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Hydroboration of Sterically Hindered Olefins under High Pressure[1]

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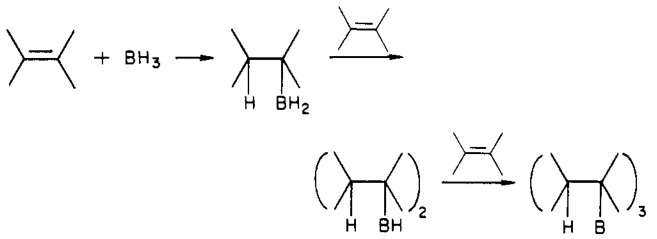
Hydroboration of sterically hindered olefins such as tetramethylethylene, tetraisopropylethylene, *trans*-1,2-di-*tert*-butylethylene, and 1,2-dimethyldi-*tert*-butylethylene has been investigated at high pressure (6000 atm). The previously unknown trithexylborane was prepared. The boron of trithexylborane was found to be isomerized much faster to a terminal carbon than that of dithexyl- and thexylboranes. *trans*-1,2-Di-*tert*-butylethylene yields a monoalkylborane at both 1 atm and high pressure (5000–6000 atm). Evidence is presented that is consistent with the hypothesis that a multialkylborane is formed at high pressure that dissociates without an isomerization upon releasing the pressure to 1 atm. Tetraisopropylethylene was found to give no hydroborated products at 1 atm or at high pressure (3500–6000 atm). (*E*)- and (*Z*)-1,2-Dimethyldi-*tert*-butylethylene was prepared, characterized, and hydroborated. A monoalkylborane is formed at 1 atm. At high pressure a trialkylborane is formed, which after returning to 1 atm, yields mainly the isomerized borane. 5β-Chol-9(11)-ene was synthesized from deoxycholic acid. This was found to yield a monoalkylborane after hydroboration at 1 atm or high pressure, in contrast to a literature report for a structurally similar steroid. An isomerized olefin was isolated after oxidation of the steroidal borane.

The addition of the elements of boron and hydrogen to multiple bonds between carbon and carbon, nitrogen, or oxygen is known as hydroboration. Since its discovery by Brown and Rao in 1956, this reaction has become one of the most important in the realm of organic chemistry.[3]

Alkenes containing two, three, or four alkyl substituents on the double bond readily undergo hydroboration. The great majority of olefins undergo complete reaction to form the corresponding trialkylborane. However, in the case of olefins with a high degree of steric hindrance, the reaction appears to proceed only to the mono- or dialkylborane.



There are many examples in the literature of large rate accelerations for sterically hindered reaction systems by the application of pressure.[4] The pressure dependence of the rate constant of a reaction is

$$(\partial \ln k/\partial p)_T = -(-\Delta V^\ddagger/RT)$$

where $\Delta V^\ddagger$ is the volume of activation. If this value is negative, i.e., the formation of the activated complex of the reactants results in an overall volume contraction, the rate, *k*, will increase with increasing pressure.[4] The effect of pressure on the rate of Menschutkin reactions such as the reaction of substituted pyridines with alkyliodides has been determined and found to result in a large acceleration, the $\Delta V^\ddagger$ being between −22 and −25 cm^3/mol.[5]

In a study of the kinetics of hydroboration of 2,3-dimethyl-2-butene it was determined that the entropy of activation for the reaction is −27 eu.[6] It has been shown that the volume of activation often parallels the entropy of activation for many chemical reactions.[7] If this is the case, a negative $\Delta V^\ddagger$ would be expected for hydroboration. Thus, the rate of hydroboration of olefins should be greatly accelerated at high pressure. We have initiated a study of the hydroboration of selected sterically hindered olefins at high pressure based upon this hypothesis.

Results and Discussion

Hydroboration of Tetramethylethylene (TME). It was observed by Brown et al. that thexylborane (2,3-dimethyl-2-butylborane) in the presence of a large excess of TME forms dithexylborane but does not proceed any further.[8] This led us to explore the possibility of synthesizing trithexylborane with excess TME at high pressure.

A solution of thexylborane in THF was prepared and excess TME added. Pressure in excess of 5000 atm was applied to a portion of the solution at room temperature for 10 h. After the product was isolated at 1 atm, an IR spectrum of the compound was recorded. The IR spectrum indicated the product to be a trialkylborane as both the terminal and bridging B–H bonds[8] had disappeared. The portion of the reaction mixture that remained at 1 atm had an IR spectrum that was identical with that of thexylborane. Oxidation of the trialkylborane with alkaline hydrogen peroxide yielded a mixture of 2,3-dimethyl-2-butanol and 2,3-dimethyl-1-butanol. The percentage of the 1-butanol was found to be much higher than that reported by Brown and co-workers for the oxidation of thexylborane.[8] Thus, an investigation of the rate of isomerization of trithexylborane as opposed to mono- and dithexylboranes was undertaken.

Trithexylborane was prepared at high pressure, and after the pressure was released to 1 atm, samples were withdrawn at various time intervals at room temperature and oxidized. It was assumed that isomerization does not occur

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[1] We dedicate this work to Professor H. C. Brown, on the occasion of his 70th birthday.

[2] This paper is abstracted from a thesis submitted to the Graduate School of the Polytechnic Institute of New York by Joseph E. Rice, in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1982.

[3] For reviews, see (a) H. C. Brown, "Organic Synthesis via Boranes", Wiley, New York, 1975; (b) H. C. Brown, *Pure Appl. Chem.*, **47**, 49 (1976).

