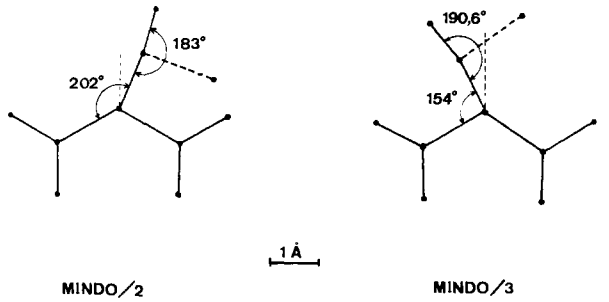
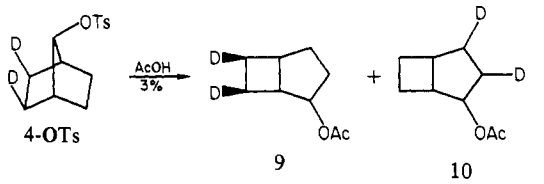


Figure 2. Head-on drawings of the 7-norbornyl cation with indicated approximate positions of the leaving group in the transition state.

of solvents used, which is obviously not the case. Finally, the formation of rearranged products of the bicyclo[3.2.0]heptyl structure cannot be brought in accord with the symmetry of the ribbon orbitals.[9] The noninteraction with these orbitals precludes any σ-bond delocalization as implied in the nonclassical structure **2** if the intermediate ion or the transition state leading to it retains the C_{2v} symmetry.

The results of the present investigation can be rationalized by assuming that the structure of the transition state leading to the 7-norbornyl cation is unsymmetrical in concord with the semiempirical MINDO calculations.

The presently available experimental evidence is insufficient for deciding which of the two bent MINDO structures should be preferred. As can be seen from a head-on drawing (Figure 2) steric, nonbonded interactions with the exo hydrogen (deuterium) atoms are stronger on each one of the sides (syn or anti) for the bent structures than for the ab initio structure. The tilting of the bridge also allows for some interaction of the p orbital with the SS-ribbon orbital on one side of the ion, thus allowing for the formation of a small amount of bicyclo[3.2.0]heptane products. However, this interaction cannot be significant in the rate-determining transition state as it would give rise to a hyperconjugative γ-effect in both endo- and exo-deuterated triflates **4-8**. Since, as Gassman[4] has observed, of the two isomeric rearrangement products **9** and **10** derived from **4** isomer **9** is the major product, the MINDO/3 structure is a better candidate for the explanation of the rearrangement reaction. An equally acceptable explanation can be provided by a bridge-flipping mechanism or



a rapid equilibrium between the two bent structures.

Conclusions

On the basis of the results obtained in the course of this work, one can conclude the following:

(1) Electronic interactions of hyperconjugative origin as implied in the nonclassical structure **2** of the 7-norbornyl cation could not be observed.

(2) Secondary deuterium γ-effects of positive value ($k_H/k_D > 1$) if present as in **4-6-OTf** are not caused by carbon-hydrogen homohyperconjugation but are of steric origin. In some other cases, as in 1- and 2-adamantyl derivatives,[30,31] they could be ascribed to carbon-carbon hyperconjugation.

(3) The solvolysis of **1-OTf** is not assisted by solvent and solvent effects are not responsible for the predominant retention of configuration at C_7 in solvolyses of 7-norbornyl derivatives.

(4) Accumulated experimental evidence gives preference to the unsymmetrical structure of the incipient 7-norbornyl cation (and the transition state leading to it) as predicted by MINDO calculations.

(5) Products of retained configuration obtained in aprotic solvents under S_N2 conditions can arise from two alternatively possible but still speculative mechanisms: (a) nucleophilic attack on sulfur or (b) pseudorotation on a pentacovalent intermediate.

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Registry No. 3, 86014-32-6; **3-OH**, 86014-39-3; **4**, 78551-26-5; **4-OH**, 23667-07-4; **5**, 78551-27-6; **5-OH**, 57233-91-7; **6**, 86014-33-7; **6-OH**, 57377-35-2; **7**, 86014-35-9; **7-OH**, 86014-37-1; **8**, 86014-36-0; **8-OH**, 86014-38-2; **9**, 86014-34-8; 7-norbornyl cation, 22318-50-9; deuterium, 7782-39-0.

Chiral Deuterium Labeling: New Method for Determination of Rotational Propensities

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Abstract: Determination of internal rotational propensities in thermal rearrangements of cyclic compounds has, in the past, involved the use of optical activity as a tracer and has required usually arduous correlation of configurations between the educt and products by chemical means. Replacement of this method by introduction of a chiral, diastereomeric deuterium hydrogen methylene group permits configurational relations to be established by NMR—either ^2H NMR or ^1H NMR alone or with LIS enhancement. As a first application of the new method, the relative rotational propensity, R_A, of the cyano and isobutenyl groups in 1-cyano-2-isobutenyl-2,3-dideuteriocyclopropane has been determined to be 3.9 ± 0.5.

