SYNTHESIS AND STRUCTURAL ANALYSIS OF -2,4,6,8-TETRABENZYL -2, 4, 6, 8- TETRAAZABICYCLO [3.3.0] OCTANE FROM CONDENSATION OF GLYOXAL, BENZYLAMINE AND FORMALDEHYDE

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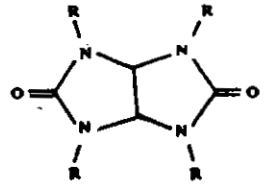
ABSTRACT : *The condensation of glyoxal with benzylamine in the presence of formaldehyde leads to 2, 4, 6, 8- Tetrabenzyl- 2, 4, 6, 8- Tetraazabicyclo [3.3.0] octane (6) in methanol. The scopes and limitations of the reaction have been determined. At low temperatures, a mixture of (6) and diol (7) is formed.*

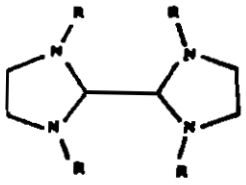
KEY WORDS : *Tetraaza - bicyclo [3.3.0] octane, Syn- dienvelope, Polyazapolycyclic*

INTRODUCTION:

The condensation of aldehydes with amines are reported to give polyazapolycyclic cage compounds.For example,the reaction of ammonia with formaldehyde produces hexamethylen-tetramine of the adamantanoid type cage structure. Recently, glycoluril *(1)* and its derivatives were synthesized via the condensation of glyoxal and urea [1-5]. Similarly glyoxal and ethylenediamine were condensed to give biimidazolidine *(2)* together with other products [6-8].



R=Alkyl , Aryl, ...
(1)



$R=C_6H_5$, $C_6H_5CH_2$-
(2)

* Correspoonding author

The reaction of anilines with glyoxal to form N, N, N, N- tetrasubstituted ethylene *(4)* has been previoulsly reported [10, 11]. Similar condensation reactions with other amines lead to formation of diimines *(5)* [9, 12, 13].

$$2RNH_2 + OCHCHO \longrightarrow R - NH - CHOH - CHOH - NH - R$$

(3)

$$(3) \xrightarrow{2RNH_2} \begin{matrix} RNH & & NHR \\ & \diagdown\ \diagup & \\ RNH & & NHR \end{matrix}$$

(4)

R = C_6H_5, O– ClC_6H_4,

$$2RNH_2 + OCHCHO \longrightarrow (3) \longrightarrow R - N = CH - CH = N - R$$

(5)

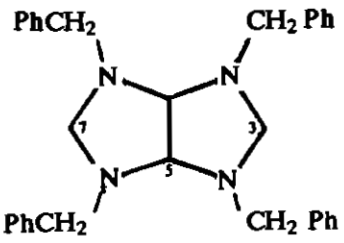
R = Alkyl , Aryl

In this report we describe a facile condensation of glyoxal with benzylamine and formaldehyde to produce a new tetraazabicyclo ring system 2, 4, 6, 8- tetrabenzyl- 2, 4, 6. 8- tetraazabicyclo [3.3.0] octane *(6)*. This and other tetraazapolycyclic derivatives are useful as precursors in the preparation of energetic materials.

RESULTS AND DISCUSSION:

The new condensation of glyoxal with benzylamine in the presence of formaldehyde in acidic media gives white crystals of (6) according to the following equation.

