I. STUDIES ON CYCLOPROPYL - STABILIZED VINYL CATION INTERMEDIATES

II. MOLECULAR ORBITAL CALCULATIONS ON CATIONIC INTERMEDIATES AND DISPLACEMENT REACTIONS

III. ON THE COMPLEXATION OF NMR LANTHANIDE SHIFT REAGENTS WITH ORGANIC SUBSTRATES

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This above all, to thine own self be true
And it must follow as the night the day
Thou canst not then be false to any man

Shakespeare

To my first and best teachers, my
mother and father

And to Clarence Hyde, who let me mess
around with B. subtilis during
physics laboratory

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Having restrained my urge to be incongruously eloquent, I take pleasure in thanking my friends and colleagues who have made these four years at Caltech enjoyable and worthwhile. I have been fortunate to have a research advisor who has been my teacher, colleague, and friend as well. I particularly thank Bob Bergman, who used to be Dr. Bergman when I first began, for his encouragement, sincere interest, and always excellent advice. I thank Shelby Sherrod, Dave White, Tom Clarke, Richard Jones, Tom Morton, Ray Carhart, Mike Sekera, and Nicki Wilson and many other friends with whom I spent many hours talking about chemistry and other things and who put up with my crazy puns. There are many special friends and associates, all of whom I could not begin to list here, to whom I extend my warmest appreciation for their help and friendship.

I thank the National Science Foundation for a Predoctoral Fellowship from 1968 through 1971.

ABSTRACTS

I. The heterogeneous and homogeneous silver-catalyzed acetolyses of E- and Z-1-cyclopropyl-1-iodopropene (1E and 1Z, R = methyl), E- and Z-1,2-dicyclopropylethylene (1E and 1Z, R = cyclopropyl), E- and Z-1-cyclopropyl-3-ethyl-1-iodopentene (1E and 1Z, R = 3-pentyl), and 1-iodo-3,4-hexadiene (4) are examined in detail. The acetate product distributions reveal small, but important, contributions of heterogeneous catalysis, clearly show overall net inversion of geometry in the formation of the corresponding vinyl acetates under homogeneous conditions, and reveal selectivity in the cyclopropyl ring-opening rearrangements of the intermediate vinyl cations. The results are consistent with the intervention of non-equilibrated ion-pair intermediates which undergo both some solvent trapping and ring-opening rearrangement with net inversion and dissociation to linear, sp-hybridized vinyl cations. It is also found that the steric effects of the β-alkyl substituents R are important in determining the extent of ion-pair contribution. The product distributions are also highly dependent upon the R substituent, with the ratio of vinyl acetates to rearranged cyclobutyl-type acetates decreasing as R changes from hydrogen, to 3-pentyl, to methyl, to cyclopropyl. It is shown that this is consistent with the conjugative electron-releasing ability of R in stabilizing the transition state for rearrangement of the vinyl cations, whereas the initial ionizations of the vinyl iodides (Z isomers) qualitatively depend upon the inductive electronic properties of R. Other

electronic and steric effects of substituent R are discussed.

It is also shown that 1E and 1Z, R = cyclopropyl, with deuterium label in the β-cyclopropyl ring, undergo reaction with no isotopic scrambling, indicating the absence (<0.2%) of 1,2-hydride shift across the double bond in the 1,2-dicyclopropylvinyl cation. A similar result (<1% rearrangement) is found for the 1,2-dicyclopropylethyl cation. These results are discussed in terms of σ-delocalization of the cyclopropyl rings adjacent to the cationic centers.

II. This part has been published in full, see D. R. Kelsey and R. G. Bergman, Journal of the American Chemical Society, 93, 1953 (1971).

III. An explicit treatment of the complexation equilibrium between organic substrates and the lanthanide nmr shift reagents is developed. It is shown that for a single equilibrium, plots of the observed shifts of two substrate protons, i and j, against one another must be linear with slopes that reflect the ratios $(\Delta_{max}^{i}/\Delta_{max}^{j})$ of the chemical shifts in the bound complex. This "internal standard proton" method is applied to sixteen vinyl and eleven allyl acetates using the acetoxy methyl protons as standard and $Eu(fod)_3$ shift reagent. Characteristic slopes are obtained which depend upon the stereochemical relationships to the reference group. The method is shown to be a valuable and reliable means of establishing substrate structures even for isomeric mixtures, since impurities and concentrations have little effect.

It is shown that at large ratios of substrate to reagent concentra-

tions, S_t/E_t, a plot of reciprocal observed shift, $1/\Delta_{obsd}$, against the total substrate concentration, S_t, should be linear if a 1:1 stoichiometry obtains. The plots of the data for representative substrates (allyl acetate, isopropenyl acetate, 2-butanone, tetrahydrofuran, 2-propanol, and dimethyl sulfoxide) with $Eu(fod)_3$ show excellent linearity and estimated bound chemical shifts, Δ_{max}, and equilibrium constants, K, are obtained. The results for dimethyl sulfoxide suggest that the major complex stoichiometry is 1:1 at room temperature, even though the literature data suggest formation of a 2:1 (DMSO:$Eu(fod)_3$) complex at low temperatures. It is observed that the limiting observed shifts, Δ_{lim}, obtained at high E_t/S_t ratios are generally less than the Δ_{max} values. This and other observations are discussed in terms of non-ideal solution behavior at high reagent concentrations. A bibliography of 240 references is included.

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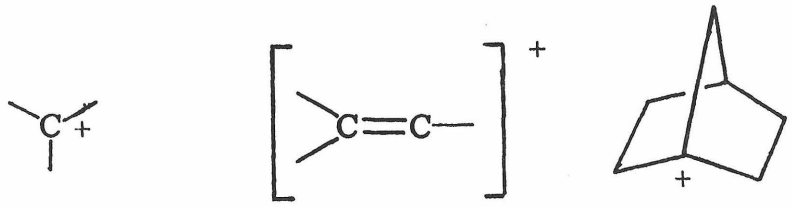
Part I: Studies on Cyclopropyl-Stabilized Vinyl Cation Intermediates

Background

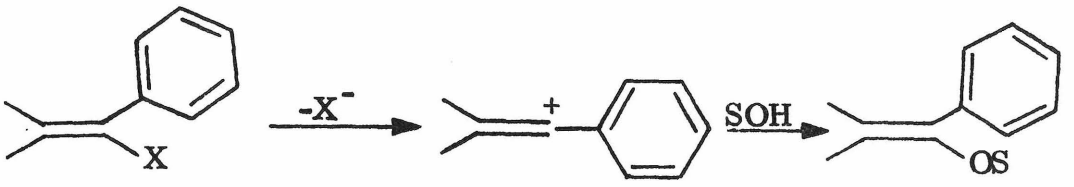
The carbonium ion, A, has played a central role in mechanistic organic chemistry due to the pioneering work of Whitmore, Hughes, Ingold, and others in the 1930's and 1940's and the significant contributions of Winstein, Roberts, Cram, Olah, and many others in the last two decades(1). It has been thoroughly established from both experimental and theoretical evidence (2) that the simple "classical" carbonium ion A prefers D_{3h} symmetry, i.e. the bonds to the cationic carbon lie in a plane and the vacant orbital is nearly pure 2p. When the ion is forced to exist in a non-planar configuration, e.g. C, it is believed to be much less stable (3).



A B C

In contrast to the fantastic quantity of work done on carbonium ions of type A, very little thought was directed toward the possibility of disubstituted ("divalent") carbonium ions -- the vinyl cation B. Jacobs and Searles (4) mentioned the possibility that vinyl cations could be formed in addition reactions of allenes in 1944, and Newman (5) mentioned them again in 1956. In both cases, the species was regarded as highly speculative and "probably without real existence" (5). It was not until 1964 that vinyl cations became a viable high-energy reaction intermediate, at least in the minds of organic chemists. Grob and coworkers (6) showed that styryl bromides

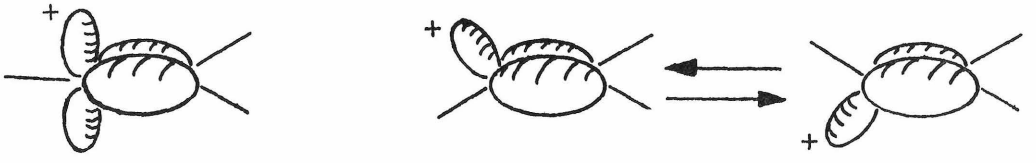
solvolyze in a first-order manner consistent with an S_N1 mechanism, eq. (d).



(d)

Since that time, a good deal of information about vinyl cations has been obtained. I shall not attempt to review here the studies in which vinyl cations have been implicated, since that has been suitably and thoroughly done in reviews of specific areas (7) and in recent comprehensive reviews of vinyl cation chemistry (8).

The basic goal of the present work I undertook with Professor Bergman in 1969 was to determine the structure of vinyl cations. Briefly, the cation may exist (in the extremes) as (a) sp-hybridized cation E having a linear configuration with a pure carbon 2p "empty" atomic orbital orthogonal to the π system, or as (b) sp^2-hybridized cation F having a bent configuration with an "empty" sp^2 orbital.



E F

The latter could exist as geometrical isomers that interconvert by inversion at the cationic center. At the time this work was begun, it was intuitively thought that linear configuration E was the most

reasonable structure (9). Theoretical calculations have now shown that the linear, sp-hybridized cation is indeed much more stable than any bent configuration (see Part II and references therein). Even at the present level of sophistication, however, theory alone cannot render complete or even completely reliable answers to many complex questions in solution chemistry. It was desirable to investigate in detail the solvolytic reactions of vinyl cation precursors.

In addition to the basic question of vinyl cation structure, I shall present our findings regarding the role of ion-pairs in vinyl cation solvolyses, the participation of adjacent cyclopropyl rings in vinyl cation reactions, the steric and electronic effects of remote substituents, the possibility of hydride shifts, and the effects of heterogeneous catalysis in silver acetate - acetic acid systems.

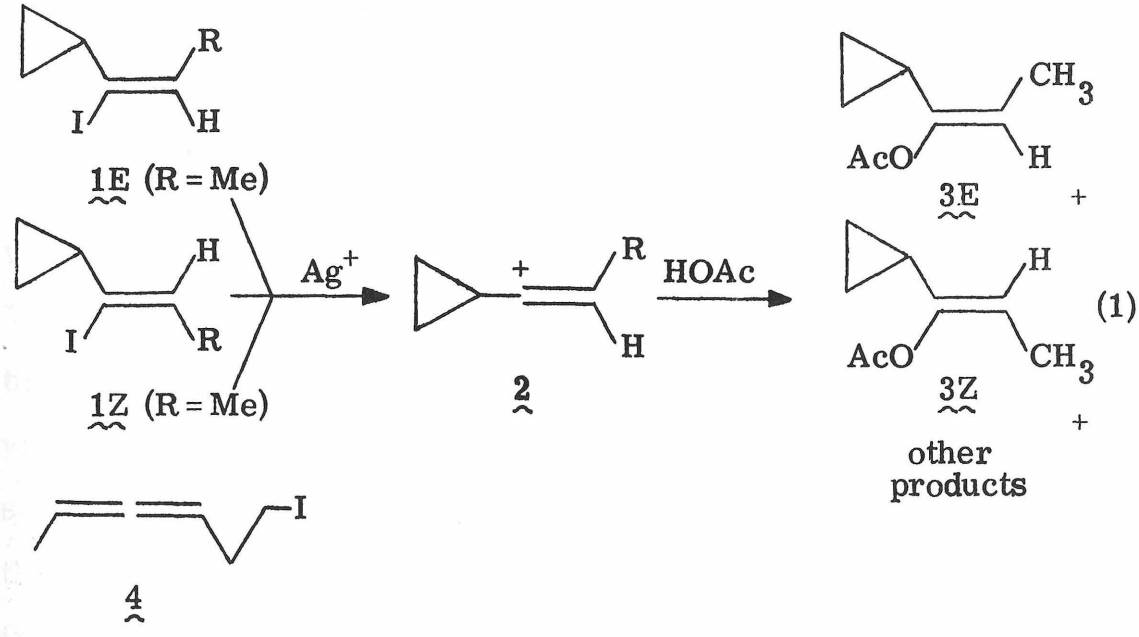
I should point out that a large portion of the work undertaken in this project has been published (10), and I will not attempt to rephrase that work here. New results and some reevaluation of our earlier work will be presented. The style of the following sections is fashioned purposely so that the material may be incorporated into pending publications by Professor Bergman and myself. (Hence, the third person plural form is used throughout.)

Introduction

Our previous investigations on vinyl cation intermediates showed that the isomeric 1-cyclopropyl-1-iodopropenes, 1Z and 1E (R=Me),*

*Throughout this Part the abbreviations Me, Cp, and 3P are used to designate methyl, cyclopropyl, and 3-pentyl substituents.

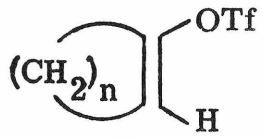
undergo silver-assisted ionization in acetic acid to give identical product mixtures within experimental error (10). We also showed that, except for a slightly enhanced formation of the corresponding homoallenic acetate, 1-iodo-3,4-hexadiene, 4, reacted under the same conditions to give the same product distribution, again within experimental error. The results for all three precursors were consistent



with the initial formation of an effectively linear (sp-hybridized) vinyl cation 2 which then underwent solvent trapping, elimination, and rearrangement (10). The major products of these reactions were the 1-acetoxy-1-cyclopropylpropenes, 3E and 3Z, eq. (1).

Concurrent with our work on the cyclopropyl-stabilized vinyl cations, Rappoport and coworkers (11) presented evidence from their study of the solvolyses of 1,2-dianisyl-2-phenylvinyl halides that the phenyl-stabilized vinyl cation is also linear. Later, the straightforward, but elegant, work of Schleyer, Hanack, Stang, and coworkers (12) showed the instability associated with bent (sp^2-hybridized) vinyl

cations. They found that the solvolysis rates of cyclic vinyl triflates, 5, exhibit a marked decrease (by up to a factor of 10^{-5}) as n decreases from six to three, a result completely consistent with the theoretical calculations showing a rapid destabilization of the vinyl cation as the deviation from preferred linearity becomes more pronounced (see Part II and references therein).

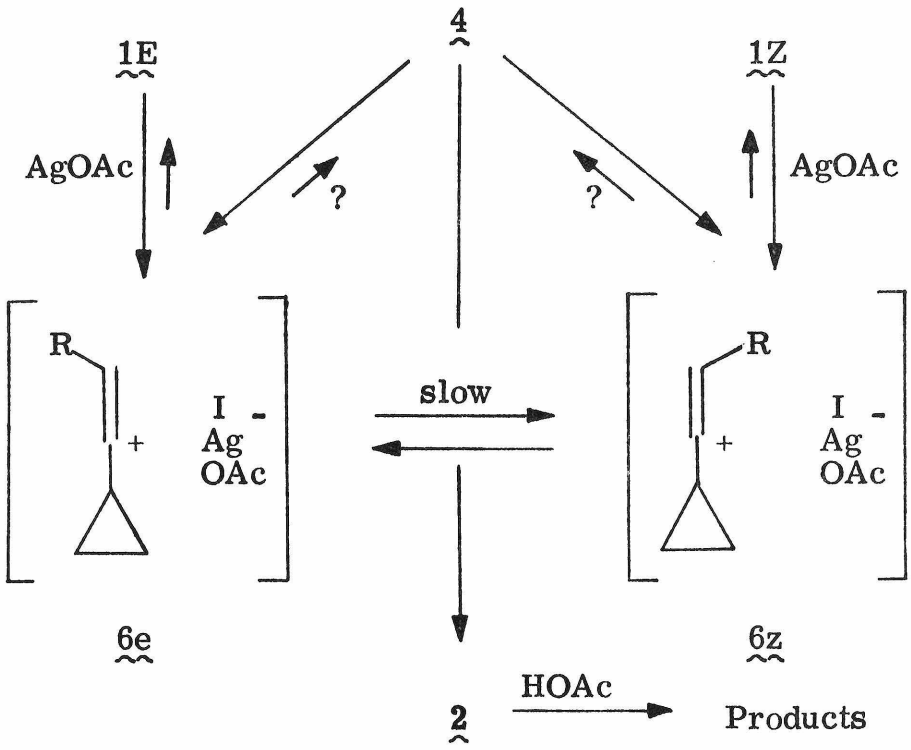


5

Thus, the experimental evidence to date strongly implies that the vinyl cation prefers a linear, sp-hybridized electronic configuration. Yet some intriguing unanswered questions remained. We noted (10) that homoallenic iodide 4 isomerized under the reaction conditions to vinyl iodides 1Z and 1E, R = Me, and that the vinyl iodides themselves likewise isomerized to a small extent. We postulated that these isomerizations occurred through ion-pair formation, as shown in Scheme I. This raised the possibility that some fraction of the reaction products could arise from trapping and rearrangements of ion-pairs 6e and 6z, as well as from the "free" cation 2. If solvent trapping of the ion-pair occurred, one should expect to see net inversion of geometry, e.g. more of acetate 3Z (eq. 1) should be formed from iodide 1E, R = Me, due to backside attack of solvent on initially formed 6e. On the other hand, predominate collapse of the ion-pairs, e.g. 6e $\longrightarrow$ 3E + AgI, should give overall net retention of geometry.

It is unlikely that both modes of reaction -- backside trapping and ion-pair collapse -- would exactly cancel in both ion-pairs,

Scheme I



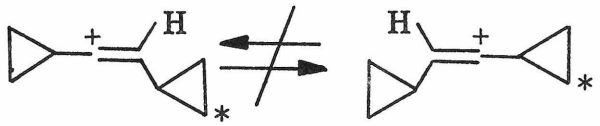
since 6e and 6z are inherently different and the minor amount of iodide isomerization suggests the interconversion between 6e and 6z is relatively slow. Therefore, one should expect to see similar, but not precisely identical, product distributions from the reactions of 1E, 1Z, and 4 if in fact the ion-pairs are involved in the ionization as postulated. Unfortunately, the precision of the analytical techniques available to us at the time of the earlier work were not adequate to detect with certainty any small differences in the product distributions.

We were also intrigued by the probability that the rates at which such ion-pairs 6 underwent external nucleophilic solvent trapping, internal ring-opening rearrangement, and/or dissociation to cation 2

might be greatly influenced by steric or electronic effects induced by substituent R.

We have, therefore, carefully reanalyzed the product mixtures obtained from 1Z, 1E, and 4, R = Me, and have extended our studies to the systems with R = Cp and R = 3P. Not only do the results of this work implicate the intervention of ion-pair intermediates, but they also strengthen the evidence previously presented in favor of linear vinyl cations and illustrate the extent to which heterogeneous catalysis may be involved in reactions of 1 with excess silver acetate in acetic acid (13a).

In addition, we have shown through the use of isotopically labled substrates, R = Cp-d_2, that the degenerate 1, 2-hydride shift across the double bond does not occur in the 1, 2-dicyclopropylvinyl cation.



This is discussed in Section B of this portion of the thesis.

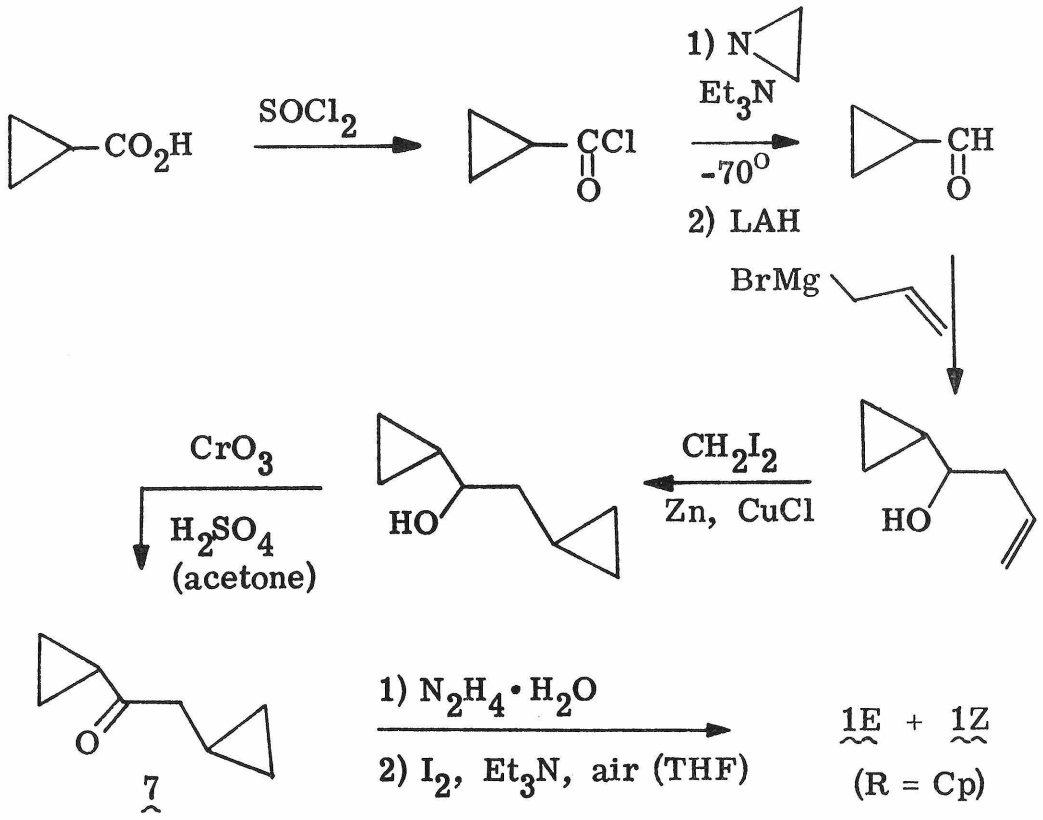
Section A.

Syntheses and Identifications of the Vinyl Iodides

The synthesis and characterization of 1, R = Me, have been previously described(10). We present here a brief outline of the syntheses of 1, 2-dicyclopropyl-1-iodoethylene (1, R = Cp) and 1-cyclopropyl-3-ethyl-1-iodopentene (1, R = 3P). Preparative and spectral details are given in the Experimental section.

As given in Scheme II, cyclopropylcarboxaldehyde was obtained from the acid chloride through a modification of Brown's aldehyde synthesis (14). Addition of the aldehyde to the Grignard reagent of

Scheme II



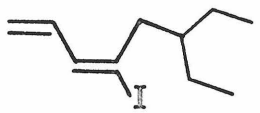
allyl bromide gave 1-cyclopropyl-3-butenol in 91% yield. The modified Simmons-Smith addition of methylene to the double bond (15) gave 1, 2-dicyclopropylethanol in ca. 65% yield. Jones oxidation (16) of the alcohol gave 1, 2-dicyclopropylethanone in 93% yield. The confirmations of these intermediate compounds from elemental analyses and from their nmr and ir spectra were quite straightforward.

We found that the normal conditions (10, 17, 18) for conversion of the hydrazone of ketone 7 to vinyl iodide 1 with iodine and triethylamine in tetrahydrofuran gave poor yields (<20%). When the reaction was run under a nitrogen atmosphere, virtually no vinyl iodides were formed. In contrast, when the reaction solution was aerated by bub-

bling air through the solution while the iodine was being added, the desired vinyl iodides (1, R = Cp) were isolated in up to 50% yield (based on starting ketone). The Z-E isomers were obtained in >99% purity by preparative gas-liquid chromotography (glc, vpc) on DEGS.

The synthesis of vinyl iodides 1, R = 3P, was similar to that shown in Scheme II, only with allyl bromide replaced by 1-chloro-2-ethylbutane. This chloride was prepared in 28% yield by reacting 2-ethylbutanol with triphenylphosphine in carbon tetrachloride (19). No attempt was made to optimize this reaction, since the starting material was so readily available. The 220 MHz nmr spectrum of the isolated chloride was consistent with an unrearranged carbon skeleton.

The Grignard of 1-chloro-2-ethylbutane was reacted with cyclopropylcarboxaldehyde to give a 79% yield of 1-cyclopropyl-3-ethylpentanol. Jones oxidation of the alcohol gave 1-cyclopropyl-3-ethylpentanone in > 98% yield. Treatment of the freshly prepared hydrazone in aerated THF - Et_3N solution with iodine (see above) gave the isomeric vinyl iodides in 62% yield based on ketone. Two fractions were collected by preparative vpc on DEGS, the first containing a small amount of ketone contaminant, and the second consisting of two iodides. The first fraction was repurified by vpc on SF96 to give pure 1Z, R = 3P. The second fraction, after a tedious vpc separation on SF96, afforded the pure E isomer and a ring-opened product whose 220 MHz nmr spectrum was consistent with structure 8. (It's geometrical isomer was not detected.) Some of the preliminary sol-



8

volyses of 1E, R = 3P, were carried out with 8 unknowingly present. Even though it was shown that 8 is unreactive under the ionization conditions (see below), the data reported are for reactions of pure (>99%) E isomer. Ring-opened products appear to be easily formed in the iodine - triethylamine reaction when R is a bulky group. Attempts to prepare 1, R = tert-butyl, were quite unsuccessful (see Appendix A).

We had previously established the identity of the E-Z isomers of 1, R = Me, through (a) the further downfield nmr chemical shift exhibited by vinyl protons cis to the vinyl iodine, (b) the rate of E2 elimination with potassium tert-butoxide in DMSO, and (c) the long-range homoallylic nmr coupling constants (10). In addition, we had observed that the rate of silver-assisted solvolysis of the E isomer was about ten times faster than that for the Z isomer.

It was considered sufficient to characterize the new iodides by the chemical shifts of their vinyl hydrogens in their nmr spectra and by their relative solvolysis rates with silver acetate in acetic acid. (The ir, nmr, and mass spectra and the elemental analyses were consistent with the overall gross structures, R = Cp and R = 3P.) These data are collected in Table I. Within each Z-E pair, the E isomer vinyl proton nmr absorption is at lower field, and the E isomer shows a much greater rate of reaction with silver acetate in acetic acid at room temperature. (Iodide 8, the ring-opened product, shows a vinyl proton absorption consistent with an E configuration, although this is less firmly established.) The results for the R = Cp and R = 3P systems are entirely consistent with the R = Me system. Therefore,

Table I. NMR Vinyl Proton Shifts and Solvolysis Rates

Compound	R	NMR[a] vinyl H	Rate[b] (10^5k, sec^{-1})	Relative rate	k_e/k_z
1	H	5.9[c] 6.3			
4			103 ± 10[d]	13.0	
1E	Me	6.25	210 ± 20	26.6	10.3
1Z	Me	5.62	20.3 ± 2[d]	2.6	
1E	Cp	5.48	99 ± 10	12.5	12.5
1Z	Cp	4.92	7.9 ± 0.2	1.0	
1E	3P	5.88	867 ± 20	110.	34.4
1Z	3P	5.16	25 ± 3	3.2	
8		6.03			
11	Cp		0.71 ± .05[e]		

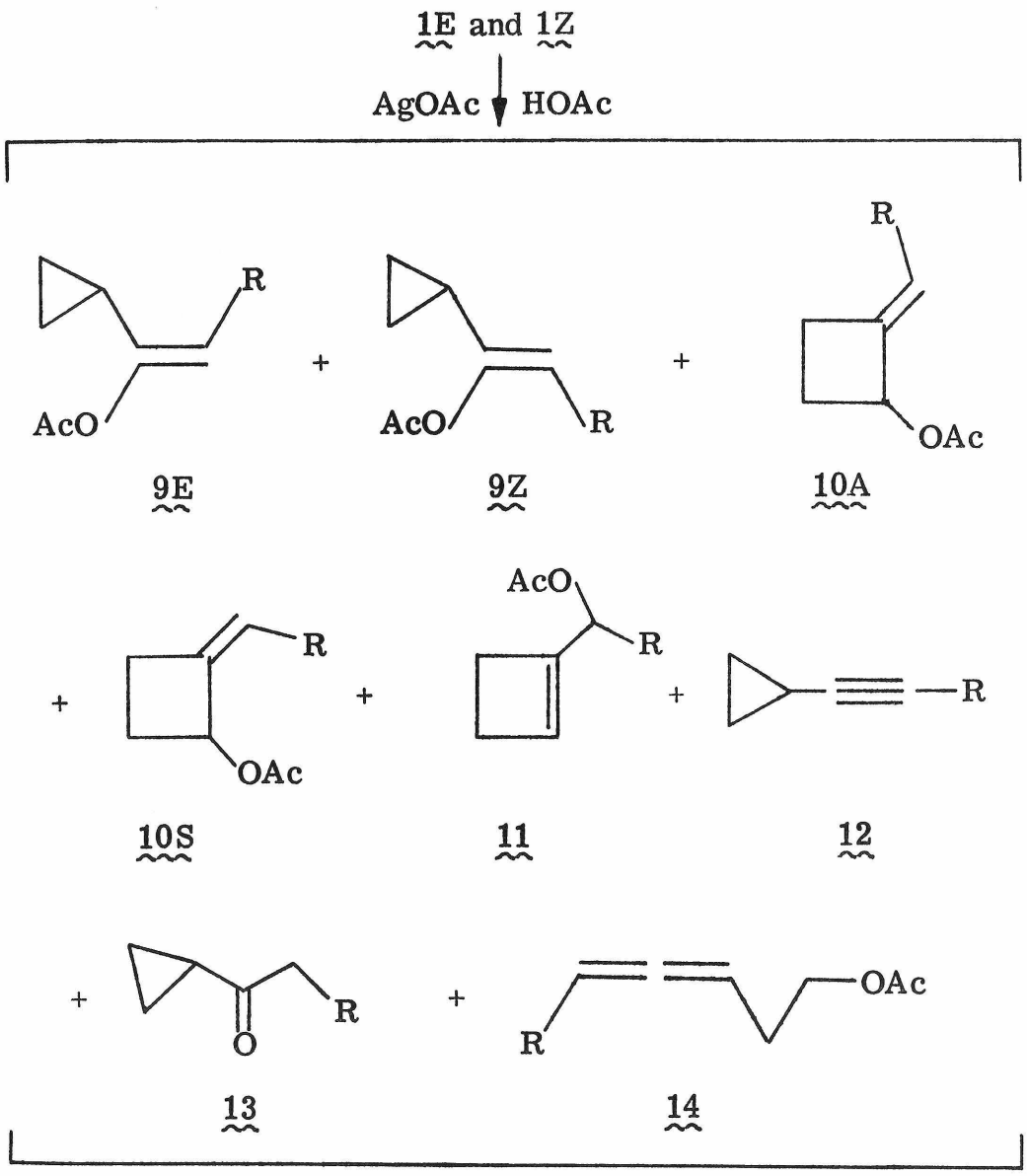
[a]In δ from TMS. [b] Pseudo first-order rate constants under heterogeneous conditions with excess silver acetate at room temperature, 24±1°; total rates including small amount of iodide isomerization (see text). [c]Ref. 17. [d]Differs slightly from rates reported in ref. 10 (see text). [e]Rate of isomerization (see text).

we believe the assigned geometries to be correct.

Preparative Ionizations of the Vinyl Iodides

Our previous work (10) would lead one to expect the products shown in Scheme III when 1 is treated with silver acetate in acetic acid.

Scheme III



R = Methyl

The isolation and characterization of the products obtained from 1, R = Me, have been previously given (10). There are some additions and corrections to be made, none of which affect the major conclusions of that report:

(1). The geometric identities of the vinyl acetates 9E and 9Z have been firmly established (20) as originally assigned from nmr spectral data obtained with paramagnetic shift reagent $Eu(fod)_3$ (see Part III). The identity of the gross structure has also been augmented by the comparison to authentic acetates prepared from cyclopropyl ethyl ketone (see Experimental section).

(2). The tenative geometrical assignments of isomers 10A and 10S given previously (10) have been shown to be incorrect and should be reversed. The assignments were established correctly with nmr shift reagent (see Part III). The spectra observed for 11 with added shift reagent are in accord with its previously assigned structure.

(3). We thought that formation of ketone 13 may have been due to minor impurities (AgO ?) in the silver acetate (10). There is a logical alternative, vis. reaction of unconsumed vinyl iodide with excess silver species during the water-ether work-up. In fact, when care is taken during the work-up to add the acetic acid reaction solution to ether first, before washing with water, formation of ketone is minimized (<1%). This explains why more ketone was observed from aliquots taken near the beginning of the reaction; more unreacted iodide was present. Therefore, the kinetic data for 1Z, R = Me, and 4, where ketone formation was greater, has been adjusted slightly by

considering the ketone as equivalent to unreacted starting material. Note, however, that this does not appreciably affect the rate data nor the calculated maximum extent of vinyl iodide isomerization (see below).

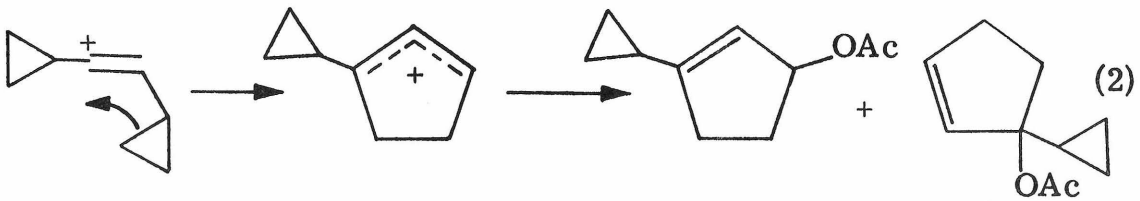
R = Cyclopropyl

Treatment of a mixture of 1E and 1Z, R = Cp, with excess silver acetate in acetic acid gave an isolated product mixture in >91% yield. Product 11 was isolated by preparative vpc on an FFAP column in a separate preparative run. The other products were partially separated by vpc on DEGS, followed in some cases by additional refractionation on TCEP. Compounds 12, 10A, and 10S were obtained in nearly pure form. Unfortunately, no preparative conditions could be found which would allow separation of vinyl acetates 9Z and 9E prepared from the corresponding ketone nor separation of reaction products 9Z, 9E, and 14 (collected together). Ketone 13 (<1% under analytical conditions) was not isolated from the solvolysis. The correspondences of the isolated products, of synthesized 9, 12, and 13, and of the vinyl iodides to the analytical vpc peaks were established by careful comparisons of exact vpc retention times obtained with an electronic integrator.

The identities of the isolated 12, 9E, and 9Z were established by comparison to authenic samples. Even for the vpc inseparable vinyl acetates, 9, this was possible through the use of nmr shift reagent and application of the "internal standard proton" method (20). Note that 9E and 9Z are amenable to analytical vpc separation using a 300' open-tubular column (TCEP).

Compound 14 was never isolated or identified. Largely by default, a small unaccounted-for peak (~1.5%) having a vpc retention time (300' TCEP) slightly shorter than acetate 9Z was assigned this structure. Approximately 1-2% of 14 would be expected on the basis of the results obtained for both the R = Me and R = 3P systems. This uncertainty in the identity of the peak assigned structure 14 does not affect the conclusions reached in this study.

The gross identities of acetates 10A, 10S, and 11 were established from their ir, nmr, and mass spectra. Analysis of the nmr spectra taken with added shift reagent allowed unequivocal assignments of the geometries (see Part III). A priori, the formation of acetates 15 and 16 could occur through rearrangement of the "remote" cyclopropyl ring, as shown in eq. (2). These products were not observed. Acetate 16 would have been easily characterized by the vinyl proton absorptions in the nmr, especially with added shift reagent. It would



(2)

15 16

have been difficult to distinguish 15 from 10A were it not for two facts: (1) Acetate 11 isomerizes to 10A and 10S (see below). It would be difficult to rationalize formation of 15 instead of 10A. (2) The 220MHz nmr spectra of 10A taken with added shift reagent are in agreement with the spectra of 10A, R = 3P, and 10, R = H, but

do not agree with the spectral characteristics of model compound 2-cyclopenten-1-yl acetate (see Part III). It seems unlikely that the small peak assigned to 14 could actually be 15 or 16, and, if it were, this would necessitate an explanation for the curious absence of 14. In any case, this sets an upper limit of ~1.5% for formation of 15 or 16.

R = 3-Pentyl

Treatment of the mixture of isomeric iodides 1, R = 3P, plus vinyl iodide 8 with silver acetate in acetic acid gave a mixture of products in >95% yield along with unreacted 8. Preparative vpc on TCEP, followed in some cases by reseparation of fractions on SF96, afforded samples of 8 and products 9E, 9Z, 10A, 10S, 12, 13, and 14 (Scheme III, R = 3P).

Vinyl acetates 9E and 9Z and ketone 13 were identified by comparison to authentic samples. Again the geometric configurations of the vinyl acetate isomers were established from their nmr spectra with shift reagent (see Part III). Acetylene 12 was assigned on the basis of its short vpc retention time and its spectra. Acetates 10A and 10S were identified on the basis of their spectra with the geometric stereoassignments based upon the nmr spectra with added shift reagent (see Part III). Homoallenic acetate 14 was characterized by its ir absorption at 1968 cm^{-1} and it nmr and mass spectra. The correspondences of the isolated compounds, of ketone 13, and of the vinyl iodides to the peaks of the analytical vpc traces (300' TCEP or SF96) were established by exact retention times measured with the electronic integrator and, in most cases, by spiking the solvolysis mixtures.

Note that no isolated fraction showed any impurity corresponding to acetate 11 even when the nmr spectra were perturbed by added shift reagent. Also all vpc peaks in the solvolysis were accounted for; compound 11, if present, surely accounted for <1% of the products.

Analytical Solvolyses of the Vinyl Iodides and 4

The solvolyses conditions and work-up procedure have been previously described for the R = Me system (10) and similar conditions were used for the R = Cp and R = 3P systems. In general, the mole ratio of silver acetate or sodium acetate to reactant iodide was 3 or 4 : 1 under heterogeneous conditions and sodium acetate concentration of 0.5 M. In addition to the various conditions previously used, we have also studied the reactions under homogeneous conditions with added sodium acetate.

R = Methyl and 4

The previous work (10) showed that 1E, 1Z, and 4 gave similar product mixtures (Scheme III). Although some small differences could be noted in the previous data (c.f. 10), the analytical methods then available could not readily detect such differences if, in fact, they were real, e.g. acetate 14 coeluted with 9Z on a packed TCEP column. We subsequently found that open-tubular vpc columns (300' x .03" ID) coated with TCEP afforded separation of all components. This improvement, together with very precise (relative) integration of the peak areas with an electronic integrator, greatly reduced the analytical error.

We carefully reanalyzed some of the previously obtained solvoly-

ses mixtures, repeated some of the solvolyses (which also showed that the product distributions had not changed during storage), and included reactions of the vinyl iodides and 4 with silver acetate under homogeneous conditions in the presence of added sodium acetate. Representative examples of the solvolysis data under the various reaction conditions are shown in Table II. (Note the reassignment of the 10 isomers from that given in Tables I, II, and III of ref. 10.) In this table, as for the subsequent data for the R = Cp and R = 3P systems, we have not shown averages for all runs of a given type because small variations in the amount of relatively volatile acetylene 12, of ketone 13, and of homoallenic acetate 14 would induce an "imaginary" error into the calculated relative percentages of the remaining products. Repeated vpc analyses of selected runs showed that the precision of the percentages was generally better than 1% (e.g. 0.01 x 30% = ±0.3%) except for the small homoallenic acetate peak, which showed variations as much as 10%, and the acetylene peak, where solvent tailing introduced some error. Similar precision limits were found in the R= Cp and R = 3P systems (see below).

Although we shall discuss this data (Table II) in detail later, note that there are obvious differences in the amounts of 9Z and 9E formed depending on whether the starting material is 1E or 1Z. Our previous data (10) indeed showed some of these differences, but we now know that the variations are real and not due to analytical imprecision.

A better idea of the changes in product distributions of Table II can be obtained by looking at the various product ratios averaged over all runs under a given set of reaction conditions. These ratios and

Table II. Representative Product Distributions Formed from Ionization of E- and Z-1-Cyclopropyl=1-iodopropenes (1E and 1Z, R = Me) and 1-Iodo-3,4-hexadiene (4) under Various Reaction Conditions at Room Temperature (24 ± 1 °).

Substrate	Conditions[a]	Products, %[b,c] 1[d,l]	9Z	9E	10S	10A	11	12	13[d]	14
1Z	HT	0.23[e]	30.20	36.58	2.94	8.00	3.52	17.46	3.05[e]	1.29
1E	HT	2.16[f]	32.64	33.10	2.71	8.76	3.91	17.72	0.29[f]	1.17
1Z	HT(.46)		30.24	35.05	2.90	7.77	3.44	19.44		1.15
1E	HT(.48)		32.39	32.67	2.81	9.08	3.88	18.01		1.15
1Z	HM	0.75[g]	30.39	35.23	3.08	8.56	4.17	17.58		0.99
1E	HM	4.02[h]	34.02	31.90	2.79	9.73	4.05	16.82		0.68
1Z	HM(.49)		29.85	34.10	2.86	7.75	4.15	20.72		0.57
1E	HM(.49)		35.30	30.89	2.97	10.11	4.22	15.70		0.81
4	HT	1.09[i] 0.74	30.99	33.75	3.23	9.28	3.69	12.36	4.26[i]	6.72
4	HT(.54)		30.80	31.98	3.20	9.07	3.65	13.68		7.62

Table II. (cont.)

Substrate	Conditions	1	9Z	9E	10S	10A	11	12	13	14
4	HM	1.89[j] 1.30	32.04	31.49	(3.09)[k]	9.21	3.53	13.91		6.25
4	HM(.50)		29.92	29.86	(3.80)[k]	8.90	3.49	14.40		9.67

[a] HT = excess AgOAc in HOAc (heterogeneous); HM = AgOAc in HOAc (homogeneous); numbers in parentheses are molarity of NaOAc. [b] Values are relative mole percentages from electronic integration of vpc peaks on 300' TCEP and uncorrected for detector response (see Experimental). [c] Repeated vpc analysis of selected runs showed relative precisions of 1% for 9Z and 9E; 2-3% for 10S, 10A, 11, 13, 1 isomer, and 14 from 4; ca. 10% for 12 and 14 from 1. [d] Percent of total reaction mixture. [e] After 20 min.; 76.9% unreacted 1Z. [f] After 4 min.; 62.2% unreacted 1E. [g] 76.5% unreacted 1Z. [h] 62.1% unreacted 1E. [i] After 3 min.; 78.2% unreacted 4; lower number 1E [j] 78.3% unreacted 4; lower number 1E. [k] Partially obscured by unreacted 4. [l] Isomeric iodide.

Table III. Product Ratios from Reactions of E- and Z-1-Cyclopropyl-1-iodopropenes (1E and 1Z, R = Me) and 1-Iodo-3,4-hexadiene (4).

Substrate	Conditions[a]	Runs[b]	Ratios[c,d] r(E/Z)	r(V/B)	r(A/S)	r(X/N)
1Z	HT	4	1.20 (.02)	4.93 (.20)	2.76 (.04)	3.23 (.08)
1E	HT	6	1.04 (.02)	4.28 (.11)	3.36 (.13)	2.98 (.12)
1Z	HT(.47)	3	1.16 (.02)	4.70 (.11)	2.67 (.02)	3.11 (.02)
1E	HT(.48)	2	1.01 (.02)	4.06 (.06)	2.88 (.36)	3.18 (.12)
1Z	HM	3	1.12 (.03)	3.88 (.30)	2.77 (.03)	2.72 (.12)
1E	HM	1	0.94 (.01)	3.98 (.03)	3.48 (.03)	3.09 (.05)
1Z	HM(.49)	1	1.14	4.33	2.71	2.56
1E	HM(.49)	1	0.88 (.01)	3.83 (.09)	3.41 (.07)	3.10 (.06)
4	HT	4	1.08 (.01)	3.91 (.05)	2.81 (.11)	3.32 (.10)
4	HT(.50)	2	1.04 (.01)	4.23 (.29)	2.93 (.11)	3.47 (.10)
4	HM	1	0.99 (.01)	e	e	e
4	HM(.50)	1	1.00 (.01)	e	e	e

[a] See footnote (a), Table II. [b] Individual samples, including aliquots

Table III. (cont.)

taken during HT runs. [c] Ratios defined in text. [d] Numbers in parentheses are average deviations observed from run to run; when only one was made, the number is the average deviation for the vpc analyses. [e] See footnote (k), Table II.

their observed average deviations are collected in Table III. The symbols for the ratios are defined:

$$r(E/Z) = \underset{\sim}{9E} / \underset{\sim}{9Z}$$

$$r(V/B) = (\underset{\sim}{9E} + \underset{\sim}{9Z}) / (\underset{\sim}{10A} + \underset{\sim}{10S} + \underset{\sim}{11})$$

$$r(A/S) = \underset{\sim}{10A} / \underset{\sim}{10S}$$

$$r(X/N) = (\underset{\sim}{10A} + \underset{\sim}{10S}) / \underset{\sim}{11}$$

R = Cyclopropyl

The pure (>99%) isomers $\underset{\sim}{1Z}$ and $\underset{\sim}{1E}$, R = Cp, were treated under the same conditions used for R = Me and $\underset{\sim}{4}$. These data are shown in Table IV and the product ratios in Table V. As in the R = Me system, a small amount of $\underset{\sim}{1Z} \rightleftarrows \underset{\sim}{1E}$ isomerization occurred during the reaction. Unlike the R = Me system, the product distribution changed during the course of the reaction -- $\underset{\sim}{11}$ decreased and $\underset{\sim}{10A}$ and $\underset{\sim}{10S}$ proportionately increased with time. When isolated acetate $\underset{\sim}{11}$ was subjected to the reaction conditions (AgOAc, AgI, HOAc), it slowly isomerized to give only $\underset{\sim}{10A}$ and $\underset{\sim}{10S}$. After 176.5 hours at room temperature, only 1.1% of $\underset{\sim}{11}$ remained and the r(A/S) ratio was ca. 9. The kinetic plot for disappearance of $\underset{\sim}{11}$ relative to appearance of isomers was very linear over the entire time (see Appendix B) and gave an estimated rate constant of $7.1 \times 10^{-6} sec^{-1}$ (Table I).

R = 3-Pentyl

Representative runs for the solvolyses of $\underset{\sim}{1E}$ and $\underset{\sim}{1Z}$, R = 3P, are given in Table VI and the averaged ratios in Table VII. The results are given for $\underset{\sim}{1E}$ which had been freed of contaminating isomer $\underset{\sim}{8}$, even though it was shown that $\underset{\sim}{8}$ was unreactive under the reaction environment. Iodide $\underset{\sim}{8}$ did interfere with accurate vpc analysis of the

Table IV. Representative Product Distributions Formed from Ionization of E- and Z-1,2-Dicyclopropyl-1-iodoethylenes (1E and 1Z, R = Cp) under Various Reaction Conditions at Room Temperature (24 ± 1°).

Substrate	Conditions[a]	Reaction time (hr.)	1[d,e]	Products, %[b,c] 9Z	9E	10S	10A	11	12	14[l]
1E	HT	0.1	1.59[f]	17.62	24.95	2.70	13.51	30.46	9.78	0.98
		2.0	1.86[g]	18.91	25.48	3.40	15.99	25.17	9.91	1.13
1Z	HT	1.0	0.19[h]	18.79	27.48	3.32	12.60	27.09	10.19	0.53
		13.0		18.61	27.18	4.46	17.77	20.84	9.95	1.20
1E	HT(.41)	6.5		19.42	25.69	3.39	17.67	21.91	10.87	1.05
1Z	HT(.43)	12.0		18.01	26.87	4.61	19.28	18.16	12.04	1.03
1E	HM	12.0	7.2[i]	18.98	23.91	5.06	25.90	17.43	7.71	1.04
1Z	HM	13.5	0.2[i]	19.85	29.35	4.96	20.99	18.41	5.43	1.02
1E	HM(.50)	3.0		20.37	22.67	3.63	20.49	21.18	11.65	[k]
1Z	HM(.50)	18.0		17.02	26.85	4.34	20.45	14.96	16.40	[k]

[a] See footnote (a), Table II. [b] See footnote (b), Table II. [c] Vpc analysis precision 1-3% for

Table IV. (cont.)

all product peaks except 1 isomer and 14; ca. 10 % for the latter. [d] Percent of total reaction mixture. [e] Isomeric iodide. [f] 72.5% unreacted 1E. [g] 0.4% unreacted 1E. [h] 78.7% unreacted 1Z. [i] 51.2% unreacted 1Z [j] 14.9% unreacted 1E [k] Not integrated. [l] Identity assumed (see text).

Table V. Product Ratios from Reactions of E- and Z-1,2-Dicyclopropyl-1-iodoethylenes (1E and 1Z, R = Cp).

Substrate	Conditions[a]	Runs[b]	Ratios[c,d] r(E/Z)	r(V/B)	r(A/S)	r(X/N)
1Z	HT	8	1.48 (.03)	1.06 (.02)	3.80[e]	0.59[e]
1E	HT	6	1.39 (.03)	0.95 (.02)	5.01[f]	0.53[f]
1Z	HT(.43)	1	1.49	1.07	4.19	1.32
1E	HT(.41)	1	1.32	1.05	5.21	0.96
1Z	HM	1	1.48 (.01)	1.11 (.01)	4.24 (.01)	1.41 (.04)
1E	HM	1	1.26 (.01)	0.88 (.01)	5.12 (.03)	1.77 (.02)
1Z	HM(.50)	1	1.57 (.02)	1.11 (.02)	4.72 (.17)	1.67 (.16)
1E	HM(.50)	1	1.11 (.01)	0.98 (.03)	5.37 (.27)	1.30 (.15)

[a] See footnote (a), Table II. [b] See footnote (b), Table III. [c] Ratios defined in text. [d] See footnote (d), Table III. [e] Initial value; after 60 min. reaction time. [f] Initial value; after 6 min. reaction time.

Table VI. Representative Product Distributions Formed from Ionization of E- and Z-1-Cyclopropyl-3-ethyl-1-iodopentenes (1E and 1Z, R = 3P) under Various Reaction Conditions at Room Temperature (24 ± 1°).

Substrate	Conditions[a]	Products, %[b-d] 1[e,f]	9Z	9E	10S	10A	12	13[f]	14
1E	HT	1.53[g]	11.75	54.49	2.80	3.37	26.05	0.12[g]	1.52
1Z	HT	0.20[h]	12.17	52.58	3.75	3.07	26.60	0.07[h]	1.82
1E	HT(.55)		13.28	51.90	2.82	3.63	26.73		1.63
1E	HT(.92)		13.80	49.04	2.87	3.70	29.03		1.56
1E	HT(1.46)		15.30	50.86	1.86	3.48	27.19		1.32
1Z	HT(.59)		11.83	52.21	3.86	2.95	27.48		1.67
1Z	HT(.98)		11.12	50.38	3.51	2.63	30.86		1.50
1E	HM	0.67[i]	12.34	53.34	3.01	3.72	26.11	0.13[i]	1.49
1Z	HM		12.11	51.89	3.82	2.76	28.07	0.06[i]	1.34
1E	HM(.50)		15.00	49.69	2.14	4.22	27.37		1.58

Table VI. (cont.)

Substrate	Conditions	1	9Z	9E	10S	10A	12	13	14
1Z	HM(.49)		10.84	52.22	3.20	2.58	30.67		0.50

[a] See footnote (a), Table II. [b] See footnote (b), Table II. [c] Vpc analysis precision 1% for 9Z and 9E; 2-5% for 10S, 10A, and 12; ca. 10% for rest. [d] Product 11 not observed, <1% (see text). [e] Isomeric iodide. [f] Percent of total reaction mixture. [g] After 7 min.; 2.3% unreacted 1E. [h] After 45 min.; 37.1 % unreacted 1Z. [i] 0.2% unreacted 1E. [j] 4.3% unreacted 1Z.

Table VII. Product Ratios from Reactions of E- and Z-1-Cyclopropyl-3-ethyl-1-iodopentenes (1E and 1Z, R = 3P).

Substrate	Conditions[a]	Runs[b]	Ratios[c,d] r(E/Z)	r(V/B)	r(A/S)	r(X/N)
1Z	HT	10	4.35 (.04)	9.8 (.4)	0.82 (.02)	e
1E	HT	7	4.65 (.03)	11.1 (.4)	1.17 (.05)	e
1Z	HT(.59)	1	4.44 (.02)	9.4	0.76	e
1Z	HT(.98)	1	4.53	10.0	0.75	e
1E	HT(.55)	1	3.83 (.05)	10.1	1.29	e
1E	HT(.92)	1	3.55	9.6	1.29	e
1E	HT(1.46)	1	3.32 (.04)	12.4	1.87	e
1Z	HM	1	4.29 (.03)	9.7	0.72	e
1E	HM	1	4.32 (.04)	9.8	1.24	e
1Z	HM(.49)	1	4.82 (.04)	10.9	0.81	e
1E	HM(.50)	1	3.31 (.03)	10.2	1.97	e

[a] See footnote (a), Table II. [b] See footnote (b), Table III. [c] Ratios defined in text. [d] See footnote (d), Table III. [e] Product 11 not observed; ratio >20 (see text).

products, however. Purity of 1E or 1Z by vpc (300' SF96) was better than 99%.

Controls

The control reactions for the R = Me system have been reported (10). Similar controls for the R = Cp and R = 3P systems were done. Treatment of acetylenes 12, R = Cp or R = 3P, with AgOAc-NaOAc-AgI in acetic acid gave no reaction, even at extended reaction times. Likewise, ketones 13, R = Cp or R = 3P, were stable to the ionization conditions. The individual vinyl acetates 9E and 9Z, R = 3P, showed no isomerization or formation of new products. The mixture of acetates 9E and 9Z, R = Cp, showed no formation of new products, and the ratio 9E/9Z remained constant at 1.46. As in the case with R = Me, vinyl iodides 1Z and 1E, R, = Cp or R = 3P, showed no reaction in acetic acid in the presence of sodium acetate and silver iodide -- in the absence of silver acetate -- and were stable to the work-up conditions. This was true even for the relatively reactive (Table I) iodide 1E, R = 3P.

In the R = Me system, we had shown that acetates 10, 11, and 14 were stable to the reaction conditions (10). As noted above, 11, R = Cp, isomerized to 10A and 10S. It is not known specifically if 10A and 10S interconvert, but the control did show that only 11, 10A, and 10S are involved. For our discussion it is largely irrelevant if 10A and 10S isomerize, since the solvolysis data is already somewhat obscured by the isomerization of 11. Products 10A, 10S, and 14, R = 3P, were not directly tested for stability, but since the observed product distributions remained constant throughout the sol-

volyses, it is highly unlikely that these acetates were unstable to the reaction conditions. As noted above, acetate 11, R = 3P, was never detected. If indeed it was formed, then its rate of isomerization must have been comparable to its rate of formation, since the expected products, 10A and 10S, showed no variation with time.

Results and Discussion

Tables II - VII illustrate the volume of data we have obtained in this work. We have examined reactions of seven compounds under four different reaction conditions which produce seven or eight products. Were identical results observed for all iodides under all conditions, we would have little to say. In her (his) characteristic fashion Nature has been too kind. There is a great deal of variation, accordingly a great deal to discuss, and -- as our reward -- some interesting information about vinyl cation and solution chemistry can be gained. We have attempted in what follows to present the results and their interrelations in a logical manner and to avoid undue repetition.

In order to avoid an endless jumble of comparisons and explanations, we have abandoned the "upside-down puzzle" approach, where one fits the pieces together and then turns the puzzle over to find out what the picture was in the first place. Instead, we shall develop the outline of the picture as quickly as possible, and then talk about the torn, missing, or alternate parts. We may stop occasionally to discuss a particular piece or the background of the picture. We begin filling in some of the background by discussing the basic nature of the solvolyses and of the reaction conditions.

The Gross S_N1 Nature of the Reactions

Sherrod and Bergman (17) showed that the parent cyclopropylvinyl iodide (1, R=H) undergoes silver-assisted ionization in acetic acid or unassisted solvolysis in methanol - water in a manner consistent with initial formation of the cyclopropylvinyl cation, 2 R=H. Alternate mechanisms, such as addition - elimination or elimination - addition, were specifically discussed and ruled out. It is not entirely presumptuous to suppose that aliphatic substituents, R, at the vinyl carbon β to the iodine will have little effect upon the basic cationic character of the reaction, especially considering the variety of systems in which vinyl cations have been implicated (8). There is more evidence than just analogy, however:

a) Elimination - addition is ruled out since all three acetylenes 12 are stable to the reaction conditions.

b) Direct S_N2 solvent displacement of iodine at the vinyl center would be unprecedented and is considered theoretically unlikely (see Part II). For the 1E isomers in particular, the steric shielding of the reaction site would be formidable. Furthermore, none of the iodides react in acetic acid in the presence of sodium acetate at room temperature without silver acetate. An S_N2 mechanism cannot be operative.

c) Simple addition - elimination mechanisms involving initial addition of a proton or acetate ion to the double bond are highly unlikely, since the vinyl iodides are unreactive in NaOAc - AgI - HOAc at room temperature. If either mechanism were involved, then minimally one should expect isomerization of the iodides. This does not occur nor are any other products formed.

d) The powerful silver catalysis of these reactions requires the involvement of a silver species in the rate determining step. In order to avoid invoking a vinyl cation, one must postulate concurrent front-side or backside participation of solvent or acetate ion. Although the exact distinction between such reactions and one involving ion-pair intermediates is perhaps somewhat "fuzzy" (21), a truly concerted reaction would preclude rearrangement to give 10, 11, and 14 and would involve little randomization of geometry in product 9, whereas as much as 50% rearranged products is observed and randomization is the predominate result (see below).

It is quite consistent, then, that vinyl iodides 1 undergo silver-assisted solvolyses which predominately, probably exclusively, involve ionizations to vinyl cation species. The same mechanism is believed to apply also to homoallenic iodide 4 , except perhaps for a small, concurrent S_N2 reaction (10). The "basic" mechanism can, in effect, be considered S_N1.

The Nature of the Reaction Medium

There are many aspects of the AgOAc - HOAc reaction system which are only poorly understood. We do know that the solubility of silver acetate in acetic acid is low, only about 4.9×10^{-3} M at 30° (22). Furthermore, the ionic dissociation constant is only 2.1×10^{-7} moles/liter (23). Thus, the "free" silver ion concentration calculates to be on the order of 3×10^{-5} M or ca. 0.7% of the dissolved silver species. It does not seem unreasonable then to suspect that the major reactive species is molecular silver acetate in acetic acid solvent.

Experiments have shown that the solubility of silver acetate in

acetic acid increases slightly when sodium acetate is added (22). One simple, though probably incomplete (22), way of explaining this behavior is to presume the following equilibrium, eq. (3). In acetonitrile,

$$NaOAc + AgOAc \rightleftharpoons Na^+Ag(OAc)_2^- \quad (3)$$

$$2AgNO_2 \rightleftharpoons Ag^+ + Ag(NO_2)_2^- \quad (4)$$

a similar equilibrium, eq. (4), is believed to obtain for silver nitrate (24). Certainly one would expect that the anion $Ag(OAc)_2^-$ would be less electrophilic toward organic halides than AgOAc. Furthermore, the presence of acetate ion should be unfavorable for ionic dissociation of silver acetate. The reaction system becomes more complicated, even when one neglects the unknown effects added acetate may have upon the solvent structure and solvation shells of reaction intermediates. Again, it is reasonable that the reactive species is molecular silver acetate, since the silver diacetate anion should be less electrophilic and the concentration of "free" silver cation should be reduced.

At least for soluble silver salts in aprotic solvents, e.g. acetonitrile, trimolecular mechanisms are believed to be viable (25), eq. (5). However, with silver acetate in acetic acid such participation

$$Y^- + RX + Ag^+ \longrightarrow \left[X^{\delta-}R^+IAg\right] \longrightarrow \text{Products} \quad (5)$$

by acetate ion is quite unlikely. When sodium acetate is present, the distinction between participation by acetate in the transition state and rapid acetate attack on an ion-pair becomes less clear, as mentioned above. (Note that a study of the kinetic effects of added acetate would probably be prohibitively difficult if meaningful results were desired. As we shall see below, homogeneous conditions would be a necessary

requirement, and this would severely complicate kinetic measurements. Furthermore, we have little tangible data on the silver species involved, on their reactivities, or on the effect of acetate upon their concentrations.) We wish to emphasize here that the existing knowledge about silver catalysis is based largely on such reactions with soluble silver salts in non-reactive solvent, whereas the conditions employed in the present work are quite the opposite.

It is also believed that heterogeneous catalysis can be important in silver salt catalysis (25). We know that silver iodide does not catalyze reactions of our vinyl halides under our reaction conditions (see Controls), so at least that possible complication is removed. However, we must recognize a priori that catalysis may occur on the surface of the undissolved silver acetate. This point will be dealt with at length shortly.

Isomerization of the Vinyl Iodides

Since we shall be concerned with differences arising in the product distributions obtained from 1E and 1Z vinyl halides, it is important that an estimate of the extent of "crossover" be made in each case, e.g. to calculate the maximum amount of products which were produced from the 1Z isomer when the 1E vinyl iodide was solvolyzed. We have used the simplified scheme (10):

$$\underset{\sim}{P}_Z \xleftarrow{k_3} \underset{\sim}{1Z} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\sim}{1E} \xrightarrow{k_2} \underset{\sim}{P}_E$$

where $\underset{\sim}{P}_Z$ and $\underset{\sim}{P}_E$ refer to the product mixtures produced from the respective isomers. The necessary data are $k_z = k_1 + k_3$, $k_e = k_{-1} + k_2$, k_{-1}/k_2, and $K_{eq} = k_{-1}/k_1$ for one to calculate the

maximum crossover. Since $k_z < k_e$ (Table I), k_{-1}/k_2 can be estimated directly from the observed formation of $\underset{\sim}{1}Z$ early in the reaction of $\underset{\sim}{1}E$, and the extent of crossover $\underset{\sim}{1}E$ to $\underset{\sim}{P}_Z$ is found. For the $\underset{\sim}{1}Z$ to $\underset{\sim}{P}_E$ crossover, it is necessary to know K_{eq}, since k_1/k_3 cannot be directly observed. With R = Me, K_{eq} was estimated to be ca. 9-10 (10).

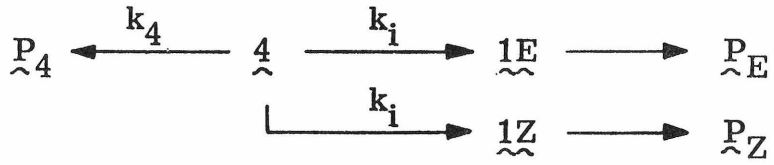
As we mentioned above, we now believe the ketone product observed, particularly for $\underset{\sim}{1}Z$, R =Me, may arise from reactions of vinyl iodide during the work-up. When these data are treated with this in mind, slightly different crossover percentages are calculated. For crossover $\underset{\sim}{1}Z$ to $\underset{\sim}{P}_E$, we obtain 6.4%; for crossover $\underset{\sim}{1}E$ to $\underset{\sim}{P}_Z$, 5.5%. The previous values were 5.9% and 5.6%, respectively. The differences are unimportant.

In view of the difficulty in inducing nondestructive isomerization between $\underset{\sim}{1}E$ and $\underset{\sim}{1}Z$, R = Me, (10), and particularly due to the limited amount of pure $\underset{\sim}{1}E$, R = 3P, available, we did not attempt to measure K_{eq} for the R = Cp and R = 3P systems. Nonetheless, reasonably reliable estimates of maximum crossover can be calculated. We have postulated (10) that the k_e/k_z ratio of ca. 10 observed for $\underset{\sim}{1}$, R = Me, is due to ground state destabilization of the sterically crowded $\underset{\sim}{1}E$ isomer. This was supported by the estimation for K_{eq} found in this case. Certainly such steric effects should be even greater when the larger Cp and 3P groups are substituted for Me. Hence, k_e/k_z should be larger for these systems, as is observed (Table I). We cannot claim that $K_{eq} \approx k_e/k_z$ in these cases, although that is quite tempting and intuitively reasonable, but we can

assume with little probable error that K_{eq} is no less than nine for the two new pairs.

The 1E to P_Z crossover is directly estimated from the data to be 3.9% and 1.7% for R = Cp and R = 3P, respectively. The 1Z to P_E crossover calculated with $K_{eq} = 9$ is 5.7% for R = Cp and 6.6% for R = 3P. Note that if $K_{eq} > 9$, then these latter values would decrease. In any case, the crossover for any of the isomers of 1 is less than 7%.

We previously gave a crossover value of <16% for homoallenic iodide 4, although the details of the calculation were not given (10). We assume the following simplified scheme, in which return from vinyl iodides 1 to 4 is neglected:



This is a good assumption since direct isomerizations of 1Z or 1E, R = Me, gave no detectable formation of 4 (10).

(We should note that our improved vpc conditions have revealed a very small peak which corresponds in retention time to 4 early in the solvolysis of 1E, R = Me. The peak disappears fairly soon, as would be expected if a small amount of 4 were formed. However, it never accounts for more than 0.2% of the products, so the irreversibility of k_i is still justified.)

We have also assumed that the formation of 1E and 1Z occur at equal rates. This is a fair choice, since the vinyl acetates, 9E

and 9Z, are formed from 4 in nearly equal amounts. Since the reaction rate for 1Z is slower than either 4 or 1E (Table I), we can use the data obtained at short reaction times to estimate k_i. A relatively straightforward calculation gives the crossover of 4 to $P_Z + P_E$ to be <12.4%. This new value assumes that the ketone observed was formed from unreacted 4 during the work-up (see above).

Heterogeneous Catalysis

We shall now examine the data presented in Tables II - VII for the silver-catalyzed acetolyses of 1. In particular, we shall examine the r(E/Z) ratios observed for the seven iodides under heterogeneous reaction conditions and compare these to the r(E/Z) values obtained under homogeneous conditions. A cursory examination of the data shows that r(E/Z) appears to characterize subtle differences much better than the other product ratios, as one might expect, and is less subject to experimental error. Minor variations in the other ratios will be pointed out later.

Examine the r(E/Z) ratios given in Table VII for 1, R = 3P. Note that within experimental error the r(E/Z) values observed under homogeneous conditions for the two isomers E and Z are identical (4.30). When heterogeneous conditions are used, the value remains about the same for the Z isomer (4.35), but for the E isomer increases to 4.65. This latter value indicates net retention has occurred under heterogeneous conditions relative to homogeneous conditions for 1E. (We will assume in later discussions that the 4.30 ratio observed for 1E and 1Z under homogeneous conditions in this system represents the "natural" ratio for solvent capture for unshielded ("free") vinyl

cation 2, R = 3P. We cannot assume, however, that this same value represents the natural ratio under heterogeneous conditions (see below).)

When R = Cp, a similar effect on r(E/Z) is observed (Table V). The homogeneous values are 1.26 for 1E and 1.48 for 1Z. But under heterogeneous conditions, the ratio for 1Z again remains the same and the value for 1E increases to 1.39. Compared to homogeneous conditions net retention has occurred under heterogeneous conditions for the 1E isomer. (Of course, comparing the data for 1E to that for 1Z under given conditions shows net overall inversion , but that will be dealt with later.)

Next, for the R = Me system and homoallenic iodide 4 (Table II), a similar trend is seen once again. In this system we have a good indication for the natural solvent trapping ratio of the vinyl cation from the data obtained for iodide 4 (see below). Under homogeneous conditions the observed r(E/Z) ratios for 4, 1Z, and 1E are 1.00 ± 0.01, 1.12 ±0.03, and 0.94. Under heterogeneous conditions the values change to 1.08 ± 0.01, 1.20 ± 0.02, and 1.04 ± 0.02, respectively. The change observed for 4 suggests that the heterogeneous component of the reaction produces the vinyl acetate isomers in a ratio quite different from that produced in homogeneous reactions. There is an apparent net inversion for 1Z and net retention for 1E when the heterogeneous reactions are compared to the homogeneous reactions. Unlike the R = Cp and R = 3P systems, the 1Z isomer is affected by the change to heterogeneous environment and shows net inversion rather than net retention.

