Summary

The mass spectra of 8,8-dicyanoheptafulvene and its derivatives, which are considered to belong to a non-benzenoid aromatic compound, were measured.

The high degree of aromaticity of 8,8-dicyanoheptafulvenes was made clear by mass spectrometry.

Low mass regions of dicyanoheptafulvene showed the elimination of hydrogen cyanide from parent ion and rearrangement to phenylpropiolonitrile ion.

The mass spectra of methoxy dicyanoheptafulvenes showed fragmentation quite different from that of 8,8-dicyanoheptafulvenes.

The structures and fragmentation processes of dicyanoheptafulvenes were discussed.

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130. Kazuo Tori, Yoshio Hamashima, and Akira Takamizawa : Nuclear Magnetic Resonance Studies of Bridged Ring Systems. V.*1 Signals of Methyl Groups in Bornane Derivatives.*2

(*Shionogi Research Laboratory, Shionogi & Co., Ltd.**3)

In recent years, many studies dealing with nuclear magnetic resonance (NMR) spectra of compounds having a bicyclo[2.2.1]heptane skeleton have been made in connection with their stereochemistry.[1~8] Kumler, *et al.*[1] investigated the spectra of some 3-halogenocamphors and assigned the three methyl signals on the bases of the magnetic anisotropy effects of the carbonyl group and halogen atoms, and the effect of freedom of rotation of the methyl groups which is reflected in sharpness (or the amplitude) of their signals. Wolinsky[9] also applied the downfield shift of a methyl signal due to the close approach of a bromine atom for structure estimation of α-bromoderivatives of 4,4-dimethylbicyclo[3.2.1]octan-2-one and 4,4-dimethylbicyclo[3.2.1]octan-3-one, inspecting the NMR spectra of several known compounds such as 3,3-dibromocamphor (XXX)

*1 Part V. K. Tori, K. Kitahonoki, Y. Takano, H. Tanida, T. Tsuji : Tetrahedron Letters, No. 11, 559 (1964).

*2 A part of this paper was delivered at "The 2nd Symposium on Nuclear Magnetic Resonance (Japan)," in Tokyo, November (1962).

*3 Fukushima-ku, Osaka (通 和夫, 浜島好男, 高見沢 映).

1) W. D. Kumler, J. N. Shoolery, F. V. Brutcher, Jr. : J. Am. Chem. Soc., **80**, 2533 (1958).
2) F. A. L. Anet : Cand. J. Chem., **39**, 789 (1961).
3) M. M. Anderson, P. M. Henry : Chem. & Ind. (London), **1961**, 2053.
4) H. E. Simmons : J. Am. Chem. Soc., **83**, 1657 (1961).
5) R. R. Fraser : Cand. J. Chem., **40**, 78 (1962).
6) J. I. Musher : Mol. Phys., **6**, 94 (1963).
7) J. Meinwald, Y. C. Meinwald, T. N. Baker, III : J. Am. Chem. Soc., **85**, 2513 (1963); J. Meinwald, Y. C. Meinwald : *Ibid.*, **85**, 2514 (1963).
8) E. I. Snyder, B. Franzus : *Ibid.*, **86**, 1166 (1964); P. Laszlo, P. von R. Schleyer : *Ibid.*, **86**, 1171 (1964) and references cited therein.
9) J. Wolinsky : J. Org. Chem., **26**, 704 (1961).

and 2-*exo*-bromobornane for comparison. On the other hand, an angular methyl signal in steroids is known to be shifted downfield when a substituent is introduced into a position 1,3-diaxial to the angular methyl group.[10~12] Further, the additivity principle for signal shifts of the angular methyl groups due to various functional groups has been well established.[10] On the basis of the NMR studies of many hydroxylated steroids, Kawazoe, *et al.*[11] have concluded that the spatial vicinity of a hydroxyl and a methyl group causes a marked downfield shift for the methyl signal and that acetylation of the hydroxyl group causes a characteristic upfield shift. They have also applied these findings to some other ring systems including 2-*endo*-hydroxybornane (borneol, Ⅲ) and 2-*exo*-hydroxybornane (isoborneol, Ⅳ)[13] and have also explained the positions of the methyl signals given by each of the four diastereoisomers of 2,3-dihydroxybornane reported by Anet,[2] who investigated the spectra of these four compounds to reveal the relation of spin-coupling constants to the stereochemistry of the bicyclo-[2.2.1]heptane system. More recently, having studied the spectra of many bornanes in carbon tetrachloride to discuss mainly the signals of protons on substituent-bearing carbon atoms in connection with the stereochemistry, Flautt and Erman[14] have also described the large downfield shift of one methyl signal due to some *exo*-substituents. However, we consider that these assignments of methyl groups in bornane derivatives are not clearly made, and hence much work will be required to establish the assignment. In this paper we present assignment of the three methyl signals of some derivatives of bornane (1,7,7-trimethylbicyclo[2.2.1]-heptane (I))*4 and camphor (1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (Ⅱ)) on much more reliable bases. Substituent effects on the methyl signals in bornanes are estimated and discussed briefly. Some other features of their spectra are described also.

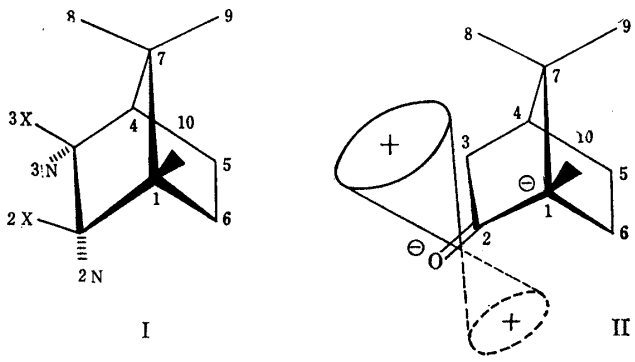


Chart 1.

Results and Discussion

All the compounds examined and their NMR spectral data are listed in Table I. In general, the spectra were analyzed by the first order treatment.

Assignment of the Spectra of Bornane Derivatives

The spectrum of I shows one sharp signal for the methyl groups at 9.17 τ in chloroform and at 9.21 τ in pyridine, as predicted by Kumler, *et al.*[1] In general, most of the 2-*exo*-substituted bornanes examined show three distinct signals for their methyl groups, one of which gives a sharp signal characteristic of a less hindered methyl

*4 The protons H_{endo} and H_{exo} are abbreviated to H_N and H_X, respectively.

10) For example, see R. F. Zürcher : Helv. Chim. Acta, **44**, 1380 (1961); *Idem* : *Ibid.*, **46**, 2054 (1963); J. C. Jacquesy, J. M. Lehn, J. Levisalles : Bull. soc. chim. France, **1961**, 2444.
11) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, K. Tsuda : This Bulletin, **10**, 338 (1962).
12) K. Tori, K. Kuriyama : Chem. & Ind. (London), **1963**, 1525.
13) T. Okamoto, Y. Kawazoe : This Bulletin, **11**, 643 (1963); Y. Kawazoe : presented at "The 16th Annual Meeting of Pharm. Soc. Japan," at Shizuoka, November (1962).
14) T. J. Flautt, W. F. Erman : J. Am. Chem. Soc., **85**,3212 (1963); and also refer to W. F. Erman, T. J. Flautt : J. Org. Chem., **27**, 1526 (1962).

