Tetrahedron, 1963, Vol. 19, pp. 869 to 872. Pergamon Press Ltd. Printed in Northern Ireland

SYNTHESES OF SOME SUBSTITUTED HEXAMINES IN AQUEOUS MEDIUM

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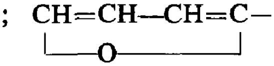
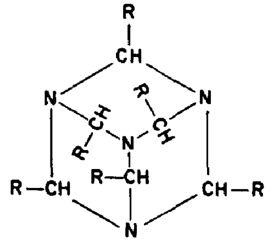
(*Received* 28 *November* 1962)

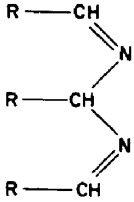
Abstract—Hexamines are obtained when aromatic, substituted aromatic and heterocyclic aldehydes are suspended in aqueous ammonium carbonate solution (10%, pH 9·2) for 15–20 days.

IN CONTINUATION of our work in aqueous medium, the reaction of various aldehydes with 10% aqueous ammonium carbonate solution—(pH 9·2) has been studied. The preliminary findings were reported in the form of a note[1]. In the present communication a detailed account of the syntheses of the hexamines along with the preparation of *m* and *p*-nitrophenylhydrobenzamides is reported.

A number of aromatic aldehydes when allowed to stand with aqueous ammonia (in 10% ammonium carbonate solution; (pH 9·2) for 10–15 days yield condensation products the analyses of which agree with both hexa-substituted hexamines (I; R = $C_6H_5^-$; *p*-$CH_3O–C_6H_4^-$; *o*-$HO–C_6H_4^-$; *o*-$Cl.C_6H_4^-$;  $CH{=}CH{-}CH{=}C{-}$ (ring closed through O); *m*-$NO_2.C_6H_4^-$ and *p*-$NO_2.C_6H_4^-$) and their corresponding hydrobenzamides (II), the molecular formulae of the hexamines being twice the molecular formulae of the corresponding hydrobenzamides.



I



II

All the hexamines obtained under these conditions, crystallize well and are completely different from their hydrobenzamides in chemical properties. The *m*- and *p*-nitro-hydrobenzamides were prepared for the first time in accordance with the method of Mignonac[9], the aldehyde was reacted in alcohol containing ammonia and ammonium chloride. The optimum pH which plays an important role in these condensations, is 12·0. Except in cases where a nitro group is present in the aromatic ring, and is reduceable, none of the hexamines obtained are reduced in the presence of 5% pd–charcoal or Raney-nickel, even at elevated temperatures and pressure indicating the absence of —C=N— group as distinct from hydrobenzamide which is reduced

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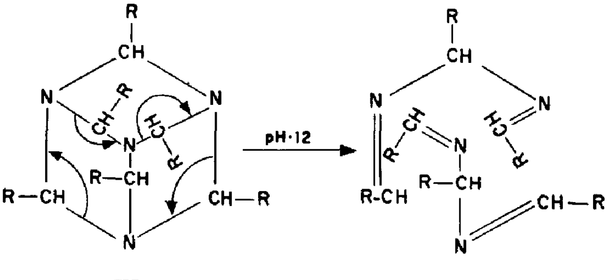
with Raney-nickel catalyst to a mixture of the corresponding benzylamine and benzalbenzylamine.[2] The compounds decompose slowly on standing (3–6 months), and immediately in acid medium (pH 5), the free aldehydes being regenerated. Molecular weight determinations (Rast) failed to give any indication of molecular weight as the compounds undergo decomposition on heating. However, on the basis of theoretical considerations, chemical properties and U.V. spectra (different from those of the corresponding hydrobenzamides) it was reasonable to regard these compounds as substituted hexamines (I) hitherto not reported.

These hexamines are easily converted to their corresponding hydrobenzamides. For instance when the hexamines: (I; R = $C_6H_5^-$; p-CH_3O–$C_6H_4^-$; o-HO–$C_6H_4^-$; o-$Cl.C_6H_4^-$; $\underbrace{\mathrm{CH{=}CH{-}CH{=}C{-}}}_{\mathrm{O}}$; m-$NO_2.C_6H_4^-$ and p-$NO_2.C_6H_4$) are dissolved in 95% ethanol containing ammonium chloride and liquid ammonia added to adjust pH to pH 12·0, the corresponding hydrobenzamides: (II; R = $C_6H_5^-$ (m.p. 102°C.[3] p-CH_3O–$C_6H_4^-$ (m.p. 125°C.)[4]; o-HO—$C_6H_4^-$ (m.p. 164°C.)[5]; o-$Cl.C_6H_4^-$ (m.p. 98°C.)[4]; $\underbrace{\mathrm{CH{=}CH{-}CH{=}C{-}}}_{\mathrm{O}}$ (m.p. 117°C.[6]; m-$NO_2.C_6H_4^-$ (m.p. 145°C.) and p-$NO_2.C_6H_4^-$ (m.p. 75°C.) are obtained, identical with authentic samples. This conversion may be explained as follows:



III IV

Attempted condensations at pH 5·3 (i.e., 10% aqueous ammonium sulphate solution) and at pH 7·1 (i.e., 10% aqueous ammonium acetate solution) resulted in unchanged aldehydes even after 20 days.

