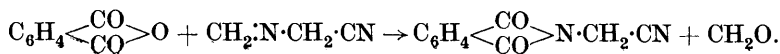


CXXIV.—*A New Synthesis of Phthalimidoacetonitriles  
and a Note on Aminoacetonitrile Sulphates.*

By HENRY STEPHEN.

WHEN phthalic anhydride or a substitution product is heated with methyleneaminoacetonitrile, formaldehyde is evolved and the corresponding phthalimidoacetonitrile produced :



The method gives excellent yields of the nitriles, from which a large number of derivatives have been prepared. In the case of phthalic anhydride and derivatives which melt below  $150^{\circ}$ , it is sufficient to mix the dry solids and heat them on the water-bath, but with higher-melting anhydrides it is desirable to add sufficient xylene to form a paste with the solids, the solvent being afterwards removed by distillation with steam. The process in most cases requires about  $\frac{1}{2}$  hour; any unchanged anhydride is extracted with cold water, and the product crystallised from hot water, alcohol, or acetic acid.

#### EXPERIMENTAL.

[With W. W. ADAMSON.]

*Phthalimidoacetonitrile*.—Phthalic anhydride (20 g.; 1 mol.) was intimately mixed with methyleneaminoacetonitrile (9 g.; 1 mol.) and heated until the evolution of formaldehyde ceased. The brown residue was extracted with cold water; the insoluble *nitrile* crystallised from hot water in leaflets, m. p.  $123\text{--}124^{\circ}$  (Found: C, 64.7; H, 3.15.  $\text{C}_{10}\text{H}_6\text{O}_2\text{N}_2$  requires C, 64.6; H, 3.2%), sparingly soluble in cold water, readily in ethyl alcohol and ethyl acetate, insoluble in ether.

The nitrile was also prepared by treating chloroacetonitrile with potassium phthalimide, and by dehydrating phthalimidoacetamide with phosphoric oxide. It dissolved slowly in dilute hydrochloric acid at  $60^{\circ}$ ; the cooled solution deposited thin plates of phthalimidoacetic acid, m. p.  $191^{\circ}$ , identical with a specimen obtained by Gabriel's method (*Ber.*, 1908, **41**, 242, footnote). Concentrated hydrochloric acid gave a mixture of phthalic acid and glycine hydrochloride.

*Phthalimidoacetamide* was prepared by dissolving the nitrile (2 g.) in sulphuric acid (8 c.c., 80%) by vigorous shaking and cooling, keeping the solution over-night, and pouring it on ice. The pale yellow needles obtained, after recrystallisation from glacial acetic acid, gave long transparent needles, m. p.  $257^{\circ}$  (Found: C, 58.8; H, 3.75.  $\text{C}_{10}\text{H}_8\text{O}_3\text{N}_2$  requires C, 58.7; H, 3.9%). The same amide was also prepared by treating phthalimidoacetyl chloride in dry ether with ammonia, and by heating a mixture of chloroacetamide with potassium phthalimide.

A new and convenient method for preparing the amide, which is also applicable to those described below, consists in heating phthalic anhydride a few degrees above the melting point and adding the hydrochloride or sulphate of aminoacetonitrile (Curtius, *Ber.*, 1894, **27**, 59; Klages, *Ber.*, 1903, **36**, 1506): the fused mass gradually

solidifies, and on crystallising the product from glacial acetic acid an excellent yield of the amide is obtained.

The amide dissolved slowly in cold sodium hydroxide solution; on acidification *phthalamic acid N-acetamide* was precipitated. It crystallised from ethyl alcohol in needles, m. p. 204—205°, and was converted into phthalimidoacetamide above the m. p. (Found : N, 12.8.  $C_{10}H_{10}O_4N_2$  requires N, 12.6%).

The following compounds were prepared in a similar manner to those described above.

*4-Chlorophthalimidoacetonitrile* formed colourless prismatic needles, m. p. 146.5°, from dilute acetic acid (Found : Cl, 15.8.  $C_{10}H_5O_2N_2Cl$  requires Cl, 16.1%). *4-Chlorophthalimidoacetic acid*, obtained from the nitrile or by condensing 4-chlorophthalic anhydride with glycine, crystallised in small yellow plates, m. p. 205°, from hot water or dilute alcohol (Found : Cl, 14.6.  $C_{10}H_6O_4NCl$  requires Cl, 14.8%). The *acid chloride* crystallised from benzene in colourless needles, m. p. 93.5° (Found : Cl, 27.3.  $C_{10}H_5O_3NCl_2$  requires Cl, 27.5%). The *amide*, obtained from the nitrile or the acid chloride, crystallised from hot water in needles, m. p. 241° (Found : Cl, 14.7.  $C_{10}H_7O_3N_2Cl$  requires Cl, 14.9%). The *ethyl ester*, obtained from the acid chloride and alcohol, crystallised from the latter in silky needles, m. p. 95.5° (Found : Cl, 13.1.  $C_{12}H_{10}O_4NCl$  requires Cl, 13.3%).