TABLE I. Nuclear Magnetic Resonance Spectral Data on Bornane, Camphor and their Derivatives[a)]

No.	Compd.	Chemical shift (τ) 10-H	9-H	8-H	4-H	3-H	2-H	other H	Coupling constant J (c.p.s.)
I	Bornane[b)]	9.17 (9.21)	9.17 (9.21)	9.17 (9.21)					
II	Camphor[c)]	9.02 (9.19) [9.35]	9.08 (9.10) [9.12]	9.15 (9.28) [9.40]		$\begin{cases}8.21_{(N)}\,^{d}\\7.61_{(X)}\,^{d-q}\end{cases}$ $\left(\begin{matrix}8.26_{(N)}\,^{d}\\7.66_{(X)}\,^{d-q}\end{matrix}\right)$			$\begin{cases}\lvert J_{3N,3X}\rvert=18.0\\J_{3X,4}=4.2\\J_{3X,5X}=2.6\end{cases}$
III	2-*endo*-Hydroxybornane[c)] (Borneol)	9.15 (9.02) [9.15]	9.14 (9.13) [9.25]	9.14 (9.13) [9.22]			5.98 d-q (5.76) d-q [6.18]		$\begin{cases}J_{2X,3X}=10.0\\J_{2X,3N}=3.8\\J_{2X,6X}=1.8\end{cases}$
IV	2-*exo*-Hydroxybornane[d)] (Isoborneol)	9.11 (8.93) [9.17]	9.17 (9.15) [9.25]	8.98 (8.72) [8.89]			6.39 t? (6.15) q [6.62]		$\begin{cases}(J_{2N,3N}=7.4)\\(J_{2N,3X}=4.0)\\(J_{2N,6N}\sim 0)\end{cases}$
V	2-*exo*,9-Dihydroxybornane[e)]	9.03 (8.77)	$\begin{cases}6.58^{d}\\6.38^{d}\end{cases}$ $\left(\begin{matrix}6.33^{d}\\6.13^{d}\end{matrix}\right)$	8.83 (8.36)			6.38 t? (6.15) q		$\lvert J_{9,9'}\rvert=10.5$
VI	2-*exo*,10-Dihydroxybornane[f)]	$\begin{cases}6.29^{d}\\6.05^{d}\end{cases}$ $\left(\begin{matrix}5.98^{d}\\5.70^{d}\end{matrix}\right)$	9.11 (9.03)	8.82 (8.57)			6.02 t? (5.70) q		$\begin{cases}\lvert J_{10,10'}\rvert=10.5\\(J_{2N,3N}=7.5)\\(J_{2N,3X}=3.8)\end{cases}$
VII	2-*endo*-Acetoxybornane[e)]	9.17	9.13	9.09			5.08 d-q	OAc 7.95	$\begin{cases}J_{2X,3X}=9.8\\J_{2X,3N}=3.6\\J_{2X,6X}=1.8\end{cases}$
VIII	2-*exo*-Acetoxybornane[e)]	9.16	9.16	9.01			5.31 t?	OAc 7.98	
IX	2-*endo*-Chlorobornane[g)]	9.13	9.13	9.07			5.83 d-q		$\begin{cases}J_{2X,3X}=10.5\\J_{2X,3N}=4.0\\J_{2X,6X}=1.9\end{cases}$
X	2-*exo*-Chlorobornane[h)]	9.00	9.13	8.90			6.03 q		$\begin{cases}J_{2N,3N}=7.9\\J_{2N,3X}=5.0\\J_{2N,6N}\sim 0\end{cases}$
XI	2-*endo*-Hydroxy-3-*endo*-aminobornane[i)]	9.14 (9.06)	9.10 (9.14)	9.10 (9.14)		6.52 n (6.48) m	6.41 m (6.07) d		$(J_{2X,3X}\sim 9)$
XII	2-*exo*-Hydroxy-3-*endo*-aminobornane[j)]	9.15 (8.97)	9.15 (9.14)	8.94 (8.70)		6.54 m (6.30) m	6.94 d (6.59) d		$J_{2N,3X}=3.4$
XIII	2-*endo*-Hydroxy-3-*endo*-methylaminobornane[k)]	9.14 (9.05)	9.10 (9.12)	9.10 (9.12)		7.00 q-d (6.93) q-d	6.30 d-d (6.02) d-d	NMe 7.65 (7.62)	$\begin{cases}J_{2X,3X}=9.2\\J_{2X,6X}=1.4\\J_{3X,4}=4.0\\J_{3X,5X}=1.0\end{cases}$

XIV	2-*exo*-Hydroxy-3-*endo*-methylaminobornane[l]	9.15 (8.97)	9.15 (9.12)	8.93 (8.68)		6.95 t (6.65) t	6.91 d (6.57) d	NMe 7.65 (7.57)	$J_{2N,3X}$ = 3.2 $J_{3X,5X}$ ~ 1
XV	2-*endo*-Hydroxy-3-*endo*-acetamidobornane[m]	9.14 (9.07)	9.09 (9.14)	9.06 (9.09)		5.81 q-q (5.33) q-q-d	6.04 d-d (5.78) d-d	NAc 7.98 (7.99) NH 3.66 d	($J_{2X,3X}$ =10.0) ($J_{2X,6X}$ ~ 1) ($J_{3X,4}$ = 3.8) ($J_{3X,5X}$ ~ 1) ($J_{3X,NH}$ = 6.4)
XVI	2-*exo*-Hydroxy-3-*endo*-acetamidobornane[n]	9.09 (8.96)	9.12 (9.16)	8.85 (8.65)		6.02 d-t-d (5.25) t-d	6.72 d (6.58) d	NAc 7.97 (7.95) NH 4.00 d	$J_{2N,3X}$ = 3.4 $J_{3X,5X}$ ~ 1
XVII	2-*endo*-Acetoxy-3-*endo*-acetamidobornane[o]	9.17 (9.20)	9.07 (9.20)	8.96 (9.10)		5.45 q-q-d (4.94) q-q-d	4.85 d-d (4.64) d-d	OAc 8.00 (7.90) NAc 7.87 (7.90) NH 4.23 d	$J_{2X,3X}$ =10.0 $J_{2X,6X}$ = 1.4 $J_{3X,4}$ = 4.0 $J_{3X,5X}$ ~ 1 $J_{3X,NH}$ = 7.5
XVIII	2-*exo*-Acetoxy-3-*endo*-acetamidobornane[p]	9.18 (9.21)	9.11 (9.19)	8.90 (8.85)		5.68 d-t-d (5.08) t-d	5.54 d (5.03) d	OAc 8.03 (8.00) NAc 7.94 (7.96) NH 3.65 d	$J_{2N,3X}$ = 4.0 $J_{3X,4}$ = 4.0 $J_{3X,5X}$ ~ 1 $J_{3X,NH}$ = 6.5
XIX	9-Hydroxycamphor[q]	9.03 (8.92)	6.49 d 6.27 d (6.36 d 6.14 d)	9.03 (8.92)					$\lvert J_{9,9'}\rvert$ =11.0
XX	10-Hydroxycamphor[q]	6.32 d 6.12 d (5.94)	8.97 (8.91)	9.01 (8.99)					$\lvert J_{10,10'}\rvert$ =11.7
XXI	9-Acetoxycamphor[q]	8.85	6.00 d 5.81 d	8.88				OAc 7.90	$\lvert J_{9,9'}\rvert$ =11.0
XXII	10-Acetoxycamphor[q]	5.73	8.94	9.01				OAc 7.96	
XXIII	9-Bromocamphor[q]	9.03	6.75 d 6.39 d-q	9.01					$\lvert J_{9,9'}\rvert$ =10.6 $J_{8,9}$ = 0.9
XXIV	10-Bromocamphor[q]	6.59 d 6.37 d	8.90	9.07	7.47 t				$\lvert J_{10,10'}\rvert$ =11.0
XXV	2-Hydroxyiminobornane[r]	9.08	8.99	9.17		8.21$_{(N)}$ d 7.61$_{(X)}$ d-q			$\lvert J_{3N,3X}\rvert$ =18.0 $J_{3X,4}$ = 4.0

