573. *Synthesis of Some Phenyl-cinnolines, -phthalazines, and -quinoxalines.*

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Unambiguous routes to 3-, 6-, and 7-phenylcinnoline, to 5- and 6-phenylquinoxaline, and to 6-phenylphthalazine are described. 4-Hydroxycinnolines have been reduced with lithium aluminium hydride.

An improved method for carrying out the Gomberg reaction is reported.

Authentic phenyl derivatives of bicyclic diazines were required in connection with work on the phenylation of the corresponding heterocyclic compounds. For the preparation of 5- and 6-phenylquinoxaline, 2 : 3- and 3 : 4-diaminodiphenyl, respectively, were required. The first of these intermediates has been reported [1] only as the unstable, oily hydrochloride. Nitration of 2-acetamidodiphenyl by the improved method of Stepan and Hamilton [2] and chromatography of the mixed nitro-amines has given a much purer sample of 2-amino-3-nitrodiphenyl; this yielded by catalytic reduction the crystalline diamine. Attempts to hydrolyse 2-acetamido-3-aminodiphenyl with acid or alkali gave a common product, presumably 2-methyl-7-phenylbenzimidazole.[3] The route to 4-amino-3-nitrodiphenyl from 4-nitrodiphenyl has been well described,[4] and catalytic reduction of both of these compounds assured an excellent overall yield.

4-Phenylphthalazine is known,[5] and for the synthesis of 5- and 6-phenylphthalazine there were required 3- and 4-phenylphthalic acid: these have been obtained [6] in about 35% yield by means of a Gomberg reaction on the dimethyl esters of the corresponding amines. In the present work, this yield has been improved to about 60% by carrying out the diazotisation with butyl nitrite, causing the product to react in benzene by addition of anhydrous sodium carbonate, and hydrolysing the insoluble intermediates. An alternative route to 3-phenylphthalic anhydride by a Diels–Alder reaction between 1-phenylbutadiene and maleic anhydride [7] was unsuccessful. The adduct could not be wholly dehydrogenated with sulphur, selenium, or *N*-bromosuccinimide; it was recovered from treatment with chloranil at low temperatures, and at high temperatures only halogeno-compounds appeared to be formed. The catalytic hydrogen-transfer method using palladised charcoal in alcohol with nitrobenzene or nitromethane also failed to bring about dehydrogenation.

Reaction of 3-phenylphthalic acid or the anhydride with hydrazine did not yield the expected 1 : 4-dihydroxy-5-phenylphthalazine; instead, a compound was obtained arising from the condensation of two molecules of acid with one of hydrazine: this formulation is supported by the analytical figures and by the behaviour of phthalic anhydride itself with hydrazine.[8] An attempt to prepare the bis-acid chloride from 3-phenylphthalic anhydride and phosphorus pentachloride [9] yielded only fluorenone-3-carboxylic acid.[6] 4-Phenylphthalic acid reacted smoothly with hydrazine to form 1 : 4-dihydroxy-6-phenylphthalazine, which was converted into the 1 : 4-dichloro-derivative: reduction of this with red phosphorus and hydriodic acid gave a low yield of 6-phenylphthalazine.

Of the six possible monophenylcinnolines, only 4-phenylcinnoline has been previously prepared.[10] For the preparation of 7-phenylcinnoline, 4-amino-3-nitrodiphenyl was converted into 4-cyano-3-nitrodiphenyl through the diazonium compound, which we found

[1] Sako, *Bull. Chem. Soc. Japan*, 1934, **9**, 55.
[2] Stepan and Hamilton, *J. Amer. Chem. Soc.*, 1949, **71**, 2438.
[3] Hofmann, "Imidazole and its derivatives," Interscience Publ. Inc., New York, 1953, p. 264.
[4] Campbell, Anderson, and Gilmore, *J.*, 1940, 446.
[5] Lieck, *Ber.*, 1905, **38**, 3918.
[6] Butterworth, Heilbron, Hey, and Wilkinson, *J.*, 1938, 1386.
[7] Kharasch, Nudenberg, and Fields, *J. Amer. Chem. Soc.*, 1944, **66**, 1276.
[8] Drew and Hatt, *J.*, 1937, 16.
[9] Ott, *Org. Synth., Coll. Vol. II*, p. 528.
[10] Stoermer and Fincke, *Ber.*, 1909, **42**, 3115.

more convenient to prepare by using nitrosylsulphuric acid rather than butyl nitrite.[11] The corresponding amino-nitrile and amino-amide were prepared by recorded methods,[11] but neither compound reacted with methylmagnesium iodide. Attempts to hydrolyse 4-cyano-3-nitrodiphenyl directly to the acid failed, but by proceeding *via* the nitroamide a high overall yield of 2-nitro-4-phenylbenzoic acid was obtained. The general method of Walker and Hauser [12] was used to convert this acid into the methyl ketone, from which 4-hydroxy-7-phenylcinnoline was obtained by reduction, diazotisation, and cyclisation.

