46. *β-Cycloylpropionitriles. Part III. Reduction to 2-Cyclyl-Δ^2-pyrrolines and 2-Cyclylpyrrolidines.*

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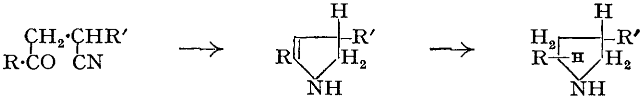
β-Cycloylpropionitriles are reduced catalytically to 2-cyclyl-Δ^2-pyrrolines and 2-cyclylpyrrolidines. α-Carboxy-β-benzoylpropionitrile on reduction gives poor yields of two amino-acids and by a peculiar reaction a 17% yield of 2-phenylpyrrole.

THE conversion of β-cycloylpropionitriles (I) into pyrrole dyes has been described in Parts I and II but hitherto no simple pyrrole derivative has been obtained. By the catalytic reduction of (I) using Raney nickel, simple 2-cyclyl-Δ^2-pyrrolines (II) and 2-cyclylpyrrolidines (III) have now been obtained in good yield. This preparation of monosubstituted reduced pyrrole ring systems is analogous to the formation of disubstituted analogues by the reduction of β-aroyl-α-arylpropionitriles (I; R, R′ = aryl) described by Rogers (*J.*, 1943, 594) who used the same catalyst (see also Rupe and Gisiger, *Helv. Chim. Acta*, 1925, 8, 338). The reaction as far as the pyrroline proceeds rapidly at room pressure and temperature (23°) but the further reduction to the pyrrolidine is a lengthy procedure under like conditions.



(I.) (II.) (III.)

A remarkable property of the pyrrolines and pyrrolidines is the great change in their odour given by small changes in the groups at the 2-positions.

The preparation of 2-cyclylpyrrolines and -pyrrolidines from the corresponding cyclyl methyl ketones is thus readily achieved by this method.*

An attempted selenium dehydrogenation of 2-phenylpyrroline did not give the required 2-phenylpyrrole; the main product was an unstable solid fluorescing strongly in alcoholic solution from which selenium separated on standing.

It was thought to be of interest to determine whether substances of type (II; R′ = H) could be obtained by catalytic reduction of α-cyano-β-aroylpropionic acids (I; R′ = CO_2H) followed by decarboxylation. This alternative synthesis would be attractive since (I; R′ = CO_2H) is readily obtained by the Friedel–Crafts condensation of the carbocycle or heterocycle with maleic anhydride to the substituted acrylic acid followed by hydrogen cyanide addition.

Reduction of the acid was rapid under conditions similar to the reduction of the nitrile. However, owing to the release of carbon dioxide during hydrogenation, the apparent volume of hydrogen absorbed was only half that required to give a pyrroline. Small yields of two amino-acids were obtained, however, the analysis of one indicating its being *4-carboxy-2-phenyl-Δ^2-pyrroline* (II; R = Ph, R′ = CO_2H); that of the other was indeterminate. Somewhat larger yields of 2-phenylpyrrole, however, were isolated (16—17%). The formation of this substance is surprising and must occur either through disproportionation of the pyrroline, or by direct loss of formic acid from the carboxypyrroline. A more careful examination of the hydrogenation products should clear that point.

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* Since this work was completed a publication by Dhont and Wibaut (*Rec. Trav. chim.*, 1944, 63, 8) has appeared. These authors obtained 2-*p*-chlorophenyl-Δ^2-pyrroline as its picrate by the zinc and hydrochloric acid reduction of *p*-chloro-α-nitrobutyrophenone. The latter was obtained by the conversion of *p*-chloroacetophenone into the Mannich base, followed by distillation to the vinyl ketone, then nitromethane addition.

EXPERIMENTAL.

(Microanalyses are by Drs. Weiler and Strauss, Oxford; m. p.s are uncorrected.)

