

3. The Condensation of Azomethines with Hydrogen Sulphide and Aldehydes.

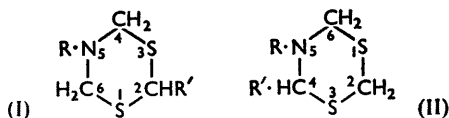
By D. COLLINS and J. GRAYMORE.

Azomethines, benzylidene-methylamine, -ethylamine, and -benzylamine and those obtained from *cyclohexylamine* and benzaldehyde, *p*-tolualdehyde or *p*-anisaldehyde, condense with formaldehyde and hydrogen sulphide, to give substituted dihydrodithiazines.

IN a previous communication,¹ we described the preparation of tetrahydrothiadiazines, thia-azetidines, and dihydrodithiazines, by the condensation of certain aromatic amines with hydrogen sulphide and formaldehyde. The aim of the work now described was the preparation of simple analogues by condensing azomethines with hydrogen sulphide, in the presence of a suitable aldehyde.

Preliminary experiments were carried out by condensing (*a*) methylenecyclohexylamine with hydrogen sulphide and benzaldehyde in the presence of formaldehyde, and (*b*) benzylidenecyclohexylamine with hydrogen sulphide and formaldehyde. Both reactions afforded the same cyclohexyldihydrophenyldithiazine, together with a non-crystalline solid soluble in chloroform, and 5-cyclohexyl-5:6-dihydro-1:3:5-dithiazine (I; R = C₆H₁₁, R' = H). The mother-liquors from the experiments with benzylidenecyclohexylamine contained free benzaldehyde.

By analogy with the dihydrothiazines obtained in previous work, the cyclohexyl dihydrophenyldithiazine is represented by structure (I) or (II). Structure (II) contains an asymmetric carbon atom and should be capable of resolution. Difficulty was



experienced in preparing well-defined salts of the compound, but eventually the dihydro-methylphenyldithiazine obtained from benzylidenemethylamine, hydrogen sulphide, and formaldehyde yielded a readily crystallisable salt with (+)-camphor-10-sulphonic acid, but attempts at resolution therefrom failed. Consequently the constitution (I; R = Me, R' = Ph) appeared the more probable.

If this is accepted, then methylenecyclohexylamine condenses directly with benzaldehyde and hydrogen sulphide to give 5-cyclohexyl-5:6-dihydro-2-phenyl-1:3:5-dithiazine (I; R = C₆H₁₁, R' = Ph), but formation of the same compound from benzylidenecyclohexylamine probably proceeds by the interaction of formaldehyde with the Schiff's base liberating benzaldehyde (it having been confirmed quantitatively that, under the conditions of the reaction, formaldehyde readily replaces benzaldehyde in benzylideneamines) in conformity free benzaldehyde was formed in reaction (*b*).

The method was applied to benzylidene-methylamine, -ethylamine, and -benzylamine and to azomethines prepared from *cyclohexylamine* and benzaldehyde, *p*-tolualdehyde, and *p*-anisaldehyde.

On hydrolysis of 5-cyclohexyl-5:6-dihydro-2-phenyl-1:3:5-dithiazine with 20% sulphuric acid the original amine, trithioformaldehyde, β -trithiobenzaldehyde, benzaldehyde, formaldehyde, and hydrogen sulphide were obtained.

EXPERIMENTAL

Azomethines.—A mixture of equivalent amounts of the aromatic aldehyde and amine was dissolved in ether, the solution washed with 2% acetic acid and with sodium hydrogen carbonate

¹ Collins and Graymore, *J.*, 1953, 4089.

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solution, dried (Na_2SO_4), and evaporated, and the residue distilled. Thus were obtained: *N*-benzylidenecyclohexylamine, m. p. 17° , b. p. 280° (Found: C, 83.2; H, 9.2; N, 7.5. $\text{C}_{13}\text{H}_{17}\text{N}$ requires C, 83.3; H, 9.2; N, 7.5%); *N*-4-methylbenzylidenecyclohexylamine, b. p. 312° (Found: C, 83.2; H, 9.6; N, 7.1. $\text{C}_{14}\text{H}_{19}\text{N}$ requires C, 83.5; H, 9.5; N, 7.0%); and *N*-*p*-anisylidenecyclohexylamine, m. p. 12° , b. p. 319° (Found: C, 77.6; H, 8.7; N, 6.2. $\text{C}_{14}\text{H}_{19}\text{ON}$ requires C, 77.4; H, 8.8; N, 6.4%).

5-cycloHexyl-5:6-dihydro-2(? 4)-phenyl-1:3:5-dithiazine.—(a) From *N*-methylenecyclohexylamine. Hydrogen sulphide was passed into a solution of 40% aqueous formaldehyde (3.4 c.c.) and benzaldehyde (5 c.c.) and *N*-methylenecyclohexylamine (5 g.) in ethanol (25 c.c.). White crystals which separated were removed and hydrogen sulphide passed through the mother-liquor until no further precipitation occurred. Recrystallisation of the solid from ethanol gave the dihydrocyclohexylphenyldithiazine (3 g.) as needles, m. p. 138° (Found: C, 64.6; H, 7.3; N, 5.1; S, 22.9. $\text{C}_{18}\text{H}_{21}\text{NS}_2$ requires C, 64.5; H, 7.6; N, 5.0; S, 22.9%). A small quantity (0.5 g.) of 5:6-dihydro-5-cyclohexyl-1:3:5-dithiazine, m. p. and mixed m. p. 58° , was recovered from the mother-liquor.

