Science Foundation Grant CHE 78-18581. High-resolution mass spectra were obtained at the Midwest Center for Mass Spectrometry a National Science Foundation Regional Instrumentation Facility (Grant CHE 8211164).

Registry No. (±)-**1**, 89362-24-3; (+)-**1**, 38129-37-2; **10**, 92098-00-5; **11**, 92098-01-6; **12**, 92216-23-4; **13**, 92098-02-7; **14**, 95782-30-2; **15**, 92216-24-5; **16**, 95694-56-7; **17**, 95782-31-3; **18a**, 95694-57-8; **19a**, 95694-58-9; **20a**, 95694-59-0; **21a**, 95694-60-3; **22a**, 95694-61-4; **23a**, 92098-06-1; **24a**, 95782-32-4; **24b**, 95694-62-5; **25a**, 95782-33-5; **25a** ($R_1 = R_2 = SiMe_2Bu$-*t*), 95694-74-9; **25b**, 95694-63-6; **26a**, 95782-34-6; **26b**, 95782-35-7; **27a**, 95782-36-8; **27b**, 95694-64-7; **28a**, 95782-37-9; **28b**, 95782-38-0; **29a**, 95782-39-1; **30**, 92098-07-2; **31**, 92125-39-8; **32**, 95739-42-7; **33**, 92125-40-1; **34**, 92125-41-2; **35**, 95694-65-8; **36**, 95694-66-9; **37**, 95694-67-0; **38**, 95739-44-9; **39a**, 95782-40-4; **39a** ([3.2.2] isomer), 95694-68-1; **39b**, 95782-41-5; **39b** ([3.2.2] isomer), 95694-69-2; **40a**, 92098-05-0; **40b**, 92098-14-1; **41a**, 95782-42-6; **41b**, 95782-43-7; **42a**, 92216-25-6; **42b**, 92098-15-2; **43a**, 92098-08-3; **43b**, 92098-16-3; **44a**, 92098-09-4; **44b**, 92098-17-4; (+)-**44b**, 95694-70-5; **45**, 63777-16-2; **46**, 92125-61-6; **47**, 92098-11-8; **48**, 92216-27-8; **49**, 92216-26-7; **50**, 92216-28-9; **51**, 92098-03-8; **52**, 92216-29-0; **53**, 95782-44-8; **54**, 92098-12-9; **55**, 95739-48-3; **57**, 95694-71-6; **58**, 95694-72-7; **59**, 92125-62-7; (+)-**59**, 95694-73-8; (±)-2,2,4-trimethyl-1,3-dioxolane-4-carboxaldehyde, 81600-36-4; (−)-2,2,4-trimethyl-1,3-dioxolane-4-carboxaldehyde, 79243-92-8; γ-butyrolactone trimethylsilyl enol ether, 51425-66-2.

Synthesis of Skeletally Labeled 3-Methylhexaborane(12) and 2-Methylpentaborane(9): ^{10}B and ^{11}B NMR Spectral Studies of Base-Catalyzed Intramolecular Rearrangements in 2-Methylpentaborane(9)

Donald F. Gaines* and Darrell E. Coons

Contribution from the Department of Chemistry, University of Wisconsin—Madison, Madison, Wisconsin 53706. *Received August 29, 1984*

Abstract: Selectively ^{10}B labeled 3-MeB_6H_{11} has been synthesized from 1-MeB_5H_8 and 96% ^{10}B labeled B_2H_6 by modification of a previously published procedure. Positions B(1), B(2), and B(6) of the labeled 3-MeB_6H_{11} each contain 46 ± 5% ^{10}B while B(3), B(4), and B(5) are isotopically normal (19% ^{10}B). Reaction of this compound with dimethyl ether produces 2-MeB_5H_8 which is ^{10}B enriched at B(4) (47 ± 5% ^{10}B) and, to a lesser extent, at B(3,5) (30 ± 5% ^{10}B). In the presence of 2,6-lutidine the ^{10}B label in the 2-MeB_5H_8 equilibrates into all boron positions except the methyl-substituted B(2). These are the first direct observations of the movement of cluster boron atoms in the isomerization of pentaborane(9) derivatives. Several proposed isomerization mechanisms are examined in light of these results.

Interest in the chemistry of cluster compounds is rapidly expanding.[1] Internal cluster rearrangement and exchange processes are an important area of cluster chemistry, though there are few examples of experimentally verified mechanisms of such rearrangements. A number of different types of intramolecular cluster rearrangements and exchange processes have been observed. For example, a cluster may undergo internal site exchange of terminal or bridging groups (or atoms) attached to the periphery of the cluster while the cluster framework atoms remain intact and static. Such exchange has been studied extensively in metal carbonyl clusters[2,3] and in metallaborane clusters.[4] A cluster may also undergo internal atom rearrangements that change the cluster shape or produce a different geometric isomer but that do not involve movement of terminal substituents to different cluster atoms. A classic example of this type of rearrangement is the isomerization of the icosahedral carboranes (eq 1).[5,6] Intramolecular cluster rearrangements may also involve a combination of terminal substituent movement and cluster atom movement.

$$1,2\text{-}C_2B_{10}H_{12} \xrightarrow{450\ ^\circ C} 1,7\text{-}C_2B_{10}H_{12} \xrightarrow{620\ ^\circ C} 1,12\text{-}C_2B_{10}H_{12} \quad (1)$$

Extending our interest in intramolecular exchange processes in boranes and metallaborane clusters, we address in this paper several aspects of the isomerization mechanism of the square-pyramidal pentaborane(9), B_5H_9, framework. Pentaborane(9) derivatives have long been known to undergo isomerization reactions in the presence of Lewis bases. The most complete example, though not the first, is trimethylsilylpentaborane(9)[7] (eq 2). The μ-$(Me_3Si)B_5H_8$ contains the Me_3Si group in a bridging position, analogous to a bridging hydrogen atom, between two adjacent boron atoms in the base of the pentaborane pyramid.

$$\mu\text{-}(Me_3Si)B_5H_8 \xrightarrow{Et_2O} 2\text{-}(Me_3Si)B_5H_8 \underset{}{\overset{HMTA}{\rightleftharpoons}} 1\text{-}(Me_3Si)B_5H_8 \quad (2)$$

