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REVERSIBLE HEMIACYLAL BRIDGING IN BICYCLO[3.3.1]NONANES: A ^{13}C NMR STUDY

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^{1}H and ^{13}C NMR conformational studies on bicyclo[3.3.1]nonanes have indicated the occurrence of chair-boat equilibria of the type $A \rightleftarrows B$[2] (fig.1)

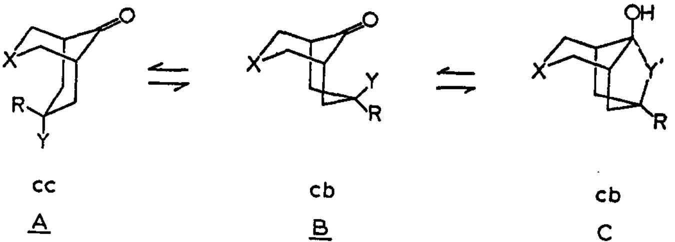
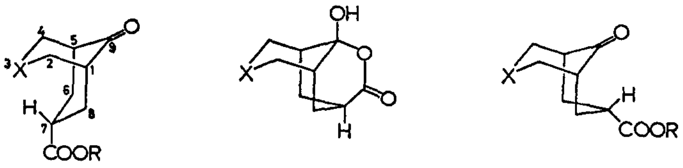


Fig. 1

Thus far the endo transannular 3,7-interaction was found to be of major importance in the stabilization of the unfavorable cb forms. Thus in carbocyclics (A: X=CH_2, R=COOMe and Y=H[3]) as well as in heterocyclics (A: X=NTs, R = COOEt, Y=H[4]) the cb form B predominates[5]. From a ^{13}C NMR study at variable temperatures we have found evidence for the existence of a second important factor favouring the cb form. Chemical interaction between suitable Y moieties and the C=O group directly governs a second equilibrium $B \leftrightarrows C$.

In the course of a ^{13}C NMR investigation of NTs-3-azabicyclo[3.3.1]nonanes[6] the C_5D_5N-spectrum of 1 at 37°C was noted to exhibit anomalous line-broadening. The presence of a small signal at 102·6 ppm and the absence of a C=O signal (at $\sim$ 200 ppm) suggested hemiacylal structure 5 to be present. To investigate this behaviour more closely, the carbocyclic analogue 2 was synthesized by known[3a)]



1 X = NTs R=H
2 X = CH_2 R=H
3 X = NTs R=Me
4 X = CH_2 R=Me

5 X = NTs
6 X = CH_2

7 X = NTs R = H
8 X = CH_2 R = H
9 X = NTs R = Et
10 X = CH_2 R = Me

Fig. 2

procedures. At 37°C, the ^{13}C NMR spectrum of 2 also showed broadened peaks; however at -25°C fourteen sharp lines were visible, corresponding to the keto-acid 2 and its tautomer the hemiacylal 6. The data are summerized in table I.

TABLE I ^{13}C NMR data of bicyclo[3.3.1]nonan-9-ones[7]

compound (conformation)	solvent (T)	$C_{1,5}$	$C_{2,4}$[a]	C_3[a]	$C_{6,8}$[a]	C_7[a]	C_9	COOR
1 (cc)	–[b]	–	–	–	–	–	–	–
2 (cc)	C_5D_5N (-25°C)	46.0	34.1	21.0	37.0	38.0	218.9	177.1
3 (cc)	$CDCl_3$ (37°C)	45.3	52.7	–	35.6	36.2	212.8	174.2
4[c] (cc)	$CDCl_3$ (35°C)	45.4	34.0	21.0	36.4	37.4	–[d]	–[d]
5 (cb)	C_5D_5N (-35°C)	36.8	48.3	–	26.9	35.1	102.9	174.8
6 (cb)	C_5D_5N (-25°C)	35.3[e]	27.1[f]	14.0	27.4[f]	36.0[e]	106.1	175.8
7 (cb)	C_5D_5N (37°C)	44.6	53.8	–	32.9	37.3	213.7	175.6
8 (cb)	$CDCl_3$ (37°C)	43.7	35.9	15.1	31.8	36.9	220.9	179.5
9 (cb)	$CDCl_3$ (37°C)	44.5	53.2	–	32.3	36.5	213.9	172.7
10[c] (cb)	$CDCl_3$ (35°C)	43.8	35.8	15.1	32.0	37.0	219.8	174.6

[a] For easier comparison of corresponding C-atoms the systematic numbering of 3-azabicyclo[3.3.1]nonanes has been maintained throughout the table.

