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PHYSICAL CHARACTERISATION OF THE NEW BIS (BENZYLPIPERIDINES)††

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1, 4-dichloromethylbenzene; 1,4-dichloromethyl-2, 5-dimethylbenzene; 1,3-dichloromethyl-4,6-dimethylbenzene and 1,4-dichloromethyl-2, 3, 5, 6-tetramethylbenzene were condensed with a saturated heterocyclic amine, 4-benzylpiperidine in absolute ethyl alcohol. Compounds listed below were prepared:

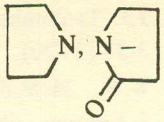
α' α' -*Bis*(benzylpiperidino)-*p*-xylene,
α, α' -*Bis*(benzylpiperidino)-2, 5-dimethyl-*p*-xylene,
1, 3 -*Bis*(benzylpiperidino)-4, 6-dimethyl-*m*-xylene
α, α' -*Bis*(benzylpiperidino)-2, 3, 5, 6-tetramethyl-*p*-xylene

An attempt has been made to characterise these compounds through physico-chemical studies.

INTRODUCTION

Since the compounds having piperidines rings had little influence on biological activity [1, 2] the authors synthesised more new diamines in having the benzyl group at the 4-position of the piperidine [3].

The structure of tremorine was earlier modified as follows:

R_1 $-CH_2-C$ and $C-CH_2R_2$, where R_i = 

and

$R_2 = -OOCH_3$ [4], $-NHC_3H_7$ [5] and $-N(CH_3)_3$ [6]

EXPERIMENTAL

1,4-dichloromethylbenzene, 1,3-dichloromethyl-4, 6-dimethylbenzene, 1,4-dichloromethyl-2, 5-dimethylbenzene and 1, 4-dichloromethyl-2, 3, 5, 6-tetramethylbenzene (dichlorodurene). 1 mole each was condensed with 2 moles *N*-benzylpiperidine, using a reflux condenser, 15 ml. absolute ethanol (medium) and heating for 4-6 hr. over an electric bulb (40W).

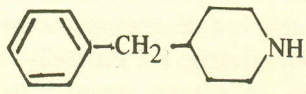
The product was cooled, filtered, washed with cold ethyl alcohol and dried in oven at 40°.

Bis-amino hydrochlorides thus obtained were characterised and were then converted into free amines.

This hydrochloride of the amine was dissolved in *iso*butyl alcohol and neutralised with 0.1N aqueous NaOH till the pH of the reaction mixture was 7.00 (pH paper).

Precipitated free amine was extracted with diethyl ether, dried over calcium chloride and filtered. The filtrate on concentration and cooling gave crystals of the free base, which was dried in a vacuum desiccator.

Reagents used. 1,4-dichloromethylbenzene; 1,4-dichloromethyl-2, 5-dimethylbenzene, 1,3-dichloromethyl-4, 6-dimethylbenzene and 1,4-dichloromethyl-2, 3, 5, 6-tetramethylbenzene were synthesised in the laboratory [7, 8].

N-Bennzylpiperidine 

used was Fluka product, m.f. $C_{12}H_{17}N$, m.w. 175, b.p.760 = 279° n_D^{20} = 0.9972 (found); n_D^{20} = 0.9972 [lit. 7].

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†† Romanian patent No. 66758 dated 13.12.1977.

(Research conducted in the laboratories of the faculty of Pharmacy, Bukharest, Romania)

RESULTS

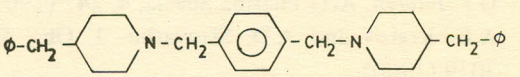
1 (a). *α,α' Bis (benzylpiperidino)-p*-xylene. m.p. 135-36°; found C,84.90; H,8.90; N,6.18; $C_{32}H_{40}N_2$; requires, C,85.20; H,9.01; N,6.14. λmax. (C_2H_5OH) 247, 254, 266.7 nm; √C-N (KBr) 1130, 1100 cm^{-1}.

Hydrochloride of i (a). yield 55.22%; m.p. 195-201° (subl.);found, C,73.12; H, 8.05; N, 5.32; $C_{32}H_{42}N_2Cl_2$; requires, C, 73.41; H,8.29; N, 4.96; λmax. (water) 218.3 sh, 222, 238, 271sh; $\sqrt{\overset{\oplus}{\underset{1}{N}}H}$, 2750, 2375 cm^{-1}.

2.a. α, α' -Bis(benzylpiperidino-2, 5-dimethyl)-p-xylene. – M.P. 137-39°; found, C,84.94; H,9.22; N,5.90; $C_{32}H_{44}N_2$; requires, C,84.89; H,8.94; N,5.90. λmax. (C_2H_5OH) 236, 274 nm $\sqrt{\underset{1}{NH}}$ (KBr) 1130, 1100 cm^{-1}.

2.b. Hydrochloride of 2. a. Yield, 48.08%; m.p. 198-202°; found C,73.76; H, 8.37; N, 5.06; $C_{34}H_{46}N_2Cl_2$; requires, C,73.55; H, 8.07; N, 5.06%. λmax (water) 236, 274 nm; $\sqrt{\overset{\oplus}{\underset{1}{N}}H}$(KBr) 2790, 2375 cm^{-1}.

