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TRICYCLIC TETRAAMINES BY GLYOXAL - LINEAR TETRAAMINE CONDENSATION

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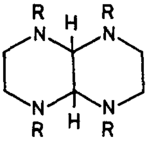
Abstract. New perhydrotetraaza- -naphtacenes, -phenalenes,phenantrenes, etc., have been obtained.The preference of formation of six- over five- and seven-membered ring structures,the *cis-trans* isomerisation,and the ring inversion in *cis*-isomers have been observed.

Glyoxal - polyamine condensations lead in one step to various bicyclic /1/ [1], tricyclic /2/,[2,3] and tetracyclic tetraamines /3/,[4,5,6]



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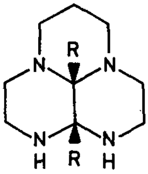

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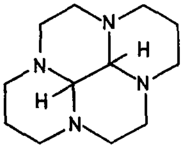

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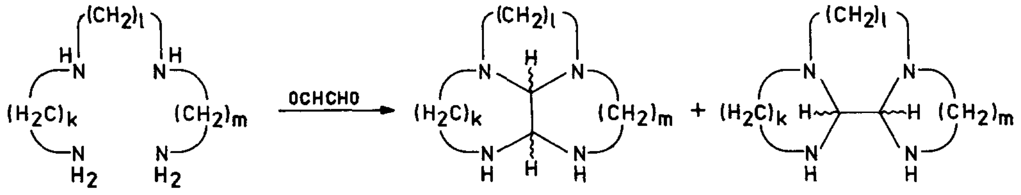
As a part of a general programme of research into the synthesis, stereochemistry, dynamics, and reactivity of polycyclic polyamines we have investigated the condensation of dicarbonyl compounds with linear and cyclic polyamines.We now wish to report that a wide variety of tricyclic tetraamines may be prepared in moderate to good yield by glyoxal - linear tetraamine condensation.Our results for reactions of a homologous series of linear tetraamines /4/ are summarised in the Figure.

Typically,a mixture of 0,01 mole of 4 /commercial reagents or prepared by known procedures / and a slight molar excess of 40% aqueous glyoxal in 50 cm^3 H$_2$O was kept at room temp. for 2-3 days.The reaction mixture was made strongly alkaline with 5 g KOH and extracted with benzene. The crude oily product />50% yield/ was distilled *in vacuo* and crystallised from hexane.



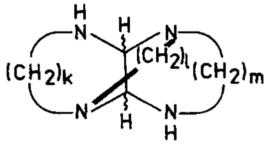
4 5 6

Starting material	k	l	m	Products /%yield/[7]		
4a	2	2	2	cis-5a /22/	+	trans-5a /trace/
4b	2	3	2	cis-5b /84/	+	trans-5b /3/
4c	2	3	3	cis-5c /trace/	+	trans-5c /12/
4d	3	2	3			trans-6d /24/
4e	3	3	3	cis-6e /4?/	+	trans-6e /10?/

Figure

The structure of compounds 5 and 6 was established by I.R., ^1H and ^{13}C N.M.R., and mass spectroscopy, and elemental analysis.[8] The physical constants and spectral data are given in the Table.

Topological considerations revealed that five isomeric compounds could be formed in the reaction: cis-5 and trans-5 by a "vertical" insertion of the CH-CH bridge, cis-6 and trans-6 by a "horizontal" insertion, and 7 by a "cross" insertion of the bridge.



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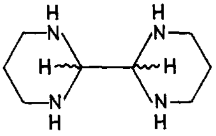

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Symmetry considerations dictate that the bridge hydrogen and carbon atoms of compounds 5 are chemically nonequivalent under any conditions of measurements of N.M.R. spectra /static or fast exchange/. The bridge protons and carbon atoms of cis-6 are chemically nonequivalent only under slow exchange conditions. Those of trans-6 compounds are chemically equivalent under any conditions. The cis-configuration of the bridge protons of compounds 5 was shown by their $^3J_{AB}$= ca.3 Hz