We pause to summarize the data: When the reaction conditions are changed from homogeneous to heterogenous conditions, (a) the 1E isomers are affected in all cases; (b) the 1Z isomers are not affected except for R = Me; (c) net retention relative to homogeneous conditions is observed for the 1E isomers ; (d) net inversion is seen for 1Z, R = Me.

The data clearly suggest that surface catalysis is a factor in the heterogeneous silver acetate-acetic acid reactions of 1 and 4. Surface catalysis does not appear to be well understood, particularly for solvolytic reactions. The trends noted above are reasonable, however, if common sense intuition about the interactions of substrate with the catalytic surface is used. We can safely propose that the heterogeneous catalysis requires interaction between the iodine atom of the substrate with a silver atom in or on the particle surface. The reactions probably occur most readily at "active sites" (26), e.g. where silver atoms are not buried by surrounding acetate anions due to defects and dislocations in the surface. The fact that 1E isomers show the larger effects in the r(E/Z) ratios suggests the reasonable idea that the more "exposed" iodine of 1E can interact most readily with the catalytic site.

The molecule, 1E, can "sit" at the active site with the R substituent directed away from the surface, whereas for 1Z the substituent would be directed toward the surface. If instead the interaction of the substrate with the surface is such that the substrate "lies" on the surface with the plane defined by the double bond parallel to the surface, it then is difficult to understand why the 1E isomers are

affected and the 1Z isomers are generally not affected, since the steric interactions of the two geometries should be similar in this "lying" position. We prefer the "sitting" hypothesis. It is evident that the steric interaction of R = Cp or R = 3P for 1Z with the catalytic surface preclude heterogeneous reactions, but for R = Me interaction with the surface is not prevented. These steric effects are entirely reasonable and gratifyingly simple.

It is not so easy to explain why the r(E/Z) ratios change in the directions observed. One thing is clear, however: in all cases there is a net formation of vinyl acetate 9E under heterogeneous conditions, which results in relative retention for all 1E isomers and relative inversion for 1Z, R = Me. In studies on the silver salt catalysis of alkyl halide in non-solvolytic media, e.g. cyclohexane, Kornblum and coworkers (27) suggested a push-pull mechanism on the catalytic surface which results in net inversion of configuration. When a non-productive, but carbonium ion stabilizing solvent is used (ether), retention is the observed path, which was explained by a double inversion mechanism involving oxonium ions (Et_2OR^+) (27).

The present system is probably more complicated, since not only can the catalytic surface be involved in trapping of the intermediate (if there is one), but the solvent is reactive as well. In view of the apparent steric dependence noted above for initial interaction of vinyl halide with the catalytic surface, one might well expect backside attack of solvent on the adsorbed species would give 9Z, i.e. relative inversion for 1E. The fact that the net effects observed all favor 9E over 9Z, even with 1Z, R = Me, suggests that the fate of intermediate

species may be independent of the geometric configuration of the reacting vinyl iodide.

If indeed a carbonium ion is involved in the heterogeneous reaction, a clearly tentative idea, then there may be rather specific cation-surface interactions which result in trapping of the cation in a specific manner. One interesting explanation is that the cation prefers a bent configuration, i.e. the "cation" is bound to the surface in a manner similar to the way it was bound to the iodine. If crowding between substituent R and the surface is more destabilizing than crowding between R and the cyclopropyl ring, then the bound species may prefer an "E" configuration (corresponding to 1E with iodine replaced by "surface"). Even if the initial species were the linear cation 2, formation of bound "E" may be more favorable kinetically than formation of bound "Z" in analogy to the behavior shown in solvent trapping of 2 (see below). Backside solvent attack on bound "E" should be severely hindered by both the cyclopropyl ring and R; hence, "E" persists until a suitable surface acetate ion captures it to form 9E.

This mechanism rationalizes the net formation of 9E, even when the reacting iodide is 1Z. It may be somewhat oversimplified, of course, since we have only circumstantial evidence about what goes on at the catalytic surface. However, we should remember that it is not axiomatic that lack of knowledge directly implies a high degree of complexity. The mechanism also implies that vinyl cations may not be intermediates, per se, in these heterogeneous reactions, i.e. formation of bound "E" or "Z" could happen concurrently with carbon - iodine bond cleavage. (Backside surface "participation" in the reac-

tion of 1Z, R = Me, could still favor formation of "E".) In fact an essentially concerted formation of "E" and "Z" does agree with the curious lack of variation in the other product ratios of Tables III, V, and VII when comparing heterogeneous data to homogeneous data for a given isomer, particularly for r(A/S), which is affected by ion-pair formation (see below).

Now we turn to another aspect of the heterogeneous reactions -- the effect of added sodium acetate. In Table VII the data show that as the concentration of sodium acetate increases from 0.0 M to 1.46 M, the r(E/Z) ratio for 1E, R = 3P, drops dramatically from 4.65 to 3.32 . Likewise, the ratio for 1Z increases from 4.35 to 4.53 when the sodium acetate concentration increases from 0.0 to 0.98 M. In each case, added sodium acetate increases the inversion component of the reaction -- a point that will be discussed at length below. At present we wish to draw attention to the molar concentration effect on the change in r(E/Z). Note that under homogeneous conditions a mere 0.5 M acetate concentration has the same effect on r(E/Z) that required 1.46 M under heterogeneous conditions for 1E and a likewise greater effect (4.82) than did 0.98 M acetate for 1Z.

An attractive explanation for this attenuation of the inversion effects of acetate under heterogeneous conditions is that the effective concentration of sodium acetate in solution is less when excess silver acetate is present. If active sites are important for surface interaction with the vinyl halides, then surface - acetate interaction should also be strongest at these sites. Adsorption of acetate ions on the silver acetate surface will not only reduce the effective solution

concentration but should interfere with the heterogeneous catalysis of the vinyl iodides. Note that the attenuated inversion effect of acetate cannot be due to some heterogeneous reaction which itself precludes intervention by acetate anion because the effect is qualitatively the same for the 1Z isomer, where presumably heterogeneous catalysis is unimportant.

The effect of such interference of acetate with heterogeneous catalysis is difficult to separate experimentally from the large inversion effects caused by acetate ion in the homogeneous phase. The R = Cp system presents little help in this regard, but at least the same effect is observed overall. At 0.5 M there is almost no effect upon 1Z under heterogeneous conditions but an increase of r(E/Z) from 1.48 to 1.57 under homogeneous conditions. For the 1E isomer, a larger drop in r(E/Z) is observed for 0.5 M acetate under homogeneous conditions (1.26 to 1.11) than under heterogeneous conditions (1.39 to 1.26).

However, some support for at least partial blockage of the heterogeneous component by acetate is gained from the data in Table III for the R = Me system. The 1E isomer acts "normally", i.e. the inversion effect of 0.5 M acetate is somewhat larger under homogeneous conditions. But for 1Z under heterogeneous conditions, an increased inversion component should produce an r(E/Z) ratio $>1.20 \pm 0.02$, which we recall was already an increase in inversion compared to the 1.12 ratio observed under homogeneous conditions. In fact, the ratio drops to 1.16 ± 0.02. There appears to be a small, if real, inversion effect of 0.5 M acetate on the homogeneous reaction (1.12 to

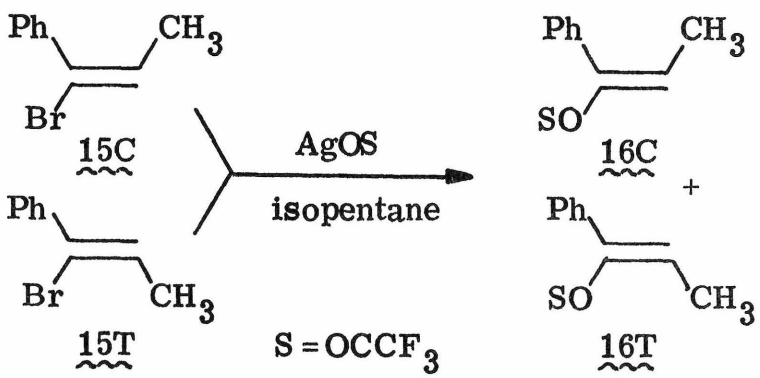
1.14). Even though the ratios 1.16 and 1.20 are almost within experimental error of one another, the drop in r(E/Z) to 1.16 is exactly what one would expect if the heterogeneous reaction of 1Z is partially blocked.

Additional evidence is found in the data for 4. Under homogeneous conditions there appears to be virtually no change in the r(E/Z) ratio (1.00 ± 0.01) when sodium acetate is added. Yet, clearly under heterogeneous conditions 0.5 M acetate reduces the ratio from 1.08 ± 0.01 to 1.04 ± 0.01. The change is outside the experimental errors for the ratios. Again, this is exactly what one would expect if the heterogeneous portion of the reaction of 4 is partially prevented by adsorbed acetate at the active sites of the catalyst. (We also note that the amount of homoallenic acetate 14 increases much more (6.25 to 9.67%) under homogeneous conditions with 0.5 M acetate than under the heterogeneous conditions (6.72 to 7.62%). This further illustrates the greater availability of acetate ion under homogeneous reaction conditions).

The results observed for 4 strongly suggest that the experimental difference observed for r(E/Z) for 1Z, R = Me, under heterogeneous conditions is also real. It is clear that added acetate interferes with the heterogeneous catalysis of 4 in some manner and apparently does not interfere with the homogeneous reaction, except for increased formation of homoallenic acetate. This does not require, per se, any change in the nature of the catalytic surface except that it then becomes difficult to also rationalize the attenuated inversion effect (and attenuated effect on formation of homoallenic acetate from 4) of acetate ion

under heterogeneous conditions. Both the attenuation (concentration) effect and the interference effect of actate in the heterogeneous reactions are logically and economically rationalized by our hypothesis that acetate ion is strongly adsorbed on the silver acetate surface and "covers over" the active sites. This partially prevents heterogeneous catalysis and, at the same time, reduces the concentration of acetate ion in the solution.

We have seen that heterogeneous catalysis may play a small, but important role in the silver-assisted ionizations of 1 and 4. The effects are most prominent when the substituent R does not interfere with approach to the surface. This result alone is rather noteworthy, since such effects have not been clearly illustrated for vinyl halides. Steric effects have been postulated to explain the low reactivity of neopentyl halides with silver salts in non-reactive solvents (25). Both cis- and trans-1-phenyl-1-bromopropene react with silver trifluoroacetate in isopentane to give vinyl trifluoroacetates, eq. (6) (28), but



(6)

qualitatively the trans bromide 15T reacted more slowly. This reactivity suggests some steric hindrance by the methyl group, in agreement with the steric effects we believe to be operative in heterogeneous

catalysis of 1.

In the above reactions of 15C and 15T, Kernaghan and Hoffmann (28) found evidence for net retention of geometry. Isomer 15C gave a ratio 16C/16T of ca. 1.30, and 15T gave a ratio of ca. 0.76 in isopentane solvent. They assumed the "natural" ratio for formation of 16C and 16T was 0.95 to 1.0 based upon the thermodynamic stabilities of 15C and 15T. Certainly one cannot regard this assumption as valid, since probably all of the reaction occurs on the silver trifluoroacetate surface. It is quite impossible to know from the available data the "natural" ratio 16C/16T under these heterogeneous conditions.

In our work we do have a good idea of the natural kinetic ratio r(E/Z) under homogeneous conditions when R = Me (1.00) and when R = 3P (4.30) (see above). Our results show that, relative to the homogeneous reactions, the heterogeneous reactions occur with a net formation of acetate 9E. In particular, the increase in r(E/Z) from 1.00 (homogeneous) to 1.08 (heterogeneous) for 4 suggests that the natural ratio for the heterogeneous portion of the reaction taken separately may be quite high. This points out the difficulty in knowing in absolute terms whether a purely heterogeneous reaction has occurred with retention or inversion, as illustrated for the reaction in eq. (6).

If we assume the natural ratio 16C/16T is indeed ca. 1.0, then the data gives ca. 13% retention of configuration for both 15C and 15T (28). However, in view of the effects noted above, it would not be unreasonable if the natural 16C/16T ratio were greater than 1.0, even 1.30 or greater on the silver catalyst. In such a case, the

data could be interpreted as showing little or no retention, even inversion, for 15C but larger (>13%) retention for 15T. On the other hand, the situation might be quite the reverse if the "true" ratio is taken to be less than one. It appears that net retention is the overall result, but we do not necessarily know which reactant gives retention nor if both reactants give net retention, as was claimed (28).

We also wonder if the one equivalent of tri-n-butylamine present during the reactions of 15C and 15T in isopentane could have participated in a double inversion mechanism, as postulated for the reaction run in ethyl ether (27, 28). This could be tested by running the isopentane reaction with a more sterically crowded base, e. g. 2, 6-di-tert-butylpyridine, and a less sterically crowded one, e.g. quinuclidine.

Turning back now to the present work, we finally note that the heterogeneous effects we have observed are relatively small. The net proportion of the reaction occurring through heterogeneous catalysis can be estimated from the r(E/Z) ratios to be about 5.0, 3.6 3.6, 5.5, and 6.1 % for 1E (R = Me), 1Z (R= Me), 4, 1E (R = Cp), and 1E (R =3P), respectively. The total proportions may be somewhat larger, of course. We have seen that even this small net component has an easily observable effect upon the r(E/Z) ratios and, if not recognized, could have led to erroneous conclusions about the stereochemical course of the solution reactions.

Stereochemistry of Vinyl Cation Reactions

Having examined the heterogeneous effects upon the silver-catylized reactions of 1 and 4, we are now able to develop a picture of the solution chemistry of these reactions. In the introduction and in our previous work (10), we postulated ion-pairs (6z and 6e, Scheme I) to account for the isomerizations of the starting vinyl iodides. We now know that such isomerization occurs for the iodides with R = Cp and R = 3P as well. It appears that the ion-pair hypothesis should be applied to these systems, too.

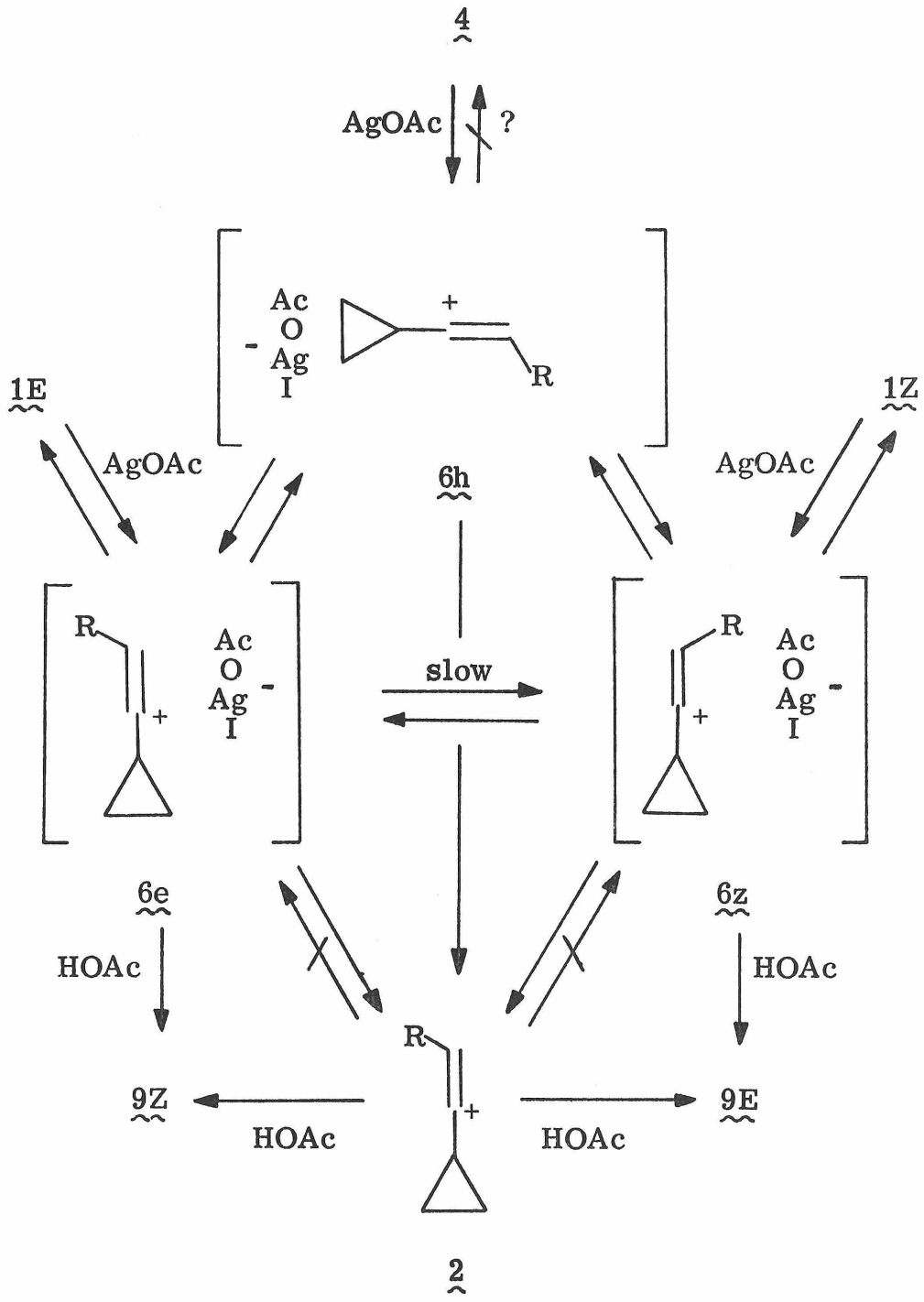
If ion-pairs are involved in isomerization of 1, then we expect to see stereochemical effects on the product distributions which depend upon the geometry of the starting material. This is perhaps the most central problem of the present work that we wished to solve. At the expense of some dramatic impact, stereochemical selectivity is observed under certain conditions, and both its presence and absences agree with the ion-pair concept. We shall begin by examining the r(E/Z) ratios. Later, we will include more subtle effects upon the product distributions. Unless specifically stated otherwise, we are dealing with the data obtained under homogeneous conditions. The number of repeated runs for a given substrate under homogeneous conditions is limited, but the precision of the data can be confidently taken to be similar to the observed deviations when repeated runs were made. When only one run was made, the vpc analysis was usually performed at least twice to assure the precision of that run. Note, too, that the average deviations given in Table III for the reaction of 1Z, R = Me, under homogeneous conditions are quite similar in magnitude

to those observed in repeated runs under heterogeneous conditions. In general, the differences we will be discussing clearly lie outside experimental errors.

1) The r(E/Z) Ratios

First, we shall look at the data for 1, R = Me, and 4 (Table III). It is clear that net inversion of geometry is observed. The ratios for 1Z, 4, and 1E are 1.12, 1.00, and 0.94, respectively. Furthermore, we feel that the data for 4 illustrates the natural ratio for solvent capture of the vinyl cation, 2. In Scheme III, a portion of the reaction sequence is shown. It is an expanded version of Scheme I and shows those steps leading to vinyl acetates. Note that we have represented the first-formed ion-pairs to show the position of the counterion as dictated by the structure of the starting material. For 4, it seems unlikely that the counterion can directly shield either side of the cation upon formation of 6h. Ion-pair 6h should be trapped by solvent in virtually the same manner as trapping of 2, the "free" ion. The observed r(E/Z) value for 4, 1.00 ± 0.01, is not unexpected, although one might have thought the cation would favor approach of solvent "anti" to the methyl group to give a slight excess of 9E. (We will see, however, that even when R = Cp, the excess formation of 9E is not terribly greater.) A high selectivity would require high stability of 2, low nucleophilicity of the solvent, and/or steric hindrance by substituent R. The steric factor is probably the key factor, and is evidently not effective for R = Me. (Remember, too, that 1Z, R = Me, is unique among the 1Z isomers studied for its involvement in heterogeneous catalysis.)

Scheme III.


4
AgOAc
?
Ac
O
Ag
I
-
+
R
1E
1Z
AgOAc
AgOAc
6h
R
Ac
O
Ag
I
-
+
slow
R
Ac
O
Ag
I
-
+
6e
6z
HOAc
HOAc
R
9Z
9E
HOAc
HOAc
+
2

The r(E/Z) values show excess 9Z is formed from 1E and excess 9E is formed from 1Z when the natural trapping ratio of 2 is taken as 1.00. This means that, within the framework of Scheme III, trapping of the ion-pairs occurs predominately by backside attack of solvent with $IAgOAc^-$ acting as a solvent shield. A priori one might expect some frontside collapse of the ion-pairs, e.g. of 6e to give 9E + AgI. This may happen some of the time, but the net effect is inversion of geometry, as shown. The calculated percentages of net reaction occurring through backside attack on the ion-pairs are 5.6% for 1Z and 3.2% for 1E. We expect trapping of 6e to be slightly hindered by the methyl group, hence the net inversion is less for 1E and for 1Z.

Now if sodium acetate is added to the reaction solution and if we naively ignore the unknown effects this may have upon the solvent structure and on the solvation shells of the various species, then we should expect the more powerful acetate nucleophile to compete with greater effectiveness in reacting with the ion-pairs. As a result, the r(E/Z) ratios should reflect greater inversion. If, however, 4 is already reacting predominately through a nonselective cation, 2, the r(E/Z) for 4 should remain constant. As expected, the r(E/Z) value drops to 0.88 for 1E and remains at 1.00 for 4. The expected increase in r(E/Z) for 1Z appears to be realized, although the effect is within the experimental error of the measurements (1.12 vs. 1.14). The calculated net inversions are now almost equal -- 6.4% for 1E and 6.6% for 1Z.

This simple, but rational, scheme qualitatively accounts for the geometric inversion observed in the formation of 9 from 1, R = Me.

The scheme will become more complicated when competing reactions are added. But first, we must see if, within the bounds of good taste, we can also use this scheme to explain the gross features of the reactions of 1 when R = Cp and R = 3P.

The reactions of vinyl iodides 1E and 1Z, R = 3P, show virtually the same r(E/Z) ratios, 4.32 and 4.29. At first thought, this was a little surprising, but not for long. If not pure coincidence, the equality of the ratios indicates that no net solvent trapping has occurred at the ion-pair stage. Thus, 4.30 represents the natural trapping ratio for vinyl cation 2, R = 3P, a value we would not otherwise have known. When we decided to include the study of this system, we expected trapping of 6e to be unlikely or at least very slow compared to R = Me, because the bulky 3P group is situated to interfere with attack by solvent. (In fact we tried originally to prepare 1, R = t-butyl; see Appendix A.) However, such steric effects may also be important in ion-pair 6z in particular, where the counterion feels the effects of the substituent. As a result, the conversion rate of 6z to 2 is accelerated, i.e. 2 is formed faster from 6z when R = 3P than when R = Me, and there may be little chance for solvent attack on 6z. Therefore, the absence of net effects in the formation of 9E and 9Z, R = 3P, does not require any particularly outrageous variation of Scheme III.

The increase in the trapping ratio of 2 from 1.00 when R = Me to 4.30 when R = 3P indicates a far greater selectivity in the latter case. Since the stability of the two cations (2, R = Me and R = 3P) should be reasonably similar and since the solvent system is the same,

it is obvious that the 3-pentyl group has a profound steric effect. On thermodynamic grounds, r(E/Z) should be less than 1.0 , since the E isomer of 9 might be more sterically crowded than the Z isomer. As discussed earlier, one clearly cannot use the thermodynamic stabilities of the products to predict the r(E/Z) ratio for trapping of 2. The Hammond postulate (29) confines the transition state for trapping of the highly unstable cation to give very stable products to resemble closely the structure of the cation. Hence, very little of the steric crowding between 3-pentyl and cyclopropyl will be "felt" in the transition state leading to 9E. Analogous to the postulated steric interactions in ion-pair 6z, steric interaction between 3-pentyl and the incoming acetic acid molecule should be felt strongly in the transition state leading to 9Z. Hence, trapping of 2 should lead to r(E/Z) > 1.0 with R = 3P. The calculated $\Delta\Delta G^{\ddagger} = 0.43$ kcal/mole for the difference in the free energy of activation of the two trapping pathways is intuitively reasonable.

When sodium acetate is added to the reaction solution, we again see overall net inversion. This is gratifying, since it indicates that ion-pairs 6e and 6z are present, as given in Scheme III. We do not necessarily know, however, if inversion is occurring for both 1E and 1Z, because we now do not know the natural ratio of trapping of 2 in the presence of acetate anion. As mentioned in the R = Me case, a more reactive necleophile should show less selectivity in trapping 2. In the present case then, the natural ratio should be ≤ 4.30, but we do not know how much less. Using a natural ratio of < 4.30, the net inversion is calculated to be $< 5.4\%$ for 1E and $> 8.8\%$ for 1Z.

Evidently trapping of 6z by acetate ion is fast compared to the conversion of 6z to 2 and much more efficient than acetic acid. As expected, the net inversion for 1E is lower; 6e is difficult to trap no matter how "slowly" it may convert to 2, even with acetate present.

For the system when R = Cp, the same qualitative behavior is observed as given in Scheme III. For isomers 1Z and 1E, the r(E/Z) ratios are 1.48 and 1.26, respectively (Table V). Again overall net inversion obtains for at least one of the isomers. Unfortunately, we have no concrete estimate for the natural r(E/Z) ratio for 2, R = Cp. In view of the behavior shown in the R = Me and R = 3P systems, we are probably justified in assuming that the natural ratio in this case lies within the 1.26 to 1.48 limits.

Note that this natural ratio again follows the pattern set by R = Me (1.00) and R = 3P (4.30). The cyclopropyl group should be sterically less bulky than 3-pentyl but more bulky than methyl. (The so-called A values for methyl, isopropyl and cyclohexyl obtained from conformational data on substituted cyclohexyl rings are 1.70, 2.15, and 2.15, respectively (30). The A value for cyclopropyl, a "contracted" isopropyl, should be somewhat less than 2.15, and the A value for 3-pentyl should be nearly the same as for isopropyl and cyclohexyl, or perhaps slightly greater.) The calculated value for $\Delta\Delta G^{\ddagger}$ in trapping of 2, R = Cp, is 0.07 to 0.12 kcal/mole at 23°C. The net inversion for 1Z within these limits is $<9.0\%$, and for 1E is $<6.7\%$.

When we compare the net inversion observed for 1E, R = Me and R = 3P, we see a drop from 3.2% to presumably 0.0% (in the absence of sodium acetate). If our steric argument is correct, then in the

first approximation the net inversion for 1E, R = Cp, should be <3.2%. For such to be the case, the natural r(E/Z) ratio must be <1.355. This in turn gives the net inversion for 1Z to be >5.1%, slightly less than the 5.6% net inversion calculated for 1Z, R = Me. The manipulation is interesting in that it again gives greater net inversion for 1Z than for 1E, which is reasonable if 6z is not too terribly destabilized by steric interactions.

When the reactions of 1, R = Cp, are run in the presence of sodium acetate, the r(E/Z) ratios again diverge. For the E isomer, r(E/Z) drops to 1.11 and for the Z isomer increases to 1.57. The divergence indicates that net inversion has increased. Again we do not know the natural ratio, but certainly it must be <1.48 (see above). This value gives minimum net inversion for 1Z of >3.5% and maximum net inversion for 1E of <11.9%. If our "calculated" natural ratio used above is reduced somewhat in the presence of acetate, i.e. <1.35, the the net inversion for 1Z is >8.6% and net inversion for 1E is <8.6%. Within the limits of the assumptions, net inversion is greater for 1Z than for 1E, although we do not know how much greater.

Lest the wrong impression be gained from this discussion, we point out that certainly we are not attempting to support the ion-pair Scheme III by manipulating the natural ratio r(E/Z) for 2. Quite the contrary. Within the limits of the information available for the R = Cp system, Scheme III appears to be valid. By imposing the above limitations derived from Scheme III, e. g. comparing 1E with R = Me and R = 3P, we then predict the natural ratio for R = Cp will be ≤1.35 under homogeneous conditions and even less with 0.5 M

sodium acetate (but >1.11). This predicted limit is then consistent with what one should expect based on Scheme III for the reactions in the presence of sodium acetate, i. e. that net inversion will be greater for 1Z than for 1E, as was observed in the R = 3P system. It would be interesting if a study of the corresponding homoallenic iodides (4 with the methyl replaced by cyclopropyl or 3-pentyl) bore this out. We expect it would. Table VIII below summarizes the net inversions observed in our studies along with the observed or predicted natural ratios for solvent capture of cation 2.

Table VIII. Observed and Estimated Net Inversion Percentages for the Vinyl Iodides (1) and Natural Solvent Trapping Ratios, r_N, for the Vinyl Cations (2).[a,b]

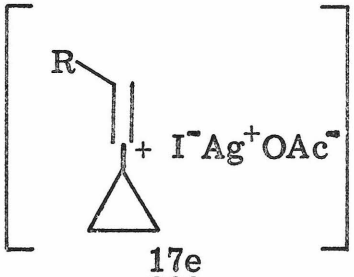
Reactant[c]	Substituent, R		
	Me	Cp	3P
2, r_N	0.99	(≤1.36)	4.30
2, r_N (NaOAc)	1.00	(≤1.35)	(≤4.30)
1E	3.2	(≤3.2)	0.0
1E (NaOAc)	6.4	(<8.6)	(≤5.4)
1Z	5.6	(≥5.1)	0.0
1Z (NaOAc)	6.6	(>8.6)	(≥8.8)

[a] Ratio r_N is the r(E/Z) ratio for cation 2. [b] Ratios and percentages in parenthesis are predicted values; see text. [c] Under homogeneous reaction conditions; (NaOAc) indicates with added sodium acetate present.

In all three systems we have studied, net geometric inversion is observed overall and, with the exception of the R = Cp case, we feel we have good direct evidence that net inversion obtains for both the E and Z isomers of 1. There is no evidence for net retention in any of these cases under homogeneous conditions. Certainly the ion-pair concept of Scheme III qualitatively accounts for these observations. Note that a "mixed" mechanism (21) in which the inversion component is produced by S_N2 displacement by solvent or acetate on 1 without silver ion involvement is specifically ruled out in these systems by the unreactive nature of 1 in the absence of silver acetate. This suggests that the overall net inversion in the solvolyses of vinyl triflates by T. C. Clarke of these laboratories (13) is also due to discrete ion-pair effects.

We should point out that the interpretation of the data given here requires that ion-pairs 6e and 6z do not equilibrate before trapping occurs. If they were rapidly equilibrating, then identical product distributions would be observed from 1E and 1Z. (Identical r(E/Z) ratios were found in the R = 3P system under homogeneous conditions, but there is additional evidence (see below) that this is not due to rapidly equilibrating ion-pairs.) Isomerization of the iodides requires some "leakage", probably by simple rotation of the cation and collapse of the ion-pair. It seems less likely that return from 2 occurs. Note too that these ion-pairs may be oversimplified. We feel that the simple cation - AgI pair does not account well for the isomerization, since the unbalanced charge makes the species inherently unstable and there is no obvious rationale for return of iodine to the

cation once AgI is formed (10). Therefore, we show the counterion as anion $IAgOAc^-$. An equivalent representation is an overall neutral quadruplet ion (31), e.g. 17e, which can collapse to give 1E (or after



17e

rotation of the cation, 1Z) + AgOAc or to 2^+ + AgI + OAc^-. In this representation it is conceptually easier to see why collapse of 17e gives 1E or 1Z but not vinyl acetate 9E or 9Z since I^-Ag^+ or IAg shields cation 2 from the quadruplet OAc^-. Of course, collapse of 17e or 6e could give 9E or 9Z -- there is no positive proof against it -- but it appears backside trapping of 17e or 6e must predominate, perhaps exclusively.

2) Cyclopropyl Ring-opening Rearrangements; r(A/S)

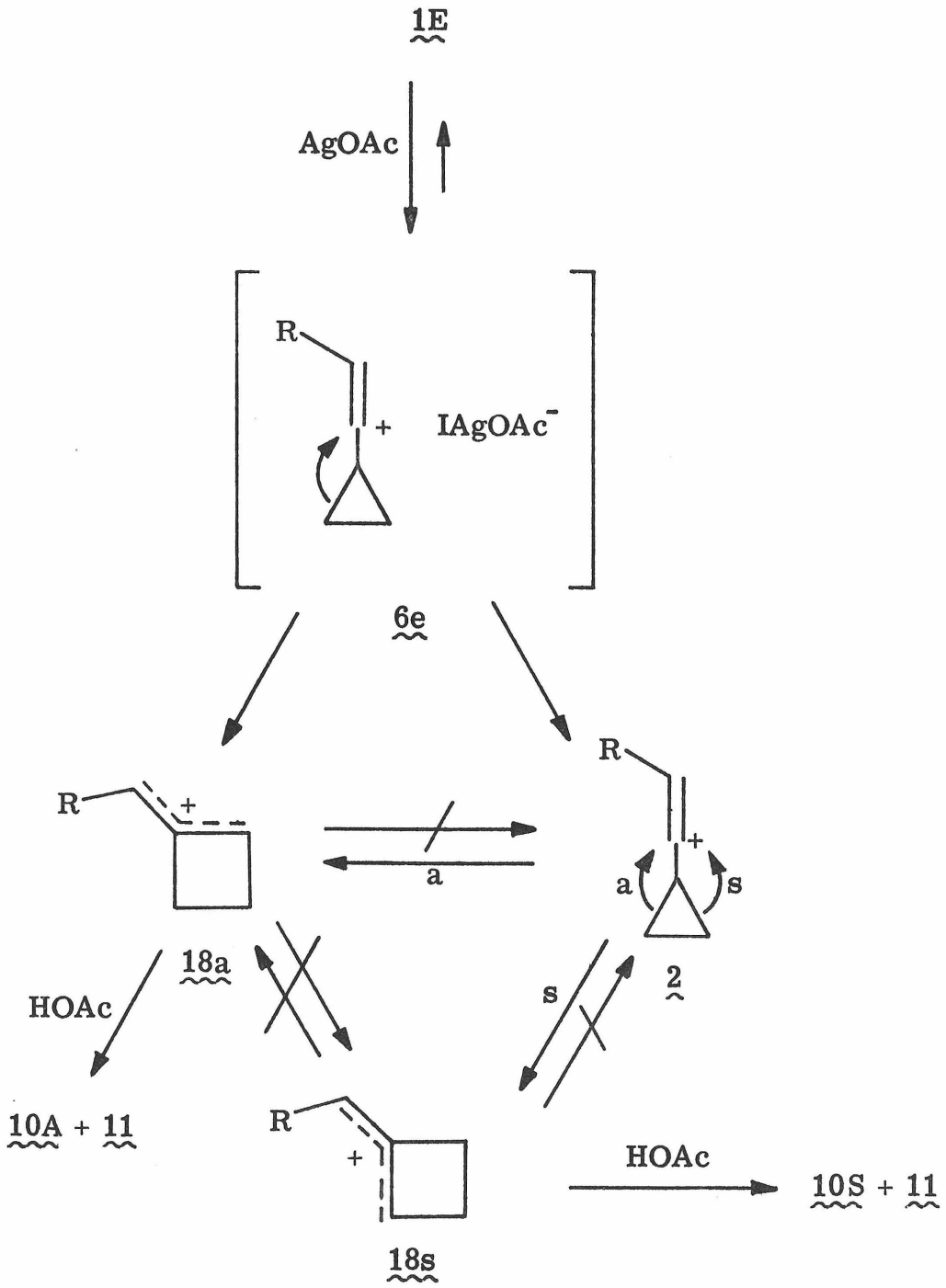
In previous work (10, 17) and in the present work (Scheme II) cyclobutyl-type acetates have been observed in all cases. Since ion-pairs have been strongly implicated in the formation of the vinyl acetates 9, we should examine the possibility that some stereoselectivity can arise in the formation of 10 and 11 from 1E and 1Z. In Scheme IV below we show formation of the cyclobutyl products from ion-pair 6e and 2. The net production of 18a from 6e is shown, a priori, on the grounds that formation of the vinyl acetates 9 evidently resulted from backside attack on 6e. We would expect the analogous reorganization of the bonds situated "opposite" the counterion to be

more likely (32). The cation 2 is shown to rearrange to both 18a and 18s, depending upon which cyclopropyl bond migrates. If interconversion between 18a and 18s is slow, as expected (33), then there should be some natural ratio for formation of 18a and 18s from 2 and hence some natural ratio 10A/10S . Also note that Sherrod and Bergman's study (17) showed that conversion of 18 back to 2 is very unlikely. Naturally, a corresponding scheme for 6z would show formation of 18s preferentially from the ion-pair, and as was shown in Scheme III ion-pair 6h from 4 should convert quickly to 2, giving the natural ratio of r(A/S).

Scheme IV (and an analogous scheme for 1Z) predicts then that the r(A/S) ratios for 1Z isomers should be lower than those for the 1E isomers. This appears to be realized, though we caution that the r(A/S) values are generally less precise than the r(E/Z) ratios because the quantities measured constitute generally a much smaller proportion of the reaction mixture.

In the R = Me system, Table III shows that r(A/S) for 1E is ca. 3.44 and for 1Z is ca. 2.75 . The difference appears to be outside the experimental error and is qualitatively accounted for by rearrangement of the cyclopropyl bonds within the ion-pair stage, either 6e or 6z or both, as shown in Scheme IV. It is unfortunate that we do not have the corresponding ratio for 4 to use as a measure of the natural r(A/S) ratio. Under homogeneous conditions, the vpc peak corresponding to the unreacted excess 4 eluted near the 10S peak and prevented accurate measurement of 10S. However, note that the r(A/S) values obtained under heterogeneous conditions for 1E and 1Z are

Scheme IV.



similar to the homogeneous values in these cases within experimental error (ca. 3.3 and ca. 2.7, respectively). If we assume that the heterogeneous conditions also do not affect r(A/S) for 4, then this value can be taken to be ca. 2.86 . This value falls between the r(A/S) ratios for 1E and 1Z ; therefore, to a first approximation net "inversion", i.e. antiparallel rearrangement, occurs for both isomers. The net "inversion" for 1Z is small, if real. This is reasonable, since we recall that the intramolecular rearrangement must compete with intermolecular trapping (Scheme III). The intermolecular trapping is more efficient for 1Z (Table VIII) and hence less intramolecular rearrangement occurs for this isomer. It is rather curious that added sodium acetate has little effect on the r(A/S) ratios, since one expects a priori that the increased competition of acetate will prevent intramolecular rearrangement at least in 6e and thus lower the r(A/S) for 1E.

Next we turn to the R = Cp system, where the situation is rather complicated by the instability of 11 under the reaction conditions (see above). Since there is little or no heterogeneous reaction for 1Z, we can use the results obtained under heterogeneous conditions in this case. The initial r(A/S) ratio for 1Z is 3.80 (Table V) and gradually rises to 4.17 during the reaction; the highest value observed is 4.72. If we assume that the heterogeneous reaction has little effect on formation of 10 and 11 from 1E, then the initial r(A/S) value is ca. 5.0. Even under homogeneous conditions where the total reaction times were the same for the two isomers, r(A/S) for 1Z is 4.24 and for 1E is 5.12. The best estimates for r(A/S) again reveal a larger

value in reactions of 1E than for reaction of 1Z, which supports Scheme IV. In this case, we have no indication of the natural r(A/S) ratio except that qualitatively compared to the R = Me case, the ratio is much larger.

In monotonous agreement with the other systems, the case where R = 3P again shows differences in r(A/S) in accord with Scheme IV. The r(A/S) for 1E is 1.24 and for 1Z is 0.75. The same values are observed under heterogeneous conditions. Even when apparently no net intermolecular trapping of the ion-pairs occurs (Table VIII), the r(A/S) values differ. This supports our contention that ion-pairs are involved in the homogeneous reactions of 1E and 1Z (without added sodium acetate) and that equilibration of the ion-pairs is not achieved. On entropy factors alone one expects intramolecular rearrangement to be favored over intermolecular trapping (34), so it is not unreasonable to find rearrangements occurring in 6e or 6z even when external trapping apparently does not occur.

With added sodium acetate present, the r(A/S) ratio for 1Z is unaffected, but increases to ca. 1.9 for 1E. The reason behind this change is not clearly evident, although we note that the natural r(A/S) ratio for rearrangement of cation 2 may be affected by the presence of acetate ion.

The most curious aspect of these r(A/S) values, R = 3P, is their low magnitude compared to the values observed in the R = Me and R = Cp systems. Certainly one would expect the product 10A to be thermodynamically more stable than 10S, particularly with R = 3P. Likewise, the steric effects of 3P should hinder solvent trapping of

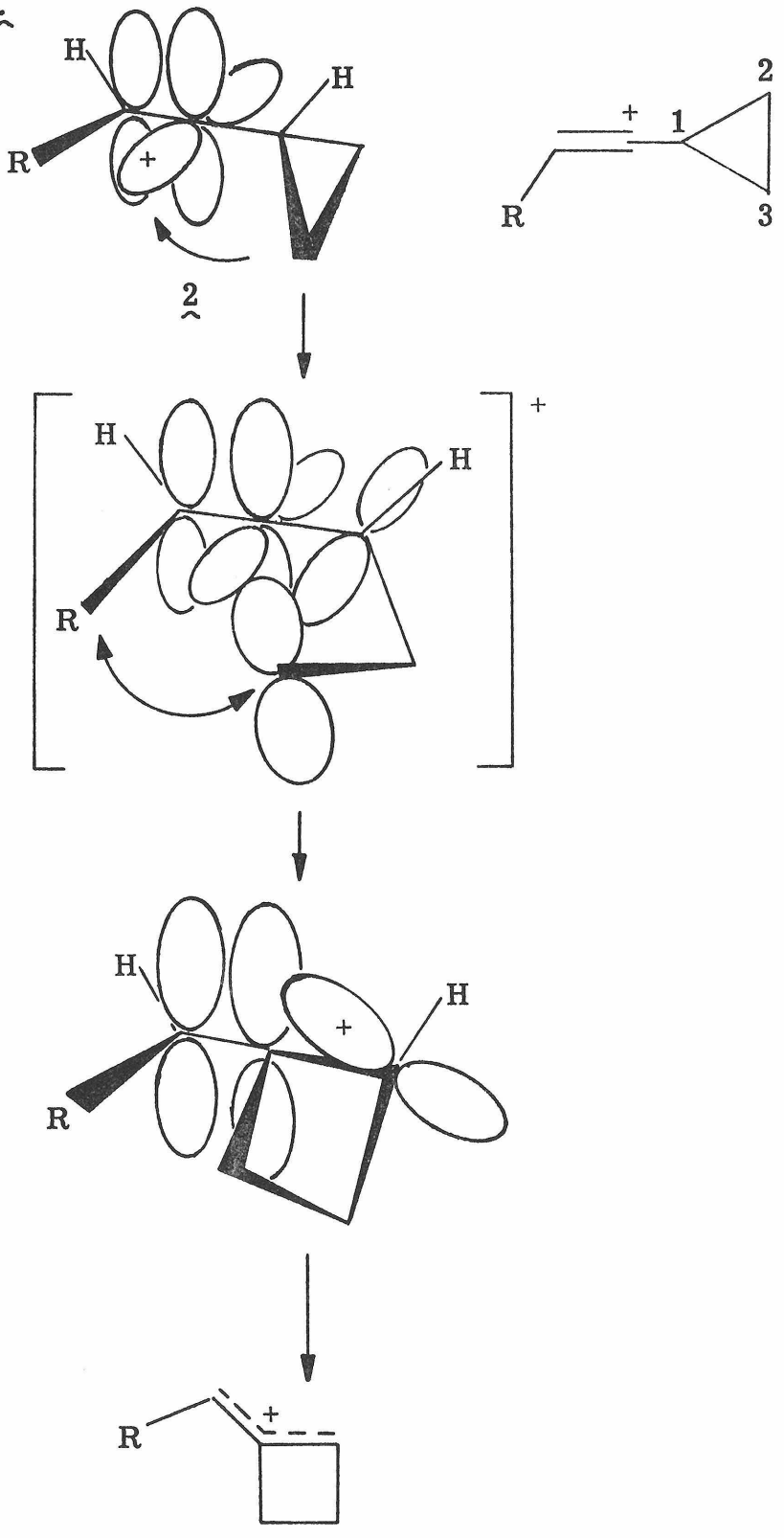
18s compared to 18a. However, if in fact interconversion of 18s and 18a is not operative, the crucial step is in the formation of 18s and 18a and not their subsequent fates.

In Scheme V below we show the conversion of 2 to 18a. In the transition state we have drawn the developing cationic center at C1 has remained nearly orthogonal to the double bond. In fact, the first-formed cyclobutyl cation may retain this partial orthogonality before relaxing to the more stable planar cation, as suggested by Sherrod and Bergman (17). The migrating methylene C3 may experience some steric interference with R, as shown. If the ring remains "buckled" on the side where the cationic center develops, then the corresponding interaction between C1 and R in the corresponding transition state (not shown) leading to "buckled" 18s cannot be as severe. Hence, formation of 18s is favored, at least when R is very bulky.

An argument similar to this was proposed by us (10) previously to explain the supposed preferential formation of 10S from 1, R = Me. We now know that the tenative assignments of stereochemistry in that case were incorrect (see above). We are quite sure that the stereoisomers have been correctly assigned in all cases now. The argument is much more reasonable in the present situation, since the steric bulk of substituent is much larger.

If solvent, and particularly acetate ion, becomes involved during this rearrangement (Scheme V), then this potentially stabilizing effect may reduce the importance of steric interaction between R and C3 and the transition state may begin to reflect the stabilities of the products. This would favor formation of 10A, as is observed with

Scheme V.



2

18a

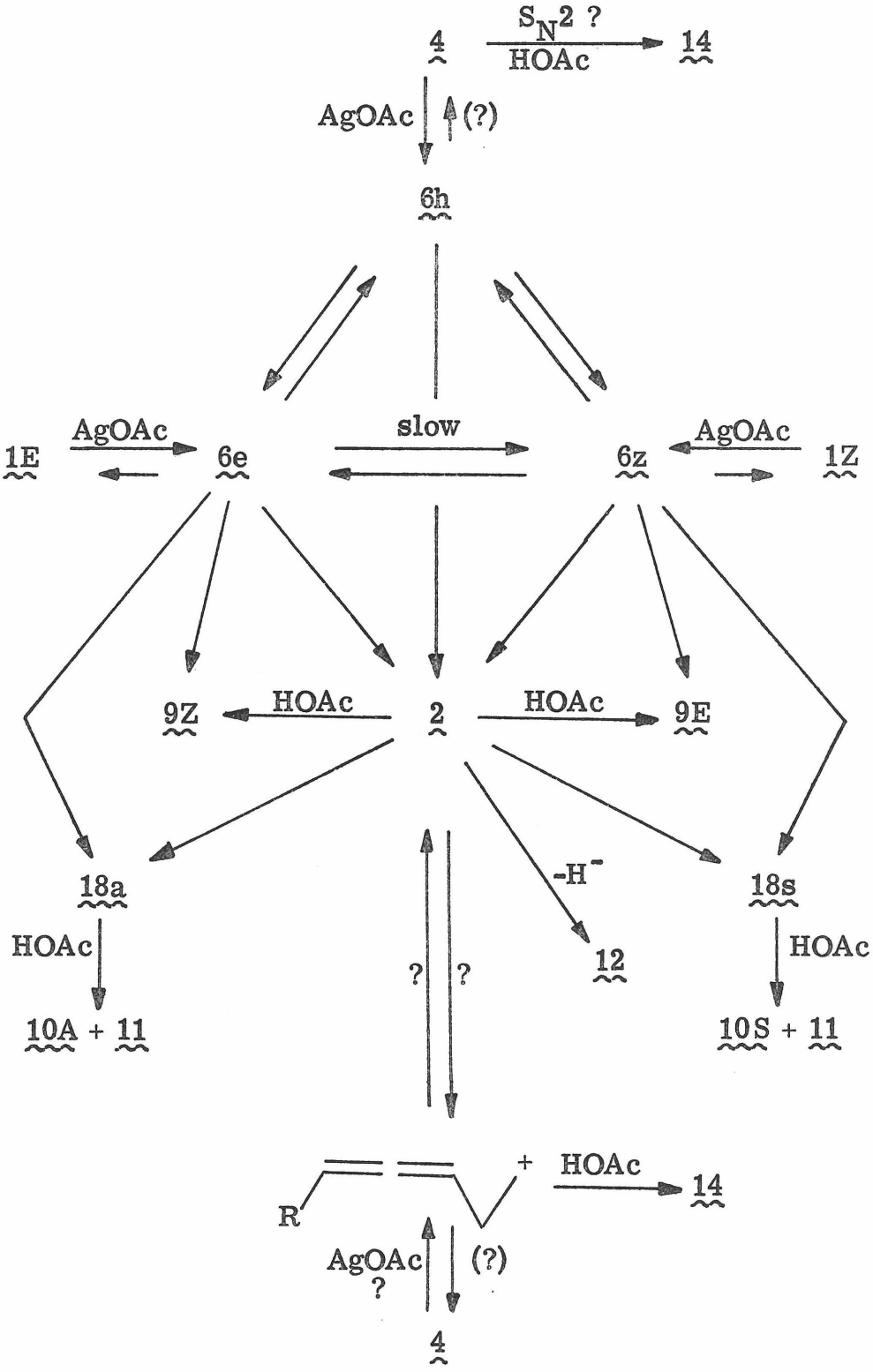
1E, R = 3P, when sodium acetate is present, but not for 1Z. It is possible, too, that 6e, R = 3P, is long-lived enough that specific exchange of counterion $IAgOAc^-$ for AcO^- occurs followed by collapse to 9E or 10A. This could result in net retention for formation of 9E and 9Z from 1E, R = 3P, which implies a natural ratio r(E/Z) of less than 3.32 under homogeneous conditions with 0.5 M NaOAc and a very large inversion component for the reaction of 1Z. This possibility cannot be altogether ruled out with the present data. In general, the behavior of r(A/S) when acetate ion is present does not follow any easily discernable pattern, except that it is usually unchanged from the ratios observed without acetate. Frankly, we do not understand this behavior, but this may just be a reflection of our lack of understanding of more complex and interrelated effects that acetate ion may have upon these reactions and upon the reaction environment.

The ion-pair concept neatly accounts for the qualitative differences that we observe in the formation of 10A and 10S from vinyl iodides 1E and 1Z as well as the differences in formation of vinyl acetates 9E and 9Z. Certainly the schemes shown may be somewhat oversimplified, for instance: (1) We do not know to what extent ion-pairs 6e and 6z interconvert, since formation of isomeric iodide may represent only a fraction of the ion-pairs that collapse. We do know that equilibrium is not reached, however. (2) We do not know the total proportion of products that arise from trapping or rearrangement at the ion-pair stage before conversion of the ion-pairs to 2. We only roughly know the net effect of the ion-pair reactions. (3) In order to account for vinyl iodide isomerization, we have shown inti-

mate or contact ion-pairs, but solvent-separated ion-pairs (35) may also be involved to some extent. (4) We do not know to what extent, if any, solvent or acetate participates in the rearrangement reactions of the ion-pairs or of the cation 2 itself. It does not seem likely that such participation occurs during the initial ionization reaction with silver species, since added acetate ion does not reduce the total proportion of rearrangement products (examine r(V/B) in the ratio tables).

These limitations represent rather subtle uncertainties which point out areas yet to be explored in vinyl cation chemistry, but they should not detract from the new understanding we have gained from these experiments. The ion-pair scheme we previously applied to account for isomerization of the vinyl iodides also qualitatively accounts for the small, but detectable, stereochemical selectivity in formation of acetates 9E, 9Z, 10A, and 10S from the vinyl iodide isomers. Below in Scheme V, we show the overall reaction pattern for which we have reasonable evidence. The scheme is similar to one already presented (10), but adds ion-pairs 6e, 6z, and 6h and shows direct paths leading from these ions to products, e.g. 6e to 9Z + 10A. We also show a direct S_N2 reaction for formation of homoallenic acetate 14 from 4, which accounts for the greater proportion of 14 found in the reactions of 4 (especially in 0.5 M NaOAc) than in those of 1 (R = Me) (Table II).

Scheme VI.

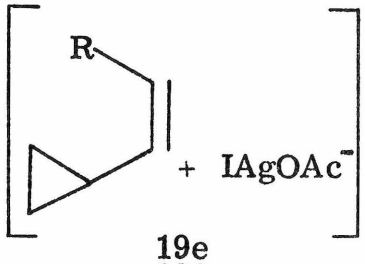

4
S_N2 ?
HOAc
14
AgOAc
(?)
6h
1E
AgOAc
6e
slow
6z
AgOAc
1Z
9Z
HOAc
2
HOAc
9E
18a
HOAc
10A + 11
?
?
-H⁻
12
18s
HOAc
10S + 11
R
+
HOAc
14
AgOAc
?
(?)
4

The Structure of the Vinyl Cation

Before proceeding to other topics of this work, we pause now to reflect upon what this new data reveals about the structure of the intermediate vinyl cation. On the basis of the earlier analytical data, we estimated (10) that the rate of interconversion of isomeric "bent" vinyl cations must be no less than 10^{10} sec^{-1} to account for the randomization of product stereochemistry. We now know that a small amount of inversion occurs for both 1E and 1Z, R = Me, and this complicates the estimation of this rate. In fact it becomes difficult to rationalize bent cations at all, since they should lead to net retention. When R= 3P, no inversion is observed, which was taken to indicate that product acetates 9 arose from cation 2. The probable error of ± 0.05 in the r(E/Z) ratio observed in this case again yields an equilibration rate of $>5 \times 10^{10}$ sec^{-1} when the steady-state treatment (10) is applied, a slight improvement over the earlier estimate. Within the detectable limits, the rate of equilibration of bent cations appears to approach the rate of a molecular vibration ($\sim 10^{13}$). Of course, in order to have detected the higher limit from differences in the r(E/Z) ratios, these ratios (for R = 3P)would have to be known to within ± 0.0003 or an error less than 0.007% !

The fact that net inversion is observed in all vinyl iodide systems examined cannot be reconciled easily with the notion of bent cations, rapidly equilibrating or otherwise. Intervention of ion-pairs becomes a less attractive solution, since the electrostatic attraction between the cation and the counterion should stabilize the bent configuration, i.e. the inversion barrier should be much higher in the ion-pairs

than for the "free" cations. Solvent attack on such ion-pairs with inversion of geometry should be quite difficult, particularly for 19e.



19e

Although we cannot completely rule out the possibility of rapidly equilibrating bent vinyl cations from this type of study, we do know that the cation behaves as if it were linear in solvolytic reactions. Furthermore, calculations (see Part II) and independent experiments (12) have shown that bent cations are energetically unfavorable. The evidence appears conclusive that the vinyl cation is sp-hybridized when not deformed by inherent structural demands.

The Steric and Electronic Effects of R

We have looked extensively at the similarities exhibited by the reactions of 1 when R = Me, Cp, and 3P, or rather, the similarity in differences in the reactions of the Z and E isomers of 1. In our examination of r(E/Z) and r(A/S) we have noted and discussed the trends as R is changed. Now we shall look further at some overall trends in these solvolyses as R is modified.

1) Effects on the Reaction Rates

In Table I the measured pseudo first-order rate constants are given for the reactions of 1 and 4 with excess silver acetate in acetic acid. The detailed plots are given in Appendix B. Linearity is generally quite good. These are rough data taken at room temperature

$(24 \pm 1^{\circ})$ and further complicated by heterogeneous reactions for some of the isomers (see above). The differences in behavior appear to be great enough to allow some contrasts to be made, however.

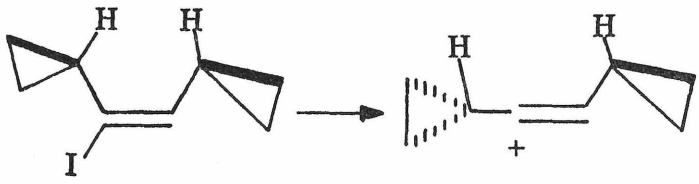
The Z isomer of 1 reacts faster in each case. In the R = Me case, this behavior was explained in terms of (a) the greater accessibility of silver species to the iodide in the E isomer and (b) ground-state destabilization of the E isomer because of steric interaction between cyclopropyl and methyl substituents (10). The estimated thermodynamic equilibrium constant K_{eq} = 1Z/1E = ca. 10 supported the second reason. The first reason is equivalent to saying that steric interaction between the silver species and substituent R destabilizes the transition state for the Z isomer relative to that for the E isomer.

The same reasons qualitatively apply to the other cases. With R = Cp, the k_e/k_z ratio increases to ca. 13 , and with R = 3P it reaches ca. 34 . As the bulk of R increases and amplifies the steric crowding, ground-state destabilization of 1E relative to 1Z should also increase. Hence, k_e/k_z should increase. Ground-state destabilization appears to be an important factor in the reactivities of 1.

Comparisons between the relative rates themselves are a little more risky than camparing the k_e/k_z ratios, since there is no direct means of comparing the ground states or transition states when R is changed, e.g. 1E with R = Me, Cp, and 3P. Note in particular that 1Z, R = Me, and 1Z, R = 3P, react at almost the same rate. Solely in terms of reason (a) above, the rate for 1Z, R = 3P, should be slower. However, if the cation formed from 1Z is more stable when

R = 3P than when R = Me, then to the extent that cation stability influences the activation barrier, there may be energetic compensation for the supposed steric destabilization. Conversely, the ground state stabilities of the iodides themselves may be such that 1Z, R = 3P, is less stable than 1Z, R = Me . Even though the transition-state is energetically less favorable for R = 3P, the ground-state destabilization compensates for this , and the activation barrier is similar to that experienced by 1Z, R = Me. The duality of these "explanations" points out the lack of proper reference points.

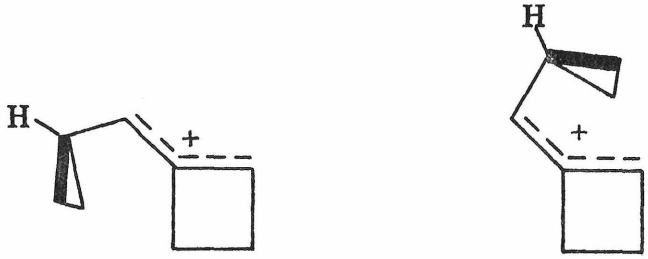
It is rather interesting that both 1Z and 1E are the least reactive when R = Cp compared to the corresponding isomers with R = Me or R = 3P. The rates for each isomer are slower by a factor of 2 - 3 compared to the R = Me isomer pair. Even though the factor is small (in terms of usual rate effects which are considered "significant"), the fact that both isomers are affected suggests that the effect is an electronic one superimposed on existing steric effects. One explanation for the slower rates is that the ground states of both isomers are stabilized by "conjugation" (36) of the cyclopropyl rings through the double bond. In the transition-states, where the cyclopropyl ring at the incipient cationic center may have rotated by nearly 90^{o} to help stabilize the developing charge (see Part II), this conjugation is partially lost. The idea is somewhat attractive, but it is rather difficult to see how the required orientation of the cyclopropyl rings for "conjugation" can be achieved in the crowded E isomer. We shall arrive at a simpler explanation for this rate behavior shortly.



2) Effects on the Product Distributions

We have already discussed the trends observed for r(E/Z) in terms of steric effects on the trapping of the vinyl cation 2, and we compared the r(A/S) ratios for R = 3P to R = Me in terms of steric effects, too. These data, along with r(V/B) and r(X/N), are summarized in Table IX.

Before discussing the r(V/B) and r(X/N) data, we note that r(A/S) for R = Cp is higher than that for R = Me. On the basis of the steric factors alone, the argument presented earlier for the R = 3P case would predict that for R = Cp r(A/S) should be between one and three. However, the cyclopropyl group may not be of the "critical size" to strongly influence r(A/S) sterically. It is quite possible that r(A/S) is influenced by electronic effects of R, particularly when R = Cp. In their nmr study of 3-cycloproplyallyl cations, Sorensen and Rajeswari (37) suggested that "trans" conjugation of cyclopropyl with the allyl cation may be more effective electronically than "cis" conjugation.



18a (R = Cp) 18s

In our case, this implies greater stability for 18a than for 18s.

Table IX. Product Ratios from the Reactions of Vinyl Iodides (1) as a function of Substituent R and Various Sigma-constants for R. [a]

R	r(E/Z)	r(V/B)	r(A/S)	r(X/N)	σ_p [d]	σ_p^+ [d]	σ_m^+ [d]	σ^* [e]
H [b]		>45		9	0.0	0.0	0.0	0.0
3P [c]	4.3	10	1	>20	-0.15	-0.27	-0.060	-0.13
Me	1	4	3	3	-0.17	-0.31	-0.066	-0.10
Cp	1.3	1	4.5	0.6	-0.24 [f]	-0.44 [g]	-0.041 [h]	

[a] Approximate ratios based on values for E and Z isomers (see Tables III, V, and VII). [b] Ratios from ref. 17. [c] Sigma parameters taken equal to those for isopropyl; σ_p^+ reduced by 0.01. [d] Values from ref. 38 except as noted. [e] Ref. 39, p. 38. [f] Ref. 40(d). [g] Average of values in ref. 40(a) and 40(b). [h] Ref. 40(a).

To the extent that this "extra" stabilization is felt in the transition state leading from 2 (or 6e) to 18a, it may dominate over any steric effects that may favor 18s. Hence, r(A/S) is larger in this case. Since the conjugative ability of cyclopropyl is rather special when compared to "normal" alkyl groups, this effect on the r(A/S) ratio should be much less important for methyl or 3-pentyl substituents. This explanation also requires that the orthogonality between the developing "empty" p orbital and the π system (see above), i.e. the "buckled" transition-state and cation leading to 18a or 18s, is relaxed to a sufficient degree to allow conjugation.

Now we focus our molecular microscope on the r(V/B) and r(X/N) ratios. These ratios were not discussed in developing the ion-pair scheme nor in discussing the heterogeneous reactions because there was no clear dependence of these ratios on the geometry of the vinyl iodides or on the reaction conditions. Furthermore, these ratios are more subject to error, since each involves sums of product percentages. For comparing the behavior of r(V/B) and r(X/N) as R is changed, rather than when E changes to Z, the differences are large enough to be useful and quite interesting.

The r(V/B) ratio falls off dramatically as R changes from H to Cp (45 to 1, Table IX). Our theoretical studies (Part II) indicate that the positive charge at the vinyl cation carbon is reduced when methyl replaces hydrogen, R, in the cyclopropyl-stabilized vinyl cation, 2. This suggests that the "remote" cyclopropyl ring, R = Cp,

may also stabilize the cation. Let us suppose then that 2, R = Cp, is stabilized relative to 2, R = Me or H, even though there are no theoretical calculations to support this contention. With this order of cation stabilities, are the r(V/B) ratios explained?

They are if bond reorganization of 2 to give cations 18a and 18s is a sufficiently activated process compared to solvent trapping of 2 to vinyl acetates. If cation 2, R = H, is relatively unstable, solvent trapping predominates, but as the cation stability improves the solvent trapping step will experience a higher activation barrier. The activation barrier for cyclopropyl bond reorganization may not be affected to the same extent, since the effects that stabilize 2 may also stabilize the transition-state leading to 18a and 18s to approximately the same extent. Thus, bond reorganization becomes competitive with solvent trapping and relatively more cyclobutyl products are formed -- the r(V/B) ratio decreases.

Table IX includes various Hammett substituent parameters (38-40). (The larger the negative value of σ, the better the electron releasing ability of R (38, 39).) While σ^* and σ_m^+ clearly show the "wrong" trend compared to r(V/B), the σ_p^+ and σ_p constants have the "correct" ordering. This invites a comparison of r(V/B) data to σ_p^+ or σ_p in terms of the familiar Hammett relationship, eq. (7) (39). In the present situation, the reactions that form the

$$\log(k/k_o) = \sigma\rho \qquad (7)$$

vinyl acetates and the cyclobutyl-type acetates can be summarized as in eq. (8). This is clearly an oversimplification of the situation,

since both k_b and k_v are sums of rates and ion-pairs are ignored.

$$\underset{\sim}{9} \xleftarrow{k_v} \underset{\sim}{2} \xrightarrow{k_b} \underset{\sim}{10} + \underset{\sim}{11} \qquad (8)$$

It is useful, nevertheless. The ratio k_v/k_b is simply r(V/B). If we take R = H as our reference system, then

$$r_R/r_H = r(V/B)_R/r(V/B)_H = (k_v/k_b)_R/(k_v/k_b)_H = \frac{k_{vR}}{k_{vH}} \cdot \frac{k_{bH}}{k_{bR}} \qquad (9)$$

and

$$\log(r_R/r_H) = \sigma\rho$$

where $\sigma = 0.0$ for R = H. In terms of the argument given above to explain the trends in r(V/B), we have assumed that $k_{bH}/k_{bR} = 1$. Therefore,

$$\log(r_R/r_H) = \log(k_{vR}/k_{vH}) = \sigma\rho \qquad (10)$$

or more conveniently, since r_H is the largest value,

$$\log(r_H/r_R) = -\sigma\rho \qquad (11)$$

The plots of $\log(r_H/r_R)$ *vs.* σ_p and σ_p^+, eq. (11), are given in Figure 1. The points for R = 3P fall a little off the lines drawn, but the remaining three points correlate remarkably well. The ρ values from the slopes are positive, which means the reaction, k_v, is less favored as R becomes a better electron-releasing substituent. (This was built into the equation by our assumptions.)

The Hammett correlation with σ_p^+ and σ_p raises some interest-

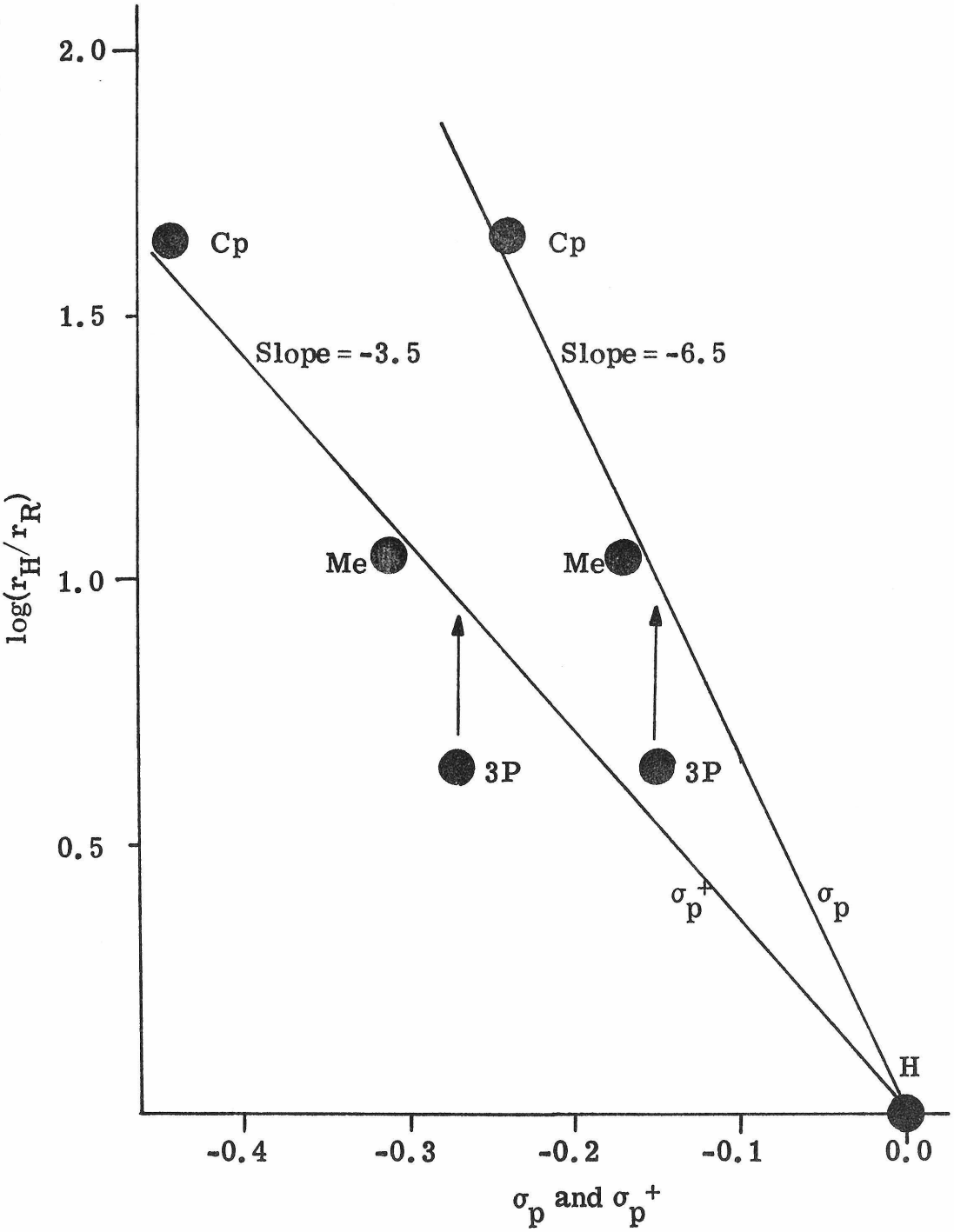
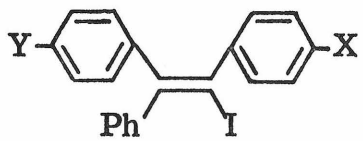


Figure 1. Hammett Plot Relating r(V/B) to σ_p^+ and σ_p for Various Substituents R (see text).

ing questions. The σ_p and σ_p^+ values are considered qualitatively to be "resonance" or conjugative parameters, whereas σ_m^+, for instance, is qualitatively an inductive parameter(38, 39). This, of course, derives from the special properties of the benzene aromatic system. The fact that r(V/B) appears to correlate with such conjugation parameters implies that the stabilization of the vinyl cation by R is also conjugative, in the present interpretation, rather than inductive.

