Stereochemical Consequences of Correlated Rotation in Molecular Propellers

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When two or more aryl rings (Ar) are attached to a single atomic center (Z), rotation about the C–Z bond axis by one of the aryl rings in Ar_nZ is sensed by the other $n-1$ rings. The motions of the n rings is coupled in the sense that none of the rings moves independently of the others. Such sympathetic motion is called *correlated rotation*.

The present Account deals with work carried out in our laboratory in the last few years on systems in which three aryl rings are attached to a central atom. We shall discuss stereoisomerism and processes of stereoisomerization for such molecules, and describe the novel stereochemistry which results from the strong coupling of the rotational motions.

Static Stereochemistry

Stereochemistry of the Ground State. Our concern is with molecules of the type Ar_3Z and Ar_3ZX, where X is a fourth substituent with conical symmetry on the time scale of observation, notably hydrogen, halogen, methyl, or a lone pair of electrons. Molecules of this type are propeller-like in shape. The aryl rings, considered as "blades", radiate from an axis of rotation (propeller axis), and each blade is twisted in the same sense so as to impart a helical (chiral) conformation to the molecule. Evidence for the propeller shape comes from a great variety of sources. In systems of the type Ar_3Z, for example, idealized D_3 symmetry is found for trimesitylborane by X-ray diffraction.[1] Systems of the type Ar_3ZX are exemplified by trimesitylmethane, whose C_3 conformation, first established by semiempirical force-field calculations,[2] was subsequently confirmed by X-ray diffraction.[3]

In summary, triaryl molecules of the type discussed are molecular propellers whose unsubstituted skeleton is of D_3 or C_3 symmetry.[4,5] They are necessarily chiral, and may be asymmetric if appropriately substituted. Each molecule of this type must therefore exist in two enantiomeric forms. Whether diastereomeric forms exist as well depends on the substitution pattern.

Consider the substituted triarylborane 1 (a $\neq$ b $\neq$ c), where the substituents a–c do not themselves contain elements of stereoisomerism on the time scale of
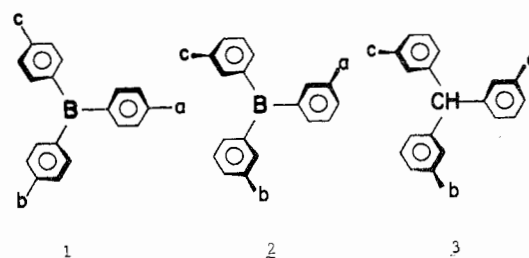
observation (e.g., halogen, methyl, ethyl). Such a molecule can exist in only two enantiomeric forms. Contrast this with the situation shown in structure 2, in which the bonds to the three substituents no longer lie along the local C_2 axis of the phenyl rings, as was the case for 1. Let us call the plane defined by the three carbon atoms attached to boron the *reference plane*. Then a may lie either above the reference plane, or below it. Similarly, b and c may each lie above or below the reference plane. A separate stereoisomer results from each of these edge interchanges, for a total stereoisomer count (N) of 2^3. Because the sense of the molecular propeller (*helicity*) may be right-handed or left-handed, 2 will exist in 2^4 stereoisomeric forms, i.e., eight diastereomeric *dl* pairs.

Replacement of the boron atom in 2 by a CH group produces a triarylmethane (3) in which the carbon atom is a chiral center. Because the configuration at the center can be either R or S, 3 will exist in 2^5 stereoisomeric forms, i.e., in 16 diastereomeric *dl* pairs.

N assumes its maximum value when all three rings are different, and when the two edges of each ring are differentiable, as in 2 and 3 (but not in 1). The structure is then said to be *maximally labeled*. The value of N in other than maximally labeled triarylboranes or triarylmethanes depends on the number and kind of degeneracies, which arise from two sources: the presence of a local C_2 axis in one or more of the aryl rings, and the identity of two or all three of the rings. Values of N for all possible combinations of degeneracies in Ar_3Z and Ar_3ZX systems have been tabulated.[4,5]

Permutational Rearrangements. We have seen that maximally labeled triarylboranes exist in 2^4 stereoisomeric forms. It can be shown that the relationship between these isomers is defined by a set of

(1) J. F. Blount, P. Finocchiaro, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **95**, 7019 (1973).

(2) J. D. Andose and K. Mislow, *J. Am. Chem. Soc.*, **96**, 2168 (1974).

(3) J. F. Blount and K. Mislow, *Tetrahedron Lett.*, 909 (1975).

(4) D. Gust and K. Mislow, *J. Am. Chem. Soc.*, **95**, 1535 (1973). This paper should also be consulted for a discussion of previous work in this field.

(5) K. Mislow, D. Gust, P. Finocchiaro, and R. J. Boettcher, *Fortschr. Chem. Forsch.*, **47**, 1 (1974).
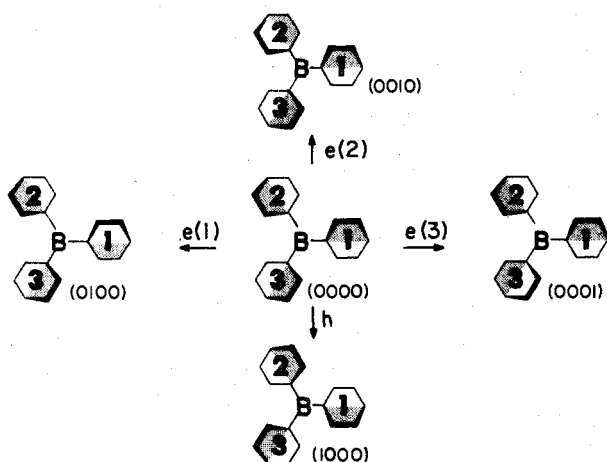
Figure 1.