TABLE

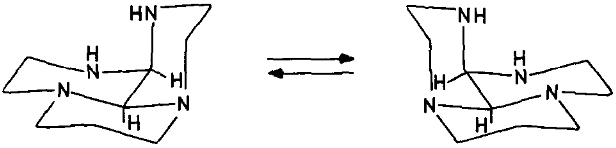
Compound	M.p. °C	M.S. m/e, %	^{1}H N.M.R./δ_H/	^{13}C N.M.R. /δ_C, CDCl$_3$, r. t./		
			NC$\underline{H}$-C$\underline{H}$N	N$\underline{C}$HN	$\underline{C}$H$_2$N	$\underline{C}$H$_2$/CH$_2$/$_2$
cis-**5a**	63-65	M$^+$168 /48/ 96/100/	3.98d/1H/ 2.91 dec. J = 2.8 Hz	77.17 66.07	50.64/2C/ 42.39	---
trans-**5a**	120-125		1.59d/1H/ J = 7.0 Hz			
cis-**5b**	98-99	M$^+$182/100/ 110 /50/	3.61d/1H/ 3.11 dec. J = 2.5 Hz	77.24 67.14	54.44br 50.02br	19.68
trans-**5b**	149-150	M$^+$182 /79/ 110/100/	3.35d/1H/ 1.73d/1H/ J = 7.0 Hz	88.46 71.62	55.17 54.08 43.96	24.42
trans-**5c**	123-124	M$^+$196 /66/ 111/100/	3.29d/1H/ J = 7.0 Hz	89.65 75.18	56.54, 55.07 54.76, 51.76 45.12, 44.88	31.49 24.43
trans-**6d**	103-105	M$^+$196 /5/ 112/100/	2.49s/2H/	79.43	54.79, 52.66 45.02	26.69
trans-**6e**	92-93	M$^+$210 /10/ 126/100/		84.39	56.55, 52.96 44.45	26.63 28.16
cis-**6e**[12]				78.11	55.53, 51.06 45.12	27.19 22.36

and the *trans*-configuration by $^3J_{AB}$= ca.7 Hz.The *trans*-configuration was ascribed to compounds **6** as their spectra are temperature independent. Computer assisted analysis of the P.M.R. spectrum of **6d** afforded $^4J_{1Heq,\ 3Heq}$= 2.0 Hz and fully corroborated the assignment.

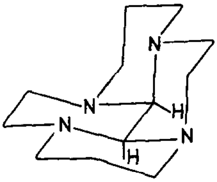
The structures of compounds obtained in this work, as well as those obtained from condensation of glyoxal with linear diamines /ethylenediamine,[1,3] /**1**/,trimethylendiamine[9] /**8**/ / and macrocyclic tetraamines[4,5,6] suggest that *products containing as many six-membered rings as possible are preferentially formed*.

We observed isomerisation of compounds *cis*-**5** with *trans*-**5**.A quantitative isomerisation of *cis*-**5b** into *trans*-**5b** was achived, as followed by P.M.R. spectroscopy, by the action of 1% aqueous H_3PO_4 in 24 hr. The isomerisation occurs probably by the ring opening mechanism.[10] This finding poses the question, are the *trans*-**5** isomers isolated from the reaction mixtures the primary products of the condensation, or are they artefacts formed by isomerisation of *cis*-isomers.

The temperature dependence of ^{1}H and ^{13}C N.M.R. spectra of *cis*-**5** compounds was observed indicating a ring inversion processes occuring in these compounds over 200°K. The interconversion occurs between two enantiomeric equally populated conformers, for instance *cis*-**5b** and *cis*-**5b′**. It involves an inversion of the two tertiary nitrogen atoms together with a change of the sign of the bridge protons dihedral angle and it is closely related to the inversion of *cis*-perhydrotetraazapyrene /**3**/[6,11]



cis-**5b** *cis*-**5b′**



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The full conformational analysis and the study of ring inversion of this interesting class of compounds are in progress.

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[7] The yield of analytically pure main isomers calculated on the starting linear tetraamine.

[8] Suitable C, H, and N elemental analyses were obtained for all compounds exept **5a** which is to hygroscopic to be exactly weighted.

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[12] The isomer was not isolated pure.

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