Thermal Stereomutations of (2R,3R)-Phenylcyclopropane-1,2,3-$^2H_3$ and (1R,2S,3R)-Phenylcyclopropane-2-^{13}C-1,2,3-$^2H_3$: Quantification of All Four Stereochemical Modes for Interconversions among the 1-Phenyl-1,2,3-trideuteriocyclopropanes

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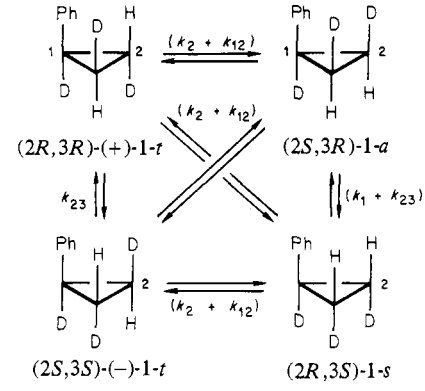
Abstract: Optically pure (2R,3R)-phenylcyclopropane-1,2,3-$^2H_3$ and (1R,2S,3R)-phenylcyclopropane-2-^{13}C-1,2,3-$^2H_3$ have been prepared and the thermal stereomutations they exhibit have been followed kinetically at 309.3 °C to provide the first complete quantification of the four one-center and two-center modes of stereomutation available to a monosubstituted cyclopropane. For phenylcyclopropane-1,2,3-$^2H_3$ at 309.3 °C in the gas phase, the unimolecular rate constants ($\times 10^5$ s) are found to be k_1 = 0.36, k_2 = 0.87, k_{12} = 0.20, and k_{23} = 0.0: one-center epimerizations are decisively dominant.

In spite of the numerous and often sophisticated efforts expended over the past 26 years in attempts to gain fresh insights on the thermal stereomutations of cyclopropanes, the reaction has not been fully elucidated.[1] Neither theoretical nor experimental work has provided a generally accepted qualitative or quantitative model useful for predicting or interpreting the absolute or relative magnitudes of all possible one-center and two-center epimerizations. The light such a model could provide on questions relating to trimethylene, one of the simplest localized diradicals, remains dim.

The central relationship between experimental fact and theoretical model for these stereomutations was perceived as early as 1964[2]: Setser and Rabinovitch studied methylcyclopropane-2,3-$^2H_2$ in hopes of distinguishing whether simultaneous (two-center, k_{ij}) or only consecutive (one-center, k_i) epimerizations occurred and of thus providing a direct crucial test between alternative mechanistic postulates. Their kinetic study, however, did not give individual rate constants for stereochemically distinct modes of epimerization, and no firm mechanistic discriminations could be rendered.

Monosubstituted cyclopropanes suitably labeled with isotopes to make stereochemically different epimerization modes observable seem to offer attractive prospects for kinetic investigations, since only four distinct paths for stereomutation are available due to symmetry. Yet the problem posed so lucidly by Setser and Rabinovitch[2] has remained unsolved. Two subsequent kinetic efforts with monosubstituted and deuterated cyclopropanes have been recorded, but neither gained a complete solution to the stereochemical problem and the partial results achieved seemed discordant. For vinylcyclopropane-2,3-$^2H_2$,[3] the combinations of epimerization rate constants ($k_1 + k_{23}$) and ($k_2 + k_{12}$) were found to be approximately equal at 325 °C, while for phenylcyclopropane-2-^2H, k_1 = 0 and k_{12}:($k_2 + k_{23}$) = 5:1 at 309.5 °C.[4,5] Further efforts[6] with chiral phenylcyclopropane-2,3-$^2H_2$ gave ($k_2 + k_{12} + k_{23}$) = 1.10 × 10^{-5} s^{-1}.

Scheme I



These incomplete studies were encumbered with unresolved synthetic problems, serious analytical difficulties, and intrinsically insufficient data, yet these pioneering attempts delineate all essential aspects of the experimental challenge posed by the goal: a complete kinetic treatment of the stereomutation modes available to a monosubstituted cyclopropane. This long-desired objective has now been attained for one exemplar, phenylcyclopropane.

In developing an approach for this kinetic investigation, we sought synthetic routes that would incorporate isotopic labels with high efficiency and stereoselectivity, reliable analytical methods, and data reduction techniques that would be straightforward and free from any assumptions respecting secondary deuterium isotope effects.[7] These design objectives were met in earlier work reporting syntheses of all three achiral forms of phenylcyclopropane-1,2,3-$^2H_3$ and of the optically pure (2R,3R)-(+) isomer, and a kinetic study of thermal stereomutations among the achiral isomers at 309.3 °C using Raman and NMR spectroscopic techniques for analyses.[8] The rate constants obtained were ($k_1 + k_{23}$) = 0.36 × 10^{-5} s^{-1} and ($k_2 + k_{12}$) = 1.07 × 10^{-5} s^{-1} (Scheme I). These analytical techniques do not distinguish (+)-**1**-*t* from (−)-**1**-*t*, and k_{23} in Scheme I could not, of course, be measured.

To follow the interconversions among all four forms (Scheme I) demands a chiral substrate and a new analytical tool able to distinguish the (2R,3R) and (2S,3S) isomers. In view of the extremely low rotations expected for these enantiomers, we decided

(1) For summaries of the field and references to earlier reviews see: Borden, W. T. In "Reactive Intermediates"; Jones, M., Moss, R. A., Eds.; Wiley: New York, 1981; Vol. II, Chapter 5. Dervan, P. B.; Dougherty, D. A. In "Diradicals"; Borden, W. T., Ed.; Wiley: New York, 1982; Chapter 3.
(2) Setser, D. W.; Rabinovitch, B. S. *J. Am. Chem. Soc.* **1964**, *86*, 564-569.
(3) Willcott, M. R., III; Cargle, V. H. *J. Am. Chem. Soc.* **1979**, *91*, 4310-4311.
(4) Berson, J. A.; Pedersen, L. D.; Carpenter, B. K. *J. Am. Chem. Soc.* **1975**, *97*, 240-242.
(5) Berson, J. A.; Pedersen, L. D.; Carpenter, B. K. *J. Am. Chem. Soc.* **1976**, *98*, 122-143.
(6) Wood, J. T.; Arney, J. S.; Cortès, D.; Berson, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 3855-3860.
(7) Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1979**, *101*, 1325-1326.
(8) Baldwin, J. E.; Patapoff, T. W.; Barden, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 1421-1426.

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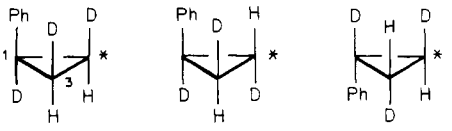
against polarimetry as an analytical method, for it would have required extremely large samples of perfectly pure phenylcyclopropanes: extremely large samples of stereoselectively isotopically labeled chiral substrates may be extremely expensive to prepare and arduous to purify, and a chiral impurity of substantial specific rotation present even in quite low concentrations could play havoc with the interpretation of polarimetric measurements for mixtures of phenylcyclopropane isomers (+)-**1**-*t*, (−)-**1**-*t*, **1**-*a*, and **1**-*s*. Instead we adopted an NMR-chiral shift reagent approach.[9]

The key intellectual challenge posed by kinetic Scheme I is this: if the interconversions among all four isomers of the phenylcyclopropane-*1,2,3*-$^2H_3$ system may only provide measures of k_1, k_{23}, and $(k_2 + k_{12})$, how can one obtain measures of the individual rate constants k_2 and k_{12} themselves? Recourse to a further substrate for kinetic study, the anti isomer **1**-*a* made chiral by virtue of a ^{13}C label at C(2) (*RSR*-**1**-*a*), answered this question; it may distinguish between k_2 and k_{12} because these conceptually distinct modes of stereomutation lead to isomers having enantiotopic and thus potentially distinguishable protons. One-center epimerization at C(2), for example, leads to the *RRR*-**1**-*t* isomer, while two-center epimerization at C(1) and C(3) generates *SSS*-**1**-*t*.

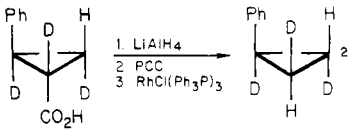


RSR-1-*a* *RRR*-1-*t* *SSS*-1-*t*

To employ this strategy required synthesis of the optically pure [^{13}C,$^2H_3$]-labeled phenylcyclopropane *RSR*-**1**-*a* and adaptation of the NMR-chiral shift reagent technique used to discriminate quantitatively between enantiotopic protons in the [$^2H_3$] systems.

