Tetrahedron Letters No.23, pp. 1829-1832, 1969. Pergamon Press. Printed in Great Britain.

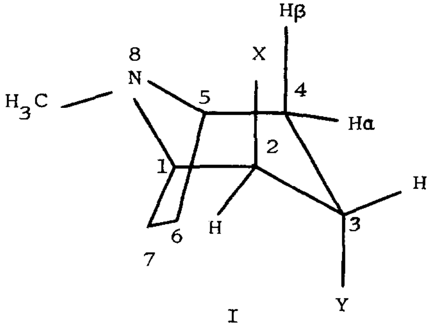
CONFORMATION OF DISUBSTITUTED TROPANES

J.H. Supple, L.N. Pridgen, and J.J. Kaminski

Department of Chemistry
State University College
Fredonia, New York 14063

(Received in USA 14 February 1969; received in UK for publication 13 April 1969)

Recent interest in the conformations of tropane and piperidine derivatives (1-9) prompts us to report our interpretation of the NMR spectra (10) of three tropanes that are substituted in the 2-and 3-positions (11). The chemical shift data listed in Table I has two particularly significant features. The absorption of the hydrogens at the 6-and 7-positions in Ia and Ib as well as in tropine (3-α-hydroxytropane, Ic) (3) is shifted downfield relative to the absorption in IIb and in pseudotropine (3-β-hydroxytropane, IIa). This deshielding of the hydrogens on the ethane bridge indicates (3) proximity of the electronegative 3-α-substituent and is possible only in a chair conformation. Similarly, the β-hydrogen on the 4-position ($H_{4\beta}$) is deshielded relative to the α-hydrogen ($H_{4\alpha}$) in compounds Ia, Ib, and IIb

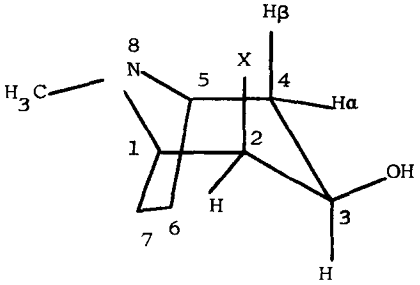


I

a: X = Y = Br

b: X = Br; Y = OH

c: X = H; Y = OH



II

a: X = H

b: X = Br

but not in the compounds lacking the 2-substituents. This deshielding, from the 1,3-diaxial proximity of $H_{4\beta}$ and the 2β-bromine, is evidence of the chair-like conformation of the three disubstituted tropanes.

Table 1

Chemical Shifts (ppm from TMS)

	H_1H_5	H_6H_7	H_2	$N-CH_3$	H_3	$H_{4\beta}$	
Tropine (3)	3.0	2.05	1.6-1.9	2.16	3.9	---	---
Pseudotropine (3)	3.07	1.5-1.8	1.5-1.8	2.22	3.7	---	---
Ia	3.25	2.25	4.60	2.31	4.49	2.77	2.05
Ib	3.15	1.99	4.05	2.23	--(a)	2.27	1.55
IIb	3.37	1.65	4.30	2.22	--(b)		

(a) The H_2 and H_3 protons were indistinguishable.

(b) This proton is believed to be hidden under the H_1, H_5 multiplet.

A somewhat better approximation of the conformations of the disubstituted tropanes is available from a consideration of the various coupling constants. The ABX system comprising $H_{4\beta}$, $H_{4\alpha}$, and H_5 was investigated using decoupling techniques by irradiation at H_3. The other pertinent coupling constants were obtained from the undecoupled spectra. Examination of the J values in Table II shows that all of the coupling constants are of the magnitude expected for axial-equatorial and equatorial-equatorial couplings. However, only the cis-bromohydrin IIb shows the identical coupling constants expected (12) from a perfect chair conformation. The inequality of $J_{4\beta-5}$ and $J_{4\alpha-5}$ as well as $J_{4\beta-3}$ and $J_{4\alpha-3}$ observed for both Ia and Ib indicates that these compounds exist in a distorted chair conformation.

All of these data are consistent with compounds Ia and Ib existing in a chair conformation distorted slightly by interactions between the 3β-substituents and the ethane bridge. When this interaction is removed, as in IIb the distortion is removed (13).

Table II

Coupling Constants (Hz)

	$J_{3-4\beta}$	$J_{3-4\alpha}$	$J_{4\beta-5}$	$J_{4\alpha-5}$	$J_{4\alpha-4\beta}$	J_{2-3}	J_{1-2}
Ia	4.0	< 1	4.0	3.0	16	< 1	< 1
Ib	4.0-4.2	< 1	4.0	3.0	15	< 1	< 1
IIb						3.5	3.5

Acknowledgement. One of us (JHS) is grateful to the Research Foundation of the State University of New York for Faculty Research Fellowships and Grants 24-64-A, B, and C. We are grateful to Mr. Jack Donovan and Dr. Earl Krakower for assistance in obtaining NMR spectra and to Mr. J. Elton Dewhurst for technical assistance.

References

1. H. Schenk, C. H. MacGillavry, S. Skolnik and J. Laan, Acta Cryst. 23, 423 (1967).
2. N. Mandava and G. Fodor, Can. J. Chem. 46, 2761 (1968).
3. R. J. Bishop, G. Fodor, A. R. Katritzky, F. Soti, L. E. Sutton, and F. J. Swinbourne, J. Chem. Soc. (C), 74 (1966).
4. G. L. Closs, J. Am. Soc. 81, 5456 (1959).
5. C. Y. Chen and R. J. W. LeFevre, J. Chem. Soc., 3467 (1965).
6. C. Y. Chen and R. J. W. LeFevre, ibid., 3473 (1965).
7. J. Parello, P. Longivialle, W. Vetter and J. A. McCloskey, Bull. Soc. Chem. 2787 (1963).
8. R. E. Lyle and C. R. Ellefson, J. Am. Chem. Soc. 89, 4563 (1967).
9. M. L. Stien, R. Ottinger, J. Reisse, and G. Chuirdoglu, Tetrahedron Letters, 1521 (1968).
10. NMR and decoupling studies were carried out in $CDCl_3$ (60MHz) on Perkin-Elmer-Hitachi R-20 and JNM-C-60 HL spectrometers.

11. The synthesis of Ia, Ib, and IIb will be the subject of a future paper. All new compounds gave satisfactory analyses.
12. J. R. Dyer, Applications of Absorption Spectroscopy of Organic Compounds, p. 117, Prentice-Hall Inc., Englewood Cliffs, New Jersey (1965).
13. X-ray studies reported (1) for pseudotropine indicated that this molecule exists in a distorted chair form in the solid state.