XXVI	Camphorquinone (Bornan-2,3-dione)[s]	8.93	8.90	9.06	7.36 q			$\begin{cases} J_{4,5X} = 4.3 \\ J_{4,5N} = 1.2 \end{cases}$
XXVII	3-Hydroxyiminocamphor[t]	9.00	8.98	9.12	6.70 q			$\begin{cases} J_{4,5X} = 3.8 \\ J_{4,5N} = 1.0 \end{cases}$
XXVIII	3-*endo*-Chlorocamphor[u]	8.93	9.03	9.07	7.66 m	5.73 q		$\begin{cases} J_{3X,4} = 4.5 \\ J_{3X,5X} = 0.6 \end{cases}$
XXIX	3-*endo*-Bromocamphor[u]	8.91	9.04	9.06	7.70 t-d	5.36 q		$\begin{cases} J_{3X,4}=J_{4,5X}=4.5 \\ J_{3X,5X} = 1.0 \\ J_{4,5N} = 1.0 \end{cases}$
XXX	3,3-Dibromocamphor[v]	8.88	8.98	8.75	7.10 d			$J_{4,5X} = 3.2$
XXXI	3-*endo*-Methylaminocamphor[s]	8.98	9.08	9.10	7.81 t-d	6.78 q	NMe 7.68	$\begin{cases} J_{3X,4}=J_{4,5X}=4.5 \\ J_{3X,5X} = 1.0 \\ J_{4,5N} = 1.0 \end{cases}$
XXXII	3-*endo*-Methylamino-9-hydroxycamphor[k]	9.03	$\begin{cases} 6.45\,d \\ 6.19\,d \end{cases}$	8.97	7.50 t-d	6.81 q	NMe 7.58	$\begin{cases} J_{3X,4}=J_{4,5X}=4.5 \\ J_{3X,5X} = 0.8 \\ J_{4,5N} = 1.0 \\ \lvert J_{9,9'}\rvert = 11.0 \end{cases}$

a) All the data are observed in $CHCl_3$. Values in parentheses are the data observed in pyridine. Values in square brackets are the data observed in benzene. d: doublet, t: triplet, q: quartet, m: multiplet (for example, t-d represents a tripling doublet signals).
b) L. Wolff: Ann., **394**, 86 (1912).
c) Commercially available.
d) L.W. Trevoy, W.G. Brown: J. Am. Chem. Soc., **71**, 1675 (1949).
e) Prepared by reduction of XIX with $NaBH_4$, m.p. 228°.
f) Prepared by reduction of XX with $NaBH_4$, m.p. 232~235°.
g) G.B. Frankforter, F.C. Frary: J. Am. Chem. Soc., **28**, 1461 (1906).
h) J. Kachler: Ann., **197**; 86 (1879); A. Reychler: Ber., **29**, 697 (1896).
i) E.E. van Tamelen, C.I, Judd: J. Am. Chem. Soc., **80**, 6305 (1958).
j) E.E. van Tamelen, W.F. Jousignant, P.E. Peckhan: *Ibid.*, **75**, 1297 (1953).
k) T. Takahashi, H. Fujimura, Y. Hamashima: Yakugaku Zasshi, **84**, 588 (1964).
l) Prepared by reduction of 2-*exo*-hydroxy-3-formamidobornane derived from XII m.p. 65~66°. See ref. 25).
m) Prepared by acetylation of XI in Et_2O, m.p. 124°.
n) Prepared by acetylation of XII in Et_2O, m.p. 184°.
o) Prepared by acetylation of XV at 100°, m.p. 141°.
p) Prepared by acetylation of XVI at 100°, colorless syrup, b.$p_{1.5}$ 148°.
q) K. Sahashi, T. Iki: J. Agric. Chem. Soc. Japan, **10**, 873 (1933).
r) E. Nägeli: Ber., **16**, 494 (1883).
s) H. Rupe, A.T. di Vignano: Helv. Chim. Acta, **20**, 1078 (1937).
t) M.O. Forster: J. Chem. Soc., **83**, 514 (1903).
u) F.S.Kipping, W.J. Pope: *Ibid.*, **63**, 548 (1893),
v) T.M. Lowry: *Ibid.*, **73**, 569 (1898).

group.[1] A broader methyl signal at a relatively lower field in the spectra of 2-*exo*-substituted bornanes can be assigned to the 8-methyl group on the basis of the conclusion of Kawazoe, *et al.*[11,13] However, assignment of the other two signals is somewhat difficult. As shown in Fig. 1, the spectrum of 2-*exo*, 9-dihydroxybornane (V) gives

