dimethylsulfone,[29] as well as with the guanidinium ion.[30] In each structure, the two guest molecules approach from the opposite sides of the crown ring, with N-H···O or C-H···O hydrogen bonds stabilizing the interaction. The 18-crown-6 ring in the sulfonamide complex has an elliptical shape, with a conformation different from that of the uncomplexed molecule[25] and from that found here, although all C-C torsion angles are gauche, near 66°. The 18-crown-6 ring in the guanidinium complex[30] has also a conformation different from that of the uncomplexed molecule and that found here, with the guanidinium ions tipped at rather high angles to the median crown plane and each joined to the crown ring by only a single hydrogen bond. The crown ring in the dinitrophenylhydrazine complex[27] has the nearly ideal crown conformation; each ring oxygen is involved in a N-H···O hydrogen bond. In the complex with dimethylsulfone,[29] one methyl group of each dimethylsulfone molecule is more or less centered over the crown ring, which also has the nearly ideal crown conformation. This arrangement is similar to that in the complex of 18-crown-6 with dimethyl acetylenedicarboxylate.[26] Cationic repulsion would make such an arrangement of two perching RNH_3^+ groups on opposite faces of a single crown ring unstable.

Molecular and Ionic Packing. We have commented already on some features of the packing in these structures; that for **2** is illustrated in Figure 4. There are no unusually short contacts in any of the structures. In each structure the shortest apparent intermolecular H···H distances are around 2.25-2.4 Å, but their significance is questionable because the hydrogen positions are of limited precision and are on the average about 0.1 Å too close to the atoms to which the hydrogens are bonded, as is common with X-ray structure determinations. The shortest intermolecular C···O distances are in the range 3.24-3.4 Å, usually involving perchlorate oxygen atoms, and do not seem of any particular significance.

Conclusion. Our principal findings are as follows. (1) Despite arguments that an ammonium or substituted ammonium ion is too large to fit into an 18-crown-6 ring, it can readily move almost to the center of the ring, as in the hydrazinium complex, if its stability in such a position is even moderately enhanced by other interactions. (2) The 18-crown-6 ring in the present structures for which we were able to measure vibrational parameters precisely is itself rigid and holds the $-NH_3^+$ group firmly as well. The atoms attached to the $-NH_3^+$ group undergo considerably greater motion, in directions predictable from their patterns of hydrogen bonding. (3) The orientation of the $N^+\cdots O$ line relative to the tetrahedral and trigonal directions at each C-O-C group of a crown ring is governed primarily by the depth of penetration of the NH_3^+ into the ring, irrespective of the disposition of hydrogen bonds to the ring oxygen atoms.

Acknowledgment. This work was supported in part by NSF Grants GP-28248, CHE77-18748, CHE80-22526, and CHE78-27084. D.S.L. has been supported in part also by a UCLA Chancellor's Fellowship. We are grateful as well to the UCLA Office of Academic Computing and to Dr. C. E. Strouse and Dr. L. H. Levine for their help and cooperation.

Registry No. 1, 80243-90-9; **2**, 80243-92-1; **3**, 80243-93-2.

Supplementary Material Available: The U values for all anisotropic atoms (Tables IIA, IIB, IIC), observed and calculated structure factors (amplitudes for **1**) (Tables IIIA, IIIB, IIIC), and values of individual bond lengths, bond angles, and torsion angles (Tables IVA, IVB, and IVC) (84 pages). Ordering information is given on any current masthead page.

(29) Bandy, J. A.; Truter, M. R.; Vögtle, F. *Acta Crystallogr., Sect. B* **1981**, *B37*, 1568-1571.
(30) Bandy, J. A.; Truter, M. R.; Wingfield, J. N.; Lamb, J. D. *J. Chem. Soc, Perkin Trans. 2* **1981**, 1025-1030.

Complete Kinetic Analysis of the Thermal Stereomutations of (+)-(1*S*,2*S*,3*R*)-*r*-1-Cyano-*t*-2-methyl-1,2,*t*-3-trideuteriocyclopropane

John E. Baldwin* and Charles G. Carter

Contribution from the Department of Chemistry, University of Oregon, Eugene, Oregon 97403.
Received June 1, 1981

Abstract: (+)-(1*S*,2*S*,3*R*)-*r*-1-Cyano-*t*-2-methyl-1,2,*t*-3-trideuteriocyclopropane has been synthesized in optically pure form. The kinetics of thermal stereomutations which interconvert this and seven other isomeric cyclopropanes have been followed: at 335.4 °C in the gas phase, the title compound undergoes stereomutations with rate constants ($\times 10^5$ s) $k_1 = 0.55$, $k_2 = 0.61$, $k_3 = 0.10$, $k_{12} = 0.88$, $k_{13} = 0.083$, and $k_{23} = 0$; the *cis*-1-cyano-2-methyl-1,2,3-trideuteriocyclopropanes exhibit stereomutation rate constants ($\times 10^5$ s) $k'_1 = 0.62$, $k'_2 = 0.69$, $k'_3 = 0.15$, $k'_{12} = 1.31$, $k'_{13} = 0.09$, and $k'_{23} = 0$. While cyclopropanes 1,2-disubstituted with potent radical-stabilizing groups such as phenyl, cyano, and vinyl give stereomutation products by way of C(1)-C(2) bond cleavage only, the deuterium-labeled 1-cyano-2-methylcyclopropanes experience thermal stereomutations consistent with the intermediacy of two distinct trimethylene diradicals, one formed through cleavage of the C(1)-C(2) bond, the other by breaking C(1)-C(3).

Even though the thermal stereomutations of cyclopropanes have been studied most intensively, they remain imperfectly understood.[1] These stereomutations may involve epimerization at one carbon, or at two carbons simultaneously; which of the two types of epimerization predominates in a given cyclopropane is often hard to rationalize in conformity with existing theory and cannot in general be predicted.[1,2]

Earlier experimental studies with unconstrained cyclopropanes have frequently been interpreted with the aid of an assumption: that only processes arising from cleavage of the most substituted

(1) Berson, J. A. "Rearrangements in Ground and Excited States"; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 1, p 311.
(2) Willcott, R. M.; Cargill, R. L.; Sears, A. B. *Prog. Phys. Org. Chem.* **1972**, *9*, 25-98.

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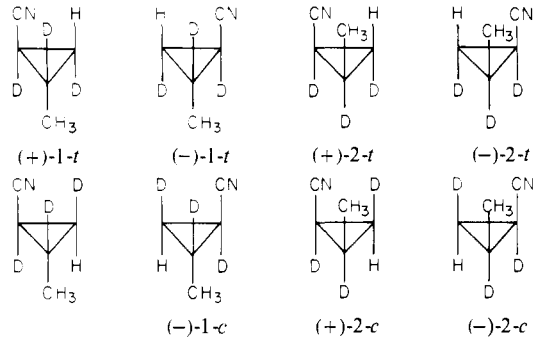
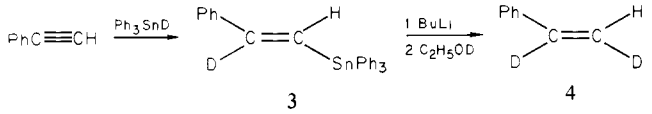
carbon–carbon bond will be involved.[3] Interpretations of kinetic data for cyclopropane stereomutations which depend upon this "most substituted bond hypothesis" being strictly valid have often been advanced with an appropriate caveat, and, in two recent studies, the hypothesis has been tested rigorously. 1-Cyano-2-phenyl-1,3-dideuteriocyclopropanes[4] and 1-cyano-2-(*cis*-propenyl)-3-methylcyclopropanes[5] show one-center epimerizations at C(1) and C(2), and two-center epimerization at C(1) and C(2) simultaneously (rate constants k_1, k_2, and k_{12}); other epimerizations are not kinetically competitive.[6]

We now report a test of the "most substituted bond hypothesis" with compounds having only one powerful radical-stabilizing substituent, the eight isomers of 1,2,3-trideuterio-1-cyano-2-methylcyclopropane. The symbols used to represent these compounds have three parts: a sign of rotation, **1** for trans cyano and methyl or **2** for cis cyano and methyl, and *t* or *c*, giving the trans or cis geometrical disposition between the cyano function and the deuterium at C(3).



