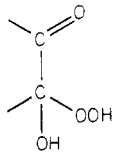
our EDTA and related results. Step 2 represents the oxidation of bound catechol to bound *o*-benzoquinone (**6**). Electrons are transferred through Fe(III) to a coordinated HOOAc ligand which is reduced to HOAc—a two-electron process. Peracetic acid is the oxidant of choice for this process since we have demonstrated that it is required for the overall conversion of catechol to MA but that it is *not* the active oxidant in the conversion of quinone to acid. The binding of *o*-benzoquinone to Fe(III) helps stablize an otherwise unstable structure, and, further, functions to make the carbonyl more susceptible to nucleophilic attack by H_2O_2 in the following step. Steps 3, 4, and 5 represent oxidative ring opening by H_2O_2. Our results with 9,10-phenanthrenequinone clearly indicate that H_2O_2 oxidizes ortho quinones to dicarboxylic acids. Thus, step 3 involves nucleophilic attack on the carbonyl group of the quinone to give **7**. Evidence for this mode of reaction comes from the work of Patchett and Witkop,[23] who isolated a peroxide adduct of the ortho quinone carbonyl group containing structure **10** in the oxidation of *o*-



10

benzoquinone *dimer* with H_2O_2. This compound results from the addition of H_2O_2 to the carbonyl of the ortho quinone structure in the dimer, and it was observed to readily decompose with C–C bond cleavage to give a dicarboxylic acid, the dimeric analogue of MA.

Step 4 involves intramolecular nucleophilic attack on the adjacent carbonyl to give the dioxetane **8**, which spontaneously decomposes (step 5) to give MA. The postulation of a 1,2-dioxetane intermediate is reasonable in light of our results and well-documented studies on the preparation and decomposition of 1,2-dioxetanes formed in singlet oxygen reactions.[24]

We have presented a resonable mechanism of a biomimetic reaction for the dioxygenase, pyrocatechase. Our studies of the model reaction have provided us with insights to the enzymic process and suggest a peroxide mechanism for pyrocatechase activity.

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Registry No. **1**, 120-80-9; **2**, 1119-72-8; **3**, 84-11-7; **4**, 482-05-3; Fe, 7439-89-6; Mo, 7439-98-7; Cu, 7440-50-8; HOOAc, 79-21-0; pyrocatechase, 9027-16-1.

(23) Patchett, A. A.; Witkop, B. *J. Org. Chem.* **1957**, *22*, 1477-1484.

(24) Schaap, A. *Tetrahedron Lett.* **1971**, 1757-1760 and references cited therein.

(25) Sillen, L. G.; Martell, A. E. "Stability Constants of Metal-Ion Complexes", Supplement 1, Spec. Publ. No. 25; The Chemical Society: London, **1971**; p 400. Reference 20, p 472.

(26) Latimer, W. M. "Oxidation Potentials", 2nd ed.; Prentice-Hall: Englewood Cliffs, NJ, 1952.

(27) Mentasti, E.; Pelizzetti, E. *J. Chem. Soc., Dalton Trans.* **1973**, 2605.

(28) Presented in part at the 183rd National Meeting of the American Chemical Society, Las Vegas, NV, April 1982.

Stereochemical Kinetics of the Thermal Stereomutations of 1-Cyano-2-phenyl-1,3-dideuteriocyclopropanes

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A complete kinetic analysis of the stereomutations that interconvert the isomers of 1-cyano-2-phenyl-1,3-dideuteriocyclopropane at 242.1 °C has been attained by following the thermolysis of (+)-(1*S*,2*S*,3*S*)-*r*-1-cyano-*t*-2-phenyl-1,*c*-3-dideuteriocyclopropane and its stereoisomers. The kinetic parameters describing the time evolution of the set of eight isomers are K_{eq}(cis/trans) = 0.40 and rate constants ($\times 10^5$ s) $k_1 = 0.76$, $k_2 = 0.33$, $k_{12} = 0.60$, $k'_{12} = 0.43$; k_{13}, k_{23}, k_3, and k'_3 are all found to be zero. In this system, and in contrast to results obtained for the 1-cyano-2-methyl-1,2,3-trideuteriocyclopropanes and the 2,3-dideuterio-2-(methoxymethyl)spiro[cyclopropane-1,1′-indenes], all stereomutations may be rationalized in terms of C(1)–C(2) bond cleavage.

Thermal interconversions of one to another cyclopropane may follow several alternative paths.[1] In an unsymmetrically disubstituted cyclopropane, for instance, the kinetic situation is defined by four possible isomers and five independent kinetic parameters (Scheme I). A kinetic study for such a system can give no more than these five parameters. In Scheme I, the independent rate constants are given symbolic names (with subscripts *d*, *h*, and *v* for diagonal, horizontal, and vertical; rate constants *k* label reactions of a trans isomer, while *k′* rate constants designate reactions of a cis isomer) and are associated with heavy arrows; the reactions symbolized with light arrows all have rate constants that may be calculated from the four rate constants given, the equilibrium constant K_{eq},

(1) Recent reviews on this topic include: Berson, J. A. In "Rearrangements in Ground and Excited States"; Academic Press: New York, 1980; Vol. 1, Chapter 5. Gajewski, J. J. "Hydrocarbon Thermal Isomerizations"; Academic Press: New York, 1981; pp 28-36. Borden, W. T. In "Reactive Intermediates"; Wiley: New York, 1981; Vol. II, Chapter 5.

