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BOAT-CHAIR CONFORMATION OF 2,4-DIOXABICYCLO[3.3.1]NONANE

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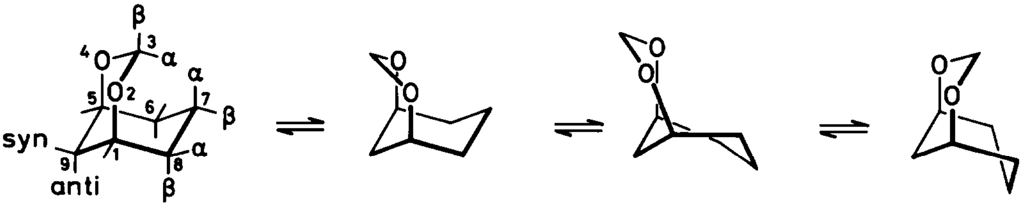
The conformation of 2,4-dioxabicyclo[3.3.1]nonane was investigated with the use of ^1H NMR spectroscopy. From the coupling constants, the Nuclear Overhauser Effects and the T_1-relaxation times it was concluded that this compound occurs predominantly in the bc conformation.

It is well-known that bicyclo[3.3.1]nonane occurs predominantly in the double-chair conformation (cc).[2,3] Severe interaction between the $H_{3\alpha}$ and $H_{7\alpha}$ atoms is avoided by substantial flattening of both wings of the system. For this compound contributions of the boat-chair (bc) and the double-twist boat conformations (t-bb) to the conformational equilibrium can be neglected. Replacement of the methylene groups at the 2- and 4-positions by ether oxygens introduces several changes in non-bonding interactions in the various conformations. The most striking alteration is the shortening of the distance between both wings in all possible conformations.



cc bc t-bb cb

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The conformation of 2,4-dioxabicyclo[3.3.1]nonane (1) has been studied by Anteunis et al.[4,5] From ^1H NMR spectra these authors concluded that compound 1, as well as its 7,7-dimethyl derivative, probably occurs in a flattened cc conformation or the t-bb conformation, although other conformations could not be excluded. The vicinal coupling constants of H_1 with both $H_{8\alpha}$ and $H_{8\beta}$, however, are small ($\leqslant$ 5 Hz). From our previous studies on vicinal coupling constants,[6] it seems rather unlikely that the cyclohexane part of compound 1 occurs in the boat conformation, as in that case $J_{18\beta}$ is expected to be 9-11 Hz. We have repeated the ^1H NMR measurements at 300 MHz and with the use of lanthanide shift reagents at 100 MHz, enabling the determination of all vicinal coupling constants.[9] Comparison of the values obtained with those of previous investigations on bicyclo[3.3.1]nonane systems shows that the cyclohexane ring in compound 1 is a somewhat flattened chair. This chair conformation is supported by a long-range coupling between H_{9syn} and $H_{6\alpha}$ ($J = \sim 2$ Hz).[7] In this conformation the bonds between H_{9syn} and $H_{6\alpha}$ exist in a W-arrangement. The close similarity of the ^1H NMR spectra of compound 1 and its 7,7-dimethyl derivative[5] indicates that both compounds occur in the same conformation. An inspection of molecular models shows that then the bc conformation is the more likely.

From the coupling constants it may be concluded that compound 1 occurs either in the flattened cc conformation or in the bc conformation. In order to obtain a definitive proof for the conformation of the dioxane ring we investigated the Nuclear Overhauser Effects (NOE) in the 300 MHz ^1H NMR spectrum. Saturation of the H_3-signal at $\delta = 5.04$ results in significant NOE's on the other H_3-signal ($\delta = 4.74$) and on the signal of H_{9syn} ($\delta = 2.16$) (see Table 1).

Table 1. Nuclear Overhauser Effects in compound 1 (1.4 mole % in C_6D_6, degassed, 300 MHz ^1H NMR)

	experimental	calculated[b]	
		cc	bc
$f_{3\beta}$ (9syn)[a]	5±3%	0.5%	8.4%
f_{9syn} (3β)	5±3	0.5	6.5
$f_{7\alpha}$ (3α)	0±3	7.0	0.7
$f_{3\alpha}$ (7α)	0±3	9.8	0.9

[a] f_i (j) is the NOE on signal i upon saturation of signal j.