Results

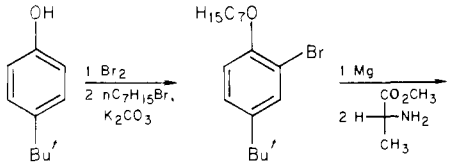
Syntheses. (+)-(1*S*,2*S*,3*R*)-*r*-1-Cyano-*t*-2-methyl-1,2,*t*-3-trideuteriocyclopropane, (+)-**1**-*t*, was prepared following methods which have been outlined in previous related work.[4,7] The reaction of triphenyltin deuteride[8] with phenylacetylene gave α-deuterio-*trans*-β-triphenylstannylstyrene[9] (**3**); this intermediate was



3 4

transmetalated with *n*-butyllithium in THF at −78 °C and the lithio derivative was quenched with C_2H_5OD to give *cis*-α,β-dideuteriostyrene (**4**),[10] estimated by NMR spectroscopy to be 98:2 cis:trans.

An optically active copper catalyst for additions of diazoesters to olefins patterned after the work of Aratani, Yoneyoshi, and Nagase[11] on asymmetric syntheses of chrysanthemic acid was prepared from 4-*tert*-butylphenol. Monobromination[12] followed by alkylation[13] with *n*-heptyl bromide using K_2CO_3 in acetone gave 2-bromo-4-*tert*-butylphenyl heptyl ether (**5**). The corresponding



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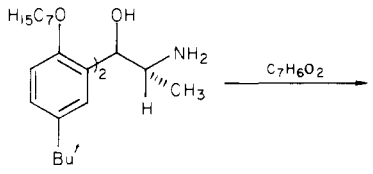

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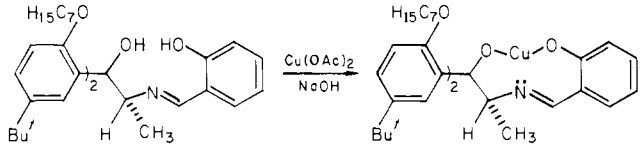

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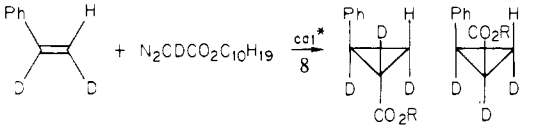
Grignard reagent was allowed to react[14] with D-alanine methyl ester in THF to give (2*R*)-1,1-diaryl-2-amino-1-propanol (**6**). This primary amine was condensed with salicylaldehyde (benzene, *p*-toluenesulfonic acid) to afford a salicylaldimine (**7**) as a bright yellow oil. When this imine was treated with cupric acetate and aqueous hydroxide in ethanol, there was obtained copper complex **8**, $[\alpha]_{546}$ +465°, as a viscous, dark-green oil.

In the presence of this chiral copper catalysis, *dl*-menthyl α-deuteriodiazoacetate[15,16] and *cis*-α,β-dideuteriostyrene gave a mixture of cis and trans esters, **9a** and **10a**, which were hydrolyzed with aqueous-methanolic NaOH at reflux. A small sample of



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a, R = *dl*-menthyl
b, R = H
c R = CH_3

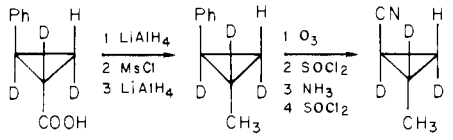
the cis and trans acids **9b** and **10b** was esterified with diazomethane; NMR analysis indicated an 85:15 trans:cis mixture. A sample of trans methyl ester **9c** was combined with the chiral shift reagent Eu–Opt in $CDCl_3$ and shown to be 80% optically pure, the (+) antipode predominating. The 85:15 mixture of trans and cis acids was converted to the corresponding quinine salts;[17] two recrystallizations from ethanol/hexanes, followed by hydrolysis of salt with dilute HCl, gave resolved trans acid. Its methyl ester (+)-**9c** had $[\alpha]_D$ +327° (lit.[17] unlabeled analogue, $[\alpha]_D$ +335°); the NMR spectrum in the presence of Eu(hfbc)$_3$[18] implied 100% optical purity.

This route has several advantages over the previously used[4] and more conventional route. While the overall yield remains about the same whether one uses $CuSO_4$ and ethyl diazoacetate or complex **8** and *dl*-menthyl diazoacetate with styrene, the **8**-catalyzed reaction gives a higher proportion of trans product and that

(3) O'Neal, H. E.; Benson, S. W. *J. Phys. Chem.* **1968**, *72*, 1866–1887.
(4) Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1978**, *100*, 3942–3944. See also Doering, W. von E.; Barsa, E. A. *Tetrahedron Lett.* **1978**, 2495–2498.
(5) Doering, W. von E.; Barsa, E. A. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 2355–2357.
(6) Doering and Barsa[5] did observe epimerization at C(3) at a 40° higher temperature.
(7) Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1979**, *101*, 1325–1326. Baldwin, J. E.; Chang, G. E. C. *Tetrahedron*, in press.
(8) Kuivila, H. G.; Beumel, O. F., Jr. *J. Am. Chem. Soc.* **1961**, *83*, 1246–1250.
(9) van der Kerk, G. J. M.; Noltes, J. G. *J. Appl. Chem.* **1959**, *9*, 106–113; *Chem. Abstr.* **1960**, *54*, 1379a.
(10) Seyferth, D.; Vaughan, L. G.; Suzuki, R. *J. Organomet. Chem.* **1964**, *1*, 437–448.
(11) Aratani, T.; Yoneyoshi, Y.; Nagase, T. *Tetrahedron Lett.* **1975**, 1707–1710; **1977**, 2599–2602.
(12) Rosenwald, R. H. *J. Am. Chem. Soc.* **1952**, *74*, 4602–4605.
(13) Allen, C. F. H.; Gates, J. W., Jr. "Organic Syntheses", Collect. Vol. III; Wiley: New York, 1955; pp 418–420.
(14) Greenstein, J. P.; Winitz, M. "Chemistry of the Amino Acids"; Wiley: New York, 1961; p 926.
(15) Harada, K.; Hayakawa, T. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 191–194.
(16) Takamura, N.; Mizoguchi, T.; Koga, K.; Yamada, S. *Tetrahedron* **1975**, *31*, 227–230.
(17) Sugita, T.; Inouye, Y. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1075–1076. Baldwin, J. E.; Löliger, J.; Rastetter, W.; Neuss, N.; Huckstep, L. L.; De La Higuerra, N. *J. Am. Chem. Soc.* **1973**, *95*, 3796–3797.
(18) 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.

product is formed with about 80% enantiomeric enrichment. These two factors make possible resolution of the trans acid directly, without prior conversion of the esters obtained in the condensation through base-catalyzed epimerization to the thermodynamically controlled trans-rich mixture. The **8**-catalyzed alternative proved more efficient overall and it avoided possible loss of deuterium at C(1) during base-catalyzed epimerizations.[4]

The sequence used to transform the resolved (+)-acid **9b** into (+)-(1*S*,2*S*,3*R*)-*r*-1-cyano-*t*-2-methyl-1,2,*t*-3-trideuteriocyclopropane is outlined in the scheme below. The acid function was

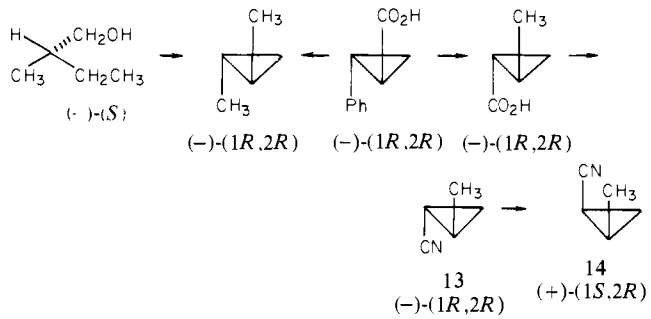


(+)-**9b** **11** (+)-**1**-*t*

reduced with $LiAlH_4$ in THF to give the cyclopropylcarbinol in quantitative yield; this alcohol was converted to the methane sulfonyl ester, which was reduced with $LiAlH_4$ to give the chiral trideuterio-*trans*-2-methyl-1-phenylcyclopropane **11**. Ozonolysis followed by oxidative work up afforded the (+)-(1*S*,2*S*,3*R*) trans acid, $[\alpha]_D$ +95.8 ± 2.7° ($CHCl_3$),[17] which was converted to the desired trans nitrile (+)-**1**-*t* by way of the acid chloride and acid amide. The product had $[\alpha]_D$ +150 ± 4° ($CHCl_3$).[19,20]

