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Hydroboration and Thermal Isomerization of Unsaturated Alcohols

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Hydroboration and thermal isomerization of undecenols (**1**, **2**, and **3**), pentenol (**11**), and 2,2-dimethyl-3-nonenol-1 (**21**) were studied. Undecane-1,3- and -1,4-diols were obtained from undecenols *via* oxaborolane and oxaborinane. π-Complex mechanism for thermal isomerization (mechanism 1) was supposed and was confirmed by the studies using diborane-d_6 and 5-ethyl-4-heptenol-1 (**39**).

Hydroboration and successive thermal isomerization of simple olefins have been studied and have become useful synthetic methods.[1] On the other hand, few examples have been reported in the case of olefins bearing functional groups.[2] From the viewpoint of mechanistic studies and of synthetic applications, the hydroboration and thermal isomerization of unsaturated alcohols were reinvestigated.

Hydroboration and Thermal Isomerization.—Three undecenols, 10-undecenol-1 (**1**), 6-undecenol-1 (**2**), and 3-undecenol-1 (**3**), were chosen and were hydroborated at room temperature and thermally isomerized at 160° followed by the usual oxidation. Products were converted into trimethylsilyl ethers and analyzed by glc and mass spectrometry.[3] The results of such analyses are shown in Table I.

$CH_2{=}CH(CH_2)_9OH$
1

$CH_3(CH_2)_mCH{=}CH(CH_2)_nOH$
2, $m = 3;\ n = 5$
3, $m = 6;\ n = 2$

$HO(CH_2)_{11}OH$
4

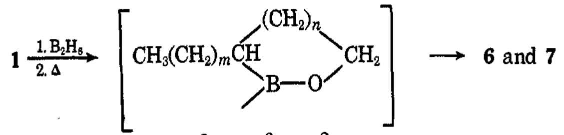
$CH_3(CH_2)_mCH(OH)(CH_2)_nOH$
5, $m = 0; n = 9$
6, $m = 6, n = 3$
7, $m = 7, n = 2$

$CH_3(CH_2)_{10}OH$
8

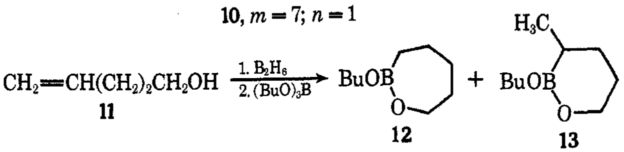
TABLE I
HYDROBORATION AND THERMAL ISOMERIZATION OF UNDECENOLS AT 160°

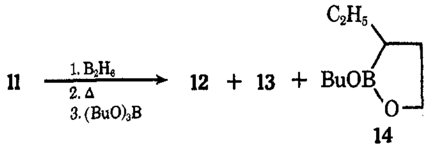
Undecenol	Reaction time, hr	Yield of undecanediol, % 1,3- (7)	1,4- (6)	1,6-	1,7-	1,10- (5)	1,11- (4)	Yield of undecanol (8), %
10-Undecenol-1	0	0	0	0	0	8	92	0
(1)	3	1	56	0	0	1	40	1
	7	11	66	0	0	1	19	1
	10	12	67	0	0	1	18	1
	22	12	70	0	0	1	15	1
	34	13	70	0	0	<1	15	2
6-Undecenol-1	0	0	0	51	49	0	0	0
(2)	2	27	57	<1	<1	<1	1	9
	5	27	58	<1	<1	<1	1	9
	10	26	55	<1	<1	<1	1	11
3-Undecenol-1	0	61	33	0	0	0	0	6
(3)	0.5	60	34	0	0	0	0	6
	2	60	32	0	0	0	0	7
	5	58	32	0	0	0	0	10
	10	53	31	0	0	0	0	16

Inspection of Table I indicates that undecane-1,3- and 1,4-diol (**7** and **6**) are the main products in each case. The formation of the diols, **6** and **7**, suggests that the boron atom was trapped on C_3 or C_4. This might be explained by the formation of oxaborolane (**10**)[4] and oxaborinane (**9**) derivatives. For experimental convenience,[5] 4-pentenol-1 (**11**) was chosen to confirm the intermediary oxaborolane and oxaborinane formation. Hydroboration of **11** at room temperature and successive treatment with tributyl borate gave a mixture of **12** and **13**. Similarly, **11** gave a mixture of **12**, **13**, and **14** by hydroboration, thermal isomerization, and successive treatment with tributyl borate. The structure of **12**, **13**, and **14** were determined by ir, mass spectral, and elemental analyses and by the analyses of their oxidation products. These results indicated the formation of oxaborinane during thermal isomerization.



9, $m = 6; n = 2$
10, $m = 7; n = 1$

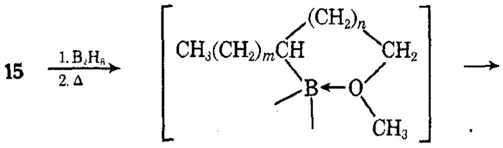




The assumption of coordinate bond formation between boron and oxygen[2b] also might explain the trapping of boron on C_3 or C_4. Provided that such a coordinate bond does exist, the oxygen atom of the

$CH_2{=}CH(CH_2)_8CH_2OCH_3$
15

$CH_3(CH_2)_6CH{=}CHCH_2CH_2OCH_3$
16



17, $m = 6; n = 2$
18, $m = 7; n = 1$

$[CH_3(CH_2)_mCH(OH)(CH_2)_nCH_2OCH_3]$
19, $m = 6; n = 2$
20, $m = 7; n = 1$

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[1] H. C. Brown, "Hydroboration," W. A. Benjamin, New York, N. Y., 1962; G. Zweifel and H. C. Brown, *Org. React.*, **13**, 1 (1963); H. C. Brown and M. V. Bhatt, *J. Amer. Chem. Soc.*, **88**, 1440 (1966).

