PART I β-FERROCENYLALKYL CARBONIUM IONS

PART II THE STEREOSPECIFIC SYNTHESES OF THE EXO AND ENDO ISOMERS OF α-HYDROXYMETHYL-1, 2-TETRAMETHYLENEFERROCENE

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To My Wife

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ABSTRACT

Part I β-Ferrocenylalkyl Carbonium Ions

Part II The Stereospecific Syntheses of the Exo and Endo Isomers of α-Hydroxymethyl-1, 2-Tetramethyleneferrocene

By

Maurice Joseph Nugent Jr.

Part I

The solvolysis mechanism of β-ferrocenylalkyl tosylates is discussed. Evidence is presented which shows that solvolysis occurs with preferential participation of the interannular electrons of the ferrocene moiety leading to intermediate formation of very stable carbonium ions. The products resulting from these solvolysis reactions demonstrate that these carbonium ions exhibit features expected for both ferrocenyl ring-bridged and iron-stabilized intermediates. The stereochemistry of solvolysis of (-)-1-ferrocenyl-2-propyl p-toluenesulfonate has also been examined and found to occur with complete retention of configuration.

Part II

The stereospecific syntheses of the exo and endo isomers of α-hydroxymethyl-1, 2-tetramethyleneferrocene is described.

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PART I β-FERROCENYLALKYL CARBONIUM IONS

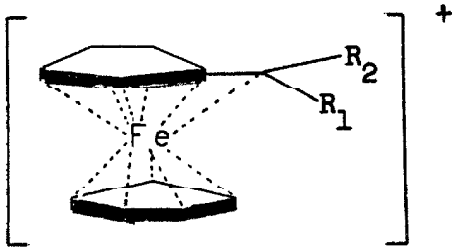
CHAPTER I

Part I

Introduction

α-Ferrocenyl Carbonium Ions

The ability of the iron atom of ferrocene to stabilize a carbonium ion in a position adjacent to the ring has been well documented (1, 2). This stability, which is manifested by the comparable rates of hydrolysis of ferrocenyl carbinyl acetate and trityl acetate in 80% acetone (3), has been attributed to iron participation (2), and the intermediate has been formulated as Ia.



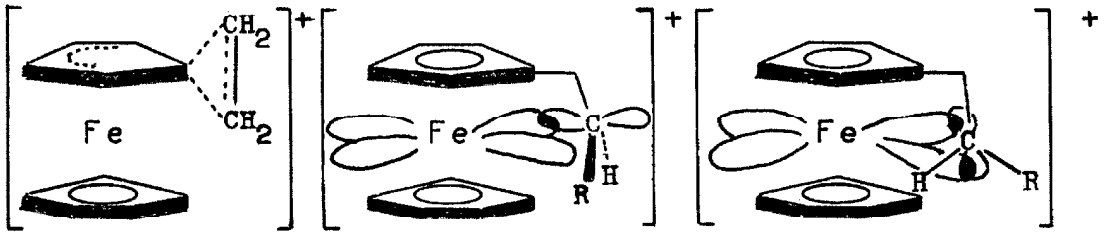
Ia

Ib: $R_1 = CH_3$, $R_2 = H$

β-Ferrocenyl Carbonium Ions

The observation (4) that 2-ferrocenylethyl p-toluenesulfonate solvolyzes 537 times faster than 2-phenylethyl p-toluenesulfonate in 80% acetone was the first published indication of the stability of ferrocenyl carbonium ions which are derived from carbon atoms that are not adjacent to the ferrocene ring.

A stable β-ferrocenyl carbonium ion was also proposed by Hill (7) to explain the rate enhancement for 2-ferrocenylethyl p-toluenesulfonate; he considered the stability of this ion to be due to participation by either the π electrons of the ferrocene ring as in II, or by a filled iron d orbital as represented by IIIa and IVa.

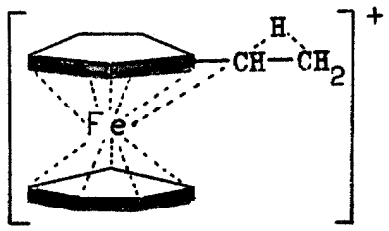


II

IIIa : R = H
IIIb : R = CH_3

IVa : R = H
IVb : R = CH_3

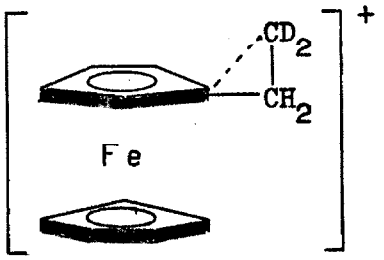
Anchimeric assistance by hydride migration from the β carbon atom, as in V, and the formation of the very stable α-ferrocenyl carbonium ion Ib was ruled out by Hill (5) when he found that the only hydrolysis product of 2-ferrocenylethyl p-toluenesulfonate in 80% acetone was the corresponding, unrearranged alcohol.



V

A possible electron-donating, inductive effect of the ferrocene moiety was also considered as an explanation for the observed rate enhancement (8). Carter rejected this possibility, however, because of the similarity in pKas of ferrocenoic and benzoic acids, and from a consideration of the dipole moments of various substituted ferrocenes (9). In fact, the actual inductive effect of the ferrocene group based on these pKas is electron-withdrawing, and would be expected to retard the rate of solvolysis of 2-ferrocenylethyl p-toluenesulfonate by a factor of approximately ten (9).

In an attempt to distinguish between ring-bridged ion II and the iron-stabilized intermediates III and IV, Carter characterized the hydrolysis and acetolysis products of 2-ferrocenylethyl-1, 1-d_2 p-toluenesulfonate (10). He found no deuterium shuffling (limit of detection ± 10%) and concluded that either carbonium ion stabilization by interaction with the π electrons of the cyclopentadienyl ring does not occur, or that if interaction occurs, the α (deuterated position) and β carbon atoms never become "equivalent" (11). Solvent collapse, in this latter case, would have to occur only at the α position to account for the failure to observe deuterium scrambling. Intermediate VI represents the ring-bridged ion considered by Carter to have "non-equivalent" α and β positions.



VI

Another explanation, presented by Carter, for the immobility of the deuterium label in a ring-bridged ion with "equivalent" α and β positions was that attack of solvent at the β position was sterically hindered by the bottom ring (11).* Although his data obtained from the solvolyses of 2-ferrocenylethyl-1, 1-d_2 p-toluenesulfonate did not exclude formation of a ring-bridged ion, Carter rejected this intermediate from consideration of the relative strength of the π-bonded hydroxyl absorptions of 2-ferrocenylethanol and 2-phenylethanol (11). The infrared absorption of the ring-bonded hydroxyl in 2-ferrocenylethanol occurs 27 cm^{-1} lower than the free hydroxyl absorption in this molecule (12, 13). For 2-phenylethanol, the π-bonded hydroxyl is 29 cm^{-1} lower than the free hydroxyl absorption (14). These data indicate that energetically the interaction of the π electrons with the hydroxyl hydrogen is similar in both the phenyl and ferrocenyl systems. Carter's extension of this argument was that the interaction

*In order to maintain continuity, the detailed discussion of possible ring-bridged ferrocenyl intermediates is discussed below (see p. 15).

of these π electrons with carbonium ions should be energetically similar for both the 2-ferrocenylethyl and 2-phenylethyl systems. Thus if a ferrocenyl ring-bridged intermediate is formed, it should stabilize a carbonium ion to the same extent as does the bridged phenyl system. Since 2-ferrocenylethyl p-toluenesulfonate hydrolyzes 537 times faster than the corresponding phenyl compound, anchimeric assistance is different in the two systems and is not, therefore, due to the formation of a bridged ion. As Carter pointed out (15), this argument is not flawless since infrared hydroxyl shifts represent ground state interactions while ring-bridged ions occur as metastable intermediates; the assumption that the interaction is the same in both states may not be valid. Another objection to this application of absorption frequency differences is that the interacting groups involved in hydrogen bonding, ring carbons and hydroxyl hydrogen, are separated by three atomic centers; i.e. two carbon atoms and one oxygen atom. In the ring-bridged carbonium ion however, the interacting partners, ring carbons and electron-deficient carbon, are separated by only one carbon atom. Accordingly, ring-hydroxyl interactions may be isoenergetic for both phenyl and ferrocenyl in the hydrogen bonding case; but the ring interactions may be of much different energy when the geometry, the distances, and the hybridizations are changed to those that apply in the phenyl and ferrocenyl ring-bridged ions.

As further evidence against a ring-bridged ferrocenyl carbonium ion. Carter cited results obtained from Garwood's studies of ω-ferrocenyl-α-alkyl p-bromobenzenesulfonates (6), and from his own

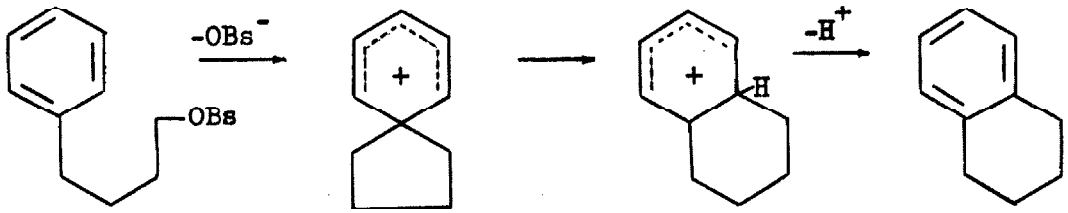
stereochemical studies of the solvolysis of optically active 1-ferrocenyl-2-propyl p-toluenesulfonate. These results are discussed below (see p. 7).

Carter's kinetic results included measurement of the secondary α deuterium isotope effect (16) of 2-ferrocenylethyl p-toluenesulfonate (k_H/k_D = 1.14) and a measurement of the α-methyl effect (17, 18, 19) from the rate of hydrolysis (80% acetone) of 1-ferrocenyl-2-propyl and 2-ferrocenylethyl p-toluenesulfonates. The isotope effect of 1.14 demonstrates that the hydrolyses of 2-ferrocenylethyl and 1-ferrocenyl-2-propyl p-toluenesulfonates are close to limiting and, in conjunction with the small α-methyl effect of 1.4, provides good evidence for neighboring group participation (8). The added significance of this small α-methyl effect is discussed below (see p. 45).

The most notable result obtained by Carter was his observation that the hydrolysis of optically active 1-ferrocenyl-2-propyl p-toluenesulfonate in either 60% or 80% acetone resulted in complete racemization (20). This result was rationalized in terms of p-d π stabilization of the carbonium ion as in intermediate IVb, which was favored over intermediate IIIb because the confirmation of IVb would minimize unfavorable steric repulsions between the ferrocene moiety and the hydrogens of the methyl group (21). Although there are certain objections to intermediate IVb (see p. 24), any discussion of these objections here is superfluous since Carter's stereochemical results cannot be reproduced. On the contrary, the acetolysis and the hydrolysis (80% acetone) of (-)-1-ferrocenyl-2-propyl p-toluenesulfonate both occur with 100 ±3% retention of configuration (see p. 76).

ω-Ferrocenyl-α-alkyl Systems

The search for other stabilized ferrocenyl carbonium ions was carried out by Garwood, who investigated the hydrolysis (80% acetone) and acetolysis of 3-ferrocenyl-1-propyl, 4-ferrocenyl-1-butyl, and 5-ferrocenyl-1-pentyl p-bromobenzenesulfonates (22). The acetolysis of the corresponding phenyl brosylates has been investigated (23), and for 4-phenyl-1-butyl p-bromobenzenesulfonate only ca. 5% proceeds via the spiro-carbonium ion:



$OBs^- = p\text{-}BrC_6H_4SO_3^-$

95% of the solvolysis occurs by an unassisted path (23). In the more nucleophilic solvent, 80% acetone (24), the weakly nucleophilic, intramolecular π system is probably unable to compete effectively with solvent for the electron-deficient carbon atom so that products are formed via S_N2 displacement of brosylate by solvent or perhaps by a special acetone mechanism (24). Since Garwood observed only minor differences in the solvolysis rates among the compounds in the ferrocene series, and because there were no large solvolytic rate differences between the corresponding ferrocenyl and phenyl brosylates, he concluded that there was no anchimeric assistance by the metallocene group in these systems (25). The fact that ω-(p-anisyl)-

α-alkyl brosylates, which solvolyze via spiro carbonium ions, react faster in acetic acid than their ferrocene and phenyl counterparts was also cited as evidence of the absence of metallocene participation in the ferrocene series. He attributed this result to ring size effects. Namely, the closure of a large ring is less probable than that of a smaller one, and rings which would result from metal participation in compounds with alkyl side chain lengths of three carbons or more would require more free energy for their formation than would result from neighboring group participation (25). Thus, metallocene participation was possible in the 2-ferrocenylethyl system (small ring), but energetically unfavorable in the longer chain derivatives. As further evidence against π electron participation and formation of spiro-carbonium ions in the ferrocene systems, Garwood cited the absence of "hydrocarbon" products in the solvolysis mixtures. It should be noted, however, that extensive decomposition occurs in these systems (6) so that a few percent of 1, 1' or 1, 2-tetramethyleneferrocene would not have been detected (see p. 26).

Present Objectives

The purpose of the research described on the following pages was to gather evidence concerning the importance of ferrocenyl ring-bridged and iron-stabilized solvolytic transition states, and to define the structure of the important intermediates. Evidence was acquired in three different ways: (1) by measuring acetolysis rates of 2-ferrocenylalkyl tosylates so that data on ferrocene compounds would be available for comparison with the wide variety of acetolysis rates

for other alkyl and aryl systems, (2) by investigating the stereochemistry of the solvolyses of 2-ferrocenylalkyl tosylates, (3) and by kinetic measurements and product studies of ferrocene derivatives with structures designed so that the effects of either iron participation or ferrocenyl ring-bridging could be identified with these results.

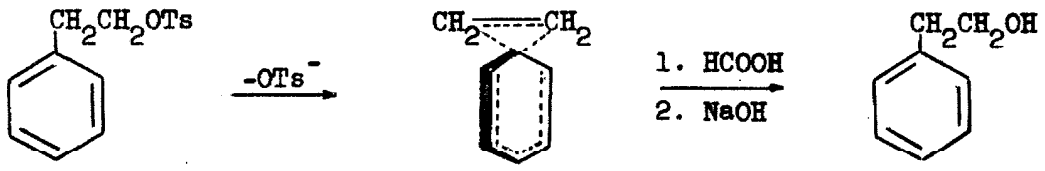
CHAPTER II

The Formulation of β-Ferrocenylalkyl Solvolytic Intermediates

β-Phenyl Participation

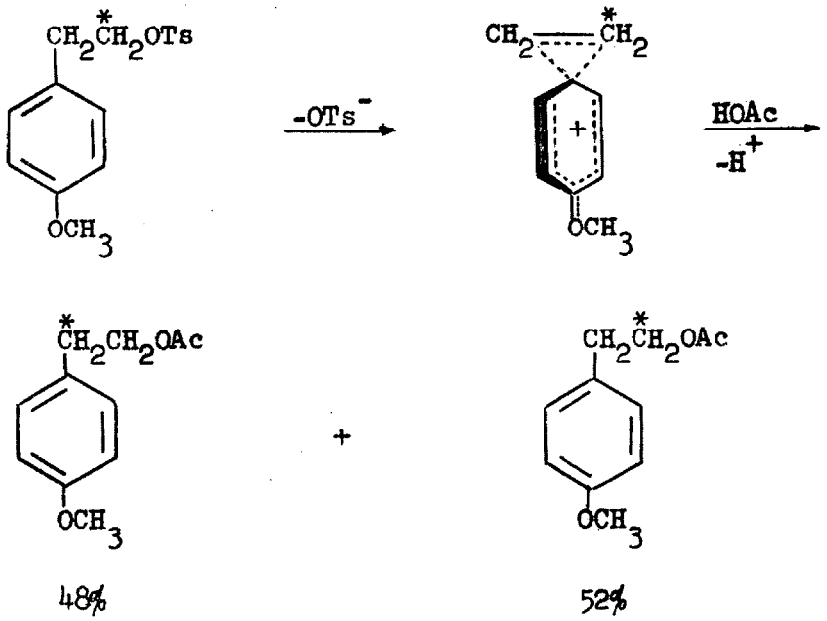
In the Introduction, it was pointed out that the main objective of this research was to determine the importance of ring-bridged and iron-stabilized intermediates in the solvolyses of β-ferrocenylalkyl tosylates. In this connection, it is appropriate to review some of the results on neighboring phenyl participation. The importance of ring-bridged ionic intermediates for the phenyl systems discussed herein has been well established and recently reviewed (26). No attempt is necessary here to justify these formulations; rather, the consequences of neighboring phenyl participation will be discussed so that ferrocenyl ring-bridging can be formulated and the expected results can be assessed. In addition, the iron-stabilized intermediates, first proposed by Hill (7) and described in detail by Carter (27), for these solvolyses will be discussed.

The simplest structure in which phenyl participation occurs is in the intermediate derived from the formolysis of 2-phenylethyl p-toluenesulfonate:



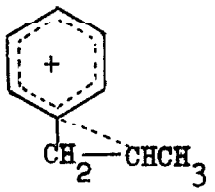
$OTs^- = p\text{-}CH_3C_6H_5SO_3^-$

It should be noted that phenyl participation is not complete in this system, and this solvolysis proceeds in part by a nucleophilic* process (17, 26, 28). Because phenyl participation leads to substantial charge delocalization by the benzene ring, phenyl substituents that stabilize positive charge increase the rate of assisted solvolysis. Furthermore, if one of the carbon atoms of the methylene groups is isotopically labeled, the extent of formation of a symmetrical intermediate can be evaluated from scrambling of the label. These experiments have been carried out (17, 29), and the results are entirely consistent with the formulation of the acetolysis of the C^{14} labeled p-anisylethyl tosylate, for the most part, as:

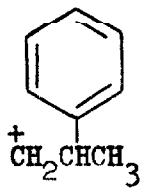


*The discussion of nucleophilic and limiting solvolyses together with the effect of these solvent properties on solvolysis rates is discussed on page 43.

The kinetic effects of α-methyl substitution in β-arylalkyl systems are discussed below (see p. 44); however, it is useful to discuss the effect of α-methyl substitution on the driving force for aryl participation (30) here. The rates and stereochemical results of the acetolysis and formolysis of 1-phenyl-2-propyl p-toluenesulfonate have been investigated (31) and the results have been interpreted in terms of neighboring phenyl participation leading to the formation of an unsymmetrical bridged ion VII where the formulated resonance structure refers to the relative unimportance of canonical form VIIa.



VII

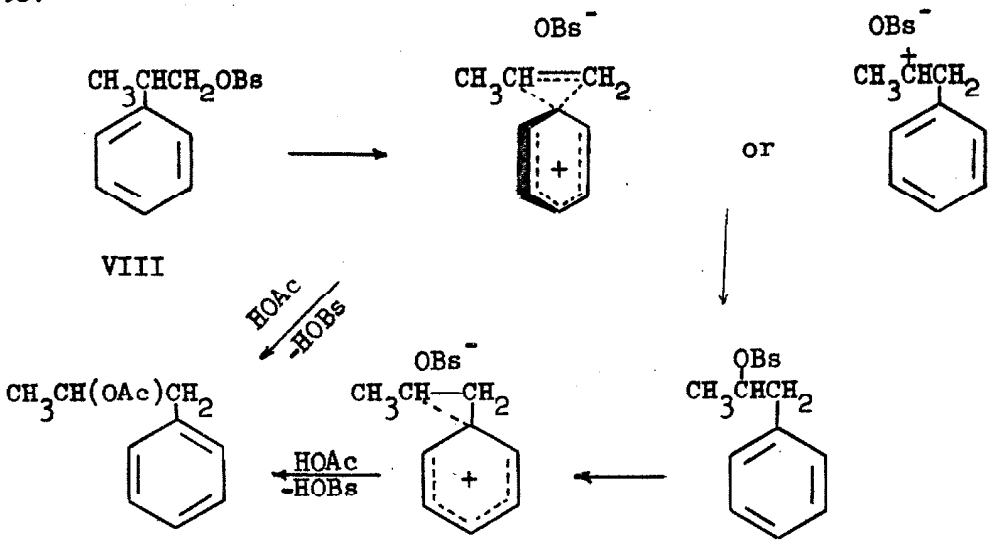


VIIa

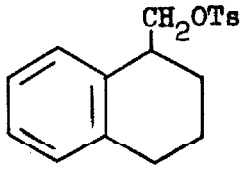
Thus α-methyl substitution results in less bonding character between the neighboring group and the electron-deficient carbon. The stereochemical outcome of such participation is retention of configuration with formation only of secondary products (31).

Secondary products are also exclusively obtained from the acetolysis and formolysis of 2-phenyl-1-propyl p-bromobenzenesulfonate VIII; this observation is in complete accord with the increased driving force for phenyl participation as a result of β-methyl substitution (30, 32). In fact, phenyl migration is complete in the

acetolysis and formolysis of such systems, even to the extent that rearranged starting brosylate is formed in acetic acid (31) according to:

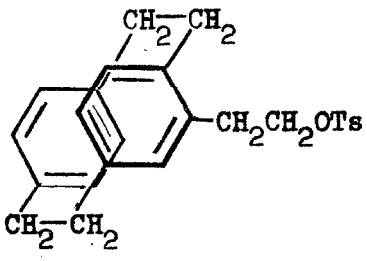


An important result of α or β-methyl substitution is that in no case does phenyl participation lead to primary esters when the phenyl group is bridged between primary and secondary carbons. This result is illustrated further by the solvolysis of 1, 2-benzocyclohexyl-3-methyl p-toluenesulfonate (IX) (33, 34). The acetolysis of this tosylate proceeds through a phenonium ion intermediate; and can be formulated analogously to VIII. As a result of the conversion of primary sulfonate to secondary sulfonate and the comparable acetolysis rates of the primary and secondary esters (factor of 30), the acetolysis of these systems is not a simple first order process. Instead, an induction period occurs as the concentration of secondary ester is increased; most of the solvolysis then occurs via the rearranged sulfonate ester.

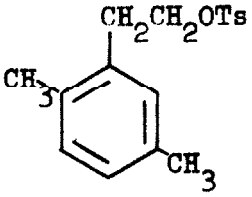


IX

The phenyl system, which is structurally most closely related to the β-ferrocenylalkyl systems, is 2-([2.2]paracyclophanyl)-ethyl p-toluenesulfonate (X) investigated by Cram (35). The molecular geometry of [2.2]paracyclophane (36) shown in Figure 1 is important for the description of the intermediate involved in the solvolysis of X and for comparison with the geometry of ferrocene (see p. 17, Figure 3).



X



XI

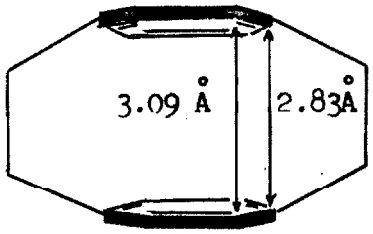
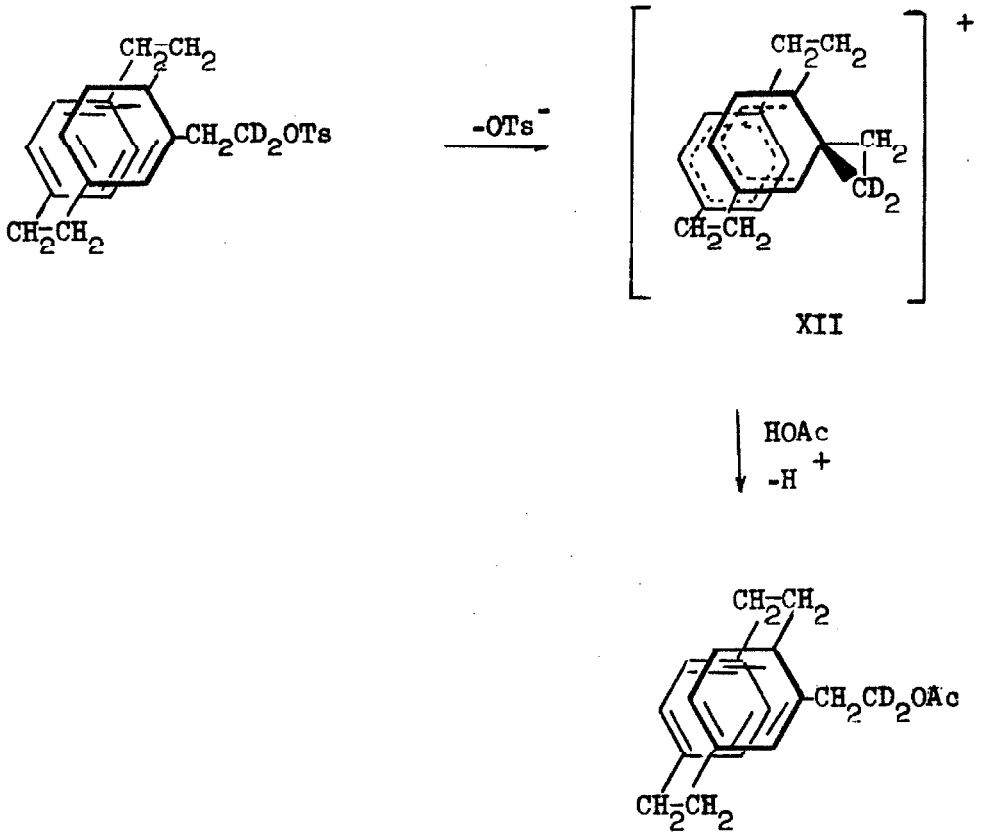


Fig. 1

Because 2-(2, 5-dimethylphenyl)-ethyl p-toluenesulfonate (XI) solvolyzes (via a bridged transition state) more slowly than X and because the entropy of activation for the paracyclophane derivative is comparable to that of systems which are known to involve ring-bridged solvolytic intermediates, a paracyclophanyl phenonium ion has been proposed as an intermediate in the acetolysis and formolysis of X.

Despite the intermediacy of this bridged ion however, no scrambling of deuterium label is observed in either the formolysis or acetolysis of deuterium labeled X, even under experimental conditions which are thought to involve repeated regeneration of the carbonium ion. This failure to observe deuterium scrambling has been cited as evidence of bridged ion XII, which for steric reasons always forms and collapses from the exo direction as shown below (35):



Formulation of π-Electron Participation in β-Ferrocenylalkyl Systems

The β-ferrocenylalkyl carbonium ions, which can be theoretically formulated as involving only π electron participation (ring-

bridged intermediates) are most conveniently discussed in terms of overlap between the vacant carbon p orbital and the more or less bonding orbitals of the ferrocene system. It should be recognized that such a formulation is necessarily approximate in this system since no quantitative molecular orbital descriptions of ferrocene are available, nor is the degree of overlap between the iron and cyclopentadienyl orbitals of proper symmetry in the ferrocene molecular a matter of consistent agreement.* Furthermore, there is no reason to expect that the molecular orbital description of ferrocene will be applicable to a positively charged ferrocenylalkyl carbonium ion.

The molecular orbital representation of ferrocene, which will be used for the description of these β-ferrocenylalkyl carbonium ions is that of Moffit (39) with the modification that overlap between the iron and ring orbitals of proper symmetry is more significant (37) than was originally suggested by this treatment. The advantage of this representation derives from the fact that it facilitates some pictorial illustration of the molecular orbitals of ferrocene. In this connection, it will be assumed that the eight iron carbon orbitals, which are involved in bonding to some extent (37), are localized for the most part in the interannular region described by the e_{1g} molecular orbitals (Figure 2); two nonbonding electrons are contained in the h_{ag}

*A review of most of the molecular orbital descriptions of ferrocene is given in reference 37; the most recent description of the method involved in molecular orbital calculations of ferrocene is presented in reference 38.

molecular orbital (bonding hydrid of the d_{z^2} and 4s iron orbitals) which forms an equatorial belt around the central iron atom (Figure 3).

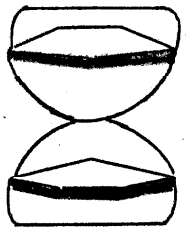


Fig. 2

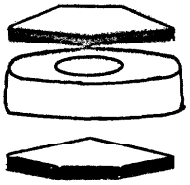
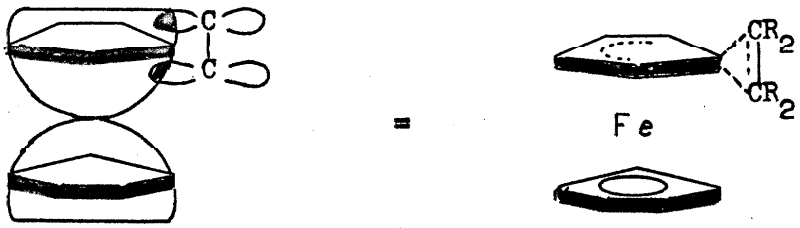


Fig. 3

The shape of the interannular bonding and nonbonding orbitals can be regarded as a result of electron correlation between these orbital networks (39) so that the highest density of nonbonding electrons is in the central interannular region, while the bonding orbitals have their largest density in the interannular regions which are close to the five-membered rings.

The description of π electron stabilization as represented by XIII will be discussed in terms of the orbitals represented in Figure 2; whereas the h_{ag} orbital (Figure 3) is important in the description of the iron-stabilized intermediate (p. 23).