Figure 2.

independent operations on an arbitrarily selected initial structure. Let us choose as the initial structure the maximally labeled borane in the center of Figure 1. The rings are individually identified by numerals, and each ring has two differentiable edges, one shaded and the other unshaded. As shown in Figure 1, we can reverse the shading independently for each ring under the operation of edge interchange, e. We can also reverse the helicity under an operation h. All possibilities for isomerism are thereby exhausted, since rigid rotation of the whole molecule does not generate any new isomers. Operations such as e and h are called *rearrangements*.[6]

The four rearrangements shown in Figure 1 are all operations of period 2, or involutions. An involution followed by another one of the same kind gives the identity, I. Let us represent the involution by the generalized group element of order 2, a. Then $a^2 = I$ is the defining relation of the two-group, abstractly written as $C_2 = \{I, a\}$, whose generator is a. This group is of paramount importance in science, and appears in many guises. To the chemist, the point groups C_2, C_i, and C_s are familiar realizations. These point groups, as well as the symmetric group of permutations on two symbols, S_2, and the groups which can be generated from a rearrangement e or h are all abstractly equal (*isomorphic*) to C_2. Their elements are therefore logically associated with the binary numeral set 0 (for the identity) and 1 (for the involution), since $\{0, 1\}$ under addition modulo 2 is a group isomorphic to C_2. In the present instance, if we assign to h, $e(1)$, $e(2)$, and $e(3)$, in that order, a value of either 0 or 1, the resulting set of four two-valued descriptors forms one of 16 ordered quadruples, which are in one-to-one correspondence with the 16 stereoisomers of a maximally labeled triarylborane. Adopting (0000) for the initial structure, it then follows that h, $e(1)$, $e(2)$, or $e(3)$ acting on (0000) gives rise to (1000), (0100), (0010), or (0001), respectively, as shown in Figure 1.

Starting with (0000), successive action of the three e rearrangements leads to a closed set of eight isomers, **K**. Figure 2 is a graph in the form of a cube, in which the eight vertices represent the isomers, and the twelve edges the rearrangements leading from one isomer to the other. Each of the three rearrange-
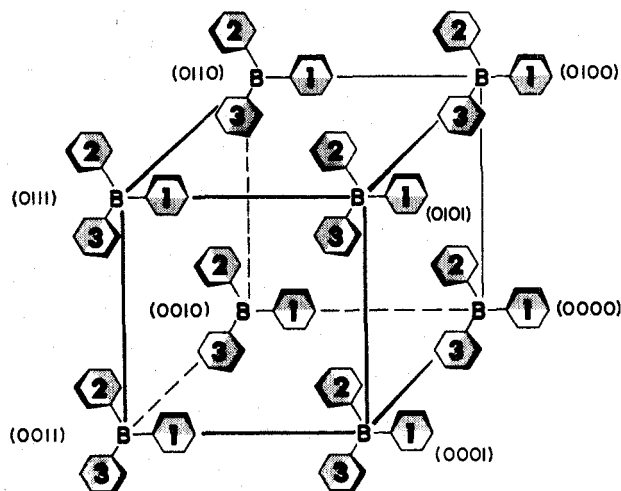
ments, $e(1)$, $e(2)$, and $e(3)$, is associated with a set of four parallel edges of the graph.

The three e rearrangements generate a mathematical group under the binary operation "followed by" and this group is isomorphic to the abstract group $C_2 \times C_2 \times C_2$, or $(C_2)^3$. The importance of this group to the subject of this Account justifies a brief explanatory diversion for the benefit of the general reader.

The direct product group $(C_2)^n$ of order 2^n is the group of n independent involutions, with n generators. Each element of the group, other than the identity, is of period 2. All elements commute, i.e., the group is abelian. We have already described the case for $n = 1$, where the abstract group is C_2. When $n = 2$, the group generators are a and b, and $(C_2)^2 = \{I, a, b, ab\}$. This group is known as the Klein four-group, and is isomorphic to the point groups D_2, C_{2v}, and C_{2h}. When $n = 3$, the group generators are a, b, and c, and $(C_2)^3 = \{I, a, b, c, ab, ac, bc, abc\}$. This group is isomorphic to the point group D_{2h}. A moment's reflection brings the realization that the operators $e(1)$, $e(2)$, $e(3)$ are similarly the generators of a group $\mathbf{R} = \{I, e(1), e(2), e(3), e(1)e(2), e(1)e(3), e(2)e(3), e(1)e(2)e(3)\}$ which is isomorphic to $(C_2)^3$, and that the eight structures in **K** are thus the products of **R** acting on (0000). In other words, the structures in **K** are, as it were, embodiments of these operations (with $I = (0000)$), in that the elements of $\mathbf{K} = \{(0000), (0100), (0010), (0001), (0110), (0101), (0011), (0111)\}$ can be mapped, one-to-one, onto the elements of **R** and of $(C_2)^3$. This explains why the graph of **K** (Figure 2) is isomorphic to the Cayley diagram of $(C_2)^3$, a graph of the group in which vertices represent group elements and edges represent group generators.[7]

Let us multiply each element in **R** by the helicity reversal operator h, and let the resulting set of rearrangements $h\mathbf{R}$ act on (0000). This will lead to a second closed set of eight isomers, $\bar{\mathbf{K}}$ (Figure 3). The same result could have been obtained by letting **R** act on (1111), the mirror image of (0000). All the elements in **K** have in common the same helicity (P),

(6) E. Ruch and W. Hässelbarth, *Theor. Chim. Acta*, **29**, 259 (1973).