This produces a conflict. First, it is intuitively not clear how the remote cyclopropyl group, or any group, can conjugate with the vinyl cation. Conjugation of cyclopropyl with the double bond may be easy, but the cationic orbital is clearly orthogonal to the π system. One can visualize some rehybridization at the β vinylic carbon, as would be the case in a hydrogen-bridged species (see Section B), to provide a conjugative link. Or one might presume a polarization of the π bond puts partial positive charge at the β carbon (9). This latter view could be construed as an indirect conjugation, of sorts.

Second, Miller and Kaufmann (9) have shown that <u>para</u>-substituents Y, specifically methoxy, in triarylvinyl iodides, 20, have little



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effect upon the solvolysis rates of these compounds (through vinyl cations). They concluded that conjugative stabilization in the β position, direct or indirect, can have little importance.

Third, the concept that 2, R = Cp, is relatively stabilized compared to the other vinyl cations makes our previous explanation for the low reactivity of these vinyl iodides, R = Cp, rather unattractive. One would predict on this basis alone that 1, R = Cp, should react faster than 1, R = Me, for both E and Z isomers.

The dilemma we have reached can be resolved by abandoning the idea that 2, R = Cp in particular, is specially stabilized by R. The correlation between $\log(r_R/r_H)$ and the sigma constants remains, of course, but an entirely different -- and consistent -- assessment of this relationship is obtained. Our first hypothesis led to the approximation that $k_{bH}/k_{bR} = 1$. Now we shall let $k_{vR}/k_{vH} = 1$ to a first approximation. This then implies from eq. (9) that

$$\log(r_R/r_H) = \log(k_{bH}/k_{bR}) = -\sigma\rho \qquad (12)$$

or

$$\log(r_H/r_R) = \log(k_{bR}/k_{bH}) = \sigma\rho \qquad (13)$$

where 'minus' has been removed in eq. (13), since the ratio on the left is now in correct form (compare eq. (10) and eq. (11)).

The assumption leading to eq. (13) is equivalent to the following hypothesis: The vinyl cation 2 does not vary greatly in stability as substituent R changes, hence trapping of the cation by solvent, k_v, is nearly the same in each case. This is consistent with our view (see above) that trapping ought to be nearly diffusion controlled. The rearrangement of 2 to the cyclobutyl-type allyl cations, 18a and 18s, is governed largely by the stability of the generated cation. To the extent that substituent R stabilizes the transition-state leading to re-

arranged cations, then the rearrangement, k_b, will become competitive with solvent capture of 2. The rearrangement transition -state and the initial rearranged cation may still be considered to be "buckled" (see above), but there is no longer a demand that it involve strict orthogonality, which was also relaxed in our discussion of the r(A/Z) ratio when R = Cp. To the extent that orthogonality is reduced, at least partial conjugation of R with the incipient allyl cation can occur. (Note that the ρ values are now negative, as required by this explanation.)

We must now reconsider the effect of substituent R on the stability of cation 2. If conjugation of R with the vinyl cation is poor, what should we expect for inductive effects , which can presumably be operative? In terms of σ_m^+ values (Table IX) methyl and 3-pentyl are expected to be rather similar inductively and perhaps cyclopropyl is slightly less electron releasing inductively. This agrees with the report of Brown and Cleveland (41) which showed that a p-cyclopropyl increases the solvolysis rate of cumyl chloride ($C_6H_5C(CH_3)_2Cl$) by a factor of 157. However, when methyl groups were placed on the benzene ring ortho to the cyclopropyl (which prevents proper orientation of the cyclopropyl ring for conjugation), the rate enhancement dropped to a factor of 9, which is even less than the rate enhancement of 18 observed for a p-isopropyl group. This implies that cyclopropyl is not as effective inductively as isopropyl (41), or in the present situation, as 3-pentyl.

We now have the proper background to explain qualitatively the solvolysis rates of 1, particularly when R = Cp. Vinyl iodides 1Z

with R = Me and R = 3P solvolyze at about the same rate (Table I) as expected on the basis of the σ_m^+ values. The rate for 1Z, R = Cp, is slower. This is quite consistent with the smaller σ_m^+ value (less negative; less electron-releasing) and the inductive effect noted by Brown and Cleveland (41) for cyclopropyl compared to isopropyl. The rate for 1E, R = Cp, is also slower than that for 1E, R = Me, even though steric crowding in the ground state is certainly higher (k_e/k_z increases). This fits in nicely with the sterically-independent inductive effects of substituent R, in contrast to the ground state "conjugation" we discussed above in regard to the solvolysis rates of 1, R = Cp.

(In an aliphatic system, the Taft σ^* constants are often used (39). There does not appear to be a report of this constant for the cyclopropyl group. The pK_a of cyclopropylacetic acid in water at 25° would give an estimation of this constant, but apparently this measurement has not been done as far as we can determine. The σ_I and σ_R^o values have been reported (42) for cyclopropyl, but since these parameters also refer to effects on a benzene nucleus, it is not clear that they would be any more valuable or reliable in the present case than σ_m^+ values.)

To sum up the advantages of our explanation: (a) It explains the trend in the r(V/B) ratios in terms of the electronic effects of R. (b) It explains why the solvolysis of 1, R = Cp, is qualitatively slow. (c) It explains why the "resonance" or conjugative parameters σ_p and σ_p^+ correlate with r(V/B). (d) One does not require conjugation of R with the vinyl cation center, in agreement with the assessment of

Miller and Kaufman (9), but conjugation with an incipient allyl cation.

In connection with point (c), the σ_p or σ_p^+ parameters have been used for non-benzenoid compounds, notably the substituted α,β - unsaturated acids and esters (43). We have not been able to locate any report where such parameters have been used to correlate substituent effects in an aliphatic carbonium ion rearrangement where the substituent "changes" its mode of interactive stabilization from a predominately inductive one to a predominately conjugative one.

The trend in the r(X/N) values (Table IX) is similar to the ordering of r(V/B). This may reflect the electronic effects of R on the charge distribution in the allyl cations, 18a and 18s. When R = 3P, r(X/N) does not fit in with the trend established by the other two cases. The large value for r(X/N), certainly >20, clearly suggests a great deal of steric hindrance for capture of ions 18a and 18s to give acetate 11. We had also noted above that steric effects of the 3-pentyl group may affect the r(A/S) ratio. It would not be unreasonable to assume that, in addition to the electronic effects of 3-pentyl, the steric effect of this substituent increases the r(V/B) ratio by slowing k_b in this case relative to k_b for the other cases. Assuming that the estimates for σ_p^+ and σ_p are reasonably correct for R = 3P, then the "true" r(V/B) ratio in the absence of steric effects of 3-pentyl will be <10. In Figure 1 verticle arrows are shown connecting the R = 3P points to the lines. The "corrected" value of r(V/B) is then estimated to be ca. 5, a rather substantial reduction. Certainly this separation of electronic and steric effects is rather crude, considering the approximations in the data used for Figure 1. Yet it agrees with

the much larger steric effect on r(X/N) and our arguments concerning the low r(A/S) ratio observed when R = 3P.

Conclusions

There are several interesting and important results of this work which we feel strengthen our understanding of vinyl cation chemistry and silver-assisted ionizations:

(a) We have shown that heterogeneous silver catalysis can occur for sterically accessible vinyl iodides and that heterogeneous reactions can be blocked by added salts. This should further amplify the caution one should use when dealing with reactions involving silver catalysis.

(b) We have found that net overall inversion of geometry obtains for three different E-Z pairs of vinyl iodides. That net inversion occurs for each E and Z isomer has been shown in the R = Me case and strongly implied in the R = 3P case (with added NaOAc).

(c) We have found that the proportions of syn and anti substituted 2-methylenecyclobutyl acetates, 10A and 10S, depend upon the initial vinyl iodide geometry.

(d) Both the results in (b) and (c), as well as vinyl iodide isomerization, are accommodated by intervention of ion-pair intermediates.

(e) Our results are entirely consistent with a vinyl cation structure that is sp-hybridized (linear).

(f) We have evidence that the electron-releasing ability of substituent R strongly affects the rates of cyclopropyl ring-opening

rearrangements of our vinyl cations.

(g) Steric effects of substituent R have been implicated in the relative rates of ionization of the vinyl iodides; in the trapping of the vinyl cations and their ion-pairs to give vinyl acetates; in the rearrangement of the vinyl cation when R = 3P (r(V/B) and r(A/S)); in the lack of ion-pair effects in the absence of added sodium acetate when R = 3P; and in the trapping of allyl cations 18 when R = 3P.

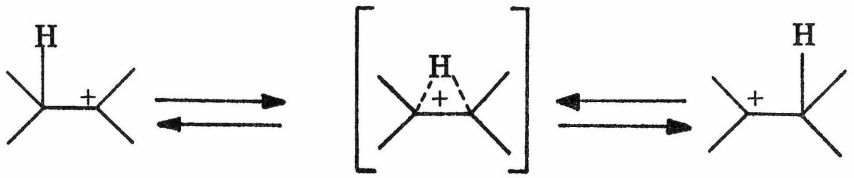
(h) Electronic effects of substituent R have been implicated, in addition to (f) above, in the ionization rates of the vinyl iodides, particularly when R = Cp ; in the favored formation of allyl cation 18a over 18s when R = Cp; and in the electronic charge distribution in the allyl cations 18 (r(X/N)).

Section B.

Background

Experimental

For many years rearrangements of groups adjacent to a carbonium ion center have received a great deal of study (44). In particular, the 1,2 - hydride shift, eq. (14), intrigued early investigators because of the possibility that the bridged ion 21 might be a stable



(14)

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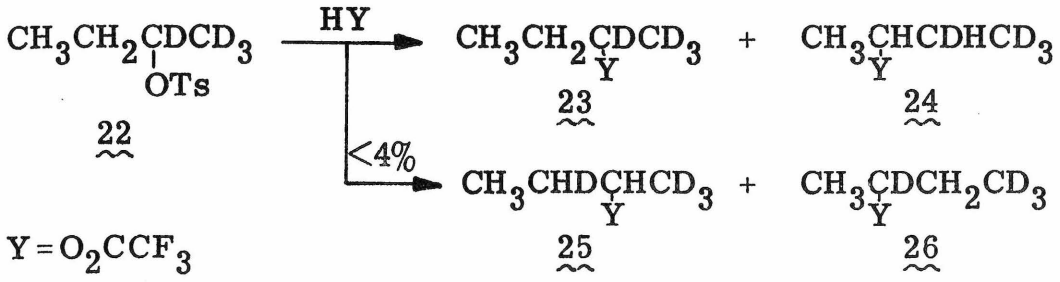
intermediate. Roberts and Yancy found only 1.5% rearrangement in the aqueous deamination of C^{14} labled ethylamine, but the rapid trapping of the cation by solvent probably accounted for the low extent of rearrangement (45). Roberts and coworkers found up to 9% rearrangement in the acetolysis of C^{14} labled 2-butyl tosylate and concluded that this low value was not consistent with a stabilized bridged ion (46).

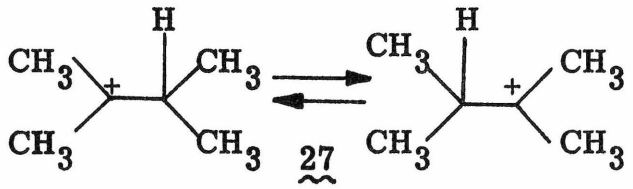
Myhre and Evans (47) studied the reactions of deuterated ethyl tosylates in fluorosulfonic acid. They postulated that ca. 42% of the products arose from a bridged ion, but their results do not, in fact, demand such an intermediate. Recently, a report appeared which claims that the hydrogen-bridged 2-butyl cation is the major inter-

mediate in the trifluoroacetolysis of 22 (48). Only products 23 and



24 were observed (1.08 : 1.00) by nmr with <4% of 25 or 26. However, when one takes into account that ca. 24% of the products may have been formed by an elimination - addition pathway (48), and that there must be a reasonably large isotope effect for deuteride migration, it is not entirely clear that rapidly equilibrating 2-butyl cations cannot explain the data. In any event, the extent of rearrangement is great.

Direct nmr observations of degenerate aliphatic cations in "magic acid" solutions (e.g. $FSO_3H - SbF_5 - SO_2ClF$, etc.) allow perhaps less equivical conclusions. Both the proton (49) and C^{13} (50) spectra of dimethylisopropylcarbonium ion 27 are consistent with rapidly



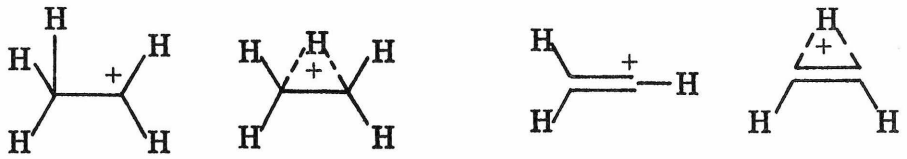
27

equilibrating ions rather than a bridged cation (49, 50). Even at -112^{o} C the cyclopentyl cation shows only a single proton absorption which indicates that very rapid 1,2 (?) shifts occur to give a five-fold degenerate cation (50, 51). The 2-butyl cation undergoes degenerate

rearrangement at a rate $>10^5$ sec^{-1} at -112° C, and the observed spectrum is consistent with equilibrating cations (52). Of course, one must consider the danger in extrapolating these results to "normal" solvents. However, the nmr evidence together with the solvolysis data give little support to the idea that the bridged cation 21 is a stabilized intermediate rather than a transition-state point of the reaction coordinate.

Theoretical

Ab initio SCF calculations have been done on both the ethyl and vinyl cations. It is found that bridged 29 is less stable than the classical ion 28 by ca. 7 - 12 kcal/mole (53a-c). The calculations also



28 29 30 31

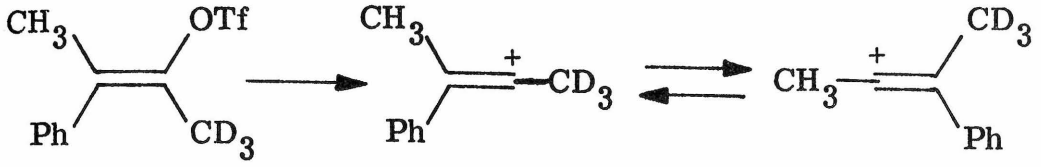
indicate that 29 is a transition state and not a stable species (53a, 53b). Semiempirical calculations give the opposite results, but this is believed to be an artifact of the approximations (53d).

The ab initio results for the vinyl cation show that 31 is less stable than 30 by 18.5 (53e) to 25 kcal/mole (53d). The calculations predict that the hydride shift should be less favorable for vinyl cations than for alkyl cations. Since the nmr studies (see above) indicate activation energies of ca. 8 kcal/mole or less in the alkyl cases, it would still seem likely that hydride shifts could be observed in vinyl cations under solvolytic conditions.

Vinyl Cation Rearrangements

Rearrangements across the double bond in vinyl cations have been observed for the thiophenyl and phenyl substituents. The thiophenyl group represents a special case (54), and phenyl migrations (55) have generally been observed only for cases where the rearranged cation is more stable than the original cation, e.g. eq. (15) (55c). Recently,

(15)



(16)

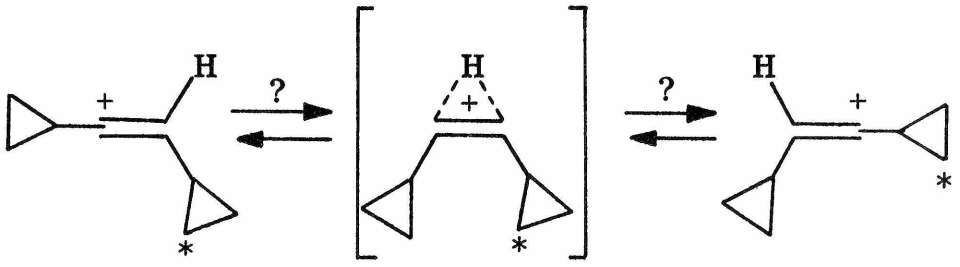
Stang and Deuber (55b) obtained evidence for the degenerate phenyl rearrangement, eq. (16). Rearrangement was more extensive when the phenyl group was <u>trans</u> to the triflate group, from which the authors inferred participation of the phenyl substituent in the ionization process (55b). No degenerate methyl rearrangement was detected in the solvolysis of labled 3-methyl-2-butenyl triflate, $(CH_3)_2C{=}C(CD_3)OTf$ (55a).

The only reports of hydride shifts across the double bond of a vinyl cation are the studies of the addition of adamantyl cation to acetylene in concentrated sulfuric acid (56). However, the existence of discrete vinyl cations has not been adequately established under these conditions.

The 1,2-hydride shift in vinyl cations would appear to be favored by two conditions inherent in the system: (1) the shorter C=C bond could facilitate overlap of the "empty" p orbital with the β C-H bond compared to alkyl cations and (2) the geometry is "frozen" so that the interacting orbitals are coplanar. The importance of coplanar orientation of a neighboring hydrogen relative to the cationic center was discussed in a classic paper by Winstein and Holness (57). Detailed invistigation of β-deuterium isotope effects have likewise shown that interaction is facilitated by coplanar geometry (58). Stang and coworkers found large β-deuterium isotope effects in vinyl cation reactions and attributed this to the favorable geometry for interaction (59).

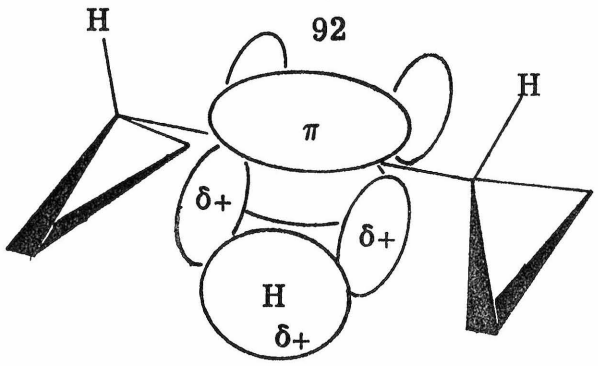
The Problem

In order to determine whether 1,2-hydride shifts might be an important reaction in cyclopropyl-stabilized vinyl cations, we chose to study the 1,2-dicyclopropylvinyl cation, 32, which can undergo a degenerate hydride shift. This system possesses the favorable



32 33 32*

geometric constraints discussed above and also could potentially stabilize the bridged species 33. A linear "protonated acetylene" representation of 33 below shows two "partial" vinyl cations, one at



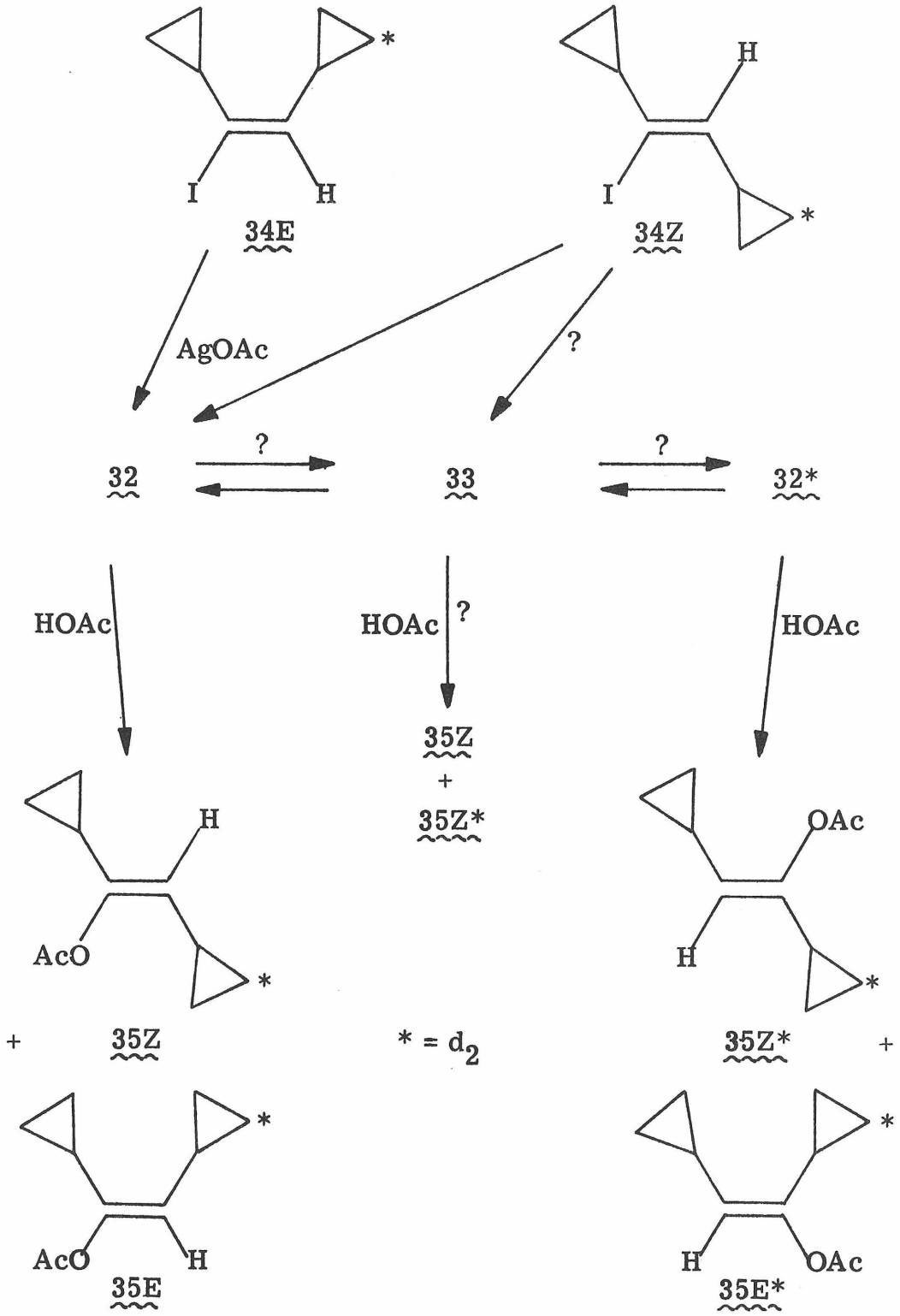
33

each vinyl carbon. Only one cyclopropyl ring can participate to any great extent in stabilization of cation 32 (see also Section A), whereas in 33 the delocalization of charge could conceivably involve the second cyclopropyl ring as well. It is therefore reasonable, a priori, that a bridged species could be involved as an intermediate in this case. Clearly neither the work in alphatic carbonium ions nor the theoretical calculations (see above) would be of any great help in assessing the relative stabilities of 32 and 33, although our results in Section A suggest that 33 cannot be a major species.

Method

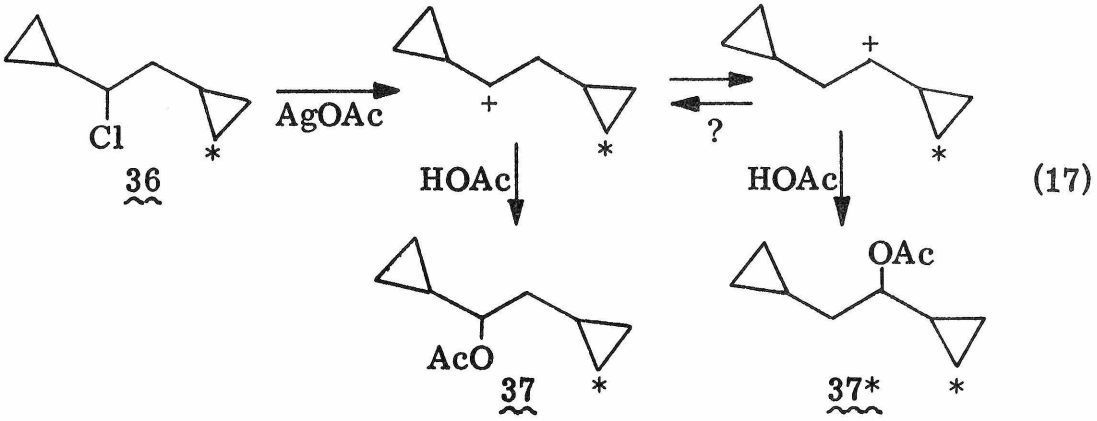
The following scheme (Scheme VII) shows the results expected if degenerate hydride shift occurred in the silver-catalyzed solvolysis or E- or Z-1,2-dicyclopropyl-1-iodoethylene, 34, in which the remote cyclopropyl ring is labled with deuterium. If hydride shift occurs, then rearranged products 35* should be observed along with vinyl acetates 35. If bridged ion 33 were an intermediate, then the rearranged vinyl acetates could be richer in 35Z* than in 35E* because of preferential solvent attack on 33 opposite from the hydrogen

Scheme VII.


*
I
H
34E
H
I
*
34Z
AgOAc
?
?
32
?
33
?
32*
HOAc
HOAc
?
HOAc
35Z
+
35Z*
H
AcO
*
OAc
H
*
+
35Z
* = d2
35Z*
+
*
AcO
H
35E
*
H
OAc
35E*

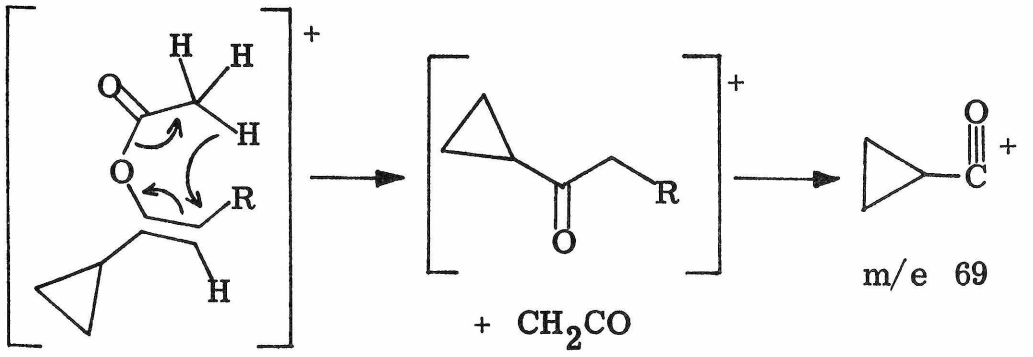
bridge. As also shown, one might expect that 33 could form preferentially from 34Z by backside trans participation by the β hydrogen during ionization.

For comparison, we studied the saturated chloride 36, eq. (17).



(17)

The detection of rearrangement by mass spectroscopy was based upon the very predominate m/e = 69 in the spectra of the various R-substituted cyclopropylvinyl acetates and their corresponding ketones used in Section A. For the ketones, this peak is expected (60) to be the cyclopropyl acylium ion. The vinyl acetates can also produce this peak by the rearrangement shown in eq. (18). It was



(18)

also observed that the isotopic peaks at m/e = 70 and 71 agree within experimental error with the theoretical values (60) for $C_4H_5O^+$ (see below). Fortunately there were no other peaks in this region that

could obscure these three peaks. Thus, if rearrangement of the vinyl cation occurred through a 1,2-hydride shift, deuterium lable originally residing in the remote cyclopropyl ring should show up in the mass spectrum as enhanced m/e = 70 or 71 peaks.

The spectra were obtained with a quadrupole mass spectrometer coupled to the outlet of a gas chromatograph (vpc-ms). An ionization energy of 70 volts was used rather than low voltages since the latter did not appear to appreciably affect the extent of the fragmentation to m/e = 69 and because it seemed unlikely that scrambling of the lable could occur in the ionization itself. This is supported by the fact that the 69 - 71 region in the deuterated control samples were unchanged (see below). The vpc columns used were an 1/8" packed DEGS or the 300' x 0.03" ID open-tubular column coated with TCEP. At least three (usually six) spectra were obtained for each vpc peak. (It was necessary to take all spectra before the eluting peak reached its maximum height. When spectra were taken as the peak height was declining, the variations in the mass spectrum peak ratios increased. This behavior might have been due to some inefficiences in the mass spectrometer's vacuum system.)

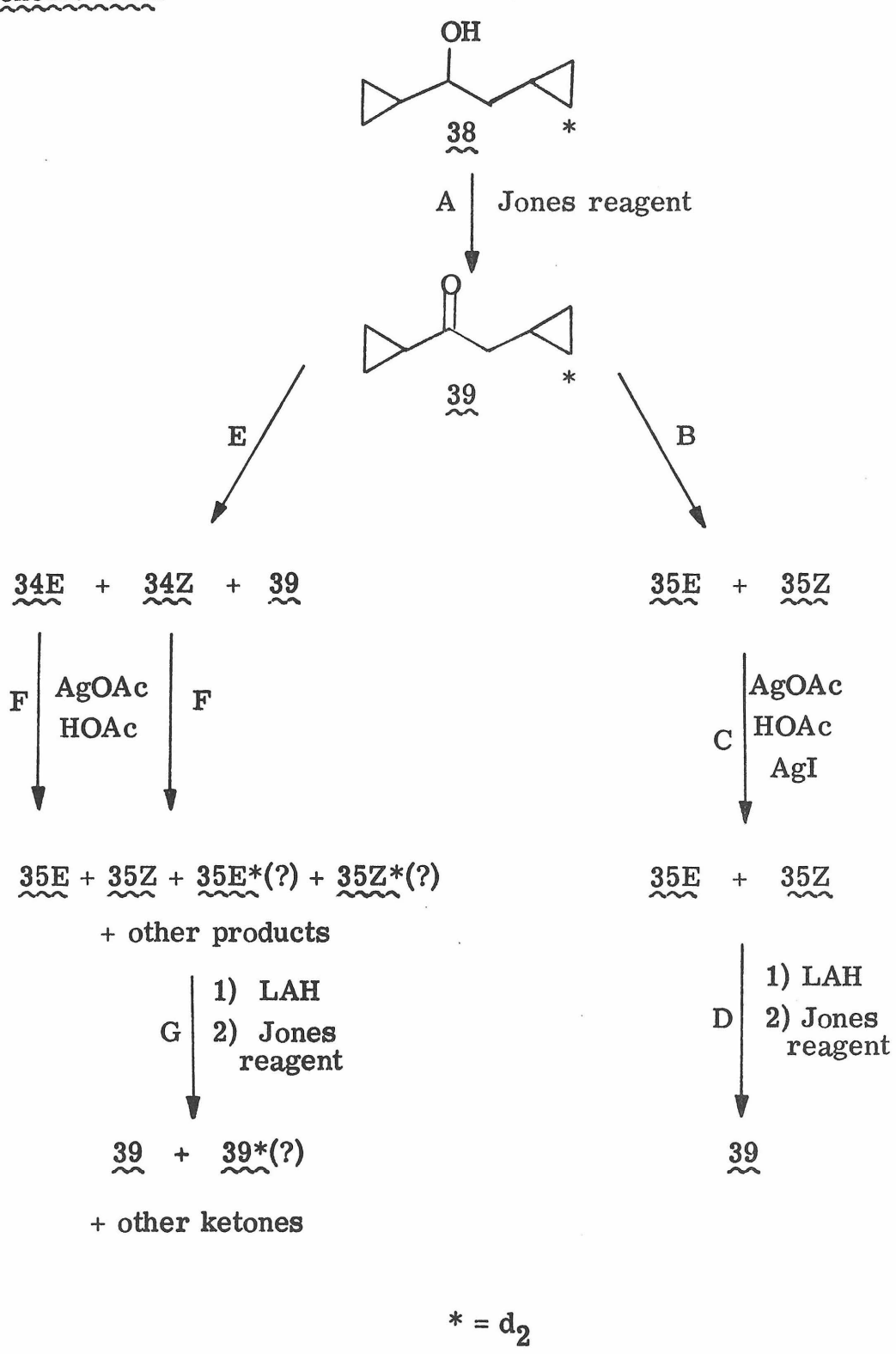
The deuterated iodides were prepared according to Scheme II in Section A using deuterated methylene iodide in the Simmons -Smith reaction. The deuterated methylene iodide was prepared by exchange with D_2O (61). Quantitative nmr showed the isotopic substitution to be 89 mole % d_2 and 11 % d_1; mass spectral data showed minimum 91 %-d_2 (see Experimental section). The ir spectrum of the ketone obtained after the Jones oxidation (Scheme II) showed

the expected weak C-D strech absorptions at 2317 and 2205 cm^{-1}, and the mass spectrum parent peaks (weak) of the ketone showed ca. 90%-d_2 and 10%-d_1. The method of synthesis and the data given below require the deuterium be located in the "remote" cyclopropyl ring. The ketone was converted to vinyl iodides (Scheme II) and to vinyl acetates (Experimental and Scheme VIII).

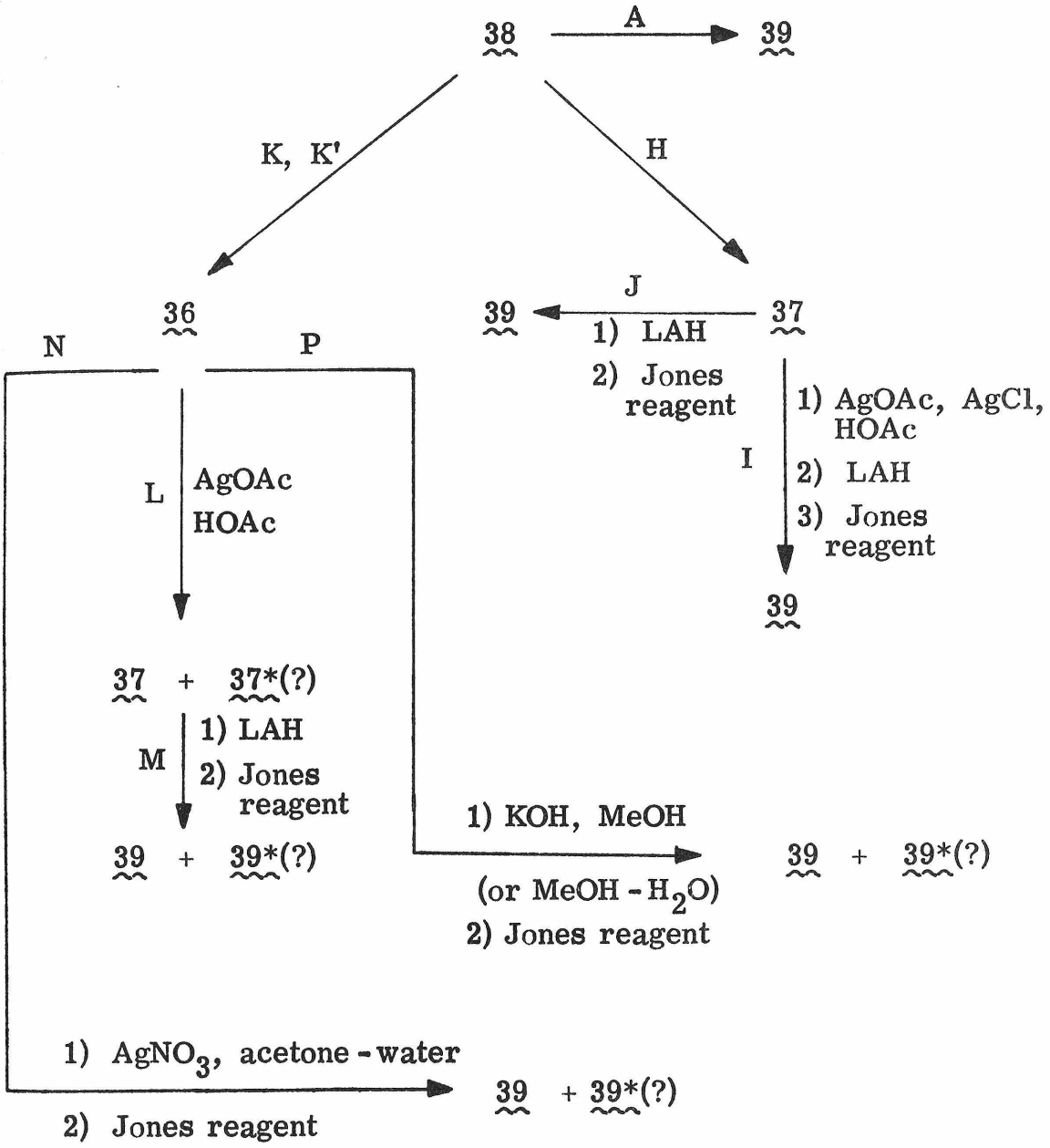
The various reactions and controls are summarized in Scheme VIII. Path A shows Jones oxidation of the alcohol 38 to ketone 39. Path B shows the synthesis of the vinyl acetates (Experimental), and treatment, path C, under the solvolysis conditions. Subsequent reduction of the (unchanged) acetates with LAH gave a mixture of ketone 39 and alcohol 38 (14:86); the alcohol was oxidized to 39 with Jones reagent, path D. Path E is the synthesis of the vinyl iodides (Section A) in which some unreacted ketone was recovered. Treatment of each isomer, path F, with silver acetate in acetic acid gave the product mixtures observed in Section A. Reduction, then oxidation, converted the acetates to ketones, path G (see Experimental).

The reactions and controls for the saturated system are shown in Scheme IX. The alcohol 38 was converted to acetate 37 (see Experimental), path H, which was then converted to ketone 39 as shown with, path I, or without, path J, subjection of the acetate to the solvolysis conditions. The labled chloride 36 was prepared by treatment of the alcohol in chloroform with thionyl chloride. Two different preparations of 36 were done under slightly different reaction conditions, paths K and K' (see Experimental). The chloride was obtained in 91% yield and could be purified by vpc if special precautions were

Scheme VIII.

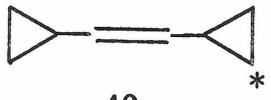

OH
38
*
A
Jones reagent
O
39
*
E
B
34E + 34Z + 39
35E + 35Z
F
AgOAc
HOAc
F
C
AgOAc
HOAc
AgI
35E + 35Z + 35E*(?) + 35Z*(?)
+ other products
35E + 35Z
G
1) LAH
2) Jones reagent
D
1) LAH
2) Jones reagent
39 + 39*(?)
+ other ketones
39
* = d2

Scheme IX.

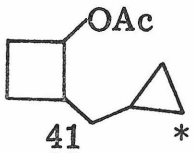

38
A
39
K, K'
H
36
39
J
37
1) LAH
2) Jones reagent
N
P
1) AgOAc, AgCl, HOAc
I
2) LAH
3) Jones reagent
L
AgOAc
HOAc
39
37 + 37*(?)
M
1) LAH
2) Jones reagent
39 + 39*(?)
1) KOH, MeOH
(or MeOH - H_2O)
2) Jones reagent
39 + 39*(?)
1) $AgNO_3$, acetone - water
2) Jones reagent
39 + 39*(?)

taken (see Experimental).

Treatment of the chloride with silver acetate in acetic acid gave acetate 37, path L. Less than 8% possible rearranged acetates were observed by vpc. A small peak having a very short vpc retention time was assumed to be the elimination product 40, but it was not isolated.



40



41

Undeuterated 40 (cis-trans mixture), prepared by reduction of undeuterated vinyl iodides 34 with tri-n-butyltin hydride (see Experimental), did not react under the solvolysis conditions. The product mixture from path L was treated with LAH and then with Jones reagent to give ketone 39, path M. Paths K, L, and M were also carried out using undeuterated alcohol to establish product identities. The mass spectrum of the undeuterated ketone obtained in this sequence of reactions showed no extraneous peaks, which indicated no "hidden" rearrangement products, e.g. 41. Path N shows the reaction of chloride 36 with silver nitrate in acetone-water and subsequent conversion of the product to ketone 39. Path P shows the reaction of the chloride with potassium hydroxide in methanol or methanol-water followed by oxidation of the alcohol product to ketone.

Results

The vpc-ms data for the vinyl acetates 35E and 35Z obtained from the reactions of vinyl iodides 34E and 34Z with silver acetate

in acetic acid, along with the control experiments, are given in Table X. It is not clear why the m/e 70 and 71 peaks for the deuterated compounds are consistently higher than for the undeuterated acetates (see below). The important comparison is between paths B (control) and F. Within experimental error no excess m/e 71 peak is observed for either acetate isomer formed from either iodide isomer.

The results for the ketones obtained from the reduction, then oxidation,treatment of the vinyl acetates are shown in Table XI. Now the differences noted between undeuterated and deuterated species in data of Table X have largely disappeared. Note that within ± 0.1, the ketone produced through the solvolysis route (path G) shows no spectral differences from that produced via control path D or from undeuterated ketone. Thus, the data of Table X are confirmed, i.e. no rearrangement ($< 0.2\%$) is observed.

The mass spectral results for the ketones obtained in the saturated system are given in Table XII. The control reactions show that no scrambling of lable has occurred during the reactions with LAH or Jones reagent (runs 2 - 5). The data clearly indicate that the m/e 71 peak has increased for paths M, M', N and P. Our initial data without path M' would have led to the conclusion that rearrangement had occurred were it not for the missing control -- showing the lack of scrambling in the synthesis of the chloride, path K. It was also very curious that virtually the same values were obtained from paths N and P, where one might expect rearrangement to be suppressed due to the increased nucleophilicity of the reaction medium (62) or possible S_N2 reactions (path P).

Table X. Mass Spectral Data of the E- and Z-1-Acetoxy-1, 2= dicyclopropylethylenes (35). [a]

Source[b]	Acetate isomer	m/e 70[c]	m/e 71[c]
d_o	E	6.57 ± 0.62	1.56 ± 0.10
d_o	Z	5.74 ± 0.14	1.00 ± 0.07
B[d]	E	10.37 ± 0.24	4.02 ± 0.15
B[d]	Z	10.58 ± 0.48	4.26 ± 0.34
F(E)	E	10.60 ± 0.34	3.92 ± 0.36
F(E)	Z	9.95 ± 0.25	3.42 ± 0.22
F(Z)	E	11.50 ± 0.70	4.58 ± 0.70
F(Z)	Z	10.87 ± 0.02	4.40 ± 0.27

[a] Vpc-ms obtained with the 300' open-tubular column, TCEP phase. [b] Capital letters refer to path in Scheme VIII; (Z) and (E) refer to vinyl iodide 34 isomers; d_o refers to undeuterated acetate. [c] Values shown are peak heights as a percentage of the m/e 69 peak heights; errors are average deviations observed for three to six spectra. [d] Data for path C, Scheme VIII, similar.

Table XI. Mass Spectral Data for 1,2-Dicyclopropylethanone (39) Obtained from Various Reaction Pathways in Scheme VIII.[a]

Source[b]	m/e 70[c]	m/e 71[c]
d_o	4.67 ± 0.04	0.41 ± 0.06
A	4.58 ± 0.37	0.58 ± 0.05
E	4.77 ± 0.05	0.67 ± 0.02
G	4.81 ± 0.06	0.57 ± 0.04
D	4.67 ± 0.12	0.51 ± 0.02

[a] Vpc-ms obtained with packed DEGS column (1/8"). [b] Capital letters refer to paths in Scheme VIII; d_o refers to undeuterated ketone. [c] Values shown are peak heights as a percentage of the m/e 69 peaks; errors are average deviations observed for three to six spectra.

Table XII. Mass Spectral Data for 1,2-Dicyclopropylethanone (39) Obtained from Various Reaction Pathways in Scheme IX.[a]

Run	Source[b]	m/e 70[c]	m/e 71[c]
1	d_o[d]	4.67 ± 0.04	0.41 ± 0.06
2	A	4.58 ± 0.37	0.58 ± 0.05
3	A	4.70 ± 0.05	0.50 ± 0.06
4	I	4.81 ± 0.18	0.55 ± 0.05
5	J	4.70 ± 0.06	0.50 ± 0.03
6	M[e]	4.72 ± 0.12	1.86 ± 0.09
7	M[f]	4.78 ± 0.07	1.76 ± 0.05
8	M[g]	4.83 ± 0.18	1.73 ± 0.03
9	M'[h]	4.73 ± 0.14	1.07 ± 0.03
10	N	4.73 ± 0.10	1.74 ± 0.05
11	P[i]	4.73 ± 0.15	1.79 ± 0.07
12	P[j]	4.36 ± 0.38	1.78 ± 0.07

[a] Vpc-ms obtained with packed DEGS column (1/8"). [b] Capital letters refer to paths in Scheme IX; d_o refers to undeuterated ketone. [c] Peak heights as percent of m/e 69. [d] Theoretical values for $C_4H_5O^+$ are 4.44 % and 0.28%. [e] Chloride 36 from path K; solvolysis time 1.5 hr. [f] Chloride 36 from path K; solvolysis time 15 min. [g] Chloride 36 from path K; solvolysis time 2.5 hr. [h] Chloride 36 from path K'. [i] 30% KOH in MeOH; 45 min. solvolysis time. [j] KOH in 2:1 water-methanol (see Experimental).

Reaction of another sample of chloride 36 prepared under slightly different conditions, gave less rearrangement (run 9, path M'). This confirmed the idea that most, if not all, of the observed rearrangement was due to isomerization during preparation or purification of the chloride (63). In any case, we know that solvolysis of chloride 36 occurs with, at most, 1% rearrangement by hydride shift. In view of the similar data obtained under very nucleophilic conditions (paths N and P), it is likely that the extent of hydride shift is much less than 1%.

It is perhaps fortunate that rearrangement during path K did occur. We note that although the m/e 71 peak increased from ca. 0.5% to ca. 1.75%, the m/e 70 peak did not change within experimental error (4.7 ± 0.2%). This is exactly the behavior one would expect for the 90% - d_2 labled substrate. The expected increase in m/e 70 from the remaining 10% - d_1 is ~0.1%, which is within the error limits. This does lend some support to the analytical method used here for the detection of rearrangement.

Discussion

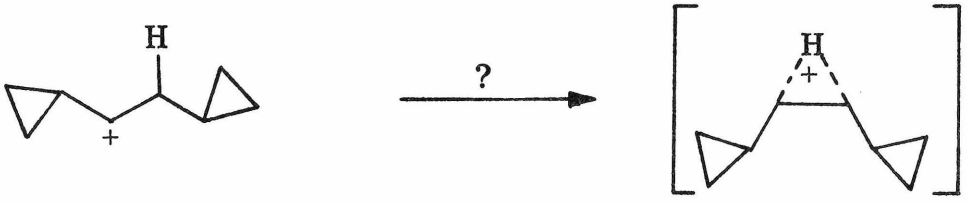
The data shows quite conclusively that, in spite the favorable geometry and possible stabilization of the transition state 33, hydride migration does not occur ($<0.2\%$) in the 1,2-dicyclopropylvinyl cation 32 under our conditions. Furthermore, the saturated system shows little or no rearrangement (<1%) either.

There are a number of competing processes which occur for cation 32, most notably solvent or ion-pair trapping and rearrange-

ment by cyclopropyl ring-opening, as discussed in Section A. We know that the cation undergoes this latter reaction to greater than 50% (based on acetate products). It is not unreasonable then that solvent trapping and C-C bond reorganization may present lower energy pathways than does hydride shift.

It is more difficult to explain the lack of hydride shift in the 1,2-dicyclopropylethyl cation, 42. This cation should be relatively more stable than the vinyl cation in acetic acid, hence hydride shift should be more competitive with solvent trapping. Furthermore, very little formation of possible rearrangement products (<5%) was observed; apparently cyclopropyl ring opening is also less competitive. It seems unlikely that the hydride shift is prevented because of solvent participation in the ionization of the chloride in silver acetate - acetic acid. Such participation should be minimal for the secondary cyclopropylcarbinyl cation system (64), particularly in the presence of silver catalyst.

It seems we must examine the hydride shift solely in terms of the relative stabilities of the cation 42 and transition state 43 compared

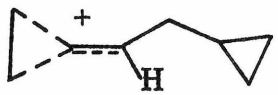


42 43

to the relative stabilities of the corresponding states of the ethyl cation system or the 2-butyl cation system, where at least some hydride shift is observed (see above). The obvious rationale is to presume

that the bridged ion 43 is stabilized by the cyclopropyl groups compared to the 2-butyl bridged ion, but that the cation 42 is stabilized even more. It is somewhat remarkable, however, that such an effect would prevent hydride shifts altogether during the lifetime of the cation.

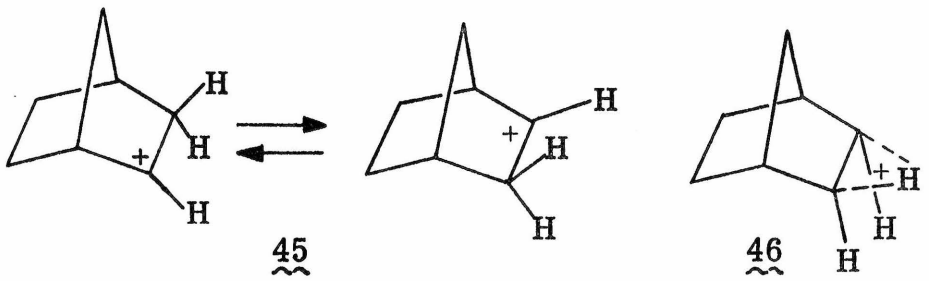
Perhaps, though, the answer rests upon the nature of the cyclopropyl ring stabilization of the cationic center. Even though the delocalization may not approach that of the primary cyclopropylcarbinyl cation (65), as evidenced by the lack of rearranged products observed here and in other cases (66), it certainly may be " σ-delocalized" enough, e.g. 44, to preclude hydride shift . In going to bridged ion 43, such delocalization stability may be largely lost. Another way of looking at the same thing is to presume that the charge at the cationic



44

center is very much reduced through interaction with the near cyclopropyl ring. The β hydrogen "sees" little charge at the α carbon and little interaction develops between the β C - H bond and the cationic center. No hydride shift can occur.

Similar arguments have been proposed by Olah and coworkers (67) to account for the much slower 3,2-hydride shift in the norbornyl cation 45 (shown as a localized cation) compared to the rate of hydride shift in the cyclopentyl cation. The non-classical delocalization of 45 is presumable lost upon forming the hydrogen-bridged transition state 46 (67). By comparison to the norbornyl system, the lack of hydride shift in cation 42 is still somewhat remarkable.



45 46

This " σ-delocalization hindrance" of 1,2-hydride shifts should also apply to the cyclopropyl-stabilized vinyl cation system as well and may be another factor, along with the competitive reactions, for the lack of hydride shifts in this system. If this is indeed true, then it implies that partial participation, i.e. hyperconjugation, by the hydrogens in the cyclopropylvinyl iodide ionizations should be less than in ionizations of "normal" vinyl cation precursors, i.e. where the group attached to the vinyl cation center is an alkyl group and not phenyl or cyclopropyl. Since Stang and coworkers (59) have found a relatively large vinyl β-deuterium isotope effect in such "normal" vinyl cation systems, it would be interesting to measure the β isotope effect in cyclopropyl-stabilized systems, e.g. iodide 1, Section A, with vinyl H replaced by D. The isotope effect could be substantially smaller in this case.

Experimental

General Methods. All boiling and melting points are uncorrected. Infrared spectra (ir) were routinely obtained from CCl_4 solutions in microcavity cells (Barnes Engineering Co., Stamford, Conn.) on a Perkin-Elmer IR-257 (grating) instrument and using polystyrene film standard. Spectra are reported in cm^{-1} and qualitative indications of the relative peak intensities and types are given: v = very, w = weak, m = medium, s = strong, d = doublet, b = broad, sh = shoulder. Routine nuclear magnetic resonance spectra (nmr) were obtained on 10% solutions in CCl_4 with tetramethylsilane (TMS) internal standard with a Varian A-60A or occasionally with a Varian T-60. Some spectra were obtained for <1% solutions on a Varian HR-220 spectrometer. Nmr spectra are reported as: chemical shift (in δ); multiplicity, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; splitting (in Hz); integration in units of H; peak assignment. Mass spectra (vpc-ms) were taken on a spectrometer-vpc system consisting of a Hewlett-Packard 7620A gas chromatograph (thermoconductivity detector, TC) coupled to an EAI (Electronic Associates, Inc.) Quad-300 quadrupole mass spectrometer. The chromatograph injector and detector temperatures were 200° and the mass spectrometer manifolds were at 220-250°. An ionization current of 100 or 200 μA and an ionization potential of 70 V were used. The vpc-ms data are reported as: m/e (% of main peak, assignment). In general, our quadrupole spectra showed more fragmentation than did spectra obtained on the CEC-21-103C instrument (10), which made

detection of parent peaks difficult in some cases. Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. 48106. Preparative and rough analytical gas chromotagraphy (glc or vpc) were done on a Varian Aerograph A90-P3 (TC) with the injector at 200°, the detector at 200°, and the helium carrier flow at 60 ml/min, unless otherwise stated. Analytical vpc was done on a Hewlett-Packard 5750 (flame ionization) connected to a Hewlett-Packard 3370A electronic integrator. Gas pressures used were He, 33; H_2, 12; air, 25 (lb/in^2). Carrier gas flow for 1/8" columns was generally 30-60 ml/min; for open-tubular columns, 5-10 ml/min. A table of the various vpc columns has been given (10). The following additional columns were used (1/4" used on Aerograph, others on Hewlett-Packard): C-4, 10'x1/4" 20% Carbowax 20M on Chromosorb P, stainless steel (ss); C-5, 5'x1/4" 10% Carbowax 20M on Chromosorb P, ss; D-3, 12'x1/8" 15% DEGS on Cromosorb W-AW-DMCS, ss; F-1, 7'x1/4" 8% FFAP on Chromosorb P, ss; S-4, 10'x1/8" 20% SE30 on Chromosorb P, ss; SF-1, 20'x1/4" 10% SF96 on Chromosorb W-AW-DMCS, aluminum; T-3, 20'x1/4" 10% TCEP on Chromosorb W-AW-DMCS, aluminum; U-3, 10'x1/4" 20% UCCW982 on Chromosorb P, glass; 300'TCEP, 300'x0.03" ID open-tubular ss column coated with TCEP; 300'SF96, same coated with SF96. (Note: The retention time and resolution characteristics of the open-tubular columns varied somewhat with successive recoatings and age of the coating. When retention times were being compared, care was taken to perform the analyses with a well-equilibrated column in one sitting and to recheck the retention times with a standard solution (usually a solvolysis mix-

ture) periodically.)

Materials. The sources of several chemicals and the purifications of triethylamine, tetrahydrofuran (THF), dimethyl sulfoxide (DMSO), and acetic acid have been given (10). The following lists addition sources: Columbia Organic Chemicals, deuterium oxide (99.8%); Allied Chemical, cuprous chloride (reagent, 98% minimum), acetone (reagent), silver nitrate (reagent); Matheson Coleman and Bell, isopropenyl acetate (practical), azirane, allyl bromide, methylene iodide, triphenylphosphine, CCl_4 (spectroscopic grade), $CHCl_3$ (spectroscopic grade), silver acetate (99.5%); Calbiochem, 2-ethylbutanol; Mallinckrodt, zinc dust (reagent, 95% minimum). Dr. Paul Condit of these laboratories provided the tri-n-butyltin hydride. Ethyl ether was distilled from lithium aluminum hydride (LAH) before use. Pyridine (reagent grade) was dried over Linde type A4 molecular sieves.

Cyclopropanecarbonyl Chloride. The preparation of the acid chloride from cyclopropylcarboxylic acid followed that previously reported (10). The yields were generally 75 - 90 %. Ir: 3105w, 3030m, 1780s, 1455m, 1430m, 1367s, 1209m, 1169s, 1120w, 1078m, 1053s, 978vs, 883s, 861w, 707s.

E- and Z-1-Cyclopropyl-1-iodopropene, 1E and 1Z, R = Me. The preparative procedure and vpc purification of these vinyl iodides has been reported (10). There was a typographical error in the reported elemental analyses. Anal. Calcd for 1, R = Me: C, 34.64; H, 4.36; I, 61.00. Found 1Z, R = Me: C, 34.78; H, 4.23; I, 61.15. Found 1E, R = Me: C, 34.47; H, 4.36; I, 61.35. Ir 1Z, R = Me: 3100m, 3023s, 2935m, 2875w, 1646wd, 1435m, 1385m,1361m, 1285s, 1219sh, 1205s, 1179sh, 1169s, 1112s, 1061m, 1035s, 1012m, 945s, 904m, 864m, 850s. Ir 1E, R = Me: 3100m, 3020s, 2930s, 2875m, 1624m, 1455md, 1431m, 1373w, 1311m, 1212w, 1155s, 1102w, 1063m, 1037s, 990s, 945s, 895w, 859s, 655w. Vpc-ms (column D-3) 1Z, R = Me: 209(.2026, P+1), 208(3.137, P), 128(3.33, HI^+), 127 (4.98, I^+), 83 (.26, P-I+2), 82(7.22, P-I+1), 81(100, P-I), 79(44.84), 77(11.53), 55 (10.85), 53 (64.44), 52(11.24), 51(15.88), 50(11.08), 41(50.07), 39 (31.37), 27(30.60). Vpc-ms (column D-3) 1E, R = Me: 209(.2267, P+1), 208(3.30, P), 128(4.50, HI^+), 127(6.00, I^+), 83(0.22, P-I+2), 82(7.33, P-I+1), 81(100.0, P-I), 79(50.00), 77(13.63), 55(11.50), 53 (69.33), 52(12.20), 51(19.17), 50(12.50), 41(54.00), 39(37.35), 27 (34.33).

E- and Z-1-Acetoxy-1-cyclopropylpropene, 3E and 3Z (9E and 9Z, R = Me). The vinyl acetates were prepared by acid-catalyzed

exchange of isopropenyl acetate (68) with cyclopropyl ethyl ketone (10). The ketone (2.5 gm, 25 mmol), a large excess of isopropenyl acetate (ca. 30 ml), and a catalytic amount (ca. 0.05 gm) of p-toluenesulfonic acid monohydrate were placed in a 100 ml flask fitted with a distillation head and condenser, and magnetic stir bar and heated in an oil bath at 110 - 118° so as to cause slow distillation of isopropenyl acetate. Additional isopropenyl acetate was added as needed. After three days, the oil bath was raised to 130° and the volatile material was distilled off. The residue was dissolved in ether, washed with water, sodium bicarbonate soln, and sat sodium chloride soln, and dried over anhyd sodium sulfate. After removal of the ether on the rotary evaporator, the resulting liquid was vacuum transferred (10 - 1 mm Hg) to give the acetates (2.2 gm) in 45% yield, 74% pure by vpc (column D-3, 160°). The E and Z isomers were obtained pure by preparative vpc (column D-2, 110°). Anal. Calcd for 3 (9, R = Me): C, 68.54; H, 8.63. Found for 3E (9E, R = Me): C, 68.10; H, 8.46. Found for 3Z (9Z, R = Me): C, 68.13; H, 8.55. Ir 3E (9E, R = Me): 3100w, 3025m, 2950sh, 2935m, 2880w, 1760sb, 1682m, 1434w, 1374s, 1309w, 1230s, 1207s, 1192s, 1110wsh, 1061s, 1073sh, 1034m, 996m, 922m, 898m. Ir 3Z (9Z, R = Me): 3100m, 3060w, 3025m, 2955sh, 2935m, 2880w, 1755vs, 1693m, 1452m, 1436m, 1375s, 1317w, 1230vs, 1205s, 1190sh, 1170s, 1127m, 1050s, 1030s, 995m, 942w, 920w, 888m, 656w. The nmr spectra were identical to those of the previously isolated acetates (10). (Ref. 10 contains two typographical errors in the nmr spectrum for 3E (9E, R = Me). The cyclopropyl ring methine hydrogen absorbs at 1.66 δ and the vinyl methyl

at 1.75 δ instead of at 1.42 δ and 1.51δ as reported.) Vpc-ms (300'TCEP, 60°) 3E (9E, R = Me): 140(2.17, P), 98 (36.62, P - CH_2CO), 83 (30.69), 79 (11.86), 69 (68.97, $C_4H_5O^+$), 56 (59.86), 55 (23.66), 43 (100.0, CH_3CO^+), 41 (37.66), 39 (26.48), 28 (33.66), 27 (18.07). Vpc-ms (300'TCEP, 60°) 3Z (9Z, M = Me): 140 (2.20, P), 98 (39.03, P - CH_2CO), 83 (31.42, 98 - CH_3), 79 (11.49), 69 (72.39, 98 - Et), 56 (61.72), 55 (24.63), 43 (100.0, CH_3CO^+), 41 (37.3), 39 (27.16), 28 (34.25), 27 (18.66).

1-Iodo-3,4-hexadiene, 4. The preparation, vpc isolation, and spectra of this iodide were previously given (10). Vpc-ms (column D-3, 130°): 208 (.1362, P), 128 (3.16, HI^+), 127 (4.40, I^+), 83 (0.24, P-I+2), 82 (7.14, P-I+1), 81 (100.0, P-I), 79 (21.25), 77 (8.31), 53 (44.56), 51 (13.91), 41 (42.78), 39 (24.66), 27 (27.25). Anal. Calcd for 4: C, 34.64; H, 4.36; I, 61.00. Found: C, 34.72; H, 4.27; I, 61.06.

Cyclopropylcarboxaldehyde. An initial preparation of this aldehyde from the acid chloride by the procedure reported by Brown and Tsukamoto (14) gave only 27% yield. The following modified procedure gave better results for us. A 1000 ml 3-necked flask fitted with a Trubor (R) mechanical stirrer (Teflon blade), a side-arm addition funnel, and nitrogen bubbler was flamed under nitrogen flow and then cooled to -70° in a Dry Ice - isopropyl alcohol bath. Azirane (11.1 gm, 258 mmol), triethylame (26.3 gm, 260 mmol, purified), and 300 ml dry ethyl ether were added to the flask, and the solution was cooled to -70° under nitrogen. Fresh cyclopropanecarbonyl chloride (26.1 gm, 250 mmol) in 100 ml dry ether was added

slowly to the reaction mixture (1 hr) at a bath temperature maintained at -75°. The reaction mixture was then stirred at -60° for 0.5 hr and then allowed to warm to room temperature. The white $Et_3N \cdot HCl$ ppt was removed by filtering the reaction mixture (sintered glass) and washed with 4 x 200 ml dry ether. The clear filtrate and washings were quickly returned to a 2000 ml flask fitted as before and the contents cooled to -60°. A slurry of lithium aluminum hydride, LAH, (2.75 gm, 72.4 mmol) in 200 ml ether, which had refluxed for 0.5 hr, was added in small portions to the reaction solution over a period of 1 hr. During this time the cooling bath temperature was allowed to warm slowly to -10°. Vpc (column D-2, 150°, 85 ml/min) of a hydrolyzed aliquot showed the reaction complete. The intermediate and excess LAH were hydrolyzed with sat sodium sulfate soln, anhyd sodium sulfate was added to the flask, the ether soln was decanted from the white ppt, and the ppt was washed thoroughly with ether. The combined ether solns were washed with sat sodium chloride soln and dried over anhyd sodium sulfate. The ether solvent was removed by gentle distillation (30 cm Vigreau + 10 cm glass helices), and the residue was distilled (10 cm Vigreau + 5 cm glass helices) to give (96 - 100°) 10.7 gm, 59% yield, of 96% pure (vpc, column D-3, 120°) aldehyde; 2,4-dinitrophenylhydrazone derivative (ethyl acetate) m.p. 185.5 - 186.5 (lit (69) 186 - 187.5). The ir and nmr spectra were in accord with the structure.

(This procedure gave 60% yields on two different occasions. When the amount of LAH was increased to 125 mmol, the yield dropped to 40% and cyclopropylcarbinol was formed as a major impurity. For

as yet unknown reasons, some later attempts to repeat the synthesis yielded a high boiling, foul-smelling material (not characterized) instead of aldehyde. This may have been due to the use of different batches of reactants, but it was not determined which one was the culprit.)

1-Cyclopropyl-3-buten-1-ol. The preparation of the Grignard reagent from allyl bromide followed easily available procedures (70). Excess Mg turnings (28.5 gm, 1.17 mol) was placed in a 2000 ml 3-necked flask fitted with a mechanical stirrer, side-arm addition funnel, condenser, and nitrogen bubbler and flamed and cooled under nitrogen flow. Dry ether (400 ml) was added and the flask was cooled in an ice bath. A small crystal of iodine was added, then allyl bromide (40.5 gm, .335 mol) in 120 ml dry ether was added to the stirred soln over 1.5 hr. After the addition was complete, the reaction mixture was stirred for .25 hr and then allowed to warm to room temperature. The Gilman test for Grignard reagent was strongly positive. Cyclopropylcarboxaldehyde (95% pure, 12.0 gm, .163 mol) in 160 ml of ether was added to the reaction mixture over 1 hr. After the first 15 min of addition, the reaction flask was heated gently on the steam bath. Heating was continued for 1 hr after the end of the addition and stirring was continued for .5 hr while the reaction mixture cooled to room temperature. The reaction mixture was poured into ice water slush, and this soln was adjusted to pH 4 with 1N sulfuric acid. The ether layer was decanted off, and the water layer was saturated with sodium chloride and then extracted with ether. The combined ether solns were washed three times with

sat sodium chloride soln and dried over anhyd sodium sulfate.

After removal of the ether on the rotary evaporator, the product was obtained by short-path distillation at 65 - 67° (19 mm Hg), 17.3 gm, 96% pure by vpc (column U-1, 90°, or column D-3, 130°), 91% yield. Yields of three runs varied from 87 to 96%. A pure analytical sample was obtained by preparative vpc (column D-2, 130°). Anal. Calcd: C, 74.95; H, 10.78. Found: C, 75.18; H, 10.72. Ir: 3605m, 3410sb, 3090s, 3008s, 2982sh, 2933sh, 2910m,2870m, 1641s, 1433s, 1415mb, 1338w, 1265mb, 1223wb, 1145wb, 1082sh, 1060sh, 1045s, 1023s, 996s, 946sh, 914s, 867w, 852sh. Nmr: 5.91, X of ABX vinyl group, 1H; 5.13 and 4.94, A and B of ABX, 2H; 2.95, q, J=6.3, 1H (integrated with alcohol proton), methine at hydroxyl; 2.65, broad s, 1H, alcohol proton; 2.27, finely split t, J= 6.4, J= ca. 1, 2H, methylene; 0.5 - 1.2, m, 1H, cyclopropyl methine; 0.1 - 0.5, m, 4H, cyclopropyl methylenes. (Double irradiation spectra obtained on a Varian T60 showed the expected changes when various protons were decoupled.)