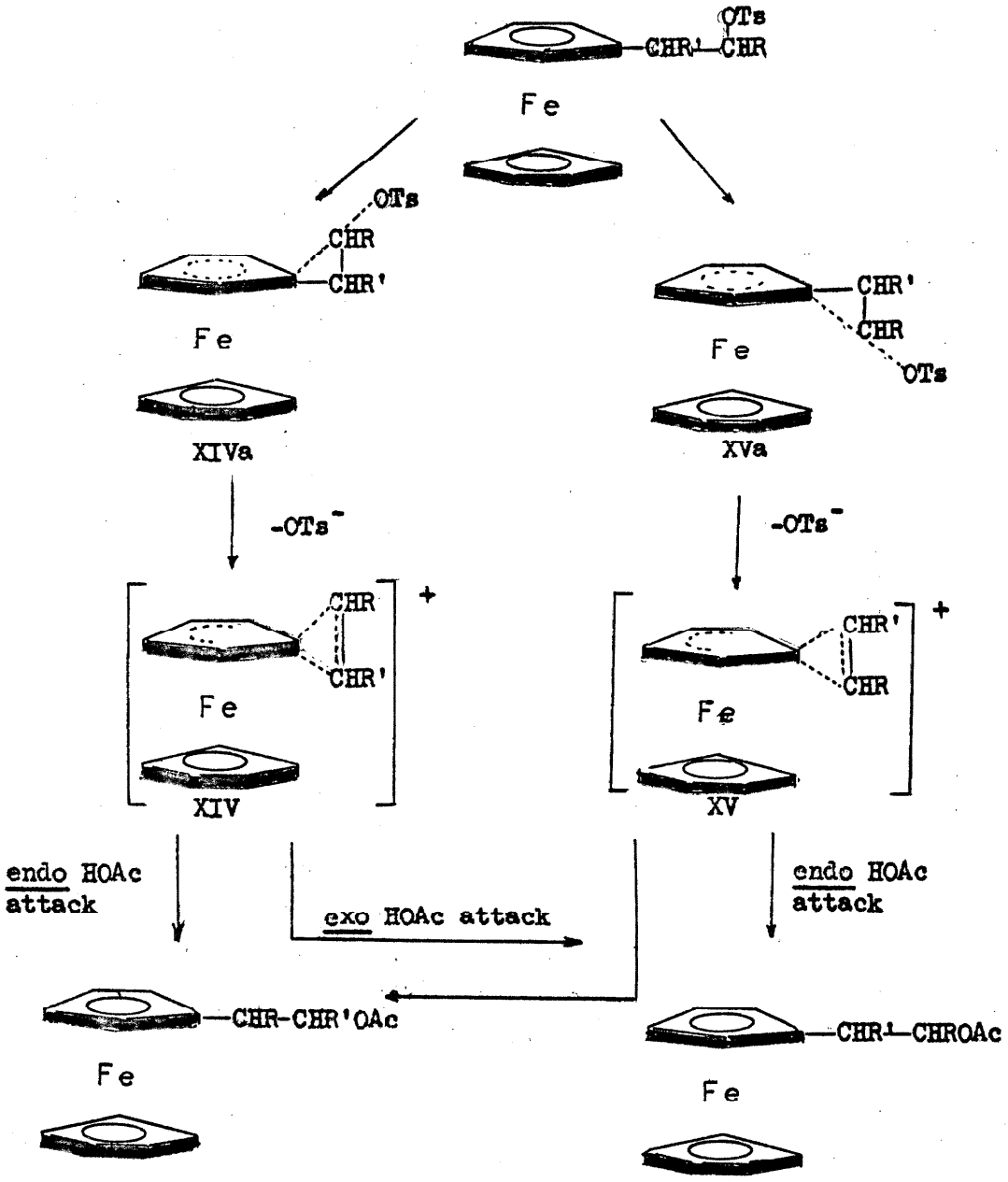
XIII

Because there is a larger availability of bonding orbitals and electron density between the two cyclopentadienyl rings than above or below these moieties, a ring-bridged intermediate (XIII) will be able to sustain positive charge much better at the endo carbon than at the exo carbon atom. In this connection, it is important to realize that intermediate XIII, with identical substituents on each carbon in the alkyl chain, represents a carbonium ion with electronically nonequivalent endo and exo carbon atoms in this alkyl chain. Of course, the relative charge density at the exo carbon will be determined by the substituents attached to this carbon.

A further implication of this formulation is that involvement of the π electrons of the cyclopentadiene ring necessarily includes the iron-carbon bonding electrons in intermediate XIII because overlap between the orbitals of the π system and the iron atom is the molecular orbital description of iron-carbon bonding in ferrocene (37, 38).

Because the interplay of various steric and electronic factors which determines the configuration of these ferrocenyl ring-bridged transition states (XIVa and XVa) and the products formed from the resulting intermediates (XIV and XV) can be most easily presented within the framework of several solvolytic processes, the solvolysis of a β-ferrocenylalkyl tosylate proceeding by way of two isomeric, ring-bridged transition states is shown in Chart I. It is emphasized that this representation of the simultaneous occurrence of two isomeric transition states and two isomeric intermediates during the solvolysis of this β-ferrocenylalkyl tosylate is purely hypothetical here and is used only for illustrative purposes.

Chart I


OTs
CHR'—CHR
Fe
OTs
CHR
CHR'
Fe
XIVa
CHR'
CHR
OTs
Fe
XVa
-OTs⁻
-OTs⁻
CHR
CHR'
+
Fe
XIV
CHR'
CHR
+
Fe
XV
endo HOAc attack
exo HOAc attack
endo HOAc attack
—CHR-CHR'OAc
Fe
—CHR'—CHROAc
Fe

Since the interannular distance in the ferrocene molecule (Figure 4) is similar to the distance between the two phenyl rings in [2.2]paracyclophane (Figure 1), the most favorable ferrocenyl, ring-bridged transition state, based only on steric interactions, would be XIVa in which a bridged ion is formed from the exo direction as is the case with the 2-([2.2]paracyclophanyl)-ethyl system (35) discussed above (p. 15). Similar steric effects will facilitate solvent attack from the exo direction.

Steric interactions are not the only important considerations in these systems, however, in view of the greater availability of bonding electrons in the interannular region. Accordingly, the steric preference for the formation of exo transition state XIVa is counterbalanced

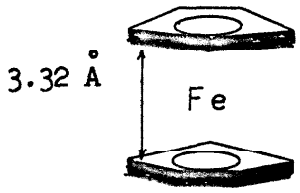
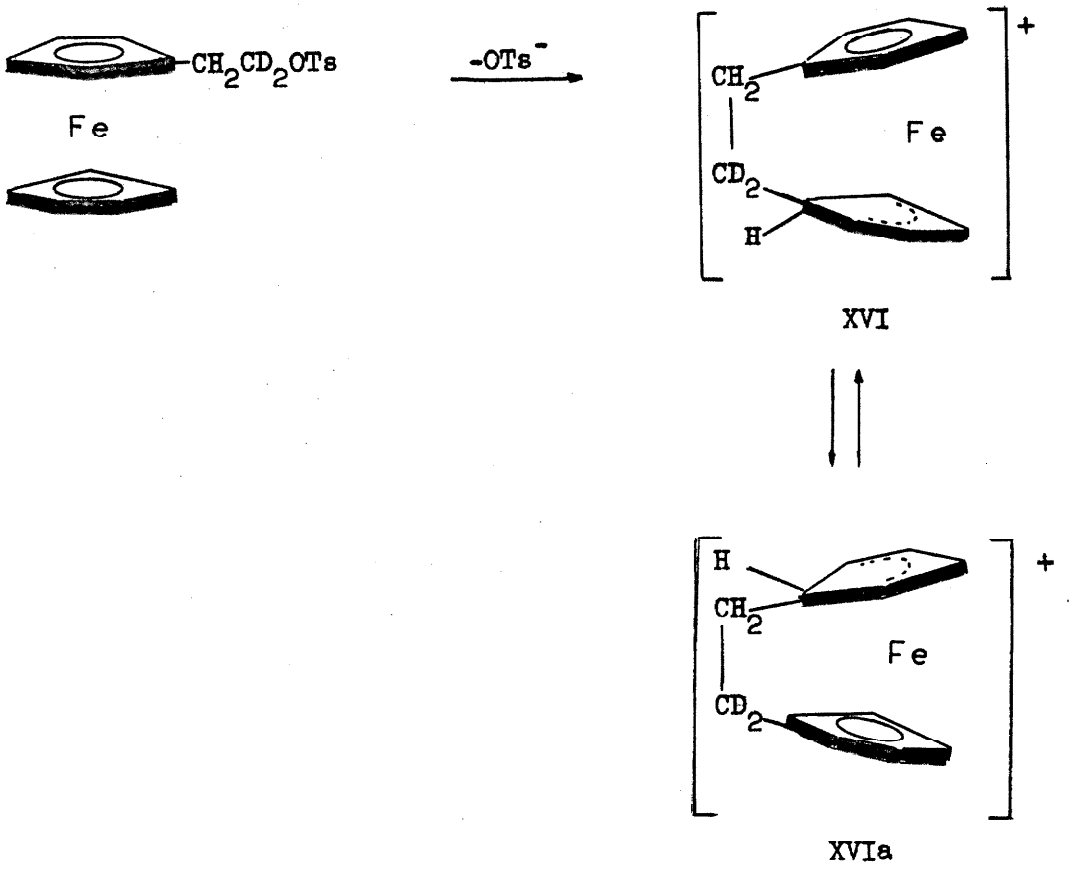


Fig. 4

by the more favorable electron participation in transition state XVa when the α and β substituents R and R' are the same. Because direct interaction between the developing positive charge and the interannular electrons can occur in transition state XVa, this mechanistic path is preferred from electronic considerations over transition state XIVa where direct interaction between the interannular bonding electrons and the electron-deficient carbon atom is not possible.

Opposing steric and electronic effects also play a role in determining the site of nucleophilic attack on these electron-deficient intermediates. As mentioned previously, the endo carbon atom in either carbonium ion XIV or XV is better able to sustain positive charge when the α and β substituents, R and R' are the same. This enhanced electron delocalization at the endo carbon atom results in a strong preference for endo nucleophilic attack on these ring-bridged ions. This preference for endo nucleophilic attack is somewhat suppressed, however, by the fact that the exo carbon in the alkyl bridge may be more accessible to attack by solvent. The importance of such a steric effect is indicated by the results of deuterium labeling experiments in the 2-([2.2]paracyclophanyl)-ethyl system (35) which were discussed earlier (p. 15).

Participation by the π electrons of the unsubstituted ring, as in XVI, could be envisioned as the source of stability in a carbonium ion intermediate derived from 2-ferrocenylethyl-1, 1-d_2 p-toluenesulfonate. The structure of this intermediate is formulated on the basis of the structure of 1, 1'-dimethyleneferrocene (41).



XVI

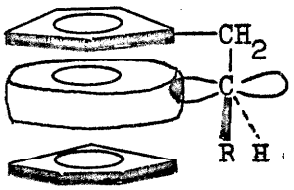
XVIa

This kind of participation is unlikely because no products having a heteroannular, two-carbon bridge have ever been isolated from these solvolysis mixtures. Additional evidence against XVI results from the observation that no scrambling of deuterium label was observed during the solvolysis of 2-ferrocenylethyl-1, 1-d_2 p-toluenesulfonate in either this research or in previous studies (42) even under conditions where repeated ionization could occur. If intermediate XVI is formed, it would be expected to equilibrate with its isomer XVIa during solvolysis, and as a result, shuffling of isotopic label would occur. The same arguments have been used previously by Cram to eliminate the analogous paracyclophane intermediate (35).

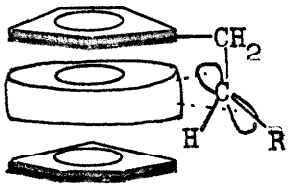
Iron Stabilization in β-Ferrocenylalkyl Systems

The term iron-stabilized carbonium ion as it is used in this thesis will denote overlap between the h_{ag} molecular orbital (Figure 3), which contains two nonbonding electrons, and a vacant carbon 2 p orbital. Since π stabilization as described above involves overlap of the iron bonding orbitals in the ferrocene system, the two terms can be distinguished even though they both involve participation by orbitals associated with the iron atom. The use of the h_{ag} molecular orbital rather than the dx^2-y^2 iron orbital used by Carter and Hill (p. 2) as the orbital containing the nonbonding pair is a result of the author's preference; the interpretation of the experimental facts concerning these carbonium ions are in no way affected by this choice.

An extensive description of the geometry of iron-stabilized carbonium ions for 2-ferrocenylethyl and 1-ferrocenyl-2-propyl cations has been given by Carter (27) and will not be repeated here. From geometric calculations and model measurements, Carter concluded that intermediate XVIIb would be of higher energy than XVIIb for the 1-ferrocenyl-2-propyl cation because the latter intermediate minimizes unfavorable steric interactions between the methyl group hydrogens and those of the unsubstituted ring.

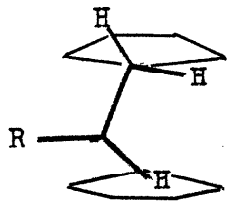


XVII
a: R = H
b: R = CH_3



XVIII
a: R = H
b: R = CH_3

Close examination of models of these cations, however, reveals that IV involves serious steric repulsions between the hydrogens attached to the electron-deficient carbon and those of the unsubstituted ring. The best conformation of either the primary or secondary iron-stabilized intermediate, as indicated by models, is one in which the carbon chain is not fully extended towards the unsubstituted ring, as previously implied (27), but one in which the chain is offset as in XIX. This conformation does not lead to steric interactions that prevent the rotation of the rings, and it does permit overlap between one lobe of carbon p orbital and one lobe of the iron nonbonding orbital as represented by XVII.



XIX

CHAPTER III

Measurement of Acetolysis Rates of β-Ferrocenylalkyl p-Toluenesulfonates

The measurement of solvolysis rates of ferrocenylalkyl sulfonate esters by determining the rate of production of sulfonic acid is often complicated by side reactions which occur during solvolysis. The first side reaction of these ferrocene derivatives is acid-promoted oxidation by molecular oxygen. This oxidation can be eliminated by degassing the reaction mixture before appreciable solvolysis has occurred. A second side reaction, which has not been eliminated, leads to decreases in the yields of p-toluenesulfonic acid of about 7% (Table I, p. 29). Because the mechanism of this latter side reaction is unknown, the values of many of the solvolytic rate constants obtained in this research are certain only within an 8% range. Although this uncertainty is larger than the standard deviations of these rate constants in most cases (Table II, p. 40), it is not large enough to affect any of the mechanistic conclusions which are based on these values. The details of the kinetic effects of these two side reactions are discussed separately below.

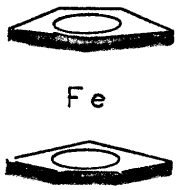
Acid Promoted Atmospheric Oxidation of Ferrocene Compounds

One of the properties of ferrocene compounds, which is often troublesome to the organic chemist, is their susceptibility to oxidation (43) and the decomposition of the resulting ferricinium species (44, 45). Although several organic and inorganic compounds are reduced by ferrocene (43), the reaction which is relevant here is that

between oxygen and ferrocene in acidic solutions:

$$4H^+ + O_2 + FcH \longrightarrow 4FcH^+ + 2H_2O$$

$$FcH^+ \longrightarrow \text{decomposition products}$$

FcH = 

Since the solvolysis of esters in non-basic, protic solutions is accompanied by the production of acid, the reaction of ferrocenyl esters with solvent can be markedly affected by the presence of oxygen. The result of oxidation in these solvolytic systems is twofold. Since the rate of production of acid is often the experimental measure of the rate of solvolysis of the ester, oxidation will cause a deviation from the first order kinetics usually observed (46).

A second result of oxidation is preferential destruction of important reaction products. This destruction is due to the formation of ferricinium species which may slowly decompose either during the course of the reaction or during isolation of the products (43, 44). The preference arises from the fact that ferricinium species with electron-donating substituents will exist in larger relative concentrations than those of ferricinium ions with electronegative substituents (47). If one assumes that both ferricinium ions are equally unstable, a larger fraction of the more easily oxidized ferrocenes

will be destroyed by this reaction. The absence of detectable quantities of 1, 1' or 1, 2-tetramethyleneferrocene in the acetolysis mixture of 4-ferrocenyl-1-butyl p-toluenesulfonate (6) could be explained by preferential oxidative destruction (see p. 8).

Fortunately, acid promoted oxidation of ferrocene does not always occur instantaneously. For example, there is apparently no oxidation during the hydrolysis of ferrocenylcarbinyl acetates in 80% acetone (1), and acetic acid solutions of 2-ferrocenylalkyl p-toluenesulfonates are sufficiently stable so that no green color,* indicative of ferricinium ion, appears for several hours at room temperature, if extensive solvolysis does not occur.

In other cases however, oxidation has seriously hampered rate measurements. Garwood experienced serious difficulties in obtaining reproducible rate constants from his acetolysis studies (48), and Carter's rate data (49) could have been affected by oxidation, since 1-ferrocenyl-2-propyl p-toluenesulfonate was found to be oxidized during hydrolysis in 80% acetone at 32° (see Experimental Section p. 121).

To prevent this kind of oxidation all acetolyses, reported herein, were carried out in evacuated, sealed ampoules. Control experiments with either methylferrocene or 1-ferrocenyl-2-propyl p-toluenesulfonate in p-toluenesulfonic acid-acetic acid mixtures did

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*The reported color of ferricinium in acidic aqueous solutions is blue (1); however, in dry acetic acid solutions in which oxidation is not extensive, the characteristic color is green.

not show any green discoloration due to the formation of ferricinium ion, even after periods of time corresponding to the ten solvolytic half lives of these tosylates. Furthermore, the agreement between duplicate infinity titers (standard deviation 0.2%) showed that no oxidation occurred in the time interval between opening of the ampoule and titration of the sample.

Other Side Reactions

Since the acid promoted oxidation of ferrocenes had been eliminated by degassing the reaction mixtures, it was expected that the determination of acetolysis rates would not be complicated. This was not the case, however, because the yield of p-toluenesulfonic acid was never quantitative (see Table I); in spite of the fact that the 2-ferrocenylethyl and 1-ferrocenyl-2-propyl p-toluenesulfonates which were used were higher melting, * and therefore probably as pure as those which give nearly quantitative yields of p-toluenesulfonic acid upon hydrolysis in 80% acetone (49). Side reactions were observed during these acetolyses; one of which probably accounts for the discrepancy between the calculated and experimental values of the infinity titers.

The first of these reactions was an oxidation which occurs by electron transfer from an iron atom to a carbonium ion intermediate.**

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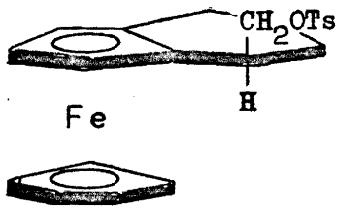
*Carter did not report the m.p. of 2-ferrocenylethyl p-toluenesulfonate in his thesis, but in his laboratory notebook (No. 1050, p. 69) he reports a m.p. of 76-78° for this tosylate.

**Evidence for the presence of carbonium ion intermediates in these systems is presented on p. 43.

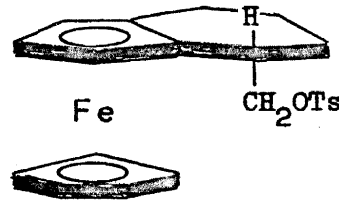
TABLE I. Solvolytic Oxidation of β-Ferrocenylalkyl p-Toluenesulfonates

Compounds which Solvolyze without Oxidation	(100) Exp. Infinity Titer[a] / Theoretical Infinity Titer	Acetate % Yield
1-Ferrocenyl-2-propyl p-Toluenesulfonate	94.3 ± 0.6	90
α-exo-Tosyloxymethyl-1, 2-tetramethylene-ferrocene (XX)	92.8 ± 0.3	70[c]
2-Ferrocenyl-1-propyl p-Toluenesulfonate		85
Compounds which Solvolyze with Oxidation		
2-Ferrocenylethyl p-Toluenesulfonate	93.8 ± 0.6	94[b]
α-endo-Tosyloxymethyl-1, 2-tetra-methyleneferrocene (XXI)	96.8 ± 0.6	80[c]

[a]Temperature invariant. [b]Corrected for chromatographic column less. [c]Products isolated from titrated solvolysis mixtures.



XX



XXI

This oxidation does not contribute significantly to the discrepancy between the theoretical and experimental values of the infinity titers since this discrepancy is larger for compounds which are not oxidized than for those which are (Table I). Although electron transfer from the iron atom of ferrocene to electron-deficient carbon has been previously observed (50, 51, 52), the detailed mechanism of this process has not been carefully studied. In addition, the small extent of oxidation in these systems precluded the isolation of the products from this electron transfer. For these reasons, no reliable mechanistic conclusions can be made on the basis of the data in Table I.

The major side reaction which does not produce p-toluenesulfonic acid probably leads to the unidentified, white solid observed in the large scale acetolysis of 2-ferrocenylethyl p-toluenesulfonate. This conclusion is supported inasmuch as there is close agreement between the yields of product acetate and p-toluenesulfonic acid in the two acetolyses (2-ferrocenylethyl and 1-ferrocenyl-2-propyl p-toluenesulfonate) where quantitative product determinations were carried out independently of the rate measurements. The lower yields of acetate for α-exo and α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene, presented in Table I, are a result of the manner in which these products were obtained. Since the supply of these tosylates was limited, their solvolysis products were isolated directly from the titrated acetic acid solutions which had been employed for the rate determinations. Yields of product acetate for these two tosylates were not comparable to those of p-toluenesulfonic acid because of the difficulty in efficiently extracting the large volumes of

aqueous potassium carbonate solution which were used to neutralize the acidic solvent. In any event, the yields of product in all cases compare favorably with those of 75% obtained from the hydrolysis (80% acetone) of ferrocenylcarbinyl acetates where no side reactions occur (1).

Rate Law Derivation

For the acetolyses of these β-ferrocenylalkyl p-toluenesulfonates, the observed rate law is

$$\ln \frac{[H^+]_f}{[H^+]_f - [H^+]} = kt \qquad 1$$

where $[H^+]_f$ is the experimentally determined infinity titer (see Experimental Section, p. 114). The following consecutive reactions are consistent with this rate law:

$$\begin{aligned}
ROTs &\xrightarrow{k_1} R^+ + OTs^- \\
R^+ + HOAc &\xrightarrow{k_2} ROAc + H^+ \\
ROTs + HOAc &\xrightarrow{k_3} P \qquad 2 \\
R^+ &\xrightarrow{k_4} P \qquad 3 \\
R^+ + HOAc &\xrightarrow{k_5} P \qquad 4
\end{aligned}$$

where P is the unidentified product. A notable exclusion in this series of reactions is the formation of P according to

$$ROTs \longrightarrow P$$

This reaction was not included because it does not involve the reaction of the tosylate with acetic acid, but rather a spontaneous decomposition of the sulfonic ester. Since there is good agreement between the theoretical and experimental infinity titers in 80% acetone (49), it appears that acetic acid is necessary for this decomposition. Reaction with acetic acid may not be necessary for conversion of the carbonium ion to side product however, since the decomposition could be favored in this solvent because the carbonium ion lives longer in acetic acid than in the more nucleophilic 80% acetone (24). For this reason, the conversion of carbonium ion to side product P in a reaction not involving acetic acid (reaction 3) has been included.

The rate expressions and the relationships of the ionization rate constant (k_1) to the measured rate constant (k) can be deduced from the derivation of the rate equations for the production of p-toluenesulfonic acid, H^+, with formation of P according to each of the above reactions, which are considered as separate cases. Only those processes which produce side product P and, at the same time, cause the yield of p-toluenesulfonic acid to be less than the theoretical value have been considered.

Case I: Exclusive formation of P according to reaction 2. The rate of production of acid is

$$\frac{d[H^+]}{dt} = k_2[R^+]\,[HOAc]$$

The steady state approximation with respect to $[R^+]$ gives

$$k_1[ROTs] = k_2[R^+][HOAc]$$

Then $$\frac{d[H^+]}{dt} = k_1[ROTs] \qquad 5$$

The rate of production of P is

$$d[P] = k_3[ROTs][HOAc]$$

$$\frac{d[P]}{d[H^+]} = \frac{k_3[HOAc]}{k_1} = \frac{[P]}{[H^+]}$$

Since [HOAc] does not change, a constant c can be defined as

$$c = \frac{[P]}{[H^+]} = \frac{k_3[HOAc]}{k_1} = \frac{[P]_f}{[H^+]_f} \qquad 6$$

where the subscript f denotes the value of the quantity after ten solvolytic half-lives; the subscript o denotes an initial value at time t = 0.

From stoichiometric considerations it is clear that

$$[ROTs]_o = [ROTs] + [H^+] + [P] \qquad 7$$

At time t_f $$[ROTs]_o = [H^+]_f + [P]_f$$

or $$[P]_f = [ROTs]_o - [H^+]_f$$

Substituting this value of $[P]_f$ into 6

$$\frac{[P]}{[H^+]} = \frac{[ROTs]_o - [H^+]_f}{[H^+]_f} = c$$

so that $$[P] = [H^+]c$$

and $$[ROTs]_o = [H^+]_f(c + 1)$$

Equation 7 then becomes

$$[H^+]_f (c + 1) = [ROTs] + [H^+] + [H^+]c$$

or $$[ROTs] = \{[H^+]_f - [H^+]\} (c + 1)$$

The differential rate equation 5 can then be written as

$$\frac{d[H^+]}{dt} = (c + 1)k_1 \{[H^+]_f - [H^+]\}$$

$$= k \{[H^+]_f - [H^+]\}$$

where $$k = (c + 1)k_1 = k_3[HOAc] + k_1 \qquad 8$$

The integrated rate expression which results is

$$\ln \frac{[H^+]_f}{[H^+]_f - [H^+]} = kt \qquad 1$$

which is the observed rate law.

Case II: Exclusive formation of P according to equation 3. The rate of production of acid is

$$\frac{d[H^+]}{dt} = k_2[R^+] [HOAc]$$

The steady state approximation for $[R^+]$ gives

$$k_1[ROTs] = k_2[R^+][HOAc] + k_4[R^+]$$

and the steady state concentration of $[R^+]$ is

$$[R^+] = \frac{k_1[ROTs]}{k_2[HOAc] + k_4}$$

Substituting this value of $[R^+]$ into the expression for the rate of acid production one obtains

$$\frac{d[H^+]}{dt} = \frac{k_1k_2[ROTs][HOAc]}{k_2[HOAc] + k_4} \qquad 9$$

The rate of production of P is

$$\frac{d[P]}{dt} = k_4[R^+]$$

Therefore a constant c can be defined for this case as

$$c = \frac{d[P]}{d[H^+]} = \frac{k_4}{k_2[HOAc]} = \frac{[P]}{[H^+]} = \frac{[P]_f}{[H^+]_f}$$

The expression for $[P]_f$ as in the previous case is

$$[P]_f = [ROTs]_o - [H^+]_f$$

Therefore the expression for c in terms of the measured quantities $[H^+]_f$ and $[ROTs]_o$ rather than $[P]_f$ is

$$c = \frac{[ROTs]_o - [H^+]_f}{[H^+]_f}$$

so that $$[ROTs]_o = [H^+]_f(c + 1)$$

Using these values of [P] and $[ROTs]_o$ in equation 7 which also applies in this case

$$[ROTs] = [H^+]_f(c + 1) - [H^+]c - [H^+]$$

$$= \{[H^+]_f - [H^+]\} \ (c + 1)$$

The rate of production of acid obtained by substituting this value of [ROTs] into equation 9 is

$$\frac{d[H^+]}{dt} = \frac{k_1k_2(c + 1)[HOAc]\{[H^+]_f - [H^+]\}}{k_2[HOAc] + k_4}$$

and since c and [HOAc] are constants one obtains the observed rate dependence

$$\frac{d[H^+]}{dt} = k\{[H^+]_f - [H^+]\}$$

where $$k = \frac{(c + 1)k_1k_2[HOAc]}{k_2[HOAc] + k_4}$$

$$= \frac{(c + 1)k_1}{1 + \frac{k_4}{k_2[HOAc]}}$$

The definition of c in terms of rate constants is

$$c = \frac{k_4}{k_2[HOAc]}$$

so for this mechanism the relationship between the measured rate constant k and the ionization rate constant k_1 is

$$k = \frac{(c+1)k_1}{1+c} = k_1 \qquad 10$$

Case III: Exclusive formation of P according to reaction 4. The rate of production of acid is

$$\frac{d[H^+]}{dt} = k_2[R^+]\,[HOAc]$$

The steady state approximation for $[R^+]$ gives

$$k_1[ROTs] = (k_2 + k_5)[R^+]\,[HOAc]$$

so that

$$[R^+] = \frac{k_1[ROTs]}{[HOAc](k_2+k_5)}$$

Using this value of $[R^+]$ in the expression for the rate of acid production one obtains

$$\frac{d[H^+]}{dt} = \frac{k_2k_1[ROTs]}{k_2 + k_5} \qquad 11$$

The rate production of P is

$$\frac{d[P]}{dt} = k_5[R^+]\,[HOAc]$$

so that a constant c can be defined for this case as

$$\frac{d[P]}{d[H^+]} = \frac{k_5}{k_2} = \frac{[P]}{[H^+]} = \frac{[P]_f}{[H^+]_f}$$

and $$[P] = [H^+]c$$

The expression for $[P]_f$ is as before

$$[P]_f = [ROTs]_o - [H^+]_f$$

The expression for c in terms of $[H^+]_f$ and $[ROTs]_o$ is then

$$c = \frac{[ROTs]_o - [H^+]_f}{[H^+]_f}$$

or $$[ROTs]_o = [H^+]_f(c + 1)$$

To obtain [ROTs] in terms of $[H^+]_f$, the above values of [P] and $[ROTs]_o$ are substituted into 7 to obtain

$$[ROTs] = \{[H^+]_f - [H^+]\} \ (c + 1)$$

The rate of production of acid, equation 11, can then be written to give the observed rate law

$$\frac{d[H^+]}{dt} = \frac{k_2k_1(c + 1)\{[H^+]_f - [H^+]\}}{k_2 + k_5}$$

$$= k[H^+]_f - [H^+]$$

where $$k = \frac{k_2k_1(c + 1)}{k_2 + k_5} = \frac{k_1(c + 1)}{1 + \frac{k_5}{k_2}}$$

The relationship between the measured rate constant k and the ionization rate constant k_1 is obtained by substituting the expression for

c in terms of rate constants in the above equation

$$c = \frac{k_5}{k_2}$$

so that $$k_{\cdot} = \frac{k_1(c+1)}{1+c} = k_1$$

for this mechanistic sequence.

Kinetic Implications

Since there are at least three mechanisms which are consistent with the observed kinetics, the ionization rate constant (k_1) cannot be unambiguously related to the experimentally determined constant (k) unless it is known whether the side product P arises via a carbonium ion reaction or by means of another side reaction of these β-ferrocenylalkyl tosylates in acetic acid.