(7) (a) E. L. Burrows and M. J. Clark, *J. Chem. Educ.*, **51**, 87 (1974), see especially Figure 11; (b) I. Grossman and W. Magnus, "Groups and Their Graphs", Random House, New York, N.Y., 1964. For readers unacquainted with elementary group theory, we strongly recommend this highly readable introductory text, which is distributed by The Mathematical Association of America, Washington, D.C.
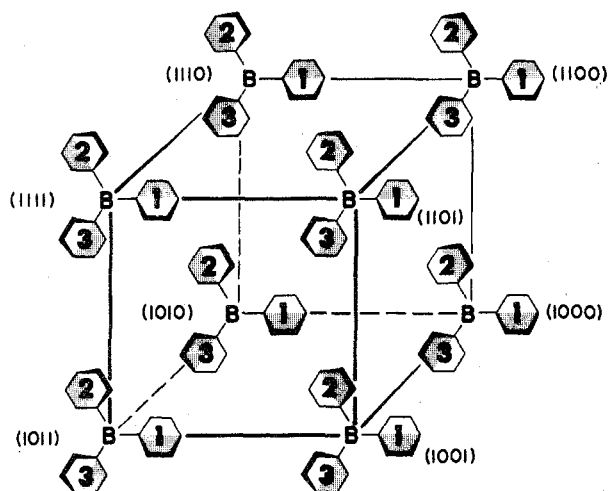
Figure 3.

while all those in $\bar{K}$ have in common the opposite helicity (M).

The 16 elements in $\mathbf{R} \cup h\mathbf{R}$ form a group, $\mathbf{G}$, which is isomorphic to the abstract group $(C_2)^4$ and whose generators are the four rearrangements $e(1)$, $e(2)$, $e(3)$, and h. The Cayley diagram of $\mathbf{G}$ can be constructed by nesting the graph of subgroup $\mathbf{R}$ inside the graph for the coset $h\mathbf{R}$ in such a manner that rearrangements which differ only in helicity are proximate, i.e., h next to I, $he(1)$ next to $e(1)$, etc. By connecting the proximate vertices pairwise by means of edges which represent h, a hypercube is generated whose 16 vertex elements represent the elements in $\mathbf{G}$. Since action of the elements in $\mathbf{G}$ on (0000) generates all of the isomers in $\mathbf{K}$ and $\bar{\mathbf{K}}$, a graph showing the interconversion of the 16 isomers by these rearrangements can be constructed simply by replacing the vertex elements in the hypercube by the corresponding isomer descriptors.

It must be emphasized that *the various ways of decomposing* $\mathbf{G}$ *into disjoint subsets (cosets) correspond to some of the ways of partitioning stereoisomers.* We have just discussed one such decomposition, i.e., with respect to the subgroup $\mathbf{R}$. But $\mathbf{R}$, as we shall see, is decidedly not the only proper subgroup of $\mathbf{G}$. This *chemically* significant point will be driven home when we discuss residual stereoisomerism.

It must also be emphasized that a rearrangement is a mathematical operation which describes only the net result of the transformation of one state of a model of a molecule (the sense in which we have used the term "isomer") to another. Rearrangements must be sharply differentiated from the physical *mechanisms* of the associated chemical transformations. A mechanism is concerned with the continuum of intermediate states in the reaction pathway, and with the associated questions of structure and energy: in other words, with the detailed description of the dynamic process. This question is addressed in the next section.

Dynamic Stereochemistry

Mechanistic Alternatives. What are the number and kinds of pathways by which isomerization of molecular propellers can take place? It seems sensible to

suppose at the outset that the various mechanisms capable of interconverting the isomers of an Ar_3Z system are not all equally favored on energetic grounds, and that only a limited number need be seriously considered. These considerations apply with equal force to the isomerization of Ar_3ZX systems with a fixed configuration at the chiral center (Z), since torsional motions around the Ar–Z bonds are the only feasible mechanisms for stereoisomerization in such compounds. Indeed, a limitation on the number of possible mechanisms which has been fully borne out by all the evidence so far[4] is this: all single-step isomerizations of Ar_3Z and Ar_3ZX systems involve a change in helicity, which may or may not be accompanied by an edge interchange. This means that a single-step isomerization of any member of the set $\mathbf{K}$ leads into the set $\bar{\mathbf{K}}$, and vice versa. Stated another way, the only allowed rearrangements belong to the set $h\mathbf{R}$. Evidently, simple edge interchange without a change in helicity involves steric congestion leading to unfavorable transition states.

The eight rearrangements in $h\mathbf{R}$ may be partitioned into four equivalence classes (*rearrangement modes*[6]) according to the number of edge interchanges, e. A single edge interchange combined with the operation of h on (0000) leads to three diastereomers, viz., (1100), (1010), or (1001), depending on which ring is involved. This mode, M_1, therefore consists of a set of three rearrangements, $he(1)$, $he(2)$, and $he(3)$. When zero edges are interchanged, the diastereomer obtained, (1000), differs from the initial structure, (0000), only in helicity. This mode, M_0, therefore contains only the rearrangement h. Similarly, M_3 contains only a single rearrangement, $he(1)e(2)e(3)$, in which edge interchange in all three rings combined with reversal of helicity leads from (0000) to the enantiomer, (1111). Finally, the three rearrangements in M_2, $he(1)e(2)$, $he(1)e(3)$, and $he(2)e(3)$, lead to three diastereomers of (0000), viz., (1110), (1101), or (1011), depending on which set of rings is involved. For completeness, we note that the eight rearrangements in $\mathbf{R}$ can of course also be partitioned into four rearrangement modes. One of these contains the identity as its only element.

The four modes M are realized physically by the four classes of *flip mechanisms* proposed by Kurland et al.[8] The torsional motion of the rings in the course of helicity reversal may involve passage through the reference plane, with concomitant edge interchange, or through a plane perpendicular to the reference plane, with no edge interchange. In the latter case, the ring is said to flip. Accordingly, rearrangements in M_3, M_2, M_1, and M_0 are the permutational consequences of the zero-, one-, two-, and three-ring flip, respectively.

