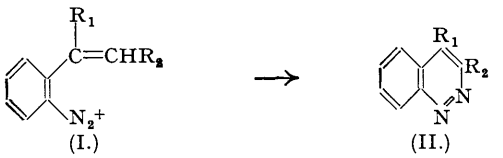
508. *Cinnolines. Part XXIV. Heterocyclic Nuclei as Substituents in the Widman–Stoermer Synthesis. Part I. Pyridyl and Quinolyl Nuclei.*

By K. SCHOFIELD.

The Widman–Stoermer synthesis (I) ⟶ (II) is applicable to the synthesis of 4-aryl-3-2′-pyridyl- and 4-aryl-3-2′-quinolyl-cinnolines, but the success of the reaction depends on the electron-releasing ability of the aryl group. 4-p-*Methoxyphenyl*-3-2′-*pyridyl*- and -3-2′-*quinolyl-cinnoline* are described, and 4-phenyl-3-2′-pyridylcinnoline has been isolated in poor yield as its *picrate*. A small yield of 4-2′-*pyridylcinnoline* is obtained by diazotisation of the appropriate ethylene and differs from the "$C_{13}H_9N_3$ base" (Schofield and Simpson, Part V, *J.*, 1946, 672) to which this structure was previously assigned.

THE work of Stoermer and Simpson and their collaborators (Stoermer and Fincke, *Ber.*, 1909, **42**, 3115; Stoermer and Gaus, *ibid.*, 1912, **45**, 3104; Simpson and Stephenson, *J.*, 1942, 353; Simpson, *J.*, 1943, 447; 1946, 673) has led to a fairly comprehensive understanding of the circumstances in which the Widman–Stoermer reaction (I) ⟶ (II) may be expected to

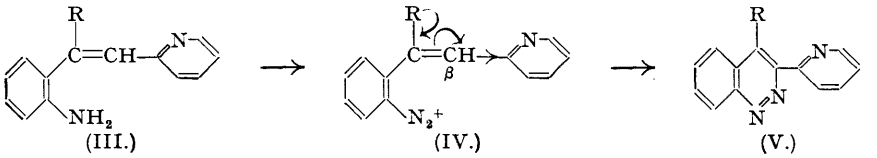


(I.) (II.)

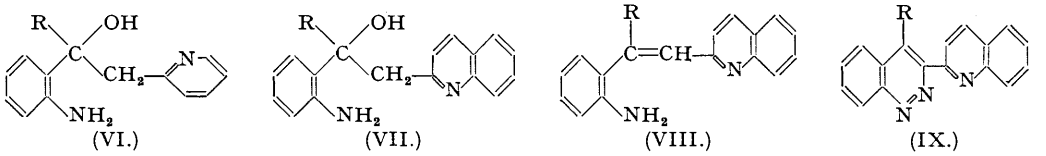
succeed. Thus, cinnoline formation does not occur for the compounds (I; R_1 = H or CO_2H) and (I; R_2 = aryl, CO_2H, CO_2Et, CN, 2-pyridyl, or 2-quinolyl). However, with (I; R_1 = aryl) cyclisation is favoured even when R_2 is also an aryl group. In the last circumstance cinnoline formation is independent of the stereochemical configuration of the ethylene, although in the case of *cis*-compounds it must be regarded as being in competition with the Pschorr phenanthrene synthesis. The example in which R_1 = Ph, and R_2 = Br, was examined by Stoermer and Fincke (*loc. cit.*), and, surprisingly, 4-phenylcinnoline was the only identified product.