1,2-Dicyclopropylethanol. The Rawson-Harrison (15a) modification of the Simmons-Smith (15b) reaction was used. Zinc dust (8.2 gm, 120 mmol), cuprous chloride (13.2 gm, 120 mmol) and 40 ml dry ether were placed in a 200 ml 3-necked flask fitted with a mechanical stirrer, reflux condenser, and nitrogen bubbler. The mixture was stirred and refluxed under nitrogen for 1.5 hr and then 1-cyclopropyl-3-buten-1-ol (96% pure, 3.34 gm, 28.6 mmol) was added followed by addition of methylene iodide (16.2 gm, 0.4 mmol). The reaction mixture was heated in an oil bath maintained at 50 - 60 ° for 18 hr,

and then cooled in an ice bath. After careful hydrolysis with a sat ammonium chloride soln , the reaction mixture was extracted with several portions of ether. The combined ether solns were washed with water , sat sodium chloride soln , and dried over anhyd sodium sulfate. After removal of the ether on the rotary evaporator, the residue was bulb-to-bulb distilled (1 - 5 mm Hg, oil bath at 50 - 70°) to give 2.87 gm product, 84% pure by vpc (column D-3, 130°), 67 % yield. An analytical sample was obtained by preparative vpc (column D-2, 160°, 40 ml/min). Anal. Calcd: C, 76.14; H 11.18. Found: C, 75.97; H, 11.10. Ir: 3602m, ca. 3410 mb, 3077s, 3002s, 2910s, 2870m, 1465m, 1431m, 1413m, 1293w, 1268wb, 1230wb, 1171w, 1060sh, 1045sh, 1017s, 975sh, 962m, 943sh, 917m, 901w. Nmr: 2.95, q, J=6 (slight additional splitting), 1H, methine at alcohol carbon; 1.98, broad s, 1H, alcohol proton; 1.42, two slightly overlapping t, J = 6-7, 2H, methylene; 0.1 - 1.2, complex m, 10H, cyclopropyls.

1,2-Dicyclopropylethanone(7). Jones reagent (16) was prepared by dissolving 7 gm chromic oxide in 50 ml water, cooling , and adding 6.3 ml conc sulfuric acid (dropwise!). The soln is ca. 1.25 M in reagent. 1,2-Dicyclopropylethanol (7.37 gm, 76% pure, 44.6 mmol) in 200 ml reagent acetone was placed in a 500 ml flask fitted with a magnetic stir bar and thermometer and cooled to 10° in an ice bath. Jones reagent (47 ml, 58 mmol) was added over 20 min during which the reaction soln was kept at 10 - 15°. After an additional 15 min of stirring, 5 ml methanol was added to consume the excess reagent and the reaction mixture was stirred for another 1 hr. The blue-green ppt

was dissolved by adding water, the flask contents was transferred to a separatory funnel, the water layer was saturated with sodium chloride, and the mixture was thoroughly extracted with ether. The combined ether extracts were washed with sat sodium chloride soln twice and dried over anhyd magnesium sulfate. After removal of the ether and acetone on the rotary evaporator, the residue was bulb-to-bulb distilled at 2 - 10 mm Hg (oil bath at 60 - 70°) to give 6.28 gm product, 82% pure by vpc (column D-3, 150°), 93% yield.

Modified work-up: After the excess reagent was consumed with methanol and the blue-green ppt had formed, the reaction soln was decanted off, and the ppt was stirred with 2 or 3 portions of ether. These ether solns were added to the decanted reaction soln and the soln was dried over anhyd sodium sulfate. The ether and acetone were then removed on the rotary evaporator. The blue-green ppt was dissolved in water along with the sodium sulfate used to dry the ether-acetone soln. The evaporation residue was added , and the mixture was extracted twice with ether. The combined ether extracts were then washed with sat sodium bicarbonate soln and sat sodium chloride soln and dried over anhyd sodium sulfate plus anhyd magnesium sulfate. After removal of ether on the rotary evaporator, the residue was then distilled. When this work-up was used, the product yields from the oxidation were generally better than 98%. The work-up removes the troublesome acetone before any washing is done.

Anal. Calcd: C, 77.38; H, 9.74. Found: C, 77.19; H, 9.69.
Ir: 3080m, 3010s, 2950w, 2885m, 1700vs, 1460sh, 1449m, 1416w,

1410w, 1390s, 1382s, 1275w, 1230w, 1201sh, 1192m, 1172m, 1159m, 1134m, 1100w, 1085sh, 1070s, 1046sh, 1042m, 1019s, 980m, 892m. Nmr: 2.36, d, J = 6.5, 2H methylene; ca. 1.9, m, cyclopropyl methine nearest carbonyl; 1.3 - 0.0, complex m, ca. 9H, cyclopropyl. The ir and nmr spectra agreed with the published data (71). Vpc-ms (column D-3, 150°): 125 (.0675, P+1), 124 (.5917, P), 123 (.136, P-1), 69 (100.0, $C_4H_5O^+$), 55 (12.13), 41 (48.11), 39 (21.12), 29 (7.93), 27 (10.36). The analytical sample was obtained by preparative vpc (column D-2, 140°).

E- and Z-1,2-Dicyclopropyl-1-iodoethylene, 1E and 1Z, R = Cp. The hydrazone of 1,2-dicyclopropylethanone was prepared (10) and used immediately in the vinyl iodide synthesis. (Ir of the hydrazone ($CHCl_3$) showed peaks at 1625, hydrazone, at 1698, ketone, and at ca. 1733, probably azine.) Attempts to prepare the vinyl iodides from the hydrazone by the previous procedures (10, 17, 18) gave very poor yields. When the reaction was carried out under nitrogen, no vinyl iodides were obtained. The following procedure, however, gave reasonably good results.

The crude hydrazone (prepared from 1.7 gm ketone, 82% pure, 11 mmol), 70 ml triethylamine, and 50 ml dry THF were placed in a 3-necked flask fitted with a side-arm addition funnel, a magnetic stir bar, a vent tube from one neck leading to the hood exhaust, and a 4-5 mm diam glass tube fitted in a side neck which was connected to house air (filtered). The reaction mixture was stirred and aerated at room temperature while iodine (5.5 gm, 21.7 mmol) in 40 ml THF was added fairly rapidly. Decolorization during the addition was

excellent, and the final mixture was yellowish-orange. The reaction mixture was stirred for another 40 min and worked up as before (10). After removal of the solvent ether and bulb-to-bulb distillation of the residue at 1 mm Hg, the distillate was stirred for 30 min at 55° with 3 ml triethylamine. This soln was cooled, the amine removed on the rotary evaporator, and the residue washed into another flask with a little ether. Vacuum transfer gave 1.72 gm product, 77% pure by vpc (column D-2, 120°), 51% yield based on ketone. The isolated yields after vpc purification (column D-2) were generally 24 - 38%. Anal. Calcd for 1, R = Cp: C, 41.05; H, 4.73; I, 54.21. Found 1E, R = Cp: C, 40.87; H, 4.62; I, 54.16. Found 1Z, R = Cp: C, 41.08; H, 4.65; I, 54.22. Ir 1E, R = Cp: 3087s, 3010s, 1612vw, 1456w, 1430sh, 1426m, 1386w, 1349w, 1294m, 1183m, 1120m, 1093w, 1052s, 1026s, 970s, 945s, 897m, 887m, 876sh, 822w, 673m. Ir 1Z, R = Cp: 3086s, 3008s, 1641vw , 1455w, 1429m, 1423sh, 1378w, 1349w, 1262s, 1191s, 1172s, 1120w, 1096w, 1050s, 1025s, 988s, 952s, 906w, 891w. Nmr (220 MHz) 1E, R = Cp: 5.48, d of d, J = 9.5 and 1.2, 1H, vinyl; 1.77, complex m, 1H, cyclopropyl methine; 1.47, complex m, 1H cyclopropyl methine; 1.05 - 0.35, complex m, 8H, cyclopropyl methylenes. Nmr (220 MHz) 1Z, R = Cp: 4.92, d, J = 8.8, 1H, vinyl; 1.59, complex m, 2H, cyclopropyl methines; 0.90 - 0.35, complex m, 8H, cyclopropyl methylenes. Vpc-ms (column D-3, 130 - 150°) 1Z, R = Cp: 235 (.1598, P+1), 234 (1.77, P), 128 (3.00, HI^+), 127 (3.64, I^+), 108 (0.66, P-I+1), 107 (7.13, P-I), 92 (10.64), 91 (49.36), 79 (100.0, 107 - C_2H_4?), 78 (20.83), 77(50.93), 67 (12.78), 66 (11.01), 65 (22.25), 53 (22.25), 52 (14.69), 51 (27.96), 50 (14.98),

41 (37.09), 39 (45.79), 29 (24.39), 27 (25.68). Vpc-ms (column D-3, 130 - 150°) 1E, R = Cp: 235 (.1653), 234 (1.851), 128 (3.88), 127 (4.41), 108 (.58), 107 (6.03), 92 (10.58), 91 (49.09), 79 (100.0), 78 (20.17), 77 (52.07), 67 (10.99), 66 (10.61), 65 (23.31), 53 (22.31) 52 (14.73), 51 (28.12), 50 (16.86), 41 (36.36), 39 (46.61), 29 (24.13), 27 (25.62).

Dicyclopropylacetylene, 12, R = Cp. Potassium t-butoxide (250 mg, 2.6 mmol) was dissolved in 2.5 ml DMSO in a vial (magnetic stir bar, serum cap) and a soln of crude vinyl iodide 1, R = Cp, (262 mg, 60% pure, 0.67 mmol) in 2.5 ml DMSO was added. After 4 hr, the reaction soln was poured into water and extracted twice with pentane. The pentane soln was washed with water and sat sodium chloride soln and dried over anhyd sodium sulfate. A portion of the pentane was carefully removed on the rotary evaporator, and the residue was purified by preparative vpc (column C-4, 180°). The product was collected in a dry ice trap over glass helices and then vacuum transferred (liquid nitrogen trap) to give 47 mg pure acetylene, 66% yield. Anal. Calcd: C, 90.51; H, 9.49. Found: C, 90.57; H, 9.40. Ir: 3095s, 3015s, 2870w, 2250vw, 1455m, 1427s, 1378s, 1216s, 1175w, 1090m, 1051s, 1029s, 1002s, 953w, 904m, 876w, 830s. Nmr: 1.3 - .75, m, 2H; .75 - .3, m, 8H. Vpc-ms (column D-3, 110°): 108 (.200, P+2), 107 (4.19, P+1), 106 (49.05, P), 105 (19.00, P-1), 91 (100.0), 79 (59.25), 78 (58.0), 77 (60.65), 65 (54.0), 63 (31.25), 52 (57.5), 51 (71.5), 50 (64.5), 41 (18.35), 39 (67.05), 28 (17.0), 27 (39.27). Dicyclopropylacetylene has been prepared prepared in two steps from dicyclopropylketone (71).

E- and Z-1-Acetoxy-1,2-dicyclopropylethylene, 9E and 9Z, R=Cp.

The vinyl acetates were prepared as above by acid-catalyzed exchanged between isopropenyl acetate and 1,2-dicyclopropylethanone, 7, in 58% yield. The acetate mixture obtained was purified by preparative vpc (column S-3, then column D-2, 150°) to give the E-Z isomer mixture, 99.4% pure by vpc (300'TCEP, 140°), with an E/Z ratio of 1.53. The individual isomers could not be separated by preparative vpc on any column tried. Anal. Calcd: C, 72.26; H, 8.49. Found (mixture E and Z): C, 72.34; H, 8.59. Ir: 3085m, 3010m, 1755vs, 1676w, 1430m, 1368s, 1290w, 1227vs, 1195vs, 1145m, 1050vs, 1026s, 972s, 928w, 904w. Nmr: 4.57 and 4.42, two overlapping d (appear to be "t"), J = 8, 1H, E and Z vinyl protons; 2.08 and 1.99, two s, ratio 1:1.5, 3H, acetoxy methyls; 1.9 - 0.9, complex m, 2H, cyclopropyl methines; 0.9 - 0.2, complex m, 8H, cyclopropyl methylenes. The nmr of the acetate mixture with added shift reagent, $Eu(fod)_3$, allowed unequivocal assignment of the geometric isomers (see Part III). The absorptions at 4.42δ and 2.08δ are due to Z isomer and those at 4.57δ and 1.99δ to E isomer. Vpc-ms (300'TCEP) 9E, R = Cp: 166 (.49, P), 138 (.31), 124 (2.58), 109 (25.63), 96 (43.27), 95 (13.53), 83 (19.53), 82 (16.55), 81 (14.92), 69 (41.45, $C_4H_5O^+$), 67 (10.29), 55 (28.0), 54 (18.87), 53 (16.98), 43 (100.0, CH_3CO^+), 41 (44.0), 39 (38.18), 28 (19.02), 27 (17.60). Vpc-ms (300'TCEP) 9Z, R = Cp: 166 (.70, P), 124 (2.95), 109 (26.29), 96 (46.0), 95 (13.99), 83 (20.0), 82 (16.81), 81 (15.02), 69 (40.38, $C_4H_5O^+$), 67 (10.52), 55 (29.58), 54 (28.45), 53 (18.78), 43 (100.0, CH_3CO^+), 41 (46.20), 39 (41.03), 28 (21.97), 27 (18.78).

1-Chloro-2-ethylbutane. The chlorination of 2-ethylbutanol was patterned after a published procedure (19). Triphenylphosphine (106 gm, 0.4 mol), carbon tetrachloride (102 gm, .66 mol), and 2-ethylbutanol (41 gm, 0.4 mol) were placed in a 500 ml 3-necked flask fitted with a magnetic stir bar and a "screw" condenser topped with a drying tube. The reaction soln was heated gradually in an oil bath. At 55° the triphenylphosphine had dissolved, and as the bath temperature slowly approached 75-76°, a rapid reaction ensued which forced some material out the top of the condenser -- even when the heating bath was quickly replaced with an ice bath. In ca. 2 min this reaction subsided, and a white ppt formed. The reaction mixture was heated to a bath temperature of 120° for 45 min and then cooled to room temperature, whereupon the reaction mixture became a solid cake. The cake was dissolved in methanol and extracted twice with pentane. The combined pentane extracts were washed with water and set aside. The methanol soln was diluted with water and extracted four times with pentane. These extracts were washed with water and added to the previous pentane extracts. The pentane soln was dried over anhyd sodium sulfate, and the solvent removed on the rotary evaporator. The residue was dissolved again in pentane (a smaller volume), washed with water, dried over anhyd magnesium sulfate, and the solvent removed on the rotary evaporator. The residue was distilled through a 15 cm Vigreaux column topped with 5 cm glass helices to give a 28% yield of the chloride, b.p. 125 - 126.5°, purity 94% by vpc (column S-4). No attempt was made to optimize this preparation. The ir showed no O-H stretch, but was otherwise

uninformative. Nmr (220 MHz): 3.45, d, J = 4.5, 2H, methylene at chlorine; 1.57 - 1.25, m (part of m is pentuplet at 1.33, J = 7), 5H, methine and ethyl methylenes; 0.87, t, J = 7, 6H, methyls. The 60 MHz spectrum was quite complex.

1-Cyclopropyl-3-ethylpentanol. Magnesium turnings (2.4 gm, 100 mmol) was placed in a 300 ml 3-necked flask fitted with a mechanical stirrer, Trubor (R) seal, Teflon blade, condenser, side-arm addition funnel, and a nitrogen bubbler, and the flask was flamed under nitrogen flow. Dry ethyl ether (25 ml), a small crystal of iodine, and ca. 5 ml of 1-chloro-2-ethylbutane (5.0 gm, 39 mmol) in 20 ml ether were added. The reaction mixture was stirred and heated in an oil bath at 50°, and the chloride soln was added slowly. Ethyl bromide (7 drops) was added, the reaction mixture was heated for 8 hr, more ethyl bromide was added, the mixture was heated for 8 hr, and then the reaction mixture was allowed to stand overnight. Vpc of an aliquot (column C-5, 110°) showed unreacted chloride. Ethyl bromide (3 drops) was added, and the reaction mixture was heated for 30 min, whereupon the vpc showed no trace of reactant chloride. Cyclopropylcarboxaldehyde (1.8 gm, 24.4 mmol) in 30 ml dry ether was added to the heated and stirred reaction mixture in small, dropwise portions. The reaction was followed by vpc (column C-5, 100°). After addition of the aldehyde, the reaction mixture was heated for another 45 min, cooled, and poured into ice water slush. The water layer was adjusted to pH 4 with 1N sulfuric acid and extracted three times with ether. The combined ether solns were washed with water, sat sodium bicarbonate soln, water, sat sodium chloride soln, and dried over an-

hyd sodium sulfate. The solvent was removed on the rotary evaporator, and the residue was dissolved in a small portion of ether and redried over anhyd magnesium sulfate. After again removing the ether, the residue was vacuum transferred at 10 mm Hg to give 3.8 gm product, 80% pure by vpc (column C-3, 150°), 79% yield . An analytical sample was obtained by preparative vpc (column C-4, 190°). Anal. Calcd: C, 76.86; H, 12.90. Found: C, 76.77; H, 12.75. Ir: 3610m, 3370mb, 3090m, 3005m, 2980s, 2920s, 2880s, 1463s, 1432m, 1409m, 1382s, 1267mb, 1065m, 1023s, 1000m, 972w, 940w, 917m, 857w, 824w. Nmr: 2.92, q (perturbed), J = ca. 6.5, 1H, methine at alcohol carbon; 2.1 - 1.1, m, ca. 8H; 2.1 - 0.75, m, ca. 7H; 0.75 - 0.0, m, ca. 4H, cyclopropyl.

1-Cyclopropyl-3-ethylpentanone. 1-Cyclopropyl-3-ethylpentanol was oxidized with Jones reagent following the procedure given above (modified work-up). After removal of solvent ether on the rotary evaporator and vacuum transfer at 20 mm Hg, the ketone was obtained in 98% yield. An analytical sample was obtained by preparative vpc (column C-4, 180°). Anal. Calcd: C, 77.87; H, 11.76. Found: C, 78.07; H, 11.68. Ir: 3095w, 3010w, 2965s, 2930s, 2880s, 1695vs, 1460m, 1448sh, 1416sh, 1405sh, 1384s, 1210w, 1196m, 1140w, 1089m, 1068s, 1025m, 975w, 948w, 895m. Nmr: 2.38, d, J = 6, 2H, methylene at carbonyl; 1.82, m, 2H, both methines; 1.25, "q", J = 6, 4H, ethyl methylenes; 1.1 - 0.65, m, 10H, methyls and cyclopropyl methylenes.

E- and Z-1-Cyclopropyl-3-ethyl-1-iodopentene, 1E and 1Z, R = 3P. The hydrazone of 1-cyclopropyl -3-ethylpentanone (5.95 mmol)

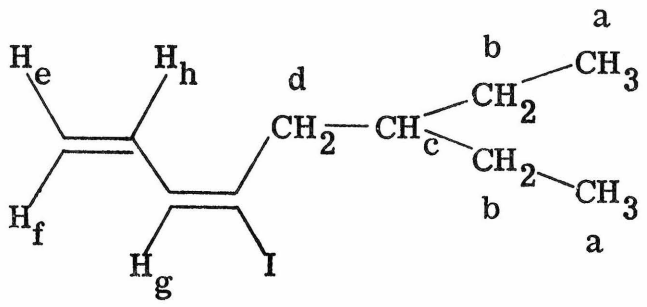
was prepared (10) (reaction mixture heated in 65° bath) and used immediately in the vinyl iodide synthesis. The vinyl iodides were prepared from the hydrazone as given above for 1, R = Cp, except that the dil hydrochloric acid wash was omitted from the work-up. The initial distillate from vacuum transfer at 1 mm Hg was stirred with 8 ml triethylamine at 55-60° for 6 hr. The amine was removed on the rotary evaporator, the residue was dissolved in a little ether, and the soln was filtered from a small amount of ppt. Evaporation of the solvent gave 1.29 gm product, 80% iodides by vpc (column C-3, 150°), 62% yield based on ketone. Preparative vpc (column D-2, 125°) gave two fractions, A and B. Preparative vpc (column C-4, 175°) of A removed ketone impurity and of B removed A impurity. Vpc (300'TCEP) showed A and B to be 98% pure. However, it was later found (300'SF96) that fraction B contained a second iodide that was not observed on DEGS, Carbowax, or TCEP vpc columns. The elemental analyses indicated that the impurity was an isomeric iodide. Anal. Calcd for 1, R = 3P: C, 45.47; H, 6.49; I, 48.04. Found fraction A, 1Z, R = 3P: C, 45.54; H, 6.39; I, 48.18. Found fraction B, 1E, R = 3P, and 8 (see below): C, 45.40; H, 6.48; I, 48.15.

The following isolation of the iodides was used: (1) The initial product mixture was separated on column D-2 (120°) to give fractions A and B. (2) Fraction A was repurified on column SF-1 (150°) to remove ketone impurity; collected Z isomer 99.5% pure (300'-SF96). (3) Fraction B gave a broad composite peak on column SF-1 (150°) that was collected in "thirds", C, D, and E. Fraction E was 99.9% pure E isomer (300'SF96, 110°). Fraction D was 89% E

isomer and 11% 8. Fraction C was 24% E isomer, 68% 8, and 8% Z isomer. (4) Fraction D was repurified on SF-1 (2 μl injections), the first "fourth" of the peak collected as fraction F, the rest as fraction G. Fraction G was 99.6% E isomer (300'SF96). (5) Fraction F was combined with fraction C and repurified on SF-1. Three fractions were collected, the second of which was 95% 8, 4.6 % E-Z isomers and .4% other impurities (300'SF96, 110°). The purified iodides were used for obtaining spectral data (1Z, fraction A; 1E, fractions E and G; 8, fraction in step (5)) and in the analytical solvolyses.

Ir 1Z, R = 3P: 3084w, 3009w, 2964s, 2925s, 2880m, 2860m, 1640w and 1627w doublet, 1463s, 1456s, 1429m, 1424m, 1380m, 1357w, 1336w, 1289m, 1239m, 1229m, 1207w, 1196m, 1169m, 1142w, 1119w, 1050m, 1025s, 977s, 934w, 911w, 870w, 854w, 844w. Ir 1E, R = 3P: 3087w, 3012w, 2962s, 2925s, 2882m, 2862m, 1617m, 1463m, 1424m, 1379m, 1334w, 1316w, 1303w, 1244w, 1158s, 1147sh, 1109w, 1050m, 1027s, 980m, 943s, 925m, 912sh, 888w, 875w, 834w, 667w. Ir 8: 3090w, 3010sh, 2982s, 2923s, 2880m, 1818w?, 1628m, 1459m, 1428w, 1412m, 1380m, 1324w, 1262m, 1199w, 1172m, 1068w, 987s, 958m, 912vs, 647w. Nmr 1Z, R = 3P, (220 MHz): 5.16, d, J = 9, 1H, vinyl proton; 2.20, m, 1H, methine on 3P; 1.63, m, 1H, cyclopropyl methine; 1.41 and 1.28, two sextets, J = 6.5 - 7, 4H, nonequivalent methylene protons on 3P; 0.86, t, J = 7, 6H, methyls; 0.77 - 0.59, m, 4H, cyclopropyl methylenes. Nmr 1E, R = 3P (220): 5.88, d, J = 10.5 (further split by ca. 1 Hz), 1H, vinyl proton; 2.38, m (9 lines), J = 4-5, 1H, methine on 3P; 1.42 and 1.23, two sextets, J = 6.5 - 7, 2H and 3H, nonequivalent methylene protons on 3P plus

cyclopropyl methine (under 1.23); 0.90, t, J=7.5 ,6H, methyls; 0.67, "d", J = 6.5, 4H, cyclopropyl methylenes. Nmr $\underset{\sim}{8}$ (220 MHz): 6.37, d of t, J_{hf}=17, $J_{he} = J_{hg}$ = 9.5-10, 1H, H_h; 6.03, d, 1H, H_g; 5.28, d, 1H, H_f; 5.18, d, 1H, H_e; 2.38, d, J_{dc} = 7, 2H, H_d; 1.66, m, 1H, H_c; 1.30, "pentuplet", $J_{ab} = J_{bc}$ = 7, H_b; 0.87, t, 6H, H_a.



E- and Z-1-Acetoxy-1-cyclopropyl-3-ethylpentene, 9E and 9Z, R = 3P. The vinyl acetates were prepared from 1-cyclopropyl-3-ethylpentanone as described above for $\underset{\sim}{9}$, R = Me. A Dean-Stark trap was used to collect the distillate. After 74% conversion, a 60% yield of the acetates was obtained in a ratio E/Z ca. 4.0 . The isomers were obtained in pure form by preparative vpc (column C-4, 180°). Anal. Calcd: C, 73.43; H. 10.27. Found 9Z, R = 3P: C, 73.37; H, 10.60. Found 9E, R = 3P: C, 73.38; H, 10.20. Ir 9Z, R = 3P: 3090w, 3015m, 2965s, 2925s, 2880m, 2860m, 1754vs, 1686m, 1464m, 1458m, 1431w, 1371s, 1247m, 1217vs, 1197vs, 1166s, 1133w, 1047vs, 1024m, 943w, 932w, 912w, 888w, 668w. Ir 9E, R = 3P: 3095w, 3015m, 2965s, 2925s, 2880m, 2860m, 1754vs, 1677m, 1464m, 1457m, 1429w, 1367s, 1298w, 1217vs, 1198vs, 1178vs, 1128m, 1052sh, 1043s, 1024s, 1005w, 927s, 904m, 872w, 659w. Nmr (220 MHz) 9Z, R = 3P: 4.63, d, J = 10, 1H, vinyl; 2.06, s, 3H, acetoxy methyl; 1.84, m,

1H, methine on 3P; 1.49, m, 1H, cyclopropyl methine; 1.32 and 1.13, two perturbed sextets, J = 7, 2H each, methylenes on 3P; 0.79, t, J = 7.5, 6H, methyls on 3P; 0.70-0.43, m, 4H, cyclopropyl methylenes. Nmr (220 MHz) 9E, R = 3P: 4.71, d, J = 10, 1H, vinyl; 2.17, m (overlapping q of t), J = 8, 1H, methine on 3P; 2.01, s, 3H, acetoxy methyl; 1.66, m, 1H, cyclopropyl methine; 1.49 and 1.21, two m (each 11 lines or more), 2H each, methylenes on 3P; 0.92, t, J = 7.5, 6H, methyls on 3P; 0.72-0.44, two m, 4H, cyclopropyl methylenes. The assignments of the methine hydrogens in 9Z and 9E were facilitated by the use of shift reagent, $Eu(fod)_3$, and the geometrical isomers were definitely established from the nmr spectra with shift reagent (see Part III). Vpc-ms (column D-3, 150°) 9Z, R = 3P: 197 (.0545, P+1), 196 (.394, P), 154 (6.03, P - CH_2CO) 126 (9.58), 125 (100.0, 154 - Et?), 83 (75.4), 79 (10.53), 69 (33.2, $C_4H_5O^+$), 55 (44.5), 43 (88.2, CH_3CO^+), 41 (53.7), 39 (25.6). Vpc-ms 9E, R = 3P: 197 (.065), 196 (.435), 154 (5.43), 126 (9.39), 125 (100.0), 83 (77.4), 79 (12.4), 69 (32.8), 55 (43.9), 53 (9.46), 43 (88.7), 41 (54.4), 39 (25.6).

Preparative Ionization of 1E and 1Z, R = Me. The isolation procedure previously given (10) was repeated on a new sample of the product mixture obtained from the reaction of 1E and 1Z, R = Me with excess silver acetate in acetic acid in order to obtain nmr spectra of the cyclobutyl acetates with shift reagent. Details of the nmr results are given in Part III. Below are listed the solvolysis products, along with the starting iodides and 4, in the order of their retention times (RT) on the 300'TCEP column. More complete spec-

tral details are given in some cases:

(1) Cyclopropylmethylacetylene, 12, R = Me. RT = 12.11 min. Vpc-ms (300'TCEP, 55°): 80 (100., P), 79 (97.3, P-1), 77 (77.4), 65 (28.2), 53 (29.9), 52 (48.2), 51 (60.5), 50 (42.5), 41 (19.9), 39 (62.5), 27 (25.2).

(2) Cyclopropyl Ethyl Ketone, 13, R = Me. RT = 23.20 min.

(3) Z-1-Cyclopropyl-1-iodopropene, 1Z, R = Me. RT = 25.98 min.

(4) 1-Cyclobutenylethyl Acetate, 11, R = Me. RT = 30.03 min. Ir: 3049w, 2982sh, 2960sh, 2925s, 2877w, 2845w, 1733s, 1447w, 1370s, 1236sb, 1174w, 1080m, 1059m, 1047sh, 1029m, 955m, 935w, 906m, 860m, 848sh. Vpc-ms (300'TCEP, 55°): Parent too weak, 112 (7.5), 98 (11.6, P - CH_2CO?), 83 (13.2), 80 (8.81, P - AcOH?), 79 (33.05), 53 (12.1), 43 (100.0, CH_3CO^+), 41 (11.43), 39 (12.38), 28 (17.62), 27 (15.48).

(5) E-1-Cyclopropyl-1-iodopropene, 1E, R = Me. RT = 32.74 min.

(6) 1-Iodo-3,4-hexadiene, 4. RT = 39.00 min.

Ir: 2980m, 2942m, 2920m, 2900sh, 2852w, 1962s, 1460w, 1443m, 1425m, 1412sh, 1371m, 1322w, 1270w, 1243s, 1230s, 1170s, 1077w, 1050w, 1000w, 874mb, 710mb. (The additional data given here was obtained on synthesized 4 (10).)

(7) syn-2-Ethylidenecyclobutyl Acetate, 10S, R = Me. RT = 41.71

min. Ir: 2990m, 2948m, 2925m, 2862w, 1735vs, 1441m, 1426m, 1370s, 1314w, 1230sb, 1146w, 1097m, 1068m, 1048sh, 938m, 888w, 845. Vpc-ms (300'TCEP, 55°): Parent too weak, 112 (4.17), 98 (11.83, P - CH_2CO?), 83 (9.50), 79 (12.0), 69 (12.50), 43 (100.0, CH_3CO^+), 41 (18.8), 39 (14.8), 28 (16.0), 27 (9.50).

(8) anti-2-Ethylidenecyclobutyl Acetate, 10A, R = Me. RT = 49.53 min. Ir: 3044w, 2986sh, 2940s, 2922wsh, 2860w, 1735vs, 1441m, 1428sh, 1371s, 1235vsb, 1200sh, 1099m, 1075s, 1060sb, 1014m, 968w, 951w, 891w. Vpc-ms (300'TECP, 55°): 140 (.724, P), 125 (.89, P-CH_3?), 112 (3.77), 98 (11.90), 97 (7.24), 83 (10.1), 79 (11.31), 69 (13.89), 43 (100.0, CH_3CO^+), 41 (18.85), 39 (15.48), 28 (16.1), 27 (11.8).

(9) Z-1-Acetoxy-1-cyclopropylpropene, 9Z, R = Me. RT = 58.01 min.

(10) 3,4-Hexadienyl Acetate, 14, R = Me. RT = 59.96 min. Vpc-ms (column D-3, 130°) on synthesized (10) compound: 141 (.024, P+1), 140 (.190, P), 98 (13.24), 80 (12.6), 79 (39.0), 43 (100.0, CH_3CO^+), 41 (21.1), 39 (15.5), 28 (9.65), 27 (9.76). The vpc-ms spectrum was the same for the corresponding peak in the solvolysis mixture.

(11) E-1-Acetoxy-1-cyclopropylpropene, 9E, R = Me. RT = 72.35 min.

Analytical Ionizations of 1E and 1Z, R = Me, and 4. Details of the procedure have been given (10). In addition to the previous conditions, the iodides were reacted with silver acetate in acetic acid as a homogeneous soln in the presence of ca. 0.5 M sodium acetate.

Several of the previous reaction solns had been stored in tightly sealed vials (Teflon cap liners) in the freezer, and these were reanalyzed. Several of the ionizations were repeated to be sure that the stored solns had not changed. The analyses were done with the 300'TCEP vpc column , and the relative peak areas were measured with the Hewlett-Packard electronic integrator. The data is given in Tables II and III in the text. The precision of the analyses is also discussed in the text. There was a slight tailing of peak 9 into peak 10 (above), but this was easily corrected for by measuring the analogous area in peak 11 . The corrected areas of peaks 9 and 10 were uniformly precise, as can be seen from the error values given in Table III.

Our previous data (10) were partially corrected for the flame detector response. The measured response factors (column T-1, 90^{O}) relative to amyl acetate were 0.913, 0.903, 0.905, 0.965, and 0.940, all ± 0.03, for 12, 1Z, 1E, 9Z, and 9E, R = Me, respectively. The values are quite close, and for this reason the response factors were not remeasured for the 300'TCEP column. (The factors could change somewhat since the eluting peaks are sharper on the open-tubular column.) The response factors for the R = Cp and R = 3 P systems were not measured since there was generally not enough of the individual compounds available . This should introduce relatively little error, and in particular cannot affect the results when comparing data for E-Z isomers. Also, since the acetate products in any given case are isomeric, there should be little, if any, difference in their response factors.

Preparative Ionizations of 1E and 1Z, R = Cp. The mixture of vinyl iodides 1E and 1Z, R = Cp, (0.29 gm, 1.24 mmol) was stirred with excess silver acetate in acetic acid for 13 hr, and the reaction mixture was worked up (10). Careful removal of ether solvent on the rotary evaporator gave 0.26 gm crude product mixture (when corrected for some remaining ether by vpc analysis, corresponds to >90% yield). Five fractions, A - E, were collected by preparative vpc (column D-2, 150°). Fractions C, D, and E were repurified (column T-3, 145°), and three fractions were obtained in each case, C1 - C3, D1 - D3, E1 - E3. Fractions E1 and E2 were repurified on the same column to remove slight discolorations. In a second reaction, 0.30 gm of the iodide mixture was solvolyzed to give 0.23 gm product mixture (yield calculated to be >91%). This mixture was separated by vpc (column F-1, 105°) to give fraction F. The correspondence of the various fractions A - F to the analytical vpc peaks (300'TCEP) was established from comparisons of exact retention times with the electronic integrator. The various products are listed below in order of their retention times (RT) on the 300'TCEP at 110°. The fractions collected and their vpc purities are given, along with with spectral data for each compound.

(1) Dicyclopropylacetylene, 12, R = Cp. RT = 11.53 min. (Fraction A.) The ir and mass spectra were identical to the prepared compound.

(2) 1,2-Dicyclopropylethanone, 13, R = Me. RT = 17.2 min. This compound was not isolated in the preparative reaction. A very small peak, generally <0.5%, in the analytical vpc was assigned on the

basis of vpc retention time.

(3) Cyclobutenylcyclopropylmethyl Acetate, 11, R = Cp. RT = 19.81 min. (Fraction F, 94% peak 3, .9% peak 6, 5% peak 7.) Ir: 3103w, 3069w, 3027m, 2975m, 2940s, 2892w, 2859m, 1772sh, 1739vs, 1433m, 1370s, 1236vsb, 1196sh, 1175w, 1070w, 1050sh, 1026s, 1017s, 967m, 939w, 910w, 896w, 860m, 832w. Nmr: 5.87, s (finely split), 1H, vinyl; 4.53, d, J = 8, 1H, methine at acetoxy carbon; 2.4, broad "s", 4H, cyclobutenyl methylenes; 2.00, s, 3H, acetoxy methyl; 1.2 - 0.7, m, 1H, cyclopropyl methine; 0.6 - 0.2, m, 4H, cyclopropyl methylenes. With added $Eu(fod)_3$ (Part III), the cyclobutenyl methylenes move downfield as two m of 2H each; extrapolation back to zero reagent gives initial absorptions to be 2.48δ and 2.34δ. Vpc-ms (300'TCEP, 70-120°) from solvolysis mixture: 166 (0.17, P), 138 (1.67), 109 (6.29), 96 (13.27), 95 (12.62), 91 (28.57), 81 (9.89), 79 (19.74), 78 (16.92), 77 (12.9), 67 (10.22), 53 (10.22), 51 (9.62), 43 (100.0, CH_3CO^+), 41 (16.0), 39 (30.6), 28 (10.86), 27 (14.1).

(4) Z-1,2-Dicyclopropyl-1-iodoethylene, 1Z, R = Cp. RT = 24.86 min. (Fraction D1.) Ir identical to that of 1Z, R = Cp.

(5) E-1,2-Dicyclopropyl-1-iodoethylene, 1E, R = Cp. RT = 27.20 min.

(6) syn-2-Cyclopropylmethylenecyclobutyl Acetate, 10S, R = Cp. RT = 32.50 min. (Fraction C2, 94% peak 6, 5% peak 7; fraction D2, 94.5% peak 6, 3.7% peak 7; fraction E1, 92% peak 6, 3.5% peak 4 (before repurification).) Ir: 3085m, 3005s, 2955s, 2930sh, 2845w, 1735vs, 1694sh, 1429m, 1370s, 1294w, 1240vs, 1101m, 1065sb, 1047sh, 1033sh, 1020sh, 952s, 923sh, 897m, 855m, 686w.

Nmr: 5.70, m, 1H, methine at acetoxy carbon; 4.63, "d", J = 10, 1H, vinyl; 2.9 - 1.7, m with sharp s at 2.02, 7H, s is acetoxy methyl and rest of m is cyclobutyl methylenes; 1.7 - 0.9, m, 1H, cyclopropyl methine; 0.9 - 0.2, m, 4H, cyclopropyl methylenes. Stereochemistry was assigned by the use of $Eu(fod)_3$ shift reagent (see Part III); the cyclobutyl methylene protons eventually separate into four 1H peaks. Vpc-ms (300'TCEP, 70-120°) from solvolysis mixture: P absent, 138 (2.84), 109 (7.84), 96 (14.4), 95 (14.1), 91 (22.1), 81 (12.0), 79 (19.4), 78 (11.4), 77 (12.3), 67 (12.3) 53 (9.22), 51 (8.96), 43 (100.0, CH_3CO^+), 41 (13.8), 39 (19.2), 28 (20.9), 27 (10.8).

(7) anti -2-Cyclopropylmethylenecyclobutyl Acetate, 10A, R = Cp. RT = 38.97 min. (Fraction C3, 98% peak 7, 2% peak 6; fraction D3, 96.5% peak 7; fraction E2, 94.5% peak 7 (before repurification).) Ir: 3085m, 3002s, 2952s, 2930sh, 2842w, 1736vs, 1700wsh, 1428m, 1371s, 1238s, 1200sh, 1106w, 1082w, 1060sb, 1047sh, 1021s, 965m, 954m, 897m, 855w, 698w. Nmr: 5.42, "t", J = 7, 1H, methine at acetoxy carbon; 4.88, "d", J = 9, 1H, vinyl; 2.9 - 1.7, m with s at 1.99, 7H, s acetoxy methyl and m cyclobutyl methylenes; 1.4 - 0.8 and 0.8 - 0.2, two m, 5H, cyclopropyl methine and cyclopropyl methylenes. Vpc-ms (300'TCEP, 70-120°) from solvolysis mixture: 166 (.25, P), 138 (2.41, P - C_2H_4?), 109 (8.0), 96 (14.9), 95 (13.7), 91 (20.9), 81 (11.3), 79 (17.7), 78 (11.3), 77 (11.7), 67 (11.7), 55 (8.60), 54 (9.33), 53 (10.7), 51 (9.47), 43 (100.0, CH_3CO^+), 41 (16.1), 39 (21.3), 28 (40.4), 27 (13.4).

(8) 5-Cyclopropyl-3,4-pentadienyl Acetate, 14, R = Cp. RT = 42.58 min. (Fraction E3, 2.2% peak 8, 39.9% peak 9, 57.4% peak 10.)

The compound was not isolated or identified. The solvolysis peak was too small for vpc-ms analysis. The peak was assigned 14, R = Cp, on the basis that its vpc retention time and its percentage of the reaction products were in agreement with the behavior observed for the R = Me system (see above and see text).

(9) Z-1-Acetoxy-1,2-dicyclopropylethylene, 9Z, R = Cp. RT = 43.92 min. (Fraction E3; see peak 8.) and

(10) E-1-Acetoxy-1,2-dicyclopropylethylene, 9E, R = Cp. RT = 45.65 min. (Fraction E3; see peak 8.) This mixture of 9Z and 9E, R = Cp, gave qualitatively the same ir, nmr, and vpc-ms spectra as the acetate mixture synthesized from the ketone (see above). The nmr spectra with shift reagent, $Eu(fod)_3$, also showed the same behavior.

Analytical Ionizations of 1E and 1Z, R = Cp, R = 3P. The amounts of reactants and the work-up procedure were similar to those reported (10). The solvolyses mixtures were vpc analyzed on the 300'TCEP column at 105 to 115° generally, and the relative peak areas obtained by electronic integration. The data are given in Tables IV-VII along with the analysis precision. The solvolyses rates of the individual isomers under heterogeneous conditions were obtained, as before (10), by removing aliquots from the reaction mixture, working them up, and analyzing them by vpc. Since the reactions are quantitative or nearly so, kinetic plots were based upon the percent of starting material in the total reaction mixture. The purity of the individual isomers used in the analytical reactions was generally $> 99\%$. Small amounts of isomerization of the starting vinyl iodides

were observed (corrected for any initial isomer impurity in the starting material), particularly formation of the slower-reacting 1Z isomer when 1E was ionized. For a discussion of the isomerization, see the text.

Isomerization of 11, R = Cp. The material obtained in fraction F above (10μl) was stirred with 50 mg silver iodide, and 100 mg silver acetate in 3.0 gm acetic acid at room temperature. Aliquots were removed over a period of 7 days, worked-up as for the analytical ionizations, and vpc analyzed on the 300'TCEP column. The kinetic plot of the fraction of 11 in the total reaction mixture was very linear even when only 2% of 11 remained. The plot is given in Appendix B. The only products observed were acetates 10A and 10S, R = Cp. The excellent linearity of the plot suggests that 10A and 10S are stable to ionization, since if they were not, i.e. if all three isomers were in equilibrium, the plot should curve. The ratio in which the 10 isomers were formed from 11 was 10A/10S ≈ 9.1.

Preparative Ionization of 1E and 1Z, R = 3P. The mixture of vinyl iodide isomers containing some vinyl iodide 8 (207 mg) was stirred with excess silver acetate in acetic acid for 25 hr and then worked up as usual (10). After careful removal of ether solvent on the rotary evaporator, 170 mg of product mixture was obtained. (After correction for the approximate percentages of acetates, acetylene, and iodide 8 by vpc, this calculates to be better than 95% yield.) The product mixture was separated into six fractions, A - F, by preparative vpc (column T-3, 115°). Fraction B and fraction F were repurified on column SF-1 (145°) with one major peak collected in each

case. Fraction C was refractionated (column SF-1, 145°) to give four fractions, C1 - C4. The same was true for fraction D, giving fractions D1 - D3. Below are given the products along with the iodides in order of their retention times (RT) on the 300'TCEP column for a representative run at 105°. The corresponding collected fractions were established by comparisons of exact retention times on the electronic integrator. In several cases, correspondence was checked by spiking the solvolysis mixture as indicated. (Since iodide 8 coeluted with the E starting material, the solvolysis mixture and the collected fractions were checked for purity and correspondence on the 300'SF96 column, which cleanly separates 1E, 1Z, and 8. No new solvolysis peaks were observed on this column, but it could not be used for analysis of solvolysis mixtures because 1Z coeluted with 9Z.)

(1) 1-Cyclopropyl-3-ethylpentyne, 12, R = 3P. RT = 9.10 min. (Fraction A, 97% 300'TCEP.) Ir:3095m, 3012m, 2965s, 2933s, 2877m, 2244vw, 1464s, 1458sh, 1429w, 1380m, 1362s, 1343w, 1203w, 1166w, 1089w, 1051m, 1028m, 1003w, 895s, 848w. Nmr (220 MHz): 2.04, m, 1H, methine on 3P; 1.37, "quintet", J = 7, methylenes on 3P; 0.94, t, J = 7, methyls; 0.94 - 1.27, m, cyclopropyl methine; (total 11H for 1.37 - 0.94); 0.77 - 0.5, m, 4H, cyclopropyl methylenes. Vpc-ms(300'TCEP) from solvolysis mixture: 137 (1.13, P+1), 136 (10.90, P), 107 (25.6), 93 (28.6), 91 (77.7), 77 (56.4), 67 (18.1), 65 (27.8), 53 (22.3), 51 (27.7), 41 (39.6), 39 (42.0), 29 (33.4), 27 (29.8), 79 (100.0).

(2) Z-1-Cyclopropyl-3-ethyl-1-iodopentene, 1Z, R = 3P. RT =

18.16 min.

(3) E-1-Cyclopropyl-3-ethyl-1-iodopentene, 1E, R = 3P. RT = 21.79 min.

(3a) 6-Ethyl-4-iodo-1,3-octadiene, 8. RT = 21.79 min. (Fraction B, 94% 300'SF96; fraction C4, 97% pure 300'TCEP.) Ir and nmr spectra identical to the material isolated from the starting iodide mixture (see above).

(4) 1-Cyclobutenyl-2-ethylbutyl acetate, 11, R = 3P. As explained in the text, this acetate was not isolated nor was it detected as an impurity in any fraction. A very small peak with a retention time of 23.12 min, which compared to the retention times (relative to the other products) for 11, R = Cp and R = Me, could have been 11, R = 3P. However, this peak never constituted more than 0.2% of the product mixture.

(5) syn-2-(3-pentylmethylene)cyclobutyl Acetate, 10S, R = 3P. RT = 25.21 min. (Fraction C3, 95% 300'SF96; solvolysis mixture spiked.) Ir: 3003sh, 2968s, 2933s, 2886m, 2868m, 1737vs, 1462m, 1452m, 1427w, 1370s, 1230vs, 1095m, 1065m, 965w, 927w, 847w. Nmr (220 MHz): 5.52, m, 1H, methine at acetoxy carbon; 5.31, d, J = 10, 1H, vinyl; 2.7-2.2, m,1.91, m, 1.97, s, 8H, cyclobutyl methylenes, 3P methine, and Ac methyl; 1.37 and 1.11, two m, 4H, methylenes of 3P; 0.818 and 0.843, two overlapping t, J = 7, 6H, methyls on 3P. The geometric configuration was established with the aid of nmr shift reagent (Part III). Vpc-ms (300'TCEP, 100°) fraction C3: 154 (3.78), 125 (12.72), 107 (35.6), 93 (24.9), 91 (30.5), 81 (11.9), 79 (57.1), 77 (25.6), 67 (18.7), 55 (33.7), 53 (19.9),

43 (100.0, CH_3CO^+), 41 (48.4), 39 (33.9).

(6) 1-Cyclopropyl-3-ethylpentanone, 13, R = 3P. RT = 26.89 min. (Fraction C1 and fraction D1, 99% 300'TCEP or 300'SF96; solvolysis mixture spiked.) The collected material showed identical ir and vpc-ms spectra to the authentic material synthesized above.

(7) Z-1-Acetoxy-1-cyclopropyl-3-ethylpentene, 9Z, R = 3P. RT = 29.78 min. (Fraction C2, 97% 300'TCEP; fraction D2, 99.8 % 300'TCEP or SF96; solvolysis mixture spiked.) The isolated material gave ir, nmr, and vpc-ms spectra identical to the prepared acetate.

(8) anti-2-(3-pentylmethylene)cyclobutyl Acetate 10A, R = 3P. RT = 30.82 min. (Fraction D3, 97.4% 300'TCEP; solvolysis mixture spiked.) Ir: 2960s, 2928s, 2877s, 2862sh, 1735vs, 1461m, 1454m, 1428w, 1370s, 1230vsb, 1200 sh, 1100m, 1078s, 1060s, 1017m, 950m, 924m, 892w, 867w. Nmr (220 MHz): 5.37, m, 1H, methine at acetoxy carbon; 5.03, d, J = 9.5, 1H, vinyl; multiplets at 2.52, 2.31, 1.95, and 1.74 with sharp s at 1.97, total 8H, cyclobutyl methylenes and methine on 3P plus acetoxy methyl; 1.54 - 1.02, m, 4H, 3P methylenes; 0.805 and 0.842, two overlapping t, J = 7, 6H, 3P methyls. The geometric configuration was established with the aid of nmr shift reagent (Part III). Vpc-ms (300'TCEP, 100°) fraction D3: 154 (2.29), 136 (15.0), 125 (9.47), 121 (11.4), 107 (66.4), 105 (14.0), 93 (47.6), 91 (60.2), 81 (15.6), 80 (10.55), 79 (100.0), 77 (48.3), 67 (30.9), 65 (26.3), 55 (43.9), 53 (31.1), 43 (89.5, CH_3CO^+), 41 (89.5), 39 (58.4), 29 (33.4), 27 (37.5).

(9) E-1-Acetoxy-1-cyclopropyl-3-ethylpentene, 9E, R = 3P. RT = 40.36 min. (Fraction E, 99.7% 300'TCEP or SF96.) The ir,

nmr, and vpc-ms of the isolated material were identical to the prepared acetate.

(10) 6-Ethyl-3,4-octadienyl Acetate, 14, R = 3P. RT = 56.24 min. (Fraction F, 99.8% 300'TCEP; solvolysis mixture spiked.) Ir: 2969s, 2929s, 2884m, 2868sh, 1968m, 1740vs, 1460m, 1430w, 1383m, 1365m, 1230vsb, 1036sb, 878m, 710w. Nmr (220 MHz): 5.02 and 4.89, m, 2H, vinyls; 4.03, t, J = 7, 2H, C1 methylene; 2.26, d of d, J = 7, J = 3, 2H, C2 methylene; 1.97, s, 3H, acetoxy methyl; 1.80, m, 1H, methine; 1.54-1.11, m, 4H, 3P methylenes; 0.888 and 0.896, two overlapping t, J = 7, 3P methyls. Vpc-ms (300'TCEP, 120°) fraction F: 167 (1.66), 107 (12.4), 91 (11.0), 79 (30.1), 55 (15.4), 43 (100.0, CH_3CO^+), 41 (18.5), 39 (10.5), 29 (12.3).

Controls. The control reactions in the R = Me system have been described (10). The control reactions for the R = Cp and R = 3P systems are discussed in the text.

Methylene iodide - d_2. Methylene iodide was exchanged twice with D_2O according to the procedure of Winstein and coworkers (61). The product was purified by distillation at 14.5-15 mm Hg, b.p. 69.5-70.5°. The ir spectrum showed a medium band at 2310 cm^{-1} and a very strong band at 832 corrsponding to CD_2I_2 and a medium band at 1076 for $CDHI_2$ (61). No absorption for CH_2I_2 was observed. The product (1.7335 gm) and acetonitrile (0.1067 gm) were weighed into an nmr tube. Careful integration of the peaks gave an isotopic composition of 89.2% - d_2 and 10.8% - d_1. This was checked by adding 0.9685 gm methylene iodide (3.615 mmol) and reintegrating the spectrum . The calculated amount of methylene iodide added was

3.598 mmol. Vpc-ms data (column D-3) showed minimum 91% - d_2 and minimum 6%- d_1.

1-Cyclopropyl-2-(cyclopropyl-2-d_2) ethanol (38). The procedure given above was used to prepare the deuterated alcohol from 1-cyclopropyl-3-butenol and the deuterated methylene iodide. The product was obtained in 62% yield, 77.8% pure. The ir spectrum of the crude product showed new peaks at 2317w cm^{-1}, 2205w, 1120wb, 1073w, and 1031sb and peaks absent at 1455, 1045, 1017, 975, 962, and 943.

1-Cyclopropyl-2-(cyclopropyl-2-d_2)ethanone (39). Jones oxidation (see above) of the deuterated alcohol 38 afforded the deuterated ketone in 87% yield, 82 % pure. Vpc-ms (column D-3) showed a parent peak at 126 ($P+d_2$). The peak distribution at m/e 124 - 128 gave a calculated isotope distribution of ca. 90% - d_2 and ca. 10% - d_1. The pattern at m/e 69 - 71 was identical within experiment error to that for the undeuterated ketone (see Table XII)

1-Cyclopropyl-2-(cyclopropyl-2-d_2)-1-iodoethylenes, 34E and 34Z. The procedure given above was used to convert ketone 39 to vinyl iodides 34E and 34Z. The ir spectrum of 34E showed new peaks at 2325 vw cm^{-1} and 2207w and peaks at 1456 and 673 were split into doublets. The ir spectrum of 34Z showed new peaks at 2325vw, 2200w, 860s, 696m, 644m and peaks at 1455, 1191, and 1120 were split into doublets. Vpc-ms showed parent peaks at 236 ($P+d_2$) for each isomer, and the peak distribution at m/e 232 - 237 gave ca. 89.5% - d_2 and 10.5% - d_1 for each isomer.

1-Chloro-1,2-dicyclopropylethane (36-d_0). (See ref. 72) Thionyl chloride (1.0 gm, 8.4 mmol) and 5 ml chloroform were placed in a

25 ml flask fitted with a magnetic stir bar and a side-arm addition funnel topped with a drying tube. The soln was cooled in an ice bath, and 1,2-dicyclopropylethanol (0.5 gm, 86% pure, 3.4 mmol) in 5 ml chloroform was added to the stirred soln dropwise. After the addition was complete, the addition funnel was replaced with a "T" tube, and a flow of nitrogen was applied across the "T" while the reaction mixture was stirred at room temperature for 7 hr. The reaction mixture was then evacuated on the rotary evaporator to remove excess HCl, poured into ice water, and extracted with ether. The ether extracts were washed with water, sat sodium bicarbonate soln, and sat sodium chloride soln and dried over anhyd magnesium sulfate. Removal of the ether on the rotary evaporator gave 0.53 gm product, ca. 85% pure by vpc (column U-3), 91% yield. The product could be purified if precautions were taken to prevent decomposition on the vpc column. The glass column U-3 (90^{o}) was used, and each shot of chloride was preceeded by 10 50 μl shots of ammonia vapor and 80 μl ether. The isolated yield of chloride was 0.32 gm, 65%. Anal. Calcd: C, 66.43; H, 9.06; Cl, 24.51. Found: C, 66.55; H, 9.15; Cl, 24.49. Ir: 3085s, 3010s, 2943m, 2910sh, 2885sh, 2865sh, 2842w, 1464m, 1445w, 1434sh, 1328s, 1394m, 1321w, 1284w, 1268m, 1251w, 1219m, 1196w, 1172m, 1157sh, 1107w, 1101w, 1050s, 1021s, 979m, 950m, 945m, 927m, 909s, 891m, 826m, 718m, 678sh, 657s. Nmr (220MHz): 3.25, d of d of d, J = 7.5, J = 9.5, J = 5.5, 1H, methine at chloro carbon; 1.76, 10 lines nearly symmetrical with upfield half peaks split by 1.5 Hz, 2H, nonequivalent methylene protons; 1.16 and 0.98, two m, 1H each, cyclopropyl methines; 0.75 -

0.05, complex m, 8H, cyclopropyl methylenes. The nmr spectrum showed no peaks in the vinyl region and no evidence of cyclobutyl protons. Vpc-ms (column D-3, 120°): 146 (.0970, P+2), 145 (.0443, P+1), 144 (.2992, P), 118 (.812), 117 (.215), 116 (2.826), 103 (3.19), 95 (12.09), 81 (60.3), 79 (14.1), 67 (100.0), 65 (10.2), 55 (13.3), 54 (27.2), 53 (17.2), 41 (70.9), 39 (38.2), 27 (21.6).

1-Chloro-1-cyclopropyl-2-(cyclopropyl-2-d_2)ethane, 36. Thionyl chloride (.5 gm) and deuterated alcohol 38 (0.26 gm) were reacted in 4 ml chloroform for 4 hr as given above. The chloride was isolated and purified by vpc as in the preceeding case. This material was used in paths M, N, and P in Table XII. This preparation is designated path K, Scheme IX.

In a second preparation 0.92 gm thionyl chloride and 0.46 gm 38 were stirred in 2 ml chloroform for 10 hr. This preparation is designated path K', and the chloride obtained was used in path M'.

The ir spectra of the chlorides from path K and K' were identical and showed new peaks (compared to the undeuterated chloride) at 2320w, 2210w, 878w, 867w, and 684m, doublets at 1464 and 1050, and a peak at 979 was absent. The 220 MHz nmr spectrum was the same as for the undeuterated chloride except that the cyclopropyl methylene region integrated for 6 protons rather than for 8 protons. The vpc-ms spectrum showed a parent peak at m/e 146 (P+d_2) and a deuterium content of ca. 88%-d_2 and 12%-d_1.

1,2-Dicyclopropylethyl Acetate (37-d_0). 1,2-Dicyclopropylethanol (.3 gm, 86% pure, 2.0 mmol) was treated with acetic anhydride (.40 gm, 3.9 mmol) in 6 ml pyridine at 60-70°. Work-up and

preparative vpc (column D-2, 150°) gave the pure acetate. Anal. Calcd: C, 71.39; H, 9.59. Found: C, 70.59; H, 9.40. Ir: 3084m, 3010s, 2970mb, 1726vs, 1463w, 1428m, 1408w, 1370s, 1245vsb, 1046m, 1028s, 1016s, 965m, 950sh, 907w, 824m. Nmr (220 MHz): 4.18, q (slightly split), J = 7, 1H, methine at acetoxy carbon; 1.95, s, 3H, acetoxy methyl; 1.50, symmetrical 10 line pattern, J = ca. 7, 2H , nonequivalent CH_2 protons; 0.94 and 0.71, two m, 2H, cyclopropyl methines; 0.6 - 0.1, complex m, ca. 8H, cyclopropyl methylenes. Vpc-ms (column D-3, 150°): 168 (very small), 139 (0.07) 126 (1.03), 113 (3.62), 93 (10.3), 80 (15.9), 79 (12.8), 71 (17.9), 67 (20.6), 55 (11.0), 43 (100.0, CH_3CO^+), 41 (14.7), 39 (13.2).

1-Cyclopropyl-2-(cyclopropyl-2-d_2) ethyl Acetate, 37. The procedure given above was used to prepare the acetate from deuterated alcohol 38. The ir spectrum of the isolated material showed peaks at 2320w, 2210w, and 682 with reduced intensity peaks at 1463 and 1046.

1,2-Dicyclopropylethylene , 40-d_0. The olefin was prepared by reduction of the corresponding vinyl iodide (E, Z) with tri-n-butyltin hydride (73). A 25 ml flask containing a magnetic stir bar was flamed, flushed with nitrogen, capped with a serum stopper, and cooled in an ice bath. Tri-n-butyltin hydride (200 μl) was added to the reaction flask with a syringe , and then the freshly vpc purified vinyl iodide mixture , 1E and 1Z, (120 mg, 0.51 mmol) was added slowly to the stirred hydride with a syringe. After 30 min the volatile material was removed by vacuum transfer to a flame-dried liq nitrogen trap at 4 mm Hg. The distillate (44 mg, 76% yield) was ca. 97%

pure by vpc and showed two major peaks (300'TCEP, 40°). The material was characterized by its mass spectrum. Vpc-ms (column D-3): 109 (1.3252, P+1), 108 (15.951, P), 107 (1.963, P-1), 93 (50.1), 91 (53.1), 80 (47.1), 79 (86.5), 78 (17.9), 77 (100.0), 67 (81.0), 66 (23.9), 65 (35.0), 54 (21.5), 53 (34.9), 52 (17.9), 51 (33.3), 50 (22.5), 41 (73.0), 40 (15.4), 39 (95.7), 29 (12.4), 27 (48.8). The cis- and trans-1,2-dicyclopropylethylenes have been prepared by reduction of dicyclopropylacetylene (71).

Ionizations of 34E and 34Z. The reactions of 34E and 34Z with excess silver acetate in acetic acid were carried out as given above. The product acetates 35E and 35Z were analyzed by vpc-ms (300'TCEP) and the data are given in Table X (path F, Scheme VII).

For the reaction shown as path G, Scheme VII, a mixture of the purified vinyl iodides was reacted with excess silver acetate in acetic acid, and the product mixture so obtained was reduced with excess LAH in ether at 0°. (The reduction reaction mixtures were worked up by carefully adding sat sodium sulfate soln and then anhyd sodium sulfate. The mixture was stirred until only white (not grey) ppt was present, and then the ether soln was decanted and the ppt washed thoroughly with ether.) Vpc analysis (300'TCEP) of the resulting product mixture showed 11.59% 12, 7.35% ketone 39, and 38.82% alcohol 38 (identified by comparisons of retention time). Other peaks, in continuing order of their retention times, were assumed to be alcohols corresponding to the other product acetates (deuterated): 21.80% (10A), 0.90% (14), 4.11% (10S), and 15.39% (11). The product distribution so assigned paralleled the product distribution ob-

served (300'TCEP) before the LAH reduction. The LAH reduction product mixture was then oxidized with Jones reagent (see above), and the peak corresponding to ketone 39 was analyzed by vpc-ms. The data are given in Table XI.

The following control reactions, paths C and D, Scheme VII, were carried out: (C) The deuterated acetates, 35E and 35Z, were stirred with excess silver acetate and silver iodide in acetic acid for 20 hr. After the usual work-up, vpc of the product soln (300'TCEP) showed that the purity (99.2%) and E/Z ratio (1.44) were unchanged. Vpc-ms data are given in Table X. (D) The acetate mixture was then reduced with a slight excess of LAH in ether. Vpc analysis (300'TCEP) of the resulting product mixture showed 13.6% ketone 39 and 86.4% alcohol 38. This mixture was treated with Jones reagent (see above) and the worked-up reaction showed only one peak (300'TCEP) which corresponded to ketone 39. The vpc-ms results are given in Table XI.

Solvolyses of 36. The deuterated chloride 36 (5 μl) was stirred with excess silver acetate (26 mg) in .5 ml acetic acid for 15 min and then worked up as usual (see above and ref. 10). Vpc analysis of the product mixture (column D-3, 110°) showed 91% acetate 37, four minor impurities, two at shorter and two at longer retention times than 37, and 1% possible olefin (40?). Reduction of the product mixture with LAH at 0° gave 93.5% pure alcohol 38. Oxidation of the alcohol with Jones reagent gave 97.9% ketone 39 with two minor impurities observed by vpc (column D-3). The vpc-ms spectrum of the major product was identical to that obtained for the ketone 39

prepared directly from alcohol 38 (path A, Scheme IX) except for very minor variations in some peak ratios. The data at m/e 69-71 is given in Table XII. The chloride used in this reaction was that prepared by path K (see above). This sequence of reactions is designated paths L and M in Scheme IX.

The above sequence was repeated twice with the solvolysis time extended to 1.5 hr and 2.5 hr. In each case the purity of the product acetate (before LAH reduction) was 91%, which indicated that the acetate 37 was stable to the reaction conditions. The vpc-ms data for the final ketone product are shown in Table XII.

The reaction sequence was repeated with chloride 36 (5 μl) prepared in path K' above. The mass spectral results are given in Table XII.

Chloride 36 (5 mg, from path K) was added to a homogeneous soln of 26 mg silver nitrate in acetone-water (1:1 by weight, 1.0 gm total). After stirring for 7 min, the reaction soln was saturated with sodium chloride and extracted with ether. The ether extract was washed with sat sodium chloride soln and dried over anhyd sodium sulfate. Vpc analysis of the soln (column D-3, 110°) showed 97% alcohol 38 and 3% total of two impurities. The product mixture was oxidized with Jones reagent, and the vpc-ms data obtained on the resulting ketone (Table XII). This reaction sequence is given as path N in Scheme IX.

Chloride 36 (5 mg , from path K) was stirred with a 30% soln of potassium hydroxide in methanol (1 ml) for 45 min. The reaction soln was poured into water, saturated with sodium chloride, and ex-

tracted with ether. The ether extract was washed with water, 1H HCl, water, sat sodium bicarbonate soln, and sat sodium chloride soln and dried over anhyd sodium sulfate. After removal of the ether solvent, the product was oxidized with Jones reagent. This sequence was repeated for a reaction of the chloride 36 in 1 ml of a soln prepared from 5.6 gm potassium hydroxide, 10 ml water, and 5 ml methanol. The ketone 39 obtained in each run was analyzed by vpc-ms, and the data are given in Table XII. These runs are given as path P in Scheme IX.

Control reactions, paths I and J, Scheme IX, were carried out: (I) Acetate 37 was stirred with excess silver acetate and silver chloride in acetic acid for 2.5 hr and the mixture was worked up. The isolated product was reduced with LAH and then oxidized with Jones reagent to give ketone 39. (J) Acetate 37 was reduced with LAH to alcohol 38, which was then oxidized to ketone 39 with Jones reagent. The vpc-ms data for the ketones obtained from these pathways are given in Table XII.

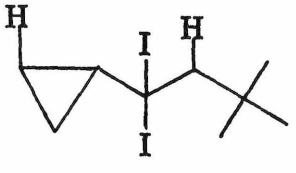
The reaction sequence path L - path M, Scheme IX, was carried out with undeuterated chloride, 1-chloro-1,2-dicyclopropylethane (36-d_0). Ir and nmr spectra of the intermediate alcohol and final ketone were identical to the authentic materials. The vpc-ms of the ketone obtained through this sequence was identical to ketone 13, R = Cp.

When the 1,2-dicyclopropylethylene (40-d_0) isomer mixture was stirred with excess silver acetate in acetic acid for 2.5 hr and worked up, the resulting product soln showed no vpc peaks (column

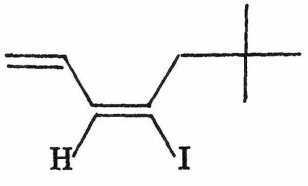
D-3, 110°) besides olefin.

Appendix A: Some notes on the vinyl iodide synthesis (10, 17, 18).

When we decided to look at the reactions of a vinyl iodide of type 1 having a bulky substituent R, our first choice was R = t-butyl. The necessary ketone, cyclopropyl neopentyl ketone, was easily obtained in 70% yield by reacting the Grignard of neopentyl chloride directly with cyclopropanecarbonyl chloride. When the hydrazone was treated with iodine and triethylamine (see Experimental for general procedure) only a high-boiling compound was obtained. The nmr of the crude material was consistent with diiodide G. The reaction of G with



G

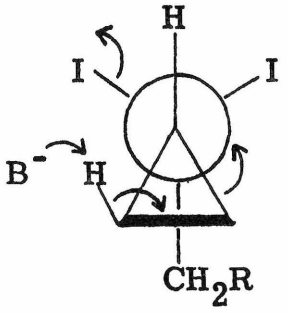


H

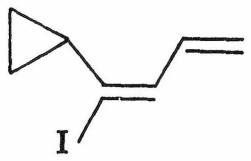
a deficiency of potassium t-butoxide in DMSO, with triethylamine at 60°, or even with tetrabutylammonium fluoride in dimethylformamide (74) gave only a product whose nmr was consistent with ring-opened structure H.

When the steric hindrance at the methylene carbon next to the diiodide center was relaxed somewhat by using R = 3P, then the desired vinyl iodides, 1E and 1Z, were formed, but some ring-opened product (8) was found (see text). The nmr spectra of H and 8 were consistent with the E isomer shown in each case, although this identi-

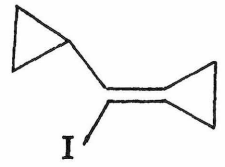
fication was not definitely established. Only one ring-opened isomer was detected in each case. If the stereoassignment is correct, then the elimination may occur as shown.



