Thermal Stereomutation of Cyclopropanes[1,2]

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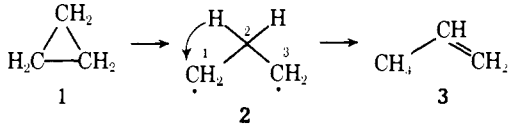
Abstract: The syntheses of optically active *trans*-1-phenylcyclopropane-*2-d*, (−)-**13** and (+)-**13**, are achieved by Haller-Bauer cleavages of the corresponding ketones (+)-**10** and (−)-**10** with $NaND_2$. The optically active cis isomer (+)-**14** is prepared from the cis ketone, (−)-**17**, by an analogous route. Three kinetic experiments on these compounds are carried out. (1) Pyrolysis of (−)-**13** and (+)-**13** to effect trans-cis isomerization at 309.5° in the gas phase. This reaction is first-order with a rate constant $k_i = 2.48 \times 10^{-5}$ sec^{-1}. (2) The loss of optical activity from a synthetic equilibrium mixture, "V", composed of 50% each of (+)-**13** and (+)-**14**, in which the enantiomeric purities of each are identical. This reaction also is first-order with a rate constant $k_\alpha^{eq} = 4.06 \times 10^{-5}$ sec^{-1}. (3) The decline of optical rotation of the kinetic samples from experiment 1. This reaction is not first-order, because the optical rotations of enantiomerically pure **13** and **14** differ slightly. The kinetics can be analyzed by numerical integration to determine k_1, the rate constant for unaccompanied single rotation of the phenyl-substituted carbon, C_1 (Scheme II) and k_{12} (and k_{13}), the rate constant for synchronous double rotation of C_1 and C_2 (or C_1 and C_3). The "best-fit" values are $k_1 = 0$, and $k_{12} = 0.96 \times 10^{-5}$ sec^{-1}. An assumed isotope effect of 10% gives $k_{13} = 1.06 \times 10^{-5}$ sec^{-1}. Thus, each rotation of C_1 is accompanied by a synchronous rotation of C_2 or C_3. The result is that expected if the stereomutation pathway passes over a 0,0 trimethylene ("π-cyclopropane"). Ozonolysis of (−)-**13** to the acid (−)-**18**, conversion of the latter to *trans*-1-benzoylcyclopropane-*2-d*, and $NaND_2$ cleavage of the ketone give *trans*-cyclopropane-*1,2-d*$_2$, α_{365} +0.168° (neat, 1 dm). Pyrolysis of this hydrocarbon at 422.5° results in first-order approach to the trans-cis equilibrium mixture (rate constant k_i) and first-order decline of optical activity (rate constant k_α). The ratio, $k_i/k_\alpha = 1.07 \pm 0.04$, is most simply interpreted again as a synchronous rotation of two methylene groups (Scheme VII).

Pyrolysis of cyclopropane or its substituted derivatives causes two major reactions:[3] structural isomerization by hydrogen shift to give an olefin (e.g., cyclopropane → propylene[4]) and stereomutation (e.g., *trans-* → *cis*-cyclopropane-*1,2-d*$_2$[5,6]). High molecular symmetry and structural simplicity have made cyclopropane a popular vehicle for testing theories of energy transfer and reaction pathway. In fact, cyclopropane isomerizations have been the most intensely studied of all thermal unimolecular reactions.[3,7] Nevertheless, the mechanisms of these apparently simple processes have remained unsettled. In this paper,[2] we report advances toward the solution of the mechanistic problem in two examples of stereomutation.

Previous Mechanistic Proposals. Stereorandom Trimethylene Biradical. Chambers and Kistiakowsky[8] were the first to suggest that the structural isomerization of cyclopropane (**1**) might occur by way of an intermediate (**2**) in which one of the ring C–C bonds had been broken. Hydrogen shift in **2**



1 **2** **3**

from C_2 to C_1 then would give propylene and complete the reaction.

The concept of a trimethylene biradical intermediate (**2**) has been taken up by others, most notably Benson, who has elaborated it into a general mechanism, not only for the cyclopropane structural isomerization but also for the stereomutations of cyclopropanes and other small-ring compounds and for a wide variety of thermal fragmentations and rearrangements.[9] The major arguments in favor of this scheme have been the agreement between the observed activation parameters determined from kinetic data and those calculated from thermochemical bond additivity assumptions.

For example, in the case of cyclopropane, the heats of formation of the transition states for the structural isomerization and for stereomutation were available from the heat of formation of cyclopropane and the observed[5,8,10] activation energies. The heat of formation of the proposed common intermediate, trimethylene (**2**), was estimated[9] from that of propane by (conceptually) breaking two C–H bonds. This led to the conclusion that **2** lies in a potential well flanked by barriers of almost equal height (8.2 and 9.0 kcal/mol, respectively) for ring closure to cyclopropane and hydrogen shift to propylene.[9e] In accord with a prior suggestion,[5] internal rotations about the C_1–C_2 bonds of the ring-opened intermediate **2** were considered to provide a mechanism for the stereomutation.[9] Note that the additivity assumption used to calculate the heat of formation of trimethylene implied the absence of energetically significant interaction between C_1 and C_3, either through-space or through the intervening bonds.

To demonstrate the utility of this approach, Benson and O'Neal[9b,c] developed additivity tables for estimation of the activation parameters and hence the rate constants of the internal rotation, ring closure, and hydrogen shift reactions of the proposed trimethylene intermediates in the pyrolyses of several substituted cyclopropanes. With some adjustments,[11] these tables correlated the extensive data on such reactions in an internally consistent manner. It is of particular significance to our discussion that this correlation provided an explanation for the effect of substituents on the rates. The activation energy for the formation of the trimethylene intermediate was considered to be lowered by about 2.5 kcal/mol for each alkyl substituent on the C–C bond being ruptured, in accord with the corresponding bond-weakening effect of alkyl substituents in acyclic hydrocarbons.[9b-d] Moreover, the internal rotation rates were supposed to be retarded by heavier substituents on C_1 and C_3 of the trimethylene, thus slowing down the stereomutation in the more highly substituted systems.[9b-d] This idea proved to be of some correlative value in other cases.[12-15]

The internal rotation rate assigned[9b-d,15] to the unsubstituted trimethylene biradical **2** was based upon an estimated rotational barrier of about 2 kcal/mol. Since E_a for ring closure had been estimated at about 8.2 kcal/mol, and since there was no reason to believe that the entropy of activation for internal rotation would be especially low, the value assigned for the rotational barrier predicted a much faster rate of internal bond rotation than of ring closure. In effect, therefore, the Benson–O'Neal scheme predicted that the

parent unsubstituted trimethylene should be a *stereorandom intermediate.*

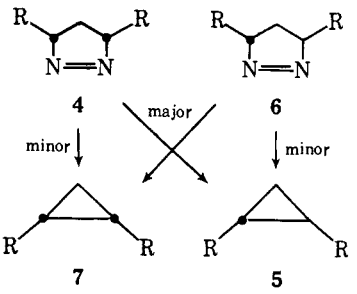
It has been noted[16,17] that the quantitative estimate[9b-d,15] of a value for the bond rotation rate in a trimethylene biradical as two-thirds that in the corresponding hydrocarbon probably was unsound since the data in the literature on the few available comparisons suggested that the factor should be more like a sixth or even less. In any case, this only reinforced the previous conclusion that an unsubstituted trimethylene of the Benson-O'Neal type, in which no interaction between the radical centers was envisioned, should lose its stereochemistry rapidly.

The single methylene rotation category includes all mechanisms in which stereomutation occurs by an unaccompanied, individual inversion of configuration of one of the ring carbons. In terms of observable stereochemical events, this process would convert an optically active trans-1,2-disubstituted cyclopropane sequentially to the cis isomer and then to the enantiomeric trans compound by successive single inversions of C_1 and C_2. In a completely general treatment, the same effect could be achieved by an even number of inversions of one center and an odd number of the other. The term *single methylene rotation* derives from the fact that the process is stereochemically equivalent to a 180° rotation of the exocyclic substituents at one center.

The first detailed proposal of a single methylene rotation was that of Smith,[18] who visualized a distorted species with one methylene group twisted by 90° from the ground configuration as a common intermediate for the structural isomerization and the stereomutation. This mechanism was later challenged,[9a,e] supported,[19] and modified.[20] Theoretical objections[9a] have become less severe, and it now seems possible[21,22] that stereomutation by way of a Smith mechanism in an "expanded ring" model (two stretched ring bonds) might not be completely out of the question.

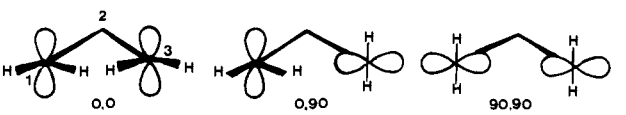
It should be obvious that the trimethylene biradical also could be responsible for the equivalent of a single methylene rotation, provided that the internal bond rotation was much slower than the ring closure. In fact, the Benson-O'Neal treatment suggested that such behavior might be approached as a limit in the more highly substituted cases, and the observed trends in the available experimental data could be interpreted in accord with this idea.[9b,11,12]

Double Methylene Rotation. In an important series of experiments, Crawford and Mishra[23] and McGreer and coworkers[24] showed that, in some cases, the pyrolytic elimination of nitrogen from a cis-3,5-disubstituted pyrazoline (**4**) gave as the major product a cyclopropane in which the substituents were trans (**5**), whereas the corresponding trans



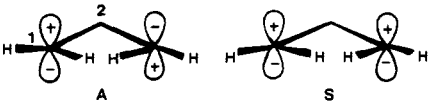
pyrazoline (**6**) gave mostly cis cyclopropane (**7**). It was clear[23] that, if trimethylene intermediates were involved in these reactions, they could not be stereorandomized. Moreover, the peculiar crossover effect suggested a conrotatory ring closure as the preferred fate of the intermediate.[23] Hoffmann's extended Hückel calculations[21] provided a theoretical justification for these conclusions.

Hoffmann considered three idealized geometries for the



trimethylene intermediate: 0,0; 0,90; and 90,90. The numbers refer to the degrees of arc by which one or both of the terminal methylene pairs of hydrogens are twisted out of the plane defined by the three carbons. These species could be taken as models of the transition states (or intermediates) in three different mechanisms of cyclopropane pyrolysis. The stereochemically random type of trimethylene could in principle be approached through any of these, provided that the barrier to internal rotation of the individual terminal methylene groups was low. A single methylene rotation pathway could include species whose structure was approximated by that of the 0,90 form. The 0,0 form (a "π-cyclopropane") could represent the half-way point of a new mechanism in which ring closure and its microscopic reverse, ring opening, occurred by a coupled, synchronous motion of both terminal methylene groups (*double methylene rotation*).

The extended Hückel calculations[21] showed that, for C_1-C_2-C_3 bond angles greater than 100°, the antisymmetric combination (A) of the formally nonbonding 2p orbitals of the 0,0 trimethylene was lower in energy than the symmetric one (S), essentially because of destabilization of the



S orbital by interaction with the bonding combination of the C_2-H σ orbitals. The highest occupied orbital then became A, which meant that, if the 0,0 form were to cyclize in a concerted manner, orbital symmetry would require it to do so by conrotation. The calculations[21] suggested that there should be a high internal rotational barrier, which would preserve the stereochemical relationships among the labels in a substituted case.

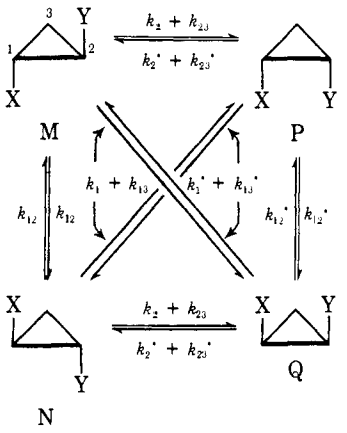
Perhaps the most significant result was the conclusion[21] that the energy of the 0,0 form passed through a minimum when the C_1-C_2-C_3 bond angle was near 125°. Moreover, the fact that the minimum occurred at a substantially lower energy than that of either the 0,90 or 90,90 forms was the basis of the bold suggestion[21] that, not only was the 0,0 species responsible for the stereochemical crossover effect in the decomposition of pyrazolines, but also it was the intermediate or transition state in the pyrolysis of cyclopropane. Although not explicitly stated,[21] this amounted to the prediction of a conrotatory double methylene rotation as the mechanism of stereomutation of the hydrocarbon.

Triple methylene rotation, in which all three methylene groups of cyclopropane invert in synchrony, has not been seriously proposed as a mechanism, nor are we aware of any theoretical attempts to evaluate it. We have mentioned it here for the sake of completeness, but also, as will become evident, because its occurrence would have definable experimental consequences.

Experimental Approaches to the Determination of the Mechanism of Stereomutation. Scheme I outlines a generalized system that in principle is capable of a solution of the problem. It involves an unsymmetrically 1,2-disubstituted cyclopropane in which both the cis and trans isomers are chiral. Six independent phenomenological rate constants characterize the network of epimerizations and enantiomerizations.

If we temporarily disregard triple methylene rotations, the most general analysis of Scheme I would permit any of

Scheme I



the three ring carbons and their attached substituents to be involved in both unaccompanied single rotations (with single index rate constants) and synchronous double rotations (with double index rate constants). Note that rotation of the unlabeled carbon C_3 results in no observable reaction and that, in the double rotation mechanism, Scheme I does not distinguish conrotation from disrotation.

The rate constant indices show which carbons are involved in each transformation. For example, the conversion of the trans compound M, at the upper left of the scheme, to the cis isomer P (upper right) can occur by a single rotation of C_2, with rate constant k_2, or by a synchronous rotation (con or dis) of C_2 and C_3, with rate constant k_{23}. In general, the reverse reaction will have different rate constants (k_2' and k_{23}' in Scheme I). Similarly, interconversion of M with Q, the enantiomer of P, can occur by single rotation of C_1 or double rotation of C_1 and C_3 (rate constants k_1 and k_{13} in the forward direction, k_1' and k_{13}' in the reverse). Direct interconversion of M with its own enantiomer N can only occur by double rotation of C_1 and C_2. The rate constant is k_{12} in both directions because the equilibrium constant is unity. Likewise, interconversion of cis enantiomers P and Q has one rate constant k_{12}', which, however, is different from the rate constant k_{12} for the trans pair. Finally, reaction N $\rightleftharpoons$ Q has the same set of rate constants as M $\rightleftharpoons$ P.

For a single rotation mechanism in, for example, a C_1–C_2 ring-opened or ring-loosened species, to appear as exclusively double rotation would require ring closure only after even numbers of successive alternate single rotations, which certainly seems implausible. Conceptually, therefore, the distinction between single and double rotation mechanisms is valid. However, the two cannot be distinguished by simple evaluation of the ten rate constants of Scheme I since only six independent quantities are measurable (Table I).

Historically, the most common strategy for circumventing this obstacle has depended upon the assumption that only C_1 and C_2 participated in the stereomutation, that is, that ring cleavage involved only the most substituted bond. The justification for this has been the bond-weakening effect of substituents, which especially in the case of conjugating groups, could be as large as 10–12 kcal/mol for each group.[9b-d] As Table I shows, this assumption reduces the number of mechanistic rate constants to six when X $\neq$ Y and to three when X = Y.

The assumption may turn out to be valid, but two points should be kept in mind. First, there is no case in which it has been tested experimentally. Second, it contains a subtle logical circularity, because it uses a bond dissociation energy as a model of the activation energy for the cyclopropane stereomutation. The bond dissociation energy refers to

Table I. Independent Mechanistic and Phenomenological Rate Constants for the Native System and Special Cases of Scheme I

	Native system		Only C_1–C_2		Unrestricted	
	X ≠ Y	X = Y	X ≠ Y	X = Y	Y = D	X = Y = D
			Mechanistic, Single			
	k_1	k_1	k_1	k_1	k_1	k_1
	k_1'	k_1'	k_1'	k_1'	k_1	k_1
	k_2	k_1	k_2	k_1	k_2	k_1
	k_2'	k_1'	k_2'	k_1'	k_2	k_1
			Mechanistic, Double			
	k_{12}	k_{12}	k_{12}	k_{12}	k_{12}	k_{12}
	k_{12}'	0	k_{12}'	0	k_{12}	k_{12}
	k_{13}	k_{13}	0	0	$k_{12}k_H/k_D$	$k_{12}k_H/k_D$
	k_{13}'	k_{13}'	0	0	$k_{12}k_H/k_D$	$k_{12}k_H/k_D$
	k_{23}	k_{13}	0	0	k_{23}	$k_{12}k_H/k_D$
	k_{23}'	k_{13}'	0	0	k_{23}	$k_{12}k_H/k_D$
Total:	10	5	6	3	$4 + k_H/k_D$	$2 + k_H/k_D$
			Phenomenological			
Total:	6	3	6	3	3	2

cleavage into two noninteracting radicals, and adoption of the assumption regarding substituent effects amounts to a prejudgment that the mechanism of the stereomutation involves a similar cleavage.

At the disubstituted cyclopropane level, other devices are needed if the assumption is to be by-passed. Isotopic substituents provide a means for this. For example, the system in which there is one true substituent (X) and one isotopic one (Y = D), because of its high symmetry, has only five independent mechanistic rate constants when all three ring bonds are allowed to participate in stereomutation. The closest possible approach to the parent cyclopropane itself is the 1,2-dideuterio compound (X = Y = D), where symmetry reduces the number of rate constants to three (Table I) for the unrestricted case. Obviously, the rigor with which the results could be interpreted would tend to increase as the systems chosen for examination approached the right side of Table I. As will become clear, however, experimental difficulties also increase in that direction.

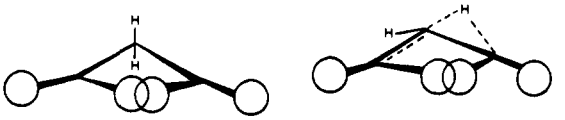
Scheme I shows that, under the substituent effect assumption, in which only C_1 and/or C_2 participate in stereomutation, the double rotation mechanism would permit interconversion of chiral trans reactant with its enantiomer (M $\rightleftharpoons$ N) or of a chiral cis reactant with its enantiomer (P $\rightleftharpoons$ Q) but would preclude trans $\rightleftharpoons$ cis interconversion. Similarly, enantiomerization also could occur in the single rotation mechanism, but only by two sequential trans $\rightleftharpoons$ cis interconversions, e.g., M $\rightarrow$ P $\rightarrow$ N because, in this mechanism, the rate constants for direct enantiomerization (k_{12} and k_{12}') would be zero. The prediction thus would be that, if the double rotation mechanism were dominant, the rate constant for racemization should far exceed that for trans $\rightleftharpoons$ cis interconversion.