$$4PhCH_2NH_2 + OCHCHO + 2CH_2O \xrightarrow[CH_3OH]{H_3O^+} (6)$$



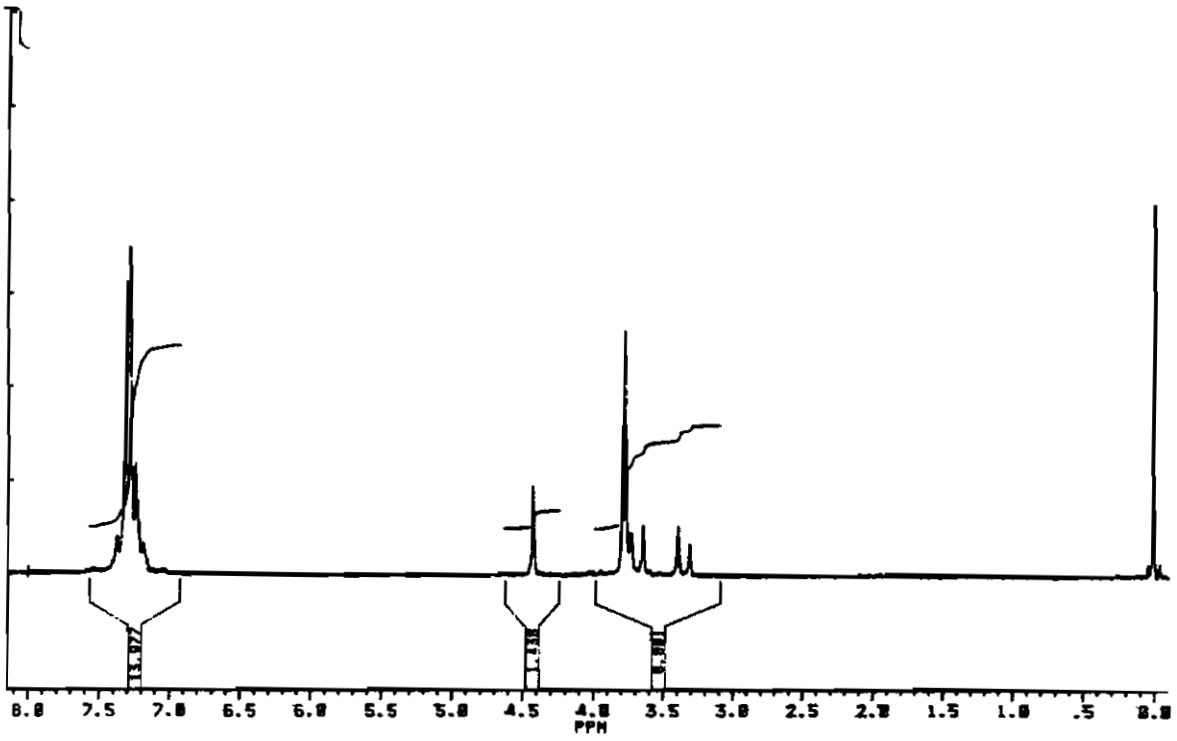
(6)

This reaction is limited to benzylamine and certain phenyl substituted amines. Primary aliphatic amines usually form dicarbinolamines *(3)* or diimines *(5)* [9-13]. Stoichiometric quantities of benzylamine and formaldehyde with 30% aqueous glyoxal in methanol solvent at 20°C leads to *(6)*. Acid catalysts such as formic acid (0.1 mole%) is added to the reaction mixture to keep the pH in the range 9-9½. The reaction is fast and is completed within a few hours. Crystalline *(6)* seperates from the reaction mixture and is recovered by recrystallization from acetonitrile solvent. Best yields (75 - 80%) are obtained at pH= 9-9½ but drastically reduced under highly basic or acidic condition (10 > pH > 7). Yield is very sensitive to the reaction temperature and optimum results are obtained in the range of 15-20°C. The reaction stays incomplete at 0°C giving a mixture of product in diol *(7)*. The white needle crystals melt at 81-83°C and contain 81.180% C, 7.28 %H and 11.51 %N.

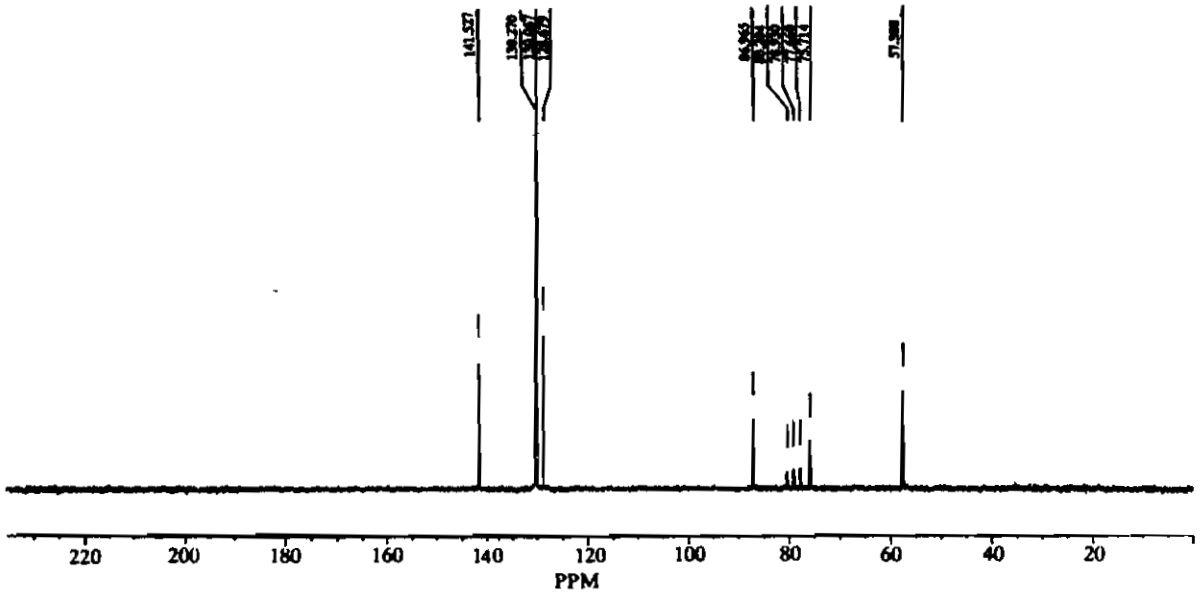
A characteristic molecular ion peak (M + 1) is seen at 475 m/e in the chemical ionization mass spectrum of *(6)*. The 100% peak, m/e = 91 is believed to be the mass of Benzyllium ion and the peak at m/e=237 is believed to be the (M+ 1) ion of N, N' - dibenzyl - 1, 2- ethanediimine *(9)*. These results suggest a molecular formula of $C_{32}H_{34}N_4$ for *(6)*. The isolated *(6)* was further characterized by NMR and IR spectroscopies.