Because it is difficult to imagine any reaction occurring at the carbon–oxygen bond of the tosylate which does not lead to solvolysis or carbonium ion formation, reaction 2 implies that polymer is formed by a reaction occurring elsewhere in the molecule, perhaps at the iron–ring carbon bond. A reaction of this kind would not be dependent on the presence of the tosylate functional group, but would be a general reaction of ferrocene compounds in degassed acetic acid. The fact that ferrocene itself is unaffected by acid in the absence of oxidizing agents (45) indicates that this reaction probably does not occur.

Further evidence against reaction 2 can be obtained from comparison of the rate of p-toluenesulfonic acid production (Table II) with

TABLE II. Acetolysis Data for β-Ferrocenylalkyl Tosylates

Compound	Temp.	$k \times 10^5$ (sec^{-1})	$H^{\ddagger}$ (kcal/mole)	$S^{\ddagger}$ (e.u.)
$FcCH_2CH_2OTs$	75.00	89.9[a]		
	59.93	17.2 ± 1.2		
	49.91	5.31 ± 0.20	22.4 ± 1.0	-8.88 ± 2.93
	39.90	1.83 ± 0.08		
	30.00	0.516[a]		
	25.00	0.268[a]		
$FcCH_2CH(OTs)CH_3$	59.93	28.1 ± 1.5		
	49.91	9.38 ± 0.60		
	39.90	2.88 ± 0.08	23.1 ± 0.09	-5.58 ± 0.23
	30.00	0.852[a]		
	25.00	0.431[a]		
exo tosylate XV	100.00	39.1 ± 0.5		
	89.75	13.5 ± 0.4	27.4	+1.37
	25.00	0.0100[a]		
endo tosylate XVI	25.07	27.8 ± 4.5		

[a]Rate constant extrapolated from other temperatures.

the yield of side product (ratio of infinity titers as shown in Table I) for the isomeric tosylates XX and XXI. According to reaction 2, the amount of polymer relative to p-toluenesulfonic acid produced in these reactions is determined by partitioning of tosylate between two reaction paths: one which produces carbonium ions and another which produces side product P. If the reaction which produces P is independent of the structure of the molecule at the carbon-oxygen bond of the tosylate, the rate of this reaction will be the same for the isomeric tosylates XV and XVI. The rates of acid production of these tosylates, however, differ by several orders of magnitude (Table II). If this competition did occur, it would be expected that the slower isomer XX would give much larger amounts of P than does the faster tosylate XXI. Examination of the data in Table I shows that these tosylates give nearly identical amounts of side product. This result is, therefore, evidence against formation of P occurring via some side reaction of the tosylate that does not involve a carbonium ion.

On the basis of the above conclusions, the observed rate constants k will be identified with the rate of ionization of these tosylates. In this connection, it is important to determine the relative maximum uncertainty in the rate constant resulting from the uncertainty in the mechanism of production of P. Since the rate of ionization is either equal to the observed rate k for reactions 3 and 4, or $k/(c + 1)$ in the case of reaction 2, the uncertainty arising from these values is

$$k - k/(c + 1) = ck/(c + 1)$$

and the maximum percent error is

$$\frac{100\,ck/(c+1)}{k/(c+1)} = 100c$$

For α-exo-tosyloxmethyl-1, 2-tetramethyleneferrocene (XVI) where the discrepancy between the theoretical and calculated infinity titers is largest, this error amounts to only 7.8%, which is smaller than the standard deviation often observed in other solvolytic systems (53). It is not large enough, in any case, to affect the mechanistic conclusions based on the values of these rate constants.

CHAPTER IV

Participation in the Solvolyses of β-Ferrocenylalkyl Tosylates

Kinetic Evidence of Carbonium Ions

The rate of solvolysis as a function of solvent can be summarized in terms of the ionizing power and the nucleophilicity of the solvent (54). Although semiquantitative mathematical relationships have been developed, a qualitative discussion of these solvent properties and their effects on solvolysis rates is sufficient here. The nucleophilicity of a solvent has been defined as its "ability to act as a displacing base on carbon" (55). Substitution reactions which proceed by attack of solvent at carbon and nearly synchronous displacement of the leaving group (S_N2 or nucleophilic reactions) occur faster in more nucleophilic solvents. For example, ethyl p-toluenesulfonate solvolyzes 60 times faster in dry ethanol than in the poorly nucleophilic solvent acetic acid (54).

Other solvolysis reactions clearly involve formation of a carbonium ion intermediate prior to the product-forming step. When the transition state leading to the formation of the carbonium ion does not involve covalent interaction between a solvent molecule and the electron-deficient carbon atom of the transition state, the solvolysis is defined as a limiting or S_N1 process (55). In limiting solvolyses, the rate depends on the ionizing power and not on the nucleophilicity of the solvent. One of the most dependable and often-used criteria, then for a limiting solvolysis is the relative constancy of the solvolysis

rate in solvents of comparable ionizing power but of different nucleophilicity (56).

While the ionizing powers of 80% acetone and acetic acid are not identical, the increase in rate due to the increased ionizing power of the aqueous solvent is small as shown by the solvolysis data in Table III for t-butyl bromide, whose solvolysis is thought to be limiting and, therefore, not dependent on the nucleophilicity differences of these two solvent systems. More pronounced is the effect of the increased nucleophilicity of 80% acetone (24) on the rate of an S_N2 solvolysis; thus ethyl tosylate, which solvolyzes by a nucleophilic mechanism (58), reacts with aqueous acetone 164 times faster than with acetic acid. For β-ferrocenylalkyl systems, the implication of the small rate increases in 80% acetone is quite clear; the solvolyses of these β-ferrocenylalkyl tosylates are nearly limiting. This conclusion is in complete accord with Carter's mechanistic deductions from his study of the α deuterium isotope effect for these tosylates (see p. 7), and it is also consistent with the stereochemical results discussed below. Because primary and secondary tosylates do not generally form stable carbonium ions (58), the stability of these primary and secondary ferrocenyl carbonium ions requires some internal source of electron supply (participation) to account for the limiting nature of these solvolyses.

α-Methyl Substituent Effect

Another indication of limiting solvolyses is the magnitude of the rate enhancement caused by the substitution of a methyl group for

TABLE III. Effect of Solvent on Solvolysis Rates

Compound	Rate in 80% Acetone Relative to Acetic Acid
CH_3CH_2OTs	164[a, b]/1
$(CH_3)_3CBr$	9.1[b]/1
$FcCH_2CH_2OTs$	2.1[c]/1
$FcCH_2CH(OTs)CH_3$	1.8[c]/1

[a]Based on rate constants which were calculated from the Winstein-Grunwald equation (46). [b]Data obtained from reference 57. [c]Data obtained from reference 49.

hydrogen at the electron-deficient carbon atom. Because of the well-known ability of a methyl group to stabilize positive charge on an adjacent carbon atom through hyperconjugative and inductive electron release, it is apparent that α-methyl substitution can result in large rate enhancements for solvolyses in which the developing positive charge is borne largely by the electron-deficient carbonium ion, i.e. in limiting solvolyses. The theory and the diagnostic application of this effect have been considered in detail for various systems (18, 19, 30), and it has been pointed out that the maximum rate enhancement attributable to the α-methyl effect, expected for a limiting solvolysis, is given by the ratio of the rate of formolysis of t-butyl bromide to the formolysis rate of isopropyl bromide or 10^6 (58). Other systems which are thought to solvolyze by limiting mechanisms give α-methyl effects of approximately 10^4 while primary systems,

which solvolyze by a nucleophilic or S_N2 process, give much lower values. These data are shown in Table IV together with the α-methyl substituent effects observed in ferrocenyl and phenyl systems.

Low α-methyl effects are not only indicative of nucleophilic processes, but also occur in cases where there is participation (19), probably because the α-methyl substituent is not the principal source of carbonium ion stability in these anchimerically assisted systems. For example, the α-methyl effect for the esters listed in Table IV, in which there is participation, ranges from 76 for the β-phenylalkyl systems to 10 for the ferrocenylcarbinyl systems. As Carter pointed out, the low value of the α-methyl substituent effect for these β-ferrocenylalkyl tosylates coupled with the secondary deuterium isotope effect of 1.14, indicative of a limiting solvolysis, is evidence of participation in the hydrolysis of 2-ferrocenylalkyl tosylates (60).

Although the interpretation of small α-methyl substituent effects are not always valid because of the dependence of the effect on solvent and temperature (19), the data for the ferrocenyl and phenyl systems in Table IV warrant additional comment. From a consideration of the relative rates of solvolysis of the phenyl and ferrocenyl systems (Table VI, p. 51) and since the ferrocenylcarbinyl cation is almost as stable as triphenylmethyl cation (1), the primary carbonium ions can be arranged in order of decreasing stability as:

$$FcCH_2^+ > FcCH_2CH_2^+ > ArCH_2CH_2^+$$

Since the stability of these primary systems is due in large measure

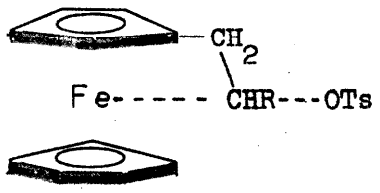
TABLE IV. Rate Factors Due to α-Methyl Substitution

Compound Pair	Solvent	Rate Ratio
$\frac{(CH_3)_3CBr}{(CH_3)_2CHBr}$	HCO_2H	10^6 [a]
$\frac{(CH_3)_2CHCH(OTs)CH_3}{(CH_3)_2CHCH_2OTs}$	HCO_2H	5.2×10^3 [b]
$\frac{C_6H_5CH_2CH(OTs)CH_3}{C_6H_5CH_2CH_2OTs}$	HCO_2H	76 [c]
$\frac{p\text{-}CH_3OC_6H_4CH_2CH(OTs)CH_3}{p\text{-}CH_3OC_6H_4CH_2CH_2OTs}$	HCO_2H	69 [c]
$\frac{CH_3CH_2OTs}{CH_3OTs}$	HCO_2H	1.8 [b]
$\frac{FcCH(OAc)CH_3}{FcCH_2OAc}$	80% $(CH_3)_2CO$	10 [d]
$\frac{FcCH_2CH(OTs)CH_3}{FcCH_2CH_2OTs}$	HOAc, 80% $(CH_3)_2CO$	1.6 and 1.4 [e] resp.

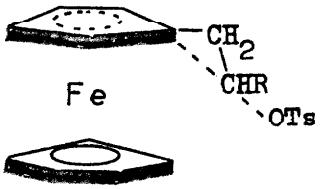
[a]Reference 59. [b]Reference 19. [c]References 17 and 31. [d]Reference 3. [e]Reference 49.

to participation, the effectiveness of an α-methyl substituent in stabilizing these ions would be expected to be most pronounced for the 2-arylethyl system, least important in the ferrocenylcarbinyl system, and of intermediate significance in the 2-ferrocenylethyl system. While the data in Table IV show that the effect in the 2-phenylethyl system is largest as expected, the α-methyl effect of 1.4 for the 2-ferrocenylethyl system is not intermediate between the 2-phenylethyl and ferrocenylcarbinyl systems, but smaller than either one. It is too

small to be rationalized only in terms of simple neighboring group participation. This small α-methyl effect is readily interpreted in terms of either an iron-stabilized transition state as represented by XXII, or an endo ring-bridged transition state XXIII.



XXII



XXIII

The net result of the methyl substituent on the stability of these transition states is a consequence of two mutually compensating effects. One effect is the previously mentioned rate-increasing ability of the methyl group due to inductive and hyperconjugative electron release. The second effect is a rate-retarding steric effect; it arises because the geometry of the transition states derived from a secondary tosylate requires a more precise alignment of the carbon chain than that required for the less bulky primary system in order to prevent steric repulsions between the hydrogens of the bottom ring and those of the methyl group. If the rate-retarding steric effect and the rate-increasing electronic effect are of nearly equal importance to the overall rate, the net effect will be the absence of significant rate enhancement resulting from α-methyl substitution.

Relative Acetolysis Rates of β-Ferrocenylalkyl Tosylates

Further evidence concerning the nature of the electron-deficient transition state for the solvolysis of β-ferrocenylalkyl tosylates can be obtained from rate comparisons among the series of compounds listed in Table V. The most striking rate enhancement is

TABLE V. Relative Rates of Acetolysis of β-Ferrocenylalkyl Tosylates

Compound	Relative Rate at 25°
exo-Tosylate XX	1[a]
$FcCH_2CH_2OTs$	27[a]
$FcCH_2CH(OTs)CH_3$	43.2[a]
endo-Tosylate XXI	2700

[a]Based on extrapolated rate constants.

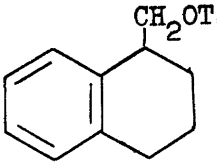
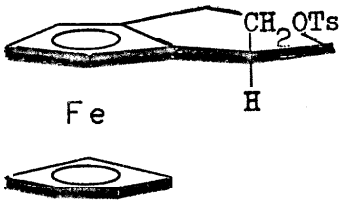
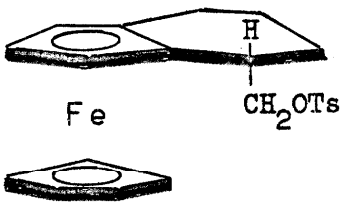
evident in the case of the endo and exo isomers of α-tosyloxymethyl-1, 2-tetramethyleneferrocene; the rate factor of 2700 again demonstrates the preference for carbonium ion formation from the endo position where interaction between the interannular electrons and the developing carbonium ion can readily occur. The assignment of the factor of 2700 entirely to iron participation, however, is not necessarily valid because the hydrogens of the unsubstituted ring can cause steric congestion of the endo methylene group which is not encountered in the exo isomer. As a result, the ground states of these two isomers

are not energetically equivalent and the factor of 2700, in part, may reflect a somewhat higher ground state energy of the endo compound. That steric factors are not entirely responsible for this rate enhancement is shown by the fact that 2-ferrocenylethyl p-toluenesulfonate, which can adopt either an endo or exo conformation, solvolyzes 27 times faster than α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene (XX) in which direct interannular electron participation is not possible. These relative rates demonstrate that formation of an exo ring-bridged transition state is the least favorable route for these solvolysis reactions. In contrast to the paracyclophane system (35), the steric repulsions, in these ferrocene systems, between the hydrogens of the bottom ring and the electron-deficient carbon atom are not large enough to compensate for the large availability of electrons in the interannular region. As a result, endo alignment of the alkyl chain leads to the most favorable positioning of the electron-deficient carbon atom in the transition state for the acetolyses of these β-ferrocenylalkyl tosylates.

Comparison of β-Ferrocenylalkyl and β-Phenylalkyl Systems

Comparison of the acetolysis rates of β-ferrocenylalkyl tosylates with those of the phenyl analogs (Table VI) shows that participation of interannular electrons results in greater rate enhancements relative to β phenylalkyl tosylates, even in cases where phenyl participation has been shown to occur during acetolysis. For example, the acetolyses of the β-(p-anisyl)-alkyl and the β-alkyl substituted tosylates listed in Table VI involve predominant phenyl

TABLE VI. Relative Acetolysis Rates of β-Phenyl and β-Ferrocenylalkyl Systems

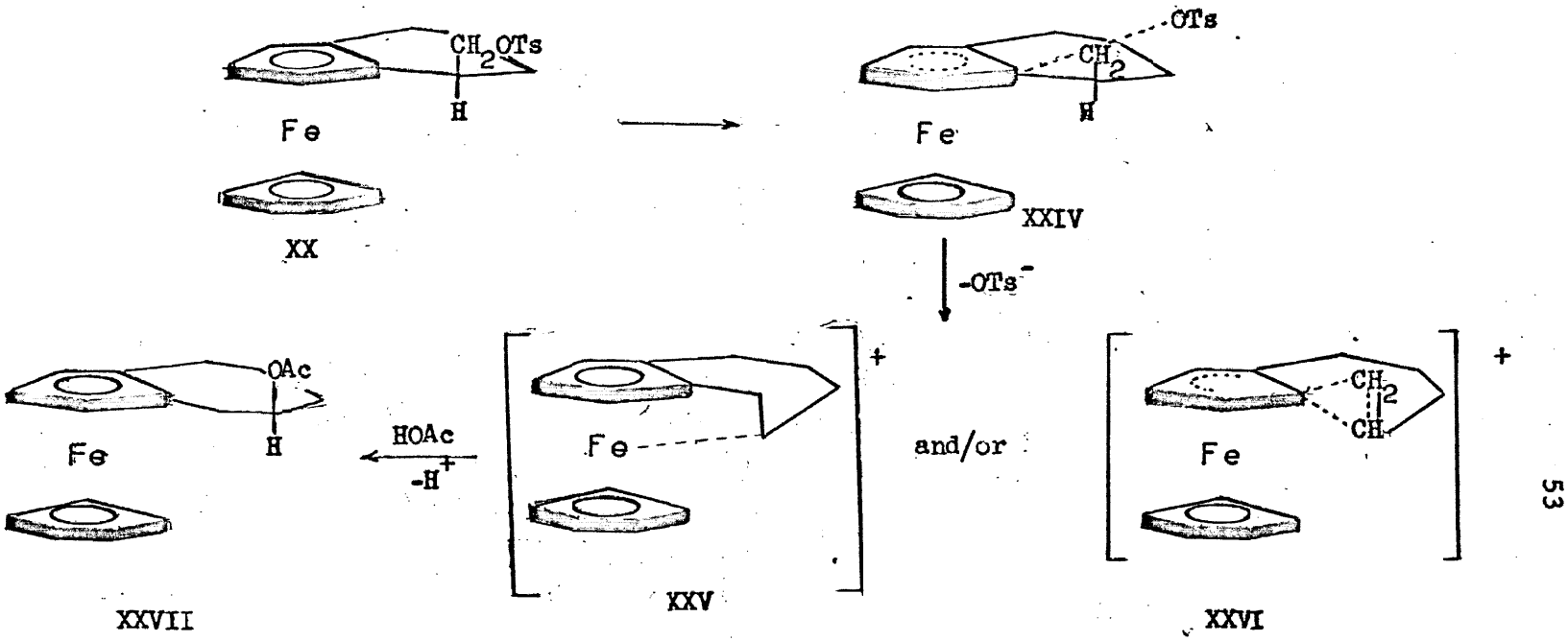
Primary Systems at 75°	Relative Rate
$C_6H_5CH_2CH_2OTs$	1
$p\text{-}CH_3OC_6H_4CH_2CH_2OTs$	23.9
$PCPCH_2CH_2OTs$ (X)	3.09
$FcCH_2CH_2OTs$	3120[a]
Secondary Systems at 50°	
$C_6H_5CH_2CH(OTs)CH_3$	1
$p\text{-}CH_3OC_6H_4CH_2CH(OTs)CH_3$	20.5
$FcCH_2CH(OTs)CH_3$	161
Cycloalkyl Systems at 25°	
 (IX)	1[a]
 (XX)	1.61[a]
 (XXI)	4480

[a]Extrapolated from data at other temperatures.

participation even in acetic acid (23, 27, 28); yet these esters react significantly more slowly than the corresponding ferrocene derivatives in which anchimeric assistance to ionization by the interannular electrons occurs.

Further information regarding the stability of an exo ring-bridged transition state derived from a β-ferrocenylalkyl tosylate can be obtained from the data in Table VI. It was pointed out that the acetolysis of tosylate IX involves participation by the π electrons of the phenyl ring resulting in partial rearrangement to a secondary tosylate, which then reacts further via a phenonium ion. As a result of phenyl participation, this tosylate solvolyzes ca. 200 times faster than cyclohexylcarbinyl tosylate and gives only rearranged product (33). The fact that α-exo-tosyloxymethyl-1, 2-tetramethyleneferrocene (XX), in which direct overlap between the developing p orbital of the electron-deficient exo carbon atom and the interannular ferrocene orbitals is not possible, solvolyzes with rearrangement (see p. 58) at nearly the same rate as its phenyl analog indicates that the acetolysis of this tosylate involves rate determining participation only by the external π cloud of the ferrocene ring (Chart II). In this connection, it is important to note that the similarity between the ferrocenyl and phenyl systems does not extend to their solvolytic rate dependencies. The first-order acetolysis rate of tosylate (XX) does not exhibit the

Chart II


CH2OTs
H
Fe
XX
OTs
CH2
H
Fe
XXIV
-OTs⁻
OAc
H
Fe
HOAc
-H⁺
Fe
+
XXV
and/or
CH2
CH
Fe
+
XXVII
XXVI

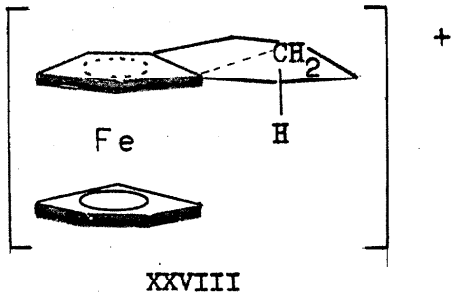
induction period* that is characteristic of the primary phenyl systems which rearrange to secondary sulfonates during solvolysis (see p. 14). Of course, no induction period will occur if rearranged tosylate is not formed, and it has been pointed out that an induction period will also not be observed if the solvolysis rate constant of the secondary system is approximately two or more orders of magnitude larger than that of the primary tosylate (33). The absence of an induction period in the acetolysis of tosylate XX is in complete accord with a solvolysis mechanism which involves rearrangement of the first-formed transition state (XXIV) to a more stable iron-stabilized (XXV) or π-stabilized carbonium ion (XXVI).

The absence of an exo ring-bridged ion (XXVIII) as a discrete intermediate in this mechanism is indicated by the relative rate data presented above. These data show that an exo ring-bridged transition state is of higher energy than a transition state in which participation of interannular electrons can occur. Since ring-bridging is a readily available pathway for conversion of an exo ring-bridged transition state into an interannular stabilized ion (XXV or XXVI), a ring-bridged intermediate such as XXVIII is precluded because such a structure would not involve the extremely favorable overlap between the

---

*In order to establish the existence of an induction period, it is useful to determine many kinetic points before 30% of the reaction has been completed (27). Unfortunately, this was not done in the present study so that the absence of an induction period is based on the absence of a trend for only three kinetic points in the one-fourth life time interval.

interannular electrons and the vacant p orbital of the electron deficient carbon atom.



XXVIII

Finally, it should be recognized that the kinetic results presented in this chapter can only give information regarding the relative stabilities of the transition states involved in these solvolysis reactions. These data establish that it is much more favorable for carbonium ion formation to occur in such a way that overlap between the interannular electrons of the ferrocene moiety and the developing p orbital of the electron-deficient carbon atom can readily take place. The rate data do not show whether this interannular electron delocalization is due to iron stabilization (participation by the non-bonding electrons in the h_{ag} molecular orbital) or due to π-electron stabilization (participation by the interannular iron-carbon bonding electrons). This interaction is discussed further in the following chapter.

CHAPTER V

Solvolysis Products

It has been recognized for some time that nucleophilic attack on aryl-bridged solvolytic intermediates can often result in skeletal rearrangement during solvolysis (p. 10); although such rearrangement, by itself, is not conclusive evidence of the formation of these bridged intermediates (26). Previously discussed kinetic results have shown that solvolyses of these β-ferrocenylalkyl tosylates are nearly limiting with participation by interannular electrons occurring when possible. In view of these kinetic results, it is possible to gain insight into the importance of ring-bridged carbonium ions and iron-stabilized carbonium ions from the nature of the solvolytic products resulting from solvolysis of these β-ferrocenylalkyl tosylates.

All of the solvolysis products described below have been conclusively identified by n.m.r. and infrared spectra comparisons with authentic samples, with the exception of the acetate derived from the acetolysis of α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene. Solvolysis mixtures were analyzed and purified by column chromatography on alumina and in most cases results were checked by thin layer chromatography on silica gel. These results are, therefore, limited by the shortcomings of chromatographic separation and are not quantitative; however, comparison of the yields of product with the yields of p-toluenesulfonic acid produced in these solvolyses (Table I, p. 29) show that no large amounts of undetected products were formed.

Solvolyses with Rearrangement

Skeletal rearrangement during acetolysis of these β-ferrocenylalkyl tosylates was observed only in cases where a β-alkyl substituent provides additional driving force for aryl migration; although β-alkyl substitution was not effective in promoting rearrangement during the acetolysis of α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene (XXI). This latter result is discussed below (p. 67). Notably, no rearranged products indicative of hydrogen or alkyl migration were obtained from the solvolyses of these β-ferrocenylalkyl tosylates. The acetolysis of α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene (XX) and 2-ferrocenyl-1-propyl p-toluenesulfonate, together with evidence regarding the structures of the rearranged product derived from acetolysis of the former tosylate, are discussed separately below.

α-exo-Tosyloxymethyl-1,2-tetramethyleneferrocene

The acetolysis of α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene (XX) was the only solvolysis which lead solely to the formation of rearranged product. Only one acetate was obtained, as evidenced by the sharp melting point (79.0-80.5°) of this product, together with a small amount of unidentified, less polar material.* It is noteworthy that no alcohols were obtained from treatment of the

*This product may have resulted from treatment of the acetolysis mixtures from the rate determinations with aqueous potassium carbonate solution for eight days.

acetolysis mixture with an aqueous acetone solution of potassium carbonate at room temperature for eight days. Apparently this acetate, unlike all of the other acetates obtained from these solvolyses, is not easily hydrolyzed because iron participation cannot readily occur during solvolysis of this ester. This result shows that the acetate group is not attached to the carbon atom adjacent to the metallocene ring since both the exo and endo isomers of α-acetoxy-1, 2-tetramethyleneferrocene would be extensively hydrolyzed under these conditions (1). High intensity mass spectral peaks at m/e 311 ± 2 and 252 (corresponding to the loss of acetic acid from the parent compound) and the elementary analysis (p. 119) show that this acetate is isomeric with α-acetoxymethyl-1, 2-tetramethyleneferrocene. The n.m.r. spectrum of this acetate is shown in Figure 4. All of these data are consistent with stereospecific formation of β-exo-acetoxy-1, 2-pentamethyleneferrocene XXVII; although exclusive formation of either the endo isomer of this ester or of one isomer of γ-acetoxy-1, 2-pentamethyleneferrocene is not eliminated on the basis of this evidence. Formation of these latter two esters seems very unlikely, however, because there is no established mechanistic pathway which could lead to stereospecific production of these esters.

The rate of this rearrangement, which is slightly faster than the acetolysis rate of 1, 2-benzocyclohexyl-3-methyl p-toluenesulfonate (IX), and the stereospecific formation of rearranged product in this ferrocene system together provide strong evidence for the formation of either a ferrocenyl ring-bridged (XXVI) or an iron-

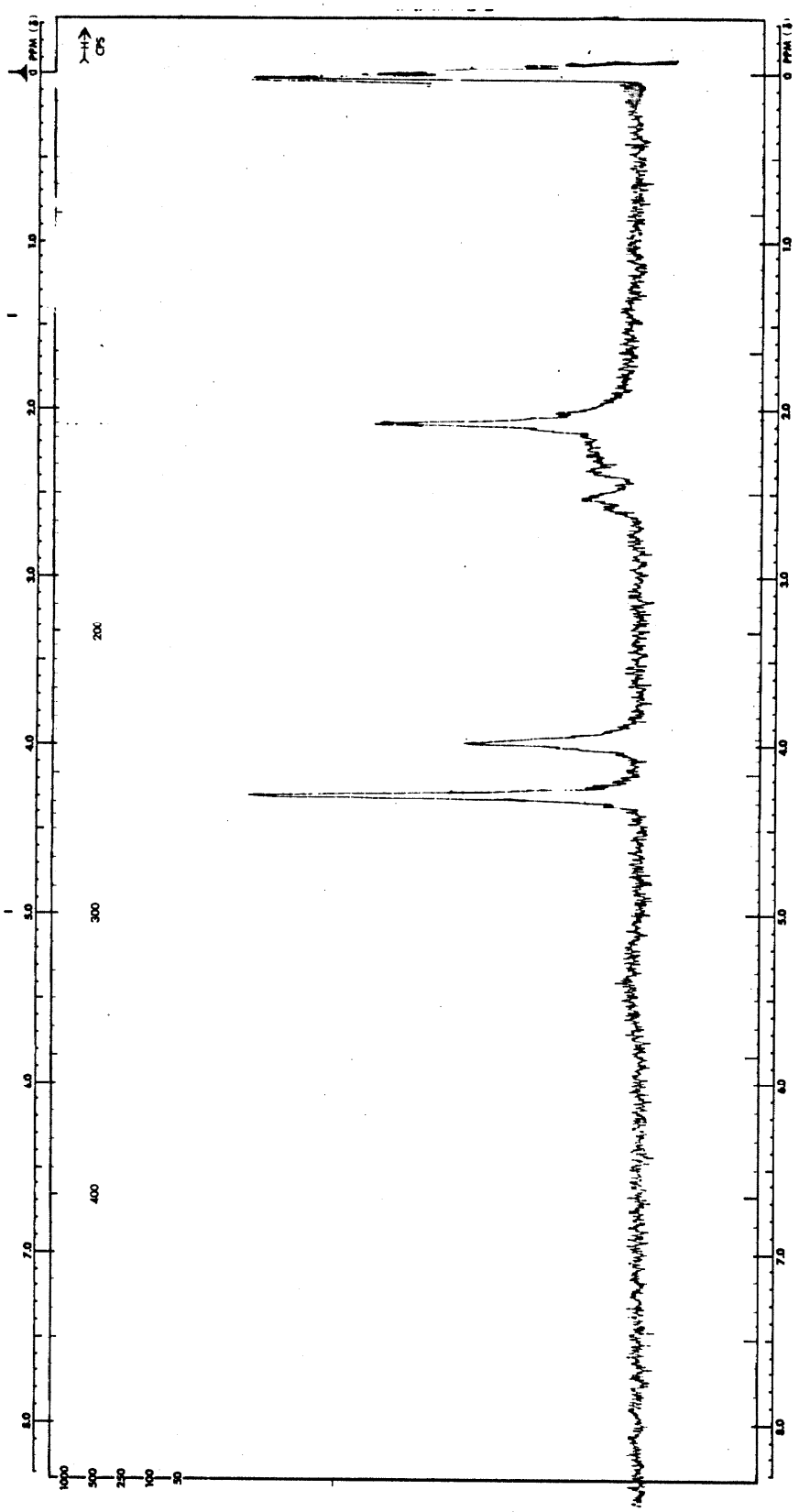


Fig. 4 N.m.r. spectrum of a carbon tetrachloride solution of the acetolysis product of α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene with TMS internal standard.

stabilized intermediate XXV* by migration of the aryl group during this solvolysis (p. 52). It is also possible that stereospecific production of acetate is a result of nucleophilic attack by acetic acid on both of these intermediates, which could occur simultaneously in this system. Since no unrearranged acetate is produced during this acetolysis, it must be concluded that nucleophilic attack on a ring-bridged ion in this system occurs exclusively at the secondary carbon. This result is not unexpected since this position is best able to support positive charge not only because it is a secondary carbon, but also because of better electron delocalization at the endo carbon in the alkyl bridge. Apparently, any steric effects which favor exo attack of solvent are entirely cancelled by these electronic factors, all of which in this case, favor endo attack.