Internal rotational propensity is the key to many types of not obviously concerted thermal rearrangements. Specifically in rearrangements of cyclopropanes and cyclobutanes, an internal rotational component determines the stereochemistry of automerization and ring enlargement.[1-7]

In the past, investigation of this factor has employed optical activity as a tracer. Relatively straightforward in clarifying the

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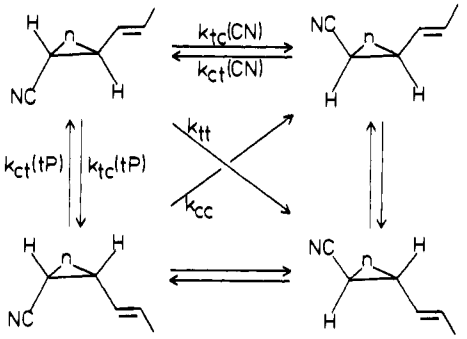

Figure 1. Set of single and double internal rotations interrelating *cis*- and *trans*-1-cyano-2-(*trans*-propenyl)carbocycles (n = 1, cyclopropane; n = 2, cyclobutane).

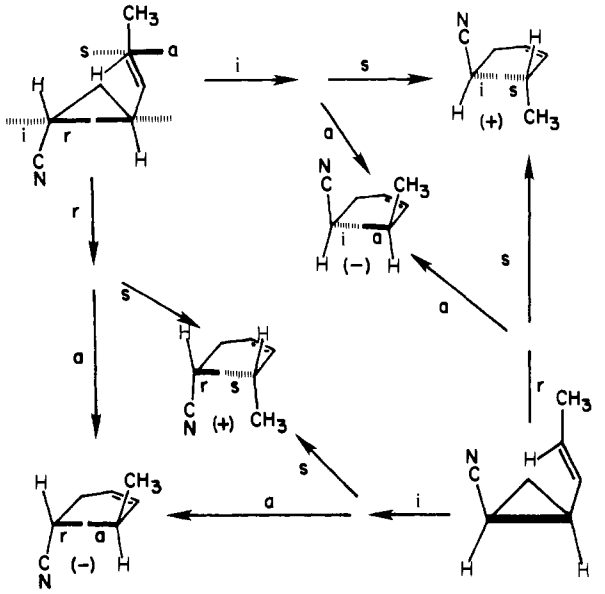

Figure 2. Internal rotational components leading to the two enantiomeric pairs of diastereomeric ring-enlarged products from rearrangement of *cis*- and *trans*-1-cyano-2-(*trans*-propenyl)cyclopropanes. The notation i and r defines inversion or retention of configuration at the cyano-bearing carbon atom; *s* and *a* represent suprafacial and antarafacial relative to the new chiral center generated at the methyl terminus of the double bond.

role of internal rotation in thermal automerizations of cis and trans cyclopropanes and cyclobutanes, the device becomes extremely burdensome when relative configurations and the relative magnitude of specific rotations between different families of chiral centers are required.

As an illustration of the use of conventional chiral techniques, cyclopropane rearrangements unravelled by Barsa may serve.[8] For the evaluation of relative internal rotational propensities,

$$R_A = k_{tc}(CN)/k_{tc}(tP) = k_{ct}(CN)/k_{ct}(tP)$$

the relative specific rotations of cis and trans diastereomers at the same degree of optical purity are required. These may be obtained by partial resolution and epimerization of the cyano group by basic catalysis, for example (see Figure 1).

Where the burden becomes excessively heavy and not easily surmountable is in ring enlargement of (*trans*-propenyl)cyclopropanes and cyclobutanes to cyclopentenes and cyclohexenes, n = 1 and 2, respectively.[8-10] The relative contribution of *ia* and

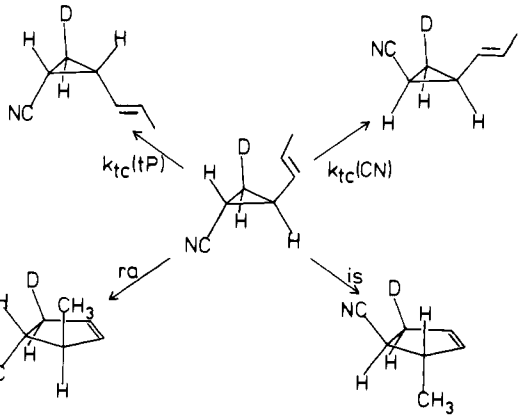

Figure 3. Use of a chiral CHD group converts the enantiomeric relation of k_{tc}(tP) and k_{tc}(CN) to a diastereomeric relation. The *ra* and *is* processes in ring enlargement of *trans*-1-cyano-2-(*trans*-propenyl)-3-deuterocyclopropane lead to diastereomeric products.

rs pathways, for example, to cis ring-enlarged product (see Figure 2), depends on an accurate knowledge of the relation of the specific rotations of educt and product of identical optical purity. It is also essential to establish the configurational relation of educt and product; otherwise there is unavoidable confusion between *ia* and *rs*. Chemical degradations or X-ray crystallographic methods can be used, but not without an expenditure of effort so large as to inhibit the accumulation of enough data to reveal the general factors controlling the role of internal rotations in ring expansion.

