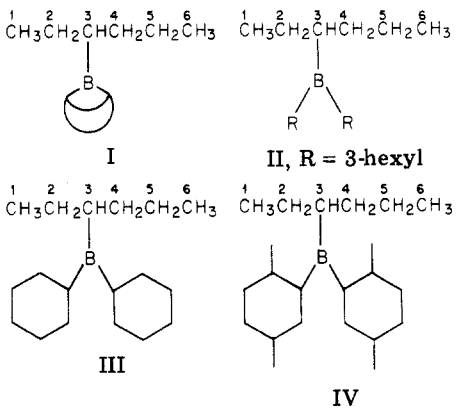
Chart I



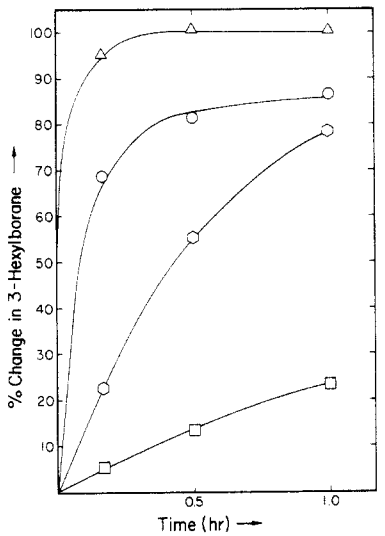
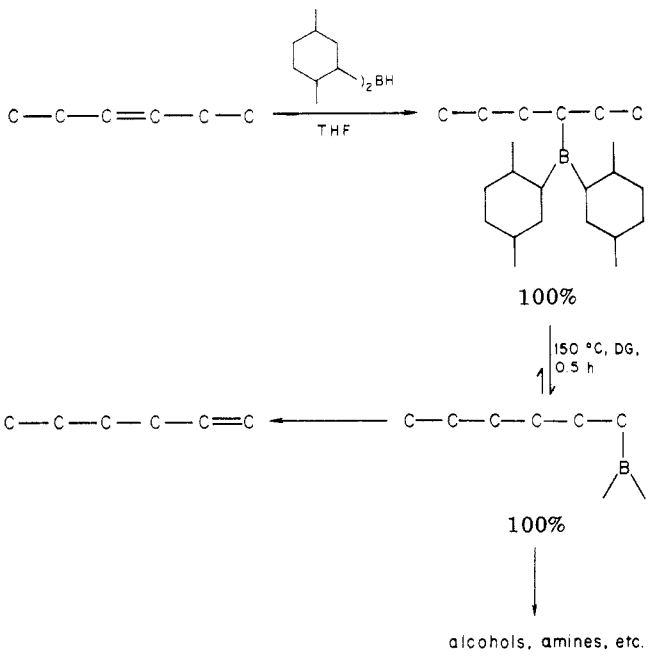



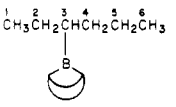
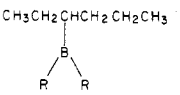
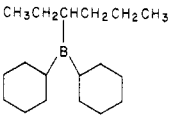
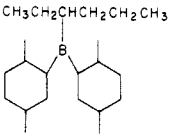

**Figure 1.** Rates of isomerization at 150 °C of *B*-(3-hexyl)dialkylboranes: □, *B*-R-9-BBN; hexagon, $RBR_2$; ○, RB-c-$Hex_2$; △, RB(2,5-$Me_2$-c-Hex)$_2$.

Scheme I




We continue to probe further into the steric influences on the rates and equilibrium involved in thermal isomerization and to explore the full scope of the isomerization of *B*-alkylbis(2,5-dimethylcyclohexyl)boranes.

Table I. Thermal Isomerization[a] of Organoboranes

| organoborane | $t_{1/2}$, s[b] | time to reach equilibrium, h | % composition of hexanols at equilibrium: 1-ol | 2-ol | 3-ol |
|---|---|---|---|---|---|
|  I | 12060 | 264 | 90 | 6 | 4 |
|  II[c] | 1500 | 72 | 90 | 6 | 4 |
|  III | 300 | 48 | 97 | 2 | 1 |
|  IV | 3 | 0.5 | 100 | 0 | 0 |

[a] All thermal isomerizations were done at 150 ± 2 °C in diglyme with 0% hydride excess. [b] $t_{1/2}$ was determined graphically from kinetic data in each case. [c] R = 3-hexyl.

**Registry No. I**, 78964-99-5; **II**, 1883-34-7; **III**, 72487-19-5; **IV**, 78965-00-1; *cis*-3-hexene, 7642-09-3; dicyclohexylborane, 1568-65-6; bis(2,5-dimethylcyclohexyl)borane, 78965-01-2; 1-hexanol, 111-27-3; 2-hexanol, 626-93-7; 3-hexanol, 623-37-0.

(6) Graduate research assistant on grants from the Exxon Research and Engineering Corp. and the National Science Foundation.
(7) Visiting scholar, 1972–1973, on funds provided by the Maruzen Oil Co., Ltd., Osaka, Japan.