In the zero- and three-ring flips, the three rings all rotate in the same direction (clockwise or counterclockwise), whereas in the one- and two-ring flips, two of the rings rotate in the same direction while the third rotates in the opposite direction. The central question of mechanism may now be posed as follows: Which of the four flip mechanisms is energetically preferred, and to what extent are the torsional motions of the individual rings interdependent?

The Two-Ring Flip. We shall immediately pro-

vide an answer to these questions and then proceed to marshal some of the evidence. It has been firmly established that the two-ring flip (i.e., the motion in which only *one* ring passes through the reference plane) is the stereoisomerization mechanism of lowest energy (*threshold mechanism*) in all systems of the type Ar_3Z and Ar_3ZX thus far examined. The torsional motions of the three rings are strongly coupled.

The experimental evidence supporting the above conclusion is based on dynamic nmr (DNMR) studies of variously substituted triarylboranes, triarylmethanes, and their cognates.[1,4,9-12] In addition to furnishing estimates of barrier heights for the isomerizations, these studies have provided the basis for a decision between the rearrangement alternatives. We shall content ourselves with one example from our work.

4
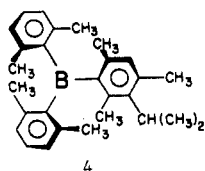
In the DNMR study[12] of 4, it was found that the coalescence of the four xylyl methyl singlets to one singlet at elevated temperatures was accompanied by the coalescence of the two isopropyl methyl doublets to one doublet, and that the activation energies for the two processes are the same ($\Delta G^{\ddagger} = 17.8$ kcal/mol). Thus, two different aspects of the *same* process had been observed. On the time scale of the slow exchange limit (ambient temperatures), the two isopropyl methyl groups reside in the asymmetric environment of the molecular propeller and are therefore diastereotopic. Only stereoisomerization by a mechanism involving a reversal of helicity can render these methyl groups enantiotopic (and therefore necessarily isochronous in an achiral solvent) on the time scale of the fast exchange limit. The coalescence of the four xylyl methyl group ligands must therefore have involved a rearrangement belonging to $h\mathbf{R}$. The three- and zero-ring flips are immediately ruled out, the first because the corresponding rearrangement (M_0), though changing helicity, does not effect any edge interchanges and would therefore lead to coalescence of the four signals to two rather than to one, and the second because the corresponding rearrangement (M_3) results not only in a change of helicity but as well in an edge interchange of each of the three rings, so that there cannot be any coalescence of the four methyls. Of the remaining two alternatives, only the two-ring flip (corresponding to M_1) is consistent with the observed coalescence.[12]

The preceding experiment, though providing compelling evidence for the operation of the two-ring flip mechanism in the permutational sense, and furnish-

ing a powerful argument for correlated ring motion, fails to provide us with details of the pathway for isomerization, and of the structure of the transition state. It must be remembered that DNMR spectroscopy deals exclusively with the phenomenon of site exchanges among nuclei and is uninformative with respect to intermediate states. To obtain information on this point we therefore had to transcend the limitations of DNMR and appeal to the computational method of molecular mechanics. The procedure was as follows.[2] One of the mesityl rings in the input structure for trimesitylmethane (corresponding to a ground state of P helicity) was rotated ("driven") about its C–Mes bond by 10° increments in a counterclockwise sense (as seen from the central carbon atom, looking toward the mesityl ring), thereby generating new structures for each incremental change. At each stage, the structure was subjected to a full-relaxation empirical-force-field calculation. The results showed that, while edge interchange was forced on the driven ring by the direction of rotation, the two dependent or "following" rings described rotations in the opposite (clockwise) direction. In the end, the helicity had been reversed and a single edge interchange (M_1 rearrangement) had taken place. When the calculation was repeated driving the ring in a clockwise direction, it was found that one of the dependent rings rotated in the same direction as the driven ring, while the other rotated in the counterclockwise direction (leading to edge exchange); once again, an M_1 rearrangement had taken place. In the transition state for the two-ring flip, as deduced from these calculations, the two flipping rings are roughly perpendicular to the third, and the computed energy, 20 kcal/mol, compares favorably with the value of 21.9 kcal/mol found experimentally for the free energy of activation.[10]

In an extension of these calculations,[13] it was found that the two-ring flip is the threshold mechanism for the whole class of trimesityl compounds in which the three mesityl groups are attached to an atom from group IIIa, IVa, or Va. The results show that energy barriers among members of this class are quantitatively correlated with Z–Mes bond lengths, which govern nonbonded interactions in the transition state. The shorter the Z–Mes bond, the higher the barrier. A fascinating prediction is the threshold barrier for trimesitylamine, 25–27 kcal/mol. According to this prediction, the resolved amine should be optically stable at room temperature.

DNMR studies in related systems have demonstrated the existence of higher barriers and hence the operation of additional mechanisms. A comparative study[11] of triarylmethanes containing two mesityl (or 2,6-xylyl) groups and a third group with a lesser steric requirement (Ar) has revealed that, whereas the threshold barriers among these compounds vary widely according to the nature of Ar (21.9, 20.1 (18.6), 17.2, ca. 13, and ca. 8 kcal/mol for Ar = mesityl, 2-methyl-1-naphthyl (two diastereomers), 9-anthryl, 2,4,6-trimethoxyphenyl,[14] and phenyl, respectively),

(8) R. J. Kurland, I. I. Schuster, and A. K. Colter, *J. Am. Chem. Soc.*, **87**, 2279 (1965).

(9) R. J. Boettcher, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **95**, 7157 (1973).

(10) P. Finocchiaro, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **96**, 2165 (1974).