2-Nitro-5-phenylacetophenone, required for the preparation of 4-hydroxy-6-phenylcinnoline, was synthesised from 5-amino-2-nitroacetophenone [13] by the usual Gomberg procedure in a yield of only 4%, and attempts to prepare (for subsequent decomposition) 2-nitro-5-*N*-nitrosoacetamidoacetophenone with nitrous fumes or nitrosyl chloride failed (cf. ref. 14). When the Gomberg reaction was carried out under anhydrous conditions, however, a 45% yield of 2-nitro-5-phenylacetophenone was attained: 4-hydroxy-6-phenylcinnoline was then available by the usual route.

For conversion of the 4-hydroxycinnolines into the parent bases a number of methods were investigated: decomposition of *N*-(6-phenyl-4-cinnolyl)-*N'*-toluene-*p*-sulphonhydrazide under a variety of conditions gave the cinnoline in an optimum overall yield of 26%; and attempt to make 6-phenyl-4-cinnolylhydrazine failed. Catalytic reduction in aqueous-alcoholic alkali (cf. ref. 15) gave only 4-ethoxy-6-phenylcinnoline. However, direct reduction of 4-hydroxycinnolines with lithium aluminium hydride was more successful: 4-hydroxycinnoline itself gave a 42% yield of cinnoline picrate which was increased to 74% by gentle oxidation of the crude product of reduction. 6- and 7-Phenylcinnoline were obtained, but in lower yields, possibly owing to the presence of more stable dihydro-compounds as intermediates which still reduced cold potassium permanganate solution after oxidation with mercuric oxide. 4-Hydroxy-3-phenylcinnoline [16] yielded by similar treatment a red, partially reduced compound which, by analogy with the red complex obtained [16] by similar reduction of 3 : 4-benzacridone, is thought to be a complex of 3-phenylcinnoline and dihydro-3-phenylcinnoline: two picrates were isolated and each gave 3-phenylcinnoline on decomposition; the possibility of picric acid's acting as an oxidising agent here may be related to the increased yields obtained when products were isolated as picrates rather than as free bases.

An attempt to prepare 8-phenylcinnoline by means of a Gomberg reaction with 8-aminocinnoline, prepared by the recorded method,[17] gave no recognisable product. Similarly, the synthesis of a 5-phenylcinnoline derivative has not yet been achieved: 2-amino-3-nitrodiphenyl was converted into the amino-nitrile but this failed to give any useful product with methylmagnesium iodide in ether or anisole. The novel method of Beech [18] for preparing methyl ketones directly from amines yielded only the deaminated product when applied to 2-amino-3-nitrodiphenyl.

Experimental

Light petroleum had b. p. 40—60° except where otherwise stated.

2-Amino-3-nitrodiphenyl.—The crude mixture (m. p. 80—90°) obtained from nitration of 2-acetamidodiphenyl (29 g.) by the method of Stepan and Hamilton [2] was added to glacial acetic acid (180 ml.) and concentrated hydrochloric acid (400 ml.) and heated under reflux for 7 hr. After cooling, the mixture was poured into an equal volume of water and made alkaline with concentrated aqueous potassium hydroxide. The brown viscous oil, obtained by extraction with benzene, was dissolved in the minimum volume of benzene and transferred to a column of alumina (200 g., type H). Elution with 1 : 5 benzene–light petroleum (700 ml.) yielded an

[11] Jones, *J. Org. Chem.*, 1945, **10**, 538.
[12] Walker and Hauser, *J. Amer. Chem. Soc.*, 1946, **68**, 1387.
[13] Simpson, Atkinson, Schofield, and Stephenson, *J.*, 1945, 646.
[14] France, Heilbron, and Hey, *J.*, 1940, 369.
[15] Stephenson, *Chem. and Ind.*, 1957, 174.
[16] Badger, Seidler, and Thomson, *J.*, 1951, 3207.
[17] Alford, Irving, Marsh, and Schofield, *J.*, 1952, 3009.
[18] Beech, *J.*, 1954, 1297.

orange oil (9·6 g.) which was further purified on a smaller column to give 2-amino-3-nitrodiphenyl as an orange solid (8·5 g., 29% yield based upon 2-acetamidodiphenyl), m. p. 50—53°.

A purer product, m. p. 53—56°, was obtained in an overall yield of 16—19% by similar chromatography of the hydrolysis product of 2-acetamido-3-nitrodiphenyl, the latter having been purified by repeated recrystallisation from benzene and aqueous alcohol.