The advent of high-resolution deuterium nuclear magnetic resonance (^{2}H NMR) spectroscopy and the power of the lanthanide induced shift (LIS)[11] to educe reliable constitutional information provide much easier access to the required relationships. The need for optical resolutions and/or the establishment by often arduous chemical means of configurational interrelations disappears. This simplification is achieved by transforming interrelations among enantiomers into interrelations among diastereomers. In an earlier time, that transformation would have involved major perturbations such as that introduced by a new chiral center on the basis of, for example, the nonidentity of hydrogen and methyl.[3] What the new analytical methods make possible is the use of a chiral element on the basis of the minimal difference between hydrogen and deuterium. Although still not a zero perturbation, resulting isotope effects need be no more than secondary.

Determination of rotational propensities no longer requires measurement of changes in optical rotation and establishment of the relative specific rotations of cis and trans isomers but instead only requires measuring the relative amounts of deuterium cis and trans to one of the groups engaged in the internal rotation. In the example shown in Figure 3, it is assumed that the problem of synthesizing the racemic trans educt with a diastereomeric deuterium atom trans to the cyano group has been overcome. It then follows that the relative rotational propensity of cyano (CN) and *trans*-propenyl (tP) can be evaluated from the relative distribution in racemic cis product of cyano cis to deuterium [k_{tc}(CN)] and trans to deuterium [k_{tc}(tP)].

When the role of internal rotation in ring expansions is under investigation, replacement of optical activity by chiral deuterium labeling is especially advantageous. In the expansion of *trans*-1-cyano-2-(*trans*-propenyl)cyclopropane to *cis*- and *trans*-4-cyano-3-methylcyclopentene (Figure 3) the introduction of a deuterium-induced chiral methylene group remote from the site of reaction allows apportionment among the four reaction paths, *is*, *ia*, *rs*, and *ra* (Figure 2), by first separating cis and trans products by gas chromatography and then bifurcating each of these

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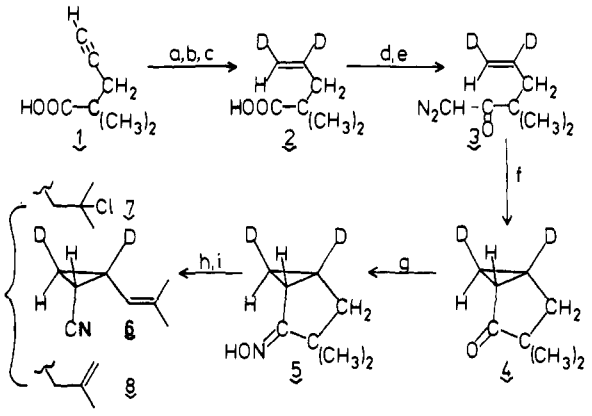

Figure 4. Synthetic scheme to *cis*-1-cyano-2,3-dideuterioisobutenylcyclopropane (patterned after a related sequence by Julia et al.[16]). Outlines of the various steps follow: (a) CH_3OH, H_2SO_4; (b) D_2, Lindlar catalyst; (c) KOH; (d) $(COCl)_2$; (e) CH_2N_2; (f) $CuSO_4$; (g) H_2NOH, HCl; (h) PCl_5; (i) $C_7H_7SO_2OH$.

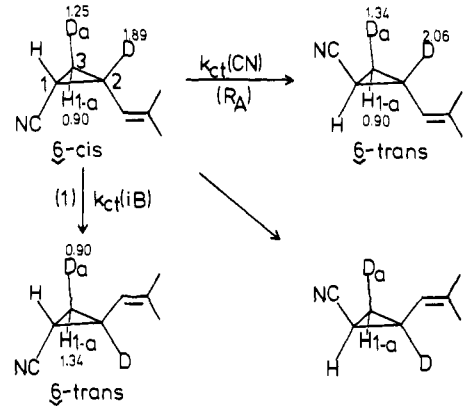

Figure 5. Thermal rearrangement of *cis*-**6** and *trans*-**6** by single rotations of the cyano (CN) group [k_{ct}(CN)] and the isobutenyl (iB) group [k_{ct}(iB)]. Chemical shifts of the various hydrogen atoms are shown and, in parentheses, the fraction of ^2H in the two positions D_a and H_{1-a} at carbon 3.

by NMR spectroscopy (trans is illustrated in Figure 3). In the trans ring-expanded product, paths *is* and *ra* are characterized by the chiral deuterium cis and trans, respectively, to the cyano group. Quantitative measurement can be made by ^2H NMR or ^1H NMR, whichever is the more convenient. In complicated molecules, having many different types of frequently overlapping ^1H, ^2H NMR has a clear advantage in giving simplified, more easily quantifiable spectra.

The method's experimental simplicity and quantitative reliability are particularly obvious in such applications. Even if struggles with degrees of relative optical purity can be avoided by application of chiral lanthanide shift reagents,[11] the often exceedingly onerous task of establishing configurational relationships may not be avoided. The trade-off for this advantage comes in having to devise stereospecific syntheses of chirally labeled starting materials.

