

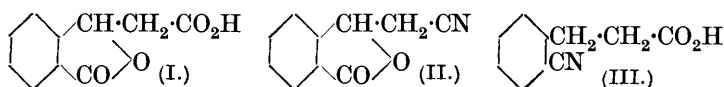
CXI.—*Synthetical Work on the isoQuinoline Alkaloids.*
Part II. A Method of Opening the Rings of Cyclic
Ketones.

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THE reactions herein described were investigated with the object of obtaining derivatives of β -*o*-cyanophenylpropionic acid and of *o*-carboxyphenylacetonitrile, such substances being required for attempts to synthesise ten-membered rings of the cryptopine type.

The sodium salt of 1-nitroso- β -naphthol when heated to 180° with sand gives sodium *o*-cyanocinnamate in poor yield (D.R.-P. 116223). This reaction was examined in the hope of bringing about the same change by less violent means. 1-Nitroso- β -naphthol was converted by benzoyl chloride and cold caustic soda solution into a benzoyl derivative, which slowly hydrolysed in warm caustic soda solution, yielding benzoic acid and the *o*-cyanocinnamic acid of m. p. 137° (D.R.-P. 411955). The separation of the benzoic acid was rather troublesome, so it is fortunate that benzoyl chloride can be replaced by either benzene- or toluene-sulphonyl chloride, the acyl derivative produced being in each case easily hydrolysed to the above cyano-acid.

This 2-cyanocinnamic acid was at first thought to be *o*-carboxycinnamonitrile, since on hydrolysis it gave *o*-carboxycinnamic acid, and since, if its formation followed the normal course of the Beckmann reaction, ring opening might take place in two ways, thus: $R \cdot C(\cdot NOH) \cdot COR' \rightarrow R \cdot CO \cdot NH \cdot COR' \rightarrow$ either $R \cdot CO_2H$ and $R'CN$ or RCN and $R' \cdot CO_2H$. *o*-Carboxycinnamonitrile was therefore synthesised as follows. Phthalylacetic acid (Neumann and Gabriel, *Ber.*, 1893, 26, 952) was reduced electrolytically to phthalideacetic acid (I). This was converted through its acid chloride into *phthalideacetamide*, which, when boiled in xylene solution with phosphorus pentoxide, lost water and gave *phthalideacetoneitrile* (II). The



lactone ring of this substance was opened on treatment with caustic soda, and by carefully heating the sodium salt in a vacuum *o*-carboxycinnamonitrile was produced.

If the acyl derivatives of 1-nitroso- β -naphthol are heated at 140° for a short time, they will give the *o*-cyanocinnamic acid of m. p. 255 — 256° on hydrolysis.

The low-melting acid itself, when heated above its melting point for a few minutes, is completely converted into the high-melting *o*-cyanocinnamic acid. Since both cyano-acids on electrolytic reduction give β -*o*-cyanophenylpropionic acid (III), the only possible conclusion is that these acids are geometric isomerides similar to cinnamic and *allocinnamic* acids. On the analogy of these, the low-melting acid has been called *o*-cyano*allocinnamic* acid.

As β -*o*-cyanophenylpropionic acid was required in quantity, the most suitable conditions for its preparation were investigated. A method is described, using toluenesulphonyl chloride, which is suitable for large-scale preparations; about 6% of the acyl derivative

is hydrolysed to 1-nitroso- β -naphthol, but this is easily separated owing to its insolubility in sodium carbonate solution.

Since in these reactions 1-nitroso- β -naphthol obviously reacted in the oxime form, it seemed probable that substances containing the group $\cdot\text{CH}_2\cdot\text{CO}\cdot$ in a ring, if first converted into their *isonitroso*-derivatives, would react with acid chlorides in the same way. This was investigated in the case of the hydrindones. Hydrindone itself gave *o*-carboxyphenylacetonitrile in 92% yield, whilst 5:6-dimethoxy- and 5:6-methylenedioxy-hydrindones gave the corresponding cyano-acids. These three cyano-acids have recently been prepared by Haworth and Pink (J., 1925, 127, 1369) by the action of phosphorus pentachloride on the nitrosohydrindones. They easily decompose on warming, but by cautious treatment with thionyl chloride may be converted into their acid chlorides, from which their esters, amides, and substituted amides may be obtained.

EXPERIMENTAL.

Action of Benzenesulphonyl Chloride upon 1-Nitroso- β -naphthol.—1-Nitroso- β -naphthol (1 g.-mol.) is mixed with benzenesulphonyl chloride (1 g.-mol.), the whole is dissolved in the minimum quantity of cold acetone, and 8% caustic soda solution (1.2 g.-mols.) is added slowly, with shaking and cooling in ice. The *benzenesulphonyl-1-nitroso- β -naphthol* that separates crystallises from a little acetone in yellow prisms, m. p. 124—125° (decomp.) (Found: C, 61.6; H, 3.6. $\text{C}_{16}\text{H}_{11}\text{O}_4\text{NS}$ requires C, 61.3; H, 3.5%). On being kept at its m. p. for a few minutes, it resolidifies and thereafter melts at 137—139°, having been converted into an isomeride which crystallises from acetone in cream needles, m. p. 141° (Found: C, 61.7; H, 3.5%).

