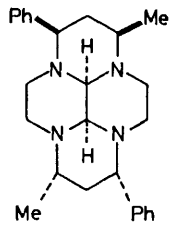
A New Tetracyclic Ring System: the Reaction of Glyoxal with a 1,4,8,11-Tetra-azacyclotetradecane and the *X*-Ray Crystal Structure of the Product

By PETER W. R. CAULKETT, DAVID GREATBANKS, and RALPH W. TURNER*
(*Pharmaceuticals Division, I.C.I. Ltd., Alderley Park, Macclesfield, Cheshire* SK10 4TG)
and JOHN A. J. JARVIS
(*Corporate Laboratory, P.O. Box* 11, *The Heath, Runcorn, Cheshire* WA7 4QE)

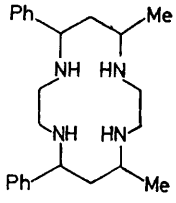
Summary The synthesis of the novel 3a,5a,8a,10a-tetra-azapyrene (**1**) from the macrocycle (**6**) is reported; *X*-ray data for (**1**) confirm its structure, and cause a revision in the previously assigned structure (**2**) of the tetra-azacyclotetradecane starting material.

REPLACEMENT of more than one oxygen atom in crown-ether molecules by an –NH– group gives rise to macrocycles capable of reacting with a variety of electrophiles to produce new ring systems. During an investigation of the chemistry of the 1,4,8,11-tetra-azacyclotetradecane ring system, the reaction of glyoxal with the macrocycle (**2**) was studied. The tetramine (**2**) was synthesised by Lloyd's procedure[1] from benzylideneacetone and ethylenediamine to give the bis-imine (**3**), followed by reduction with sodium borohydride. The *cisoid* structure for (**2**), postulated by Lloyd was supported by chemical degradation and reformation. Treatment of (**2**) with glyoxal in acetonitrile at 60 °C for 30 min gave a 75% yield of a product, $C_{26}H_{34}N_4$, m.p. 164—165 °C (from EtOAc). The ^1H n.m.r. spectrum at ambient temperature in a variety of solvents produced broad signals. Higher-temperature studies at 140 °C in $(CD_3)_2SO$ gave a sharp spectrum showing the two aminal hydrogen atoms as two doublets at δ 3·95 and 3·28, the two benzylic hydrogen atoms at δ 3·86 (t) and 3·60 (dd), and the methyl groups as two doublets at δ 1·05 and 0·70. Four tetracyclic structures, the *cis* and *trans* isomers of (**4**) and (**5**), could be written for the glyoxal reaction product, and therefore a *X*-ray crystallographic study was undertaken.

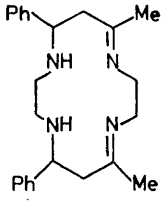
Crystal data: $C_{26}H_{34}N_4$, $M = 402·6$, $a = 11·226(5)$, $b = 7·793(4)$, $c = 27·21(1)$ Å, $\beta = 111·23(8)°$, $U = 2219(1)$ Å^3,



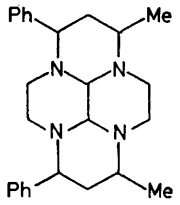
(1)



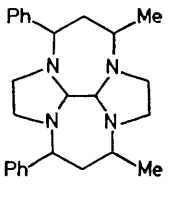
(2)



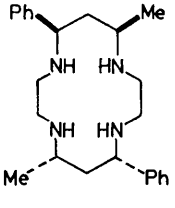
(3)



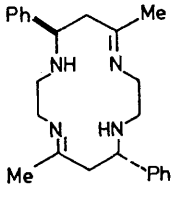
(4)



(5)



(6)



(7)

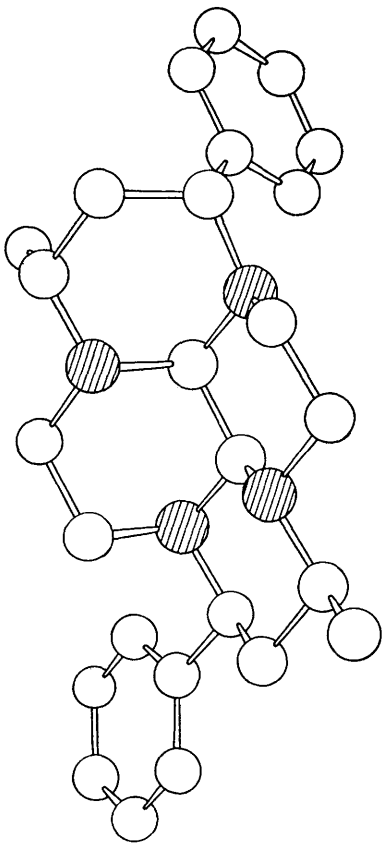


FIGURE. Molecule of the glyoxal product $C_{26}H_{34}N_4$.

space group $P2_1/c$, $D_c = 1{\cdot}205$ g cm^{-3} for $Z = 4$, Mo-K_α radiation (Nb filter).

Cell dimensions and full three-dimensional intensity data ($2\theta \leqslant 45°$) were measured on a Picker automatic diffractometer. The structure was solved by direct methods (MULTAN) and refined with isotropic temperature factors to $R = 0{\cdot}126$ for 1709 reflections. All the peaks on an electron-density difference map were less than 0·6e and were in plausible positions for hydrogen atoms. All bonds in the tetracyclic group were close to the expected values, C–C 1·54 and C–N 1·47 Å, for C–C and C–N single bonds and the bond angles were close to tetrahedral values. A three-dimensional view of the molecule is shown in the Figure.†

The glyoxal product thus possessed the *transoid* structure (**1**) and was not an isomer of the expected *cisoid* structures (**4**) and (**5**), and is the first representative of the perhydro-3a,5a,8a,10a- tetra-azapyrene system. The rings are all chair-shaped, though not all in the same orientation and the two aminal hydrogen atoms are in a *cis*-relationship. The stability of the ring system is reflected in the inertness of (**1**) towards acidic conditions and a variety of reducing agents, properties which contrast with those of simple cyclic aminals.[2,3] A derivative of the related perhydropyrene ring system has been recently described,[4] *X*-ray studies demonstrating that four *trans*-fused cyclohexane rings, all in the chair conformation, form the body of the molecule.

This *X*-ray evidence also suggested that Lloyd's tetramine possessed the *transoid* structure (**6**) rather than the *cisoid* structure and that the bis-imine has the structure (**7**), unless an unprecedented rearrangement occurred either during the borohydride reduction or the glyoxal reaction. Recently Cook[5] has come to a similar conclusion following an *X*-ray examination of a copper(II) complex of Lloyd's macrocycle.

(*Received, 2nd December* 1976; *Com.* 1319.)

† The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

[1] K. Hideg and D. Lloyd, *J. Chem. Soc.* (*C*), 1971, **3441**; O. H. Honkovszhy, K. Hideg, D. Lloyd, and H. McNab, *J.C.S. Chem. Comm* 1974, 378.
[2] R. F. Evans, *Austral. J. Chem.*, 1967, **20**, 1643.
[3] R. C. Northrop, Jr., and P. L. Russ, *J. Org. Chem.*, 1975, **40**, 558.
[4] J. T. Baker, R. J. Wells, W. E. Oberhänsli, and G. B. Hawes, *J. Amer. Chem. Soc.*, 1976, **98**, 4010.
[5] D. C. Cook, *Inorg. Nuclear Chem. Letters*, 1976, **12**, 103.