Before we proceed to the specific illustration of the method it is worth noting that the method of chiral deuterium labeling complements the chiral LIS method for the establishment of specific rotations of the products of rearrangement by permitting relatively easy establishment of the configurational relation between the educt and the product. If the optical purity of a chirally labeled educt is known from its source, by application of the Berson radioactive-dilution method[12] or the chiral LIS method,[13] then the optical rotation of a product can be translated into the specific rotation of an enantiomer of configuration known relative to that of the educt, provided configurational integrity of the chiral deuterium label has been maintained in its passage from educt to product. If the optical purity of the chiral marker in the educt is x, its rotation is given by the following expression:

$$\alpha_{is} = x[\alpha]_{is}\frac{(is - ra)}{(is + ra)}$$

Admittedly, the value will be in error to the extent that the chiral methylene group contributes to the observed rotation, α_{is}.

Results

The synthetic obstacles to be overcome are stereochemical. Relative to the two substituents about which the thermal rearrangement will occur, the remote chiral deuterium center must be incorporated with a diastereospecificity of as high a degree as possible.

In the present scheme (Figure 4), two stages are critical. The first is the deuteration of a monosubstituted acetylene to a cis (*E*) dideuterioethylene where contamination by trans (*Z*) must be held to a minimum. The second is the addition of a carbene to the dideuterio olefin, in which reaction only one of two diastereomers should be produced.

In light of the success in obtaining cis olefins by reduction of acetylenes with Lindlar catalyst,[14] it was confidently expected that the deuteration of the monoacetylene would proceed in a similarly configurationally homogeneous fashion. In the event, this expectation was not well fulfilled nor were efforts to improve the configurational and constitutional specificity successful.

Spectroscopic analysis of compound **6** by ^1H NMR revealed the unexpected appearance of some ^1H at carbon atom 2 and, concomitantly, the appearance of some ^2H in the *Z* position at carbon atom 3. Although the former of these leakages was of no consequence to the experiment, the second reduced the purity of the desired *E* configuration of 1-deuterio olefin to 70%. Although this result led to a disappointing degradation of the accuracy of the final R_A value, the usefulness of the method itself could still be demonstrated.

The second critical stage involves an intramolecular carbene cyclization[15,16] to the bicyclo[3.1.0]hexan-2-one, **4**. Its diastereospecificity is fixed by the configuration of **3** and the unlikelihood of the five-membered ring becoming fused to the three-membered ring in any but a cis fashion.

The geminate dimethyl group in **1** leads in **6** to an isobutenyl group, the rotational propensity of which has not been examined previously. This grouping is present, incidentally, in chrysanthemic acid, the thermal behavior of which has interest for reasons of rotational hindrance. The geminate dimethyl group, according to Julia et al.,[16] fortunately directs the Beckmann rearrangement to the 2,3-bond and by good hap converts the rearrangement into its abnormal, nitrile-generating modification. Degradation of the isobutenyl group to aldehyde, by ozonolysis for example, would generate a versatile precursor of many substituted cyclopropanes apposite to the elucidation of the internal rotational factor.

The final step, (i), serves the purpose of establishing an equilibrium between the isobutenyl group (favored at equilibrium) and the 2-methylallyl group, which is formed in much larger amount under the initial kinetic control.

For the evaluation of the R_A factor, the relative rates at which *trans*-**6** is produced from *cis*-**6** by single rotations of the cyano [k_{ct}(CN)] and isobutenyl [k_{ct}(iB)] groups must be determined. The deuterium label at C_3 functions as the observer of the extent to which the cyano group at C_1 moves from a trans relation in *cis*-**6** to a cis relation in *trans*-**6** [k_{ct}(CN)] or remains in the trans relation in *trans*-**6** [k_{ct}(iB)] (see Figure 5). In practice, the reverse is measured—how much of the deuterium label appears cis to the cyano group in *trans*-**6** and how much appears trans.

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Table I. Thermal Diastereoisomerization of Deuterated *cis*-6

time, s	$^2H(1.34)/^2H(0.90)$		
3000	1.537[a]	1.549[b]	1.519[b]
4200	1.552	1.501	1.496
6300	1.500	1.459	1.455
9000	1.398	1.393	1.395
0000[c]	1.637	1.616	1.582
	±0.038	±0.012	±0.003

[a] By electronic integration. [b] Area measurement by two observers, independently. [c] The ratio of $^2H(1.34)/^2H(0.90)$ calculated by extrapolation to zero time from the equation $r = a_0 + a_1 t$, fitted by the method of least squares.

In the present instance the chiral deuterium label at C_3 is not as pure as had been hoped: "D" at C_3 is in fact 0.698 ^2H and "H" at C_3 is 0.302 "^2H" instead of the 1.000 and 0.000, respectively, needed for maximum sensitivity. The ratio of "D" (0.698 ^2H at 1.25 ppm) to "H" (0.302 ^2H at 0.90 ppm) in *cis*-**6** becomes inverted in *trans*-**6** generated by internal rotation of isobutenyl: "H" (0.302 ^2H at 1.34 ppm) to "D" (0.698 ^2H at 0.90 ppm).