Several previous experiments have been carried out under the assumption of exclusive C_1–C_2 participation in attempts to detect this behavior. Pyrolyses of optically active *trans*-1,2-diphenylcyclopropane,[25] *cis*- and *trans*-1-methyl-2-ethylcyclopropane,[12,26] *cis*- and *trans*-1-cyano-2-isopropenylcyclopropane,[27] *cis*- and *trans*-1,2-diphenyl-1-carbomethoxycyclopropane,[28] and *trans*-1,2-dimethyl-1,2-bis(trideuteriomethyl)cyclopropane[29] each occurred with a trans $\rightleftharpoons$ cis interconversion rate that was at least competitive with and in some cases larger than the rate of racemization. The results usually were interpreted with a mechanism in which a biradical could undergo internal rotations at rates dependent on the nature of the substituent. We defer further discussion of this mechanism but emphasize here that none of

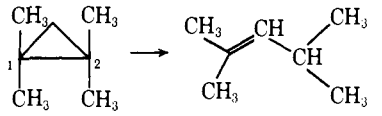
the experiments were considered to provide support for any substantial contribution from a double methylene rotation process.

An experiment of a slightly different type led to a similar conclusion. The pyrolysis of *cis*-1,2-dideuterio-*trans*-3-vinylcyclopropane gave *trans*-2,3-dideuterio-1-vinylcyclopropane at a rate twice the rate of formation of *cis*-2-3-dideuterio-*cis*-1-vinylcyclopropane.[30] The achiral starting material precluded a study of the enantiomerization kinetics outlined in Scheme I, but the apparently statistical product distribution was consistent with the formation of a biradical intermediate in which bond rotation was much faster than recyclization. Again, the synchronous double rotation seemed not to be a major factor.

It is not obvious that the conclusions drawn from these experiments can be safely applied to cyclopropane itself. For example, in the case of tetramethylcyclopropane, there might well be a severe steric impediment to the double rotation mechanism, because the synchronous motion of both of the fully substituted carbons, C_1 and C_2, would cause two methyl groups to clash at some point along the reaction coordinate.[29] For a given C_1–C_2–C_3 angle, the methyl-methyl repulsion would be most severe in a planar array (circles represent methyl groups), but even nonplanar species could not avoid all of the difficulty.



In fact, there are some indications of a similar steric inhibition in the *structural* isomerization of tetramethylcyclopropane to 2,4-dimethylpent-2-ene, presumably by way of a transition state resembling that shown. This reaction has an activation energy (E_a = 64.4 kcal/mol[31]) 10 kcal/mol higher than that of the stereomutation of the hexadeuterio derivative (E_a = 54.4 kcal/mol[29]), whereas the corresponding ΔE_a between structural isomerization and stereomutation of the parent dideuteriocyclopropane is only 0.8 kcal/mol.[5b,d,8] One explanation of the discrepancy could be that, in the tetramethyl case, the hydrogen-shift transition state necessarily would embody a methyl-methyl clash. The developing double bond and the stereoelectronic requirements for reception of the hydrogen at the migration terminus each would force a methyl group to the inside, which might substantially raise the energy relative to that of the reactant ground state. The geometry of this transition state would be very similar to that of the 0,0 intermediate in a hypothetical double rotation mechanism for stereomutation, and consequently the E_a for the double rotation would be raised also. It is therefore possible that the major stereomutation process for tetramethylcyclopropane by-passes the planar array in favor of a completely different mechanism, for example, a double rotation of the unsubstituted carbon C_3 with C_1 or C_2. This would be indistinguishable from predominant single rotation of C_1 or C_2 and therefore in agreement with the experimental results.[29] Although there is no independent support at present for this mechanism, it illustrates the potential pitfalls of extrapolation from the substituted cases to cyclopropane itself.



Newer Theoretical Calculations. Hoffmann's extended Hückel calculation[21] was followed by several more elaborate studies. Buenker and Peyerimhoff[32] showed by self-consistent field molecular orbital (SCF-MO) calculations that the inclusion of configurational interaction substantially lowered the energy cost for opening cyclopropane to the 90,90 trimethylene, but the significance of this finding for the pyrolysis itself was unclear since pathways to other trimethylene geometries were not investigated. However, SCF-MO calculations by Hayes and co-workers[33] showed the 0,0 trimethylene to be favored with respect to the 0,90 form by 2.5 kcal/mol, in qualitative agreement with the extended Hückel calculation.

Ab initio calculations of the full 21-dimensional hypersurface for the cyclopropane stereomutation have been carried out by Salem et al.[34] The *single rotation pathway* was described as a complex collaborative series of "wavings" of C_1 and C_3, with the transition state energy being lowered substantially when the rotating methylene groups were allowed to relax from a planar trigonal to a pyramidal configuration. This transition state and the paths to and from it were discussed at some length, but the calculation clearly showed the transition state for the *double rotation* to be 0.6 kcal/mol lower in energy.[34]

Similarly, generalized valence bond calculations by Goddard and co-workers[35] again showed a slight preference (0.4 kcal/mol) for double rotation when the methylene groups were considered to be planar (0,0 configuration). The Goddard calculation also recognized the importance of hybridization effects, but since a complete surface was not explored, one could not deduce whether the calculated preference for double over single rotation might be reversed by pyramidalization. Therefore, the Goddard prediction must be said to have favored double rotation somewhat less definitely than that of Salem.

All of the more elaborate calculations predicted a weaker preference for double methylene rotation than the 6–10 kcal/mol gap between 0,0 and 0,90 trimethylenes suggested by the extended Hückel calculation. With such small differences, it was difficult to make a clear-cut prediction of the mechanism. However, it seems to us significant that all of the calculations persisted in the prediction that the 0,0 species was a low-energy form of trimethylene and hence should be near if not upon the most favored pathway. This prediction, made in the face of the apparently strong countervailing experimental evidence[36] from studies of the substituted compounds, suggested at least a remarkable consistency of several independent quantum mechanical approaches. Clearly, an unperturbed test of the theoretical calculations was desirable, and the closest possible approach to this required a study of the pyrolysis of the parent compound, optically active *trans*-cyclopropane-*1,2-d*$_2$. The present paper describes this experiment and also the related case of 1-phenylcyclopropane-*2-d*.

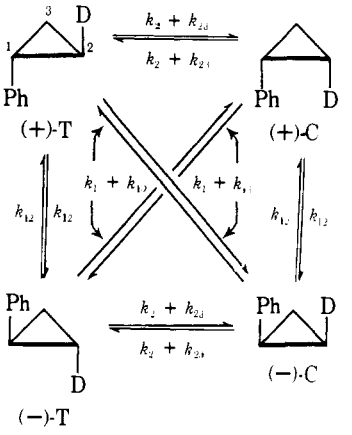
Synthesis and Pyrolysis of Optically Active *trans*- and *cis*-1-Phenylcyclopropane-*2-d*. Scheme I and Table I show that, when one of the substituents of a disubstituted cyclopropane is deuterium, all of the primed rate constants of Scheme I become essentially equal to their unprimed counterparts. This simplification is expected because the trans/cis equilibrium constant should be very close to unity and in fact is observed to be so within experimental error (see below).

The molecular symmetry causes a further simplification in that the rate constant for the double rotation of C_1 and C_2 must be the same as that for the double rotation of C_1 and C_3, modified only by the secondary kinetic isotope effect. Therefore,

$$k_{13} = k_{12}z \qquad (1)$$

where z is the secondary kinetic isotope effect (k_H/k_D). The complete kinetic array is set out in Scheme II.

Scheme II

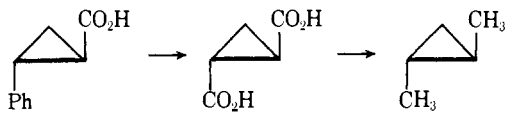


Scheme II contains five-independent mechanistic rate constants, but eq 1 would permit the number to be reduced to four if the kinetic isotope effect were known or could be assigned. As will be seen, this assignment can be made with some confidence, but, even so the system remains underdetermined because only three independent phenomenological rate constants (for the reactions (+)-T → (−)-T, (+)-T → (+)-C, and (+)-T → (−)-C) are available (Table I).

It is tempting to simplify the kinetics further by the usual assumption that the unsubstituted bond (C_2–C_3) is not involved, that is, that $k_{23} = 0$. The C_1 phenyl group should be very effective in weakening the other two ring bonds (C_1–C_2 and C_1–C_3), and the assumption should be at least as justifiable here as in many of the previous systems. However, we prefer to avoid this expedient entirely and to aim, for the present, at a partial but unclouded kinetic characterization of the system.

One such partial solution in the unrestricted, assumption-free system involves a determination of k_1, the rate constant for the single rotation of the phenyl-bearing carbon. If the single methylene rotation mechanism dominates, $k_1 \gg k_{12}$. If the double methylene rotation mechanism dominates, $k_{12} \gg k_1$.

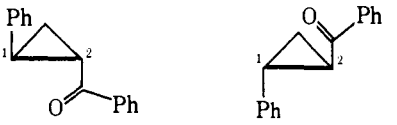
Synthesis of Optically Active *cis*- and *trans*-2-Deuterio-1-phenylcyclopropane. The starting material for the synthesis of optically active *trans*-1-phenylcyclopropane-*2-d* is *trans*-2-phenylcyclopropanecarboxylic acid (**8**). Inouye, Sugita, and Walborsky[37] had resolved this acid via the quinine salt, obtained material of constant rotation, $[\alpha]_D$ +381° (chloroform), and assigned the absolute configuration by conversion of the (−) isomer to (−)-*trans*-1,2-dimethylcyclopropane (**9**), the configuration of which had been established by Doering and Kirmse.[38]



(1*R*:2*R*)-(−)-**8** (1*R*:2*R*)-(−) (1R:2R)-(−)-**9**

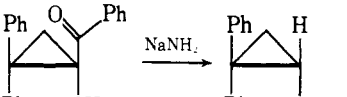
After resolution by a modification (see Experimental Section) of the Walborsky procedures, 2 kg of racemic **8** give 400 g of (+)-**8**, $[\alpha]$+354.6°, and 80 g of (−)-**8**, $[\alpha]_D$ −322.9°, corresponding to materials of 93 and 85% enantiomeric purity, respectively.

The (+) and (−) acids each react with phenyllithium to give (+)- and (−)-*trans*-1-phenyl-2-benzoylcyclopropane (**10**) in high yield. The optical rotations of these ketones, $[\alpha]_D$ +371.4 and −352.8°, have a ratio within experimental error of that of the acid precursors.



(+)-**10** (−)-**10**

The key step in the synthesis of 1-phenylcyclopropane-*2-d* is a stereospecific Haller–Bauer cleavage of ketone **10**, a reaction for which there is at least formal precedent. Impastato and Walborsky[39] showed that sodium amide in benzene cleaved (−)-2,2-diphenyl-1-methyl-1-benzoylcyclopropane (**11**) to (+)-2,2-diphenyl-1-methylcyclopropane (**12**) with complete retention of enantiomeric purity.



11 **12**

There is, of course, a major hazard in attempting to apply this reaction to the synthesis of 1-phenylcyclopropane-*2-d* from ketone **10** and $NaND_2$. In contrast to **11**, **10** has a hydrogen at C_2 adjacent to the carbonyl group, and the configurational integrity of that site therefore is questionable. Achievement of a stereospecific substitution of deuterium for PhCO by the Haller–Bauer reaction would depend on the relative rates of cleavage and epimerization. Moreover, if the $NaND_2$ were to deprotonate **10** before cleavage, the resulting cyclopropyl anion might react with the NHD_2 formed to give **10**-*2-d*, which upon Haller–Bauer cleavage could give 1-phenylcyclopropane-*2,2-d*$_2$. The dideuterated material no longer would have a chiral center at C_2 and would not be a suitable substrate for the proposed kinetic experiment based on Scheme II.

In fact, however, the reactions of (+)-**10** and (−)-**10** with $NaND_2$ in benzene at 80° give the trans monodeuterated hydrocarbons (**13**) with high epimeric stereospecificity. Ke-

(−)-**13** (+)-**13**

tone (+)-**10** gives (−)-*trans*-1-phenylcyclopropane-*2-d* (**13**) in 56% yield, α^{365} −1.112° (neat, 1 dm); (−)-**10** gives (+)-**13** in 56% yield, α^{365} +1.053° (neat, 1 dm). The ratio of optical rotations of the hydrocarbon samples is the same as that of the ketone precursors.[41]

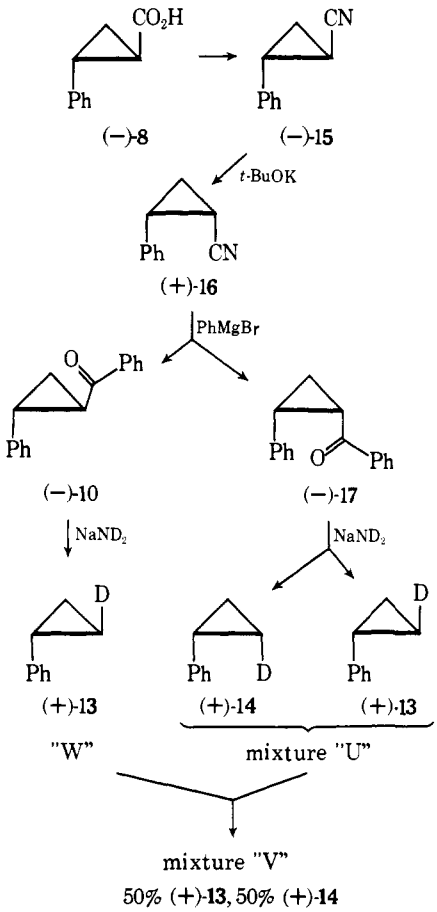
The kinetic analysis of Scheme II to be described requires a study of the pyrolysis of an equilibrium (50:50) mixture of *trans*- and *cis*-1-phenylcyclopropane-*2-d* in which the isomers are optically active and of identical initial enantiomeric purity. The preparation of this mixture "V" is outlined in Scheme III.

The Experimental Section describes the completion of Scheme III and the preparation of the final equilibrium composition mixture "V" by combination of an appropriate quantity of sample "W" (1.1% cis and 98.9% trans in the d_1 component) and sample "U" (56.2% cis and 43.8% trans).

Kinetic Analysis of Scheme II. Scheme II is a special case of Scheme I, where Y = D. Although as Table I shows, the number of independently measurable rate constants is insufficient to permit a complete analysis, some decisive information can be extracted.

In the stereomutation of optically active 1-phenylcyclopropane-*2-d*, the two observables are the loss of activity and the approach to a cis/trans (C/T) equilibrium mixture. For the isomerization of a predominantly trans reactant sample

Scheme III



to the equilibrium mixture, the differential rate law is

$$-dT/dt = (k_2 + k_{23} + k_1 + k_{13})(T - C) \quad (2)$$

where T and C represent concentrations. From eq 2 and the equilibrium constant, $K_{eq} = 1.00 = C_{eq}/T_{eq}$, the integrated rate expression (eq 3)

$$k_i = -\frac{1}{t}\ln\frac{(T-C)}{(T_0 - C_0)} = 2(k_2 + k_{23} + k_1 + k_{13}) \quad (3)$$

can be derived (Appendix). The trans-cis stereomutation thus is a first-order reaction with a phenomenological rate coefficient, k_i, that can be expressed as a sum of mechanistic rate constants.

The loss of optical rotation of a mixture containing an initial predominance of (+)-T reactant can be expressed (Appendix) as in eq 4

$$-d\alpha_{obsd}/dt = \alpha_t^{max}(k_a\Delta T + k_b\Delta C) + \alpha_c^{max}(k_a\Delta C + k_b\Delta T) \quad (4)$$

where α_{obsd} is the rotation of the total sample, α_t^{max} and α_c^{max} are the rotations of the enantiomerically pure trans and cis isomers, $k_a = k_2 + k_{23} + 2k_{12} + k_1 + k_{13}$, $k_b = k_1 + k_{13} - k_2 - k_{23}$, and ΔT and ΔC are the differences in concentrations of the (+) and (−) enantiomers of T and C.

Equation 4 in general does not correspond to a first-order reaction. However, in the special case where the rotations of enantiomerically pure *trans*- and *cis*-1-phenylcyclopropane-*2-d* are identical ($\alpha_t^{max} = \alpha_c^{max}$), eq 4 becomes

$$-d\alpha_{obsd}/dt = \alpha^{max}(k_a + k_b)(\Delta T + \Delta C) \quad (5)$$

Since $\alpha_{obsd} = \alpha^{max}\Delta T + \alpha^{max}\Delta C$ in this hypothetical case, eq 5 becomes a simple first-order rate law with the rate coefficient $k_\alpha = k_a + k_b = 2(k_1 + k_{12} + k_{13}) = (1/t)\ln(\alpha_0/\alpha)$. It is already known that α_t^{max} and α_c^{max} differ by a small but significant amount since results of the Haller-Bauer cleavages of ketones **10** and **17** show $\alpha_t^{max}/\alpha_c^{max} = 1.28$ (see Experimental Section). A first-order plot (log (α_0/α) vs. time) of the loss of optical activity of (+)-T therefore should be nonlinear.

However, inspection of eq 4 shows that there is another set of conditions under which the polarimetric reaction becomes first-order, namely when T and C have equal enantiomeric purities which remain equal with time i.e., $\Delta T = \Delta C$. This time independence could be provided by an *equilibrium mixture* of equal parts of T and C at equal enantiomeric purity. Under these conditions, eq 4 becomes

$$-d\alpha_{obsd}/dt = (\alpha_t^{max} + \alpha_c^{max})(k_a + k_b)(\Delta T) \quad (6)$$

The phenomenological first-order rate coefficient is given by

$$k_\alpha^{eq} = k_a + k_b = 2(k_1 + k_{12} + k_{13}) = (1/t)\ln(\alpha_0/\alpha) \quad (7)$$

just as in the previous nonequilibrium special case, where $\alpha_t^{max} = \alpha_c^{max}$. Heating the equilibrium mixture would cause no net trans ⇌ cis isomerization, and the total reaction would consist of a first-order decline of the optical activity to zero, regardless of whether or not $\alpha_t^{max} = \alpha_c^{max}$.

Accordingly, there are three kinetic experiments that are useful in the present system: (1) the first-order trans → cis + trans isomerization, with rate constant k_i (eq 3); (2) the first-order decay, with rate constant k_α^{eq} (eq 7), of optical rotation of the previously described equilibrium mixture "V", in which trans and cis are present in equal amounts and equal enantiomeric purities; (3) the nonfirst-order decay of optical rotation of a nonequilibrium sample, "W", consisting initially of mostly trans isomer.

