J. Am. Chem. Soc. 1981, 103, 1579-1581

Trispiro[tricyclo[3.3.3.0^{1,5}]undecane-2,1′:8,1″:9,1‴-tris[cyclopropane]], a Chiral Fluxional Hydrocarbon

John E. Maggio and Howard E. Simmons III*[†]

Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138

Jay K. Kouba

Department of Chemistry, Purdue University
West Lafayette, Indiana 47907

Received October 6, 1980

The title compound (**1**) adopts a chiral conformation of C_3 point-group symmetry due to geometric constraints caused by severe crowding of the cyclopropyl groups (Figure 1).[1] The compound is in fact fluxional, and ^{13}C and ^{1}H NMR spectroscopy can be used to observe the interconversion of the enantiomers[2] (Figure 2) at temperatures between −43 and +147 °C. This novel inversion apparently does not proceed through a higher symmetry C_{3v} intermediate.

1 was prepared by cyclopropanation of 2,8,9-trimethylene-[3.3.3]propellane[3] (**2**) as shown in Scheme I.[4] The third cyclopropanation is quite slow, and a large excess of reagents is necessary to force the reaction to completion. Purification by preparative gas chromatography (20% SE-30 on Chromosorb-W) gave colorless crystalline **1**.[5]

Variable-temperature ^{1}H NMR spectra (270 MHz) of **1** are shown in Figure 3. At −43 °C (Figure 3A) the cyclopentyl and cyclopropyl protons are each resolved into ABCD spin patterns, one resonance of each further split by a single long-range coupling. Chemical shift assignments and coupling constants are reported in Table I (values for the model compound spiro[2.4]heptane are included for comparison). At 147 °C (Figure 3B) the system is approaching fast exchange and two AA′BB′ patterns are observed.[6]

The conformation of **1** is readily deduced from the coupling constants in the low-temperature ^{1}H NMR spectrum. The magnitudes of the four three-bond vicinal couplings can be used to define the configuration of the cyclopentyl ethano bridges and hence the approximate geometry of the entire molecule.[7] The conformation thus derived matches very closely that derived from force-field calculations (Allinger's MM2).[8] For example, in the geometry predicted by the force-field calculation, the dihedral angle between H_6 and H_8 is 166°. The large value of $^{3}J_{68}$ (13.4 Hz) is consistent with a trans relationship between these protons in the constrained five-membered rings. The notably high-field cyclopentyl proton (H_4, δ 0.76) lies over the shielding region of a cyclopropyl ring in the theoretical conformation as well as in that deduced from coupling constants, while its low-field geminal partner (H_8, δ 2.07) lies in the deshielding region of two cyclopropyl rings.[9,10] H_5 and H_8, which show long-range coupling ($^{4}J_{58}$ = 1.8 Hz), lie approximately in a "W" configuration in the calculated geometry.[11] The force-field calculation even predicts which of the methylenes of the cyclopropyl rings displays a larger HCH angle and hence has a more negative $^{2}J_{\mathrm{HH}}$.[12]

Scheme I

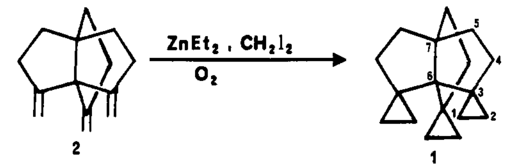


Table I. Chemical Shifts and Coupling Constants in 1

	chemical shifts, ppm		
	1[a]		spiro[2,4]-heptane[b]
	out	in	
cyclopropyl			
protons	H_1 0.04	H_2 0.18	0.41
	H_5 0.86	H_3 0.35	
methylene carbons	C_2 8.63	C_1 4.85	13.1
spiro carbons	C_3 27.73		22.5
cyclopentyl	"α"	"β"	
protons	H_4 0.76	H_6 1.45	H_α 1.40
	H_8 2.07	H_7 1.70	H_β 1.56
methylene carbons	C_4 36.69	C_5 37.92	C_α 36.2
quaternary carbons	C_6 56.73	C_7 65.44	C_β 32.6

proton–proton coupling[c] in 1, Hz

cyclopropyl			cyclopentyl	
$^{2}J_{15} = -3.28$	$^{2}J_{23} = -4.73$	geminal	$^{2}J_{48} = -11.86$	$^{2}J_{67} = -11.62$
$^{3}J_{13} = 9.31$	$^{3}J_{25} = 9.33$	cis	$^{3}J_{46} = 5.97$	$^{3}J_{78} = 5.80$
$^{3}J_{12} = 5.20$	$^{3}J_{35} = 5.11$	trans	$^{3}J_{68} = 13.42$	$^{3}J_{47} < 0.5$
		long-range coupling[d] $^{4}J_{58} = 1.80$		