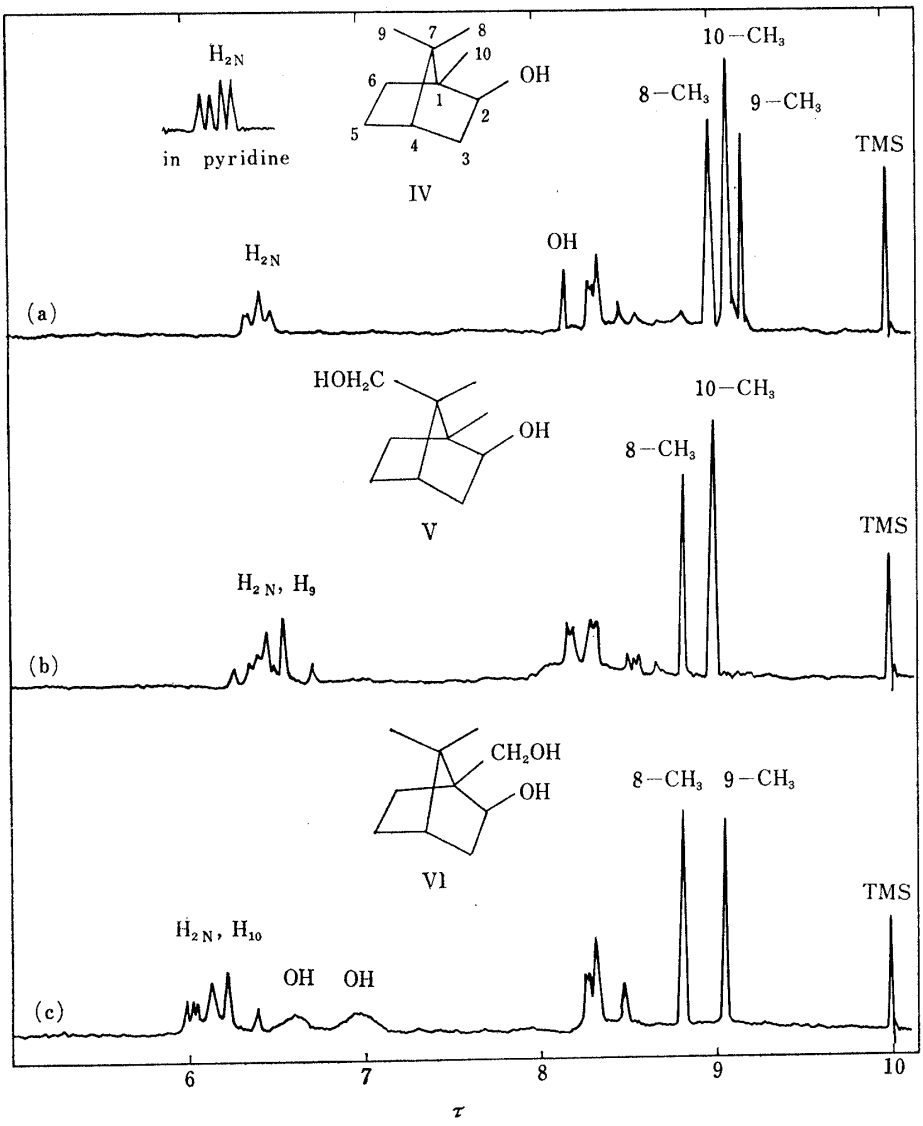


Fig. 1. Nuclear Magnetic Resonance Spectra of 2-*exo*-Hydroxybornane (Ⅳ), 2-*exo*, 9-Dihydroxybornane (V), and 2-*exo*, 10-Dihydroxybornane (Ⅵ) in Chloroform at 60 Mc.p.s.

two methyl signals, the one at a higher field having a greater amplitude than the other, whereas the spectrum of 2-*exo*,10-dihydroxybornane (Ⅵ) shows two methyl signals of an equal amplitude. These observations show that the sharpest methyl signal at 9.11 τ and the methyl signal at a field lower than the other two (8.98 τ) in Ⅳ are due to the 10- and 8-methyl groups, respectively. This result is consistent with that reached by Wolinsky[9] who examined 2-*exo*-bromobornane. The spectra of Ⅳ, V, and Ⅵ observed in pyridine are essentially the same as when observed in chloroform. However, the signals of the 8- and 10-methyl groups are shifted markedly to lower fields, whereas the signal of the 9-methyl group is shifted slightly. Such a large downfield shift of a methyl group in pyridine is usually seen when the methyl group and a hydroxyl

group are located closely in a molecule.[14,15] This finding is believed to be useful for assigning the methyl signals exhibited by 2-*exo*-hydroxybornane derivatives. For example, the spectrum of 2-*exo*-hydroxy-3-*endo*-aminobornane (XII) shows only two methyl signals in chloroform; the signal at 8.93 τ corresponds to one methyl group and the other at 9.15 τ to two methyl groups. In the spectrum of XII in pyridine, these methyl signals are found well-separated at 8.70, 8.97, and 9.14 τ, and accordingly are assigned to the 8-, 10-, and 9-methyl groups, respectively. In addition, the 10-methyl signal at 8.97 τ has the greatest amplitude as expected. The methyl signals given by other bornane derivatives having a 2-*exo*-substituent were assigned in a similar manner.

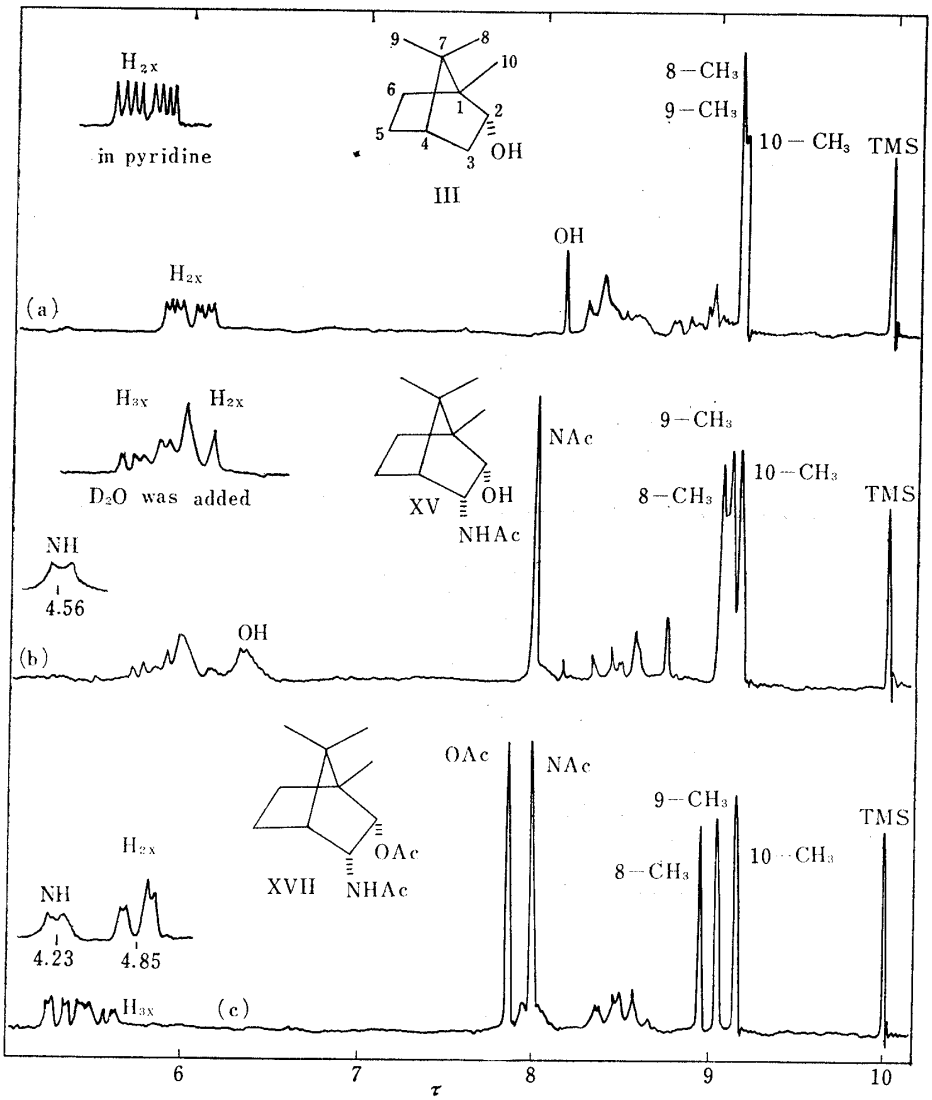


Fig. 2. Nuclear Magnetic Resonance Spectra of 2-*endo*-Hydroxybornane (III), 2-*endo*-Hydroxy-3-*endo*-acetamidobornane (XV), and 2-*endo*-Acetoxy-3-*endo*-acetamidobornane (XVII) in Chloroform at 60 Mc.p.s.