Unlike hexamine, all the C-substituted hexamines fail to give salts with picric acid and hydrochloric acid as they decompose into their components in even slightly acidic media.

EXPERIMENTAL

All points are corrected. U.V. absorption spectra were determined with a Beckman Spectrophotometer Model D.B.

Syntheses of hexamines

General method. The aldehyde (0·006 mole) was added to an aqueous ammonium carbonate solution (10%; 50 ml; pH 9·2); and shaken for ½ hr. After keeping 20 days at room temp. the condensation product, if solid, was filtered off, but if oily, it was isolated by means of ethyl acetate and recrystallized from an appropriate solvent.

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2,4,6,8,9,10-*Hexaphenyl-hexamine.* Benzaldehyde (0·64 g; 0·006 mole) yielded a crystalline product; m.p. 110°, 0·42 g; (69·9%) which recrystallized from ethanol in long microscopic colourless needles; 0·38 g, (64%); m.p. 115°. (clear melt).

It is easily soluble in acetone, benzene, chloroform, ethyl acetate, ether; sparingly in ethanol and methanol, and insoluble in water, ligroin and light-petroleum (60–80°). It decomposes on standing. Found: C, 84·15; H, 6·12; N, 9·54, $C_{42}H_{36}N_4$; (M.W. 596); requires: C, 84·53; H, 6·08; N, 9·39%. Its U.V. absorption bands are at λ_{max} 233 mμ (log ε 4·7) and 271 mμ (log ε 4·65) and λ_{min} at 255 mμ (log ε 4·58) with shoulder at 278 mμ (log ε 3·61); hydrobenzamide shows absorption at λ_{max} at 235 mμ (log ε 4·66) and 205 mμ (log ε 4·76) and λ_{min} at 278 mμ (log ε 4·72) and 208 mμ (log ε 3·32).

2,4,6,8,9,10-*Hexa-(4′-methoxyphenyl)-hexamine.* Anisaldehyde (0·816 g; 0·006 mole) yielded an oily product; 0·39 g (49%) which crystallized from ethyl acetate–ligroin in light brown needles; 0·36 g; (46%); m.p. 158° (clear melt). It is easily soluble in acetone, benzene, chloroform, ethyl acetate, ether and insoluble in light-petroleum (60–80°). It decomposes on standing. (Found: C, 74·42; H, 6·10; O, 12·36; N, 7·26; $C_{48}H_{48}O_6N_4$; (M.W. 776); requires: C, 74·20; H, 6·23; O, 12·36; N, 7·21%).

2,4,6,8,9,10-*Hexa-(2′-hydroxyphenyl)-hexamine.* Salicylaldehyde (0·73 g; 0·006 mole) yields an oily product; 0·45 g; (65%) which crystallized from methanol in golden yellow prisms; 0·43 g; (62%); m.p. 130° (clear melt). It is easily soluble in acetone, benzene, chloroform, ethyl acetate; sparingly soluble in ethanol and methanol and insoluble in water and light petroleum (60–80°) and decomposes on standing. (Found: C, 72·75; H, 5·60; O, 13·92; N, 8·00; $C_{42}H_{36}O_6N_4$; (M.W. 692); requires: C, 72·82; H, 5·24; O, 13·86; N, 8·09%). It shows U.V. absorption bands at λ_{max} 255 mμ (log ε 4·73); 206 mμ (log ε 4·79) and λ_{min} 279 mμ (log ε 3·54) and 233 mμ (log ε 4·04). Hydrosalicylamide: λ_{max} at 254 mμ (log ε 4·68) and 206 mμ (log ε 4·54) and λ_{min} at 280 mμ (log 3·32) and 237 mμ (log ε 4·06).

