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^{13}C NMR SPECTROSCOPY OF SOME 3- AND 7-SUBSTITUTED BICYCLO[3.3.1]NONANES

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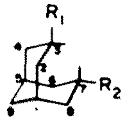
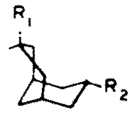
Abstract—The ^{13}C NMR spectra of a series of 3,7-substituted bicyclo[3.3.1]nonane derivatives are examined. Taken into account substituent influences, the ^{13}C chemical shifts appear to be diagnostic for the conformation of the bicyclo[3.3.1]nonane derivative.

Due to its conformational features, the bicyclo[3.3.1]nonane system is an attractive subject of study. It has been shown that bicyclo[3.3.1]nonane and its 3-*exo* and/or 7-*exo* substituted derivatives exist in a somewhat flattened double-chair conformation (cc).[1] Substitution of the 3-*endo*-position causes severe 3,7-interaction. Consequently these compounds prefer a rigid chair-boat conformation (cb), with the 3-*endo*-substituent (R_1) in the boat part. When both the 3-*endo* and 7-*endo*-position are substituted with bulky groups the double-boat conformation (bb) will be favoured.



cc



cb

bb

Previously we have studied the conformation of 3,7-substituted (9-oxo-)bicyclo[3.3.1]nonanes by means of the vicinal proton-proton coupling constants. We are at present investigating some alternative tools for conformational analysis of compounds in which these coupling constants are not conclusive.

It has been shown that the ^{13}C NMR chemical shifts are sensitive to stereochemical factors. Moreover, the effects of substituents on ^{13}C shielding are often additive within a class of compounds.[2] These features make ^{13}C NMR a powerful method for conformational analysis. So far only a few papers on ^{13}C NMR spectroscopy of bicyclo[3.3.1]nonanes—all dealing with compounds in the cc and/or cb conformation—have been published.[3-5]

In this paper, the ^{13}C NMR spectra of a series of 3- and 3,7-substituted bicyclo[3.3.1]nonanes and the corresponding 9-oxo derivatives are presented and discussed. The conformations of these compounds were established earlier by means of ^{1}H NMR spectroscopy with the aid of lanthanide shift reagents.[1,6] This study includes compounds, which prefer cc, cb as well as bb conformations.

EXPERIMENTAL

The 25.2 MHz ^{13}C NMR spectra were recorded with a Varian XL-100-15 NMR spectrometer system, equipped with a V-4415 universal probe, in the PFT-mode. All spectra were obtained from $CDCl_3$-solutions at 39°. The chemical shifts are given in ppm relative to TMS (δ).

9-Oxobicyclo[3.3.1]nonane and its 7-*endo*- and 7-*exo*-t-butyl derivative were prepared by a Hunsdiecker reaction of the corresponding 9-oxo-bicyclo[3.3.1]nonane-3-carboxylic acid,[6] followed by hydrogenation of the resulting bromide.

Hunsdiecker reaction. To a stirred soln of 16 g dry Br_2 in 100 ml CCl_4 (dried over molecular sieve 3A) 0.088 mole of the silver salt of the carboxylic acid was added in small portions. During the addition of the salt the temp. was maintained at 20–25°. Then the temp. was raised until 50°. After 30 min the mixture was filtered and from the filtrate the solvents were evaporated. A soln of the residue in 50 ml ether was washed with $NaHSO_3$ aq and then with H_2O. After drying over $MgSO_4$ the solvents were evaporated to yield the bromide with a yield of about 70%. This product was used in the next step without further purification.

Hydrogenation. A mixture of 0.01 mole of the bromide in 20 ml EtOAc and 1.0 g NaOAc was hydrogenated at 50° with 10% Pd/C as the catalyst. After the calculated amount of hydrogen was consumed the soln was filtered. After evaporation of the solvents the residue was recrystallized from light petroleum and sublimed at 10 mm. 9-*Oxobicyclo*[3.3.1]*nonane*; m.p. 156–157°. 7-Exo-*t*-*butylbicyclo*[3.3.1]*nonane*; m.p. 68.5–69.5°; ^{1}H NMR (60 MHz, $CDCl_3$): δ 0.87 (9H, s), 1.5–2.5 (13H). 7-Endo-*t*-*butylbicyclo*[3.3.1]*nonane*; m.p. 61.5–62.5°; ^{1}H NMR (60 MHz, $CDCl_3$): δ 0.89 (9H, s), 0.9–2.7 (13H).