2-Ferrocenyl-1-propyl p-Toluenesulfonate

The acetolysis of 2-ferrocenyl-1-propyl p-toluenesulfonate at 60.0° leads to the formation of a mixture of 2-ferrocenyl-1-propyl acetate (XXIX) and the product of ferrocenyl migration 1-ferrocenyl-2-propyl acetate (XXX). Although these acetates were not separable by either column or thin layer chromatography, their formation is evident from the infrared and n.m.r. spectra of the acetate product (Figures 5 and 6) which is a composite of the corresponding spectra

*Evidence for the existence of iron-stabilized intermediates as separate entities is presented on page 71.

Fig. 5 Part of the infrared spectrum of a carbon tetrachloride solution of the acetolysis products of 2-ferrocenylpropyl p-toluenesulfonate

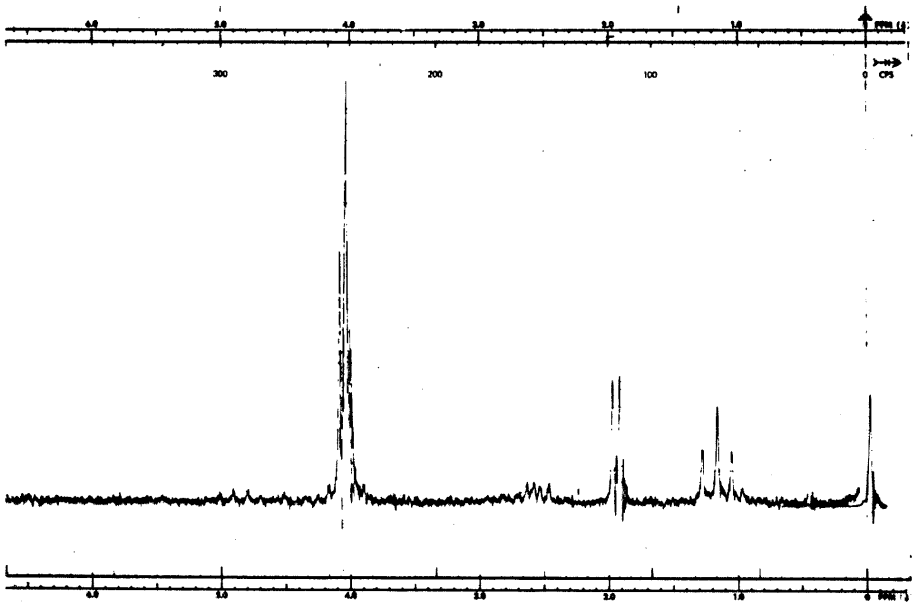


Fig. 6 N.m.r. spectrum of a carbon tetrachloride solution of the acetolysis products of 2-ferrocenylpropyl p-toluenesulfonate with TMS internal standard

of 2-ferrocenyl-1-propyl acetate (Figures 7 and 8) and 1-ferrocenyl-2-propyl acetate (Figures 9 and 10).

The relative intensities of the proton resonances of the methyl groups adjacent to the carbonyl functions in the n.m.r. spectrum of the acetate product derived from this solvolysis (Figure 6) show that acetolysis of 2-ferrocenyl-1-propyl p-toluenesulfonate leads to an equimolar mixture of primary acetate XXIX and secondary acetate XXX after 11 hours (ten solvolytic half lives of 2-ferrocenylethyl p-toluenesulfonate). This result was further substantiated by spectrophotometric determination of the extent of rearrangement from the 1136 cm^{-1} infrared absorption due to 2-ferrocenyl-1-propyl acetate (XXX) in the acetolysis mixture. No residual 2-ferrocenyl-1-propyl p-toluenesulfonate was found after the 11 hour solvolysis period. The overall yield of isomeric acetates was 85%.

In order to show that formation of these products was kinetically controlled, 2-ferrocenyl-1-propyl p-toluenesulfonate was allowed to solvolyze in acetic acid for 22 hours, and the ratio of secondary acetate XXX to primary acetate XXIX was again determined. Since the acetolysis of 1-ferrocenyl-2-propyl p-toluenesulfonate does not lead to the formation of primary acetate XXIX (see p. 73), there is no rearrangement of secondary acetate XXX to primary acetate XXIX. Therefore, conversion of initially formed primary acetate XXIX to 1-ferrocenyl-2-propyl acetate in a thermodynamically controlled process should lead to a threefold excess of the secondary isomer XXX after 22 hours, if the equimolar mixture of these isomers

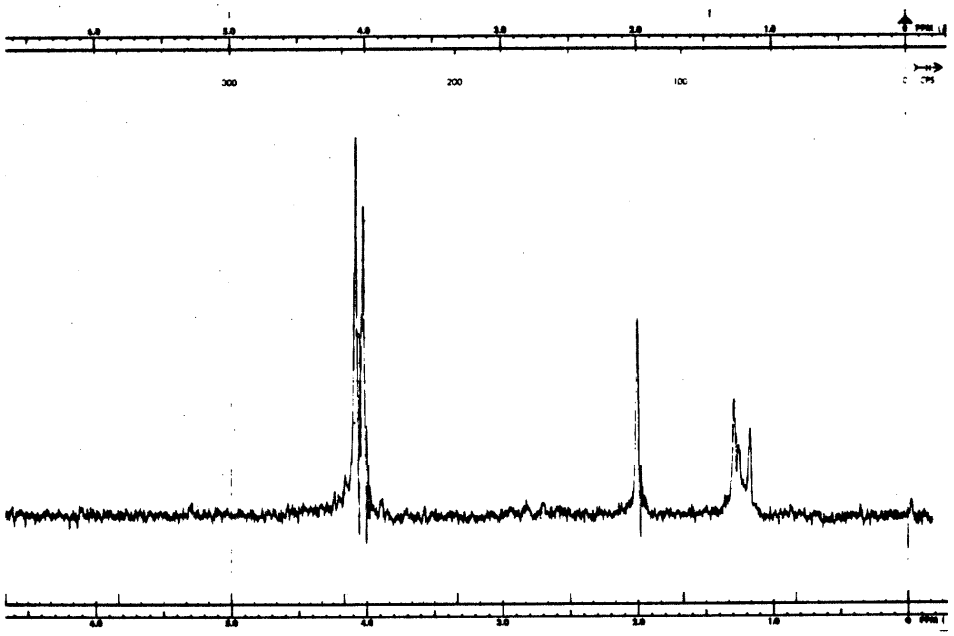


Fig. 7 N.m.r. spectrum of a carbon tetrachloride solution of 2-ferrocenyl-1-propyl acetate

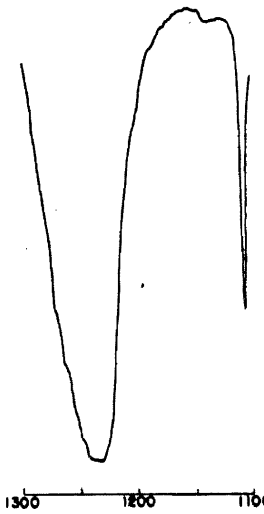


Fig. 8 Part of the infrared spectrum of a carbon tetrachloride solution of 2-ferrocenyl-1-propyl acetate

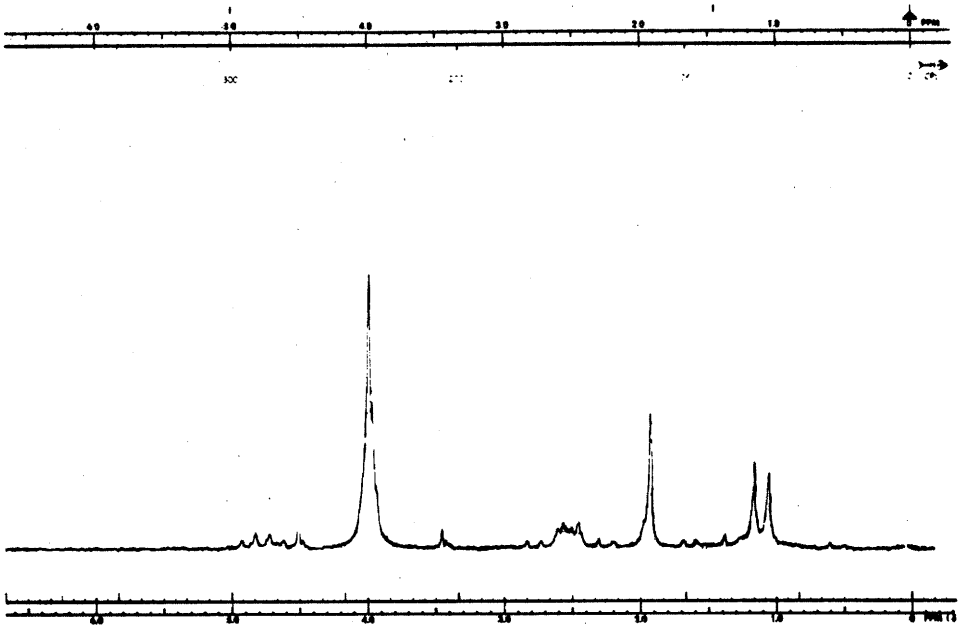
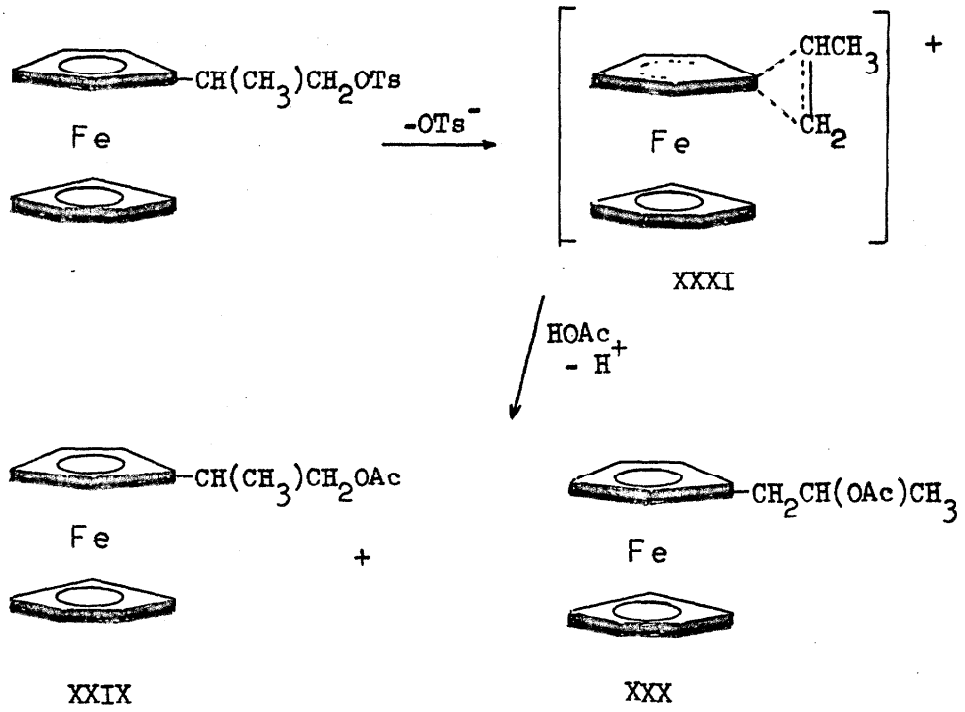


Fig. 9 N.m.r. spectrum of a carbon tetrachloride solution of 1-ferrocenyl-2-propyl acetate

Fig. 10 Part of the infrared spectrum of a carbon tetrachloride solution of 1-ferrocenyl-2-propyl acetate

observed after 11 hours was due to product equilibration. The fact that the secondary acetate XXX comprised only 56% of the reaction mixture after 22 hours shows that the equimolar mixture of primary and secondary acetates is a result of kinetic control.



Although the rate of acetolysis of 2-ferrocenyl-1-propyl p-toluenesulfonate has not been measured, it would be expected that this tosylate would solvolyze faster than 2-ferrocenylethyl p-toluenesulfonate. This conclusion is based on the fact that the effect of a β-alkyl substituent will be a rate-enhancing one regardless of the detailed mechanism of this S_N1 reaction.

Partial migration of the metallocene ring system during this solvolysis indicates that a π electron stabilized intermediate (XXXI) is involved prior to the product forming step. That rearrangement occurs in this system at a rate which is faster than the acetolysis rate of α-exo-tosyloxymethyl-1, 2-tetramethyleneferrocene demonstrates that the formation of a ring-bridged ion from the endo direction where direct overlap with the interannular bonding electrons can occur is more favorable than formation of a ring-bridged ion from the exo direction where overlap between the external π cloud and the developing carbonium ion is the only possibility. This fast rate also shows that previously mentioned steric effects, which would be expected to favor exo formation of a ring-bridged ion (p. 20), are overwhelmed by the greater stabilization due to participation by these interannular bonding electrons.

The equimolar mixture of primary and secondary acetates resulting from nucleophilic attack of acetic acid on the π stabilized intermediate XXXI is also a result of opposing electronic and steric effects. The fact that the secondary carbon in the alkyl bridge is more sterically accessible to solvent than the endo carbon, as indicated by labeling experiments in the paracyclophane system (p. 20), coupled with the stabilization of positive charge at the secondary position by the adjacent methyl group is counterbalanced by the greater electron delocalization at the endo carbon atom. The equimolar mixture of acetates derived from this solvolysis results from these mutually compensating effects. An alternative mechanism which

involves both a π-stabilized ring-bridged ion like XXXI and an iron-stabilized intermediate with rearrangement resulting solely from attack of solvent on the ring-bridged ion while possible is unlikely, since it is not certain that solvent attack on this ring-bridged intermediate (XXXI) would result in exclusive formation of secondary acetate XXX, in view of the previously mentioned interannular electronic factors which facilitate solvent attack at the endo carbon atom.

Solvolyses without Rearrangement

The previous section described experimental results which required the formulation of acetolysis mechanisms that involved intermediate formation of π-stabilized, ferrocenyl, ring-bridged intermediates. The experimental results presented in this section are no less important, since the absence of rearrangement in these solvolyses, particularly in the case of α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene (XXI), demonstrates that solvolysis occurs by intermediates in which iron stabilization is the important feature.

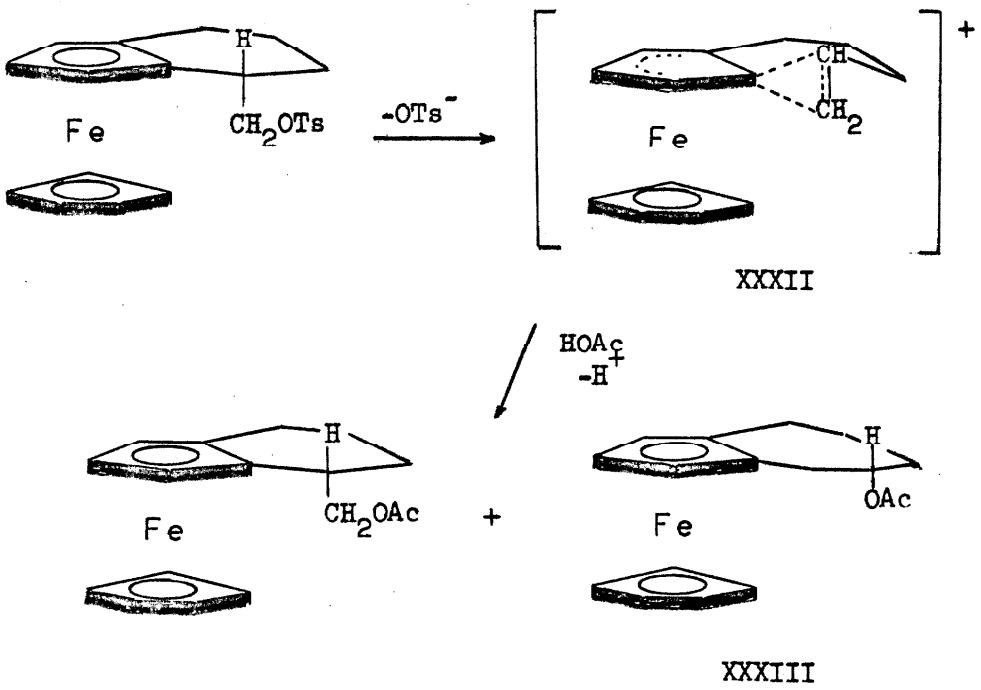
α-endo-Tosyloxymethyl-1,2-tetramethyleneferrocene

The acetolysis of α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene (XXI) proceeds without rearrangement to give only α-endo-acetoxymethyl-1,2-tetramethyleneferrocene. The fast rate of this acetolysis (Table V, p. 49) and the complete absence of products which would result from a ring-bridged ion require anchimerically assisted formation of a stable carbonium ion intermediate which undergoes nucleophilic attack only at the primary endo carbon atom.

This is in complete contrast to the acetolysis of 1-ferrocenyl-2-propyl p-toluenesulfonate in which there is also participation by the interannular electrons that leads to the formation of a carbonium ion which is attacked at both the primary endo carbon and the secondary exo carbon atom. As a result, an equimolar mixture of primary and secondary acetates is produced (see p. 65).

That nucleophilic attack on a ring-bridged intermediate (XXXII) derived from the acetolysis of endo tosylate XXI could lead to significant amounts of rearranged product can be ascertained by considering the electronic and steric factors which influence the product distribution resulting from nucleophilic attack on a ring-bridged ion in this system. Indeed, similar factors have been previously shown to account for varying amounts of rearrangement accompanying the acetolysis of both α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene (XX) and 1-ferrocenyl-2-propyl p-toluenesulfonate.

Solvolysis involving participation by interannular electrons and leading to formation of a ferrocenyl ring-bridged ion XXXII can be formulated as



Rearrangement to β-endo-acetoxymethyl-1, 2-pentamethylene-ferrocene (XXXIII) will be favored by those factors which facilitate nucleophilic attack at the secondary exo carbon atom. Because of the adjacent alkyl group, the exo position is well-suited to sustain positive charge. This same electronic factor leads to the partial rearrangement observed during the acetolysis of 1-ferrocenyl-2-propyl p-toluenesulfonate. Attack of nucleophile at the exo position may also be favored by any steric factors which make the endo carbon atom relatively inaccessible to solvent attack; however, possible steric effects of the fused ring system make it difficult to predict the magnitude or the direction of the net steric effect in this solvolysis.

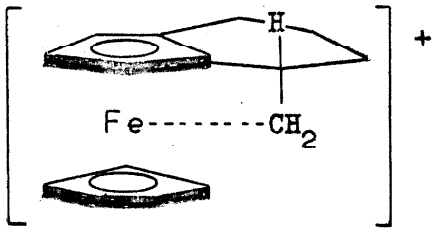
Conceivably, it could be argued that nucleophilic attack at the exo carbon atom in this ion (XXXII) would be deterred, since such

attack would lead to the formation of a strained seven-membered ring* (61). According to the Hammond postulate (62), however, this effect should be very small since the stability of the product is not an important consideration in determining the site of nucleophilic attack on a positively charged carbonium ion.

These results, in conjunction with the previously discussed kinetic data (p. 49), require formulation of a solvolytic pathway which leads to formation of a very stable carbonium ion via participation by the interannular electrons. Iron stabilization involving overlap between the equatorial belt of nonbonding electrons around the iron atom and the developing carbon p orbital leading to the formation of an iron-stabilized carbonium ion XXXIV is completely consistent with the energetic and stereochemical requirements demanded by the experimental observations in this system. Furthermore, the fact that ring-bridging is minimal in this system requires that the effect of the fused six-membered ring, which results in positioning the developing carbonium ion in the central interannular region shown by XXXIV, makes iron participation more favorable than ring-bridging in this system. Or alternatively, that iron bonding with the electron-deficient carbon atom is the energetically preferred solvolytic pathway

---

*Actually, there is no reason to suspect that the observed product, α-endo-acetoxymethyl-1, 2-tetramethyleneferrocene is more stable than XXXIII since nonbonded repulsions between the hydrogens of the unsubstituted ring and the acetoxymethyl group contribute to the instability of this primary endo acetate.



XXXIV

in these systems in the absence of special effects such as β-alkyl substitution which does not involve special disposition of the tosyloxymethyl group. Although it is not possible to choose between these two alternatives on the basis of the evidence presented in this thesis, the extraordinarily fast solvolysis rate of this endo tosylate XXI (p. 40) suggests that iron participation is the lowest energy solvolytic pathway in the absence of special effects which increase the driving force for ring-bridging.

2-Ferrocenylethanol-1, 1-d_2

The alcohol obtained from equilibration of 2-ferrocenylethanol-1, 1-d_2 in 80% acetone d_6-20% deuterium oxide with benzenesulfonic acid shows no scrambling of deuterium label between the α and β carbon atoms after approximately 8 solvolytic half lives.* The n.m.r. spectrum of this product is shown in Figure 11. This experiment supplements the original deuterium scrambling experiment performed

*This calculation is based on a first-order rate constant of 8.67×10^{-7} sec^{-1} for 2-ferrocenylethyl-1, 1-d_2 p-toluenesulfonate (49) and on the approximation that the tosylate solvolyzes 3.8 times faster than the protonated alcohol (46, 63).

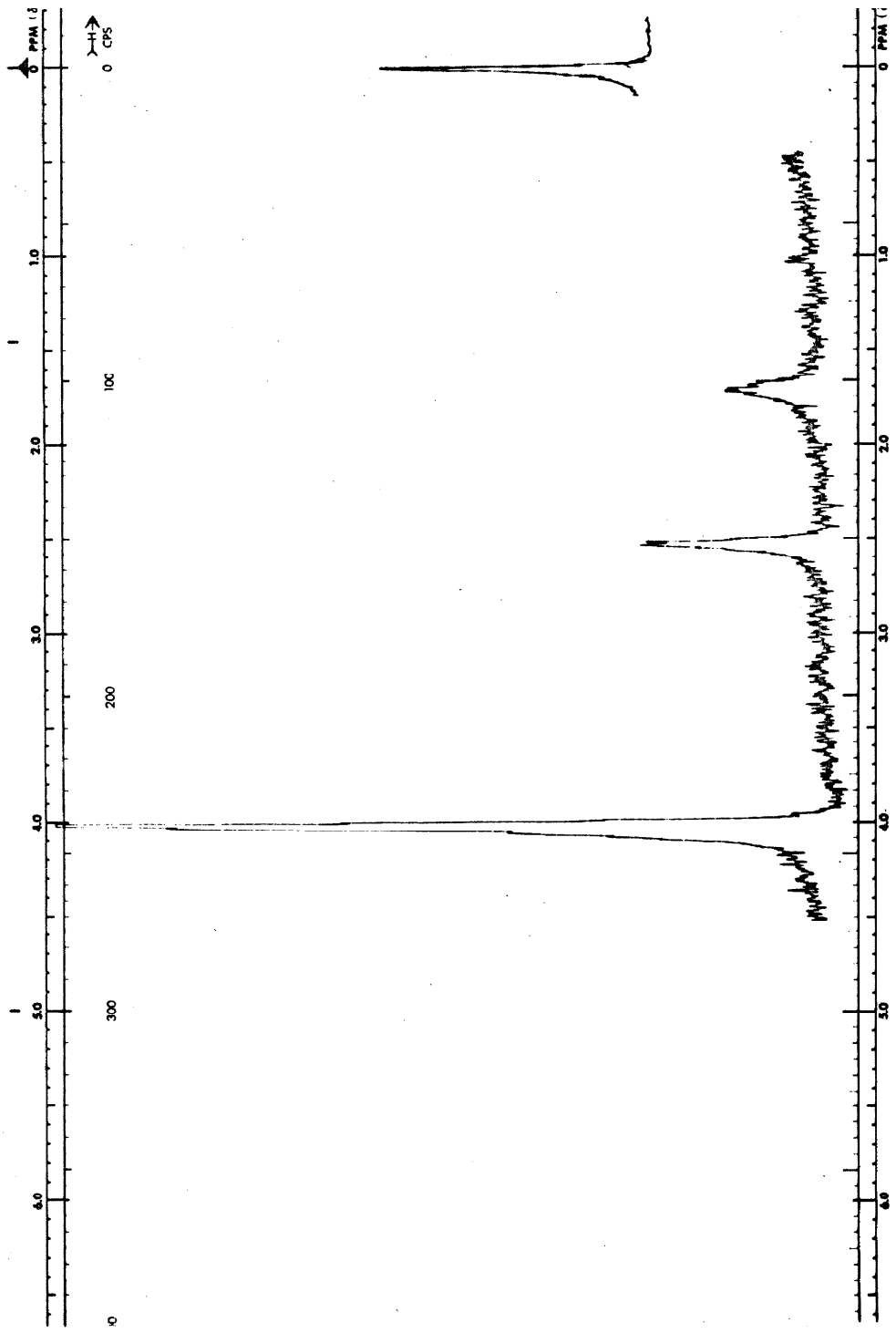
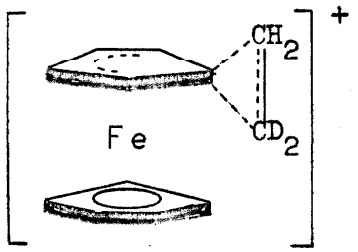


Fig. 11 N.m.r. spectrum of a carbon tetrachloride solution of the hydrolysis product of 2-ferrocenylethanol-1, 1-d_2 with TMS internal standard

on 2-ferrocenylethyl-1, 1-d_2 p-toluenesulfonate by Carter (42); and differs only inasmuch as the equilibration could continuously regenerate the carbonium ion, if this is an S_N1 process, so that accumulation of rearranged product would occur.

This immobility of deuterium label is completely consistent with the formation of an iron-stabilized carbonium ion during this hydrolysis. Since this intermediate is best able to support positive charge at the α carbon atom, solvent attack occurs exclusively at this position. The absence of deuterium scrambling does not rule out the possibility of forming a ring-bridged ion XXXV in this system, since exclusive endo attack of solvent could occur because of the previously described preference for nucleophilic attack at the endo carbon, which is better able to sustain positive charge because of the interannular electrons.



XXXV

1-Ferrocenyl-2-propyl p-Toluenesulfonate

The assumption that the acetolysis of 2-ferrocenylethyl p-toluenesulfonate does not involve large contributions from a ring-bridged ion, but occurs via participation by the nonbonding electrons

of the iron atom has important implications concerning the acetolysis of 1-ferrocenyl-2-propyl p-toluenesulfonate. Since an α-methyl substituent decreases to driving force for ring bridging (p. 12), iron participation will be the dominant feature in the solvolysis of this secondary tosylate. All of the kinetic results previously discussed for this secondary system are consistent with this conclusion. Evidence regarding the structure of this carbonium ion intermediate is presented in Chapter VI.

CHAPTER VI

The Structure of 1-Ferrocenyl-2-propyl Cation

In the preceding chapters evidence of interannular π electron participation was presented. This chapter is concerned with the stereochemical result of acetolysis and hydrolysis (80% acetone) of (-)-1-ferrocenyl-2-propyl p-toluenesulfonate, and therefore presents evidence concerning the structure of this stabilized carbonium ion.

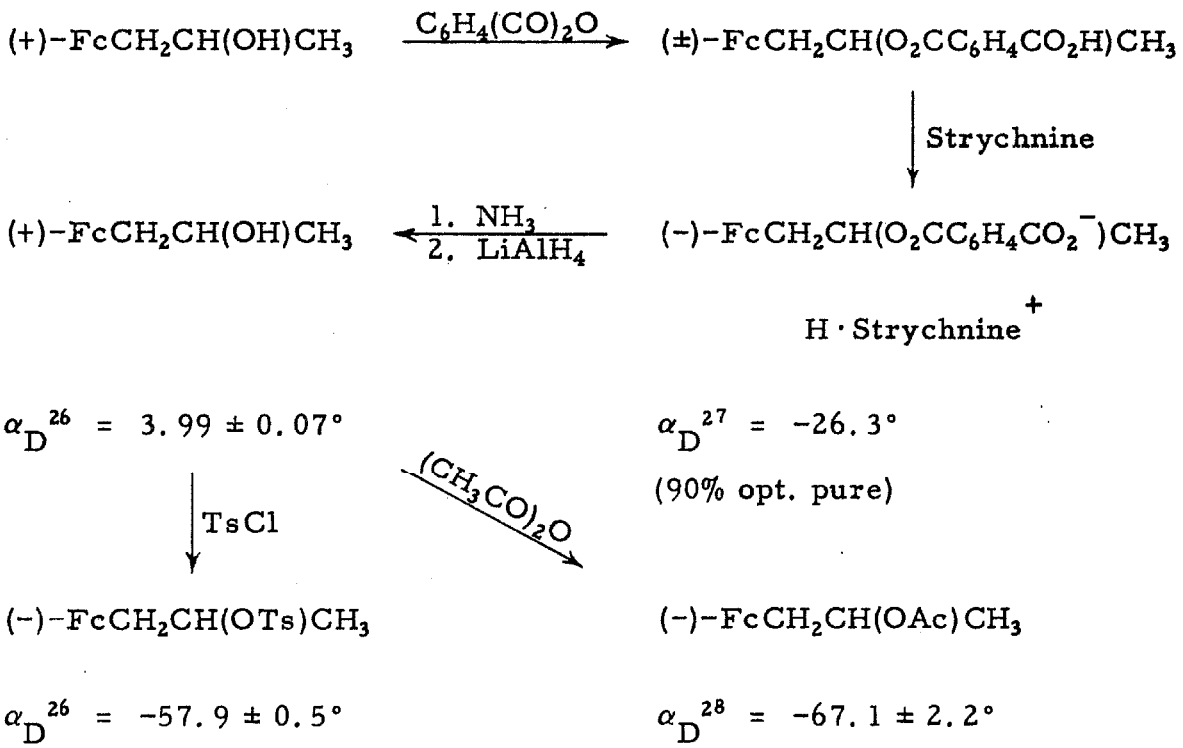
Resolution of 1-Ferrocenyl-2-propanol

This alcohol was first resolved by Carter (64), and the method described here is the one which he used. All rotations were measured on an ETL-NPL Electric Polarimeter so that no difficulties were encountered because of the yellow color of these ferrocene solutions.