Results

Syntheses. The (2*R*,3*R*) isomer of 1-phenyl-1,2,3-trideuteriocyclopropane ((+)-**1**-*t*) was prepared from the optically pure *t*-2-phenyl-1,2,3-trideuteriocyclopropanecarboxylic acid isomer **2** through a Wilkinson's catalyst promoted decarbonylation of the corresponding aldehyde.[8] According to Raman spectroscopic analysis, this labeled chiral substrate for kinetic studies [ref 8, Table I, line 5] was 96.4% the desired trans product, contaminated by 2.2% of the anti-(2*S*,3*R*) and 1.3% of the syn-(2*R*,3*S*) isomers **1**-*a* and **1**-*s*. The 100% optical purity of the trans mateial followed from the complete resolution of the acid precursor.[8]

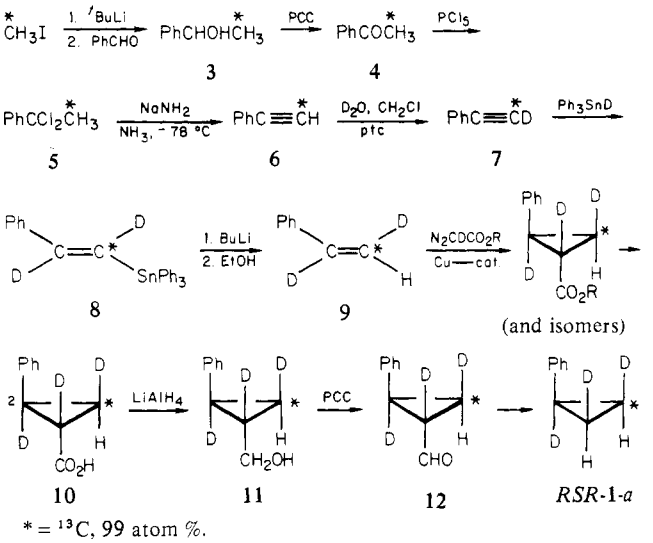


(+)-**2** (+)-**1**-*t*

The sequence of reactions used to prepare the chiral [^{13}C,$^2H_3$]-labeled substrate *RSR*-**1**-*a* is outlined in Scheme II. It proved quite efficient in terms of the cost of labeled precursors, overall yield, and reutilization of previously developed chemistry. Most importantly, it provided product of high isotopic and stereochemical purity.

Iodomethane-^{13}C and *tert*-butyllithium at −78 °C underwent lithium halide exchange;[10] subsequent addition of benzaldehyde followed by reaction of the excess *tert*-butyllithium with isopropyl alcohol and water at −78 °C gave the labeled 1-phenylethanol (**3**). Oxidation of this alcohol with PCC provided the labeled acetophenone (**4**) which was converted to dichloride **5** with PCl_5.[11]

Scheme II



3 4 5 6 7 8 9 10 11 12 *RSR*-1-*a*

* = ^{13}C, 99 atom %.

Addition of the dichloride to a freshly prepared suspension of $NaNH_2$ in liquid ammonia at −78 °C[12] generated the ^{13}C-labeled phenylacetylene (**6**), thus providing an entry into the synthetic sequence used to prepare other labeled phenylcyclopropanes.[8]

The acetylenic hydrogen was exchanged for deuterium with the aid of benzylhexadecyldimethylammonium chloride as a phase-transfer catalyst in D_2O/CH_2Cl_2 with a trace of NaOD to provide the [^{13}C,^2H]-labeled phenylacetylene (**7**).

This dilabeled synthetic intermediate, with 99% ^{13}C and better than 99% deuterium incorporation, was secured in an overall yield of 43.5% from iodomethane-^{13}C through the six-step route of Scheme II—an average of 87% for each reaction. The ^1H NMR spectrum of **6**, its immediate precursor, showed the acetylenic proton as a doublet centered at 3.05 ppm, with $J_{^{13}C-H}$ = 251 Hz; no singlet from acetylenic ^{12}C–H was apparent above baseline noise. The ^1H NMR spectrum of **7** itself exhibited no detectable acetylenic proton signal at all.

Conversion of the dilabeled phenylacetylene (**7**) to the stereoselectively [^{13}C,$^2H_2$]-labeled styrene (**9**) was accomplished by way of the triphenyltin deuteride adduct **8**, a transmetalation with *n*-butyllithium at −78 °C, and quenching the vinyllithio intermediate with ethanol.[8]

The olefinic region in the ^1H NMR spectrum of styrene **9** matched theoretical expectations exactly. A sixfold spectral amplification was necessary before any resonances expected from stereoisomers of **9** or less highly labeled analogues of **9** could be just barely distinguished. Although NMR integrations were too insensitive to quantify the small amounts of impurities present, the stereochemical integrity and overall isotopic incorporation of [^{13}C,$^2H_2$]styrene (**9**) both appeared to be in excess of 99%.

A chiral copper catalyst[13] was employed to condense styrene **9** with *dl*-menthyl α-deuteriodiazoacetate;[8] with slow addition of the neat diazo ester using a syringe pump, high stereoselection favoring the trans adduct and asymmetric induction of about 90% favoring the (1*S*,2*S*,3*R*) form are realized. The mixture of menthyl esters from the reaction was saponified, and the mixture of acids obtained was esterified with diazomethane, giving *cis*- and *trans*-methyl esters which were easily separable by low-pressure liquid chromatography. The *trans*-methyl ester obtained was converted to the trans acid, which was efficiently resolved to complete optical purity through several recrystallizations of its quinine salt[14] to yield acid **10** having the absolute configuration shown.[15] A small sample was treated with diazomethane and

(9) Kime, K. A.; Sievers, R. E. *Aldrichim. Acta* **1977**, *10*, 54–62. Sullivan, G. R. *Top. Stereochem.* **1977**, *10*, 287–329.
(10) Lansbury, P. T.; Haddon, V. R.; Stewart, R. C. *J. Am. Chem. Soc.* **1974**, *96*, 896–898.
(11) Fringuelli, F.; Mancini, V.; Taticchi, A. *Tetrahedron* **1969**, *25*, 4249–4256.
(12) Brandsma, L. In "Preparative Acetylenic Chemistry"; Elsevier: New York, 1971; Chapter 2, pp 19–20.
(13) Compare: Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, 1707–1710; *Ibid.* **1977**, 2599–2602.
(14) Baldwin, J. E.; Lötiger, J.; Rastetter, W.; Neuss, N., Huckstep, L. L.; De La Higuerra, N. *J. Am. Chem. Soc.* **1973**, *95*, 3796–3797.

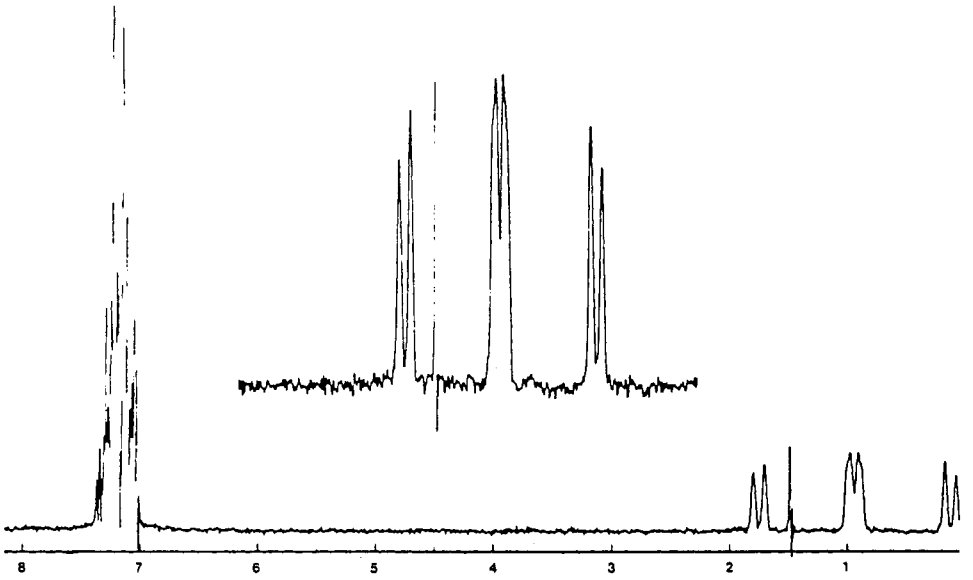
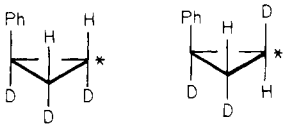


Figure 1. The 100-MHz ^{1}H NMR spectrum of (1*R*,2*S*,3*R*)-phenylcyclopropane-2-^{13}*C*-1,2,3-$^2H_3$ (*RSR*-**1**-*a*). A trace of water is apparent in the NMR sample. The anti protons come at 0.94 ppm; the syn protons in phenylcyclopropane appear at 0.70.

the VPC-purified methyl ester was examined by NMR in the presence of increasing portions of the chiral shift reagent, Eu(hfc)$_3$.[16] Optical purity was confirmed by observing that the methyl singlet remained unsplit under conditions known to give two methyl singlets with racemic or partially racemic material. The final synthetic sequence involving reduction to alcohol **11**, oxidation to aldehyde **12**, and decarbonylation with a stoichiometric amount of Wilkinson's catalyst provided the labeled phenylcyclopropane *RSR*-**1**-*a* without complications.