The silicon is considered to be bonded to the two adjacent boron atoms by a boron–silicon–boron, three-center, two-electron bond.[8] Isomerization of the μ-$(Me_3Si)B_5H_8$ occurs in diethyl ether to form 2-$(Me_3Si)B_5H_8$, in which the Me_3Si group occupies a terminal substituent position on the base of the pentaborane pyramid. Further isomerization to 1-$(Me_3Si)B_5H_8$ occurs at elevated temperatures or in the presence of stronger bases such as hexamethylenetetramine. The mechanisms of these processes in various pentaborane(9) derivatives have been studied in our laboratories[9] and elsewhere.[10]

(1) See, for example: Behnken, P. E.; Belmont, J. A.; Busby, D. C.; Delaney, M. S.; King, R. E., III; Kreimendahl, C. W.; Marder, T. B.; Wilczynski, J. J.; Hawthorne, M. G. *J. Am. Chem. Soc.* **1984**, *106*, 3011-3025.
(2) Band, E.; Muetterties, E. L. *Chem. Rev.* **1978**, *78*, 639-658.
(3) Geoffroy, G. L. *Acc. Chem. Res.* **1980**, *13*, 469-476.
(4) See, for example: Gaines, D. F.; Hildebrandt, S. J. In "Metal Interactions with Boron Clusters"; Grimes, R. N., Ed.; Plenum Press: New York and London, 1982; pp 132-143.
(5) Grafstein, D.; Dvorak, J. *Inorg. Chem.* **1963**, *2*, 1128-1133.
(6) Papetti, S.; Heying, T. L. *J. Am. Chem. Soc.* **1964**, *86*, 2295.
(7) (a) Gaines, D. F.; Iorns, T. V. *J. Am. Chem. Soc.* **1968**, *90*, 6617-6621. (b) Gaines, D. F.; Iorns, T. V. *Inorg. Chem.* **1971**, *10*, 1094-1095.
(8) Calabrese, J. C.; Dahl, L. F. *J. Am. Chem. Soc.* **1971**, *93*, 6042-6047.
(9) (a) Gaines, D. F.; Iorns, T. V. *J. Am. Chem. Soc.* **1967**, *89*, 3375. (b) Gaines, D. F.; Iorns, T. V. *Ibid.* **1970**, *92*, 4571-4574. (c) Gaines, D. F.; Walsh, J. L. *Inorg. Chem.* **1978**, *17*, 806-809. (d) Heppert, J. A.; Gaines, D. F. *Ibid.* **1983**, *22*, 3155-3163.
(10) (a) Onak, T. P. *J. Am. Chem. Soc.* **1961**, *83*, 2584. (b) Onak, T. P.; Gerhard, F. J. *Inorg. Chem.* **1962**, *1*, 742-744. (c) Hough, W. V.; Edwards, L. J.; Stang, A. F. *J. Am. Chem. Soc.* **1963**, *85*, 831. (d) Onak, T. P.; Gerhart, F. J.; Williams, R. E. *Ibid.* **1963**, *85*, 1754-1756. (e) Burg, A. B.; Sandhu, J. S. *Ibid.* **1965**, *87*, 3787-3788. (f) Friedman, L. B.; Lipscomb, W. N. *Inorg. Chem.* **1966**, *5*, 1752-1757. (g) Onak, T. P.; Dunks, G. B.; Stearcy, J. W.; Spielman, J. *Ibid.* **1967**, *6*, 1465-1471. (h) Johnson, H. D.; Geanangel, R. A.; Shore, S. G. *Ibid.* **1970**, *9*, 908-912. (i) Tucker, P. M.; Onak, T.; Leach, J. B. *Ibid.* **1970**, *9*, 1430-1441. (j) Brice, V. T.; Shore, S. G. *Ibid.* **1973**, *12*, 309-313.

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Using a combination of ^1H, ^2H, and ^{11}B NMR studies of selectively deuterium labeled pentaborane derivatives, we have verified that at least two very different activation barriers are represented by the isomerizations in eq 2. In the first (lower energy) process, the Lewis base apparently becomes associated with a boron atom in the base of the pentaborane pyramid to produce an arachno intermediate having a B_5H_{11}-type structure. In this complex a bridging trimethylsilyl group is able to exchange into an adjacent, less sterically crowded terminal position forming 2-$(Me_3Si)B_5H_8$ quantitatively. The mechanism for the isomerization of 2-$(Me_3Si)B_5H_8$ to 1-$(Me_3Si)B_5H_8$ is more complex and has not been directly addressed by previous studies. Many pentaborane derivatives undergo such isomerizations, presumably via similar mechanisms. The primary question regarding movement of substituents between 1- and 2-positions (apical and basal positions, respectively) is whether these terminal substituents move from one boron atom to another on the surface of the cluster via a 1,2-shift or move by rearrangement of the boron atoms without breaking the boron-substituent bond, via a cluster rearrangement. In order to address this question we have undertaken the synthesis of a selectively ^{10}B labeled pentaborane derivative.

Selective isotopic labeling of molecular cluster atoms, though generally difficult to achieve, potentially provides a direct method for obtaining detailed information about cluster rearrangements. In this area, boron hydrides offer clear advantges over most other cluster systems. The natural isotopic composition of boron is approximately 81% ^{11}B and 19% ^{10}B,[11] and both isotopes are readily observable by NMR spectroscopy ($I_{^{11}B} = {}^3/_2$; $I_{^{10}B} = 3$) and exhibit strong chemical shift–structural correlations. As both isotopes are quadrupolar, coupling among the boron nuclei within borane clusters does not generally complicate their spectra. Several boron compounds enriched to 96% ^{10}B are commercially available and affordable.