Racemic samples of *trans*- and *cis*-trideuterio nitriles were prepared similarly, using $CuSO_4$ as catalyst for the diazoester condensation.[21]

Stereochemical Assignments. The absolute configuration of (−)-(1*R*,2*R*)-*trans*-2-methylcyanocyclopropane (**13**) and its (+)-(1*S*,2*R*) cis isomer **14** have been established by correlation with (−)-(1*R*,2*R*)-2-phenylcyclopropanecarboxylic acid using (−)-(1*R*,2*R*)-2-methylcyclopropanecarboxylic acid as a relay point.[17,20] The absolute stereochemistry of (−)-(1*R*,2*R*)-2-phenylcyclopropanecarboxylic acid has been related to (−)-(1*R*,2*R*)-1,2-dimethylcyclopropane,[22] a compound of securely established absolute stereochemistry;[23] it has been related with (−)-(*S*)-2-methylbutanol-1, which in turn has been correlated with L-(+)-isoleucine. Since deuterium substitution will not affect



the absolute stereochemistry, (+)-**1**-*t* must have the (1*S*,2*S*,3*R*) configuration and (−)-**2**-*t* the (1*R*,2*S*,3*R*) configuration.

Kinetics. Pyrolyses were done in a static gas-phase reactor at 335.4 °C. At this temperature, stereomutations of the trideuterio-1-cyano-2-methylcyclopropanes are about two orders of magnitude faster than structural isomerizations giving trideuterio-*cis*- and *trans*-2-pentenonitriles,[24] with both *cis*- and *trans* cyclopropane isomers forming olefins at the same rate, within estimated experimental uncertainties. This competitive first-order isomerization to olefins with rate constant $k_0 = 2.85 \times 10^{-7}$ s^{-1} was included in the kinetic analyses.

Table I. Calculated and Observed Mole Percent Concentrations of the Cyclopropanes 1-*t*, **1**-*c*, 2-*c*, and 2-*t* at 335.4 °C

time, min	1-*t*	1-*c*	2-*c*	2-*t*
0	98.1	1.9	0	0
150	80.2	10.1	4.5	5.2
	(80.8)[a]	(9.1)	(4.5)	(5.4)
200	75.3	11.4	6.7	6.6
	(76.0)	(11.0)	(5.8)	(6.9)
250	70.2	13.6	7.8	8.0
	(71.6)	(12.6)	(7.1)	(8.3)
350	64.6	15.5	9.0	10.3
	(64.0)	(15.5)	(9.2)	(10.6)
425	59.8	17.1	10.8	11.5
	(59.3)	(17.2)	(10.7)	(12.1)
450	57.7	17.0	11.9	12.4
	(57.7)	(17.8)	(11.2)	(12.6)
625	49.6	19.9	14.0	15.3
	(49.0)	(20.6)	(14.0)	(15.3)
0	96.8	3.2	0	0
300	67.0	14.6	8.4	9.4
	(66.9)	(14.8)	(8.3)	(9.6)
500	55.8	18.3	12.2	12.8
	(54.4)	(19.1)	(12.1)	(13.5)
0	0.9	0	1.9	97.2
150	6.2	6.1	12.1	75.6
	(6.8)	(5.1)	(11.8)	(76.1)
200	8.8	6.6	14.3	70.3
	(8.4)	(6.6)	(14.2)	(70.7)
250	10.7	7.0	16.5	65.3
	(9.9)	(8.0)	(16.1)	(65.7)
300	11.6	9.6	17.6	60.9
	(11.1)	(9.3)	(17.8)	(61.3)
350	13.0	10.1	19.6	56.7
	(12.4)	(10.4)	(19.2)	(57.4)
450	13.8	13.5	20.3	51.8
	(14.5)	(12.6)	(21.3)	(50.7)
500	17.0	12.0	21.8	48.4
	(15.5)	(13.6)	(22.2)	(48.0)
550	16.1	14.4	22.8	45.8
	(16.2)	(14.5)	(22.3)	(45.5)
600	17.1	14.4	23.0	44.6
	(17.0)	(15.3)	(23.4)	(43.3)

[a] Calculated values (in parentheses) for the parameters (× 10^5 s) $(k_1 + k_{23}) = 0.55$; $(k_2 + k_{13}) = 0.69$, $(k_3 + k_{12}) = 0.98$, $(k'_3 + k'_{12}) = 1.46$; $K_{eq} = 0.89$, and $k_0 = 2.85 \times 10^{-7}$ s^{-1}.

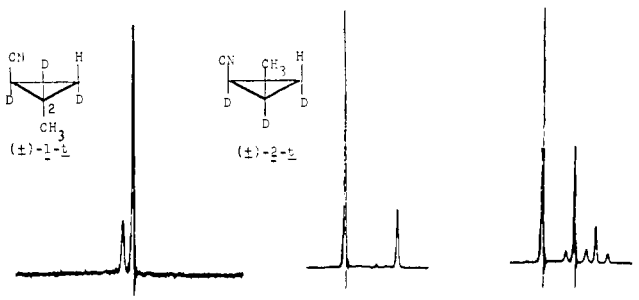


Figure 1. ^{1}H NMR spectra of **1**-*t* (left), **2**-*t* (center), and a mixture of **1**-*t*, **1**-*c*, **2**-*t*, and **2**-*c* (right) recovered from pyrolysis of **2**-*t* for 600 min at 335.4 °C.

The isomerizations interconverting the four trans isomers **1** and the four cis isomers **2** were followed by analytical GLPC. The usual kinetic treatment for reversible first-order isomerizations provided values for the rate constant for conversion of **1** to **2** $(k_1 + k_2 + k_{13} + k_{23}) = 1.24 \times 10^{-5}$ s^{-1} and the equilibrium constant $K = 0.89$. The data are summarized in Table I.

After pyrolysis samples had been analyzed chromatographically, NMR spectroscopy was employed to measure the mole fractions of the four distinguishable isomers; the singlet C(3)H absorptions in the four compounds were clearly separated when C_6D_6 was used as solvent: 0.49 (**1**-*t*), −0.15 (**1**-*c*), 0.08 (**2**-*t*), 0.18 (**2**-*c*). Figure

(19) Bergman[20] converted (−)-(1*R*,2*R*)-*trans*-2-methylcyclopropanecarboxylic acid of $[\alpha]_D$ −46.4° to the corresponding nitrile, $[\alpha]_D$ −63.1° ($CHCl_3$), and estimated it to be 60% optically pure.

(20) Bergman, R. G. *J. Am. Chem. Soc.* **1969**, *91*, 7405–7411.

(21) Berger, A.; Yost, W. L. *J. Am. Chem. Soc.* **1948**, *70*, 2198–2201. DePuy, C. H.; Dappen, G. M.; Eilers, K. L.; Klein, R. A. *J. Org. Chem.* **1964**, *29*, 2813–2815.

(22) Inouye, Y.; Sugita, T.; Walborsky, H. M. *Tetrahedron* **1964**, *20*, 1695–1699.

(23) Doering, W. von E.; Kirmse, W. *Tetrahedron* **1960**, *11*, 272–275, and references therein.

(24) Gajewski, J. J.; Weber, R. J.; Braun, R.; Manion, M. L. *J. Am. Chem. Soc.* **1977**, *99*, 816–821.

