Acrylonitrile in Organic Syntheses. Part I. Synthesis of 3a : 4 : 5 : 6-*Tetrahydroperinaphthane*-3a-*carboxylic Acid.*

By A. D. CAMPBELL.

[Reprint Order No. 5041.]

Acid hydrolysis of γ-cyano-γ-phenylpimelonitrile (III) gave α-2-carboxyethyl-α-phenylglutarimide (IV) which was cyclised to 1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene-1-*spiro*-α-glutarimide (V). γ-Carboxy-γ-phenylpimelic acid (VI), obtained by prolonged hydrolysis of (III) or (IV) by acid or alkali, was cyclised to 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII). After reduction by the Clemmensen procedure (VII) was further cyclised to 3*a* : 4 : 5 : 6-tetrahydro-1-oxoperinaphthane-3*a*-carboxylic acid (X). This keto-acid (X) gave 3*a* : 4 : 5 : 6-tetrahydroperinaphthane-3*a*-carboxylic acid on reduction. A method for the synthesis of α-phenylglutaric anhydride is described.

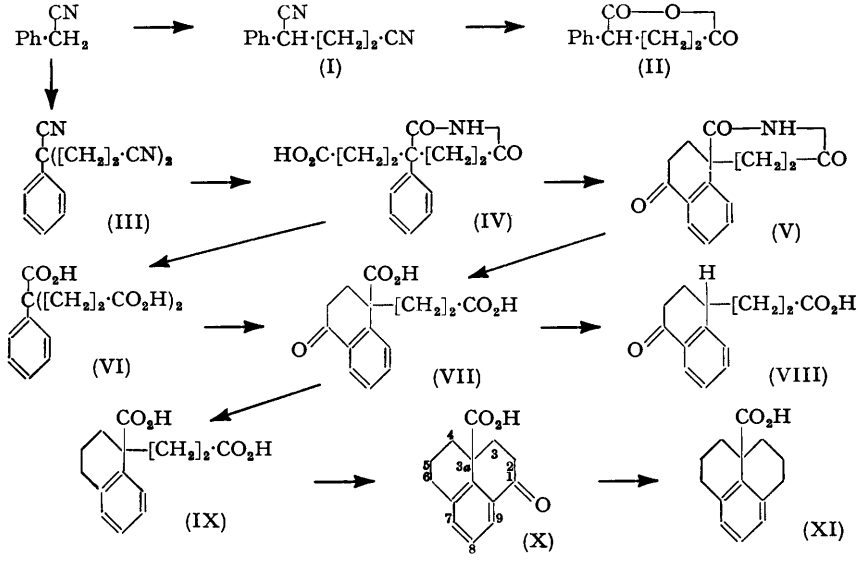
ACRYLONITRILE is a reagent whose many reactions (Bruson, *Organic Reactions*, 1949, **5**, 77) have found numerous uses in synthetic organic chemistry. The present communication describes the use of acrylonitrile in the preparation of a number of derivatives of tetrahydronaphthalene and tetrahydroperinaphthane.

When equimolar quantities of acrylonitrile and phenylacetonitrile reacted in *tert.*-butyl alcohol containing an alkaline catalyst (methyl-alcoholic potassium hydroxide or Triton B) at temperatures from 15° to 100° the product was invariably γ-cyano-γ-phenylpimelonitrile (III). By using Roger's method (*Chem. Abs.*, 1949, **43**, 3446; U.S.P. 2,460,536/1949) in which acrylonitrile is added to an excess of boiling phenylacetonitrile in the presence of sodium cyanide a 65% yield of α-phenylglutaronitrile (I) has been obtained. Where dicyanoethylation is possible it is normally difficult to isolate the monocyanoethylation product (Bruson, *op. cit.*) but it appears that elevated temperatures favour monosubstitution. However, Koelsch (*J. Amer. Chem. Soc.*, 1943, **65**, 437) obtained a 20—33% yield of α-phenylglutaronitrile by treating acrylonitrile with phenylacetonitrile in molar proportions in the absence of a solvent (sodium ethoxide as catalyst), and when ether was used as solvent the yield rose to 36%. The effect of temperature

on the course of the cyanoethylation reaction is being further investigated. Hydrolysis of the nitrile (I) by aqueous sulphuric acid gave α-phenylglutaric acid which was isolated as the anhydride (II): Hornig and Finelli (*ibid.*, 1949, **71**, 3204) prepared this anhydride by a similar but more indirect method, converting the phenylacetonitrile into ethyl α-cyano-α-phenylacetate where only monocyanoethylation is possible.

