I. STUDIES IN ISOMERISM: PERMUTATIONS, POINT GROUP SYMMETRIES, AND ISOMER COUNTING

II. STUDIES IN THE PHOTOCHEMISTRY OF COUMARIN AND CERTAIN COUMARIN DERIVATIVES

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To an exceptional succession of teachers who have known when to prod and when to leave me alone:

my parents
Opel Sanders
Lottie Clymer
Robert Ingersol
my wife
Schubert M. Ogden
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ABSTRACT

PART I

Polya's group theoretical method for calculating the permutation isomers of a rigid molecular framework is extended to certain nonrigid systems. Symmetry operators are defined which allow the high symmetry of freely rotating, rapidly inverting, or ring-flipping molecules to be handled by group theoretical methods.

In the second portion of this discussion the effect of chiral ligands on the number of possible permutation isomers is discussed and a number of unusual possible <u>meso</u> compounds are presented.

PART II

The unusually high rate of energy dissipation in coumarin is discussed. In the raman spectrum of ultraviolet irradiated coumarin at 98°K evidence is found for the formation of an oxabicyclobutane derivative via the rearrangement:

Bands at 875 and 1231 cm^{-1} in the raman spectrum appear to arise from the oxabicyclobutane.

When coumarin (or N-alkyl <u>o</u>-coumaramides) is irradiated in amine solution, N,N′-dialkyl-<u>o</u>-tyrosine amide derivatives are formed. This is a new pathway to <u>o</u>-tyrosine derivatives, but its generality is not known.

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I. STUDIES IN ISOMERISM: PERMUTATIONS, POINT GROUP SYMMETRIES, AND ISOMER COUNTING

A. Introduction to the Classification of Isomers

In a very thoughtful paper written in 1936 entitled "On Certain Chemical Definitions," J. K. Senior(1) argued that there were basically two ways of defining chemical concepts:

(a) in terms of verifiable observations and reproducible laboratory operations;

(b) in terms of the theory adopted to explain certain phenomena. That is to say, a particular part of chemistry may be defined as the field of application of a given chemical theory.

He defended the thesis that, insofar as it is possible, concepts should be defined by the first method, both because of its pedagogical straightforwardness, and because "if a concept is defined in terms of a theory, any future observation which invalidates the theory at the same time annihilates the concept."

Senior's thesis, though praiseworthy, did not outlast the first page of his work. For in order to define "isomerism" he not only introduced the observational bases of elemental analysis (leading to an elemental formula), and molecular weight determination, but he was also forced to admit the atomic-molecular hypothesis, for without it the numerical data are gibberish. But his analysis is valuable not because of its success as a thesis, but for its clarity in setting forth the basis on which our concept of isomerism is, in fact, based, or rather, was in 1936. And he did judiciously employ Ockam's razor--he did not unnecessarily multiply hypotheses.

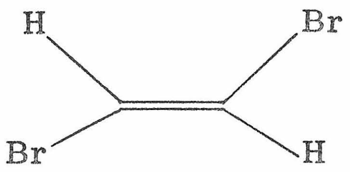
In surveying the changes in our understanding of isomerism since 1936, two developments stand out. Foremost is the growth of diffraction techniques--x-ray, electron, and neutron--as tools for structural determinations, even for the determination of the absolute configuration of enantiomeric compounds. Second is the growing use of molecular symmetry as a key to physical properties, especially in Raman, infrared, and magnetic resonance spectroscopy.

Thus, a new basis for a study of isomerism should expand on Senior's definitions to include the immense possibilities opened up by diffraction methods and symmetry analysis. One of two far ranging papers in the past decade, the system of Noyce(2) moves in the direction of a less, rather than more, operational basis for distinguishing types of isomers.

Noyce distinguishes stereoisomers into two basis classes: inversional and rotational.

> Rotational isomers are stereoisomers which are formally convertible by the rotation of one part of the molecule with respect to the rest of the molecules about a sigma bond without the necessity of disrupting and reforming sigma bonds.

Examples of such compounds are I - V below. Compounds Ia, b and IIa, b exhibit π-bond hindrance to rotation. Compounds IIIa, b and IVa, b exhibit nonbonded hindrance to rotation. Sigma bond hindrance to rotation characterizes compounds Va, b, c, d.



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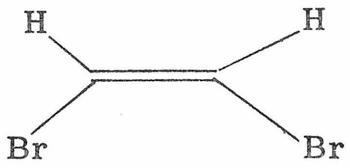

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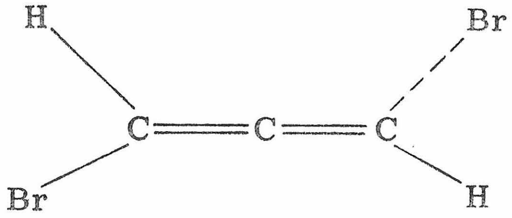
I



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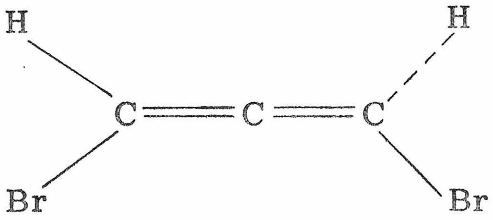

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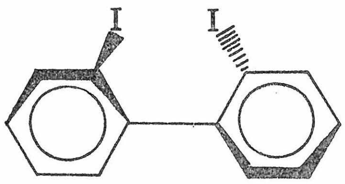

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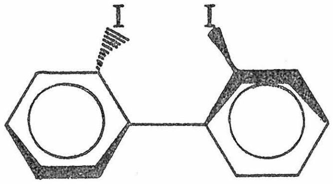

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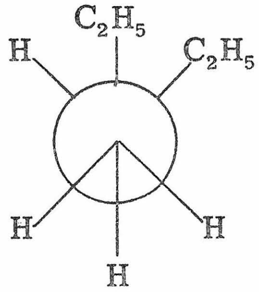

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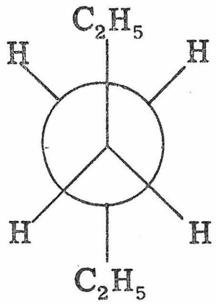

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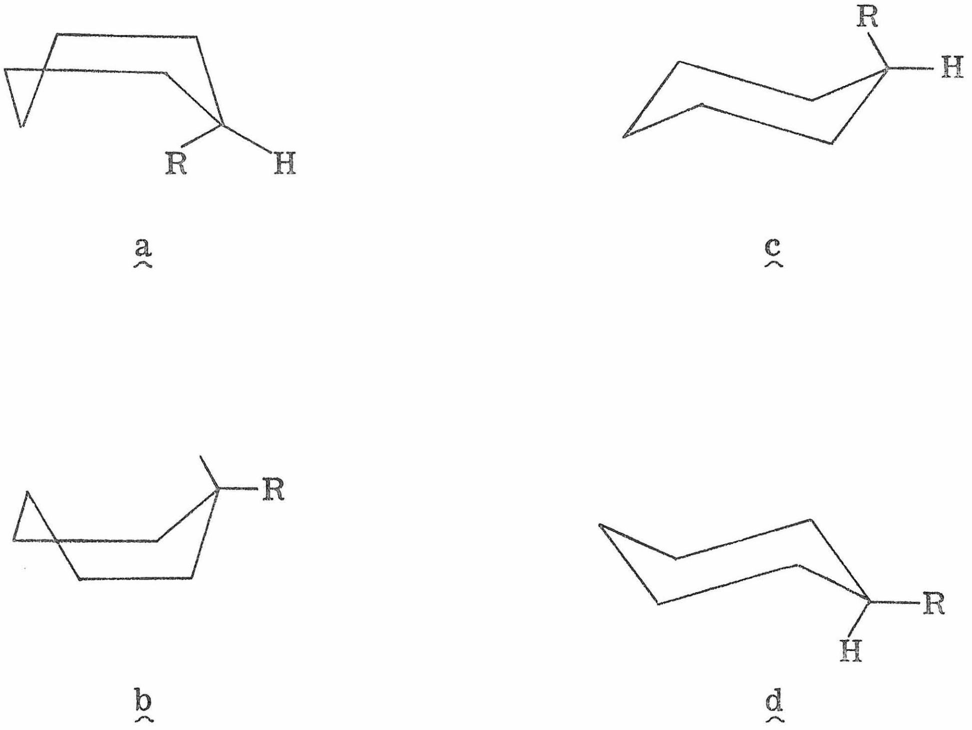
IV



V

Noyce continues:

> Inversional isomers are stereoisomers which are formally interconvertible only by inversion of one or more carbon atoms with the breaking of one or more sigma bonds and the formation of a corresponding number of sigma bonds.

The strengths of Noyce's classification scheme are threefold. First, it very easily includes conformational analysis as a natural division. (In Noyce's terminology, a rotational isomer is a conformation; an inversional isomer is a configuration.) Second, it levels the misleading distinction between optical and geometric isomers. Thus, the dibromoallenes, IIa and b, are geometrical isomers by the usual definition. ("Isomerism depending on restricted rotation about a carbon-carbon bond is known as geometrical isomerism". (3)) Yet they are also optical isomers. Finally, it appears to be a complete definition of stereoisomer types.

However, it falls short at several places. Most seriously, some compounds are clearly in both classes. Inversion of the starred carbon atom in the cyclohexane conformation Va leads to compound Vb, even as rotation does; similarly for Vc and Vd.

Furthermore (applying Senior's objection), the bonding theory underlying Noyce's theory is inadequate, and hence the definitions themselves are suspect. First of all, the sigma and pi bond designation is an artifact of a particular mathematical approximation for handling molecular quantum mechanical calculations. And even when calculations have been performed, the designations may be of little use for Noyce's purpose. A good example is cyclopropane; bonds directed along the C-C internuclear axes (the definition of sigma bonds) would produce unrealistically large H-C-H bond angles. Calculations show that cyclopropane does not have sigma bonds, so, by Noyce's definitions, it can have neither rotational nor inversional isomers.

A different approach to the problem of classifying isomers was taken in a recent paper by Ugi, Marquarding, Klusacek, Gobel, and Gillespie. (3) The problems of classifying isomers and developing nomenclature are interrelated. An ideal nomenclature system should have a one-to-one correspondence between possible isomers and possible names. Ugi and his co-workers approach the problem of nomenclature through the idea of <u>permutation</u> isomerism. In this, a molecular skeleton is considered to be substituted by a set of ligands which can be permuted between various skeletal positions, giving rise to a set of isomers each of which can be uniquely named. Their system even allows for the designation of the absolute configuration of enantiomers in cases where the R, S nomenclature(4) of Cahn, Ingold, and Prelog is not applicable. An approach to classifying isomers through permutational isomerism was also utilized recently by Prelog in his study of pseudo-asymmetry.(5)

In this paper we have adopted the permutational isomer as the basic structural category and show in Part B how it is possible to mathematically calculate the number of possible structural isomers, both in rigid systems and in systems having internal rotation, by Polya's method. In Part C we consider the consequences of chiral substitution on the number and type of possible isomers.

B. Isomer Counting in Rigid and Rotating Systems: Permutation Isomers with Achiral Ligands

1. History of the Problem

As pointed out by Senior,(1) the problem of isomerism arises only when molecular formulas can be determined and it is found that compounds with the same formula have different chemical and physical properties. A general theory of isomerism would be able to take a molecular formula, calculate all the possible isomers, and provide a convenient method for drawing and naming each isomer, without resorting to trial and error model building. The only compounds for which this is possible at present are the saturated acyclic hydrocarbons, C_nH_{2n+2}, and a few related compounds. In a series of papers in the early 1930's, Henze and Blair(6) developed finite recursion formulas for calculating the number of possible isomers for substituted paraffinic hydrocarbons.

Henze and Blair's first calculations (6a, b) did not consider the problem of stereoisomerism, which in saturated hydrocarbon systems is related to the number of asymmetric carbon atoms in the molecule. They later included stereoisomerism, but they did not fully consider the problem of a molecule containing several equivalent asymmetric carbon atoms. Allen and Diehl(7) developed a method of considering this problem by an "asymmetry number" index, and they applied it to carbinols with up to twenty carbon atoms. Carr(8) utilized Polya's method to develop a similar series of formulas for linear and branched hydrocarbons and their derivatives. Table I summarizes the results of these calculations.

Since carbon atoms can be incorporated into chains, such calculations are especially useful for isomers based on the saturated hydrocarbons. However, with most elements, simple chain-forming is *not* a major form of isomerism. Moreover, the asymmetric carbon atom is not the only source of enantiomerism. For these reasons the most general class of isomers for which routine numerical computation of isomer numbers can be performed is the class of *permutation isomers*(3) of a given empirical formula.

2. Definitions

Before defining permutation isomers, it is necessary to define *chirality.* The term, deriving from the Greek work for *hand*, was apparently introduced into physical theory by Lord Kelvin in his Baltimore lectures(9):

> I call any geometrical figure or group of points chiral and say it has *chirality* if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself.

An achiral figure, of course, would be superimposable on its mirror image. We have used the symbol $\overset{\circ}{\rightarrow}$ throughout to indicate the operation of reflection in a plane mirror.

Ugi and his co-workers(3) have called attention to a class of *amphichiral* objects which are chiral under Lord Kelvin's definition, but behave physically as achiral objects. For the purposes of the present work, however, we need not consider this complication.

Table I

Number of Possible C_{20} Saturated Alcohols

	Primary	Secondary	Tertiary	Nonenantiomorphic	Total
Henze and Blair(6a)	2,156,010	2,216,862	1,249,237	--	5,622,109
Henze and Blair(6c)				11,759	82,300,275*
Allen and Diehl(7)	27,012,286	40,807,290	14,480,699	11,759	82,300,275
Carr(8)				19,059	82,300,275

---

* Henze and Blair made a numerical error which was corrected by Allen and Diehl.(7) It is corrected here.

There is another useful definition of a chiral configuration which had long been applied to enantiomorphism, namely, a configuration which lacks an alternating axis of symmetry. Wheland(10) shows that the existence of such an axis renders an organic molecule non-superimposable on its mirror image. P. Woodward(11) had suggested as a defining characteristic for achirality: the presence of an inversion-rotation axis. However, these crystallographic axes are equivalent to the alternating axes of point group symmetry--inversion center ($i = \bar{1}$), mirror plane ($\sigma = \bar{2}$), and improper rotation or rotation-reflection axes ($S_6 = \bar{3}$, $S_4 = \bar{4}$, etc.). Since we will be employing point group symmetries,(12) we will use Wheland's formulation.

Note that we have implicitly distinguished between physical and conceptual symmetry operations. For molecular isomerism, the only relevant physical symmetry operations are rotation and vibration. As we will discuss further below, such physical operations can be properties of the molecule as a whole (rigid rotation or molecular vibration) or of a portion of the molecule. Nonphysical or conceptual operations are represented by the alternating axes of symmetry. Note, however, that in some cases, such as nitrogen inversion in ammonia derivatives, vibration can lead to the same result as an alternating axis.

Calculations are performed on figures--they may or may not represent the actual structure of the molecule under the conditions of a given structure determination. Thus, for an appropriately substituted amine (such as methyl ethyl amine), there certainly are enantiomorphs (representations which are not superimposable), but there are not chemically isolable enantiomers (enantiomorphic isomers), although such solutions at any given moment are probably an equimolar mixture of the two enantiomers.

Permutation isomers are isomers based on an achiral skeleton such as a tetrahedral carbon or a benzene ring, which is substituted with a given set of ligands. By permutation of these ligands among the possible skeletal positions, isomers which are not physically identical may be obtained. These isomers are permutation isomers. In the words of Ugi and his co-workers(3):

> Two molecules will be called permutational isomers if, and only if, they can be shown to derive from the same achiral skeleton, S_n, with n ligand positions by substitution with the same set of n ligands, L_n, but they cannot be superimposed on one another by any allowed rotation of the molecule.

Two kinds of ligands will be considered: chiral and achiral. A ligand is chiral if it contains no alternating axis of symmetry when its directed valence is considered an achiral substituent. Examples of such ligands are shown in Figure 1.

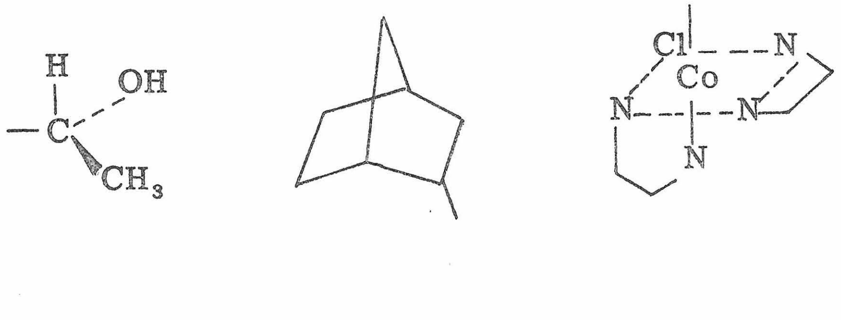


Figure 1

Chiral Ligands

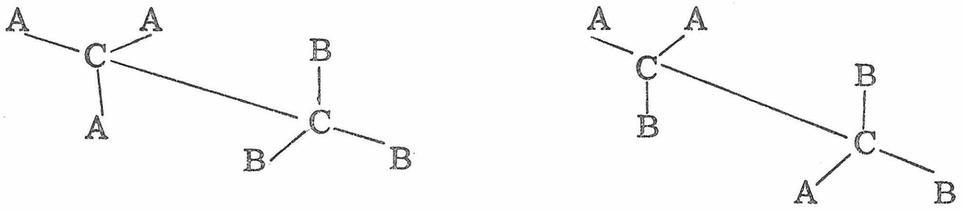
We will use Prelog's notation(5) for chiral and achiral ligands; the basis for this notation is explained in Part C.

Chiral ligands: G J L N P Q R Z

Achiral ligands: A B D E K M T U V W X Y or a blank ligand position.

In this part we will only consider substitution by achiral ligands; we will postpone the problem of chiral substituents until Part C.

Permutation isomers are of two types: structural or stereoisomeric. Structural isomers such as compounds VIa and VIb differ in *connectivity*, that is, in which ligands are attached to which atom. In VIa one carbon has a ligand set $\{A, A, A, CB_3\}$ and the other has the set $\{B, B, B, CA_3\}$. In VIb the sets are $\{A, A, B, CAB_2\}$ and $\{B, B, A, CA_2B\}$.



a

b

VI

All other permutation isomers are stereoisomers. Both Senior(1) and Noyce(2) argue convincingly that distinguishing stereoisomers into geometric and optical isomers is a false dichotomy, and I do not intend to revive it here. Indeed, using the nomenclature system proposed by Ugi, even the *cis*, *trans* nomenclature of geometric isomerism is unnecessary.

Since the reflection of a molecular representation in a plane mirror is incapable of altering connectivity, enantiomers are stereoisomers of each other. Stereoisomers which are not enantiomers of each other are diastereomers. This usage is somewhat broader than customary (for example, it makes *cis*- and *trans*-2-butenes diastereomers), but it is the only consistent usage.(5)

For the purposes of counting isomers, we need to define another term, diamutamer, to indicate the relationship between permutation isomers which are not enantiomorphic. Thus, for a given framework and ligand set, the diamutamers constitute a set of permutation isomers, none of which can be made equivalent to any other member of the set by reflection of the molecular representation in a plane mirror. When there are enantiomorphic permutation isomers, there are at least two non-equivalent sets of diamutamers, but every set has the same number of members.

This classification scheme has, in addition to preciseness, a great utility in the calculation of the number of possible permutation isomers. In particular, it is the scheme which arises naturally from the application of Polya's group theoretical method of counting isomers.

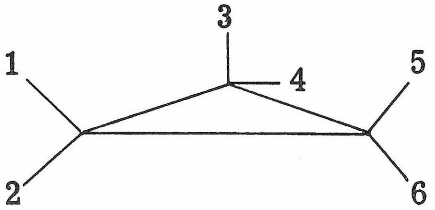
3. Polya's Method in Rigid Molecules

The use of permutational analysis for calculating isomers numbers, both by recursion formulas such as Henze and Blair's, and by group theoretical methods such as Polya's, had its inspiration in a pivotal paper by A. C. Lunn and J. K. Senior in 1929.(13) In it they showed the value of this approach and gave tables for use in isomer counting in certain systems.

The great advance made by Georg Polya(14) was the introduction of Polya's theorem (below) which reduced the tables of Lunn and Senior to a matter of algebraic manipulation. The method used herein is that of Polya, modified by using point groups rather than permutation groups. This modification was introduced by Kennedy, McQuarrie, and Brubaker.(15)

In counting permutation isomers we are given an achiral molecular skeleton S_n with n ligand positions which has point group symmetry H (a group of order h). Each operation in H corresponds to a permutation of the n ligand positions. For example, consider the cyclopropane skeleton under the operations of the rotation group D_3.

$\underline{D}_3$: $E2C_2 3C_2$



Under the three-fold rotation operation C_3, position 1 goes to position 3 which goes to position 5 which goes to position 1. Thus, the cycle includes the permutation of three positions, and is usually written (135). The cycle (135) is said to be of length three. In addition, C_3 also carries out the simultaneous permutation (246), so that the operation C_3 corresponds to the permutation (135) (246), or two cycles of length three. We can represent this permutation as f_3^2, which is read as two cycles of length three. The other three-fold operation, C_3^2 is also f_3^2. The two-fold operations are of the type (12)(36)(45), or f_2^3.

The identity operator is (1)(2)(3)(4)(5)(6) or f_1^6. Thus, by knowing n, the number of points to be permuted, and the group H, we can define a cycle index, Z(H;n). In this case,

$$Z(D_3;6) = \frac{1}{6}[f_1^6 + 2f_3^2 + 3f_2^3]$$

If we had only three points in D_3, such as the vertices of an equilateral triangle, we would have obtained

$$Z(D_3;3) = \frac{1}{6}[f_1^3 + 2f_3 + 3f_2f_1]$$

In general, a permutation of n points can be represented as $f_1^{j_1}f_2^{j_2}\ldots f_n^{j_n}$ or $\prod_{i=1}^{n} f_i^{j_i}$. Note that the sum $\sum ij_i$ is equal to n, the number of points. It should be clear that any given $\prod_{i=1}^{n} f_i^{j_i}$ has several j_i equal to zero. The general cycle index is defined as

$$Z(H;n) = \frac{1}{h}\sum a_{j_1j_2\ldots j_n}\prod_{i=1}^{n} f_i^{j_i}$$

where the summation is over all sets $\{j_i\}_{i=1}^{n}$ consistent with the above condition that $\sum ij_i = n$. The coefficient $a_{j_1j_2\ldots j_n}$ is the number of permutations of H which consist of j_1 cycles of length 1, j_2 cycles of length 2, etc. These coefficients depend on both H and n and are either zero or a positive integer. Thus the cycle index carries information about both the number and type of possible permutations.

Given a set of possible ligands $\{x_\ell\}_{\ell=1}^{m}$ we can define a configuration counting series, $F(x_1, x_2, \ldots, x_m)$ which gives us the total number of possible distinct substitutions of these m ligands (any one of which can occur from 0 to n times) on the n ligand positions of S_n. This series is

$$F(x_1, x_2, \ldots, x_m) = \sum A_{k_1 k_2 \ldots k_m} \prod_{\ell=1}^{m} x_\ell^{k_\ell}$$

where the summation is over $k_\ell = 0$ to n for each ℓ from 1 to m. The coefficient $A_{k_1 k_2 \ldots k_m}$ is the number of isomers possible when the molecular framework is substituted with k_1 ligands of type x_1, k_2 of type x_2, etc.

Polya's theorem (14, 16) allows us to derive the configuration counting series from the cycle index by replacing $f_i^{j_i}$ by

$$\left(\sum_{\ell=1}^{m} x_\ell^i\right)^{j_i} .$$

This substitution gives rise to a new cycle index, $Z[H;n;f(x_1, x_2, \ldots, x_m)]$. We can summarize Polya's theorem by the equation

$$F(x_1, x_2, \ldots, x_m) = Z[H;n;f(x_1, x_2, \ldots, x_m)].$$

Returning to cyclopropane, we can compute number of isomers with all possible combinations of two different ligands, A and B.

$$\begin{aligned} Z[D_3;6;f(A,B)] &= \tfrac{1}{6}\left[(A^1 + B^1)^6 + 2(A^3 + B^3)^2 + 3(A^2 + B^2)^3\right] \\ &= \tfrac{1}{6}\left[6A^6 + 6A^5B + 24A^4B^2 + 24A^3B^3 + (24B^4A^2 + 6B^5A + 6B^6)\right] \\ &= A^6 + A^5B + 4A^4B^2 + 4A^3B^3 + K(A,B) \end{aligned}$$

where $K(A, B)$ is a polynomial containing redundant information, denoted by the parenthetic material in the second line of the equation. Thus, there is one possible isomer with six identical ligands, one possible with one ligand substitution, four isomers with four A ligands and two B ligands, etc.

