Carbon-13 Nuclear Magnetic Resonance Spectra of 3,7-Disubstituted Bicyclo[3.3.1]nonanes: Conformation and Through-space Interaction

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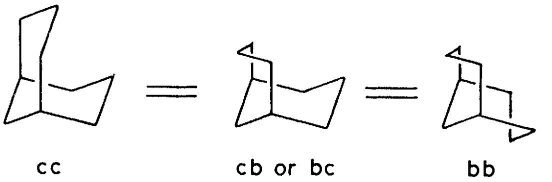
Carbon-13 n.m.r. spectra of several bicyclo[3.3.1]nonane derivatives were measured. The conformation of the framework of bicyclo[3.3.1]nonanes in this study was confirmed by the carbon chemical shifts. The π-electron delocalization was recognized in 3,7-dimethylenebicyclo[3.3.1]nonane and 7-methylenebicyclo[3.3.1]nonan-3-one due to the intramolecular through-space interaction between two π-orbitals.

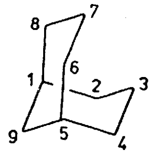
CARBON-13 n.m.r. chemical shifts are sensitive to steric and electronic factors, and provide useful information about the structure of organic molecules. Due to its conformational features the bicyclo[3.3.1]nonane system is an attractive subject of study. In this system, three groups of conformation can be envisaged, double chair (cc), chair-boat (cb or bc), and double boat (bb).[1]



Substitution at the 3-*endo*- or both 3-*endo*- and 7-*endo*-positions introduces severe transannular 3,7-interactions and 1,3-diaxial interactions in the double chair conformation, so that substituents at these positions govern the conformation of this system. Since C-3 and -7 are close to each other, transannular reactions involving these carbons have been observed, such as hydride transfer between these carbons,[2] and 2-oxa-adamantane formation in the reduction of 7-methylenebicyclo[3.3.1]nonan-3-one with $LiAlH_4$ or $NaBH_4$.[3] In this paper, the carbon-13 n.m.r. spectra of a series of 3,7-disubstituted bicyclo[3.3.1]nonanes are presented and the conformation is discussed. Intramolecular orbital interaction is expected in bicyclo[3.3.1]nonanes which carry substituents containing π- and n-orbitals at C-3 and -7. This interaction may play an important role in determining the conformation of the molecule and the selectivity of the reaction. This interaction is also discussed.

RESULTS AND DISCUSSION

Table 1 collects the chemical shift data of various substituted bicyclo[3.3.1]nonanes. The assignments of the chemical shifts were based on standard methods, *i.e.*, relative intensities, off-resonance continuous wave decoupling, and a comparison of the signal shift between closely related compounds.



Taking into account the orientation of the substituents, there are four conformations (1)—(4) of the stereoisomeric 3-hydroxy-7-methylbicyclo[3.3.1]nonanes.[4] The ^{13}C chemical shifts were compared with the corresponding values for 3-methyl-[5] and 3-hydroxy-bicyclo[3.3.1]nonane [5] whose preferred conformation are already known. Thus, for example, the methylcyclohexane