The optical purity of the multiply labeled cyclopropane *RSR*-**1**-*a* follows from the optical purity of the precursor acid **10**, $[\alpha]_{546}$ +433°, demonstrated for the corresponding methyl ester with the chiral shift reagent Eu(hfc)$_3$. Possible stereoisomers of *RSR*-**1**-*a*, such as *RRR*-**1**-*t*, *RRS*-**1**-*s*, and *RSS*-**1**-*t*, well as incompletely



RRS-**1**-*s* *RSS*-**1**-*t*

deuterated analogues, could not be quantified by ^{1}H NMR spectroscopy for they could not be seen at all: signals attributable to these potential synthetic coproducts all having C(2 or 3)–H cis to the phenyl substituent are conspicuously absent in the spectrum (Figure 1). They are just not present to any significant degree.

Stereochemical Analyses of Thermolysis Reaction Mixtures from Chiral Substrates. Samples of (+)-**1**-*t* heated at 309.3 °C in the gas phase for various times generated mixtures of the four isomers shown in Scheme I.[8] Concentrations ([(+)-**1**-*t*] + [(−)-**1**-*t*]), [**1**-*a*], and [**1**-*s*] in these product mixtures were determined by Raman and NMR spectroscopy [ref 8, Table I, last four lines].

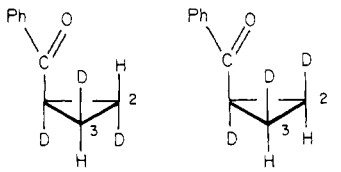
Proton NMR spectroscopy in the presence of the chiral shift reagent Eu(hfc)$_3$ gave the additional information needed to determine the relative amounts of (+)-**1**-*t* and (−)-**1**-*t* in these kinetic mixtures. To facilitate this technique, the mixture of the four isomers (Scheme I) derived thermally from (+)-**1**-*t* was subjected first to Sharpless oxidation,[17] converting the phenyl group to a carboxylic acid, followed by reaction of the acid with phenyllithium.[18] Thus, a reaction mixture containing all four cyclopropanes (Scheme I) provided through this two-step sequence a mixture of the four benzoylcyclopropanes **13**.

Table I. Observed and Calculated Mol Percent Concentrations[a] of Phenylcyclopropane-1,2,3-$^2H_3$ Isomers from (2*R*,3*R*)-(+)-**1**-*t* at 309.3 °C

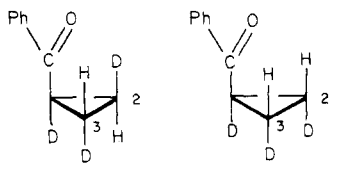
time (min)	**1**-*a*	**1**-*s*	(+)-**1**-*t*	(−)-**1**-*t*
0	2.3	1.3	96.4	0.0
400	17.0	16.3	62.1	4.5
	(16.9)	(16.5)	(62.1)	(4.5)
800	21.6	21.0	45.6	11.8
	(22.1)	(21.9)	(45.2)	(10.7)

[a] According to the parameters $k_1 = 0.36 \times 10^{-5}$ s^{-1}, $k_{23} = 0.0$, $(k_2 + k_{12}) = 1.07 \times 10^{-5}$ s^{-1}. Calculated values are in parentheses.

The electron-rich benzoyl moiety complexed well with Eu(hfc)$_3$, and the NMR absorptions for protons on C(2) and C(3) disposed cis to the benzoyl group shifted rapidly downfield. The cis proton on C(2) shifts further downfield than the enantiotopically related cis proton on C(3). The ratio of the two signal intensities thus gives a measure of the concentration ratio ([2*R*,3*R*)-**13**-*t*] + [(2*R*,3*S*)-**13**-*s*]):([2*S*,3*S*)-**13**-*t*] + [(2*R*,3*S*)-**13**-*s*]). Since the



(2*R*,3*R*)-**13**-*t* (2*S*,3*R*)-**13**-*a*



(2*S*,3*S*)-**13**-*t* (2*R*,3*S*)-**13**-*t*

concentrations ([(+)-**1**-*t*] + [(−)-**1**-*t*]) and [2*R*,3*S*-**1**-*s*] are already

(15) Doering, W. von E.; Kirmse, W. *Tetrahedron* **1960**, *11*, 272–275. Inouye, Y.; Sugita, T.; Walborsky, H. M. *Ibid.* **1964**, *20*, 1695–1699. Sugita, T.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1075–1076.

(16) Eu(hfc)$_3$ is tris[3-(heptafluoropropylhydroxymethylene)-*d*-camphorato]europium(III) from Aldrich Chemical Co.; also abbreviated Eu(hfbc)$_3$. Fraser, R. R.; Petit, M. A.; Saunders, J. K. *J. Chem. Soc., Chem. Commun.* **1971**, 1450–1451. Goering, H. L.; Eikenberry, J. N.; Koermer, G. S. *J. Am. Chem. Soc.* **1971**, *93*, 5913–5914.

(17) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936–3938.

(18) On the small scales employed, this reaction was somewhat capricious under standard conditions. The most reproducible results were obtained followed the procedures described by: Rubottom, G. M.; Kim, C. *J. Org. Chem.* **1983**, *48*, 1550–1552.

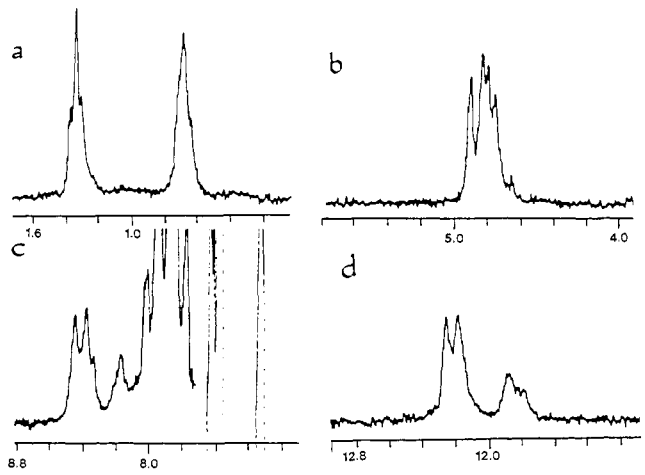
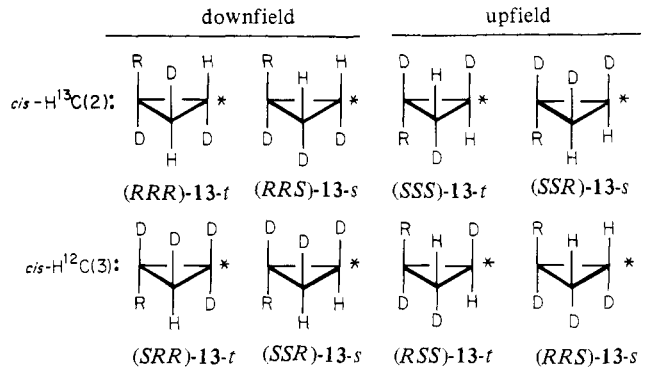


Figure 2. Lower field resonance of the 800-min kinetic point, benzoyl derivatives **13**: (a) without $Eu(hfc)_3$; (b) partially resolved at δ 4.8; (c) passing benzene protons at δ 8.2; (d) fully resolved at δ 12.3.

Scheme III. Enantiotopic Distinctions in the Presence of $Eu(hfc)_3$[a]



[a] R = PhCO–; * = ^{13}C, 99 atom %.

known, [(+)-**1**-*t*] and [(−)-**1**-*t*] may be calculated. The enantiotopic trans hydrogens moved downfield more slowly than those cis to the benzoyl function and were not separated appreciably.

This analytical strategy was applied to the mixtures of isomers obtained from 400- and 800-min thermolyses. After analysis by Raman and NMR spectroscopy, the mixtures of phenylcyclopropane-*1,2,3*-$^2H_3$ isomers were converted to benzoylcyclopropane-*1,2,3*-$^2H_3$ isomers; these ketones were examined by ^1H NMR spectroscopy in the presence of increasing amounts of $Eu(hfc)_3$. The experimental ratios of enantiotopic cis-to-benzoyl H-C(2):H-C(3) signals were found to be 79:21 and 67:33 (Figure 2). Simple arithmetic then led from the relationship given above between this ratio and the mole percents of (2*R*,3*R*)-**13**-*t*, (2*S*,2*S*)-**13**-*t*, and (2*R*,3*S*)-**13**-*s* to the mole percent concentrations reported in Table I.