[2] (a) S. P. Fore and W. G. Bickford, *J. Org. Chem.*, **24**, 920 (1959); (b) T. J. Logan, *ibid.*, **26**, 3657 (1961).

[3] (a) J. Diekman, J. B. Thomson, and C. Djerassi, *ibid.*, **32**, 3904 (1967); **33**, 2271 (1968); (b) G. H. Draffan, R. N. Stillwell, and J. A. McCloskey, *Org. Mass Spectrom.*, **1**, 669 (1968).

[4] Isolation of oxaborolane: B. M. Mikhailov and V. A. Dorohov, *Izv. Akad. Nauk SSSR*, 1661 (1964).

[5] The method used in this experiment is conveniently applicable when the boiling point of the organoboron compound is lower than that of tributyl borate.

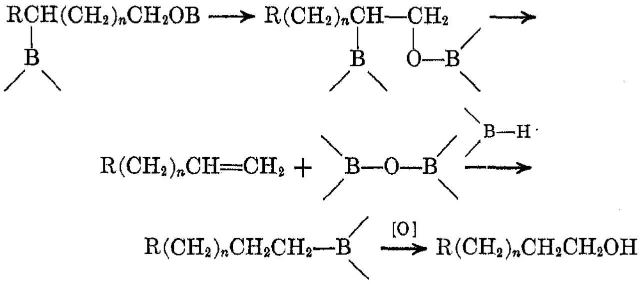
methoxy group, instead of the hydroxy group, may similarly trap the boron atom at the C_3 or C_4 position. From the results of hydroboration and thermal isomerization of methyl 10- and 3-undecenyl ether (**15** and **16**), no evidence of intramolecular coordinate bond formation was obtained (Table II).

TABLE II

HYDROBORATION AND THERMAL ISOMERIZATION OF METHYL UNDECENYL ETHER AT 160° (CH_3OR)

R	Reaction time, hr	Solvent	Yield of hydroxyundecyl methyl ether, % 3- (**20**)	4- (**19**)	10-	11-	Yield of undecanol (**8**), %
10-Undecenyl	0	Diglyme	0	0	16	84	0
(**15**)	20	Diglyme	0	0	3	29	59
	20	Decalin	0	0	5	74	17
3-Undecenyl	0	Diglyme	51	43	0	0	6
(**16**)	8	Diglyme	<1	<1	<1	7	93

The formation of the monofunctional alcohol, undecanol-1, may be explained by rehydroboration of 1-undecene, produced by 1,2 elimination of a hydroxyl group and the vicinally situated boron, by a mechanism similar to that of Brown and Cope.[6] This consideration was supported by the reaction of 2,2-dimethyl-3-nonenol-1 (**21**) with diborane. Hydroboration and thermal isomerization of **21** gave a mixture of **22** (8%), **23** (90%), and **24** (2%), but 2,2-dimethylnonanol-1 (**25**) could not be detected. Considering these facts, as well as Brown's thermal isomerization mechanism,[7] the above-mentioned explanation for the formation of undecanol seems plausible.



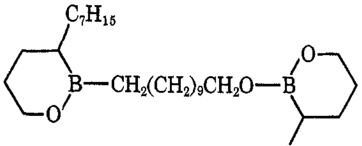
$$RCH(CH_2)_nCH_2OB \longrightarrow R(CH_2)_nCH{-}CH_2 \longrightarrow R(CH_2)_nCH{=}CH_2 + \,{>}B{-}O{-}B{<} \xrightarrow{>B{-}H} R(CH_2)_nCH_2CH_2{-}B{<} \xrightarrow{[O]} R(CH_2)_nCH_2CH_2OH$$

$$\underset{\mathbf{21}}{CH_3(CH_2)_4CH{=}CHC(CH_3)_2CH_2OH} \xrightarrow[2.\ [O]]{1.\ B_2H_6} \underset{\mathbf{22}}{CH_3(CH_2)_4CH_2CH(OH)C(CH_3)_2CH_2OH} + \underset{\mathbf{23}}{CH_3(CH_2)_4CH(OH)CH_2C(CH_3)_2CH_2OH}$$

$$\mathbf{21} \xrightarrow[3.\ [O]]{1.\ B_2H_6\ \ 2.\ \Delta} \mathbf{22} + \mathbf{23} + \underset{\mathbf{24}}{HOCH_2(CH_2)_6C(CH_3)_2CH_2OH}$$

$$\underset{\mathbf{25}}{[CH_3(CH_2)_6C(CH_3)_2CH_2OH]}$$

A comparison between entries 3 (10-undecenol-1, 7-hr thermal isomerization) and 12 (3-undecenol-1, 0.5-hr thermal isomerization) of Table I shows that the yield of 1,3-diol was only 11% in the former case and 60% in the latter case. This difference may be explained by the following considerations. In the case of 10-undecenol-1, 19% of 1,11-diol was obtained. The organoboron compound which gave rise to undecane-1,11-diol might be compound **26** rather than **27**. The reaction mixture from 10-undecenol-1 was considered to be a mixture of compounds **26**, **28**, and **29**. On the other hand, the reaction mixture from 3-undecenol-1 was considered to be a mixture of **28** and **29**. Formation of **29** from **1** also indicated that **28** was the precursor of **29**.



