248. *The Reaction between Amines and Unsaturated Compounds containing Halogen attached to one of the Ethylenic Carbon Atoms. Part I. The Reaction between Ethyl α-Chlorocrotonate and Dimethylamine.*

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THE reaction between unsubstituted unsaturated esters and ammonia (or an amine) has formed the subject of many investigations (cf. Engel, *Compt. rend.*, 1887, **104**, 1805; 1888, **106**, 1677; Wender, *Ber.*, 1889, **22**, 736; Bougault, *Ann. Chim.*, 1908, **15**, 491; Körner and Menozzi, *Ber.*, 1888, **21**, Ref. 86; 1889, **22**, Ref. 735), notably by Philippi and his co-workers (*Monatsh.*, 1913, **34**, 717, 1187; 1932, **60**, 50), who conclude that the product at the ordinary temperature is mainly an amide, whereas a higher temperature, and also the use of a solvent, tend to favour addition at the point of unsaturation. αβ-Unsaturated esters seem to be the most active with regard to the latter reaction (*Monatsh.*, 1929, **51**, 253), which often takes place to the exclusion of amide formation (*ibid.*, 1915, **36**, 97). It is generally accepted that, in the process of addition, the amino-group attaches itself to the carbon atom more remote from the ester group.

Reactions between amines and unsaturated compounds containing halogen attached to an ethylenic carbon atom do not appear to have been investigated to any extent. Ammonia and vinyl chloride (or bromide) in alcoholic solution react only at 150—160° with the production of ethylenediamine (Engel, *Compt. rend.*, 1887, **104**, 1621). Ethyl β-chlorocrotonate reacts with phenylhydrazine, halogen and ethyl alcohol being eliminated and ring closure occurring (Autenrieth, *Ber.*, 1896, **29**, 1653).

In an attempt to prepare ethyl α-dimethylaminocrotonate, ethyl α-chlorocrotonate was treated with an alcoholic solution of dimethylamine. A vigorous reaction took place at ordinary temperature, considerable heat being evolved. With 2 mols. of dimethylamine about 85—90% of the total halogen was replaced in 24 hours at room temperature, and with 3 mols. all the halogen was replaced within one hour at room temperature. In both instances the product was *ethyl αβ-bis(dimethylamino)butyrate.*

The nature of this reaction is not in agreement with Philippi's generalisations that negative substituents hinder addition and that an amino-group already attached to a doubly linked carbon atom entirely prevents the further addition of a like group (Philippi and Spenner, *Monatsh.*, 1915, **36**, 97). It is not possible to state which reaction takes place first—replacement of chlorine or addition to the double bond—but in either case the generalisation fails. It is interesting that the reaction should take place so readily, since, in general, addition of ammonia (or amines) to an unsaturated compound involves heating under pressure at a high temperature (cf., however, slow addition at ordinary temperatures, Morsch, *ibid.*, 1932, **60**, 50).

EXPERIMENTAL.

Ethyl α-Chlorocrotonate.—α-Chlorocrotonic acid was prepared from butylchloral hydrate and potassium ferrocyanide (Wallach, *Ber.*, 1877, **10**, 1530) and had m. p. 99° (Wislicenus, *Annalen*, 1888, **248**, 293, gives 99·2°). The acid was esterified by refluxing for 3 hours with either (i) absolute alcohol saturated with dry hydrogen chloride or (ii) 98% alcohol containing 10% by volume of concentrated sulphuric acid, which gave a better yield. The ester, b.p. 174—176° (corr.) (Perkin, J., 1894, **65**, 424, gives 175—176°, corr.), was isolated in the usual way in either case.

Reaction between Ethyl α-Chlorocrotonate and Dimethylamine.—(i) 2 *Mols. of base.* 2·58 G. of the ester were mixed with 4·94 g. of 33% w/w solution of dimethylamine in absolute alcohol in a loosely corked graduated test-tube, giving a total volume of 8·9 c.c. In 5—10 minutes much heat was developed and the mixture was cooled under the tap. At intervals, 0·3 c.c. of the mixture was abstracted (by means of a 1 c.c. pipette graduated in 0·1 c.c.) and added to 10 c.c. of dilute nitric acid. The ionisable chlorine was then determined by back-titration in the usual way.

