236. *The Constitution of a By-product from the Preparation of Trichloropyrimidine from Barbituric Acid.*

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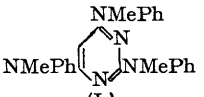
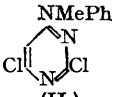
The constitution of a high-boiling crystalline by-product from the reaction between barbituric acid, phosphoryl chloride, and dimethylaniline is shown by synthesis to be 4 : 6-*dichloro*-2-N-*methylanilinopyrimidine* and not the expected 2 : 6-dichloro-4-*N*-methyl compound.

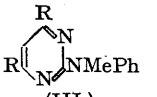
WHEN preparing 2 : 4 : 6-trichloropyrimidine from barbituric acid by the improved method of Baddiley and Topham (*J.*, 1944, 679), using phosphoryl chloride and dimethylaniline, a crystalline by-product was isolated from the residue, after distillation of the trichloro-compound, as a fraction of b. p. 240—300°. The yield of recrystallised product averaged 5%, and it was at first believed to be a partly chlorinated barbituric acid. However, analyses indicated the structure to be that of a dichloropyrimidine containining a monomethylaniline residue, thus suggesting either 4 : 6-dichloro-2- or 2 : 6-dichloro-4-*N*-methylanilinopyrimidine as the correct constitution. The by-product was still obtained even when dimethylaniline carefully freed



(I.)



(II.)



(III.)

from traces of the monomethyl compound was employed, and its formation is therefore similar to that of 2 : 4 : 6-tri-*N*-methylanilinopyrimidine (I) from trichloropyrimidine and dimethylaniline (Kawai and Miyoski, *Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1931, **16**, 20), in which the loss of methyl chloride from an intermediate quaternary salt is involved.

Since the action of aniline on trichloropyrimidine is presumed to give 2 : 6-dichloro-4-anilinopyrimidine (Winkelmann, *J. pr. Chem.*, 1927, **115**, 305), the constitution of the new pyrimidine was thought to be analogous. This supposition was, however, disproved when the condensation of monomethylaniline and trichloropyrimidine in ethanol gave the non-identical 2 : 6-*dichloro*-4-N-*methylanilinopyrimidine* (II). Its 2-*methylanilino*-isomer (III, R = Cl) was therefore synthesised from α-phenyl-α-methylguanidine and ethyl malonate in alcoholic sodium ethoxide solution, the intermediate N-*methylanilinodihydroxypyrimidine* (III, R = OH) giving on treatment with phosphoryl chloride a product indistinguishable from the substance under investigation.

By means of the phosphoryl chloride–dimethylaniline method, 4 : 6-*dichloro*-5-p-*chlorobenzeneazo*-2-*methylpyrimidine* has been prepared from the corresponding dihydroxypyrimidine (Lythgoe, Todd, and Topham, *J.*, 1944, 3151), but under similar conditions the 2 : 4 : 6-*trihydroxy*-5-p-*chlorobenzeneazo*-compound gave only tarry products.

EXPERIMENTAL.

2 : 6-*Dichloro*-4-N-*methylanilinopyrimidine*.—Methylaniline (11 g., 2 mol.) was added to a solution of trichloropyrimidine (9·2 g., 1 mol.) in ethanol (40 c.c.) at room temperature. After 3 hours the colourless product was collected and crystallised from alcohol. The *dichloromethylanilinopyrimidine* (II) separated in tiny prisms, m. p. 106—107° (Found : C, 51·7; H, 3·8; Cl, 27·8. $C_{11}H_9N_3Cl_2$ requires C, 52·0; H, 3·5; Cl, 27·9%).

2-N-*Methylanilino*-4 : 6-*dihydroxypyrimidine*.—α-Phenyl-α-methylguanidine hydrochloride (8 g.) dissolved in ethanol (20 c.c.) was added to a solution of sodium (2 g.) in ethanol (40 c.c.), and, with the addition of ethyl malonate (6·3 g.), the mixture was heated under reflux on a steam-bath for 8 hours. After standing overnight, the precipitated sodium salt was collected and treated with dilute acetic acid. Crystallisation of the product from boiling water gave the *pyrimidine* (III, R = OH) (2·5 g.) as nearly colourless flat prisms, m. p. 219° (Found : C, 60·8; H, 4·9; N, 19·5. $C_{11}H_{11}O_2N_3$ requires C, 60·8; H, 5·0; N, 19·4%).

4 : 6-*Dichloro*-2-N-*methylanilinopyrimidine*.—(*a*) The colourless distillate obtained from the residue of the trichloropyrimidine preparation was crystallised from alcohol, and the *pyrimidine* (III, R = Cl) obtained in thick rhombic plates, m. p. 92—93° (Found : C, 52·0; H, 3·6; Cl, 27·6. $C_{11}H_9O_3Cl_2$ requires C, 52·0; H, 3·5; Cl, 27·9%).

(*b*) The dihydroxypyrimidine (III, R = OH) (2 g.) was heated under reflux with phosphoryl chloride (6 c.c.) for 15 minutes. The liquid was then poured on ice, and the precipitated solid collected and crystallised from ethanol (Found : C, 53·4; H, 3·8%). Admixture of the product with a specimen from the trichloropyrimidine preparation did not depress its m. p. of 92°.

4 : 6-*Dichloro*-5-p-*chlorobenzeneazo*-2-*methylpyrimidine*.—A mixture of 4 : 6-dihydroxy-5-*p*-chlorobenzeneazopyrimidine (5 g.), phosphoryl chloride (6 c.c.), and dimethylaniline (3 c.c.) was warmed until the solid dissolved. The black liquid was poured on ice, and after 1 hour the resinous product was separated by decantation and triturated with alcohol. Crystallisation of the orange solid (2·9 g.,

47%) from ethanol afforded the *azopyrimidine hemi-alcoholate* as clusters of bright red needles, m. p. 104° (Found : C, 44·7; H, 3·1. $C_{11}H_7N_4Cl_3,\frac{1}{2}EtOH$ requires C, 44·3; H, 3·1%).

2 : 4 : 6-*Trihydroxy*-5-p-*chlorobenzeneazopyrimidine* (cf. Lythgoe, Todd, and Topham, *loc. cit.*).—A cold aqueous solution of barbituric acid (15 g.) was treated with a solution of *p*-chlorobenzenediazonium chloride (from 15 g. of *p*-chloroaniline) in excess of concentrated hydrochloric acid. The solid which separated on basification with sodium hydrogen carbonate was collected, washed, and dried at 100°; the very sparingly soluble *azopyrimidine* crystallised from *cyclo*hexanone in minute yellow needles, m. p. 300° (Found : C, 45·0; H, 2·7. $C_{10}H_7O_3N_4Cl$ requires C, 44·9; H, 2·6%). The action of phosphoryl chloride–dimethylaniline on the azo-derivative gave an uncrystallisable resin.

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