(11) P. Finocchiaro, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **96**, 2176 (1974).

(12) J. P. Hummel, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **96**, 3679 (1974).

(13) M. R. Kates, J. D. Andose, P. Finocchiaro, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **97**, 1772 (1975).

(14) M. J. Sabacky, S. M. Johnson, J. C. Martin, and I. C. Paul, *J. Am. Chem. Soc.*, **91**, 7542 (1969).

the higher barriers (22.3 (22.9) and 22.0 kcal/mol for Ar = 2-methyl-1-naphthyl and 2,4,6-trimethoxyphenyl[14]) are all close to 22 kcal/mol. This result fits nicely into the scheme developed above. For compounds of the type under discussion, there are two distinct two-ring-flip transition states, A and B (see schematic sketch). In A, one of the flipping rings is Ar and the other is mesityl or 2,6-xylyl, whereas in B they are both mesityl or 2,6-xylyl. The principal repulsive nonbonded interaction takes place between the four paired ortho substituents of the two flipping rings, especially the pair distal to the hydrogen on the central carbon atom, while the two ortho substituents of the ring undergoing edge interchange are relatively unencumbered. Thus, to a first approximation, the energy of the transition state will be primarily determined by the interaction of the flipping rings. It follows that the energy of A will be variable, whereas the energy of B will be relatively constant, and that threshold barriers, corresponding to A, will therefore be variable whereas the higher barriers, corresponding to B, will all have values close to that found for trimesitylmethane.

A   B
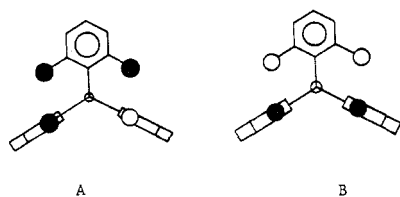
The preceding discussion points up an important reason for the favored position of the two-ring flip among competing mechanisms. In the three-ring flip, instead of the two unfavorable interactions described above, there will be six. In the zero-ring flip, the repulsive interactions, though of a different sort, will predictably be even more severe, assuming correlated rotation.[13] The two- and one-ring flips may thus be regarded as compromises between these two extremes, with the two-ring flip favored according to all the evidence.

Stereochemical Correspondence

At the very beginning of our work in this area, it was recognized that two chemically unrelated classes, the Ar_3Z systems and the transition metal tris chelates, were intrinsically similar in their static and dynamic stereochemistry.[4] Both systems can be described as molecular propellers, with D_3 symmetry in the ground state of the basic skeleton (e.g., $(C_6H_5)_3C^+$ and $Co(en)_3{}^{3+}$). Both systems can undergo stereoisomerizations by mechanisms which are formally analogous; thus, the Bailar and Rây-Dutt intermediates proposed for interconversions in the tris chelates have their counterparts in the three- and two-ring flips, respectively. The formal resemblance between the two systems can sometimes be quite striking. For example, tris(2-methyl-1-naphthyl)borane (5)[1] and tris(α-isopropenyltropolonato)cobalt(III) (6)[15] both exist as mixtures of two diastereomeric *dl* forms, one cis (C_3) and the other trans (C_1). At the slow exchange limit either mixture gives rise

to four methyl proton signals, and at the fast exchange limit to one. The coalescence behavior in both cases points to the existence of two barriers and hence to two stereoisomerization processes. Only in one important respect is there a distinction: although in both systems the threshold mechanism entails the enantiomerization of the trans form, in **5** this occurs by the two-ring flip but in **6** by the trigonal (Bailar) twist, i.e., by the three-ring flip equivalent.

5   6
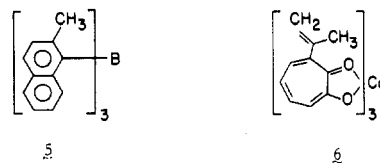
It is thus apparent that some kind of equivalence relation exists between systems whose static and dynamic stereochemistry shows the above described similarities. To frame this relationship, which we call *stereochemical correspondence*, in more exact terms, one must resort to mathematical abstractions, for *the essential stereochemical features of any system can be given precise expression only in the language of group theory:* static stereochemistry by point groups, and dynamic stereochemistry by permutation groups.[5,16] Reduced to its simplest terms, two systems are stereochemically correspondent when they have the same point group and the same permutation group.[17] The essential stereochemical features, static and dynamic, of such systems, no matter how chemically disparate, are in a one-to-one correspondence with each other and can be isomorphically mapped onto the same mathematical model. An equivalence relation is thereby established between the two systems.

This abstraction has proven to be a powerful and unifying tool. Thus, the stereochemical analysis of Ar_3Z systems in this Account, insofar as it does not deal with intermediates or transition states, is applicable in toto to the tris chelates. The two systems have the same number and kind of stereoisomers, interconvertible by the same number and kind of permutational rearrangements. The groups of rearrangements of the two systems are abstractly equal. In the tris chelates, M_0 and M_1 are realized by the trigonal twist and Rây-Dutt mechanisms, respectively; one need merely remember that in the case of tris chelates edge interchanges refer to bidentate ligands. The group of 16 rearrangements of stereochemically nonrigid tris chelates[18] is isomorphic to G. The dynamic stereochemistry of three-coordinate transition-metal compounds with D_3 symmetry[19] can predictably be analyzed in the same manner.

Stereochemical correspondence does not inform us on mechanisms and energetics. That the threshold mechanisms for the stereoisomerization of **5** and **6** belong to different rearrangement modes (M_1 and M_0, respectively) does not alter the fact that the two systems are stereochemically correspondent.

(15) S. S. Eaton, J. R. Hutchison, R. H. Holm, and E. L. Muetterties, *J. Am. Chem. Soc.*, **94**, 6411 (1972).