The low-melting acyl derivative is hydrolysed when dissolved in a slight excess of 8% caustic soda solution at 60°. The filtered cooled solution on acidification deposits *o*-cyanoallicinnamic acid in almost colourless needles. This crystallises from water, containing a little animal charcoal, in colourless, felted needles, m. p. 137° (Found: C, 69.7; H, 4.4. Calc. for $\text{C}_{10}\text{H}_7\text{O}_2\text{N}$: C, 69.4; H, 4.1%). When the benzenesulphonyl derivative, m. p. 141°, is treated in the same way, *o*-cyanocinnamic acid separates in a gelatinous form; it crystallises from glacial acetic acid in slightly brown, glistening plates, m. p. 256°, identical with the product of heating the sodium salt of 1-nitroso- β -naphthol with sand at 180°.

Direct Preparation of o-Cyanoallicinnamic Acid.—A solution of 1-nitroso- β -naphthol (43 g.) and toluenesulphonyl chloride (47 g.) in the minimum quantity of acetone is kept at 55—60° while caustic soda (8% solution) is added slowly, with constant shaking, so that

the solution is kept faintly alkaline. When the solution finally becomes permanently alkaline, it is cooled, filtered, and acidified, 38 g. of crude *o*-cyanoallocinnamic acid being precipitated. For the preparation of *o*-cyanophenylpropionic acid further purification is unnecessary.

o-Carboxycinnamic acid, m. p. 182°, is produced when either of the *o*-cyanocinnamic acids is refluxed for 2 hours with 10% caustic soda solution, and is precipitated on acidification.

β-*o*-Cyanophenylpropionic Acid (III).—A solution of crude *o*-cyanoallocinnamic acid (40 g.) in 14% sodium carbonate solution (150 c.c.) is filtered from insoluble gummy impurities and reduced electrolytically for 3 hours at a lead cathode, the current density being 2 amps./100 sq. cm.; the anode cell consists of a lead electrode in 20% caustic soda solution. The product on acidification deposits a slightly brown, sandy powder, which crystallises from water in prisms, m. p. 127° (Found: C, 68.9; H, 5.0. C₁₀H₉O₂N requires C, 68.6; H, 5.2%).

o-Carboxycinnamionitrile, CO₂H·C₆H₄·CH:CH·CN.—Phthalyl-acetic acid (40 g.) dissolved in caustic soda (200 c.c. of 15% solution) is reduced electrolytically under the conditions described above. The hot solution is acidified with hydrochloric acid and filtered; on cooling, phthalideacetic acid separates in colourless plates, m. p. 151°, identical with the substance obtained by the reduction of phthalylacetic acid with sodium amalgam (Gabriel and Michael, *Ber.*, 1877, 10, 391). The acid (10 g.) is boiled with thionyl chloride (20 c.c.) for 15 minutes, the excess of thionyl chloride distilled away, the gummy residue dissolved in a little chloroform, and the solution slowly added to aqueous ammonia (60 c.c.; *d* 0.880) cooled in ice, the temperature being kept below 10° during the addition. The chloroform is then evaporated on the water-bath; on cooling, *phthalideacetamide* separates in rectangular plates, m. p. 182–183° (Found: N, 7.5. C₁₀H₉O₃N requires N, 7.3%). This amide (2 g.) is heated in boiling xylene (16 c.c.) with phosphorus pentoxide (4 g.) for 15 minutes. The boiling filtered xylene, on cooling, deposits pure white needles, m. p. 111°, of *phthalideacetoneitrile*, and more may be obtained by extracting the brown, gummy residue from the xylene with boiling water, the latter depositing slightly brown needles on cooling. The nitrile is insoluble in cold alkali, but dissolves readily on warming, ammonia being evolved from the boiling solution.

A solution of phthalideacetoneitrile in the theoretical quantity of warm caustic soda solution is evaporated to dryness on the water-bath, the residue kept at 200° in a vacuum for 10 minutes, cooled, and dissolved in water. On acidification a slightly yellow powder

separates which crystallises from water as a microcrystalline powder, m. p. 169—172° (Found: N, 7.3. $C_{10}H_9O_3N$ requires N, 7.3%). This is *o*-carboxycinnamionitrile and yields *o*-carboxycinnamic acid, m. p. 182°, on hydrolysis (as above).

o-Carboxyphenylacetoneitrile.—2-isoNitroso-1-hydrindone (7.2 g.) is dissolved in caustic soda (80 c.c. of 8% solution), and benzenesulphonyl chloride (9 g.) added with constant shaking. The benzenesulphonyl derivative first separates as a white gum, which slowly dissolves on raising the temperature to 80° for a few minutes. The cooled filtered solution on acidification deposits *o*-carboxyphenylacetoneitrile as a white powder crystallising from water in colourless needles, m. p. 126°, identical with the substance obtained by Haworth and Pink (*loc. cit.*).

2-Carboxy-4 : 5-dimethoxyphenylacetoneitrile is obtained from dimethoxyisonitrosohydrindone (3 g.), caustic soda (3 g. in 25 c.c. of water), and benzenesulphonyl chloride (2.2 c.c.) by the method described above; it crystallises slowly in needles, m. p. 166—167°.

2-Carboxy-4 : 5-methylenedioxyphenylacetoneitrile, obtained in exactly the same way as the dimethoxy-compound, crystallises in slightly yellow prisms, m. p. 195° (Found: C, 58.3; H, 3.4. Calc., C, 58.5; H, 3.4%).

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