2-*Phenyl-Δ^2-pyrroline* (II; R = Ph).—β-Benzoylpropionitrile (31·8 g., 0·2 mol.), dissolved in methyl alcohol (300 c.c.), was shaken with Raney nickel (5 g.) at room temperature and pressure. After the absorption of hydrogen (0·4 mol.) had been completed, the catalyst was filtered off and the alcohol distilled. The greenish oil had b. p. 252°/760 mm. and weighed 25 g. (86%). It crystallised on standing and formed large plates, m. p. 46°, from light petroleum (Gabriel and Colman, *Ber.*, 1908, **41**, 517, give m. p. 44—45°) (Found: C, 82·3; H, 7·5; N, 9·55. Calc. for $C_{10}H_{11}N$: C, 82·25; H, 7·55; N, 9·6%). The *picrate* formed yellow blades, m. p. 198°, from ethyl alcohol (Found: N, 15·1. $C_{16}H_{14}O_7N_4$ requires N, 15·0%). It was further characterised by shaking with benzoyl chloride and aqueous sodium hydroxide according to the directions of Gabriel *et al.* (*loc. cit.*), giving γ-benzamidobutyrophenone m. p. 125—126° (Found: N, 5·3. Calc. for $C_{16}H_{15}O_2N$: N, 5·55%).

2-*Phenylpyrrolidine* (III; R = Ph).—β-Benzoylpropionitrile (7·95 g., 0·05 mol.) was reduced in presence of Raney nickel (2 g.) and methyl alcohol (100 c.c.) by shaking with hydrogen until 0·15 mol. was absorbed. The last 0·05 mol. was absorbed slowly. Removal of the alcohol left an oil (5·7 g., 77·5%), b. p. 239°/756 mm. (Gabriel and Colman, *loc. cit.*, give b. p. 241°/771 mm.) (Found: N, 9·55. Calc. for $C_{10}H_{13}N$: N, 9·55%); *picrate*, m. p. 149° (lit. m. p. 148—149°) (Found: N, 15·1. Calc. for $C_{16}H_{16}O_7N_4$: N, 14·9%).

2-p-*Tolyl-Δ^2-pyrroline* (II; R = p-Me·C_6H_4).—β-p-Toluoylpropionitrile, reduced as for the benzoyl analogue, gave a crystalline solid (6·3 g., 79·5%) forming cream aggregates, m. p. 65°, from light petroleum. It had a peculiar caraway odour when heated alone or in water (Found: N, 8·75. $C_{11}H_{13}N$ requires N, 8·5%). Its *picrate* was obtained as irregular plates, m. p. 184°, from spirit (Found: N, 14·1. $C_{17}H_{16}O_7N_4$ requires N, 14·4%).

2-p-*Tolylpyrrolidine* (III; R = p-Me·C_6H_4), obtained analogously, formed a colourless oil, b. p. 354—356°/755 mm., with an odour similar to that of the phenyl analogue (Found: N, 8·75. $C_{11}H_{15}N$ requires N, 8·7%). Its *picrate* formed large, yellow plates, m. p. 170—172°, from alcohol (Found: N, 14·2. $C_{17}H_{18}O_7N_4$ requires N, 14·35%).

2-p-*Anisyl-Δ^2-pyrroline* (II; R = p-MeO·C_6H_4).—This was obtained analogously in 89% yield by reducing β-4-methoxybenzoylpropionitrile. It was obtained as glistening, pale yellow plates, m. p. 74°, from light petroleum. After repeated recrystallisation it had m. p. 69°. It possesses a pleasant odour not unlike that of piperonal (Found: N, 7·7. $C_{11}H_{13}ON$ requires N, 8·0%). Its *picrate* formed flat yellow needles, m. p. 175°, softening at 171°, from alcohol (Found: N, 13·9. $C_{17}H_{16}O_8N_4$ requires N, 13·85%).

2-p-*Anisylpyrrolidine* (III; R = p-MeO·C_6H_4).—The nitrile absorbed the third hydrogen molecule very slowly (2 days) even with a large amount of nickel. It formed a colourless oil, b. p. 284°/760 mm., in 78% yield. It possesses a peculiar fishy odour (Found: N, 7·8. $C_{11}H_{15}ON$ requires N, 7·9%). Its *picrate* was obtained as yellow needles, m. p. 172—173°, from alcohol (Found: N, 14·2. $C_{17}H_{18}O_8N_4$ requires N, 13·8%).