2 : 3-*Diaminodiphenyl.*—2-Amino-3-nitrodiphenyl (2 g.) in alcohol (35 ml.) with 5% palladised charcoal (0·4 g.) was hydrogenated (5 atm.) for 2 hr. The brown oil left after removal of solvent was digested with hot light petroleum (2 × 25 ml.; b. p. 80—100°) and decanted from an insoluble tar. Evaporation of this extract to about 30 ml. furnished a pale yellow crystalline solid (1·2 g.), m. p. 86—87°, which on recrystallisation from light petroleum (b. p. 80—100°) gave very pale yellow rectangular prisms of the pure *diamine* (0·96 g., 55%), m. p. 89° (Found: C, 78·0; H, 6·6; N, 15·1. $C_{12}H_{12}N_2$ requires C, 78·2; H, 6·5; N, 15·2%).

5-*Phenylquinoxaline.*—2 : 3-Diaminodiphenyl (0·95 g.) and glyoxal sodium bisulphite (1·45 g.) in 50% alcohol (10 ml.) were stirred at 60° for 1 hr. A further portion of glyoxal sodium bisulphite (0·15 g.) was then added, and stirring at 60° continued for 2 hr. After evaporation of the alcohol, the solution was made alkaline with 6N-sodium hydroxide and extracted with ether. The dried ($MgSO_4$) extract yielded a brown solid (0·8 g.), m. p. 112—118°, which was digested with boiling light petroleum (b. p. 80—100°). The filtered digest yielded, on concentration to *ca.* 15 ml., a brown, microcrystalline solid (0·42 g., 39%), m. p. 124—124·5°, which on further recrystallisation from *n*-hexane and from aqueous methanol gave colourless needles, m. p. 124·5°, of 5-*phenylquinoxaline* (Found: C, 81·85; H, 5·0; N, 13·2. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%). A yellow picrate, m. p. 148°, was prepared in methanol but attempted recrystallisation led only to recovery of the base.

3 : 4-*Diaminodiphenyl.*—A solution of 4-amino-3-nitrodiphenyl (14·8 g.) in alcohol (193 ml.) was hydrogenated at 3—5 atm. for 30 min. in the presence of Adams catalyst. The filtrate was evaporated to *ca.* 40 ml., and the crude product (12·1 g., 95%), m. p. 101°, was precipitated by addition of water. 3 : 4-Diaminodiphenyl formed colourless plates, m. p. 102° (lit.,[19] m. p. 103°), from benzene–light petroleum or from dilute alcohol (Found: C, 78·2; H, 6·7; N, 15·3. Calc. for $C_{12}H_{12}N_2$: C, 78·2; H, 6·5; N, 15·2%).

6-*Phenylquinoxaline.*—3 : 4-Diaminodiphenyl (5 g.) in water (50 ml.) was treated with two portions of glyoxal sodium bisulphite (7·3 g. and 0·7 g.) as above. The cold solution was made alkaline with potassium hydroxide, and the crude material (5·6 g.), m. p. 104—106°, was powdered and extracted with boiling light petroleum, from which colourless needles (3·4 g.), m. p. 109—111°, were obtained after evaporation to about 50 ml. Successive recrystallisation from light petroleum and aqueous ethanol gave colourless needles, m. p. 112°, of 6-*phenylquinoxaline* (Found: C, 81·8; H, 4·7; N, 13·2. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·6%). A bright yellow picrate, m. p. 170° unchanged by recrystallisation from methanol, was obtained on mixing concentrated methanolic solutions of 6-phenylquinoxaline and picric acid.

2-*Acetamido*-3-*aminodiphenyl.*—2-Acetamido-3-nitrodiphenyl (3 g.) was suspended in alcohol (39 ml.) with Adams catalyst (0·1 g.) and hydrogenated at 2—5 atm. 2-*Acetamido*-3-*aminodiphenyl* formed colourless needles, m. p. 179°, from water or benzene (Found: C, 74·5; H, 6·3; N, 12·5. $C_{14}H_{14}ON_2$ requires C, 74·3; H, 6·2; N, 12·4%).

The Action of Acid and Alkali on 2-*Acetamido*-3-*aminodiphenyl.*—2-Acetamido-3-aminodiphenyl (1·75 g.) was boiled with concentrated hydrochloric acid (17·5 ml.) for periods of 1 to 6 hr.; glassy residues were obtained by making the solutions alkaline with 6N-sodium hydroxide, followed by chloroform-extraction. These crystallised with loss of solvent when heated on the water-bath, to form a white solid, m. p. 150—166°. Recrystallisation from aqueous ethanol gave colourless crystals, m. p. 180°, decreasing to 172° after recrystallisation from benzene–light petroleum; the higher-melting product was regained either by recrystallisation from aqueous alcohol or by drying, for 6 hr. at 110°/0·1 mm. 2-*Methyl*-7-*phenylbenzimidazole* was also obtained when 2-acetamido-3-aminodiphenyl was heated under reflux with 6N-sodium hydroxide for 2½ hr. (Found: C, 80·1; H, 5·8; N, 14·6. $C_{14}H_{12}N_2$ requires C, 80·7; H, 5·8; N, 13·5%).