I)



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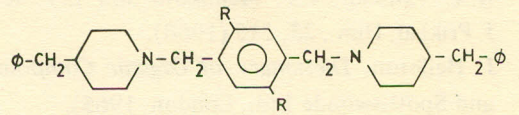
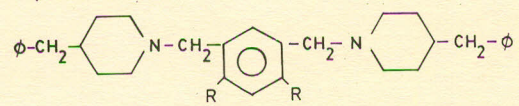
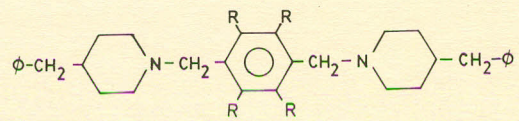


III)



IV)



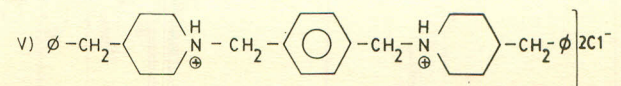
3. a. 1,3-Bis(benzylpiperidino)-4,6-dimethyl-m-xylene. – M.P. 124-25° ; found, C, 84.94; H, 9.22; N, 5.82; $C_{34}H_{44}N_2$; requires, C,84.87; H, 9.01; N, 5.71. λmax. (C_2H_5OH) 217, 267, 275.5 nm; √C-N (KBr) 1140 cm^{-1}.

3. b. Hydrochloride of 3.a. – Yield, 44.08 %, m.p. 155-56° (subl.); found, C,73.76; H,8.37; N,5.06; $C_{34}H_{46}N_2Cl_2$; requires, C,73.83; H, 8.49; N, 5.11%. λmax. (water) 217, 255(sh), 259.7, 268.8 nm; $\sqrt{\overset{\oplus}{\underset{1}{N}}H}$ (KBr) 2375 cm^{-1}.

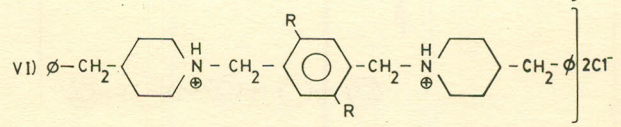
4. a. α, α' -Bis(benzylpiperidine) -2, 3, 5, 6-tetramethyl-p-xylene. – M.P. 190-92°c, found, C 84.98; H, 9.50; N, 5.50; $C_{36}H_{48}N_2$; requires, C,85.29; H, 9.23; N, 5.39 %. λmax. (C_2H_5OH) 218, 227, 278nm √C-N (KBr) 1120, 1105 cm^{-1}.

Hydrochloride of 4.a. – Yield, 50%, m.p. 193-95° (subl.); found, C, 74.32; H, 8.66; N, 4.81; $C_{36}H_{50}N_2Cl_2$; requires, C, 74.43; H, 8.74; N,4.33 %. λmax. (water), 218.8, 264, 268.8, 290.7 nm; $\sqrt{\overset{\oplus}{\underset{1}{N}}H}$ (KBr), 2780, 2735 cm^{-1}.

V)

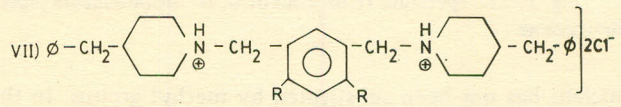


VI)

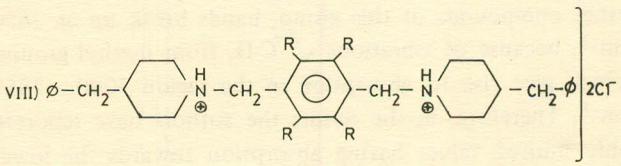


R = -CH_3

VII)



VIII)



DISCUSSION

Substitution with benzyl group results in the rise of the melting points of the diamines as compared to the unsubstituted diamine [3]. On the other hand melting points of the hydrochlorides of the benzyl substituted diamines are lowered as compared to the hydrochlorides of the piperidino compounds [3].

The solubility of the hydrochlorides of *bis*(benzylpiperidino)-xylenes in water was found to be lower than that of the hydrochlorides of *bis*(piperidino)xylenes. In fact, the former are soluble in organic solvents.

The IR spectra of *α, α' -bis(4-benzylpiperidino)* xylenes show that for C-N vibrations, two bands are found at 1120-1140 cm^{-1} and at 1105 - 1100 cm^{-1} 4-Benzylpiperidino itself presents a band at 1180 cm^{-1} (√C-N).

Compared to the spectra of diamines prepared from piperidine, those of the diamines obtained from 4-benzylpiperidine have an additional band. This is due to vibrations √C - C from the benzene ring (Fig. 1).

Hydrochlorides of *α, α' -bis(*4-benzylpiperidino)xylenes have very powerful/strong absorption in the same region of IR spectrum in between 2790 and 2375 cm^{-1}.

The maximum value is 2750 cm^{-1} in the case of α, α' -*bis*(4-benzylpiperidino)-*p*-xylene in which the central

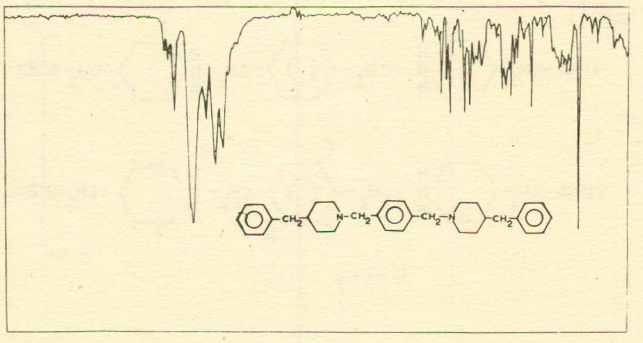


Fig. 1. I.R. spectrum (KBr disc) of α, α' -bis(4-benzyle piperidino xylene.

nucleus has not been substituted by methyl groups. In the other compounds of this group, bands break up at 2850 cm^{-1}, because of vibrations $\sqrt{}$C-H, from methyl groups, which give rise to absorption in the region 3000 - 2850 cm^{-1}. Therefore, in the results the authors have reported only limited values having absorption towards the lower number of waves.

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