**Herbert C. Brown,* Uday S. Racherla[6] Hiroaki Taniguchi[7]**
*Richard B. Wetherill Laboratory*
*Purdue University*
*West Lafayette, Indiana 47907*
*Received June 29, 1981*

## Mechanism of the Backbone Rearrangement of Amino Steroids. A High-Field Proton, Deuterium, Carbon-13, and $^1$H Two-Dimensional Nuclear Magnetic Resonance Spectroscopic Study of Isoholamine and Polydeuterated Isoholamine

*Summary:* The determination of the label distribution in polydeuterated isoholamine resulting from $D_2SO_4$-catalyzed rearrangement of holamine has been carried out. A mechanism for the rearrangement is proposed.

*Sir:* Considerable effort has been directed in recent years toward the elucidation of the mechanism of the backbone rearrangement of steroids.[1] Deuterated reagents were used in a number of cases,[1] but no appropriate technique

(1) Ph.D. Thesis, J. Thierry, Université de Paris-Sud, Centre d'Orsay, France, 1976 and references cited therein.

0022-3263/81/1946-4314$01.25/0 

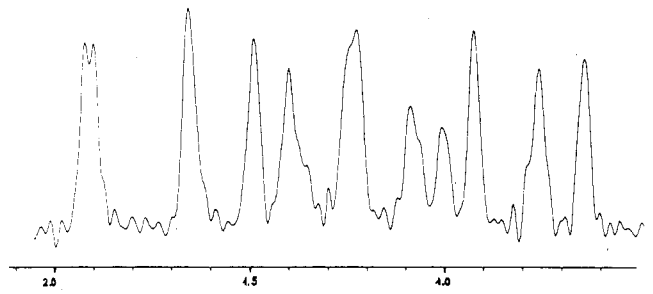
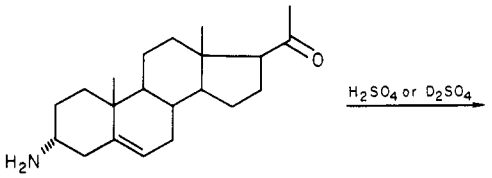
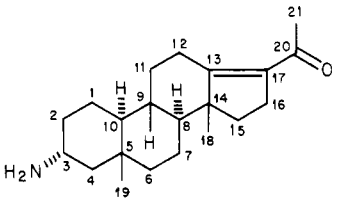


**Figure 1.** The 61.4-MHz proton-decoupled deuterium NMR spectrum of 2-$d_x$ in $CDCl_3$ solution. Deuterium chemical shifts were measured with respect to the solvent and are given for $Me_4Si$ = 0.

was available for the determination of the label distribution in the complex polydeuterated molecules. We report here high-field NMR spectroscopic evidence concerning the mechanism of the rearrangement of holamine 1 into isoholamine (2).[2]




1




2 or 2-$d_x$

Holamine 1 treated with $D_2SO_4$ at 0 °C afforded as expected[3] an isotopic mixture of polydeuterated isoholamine (2-$d_x$). Spectral comparison between the 400-MHz $^1H$ and 62.89-MHz $^{13}C$ NMR spectrum of 2 and 2-$d_x$ showed that a maximum of 13 deuterium atoms attached to eight carbon centers were incorporated, which is in agreement with chemical ionization mass spectrometric results. Furthermore, the 61.4-MHz proton-decoupled deuterium NMR spectrum of labeled isoholamine exhibited 10 resolved signals (Figure 1). A comparison of this $^2H$ NMR spectrum with the proton spectrum of 2 and 2-$d_x$ afforded evidence that three of the 10 signals correspond each to the two resonances of partially labeled atoms.

In view of the highly extended spin systems, analysis of the cross sections of the two-dimensional $J$ spectrum of isoholamine (2) was not very useful for the assignment of its hydrogens.[4] However, this technique permitted the determination of the precise chemical shift of all protons of 2,[4] and this information was important in the interpretation of the $^2H$ NMR spectrum of 2-$d_x$. Spin-decoupling experiments allowed the assignment of some of the hydrogen signals of isoholamine (2). These assignments were easier for those protons in 2-$d_x$ which are not labeled: $^1H$ NMR ($CDCl_3$) $\delta$ 3.32 ($H_{16\alpha}$ or $H_{16\beta}$), 2.85 ($H_{3ax}$, t of t and integrated intensity identical in 2 and 2-$d_x$), 2.48 ($H_{12ax}$ or $H_{12eq}$), 2.43 ($H_{12eq}$ or $H_{12ax}$), 2.20 ($3H_{21}$), 1.97 ($H_{16\beta}$ or $H_{16\alpha}$), 1.91 ($H_{2eq}$), 1.51 ($H_{4eq}$), 0.94 ($3H_{18}$ or $H_{19}$), 0.91 ($H_{2ax}$), 0.81 ($3H_{19}$ or $H_{18}$), 0.78 ($H_{4ax}$). Deuterium incorporation at rates varying between 50–90%, based on integration of the $^2H$ NMR spectrum of 2-$d_x$, could be determined at all remaining sites ($^1H$ NMR chemical shifts from the 2D $J$ spectrum[4] of 2): 1.95, 1.70, 1.69, 1.51, 1.45, 1.40, 1.30, 1.25, 1.12, 1.03, 0.97, 0.75, 0.69.