4-*Phenylphthalic Acid.*—Dimethyl 4-nitrophthalate (30 g.), alcohol (300 ml.), and Adams catalyst (0·3 g.) were shaken with hydrogen for 2½ hr. After filtration from the catalyst, the solution was evaporated to dryness and the residue was digested with 3N-hydrochloric acid. The filtrate was neutralised with concentrated aqueous ammonia, then extracted continuously

[19] Bell and Kenyon, *J.*, 1926, 2710.

with benzene, and the extract was evaporated to provide the amine (26 g.), m. p. 78—82°. A solution of this amine (5 g.) in glacial acetic acid (8 ml.) and benzene (15 ml.) was treated with concentrated sulphuric acid (1·5 ml.) and then stirred, at 10—15°, during the addition (in 20 min.) of freshly distilled butyl nitrite (8·5 ml.). After ¾ hr., benzene (70 ml.) was added, followed by small portions of anhydrous sodium carbonate (3·9 g.) during 1 hr. After 3 hr. the cooling-bath was removed, stirring was continued overnight, and the mixture was heated during 2 hr. to the b. p. and maintained thus for a further 2 hr. The mixture was filtered cold, the solvent removed under reduced pressure, and the semi-crystalline residue was heated with 6N-sodium hydroxide (50 ml.) under reflux for 5 hr. The ice-cooled, stirred solution was acidified with concentrated hydrochloric acid, then set aside for 1 hr., and the brown solid (3·5 g., 60%), m. p. 190—194° (decomp.), was collected, washed with water, and dried *in vacuo*.

3-*Phenylphthalic Anhydride*.—Dimethyl 3-aminophthalate (15 g.), under the conditions applied to dimethyl 4-aminophthalate above, afforded 3-phenylphthalic acid (11·1 g.), m. p. 175—177° (decomp.). The crude acid (11·8 g.) was heated with acetic anhydride (12 ml.), at 120° for 20 min., cooled, triturated with ether (2 × 20 ml.), and dried at 95°. The brown powder (8·0 g.), m. p. 143—146°, after three recrystallisations from ligroin, yielded colourless needles (5·1 g.) of the anhydride, m. p. 146—146·5° (Found: C, 74·5; H, 4·35. $C_{14}H_8O_3$ requires C, 75·0; H, 3·6%).

1 : 4-*Dihydroxy*-6-*phenylphthalazine*.—Crude 4-phenylphthalic acid (3·1 g.), 50% acetic acid (50 ml.), and 98—100% hydrazine hydrate (1·2 ml.) were heated under reflux for 5 hr. The solid was collected cold, washed successively with water, sodium hydrogen carbonate solution, and water, then dried at 90°. This product (2·6 g.), m. p. 307—311°, was digested with boiling acetic acid, and provided a buff-coloured solid (2·2 g.), m. p. 315°; this was sparingly soluble in the usual organic solvents, but dissolved in dilute sodium hydroxide solution after warming.

1 : 4-*Dichloro*-6-*phenylphthalazine*.—1 : 4-Dihydroxy-6-phenylphthalazine (1 g.) was heated with phosphorus pentachloride (approx. 3 g.) at 150—160° for 4 hr. Phosphorus oxychloride was removed at 120° under reduced pressure and the residue was extracted with boiling benzene (2 × 30 ml.). The benzene extract gave, by evaporation under reduced pressure, a waxy brown solid, easily soluble in benzene and sparingly soluble in light petroleum. From a mixture of these solvents, some red sticky solid separated; this was discarded and the liquors were evaporated to dryness. The residue was digested with boiling ligroin, cooled, filtered, and washed with light petroleum. After drying at 90°, the buff-coloured chloro-compound (0·5 g.), m. p. 150—153°, was not further purified. This product was insoluble in dilute alkali.