7 - Endo - *t* - *butyl* - 3 - endo[2 - (2 - *hydroxypropyl*)] - 9 - *oxobicyclo*[3.3.1]*nonane* was synthesized by reaction of methyl 7 - *endo* - t - butyl - 9,9 - dimethoxybicyclo[3.3.1]nonane - 3 - *endo* - carboxylate[6] with MeMgBr, followed by hydrolysis; m.p. 111–111.5°; ^{1}H NMR (60 MHz, $CDCl_3$): δ 0.87 (9H, s), 1.20 (6H, s), 1.2–2.6 (13H).

The syntheses of all other compounds have been described in previous publications.[1,6]

Spectral assignments. The ^{13}C chemical shift data of the 3,7-substituted bicyclo[3.3.1]nonane derivatives are collected in Table 1; those of the corresponding 9-oxo derivatives in Table 2. Peak assignments were made with the use of the off-resonance technique, the relative intensities and intercomparison of the chemical shifts within families of derivatives. Moreover, substituent effects, estimated from the corresponding cyclohexane derivatives, were taken into account.

DISCUSSION

In order to get an impression of conformational effects on the ^{13}C chemical shifts given in Tables 1 and 2, it is necessary to correct for substituent influences. When the δ and ϵ effects are neglected, the α, β and γ substituent effects in the cc system can be derived from a comparison of the data of the compounds concerned. The values obtained (see Table 3) are in good agreement with the corresponding values for cyclohexane derivatives.

For geometric reasons, the interactions, introduced by a 3-*endo* or 7-*endo*-substituent in a boat ring of a cb or bb conformation, are analogous to those introduced by a 3-*exo*- or 7-*exo*-substituent in the cc conformation or an equatorial substituent in cyclohexane. Therefore we

Table 1. ^{13}C chemical shift data for 3,7-substituted bicyclo[3.3.1]nonanes

substituents	conformation[b]	chemical shifts								
		C_1	C_2	C_3	C_6	C_7	C_9	OMe	CO_2Me	alkyl group
nil[a]	cc	27.9	31.6	22.5	31.6	22.5	35.1	--	--	--
3-*exo*-CO_2Me	cc	27.5	34.0	39.1	30.9	22.1	34.1	51.4	177.1	--
3-*exo*-CO_2Me, 7-*exo* t-Bu	cc	28.1	34.0	39.2	33.3	42.3	33.8	51.4	176.9	27.0, 32.0
3 *exo* CMe_2OH	cc	27.0	32.2	43.2	31.5	22.3	34.5	--	--	28.2, 73.2
3-*endo*-CO_2Me	cb	25.0	29.1	36.0	33.1	16.0	29.1	51.4	177.2	--
3-*endo*-CO_2Me, 7 *exo*-t-Bu	cb	25.4	29.6	35.8	34.0	36.5	29.0	51.4	177.2	27.5, 32.1
3-*endo*-CMe_2OH	cb	25.4	27.2	40.3	33.7	16.0	28.9	--	--	27.1, 73.1
3-*endo*-t-Bu, 7-*exo*-CO_2Me	cb	25.2	27.8	38.8	36.4	33.9	27.2	51.4	177.0	27.5, 32.5
3-*endo*-CMe_2OH, 7-*endo*-CMe_2OH	bb	24.5	32.0	41.4	32.0	41.4	23.7	--	--	27.0, 72.7

[a] Ref. 3.

[b] As indicated by ^1H-NMR spectroscopy

Table 2. ^{13}C chemical shift data for 3,7-substituted 9-oxobicyclo[3.3.1]nonanes

substituents	conformation[a]	chemical shifts								
		C_1	C_2	C_3	C_6	C_7	C_9	OMe	CO_2Me	alkyl group
nil	cc	46.5	34.3	20.6	34.3	20.6	221.4	--	--	--
3-*exo*-t-Bu	cc	46.1	35.9	40.7	34.2	21.3	221.3	--	--	27.2, 32.8
3-*exo*-CO_2Me	cc	45.4	36.4	37.4	34.0	21.0		51.8	--	--
3-*exo*-CO_2Me, 7-*exo*-t-Bu	cc	45.2	36.4	38.1	35.7	41.5		51.9		27.2, 31.0
3-*endo*-t-Bu	cb	44.6	30.7	41.3	36.1	15.2	222.2	--	--	27.3, 32.4
3-*endo*-CO_2Me	cb	43.8	32.0	37.0	35.6	15.1	219.8	51.8	174.6	--
3-*endo*-CO_2Me, 7-*exo*-t-Bu	cb	43.0	32.5	36.8	36.8	33.0	220.6	51.8	174.6	27.9, 31.9
3-*endo*-CO_2Me, 7-*exo*-i-Pr	cb	43.0	32.6	36.8	39.1	31.7	220.6	51.8	174.7	20.3, 32.3
3-*endo*-t-Bu, 7-*exo*-CO_2Me	cb	43.1	32.4	40.9	37.9	33.2	219.9	51.9	184.9	27.4, 32.4
3-*endo*-CMe_2OH, 7-*endo*-t-Bu	bb	42.4	34.4	42.7	34.6	42.2	224.7	--	--	27.0, 27.0, 32.1