By simple algebra, eq 1, 3, and 7 may be combined to give eq 8-11.

$$k_{12} = \frac{(k_\alpha^{eq}/2) - k_1}{1 + z}, \text{ where } z = k_H/k_D \quad (8)$$

$$k_{13} = k_{12}z = \frac{z[(k_\alpha^{eq}/2) - k_1]}{1 + z} \quad (9)$$

$$k_2 + k_{23} = \frac{(k_\alpha^{eq}/2) - k_1}{1 + z} - \frac{k_\alpha^{eq} - k_i}{2} \quad (10)$$

$$0 \leq k_1 \leq \frac{(1 + z)k_i - zk_\alpha^{eq}}{2} \quad (11)$$

Equation 11 gives an upper limit for k_1 in terms of the observable rate constants, k_i and k_α^{eq}, and the isotope effect, z. The lower limit of k_1 of course is zero. The remaining rate constants of the system, k_{12}, k_{13}, and the sum $k_2 + k_{23}$, all can be expressed in terms of k_1, the isotope effect (z), and the observable rate constants for the two first-order reactions (experiments 1 and 2). The strategy for the kinetic analysis thus becomes evaluation of the upper limit for k_1 from the first-order data of experiments 1 and 2, eq 11, and assumed values of the isotope effect, followed by empirical matching of the nonfirst-order data of experiment 3, using eq 8-11 as boundary conditions, with k_1 and z as adjustable parameters.

Experiment 1 (two separate runs) involves gas phase pyrolysis at 309.5° (725 Torr) of samples of (+)- and (−)-*trans*-1-phenylcyclopropane-*2-d* contained in glass ampules. Although slightly higher temperatures lead to complex side reactions,[42] the conditions used in this work permit the stereomutation to proceed with very little degradation. The sample for each kinetic point is purified by vapor chromatography to eliminate even these minor by-products.

The approach of the (+)- and (−)-trans isomers to the

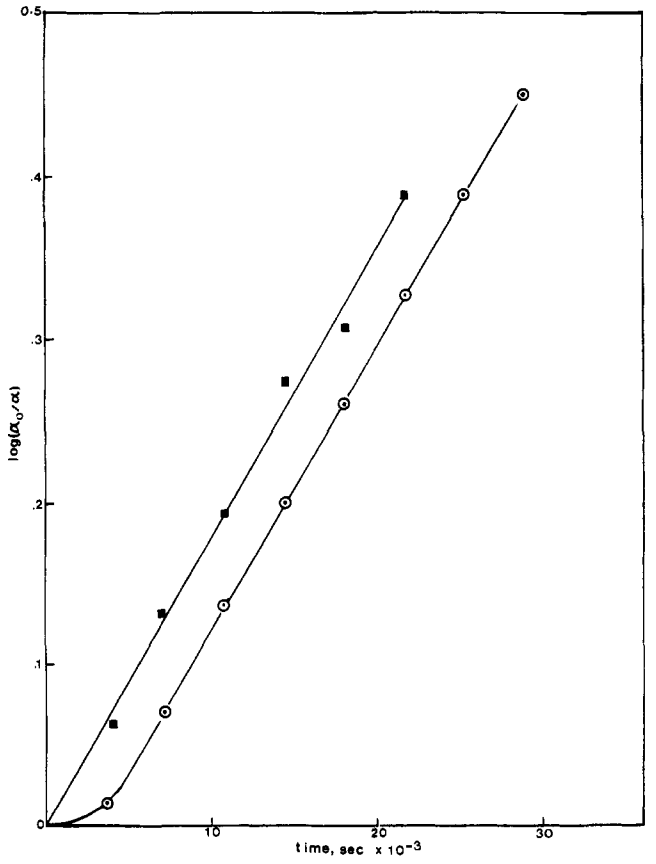


Figure 1. Loss of optical rotation from (−)-*trans*-1-phenylcyclopropane-*2-d* (experiment 3) plotted as a first-order reaction (circles), and from the trans–cis equilibrium mixture "V" (squares, experiment 2).

equilibrium mixture of equal amounts of *cis*- and *trans*-2-phenylcyclopropane-*1-d* is followed by monitoring the 793 cm^{-1} infrared absorption band characteristic of the cis isomer. The spectra of an independently prepared cis–trans mixture of known composition show that this absorption band follows the Beer–Lambert law. The error in the analysis for the cis isomer is estimated to be about 0.5% absolute (i.e., about 1% relative error in mixtures near the equilibrium composition).

The trans → cis + trans stereomutation of 1-phenylcyclopropane-*2-d* is a clean first-order reaction. The rate constant k_i, defined as in eq 3 and observed from the pyrolysis of the (−) and (+) isomers (eight points each during 1.2 half-lives), is, respectively, $(2.49 \pm 0.16) \times 10^{-5}$ and $(2.47 \pm 0.11) \times 10^{-5}$ sec^{-1}.

Experiment 2. The loss of optical rotation of the equilibrium mixture "V" also is a first-order reaction. The rate constant k_α^{eq}, defined as in eq 7 and observed from six points over 1.5 half-lives, is $(4.06 \pm 0.14) \times 10^{-5}$ sec^{-1}.

Experiment 3. The optical rotations of the kinetic samples used for the determination of the trans → cis + trans reaction (experiment 1) are measured. As expected, the polarimetric reaction does not follow first-order kinetics overall, but a plot of the data in first-order form, log α_0/α vs. time (Figure 1, circles), shows that, after about a quarter of the total reaction period examined, the reaction quite accurately approaches first order, with the same rate constant as that, k_α^{eq}, obtained from experiment 2 (see Figure 1). The initial deviation is a consequence of the nonequivalence of α_t^{max} and α_c^{max}. The approach to linearity occurs because mixture "W" contains unequal proportions (1.1% C, 98.9% T) but equal optical purities of the isomers. During the kinetic runs of experiment 3, the proportions of C and T approach the 50:50 equilibrium composition, thereby satisfying a sufficient condition for first-order kinetics. The close correspondence between $k_\alpha^{eq}/2.303$ from experiment 2 and the slope of the linear portion of the experiment 3 plot provides a check on the consistency of the data from the two experiments.

Control Experiments. The rates of trans → cis + trans isomerization and loss of optical rotation are unaffected by the presence of glass wool. Similarly, a decrease in pressure from 725 to 300 Torr has no effect on the value of k_i. The method of VPC purification does not cause any change in the trans–cis composition or optical rotation of samples of 1-phenylcyclopropane-*2-d*. The mass spectrometrically determined isotopic composition of a sample before and after a 28800 sec pyrolysis is unchanged, which excludes the possibility of intermolecular hydrogen exchange reactions.

Mechanistic Rate Constants. Substitution of the experimentally determined values of k_i and k_α^{eq} into eq 11 combined with the assumption (see below) that the isotope effect z has a value $1.00 \leqslant z \leqslant 1.10$ permits an upper limit for k_1 of $(0.37\text{–}0.45) \times 10^{-5}$ sec^{-1}. From eq 7 and the experimental value of k_α^{eq}, we see that the sum of all the rate constants measuring C_1 stereomutation has the value $k_1 + k_{12} + k_{13} = 2.03 \times 10^{-5}$ sec^{-1}. We are thus led immediately to the striking result that k_1, which measures the unaccompanied single rotation of C_1, represents not more than 18–22% of the total C_1 rotation. At least 78–82% of the C_1 stereomutation must occur by the synchronous double rotations measured by k_{12} and k_{13}.

To refine the values of k_1 and the other mechanistic rate constants, the nonfirst-order decline of optical activity (experiment 3) of (−)- and (+)-*trans*-1-phenylcyclopropane-*2-d*, (−)-T and (+)-T, is analyzed by numerical integration of the differential equations (Appendix) leading to eq 4. The actual numerical integrations are carried out by digital computation, using either a Runge–Kutta scheme (program RUNGG)[43] or a program MTRX written by one of us (B.K.C.) which solves the secular determinantal form[44] of the differential equations. In the latter case, the symmetry of the kinetic problem of Scheme II lends itself particularly well to numerical solution because the determinant is symmetric and can be diagonalized easily by the Jacobi method.

An input subroutine for both programs includes eq 8–11, with the experimental values of k_i and k_α^{eq} specified, as boundary conditions. The initial geometric and enantiomeric compositions being known, the choice of the isotope effect, z, and the single rotation rate constant, k_1, then generate a set of concentrations of the four components (−)-T, (+)-T, (−)-C, and (+)-C, and hence of the observed optical rotation, as functions of time. In practice, each programmed search uses a fixed value for the assumed isotope effect and varies k_1 within the limits of eq 11 so as to minimize the root-mean-square (rms) deviation of the computed optical rotations from the observed values.

These "best-fit" values of k_1 derived from either computational procedure are identical to within three significant figures. Table II gives the results for both runs of experiment 3, one starting with (−)-T and the other with (+)-T. The latter data are somewhat less accurate but lead to essentially the same conclusions as the first set. The (−)-T data are particularly smooth and can be fitted with an rms error of 0.00074° in α_{obsd}, which is within the experimental error of each point.

A justification for restricting the isotope effect z to the range 1.00–1.10 will be given later. It is already clear from Table II, however, that values of z larger than about 1.10 lead to negative values of k_1, an absurd result. The overall conclusion from Table II is that k_1 is confined to a small range of values near zero.

Table II. Computer Generated "Best-Fit" Values for k_1 in the Pyrolysis of Optically Active *trans*-1-Phenylcyclopropane-*2-d*

z ($=k_H/k_D$)	Best-fit $k_1 \times 10^5$ sec	
	From (−)-T[a]	From (+)-T[b]
0.90	0.103	
1.00	0.098	0.044
1.10	0.000	−0.005
1.20	−0.095	

[a] Rms error in α_{obsd} 0.00074°. [b] Rms error in α_{obsd} 0.065°.

Some idea of the sensitivity of the numerical integration method for the evaluation of k_1 is given by Figure 2, which shows the computer-generated curves for the optical rotation as a function of time in the pyrolysis of (−)-T. These curves are based upon an assumed isotope effect z of 1.10. The dashed curve is the behavior calculated for $k_1 = 0.395 \times 10^{-5}$ sec^{-1}, which is near the experimentally established upper limit of k_1 and corresponds to a contribution of about 19% of single rotation to the overall stereomutation of C_1, i.e., $k_1/(k_1 + k_{12} + k_{13}) = 0.19$. The solid curve shows the behavior calculated for $k_1 = 0$. The fit to the experimental points is obviously better in the case where $k_1 = 0$.

Since the two computed curves lie nearly parallel, it might be argued that a small change in the determination of the initial trans/cis composition or optical rotation would shift the dashed curve leftward and provide a good fit to the experimental points. However, although it is not apparent from inspection of the curves, the insertion of test initial data differing only slightly from the measured values causes not only a shift of the computed curve but also a marked increase in the rms error.

As will be discussed in the case of dideuteriocyclopropane, there are good grounds for the assumption that the isotope effect should be normal rather than inverse, i.e., that $k_H/k_D \geq 1.00$. If this is correct, the data of (−)-T from Table II suggest that $k_1 \leq 0.098 \times 10^{-5}$ and hence that no more than about 4% of the stereomutation of C_1, the phenyl-substituted carbon, can occur by single rotation. The major pathway is a reaction in which every rotation of CHPh is accompanied by a synchronous rotation of CH_2 (rate constant k_{13}) or CHD (rate constant k_{12}).

A partial analysis of the stereomutation of the deuterium-substituted carbon, C_2, starts with the experimental value $k_i = 2.48 \times 10^{-5}$ sec^{-1}. From eq 3 and the observation that $k_1 = 0$ for an isotope effect $k_H/k_D = 1.10$, we may write $k_i = 2.48 \times 10^{-5}$ sec^{-1} $= 2(k_2 + k_{23} + k_{13})$. Also, since by definition $k_{12} = k_{13}/z$, we find that

$$k_{12} = 1.13 \times 10^{-5}\ \text{sec}^{-1} - (k_2 + k_{23}) \qquad (12)$$

We may evaluate the sum $k_2 + k_{23}$ by insertion of the experimental values of k_α^{eq} and k_i into eq 10, together with the substitutions $k_1 = 0$ and $z = 1.10$. This leads to $k_2 + k_{23} = 0.19 \times 10^{-5}$ sec^{-1}, which when inserted into eq 12 gives $k_{12} = 0.96 \times 10^{-5}$ sec^{-1}.

The total rate constant for all C_2 stereomutation is the sum $k_{12} + k_2 + k_{23} = 1.13 \times 10^{-5}$ sec^{-1}. Thus, k_{12}, the rate constant characterizing that double rotation of C_2 which occurs in synchrony with C_1, is 80% of the total C_2 stereomutation. The remainder of the C_2 stereomutation is made up of k_2 and k_{23} in a ratio that is not determinable from the present experiments.[45] It is already clear, however, that the major reaction at C_2, just as at C_1, is a synchronous double rotation. A summary of the known rate constants of Scheme II based upon an isotope effect $k_H/k_D = 1.10$ is given in Table III.

Synthesis and Stereomutation of Optically Active *trans*-Cyclopropane-*1,2-d*$_2$. The conversion of optically active

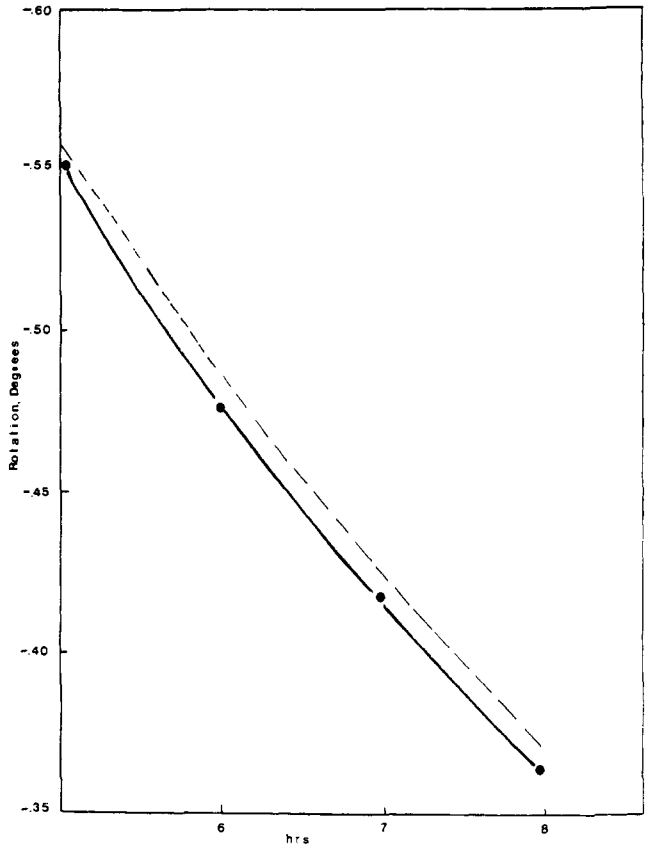
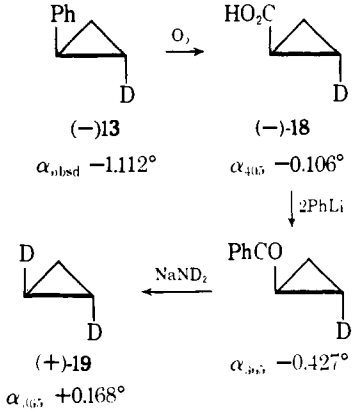


Figure 2. Loss of optical activity in the pyrolysis of (−)-*trans*-1-phenylcyclopropane-*2-d*. Only the later experimental kinetic points are shown (circles). Both curves are calculated using $k_H/k_D = 1.10$. The dashed curve is for $k_1 = 0.395 \times 10^{-5}$ sec^{-1}; the solid one is for $k_1 = 0$.

Table III. Rate Constants of Scheme II Based on $k_H/k_D = 1.10$

Rate constant	Value $\times 10^5$ sec, at 309.5°
k_1	0.00
$k_2 + k_{23}$	.19
k_{13}	1.06
k_{12}	0.96

trans-1-phenylcyclopropane-*2-d* (−)-**13** to *trans*-cyclopropane-*1,2-d*$_2$ (**19**) is carried out as follows. Ozonolysis of (−)-**13**, α_{365} −1.112°, gives (−)-*trans*-cyclopropanecarboxylic acid-*2-d* (**18**), α_{405} −0.106°, in a yield of 33% of isolated product. Another 33% of the starting material (−)-**13** is recovered. Conversion of the acid **18** to (−)-*trans*-



benzoylcyclopropane-*2-d*, α_{365} −0.427°, with phenyllithium proceeds in 71% yield. Haller-Bauer cleavage of two 15-g batches of the ketone with sodium amide-*d*$_2$ gives 1.5

g (17% isolated yield after two vapor chromatographic purifications) of cyclopropane. Mass spectrometry shows this material to consist of 1% d_3, 62.6% d_2, 32.7% d_1, and 3.7% d_0 species. Infrared spectrometry indicates that the d_2 component is 2.3% *cis*-1,2-cyclopropane-d_2 and 97.7% trans.

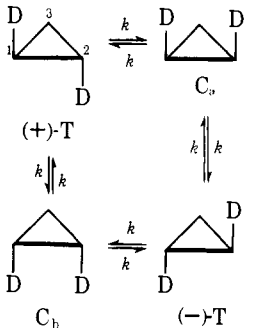
It is not obvious that *trans*-cyclopropane-d_2 should have an observable optical rotation at a convenient wavelength since the basis of the chirality is merely the isotopic substitution. Moreover, it is a nuisance that the substance is a gas (bp −33°) since measurement of the expected low rotation in that state would necessitate the use of an exceptionally long or multiple reflection light path. The latter problem is overcome by the use of a special 1-dm cell designed to permit measurements on the pure liquid[46] (see Experimental Section).

The sample of *trans*-cyclopropane-*1,2-d*$_2$ (**19**) shows α_{365} +0.168°. Since the precursor (−)-**13** contains 87.4% d_1 species, its rotation at 100% isotopic purity would be −1.112/0.874 = −1.28°, which is 88.3% of the rotation (−1.446°) of enantiomerically pure (−)-**13.** The sample of cyclopropane ((+)-**19**) contains 36.4% of achiral material (cis, d_1 and d_0). Thus, pure *trans*-cyclopropane-*1,2-d*$_2$ ((+)-**19**), at 100% enantiomeric, geometric, and isotopic purity, would have α_{365} = +0.168/[(0.883)(0.636)] = +0.298°, with the absolute configuration shown.

Kinetic Analysis. The observable phenomena in the stereomutation of optically active *trans*-cyclopropane-*1,2-d*$_2$ are the approach to the trans-cis equilibrium composition (50:50),[47] with rate constant k_i, and the loss of optical activity, with rate constant k_α. Both of these processes would be first-order for any of the four mechanisms to be considered, but each mechanism predicts a different ratio of k_i/k_α.