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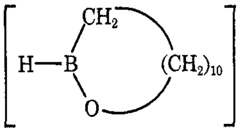

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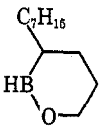

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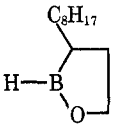

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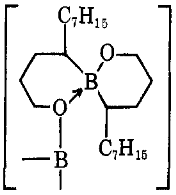

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From these considerations, migration of the boron atom from the C_4 position to the C_3 position was considered to be explained by the following mechanism (using as an analogy a previously proposed mechanism).[8,9] The thermal isomerization of organoboron compounds seems to proceed *via* dehydroboration to form a π complex (**32** → **33**) followed by rehydroboration (**33** → **34** → **35**). The boron atom eliminated from the C_4 position of the six-membered cyclic organoboron compound forms a π complex with the newly produced olefinic linkage, and the rotation around the π complex results in the original hydrogen atom (H_a) being situated close to the C_4 position (**34**). Then rehydroboration gives the five-membered cyclic organoboron compound (**35**). Thus, the isomerization from oxaborinane to oxaborolane proceeds without difficulty, and is also considered to be reversible. This thermal isomerization is considered to be rather difficult when the boron atom of complex **37** has only one hydrogen on boron, as in the case of **36** (R' = alkyl or alkoxy). In this case, the transformation of **36** into **41** is considered to be rather difficult without first destroying the intramolecular π complex (**37**). Upon destroying the π complex followed by rotation around the C_2–C_3 bond or the B–O bond, the complex **39** would be reconstructed and oxaborolane (**41**) would be formed *via* **40**. This rotation around the C–C or B–O bond is, however, hindered by the bulkiness of the alkyl or alkoxy group attached to the boron atom and/or of the remaining alkyl residue of the olefinic group. Using this reasoning, rehydroboration from the complex **37** is considered to give oxaborinane **36** rather than oxaborolane **41**.

Mechanistic Studies.—In order to obtain further evidence for the thermal isomerization mechanism (mechanism 1), deuterium-labeling experiments were undertaken. Taking account of the conceivable facility of oxaborinane formation, 5-ethyl-4-heptenol-1 (**42**)

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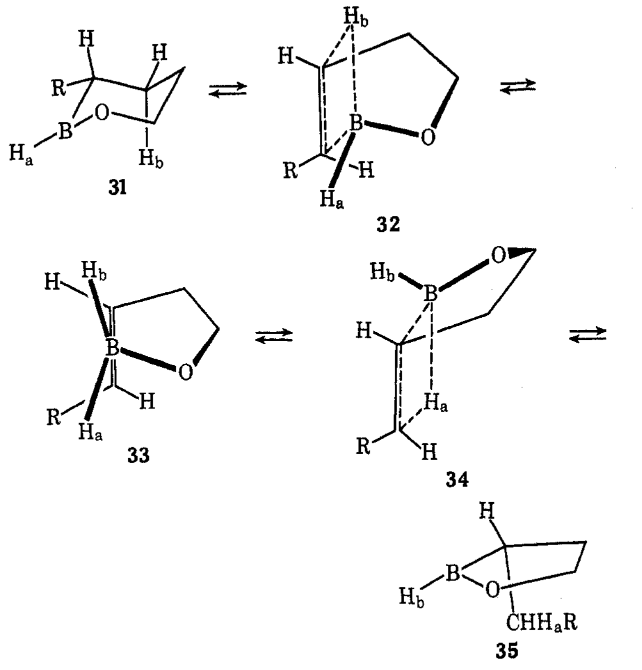
(6) H. C. Brown and O. J. Cope, *J. Amer. Chem. Soc.*, **86**, 1801 (1964).

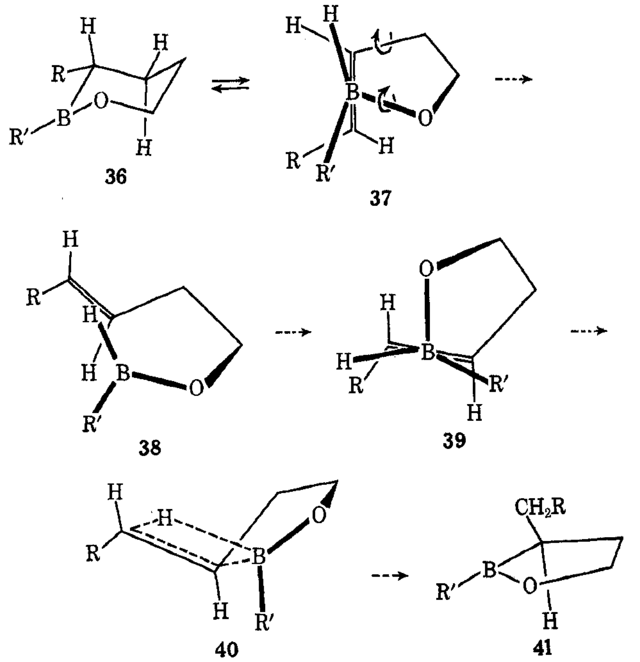
(7) H. C. Brown and G. Zweifel, *ibid.*, **82**, 1504 (1960).

(8) A. Streitwieser, Jr., L. Verbit, and R. Bittman, *J. Org. Chem.*, **32**, 1530 (1967).

(9) F. M. Rossi, P. A. McCusker, and G. F. Hennion, *ibid.*, **32**, 450 (1967).



(mechanism 1)



was chosen and was treated with diborane-d_6 (deuterium content 86%[10]).

Reaction of **42** and diborane-d_6 in the molar ratio of 2:1 at room temperature afforded a mixture of 1,4-diol **43** (99%) and 1,5-diol **44** (1%). Deuterium analysis showed that the total deuterium content in **43** was 87% and the deuterium was exclusively located at C_5. Thermal isomerization of the reaction mixture at 160° for 2 hr gave 1,4-diol **43** (64%), 1,3-diol **45** (26%), 1,7-diol **46** (4%), and 5-ethylheptanol-1 (**47**) (6%). From this mixture, 1,3-diol **45** was isolated *via* the six-membered cyclic butaneborinic ester **49**.[11]

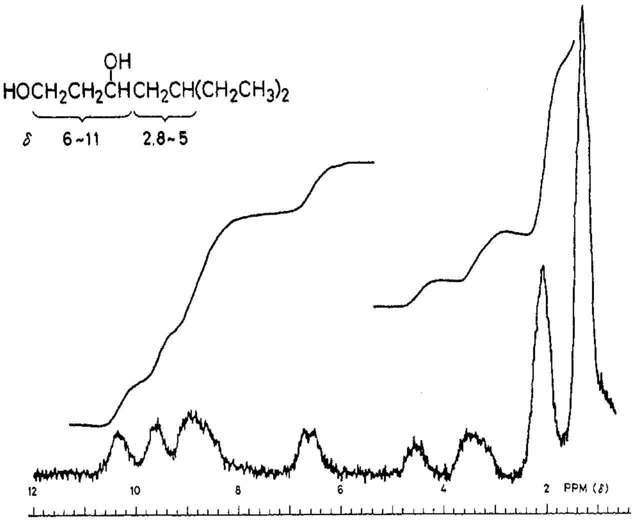
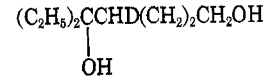


Figure 1.—60-MHz nmr spectrum of deuterated **45** (12 mg) in CCl_4 (150 μl) after addition of Eu(dpm)$_3$ (30 mg).