In another case, the hydrazone of dicyclopropyl ketone gave what appeared to be dicyclopropyldiiodomethane. Treatment of the diiodide under a variety of basic conditions (those given above, sodium hydroxide in DMSO-water, or sodium methoxide in DMSO) gave 1-cyclopropyl-1-iodo-1,3-butadiene J (probably a mixture of geometric isomers). This in fact is a rather efficient synthesis of J from the readily available ketone. The "normal" reaction in this case would have given iodide K, which must be rather strained.



J



K

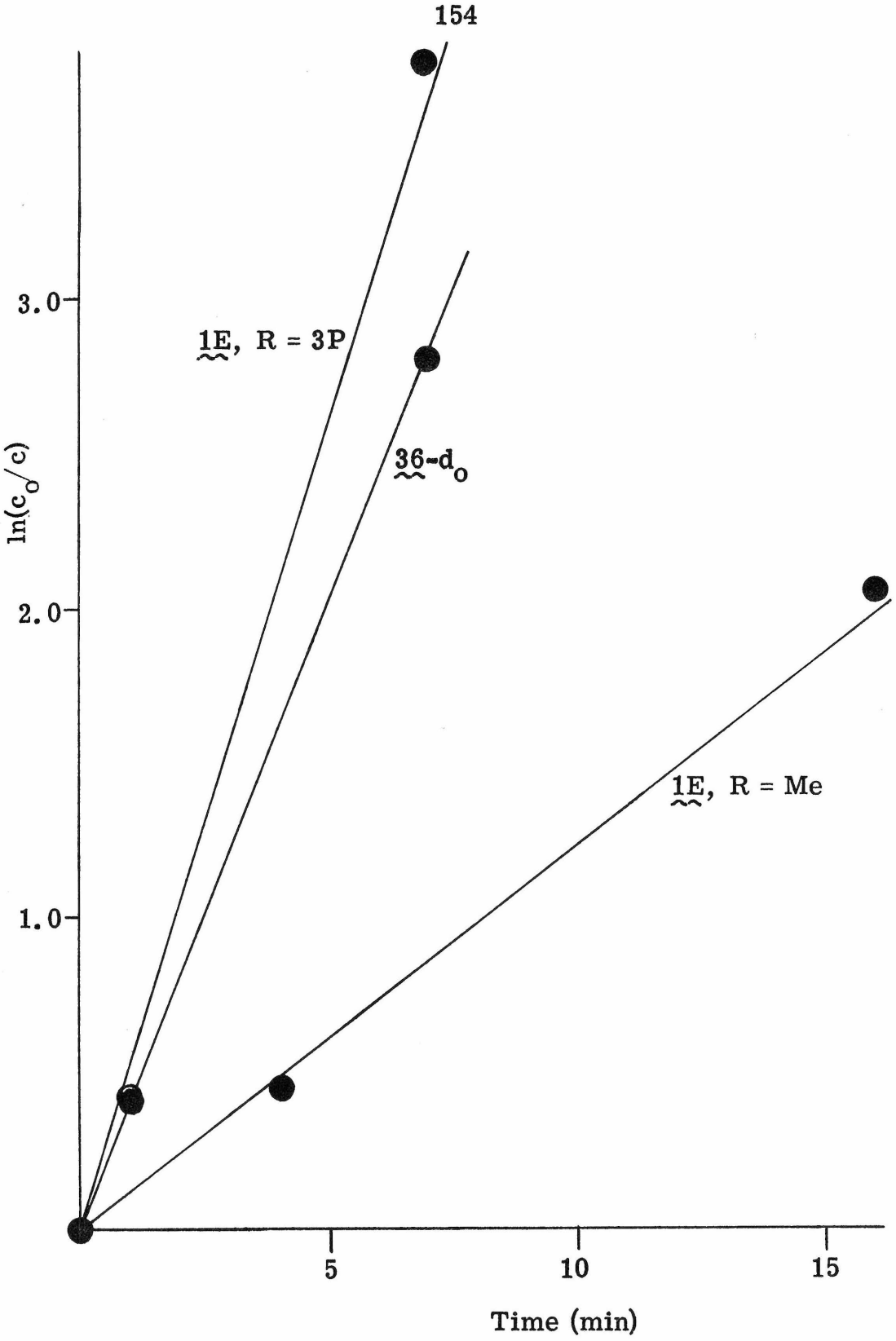
The "normal" elimination reaction is apparently blocked in these reactions, and a cyclopropyl methylene proton is attacked by the base. It would be rather interesting to explore this reaction further, either with hindered diiodides or with monohalo compounds, to determine

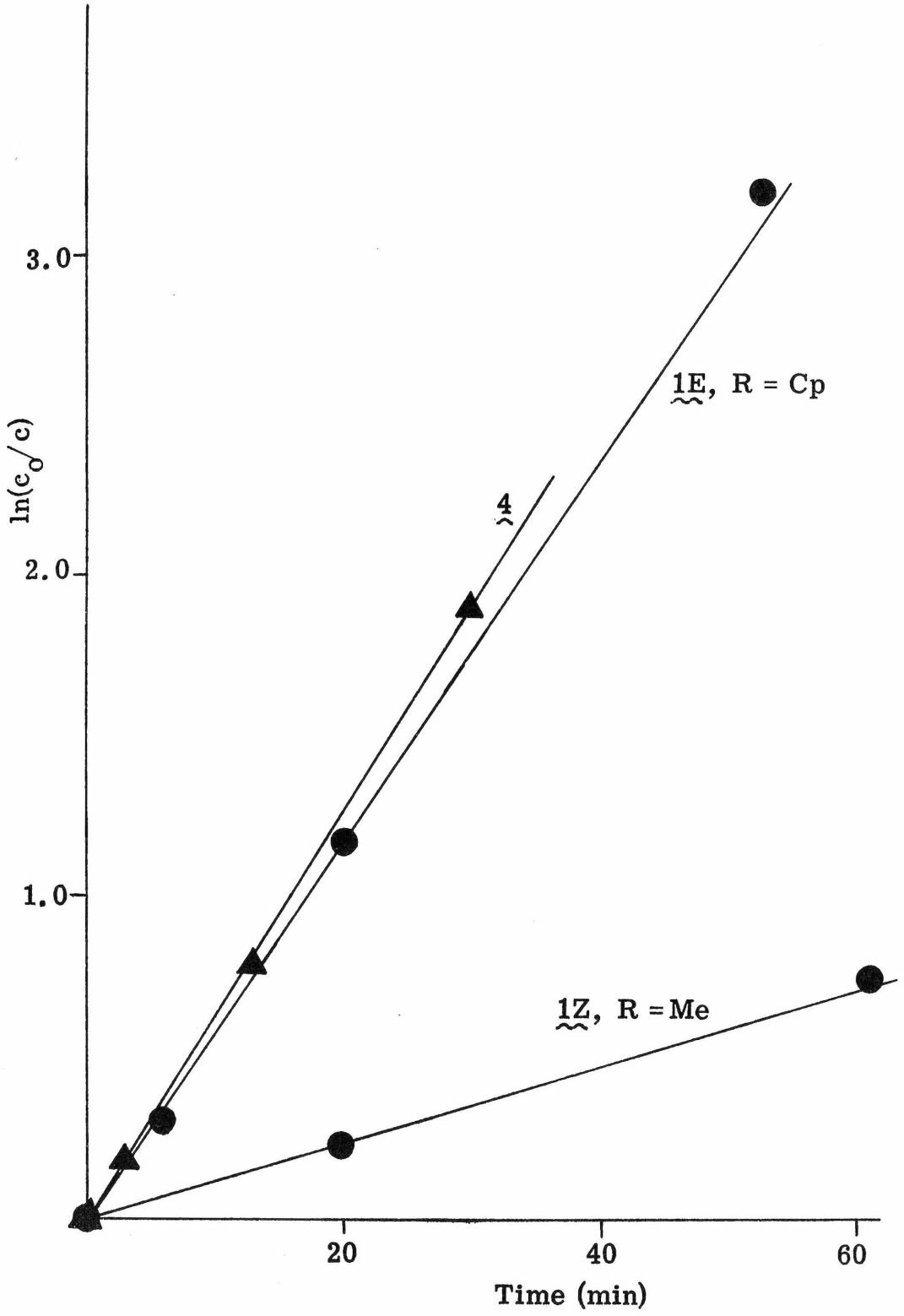
the extent to which stereoselectivity obtains or can be changed.

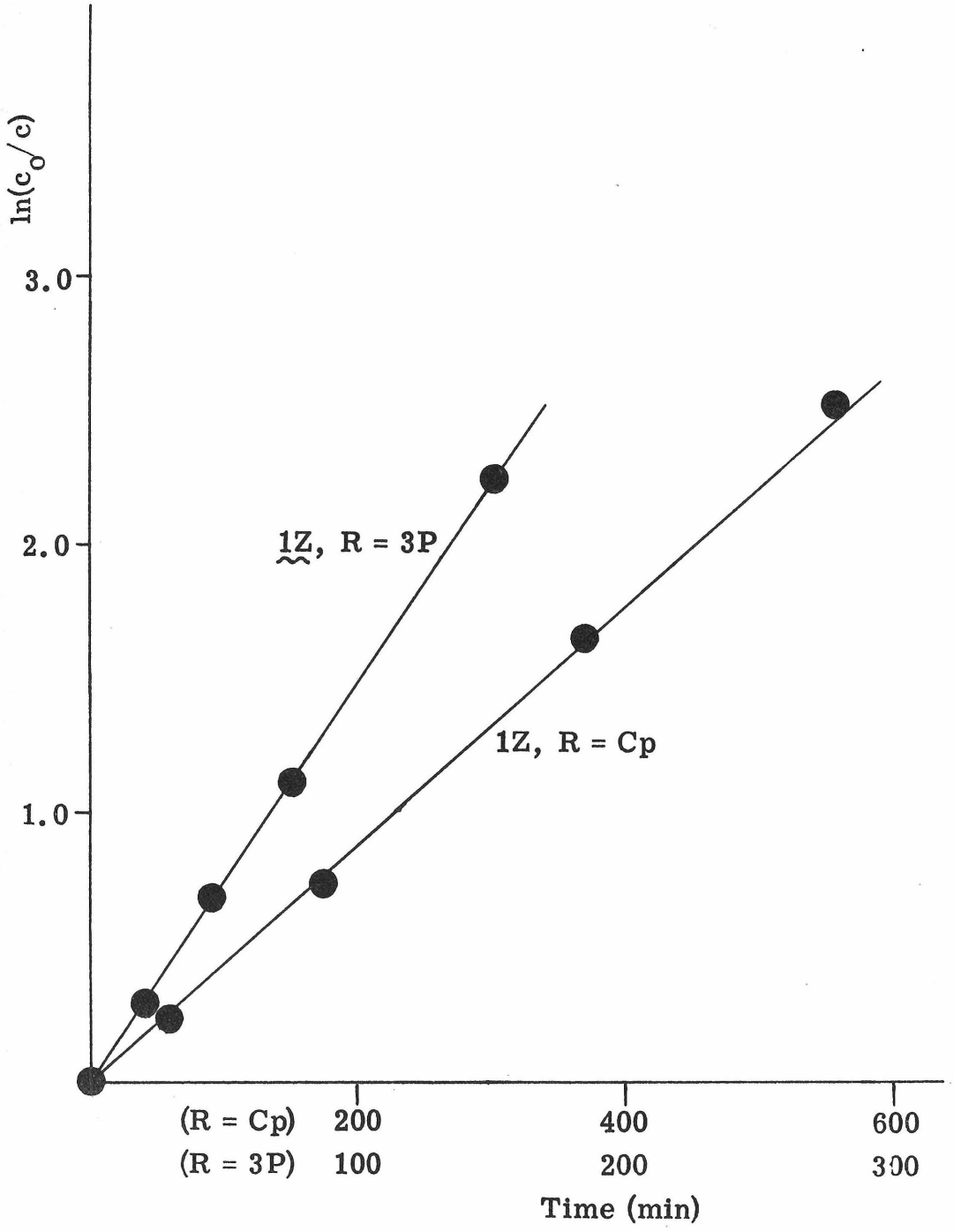
Appendix B. Kinetic plots.

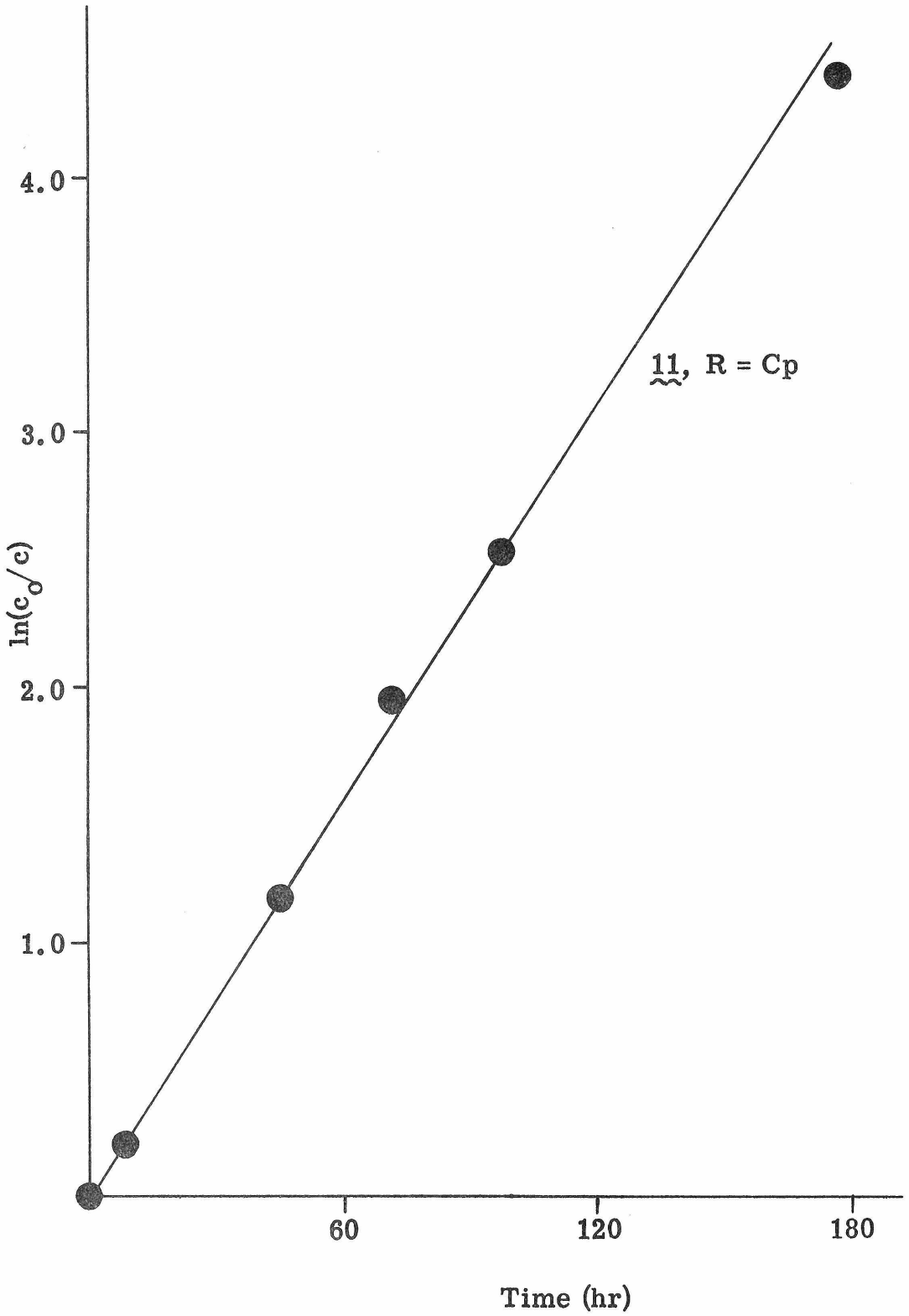
The following graphs show the experimental rate data for the reactions of 1E and 1Z, R = Me, R = Cp, and R = 3P, of 4, and of 1-chloro-1,2-dicyclopropylethane, 36-d_0, with excess silver acetate in acetic acid at room temperature, 24 ± 1°. On the ordinate, c_0 is the initial concentration of the reactant, and c is the concentration at time t, both concentrations taken as the mole % of reactant in the reaction mixture as found by vpc. The rate constants are given in Table I except that for 36-d_0, which is 6.7×10^{-3} ($\pm 0.3 \times 10^{-3}$) sec^{-1}.

Also shown is the plot obtained for the isomerization of 11, R = Cp, to 10A and 10S in acetic acid in the presence of silver acetate. The rate constant is given in Table I.


154
3.0
2.0
1.0
ln(c_o/c)
1E, R = 3P
36-d_o
1E, R = Me
5
10
15
Time (min)


3.0
2.0
1.0
ln(c_o/c)
1E, R = Cp
4
1Z, R = Me
20
40
60
Time (min)


ln(c$_o$/c)
3.0
2.0
1.0
1Z, R = 3P
1Z, R = Cp
(R = Cp) 200 400 600
(R = 3P) 100 200 300
Time (min)


4.0
3.0
2.0
1.0
ln(c_o/c)
11, R = Cp
60
120
180
Time (hr)

References

1. For discussions of carbonium ion history, see: (a) D. Bethell and V. Gold, "Carbonium Ions," Academic Press, London, 1967, pp 6-11; (b) C. D. Nenitzescu, in "Carbonium Ions," vol. 1, G. A. Olah and P. v. R. Schleyer, Ed., Interscience, New York, N. Y., 1968, p 1.

2. See ref. 1(a), p 13ff.

3. R. C. Fort, Jr., and P. v. R. Schleyer, Adv. Alicylic Chem., 1, 283 (1966).

4. T. L. Jacobs and S. Searles, Jr., J. Amer. Chem. Soc., 66, 686 (1944).

5. M. S. Newman and A. E. Weinberg, ibid., 78, 4654 (1956).

6. C. A. Grob and G. Cseh, Helv. Chim. Acta, 47, 194 (1964); C. A. Grob, J. Csapilla, and G. Cseh, ibid., 1590.

7. (a) M. Hanack and H.-J. Schneider, Angew. Chem. Int. Ed. Eng., 6, 666 (1967); (b) C. A. Grob, Chimia, 25, 87 (1971); (c) Z. Rappoport, T. Bässler, and M. Hanack, J. Amer. Chem. Soc., 92, 4985 (1970); (d) R. C. Fahey, Top. Stereochem., 3, 237 (1968); (e) H. G. Richey and J. M. Richey, in ref. 1(b), vol. 2, 1970, p 38.

8. (a) G. Modena and U. Tonellato, Adv. Phys. Org. Chem., 9, 185 (1971); (b) M. Hanack, Accounts Chem. Res., 3, 209 (1970); (c) P. J. Stang, Prog. Phys. Org. Chem., 10, in press.

9. L. L. Miller and D. A. Kaufman, J. Amer. Chem. Soc., 90, 7282 (1968).

10. D. R. Kelsey and R. G. Bergman, ibid., 92, 228 (1970); ibid., 93, 1941 (1971).

11. Z. Rappoport and Y. Apeloig, ibid., 91, 6734 (1969); Z. Rappoport and A. Gal, ibid., 5246; see also Z. Rappoport and Y. Apeloig, Tetrahedron Lett., 1817, 1845 (1970); Z. Rappoport and M. Atida, ibid., 4085; Z. Rappoport and A. Gal, ibid., 3233; Z. Rappoport and J. Kaspi, ibid., 4039 (1971); J. Amer. Chem. Soc., 92, 3220 (1970).

12. W. D. Pfeifer, C. A. Bahn, P. v. R. Schleyer, S. Bocher, C. E. Harding, K. Hummel, M. Hanack, and P. J. Stang, ibid., 93, 1513 (1971).

13. (a) A portion of this work as been presented in preliminary

form: T. C. Clarke, D. R. Kelsey, and R. G. Bergman, ibid., 94, 3626 (1972); (b) T. C. Clarke and R. G. Bergman, ibid., 3627.

14. H. C. Brown and A. Tsukamoto, ibid., 83, 4549 (1961).

15. (a) R. J. Rawson and I. T. Harrison, J. Org. Chem., 35, 2057 (1970); (b) H. E. Simmons and R. D. Smith, J. Amer. Chem. Soc., 80, 5323 (1958); ibid., 81, 4256 (1959).

16. See L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," vol. 1, Wiley, New York, N. Y., 1967, p 142.

17. S. A. Sherrod and R. G. Bergman, J. Amer. Chem. Soc., 91, 2115 (1969); ibid., 93, 1925 (1971).

18. D. H. R. Barton, R. E. O'Brien, and S. Sternhell, J. Chem. Soc., 470 (1962); A. Pross and S. Sternhell, Aust. J. Chem., 23, 989 (1970).

19. R. G. Weiss and E. I. Snyder, J. Org. Chem., 35, 1627 (1970).

20. D. R. Kelsey, J. Amer. Chem. Soc., 94, 1764 (1972).

21. E.g. see R. A. Sneen and J. W. Larsen, ibid., 91, 6031 (1969); J. L. Kurz and J. C. Harris, ibid., 92, 4117 (1970); D. J. Raber, J. M. Harris, R. E. Hall, and P. v. R. Schleyer, ibid., 93, 4821 (1971).

22. R. K. Birdwhistell and E. Griswold, ibid., 77, 873 (1955).

23. M. M. Jones and E. Griswold, ibid., 76, 3247 (1954).

24. Y. Pocker and D. N. Kevill, ibid., 87, 4760, 4771, 4778, 5060 (1965).

25. G. S. Hammond, M. F. Hawthorne, J. H. Waters, and B. M. Graybill, ibid., 82, 704 (1960).

26. See A. A. Baladin, Adv. Catalysis, 19, 1 (1969).

27. N. Kornblum, W. J. Jones, and D. E. Hardies, J. Amer. Chem. Soc., 88, 1704 (1966); N. Kornblum and D. E. Hardies, ibid., 1707.

28. G. F. P. Kernaghan and H. M. R. Hoffmann, ibid., 92, 6988(1970).

29. G. S. Hammond, ibid., 77, 334 (1955).

30. J. A. Hirsch, Top. Stereochem., 1, 199 (1966).

31. A. Streitwieser and T. D. Walsh, J. Amer. Chem. Soc., 87, 3686 (1965).

32. E.g. see ref 1(a), p 208ff.

33. W. G. Young, S. H. Sharman, and S. Winstein, J. Amer. Chem. Soc., 82, 1376 (1960); ref 1(a), p 177ff.

34. See discussion by A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed., Wiley, New York, N. Y., 1961, pp 296-300.

35. S. Winstein, E. Clippinger, A. H. Fainberg, and G. C. Robinson, J. Amer. Chem. Soc., 76, 2597 (1954).

36. R. A. Clark and R. A. Fiato, ibid., 92, 4736 (1970); and references therein.

37. T. S. Sorensen and K. Rajeswari, ibid., 93, 4222 (1971).

38. L. M. Stock and H. C. Brown, Adv. Phys. Org. Chem., 1, 35 (1963).

39. P. R. Wells, "Linear Free Energy Relationships," Academic Press, London, 1968.

40. (a) R. C. Hahn, R. F. Carbin, and H. Shechter, J. Amer. Chem. Soc., 90, 3404 (1968); (b) L. B. Jones and V. K. Jones, Tetrahedron Lett., 1493 (1966); (c) L. B. Jones and S. S. Eng, ibid., 1431 (1968); (d) R. Ya. Levina, P. A. Genbitskii, L. P. Guseva, and P. K. Agasyan, Zh. Obshch. Khim., 34, 146 (1964); J. Gen. Chem. USSR, 34, 144 (1964).

41. H. C. Brown and J. D. Cleveland, J. Amer. Chem. Soc., 88, 2051 (1966).

42. R. G. Pews, ibid., 89, 5605 (1967); R. T. C. Brownlee, R. E. J. Hutchinson, A. R. Katritzky, T. T. Tidwell, and R. D. Topsom, ibid., 90, 1757 (1968).

43. M. Charton and H. Meislich, ibid., 80, 5940 (1958); J. Hine and W. C. Bailey, Jr., ibid., 81, 2075 (1959).

44. For discussions of 1,2 shifts, see: J. L. Fry and G. J. Karabatsos, in ref 1(b), vol. 2, p 521; ref 1(a), pp 204-218; Y. Pocker, in "Molecular Rearrangements," vol. 1, P. deMayo, Ed., Interscience, New York, N. Y., 1963, pp 9-25; J. A. Berson, in ibid., pp 139-155.

45. J. D. Roberts and J. A. Yancey, J. Amer. Chem. Soc., 74, 5943 (1952).

46. J. D. Roberts, W. Bennett, R. E. McMahon, and E. W. Holroyd, Jr., ibid., 74, 4283 (1952).

47. P. C. Myhre and E. Evans, ibid., 91, 5641 (1969).

48. J. J. Dannenberg, D. H. Weinwurzel, K. Dill, and B. J. Goldberg, Tetrahedron Lett., 1241 (1972).

49. G. A. Olah and J. Lukas, J. Amer. Chem. Soc., 89, 4739, (1967).

50. G. A. Olah and A. M. White, ibid., 91, 5801 (1969).

51. G. A. Olah and J. Lukas, ibid., 90, 933 (1968).

52. M. Saunders, E. L. Hagen, and J. Rosenfeld, ibid., 90, 6882 (1968).

53. (a) J. E. Williams, Jr., V. Buss, L. C. Allen, P. v. R. Schleyer, W. A. Lathan, W. J. Hehre, and J. A. Pople, ibid., 92, 2141 (1970); (b) G. V. Pfeiffer and J. G. Jewett, ibid., 92, 2143 (1970); (c) W. A. Lathan, W. J. Hehre, and J. A. Pople, ibid., 93, 808 (1971); (d) R. Sustmann, J. E. Williams, M. J. S. Dewar, L. C. Allen, and P. v. R. Schleyer, ibid., 91, 5350 (1969); (e) A. S. Denes, I. G. Csizmadia, and G. Modena, Chem. Commun., 8 (1972).

54. See discussion by Modena and Tonellato, ref 8(a).

55. (a) M. A. Imhoff, R. H. Summerville, P. v. R. Schleyer, A. G. Martinez, M. Hanack, T. E. Dueber, and P. J. Stang, J. Amer. Chem. Soc., 92, 3802 (1970); (b) P. J. Stang and T. E. Dueber, unpublished results, see ref 8(c); (c) W. M. Jones and F. W. Miller, J. Amer. Chem. Soc., 89, 1960 (1967); (d) D. Y. Curtin, J. A. Kampmeier, and B. R. O'Connor, ibid., 87, 863 (1965).

56. K. Bott, Tetrahedron Lett., 1747 (1969); Chem. Commun., 1349 (1969); T. Sasaki, S. Eguchi, and T. Toru, ibid., 780 (1968).

57. S. Winstein and N. J. Holness, J. Amer. Chem. Soc., 77, 5562 (1955).

58. V. J. Shiner, Jr., and J. G. Jewett, ibid., 86, 945 (1964); ibid., 87, 1382, 1383 (1965); and references therein.

59. R. J. Hargrove, T. E. Dueber, and P. J. Stang, Chem. Commun., 1614 (1970); see also ref 8(c).

60. R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," 2nd ed., John Wiley and Sons, New York, N. Y., 1967, pp 19-35.

61. S. Winstein, E. C. Friedrich, R. Baker, and Y.-I. Lin, Tetrahedron, Suppl. No. 8, 22, 621 (1966).

62. P. v. R. Schleyer, J. L. Fry, L. K. M. Lam, and C. J. Lancelot, J. Amer. Chem. Soc., 92, 2542 (1970); A. Diaz and S. Winstein, ibid., 91, 4300, 5635 (1969); T. W. Bently, F. L. Schadt, and P. v. R. Schleyer, ibid., 94, 944 (1972).

63. Rearrangement occurs when cyclopropylcarbinol is treated with thionyl chloride: M. C. Caserio, W. H. Graham, and J. D. Roberts, Tetrahedron, 11, 171 (1960).

64. Z. Majerski and P. v. R. Schleyer, J. Amer. Chem. Soc., 93, 665 (1971); c.f. D. J. Raber, J. M. Harris, and P. v. R. Schleyer, ibid., 4829.

65. See G. A. Olah, C. L. Jeuell, D. P. Kelly, and R. D. Porter, ibid., 94, 146 (1972); and references therein.

66. H. Hart and J. M. Sandri, ibid., 81, 320 (1959); M. Vogel and J. D. Roberts, ibid., 88, 2262 (1966).

67. G. A. Olah, A. M. White, J. R. DeMember, A. Commeyras, and C. Y. Lui, ibid., 92, 4627 (1970).

68. H. O. House and H. W. Thompson, J. Org. Chem., 26, 3729 (1961).

69. C. L. Wilson, J. Amer. Chem. Soc., 69, 3002 (1947).

70. See J. C. H. Hwa and H. Sims, Org. Syn., 41, 49 (1961).

71. G. Köbrich. D. Merkel, and K.-W. Thiem, Chem. Ber., 105, 1683 (1972).

72. See W. R. Kirner and W. Windus, Org. Syn., Coll. Vol. II., 136 (1943).

73. See H. G. Kuvila, Accounts Chem. Res., 1, 229 (1968) for leading references.

74. R. A. Bartsch, J. Org. Chem., 35, 1023 (1970).

Part II: Molecular Orbital Calculations on Cationic Intermediates and Displacement Reactions

This part has been published in full: D. R. Kelsey and R. G. Bergman, "Application of the Extended Hückel Molecular Orbital Method to the Properties of Vinyl Cations. Conformational Energies of Some 1-Cyclopropylvinyl Cations and a Comparison of S_N2 Displacements at Saturated and Vinyl Carbon," Journal of the American Chemical Society, 93, 1953 (1971).

Part III. On the Complexation of NMR Lanthanide Shift Reagents with Organic Substrates.

Although rare-earth ions and complexes had been used in nuclear magnetic resonance (nmr) spectroscopy prior to 1969 (1-4), it was not until that time that the utility of such "shift reagents" became evident. Hinckley's report (5) on the effect of $Eu(dpm)_3 \cdot 2py$ * on the nmr spectrum of cholesterol initiated an increasing interest in the use and properties of such reagents (6). Shortly thereafter, Sanders and Williams (7) showed that $Eu(dpm)_3$ itself was a superior reagent. Numerous reagents and variations have been proposed (8-15), but the $Eu(fod)_3$ and $Pr(fod)_3$ reagents reported by Rondeau and Sievers (16) appear to be the most useful to date.

It was proposed initially (5) that the shifts induced by the reagents could be related to the pseudo-contact model, such as the equation of McConnell and Robertson (17), eq 1, where δ^i is the paramagnetic shift in ppm , r_i is the distance of proton i from the metal atom in the substrate-reagent complex, C is a collection of constants including a 1/T temperature dependence, and θ_i is the angle between the principle magnetic axis and vetor r_i. This equation strictly applies only

$$\delta^i = C(3\cos^2\theta_i - 1)/ r_i^3 \qquad (1)$$

to axially symmetric complexes (9, 17), and more complex equations are available for complexes of C_2 symmetry (5, 18-19). Hinckley

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* $Eu(dpm)_3$ = tris(2, 2, 6, 6-tetramethylheptane-3, 5-dionato)europium (III); py = pyridine; $Eu(fod)_3$ = tris(1, 1, 1, 2, 2, 3, 3, -heptafluoro-7, 7= dimethyloctane-4, 6-dionato)europium (III).

5, 20) pointed out that such symmetry may not obtain for the substrate-reagent complex or that the assumptions used to develop the equations might not apply. It has also been suggested that the principle magnetic axis may not be known for the calculation of θ_i (eq 1) and that second-order paramagnetic effects rather than pseudo-contact effects may predominate for europium reagents (21). Nonetheless, numerous investigations have used eq 1 to assign observed proton shifts, particularly the successful treatment of Willcott and coworkers (22). The pseudo-contact model appears to be a good approximation, although there may be some cases in which it is neither strictly (5, 9) or usefully (23) applicable.

It was found quite early in the work on shift reagents that plots of the observed shift, Δ_{obsd}^{i}, of proton i against the E_t/S_t ratio were apparently linear (24), where E_t is the total concentration of reagent E, and S_t is the total concentration of substrate S. We noted however that there were indications of non-linearity at low (7b, 24-28) and high (16, 29-31) E_t/S_t and that the slope of such plots depended upon the substrate concentration (8b, 32, 33).

It had been recongnized that the shift reagent phenomenon was related to a rapid equilibrium on the nmr time scale between free and complexed substrate, eq 2 (7b, 20, 34). However, at the time

$$pS + qE \rightleftharpoons (S_pE_q) \qquad (2)$$

this work was undertaken and presented in preliminary form (35), there had been no explicit treatment of the equilibrium. We briefly

outlined (35) two derivations which led to (1) a method for characterizing spectral shifts that is largely independent from the pseudo-contact model (eq 1) and from concentration effects and to (2) a method for estimating the complex formation equilibrium constants, K, and the bound induced shifts, Δ_{max}. We present here a more complete analysis and discussion of these methods and applications to an extended set of substrates.

A. The Standard Proton Method.

If we assume a single equilibrium, eq 2, then the observed shifts of proton i must be the weighted average (4) of the environments of i, eq 3, where δ_{obsd}^{i} is the observed chemical shift of proton i, δ_{o}^{i} is

$$\delta_{obsd}^{i} = (\delta_{o}^{i}[S] + p \cdot \delta_{max}^{i}[S_pE_q])/S_t \qquad (3)$$

the chemical shift of i in the absence of reagent E, [S] is the concentration of free substrate, and δ_{max}^{i} is the chemical shift of i in the complex $[S_pE_q]$*. One can then derive the relationship between Δ_{obsd}^{i} and E_t/S_t, eq 4, where $\Delta_{obsd}^{i} = \delta_{obsd}^{i} - \delta_{o}^{i}$ and $\Delta_{max}^{i} = \delta_{max}^{i} - \delta_{o}^{i}$, and E is the concentration of free reagent (36). When

$$\Delta_{obsd}^{i} = (p/q)\,\Delta_{max}^{i}(1 - E/E_t)(E_t/S_t) \qquad (4)$$

---

* For simplicity, concentration brackets are generally omitted.

the complex formation is 1:1, p=q=1, then this equation is the same as previously given (35). The equation qualitatively accounts for the observed behavior in plots of Δ_{obsd}^{i} vs. E_t/S_t. At high E_t/S_t, the slope must approach zero, as is observed (16). At low E_t/S_t, the plot can be linear only if the factor E/E_t is constant. At high S_t, E/E_t approaches zero, and the limiting slope is predicted to be $(p/q)\Delta_{max}^{i}$. Plots of Δ_{obsd}^{i} vs. E_t/S_t have been extrapolated to $E_t/S_t = 1.0$ to obtain what were believed to be characteristic shifts, Δ_{Eu} (24). Equation 4 shows that such extrapolated values are related to Δ_{max}^{i} if the substrate concentration, S_t, is high, as has been recently pointed out by Armitage and coworkers (37).

Equation 3 is somewhat oversimplified, since if proton i of the bound substrate exists in one or more preferred orientations with respect to the lanthanide atom, then the finite (or infinite) sum of these configurations is required, e.g. eq 5, where n_k is the fraction

$$\delta_{max}^{i}(S_pE_q) = \sum_k n_k \delta_{max_k}^{i}(S_pE_q)_k \qquad (5)$$

of complex in form $(S_pE_q)_k$. At a given temperature, the effect of such a sum will be constant, so the effective equation is still of the form of eq 4. This can be extended to treat systems (38) where substrate conformational equilibria are perturbed by complexation of the substrate to the reagent.

Of course, more than a single equlibrium process may occur between reagent and substrate. If we assume a two-stage equilibrium

that is 2:1 overall, eqs 6 and 7, then a similar treatment to that

$$S + E \underset{}{\overset{K_1}{\rightleftharpoons}} (SE) \qquad (6)$$

$$(SE) + E \underset{K_2}{\overset{}{\rightleftharpoons}} (S_2E) \qquad (7)$$

given above gives eq 8, where subscripts 1 and 2 refer to mono- and dicomplexed species, respectively.

For two protons, i and j , in the same substrate molecule, one obtains by division eqs 9 and 10 from eqs 4 and 8, respectively. Equation 9 shows that if a single equilibrium obtains, then no matter

$$\Delta_{obsd}^{\,i} = [(\Delta_{max_1}^{\,i}(SE) + 2\Delta_{max_2}^{\,i}(S_2E))/E_t](E_t/S_t) \qquad (8)$$

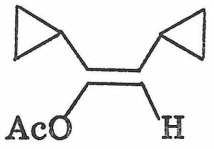
$$\Delta_{obsd}^{\,i} = (\Delta_{max}^{\,i}/\Delta_{max}^{\,j})\,\Delta_{obsd}^{\,j} \qquad (9)$$

$$\Delta_{obsd}^{\,i} = \frac{[\Delta_{max_1}^{\,i}(SE) + 2\Delta_{max_2}^{\,i}(S_2E)]}{[\Delta_{max_1}^{\,j}(SE) + 2\Delta_{max_2}^{\,j}(S_2E)]}\,\Delta_{obsd}^{\,j} \qquad (10)$$

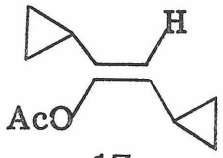
what the stoichiometry (p:q) , a plot of $\Delta_{obsd}^{\,i}$ vs. $\Delta_{obsd}^{\,j}$ will be a straight line whose slope is independent of substrate or reagent concentrations and whose intercept is zero. On the other hand, if two or more complexes are important, eq 10, then the slope is not constant unless $(SE)/(S_2E)$ is constant or the $\Delta_{max_1}/\Delta_{max_2}$ ratio is the same for both protons i and j.

Initially the correct assignments of geometrical isomers 1E and

1Z were particularly important to us in connection with our studies with Professor Bergman on the stereochemistry of vinyl iodide



1E



1Z

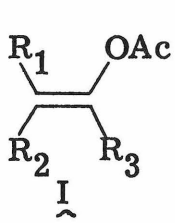
reactions (39). Unfortunately, the isomer mixture was completely inseparable under a variety of preparative gas chromotography conditions, although the relative ratio of the isomers (1:1.5, unassigned) could be determined by analytical vpc (39b). The unshifted nmr spectrum of the mixture did not allow unequivocal assignments to be made. A priori, the pseudo-contact equation (eq 1) qualitatively predicts that the vinyl proton in 1E should show a larger shift than the vinyl proton in 1Z for complexation of reagent at the carbonyl oxygen (40). Thus, the slope of the plot of Δ_{obsd}^{i} vs. E_t/S_t should be larger for the 1E vinyl proton than for the 1Z vinyl proton (7, 24). However, since the complexations of 1E and 1Z with reagent are dependent upon their concentrations and the equilibrium constants, the competition for reagent could obscure the expected slope relationships.

However, eq 9 predicts that the plot of the vinyl proton shifts with added reagent versus the acetoxy methyl (Ac) shifts will be independent of competition effects. Furthermore, since there is no obvious reason why Δ_{max} for Ac will change greatly for different substrates, we reasoned that the observed slopes $\Delta_{max}^{Ac}/\Delta_{max}^{j}$ should be characteristic of the relationship between Ac and proton j.

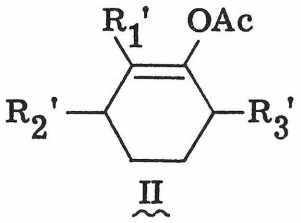
Thus when the same treatment is applied to model compounds in which the protons can be readily assigned, similar slopes should be found for protons of a given stereochemical relationship to Ac.

Experimental Method and Results

When the nmr spectra of the mixture of 1E and 1Z were taken with successive additions of $Eu(fod)_3$, not only did the shifted spectra allow separate integrations of each vinyl proton and Ac so as to assign the correct pairing and isomer ratio (1:1.5, same as vpc), but the plots of Δ_{obsd}^{Ac} vs. Δ_{obsd}^{vinyl} for each isomer gave excellent straight lines with least-squares slopes of 1.92 and 1.34 and nearly zero intercepts. We then applied the analysis to model compounds 4 - 11 of general structure I and II (see Experimental). We have also assigned the isomers of 2 and 3 by this method. The slopes are given in Table I.



I



II

In general, substrate concentrations were 10% or less in CCl_4 and $Eu(fod)_3$ was added as a 0.1 - 0.5 M solution in CCl_4. The maximum E_t/S_t ratio used was ~1.0, although no attempt was made to determine the precise concentrations for these experiments. The reproducibility of the slopes given in Table I was quite good (<3% variation in those cases tested). The correlation coefficients for the plots were never <0.9996 and usually >0.9999. The calculated intercepts were always $<|0.10$ ppm$|$ and normally $<|0.05$ ppm$|$.

Table I. The Characteristic $\Delta_{max}^{Ac}/\Delta_{max}^{j}$ Slopes for Vinyl Acetates I and II with Eu(fod)$_3$. [a,b]

Compd	R_1	R_2	R_3 [c]
1E [d,e]	H, 1.34 ±.03	Cp	Cp
1Z [d,e]	Cp	H, 1.92 ±.01	Cp
2E [e]	H, 1.10 ±.02	$Et_2C\underline{H}$, 2.41	Cp, 1.19
2Z [e]	$Et_2C\underline{H}$, 1.18	H, 1.69 ±.02	Cp, 1.14
3E [e]	CH_3, 2.09	$PrC\underline{H}_2$, 3.92	CH_3, 1.62
3Z [e]	$PrC\underline{H}_2$, 1.88	CH_3, 4.16	CH_3, 1.60
4	H, 1.55	H, 2.63	CH_3, 1.71
5E	H, 1.58	CH_3, 5.25	CH_3, 1.64
5Z [d]	CH_3, 2.36	H, 2.48	CH_3, 1.77
6 [d]	H, 1.46	H, 2.54	CH_3CH_2, 3.53 1.60
7	H, 1.44	H, 2.51	Cp, 1.56
8E	H, 1.38 ± .03	CH_3, 5.20 ±.04	Cp
8Z	CH_3, 2.11	H, 2.21	Cp
9	H', 1.53	H', 5.49	H', 1.38
10 [d]	CH_3', 2.13	H'	H', 1.33
11 [d]	H', 1.40	H'	CH_3', 2.33

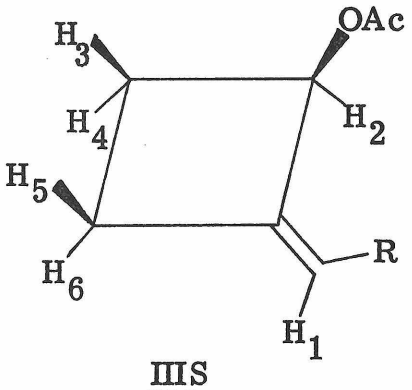
[a] Cp = cyclopropyl; Pr = n-propyl . [b] Errors shown in some cases are for duplicate runs using different substrate concentrations. [c] Value given for Cp is the methine proton; for 6, lower value is for methylene protons. [d] Data obtained for mixtures: 1Z + 1E, 5Z + 6, and 10 + 11. [e] Assigned isomer.

This allowed confident extrapolation back to $E_t = 0.0$ to find δ_o^j in cases where the unshifted spectrum peaks were obscured or not readily assigned initially (see Experimental).

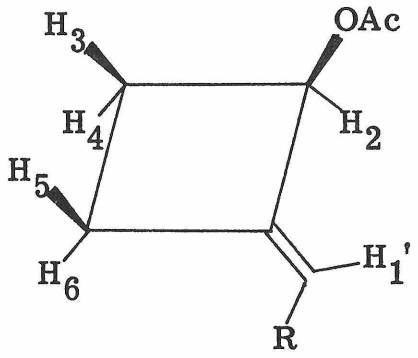
The slopes in Table I fall into the following ranges: 1.69 - 2.63 for vinyl protons trans to Ac; 1.10 - 1.58 for vinyl protons cis to Ac; 2.41 - 5.49 for allylic protons trans to Ac; 1.18 - 2.13 for allylic protons cis to Ac; 1.14 - 1.77 for allylic protons gem to Ac; and 2.33 - 3.53 for homoallylic protons gem to Ac.

We have also applied this method to several allyl acetates of general structures IIIS, IIIA, and IV. These acetates were obtained from the solvolyses of 1-cyclopropyl-1-iodo-2-substitutedethylenes (39), and the correct syn-anti assignments for III were necessary for correct interpretation of our data in those studies (39). The compounds were available in nearly pure form, but often in very small amounts (<2 mg). The standard proton method offered a quick and reliable means of assigning the isomers without worrying about concentration determinations. The data for these compounds along with those for compounds 12, 17, and 18 are given in Table II.

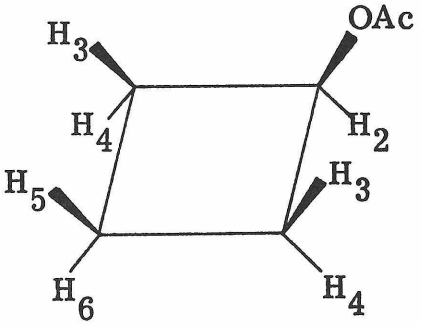
The vinyl protons are the key structural feature of III, and show well-defined ranges of 1.85 - 1.96 and 4.41 - 4.69, for syn and anti relationships, respectively. The assignments of the slopes of the vinyl protons and the protons of substituent R rest upon the obvious qualitative distance factor shown in the series of vinyl acetates, i.e. protons trans (anti) from the Ac standard show larger slopes than do cis (syn) protons. The data in Table II showed that our tentative previous assignments (39a) of 14S and 14A were reversed.



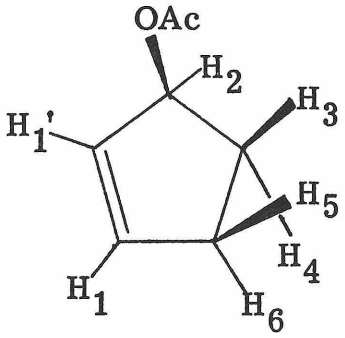
IIIS



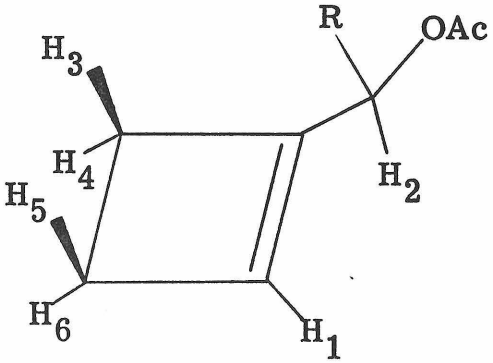
IIIA



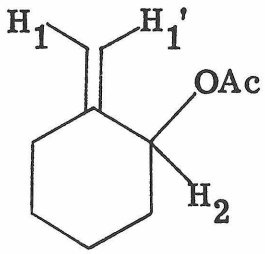
12



17



IV



18

Table II. The Characteristic $\Delta_{max}^{Ac}/\Delta_{max}^{j}$ Slopes for Allyl Acetates IIIS, IIIA, IV, 17, and 18 and Cyclobutyl Acetate, 12, with Eu(fod)$_3$. [a,b]

Compd	$H_1(H_1')$	H_2	H_3	H_4	H_5	H_6	R
12 [c]		.80 ± .02	1.92 ± .02	2.49 ± .03	4.87 ± .04	6.15 ± .15	
13 [d]	4.69 1.89'	.78	1.85	2.62	4.35	5.98	H
14S	4.73	.78					CH_3, 3.06
14A	1.85'	.81					CH_3, 8.97
15S	4.50	.78					Cp
15A [e]	1.95'	.75	1.74	3.04	4.14	6.27	Cp, 8.93
16S	4.41	.76	1.88	2.39	3.96	5.36	$Et_2C\underline{H}$, 1.51
16A	1.96'	.75	1.69	2.44	4.04	5.47	$Et_2C\underline{H}$, 6.55
17	5.60 1.78'	.78	1.67	2.94	4.08	6.95	
18	4.71 2.22'	.78					
19 [f]	3.53	.74	3.15		7.69		CH_3, 2.19
20 [f]	3.33	.73	3.11		8.22		Cp

Table II. (cont)

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[a] Ring proton (H_3 - H_6) slopes for 12 - 17 from 220 MHz spectra. [b] Ring proton (H_3 - H_6) slopes for 19 and 20 from 60 MHz spectra. [c] Errors given for 12 are estimated error in slope for the least-squares plot. [d] Structure III, R = H. [e] Value given under R is for cyclopropyl methine. [f] Structure IV.

Included in Table II are the slopes found for the ring protons. The 220 MHz spectra showed four single-proton multiplets for compounds of type III, and these were assigned by comparing the slopes to those found for model compound 12, cyclobutyl acetate. The shifted 220 MHz spectra of 12 showed two two-proton multiplets and two one-proton multiplets. The observed slopes of each pair of multiplets were assigned according to the cis or trans relationship to the acetoxy group (see above). Even though 12 may be conformationally more mobile than the 2-exo-methylenecyclobutyl acetates, IIIS and IIIA, the slopes found for the ring protons in these cases are quite comparable to those for 12. 2-Cyclopentenyl acetate, 17, was included in this series to determine if this structure could be distinguished from IIIA. Both H_1 and H_6 of 17 show larger slopes than the corresponding protons in 12, 13, 15A, or 16.

Isomers 19 and 20 (structure IV) are easily differentiated from the III isomers by their vinyl proton slopes. The ring protons in the shifted spectra consisted of two two-proton multiplets, as required, and the large slopes found for the H_5-H_6 methylenes indicate the remote location from the acetoxy complexation site.

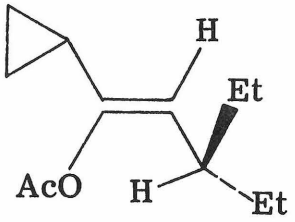
Again, all plots were quite linear (correlation coefficients >0.99995). Only in those cases where the relative shift was small, e.g. the methyl protons of 14A, or where the peaks were broad multiplets, e.g. ring protons in 19 and 20, did the correlation coefficients drop to as low as 0.9993. The calculated statistical error for the slopes was always $< 3\%$.

Discussion

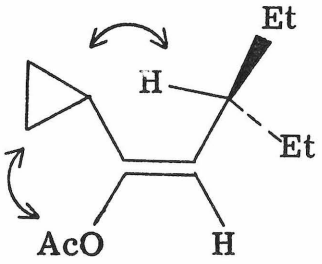
Conformational Effects.

The ranges of the slopes observed for the various types of protons in the vinyl acetates (Table I) were summarized above. However, note that when substituent R_1 or R_2 is relatively bulky, e.g. 3-pentyl or n-butyl, the slopes are often at the extremes of the ranges. In particular, the values for R_2 = H of 1Z and 2Z fall at 1.92 and 1.69, respectively, but the other protons of this class show slopes in the range 2.21 - 2.63. The slopes for R_2 = allylic protons for 2E, 3E, and 3Z are 2.41, 3.92, and 4.16, respectively, but the others have slopes of 5.20 - 5.49. The slope for R_1 = H of 2E is particularly low, as are the slopes for R_1 = allylic for 2Z and 3Z.

We feel this reflects steric effects of the 3-pentyl, n-butyl, or cyclopropyl substituents upon the conformations of the free and/or complexed substrates. The 3-pentyl group in particular should prevent free rotation about the carbon-carbon bond connecting the substituent to the double bond. The allylic methine will be held, on the average, closer to the complexation site (Ac) in 2Z, as compared to, say, the methyl protons of 8Z. Therefore, the slope for this methine proton will be less, and this is observed. Steric crowding between

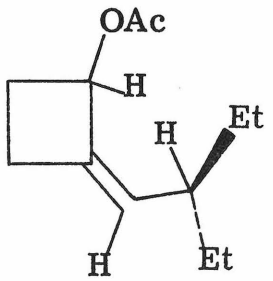


2Z



2E

the 3-pentyl group and the reagent-complexed acetoxy group may force the lanthanide atom to be situated somewhat above the plane defined by the double bond, and this may account for the low slope observed for the trans proton in 2Z. In 2E, a similar conformational restriction holds the 3-pentyl methine nearer to the acetoxy which results in a low slope. There can also be a "domino" steric effect (as shown by the arrows above) which can reduce the slope for the cis vinyl proton of 2E because the acetoxy carbonyl may be restricted to spending more time nearer the vinyl proton than is the case for, say, 8E. The coupling constants between the vinyl protons and the 3-pentyl methines are 10 Hz for both 2Z and 2E (39b), which suggest dihedral angles of ca. 180° (41) as shown above. Similar steric effects are probably operative for n-butyl and possibly cyclopropyl substitutents. A restricted rotation effect also explains the low methine slopes for 16S and 16A compared to the methyl slopes in 14S and 14A (Table II). Here again, the methine - vinyl coupling constant is large (~10 Hz for 16S and ~9.5 Hz for 16A) (39b).



16S

We have only a qualitative indication of the conformational effects that can be operative in these substrates, but clearly the results indicate that care must be taken in assuming conformationally rigid

models when applying the pseudo-contact equation, eq 1 (see above), or in assuming the axial symmetry required for strict application of eq 1 (9, 42). In particular, the above discussion suggests that the averaged proton-lanthanide relationships, e.g. r_i and θ_i, must be used when considering protons located on conformationally mobile portions, e.g. methyl, of the substrate structure in question.

Even when sterically bulky groups may perturb the conformations of the free or complexed substrate, the characteristic slopes for the various classes of protons in the vinyl acetates studied here are separated into distinct ranges. However, the effects noted above serve as a caution that assignments made by the standard proton method are best made when the model (known) compounds most closely resemble the substrate (unknown) structure.

The Linearity of the Plots.

As noted above, the linearity of the Δ_{obsd}^{Ac} vs. Δ_{obsd}^{j} plots in all cases was excellent through a range of E_t/S_t = 0.0 - ca. 1.0. This implies a predominant single equilibrium in this ratio range for the acetates, which was assumed in deriving eq 9. The coefficients p and q in eq 4 cannot be obtained, of course, from these experiments. We have noted some generally small variations in the Δ_{obsd}^{i} vs. Δ_{obsd}^{j} plots for other substrates, however. The slopes at low ($0.0 < E_t/S_t < \sim 1$) and high ($\sim 1 < E_t/S_t < \sim 5$) E_t/S_t for various proton pairs (i/j) are: 2-butanone, 1.04 and 0.95 (Ac/CH_2), 1.48 and 1.44 (Ac/CH_3); tetrahydrofuran (THF), 2.40 and 2.11 (α/β); and 2-propanol, 1.79 and 2.30 (CH/CH_3). The linearity within a given E_t/S_t range is good in these cases, but the overall plots show

some curvature at high E_t/S_t, particularly for THF and 2-propanol This curvature suggests that more than one equilibrium is operative over the entire E_t/S_t range, e. g. eq 10. (This does not suggest, however, that 2:1 complexation necessarily obtains, since two competing 1:1 equilibria will give an equation of the same form as eq 10.) We shall have more to say about this observation in Section B.

In spite of such effects at very large E_t/S_t ratios, the linearity of the plots is generally excellent over a wide, experimentally useful range of Δ_{obsd}, and extrapolations of the plots to $E_t = 0.0$ can be confidently made in most cases. Caution may be needed, however, in extrapolating data obtained only at large E_t/S_t to $E_t = 0.0$, since slight curvatures in the plots, not necessarily evident in a limited E_t/S_t range, could lead to some inaccuracy in the δ_o^i obtained.

Conclusions

It is evident from the above results that the standard proton treatment of the $Eu(fod)_3$-shifted nmr spectra of several vinyl and allyl acetates allows rapid and reliable structural assignments to be made. The method has several advantages: (1) The concentrations of substrate and reagent need not be known, a particular advantage when only a small amount of substrate is available. (2) The pseudo-contact parameters (eq 1) need not be "guesstimated" so long as suitable model substrates are available. (3) Conformational effects which might otherwise obscure direct application of eq 1 can probably be circumvented in most cases. (4) Uncertainties in the appropriateness of the pseudo-contact model (see above) are avoided altogether. (4)

Mixtures of compounds of isomers can be explicitly analyzed. We know of no other treatment at present which can deal with this situation as effectively. (5) Impurities in the substrate, inert impurities in the shift reagent, and small amounts of solvent impurity (water) can have little effect upon the slopes.

Intramolecular standards have been recently used, although generally in a somewhat different manner and for different purposes than given in this report. In some cases, a given proton was assigned an arbitrary relative shift (1.0, 10, 100, etc) and the other proton shifts were normalized accordingly (43-46). In other cases, relative shift ratios (47-49) were used, especially in comparisons of the effects of different shift reagents (9a, 50-52). Peters and coworkers (53) plotted observed proton shifts against one another in order to extrapolate to $E_t = 0.0$, and Tsukida and Ito (44) analyzed a mixture of tocopherols using acetoxy protons as a standard. The Δ_{Eu} values (24, 54) (see above) represent characteristic shifts, of course, if the substrate concentration is large.

Of course, any pair of proton (or carbon, etc.) shifts can be plotted against each other, and such relationships may be useful in particular cases. Our approach here was to choose a reference proton whose Δ_{max} remains nearly constant for a large number of substrates. The acetoxy protons serve quite well in this regard. The variations in the slopes of different classes of protons that we have observed are rationalized quite effectively by conformational - steric effects, rather than by any variation in Δ_{max}^{Ac}. The reference proton itself is not structurally significant, which is an advantage

when different substrates are to be compared. Other functional groups may serve equally well as internal standards, particularly esters, amides, and perhaps sulfonates. Methyl ether protons could be used, although since the complexation site is much "closer" to the rest of the molecule compared to carbonyl oxygen of acetoxy, steric effects in the complexed substrate may complicate comparisons of methyl ethers.

B. The Estimation of K and Δ_{max}

If we assume a single equilibrium, eq 2, and further assume that $p = q = 1$, then at $S_t/E_t \gg 0.0$, where $S \approx S_t$, $K \approx (E_t - E)/(S_t)(E)$, and eq 11 is obtained from eq 4 (35). The exact solution of eq 4 in

$$(\Delta_{obsd})^{-1} \cong (\Delta_{max}{}^{i} E_t)^{-1} S_t + (\Delta_{max}{}^{i} E_t K)^{-1} \qquad (11)$$

$$(\Delta_{obsd})^{-1} \cong (2\Delta_{max} E_t)^{-1} S_t + (2\Delta_{max} E_t K S_t)^{-1} \qquad (12)$$

terms of E_t, S_t, K, and Δ_{max} (which involves solving a simple quadratic) has been given recently by Bouquant and Chuche (55) and by Wittstruck (56) in a slightly different, but equivalent, form. These

authors (55, 56) have reported K and Δ_{max} values for cholesterol obtained by a dilution method with $E_t/S_t = 1.0$. The simplified equation, eq 11, shows that at large S_t/E_t ratios, a plot of $(\Delta_{obsd})^{-1}$ vs. S_t will be linear at constant E_t if a 1:1 complex equilibrium obtains. The equilibrium constant K can be found without any knowledge of E_t, but if E_t is known, then Δ_{max} can be calculated from the observed slope. Alternatively, one can plot E_t/Δ_{obsd} vs. S_t if E_t changes.

If the assumed single equilibrium were such that p = 2 and q = 1, then a similar derivation for the condition $S_t/E_t \gg 0.0$, where $(S_t)^2 \approx (S)^2$, gives eq 12, in which a factor of 1/2 has been introduced into both terms on the right and a factor of $1/S_t$ into the "intercept" term. (In this case, as for mixed 1:1 + 2:1 equilibria, the solution of the exact equation is tedious and complex.)

A plot of $(\Delta_{obsd})^{-1}$ vs. S_t at constant E_t should be curved in this instance, particularly at low values of S_t, where the "apparent" intercept should increase, i.e. the plot should show positive curvature at low S_t provided K and/or Δ_{max} are not too large relative to E_t. In this case, neither K nor Δ_{max} can be obtained from the simple plot.

Experimental Method and Results.

We have briefly studied several representative organic substrates under the conditions of $S_t/E_t \gg 0.0$. Measured aliquots of substrate were added to a calculated concentration (0.008 to 0.025 M) of $Eu(fod)_3$ in CCl_4. In general, the proton shifts were measured

with S_t/E_t in the range 5 to 50, and the least-squares plots of $(\Delta_{obsd})^{-1}$ vs. S_t were made. At $S_t/E_t < 5$, where the assumption $S \approx S_t$ begins to break down, slight negative curvatures (but never positive curvatures, see above) were apparent (57). Alternatively, E_t/Δ_{obsd} vs. S_t plots were made, which allowed for minor corrections due to slight dilution of the reagent by added substrate volumes. The Δ_{max} and K values were calculated according to eq 11 from the least-squares slopes and intercepts. This data and the minimum observed correlation coefficients are given in Table III.

The K values listed are the averages of values calculated in repeated experiments, except for allyl acetate and DMSO, for the the various protons for which Δ_{max} is given. The calculated K values are not dependent upon the value given to E_t when treating the data in terms of eq 11, but are quite sensitive to δ_o^i, the initial unshifted reference point. When δ_o^i was arbitrarily varied by ±.2 Hz, K was affected by as much as 10% for $K < 100$ and up to 100% or more for $K > 100$. However, when δ_o^i was changed, the correlation coefficients for the plots also changed and gave an indication of the "best" δ_o^i value (within ±.4 Hz of the nominal measured value). This behavior reflects the fact that the intercept is very small when K is large, and small changes can cause large errors. Such errors are much smaller when K is <100. (Such errors can be reduced by using smaller E_t concentrations.)

The Δ_{max} values listed are estimated to be accurate to ±5-10%. The calculated Δ_{max} are not very sensitive to the choice of δ_o^i, but are affected by the value of E_t, i.e. errors in calculation of the

Table III. Estimations of K and Δ for Various Representative Organic Substrates with $Eu(fod)_3$. [a]

Compd	K [b]	CC [c]	Proton	Δ_{max} [d]	Δ_{lim} [e]	Δ_{Eu} [f]
Allyl acetate	26 ± 3	.99988	Ac	16.7 [h]	18.2	
			CH_2	16.8	14.6	
Isopropenyl acetate	25 ± 4	.99989	Ac	19.8		
			CH_3	10.9		
2-Butanone	30 ± 4	.99962	Ac	21.3	15.8	23.0
			CH_2	18.5	15.7	20.2
			CH_3	14.0	10.8	15.1
THF	58 ± 4	.99991		38.5	28.4	41.8
				15.5	12.7	16.7
2-Propanol	160 ± 60	.9998	CH	30.3	24.2	
			CH_3	17.0	12.8	
			OH		~80	
DMSO	318 ± 180	.99995	CH_3	8.6	7.2	9.3
					3.6 [g]	

Table III. (cont)

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[a] Probe temperature at 32° or 38°; there was no observable variation within this range. [b] Allyl acetate, 1 run; Isopropenyl acetate, 2 runs; 2-Butanone, 2 runs; THF, 3 runs; 2-Propanol, 2 runs; DMSO, 1 run. [c] CC = correlation coefficient; minimum value observed. [d] Calculated from $(\Delta_{obsd})^{-1}$ vs. S_t, eq 11. [e] Estimated from Δ_{obsd_f} vs. E_t/S_t at "saturation" (see text); obtained at 220 MHz, except for DMSO. [f] Approximates $(p/q)\Delta_{max}$, eq 4 (see text). [g] At -78° to -91° (see text). [h] Values probably too small do to inert impurities in one sample of reagent from Norell Chemical Co.

reagent concentration will be reflected in the Δ_{max} values. Since we have assumed that the purity of the reagent was 100% in calculating E_t and have implicitly assumed that the activity coefficient is 1.0 at 0.008 - 0.025 M, both of which would be difficult to determine, the effective concentration of reagent may be somewhat less than the calculated concentration. However, this means then that the calculated Δ_{max} are minimum values.

The ratios of various Δ_{max} values, $\Delta_{max}{}^{i}/\Delta_{max}{}^{j}$, are quite comparable to the independently obtained slopes from plots of $\Delta_{obsd}{}^{i}$ vs. $\Delta_{obsd}{}^{j}$ at $E_t/S_t < \sim 1$ (ratio from Table III, ratio eq 9, (proton i/ proton j)): allyl acetate, 0.99, 0.94 (Ac/CH_2); isopropenyl acetate, 1.82, 1.71 (Ac/CH_3); 2-butanone, 1.15, 1.04 (Ac/CH_2); 1.52, 1.48 (Ac/CH_3); THF, 2.48, 2.40 (α/β); 2-propanol, 1.78, 1.79 (CH/CH_3).

We also carried out "direct" estimations of Δ_{max} in some cases by plotting Δ_{obsd} (220 MHz) vs. E_t/S_t with the ratio carried out to ~5, where little incremental change in Δ_{obsd} occurred with additional reagent. Such plots allowed an estimation of the maximum observable shift, Δ_{lim}. These are given in Table III and are estimated to be accurate to ± 5%.

In Section A, we mentioned that at high S_t, the initial slope of eq 4 (at low E_t/S_t) is $(p/q)\Delta_{max}{}^{i}$. These slopes, Δ_{Eu}, found for plots of Δ_{obsd} vs. E_t/S_t with S_t = 1.9 - 2.7 M and E_t/S_t in the range 0.0 to 0.04, are given in Table III for the three substrates examined.

Discussion

The Equilibrium Constants, K.

The trend in K values shown in Table III follows the qualitative estimates given by Hart and Love (54) as esters≈ketones<ethers < alcohols. As pointed out above and by Armitage (37), when K is large, the intercept of eq 11 is very small and large errors can occur. The value given for 2-propanol (slightly larger than our previous estimate (35)) and for DMSO are both probably lower limits. Wittstruck (56) reports an equilibrium constant of 237 for cholesterol with $Eu(fod)_3$. At present, the equilibrium constants given in Table III should be regarded as semi-quantitative estimates of K.

The Stoichiometry of the Equilibrium.

There now exists some evidence that the major equilibrium in many cases is that forming a 1:1 complex. The dilution methods of Wittstruck (56) and Bouquant and Chuche (55) are based upon the assumption of 1:1 complexation at $E_t/S_t = 1.0$, and their data appear to fit this assumed stoichiometry. In another method, Roth and coworkers (58) found 1:1 complexation of $Eu(fod)_3$ with t-butyl alcohol but possibly mixed 1:1 and 2:1 (p:q) complexations for t-butylamine. Huber and Seelig (59) reported 1:1 complexation between pyridine and $Eu(dpm)_3$ at $S_t/E_t \gg 0$. The $Eu(fod)_3$ reagent is reported to pick up one mole of water upon standing exposed to the atmosphere (16), which indicates predominant 1:1 complex. The hydrates of several $Ln(fod)_3$ complexes were found to be monomeric in $Ln(fod)_3$ and monohydrated (60).

Solid crystals of lanthanide complexes have shown both dicom -

plexed (9b, 61) and monocomplexed (62) structures. On this basis, it has been suggested (9, 16) that dicomplexed species may be important in solution. Since at least one lanthande reagent has been crystallized as a dimer (63), it has also been suggested (9) that these reagents may exist in solution as dimeric species in equilibrium with their monomers. Recent reports have suggested that this may be true for $Eu(dpm)_3$ (64, 65), although the evidence is at present somewhat circumstantial. Roth and coworkers evidently found $Eu(fod)_3$ to be monomeric in CCl_4 (66).

Evans and Wyatt (67) recently reported that the spectrum of DMSO with $Eu(fod)_3$ in CD_2Cl_2 at -80^o shows two peaks which correspond to free and complexed substrate in ratios consistent with formation of $Eu(fod)_3 \cdot 2DMSO$. The observed Δ_{max} was 3.42 ppm. We found this Δ_{max} surprisingly small, since at 38^o the "observed" Δ_{lim} is 7.2 ppm in CCl_4 with excess $Eu(fod)_3$ (Table III). We repeated the low temperature experiment in CD_2Cl_2 but with an excess, rather than a deficiency, of reagent so that at 25^o the initial observed shift, Δ_{obsd}, was ~6.5 ppm. Upon cooling the sample to -50^o and below, the peak broadened and moved upfield to Δ_{max} = 3.6 ppm at -78^o to -91^o, in qualitative agreement with the reported value (67).