As indicated above, the only compounds hitherto examined in which one of the substituents was a heterocyclic nucleus have been (III; R = H) and (VIII; R = H) (Simpson, *J.*, 1946, 673). In view of the dominating influence of an aryl group at R_1 in (I) it seemed reasonable to expect that successful ring-closure would ensue on diazotisation of ethylenes of the type (I; R_1 = aryl, R_2 = heterocyclic nucleus), for, if the probable mechanism of the Widman–Stoermer synthesis is borne in mind (Schofield and Simpson, *J.*, 1945, 520), a heterocyclic nucleus at R_2, if it were basic, would probably encourage the necessary polarisation of the ethylenic linkage [*e.g.*, (III) ⟶ (IV) ⟶ (V)]. On the same grounds, cinnoline formation might be discouraged if R_1 were a basic heterocyclic residue. Successful cyclisation would give products of interest for their similarity to various pyridylquinolines (Cook, Heilbron, Hey, *et al.*, *J.*, 1943, 401, *et seq.*), and furthermore if it occurred with the compound (I; R_1 = 2-pyridyl, R_2 = H), it would yield authentic 4-2′-pyridylcinnoline and so provide a crucial test of the hypothesis put forward (Part V, *loc. cit.*) to explain the complex reaction which occurs

between pyridine, acetic anhydride, and 4-hydroxycinnoline-3-carboxylic acid. The present paper describes preliminary experiments along these lines.

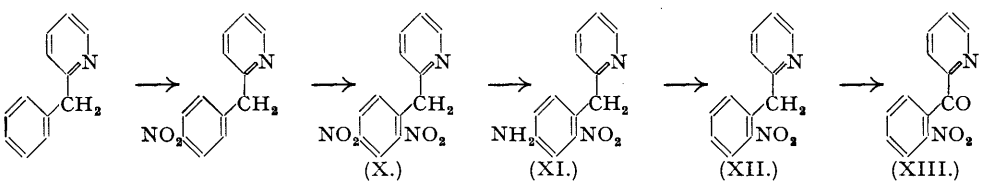


(III.) (IV.) (V.)



(VI.) (VII.) (VIII.) (IX.)

Ethylenes of the first type mentioned above (I; R_1 = aryl; R_2 = heterocyclic nucleus) are comparatively accessible. Although examination of the reactions is not yet complete, 2-aminobenzophenone reacted with 2-pyridylmethyl-lithium and 2-quinolylmethyl-lithium to give *phenyl*-o-*aminophenyl*-2-*pyridylmethyl*- (VI; R = Ph) and *phenyl*-o-*aminophenyl*-2′-*quinolylmethyl-carbinol* (VII; R = Ph), respectively, and similarly o-*aminophenyl*-p-*methoxyphenyl*-2-*pyridylmethyl*- (VI; R = *p*-methoxyphenyl) and o-*aminophenyl*-p-*methoxyphenyl*-2-*quinolylmethyl-carbinol* (VII; R = *p*-methoxyphenyl) were obtained from 2-amino-4′-methoxybenzophenone. Dehydration of these carbinols furnished 1-*phenyl*-1-o-*aminophenyl*-2-2′-*pyridylethylene* (III; R = Ph), and 1-*phenyl*-1-o-*aminophenyl*- (VIII; R = Ph) and 1-o-*aminophenyl*-1-p-*methoxyphenyl*-2-2′-*quinolyl-ethylene* (VIII; R = *p*-methoxyphenyl). 1-*o*-Aminophenyl-1-*p*-methoxyphenyl-2-2′-pyridylethylene (III; R = *p*-methoxyphenyl) was isolated as its *picrate*. The dehydrations proceeded more readily with the derivatives of 2-amino-4′-methoxybenzophenone than with those of 2-aminobenzophenone (there are indications of the similar effect of a hydroxyl group in the work of Simpson and Stephenson, *loc. cit.*).



(X.) (XI.) (XII.) (XIII.)