Time of reaction, hrs.	½	3	24
$0·1N$-$AgNO_3$, c.c.	4·85	4·95	5·20
Chlorine replaced, %	83	84	89

(ii) 3 *Mols. of base.* 2·38 G. of ester were mixed with 6·66 g. of a solution of the base, as described above, giving a volume of 10·8 c.c. After 1 hour 0·4 c.c. of the reaction mixture contained 0·0217 g. of ionisable chlorine (Calc. for ester present: 0·0210 g.).

Ethyl αβ-Bis(dimethylamino)butyrate.—14·85 G. of ethyl α-chlorocrotonate were mixed with 40·5 g. (*ca.* 3 mols.) of dimethylamine solution (as described above) in a 250 c.c. loosely corked R.B. flask. In 10 minutes the temperature rose to about 60°, but a slight diminution in pressure was observed. The mixture was left for 1 hour, neutralised with concentrated hydrochloric acid to litmus, and the bulk of the alcohol (25 c.c.) distilled off on a water-bath. The mixture was cooled and dissolved in 100 c.c. of water. The aqueous solution was made distinctly acid with concentrated hydrochloric acid and extracted with ether (25 c.c. + 20 c.c.). Ice and a large excess of cold 33% sodium hydroxide solution were added; the brown oil which rose to the surface was separated, and the aqueous portion, after addition of more alkali, was extracted with ether (30 c.c. + 25 c.c.). The separated oil was dissolved in the ethereal extracts, which were washed with water (20 c.c. + 20 c.c.), dried (sodium sulphate), and the solvent evaporated. The residue was distilled in a vacuum (yield 11 g.).

Ethyl αβ-bis(dimethylamino)butyrate is a colourless oil, of faint unpleasant odour, b. p. 89°/3 mm., 91°/6 mm., very sparingly soluble in water (Found: C, 58·8; H, 11·0; N, 14·0, 14·1. $C_{10}H_{22}O_2N_2$ requires C, 59·3; H, 11·0; N, 13·9%). Its picrate (from a saturated alcoholic solution of picric acid and a 50% alcoholic solution of the ester) formed bright yellow prisms, m. p. 147°. Its *platinichloride* crystallised in small, orange-coloured, hexagonal plates, m. p. 180° (decomp.) (Found: Pt, 31·5. $C_{10}H_{22}O_2N_2,H_2PtCl_6$ requires Pt, 31·9%).

Monohydrochloride. The ester was dissolved in 3 vols. of dry ether and dry hydrogen chloride was passed through the solution. The crystals were filtered off, washed with dry ether, dissolved in absolute alcohol, and reprecipitated by addition of dry ether. Small colourless prisms were obtained, which were filtered off, washed with dry ether, and dried in a vacuum over concentrated sulphuric acid, m.p. 117° (Found: Cl, 15·1, 15·0. $C_{10}H_{22}O_2N_2,HCl$ requires Cl, 14·9%).

In view of the possibility of amide formation it was thought necessary to establish conclusively the presence of the carbethoxy-group. 1 G. of the product was therefore hydrolysed with dilute sulphuric acid, the mixture fractionated, and the distillate oxidised with chromic acid. The presence of acetaldehyde was established by preparation of its 2 : 4-dinitrophenylhydrazone (m. p. and mixed m. p.).

All attempts to prepare a dimethiodide of the base failed. On treatment with methyl iodide in methyl-alcoholic solution, the base yields a mixture containing tetramethylammonium iodide (Found: I, 62·7. Calc.: I, 63·2%). If the base undergoes with methyl iodide a reaction similar to that of ethylenediamine, as appears probable, it may be possible to obtain piperazine derivatives. Investigations on this point are proceeding.

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