A computer program[19] based on the exact integrated solutions to the differential equations appropriate to the kinetic situation portrayed in Scheme I was employed to find the best values of k_1 and k_{23}. From the known parameters $(k_1 + k_{23}) = 0.36 \times 10^{-5}$ s^{-1} and $(k_2 + k_{12}) = 1.07 \times 10^{-5}$ s^{-1} and the experimental concentration vs. time data in Table I, the optimum match between observed and calculated concentrations resulted when k_{23} was zero. The χ^2 measure of discrepancy between observed and calculated concentrations[20] rapidly became worse as k_{23} increased.

The same analytical technique applied to product mixtures from the chiral [^{13}C,$^2H_3$] system *SSS*-**1**-*a* worked in an analogous fashion, with an additional and decisively important complication stemming from ^{13}C–^1H spin–spin coupling: the contributions to

(19) Baldwin, J. E.; Baldwin, C. M., unpublished.
(20) See: Cooper, J. W. "Introduction to Pascal for Scientists"; Wiley: New York, 1981; Chapter 18, and references cited therein.

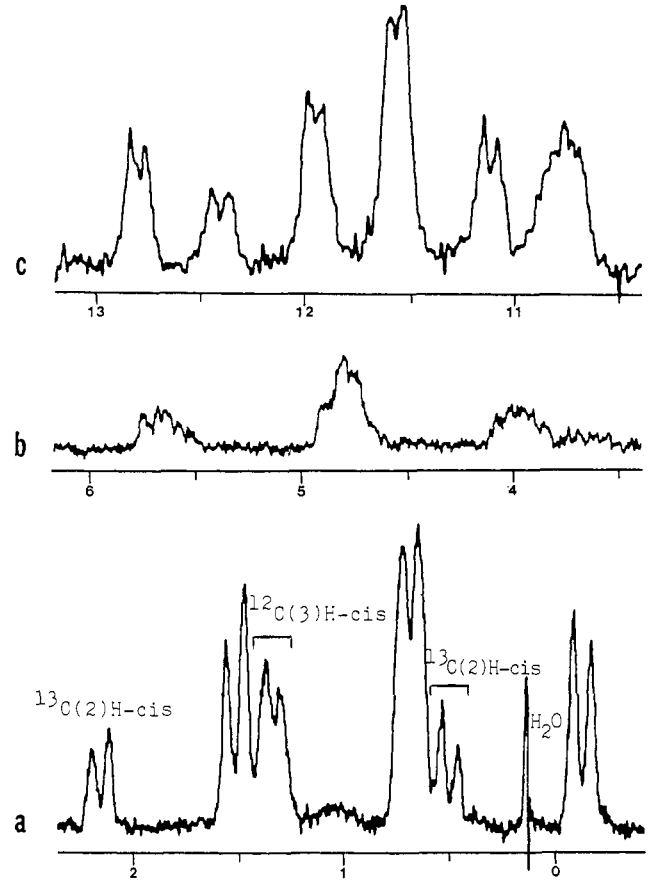


Figure 3. Separation of enantiotopic cis-to-benzoyl hydrogens in the benzoylcyclopropane-^{13}C,$^2H_3$ isomers derived from *RSR*-**1**-*a* through addition of $Eu(hfc)_3$; spectrum a is before addition of shift reagent. The signals from hydrogens at $^{13}C(2)$ and $^{12}C(3)$ cis to benzoyl are labeled (cf. Scheme III). Only these absorptions are retained in the most downfield region and are progressively separated into enantiomeric components in b and c. Spectrum b shows some separation at δ 4.8, while c gives fully resolved absorptions at δ 11.8. An extraneous peak from the shift reagent obscures the farthest upfield "doublet" in c.

downfield and upfield signal strength for cis protons at $^{13}C(2)$ and $^{12}C(3)$ in the presence of $Eu(hfc)_3$ relate to structure as summarized in Scheme III.

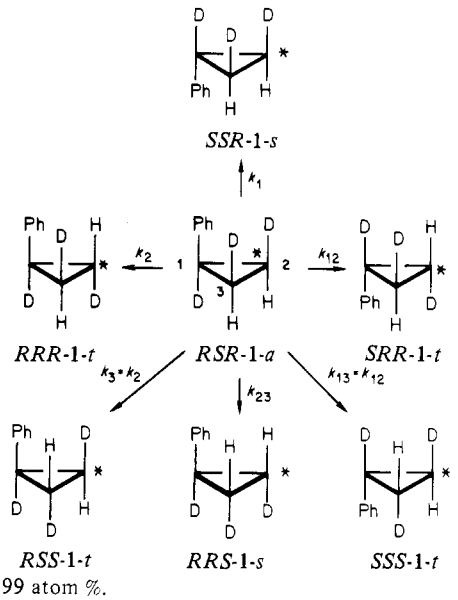
The isomers with two hydrogens cis to (*SSR*)-**1**-*s* and (*RRS*)-**1**-*s*, each appear twice in Scheme III, for they contribute to two signal intensities. The isomers with two hydrogens trans to benzoyl, (*RSR*)-**1**-*a* and (*SRS*)-**1**-*a*, do not contribute at all to the experimentally discriminating ratio of enantiotopically related cis hydrogens.

The summary of Scheme III makes clear that the ratio of enantiotopically related cis $H^{13}C(2)$ signal intensities in a mixture of all eight [^{13}C,$^2H_3$] isomers should be just the inverse of the ratio of enantiotopically related cis $H^{12}C(3)$ absorptions. Since ^{13}C–H spin–spin coupling makes these ratios independently observable, two independent measurements of the same quantity may be made in one product mixture.

A 100-mg sample of (*RSR*)-**1**-*a* and dry pentane heated at 309.3 °C for 600 min gave a mixture of labeled phenylcyclopropanes which were converted in two steps to a mixture of isotopically labeled benzoylcyclopropanes. Added chiral shift reagent $Eu(hfc)_3$ had the qualitatively anticipated effect on the ^1H NMR spectrum of the [^{13}C,$^2H_3$] benzoylcyclopropane isomers: the enantiotopic cis-to-benzoyl protons were differentiated, and the downfield:upfield ratios were found to be 1.4:1 and 1:1.5 for $^{13}C(2)H$ and $^{12}C(3)H$ (Figure 3).

The relationship between the two ratios of enantiotopic hydrogens observed (Figure 3) and distinct values for the rate constants k_2 and k_{12} is straightforward. The kinetic situation appropriate to the situation involves 48 rate constants—six rate constants for six distinct stereomutations from each of the eight

Scheme IV



* = ^{13}C, 99 atom %.

stereoisomers in the [^{13}C,$^{2}H_3$]-labeled set, as exemplified in Scheme IV for *RSR*-**1**-*a* as thermal reactant. Yet, there is only one variable to be found: knowing values of k_1, k_{23}, and (k_2 + k_{12}), one may vary a single parameter, say k_{12}, and calculate the time vs. concentration behavior of the entire set of isomers; these concentrations then give theoretical values for the experimentally accessible observables to be compared with the enantiomeric ratios measured spectroscopically.

The optimum value of k_{12} was quickly found, for the problem is a simple one-unknown optimization exercise. The calculated dependence of the ratios of enantiotopic protons turns out to be a sensitive function of k_{12}: the $^{13}C(2)H$ ratio 1.4:1 implies k_{12} = 0.19 × 10^{-5} s^{-1}, while the $^{12}C(3)H$ ratio 1:1.5 corresponds to k_{12} = 0.21 × 10^{-5} s^{-1}.[21] These values separate the final sum (k_2 + k_{12}): k_2 = 0.87 × 10^{-5} s^{-1} and k_{12} = (0.20 ± 0.01) × 10^{-5} s^{-1}.

Uncertainties in Rate Constants. From the two data sets for achiral isomers,[8] the kinetic expression ln |(2[**1**-*t*] − 1)| = constant − 4(k_2 + k_{12})*t* for the reversible first-order equilibration between **1**-*t* and (**1**-*a* + **1**-*s*) and a standard weighted least-squares treatment[22] leads to (k_2 + k_{12}) = (1.06 ± 0.02) × 10^{-5} s^{-1}. Simplex optimization of the data fit to the complete kinetic scheme gives (k_2 + k_{12}) = 1.07 × 10^{-5} s^{-1} and (k_1 + k_{23}) = 0.36 × 10^{-5} s^{-1}.[8] The χ^2 values calculated for the concentration data with **1**-*a* as substrate are less sensitive by a factor of ~1.5 to systematic variations from the best value of (k_1 + k_{23}) than (k_2 + k_{12}). Hence from the achiral kinetic study one may estimate the parameters (k_2 + k_{12}) = (1.07 ± 0.02) × 10^{-5} s^{-1} and (k_1 + k_{23}) = (0.36 ± 0.03) × 10^{-5} s^{-1}.