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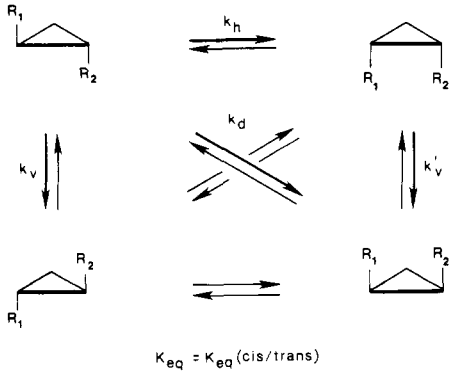
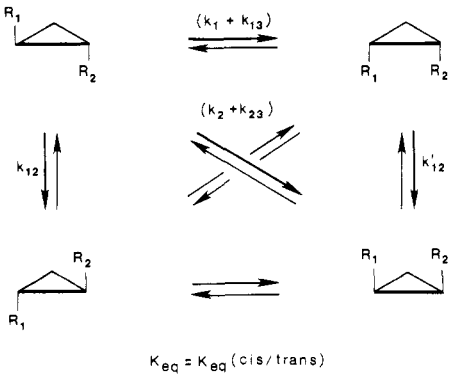
Scheme I. Phenomenological Kinetic Parameters



Scheme II. Individual Stereochemical Rate Constants

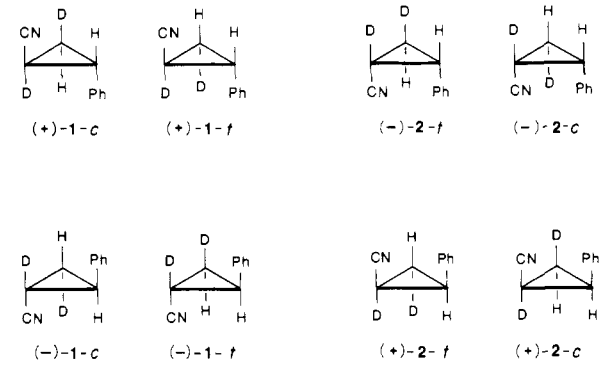


and the principle of microscopic reversibility.

A number of such chiral unsymmetrical 1,2-disubstituted cyclopropanes have been subjected to careful kinetic scrutiny in efforts to perceive the mechanistic essentials of cyclopropane stereomutations.[2] Mechanistic interpretations of these kinetic results have required some correlation between phenomenological rate constants and individual rate constants for one-center and two-center epimerizations (k_i and k_{ij}; Scheme II). An assumption-free reduction of observed rate constants to individual k_i and k_{ij} rate constants is not, however, directly accessible. Five phenomenological kinetic parameters are measurable, and seven stereochemical kinetic parameters are to be deduced. Either a trustworthy assumption or another experimental approach, then, must be used to infer or to find all the k_i and k_{ij} values.

Prior to this work, an assumption dubbed the most substituted bond hypothesis was often invoked to resolve the kinetic dilemma posed by Schemes I and II; since these stereomutations of cyclopropanes probably involve trimethylene diradicals,[3] and since these diradicals are stabilized by most substituent groups,[4] one plausibly supposed that only the most substituted cyclopropyl C–C bond would be cleaved, and that therefore only k_1, k_2, k_{12}, and k'_{12} would be of significance. This hypothesis disposed of the kinetic dilemma by setting two independent stereochemical rate constants of Scheme II, k_{13} and k_{23}, equal to zero, thus establishing a one-to-one correspondence

Scheme III



between phenomenological and individual kinetic parameters.

In this and in two related studies[5,6] we have sought to demonstrate that a complete kinetic solution to the dilemma posed by Schemes I and II is accessible through appropriate experimentation, without the aid of convenient and possibly valid assumptions,[7] and to probe for the limits of applicability of the most substituted bond hypothesis. Here, we give in full detail the first unequivocal test of the most substituted bond hypothesis.[8]

Results

The set of eight isomers at issue in this work is depicted in Scheme III. Each 1-cyano-2-phenyl-1,3-dideuteriocyclopropane is named according to sign of rotation, trans (**1**) or cis (**2**) disposition of cyano and phenyl substituents, and cis (*c*) or trans (*t*) stereochemistry of the deuterium at C(3), relative to the cyano group at C(1). Absolute stereochemistry is given in Scheme III as well; while not required, assignments of absolute stereochemistry were readily made.

Syntheses. The main comprehensively labeled substrate employed in this study, (+)-(1*S*,2*S*,3*S*)-1,*c*-3-dideuterio-*t*-2-phenyl-*r*-1-cyanocyclopropane, (+)-**1-c**, was prepared by using the sequence of reactions shown in Scheme IV.

