Nuclear Magnetic Resonance Study of Tricrotonylidenetetramine (1,2,3,3a,4,5,6,6a,7,8,9,9a-Dodecahydro-2,5,8-trimethyl-1,4,7,96-tetraazaphenalene)

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The less soluble isomer of 1,2,3,3a,4,5,6,6a,7,8,9,9a-dodecahydro-2,5,8-trimethyl-1,4,7,96-tetra-azaphenalene has trans-fused rings in chair forms with all methyl groups in equatorial positions. The more soluble isomer has one methyl group in an axial position.

THE structure of tricrotonylidenetetramine was proved by Delépine¹ who also isolated a second, more soluble, isomer which he named base B. He suggested that in base A the three asymmetric carbon atoms which bear methyl groups had the same configuration, whereas in base B the configuration of one of these atoms was reversed. This assignment was based solely on the relative proportions of the isomers formed in the reaction of crotonaldehyde with ammonia, but we have now obtained definite information about the structures from the n.m.r. spectra.

EXPERIMENTAL

The isomers were prepared and separated by the method of Delépine,¹ but since base B forms no derivatives with well defined m.p.s, it was necessary to show that it was free from base A. This was done by t.l.c. on silica gel. The $R_{\rm F}$ values of bases A and B were 0.44 and 0.38 respectively in ethanol-25% ammonia (19:1). The first crop of crystals of base B was discarded because it contained a small amount of base A, but subsequent crops obtained by the addition of ether to the solution in wet acetone were pure. The anhydrous form of base B was a syrup, but its i.r. spectrum in chloroform was nearly identical with that of base A; it showed small differences only in the region 950-1350 cm.⁻¹. The mass spectra of the isomers were identical, and showed the molecular ion at m/e 224. N.m.r. spectra were obtained from solutions (10% w/v) in deuteriochloroform with a Varian HA-100 spectrometer, with tetramethylsilane as internal reference (probe temperature ca. 32°).

N.M.R. ASSIGNMENTS AND ANALYSIS

The 100 MHz spectrum of base A is reproduced in the Figure.[†] The simple pattern shows that all three CHMe·CH₂·CH portions must be identical. The protons are easily assigned from splittings and chemical shifts. Protons next to nitrogen atoms occur at lowest field [τ 6.953 (H-3a) and 7.164 (H-2)]; H-2 was identified by the complexity of its signal, due to the interaction with the methyl group. A rather large chemical shift difference is observed between the two methylene proton signals [$\tau 8.093$ (H-3_{eq}) and 8.975 (H- 3_{ax})]. The proton at higher field is partly obscured by the strong methyl doublet (τ 8.896).

The CH·CH₂·CH portion was analysed on an ABXY basis² after removing the effect of the methyl group on the 2-proton resonance. The full spectrum including the methyl group was then calculated on an IBM 360/40

computer. Chemical shifts and coupling constants were varied slightly until a satisfactory agreement between the observed and calculated spectrum was obtained (Figure). The final parameters are summarised in Table 1.

		TABLE 1
Proton	Chemical shift $(\tau \text{ value})$	Coupling constants (in Hz)
3a	6.953	³ I(3a, 3eg) 2.86, ³ I(3a, 3ax) 10.67
3_{eq}	8.093	${}^{2}J(3_{eq},3_{ax}) - 12.81, {}^{3}J(3_{eq},2) 2.92$
3 _{ax}	8.975	$^{3}J(3_{ax},2)$ 11.61
2	7.164	$^{3}J(2, \text{Me}) 6.36$
Me	8·896	

The n.m.r. spectrum of base B showed two identical secondary methyl groups at a similar τ value (8.91) to those of base A and one secondary methyl group at lower field $(\tau 8.77)$. Loss of the threefold symmetry in base B resulted in the superposition of three rather similar n.m.r. spectra, a detailed analysis of which was impossible. The integral measurements indicated that there were six protons, $\tau 6.5$ — 7.3, four τ 8.0–8.4, and eleven (including three methyl groups) τ 8.7–9.1.

DISCUSSION

Tricrotonylidenetetramine contains six asymmetric carbon atoms and one trisubstituted nitrogen atom which should not invert freely in the rigid structure expected. There is consequently a maximum of 128 (27) different configurations possible. Symmetry considerations as well as steric requirements will reduce this number considerably, but conformational differences may lead to an increased number of conformers. The n.m.r. spectrum of base A showed that this isomer has a threefold symmetry. The large difference in chemical shift between the axial and equatorial protons of the methylene group, as well as the magnitude of the vicinal coupling constants indicates that base A exists in one conformation only.

The analysis of the n.m.r. spectrum of base A (Table 1) yielded a large (ca. 11 Hz) and a small (ca. 3 Hz) coupling between each of the methine protons H-3a and H-2, and the methylene group (H-3). Thus³ the dihedral angle between the methine protons and one of the methylene protons (at higher field, τ 8.975) must be near 0 or 180° (J ca. 11 Hz), while the angle with the other methylene proton will be ca. 120 or 60° . Dihedral angles of 0 and 120° would suggest ' boat ' forms for the individual six-membered rings, but this conformation

For convenience, protons referred to as numbered 2-3a in the Figure refer to all three equivalent positions in the case of base A.

¹ M. Delépine, Compt. rend., 1943, 216, 649, 697, 785.