[a] As indicated by ^1H-NMR spectroscopy

Table 3. Substituent effects on ^{13}C chemical shifts in bicyclo[3.3.1]nonane derivatives[a]

	α	β	γ
CO_2Me	16.7	2.3	-0.5
	(16.2)	(1.7)	(-1.6)
CMe_2OH	21.7	0.5	-0.9
	(22.9)	(1.0)	(0.2)
t-Bu	20.0	1.7	0.0
	(21.4)	(0.7)	(0.0)

[a] Derived from cc conformations; the corresponding values for equatorial substitution in cyclohexane[7,8] are given in parenthesis

assume that substituent effects derived from **cc** conformations or from cyclohexane derivatives are in good approximation also applicable for *endo* substituents R in **cb** and **bb** conformations.

cb

cc

After correcting for substituent effects, the agreement of the chemical shifts of corresponding carbons within a series of compounds with the same conformation is very good with a standard deviation of less than 1 ppm. The average values are given in Tables 4 and 5.

As already mentioned by Wiseman and Krabbenhoft[4] the chemical shift of the C_7-atom in the **cb** conformation

Table 4. Average ^{13}C chemical shifts of bicyclo[3.3.1]nonane

conformation	^{13}C chemical shift					
	C_1	C_2	C_3	C_6	C_7	C_9
double-chair	28.1	31.5	22.3	31.5	22.3	34.4
chair-boat[a]	25.9	26.7	19.0	33.3	16.4	28.6
double-boat	26.3	31.4	20.7	31.4	20.7	23.7

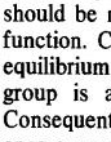
[a] C_2 and C_3 are assigned to the boat part

Table 5. Average ^{13}C chemical shifts of 9-oxobicyclo[3.3.1]nonane

conformation	^{13}C chemical shift					
	C_1	C_2	C_3	C_6	C_7	C_9
double-chair	46.0	34.2	21.0	34.2	21.0	221.4
chair-boat[a]	44.0	29.9	20.6	35.7	15.7	220.6
double-boat	43.3	33.5	21.6	33.5	21.6	224.7

[a] C_2 and C_3 are assigned to the boat part

shows appreciable shielding. This may be attributed to the γ-gauche interactions between the 7-*endo* and the 2- and 4-*endo*-hydrogens, which are operative in this conformation.[9] Probably due to this effect in the **cb** conformation, C_2 and C_4 are also shielded. This explanation would account for the observation that the ^{13}C chemical shifts of C_2 and C_7 in the **bb** conformation are more close to those in the **cc** conformation. The shielding of C_2 and C_4 in the **cb** conformation seems to be in contradiction with the investigation of Wiseman and Krabbenhoft.[4] From the similarity of the chemical shifts of C_2/C_4 in the granatols **1** and **2** these authors concluded that in this case there is no reciprocity for the chemical shifts of the sterically interacting moieties. In our opinion, however, a correction should be made for steric effects caused by the N–Me function. Compound **1** occurs approximately as an 1:1 equilibrium of **1a** and **1b**, but in compound **2** the N–Me group is almost exclusively axial to the chair-ring. Consequently C_2 and C_4 in the *exo*-compound **1** experience a considerable γ-gauche effect; in *endo*-compound **2** no γ-gauche interaction between C_2/C_4 and N–Me occurs. After correction for this difference, the trends in ^{13}C chemical shifts of **1** and **2** would seem in agreement with our results.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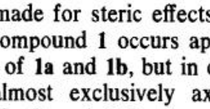
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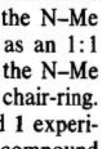
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In the **cb** and **bb** conformations, C_1 is also somewhat shielded with respect to the **cc** conformation. This might be due to eclipsing of H_1 and $H_{2\text{-exo}}$ in the former conformations. Going from the **cb** to the **bb** conformation, no further shielding is observed. This may be associated with twisting in the flexible **bb** conformation.

We did not correct for δ-substituent effects. The differences in chemical shifts of C_9 in the bicyclo[3.3.1]nonane derivatives, however, are large enough to be significant. Probably a γ-eclipsing of C_9 and C_3 and/or C_7 is responsible for the shielding of C_9 in the **cb** and **bb** conformations.

It may be concluded that, after correcting for substituent effects, the ^{13}C chemical shifts of bicyclo[3.3.1]nonane derivatives are characteristic for their conformation. The data presented prove to be useful in the estimate of the conformational preferences of these compounds and may be helpful in signal assignment in ^{13}C NMR spectra of bicyclo[3.3.1]nonane derivatives.

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