Addition of triphenyltin hydride to phenylacetylene gave *trans*-β-(triphenylstannyl)styrene (**3**).[9] Transmetalation of this tin compound using butyllithium in tetrahydrofuran, followed by deuteration of the styryllithium intermediate with *O*-deuterioethanol, gave *trans*-β-deuteriostyrene (**4**) contaminated with some 3% of the cis isomer.[10]

Condensation of *trans*-β-deuteriostyrene with ethyl α-deuteriodiazoacetate in the presence of copper sulfate led to a 60:40 mixture of *trans*- and *cis*-1-(ethoxycarbonyl)-2-phenylcyclopropanes (**5** and **6**).[11] Treatment of this mixture with potassium *tert*-butoxide in *O*-deuterio-*tert*-butyl alcohol at reflux afforded trans ester

(2) Carter, W. L.; Bergman, R. G. *J. Am. Chem. Soc.* **1968**, *90*, 7344–7346; **1969**, *91*, 7411–7425. Doering, W. von E.; Sachdev, K. *Ibid.* **1974**, *96*, 1168–1187; **1975**, *97*, 5512–5520. Andrews, G. D.; Baldwin, J. E. *Ibid.* **1976**, *98*, 6705–6706. Doering, W. von E.; Barsa, E. A. *Tetrahedron Lett.* **1978**, 2495–2498.

(3) Rabinovitch, B. S.; Schlag, E. W.; Wiberg, K. B. *J. Chem. Phys.* **1958**, *28*, 504–505. Benson, S. W. *Ibid.* **1961**, *34*, 521–526. Hoffmann, R. *J. Am. Chem. Soc.* **1968**, *90*, 1475–1485.

(4) Rodewald, L. B.; DePuy, C. H. *Tetrahedron Lett.* **1964**, 2951–2953. Crawford, R. J.; Lynch, T. R. *Can. J. Chem.* **1968**, *46*, 1457–1458.

(5) Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1982**, *104*, 1362–1368.

(6) Baldwin, J. E.; Black, K. A. *J. Am. Chem. Soc.*, accepted for publication.

(7) Attempts to circumvent the kinetic dilemma through deuterium labeling and assumptions regarding secondary deuterium kinetic isotope effects are of uncertain reliability. See: Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1979**, *101*, 1325–1326.

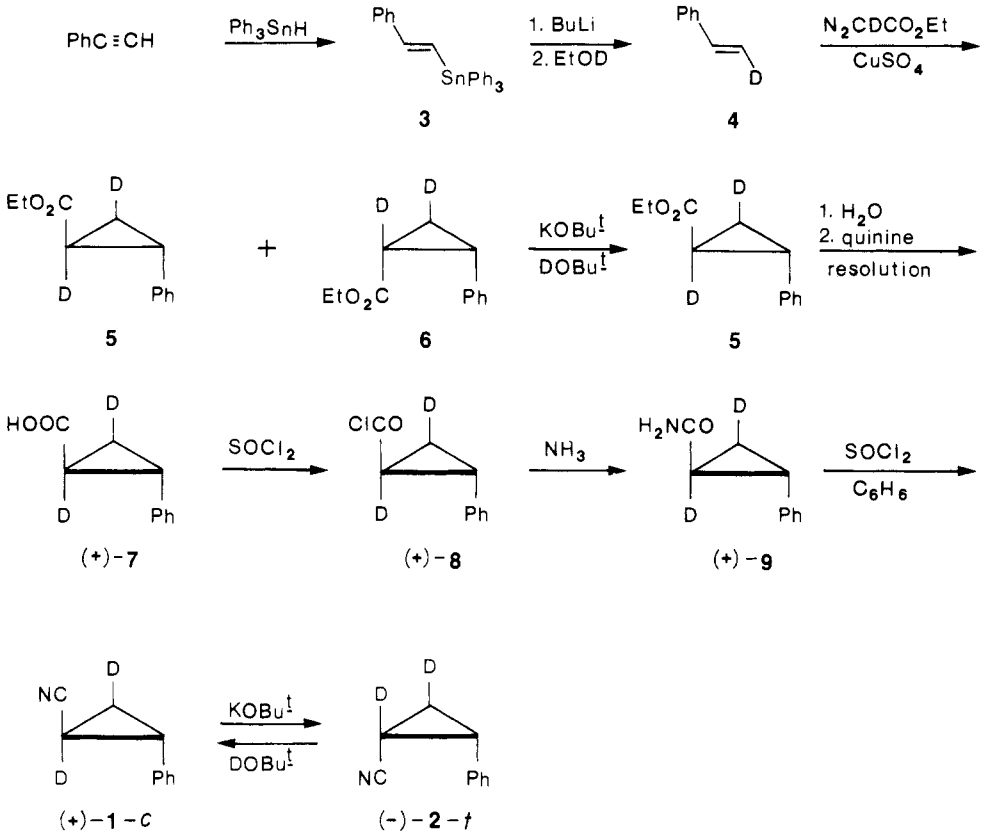
(8) Baldwin, J. E.; Carter, C. G. *J. Am. Chem. Soc.* **1978**, *100*, 3942–3944.

(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. Compare the use of tributyltin hydride to prepare selectively deuterated styrenes reported by: Quintard, J. P.; Pereyre, M. *J. Labelled Cmpd. Radiopharm.* **1978**, *14*, 653–661.

(11) Burger, A.; Yost, W. L. *J. Am. Chem. Soc.* **1948**, *70*, 2198–2201.

Scheme IV



5, which was hydrolyzed to the corresponding trans acid (±)-7.