6-*Phenylphthalazine*.—1 : 4-Dichloro-6-phenylphthalazine (0·5 g.), m. p. 150—153°, concentrated hydriodic acid (8·5 ml.; *d* 1·94), and red phosphorus (0·4 g.) were heated under reflux for 1½ hr. The mixture was diluted with water (8·5 ml.), cooled in ice, and made alkaline with solid potassium hydroxide. The solid was collected and washed with benzene, and the washings were used (6 × 20 ml.) to extract the aqueous filtrate. The benzene extract, after being washed with water, yielded a waxy residue which formed a yellow picrate (140 mg.), m. p. 202°, from methanol; this was decomposed by 3N-sodium hydroxide (35 ml.) on the water-bath for 1½ hr. The cooled solution was extracted continuously with benzene to yield pale yellow needles (65 mg.), m. p. 137—139° (from ligroin); further recrystallisation gave colourless needles of 6-*phenylphthalazine*, m. p. 138·5—139° (Found: C, 80·9; H, 4·6. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9%).

2-*Cyano*-3-*nitrodiphenyl*.—2-Amino-3-nitrodiphenyl (44·8 g.) was warmed and stirred with concentrated hydrochloric acid (450 ml.) to provide the colourless hydrochloride. The mixture was stirred at 0—5° during portionwise addition of sodium nitrite (16·5 g.) in ½ hr., then for a further ½ hr. The ice-cold diazonium salt solution was led, during 1 hr., beneath the surface of a stirred cuprous cyanide solution (⩾15°) to which had been added aqueous ammonia (*d* 0·880; 230 ml.) and sufficient benzene to cover the surface of the liquid (about 150 ml.). After 2 hr., the cooling-bath was removed and the mixture was stirred overnight. A benzene extract, after being washed successively with water, sodium hydroxide solution, and water, yielded an oily brown residue. This was digested repeatedly with boiling ligroin (total 1500 ml.), and the oily discoloured needles obtained on cooling were collected and washed with light petroleum. Recrystallisation from alcohol (350 ml.) yielded pale brown needles of 2-*cyano*-3-*nitrodiphenyl* (20·5 g., 44%), m. p. 130—131° (Found: C, 69·8; H, 3·4; N, 12·8. $C_{13}H_8O_2N_2$ requires C, 69·7; H, 3·6; N, 12·55%).

3-*Aminodiphenyl*-2-*carboxyamide*.—2-Cyano-3-nitrodiphenyl (1 g.) was suspended in hot alcohol (10 ml.) and added to a solution of stannous chloride (3·3 g.) in concentrated hydrochloric acid (10 ml.). The mixture was heated on the water-bath for ½ hr., cooled, made alkaline with concentrated aqueous potassium hydroxide, and extracted with ether. The oily residue afforded slightly coloured needles (210 mg., 22%), m. p. 169—170° (from benzene). Recrystallisation from water gave colourless needles of the *amide*, m. p. 171° (Found: C, 73·5; H, 5·95; N, 13·0. $C_{13}H_{12}ON_2$ requires C, 73·6; H, 5·7; N, 13·2%).

3-*Amino*-2-*cyanodiphenyl*.—A solution of 2-cyano-3-nitrodiphenyl (6 g.) in glacial acetic acid (120 ml.) was treated at 18—22° with stannous chloride–acetic anhydride reagent [20] (120 ml.), and set aside for 2 hr. The solid was collected, washed with acetic acid, and transferred to a separating funnel containing 6N-sodium hydroxide (75 ml.) and ether (75 ml.). When the solid had dissolved, the aqueous layer was extracted with ether, and the combined ether solutions were washed with water, dried ($MgSO_4$), and evaporated. Recrystallisation of the pale brown residue from ligroin gave colourless prisms of the *amino-nitrile* (3·4 g., 65%), m. p. 103—104° (Found: C, 80·4; H, 5·1; N, 14·2. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2; N, 14·4%).

3-*Nitrodiphenyl*-4-*carboxyamide*.—Finely powdered sodium nitrite (10 g.) was added during 10 min. to stirred concentrated sulphuric acid (120 ml.). The solution was cooled to 20° and powdered 4-amino-3-nitrodiphenyl (24 g.) was added during 20 min. at this temperature. After a further hour (when a drop of the solution gave no red precipitate of the amine on addition to water), the solution was poured cautiously, with stirring, into water and crushed ice (final volume *ca.* 500 ml.).