This behavior is rather curious, since the pseudo-contact equation (or contact equation for that matter) has a 1/T dependence (17-19). Therefore, Δ_{max} should increase as the temperature is lowered, but the opposite behavior is observed for DMSO. Several investigators have noted larger shifts at lower temperatures (25, 32,

50, 68-71) and have correctly pointed out, we think, that such temperature effects can be due to a combination of effects upon the magnetic phenomenon and upon the equilibria (69, 70).

This suggests that the observed low-temperature Δ_{max} (3.5ppm) for DMSO with $Eu(fod)_3$ may be due to a true 2:1 complex as proposed (67), but at room temperature the major species is the 1:1 complex. This is supported by the fact that the calculated Δ_{max}, obtained by applying eq 11 derived for a 1:1 equilibrium, is 8.6 ppm, only slightly greater than the "observed" 7.2 ppm at the same temperature.

(Since K is large in this case, deviations in the $(\Delta_{obsd})^{-1}$ vs. S_t plot may not be particularly noticeable. If eq 12 is used, the calculated Δ_{max} is halved to 4.3, which clearly underestimates the room temperature value (7.2). If the reagent (at ca. 0.01 M) were exclusively dimer, then E_t used in eq 12 must be reduced by a factor of 1/2. This cancels the factor of 1/2 already present in eq 12, and so gives Δ_{max} to be 8.6 again. We think this combination -- 2:1 complexation with a dimeric reagent -- is rather unlikely, although difficult to rule out altogether from the available data.)

We believe this supports the predominant formation of a 1:1 complex between DMSO and $Eu(fod)_3$ at room temperature, which was also implied by the excellent linearity found for the $(\Delta_{obsd})^{-1}$ vs. S_t plot in this case. In fact, the conditions under which these data were obtained, with $S_t/E_t \gg 0$, should favor 2:1 complex formation, yet the 1:1 assumption gives Δ_{max} in reasonable agreement with Δ_{lim}. This is not particularly surprising, since the Lewis acidity of (SE)

should be greatly reduced because of electron donation by the substrate, as evidenced by the upfield shifts of the fod ligand protons (67, 72) when DMSO is present in excess. Thus, further complexation of S to (SE) may be unlikely. The small Δ_{max} at low temperature compared to the larger room temperature value suggests that $\Delta_{max_2} < \Delta_{max_1}$ (see eq 8). This is reasonable if the second molecule of substrate forms only a weak complex because of the reduced Lewis acidity of (ES). Of course, at low temperature the 2:1 complex can be "frozen out" even though it may be only a minor component at room temperature. We suggest that caution is required in inferring room temperature solution behavior of the shift reagents or their complexes with substrates from their properties at low temperature or in the solid state.

We have no direct evidence regarding the stoichiometry for the equilibria of the other substrates listed in Table III, but considering the behavior observed for DMSO, we suspect that the predominant equilibria , even with $S_t/E_t \gg 0$, are 1:1 in these cases, too. The linearity of the $(\Delta_{obsd})^{-1}$ vs. S_t plots was generally excellent, and the calculated Δ_{max} values as given in the table appear to agree with the Δ_{lim} values better than would $(1/2)\Delta_{max}$.

Discrepancies in Δ

In Table III three sets of Δ values are given, Δ_{lim}, Δ_{max}, and Δ_{Eu}. The three values generally increase in magnitude in this order for a given proton. As noted above, Δ_{max} is probably a lower limit due to activity effects or due to trace impurities (particularly since very small amounts of water can reduce the

effective concentration of active reagent (64)). With this in mind, Δ_{max} and Δ_{Eu} agree quite well with each other, but Δ_{lim} is consistently lower. Either Δ_{max} is overestimated or Δ_{lim} does not represent the true Δ_{max} .

Roth and coworkers (58) found that the plot of Δ_{obsd} vs. E_t/S_t can reach a maximum value and then decrease as E_t/S_t is increased further. They inferred from this that at high E_t/S_t, a 2:1 complex may become important and that the observed shift decreases because $\Delta_{max_2} < \Delta_{max_1}$ (see above). However, in terms of eq 6 and eq 7, even though excess E favors formation of (SE), with E $\gg$ (ES) , formation of (S_2E) is unlikely, i.e. formation of (S_2E) does not "consume" reagent. Recently, Sanders and coworkers (64)have noted the same effect and suggested that at low E_t/S_t a 2:1 complex may be important but at high E_t/S_t the 1:1 obtains. This agrees with a process which is capable of reagent "consumption", but also implies that $\Delta_{max_2} > \Delta_{max_1}$, which is precisely opposite from what one expects considering the apparent behavior of the DMSO complexes (see above).

There is an alternative explanation which covers both the "falling off" behavior at very high E_t/S_t and the generally lower values observed for Δ_{lim} compared to the other Δ values. Since the observed shift in the nmr reflects the weighted average of all species, any event or complex which brings a substrate molecule into the vicinity of the lanthanide atom, whether or not such an event is productive as far as formation of the major 1:1 (?) complex, will have an observable effect. It has been shown that shifts can be observed

for protons >13 Å from the coordinated lanthanide atom (5). Therefore, any collision or weak complex which brings the substrate protons to within roughly this distance will affect the spectrum. If these collisions or weak complexes become highly probable, then their collective effect may dominate the weighted average. By definition, the chemical shift of proton $\underline{i}$ in these secondary species, δ_{sec}^{i}, is generally less than that experienced in the "true" primary complex, δ_{max}^{i}, i.e. $\Delta_{sec}^{i} < \Delta_{max}^{i}$.

One such weak complex is suggested by the crystal structure of $(fod)_2Pr(fod)_2(H_2O)Pr(fod)_2 \; H_2O$ (73) in which evidently one water molecule is strongly bound to the lanthanide atoms, but the other is possibly hydrogen bonded to the perfluoro side chains. Another effect may be due to what one may term less productive collision complexes, i.e. collisions which are somewhat non-elastic and which orient the substrate molecule due to electrostatic interactions between the Lewis acid and Lewis base centers, but which do not lead to formation of the primary 1:1 complex.

These secondary 1:1 complexes can be summed to give an effective Δ_{sec}^{i}, as was shown in eq 5 for treatment of conformations within the primary complex, and one can assign an effective "equilibrium constant" K_{sec}, eqs 13 and 14, where $\underline{l}$ labels the different secondary complexes. Applying the method used to derive eq 6, one can obtain eq 15. This equation is in the same

$$\Delta_{sec}^{i}(SE)_{sec} = \sum_{l} n_l \Delta_{sec_l}^{i}(SE)_l \qquad (13)$$

$$K_{sec} = \sum_{l} K_l \qquad (14)$$

$$\Delta_{obsd}^{i} = \frac{K\ \Delta_{max}^{i} + K_{sec}\ \Delta_{sec}^{i}}{K + K_{sec}}\ (1 - E/E_t)(E_t/S_t) \qquad (15)$$

form as eq 6, except now the limiting slope (at low E_t/S_t and high S_t) is more complex.

Of course, some secondary complexes may occur under all conditions so that one cannot obtain from this treatment the true Δ_{max} of the primary complex. However, we postulate that the number of secondary complexes, index l in eqs 13 and 14, can change depending upon the solution conditions. This means that the effective "equilibrium constant" K_{sec} is not constant, as is presumably K. In particular, we postulate that such factors as cage and viscosity effects (74, 75) will be important at large E_t concentrations. K_{sec} is then a function of E_t (or E_t/S_t) and may be relatively small or zero at low E_t/S_t, but at large E_t/S_t, K_{sec} may become competitive with K, and in the limit that $K_{sec} \gg K$, $\Delta_{obsd} \approx \Delta_{sec}$. Whether or not this limit is reached, this suggests that Δ_{lim} cannot measure Δ_{max} since an increasing proportion $(K_{sec}/(K + K_{sec}))$ of Δ_{obsd} is due to Δ_{sec} $(< \Delta_{max})$.

In Figure 1a we show a hypothetical example in which the observed shift, Δ_{obsd}, is divided between its competing components,

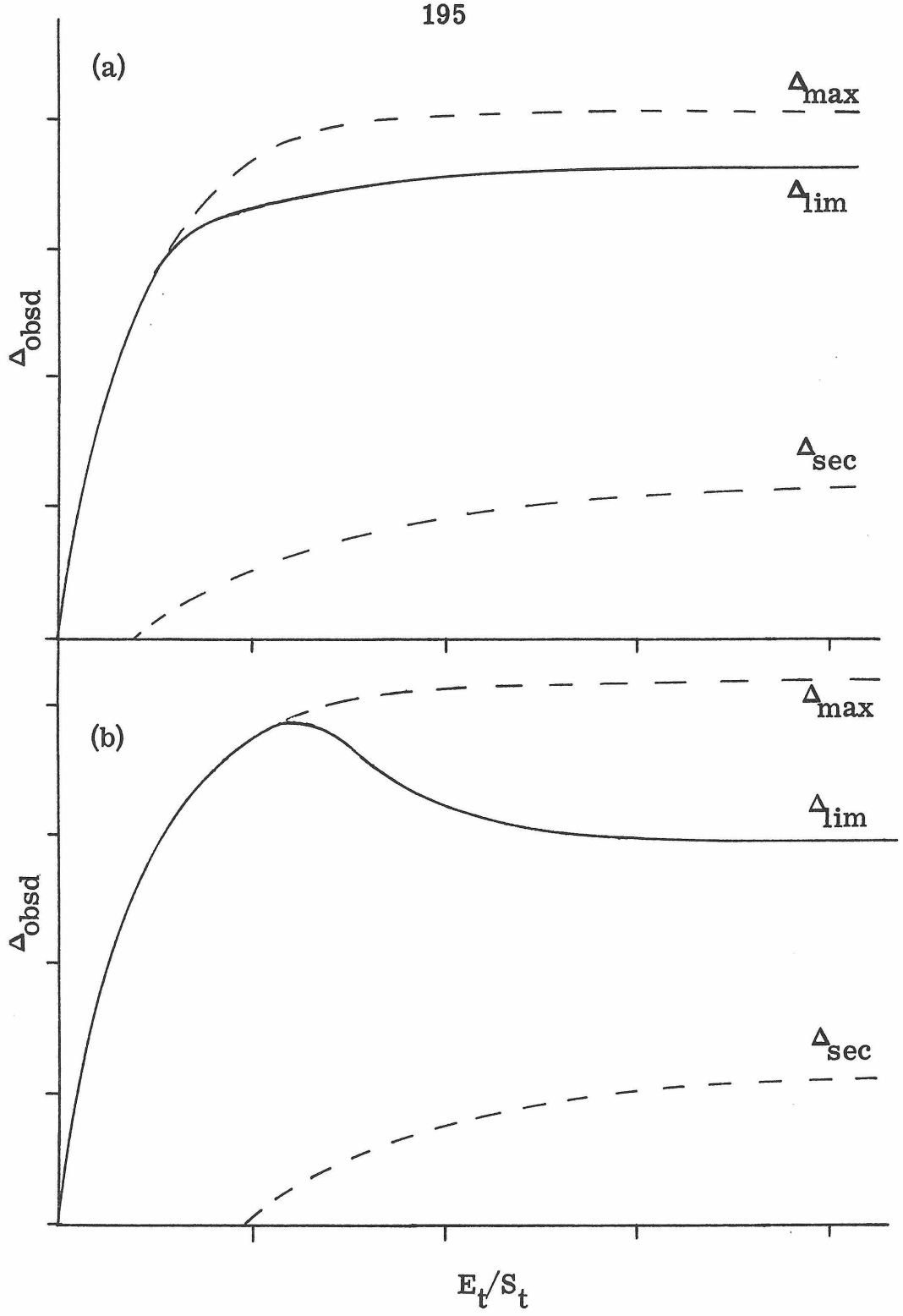

Figure 1. Stylized representation of the effect of competing secondary complexes on Δ_{obsd} due to non-ideal solution behavior (arbitrary coordinate scales; solid curve is Δ_{obsd}).

one due to the primary complex, Δ_{max}, and "one" due to the secondary complexes. The observed shift behavior is obtained by proportinately reducing the Δ_{max} curve due to increasing K_{sec} (eq 15). For simplicity, we have assumed a threshhole value at which Δ_{sec} becomes important. The resultant curve reproduces the behavior of "normal" substrate curves, where the observed shift levels off or appears to approach some limiting value. In Figure 1b, we show the case where the competing Δ_{sec} curve has been displaced to the right somewhat. In this case, the observed shift appears to reach a maximum value and then drops as K_{sec} becomes competitive with K. Such a case can occur if K is particularly large or if K_{sec} is a more slowly increasing function of E_t/S_t in a particular case. The resultant curve in Figure 1b resembles the published curves (58, 64) for some substrate protons. We note that since the orientation of a given proton to the lanthanide atom in the secondary complexes may be quite different from the orientation in the primary complex, all protons of a given substrate may not be proportionately affected, i.e. Δ_{sec}^{i} is not proproportional to Δ_{max}^{i}. Hence, some protons may behave "normally" as in curve (a) or abnormally as in curve (b). These examples are necessarily simplified, since the lower curve is a function of K_{sec} as well as E_t/S_t and, of course, we do not know the postulated dependence of K_{sec} on E_t/S_t or E_t nor do we know the magnitude of Δ_{sec}^{i}.

At present, the above explanation must remain an hypothesis, yet it offers an attractive explanation for the behavior of the type shown in Figure 1b and it accounts for the generally "low" Δ_{lim} values.

In section A of this report, we noted that the slopes of the Δ_{obsd}^{i} vs. Δ_{obsd}^{j} plots for several of the substrates used in this section do show curvature at high E_t/S_t. We feel that this behavior reflects the changing competition between the primary complex formation and the formation of secondary complexes rather than changes in the reaction stoichiometry. In eq 15, if K_{sec} were a constant, then plots of Δ_{obsd}^{i} vs. Δ_{obsd}^{j} must be linear, but if K_{sec} is an increasing function of E_t or E_t/S_t, then such plots need not be linear. We also note that the above explanation implies that care should be taken when the dilution method (55, 56) is used to obtain K and Δ_{max} values. Even though the $E_t/S_t = 1.0$ at all times in this procedure, the absolute concentration is varied, and since K_{sec} may be a function of E_t (particularly if viscosity effects are important), the observed shifts may be somewhat illusionary at high absolute concentrations. The data may appear to be quite "normal", however (e.g. figure 1a).

Conclusions

The method presented in this report allows reasonable estimations of the complex formation equilibrium constants and the bound chemical shifts if the major equilibrium is the formation of a 1:1 complex. Generally, the method appears to be less subject to error if the formation constant is relatively low. Our data for DMSO with $Eu(fod)_3$ at room temperature suggest that the 1:1 complex is predominant, even though the low temperature results imply 2:1 complexation (67). We suggest that the 1:1 complexes also predominate for the weaker Lewis bases. These measured estimations for K

must necessarily include perturbations due to competing processes, including probably a small amount of 2:1 complex formation, associations between substrate molecules, e.g. alcohols in CCl_4, associations between substrate and solvent, e.g. ketones in $CHCl_3$, and associations between shift reagent and solvent or trace amounts of impurities (water) (64). Until such effects are corrected for, the K values reported here cannot be considered to be "true" equilibrium constants. In spite of these uncertainties, we feel the present results are of considerable value for studying the relative affinities of functional groups toward the shift reagents, particularly when $K < 100$.

We have observed that Δ_{Eu} and Δ_{max} are generally comparable in magnitude, but that the observed limit, Δ_{lim}, is consistently lower. We have postulated that, in fact, Δ_{lim} may not reflect the true bound chemical shift in the 1:1 complex due to increasing competition for formation of less tightly bound complexes at high concentrations, especially due to cage and viscosity effects. We have noted that decreases in $\Delta_{obsd}{}^{i}$ at high E_t/S_t (58, 64) as shown in Figure 1b may not be easily rationalized by either a change from a 1:1 complex to a 2:1 complex or from 2:1 to 1:1 as E_t/S_t increases. However, such decreases are rationalized by the increasing importance of secondary 1:1 complexes at large E_t (or E_t/S_t). This interpretation also accounts for slight (usually) changes in the proton $\Delta_{max}{}^{i}$ ratios observed at large E_t/S_t. At present, our interpretation must be regarded as an hypothesis, but it does emphasize the quite reasonable idea that solution non-ideality may be an important factor

particularly at high concentrations of shift reagents. Since the nmr experiment observes all environments in which the substrate is found, it is not surprising that such observations will reflect any non-ideal solution behavior. At the present time, we believe our Δ_{max} values or the Δ_{Eu} values (24) (provided S_t is large) are better estimates of the chemical shifts experienced by substrate nuclei in the primary 1:1 complex than are the "observed" Δ_{lim} values.

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Experimental

General. The nuclear magnetic resonance (nmr) spectra were taken in CCl_4 solution with tetramethylsilane (TMS) internal standard on a Varian A60-A at a probe temperature of 32° or 38°. The 220 MHz spectra were obtained on a Varian HR-220 at 18°. The low temperature spectra of DMSO in CD_2Cl_2 (Merck Sharp and Dohme, 99% d_2) were taken on a Varian T-60 equipped with a low temperature probe. CCl_4 (Matheson Coleman and Bell, "spectroquality") was used as received. $Eu(fod)_3$ (Norell Chemical Co. or Alfa Inorganics) was stored over P_2O_5 at 1 mm Hg pressure for a minimum of one week prior to use. Precision nmr sample tubes were washed thoroughly with acetone, with CCl_4, air dried, and then flamed dried prior to use. Calculated molarity solutions of $Eu(fod)_3$ in CCl_4 were obtained by weighing the solid reagent in a capped nmr tube which had been calibrated for conversion of the height of the liquid level in mm to volume in ml with both CCl_4 and distilled water. (The error in the volume measurement by this method is estimated to be ± 2%.) The reagent was then dissolved in CCl_4 (containing ~1% TMS), and the solution volume and molarity were calculated. The solution was then quickly transferred to a flamed-dried serum bottle, and this was sealed with a serum cap. The reagent solution and pure organic compounds were measured with a 10 μl syringe which had been calibrated for actual delivery of 10 μl aliquots of CCl_4 or the organic compound being measured.

Data. The "standard proton" data (section A) were obtained by adding a 0.1 - 0.5 M $Eu(fod)_3$ solution to the substrate solu-

tion in successive portions and recording the spectrum after each addition. In general, the spectra for the acetates were shifted until Δ_{obsd} for the acetoxy protons was >7 ppm (60 MHz) or >10 ppm (220 MHz). The plots of Δ_{obsd}^{i} vs. Δ_{obsd}^{j} for each data set were analyzed with a least-squares program (Fortran IV) which calculated the slope and intercept of the plot in terms of δ_{obsd} and Δ_{obsd} (both in Hz and ppm), the correlation coefficient, and the statistical standard errors of estimates (76) for the slope, intercept, $\underline{x}$, and $\underline{y}$ values.

For the equilibrium experiments (section B), a known volume of a concentrated solution of calculated molarity of $Eu(fod)_3$ in CCl_4 (0.1 - 0.3 M) was diluted with CCl_4 in a dried, calibrated nmr tube to a known volume to give a final calculated concentration of 0.008 - 0.024 M. Successive aliquots of substrate were added with a 10 μl syringe, and the nmr spectrum was recorded after each aliquot after allowing the sample solution to warm to probe temperature (~10 min). The solution volume (in mm) was rechecked after each sample was removed from the probe for the next addition of substrate. Substrate was added until Δ_{obsd} was generally 20 Hz or less for those protons examined, which generally corresponded to a calculated S_t/E_t ratio of >50. The δ_o^{i} values were taken separately from the normal spectra (see text). In the case of DMSO, δ_o exhibits a small concentration dependence (~ 2Hz) over the concentration range used in the equilibrium experiment, and the data was corrected accordingly. A Fortran IV program was used to calculate the least-squares slopes, intercepts, and correlation coefficients for plots of $(\Delta_{obsd})^{-1}$ vs. S_t

at a given E_t or (E_t/Δ_{obsd}) vs. S_t directly from raw data input. The program calculated Δ_{max} and K according to eq 11 and their estimated standard deviations.

The data for Δ_{Eu} were obtained by adding small aliquots of an $Eu(fod)_3$ solution (calculated concentration) to a substrate solution of known high concentration. The following lists the initial substrate concentration and the final E_t/S_t ratios used: THF, 1.916M, 0.0437; 2-butanone, 2.140M, 0.0272; DMSO, 2.752M, 0.0206. The least-squares slope of the plot of Δ_{obsd} vs. E_t/S_t was then calculated from the spectral data.

The Δ_{lim} values were obtained from dilute (0.03 - 0.05 M) solutions of substrate with added $Eu(fod)_3$ at 220 MHz. Enough reagent solution was eventually added to give $E_t/S_t \geq 5$, where little additional change was noted upon addition of more reagent. A direct estimate of Δ_{lim} was made from the leveling off found in the Δ_{obsd} vs. E_t/S_t plots.

Substrates. THF was distilled from lithium aluminum hydride (LAH) prior to use. DMSO (Baker, reagent) was distilled through a 35 x 2.5 cm column of Linde A-4 molecular seives at ~12 mm Hg (b.p. 71 - 72°, uncorrected) and stored over molecular seives. 2-Propanol (Eastman, "spectro" grade) was stored over molecular seives for two weeks prior to use. The preparation of acetates 1E, 1Z, 2E, 2Z, 8E, and 8Z and their nmr spectra (with chemical shift assignments in some cases made with aid of the data given in Table I) have been given (39b). Acetates 14S, 14A, 15S, 15A, 16S, 16A, 19 and 20 (Table II) were isolated from the solvolyses of vinyl

iodides as described (39b). Their ir, nmr, and mass spectra were in accord with the gross structures (39b) and the geometrical isomers were assigned on the basis of the data given in Table II. Acetate 13 was isolated by preparative gas chromotography (vpc) from the solvolysis products obtained by treating 1-cyclopropyl-1-iodoethylene with excess silver acetate in glacial acetic acid according to Sherrod and Bergman (77). Its spectral properties were in accord with those reported (77).

Isopropenyl acetate, 4, (Matheson Coleman and Bell) was purified by preparative vpc on Carbowax. Vinyl acetates 3E, 3Z, 5E, 5Z, 6, 7, and 9-11 were obtained by acid-catalyzed exchange of the corresponding ketones with isopropenyl acetate (39b, 78). The products were purified by preparative vpc on Carbowax or DEGS. The ir and nmr spectra were in accord with the assigned structures. Isomers 5Z and 6 and 10 and 11 were isolated as mixtures. The cis and trans protons of 4, 5E, 5Z, 6, and 7 were readily distinguishable in the shifted spectra due to the differences in allylic and homoallylic coupling constants (79). Acetates 3E and 3Z and their shifted nmr spectra with $Eu(fod)_3$ were kindly provided by T. C. Clarke of these laboratories in connection with other work (80). A generous sample of 2-methylenecyclohexyl acetate, 18, was provided by M. H. Sekera of these laboratories and purified by preparative vpc on DEGS.

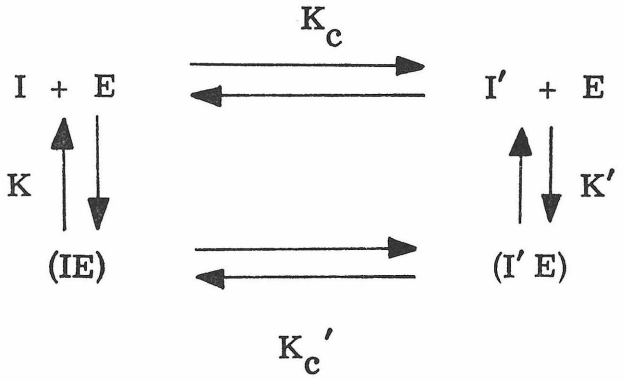
Cyclobutyl acetate, 12, was prepared by treating cyclobutanol (Chemical Samples Co., Inc.) with acetic anhydride in pyridine. The isolated product was purified by preparative vpc on DEGS, and its ir and nmr spectra were in accord with the structure.

2-Cyclopentenyl acetate, 17, was prepared in two steps from 2=cyclopentenone (Aldrich). The ketone (4.1 gm) in 10 ml dry ether was added dropwise to a stirred slurry of LAH (0.6 gm) in 30 ml dry ether. The reaction mixture was cooled to -15 to -20° in a Dry Ice - 2-propanol bath during the addition (81). After the addition was complete, 3 ml of a saturated sodium sulfate solution was added dropwise and then 3-5 gm anhydrous sodium sulfate was added. The reaction mixture was filtered (sintered glass) and the white precipitate was washed with ether. The filtrate and washings were combined and dried over anhydrous sodium sulfate. When the ether solvent was removed on the rotary evaporator, 4.2 gm crude product was obtained. This was not characterized, but directly treated with acetic anhydride in pyridine for 12 hr. The isolated crude acetate showed one major product peak (~90 %) and five minor products by vpc (flame ionization, Carbowax). (One of the minor products corresponded in retention time to cyclopentanone (81).) The major product was collected by preparative vpc on SF96 at 90°. Its ir and nmr spectra were in complete accord with the structure of the desired acetate.

Appendix: Mathematical Treatment of the Complexation Equilibrium between a Conformationally Mobile Substrate and NMR Shift Reagent.

This appendix treats the data given by W.G. Bentrude, H.-W. Tan, and K.C. Yee (38) for a conformationally mobile substrate.

Designate 2a as I, 2b as I′, the corresponding complexed conformers (IE) and (I′E), and the free reagent as E. Assume the equilibrium scheme



where $K_c = I'/I$, $K_c' = (I'E)/(IE)$, $K = (IE)/(I)(E)$, and $K' = (I'E)/(I')(E)$. (It can be readily shown that $(K'K_c)/(KK_c') = 1.$) Assume, as the authors did, that J_{ax} and J_{eq} remain constant, then write the observed coupling J_{obs} as a weighted average (looking at the B protons), eq. (1).

$$J_{obs} = \frac{J_{eq}(I) + J_{ax}(I') + J_{ax}(I'E) + J_{eq}(IE)}{I + I' + (I'E) + (IE)} \qquad (1)$$

The initial coupling is

$$J_0 = \frac{J_{eq}(I) + J_{ax}(I')}{I + I'} = \frac{J_{eq} + J_{ax}K_c}{1 + K_c}$$

and the coupling when bound is

$$J_{max} = \frac{J_{eq}(IE) + J_{ax}(I'E)}{(IE) + (I'E)} = \frac{J_{eq} + J_{ax}K_c'}{1 + K_c'}$$

Using the material balance $I_t = I + I' + (IE) + (I'E)$, equation (1) becomes

$$J_{obs} = \frac{J_{eq} + J_{ax}K_c}{1 + K_c} + \frac{(1 + K_c)[J_{eq}(IE) + J_{ax}(I'E)] - (J_{eq} + J_{ax}K_c)[(IE) + (I'E)]}{(1 + K_c)(I_t)}$$

This then gives

$$\Delta J_{obs} = J_{obs} - J_0 = \Delta J_{max}(1 - E/E_t)\, E_t/I_t \qquad (2)$$

where

$$\Delta J_{max} = J_{max} - J_0 = \frac{K(J_{eq} - J_{ax}) + K'(J_{ax} - J_{eq})}{K + K'K_c} \cdot \frac{K_c}{1 + K_c}$$

For A protons, $J_0 = (J_{ax} + J_{eq}K_c)/(1 + K_c)$

$$\text{and } \Delta J_{max} = \frac{K(J_{ax} - J_{eq}) + K'(J_{eq} - J_{ax})}{K + K'K_c} \cdot \frac{K_c}{1 + K_c}$$

Since the J's and K's are presumably constant, ΔJ_{max} is a constant. A plot of ΔJ_{obs} vs. E_t/I_t will be a straight line, in the limit $E/E_t \approx$ a constant, with slope ΔJ_{max}. This probably holds for $E_t/I_t < 0.8$ if I_t is sufficiently large. At high E_t/I_t, the slope approaches zero. The limit $E/E_t \approx 0$ is reached if K, K', and I_t large, as is likely in the present case.

The authors' data for 2 and 3 does plot well as ΔJ_{obs} (or $-\Delta J_{obs}$ for B protons) vs. E_t/I_t. In each case, both A and B protons appear to fall near the same line. The plot reveals that $E_t/I_t = 0.95$ for 3 may be an error (0.75?). The slope is approximately 6.2 for 2 and 7.5 for 3, and one can assume that these values approximate ΔJ_{max} in each case. Neither plot, however, passes through $\Delta J_{obs} = 0$. I assume this indicates that the authors' computer data for 2 and 3 (and 1?) at $E_t/I_t = 0$ may be in error. The intercepts are ~0.75 Hz for 3 and ~2.45 Hz for 2. This gives calculated values for 2 of $J_{BP} \approx 13.9$, $J_{AP} \approx 9.25$ and for 3 of $J_{BP} \approx 16.95$, $J_{AP} \approx 6.5$ at $E_t/I_t = 0$. These values give different results for the corresponding entries in columns 13 and 14.

Next one can show that a plot of ΔJ_{obs} for A protons against B protons should be linear with a slope of minus one. Using equation (2) one obtains

$$\frac{\Delta J^{A}_{obs}}{\Delta J^{B}_{obs}} = \frac{\Delta J^{A}_{max}}{\Delta J^{B}_{max}} = \frac{K(J_{ax} - J_{eq}) + K'(J_{eq} - J_{ax})}{K(J_{eq} - J_{ax}) + K'(J_{ax} - J_{eq})} = -1.$$

The authors' data come reasonably close to fulfilling this criterion. Note that equation (2) can be derived in the case where conformations are not changing and complexation with reagent changes the coupling constants due to perhaps obscure electronic effects. But then $\Delta J_{max} = (J_{max} - J_0)$, where J_{max} represents a new coupling constant. The ratio of $\Delta J^{A}_{max}/\Delta J^{B}_{max}$ would not necessarily be minus one. The minus one slope further suggests the idea that conformational changes are occurring and that the assumption of constant $J_{HP(ax)}$ and $J_{HP(eq)}$ is valid.

Now, what does "%2a" represent? What one is actually finding (for the B proton, for example) is

$$\text{percent} = P = \frac{J_{obs} - J_{ax}}{J_{eq} - J_{ax}} \cdot 100.$$

Using equation (1) written as $J_{obs} = J_{eq}(n_1 + n_{IE}) + J_{ax}(n_{(I')} + n_{(I'E)})$, where n_i is the mol fraction of component i, one can write

$$\frac{P}{100} = \frac{J_{eq}(n_I + n_{IE}) + J_{ax}(1 - n_I - n_{IE}) - J_{ax}}{J_{eq} - J_{ax}} = n_I + n_{IE}$$

So the values represent the percent of 2a plus percent of complexed 2a. It is easy to show that a plot of P vs. E_t/I_t should be in the same

form as equation (2):

$$J_{obs} - J_{ax} = \Delta J_{max}(1 - E/E_t)E_t/I_t + J_o - J_{ax}$$

$$\frac{P}{100} = \frac{J_{obs} - J_{ax}}{J_{eq} - J_{ax}} = \frac{\Delta J_{max}(1 - E/E_t)}{J_{eq} - J_{ax}} (E_t/I_t) + \frac{J_o - J_{ax}}{J_{eq} - J_{ax}}$$

Again, in the limit $E/E_t \approx 0$, a straight line with slope $\Delta J_{max}/(J_{eq} - J_{ax})$ and intercept P_0 (composition at zero reagent) should be found for a plot of P vs. E_t/I_t. This is the case, in fact. The slope for $\underset{\frown}{2}$ is ~0.34 and for $\underset{\frown}{3}$ is ~0.45. Using the ΔJ_{max} values from the ΔJ_{obs} vs. E_t/I_t plot and the assumed J_{eq} and J_{ax} values, one calculates these slopes should be 0.35 and 0.42, respectively. (Note: The intercepts of the lines, P_0, agree with the revised coupling constants quoted earlier, whereas the computer-assisted values at $E_t/I_t = 0$ give P_0 which does not fall on the plot. My values calculated for Table I, column 13, are 63, 59, 43, 38 and for column 14 are 80, 75, 69, 64, 59, 53, 47 using estimated "best fit" values, obtained from the ΔJ_{obs} vs. E_t/I_t plots.)

One can also show that P should change as reagent concentration increases. The following relationship

$$\frac{P}{1 - P} = \frac{I + (IE)}{I' + (I'E)} = \frac{1 + K(E)}{1 + K'(E)} \cdot \frac{1}{K_c}$$

shows the fraction cannot remain constant if $K \neq K'$ and if the concentration of free reagent changes. Since E starts at zero and

increases, the value of P will decrease if $K' > K$. Naturally, if $K = K'$, the ratio is constant, as expected.

One further point. Since the slope of ΔJ_{obs} vs. E_t/I_t approximately equals ΔJ_{max}, then one can obtain

$$\frac{K'}{K} \approx \frac{K_c(J_{eq} - J_{ax}) + \Delta J_{max}(1 + K_c)}{K_c[-\Delta J_{max}(1 + K_c) + (J_{eq} - J_{ax})]}$$

This gives K'/K of ~ 4.37 for $\underset{\frown}{2}$ and ~ 6.65 for $\underset{\frown}{3}$. Using $K' K_c/KK_c' = 1$, K_c' is calculated to be ~ 2.56 for complexed $\underset{\frown}{2}$ and ~ 1.66 for complexed $\underset{\frown}{3}$. In view of the changes seen for P, these values are expected to be > 1. It would be interesting to know if these values for K'/K and K_c' reflect the differences in the substrates ($\underset{\frown}{2}$ or $\underset{\frown}{3}$) or are more sensitive to the type of shift reagent used ($Eu(dpm)_3$ or $Eu(fod)_3$).

References

1. J. Reuben and D. Fiat, Chem. Commun., 729 (1967).

2. J. Reuben and D. Fiat, J. Chem. Phys., 47, 5440 (1967); ibid., 51, 4909, 4918 (1969).

3. J. E. Schwarberg, D. R. Gere, R. E. Sievers, and K. J. Eisentraut, Inorg. Chem., 6, 1933 (1967).

4. E. R. Birnbaum and T. Moeller, J. Amer. Chem. Soc., 91, 7274 (1969).

5. C. C. Hinckley, ibid., 91, 5160 (1969).

6. Over 240 pertinent references are given in the bibliography immediately following the reference list.

7. (a) J. K. M. Sanders and D. H. Williams, Chem. Commun., 422 (1970); (b) J. Amer. Chem. Soc., 93, 641 (1971).

8. (a) D. R. Crump, J. K. M. Sanders, and D. H. Williams, Tetrahedron Lett., 4419 (1970); (b) ibid., 4949(1971).

9. (a) W. DeW. Horrocks, Jr., and J. P. Sipe III, J. Amer. Chem. Soc., 93, 6800 (1971); (b) W. DeW. Horrocks, Jr., J. P. Sipe III, and J. R. Luber, ibid., 93, 5258 (1971).

10. J. E. Maskasky and M. E. Kenney, ibid., 93, 2060 (1971); J. E. Maskasky, J. R. Mooney, and M. E. Kenney, ibid., 94, 2132 (1972).

11. G. P. Schiemenz, J. Magn. Resonance, 6, 291 (1972)

12. C. Beute, Z. W. Wolkowski, and N. Thoai, Chem. Commun., 700 (1971).

13. F. A. Hart, G. P. Moss, and M. L. Staniforth, Tetrahedron Lett., 3389 (1971).

14. H. L. Georing, J. N. Eikenberry, and G. S. Koermer, J. Amer. Chem. Soc., 93, 5913 (1971).

15. G. M. Whitesides and D. W. Lewis, ibid., 92, 6979 (1970); ibid., 93, 5914 (1971).

16. R. E. Rondeau and R. E. Sievers, ibid., 93, 1522 (1971).

17. H. M. McConnell and R. E. Robertson, J. Chem. Phys., 29, 1361 (1958).

18. G. N. LaMar, W. DeW. Horrocks, Jr., and L. C. Allen, ibid., 41, 2126 (1964); G. N. LaMar, ibid., 43, 1085 (1965).

19. R. J. Kurland and B. R. McGarvey, J. Magn. Resonance, 2, 286 (1970).

20. C. C. Hinckley, J. Org. Chem., 35, 2834 (1970).

21. C. L. Honeybourne, Tetrahedron Lett., 1095 (1972).

22. M. R. Willcott III, R. E. Lenkinski, and R. E. Davis, J. Amer. Chem. Soc., 94, 1742 (1972); R. E. Davis and M. R. Willcott III, ibid., 94, 1744 (1972).

23. M. R. Willcott III, private communication.

24. P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert, J. Amer. Chem. Soc., 92, 5734, 5737 (1970).

25. D. L. Rabenstein, Anal. Chem., 43, 1599 (1971).

26. D. E. U. Ekong, J. I. Okogun, and M. Shok, J. C. S. Perkin I, 653 (1972).

27. J. W. de Haan and L. J. M. van de Ven, Tetrahedron Lett., 2703 (1971).

28. B. L. Shapiro, J. R. Hlubucek, G. R. Sullivan, and L. F. Johnson, J. Amer. Chem. Soc., 93, 3281 (1971).

29. A. F. Cockerill and D. M. Rackham, Tetrahedron Lett., 5149 (1970).

30. E. Wenkert, D. W. Cochran, E. W. Hagaman, R. B. Lewis, and F. M. Schell, J. Amer. Chem. Soc., 93, 6271 (1971).

31. H. v. Brederode and W. G. B. Huysmans, Tetrahedron Lett., 1695 (1971).

32. L. Tomic, Z. Majerski, M. Tomic, and D. E. Sunko, Chem. Commun., 719 (1971).

33. K. K. Anderson and J. J. Uebel, Tetrahedron Lett., 5253 (1970).

34. G. H. Wahl, Jr., and M. R. Peterson, Jr., Chem. Commun., 1167 (1970).

35. D. R. Kelsey, J. Amer. Chem. Soc., 94, 1764 (1972).

36. A similar equation has been derived for charge-transfer complexes; see R. Foster and C. A. Fyfe, Prog. N.M.R. Spectrosc., 4, 1 (1969).

37. I. Armitage, G. Dunsmore, L. D. Hall, and A. G. Marshall, Chem. Commun., 1281 (1971); Chem. Ind. (London), 79 (1972); Can. J. Chem., 50, 2119 (1972).

38. W. G. Bentrude, H.-W. Tan, and K. C. Yee, J. Amer. Chem. Soc., 94, 3264 (1972); see Appendix.

39. (a) D. R. Kelsey and R. G. Bergman, ibid., 92, 228 (1970); ibid., 93, 1941 (1971); (b) Part I this thesis.

40. C. Beaute, Z. W. Wolkowski, J. P. Merda, and D. Lelandais, Tetrahedron Lett., 2473 (1971).

41. A. A. Bothner-By, C. Naar-Colin, and H. Günther, J. Amer. Chem. Soc., 84, 2748 (1962); E. W. Garbish, Jr., ibid., 86, 5561 (1964).

42. W. L. F. Armarego, T. J. Batterham, and J. R. Kershaw, Org. Magn. Resonance, 3, 575 (1971).

43. J. Paasivirta, Suomen Kemistilehti B, 44, 131, 135 (1971).

44. K. Tsukida and M. Ito, Experientia, 27, 1004 (1971).

45. D. G. Buckley, G. H. Green, E. Ritchie, and W. C. Taylor, Chem. Ind. (London), 298 (1971).

46. F. - G. Klärner, Tetrahedron Lett., 3611 (1971).

47. H. G. Richey, Jr., and F. W. Von Rein, ibid., 3781 (1971).

48. R. M. Cory and A. Hassner, ibid., 1245 (1972).

49. R. Seux, G. Morel, and A. Foucaud, ibid., 1003 (1972).

50. I. Armitage and L. D. Hall, Can. J. Chem., 49, 2770 (1971).

51. P. Kristiansen and T. Ledaal, Tetrahedron Lett., 4457 (1971).

52. J. Reuben and J. S. Leigh, Jr., J. Amer. Chem. Soc., 94, 2789 (1972).

53. J. A. Peters, J. D. Remijnse, A. van der Wiele, and H. van Bekkum, Tetrahedron Lett., 3065 (1971).

54. H. Hart and G. M. Love, ibid., 625 (1971).

55. J. Bouquant and J. Chuche, ibid., 2337 (1972).

56. T. A. Wittstruck, J. Amer. Chem. Soc., 94, 5130 (1972).

57. See fig. 1, reference 35.

58. K. Roth, M. Grosse, and D. Rewicki, Tetrahedron Lett., 435 (1972).

59. H. Huber and J. Seelig, Helv. Chim. Acta, 55, 135 (1972).

60. C. S. Springer, Jr., D. W. Meek, and R. E. Sievers, Inorg. Chem., 6, 1105 (1967).

61. R. E. Cramer and K. Seff, Chem. Commun., 400 (1972).

62. C. S. Erasmus and J. C. A. Boeyens, J. Cryst. Mol. Struct., 1, 83 (1971).

63. C. S. Erasmus and J. C. A. Boeyens, Acta Crystallogr., Sect. B, 26, 1843 (1970).

64. J. K. M. Sanders, S. W. Hanson, and D. H. Williams, J. Amer. Chem. Soc., 94, 5325 (1972).

65. M. K. Archer, D. S. Fell, and R. W. Jotham, Inorg. Nucl. Chem. Lett., 7, 1135 (1971).

66. See footnote 7 in reference 58.

67. D. F. Evans and M. Wyatt, Chem. Commun., 312 (1972).

68. N. Ahmad, N. S. Bhacca, J. Selbin, and J. D. Wander, J. Amer. Chem. Soc., 93, 2564 (1971).

69. R. R. Fraser, M. A. Petit, and J. K. Saunders, Chem. Commun., 1450 (1971).

70. R. D. Bennett and R. E. Schuster, Tetrahdron Lett., 673 (1972).

71. C. Beaute, S. Cornuel, D. Lelandais, N. Thoai, and Z. W. Wolkowski, ibid., 1099 (1972).

72. Unpublished observations. Excess DMSO, THF, or 2-propanol cause the major ligand peak of $Eu(fod)_3$ to move upfield from 1.74 ppm to 0.2 - 0.0 ppm. Acetates and 2-butanone do not have such a pronounced effect, with the ligand peak shifted to 1.1 - 0.7 ppm.

73. J. P. R. de Villiers and J. C. A. Boeyens, private communication to R. E. Sievers reported in reference 16.

74. E. g. see A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1961, pp 129-131.

75. Concentrated solutions of $Eu(fod)_3$ in CCl_4 appear to be rather viscous.

76. C. L. Perrin, "Mathematics for Chemists," Wiley-Interscience, New York, N. Y., 1970.

77. S. A. Sherrod and R. G. Bergman, J. Amer. Chem. Soc., 91, 2115 (1969); ibid., 93, 1925 (1971).

78. H. O. House and H. W. Thompson, J. Org. Chem., 26, 3729 (1961).

79. See S. Sternhell, Rev. Pure Appl. Chem., 14, 15 (1964).

80. T. C. Clarke, D. R. Kelsey, and R. G. Bergman, J. Amer. Chem. Soc., 94, 3626 (1972); T. C. Clarke and R. G. Bergman, ibid., 94, 3627 (1972).

81. See H. C. Brown and H. M. Hess, J. Org. Chem., 34, 2206 (1969).

Bibliography

The following is a reasonably complete list of pertinent references to research on the nmr shift reagents and related topics up to approximately September 1, 1972. Reports labelled m generally are concerned with other topics, but have used shift reagents.

1. O. Achmatowicz, Jr., A. Ejchart, J. Jurczak, L. Kozerski, and J. St. Pyrek, Chem. Commun., 98 (1971).

2. N. Ahmad, N.S. Bhacca, J. Selbin, and J.D. Wander, J. Amer. Chem. Soc., 93, 2564 (1971).

3. L.J. Altman, R.C. Kowerski, and H.C. Rilling, J. Amer. Chem. Soc., 93, 1782 (1971).

4. R. von Ammon, R.D. Fischer, and B. Kanellakopulos, Chem. Ber., 104, 1072 (1971).

5. K.K. Andersen and J.J. Uebel, Tetrahedron Lett., 5253 (1970).

6. J.W. ApSimon and H. Beierbeck, Chem. Commun., 172 (1972).

7. J.W. ApSimon and J.D. Cooney, Can. J. Chem., 49, 2378 (1971).

8. M.K. Archer, D.S. Fell, and R.W. Jotham, Inorg. Nucl. Chem. Lett., 7, 1135 (1971).

9. W.L.F. Armarego, T.J. Batterham, and J.R. Kershaw, Org. Magn. Resonance, 3, 575 (1971).

10. I. Armitage, G. Dunsmore, L.D. Hall and A.G. Marshall, Can. J. Chem., 50, 2119 (1972).

11. I. Armitage, G. Dunsmore, L.D. Hall, and A.G. Marshall, Chem. Commun., 1281 (1971).

12. I. Armitage, G. Dunsmore, L.D. Hall, and A.G. Marshall, Chem. Ind. (London), 79 (1972).

13. I. Armitage and L.D. Hall, Can. J. Chem., 49, 2770 (1971).

14. (m) I. Armitage and L.D. Hall, Chem. Ind. (London), 1537 (1971).

15. J. Barciszewski, A.J. Rafalski, and M. Wiewiorowski, Bull. Acad. Pol. Sci., Ser. Sci. Chim., 19, 545 (1971).

16. (m) C.D. Barry, A.C.T. North, J.A. Glasel, R.J.P. Williams, and A.V. Xavier, Nature, 232, 236 (1971).

17. R.A. Bauman, Tetrahedron Lett., 419 (1971).

18. C. Beauté, S. Cornuel, D. Lelandais, N.Thoai, and Z.W. Wolkowski, Tetrahedron Lett., 1099 (1972).

19. C. Beauté, Z.W. Wolkowski, J.P. Merda, and D. Lelandais, Tetrahedron Lett., 2473 (1971).

20. C. Beauté, Z.W. Wolkowski, and N. Thoai, Chem. Commun., 700 (1971).

21. C. Beauté, Z.W. Wolkowski, and N. Thoai, Tetrahedron Lett., 817 (1971).

22. P. Bélanger, C. Freppel, D. Tizané, and J.-C. Richer, Can. J. Chem., 49, 1985 (1971).

23. P. Bélanger, C. Freppel, D. Tizané, and J.-C. Richer, Chem. Commun., 266 (1971).

24. R.D. Bennett and R.E. Schuster, Tetrahedron Lett., 673 (1972).

25. W.G. Bentrude, H.-W. Tan, and K.C. Yee, J. Amer. Chem. Soc., 94, 3264 (1972).

26. K.D. Berlin and S. Rengaraju, J. Org. Chem., 36, 2912 (1971).

27. (m)J.A.Berson, R.T. Luibrand, N.G. Kundu, and D.G. Morris, J. Amer. Chem. Soc., 93, 3075 (1971).

28. (m) J.A. Berson and R.G. Salomon, J. Amer. Chem. Soc., 93, 4620 (1971).

29. N.S. Bhacca and J.D. Wander, Chem. Commun., 1505 (1971).

30. B. Birdsall, J. Feeney, J.A. Glasel, R.J.P. Williams, and A.V. Xavier, Chem. Commun., 1473 (1971).

31. (m) E.R. Birnbaum, J.E. Gomez, and D.W. Darnall, J. Amer. Chem. Soc., 92, 5287 (1970).

32. E.R. Birnbaum and T. Moeller, J.Amer. Chem. Soc., 91, 7274 (1969).

33. (m) F. Bohlmann and C. Zdero, Tetrahedron Lett., 851 (1972).

34. J. Bouquant and J. Chuche, Tetrahedron Lett., 2337 (1972).

35. (m) A.F. Bramwell, G. Riezebos, and R.D. Wells, Tetrahedron Lett., 2489 (1971).

36. H.v. Brederode and W.G.B. Huysmans, Tetrahedron Lett., 1695 (1971).

37. J. Briggs, G.H. Frost, F.A. Hart, G.P. Moss, and M.L. Staniforth, Chem. Commun., 749 (1970).

38. J. Briggs, F.A. Hart, and G.P. Moss, Chem. Commun., 1506 (1970).

39. J. Briggs, F.A. Hart, G.P. Moss, and E.W. Randall, Chem. Commun., 364 (1971).

40. A. van Bruijnsvoort, C. Kruk, E.R. de Waard, and H.O. Huisman, Tetrahedron Lett., 1737 (1972).

41. D.G. Buckley, G.H. Green, E.Ritchie, and W.C. Taylor, Chem. Ind. (London), 298 (1971).

42. H. Burzynska, J. Dabrowski, and A. Krowczynski, Bull. Acad. Pol. Sci., Ser. Sci. Chim., 19, 587 (1971).

43. R.F. Butterworth, A.G. Pernet, and S. Hanessian, Can. J. Chem., 49, 981 (1971).

44. C.A. Cabrera, G.M. Woltermann, and J.R. Wasson, Tetrahedron Lett., 4485 (1971).

45. R. Caple and S.C. Kuo, Tetrahedron Lett., 4413 (1971).

46. J.F. Caputo and A.R. Martin, Tetrahedron Lett., 4547 (1971).

47. F.A. Carey, J. Org. Chem., 36, 2199 (1971).

48. (m) F.I. Carroll and J.T. Blackwell, Tetrahedron Lett., 4173 (1970).

49. P.-F. Casals and G. Boccaccio, Tetrahedron Lett., 1647 (1972).

50. (m) C.P. Casey and R.A. Boggs, Tetrahedron Lett., 2455 (1971).

51. (m) C.P. Casey and C.R. Cyr, J. Amer. Chem. Soc., 93, 1280 (1971).

52. M. Christl, H.J. Reich and J.D. Roberts, J. Amer. Chem. Soc., 93, 3463 (1971).

53. A.F. Cockerill and D.M. Rackham, Tetrahedron Lett., 5149 (1970).

54. A.F. Cockerill and D.M. Rackham, Tetrahedron Lett., 5153 (1970).

55. J.R. Corfield and S. Trippett, Chem. Commun., 721 (1971).

56. R.M. Cory and A. Hassner, Tetrahedron Lett., 1245 (1972).

57. R.E. Cramer and K. Seff, Chem. Commun., 400 (1972).

58. D.R. Crump, J.K.M. Sanders, and D.H. Williams, Tetrahedron Lett., 4419 (1970).

59. D.R. Crump, J.K.M. Sanders and D.H. Williams, Tetrahedron Lett., 4949 (1971).

60. B.D. Cuddy, K. Treon and B.J. Walker, Tetrahedron Lett., 4433 (1971).

61. J. Dale and P.O. Kristiansen, Chem. Commun., 670 (1971).

62. R.E. Davis and M.R. Willcott, III, J. Amer. Chem. Soc., 94, 1744 (1972).

63. P.V. Demarco, T.K. Elzey, R.B. Lewis and E. Wenkert, J. Amer. Chem. Soc., 92, 5734 (1970).

64. P.V. Demarco, T.K. Elzey, R.B. Lewis and E. Wenkert, J. Amer. Chem. Soc., 92, 5737 (1970).

65. H. Donato, Jr., and R.B. Martin, J. Amer. Chem. Soc., 94, 4129 (1972).

66. J.C. Duggan and W.H. Urry, Tetrahedron Lett., 4197 (1971).

67. D.R. Eaton, J. Amer. Chem. Soc., 87, 3097 (1965).

68. D.R. Eaton and W.D. Phillips, Adv. Magn. Resonance, 1, 103 (1965). Review.

69. K.J. Eisentraut and R.E. Sievers, J. Amer. Chem. Soc., 87, 5254 (1965).

70. D.E.U. Ekong, J.I. Okogun, and M. Shok, J. C. S. Perkin I, 653 (1972).

71. C S. Erasmus and J.C.A. Boeyens, Acta. Crystallogr., Sect. B, 26, 1843 (1970).

72. C.S. Erasmus and J.C.A. Boeyens, J. Cryst. Mol. Struct., 1, 83 (1971).

73. L. Ernst and A. Mannschreck, Tetrahedron Lett., 3023 (1971).

74. D.F. Evans and M. Wyatt, Chem. Commun., 312 (1972).

75. S. Farid, A. Ateya and M. Maggio, Chem. Commun., 1285 (1971).

76. (m) D. Fleischer and R.C. Schutz, Makromol. Chem., 152, 311 (1972).

77. I. Fleming, S.W. Hanson and J.K.M. Sanders, Tetrahedron Lett., 3733 (1971).

78. M.I. Foreman and D.G. Leppard, J. Organometal. Chem., 31, C31 (1971).

79. R. Foster and C.A. Fyfe, Prog. N. M. R. Spectrosc., 4, 1 (1969). Review.

80. R.R. Fraser, M.A. Petit, and M. Koskow, J. Amer. Chem. Soc., 94, 3253 (1972).

81. R.R. Fraser, M.A. Petit and J.K. Saunders, Chem. Commun., 1450 (1971).

82. R.R. Fraser and Y.Y. Wigfield, Chem. Commun., 1471 (1970).

83. (m) R.R. Fraser and Y.Y. Wigfield, Tetrahedron Lett., 2515 (1971).

84. O.A. Gansow, M.R. Willcott, and R.E. Lenkinski, J. Amer. Chem. Soc., 93, 4295 (1971).

85. M. Grielen, N. Goffin and J. Topart, J. Organometal. Chem., 32, C38 (1971).

86. (m) E. Gillies, W.A. Szavek, and M.C. Baird, Can. J. Chem., 49, 211 (1971).

87. (m) P. Girard, H. Kagan and S. David, Bull. Soc. Chim. Fr., 4515 (1970).

88. H.L. Goering, J.N. Eikenberry, and G.S. Koermer, J. Amer. Chem. Soc., 93, 5913 (1971).

89. J. Goodisman and R.S. Matthews, Chem. Commun., 127 (1972).

90. P. Granger, M. M. Caludon, and J. F. Guinet, Tetrahedron Lett., 4167 (1971).

91. J.L. Greene, Jr., and P.B. Shevlin, Chem. Commun., 1092 (1971).

92. A.M. Grotens, C.W. Hilbers, and E. de Boer, Tetrahedron Lett., 2067 (1972).

93. A.M. Grotens and J. Smid, J. Magn. Resonance, 6, 612 (1972).

94. A.M. Grotens, J. Smid, and E. de Boer, Tetrahedron Lett., 4863 (1971).

95. J.E. Guillet, I.R. Peat, and W.F. Reynolds, Tetrahedron Lett., 3493 (1971).

96. J.W. de Haan and L.J.M. van de Ven, Tetrahedron Lett., 2703 (1971).

97. F.A. Hart, G.P. Moss, and M.L. Staniforth, Tetrahedron Lett., 3389 (1971).

98. F.A. Hart, J.E. Newbery and D. Shaw, Chem. Commun., 45 (1967).

99. F.A. Hart, J.E. Newbery and D. Shaw, J. Inorg. Nucl. Chem., 32, 3585 (1970).

100. H. Hart and G.M. Love, Tetrahedron Lett., 625 (1971).

101. J.E. Herz, V.M. Rodriguez and P. Joseph-Nathan, Tetrahedron Lett., 2949 (1971).

102. C.C. Hinckley, J. Amer. Chem. Soc., 91, 5160 (1969).

103. C.C. Hinckley, J. Org. Chem., 35, 2834 (1970).

104. C.C. Hinckley, W.A. Boyd and G.V. Smith, Tetrahedron Lett., 879 (1972).

105. C.C. Hinckley, M.R. Klotz, and F. Patil, J. Amer. Chem. Soc., 93, 2417 (1971).

106. (m) H. Hogeveen, C.F. Roobeek, and H.C. Volger, Tetrahedron Lett., 221 (1972).

107. J. Homer, C.J. Jackson, P.M. Whitney, and M.A. Everdell, Chem. Commun., 956 (1971).

108. C.L. Honeybourne, Tetrahedron Lett., 1095 (1972).

109. W. DeW. Horrocks, Jr., and J.P. Sipe, III, J. Amer. Chem. Soc., 93, 6800 (1971).

110. W. DeW. Horrocks, Jr., J.P. Sipe, III, and J.R. Luber, J. Amer. Chem. Soc., 93, 5258 (1971).

111. D. Horton and J.K. Thomson, Chem. Commun., 1389 (1971).

112. H. Huber and C. Pascual, Helv. Chim. Acta, 54, 913 (1971).

113. H. Huber and J. Seelig, Helv. Chim. Acta, 55, 135 (1972).

114. L.R. Isbrandt and M.T. Rogers, Chem. Commun., 1378 (1971).

115. H. Ishitobi, H. Tanida, K. Tori and T. Tsuji, Bull. Chem. Soc. Jap., 44, 2993 (1971).

116. S. Ito and I. Itoh, Tetrahedron Lett., 2969 (1971).

117. A. Ius. G. Vecchio and G. Carrea, Tetrahedron Lett., 1543 (1972).

118. A. Johnson and G.W. Everett, Jr., J. Amer. Chem. Soc., 94, 1419 (1972).

119. L.F. Johnson, J. Chakravarty, R. Dasgupta and U.R. Ghatak, Tetrahedron Lett., 1703 (1971).

120. (m) Y. Kashman, Tetrahedron Lett., 4045 (1971).

121. (m) A. Kato and M. Numata, Tetrahedron Lett., 203 (1972).

122. (m) A.R. Katritzky and A. Smith, Tetrahedron Lett., 1765 (1971).

123. L.H. Keith, Tetrahedron Lett., 3 (1971).

124. H.J. Keller and K.E. Schwarzhans, Angew. Chem. Int. Ed. Eng, 9, 196 (1970). Review.

125. D.R. Kelsey, J. Amer. Chem. Soc., 94, 1764 (1972).

126. (m) A.S. Kende, J.K. Jenkins and L.E. Friedrich, Chem. Commun., 1215 (1971).

127. M. Kishi, K. Tori, and T. Komeno, Tetrahedron Lett., 3525 (1971).

128. F.-G. Klarner, Tetrahedron Lett., 3611 (1971).

129. R.W. Kluiber and W. DeW. Horrocks, Jr., J. Amer. Chem. Soc., 88, 1399 (1966).

130. P. Kristiansen and T. Ledaal, Tetrahedron Lett., 2817 (1971).

131. P. Kristiansen and T. Ledaal, Tetrahedron Lett., 4457 (1971).

132. R.J. Kurland and B.R. McGarvey, J. Magn. Resonance, 2, 286 (1970).

133. L. Lacombe, F. Khuong-Huu, A. Pancrazi, Q. Khuong-Huu, and G. Lukacs, C.R. Acad. Sci., Paris, Ser. C., 272, 668 (1971).

134. F. Lafuma and C. Quivoron, C.R. Acad. Sci., Paris, Ser. C., 272, 2020 (1971).

135. (m) L.K. Lala, J. Org. Chem., 36, 2560 (1971).

136. G.N. LaMar, J. Chem. Phys., 43, 1085 (1965).

137. G.N. LaMar, W. DeW. Horrocks, Jr., and L.C. Allen, J. Chem. Phys., 41, 2126 (1964).

138. S.G. Levine and R.E. Hicks, Tetrahedron Lett., 311 (1971).

139. A.H. Lewin, Tetrahedron Lett., 3583 (1971).

140. Y.-Y. Lim and R.S. Drago, J. Amer. Chem. Soc., 94, 84 (1972).

141. K.J. Liska, A.F. Fentiman, Jr., and R.L. Foltz, Tetrahedron Lett., 4657 (1970).

142. H.-P. Loffler, Tetrahedron Lett., 4893 (1971).

143. (m) G. Lukacs, X. Lusinchi, P. Girard, and H. Kagan, Bull. Soc. Chim. Fr., 3200 (1971).

144. L.J. Luskus and K.N. Houk, Tetrahedron Lett., 1925 (1972).

145. (m) G. Maier, G. Fritschi and B. Hoppe, Tetrahedron Lett., 1463 (1971).

146. T.J. Marks, J.S. Kristoff, A. Alich, and D.F. Shriver, J. Organometal. Chem., 33, C35 (1971).

147. J.E. Maskasky and M.E. Kenney, J. Amer. Chem. Soc., 93, 2060 (1971).

148. J.E. Maskasky, J.R. Mooney, and M.E. Kenney, J. Amer. Chem. Soc., 94, 2132 (1972).

149. P.H. Mazzocchi, H.J. Tamburin, and G.R. Miller, Tetrahedron Lett., 1819 (1971).

150. H.M. McConnell and R.E. Robertson, J. Chem. Phys., 29, 1361 (1958).

151. C.C. McDonald and W.D. Phillips, Biochem.Biophys. Res. Commun., 35, 43 (1969).

152. B.R. McGarvey, J. Amer. Chem. Soc., 94, 1103 (1972).

153. B.R. McGarvey, J. Chem. Phys., 53, 86 (1970).

154. J.D. McKinney, L.H. Keith, A. Alford and C.E. Fletcher, Can. J. Chem., 49, 1993 (1971).

155. K.G. Morallee, E. Nieboer, F.J.C. Rossotti, R.J.P. Williams, A.V. Xavier and R.A. Dwek, Chem. Commun., 1132 (1970).

156. K. Nakanishi and J. Dillon, J. Amer. Chem. Soc., 93, 4058 (1971).

157. (m) H. Newman, Tetrahedron Lett., 4571 (1971).

158. (m) J. E. Nordlander, and T.J. McCrary, Jr., J. Amer. Chem. Soc., 94, 5133 (1972).

159. M. Ohashi, I. Morishima, K. Okada, T. Yonezawa, and T. Nishida, Chem. Commun., 34 (1971).

160. M. Ohashi, I. Morishima, and T. Yonezawa, Bull. Chem. Soc. Jap., 44, 576 (1971).

161. T. Okutani, A. Morimoto, T. Kaneko and K. Masuda, Tetrahedron Lett., 1115 (1971).

162. J. Paasivirta, Suomen Kemistilehti B, 44, 131 (1971).

163. J. Paasivirta, Suomen Kemistilehti B, 44, 135 (1971).

164. T.B. Patrick and P.H. Patrick, J. Amer. Chem. Soc., 94, 6230 (1972).

165. J. Paul, K. Schlogl, and W. Silhan, Monatsh. Chem., 103, 243 (1972).

166. W.D. Perry and R.S. Drago, J. Amer. Chem. Soc., 93, 2183 (1971).

167. J.A. Peters, J.D. Remijnse, A. van der Wiele, and H. van Bekkum, Tetrahedron Lett., 3065 (1971).

168. W. Platzer and P. Demerseman, Bull. Soc. Chim. Fr., 192 (1972).

169. D.L. Rabenstein, Anal. Chem., 43, 1599 (1971).

170. A.J. Rafalski, J. Barciszewski, and M. Wiewiorowski, Tetrahedron Lett., 2829 (1971).

171. D.C. Remy and W.A. Van Saun, Jr., Tetrahedron Lett., 2463 (1971).

172. J. Reuben and D. Fiat, Chem. Commun., 729 (1967).

173. J. Reuben and D. Fiat, J. Chem. Phys., 47, 5440 (1967).

174. J. Reuben and D. Fiat, J. Chem. Phys., 51, 4909 (1969).

175. J. Reuben and D. Fiat, J. Chem. Phys., 51, 4918 (1969).

176. J. Reuben and J.S. Leigh, Jr., J. Amer. Chem. Soc., 94, 2789 (1972).

177. C. Reyes-Zamora and C.S. Tsai, Chem. Commun., 1047 (1971).

178. H.G. Richey, Jr. and F.W. Von Rein, Tetrahedron Lett., 3781 (1971).

179. R.E. Rondeau, M.A. Berwick, R.N. Steppel, and M.P. Serve, J. Amer. Chem. Soc., 94, 1096 (1972).

180. R.E. Rondeau and R.E. Sievers, J. Amer. Chem. Soc., 93, 1522 (1971).

181. A.A.M. Roof, A. van Wageningen, C. Kruk and H. Cerfontain, Tetrahedron Lett., 367 (1972).

182. K. Roth, M. Grosse and D. Rewicki, Tetrahedron Lett., 435 (1972).

183. J.K.M. Sanders, S.W. Hanson, and D.H. Williams, J. Amer. Chem. Soc., 94, 5325 (1972).

184. J.K.M. Sanders and D.H. Williams, Chem. Commun., 422 (1970).

185. J.K.M. Sanders and D.H. Williams, J. Amer. Chem. Soc., 93, 641 (1971).

186. J.K.M. Sanders and D.H. Williams, Tetrahedron Lett., 2813 (1971).

187. H.-D. Scharf and M.-H Feilen, Tetrahedron Lett., 2745 (1971).

188. (m) J.R. Scheffer and B.A. Boire, J. Amer. Chem. Soc., 93, 5490 (1971).

189. G.P. Schiemenz, J. Magn. Resonance, 6, 291 (1972).

190. G.P. Schiemenz and H. Rast, Tetrahedron Lett., 4685 (1971).

191. (m) G.P. Schiemenz and H. Rast, Tetrahedron Lett., 1697 (1972).

192. J.E. Schwarberg, D.R. Gere, R.E. Sievers, and K.J. Eisentraut, Inorg. Chem., 6, 1933 (1967).

193. J. Selbin, N. Ahmad and N. Bhacca, Inorg. Chem., 10, 1383 (1971).

194. R. Seux, G. Morel and A. Foucaud, Tetrahedron Lett., 1003 (1972).

195. B.L. Shapiro, J.R. Hlubucek, G.R. Sullivan, and L.F. Johnson, J. Amer. Chem. Soc., 93, 3281 (1971).

196. B.L. Shapiro, M.D. Johnston, Jr., and R.L.R. Towns, J. Amer. Chem. Soc., 94, 4381 (1972).

197. J.S. Sheppard and J.L. Burdett, Inorg. Chem., 5, 921 (1966).

198. T. Shingu, T. Hayashi and H. Inouye, Tetrahedron Lett., 3619 (1971).

199. T.H. Siddall, III, Chem. Commun., 452 (1971).

200. J. Skolik, J. Barciszewski, A.J. Rafalski and M. Wiewiorowski, Bull. Acad. Pol. Sci., Ser. Sci. Chem., 19, 599 (1971).

201. G.V. Smith, W.A. Boyd, and C.C. Hinckley, J. Amer. Chem. Soc., 93, 6319 (1971).

202. W.B. Smith and D.L. Deavenport, J. Magn. Resonance, 6, 256 (1972).

203. C.S. Springer, Jr., D.W. Meek and R.E. Sievers, Inorg. Chem., 6, 1105 (1967).

204. K.-E. Stensio, and U. Ahlin, Tetrahedron Lett., 4729 (1971).

205. G.E. Stolzenberg, R.G. Zaylskie, and P.A. Olson, Anal. Chem., 43, 908 (1971).

206. (m) H.H. Strain, W.A. Svec, K. Aitzetmuller, M.C. Gradolfo, J.J. Katz, J. Kjosen, S. Norgard, S. Liaaen-Jensen, F.T. Haxo, P.Wegfahrt, and H. Rapoport, J. Amer. Chem. Soc., 93, 1823 (1971).

207. D. Swern and J.P. Wineburg, J. Amer. Oil Chem. Soc., 48, 371 (1971).

208. (m) W.A. Szarek and M.C. Baird, Tetrahedron Lett., 2097 (1970).

209. M. Tada, Y. Moriyama, Y. Tanahashi, T. Takahashi, M. Fukuyama, and K. Sato, Tetrahedron Lett., 4007 (1971).

210. R.C. Taylor and D.B. Walters, Tetrahedron Lett., 63 (1972).

211. Y. Takagi, S. Teratani, and J. Uzawza, Chem. Commun., 280 (1972).

212. (m) Y. Tamura, Y. Kita, H. Ishibashi, and M. Ikeda, Chem. Commun., 1167 (1971).

213. (m) H. Tanida and T. Tsushima, Tetrahedron Lett., 395 (1972).

214. (m) H. Tanida, T. Tsushima, and Y. Terui, Tetrahedron Lett., 399 (1972).