[4] For general review, see W. J. le Noble and H. Kelm, *Angew. Chem., Int. Ed. Engl.* **19**(11), 841 (1980).

[5] W. J. le Noble and Y. Ogo, *Tetrahedron*, **26**, 4119 (1970).

[6] D. J. Pasto, B. Lepeska, and T. C. Cheng, *J. Am. Chem. Soc.*, **94**, 6083 (1972).

[7] N. S. Isaacs, "Liquid Phase High Pressure Chemistry", Wiley, New York, 1981, p 197.

[8] H. C. Brown, E. Negish, and J. J. Katz, *J. Am. Chem. Soc.*, **97**, 2791 (1975).

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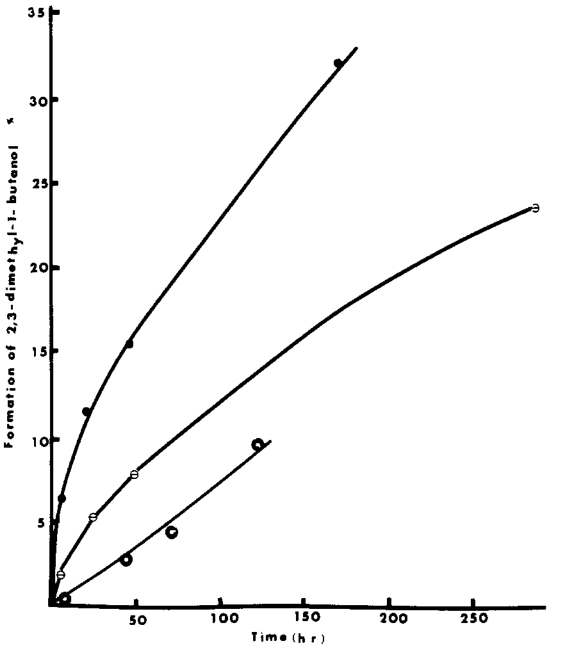
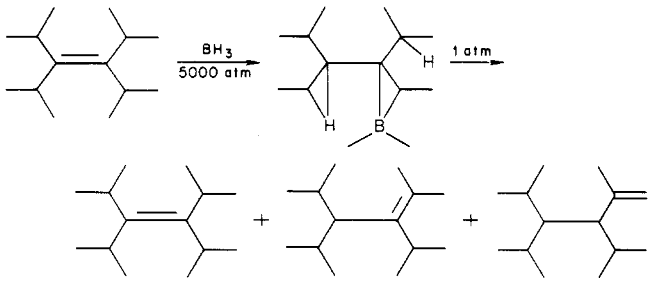


Figure 1. Rate of isomerization at room temperature of trithexylborane (●), dithexylborane (⊖), and monothexylborane (○). The data for monothexylborane was taken from ref 8.

at high pressure as this would involve a dissociation–recombination step that should be suppressed at high pressure. The alcohol formed was determined by gas chromatography. Dithexylborane was prepared at 1 atm and treated in a similar fashion. The isomerization rates of these boranes are plotted in Figure 1. The boron of trithexylborane was isomerized much faster to a terminal carbon than those of dithexyl- and thexylboranes. This sterically accelerated isomerization at room temperature is analogous to the well-known isomerization of alkylboranes at elevated temperature in diglyme.[9]

Hydroboration of Tetraisopropylethylene (TIPE). One of the most hindered olefins, tetraisopropylethylene, was synthesized from diisopropyl ketone by McMurry's procedure.[10]

Attempted hydroboration of TIPE at >5000 atm led to quantitative recovery of starting material. Varying the concentrations, reaction time, temperature, and pressure had no effect on the outcome of the reaction. A possibility for this reaction is that an alkylborane is formed at high pressure and then dissociates to TIPE and isomerized products upon returning to 1 atm. The product, however, was found to be a single compound identical with TIPE by NMR and GC.



There is NMR evidence that TIPE does possess unusual steric interactions.[11] The structure of TIPE is such that the methyl groups all lie above and below the plane of the double bond. The methine protons are coplanar with the double bond and lie alternately alongside the double bond and its ends (Figure 2a). If the alkylborane is formed at high pressure and the borane is isomerized at 1 atm to less hindered olefins, the transition state for the isomerization would involve the rotation of two methyl groups into the plane of the double bond so a syn elimination of B–H could occur (Figure 2b). This would put a tremendous steric strain on the molecule, which would be difficult to compensate for by rotation of the other group. Thus, the most likely mode of dissociation is to reform TIPE. Thus, this result indicates that either TIPE is not hydroborated at high pressure or an alkylborane is formed at high pressure but dissociates without isomerization upon returning to atmospheric pressure.

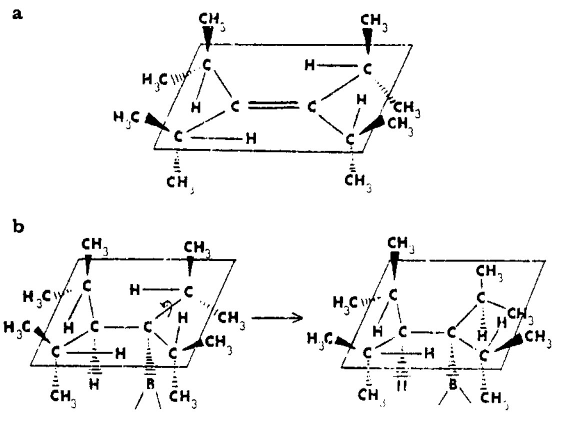
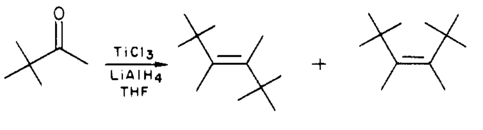


Figure 2. (a) Structure of TIPE. (b) Transition state for isomerization.