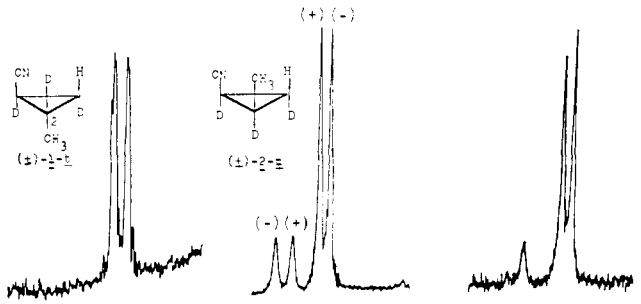
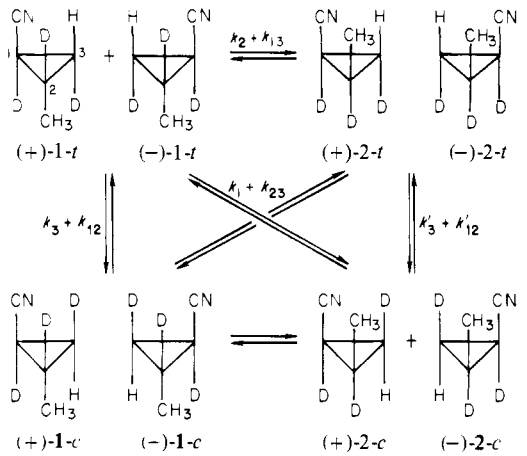


Figure 2. ^{1}H NMR spectra taken in the presence of Eu(hfbc)$_3$ of C(3)H in (±)-**1**-*t* (left), (±)-**2**-*t* (center), and the four isomers of **2** derived from thermal isomerization of (+)-**1**-*t* (right).

1 shows the ^{1}H NMR spectra of racemic **1**-*t* and **2**-*t* and of a pyrolysis mixture derived from **2**-*t*; the more downfield methyl singlet corresponds to **2**-*t* and **2**-*c*.

The concentration vs. time data (Table I; 21 sets, 11 from **1**-*t*, 10 from **2**-*t*) were fit to theoretical curves based on exact solutions to the kinetic expressions appropriate to the stereomutations to give the parameters (×10^5 s) $(k_1 + k_{23}) = 0.55$, $(k_2 + k_{13}) = 0.69$, $(k_3 + k_{12}) = 0.98$, and $(k'_3 + k'_{12}) = 1.46$. Other rate constants in the scheme are evident from microscopic reversibility and K_{eq}.



Complete analysis of all eight isomers may not be reached through chromatography, NMR spectroscopy, and polarimetry, but NMR with the aid of the chiral shift reagent tris[3-(heptafluorobutyryl)-*d*-camphorato]europium(III), Eu(hfbc)$_3$,[18] provided the required analytical discriminations. In the presence of Eu(hfbc)$_3$, the enantiotopic C(3)H singlets in **1**-*t* and **2**-*t* are separated, and the methyl group cis to cyano in (+)-**2** and (−)-**2** can be distinguished; the more downfield of the two methyl singlets is due to the (+) isomer. Figure 2 demonstrates these separations of enantiotopic proton resonance lines.

A sample of **2**-*t* enriched in the (+) antipode was prepared[20] and examined with the aid of Eu(hfbc)$_3$; the more downfield C(3)H line proved to be associated with the (−) isomer, (−)-**2**-*t*.

The trans products from pyrolyses of (+)-**1**-*t* were found to contain no (−)-**1**-*t*; only one of the pair of resonance lines observed with racemic material (Figure 2, left) could be detected. One may conclude, then, that k_{123}, the rate constant for the triple isomerization process, is zero, as expected, and that indirect routes from (+)-**1**-*t* to (−)-**1**-*t* are not important at relatively short reaction times. This fact, together with the NMR-determined ratio of **1**-*t* to **1**-*c* and the observed rotation of **1**, permitted calculation of concentrations of all of the trans isomers.

The optical purity of cis products could be calculated from the relative intensities of the enantiotopic methyl singlets in the presence of Eu(hfbc)$_3$ (Figure 2). Thermolysis of (+)-**1**-*t* leads to cis isomers slightly enriched in the (−) antipodes, and (+)-**2**-*t* is formed much more rapidly than (−)-**2**-*t* (85:15 ratio). From these data and the results of the kinetic study with optically inactive substrates, the concentrations of all four cis isomers in a pyrolysis mixture could be calculated.

Table II. Calculated[a] and Observed Mole Percent Concentrations of the Eight 1,2,3-Trideuterio-1-cyano-2-methylcyclopropanes from the Pyrolysis of (+)-1-*t* at 335.4 °C

	300 min		500 min	
isomer	exptl	calcd	exptl	calcd
(+)-1-*t*	67.0	66.3	55.8	53.3
(+)-1-*c*	2.7	3.5	4.4	3.7
(−)-**1**-*t*	0	0.7	0	1.3
(−)-1-*c*	11.9	11.2	13.9	15.3
(+)-2-*t*	7.8	8.1	10.9	11.5
(+)-2-*c*	0.6	0.6	1.0	1.2
(−)-2-*t*	1.6	1.4	1.9	2.0
(−)-**2**-*c*	7.8	7.6	11.2	10.9

[a] Calculated for the parameters $K = 0.89$, $k_1 = 0.55 \times 10^{-5}$ s^{-1}, $k_2 = 0.61 \times 10^{-5}$ s^{-1}, $k_3 = 0.10 \times 10^{-5}$ s^{-1}, $k_{12} = 0.88 \times 10^{-5}$ s^{-1}, $k_{13} = 0.083 \times 10^{-5}$ s^{-1}, $k_{23} = 0$, $k_3' = 0.15 \times 10^{-5}$ s^{-1}, $k_{12}' = 1.31 \times 10^{-5}$ s^{-1}; and $k_0 = 2.85 \times 10^{-7}$ s^{-1}. The starting material was 96.8% (+)-1-*t* and 3.2% (+)-**1**-*c*.

The symmetry of the kinetic scheme appropriate to stereomutations among the eight isomers of **1** and **2** makes an exact solution of the kinetic expressions possible.[25] A computer program based on these exact integrated expressions for the concentrations of each of the eight isomers as a function of time, given initial concentrations and rate constants, was used to compare calculated and observed concentrations and to find optimum values of rate constants.

Given the earlier results with racemic substrates, and the direct experimental indication that [(−)-**1**-*t*] in pyrolysis mixtures is zero or nearly zero, the computer-aided search for best rate constants proceeded with but three unknowns: k_2/k_{13}, k_1/k_{23}, and k_3/k_{12}. Starting from trans material, we could not gain experimental data suitable for a clear separation of $(k'_3 + k'_{12})$ into its component parts, for the calculated concentrations are relatively insensitive to k'_3/k'_{12}. The calculations were done, then, assuming $k_3/k_{12} = k'_3/k'_{12}$.

Table II gives experimental and calculated values for concentrations of the eight isomers obtained through pyrolysis of (+)-**1**-*t* for 300 and for 500 min at 335.4 °C; the calculated concentrations are based on the parameters (×10^5 s) $k_1 = 0.55$, $k_2 = 0.61$, $k_3 = 0.10$ $k_{12} = 0.88$, $k_{13} = 0.083$, $k_{23} = 0$, $k'_3 = 0.15$, and $k'_{12} = 1.31$; $K_{eq} = 0.89$; and $k_0 = 2.85 \times 10^{-7}$ s^{-1}.

For the experimental and calculated concentrations summarized in Table I, the mean and standard deviation in the 72 comparisons is +0.02 ± 0.65%. For the data of Table II, the mean and standard deviation in the 16 comparisons between experimental and calculated concentrations is −0.01 ± 0.94%. For a calculation with the rate constants (×10^5 s) $k_1 = 0.55$, $k_2 = 0.69$, $k_{12} = 0.98$, $k'_{12} = 1.46$, and $k_3 = k_{13} = k_{23} = k'_3 = 0$, the standard deviation between experimental (Table II) and calculated concentrations increased to ±1.5%. The two sets of parameters differ most strikingly in predictions for the mole percent ratio (−)-**2**-*t*/(+)-**2**-*t*; the observed ratios at 300 and 500 min are 0.21 and 0.17; the calculated ratios of Table II are 0.17 and 0.17; the parameter set with $k_3 = k_{13} = k_{23} = k'_3 = 0$ give as calculated values of these ratios 0.03 and 0.03.