If, instead of considering only the rotation operators, we had included the alternating axes, we would generate the cycle index for D_{3h}, which consists of the operations E, $2C_3$, $3C_2$, σ_h, $2S_3$, $3\sigma_v$:

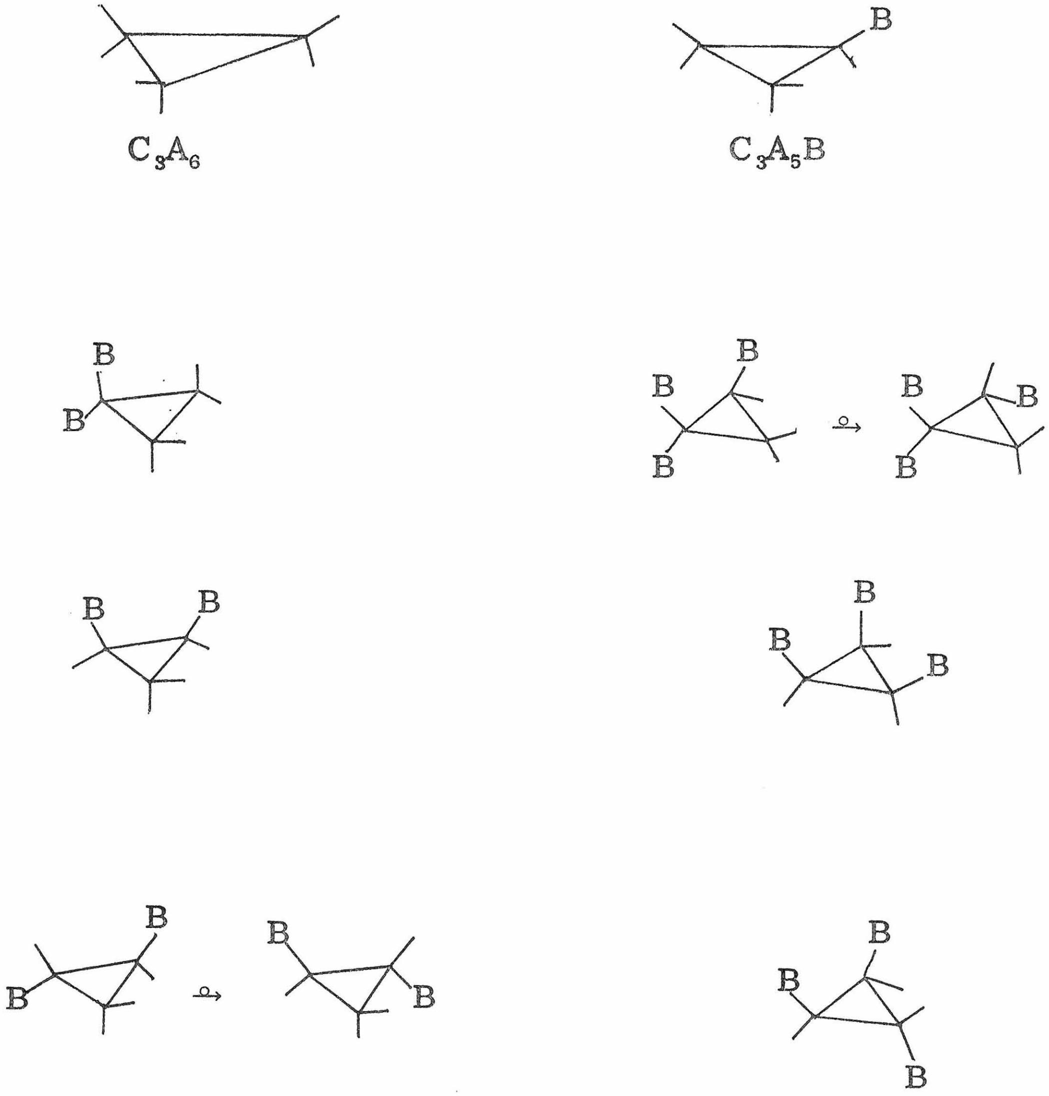
$$\begin{aligned} Z(D_{3h};6) &= \frac{1}{12}[f_1^6 + 2f_3^2 + 3f_2^3 + f_2^3 + 2f_6^1 + 3f_2^2 f_1^2] \\ &= \frac{1}{12}[f_1^6 + 2f_3^2 + 4f_2^3 + 2f_6^1 + 3f_2^2 f_1^2] \end{aligned}$$

Again substituting the appropriate $A^i + B^i$ binomials, we obtain the configuration counting index for two different ligands:

$$Z[D_{3h};6;f(A, B)] = A^6 + A^5B + 3A^4B^2 + 3A^3B^3 + K(A, B)$$

The decrease from 4 to 3 of the coefficients of A^4B^2 and A^3B^3 indicates that the rotationally distinct permutation isomers in each case includes an enantiomorphic pair which leads to only three diamutamers when the alternating axes are included. Figure 2 shows the $A_\ell B_{6-\ell}$ isomers of cyclopropane for $\ell = 3$ to 6.

William J. Taylor$^{(17)}$ showed that by introducing to the point group D_{3h} a permutation operator which permutes the two ligand positions on each skeletal atom, one could render all isomers except structural isomers indistinguishable, so that there are only two isomers each of $C_3A_4B_2$ and $C_3A_3B_3$ as shown in Figure 3.



C_3A_6

C_3A_5B

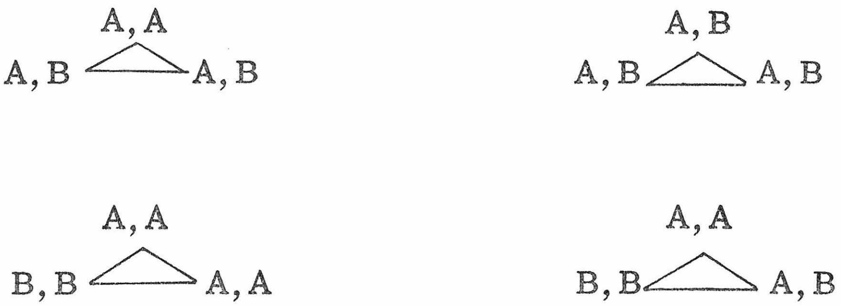
$C_3A_4B_2$

$C_3A_3B_3$

Figure 2

Isomers of $C_3A_\ell B_{6-\ell}$ (ℓ = 3 to 6)

A's are omitted for clarity



$C_3A_4B_2$ $C_3A_3B_3$

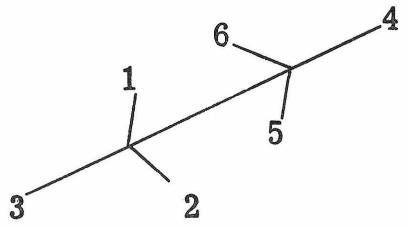
Figure 3

Structural Isomers of Cyclopropane
with Two Achiral Ligands

Kennedy, McQuarrie, and Brubaker(15) give the cycle indices of a number of rigid systems of interest to inorganic chemists. Additional applications of Polya's method to rigid systems are listed in Reference 18. Table II gives the indices for a number of organic skeletons not previously published.

4. Polya's Method in Nonrigid Molecules

There has been, to my knowledge, no previously reported attempt to calculate the number of isomers in a freely rotating system by Polya's method. The problem is well illustrated by considering the isomers of dichloroethane, which is usually represented as based on an ethane skeleton in the staggered form of D_{3d} symmetry.



The cycle index $Z(D_{3d};6)$ is the same as $Z(D_{3h};6)$. Thus, the number of isomers should be the <u>same</u> as in the case of the $C_3A_4B_2$ system: four. However, attempts to isolate isomers in this sytem have only succeeded in obtaining two forms, 1,1- and 1,2-dichloroethane. Thus, the system as a whole is for many chemical purposes best represented as two isomers, even though, as we noted above, the system actually is probably a mixture of the rotamers which are counted by Polya's method on the rigid skeleton. Figure 4 shows the four dichloroethane isomers.

Table II

Cycle Indices of Certain Rigid Organic Structures

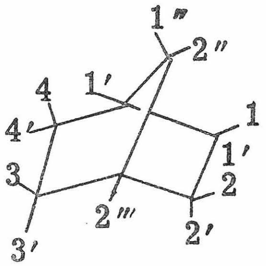
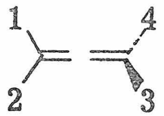
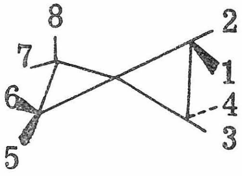
Point Group	S_n	Cycle Index
C_{2v}		$Z(C_2;12) = \frac{1}{2}(f_1^{12} + f_2^{6})$ $Z(C_{2v};12) = \frac{1}{4}(f_1^{12} + f_2^{6} + 2f_1^{2}f_2^{5})$
D_{2d}		$Z(D_2;4) = \frac{1}{4}(f_1^{4} + 3f_2^{2})$ $Z(D_{2d};4) = \frac{1}{8}(f_1^{4} + 3f_2^{2} + 2f_4^{1} + 2f_2^{1}f_1^{2})$
		$Z(D_2;8) = \frac{1}{4}(f_1^{8} + 3f_2^{4})$ $Z(D_{2d};8) = \frac{1}{8}(f_1^{8} + 5f_2^{4} + 2f_4^{2})$

Table II (Continued)

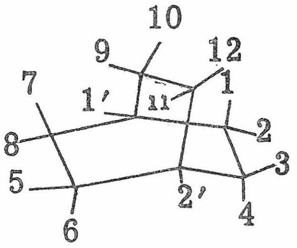
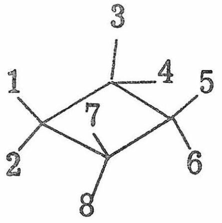
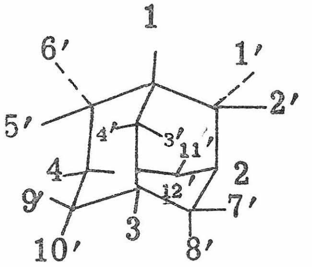
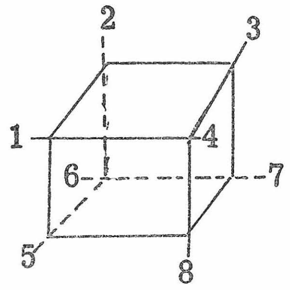
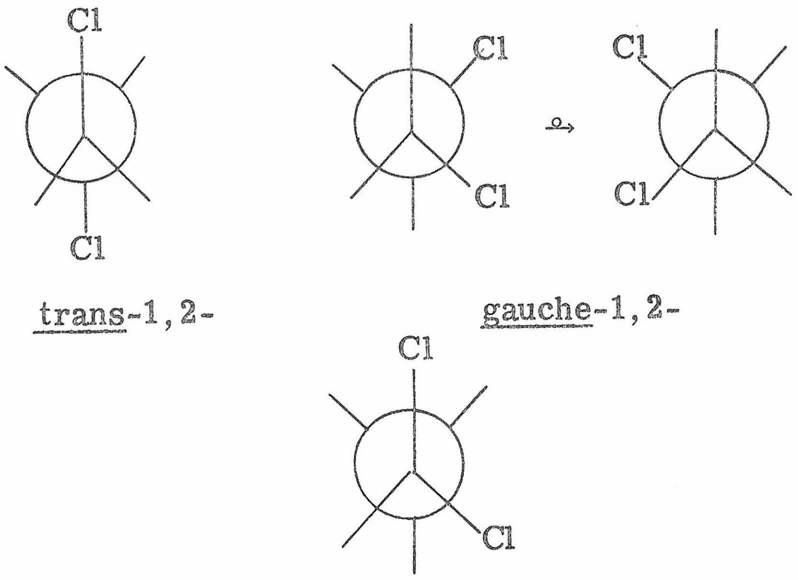
Point Group	S_n	Cycle Index
D_{3h}		$Z(D_3;14) = \frac{1}{6}[f_1^{14} + 2f_1^2 f_3^4 + 3f_2^7]$ $Z(D_{3h}:14) = \frac{1}{12}[f_1^{14} + 2f_1^2 f_3^4 + 4f_2^7 + 2f_1^2 f_6^2 + 3f_1^2 f_2^6]$
D_{4h}		$Z(D_4;8) = \frac{1}{8}(f_1^8 + 5f_2^4 + 2f_4^2)$ $Z(D_{4h};8) = \frac{1}{16}(f_1^8 + 9f_2^4 + 2f_4^2 + 2f_8^1 + 2f_2^2 f_1^4)$
T_d		$Z(T;16) = \frac{1}{12}[f_1^{16} + 8f_1^1 f_3^5 + 3f_2^8]$ $Z(T_d;16) = \frac{1}{24}[f_1^{16} + 3f_2^8 + 8f_1 f_3^5 + 6f_4^4 + 6f_1^4 f_2^6]$

Table II (Continued)

Point Group	S_n	Cycle Index
		$Z(O;8) = \frac{1}{24}[f_1^8 + 6f_4^2 + 9f_2^4 + 8f_1^2 f_3^2]$ $Z(O_h;8) = \frac{1}{48}[f_1^8 + 12f_4^2 + 13F_2^4 + 6f_1^4 f_2^2 + 8f_6^1 f_1^2 + 8f_1^2 f_3^2]$



trans-1,2-   gauche-1,2-

1,1-

Figure 4

Isomers of Dichloroethane in D_{3d} Symmetry

The problem, then, is to find a way in which Polya's method can be made to represent the state of the chemical system rather than the individual molecules. In order to do this we need to reduce the effective number of isomers. Now for any given n in Polya's method, a reduction in the number of isomers corresponds to going to a group of higher order symmetry. Hence, the ethane skeleton shows a chemical behavior of a symmetry higher than D_{3h} or D_{3d}. Chemists have long known that this higher effective symmetry derives from rotation about the C-C bond which occurs more rapidly than chemical separations can be performed. However, to my knowledge, this knowledge has never been formalized into a symmetry group representation.

In the ethane skeleton above, let us define one free rotation operation as the permutation (123)(4)(5)(6), that is, we hold the right end of the skeleton fixed and rotate the left end by $2\pi/3$. We can designate this operation F_3. Operating twice gives us F_3^2 or (132)(4)(5)(6). A similar rotation can occur about the right end of the skeleton, yielding $F_3' = (1)(2)(3)(456)$ and $F_3^{2\prime} = (1)(2)(3)(465)$. Combining the free rotations with the rigid rotations of point group D_3, we obtain a new point group $D_3F_3^2$, where the notation indicates that two three-fold free rotation axes have been added to the D_3 rotation group. Table III shows the group $D_3F_3^2$ and its character table and irreducible representations.

The cycle index for the ethane skeleton in the group $D_3F_3^2$ is $Z(D_3;6) = \frac{1}{18}[f_1^6 + 4f_3^2 + 3f_2^3 + 4f_1^3f_3 + 6f_6]$. Table IV gives the number of substituted ethanes expected.

The number of diamutamers and enantiomorphs is calculated from the rotation-reflection group:

$$D_{3d}F_3^2\text{: } E, 2C_3, 3C_2, 2F_3\cdot C_3, 6F_3\cdot C_2, i, 2S_6, 36_d, 4F_3\cdot i, 2F_3\cdot S_6, 6F_3\cdot 6_d$$

$$Z(D_{3h};6) = Z(D_{3d};6) = \frac{1}{36}[f_1^6 + 4f_3^2 + 6F_2^3 + 4f_1^3f_3 + 12f_6 + 9f_1^2f_2^2].$$

Ferrocene is a molecule which similarly shows free rotation, with a preference for a staggered configuration of the cyclopentadienyl anions. It belongs to the rotation group $D_5F_5^2$ and the reflection group $D_{5d}F_5^2$. Table V shows the operations and cycle indices for these groups and the possible isomers of ferrocene.

Table III

The Symmetry Group $D_3F_3^2$

$\epsilon = \exp(2\pi i/3)$

$D_3F_3^2$	E	$2C_3$	$3C_2$	$2F_3$	$F_3 \cdot C_3$	$3F_3 \cdot C_2$	$2F'_3$	$F'_3 \cdot C_3$	$3F'_3 \cdot C_3$	$h = 18$
	1	1	1	1	1	1	1	1	1	
	1	1	1	ϵ	ϵ	ϵ	ϵ^2	ϵ^2	ϵ^2	
	1	1	1	ϵ^2	ϵ^2	ϵ^2	ϵ	ϵ	ϵ	
	1	1	-1	1	1	-1	1	1	-1	
	1	1	-1	ϵ	ϵ	$-\epsilon$	ϵ^2	ϵ^2	$-\epsilon^2$	
	1	1	-1	ϵ^2	ϵ^2	$-\epsilon^2$	ϵ	ϵ	ϵ	
	2	-1	0	-1	2	0	-1	2	0	
	2	-1	0	$-\epsilon$	$2\epsilon^2$	0	$-\epsilon$	$2\epsilon^2$	0	
	2	-1	0	$-\epsilon^2$	2ϵ	0	$-\epsilon$	2ϵ	0	

Table IV

Empirical Formula	Permutation Isomers	Diamutamers	Enantiomorphic Pairs
C_2A_6	1	1	0
C_2A_5B	1	1	0
$C_2A_4B_2$	2	2	0
C_2A_4BD	3	2	1
$C_3A_3B_3$	2	2	0
$C_2A_3B_2D$	4	3	1
C_2A_3BDE	8	4	4
$C_2A_2B_2D_2$	6	5	1
$C_2A_2B_2DE$	10	6	4
C_2A_2BDEK	20	10	10
$C_2ABDEKM$	40	20	20

Table V

Isomerism of Ferrocene

$\underline{D_5F_5}^2$: E, $2C_5$, $5C_2$, $4[2F_5, 3F_5\cdot C_5, 5F_5\cdot C_2]$

$$Z(D_5F_5{}^2;10) = \frac{1}{50}[f_1^{10} + 16f_5^2 + 5f_2^5 + 8f_1^5f_5 + 20f_{10}]$$

$\underline{D_{5d}F_5}^2$: E, $2C_5$, $2C_5^2$, $5C_2$, i, $2S_{10}$, $5\sigma_d$, $2[4F_5, 6F_5\cdot C_5, 10F_5\cdot C_2,$ $4F_5\cdot i, 2(F_5\cdot C_5\cdot i), 2(F_5^2\cdot C_5^2\cdot i), F_5\cdot C_5^2\cdot i, F_5^2\cdot C_5\cdot i, 10F_5\cdot\sigma_d]$

$$Z(D_{5d}F_5{}^2;10) = \frac{1}{100}[f_1^{10} + 16f_5^2 + 40f_{10} + 16f_1^5f_5 + 25f_1^2f_2^4]$$

$$= Z(D_{5h}F_5{}^2;10)$$

X = Ferrocene Skeleton: $C_{10}Fe$

Formula	Permutation Isomers	Diamutamers	Enantiomorphic Pairs
XA_{10}	1	1	0
XA_9B	1	1	0
$*XA_8B_2$	3	3	0
$*XA_7B_3$	4	4	0
XA_6B_4	6	6	0
$XA_5{}^6B_5$	6	6	0
$*XA_8BD$	5	3	2
$**XA_7B_2D$	12	8	4
XA_6B_3D	20	12	8
$XA_6B_2D_2$	32	22	10
XA_5B_4D	26	16	10

Table V (Continued)

Formula	Permutation Isomers	Diamutamers	Enantiomorphic Pairs
$XA_5B_3D_2$	52	32	20
$XA_4B_4D_2$	66	42	24
$XA_4B_3D_3$	84	48	36
**XA_7BDE	24	12	12
XA_6B_2DE	60	32	28
XA_5B_3DE	104	52	52
$XA_5B_2D_2E$	156	84	72
XA_5B_4DE	126	66	60
$XA_4B_3D_2E$	252	132	120
$XA_4B_2D_2E_2$	384	201	183
$XA_3B_3D_3E$	336	168	168
$XA_3B_3D_2E_2$	504	264	240
XA_6BDEK	120	60	60
XA_5B_2DEK	310	155	155
XA_4B_3DEK	504	252	252
$XA_4B_2D_2EK$	756	390	366
$XA_3B_3D_2EK$	1010	505	505
$XA_3B_2D_2E_2K$	1512	762	744
$XA_2B_2D_2E_2K_2$	2280	1176	1104
XA_5BDEKM	624	312	312
XA_4B_2DEKM	1512	756	756
XA_3B_3DEKM	2016	1008	1008

Table V (Continued)

Formula	Permutation Isomers	Diamutamers	Enantiomorphic Pairs
$XA_3B_2D_2EKM$	3024	1512	1512
$XA_2B_2D_2E_2KM$	4536	2270	2266
XA_4BDEKM	3024	1512	1512
XA_3B_2DEKMT	6048	3024	3024
$XA_2B_2D_2EKMT$	9072	4536	4536
$XA_3BDEKMTU$	12,096	6048	6048
$XA_2B_2DEKMTU$	18,144	9072	9072
XABDEKMTU	72,576	36,288	36,288

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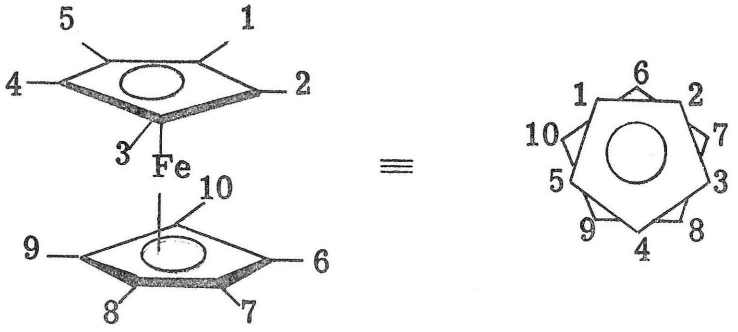
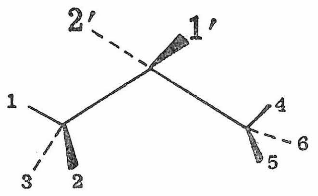
* These values agree with those in Schlögl.(19)

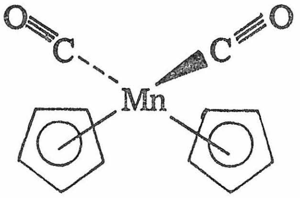
** These values have been checked with models; Schlögl(19) has incorrect values for them.



Up to now we have only considered molecules of symmetries in which the two rotating groups are related by n dihedral axes. Lower symmetry skeletons with free rotation are present in propane and in dicyclopentadienyl manganese dicarbonyl.

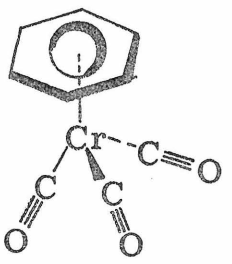


$C_{2v}F_3^2$

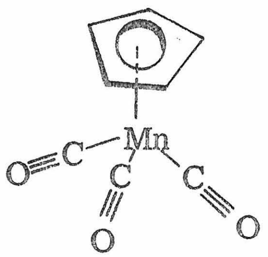


$C_{2v}F_5^2$

There is also no need for the two rotating groups to have the same rotation order. Excellent examples of this are benzenechromium tricarbonyl and cyclopentadienyl manganese tricarbonyl which belong to the $C_{3v}F_6F_3$ and $C_sF_5F_3$ symmetry groups.



$C_{3v}F_6F_3$



$C_sF_5F_3$

In these cases, as indeed in all cases in which Polya's method is employed, the problem can be simplified by only considering positions which are symmetrically equivalent. Thus, we can consider substitution of the ring apart from substitution of the carbonyl moieties. Table VI shows the cycle index and results for benzenechromium tricarbonyl.

Table VII summarizes the free rotation groups of a number of molecular skeletons.

A special kind of free rotation occurs in ring systems, such as the cyclohexane skeleton which is nominally D_{3d}.

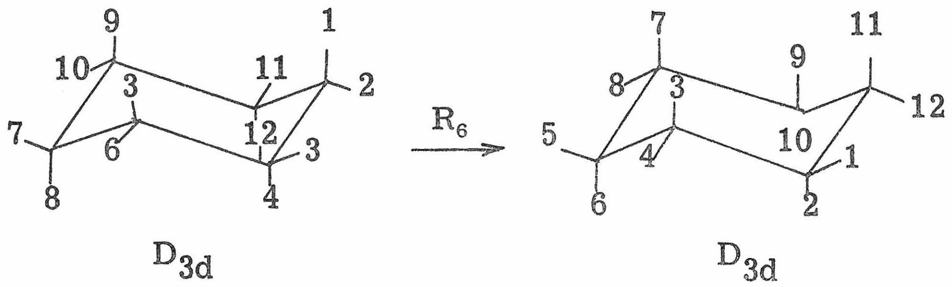
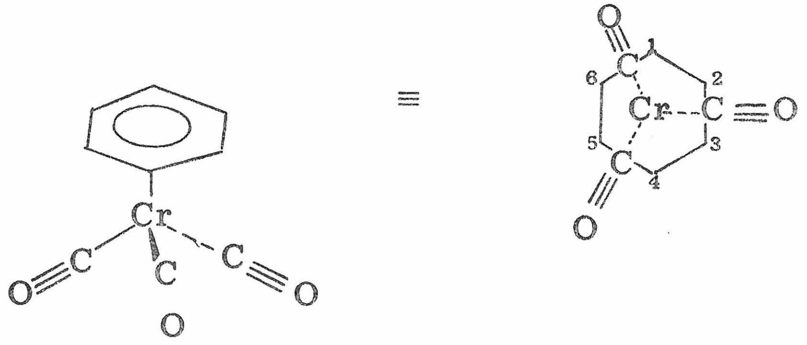


Figure 5

Ring Flip-Rotation Operation in the Cyclohexane Structure

Table VI

Isomerism of Benzenechromium Tricarbonyl



$\underline{C}_3\underline{F}_6\underline{F}_3$: E, C_3, C_3^2, F_6, F_6^2, F_6^3, F_6^4, F_6^5, F_3, F_3^2, $F_6 \cdot F_3$, $F_6 \cdot F_3^2$, $F_6^2 \cdot F_3^2$, $F_6^3 \cdot F_3$, $F_6^3 \cdot F_3^2$, $F_6^4 \cdot F_3$, $F_6^5 \cdot F_3$, $F_6^5 \cdot F_3^2$

$$Z(C_3F_6F_3;6) = \frac{1}{18}[3f_1^6 + 6f_3^2 + 6f_6 + 3f_2^3]$$
$$= \frac{1}{6}[f_1^6 + 2f_3^2 + 2f_6 + f_2^3]$$

$\underline{C}_{3v}\underline{F}_6\underline{F}_3$: E, $2C_3$, $2F_6$, $2F_6^2$, F_6^3, $2F_3$, $2F_6 \cdot F_3$, $2F_6 \cdot F_3^2$, $2F_6^2 \cdot F_3^2$, $2F_6^2 \cdot F_3^2$, $2F_6^3 \cdot F_3$, $3\sigma_v$, $2F_6 \cdot \sigma_v$, $2F_6^2 \cdot \sigma_v$, $2F_3 \cdot \sigma_v$, $2F_6 \cdot F_3 \cdot \sigma_v$, $2F_6 \cdot F_3^2 \cdot \sigma_v$, $2F_6^2 \cdot F_3^2 \cdot \sigma_v$, $2F_6^3 \cdot F_3 \cdot \sigma_v$

$$Z(C_{3v}F_6F_3;6) = \frac{1}{36}[3f_1^6 + 6f_3^2 + 6f_6 + 12f_2^3 + 9f_2^2f_1^2]$$
$$= \frac{1}{12}[f_1^6 + 2f_3^2 + 2f_6 + 4f_2^3 + 3f_2^2f_1^2]$$

X = Benzenechromium tricarbonyl skeleton = $Cr(CO)_3C_6$

Formula	Permutation Isomers	Diamutamers	Enantiomorphic Pairs
XA_6	1	1	0
XA_5B	1	1	0

Table VI (Continued)

Formula	Permutation Isomers	Diamutamers	Enantiomorphic Pairs
*XA_4B_2	3	3	0
*XA_3B_2	4	3	1
*XA_4BD	5	3	2
*XA_3B_2D	10	6	4
$XA_2B_2D_2$	16	11	5
*XA_3BDE	20	10	10
XA_2B_2DE	30	16	14
XA_2BDEK	60	30	30
XABDEKM	120	60	60

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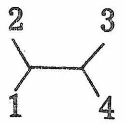
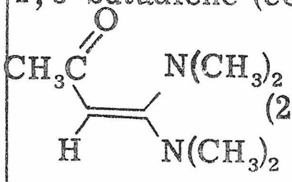
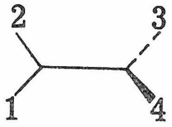
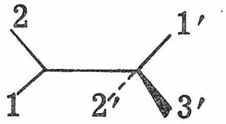
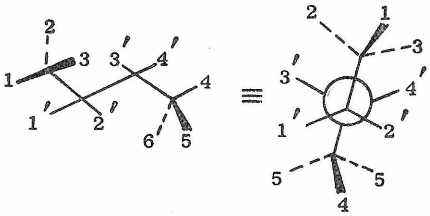
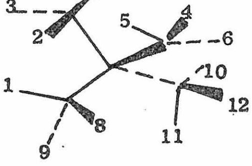
* These isomer counts agree with those given by Schlögl.(19)

Table VII

Freely Rotating Molecular Skeletons

Skeleton	Symmetry Group	Example
	$D_{2h}F_2^2$	1,3-butadiene (central bond),  (20), oxalic acid
	$D_{2d}F_2^2$	B_2Cl_4 (vapor (21)), biphenyl
	$C_sF_3F_2$	acetaldehyde, propene
	$D_{2h}F_3^2$	*n*-butane
	$T_dF_3^4$	*neo*-pentane

By flipping from one chair form to the other, and rotating by $2\pi/6$ radians, we obtain an equivalent ring as shown in Figure 5. This ring flip-rotation constitutes a symmetry operator which I have designated R_6. By combining this operator with the rigid point group D_{3d}, we obtain the group $D_{3d}R_6$, whose operations, and cycle in box are shown in Table VIII. For comparison, Table VIII also lists the cycle index and operations for D_6 and D_{6h}.