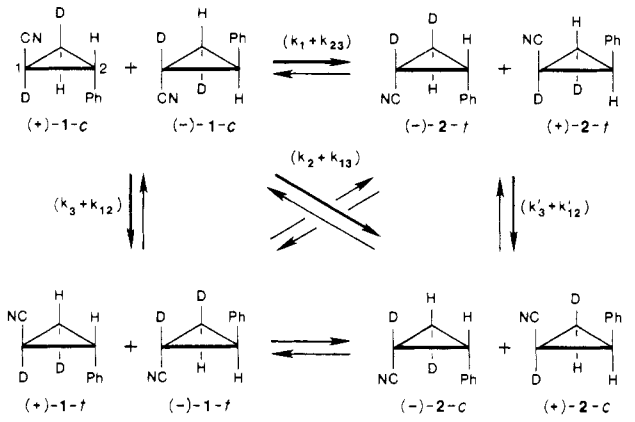
Resolution of this acid through its diastereomeric quinine salts[12] gave (+)-7, $[\alpha]_D$ +350° ($CHCl_3$); the methyl ester of this acid showed only one NMR doublet for the C(3)–H signal in the presence of the chiral lanthanide shift reagent Eu-Opt[13] under conditions known to separate the doublets of a racemic mixture. The acid was therefore taken to be optically pure.

The acid function was converted to a cyano group by way of acid chloride (+)-8 and carbamoyl ((+)-9) intermediates;[14] the nitrile (+)-1-*c*, of 1*S*,2*S*,3*S* absolute stereochemistry, had $[\alpha]_D$ +369° ($CHCl_3$).[15,16]

Treatment of trans isomer (+)-1-*c* with potassium *tert*-butoxide in *O*-deuterio-*tert*-butyl alcohol gave a mixture of starting material and its C(1) epimer, (−)-2-*t*. The cis isomer (−)-2-*t*, $[\alpha]_{436}$ −39.6°, was obtained as a pure compound through chromatography.[15,16] Neither isomer had incorporated any deuterium at C(2).

The substrates (+)-1-*c* and (−)-2-*t* were, according to NMR analysis, completely monodeuterated at C(3) but only 90% deuterated at C(1). Since the deuterium at C(1) served only to simplify NMR spectra and not as a stereochemical marker, the lack of complete deuteration at C(1) did not pose a substantial impairment to the stereochemical kinetic study undertaken.

Scheme V



Absolute Stereochemistry. The absolute stereochemistry of (−)-(1*R*,2*R*)-2-phenylcyclopropanecarboxylic acid is well established.[17] The (+)-1*S*,1*S* isomer in a deuterated variant, (+)-7, a direct precursor to the cyanocyclopropanes (+)-1-*c* and (−)-2-*t*, enables sure assignments for the absolute stereochemistry of these compounds, 1*S*,2*S*,3*S* and 1*R*,2*S*,2*S*, respectively.

Kinetics. Pyrolyses of the trans nitrile (+)-1-*c* and cis isomer (−)-2-*t* as solutions in 1-methylnaphthalene were carried out in sealed ampules at 242.1 °C. Interconversions between the trans and cis isomers were followed by gas chromatography. A standard least-squares fit of the concentration vs. time data in the form appropriate to such a reversible process provided values for the phenomenological rate constant $k_{t\rightarrow c} = (1.09 \pm 0.04) \times 10^{-5}$ s^{-1} and the equilibrium constant $K_{eq} = K_{eq}$ (cis/trans) = 0.40. No

(12) Baldwin, J. E.; Lötiger, J. ; Rastetter, W.; Neuss, N.; Huckstep, L. L.; De La Higuerra, N. *J. Am. Chem. Soc.* **1973**, *95*, 3796–3797. See also: Overberger, C. G.; Shimokawa, Y. *Macromolecules* **1971**, *4*, 718–725.

(13) Goering, H. L.; Eikenberry, J. N.; Koermer, G. S. *J. Am. Chem. Soc.* **1971**, *93*, 5913–5914.

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

(15) Doering and Barsa[2] studied unlabeled (1*S*,2*S*) trans nitrile 1, $[\alpha]^{25}_D$ +337.5° (EtOH), and the corresponding C(1) epimer, the (1*R*,2*S*) cis nitrile 2, $[\alpha]^{25}_D$ −21.8° (EtOH).

(16) Berson et al. [Berson, J. A.; Pedersen, L. D.; Carpenter, B. K. *J. Am. Chem. Soc.* **1976**, *98*, 122–143] record rotations of $[\alpha]_D$ −322.6° ($CHCl_3$) and $[\alpha]_D$ +20.0° ($CHCl_3$) for the 1*R*,2*R* and 1*S*,2*R* isomers.

(17) Doering, W. von E.; Kirmse, W. *Tetrahadron* **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.