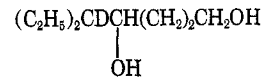
Since mass spectrometric determination of the deuterium distribution in **45** was considered to be unreliable,[12] it was performed by nmr and mass spectrometry.

$$\underset{\mathbf{42}}{(C_2H_5)_2C{=}CH(CH_2)_2CH_2OH} \xrightarrow[2.\ \Delta\ 2\,hr \quad 3.\ [O]]{1.\ >BD}$$



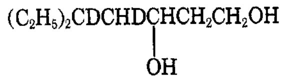
$$(C_2H_5)_2C(OH)CHD(CH_2)_2CH_2OH$$

44



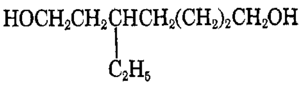
$$(C_2H_5)_2CDCH(OH)(CH_2)_2CH_2OH$$

43



$$(C_2H_5)_2CDCHDCH(OH)CH_2CH_2OH$$

45



$$HOCH_2CH_2CH(C_2H_5)CH_2(CH_2)_2CH_2OH$$

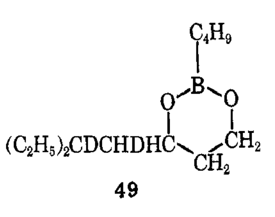
46

$$(C_2H_5)_2CHCH_2(CH_2)_2CH_2OH$$

47

$$\mathbf{45} \xrightarrow[2.\ -CO_2 \quad 3.\ -OH]{1.\ [O]} (C_2H_5)_2CDCH_2COCH_3$$

48



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Total deuterium content at C_4 and C_5 was determined by the nmr spectrum (Figure 1) of a carbon tetrachloride solution of **45** and tris(dipivaloylmethanato)europium.[13] The protons situated on C_1–C_3, C_4–C_5, C_6, and C_7 were assigned[14] as shown in Figure

---

[10] Diborane-d_6 was generated from sodium borodeuteride and boron trifluoride etherate in Diglyme and used in THF solution. Deuterium content of the diborane-d_6 was calculated from that of the cyclohexanol produced by the reaction of diborane-d_6 with excess cyclohexene followed by oxidation.

[11] G. M. Anthony, C. J. W. Brooks, I. Maclean and I. Sangster, *J. Chromatogr. Sci.*, **7**, 623 (1969).

[12] Because the mass spectra of the TMS derivative of **45** showed a very small parent peak (0.07%) and large M − 1 peak (0.15%), the total deuterium content in **45** was difficult to determine using the molecular ion peak. The M − 15 ion was prominent and considered to be possible to use for the determination of deuterium content, but was less accurate, for this fragment is said to be the one due to methyl group loss from the trimethylsilyl group, but there is no evidence that there is no intramolecular hydrogen–hydrogen exchange before fragmentation.

[13] (a) A. F. Cockerill and D. M. Rackham, *Tetrahedron Lett.*, 5153 (1970); (b) J. K. M. Sanders and D. H. Williams, *J. Amer. Chem. Soc.*, **93**, 641 (1971), and references cited therein.

[14] The assignment of the signals shown in Figure 1 was sufficient for the calculation of the deuterium content on C_4 and C_5.

1, analogously to the case of 2-hydroxy-1-(2-hydroyethyl)adamantane.[13a] The integration of the hydrogen atoms at C_1, C_2, and C_3 was used for deuterium analyses, because the deuterium content at these positions was considered to be negligible. The total deuterium content on C_4 and C_5 was observed to be 1.56 from the integral of Figure 1. The 1,3-diol **45** was converted into 4-ethyl-2-hexanone (**48**) by oxidation and decarboxylation. After complete deuterium–hydrogen exchange of the hydrogens α to the carbonyl group by aqueous base treatment, the deuterium content on C_4 and C_5–C_6 (C_5 and C_6–C_7 positions, respectively, in the precursor **45**) was determined to be 0.72 and 0.06, respectively, by mass spectrometry. The deuterium distribution in **45** was calculated from the above described data, and is summarized in Table III.

TABLE III

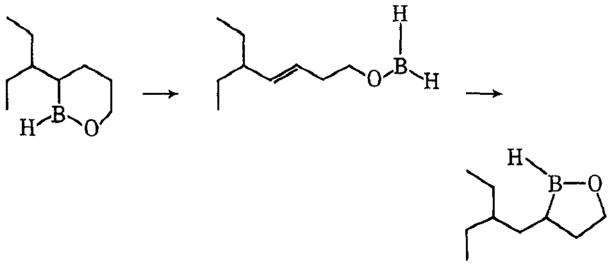
DEUTERIUM CONTENT IN 45

	Amount of deuterium atom at position 4	5	6
Observed	0.84	0.72	0.06
Mechanism 1	0.86	0.86	*a*
Mechanism 2	0.43	0.86	*a*

[a] Deuterium content on C_6 could not be obtained by mechanism 1 and 2.