Table VIII

Symmetry Groups D_3R_6 and $D_{3d}R_6$

$\underline{D_3R_6}$: $E,\ 2C_3,\ 3C_2,\ 2R_6,\ R_6^3,\ 3R_6\cdot C_2$

$\underline{D_6}$: $E,\ 2C_3,\ 3C_2',\ 2C_6,\ C_2,\ 3C_2''$

$$Z(D_3R_6;\,12) = Z(D_6;12) = \frac{1}{12}\left[f_1^{12} + 2f_3^4 + 3f_2^6 + 2f_6^2 + f_2^6 + 3f_2^6\right]$$
$$= \frac{1}{12}\left[f_1^{12} + 2f_3^4 + 7f_2^6 + 2f_6^2\right]$$

$\underline{D_{3d}R_6}$: $E,\ 2C_3,\ 3C_2,\ 2R_6,\ R_6^3,\ 3R_6\cdot C_2,\ i,\ 2S_6,\ 3\gamma_V,\ 2R_6\cdot i,$
$R_6^3\cdot i,\ 3_{6V}\cdot R_6$

$\underline{D_{6h}}$: $E,\ 2C_3,\ 3C_2,\ 2C_6,\ C_6^3,\ 3C_2'',\ i,\ 2S_6,\ 3\gamma_V,\ 2S_3,\ 6_h,\ 3_{6d}$

$$Z(D_3R_6;\,12) = Z(D_{6h};\,12) = \frac{1}{24}\left[f_1^{12} + 12f_2^6 + 4F_6^2 + 3f_1^4f_2^4 + 4f_3^4\right]$$

The comparison of $D_{3d}R_6$ and D_{6h} is instructive; the two groups not only have identical cycle indices, but they are in fact the same permutation group. Carbohydrate chemists and others have long represented the inositols and other cyclohexane derivatives by a planar ring structure. Once it was found that cyclohexanes are *not* planar, two major explanations were used to justify the fact that this device actually accounted for the isolable isomers of the cyclohexane system. The older explanation invoked a planar transition state in the ring-flipping process, a transition state which would be unreasonably high in energy. The more usual explanation is given in a statement by Prelog(22) in an excellent paper on chiral substitution of ring systems. Speaking of such rings, he states that

> Because of the ability to rotate freely, however, these stereoisomers behave statistically as though they had a twofold symmetry, and thus as though they belonged to a higher symmetry group....

Actually their statistical behavior would tend toward a favored conformation which would not necessarily time average to a planar state (required to generate the twofold axis he speaks of). What *is* true in these cases, though, is that the appropriate ring torsion mode, R_n, can occur faster than the compounds can be isolated, so that the *permutation group* of the molecule corresponds to a *point group* with a twofold axis.

An operation of still another kind occurs in the nitrogen inversion of amine derivatives.(23) As shown in Figure 5a, such an operator effectively permutes the enantiomorphic representations of the amine compounds so that the effective symmetry of an amine is higher than the C_{3v} symmetry of a rigid ammonia skeleton. I have denoted this operation Iv_2 since it is a composite operation involving

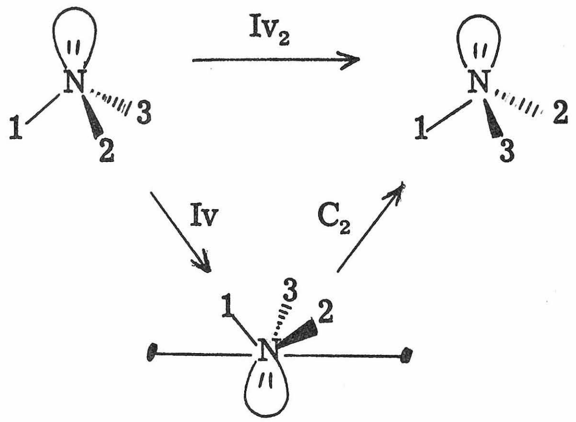
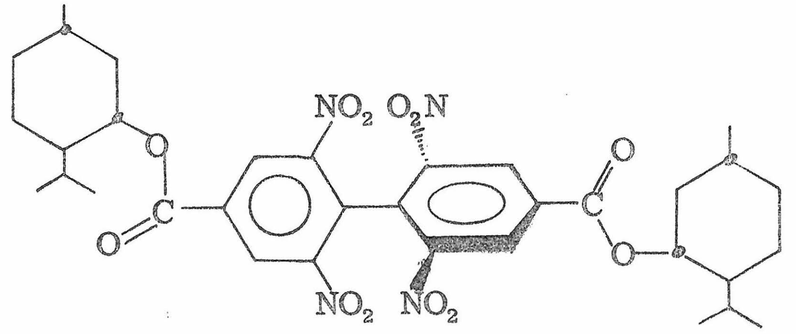


Figure 5a

The Inversion-Rotation Operator

inversion of the position of the lone pair electrons, followed by a two-fold rotation as indicated in Figure 5a. In aziridines this inversion is sufficiently slow that the separate enantiomers can be obtained. Notice that if any of the ligand set $\{1, 2, 3\}$ are chiral, this inversion does not lead to the enantiomers, but to a diastereomeric molecules.

A final instance of the usefulness of the special rotation-vibration groups is afforded by a compound prepared and commented on by Mislow and his co-workers.(24) The molecule prepared was d̲-menthyl ℓ̲-menthyl 2,2′,6,6′-tetranitro-4,4′-diphenate, compound VII.



VII

A simplified representation of Mislow's compound is shown in Figure 6.

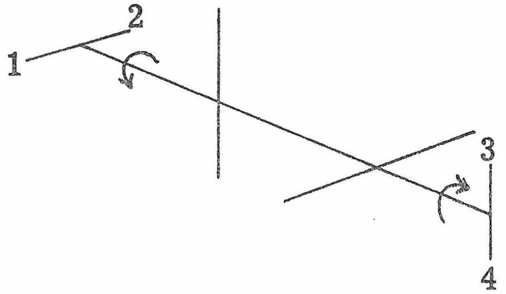


Figure 6

Simplified Skeleton of Mislow's Compound

If 1, 2, 3, and 4 are all oxygens, we would have the dicarboxylate ion. This ion would have a high symmetry, even as a rigid molecule, since it would be in group S_4. Because of the steric bulk and dipolar repulsion of the nitro groups, the central bond can be treated as a rigid structure; rotation about this band takes considerably longer than isolation of the enantiomeric compounds.

Rotation about the bond joining the carboxylate groups to the ring is relatively free, however, so that we have F_2 operation possible at each end, leading to an effective molecular symmetry of $S_4F_2^2$.

An interesting thing happens, though, when we substitute, say, positions 1 and 3 with an achiral ligand, such as an n-butyl group. The pure S_4 axis is destroyed, but the composite S_4F_2 axis is not! This is shown in Figure 7.

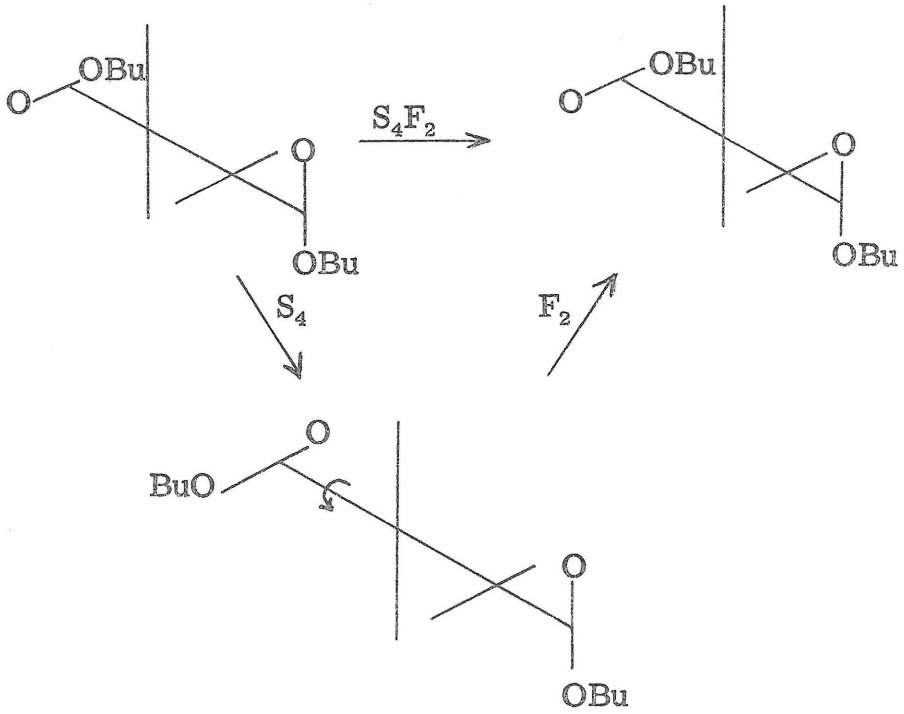


Figure 7

Operation of S_4F_2 Axis

By the same token, the $C_2F_2^2$ axis is preserved in this compound as shown in Newman projections of Figure 8.

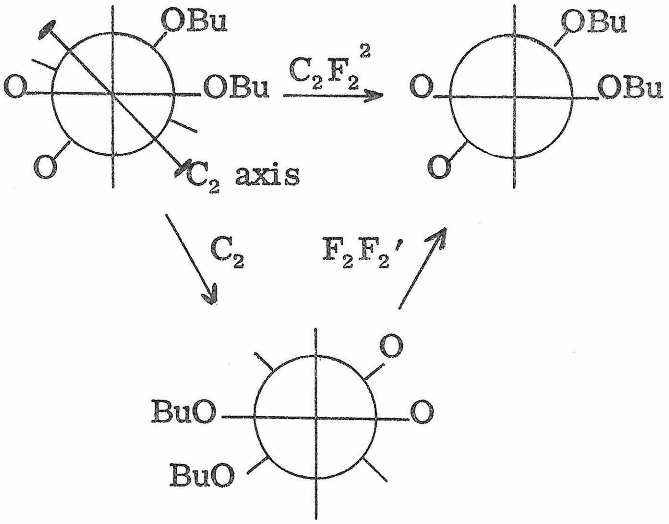


Figure 8

Operation of the $C_2F_2^2$ Axis

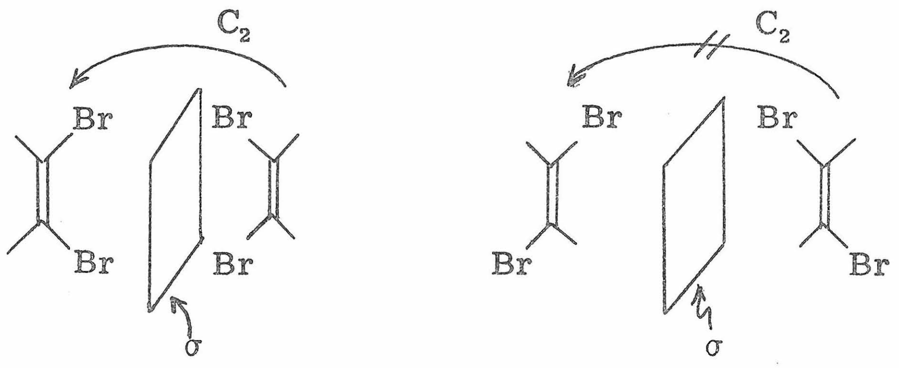
If, instead of the achiral n-butyl ligand we had used one each of the chiral d- and ℓ-menthyl ligands, we have Mislow's compound. Since the S_4F_2 axis interconverts d and ℓ menthyl, this axis (an alternating axis of symmetry) is preserved, and hence the compound should not possess isolable enantiomers. Interestingly, the $C_2F_2^2$ axis demonstrated above is no longer present, so that the molecule belongs to the symmetry group $\overline{S_4F_2}$ of order 4. The vincula is used to indicate that this group is not made by adding an F_2 axis to the S_4 group, but is based on the complex rotation-reflection operator, S_4F_2.

In a large number of examples, then, the free rotation, ring flip-rotation and atomic inversion operators serve very well to describe the gross behavior of chemical compounds, because they are simply mathematical formulations of known chemical pathways. As Mislow's compound illustrates, not all possible rotations can occur. The bond joining the phenyl rings does not have "free rotation" in the chemical sense; that is, we can isolate compounds which differ only by a rotation about that kind of bond. But the mathematical method is indifferent; if that bond were free to rotate Mislow's compound would still be a racemate. What the operators do, however, is to provide the isomer numbers for more and less restrictive condition on physical operations (free rotation, atomic inversion, and ring flipping) which can then lead to experimental verification--or falsification--of the types of physical transformations occurring in a given chemical system.

C. Permutational Isomerism and Chiral Ligands

1. History and Definition of the Problem

In a recent lecture on pseudoasymmetry, Prelog(5) called attention to the fact that enantiomerism is a function of the dimensionality of the space in which a compound exists. In a one-dimensional world such as Lineland,(25) the only possible physical operations are vibration along and rotation about the "world axis". Thus, compounds such as $C\equiv O$ and $HC\equiv N$ (supposing for the moment that they are composed of point atoms) could exist in two enantiomeric forms, $C\equiv O$ plus $O\equiv C$ and $HC\equiv N$ plus $N\equiv CH$. In a two-dimensional world such as Flatland,(25) where rotation in a plane is allowed, these two compounds cease to have enantiomeric forms. But *trans*-olefins now exist as enantiomers, whereas *cis*-olefins do not; see Figure 9. Whereas three-dimensional enantiomorphism (chirality) is *handedness*, two-dimensional is *sidedness*, and one-dimensional is *directedness*.



Rotation in the plane = C_2

Mirror plane ⊥ to the plane = σ

Figure 9

Two-Dimensional Enantiomorphism

Of course, in three dimensions, such two-dimensional enantiomers are interconvertible by an out of plane rotation. The implication, of course, is that in n-dimensions ($n > 3$) angles and ghosts could freely interconvert our 3-dimensional enantiomers, but they would face the chemical problem of resolving n-dimensional enantiomers.

In line with this observation, Prelog proposed(5) a notation for chiral ligands(26) involving the fact that certain Roman capital letters are chiral in two dimensions, and other are achiral. We have used this notation throughout Part B without explanation. The chiral letters are F G J L N P Q R S Z; the achiral are A B C D E H I K M O T U V W X Y. In order to avoid confusion, we have reserved the letters C, F, H, I, O, P, and S for their normal use as symbols for common elements.

The usual rule for chiral ligands, Van't Hoff's rule,(27) is that a molecule substituted with X chiral groups has 2^X possible stereoisomers, divided into 2^{X-1} sets of enantiomers.

The proof for this rule is straightforward. If we have X positions which can have chiral ligands, and each position can carry either enantiomorphic form, + or - (R or S) then we can generate all possible permutations by taking the product $(R + S)^X = R^X + XR^{X-1}S + \ldots$ where each term has the appropriate binary coefficient specifying the number of permutations of $(X - m)$ R-configurations and m S-configurations. The problem is formally identical to the distribution of heads and tails in flipping a coin X times. In an achiral environment, the R and S forms are equally probable, so that we get $(1 + 1)^X = 2^X$ isomers.

In Table IX we have listed the possible permutations for X = 1 - 4. We have grouped the permutations as enantiomorphic pairs having (X - m) R (or S for the enantiomorph) and m S (or R) ligands, as indicated in parentheses: (X - m, m).

If each position carries a different chiral ligand, or if the different positions are not related by any symmetry element of the molecule, then the maximum number of isomers can often be obtained.* However, if there are positions which carry enantiomorphically equivalent ligands (that is, ones which are identical or differ only in chirality) and which are related to each other by some symmetry element of the molecular skeleton as substituted, then fewer than 2^X isomers may result.

Van't Hoff and others have discussed the case of the tartaric acids in which the joining of two asymmetric carbons leads not to four, but only to three stereoisomers.(27-9) The (2,0) permutations remain a d,ℓ pair because no physical operation can interconvert the + and - forms of a chiral substituent.** The (1,1) permutations, however,

---

* It should be emphasized that with several chiral ligands the environment is not achiral, so that some possible (in the mathematical sense) diastereomers can not be obtained. Such a case might arise from trying to add too many bulky ligands to a central atom, for example.

** Our discussion of the nitrogen inversion operation in Part B is a relatively minor complication. Because of this operation, amines may have two enantiomers chemically present, but as a chemical system they are not enantiomorphic, and hence they should be considered achiral ligands. If the inversion is slower than chemical separation techniques, then the separate isomers could be obtained, and the enantiomers are also enantiomorphic as chemical systems and hence are chiral ligands.

Table IX

Permutations of X Chiral Ligands for X = 1 to 4

Number of Chiral Ligands	Position		a	b	c	d
one: 2^1 = 2 permutations	(1,0)	{	+ -			
two: 2^2 = 4 permutations	(2,0)	{	+ -	+ -		
	(1,1)	{	+ -	- +		
three: 2^3 = 8 permutations	(3,0)	{	+ -	+ -	+ -	
	(2,1)	{	+ -	+ -	- +	
	(2,1)	{	+ -	- +	+ -	
	(2,1)	{	- +	+ -	+ -	
four: 2^4 = 16 permutations	(4,0)	{	+ -	+ -	+ -	+ -
	(3,1)	{	+ -	+ -	+ -	- +
	(3,1)	{	+ -	+ -	- +	+ -
	(3,1)	{	+ -	- +	+ -	+ -
	(3,1)	{	- +	+ -	+ -	+ -
	(2,2)	{	+ -	+ -	- +	- +
	(2,2)	{	+ -	- +	+ -	- +
	(2,2)	{	+ -	- +	- +	+ -

give rise to only one stereoisomer, since the two positions, a and b, are equivalent if free rotation of the groups is allowed. This process of reducing a d,ℓ pair to a meso form through symmetrical substitution we shall call enantiomeric reduction.

E. Mohr(28) gives the best early description of this enantiomeric reduction. Early workers often assumed that the meso isomer corresponded to a (2,0) permutation since, by the definition of an asymmetric carbon atom, it should have four different ligands. The tartaric acid with both ends of the same chirality would have two identical ligands, and hence should be symmetric. Mohr clearly understood the significance of the alternating axis of symmetry. In addition to this problem and that of enantiomerism in ring compounds he discussed the hypermeso tetrahedral compound of S_4 symmetry which we will discuss further below.

The how of the equivalence in the meso form is important. As I noted above, a configuration which has no alternating axis of symmetry is inherently chiral, and hence has an associated enantiomorph. Thus, a two-fold rotation can never accomplish an enantiomeric reduction. As an illustration of this I have included the Newman projections of the nine conformations of staggered meso-tartaric acid in Figure 10. If rotation about the C-C bond were slower than chemical separation, all nine of these would be theoretically isolable. However, since rotation is faster than isolation techniques, the system appears to contain only one isomer. Interestingly, the predominant form may be an equimolar mixture of enantiomorphic rotamers. It is known to be such in certain crystalline salts.(29)

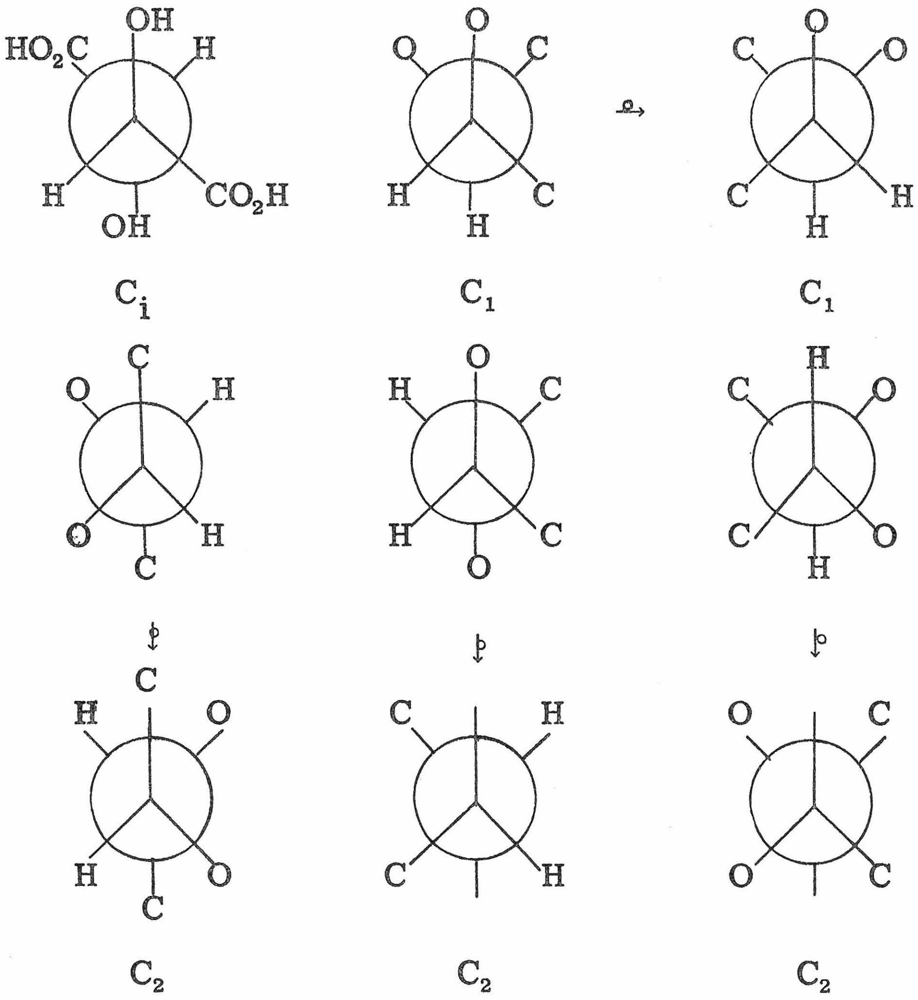


Figure 10

Rotational Conformations of meso-Tartaric Acid and Their Group Symmetries

In what follows we will assume that free rotation is present to permit the proper symmetry axis to operate to accomplish a reduction in the number of isomers.

Although rigid rotations alone cannot produce a non-enantiomeric form, they can reduce the number of diastereomers (diastereomeric reduction). In Table IX there are three enantiomeric pairs designated (2,1) in the case of three chiral ligands. If these three chiral ligands are enantiomorphically equivalent, and in addition, if positions a, b, and c are related by a three-fold operation, then all three (2,1) pairs become identical. This is shown in Figure 11.

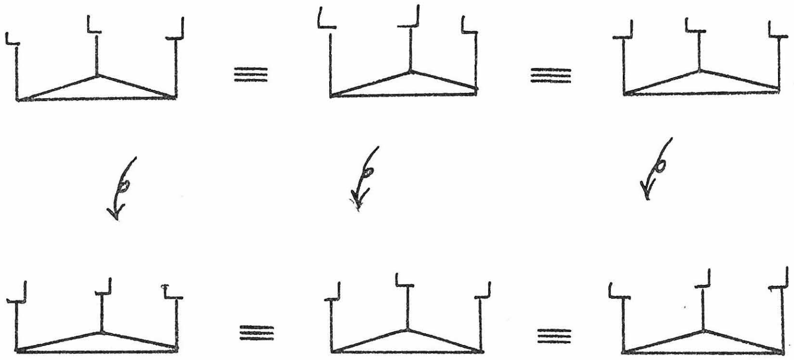
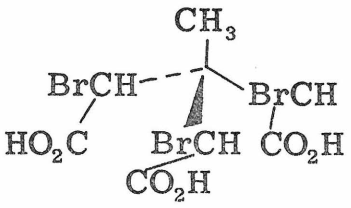


Figure 11

Diastereomeric Reduction with Three Chiral Ligands

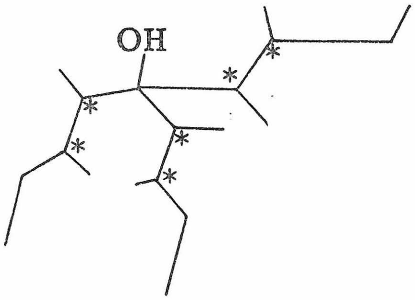
This diastereomeric reduction was first discussed by J. K. Senior(30) in 1927. He noted that compound VIII, which had been (reportedly(31)) prepared by Beesley and Thorpe(32) shows such reduction. Senior points out that despite the presence of three asymmetric carbons, there are two, not four, possible diastereomers.