With these values held constant, the best fit to the full data set made available through analysis for (+)-**1**-*t* and (−)-**1**-*t* (Table I) was when k_{23} was zero. Such close agreement between the observed and calculated concentrations of the four-isomer set with k_{23} = 0 increases the confidence level for the (k_1 + k_{23}) and (k_2 + k_{12}) values. In addition, this result may be taken as experimental confirmation of a value one might have predicted confidently on thermochemical grounds.

If k_{23} is taken to be exactly zero, then k_1 = (0.36 ± 0.03) × 10^{-5} s^{-1}. Any assignment of experimental uncertainty to k_{23} decreases the estimated error for k_1. Finally, since k_{12} = (0.20 ± 0.01) × 10^{-5} s^{-1}, k_2 = (0.87 ± 0.02) × 10^{-5} s^{-1}.

The rate constant k_2 is known with the greatest precision, and k_1 with the least; yet all of the error estimates are quite small and could be doubled without impinging on any conclusions to be drawn from the kinetic results.

Of more importance than formal estimates of random uncertainties, possible systematic errors in the rate constants must be pondered. Two aspects of the experimental work mitigate against serious errors of this sort. First, the analysis of achiral kinetics gave comparable values for the parameters (k_1 + k_{23}) and (k_2 + k_{12}) using either Raman or NMR spectroscopy. Second, the same analytical method employing a chiral shift reagent was used to find k_1 vs. k_{23}, and k_2 vs. k_{12}, and any unconsidered sources of error should have influenced both measurements comparably; insofar as the one finding, k_{23} = 0, was thoroughly expected, the second finding, k_2 >> k_{12}, is rendered more secure.

Summary, Discussion, and Conclusions

This study provides values for all four one-center and two-center stereomutation rate constants shown by a deuterium-labeled monosubstituted cyclopropane. The previously unsolved problem posed by the kinetic situation of Scheme I (three experimental observables and four unknown rate constants) has been dispatched through a progressive approach: two parameters were obtained through a kinetic study of the achiral isomers;[8] a third was deduced by following stereomutations among all four isomers of Scheme I; and the fourth independent observable was secured through synthesis and thermal isomerization of a chiral [^{13}C,$^{2}H_3$]-labeled version of phenylcyclopropane.

The reliability of the kinetic work on achiral isomers was corroborated through securing wholly consistent results using two different analytical techniques, Raman and NMR spectroscopy, and through the narrow error limits defined by statistical treatments of the nine (time, three concentrations) data sets. The kinetic parameters obtained and chiral analyses of trans isomers (+)-**1**-*t* and (−)-**1**-*t* gave a thoroughly anticipated result, k_{23} = 0, with high precision. The [^{13}C,$^{2}H_3$] system, completely defined kinetically save for a single parameter, then provided that last unknown.

The four rate constants determined through this experimental effort make possible a strong distinction between alternative mechanistic models for stereomutations in phenylcyclopropane: the preponderance of one-center epimerizations is completely consistent with anticipations for diradical-mediated reactions but is not conformable to expectations based on some hypothetical energetic advantage for synchronous two-center stereomutations. The preference of one-center over two-center epimerizations here may not be ascribed to a competition between the Smith mechanism[23] and an orbital symmetry-controlled simultaneous stereomutation at two centers;[24] recent theoretical calculations and experimental studies have served to make the Smith mechanism a very implausible rationale for one-center epimerizations.[25]

The present work permits deduction for the first time of rate constants for one-center and two-center epimerizations associated with a single monosubstituted cyclopropane bond; thanks to symmetry, the measured value of k_1 reflects contributions from two equally important bond cleavages. The symmetry-corrected rate constants appropriate to stereomutations involving the C(1)–C(2) bond in phenylcyclopropane-*1,2,3*-$^{2}H_3$ (×10^5 s) are k_1 = 0.18, k_2 = 0.87, and k_{12} = 0.20. Relative to (k_1 + k_2 + k_{12}), one-center epimerizations contribute 84%.

The rotational propensity of an unemcumbered methylene can thus be seen clearly, relative to the phenyl-substituted unit, for k_2 >> k_1. Earlier kinetic work on the 2-methoxymethyl-1-spiroindenylcyclopropane-*2,3*-$^{2}H_2$ isomers indicated the trend with the finding k_2 > k_1, a larger rotational propensity for the secondary than for the tertiary radical locus.[25] The same pattern is observed in rotational barriers for alkyl radicals.[26]

(21) Qualitatively, the result k_2 > k_{12} is evident without any computation from a consideration of Schemes III and IV and the top spectrum in Figure 3.

(22) Perrin, C. L. "Mathematics for Chemists"; Wiley-Interscience: New York, 1970; pp 161–163.

(23) Smith, F. T. *J. Chem. Phys.* **1958**, *29*, 235–236.

(24) Hoffmann, R. *J. Am. Chem. Soc.* **1968**, *90*, 1475–1485.

(25) Baldwin, J. E.; Black, K. A. *J. Am. Chem. Soc.* **1984**, *106*, 1029–1040.

(26) Krusic, P. J.; Meakin, P.; Jesson, J. P. *J. Phys. Chem.* **1971**, *75*, 3438–3453. See also: Pacansky, J.; Schubert, W. *J. Chem. Phys.* **1982**, *76*, 1459–1466. There may be dramatic changes in geometry at a hydrocarbon radical center as internal rotation occurs.

The dominance of one-center epimerizations demonstrated now for phenylcyclopropane is commonly seen in other cyclopropanes: for 1,2-diphenyl-, 1,2-divinyl-, and 1-isopropenyl-2-phenylcyclopropane, kinetic studies interpreted after well-justified invocations of the "most substituted bond hypothesis" have shown that $(k_1 + k_2)$ represents 80, 74, and 68%, respectively, of the sum $(k_1 + k_2 + k_{12})$.[27-30]

For vinylcyclopropane, a consistent picture now emerges: the report of Willcott and Cargle[3] that $(k_1 + k_{23}) \approx (k_2 + k_{12})$ may now be extrapolated with confidence to anticipate $k_{23} = 0$ and $(k_1 + k_2) > k_{12}$, and the baffling apparent disparity between the behavior of vinylcyclopropane and phenylcyclopropane vanishes.

Earlier work by Berson and co-workers[6] on the 1-phenyl-2,3-dideuteriocyclopropanes at 309.5 °C led to the kinetic parameter $(k_2 + k_{12} + k_{23}) = 1.10 \times 10^{-5}$ s^{-1}, a value in excellent agreement with our present results at 309.3 °C, $(k_2 + k_{12} + k_{23}) = (1.07 \pm 0.02) \times 10^{-5}$ s^{-1}. Such a close agreement lends enhanced credibility to both studies, for very different analytical methods were employed.

Such agreement does not obtain, however, for comparisons between the present results and kinetic studies with 1-phenyl-2-deuteriocyclopropane[4,5] in which analyses of geometrical isomerization by infrared spectroscopy provided the parameter $(k_1 + k_2 + k_{12} + k_{23}) = (1.24 \pm 0.10) \times 10^{-5}$ s^{-1}, and first-order racemization of a chiral 50:50 mixture of cis and trans isomers followed polarimetrically gave $(k_1 + k_{12} + k_{13}) = (2.03 \pm 0.07) \times 10^{-5}$ s^{-1}. For these two combinations of rate constants we find $(1.43 \pm 0.04) \times 10^{-5}$ and $(0.76 \pm 0.03) \times 10^{-5}$ s^{-1}. The first comparison is fair, and the second well beyond the uncertainties of random experimental error or possible differences in secondary deuterium kinetic isotope effects. This 2.7-fold higher value in a measured kinetic parameter for racemization led inexorably to strikingly different individual rate constants and a totally reversed mechanistic impression: $k_1 = 0$ and $k_{12}:(k_2 + k_{23}) = 5:1$ (two-center epimerization dominant).[4,5] Our values contrast markedly: $k_1 = (0.36 \pm 0.03) \times 10^{-5}$ s^{-1} and $k_{12}:(k_2 + k_{23}) = 1:4.4$.

Berson, Pedersen, and Carpenter[4,5] expended considerable care to purify chiral substrates for kinetic work, recognizing clearly that even traces of chiral impurities could contribute significantly to the small rotations observed for the 1-phenyl-2-deuteriocyclopropanes (α_{365} +1.086° and smaller for neat liquids), so hypothetical trace levels of chiral impurities in kinetic samples seem an unwarranted subject for speculation. We do not know the origin of the 2.7-fold difference in experimental values for $(k_1 + k_{12} + k_{13})$ reported now by us and earlier by the Berson group,[4,5] but are continuing efforts to identify the source of the disparity.