The spectrum of III in chloroform exhibits an almost single peak for the methyl signals as shown in Fig. 2(a). In contrast, the spectrum of 2-*endo*-hydroxy-3-*endo*-acetamidobornane (XV) in chloroform shows three peaks for the methyl groups, one of

15) Refer to N. Nakagawa, S. Tsuji, M. Onishi: presented at "The 16th Annual Meeting of Chem. Soc. Japan," in Tokyo, April (1963); G. Slomp, F. McKellar: J. Am. Chem. Soc., 82, 999 (1960).

which gives the sharper signal at 9.14 τ assignable to the 10-methyl group (Fig. 2 (b)). Further, in the spectrum of XV in pyridine, the 10-methyl signal is shifted downfield (9.07 τ), whereas the other two methyl signals are slightly shifted upfield. The solvent effect of pyridine appears to exert the downfield shift only on the 10-methyl signal. Thus the methyl signal at the lower field in the spectrum of III in pyridine can be assigned to the 10-methyl group. In the spectra of 2-*endo*-hydroxy-3-*endo*-aminobornane (XI) and 2-*endo*-hydroxy-3-*endo*-methylaminobornane (XIII), the methyl signal at the highest field in chloroform which moves to a lower field in pyridine was assigned to the 10-methyl group. These results also support the assignment for the methyl signals of III in carbon tetrachloride made by Tiers.[16] The methyl groups of other 2-*endo*-substituted bornanes were assigned in a similar manner.

Other signal assignments in the spectra of bornane derivatives of III~XVIII were carried out in the usual way. In general, the signal of the bridgehead proton H_4 is obscured by other signals. In regard to signal patterns and coupling constants of protons on the substituent-bearing C_2- and C_3-atoms, we obtained results similar to those reported by other workers.[2,6,14] The proton H_{2N} of 2-*exo*-chlorobornane (X) shows its signal as a distinct quartet which is easily analyzed by the first order treatment. This is also the case with the signal of the proton H_{2N} of IV in pyridine, which appears as a second order pattern of the X part of an ABX system in chloroform[6,14] (see Fig. 1 (a)). As has been observed frequently,[12,17] the CONH proton of 3-*endo*-acetamido group is coupled with the proton H_{3X}. In Figs. 2 (b) and (c) are shown typical examples of this coupling. This spin coupling was removed by addition of a small amount of deuterium oxide to the solutions examined.[18]

Assignment of the Spectra of Camphor Derivatives

The spectrum of II in chloroform shows one sharp and two broader signals for the methyl groups, as shown in Fig. 3 (a). Kumler, *et al.*[1] reported that the former signal and the lower field signal of the latter arise respectively from the 9- and 10-methyl groups. The spectrum of XXX also exhibits one sharp and two hindered-methyl signals, implying that one of the hindered-methyl signals can be assigned to the 8-methyl group because of the close approach of the 3-*exo*-bromine atom as described by Kumler, *et al.*[1] To establish the assignment of the methyl groups in camphor derivatives, we measured the spectra of 10-substituted camphors. The spectra of 10-hydroxy-, 10-acetoxy-, and 10-bromocamphors (XX, XXII, and XXIV) show two signals with a greater and a smaller amplitude for the methyl groups. Thus all the three methyl signals in II were assigned as shown in Fig. 3 (a). These assignments are consistent with those reported by Kumler, *et al.*[1] and Wolinsky.[9] Then the 9-methyl group in camphors was revealed to give the sharpest signal in contrast to the case of bornanes. Further, it should be noted that the 10-methylene signal in XX appears as an AB-type quartet whereas that in XXII appears as a singlet. The former fact can be ascribed to the hydrogen-bonding between the 10-hydroxyl and the 2-carbonyl group because the AB-type quartet in XX turns into a singlet in pyridine. The spectra of 9-hydroxy-, 9-acetoxy-, and 9-bromocamphors (XXI, XXIII, and XXV) show an AB-type quartet for the 9-methylene groups, whose lower field half peaks are broadened or further split into quartets. On the other hand, the 8-methyl signals of these compounds are somewhat broadened (in XXI and XXIII) or split

16) G. V. D. Tiers: "Characteristic Nuclear Magnetic Resonance *Shielding Values* for Hydrogen in Organic Structures," Minnesota Mining & Manufacturing Co., St. Paul, Minn. (1958).
17) For example, see H. S. Gutowsky, C. H. Holm: J. Chem. Phys., **25**, 1228 (1957); K. Tori: Ann. Rept. Shionogi Research Lab., **12**, 114 (1962).
18) H. M. Fales, A. V. Robertson: Tetrahedron Letters, No. 3, 111 (1962).