In a general formulation, if the ratio of ^2H in "D" (1.25 ppm) to ^2H in "H" (0.90 ppm) is $a/(1 - a)$ in *cis*-**6** (see Figure 5) and the experimental ratio of ^2H in "D" (1.34 ppm) to that in "H" (0.90 ppm) in *trans*-**6** is r, then R_A, the ratio of $k_{ct}(CN)$ to $k_{ct}(iB)$, is given in the following derivation:

$$r = \frac{R_A a + (1 - a)}{R_A(1 - a) + a} \quad \text{whence} \quad R_A = \frac{a(1 + r) - 1}{a(1 + r) - r}$$

At maximum sensitivity, when $a = 1$, $R_A = r$; when $a = {}^1/_2$ (and $r = 1$), R_A becomes indeterminate.

The experimental ratio of ^2H (1.34 ppm) to ^2H (0.90 ppm) is needed at zero time in order to remove the degradation of the ratio occasioned by three processes: the reverse rearrangement of *trans*-**6** to the other diastereomer of *cis*-**6**, the interconversion of one diastereomer of *trans*-**6** into the other by a double-rotational process, and a similar double-rotational interconversion between the two diastereomers corresponding to *cis*-**6**. Ratios are therefore determined at four, short times of reaction as indicated in Table I and, being found to decrease in a satisfactorily linear fashion, they are fit to a linear equation by least-squares treatment and afford a value for the ratio at zero time, $r = 1.612 \pm 0.015$. The resulting value of $R_A = 3.9 \pm 0.5$.

The other groups with which this value may be compared are isopropenyl (2.20),[5] *trans*-propenyl (2.36),[3] and phenyl (2.47).[2] A value for *cis*-propenyl of 2.25 has been predicted but not as yet confirmed experimentally.[3] The value obtained here for isobutenyl is significantly higher. Whether another clue to the effect of structure on R_A is being revealed will depend on examination of additional systems and confirmation of the value obtained here.

As regrettable as the lack of constitutional and configurational integrity in the Lindlar reduction of the terminal acetylene may be, this example serves to illustrate the method of chiral deuterium labeling as a means of determining internal rotational propensities. Work in progress on the ring enlargement of 1-cyano-2-(*trans*-propenyl)cyclobutane is intended to further illustrate the usefulness of the method.

Experimental Section

2,2-Dimethylpent-4-enoic Acid. This material was prepared according to the procedure of Brannock, Pridgen, and Thompson.[17]

2,2-Dimethylpent-4-ynoic Acid (1). This procedure is patterned after that of Creger for 2,2-dimethyl-4-phenylbutyric acid.[18] Diisopropylamine (23.25 g, 0.224 mol), sodium hydride in mineral oil (54%) (11.04 g, 0.248 mol), and THF (225 mL) were placed in a 1-L, three-necked flask. To the stirred mixture, isobutyric acid (19.8 g, 0.225 mol) was added dropwise over 10 min. The internal temperature rose to 50–60 °C. Hydrogen evolution was completed by heating the mixture at reflux for 15 min. A 1.44 M solution of *n*-butyllithium in hexane (156 mL, 0.225 mol) was then added to the cooled (0 °C) mixture by injection through a stopple, keeping the temp below 10 °C. After 15 min of standing at 0 °C, the mixture was heated to 30–35 °C for 30 min to complete the metalation and then cooled to 0 °C. Propargyl bromide (34.5 g as an 80% solution in toluene, 0.225 mol) was added from a dropping funnel at such a rate as to keep the temp below 5 °C (40 min). Sodium bromide began to precipitate almost immediately. The ice bath was retained for 30 min, after which the mixture was heated to 25–30 °C for 1 h.

Water (300 mL) was then added at a rate to keep the temperature below 15 °C. The aqueous layer was separated, and the reaction flask and organic layer were washed with a mixture of water (150 mL) and ether (225 mL). The combined aqueous layers were extracted with two 100-mL portions of ether (discarded), acidified with 6 N HCl, and extracted with three 120-mL portions of ether. These combined ether extracts were washed with saturated aqueous NaCl (100 mL), dried ($MgSO_4$), and concentrated. The remaining liquid was distilled to separate recovered isobutyric acid and gave 2,2-dimethylpent-4-ynoic acid (1): 9.25 g (32.6%); bp 115–118 °C (3.33 kPa); ^1H NMR ($DCCl_3$) δ 1.31 (s, 6), 2.01 (t, 1, J = 6 Hz), 2.47 (d, 2, J = 6 Hz).

Methyl 2,2-Dimethyl-4-pentynoate. A solution of the acid 1 (11.98 g, 0.095 mol) in benzene (58 mL) and methanol (18 mL) was treated with concentrated H_2SO_4 (1.2 mL), refluxed for 18 h in a 125-mL flask equipped with a Dean-Stark apparatus, cooled, and diluted with ether (50 mL). The organic layer was washed with water (10 mL), twice with sat aq $NaHCO_3$ (10 mL each), and water (10 mL) and then dried ($MgSO_4$). Distillation gave methyl 2,2-dimethyl-4-pentynoate as a colorless liquid: 10.94 g (82%); bp 145–150 °C (101.3 kPa); ^1H NMR ($DCCl_3$) δ 1.26 (s, 6), 1.99 (t, 1, J = 5 Hz), 2.43 (d, 2, J = 5 Hz), 3.67 (s, 3).