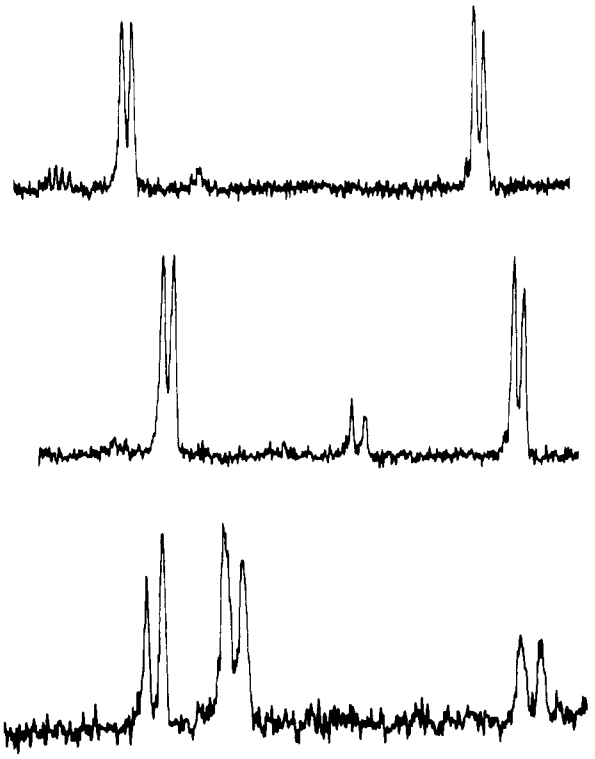


Figure 1. 100-MHz ^1H NMR spectra for 1-cyano-2-phenylcyclopropanes in $CDCl_3$ in the presence of $Eu(fod)_3$-d_{30}: top, **1-*c***; middle, **1-*c*** and **1-*t*** from pyrolysis of **1-*c*** for 375 min; bottom, **2-*c*** and **2-*t*** from pyrolysis of **1-*c*** for 375 min.

other products from thermolyses of **1** and **2** were detected by gas chromatography or NMR spectroscopy after four half-lives for the geometrical isomerization. The rate constant $k_{t\rightarrow c}$ is equal to the sum of four mechanistic rate constants, $k_1 + k_2 + k_{12} + k_{13}$.

Pyrolyses with the same substrates on a somewhat larger scale were conducted in the same manner, and reaction mixtures were examined by gas chromatography and by NMR spectroscopy. Analysis by gas chromatography gave [1/2]; after removal of 1-methylnaphthalene by column chromatography over silica gel, the cis and trans isomers were separated on 1000-mm alumina thick-layer plates, purified by gas chromatography on a Carbowax 20 M column, and then examined by NMR spectroscopy. Analysis of chromatographically pure samples of **1** and **2** by NMR spectroscopy with the aid of an optically inactive but deuterated shift reagent, $Eu(fod)_3$-d_{30},[18] provided the ratios of **1-*c*** to **1-*t*** and **2-*c*** to **2-*t*** in the thermolysis mixture. Representative NMR spectra (Figure 1) show the separation of the ring protons in a sample of **1-*c*** and in the **1** and **2** isolated from a 375-min pyrolysis of **1-*c***. Thus the kinetic situation of Scheme V in which isomers are considered as enantiotopic pairs may be treated.

The concentration vs. time data acquired in this manner are summarized in Table II. The kinetic parameters that lead to calculated concentration vs. time values in best agreement with the experimental findings are, in terms of individual rate constants, $(k_1 + k_{23}) = 0.76 \times 10^{-5}$ s^{-1}, $(k_2 + k_{13}) = 0.33 \times 10^{-5}$ s^{-1}, $(k_3 + k_{12}) = 0.60 \times 10^{-5}$ s^{-1}, and $(k'_3 + k'_{12}) = 0.43 \times 10^{-5}$ s^{-1}. Other rate constants in the scheme are evident from microscopic reversibility and K_{eq}.

If one pairs the isomers in an alternative fashion, so that optical activity is followed while the stereochemistry of C(3)–D is ignored, Scheme VI applies and some different

Scheme VI

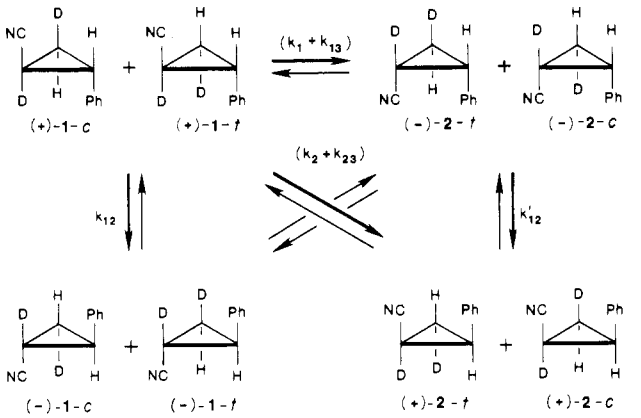


Table I. Calculated[a] and Observed Mole Percent Concentrations of the Cyclopropane Isomers of Scheme V