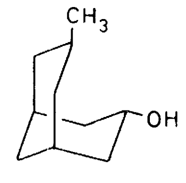
TABLE 1

Carbon chemical shifts of bicyclo[3.3.1]nonane derivatives

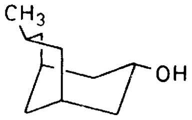
Bicyclo[3.3.1]nonane	Chemical shifts [δ(p.p.m.)] C-1, -5	C-2, -4	C-3	C-6, -8	C-7	C-9	=CH_2	CH_3	OCH_3
3-*exo*-Hydroxy-7-*exo*-methyl- (1)	30.2	41.4	66.7	40.5	28.8	34.7		24.3	
3-*exo*-Hydroxy-7-*endo*-methyl- (2)	26.6	43.2	64.1	35.7	24.2	28.2		22.0	
3-*endo*-Hydroxy-7-*exo*-methyl- (3)	26.9	36.2	65.2	42.3	22.8	28.9		22.1	
3-*endo*-Hydroxy-7-*endo*-methyl- (4)	25.3	(36.2) [a]	68.0	(40.9)	28.1	25.0		22.6	
3,7-Dimethylene- (5)	29.4	40.8	145.2	40.8	145.2	33.7	110.4		
7-Methylene-3-one (6)	31.0	47.3	209.3	41.6	141.8	32.2	114.2		
7-*exo*-Methyl-3-one (7)	30.9	47.6	212.2	41.1	24.1	32.5		23.0	
7-*endo*-Methyl-3-one (8)	28.9	50.4	211.8	36.5	23.7	28.5		22.1	
3-*exo*-Hydroxy-7-methylene- (9)	30.9	42.0	63.8	40.2	148.8	33.9	108.8		
3-*endo*-Hydroxy-7-methylene- (10)	28.6	(37.9)	63.3	(40.6)	147.9	32.2	112.2		
3-*exo*-Methoxy-7-methylene- (11)	30.9	38.7	72.9	40.6	148.8	34.2	109.2		55.5
3-*endo*-Methoxy-7-methylene- (12)	28.3	32.5	74.0	43.0	144.0	29.4	111.9		55.5
3-*exo*-Methyl- (13)	29.2	41.7	28.5	31.6	24.9	35.4		24.9	
3-*endo*-Methyl- (14) [b]	26.2	36.1	25.7	34.3	16.1	29.7		22.7	
3-*exo*-Hydroxy- (15) [b]	30.9	41.8	66.7	31.0	22.7	34.7			
3-*endo*-Hydroxy- (16) [b]	26.7	36.1	65.5	33.2	16.4	29.4			
3-Methylene- (17)	29.8	40.7	150.2	32.8	20.1	34.7	107.3		
3-One (18)	30.8	47.5	212.5	32.3	18.4	33.1			

[a] Values in parentheses may be interchanged. [b] Ref. 5.

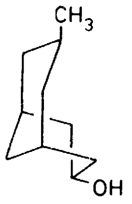
moiety of 3-*exo*-hydroxy-7-*exo*-methylbicyclo[3.3.1]nonane (1) was compared with that of 3-*exo*-methylbicyclo[3.3.1]nonane (13) and the cyclohexanol moiety with that of 3-*exo*-hydroxybicyclo[3.3.1]nonane (15).


3-*exo*, 7-*exo*

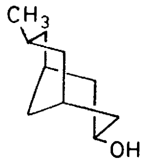
(1)


3-*exo*, 7-*endo*

(2)


3-*endo*, 7-*exo*

(3)


3-*endo*, 7-*endo*

(4)

The agreement of the chemical shifts of the corresponding carbons is very good between mono- and di-substituted bicyclo[3.3.1]nonanes.

Peters and his co-workers have estimated the chemical shifts of cc, cb, and bb conformation of bicyclo[3.3.1]nonane itself.[6] The C-9 chemical shifts of the parent bicyclo[3.3.1]nonane, and several 3-substituted and 3,7-disubstituted bicyclo[3.3.1]nonanes whose ring conformations are already known show that these signals appear in a limited region of the magnetic field depending on the conformation of the bicyclo[3.3.1]nonane framework.[5,6] These values are in Table 2. The C-9 chemical shifts of cc come in the region around δ 33.8—34.7, cb around δ 28.6—30.2, and bb δ 23.7 p.p.m. This indicates that the C-9 chemical shift is not very sensitive to δ-substitution at C-3 and -7, and can be used to establish the conformation of the framework. The C-9 chemical shifts of the four stereoisomers were compared with those of the corresponding conformation of the bicyclo-[3.3.1]nonane framework. These chemical shifts are consistent with the assigned conformations. It has been reported that 3-*endo*-hydroxy-7-*endo*-methylbicyclo-[3.3.1]nonane (4) preferably exists in the cb conformation from a study of the ^{1}H n.m.r. spectra,[4] but the C-9 chemical shift indicates that this isomer exists in 70—80% bb conformation by simple estimation using the method of Eliel.[7] Carbon-13 n.m.r. spectra of stereoisomeric 1-t-butyl-4-methylcyclohexanes show that the chemical shift for an axial methyl group on the cyclohexane ring is at δ 17.5 p.p.m. and that for an equatorial methyl group on the cyclohexane ring is at δ 22.8 p.p.m.[8] In addition, the carbon chemical shift of the equatorial methyl group in the boat conformation is not so different from that in the chair conformation; the methyl signal of 3-*endo*-methylbicyclo[3.3.1]nonane (14) is at δ 22.7 p.p.m. The chemical shifts for the methyl carbons of these four stereoisomers indicate that all the 7-methyl groups preferably exist in an equatorial orientation. This also supports the assigned conformation.

