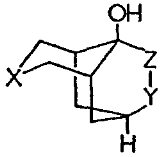
Tetrahedron Letters No. 7, pp 657 - 660, 1978. Pergamon Press. Printed in Great Britain.

HEMI-ACETAL STABILIZATION OF THE CHAIR-BOAT FORM IN BICYCLO[3.3.1]NONANES. A ^{13}C NMR INVESTIGATION.

Th. Reints Bok[1], C. Kruk and W.N. Speckamp*,
(Laboratory for Organic Chemistry, University of Amsterdam,
Nieuwe Achtergracht 129, Amsterdam. The Netherlands).

(Received in UK 2 December 1977; accepted for publication 23 December 1977)

In a preceding communication the hemi-acylal formation leading to a fixed chair-boat form A in bicyclo[3.3.1]nonanes has been discussed[2]. Aiming at a better understanding of this unusual phenomenon[3] two hydroxyketones capable of formation of the acetal derivative B were synthesized in which the eventual Y-Z bridge had been shortened by one carbon atom.

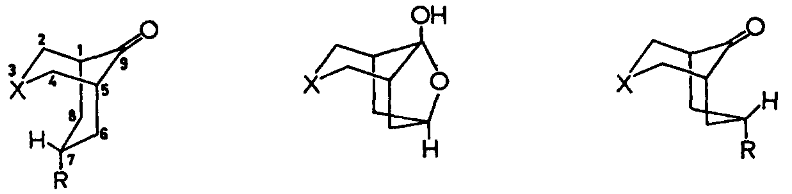


A $X = CH_2$ or NTs , $Y = -\overset{O}{\overset{\|}{C}}-$, $Z = O$
B $X = CH_2$ or NTs , $Y-Z = O$

Fig.1

The N-tosyl-3-aza-7-*exo* acetate 3 prepared in an unequivocal manner[4] from the known N-tosyl-3-aza-7-carbohydroxy-9-oxo-bicyclo[3.3.1]nonane[5] gave upon hydrolysis (NaOH-H_2O/CH_3OH) a mixture of two isomeric compounds to which structures 1a and 1b were assigned on the basis of the following ^{1}H and ^{13}C NMR evidence. C_7-H signals in the ^{1}H NMR spectrum ($CDCl_3$; 35°) were found at 5·20 ppm for 1a (H_{ax}) and at 4·25 ppm for 1b (H_{eq}); the ratio of the two C_7-H absorptions being determined at 45:55 for 1a:1b[6] respectively. From variable temperature ^{1}H NMR studies in different solvents the amount of 1a present at -60°C ($CDCl_3/C_5D_5N$) is estimated at 15% while at 90°C (toluene-d8) the ratio of 1a and 1b is almost equal. In diphenylether the ratio of 1a and 1b at 35°C was found to be 30:70 while at 130° coalescence of the C_7-H signals occurred.

Acetylation of the mixture 1a+1b (BF_3OEt_2/HOAc) yielded 3 in quantitative yield indicating that upon hydrolysis isomerization at C_7 had not taken place. The C_7-*endo* isomer 4 possessing the chair-boat conformation is synthesized via an independent route[4] and shows completely different spectral behaviour. These results strongly point to the existence of a conformational or tautomeric equilibrium between the two isomers 1a and 1b, however without proving the hemi-acetal form of 1b.



1a X=NTs R=OH
2a X=CH_2 R=OH
3 X=NTs R=OAc

1b X=NTs
2b X=CH_2

4 X=NTs R=OH
5 X=CH_2 R=OH

Fig. 2

A ^{13}C NMR spectrum in C_5D_5N of the mixture 1a+1b demonstrated a conspicuous signal at 104·9 ppm (Table) in addition to the C (9) = O signal at 213·8 ppm. At -35°C the latter signal had almost vanished together with the other absorptions assigned to 1a, while at higher temperature (70°C) the peaks of both isomers were still present. The assignment of the ^{13}C data was based upon analysis of the off-resonance decoupled spectra at different temperatures and selective ^{13}C-$\{^1$H$\}$ decoupling experiments and is given in the table. The spectral data of 1a clearly indicate the double chair conformation[7]. The signal at 104·9 ppm is most likely attributed to the hemi-acetal carbon at C_9 of 1b[8][9].

TABLE ^{13}C Chemical shift data of 7-hydroxy-9-oxo-bicyclo [3.3.1]nonanes in C_5D_5N at 37° a)b).

Compound	$C_{1,5}$	$C_{2,4}$ c)	C_3 c)	$C_{6,8}$ c)	C_7 c)	C_9
1a	45·8	53·3		41·7	62·9	213·8
1b	40·5	46·2		35·4	71·0	104·9
2a	45·2	35·2	19·6	41·6	63·8	218·6
2b	35·6	25·0	15·1	39·9	70·8	107·1

a) Spectra were recorded on a Varian XL-100 15 in FT-spectrometer in 5 mm tubes at 25·2 MHz. Chemical shifts, relative to internal TMS, were obtained from the proton noise decoupled spectra.

b) Data were measured from -35°C to 70°C; no appreciable solvent effects could be found.

c) See note 10.