215. S.B. Tjan and F.R. Visser, Tetrahedron Lett., 2833 (1971).

216. L. Tomic, Z. Majerski, M. Tomic, and D.E. Sunko, Chem. Commun., 719 (1971).

217. K. Tori, Y. Yoshimura, and R. Muneyuki, Tetrahedron Lett., 333 (1971).

218. J.M.J. Tronchet, F. Barbalat-Rey, and N. Le-Hong, Helv. Chim. Acta, 54, 2615 (1971).

219. K. Tsukida and M. Ito, Experientia, 27, 1004 (1971).

220. E. Vedejs and M.F. Salomon, J. Amer. Chem. Soc., 92, 6965 (1970).

221. M.R. Vegar and R.J. Wells, Tetrahedron Lett., 2847 (1971).

222. G.H. Wahl, Jr., and M.R. Peterson, Jr., Chem. Commun., 1167 (1970).

223. W. Walter, R.F. Becker and J. Thiem, Tetrahedron Lett., 1971 (1971).

224. H. Wamhoff, H.W. Durbeck and P. Sohar, Tetrahedron, 27, 5873 (1971).

225. T.M. Ward, I.L. Allcox and G.H. Wahl, Jr., Tetrahedron Lett., 4421 (1971).

226. G.A. Webb, Annual Rep. NMR Spectrosc., 3, 211 (1970).

227. S.I. Weissman, J. Amer. Chem. Soc., 93, 4928 (1971).

228. E. Wenkert, D. W. Cochran, E. W. Hagaman, R. B. Lewis, and R. M. Schell, J. Amer. Chem. Soc., 93, 6271 (1971).

229. N. H. Werstiuk and T. Kadai, Chem. Commun., 1349 (1971).

230. G. M. Whitesides and J. S. Filippo, Jr., J. Amer. Chem. Soc., 92, 6611 (1970).

231. G. M. Whitesides and D. W. Lewis, J. Amer. Chem. Soc., 92, 6979 (1970).

232. G. M. Whitesides and D. W. Lewis, J. Amer. Chem. Soc., 93, 5914 (1971).

233. M. R. Willcott, III, R. E. Lenkinski, and R. E. Davis, J. Amer. Chem. Soc., 94, 1742 (1972).

234. M. R. Willcott, J. F. M. Oth, J. Thio, G. Plinke, and G. Schröder, Tetrahedron Lett., 1579 (1971).

235. D. E. Williams, Tetrahedron Lett., 1345 (1972).

236. M. Witanowski, L. Stefaniak, and H. Januszewski, Chem. Commun., 1573 (1971).

237. M. Witanowski, L. Stefaniak, H. Januszewski, and Z. W. Wolkowski, Tetrahedron Lett., 1653 (1971).

238. T. A. Wittstruck, J. Amer. Chem. Soc., 94, 5130 (1972).

239. Z. W. Wolkowski, Tetrahedron Lett., 821 (1971).

240. Z. W. Wolkowski, Tetrahedron Lett., 825 (1971).

241. K. C. Yee and W. G. Bentrude, Tetrahedron Lett., 2775 (1971).

242. T. Yonezawa, I. Morishima, Y. Akana, and K. Fukuta, Bull. Chem. Soc. Jap., 43, 379 (1970).

Abstracts of Propositions

I. A study of the electrocyclic reactions of potentially singlet state trimethylenemethane intermediates is proposed.

II. A detailed study of the complex formed between lanthanide nmr shift reagents and rigid, bicyclic ethers is proposed in order to elucidate the nature of the interaction between the reagent metal atom and heteroatom lone-pair electrons.

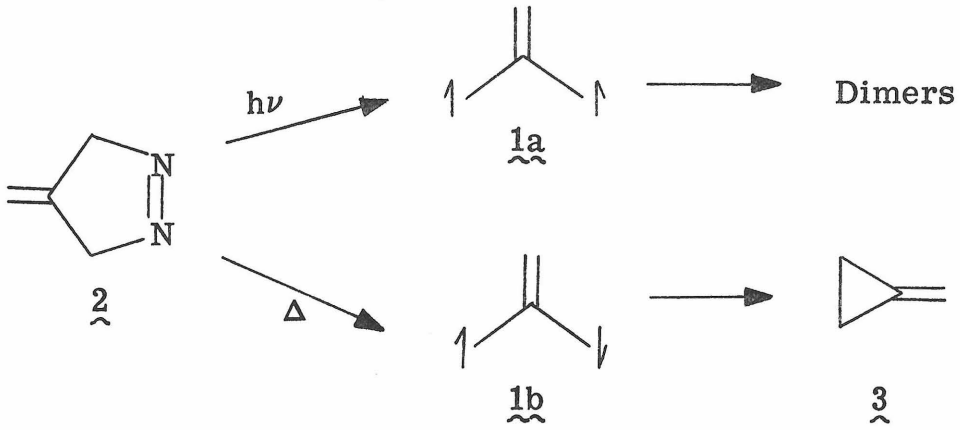
III. It is proposed that cyclopropenyl-stabilized vinyl cations may be generated upon ionization of 2-methylenebicyclobutyl precursors.

IV. A topological approach to unimolecular transformations is developed along with a computer overlap analysis procedure relating reactant and product topologies. Several symmetrical and non-symmetrical transformations and possible extensions to other systems are discussed.

V. Two experimental studies are proposed in order to help elucidate the nature of solvent effects on the infrared absorption (stretch) of the carbonyl group.

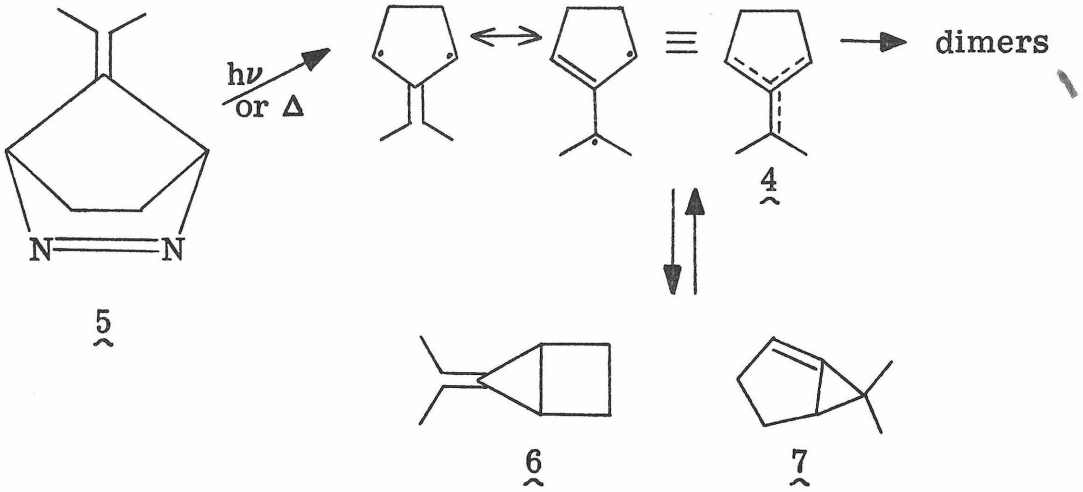
PROPOSITION I

Theoretical studies have predicted the trimethylenemethane molecule 1 to exist as a ground state triplet diradical 1a (1, 2). The



singlet state 1b is predicted to be as much as 58 kcal/mole higher in energy (2). The triplet ground state has been observed by electron spin resonance spectroscopy of 1 generated by low temperature photolysis of 4-methylene-1-pyrazoline, 2, or of 3-methylenecyclobutanone (3). Pyrolysis of 2 gave only methylenecyclopropane (4). Borden (5) has suggested that, based on orbital symmetry considerations (6), photolysis of 2 could give the triplet ground state 1a directly from the triplet excited state of 2, but that pyrolysis should give the excited singlet state of 1 (if nitrogen leaves in a singlet state). The singlet state 1b can close to methylenecyclopropane, but triplet 1a cannot form 3 and can only dimerize. The fact that Crawford and Cameron (4) obtained only 3 upon pyrolysis of 2 suggests that singlet 1b was formed and that ring closure (concerted ?) to 3 was much faster than intersystem-crossing to 1a (5).

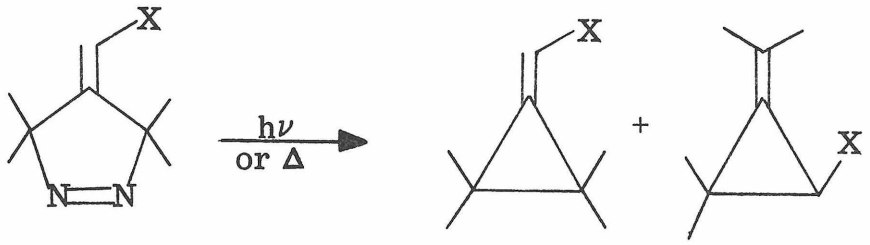
Berson and coworkers have recently reported the generation of 4 by photolysis and pyrolysis of pyrazoline 5 (7). The products were dimers of 4, and the chemically induced dynamic nuclear spin polarization emission observed for the dimeric products, along with the esr



5 4 6 7

spectrum of 4, support the intervention of a triplet species (7, 8). A singlet intermediate would not be expected to close to the highly strained compounds 6 or 7, and thus singlet 4 exists until intersystem-crossing to the ground state triplet can occur. Dimerization products from presumed trimethylenemethane intermediates have also been observed by Doerr and Skell (9), Schirmann and Weiss (10), and Kobrich and Heinemann (11).

Day and coworkers (12) have studied the reactions of pyrazolines of structure 8. Both direct and triplet sensitized photolyses and pyrolyses of the pyrazolines gave the products shown. The distribution of isomers depended upon the reaction conditions. It is impor-



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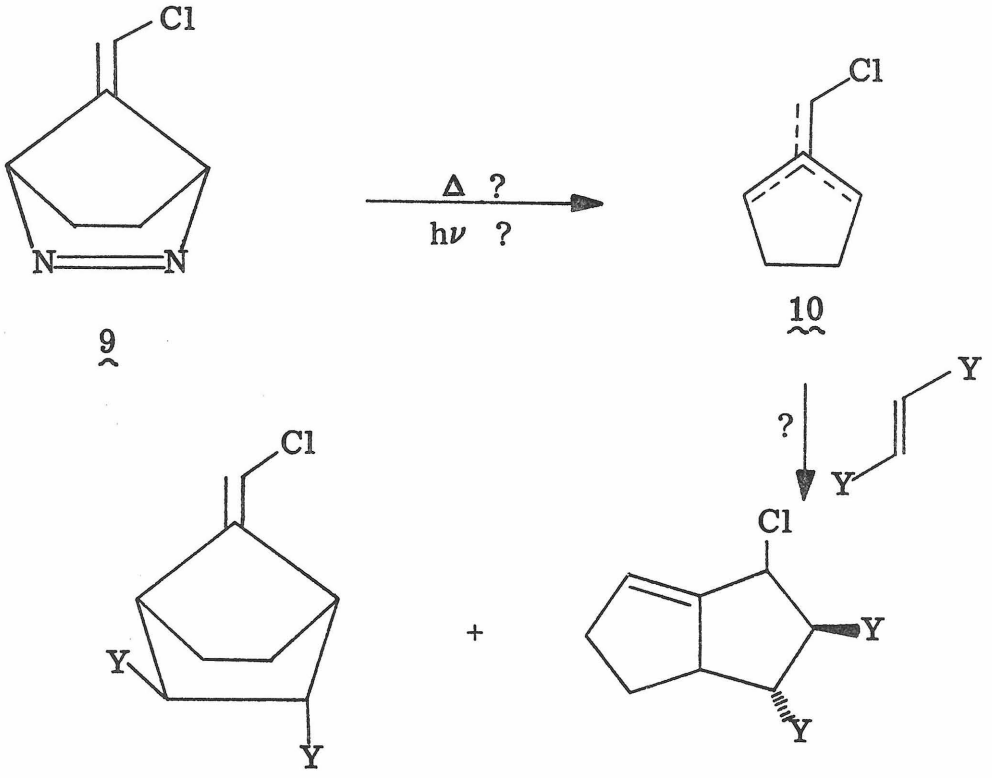
(X = -Cl or -CO_2Et)

tant to note that ring-closed products, not dimers, were the reaction products -- even in the sensitized photolyses, which according to Borden's analysis (5) should give triplet ground state trimethylenemethane. A plausible explanation, recognized at least in part by Day and coworkers, is that singlet intermediates are involved as ground state species.

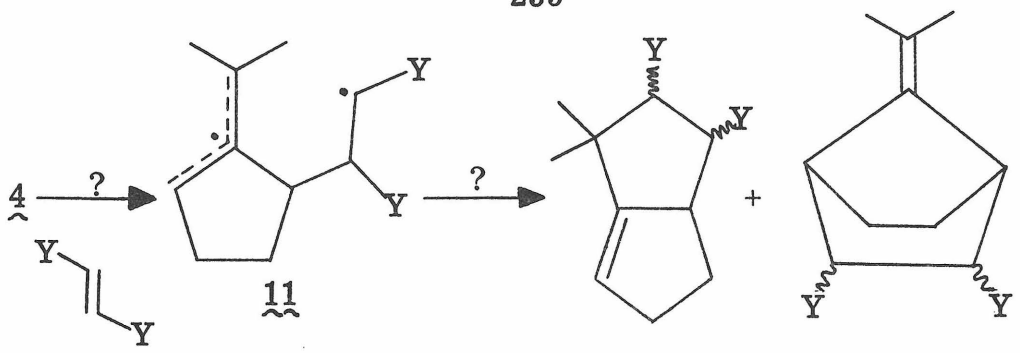
I propose the following hypothesis: An electron rich or deficient substituent on the trimethylenemethane intermediate (e.g. Cl, F, CN, CO_2R, etc.) causes the ground state to be a singlet species through perturbation of the molecular orbitals. It is then possible for the system to no longer act as a diradical, but as a delocalized π-system. Therefore, reactions such as cycloadditions to olefins and dienes could occur according to "orbital symmetry" control.

The following experiment is designed to test this hypothesis. A simple modification of Berson and coworkers' synthesis of 5, using 6-chlorofulvene (13) as the starting material, would give pyrazoline 9. If the chlorine substituent effectively removes the orbital degeneracy in the intermediate (and at least CNDO/2 calculations indicate that it may) so that 10, generated by photolysis or pyrolysis of 9, is a singlet, then the esr should not give triplet species signals and the

dimeric products should not exhibit CIDNP emissions . It is important, too, that 10 is not expected to form internal cyclization products (e.g. 6 and 7) due to the high strain energy involved, even though an "unrestrained" singlet would be expected to give methylenecyclopropanes quickly (see above). Therefore, trapping with olefins should be efficient.



In comparing the reactions of intermediates 10 and 4 with olefins or dienes, the trapped triplet species 11 (from 4) must await spin inversion before ring closure to products can occur. But a singlet species 10 may react to form products in a one-step, concerted manner. Trapping of 4 with, say, a trans-disubstituted olefin for example may give products of scrambled stereochemistry, whereas



with 10, the trans relationship may be retained in the products. If triplet sensitized photolysis led to an excited state triplet 10, then scrambled stereochemistry in the products can occur if trapping competes effectively with intersystem-crossing to the ground state singlet 10. If the intermediate singlet 10 behaves as a delocalized π-system, rather than as a diradical, then "orbital symmetry" may influence the cycloadditions, i.e. some additions may be allowed and others may be forbidden, depending upon the substrate and the reaction conditions.

It would be nice to be able to present, out of hand, a complete correlation diagram (6) to "prove" the proposed orbital symmetry control. However, we have assumed that the substituent perturbation is large enough so that the symmetry of the molecule is vastly disrupted and none of the essential symmetry elements remain for analysis. One cannot simply ignore the dissymmetric substituent nor make arbitrary assumptions about the orbitals involved in the reaction, because the dissymmetric perturbation is crucial to the existence of the ground state singlet species in the first place. The experiments themselves would have to decide whether or not orbital control is im-

portant in these reactions.

Of course, 10 may act as a singlet diradical, rather than as a π-system, and all cycloadditions may be allowed, although there might be differences in stereoselectivity depending upon whether the diradical was ground state or excited state species.

A variety of disubstituted olefins and dienes could be tested for reaction with 10 (and 4), and the reaction system may be modified by replacing the chlorine substituent of 9 by cyano, carboethoxy, etc., in order to test the effect these modifications would have upon the stereoselectivity of the addition reactions.

After this proposal was intially prepared, Berson and coworkers (14) indeed showed that cycloadditions of 4 with olefins and dienes do occur. The product distributions with dimethyl maleate and dimethyl fumarate, while not identical, indicated low stereoselectivity. The above proposal then suggests that these reactions may become stereospecific when the appropriate perturbing group is conjugated with the trimethylenemethane π-system.

The experiments outlined here could provide answers to some theoretically important and useful problems: (1) the effect of electronic perturbation upon the state energies of trimethylenemethanes, (2) the nature of the singlet trimethylenemethane intermediates (diradical?), (3) the applicability of orbital symmetry control to reactions of trimethylenemethane singlet states and to intrinsically unsymmetric orbital systems, (4) the possible stereoselective syntheses of bicyclo[2.2.1]heptanes, 1-bicyclo[3.3.0]-

octenes, 3-bicyclo[4.2.1.]nonenes, and 3.7-bicyclo[5.3.0.]deca-dienes.

References

1. D. P. Chong and J. W. Linnett, J. Chem. Soc., 1798 (1965); A. Streitwieser, Jr., "Molecular Orbital Theory for Organic Chemists," Wiley, New York, N.Y., 1961, p 43.

2. M. J. S. Dewar and S. D. Worley, J. Chem. Phys., 51, 1672 (1969)

3. P. Dowd, J. Amer. Chem. Soc., 88, 2587 (1966); P. Dowd and K. Sachdev, ibid., 89, 715 (1967); P. Dowd, A. Gold, and K. Sachdev, ibid., 90, 2715 (1968).

4. R. J. Crawford and D. M. Cameron, ibid., 88, 2589 (1966).

5. W. T. Borden, Tetrahedron Lett., 259 (1967).

6. For a definitive discussion of orbital symmetry, see R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N.Y., 1970.

7. J. A. Berson, R. J. Bushby, J. M. McBride, and M. Tremelling, J. Amer. Chem. Soc., 93, 1544 (1971).

8. G. L. Closs, ibid., 93, 1546 (1971).

9. R. G. Doerr and P. S. Skell, ibid., 89, 3062, 4688 (1967).

10. J.-P. Schirmann and F. Weiss, Tetrahedron Lett., 5163 (1967).

11. G. Kobrich and H. Heinemann, Chem. Commun., 493 (1969).

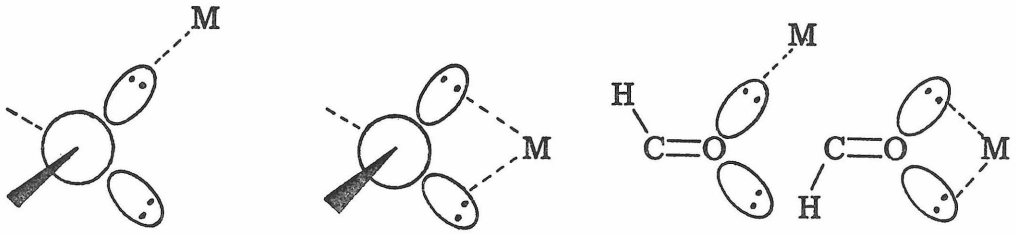
12. A. C. Day and M. C. Whiting, J. Chem. Soc. (C), 464 (1966); S. D. Andrews and A. C. Day, Chem. Commun., 667 (1966); J. Chem. Soc. (B), 1271 (1968).

13. M. B. D'Amore and R. G. Bergman, Chem. Commun., 461 (1971).

14. J. A. Berson, D. M. McDaniel, L. R. Corwin, and J. H. Davis, J. Amer. Chem. Soc., 94, 5508 (1972); J. A. Berson, D. M. McDaniel, and L. R. Corwin, ibid., 94, 5509 (1972).

PROPOSITION II

As the bibliography included in Part III of this thesis shows, there has been considerable interest in the nmr shift reagents since Hinckley's report in 1969 (1). However, very little is known about the manner in which these reagents complex to electron rich centers. Specifically, I propose here a study that may help reveal how these reagents complex with oxygen. The possible modes of complexation between reagent (the metal atom, M, shown) and ether and carbonyl oxygen are shown below. The lone-pair electrons are shown as occupying sp^2-hybridized orbitals, since hydrogen bonding studies (2) appear to justify this representation. In 1 or 3 the coordination is shown with one of the lone-pairs ("angular" coordination), but in 2 or 4 the coordination involves both lone-pairs ("linear" coordination). These two different modes, angular and linear, are inherently differ-



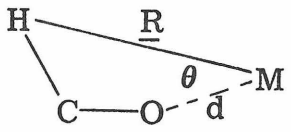
1 2 3 4

ent, since the orientations of the substrate atoms (protons) in relation to the metal atom may be quite different in the two cases.

The published work on shift reagent complexes has invariably been based upon the pseudo-contact model (1, 3), which for axially symmetric complexes gives an equation of the form of eq 1, where Δ is the

$$\Delta = C(3\cos^2\theta - 1)/R^3 \qquad (1)$$

paramagnetic (or diamagnetic) shift in ppm, C is a constant, and θ and $\underline{R}$ are angle and distance factors defined below. Innumerable



variations have been tried using this basic model. Some studies have measured $\underline{R}$ from the heteroatom, some have included the angle term, some have ignored the angle term, some have found a $1/R^2$ relation, etc. (4-6). Since upfield shifts, rather than the usual downfield shifts, have been observed with europium reagents (7, 8), this has been taken as evidence for the applicability of eq 1 because the equation predicts reversed shifts in the angle dependence. The most detailed analysis of the <u>effective</u> reagent-substrate complex structure has been done by Willcott and coworkers (9), who have carried out computer analyses of rigid substrates using the pseudo-contact model and statistical correlations.

There are at least two important factors which can cause problems in calculating the structure of the complex: (1) the applicability of the pseudo-contact model and (2) the possibility of two or more complexation configurations. The pseudo-contact model, and particularly the equations derived from symmetry assumptions, have been criticized as approximate or perhaps not applicable (1, 8, 10, 11). There

is general experimental support for the model (5, 6, 10, 12), particularly from the calculations by Willcott and coworkers (9), but there is also some indication that contact shift contributions may be important in some cases (13). In view of the existing uncertainties concerning the mechanism of the induced shifts, one should approach the use of the pseudo-contact equations with some caution when trying to deduce the specific reagent - complex structure itself, although such care may not be necessary when the primary objective is the useful application of shift reagents for solving substrate structure only (9).

Now concerning the second point above, in all calculations reported so far, the metal atom is generally positioned at some point near the heteroatom, the angle and distance factors are calculated for each nucleus, eq 1 is applied, and the relative shifts for each nucleus are obtained. The position of the metal atom is varied until the calculated shifts agree best with the observed shifts. The procedure generally ignores rotation about single bonds, e.g. methyl, changes in substrate conformations, and the possibility that more than one "coordination site" may be significant -- even for monofunctional compounds.

For example, if the reagent complexes to a carbonyl oxygen in the angular mode, $\underset{\frown}{3}$ above, there are in effect two coordination sites, one on either side of the axis through the C-O bond. However, when a calculation is performed on the complex in one configuration, the pseudo-contact model may give poor correspondence to experiment because the effect of the "other" configuration has been ignored

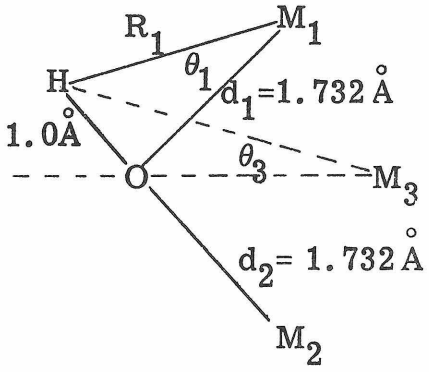
-- the shift of a given proton is due to the combined effect of the reagent in two different angular modes. For the proton shown in 3, the observed shift is the combined effect, to a first approximation, of two equilibria, one with M syn to the proton and the other anti to the proton. Each equilibrium complex (call C_a and C_s) results in a paramagnetic shift, Δ_a and Δ_s, so that the observed shift is given by eq 2 (see Part III). If one assumes that the equilibrium

$$\Delta_{obsd} = (\Delta_a[C_a] + \Delta_s[C_s])/S_t \qquad (2)$$

constants for the two complexation geometries are the same, the the pseudo-contact model gives eq 3.

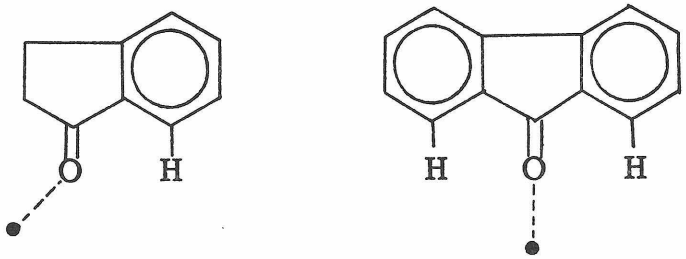
$$\Delta = (\Delta_a + \Delta_s)/2 = (C/2)[(3\cos^2\theta_a - 1)/R_a^3 + (3\cos^2\theta_s - 1)/R_s^3] \qquad (3)$$

Assumption of a single complexation site may give the effective position of the metal atom as shown in 4 above, even though this is not the true mode. As a hypothetical case, consider a proton with an observed shift of 25.5 ppm that is the result of two "equal" complexations of the metal atom shown below, M_1 and M_2. In this case, $\theta_1 = 30^o$, $R_1 = 2.0$ Å, $\theta_2 = 0^o$, and $R_2 = 2.732$ Å. Equation 3 then allows the calculation of constant C = 200. Knowing C, we can



then calculate from eq 1 the effective parameters if the metal atom is positioned along the axis, M_3. A shift of 24.5 ppm is obtained when $\theta_3 = 17^{o}$ and $R_3 = 2.42$. The O-M distance has shortened slightly from 1.732 Å to ~1.6 Å . A real system is more complex since many more protons must be correlated, but the example illustrates the possibility that only effective complex configurations may result from single configuration calculations.

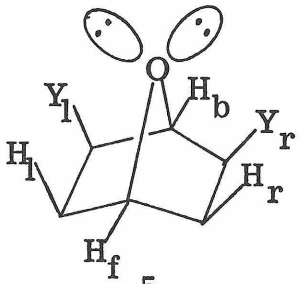
For a specific example, Wolkowski (14) calculated the lanthanide positions (dot) for the compounds shown below. (Unfortunately, the angle term of eq 1 was ignored, but the example is still qualitatively valid.) In benzocyclopentenone the metal lies off the C-O axis pre-



sumably because of steric interactions with the hydrogen (shown) (14). In the dibenzo compound, the symmetry dictates that a single cal-

culation must place the lanthanide on the C-O axis, but the true mode might just as well be two equivalent complexations on either side of the axis (see 3 above). The author attributed the behavior to complexation in the dibenzo compound at a carbonyl sp-hybridized (15) lone-pair when the complexations to the p-orbital lone-pair (15) are blocked (14). (Representing the carbonyl lone-pairs in this way (15), rather than as sp^2 orbitals (2), results in three "complexation sites", but this does not materially affect the rationale of this proposal.)

In order to answer the questions raised at the beginning of this proposal regarding the specific configurations for complexation of shift reagents with ethers and carbonyl oxygens, I propose a study of substituted 7-oxanorbornanes and 7-norbornanones, 5 and 6, both of which have a "right" and "left" side with respect to the oxygen lone-pairs. In view of some uncertainties mentioned above about the appropriateness of the pseudo-contact model, the "standard proton"



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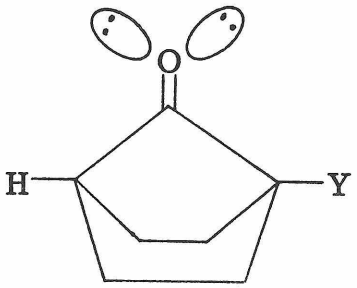


6

method (see Part III) would be used to assess the interaction mode.

If the complexation of 5 is a linear one, corresponding to 2 above, then when substituent Y_r (right side) is changed from H to methyl, there may be little effect upon the relative shifts of the other

protons. That is, we can use the bridgehead protons, H_f and H_b, as reference protons. If the complexation is linear, then the slopes of the plots of the observed shifts of H_f vs. the observed shifts of H_r and H_l should be the same, even when Y_r or Y_l or both are methyl groups. Of course, the absolute slope values may change somewhat as the substituents are changed, but for any given case, the "right" and "left" protons will be equivalent with respect to the linearly complexed metal atom.

The situation is quite different if the angular mode, corresponding the 1 above, obtains for 5. There are two complexation sites -- one on the left side of the H_f-O-H_b plane and one on the right. When $Y_r = Y_l = H$, then plots of shifts of H_r vs. H_f and H_l vs. H_f must result in equal slopes. If Y_r = methyl, then complexation of reagent on the right may be partially or completely blocked. In contrast to the linear situation above, the left and right slopes, S^l and S^r, for the left and right hydrogens, H_l and H_r, cannot be equal. (S^l means the slope of the plot obtained when the observed shifts of H_l are plotted against the observed shifts of H_f or H_b.) In fact, one predicts that S^l should be much less than S^r in this case, and that S^l should be less than the corresponding slope when Y_r was hydrogen.

To see this, we obtain eq 4 for the observed shift of proton i, $\Delta_{obsd}{}^i$, in the manner used in Part III. In this

$$\Delta_{obsd}{}^i = [\, \Delta_L{}^i(L) + \Delta_R{}^i(R) \,] / S_t \qquad (4)$$

equation (L) and (R) are the concentrations of substrate - reagent complexes where the configuration is with the metal atom on the left and right side of the molecule, respectively, S_t is the total concentration of substrate, and Δ_L^i and Δ_R^i are the paramagnetic shifts of proton i in the two different complexes. Since (L) = (R) when $Y_r = Y_l = H$ and $\Delta_L^f = \Delta_R^f = \Delta^f$ for H_f, one can show that the slope of a plot of Δ_{obsd}^f vs. Δ_{obsd}^i is

$$S_H^i = [2\Delta^f/(\Delta_L^i + \Delta_R^i)] \quad .$$

in this case, and of course $S_H^r = S_H^l$ (where superscripts r and l refer to protons H_r and H_l). For the case where Y_r = methyl and complexation on the right side is assumed to be totally blocked, then one can show that the slopes are

$$S_Y^l = \Delta^f/\Delta_L^l \qquad S_Y^r = \Delta^f/\Delta_L^r \quad .$$

Since proton H_r is much farther from the metal atom than is H_l when the reagent is complexed on the left, then qualitatively we expect $\Delta_L^l > \Delta_L^r$. Thus, $S_R^l < S_R^r$, since Δ^f is the same in slope expression. To see that $S_H^l > S_Y^l$, we write the inequality

$$S_H^l = [2\Delta^f/(\Delta_L^l + \Delta_R^l)] \quad > \quad \Delta^f / \Delta_L^l = S_Y^l$$

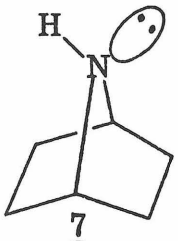
Since Δ^f presumably remains nearly constant and since $\Delta_R^l < \Delta_L^l$ (see above), then the inequality follows directly. Of course, the

corresponding effect for the two cases (Y_r = H and Y_r = methyl) for H_r is $S_Y{}^r > S_H{}^r$.

If the angular mode is correct, then if $Y_r = Y_1$ = methyl, complexation may be drastically reduced, i.e. the equilibrium constant for complexation may be much smaller because both complexation modes are hindered. Presumably, the equilibrium constants for the linear mode should not be greatly different in these cases. The procedure given in section B of Part III might be used to estimate the equilibrium complexation constants for the mono-, di-, and unsubstituted substrates. This information could be quite valuable.

The Y substituents could be varied somewhat, and in particular the bulky t-butyl group could be used to assure blockage of angular complexation. A symmetrical substituent would be an exo fused cyclopropyl ring.

A good model compound to which the results from 5 could be compared is 7-azanorbonane, 7, and its substituted derivatives corresponding to those used for 5. Most certainly, the reagent cannot complex in the linear mode, but lies to the right or to the left of



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the C_1-N-C_4 plane. Rapid inversion at the nitrogen should make each side of the compound equivalent and effectively simulate the oxygen lone-pairs of 5. If angular complexation is important for 5, then the standard proton results for 7 and its exo-substituted deriva-

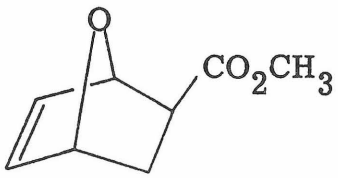
tives should be similar to the results for the ether system. If, in fact, $S_Y^l \neq S_Y^r$ when Y_r = methyl in 5, then the question may arise whether or not we are perturbing a linear mode rather than an angular mode . This may be answered in part by comparing the ratio S_Y^l/S_Y^r for 5, Y_r = methyl, to the same ratio for 7, Y_r = methyl. The ratios should be similar if angular complexation is important for 5 , but quite different if the methyl substituent on 5 is merely causing a slight perturbation of an essentially linear complexation.

The basic ideas are the same for the carbonyl compound 6 except that the "left" and "right" sides have been rotated by 90°. The exo and endo protons would be the reference protons for the bridgehead proton as substituent Y is varied. Molecular models show that a bridgehead methyl may have little effect sterically on angular complexation in this case, but t-butyl might be effective. The obvious model compound in this case is the corresponding imine, but to my knowledge this compound has not been reported. My main concern here is the study of the ether (5), and if the results proved reasonably conclusive for the ether (particularly in angular complexation were found), then the study of 6 would be a logical extension.

I should note that the systems lend themselves to much more analysis and substituent variations than outlined here. For example, the endo protons of 5 can be treated along with H_r and H_l, other substituents (neopentyl, etc.) could be used, and the data could be analyzed by the usual computer methods.

Syntheses of the compounds should not be terribly formidable.

Parent 5, 7-oxabicyclo[2.2.1.]heptane, is commercially available. Substituted derivatives could be made by appropriate transformations of Diehls-Alder adducts of olefins with furans, e.g. 8 (16). The intra-



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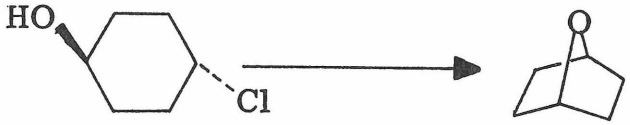
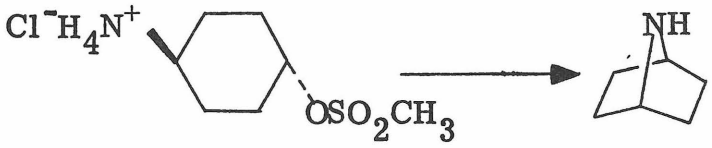
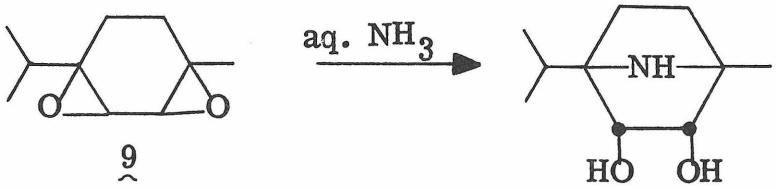
molecular displacement route used to prepare 5 (17) might lend



itself to incorporation of substituents, but this may be more difficult than the Diehls-Alder scheme. The intramolecular displacement reaction appears to be the best route to 7-azabicyclo[2.2.1.]heptane, 7 (18), and substituted derivatives have been reported (19) for



Diehls-Alder reactions. The observed transformation of 9 (20)



9

might also lend itself to preparation of suitably substituted derivatives.

The experiments outlined here should reveal some important characteristics of the nmr shift reagents and lead to a better understanding of the manner in which complexation with organic substrates occurs. It may turn out, of course, that the reagent really does not care about finding the highest electron density, and the reagent - substrate complex may be the sum of a wide variety of configurations in which steric considerations control the relative preferences. The selectivity of configurations should depend upon the Lewis acidity of the reagent, in which case $Eu(dpm)_3$ may show "more" angular complexation than $Eu(fod)_3$.

If the linear complexation is found, this may have important ramifications on interpretations of the equilibrium stoichiometry. Huber and coworkers (21) have some evidence that t-butyl alcohol forms a 1:1 complex with $Eu(fod)_3$ but that t-butylamine forms both 1:1 and 2:1 (amine:reagent) complexes. A possibly important distinction is that the amine has only one lone-pair, whereas the oxygen has two. The oxygen may act as a difunctional "ligand", and the coordination number of the metal may be maximal. It would take two amine molecules to satisfy this coordination number. Thus, 2:1 complexation can occur for amines, but "1:1" complexation obtains for alcohols, ethers, esters, etc. (This assumes that the organic substrates can be considered to form some type of covalent bond with the reagent metal atom, but the nature of this interaction is quite obscure at this time.)

On the other hand, if the angular complexations were shown to be

important, then this could require a rather drastic reappraisal of the usual single configuration computer fitting. For conformationally mobile groups, such as alcohols, methyl ethers, etc., there is no need to consider two complexation sites at the oxygen function, but for compounds in which the geometry is either fixed or energetically favorable, i.e. α,β-unsaturated aldehydes, the recognition of two complexation sites, both of which affect the averaged chemical shift of the substrate nuclei, may be quite important in establishing the structure of a given substrate and in examining the pseudo-contact model itself.

References

1. C. C. Hinckley, J. Amer. Chem. Soc., 91, 5160 (1969); J. Org. Chem., 35, 2834 (1970).

2. P. A. Kollman, J. Amer. Chem. Soc., 94, 1837 (1972); and references therein.

3. H. M. McConnell and R. E. Robertson, J. Chem. Phys., 29, 1361 (1958); for more complex equations applicable to complexes of lower symmetry, see G. N. LaMar, W. DeW. Horrocks, Jr., L. C. Allen, ibid., 41, 2126 (1964); G. N. LaMar, ibid., 43, 1085 (1965); R. J. Kurland and B. R. McGarvey, J. Magn. Resonance, 2, 286 (1970).

4. J. W. ApSimon and J. D. Cooney, Can. J. Chem., 49, 2378 (1971); W. L. F. Armarego, T. J. Batterham, and J. R. Kershaw, Org. Magn. Resonance, 3, 575 (1971); J. Barciszewski, A. J. Rafalski, and M. Wiewiorowski, Bull. Acad. Pol. Sci., Ser. Sci. Chim., 19, 545 (1971); P. Belanger, C. Freppel, D. Tizane, and J.-C. Richer, Can. J. Chem., 49, 1985 (1971); C. Beaute, Z. W. Wolkowski, J. P. Merda, and D. Lelandais, Tetrahedron Lett., 2473 (1971); J. Briggs, F. A. Hart, and G. P. Moss, Chem. Commun., 1506 (1970); J. Briggs, F. A. Hart, G. P. Moss, and E. W. Randall, ibid., 364 (1971); R. Caple and S. C. Kuo, Tetrahedron Lett., 4413 (1971); P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert, J. Amer. Chem. Soc., 92, 5734 (1970); O. A. Gansow, M. R. Willcott, and R. E. Lenkinski, ibid., 93, 4295 (1971); J. Goodisman and R. S. Matthews, Chem. Commun., 127 (1972); P. Granger, M. M. Claudon, and J. F. Guinet, Tetrahedron Lett., 4167 (1971); L. H. Keith, ibid., 3 (1971); J. Paasivirta, Suomen Kemistilehti B, 44, 131, 135 (1971); J. Reuben and J. S. Leigh, Jr., J. Amer. Chem. Soc., 94, 2789 (1972); J. K. M. Sanders and D. H. Williams, ibid., 93, 641 (1971); W. Walter, R. F. Becker, and J. Thiem, Tetrahedron Lett., 1971 (1971).

5. R. R. Fraser and Y. Y. Wigfield, Chem. Commun., 1471 (1970).

6. A. F. Cockerill and D. M. Rackham, Tetrahedron Lett., 5149 (1970).

7. N. S. Bhacca and J. D. Wander, Chem. Commun., 1505 (1971); D. E. U. Ekong, J. I. Okogun, and M. Shok, J. C. S. Perkin I, 653 (1972); M. Kishi, K. Tori, and T. Komeno, Tetrahedron Lett., 3525 (1971); P. H. Mazzocchi, H. J. Tamburin, and G. R. Miller, ibid., 1819 (1971); R. E. Rondeau, M. A. Berwick, R. N. Steppel, and M. P. Serve, J. Amer. Chem. Soc., 94, 1096 (1972); B. L. Shapiro, J. R. Hlubucek, G. R. Sullivan, and L. F. Johnson, ibid., 93, 3281 (1971); T. H. Siddall, III, Chem. Commun.,

452 (1971); S. B. Tjan and F. R. Visser, Tetrahedron Lett., 2833 (1971); M. R. Willcott, J. F. M. Oth, J. Thio, G. Plinke, and G. Schroder, ibid., 1579 (1971).

8. A. M. Grotens and J. Smid, J. Magn. Resonance, 6, 612 (1972).

9. M. R. Willcott, III, R. E. Lenkinski, and R. E. Davis, J. Amer. Chem. Soc., 94, 1742 (1972); R. E. Davis and M. R. Willcott, III, ibid., 94, 1744 (1972).

10. W. DeW. Horrocks, Jr., and J. P. Sipe, III, ibid., 93, 6800 (1971).

11. C. L. Honeybourne, Tetrahedron Lett., 1095 (1972).

12. H. Huber and C. Pascual, Helv. Chim. Acta, 54, 913 (1971).

13. M. R. Willcott, III, private communication.

14. Z. W. Wolkowski, Tetrahedron Lett., 821 (1971).

15. H. Suzuki, "Electronic Absorption Spectra and Geometry of Organic Molecules," Academic Press, New York, N.Y., 1967, p 429.

16. R. J. Ouellette, A. Rosenblum, and G. Booth, J. Org. Chem., 33, 4302 (1968).

17. A. W. Heine, J. Amer. Chem. Soc., 79, 6268 (1957).

18. R. R. Fraser and R. B. Swingle, Can. J. Chem., 48, 2065 (1970).

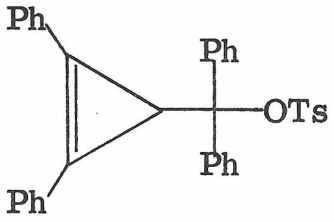
19. A. Shafi'ee and G. Hite, J. Org. Chem., 33, 3435 (1968); see also R. Kitzing, R. Fuchs, M. Joyeaux, and H. Pinzbach, Helv. Chim. Acta, 51, 888 (1968).

20. A. Runquist, G. Pierson, and O. Runquist, J. Org. Chem., 34, 3192 (1969).

21. H. Huber and J. Seelig, Helv. Chim. Acta, 55, 135 (1972).

PROPOSITION III

The solvolyses of cyclopropenylcarbinyl derivatives, e.g. 1, are thought to occur through a delocalized transition state such as 2, which involves the β,γ σ-bond, rather than the π-system (1-3). The



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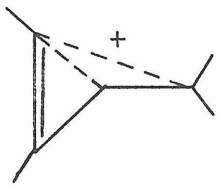
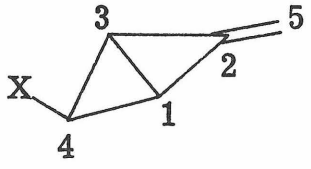


2

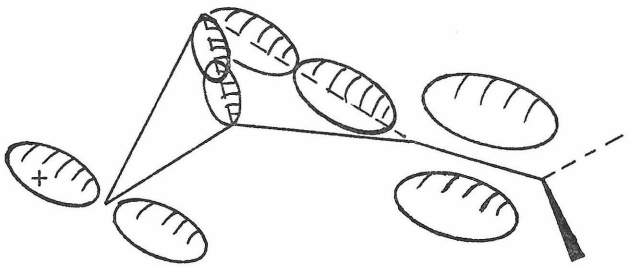
main products of these reactions are thought to arise from cyclobutenyl cation intermediates (1-3). Likewise, a large portion of the products from the solvolysis of cyclopropylcarbinyl derivatives are cyclobutanes (4). In contrast, a relatively small amount of cyclobutyl compounds are formed when 1-cyclopropyl-1-iodopropene or 1-iodo-3,4-hexadiene are reacted with silver actate in acetic acid (5).

It is proposed that one way of generating a vinyl cation stabilized by an adjacent cyclopropene ring is through solvolysis of a bicyclobutane derivative of structure 3, where X is an appropriate leaving



3

group. S_N1 solvolysis can involve participation of (or rearrangement involving) the 1-3 and/or 2-3 bonds, shown in intermediate 4. (The orbitals are shown along the atom centers for simplicity.)



4

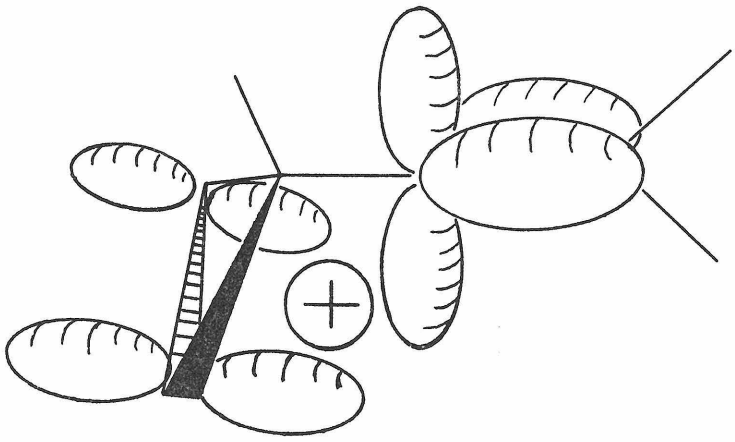
If the 1-3 σ-bond is involved, then the transition state or intermediate ion can be depicted as 5 , which can lead to the allylic cation 6. Allylic stabilization of 5 cannot be very important unless the transition state resembles 6, i.e. unless considerable twisting about

5 6

1-4 and 3-4 bonds occurs to achieve overlap. If the 2-3 bond participates in the ionization to 4 or is involved in rearrangement, then an alternate transition state or intermediate is 7, which can convert to the vinyl cation 8. Note that relatively little twisting may

7 8

be involved in this case for the developing cation at the vinyl center to achieve stabilization from the cyclopropene ring in the "bisected" conformation, in analogy to the proposed conformation for the cyclopropyl-stabilized vinyl cation (6). More twisting is involved to form the "homocyclopropenium" ion 9, which is thought to make little contribution to the stabilization of cyclopropenylcarbinyl cations (2, 3).



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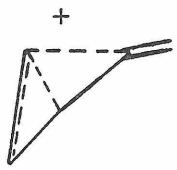
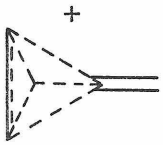
More extensively delocalized intermediates, such as 10 or 11, might be possible. Cation 10 could lead to cations 6 and/or 8 or trapped to give products derivable from 6 and 8. Cation 11 seems overly confusing.

Whether ions 5, 7, or 10 are involved as intermediates or as



10

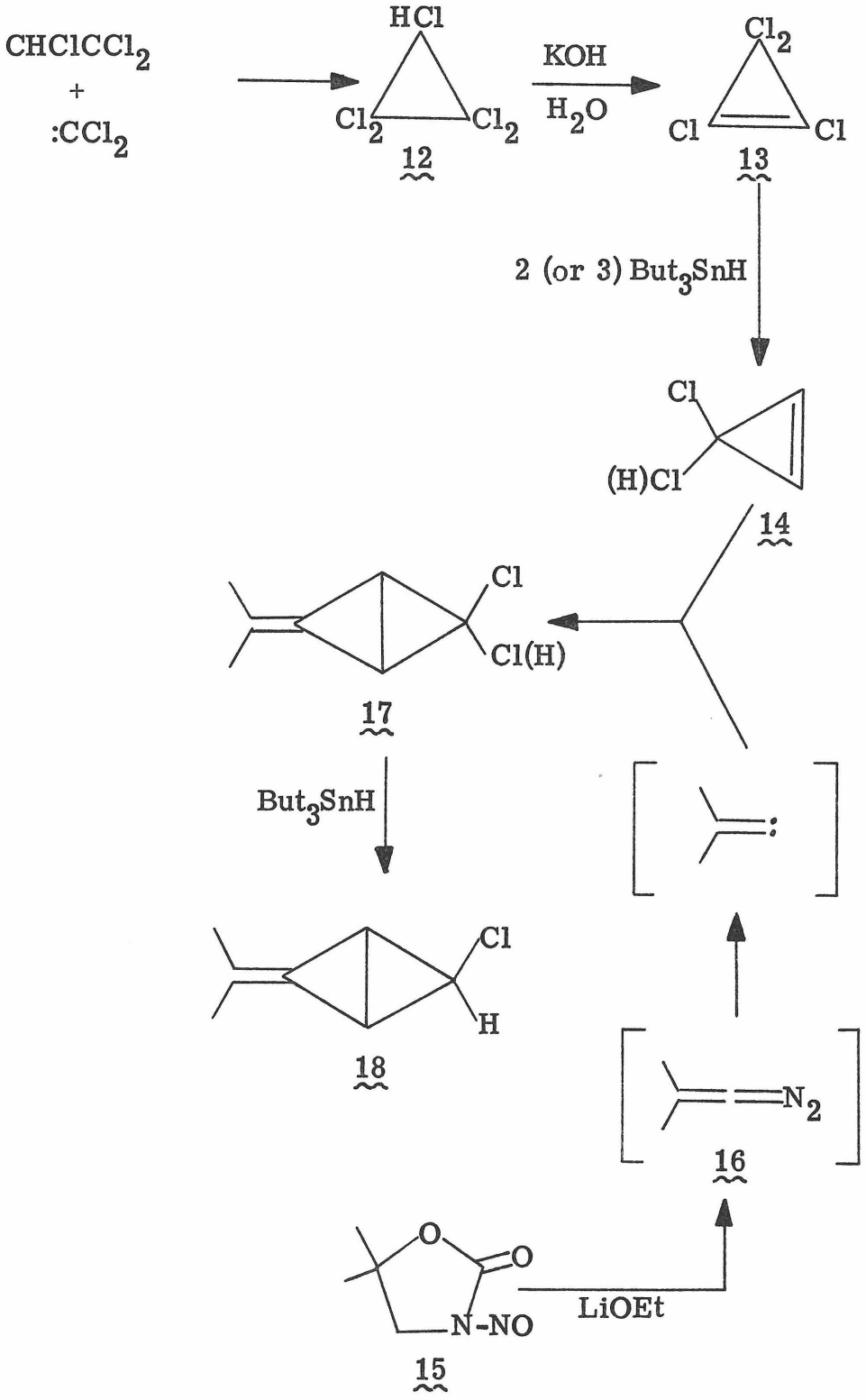


11

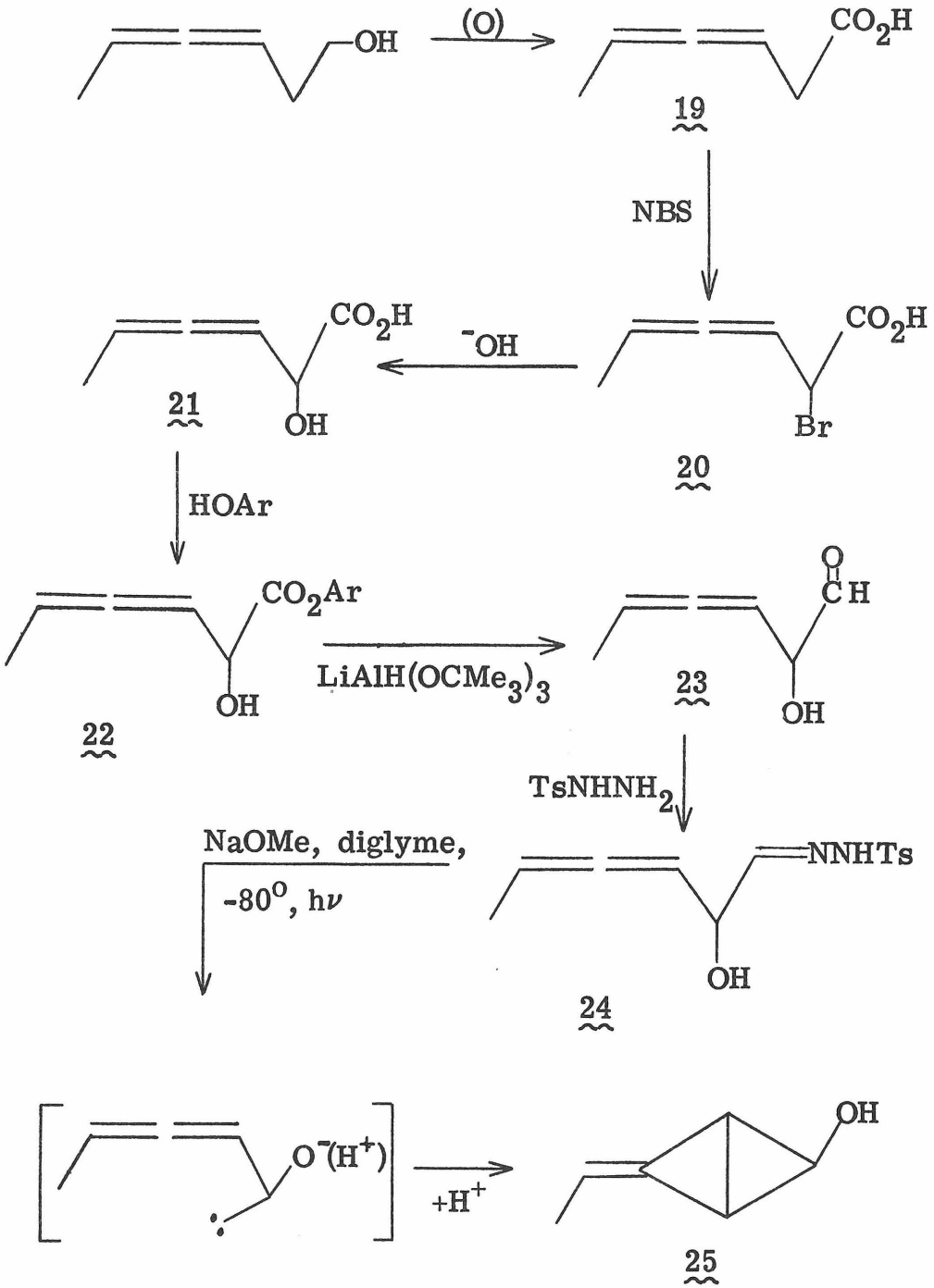
transition states leading to 6 or 8, the product distributions for vinyl iodide solvolyses (5) suggest that products arising from vinyl cation 8 may be found when compounds of structure 3 are solvolyzed, in contrast to the solvolyses products observed thus far for other cyclopropenylcarbinyl derivatives (2, 3).

One possible synthetic route for preparation of 3 is shown in Scheme I. Pentachlorocyclopropane 12 (7) is dehydrochlorinated to tetrachlorocyclopropene 13 (8). Careful reduction of 13 with two equivalents of tri-n-butyltin hydride can yield the dichloro compound 14 (9). (It may also be possible to obtain the monochloro reduction product.) Ethylidenecarbenes are believed to be produced when 5, 5-disubstituted-N-nitrosooxazolidones, 15, are treated with base, since methylenecyclopropanes are formed in the presence of olefins (10). Addition of the carbene to 14 can give 17, which can probably be reduced safely (without breaking the bridgehead bond) to the monochloro derivative 18 with tri-n-butyltin hydride. Barring difficulties in obtaining 14, the main forseeable obstacle may be the reaction of base in the carbene reaction with the cyclopropene 14. However, it may be possible to vacuum transfer the presumed diazo intermediate as it is formed, so that subsequent reaction with the cyclopropene can occur in the absence of base.

Scheme I


CHClCCl2
+
:CCl2
HCl
Cl2
Cl2
12
KOH
H2O
Cl2
Cl
Cl
13
2 (or 3) But3SnH
Cl
(H)Cl
14
Cl
Cl(H)
17
But3SnH
Cl
H
18
[:]
[N2]
16
O
O
N-NO
15
LiOEt

Scheme II


OH
(O)
CO2H
19
NBS
CO2H
Br
20
-OH
CO2H
OH
21
HOAr
CO2Ar
OH
22
LiAlH(OCMe3)3
O
CH
OH
23
TsNHNH2
NaOMe, diglyme,
-80°, hν
NNHTs
OH
24
O-(H+)
+H+
OH
25

Another route is given in Scheme II. 3,4-Hexadiene-1-ol (11) is oxidized to the corresponding acid, 19, which is treated with N-bromosuccinimide to give the α-bromo compound 20 (12). Displacement of the bromine by hydroxyl and subsequent esterification gives aryl ester 22. Reduction (13) may give aldehyde 23, which is then converted to tosylhydrazone 24. Photolysis of the sodium salt of 24 at low temperature (14) (or pyrolysis (15), if no too high a temperature is required) can lead to the intramolecular addition product 25 after careful acidification.

Bicyclobutanes have been prepared by carbene additions to cyclopropenes and by intramolecular carbene additions (16). Schemes I and II given here employ these overall approaches, but must also provide the exocyclic double bond and the leaving group (or a group readily converted to a leaving group, e.g. -OH) required by structure 3.

References

1. D. Bethell and V. Gold, "Carbonium Ions," Academic Press, London, 1967, p 254.

2. G. L. Closs, Adv. Alicyclic Chem., 1, 53 (1966).

3. R. Breslow, J. Lockhart, and A. Small, J. Amer. Chem. Soc., 84, 2793 (1962).

4. Ref 1, p 266ff.

5. This work, Part I.

6. This work, Part II.

7. S. W. Tobey and R. West, J. Amer. Chem. Soc., 88, 2478 (1966).

8. S. W. Tobey and R. West, ibid., 88, 2481 (1966).

9. R. Breslow and G. Ryan, ibid., 89, 3073 (1967).

10. M. S. Newman and T. B. Patrick, ibid., 91, 6461 (1969).

11. D. R. Kelsey and R. G. Bergman, ibid., 93, 1941 (1971).

12. R. C. Fuson, "Reactions of Organic Compounds," Wiley, New York, N. Y., 1962, pp 610-611.

13. H. O. House, "Modern Synthetic Reactions," 2nd ed., W.A. Benjamin, New York, N. Y., 1972, p 73.

14. W. G. Dauben, J. Amer. Chem. Soc., 84, 1497 (1962).

15. W. Kirmse, "Carbene Chemistry," 2nd ed., Academic Press, New York, N. Y., 1971, pp 29-34.

16. K. B. Wiberg, Adv. Alicyclic Chem., 2, 185 (1968).

PROPOSITION IV

Orbital symmetry control of chemical reactions, as developed largely by Woodward and Hoffmann (1), is clearly one of the major events in organic chemistry. The concept has explained a large body of data, has led to reliable predictions of chemical reactions, and has provided a challenge to the organic chemist to understand chemical systems in terms of more complete interactions, rather than as collections of atoms, bonds, and functional groups.

The Woodward-Hoffmann rules appear to work, but there is yet very little understanding of why they work or if they merely represent a simplified tool based upon a more elusive concept. Other approaches to orbital control have been postulated, notably the concept of transition state aromaticity by Zimmerman (2) and Dewar (3) and the perturbation approaches of Dougherty (4) and Epiotis (5). Goddard (6) has recently proposed the orbital phase continuity principle, which in essence contains the Woodward-Hoffmann rules as a subset but does not rely upon molecular symmetry.

For some time I have been intrigued with the idea that a molecular orbital, or rather the composite whole of the molecular orbitals as a description of a molecule, is a topological space which retains its identity under transformation -- not in a chemical sense, but in a topological sense. This then leads directly to the hypothesis that there is a " topological control" of molecular transformations, and that orbital symmetry would represent a special accessible case. Trindle (7) recently reported an approach to orbital control based upon sophisticated topological mapping calculations. The apparent success

of his approach has led me to explore the topological concept from an independent, though complementary, point of view.

Another concern of mine is the basic symmetry requirements of the Woodward-Hoffmann approach. In cases which are clearly unsymmetrical, one generally assumes that only a core set of orbitals control the reation and that perturbing influences of substituents are minimal, e.g. the electrocyclic ring-opening of 2-methylcyclobutene would be treated as if it were cyclobutene itself. The assumption is probably valid for many cases, but I suspected strongly influential substituents whose perturbations could not be ignored could be found. If such substituents were interacting with the core orbitals in a non-symmetric manner, then symmetry correlations could not be used to assess the orbital control.

My work here deals with these two concepts: (a) the topological approach to molecular transformations and (b) the application of the derived method to non-symmetric reactions. Note that my goal has not been to find a detailed theoretical treatment of topological or orbital control. I was much more interested in developing a computer method based on approximate, but inexpensive, extended Huckel (EHT) (8) or CNDO/2 (9) calculations that would allow a qualitative answer to the stereochemical consequences of a reaction. The approach developed here is certainly not a "pencil and paper" method, but it does apparently avoid the necessity for detailed energy surface calculations. It will be implicite in the following discussions that I am considering ground state (thermal) reactions only. I shall develop the topological rationale and then present the test of the procedure

with "known" reactions. Preliminary results for unknown reactions, generally the non-symmetrical cases, are then discussed.

The Topological Approach

I begin by making a broad and basic assumption: the total electronic (and nuclear) behavior that we call an atom or molecule is a unique topological space. I shall explain mathematically below what is meant by a topological space. In conceptual terms, we can view a particular molecule as a surface or "shape" which determines its identity and properties. When one describes a molecule in terms of atoms, bonds, and lone-pairs, then one is merely attempting to describe the shape of the space in terms of easily recognizable forms. In principle, there is a quantum mechanical function that will completely describe this shape. In practice of course, the exact function is undetermined, and we resort to less exact descriptions. The concept of molecular orbitals, as derived from the linear combination of atomic orbitals (LCAO), is such a description. The MO-LCAO orbitals approximate the topological "shape" of the molecule . Just as the joining of atoms with bonds allows us to "construct" a molecule, the total combination of molecular orbitals should allow us to approximate the topological space of a molecule. The total shape is not easily grasped since the "surface" is multidimensional, but this need not deter us from using the concept of the total space.

The second basic assumption regards chemical transformations: in a unimolecular reaction, the topological space of the reactant

transforms smoothly and continuously into the topological space of the product. The spaces are said to be homeomorphic in such a case. Trindle (7) justified a similar assumption on the basis that creating a node in a molecular orbital raised its energy and was equivalent to cutting or tearing the topological surface, i.e. the node creates a discontinuity in the transformation. In my view, however, such justification is unnecessary. The assumption itself does not require justification since it is an hypothesis to be tested. Furthermore, since a particular molecular orbital represents only part of the total surface, it is quite impossible to say that creation of a node in that orbital results in a discontinuity in the total surface. In fact, I could logically propose that one has merely moved the node from one MO to another while keeping the total surface homeomorphic (equivalent). The idea is intriguing and certainly not outside the concepts presented here.

Definitions

A more precise idea of topological space is required, and at this point the concepts become rather abstract. The definitions are taken from point set topology (10).

Neighborhoods: Let X be a set of points $\underline{x}$ (where $\underline{x}$ can be MO's, chairs, underwear, etc.). For each $\underline{x}$ in X, we must have a non-empty family, U_x^*, of subsets of X, U(x), i.e. $U_x^* = \{U(x)\}$. U_x^* is then a system of neighborhoods at $\underline{x}$ if:

(a) $\underline{x}$ is a member of all the subsets U(x) in U_x^*,

(b) if V is another subset of X that contains a U(x) as a subset,

then V is also in U_x*,

(c) if both sets P and Q are in U_x*, then the intersection of P with Q is also a member of U_x*,

(d) and if U(x) is a member of U_x*, then there must be at least one subset V of U(x) that is also a member of U_x* such that if another point y is in V, then U(x) is a member of the neighborhood U_y*.

Topological space: Given a set X with a neighborhood system defined for each point x in X, then X is a topological space.

Homeomorphism: Let X and Y be topological spaces. A function $f: X \rightarrow Y$ is a homeomorphism if f is one-to-one, onto, and both f and f^{-1} are continuous.

The MO Topological Space

The definition of a topological space in terms of neighborhoods is quite general. A priori, there is no mathematical (10) or conceptual basis on which to construct the "proper" topology of a molecule. The elements of X could be electrons, atomic orbitals, or MO's. Once the elements of X were chosen, they could be grouped in any number of ways under the restrictions of the definition to form many topologies.

One could also begin with the assumption that the MO's represent sets, rather than elements, of X. The elements of the MO sets could be taken as atomic orbitals or as points in three dimentional metric space. There are mathematical procedures (10) for generating topologies from sets rather than from elements, but in the present context this requires concepts such as unions and intersections of

MO's. For example, if one attempts to generate what is called a sub-basis (10) for a topology of X from the MO sets composed of metric space points and if one defines the intersection of two MO sets to be their overlap space, one quickly finds that the number of generated sets can soon exceed the storage capacity of most computers and that one must deal with three- and multicentered overlaps.

I therefore chose the elements of X to be the MO's themselves. I also chose to define the neighborhood systems for each MO, ψ , in X so that

$$U_{\psi}^{*} = \{ U \mid \psi \in U \}$$

i.e. the neighborhood of ψ consists of all subsets of X that contain ψ . This type of topology is called the discrete topology of X (10). The total number of sets needed for a system of n MO's is $2^n - 1$.

The properties of discrete topologies (10) are advantageous for arriving at a solution for transforming topology X into topology Y. We are interested in finding a function f that will do this properly. In a physical sense, f is a complex function that changes the internal coordinates of the atoms of X into those of Y. As the coordinates change, the MO's will change accordingly. Among other things, f must be a continuous function if it is to be a homeomorphism. Yet, a priori, we cannot be certain that f itself or that an approximation to f will be continuous. However, by defining the discrete topologies for X and Y, then any function $f: X \rightarrow Y$ is continuous (10). If f is also onto and one-to-one as well, then f is a homeomorphism.

The above definition of the molecular discrete topology is in

terms of all MO's of the molecule, but in physical reality, we are interested only in the orbitals occupied by electrons. These MO's constitute a filled subspace, F_x, of X. Since X is discrete, F_x is also discrete (10). There are then two essential questions: (1) Given F_x and F_y, the filled subspaces of X and Y, is an approximate function $\underline{f}$, $\underline{f}: F_x \rightarrow F_y$, a homeomorphism? (2) Given F_x and Y and a homeomorphism $\underline{f}: X \rightarrow Y$, then it can be shown(10) that $\underline{f}: F_x \rightarrow Z_y$, where Z_y is some subspace of Y. Is $Z_y = F_y$, i.e. do the filled orbitals of X transform into the filled orbitals of Y, or is some other subspace of Y generated under the particular homeomorphism?

The reactant (X) and product (Y) spaces are defined once the MO's for the two molecules are known. The function relating X and Y must be found if it is required that $\underline{f}: F_x \rightarrow F_y$ or must be defined if $\underline{f}: F_x \rightarrow Z_y$. Since the stereochemistry of the reaction is generally the important feature, the properties of function $\underline{f}$ can be defined by specifying intermediate structures which $\underline{f}$ must generate in the transformation of X into Y (or the reverse). When such an intermediate space, M, is given, then there is a function $\underline{g}$ such that $\underline{g}: X \rightarrow M$ and a function $\underline{h}$ such that $\underline{h}: M \rightarrow Y$. Since homeomorphism is an equivalence relation (10), then $\underline{gh}: X \rightarrow Y$ is a homeomorphism.