γ-Cyano-γ-phenylpimelonitrile (III), the condensation product formed when two mols. of acrylonitrile condense with one of phenylacetonitrile (Bruson, *ibid.*, 1942, **64**, 2858), resisted normal hydrolysis. Prolonged hydrolysis by alkali gave γ-carboxy-γ-phenylpimelic acid, but acid hydrolysis gave, after 6 hr.' refluxing, α-2-carboxyethyl-α-phenylglutarimide (IV) which could be converted into the required acid by further prolonged hydrolysis with acid or alkali. This imide was monobasic to phenolphthalein and the keto-imide, 1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene-1-*spiro*-α-glutarimide (V), formed on cyclisation with sulphuric acid was neutral to phenolphthalein although it dissolved in alkali. The keto-imide (V) was readily hydrolysed to 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII) by aqueous alkali.

Cyclisation of γ-carboxy-γ-phenylpimelic acid (VI), previously prepared by the oxidation of γ-acetyl-γ-phenylpimelic acid (Bruson, *loc. cit.*), with anhydrous hydrogen fluoride or concentrated sulphuric acid at 70° gave a good yield of 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII), which exists in two crystalline forms; no perinaphthane derivative was isolated. It is interesting that although Manske (*ibid.*, 1931, **53**, 1104) obtained mainly 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene and only a very small yield of 3*a* : 4 : 5 : 6-tetrahydro-1 : 6-dioxoperinaphthane von Braun and Weissbach (*Ber.*, 1931, **64**, 1785) claimed that this cyclisation produced mainly the



diketone. In general, *meta*-directing groups inhibit intermolecular acylation (Johnson, *Organic Reactions*, 1944, **2**, 120). Cyclisation of γ-carboxy-γ-phenylpimelic acid with concentrated sulphuric acid at 100° gave a low yield of the expected keto-acid together with a compound which was an acid–base indicator. Analytical figures suggest that it is the potassium salt of a sulphonic acid and may be an oxidation product of the doubly cyclised 3*a* : 4 : 5 : 6-tetrahydro-1 : 6-dioxoperinaphthane-3*a*-carboxylic acid.

1-2'-Carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid was readily decarboxylated to 1-2'-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxonaphthalene (VIII), previously prepared by Manske (*J. Amer. Chem. Soc.*, 1931, **53**, 1109) as one of the products from the cyclisation of γ-phenylpimelic acid. Although the carboxyl group attached to the

quaternary carbon atom was easily eliminated in this case, attempts to decarboxylate γ-carboxy-γ-phenylpimelic acid with copper powder in quinoline at 210° were unsuccessful.

By using the Clemmensen–Martin procedure (*ibid.*, 1936, **58**, 1438) 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (VII) was reduced to the acid (IX) and then cyclised with anhydrous hydrogen fluoride to 3*a* : 4 : 5 : 6-tetrahydro-1-oxoperinaphthane-3*a*-carboxylic acid (X), which was very easily decarboxylated by heat. The 2 : 4-dinitrophenylhydrazone of this keto-acid was decarboxylated in boiling ethanol, giving the 2 : 4-dinitrophenylhydrazone of 3*a* : 4 : 5 : 6-tetrahydroperinaphthan-1-one; this ketone had been prepared by von Braun and Reutter (*Ber.*, 1926, **59**, 1922) by cyclisation of 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydronaphthalene. 3*a* : 4 : 5 : 6-Tetrahydro-1-oxoperinaphthane-3*a*-carboxylic acid was reduced by the Clemmensen procedure to 3*a* : 4 : 5 : 6-tetrahydroperinaphthane-3*a*-carboxylic acid (XI) in which the carboxyl group is attached to a quaternary carbon atom at the point of fusion of the two saturated rings.

Experimental

α-Phenylglutaric Anhydride (II).—A mixture of phenylacetonitrile (150 g.) and sodium cyanide (1 g.) was heated (oil-bath) to 225°; water (0·5 c.c.) and then acrylonitrile (14 g.) were added dropwise with stirring. The mixture was stirred at 225° for 30 min. and then fractioned under reduced pressure, to give α-phenylglutaronitrile (30 g.), b. p. 200—205°/15 mm., as a colourless liquid. Rogers (*loc. cit.*) gives b. p. 163°/1 mm. The nitrile (28 g.) was refluxed with water (40 c.c.), concentrated sulphuric acid (40 c.c.), and glacial acetic acid (40 c.c.) for 5 hr., poured into water, extracted with ether–ethyl acetate, and dried and the solvent was removed under reduced pressure. The residue was refluxed with acetic anhydride (30 c.c.) for ½ hr. and distilled. The anhydride, b. p. 235—240°/15 mm. (26 g.), had m. p. 95°. Hornig and Finelli (*loc. cit.*) give m. p. 95—96°.