Because a large number of recrystallizations are necessary to obtain diastereomeric strychnine salt with a constant specific rotation of $\alpha_D^{26} = -29.2 \pm 1.4°$ (assumed to be optically pure), the optically active alcohol and its derivatives were obtained from strychnine salt with $\alpha_D^{27} = -26.3$; and therefore represent samples of 90% optical purity.

Only optically active strychnine salt and tosylate were easily crystallized; both (-)-1-ferrocenyl-2-propyl acetate and (+)-1-ferrocenyl-2-propanol were oils which were purified by column chromatography and dried under vacuum at 55° for at least one hour prior to each measurement. The standard deviations listed in Chart III indicate the reproducibility achieved by this method. Appropriate control

Chart III

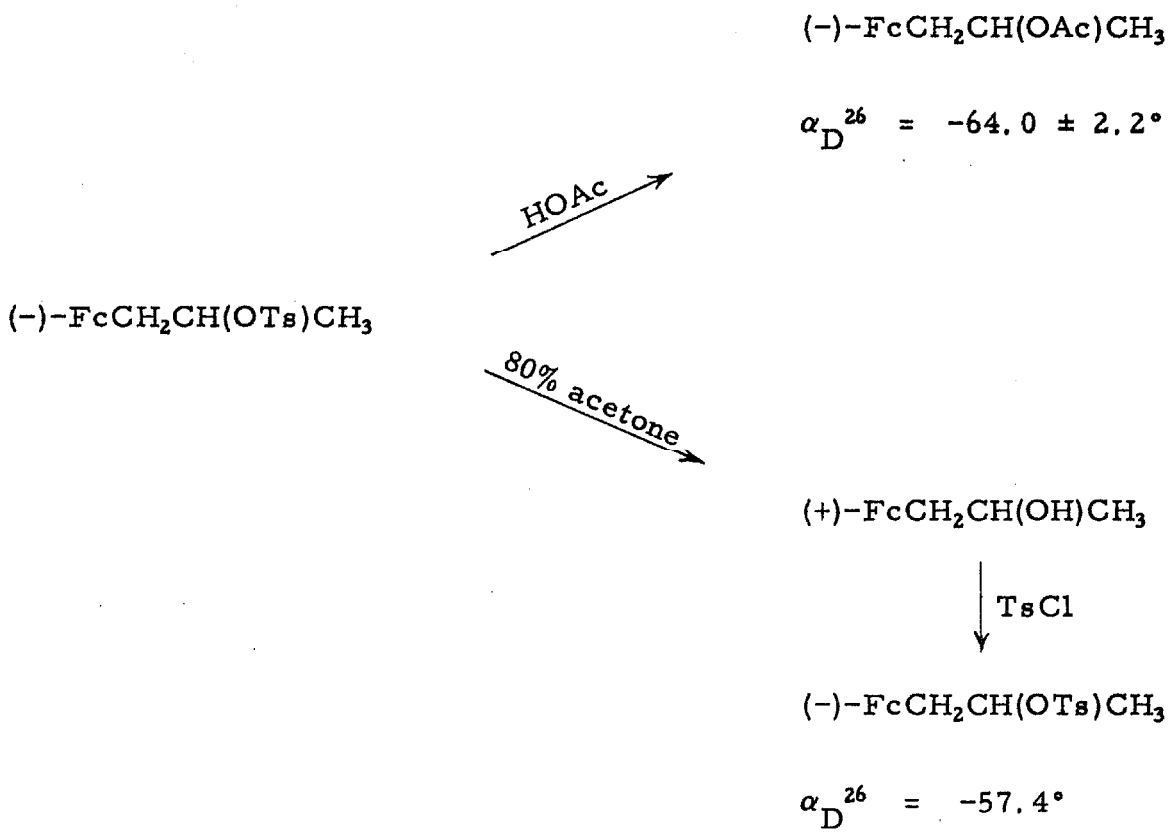


experiments also showed that neither purification procedure resulted in any racemization of these compounds.

Stereochemical Results of Interannular Electron Participation

Comparison of the specific rotations of (-)-1-ferrocenyl-2-propyl p-toluenesulfonate and acetate obtained via solvolysis reactions (Chart IV) with the rotations of the same compounds obtained by resolution of the corresponding alcohol shows that solvolysis in both acetic acid and 80% acetone occurs with complete retention of configuration. These experimental results are irreconcilable with Carter's previous report of complete racemization accompanying hydrolysis in the

Chart IV



former solvent (20), and nullify his conclusion (see p. 6) that the p-dπ stabilized intermediate XVIIIb is more stable than the π-dσ intermediate XVIIb (21). In contrast, complete retention of configuration, in conjunction with kinetic results discussed earlier, indicates that interannular participation results in the formation of a carbonium ion like XIII or XVIIb (pp. 17 and 23) in which overlap occurs between the interannular orbitals and one lobe of the vacant carbon p orbital.

CHAPTER VII

Summary and Conclusions

The kinetic data in Chapter IV and the product studies presented in Chapter V show that the acetolysis of these β-ferrocenylalkyl p-toluenesulfonates occurs with participation leading to formation of what has been described as either a π-stabilized, ring-bridged ion or an iron-stabilized carbonium ion.

Participation by the external π electrons of the ferrocene moiety is evident in the acetolysis of α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene (XX). That the rate of acetolysis of this exo tosylate (XX), in which direct interaction of the interannular electrons and the developing carbonium ion cannot occur, is slightly faster than the acetolysis rate of 1,2-benzocyclohexyl-3-methyl p-toluenesulfonate (IX), which is also an assisted solvolysis (33), shows that exo formation of a ring-bridged ion leads to rate enhancements similar to those due to participation in the corresponding phenyl derivatives. Because the rearrangement observed during this acetolysis can occur through either a ring-bridged or iron-stabilized carbonium ion, it is not possible to establish the identity of the solvolytic intermediate or intermediates on the basis of the available evidence for this solvolysis.

The only solvolysis which necessarily leads to formation of a ring-bridged ion is the acetolysis of 2-ferrocenyl-1-propyl p-toluenesulfonate in which the driving force for ring-bridging is provided by the β-methyl substituent. The partial migration of the metallocene

system during this solvolysis can only be satisfactorily explained in terms of a ring-bridged, electron-deficient intermediate, which undergoes nucleophilic attack at both the primary and secondary carbon atoms. The kinetic advantage of forming a ring-bridged ion from the endo direction rather than from the exo direction is demonstrated by the fact that acetolysis of this tosylate must be faster than the acetolysis rate of exo tosylate XX* which also proceeds through a ring-bridged transition state. This kinetic advantage is explained in terms of the greater availability of bonding electrons in the interannular region.

The product distribution from the acetolysis of 2-ferrocenyl-1-propyl p-toluenesulfonate is accounted for by the steric and electronic factors which facilitate exo solvent attack at the secondary carbon, and the compensating effect of the greater availability of interannular bonding electrons which favors attack of solvent at the endo primary carbon.

While the β-methyl substituent is effective in promoting partial rearrangement in the 2-ferrocenyl-1-propyl system, the acetolysis of α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene (XXI) does not lead to any observable rearrangement in spite of the β-alkyl

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*This conclusion is based on the fact that the rate of acetolysis of 2-ferrocenyl-1-propyl p-toluenesulfonate will be faster than the rate of acetolysis of 2-ferrocenylethyl p-toluenesulfonate because of the β-methyl substituent. This latter sulfonate solvolyzes 27 times faster than the exo tosylate XX.

substituent. Furthermore, the acetolysis of this endo tosylate (XXI) is much faster than any of the other acetolysis rates determined in the course of this research. If a ring-bridged ion were formed in this system, it could have similar steric and electronic contributions at the primary and secondary carbons in the alkyl bridge which lead to partial rearrangement in the 2-ferrocenyl-1-propyl ring bridged ion. The fact that no rearrangement occurs during acetolysis of this endo tosylate (XXI) demonstrates that a simple ring-bridged ion is not formed, and that there must be another kind of interannular electron participation in this system which causes the very fast acetolysis rate and leads to exclusive nucleophilic attack at the primary, endo carbon atom. Participation of the nonbonding electrons in the equatorial belt around the iron atom resulting in formation of an iron-stabilized intermediate is entirely consistent with these experimental requirements.

Special effects such as β-alkyl substitution, which does not result in placing the developing positive charge near the nonbonding iron orbitals in the central interannular region, or disposition of the tosyloxymethyl group in such a way that direct participation of these nonbonding electrons is prevented, make ring-bridging rather than iron-stabilization the dominant feature in these solvolysis reactions. A result of this conclusion is the implication that both 2-ferrocenylethyl p-toluenesulfonate and 1-ferrocenyl-2-propyl p-toluenesulfonate solvolyze via intermediate formation of what are best described as iron-stabilized carbonium ions. The results of labeling experiments

described in Chapter V for the 2-ferrocenylethyl system and the complete retention of configuration accompanying the solvolysis of 1-ferrocenyl-2-propyl p-toluenesulfonate (Chapter VI) are completely consistent with these conclusions.

PART II THE STEREOSPECIFIC SYNTHESES OF THE EXO AND ENDO ISOMERS OF α-HYDROXYMETHYL-1,2-TETRAMETHYLENEFERROCENE

CHAPTER I

Part II

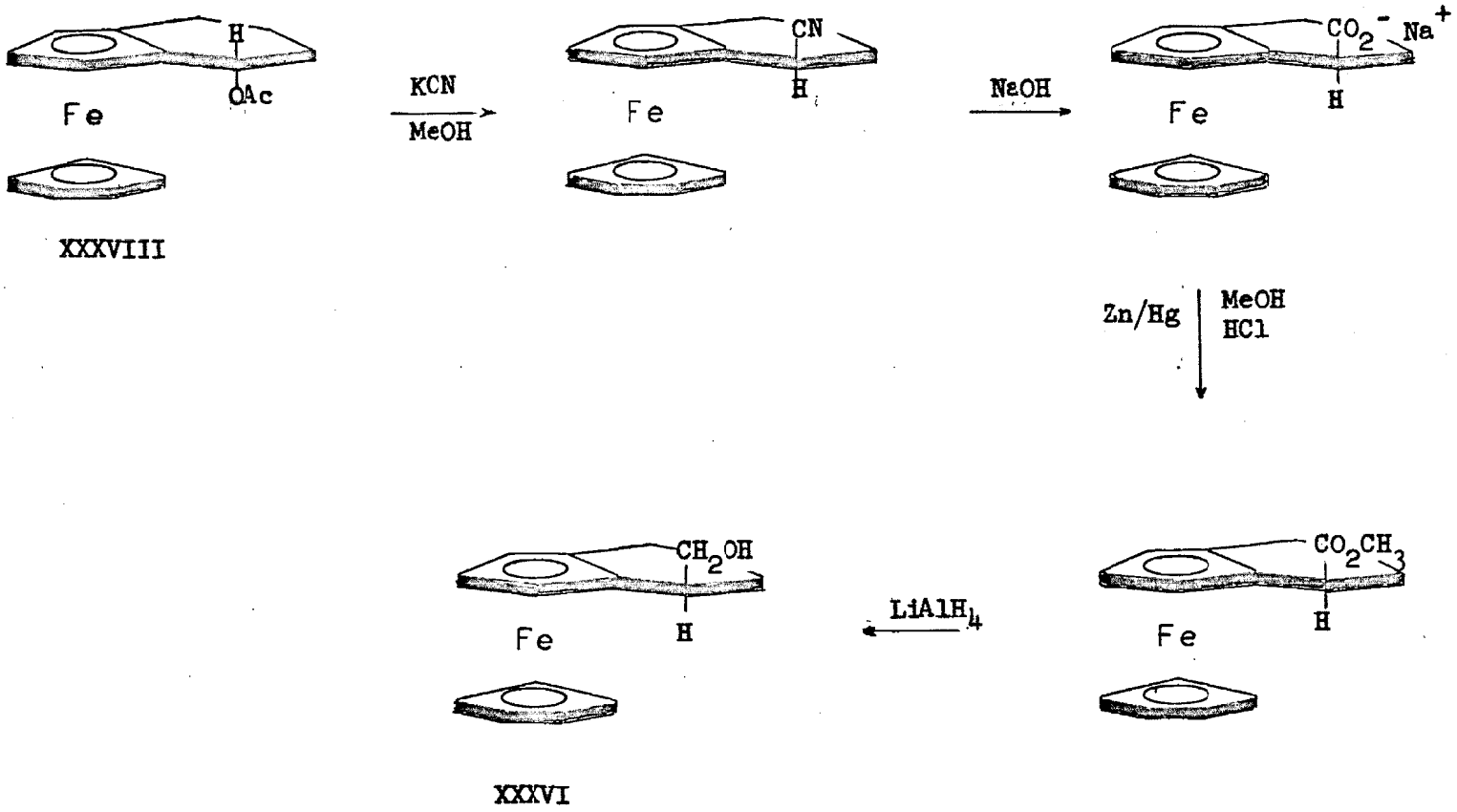
Syntheses

The syntheses of α-exo-hydroxymethyl-1, 2-tetramethylene-ferrocene (XXXVI) and α-endo-hydroxymethyl-1, 2-tetramethylene-ferrocene (XXXVII) were carried out in order to obtain the corresponding tosylates for the mechanistic studies described in Part I of this thesis.

Synthesis of α-exo-Hydroxymethyl-1, 2-tetramethyleneferrocene

The synthesis of α-exo-hydroxymethyl-1, 2-tetramethylene-ferrocene, beginning with α-endo-acetoxy-1, 2-tetramethyleneferrocene (XXXVIII), which was prepared by the previously described methods (2), is shown in Chart I. The success of this sequence of reactions is a result of the ability of a carbon atom adjacent to a ferrocene ring to sustain positive charge (1) thereby promoting nucleophilic substitution of cyanide for acetate in the first step. The stereospecificity of this synthesis is due to the fact that attack of cyanide ion and displacement of acetate in this step leads to formation of exo nitrile, regardless of the S_N2 or S_N1 character of this substitution. Obviously, S_N2 attack of cyanide with synchronous backside displacement of acetate from XXXVIII must produce exo nitrile; the same nitrile results from the reaction of the carbonium ion derived from XXVIII with cyanide ion, since overlap between an iron orbital and one lobe of the carbon p orbital prevents the formation of

Chart I



XXXVIII

XXXVI

endo product (2).

Because α-exo-cyano-1, 2-tetramethyleneferrocene and the corresponding acid decompose rapidly in solution, this nitrile was not isolated; but was converted immediately to the sodium salt of the corresponding acid, which was easily separated from the other organic by-products that were not water soluble. This sodium salt was then converted to α-exo-carbomethoxy-1, 2-tetramethyleneferrocene by refluxing in aqueous, acidic methanol in the presence of zinc amalgam which prevented decomposition of the intermediate acid. The ester was isolated as an oil, and although it could be chromatographed on deactivated alumina, attempts to recover this material from solution resulted in extensive decomposition. The infrared and n. m. r. spectra were in accord with the assigned structure.

Lithium aluminum hydride reduction of this ester to exo-alcohol I was straightforward. This alcohol was characterized by elemental analysis of its acetate and tosylate derivatives. The n. m. r. spectrum of the acetate is shown in Figure 12. The exo tosylate (Compound XX, p. 29) melted, without decomposition in air, at exactly the same temperature (100-101°) as its endo isomer (XXI); the melting point of this latter compound had to be determined in a sealed evacuated capillary to prevent decomposition. The configurational assignment of this alcohol is based on infrared spectral analysis of the hydroxyl region, which is discussed below.

Synthesis of α-endo-Hydroxymethyl-1, 2-tetramethyleneferrocene

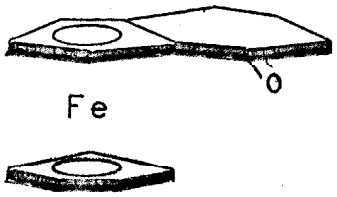
The reaction sequence for the synthesis of endo alcohol XXXVII

beginning with α-oxo-1, 2-tetramethyleneferrocene (2) is shown in Chart II. The Wittig reagent, triphenylmethylene phosphorane, which was generated in the first step, was prepared according to the method of Corey and co-workers (65). A phosphorane-ketone ratio of 2:1 gave consistently good yields (70%) of α-methylene-1, 2-tetramethylene-ferrocene. Attempted vacuum distillation of this latter olefin resulted in extensive decomposition, as evidenced from the change in the n.m.r. spectrum accompanying this treatment.

The stereospecificity of this synthesis is due to the fact that hydroboration with disiamylborane (bis-3-methyl-2-butylborane) proceeds exclusively from the least hindered, exo side, of the olefin. This result is in complete accord with the selectivity exhibited by this reagent (66) and the proposed steric control of addition of the boron-hydrogen linkage to the carbon-carbon double bond in similar reactions of disiamylborane (67).

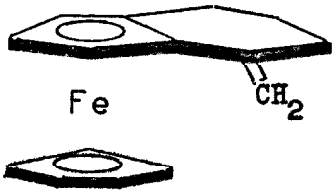
In contrast to the intermediate compounds involved in the synthesis of exo alcohol XXXVI, all of the intermediate products in the synthesis of endo isomer XXXVII showed no great tendency to decompose; however, the endo alcohol XXXVII was considerably more reactive than its exo isomer XXXVI as evidenced by the fact that it decomposes when stored in air for long periods even at 10°, while the exo alcohol XXXVI is stable under these conditions. The endo alcohol XXXVII was characterized by elemental analysis of its acetate and benzoate derivatives (the tosylate was too reactive to give a satisfactory analysis). The n.m.r. spectrum of the acetate derived from

Chart II

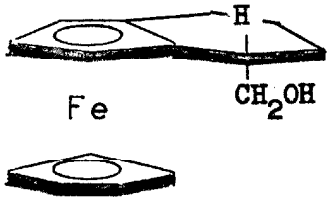


$(C_6H_5)_3PCH_3Br$

NaH
DMSO



1. Disiamylborane
2. NaOH, H_2O_2



XXXVII

endo alcohol XXXVII is shown in Figure 13, p. 88. This spectrum is notably different from the n.m.r. spectrum of α-exo-acetoxymethyl-1, 2-tetramethyleneferrocene (Figure 12). The ring proton resonances appear further downfield for the former compound than for the exo acetate derived from alcohol XXXVI. Furthermore, the endo derivative has a doublet at 4.4 p.p.m.; whereas, the exo acetate derived from XXXVI has only a partially resolved doublet in this region. The assignment of an endo configuration to this alcohol is based not only on the synthetic sequence, but also on the infrared spectrum described below.

Configurational Assignments--Hydrogen Bonding Study

A major difference in the infrared spectra of the exo XXXVI and endo XXXVII isomers of α-hydroxymethyl-1, 2-tetramethyleneferrocene is due to the fact that the endo isomer can form an intramolecular hydrogen bond with the iron atom (1, 2, 12); whereas, the geometry of alcohol XXXVI prevents this interaction in the exo isomer. Infrared spectral analyses of dilute solutions of various ferrocenylcarbinols have been reported (2, 12); and the results have been summarized in terms of free, iron-bonded, and π-bonded hydroxyl absorptions. The most complete study, and the one most nearly analogous to the present work is the analysis of the infrared spectrum of 2-ferrocenylethanol reported by Trifan and Bacskai (12). The hydroxyl absorptions and the assignments for this alcohol are shown in Table VII together with the data for the exo XXXVI and endo XXXVII isomers of α-hydroxymethyl-1, 2-tetramethyleneferrocene. The

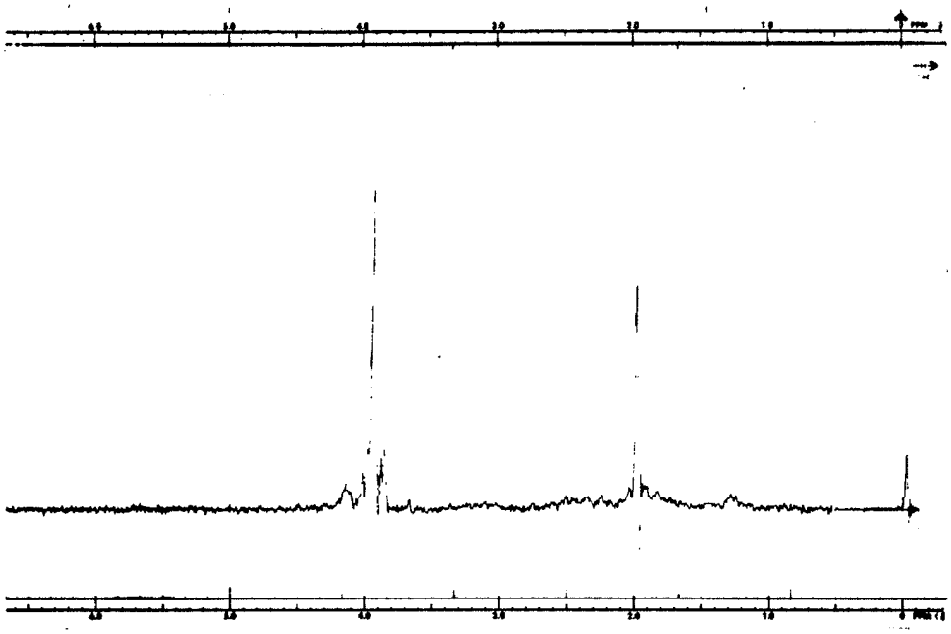


Fig. 12 N.m.r. spectrum of a carbon tetrachloride solution of α-exo-acetoxymethyl-1, 2-tetramethylene-ferrocene with TMS internal standard

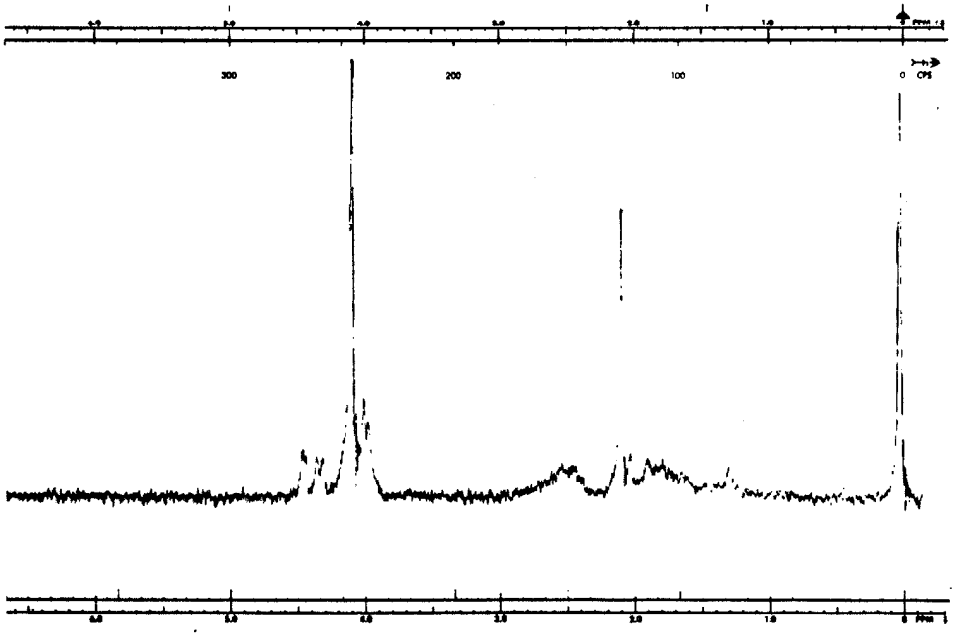


Fig. 13 N.m.r. spectrum of a carbon tetrachloride solution of α-endo-acetoxymethyl-1, 2-tetramethylene-ferrocene with TMS internal standard

TABLE VII. Infrared Hydroxyl Absorptions of β-Ferrocenylalkyl Alcohols in Carbon Tetrachloride Solution

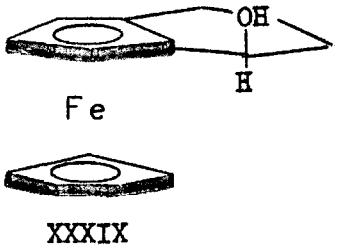
Compound	Concentration	Absorption (cm^{-1})	Assignment
2-Ferrocenylethanol[a]	0.005 M	3533	Fe-bonded OH
		3605	π-bonded OH
		3632	Free OH
exo Alcohol XXXVI	0.005 M	3610	π-bonded OH
		3645	Free OH
endo Alcohol XXXVII	0.005 M	3527	Fe-bonded OH
		3645	Free OH

[a]Data from reference 12.

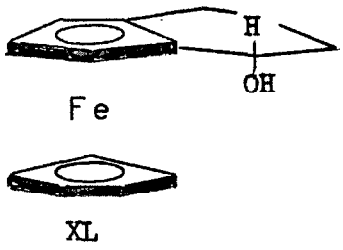
infrared spectra of the hydroxyl region of dilute carbon tetrachloride solutions (0.005 M) of these alcohols are shown in Figures 14 and 15.

The infrared data shown in Table I unequivocally establish the configurations of the two alcohols. The high degree of stereospecificity attained in these syntheses is demonstrated by the absence of any iron-bound hydroxyl absorption in the infrared spectrum of exo alcohol XXXVI (Figure 1) and by the absence of any π-bonded hydroxyl absorption in the infrared spectrum of endo isomer XXXVII.

Similar hydrogen bonding differences between the exo XXXIX and endo XL isomers of α-hydroxy-1, 2-tetramethyleneferrocene (the next lower homologs of *I* and *II* respectively) have been used to advantage in the separation of these compounds by chromatography on deactivated alumina (2). The endo isomer XL is eluted much faster than the exo isomer XXXIX because of intramolecular hydrogen



XXXIX



XL

bonding in the former compound. In fact, no free hydroxyl absorption (3650 cm^{-1}) occurs in these or the closely related alcohols which have been chromatographically separated; although absorptions near 3610 cm^{-1}, which are indicative of π-bound hydroxyl groups have been noted for these alcohols (2).

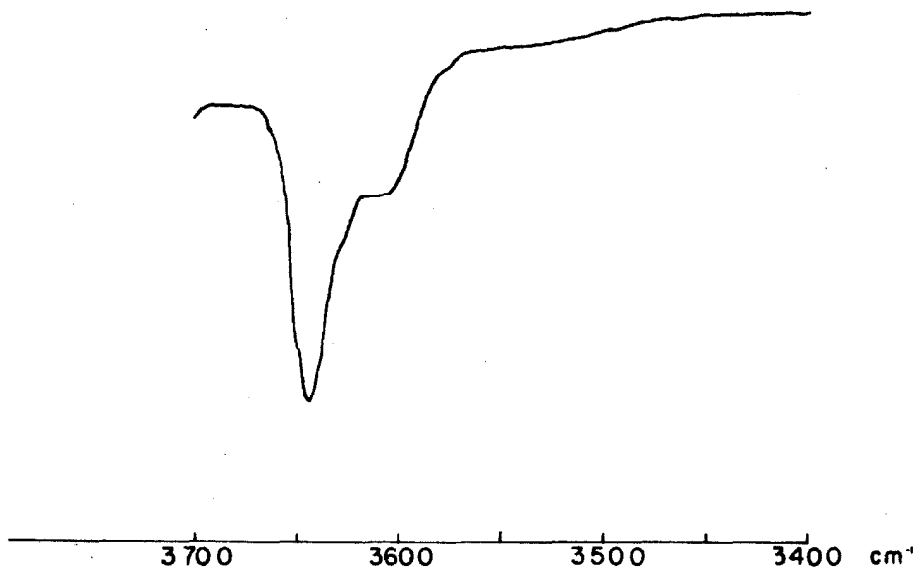


Fig. 14 Infrared hydroxyl absorptions of a 0.005 M carbon tetrachloride solution of α-exo-hydroxymethyl-1,2-tetramethyleneferrocene

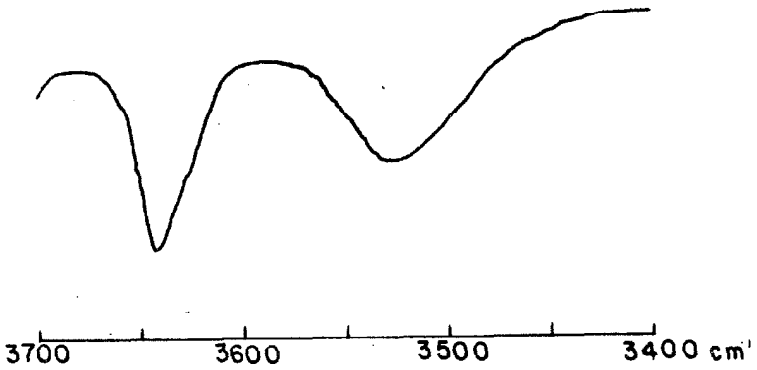


Fig. 15 Infrared hydroxyl absorptions of a 0.005 M carbon tetrachloride solution of α-endo-hydroxymethyl-1,2-tetramethyleneferrocene

Chromatographic separation of alcohols XXXVI and XXXVII was not possible, however, apparently because the hydroxyl hydrogen of endo alcohol XXXVII is not so constrained as is the hydroxyl hydrogen of α-endo-hydroxy-1,2-tetramethyleneferrocene XL. As a result, the hydroxyl hydrogen of endo isomer XXXVII is more available for bonding to alumina or silica gel thus diminishing the differences in chromatographic adsorption between these endo and exo isomers. The existence of a free hydroxyl absorption at 3645 cm^{-1} for alcohol XXXVII and the previously mentioned absence of this band for alcohols which are chromatographically separable supports this conclusion.

Experimental

All temperatures reported herein have been corrected.

Analyses were determined by either Schwarzkopf Microanalytical Laboratory, Woodside 77, New York (S); or Spang Microanalytical Laboratory, Ann Arbor, Michigan (Sp).