Hydroboration of *trans*-1,2-Di-*tert*-butylethylene (DBE). The hydroboration of *trans*-1,2-di-*tert*-butylethylene was investigated by Logan and Flautt and found to yield only a monoalkylborane at 1 atm.[12] The monoalkylborane was prepared and allowed to react with excess DBE at high pressure. Various reaction conditions were utilized. An IR spectrum of the product isolated, however, showed that it was identical with the starting alkylborane and oxidation of the borane with alkaline hydrogen peroxide yielded the expected 2,2,5,5-tetramethyl-3-hexanol. Since olefin isomerization was observed for TME and not DBE, it must be concluded that at least one hydrogen on the carbon β to boron must be available for isomerization to occur.

Hydroboration of 1,2-Dimethyldi-*tert*-butylethylene (DMDBE). 1,2-Dimethyldi-*tert*-butylethylene was prepared from pinocolone by use of the McMurray olefin synthesis.[10] This compound has not been reported in the literature and so its structure was determined rigorously. A mixture of the *E* and *Z* isomers was formed, consisting of 63% *Z* isomer and 37% *E* isomer. Space filling models show that these two isomers have similar degrees of steric hindrance. Separation of the mixture of isomers was found to be difficult and so the mixture was employed for the subsequent reactions.



(*E*)-DMDBE (*Z*)-DMDBE

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(9) H. C. Brown, U. S. Racherla, and H. Taniguchi, *J. Org. Chem.*, **46**, 4314 (1981).

(10) (a) J. E. McMurray, *Acc. Chem. Res.*, **7**, 281 (1974); (b) J. E. McMurray and M. P. Fleming, *J. Am. Chem. Soc.*, **96**, 4708 (1974).

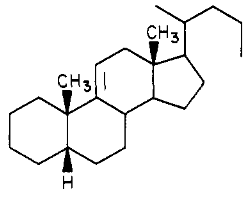
(11) (a) R. F. Langler and T. T. Tidwell, *Tetrahedron Lett.*, 777 (1975); (b) D. S. Bomse and T. H. Morton, *Tetrahedron Lett.*, 781 (1975).

(12) T. J. Logan and T. J. Flautt, *J. Am. Chem. Soc.*, **82**, 3446 (1960).

Hydroboration of DMDBE at 1 atm yielded a monoalkylborane as a bridged dimer (determined by IR). Reaction of the monoalkylborane with excess DMDBE at 5500 atm yielded the corresponding trialkylborane as demonstrated by the disappearance of all B–H peaks in the IR spectrum. This result was surprising in view of the fact that DBE forms only a monoalkylborane at high pressure and DMDBE is more sterically hindered than DBE. Oxidation of the trialkylborane with alkaline hydrogen peroxide gave an alcohol that was shown by its NMR spectrum to be predominantly the isomerized product, 2-*tert*-butyl-3,4,4-trimethylpentanol. Apparently the same mechanism that accounted for the rapid isomerization of sterically hindered trithexylborane also applies in this case. The trialkylborane of DMDBE formed at high pressure is extremely hindered. When pressure is released, a rapid isomerization to the less hindered structure occurs to relieve steric hindrance. This result suggests that the less hindered olefin DBE should form a trialkylborane at high pressure that dissociates to the monoalkylborane and DBE upon releasing the pressure.

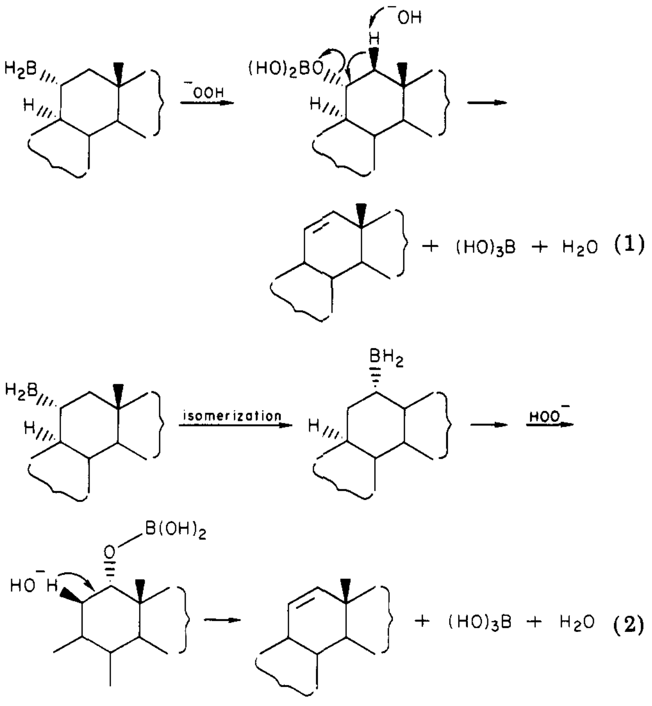
In order to examine this possibility, an attempt was made to examine the IR spectrum of the monoalkylborane with excess DBE directly under high pressure, using a diamond anvil pressure cell.[13] However, due a lack of resolution, the formation of the trialkylborane could not be detected. Another approach to this problem involved allowing the monoalkylborane of DBE to react at 5000 atm with an excess of DMDBE. Upon releasing of the pressure, an IR spectrum of the product showed the absence of B–H peaks. This observation indicated that the monoalkylborane of DBE did react with DMDBE at high pressure to yield the trialkylborane. This result lends support to the hypothesis that DBE does form a trialkylborane at high pressure, which then dissociates upon return to 1 atm.