The only known route to B_5H_9 that is suitable for introduction of a boron isotopic label is not from smaller boranes but from hexaborane(12), B_6H_{12}, by its reaction with dimethyl ether (eq 3).[12] A high-yield synthetic route to B_6H_{12} (eq 4–6)[13] and

$$B_6H_{12} \xrightarrow{Me_2O} B_5H_9 + {}^1/_2B_2H_6 \qquad (3)$$

3-MeB_6H_{11} (eq 7–9)[16] was recently developed by Shore et al. We report here the modification of this synthetic route for the preparation of the first examples of ^{10}B labeled hexaborane(12) and pentaborane(9) derivatives and a study of the isomerization mechanism of ^{10}B labeled 2-methylpentaborane(9) with ^{10}B and ^{11}B NMR spectroscopy.

$$B_5H_9 + KH \xrightarrow[Me_2O]{-78\ ^\circ C} K[B_5H_8] + H_2 \qquad (4)$$

$$K[B_5H_8] + {}^1/_2B_2H_6 \xrightarrow[Me_2O]{-78\ ^\circ C} K[B_6H_{11}] \qquad (5)$$

$$K[B_6H_{11}] + HCl \xrightarrow{-112\ ^\circ C} B_6H_{12} + KCl \qquad (6)$$

$$1\text{-}MeB_5H_8 + KH \xrightarrow[Me_2O]{-78\ ^\circ C} K[1\text{-}MeB_5H_7] + H_2 \qquad (7)$$

$$K[1\text{-}MeB_5H_7] + {}^1/_2B_2H_6 \xrightarrow[Me_2O]{-78\ ^\circ C} K[MeB_6H_{10}] \qquad (8)$$

$$K[MeB_6H_{10}] + HCl \xrightarrow{-112\ ^\circ C} 3\text{-}MeB_6H_{11} + KCl \qquad (9)$$

Results

Synthesis of ^{10}B Labeled 3-MeB_6H_{11}. Selectively ^{10}B labeled 3-MeB_6H_{11} was obtained by modification of the published synthetic procedure for isotopically normal 3-MeB_6H_{11} (eq 7–9)[14] with 96% ^{10}B labeled diborane, $^{10}B_2H_6$, as the label source. Reaction times were kept to 30 min or less per step, including solvent removal, and the temperature of the reaction mixture was not allowed to rise above −78 °C. Following the protonation at −112 °C (eq 9), the 3-MeB_6H_{11} was isolated in greater than 80% yield. It is important to note that in our initial experiments with $^{10}B_2H_6$ in the synthesis of B_6H_{12} (eq 4–6) and 3-MeB_6H_{11} (eq 7–9) according to the published procedures,[13,14] we found, via NMR analysis, that in both cases the ^{10}B label was totally scrambled.

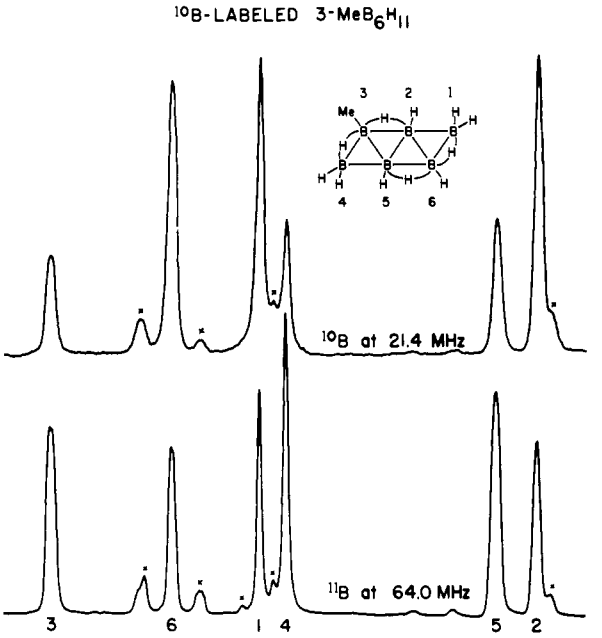


Figure 1. Proton-decoupled ^{10}B (21.4 MHz) and ^{11}B (64.0 MHz) NMR spectra of ^{10}B labeled 3-MeB_6H_{11} in pentane solution. Proposed resonance assignments are shown below the ^{11}B spectrum (x = impurities).

^{10}B and ^{11}B NMR spectra of the ^{10}B labeled 3-MeB_6H_{11} indicated that the ^{10}B isotopic enrichment was restricted almost entirely to three of the six positions in the molecule (Figure 1), corresponding to one of each of the boron positions that are equivalent in the parent B_6H_{12}. The extent of ^{10}B enrichment in the ^{10}B labeled 3-MeB_6H_{11} was determined by integration of the ^{10}B and ^{11}B NMR spectra. On the basis of a proposed mechanism for eq 11 (see Discussion section), the ^{10}B labeled positions are B(1), B(2), and B(6). The percentages of ^{10}B and ^{11}B in each position were estimated by two independent methods. In each case it was assumed that the boron in our laboratory stock of B_5H_9 was from California borax, which has an average composition of 19% ^{10}B and 81% ^{11}B.[11] In method 1 the total ^{10}B in the molecule was calculated on the basis of the introduction of exactly one boron enriched to 96% ^{10}B. Each peak integral in the ^{10}B and ^{11}B NMR spectra then corresponds to the relative isotopic composition at that position. In method 2 it was assumed only that no exchange of ^{10}B into the methyl-substituted position, B(3), occurred. The B(3) isotopic composition remained fixed at 19% ^{10}B and 81% ^{11}B, and the isotopic compositions of the other boron positions were related to the B(3) composition on the basis of their relative areas in the NMR spectra. The estimated uncertainty of the area measurements is ±5% with the exception of the B(5) resonance. Resonances due to inseparable impurities are observed in the NMR spectra, and since the measured ^{11}B in the B(5) position is unrealistically high, we assume that an impurity is responsible. The estimated uncertainty for this resonance is ±12%. Nevertheless, the relative ^{10}B enrichment is clear. Table I lists the measured ^{10}B and ^{11}B NMR peak areas and isotopic compositions at each position of the ^{10}B labeled 3-MeB_6H_{11} calculated on the basis of these two methods. The close numerical agreement between these methods supports the validity of the assumptions. Average values are also listed and are used in the discussion below.

Reaction of 3-MeB_6H_{11} with Dimethyl Ether. The reaction of 3-MeB_6H_{11} with dimethyl ether produced 2-MeB_5H_8 in good yield

(11) Shima, M. *Geochim. Cosmochim. Acta* **1963**, *27*, 911–913.
(12) Gaines, D. F.; Schaeffer, R. *Inorg. Chem.* **1964**, *3*, 438–440.
(13) Remmel, R. J.; Johnson, H. D., II; Jaworiwsky, I. S.; Shore, S. G. *J. Am. Chem. Soc.* **1975**, *97*, 5395–5403.
(14) Jaworiwski, I. S.; Long, J. R.; Barton, L.; Shore, S. G. *Inorg. Chem.* **1979**, *18*, 56–60.
(15) Young, D. E.; Shore, S. G. *J. Am. Chem. Soc.* **1969**, *91*, 3497–3504.
(16) Gaines, D. F. In "Boron Chemistry"; Parry, R. W., Kodama, G., Eds.; Pergamon Press: Oxford, 1980.