[a] ^{1}H NMR spectra in toluene-d_8 at −43 °C, ^{13}C NMR spectra in CDCl$_3$ at −38 °C, referenced to internal Me$_4$Si. Resonances are uniquely assigned by various double-resonance techniques: decoupling, saturation spin transfer, spin tickling, and nuclear Overhauser effects. ^{1}H and ^{13}C resonances are arbitrarily numbered from upfield to downfield; out and in refer to cyclopropyl methylenes; α and β refer to positions 1 and 2 bonds from the spiro carbon, respectively (see Figures 1 and 2, and Scheme I). [b] ^{1}H NMR: Lambert, J. B.; Magyar, E. S. *Org. Magn. Reson.* 1973, *5*, 403. ^{13}C NMR: Strong, A. B. Ph.D. Thesis, University of Utah, UT, 1971. [c] Coupling constants were obtained by analysis of first-order spectra at 270 MHz, then refined by iterative fit to 100-MHz spectra by using the program ITRCAL supplied by Nicolet Corporation. [d] There are two potential coupling "pathways", one over four and one over five bonds.

Representative variable-temperature ^{13}C NMR spectra of the cyclopropyl methylene carbons of **1** are shown in Figure 4. As expected, two resonances are observed at lower temperatures. At higher temperatures the two resonances coalesce to a single line, indicating fast exchange of the cyclopropyl methylene carbons. Line-shape analysis based on uncoupled two-site exchange was performed by using 11 spectra between −20 and +35 °C. The appropriate Eyring plot gave activation parameters of $\Delta H^{\ddagger} = 11.3 \pm 0.6$ kcal/mol $\Delta S^{\ddagger} = -6.1 \pm 2.2$ eu.[13] The remaining ^{13}C resonances of **1** remain sharp from −60 to +53 °C.

While the negative value of $\Delta S^{\ddagger}$ obtained is consistent with an intramolecular rearrangement with an ordered transition state, the ^{13}C NMR results do not distinguish between synchronous or

---

[†] Photoproducts Dept., E. I. du Pont de Nemours and Co., Wilmington, DE 19898.

(1) For other examples of conformational chirality, see: Binsch, G. *Top. Stereochem.* **1968**, *3*, 97–192 and references therein. For other examples of C_3 point-group symmetry, see: Mislow, K. *Acc. Chem. Res.* **1976**, *9*, 26–33. Nakazaki, M.; Yamamoto, K.; Toya, T. *J. Org. Chem.* **1980**, *45*, 2553–4.

(2) The inversion is perhaps best visualized as reversing the pitch of the blades of a fan.

(3) Drouin, J.; Leyendecker, F.; Conia, J. M. *Tetrahedron Lett.* **1975**, 4053–4056; *Tetrahedron* **1980**, *36*, 1203–1208.

(4) This compound has been independently prepared: Drouin, J. Ph.D. Thesis, Université de Paris-Sud, Paris, 1976.

(5) Anal. ($C_{17}H_{24}$) C, H. mp 270–289 °C. Beautiful colorless crystals (hexagonal plates) were grown from "wet" MeOH, but a crystal structure failed as the crystals decomposed in the X-ray beam.

(6) This temperature was the upper limit of the spectrometer.

(7) Karplus, M. *J. Chem. Phys.* **1959**, *30*, 11–15. Booth, H. *Prog. Nucl. Magn. Reson. Spectrosc.* **1969**, *5*, 149–381.

(8) Allinger, N. *J. Am. Chem. Soc.* **1977**, *99*, 8127–8134; *Adv. Phys. Org. Chem.* **1976**, *13*, 1–82. We are grateful to Dr. D. Pensak (Central Research and Development Dept., E. I. du Pont de Nemours and Co., Wilmington, DE) and Dr. G. Graham (Dept. of Chemistry, Harvard University, Cambridge, MA) for assistance with these calculations.

(9) Tori, K.; Kitahonoki, K. *J. Am. Chem. Soc.* **1965**, *87*, 386–387 and references therein.