As described in the above section, hydroboration and thermal isomerization of 5-ethyl-4-heptenol-1 (**42**) was considered to proceed mainly from oxaborinane **31** to oxaborolane **35**, since 99% of **43** was obtained by hydroboration and successive oxidation. The expected deuterium distribution for each of the mechanisms, mechanism 1 and 2, is shown in Table III.

Inspection of the data shown in Table III indicates that mechanism 1 is considered to be the probable one because of the good agreement between the observed values and the expected ones. Mechanism 2 is not considered to be suitable for this case since the deuterium content on C_4 is too small.



(mechanism 2)

The above-mentioned inspection for each mechanism indicated that thermal isomerization of oxaborinane **31** to oxaborolane **35** proceeds *via* an intramolecular π complex (mechanism 1).[15]

Experimental Section

Gas chromatography was performed on a Shimazu GC-4APT and a Hitachi K-23 with a 3 m × 3 mm column packed with 15% polyethylene glycol and 10% HVSG on Chromosorb W (80–100 mesh), and with a 45 m × 0.5 mm BDS Golay column. Mass spectra were obtained with an Hitachi RMS-4 spectrometer with 70 eV ionization potential. Nuclear magnetic resonance spectra were recorded with a Jeolco CL-60 spectrometer, with tetramethylsilane as internal standard and carbon tetrachloride as solvent.

6-Undecenol-1 (2).—6-Undeconic acid was prepared by the Wittig reaction between valeraldehyde and the phosphonium salt made from triphenylphosphine and 6-bromohexenoic acid. Methyl esterification of 6-undecenoic acid followed by lithium aluminum hydride reduction gave **2**: bp 130° (16 mm); mass spectrum *m/e* (rel intensity) 170 (M^+, 1); ir 3330 and 1655 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.31; H, 12.90.

3-Undecenol-1 (3).—3-Undecenoic acid was prepared *via* the Knoevenagel reaction of malonic acid, nonyl aldehyde, and triethanolamine. Methyl esterification of 3-undecenoic acid followed by lithium aluminum hydride reduction gave **3**: bp 121° (12 mm); ir 3320 cm^{-1}; mass spectrum *m/e* (rel intensity) 170 (M^+, 0.9).

Methyl 10-Undecenyl Ether (15).—Excess sodium hydride treatment of a THF solution of **1** followed by excess methyl iodide treatment gave **15**: bp 116–119° (18 mm); ir 3100, 1640, 1110 cm^{-1}.

Anal. Calcd for $C_{12}H_{24}O$: C, 78.19; H, 13.13. Found: C, 78.28; H, 13.35.

Methyl 3-Undecenyl Ether (16).—This ether was prepared as described above: bp 124° (35 mm); ir 1110 cm^{-1}; mass spectrum *m/e* (rel intensity) 184 (M^+, 1), 55 (100).

Anal. Calcd for $C_{12}H_{24}O$: C, 78.19; H, 13.13. Found: C, 78.26; H, 13.36.

2,2-Dimethyl-3-nonenol-1 (21).—Wittig reaction between *n*-hexylidenetriphenylphosphorane and 2,2-dimethyl-3-tetrahydropyranyloxypropanal gave 1-tetrahydropyranyloxy-2,2-dimethyl-3-nonene. Acid-catalyzed hydrolysis of this tetrahydropyranyl ether gave **21**: bp 114° (19 mm); ir 3350, 1640 cm^{-1}; mass spectrum *m/e* (rel intensity) 170 (M^+, 1), 69 (100).

Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.43; H, 13.03.

General Procedure for Hydroboration–Isomerization. **A.**—To the ice-cooled solution of unsaturated alcohol in diglyme a THF solution of diborane (molar ratio alcohol/diborane = 2) was added during 5 min under nitrogen. The mixture was stirred at room temperature for over 4 hr. THF was distilled off *in vacuo* and the mixture was refluxed. A 5-ml portion of the reaction mixture was periodically taken out and treated with excess alkaline hydrogen peroxide. The resulting mixture was extracted with ether and dried (Na_2SO_4), and ether and diglyme were distilled off. The crude product was converted to the trimethylsilyl ether derivative[3] and analyzed by glc.

B.—For the purpose of confirming the yield of reaction product, heat treatment was continued for 20 hr. After alkaline hydrogen peroxide oxidation the reaction mixture was extracted with ether and dried (Na_2SO_4), ether and diglyme were distilled off, and then distillation gave the product mixture. The product mixture was converted to the trimethylsilyl derivatives and analyzed by glc.

Hydroboration–Isomerization of 10-Undecenol-1 (1). **A.**—Besides the general procedure, **1** (4.25 g, 25 mmol) was hydroborated internally with sodium borohydride (0.71 g, 18.8 mmol) and boron trifluoride etherate (3.55 g, 25 mmol) in diglyme (120 ml). After completion of hydroboration at room temperature (overnight), the reaction mixture was refluxed and a 20-ml portion of the mixture was taken out after 3, 7, 10, 22, 34, and 48 hr, and was treated as described above. The results are shown in Table I.

B.—Hydroboration–isomerization of **1** (1.7 g, 10 mmol) in diglyme (20 ml) was performed by general procedure B, yield 1.76 g, bp 140–145° (4 mm). Glc analysis of the trimethylsilyl ether of the product showed that the product was a mixture of **4** (23%), **6** (55%), **7** (15%), **8** (2%), and other diols (5%).

Hydroboration–Isomerization of 6-Undecenol-1 (2). **A.**—Hydroboration–isomerization and work-up of **2** (500 mg, 2.93

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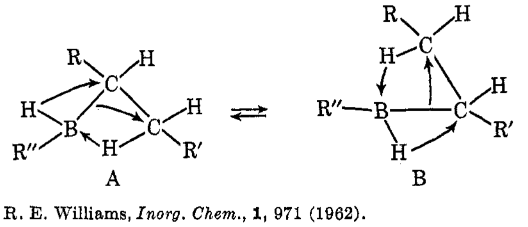
[15] Williams' mechanism[16] (A ⇄ B) was omitted. Inspection of Dreiding models indicated that the application of this mechanism to oxaborinane was considered to be difficult.