Hydroboration of a Sterically Hindered Steroidal System. Since we have observed that hydroboration of sterically hindered olefins can be achieved by the application of pressure,[14] we sought to utilize this high-pressure technique for the hydroboration of sterically hindered steroidal systems. Highly hindered steroidal olefins such as Δ^7, 5β-$\Delta^{9(11)}$, and $\Delta^{8(14)}$ were reported to be inert to hydroboration by Sondheimer and co-workers.[15] There is a great deal of interest in methods for oxygenating C-11 in certain steroids. Therefore, an investigation of the hydroboration of 5β-chol-9(11)-ene, which is structurally similar to those steroids reported by Sondheimer, has been initiated. During the course of the present investigation, Mincione and co-workers[16] reported that hydroboration of $\Delta^{7(8)}$ and 5β-$\Delta^{9(11)}$ steroidal olefins could be achieved at 40–60 °C at 1 atm. Hydroboration of 5β-chol-9(11)-ene at 1 atm yielded a product that showed weak B–H peaks in the IR spectrum. These became more intense after the reaction was performed at high pressure. This finding agrees with the observation of Mincione that some hindered steroidal olefins can be hydroborated at 1 atm.



5β-chol-9(11)-ene

Scheme I



Oxidation with alkaline hydrogen peroxide yielded a crystalline compound with a melting point about 30 °C below that of 5β-chol-9(11)-ene. The mass spectrum revealed it to be of identical molecular weight with that of the starting compound. The olefinic doublet of doublets of the starting olefin was not evident in the NMR spectrum of the product. It appeared that an isomer of 5β-chol-9-(11)-ene is formed upon oxidation. Although the structure of the isomer was not determined rigorously, the most logical isomer should be Δ^{11}-cholene, which could arise by one of the mechanisms shown in Scheme I. Mincione found the same type of borane isomerization.[16]

This observation may offer an explanation of Sondheimer's results.[15] Since he was interested in the hydroboration–oxidation of unsaturated steroids, the failure to obtain alcohols might have been taken to mean that the reaction did not proceed. In fact, an isomer of the starting olefin was most likely formed.

In conclusion, it has been shown that hydroboration of sterically hindered olefins can be achieved at high pressure. The hindered boranes obtained at high pressure are thermally unstable and tend to isomerize rapidly at room temperature and 1 atm to less hindered structures if at all possible. Otherwise, dissociation to starting materials occurs. Although the range of pressures required was not optimized, it has been demonstrated that the application of high pressure on some hydroboration reactions may offer additional utilization of this fascinating hydroboration reaction in organic chemistry.

Experimental Section

General Procedures. Infrared spectra were recorded on a Perkin-Elmer Model 457 grating infrared spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian A-60 NMR spectrometer or a JEOL JNM FX90Q spectrometer. Abbreviations used are as follows: s, singlet; d, doublet; t, triplet,

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[13] C. E. Weir, A. Van Valkenburg, and E. Lippincott in "Modern Very High Pressure Techniques", R. H. Wentorf, Jr., Ed., Butterworths, Washington, DC, 1962, p 51.

[14] Y. Okamoto. Proceedings of the 6th AIRAT International High Pressure Conference, Boulder, CO, July 1977.

[15] M. Nussin, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, **29**, 1120 (1964).

[16] (a) E. Mincione and A. Sirna, *Ann. Chim. (Rome)*, **65**, 473 (1975); (b) E. Mincione and A. Sirna, *ibid.*, **65**, 421 (1975); (c) E. Mincione and F. Feliziani, *Chem. Commun.*, 942 (1973).

q, quartet, m, multiplet. Ultraviolet spectra were recorded on a Cary 15 UV–vis spectrophotometer. Mass spectra were recorded at the Rockefeller University mass spectrometry resource center or at Columbia University on a Finnigan 3300 GC/MS system. Raman spectra were recorded in glass capillary tubes irradiated by a Spectra Physics argon ion laser with scattered light collected at 90° in a Jobin Yvon Ramanor HG-2 double-grating monochromator. Gas chromatograms were recorded with a Perkin-Elmer 800 equipped with flame-ionization detector with a 10% Carbowax 20 M TPA on a Chromosorb W stainless steel column. Melting points were measured on an electrothermal apparatus and are uncorrected. Elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY.

High-pressure experiments were performed in Teflon capsules (3-mL capacity) in a stainless steel die and compressed via a piston with a Clifton 200-ton hydraulic press.[17]

Tetramethylethylene and *trans*-1,2-di-*tert*-butylethylene were purchased from Tridom-Fluka and were distilled from CaH_2 prior to use. Titanium(III) chloride and lithium aluminum hydride were obtained from Alfa. All other reagents were purchased from Aldrich Chemical Co. THF and diglyme were distilled from purple solutions of sodium benzophenone ketyl prior to use. A solution of BH_3·THF was prepared according to the procedure of Brown and stored under N_2 at 0 °C.[19] Concentration was checked prior to use by hydrolysis in glycerol–water (1:1), collecting the evolved hydrogen in a gas burette as described by Brown.[20]

All reactions were done in oven-dried glassware (120 °C, overnight), cooled in a stream of dry nitrogen. Transfer of liquid reagents was accomplished with oven-dried syringes, purged with N_2 prior to use. Infrared spectra of organoboranes were obtained in THF solution, utilizing the double syringe technique of Brown.[18] Teflon capsules for high-pressure experiments were filled under N_2 in a glovebag containing dishes of P_2O_5 as a dessicant.