Discussion

The rate constants which describe the thermal stereomutations interconverting the eight isomers of 1,2,3-trideuterio-1-cyano-2-methylcyclopropane imply that processes arising from cleavage of the C(1)–C(2) bond are favored, but two ascribable to breaking C(1)–C(3), k_3 and k_{13}, do contribute significantly. The stereomutations are consistent with the intermediacy of two distinct trimethylene diradicals.

The most substituted bond hypothesis is not rigorously valid here; an alkyl-substituted carbon is not sufficiently different from an unsubstituted or a deuterium-labeled carbon in a cyanocyclopropane at 335.4 °C to control the locus of bond cleavage perfectly.

(25) Baldwin, J. E.; Carter, C. G.; Chang, G. E. C., unpublished results.

Our experiments give no indication of how much of the overall observed one-center epimerization at C(1) is achieved through C(1)–C(3) fragmentation. Comparisons of relative rates with other systems, then, must be restricted to k_2/k_{12}. For 2-substituted-1-cyanocyclopropanes, in which the substituent is isopropenyl,[26] phenyl,[4] methyl, and deuterium, the k_2/k_{12} ratio varies but little: 0.4, 0.5–0.6, 0.7, and 1.2. The balance between one-center and two-center epimerization in such a congruent series of 1,2-disubstituted cyclopropanes does not show marked sensitivity to the character of the C(2) substituent, even though these substituents have substantial influence on $(k_2 + k_{12})$.

The trideuterio-1-cyano-2-methylcyclopropane system is the third 1,2,3-trisubstituted cyclopropane subjected to a full stereochemical study,[4,5] and the first to show the involvement of two distinct trimethylene diradicals. The most substituted bond hypothesis breaks down in this case although in a qualitative sense its logic is still apparent.

For other cyclopropanes having but one powerful radical-stabilizing substituent or cyclopropanes lacking even one, thermal stereomutations observed at relatively elevated temperatures may be expected now to involve to various extents departures from the behavior expected from the most substituted bond hypothesis.

If this investigation had been conducted with an equimolar mixture of (+)-**1**-*t* and (+)-**1**-*c*, no stereochemical distinctions at C(3) could have been made, yet some stereomutations could have been followed chromatographically and polarimetrically. With the aid of the most substituted bond hypothesis, the kinetic data would have given accurate values for k_2 and k_{12}, but k_1 would have appeared 15% too high—0.63 rather than 0.55×10^{-5} s^{-1}.

For some purposes, an error of this magnitude would never impair understanding or confuse a mechanistic issue; yet several of the remaining puzzles associated with the stereomutations of cyclopropanes may require knowing rate constants for k_i and k_{ij} processes to much higher tolerances, and the limits of applicability of the most substituted bond hypothesis will have to be countered with appropriate experimentation.

Experimental Section

Solutions of volatile liquids encountered in this work were ordinarily concentrated by distillation through an 11 mm × 1 m vacuum-jacketed column packed with glass helices. Reaction mixtures following lithium aluminum hydride reductions were worked up by adding sequentially *n* mL of H_2O, *n* mL of 15% aqueous NaOH, and 3*n* mL of H_2O for each *n* g of $LiAlH_4$, followed by drying ($MgSO_4$), filtration, and concentration.[27] ^{1}H NMR spectra were taken on a Varian XL-100 instrument using $CDCl_3$ solutions. The chemical shifts reported in ppm downfield from Me_4Si are uncalibrated and measured relative to $CHCl_3$, δ 7.25.[28] Optical rotations were recorded on a Perkin-Elmer 141 polarimeter. Melting points are uncorrected and were obtained using a Kofler micro hot stage equipped with a Reichert Thermopan microscope.

Analytical GLPC work was done on either a Varian Aerograph 1520 chromatograph or a Perkin-Elmer F-11 chromatograph using column A, 2.4 m × 3 mm 10% free fatty acid phase (FFAP) on 50/80 mesh non-acid-washed dimethyldichlorosilane-treated Chromosorb W. Preparative GLPC separations were carried out on the Varian 1520 or on a Varian A-90P3 chromatograph with one of two aluminum columns: B, 0.3 m × 6 mm 25% Carbowax 20M on 60/80 mesh Chromosorb W; C, 3.2 m × 6 mm 10% Carbowax 20M on 60/80 mesh Chromosorb G.

Triphenyltin Deuteride.[8] Triphenyltin chloride (75 g, 0.19 mol) was reduced with lithium aluminum deuteride to give 64.3 g (94%) of triphenyltin deuteride.

α-Deuterio-*trans*-β-triphenylstannylstyrene (3).[9,10] The entire sample of triphenyltin deuteride prepared above (0.18 mol) was added to phenylacetylene (17.6 g, 0.17 mol) in a 1-L three-necked flask fitted with a mechanical sitrrer and nitrogen inlet. After 5 min the solution had solidified enough to stop the stirrer. The cake of reaction products was broken up and slurried in pentane. The slurry was filtered; the resulting white solid, collected after repeated washing with pentane and drying, amounted to 61.3 g (74%) of α-deuterio-*trans*-β-triphenylstannylstyrene, mp 114–119 °C (lit.[9] mp 119–120 °C for unlabeled compound).

***cis*-α,β-Dideuteriostyrene (4).** A solution of the stannylstyrene prepared above (49.5 g, 0.11 mol) in 300 mL of THF was cooled to −78 °C under an atmosphere of nitrogen. The solution was mechanically stirred while 1 equiv of *n*-butyllithium in hexane (2.4 M; Ventron) was added dropwise.[10] After the addition had been completed, stirring was continued as the reaction mixture was allowed to warm to 0 °C over a period of 2.5 h. It was cooled to −78 °C again and quenched with 15 mL of *O*-deuterioethanol. Pentane (300 mL) was added and the resulting suspension was suction filtered through a sintered glass funnel containing a Celite pad. Hydroquinone (ca. 50 mg) was added to the filtrate, which was then concentrated at room temperature under aspirator pressure. A second portion of pentane was added to the concentrate to precipitate additional butyltriphenyltin still present. After filtration and concentration of the pentane solution, flash distillation of the concentrate at 0.1 Torr into a dry ice cooled receiver yielded 5.5 g (47%) of *cis*-α,β-dideuteriostyrene: NMR δ 5.24 (0.023 H, br s), 5.74 (0.977 H, t, J = 2.5 Hz), 7.2–7.5 (5 H, m).

2-Bromo-4-*tert*-butylphenol. Bromination[12] of 4-*tert*-butylphenol (150 g, 1 mol) gave 219 g (100%) of crude product as a viscous oil.

2-Bromo-4-*tert*-butylphenyl Heptyl Ether (5). The crude phenol (219 g, 1 mol) was alkylated with heptyl bromide (200 g, 1.1 mol) using potassium carbonate (138 g, 1 mol) in acetone.[13] Kugelrohr distillation at 160 °C (0.1 mm) gave 269.3 g (85%) of ether **5**, a viscous oil whose NMR spectral properties agreed with expectations.

(2*R*)-2-Amino-1,1-bis(5-*tert*-butyl-2-heptyloxyphenyl)-1-propanol (6). D-Alanine methyl ester hydrochloride (2.2 g, 16 mmol) was allowed to react with the Grignard reagent derived from 2-bromo-4-*tert*-butylphenyl heptyl ether (50.4 g, 0.159 mol) in refluxing tetrahydrofuran.[14] The reaction solution was cooled and poured into ice water containing sulfuric acid; the organic and aqueous layers were separated and the aqueous phase was extracted with ether. The combined organic solutions were washed with 10% sulfuric acid and brine, dried ($MgSO_4$), filtered, and concentrated. Most of the unreacted 4-*tert*-butylphenyl heptyl ether was removed by distillation at reduced pressure. The residue was chromatographed with 2:1 hexane:benzene on 75 g of silica gel to give 3.6 g (41%) of amino alcohol **6** as a clear viscous oil.

Salicylaldimine 7 Derived from Amino Alcohol 6 and Salicylaldehyde. Amino alcohol **6** (3.6 g, 6.4 mmol) and salicylaldehyde (0.78 g, 6.4 mmol) were heated to reflux for 48 h in benzene with a trace of *p*-toluenesulfonic acid as water was removed azeotropically. Concentration of the benzene solution and chromatography (silica gel, 1% ether/hexanes) gave 1.75 g (41%) of salicylaldimine **7** as a bright yellow oil.