2-m-*Hydroxyphenyl-Δ^2-pyrroline* (II; R = m-HO·C_6H_4).—Hydrogenation of β-3-hydroxybenzoylpropionitrile with subsequent filtration and removal of alcohol gave a solid which on dissolving in hot methyl alcohol gave an intensely blue solution. It is recrystallised preferably from benzene since no blue colour develops in this solvent. It was thus obtained as colourless needles, m. p. 156°, containing solvent lost on exposure to the atmosphere (Found: N, 8·7. $C_{10}H_{11}ON$ requires N, 8·7%). Its *picrate*, unlike others of this series, crystallised very slowly on adding alcoholic picric acid to the alcoholic solution of the base. It formed needles, m. p. 197—199°, from spirit (Found: N, 14·0. $C_{16}H_{14}O_8N_4$ requires N, 14·35%).

In an attempt to prepare the pyrrolidine, the nitrile was shaken to absorb 3 mols. of hydrogen, and the alcohol removed. A resin, soluble in alkali or acid, was obtained, which, however, could not be distilled, and formed an oily picrate.

2-(2'-*Naphthyl*)-Δ^2-*pyrroline* (II; R = 2-$C_{10}H_7$).—This was obtained, in 82% yield, on reducing β-2-naphthoylpropionitrile, as almost colourless needles, m. p. 96°, from light petroleum. It had an odour not unlike that of quinoline (Found: N, 7·45. $C_{14}H_{13}N$ requires N, 7·2%). Its *picrate* formed jagged needles, m. p. 182°, from spirit (Found: N, 13·7. $C_{20}H_{16}O_7N_4$ requires N, 13·2%).

2-(3' : 4'-*Dimethoxyphenyl*)-Δ^2-*pyrroline*.—β-3 : 4-Dimethoxybenzoylpropionitrile (4·38 g.) was reduced in presence of Raney nickel (1 g.) and methyl alcohol (50 c.c.) to give the *pyrroline* in 88% yield, which was obtained as colourless needles, m. p. 77—79°, from benzene–light petroleum (Found: N, 6·95. $C_{12}H_{15}O_2N$ requires N, 6·85%). Its vapour had a peculiar, sharp odour. Its picrate formed flat needles, m. p. 205—207°, from spirit (Found: N, 13·0. $C_{18}H_{18}O_9N_4$ requires N, 12·9%).

2-(3' : 4'-*Dimethoxyphenyl*)*pyrrolidine*.—This *base* was obtained as a thick oil, b. p. 289—291°/758 mm., with a strong odour of bloaters (Found: N, 6·8. $C_{12}H_{17}O_2N$ requires N, 6·75%). Its *picrate* formed needles, m. p. 200° (previous softening), from ethyl alcohol (Found: N, 13·2. $C_{18}H_{20}O_9N_4$ requires N, 12·85%).

2-p-*Chlorophenyl-Δ^2-pyrroline* (II; R = p-Cl·C_6H_4).—β-p-Chlorobenzoylpropionitrile (3·87 g.), methyl alcohol (50 c.c.) and Raney nickel (1 g.) were shaken to absorb hydrogen (0·04 mol.). The nickel was filtered off, the alcohol removed, and the solid residue dissolved in light petroleum (100 c.c.), filtered to remove a cloudiness, and concentrated to 10 c.c. The *pyrroline* crystallised as pale green needles. Further concentration gave a second crop, 3·1 g. in all (86%). It formed colourless glassy needles, m. p. 67°, from light petroleum. It had a strong minty odour, particularly on heating (Found: N, 7·75. $C_{10}H_{10}NCl$ requires N, 7·8%). Its picrate formed irregular plates, m. p. 209—210°, from spirit (Dhont and Wibaut, *Rec. Trav. chim.*, 1944, **63**, 81, give m. p. 210—211°. They did not isolate the base) (Found: N, 14·2. Calc. for $C_{16}H_{13}O_7N_4Cl$: N, 13·7%).

2-(2'-*Thienyl*)-Δ^2-*pyrroline* (II; R = 2-C_4H_3S).—β-2-Thienoylpropionitrile was reduced as for the benzoyl analogue. Removal of the solvent left an oil with an odour not unlike that of quinoline. It was fractionally distilled under 750 mm., and the fractions b. p. 250—255° and 255—265° collected. The lower-boiling fraction solidified completely, and the other partly crystallised after inoculation. From light petroleum the *pyrroline* (26·5%) formed long flat needles, m. p. 59° (Found: N, 9·4; S, 21·2. C_8H_8NS requires N, 9·25; S, 21·2%). Its *picrate*, m. p. 195—197°, formed long, flat needles from alcohol (Found: N, 14·3. $C_{14}H_{12}O_7N_4S$ requires N, 14·75%).