Characteristics of the proton spectra are a singlet peak for the two ring methine protons at δ4.43 . Also seen are the two doublets of methylene protons near δ3.3 and δ3.7 (J=8 Hz). Signals belonging to eight adjacent benzyl methylene protons appear at δ3.8. The ^{13}C - NMR spectra reveals a signal for the two ring methinic carbon atoms at 86.9 ppm. Also seen is the signal corresponding to benzyl methylene carbons at 57.4 ppm and ring methylene carbons at 75.7 ppm. The IR (KBr) spectra shows absence of N-H and C=O bands.

The formation of tetraazabicyclooctane *(6)* is believed to first go through diol *(7)* which can be isolated at 0°C (Scheme 1). When formal-

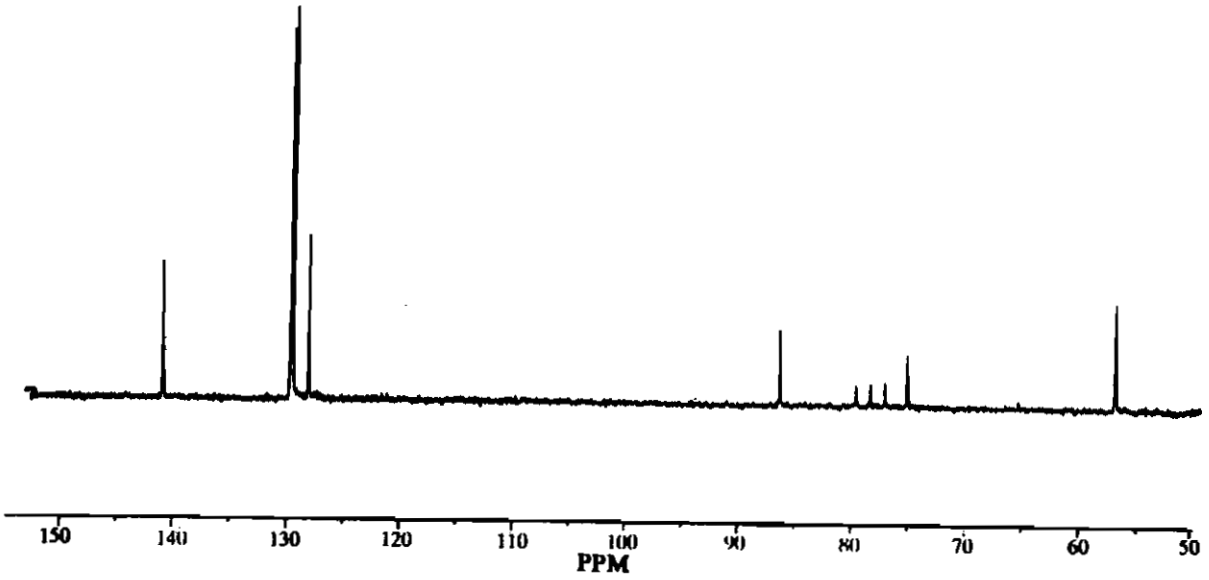


^1H - NMR spectrum of compound (6)



^{13}C - NMR spectrum of compound (6) (Decop)

dehyde is present, the diol *(7)* further reacts with additional amines [9-13] to give tetramine *(8)* which is then rapidly cyclized to *(6)*. In the absence of formaldehyde and under acidic conditions diol *(7)* dehydrates rapidly to give diimine *(9)*. In the case of benzylamine, diimine *(9)* is trimerized to yet another polyazapolycyclic product, which will be reported separately.