*3-Nitrophthalimidoacetonitrile* formed small yellow needles, m. p. 156°, from glacial acetic acid (Found : N, 18.0.  $C_{10}H_5O_4N_3$  requires N, 18.2%). The *acid*, which crystallised in transparent yellow plates, m. p. 208°, from hot water (Found : N, 10.9.  $C_{10}H_6O_6N_2$  requires N, 11.2%), gave with thionyl chloride or phosphorus pentachloride the *acid chloride*, which formed clusters of small prismatic needles, m. p. 119.5°, from benzene (Found : Cl, 13.2.  $C_{10}H_5O_5N_2Cl$  requires Cl, 13.2%). The *ethyl ester* formed long needles, m. p. 77.5°, from alcohol (Found : N, 9.8.  $C_{12}H_{10}O_6N_2$  requires N, 10.0%), and the *amide* transparent needles, m. p. 212°, from dilute acetic acid (Found : N, 17.3.  $C_{10}H_7O_5N_3$  requires N, 16.9%).

*4-Nitrophthalimidoacetonitrile* formed thin yellow plates, m. p. 134—135°, from water (Found : N, 18.3%), the *acid* thin shimmering plates, m. p. 193° (Found : N, 11.2%), and the *acid chloride* buff-coloured prisms, m. p. 129°, from benzene (Found : Cl, 13.4%). The *ethyl ester* crystallised from ethyl alcohol in yellow hexagonal prisms, m. p. 78°; a mixture with the 3-nitro-ester had m. p. 52—65° (Found : N, 10.2%). The *amide* formed thin rectangular transparent plates, m. p. 214°, from dilute acetic acid (Found : N, 16.65%). It is less soluble in water than the 3-nitro-amide. A mixture of the two softened at 196° and melted slowly at 202.5°.

*3 : 6-Dichlorophthalimidoacetonitrile* formed long needles, m. p.

175—176°, from glacial acetic acid (Found: N, 11.1; Cl, 27.8.  $C_{10}H_4O_2N_2Cl_2$  requires N, 11.0; Cl, 27.8%), the *acid* white needles, m. p. 243—244.5° (Found: N, 5.2; equiv., 291.7.  $C_{10}H_5O_4NCl_2$  requires N, 5.1%; equiv., 292), and the *acid chloride* hexagonal prisms, m. p. 135°, from benzene (Found: Cl, 36.2.  $C_{10}H_4O_3NCl_3$  requires Cl, 36.4%). The *ethyl* ester crystallised in transparent leaflets, m. p. 193°, from benzene (Found: Cl, 35.1.  $C_{12}H_9O_4NCl_2$  requires Cl, 35.1%), and the *amide* from glacial acetic acid in transparent needles, m. p. 262—263° (Found: N, 10.4; Cl, 26.2.  $C_{10}H_6O_3N_2Cl_2$  requires N, 10.25; Cl, 26.0%).

3:6-Dibromophthalimidoacetoneitrile crystallised from glacial acetic acid in long needles, m. p. 228° (Found: Br, 46.3.  $C_{10}H_4O_2N_2Br_2$  requires Br, 46.5%), the *acid* in small rhombic prisms, m. p. 239—242° (Found: Br, 43.9.  $C_{10}H_5O_4NBr_2$  requires Br, 44.1%), and the *amide* in needles, m. p. 285—287° (Found: Br, 44.1.  $C_{10}H_6O_3N_2Br_2$  requires Br, 44.2%).