γ-Carboxy-γ-phenylpimelic Acid (VI).—(*a*) γ-Cyano-γ-phenylpimelonitrile (12 g.) was refluxed for 60 hr. with potassium hydroxide (20 g.) in water (100 c.c.). The mixture of acid and potassium chloride which separated on acidification with concentrated hydrochloric acid was filtered off and the acid was taken up in acetone. Evaporation gave an oil which crystallised from nitromethane, to give the acid (8 g.), m. p. 154° (Bruson, *loc. cit.*, gives m. p. 154°). (*b*) γ-Cyano-γ-phenylpimelonitrile (10 g.) was refluxed for 40 hr. with concentrated sulphuric acid (50 g.), glacial acetic acid (50 g.), and water (50 c.c.). The mixture was cooled and poured on cracked ice, and the solid which separated was filtered off and recrystallised from water, to give the acid (7·5 g.), m. p. 153—154°.

1-2′-*Carboxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*oxo*-1-*naphthoic acid* (VII).—(*a*) γ-Carboxy-γ-phenylpimelic acid (10 g.) was treated with anhydrous hydrogen fluoride (approx. 100 g.) in a copper beaker. After 48 hr. the remaining hydrogen fluoride was allowed to evaporate, ice was added, and the product extracted with ether. The solid obtained on evaporation of the ether was recrystallised from water, to give the *keto-acid* (6 g.), m. p. 135—136°. Further recrystallisation from water or ethyl acetate gave white cubes or needles, respectively, both of m. p. 167° (Found: equiv., 125; C, 64·2; H, 5·5%. $C_{14}H_{14}O_5$ requires equiv., 131; C, 64·1; H, 5·3%). The acid of m. p. 135—136° gave a similar equivalent weight. Both acids gave a *semicarbazone*, m. p. 239—240° (decomp.), as fine white crystals from ethanol (Found: N, 13·0. $C_{15}H_{17}O_5N_3$ requires N, 13·2%), and a 2 : 4-*dinitrophenylhydrazone* as orange-red crystals, m. p. 208° with resolidification, remelting at 225—226° (Found: N, 12·8. $C_{20}H_{15}O_8N_4$ requires N, 12·7.

(*b*) γ-Carboxy-γ-phenylpimelic acid (10 g.) was warmed to 70—80° for 2 hr. with concentrated sulphuric acid (50 c.c.). The mixture was poured on cracked ice, and the acid which separated was filtered off and recrystallised from water; it melted at 135—136°, resolidifying immediately to remelt at 166—167°.

(*c*) When the above reaction was carried out at 100° the deep red solution formed when the product was poured on ice water was extracted with ether–ethyl acetate. Extraction of the organic layer with concentrated aqueous potassium hydroxide, followed by acidification, gave the keto-acid (VII) together with a red powder which was sparingly soluble in ethyl acetate. Recrystallisation of this red compound from water gave a brick-red hygroscopic powder, decomp. >300° (Found: C, 50·2; H, 3·2; K, 12·2%). This compound which also contained sulphur acts as an acid–base indicator changing colour at pH 4·5—5 from a pink fluorescence in alkali

to a yellow fluorescence in acid. A very marked colour change is noticed in acid–base titrations containing 0·1 mg. of the compound per 100 c.c. of solution.

1-2′-*Carboxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-1-*naphthoic Acid* (IX).—1-2′-Carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (6 g.) was refluxed for 6 hr. with amalgamated zinc (20 g.), concentrated hydrochloric acid (35 c.c.), water (15 c.c.), acetic acid (2 c.c.), and toluene (10 c.c.). The acid remaining after evaporation of the combined toluene layer and ether-extracts of the aqueous layer failed to crystallise. It was taken up in aqueous alkali (charcoal), reprecipitated, and taken up in ether. A semisolid *acid* remained after evaporation of the ether (Found: C, 67·5; H, 6·6. $C_{14}H_{16}O_4$ requires C, 67·7; H, 6·5%).

3a : 4 : 5 : 6-*Tetrahydro*-1-*oxoperinaphthane*-3a-*carboxylic Acid* (X).—The preceding acid (4 g.) was treated with anhydrous hydrogen fluoride (approx. 60 g.) in a copper beaker for 20 hr. The remaining hydrogen fluoride was allowed to evaporate, ice was added, and the product was extracted with ether and taken up in aqueous sodium hydroxide (charcoal), and reprecipitated by acid. Clusters of white needles of the *keto-acid* (2·5 g.), m. p. 203°, separated on cooling (Found: equiv., 223; C, 73·1; H, 6·4%. $C_{14}H_{14}O_3$ requires equiv., 230; C, 73·1; H, 6·1%). It gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 266° (with previous darkening), as red needles from warm ethanol (Found: N, 13·9. $C_{20}H_{18}O_6N_4$ requires N, 13·7%).