(+)-(*R*)-Copper(II) Complex of Aldimine 7 ((+)-8). Salicylaldimine **7** (1.75 g, 2.6 mmol) and cupric acetate monohydrate (0.53 g, 2.6 mmol) were dissolved in 200 mL of ethanol. Aqueous sodium hydroxide (10%, 10 mL) was added and the mixture was stirred for 1 h. The solution was diluted with water and extracted three times with benzene. The benzene extracts were dried (K_2CO_3), filtered, and concentrated to give 1.9 g (100%) of complex (+)-**8** as a viscous, dark-green oil which had $[\alpha]_{546}$ +465° (*c* 2.78, EtOH). The complex was dissolved in cyclohexane and the solution was stored over anhydrous potassium carbonate.

Menthyl Glycinate Hydrochloride.[15] Glycine (25 g, 0.33 mol), *dl*-menthol (61.5 g, 0.39 mol) and *p*-toluenesulfonic acid monohydrate (75 g, 0.39 mol) were heated to reflux in benzene until the theoretical amount of water had been collected in a Dean-Stark trap. The reaction solution was cooled, filtered, and concentrated at reduced pressure. The residue was dissolved in ether and repeatedly extracted with saturated sodium bicarbonate solution to remove acidic material. The ethereal portion was washed with water and brine, dried ($MgSO_4$), and filtered. Anhydrous hydrogen chloride was bubbled through the solution, precipitating the ester as a hydrochloride. The white crystals were washed with ether and dried (79.0 g, 96%).

Menthyl Diazoacetate.[16] A benzene solution of menthyl glycinate (74.9 g, 0.352 mol; regenerated from the corresponding hydrochloride), acetic acid (6.0 g, 0.01 mol), and isoamyl nitrite (42.9 g, 0.367 mol) was heated to reflux for 6 h, at which time a positive ninhydrin test was no longer obtained. The reaction mixture was cooled and washed in sequence with cold 10% sulfuric acid, ice water, cold saturated sodium bicarbonate, again with ice water, and finally with cold brine. It was then dried (Na_2SO_4), filtered, concentrated, and chromatographed on silica gel with benzene giving 57.3 g (73%) of diazoester: NMR δ 0.78 (3 H, d, J = 7 Hz), 0.89 (6 H, d, J = 6 Hz), 0.90–2.15 (9 H, m), 4.69 (1 H, s), 4.76 (1 H, t of d, J = 10, 4.5 Hz).

Ethyl α-Deuteriodiazoacetate.[29] Ethyl diazoacetate (25 g, 0.22 mol) was dissolved in 50 mL of methylene chloride in a 250-mL three-necked Morton flask. To this solution was added 10 mL of deuterium oxide (J.

(26) Doering, W. von E.; Sachdev, K. *J. Am. Chem. Soc.* **1974**, *96*, 1168–1187.
(27) Mičovič, V. M.; Mihailovič, M. L. J. *J. Org. Chem.* **1953**, *18*, 1190–1200.
(28) Silverstein, R. M.; Bassler, G. C. "Spectrometric Identification of Organic Compounds", Wiley: New York, 1967, p 135.
(29) Saegusa, T.; Ito, Y.; Shimizo, T.; Kobayashi, S. *Bull. Chem. Soc. Jpn.* **1969**, *42*, 3535–3538.

T. Baker), 10 drops of a 10% solution of sodium deuteroxide in deuterium oxide, and about 25 mg of benzylhexadecyldimethylammonium chloride. The mixture was stirred magnetically for 24 h under a nitrogen atmosphere. The layers were separated and the process was repeated two more times. After drying ($MgSO_4$), filtration, and concentration, there remained 25 g (100%) of diazoester that was shown by NMR analysis to have 98.5% deuterium incorporation at the α position: NMR δ 1.26 (3 H, t, J = 7 Hz), 4.22 (2 H, q, J = 7 Hz), 4.70 (0.015 H, s).

Menthyl α-Deuteriodiazoacetate. Menthyl diazoacetate (57.3 g, 0.256 mol) was deuterated through the procedure used to prepare ethyl α-deuteriodiazoacetate. The time for each exchange was extended, however, to 48 h. Three exchanges gave 48.2 g (84%) of diazoester having 99% deuterium incorporation at the α position as measured by NMR: 0.78 (3 H, d, J = 7 Hz), 0.89 (6 H, d, J = 6 Hz), 0.90–2.15 (9 H, m), 4.59 (0.01 H, s), 4.76 (1 H, t of d, J = 10, 4.5 Hz).

Menthyl *t*-2-Phenyl-1,2,*c*-3-trideuteriocyclopropanecarboxylate (9a) and Menthyl *c*-2-Phenyl-1,2,*t*-3-trideuteriocyclopropanecarboxylate (10a). Copper catalyst (+)-**8** (0.8 g, 1.1 mmol) was added to a dried (Na_2SO_4) and filtered solution of *cis*-α,β-dideuteriostyrene (7.0 g, 6.6 mmol) in 40 mL of cyclohexane. The solution was heated with a 75° oil bath under a nitrogen atmosphere as *dl*-menthyl α-deuteriodiazoacetate (20 g, 89 mmol) in 30 mL of cyclohexane was added dropwise over a period of 9 h.[11] The reaction mixture was cooled and concentrated, and the residue was subjected to Kugelrohr distillation (150 °C, 0.1 Torr) to afford 14.8 g (74%) of esters **9a** and **10a**, contaminated with small amounts of fumaric and maleic esters.

***t*-2-Phenyl-1,2,*c*-3-trideuteriocyclopropanecarboxylic Acid (9b) and *c*-2-Phenyl-1,2,*t*-3-trideuteriocyclopropanecarboxylic Acid (10b).** The mixture of the two menthyl esters prepared above (19.1 g, 63 mmol) was heated to reflux for 20 h with 100 mL of methanol and 60 mL of 25% aqueous sodium hydroxide. When the solution had cooled, it was diluted with water and extracted with ether. The aqueous phase was acidified with concentrated hydrochloric acid and extracted with ether. This second ether extract was washed with brine, dried ($MgSO_4$), filtered, and concentrated; the residue was 9.5 g (91%) of a mixture of *cis* and *trans*-2-phenylcyclopropanecarboxylic acids **9b** and **10b**. A small amount of the mixture was methylated with diazomethane.[30] The ratio of **9c** to **10c** was 85:15, determined by integration of the methyl ester NMR absorptions of the two isomers. A sample of the *trans*-ester **9c** was analyzed with the aid of the optically active shift reagent Eu-Opt in chloroform and shown to have an optical purity of 80%.

(+)-(1*S*,2*S*,3*S*)-*t*-2-Phenyl-1,2,*c*-3-trideuteriocyclopropanecarboxylic Acid ((+)-9b). The optically active acid was crystallized from 9.5 g of the 85:15 mixture of **9b** and **10b** as its quinine salt.[17] After hydrolysis of the salt with dilute hydrochloric acid, the resolved acid (5.8 g, 61%) had NMR absorptions at δ 1.40 (1 H, s), 7.25 (5 H, m), 9.5 (1 H, broad s).

Methyl (+)-(1*S*,2*S*,3*S*)-*t*-2-Phenyl-1,2,*c*-3-trideuteriocyclopropanecarboxylate ((+)-9c). A small sample of (+)-**9b** was esterified with diazomethane.[30] The methyl ester was purified by GLPC on column B: $[\alpha]_D$ +327° (*c* 2.52, $CHCl_3$) (lit.[17] $[\alpha]_D$ +335° (*c* 3.79, EtOH)); NMR δ 1.32 (1 H, s), 3.74 (3 H, s), 7.04–7.32 (5 H, m). The NMR spectrum of (+)-**9c** in the presence of $Eu(hfbc)_3$ had only one methyl signal under conditions where racemic material showed two absorptions.

(+)-(1*S*,2*S*,3*S*)-*t*-2-Phenyl-1,2,*c*-3-trideuteriocyclopropylmethanol. Reduction of acid (+)-**9b** (5.3 g, 32 mmol) with $LiAlH_4$ in THF gave 4.1 g (100%) of alcohol as a colorless, viscous oil: NMR 0.95 (1 H, s), 2.60 (1 H, broad s), 3.60 (2 H, s), 7.20 (5 H, m).