Experimental information on the kinetic and stereochemical behavior of substituted cyclopropanes now seems to delineate a consistent picture for all systems bearing at least one group such as phenyl or vinyl able to stabilize a radical center and thus facilitate formation of diradical structures: thermochemical factors control the rates of bond cleavages,[31] and subtle steric or stereoelectronic factors influence the relative rates of one-center and two-center epimerizations.[32] One-center epimerizations are more significant kinetically than two-center stereomutations; for such 1,2-disubstituted cyclopropanes and for 1-phenyl- and 1-vinylcyclopropane, $(k_1 + k_2) > k_{12}$.[33]

For monoalkyl- or 1,2-dialkylcyclopropanes the situation may be different; currently available experimental results are too incomplete to permit any influence. Its seems evident now that the "most substituted bond hypothesis" will not be valid for 1-ethyl-2-methylcyclopropane, and the partial kinetic study[34] on this system cannot be intepreted unambiguously. Methylcyclopropane, an attractive subject for both experimental and theoretical investigation,[35] should provide telling results: will it behave like phenylcyclopropane, with one-center epimerizations dominant, or like cyclopropane, the parent system, where a double rotation mechanism predominates[36] over one-center epimerizations by a substantial factor?

Experimental Section

Most reactions were conducted under a nitrogen atmosphere in flame-dried or oven-dried (130 °C, overnight) glassware; organic solutions of crude products were dried over magnesium sulfate, filtered, and concentrated by rotary evaporation. Commercial *n*-butyllithium and *tert*-butyllithium were standardized with diphenylacetic acid.[37] Tetrahydrofuran (THF) was dried over sodium and benzophenone, and diethyl ether was dried over lithium aluminum hydride ($LiAlH_4$); each was distilled under a positive pressure of nitrogen directly into a reaction vessel as required. Dichloromethane was dried by storage over 3A molecular sieves. Benzene was purified by bubbling nitrogen through reagent grade benzene for 15 min followed by distillation, under nitrogen, from CaH_2 or sodium, onto activated 3A molecular sieves.

Vapor-phase chromatography (VPC) was performed on a Varian Aerograph A90-P3. The following 6.4-mm i.d. aluminum columns were used for analyses and VPC purifications: A, 2-m Carbowax 20 M (20% on 60/80 mesh Chromosorb W-HP); B, 2.5-m Apiezon L (14% on 60/80 mesh Chromosorb G-HP); C, a 1.2-m version of column A. Infrared (IR) spectra were recorded on a Sargent-Welch 3-200 spectrophotometer in $CHCl_3$ solutions. Polarimetry was performed on a Perkin-Elmer 141 polarimeter. A Varian XL-100 instrument was used to obtain ^1H NMR spectra. Chemical shift values are reported in ppm ($CDCl_3$ solutions) relative to Me_4Si (δ 0.00 ppm) or $CHCl_3$ (δ 7.27 ppm).

Nonisotopically labeled versions of all compounds are described in the literature and have been well characterized. The physical and spectral properties of the labeled materials were consistent with those reported earlier for the unlabeled analogues.

1-Phenylethanol-2-^{13}C (3). Iodomethane-^{13}C (99 atom %, Merck and Co., 12.30 g, 86.0 mmol) in ether (100 mL) under a blanket of argon was cooled to −78 °C. A 1.9 M solution of *tert*-butyllithium in pentane (48.0 mL, 91.2 mmol) was added in 45 min, and the reaction mixture was stirred an additional 2 h at −78 °C. Benzaldehyde (9.87 g, 93.0 mmol) in ether (10 mL) was added over the course of 1 h; after being stirred another 6 h at −78 °C, the reaction mixture was quenched by adding a 1:1 mixture of isopropyl alcohol and water (15 mL). The cooling bath was removed and brine (50 mL) was added as the solution warmed to room temperature. The layers were separated; the aqueous phase was acidified and extracted with ether (80 mL), and the combined ethereal phases were washed with brine (50 mL), dried, and concentrated to give 15.09 g of crude alcohol **3** with some benzaldehyde and isopropyl alcohol still present. The product was not further purified but was carried on directly to the next reaction. Alcohol **3**: NMR δ 7.36 (s, 5 H), 4.85 (d of q, J = 2, 6 Hz, 1 H), 2.38 (s, 1 H), 1.46 (d of d, J = 7, 126 Hz, 3 H).

1-Phenylethanone-2-^{13}C (4). The entire sample of the alcohol prepared above (15.09 g) was oxidized with PCC (33.6 g, 156 mmol) in CH_2Cl_2 (300 mL) and was subjected to workup.[38] The crude product was taken up in either (50 mL) and was shaken well with a 40% aqueous solution of $NaHSO_3$ (20 mL) to remove the last traces of benzaldehyde. The organic phase was then dried and carefully concentrated to give 9.88 g of yellow liquid. Analysis by NMR indicated that 8.84 g was the desired ketone **4** (85% from iodomethane-^{13}C): NMR δ 7.68–8.04 (m,

(27) Crawford, R. J.; Lynch, T. R. *Can. J. Chem.* **1968**, *46*, 1457–1458.
(28) Arai, M.; Crawford, R. J. *Can. J. Chem.* **1972**, *50*, 2158–2162.
(29) Two recent reviews on cyclopropane stereomutations [Berson, J. A. In "Rearrangements in Ground and Excited States"; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. I, Chapter 5. Gajewski, J. J. "Hydrocarbon Thermal Isomerizations"; Academic Press: New York, 1981; pp 27–42] apparently misinterpreted the results reported by Crawford and Lynch,[27] for they quote $2k_1:k_{12}$ ratios of 2:3.3 and 1:4, respectively, indicating preferential two-center epimerization rather than the actually reported preponderance of one-center turnover. The rate constants k_{rac} and k_{tc}[27] correspond to the sums $2(k_{12} + k_1)$ and $2k_1$, respectively, a point confirmed by the senior author (Crawford, R. J., personal communication, Sept 1983). Curiously, the related work showing dominant one-center epimerization in 1,2-divinylcyclopropane[28] was overlooked by both review articles.
(30) Doering, W. von E.; Barsa, E. A. *Tetrahedron Lett.* **1978**, 2495–2498.
(31) For a current thermochemical analysis of cyclopropane and trimethylene, see: Doering, W. von E. *Proc. Natl. Acad. Sci. U.S.A.* **1981**, *78*, 5279–5283.
(32) See: Doering, W. von E; Robertson, L. R.; Ewing, E. E. *J. Org. Chem.* **1983**, *48*, 4280–4286, and references therein, for recent work on internal rotational propensities.
(33) This preference is generally less pronounced in cyanocyclopropanes: for instances, see ref 30 and Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1978**, *100*, 3942–3944; *J. Org. Chem.* **1983**, *48*, 3912–3917. Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1982**, *104*, 1362–1368.
(34) Bergman, R. G.; Carter, W. L. *J. Am. Chem. Soc.* **1969**, *91*, 7411–7425.
(35) Schoeller, W. W. *Z. Naturforsch. A* **1979**, *34*, 858–861.
(36) Berson, J. A.; Pedersen, L. D. *J. Am. Chem. Soc.* **1975**, *97*, 238–240.
(37) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879–1880.
(38) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2657–2650.

2 H), 7.40–7.60 (m, 3 H), 2.59 (d, J = 128 Hz, 3 H); a small singlet at δ 2.59 was present ($^{12}CH_3$) that integrated to <1% of the large doublet centered at the same chemical shift.

Phenylacetylene-2-^{13}C (6). The entire sample of the ketone prepared above (8.84 g, 73.0 mmol) in dry benzene (10 mL) was cooled to 0 °C, and solid PCl_5 (18.2 g, 87.4 mmol) was added in 2-g portions over a 1-h period. The reaction mixture was stirred at 0 °C for 5 h and then overnight at room temperature, attaining the color and consistency of split pea soup. It was poured onto ice (50 g), the phases were well mixed, and the two layers were separated. The aqueous layer was extracted with ether (30 mL), and the combined organic phases were washed with ice water (50 mL) and ice-cold brine (50 mL), dried over Na_2SO_4, filtered, and concentrated. The NMR spectrum of the product, 15.03 g of a dark yellow oil, was consistent with the desired product dichloride **5** (~70%) together with the monodehydrochlorinated compound, α-chlorostyrene-β-^{13}C (~30%). The characteristic, nonaromatic NMR absorbances were δ 2.56 (d, J = 132 Hz, 3 H) for **5** while the monochloro olefin had nonaromatic signals at δ 5.74 (d of d, J = 2 Hz, 158, 1 H) and 5.50 (d of d, J = 2 Hz, 166, 1 H).