Hydroboration of Olefins. Each reaction was repeated at least twice. Representative reactions are cited in this report.

Hydroboration of Tetramethylethylene (TME). Into a 50-mL three-neck flask fitted with a condenser, addition funnel, septum, and spin bar was added via syringe BH_3·THF (10 mL, 95 mmol, 9.55 M). A solution of TME (3 mL, 25 mmol) in THF (10 mL) was added under nitrogen over a 30-min period at −10 °C. After the mixture was stirred for 2 h at 0 °C, THF and excess BH_3 were removed under vacuum, leaving behind a colorless oil: IR (Nujol) 2505 (s), 1610 (w), 1555 (s) cm^{-1}. The oil was dissolved in THF (15 mL) and TME (8 mL, 67 mmol) was added. A portion (3 mL) of this mixture was pressurized at 4900 atm and room temperature for 22 h. After release of the pressure, excess TME and THF were evaporated under vacuum. A colorless oil remained: IR (Nujol) 2440 (vw), 1555 (vw) cm^{-1}. This procedure generally required 0.5–3 h. The solution, which was not pressurized, was evaporated under vacuum, yielding a colorless oil: IR (Nujol) 2500 (w), 2440 (w), 1610 (w), 1560 (s) cm^{-1}.

Oxidation of Thexylboranes Prepared at 1 atm and High Pressure. After 20 h trithexylborane (3 mmol) was dissolved in ethanol (2 mL) and sodium hydroxide (0.5 mL, 3 mmol, 6 N) was added dropwise followed by hydrogen peroxide (1 mL, 10 mmol, 30%). The mixture was stirred at 40 °C for 1 h and then extracted twice with ether, washed with water and brine, dried over K_2CO_3, filtered, and evaporated, leaving a colorless liquid. GC showed this to be a mixture of 2,3-dimethyl-2-butanol and 2,3-dimethyl-1-butanol in the ratio of 7.2:1.

After 26 h dithexylborane (21 mmol) was dissolved in ethanol (10 mL) and sodium hydroxide (4 mL, 24 mmol, 6 N) was added dropwise followed by hydrogen peroxide (7 mL, 70 mmol, 30%). After workup as above, the mixture was shown by GC to be a mixture of 2,3-dimethyl-2-butanol and 2,3-dimethyl-1-butanol in the ratio of 17.5:1.

Determination of Rate of Isomerization. An investigation of the rate of isomerization of trithexylborane as opposed to di- and monothexylborane was undertaken. Trithexylborane was prepared at high pressure, and after release of the pressure to 1 atm, samples were withdrawn at various time intervals at room temperature and oxidized. It was assumed that isomerization does not occur at high pressure as this would involve a dissociation–recombination step that should be suppressed at high pressure. Dithexylborane was prepared at 1 atm and treated in a similar fashion. The percentage of the various alcohols was determined by gas chromatography. The results are summarized in Table I.

Table I. Isomerization of Tri-, Di-, and Monothexylborane

time, h	% 1-ol
Trithexylborane	
0.5	6.5
20.5	11.5
44.1	15.5
167.5	31.3
Dithexylborane	
1	2.1
26.7	5.5
50.3	7.8
310.75	24.6
Thexylborane[8]	
1	~0
24	~0
48	3.1
72	4.5
120	9.6

Table II. Conditions for the Reaction of 2,2,5,5-Tetramethyl-3-hexylborane with DBE

expt. no.	DBE, mmol	alkylborane, mmol	*T*, °C	*P*, atm	*t*, h
1	6.0	1.5	25	5400	5
2	6.0	1.5	25	5400	22
3	7.0	2.0	25	5300	44
4	7.0	2.0	25	5100	71
5	22.0	2.0	25	6200	19

Hydroboration of *trans*-1,2-Di-*tert*-butylethylene (DBE). DBE (3 mL, 15 mmol) was dissolved in THF (3 mL) and this was dropped into BH_3·THF (15 mL, 56 mmol, 3.7 M) at 0 °C and stirred for 1 h. THF and excess BH_3 were evaporated under vacuum, leaving a white powder: IR (Nujol) 2490 (s), 1600 (s), 1580 (s) cm^{-1}. The powder was dissolved in THF (10 mL) and DBE (10 mL, 51 mmol) was added. A portion (3 mL) of this was pressurized at 5400 atm and room temperature for 16 h. After release of the pressure, excess DBE and THF were evaporated under vacuum, leaving a white powder: IR (Nujol) 2490 (s), 1700 (w), 1600 (w), 1575 (s) cm^{-1}.

This reaction was repeated a number of times under varying reaction conditions and a summary of the conditions used is shown in Table II.

Oxidation of Hydroboration Products of DBE at 1 atm and High Pressure. The alkylboranes isolated were oxidized by a method similar to that described above: NMR ($CDCl_3$) δ 5.43 (s), starting olefin 3.83 (t, $J = 6$, CHOH), 1.88 (m), 1.27 (d, $J = 6$, CH_2COH), 0.98 (s, *t*-Bu), 0.93 (s, *t*-Bu).