[16] R. E. Williams, *Inorg. Chem.*, **1**, 971 (1962).

mmol) in diglyme (25 ml) was performed by general procedure A. The results are shown in Table I.

B.—Hydroboration–isomerization of **2** (340 mg, 2 mmol) in diglyme (15 ml) was performed by general procedure B, yield 301 mg, bp 146° (4 mm). Glc analysis of the trimethylsilyl ether of the product showed that the product was a mixture of **4** (2%), **6** (77%), **8** (3%), **7** (17%), and other diols (1%).

Hydroboration–Isomerization of 3-Undecenol-1 (3). A.—3-Undecenol-1 (3) was hydroborated and isomerized by general procedure A. The results are shown in Table I.

B.—Hydroboration–isomerization of **3** (340 mg, 2 mmol) in diglyme (15 ml) was performed by general procedure B, yield 306 mg, bp 142° (4 mm). Glc analysis of trimethylsilyl ethers of the products showed that the products were **6** (42%), **7** (52%), and **8** (6%).

Hydroboration–Isomerization of Methyl 10-Undecenyl Ether (15). A. In Diglyme.—Methyl 10-undecenyl ether (**15**) (0.43 g, 11.3 mmol) was hydroborated internally with sodium borohydride (0.43 g, 11.3 mmol) and boron trifluoride etherate (2.17 g, 15 mmol) in diglyme (50 ml) at 0°. After completion of the hydroboration at room temperature, a half of the mixture was taken out. Usual work-up and distillation gave 0.90 g of a mixture, bp 136–143° (8 mm). The residue was refluxed for 20 hr. Usual work-up and distillation of this isomerization product gave 0.89 g of a product mixture, bp 110–134° (10 mm). The results are shown in Table II.

B. In Decalin.—To the solution of **15** (0.81 g, 4.4 mmol) in decalin (50 ml), a THF solution of diborane (4.2 mmol in 4.0 ml) was added at 0°. The reaction mixture was stirred overnight, THF was distilled off, and the mixture was heated at 160° for 20 hr. General work-up and distillation of this resulting mixture gave 0.71 g of product mixture, bp 136–140° (6 mm). The results are shown in Table II.

Hydroboration of Methyl 3-Undecenyl Ether (16).—To the solution of **16** (461 mg, 2.5 mmol) in diglyme (10 ml), a THF solution of diborane (0.62 mmol in 0.5 ml) was added at 0°. The reaction mixture was stirred at room temperature for 3 hr and allowed to stand overnight. After the general work-up, the crude product was analyzed. The results are shown in Table II.

Hydroboration–Isomerization of Methyl 3-Undecenyl Ether (16).—To the solution of **16** (461 mg, 2.5 mmol) in diglyme (10 ml), a THF solution of diborane (1.25 mmol in 1.1 ml) was added at 0°. The reaction mixture was stirred for 6 hr at room temperature, and the mixture was refluxed for 8 hr. General work-up and distillation gave 393 mg of product mixture, bp 110–125° (10 mm). The results are shown in Table II.

1-*n*-Butoxy-2-oxaborepane (12), 1-*n*-Butoxy-2-oxa-6-methylborinane (13), and 1-*n*-Butoxy-2-oxa-5-ethylborolane (14). A.—To a solution of **11** (2.15 g, 25 mmol) in THF (15 ml), a THF solution of diborane (12.5 mmol in 10 ml) was added at 0°. The reaction mixture was stirred overnight at room temperature, and the solvent and excess of diborane were removed *in vacuo*. To the residue, tributyl borate (3.3 g, 14.3 mmol) was added. About 4 g of liquid was distilled out during heating at 210–225° for 10 hr. Redistillation gave a mixture of boron compounds: yield 3.12 g (73%) from 4-pentenol-1; bp 80–96° (16.5 mm); ir 1330 cm^{-1}, absence of -OH absorption; mass spectrum *m/e* (rel intensity) 170 (M$^+$, 1), 56 (100).

Anal. Calcd for $C_9H_{19}O_2B$: C, 63.57; H, 11.26. Found: C, 63.68; H, 11.37.

The components of this organoboron mixture were determined by alkaline hydrogen peroxide oxidation of these organoboron compounds. Glc analysis of the oxidation products, with *n*-octyl alcohol as internal standard, showed that these oxidation products were *n*-butyl alcohol (51%) and some pentanediols (total 49%). Yield of the oxidation reaction was 89% (by glc), and diols were pentane-1,5-diol (75%) and pentane-1,4-diol (25%). These results showed that the initial organoboron compounds were **12** (75%) and **13** (25%).

B.—To a solution of **11** (2.15 g, 25 mmol) in diglyme (20 ml), a THF solution of diborane (12.5 mmol in 10 ml) was added at 0°, the mixture was stirred at room temperature, and THF was removed and then refluxed for 6 hr. Then the solvent was removed *in vacuo*. To the residue, tributyl borate (3.3 g, 14.3 mmol) was added and the mixture was heated to 220–225° for 7 hr. The distilled liquid was redistilled, bp 90–96° (15 mm), yield 1.5 g (35%) from **11**. Product analysis as described above showed that the products were **12** (76%), **13** (23%), and **14** (1%).

Hydroboration–Isomerization of 2,2-Dimethyl-3-nonenol-1 (21). A.—Hydroboration–isomerization and work-up was performed by general procedure A. The products are (i) before heating, **22** (44%) and **23** (56%); and (ii) after heating, **22** (8%), **23** (90%), and **24** (2%).

B.—Hydroboration–isomerization of **21** (340 mg, 2 mmol) in diglyme (15 ml) was performed by general procedure B, yield 293 mg, bp 122° (3.5 mm). The products were **22**, **23** (total 99%), and **24** (1%).