Single Methylene Rotation (Scheme IV). For didactic purposes, the cis component of the reaction mixture is divided

Scheme IV. Single Methylene Rotation



into two equal parts, C_a and C_b. Starting from (+)-T, enantiomerization to give (−)-T necessarily would occur by way of C_a or C_b. Since the only way to effect stereomutation by this mechanism would involve single rotation of one of the deuterated carbons (C_1 or C_2), the rate constants for all the steps of the scheme should be identical if there were no secondary kinetic isotope effect. As we already have mentioned, it is true that single rotation could be simulated by a process in which a C_1-C_2, C_1-C_3, or C_2-C_3 bond was broken and in which bond rotation was slow relative to ring closure. There should be an appreciable isotope effect on the competition because the C_1-C_2 bond is dideuterated, whereas the C_1-C_3 and C_2-C_3 bonds are monodeuterated. Also, if the turnover of one methylene group is strongly coupled with motions of another one, as is suggested by a detailed theoretical analysis[34] of the single rotation reaction path, there should be an isotope effect in the competition between turnover of, for example, C_1 coupled with the monodeuterated carbon C_2 vs. C_1 coupled with the undeuterated carbon C_3.

However, the symmetry of the molecule requires that the isotope effects associated with the *number* of deuteriums involved must be present in each interconversion of Scheme IV. That is, the rate constant for each interconversion of Scheme IV could be a weighted average of several rate constants which differ slightly among themselves because of the *number* isotope effect, but the overall rate constant for each step would not differ from that of any other step.

Another imaginable type of isotope effect is the one that depends upon a difference in *stereochemical configuration* of the deuteriums, rather than on the number of deuteriums attached to the breaking bond. This stereochemical isotope effect should be and is quite small, as is demonstrated by the earlier observation,[5b,d] confirmed in the present work, that the cis-trans equilibrium constant in the cyclopropane-*1,2-d*$_2$ system is unity within the experimental accuracy of the infrared spectrophotometric analysis (±1%). We conclude that there should be no significant isotope effect on the k_i/k_α ratio in the single rotation mechanism.

From Scheme IV, we derive by inspection the differential eq 13 (where $C = C_a + C_b = 2C_a$, $T = (+)\text{-}T + (-)\text{-}T$, and T_0 and C_0 are initial concentrations).

$$dC/dt = -dT/dt = 2k(T - C) \qquad (13)$$

But $C = T_0 + C_0 - T$. Substitution for C in eq 13 and integration yield eq 14.

$$-\ln [(T - C)/(T_0 - C_0)] = 4kt \qquad (14)$$

The approach to the equilibrium cis-trans mixture is thus a first-order reaction with a phenomenological rate constant k_i which can be expressed in terms of Scheme IV as $k_i = 4k$.

The loss of optical activity of the total sample during pyrolysis will be caused by formation of propylene, isomerization of trans to (achiral) cis, and enantiomerization of (+)-T to (−)-T. However, since the recovered cyclopropane is carefully separated from propylene by vapor chromatography of the sample at each kinetic point, the diversion to propylene, although of practical consequence because it consumes starting material, does not appear in the kinetic equations. By addition of the differential equation for the formation of cis and twice the equation for the formation of (−)-T, we obtain (after substitution of dC/dt by $-dT/dt$ from eq 13)

$$d[2(-)\text{-}T + C]/dt = -d\Delta T/dt = 2k\Delta T \qquad (15)$$

where ΔT is the difference in concentration of (+)-T and (−)-T. Integrating eq 15, we find

$$-\ln (\Delta T/\Delta T_0) = 2kt \qquad (16)$$

But the observed optical rotation α is given by

$$\alpha = [\alpha]_{max}\Delta T \qquad (17)$$

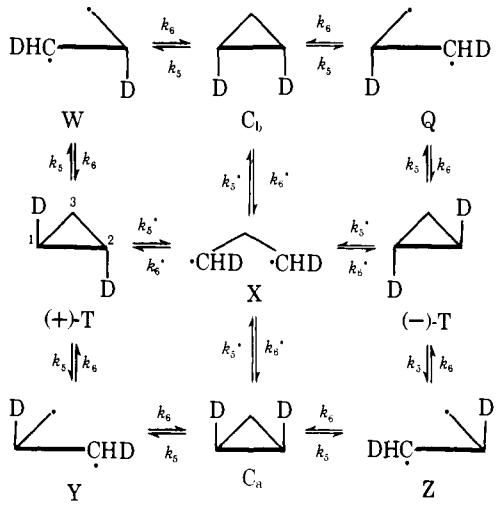
where $[\alpha]_{max}$ is the specific rotation of enantiomerically pure T, and the measurements are carried out on the neat liquid in a 1 dm tube. Substituting eq 17 into eq 16, we obtain

$$-\ln (\alpha/\alpha_0) = 2kt \qquad (18)$$

The loss of optical activity of the total cyclopropane sample is thus a first-order reaction with rate constant k_α which can be expressed in terms of Scheme IV as $k_\alpha = 2k$. The single methylene rotation mechanism thus predicts $k_i/k_\alpha = 4k/2k = 2$.

Random Intermediate Mechanism (Scheme V). From (+)-T, formation of products C ($\equiv C_a + C_b$) or (−)-T requires opening of the cyclopropane ring between two deu-

Scheme V. Random Intermediate Mechanism



terated carbons (C_1 and C_2) or between a deuterated and an undeuterated carbon (C_1 and C_3 or C_2 and C_3), followed by ring closure of the same two carbons. Both the cleavage and closure reactions should be subject to a secondary kinetic isotope effect. Before discussing how large this effect should be, we derive the phenomenological ratio k_i/k_α in general terms, using k_5' and k_6' to refer to the cleavage and cyclization rate constants involving the dideuterated bond (C_1 and C_2). The corresponding rate constants for the monodeuterated bonds are k_5 and k_6. In the following equations, brackets are omitted, and the terms denoting concentrations of species are in italics. The symmetry of the scheme requires that, at any time, $Y = W$, $C_a = C_b = C/2$, and $Q = Z$.

By inspection

$$dC/dt = 2k_6(W + Q) + 2k_6'X - (2k_5 + k_5') \quad (19)$$

From the steady-state assumption, we find that

$$W + Q = 2k_5(C + T)/4k_6 \quad (20)$$

$$X = k_5'(C + T)/4k_6' \quad (21)$$

Substitution of eq 20 into eq 19 gives

$$dC/dt = [(2k_5 + k_5')/2](T - C) \quad (22)$$

Note that because the terms for $W + Q$ and X in the substituted form of eq 19 respectively have k_6 and k_6' in both the numerator and denominator, these ring-closure rate constants cancel identically from the expression for dC/dt (eq 22). The integrated form of eq 22 is eq 23, from which it is clear that $k_i = 2k_5 + k_5'$.

$$-\ln [(T - C)/(T_0 - C_0)] = (2k_5 + k_5')t \quad (23)$$

The loss of optical activity may be shown similarly to be characterized by eq 24

$$d[2(-)\text{-}T + C]/dt = -d\Delta T/dt = (k_5 + k_5')\Delta T \quad (24)$$

which upon integration gives eq 25

$$-\ln (\Delta T/\Delta T_0) = -\ln (\alpha/\alpha_0) = (k_5 + k_5')t \quad (25)$$

Thus, $k_\alpha = k_5 + k_5'$, and

$$k_i/k_\alpha = (2k_5 + k_5')/k_5 + k_5') \quad (26)$$

Again, the ring-closure rate constants, k_6 and k_6', do not appear in the final expressions.

Equation 26 reduces to $k_i/k_\alpha = 3/2 = 1.50$ if the secondary kinetic isotope effect is negligible. If the isotope effect retards the rate of bond-breaking by about 10% per deuterium (see below), $k_5 = 1.10\ k_5'$, and eq 26 becomes $k_i/k_\alpha = 2.91/1.91 = 1.53$.

Competitive Rotation and Ring Closure (Scheme VI). In a formal sense, both the single methylene rotation and random intermediate mechanisms can be derived as limiting cases of a more general scheme in which a trimethylene biradical is formed (with rate constant k_7), one methylene group rotates (with rate constant k_r) to a new geometry, and the new trimethylene suffers internal rotation of the other terminal methylene (rate constant k_r) in competition with ring closure (rate constant k_c). In Scheme VI, we assume for simplicity that the secondary kinetic isotope effect is negligible so that the rate constants k_7, k_r, and k_c apply everywhere.

Qualitatively, it is obvious from Scheme VI that, when $k_r \gg k_c$, we have the equivalent of the random intermediate and, when $k_r \ll k_c$, we have the single methylene rotation. It is instructive to use this scheme to calculate what values of the rotation vs. ring-closure competition ratio, k_r/k_c, would be necessary to produce the extremes of behavior.

Imagine that reaction is initiated from (+)-T. The scheme is mechanistically symmetrical under reflection in a plane perpendicular to the page and running through (+)-T, E, A, and (−)-T. Consequently, using italic capitals to denote concentrations, we write $B = F$, $M = K$, $N = J$, $O = H$, and $P = G$. Also, $C_a = C_b = C/2$. Also

$$dC/dt = 2k_c(N + B + O) - 3k_1C \quad (27)$$

Solving for the steady-state concentrations of N, B, and O in terms of T and C, and substituting these expressions into eq 27, we obtain

$$dC/dt = -dT/dt = \frac{k_7k_r(12k_r + 4k_c)(T - C)}{(k_c + 2k_r)(k_c + 4k_r)} \quad (28)$$

Substitution of $C = T_0 + C_0 - T$ into eq 28 and integration give

$$k_it = -\ln \frac{(T - C)}{(T_0 - C_0)} = \frac{8k_7k_r(k_c + 3k_r)}{(k_c + 2k_r)(k_c + 4k_r)}t \quad (29)$$

Similarly, we can calculate a first-order rate law for the loss of optical activity.

$$k_\alpha t = -\ln (\alpha/\alpha_0) = \frac{4k_7k_r(k_c^2 + 5k_ck_r + 4k_r^2)}{(k_c + k_r)(k_c + 2k_r)(k_c + 4k_r)}t \quad (30)$$

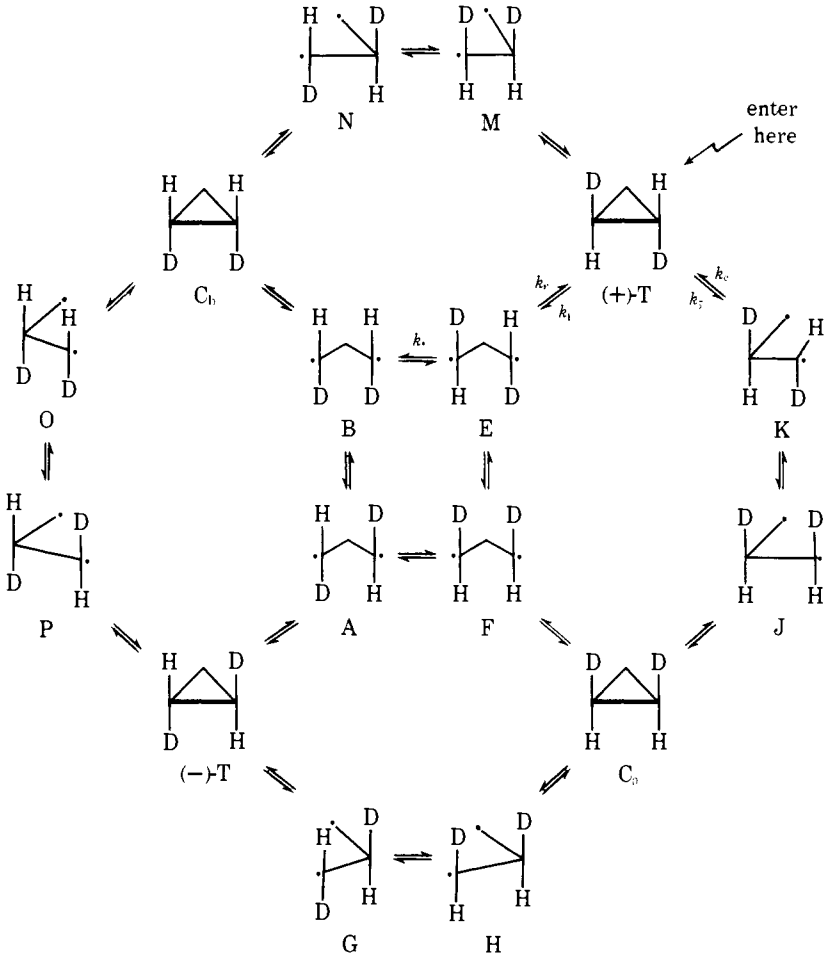
From eq 29 and 30, we obtain

$$k_i/k_\alpha = \frac{2[1 + 4(k_r/k_c) + 3(k_r^2/k_c^2)]}{1 + 5(k_r/k_c) + 4(k_r^2/k_c^2)} \quad (31)$$

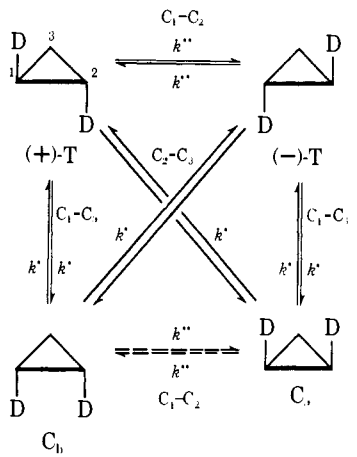
Equation 31 shows that when $k_r/k_c \gg 1$, that is, in the limit of fast internal rotation, k_i/k_α approaches the value $6/4 = 1.5$, the same ratio derived above for the random intermediate mechanism. The k_i/k_α ratio does not rise very much as rotation is slowed down relative to ring closure. Thus, a value of $k_r/k_c = 10$ gives $k_i/k_\alpha = 1.51$, and even $k_r/k_c = 5$ still gives a k_i/k_α ratio of 1.52. Thus, even moderately fast rotations in the biradical intermediate would suffice to give a k_i/k_α value indistinguishable from complete randomization. The approach to the single rotation value of 2.00 for k_i/k_α requires a pronounced retardation of the rotation. For example, $k_r/k_c = 0.1$ substituted into eq 31 gives $k_i/k_\alpha = 1.86$.

Double Methylene Rotation Mechanism (Scheme VII). Isomerization of trans to cis or vice versa occurs by synchronous rotation of C_1 and C_3 or C_2 and C_3. Rotation of C_1 and C_2 interconverts the enantiomers of the trans compound but is without effect on the cis. Reaction at the di-

Scheme VI. Competitive Rotation and Ring Closure



Scheme VII. Double Methylene Rotation



deuterated bond is denoted k'', elsewhere k'.

$$dC/dt = -dT/dt = 2k_1(T - C)$$

As before, $C = T_0 + C_0 - T$. Substitution and integration give

$$-\ln \frac{(T - C)}{(T_0 - C_0)} = 4k't \tag{32}$$

The trans-cis stereomutation is a first-order reaction with rate constant $k_i = 4k'$. Note that because the double rotation at the dideuterated centers is ineffective in this process, the rate constant k'' does not appear in the kinetic expression.

Optical activity declines at a rate given by

$$d[2(-)\text{-}T + C]/dt = -d\Delta T/dt = 2(k'' + k')\Delta T \tag{33}$$

Expression of the integrated form of eq 33 in terms of the optical rotation of the sample (see eq 16-18) gives

$$-\ln (\alpha/\alpha_0) = 2(k'' + k')t \tag{34}$$

so that the phenomenological rate constant $k_\alpha = 2(k'' + k')$. Thus, for the double methylene rotation mechanism

$$k_i/k_\alpha = 4k'/2(k'' + k') = 2/(1 + (k''/k'))$$

If the isotope effect is negligible, $k'' = k'$, and $k_i/k_\alpha = 1.00$. With an isotope effect of 10% per deuterium, $k'' = 0.91\ k'$, and k_i/k_α becomes 1.05.

In principle, it is possible to imagine that there are isotope effects on both the ring-cleavage and ring-closure[49] aspects of Scheme VII. The distinction between k'' and k' in that scheme therefore might be complex and, in fact, it would be possible for the isotope effects on the hypothetical ring-cleavage and ring-closure steps to be different. It can be shown however, that, just as is the case in the random intermediate mechanism (Scheme V), any secondary isotope effect on the ring-closure of a π-cyclopropane would not appear in the kinetic expression for the k_i/k_α ratio and therefore need not be considered here.

Triple Methylene Rotation. In this mechanism, all three methylene groups rotate simultaneously. Enantiomerization of the trans compound can occur, but isomerization of trans to cis, or vice versa, cannot. Therefore, $k_i = 0$, and $k_i/k_\alpha = 0$. There would be no kinetic isotope effect on this ratio.

Table IV summarizes the results of the kinetic analysis of the mechanisms considered. The predicted values of k_i/k_α

Table IV. Predicted Ratios of Rate Constants for Stereomutation of *trans*-Cyclopropane-*1,2-d*$_2$

Mechanism	Kinetic form of k_i/k_α[a]	k_i/k_α if k_H/k_D = 1.00	k_i/k_α if k_H/k_D = 1.10
Single CH_2 rot	2.00	2.00	2.00
Random int	$(2k_s + k_s')/(k_s + k_s')$	1.50	1.53
Double CH_2 rot	$2/(1 + (k''/k'))$	1.00	1.05
Triple CH_2 rot	$0/k_\alpha$	0.00	0.00

[a] k_s and k' refer to reactions at monodeuterated C–C bonds, k_s' and k'' at dideuterated bonds.

for each mechanism are calculated for isotope effects of either 1.00 or 1.10, which should represent the extremes of the range of isotope effects that might operate in this system. The basis for this opinion follows.

The Kinetic Isotope Effect. Both the random intermediate and double methylene rotation mechanisms are subject in principle to a secondary kinetic isotope effect of deuterium. There have been two points of view on how large this isotope effect should be in cyclopropane isomerizations. Al-Sader and Crawford[49] have suggested that k_H/k_D should be negligibly different from unity because little or no change in C–H vibrational force constants should occur in the cyclization of a terminally deuterated trimethylene biradical to cyclopropane. A similar argument could be applied to the reverse reaction. These authors considered C–H stretching, bending, and wagging modes in their analysis but did not examine the effect of other fundamental vibrations.

Simons and Rabinovitch also concluded[50] that these C–H modes would make little contribution to an isotope effect. However, they stated that the methylene twisting vibrations of cyclopropane would be converted into two methylene hindered rotor vibrations in a reasonable model of the transition state for stereomutation. This would result in a decrease of about 400 cm^{-1} in the CH_2 twisting vibrational frequency.

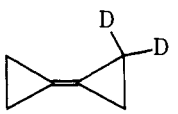
We may substitute this value for $\nu - \nu^\ddagger$ in the Streitwieser approximation[51] (eq 35) of the Biegeleisen equation

$$\ln (k_H/k_D) = (0.187/T)(\nu - \nu^\ddagger) \qquad (35)$$

where T is the absolute temperature and $\nu - \nu^\ddagger$ is the change in frequency of the relevant vibration between the reactant and the transition state. The k_H/k_D value predicted is that for the molecule fully deuterated at the site undergoing the change in frequency. For a hypothetical "stereomutation" of cyclopropane-*1,1-d*$_2$, eq 35 predicts k_H/k_D = 1.11 at 695 K. On the assumption of additivity of the isotope effects, this would correspond to k_H/k_D of about 1.06 per deuterium at 695 K.