TABLE 2

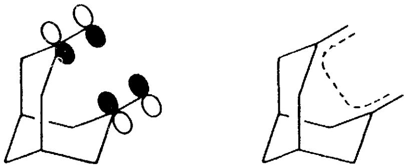
C-9 Chemical shifts of some bicyclo[3.3.1]nonane derivatives whose conformations are aready known

cc Conformation	
Parent (estimated) [a]	34.4
3-*exo*-Methoxycarbonyl- [a]	34.1
3-*exo*-t-Butyl-7-*exo*-methoxycarbonyl- [a]	33.8
3-*exo*-[2-(2-Hydroxypropyl)]- [a]	34.5
3-*exo*-Chloro- [b]	34.3
3-*exo*-Bromo- [b]	34.1
3-*exo*-Hydroxy- [b]	34.7
cb Conformation	
Parent (estimated) [a]	28.6
3-*endo*-Methoxycarbonyl- [a]	29.1
3-*exo*-t-Butyl-7-*endo*-methoxycarbonyl- [a]	29.0
3-*endo*-[2-(2-Hydroxypropyl)]- [a]	28.9
3-*endo*-Hydroxy- [b]	29.4
3-*endo*-Methoxy- [b]	28.8
3-*endo*-Acetoxy- [b]	30.2
3-*endo*-Ethoxycarbonyl- [b]	29.1
3-*endo*-Methyl- [b]	29.7
bb Conformation	
Parent (estimated) [a]	23.7
3,7-*endo*-Bis-[2-(2-Hydroxypropyl)]- [a]	23.7

[a] Ref. 6. [b] Ref. 5.

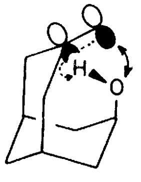
The C-9 chemical shifts of 7-*exo*-methylbicyclo[3.3.1]-nonan-3-one (7) and bicyclo[3.3.1]nonan-3-one (18) are at δ 32.5 and 33.1 p.p.m., respectively, whereas that of 7-*endo*-methylbicyclo[3.3.1]nonan-3-one (8) is at δ 28.5 p.p.m. The framework of (7) and (18) is supposed to be cc and (8) to be cb. The chemical shifts of the 7-methyl groups also support these conformations.

The conformation of 3,7-dimethylenebicyclo[3.3.1]-nonane (5) is expected to be cc, since its C-9 chemical shift is at δ 33.7. The chemical shifts of C-3 and -7 and the *exo*-methylene carbon were compared with those of 3-methylenebicyclo[3.3.1]nonane (17). The signals of C-3 and -7 are shifted upfield by 5 p.p.m., while that of terminal methylene carbon is shifted downfield by 3.1 p.p.m. If the upfield shift of C-3 and -7 signals is only due to the magnetic anisotropy effect of the π-electrons,[9] the terminal methylene carbon signal should have been shifted upfield. Taking into account the Dreiding models of a series of bicyclo[3.3.1]nonanes, the distance between C-3 and -7 for (5) seems to be almost the same as that for bicyclo[3.3.1]nonane itself, which has been obtained by the *X*-ray analysis to be 3.06 Å.[10] Both ethylenic moieties of (5) are on the same plane of symmetry and they face each other. Since the π-orbital extends above and below its nodal plane by *ca.* 1.7 Å, respectively,[11] some through space interaction is expected between two π-orbitals of this compound by the overlapping of them. As a consequence, the electron delocalization between two π-orbitals may occur. Similar trends of sp^2 carbon chemical shifts are observed in (6). The resonance of C-7 is shifted upfield by 8.4 p.p.m., while that of *exo*-methylene carbon is shifted downfield by 6.9 p.p.m. The carbonyl carbon signal appears at the field 3.2 p.p.m. higher than that of (18). The ketone (18) shows $\lambda_{max.}$ for an n–π^* transition at 289 nm (ε 11) in cyclohexane. The maximum absorption of (6) is slightly shifted to longer wavelength than that of (18), $\lambda_{max.}$ 294 nm (ε 14) in cyclohexane. In the i.r. spectra, stretching bands for the carbonyl group and the carbon–carbon double bond appear at 1 706 and 1 655 cm^{-1}, respectively. There is no appreciable difference in the position of these absorption bands compared with the correspondings of (17) and (18). These spectral data indicate that carbon-13 n.m.r. spectrum is sensitive to the electronic situation of the carbon atom and one of the powerful methods for analysis of the intramolecular interaction.