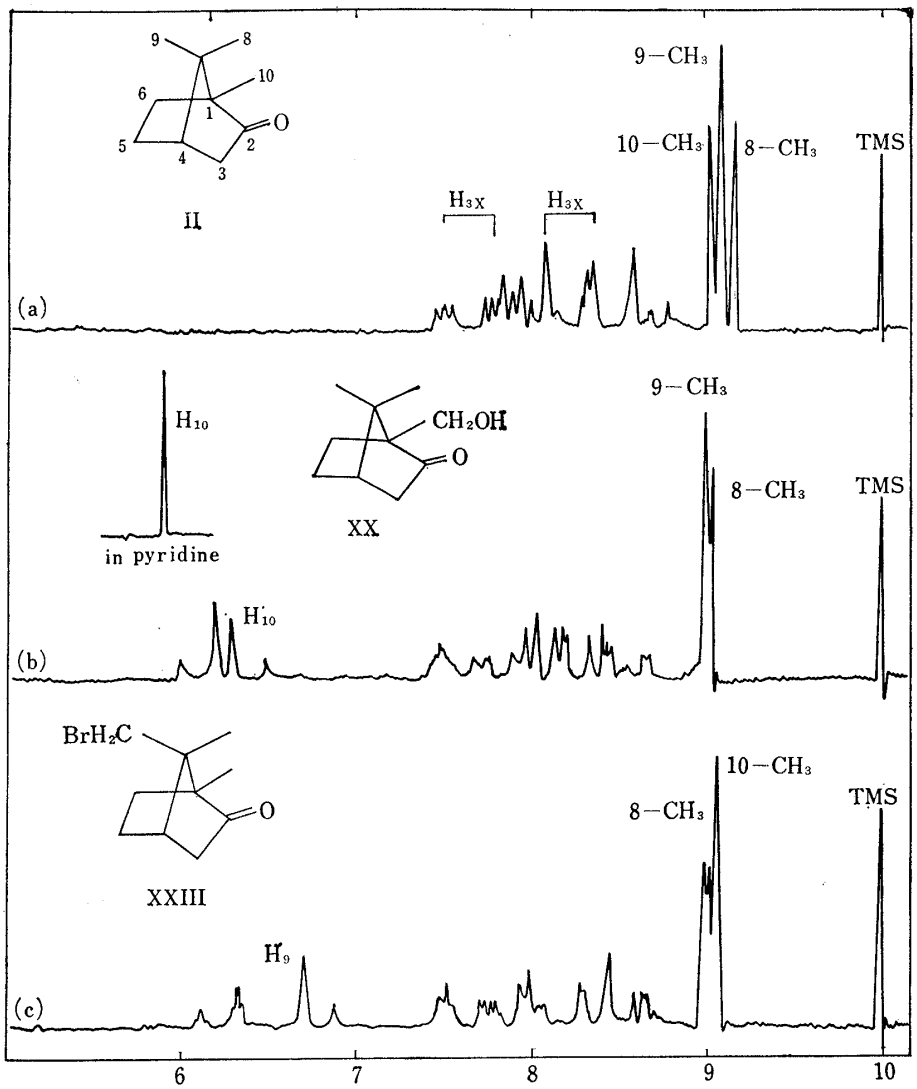


Fig. 3. Nuclear Magnetic Resonance Spectra of Camphor (II), 10-Hydroxycamphor (XX), and 9-Bromocamphor (XXIII) in Chloroform at 60 Mc.p.s.

into a doublet (in XXV shown in Fig. 3 (c)), indicating the long-range spin coupling between the 8-methyl and the 9-methylene group.[19] Therefore, the spectra of XXI, XXIII, and XXV could not be used for assignments of the methyl signals.

Other signal assignments in the spectra of camphor derivatives of XIX~XXXII were made in the usual way. In the case of 3-substituted camphors, the signal of the bridgehead proton H_4 appears separated.[14,20] The protons H_{3N} and H_{3X} in II and XXV were tentatively assigned to the AB-type quartet, whose peaks in the lower field are further split into quartets, as shown in Fig. 3 (a).

Other NMR features except for the methyl signals in all the compounds examined are consistent with those already reported by other workers.[1,2,6,14] Thus we will discuss only the methyl signals in the following sections.

19) D. R. Davis, R. P. Lutz, J. D. Roberts : J. Am. Chem. Soc., 83, 246 (1961); D. R. Davis, J. D. Roberts : *Ibid.*, 84, 2252 (1962).
20) Refer to S. L. Manatt, D. D. Elleman : *Ibid.*, 83, 4095 (1961).

Table II. Substituent Effects on the Chemical Shifts of Methyl Groups in Bornanes, in p.p.m.[a)]

Substituent	Compounds to be compared	8-H	9-H	10-H
2-*endo*-OH	I～III	−0.03	−0.03	−0.02
		−0.04[b)]	−0.04[b)]	−0.01[b)]
		(−0.08)	(−0.08)	(−0.19)
2-*exo*-OH	I～IV	−0.19	0.00	−0.06
		−0.20[b)]	−0.01[b)]	−0.07[b)]
		(−0.50)	(−0.06)	(−0.28)
2-*endo*-OAc	I～VII	−0.08	−0.04	0.00
		−0.11[b)]	−0.05[b)]	+0.01[b)]
2-*exo*-OAc	I～VIII	−0.16	−0.01	−0.01
		−0.16[b)]	−0.01[b)]	−0.01[b)]
2-*endo*-Cl	I～IX	−0.10	−0.04	−0.04
		−0.12[b)]	−0.07[b)]	−0.08[b)]
2-*exo*-Cl	I～X	−0.27	−0.04	−0.17
		−0.29[b)]	−0.05[b)]	−0.20[b)]
2-*exo*-Br	I～2-*exo*-bromobornane[c)]	−0.31[c)]	−0.04[c)]	−0.18[c)]
2-*endo*-(p-HO·C_6H_4)	I～XXXIII[b)]	−0.20[b)]	−0.11[b)]	+0.12[b)]
2-*exo*-(p-HO·C_6H_4)	I～XXXIV[b)]	+0.10[b)]	+0.01[b)]	+0.01[b)]
2-*endo*-OC_6H_5	I～XXXV[b)]	−0.10[b)]	−0.10[b)]	−0.10[b)]
2-*exo*-OC_6H_5	I～XXXVI[b)]	−0.23[b)]	−0.04[b)]	−0.16[b)]
2-C=O	I～II	−0.02	−0.09	−0.12
		(+0.07)	(−0.11)	(−0.03)
2-C=NOH	I～XXV	0.00	−0.18	−0.09
3-*endo*-Cl	II～XXVIII	−0.08	−0.05	−0.09
3-*exo*-Cl	II～3-*exo*-chlorocamphor[d)]	−0.13[d)]	−0.13[d)]	−0.18[d)]
3-*endo*-Br	II～XXIX	−0.09	−0.04	−0.11
		−0.13[d)]	−0.13[d)]	−0.20[d)]
3-*exo*-Br	XXIX～XXX	−0.31	−0.06	−0.03
		−0.30[c,d)]	−0.07[c,d)]	−0.03[c,d)]
3-*endo*-NH_2	III～XI	−0.04	−0.04	−0.01
		(+0.01)	(+0.01)	(+0.04)
	IV～XII	−0.04	−0.02	+0.04
		(−0.02)	(−0.01)	(+0.04)
3-*endo*-NHMe	III～XIII	−0.04	−0.04	−0.01
		(−0.01)	(−0.01)	(+0.03)
	IV～XIV	−0.05	−0.02	+0.04
		(−0.04)	(−0.03)	(+0.04)
	II～XXXI	−0.05	0.00	−0.04
	XIX～XXXII	−0.06		0.00
3-*endo*-NHAc	III～XV	−0.08	−0.05	−0.01
		(−0.04)	(+0.01)	(+0.05)
	IV～XVI	−0.13	−0.05	−0.02
		(−0.07)	(+0.01)	(+0.03)
	VII～XVII	−0.13	−0.06	0.00
	VIII～XVIII	−0.11	−0.05	+0.02
3-C=O	II～XXVI	−0.09	−0.18	−0.07
3-C=NOH	II～XXVII	−0.03	−0.10	−0.02

