

**81. Preparation of Aldehydes from Nitriles (Stephen's Method).
γ-Phthalimidobutaldehyde.**

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THE marked tendency of certain aliphatic aldehydes, such as those used in alkaloid synthesis, to undergo irreversible self-condensation often renders them difficult of access except from nitriles, which, being converted into the so-called iminochlorides, can be reduced by means of anhydrous stannous chloride at the ordinary temperature (Stephen, J., 1925, 127, 1874). The products are double salts of the type $(R \cdot CH : NH, HCl)_2, SnCl_4$, from which the aldehydes may be obtained merely by the action of water.

Of the many illustrations offered by Stephen, α -naphthonitrile and *o*-toluonitrile alone give poor yields, but in three recently investigated examples, *viz.*, γ -phenoxy- α -methylbutaldehyde (King and Robinson, J., 1933, 273), γ -phthalimido- α -methylbutaldehyde (King, Liguori, and Robinson, *ibid.*, p. 1477), and γ -phenoxybutaldehyde (forthcoming publication), no precipitation of stannichloride occurred unless the reactants were heated for some time; the good yields normally associated with the method were then obtained. Even under these more drastic conditions, however, the two exceptional nitriles mentioned by Stephen (*loc. cit.*) gave no noticeable improvement in yield.

Prior to the 1925 memoir of Stephen, several aromatic aldehydes were synthesised by Sonn and Müller from anilides, these first reacting with phosphorus pentachloride to give iminochlorides, $R \cdot CCl : NPh$, which were reduced by stannous chloride under conditions parallel with those used in the Stephen method (*Ber.*, 1919, 52, 1927; Houben-Weyl, "Die Methoden der Organischen Chemie," 1923, III, 398). In view of the failure of *o*-toluonitrile to afford more than a small proportion of the related aldehyde, it is of interest to record that, by applying the process of Sonn and Müller to *o*-toluanilide, almost quantitative yields have now been obtained.

The method of Stephen has been extended to the preparation of γ -phthalimidobutaldehyde, which is of possible synthetical value. The requisite nitrile (Gabriel, *Ber.*, 1889, 22,

3337) was obtained by improved methods from γ -phthalimidobutyric acid through the usual intermediates.

EXPERIMENTAL.

α -Naphthaldehyde.—Hydrogen chloride was passed into a suspension of anhydrous stannous chloride in dry ether (9 g. in 35–40 c.c., *i.e.*, approximately the proportion recommended by Stephen). Saturation was expedited by cooling to 0°; the solid was then completely dissolved without the formation of a second layer. α -Naphthonitrile (5 g.) was then added. After 12 hours, the homogeneous liquid deposited a small amount of stannichloride, which refluxing for 6 hours and re-saturation with hydrogen chloride at 0° only slightly augmented. The precipitate was collected and decomposed with warm water, and the aldehyde (less than 1 g.) extracted with ether. The 2 : 4-dinitrophenylhydrazone crystallised from a fairly large volume of acetic acid in a deep yellow mass of minute needles (Found: C, 60.6; H, 3.5. $C_{17}H_{12}O_4N_4$ requires C, 60.7; H, 3.6%).

o -Tolualdehyde.—Although three experiments were made under various conditions, only a very small yield of aldehyde was obtainable from *o*-toluonitrile. To effect its preparation by the method of Sonn and Müller (*loc. cit.*), *o*-toluic acid (25 g.) was converted by boiling thionyl chloride (40 c.c.) into the acid chloride, which on dilution with benzene (60 c.c.) and addition to an ice-cold chloroform solution (200 c.c.) of aniline (35 g.) afforded *o*-toluanilide. By evaporating the washed and dried solution, and crystallising the residue from benzene, it was obtained as colourless needles, m. p. 125–126°. The gentle reaction between phosphorus pentachloride (10 g.) and the anilide (10 g.), dissolved in toluene (35 c.c.), began at 50° and was completed at 100°; both solvent and phosphorus oxychloride were then removed under diminished pressure. On addition of the residual pale red syrup to a solution prepared from ether (100 c.c.) and stannous chloride (25 g.) saturated at 0° with hydrogen chloride, a yellow precipitate began to separate. After several hours the solid was collected and placed in boiling dilute hydrochloric acid. The aldehyde (4.9 g.) collected in the steam distillate and was removed by ether extraction. It was recognised by the semicarbazone, m. p. 210–211°, and by the 2 : 4-dinitrophenylhydrazone, which crystallised from acetic acid in orange-red rectangular plates, m. p. 193–194° (30° depression when mixed with the hydrazine) (Found, after drying at 120°: C, 56.2; H, 3.9. $C_{14}H_{12}O_4N_4$ requires C, 56.0; H, 4.0%).