A solution of cuprous cyanide (210 ml.; prepared as usual from 87 g. of crystalline copper sulphate), aqueous ammonia (*d* 0·880; 220 ml.), and benzene (*ca.* 200 ml.) were stirred and the temperature kept below 15° by strong cooling, whilst the ice-cold diazonium salt solution was added beneath the surface during 1 hr. After being stirred for a further ½ hr., the mixture was set aside overnight. A benzene extract of the product was washed with sodium carbonate solution and with water, and evaporated, yielding a brown oil which was mixed with " Hyflo " and extracted with *n*-hexane (300 ml.) in a Soxhlet apparatus. The brown product which crystallised on cooling (11·2 g.; m. p. 110—116°) was collected, air-dried, and recrystallised from ethanol, giving discoloured needles (10·3 g., 41%), m. p. 117—119°. A solution of this nitro-nitrile (3·5 g.) in acetone (100 ml.) and N-sodium hydroxide (50 ml.) was treated with 100-vol. hydrogen peroxide (30 ml.). The solution was warmed gently for 1½ hr., then heated under reflux for ½ hr., the acetone was distilled off, and, from the cooled residue, after dilution with water (150 ml.), a pale brown solid (3·67 g., 97%), m. p. 192—193°, was collected. Recrystallisation from aqueous alcohol and from benzene afforded colourless needles of the *nitro-amide*, m. p. 195° (Found: C, 64·25; H, 4·0; N, 10·3. $C_{13}H_{10}O_3N_2$ requires C, 64·45; H, 4·2; N, 11·6%).

3-*Nitrodiphenyl*-4-*carboxylic Acid*.—The last-mentioned amide (18·5 g.; m. p. 191—192°), in acetic acid (300 ml.), water (164 ml.), and concentrated sulphuric acid (212 ml.), was stirred at 5—10° during portionwise addition (20 min.) of sodium nitrite (10·3 g.), and for a further 1½ hr. The solution was set aside overnight and diluted to *ca.* 1 l., and the brown solid (18·3 g.), m. p. 200—203°, was reprecipitated from N-sodium carbonate with concentrated hydrochloric acid. Recrystallisation from aqueous alcohol gave colourless needles of the *acid*, m. p. 205° (Found: C, 64·5; H, 4·3; N, 5·4. $C_{13}H_9O_4N$ requires C, 64·2; H, 3·7; N, 5·8%).

4-*Acetyl*-3-*nitrodiphenyl*.—The foregoing acid (17 g.) and thionyl chloride (56 ml.) were heated under reflux for ½ hr. The excess of thionyl chloride was removed on the water-bath, finally under reduced pressure, and the brown residue was warmed with dry ether (70 ml.) and filtered. The pale yellow solution of the acid chloride was used directly as described below.

To a mixture of magnesium turnings (1·9 g.), absolute ethanol (1·75 ml.) and carbon tetrachloride (0·4 ml.), were added sodium-dried ether (52·5 ml.), and then diethyl malonate (12·3 g.) and absolute ethanol (7 ml.) in sodium-dried ether (9·1 ml.), at a rate sufficient to maintain boiling. Heating under reflux was continued for 3 hr. and an ethereal solution of the acid chloride was added in 15 min. with stirring. After 2½ hours' boiling, the white viscous gum was cooled and a solution of concentrated sulphuric acid (5 ml.) in water (70 ml.) was added. The aqueous layer was extracted once with ether, and the combined extracts were evaporated to dryness; the residue was heated under reflux with acetic acid (21 ml.), water (14 ml.), and

[20] Albert and Linnell, *J.*, 1936, 1617.

concentrated sulphuric acid (2·6 ml.) for 10 hr. After dilution with an equal volume of water and cooling, the oily solid was collected and dried *in vacuo*. The crude product yielded, by digestion with small portions of boiling light petroleum (b. p. 60—80°; 650 ml.), yellow needles (12·8 g.), m. p. 75—79°, which, on further recrystallisation from light petroleum (b. p. 80—100°) and from *n*-hexane, gave colourless needles of the *nitro-ketone*, m. p. 79·5° (Found: C, 69·95; H, 4·85; N, 5·15. $C_{14}H_{11}O_3N$ requires C, 69·7; H, 4·6; N, 5·8%).

4-Acetyl-3-aminodiphenyl.—4-Acetyl-3-nitrodiphenyl (7·3 g.) was dissolved in glacial acetic acid (60 ml.), and the stannous chloride–acetic anhydride reagent [20] (170 ml.) was added fairly rapidly at $<22°$. After 4 hr., working up as for 3-amino-2-cyanodiphenyl (above) yielded a yellow residue, m. p. 109—114°. Two recrystallisations from *n*-hexane gave colourless needles (4·7 g., 73%), m. p. 119·5°, of the *amino-ketone* (Found: C, 79·1; H, 4·9; N, 7·5. $C_{14}H_{13}ON$ requires C, 79·6; H, 6·2; N, 6·6%).