(10) This is the largest $\Delta\delta_{\mathrm{gem}}$ reported in an aliphatic system, to the best of our knowledge. The exact magnitude is solvent dependent.

(11) Rassat, A.; Jefford, C. W.; Lehn, J.-M.; Waegell, B. *Tetrahedron Lett.* **1964**, 233–243. Barfield, M.; Chakrabarti, B. *Chem. Rev.* **1969**, *69*, 757–778.

(12) Gutowsky, H. S.; Karplus, M.; Grant, D. M. *J. Chem. Phys.* **1959**, *31*, 1278–1289. Kowalewski, J. *Prog. Nucl. Magn. Reson. Spectrosc.* **1977**, *11*, 33–42.

(13) Calculations were performed on an IBM 360 computer by using DNMR-3 (Kleier, D. A.; Binsch, G. *J. Magn. Reson.* **1970**, *3*, 146–160) modified as described by: Bushweller, C. H.; Bhat, G.; Letendre, L. J.; Brunelle, J. A.; Bilofsky, J. S.; Ruber, H.; Templeton, D. H.; Zalkin, A. *J. Am. Chem. Soc.* **1975**, *97*, 65–73.

0002-7863/81/1503-1579$01.25/0

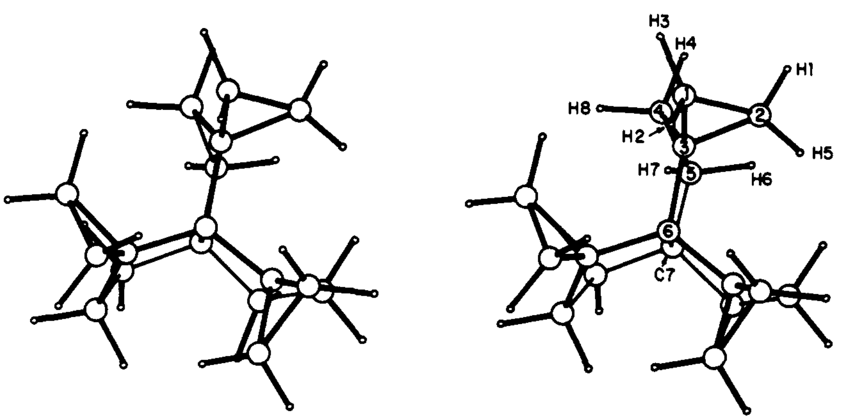


Figure 1. PLUTO stereodrawing of one enantiomer of **1** derived from Allinger's MM2 force field (see text). Numbering refers to the resonance assignments of Table I.

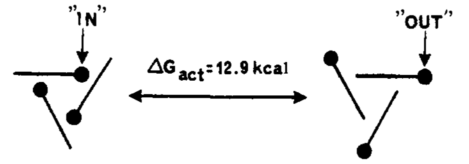


Figure 2. Schematic representation of the inversion of **1**, showing only cyclopropyl methylene carbons. After inversion, the in set of CH_2 groups (C1 in Figure 1) has become the out set (C2 in Figure 1).

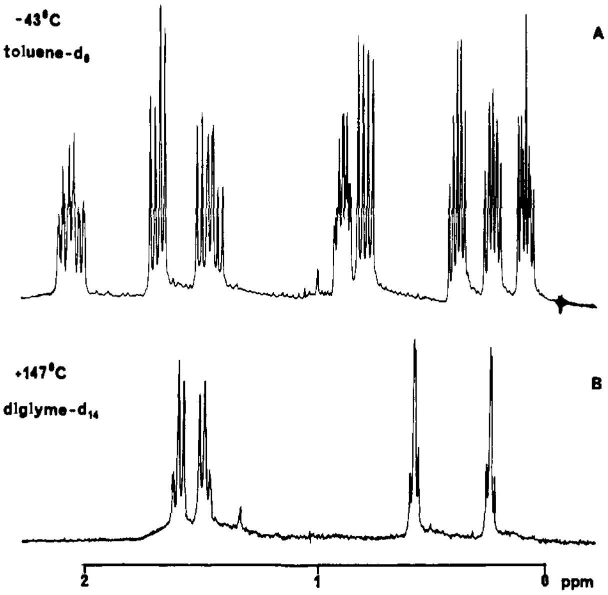


Figure 3. 270-MHz ^1H NMR spectra of **1**.