VIII

He includes in his paper tables for chirally substituted carbon atoms with X = 0-4 chiral and 4-X achiral ligands. He did not, however, discuss the general problem of enantiomeric and diastereomeric reduction, nor did he describe the symmetry basis for the reduction in the case of compound VIII. In a brief note on Senior's paper, Hahn(33) pointed out that the reduction is a consequence of the equivalence of the three substitutent positions, but he did not develop the thought further.

Allen and Diehl(7) considered diastereomeric reduction while calculating the isomers of C_1-C_{20} paraffinic alcohols, and they developed a formula for this reduction. They noted one interesting C_{19} molecule, 3,4,6,7-tetramethyl-5-(1,2-dimethyl)butyl-5-nonanol, IX, which has twenty-four diastereomeric forms, in which one-third, or eight, have an asymmetric carbinol carbon. The other asymmetric carbon atoms are noted with asterisks



IX

Thus, the problem is to find ways to predict or calculate the amount of diastereomeric or enantiomeric reduction that can occur when chiral ligands are included in the substituent set of permutation isomers.

2. Isomer Counting with Chiral Ligands

The problem of isomer counting is immediately solved if there is an odd number of chiral ligands, i.e., $X = 2p + 1$. Since X *must* be the sum of an odd number of ligands of one chirality and an even number of the opposite chirality, only diastereomeric reduction can occur. No physical symmetry operation suffices to change the ligands of one chirality into ligands of the opposite chirality.

Indeed, we can treat the ligands L and ⅃ as a pair of non-identical achiral ligands. Thus, to determine the number of cyclopropane isomers of the type $C_3A_3L_2$⅃ (= number of C_3A_3L⅃$_2$ isomers), we merely need to look at the number of isomers of the type $C_3A_3B_2D$. In Table X are the results for Polya's method calculations for all the isomer numbers of cyclopropane derivatives, which will serve as a basis for calculating the number of isomers with various chiral ligand substitutions.

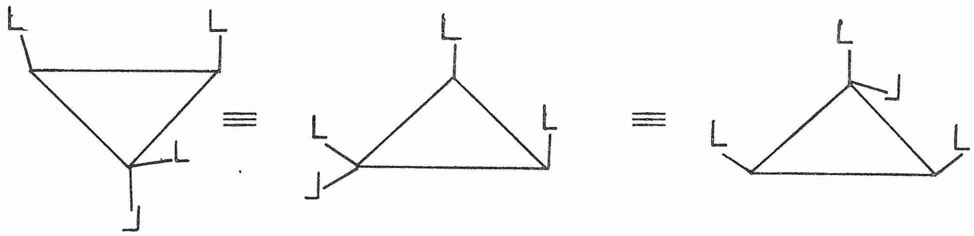
Table X

Substitution Isomers of Cyclopropane

Formula	Permutation Isomers	Diamutamers	Enantiomorphic Pairs
C_3A_6	1	1	0
C_3A_5B	1	1	0
$C_3A_4B_2$	4	3	1
C_3A_4BD	5	3	2
$C_3A_3B_3$	4	3	1
$C_3A_3B_2D$	10	6	4
C_3A_3BDE	20	10	10
$C_3A_2B_2D_2$	18	11	7
$C_3A_2B_2DE$	30	16	14
C_3A_2BDEK	60	30	30
$C_3ABDEKM$	120	60	60

For a compound $C_3A_3L_3$, then, there would be four isomers for the L form and four for the ⅃ form, whereas there are only four for the compound $C_3A_3B_3$. In addition, there would be ten isomers each for the compounds $C_3A_3L_2\text{⅃}$ and $C_3A_3L\text{⅃}_2$. Thus, if we change from the achiral ligand B to the chiral ligand L (or ⌋), we increase from four isomers to twenty-eight. By Van't Hoff's rule, we should get $4 \cdot 2^3 = 32$ isomers, so the threefold axis present in one of the $C_3A_3B_3$ isomers has produced a diastereomeric reduction in the number of isomers.

The difficult problem arises, then, when there are an even number of <u>each</u> <u>kind</u> of enantiomorphically equivalent chiral ligand present in the molecule. Even in this case the problem is simplified if the number of + and - forms of each kind of chiral ligand are not equal. Thus, for the case of four chiral ligands in Table IX, diastereomeric and enantiomeric reduction cannot occur in the (4,0) case. Only diastereomeric reduction can occur in the (3,1) cases. We can treat this case <u>exactly</u> as we treated that of an odd number of chiral ligands. Thus, we can look at the diastereomeric reduction as a change from $C_3A_4B_2$ to C_3A_3BD in the cyclopropane case. This is a change from four to ten for $C_3L_4B_2$ going to $C_3L_3\rfloor B_2$ and also for $C_3\rfloor_4B_2$ to $C_3\rfloor_3LB$. Since there are three possible (3,1) permutations, we would expect a change of four to $4 \cdot 3 = 12$, so diastereomeric reduction occurs in this case. The relevant structure is shown as compound X.



X

With a higher order axis, even larger diastereomeric reduction can occur. Thus, a compound with a four-fold rotation is capable of reducing the four (3,1) d,ℓ pairs of four enantiomorphically equivalent chiral ligands to one d,ℓ pair, as shown in Figure 12. Even in this case, though, we could easily compute this reduction by Polya's method.

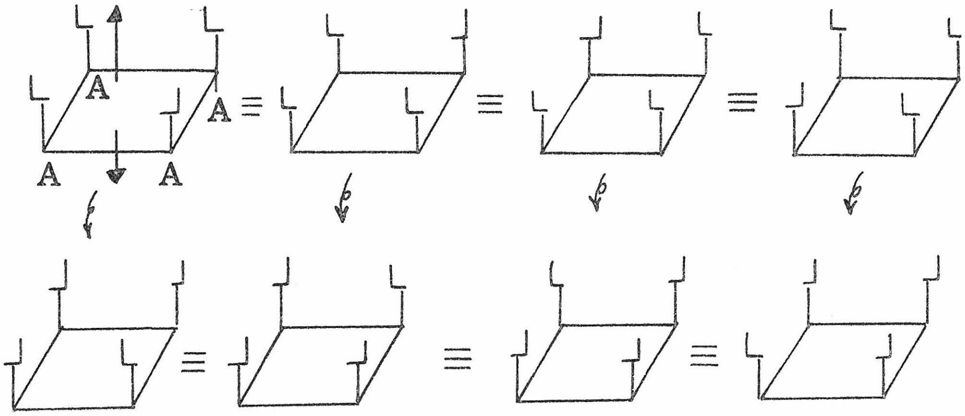


Figure 12

Four Chiral Substituents Under the Influence of a Fourfold Rotation Axis

The real counting problem arises, then, when X is even and all enantiomorphically equivalent chiral ligands occur in pairs. In such cases, the possibility of enantiomorphic reduction arises, and such reduction cannot (by present techniques) be handled by Polya's method. Instead, the Polya's method calculation merely sets an upper limit on the number of isomers, since it can only account for the diastereomeric reductions.

Since the case of $X = 2$ and the (1, 1) permutation is well known, let us divert our attention for the present to the (2, 2) permutation for the case $X = 4$. There are six possible isomers in the low symmetry limit. We can reduce these six (three *d,ℓ* pairs) to three *meso* forms by using any alternating axis, such as an inversion center, a mirror plane, or a fourfold rotation-reflection axis, as shown in Figure 13.

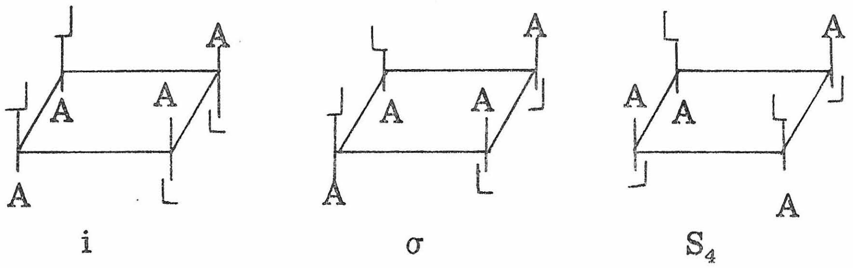


Figure 13

Meso Compounds with Four Chiral Ligands

The molecular skeleton itself need *not* have a fourfold axis of any kind in order to generate such *meso* compounds, as can be seen in Figure 14.

Figure 14

Meso Compounds with Four Chiral Ligands

To my knowledge no <u>meso</u> compounds with four chiral ligands of the above type have yet been made and their structures confirmed.

Since there is no direct method for calculating the amount of enantiomorphic reduction, I can only propose the following procedure for locating such reductions.

Given a molecular skeleton, S_n, with X chiral ligands and n-X achiral ligands, such that the set of X chiral ligands can be divided into exactly two subsets which differ only in chirality (i. e., one subset is the enantiomorph of the other):

1. Replace the X chiral ligand representations on the skeleton by X achiral ligand representations. All enantiomorphically equivalent ligands should have the same achiral representation; nonequivalent sets should have different representation.
2. If the skeleton as substituted possesses no alternating axis of symmetry, only diastereomeric reduction is possible.
3. The converse of Rule 2 is <u>not</u> true. The representation <u>may</u> possess an alternating axis and yet have no possible <u>meso</u> structure. Figure 15 illustrates such a case.

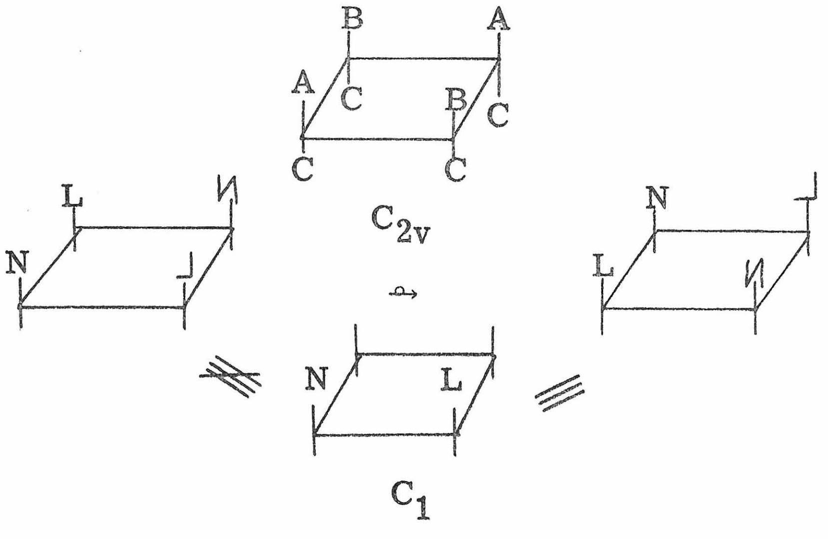


Figure 15

Meso forms will occur if none of the chirally substituted positions lie on the alternating axis of symmetry. Thus, an inversion center in the achiral representation will *always* produce *meso* chiral representations, since at most one ligand can occupy the center. This ligand must be achiral, for if there were a chiral ligand at the center, its enantiomorphic ligand would *not* possess a corresponding ligand at the position arising from inversion through the center, clearly a contradiction of the hypothesis that such ligands occur in pairs. With any higher order alternating axis, *meso* forms may not occur, since pairs of ligands may lie on the mirror plane or S_m axes.

4. As a corollary to the preceding, the number of *meso* isomers possible when there is more than one set of enantiomorphically equivalent chiral ligands corresponds *at most* to the *product* of the number possible for each set separately. However, this number may be reduced if the production of *meso* forms for one set of chiral ligands is carried out by one alternating axis which includes another set. Figure 15 above illustrates such a reduction, since for the separate L and N ligand sets there are *meso* forms, but none when they are placed together.

5. For forms corresponding to an enantiomorphic pair in the achirally substituted structure, it is generally true that the enantiomorph of a chirally substituted form is *not* the same as the chirally substituted enantiomorphic form; see Figure 16. Thus, new diamutamers can be obtained. However, at most one new diamutamer will be produced for each enantiomorphic pair in the corresponding achiral structure. Therefore, the number of *diamutamers* of the chirally substituted form will be less than or equal to the number of *permutation isomers* in the corresponding achirally substituted form.

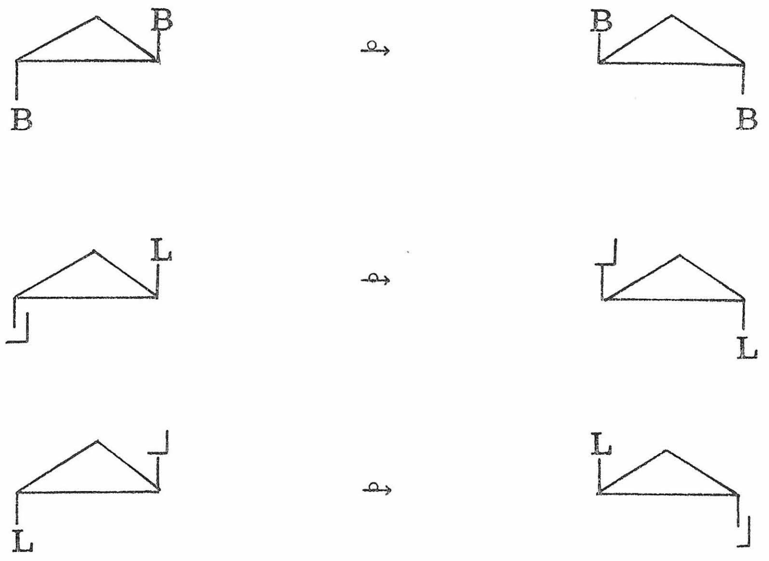


Figure 16

Effect of Chiral Substitution on Enantiomorphs:

Two Permutation Isomers → Two Diamutamers

Another interesting question can be asked of systems which show both diastereomeric and enantiomeric reduction. Suppose we are given a skeleton S_n with an even number, n, of ligand positions which is substituted with n enantiomorphically equivalent chiral ligands of the permutation type (n/2, n/2). Can enantiomeric and diastereomeric reduction proceed completely? That is, can all $n!/((n/2)!)^2$ permutations be reduced to one and only one isomer? If such a structure exists, we will call it a <u>hypermeso</u> isomer. For n = 2 <u>any</u> achiral skeleton with only two ligand positions can have a <u>hypermeso</u> form, since there is only one <u>meso</u> isomer of the type LX⅃ where X is a divalent atom or other S_2. A more interesting case occurs when n = 4.

In this case there are six permutations of the (2,2) type which would be reduced to one in a hypermeso form. The tetrahedral skeleton can give rise to hypermeso isomers. Figure 17 shows that all four ligand positions (a, b, c, and d) for the permutations in Table IX are equivalent in such a compound.

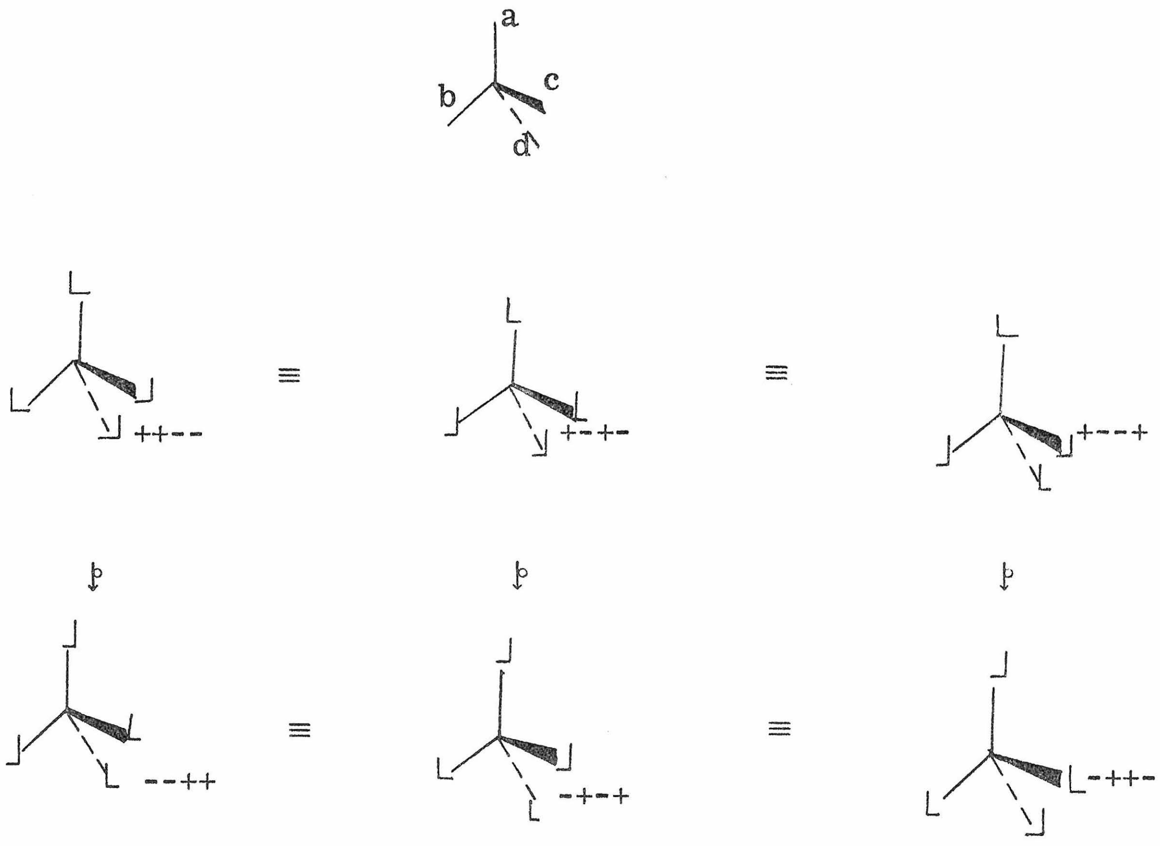


Figure 17

The n = 4 Hypermeso Structure

Such a compound was first discussed by Mohr,(28) and one was prepared fifty years later by McCasland, Horvart, and Roth,(34) in their investigation of compounds possessing S_4 symmetry. The compound they prepared was pentaerythritol di-(+)menthyloxyacetate di-(-)-menthyloxyacetate.

In addition to the n = 4 hypermeso compound shown in Figure 17, other possible hypermeso skeletons are shown in Figure 18.

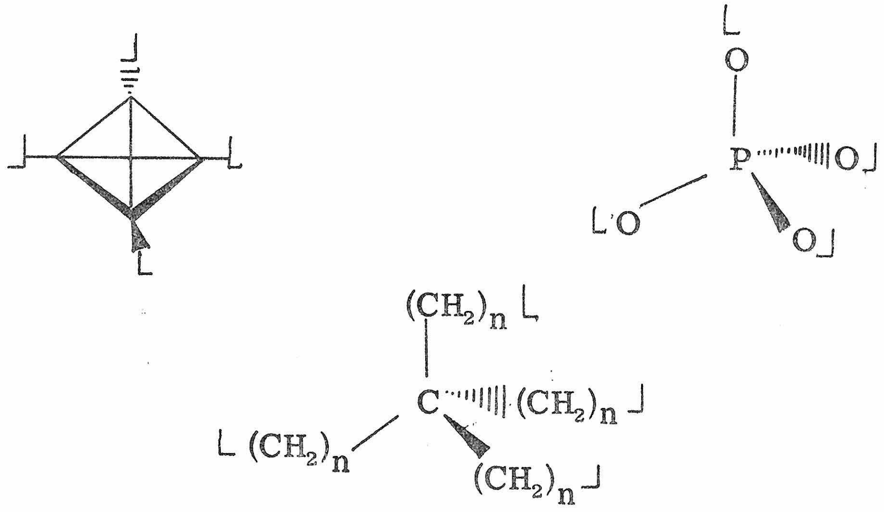


Figure 18

n = 4 Hypermeso Structures

But are there higher hypermeso compounds, such as for n = 6, n = 8, etc? No. That answer, interestingly enough, is provided by Polya's method. In order to give rise to a hypermeso isomer, a molecular skeleton X has to be such that for the compound $XA_{n/2}B_{n/2}$ there is only one permutation isomer. Otherwise, there are distinguishable patterns for substituting the skeleton with L and ⅃, and at least *two* *meso* (or d, ℓ) forms arise.

For six ligands the octahedron is the highest symmetry framework available, but an XA_3B_3 species has two isomers: one in which the A ligands share a face, and one in which they do not. Similarly, for eight ligands, twelve ligands, and twenty ligands (cube, dodecahedron, and icosahedron, respectively). In all three cases there is more than one $XA_{n/2}B_{n/2}$ isomer. But clearly, if the regular polyhedra are of too low a symmetry, then any less ordered arrangement of the ligands cannot generate a *hypermeso* structure. In the same way it can be shown that there is no $n = 4$ *hypermeso* compound other than those with T_d symmetry. All distortions of the tetrahedron immediately make possible *cis* and *trans* forms, and hence generate at least two *meso* isomers.

Although *hypermeso* structures cannot be generated for $n > 4$, a considerable amount of diastereomeric and enantiomeric reduction can be accomplished by substituting a regular polygon or polyhedron. For $n = 6$ ligands there are twenty possible (3, 3) permutations. If these six ligands are arrayed on a benzene skeleton, three *meso* forms result, shown in Figure 19. On an octahedron only two forms are required to represent all twenty permutations, as seen in Figure 20. The facial form may be one of the few possible S_6 structures in chemistry.

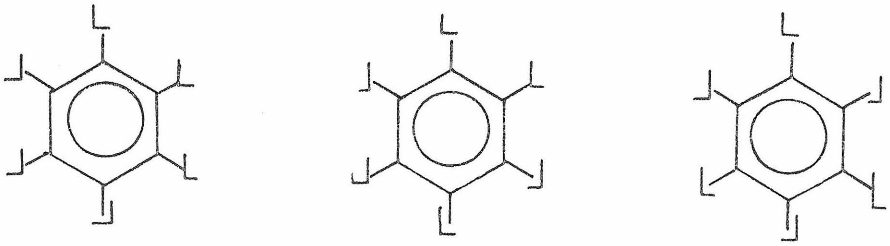


Figure 19

Meso Forms of $C_6L_3\text{⅃}_3$

Facial Form

S_6

Meridional Form

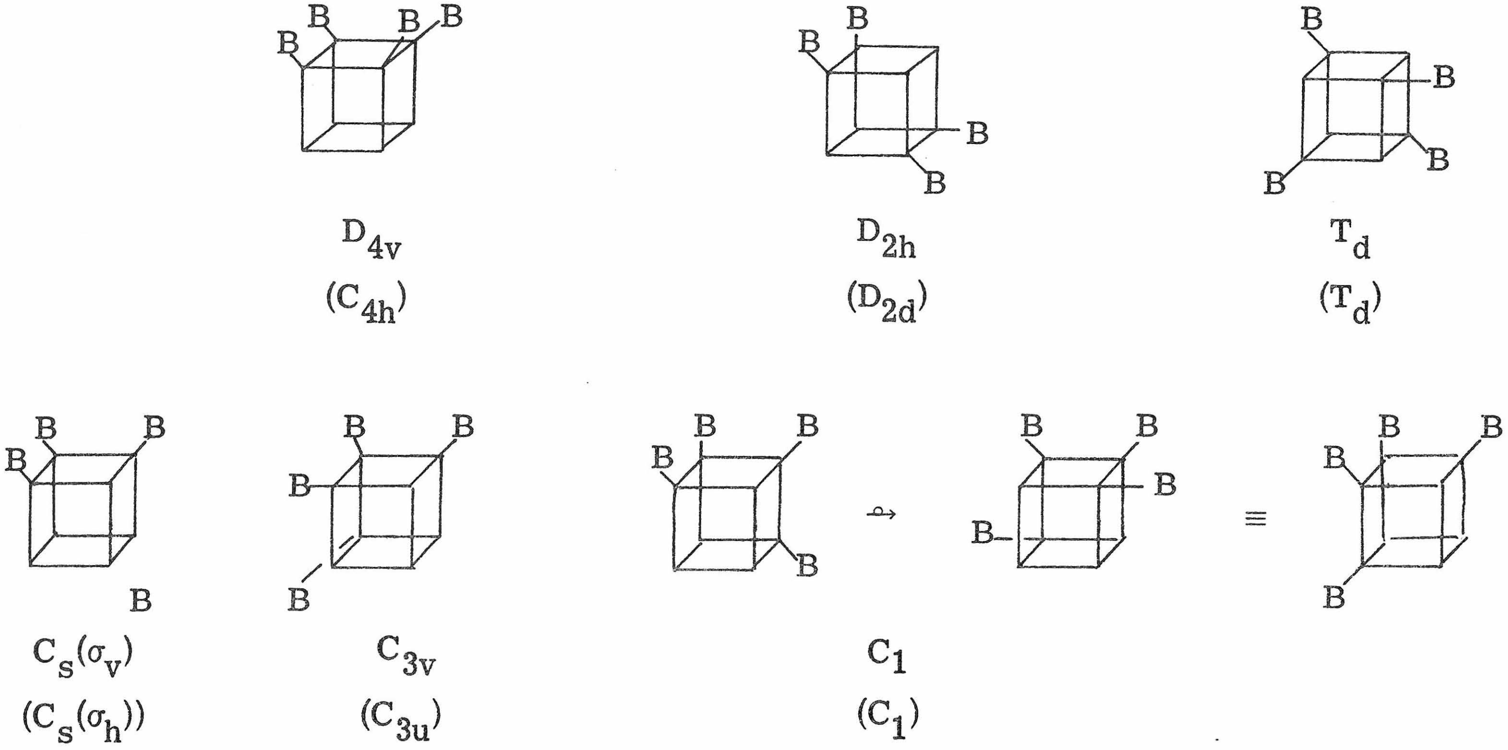
S_4

Figure 20

Meso Forms of $XL_3\text{⅃}_3$ on an Octahedral Skeleton

With eight chiral ligands there are seventy possible permutations. In Table II, Part B, we gave the cycle indices for a cubane type skeleton with eight ligands: $Z(O;8)$ and $Z(O_h;8)$. The solution for XA_4B_4 is seven permutation isomers, six diamutamers, and one enantiomorphic pair. (Note that the complete expansion of $Z(O;8;f(A,B))$ and $Z(O_h;8;f(A,B))$ need not be solved to obtain this information.) Inspection of these forms in Figure 21 shows that five meso forms and two enantiomorphic pairs are required to account for the seventy permutations of $XL_4⅃_4$.