(b) From *N*-benzylidenecyclohexylamine. (General method.) Hydrogen sulphide was passed into a solution of 40% formaldehyde (4 c.c.) and the azomethine (5 g.) in ethanol (25 c.c.). A white solid separated. Recrystallisation from ethanol gave needles, m. p. and mixed m. p. 138° (6.5 g.).

A solution of the dithiazine in benzene was saturated with hydrogen chloride. A white hydrochloride separated, which crystallised from ethanol in needles, m. p. 178° (Found: Cl, 11.2. $\text{C}_{18}\text{H}_{23}\text{NS}_2\text{Cl}$ requires Cl, 11.2%).

Method (b) afforded also the following:

5-cycloHexyl-5:6-dihydro-2(? 4)-*p*-tolyl-1:3:5-dithiazine (6.2 g.), needles, m. p. 127° (from ethanol) (Found: C, 65.3; H, 7.9; N, 4.7; S, 22.0. $\text{C}_{16}\text{H}_{23}\text{NS}_2$ requires C, 65.5; H, 7.9; N, 4.8; S, 21.9%) [*hydrochloride*, needles, m. p. 120° (from ethanol) (Found: Cl, 10.9. $\text{C}_{16}\text{H}_{24}\text{NS}_2\text{Cl}$ requires Cl, 10.8%)].

2(? 4)-*p*-Anisyl-5-cyclohexyl-5:6-dihydro-1:3:5-dithiazine (6.2 g.), needles, m. p. 166° (from ethanol) (Found: C, 62.1; H, 7.5; N, 4.4; S, 20.6. $\text{C}_{16}\text{H}_{23}\text{ONS}_2$ requires C, 62.1; H, 7.5; N, 4.5; S, 20.7%) [*hydrochloride*, needles, m. p. 162° (Found: Cl, 10.1. $\text{C}_{16}\text{H}_{24}\text{ONS}_2\text{Cl}$ requires Cl, 10.2%)].

5:6-Dihydro-5-methyl-5:6-dihydro-2(? 4)-phenyl-1:3:5-dithiazine (4 g.), plates, m. p. 167° (from ethanol) (Found: C, 56.8; H, 6.1; N, 6.4; S, 30.4. $\text{C}_{10}\text{H}_{13}\text{NS}_2$ requires C, 56.8; H, 6.2; N, 6.6; S, 30.4%) [*hydrochloride*, leaflets, m. p. 182° (from ethanol) (Found: Cl, 14.1. $\text{C}_{10}\text{H}_{14}\text{NS}_2\text{Cl}$ requires Cl, 14.3%)]. The (+)-*camphor*-10-sulphonate prepared by dissolving equivalent amounts of the dithiazine (10 g.) and camphorsulphonic acid (11.1 g.) in boiling acetone, separated as matted needles, m. p. 175 — 177 (decomp.), $[\alpha]_D^{25}$ 25.5 in CHCl_3 (Found: N, 3.2; S, 21.6. $\text{C}_{20}\text{H}_{29}\text{O}_4\text{NS}_2$ requires N, 3.2; S, 21.7%), soluble in acetone and ethyl acetate, very soluble in ethanol and methanol. It was not resolved by crystallisation from acetone.

5-Ethyl-5:6-dihydro-2(? 4)-phenyl-1:3:5-dithiazine (1.8 g.), leaflets, m. p. 129° (from ethanol) (Found: C, 58.4; H, 6.8; N, 6.3; S, 28.2. $\text{C}_{11}\text{H}_{16}\text{NS}_2$ requires C, 58.6; H, 6.7; N, 6.2; S, 28.4%) [*hydrochloride*, leaflets, m. p. 192° (from ethanol) (Found: Cl, 13.5. $\text{C}_{11}\text{H}_{16}\text{NS}_2\text{Cl}$ requires Cl, 13.5%)].

N-Benzylidenebenzylamine gave a sticky solid from which only 0.8 g. of 5-benzyl-5:6-dihydro-2(? 4)-phenyl-1:3:5-dithiazine could be isolated; it formed needles, m. p. 147° , from ethanol (Found: C, 66.9; H, 6.0; N, 4.8; S, 22.0. $\text{C}_{16}\text{H}_{17}\text{NS}_2$ requires C, 66.8; H, 6.0; N, 4.9; S, 22.3%) [*hydrochloride*, needles, m. p. 161° (from ethanol) (Found: Cl, 11.0. $\text{C}_{16}\text{H}_{18}\text{NS}_2\text{Cl}$ requires Cl, 11.0%)].

Hydrolysis of 5-cycloHexyl-5:6-dihydro-2(? 4)-phenyl-1:3:5-dithiazine.—The base (1 g.) was refluxed with 20% sulphuric acid (100 c.c.) until evolution of hydrogen sulphide ceased (2—3 hr.). β -Trithiobenzaldehyde (0.18 g.) (m. p. and mixed m. p. 226°) was removed from the hot acid liquor by filtration; as the filtrate cooled, trithioformaldehyde (0.06 g.) (m. p. and mixed m. p. 216°) separated. Free formaldehyde and benzaldehyde were liberated during the hydrolysis; cyclohexylamine was recovered quantitatively from the filtrate as the benzoyl derivative.