Tetrachlorophthalimidoacetoneitrile, prepared by heating tetrachlorophthalic anhydride with methyleneaminoacetoneitrile in suspension in xylene at 130°, crystallised from ethyl acetate-glacial acetic acid in small colourless prisms, m. p. 259° (Found: N, 8.6; Cl, 43.7.  $C_{10}H_2O_2N_2Cl_4$  requires N, 8.6; Cl, 43.8%), sparingly soluble in hot water and alcohol. The *acid* crystallised from dilute acetic acid in thin lustrous plates, m. p. 298° (decomp.) (Found: Cl, 41.3.  $C_{10}H_3O_4NCl_4$  requires Cl, 41.4%), and the *acid chloride* from benzene in leaves, m. p. 209° (Found: Cl, 49.0.  $C_{10}H_2O_3NCl_5$  requires Cl, 49.1%). The *methyl* ester formed long needles, m. p. 181°, from benzene (Found: Cl, 39.9.  $C_{11}H_5O_4NCl_4$  requires Cl, 40.0%), and the *ethyl* ester long needles, m. p. 180.5°, from alcohol-benzene (Found: Cl, 38.2.  $C_{12}H_7O_4NCl_4$  requires Cl, 38.3%). The *amide* crystallised from glacial acetic acid in bundles of needles, which melted at 294° if rapidly heated, but decomposed if slowly heated and melted at 285° (Found: Cl, 41.4.  $C_{10}H_4O_3N_2Cl_4$  requires Cl, 41.5%).

Naphthalimidoacetoneitrile was readily obtained by condensing naphthalic anhydride with methyleneaminoacetoneitrile in boiling xylene. It crystallised from glacial acetic acid in pale yellow, transparent needles, m. p. 248° (decomp.) (Found: N, 11.9.  $C_{14}H_8O_2N_2$  requires N, 11.9%). The nitrile was readily hydrolysed by dilute hydrochloric acid, giving the *acid*, which crystallised from dilute acetic acid in white plates, m. p. 259—260° (Found: N, 5.4.  $C_{14}H_9O_4N$  requires N, 5.5%).

Naphthalimidoacetyl chloride formed pale yellow needles, m. p. 232° (Found: Cl, 12.6.  $C_{14}H_8O_3NCl$  requires Cl, 12.6%). The corresponding *amide* crystallised in small yellow needles, m. p. 319°

(decomp.), from water (Found : N, 10.9.  $C_{14}H_{10}O_3N_2$  requires N, 11.0%).

*Aminoacetonitrile Sulphates*.—Klages (*loc. cit.*) isolated a mono- and a di-sulphate of aminoacetonitrile, m. p.  $101^\circ$  (leaves) and  $165^\circ$  (long flat prisms) respectively. He obtained the former by treating methyleneaminoacetonitrile with one molecular equivalent of concentrated sulphuric acid dissolved in alcohol, the salt being precipitated by addition of ether. From a perusal of his paper it is not clear how he obtained the disulphate, and some difficulty was experienced at first in obtaining specimens for the preparation of the amides mentioned above. Klages's experimental details were followed closely, and in several preparations the white crystalline powder precipitated by the addition of ether, which according to Klages should be the monosulphate (m. p.  $101^\circ$ ), began to melt at  $127^\circ$  and was completely melted at  $166^\circ$  with decomposition. It was treated with alcohol containing a few drops of water : the portion of the salt remaining undissolved melted sharply at  $166^\circ$  (decomp.) (Found : 0.14 g. required 13.5 c.c. 0.1N-NaOH to neutralise the mineral acid. Calc. for disulphate : 13.5 c.c.). The filtrate deposited thin plates with leaf-like formation, m. p.  $101-127^\circ$ , and analysis showed that this was a mixture of the mono- and the di-sulphate. A similar mixture (m. p.  $101-109^\circ$ ) was obtained by crystallising the powder from absolute alcohol. The disulphate is therefore the less soluble portion, and its properties are in agreement with Klages's statements. The *monosulphate* prepared by the following method is entirely different from that obtained by Klages. Methyleneaminoacetonitrile (3 g.; 1 mol.) was treated with concentrated sulphuric acid ( $d$  1.84) (3 c.c.; a slight excess over 1 mol.) dissolved in alcohol (12.5 c.c.) cooled in ice. The solution became clear, and began to deposit a snow-white crystalline powder after  $\frac{1}{2}$  hour, the deposition being hastened by the addition of ether. This first crop of crystals consisted of small hard prisms, m. p.  $127-164^\circ$  (decomp.). The alcohol-ether solution afterwards deposited thin shimmering leaves, which were hygroscopic; m. p.  $121^\circ$  (Found : 0.1 g. required 12.7 c.c. 0.1N-NaOH to neutralise the mineral acid. Calc. for monosulphate : 12.9 c.c.).

Both the mono- and the di-sulphate react with phthalic anhydride and derivatives to give the corresponding amides, the intermediate nitrile being hydrolysed by the molecule of water liberated during the first stage of the reaction.

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