As a result of the labeling, the $^{13}C$ NMR spectrum of 2-$d_x$ exhibited considerably decreased intensity for 10 resonances with respect to the spectrum of 2[5]. The carbon signals of relatively low intensity correspond to the eight labeled sites and to the two quaternary centers which are in highly deuterated environments.[6] $^{13}C$ chemical shift assignment for isoholamine[7] is as follows (signals of relatively low intensity in the spectrum of 2-$d_x$ are in italics[8]) ($CDCl_3$) $\delta$ *24.7* ($C_1$), 37.9 ($C_2$), 46.2 ($C_3$), 52.8 ($C_4$), *34.5* ($C_5$), *41.8* ($C_6$), *21.8* ($C_7$), *50.2* ($C_8$), *35.8* ($C_9$), *55.3* ($C_{10}$), *34.9* ($C_{11}$), 31.4 ($C_{12}$), 162.7 ($C_{13}$), *52.2* ($C_{14}$), *37.5* ($C_{15}$), 24.2 ($C_{16}$), 131.2 ($C_{17}$), 18.4/17.8 ($C_{18/19}$), 199.1 ($C_{20}$), 30.3 ($C_{21}$).

Thus all the hydrogen atoms attached to $C_1$, $C_6$, $C_7$, $C_8$, $C_9$, $C_{10}$, $C_{11}$, and $C_{15}$ are labeled between 50% and 90% in 2-$d_x$ while the other protons of this amino steroid do not show deuterium incorporation.[9]

In the light of these results the following mechanism may be considered for the backbone rearrangement: the reaction starts by the formation of a carbocation at $C_5$ in equilibrium with the olefin $\Delta_{5\text{-}6}$. This is followed by the migration of the $C_{19}$ methyl group from $C_{10}$ to $C_5$. The olefin $\Delta_{4\text{-}5}$ is not involved in the reaction and no incorporation takes place at $C_4$. The charge then migrates along the backbone from $C_{10}$ toward $C_{14}$ and the intermediate tertiary carbocations are in equillibrium with the corresponding trisubstituted olefins. The interconversion between $C_{10}^+$, $C_9^+$, $C_8^+$, and $C_{14}^+$ proceeds by 1,2 hydrogen shifts or by a protonation–deprotonation mechanism.[10] The migration of the $C_{18}$ methyl group from $C_{13}$ to $C_{14}$ should be energetically favored. The absence of deuterium incorporation at the allylic sites $C_{12}$ and $C_{16}$ is probably the result of the nature of the carbocation at $C_{13}$, which may be stabilized, under the reaction conditions, by resonance with the enolized ketone at $C_{20}$.[11]

**Registry No.** 1, 28840-94-0; 2, 24376-22-5.

(2) Frappier, F.; Khuong-Huu, Q.; Jarreau, F.-X. *Bull. Soc. Chim. Fr.* **1969**, 3265.
(3) Janot, M.-M.; Frappier, F.; Thierry, J.; Lukacs, G.; Jarreau, F.-X.; Goutarel, R. *Tetrahedron Lett.* **1972**, 3499.
(4) Hall, L. D.; Sanders, J. K. M.; Sukumar, S. *J. Chem. Soc., Chem. Commun.* **1980**, 366.
(5) Stothers, J. B. "Carbon-13 NMR Spectroscopy"; Academic Press: New York, 1972.
(6) Wehrli, F. W. *J. Chem. Soc., Chem. Commun.* **1973**, 379.
(7) Reich, H. J.; Jautelat, M.; Messe, M. T.; Weigert, F. J.; Roberts, J. D. *J. Am. Chem. Soc.* **1969**, *91*, 7445.
(8) In the $^{13}C$ NMR spectrum of 2-$d_x$ an upfield isotopic shift of 0.1–0.2 ppm was detected for $C_2$, $C_{12}$, and $C_{16}$ in agreement with the signal assignments.
(9) Labeling below 5% would not be detected by the technique used.
(10) Thierry, J.; Frappier, F.; Pais, M.; Jarreau, F.-X. *Tetrahedron Lett.* **1974**, 2149.
(11) Berthelot, J.-P.; Levisalles, J. *Bull. Soc. Chim. Fr.* **1971**, 1888.

**Francois Frappier**
*Laboratoire de Chimie Organique Biologique*
*Université Pierre et Marie Curie*
*75230 Paris, France*

**William E. Hull**
*Bruker-Physik AG.*
*Am Silberstreifen*
*D-7512 Rheinstetten-Fo., Germany*

**Gabor Lukacs***
*Institut de Chimie des Substances Naturelles*
*CNRS*
*91190 Gif-sur Yvette, France*

*Received April 9, 1981*