Hopefully this analysis of the effect of chiral ligand substitution on molecular isomerism will add some additional direction to the ferment in this area produced by Prelog's work.(5, 22, 35) The most recent work in this area was on meso forms of 1,2-disubstituted ferrocenes by Goldberg and Bailey.(36) There are still new veins to be worked, even in so old a mine as optical isomerism.



D_{4v} (C_{4h})

D_{2h} (D_{2d})

T_d (T_d)

$C_s(\sigma_v)$ ($C_s(\sigma_h)$)

C_{3v} (C_{3u})

C_1 (C_1)

Figure 21

Substitution Isomers of XA_4B_4 ($XL_4\ \ _4$).

(A's Omitted for Clarity)

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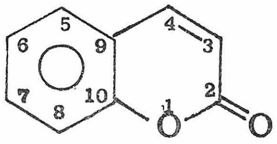
II. STUDIES IN THE PHOTOCHEMISTRY OF COUMARIN AND CERTAIN COUMARIN DERIVATIVES

A. Introduction

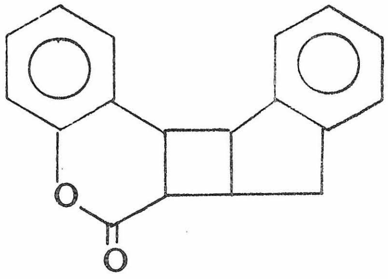
Coumarin, compound I, was first isolated by A. Vogel in 1820 from clover blossoms and Guianaian Tonka beans.(1) Interest in the natural product originally centered on its sharp cloverlike odor; indeed, it was this odor plus the crystal form which lead Vogel to equate the compounds from these two sources. Coumarin is used heavily as a flavoring and perfume ingredient. The 1966 production of over a million pounds of coumarin was almost entirely from synthesis from phenols via a modified Perkin reaction. William H. Perkin first synthesized this compound in 1868 via the condensation of salicylaldehyde and acetic anhydride.



I

Recent industrial interest in coumarin has been primarily in its pharmaceutrical and fluorescent derivatives. Dicoumarol, which is produced in fermented sweet clover, interferes with blood-clotting and has been used in thrombosis chemotherapy. Warfarin performs a similar function but is fairly species-specific in action and has found extensive use as a rat poison. A number of natural coumarin derivatives and furanocoumarins are efficient fluorescers and are used as laundry whiteners.

Photochemical interest in coumarin has derived from cycloaddition reactions across the 3,4-double bond. The original reaction involved dimerization which was found by Ciamacian and Silder in 1902.(2) In addition to the dimerization reaction, other double bond additions occur to form products such as the indene adduct, II.(3) One result of the studies of the mechanisms of these reactions has been evidence, as outlined below, that coumarin has an unusually high quantum yield for radiationless deactivation. In what follows I will first try to outline the evidence for this high dissipation rate and the mechanism proposed for it by Ronald Cole. Then the evidence for a new mechanism will be presented, and then some new photochemistry which resulted from unsuccessful attempts at verifying the Cole mechanism.



II

B. Spectroscopy and Photochemistry of Coumarin

The ultraviolet absorption spectrum of coumarin has been reported in a number of places.(4-8) Figure 1 shows the spectrum as given in Reference 4. Essentially all of the photochemical studies of coumarin have involved excitation into the 310 nm band. The high excitation coefficient of this band ($\epsilon = 6000$ liter mole^{-1}cm^{-1}) and its relative indifference to solvent shows it to be a (π, π^*) transition. It does not show any vibrational structure, which Gallivan(6) interprets as being evidence of a large difference in internuclear coordinates between the ground to the first singlet state. This lack of structure is present even at 77°K in the fluorescence and absorption spectrum in polar solvents.(6,7) In contrast the phosphorescence and singlet-triplet absorption spectra show well-resolved vibrational structure.

Calculations of the absorption spectrum by Perel'son and Sheinker(5) and by Song and Gordon(7) both show that the lowest energy singlet transitions should all be (π, π^*) in character.

Ordinarily (π, π^*) singlet states are fluorescent. Although fluorescence from coumarin has been reported from this laboratory,(9,10) both older studies(8,11) and the most recent studies(6,7) have failed to show room temperature fluorescence with a quantum yield of greater than 10^{-4}. Interestingly, at 77°K, coumarin is fluorescent, but the quantum yield is solvent dependent. In nonpolar solvents, the ratio of fluorescence to phosphorescence quantum yield was greater than 50. In polar solvents it was about 0.2. Polarization studies of the fluorescence and phosphorescence at 77°K confirms their (π, π^*)

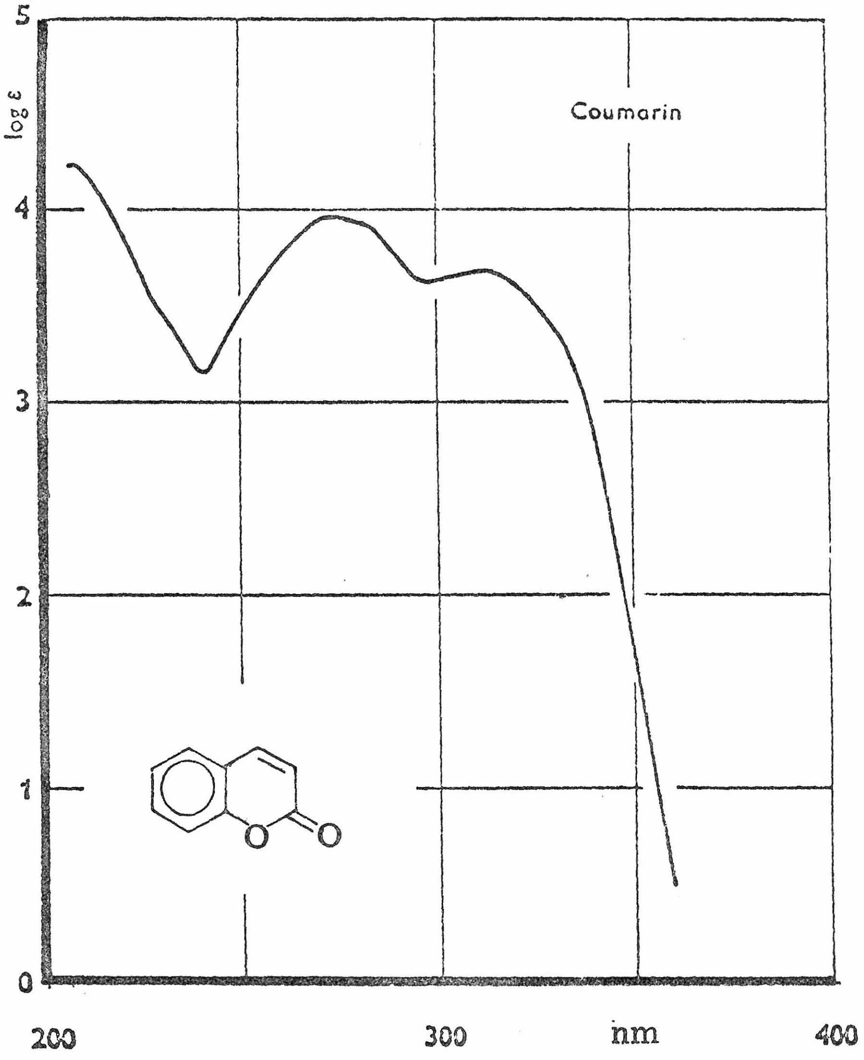
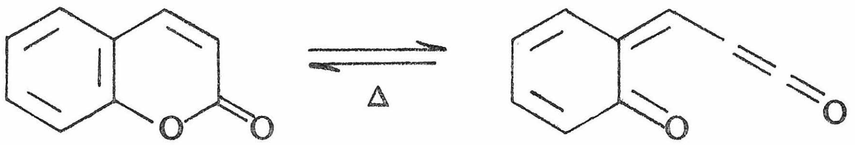


Figure 1

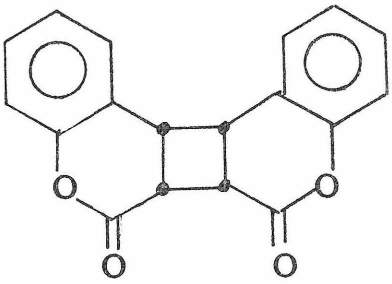
character. The phosphorescence lifetime is about 0.5 sec. at 77°K and 0.3 sec. in poly(methylmethacrylate) glass at room temperature. The electron spin resonance spectrum verifies the (π, π^*) character of the triplet state.(12,13)

Two explanations have been offered for this luminescence behavior. Song and Gordon(7) propose that the change in phosphorescence character in going from non-polar to polar solvents is due to the shift in the amount of (n, π^*) character in the first excited states, leading to a decreased intersystem crossing probability; such behavior has been discussed by Kasha.(14) They ascribe the absence of room temperature fluorescence to "thermally enhanced intersystem crossing and internal conversion," but they are not specific as to mechanism. Gallivan(6) argues that the change in fluorescence and phosphorescence properties is due to aggregation in the rigid matrices. This aggregation then bends to exciplex emission and to a decreased intersystem crossing. It may also lead to dimerization.(15-17) Song and Gordon argue that the stability of phosphorescence intensity with time excludes dimerization; however, if only monomeric, isolated, and solvated molecules phosphoresce, then there is no reason to expect dimerization, which would occur in aggregates, to lead to a decrease in the phosphorescence quantum yield. Gallivan further argues, following Cole,(10) that the absence of room temperature fluorescence is due to a thermally reversible photochemical ring opening to the ketene III.

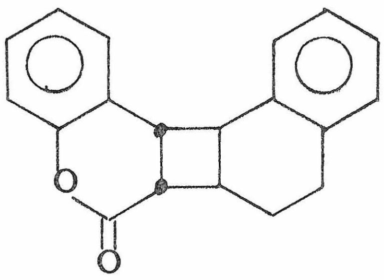


I　　　　　III

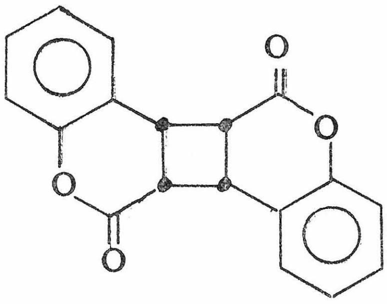
Cole proposed this ring-opening following a very careful study of the photodimerization of coumarin. As mentioned above, Ciamician and Silber(2) showed that coumarin photodimerizes in alcoholic solution. Later studies by Anet,(18) Krauch, Farid, and Schenck,(16) and Hammond, Strout, and Lamola(9) have shown that four dimers, IV-VII, are formed under direct and sensitized irradiations.



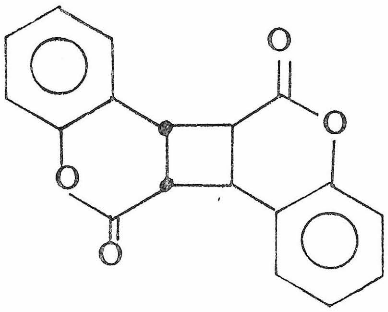
IV



V



VI



VII

The two head-to-head dimers (IV, V) are the predominant isomers formed; by sensitization and quenching it has been shown that IV is the singlet reaction product and V arises from triplet coumarin. There is a marked solvent and salt dependence on this reaction. (16,17,19)

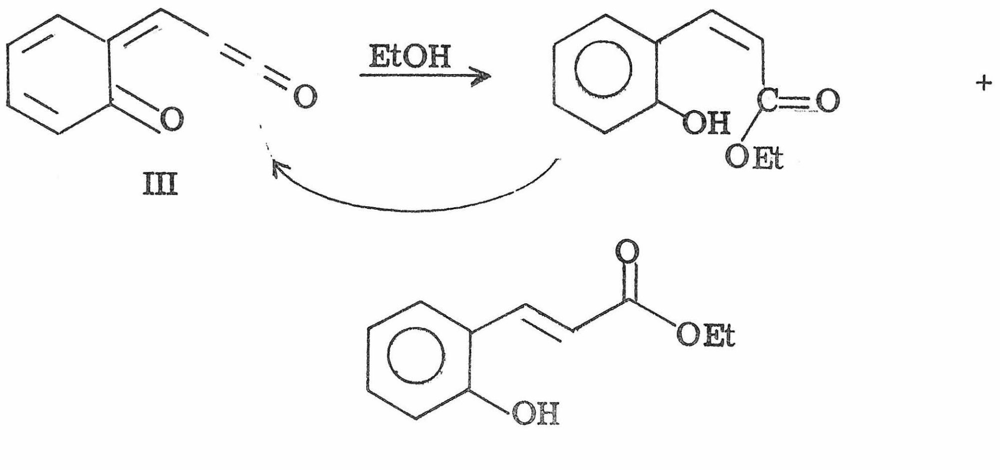
In his study of the coumarin system, Cole measured quantum yields for both direct and sensitized irradiation in benzene and ethanol. Under favorable concentration conditions in benzene the quantum yield for dimerization (direct irradiation) is 2.3×10^{-4}. Based on the sensitized dimerization he was also able to set the intersystem crossing efficiency at 2.2%. Combined with a fluorescence yield of less than 10^{-4}, this leaves 98% of the absorbed energy unaccounted for. From the (π, π^*) band intensity of 6000 liter/mole/cm and the relation $\underset{\frown}{1}$ we can calculate that the expected natural fluorescence lifetime of the first singlet state should be about 20 nsec. Furthermore, from the

$$\tau_0 = \frac{10^{-4}}{\epsilon_{max}} = \frac{10^{-4}}{6 \times 10^{3}} \sim 2 \times 10^{-8} \qquad \underset{\frown}{1}$$

fluorescence quantum yield of less than 10^{-4} and relation 2, we can estimate the upper limit of the coumarin singlet lifetime as 2 psec. or roughly one vibration. Even if this value is off by three orders of magnitude, we must invoke a fairly direct rearrangement pathway to account for such a rapid reaction.

$$\phi_f \tau_0 = \tau = 10^{-4} \times 2 \times 10^{-8} = 2 \times 10^{-12} \qquad \underset{\frown}{2}$$

Cole had only one piece of positive evidence to support his position of the ketene formation, namely the observation that ethyl coumarate is formed in ethanol upon long irradiation.(20) This product (VIII) might arise from the ketene by nucleophilic attack.



III

VIII

It was as a follow-up to Cole's suggestion that I undertook the detection of this ketene by two methods:

a) low-temperature spectroscopic methods, and

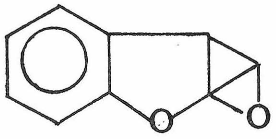
b) nucleophilic trapping at room temperature.

C. Low Temperature Spectroscopy of Coumarin

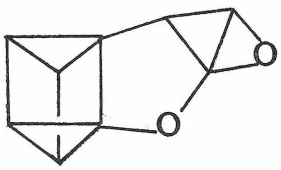
The conjugated ketene III should be highly colored. Ketene itself$^{(20)}$ shows absorption to 370 nm with $\lambda_{max} = 330$ nm, $\epsilon = 12$. The eight additional π electrons should increase the extinction coefficient (by mixing in additional (π, π^*) character) of this absorption and red shift it. Thus, flash photolysis should reveal this intermediate if it is present for longer than a few microseconds. The formation of ethyl o-coumarate suggests that it might be long-lived. However, Cole$^{(10)}$ attempted flash spectroscopy and failed to locate the ketene. A repeat of the experiment at low concentrations in methanol and benzene failed to show any evidence of ketene formation. Cole argued that the negative result could be due to photochemical cyclization induced by the spectral analysis lamp. However, a cyclization of this kind from an (n, π^*) excited state is unusual if not unprecedented.

In addition to changes in the electronic spectrum, changes would be expected to occur in the vibrational spectrum. In particular carbonyl stretches would appear at about 2100 cm^{-1} due to the conjugated ketene and about 1665 cm^{-1} due to the conjugated ketone. Several groups$^{(22)}$ have recently observed ketene stretches in the low temperature infrared of irradiated dienones with (n, π^*) excited states.

An examination of the infrared spectrum of 10^{-2} M coumarin in ethanol-isopentane-ethyl ether(EPA; 2:5:5 by volume) glass at 77°K showed a reduction of all bands in the region 1600-1750 cm^{-1} without the appearance of any new bands from 1500-2400 cm^{-1}. I originally interpreted this result as a net loss of coumarin without ketene formation. However, not only the carbonyl band at 1738 cm^{-1} went down by 50%, but so did the aromatic carbon-carbon double bond stretches at 1624 and 1610. The ketene should show double bond stretches in this region, as should the oxabicyclobutane IX which was proposed to account for the net loss of carbonyl, or any other reasonable coumarin isomer which might be proposed. An unreasonable isomer might be the prismaneoxabicyclobutane X. In benzene the prismane form is only produced by



IX



X

irradiation in the Schumann ultraviolet, (23) and the high strain energy of this molecule makes it unlikely to be produced at a photon energy of 92.3 kcal/mole (310 nm). The intensity loss must thus be attributed to net sample loss due to leakage of the indium wire sealed cell.

To circumvent this problem the irradiation was performed on coumarin in a KBr pellet. The only obvious major change after six hours irradiation was a broadening of the carbonyl band and a concomitant strengthening of the shoulder band at about 1750 cm^{-1} (main band at 1722) which persisted when the sample was warmed to room temperature.

Low temperature ultraviolet spectra were run in both EPA glass and KBr pellets. A photoproduct without a maximum at 310 nm is formed irreversibly. That is, warming to room temperature does not cause the disappearance of the new bands formed at low temperature. In both cases the product spectrum is superimposed on the coumarin spectrum. In EPA the new band is extremely broad with no well-defined maximum. In KBr the short wavelength maxima (225 and 275 nm in coumarin in KBr) shift together to 230 and 268 nm in the photoproduct. In both the infrared and ultraviolet experiments the results are consistent with photodimerization, although photodimerization has <u>not</u> been carefully examined in these solid systems. However, both the ultraviolet and carbonyl vibrational absorptions of the dimer lie at higher energy in the dimer than in coumarin, and photodimerization in frozen solutions and crystallites has been previously observed. (16,17)

With the exception of the initial infrared experiment, all of these experiments were made on the assumption that the oxabicyclobutane IX was the thermally isomerizing photoproduct responsible for the observed deactivation of coumarin singlets. None of the experiments thus far have supported this conclusion. However, in a further attempt to locate an intermediate, a large (imperfect) single crystal of coumarin was subjected to low temperature ultraviolet irradiation and examination by laser raman. After only twenty minutes, irradiation a small peak was observed growing in at 875 cm^{-1}. After three hours irradiation this band was almost the strongest in the spectrum. After six hours irradiation what may be new peaks are emerging at 1635 and 1680 cm^{-1}, but they are very small and in a noisy region. Table I shows the charge of various raman bands after irradiation at 98°K. The sample accidently warmed to -70°C (203°K) for a short time and was recooled without significant loss of the 875 cm^{-1} band. However, when the sample was warmed to room temperature the 875 cm^{-1} band disappeared and the original spectrum was restored. The changes in the relative room temperature band intensities before and after irradiation are also shown in Table I. Because peak heights rather than peak areas are used, and since the noise level makes for considerable baseline error, a change of ten percent is probably within experimental error.

Four lines decrease about thirteen percent: the carbonyl bands at 1724 and 1703 cm^{-1}, the C–O–C stretch at 1180 cm^{-1}, and a band

Table I

Raman Peak Heights

Relative to the 1566 cm^{-1} Band

		Room Temperature		98°K	
Frequency	Assignment (24)	After Irradiation	% Change After/Before	After Irradiation	% Change After/Before
1724	C=O	0.24	+19	0.18	-13
1703	C=O	0.38	+ 6	0.43	-15
1619	aromatic C=C	0.44	+ 4	0.95	+ 8
1603	aromatic C=C	0.92	--	≡1.000	+ 6
1566	aromatic C=C	≡1.000	--	0.28	--
1486		0.26	-13	0.22	- 2
1452		0.19	+ 1	0.45	- 2
1325		0.44	--	0.71	+ 3
1231		0.54	+ 5	1.45	+33
1180	C–O–C	1.18	- 1	0.39	-13
1156		0.42	-11	0.40	-10

Table I (Continued)

		Room Temperature		98°K	
Frequency	Assignment (24)	After Irradiation	% Change After/Before	After Irradiation	% Change After/Before
1124		0.38	-16	0.40	+ 4
1030	vinylic C–C?	0.34	+ 6	0.30	-14
875		--	--	1.09	∞
762	aromatic ring deformations	0.31	- 1	0.34	- 1
735	aromatic ring deformations	0.38	-13	0.42	+13

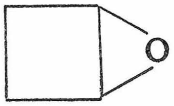
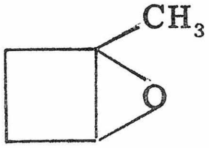
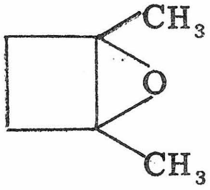
tentatively assigned as the 3,4 double band stretching frequency at 1030 cm^{-1}. Eight bands remain close to the same: the aromatic double band stretches (the increases may be real, since they are less polar in the oxabicyclobutane derivative then in coumarin) at 1619, 1603, 1566, and (probably) 1486 and 1452 cm^{-1}, the aromatic ring deformation at 762 cm^{-1}, and unassigned bands at 1325 and 1124 cm^{-1} (this loss is possibly an aromatic frequency indicating 1,2 substitution).

Three lines appear in the spectrum, or, more precisely, one line (875 cm^{-1}) appears and two lines (1230 cm^{-1}, 735 cm^{-1}) increase in intensity. Notably absent, even after six hours, is any line in the region of 2100 cm^{-1}. If any 2-oxabicyclobutanes were known, we could compare these three lines of calculated intensity ratio 0.17:1.000:0.05 (1231:875:735) to the known spectra. However, none are known, so we shall have to argue by analogy. Bicyclobutane and 3-azabicyclobutane are known. In addition, the next higher homologous oxabicyclo compound--5-oxabicyclopentane, IX--is known and its strong infrared bands (other than characteristic CH stretches which are not easily studied on the laser raman used in these experiments) assigned to the ring modes were found and are tabulated in Table II.

The band at about 930 cm^{-1} is due to the cyclobutane moiety(25-6) and the remaining bands are characteristic of epoxides. Note that the band below 900 cm^{-1} is a stronger infrared band than the band near 1260 cm^{-1}. Szymanski(26) points out that in the raman the intensity of these two bands is reversed; he assigns the 1260 cm^{-1} band to the asymmetric CH_2 wag. In addition to the epoxide modes, we

Table II

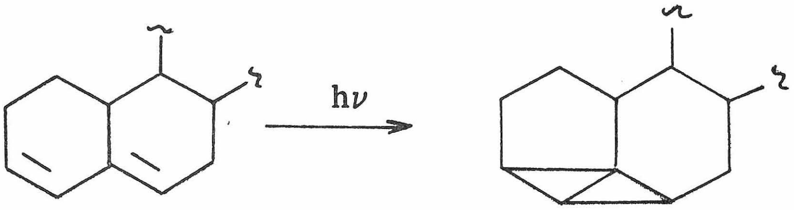
Infrared Absorptions Arising from Ring Vibrations in 5-Oxabicyclopentanes(27)

	1248 (medium)	929 (strong)	882 (strong)
	1252 (medium)	940 (medium)	824 (very strong)
	1289 (medium)	933 (weak)	836 (very strong)

would expect cyclopropane modes near 1190 cm^{-1} (strong; symmetric ring stretch) and 1029 cm^{-1} (weak; asymmetric wag). Haller and Srinivasan(28) carried out the analysis of the infrared and raman spectrum of bicyclobutane (C_4H_6) and the infrared spectrum of C_4D_6. For our purposes the important result is that the ring stretch modes in bicyclobutane (C_{2v} symmetry; allowed stretches $2A_1 + B_1 + B_2$) are not located in the same position as in cyclopropane nor are they the most prominent peaks in the spectrum. The symmetric (A_1) stretch has moved to 1245 cm^{-1}, and the strongest band is at 1091 cm^{-1} (an A_2 wag motion) which is normally weak in cyclopropane. A similar inversion could occur in the 2-oxabicyclobutane spectrum and thus lead to the strong 875 cm^{-1} band. A bicyclobutane mode of the same symmetry occurs at 914 cm^{-1} and the 875 cm^{-1} band may be a mode produced by the interaction of the epoxide and bicyclobutane modes. The 1231 cm^{-1} band would then correspond to the A_1 bicyclobutane mode. The 735 cm^{-1} band is due to an aromatic mode. Thus, the raman data are consistent with an enone → oxabicyclobutane rearrangement in the radiationless deactivation of excited singlet coumarin.

The mechanism of this rearrangement is interesting. The transition moment of the (π, π^*) transition in coumarin is highly localized in the α-pyrone portion.(7) Indeed, the first transition in coumarin (λ_{max} = 310 nm, ϵ = 6000 liters/mole/cm) is remarkably similar to that of 5-methyl-α-pyrone (λ_{max} = 300 nm, ϵ = 5000). These same calculations indicate further that the carbonyl carbon becomes more electrophilic, unlike many other (π,π^*) carbonyl compounds. The situation is very similar, then, to the well-known formation of bicyclobutanes from the singlet states of s-trans dienes, as shown in equations 3(29) and 4.(30)

3

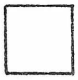
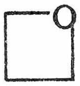
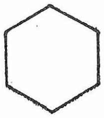
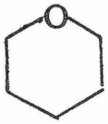


4

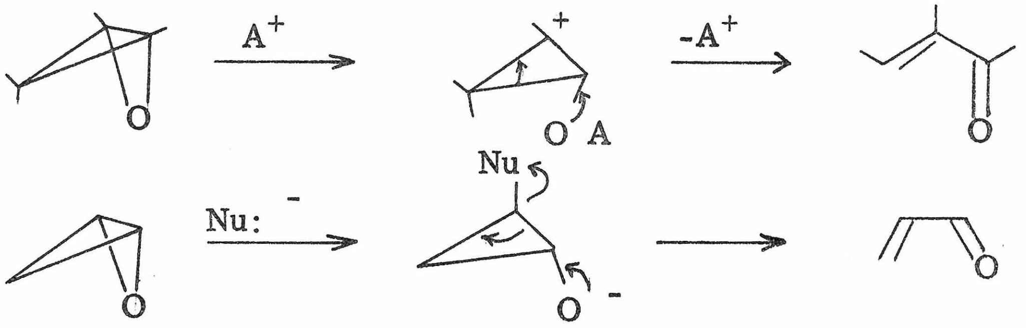
The thermodynamic enthalpy change in reaction 3 has been measured by Wiberg and is 25.9 kcal/mole.(31) The calculated strain energy of bicyclobutane is 66 kcal/mole.(32) The stability of the compound derives from the fact that ring-opening is a thermally forbidden reaction as a concerted process, so that an activated ($E_a > 40$ kcal/mole) radical mechanism is required to effect the reverse of 3.(32) Table III shows the strain energies of a few alicyclic rings and their oxa analogs, calculated from additivity relations in the thermochemical data. The introduction of an oxygen in the ring apparently makes no significant difference in the strain energy, so the instability of the oxabicyclobutane ring is probably kinetic. As illustrated in equations 5 and 6, the cyclopropene oxide system is subject to both general acid and nucleophilic catalysis, respectively. Thus, it is the polarization of the bonds rather than

Table III

Ring Strain Energies(33)

Compound	Strain Energy (kcal/mole)	
	27.6	ΔE = 0
	27.6	
	26.2	ΔE = 0.2
	26.4	
	0.0	ΔE = 2.2
	2.2	

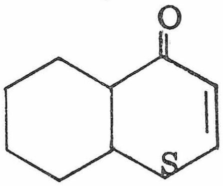
the inherent differences in the energies of the system which make the oxabicyclobutanes less stable than their carbocyclic counterparts. If, as I believe, the new raman spectrum is due to the oxabicyclobutane isomer, its thermal stability should allow its detection in a suitable solvent at -80 °C via the ^{1}H nmr spectrum of the vinylic protons.