A reaction vessel was fitted with a mechanical stirrer and a dry ice/acetone condenser and the vessel was cooled to −78 °C. Ammonia (250 mL) was condensed into the reaction flask and a small ball of sodium (diameter 4 mm) was added. After the solution had completely turned blue, $Fe(NO_3)_3 \cdot 9H_2O$ (~50 mg) was mixed in; the blue color quickly changed to tan and the rest of the sodium balls (diameter 4–6 mm, 7.11 g, 309 mmole were dropped into the flask; there followed 1 h of stirring at −78 °C to allow for complete formation of $NaNH_2$. The chlorides prepared immediately above in ether (50 mL) were added dropwise over 1 h and the mixture was stirred another 2 h at −78 °C. The cooling bath was removed, the dry ice/acetone condenser was replaced with a water-cooled spiral condenser, and the ammonia was allowed to evaporate overnight under a positive nitrogen pressure. Saturated aqueous NH_4Cl (100 mL) was added, and the two layers were mixed well and separated. The aqueous phase was extracted with ether (2 × 50 mL), and the combined ethereal phases were washed with brine (50 mL), dried, and concentrated to about 50 mL by rotary evaporation at 10 °C. Distillation gave labeled phenylacetylene **6** (5.05 g, 67% from **4**, bp 139–141 °C: NMR δ 7.14–7.62 (m, 5 H), 3.05 (d, J = 251 Hz, 1 H).

Phenylacetylene-2-^{13}C-2-^{2}H (7). The entire sample of phenylacetylene **6** prepared above (5.05 g) was deuterated to >99% deuterium incorporation through the phase-transfer catalysis technique previously described (4.39 g, 87% recovery).[8,39] The NMR spectrum of the material obtained after the last deuterium oxide wash only exhibited resonances attributable to solvent and the aromatic protons of **7**; the resonances expected for residual proton on the ^{13}C were indistinguishable from baseline noise at a spectrum amplitude sufficient to bring the aromatic resonances to full scale.

***trans*-β-Triphenylstannylstyrene-β-^{13}C-α,β-$^{2}H_2$ (8).** A mechanically stirred solution of dilabeled phenylacetylene **7** (4.39 g, 42.1 mmol) and triphenyltin deuteride (24.8 g, 70.4 mmol) was irradiated 20 min with a sunlamp. The solids produced were finely ground with a mortar and pestle and were washed with pentane. The resulting fine, white powder (13.10 g, 68%) had mp 116–122 °C.

Styrene-β-^{13}C-α,β-*trans*-$^{2}H_2$ (9). The mechanically stirred solution of triphenylstannylstyrene **8** (12.85 g, 28.2 mmol) in THF (100 mL) was cooled to −78 °C and was transmetalated by slow addition of a 1.55 M solution of *n*-butyllithium in hexanes (21.0 mL, 32.6 mmol) over 30 min. After 3.75 h at −78 °C the cooling bath was removed and the mixture was allowed to warm to 0 °C; the solution was recooled to −78 °C and ethanol (5.0 mL, 83.3 mmol) was added to quench the reaction. The reaction mixture was diluted with pentane (300 mL), hydroquinone (100 mg) was added, and the solution was warmed to 10 °C. The reaction mixture was kept cool and under nitrogen as much as possible as it was quickly filtered through a 15-cm column of Florisil (2.5-cm i.d.) to remove the solids present; the column was washed with an additional 150 mL of pentane. The filtrate, with hydroquinone (100 mg) added, was concentrated by rotary evaporation at 10 °C until the majority of the THF had evaporated; the product was further purified by vacuum transfer (0.05–0.10 torr, 10–25 °C) into a liquid-nitrogen-cooled flask containing 50 mg of hydroquinone. Analysis by NMR showed that the resulting 6.14 g of colorless liquid contained 2.36 g (78%) of the desired styrene **9**: NMR δ 7.20–7.50 (m, 5 H), 5.19 (t of d, J = 2 Hz, 161, 1 H). No other resonances in the olefinic region were observed.

Menthyl Cyclopropanecarboxylates from Asymmetric Condensation of [^{13}C,$^{2}H_2$]Styrene (9) and *dl*-Menthyl α-Deuteriodiazoacetate. A mixture of the chiral copper(II) catalyst previously described[8] ([α]$_{546}$ +425° (*c* 0.16, ethanol, 0.17 g) and styrene **9** (2.36 g, 22.0 mmol) in cyclohexane (40 mL) was heated to 70 °C. *dl*-Menthyl α-deuteriodiazoacetate[33,40] (5.6 g, 24.8 mmol) was added by syringe pump (Sage Instruments, Model 352) at a rate of 0.6 mL/h. After the addition, the solution was concentrated by rotary evaporation; Kugelrohr distillation (0.2 torr, 100–140 °C) gave 6.72 g of colorless, viscous oil. Analysis by NMR indicated that most of this oil (5.14 g, 77%) was a mixture of the desired labeled *trans*- and *cis*-2-phenylcyclopropanecarboxylates.

(1*S*,2*S*,3*R*)-(+)-2-Phenylcyclopropanecarboxylic-3-^{13}C-1,2,3-$^{2}H_3$ Acid (10). The menthyl esters prepared above (5.14 g, 16.9 mmol) were saponified with 25% NaOH (15 mL) in methanol (20 mL) to give 2.30 g (82%) of crude trans and cis acids; the acid mixture was treated with diazomethane[41] to give the corresponding methyl esters. Comparison of the methyl singlets in the NMR spectrum of this mixture demonstrated that carbenoid addition had produced the trans and cis isomers in a 9:1 ratio. Low-pressure liquid chromatography on silica gel with 9:1 hexanes/ethyl acetate provided 2.06 g of the *trans*-methyl ester with <1% of the cis isomer present: NMR δ 7.02–7.20 (m, 5 H), 3.71 (s, 3 H), 1.60 (br d, J = 168 Hz, 1 H). The trans ester was saponified with 25% NaOH (8.0 mL) in methanol (15 mL) to give a quantitative yield (1.90 g) of trans acid. The acid was dissolved with quinine (4.00 g, 12.33 mmol) in 85 mL of hot ethanol/hexanes (3:7), and the resulting quinine salt was systematically recrystallized to diasteromeric purity.[14] The crops having the highest optical rotations ([α]$_{546}$ +67.5 to +70.1°) were combined (2.12 g) and were hydrolyzed to give optically pure carboxylic acid **10** (0.718 g). To confirm optical purity, a small sample of **10** was esterified with diazomethane; the ester was purified by VPC on column A at 180 °C and examined as a deoxygenated C_6D_6 solution by NMR in the presence of Eu(hfc)$_3$. The CH_3 singlet remained unsplit as it was shifted downfield to δ 9.00. Previous experiments with partially racemic material had shown that the enantiotopic methyl resonances were well separated at δ 6.5. Carboxylic acid **10** had [α]$_{546}$ +433° (*c* 2.61, $CHCl_3$); NMR δ 12.02 (br s, 1 H), 7.0–7.4 (m, 5 H), 1.62 (br d, J = 168 Hz, 1 H); IR 3020, 2890, 2680, 2630, 2550, 2400, 1690, 1605, 1500, 1425, 1290 cm^{-1}.

(1*S*,2*S*,3*R*)-2-Phenylcyclopropanemethanol-3-^{13}C-1,2,3-$^{2}H_3$ (11). Carboxylic acid **10** (0.416 g, 2.50 mmol) was reduced with $LiAlH_4$ (0.29 g, 7.64 mmol) in THF (5 mL). Alcohol **11** was obtained by Kugelrohr distillation (0.05 torr, 62 °C): NMR δ 6.98–7.36 (m, 5 H), 3.58 (br d, J = 3 Hz, 2 H), 1.89 (br s, 1 H), 0.87 (br d, J = 160 Hz, 1 H); IR 3610, 3440, 3080, 3060, 3020, 3010, 2950, 2930, 2880, 2240, 1605, 1495, 1445, 1395 cm^{-1}.

(1*R*,2*S*,3*R*)-Phenylcyclopropane-2-^{13}C-1,2,3-$^{2}H_3$ (*RSR*-1-*a*). The entire sample of alcohol **11** prepared above (0.363 g, 2.38 mmol) was oxidized with PCC (0.913 g, 4.24 mmol) in CH_2Cl_2 (8 mL). The aldehyde obtained (0.346 g, 97% crude yield) was immediately subjected to decarbonylation with Wilkinson's catalyst (2.24 g, 2.42 mmol) in benzene (20 mL). Final purification by VPC on column B at 135 °C gave pure hydrocarbon *RSR*-**1**-*a* (123.6 mg, 42% from **11**) as a colorless liquid: NMR δ 7.00–7.40 (m, 5 H), 0.95 (br d, J = 6 Hz, 1 H), 0.95 (br d of d, J = 10, 172 Hz, 1 H).