Anal. Calcd for $C_{11}H_{24}O_2$: C, 70.16; H, 12.85. Found: C, 70.02; H, 12.95.

5-Ethyl-4-heptenol-1 (42).—5-Ethyl-4-heptenal was prepared by the reported method[17] from 15 g of 3-vinyl-3-pentanol and 19.7 g of ethyl vinyl ether, yield 5.4 g (24%). Lithium aluminum hydride reduction of this aldehyde gave **42** in quantitative yield: bp 106° (21 mm); ir 3370, 2950, 2890, 1660 cm^{-1}; mass spectrum *m/e* (rel intensity) 55 (100), 142 (M$^+$, 24).

Anal. Calcd for $C_9H_{18}O$: C, 75.99; H, 12.76. Found: C, 75.87; H, 13.00.

Hydroboration–Isomerization of 5-Ethyl-4-heptenol-1 (42).—Hydroboration–isomerization of **42** (0.71 g, 5 mmol) in diglyme (20 ml) was performed by general procedure A. The products were (a) before heating, **43** (99%), **44** (1%); (b) 20 min, **43** (85%), **45** (15%); (c) 60 min, **43** (83%), **45** (17%); (d) 120 min, **43** (82%), **45** (18%).

Deuterioboration of 5-Ethyl-4-heptenol-1 (42).—To the stirred solution of **42** (710 mg, 5 mmol) in diglyme (20 ml), THF solution of diborane-d_6 (2.5 mmol in 2.7 ml) was added at 0° under nitrogen. The mixture was stirred for 3 hr at room temperature. Then a quarter portion of this mixture was taken out. Usual work-up followed by distillation of this portion gave 187 mg of a mixture of **43** (99%) and **44** (1%). The mass spectrum of the trimethylsilyl derivative of **43** follows: *m/e* (rel intensity) 305 (M$^+$, 0.01), 304 (0.04), 290 (0.07), 233 (17.8), 143 (100), 73 (57); relative abundance of M − 15 fragments,[18] 289 (15.5), 290 (100), 291 (28.8), 292 (12.0).

Deuterioboration–Isomerization of 5-Ethyl-4-heptenol-1 (42).—To the stirred solution of **42** (1.14 g, 8 mmol) in diglyme (23 ml), a THF solution of diborane-d_6 (4 mmol in 6.4 ml) was added at 0° under nitrogen. The mixture was stirred for 4 hr at room temperature. Then the mixture was heated and THF was distilled off after 30 min refluxing, and the mixture was refluxed for a further 1.5 hr. After general work-up, the crude yield was 1.10 g. The products were **43** (64%), **45** (26%), **46** (4%), and **47** (6%).

Isolation of 5-Ethylheptane-1,3-diol (45).—To the crude product (1.10 g) obtained above, 0.95 g of *n*-butaneboronic acid and 5 ml of pyridine were added. After standing for 30 min, pyridine was distilled off under nitrogen. The residue was chromatographed on silica gel by elution with ethyl acetate–carbon tetrachloride (1:1). The cyclic boronate **49** was isolated. The boronate **49** was oxidized by alkaline hydrogen peroxide, extracted with ether, and dried (Na_2SO_4). Distillation and preparative glc gave 40 mg of pure **45**.

Deuterioboration of Cyclohexene.—To a solution of diborane-d_6 in THF, a large excess of cyclohexene was added at 0° under nitrogen. The reaction mixture was stirred for 10 hr at room temperature, oxidized by alkaline hydrogen peroxide, extracted with ether, and dried (Na_2SO_4); ether and THF were distilled off under reduced pressure and the residue was separated by glc. The deuterium content of cyclohexanol was determined by mass spectrography at 70 eV using molecular ion: mass spectrum *m/e* (rel intensity) 57 (100), 83 (55), 101 (M$^+$, 4); relative abundance of molecular ions,[19] 99 (7.0), 100 (58.2), 101 (100), 102 (8.9).

4-Ethyl-2-hexanone (48).—To the stirred solution of diols obtained by deuterioboration and thermal isomerization of **42**, Jones reagent (8 *N*) was added dropwise until the reddish-brown color remained. The stirring was continued for a further 15 min, the organic layer was decanted, diluted with ether, and washed with water, and the solvents were removed under reduced pressure. The remainder was stirred with about 20% aqueous

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(17) R. Marbet and G. Saucy, *Helv. Chim. Acta*, **50**, 2095 (1967).

(18) Relative abundances of M − 15 fragments of trimethylsilyl derivatives of undeuterated **43** were as follows: *m/e* (rel intensity) 289 (100), 290 (23.8), 291 (15.9). Relative abundances of M − 3-pentyl fragments of trimethylsilated **43** (*m/e* 233–235) were superimposable with those of undeuterated **43**.

(19) Relative abundances of molecular ions of undeuterated cyclohexanol were as follows: *m/e* (rel intensity) 99 (42.8), 100 (100), 101 (9.1).

sodium carbonate solution for 4 hr, extracted with ether, and dried (Na$_2$SO$_4$), and ether was separated by glc: mass spectrum *m/e* (rel intensity) 43 (85), 85 (100), 110 (25), 129 (M$^+$, 9); relative abundance of molecular ions,[20] 128 (45.5), 129 (100), 130 (17.1), 131 (3.0).

5-Ethylheptane-1,3-diol (45).—Methyl 5-ethyl-3-oxoheptanoate was synthesized by the method of Weiler[21] from methyl acetoacetate (3.48 g, 30 mmol) and 3-bromopentane (6.6 g, 33 mmol), bp 116–118° (18 mm), yield 1.4 g, (40%) from methyl acetoacetate. Reduction of this β-keto ester by the method of Cope and Wood[22] gave **45** in 83% yield: bp 126–130° (8 mm); ir 3320, 2925, 1460, 1380, 1050 cm^{-1}; mass spectrum of trimethylsilyl derivative *m/e* (rel intensity) 304 (M$^+$, 0.07), 289 (2), 261 (4), 219 (53), 187 (46), 103 (100), 73 (79).