The concept of homeomorpic relationships between reactants and products agrees in many respects with our concepts about chemical reactions. It demands that the reaction path be microscopically reversible, and it requires the transformations to be continuous. Homeomorphism says nothing about energy, however. If two species

are homeomorphic, then function f relating them need not be unique. This means that reactants can transform into products over numerous reaction pathways, all of which may be topologically feasible, but some of which may be favored energetically.

Since homeomorphism is an equivalence relationship, all intermediate spaces that are homeomorphic to X are also homeomorphic to each other as well. This simplifies the need to specify intermediate space M, since the structure specified can represent a rather high energy intermediate of low probability, but as long as M can be related homeomorphically to an energetically more probable intermediate point along the reaction coordinate, it remains a valid structure for specifying the stereochemical path of the reaction. This property is useful, since it implies that minimum energy reaction pathways are not necessary. As long as a given intermediate point is "close" (homeomorphic) to the correct minimum energy structure at a point on the reaction coordinate, then it is valid. I should also point out that if a composite function, e.g. ijk: $X \rightarrow Y$, shows X and Y to be homeomorphic, then ijk(x), the MO in Y that is obtained upon the transformation of MO x in X, may not necessarily equal f(x), where f is the "true" low-energy pathway. It remains true, however, that if X and Y are shown to be homeomorphic under ijk transformation, then they are homeomorphic under transformation by f so long as the intermediate points of function ijk are themselves homeomorphic to points along the path defined by f.

In more concrete terms, if a reaction transforming X to Y can occur in one of two possible modes, conrotatory (CON) or disrotatory

(DIS), and the "true" minimum-energy reaction paths (functions) are f and g, respectively, then an approximation to the correct functions can be made by specifying non-minimized transition states, TS_{con} and TS_{dis}, which by their geometry characterize the reaction mode. The two reaction paths, f and g, have thus been approximated by functions i: $X \rightarrow TS_{con}$ then j: $TS_{con} \rightarrow Y$ and a: $X \rightarrow TS_{dis}$ then b: $TS_{dis} \rightarrow Y$. If it is found that function ij is homeomorphic, but function ab is not, then it follows from the above discussion that f is homeomorphic but g is not. It also follows that ij(x) does not necessarily equal f(x), but this does not alter the overall result. Of course, if the point TS_{con} did happen to be an energy-minimized structure, if the MO's were correctly calculated to begin with, and if the evaluation of the functions i and j were correct, then ij(x) = f(x).

Since the exact functions, f, g, etc., are elusive because of their complexity, an index of the functions must be used. A likely choice for this index is overlap. The orbital symmetry correlations are implicitly based upon overlap, i.e. orbitals or states of opposite symmetries cannot overlap effectively and, thus, cannot be transformed into one another. In Trindle's elegant approach (7), the initial total wavefunction in terms of CNDO/2 eigenvectors was transformed into a "virtual" total wavefunction of the product by explicit movement and twisting of the component atomic orbitals as demanded by the reaction path assumed and subject to the constraint that no nodes be created in a given MO. The virtual wavefunction was then compared to the true CNDO/2 wavefunction of the product by their overlap. A localization procedure was used to deter-

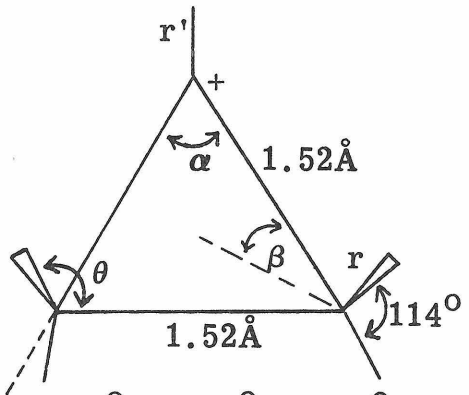
mine which bonds had been acceptably transformed.

My approach is somewhat different from either the symmetry criterion (1) or initial wavefunction transformation (7). The eigenvectors of the reactant, the desired product, and one or more intermediate points along the assumed reaction path are calculated. The overlaps between successive structures are then directly calculated. If MO ψ_x in X has a high overlap with MO ψ_m in M, this is taken to indicate that $\underline{f}(\psi_x) = \psi_m$. If the best overlaps of the filled subspace F_x of X are with the filled subspace F_m of M with each pair of orbitals (ψ_x, ψ_m) uniquely correlated, i.e. onto, and one-to-one, the this is taken to indicate that F_x and F_m are homeomorphic. On the other hand, if F_x and F_m are not homeomorphic, then if overlap is a proper criterion of correspondence, at least one orbital if F_x will show very low overlap with all orbitals of F_m. When the "available" orbitals of the correlation are all orbitals of M, rather than the subspace F_m, in this case, then F_x may be found to be homeomorphic to a different subspace Z_m, which necessarily contains at least one unfilled orbital. In the usual Woodward-Hoffmann sense, this indicates that the reaction is "disallowed" since the ground state of the reactant transforms into some excited state of intermediate M. This means, of course, that the total reaction of X to Y is disallowed. If all pairs of structures are homeomorphic, then X and Y are homeomorphic and the reaction is allowed.

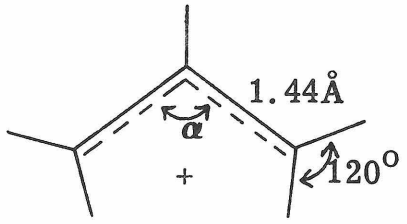
The Calculation Methods

The bond lengths and angles for the various reactants and pro-

ducts to be discussed in the following sections were arbitrarily set at their experimentally determined values for compounds of similar structure (11). Otherwise, they were set at the average values for the type of bonds involved (11). For structures in which delocalization would obviously alter the bond lengths from their "normal" values, a reasonable estimation was used, e.g. for allyl cation the C-C bond lengths were taken as 1.44 . In general, the intermediate structures were assumed to develop as "smooth" transformations of all variables. For example, in a conrotatory ring-opening of cyclopropyl cation to allyl cation with initial and final variables shown, the stereochemically important variable is the twist angle θ of the methylenes from 90° in cyclopropyl cation to 0° in allyl cation. At a given point, say $\theta = 45^{\circ}$, the percent of change in θ (50%) was used as a factor to determine the changes in the remaining variables, e.g. the central angle α changes overall from 60° to 120° and the C-C bond lengths



$\theta = 90^{\circ}$, $\alpha = 60^{\circ}$, $\beta = 30^{\circ}$,
r = 1.10Å, r' = 1.08Å



$\theta = 0^{\circ}$, $\alpha = 120^{\circ}$, $\beta = 0^{\circ}$,
r = r' = 1.08Å

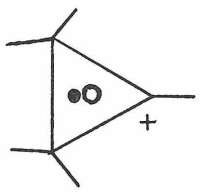
(non-breaking) change from an arbitrary 1.52 Å to 1.44 Å, so that at $\theta = 45^{\circ}$, $\alpha = 90^{\circ}$ and the C-C bond lengths were 1.48Å. In this

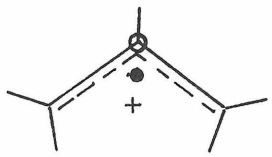
procedure, the length of the bond being broken was determined by the remaining variables at any given reaction coordinate point and was not taken proportionately. The xyz coordinates of the atoms were calculated from the given variables with respect to an arbitrary origin taken in the major molecular plane and along a pseudo-symmetry axis.

The overlap subroutine of the CNDO/2 program (9) was modified to calculate molecular orbital overlaps,

$$S_{ij} = \sum_{k,l} c_{ik} c_{jl} \langle \phi_{ik} | \phi_{jl} \rangle$$

where S_{ij} is the overlap between MO ψ_i of structure I and MO ψ_j of structure J, and $\psi_i = \sum c_k \phi_k$ in terms of atomic orbitals ϕ_k. This simple overlap program requires the coordinates of both I and J atoms and the eigenvectors of each structure. Since the overlap $\langle \phi_{ik} | \phi_{jl} \rangle$ depends upon the distance separating the two atomic centers, the coordinates of I and J were automatically adjusted before the calculation so as to place the coordinate origin for each structure at its center of mass. For example, the input coordinates for cyclopropyl cation and allyl cation used a convenient origin in the carbon atom plane as shown by the open circles, but the program then adjusted all coordinates to put the origin at the centers of mass, filled circles. In a chemical sense, it is reasonable to expect that,





in the absence of conversion of vibrational energy to translational energy during the transformation, the center of mass will remain stationary to an outside observer. Using a fixed center of mass is also implied by the principle of least motion (12). From a computational standpoint, this procedure maximizes the overlaps between a pair of structures, although in principle this would not be needed if the true molecular orbitals and overlap integrals, rather than approximations, were known.

A program which determines the best overlaps between two given sets of molecular orbitals was written. The program picks ψ_i of I and calculates its overlap with all ψ_j of J. It saves the particular ψ_j which gives the highest absolute overlap with the ψ_i, and the calculation is repeated until all ψ_i have been used. The sets from which ψ_i and ψ_j are picked can be the full space I and J or the limited subspaces F_i and F_j. When all allowable ψ_i have been correlated, the program tests to see if the correspondence is one-to-one and onto . If such is not the case, then there will be some ψ_j that has been picked at least twice. The (ψ_i, ψ_j) pair that has the larger overlap is saved, and the program recycles to find the next best overlap for the rejected ψ_i . This process continues until a one-to-one correspondence is established, i.e. the MO sets are forced into a one-to-one correspondence if necessary.

In the present version, TOPCNDO accepts xyz coordinates for the initial structure, adjusts the origin to the center of mass, calculates the CNDO/2 eigenvectors, and saves the coordinates and overlap-normalized eigenvectors. The next structure is then accepted

the above procedure is repeated, the MO overlaps with the previous structure are calculated, and the correspondences between the MO's are established. The program saves the coordinates and eigenvectors of the second structure and proceeds to the third structure, and so on. The TOPEHT program functions in a similar manner, but the eigenvector matrix calculated in the EHT program requires extensive rearrangement of the rows and columns in order to be compatible with the overlap procedure used in the MO correlation. The usual Slater exponents and coulomb integrals were used (13).

I have used flourine and cyano substituents in several of the molecules to be discussed below. These substituents were chosen because (a) they do not require a conformational assignment, as would methoxy for example, (b) only first-row elements are involved so that the parametrization may be less subject to error, and (c) both are strongly electron withdrawing but interact with π systems in opposite senses, fluorine being a π donor and cyano a π acceptor (14).

Tests with Known Reactions

The first task was to test the procedure outlined above on reactions for which the Woodward-Hoffmann rules give clear predictions. This would indicate (a) if the overlap procedure gave the correct results and (b) how many intermediate points between reactant and product were necessary

Cyclobutene - Butadiene

The thermal conrotatory opening of cyclobutene to butadiene is

one of the fundamental reactions which led to the Woodward-Hoffmann rules (1). Numerous experimental and theoretical investigations have established that the overall reaction is clearly conrotatory (15, 16, 17). I initially tried the overlap correlation with the fewest number of structures that would define the CON and DIS pathways, i.e. cyclobutene, a CON "midpoint" with the methylenes twisted 45^{o}, a similar DIS "midpoint", and two (since the hydrogens are labled) cisoid butadienes. These 3-point pathways were unsuccessful since the overlap correlation showed both to be disallowed. This failure was attributed to the large changes in geometry between the structures which could cause errors in the overlap calculations. However, when the total number of structures along the pathways was increased to five or more, the correct correlations, i.e. allowed for CON and disallowed for DIS, were found with both EHT and CNDO/2 eigenvectors. The orbital correlations are given in Tables I and II. In these tables, the abbreviation "2-3" means that MO 2 of cyclobutene (where MO 1 is the lowest energy orbital) was ultimately paired with MO 3 of butadiene. Also shown in the tables are the pairings obtained from symmetry, i.e. by explicitly analyzing the eigenvectors for their symmetry with respect to the symmetry plane (DIS) or axis (CON) in butadiene and cyclobutene and correlating the two sets after invoking the "non-crossing rule" (1).

In all cases with five of more pathway points, the results are the same with respect to reaction stereochemistry. For the CON mode, each set of filled orbitals was overlap-paired with the filled orbitals of the structures immediately preceeding and following on the chosen

Table I. Overall Overlap Correlations for EHT Molecular Orbitals of Cyclobutene with Butadiene (11 filled orbitals).

Points	symmetry		five		six		eleven	
Mode	DIS	CON	DIS	CON	DIS	CON	DIS	CON
	1-1	1-1	1-1	1-1	1-1	1-1	1-1	1-1
	2-3	2-3	2-3	2-3	2-3	2-3	2-3	2-3
	3-2	3-2	3-2	3-2	3-2	3-2	3-2	3-2
	4-4	4-4	4-4	4-4	4-4	4-4	4-4	4-4
	5-5	5-6	5-5	5-6	5-5	5-6	5-5	5-6
	6-7	6-5	6-7	6-5	6-7	6-5	6-7	6-5
	7-6	7-7	7-6	7-7	7-6	7-7	7-6	7-7
	8-9	8-10	8-10	8-10	8-10	8-10	8-10	8-10
	9-10	9-11	9-9	9-11	9-9	9-11	9-9	9-11
	10-8	10-8	10-8	10-8	10-8	10-8	10-8	10-8
	11-12	11-9	11-12	11-9	11-a	11-9	11-12	11-9
	12-11	12-13	12-13	12-13			12-11	12-13
	13-13	13-12	13-11	13-12			13-13	13-12

a Restricted set pairs 11-11, but overlap is extremely small, see text.

Table II. Overall Overlap Correlations for CNDO/2 Molecular Orbitals of Cyclobutene with Butadiene (11 filled orbitals).

Points	symmetry		six[a]		ten[b]		eleven[c]	
Mode	DIS	CON	DIS	CON	DIS	CON	DIS	CON
	1-1	1-1	1-1	1-1	1-1	1-1	1-1	1-1
	2-3	2-3	2-3	2-3	2-3	2-3	2-3	2-3
	3-2	3-2	3-2	3-2	3-2	3-2	3-2	3-2
	4-4	4-5	4-6	4-9	4-6	4-7	4-6	4-9
	5-6	5-4	5-4	5-4	5-4	5-4	5-4	5-4
	6-5	6-7	6-5	6-5	6-5	6-5	6-5	6-5
	7-7	7-6	7-7	7-6	7-7	7-10	7-7	7-10
	8-8	8-10	8-8	8-10	8-8	8-6	8-8	8-6
	9-10	9-11	9-12	9-11	9-12	9-11	9-12	9-11
	10-12	10-8	10-10	10-8	10-10	10-9	10-10	10-7
	11-9	11-9	11-9	11-7	11-9	11-8	11-9	11-8
	12-11		12-11		12-14		12-14	
					19-11		19-11	

[a] "Smooth" reaction. [b] Two-stage reaction, methylenes rotated at 60% point, see text. [c] Two-stage reaction, methylenes rotated at 80% point, see text.

reaction coordinate. For the DIS mode, the overlap-pairing correlated a filled orbital with an unfilled orbital of the next structure along the path, i.e. F_x was mapped into Z_m rather than into F_m at some point. It is interesting to look at the results for the 6-point paths for the reaction with EHT eigenvectors. In this case, the program was restricted to pick only orbitals from the filled subspace at each point. For the CON mode, this caused no problems, and the program easily traced the orbitals from reactant to product. However, in the DIS mode, this restriction sent the program into psychosomatic shock. At the point where it compared the structure with the methylenes twisted to $\theta = 50^{\circ}$ to the structure with $\theta = 30^{\circ}$ (and the other variables adjusted accordingly, see above), an overlap of -.923 was found for the pair 5-5 and 0.1428 for 11-5. It saved the 5-5 pair and searched for the proper pairing for orbital 11. After trying orbitals (of $\theta = 30^{\circ}$) 8, 6, 3, 1, 10, 9, 7, and 4, all of which had already been paired, it finally settled on the only orbital left, 11. A one-to-one correspondence was established, but the 11-11 overlap was 0.00000175, where as the other orbital pairs in the correspondence were all greater than $|.916|$. Clearly, the filled subspaces do not correlate. Of course, when the restriction was removed and all orbitals could be chosen, orbital 11 then correlated with an unfilled orbital, as shown in the 5-point and 11-point paths in Table I.

Even though the results in Tables I and II all show that the ground state reactant and ground state product are homeomorphic only under a conrotatory transformation, the exact orbital pairings differ slightly depending upon the number of reaction points. For example,

in the CON reaction, the orbital pairing is the same for the 5-point, 11-point, and symmetry correlations. But for the DIS reaction, symmetry gives pairs 8-9 and 9-10 and the 11-point or 5-point paths give 8-10 and 9-9. Actually, the total energy change is the same for the two pairings so the difference is not crucial. (In fact, the distribution of the coefficients in the eigenvectors suggests that the overlap analysis has indeed picked the correct pairs.) When one compares the DIS results for the 5-point and 11-point paths, it is evident that the two paths give different pairings for orbitals 11, 12, and 13, even though the overall disallowed nature of the pathway is found in each case. Part of this behavior may have been due to a greater error in calculating the overlaps between points in the 5-point path, since the successive structures along this path show greater geometrical changes than do successive structures along the 11-point path.

Extensive calculations have recently suggested that, rather than a gradual transformation of all variables, the ring-opening may involve two stages (15) where the breaking bond length increases to about 2.3Å without rotations of the methylenes, then the methylenes then rotate conrotatory from $\theta = 90^{o}$ to 0^{o}. Two such two-stage transformations are shown in Table II. The notation "60%" refers to 0.6 factor of the change in all variables, except methylene rotation, between their initial values in cyclobutene and their final values in butadiene. This structure corresponds roughly to the stretched configuration (15) with the breaking bond length $\cong 2.3$ Å. In the "80%" path, the breaking bond had almost reached its final value before methylene rotation was begun. The overall results for the

CON and DIS paths in these cases are the same as the smooth reactions -- the CON path is allowed and the DIS path is not. However, the orbital pairing obtained for the two-stage pathways is rather different from the pairing found in the 6-point smooth transformation or in the symmetry analysis. This may reflect, in part, the different overall pathways. I discussed at length above the fact that the topological rationale dictates that ijk(x) need not be the same as f(x) for a particular x, but that this cannot affect the overall relationship between X and Y as long as function ijk is a good approximation for function f. If one assumes that the true reaction path f would give the pairing obtained by the symmetry analysis, and if one designates the 6-point smooth path conrotatory function as ij and the 10-point two-stage conrotatory path as composite function mn, then the mappings for orbital 11 of cyclobutene are f(11) = 9, ij(11) = 7, and mn(11) = 8. The mappings are different, but all retain the essential conrotatory stereochemistry, i.e. functions ij and mn both approximate f. Therefore, the overall homeomorphism between cyclobutene and butadiene is observed for all three functions. When the opposite disrotatory mode is approximated by three analogous functions, the mappings are again slightly different, but all are non-homeomorphic. These results appear to support the topological rationale of treating the transformations as homeomorphisms and approximating the mapping functions by specifying non-energy-minimized structures.

I should note that the overlap analysis usually assigned one-to-one pairings (when all orbitals were available, see above) on the first trial. In a few instances, degeneracies were obtained on the first

trial, but these involved either very high energy, unoccupied orbitals or orbitals deeply "buried" within the filled subspace, i.e. at no time was there an indication that the analysis was having difficulty in choosing between a filled or unfilled orbital.

Cyclopropyl cation - Allyl cation

Orbital symmetry (1) and detailed calculations (16) show that the ring-opening of cyclopropyl cation to allyl cation is thermally allowed if the motion is disrotatory. My analysis of the conrotatory and disrotatory paths using the reactant and product and four intermediate points for each path showed the transformation of the occupied orbitals to be homeomorphic under a disrotatory function, but not homeomorphic under the conrotatory mode with both EHT and CNDO/2 eigenvectors.

Cyclopropyl anion - Allyl anion

With EHT calculations, increasing the occupied levels calculated for the cyclopropyl cation gives the anion. The overlap analysis then showed the conrotatory to be allowed and the disrotatory not allowed. A separate CNDO/2 calculation for the anion (again with a 6-point path) gave the same results. These results agree with the previous theoretical predictions (1, 16), although it appears there is no clear experimental verification for this stereochemistry as yet (18).

"Breathing" Cyclopropyl Cation

As a test to see how much distortion one could induce into a structure and have homeomorphism preserved, the cyclopropyl cation was symmetrically contracted and expanded. The molecule with an initial geometry with all C-C bonds at 1.52 Å and C-H bonds at ~1.09 Å was "shrunk" to give C-C bond lengths of 0.81 Å and C-H ~0.90 Å and stretched to give C-C lengths of 2.17 Å and C-H ~1.30 Å. An intermediate structure was included between each of these extremes and the initial structure. The overlap correlation with CNDO/2 eigenvectors showed that the cyclopropyl cation was homeomorphic under this distortion, even though the calculated energy rises by 804 kcal/mole and by 3870 kcal/mole for the stretched and contracted extremes, respectively, compared to the energy of the of the undistorted structure. When the C-C bonds were set at 2.6 Å the orbitals no longer correlated.

This distortion is analogous to a torus ("doughnut"), which topologically can be shrunk, twisted, or stretched in any manner without affecting the identity of the space, i.e. the resulting shape is homeomorphic to the original torus. The only restriction is that the surface not be torn or cut. The cyclopropyl cation appears to behave very much like the torus under the deformation described above. Within the approximations used to calculate the orbitals by either EHT or CNDO/2, it is also quite reasonable that the structure is no longer homeomorphic when the C-C bond lengths become too large. Qualitatively, the surface has been "torn" when the C-C bond lengths equal or exceed 2.6 Å which agrees with the expectation that

a symmetrical stretching of the C-C bonds must eventually result in fragmentation of the molecule.

Comments

The above test cases indicate that the approach used here to correlate reactants and products under various transformations is a valid method. In every case, the correct mode of ring opening was obtained. Even when gross distortions in the intermediate structures were made, as in the case of the gradual vs. two-stage opening of cyclobutene, the results were stereochemically correct. The large distortions induced on the cyclopropyl cation also show that the analysis will tolerate a large amount of uncertainty in the structure geometries. This appears to support the contention arrived at on topological grounds that energy-minimized configurations are unnecessary as long as the arbitrarily chosen structures are homeomorphic to configurations along the true pathway. In essence, this means that if the approximate MO's obtained from EHT or CNDO/2 calculations on an arbitrary structure correctly approximate the "shape" of the molecular topological space, then the reactants and products can be topologically related. The exact "shapes", i.e. accurate geometries and accurate wavefunctions and energies, are not required.

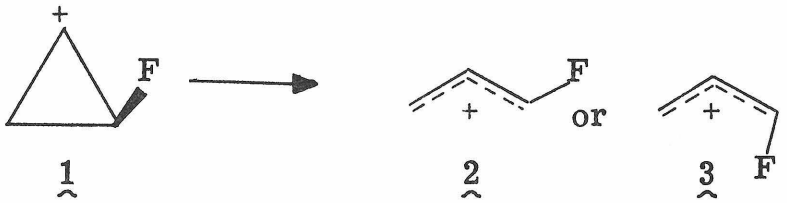
Applications to Unsymmetrical Reactions

The goal of this approach is not, of course, to treat reactions that can be analyzed by symmetry. The symmetric cases treated above did indicate that extension to unsymmetrical reactions would be

reliable if the reaction paths were sufficiently defined, i.e. if enough points were chosen. Five-point paths were sufficient for the cyclobutene reaction (and in fact, three-point paths were sufficient for the cyclopropyl cation reaction with CNDO/2 eigenvectors). In the following section, I shall briefly discuss the preliminary results for several unsymmetrical systems. In general, smooth changes of all variables were used and, unless otherwise specified, six-point reaction paths were chosen.

2-Fluorocyclopropyl Cation

In principle, the ring-opening of this planar cation to 1-fluoroallyl cation is an unsymmetrical reaction. The reaction could proceed CON or DIS to give ions $\underset{\wedge}{2}$ or $\underset{\wedge}{3}$. Each of these four paths was



$\underset{\wedge}{1}$ $\underset{\wedge}{2}$ $\underset{\wedge}{3}$

tested using CNDO/2 eigenvectors, and only the disrotatory paths were homeomorphic leading to either $\underset{\wedge}{2}$ or $\underset{\wedge}{3}$. This requires that $\underset{\wedge}{2}$ and $\underset{\wedge}{3}$ also be homeomorphic to each other, although interconversion through $\underset{\wedge}{1}$ need not be a unique homeomorphic function. These results are the same as the reaction for the unsubstituted cation. The fluoride evidently does not perturb the basic surface sufficiently to alter the reaction mode.

2-Cyanocyclopropyl Cation and Anion

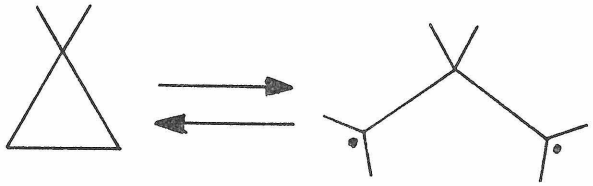
The CON and DIS ring openings were examined using EHT eigenvectors. The cation reaction was homeomorphic under disrotatory opening and the anion under conrotatory opening. As with the fluoro case, the results for this system are the same as for the unsubstituted system.

I should perhaps note here that such unsymmetrical substituents tilt the cyclopropyl ring with respect to the coordinate planes when the origin is adjusted to the center of mass of the molecule in the calculation procedure (see above). As the "reaction" proceeds, the relative movement of the "heavy" substituent will be less. The overlap analysis could overemphasize the importance of the substituent, since the overlaps of the substituent with itself will be favored by the smaller distances. However, the results for the cyclopropyl cases suggest that such emphasis does not occur or does not affect the results. In the remaining discussions, the fluorine and cyano groups are attached to larger molecules, so any emphasis of the substituent will be reduced.

Cyclopropane and Fluorocyclopropane

The isomerization of cyclopropane derivatives has been the subject of much experimental and theoretical investigation (19, 20). Hoffmann (19) found that the opening of the ring, if concerted, should be conrotatory. He also suggested that the interaction between the "radical" centers might be achieved through overlap with the central C-H bonds. Salem and coworkers (20) have recently presented very

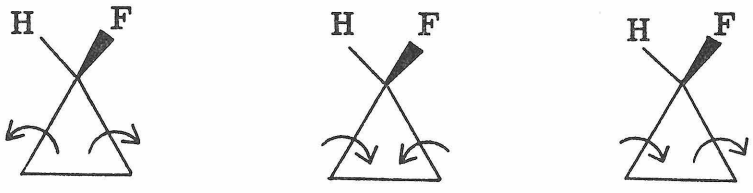
detailed calculations which reveal changes in the relative rotational directions during the reaction, but the overall result is still conrotatory.



4 5

I briefly examined this reaction with smooth six-point paths using equal, concerted rotations of the methylenes from 0^{o} twist in cyclopropane to 90^{o} twist in the "planar" intermediate 5. Both EHT and CNDO/2 eigenvector calculations showed the ring-opening to be homeomorphic in the conrotatory mode but not in the disrotatory mode, in agreement with the previous more detailed calculations (19, 20). In the disrotatory mode, the disallowed mapping occurred between 60^{o} and 80^{o} twisting of the methylenes.

If Hoffman's analysis concerning the importance of the central C-H bonds (19) were correct, then a substituent at the central carbon could greatly affect the reaction pathway. The fluoro-substituted structure was used to examine this possibility. There are two possible disrotatory modes as shown in 6 and 7 and a conrotatory mode, 8.



6 7 8

When the overlap analyses were done with EHT calculations, the initial results showed no correspondence for any of the three paths. However, the reactions shown in 7 and 8 did not correlate between 80^{o} and 90^{o} twisting of the methylenes, which is qualitatively very "late" in the reaction. When another point at 85^{o} twist was added, then the correlation was successful for the conrotatory path 8, but not for 7. In the latter case, the overlap data indicated that the non-correspondence was correct. The overall result, then, was the same as for the unsubstituted case.

When the same calculations were carried out with CNDO/2 eigenvectors, the opposite correlation was found. Both disrotatory modes were homeomorphic, but the conrotatory mode did not correlate between 60^{o} and 75^{o} twists. Unfortunately, these results are obscured by an apparent failure of the CNDO/2 program in some of the conrotatory structures. With the methylenes rotated by 75^{o}, 80^{o}, or 85^{o}, the iterations did not reduce the electronic energy, but increased it. After several interations, the resulting orbitals showed almost random overlaps with either the 60^{o} or 90^{o} structures (for which the calculations appeared to proceed normally). When iteration of the electronic energy was not allowed for these cases, the resulting eigenvectors did correlate with only a few initial degeneracies and showed correspondences of the filled orbitals except at the point between 60^{o} and 75^{o} rotation.

The above results give a strong hint that the EHT and CNDO/2 calculations do not give the same energy level ordering and that this leads to reversed predictions. It is quite impossible to know which

correlation is correct, in spite of the strange behavior of the CNDO/2 calculations for some of the conrotatory structures. The CNDO/2 results indicate that the fluorine might have changed the interaction between the radical centers, but at present this remains still only a possibility. More extensive calculations on this system are needed to explore this possibility further. The effect of cyano or other substituents at the central carbon and of disubsituted derivatives should be explored.

2-Cyclobutenones

Trindle applied the mapping analysis (7) to the highly dissymetric opening of 2-cyclobutene 9 to ketene 10 where R = H or methyl. I have treated this reaction with one important difference: whereas the

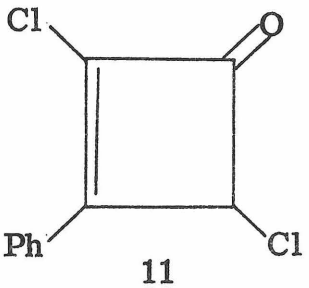
9 10

mapping analysis can rotate the carbonyl group explicitly, the overlap procedure described here uses the calculated eigenvectors at each intermediate structure. Hence, a "rotation" of the carbonyl will be reflected in a repopulation of the atomic orbital basis set as the reaction proceeds to 10. The analysis cannot force the carbonyl to rotate, but if it does rotate, this will be taken care of automatically.

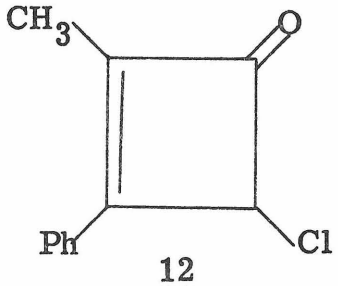
The correlation for 2-cyclobutenone itself was carried out with

both EHT and CNDO/2 eigenvectors. (The initial structure, 9 (R=H), was taken with C_1-C_2 bond length equal to C_3-C_4 for convenience, and the remaining parameters taken appropriately for the structural features involved (11).) The reaction was found to be homeomorphic. When the substituent at C_4 was methyl (with one C-H bond fixed to lie over and parallel to the C_3-C_4 bond), both EHT and CNDO/2 correlations showed homeomorphic transformations to both the cis and trans ketene. The same result was found with R = chlorine using CNDO/2 eigenvectors.

These results are interesting, since Trindle's overlap index suggested that the reaction of the parent system (R = H) was highly disfavored but became allowed when R = methyl. He suggested that the influence of the methyl group was due to hyperconjugative interaction with the π system (7). It seems to me that this would indicate a very delicate balance of factors involved for the methyl to be so effective. My results indicate that no such difference exists and that all cases are topologically homeomorphic, i.e. thermally allowed. Whether or not the reactions will be observed depends, of course, upon the activation energy, especially in relation to competing transformations. To my knowledge, data on these particular reactions are not available. The example cited by Trindle (7) was Baldwin and McDaniel's study of thermal and photochemical reactions of 11, 12, and 13 (21). In these systems, it may not matter what the substituent at C_4 is because the phenyl at C_3 may perturb the system far more effectively. It is not clear that a concerted reaction obtains for the reactions of 11-13 in the first place (21).



11



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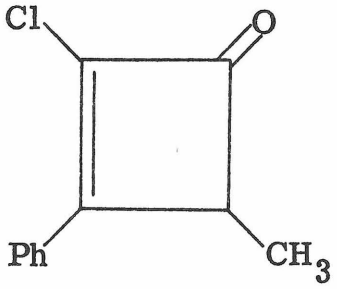


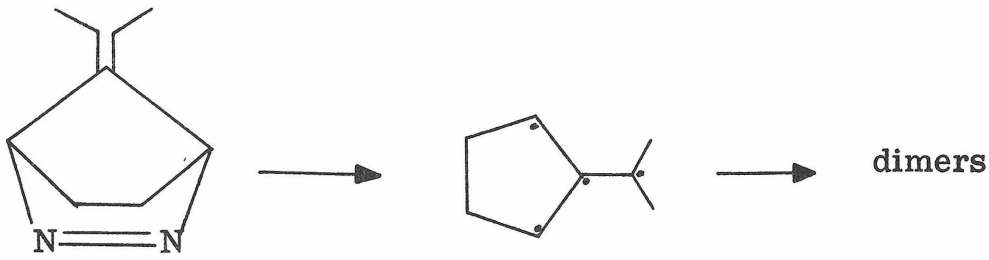
13

For the reaction of 9 and its 4-substituted derivatives, my results, in contrast to those of Trindle (7), show that concerted ring-opening may obtain no matter what substituent R is. In fact, very qualitatively, the activation barriers are fairly insensitive to the nature of R, although the CNDO/2 calculations indicate that R = methyl or chlorine may be slightly more favorable that R =H.

Trimethylenemethane

According to Borden (22), the ring opening of methylenecyclopropane to trimethylenemethane can be either conrotatory or disrotatory and that the ground state should be a triplet. Indeed, the

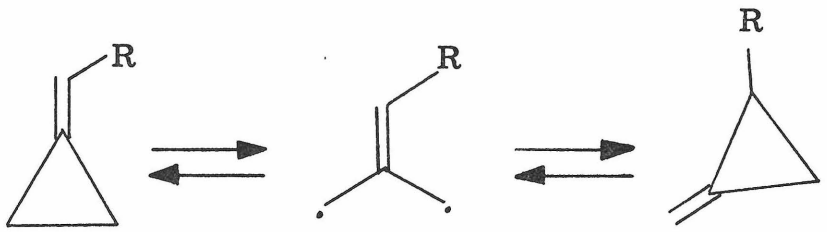
direct esr observation of the triplet species by Dowd and coworkers (23) gives strong support for such a ground state electronic configuration. Berson and coworkers (24) have obtained dimers from the pyrolysis or photolysis of 14 which show CIDNP emissions, which



14

is in accord with a dimerization in which at least one of the participants is a triplet (24, 25). The elegant investigations by Doering and Roth (26) and Gajewski (27) have shown that the isomerizations of methylenecyclopropanes cannot occur exclusively through a planar trimethylenemethane intermediate, since optical activity is retained.

Since the planar intermediate trimethylenemethane should be a triplet (see above), fluoro and cyano substituents were used to remove the orbital degeneracy. (The planar species, in which all atoms lie in one plane, is designated (0, 0, 0).) The ring openings of 15 and 17 to give 16 (0, 0, 0) were calculated with six-point pathways (eleven points overall for isomerization between 15 and 17). Isomer



15 16 17

15 can open in a CON or DIS mode to 16, and 17 can open in two CON and two DIS modes to 16, i.e. with the substituent rotating "in" or "out." The results of these calculations with CNDO/2 eigenvectors are rather interesting. With R = F, the overlap correspondence shows that 15 and 16 are homeomorphic under the CON pathway but not under the DIS mode. The behavior reverses for 17 and 16, where the DIS opening is homeomorphic but the CON is not. When R = CN, the pattern changes again. Isomer 15 is homeomorphic to 16 under DIS transformation, and 17 and 16 are homeomorphic

also under DIS transformation (nether transformation correlates under CON motion). Thus, the correlations predict that a planar, substituted trimethylenemethane will close to isomer 17 in a disrotatory manner, but closure to isomer 15 can be either conrotatory of disrotatory (but not both) depending upon the substituent. If this is true (and at this point some caution is still required), then it implies a remarkable control on the stereochemistry by substituent R.

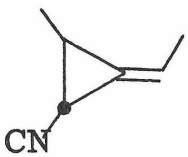
Non-planar intermediates were briefly studied. One such species would be the intermediate in which the perimeter p lobes are all tilted at 45^{o} with respect to the plane of the carbon atoms, i.e. the (45, 45, 45) species. There are four modes of opening 15 (R = F) and eight modes of opening 17 (R = F) to such an intermediate, depending upon on how the double bond methylene twists during CON or DIS opening of the cyclopropyl ring and whether the substituent in 17 rotates in or out. The correlation with CNDO/2 eigenvectors showed that all twelve modes were allowed. It would appear then that the disallowed pathways through the planar intermediates (above) can be circumvented by twisted intermediates, although these results do not tell us the relative energetics involved.

Another possible intermediate is the so-called "orthogonal" species suggested by Gajewski (27), in which one methylene in 15 or 17 acts as a pivot while the other methylene rotates. The resulting intermediate has two methylenes lying in the carbon plane and one (the pivot) at 90^{o} with respect to the plane, i.e. the (0, 0, 90) species. The isomer is then formed by rotation of the (formerly) double bond

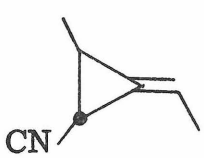
methylene to bond with the pivot (90^{o}) methylene. When six such pathways were tried, the overlap correspondence showed both CON and DIS modes to be homeomorphic.

There remain other variations which have not been studied by the overlap correlation. If the cyclopropyl ring reacting bond breaks without rotation of the methylenes of the ring but with simultaneous rotation of the double bond methylene, the resulting intermediate is (90, 90, 90). A variation of the "pivot" mechanism is where the double bond methylene rotated concertedly with the other ring methylene to give a (45, 45, 90) species.

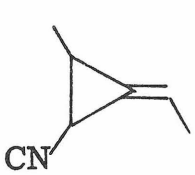
These various mechanisms have been summarized by Doering and Birladeanu (28), who studied the thermal rearrangement of the diastereomeric methylenecyclopropanes 18a - 18d . Of course, the (0, 0, 0) and (45, 45, 45) pathways can lead to complete or partial racemization and may not be exclusive pathways (see above), but can not be specifically excluded in Doering and Birladeanu's study because the enantiomeric pairs were not studied. The (45, 45, 90) intermediates can be formed through either conrotatory or disrotatory modes, the exclusive operation of which Doering and Birladeanu (28) exclude on the basis that both 18a and 18d form the remaining three isomers in each case, although the results can be explained in terms



18a



18b



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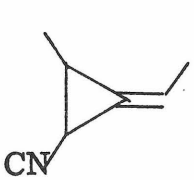


18d

of concurrent conrotatory and disrotatory transformations to the (45, 45, 90) transition state (28). This, in fact, may not be so far-fetched considering the correlation results given above with the (45, 45, 45) and (0, 0, 90) intermediates (transition states). The authors prefer the view that either the (0, 0, 90) or (90, 90, 90) pathway accounts for their results.

Certainly, further calculations are necessary, particularly for the reaction modes with (45, 45, 90) and (90, 90, 90) transition states. In view on the interesting specificity found for the planar (0, 0, 0) transition state, it would be important to examine this path in more detail. Note that detailed energy surface calculations of all these possibilities with fluorine and cyano or other substituents would be prohibitively expensive, yet the success of the present overlap approach in the model test cases suggests that the essential stereochemical features in this system, if such exist, can be found with much less effort and expense.

Conclusions

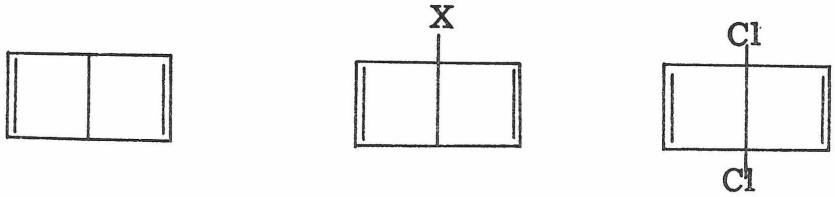
The topological approach presented here leads to a rather straightforward method for correlating thermal reactions through overlap correspondence. The calculation procedure could have been arrived at from other viewpoints, but the topology framework suggests that the equivalence relationship, homeomorphism, allows not only approximate semi-empirical molecular orbital calculations to be used, but that even approximate reaction structures can be used without threatening the validity of the results. The major likely sources of

error appear to be (1) in the direct overlap calculations, where a too drastic structural change from one reaction point to the next cannot be tolerated,and (2) in the semi-empirical calculations themselves, which must correctly define the filled subspace, i.e. the energy level ordering within the filled subspace is unimportant, but the orbitals must be the ground state orbitals.

The overlap analysis gave the correct results for the thermal ring-opening reactions of cyclobutene, cyclopropyl cation, and cyclopropyl anion. Fluoro and cyano substituents did not appear to affect the cyclopropyl cation orbital control, as would have been assumed for the usual orbital symmetry correlation (1). The rearrangement of cyclopropane through the trimethylene "diradical" gave the same overall stereochemistry by overlap analysis as predicted for a concerted reaction from more sophisticated and expensive calculations (see above). The thermal ring openings of 2-cyclobutenones were found to be allowed. Several reaction modes for isomerizations of methylenecyclopropanes have been studied.

There is some indication, particularly in the cyclopropane isomerization and the trimethylenemethane studies, that fluorine or a cyano group may affect the stereochemical path because of their perturbation of the molecular orbital hypersurface. There is at present no clear experimental case in which such effects have been observed. Breslow and coworkers (29) have observed that the thermal (disallowed) rearrangement of Dewar benzene, 19, to benzene is facilitated by unsymmetrical substitution. Their kinetic data show that the monochloro compound, 20 (X = Cl), rearranges nine times

faster than does 19 , and the monofluoro compound, 20 (X=F), rearranges thirty six times faster. In contrast, the symmetrically substituted dichloro compound 21 reacts more slowly than does 19 by a factor of 615. The fact that Dewar benzene, 19, itself undergoes disallowed thermal rearrangement attests to the high degree of strain in the molecule, and the halogen substituents could lower the activation energy by their stabilizing effect on some sort of diradical transition state. However, it is curious that the dichloro species appears



19 20 21

to be a much more stable compound. One can speculate on several "reasons" for the behavior of these compounds, and a particularly interesting hypothesis is that the unsymmetrical substitution causes the concerted, disrotatory thermal rearrangement to be allowed rather than forbidden. The overlap analysis method presented here should be applied to this system to see if such substituent effects are possible.

Finally, I should point out that the approach to chemical reactions from topological viewpoints can be quite varied. I adopted a rather simple topological model and used a rather simple homeomorphic index (overlap). If there is a "proper" topological description of a molecule, this topology may be computationally and conceptually more complex than that presented here.

Acknowledgement

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References

1. R. B. Woodward and R. Hoffmann, "The Conservation of Orbital Symmetry," Academic Press, New York, N.Y., 1970.

2. H. E. Zimmerman, J. Amer. Chem. Soc., 88, 1564, 1566 (1966).

3. M. J. S. Dewar, Tetrahedron, Suppl., 8, 75 (1967).

4. R. C. Dougherty, J. Amer. Chem. Soc., 93, 7187 (1971).

5. N. D. Epiotis, ibid., 94, 1924, 1935, 1941, 1949 (1972).

6. W. A. Goddard, III, ibid., 94, 793 (1972).

7. C. Trindle, ibid., 92, 3251, 3255 (1970); see also P. W. Lert and C. Trindle, ibid., 93, 6392 (1971).

8. R. Hoffmann, J. Chem. Phys., 39, 1397 (1963).

9. J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N.Y., 1970.

10. J. D. Baum, "Elements of Point Set Topology," Prentice= Hall, Englewood Cliffs, N.J., 1964.

11. See "Tables of Interatomic Distances and Configuration in Molecules and Ions," Chem. Soc., Spec. Publ., No. 11, M164, M182, M218 (1958); No. 18, S15s-S18s, S20s, S21s, M75s, M95s, M97s, M107s, M109s (1965).

12. O. S. Tee, J. Amer. Chem. Soc., 91, 7144 (1969); O. S. and K. Yates, ibid., 94, 3074 (1972).

13. Slater exponent for H was 1.2, all others from R. S. Mulliken, C. A. Rieke, D. Orloff, and H. Orloff, J. Chem. Phys., 17, 1248 (1949); H_{ii} from J.A. Pople and G.A.Segal, ibid., 43,S136 (1965).

14. See W. J. Hehre, L. Radom, and J. A. Pople, J. Amer. Chem. Soc., 94, 1496 (1972).

15. K. Hsu, R. J. Buenker, and S. D. Peyerimhoff, ibid., 93, 2117 (1971); ibid., 94, 5639 (1972); and references therein.

16. M. J. S. Dewar and S. Kirschner, ibid., 93, 4290, 4291, 4292 (1971); and references therein.

17. For a particularly interesting study of the cyclobutene ring opening, see J. I. Brauman and W. C. Archie, Jr., ibid., 94, 4262 (1972).

18. P. Eberhard and R. Huisgen, ibid., 94, 1345 (1972); R. Huisgen and P. Eberhard, ibid., 94, 1346 (1972); and references therein.

19. R. Hoffmann, ibid., 90, 1475 (1968).

20. J. A. Horsley, Y. Jean, C. Moser, L. Salem, R. M. Stevens, and J. S. Wright, ibid., 94, 279 (1972); see also P. J. Hay, W. J. Hunt, and W. A. Goddard, III, ibid., 94, 638 (1972).

21. J. E. Baldwin and M. C. McDaniel, ibid., 90, 6118 (1968).

22. W. T. Borden, Tetrahedron Lett., 259 (1967).

23. P. Dowd, J. Amer. Chem. Soc., 88, 2587 (1966); P. Dowd and K. Sachdev, ibid., 89, 715 (1967); P. Dowd, A. Gold, and K. Sachdev, ibid., 90, 2715 (1968).

24. J. A. Berson, R. J. Bushby, J. M. McBride, and M. Tremelling, ibid., 93, 1544 (1971).

25. G. L. Closs, ibid., 93, 1546 (1971).

26. W. von E. Doering and H. D. Roth, Tetrahedron, 26, 2825 (1970).

27. J. J. Gajewski, J. Amer. Chem. Soc., 93, 4450 (1971).

28. W. von E. Doering and L. Birladeanu, Tetrahedron, submitted for publication; copy from M. R. Willcott, III.

29. R. Breslow, J. Napierski, and A. H. Schmidt, J. Amer. Chem. Soc., 94, 5906 (1972).

PROPOSITION V

Some infrared stretching frequencies, most notably C=O, N-H, and O-H are sensitive to solvent. Several years ago Kirkwood (1) and Bauer and Magat (2) treated the problem in terms of a point dipole in a spherical cavity within a medium of macroscopic dielectric constant D and derived the "KBM" equation, eq 1, where ν_o is the frequency of the absorption in the gas phase, ν_s is the frequency in the solvent,

$$\frac{\nu_o - \nu_s}{\nu_o} = \frac{C(D - 1)}{2D + 1} \qquad (1)$$

and C is a constant that depends on the solute molecule. The relation is simple, but only works for non-polar solvents, and then usually not very well (3-7). Since $D = n^2$ for a molecule without a permanent dipole moment (8), where n is the refractive index, the relation (eq 1) was tried with D replaced by n^2 in the belief that the main solvent effect was due to the polarizability of the solvent molecules and that the permanent dipole component of D for polar solvents should have little influence (4, 9). A little, but not much, improvement was found. A very complicated quantum mechanical treatment by Buckingham (10) gives an expression similar to eq 1 but containing a constant term and a term in n^2. Pullin (11) also obtained a complex expression in terms of $(n^2 - 1)/(2n^2 + 1)$ and $(D - 1)/(2D + 1)$. Caldow and Thompson (12) complicate the Buckingham relation still further.

None of these relations has been justified by experimental measurements, except on a very limited basis. One feature of these relations I find rather unreasonable: The relations compare the solvent frequency to the frequency in the vapor state. Theoretically, this is justified because the vapor phase absorption supposedly represents the vibration of an isolated molecule. However, to my knowledge no one has calculated what the effect would be on the stretching frequencies of a molecule if the molecule were immersed in a completely inert, non-polarizable medium. I conjecture that the present mathematical models would show that such an ideal solvent would have no effect on vibrational levels, or else the effect would be too complex to treat. That the presence of solvent molecules can drastically affect the infrared spectrum is evident by the disappearance of rotational fine structure, by an increase in band intensities (4), and by a large shift in absorption frequency in going from the vapor state to non-polar* solvents of very low dielectric constant (e.g. cyclohexane) (9, 11).

In the other extreme, completely empirical relations have been used by Bellamy and coworkers (13-17). If one plots $(\nu_o - \nu_s)/\nu_o$ of, say, a C=O absorption of a given solute in a series of solvents against the $(\nu_o - \nu_s)/\nu_o$ of a standard substrate, e.g. acetophenone, in the same solvents, one gets a straight line. (Here ν_o is the absorption in the vapor state or sometimes in a reference solvent.) Linearity is obtained for both polar and non-polar solvents. This behavior

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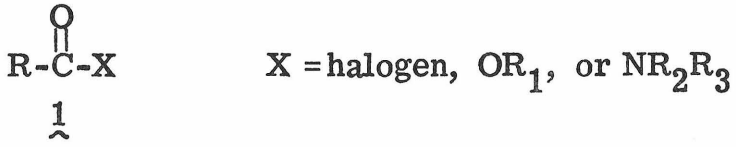
* "Polar" means any solvent with a permanent, measurable dipole moment.

was interpreted (15) as evidence that only "specific" interactions between solute and solvent are responsible for the solvent shifts, and that bulk (macroscopic) effect of the solvent are unimportant.

It seems to me that these plots only show that the solvent effects are quite similar for all the solute molecules, regardless of what the reason is for the effect, at least as long as the reference compound and the other solutes do not differ too much in structure. These plots do not necessarily show that bulk effects do not contribute to the shifts.

Another empirical relation has been found by Horak and coworkers (18). For compounds of type 1, eq 2 was found to hold for a given



1

R group, where A and ω are experimental parameters. The treat-

$$\Delta\nu = \nu_{hexane} - \nu_{CHCl_3} = A(1 - \omega\nu_{hexane}) \qquad (2)$$

ment is essentially equivalent to Bellamy's $\Delta\nu$ vs. $\Delta\nu$ plots, e.g. the effect of chloroform on a C=O absorption is roughly the same for different solutes (however, see below).

A linear free energy relationship (eq 3) was proposed by Brownstein (19) to include reaction rates, equilibrium constants, or spectral shifts (eq 4), where S is a function of the solvent and R is a measure of the sensitivity of the solute to solvent effects. Plots for C=O ir shifts were not given, but the R values given (19) do not appear

$$\log(k_{solv}/k_{EtOH}) = SR \qquad (3)$$

$$(\nu_{solv} - \nu_{EtOH})/\nu_{EtOH} = SR \qquad (4)$$

to correlate very well, e.g. for acetone C=O, R = -0.036 with a "deviation" of 0.021 (19).

More recently, Allerhand and Schleyer (20) proposed a similar free energy relationship, eq 5, where ν_o is the stretching frequency in the vapor phase, a is a measure of the sensitivity of the

$$\frac{\nu_o - \nu_s}{\nu_o} = aG \qquad (5)$$

solute to solvent effects, and G is a function of the solvent only. The G values were determined from correlations with benzophenone and dimethylsulfoxide in various solvents and fixed at 0.0 and 100 for the vapor phase and methylene chloride solvent, respectively. These authors pointed out that eq 5 is just the KBM equation, eq 1, with (D - 1)/(2D + 1) replaced by an empirical parameter G. They also stated that no straightforward relationship of G to n^2 or D, or a combination thereof, could be deduced. This work was primarily concerned with hydrogen bonding effects, and the plots shown for X-H bonds were generally good. The authors indicated that plots for the C=O absorptions were "excellent." Since the same G parameters could be used for both C=O and O-H absorptions (H-N plots gave poorer correlations), Allerhand and Schleyer concluded that bulk

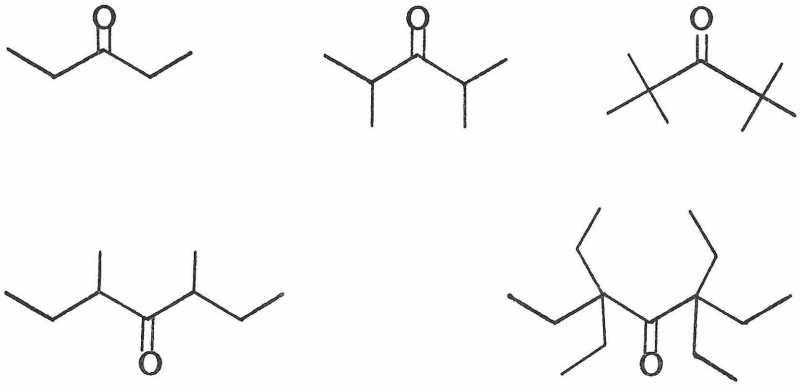
effects of solvents are the primary cause of solvent shifts, in contrast to Bellamy's arguments.

Two points can be raised regarding Allerhand and Schleyer's work: First, although ν_o could be estimated from the graphs and found to correspond with the observed ν_o to within 8 cm^{-1} (20), this error is too large when compared to the magnitude of the shifts involved. I believe, as pointed out earlier, that one should dispense with ν_o (in the vapor state) altogether. Second, the empirical relation found in this instance is equivalent to Bellamy's $\Delta\nu$ vs. $\Delta\nu$ plots, only the relation has been generalized by fixing the standard and the scale for the solvent parameters. Thus, the treatment is considering the total effect of solvent, whether it be due to bulk effects of to specific interaction effects, or a combination of both.

It is proposed that neither bulk continuum effects nor specific interaction effects are solely responsible for the spectral shifts in many cases. A combination of both effects should be responsible for the observed solvent shifts, and these two basic factors can probably in some cases, be separated, at least in an empirical manner if not in a full theoretical treatment. The C=O absorptions of ketones, esters, and aldehydes seem most appropriate for study, since these absorptions are very intense, allowing studies with very dilute solutions, and unlike X-H absorptions, they appear to be reasonably free (however, see below) from strong hydrogen bonding effects.

One way of possibly separating "bulk" effects from "specific" effects is to study solvent effects in substrates having steric "shielding." A detailed study of compounds such as shown in Series I - III

Series I.



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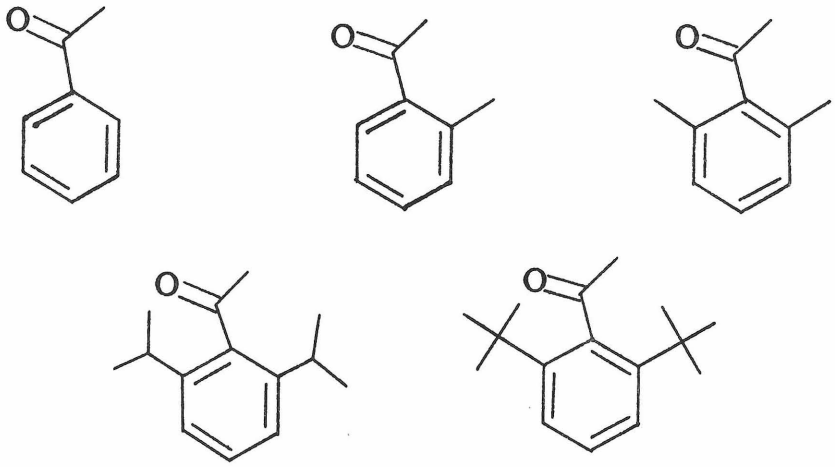

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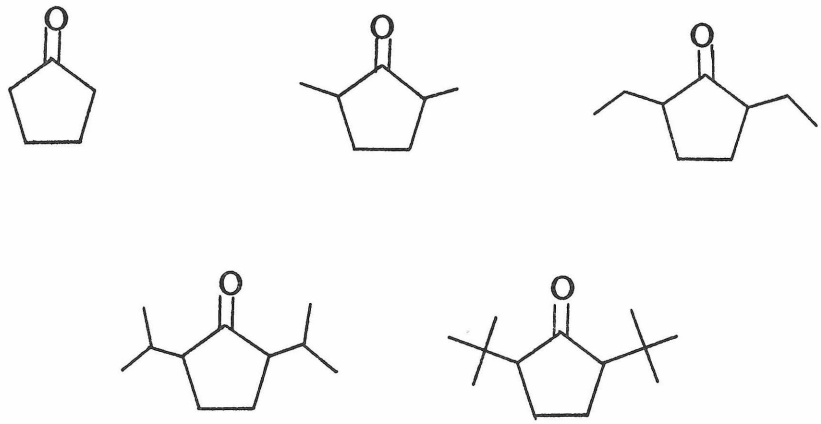

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is needed. If bulk properties are important, then plots of the solvent shifts, $\Delta\nu$, for $\underset{\sim}{2}$ (taken relative to a reference solvent) vs. $\Delta\nu$ for an unhindered ketone (acetone) may show a correlation. For those solvents where a "specific" interaction is also important, the shifts may no longer correlate, since the protected carbonyl group of $\underset{\sim}{2}$ can not interact as easily at the molecular level with the solvent. A similar effect should be seen for $\underset{\sim}{3}$ and $\underset{\sim}{4}$ compared to acetophenone and cyclopentanone, respectively. The correlation with the reference compound in each series could become progressively worse (for the "special" solvents) as the steric "protection" increases. Of course, if the carbonyl group is too deeply buried in the surrounding side chains, then there is the possibility that no solvent effect will be seen even with the non-polar solvents, i.e. the side chains may effectively be "solvent" to the carbonyl. If $\underset{\sim}{2}$, $\underset{\sim}{3}$, and $\underset{\sim}{4}$ do show solvent dependences on their carbonyl absorptions and if deviations occur when these protected substrates are compared to unhindered ketones, then one may be able to ascribe the solvent dependences for $\underset{\sim}{2}$, $\underset{\sim}{3}$, and $\underset{\sim}{4}$ to bulk effects, perhaps even correlating with eq 1. One then could separate the solvent effects seen for the unshielded molecules into two effects and study the "specific" effects of the solvents.

A second approach can be used, at least in some instances, for separating special effects from more general solvent interactions. Quite independently of Brownstein's (19) and Allerhand and Schleyer's (20) relationships, I found (21) that solvent shifts for some selected ketones and esters can be correlated by eq 6, where D is the dielectric constant of the solvent, K is a parameter dependent on the solute, and

$$\Delta\nu = \nu_{\text{cyclohexane}} - \nu_{\text{solv}} = K D^{1/a} \qquad (6)$$

a is a parameter independent of solute and dependent on solvent. Of course, the expression is equivalent to eq 7, where α is the "attenuation" factor, rather than 1/a. For carbon tetrachloride and

$$\Delta\nu = K(\alpha D) \qquad (7)$$

and benzene, a $\cong$ 1.0, and for chlorobenzene and 1,2-dichloroethylene, a $\cong$ 2.0 and 2.5, respectively.

The overall form of eq 6 is, of course, equivalent to eq 5, but the manner in which the parameters are derived differs. My data (21) indicated that for solvents with no permanent dipole and of low dielectric constant, such as hexane, cyclohexane, carbon tetrachloride and possibly benzene, the plot of $\Delta\nu$ (cm^{-1}) against D was linear, i.e. a = 1.0. (Some data gleaned from the literature also show this linear dependence in these solvents, but generally the reported measurements are far too inaccurate.) A reference compound, 2-butanone, was used to find the effective dielectric constants, i.e. $D^{1/a}$, for the polar solvents. When the shifts for the other solutes (benzophenone, acetophenone, p-nitrophenyl acetate, methyl cinnamate, ethyl benzoate, and ethyl acetate) were plotted against these D_{eff} values, straight line correlations were obtained. Thus, D_{eff} depends only on the solvent, and K (the slope of the plot) depends on the solute. If one can infer that the absorptions in cyclohexane, carbon tetrachloride, and benzene reflect mainly bulk solvent effects,

then K may be a measure of the sensitivity of the substrate to these bulk effects. However, the relation (eq 6) does not really distinguish whether the solvent effects are due to bulk or to special properties thus far (see above discussion regarding eq 5).

When $\Delta\nu$ was plotted directly against D, curves such as shown in Figure 1 were obtained. When 2-butanone was used to find D_{eff} for chloroform (total effect), the value found did not generally correlate with the other solutes, i. e. D_{eff} (total) for chloroform is dependent upon the solute. However, when the total shift was broken down as shown in the figure, D_{eff} could be obtained for the "ordinary" shift for 2-butanone ($D^{1/a}$ with $\underline{a} \cong 1.8$). When the chloroform shifts for the other solutes were dissected in the same manner, and the "ordinary" shift vs. D_{eff} (found with 2-butanone) added to the plots for the other solvents, the new points fell on the lines in each case. For the compounds used, the total shift in chloroform ranges from 9.5 to 21.5 cm^{-1}, and the "special" shift accounts for 34-58% of the total shift.

This special effect of chloroform has been generally attributed to formation of some sort of weak hydrogen bond between the carbonyl group and chloroform (22, 23). The treatments of Bellamy and coworkers or of Allerhand and Schleyer (see above) do not separate out any special effect for chloroform, although the above results indicate that a large portion of the shift may be due to this specific interaction. The shifts (relative to n-hexane) in chloroform for ethyl acetate, ethyl trichloroacetate, and ethyl trifluoroacetate are 18.2, 10.8, and 8.6 cm^{-1}, respectively (22). This indicates, in contrast

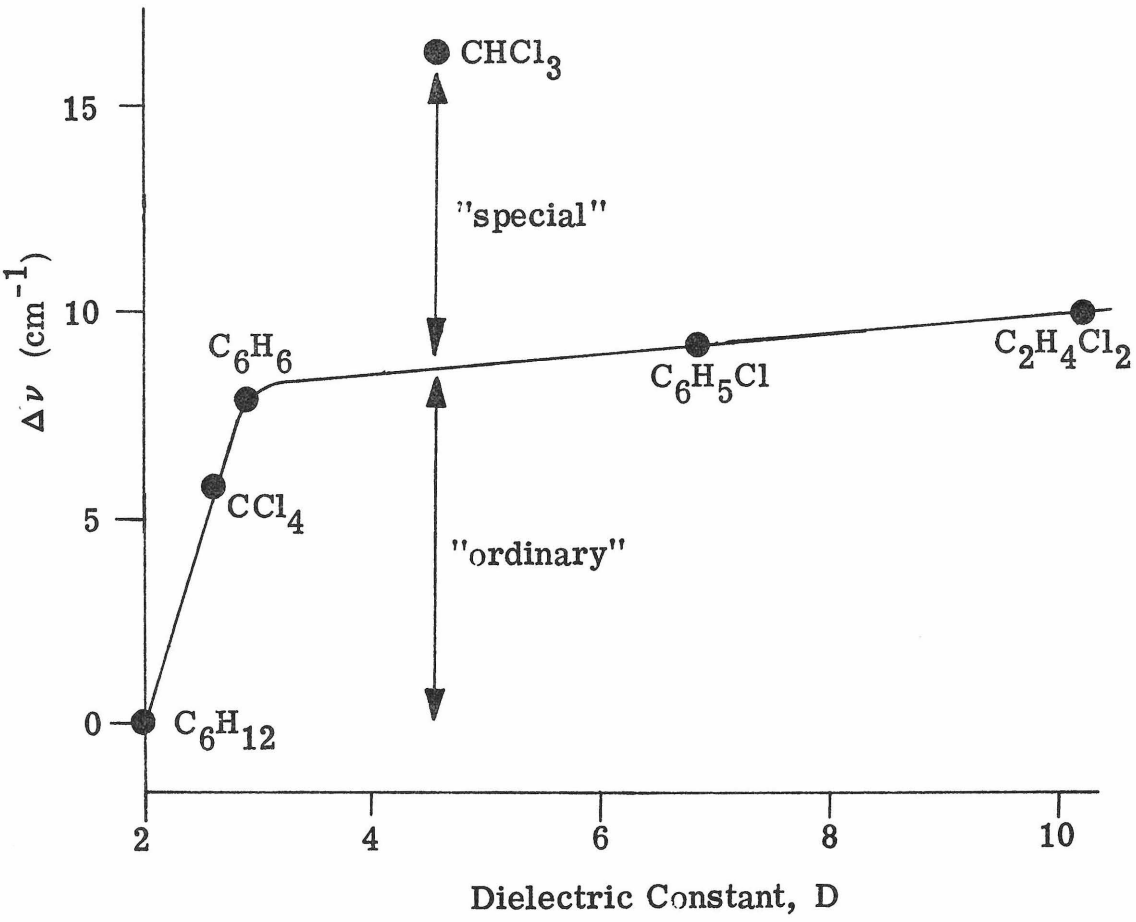

Figure 1. Carbonyl stretching frequency of 2-butanone as a function of solvent dielectric constant.

to other conclusions (18), the hydrogen bonding effect of chloroform is quite dependent upon the solute molecule in question.

The literature shows a considerable lack of reliable absorption data for the carbonyl group even though a considerable number of infrared studies have been done on this group. Absorptions accurate to a least ± 0.5 cm^{-1} (if possible, to ± 0.2 cm^{-1}) are needed (also checked for dilution effects and extrapolated to infinite dilution if necessary). A wider range of carbonyl compounds and solvents than used in my preliminary study should be used, since the evidence for the solute independence of the D_{eff} values is far from established. In addition to the hydrogen bonding effects between carbonyls and chloroform, a detailed study could reveal such effects and their relative importance for other solvents, especially for hydroxylic solvents were large dielectric constants may also cause large "bulk" effects. The substrates shown in Series I - III could be used in this second approach also.

The two general studies proposed here should, hopefully, provide an experimental basis upon which to construct a better understanding of interactions in the liquid phase and perhaps a more intimate knowledge about the vibrational states of organic molecules.

References

1. J. G. Kirkwood, in W. West and R. T. Edwards, J. Chem. Phys., 5, 14 (1937).

2. E. Bauer and M. Magat, J. Phys. Radium, 9, 319 (1938).

3. M. Horak and J. Pliva, Spectrochim. Acta, 21, 911 (1965).

4. H. E. Hallam, in "Infra-red Spectroscopy and Molecular Structure," M. Davies, Ed., Elsevier, Amsterdam, 1963, pp 419-438.

5. R. E. Kagarise and K. B. Whetsel, Spectrochim. Acta, 18, 341 (1962).

6. H. W. Thompson and D. J. Jewell, ibid., 13, 254 (1958).

7. M. L. Josien, Pure Appl. Chem., 4, 33 (1962).

8. G. M. Barrow, "Physical Chemistry," 2nd ed., McGraw= Hill, New York, N. Y., 1966, pp 420-434.

9. N. S. Bayliss, A. R. H. Cole, and L. H. Little, Aust. J. Chem., 8, 26 (1955).

10. A. D. Buckingham, Proc. Roy. Soc., Ser. A, 248, 169 (1958).

11. A. D. E. Pullin, Spectrochim. Acta, 16, 12 (1960).

12. G. L. Caldow and H. W. Thompson, Proc. Roy. Soc., Ser. A, 254, 1 (1960).

13. L. J. Bellamy, H. E. Hallam, and R. L. Williams, Trans. Faraday Soc., 54, 1120 (1958).

14. L. J. Bellamy and R. L. Williams, ibid., 55, 14 (1959).

15. L. J. Bellamy, K. J. Morgan, and R. J. Pace, Spectrochim. Acta, 22, 535 (1966).

16. L. J. Bellamy and P. E. Ragasch, ibid., 16, 30 (1960).

17. See also reference 6.

18. M. Horak, J. Janas, and J. Pliva, Tetrahedron Lett., 19 (1959).

19. S. Brownstein, Can. J. Chem., 38, 1590 (1960).

20. A. Allerhand and P. v. R. Schleyer, J. Amer. Chem. Soc., 85, 371 (1963).

21. Unpublished data, 1967-68.

22. K. B. Whetsel and R. E. Kagarise, Spectrochim. Acta, 18, 329 (1962).

23. G. C. Pimentel and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman, San Francisco, Ca., 1960, pp 197-198; and references therein.