stepwise flipping of the three cyclopropyl rings. It was anticipated that analysis of the variable-temperature ^1H NMR spectra would be more informative about the mechanism of the rearrangement. ^1H NMR spectra of **1** at 100 and 270 MHz in the slow-exchange limit were satisfactorily simulated as static spectra.[14] Spectra simulated for intermediate exchange rates based on the same nuclear permutation, however, did *not* satisfactorily match experimental spectra.[16] This result is consistent with the existence of one or more long-lived intermediates in the exchange process

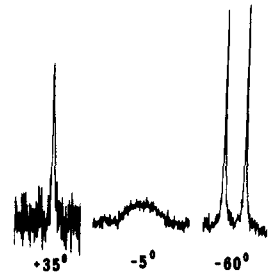


Figure 4. Representative proton-decoupled ^{13}C NMR spectra (25.2 MHz) of the cyclopropyl methylene region (11 → 2 ppm) of **1** in CD_2Cl_2.

and not consistent with synchronous inversion[17] of the three cyclopropyl groups via a conformer of C_{3v} symmetry.

The dicyclopropane 2-methylenedispiro[tricyclo[3.3.3.0^{1,5}]undecane-8,1′:9,1″-bis[cyclopropane]] also adopts a chiral conformation in the cold. Its inversion proceeds with Eyring activation parameters of $\Delta H^{\ddagger} = 8.0 \pm 0.6$ kcal/mol and $\Delta S^{\ddagger} = -0.6 \pm 0.3$ eu. Assuming these values approximate the barrier imposed by a single cyclopropyl–cyclopropyl interaction on the [3.3.3.0] skeleton, it is clear that the inversion barrier in **1** is considerably lower than would be expected for inversion through a single intermediate of C_{3v} symmetry.[18] We consider it likely that **1** inverts in a stepwise process, one-third of the molecule at a time, perhaps cooperatively where twisting of one ethano bridge induces the twisting of the other two.[19]

Epoxidation of **2** gives a mixture of symmetrical and unsymmetrical triepoxide analogues of **1**.[20] The symmetrical triepoxide trispiro[tricyclo[3.3.3.0^{1,5}]undecane-2,2′:8,2″:9,2‴-tris[oxirane] heptadecane (**3**) adopts a conformation analogous to that of **1** with the oxygens occupying the "inner" positions.[21] This is anticipated on the basis of the smaller steric requirement of oxygen relative to a methylene group.[22] No significant changes are observed in

---

[14] By averaging the coupling constants and chemical shifts in a manner consistent with the molecular inversion of Figure 2, spectra in the fast-exchange limit were also simulated[15] and are in fairly close agreement with the experimental spectrum at 147 °C. Since high-field spectra at the fast-exchange limit were not obtainable and since temperature dependence of coupling constants at higher temperatures cannot be excluded, detailed comparison of experimental and theoretical fast-exchange spectra cannot be made.

[15] Simulations were performed by using the program NTCSIM supplied by Nicolet Corporation.

[16] Calculations were performed on a CDC-7700 computer by using the program described in ref 13.

[17] For other examples, see: Meakin, P.; Guggenberger, L. J.; Tebbe, F. N.; Jesson, J. P. *Inorg. Chem.* **1974**, *13*, 1025–1032. Binsch, G.; Kesler, H. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 411–428.

[18] Force-field calculations as described in ref 8 suggest that the C_{3v} conformer is prohibitively high in energy. Inspection of Dreiding models intuitively suggests the same conclusion.

[19] Osawa, E. *J. Am. Chem. Soc.* **1979**, *101*, 5523–5529.

[20] Reaction of **2** with *m*-chloroperbenzoic acid gives a ≃50:50 mixture (85% yield) of the diastereomeric symmetrical and unsymmetrical triepoxides, which can be separated by preparative thin-layer chromatography (silica gel, 2:1 hexane:ether).