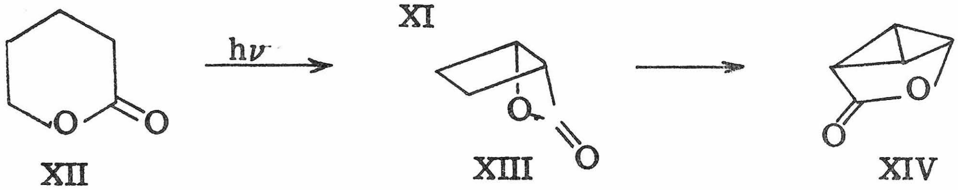
5

6

If the mechanism written is correct, other carbonyl compounds with transoid diene structures and a (π, π*) ground state might give oxabicyclobutanes. Besides coumarin derivatives, 1-thio- and 1-selenocoumarins and 1-thio chromones such as XI might show a similar behavior.(34) The 1-azacoumarin (carbostyril) has an (n, π*) first singlet state and should not show this rearrangement. Interestingly, α-pyrone, XII, gives a Dewar benzene-like structure, XIII, which thermally isomerizes to the bicyclobutane XIV.(35)



XI

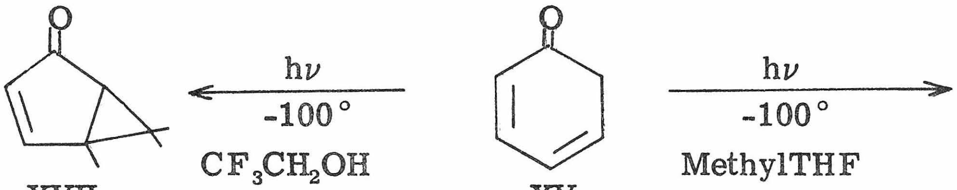


XII

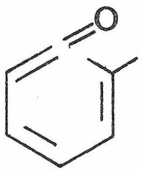
XIII

XIV

The nonopening of coumarin to the ketene III is consistent with previous studies. It would proceed by an α-cleavage reaction of a carbonyl compound (Norrish Type I) which is well-documented for (n,π^*) excited states. In the case of 6,6-disubstituted-2,4-cyclohexadienones the ketene rearrangement is frequently observed.(22,36) In investigating the reaction of 3,4,6,6-tetramethyl-2,4-cyclohexadienone XV, Griffiths and Hart(22b) found that they could observe the ketene XVI at -100° in a series of solvents. However, in 2,2,2-trifluoroethanol they could not observe ketene forming. On examining the absorption spectrum they found that the (n,π^*) and (π,π^*) states had crossed and that the bicyclohexenone XVII was now the observed product. The same result could be obtained by photolyzing XV in a cyclohexane-silica gel-benzene slurry. Thus, the change to a (π,π^*) singlet abolishes the cleavage to a ketene.



XVII XV

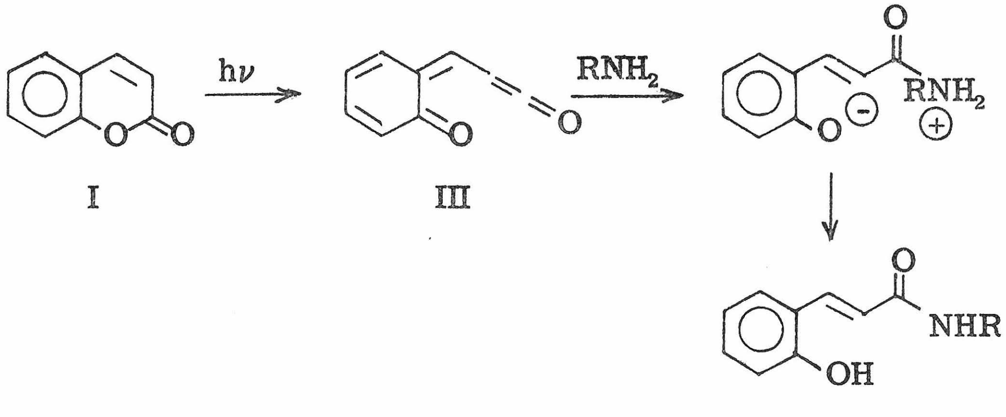


XVI

Although the present study is suggestive, further study is required to firmly establish the enone-oxabicyclobutane rearrangement and to test its generality.

D. Addition of Amine to N-Alkyl-o-coumaramide

In the course of trying to identify the ketene III as the coumarin rearrangement product, I attempted to trap it by means of nucleophiles. Stout's observation(9) that ethyl-o-coumarate is produced on photolysis seemed to indicate that such trapping should be possible. Ketene trapping had been the standard method of identifying these reactive intermediates prior to the development of low temperature spectroscopic techniques.(36) If Cole's mechanism is correct, we should expect to form the o-coumaramide XVIII.



XVIII

The initial attempt to trap the intermediate was carried out in benzene solution using cyclohexylamine as the nucleophile. The reaction product was definitely not the N-cyclohexyl amide, although it appeared to revert to the amide on standing. Physical data are shown in Table IV. Even the most cursory examination of the data confirms

Table IV

	Cyclohexyl Amide				Cyclohexylamine Adduct*			
Melting Point	231 °C				Liquid at 20 °C			
UV Spectrum								
λ_{max} (nm)	218	226 (sh)	275	323	206	218	273	281
Relative Intensity	0.78	0.71	1.00	0.53	1.00	0.55	0.07	0.06
NMR Spectrum								
δ(ppm TMS)	0.6-2.0 (mult.)	**	6.0-8.0 (mult.)		0.7-2.0 (mult.)	4.19, 4.28 (doublet?)	7.33-7.82*** (mult.)	
Relative Intensity	10.00		6.00		8.62	0.99	1.00	
IR Spectrum								
ν_{max} (Intensity)					3420 (w) 2910 (s) 1715 (s) 1468 (m) 1376 (m) 1270 (s)			
Molecular Weight	245.33				380 ± 60 (Rast melting point method)			

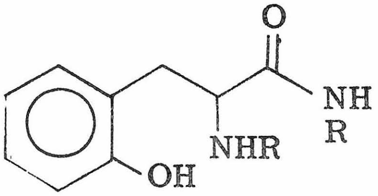
* Purity was indicated by a single spot on silica gel TLC regardless of solvent polarity, an unchanging UV spectrum over forty 2-ml fractions during column chromatography, and a single peak on a Carbomarx 20M GLC Column.

** The $O\underline{H}$, $N\underline{H}$, $NC\underline{H}$ peaks are obscured by the d_5-DMSO solvent peak.

*** In $CDCl_3$; slightly more complex in CCl_4.

the nonidentity of the adduct and the amide. However, the data, especially the nmr spectrum, are hard to interpret. The mass spectrum gave no peak larger than 167 daltons/charge unit.

The complexity of the alkyl region in the cyclohexylamine adduct made the nmr difficult to interpret, so a simpler amine, isopropylamine, was selected. Irradiation of coumarin in neat isopropylamine led to the formation of isopropylcoumaramide and a product which has been identified as N,N′-diisopropyl-o-tyrosine amide XIX. Table V lists the physical data for this compound and its hydrochloride.



$R = CH(CH_3)_2$

XIX

The identification of the adduct as the isomer with the amine group α to the carbonyl is based on its formation of a stable hydrochloride and its carbonyl peak in the infrared. The β-amino acid would be expected to undergo a retro-Michael addition to yield the amide and isopropylamine; the existence of a stable hydrochloride makes it probable that it is not the β isomer. Furthermore, it has been found that the carbonyl frequency of β amino acids occurs about 20 cm^{-1} lower than the corresponding α-amino acids.(25) A sample of o-tyrosine isopropylamide was prepared from an authentic sample of o-tyrosine. The hydrochloride of this amide showed an absorption

Table V

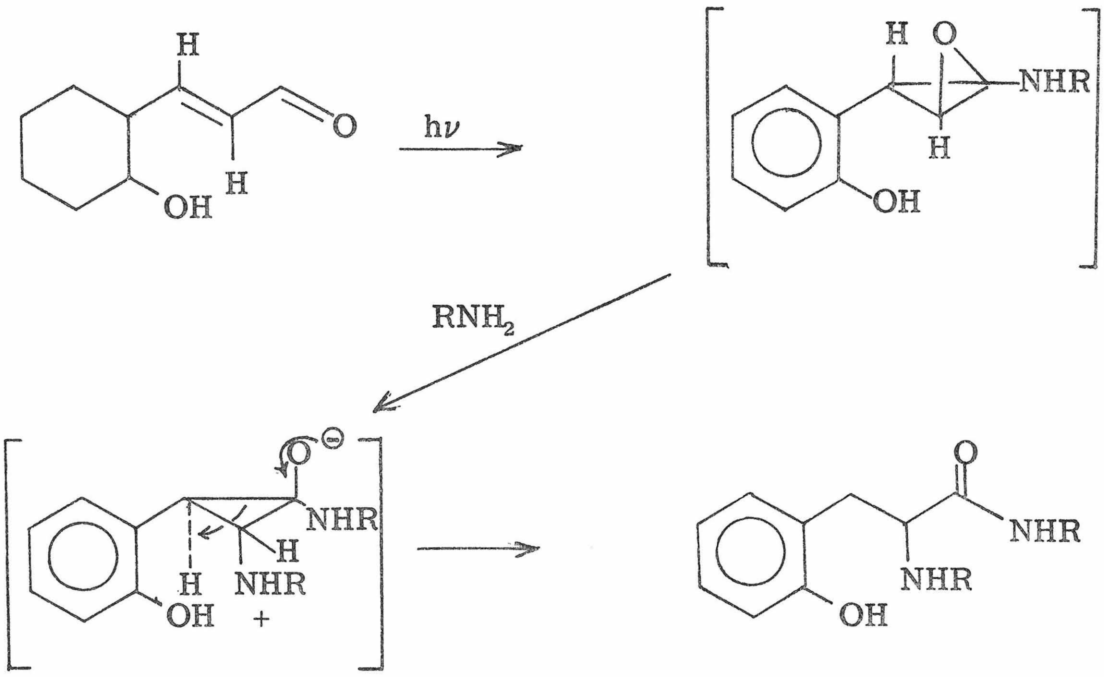
	Isopropylamine Adduct	Isopropylamine Adduct Hydrochloride
Melting Point	51°	85-105° dec.
UV Spectrum		
	λ_{max} = 278 nm	--
	ϵ = 2600	
NMR Spectrum (220 Hz)		
δ (structure, H)	($CDCl_3$)	(D_2O, DCl, $CDCl_3$)
	1.09 (mult., 12.1)	1.10 (mult., 12.25)
	2.40 (2 doubl., 1.0)	2.37 (2 doubl., 1.03)
	2.68 (mult., 2.0)	2.65 (mult., 2.00)
	4.00 (sept., 1.0)	4.00 (sept., 0.97)
	4.25 (2 doubl., 0.9)	4.26 (2 doubl., 0.96)
	6.71, 6.87 (mult., 3.8)	6.73, 6.90 (doubl., 0.98)
	7.07 (trip., 1.1)	6.73, 6.90 (doubl., 0.98)
		7.10 (trip., 1.08)

Table V (Continued)

	Isopropylamine Adduct	Isopropylamine Adduct Hydrochloride
IR Spectrum		
ν_{max} (intensity)	3310 (m) 3270 (ms) 2965 (m) 1647 (s)	3250 (m) 2965 (s) 2805 (m) 1645 (s)
	1542 (m) 1455 (m)	1592 (m) 1547 (m) 1450 (s) 1372 (m) 1128 (m)
	1364 (m) 1262 (m) 753 (ms)	1283 (m) 778 (s)
Molecular Weight	264.36 (calculated)	
	276 (osmometry in CHO_3)	

of 1655 cm^{-1} compared to 1655 and 1645 in the hydrochloride of the isopropylamine adduct.

The reaction proceeds via the amide or its anion, since it is formed in amine solution thermally before the photoadduct appears. The amide electronic spectrum is very similar to the coumarin spectrum, but more intense, so that it, too, has a (π,π^*) first excited state. A possible, but certainly not the only possible mechanism is shown in equation 7.



7

The generality of this amine addition reaction is not known; t-butylamine, which does not efficiently form an amide, does not appear to give a photoproduct even after three weeks irradiation. The relation of the isopropylamine reaction to the cyclohexylamine adduct is unclear.

E. Experimental

Spectra: The nmr spectra were performed on a Varian A-60 spectrometer unless mentioned; the isopropylamine adduct and its hydrochloride were also run on the Varian 220 Hz spectrometer by Mr. David Live. Ultraviolet spectra were run on a Cary 14 spectrophotometer. Infrared spectra were run on Perkin-Elmer 225 and 457 instruments in 400 mg KBr pellets unless otherwise mentioned. The raman spectra were run on a Cary 81 spectrometer with a neon-argon laser exciting source.

Irradiation: All irradiations were performed through pyrex. Low temperature irradiations were performed with an Osram 150 watt focusable xenon lamp. All other irradiations were carried out with a 450 watt Hanovia medium pressure mercury source.

Materials: MC and B coumarin was recrystallized from benzene-petroleum ether. MC and B amines were distilled from KOH or BaO. Benzene and methanol were MC and B spectrograde when used for spectra or photolyses, reagent grade when used for chemical preparation. Aldrich *o*-tyrosine was used without purification.

Low Temperature Studies: The low temperature UV studies were performed with the sample immersed in liquid nitrogen in a Dewar fitted with quartz windows. The low temperature infrared experiment was performed in the Perkin-Elmer low temperature dewar adapted to take 13 mn KBr pellets. The raman studies were performed in an apparatus designed by Mr. Jeff Hare of this department; details of its design may be obtained from him. Three hour irradiations were performed.

Preparation of Amine Adducts: Corning 13 mm × 100 mm Pyrex test tubes were cleaned in alcoholic KOH, rinsed with distilled water three times after the pH had reached neutrality. The tubes were then washed with sodium dodecyl sulfate and rinsed with distilled water three times after no foaming was observed. The tubes were dried overnight and constricted. Three ml aliquots of 0.8 M coumarin in amine were placed in each tube and the tubes were sealed following three freeze-pump-thaw cycles to 5×10^{-4} Torr. Irradiation was performed with the tubes taped to the cooling well of the lamp, a 24 hr. irradiation was generally adequate. Following irradiation the solvent was removed under reduced pressure. The adduct could be purified by forming its hydrochloride in benzene or by column chromatography on silica gel with 2:1 30°-60° ligroin:ethyl acetate.

Preparation of N-Isopropyl Coumaramide: 4.1 g (2.8 m moles) of coumarin and 2 ml (28 m moles) thionyl chloride were heated together on a steam plate until HCl evolution ceased. An additional 2 ml of thionyl chloride was added and heated one hour. After cooling, 100 ml of ethyl ether was added, followed by 9 ml (160 m moles) of amine in 50 ml ether. After stirring for an hour, the solvent and excess amine were removed on the steam bath. The solid was broken up and stirred with 200 ml 4N HCl. The precipitate was collected and stirred over the weekend with 150 ml 5% sodium bicarbonate. After filtering and washing with additional bicarbonate, the solid was dried under vacuum. Yield: 4.21 g (73%), m. 229-229.5 (uncorr.).

The amide could also be prepared by refluxing 0.2g of coumarin in 30 ml isopropylamine.

The amide could be purified by dissolving 1.5 g in 55 ml n-butanol and adding 100 ml 60°-70° ligroin.

Preparation of o-Tyrosine Isopropyl Amide Hydrochloride: Fifty ml of methanol saturated with hydrogen chloride was refluxed with 0.1 g o-tyrosine for two days. The solvent was removed under reduced pressure and replaced by 30 ml isopropylamine. Refluxing was continued for two days and the solvent was removed and the viscous liquid dried for a week under vacuum. The flask was washed with 15 ml benzene and the benzene solution in an erlenmeyer flask was saturated with hydrogen chloride. The solvent was decanted and the solid dried fifteen minutes at 70°.

Flash Spectroscopy of Coumarin: Two samples--one in methanol and one in benzene--were prepared to give an absorbance of 1.0 (2×10^{-4}) in a 10 cm flask cell. The cells were not degassed and were flashed without filtering. The spectrum of the flashed solutions were determined photographically. The apparatus and techniques have been discussed elsewhere.(37)

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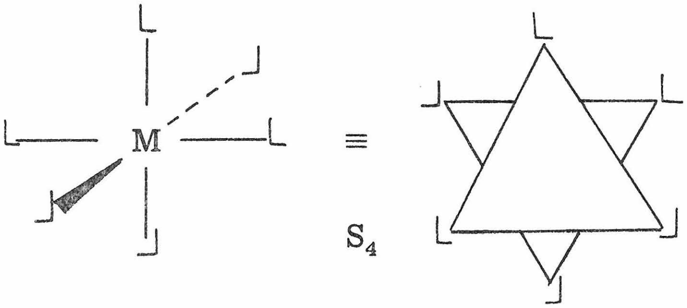
PROPOSITION I

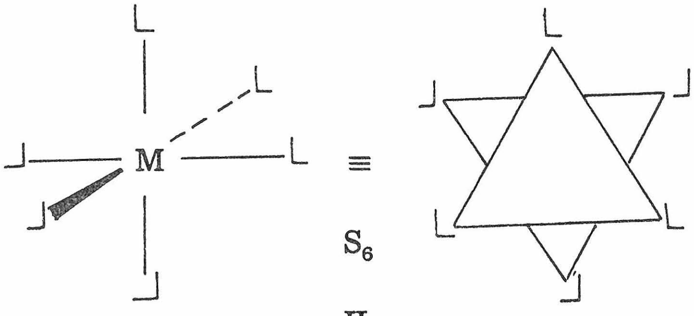
Synthesis of an Optically Inactive Compound with Chiral Ligands and a Sixfold Alternating Axis

Proposition: The compound below should be prepared. It would be the first optically inactive compound with chiral ligands and an S_6 axis; indeed it may be the first S_6 compound known. It would also be one of the few octahedral *meso* compounds.

As described in Part I of this thesis, there are two possible *meso* isomers of the type $ML_3⅃_3$ (where L and ⅃ are related as non-superimposable mirror images. These isomers are the meridional (I) and the facial (II) form shown below.



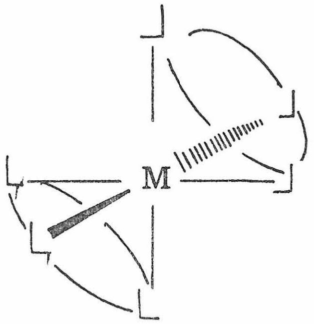
I



II

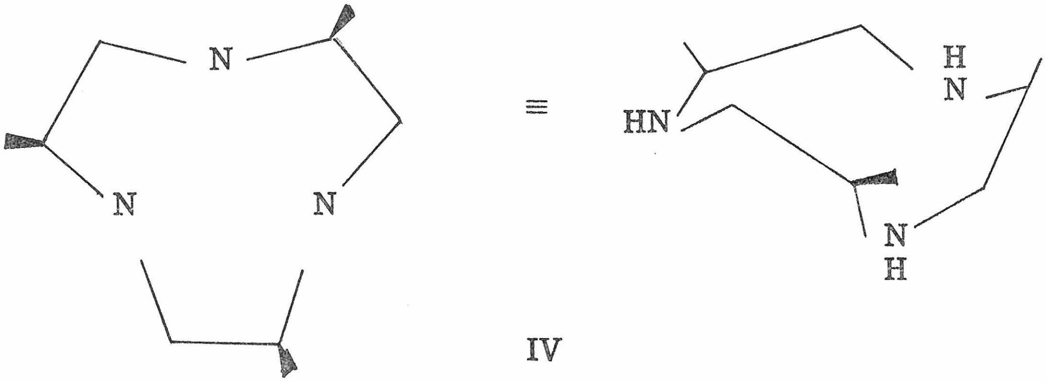
As noted, the meridional isomer has point group symmetry S_4. Indeed, this compound too is of interest, since it is an S_4 meso compound which McCasland(1) did not consider in his classic studies of compounds which are optically inactive because of a four fold alternating axis. The facial isomer has S_6 symmetry (operations $E\ 2C_3\ i\ 2S_6$). In both cases, the symmetries achieved depend on substitution of the octahedron with chiral ligands, since the corresponding substitution with achiral ligands would be of O_h (MA_6), D_{2d} (MA_3B_3, meridional substitution), or C_{3v} (MA_3B_3, facial isomer).

Synthesizing the S_6 compound would be simplified if the ligands of the same chirality were bound together as in III.



III

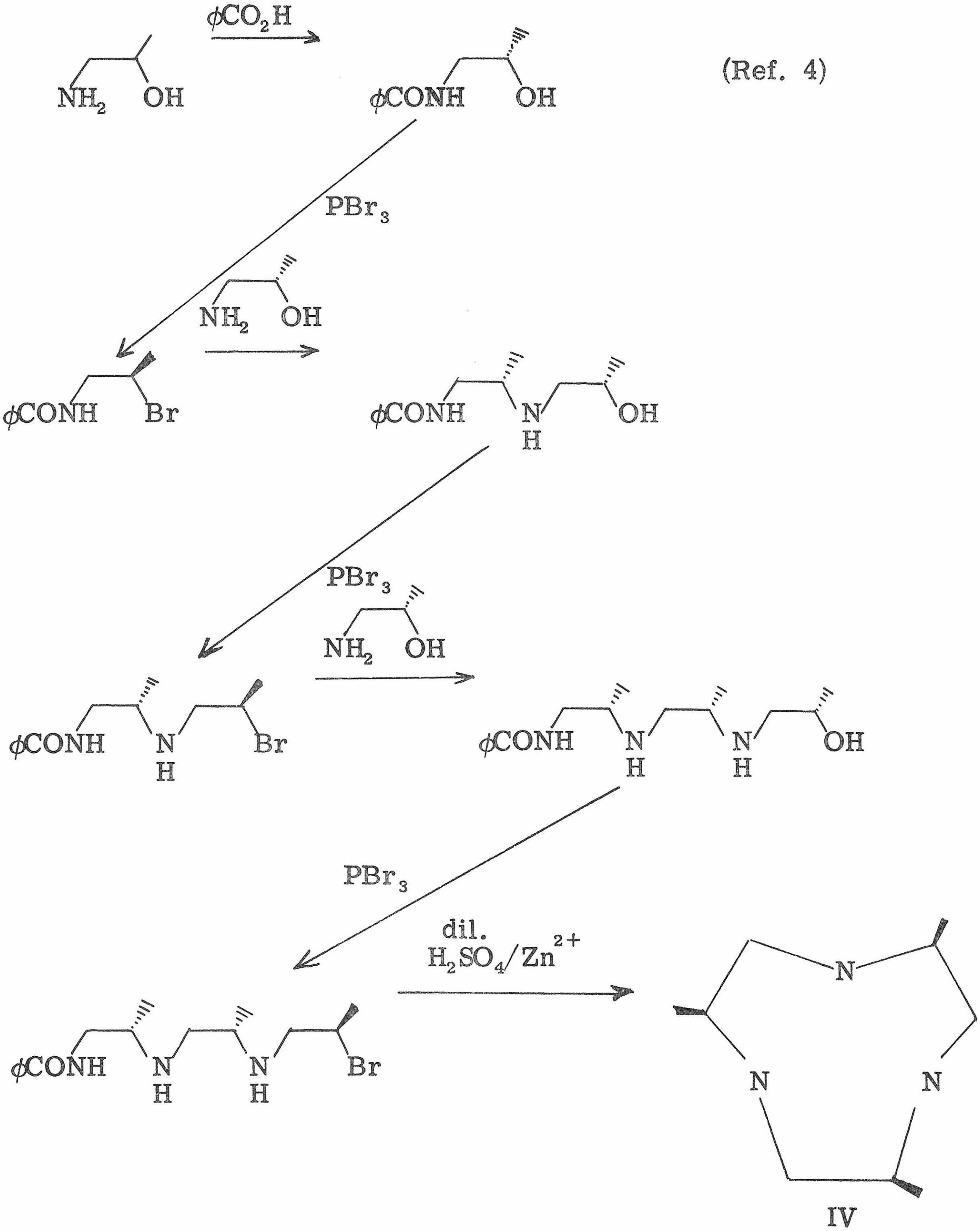
A ligand possessing the desired properties is shown as IV below. This ligand has not been made, although there are a few references$^{(2)}$ to the triazocyclononane system (also referred to as octahydro-1H-1,4,7-triazonine).



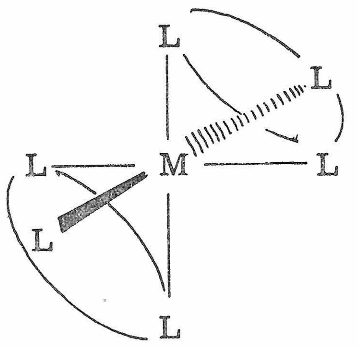
IV

Compound IV, 2,5,8-trimethyl-1,4,7-triazacyclononane, can be prepared by resolving the commercially available (and cheap) 1-amino-2-propanol by the method of Sullivan$^{(3)}$ and then putting the isomers separately through the scheme below.