Synthesis of Tetraisopropylethylene (TIPE). Tetraisopropylethylene was prepared according to the literature preparation,[10] yielding 21.1 g (41% yield). Purification was accomplished by vacuum sublimation at 105 °C. The white needles melted at 117 °C (lit.[10] mp 116–117 °C); IR (Kbr) 3015 (w), 2960 (s), 2930 (s), 2875 (s), 1650 (w), 1460 (w), 1385 (w), 1370 (w) cm^{-1}; Raman 1641 (w) cm^{-1}; NMR ($CDCl_3$) δ 2.96 (m), 2.25 (m), 1.05 (m).

Hydroboration of Tetraisopropylethylene (TIPE). Hydroboration of TIPE was carried out under various conditions (Table III). The product was identified as unreacted TIPE by IR and GC.

Synthesis of (*E*)- and (*Z*)-1,2-Dimethyldi-*tert*-butylethylene (DMDBE). A slurry of titanium(III) chloride (195.7 g, 1.3 mol) in THF (1.5L) was prepared in a 3-L flask under

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[17] Y. Okamoto and H. Shimizu, *J. Am. Chem. Soc.*, **90**, 6145 (1968).

[18] Reference 3a, p 240.

[19] Reference 3a, p 18.

[20] Reference 3a, p 241.

Scheme II. Synthesis of 5β-Chol-9(11)-ene

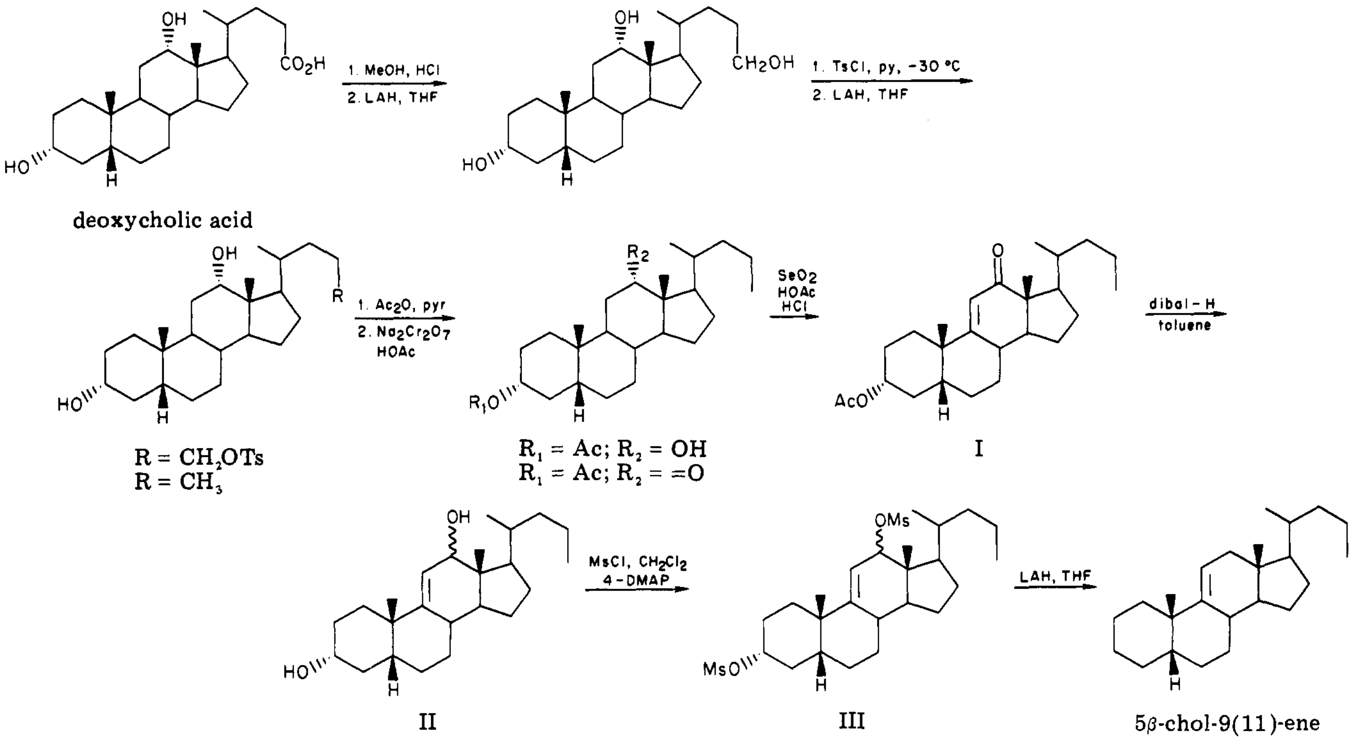

Table III. Conditions for the Reaction of TIPE with BH_3·THF

expt no.	TIPE, mmol	BH_3, mmol	T, °C	P, atm	t, h
1	0.5	LE[a]	25	5200	2
2	1.5	12	25	4700	23
3	1.7	2.0	25	6000	26
4	1.7	LE	25	3500	67
5	0.7	LE	60	5300	22

[a] LE = a large excess.