[21] The cyclopentyl region of the ^1H NMR spectrum of **3** is virtually identical with that of the low-temperature spectrum of **1** (Figure 3A). The conclusion that the oxygens in **3** are "in" (see Figure 2) is based on analysis of shift reagent studies (^{13}C and ^1H) of both **3** and the unsymmetrical triepoxide,[20] as well as consideration of ^{13}C and ^1H chemical shifts and coupling constants of the compounds over a wide range of temperatures and solvents, and their TLC behavior. The chirality of **3** was established by using the chiral shift reagent tris[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]europium(III). Hinckley, C. C. *J. Am. Chem. Soc.* **1969**, *91*, 5160. Rueben, J. *Prog. Nucl. Magn. Reson. Spectrosc.* **1975**, *9*, 1–70. Willcott, M. R., III; Davis, R. E. *Science (Washington, DC)* **1975**, *190*, 850–857.

the ^{1}H or ^{13}C NMR spectra of **3** over the temperature range -80–+140 °C, reflecting the thermodynamic stability of the oxygens "in" conformer relative to the unobserved oxygens "out" conformer.

Acknowledgment. H.E.S. is indebted to the late Professor R. B. Woodward for his knowledgeable guidance and generous support (NSF Grant CHE 78-25699). J.E.M. is grateful to Professor K. E. Bloch for support and encouragement. Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support (J.K.K.) of this research. The high-field NMR experiments were performed at the F. Bitter National Magnet Laboratory, Massachusetts Institute of Technology. The NMR facility is supported by Grant RR00995 from the Division of Research Resources of the National Institutes of Health and the National Science Foundation under Contract C-670. We thank Professor J. D. Roberts for comments on the manuscript.

---

(22) Pauling, L. "The Nature of the Chemical Bond", 3rd ed.; Cornell University Press: Ithaca, NY, 1960; p 361. Flory, P. J.; Mark J. E. *Makromol. Chem.* **1964**, *75*, 11–21; *J. Am. Chem. Soc.* **1965**, *87*, 1415–1423.

Rearrangement of a Geometrically Restricted Triepoxide to the First Topologically Nonplanar Molecule: A Reaction Path Elucidated by Using Oxygen Isotope Effects on Carbon-13 Chemical Shifts

Steven A. Benner, John E. Maggio, and
Howard E. Simmons III*†

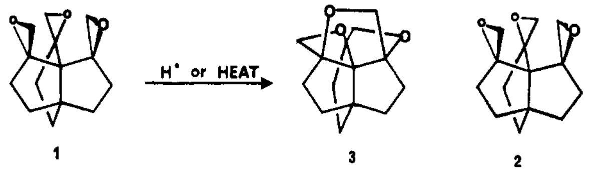
Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138

Received October 6, 1980

The symmetrical triepoxide trispiro[tricyclo[3.3.3.0^{1,5}]undecane-2,2':8,2'':9,2'''-tris[oxirane]] (**1**[1]) cleanly undergoes rearrangement to the triether 2,5,14-trioxahexacyclo[5.5.2.1.2^{4,10}.0^{4,17}.0^{10,17}]heptadecane (**3**), both thermally and with acid catalysis (Scheme I).[2] To elucidate the reaction pathway for this novel rearrangement, we have developed and applied a new method of double-isotope labeling based on the perturbation of ^{13}C NMR chemical shifts by isotopes of oxygen.[3,4]

Triether **3** has been a target of our synthetic efforts because it is topologically unique. To our knowledge, it is the first organic molecule known which has a structure which cannot be represented as a planar graph.[5] In addition, the rearrangement that produces **3** was especially interesting, because it could proceed via an unprecedented $2\sigma + 2\sigma + 2\sigma$ to $2\sigma + 2\sigma + 2\sigma$ electrocyclic rearrangement[6] (Scheme II, path a). Consideration of the conformations of **1**, unsymmetrical triepoxide **2**, and the all-carbon analogue of **1**, trispiro[tricyclo[3.3.3.0^{1,5}]undecane-2,1':8,1'':9,1'''-tris[cyclopropane]],[7] suggested that a conformation of **1** is possible which directs the lone pairs on each oxygen into the region of the antibonding orbitals of an adjacent C–O bond[8] (Figure 1). These considerations, combined with the fact that the electrocyclic reaction represented in path a is orbital-symmetry allowed,[9] made us optimistic that the rearrangement of **1** to **3** might be the first case of an electrocyclic reaction involving only σ bonds. However, an alternative route from **1** to **3** (path b) was also conceivable. Although unprecedented in its details, this route is more reminiscent of conventional epoxide chemistry.[10]

Scheme I



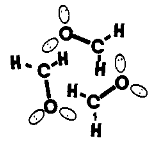


Figure 1. Schematic representation of **1** observed from the "top" along the C_3 axis.