Table I. ^{10}B and ^{11}B NMR Integration Results for ^{10}B Labeled 3-MeB_6H_{11}

	position					
	1	2	3	4	5[d]	6
rel peak areas[a]						
^{10}B	191	196	78	84	92	205
^{11}B	165	185	248	249	285	177
isotopic composition method 1[b]						
^{10}B	43	44	18	19	21	46
^{11}B	52	58	77	78	89	55
method 1 sum	95	102	95	97	110	101
isotopic composition method 2[c]						
^{10}B	47	48	19	20	22	50
^{11}B	54	60	81	81	93	58
method 2 sum	101	108	100	101	115	108
average						
^{10}B	45	46	19	20	22	48
^{11}B	53	59	79	80	91	57
average sum	98	105	98	100	113	105

[a] Arbitrary units. [b] Relative percentages (±5) of that isotope in the indicated position based on the premise that one 96% ^{10}B atom per molecule was introduced during its synthesis. [c] Relative percentages (±5) of that isotope in the indicated position based on the premise that the B(3) position contains natural abundance boron. [d] A sample impurity reduces the certainty of these values, which are ~10% higher than possible.

Table II. ^{10}B and ^{11}B NMR Integration Results for ^{10}B Labeled 2-MeB_5H_8 before and after Isomerization

		position			
		1	2	3,5	4
rel peak areas[a]	^{10}B before	126	93	299	237
	^{10}B after	191	114	384	189
	^{11}B before	193	197	360	124
	^{11}B after	143	157	272	132
isotopic composition					
^{10}B before	method 1[b]	25	18	29	46
	method 2[c]	26	19	31	48
	average	26	19	30	47
^{10}B after	method 1	32	19	32	32
	method 2	32	19	32	31
	average	32	19	32	32
^{11}B before	method 1	79	80	74	51
	method 2	79	81	74	51
	average	79	81	74	51
^{11}B after	method 1	73	81	69	67
	method 2	74	81	70	68
	average	74	81	70	68

[a] Arbitrary units. [b] Relative percentages (±5%) of the indicated isotope in the various positions based on the premise that, in the reaction of 3-MeB_6H_{11} with Me_2O, B(1) is cleaved leaving B(2)–B(6) to form the 2-MeB_5H_8. [c] Relative percentages of the indicated isotope in the various positions based on the premise that the B(2) position contains natural abundance boron.

as well as diborane, methyldiborane, and pentaborane. Separation of the B_5H_9/2-MeB_5H_8 mixture was accomplished with use of a high-vacuum, low-temperature distillation column. The 2-MeB_5H_8 was ^{10}B enriched primarily in the 4 position and secondarily in the 3- and 5-positions. Table II gives the measured ^{10}B and ^{11}B NMR peak areas for this compound and the isotopic composition in each position with use of methods analogous to those described above for 3-MeB_6H_{11}. In method 1 it was assumed that the overall isotopic composition of the ^{10}B labeled 2-MeB_5H_8 was that expected if B(1) was removed from the ^{10}B labeled 3-MeB_6H_{11}. In method 2 it was assumed only that no exchange of ^{10}B into the methyl substituted position, B(2), occurred so its isotopic composition remained normal. Again, the two methods are in close agreement.

Isomerization of ^{10}B Labeled 2-MeB_5H_8. The distribution of ^{10}B and ^{11}B in the different positions of the specifically ^{10}B labeled 2-MeB_5H_8 changed when it was treated with 2,6-lutidine. Table II lists the measured ^{10}B and ^{11}B NMR peak areas and the isotopic composition in each position before and after treatment with 2,6-lutidine. Figure 2 shows the ^{10}B NMR spectra. Within the limits of experimental error (±5%), no change was observed in the isotopic composition at the 2-position. In contrast, the remaining four positions equilibrated completely. A sample con-

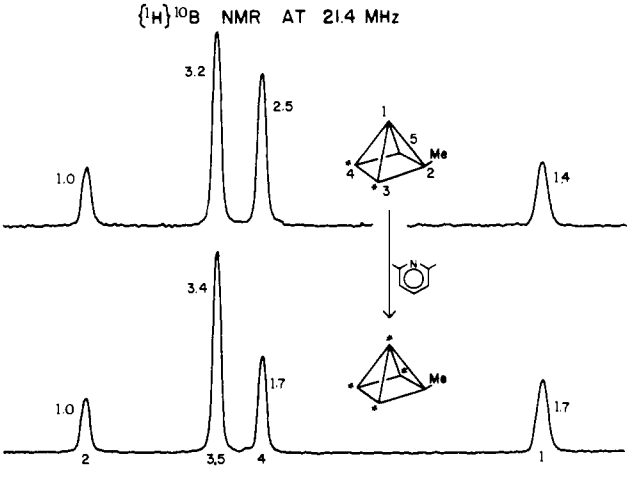


Figure 2. Proton-decoupled ^{10}B NMR spectra (21.4 MHz, pentane solution) of ^{10}B labeled 2-MeB_5H_8 before and after isomerization with 2,6-lutidine catalyst. Upper trace is before isomerization. Resonance assignments are shown below the lower trace. Numbers beside resonances represent relative peak areas.

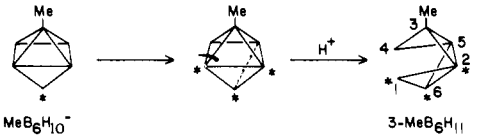
taining a large excess of 2,6-lutidine reached equilibrium in 3 h at room temperature. Using a 2,6-lutidine:2-MeB_5H_8 ratio of 1:10 increased the equilibration time to approximately 100 h.

Discussion

Synthesis of ^{10}B Labeled 3-MeB_6H_{11}. The $B_6H_{11}^-$ anion is formed by reaction of B_2H_6 with $B_5H_8^-$ anion in dimethyl ether solution according to eq 5.[13] On the basis of its ^{11}B and ^{1}H NMR spectra a structure was proposed for $B_6H_{11}^-$ in which a BH_3 group occupies the vacant bridge position of the $B_5H_8^-$ anion. Fluxionality of the hydrogen atoms in $B_6H_{11}^-$ was observed with variable-temperature ^{1}H NMR spectroscopy.[12] Our experiments with 96% ^{10}B labeled diborane, $^{10}B_2H_6$, in this system have demonstrated the fluxional character of the boron atoms as well. The added $^{10}BH_3$ group exchanged into all boron atom positions in the anion such that, after protonation, the ^{10}B and ^{11}B NMR spectra of the isolated B_6H_{12} contained equal ^{10}B:^{11}B ratios in all resonance positions. Three resonances of equal area would also be observed if the exchange were limited to one of each of the pairs of equivalent positions. This is unlikely in light of other experiments with 3-MeB_6H_{11} (vide infra).