 ² N. V. Riggs, Austral. J. Chem., 1963, 16, 521.
 ³ M. Karplus, J. Chem. Phys., 1959, 30, 11.

can be ruled out as it is of considerably higher energy than the thermodynamically favoured ' chair ' conformation. (Values calculated for cyclohexane 4,5 vary from 5 to 8 kcal./mole, while the flexible 'skew boat', more stable ⁴ by ca. 1.5 kcal./mole, does not show the required dihedral angles.) The ' chair ' form, however, is a rigid strain-free molecule with dihedral angles of 60 and 180° between methine and methylene protons. Both the methine protons H-3a and H-2 are axial and the second-

axial position. An alternative structure for base B involving a *cis*-fusion of one of the rings is shown in (II). Both possibilities would account for the ratio 1:3 in which base A and base B are formed, but we prefer the first explanation, since the difference in conformational energy between axial and equatorial methyl groups 4,7 is only 1.7-1.9 kcal./mole, while a cis-fused molecule should be of much higher energy.*

The n.m.r. spectrum of base B fully supports this



ary methyl group is in an equatorial position as shown in (I). This is the conformation expected to be of lowest energy.6



(I) trans-Fused tricrotonylidenetetramine

The n.m.r. spectrum of base B indicates that one of the methyl groups is in an environment different from that of the methyl groups in base A. This would be expected if one of the methyl groups had moved into an conclusion. The very similar chemical shifts of the methyl groups in base A and of two of the methyl groups



cis-Fused tricrotonylidenetetramine

in base B indicate that there are only minor configurational changes. The lower τ value observed for the ⁵ D. L. Robinson and D. W. Theobald, Quart. Rev., 1967, 21,

- 314.
 ⁶ F. G. Riddell, *Quart. Rev.*, 1967, 21, 364.
 ⁷ M. Hanack, 'Conformation Theory,' Academic Press, New
- ⁸ C. D. Johnson, R. A. Y. Jones, A. R. Katritzky, C. R. Palmer, K. Schofield, and R. J. Wells, *J. Chem. Soc.*, 1965, 6797. ⁹ H. S. Aaron, Chem. and Ind., 1965, 1338.

^{*} trans-Quinolizidine is more stable by 4.4 kcal./mole than its cis-isomer.^{6,8,9}

⁴ E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, Conformational Analysis, 'Interscience, New York, 1965.

third secondary methyl group in base B is in agreement with differences in chemical shifts between equatorial and axial methyl groups observed in a variety of related compounds.¹⁰⁻¹⁴ Further evidence for the configuration of C-2 (Figure) is obtained from the coupling constants. It is often found that CH₃-CH couplings in six-membered rings are slightly larger for axially orientated methyl groups. Although apparent couplings which were strongly affected by second-order perturbations have been quoted in some cases, 12, 15, 16 recent results show that this difference is genuine.^{11,13} We have measured CH_a-CH coupling constants of 6.4 Hz for the equatorial methyl groups in base A and base B (τ 8.91), and of 7.2 Hz for the axial methyl group ($\tau 8.77$) in base B. These values should represent true coupling constants, as they were not affected by the spectrometer frequency (60 MHz and 100 MHz). A detailed examination of the chemical shifts of the ring protons lends further support to the suggested structure of base B. If the τ values of base A are taken as a reference, one can calculate approximate chemical shifts from known substituent effects of alkyl groups in six-membered rings, 10, 11, 13, 17, 18 for a trans-fused tricrotonylidenetetramine with one axial methyl group (Table 2). The overall agreement between calculated and observed τ values is as good as can be expected.

The observation that all three ring-junction protons in base B appear as a four-line pattern with one large and

¹⁰ H. Booth, N. C. Franklin, and G. C. Gidley, Tetrahedron, 1965, **21**, 1077. ¹¹ H. Booth, J. H. Little, and J. Feeney, *Tetrahedron*, 1968,

24, 279.
 ¹² H. Feltkamp, N. C. Franklin, K. D. Thomas, and W. Brügel,

Annalen, 1965, 683, 64.

¹³ A. Segre and J. I. Musher, J. Amer. Chem. Soc., 1967, 89, 706.

TABLE 2

		τ-Value
Proton 3a	Calc. 6.95	Obs. 6·85 (1)
6a 9a	$6.75 \\ 6.75$	$\left. ight\} = 6.7~(2)$
$\begin{array}{c} 3_{eq} \\ 6_{eq} \\ 9_{eq} \end{array}$	8·09 8·09 8·1	} 8.1-8.3 (3)
3_{ax} 6_{ax}	8·98 8·98	} 8.9 (2)
9_{ax}	8.3	8.1-8.3 (1)
2 5	$7.16 \\ 7.16$	brace 7.2 (2)
8	6.7	6 ·9 (1)

one small splitting cannot be reconciled with a *cis*-fused ring system.

Finally, both base A and base B show i.r. bands of comparable intensity at 2730, 2800, and 2840 cm.⁻¹. According to the Bohlmann correlation ^{19,20} these arise from two or more axial CH groups trans to the lone electron pair of a nitrogen atom. These bands could originate from all four nitrogens in base A, from three in the trans-fused structure for base B, but from only one in the alternative structure. The near identity of the i.r. spectra is further evidence for the trans-fused structure.

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¹⁴ T. M. Moynehan, K. Schofield, R. A. Y. Jones, and A. R. ¹⁵ J. I. Musher, Soc., 1962, 2637.
 ¹⁵ J. I. Musher, Spectrochim. Acta, 1960, 16, 835.
 ¹⁶ N. Muller and W. C. Tosch, J. Chem. Phys., 1962, 37, 1167.
 ¹⁷ H. Booth, Tetrahedron, 1966, 22, 615.
 ¹⁸ H. Fatherer and W. C. Tosch, J. Tarakakan, 1967, 21

18 H. Feltkamp and N. C. Franklin, Tetrahedron, 1965, 21, 1541. ¹⁹ F. Bohlmann, Chem. Ber., 1958, **91**, 2157.

²⁰ W. E. Rosen, Tetrahedron Letters, 1961, 482.