[b] calculated according to Noggle and Schirmer[8] with the use of distances obtained from force field calculations[10]

Upon saturation of the signal at $\delta = 4.74$ only a NOE on the signal at $\delta = 5.04$ could be detected, whereas saturation of H_{9syn} induces significant NOE's on H_{9anti} and on the H_3-signal at $\delta = 5.04$. Thus, it may be concluded that compound 1 occurs predominantly in the bc conformation: the agreement of the experimental NOE's with the calculated values for the bc conformation is rather good. Moreover, these results allow the assignment of the signals at $\delta = 5.04$ and 4.54 to $H_{3\beta}$ and $H_{3\alpha}$, respectively. These assignments are difficult to achieve otherwise.

The above conclusions are supported by T_1-relaxation times of the protons in compound 1 (see Table 2). The experimental values agree distinctly better with the calculated values for the bc conformation than with those calculated for the cc conformation.

Table 2. T_1 values in compound 1 (1.4 mole % in C_6D_6, degassed, 300 MHz ^1H NMR)

	experimental		calculated[b] $T_{1i}/T_{6\beta}$	
	T_{1i}[a] (s)	$T_{1i}/T_{16\beta}$	cc	bc
H_1	∿22	∿2.9	2.69	2.73
$H_{3\alpha}$	13.2	1.74	1.03	1.43
$H_{3\beta}$	9.5	1.25	1.38	1.17
$H_{6\alpha}$	8.7	1.14	1.08	1.07
$H_{6\beta}$	7.6	1.00	1.00	1.00
$H_{7\alpha}$	8.4	1.11	0.74	1.02
$H_{7\beta}$	6.8	0.89	0.80	0.96
H_{9syn}	6.7	0.88	1.27	0.90
H_{9anti}	6.6	0.87	1.14	0.92
agreement factor[c]			0.94	0.15

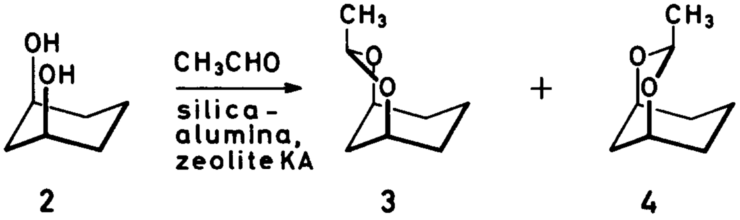
[a] As the T_1^{-1} value was taken the slope at the magnetization recovery curve at the time zero after the inverting π-pulse in the inversion recovery method.

[b] Calculated with the use of interatomic distances, obtained from force field calculations,[10] assuming that there is isotropic tumbling of the molecule. Cross relaxation was taken into account, cross correlation effects were neglected.

[c]
$$\sum_{i=1}^{n} [(T_{1i}/T_{16\beta})_{exp} - (T_{1i}/T_{16\beta})_{calc}]^2$$

Moreover, the preference of compound 1 for the bc conformation is shown by force field calculations.[10] The bc conformation is calculated to be 1.98 kcal/mole more stable than the cc conformation and 2.35 kcal/mole more stable than the cb conformation. The t-bb is the less stable conformation.

The relative high stability of the bc conformation is demonstrated by the acetalisation of *cis*-1,3-cyclohexanediol (2) with acetaldehyde under supposed thermodynamically conditions,[9] using silica-alumina (HA-LPV) as the catalyst.[11] The main product was 3α-methyl-2,4-dioxabicyclo[3.3.1]nonane (3). Less than 1% of a second compound, probably the 3β-epimer (4), which is expected to occur in the cc conformation, could be detected. The structure of compound 3 was proven by an independent selective synthesis.[9]



A more detailed study of 2,4-dioxabicyclo[3.3.1]nonane derivatives with the aid of several NMR techniques is in progress. A comparison is made with some model compounds with fixed conformations.[9]

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