(+)-(1*S*,2*S*,3*H*)-*r*-1-Phenyl-*t*-2-methyl-1,2,*t*-3-trideuteriocyclopropane (11). Mesylation of 4.1 g of the alcohol prepared immediately above followed by $LiAlH_4$ reduction gave 2.1 g (48%) of the deuterated phenylcyclopropane **11**,[17] bp 71–74 °C (17 mm): NMR δ 0.86 (1 H, s), 1.20 (3 H, s), 7.0–7.35 (5 H, m). The major side product, which was isolated by GLPC and identified by NMR, proved to be 0.37 g of 4-phenylbut-1-ene-d_3.

(+)-(1*S*,2*S*,3*R*)-1,2,*t*-3-Trideuterio-*t*-2-methylcyclopropanecarboxylic Acid. A carbon tetrachloride solution of 2.1 g (16 mmol) of the deuterated phenylcyclopropane **11** was subjected to ozonolysis followed by an oxidative workup with 30% hydrogen peroxide.[17] The organic and aqueous layers were separated and the aqueous portion was extracted once with carbon tetrachloride. The combined organic solutions were extracted four times with 15% sodium hydroxide. The basic solution was acidified with concentrated hydrochloric acid, saturated with sodium chloride, and continuously extracted for 2 days with ether. The resulting ethereal solution was dried ($MgSO_4$), filtered, and concentrated by distillation using the 1-m glass helix-packed column. The undistilled residue was used in the next reaction without further purification. The presence of the desired product in the residue was confirmed by GLPC and NMR spectroscopy: the retention time of the major component of the residue on column A (15 min at 150 °C, flow rate 30 ml/min) and the NMR spectrum were identical to those of racemic d_3-material. A purified sample of the acid had rotation $[\alpha]_D$ +95.8 ± 2.7° (*c* 2.85, EtOH) (lit.[17] $[\alpha]_D$ +99.2° (*c* 3.09, EtOH): NMR δ 0.72 (0.04 H, s), 1.13 (3 H, s), 1.22 (0.96 H, s), 9.5 (1 H, broad s).

(+)-(1*S*,2*S*,3*R*)-1,2,*t*-3-Trideuterio-*t*-2-methylcyclopropanecarboxamide. The concentrate of acid prepared immediately above, which still contained some ether, was stirred overnight with thionyl chloride (2.0 g, 18 mmol).[20] More ether was then added and anhydrous ammonia was bubbled into the solution until examination of an aliquot by NMR showed that all of the acid chloride had been consumed. The mixture was filtered and the precipitate was washed well with methylene chloride. Solvent was removed from the filtrate under vacuum; pentane was added and solvent was removed again, to eliminate traces of methylene chloride, leaving 1.2 g (75% based on **11**) of the crude amide: NMR δ 1.10 (3 H, s), 1.16 (1 H, s), 6.0 (2 H, broad s).

(+)-(1*S*,2*S*,3*R*)-1,2,*t*-3-Trideuterio-*t*-2-methyl-*r*-1-cyanocyclopropane ((+)-1-*t*). The unpurified amide described immediately above (1.2 g, 11 mmol) and thionyl chloride (3.0 g, 25 mmol) in benzene were heated to reflux overnight. The following morning it was discovered that the solvent had been boiled off during the night. More benzene and thionyl chloride (1.0 g, 8 mmol) were added and the solution was heated to reflux for an additional 12 h. After cooling and addition of water, the aqueous and organic phases were separated. The organic solution was washed with water and brine, dried ($MgSO_4$), filtered, and concentrated by distillation through a 10-cm Vigreux column. Purification by GLPC on column B yielded about 75 μL of (+)-**1**-*t*, enough material for two kinetic points. The purified cyclopropane (+)-**1**-*t* had $[\alpha]_D$ +150 ± 4° (*c* 1.95, $CHCl_3$) (lit.[20] $[\alpha]_D$ −134° ($CHCl_3$), calculated for optically pure (1*R*,2*R*) unlabeled material); $[\alpha]_{578}$ 154 ± 5° (*c* 1.6–1.95, $CHCl_3$), $[\alpha]_{546}$ +176 ± 5°, $[\alpha]_{436}$ +284 ± 7°, $[\alpha]_{365}$ +418 ± 10°: NMR (C_6D_6) δ −0.15 (0.03 H, s), 0.37 (3 H, s), 0.49 (0.97 H, s).

1,2,*c*-3-Trideuterio-*t*-2-phenylcyclopropylmethanol and 1,2,*t*-3-Trideuterio-*c*-2-phenylcyclopropylmethanol. *cis*-α,β-Dideuteriostyrene (21.9 g, 0.207 mol) was condensed with a mixture of ethyl α-deuteriodiazoacetate (26.2 g, 0.228 mol) and menthyl α-deuteriodiazoacetate (5.0 g, 0.022 mol) using the copper sulfate catalyzed procedure.[4,21] The identity of the product esters was verified by NMR spectroscopy. The mixture of cyclopropanecarboxylates was reduced with $LiAlH_4$, leaving, after workup and concentration at reduced pressure, 20.8 g (67%) of a mixture of alcohols. The mixture was characterized by NMR.

1,2,*t*-3-Trideuterio-*t*-2-methylphenylcyclopropane and 1,2,*t*-3-Trideuterio-*c*-2-methylphenylcyclopropane. The crude alcohols described immediately above were mesylated and reduced, using the previously detailed procedures. The product obtained after distillation, bp 64–66 °C (13 mm) (lit.[17] bp 74–76 °C (18 mm)) was a mixture of geometric isomers (10.8 g, 58%) according to NMR spectroscopic analysis.

1,2,*t*-3-Trideuterio-*t*-2-methylcyclopropanecarboxamide and 1,2,*t*-3-Trideuterio-*c*-2-methylcyclopropanecarboxamide. The cis and trans trideuterio-1-phenyl-2-methylcyclopropanes prepared immediately above were ozonized in carbon tetrachloride, and the resulting acids were converted to the corresponding acid chlorides by the methods detailed above. Treatment of the acid chlorides with ammonia gave 3.6 g (44%) of a mixture of the amides. The NMR spectrum of the mixture was consistent with structural anticipation.

1,2,*t*-3-Trideuterio-*t*-2-methylcyanocyclopropane ((±)-1-*t*) and 1,2,*t*-3-Trideuterio-*c*-2-methylcyanocyclopropane ((±)-2-*t*). Dehydration of the amides (3.6 g, 43 mmol) with thionyl chloride in benzene afforded 1.7 g (57%) of a mixture of the racemic methylcyanocyclopropanes 1-*t* and 2-*t*. The nitriles were separated and purified by GLPC on column C. Trans isomer 1-*t* had NMR (C_6D_6) δ 0.37 (3 H, s), 0.49 (1 H, s). Cis isomer 2-*t* had NMR δ 0.08 (1 H, s), 0.88 (3 H, s).

Base-Catalyzed Epimerization of (+)-1-*t*. A small sample of optically impure (+)-1-*t* was epimerized with potassium *tert*-butoxide in Me_2SO-d_6/ether under nitrogen at 25 °C for 3 h to secure a sample of (−)-2-*c*.[20] The reaction mixture was quenched with D_2O and extracted with ether. Analysis by NMR indicated a 1:1 mixture of 1 and 2. The cis isomer 2 was isolated by preparative GLPC and examined by NMR with the aid of $Eu(hfbc)_3$; the predominant methyl resonance was the more upfield of the two methyl singlets.