(*E*)-2,2-Dimethyl-4,5-dideuteriopent-4-enoic Acid (2). Methyl 2,2-dimethyl-4-pentynoate (2.01 g, 24.3 mmol) in *n*-hexane (70 mL) was treated with 2.2 mL of a 5% solution of quinoline in *n*-hexane and Lindlar catalyst (200 mg), freshly prepared according to published procedure.[19] Deuteration was effected at atmospheric pressure and required 95 min for the absorption of 1 molar equiv. This operation was repeated several times until 14.59 g (0.104 mol) of the ester had been deuterated. The combined reaction mixture was distilled in a Vigreux column to give a pale yellow liquid, which was dissolved in methanol (300 mL) containing 8% by weight KOH and stirred at room temperature for 50 h. Concentrated to 50 mL under reduced pressure, the solution was diluted with water (100 mL) and extracted with ether (50 mL) to remove recovered ester. The aqueous layer was acidified with 6 N HCl and extracted 4 times with ether (50 mL each). The ether extracts were washed twice with brine (30 mL) and dried ($MgSO_4$). Evaporation gave a pale yellow liquid which was distilled to give (*E*)-2,2-dimethyl-4,5-dideuteriopent-4-enoic acid (**2**) as a colorless liquid: 10.05 g (77%); ^1H NMR ($DCCl_3$) δ 1.22 (s, 6), 2.36 (s, 2), 5.06 (s, 1, *Z* H_4). Methyl ester: ^1H NMR ($DCCl_3$) δ 1.18 (s, 6), 2.25 (s, 2), 3.64 (s, 3), 5.40 (s, <1).

2,2-Dimethylpent-4-enoate (2,2-diprotio): ^1H NMR ($DCCl_3$) δ 1.20 (s, 6), 2.31 (d, 2, J = 7.6 Hz), 5.05 (s, 1), 5.10 (s, 1), 5.70–5.83 (m, 1). Methyl 2,2-dimethylpent-4-enoate: ^1H NMR ($DCCl_3$) δ 1.17 (s, 6), 2.25 (d, 2, J = 7.2 Hz), 3.63 (s, 3), 4.93 (m, 1), 5.10 (br s, 1), 5.45–6.00 (m, 1); LIS ($Eu(fod)_3$) relative rates of shift: CH_3O 1.00, CH_2 0.68, $C(CH_3)_2$ 0.63, H_4 0.49.

3,3-Dimethylbicyclo[3.1.0]hexan-2-one (4). The sodium salt of **2** (10.05 g, 0.0773 mol) was prepared by dissolving it in aqueous sodium hydroxide (3.25 g, 0.081 mol), evaporating the solution under reduced pressure, and drying the residue in a vacuum oven at 70 °C for 2 h. To a stirred suspension of the resulting dry sodium salt at 0 °C in dry benzene (75 mL) containing dry pyridine (2.0 mL), oxalyl chloride (30 g) was added carefully. The reaction mixture was stirred below 5 °C for 2 h, filtered, and evaporated under reduced pressure to give crude acid chloride, which was dissolved in dry ether (75 mL) and added to an excess of alcohol-free ethereal diazomethane (dried over KOH pellets). This mixture was stirred at 0–5 °C for 1 h and then at room temperature for 2 h and evaporated to afford crude diazoketone, which was then dissolved in cyclohexane (750 mL) and treated with anhydrous $CuSO_4$ (2.5 h). The resulting suspension was refluxed for 20 h, after which time the IR spectrum no longer showed any diazoketone. The filtered solution was concentrated by distillation in a Vigreux column to an orange oil and distilled to give 3,3-dimethylbicyclo[3.1.0]hexan-2-one (**4**) as a pale yellow oil: 6.15 g (63.1%). 3,3-Dimethyl-5,6-dideuteriobicyclo[3.1.0]-hexan-2-one: ^1H NMR ($DCCl_3$) δ 0.82 (d, 1, J = 3.1 Hz, endo H_6), 1.00 (s, 3), 1.05 (s, 3), 1.84 (1, d, H_1), 1.85 (d, 1, J = 12 Hz), 2.05 (d, 1, J = 12 Hz, exo/endo H_4).