Pyrolyses of (+)-1-*t* and *RSR*-1-*a*. A detailed description of the 300-mL Pyrex pyrolysis bulb, the kinetic bath, and the vacuum line used in the pyrolyses can be found elsewhere.[33] These references also give the general operational procedures used. The kinetic samples and pentane were injected directly into the pyrolysis bulb with a gas-tight 100- or 250-μL Hamilton syringe. After recovery by vacuum transfer the kinetic mixtures were washed from the U-tube collector with a small amount of pentane. About 15 mg of labeled phenylcyclopropanes from each kinetic point derived from (+)-**1**-*t* (for Raman spectroscopic analysis) and *RSR*-**1**-*a* (for record NMR spectra) was reisolated in pure form by VPC on column B at 155 °C. The remainder of each sample was carefully concentrated to about 1 mL total volume and was subjected to the oxidation procedure described below.

General Procedure for Oxidation of Kinetic Samples Derived from (+)-1-*t* and *RSR*-1-*a*. The isotopically labeled phenylcyclopropanes (~80 mg, ~0.7 mmol) in pentane were combined with water (4.5 mL), CH_3CN (3.0 mL), CCl_4 (3.0 mL), and $NaIO_4$ (2.4 g, 11.2 mmol); a catalytic amount of ruthenium(III) chloride monohydrate (5–10 mg, Alfa Products) was added and the resulting mixture was vigorously stirred for 1.5–2 days at room temperature while open to the atmosphere. Saturated aqueous Na_2CO_3 (2.5 mL) was poured in and the system was mixed well. The solids were vacuum filtered and were washed successively with water (2 × 5 mL) and CH_2Cl_2 (3 × 5 mL). The combined filtrates were shaken in a separatory funnel and separated, and the yellow aqueous phase was washed with CH_2Cl_2 (4 × 10 mL). The aqueous phase was

(39) A large amount of base must be avoided; excess base causes undesirable side reactions.

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acidified to pH 4–5 and was subjected to continuous extraction for 1 week with ether using a modified Dean-Stark trap. (Strongly acidic conditions had to be avoided to suppress the generation of I_2 during the continuous extraction process, presumably arising from residual iodate salts in the aqueous phase; otherwise, further purification became awkwardly complicated.) After continuous extraction, the ether solution was dried and carefully concentrated to 0.5–1.0 mL, and the isotopically labeled cyclopropanecarboxylic acids were purified by VPC on column C at 170 °C. The yields ranged from 50 to 70%.

Typical Procedure for Preparation of Labeled Phenyl Cyclopropyl Ketones for NMR Chiral Shift Reagent Analysis. The isotopically labeled cyclopropanecarboxylic acid (26.2 mg, 0.29 mmol) was washed from a VPC collection tube into the reaction vessel with dry THF (3 mL) and the flask was cooled to 0 °C. A 2.7 M solution of phenyllithium (0.77 mL, 2.08 mmol, Aldrich Chemical Co.) in 7:3 cyclohexane/ether was quickly syringed into the solution followed by 1.5 h of stirring at 0 °C. Trimethylsilyl chloride[18] (0.76 mL, 7.00 mmol) was rapidly added, the cooling bath was removed, and the mixture was stirred 30 min at room temperature. The bis(trimethylsilyl) derivative was then hydrolyzed by addition of aqueous 1 M HCl (2 mL) and rapid stirring for 1 h. The layers were separated, the aqueous phase was extracted with ether (2 × 10 mL), and the combined organic phases were dried and concentrated to ~0.5 mL. The ketone product was purified for shift reagent analysis by VPC on column A at 145 °C. Yields of 80 to 90% were realized.

General Procedure Used for Determining Enantiomeric Ratios with NMR Chiral Shift Reagent Eu(hfc)$_3$. The VPC purified sample was dissolved in dry benzene-d_6. The optimum sample size was about 15 mg. This gave an adequate signal-to-noise ratio in the NMR allowing reasonably accurate and precise integrations to be measured, yet kept the substrate concentration low enough so that an excessively large amount of shift reagent was not required to produce the necessary peak separations. The shift reagent was added in about 50-mg portions to the NMR tube. After each addition the solution was agitated to dissolve the shift reagent, nitrogen was bubbled through the solution for 5 min with a drawn out Pasteur pipet, and the spectrum was measured. The integral ratios reported were an average of at least 10 scans with a 30-s delay between each scan. Commercial Eu(hfc)$_3$ contains an insoluble trace impurity; samples requiring large amounts of shift reagent (>300 mg) were therefore filtered and deoxygenated once more before the final spectral determinations were made.

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Registry No. (2*R*,3*R*)-(+)-**1**-*t*, 88546-86-5; (*S*,*S*,*S*)-**1**-*a*, 91230-87-4; **3**, 91230-88-5; **4**, 71777-36-1; **6**, 54522-92-8; **7**, 91230-89-6; **8**, 91230-90-9; **9**, 91230-91-0; **10**, 91230-93-2; **11**, 91230-94-3; $I^{13}CH_3$, 4227-95-6; *dl*-menthyl α-deuteriodiazoacetate, 80594-25-8; *d*-menthyl *trans*-1-(*S*),2(*R*),3(*R*)-trideuterio-2-phenylcyclopropanecarboxylate-*3*-^{13}C, 91230-92-1; *l*-menthyl *trans*-1(*S*),2(*R*),3(*R*)-trideuterio-2-phenylcyclopropanecarboxylate-*3*-^{13}C, 91279-52-6; *d*-menthyl *cis*-1(*R*),2(*R*),3(*R*)-trideuterio-2-phenylcyclopropanecarboxylate-*3*-^{13}C, 91279-51-5; *l*-menthyl *cis*-1(*R*),2(*R*),3(*R*)-trideuterio-2-phenylcyclopropanecarboxylate-*3*-^{13}C, 91279-53-7.

Precise Structural Characterizations of the Hexaaquovanadium(III) and Diaquohydrogen Ions. X-ray and Neutron Diffraction Studies of $[V(H_2O)_6][H_5O_2](CF_3SO_3)_4$

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Abstract: The title compound, a new one, the preparation of which is described, has been investigated structurally by both X-ray diffraction at ca. 295 K and neutron diffraction at ca. 20 K. The space group is $P\bar{1}$ and the unit cell has the following dimensions, where in each case the X-ray value is given first followed by the neutron value: a = 8.950 (1) Å, 8.942 (8) Å; b = 9.112 (1) Å, 8.902 (8) Å; c = 8.928 (2) Å, 8.774 (8) Å; α = 103.38 (1)°, 103.4 (2)°; β = 93.75 (2)°, 95.2 (1)°; γ = 70.19 (1)°, 69.9 (2)°; V = 666.4 (3) Å^3, 638 (2) Å^3. The structure was first solved and refined (211 variables) by using 2605 independent X-ray reflections with $F^2 > 3\sigma(F^2)$ to R = 0.046. Neutron data, 2137 reflections with $F^2 > 2\sigma(F^2)$, were then used to refine 261 variables including all hydrogen atoms anisotropically to R = 0.067. The structure consists of centrosymmetric $[V(H_2O)_6]^{3+}$ and $H_5O_2^+$ cations and $CF_3SO_3^-$ anions. All hydrogen atoms participate in hydrogen bonds. The $H_5O_2^+$ ion appears to be truly centrosymmetric with an O···O distance of 2.430 (3) Å at 20 K; the configuration at each oxygen atom is highly pyramidal. The $[V(H_2O)_6]^{3+}$ cation has nearly flat water molecules (i.e., sums of bond angles about oxygen atoms are 357.7–359.7°), and these are arranged to give the hexaaquo ion essentially D_{3d} symmetry of the sort in which the six hydrogen atoms of three mutually cis water molecules are essentially coplanar. Possible reasons for the adoption of this particular highly symmetric arrangement are discussed.

Definitive structural information on hydrated ions is surprisingly scarce,[2-7] considering the importance of the subject. The principal difficulty, of course, is that a full description of such species requires accurate knowledge of hydrogen atom positions and the only generally applicable source of precise data on this point is neutron crystallography. Of course, there are several requirements to obtain accurate and useful neutron diffraction data. Crystals of considerably greater volume than those used for X-ray crystalography are needed (typically at least 100 times greater), and for many interesting compounds such crystals cannot be grown. Furthermore, as in X-ray work, it is desirable to have well-ordered crystals. Finally, to obtain the fullest benefit from the neutron diffraction data, it is best to collect it at a very low temperature and this means that the crystal must not undergo any interfering

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