2-(2'-*Furyl*)-Δ^2-*pyrroline* (II; R = 2-C_4H_3O).—Removal of the solvent after the reduction of β-2-furoylpropionitrile left an oil which crystallised. It was dissolved in dilute hydrochloric acid, giving a bright yellow solution of the salt, filtered from a little tar, made alkaline with solid sodium carbonate, and the water-soluble base extracted with ether. After drying, the ether was removed, leaving the base, which crystallised. It tended to crystallise with a sticky impurity so it was converted into its *picrate* forming flat needles, m. p. 175—177°, from ethanol (Found: N, 15·3. $C_{14}H_{12}O_8N_4$ requires N, 15·4%). The *base*, released by conversion into its hydrochloride followed by basifying the aqueous solution of the latter, and extraction with ether as above, was then obtained pure as tiny, flat, pale yellow needles, m. p. 55—56°, from light petroleum, with an odour of thiazole (Found: N, 10·3. C_8H_9ON requires N, 10·3%).

2-(2'-*Coumaronyl*)-Δ^2-*pyrroline*.—2-Coumaronyl β-cyanoethyl ketone was reduced to give an oil which crystallised. It tended to crystallise from light petroleum with a sticky contamination so it was converted into its *picrate*, m. p. 192—194°, obtained as tiny glistening plates from 95% alcohol (Found: N, 13·25. $C_{18}H_{14}O_8N_4$ requires N, 13·5%). The *base* regenerated from the picrate formed tiny, cream needle rosettes, m. p. 97—99°, from light petroleum. Its vapour (in steam) has a pleasant aromatic odour (Found: N, 7·75. $C_{12}H_{11}ON$ requires N, 7·55%).

Attempted Selenium Dehydrogenation of 2-Phenyl-Δ^2-pyrroline.—The pyrroline (5 g.) and selenium (5 g.) were refluxed gently for 3 hours. The reddish liquor partly solidified. It was extracted three times with boiling ligroin, leaving a buff powder (2 g.), which fluoresced strongly in methyl alcohol solution, but was unstable and deposited selenium on attempted crystallisation. The ligroin extract gave a little crystalline solid contaminated with a resinous oil on concentration. Neither solid was investigated further.

Catalytic Reduction of α-Cyano-β-benzoylpropionic Acid.—The acid hydrate (22·1 g., 0·1 mol.), methyl alcohol (50 c.c.), and Raney nickel (5 g.) were shaken to absorb hydrogen. Owing to carbon dioxide evolution the amount of hydrogen absorbed was unknown, but after a volume had been absorbed corresponding to 0·2 mol. of hydrogen the absorption became slow and a solid separated. The nickel and solid (A) were filtered off, and the filtrate (B) left overnight. The solid (A) was dissolved in 2N-sodium carbonate, the solution filtered, and the *acid* (II; R = Ph, R' = CO_2H) reprecipitated with acetic acid. It formed colourless grains, m. p. 192—193°, from methyl alcohol (Found: C, 71·65; H, 5·45; N, 7·4. $C_{11}H_{11}O_2N$ requires C, 69·8, H, 5·85; N, 7·4%).

The filtrate (B) deposited a further crop of (A) on standing (1·2 g.). The methyl alcohol was distilled off, and the residue extracted twice with boiling benzene. The residue consisted chiefly of (A) but was difficult to purify. The benzene extract deposited a mass of crystals on cooling. They (2 g.) formed bundles of asbestos-like needles, m. p. 140°, from methyl alcohol, soluble in acid and alkali (Found: C, 67·55; H, 5·3; N, 6·45%).

The benzene filtrate was distilled to remove the benzene, and the residue extracted repeatedly with ligroin to give 2-phenylpyrrole (2·4 g., 16·8%), m. p. 129°, mixed m. p. with authentic specimen 129° (Found: N, 9·85. Calc. for $C_{10}H_7N$: N, 9·8%).

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