3,3-Dimethylbicyclo[3.1.0]hexan-2-one Oxime (5). The bicyclic ketone **4** (6.010 g, 0.048 mol) and $NH_2OH{\cdot}HCl$ (7.29 g, 0.105 mol) were dissolved in a mixture of dry ethanol (25 mL) and dry pyridine (25 mL)

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Table II. Geometrical Isomerization of *cis*-6 (No Deuterium)

sample, T, °C	time, s	*cis*-6	*trans*-6
D free, 218.2	000	0.9913	0.0087
	4200	0.668	0.332
	5400	0.615	0.385
	14400	0.452	0.548
	19800	0.423	0.577
	23400	0.424	0.576
	86400	0.424	0.576
D free, 207.5	000	0.9913	0.0087
	3600	0.837	0.163
	7200	0.720	0.280
	14400	0.573	0.427
	19800	0.515	0.485
	90000	0.418	0.582
D_2, 206.7	000	0.986	0.014
	3000	0.883	0.117
	4200	0.848	0.152
	6300	0.784	0.216
	9000	0.730	0.270

and heated at reflux for 3 h. Solvents were removed under reduced pressure (rotary evaporator) to give a noncrystalline residue, which was suspended in water (50 mL) and extracted 4 times with ether (50 mL each). The ether solution was washed twice with water (10 mL), dried ($MgSO_4$), and concentrated to a pale yellow oil. Crystallization from *n*-hexane (1 mL) gave colorless crystals: 3.56 g; mp 69–71 °C. Second crop: 0.44 g, mp 68–70 °C. Total yield: 59%. Although a third crop was not obtained, the filtrate contained mainly oxime as judged from its NMR spectrum. 3,3-Dimethyl-5,6-(*exo*)-dideuteriobicyclo[3.1.0]hexan-2-one oxime: ^{1}H NMR ($DCCl_3$) δ 0.62 (d, 1, J = 2.3 Hz, endo H_6), 1.15 (s, 3), 1.25 (s, 3), 1.61 (s, < 1, exo H_6), 1.80 (s, 1), 1.95 (s, 1, exo/endo H_4), 2.11 (s, <1, H_5), 2.42 (br s, 1, H_1).

***cis*-1-Cyano-2-isobutenylcyclopropane.** To a solution of phosphorus pentachloride (2.7 g) in ether (80 mL), cooled in an ice-water bath, dry pyridine (1.5 mL) was added. After 3 min, the oxime **5** (1.50 g, 0.0106 mol) in dry ether (10 mL) containing dry pyridine (1.23 mL) was added gradually. The reaction mixture was stirred in the ice-water bath for 2 h and then at room temp for 23 h. The resulting solution was poured into a water–ice mixture (40 mL) and extracted 4 times each with 40 mL of ether. The ether layer was washed twice each with 12 mL of saturated aqueous $NaHCO_3$ and with brine (12 mL) and dried ($MgSO_4$). Evaporation gave a brown oil that was dissolved in dry toluene (15 mL) and refluxed for 2 h with *p*-toluene sulfonic acid (300 mg). The reaction mixture was poured into 15 mL of saturated $NaHCO_3$ and treated with ether (15 mL). The separated organic layer was washed twice each with 10 mL of saturated $NaHCO_3$ and brine (10 mL) and dried ($MgSO_4$). Evaporation afforded a pale yellow oil consisting of three products: *cis*-1-cyano-2-isobutenylcyclopropane (*cis*-**6**), *cis*-1-cyano-2-(2-chloro-2-methylpropyl)cyclopropane (**7**), and *cis*-1-cyano-2-(2-methylallyl)cyclopropane (**8**) in the ratios 10:2:1, respectively, as determined by GLC (2 m × 0.25 in., Carbowax 20M on Anakrom ABS 50/60 at 135 °C and a flow rate (He) of 60 mL/min): retention times 9, 21, and 7 min, respectively.

cis-1-Cyano-2-isobutenylcyclopropane: ^{1}H NMR ($DCCl_3$) δ 0.98 (br m, 1, H_{3c}), 1.33 (br m, 1, H_{3t}), 1.68 (br m, 1, H_1), 1.760 (s, 3), 1.764 (s, 3), 1.99 (br m, 1, H_2), 4.90 (d, 1, J = 8.6 Hz, H_v).

1-Cyano-2,3-dideuterio-2-isobutenylcyclopropane (*cis*-**6**): ^{1}H NMR ($DCCl_3$) δ 0.96 (d, 1, J = 5.4 Hz, H_{3c}), 1.35 (br s, <1, H_{3t}), 1.59 (d, 1, J = 5.4 Hz, H_1), 1.76 (s, 6), 1.98 (br s, <1, H_2), 4.90 (s, 1, H_v); LIS ($Eu(fod)_3$) relative rate of shift H_1 1.00, H_v 0.74; H_{3c} 0.61, *gem*-$(CH_3)_2$: 0.20, 0.12; ^{2}H NMR ($DCCl_3$) δ 0.90 (s, <1, $^2H_{3c}$), 1.25 (s, 1, $^2H_{3t}$), 1.88 (s, 1, $^2H_2$).

Thermal Isomerization of *cis*-1-Cyano-2-isobutenylcyclopropane. Compound *cis*-**6** (no D) was collected by GLC and purified further by rechromatographing: 98.9%, contaminated by **8** (0.3%), *trans*-**6** (no D) (0.8%). A 2-mg sample was sealed in a 2-mL Pyrex tube in vacuo. Prior to use, the tubes were soaked in concentrated NH_4OH solution, washed with distilled water and acetone, and dried. The sealed tubes were heated in the vapors of a refluxing naphthalene bath at 218.2 °C and a refluxing tetralin bath at 207.5 °C. Analysis was by a 300 ft × 0.01 in. Carbowax 20M capillary column (Perkin-Elmer) at 125 °C and 34 psi He and an integrator. Retention times of *cis*-**6** and *trans*-**6** were 23 and 19 min, respectively.