data set	time, min	1-*c*	2-*t*	1-*t*	2-*c*
A	0	0	98.7	0	1.3
	60	7.1 (6.3)[b]	85.1 (88.3)	4.8 (2.8)	3.0 (2.6)
	131	14.5 (12.6)	75.0 (77.6)	6.7 (5.9)	3.8 (3.9)
	212	20.4 (18.5)	65.2 (67.3)	10.0 (9.0)	4.3 (5.2)
	450	29.7 (29.6)		17.4 (16.3)	
	458	30.3 (29.9)	45.7 (45.5)	17.3 (16.5)	6.7 (8.1)
	600	34.6 (33.6)	37.4 (37.3)	20.6 (19.8)	7.4 (9.3)
B	0	98.7	0	1.3	0
	156	84.6 (85.2)	5.4 (5.8)	7.3 (6.3)	2.7 (2.8)
	240	78.5 (79.2)	8.6 (8.1)	8.7 (8.7)	4.1 (4.0)
	300	75.9 (75.5)	9.6 (9.4)	9.6 (10.3)	4.9 (4.8)
	450	68.4 (67.6)	11.6 (11.9)	13.4 (14.0)	6.6 (6.5)
	600		13.0 (13.4)		7.8 (7.9)
C	0	95.5	0	4.5	0
	375	68.4 (69.4)	10.9 (10.6)	14.3 (14.2)	6.4 (5.9)

[a] According to the parameters $K_{eq} = 0.40$, $(k_1 + k_{23}) = 0.76 \times 10^{-5}$ s^{-1}, $(k_2 + k_{13}) = 0.33 \times 10^{-5}$ s^{-1}, $(k_3 + k_{12}) = 0.60 \times 10^{-5}$ s^{-1}, and $(k'_3 + k'_{12}) = 0.43 \times 10^{-5}$ s^{-1}. [b] Calculated values in parentheses.

rate constants become available. But the kinetic analysis remains incomplete: the pairs of rate constants $(k_1 + k_{23})$, $(k_2 + k_{13})$, $(k_1 + k_{13})$, and $(k_2 + k_{23})$ may each be associated with an observable phenomenological rate constant (Schemes V and VI), but they will not provide all individual stereochemical rate constants since they constitute a set of linearly dependent equations.[19] Thus additional data are required to obtain the values of the individual rate constants contained in these sums.

To gain data appropriate to kinetic treatment according to Scheme VI, and to secure the additional data permitting deductions of concentrations for individual isomers, and hence of individual stereochemical rate constants, larger samples of **(+)-1-*c*** were thermolyzed, purified, and analyzed polarimetrically, as well as by gas chromatography and NMR (Tables II, III).

From the data of Tables I and II, mole percent figures for the pairs of isomers shown in Table III may be calculated, and from them and the synthetic route employed may be derived the time zero distribution of individual isomers for each data set. For set I, for example, 97.3% **(+)-1** and 98.7% **1-*c*** imply 96.0% **(+)-1-*c***, 1.3% **(+)-1-*t***, 2.7% **(-)-1-*c***, and <0.1% **(-)-1-*t***. Similarly, the various isomers at time zero for data sets II and III may be cal-

(18) Rondeau, R. E.; Sievers, R. E. *J. Am. Chem. Soc.* **1971**, *93*, 1522–1524.

(19) The Gram determinant for these equations is zero. Cf.: Margenau, H.; Murphy, G. M. "The Mathematics of Physics and Chemistry", 2nd ed.; Van Nostrand: Princeton, NJ, 1956; pp 132–134. Perrin, C. L. "Mathematics for Chemists"; Wiley-Interscience: New York, 1970; p 252.

Table II. Optical Rotations of 1-Cyano-2-phenyl-1,3-dideuteriocyclopropanes in Scheme VI

		starting substrate		*trans*-product 1		*cis*-product 2	
data set	time, min	$[\alpha]_D$, deg	optical purity, %	$[\alpha]_{578}$, deg	optical purity, %	$[\alpha]_{436}$, deg	optical purity, %
I	0	1: +349	94.6				
	240			+301	79.8[a]	−14.7	37.1
II	0	1: +369	100				
	375			+260	69.0	−14.0	35.4
III	0	2[b]	94.6				
	450			+95.4	25.3		

[a] Optically pure trans and cis nitriles had $[\alpha]_D$ +369° ($[\alpha]_{578}$ +377°) and $[\alpha]_{436}$ −39.6°, respectively. [b] From the base-catalyzed epimerization of (+)-1-*c*, $[\alpha]_D$ +349°.

Table III. Observed[a] and Calculated[b] Mole Percent Concentrations for Isomer Pairs in Scheme VI Followed by Chromatography and Polarimetry[a]

data set	time, min	(+)-1	(−)-2	(−)-1	(+)-2
I[a]	0	97.3	0	2.7	0
	240	78.4 (78.2)	8.7 (7.9)	8.8 (9.8)	4.0 (4.1)
II	0	100	0	0	0
	375	69.9 (71.9)	11.7 (10.8)	12.8 (11.6)	5.6 (5.8)
III	0	0	97.3	0	2.7
	450	29.5 (29.2)		17.6 (16.7)	

[a] From data of Tables I and II. [b] In parentheses; see text and Table IV for kinetic parameters used.