4-Hydroxy-7-phenylcinnoline.—Powdered 4-acetyl-2-aminodiphenyl (2·25 g.) was stirred with concentrated hydrochloric acid (75 ml.) until dissolved and then diazotised in the usual way. The solution was stirred at 55—60° for 3½ hr. (by which time it no longer coupled with alkaline β-naphthol), diluted with about twice its volume of water, cooled, and filtered. The dark residue was extracted with hot 3N-sodium hydroxide which yielded on acidification a white solid (1·14 g.), m. p. 312—316°. This dissolved slowly in boiling alcohol and concentration of the solution gave colourless needles of the *hydroxycinnoline* (0·88 g., 37%), m. p. 323—325° (unchanged by recrystallisation from methanol or acetic acid) (Found: C, 75·9; H, 4·7; N, 11·6. $C_{14}H_{10}ON_2$ requires C, 75·65; H, 4·5; N, 12·6%).

3-Acetyl-4-nitrodiphenyl.—5-Amino-2-nitroacetophenone [13] (15 g.) was dissolved in warm glacial acetic acid (45 ml.), concentrated sulphuric acid (5 ml.) and benzene (50 ml.) were added, and the solution was stirred at 15° during addition of butyl nitrite (13·5 ml.) in 15 min. Benzene (250 ml.) was added, the mixture was stirred for ½ hr., and anhydrous sodium carbonate (10 g.) was added in small portions during ¾ hr. After 3 hours' stirring at 15°, the cooling-bath was removed and stirring was continued overnight. A yellow, thermally unstable solid was collected and washed with benzene, and the filtrate washed successively with dilute sodium hydroxide (3×) and finally with water. The dried ($MgSO_4$) extract was evaporated to dryness on the water-bath, finally at reduced pressure to remove butyl acetate. The oily brown residue was transferred in benzene (30 ml.) and light petroleum (*ca.* 15 ml.) to a column of alumina (150 g., type H), which was eluted with 2 : 3 benzene–light petroleum. Evaporation of the coloured eluate (1 l.) and recrystallisation of the residue from light petroleum (b. p. 60—80°) gave pale yellow needles of *3-acetyl-4-nitrodiphenyl* (8·1 g., 45%), m. p. 86° (Found: C, 68·9; H, 4·5; N, 5·45. $C_{14}H_{11}O_3N$ requires C, 69·6; H, 4·6; N, 5·8%).

4-Hydroxy-6-phenylcinnoline.—The stannous chloride–acetic anhydride reagent (375 ml.) was stirred below 25° during portionwise addition of 3-acetyl-4-nitrodiphenyl (15 g.) and then set aside at room temperature for 4 hr. The mixture was worked up as usual and yielded from *n*-hexane pale yellow prisms (11·0 g.), m. p. 80—84°.

This crude, finely powdered amine was stirred with concentrated hydrochloric acid (350 ml.) and treated at 0—5° with a saturated solution of sodium nitrite (4·05 g.). After a further ½ hr. at this temperature, the solution was stirred at 55—60° until it no longer coupled with alkaline β-naphthol (4 hr.), diluted with twice its volume of water, and allowed to cool. The solid was extracted with hot 3N-sodium hydroxide, from which the crude *hydroxycinnoline* (7·0 g.), m. p. 282—288°, was obtained by acidification with concentrated hydrochloric acid. It separated from alcohol as colourless needles (5·3 g., 38% overall), m. p. 292—295° raised to 294—296° by further recrystallisation (Found: C, 74·7; H, 4·6; N, 12·1. $C_{14}H_{10}ON_2$ requires C, 75·6; H, 4·5; N, 12·6%).

4-Chloro-6-phenylcinnoline.—4-Hydroxy-6-phenylcinnoline (3·9 g.; m. p. 292—295°) and phosphorus oxychloride (40 ml.) were heated under reflux for 15 min., cooled, and added slowly to 6N-sodium hydroxide (100 ml.) and crushed ice. Recrystallisation of solid (4·1 g.), m. p. 146—148°, from ligroin gave pale yellow needles of the *chloro-compound* (3·75 g., 89%), m. p. 150—152° raised to 151—152° on further recrystallisation (Found: C, 70·2; H, 3·8; N, 11·5; Cl, 14·4. $C_{14}H_9N_2Cl$ requires C, 69·85; H, 3·8; N, 11·6; Cl, 14·75%).

4-Chloro-7-phenylcinnoline.—4-Hydroxy-7-phenylcinnoline (250 mg., m. p. 232—235°) and phosphorus oxychloride (3 ml.), under the conditions used for the 6-phenyl isomer, yielded a green solid (230 mg.; m. p. 105—108°), which on recrystallisation from ligroin or light petroleum gave pale yellow plates of the *chloro-compound* (150 mg., 55%), m. p. 124—125°

(Found: C, 68·8; H, 3·8; N, 11·8; Cl, 15·0. $C_{14}H_9N_2Cl$ requires C, 69·95; H, 3·8; N, 11·6; Cl, 14·75%).