Ethyl β -Phthalimidoethylmalonate and γ -Phthalimidobutyric Acid.—Robinson and Suginome (J., 1932, 307) have shown that the use of alcohol as a solvent for condensations which involve phthalo- β -bromoethylimide and sodio-compounds may lead to inferior yields owing to a by-reaction, so in a repetition of Aschan's preparation of ethyl β -phthalimidoethylmalonate (*Ber.*, 1891, 24, 2449), the powdered bromide (70 g.), with 2 g. of sodium iodide, was added to a benzene suspension of ethyl sodiomalonate prepared by refluxing ethyl malonate (70 g.) and pulverised sodium (9.4 g.) in dry benzene (200 c.c.) for 2 hours on a steam-bath. After 16 hours' heating under reflux, the mass was made neutral with acetic acid and exhaustively steam-distilled. The non-volatile residue was removed by ether and fractionated, the substituted malonate (58 g.) having b. p. 225–235°/4.5 mm.

To hydrolyse the ester without removing the phthalimido-group, Radde (*Ber.*, 1922, 55, 3177) used cold hydrobromic acid (yield, 60%), but the following method, based on the preparation of γ -phthalimido- α -methylbutyric acid (King, Liguori, and Robinson, *loc. cit.*), is more satisfactory. A mixture of acetic anhydride (80 c.c.) and concentrated hydrochloric acid (120 g.) with the ester (10 g.) in solution was boiled in an open flask for exactly 50 minutes; the remaining solvents were then removed under diminished pressure at 100°. The residue (7.5 g.), after one crystallisation from alcohol, had m. p. 167–168° and was almost pure, the m. p. of β -phthalimidoethylmalonic acid being given by Radde as 168°. It was decarboxylated by heating for 5–10 minutes in an oil-bath at 180°; the residue, crystallised from benzene and then from aqueous alcohol (50%), gave γ -phthalimidobutyric acid in colourless prisms, m. p. 116–117° (Found: C, 61.8; H, 4.9. Calc. for $C_{12}H_{11}O_4N$: C, 61.8; H, 4.7%). Gabriel and Colman (*Ber.*, 1908, 41, 513) record m. p. 117–118° after sintering at *ca.* 115°.

γ -Phthalimidobutyramide.— γ -Phthalimidobutyric acid (10 g.) was refluxed with thionyl chloride (20 c.c.) for $\frac{1}{2}$ hour, and the solution evaporated to dryness under reduced pressure at 100°. The residual yellow crystalline acid chloride was dissolved in absolute ether (150 c.c.), and the solution saturated at 0–10° with dry ammonia. The resulting white paste was freed from solvent by filtration, and shaken with water to dissolve ammonium chloride. Gabriel and Colman (*loc. cit.*) record for γ -phthalimidobutyramide m. p. 165–166°, and our product (9.5 g.), after one

crystallisation from alcohol, had m. p. 166—167°, which further treatment did not advance beyond 167° (Found : C, 62.1; H, 5.3. Calc. for $C_{12}H_{12}O_3N_2$: C, 62.1; H, 5.2%).

γ-Phthalimidobutyronitrile (cf. Gabriel, *loc. cit.*).—The amide (10 g.) and thionyl chloride (20 g.) were refluxed for $\frac{1}{2}$ hour, and the excess of dehydrating agent then removed under diminished pressure. The residue, which immediately solidified, was washed with sodium bicarbonate solution and then with water. The dried product (9.2 g.), crystallised from benzene–light petroleum, yielded phthalimidobutyronitrile, m. p. *ca.* 81°, and one recrystallisation from alcohol gave the pure substance, m. p. 81—82° (Found : C, 67.4; H, 4.8. Calc. for $C_{12}H_{10}O_2N_2$: C, 67.3; H, 4.7%).

γ-Phthalimidobutaldehyde.—Unlike the three recent examples cited in the introduction, when the nitrile (6 g.) was added to stannous chloride (9 g.) in absolute ether (50 c.c.) saturated with hydrogen chloride, the stannichloride was slowly precipitated at room temperature. After 12 hours, the solid was collected, but it proved unusually stable towards water, and as the resultant *aldehyde* rapidly polymerised, the tin salt was best hydrolysed by being mechanically shaken with equal volumes of ether and water for 3 hours. After filtration, the ethereal solution was rapidly dried (magnesium sulphate) and evaporated at room temperature. The residue (4.5 g.) was a colourless oil, but it shortly became turbid owing to the production of an amorphous polymeride. The 2 : 4-*dinitrophenylhydrazone*, prepared at room temperature, crystallised from acetic acid in yellow minute prisms, m. p. 184° (Found : N, 17.3. $C_{18}H_{15}O_6N_5$ requires N, 17.6%).

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