^{13}C - NMR spectrum of compound (6)

Scheme 1

$$2C_6H_5CH_2NH_2 + OCHCHO \longrightarrow C_6H_5CH_2NHCHOHCHOHNHCH_2C_6H_5$$

(7)

$$(7) \xrightarrow{2C_6H_5CH_2NH_2} \begin{matrix} C_6H_5CH_2NH & & NHCH_2Ph \\ & \diagdown\ \diagup & \\ C_6H_5CH_2NH & & NHCH_2Ph \end{matrix}$$

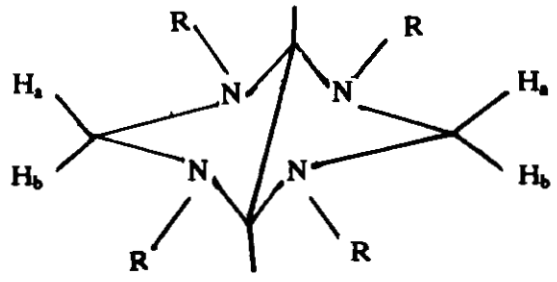
(8)

$$(8) \xrightarrow{CH_2O} (6)$$

$$(7) \xrightarrow{H^+} C_6H_5CH_2N = CHCH = NCH_2C_6H_5$$

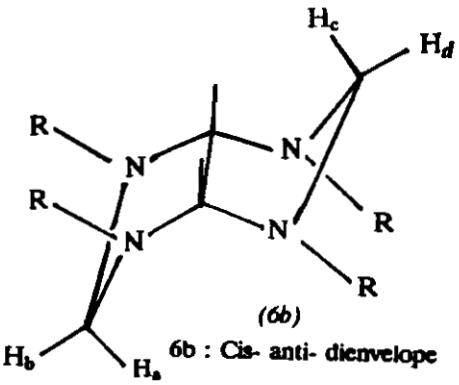
(9)

For compound *(6)* three possible conformers exist, trans *(6a)*, anti *(6b)* and syn *(6c)*. These can be distinguished by the coupling pattern of hydrogens of the ring and from the results of ^1H and ^{13}C-NMR spectra.



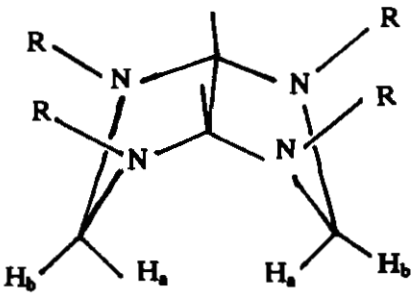
(6a)

R = $C_6H_5CH_2$



(6b)

6b : Cis- anti- dienvelope

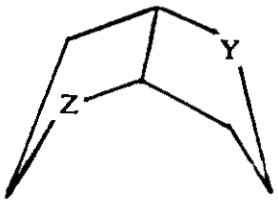


(6c)

6c: Cis- syn- dienvelope

The ^1H-NMR spectra of *(6)* shows two doublets of equal intensity for methylene protons 3 and 7. This clearly indicates an AB system and hence protons A and B resonate in non- equivalent environment. The trans structure *(6a)* is ruled out since it has a rotational symmetry (C_2) and mirror planes by which the protons 3 and 7 are interchanged and therefore the coupling of protons at 3 and 7

should not be observed by ^{1}H-NMR spectroscopy; Moreover the structural consideration of *(6a)* shows increased strain at the molecular level that makes the formation of *(6a)* very unlikely. Also the NMR data do not conform with coupling of methylene protons 3 and 7 in the anti form *(6b)* which are predicted to resonate in an AB, CD system. The syn-conformation *(6c)* agrees completely with ^{1}H-NMR results and must be the most stable of the three structures. There are several reports regarding the stability of the syn- conformation in similar bicyclooctane derivatives. For example [10] and its derivatives [6,7] show a syn-envelope conformation and are energetically more stable.



(10)

Z = Y = O, S, NH, NR

Based on the NMR results and in the absence of X- ray data the cis structure with a syn- envelope conformation is proposed for 2, 4, 6, 8- tetrabenzyl- 2, 4, 6, 8- tetraazabicyclo [3.3.0] octane.

EXPERIMENTAL:

Materials

Glyoxal, formaldehyde and amines were obtained from the Merck, Inc. and were all synthesis grade.