The literature contains a number of experimental examples of normal secondary isotope effects ($k_H/k_D > 1$) in pyrolysis reactions in which deuterium is substituted for hydrogen at the carbon–carbon bond undergoing rupture.[52-53] In many of these cases, $k_H/k_D \sim 1.1$ per deuterium.

Perhaps the closest analogy to the case of cyclopropane can be found in the pyrolysis of dideuteriobis(cyclopropylidene) (**20**),[53] where the isotope effect retards the rate of



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rupture of the deuterated ring by a factor of 1.24 at 487 K. Extrapolation to 695 K gives a value of 1.18, which corresponds to k_H/k_D = 1.09 per deuterium.

Since there appear to be no obvious reasons for expecting a substantial *inverse* isotope effect, and since both theoretical arguments[49,51] and experimental precedent[52,53] suggest values between 1.00 and 1.10, we adopt this as the proper range for k_H/k_D per deuterium. It should be clear from Table IV that, if one of the pathways predominates strongly, the assignment of mechanism will not be very sensitive to the exact choice of k_H/k_D within this range.

Pyrolysis of (+)-*trans*-Cyclopropane-*1,2-d*$_2$. The effort and expense incorporated in the precious sample of (+)-*trans*-cyclopropane-*1,2-d*$_2$ provide strong motivation for a choice of pyrolysis conditions for the stereomutation that would minimize the competing structural isomerization to propylene. Since the stereomutation has a slightly lower activation energy than the structural isomerization,[5] the competition would be most favorable to our purpose at the lowest possible temperature. A compromise between conveniently short reaction times and a high preference for stereomutation over structural isomerization is achieved at 422.5 ± 0.5° (695.5 K). The pyrolyses are carried out in a seasoned static reactor at 630 Torr, a pressure that has been shown[5] to be near the high-pressure limit for the stereomutation.

The trans–cis isomerization is monitored at the 846 cm^{-1} infrared spectroscopic absorption maximum, as in the work of Rabinovitch.[5] At the sample pressures used for our analyses, this band obeys the Beer–Lambert law. Empirical calibration using mixtures prepared from the starting material and an equilibrium mixture (already shown[5] to be 50:50) provides an analysis for trans/cis composition that is accurate to better than 1% absolute.

The loss of optical activity is monitored polarimetrically on the same samples used for the infrared analysis. Rotations are easily reproducible to 0.001–0.002° with the Rudolph Model 80 polarimeter equipped with oscillating polarizer using photoelectric observation.

Both the trans–cis isomerization (rate constant k_i) and the loss of activity (rate constant k_α) obey first-order kinetics as measured for six points during 2 half-lives. The trans–cis isomerization rate, duplicated on a separate small sample, agrees well with that obtained from the large polarimetric sample and also with a value interpolated from data of Schlag and Rabinovitch[5b,d] at other temperatures.

The values (± standard deviations) determined for k_i are $(6.70 \pm 0.17) \times 10^{-5}$ sec^{-1} (small check sample) and $(6.75 \pm 0.14) \times 10^{-5}$ sec^{-1} (polarimetric sample). The value for k_α is $(6.33 \pm 0.14) \times 10^{-5}$ sec^{-1}. These give the ratio k_i/k_α = 1.06 with an rms error of 0.04 in the ratio.

The ratio does not depend upon a single determination of k_α, however. Since the polarimetric and infrared analyses for each data point are made on the same sample, each of the six data points provides a valid comparison of k_i and k_α. The average value (± standard deviation) found in this way is $k_i/k_\alpha = 1.07 \pm 0.04$.

The mass spectrum of the pyrolysis mixture after 2 half-lives is identical with that of the starting material. Moreover, the infrared spectrum of the starting material is unchanged by passage through the VPC column used for the separations of the analytical samples. These control experiments show that no intermolecular exchange processes occur during pyrolysis and that no isotopic fractionation or trans–cis isomerization occurs during the VPC isolation.

Rabinovitch and Schlag[5b,d] have shown the insensitivity of the trans–cis isomerization to surface catalysis. The small amount of optically active dideuterio compound available precludes a similar test for the polarimetric reaction, but we assume that no such catalysis is present there since our values for the rate constant for trans–cis isomerization, k_i, and for the rate constant for the structural isomerization

to propylene (separately measured) check quite well with the values reported by these authors.

Formally, the experimental ratio $k_i/k_\alpha = 1.07$ could signify a blend of mechanisms containing a large component of triple methylene rotation (see Table IV). For example, mixtures of about 53% single methylene rotation and 47% triple methylene rotation or 70% random intermediate and 30% triple methylene rotation would produce the observed value. We confess that our present reluctance to embrace the triple methylene rotation process is prejudiced. However, it does seem unlikely that such a reaction, in which there is enough loosening of all three carbon–carbon bonds to permit triple rotation, could compete with processes that preserve two of the three bonds essentially intact. Perhaps future events will provide stronger reasons, either theoretical or experimental, for acceptance or rejection of the triple methylene rotation mechanism.

For the present, a preferable interpretation would ascribe the observed k_i/k_α to a predominance of the double methylene rotation mechanism. The case least favorable to this interpretation would be one in which k_H/k_D is assumed to be 1.00 and in which twice the standard deviation is taken as the experimental error and added to the observed k_i/k_α. The ratio k_i/k_α then could have a value as high as 1.15, which could be interpreted as a mixture of 70% of double methylene rotation and 30% of random intermediate, or 85% double and 15% single methylene rotation. A more favorable case for the double methylene rotation mechanism would be derived by taking the observed k_i/k_α ratio of 1.07 at face value and assuming that $k_H/k_D = 1.10$. These data would be fit by 96 and 98% of double methylene rotation, contaminated by only 4 and 2%, respectively, of random intermediate and single methylene rotation. The uncertainty about the size of the isotope effect precludes a quantitative partitioning of the pathways, but there is no doubt that the double rotation mechanism predominates by a substantial factor.

Discussion

A synchronous double rotation mechanism is prominent in the stereomutations of phenylcyclopropane and cyclopropane itself. Before we proceed to compare the experimental data with theoretical considerations, it would be well to emphasize some of the important questions to which our results *do not* provide answers.

There has been considerable discussion[9,27,33-35] of whether or not the energy surface has a local minimum representing a true intermediate near the stereomutation transition state. We are not aware of any experimental results, including our own, that resolve this issue.

For example, Doering and Sachdev[27] have argued that it is not useful to describe the stereomutations of the 1-cyano-2-isopropenylcyclopropanes in terms of a mechanism in which each enantiomer of trans and each of cis is separately connected to a configurationally related metastable biradical intermediate, and in which stereomutation occurs by sequential single rotational interconversions around a square array of the biradicals. They have proposed instead a scheme in which the "biradical" is to be considered as a transition state and in which no local minima are encountered on the pathway of stereomutation.

However, the experimental data[27] on the 1-cyano-2-isopropenylcyclobutane stereomutations can be accommodated to a square array if one permits direct interconversions of the biradicals diagonally across the square, which would correspond to double methylene rotations. The experiments[27] do not rule out such interconversions, and therefore the question remains open whether there are one or more metastable intermediates on the reaction pathway.

In experiments based on Scheme I, "rotations" refer to stereochemically identifiable acts transforming ground state reactant to ground state product molecules, not to motions in species on the upper reaches of the energy surface. Therefore, such experiments cannot provide direct information on such questions as rehybridization[34,35] or partial rotations ("wavings") of groups[34] that may occur along the reaction path.

Theory suggests[21,34] that the double methylene rotation passes over a saddle point species (0,0 trimethylene or "π-cyclopropane") with C_{2v} symmetry, in which all four of the terminal methylene hydrogens lie in the plane of the three carbon atoms. A consideration of this question helps to sharpen the definition of the word "synchronous", which we use to describe the double rotation mechanism. Our experimental results do not require that a C_{2v} species lie along the reaction coordinate. The rotations of the two methylene groups are "synchronous" in the sense that they are coupled and occur at the same time, but there may be a phase lag between them, which would permit an unsymmetrical configuration at the saddle point of the mechanism.[55]

The theoretical studies[21,34,35] agree that conrotation should be favored over disrotation in the double methylene rotation mechanism. Our experiments cannot distinguish these two subcategories of synchronous rotation. It is tempting to ascribe the apparently conrotatory stereochemical crossover effect in the thermal decomposition of pyrazolines[23,24] to the same cause as the synchronous double methylene rotation we now observe, but we can offer no direct evidence that the reaction pathway for pyrazoline decomposition intersects that for the cyclopropane stereomutation.

As Hoffmann has pointed out,[21] in the ring opening of cyclopropane, a pair of the C_2–H σ bond electrons play an orbital symmetry role analogous to that of a lone pair in the ring openings of cyclopropyl anion and its analogs, oxirane and aziridine. There is strong experimental evidence for conrotation in the latter two systems,[54] but full confirmation of the theoretical analogy awaits the demonstration that the cyclopropane stereomutation also is conrotatory.

Moreover, it is not clear whether the stereomutation and the structural isomerization to propylene share part of a common pathway. The evidence so far permits but does not require the 0,0 trimethylene to be an intermediate for both processes.

Turning to some answerable questions, we may use the calculation of Salem and co-workers[34] as a model against which to compare our own and previous experimental results. The calculated activation energy for the single methylene rotation is 0.6 kcal/mol above that for the double methylene rotation. As we have mentioned, the preferred pathway is qualitatively the same as that predicted by Hoffmann. The theoretical energy surface[34] makes no direct prediction of an activation energy for the process we have called the random intermediate mechanism, since it does not contain a metastable species that could survive long enough to become randomized by internal rotations.

Doering and Sachdev[27] have used the calculated[34] energy difference between the transition states for the single and double methylene rotation of cyclopropane itself to compute a predicted rate difference between these pathways for the stereomutation of the 1-cyano-2-isopropenylcyclopropanes. At their experimental temperature of 217.8° (491 K), they deduced from the activation energy difference of 0.6 kcal/mol (on the assumption that this could be equated to $\Delta\Delta F^{\ddagger}$) a predicted ratio of 35:65 for single vs. double rotation. By an analysis of the observed kinetics in the pyrolyses of the optically active cis and trans isomers, Doering and Sachdev assigned phenomenological rate constants for the dia-

stereomerization of the optically active trans isomer to each of the enantiomers of cis, and of the optically active cis isomer to each of the enantiomers of trans. Similarly, they deduced rate constants for the enantiomerizations of (−) to (+) in both the cis and trans series.

For comparison with the predictions of theory, Doering and Sachdev assumed that bond cleavage occurred only between the substituted carbons, C_1 and C_2. The system may be visualized by reference to Scheme I, with X = CN and Y = isopropenyl, with all the reactions at C_1–C_3 and C_2–C_3 assumed to be absent ($k_{13} = k_{23} = k_{13}' = k_{23}' = 0$). The (−)-trans isomer would be represented by M, the (+)-trans by N, the (+) cis by Q, and the (−)-cis by P. Enantiomerization of M and P would be represented by double rotations with rate constants k_{12} and k_{12}', respectively, whereas diastereomerizations would occur by reactions with the single rotation rate constants k_2 (M → P and N → Q), k_2' (P → M and Q → N), k_1 (M → Q and N → P), and k_1' (Q → M and P → N).

The experimental values ($\times 10^6$ sec) of the six phenomenological rate constants[27] may be expressed in terms of the above assumption as $k_{12} = 8.16$, $k_{12}' = 10.84$, $k_2 = 3.15$, $k_2' = 8.70$, $k_1 = 6.83$, and $k_1' = 18.66$. On this basis, if the total stereomutation of trans isomer M is given by $(k_{12} + k_1 + k_2)$. diastereomerization $(k_1 + k_2)$ may be said[27] to account for 54% and enantiomerization (k_{12}) for 46%. From cis isomer P, diastereomerization $(k_1' + k_2')$ accounts for 72% and enantiomerization (k_{12}') for 28% of the total stereomutation. Doering and Sachdev[27] concluded that these distributions were in excellent agreement with the 35/65 ratio of diastereomerization to enantiomerization predicted by the Salem calculations.[34] Since the predicted order of preference[34] is the reverse of that reported experimentally,[27] the nature of the alleged agreement is not clear.

Moreover, the ratios of *total* diastereomerization to enantiomerization are not really appropriate for comparison with theory. The theoretical calculations[34] mark the relative heights of two transition states, that is, a difference in activation energy between a single methylene rotation and a double methylene rotation. Properly, the ratios of diastereomerization to enantiomerization therefore should be taken pairwise. They are, from trans, $k_1/k_{12} = 46/54$, and $k_2/k_{12} = 28/72$; from cis, $k_1'/k_{12}' = 63/37$, and $k_2'/k_{12}' = 45/55$. It is these numbers that must be used for matching with the theoretical ratio[34] of 35/65 or with qualitative prediction.[21] Clearly, a summation of the diastereomerization rate constants would tend to mask the importance of the double rotation. The proper pairwise comparisons of the Doering–Sachdev experimental data now show in two cases that the double rotation pathway is about as facile as the single rotation, and in the case $k_2/k_{12} = 28/72$, double rotation actually is preferred.

Of course, it is not certain that calculations made for cyclopropane itself[21,34] should apply quantitatively or even qualitatively to substances structurally so different as the cyanoisopropenyl derivatives examined by Doering and Sachdev.[27] Furthermore, the calculated contributions of the double rotation pathway in the cyanoisopropenyl series still depend upon the most substituted bond assumption. Nevertheless, there is now no experimental basis for the conclusion[27] that the study of this series "provides another example of failure to observe the preference predicted by Hoffmann".

For the case of cyclopropane-*1,2-d*$_2$, at our experimental temperature of 695 K, the theoretical activation energy difference,[34] if interpreted as $\Delta\Delta F^{\ddagger}$ (that is, if $\Delta\Delta S^{\ddagger} = 0$), predicts a 69/31 ratio of double to single methylene rotation. This is somewhat below the minimum experimental ratio of 85/15 derived above on the assumptions least favorable to double rotation. It is only in qualitative agreement with the experimental ratio of 98/2 that results from the less extreme assumptions. Since the "resolving power" of the Salem ab initio calculation probably is not very great,[34] one perhaps should not expect quantitative agreement with experiment. Moreover, competition between single and double rotation may depend not only upon the difference in barrier heights, but also upon dynamic effects arising from the nature of the energy surface and the way in which the energized molecules approach and pass over the region of the saddle point.[34,55]

It is not obvious why the double rotation mechanism has not been observed in previous cases. For example, there is a disturbing apparent difference in behavior between vinylcyclopropane, which is reported[30] to stereomutate via a random intermediate, and phenylcyclopropane, which we find adheres to the double rotation mechanism. Conceivably, the reason may be that the various mechanistic pathways are closely balanced, as is suggested by the most recent calculations,[22,33-35] and that substituents perturb the order of preference in some way yet to be elucidated.

Alternatively, it is also conceivable that the assumption of reaction only at the most substituted bond is invalid in some of the previous cases. Substantial contributions by double rotation of a substituted carbon with an unsubstituted one then could be hidden in the kinetic results. Since the activation energies for stereomutation in the substituted cases are lower than in cyclopropane itself, a significant contribution from reaction at the unsubstituted or (monosubstituted) bond in a mono- (or di-) substituted cyclopropane logically would require that the substituent's bond-weakening effect on the remote, unsubstituted bond be about as large as it is on the adjacent, substituted bond. Although such an explanation may seem rather implausible in the absence of any independent precedent, some actual tests would be useful.

Moreover, the emergence of the double rotation pathway in cyclopropane-d_2 raises other questions about the significance of the substituent effect in lowering the activation energy for stereomutation. Suppose, for example, that the most substituted bond assumption should turn out to be incorrect, and the previously studied disubstituted cyclopropanes were shown to use the double rotation mechanism. It would follow that *bond-stretching* models of the transition state, as in the Benson–O'Neal treatment, will have served satisfactorily as predictive tools for the estimation of the effect of substituents on the activation energy of quite a different mechanistic pathway, which involves a large *bond-twisting* component. This result would seem to provide a fruitful basis for theoretical investigation.

On the other hand, should the most substituted bond assumption prove correct, the previously studied examples all would have been shown to employ the single rotation pathway to a substantial or even predominant extent. Then the substituent effect would measure the decrease in activation energy between two different mechanisms, double rotation in cyclopropane-d_2 and single rotation in the disubstituted example. The decrease thus would represent a *minimum value* for the substituent effect on the single rotation mechanism. The actual value would be unknown until the determination of the activation energy for the single rotation pathway in cyclopropane-d_2, a mechanism that so far has eluded detection.

These speculations may suggest future lines of inquiry. For the present, the experimental status of the cyclopropane stereomutation problem permits only the statement that, in cyclopropane and phenylcyclopropane, two cases free of the most substituted bond assumption, the theoretically predicted double rotation mechanism predominates.

Experimental Section

Melting points were obtained using a Thomas-Hoover capillary apparatus and are uncorrected.

Infrared spectra were recorded on a Perkin-Elmer 237B infrared spectrophotometer or a Perkin-Elmer Model 421 infrared spectrophotometer. The positions of diagnostic absorption bands are reported in reciprocal centimeters (cm^{-1}).

NMR spectra were recorded on Jeolco 100 mHz or Varian 60 mHz (Model A60-A) instruments. The solvent for all NMR spectra was chloroform-*d* containing 1% tetramethylsilane (Me_2Si). Chemical shifts are given as parts per million (ppm) downfield from Me_2Si in δ units. NMR data are reported in the order: chemical shift; multiplicity, s = singlet, d = doublet, t = triplet, m = multiplet; number of protons (integrated intensity); coupling constants (in hertz); assignment.

Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6 instrument.

Preparative vapor phase chromatographic (VPC) separations of liquids were performed on Aerograph A-90P instruments using a 10-ft Carbowax 20M on Chromosorb P ⅜-in. column (Column A) unless otherwise specified. All separations involving cyclopropane gas were made on a special chromatograph[56] kindly provided by Dr. K. B. Wiberg, using a 20% squalane on Fluoropak 80 column, as suggested by Dr. B. S. Rabinovitch.[57]

Optical rotations were measured with a Rudolph Research, Inc. Model 80 high precision polarimeter equipped with a Model 200 photometer unit, a Model 340 oscillating polarizer, and a Model 313 tube trough. All observed rotations were read to 0.001°. An estimate of the error is included as a standard deviation for all rotations which were measured on the same sample more than five times. All rotations were corrected by means of a blank rotation using the solvent for the sample or the racemic sample (for liquids measured neat). The volumetric error in the solutions measured is estimated to be 1%.