(16) D. Gust, P. Finocchiaro, and K. Mislow, *Proc. Natl. Acad. Sci. U.S.A.*, **70**, 3445 (1973).

(17) M. G. Hutchings, J. G. Nourse, and K. Mislow, *Tetrahedron*, **30**, 1535 (1974).

(18) S. S. Eaton and G. R. Eaton, *J. Am. Chem. Soc.*, **95**, 1825 (1973).

(19) M. B. Hursthouse and P. F. Rodesiler, *J. Chem. Soc., Dalton Trans.*, 2100 (1972).

The concept of stereochemical correspondence has proven particularly fruitful in a comparison of spirophosphoranes with molecules of the type Ar_2ZX.[5,16] Both systems may be regarded as two-bladed molecular propellers and their stereochemical correspondence, obvious at the static level (the basic skeleton of both systems has C_2 symmetry), can be expressed at the dynamic level by the statement that the groups of rearrangements for both systems are isomorphic to $(C_2)^3$ and therefore to each other.

An algebraic description which expands and generalizes the concept of stereochemical correspondence has been provided by Nourse,[20] in terms of homomorphisms between the point and permutation groups.

Residual Stereoisomerism

We have learned that the threshold mechanism for stereoisomerization in systems of type Ar_3Z and Ar_3ZX is, without known exception, the two-ring flip, and that the permutational consequences of that mechanism are the rearrangements contained in M_1. Now the rearrangements in M_1 form a set of three generators for the group $T_1 = \{I, he(1), he(2), he(3), e(1)e(2), e(1)e(3), e(2)e(3), he(1)e(2)e(3)\}$, which is a subgroup of G and is isomorphic to $(C_2)^3$. Consequently, the full group of rearrangements is decomposed into two cosets with respect to the subgroup T_1. We may express this fact by writing $G = T_1 \cup hT_1$, though it should be noted that h, the representative of the coset, is not unique since any one of the eight elements in G not in T_1 (e.g., $e(1)$, etc.) serves equally well to generate the coset. If T_1 and hT_1 act on (0000), then the two disjoint sets are given by {(0000), (1100), (1010), (1001), (0110), (0101), (0011), (1111)} and {(1000), (0100), (0010), (0001), (1110), (1101), (1011), (0111)}, respectively. Each set consists of eight stereoisomers (four dl pairs) which are interconvertible by an M_1 rearrangement. However, no isomer in one set can be converted to an isomer in the other by a rearrangement belonging to M_1. *The chemical consequences are that any maximally labeled system Ar_3Z will exist in two achiral diastereomeric forms under the full operation of the two-ring flip.*

The phenomenon we have just described exemplifies what we have called *residual stereoisomerism*,[21] and results whenever closed subsets of appropriately substituted interconverting isomers are generated from the full set at a particular time scale of observation and under the operation of a given stereoisomerization. Succinctly put, the number of residual stereoisomers is the index of the subgroup generated by a given set of rearrangement modes (at a particular time scale of observation) in the full rearrangement (permutation) group;[22] i.e., it is the order of that group divided by the order of the subgroup. In the above example, $|G|/|T_1| = 16/8 = 2$, the number of residual diastereomers.

The number of residual stereoisomers in maximally labeled systems of the type Ar_3Z under the operation of each of the three remaining flip mechanisms is

now easily computed. The rearrangement in M_0 is the generator for the group $T_0 = \{I, h\}$, a subgroup of index 8 in G. Each coset corresponds to an interconverting pair of chiral diastereomers, e.g., (0000) and (1000), leading to four residual dl pairs under the three-ring flip. The rearrangement in M_3 is the generator for the group $T_3 = \{I, he(1)e(2)e(3)\}$, a subgroup of index 8 in G. Each coset corresponds to an interconverting pair of enantiomers, e.g., (0000) and (1111), leading to eight achiral residual diastereomers under the zero-ring flip. Finally, the rearrangements in M_2 are the generators for the group $T_2 = \{I, he(1)e(2), he(1)e(3), he(2)e(3), e(2)e(3), e(1)e(3), e(1)e(2), h\}$, a subgroup of index 2 in G. Each coset corresponds to eight interconverting chiral diastereomers, leading to two residual enantiomers (one residual dl pair) under the one-ring flip. Note that since all subgroups of G are invariant (G is abelian), the cosets resulting from the decomposition of G with respect to T themselves form the elements of factor groups, G/T, which are isomorphic to C_2 (for T_1 and T_2) and $(C_2)^3$ (for T_0 and T_3).

In systems of the type Ar_3ZX, the presence of a chiral center in the maximally labeled structure doubles the number of stereoisomers. Assuming no inversion at Z, there will then be eight residual dl pairs under the zero-ring flip and eight *different* residual dl pairs under the three-ring flip, and there will be two residual dl pairs under the one-ring flip and two *different* residual dl pairs under the two-ring flip.

We now proceed to describe the realization[21] of one of these predictions:[4] that under the full operation of the two-ring flip, a maximally labeled Ar_3ZX system exists in the form of two diastereomeric dl pairs.

7
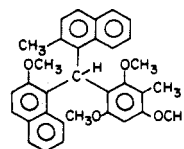
Crystallization of triarylmethane **7** from benzene afforded two fractions, one enriched to the extent of 95% in the α isomer, mp 210–213°, and the other enriched to the extent of 70% in the β isomer, mp 158–163°. Since three of the six methyl proton signals in the NMR spectrum of the α isomer (at 87°) were significantly shifted from the corresponding set of three methyl proton signals of the β isomer, the progress of the separation could be easily followed, and stereomutation at elevated temperatures could be conveniently monitored as a function of time. The barriers for diastereomerization at 122° were thus found to be $\Delta G^{\ddagger} = 30.6$ kcal/mol for $\alpha \rightarrow \beta$ and $\Delta G^{\ddagger} = 30.4$ kcal/mol for $\beta \rightarrow \alpha$; $K_{\beta/\alpha} = 0.7$ at 122°. The two isomers are residual diastereomers.

