32. *Structure and Amœbicidal Activity. Part II.* Aliphatic Diamines.*

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7 : 13-Diamino-5 : 15-diethylnonadecane dihydrochloride has been synthesised and found to possess amœbicidal activity.

PREVIOUS work (*J.*, 1950, 1842) has been extended by the synthesis of 7 : 13-diamino-5 : 15-diethylnonadecane (dihydrochloride), by use of the Schmidt reaction on the corresponding 7 : 13-dicarboxy-compound, obtained by a malonic ester synthesis. The hydrochloride was active at a concentration of 1 in 500,000 against *Entamœba histolytica* (*in vitro* test by Dr. J. D. Fulton).

A second route to diamines was examined. By the action of cadmium alkyls on adipoyl chloride it is possible to prepare diketones of the type $R{\cdot}CO{\cdot}[CH_2]_4{\cdot}CO{\cdot}R$, whence diamines are obtainable by reducing the diketone dioximes. In this way 5 : 10-diaminotetradecane (dipicrate) was synthesised. When, however, an attempt was made to employ ββ-dialkylglutaric acids instead of adipic acid as starting material, the synthesis broke down, since we were unable to prepare 2 : 2-dimethylglutaroyl chloride; the acid was converted mainly into the anhydride by thionyl chloride.

A third route tried was from 2 : 2-dialkylpropane-1 : 3-diols, obtainable by reducing ethyl dialkylmalonates with ethereal lithium aluminium hydride. Conversion of 2 : 2-dimethylpropane-1 : 3-diol into the corresponding 1 : 3-dibromide, and condensation of the latter with ethyl *n*-amylmalonate, followed by a normal series of reactions, led to 6 : 10-diamino-8 : 8-dimethylpentadecane (dihydrochloride). This was active at 1 : 1000 against *E. histolytica.*

EXPERIMENTAL

Ethyl 5 : 15-*Diethylnonadecane*-7 : 7 : 13 : 13-*tetracarboxylate*.—Pentamethylene dibromide (76 g., 0·33 mole) was added to a solution of ethyl 2-ethylhexylmalonate (180 g., 0·7 mole) in absolute ethyl alcoholic sodium ethoxide (sodium, 14·95 g., 0·65 g.-atom). The mixture was

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* Part I, *J.*, 1950, 1842.

stirred and boiled under reflux for 8 hours. The bulk of the alcohol was distilled off, water was added, and the cooled residue was extracted with ether. The ethereal solution was dried (Na_2SO_4) and the ether distilled off. The *ester* (yield 35%) boiled at 256—257°/4 mm. (Found: C, 69·6; H, 10·7. $C_{35}H_{64}O_8$ requires C, 68·6; H, 10·5%).

7 : 13-*Diamino*-5 : 15-*diethylnonadecane*.—Hydrolysis of the tetracarboxylic ester, followed by half-decarboxylation, gave a product which could not be crystallised. It was dissolved in 50 c.c. of benzene, and 25 c.c. of concentrated sulphuric acid were added. To the mixture sodium azide (2·5 g.) was added at 30—45°, followed by ice and then 30% sodium hydroxide solution. The mixture was extracted with benzene–ether, and the extracts were dried (Na_2SO_4). The solution obtained was used for making the *dihydrochloride* (Found: Cl, 16·4. $C_{23}H_{50}N_2,2HCl$ requires Cl, 16·5%) and the *dipicrate*, m. p. 142—144° (from aqueous alcohol) (Found: C, 50·3; H, 6·9; N, 13·8. $C_{35}H_{56}O_{14}N_8,H_2O$ requires C, 50·5; H, 7·0; N, 13·2%).

Tetradecane-5 : 10-*dione*.—This was prepared from di-*n*-butylcadmium and adipoyl chloride (cf. Cason and Prout, *J. Amer. Chem. Soc.*, 1944, **66**, 46; Burnett and Tarbell, *ibid.*, 1945, **67**, 1944; Cason, *Chem. Reviews*, 1947, **40**, 15). The crude diketone was converted into the *dioxime* which after being crystallised from benzene had m p. 117—119° (Found: C, 66·8; H, 11·0; N, 10·7. $C_{14}H_{28}O_2N_2$ requires C, 65·5; H, 11·0; N, 10·9%). Reduction of the dioxime with sodium and absolute alcohol, etc., led to 5 : 10-*diaminotetradecane dipicrate*, m. p. 205—207°, which was crystallised from alcohol (Found: C, 45·8; H, 5·3; N, 16·2. $C_{26}H_{38}O_{14}N_8$ requires C, 45·4; H, 5·5; N, 16·3%).

2 : 2-*Diethylpropane*-1 : 3-*diol*.—This diol was (95%) obtained by reduction of ethyl diethylmalonate with ethereal lithium aluminium hydride. It had b. p. 112°/5 mm., 118°/8 mm., and when crystallised from benzene had m. p. 65° (Found: C, 63·1; H, 12·0. Calc. for $C_7H_{16}O_2$: C, 63·5; H, 12·1%). It has previously been made by condensation of 2-ethylbutaldehyde and formaldehyde (Shortridge, Craig, Greenlee, Derfer, and Boord, *J. Amer. Chem. Soc.*, 1948, **70**, 946; McKusick, *ibid.*, p. 1982). The diol was treated with phosphorus tribromide but the resulting 1 : 3-dibromo-2 : 2-diethylpropane proved unsatisfactory for further synthetic work.

6 : 10-*Diamino*-8 : 8-*dimethylpentadecane Dihydrochloride*.—Condensation of 1 : 3-dibromo-2 : 2-dimethylpropane with an alcoholic solution of sodium ethoxide and ethyl *n*-amylmalonate gave a low yield of ethyl 8 : 8-dimethylpentadecane-6 : 6 : 10 : 10-tetracarboxylate. Hydrolysis, followed by half-decarboxylation and application, as above, of the Schmidt reaction, gave 6 : 10-*diamino*-8 : 8-*dimethylpentadecane dihydrochloride* as a deliquescent solid (Found: C, 60·1; H, 11·4; Cl, 19·7. $C_{17}H_{40}N_2Cl_2$ requires C, 59·4; H, 11·7; Cl, 20·6%).

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