Instruments

MS analysis of the product was conducted on a Finnigan Matt 8430 GC - MS spectrograph equipped with a Propak column. NMR experiments were run via a Brucker AE100 MHz and the IR (KBr) spectra were obtained via a Shimadzu 4300 FT- IR spectrophotometer. All elemental analysis were done with C, H, N, O-rapid Hereous analyser and the melting points were determined with a Gallenkamp instrument.

Synthesis of 2, 4, 6, 8- tetrabenzyl- 2, 4, 6, 8- tetraazabicyclo [3.3.0] octane (6)

A Solution of benzylamine (5.4 g, 50 mmole), formic acid (0.27 g, 5.25 mmole), distilled water (1.8 ml) and methanol (50 ml) were prepared in a 250 ml flask. To this solution at 20°C and while being continiously stirred was added glyoxal (2.42 g 30% , 2.5 mmole) dropwise and then formaldehyde (2.03 g 37%, 25 mmole) was added gradually in a period of ten minutes. The solution was stirred for an additional sixty minutes and cooled subsequently to 0°C until white precipitates were formed. The precipitates were then filtered and the filtrate concentrated to get residual precipitates. Overall yield: 4.74 g (79.1%) of crude product mp 74 - 77°C. Recrystallization in aceto- nitrile yielded white pure crystals of *(6)* (4.53 g, 75%) mp 81- 83°C.

Anal. calc for $C_{32}H_{34}N_4$

C, 81.18% H, 7.28; N, 11.51. Found: C, 80.98; H, 7.22; N, 11.80.

^{1}H-NMR: ($CDCl_3$), δ3.345 (d, 2H, J= 8 Hz, $H_{3,7}$)δ3.7 (d, 2H, J= 8 Hz, $H_{3,7}$) δ3.79 (S, 8H, -CH_2-Ph)δ4.43 (S, 2H, $H_{1,5}$) δ7.22 (S, 2OH, C_6H_5).

^{13}C-NMR: ($CDCl_3$) 57.39 ppm (4C, -CH_2-Ph)75.71 ppm (2C, 3.7) 86.96 ppm (2C, 1, 5) 128.68 ppm (4C, Para) 130.08 ppm (8C, Ortho) 130.27 ppm (8C, Meta) 141.53 ppm (4C, Ipso).

GC - MS: m/e (rel. intensity) 475 (MH^+, 4%) 384 ($C_{25}H_{27}N_4^+$, 10%). 91 (Ph-CH_2^+, 100%).

IR (KBr): N - H and C = O bands were absent.

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REFERENCES:

[1] Pinner, A., *Chem. Ber.*, 1997 (1887).
[2] Bottinger, C., *Chem. Ber.*, 10 (1923).
[3] Mock, W. L., Manimaran, T., Freeman, W. A., Kuksuk, R. M., Maggio, J. E. and Williams, D. H., *J. Org. Chem.* 50, 60 (1985).
[4] Freeman, W. A., Mock, W. L., and Shih, N. Y., *J. Am. Chem. Soc.*, 103, 2307 (1981).
[5] Smeets, J. W. H., Sijbesma, R. P., Niele, F. G., Spek, A. L., Smeets, W. J. J., and Nolte, R. J. M., *J. Am. Chem. Soc.* 109, 928 (1987).
[6] Wanzlick, H. W., and Lochel, W. L., *Chem. Ber.* 86, 1463 (1953).
[7] Wanzlick, H. W., Liebiegs, *Ann. Chem.* 195, 196-8 (1975).
[8] Willer, R. L., and Moore, D. W., *J. Org. Chem.* 50, 2365 (1985).
[9] Kliegman, J. M., and Barnes, R. K., *Tetrahedron*, 26, 2555 (1970).
[10] Kliegman, J. M., and Barnes, R. K., *J. Org. Chem.* 35, 3140 (1970).
[11] Kliegman, J. M., and Barnes, R. K., *J. Hetero. Chem.* 7, 1153 (1970).
[12] Tom Dieck, H., and Renk, I. W., *Chem. Ber.* 104, 92 (1971).
[13] Tom Dieck, H., Dietrich, J., *ibid.* 117, 694 (1984).
[14] Cope, A. C., and Shea, T. V., *J. Am. Chem. Soc.* 78, 5912, *ibid* 5916 (1956).
[15] Jeffrey, G. A., and Kim, S. H., *Chem. Commun.* 211 (1966).
[16] Riddell, G., "The Conformational Analysis Of Heterocyclic Compounds" Academic Press (1980).