(+)-(1*S*,2*R*,3*S*)-1,2,*t*-3-Trideuterio-*c*-2-methyl-1-cyanocyclopropane. A sample of GLPC-purified racemic 1,2,*t*-3-trideuterio-*c*-2-methyl-1-cyanocyclopropane (2-*t*) was hydrolyzed with aqueous KOH[28] to give racemic acid (160 mg) which was resolved by way of the quinine salt following Bergman.[20] The first crop of quinine salt (320 mg) was recrystallized twice from fresh acetone to give 205 mg of salt enriched in the (+)-(1*S*,2*R*,3*S*) carboxylate, which was decomposed with 17% aqueous HCl and ether. The crude acid was converted[20] by way of the

(30) Monson, R. S. "Advanced Organic Synthesis", Academic Press: New York, 1971; p 155.

corresponding acid chloride and acid amide to (+)-(1*S*,2*R*,3*S*)-1,2,*t*-3-trideuterio-*c*-2-methyl-1-cyanocyclopropane. A sample of this product was purified by GLPC on column C and combined with a dry saturated C_6D_6 solution of the chiral NMR shift reagent Eu(hfbc)$_3$. The enantiotopic methyl resonances confirmed the (+)-(1*S*,2*R*,3*S*) absolute stereochemistry anticipated from the synthetic route and published resolution[20] (downfield methyl larger; 30% optical purity); the enantiotopic C(3)H singlets came with the (−) isomer at lower field, the (+), preponderant isomer at higher field (cf. Figure 2).

Gas-Phase Kinetics. Pyrolyses of the deuterated 2-methyl-1-cyanocyclopropanes were carried out in a 300-mL Pyrex bulb encased in an aluminum block. A spherical cavity machined in the block accommodated the flask; the aluminum top hemisphere was halved to allow facile dismantling of the apparatus. Eight cartridge heaters in vertical holes around the block were connected alternately to a Variac and to a Bailey Instruments Model 253 precision temperature controller. Temperature measurements were made with a Hewlett-Packard Model 2802A digital thermometer; the probe of the thermometer was placed in a well in the bulb.

The aluminum block was supported with firebrick and enclosed in a plywood box (34 cm × 34 cm × 27 cm) packed with diatomaceous earth. The stem of the Pyrex bulb connected, just after emerging from the plywood box, through a Quartz-General No. W-1831 Teflon-barreled vacuum stopcock and to an adjustable electrode adaptor (Ace Glass No. 5037-03) fitted with a silicone rubber septum.

The portions of the vacuum line outside the box between the septum or stopcock and the reactor were insulated with glass wool.

Prior to pyrolyses the bulb was evacuated to $<10^{-4}$ Torr and the stopcock was closed. Samples were injected into the bulb through the septum with a gas-tight syringe (Hamilton, 50 μL). When a pyrolysis was finished, the stopcock was opened and the contents of the pyrolysis bulb as pumped into a liquid nitrogen cooled U-tube attached to the vacuum line with O-ring seals and threaded connectors (Ace Glass No. 5027-30).

This method resulted in immediate recovery of the sample, in contrast with the longer times required by methods that depend on the vapor pressure of the sample to effect transfer in a vacuum line. After manipulating appropriate stopcocks on the line, the trap was removed and its contents was dissolved in either benzene-d_6 or ether.

The bulb was conditioned before use in kinetic runs as follows. Trimethylsilyl chloride (40 μL) was introduced and heated for 24 h at 350 °C. After evacuation, the system was subjected to a similar treatment with triethylamine. The reactor was then seasoned by heating a 25-μL sample of 2-methylcyanocyclopropane (prepared according to Applequist and Peterson[31]) in it for 10 days. This seasoning was necessary to obtain reproducible kinetic rates. Further seasoning had no effect on the rate of isomerization of **1** or **2**.

The flask was henceforth maintained under vacuum except during pyrolyses or when a septum was changed. Septums were generally used for an average of 10 injections. To avoid admitting oxygen into the pyrolysis bulb, the line was filled with a positive pressure of nitrogen while a septum was being replaced.

Samples of deuterated 2-methyl-1-cyanocyclopropanes were thermolyzed at 335.4 °C and a pressure of 17 mm (calculated from the ideal gas equation). The solutions of thermal rearrangement products were analyzed directly by GLPC on column A for the relative amounts of *cis*-2-methylcyanocyclopropane (**2**), *trans*-2-methylcyanocyclopropane (**1**), and the 2-pentenonitriles. Integrated areas were determined by cutting out and weighing the peaks from Xerox copies of the GLPC traces. The NMR measurements of the products from the pyrolysis of racemic **1** or **2** were carried out on the benzene-d_6 solutions used in GLPC analysis.

The products from the pyrolysis of (+)-**1**-*t* were handled differently. The material was rinsed from the trap with ether. After GLPC analysis of the ethereal solution, 1 and **2** were isolated by preparative GLPC on column C. The cis isomer, **2**, was dissolved in benzene-d_6. After NMR determination of the ratio H(3-exo):H(3-endo), the sample of **2** was reisolated by GLPC and dissolved in a solution of Eu(hfbc)$_3$ in perdeuteriobenzene (300 mg per mL). The ratio of (+)-**2** to (−)-**2** was computed from the relative intensities of the singlets due to the enantiotopic methyl groups (Figure 2). The resonances of the enantiotopic endo C(3)H protons of **2** were also split under these conditions.

The trans isomers, **1**, were first dissolved in chloroform and the rotation of the solution was measured. The sample of 1 was reisolated by GLPC on column C and dissolved in benzene-d_6. The ratio **1**-*t*:**1**-*c* was determined by NMR spectroscopy. The sample was reisolated again, dissolved in a solution of Eu(hfbc)$_3$ in benzene-d_6 (300 mg/mL) and examined by NMR to determine the ratio of (+)-1-*t* to (−)-1-*t*.

Acknowledgment. We thank the National Science Foundation for partial support of this work.

Registry No. (+)-**1**-*t*, 80594-17-8; (+)-1-*c*, 80655-83-0; (−)-**1**-*t*, 80655-84-1; (−)-**1**-*c*, 80655-85-2; (±)-**1**-*t*, 80655-86-3; (+)-**2**-*t*, 80655-87-4; (+)-**2**-*c*, 80655-88-5; (−)-**2**-*t*, 80655-89-6; (−)-**2**-*c*, 80655-90-9; (±)-**2**-*t*, 80655-91-0; **3**, 80594-18-9; **4**, 52751-11-8; **5**, 65456-43-1; **6**, 80594-19-0; **7**, 80594-20-3; **8**, 80594-55-4; **9b**, 80594-21-4; **9c**, 80594-22-5; **10a**, 80594-23-6; **10b**, 80655-92-1; **10c**, 80655-93-2; **11**, 80594-24-7; triphenyltin deuteride, 6181-00-6; phenylacetylene, 536-74-3; 2-bromo-4-*tert*-butylphenol, 2198-66-5; 4-*tert*-butylphenol, 98-54-4; heptyl bromide, 629-04-9; D-alanine methyl ester HCl, 14316-06-4; salicylaldehyde, 90-02-8; menthyl glycinate HCl, 80655-94-3; glycine, 56-40-6; *dl*-menthol, 15356-70-4; *dl*-menthyl diazoacetate, 63323-84-2; ethyl α-deuteriodiazoacetate, 26697-95-0; *dl*-menthyl α-deuteriodiazoacetate, 80594-25-8; (+)-(1*S*,2*S*,3*s*)-*t*-2-phenyl-1,2,*c*-3-trideuteriocyclopropylmethanol, 80594-26-9; (+)-(1*S*,2*S*,3*R*)-1,2,*t*-3-trideuterio-*t*-2-methylcyclopropanecarboxylic acid, 80594-27-0; (+)-(1*S*,2*S*,3*R*)-1,2,*t*-3-trideuterio-*t*-2-methylcyclopropanecarboxamide, 80594-28-1; 1,2,*c*-3-trideuterio-*t*-2-phenylcyclopropylmethanol, 80655-95-4; 1,2,*t*-3-trideuterio-*c*-2-phenylcyclopropylmethanol, 80655-96-5; 1,2,*t*-3-trideuterio-*t*-2-methylphenylcyclopropane, 80655-97-6; 1,2,*t*-3-trideuterio-*c*-2-methylphenylcyclopropane, 80655-98-7; 1,2,*t*-3-trideuterio-*t*-2-methylcyclopropanecarboxamide, 80655-99-8; 1,2,*t*-3-trideuterio-*c*-2-methylcyclopropanecarboxamide, 80656-00-4.

(31) Applequist, D. E.; Peterson, A. H. *J. Am. Chem. Soc.* **1960**, *82*, 2372–2376.