N.m.r. spectra were taken on a Varian A-60 Spectrometer; all peaks are reported in p.p.m. relative to tetramethylsilane internal standard.

Nitrogen Purification

Purified nitrogen was prepared by passing Linde Hi Purity Nitrogen through a gas washing apparatus which consisted, in series, of: a column (5 by 54 cm) containing activated BTS Copper Catalyst (purchased from Badische Anilin Soda-Fabrik A G, Ludwigshafen am Rhein, Germany); and three gas washing bottles which contained concentrated sulfuric acid, Ascarite, and phosphorous pentoxide on glass wool respectively. A test tube, which contained mercury and was equipped with a T-joint and a side arm, was used as a safety valve between the gas washing apparatus and the reaction mixture.

When purified nitrogen was not necessary, Linde Hi Purity Nitrogen was used directly from the cylinder.

Ferrocene

Ferrocene was purchased from K & K Laboratories, Plainview, New York. It was used directly from the container without further purification.

2-Ferrocenylethanol

This alcohol was prepared according to the procedure of Hauser and co-workers (68) from the lithium aluminum hydride reduction of ferrocenylacetic acid.

The deuterated alcohol, 2-ferrocenylethanol-1, 1-d_2, was also prepared by this method. Lithium aluminum deuteride (98.8%) was purchased from Metal Hydrides Inc., Beverly, Massachusetts. After two crstallizations from petroleum ether (b.p. 60-70°), the deuterated alcohol melted at 37-38°.

2-Ferrocenylethyl p-Toluenesulfonate

The method used for the purification of this sulfonic ester was a modification of the procedure described by Hill (69). The crude alcohol (46 g., 204 mmoles) was dissolved in 75 ml. of pyridine, which had been stored over barium oxide. An equivalent amount of recrystallized p-toluenesulfonyl chloride was then added, and the reaction mixture was allowed to stand in a stoppered flask at 0° overnight. The contents of the flask were then poured into a mixture of ice, 75 ml. concentrated phosphoric acid, and methylene chloride. The organic layer was extracted and washed three times with water. The aqueous washings were then extracted once with methylene chloride. The combined methylene chloride extracts were dried over sodium sulfate, and then added dropwise to boiling hexane. Orange crystals were obtained from the cold hexane solution in 24% yield, m.p. 78-79° after two crystallizations.

Anal. (Sp) Calcd. for $C_{19}H_{20}O_2SFe$: C, 59.38; H, 5.25; Fe, 14.53.
Found: C, 59.47; H, 5.24; Fe, 14.59.

2-Ferrocenylethyl Acetate

This ester was prepared in 90% yield according to the method described by Carter (70). The acetate, obtained as an oil after chromatography on grade III neutral alumina, was purified by molecular distillation at 97° (10 μ).

Anal. (S) Calcd. for $C_{14}H_{16}O_2Fe$: C, 61.79; H, 5.93; O, 11.76.
Found: C, 62.02; H, 5.99; O, 11.93.

1-Ferrocenyl-2-propanone

The synthesis of this ketone has been reported (71), but not in detail. For this reason, the method will be described here.

Crude, dry ferrocenylacetic acid (68) (133 g., 545 mmoles) was extracted from a soxhlet thimble into 650 ml. of anhydrous ether. A residue of 18 g. remained in the thimble. Methyllithium, 860 ml. of a 2 M ethereal solution (Lithium Corporation of America), was slowly added to the suspension of 115 g. (472 mmoles) of acid in 1.5 l. of anhydrous ether at −10°. A static pressure of purified nitrogen was maintained over the reaction mixture, which was stirred at high speed. After the reaction mixture had been allowed to proceed for five hours at −10°, it was refluxed for five additional hours. Stirring was then discontinued and the mixture was allowed to stand at room temperature overnight. Phosphoric acid (200 ml. of a 5% aqueous solution) was then added dropwise with stirring while methane was continuously evolved. The ethereal layer was then extracted,

washed once with saturated sodium bicarbonate solution, and dried over sodium sulfate. The product ketone was not isolated because of its instability as evidenced by the fact that the low temperature evaporation of ether produced only tars.

1-Ferrocenyl-2-propanol

The ethereal solution of 1-ferrocenyl-2-propanone, obtained above, was added dropwise to a suspension of 18.1 g. (479 mmoles) of lithium aluminum hydride. The reaction mixture was refluxed for twelve hours; after which excess hydride was decomposed by the dropwise addition of water. The ethereal layer was extracted, washed three times with water, and dried over sodium sulfate. The ether was removed at reduced pressure, and the crude alcohol was obtained as a viscous orange-brown oil in 76% yield. For specific uses, this alcohol was purified by chromatography on grade III, neutral alumina. It was eluted from the column with 1:1 methylene chloride-hexane. The infrared spectrum of this material, in carbon tetrachloride, had characteristic, sharp absorptions at 1020, 1140 and 3100 cm^{-1}. Broad hydroxyl absorption appeared at 3480 cm^{-1}. The n.m.r. spectrum had resonances at: 4.23 p.p.m., singlet; 3.70 p.p.m., multiplet; 3.09 p.p.m., singlet; 2.61 p.p.m., doublet; and 1.23 p.p.m., doublet.

1-Ferrocenyl-2-propyl p-Toluenesulfonate

The procedure for the preparation of this tosylate was the same as that described above for 2-ferrocenylethyl p-toluenesulfonate. The yield of yellow crystalline product, m.p. 71-72°, was 33%.

Anal. (S) Calcd. for $C_{20}H_{22}O_3SFe$: C, 60.31; H, 5.58; O, 12.05.
Found: C, 60.16; H, 6.02; O, 12.03.

1-Ferrocenyl-2-propyl Acetate

This compound was prepared in 95% yield according to the procedure described above for 2-ferrocenylethyl acetate. The red-brown oil, obtained by molecular distillation at 71° (18 μ), had an acetate absorption at 1250 cm^{-1} and a carbonyl stretching frequency at 1745 cm^{-1} in the infrared.

Anal. (S) Calcd. for $C_{15}H_{18}O_2Fe$: C, 62.96; H, 6.34.
Found: C, 63.10; H, 6.43.

2-Ferrocenylpropanoic Acid

1-Ferrocenyl-1-ethyl acetate was prepared according to the method described by Hill (1). The ester (36 g., 91 mmoles) was dissolved in 100 ml. of reagent methanol together with 13 g. (200 mmoles) of freshly opened potassium cyanide. The reaction mixture became very dark during the twelve hour reflux period; therefore, the nitrile intermediate was not isolated, but hydrolyzed by the addition of 80 g. of potassium hydroxide in 700 ml. of water and refluxing for ten hours. The reaction mixture was cooled, and its volume then reduced to ca. 500 ml. The resulting aqueous solution was washed three times with ether, and then acidified with concentrated phosphoric acid. The precipitated acid was collected to yield 15 g. (58%) of yellow-brown crystals. An analytical sample was obtained by sublimation at 70° (6 μ); this compound darkened at 121°, but did not melt. The infrared spectrum of this sample (potassium

bromide pellet) showed hydroxyl absorptions at 3500 and 2775 cm^{-1}, and a carbonyl stretch at 1699 cm^{-1}.

Anal. (S) Calcd. for $C_{13}H_{14}O_2Fe$: C, 60.49; H, 5.47; O, 12.40.

Found: C, 60.62; H, 5.40; O, 12.39.

2-Ferrocenyl-1-propanol

A suspension of 15 g. (58 mmoles) of 2-ferrocenylpropanoic acid in ether was added dropwise to a stirred ethereal suspension of 2 g. (53 mmoles) of lithium aluminum hydride. The mixture was then refluxed for 8.5 hours; after which water was slowly added and the ethereal layer extracted. The organic solution was washed three times with water, and dried over anhydrous sodium sulfate. Evaporation of the ether and chromatography of the resulting oil on grade III, neutral alumina yielded 9.5 g. (67%) of 2-ferrocenyl-1-propanol. The alcohol was eluted with methylene chloride after two, more mobile bands had been eluted with hexane. The infrared spectrum of a carbon tetrachloride solution of this alcohol had hydroxyl absorption at 3660 and 3550 cm^{-1}. The n.m.r. spectrum of this solution exhibited the following resonances: 4.05 p.p.m., singlet; 3.45 p.p.m., doublet; 2.57 p.p.m., multiplet; 2.06 p.p.m., broad singlet; 1.20 p.p.m., doublet.

2-Ferrocenyl-1-propyl p-Toluenesulfonate

This sulfonic ester was obtained in 77% yield according to the procedure described above for 2-ferrocenylethyl p-toluenesulfonate. The yellow, crystalline product melted at 74-76°.

Anal. (S) Calcd. for $C_{20}H_{22}O_3SFe$: C, 60.31; H, 5.58; Fe, 14.02.
Found: C, 60.30; H, 5.98; Fe, 13.95.

2-Ferrocenyl-1-propyl Acetate

The method of preparation of this ester from the alcohol was the same as that previously described (70). The acetate was obtained in 17% yield, b.p. 85° (12 μ).

Anal. (S) Calcd. for $C_{15}H_{18}O_2Fe$: C, 62.96; H, 6.34.
Found: C, 63.03; H, 6.28.

α-exo-Carbomethoxy-1,2-tetramethyleneferrocene

Crude α-endo-acetoxy-1,2-tetramethyleneferrocene (2) (5.05 g., 16.9 mmoles) was dissolved in 270 ml. of methanol contained in a three-necked flask. The flask was equipped with a magnetic stirrer, a reflux condenser, and a nitrogen inlet; the outlet was at the top of the condenser. After the addition of 50.5 g. (1030 mmoles) of freshly opened sodium cyanide, nitrogen was bubbled through the reaction mixture for ten minutes. The solution was then refluxed under nitrogen for seven hours. The nitrile, thus formed, was hydrolyzed immediately by the addition of 17 g. (420 mmoles) of sodium hydroxide and refluxing for ten hours. The aqueous solution was then cooled, washed three times with ether, and then added to a mixture of 50 g. of 10% zinc amalgam (to prevent oxidation), 333 ml. of concentrated hydrochloric acid, 333 ml. of methanol, and 250 ml. of benzene. Hydrogen cyanide was evolved during this addition. The reaction mixture was refluxed until the aqueous layer was colorless. The benzene layer was extracted and washed three times with water.

After the benzene was removed at reduced pressure, the resulting brown oil was chromatographed on neutral, grade III alumina. The ester was cluted with 50% hexane-benzene in 65% yield. The infrared spectrum of this ester, in carbon disulfide, has a carbonyl absorption at 1743 cm^{-1} and a carbon-oxygen vibration at 1160 cm^{-1}. The n.m.r. spectrum was also consistent with this structure. This ester decomposes rapidly on standing, and when dissolved in chlorinated solvents.

α-exo-Hydroxymethyl-1,2-tetramethyleneferrocene

This alcohol was obtained from the reduction of 10 g. (33.6 mmoles) of α-exo-carbomethoxy-1,2-tetramethyleneferrocene with 2 g. (52.5 mmoles) of lithium aluminum hydride in ether. The reaction mixture was stirred for twenty minutes after the addition had been completed. Water was then carefully added to destroy the excess hydride. The reaction mixture was filtered through a glass wool plug and dried over sodium sulfate. Evaporation of the ether yielded a brown oil, which was chromatographed on grade III, neutral alumina. The alcohol was eluted with 50% methylene chloride-hexane in 25% yield. The n.m.r. spectrum of this material had the following resonances: 0.8 to 3.10 p.p.m., multiplets; 3.90 p.p.m., broad singlet; 3.95 and 4.27 p.p.m. singlets. The infrared spectrum had a broad hydroxyl absorption from 3130 to 3640 cm^{-1}. A dilute solution (0.005 M) was carefully examined (see the Hydrogen Bonding Study), in this region, and had only a π-bonded hydroxyl absorption at 3610 cm^{-1} and a stronger free hydroxyl absorption at 3645 cm^{-1}.

α-exo-Tosyloxymethyl-1,2-tetramethyleneferrocene

The procedure used for the preparation of this tosylate is the same as that described above for 2-ferrocenylethyl p-toluenesulfonate. The sulfonic ester was crystallized from 50% ether-hexane at -77°. The crystals obtained were used to seed the mother liquor and for subsequent recrystallizations so that only one low temperature crystallization was necessary. The exo tosylate was obtained in 49% yield, m.p. 100-101°.

Anal. (S) Calcd. for $C_{22}H_{24}O_3Fe$: C, 62.27; H, 5.70; O, 11.31; Fe, 13.16.
Found: C, 62.30; H, 5.96; O, 10.94; Fe, 13.36.

α-exo-Acetoxymethyl-1,2-tetramethyleneferrocene

This acetate was prepared according to previously described methods (70). After chromatography, the ester was distilled at 85-86° (18 μ) in 94% yield. The n.m.r. spectrum of this material had the following resonances: 0.8-2.00 p.p.m. and 2.18-3.70 p.p.m., multiplets; 2.09 p.p.m., singlet; 3.95 p.p.m., multiplet; 4.05 p.p.m., singlet.

Anal. (S) Calcd. for $C_{17}H_{20}O_2Fe$: C, 65.40; H, 6.46.
Found: C, 65.87; H, 6.65.

α-Methylene-1,2-tetramethyleneferrocene

This olefin was obtained from a Wittig reaction of α-oxo-1,2-tetramethyleneferrocene (2). The Wittig reagent, triphenylmethylene phosphorane, was prepared as described by Corey and co-workers (65). A solution of 1.0 g. (3.9 mmoles) of ketone in 8 ml. of dimethylsulfoxide was added to 7.8 mmoles of the yield maintained at

room temperature in a purified nitrogen atmosphere. The reaction mixture was then stirred for twenty hours at room temperature, after which it was poured into 100 ml. of water. The resulting aqueous solution was extracted with ether until the ethereal extract was pale brown. The organic layer was then washed four times with water and dried over sodium sulfate. The dark oil, obtained after evaporation of the ether, was chromatographed on grade III, neutral alumina. The olefin was eluted with hexane as an orange oil in 73% yield. A second band was eluted with 1:4 methylene chloride-hexane, which proved to be the starting ketone in 25% recovery. The infrared spectrum had absorptions at 1630 cm^{-1} (conjugated olefin) and 1288 cm^{-1} (methylene in plane deformation). The n.m.r. spectrum showed resonances at: 1.65-2.65 p.p.m., multiplet; 3.85 p.p.m., singlet; 4.00 p.p.m., singlet; and 4.30 p.p.m., triplet; 4.70 and 4.98 p.p.m., singlets. Additional support for this structure comes from the fact that the ultraviolet spectrum of this material has λ_{max} at 2775 and 4500 Å which are similar to those reported for vinylferrocene (72).

α-endo-Hydroxymethyl-1,2-tetramethyleneferrocene

Disiamylborane (61.2 mmoles) was prepared according to the external generation method described by Brown and co-workers (73, 74). A solution of 5.15 g. (20.4 mmoles) of α-methylene-1,2-tetramethyleneferrocene was added via syringe to a solution of 61.2 mmoles of disiamylborane in 15 ml. of tetrahydrofuran at 0°. The stirred reaction mixture was maintained in a purified nitrogen

atmosphere for twenty-four hours, after which 15 ml. of water was added. Sodium hydroxide (22 ml. of 3 N solution) was then added followed by the careful addition of 22 ml. of 30% hydrogen peroxide. Extensive decomposition occurred during the peroxide addition; the temperature of the reaction mixture was maintained between 50 and 60° during this time. The organic layer was then extracted and washed three times with water. After drying the organic solution over sodium sulfate, the ether was removed at reduced pressure. Chromatography of the resulting brown oil on grade III, neutral alumina yielded 2.6 g. (47%) of endo alcohol together with 1.2 g. (23%) of starting olefin. The n. m. r. spectrum of this alcohol was very similar to that described for the exo isomer. Furthermore, the Rf values on silica gel thin layer plates were identical for the endo and exo alcohols in a 50% acetone-hexane solvent system. A dilute (0.005 M) carbon tetrachloride solution of α-endo-hydroxymethyl-1,2-tetramethyleneferrocene had infrared hydroxyl absorptions at 3527 cm^{-1} and 3642 cm^{-1}, which can be assigned (12) to the iron-hydroxyl hydrogen bond and the free hydroxyl absorptions respectively (see the Hydrogen Bonding Study below).

α-endo-Tosyloxymethyl-1,2-tetramethyleneferrocene

The procedure for the preparation of this sulfonic ester is exactly the same as that described for the exo isomer. The yellow crystals, obtained in 66% yield, melted at 100-101° (sealed evacuated capillary to prevent decomposition). This is the same melting point as that of the exo isomer; however, a mixture of the two isomeric

tosylates melted from 82–94°. Elemental analysis of this reactive sulfonate was not satisfactory.

α-endo-Acetoxymethyl-1,2-tetramethyleneferrocene

This acetate was prepared according to previously described methods (70). The ester was distilled at 112° (20 μ). The n.m.r. spectrum differed notably from the exo isomer: 1.19–3.02 p.p.m., multiplet; 2.05 p.p.m., singlet; 3.95 p.p.m., partially resolved doublet; 4.05, 4.30, and 4.39 p.p.m., singlets. The infrared spectrum was nearly superimposable with that of the exo isomer.

Anal. (S) Calcd. for $C_{17}H_{20}O_2Fe$: C, 65.40; H, 6.46.

Found: C, 65.36; H, 6.80.

α-endo-Benzoxymethyl-1,2-tetramethyleneferrocene

Because satisfactory analysis of the very reactive sulfonate, α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene, could not be obtained, the alcohol was converted to the benzoate by treatment of 100 mg. (0.37 mmoles) of the alcohol with 2 ml. of benzoyl chloride in 0.5 ml. of pyridine. Thin layer chromatography on silica gel in hexane indicated that the reaction was completed in ten minutes at room temperature. The reaction mixture was chromatographed on grade III, neutral alumina; the ester was eluted with hexane as a brown oil. Low temperature crystallization (-77°) from hexane produced crystals which were then used to seed hexane solutions of the liquid benzoate. After three crystallizations, the ester, produced in 44% yield, melted at 80–81.5°.

Anal.* Calcd. for $C_{22}H_{22}O_2Fe$: C, 70.60; H, 5.93.

Found: C, 70.51; H, 5.72.

Resolution of 1-Ferrocenyl-2-propanol

This resolution was carried out according to the method described by Carter (64); however, the rotations which he reported are not correct. For this reason, the procedures and the polarimetric results will be described in detail here.

Measurement of rotations could not be carried out visually because all of the solutions were deeply colored. Polarimetric determinations were, therefore, made on an ETL-NPL Electric Polarimeter, Type 143-A. A quartz cell (0.1 dm.) and a glass cell (0.4 dm.) were used for each determination.

(-)-1-Ferrocenyl-2-propyl Acid Phthalate Strychnine Salt

A chloroform solution of 4.87 g. (14.6 mmoles) of strychnine was added to an acetone solution of 5.73 g. (14.6 mmoles) of 1-ferrocenyl-2-propyl acid phthalate (75). The reaction mixture was stirred overnight. The volume was reduced, and the unreacted strychnine was removed by filtration. The filtrate was cooled, and yellow crystals of the levorotatory salt were collected. Six crystallizations from acetone produced material which melted at 175-177°, with $\alpha_D^{26} = 29.2 \pm 1.4°$ (c = 9.2, methanol). The melting point and specific rotation did not change on further crystallization.

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*Elek Microanalytical Laboratories, Torrance, California.

Anal. (S) Calcd. for $C_{42}H_{42}N_2O_6Fe$: C, 69.41; H, 5.84; O, 13.21; N, 3.86; Fe, 7.68.

Found: C, 69.50; H, 5.76; O, 13.28; N, 3.84; Fe, 7.62.

(+)-1-Ferrocenyl-2-propanol

An excess of aqueous ammonia was added to an ethanolic solution (1.42 g./50 ml.) of (-)-1-ferrocenyl-2-propyl acid phthalate strychnine salt, $\alpha_D^{27} = -26.3°$ (c = 5.1, methanol). Precipitated strychnine was filtered, and concentrated hydrochloric acid was added to bring the filtrate to pH 6. The acidic solution was then extracted with ether; the organic layer dried over sodium sulfate and evaporated. The resulting brown oil was suspended in a benzene-ether solution and added to a suspension of 0.2 g. (50 mmoles) of lithium aluminum hydride in ether. The reaction mixture was then refluxed for six hours; after which, water was added to destroy the unreacted hydride and the organic layer was extracted and evaporated. Chromatography of the residue yielded 58% of dextrorotatory alcohol, which was dried at 55° (1 mm.) for one hour. This compound had $\alpha_D^{26} = 3.99°$ (c = 15.2, carbon tetrachloride).

(-)-1-Ferrocenyl-2-propyl p-Toluenesulfonate

This sulfonic ester was prepared according to the method described above for 2-ferrocenylethyl p-toluenesulfonate. The starting material (+)-1-ferrocenyl-2-propanol had $\alpha_D^{26} = 3.99°$ (c = 3.2, carbon tetrachloride). Bright yellow crystals of tosylate were obtained in 57% yield. After two recrystallizations, the solid

melted at 78–81°, and had $\alpha_D^{26} = -57.9 \pm 0.5°$ (c = 3, carbon tetrachloride).

In order to show that there was no optical fractionation of (-)-1-ferrocenyl-2-propyl p-toluenesulfonate during its crystallization, nearly equivalent amounts of pure, racemic tosylate (m. p. 71–72°) and optically active ($\alpha_D^{26} = -57.9 \pm 0.5°$) material were mixed, and recrystallized twice from hexane. The calculated value of the specific rotation of this mixture was -29.1°, the values obtained after the first and second crystallizations were -28.6 and -29.1° respectively.

(-)-1-Ferrocenyl-2-propyl Acetate

This ester was prepared by the same methods as were used for the racemic compound (70). A sample prepared from alcohol with $\alpha_D^{26} = 3.99°$ (c = 15.2, carbon tetrachloride) had $\alpha_D^{28} = -67.1 \pm 2.2°$ (c = 3.1, carbon tetrachloride). Appropriate control experiments showed that no racemization occurred either during chromatography of the liquid acetate, or drying at 55° (1 mm.).

Kinetic Procedure

Solvent

DuPont Glacial Acetic Acid was purified according to the procedure described by Wiberg (76).

Rate Measurements

All acetolysis rates were determined by measuring the p-toluenesulfonic acid concentration as a function of time. Solvolyses

were carried out in degassed ampoules to prevent atmospheric oxidation of these ferrocene compounds in acidic solutions (45). Culture tubes (18 by 150 mm.) were fitted with 19/38 standard taper, female ground glass joints. The tubes were washed with chloroform, water, and finally with potassium dichromate-sulfuric acid cleaning solution. The sample tubes were then rinsed ten times with tap water, five times with distilled water, and dried at 120° for at least three hours. The dry tubes were constricted about four inches from the bottom.

Approximately 0.5 g. of the β-ferrocenylalkyl p-toluene-sulfonate was weighed into a 50.00 ml. volumetric flask. The solid tosylate was dissolved in a small amount of purified acetic acid (76); the flask was then filled to the mark. Aliquots (5.00 ml.) of this solution were pipetted into the previously prepared tubes. Special care was taken to treat the samples, within a run, identically with respect to air exposure and temperature. Nine aliquots were prepared (eight points plus an infinity titer); these were then sealed with ground glass stoppers and frozen in liquid nitrogen. The sample tubes were attached to the degassing apparatus (Figure 16) by means of the ground glass joint. After the aliquots were cooled at -196° for fifteen minutes, the tubes were evacuated until the pressure inside was less than one micron. The vacuum line was then disconnected from the sample tubes by closing the stopcocks on the degassing apparatus, and the solutions were thawed at room temperature. This alternate freeze-evacuation cycle was repeated twice (a total of three

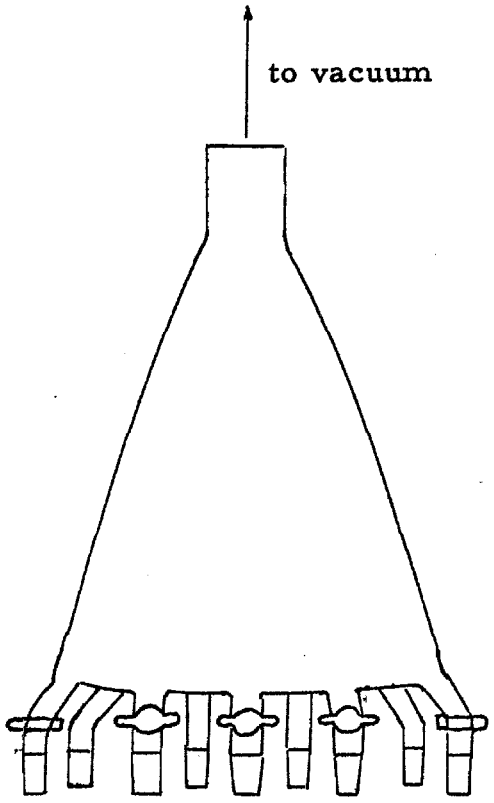

Fig. 16 Degassing apparatus

evacuations). After the final evacuation, the cold sample tubes were sealed at the constriction.

This procedure eliminated acid-promoted atmospheric oxidation in acetic acid solutions of methylferrocene, which were thermostated at typical solvolysis temperatures (60°) for extended periods of time.

The frozen samples were thermostated at the desired temperature, which was maintained to ±0.01°. An initial point was withdrawn fifteen minutes after the ampoules had been thermostated. All samples were quenched by shaking the ampoule in and ice slush for one minute; time was recorded at the instant the ampoule was removed from the thermostat. After the cold ampoule was opened, the contents were poured into a 150 ml. beaker, which contained ca. 20 ml. of purified acetic acid. The ampoule was then rinsed three times with purified acetic acid, and the washings were added to the beaker.

The liberated toluenesulfonic acid was titrated potentiometrically (Leeds and Northrup pH Indicator) with 0.2 N sodium acetate in acetic acid (19). A capillary buret was used which could be read accurately to 0.002 ml., and had a total volume of 1.000 ml. The buret tip was submerged under the surface of the stirred solution during the titration. Endpoints were determined from a plot (Figure 17) of potential versus volume of base added. Control experiments with acetic acid solutions of p-toluenesulfonic acid showed that endpoints could be reproduced to ±3% over the p-toluenesulfonic acid concentration range of a typical solvolysis. The normality of the

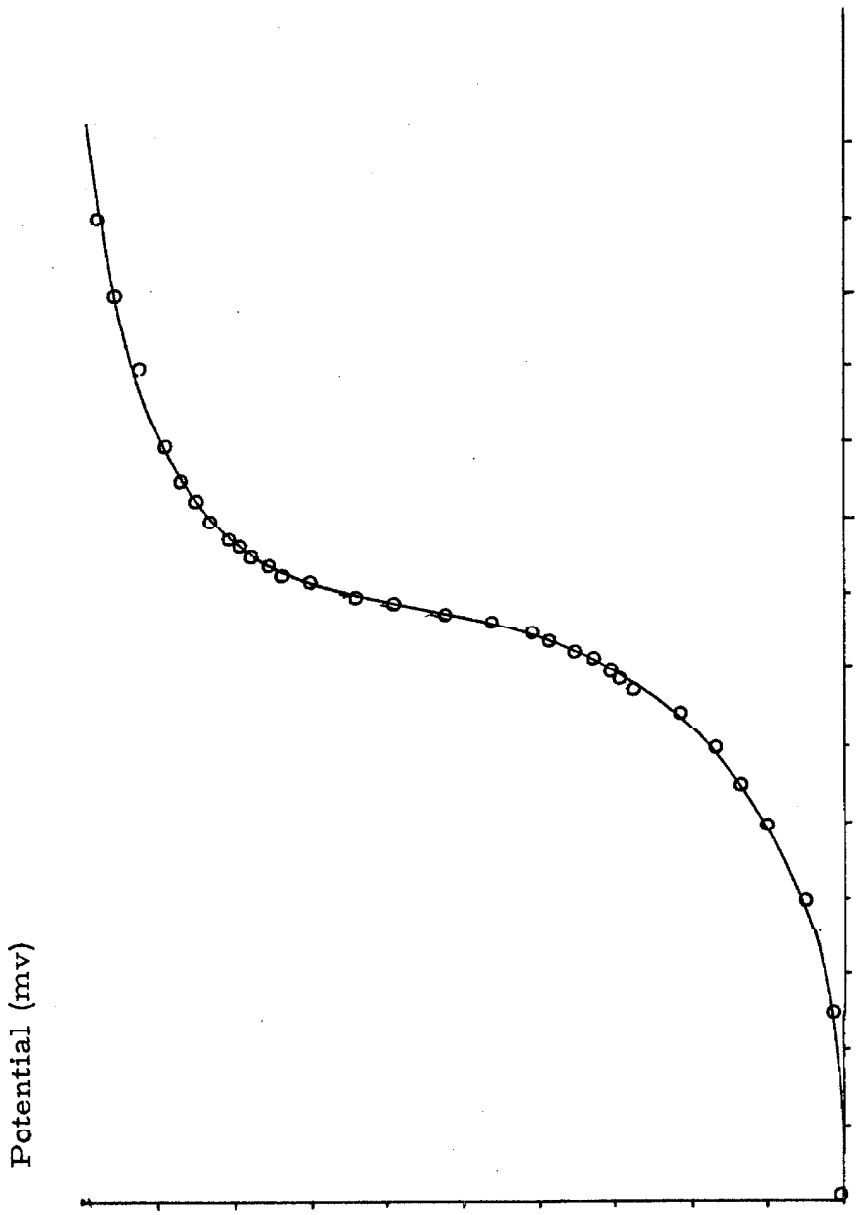

Fig. 17 Potentiometric titration curve for acetolysis of α-<u>exo</u>-tosyloxy-methyl-1,2-tetramethyleneferrocene

sodium acetate titrant was checked periodically with standardized perchloric acid in acetic acid solvent. The perchloric acid solution was standardized against potassium acid phthalate in acetic acid.