The 16 stereoisomers of **7** which have in common the R configuration at the chiral center are depicted in Figure 4. The dot at the center of each structure stands for C–H, with the hydrogen pointing at the observer, the small circles denote methoxy groups, and the short lines denote methyl groups. The set shown on the left (λ) results from the action of T_1 on the structure designated (0000), while the set on the

(20) J. G. Nourse, *Proc. Natl. Acad. Sci. U.S.A.*, **72**, 2385 (1975).

(21) P. Finocchiaro, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **96**, 3198 (1974).

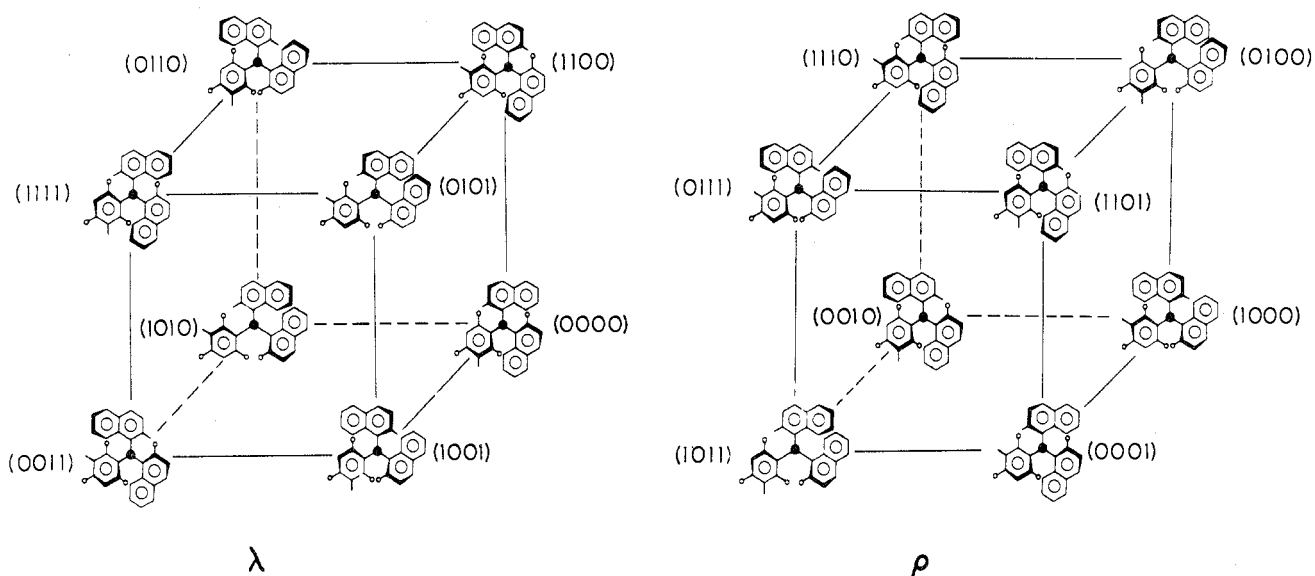(22) J. G. Nourse and K. Mislow, *J. Am. Chem. Soc.*, **97**, 4571 (1975).

Figure 4.

right (ρ) results from the action of $h\mathbf{T}_1$ on (0000). Note that, according to the convention adopted in Figures 1–3, rings numbered 1, 2, and 3 correspond to 2-methoxy-1-naphthyl, 2-methyl-1-naphthyl, and 3-methyl-2,4,6-trimethoxyphenyl, respectively, and shaded edges in the three rings correspond to edges marked by methoxy in ring 1 and by methyl in rings 2 and 3. Each of the three generators of $\mathbf{T}_1$ (i.e., each of the three rearrangements in M_1) is associated with a set of four parallel edges in the graph for λ and for ρ.

The 16 enantiomers, having in common the S configuration at the chiral center, can be represented by the same figure, the only change being that the hydrogen now points away from the observer ($\bar{\lambda}$ and $\bar{\rho}$). If we arbitrarily associate the (R)-α isomer with λ, then ρ, $\bar{\lambda}$, and $\bar{\rho}$ correspond to (R)-β, (S)-α, and (S)-β isomers, respectively. Each of the 32 conformers can be unambiguously described by an ordered pentuple, the fifth two-valued descriptor designating configuration at the chiral center.

From evidence adduced earlier we can safely conclude that, since the aryl groups in **7** are sterically less demanding than mesityl, the threshold barrier, corresponding to the two-ring flip, will be far less than 22 kcal/mol. Stereoisomerizations by that mechanism will therefore occur extremely rapidly at 87°, a temperature at which the rate of interconversion of the residual diastereomers α and β is too slow to be conveniently measured, and at which a mixture of these two isomers shows nine sharp signals in the methyl proton region (there should be twelve, but two sets of three are accidentally isochronous). As the temperature is lowered to 37°, these signals are seen to broaden, and at even lower temperatures, new signals grow in. The operation of the two-ring flip is thus revealed, and the temperatures at which it appears to be sufficiently slow for observation are consistent with barriers of the expected magnitude (10–15 kcal/mol). Note that at the slow exchange limit there should be, for each residual diastereomer, $8 \times 6 = 48$ methyl proton signals (barring accidental isochrony), 24 barriers, and 12 equilibrium constants.