Reduction of 4-Hydroxycinnoline.—4-Hydroxycinnoline (500 mg.) was heated under reflux in tetrahydrofuran (10 ml.) with lithium aluminium hydride (270 mg.) for 8 hr. Next day, benzene (30 ml.) was added, the complex was decomposed by water, and inorganic material was filtered off. The benzene layer was evaporated to 10 ml. and heated under reflux with an excess of red mercuric oxide for 3 hr. Evaporation of the filtrate to dryness and treatment with methanolic picric acid gave cinnoline picrate (900 mg.), m. p. 190—194°.

6-Phenylcinnoline.—4-Hydroxy-6-phenylcinnoline (300 mg.) was heated under reflux in tetrahydrofuran (6 ml.) with lithium aluminium hydride (140 mg.) for 15 hr. By the above procedure, an oily residue was obtained, which, on recrystallisation from ligroin, gave a yellow solid (110 mg.), m. p. 102—106°. Five recrystallisations from ligroin gave pale yellow needles, m. p. 111—111·5°, which readily formed a picrate, m. p. 176°. The same picrate was obtained by boiling the crude reduction product (m. p. 102—106°) with picric acid in methanol solution. Recrystallisation from alcohol or benzene gave deep yellow needles of *6-phenylcinnoline picrate*, m. p. 176° (Found: C, 55·2; H, 3·1; N, 14·8. $C_{20}H_{13}O_7N_5$ requires C, 55·2; H, 3·0; N, 16·1%).

7-Phenylcinnoline.—4-Hydroxy-7-phenylcinnoline (150 mg.), tetrahydrofuran (3 ml.), and lithium aluminium hydride (70 mg.), by the above procedure, yielded an oily residue, which was dissolved in the minimum volume of methanol and boiled with methanolic picric acid for 10 min. The somewhat gummy picrate separated from methanol as brown needles (140 mg., 48%), m. p. 175·5—177° unchanged by recrystallisation from aqueous alcohol or benzene.

In a similar experiment, 380 mg. of the hydroxycinnoline provided a yellow solid (100 mg.; m. p. 103—106°) by extraction of the crude reduction product with 5N-hydrochloric acid. Five recrystallisations from aqueous alcohol gave very pale yellow needles of *7-phenylcinnoline*, m. p. 116° (Found: C, 80·8; H, 5·1; N, 12·7. $C_{14}H_{10}N_2$ requires C, 81·5; H, 4·9; N, 13·5%). This compound gave the same picrate (m. p. 177°) as was obtained in the previous experiment.

Reduction of 4-Hydroxy-3-phenylcinnoline.—4-Hydroxy-3-phenylcinnoline (5 g.), tetrahydrofuran (100 ml.), and lithium aluminium hydride (2·5 g.) were heated under reflux for 16 hr. After decomposition of the complex, as before, the residue was boiled with red mercuric oxide (15 g.) in benzene (75 ml.) for 4½ hr. Filtration and evaporation yielded a sticky solid, which gave red needles (1·0 g.), m. p. 119—120°, after several recrystallisations from *n*-hexane and from aqueous alcohol (Found: C, 80·8; H, 4·9; N, 13·7. $C_{28}H_{22}N_4$ requires C, 81·1; H, 5·3; N, 13·5%). An acetone solution of this compound decolorised 0·1% potassium permanganate solution in the cold. A yellow picrate, m. p. 150—151°, was prepared in methanol.

The residue obtained by evaporation of the hexane mother-liquors was boiled with picric acid in methanol, whereby a mixture of picrates (1·8 g.; 148—151°) was obtained. Recrystallisation from alcohol and benzene gave green needles (1·2 g.), m. p. 151°, not depressed on admixture with the picrate obtained from the red compound above; a yellow picrate, m. p. 157°, was also obtained from the mixture. Each of these picrates was decomposed by heating it for 20 min. with 4N-sodium hydroxide, to yield the same product which crystallised in yellow needles, m. p. 118—119°, from ligroin, differing from the red compound, m. p. 119—120°, and not decolorising potassium permanganate solution. With methanolic picric acid, the green *3-phenylcinnoline picrate*, m. p. 151°, was regenerated (Found: C, 54·3; H, 3·2; N, 15·45. $C_{20}H_{13}O_7N_5$ requires C, 55·2; H, 3·0; N, 16·1%).

4-Ethoxy-6-phenylcinnoline.—This was obtained during attempted hydrogenolysis of 4-chloro-6-phenylcinnoline in 0·4N-aqueous-alcoholic sodium hydroxide. The *derivative* separated as colourless needles, m. p. 176°, from ligroin or aqueous alcohol (Found: C, 76·1; H, 5·4; N, 10·7. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%). This product formed a picrate, m. p. 168°, in methanol.

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