[b] No data obtainable due to low relative concentration.

[c] From ref. 3b.

[d] Not mentioned.

[e,f] Reversed assignment possible.

The spectral assignments of 6 were based on the following analysis: since the spectra of the endo-keto-acid 8 and ester 10 are very similar, both possessing the cb conformation[3b], the keto-acid 2 would be expected to give a spectrum resembling the known ester 4 both having the cc conformation. On the basis of this assumption the absorptions of 2 in the mixture 2+6 can be attributed. The hemiacylal 6 is likely to possess a completely different spectrum due to its forced cb conformation. The position of C_3 at $\delta = 14{\cdot}0$ ppm relative to C_3 in 2 at $\delta = 21.0$ ppm is in this respect diagnostic for the cb conformation; an upfield shift of ≈ 6 ppm for C_3 going from cc to cb was found in a series of structurally related bicyclo[3.3.1]nonan-9-ones[3b)]. Furthermore the δ value of ≈ 100 ppm is indicative for a hemiacetal structure[8)], while the upfield shifts for $C_{1,5}$, $C_{2,4}$ and $C_{6,8}$ may be largely ascribed to a change in substituents[9)] at C_9.

Upon raising the temperature of the sample containing the mixture of 2 and 6, line-broadening and coalescence (at about 70°C) takes place, while at 110°C a spectrum is observed consisting of only six[10)] signals found at positions between the original absorptions in 2 and 6[11)] (see table II)

TABLE II ^{13}C NMR spectra of $2 \leftrightarrows 6$ and $1 \leftrightarrows 5$ at different T[a)].

		$C_{1,5}$	$C_{2,4}$	C_3	$C_{6,8}$	C_7	C_9
2	(-25°C)	46.0	34.1	21.0	37.0	38.0	218.9
6	(-25°C)	36.0	27.1	14.0	27.4	35.3	106.1
2+6	(+110°C)	43.3	32.2	18.9	33.9	37.2	-[c)]
5	(-35°C)	36.8	48.3	-	26.9	35.1	102.9
1+5	(+100°C)	39.1	48.6	-	29.2	34.6	-[c)]

[a)] Solvent: C_5D_5N.

[b)] See note 10.

This spectrum is likely to represent an average between 2 and 6 caused by fast interconversion in a dynamic equilibrium. A similar effect was reported in pH-dependent hemiacetal formation in pyridoxal[12)].

The aforementioned behaviour was also found for 5[13)]. Unfortunately, the relative amount of the open form 1 is too low to be detected by NMR. This is ascribed to enhanced steric hindrance of C_7-H with the large tosylsubstituent, thereby favouring the cb form. The actual presence of 1 in the equilibrium $1 \leftrightarrows 5$ could be proven by reaction of 5 with diazomethane thus affording ester 3. Following the same reasoning as before, the high-temperature spectrum (C_5D_5N, +100°C) may represent an average between 1 and 5.

In conclusion it can be stated that the combined techniques of ^{1}H and ^{13}C

NMR provides new and otherwise inaccessible information on the bicyclo[3.3.1] nonane chair-boat equilibrium.

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7. Spectra were recorded on a Varian XL-100 FT spectrometer at 25.2 MHz with TMS as an internal standard. Assignments were made by comparison with related compounds$^{6)}$ and by examination of the off-resonance spectra.

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10. Presumably the width of C_9 (C = O) was too large to make the detection of the signal possible.

11. Temperature dependency of the chemical shifts was neglected.

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13. IR and ^{1}H NMR spectra of 5 and 6 are in agreement with the proposed structures. IR: sharp OH at 3400 cm^{-1} for both, C = O for 5 1750 cm^{-1} (lactone), for 6 1730-1710 cm^{-1} (broad); ^{1}H NMR: OCOH at δ = 5,8 and 4,0.