Most reagent grade chemicals were used without purification unless otherwise specified. Phenyllithium was prepared by the standard method and analyzed by titration with *sec*-butyl alcohol in xylene using 1,10-phenanthroline as indicator.[58] Ethyl diazoacetate was also prepared by the standard procedure.[59]

***trans*-2-Phenylcyclopropanecarboxylic Acid.** The large quantity of *trans*-phenylcyclopropanecarboxylic acid required for the resolution to be described was purchased from Aldrich Chemicals, Inc. Small quantities used in trial reactions were prepared by the method of Burger and Yost[60] and had mp 91-93° (lit.[60] mp 89-92°).

Optical Activation of *trans*-2-Phenylcyclopropanecarboxylic Acid (8). The quinine salt[37] was prepared from 2000 g of **8** and subjected to a systematic fractional crystallization from ethyl acetate. Regeneration of the acid from the salt permitted the course of the resolution to be monitored polarimetrically. Fractions of roughly equal enantiomeric purity were combined at several points in the scheme to conserve material. After about 60% resolution, the acid was regenerated from the quinine salt and converted to the dehydroabietylamine salt, which was further recrystallized from ethyl acetate. Altogether, the resolution required about 4000 g of quinine and 3000 g of dehydroabietylamine. The specific rotations of the most highly resolved samples were $[\alpha]D$ +354.6° (*c* 1.95, $CHCl_3$) and $[\alpha]D$ −322.9° (*c* 2.23, $CHCl_3$), which correspond to 93 and 85% enantiomeric purity, respectively. The salts of the (+) acid were the less soluble and constituted the head fractions. The salts of the (−) acid were recovered from the mother liquors, and the acid itself, after liberation, was purified by distillation at 128-130° (2.5 Torr).

A pilot partial resolution on a smaller scale was carried out as follows. A solution of 100 g of **8** and 200 g of quinine in 2.5 l. of boiling ethyl acetate was allowed to cool to room temperature and stored overnight. The resulting 213 g of quinine salt was recrystallized twice more, dissolved in 1000 ml of dilute hydrochloric acid, and extracted with ether. The combined ether extracts were dried over $MgSO_4$, filtered, and evaporated to dryness to give 32.4 g of acid, $[\alpha]D$ +191.4°.

The partially resolved acid and 57.3 g of dehydroabietylamine[61] were dissolved in 5 l. of boiling ethyl acetate. After storage overnight at room temperature, the crystalline precipitate was filtered and air dried to give 30 g of salt. This material was shaken with 160 ml of 1 *N* NaOH and three 100-ml portions of ether. The aqueous layer was acidified to pH 2 with concentrated hydrochloric acid, and the product was extracted with ether. After having been dried over $MgSO_4$, the extacts were filtered and evaporated to give 9.1 g of *trans*-2-phenylcyclopropanecarboxylic acid, $[\alpha]D$ +367.9° (95% enantiomerically pure).

Concentration of the mother liquors from the first quinine salt formation to half the original volume gave 52 g of solid salt. A further concentration and filtration of the remaining mother liquor gave 41 g of salt. The filtrate was concentrated to dryness to give 26 g of a brown syrup, from which the acid was liberated by dissolution in 80 ml of 1 *N* aqueous NaOH. The aqueous layer was washed with CH_2Cl_2, acidified to pH 2 with concentrated HCl, and extracted with ether. The dried ($MgSO_4$) extract was filtered, and the solvent was evaporated to give 7 g of acid, $[\alpha]D$ −307.6°.

The (−) acid was converted to the dehydroabietylamine salt with 12.7 g of amine in 400 ml of boiling ethyl acetate. The precipitated salt was filtered off, and the mother liquor was concentrated to give 13.5 g of a brown gum. Isolation of the acid from the latter sample of salt gave 4 g of (−)-**8**, $[\alpha]D$ −322.5° (85% optically pure).

(−)- and (+)-*trans*-2-Phenyl-1-benzoylcyclopropane (10). By the method of Walborsky and Plonsker,[62] 8 g of the acid (−)-**13**, $[\alpha]D$ −322.9°, in 50 ml of ether was added during 30 min to a 0.148 *M* solution of PhLi in ether. After an additional 10 min, the reaction mixture was poured into 200 ml of 3 *N* aqueous NH_4Cl, and the ether layer was washed with saturated brine until neutral. After having been dried over $MgSO_4$, the ether solution was evaporated and the residue was chromatographed on alumina to give 9.1 g (82%) of (−)-**10**, mp 73-75°, $[\alpha]D$ −352.8° ($CHCl_3$), 86.7% optically pure. The ir and NMR spectra were identical with those of an independently prepared[62] racemic sample.

Similarly, eight 32.4-g batches of (+) acid **13**, $[\alpha]D$ +354.6°, were converted to 290 g of (+)-**10**, $[\alpha]D$ +371.4° ($CHCl_3$). The ir and NMR spectra were identical with those of the racemic ketone **10**.

The ir spectra of all three samples showed a strong band at 1670 cm^{-1}. The NMR spectra showed the following absorptions: 1.42-1.64 (m, 1 H, ring CH_2); 1.64-2.08 (m, 1 H, ring CH_2); 2.64-2.83 (m, 1 H, PhC*H*); 2.83-3.04 (m, 1 H, PhCOC*H*); 7.24-7.52 (m, 5 H, *Ph*CH); 7.52-7.8 (m, 3 H, meta and para *Ph*CO); 8.04-8.20 (m, 2 H, ortho *Ph*CO).

(−)-*trans*-2-Phenylcyclopropanecarbonitrile (15). The reaction of 65 g (0.4 mol) of (−)-*trans*-2-phenylcyclopropanecarboxylic acid [(−)-**8**, $[\alpha]D$ −322.9°] with 0.76 mol of thionyl chloride gave 71 g (98%) of (−)-*trans*-2-phenylcyclopropanecarboxylic acid chloride, $[\alpha]D$ −310.4°, chloroform, bp 73-76° (0.4 mm), which had ir and NMR spectra identical with those of the racemic acid chloride.[60]

Addition of this material to ice cold concentrated NH_3 and isolation of the product by ether extraction gave 62.5 g of the amide, $[\alpha]D$ −109.5° ($CHCl_3$), which showed ir and NMR spectra identical with those of the racemate.[60] A solution of 62 g of the amide in 120 ml of benzene was treated with 40 ml of thionyl chloride and heated at reflux for 4.5 hr. The reaction mixture was poured into 200 ml of water and neutralized with 50% KOH, and the product was isolated by extraction with benzene. After having been washed with 1% Na_2CO_3 and water and dried over $MgSO_4$, the benzene solution was evaporated to give 49 g (89%) of the nitrile **15**. Recrystallization from petroleum ether gave material of $[\alpha]D$ −322.6° ($CHCl_3$). The ir and NMR spectra were identical with those of the racemic nitrile prepared from the racemic amide in like manner. The racemic nitrile had mp ca. 30° (lit.[63] mp 27-30°).

Epimerization of *trans*-2-Phenylcyclopropanecarbonitrile (15). To a solution of 11.0 g (0.077 mol) of racemic **15** in 150 ml of dry dimethyl sulfoxide under a nitrogen atmosphere was added 0.85 g (0.0076 mol) of potassium *tert*-butoxide in two portions. After having been stirred for 15 min at room temperature, the mixture was treated with 40 ml of cold water. The resultant solution was extracted with pentane (3 × 200 ml). The combined pentane extracts were washed with water (2 × 100 ml), dried with magnesium sulfate, and concentrated to the point at which a precipitate just started to appear. A sample of this pentane solution was analyzed by VPC on column A at 175°. Only two peaks other than the solvent peak were present. These two peaks were at retention times of 40 and 58 min and were in the ratio of 70:30, respectively. Collection of these two peaks and subsequent spectral analysis showed

that the shorter retention time peak was due to the trans nitrile **15** and the longer retention time peak to the cis nitrile **16.**

The pentane solution of this mixture of nitriles was evaporated to dryness. The solid residue was column chromatographed on an alumina column using 10% ether in pentane as the eluent. Fractions 1 (1000 ml), 2 (1500 ml), 3 (275 ml), and 4 (1475 ml) were taken. Fraction 1 was blank, fractions 2 and 4 consisted of essentially pure **15** (6.9 g) and **16** (3.3 g), respectively, and fraction 3 was a mixture of **15** and **16** (0.2 g).

Analysis of the cis isomer **16** by VPC showed no trace of the trans isomer. The NMR of the cis compound also attested to the purity of the compound. The spectral data for the trans compound were the same as for the starting trans nitrile. The spectral data for the cis nitrile were the same as those of the optically active compound described below.

Doubling the reaction time for the epimerization caused no appreciable difference in the cis–trans ratio.

The epimerization of 24 g (0.17 mol) of (−)-**15** yielded, after column chromatography on alumina, 6.2 g of (−)-cis isomer **16,** and 14.0 g of recovered trans isomer, (−)-**15,** ([α]D −321.5°). The cis nitrile ([α]D +20.0°, chloroform) had the following properties: infrared 2245 cm^{-1}; NMR 1.36–1.62 (m, 2 H), 1.64–2.0 (m, 1 H), 2.36–2.66 (complex quartet, 1 H), 7.1–7.4 (m, 5 H); mass spectrum similar to that of the trans nitrile, molecular ion at *m/e* 143.

Preparation of *cis*-2-Phenyl-1-benzoylcyclopropane (17). This ketone was prepared by the method of Mohrbacher and Cromwell.[64] Phenylmagnesium bromide was prepared in a flame-dried reaction flask under nitrogen atmosphere by the addition of 2.6 g (0.0165 mol) of bromobenzene to 0.42 g (0.017 mol) of magnesium turnings in anhydrous ether over a period of 15 min. After this mixture had stirred for an additional 30 min, a solution of 2.0 g (0.014 mol) of *cis*-2-phenylcyclopropanecarbonitrile (**16**) in 10 ml of ether was added over a period of 15 min and allowed to stir an additional 30 min. The reaction was quenched by the addition of 25 ml of 3 *N* ammonium chloride. The ether was then removed by distillation and the residue heated at 95° for 1 hr. The aqueous mixture was extracted with ether (2 × 30 ml). The ether extracts were dried over magnesium sulfate and evaporated to a thick syrup (3.15 g), which was column chromatographed on alumina using 5% ether in petroleum ether as the eluent. Bromobenzene emerged first, followed by a blank fraction (1150 ml), fraction 1 (500 ml) containing 0.51 g of pure trans ketone **10,** fractions 2 and 3 (850 and 400 ml) containing 0.53 and 0.40 g of mixtures of mainly **10** and mainly **17,** respectively, and fraction 4 (1000 ml) containing 0.60 g of pure cis ketone **17.**

Thin-layer chromatography of fraction 4 on alumina and silica plates using 15% ether in petroleum ether showed only one spot, corresponding to the cis isomer **17.** This substance had the following properties: mp 75° (lit.[65] mp of a cis–trans mixture 45.5–50°); ir 1675 cm^{-1} (carbonyl stretch); the trans absorption at 1475 was not present in the spectrum of the cis compound; NMR 1.32–1.64 (m, 1 H), 2.04–2.28 (m, 1 H), 2.72–3.28 (m, 2 H), 7.20–7.42 (m, 5 H), 7.52–7.72 (m, 3 H), 8.0–8.1 (d × d, 2 H); mass spectrum molecular ion at *m/e* 222.

The spectral data for the trans ketone **10** were identical with those of the trans ketone prepared from the addition of phenyllithium to *trans*-2-phenylcyclopropanecarboxylic acid.

Using this procedure (but with a longer chromatographic column, 35 cm as compared with 25 cm), 17.15 g (0.12 mol) of (+)-*cis*-2-phenylcyclopropanecarbonitrile (**16**) ([α]D +20.0°) was converted to 6.9 g (26% yield) of (−)-**17** ([α]D −233.1° (chloroform)) and 5.0 g of (−)-**10** ([α]D −392.1°). Since it is imperative that the optical purity of these two compounds be identical, both were rechromatographed under conditions identical with those of the first separation. The recovered cis and trans ketones had rotations identical with those before the second chromatography.

The spectroscopic properties of these ketones were identical with those of the racemic ketones prepared above.

Preparation of Phenylcyclopropane-d_0 by the Haller–Bauer Reaction.[40] A solution of *trans*-2-phenyl-1-benzoylcyclopropane (8 g, 0.036 mol), 3.5 g (0.085 mol) of sodium amide, and 100 ml of benzene (distilled from calcium hydride) was heated at reflux under nitrogen for 2 hr. After cooling, the reaction was quenched by the cautious addition of water via a syringe, causing the reaction mixture to change from a brown-green color to a light yellow with the concurrent formation of a fluffy precipitate. The reaction mixture was added to 100 ml of water. The organic layer was separated and washed with brine (4 × 50 ml). Concentration of the benzene solution by partial distillation of the solvent resulted in the formation of a precipitate which was then washed with pentane (3 × 50 ml). These washings (containing the small amount of benzene left after concentration) were concentrated by removal of the pentane and benzene by distillation. Distillation of the residue afforded 2.2 g (51% yield) of phenylcyclopropane-d_0 [bp 100° (70 mm)]. The infrared and NMR spectra were identical with those taken on commercially obtained (Chemical Samples, Inc.) phenylcyclopropane. The NMR had the following absorptions (assignments are those reported by Wiberg et al.,[66] based upon the magnitudes of the various coupling constants) for the structure in which H_2 and H_3 represent protons trans and cis to Ph, respectively: 0.60–0.70 (m, 2 H, H_3); 0.70–1.08 (m, 2 H, H_2); 1.72–2.08 (m, 1 H, H_1); 6.76–7.34 (m, 5 H, phenyl protons).

Preparation of *trans*-1-Phenylcyclopropane-2-d_1. *trans*-1-Phenylcyclopropane-2-d_1 was prepared by the method described above for the preparation of the d_0 compound, with the exception that sodium amide-d_2[67] was used in place of the d_0 reagent, and deuterium oxide was used to quench the reaction rather than water. After initial quenching, the reaction mixture was worked up, however, using light water. The crude phenylcyclopropane-d_1 obtained from a bulb-to-bulb distillation was purified by VPC (retention time on column A, 4.9 min at 150°). Phenylcyclopropane was the only reaction product found in the distillate. From 8 g (0.036 mol) of racemic *trans*-2-phenyl-1-benzoylcyclopropane was obtained 2.3 g of *trans*-1-phenylcyclopropane-2-d_1 (53% yield). The product was determined to be the trans isomer by noting that the NMR signal arising from absorption of the protons trans to the phenyl group (i.e., the multiplet between 0.70 and 1.08) had decreased substantially relative to the remainder of the absorptions: NMR 0.60–0.70 (m, 2 H), 0.70–1.08 (m, 1.1 H), 1.72–2.08 (m, 1 H). On this basis, there was approximately 90% deuterium incorporation exclusively in the trans position. The infrared spectrum showed a C–D stretching absorption at 2250 cm^{-1}. The mass spectrum taken at 70 eV gave a molecular ion peak at *m/e* 119. A more detailed description of the infrared and mass spectral data is given below.

Preparation of (−)-*trans*-Phenylcyclopropane-2-d_1 and (+)-*trans*-Phenylcyclopropane-2-d_1 (13). The chiral *trans*-1-phenylcyclopropanes were prepared in precisely the same manner as the phenylcyclopropane-d_1 described above. From 57 g (0.256 mol) of (+)-trans ketone **10,** [α]D +371.4°, and 25 g (0.61 mol) of sodium amide-d_2 (99% isotopically pure) in refluxing benzene for 2 hr, 17 g of distilled (−)-*trans*-1-phenylcyclopropane-2-d_1 was obtained. This procedure was repeated four more times. From a total of 285 g of (+)-**10** was obtained 85 g (56% yield) of (−)-*trans*-1-phenylcyclopropane-2-d_1 (shown to be pure by VPC analysis). A portion (1.5 g) of this material was further purified by VPC on column A at 150° for use in the kinetic studies. It had α_{365} −1.112° (neat, 1 dm).

Similarly, the reaction carried out on 8.0 g (0.036 mol) of (−)-trans ketone **10,** [α]D −352.8°, gave 2.4 g of *trans*-1-phenylcyclopropane-2-d_1 ((+)-**13**), α_{365} +1.053°. Also (+)-**10,** [α]D −392.1°, gave 1.9 g of (+)-**13** (55% yield), [α]D +1.213° (neat, 1 dm). The latter sample was obtained from the sample of **10** which has been shown above to have the same optical purity as its congener, the cis ketone (−)-**17** of [α]D −233.1°. This sample of (+)-**13** is referred to below as "W".

Preparation of Mixtures "U" and "V". By using the procedure described above, the reaction of 6.5 g of (−)-cis ketone **17,** [α]D −233.1°, with 3.0 g of sodium amide-d_2 afforded 0.9 g (26% yield) of a mixture "U" of *cis*- and *trans*-1-phenylcyclopropane-2-d_1, α_{365} +1.114° (neat). By infrared analysis (see below), the composition of the mixture was determined to be 56.2% cis and 43.8% trans. The data for mixtures "W" and "U" may be combined into two simultaneous equations, from which $\alpha_t^{max}/\alpha_c^{max}$ can be calculated to be 1.28. Since the enantiomeric purities of T and C in "W" and "U" are identical, the absolute values of the maximum rotations are not needed, and the ratio suffices for all further purposes of this study.

The 50:50 mixture "V" of (+)-*trans*- and (+)-*cis*-1-phenylcyclopropane-2-d_1 was prepared by combining 0.8914 g of mixture "U" with 0.1130 g of "W". The mixture "V" had an observed rotation α_{365} +1.086°.

Because all of the above phenylcyclopropane-d_1 samples were

Table V. Mass Spectra[b,f] and Infrared Analysis[a] Results

Sample	Mass spectral relative abundances[c] m/e 120	119	118	117	Cis–trans composition[a] of d_1 species % cis	% trans
(−)-10	10.5	100	13.9	0.5	1.1	98.9
(−)-10[d]	10.5	100	14.0	0.5	1.1	98.9
(+)-10	10.4	100	13.8	0.5	1.1	98.9
(+)-10[d]	10.5	100	13.9	0.5	1.1	98.9
(+)-10 ("W")	10.5	100	13.9	0.5	1.1	98.9
Mixture "V"	10.6	100	13.8	0.5	50.0	50.0
Mixture "V"[d,e]	10.5	100	14.0	0.5	50.0	50.0

[a] See below for method of analysis. [b] All relative abundances are ±0.1. [c] Analyses with Hitachi Perkin-Elmer RMU-6 instrument at 15.2 eV. [d] After second VPC purification. [e] After pyrolysis at 309.5° for 28800 sec. [f] The values 87.4% d_1, 12.6% d_0 were computed by the method of K. Biemann, "Mass Spectrometry", and represent the average of the values computed on the alternative assumptions 0 and 100% loss of D in the P − 1 and lower mass peaks.

purified by VPC on column A at 150° and because each kinetic point was likewise purified under these conditions, two samples of optically active **13** and the sample of mixture "V" each were subjected to a second vapor phase chromatography on column A. The mass spectra, infrared spectra (Table V), and observed optical rotation of these compounds were identical before and after this second chromatography. The cis/trans composition of the equilibrium mixture "V" was unchanged after pyrolysis at 309.5° for 28800 sec.