9-OH	Ⅳ～Ⅴ	−0.15 (−0.36)		−0.08 (−0.16)
	Ⅱ～XIX	−0.12		+0.01
	XXXI～XXXⅡ	−0.13		+0.05
9-OAc	Ⅱ～XXI	−0.27		−0.17
9-Br	Ⅱ～XXⅢ	−0.14		+0.01
10-OH	Ⅳ～Ⅵ	−0.16 (−0.15)	−0.06 (−0.12)	
	Ⅱ～XX	−0.14	−0.11	
10-OAc	Ⅱ～XXⅡ	−0.14	−0.14	
10-Br	Ⅱ～XXIV	−0.08	−0.18	
2-*endo*-O, 3-*endo*-N(Me)–C=O	I～XXXVⅡ[25]	−0.14	−0.10	−0.13
2-*exo*-O, 3-*exo*-N(Me)–C=O	I～XXXVⅢ[25]	−0.08 or −0.14	−0.14 or −0.08	−0.20

a) Displacement of the signal positions in $CHCl_3$ due to introduction of a substituent into a bornane skeleton. Plus sign represents an upfield shift. Values in parentheses are the shift values observed in pyridine.
b) Values derived from the data observed in CCl_4 by Flautt and Erman.[14]
c) Values derived from the data observed in CCl_4 by Wolinsky.*5,9
d) Values derived from the data observed in CCl_4 by Kumler, *et al.**5,11

Substituent Effects on the Chemical Shifts of Methyl Groups

Table Ⅱ summarizes some substituent effects on the chemical shifts of the methyl groups derived from the data in Table Ⅰ and in the literature.*5,1,9,14)

As indicated in Table Ⅱ, signal shifts of the methyl groups due to shielding by some functional groups appear to hold an additivity principle. In steroids, this principle for the angular methyl groups has been well established.[10] However, it has become apparent that when conformational changes of rings occur, this additivity principle can be no longer valid because a change in the spatial relation of a substituent to a methyl group will generally lead to a different shielding effect on the methyl group.[21] Especially, when a group possessing strong diamagnetic anisotropy such as a carbonyl group is present in the ring, considerable caution must be exercised.[22] Therefore, the shielding values of the methyl groups by substituents may vary depending on the skeleton, either bornane or camphor, to which they are attached. However, no substantial difference in the shielding effect between both series was observed, as seen from Table Ⅱ, except for a little difference in the shielding of the 10-methyl group. An *exo*-substituent has a special feature for shielding of the 8-methyl group, which is remarkably less shielded than the others by an *exo*-substituent. This phenomenon is understood from the fact that the spatial relation of the 8-methyl group to an *exo*-substituent is 1,3-diaxial-like, as quoted by Kawazoe, *et al.*[11] The observed shift values of the 8-methyl group due to a 2-*exo*-hydroxyl, a 2-*exo*-acetoxyl, a 2-*exo*-chlorine, and a 2-*exo*- or a 3-*exo*-bromine are about −0.20, −0.16, −0.27, and −0.31 p.p.m., respectively. These

*5 To convert the available NMR information to values relative to a common internal reference (TMS), we have taken $\delta_{TMS\text{-}benzene}=6.45$ p.p.m. from comparison of the data on XXX observed by us with those of the different workers.[1,9]

21) A. D. Cross : J. Am. Chem. Soc., 84, 3206 (1962); K. Tori, T. Komeno : Tetrahedron to be published.

22) A. D. Cross, I. T. Harrison : J. Am. Chem. Soc., 85, 3223 (1963).

values are of a similar order of magnitude to the observed angular methyl shifts due to 1,3-diaxial substituents in steroids. For example, the values of the 19-methyl shifts due to a 6β-hydroxyl, a 6β-acetoxyl, a 6β-chlorine, and a 6β-bromine were reported to be about −0.23, −0.18, −0.32, and −0.26 p.p.m., respectively.[10] These large shift values have generally been ascribed to the diamagnetic anisotropy, the bond dipole effect and the steric interaction of a substituent,[10~12,22,23] although a clear explanation has not been made so far. The effects of a carbonyl and a hydroxyimino group are readily explained as their anisotropic shielding effects,[24] as shown in Chart 1: the 10-methyl group is most deshielded and the 8-methyl group is most shielded in II.

Recently, some interesting NMR data on many phenyl-substituted bornanes have been reported by Flautt and Erman,[14] though they did not assign the methyl signals. Hence, from the reported data we have tentatively assigned the methyl signals of *p*-bornylphenol (XXXIII), *p*-isobornylphenol (XXXIV), bornyl phenyl ether (XXXV), and isobornyl phenyl ether (XXXVI) (see Chart 2) as typical examples, and have given the shift

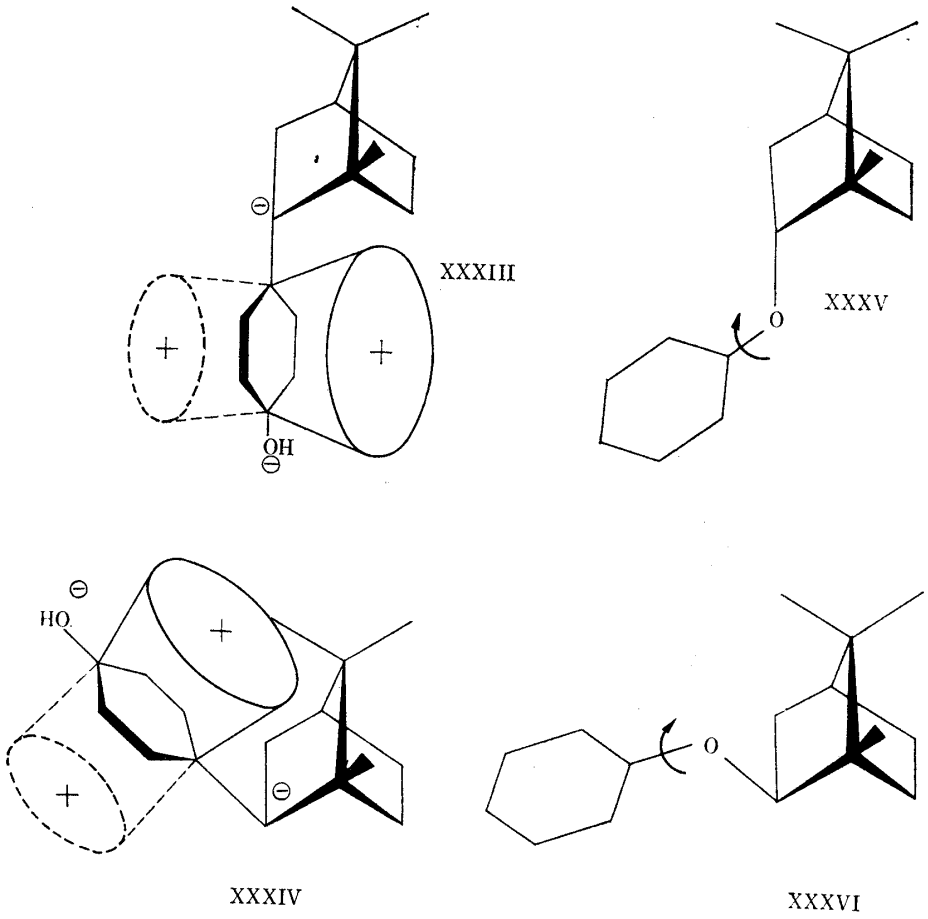


Chart 2.