Because extensive acetolysis of α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene occurred at room temperature, two different sampling methods were used for the measurement of this rate. The multiple ampoule technique, described above, was modified so that the sample tubes were evacuated only once before they were sealed. Even with this change, however, only the latter half of the reaction could be monitored. In order to take measurements during the first half life, the acetic acid solvent and the endo tosylate were degassed separately in a specially constructed sample container (Figure 18). A 0.5 g. sample of the tosylate was placed in the small tube, and 50.00 ml. of acetic acid was pipetted into the large one. The joint at the top of the large compartment was sealed with a rubber serum cover, and the apparatus was attached to the vacuum system by means of the ground glass joint above the small sample compartment. The acetic acid was degassed three times, as described above, and the apparatus sealed at the constriction. Purified nitrogen was then admitted into the ampoule, and the apparatus was thermostated at 25.07°. After fifteen minutes, the contents of the ampoule were mixed thoroughly, and consecutive aliquots (4.87 ml.) were removed by means of a syringe equipped with a calibrated deliverer. The aliquots were transferred to tubes at -196°; time was recorded when the syringe was half empty. The cold tubes were then stoppered, and the

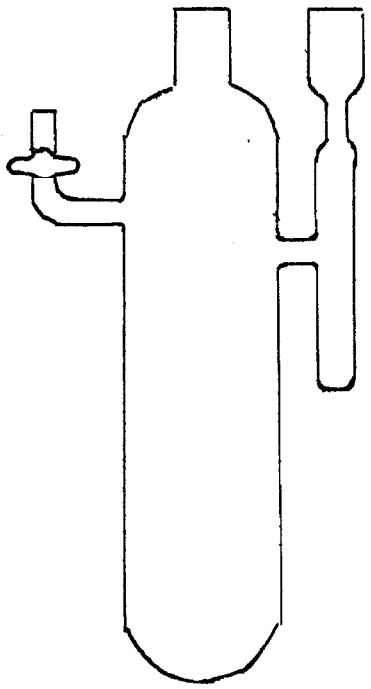

Fig. 18 Special sample and solvent ampoule

frozen samples stored in an ice bath. The aliquots were removed from the tubes with a spatula while they were still frozen and added to ca. 25 ml. of acetic acid in a 150 ml. beaker. The tube was then rinsed twice with acetic acid and the washings were added to the beaker. The liberated p-toluenesulfonic acid was then titrated as described above.

Data Treatment

Rate constants for the acetolysis of these β-ferrocenyl p-toluenesulfonates were obtained from unweighted least squares plots of the data according to the equation:

$$\ln \frac{[H^+]_f}{[H^+]_f - [H^+]} = kt$$

where $[H^+]_f$ is the experimental value of the titer after ten half lives. The initial acid concentration at time t = 0 was subtracted from all subsequent values. Straight lines were obtained in all cases (see Figure 19). The number of kinetic runs, at a given temperature, was dictated by the standard deviation of consecutive values of the rate constant. A satisfactory value of the standard deviation was arbitrarily chosen as 7% or less. Two to four runs were usually necessary to achieve this value. In the case of the very reactive α-endo-tosyloxymethyl-1,2-tetramethyleneferrocene, the standard deviation was much larger than 7%. The reason for this is that only the latter half of the reaction could be monitored when the multiple ampoule technique was used; thus, the rate constant was based on

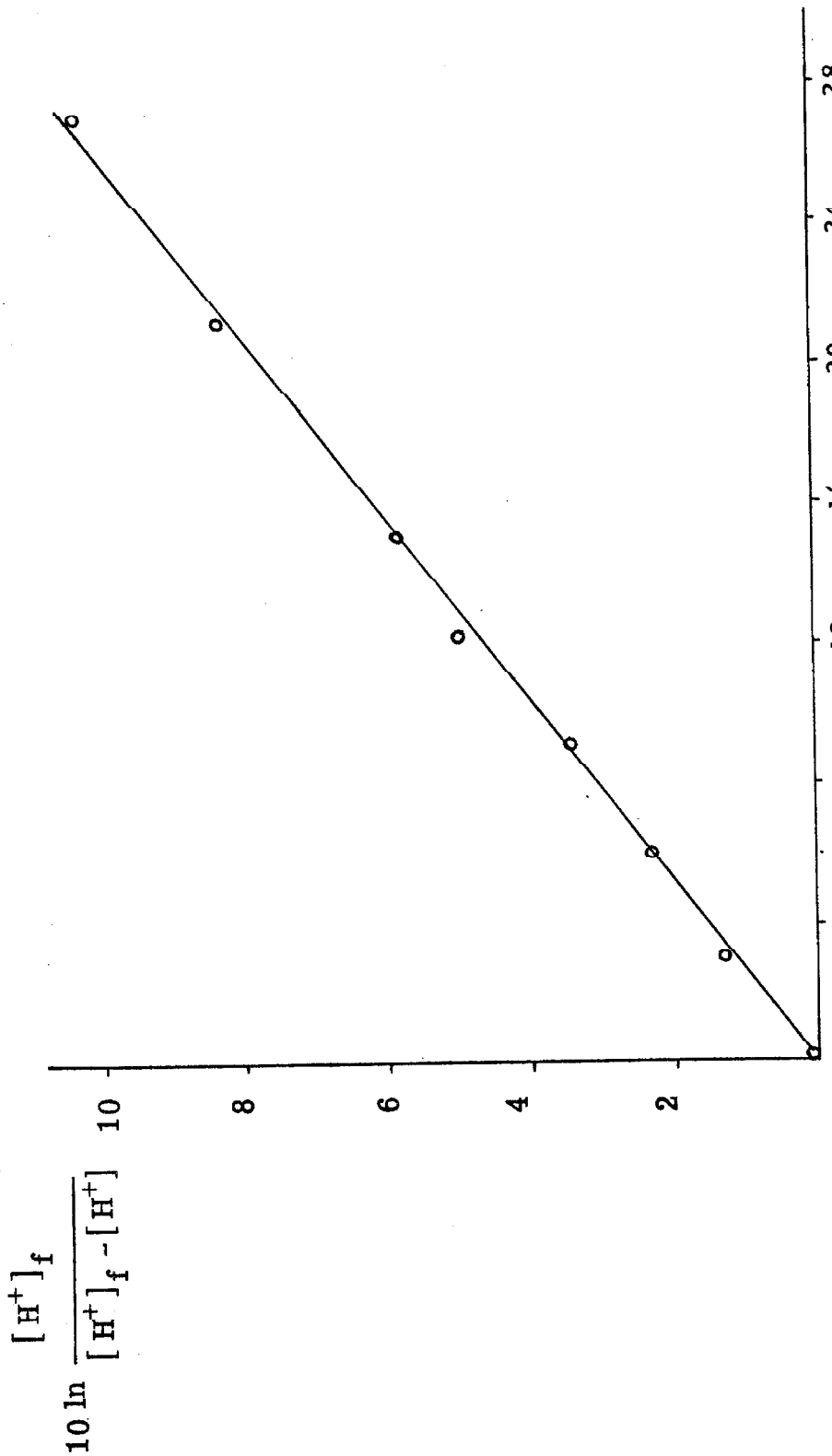

Fig. 19 Rate plot for acetolysis of α-exo-tosyloxymethyl-1,2-tetramethyleneferrocene (XX) at 100.08°.

small differences between large numbers and therefore subject to large errors. When the single ampoule technique was used, the fast acetolysis rate made the hypodermic sampling method awkward and impractical. In this latter case, large errors were apparent from the fit of the data.

Activation parameters were obtained from the equation (77):

$$k = \frac{k_B T e^{S^*/R} e^{-H^*/RT}}{h}$$

where k is the rate constant for solvolysis of the tosylate, and k_B is the Boltzmann constant.

Acetolyses

2-Ferrocenylethyl p-toluenesulfonate

The sulfonic ester (0.623 g., 1.64 mmoles) was dissolved in 10 ml. of purified acetic acid (76) and degassed according to the procedure described above (see p. 24). The sample was then thermostated at 50°. After ten half lives, the ampoule was opened, and the acetic acid solutions poured into a mixture of ligroin and aqueous sodium bicarbonate. Ascorbic acid was added to the basic solution to reduce ferricinium compounds; these probably resulted from oxidation of ferrocene by carbonium ion intermediates (p. 28), since it has been shown (see p. 110) that no atmospheric oxidation occurs in these systems. Thin layer chromatography, on silica gel in a 1:9 acetone-hexane solvent system, showed that three different compounds

were present: 2-ferrocenylethyl acetate, a very small amount of another compound which was not separable from the acetate, and 2-ferrocenylethanol. This alcohol was not present in reaction mixtures which were not treated with sodium bicarbonate solution; therefore, it results from hydrolysis of the acetate by the basic bicarbonate solution. In addition to the products separated by thin layer chromatography, a small amount (30 mg.) of a ligroin-insoluble, white powder was obtained from this solvolysis; this material was not identified. Larger scale separation of the acetolysis products was achieved by chromatography on grade III, neutral alumina. The products were identified by comparisons of their infrared spectra with those of authentic samples. The combined yield of 2-ferrocenylethyl acetate and 2-ferrocenylethanol was 94.3%. This yield has been corrected for chromatographic column loss, but not for the small amount of impurity present. The yield of p-toluenesulfonic acid, from the acetolysis data, was 93.8 ± 0.6%. This latter yield was independent of the acetolysis temperature over a 20° range.

(-)-1-Ferrocenyl-2-propyl p-Toluenesulfonate

The optically active tosylate (0.416 g., 1.04 mmoles, $\alpha_D^{27} = -57.9 \pm 0.5°$, c = 3 in carbon tetrachloride) was dissolved in 5 ml. of previously purified acetic acid (76) and degassed as described above (see p. 24). After ten half lives, the sample tube was opened and poured into 5 ml. of pyridine. Solvent was removed at reduced pressure, and the resulting oil was chromatographed on grade III, neutral alumina. The product was eluted from a small, immobile,

yellow band with 1:1 methylene chloride-hexane. This material was identified as (-)-1-ferrocenyl-2-propyl acetate by infrared spectral comparison with an authentic sample. This ester, obtained in 90% yield, had $\alpha_D^{26} = -64.0 \pm 2.2°$ (c = 5.5, carbon tetrachloride). This rotation corresponds to 100% retention of configuration. No noticeable oxidation took place during the acetolysis of either this optically active, or the corresponding racemic secondary tosylate. However, the yield of p-toluenesulfonic acid, calculated from the rate data for racemic 1-ferrocenyl-2-propyl p-toluenesulfonate, was 94.3 ± 0.6%. This latter yield was also independent of the acetolysis temperature.

2-Ferrocenyl-1-propyl p-Toluenesulfonate

A solution of 0.590 g. (1.48 mmoles) of 2-ferrocenyl-1-propyl p-toluenesulfonate in purified acetic acid (76) was degassed as described above. After the solution had been thermostated at 60.0° for eleven hours (ten half lives of 2-ferrocenylethyl p-toluenesulfonate), it was added to 25 ml. of dry pyridine and evaporated to dryness at 30° (1 mm.). The residue was chromatographed on grade III, neutral alumina. Only one colored band formed. This band was eluted with hexane, and no further separation was achieved by thin layer chromatography on silica gel in a 1:9 acetone-hexane solvent system. Control experiments indicated that 2-ferrocenyl-1-propyl acetate would not be separated from 1-ferrocenyl-2-propyl acetate by these methods. The infrared spectrum of this product and the n.m.r. spectrum can be completely described as a composite of the spectra of the isomeric 1-ferrocenyl-2-propyl and 2-ferrocenyl-1-propyl acetates. There is

no spectral evidence of the presence of any other acetates. This experiment was repeated with an acetic acid solution of 0.300 g. (0.753 mmoles) of tosylate which was thermostated at 60.0° for twenty-two hours. Spectral analysis of this reaction mixture showed that both the primary and secondary acetates were present in nearly identical amounts. The overall yield of acetate product was 85%.

α-endo-Tosyloxymethyl-1,2-tetramethyleneferrocene

No specific acetolysis experiment was carried out in this case; instead, the products were recovered from the acetolysis mixtures, which had been used for kinetic determinations. Each titrated aliquot of the reaction mixture was poured into a solution of potassium carbonate in aqueous acetone. A period of two weeks elapsed between neutralization of the first aliquot and isolation of the products. The basic solution was extracted with ether until the aqueous layer was colorless. The ethereal extract was dried over sodium sulfate and evaporated to yield a brown oil, which was chromatographed on grade III, neutral alumina. The product, α-endo-acetoxymethyl-1,2-tetramethyleneferrocene was eluted with hexane in 80% yield; 10% of the unrearranged alcohol was also obtained. A small amount of decomposed material remained at the top of the column. The yield of p-toluenesulfonic acid from this endo tosylate was 96.8 ± 0.6%. This yield was also independent of the acetolysis temperature.

α-exo-Tosyloxymethyl-1,2-tetramethyleneferrocene

The products of this acetolysis were isolated in the manner described above for the endo isomer. A period of ca. eight days

elapsed between the titration of the first aliquot and the isolation of the acetolysis products. Chromatography of the reaction mixture (1.79 g.) on grade III, neutral alumina produced three bands. The first band, eluted with hexane, was an orange oil (30 mg.), which exhibited broad infrared absorption from 1000 to 1125 cm^{-1}, and had no other absorptions indicative of any functional groups. This material was not identified. The second band eluted with hexane was a solid, (350 mg.), which melted at 79.0-80.5 after three crystallizations from hexane. This material was shown by mass spectral analysis to have a molecular weight of 311 ± 2; this spectrum also exhibited a high intensity peak at m/e 252. The infrared spectrum of this product showed absorptions at 1003 and 1107 cm^{-1} indicative of a homoannularly substituted ferrocene; acetate absorptions were at 1250 and 1735 cm^{-1}. Spectral comparisons showed that this material was not α-exo-acetoxymethyl-1,2-tetramethyleneferrocene. The n.m.r. spectrum is shown in Figure 4.

Anal. (Sp) Calcd. for $C_{17}H_{20}O_2Fe$: C, 65.40; H, 6.46; Fe, 17.89.
Found: C, 65.20; H, 6.47; Fe, 17.96.

The third band (1.11 g.) was eluted with 1:1 hexane-methylene chloride and was shown by mixed m.p., infrared, and n.m.r. spectral analysis to be unreacted exo tosylate starting material.

In an effort to recover any alcohols, which are usually formed under the basic work-up conditions of the other tosylate solvolysis mixtures, the tosylate obtained from chromatography and before crystallization was treated with pyridine and acetyl chloride at room

temperature for twenty-four hours. The acetylated reaction mixture was then rechromatographed; however, only tosylate was obtained, no traces of other acetates were evident. The purity and quality of all of these separations were checked by thin layer chromatography on silica gel in a 9:1 hexane-acetone solvent system.

Hydrolyses

2-Ferrocenylethanol-1, 1-d_2

The deuterated alcohol (0.168 g., 0.724 mmoles) was dissolved in 0.5 ml. of acetone d_6 (Merck Sharp and Dohme) in a culture tube, which had been fitted with a 19/38 female, ground glass joint. The acetone solution was frozen at -196°, and 0.05 g. (429 mmoles) of benzenesulfonic acid in 0.125 ml. of deuterium oxide was added to the frozen solution. The sample tube was then attached to a vacuum system, by means of the ground glass joint, and the reaction mixture was degassed as described above (see p. 107). Equilibration between the protonated alcohol and the carbonium ion was allowed to proceed at room temperature. After ca. eight half lives (see p. 71) the ampoule was opened, and the reaction mixture was percolated through sodium carbonate onto a column of grade III, neutral alumina. The starting alcohol was recovered in 59.5% yield together with 20 mg. of an unidentified, non olefinic ferrocene compound. This material is probably a short chain polymer, which results from an acid catalyzed reaction of vinylferrocene (72). Examination of the product alcohol by n.m.r. spectroscopy showed that the ratio of ring proton to β

methylene proton resonances was 4.3 ± 0.2. The calculated value, based on the assumption that there is no deuterium attached to the β carbon atom is 4.5. The experimental ratio was calculated from ten integrals of the n.m.r. spectrum of the product alcohol (Figure 11). The n.m.r. spectrum of this product also shows no resonance due to hydrogen attached to the α carbon atom.

(-)-1-Ferrocenyl-2-propyl p-Toluenesulfonate

The sulfonic ester (0.374 g., 0.939 mmoles, α_D^{27} = -57.9 ± 0.5°) was dissolved in 10 ml. of 80% acetone-water (5) in a 50.00 ml. volumetric flask and thermostated at 32.0°. The reaction mixture gradually became blue because of the acid catalyzed, oxidative formation of ferricinium ion (45). A small quantity, ca. 10 mg., of ascorbic acid was added to reduce ferricinium ion; the blue color did not reappear during the remainder of the solvolysis. After ten half lives (49), pyridine (1 ml.) was added to the reaction mixture and the organic products were extracted with ether. The ethereal solution was dried over sodium sulfate and chromatographed on grade III, neutral alumina. The alcohol, thus obtained, was reconverted to the tosylate (see p. 7). One crystallization from hexane produced yellow needles of the sulfonate ester, which melted at 77-79° and had α_D^{23} = -57.4° (c = 1.1, carbon tetrachloride). This rotation corresponds to 100% retention of configuration. The overall yield of tosylate was 51%.

Hydrogen Bonding Study

All measurements were made on a Beckmann IR-7 grating spectrophotometer. The region between 3300 and 3800 cm^{-1} was examined on the double beam instrument at a scanning speed of 6.4 cm^{-1}/min. The resolution was 5 cm^{-1}, and the tracking error was less than 2%.

Spectra were obtained for both 0.01 and 0.005 M carbon tetrachloride solutions of the alcohol according to the procedure described by Kuhn (78) and Trifan and Bacskai (12). Circular, 10 mm. silica cells (No. S-22-350, Pyrocell Manufacturing Company) were used for these measurements. Although these cells transmit 90% of the light in this hydroxyl region, a weak, broad absorption did occur at 3715 cm^{-1} because the cells used were not a matched pair.

The concentration independent absorptions of α-endo-hydroxymethyl-1,2-tetramethyleneferrocene, in the hydroxyl region, were at 3527 and 3643 cm^{-1}. These absorptions can be assigned to the iron-hydroxyl hydrogen bond, and the free hydroxyl absorptions respectively (12). The exo isomer had absorptions at 3606 and 3644 cm^{-1}, which can be assigned to the π-bonded and free hydroxyl absorptions respectively (12).

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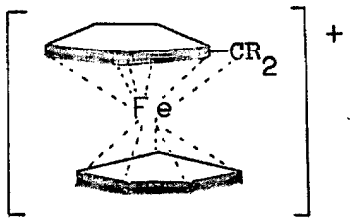
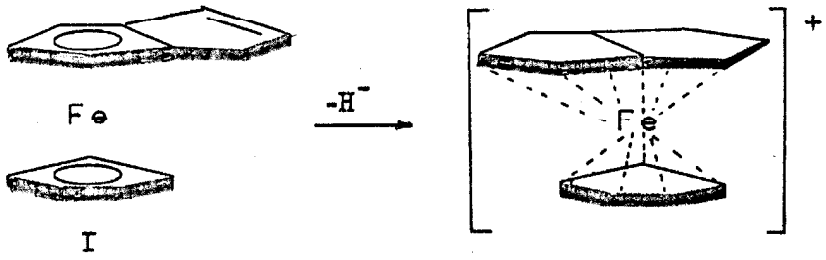
PROPOSITION I

A simple synthesis of 1, 2-ferrocenocyclopent-4-ene (I) is proposed.

The ability of a carbon atom adjacent to a metallocene ring to sustain positive charge is well documented (1, 2), and has been shown to result from stabilization of this electron-deficient carbon by the interannular electrons of the ferrocene system. A molecular orbital description of this carbonium ion has been proposed, in which the ring bearing the carbinyl carbon is shifted with respect to the rest of the molecule so that overlap between an interannular iron orbital and the vacant carbon p orbital can readily occur (1).



It has been suggested that this ring shift can be detected by examination of the carbonium ion derived from 1, 2-ferrocenocyclopent-4-ene (I), since this ion may be expected to have equivalent, electron-deficient fused rings (3).



The synthesis of I is not straightforward since it has been shown that 3-ferrocenylpropionic acid when treated with polyphosphoric acid gives only 1, 1'-(α-oxo-trimethylene)-ferrocene (4). This result strongly implies that synthetic routes to I which are based on intramolecular, electrophilic ring substitution will not be successful.

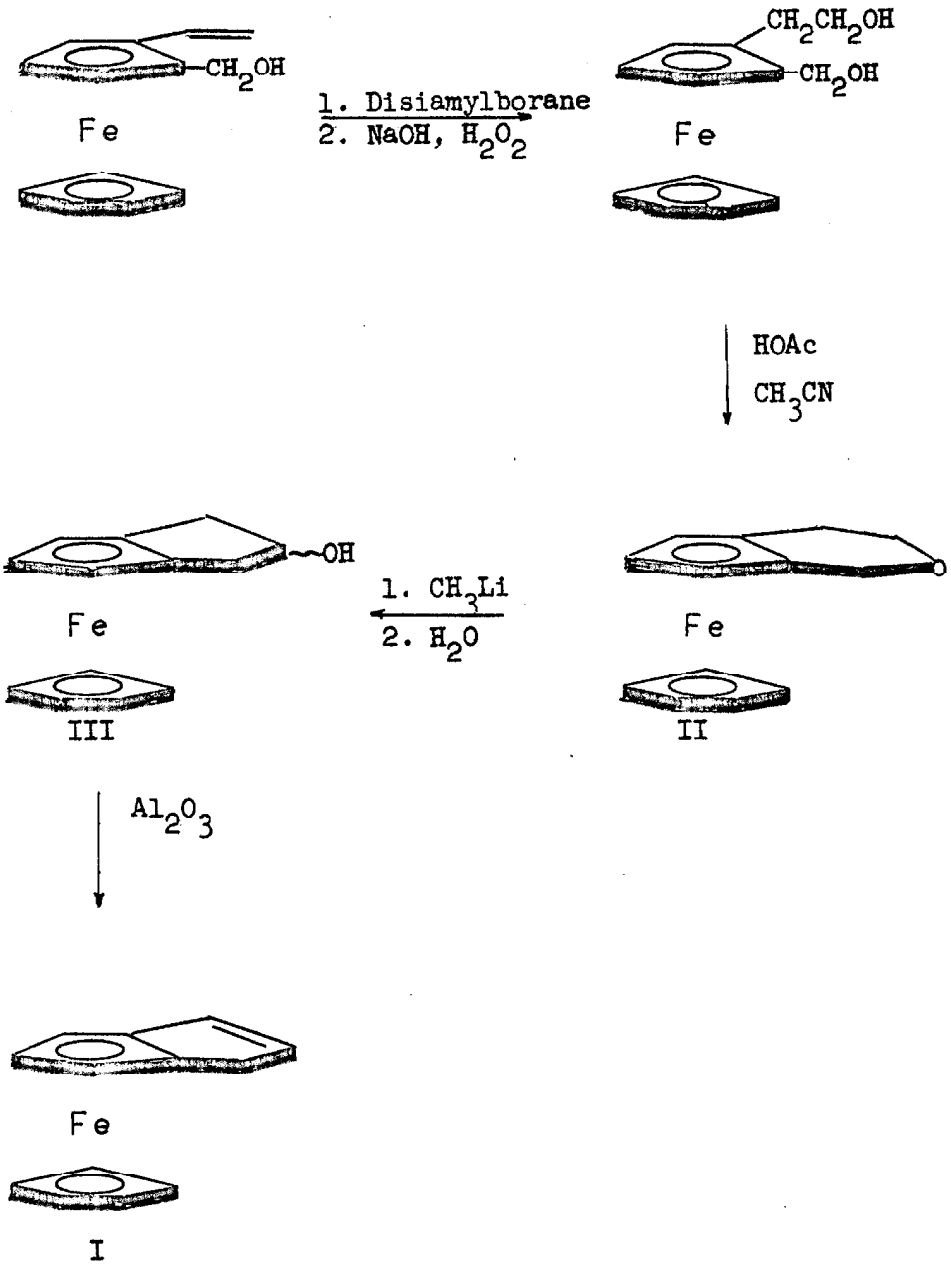
A synthetic sequence for the preparation of I beginning with 1-vinyl-2-hydroxymethylferrocene (5) is shown in Chart I.

The first step is a simple hydroboration with disiamylborane. That the terminal alcohol will be the major product is indicated by the fact that hydroboration of styrene with disiamylborane gives 98% 2-phenylethanol and only 2% 1-phenylethanol (6).

The second step in this synthesis has not been previously carried out. However, the facile preparation of ferrocenylcarbinylmethyl ether from ferrocenylcarbinol and methanol in the presence of a catalytic amount of acetic acid suggests that this intramolecular cyclization will not be difficult (7).

The Wittig rearrangement of 1, 2-ferroceno-4-oxacyclohexane (II) to alcohol III is the key step in this synthetic sequence. The

Chart I


CH2OH
Fe
1. Disiamylborane
2. NaOH, H2O2
CH2CH2OH
CH2OH
Fe
HOAc
CH3CN
OH
Fe
III
1. CH3Li
2. H2O
Fe
II
Al2O3
Fe
I

ability of ferrocenylcarbinyl ethers to undergo this rearrangement has recently been established (8). Although the yields are not large in this reaction (ca. 25%), unchanged starting material is recovered so that high conversions to alcohol III can be attained.

The product olefin 1, 2-ferrocenocyclopent-4-ene (I) can be easily prepared by low temperature dehydration of the secondary alcohol III with alumina. This procedure is a standard method for the preparation of olefins from ferrocenylcarbinols (9).

References for Proposition I

1. E. A. Hill and J. H. Richards, J. Am. Chem. Soc., 83, 3840 (1961).

2. E. A. Hill and J. H. Richards, J. Am. Chem. Soc., 83, 4216 (1961).

3. This experiment was suggested by Professor J. D. Roberts.

4. K. L. Rinehart and R. J. Curbey, J. Am. Chem. Soc., 79, 3290 (1957).

5. D. Lednicer and C. R. Hauser, J. Org. Chem., 24, 43 (1959).

6. G. Zweifel, N. R. Ayyangar and H. C. Brown, J. Am. Chem. Soc., 85, 2072 (1963).

7. A. N. Nesmeyanov, E. G. Perevalova and Yu. A. Ustynyuk, Doklady Akad. Nauk., SSSR, 133, 1105, English Translation, p. 921.

8. Uy. A. Ustynyuk, E. G. Perevalova and A. N. Nesmeyanov, C. A., 60 : 9310 g (1964) [Izv. Akad. Nauk., SSSR, Ser. Khim., 1964, 70].

9. K. Schogl and A. Mohar, Monatsh. Chem., 92, 233 (1961).

PROPOSITION II

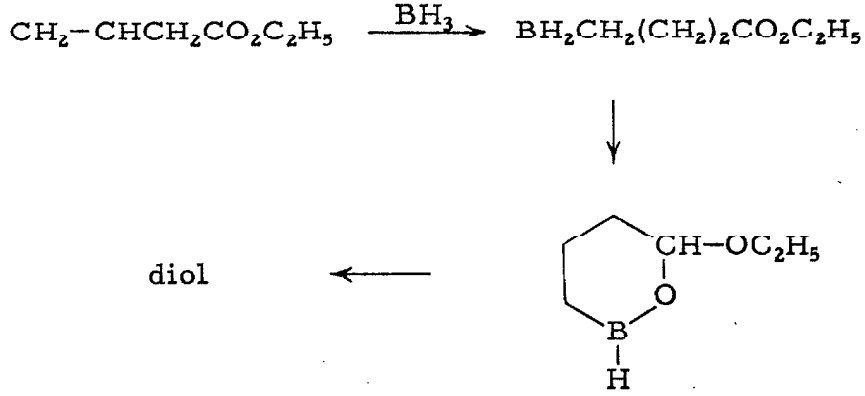
It is proposed that the reaction of diborane with the anti (I) and syn (II) isomers of 7-carboethoxynorbornene be examined in order to establish the stereochemistry of the addition of the hydrogen-boron bond of diborane to these alkenes.

The facile synthesis of organoboranes from the reaction of diborane with various alkenes and the easy conversion of these organometallics to alkanes and alcohols has become a preparative method of considerable utility (1). The addition of diborane to alkenes and subsequent protonolysis with carboxylic acids or hydrolysis with hydrogen peroxide has been shown to result in overall cis addition of hydrogen or water to the double bond (2). Unfortunately, the stereochemistry of the protonolysis or hydrolysis is not known so that the stereochemistry of the addition of the hydrogen-boron bond to the carbon-carbon double bond has not been unambiguously determined (2); however, the stereochemistry of this addition can be established for the 7-carboethoxynorbornene system by utilizing a recently described reaction between unsaturated esters and diborane (3).

The reaction of diborane with esters is usually much slower than the addition of diborane to alkenes. Consequently, it is often possible to achieve selective reduction of the carbon-carbon double bonds of unsaturated esters by using this reagent (4). It has recently been observed, however, that during the hydroboration of several

unsaturated esters the rate of consumption of hydride,* in excess of that needed to reduce the carbon-carbon double bond, is much faster than excess hydride consumption in equimolar synthetic mixtures of 1-hexene and ethyl benzoate. In addition, large quantities of diol resulting from reduction of both the ester and the double bond are obtained from the more reactive unsaturated esters after hydrolysis of the organoborane with hydrogen peroxide.