To ensure that the observed rotation was not due to some impurity in the phenylcyclopropanes, a sample of each was analyzed by VPC on each of four ⅛ in. columns listed below (using a Perkin-Elmer Model 900 instrument with nitrogen carrier gas and a flame ionization detector): B, 5-ft 5% Carbowax 20M on 100–100 Anachrom 5D; C, 10-ft 10% Dow-Corning 550 on 80–100 Chromosorb P; D, 10-ft 4% FFAP on 100–120 Anachrom SD; E, 5-ft 5% Apiezon L on 100–120 Chromosorb P. On each of these columns, each of the above listed samples showed only one peak. We conclude that the samples used for the kinetic studies are greater than 99.9% pure phenylcyclopropanes.

All of the 1-phenylcyclopropane-*2*-d_1 samples had NMR peaks at the same chemical shifts, but the integrations were different for the various samples. The samples of (−)-**13**, (+)-**13**, and "W" all showed ratios of 2:1:1:5 for the absorptions at 0.60–0.70, 0.70–1.08, 1.72–2.08, and 6.76–7.34, respectively. Samples "U" and "V" showed respectively ratios of 1.4:1.6:1:5 and 1.5:1.5:1:5.

Preparation of Cyclopropanecarboxylic Acid by Ozonolysis of Phenylcyclopropane. A solution of 1.2 g of phenylcyclopropane (0.01 mol) in 60 ml of methanol was placed in a 100-ml gas dispersion apparatus. A stream of ozone, generated by a Welsbach ozonator, was bubbled through this solution cooled to 0° by an ice bath over a period of 5 hr. The ozonolysis solution was then poured into a solution of 16 ml of hydrogen peroxide in 60 ml of 10% sodium hydroxide. After standing for 12 hr, the reaction mixture was heated at reflux for 30 min. Methanol was removed by distillation. VPC analysis of the first 10 ml of methanol collected showed a substantial amount of phenylcyclopropane present. Subsequent fractions, however, showed only a trace amount of phenylcyclopropane. Preparative VPC afforded 0.39 g of unreacted phenylcyclopropane. The residue from the distillation was acidified to pH 3 with concentrated hydrochloric acid and extracted with ether (7 × 20 ml). The acidic residue left after evaporation of the ether was extracted with pentane (7 × 5 ml). Removal of the pentane by evaporation afforded 0.3 g of a slightly yellow liquid which was shown by NMR to contain 13% formic acid and 87% cyclopropanecarboxylic acid (0.26 g, 46% yield based upon unrecovered phenylcyclopropane). All of the peaks in the NMR could be correlated with peaks of commercially obtained samples of formic acid and cyclopropanecarboxylic acid.

The same technique as described above was used for the ozonolysis of (−)-*trans*-1-phenylcyclopropane-*2*-d_1 [α_{365} −1.112° (neat, 1 dm)]. The only changes in procedure were that 2.5-g (0.021 mol) samples in 60 ml of methanol were used and that batches of three such samples were worked up at a time. All of the methanol solutions containing unreacted phenylcyclopropane were combined and distilled through a Vigreux column. The recovered phenylcyclopropane was then used for further ozonolyses. The final pentane extracts were combined from all of the ozonolyses. The pentane was removed and the cyclopropanecarboxylic acid purified by distillation, bp 100° (30 Torr).

From a total of 80 g of (−)-**13** (32 × 2.5-g samples) and 25 g of recovered (−)-**13** (10 × 2.5-g samples), ozonolysis yielded 26.55 g [33% yield based on 80 g of (−)-**13**] of (−)-*trans*-cyclopropanecarboxylic acid [(−)-**18**; α_{435} −0.106°, α_D +0.055° (neat, 0.5 dm)]. The NMR spectrum for commercial cyclopropanecarboxylic acid showed multiplets at δ 0.70–1.14 (4 H) and 1.40–170 (1 H), and a singlet at 10.0 (1 H). The sample of (−)-**18** showed absorptions in the same regions with intensities 3.1:1:1.

Preparation of Benzoylcyclopropane. This ketone was prepared by the same method as was used in the preparation of *trans*-2-phenyl-1-benzoylcyclopropane. To a solution of 4.3 g (0.05 mol) of cyclopropanecarboxylic acid (commercial) in 75 ml of anhydrous ether was added 100 ml of a 1.14 *M* solution of phenyllithium (0.114 mol) in ether over a period of 45 min. After stirring an additional 15 min, the reaction mixture was poured onto 200 ml of 3 *N* ammonium chloride and agitated. The ether layer was separated, washed with brine (3 × 35 ml), and dried with magnesium sulfate. The ether was removed by rotary evaporation. Benzene and bromobenzene were removed by distillation at 100 Torr. Distillation of the residue afforded 5.21 g (71%) of benzoylcyclopropane: bp 72–74° (0.5 Torr); ir 1680 cm^{-1}, carbonyl stretch; NMR 0.60–0.84 (m, 2 H), 0.84–1.06 (m 2 H), 2.28–2.50 (m, 1 H), 7.0–7.48 (m, 3 H), 7.76–7.92 (m, 2 H); mass spectrum molecular ion at *m/e* 146.

Similarly, 26 g (0.3 mol) of (−)-**18** gave 30 g (71%) of (−)-*trans*-2-deuterio-1-benzoylcyclopropane: α_{365} −0.427° (neat, 0.5 dm); ir 1680 (carbonyl stretch), 2255 (C–D stretch); NMR same as d_0 compound except the 0.60–0.84 absorption had intensity corresponding to 1.15 H rather than 2.0 H; mass spectrum molecular ion at *m/e* 147.

Preparation of Cyclopropanes. All manipulations of sodium amide were made in a drybox under a nitrogen atmosphere. The reaction itself was carried out on a bench top lattice. While being purged with a slow stream of helium, a mixture of 3.0 g (0.0206 mol) of benzoylcyclopropane and 2.0 g (0.0515 mol) of sodium amide in 35 ml of benzene (distilled from calcium hydride) was heated at reflux for 2 hr in a two-necked flask apparatus equipped with a water-cooled condenser. The top of the condenser was connected through a stopcock (1) to a trap (A) cooled with solid CO_2-acetone mixture. Trap A was in turn connected through stopcocks (2 and 3) to trap B, which was also cooled with CO_2-acetone and was connected to a mineral oil bubbler through stopcock 4.

After 2 hr, trap A was found to contain a mixture of a solid and a liquid. After closing stopcock 1, trap A was heated to 0° with an ice water bath. The liquid portion of the contents of trap A distilled into trap B, leaving the solid (benzene) behind. An infrared spectrum of the contents of trap B showed it to contain a mixture of cyclopropane and ammonia. The cyclopropane was purified by distilling the contents of trap B through a column of cotton saturated with water. Thus was obtained approximately 0.2 ml of cyclopropane (0.144 g based upon its density, 0.72 at −79°). The infrared spectrum was identical with that of commercial cyclopropane.

Similarly, by starting with 3 g of benzoylcyclopropane and 2.0 g of sodium amide-d_2, an identical yield of cyclopropane-d_1 was obtained. The infrared and mass spectral data are given in Table VI.

The preparation of (+)-*trans*-cyclopropane-*1,2*-d_2 was carried out on a larger scale but using the same technique as described above. A total of 30 g of (−)-*trans*-2-deuterio-1-benzoylcyclopropane, α_{365} −0.427° (neat, 0.5 dm) was treated in two 15 g (0.103 mol) batches with a total of 50 g of sodium amide-d_2 (2 × 25 g). The cyclopropane obtained from the two batches was combined and vapor chromatographed at room temperature on a column of 25% squalane on Fluoropak 80. Thus we obtained 2.1 ml of pure (+)-cyclopropane-*1,2*-d_2 [(+)-**19** 1.5 g based upon the density 0.72 g/ml at −79°; α_{365} +0.168° (neat 1 dm at 3°, see below for discussion of the polarimetry)]. A second purification made by the above VPC method also served as a control experiment. The cyclopropane was recovered quantitatively and was found to have undergone no cis–trans isomerization or loss of optical activity.

Table VI. Spectroscopic Properties of Cyclopropane Isotopic Relatives

Sample	Mass spectra relative abundances[a] m/e 45	44	43	42	41	40	Infrared absorptions in analytic regions, cm^{-1}
d_0		0.4	4.5	100	26.4	6.2	863, 867, 1023
d_1	<0.1	3.6	100	30.6	12.9	3.0	849, 858, 861, 863 (sh), 1024
d_2, (+)-I9	5.7	100	65.0	26.4	8.2	1.8	846, 849, 858, 861, 1024 1036, 1041
d_2, (+)-19[b]	5.8	100	64.8	26.3	8.4	1.9	

[a] Relative abundances ±0.1. [b] After second purification.

The above column was shown to give a good separation of cyclopropane-d_0 from propene at ambient temperatures (19 to 21°), with retention times of 40 and 25 min, respectively. Table VI shows the mass spectral and infrared data of the above mentioned cyclopropanes.

Kinetic Studies. The heat bath[68] for the pyrolyses of phenylcyclopropane and cyclopropane consisted of an insulated 8-l. stainless steel beaker containing 14 kg of an approximately 1:1:1 (by weight) mixture of sodium and potassium nitrites and sodium nitrate. The salt was heated by two blade-type immersion heaters. The heavy-duty heater (500 W) was controlled by a variable transformer while the 125-W fine-duty heater was controlled by a Bayley Model 124 proportional temperature controller. The bath was agitated with a Lightnin' constant speed stirrer. The temperature was measured by chromel-alumel thermocouples (reference junction at 0°) which had been checked by a determination of the boiling point of benzophenone. The thermocouple output was measured with a Leeds and Northrup Model 8690-mV potentiometer reading to 0.01 mV (0.25°). The temperature gradient in the region of the bath containing the reaction chamber was 0.3–0.4°. Temperature control for the phenylcyclopropane runs was held at 309.5 ± 0.3°; for the cyclopropane runs, it was 422.5 ± 0.3°. The bath temperature dropped about 1° upon introduction of the sample and returned to the original value within 120–150 sec.

Pyrolysis of Phenylcyclopropane. The kinetic studies of the isomerization of the phenylcyclopropanes were made on 120-mg samples in sealed degassed 50-ml Pyrex tubes held vertically at the bottom of the bath with a stainless steel holder. The pressure in these tubes at 309.5° was about 720 Torr. For data points of longer than 1 hr, the pyrolysis tubes were pulled out after each additional hour, allowed to cool for 5 min, and replaced so as to equalize as nearly as possible the fractional errors arising from warm-up and cool-down times. Each pyrolyzed kinetic sample was purified to >99.9% homogeneity by VPC at 150° on column A.

Pyrolysis of cyclopropane was carried out in the apparatus shown in Figure 3. The line was connected to a diffusion-pumped vacuum system held at a pressure of 2×10^{-5} Torr. The total volume of the reaction chamber C up to stopcock 5 was 276 ml. The dead space between stopcock 5 and the level of the molten salt was 2 ml. The volume of the freeze-out section (between stopcocks 3, 4, and 5) was 11 ml. The volume of the reservoir section (between stopcocks 2 and 3 and the mercury level in the manometer) was 229 ml.

The gaseous sample to be pyrolyzed, contained in storage vessel G, was connected to the system by joints m and f, as shown in Figure 3. The system was evacuated and the sample introduced into reservoir E. The reservoir and freeze out sections were isolated from the rest of the system by stopcocks 2, 4, and 5, and the pressure of the sample was recorded. The sample was then isolated in the freeze-out bulb D by cooling with liquid nitrogen. Stopcock 3 was closed, and stopcock 5 was opened. The liquid nitrogen was removed from the freeze-out bulb, and the timer was started. Warming the freeze-out bulb with a beaker of hot water caused an almost instantaneous transfer of most of the sample into the pyrolytic chamber C. Stopcock 5 was closed and stopcock 3 opened. The pressure of any untransferred sample was recorded. This unreacted sample was then returned to its storage vessel G, and stopcock 2 was closed.

After the desired reaction time had elapsed, freeze-out bulb D was cooled with liquid nitrogen, and stopcock 5 was opened. The transfer of the sample to the freeze out bulb was instantaneous and quantitative. Stopcock 5 was closed and the freeze-out bulb and sample were allowed to warm up by removal of the coolant liquid nitrogen. The pressure (P_r) of the sample (in the section between stopcocks 2, 4, and 5) was measured after thermal equilibration for 0.5 hr. This pyrolyzed sample was transferred to a second storage vessel G'.

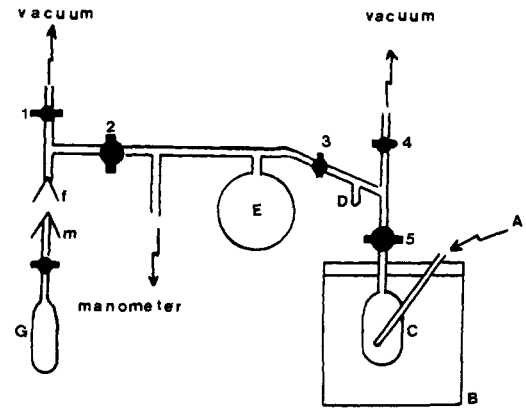

Figure 3. Apparatus for pyrolysis of cyclopropane: (A) thermocouple well; (B) molten salt bath; (C) reaction chamber; (D) freeze-out bulb; (E) 200 ml reservoir; (G) sample storage vessel; (1–4) glass stopcocks; (5) high-vacuum Teflon stopcock; (f and m) female and male standard taper joints.

By knowing the volume of the reservoir section and the freeze-out bulb (V_r), the pressure of the sampie after pyrolysis (P_r), and the laboratory temperature T_r, the number of moles of sample that had been subjected to pyrolysis (n_p) could be determined. Similarly, using the ideal gas law and knowing the number of moles of sample in the reaction chamber, the volume of the reaction chamber (V_p), and the temperature of the pyrolysis (T_p), the pressure of the sample in the pyrolysis chamber (P_p) was determined from the equation

$$P_p = (n_r/n_p)(P_r V_r T_p / T_r V_p)$$

and the fact that the transfer was quantitative ($n_r = n_p$).

Infrared analysis of the cis–trans isomer ratio in the case of phenylcyclopropane was carried out as follows. Equilibrium mixtures of *cis*- and *trans*-1-phenylcyclopropane-*2-d* were prepared by the prolonged pyrolysis (18 hr at 350°) of three samples: (−)-**13**, (+)-**13**, and mixture "U". The phenylcyclopropane recovered by VPC from the pyrolyzed samples was examined as neat liquid with the Perkin-Elmer Model 421 infrared spectrometer and found to be identical. The pyrolyzed sample from (−)-**13** was pyrolyzed a second time for 2 hr at 350°. The phenylcyclopropane recovered again had the same ir spectrum as the previous pyrolysis samples.

An inspection of the differences between the equilibrium mixture's infrared spectrum and that of either of the *trans*-1-phenylcyclopropane-*2-d*$_1$ samples showed that the only absorptions well enough resolved to be useful for the purposes of quantitative analysis were the trans and cis absorption bands at 772 and 793 cm^{-1}, respectively. Assignments of these two bands to the trans and cis isomers were made by noting that the peak at 772 cm^{-1} decreased in intensity with respect to the rest of the spectrum after the pyrolysis and that the peak at 793 cm^{-1}, barely discernible in the spectrum of (−)-**13** and (+)-**13**, was quite prominent in the spectra of the equilibrium mixtures and mixture "U".

The peak at 772 cm^{-1} was positioned on the side of an extremely intense absorption at 763 cm^{-1} and therefore was not suitable as an analytical absorption band. Consequently, we decided to use the 793 cm^{-1} absorption for the analyses of the cis-trans composition of pyrolyzed samples. For the calculation of the relative extinction

coefficient a_{793}, it was assumed that the equilibrium mixture had a 1:1 cis:trans composition in the d_1 component. The d_0 component does not absorb in the analytical region and hence would not affect the kinetic analysis for the geometric isomerization of *trans*-1-phenylcyclopropane-2-d_1.

All of the phenylcyclopropane ir spectra were obtained at 19° using one 0.02-mm NaCl liquid cell. The baseline for the 793 cm^{-1} peak was drawn between the minima on either side of the peak, by the method of Wright.[69] In the following discussion, h is the measured distance between the maximum of the 793 cm^{-1} absorption and the 0% transmittance line (recorder trace at full extinction), and R is the vertical distance between the 0% transmittance line and the intersection of the baseline and the 793 cm^{-1} abscissa.

We found that, when spectra were taken of different samples using the same cell and identical instrument settings, the baseline for the 793 cm^{-1} peak did not shift. This made it possible to obtain very accurate relative peak heights by fixing the spectrometer frequency at 793 cm^{-1} and manually advancing the recorder drum, thereby generating a series of measurements of the peak height without repeated scanning through the entire frequency region. The average peak height obtained by drawing a straight line through the points is free of any error due to variation in the response time of the recorder pen.

The relative optical density a_{793} of the cis isomer was calculated by application of eq 36 to measurements on the equilibrium mixture.

$$a_{793} = -2 \log (h/R) \tag{36}$$

This equation was derived upon the assumption that, at equilibrium, half of the d_1 component of the sample is cis, which is responsible for the 793 cm^{-1} absorption. The term h/R is equal to I/I_0. The values of a_{793} obtained from (−)-**13**, (+)-**13**, and "U" were respectively 0.7726, 0.7695, and 0.7686, for an average of 0.7702 ± 0.0016. Adherence to the Beer-Lambert law was assumed by analogy to the strict adherence observed in the cyclopropane-d_2 case. A check of this assumption was provided (see below) when it was observed that the value of the 793 cm^{-1} transmittance of the equilibrium mixtures prepared by pyrolysis was accurately reproduced in the spectrum of the gravimetrically prepared equilibrium mixture "V".

The fractions of the cis and trans isomers in the phenylcyclopropane-d_1 component, C' and T', were calculated from eq 37 and 38.

$$C' = C/(C_0 + T_0) = [-\log h/R]/a_{793} \tag{37}$$

$$T' = T/(C_0 + T_0) = 1 - C' \tag{38}$$

Analyses of the cis-trans composition of the cyclopropane-d_2 samples also were carried out by ir spectrometry. The samples were contained in a 1-dm gas cell with NaCl windows at pressures which were measured to 0.1 ± 0.1 Torr with a mercury manometer. Although several bands (at 842, 846, 849, 1036, 1041, and 2271 cm^{-1} are present in the spectrum of the cis isomer and absent in the trans, the band at 846 cm^{-1} was the most suitable for analytical work. This band previously had been used by Rabinovitch and co-workers[5] and had been shown by them to obey the Beer-Lambert law under their range of pressures.