The bonds broken and created in path a are different from those broken and created in path b, making the two paths distinguishable. To make this distinction, we have exploited the known ability of isotopic substitution of ^{18}O for ^{16}O to produce perturbations in the NMR chemical shifts of atoms directly attached to oxygen.[3,4] While the precise magnitude of this isotopic perturbation of chemical shift ($\Delta\delta$) depends on the nuclei involved and molecular structure, the ^{13}C NMR spectrum of a compound partially labeled with ^{16}O and ^{18}O at a position adjacent to a single ^{13}C-labeled atom will show two resonances, the downfield resonance arising from those ^{13}C atoms bonded to ^{16}O and the upfield resonance arising from those bonded to ^{18}O.[11] The relative intensity of the two resonances corresponds to the ratio of ^{16}O and ^{18}O labels in the adjacent position.[12] In contrast, should the ^{13}C

[†] Photoproducts Department, E. I. du Pont de Nemours and Co., Wilmington, DE 19898.

(1) **1**–**3** are all chiral molecules. In our experiments, **1** is in fact a racemic mixture of the 2*S*,8*S*,9*S* enantiomer (shown) and the 2*R*,8*R*,9*R* enantiomer, while **2** is a racemic mixture of 2*R*,8*S*,9*S* enantiomer (shown) and the 2*S*,8*R*,9*R* enantiomer. The chirality of these species was established by NMR spectroscopy using the chiral shift reagent tris[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]europium (III).

(2) Thermal reactions were carried out at 225 °C for 1 h in 0.3-i.d. × 12-cm sealed lead–potash glass tubes, prewashed with NH_4OH, distilled H_2O, MeOH, and EtOH, and then dried. Acid-catalyzed rearrangements were carried out in refluxing $CHCl_3$ over Amberlite 120 resin (sulfonic acid form) previously dried by azeotropic distillation of water with benzene.

(3) Cohn, M.; Hu, A. *Proc. Natl. Acad. Sci.* U.S.A. **1978**, *75*, 200–203. Batiz-Hernandez, H.; Bernheim, R. *Prog. Nucl. Magn. Reson. Spectrosc.* **1967**, *3*, 63–85.

(4) While this work was in progress, other examples of ^{18}O perturbation of ^{13}C chemical shifts were reported: Risley, J. M.; Van Etten, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 252–254; *Ibid.* **1980**, *102*, 4609–4614; *Ibid.* **1980**, *102*, 6699–6702. Vederas, J. C. *Ibid.* **1980**, *102*, 374–376.

(5) Balaban, A. T., Ed., "Chemical Applications of Graph Theory"; Academic Press: New York, 1976; p 84. Simmons, H. E., III; Maggio, J. E. *Tetrahedron Lett.* **1981**, 287–290. For a molecule to have a topologically nonplanar graph, it is necessary (but not sufficient) that no planar representation of the molecule exists that has no bonds crossing. The catenanes (two interlocked rings) would be considered simply as two disconnected graphs in graph theory and are therefore planar. For a graph theoretical discussion of this, see: Busacker, R. G.; Saaty, T. L. "Finite Graphs and Networks: An Introduction with Applications"; McGraw-Hill: New York, 1965; p 7. Because double-bond isomerization (geometry) is not considered in graph theory, the more recent "betweenanenes" can be drawn without edge crossings and are also planar.

(6) A reaction similar to that reported here, although almost certainly not "electrocyclic" in nature, has been reported: Weitemeyer, C.; deMeijere, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 686–687.

(7) Maggio, J. E.; Simmons, H. E., III; Kouba, J. K. *J. Am. Chem. Soc.*, preceding paper in this issue.

(8) Deslongchamps, P. *Heterocycles* **1977**, *7*, 1271–1317.

(9) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Academic Press: New York, 1970.

(10) Pritchard, J. G.; Siddiqui, I. *J. Chem. Soc., Perkin Trans. 2* **1973**, 452–457.

(11) In this work, the downfield and upfield resonances were assigned to the ^{16}O- and ^{18}O-labeled molecules, respectively, by comparing the intensities of the resonances with the amounts of M and M + 2 ions appearing in the mass spectrum. All observed isotope effects on chemical shifts over one chemical bond are in this direction; upfield signals arise from the nuclei bound to the heavier isotope.[3,4] A single example of a two-bond effect (0.004 ppm) has been reported by Vederas.[4]

0002-7863/81/1503-1581$01.00/0