Anal. Calcd for C$_9$H$_{20}$O$_2$: C, 67.45; H, 12.58. Found: C, 67.57; H, 12.66.

5-Ethylheptane-1,4-diol (43).—Hydroboration of **42** at 0° under nitrogen and usual work-up gave **43** (purity 99% by glc): bp 120–125° (6 mm); mass spectrum of trimethylsilyl derivative *m/e* (rel intensity) 304 (M$^+$, 0.05), 289 (1), 247 (2), 233 (19), 143 (100), 73 (57).

Anal. Calcd for C$_9$H$_{20}$O$_2$: C, 67.45; H, 12.58. Found: C, 67.48; H, 12.84.

Registry No.—**1**, 112-43-6; **2**, 32970-48-2; **3**, 32970-49-3; **12**, 32970-50-6; **13**, 32970-51-7; **14**, 32970-52-8; **15**, 7289-47-6; **16**, 32970-54-0; **21**, 32970-55-1; **22**, 32970-56-2; **23**, 32970-57-3; **24**, 32970-58-4; **42**, 998-67-4; **43**, 32970-60-8; **45**, 33021-05-5; **48**, 6022-26-0.

Acknowledgment.—The authors are indebted to Mr. H. Kusakabe for mass spectra and Mrs. K. Huzimoto for elemental analyses.

[20] Relative abundances of molecular ions of undeuterated **48** were as follows: *m/e* (rel intensity) 128 (100), 129 (9.3), 130 (0.6).

[21] L. Weiler, *J. Amer. Chem. Soc.*, **92**, 6702 (1970).

[22] A. C. Cope and G. W. Wood, *ibid.*, **79**, 3885 (1957).

Conformational Aspects of the Directive Effect of the Homoallylic Hydroxyl Group in the Simmons–Smith Reaction

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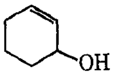
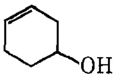
A series of substituted 3-cyclohexenols was prepared and subjected to the iodomethylzinc iodide methylenation reaction. Competitive kinetics establish that, in contrast to the allylic 2-cyclohexenols, the homoallylic 3-cyclohexenols react through the axial hydroxyl conformer. The compounds examined ($k_{\rm rel}$) are 3-cyclohexenol (1.0), *cis*-6-methyl-3-cyclohexenol (5.2), 1-methyl-3-cyclohexenol (4.0), *trans*-6-methyl-3-cyclohexenol (2.6), *trans*-1,4,5,6,7,8-4a(8a*H*)-hexahydronapthol (1.6), and 4-methoxycyclohexene (0.18). All of these olefins exhibited stereospecific methylenation reactions.

Since its introduction in 1958, the Simmons–Smith methylenation reaction[2] has been widely used in organic synthesis. A particularly interesting aspect is the directive effect of a neighboring hydroxyl group in the substrate olefin.[3] In cyclopentenes and cyclohexenes, an allylic or homoallylic hydroxyl group leads to stereospecific cis introduction of the methylene group. Higher cyclic olefins can give trans product with high selectivity provided the hydroxyl group–organometallic complex affords more facile access to the trans face of the olefin.[3] In our earlier work[4] it was established that both allylic and homoallylic hydroxyl groups in cyclohexene cause very large rate enhancement. In fact, both types of alcohols react immeasurably faster than the parent unsubstituted olefin, although a significant factor also separates the rates of 1 and 2. Interestingly,



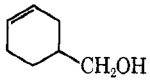
1

$k_{\rm rel} = 11$



2

1.0



3

very slow

when the hydroxyl group is removed to the γ position, as in **3**, the rate becomes comparable to that of cyclohexene itself, and the reaction becomes effectively nonstereoselective.[4] By determining the relative rates of methyl-substituted 2-cyclohexenols, it was established that the cis directive effect of the allylic hydroxyl group is exerted by this group in the pseudoequatorial conformation. This result bears on the question of the structure of the Simmons–Smith reagent in ether solution; models indicate that a monomeric iodomethylzinc species, in which the metal is complexed to the pseudoequatorial hydroxyl oxygen, cannot attain the necessary geometry for reaction with the double bond. For this reason a dimeric structure for the reactive organometallic species was proposed.[4]

The rate difference between **1** and **2**, as well as the lack of any significant influence (stereochemical or kinetic) of the hydroxyl group in compound **3**, clearly indicates, that the directive effect of the hydroxyl group has very specific geometric requirements. It was therefore of interest to determine which conformer of the homoallylic cyclohexenol causes cis selectivity.

Ginsig and Cross,[5] in applying the Simmons–Smith reaction to estr-5(10)-ene-3,17-diol, found that both the 3α and 3β alcohols gave stereospecific methylenation (cis to the homoallylic 3-OH group in both cases), but the 3α isomer was quite sluggish in reaction and required forcing conditions. Levine and coworkers[6] have presented convincing evidence that the preferred half-chair conformation of ring A in estr-5(10)-ene is such that the 3α hydroxyl group would be equatorial, and conversely the 3β group would be axial. The methylenation results[5] therefore would support the

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[1] Author to whom correspondence should be addressed.

[2] H. E. Simmons and R. D. Smith, *J. Amer. Chem. Soc.*, **80**, 5323 (1958).

[3] A recent discussion of this phenomenon and references to earlier work are found in the work of C. D. Poulter, E. C. Friedrich, and S. Winstein, *ibid.*, **91**, 6892 (1969).

[4] J. H. Chan and B. Rickborn, *ibid.*, **90**, 6406 (1968).

[5] R. Ginsig and A. D. Cross, *ibid.*, **87**, 4629 (1965).

[6] S. G. Levine, N. H. Eudy, and E. C. Farthing, *Tetrahedron Lett.*, 1517 (1963); S. G. Levine, D. M. Feigl, and N. H. Eudy, *ibid.*, 4615 (1967).