The transmittances (h/R) were determined by the same baseline method used in the phenylcyclopropane study already described. The relative extinction coefficient was calculated from eq 39, based upon measurements of the transmittances of samples of the equilibrium mixture.

$$a_{846} = [-2 \log (h/R)]/P_{TOT} \tag{39}$$

where P_{TOT} is the manometric gas pressure in the sample cell.

That the absorption at 846 cm^{-1} obeyed the Beer-Lambert law within 0.5% relative error was established by measurements on the cis-trans equilibrium mixture, prepared by pyrolysis of a small sample of (−)-*trans*-cyclopropane-*1,2*-d_2 at 446° (719 K) (680 Torr) for 12 hr (24 half-lives, based upon the rate constant reported by Rabinovitch[5b]). The sample, purified by VPC, was examined at pressures of 14.6, 26.0, 44.4, and 64.5 Torr. The observed values of a_{846} were 0.02186, 0.02221, 0.02196, and 0.02183, respectively, for an average of 0.02197 ± 0.00013 $Torr^{-1}$.

Since the isotopic composition does not change during a pyrolysis run, the fraction of the total sample that is d_2 does not change.

The accuracy of the analytical method was evaluated by spectrophotometry of known cis-trans mixtures prepared by admixture of appropriate amounts of the cis-trans equilibrium mixture (50:50) and the sample of (+)-*trans*-cyclopropane-*1,2*-d_2, which had been analyzed by ir as 97.7% trans and 2.3% cis. For the calibration, four mixtures were prepared at compositions chosen to correspond to those of four of the kinetic points in the pyrolysis of the (+)-trans compound to be described. The partial pressures of cis and trans (P_C and P_T) in each ir determination were calculated from eq 40 and 41.

$$P_C = [-\log (h/R)]/a_{846} \tag{40}$$

$$P_T = P_{TOT} - P_C \tag{41}$$

The values found spectrometrically were as follows, with the manometrically established calibrating composition in parentheses: 11.40 (11.49), 26.71 (26.59), 36.53 (36.57), 43.69 (43.81). The relative average deviation is ±0.5%.

Polarimetry. The optical rotations of phenylcyclopropane samples were taken at 19.5° on the neat liquid using a Rudolph type 2 cell of 1.6-mm bore, 0.5-dm length, and 0.1-ml capacity. Optical rotations of cyclopropane were measured in a cold room at 3° on the neat liquid using a pressure cell (Figure 4) made by Mr. Ralph Stevens.[46] The cell was a modification of a Rudolph type 14 cell with a 3-mm bore, 1-dm length, and 0.9-ml capacity. Samples were transferred into this cell directly through female joint f of the vacuum line assembly of Figure 3 by cooling the freeze-out reservoir to 77 K and closing the vacuum stopcock. The cell was then transferred to the cold room, tipped so that the sample would fill the observing volume, and allowed to come to thermal equilibrium during about 45 min, whereupon the rotation was measured at 365 nm. All rotations were taken at least ten times per sample. Normally, the observed rotations were reproducible to ±0.001-0.002°.

Rate constants were calculated for the trans-cis isomerizations from eq 37, 38, and 42 (for phenylcyclopropane), and 40, 41, and 43 (for dideuteriocyclopropane).

$$k_i(\text{Ph}) = -\frac{1}{t} \ln \frac{(T - C)}{(T_0 - C_0)} = -\frac{1}{t} \ln \frac{(1 - 2C')}{(1 - 2C_0')} \tag{42}$$

$$k_i(d_2) = -\frac{1}{t} \ln \frac{[(P_T/P_{TOT}) - (P_C/P_{TOT})]}{[(P_{T_0}/P_{TOT_0}) - (P_{C_0}/P_{TOT_0})]} \tag{43}$$

Rate constants for all of the first-order polarimetric reactions were calculated from eq 44

$$k_\alpha = \frac{1}{t} \ln (\alpha_0/\alpha) \tag{44}$$

The kinetic data for the pyrolyses of (−)- and (+)-*trans*-1-phenylcyclopropane-*2-d* (first-order trans-cis isomerization, non-first-order polarimetric reaction) and of the trans/cis equilibrium mixture "V" (first-order polarimetric reaction) are given in Tables VII and VIII. The ir spectrum of the final kinetic point in the pyrolysis of "V" was identical with that of the starting material.

Neither the trans-cis isomerization nor the polarimetric reaction of phenylcyclopropane seemed to be sensitive to surface. Pyrolysis of a 120-mg sample of (−)-**13** for 7200 sec at 309.5° in a tube packed with glass wool and analysis of the cis-trans composition gave a one-point rate constant, $k_i = 2.37 \times 10^{-5}$ sec^{-1}, which was within experimental error of that observed (Table VII) in unpacked tubes. Moreover, the optical rotation of the sample, −0.841°, was in good agreement with the corresponding value, −0.842°, observed for the 7200-sec point (Table VII) in an unpacked tube.

Kinetic measurements on (+)-*trans*-cyclopropane-*1,2*-d_2 were carried out in the reaction chamber already described. The chamber was "seasoned" by the pyrolysis of light cyclopropane for 24 hr at 460°.

Two kinetic runs were carried out. In Run 1, ir and polarimetric data were collected on the sample at each kinetic point after VPC separation of any propene formed. Each data point sample was obtained by combining the pyrolysis product from six equal aliquots. Because of the limited quantity of the reactant available, the cyclopropane recovered from each data point was used as the sample for the subsequent data point pyrolysis. The time shown for each data point, therefore, is the total elapsed time of pyrolysis of the sample up to that point.

Table VII. Kinetics of the Trans–Cis Isomerization of (−)- and (+)-*trans*-1-Phenylcyclopropane-*2-d*$_1$ at 309.5°

Time, sec	Transmittance, *h*/*R* From (−)	From (+)	$k_i \times 10^5$ sec From (−)	From (+)	α_{obsd}, deg From (−)	From (+)
0	0.981	0.979			−1.112	+1.053
3600	0.913	0.912	2.39	2.44	−0.963	0.920
7200	0.840	0.860	2.72	2.27	−0.842	0.801
10800	0.818	0.800	2.17	2.48	−0.731	0.690
14400	0.755	0.749	2.48	2.58	−0.633	0.598
18000	0.718	0.715	2.47	2.52	−0.552	0.522
21600	0.681	0.683	2.52	2.50	−0.477	0.456
25200	0.641	0.669	2.64	2.31	−0.417	0.395
28800	0.625	0.617	2.54	2.62	−0.360	0.345
Mean:			2.49 ± 0.16	2.47 ± 0.12		

Table VIII. Kinetics of the Loss of Optical Activity from the Synthetic Equilibrium Mixture "V"

Time, sec	α_{365}, deg.	$k_\alpha \times 10^5$ sec
0	+1.086	
3600	0.942	3.95
7200	0.806	4.14
10800	0.702	4.04
14400	0.582	4.33
18000	0.544	3.84
21600	0.450	4.08
		Mean: 4.06 ± 0.12

The re-use of the same sample caused a drop in the pressure in the pyrolysis chamber from 670 to 590 Torr during the run since there were some small losses in transfer and in the formation of propene. Propene formation thus amounted to <10% during about 2 half-lives of stereomutation. From an inspection of the "fall-off" curve[5d] of the stereomutation rate constant with declining pressure, it was clear that the pressure drop during the present series of measurements would have affected the rate constant by only 2%, which is within our experimental error.

Run 2 involved the pyrolysis of a small sample of (+)-*trans*-cyclopropane-*1,2-d*$_2$ and observation of the trans-cis isomerization only. The pressure change in this case was from an initial value of 680 Torr to a final one of 580 Torr. The data for runs 1 and 2 are given in Tables IX and X.

None of the rate constants of Tables IX and X were corrected for dead space since the correction cancels in the ratio k_i/k_α.

Pyrolysis of Light Cyclopropane. As a check on the experimental techniques, we studied the structural isomerization of cyclopropane to propene at 460° (630 Torr). The rate of structural isomerization was monitored by ir analysis, using the 1600 cm^{-1} band of propene. After having determined the relative extinction coefficient, the pyrolysis samples were examined in the gas cell at the analytical wavelength. Rate constants were calculated from equation $k_p = (1/t)\{\ln [1 - (P_p/P_{TOT})]\}$, where P_p is the partial pressure of propene. Only three kinetic points were taken, from which the rate constant (5.28 ± 0.28) × 10^{-5} sec^{-1} was obtained. From the temperature dependence of the structural isomerization rate constant[5] in the high pressure limit, the value 5.62 × 10^{-5} sec^{-1} may be calculated. Our value at 630 Torr should be corrected upward by about 10% to bring it to the high pressure limit so that the agreement is excellent.

A comparison of the k_i value at our average pressure of 630 Torr with the high pressure value again would require an increase of about 10%, which would raise k_i from 6.7 to 7.3 × 10^{-5} sec^{-1}. A dead space correction would raise it an additional small amount. The value interpolated to 422.5° from the Arrhenius plot of Rabinovitch and Schlag[5d] is 8.5 × 10^{-5} sec^{-1}.

Since the pressure and temperature interpolations are necessarily somewhat uncertain, and since a 1° error in temperature control or measurement would produce a 7% change in the rate constant, the 14% discrepancy between values obtained in two different apparatuses does not seem significant.

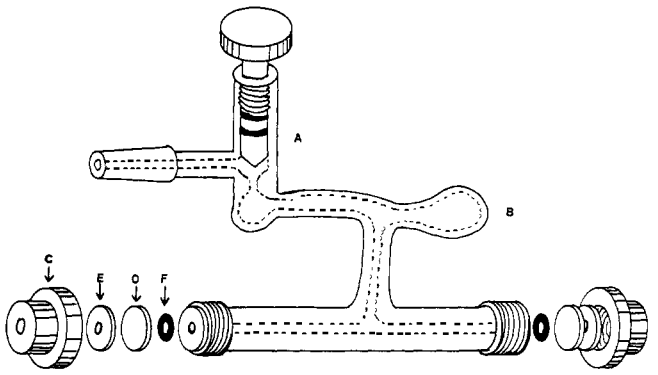

Figure 4. Pressure cell for polarimetry: (A) Teflon high-vacuum stopcock; (B) reservoir; (C) screw cap; (D) silica window; (E) Teflon spacer; (F) Buna N rubber O ring.

Table IX. Kinetics of the Trans–Cis Isomerization and Loss of Optical Activity of (+)-*trans*-Cyclopropane-*1,2-d*$_2$ at 422.5° (Run 1)

Time, sec	P_{TOT},[a] Torr	$(h/R)^b$	$k_1 \times 10^5$ sec	α_{365}, deg	$k_\alpha \times 10^5$ sec	k_1/k_α
0	35.4	126.0/131.3		+0.168		
4000	55.4	88.8/129.4	6.65	0.131	6.22	1.07
8000	52.5	65.2/117.2	6.71	0.100	6.48	1.03
12000	54.0	58.5/127.0	6.59	0.077	6.50	1.01
16000	46.3	59.2/132.3	6.95	0.062	6.23	1.12
20000	52.9	47.8/132.0	6.89	0.047	6.37	1.08
24000	39.6	58.5/131.5	6.70	0.038	6.19	1.08
			Mean: 6.75 ± 0.14		6.33 ± 0.12	1.07 ± 0.04

[a] Pressure of the analytical sample. [b] Transmittance at 846 cm^{-1}.

Table X. Kinetics of the Trans–Cis Isomerization of (+)-*trans*-Cyclopropane-*1,2-d*$_2$ at 422.5° (Run 2)

Time, sec	P_{TOT},[a] Torr	$(h/R)^b$	$k_1 \times 10^5$ sec
0	35.4	126.0/131.3	
4000	50.0	97.7/136.9	6.59
8000	56.7	70.5/131.5	6.53
12000	46.8	54.8/107.9	6.69
16000	34.9	62.0/114.0	7.00
20000	40.9	48.0/103.2	6.50
24000	39.4	51.4/115.3	6.72
30000	49.1	42.2/121.0	6.74
36000	32.1	57.3/120.8	6.85
			Mean: 6.70 ± 0.17

[a] Total pressure of the ir sample. [b] Transmittance at 846 cm^{-1}.

Appendix. Derivation of the Differential Equation for Loss of Optical Activity from *trans*-1-Phenylcyclopropane-*2-d*

The differential equations for the stereomutation of phenylcyclopropane-*2-d* (Scheme II) are:

$$-\frac{d((+)\text{-}T)}{dt} = (k_2 + k_{23} + k_{12} + k_1 + k_{13})((+)\text{-}T) - (k_2 + k_{23})((+)\text{-}C) - (k_1 + k_{13})((-)\text{-}C) - k_{12}((-)\text{-}T) \quad (A1)$$

$$-\frac{d((+)\text{-}C)}{dt} = (k_2 + k_{23} + k_{12} + k_1 + k_{13})((+)\text{-}C) - (k_2 + k_{23})((+)\text{-}T) - (k_1 + k_{13})((-)\text{-}T) - k_{12}((-)\text{-}C) \quad (A2)$$

$$-\frac{d((-)\text{-}T)}{dt} = (k_2 + k_{23} + k_{12} + k_1 + k_{13})((-)\text{-}T) - (k_2 + k_{23})((-)\text{-}C) - (k_1 + k_{13})((+)\text{-}C) - k_{12}((+)\text{-}T) \quad (A3)$$

$$-\frac{d((-)C)}{dt} = (k_2 + k_{23} + k_{12} + k_1 + k_{13})((-)C) - (k_2 + k_{23})((-)T) - (k_1 + k_{13})((+)\text{-}T) - k_{12}((+)\text{-}C) \quad (A4)$$

Summation of eq A1 and A3 gives

$$-\frac{dT}{dt} = (k_2 + k_{23} + k_1 + k_{13})(T - C) \quad (A5)$$

But $C = T_0 + C_0 - T$, which when substituted into eq A5 converts it to integrable form with T as the variable. The integrated equation is A6, which is given in the main text as eq 3.

$$k_i = -\frac{1}{t}\ln\frac{(T - C)}{(T_0 - C_0)} \quad (A6)$$

The optical activity of the phenylcyclopropane may be expressed as in eq A7.

$$\alpha_{obsd} = \alpha_t^{max}\Delta T + \alpha_c^{max}\Delta C \quad (A7)$$

Upon differentiation, we obtain

$$d\alpha_{obsd}/dt = \alpha_t^{max}d(\Delta T)/dt + \alpha_c^{max}d(\Delta C)/dt \quad (A8)$$

We may substitute for $d(\Delta T)/dt$ and $d(\Delta C)/dt$ the expressions obtained by subtraction of eq A3 from A1 and A4 from A2, respectively, which gives eq 4 of the main text.

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Cycloaddition. XIX. Competing Concerted and Stepwise [2 + 4] Cycloaddition of the Dichlorodifluoroethylenes to Butadiene and 2,4-Hexadiene

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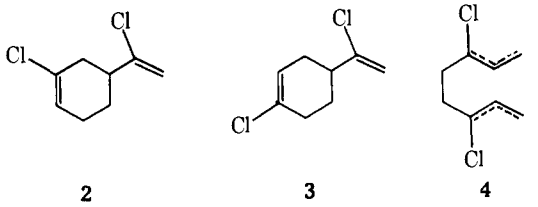
Abstract: The [2 + 4] cycloaddition of dichlorodifluoroethylenes to 1,3-dienes, though allowed as a concerted process by orbital symmetries, also occurs favorably by way of biradicals. Available criteria of mechanism are applied in detail to 1,1-dichloro-2,2-difluoroethylene (1122) and to *cis*- and *trans*-1,2-dichloro-1,2-difluoroethylene (1212) in their [2 + 4] cycloadditions to 1,3-butadiene and 2.4-hexadiene, and the competing mechanisms are sorted out. The 1122 isomer gives *less* [2 + 4] adduct with 2,4-hexadiene than with butadiene, a behavior compatible only with a stepwise mechanism having little or no competition from a concerted one. On the other hand, 1212 gives eight times as much [2 + 4] adduct with the hexadiene as with the butadiene, and the stereochemical retention index of the six-ring product is up from 4.5 for butadiene to 215 for 2,4-hexadiene, clearly indicating important competition from the concerted mechanism. The configuration of the methyl groups in the two sets of [2 + 4] products from 2,4-hexadiene is not randomized, a fact attributed to the rotation of the *cis*-allylic group being slower than the other rotations determining configuration. It is concluded that, among these reactions, only the addition of 1212 to 2,4-hexadiene involves any appreciable concerted character.

Ethylene and its halogen substitution products form a series of reagents exhibiting a wide range of reactivities and selectivities toward dienes. Butadiene reacts with ethylene to give a cross-adduct consisting 99.98% of cyclohexene.[2] Only through the concerted Diels–Alder mechanism could this result occur without substantial amounts of the [2 + 2] cycloadducts that are so much more characteristic of biradical mechanisms.[3,4]

At the other extreme, 1,1-dichloro-2,2-difluoroethylene ("1122") (**1**) adds to butadiene to give a vinylcyclobutane and, at 60°, less than 1% of a cyclohexene.[5] Trifluoroethylene is a borderline reagent, whose behavior toward dienes can be accounted for only by balanced capabilities for concerted [2 + 4] cycloaddition and biradical formation.[6a]

These facts do not allow the assignment of a mechanism to a cycloaddition by simply noting whether concert is allowed or forbidden by the orbital symmetry rules since stepwise reactions are always allowed and may compete even with normally favorable Diels–Alder mechanisms. We have noted, however, that in freely rotating dienes the amount of [2 + 4] product in a biradical reaction is limited by the diene's preference for an *s*-trans conformation.[5,7] A quantitative determination of how [2 + 4] cycloaddition to a diene is distributed between concerted and stepwise mechanisms should afford insight into the structural factors required for rapid reaction by one or the other mechanism.

A more specific criterion of mechanism than the amount of accompanying [2 + 2] addition is the effect of pressure on the rate of the [2 + 4] cycloaddition itself. Stewart[8] has shown that, in the dimerization of chloroprene, high compression favors relatively not all the [2 + 4] adducts but only those isomers (**2** and **3**) which *could not* have been formed by way of the most favored biradical (**4**); at atmospheric pressure, the biradical mechanism competes successfully where the concerted mechanism is allowed as well as where it is forbidden.



2 **3** **4**

A very general accompaniment of stepwise mechanisms is configuration loss. We have previously applied this criterion to the two centers of geometrical configuration in 2,4-hexadiene, 1,4-dichlorobutadiene, and their [2 + 2] cycloadducts[9-11] with 1122 and tetrafluoroethylene but, in those cases, the [2 + 4] cycloadducts were so minor as to escape detection. A second application of this criterion is to observe retention or loss of configuration in the *ene* component of a diene reaction. Application of this test to 1,2-dichloro-1,2-difluoroethylene ("1212") (*cis*-**5** and *trans*-**5**) and cyclopentadiene gave the simple answer that configuration was lost in the [2 + 2] product and retained in the [2 + 4] product.[12]