3a : 4 : 5 : 6-*Tetrahydroperinaphthan*-1-*one*.—The acid (X) (0·1 g.) was distilled, to give the neutral ketone, m. p. 72°. Its 2 : 4-*dinitrophenylhydrazone* had m. p. 246° (Found: N, 15·6. $C_{19}H_{18}O_4N_4$ requires N, 15·3%) and was also obtained when the 2 : 4-dinitrophenylhydrazone of the keto-acid (X) was recrystallised from boiling ethanol. The semicarbazone formed white crystals, m. p. 233°, from ethanol. Von Braun and Reutter (*loc. cit.*) give ketone, m. p. 72°, and semicarbazone, m. p. 235°.

3a : 4 : 5 : 6-*Tetrahydroperinaphthane*-3a-*carboxylic Acid* (XI).—3a : 4 : 5 : 6-Tetrahydro-1-oxoperinaphthane-3a-carboxylic acid (0·12 g.) was reduced by the Clemmensen procedure during 1 hr. The *acid* produced was isolated in the usual way, as white needles (0·08 g.), m. p. 205—206° (from aqueous ethanol; charcoal) (Found: C, 77·7; H, 7·5. $C_{14}H_{16}O_2$ requires C, 77·7; H, 7·4%).

α-2′-*Carboxyethyl*-α-*phenylglutarimide* (IV).—γ-Cyano-γ-phenylpimelonitrile (30 g.) was refluxed for 6 hr. with concentrated sulphuric acid (100 c.c.) and water (100 c.c.). The resulting solution was cooled and poured on cracked ice, and the precipitate was filtered off and recrystallised from water, to give the *imide* (24 g.) as white needles, m. p. 165° [Found: equiv., 250 (phenolphthalein); C, 64·0; H, 5·6; N, 5·3%. $C_{14}H_{15}O_4N$ requires equiv., 261; C, 64·4; H, 5·7; N, 5·4%]. The imide (10 g.), after hydrolysis with aqueous potassium hydroxide until ammonia ceased to be evolved (50 hr.), gave γ-carboxy-γ-phenylpimelic acid (8·5 g.), m. p. 153° on acidification of the reaction mixture.

1 : 2 : 3 : 4-*Tetrahydro*-4-*oxonaphthalene*-1-spiro-α-*glutarimide* (V).—α-2-Carboxyethyl-α-phenylglutarimide (10 g.) was warmed at 90° for 2 hr. with concentrated sulphuric acid (50 c.c.). The cooled mixture was poured on cracked ice, and the precipitate of *keto-imide* was filtered off and recrystallised from aqueous alcohol, to give white needles (6 g.), m. p. 198° (Found: C, 68·7; H, 5·2. $C_{14}H_{13}O_3N$ requires C, 69·1; H, 5·4%). The keto-imide was neutral to phenolphthalein but soluble in 2N-sodium hydroxide from which it was reprecipitated by hydrochloric acid. It gave a 2 : 4-*dinitrophenylhydrazone*, m. p. 292°, as fine orange needles from glacial acetic acid (Found: N, 16·1. $C_{20}H_{17}O_6N_5$ requires N, 16·5%), and a *semicarbazone*, m. p. 258—259° (decomp.), as white needles from ethanol (Found: N, 18·3. $C_{15}H_{16}O_3N_4$ requires N, 18·7%). The imide (1·0 g.), after hydrolysis with aqueous alkali and acidification of the reaction mixture, gave 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (0·9 g.), m. p. 136° (from water).

1-2′-*Carboxyethyl*-1 : 2 : 3 : 4-*tetrahydro*-4-*oxonaphthalene* (VIII).—1-2′-Carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-1-naphthoic acid (0·1 g.) was decarboxylated by being heated under reflux for 5 min. The cooled semisolid acid product (VIII) was taken up in aqueous potassium hydroxide, reprecipitated by acid, and recrystallised from water; it had m. p. 106—107° (60 mg.). Manske (*J. Amer. Chem. Soc.*, 1931, **53**, 1109) gives m. p. 105—106°.

The author is indebted to Prof. S. N. Slater for suggesting the subject of the investigation and for his interest throughout its course. The work was assisted by grants for apparatus and chemicals from the Mellor Research Fund and the University of New Zealand.

UNIVERSITY OF OTAGO, DUNEDIN, NEW ZEALAND. [*Received, January 21st*, 1954.]