Each sample was analyzed 3 times. The data are summarized in Table II. Rate constants ($k_1 + k_{-1}$) are calculated by linear regression of the expression for a reversible first-order reaction:

$$\ln [(T_e - T_0)/(T_e - T_i)] = (k_1 + k_{-1})t_i$$

The values of ($k_1 + k_{-1}$) at 218.2 and 207.5 °C are (2.14 ± 0.01) × 10^{-4} s^{-1} ($K = T/C$ = 1.360) and (8.9 ± 0.2) × 10^{-5} s^{-1} (K = 1.392), respectively.

Thermal Isomerization of Deuterated *cis*-6. Deuterated *cis*-**6** was rechromatographed before use. It was 98.6% of purity, being contaminated with *trans*-**6** (1.3%) and **8** (1.0%). Pyrex tubes were soaked in concentrated NH_4OH for 30 h, washed with distilled water and acetone, and dried. Samples of deuterated *cis*-**6** of 100, 150, 200, and 300 mg were sealed in vacuo in Pyrex ampules of 80, 110, 125, and 130 mL, respectively. The thermal reaction was performed at 206.7 °C in the vapors of refluxing tetralin. Analysis of geometrical isomerization was effected as described above on the Carbowax 20M capillary column. The data are given as the third set in Table I. The value of ($k_1 + k_{-1}$) calculated in the same manner as above is (6.7 ± 0.3) × 10^{-5} s^{-1} ($K = T/C$ = 1.392).

Deuterium was analyzed on a Brucker Spectrospin NMR spectrometer. The starting material, *cis*-**6**, showed three ^{2}H absorptions: at 1.89 ppm (downfield from Me_3Si), the allylic ^{2}H at C_2 (see Figure 5); at 1.25 ppm, ^{2}H at C_3 trans to the cyano (CN) and isobutenyl (iB) labeled "D" in Figure 5; and at 0.90 ppm, ^{2}H contaminating H at C_3. Quantitative analysis of their relative areas in two different experiments led to a ratio of ^{2}H (1.25 ppm) to ^{2}H (0.90 ppm) of 2.31 ± 0.19.

The four samples of *trans*-**6** recovered from the rearrangement above were isolated and purified by GLC. Analysis of a sample of *trans*-**6** prepared from *cis*-**6** by epimerization of the cyano group with potassium *tert*-butylate in Me_2SO revealed minor changes in chemical shift: the allylic ^{2}H at C_2 shifted to 2.06 ppm; ^{2}H at C_3 cis to CN and trans to iB shifted to 1.34 ppm; and ^{2}H at C_3 trans to CN and cis to iB is unchanged at 0.90 ppm.

trans-1-Cyano-2-isobutenylcyclopropane: ^{1}H NMR ($DCCl_3$) δ 0.82–1.47 (m, 3, H_1, H_{3c}, H_{3t}), 1.68 (s, 3), 1.76 (s, 3), 1.93–2.28 (m, 1, H_2), 4.55 (d of m, 1, J = 8.5 Hz, H_v).

trans-1-Cyano-2,3-dideuterio-2-isobutenylcyclopropane *trans*-**6**: ^{1}H NMR ($DCCl_3$) δ 0.94 (d, 1, J = 2.4 Hz, H_{3c}), 1.21 (d, 1, J = 2.4 Hz, H_1), 1.69 (d, 3, J = 1.4 Hz), 1.77 (d, 3, J = 1.3 Hz), 4.52 (m, 1, H_v); ^{2}H NMR ($DCCl_3$) δ 0.93 (s, <1, $^2H_{3c}$), 1.37 (s, 1, $^2H_{3t}$), 2.09 (s, 1, $^2H_2$).

Quantitative analysis was effected in the manner above. The relative areas of ^{2}H (1.34 ppm) to ^{2}H (0.90 ppm) in each of the four samples were determined by two independent observers working from the traces and from the printout of relative intensities. These results are given in Table I.

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Registry No. 1, 86101-48-6; **2**, 86101-50-0; **2** methyl ester, 86101-51-1; **2**·Na, 86101-53-3; **2** acid chloride, 86101-54-4; **3**, 86101-55-5; **4**, 74454-53-8; **4**-d_2, 86101-56-6; **5**, 86101-57-7; **5**-d_2, 86101-58-8; *cis*-**6**, 86101-59-9; *cis*-**6**-d_2 (isomer 1), 86101-62-4; *cis*-**6**-d_2 (isomer 2), 86161-28-6; *trans*-**6**, 86101-63-5; *trans*-**6**-d_2 (isomer 1), 86161-27-5; *trans*-**6**-d_2 (isomer 2), 86161-29-7; **7**, 86101-60-2; **8**, 86101-61-3; methyl 2,2-dimethyl-4-pentynoate, 86101-49-7; 2,2-dimethylpent-4-enoate, 86101-52-2; methyl 2,2-dimethylpent-4-enoate, 76352-72-2; isobutyric acid, 79-31-2; propargyl bromide, 106-96-7.