2,4,6,8,9,10-*Hexa-(2-′chlorophenyl)-hexamine.* *o*-Chlorobenzaldehyde (0·84 g; 0·006 mole) yielded a crystalline product; 0·78 g; (97·5%); m.p. 78° which recrystallized from ethyl acetate and light-petroleum (60–80°) in long colourless needles; 0·73 g; (91%); m.p. 81° (clear melt). It is easily soluble in acetone, benzene, chloroform, ethanol and methanol, sparingly soluble in ethyl acetate and water and insoluble in light-petroleum (60–80°), and ether. It decomposes on standing. (Found: C, 62·68; H, 3·72; N, 7·00; Cl, 26·53; $C_{42}H_{30}N_4O_6$ (M.W. 800); requires: C, 63·0; H, 3·75; N, 7·0; Cl, 26·25%).

It shows U.V. absorption bands at λ_{max} 293 mμ (log ε 3·74); 250 mμ (log ε 4·90); 210 mμ (log ε 5·19) and λ_{min} 285 mμ (log ε 3·72) and 226 mμ (log ε 4·56). Hydro-*o*-chlorobenzamide: λ_{max} at 252 mμ (log ε 4·32) and 210 mμ (log ε 4·53) and λ_{min} 228 mμ (log ε 4·19) with shoulder at 290 mμ (log ε 4·42).

2,4,6,8,9,10-*Hexa-(3′-nitrophenyl)-hexamine.* *m*-Nitrobenzaldehyde (0·91 g; 0·006 mole) yielded a crystalline product m.p. 172°; 0·721 g; (83%) which recrystallized from ethyl acetate in colourless microscopic needles; 0·68 g; (78%); m.p. 176° (dec). It is easily soluble in acetone, benzene, chloroform, ethanol and methanol, sparingly soluble in ethyl acetate and insoluble in water, light-petroleum (60–80°) and carbon-tetrachloride. It decomposes on standing. (Found: C, 58·1; H, 3·7; O, 22·4; N, 16·3; $C_{42}H_{30}O_{12}N_{10}$; (M.W. 866); requires: C, 58·20; H, 3·50; O, 22·20; N, 16·20%). It shows U.V. absorption bands at λ_{max} 234 mμ (log ε 4·84), shoulder at 264 mμ (log ε 4·72).

Raney-nickel reduction of 2,4,6,8,9,10-*Hexa-(3′-nitrophenyl)-hexamine.* 2,4,6,8,9,10-Hexa-(3′-nitrophenyl)-hexamine (0·87 g; 0·001 mole) was dissolved in absolute ethanol (50 ml), Raney nickel (½ teaspoonful) was added and the contents shaken in an hydrogen atmosphere (6 hr). The product recrystallized from benzene light-petroleum (60–80°) in microscopic rectangular plates; 0·57 g; (83%); m.p. 152°. It is soluble in benzene, acetone, ethyl acetate, ethanol and methanol, and insoluble in light-petroleum (60–80°). (Found: N, 20·52; $C_{42}H_{42}N_{10}$; (M.W. 686); requires: N, 20·39%).

3,4,6,8,9,10-*Hexa-(4′-nitrophenyl)-hexamine.* *p*-Nitrobenzaldehyde (0·91 g; 0·006 mole) yielded a crystalline yellow product; m.p. 140° (dec) 0·69 g; (79·6%) which recrystallized from ethyl acetate-light-petroleum (60–80°); 0·63 g; (72·6%); m.p. 143° (clear melt). It is easily soluble in acetone, chloroform, ethanol and methanol, sparingly in benzene, ethyl acetate and insoluble in water, carbon-tetrachloride and light-petroleum (60–80°). It decomposes slowly on standing. (Found: C, 57·58; H, 3·49; O, 22·87; N, 15·92; $C_{42}H_{30}O_{12}N_{10}$; (M.W. 866); requires C, 58·20; H, 3·50; O, 22·20; N, 16·20%). It shows U.V. absorption bands at λ_{max} 267 mμ (log ε 4·67) and λ_{min} 223 mμ (log ε 4·34).

2,4,6,8,9,10-*Hexafuryl-hexamine.* Furfuraldehyde; (0·58 g; 0·006 mole) yielded a crystalline product; m.p. 76° (clear melt); 0·47 g; (87.7%) which recrystallized from benzene–light-petroleum

(60–80° in dark-brown microscopic needles; 0·40 g; (74·5%), m.p. 80° (clear melt). It is easily soluble in acetone, chloroform, dioxane, carbon-tetrachloride, ethanol and methanol, sparingly in benzene (60–80°) and insoluble in water, ligroin and light-petroleum (60–80°). It decomposes on standing. (Found: C, 66·94; H, 4·65; O, 18·09; N, 10·42; $C_{30}H_{24}O_6N_4$; (M.W. 536); requires: C, 67·15; H, 4·51; O, 17·89; N, 10·44%).