Table IV. Calculated[a] Mole Percents for the Eight Isomers of 1-Cyano-2-phenyl-2,3-dideuteriocyclopropane

data set	time, min	(+)-1-*c*	(−)-2-*t*	(−)-1-*t*	(+)-2-*c*	(−)-1-*c*	(+)-2-*t*	(+)-1-*t*	(−)-2-*c*
I	0	96.0	0	0	0	2.7	0	1.3	0
	240	76.9	7.7	7.5	3.8	2.3	0.3	1.3	0.2
II	0	95.5	0	0	0	0	0	4.5	0
	375	68.7	10.3	11.1	5.5	0.5	0.3	3.2	0.5
III	0	0	96.7	0	0	0	2.7	0	1.3
	450	28.4	44.5	15.7	7.4	1.0	1.4	0.8	0.8

[a] Kinetic parameters $K_{eq} = 0.40$, $k_1 = 0.76 \times 10^{-5}$ s^{-1}, $k_2 = 0.33 \times 10^{-5}$ s^{-1}, $k_{12} = 0.60 \times 10^{-5}$ s^{-1}, and $k'_{12} = 0.43 \times 10^{-5}$ s^{-1}. From these parameters and microscopic reversibility, $k'_1 = 1.90 \times 10^{-5}$ s^{-1} and $k'_2 = 0.83 \times 10^{-5}$ s^{-1}.

culated (Table IV, zero time entries only).

Two thermolysis product mixtures, derived from two separate preparations of (+)-1-*c*, were analyzed by all three methods. These pyrolysis samples were also analyzed by NMR spectroscopy with the aid of Eu(hfbc)$_3$,[20] an optically active lanthanide shift reagent. In its presence the enantiotropic C(3)–H protons in 2-*t* can be distinguished: the more downfield of the two C(3)–H doublets is due to the (−)-isomer of 2-*t*. The NMR spectrum at the top of Figure 2 shows the resolution of the C(3)–H protons of a sample of (±)-2-*t* into two doublets.

The NMR spectra of the cis products from (+)-1-*c* contained only one doublet in the presence of Eu(hfbc)$_3$. Since a major fraction of the cis products contained a proton at C(3) endo to the cyano group and exhibited a negative rotation, this doublet was assigned to (−)-2-*t*, and therefore $k_{23} = 0$. This fact, together with the observed rotation of 2 and the NMR-determined ratio of 2-*t* to 2-*c*, implied that the concentration of (−)-2-*c* in the product mixture was zero, or zero within the experimental limits of detectability, and hence $k_{13} = 0$.

The trans starting material recovered after pyrolysis of optically pure (+)-1-*c* for 375 min was epimerized with base at C(1). The 2 isomers obtained, in the presence of Eu(hfbc)$_3$, showed only one C(3)–H NMR doublet, which had to be assigned to (−)-2-*t*, the epimerization product derived from the starting material in the pyrolysis, (+)-1-*c*. Thus, as expected, the triple epimerization process was not competitive ($k_{123} = 0$), and indirect routes to (−)-1-*c* were unimportant during thermolysis times of up to 375 min.

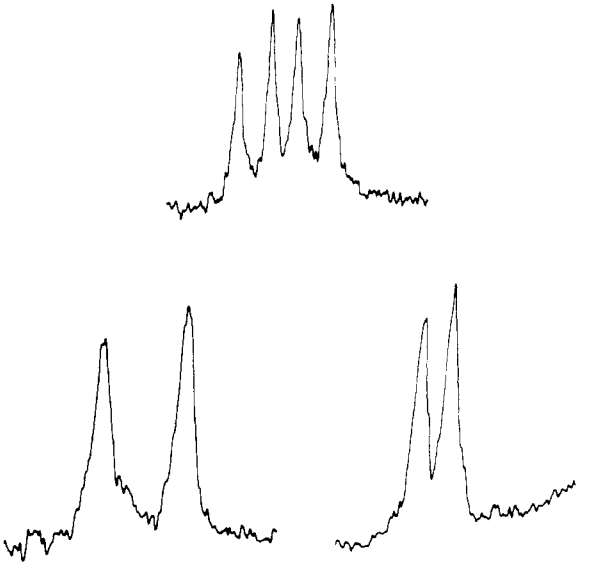
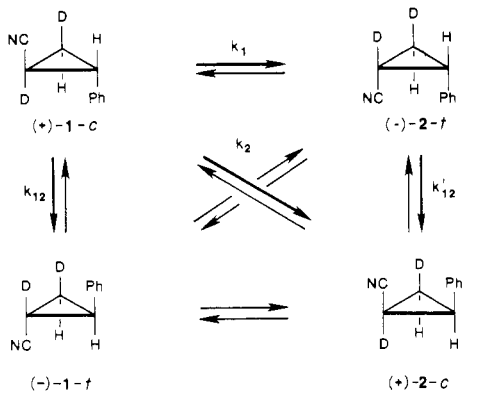


Figure 2. ^{1}H NMR spectra of C(3)–H in the presence of Eu(hfbc)$_3$ for isomers 2-*t*: top, (±)-2-*t*; bottom left, (−)-2-*t* from 375-min thermolysis of (+)-1-*c* (recorded at expanded sweep width); bottom right, (−)-2-*t* from base-catalyzed epimerization of 1 recovered from 375-min pyrolysis of (+)-1-*c*.

The pair of doublets due to enantiotopic C(3)–H in (−)-1-*t* and (+)-1-*t* were slightly separated in the presence of Eu(hfbc)$_3$. The trans isomer set recovered from thermolyses of (+)-1-*c* for 240 min showed only a trace of the (+)-1-*t* doublet, ascribed to the 1.3 percent (+)-1-*t* stereochemical contaminant in the kinetic substrate (Table IV), and thus it was evident that $k_3 = 0$.