The analogous 3-MeB_6H_{11} synthesis (eq 7–9)[14] was performed with $^{10}B_2H_6$ in the hope that the methyl substituent would hinder the isotopic exchange. However, when the published reaction conditions were employed, the ^{10}B was distributed equally over the six positions in the 3-MeB_6H_{11} molecule. This result indicates that movement of the methyl group from one boron atom to another (1,2-shift) has occurred as well as rearrangement of the boron and hydrogen atoms in the $MeB_6H_{10}^-$ anion.

Selectively ^{10}B labeled 3-MeB_6H_{11} was produced when the reaction conditions were appropriately modified. Three of the six inequivalent boron positions in this product contained nearly 50% ^{10}B while the other three remained approximately normal (~20% ^{10}B) (see Table 1). No further scrambling of boron isotopes appears to occur after protonation of the $MeB_6H_{10}^-$ ion. Boron isotope exchange must occur exclusively in the $MeB_6H_{10}^-$ anion or its immediate precursor. Protonation opens the $MeB_6H_{10}^-$ cage in a very specific manner to give the labeled 3-MeB_6H_{11} (eq 10, an asterisk indicates ^{10}B enrichment). It is difficult to describe a mechanism that will equilibrate only three boron positions in the $MeB_6H_{10}^-$ ion, but the observed ^{10}B distribution indicates a very low activation energy for the exchange. Further investigations of this mechanism are in progress.



(10)

Reaction of 3-MeB_6H_{11} with Dimethyl Ether: Synthesis of ^{10}B Labeled 2-MeB_5H_8. Ammonia cleaves 3-MeB_6H_{11} unsymmetrically to produce $MeB_5H_9^-$ (eq 11),[14] and protonation of the latter gives 3-MeB_5H_{10} (eq 12). Shore et al. have discussed the regioselectivity of this reaction. The methyl substituent is thought

$$3\text{-}Me_6H_{11} + 2NH_3 \rightarrow [H_2B(NH_3)_2][MeB_5H_9] \quad (11)$$

$$[H_2B(NH_3)_2][MeB_5H_9] + HCl \rightarrow [H_2B(NH_3)_2]Cl + 3\text{-}MeB_5H_{10} \quad (12)$$

to release electron density to the neighboring B(4) which leaves B(1) as the most positive boron and the preferred site of attack by a base.[15] Symmetrical cleavage of B_6H_{12} by dimethyl ether to B_5H_9 and B_2H_6 is also known (eq 3).[12] Dimethyl ether apparently cleaves 3-MeB_6H_{11} symmetrically in at least two ways. The primary reaction parallels the reaction with ammonia (eq 11), i.e., attack at B(1), as indicated by the reaction of dimethyl ether with the ^{10}B labeled 3-MeB_6H_{11} described above. The reaction produces 2-MeB_5H_8 which is ^{10}B enriched primarily at B(4) and secondarily at B(3,5). The smaller excess of ^{10}B at B(3,5) corresponds to what would be expected if one of the positions were labeled to the same extent as B(4) while the others were normal.

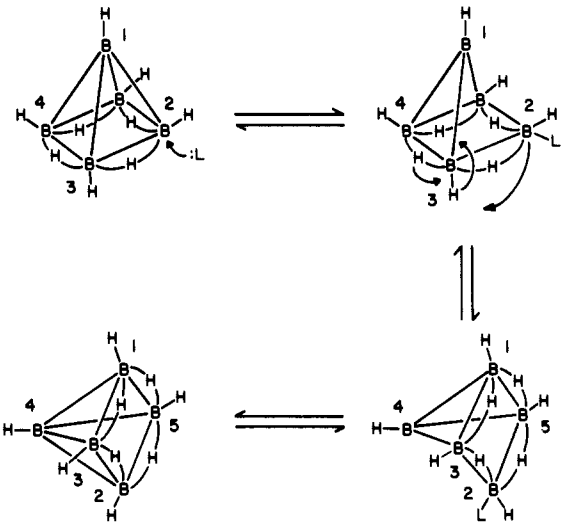
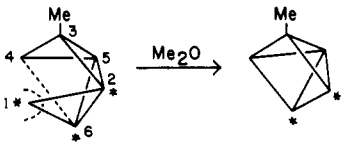


Figure 3. Base-swing mechanism for pentaborane isomerization.

Equation 13 illustrates a mechanism that is consistent with these data and requires very little relative motion of the boron atoms in closing the cage to form 2-MeB_5H_8.



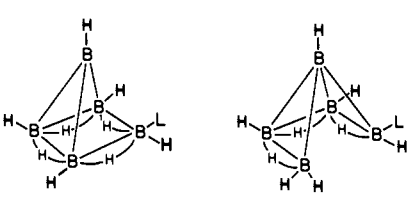
(13)

If dimethyl ether attack were to occur at B(4), closure by the mechanism described above would give 2-MeB_5H_8 enriched with ^{10}B at B(1), B(3), and B(4). The extremely small excess of ^{10}B observed at B(1) indicates that this occurs only to a very small extent. Pentaborane(9) and MeB_2H_5 were observed as minor products in the reaction of dimethyl ether with 3-MeB_6H_{11}, indicating some base attack at B_3 (eq 14). The mechanism of the

$$3\text{-}MeB_6H_{11} \xrightarrow{Me_2O} B_5H_9 + [MeBH_2] \quad (14)$$

formation of B_5H_9 is more difficult to visualize than that of 2-MeB_5H_8. Pentaborane isolated from the reaction of dimethyl ether with ^{10}B labeled 3-MeB_6H_{11} showed a base:apex ratio of 4.3 in its ^{11}B NMR spectrum, clear indication that a less specific cage closure process has occurred.