It shows U.V. absorption bands at λ_{max} 265 mμ (log ϵ 4·45); 212 mμ (log ϵ 4·49) and λ_{min} 239 mμ (log ϵ 4·36). Hydrofuramide: λ_{max} at 259 mμ (log ϵ 4·18) and 215 mμ (log ϵ 4·16) and λ_{min} at 235 mμ (log ϵ 4·11).

Hydro-p-*nitrobenzamide*. *p*-Nitrobenzaldehyde (0·45 g; 0·003 mole), was disolved in ethanol (25 ml), ammonium chloride (0·2 g) and ammonium hydroxide (25 ml), was added; (pH 12); shaken (½ hr) and filtered; 0·36 g; (83%) m.p. 70° (dec). The product recrystallized from dil. methanol in pale yellow microscopic needles; 0·34 g; (78·5%); m.p. 75° (dec). It is easily soluble in acetone, benzene, chloroform, ethyl acetate, dioxane, sparingly in ethanol and methanol and insoluble in water and light-petroleum. (Found: C, 57·86; H, 3·68; O, 22·60; N, 15·87; $C_{21}H_{15}O_6N_5$; (M.W. 433); requires: C, 58·20; H, 3·50; O, 22·20; N, 16·20%). It shows U.V. absorption bands at λ_{max} 254 mμ (log ϵ 4·81) and 210 mμ (log ϵ 4·69) and λ_{min} at 233 mμ (log ϵ 4·32).

Hydro-m-*Nitrobenzamide*. The method was the same as employed for the preparation of hydro-*p*-nitrobenzamide. The product m.p. 143° was crystallized from dil. methanol in long needles, 0·34 g; (78·5%) m.p. 145° (dec). Its solubilities are the same as those of hydro-*p*-nitrobenzamide. (Found: N, 15·9; $C_{21}H_{15}O_6N_5$; (M.W. 433); requires: N, 16·20%). It shows U.V. absorption bands at λ_{max} 230 mμ (log ϵ 4·57) and λ_{min} 260 mμ (log ϵ 4·46).

Conversion of hexamines into their corresponding hydrobenzamides (*General method*). Hexamine: (I; R = $C_6H_5^-$; *o*-CH_3O—$C_6H_4^-$; *o*-HO . $C_6H_4^-$; *o*-Cl . $C_6H_4^-$; α-Furyl-; *m*-$NO_2C_6H_4^-$; *p*-NO_2 . $C_6H_4^-$), (0·003 mole) was dissolved in ethanol (25 ml) to which ammonium chloride (0·2 g) and ammonium hydroxide (25 ml) was added (pH 12). The mixture was shaken (½ hr) and the separated hydrobenzamide recrystallized from an appropriate solvent. The hydrobenzamides were identical in U.V. spectra and their melting points undepressed by admixture with authentic samples.

Hexamine employed	*Hydrobenzamide obtained*
2,4,6,8,9,10-Hexa-phenylhexamine I, R = $C_6H_5^-$	Hydrobenzamide m.p. 102° (lit.[3] 102–105°).
2,4,6,8,9,10-Hexa(4′-methoxy-phenyl)-hexamine: I, R = *p*-CH_3O—$C_6H_4^-$	Hydroanisamide m.p. 125° (lit.[4] 125°).
2,4,6,8,9,10-Hexa(2′-hydroxyphenyl) hexamine; I, R = *o*-HO·$C_6H_4^-$	Hydrosalicylamide; m.p. 164° (dec) (lit.[5] 165°).
2,4,6,8,9,10-Hexa(2′-Chlorophenyl) hexamine: I, R = *o*-Cl·$C_6H_4^-$	Hydro-*o*-chlorobenzamide, m.p. 100° (lit.[4] m.p. 98°).
2,4,6,8,9,10-Hexa-α-furyl-hexamine: I, R = α-furyl.	Hydrofuramide; m.p. 115° (lit.[6] m.p. 117°).
2,4,6,8,9,10-Hexa(3′-nitrophenyl) hexamine: I, R = *m*-NO_2·$C_6H_4^-$	Hydro-*m*-nitrobenzamide, m.p. 145° (dec).
2,4,6,8,9,10-Hexa-(4′-nitrophenyl)-hexamine: I, R = *p*-NO_2·$C_6H_4^-$	Hydro-*p*-nitrobenzamide, 75° (dec).

Acknowledgement—Our thanks are due to Dr. M. K. Bhatty for carrying out the nitrogen determinations.

All C, H, and O estimations were carried out by Dr. A. Bernhardt, Microanalytisches Laboratorium, 22 a, Mulheim (Ruhr), (W. Germany).