The interconversion of the two residual diastereomers at elevated temperatures can obviously not occur by the two-ring flip route. The zero-ring flip can also be excluded, quite aside from steric arguments, on the grounds that $\mathbf{T}_3$ is a subgroup of $\mathbf{T}_1$, i.e., the rearrangement in M_3 converts a given structure in λ or ρ to another one in the *same* set. The one- and three-ring flips, however, remain as candidates because neither $\mathbf{T}_2$ nor $\mathbf{T}_0$ is a subgroup of $\mathbf{T}_1$. For example, M_2 and M_0 acting on (0000), which is in λ, yield, inter al., (1110) and (1000), respectively, both of which are in ρ. Our empirical-force-field calculations[2,13] permit a decision in favor of the one-ring flip, in agreement with qualitative considerations (see above).

A particularly noteworthy feature is that the structures in λ are not converted to those in ρ, and vice versa, by the two-flip route even though each of the multiples of π. Consider, for example, the circuit (0000) $\rightarrow$ (1001) $\rightarrow$ (0101) $\rightarrow$ (1100) $\rightarrow$ (0000) in λ and the circuit (1000) $\rightarrow$ (0100) $\rightarrow$ (1101) $\rightarrow$ (0001) $\rightarrow$ (1000) in ρ. In both cases, the 2-methyl-1-naphthyl ring just oscillates and does not undergo edge interchange (the descriptor for ring 2 remains invariant), while the other two rings simultaneously perform a unidirectional rotation by 2π, clockwise (as defined above) for 2-methoxy-1-naphthyl and counterclockwise for 3-methyl-2,4,6-trimethoxylphenyl. Other circuits pair different sets of rings. Thus, although all three aryl rings are rapidly spinning about their bonds to the central carbon during the two-ring flips, the structures are locked into their respective sets (λ or ρ), and there is no escape under the constraint of the rearrangement mode M_1. Hence there are no restrictions upon the *individual* torsional angles of any of the bonds to the central carbon atom in the α or β isomer. However, there are restrictions upon the *relationships* of the three torsional angles, as a consequence of the correlated character of the rotational motion.

Residual stereoisomerism has yet to be demonstrated in a representative of a maximally labeled Ar_3Z system, e.g., a borane or amine (whose nitrogen atom is certain to undergo extremely rapid inversion on the NMR time scale). The two achiral diastereomers can be exemplified by λ and ρ, where the dot at

the center now stands for a boron or nitrogen atom. We note in passing that enantiomerization, requiring a minimum of three two-ring flips, e.g., $(0000) \rightarrow (1001) \rightarrow (0011) \rightarrow (1111)$, cannot proceed by way of an achiral structure so that (by the principle of microscopic reversibility) enantiomerically paired pathways always exist, e.g., $(0000) \rightarrow (1100) \rightarrow (0110) \rightarrow (1111)$.

Residual Stereotopism

By removing the 3-methyl group from 3-methyl-2,4,6-trimethoxyphenyl in **7**, to form **8**, virtually no change occurs in the nonbonded interactions which determine the magnitude of energy barriers in these systems, and which are concentrated in the ortho positions. However, a degeneracy has been introduced, rendering the two edges of the 2,4,6-trimethoxy-1-phenyl ring nondifferentiable *in the permutational sense.*

Granted the two-ring flip as the threshold mechanism, let us allow T_1 and hT_1 to act on a reference structure of **8**, and for reasons which will become clear below, let us retain the descriptor for ring 3 even though, given the local C_2 axis, $e(3)$ seems to accomplish nothing. If the reference structure is (0000), the result will be exactly as depicted in λ and ρ, with the exception that the 3-methyl group in ring 3 is missing, and that all structures having in common the first three descriptors $(h, e(1), e(2))$ are identical. Thus (0000) in λ and (0001) in ρ are the same, etc. It follows that λ and ρ are equally valid representations for **8**. This compound exists in 16 stereoisomeric forms, consisting of eight diastereomers which are interconverted by the two-ring flip and which have the R configuration at the center, plus the mirror image set of interconverting diastereomers with the S configuration at the center.[23]

Now if rotation of the three rings were not correlated, the two edges of ring 3 would be nondifferentiable also in the operational sense, for all that would be required to make the two edges equivalent would be an independent rotation by π of that ring, unaccompanied by motion in the other two rings. But

(23) P. Finocchiaro, D. Gust, and K. Mislow, *J. Am. Chem. Soc.*, **96**, 3205 (1974).

rotation *is* correlated, i.e., rotation of ring 3 is accompanied by coupled rotation of the other two rings. Under the constraint of M_1, interconversion of the edges in ring 3 must therefore follow the pattern depicted in Figure 4. Let us imagine that the line drawn in the 3 position of ring 3 (Figure 4) which represents a methyl group in **7** merely serves to mark that particular ring edge in **8**. It immediately becomes apparent that although the marked edge takes up a variety of positions, no two structures in the same set (λ or ρ) are related in such a way that they differ only in a single edge interchange for ring 3. For example, although (0000) in λ and (0001) in ρ are the same, they cannot interconvert under any rearrangement in M_1. The reason for this is that decomposition of G with respect to T_1 places I and any *single* edge interchange e into different cosets. It follows that the condition for operational equivalence described above is not met, that *the two edges in the 2,4,5-trimethoxyphenyl group are therefore operationally differentiable,* and that the two ortho methoxy groups are diastereotopic. Furthermore, the two ortho methoxy proton signals are not expected to coalesce even at elevated temperatures. These expectations are fully borne out by experiment.[23] Not even the beginnings of coalescence are observed at 191°, and a lower limit of 26 kcal/mol may be assigned to the process of site exchange (topomerization). This process will have to accomplish interconversion of elements of λ and ρ, presumably by the one-ring flip mechanism which, as we saw, has a barrier of ca. 30 kcal/mol.

This phenomenon, which may be dubbed *residual diastereotopism,* has been depicted as the ghost of residual stereoisomerism.[23] Residual enantiotopism is similarly related to residual enantiomerism.[23]