nitrogen in a glovebag. The flask was cooled to −78 °C and solid lithium aluminum hydride (24.3 g, 0.6 mol) was added slowly under a strong flow of nitrogen with mechanical stirring. The mixture turned black and evolved heat. When the mixture warmed to 0 °C, pinacolone (65.1 g, 0.7 mol) was added dropwise. After the addition was complete, the solution was refluxed for 24 h, cooled to room temperature, and slowly poured into ice/water (1 L). The mixture was extracted four times with hexane, washed with water and brine, dried over $MgSO_4$, filtered, and evaporated, yielding 54.8 g of crude liquid. Vacuum distillation [56–58 °C (5–6 mmHg)] yielded 38 mL of colorless liquid. This was chromatographed (in batches) on a silica gel column eluting with hexane/ether (4:1), yielding 27.7 g (47%) of pure (by TLC) DMDBE: IR (neat) 3030, 2940, 2900, 2860, 2710, 1470, 1440, 1388, 1370, 1357, 1225, 1190, 1135, 1060, 1010, 865 cm^{-1}; Raman 1600 (w), 1560 (w), 812 (s) cm^{-1}; NMR ($CDCl_3$) δ 1.74 (s, 6 H), 1.68 (s, 6 H), 1.24 (s, 18 H), 1.16 (s, 18 H); MS (CI) 169 (10), 168 (85), 153 (65), 113 (70), 111 (80), 99 (85), 97 (100), 85 (40), 83 (42).

Hydroboration of (*E*)- and (*Z*)-1,2-Dimethyldi-*tert*-butylethylene (DMDBE). DMDBE (1.8 g, 10.7 mmol) was added via syringe with stirring to BH_3·THF (10 mL, 25 mmol, 2.5 M) at 0 °C under N_2. After the mixture was stirred for 3 h, THF and excess BH_3 were evaporated under vacuum, leaving a water white oil: IR (Nujol) 2490, 1550 cm^{-1}. This was redissolved in THF (5 mL) and DMDBE (8.9 g, 53 mmol) was added. The solution was stirred under N_2 for 18.5 h and then a portion (3 mL) was pressurized at 5350 atm and room temperature for 19 h.

Oxidation of the Hydroboration Product of DMDBE. The borane obtained at high pressure was isolated and oxidized with $NaOH/H_2O_2$. The product isolated was an oily compound: NMR ($CDCl_3$) δ 5.37 (s), 3.9 (m, CH_2OH), 1.93 (m, CHCOH), 1.20 (m), 1.02 (s, CH_3), 0.97 (s, *t*-Bu), 0.93 (s, *t*-Bu).

Synthesis of 5β-Chol-9(11)-ene. 5β-Chol-9(11)-ene was synthesized according to Scheme II. This scheme is taken from a synthesis done by Klein and Djerassi[21] up to 3α-acetoxy-5β-chol-9(11)-en-12-one (I).

Preparation of 3α,12-Dihydroxy-5β-chol-9(11)-ene (II). Enone I (3.0 g, 7.5 mmol) was dissolved in toluene (70 mL) and cooled to −13 °C under a blanket of N_2. Diisobutylaluminum hydride (16.4 mL, 16.4 mmol, 1 M in toluene) was added dropwise with stirring over a 10-min period. The mixture was stirred for 19 h, warming to room temperature. Methanol (75 mL) was added at 0 °C to quench the reaction. The white precipitate was filtered and washed with hot methanol, and the solvents were evaporated, yielding 3.0 g of crude solids. Attempted crystallization from methanol/benzene (4:1) yielded a golden solid foam (1.6 g, 59%): IR (Nujol) 3560, 3320, 1020, 785 cm^{-1}; NMR ($CDCl_3$) δ 5.22 (m, C=CH), 4.07 (m, C=CCHOH), 3.58 (m, CHOH), 0.62 (s, CH_3), 0.58 (s, CH_3).

Preparation of 3α,12-Dimesitoxy-5β-chol-9(11)-ene (III). Enediol II (2.9 g, 8 mmol) was dissolved in methylene chloride (50 mL) and 4-(dimethylamino)pyridine (2.48 g, 20 mmol) was added. As the solution was stirred under N_2 at −10 °C, methanesulfonyl chloride (1.5 mL, 20 mmol) was added dropwise via syringe. A precipitate formed immediately. After being stirred for 24 h, the mixture was filtered, the filtrate was poured into water, and the organic layer was separated, washed with water, brine, dried over Na_2SO_4, filtered, and evaporated, yielding an oil: 3.5 g (85%); IR (neat) 3020, 1640, 1170 cm^{-1}; NMR ($CDCl_3$) δ 5.80, 5.70 (C=CH), 4.63 (m, CHOMs), 4.23 (m, CHOMs), 3.73 (s, CH_3SO_3), 3.02 (s, CH_3SO_3), 1.42 (m), 1.08 (m), 0.70 (m).

Preparation of 5β-Chol-9(11)-ene. Dimesylate III (5.4 g, 10.5 mmol) was dissolved in THF (50 mL) and added dropwise at 0 °C under nitrogen to a suspension of lithium aluminum hydride (4.5 g, 118.4 mmol) in THF (50 mL). After the addition was complete, the mixture was refluxed for 17 h and cooled to room temperature and then to 0 °C. Saturated NH_4Cl (50 mL) was added dropwise. The precipitate was filtered and washed with THF and solvent was then evaporated. The residue was taken up in ether, washed with water and brine, dried over $MgSO_4$, filtered through Celite/$MgSO_4$, and evaporated, yielding an oil: 3.4 g (∼100%). Crystallization from methanol/benzene (4:1) gave

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[21] H. Klein and C. Djerassi, *Chem. Ber.*, **106**, 1897 (1973).

white needles: mp 91–92 °C; NMR ($CDCl_3$) δ 6.04 (d of d, J_1 = 2, J_2 = 16 Hz), 1.89 (d of m, J_2 = 16 Hz); MS (isobutane), 329 (M + 1), 327 (100, M – 1).