Reaction of equimolar amounts of the two enantiomers of IV with cobalt(II) sulfate, using air as an oxidant should lead to a mixture of the S_6 meso compound and the D_3 enantiomers (V).



Scheme



D_3

V

Construction of the molecular representations with CPK space-filling models indicates that the enantiomeric material should be more stable, since there is an unfavorable H-H nonbonded interaction between the NH and methine CH groups on the separate ligands in the meso compound. In the racemic compound these hydrogens are separated. If the reaction is thermodynamically controlled, the presence of these six H-H interactions would probably mean that we would expect less than 10% meso material.

However, the formation of Co(III) complexes from Co(II) compounds is usually kinetically controlled by the oxidation step which, in the present case, must occur before all six nitrogens are bound. In addition, the Co-N bond lengths are longer in the Co(II) complex, so the full effect of these interactions may not be felt in the formation of this complex, and we may be able to obtain a reasonable yield of the S_6 compound.

It should be noted that the enantiomeric material is also of interest, since it would be the first compound of D_3 symmetry prepared.

Because of the interaction of the NH and CH hydrogens, the *meso* and *d*,*ℓ* compounds should be easily distinguishable by ^{1}H nmr. If need be, however, the racemic material could be resolved, probably by means of the tartrate salt, as in the classic synthesis of Werner.(5)

In order to establish that the compound is in fact of S_6 symmetry, X-ray diffraction might be required, since the center of inversion could be retained by distorting the molecule. If the molecule were C_i instead of S_6, we would still expect a *meso* compound, and the compound would show complementary infrared and raman spectra. However, the nmr spectrum would change, which should be especially noticeable in the ^{13}C nmr spectrum, since the chemical shifts and coupling constants would be larger than in the ^{1}H spectrum.

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PROPOSITION II

An Experimental Freshman Program

Proposition: California Institute of Technology should institute an experimental program, as described below, in the freshman year. The purpose of this program would be to find ways to increase student initiative in the learning process through group interaction.

I. THE PROGRAM: JOE FROSH MEETS FRED1

As Joe walked to 117 Noyes, he was thinking about how he had gotten into Freshman Education 1, and he was wondering about how the course would come out. It struck him as odd when he had wandered over to the bookstore after registering for second term and hadn't found any texts listed for FRED1.

After thinking about it, though, it had struck him as only right, since he had been told at the sign-up meeting for the course that there would be no predetermined course structure. The idea of working on a research problem had been brought out at the meeting, and it had caught his attention from the start. He had put down the space project as his first choice and his second choice had been the global circulation of pollutants.

Having arrived at the classroom, Joe found a seat at one of the tables away from the blackboard and facing the door so he could see who was coming in. Other freshmen wandered in and found places. A faculty member drifted in talking with two grad students, and gradually other faculty members and grad students came in . When everyone was seated, Joe counted nineteen freshmen, three faculty members, and four grad students.

One of the grad students stood up and welcomed the group. He passed out a list of the course staff and students and then he gave a short rundown on the history of the program. Enough freshmen had signed up to fill two sections; the other section was working on Joe's second choice problem. The grad student turned the floor over to one of the faculty members, a physics prof. The prof told them that there would be no syllabus and no assigned text, and Joe again drifted off into speculations on whether the course would become one long sensitivity conference. The course, the prof continued, was to concern itself with the problem assigned: designing an interstellar space program. The staff did have a couple of things which they thought might be helpful starting points, and there would be lectures arranged if the class requested them. But under no circumstances would there be more than about five hours of lecture time a week, since most of the information that might be needed was in textbooks or in the literature where the students could find it for themselves. A special library for the course had been set up in the old Aeronautics library in Firestone; at present, the prof went on, there were only some textbooks and science fiction novels, but arrangements had been made with the other libraries to transfer materials to Firestone as needed. Following the talk there was a brief recess and the staff circulated among the students. Name tags had been passed out, and the staff had chipped in to provide milk, coffee, soft drinks, and donuts.

Following the recess they saw NASA films on the manned space flight program and on the Grand Tour of the Planets. Following the films they broke into small groups to discuss the films and in particular to evaluate the planning required for long-distance space travel. Shortly before noon, the class broke up; their assignment for the next day was to prepare a list of major planning areas for manned and unmanned interstellar or interplanetary flight.

As Joe walked back to Ruddock with Jerry Greenhorn, they talked about the morning's session. Joe couldn't help feeling uneasy about the course. For thirteen years he had been doing assigned reading and taking tests on the material. He liked doing it; it was easy for him, and it was dependable. As they reached the House, other guys were coming back from courses. Rather than talk about how FRED1 was coming, they shifted the talk to coeds and Christmas vacation.

After lunch Joe fooled around awhile and then headed over to the library. The assignment was pretty ambiguous, and he thought that maybe there was some clue to be found in the library as to what was expected. But like the prof had said, there were only some textbooks and some science fiction paperbacks. Having run out of ideas he picked up Clarke's 2001 A.D. and began to scan it. He had seen the flick, but hadn't been able to make heads nor tails of the plot. If he couldn't work he could at least clear up one confusion.

He finished the book about supper time. After supper he wandered back upstairs and laid on his bed for awhile. He wrote a letter to his girl at home, and then sat and stared at his typewriter for awhile. Finally, he dashed off a few sentences about life support systems and computer-human interactions and turned in. That would just have to be it for the assignment.

In the cold light of day it looked even worse. Some of the others had written lengthy plans for their voyage. One guy had even proposed a map, for chrissake! But the TA in Joe's small discussion group didn't seem to be too disturbed that Joe had only given a sketchy plan. And he even went out of his way to point out the importance of Joe's remark about the use of advanced computer technology.

By halfway through the morning, following the composite reports by the small groups, a long list of planning areas, and even some ideas about planning priorities had come up. But some things were going to have to be settled and soon, especially the question of whether the flight should be interstellar or interplanetary and whether it should be manned or not. For the day after next (Friday) they were asked to prepare a bibliography of sources about the problems and be prepared to discuss them. The next week was taken up with those two questions. The class didn't meet on two days so that small groups could prepare briefs defending opposing views. Joe was on a group advocating manned space flight ("we need a hand and a heart or a brain") but from the drift of the conclusion his group had guessed (correctly) that the class would vote to support an interstellar flight, which would almost surely be unmanned. So they wrote a compromise report suggesting the necessity of biological experiments and proposing that lower organisms be carried along and their behavior under deep space flight conditions be studied. Although the rocket purists put up a stout argument ("equipment is a more efficient payload"), the goldfish faction prevailed.

In the weeks that followed the route was gradually laid out. Following some lectures and guided reading on astronomical observations and spectroscopy, it was decided to set a course in the plane (including the earth) perpendicular to the crab nebulae in order to carry out long baseline optical distance charting of objects associated with the quasar in that region. There were also a few lectures on gravitational theory (and some tutoring by some members of the class for others on calculus; the high school backgrounds varied). Some of the time in the course had been used by a few for learning computer techniques, and practice programs on the PDP-10 had been expanded for the 360-75. JPL, at the class's request, made available their tapes on the planetary positions over the next century. Gradually a picture of the route to be taken was arrived at.

While the digital freaks were doing their thing, another group was studying propulsion systems. Their periodic reports to the whole group provided a little reality therapy for the astro-nuts who were planning explorations of the region of the center of the universe. They had made a number of calculations of the relative efficiencies of various chemical and nuclear power systems, and had a system which they felt would do the job.

Joe first got into the communications group which was working on maximizing information transmission. Together they got a healthy dose of information theory. But when the discussions came down to hardware, Joe and some others on other aspects of the problem set to work on the biological experiments to be performed on board. They wrangled some lab space in the bio labs and even tried their hands at culture growing.

By the middle of the last quarter the class had gotten together an extensive report on their work. By mutual consent the class had decided to spend the last of the year in independent study, brushing up on subjects they individually had not covered as deeply as they wanted to. The staff reshuffled itself to serve as tutors where needed. In their final course evaluation the students expressed enthusiasm to the man (and woman), but some, like Joe, felt some apprehension over the coming year and the return to the lecture system.

II. PROGRAM NOTES

The story fairly well speaks for itself on the main topics, but some illumination of the behind the scenes events is in order. Before such a program could be initiated, two important things must happen: a staff must be found, and topics must be chosen. The two tasks are interrelated, since not everyone would be happy to serve on every topic. Hopefully, though, a reasonably balanced staff for each of two sections could be found. By balanced, I mean that most of the departments would be represented by faculty or graduate students. I do <u>not</u> think, however, that it is essential that there be a physics prof in every section. There is nothing immoral about a physics grad student or an aeronautics professor being the one who gave lectures in Joe's section on gravitation. The staff must be willing to learn also, or the program would be of no avail. In addition, the staff should train itself in the art of constructive criticism. Such balance as a curriculum like this has will be imparted by (1) the students' interests and (2) the balance which the faculty imparts by showing the students where a greater thoroughness is called for. This last is absolutely essential to keep this program from degenerating into a series of bull sessions. Frequent student reports, criticized and revised in class by students and staff together, should be the main form of assignment. (Note that this decreases the time the staff spends in grading--a relatively distasteful endeavor in most cases.) The staff should be willing to guide student interest so long as there is an interest, but it would be fruitless to require extensive problem sets, for example, except when the students have requested them to gain proficiency with, say, mathematical skills.

Problem selection is no less important, as it establishes the only framework for the course. The ideal problem, then, should have ramifications which touch on a wide variety of areas, and should be of inherent interest but difficult to solve. I have suggested two such areas--there are surely more. The staff together should initially set the problem, subject to later modification by students and staff together.

If this program were adopted, a special committee of faculty and students would be assigned a year in advance of starting the course to recruit staff, locate facilities, set up the selection process, and, most importantly, to establish criteria for evaluating the program's success. However, the five-year experiment will have little value unless good procedures are set up in advance, involving both subjective and objective evaluation techniques, to determine whether students are better or worse off following the experience.

III. THE EDUCATION PRINCIPLE

As stated in the proposition, the purpose of this program is to increase student initiative in the learning process through group interaction. The first part of this purpose--increasing student initiative in the learning process--stands squarely in the tradition of progressive education, an ideal which was seldom realized in primary and secondary education, and seldom attempted in colleges. It is, strangely enough, a reasonably frequent paradigm for graduate scientific education in this country.

The goals of such an education are summarized ably by Carl Rogers(1):

> The goal ... is to assist students to become individuals
> who are able to take self-initiated action and to be responsible for these actions;
>
> who are capable of intelligent choice and self-direction;
>
> who are critical learners, able to evaluate the contributions made by others;
>
> who, even more importantly, are able to adapt flexibly and intelligently to new problem situations,

> who have internalized an adaptive mode of approach to problems, utilizing all pertinent experience freely creatively;
>
> who are able to cooperate effectively with others in these various activities;
>
> who work, not for the approval of others, but in terms of their own socialized purposes.

When college education has moved in this direction, it has tended to move toward independent study programs or guided reading, both of which tend to reduce the amount of interaction on common intellectual ground between students. Since student-student interaction is probably (in my opinion) the single most important environmental factor in a student's education, independent study seems to move counter to sound educational practice. If nothing else, it places no stress at all on the sixth of Roger's characteristics of an educated person.

In order to plunge the student into self-initiated learning, the program places into the student's hand the very important decision of selecting educational resources. Traditionally, it has been the view that the choice of resources available to the student is not important in education. That is, a student chooses a college and a major, and the choide of resources (aside from minor exceptions, such as, "read one of the following books and report on it") is left up to the teacher. The advantages of this traditional system are manifold. First (and of prime historical importance) is the ease with which it can be used with large numbers of students, either simultaneously or sequentially. Having mastered a certain body of information the teacher can pick what he considers most relevant and pass it on to one or a thousand students without having to alter his presentation materially. Second, the method is particularly useful when a reasonably fixed body of knowledge is considered by most men of practical wisdom to be the essentials of a subject. Arithmetic, for example, is such a subject; despite the endless intellectual variations which can be played on it, there is still a core of material that most would point to as indispensable. Third, it allows the teacher to tie his teaching to his own studies. This latter phenomenon is often seen in chemistry courses where the core of the subject is related to the professor's own research interests. And this practice results in a very admirable saving of time on the teacher's part--a not inconsiderable advantage in these days of publish or perish. Fourth, this method is easily evaluated by the usual methods of testing. The Regents exams, the College Boards, and the Graduate Record exams are all based on the assumption that there is a reasonably fixed body of knowledge being imparted. (The Student as an Interchangeable Part).

Let me hasten to add that the traditionalist arguments should _not_ be lightly dismissed. They are the very substantial justifications for the system of education from which you and I arose. Indeed, as Kuhn(2) has pointed out, it has served quite well to transmit paradigms without which scientific research is impossible. The traditional system has proved many times over its value as _an_ education device.

But it has never proved the implicit claim that it is _the_ educational device; that is, that the role of the teacher is to define education as the mastery of a certain body of material. Indeed, there are serious problems in its proving this claim. Through its heavy dependence on the subject, it has in many ways hindered the advance of knowledge and served to choke inquiry. It is not an accident, for example, that interdisciplinary approaches are more characteristic of industrial than of academic research. Being problem-centered, the former is not bound by the disciplinary requirements of the latter. Further, there are fewer and fewer areas of knowledge in which there is a well-defined "subject" which can easily be encapsulated for student consumption. This very tendency, in fact, is what allows our above-mentioned researcher to structure his courses around the basic material involved in his research. Chemistry, of course, is an example of this tendency; the variety of subject matters taught under rubric of, say, Chemistry 21 is a wonder to behold. The orientation of education to subject matter can lead to a form of academic arteriosclerosis. As Hammond(3) has ably argued, the traditional division of chemistry into Organic, Inorganic, Physical, and Analytical has often served to obscure the similarities among the things being studied in those separate areas.

Thus, the traditional system has certain inherent disadvantages. To some extent those disadvantages have been recognized and a number of different approaches to new forms of scientific education are developing.(4) Interestingly, most of these approaches deal with science for nonmajors. There seems to be a feeling that we need not be as responsible to them as to the majors. Note that I do not feel that so-called "interdisciplinary" courses, taught by traditional methods, alleviates these disadvantages. The student is merely being exposed to a novel subject; he is still not being challenged to utilize educational resources in an innovative way.

The core of the proposed program attempts to overcome these disadvantages by three means:

1) the "subject" of the course is defined as broadly as possible;
2) the teaching staff is drawn from a variety of educational backgrounds and <u>no</u> seniority is recognized within this staff;
3) the requirements placed on the students are selected to reward actual effort toward solving the problem posed as the "subject" of the course.

The Program section, above, shows those techniques in action, and need not be further expanded here.

One further point that needs to be touched upon is why I have proposed using the freshman year for this experiment.

The first reason is inherent in the nature of the freshman year. It marks one of the few (aside from first grade, perhaps the only) major transitions in a college student's career. This is particularly true of Caltech which draws students on a nationwide bases (making it a geographical transition for most) and from a fairly homogeneous intellectual group (making it an intensified, competitive period for those students who were all at the top in their previous school work). Pasadena City College, by contrast, represents a minimal transition period for most of its students. The program I have outlined takes advantage of student expectations (they <u>expect</u> that Tech won't be like high school) by not trying to change college students who have already beaten down a smooth academic path, but by taking freshmen and showing them a new manner of formal education.

The second reason has to do with aspects of freshmen education peculiar to Caltech--the uniform curriculum and the pass-fail grading. Since the program depends on attracting students, the fact that it is a clear alternative to the uniform curriculum may make it attractive to the more ambitious. Further, it precedes the time when the students must make choices of a major, and hence the students will probably be less anxious about falling behind in their specialty and it will provide them with a testing ground for trying out various majors. And, pass-fail grading is the only logical method for a course in which standard "objective" methods of grading are inappropriate and misleading.

IV. THE OBJECTIONS

There is clearly a strong impetus to _not_ initiate such a program, as evidenced by the fact that such a program does not exist. First, of course, there is the fact of lack of knowledge. It has never occurred to many faculty members that such an option might exist, and inertia resulting from such persons is always a major obstacle to educational innovation. Insofar as this _is_ the obstacle, though, education should suffice to remove it.

But more substantive objections can be raised. Specifically, three areas come to mind: philosophical, psychological, and economic. The philosophical objections can come from either the right or the left of the present proposal. Objections from the right will primarily point to the _success_ of the traditional method, a success on which I tried to amplify previously. But that success has been bought at the price of a very heavy specialization and at the cost of selecting for honors students whose main characteristics tend to be rapidity of memorization, facility of recall, and the ability to close off questions about the importance of what they are required to memorize. (This has, for example, led to the frequent objection by industrial firms that good students often make poor employees because they are not particularly good at working with others in corporate problem-solving(s). Since neither cooperation nor the imaginative use of resources is stressed in undergraduate education in general, it is hardly surprising that this objection is raised. Thus, the inquiry method stressed in this program might serve as a counterbalance to the present emphasis.)

But it may fairly be asked how much of the success of the traditional system is in fact due to the system itself, and how much is due to the adaptability of the students involved. A study of M. I. T. freshmen showed the following results(6):

a) Only a minority (10-20%) of freshmen consistently learn from attending science and mathematics lectures.

b) A majority (60-80%) attend lectures to calibrate their home-study, and to find out what will be asked on the next hour exam.

c) A minority are usually absent (in the cases of a few lectures observed, this number may actually constitute a majority). Nevertheless many of these absentees receive honors grades in the subject.

d) Of those students who stay absent from lectures the most common characteristic is one of personality: they are "risk-takers," etc.

e) The average grades of freshmen in mathematics and science recitation classes do not correlate with the age, or the reputation for teaching, or the professional competence of their instructors. There is some correlation with the average high school and college board grades of these students, although this correlation explains only about 20% of the observed variance.

f) A study of the Class of 1965 by Dr. (now Dean) Benson Snyder, revealed that instructors in physics were regarded as deficient in teaching ability, student awarness, etc., by students. Nevertheless the freshman questionnaires showed that freshman physics was overwhelmingly the most popular subject.

Thus, it can fairly be asked whether some other system might use student talent more efficiently. I do not for one minute envision the total disappearance of the traditional system; I merely hope for more diversity in styles of teaching and learning.

On my philosophical left are those who will claim that I am not going far enough to remove the structure and stricture of the traditional method, that I am introducing a new rigidity by the problem-solving orientation. To some extent that is the case. But science is distinguished from pre-science (see ref. 2) by the existence of certain kinds of communal paradigms for understanding nature, paradigms which must be transmitted if science is to continue. I have already raised by objection to independent study as the sole alternative to traditional instruction. I can only say that my vision of group learning is sufficiently dim that I see no clear alternative to a problem-oriented approach.

The psychological objections are perhaps the strongest. By its very nature, this course will primarily attract students who are risk-takers, who can tolerate fair amounts of ambiguity. The self-selection process virtually guarantees this will be the case. The staff, too, should be primarily self-selected to provide the same quality. But even given this, there is always a very real element of risk involved for the students who take the course. Consideration should be given to providing summer courses, should they be needed, to students who would be ill-prepared to enter the normal sophomore courses. Further, special sections of the sophomore courses could be run for these students. Since the course is only two terms in duration, it is not expected that <u>at the worst</u> the students would be thrown hopelessly behind their academic class. To provide an escape mechanism, the course should be reconstituted at the beginning of the third term, so that those who feel the need to bail out may begin independent study on the normal freshman materials.

The economic objections are always difficult to counter with any educational innovation. New courses require heavier doses of staff time and educational aids than do established courses. However, it is the plan for this course that <u>most</u> of the staff time will be put in <u>during</u> the class period. The overall effect of this on an individual instructor's schedule is not clear, although it could lead in some cases to a net reduction of time required for teaching as the instructor becomes a consultant rather than a performer on the lecture stage. I have not worked out in detail the comparative costs of this program and the normal undergraduate program. However, by the judicious use of experienced graduate student teaching, it should be possible to keep the costs at a reasonable level. After talking with several persons on campus, I have some confidencd that there are enough able risk-takers around to give the course a good chance of succeeding.

References

1. In Carl R. Rogers and Barry M. Stevens, *Person to Person: The Problem of Being Human,* (Lafayette, Cal: Real People Press, 1967) p. 58.

2. Thomas Kuhn, *The Structure of Scientific Revolutions,* 2nd ed., (Chicago: The University of Chicago Press, 1970).

3. George S. Hammond, "Restructuring of Chemistry and Chemical Curricula," speech given at the International Symposium on University Chemical Education, Frascati (Rome), Italy, October 16-19, 1979.

4. (a) Colin Eaborn, *Chem. Brit.*, **6**, 330 (1970).

   This article describes the program in the Chemistry Department at Sussex, England, where students are immediately assigned to undergraduate research under an advisory board.

   (b) E. L. Wehry, *J. Chem. Ed.*, **47**, 843 (1970); Verlin Richardson, John W. Renner, *ibid.*, **77**; J. E. Fernandez, *ibid.*, **624**; J. D'Auria, A. Gilchrist, J. Johnstone, *ibid.*, **508**.

   These papers all describe open-ended laboratory teaching methods; the first two are one for majors, the other two for non-majors. Richardson and Renner provide a statistical comparison of student performance in the inquiry method and the traditional lab.

   (c) Richard L. Hoffman, Doris K. Kalb, *ibid.*, **383**.

   This article describes a method of letting non-majors select topics to be covered in a one-semester physical sciences survey course.

(d) A. J. Dessler, Rice University Review, Spring 1971, 9.

> This article describes the use of the "Keller method" to teach an astronomy course for non-majors. The method involved modules which the student must master on his own in sequential manner. Although Dessler uses it within a traditional subject framework, the method could provide a means of structuring a smorgasbord course for a large number of students with different interests.

5. Report of Panel II, International Conference on Education in Chemistry, in *J. Chem. Ed.*, **48**, 14 (1970).

6. From "The M. I. T. Experimental Study Group, First Term 1969-70." I am indebted to Dean Robert Huttenback at Caltech for making this and several other documents available to me.

PROPOSITION III

A New Approach to Chemistry 21

Proposition: Chemistry 21--the junior physical chemistry course--should be taught as a combination of Keller method instruction and student-developed curriculum. The purpose of this would be to allow a wider variety of subjects to be taught and to introduce upper level students to the problems and possibilities of teaching.

Chemistry 21 offers special problems and opportunities in chemical education at Caltech. Students who take the course have already had two years each of college physics, mathematics, and chemistry. This preparation means that they can be taught almost any chemical subject. At the same time, though, their chemical backgrounds have developed to the point that they have definite interests in what they wish to learn. Thus, a class of thirty students have interests which would require five years of physical chemistry to provide them with even the fundamentals.

The usual solutions to this dilemma are either to teach what the particular instructor considers a survey of basic physical chemistry or to specialize in some one area, such as molecular quantum mechanics, statistical mechanics, or chemical dynamics.

The crux of the problem is that Chem 21, like most other courses at Caltech, is taught as a lecture course, so that all students in the course must cover the same material at the same pace. To my knowledge Biology 110 is the only science course on campus (other than various independent study and undergraduate research programs) which allows the students to select their own materials and to proceed at their own pace. The difficulty with Biology 110 has been that it is difficult for the course staff to provide enough guidance to individual students to keep them from floundering for much of the time.

Recently, a number of colleges have begun offering Keller method courses. The method is named for psychologist Fred Keller of Arizona State University.(1)

Rather than describe the theoretical background of the method, which is discussed in reference (1), a better way to describe the method is in the course description of an astronomy course for non-majors offered at Rice University and taught by Professor A. J. Dessler.(1, 2)

> The course operates as follows: Each student receives a written study guide that details his reading, problem, and laboratory assignments. The study guide also presents both helpful clarifications of the text material and supplementary material that is not in the assigned text....
>
> The subject matter for this course is divided into units, each unit having a separate study guide that covers one chapter of the basic text. There is supplementary reading assigned from a second book....
>
> The student, following the study guide, reads the text material and works the assigned problems, usually outside of class hours. The student then lectures (or explains) to one other student on what he learned and how he worked the problems. Thus, the student "lectures", not the professor. These "lectures" (or oral exercises as they are called) may be performed only in the classroom....
>
> The class is divided into sections. Each section contains 10 students and has one tutor assigned to it. The tutor is ideally an undergraduate who completed the course satisfactorily the year before. The tutor administers the written exercises, keeps progress records for each student in his section, finds a listener when a student is ready to present an oral exercise, and answers questions that arise from students in his section....

> If the tutor has trouble answering the student's questions, either the tutor or the student can come to me for help. I make it a point to be present at nearly all the class meetings, primarily to help the tutors, but also to make personal contact with the students.
>
> After the required oral and laboratory exercises are completed, the student takes a closed-book written exercise with which he can demonstrate his mastery of the unit material. These written exercises differ from the usual tests in several significant ways. Only two scores are possible--Perfect or Incomplete. A score of Perfect is required before the student is allowed to go on to the next unit. An Incomplete means only that more study is required. There is no penalty associated with an Incomplete.... After an analysis of the weakness, the student is sent back to some specific material for more study, after which he may try again on a new written exercise. (There are usually four different written exercises available for each unit.)....
>
> Each student proceeds at his own pace through the course. His mastery of the material is checked constantly. The average student is tested for mastery of the material approximately twenty times each semester....
>
> Grades are determined by how many units a student completes. The standards of performance are set by the instructor and announced the first time the class meets....The responsibility for learning thus rests with the students. The instructor is responsible for overall course direction, maintenance of standards, and (with his tutors) teaching....
>
> To avoid the problem of the student who procrastinates unduly, an early deadline is set for completion of Unit 1 to assure that everyone at least gets off to a good start. The only other prod is a one-hour, open-book mid-term examination covering the first few units. The mid-term exam does not count toward the student's final grade but rather serves as a recheck of his mastery of these units. A grade of less than 70% requires that he retake the mid-term after more study and redoing certain of the units. There is no final examination.

The main virtues of this method are that it removes the instructor from the adversary role which the usual lectures plus hour exams and finals puts him into, that it makes the student responsible for his own education, and that it is a powerful technique for building a strong base of information, since the student is required to master each unit before he can go on to the next.

The Keller method itself is not enough to solve our problem, however. By itself it would require an immense amount of instructor time preparing study units, and a great deal of instructor prescience to know what units should be prepared.