(20) Fraser, R. R.; Petit, M. A.; Saunders, J. K. *J. Chem. Soc., Chem. Commun.* **1971**, 1450–1451.

Scheme VII



Close examination, then, of thermolysis products led to the conclusion that k_3, k_{13}, k_{23}, and k_{123} are all zero, since the products that could be formed directly from (+)-1-*c* by these stereochemically discrete paths were not found in reaction mixtures. The stereomutations of any one of the 1-cyano-2-phenyl-1,3-dideuteriocyclopropanes involve just four isomers, not eight, and kinetic Scheme VII applies. According to this scheme, the kinetics of the stereomutations may be followed by chromatography and either polarimetry or NMR spectroscopy. When the scheme is valid and both techniques are employed, the same data are secured. Tables I, III, and IV illustrate the point.

For the ten common comparisons between theory based on Scheme VII (Table IV) and experimental mole percent concentrations, the NMR data (Table I: lines A 450, B 240, and C 375) give a mean difference and standard deviation values of 0.10 ± 0.60%, while the polarimetric data (Table III) values are 0.10 ± 0.99%.

Discussion

The polarimetric data serve here to demonstrate the validity of the most substituted bond hypothesis when applied to the 1-cyano-2-phenylcyclopropanes under the reaction conditions used in this study. If there had been significant discrepancies between experimental concentrations for different pairs of stereoisomers secured by polarimetry and by NMR spectroscopy, then substantially more polarimetric data and close scrutiny of kinetic samples with chiral shift reagents would have been required to find reliable values for k_3, k'_3, k_{13}, and k_{23}.[5,6]

Here, and no doubt in other situations where detailed stereochemical information for alternative reaction paths is required, deuterium-labeling methods may prove simpler to implement than techniques based on optical activity if two conditions may be met: the appropriate stereoselectivity deuterated substrates must be reasonably accessible synthetically, and the range of stereochemical options must be encompassed by the range expressible through the deuterium labeling. When the most substituted bond hypothesis is valid for a cyclopropane system, the second condition is satisfied by a stereochemically well-defined 1-R_1-2-R_2-3-deuteriocyclopropane. Conversely, when the most substituted bond hypothesis is not valid, the study of achiral deuterium-labeled cyclopropanes will not provide the information sought. Only the kinetic parameters of Scheme V will be measurable. Similar potential advantages and plain limitations of an obvious sort apply for other types of reactions in which deuterium labeling and polarimetric strategies for stereochemical kinetic work may be considered as possible options.

The relative values of the kinetic parameters found in this work are in fair agreement with those reported by Doering and Barsa[2] in their study of the undeuterated chiral nitriles **1** and **2** at 217.8 °C. These authors have also reported a test of the most substituted bond hypothesis:[21] the 1-cyano-2-(*cis*-prop-1-enyl)-3-methylcyclopropanes suffer stereomutations at 217.8 °C in the gas phase over 36 h without detectable loss in chiral integrity at C(3).

The significance of the results obtained in this study may be clearer now than when a preliminary account[8] was communicated. For the 1-cyano-2-phenylcyclopropanes, stereomutations are reflected in rate constants k_1, k_2, k_{12}, and k'_{12}, and the most substituted bond hypothesis has been confirmed experimentally. In subsequent work,[5,6] we have shown that this hypothesis breaks down when a cyclopropane lacks two strongly radical-stabilizing substituents on adjacent carbons. The stereochemical techniques developed may serve to either confirm the applicability or reveal the shortcomings of the most substituted bond hypothesis, depending on the particular cyclopropane system under investigation.

With three or four sure points of reference, one may extrapolate with considerable confidence to other substituted cyclopropanes of the sort symbolized in Scheme I and assert that for those with substituents like cyano, phenyl, and alkenyl at C(1) and C(2), the most substituted bond hypothesis is a perfectly reliable tool for the conversion of phenomenological to individual stereochemical rate constants, while for systems in which only one or not even one such group is present, the hypothesis does[5,6] and in general will break down.

The rate constants k_i and k_{ij} relate to specific reactions characterized individually by the stereochemistry of starting material and product. They do not imply any particular mechanistic model for cyclopropane stereomutations. When suitably detailed models, or mechanisms, are delineated for such thermal reactions, the magnitudes of the stereochemically significant k_i and k_{ij} values will be explained or even estimated. From the standpoint of that still elusive but important goal, reliable values for k_i and k_{ij} in a variety of representative substituted cyclopropanes are of crucial significance in directing mechanistic speculations and in framing detailed hypotheses.

Experimental Section

The compounds described are deuterated versions or isomeric deuterated versions of compounds that have been well-characterized earlier.[5] Experimental details of the present work are available as supplementary material (see paragraph at end of paper).

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Registry No. (+)-1-*c*, 67520-66-5; (−)-2-*t*, 67530-20-5.

Supplementary Material Available: Full experimental details on the synthetic and kinetic work reported in this manuscript (8 pages). Ordering information is given on any current masthead page.

(21) Doering, W. von E.; Barsa, E. A. *Proc. Natl. Acad. Sci. U.S.A.* **1980**, *77*, 2355–2357.