Hydroboration of 5β-Chol-9(11)-ene. To a solution of 5β-chol-9(11)-ene (300 mg, 0.91 mmol) dissolved in THF (3 mL) was added BH_3·THF (1 mL, 1 mmol, 1 M). A portion (3 mL) of this was pressurized at 5000 atm and room temperature for 20 h. After release of the pressure, excess THF and BH_3 were evaporated, leaving an oily residue: IR (Nujol) 2500, 1555 cm^{-1}. The residue was dissolved in THF (2 mL) and oxidized by sequential addition of water (1 mL), 3 N NaOH (0.3 mL, 0.90 mmol), and 30% H_2O_2 (0.3 mL, 3 mmol), followed by heating at 40–50 °C for 2 h. The mixture was extracted with pentane, washed with water and brine, dried over Na_2SO_4, and evaporated, yielding an oil that crystallized from methanol/benzene (4:1): mp 65–66 °C; MS (EI) M^+ 328 (M^+). The solution, which was not pressurized (~1 mL), was evaporated and yielded an oily residue: IR (Nujol) 2500 (w), 1555 (w) cm^{-1}. This was identical with the high-pressure product.

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Registry No. I, 42921-47-1; II, 82979-02-0; III, 82979-03-1; TME, 563-79-1; DBE, 692-48-8; TIPE, 7090-88-2; (*E*)-DMDBE, 54290-40-3; (*Z*)-DMDBE, 54429-93-5; trithexylborane, 82978-96-9; thexylborane, 3688-24-2; dithexylborane, 20622-63-3; 2,2,5,5-tetramethylhex-3-ylborane, 82978-97-0; pinocolone, 75-97-8; 2-*tert*-butyl-3,4,4-trimethylpentylborane, 82978-98-1; tris(2-*tert*-butyl-3,4,4-trimethylpentyl)borane, 82978-99-2; tris(2,3-dimethylbutyl)borane, 64001-87-2; tris(2,2,5,5-tetramethylhexyl)borane, 82979-00-8; 5β-chol-9(11)-ene, 82979-01-9; deoxycholic acid, 83-44-3.

Carbon-13 Nuclear Magnetic Resonance Study of the Conformations of Disulfides and Their Oxide Derivatives[1,2]

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The carbon-13 nuclear magnetic resonance spectra and substituent effects of several acyclic disulfides and their oxidized derivatives are reported. Oxidation of a disulfide to a thiosulfinate or a thiosulfonate has a deshielding effect on the α-carbon atom and a shielding effect on the α′-carbon atom. The chemical shifts of α- and α′-carbon atoms of sulfinyl sulfones can best be correlated with the shifts of the α- and α′-carbon atoms in the corresponding thiosulfinates. On the basis of ^{13}C NMR shielding trends, it appears that conformational preferences of all the oxidized derivatives of disulfides are similar. A modified gauche effect is proposed to account for the difference in chemical shifts of the α-carbon atoms in the oxidized derivatives of disulfides.

The ^{13}C NMR chemical shifts of selected model molecules in various groups of organic compounds have proved to be of great diagnostic value in the analysis of unknown mixtures or structures. Organosulfur compounds, as a class, are of particular interest owing to some of their unique conformational and stereochemical properties and to the various oxidation states of sulfur. Sulfur atoms participating in disulfide bonds have electron pairs available for covalent bonding with oxygen. The possible structures are shown below.

Although there are numerous scattered references in the literature concerning ^{13}C NMR studies of organosulfur compounds,[2–4] there are only a few systematic studies of disulfides (**1**),[3,5–7] thiosulfinates (**2**),[2,5,6] and α-disulfoxides (**3**, not yet isolated).[8–11] The ^1H NMR spectra of **1**,[3,5–7] **2**,[3,5,6,12,13] **4**,[3,5,6] and several α-disulfones (**6**)[14] have been reported. Thus, we have carried out a systematic study of the ^{13}C NMR spectra of simple symmetrical acyclic disulfides and some of their oxide derivatives (**2**–**6**). These data and previous reports[2,3,5,6] are used to obtain useful ^{13}C NMR chemical shift trends for **2**–**6** and to give some insight into the preferred conformations of these compounds in solution.

Results

The ^{13}C NMR chemical shifts for a series of disulfides (**7**–**15**), thiosulfinates (**16**–**24**), thiosulfonates (**25**–**33**), sulfinyl sulfones (**34**–**36**), and α-disulfones (**37**–**41**) are shown in Tables I and II. The assignments were made by off-resonance decoupling techniques and by observation of the expected downfield shifts owing to changes in the electronegativity of divalent sulfur after oxidation.

The ^{13}C NMR substituent effects of thiosulfinates (**2**) and thiosulfonates (**4**), which were calculated from the spectral data tabulated in Table I, are shown in Table III. The α_{SO} values [$\alpha_{SO} = \delta_{C_\alpha}$(thiosulfinate) – δ_{C_α}(disulfide)] vary from 13.18 to 19.30 ppm, and the α'_{SO} values [$\alpha'_{SO} = \delta_{C_{\alpha'}}$(thiosulfinate) – $\delta_{C_{\alpha'}}$(disulfide)] range from –9.03 to 2.30

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