Pentaborane Isomerization. The first observation of the isomerization of pentaborane(9) derivatives was the conversion of 1-MeB_5H_8 to 2-MeB_5H_8 in 2,6-lutidine.[10a] Although the reaction appears quantitative by ^{11}B NMR, it is thought to be an equilibrium process that greatly favors the basal (2-Me-) isomer. This is supported by the fact that the equilibrium constants for the isomerization of various pentaborane(9) derivatives differ by several orders of magnitude. The first mechanistic model for these reactions involved deprotonation of the borane by the base followed by rearrangement of the resulting borane anion.[10a,c] Subsequent studies have shown that deprotonation is an unlikely step in the isomerization process.[9a] Several types of base–borane adducts proposed as intermediates have been discussed in a recent paper, and two of these, I and II, appear to be consistent with the available data.[16] In either case the base is coordinated to a basal



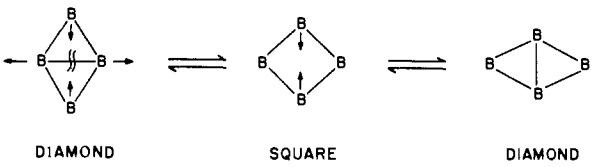


Figure 4. Diamond–square–diamond mechanism for triangulated cluster rearrangements.

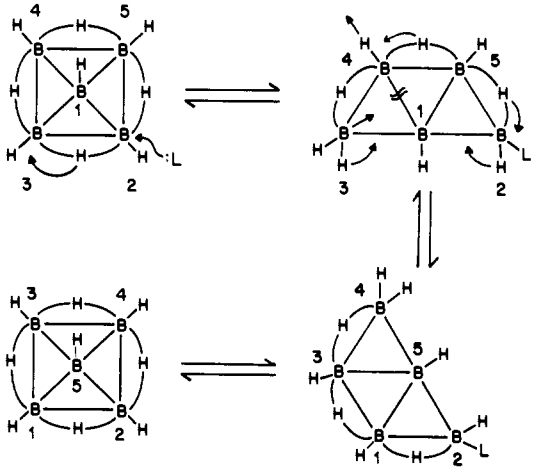


Figure 5. Diamond–square–diamond mechanism for pentaborane isomerization.

boron atom. This coordination may interrupt the bonding interaction between the coordinated boron and the apex to give intermediate I. The coordinated boron may then swing around to a new position (Figure 3). Repetition of this "base-swing" process equilibrates all positions in the cluster. Alternatively, Lewis base coordination may cause cleavage of an adjacent boron–hydrogen bridge bond that would open one basal edge of the cluster to give intermediate II. Two mechanisms have been proposed for the rearrangement of II. The first involves movement of the substituents by a 1,2-shift mechanism in which the skeletal atoms maintain their original positions. This mechanism equilibrates the four basal atoms while the apical boron remains unique. The other proposed mechanism requires no movement of terminal substituents from one boron to another. Instead, the boron atoms themselves rearrange, taking their substituents with them, via a cluster rearrangement mechanism. Rearrangement of the boron atoms via intermediate II may occur through one or more diamond–square–diamond operations[9d,17] (Figures 4 and 5). If there is a non-hydrogen substituent, only a 1,2-shift will allow exchange of the substituted boron with the others. The synthesis of ^{10}B labeled 2-MeB_5H_8, the first example of a skeletally labeled pentaborane(9) derivative, allows differentiation between these possibilities. When the ^{10}B labeled 2-MeB_5H_8 was treated with 2,6-lutidine, the ^{10}B label migrated smoothly into all positions **except** the methyl substituted B(2). While this result is consistent with either the base-swing or diamond–square–diamond mechanisms for cluster rearrangement (intermediates I and II), it clearly demonstrates that 1,2-shifts do not occur in this system.

No available data can distinguish between the base-swing and diamond–square–diamond mechanisms. Both require movement of four hydrogen atoms (two bridge-to-terminal and two terminal-to-bridge) in the course of one cluster rearrangement. We presently favor the diamond–square–diamond mechanism for two reasons. First, intermediate II has precedent in boron hydride chemistry. Addition of two electrons to the nido B_5H_9 pyramid to give an arachno B_5H_{11} type structure is logical. Second, the diamond–square–diamond mechanism, combined with our recently proposed mechanism for the lower energy μ- to 2-isomerization with use of the same intermediate,[9b,16] forms a reasonable and complete picture of the rearrangement of pentaborane(9) derivatives.

Experimental Section

Apparatus. All manipulations were performed in a nitrogen-filled glove box or in a standard high-vacuum line. The ^{10}B and ^{11}B NMR spectra were obtained at 21.4 and 64.0 MHz, respectively, on a JEOL FX-200 spectrometer. Boron-11 NMR spectra at 86.7 MHz were obtained on a Brucker WH-270 spectrometer. Pulse delays of 2 s were used in all cases to ensure complete relaxation of the boron nuclei.[18] Relative peak areas were measured on expanded spectra with a planimeter. Repeated measurements agreed to within 4%. The value used for the area of each peak was the average of three measurements.

Starting Materials. Dimethyl ether and pentane were stored over $LiAlH_4$ and were vacuum transferred directly into the vacuum line as needed. The 2,6-lutidine was dried over CaH_2 before use. Hdyrogen chloride (Matheson) was purified by repeated passage through a −126 °C U-trap into a −196 °C U-trap. Potassium hydride was obtained from Alfa Products as an oil dispersion and washed with pentane to remove the oil. Lithium aluminum hydride was purified by extraction with diethyl ether followed by removal of the ether by vacuum. Pentaborane(9) was obtained from laboratory stock. 1-Methylpentaborane(9) was prepared according to a literature method.[10b] The ^{10}B labeled BF_3-CaF_2 (96% ^{10}B) was purchased from Eagle Picher Industries, Miami, OK. Boron-10 boron trifluoride was liberated from this complex with use of a procedure adapted from one obtained from the supplier: the complex was outgased by heating at 90 °C for 5 h in a stainless steel tube attached to a high-vacuum line. The $^{10}BF_3$ was collected in a −196 °C U-trap as the temperature was raised slowly from 200 to 350 °C and subsequently purified by passing through a −126 °C U-trap into a −196 °C U-trap. Boron-10 diborane(6) was obtained from $^{10}BF_3$ by modifications on a published procedure.[19] Modifications included the use of 1,2-dimethoxyethane in place of diethyl ether to complex the BF_3 and as solvent and the use of helium in place of nitrogen to carry the $^{10}B_2H_6$ into the vacuum line. The $^{10}B_2H_6$ was purified by repeated passage through a −126 °C U-trap into a −196 °C U-trap.