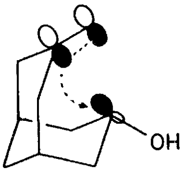


Through-space interactions of 3,7-dimethylenebicyclo[3.3.1]nonane (5)

The sp^2 carbon chemical shifts of 3-hydroxy-7-methylenebicyclo[3.3.1]nonanes were compared with those of (17). The signal of ring sp^2 carbon is shifted to higher field and that of the *exo*-methylene carbon to lower field, as in the case of dimethylene compound (5) and methylene-ketone (6). In 3-*endo*-hydroxy-7-methylenebicyclo[3.3.1]nonane (10), the C-9 chemical shift shows that this compound exists in the cc rather than the cb conformation. In i.r. spectra, the hydroxy-stretching band of 2-*exo*-hydroxy-7-methylenebicyclo-[3.3.1]nonane (9) appears at 3 630 cm^{-1} which indicates a free hydroxy-group. The hydroxy-group of (10) appears at 3 520 cm^{-1}. Normally speaking, this indicates hydrogen bonding with the π-orbital. But if the hydroxy-group is oriented to give maximum overlap of hydrogen with the π-orbital, this hydrogen is placed too close to C-7 and a drastic van der Waals repulsion operates. It is more likely that the hydroxy-group twists about the connecting carbon–oxygen bond to relieve this repulsion while maintaining hydrogen bonding to some extent. The distortion of the π-orbital by the formation of the hydrogen bond as well as the repulsive interaction with the n-orbital of the oxygen atom results in a discrepancy between the chemical shifts for the sp^2 carbons of (10) and those for (17). The sp^2 carbon chemical shifts of (9), the conformation of which is expected to be cc from the C-9 chemical shift, show similar trends as those of (10). The C-7 signal is shifted upfield, while that of the *exo*-methylene carbon is shifted downfield compared to the corresponding values for (17). In this case intramolecular hydrogen bonding is negligible. We tentatively speculate that the π-electron partially transfers to the vacant σ^*-orbital of the carbon–oxygen bond.



π-Orbital distortion by the hydroxy-group in (10)



Interaction between π- and σ^*-orbitals in (9)

As opposed to the position in (10), the C-9 chemical shift of 3-*endo*-methoxy-7-methylenebicyclo[3.3.1]nonane (12) indicates that it exists preferably in the cb conformation even though the value of the conformational free enegry of a methoxy-group is almost equal to that of a hydroxy-group.[12] Consequently, it was impossible to examine the interaction between the oxygen atom and the π-orbital by comparison of the chemical shifts of the alcohol (10) with the methyl ether (12).

EXPERIMENTAL

N.m.r. Spectra.—Carbon-13 Fourier transform n.m.r. spectra were obtained at 25.15 MHz with a JEOL JNM-MH-100 instrument equipped with a JNM-MFT-100 Fourier transform accessory; the instrument was controlled with a JEC-6 spectrum computer. Samples were dissolved into $CDCl_3$, the deuterium signal of which provided a field frequency lock; the concentrations were 15—20% (w/v). Measurement conditions were as follows: pulse width 27.5 μs (*ca.* 45°); repetition time 4 s; spectral width 6.25 kHz; data points 8 192. Noise-modulated proton decoupling was carried out at a nominal power of 20 W. All chemical shifts (δ) are expressed in p.p.m. downfield from internal Me_4Si. Each observed chemical shift is estimated to be accurate to within $\delta \pm 0.1$ p.p.m.

Materials.—All compounds employed in this study have been previously reported: (1),[13] (2),[4] (3),[14] (4),[4] (5),[15] (6),[16] (7),[13] (8),[4] (9),[17] (10),[18] (11),[5] (12),[5] (13),[19] (17),[20] and (18).[21] The structure of each substituted bicyclo[3.3.1]nonane was confirmed by ^1H n.m.r. and analytical g.l.c.

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