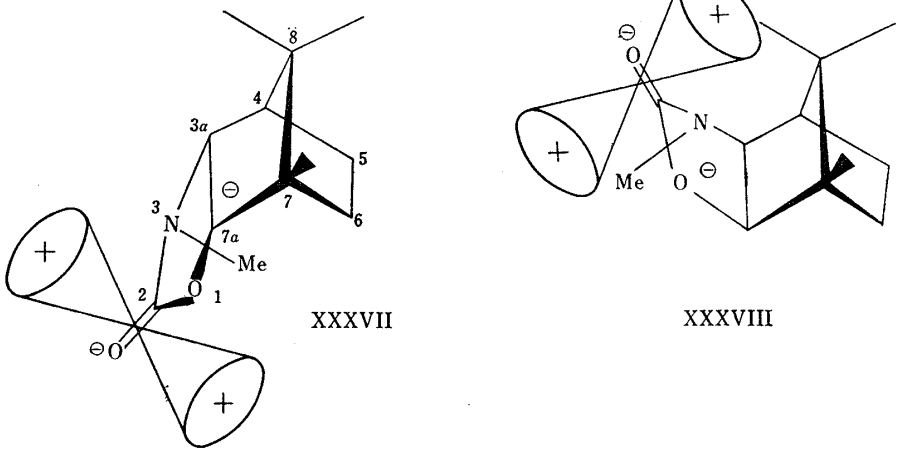
values due to the *p*-hydroxyphenyl and phenoxyl substituents in Table II. The shielding effect of a benzene ring is well known as the ring current effect.[24] An examination of Dreiding models*[6] shows that the 2-*endo*-*p*-hydroxyphenyl group in XXXIII can not

*[6] In Dreiding models, a "tetravalent carbon for a four membered-ring" was utilized for the C_7-atom in bornane skeleton for convenience.

23) W. Nagata, T. Terasawa, K. Tori: J. Am. Chem. Soc., 86 (1964), in press.
24) L. M. Jackman: "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Chap. 7 (1959), Pergamon Press, New York, N. Y.

freely rotate around the C_2–ϕ bond. Therefore, the shielding effect of the 2-*endo*-*p*-hydroxyphenyl group is qualitatively consistent with that anticipated from the Dreiding models. Interestingly, the 2-*exo*-*p*-hydroxyphenyl group in XXXIV is face to face with the 8-methyl group, as shown in Chart 2. In this situation, the 8-methyl group is highly shielded by the benzene ring, and accordingly the shift value of +0.10 p.p.m. is very reasonable. On the other hand, the 2-*endo*- and 2-*exo*-phenoxyl groups produce effects similar to those of other substituents upon the methyl groups in XXXV and XXXVI, as given in Table II. Dreiding models*[6] show that the phenoxyl group can freely rotate around the O–ϕ bond, but not around the C_2–O bond in XXXV and XXXVI as shown in Chart 2. Therefore, the benzene ring of the 2-*exo*-phenoxyl group in XXXVI is situated at a position where it has less shielding effects on the methyl groups, whereas the effects of the 2-*endo*-phenoxyl group are relatively small, as expected. The other data on the methyl groups in phenyl substituted bornane derivatives described by Flautt and Erman[14] can be explained by the above concept.

We have recently synthesized 3-methyl-3*a*-*exo*, 7*a*-*exo*-bornano[3,2-*d*]oxazolidin-2-one (XXXVII) and 3-methyl-3*a*-*endo*, 7*a*-*endo*-bornano[3,2-*d*]oxazolidin-2-one (XXXVIII) (see Chart 3) whose structures were confirmed from the NMR signals of their protons H_{3a} and H_{7a}.[25] The shift values of the methyl signals due to the oxazolidinone group are given in Table II. Although assignment of the 8- and 9-methyl groups in XXXVIII can not be made, a fairly small value should be obtained for the 8-methyl shift produced by the *exo*-oxazolidinone group in XXXVIII, as compared with other *exo*-substituents. A plausible explanation for this small shift is that the carbonyl group in the *exo*-oxazolidinone ring exerts a strong shielding effect on the 8-methyl group, as illustrated in Chart 3,[24] and this can decrease the deshielding effects due to the 2-*exo*-oxygen and 3-*exo*-nitrogen atoms.



XXXVII XXXVIII

Chart 3.

Thus considerable caution must be taken when estimating the configuration of a substituent which involves a group having a powerful anisotropy, such as a carbonyl or a benzene ring, from the methyl signals.

Solvent Effect on the Chemical Shifts of the Methyl Groups

As described earlier, considerable changes in the signal positions of the methyl groups in hydroxy derivatives of bornanes are caused by altering the solvent from

25) Y. Hamashima, K. Tori, A. Takamizawa : to be published.

chloroform or carbon tetrachloride to pyridine or benzene. As seen from Tables I and II, the signal of a methyl group closely situated to a hydroxyl group is shifted to a lower field in pyridine,[14,15,26] whereas most of the methyl signals move to higher fields in benzene.[15] This solvent effect of pyridine is due probably to the hydrogen-bonding between the hydroxyl group and a pyridine molecule, which can exert a deshielding effect on neighboring protons.[14,15,26] On the other hand, the methyl signals in II are shifted to higher fields in pyridine and benzene. Such phenomenon was usually ascertained when a carbonyl group is present in a molecule studied.[26]

Experimental

All the spectra were taken with a Varian A-60 spectrometer, the calibration of which was checked according to Tiers and Hotchkiss,[27] on 10% (w/v) solutions of the samples in $CHCl_3$, CCl_4, pyridine, and benzene containing tetramethylsilane (TMS) as an internal reference at room temperature. For the assignment of a hydroxyl and an amino signal and for the removal of spin coupling effect of a hydroxyl and an amino proton, a small amount of D_2O was added to the solutions.[18] Chemical shifts are expressed in τ-values, and coupling constants in c.p.s. Accuracy limits of the measurements are about $\pm 0.02\,\tau$ for chemical shifts and about ± 0.3 c.p.s. for coupling constants.

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Summary

Nuclear magnetic resonance spectra of many bornane derivatives have been studied. The signals of the three methyl groups in the bornane derivatives were assigned. Substituent effects due to various substituents upon the signal positions of the methyl groups were evaluated and discussed briefly. The effect on the signal position of a methyl group on the bridge carbon is considerably greater when a substituent is *exo*-oriented than when it is *endo*. However, an *exo*-substituent which involves a group possessing a powerful diamagnetic anisotropy such as a phenyl and a carbonyl group does not always give a downfield shift to a methyl signal. In such a case, considerable caution must be exercised when considering the configuration of a substituent.

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26) J. P. Kutney : Steroids, **2**, 225 (1963).
27) G. V. D. Tiers, D. R. Hotchkiss : J. Phys. Chem., **66**, 560 (1962).