Preparation of ^{10}B Labeled 3-MeB_6H_{11}. B_6H_{12}[12] and 3-MeB_6H_{11},[14] which were prepared according to the published procedures with $^{10}B_2H_6$, were not selectively ^{10}B labeled by ^{10}B and ^{11}B NMR. In an NMR tube experiment, no boron exchange was observed between B_6H_{12} and $^{10}B_2H_6$.

Selectively ^{10}B labeled 3-MeB_6H_{11} was isolated when the published procedure was appropriately modified. Typically, 5.3 mmol of K[1-MeB_5H_7] were prepared in 5 mL of Me_2O in a 100-mL round-bottom reactor equipped with a 12-mm Kontes O-ring stopcock and a stirring bar. After condensation of 2.7 mmol of $^{10}B_2H_6$ into the flask at −196 °C, it as sealed, warmed to −78 °C, and stirred for 15 min. The stopcock was then opened, and volatiles were removed by vacuum distillation at −78 °C over a period of 15 min. The flask was immediately cooled to −196 °C, and 3–4 mL of anhydrous HCl were condensed onto the remaining solid. This mixture was warmed to −112 °C and stirred for 10 min. After HCl was removed by distillation at −112 °C, the flask was allowed to warm to ambient temperature, the volatiles distilling into a series of U-traps at −45, −78, and −196 °C. The −78 °C trap contained 0.389 g of 3-MeB_6H_{11} (4.3 mmol), an 81% yield based on 1-MeB_5H_8. Neither repeated trap-to-trap distillations nor careful purification on a high-vacuum, low-temperature distillation column were successful in removing impurities observed in the ^{10}B and ^{11}B NMR spectra of this compound.

Reaction of ^{10}B Labeled 3-MeB_6H_{11} with Dimethyl Ether. In a typical experiment, 0.097 g of ^{10}B labeled 3-MeB_6H_{11} (1.08 mmol), prepared as described above, and excess dimethyl ether (~9 mmol) were condensed into a 1-L reactor. The flask was sealed, warmed to ambient temperature, and left overnight. The volatiles were separated by fractional distillation with U-traps at −95 and −196 °C. The −95 °C trap contained 0.065 g of material shown by ^{11}B NMR to be 2-MeB_5H_8 plus a small amount of B_5H_9. These were separated on a high-vacuum, low-temperature distillation column.

Reaction of ^{10}B Labeled 2-MeB_5H_8 with 2,6-Lutidine. ^{10}B labeled 2-MeB_5H_8 (1.0 mmol), prepared as described above, was condensed into a 5 mm o.d., 3 mm i.d. NMR tube along with 0.1 mmol of 2,6-lutidine and pentane solvent. The tube was flame sealed and then warmed to ambient temperature, and ^{10}B NMR spectra were obtained periodically until no further changes could be observed in the spectra (100 h). The

(17) (a) Kaczmarczyk, A.; Dobrott, R.; Lipscomb, W. N. *Proc. Natl. Acad. Sci. U.S.A.* **1962**, *48*, 729–733. (b) Hoffmann, R.; Lipscomb, W. N. *Inorg. Chem.* **1963**, *2*, 231–232.

(18) Weiss, R.; Grimes, R. N. *J. Am. Chem. Soc.* **1978**, *100*, 1401–1405.

(19) Shapiro, I.; Weiss, H. G.; Schmich, M.; Skolnik, S.; Smith, G. B. L. *J. Am. Chem. Soc.* **1952**, *74*, 901–905.

sample remained homogeneous throughout the experiment.

In another experiment, 1.0 mmol of ^{10}B labeled 2-MeB_5H_8 in a large excess of 2,6-lutidine reached equilibrium in 3 h.

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Registry No. B_5H_9, 19624-22-7; B_2H_6, 19287-45-7; MeB_2H_5, 23777-55-1; K[1-MeB_5H_7], 56009-96-2; $^{10}B_2H_6$, 19465-29-3; Me_2O, 115-10-6; 2,6-lutidine, 108-48-5.

The Convergent Synthesis of Polyether Ionophore Antibiotics: The Synthesis of the Monensin Spiroketal[1]

Robert E. Ireland,* Dieter Häbich,[2] and Daniel W. Norbeck[3]

Contribution No. 7074 from the Chemical Laboratories, California Institute of Technology, Pasadena, California 91125. *Received September 28, 1984*

Abstract: The monensin spiroketal **2**, a versatile intermediate for the synthesis of polyether ionophore antibiotics, is prepared from D-fructose. Key steps include the ester enolate Claisen rearrangement of a glycal propionate, expansion of a furanoid to a pyranoid ring, and the acid-catalyzed equilibration of a bicyclic ketal to a spiroketal. An alternative approach, entailing the hetero-Diels–Alder condensation of the exocyclic enol ether **15** with acrolein, is thwarted by facile isomerization to the endocyclic enol ether **18**.

The complex chemistry and potent biological activity of the polyether antibiotics have engaged widespread interest.[4] As ionophores, these compounds possess a striking ability to perturb ionic gradients by catalytically transporting cations across lipid barriers.[5] While optimal membrane and ion selectivity remain elusive goals, the commercial use of monensin for control of poultry coccidiosis[6] and enhancement of ruminant feed utilization[6] have encouraged intensive efforts in the isolation and study of these compounds. Several have demonstrated potential in human medicine, particularly as cardiovascular agents.[7] In addition to their diverse biological activity, these antibiotics display a formidable molecular complexity, and the attendant challenge of total synthesis has been taken up by numerous research groups.[8] Structurally, most of the polyether ionophores feature linear chains of substituted tetrahydropyran and tetrahydrofuran rings. Comparison reveals that nearly all these rings recur with high frequency, often in stereochemically indistinguishable sequences. The unified biosynthetic pathway proposed by Cane, Celmer, and Westley underscores the structural identities and combinatorial diversity of these antibiotics.[9]

We have recently developed a versatile, building-block approach to the polyethers in which prefabricated tetrahydrofuran and tetrahydrogen rings are joined via the ester enolate Claisen rearrangement. This work has culminated in the total synthesis of lasalocid A[8b] and its enantiomer[10] from readily available carbohydrates. In this and the following two papers in this issue, we report the preparation of several additional subunits for the synthesis of naturally occurring polyethers and potentially informative analogues.