Instead of relying on the instructor's endurance and prescience, though, it should be possible to structure the course so that the students perform this work. The outline I propose for the course is that the first semester should cover the basics (in Caltech terms) of quantum theory and statistical mechanics. If need be, group theoretical methods should also be introduced; the students may have an an introduction earlier. These topics should all be covered by Keller method instruction. Either graduate or undergraduate tutors could be employed. The purpose of this semester is to provide a common grounding in the concepts of chemical physics and to familiarize the students with the Keller method. The remaining two terms will each be divided into two parts. The first month of the term each student will write two study units on a topic of his own choice. During the final two-thirds of each term, each student will do four study units from these written by the other students. During the first part of each term the instructor and tutors will serve as resource persons and they will also judge the adequacy of the submitted study units. Here again the only grades will be Perfect or Incomplete. The student will submit a reading and problem assignment, a study guide, and four written exercises for each unit. In order to help the students, the teaching staff will provide a list of suggested topics and a bibliography of texts and monographs on these topics. A list of possible topics appears as Table I. During the last part of the term the tutors would again serve as tutors in a Keller method course. In addition to the usual work, each student will be required to write a one-page critique of the study guides he uses during this part of the course.

After a number of study units have been built up, it would probably be good to utilize only the third term for student preparation of these units. However, the task of organizing knowledge so that others can learn from it is itself a reason for retaining this exercise.

Note that nothing in the format would prohibit the instructors from making study units available on material in which he has a special interst. He should refrain, however, from making them compulsory during the terms when student-written units are used.

Table I

Topics for Physical Chemistry

1. Thermodynamics
    - a) Thermodynamics of solutions
    - b) Osmotic pressure
    - c) Phase equilibrium and changes of state
    - d) Sedimentation equilibria
    - e) Electrostatic free energy and polyelectrolytes
    - f) Multiple equilibria
    - g) Third Law problems
    - h) Gases--ideal and nonideal
    - i) Activities and standard states
    - j) Free energy functions
    - k) Electrochemistry

2. Statistical Mechanics
    - a) Gases
    - b) Macromolecules

3. Dynamics
    - a) Kinetics of radical reactions
    - b) Enzyme kinetics
    - c) Ion-molecule reaction mechanisms and kinetics
    - d) Transition state theory
    - e) Catalysis
    - f) Collision theory

Table I (Continued)

- g) Scattering theory
- h) Mass spectroscopy
- i) Electrochemical reactions

4. Spectroscopy
   - a) Atomic
   - b) Molecular
     - 1) Electronic
     - 2) Vibrational
     - 3) Rotational
   - c) Photoelectron
   - d) Magnetic resonances
     - 1) Electron
     - 2) Nuclear

5. Diffraction Methods
   - a) X-ray
   - b) Neutron
   - c) Electron

6. Interaction of Electromagnetic Radiation with Matter
   - a) Absorption phenomena
   - b) Emission phenomena
     - 1) Spontaneous
     - 2) Induced (lasers)
   - c) Scattering
     - 1) Rayleigh
     - 2) Raman

Table I (Continued)

7. Photochemistry
    a) Light absorption
    b) Energy transfer
        1) Intramolecular
        2) Intermolecular
    c) Photochemical reactions and mechanisms
    d) Biological photosynthesis

8. Molecular Quantum Mechanics--Calculation of Structures
    a) Ab initio methods
    b) π bond methods

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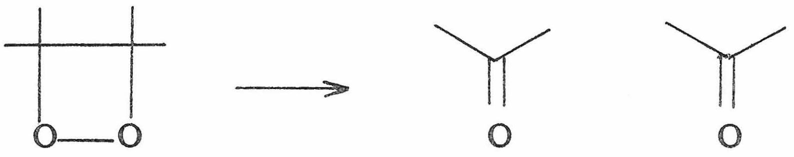
PROPOSITION IV

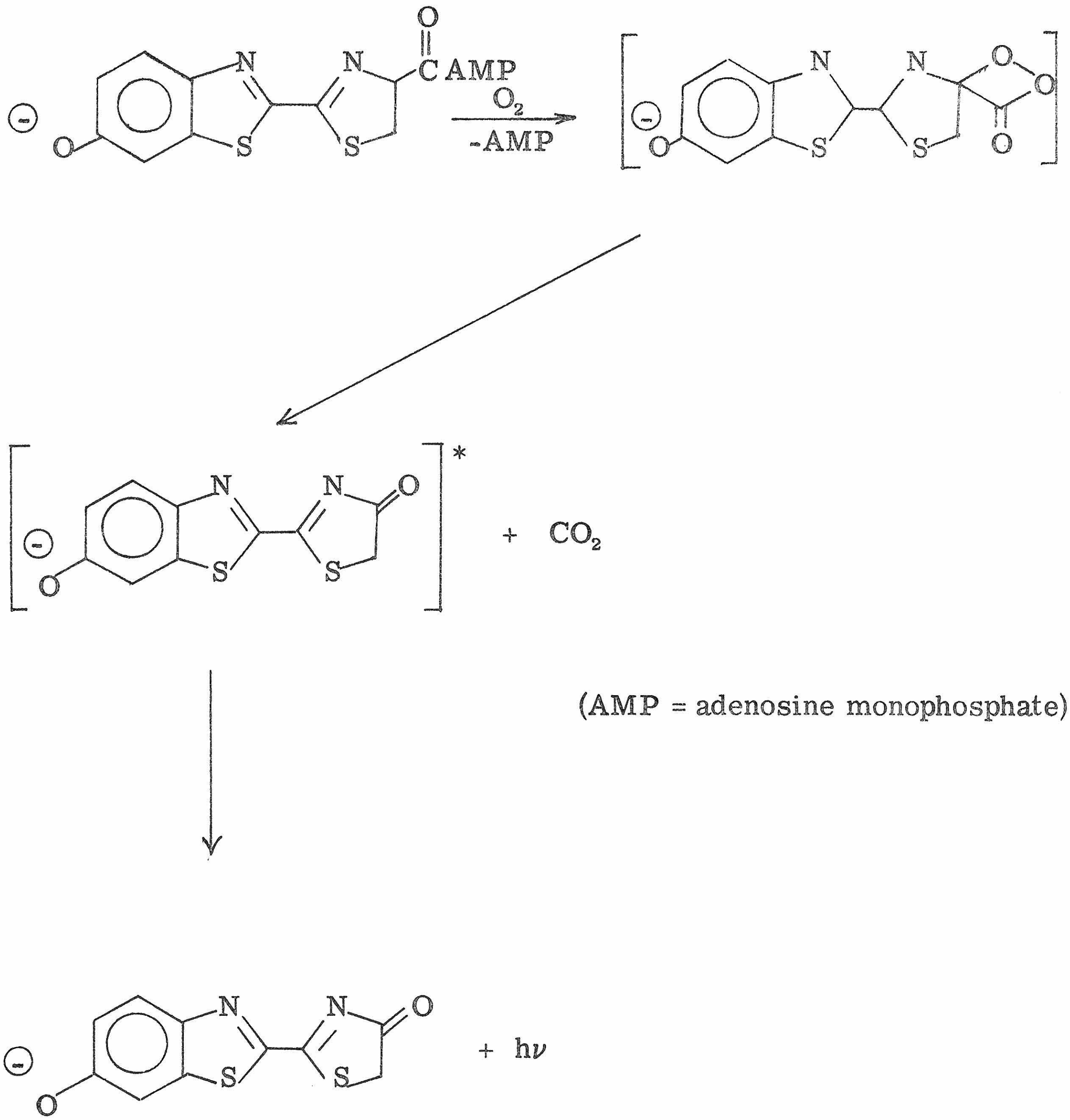
Spectroscopic Identification of 1,2-Dioxetane-3,4-dione

Proposition: The hydrogen peroxide oxidation of certain oxalic acid derivatives is believed to proceed via the formation of a high energy dioxetanedione intermediate. This intermediate can decay by transfer of electronic energy to a fluorescent compound, producing chemiluminescence. It is proposed to study the structure of this intermediate by long pathlength infrared and raman spectroscopy.

A number of recent studies of chemiluminescence accompanying hydrogen peroxide oxidation of organic compounds have pointed to the possibility of dioxetane intermediates.(1-4) Interest in these possible intermediates increased following the formulation of the Woodward-Hoffman rules for electrocyclic reactions,(5) since these rules predict that for reaction 1 at least one of the product molecules should be formed in an electronically excited state.

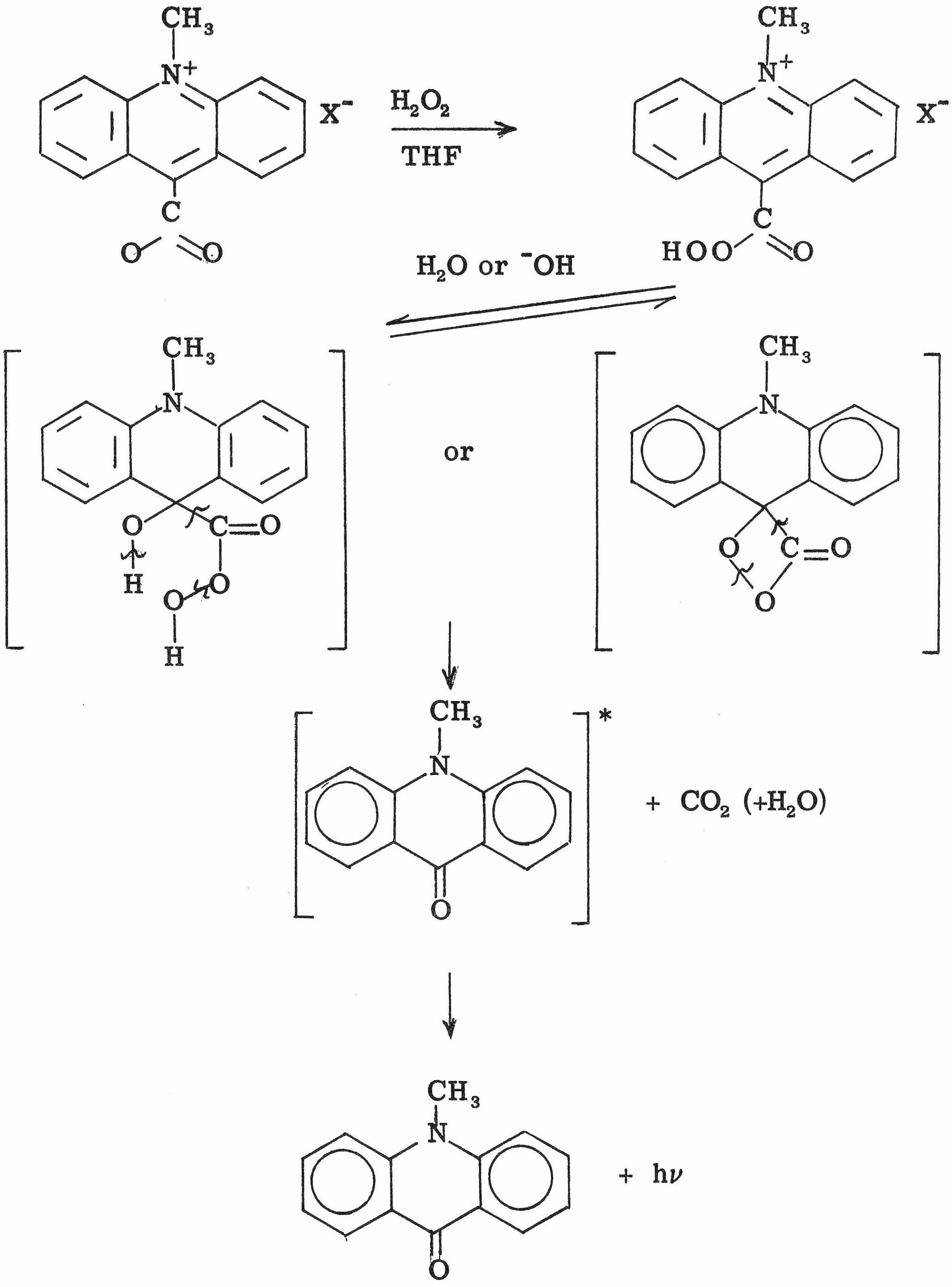

(1)

Oxidations which are typical of those believed to involve such intermediates are those of firefly luciferin (reaction 2; ref. 6) and N-methyl acridine derivatives (reaction 3; ref. 3). Note that in this second case some doubt exists as to the actual existence of the dioxetane intermediate, since oxidants such as peroxylauric acid can alse be used, which presumably would not lead as easily to the dioxetane.



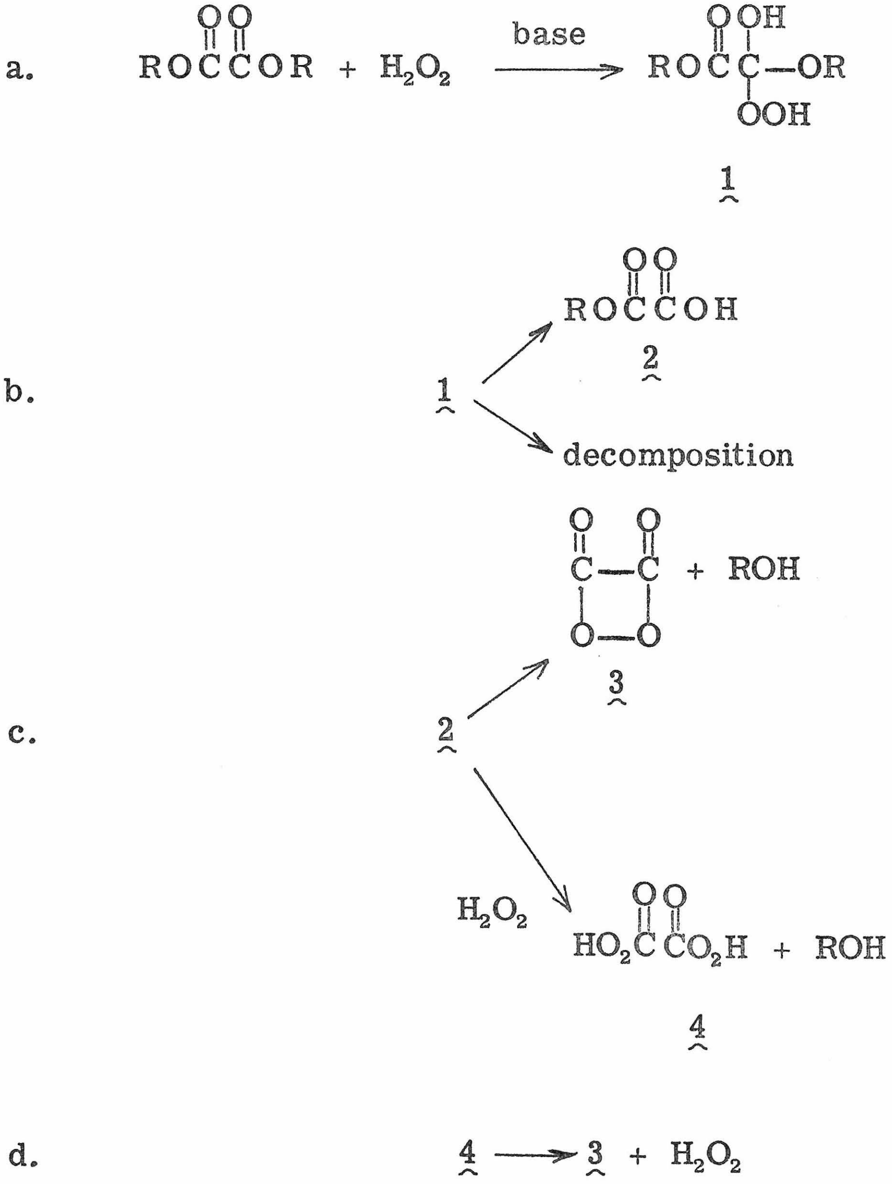
(AMP = adenosine monophosphate)

Reaction 2

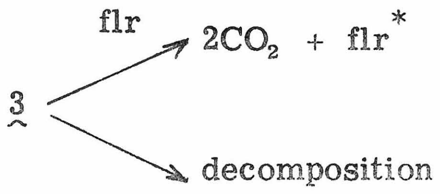


Reaction 3

Chandross(7) and Rahut and his co-workers at American Cyanamid have found an entire series of oxalic acid derivatives which are efficiently luminescent in the presence of an efficient fluorescer such as 9,10-diphenylanthracene or rubrene.(8-16) They have most extensively studied the decomposition of oxalic acid esters, certain of which are as efficient as 23% in the production of light. The Scheme below shows the pathway which they have proposed for this reaction.



e.



$$3 \begin{array}{l} \xrightarrow{flr} 2CO_2 + flr^* \\ \longrightarrow \text{decomposition} \end{array}$$

f. $flr^* \longrightarrow flr + h\nu$

(flr = fluorescer)

Mechanism of Oxalic Ester Chemiluminescence
Scheme

The reaction is of interest not only because of its high efficiency (the highest nonbiological chemiluminescence known), but also because of the absolute requirement for an energy acceptor such as the fluorescer shown. Presumably the highly symmetrical intermediate 3 cannot easily decay to $^1CO_2^* + CO_2$, and yet it is forbidden by orbital symmetry to decay to two vibrationally excited ground state molecules.

Both Chandross(7) and Rauhut(3) have commented on the fact that the intermediate is volatile enough to cause luminescence in fluorescer solution outside of the initial reaction vessel. Cordes, Richter, and Heller,(7) following Rauhut's suggestion, undertook the mass spectral analysis of the volatile products and observed ions of mass 17 (OH), 18 (H_2O), 28 (CO), 32 (O_2), 34 (H_2O_2), 44 (CO_2), 60 (CO_3), and 88 (C_2O_4). Chandross had earlier failed to observe these last two ions; Cordes mentions that they are only 10^{-3} the mass 44 intensity at certain times during the reaction. They are 10% of the reference ion at other times, however.

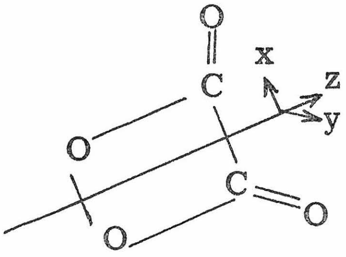
This does not constitute a definitive identification of the chemiluminescent species, however, and it does not easily lead to a general tool for characterizing such dioxetane intermediates. The infrared and raman spectroscopy of this molecule would serve both those functions.

Table I summarizes the symmetries of the expected molecular motions of the dioxetanedione. Note that all stretches are both raman and infrared allowed, and we would expect the C–C and C–O vibrations especially to mix since they are of the same symmetry and close in energy. Of more diagnostic value, however, is the information that two bending vibrations are raman allowed and ir forbidden. In addition, the C=O and the unmixed C–O vibrations are both totally symmetric and unpolarized in the raman spectrum. Together with approximate values for the group frequencies, this information should serve to characterize the molecule. In addition, we would gain information applicable to the identification of other dioxetane systems.

The experiment could be carried out as in the mass spectral work, with the addition of a carrier gas such as argon to increase the amount of compound volatilized. The gas would be led into an initially evacuated 40 m pathlength cell for analysis.

Table I

Vibrational Modes of C_2O_4



IR allowed symmetries and polarizations: $A_1(z)$, $B_1(y)$, $B_2(x)$

Raman allowed symmetries: A_1, A_2, B_1, B_2

$$\Gamma_{C=O} = A_1 + B_1$$

$$\Gamma_{C-O} = A_1 + B_1$$

$$\Gamma_{C-C} = B_1$$

$$\Gamma_{O-O} = B_1$$

$$\Gamma_{\text{stretch}} = 2A_1 + 4B_1$$

$$\Gamma_{\text{vib}} = 5A_1 + 2A_2 + 4B_1 + B_2$$

$$\Gamma_{\text{bond}} = 3A_1 + 2A_2 + B_2$$

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PROPOSITION V

Photoproduction of Amino Acids Under Martian Conditions

Proposition: It is proposed that the photoproduction of amino acids could be carried out in conditions approximating the Martian atmosphere.

Hubbard, Hardy, and Horowitz(1) reported recently that ^{14}C-formaldehyde, -acetaldehyde, -glycolic acid, and certain unindentified organic compounds are produced when ^{14}CO and H_2O are photolyzed with a xernon lamp through quartz in the presence of a catalytic surface of Vycor glass. The proportion of the gases (CO, CO_2, and H_2O) was designed to approximate a condensed (1000 m bar) Martian atmosphere (6 m bar).

This production of organic materials was totally unexpected, since none of the gases present absorbs radiation in the region of the spectrum which quartz passes. The mechanism of this photoreaction is apparently due to absorption by species adsorbed on the Vycor, similar to the photodissociation of adsorbed water or ammonia on silica gel and aluminum oxide reported by Terenin.(2)

This photosynthesis is most significant because it proceeds at wavelengths longer than the vacuum ultraviolet used in most other photochemical syntheses of biological molecules. Terenin(2) had succeeded in producing amino acids by irradiating mixtures of methane, ammonia, and carbon monoxide with the 124 and 116 nm lines of krypton.

Calvin(3) and others (ref. in 1) have argued that the ratio of photoproduction to photodestruction of biological molecules by light at wavelengths shorter than about 300 nm is too low to provide a prebiotic mechanism for the production of biological molecules. For this reason Calvin(3) and others(4) have concentrated on electron bombardment, electrical discharge, and other energy sources to explain the origin of life on earth. However, these other energy sources probably provide less than one percent of the energy available at 250 nm in the solar spectrum. Clearly a photosynthetic mechanism for the prebiotic formation of organic molecules would be more efficient.

Synthesis of amino acids at even longer wavelength was reported in 1934 by Dhar and Mukherji, starting from glucose.(5) Later work, reported by Bahadur,(6) showed that formaldehyde, and in some cases CO_2, would serve equally well as a starting material.

This reaction proceeds in the presence of transition metal oxides in aqueous solution of formaldehyde and potassium nitrate. It proceeds rapidly in sunlight or ordinary incandescent light. Since the reaction is usually performed in vessels with a terrestial atmosphere, photo-oxidation limits the yield of products.

The Martian atmosphere is known to have less than five percent gaseous hydrogen, but there is a possibility of soil nitrates derived from volcanic activity and N_2-O_2 photoreactions.

By using crushed ilmenite ($Fe_2O_3 \cdot TiO$), potassium nitrate, carbon monoxide and dioxide, and water vapor as a reaction system, amino acids could be produced. The use of ilmenite is reasonable since it is a major constituent in the crust of both the earth and Mars. The photoproduction of amino acids at long wavelengths should also be reinvestigated, since automatic amino acid analysis and tracer techniques should make elucidations of the mechanism possible. Furthermore, the use of a CO, CO_2, N_2 atmosphere is a more realistic representation of the prebiotic conditions.(7)

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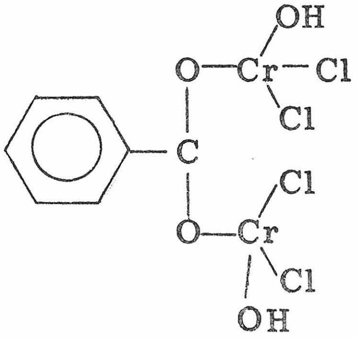
PROPOSITION VI

Magnetic Studies of a Cr(IV)-O Polymer

Proposition: A structure is proposed for the intermediate formed in Étard's Reaction--the oxidation of toluene with dichlorodioxychromium--and a study of the compound's magnetic behavior is proposed as a means of structure proof.

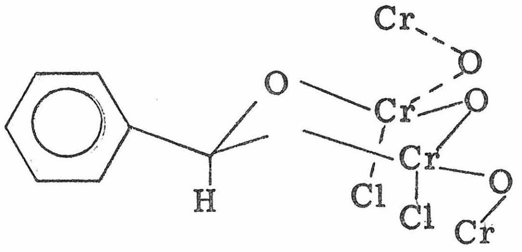
In 1881 Alexander Leon Étard published the results of his studies on the interaction of chromyl chloride (now listed in Chem. Abstr. as dichlorodioxochromium) with toluene.$^{(1)}$ In an inert solvent, such as carbon tetrachloride or disulfide, it forms a brown tarry precipitate which can readily be hydrolyzed to benzaldehyde. He proposed compound I as the intermediate in this reaction.



I

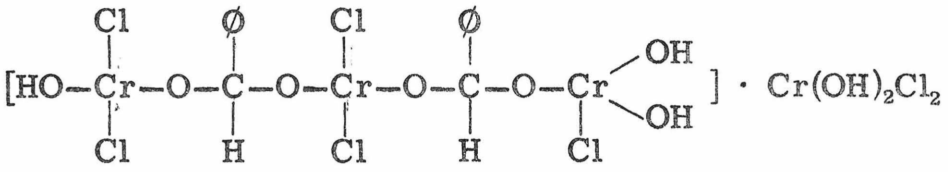
Recent magnetic susceptibility and electron spin resonance studies of this complex have shown it to have two Cr(IV) atoms per mole of complex.(2, 3) It obeys the Curie law to 77°K and shows a magnetic susceptibility of 3.21 ± 0.07 Bohr magnetroms, only slightly higher than the spin only moment of 2.83 B.M

A great deal of study has been devoted to Étard's reaction,(4) but for the most part they have not provided any definitive answers to the question of the intermediate. The insolubility and reactivity of the intermediate have made studies of it very difficult. Étard observed that if the initially formed intermediate is heated to 160°C, it loses one mole of HCl for each mole of chromium. This result can be rationalized on the basis of Étard's structure by assuming that the loss of HCl leads to a dehydrochlorinated polymer, II.



II

Differential thermal analysis(5) of the material produced by heating Étard's intermediate shows that there is indeed an exothermic reaction between 150° and 200°C which irreversibly transforms the initial intermediate. Interestingly, it makes no *apparent* difference in the intermediate. Probably the initially formed intermediate is itself polymeric in nature, possibly as shown schematically in III



III

Thus, the effect of heating is to incorporate the polymers into cyclic systems. Such oxo-bridged species may show metal-ligand-metal spin exchange phenomena such as have been observed in a number of inorganic complexes.(6) If this is the case, we would expect an anomalous temperature dependence of the magnetic susceptibility of the complex II. That is, we would expect a strong deviation from Curie law behavior at low temperature due to spin coupling of the chromium ions along the polymer chain.

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It is seriously outdated and its mechanistic proposals seem to be sheer fantasy, but there is no other comparable compilation of experimental results.

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