In order to ascertain the above conclusion the corresponding carbocyclic derivatives were also prepared. The 7-exo-hydroxy-9-oxo-bicyclo[3.3.1]nonane 2a[10)] was obtained as a byproduct in the decarboxylation of 7-endo-carbohydroxy-9-oxo bicyclo[3.3.1]nonane[11)] with $Pb(OAc)_4$. Hydrolysis by base and chromatography of the two isomeric alcohols yields 16% of 2a and 8% of 5. C_7-H_{ax} signals in the ^1H NMR spectra ($CDCl_3$) were found at 4·60 ppm for 2a and 3·70 ppm for 5.

Variable temperature ^{13}C NMR experiments in C_5D_5N of 2a+2b also showed an absorption at 107·1 ppm next to other characteristic signals assigned to 2b (Table). The latter peaks indicate a minor contribution of 2b to the equilibrium at 37°C and also explain the virtual absence of 2b signals in ^1H NMR. At lower temperatures the proportion of 2b increases while at 70°C absorptions of 2b cannot be detected. As compared to 1b however the hemi-acetal form 2b appears to be present in significantly lesser amounts suggesting an extra stabilizing effect on the boat form of the bulky tosyl substituent in 1b. The spectral data for 2a are in agreement with a double chair conformation[12)].

Apart from the signals at 104·9 ppm and 107·1 ppm a number of other data also support the cyclic hemi-acetal structure. The value of $^1J(^{13}C$-$^1H)$ for C_7 of 158·9 Hz for 1b and 156·9 Hz for 2b is in entire agreement as to the literature value for the corresponding carbon atom in 7-oxa-bicyclo[2.2.1]heptane (157 Hz)[13]. The influence of the hemi-acetal moiety is noticeable by the shift of $C_{2,4}$ from 53·3 ppm for 1a to 46·2 ppm for 1b and from 35·2 ppm for 2a to 25·0 ppm for 2b[14)]. Furthermore $C_{6,8}$ in 1b and $C_{6,8}$ and C_3 in 2b are shielded by the effect of interactions of the tosylgroup and the C_3-endo protons respectively[12)]. The C_7 signals at 71·0 ppm for 1b and 70·8 ppm for 2b are highly indicative for an ether bonding rather than the free C_7-OH moiety which shows an absorption at higher field[15)16)].

The presently discussed examples of a chair-boat equilibrium once again illustrate the importance of chemical stabilization of an a priori unfavorable conformation. It should be noted that the presence of the hemi-acetal form can only be verified by ^{13}C NMR; the combination of ^{13}C NMR and ^1H NMR therefore proves to be a method of choice for studying these phenomena.

References

1. Part of the forthcoming Ph.D.Thesis of Th. Reints Bok, University of Amsterdam.
2. H. van Oosterhout, C. Kruk and W.N. Speckamp, preceeding communication.
3. P. Hanisch, A.J. Jones, A.F. Casy and J.E. Coates, *J.C.S. Perkin II*, 1202 (1977).
4. Th. Reints Bok and W.N. Speckamp, to be published.
5. W.N. Speckamp, J. Dijkink, A.W.J.D. Dekkers and H.O. Huisman, *Tetrahedron*, **27**, 3143 (1971).
6. The ratio of *1a*:*1b* was obtained by integration of the C_7-H and the N-CH_2 absorptions in ^{1}H NMR (accuracy 5%).
7. Th. Reints Bok, H. van Oosterhout and W.N. Speckamp, to be published.
8. R.D. Lapper, H.H. Mantsch and I.C.P. Smith, *Can.J.Chem.*, **53**, 2406 (1975).
9. Possible hydrate formation at C (9) = O could be excluded by working under extremely dry conditions. See also A.J. Jones and M.M.A. Hassan, *J.Org.Chem.*, **37**, 2322 (1972).
10. For easier comparison of corresponding C-atoms the systematic numbering of 3-azabicyclo[3.3.1]nonanes has been maintained.
11. J. McEuen, R.P. Nelson and R.G. Lawton, *J.Org.Chem.*, **35**, 690 (1970).
12. J.A. Peters, J.M. van der Toorn and H. van Bekkum, *Tetrahedron*, **33**, 349 (1977)
13. M. Tamres, S. Searles Jr. and J.M. Goodenow, *J.Am.Chem.Soc.*, **86**, 3934 (1964).
14. H.-J. Schneider, M. Londsdorfer and E.F. Weigand, *Org.Magn.Reson*, **8**, 363 (1976)
15. J.R. Wiseman and H.O. Krabbenhoft, *J.Org.Chem.*, **40**, 3222 (1975).
16. H.-J. Schneider and W. Ansorge, *Tetrahedron*, **33**, 265 (1977).

+++++++++++++