Serving as rigid bands in the polyether backbone, spiroketals play a critical role in establishing the coordination geometry necessary for ion complexation.[11] Since one of the spiro oxygens usually acts as a ligand as well, spiroketals are prominent features of the polyether class.[12] Monensin's[13] spiroketal is a particularly attractive synthetic target, as it occurs in at least eight other ionophores. Disconnection of the C2,3 and C12,13 bonds of monensin generates the common structural subunit **2**, and the results of an aldol and ester enolate Claisen transform are shown in Scheme I.

Our synthetic plan for this polyether building block developed out of model studies which demonstrated the value of the hetero-Diels–Alder condensation in the construction of spiroketals (Scheme II).[14] Although the rigidity of the spiroketal system itself can mediate control of relative stereochemistry,[15] in this

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(2) Fellow of Deutscher Akademischer Austausendienst.

(3) National Science Foundation Research Fellow, 1981–1984.

(4) Westley, J. W., Ed. "Polyether Antibiotics: Naturally Occurring Acid Ionophores"; Marcel Dekker, Inc.: New York, 1982; Vols. I and II.

(5) Pressman, B. C.; Harris, E. J.; Jagger, W. S.; Johnson, J. M. *Proc. Natl. Acad. Sci. U.S.A.* **1967**, *58*, 1949.

(6) Ruff, Michael D. In "Polyether Antibiotics: Naturally Occurring Acid Ionophores"; Westley, J. W., Ed.; Marcel Dekker, Inc.: New York, 1982; Vol. I, Chapter 6.

(7) Hanley, H. G.; Slack, J. D., ref 6, Chapter 8. Reed, P. W.; Bokoch, G. M., ref 6, Chapter 9. Osborne, M. W.; Wenger, J.; Zanko, M.; Kovzelove, F.; Cohen, M. R., ref 6, Chapter 10.

(8) (a) Calcimycin: Evans, D. A.; Sacks, C. E.; Kleschick, W. A.; Tabor, T. R. *J. Am. Chem. Soc.* **1979**, *101*, 6789–6791. Grieco, P. A.; Williams, E.; Tanaka, H.; Gilman, S. *J. Org. Chem.* **1980**, *45*, 3537–3539. (b) Lasalocid A: Nakata, T.; Schmid, G.; Vranesic, B.; Okigawa, M.; Smith-Palmer, T.; Kishi, Y. *J. Am. Chem. Soc.* **1978**, *100*, 2933–2935. Ireland, R. E.; Anderson, R. C.; Badoud, R.; Fitzsimmons, B. J.; McGarvey, G. J.; Thaisrivongs, S.; Wilcox, C. S. *Ibid.* **1983**, *105*, 1988–2006. (c) Monensin: Fukuyama, T.; Akasaka, K.; Karanewsky, D. S.; Wang, C.-L. J.; Schmid, G.; Kishi, Y. *Ibid.* **1979**, *101*, 259–263. Still, W. C.; McDonald, J.; Collum, D. *Ibid.* **1980**, *102*, 2117–2121. (d) X-14547A: Nicolaou, K. C.; Papahatjis, D. P.; Claremon, D. A.; Dolle, R. E., III. *Ibid.* **1981**, *103*, 6967–6969. Roush, W. R.; Meyers, A. G. *J. Org. Chem.* **1981**, *46*, 1509. Edwards, M. P.; Ley, S. V.; Lister, S. G. *Tetrahedron Lett.* **1981**, 361. (e) Narasin: Kishi, Y. *Aldrichim. Acta* **1980**, *13*, 23–30. (f) Salinomycin: Kishi, Y.; Hatakeyama, S.; Lewis, M. D. *Front. Chem., Plenary Keynote Lect. IUPAC Congr., 28th* **1981** (Pub. 1982), 287–304. Laidler, K. J., Ed., Pergamon: Oxford, U.K. (g) General Methods: Walba, D. M.; Stoudt, G. S. *Tetrahedron Lett.* **1982**, 727–730. Amouroux, R.; Folefoc, G.; Chastrette, F.; Chastrette, M. *Tetrahedron Lett.* **1981**, 2259. Walba, D. M.; Wand, M. P. *Tetrahedron Lett.* **1982**, 4995–4998. (h) Reviews: Kishi, Y. In "Polyether Antibiotics: Naturally Occurring Acid Ionophores"; Westley, J. W., Ed.; Marcel Dekker, Inc.: New York, 1982; Vol. II, Chapter 1. Wierenga, W. In "The Total Synthesis of Natural Products"; ApSimon, J., Ed.; Wiley: New York, 1981; Vol. IV, p 263q.

(9) Crane, D. E.; Celmer, W. D.; Westley, J. W. *J. Am. Chem. Soc.* **1983**, *105*, 3594–3600.

(10) Ireland, R. E.; Courtney, L.; Fitzsimmons, B. J. *J. Org. Chem.*, **1983**, *48*, 5186–5198.

(11) Dobler, M. "Ionophores and Their Structures"; Wiley: New York, 1981.

(12) For other spiroketal containing natural products, see: Danishefsky, S. J.; Pearson, W. H. *J. Org. Chem.* **1983**, *48*, 3865–3866. Schreiber, S. L.; Sommer, T. J. *Tetrahedron Lett.* **1983**, 4781–4784. Crimmins, M. T.; Bankaitis, D. M. *Ibid.* 4551–4554. Phillips, C.; Jacobson, R.; Abrahams, B.; Williams, H. J.; Smith, L. R. *J. Org. Chem.* **1980**, *45*, 1920–1924 and references contained in these articles.

(13) Agtarap, A. G.; Chamberlain, J. W.; Pinkerton, M.; Steinrauf, L. *J. Am. Chem. Soc.* **1967**, *89*, 5737.

(14) Ireland, R. E.; Häbich, D. *Tetrahedron Lett.* **1980**, 1389. Ireland, R. E.; Häbich, D. *Chem. Ber.* **1981**, *114*, 1418–1427.

(15) Ireland, R. E.; Daub, J. P. *J. Org. Chem.* **1983**, *48*, 1303–1312. Ireland, R. E.; Daub, J. P.; Mandel, G. S.; Mandel, N. S. *J. Org. Chem.* **1983**, *48*, 1312–1325.

0002-7863/85/1507-3271$01.50/0