These results have been attributed to an intramolecular cyclization of initially formed organoborane, which effectively competes with intermolecular addition of this organoborane to another alkene molecule. This reaction can be formulated for ethyl 3-butenoate as

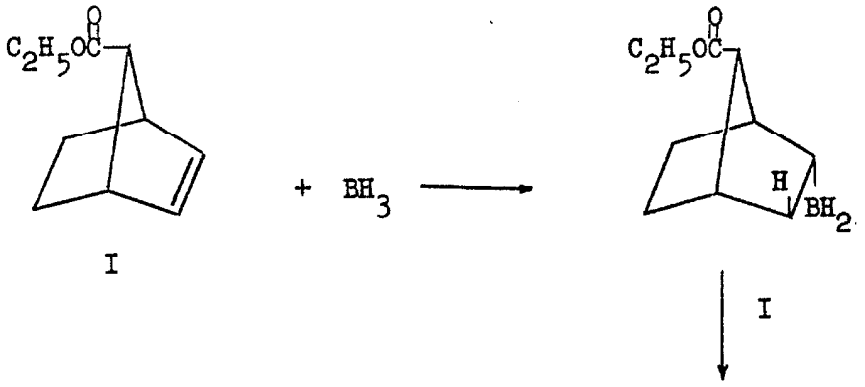


The fastest rate of excess hydride consumption is observed with ethyl 3-butenoate which can form a six-membered ring by this

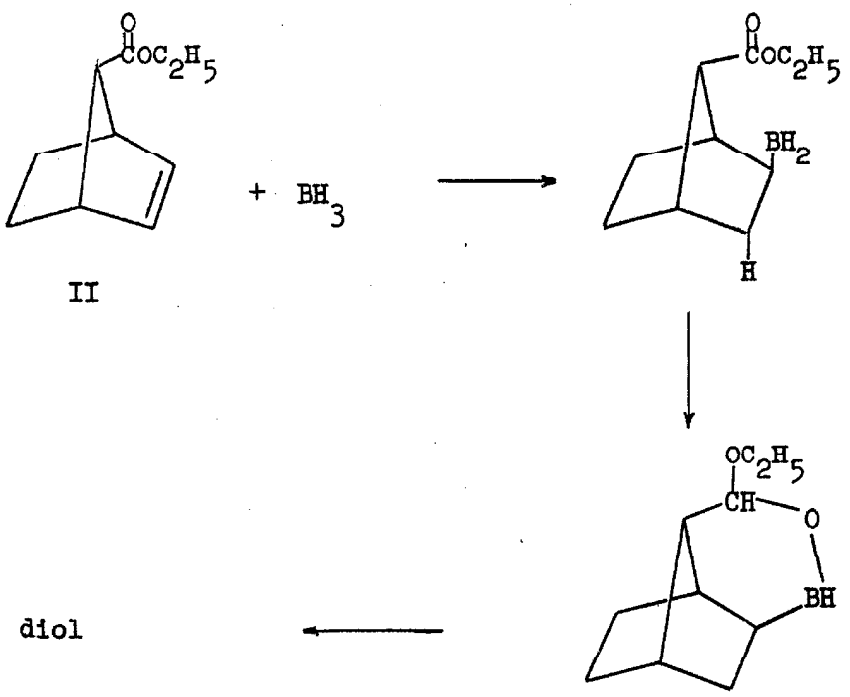
*The stoichiometry of hydroboration is conveniently discussed in terms of hydride consumption. One mole of borane, BH_3, contains three hydrides (3).

intramolecular cyclization. A slower rate is observed for ethyl 10-undecenoate, which would necessarily form a thirteen-membered ring to undergo intramolecular cyclization. Thus, each mole of this latter unsaturated ester utilizes only 1.3 moles of hydride after four hours, while each mole of ethyl 3-butenoate consumes more than two moles of hydride in the same time interval.

This intramolecular cyclization can be used to advantage in determining the stereochemistry of addition of diborane to the anti (I) and syn (II) isomers of 7-carboethoxynorbornene. For trans addition of diborane, with hydrogen adding to each of these unsaturated esters from the least hindered side,* the reactions are



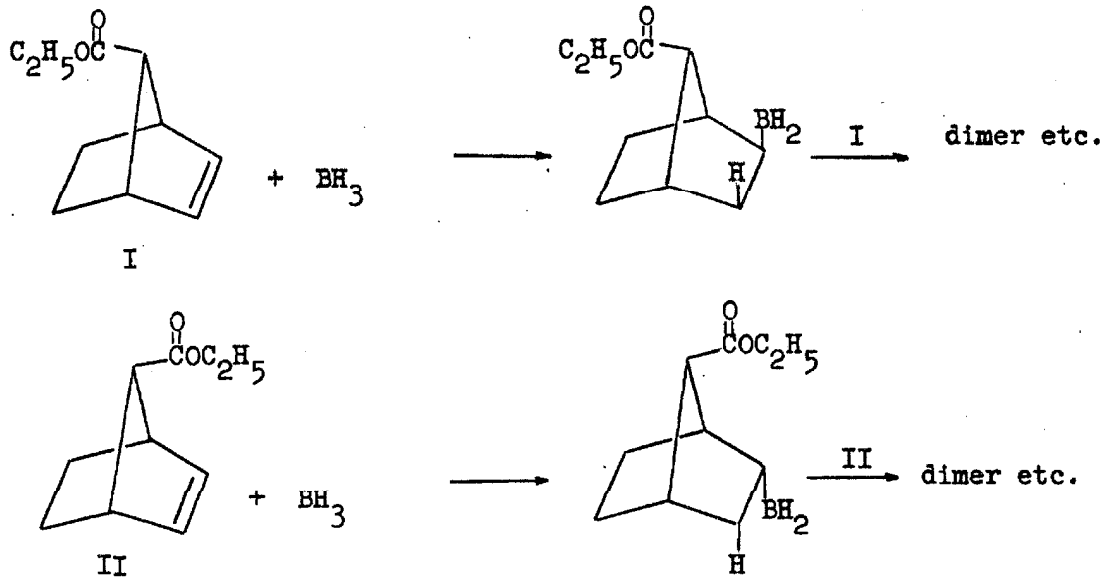
*It has been established that addition of hydrogen to norbornene during the hydroboration step proceeds exclusively from the exo direction (5). It is anticipated that hydrogen addition to anti-7-carboethoxynorbornene will occur in an analogous manner; whereas hydrogen will add to the syn isomer (II) from the endo direction because of the bulky carboethoxy group at the 7 position. The validity of these conclusions can be tested by examination of the products resulting from deuteroboration of these unsaturated esters by the method described in reference 5.



Thus if trans addition of the boron-hydrogen bond occurs, it will be expected that the rate of excess hydride consumption for the syn isomer (II) will be greater than the rate for the anti isomer I. Since a six-membered ring is formed during the cyclization step in the trans addition of diborane to II, it can be anticipated that the rate of excess hydride consumption will be similar to the rate observed in the ethyl 3-butenoate system. The rate of excess hydride consumption for the anti isomer will be similar to that observed for the equimolar synthetic mixture of 1-hexene and ethyl benzoate.

For cis addition of diborane, neither the anti (I) or syn (II) isomers of 7-carboethoxynorbornene can undergo intramolecular

cyclization.



Therefore, the rates of excess hydride consumption should be almost identical for the syn and anti isomers, and should correspond closely to the rate of excess hydride consumption observed for the 1-hexene-ethyl benzoate mixture if cis addition of diborane occurs.

References for Proposition II

1. H. C. Brown, Hydroboration, 1st ed., W. A. Benjamin, Inc., New York, 1962.

2. Reference 1, pp. 129 and 130.

3. H. C. Brown and K. A. Keblys, J. Am. Chem. Soc., 86, 1795 (1964).

4. Reference 1, p. 272.

5. H. C. Brown and K. J. Murray, J. Org. Chem., 26, 631 (1961).

PROPOSITION III

It is proposed that β-deuterium isotope effects be determined for the formolysis of various para-substituted 1-phenyl-2-propyl p-toluenesulfonates with deuterium label at the 3 position. These isotope effects when compared with the stereochemistry of these solvolyses will provide useful information regarding the significance of secondary isotope effects in phenyl-bridged systems.

Secondary deuterium isotope effects have been extensively used to elucidate the geometry of transition states in solvolysis reactions which proceed via formation of carbonium ion intermediates (1). The secondary α-deuterium isotope effect for these S_N1 solvolyses is remarkably constant with the protium compound solvolyzing ca. 15% faster than the deuterium derivative (2). This isotope effect of the first kind* is usually associated with conversion of an initially tetrahedral carbon, which bears the leaving group, to a more nearly trigonal electron-deficient carbon atom in the transition state of these solvolysis reactions.

The usual effect of β-deuterium substitution on S_N1 solvolyses is also rate-retarding; however, the origin of this solvolytic isotope effect of the second kind* is probably not the same as that of the secondary α-deuterium effect in simple systems, since bond rupture

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*An isotope effect of the first kind is defined as one in which the bonds to isotopic atoms have undergone spatial reorientation; an effect of the second kind does not involve spatial reorientation of the carbon deuterium bonds (3).

occurs only at the α carbon atom. The hydrolyses of 1-p-tolylethyl-1-d and 1-p-tolylethyl-2, 2, 2-d_3 chlorides illustrate these formal differences.

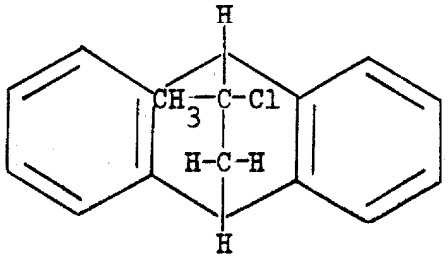
α-deuterium isotope effect (effect of the first kind)

$$C_6H_5CD(Cl)CH_3 \xrightarrow{-Cl^-} C_6H_5\overset{+}{C}DCH_3 \xrightarrow{80\% \text{ acetone}} C_6H_5CD(OH)CH_3$$

β-deuterium isotope effect (effect of the second kind)

$$C_6H_5CH(Cl)CD_3 \xrightarrow{-Cl^-} C_6H_5\overset{+}{C}HCD_3 \xrightarrow{80\% \text{ acetone}} C_6H_5CH(OH)CD_3$$

Since the magnitude of the β-deuterium isotope effect is not constant even in limiting solvolyses, but depends on the nature of the solvolysis system (4), the connection between solvolysis mechanism and β-deuterium isotope effect has not been well established. A notable improvement in this situation has resulted from the elegant demonstration by Shiner and Humphrey (5) of the dependence of the β-deuterium isotope effect on hyperconjugation. The hydrolysis of 11-methyl-11-chloro-9, 10-dihydro-9, 10-ethanoanthracene (I) has a β-deuterium isotope effect of $k_H/k_D = 1.14$ when the methylene group in the carbon bridge is deuterated; however, when deuterium is substituted for hydrogen at the tertiary, bridgehead positions, the isotope effect is small and inverted ($k_H/k_D = 0.986$).



I

The β-deuterium isotope effect at the methylene group in the carbon bridge is explained by the fact that these carbon-hydrogen bonds nearly bisect the nodal plane of the developing p orbital of the electron-deficient carbon atom (Figure 1) so that hyperconjugative stabilization of the solvolytic transition state can readily occur. The bridgehead carbon-hydrogen bonds, however, are not suitably located for hyperconjugation with the developing carbon p orbital (Figure 2) so that only a small inverse effect is observed.*

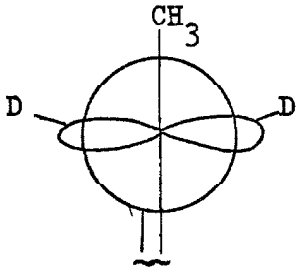


Fig. 1

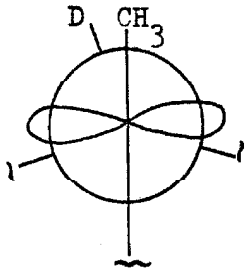
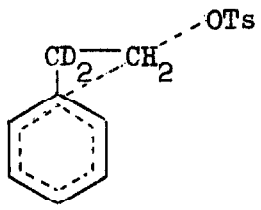


Fig. 2

*The inverted isotope effect is consistent with the electron-donating inductive effect of deuterium relative to protium (4).

Secondary kinetic isotope effects in systems involving phenyl participation are not well understood. For example, formolysis of 2-phenylethyl and 2-p-anisylethyl p-toluenesulfonates have α-deuterium isotope effects of 10-12% (2); however, substitution of deuterium for hydrogen at the β carbon atom, which bears the phenyl substituent produces no kinetic effect (6, 7). These differences in secondary α and β-deuterium isotope effects in these systems have been interpreted in terms of a transition state represented by II in which the phenyl group has not become significantly detached from the β carbon atom.

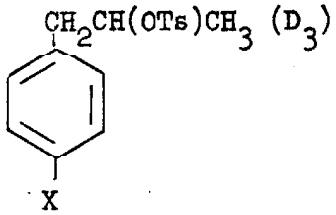


II

This interpretation explains the absence of an isotope effect of the first kind. It does not explain the absence of a secondary deuterium isotope effect of the second kind, however, since hyperconjugated stabilization by the β carbon-hydrogen σ bonds could presumably occur as long as this carbon is tetrahedral in the transition state of this reaction.

These apparently conflicting data are readily resolved by considering the importance of hyperconjugative stabilization in these

bridged transition states. Certainly, electron donation from adjacent carbon-hydrogen σ bonds will become relatively less important as other sources of electron supply, such as bridging phenyl group, become available to the electron-deficient carbon atom. The diminished importance of hyperconjugation and the resulting decrease in the β-deuterium isotope effect can be experimentally verified by determining this isotope effect for formolysis of a series of para-substituted 1-phenyl-2-propyl p-toluenesulfonates (III) in which the methyl carbon is isotopically substituted.



III

X = NO_2, Cl, CH_3CO, H, CH_3 etc.

Because the extent of phenyl participation in this system is a function of the para substituent, and can be determined by the percent retention accompanying these solvolyses (8), and since the isotope effects can be measured by independent kinetic methods, this system is suitably designed so that an unambiguous correlation can be observed.

It is anticipated that the isotope effect will decrease as anchimeric assistance (percent retention) increases thereby demonstrating that isotope effects of the second kind can be substantially reduced by neighboring group participation.

References for Proposition III

1. E. A. Halevi, "Secondary Isotope Effects" in Progress in Physical Organic Chemistry, Interscience Publishers, New York, 1963, p. 167 ff.

2. A. Streitweiser, Jr., Solvolytic Displacement Reactions, 1st ed., McGraw-Hill Book Company, New York, 1962, p. 173.

3. Reference 1, p. 111.

4. Reference 2, p. 98.

5. V. J. Shiner, Jr. and J. S. Humphrey, Jr., J. Am. Chem. Soc., 85, 2416 (1963).

6. W. H. Saunders, S. Asperger and D. H. Edison, J. Am. Chem. Soc., 80, 2421 (1958).

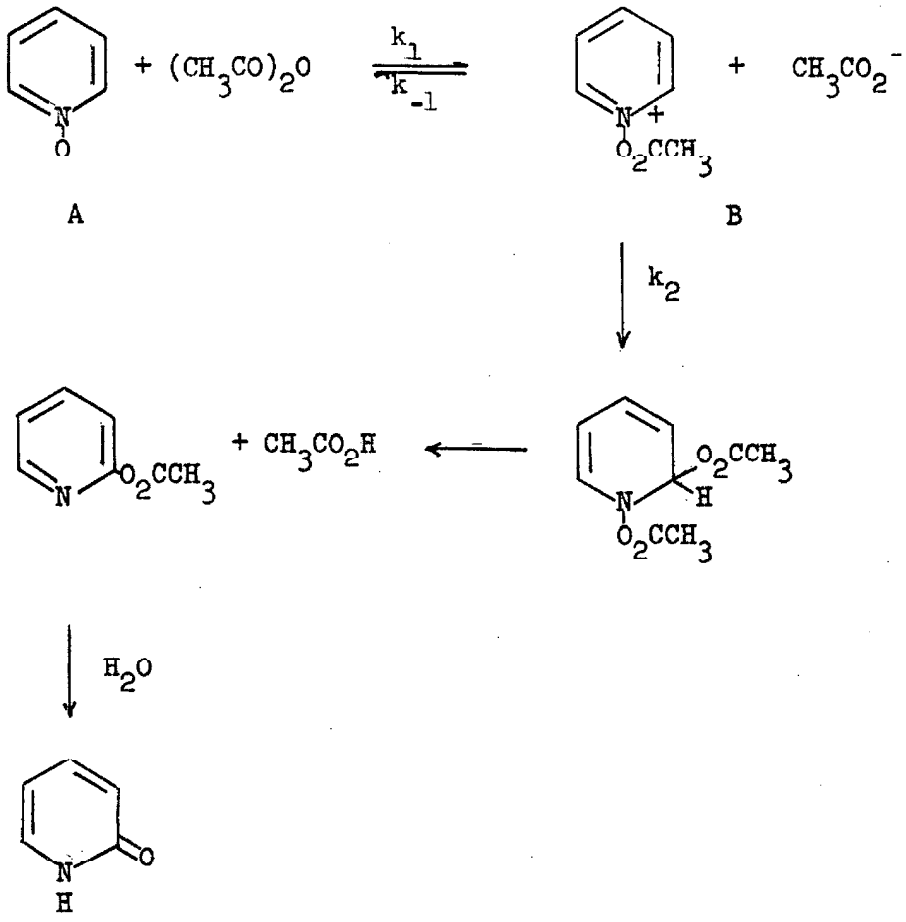
7. W. H. Saunders and R. Glazer, J. Am. Chem. Soc., 82, 3586 (1960).

8. S. Winstein, M. Brown, K. S. Schreiber and A. H. Schlesiger, J. Am. Chem. Soc., 74, 1140 (1952).

PROPOSITION IV

It is proposed that the determination of the position and relative amount of ^{18}O label in 2-acetoxypyridine and 2-pyridone, resulting from the rearrangement of pyridine N-oxide-^{18}O in acetic anhydride, will distinguish between an intramolecular cyclic mechanism and a recently proposed ionic process.

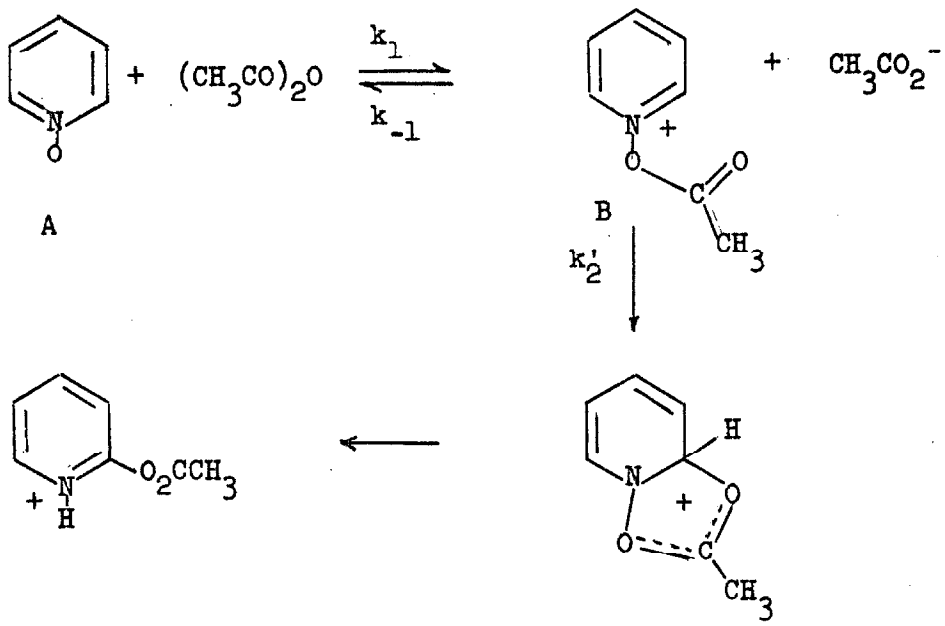
The rearrangement of pyridine N-oxide in acetic anhydride to give 2-acetoxypyridine has been formulated in terms of an ionic process which involves rate-determining attack of acetate ion on a pyridinium cation (1).



The kinetics of this reaction have been studied, and the observed first-order dependence on amine oxide concentration has been cited as evidence in support of this intermolecular mechanism (1).

$$\text{rate} = k_2[B][CH_3CO_2^-] = \frac{k_2k_1}{k_{-1}}[A][(CH_3CO)_2O]$$

For the intramolecular cyclic mechanism



it was assumed that the acetic acid produced during the course of this reaction was unionized and that the only significant contribution to the concentration of acetate ion resulted from the formation of pyridinium ion B. Then

$$[B] = [CH_3CO_2^-] = \left\{\frac{k_1}{k_{-1}}[A][(CH_3CO)_2O]\right\}^{\frac{1}{2}}$$

$$\text{rate} = k_2'[B] = k_2'\left\{\frac{k_1}{k_{-1}}[A][(CH_3CO)_2O]\right\}^{\frac{1}{2}}$$

The integrated form of this rate law was tested and found not to fit the kinetic data; therefore, this intramolecular cyclic mechanism was rejected.

The assumption that the concentration of B is equal to the acetate ion concentration is not obviously correct, since the product of this reaction is a substituted pyridine which may react with acetic acid to produce acetate ion. Therefore, the failure to observe the above rate law is not evidence against a mechanism involving unimolecular rearrangement of B. In fact, the kinetic data show that the rate of the reaction is decreased by 27 percent upon addition of tetrabutylammonium acetate (0.290 M), while a comparable concentration of sodium perchlorate reduces the rate by only 1.7 percent. These data are in accord with a rate-determining step involving rearrangement of the pyridinium ion B.

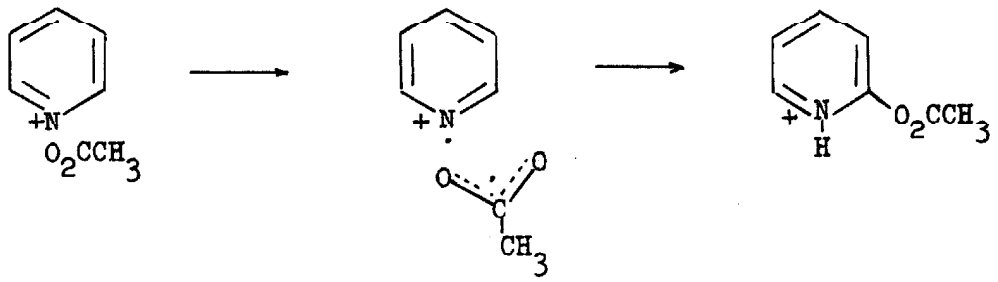
$$[B] = \frac{k_1[A][(CH_3CO)_2O]}{k_{-1}[CH_3CO_2^-]}$$

$$\text{rate} = k_2'[B] = \frac{k_2'k_1[A][(CH_3CO)_2O]}{k_{-1}[CH_3CO_2^-]}$$

An intramolecular cyclic mechanism is also suggested by the fact that in the reactions of various pyridine N-oxides, which do not have a methyl group in the 2 or 4 position, only the 2-acetoxypyridine is obtained upon treatment with acetic anhydride (2, 3, 4). If the reaction proceeded by intermolecular attack of acetate ion on the pyridinium cation, it would be expected that some 4-acetoxypyridine would be obtained, since nucleophilic substitution on pyridine N-oxides leads

to α and γ substitution in cases where the oxygen atom is coordinated with an electron-deficient species (5).

A third mechanistic possibility involves homolytic cleavage of the nitrogen-oxygen bond in B to produce a radical cation and an acetoxy radical which recombine in the solvent cage to give 2-acetoxypyridine before the acetoxy radical can decompose to give carbon dioxide and methane.



This mechanism is similar to that proposed for the rearrangement of 2-picoline N-oxide which proceeds by a homolytic cleavage of the nitrogen-oxygen bond (6). Apparently, homolysis and decomposition of acetoxy radical can occur in the unsubstituted pyridine system at higher temperatures as evidenced by the formation of carbon dioxide and methane (7).

In order to distinguish between the intramolecular cyclic and caged radical mechanisms on the one hand, and the non cyclic intermolecular ionic process on the other, it is proposed that the ^{18}O content of the products resulting from the reaction of ^{18}O labeled

pyridine N-oxide be examined.*

If the reaction is an intermolecular non cyclic process, the ^{18}O distribution in both the 2-pyridone and the 2-acetoxypyridine isolated from the reaction mixture after small conversion to product before ^{18}O label is introduced into the acetic anhydride solvent will be given by:

$$\text{atom } \%\ ^{18}O = {}^{18}O_S$$

where $^{18}O_S$ is the natural abundance of ^{18}O present in the acetic anhydride solvent.

If the rearrangement proceeds by an intramolecular cyclic process, the distribution of label will be as follows:

2-acetoxypyridine	$\text{atom } \%\ ^{18}O = \dfrac{^{18}O_N + {}^{18}O_S}{2}$
2-pyridone	$\text{atom } \%\ ^{18}O = {}^{18}O_S$

where $^{18}O_N$ refers to the atom percent oxygen label present in the amine oxide.

For the radical mechanism there are two possibilities. If the oxygen atoms of the acetoxy radical do not become equivalent with respect to the site of attack on the pyridine ring, the radical recombination occurs before rotation around the methyl-carbon, carbonyl-carbon bond, this reaction path will be indistinguishable from the

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*In order that the labeling experiment is unambiguous it is necessary to show by appropriate control experiments that ^{18}O label is not shuffled in the equilibrium between A and B, nor in equilibration of C.

intramolecular cyclic path. If however, the two oxygen atoms do become equivalent by rotation, the ^{18}O distribution will be the same for the 2-pyridone and the 2-acetoxy pyridine.

$$\text{atom \% } ^{18}O = \frac{^{18}O_N + ^{18}O_S}{2}$$

Thus by labeling the oxide oxygen of pyridine N-oxide, it will be possible to distinguish between an intermolecular non cyclic mechanism, a free radical mechanism in which the oxygen atoms become equivalent before coupling, and an intramolecular cyclic path.

References to Proposition IV

1. J. H. Markgraf, H. B. Brown, Jr., S. C. Mohr and R. G. Peterson, J. Am. Chem. Soc., 85, 958 (1963).

2. B. M. Bain and J. E. Saxton, J. Chem. Soc., 5216 (1961).

3. M. P. Cava and B. Weinstein, J. Org. Chem., 23, 1616 (1958).

4. F. C. Taylor and J. S. Driscoll, J. Org. Chem., 25, 1716 (1960).

5. A. R. Kitritzky, Quart. Revs., 10, 395 (1956).

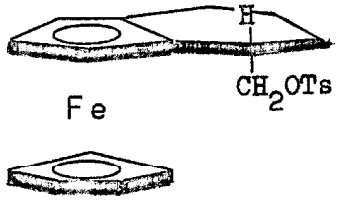
6. T. Kitao and Y. Kitaoka, J. Am. Chem. Soc., 84, 3359 (1962).

7. Reference 1, footnote 32.

PROPOSITION V

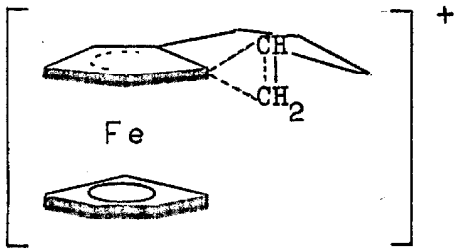
It is proposed that the rate of acetolysis of α-endo-tosyloxymethyl-1, 2-trimethyleneferrocene (III) be measured and compared with the acetolysis rate of α-endo-tosyloxymethyl-1, 2-tetramethyleneferrocene (I). This relative rate, in conjunction with the extent of rearrangement observed during the acetolysis of III, will provide evidence regarding the important structural features of the electron-deficient species involved in these solvolyses.

The partial rearrangement accompanying the acetolysis of 2-ferrocenyl-1-propyl p-toluenesulfonate has been cited as evidence for the formation of a ring-bridged β-ferrocenylalkyl carbonium ion intermediate during this solvolysis (1). For other primary β-ferrocenylalkyl systems, however, no solvolytic rearrangement occurs even though these acetolyses obviously involve participation by the neighboring ferrocene group (2). The most significant example of this latter class of compounds is α-endo-tosyloxymethyl-1, 2-tetramethyleneferrocene (I).



I

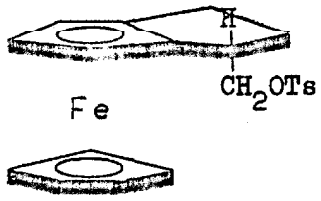
The absence of observable rearrangement in this system can be attributed to iron participation which does not involve significant contributions from ring-bridged structures, or to the possibility that nucleophilic attack at the exo carbon atom of this ring-bridged ion (II) is sterically prevented (3).



II

The steric effects which may hinder nucleophilic attack at the exo carbon atom have been associated with the presence of the fused ring system. Since the six-membered ring can cause steric constraint of this ring-bridged ion, the electron-deficient exo carbon atom may not be in the proper configuration to undergo nucleophilic attack. Solvent attack at the exo carbon atom may also be hindered by any seven-membered ring character of the transition state for neutralization of this ring-bridged ion because of the strain associated with the formation of a seven-membered ring (4). These steric effects have important implications regarding the rate and the extent of rearrangement in the α-endo-tosyloxymethyl-1,2-trimethyleneferrocene

system (III).



III

The importance of ferrocenyl ring bridging in the transition states of these two systems can be ascertained by determination of the relative acetolysis rates of the two tosylates I and III. Since the formation of a ring-bridged ion from tosylate III is probably more difficult than for tosylate I because of the constraint imposed by the fused, five-membered ring, it is expected that tosylate III will solvolyze significantly more slowly than its next higher homolog I* if ring bridging is important in the description of this transition state. If, however, ring bridging is not well developed in the transition state for these acetolyses, the solvolysis rates should be nearly identical.

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*Presumably, the acetolysis rate of tosylate III could be faster than that of tosylate I because of steric acceleration in going from a fused cyclopentene ground state to more nearly cyclohexenyl transition state.

The fused, five-membered ring may also affect the products derived from the acetolysis of tosylate III. It was mentioned above that the failure to observe rearrangement during the acetolysis of I may be due to strain associated with the transition state for nucleophilic attack at the exo carbon atom of II since some seven-membered ring character could be involved. For the ring-bridged ion derived from tosylate III, attack at the exo carbon atom would be favored by this kind of steric effect since it would involve conversion of a strained cyclopentene ring to a less strained cyclohexene ring (5). As a result, significant amounts of rearranged product, β-endo-acetoxy-1,2-tetramethyleneferrocene, would be observed.

The absence of rearrangement during the acetolysis of III would provide evidence against the importance of steric repulsions, which are associated with the product, in determining the site of nucleophilic attack on these carbonium ions, and in conjunction with the kinetic data would furnish important information regarding the best structural description of these electron-deficient species.

References for Proposition V

1. M. J. Nugent, Jr. Ph. D. Thesis, California Institute of Technology, 1965, p. 66.

2. Reference 1, p. 67.

3. This interpretation was first suggested by J. H. Richards; several of these factors have been described to the author by G. S. Hammond.

4. E. Eliel, Stereochemistry of Carbon Compounds, 1st ed., McGraw-Hill Book Company, New York, 1962, p. 189.

5. R. B. Turner and W. R. Meador, J. Am. Chem. Soc., 79, 4133 (1957).