Ethylenes of the type (I; R_1 = heterocyclic nucleus) are difficult to obtain. In small-scale experiments Wilson (*J.*, 1931, 1936) prepared 2-*o*-nitrobenzoylpyridine (XIII) by the method illustrated above. 2-Benzylpyridine is now fairly readily obtained (Crook, *J. Amer. Chem. Soc.*, 1948, **70**, 416), and we found it convenient to prepare its dinitro-derivative (X) in two stages, instead of by direct dinitration (Tschitschibabin, Kuindshi, and Benewolenskaja, *Ber.*, 1925, **58**, 1580; cf. Bryans and Pyman, *J.*, 1929, 549). Wilson's original method for reducing (X) to (XI) was readily adapted to the larger scale used in this work, but efficient deamination of (XI) to (XII), isolated as its *picrate*, required treatment of the diazonium derivative with a larger excess of hypophosphorous acid than was used by the earlier worker (*cf.* Kornblum, "Organic Reactions," Vol. II, p. 278). The oxidation of (XII) to 2-*o*-nitrobenzoylpyridine (XIII) was improved, and subsequent reduction gave 2-o-*aminobenzoylpyridine*, which with the appropriate Grignard reagents provided o-*aminophenyl*-2-*pyridylmethylcarbinol* and o-*aminophenyl*-2-*pyridylbenzylcarbinol*. The latter has not yet been examined, but dehydration of the former carbinol furnished 1-*o*-aminophenyl-1-2′-pyridylethylene, isolated as its *picrate*.

Diazotisation of these various ethylenes led to interesting results. The two carrying *p*-methoxyphenyl groups gave, in yields greater than 70%, the corresponding 4-p-*methoxyphenyl*-3-2′-*pyridyl*- (V; R = *p*-methoxyphenyl) and 4-p-*methoxyphenyl*-3-2′-*quinolyl-cinnoline* (IX; R = *p*-methoxyphenyl), but, in the cases where the methoxy group was lacking, diazotisation led to tarry products. With (III; R = Ph) a small yield (25%) of 4-*phenyl*-3-2′-*pyridylcinnoline picrate* was isolated, but (VIII; R = Ph) has not so far yielded a homogeneous product.

These results seem to suggest that a pyridyl or quinolyl group in the potential $C_{(3)}$ position of cinnoline, being electron-attracting in acid media, removes some of the electronic charge

accumulated at $C_{(\beta)}$ in (IV), and unless the supply of electrons is sufficiently great, as is ensured by the presence of the methoxyl-group in the above examples, cinnoline formation is greatly hindered. It is unlikely that the steric configuration of the ethylenes is responsible for this result in view of the findings on this point mentioned above. The situation recalls the behaviour of the tolazoles described in an accompanying paper (Part XXI, this vol., p. 2393).

Equally interesting was the diazotisation of 1-*o*-aminophenyl-1-2′-pyridylethylene. For the reasons already mentioned this was effected in dilute acid, and it proved possible to isolate 4-2′-*pyridylcinnoline picrate*, m. p. 201—203°, from the reaction product, in about 25% yield. Alkaline decomposition of the picrate gave 4-2′-*pyridylcinnoline*, m. p. 128—129°. Evidently the diazonium group can sufficiently influence the polarisation of the ethylenic linkage in this case to permit some cinnoline formation, despite the influence of the weakly basic 2-pyridyl group.

As indicated, an authentic specimen of 4-2′-pyridylcinnoline was required for comparison with a compound to which this structure had previously been assigned, which arose from a series of transformations carried out on the reaction product of pyridine, acetic anhydride, and 4-hydroxycinnoline-3-carboxylic acid (Part V, *loc. cit.*). This compound, a yellow base $C_{13}H_9N_3$, m. p. 152·5—153·5°, differs entirely from the synthetic product now obtained, and the picrates of the two compounds confirm this difference. Clearly, the hypothesis put forward to explain the origin of the " $C_{13}H_9N_3$ base " is wholly or partly mistaken. The properties of 4-2′-pyridylcinnoline make it unlikely that the other compound has the alternative γ-pyridyl structure, but this point should be confirmable by a synthesis similar to that described here. We are re-examining the reaction between pyridine, acetic anhydride, and 4-hydroxycinnoline-3-carboxylic acid.

The properties of the new cinnolines are being examined, as are those of some related quinoline derivatives prepared from 2-*o*-aminobenzoylpyridine, and more convenient syntheses of this and similar ketones are being sought. The present examples clearly offer an interesting field for the study of the effect of pH on the Widman–Stoermer synthesis, and experiments along these lines are in hand.

Experimental.

M.p.s are uncorrected. Ether extracts were dried with sodium sulphate unless otherwise stated, and diazotisations were effected at 0—5°.

2-Pyridylmethylcarbinols.—2-Amino-4′-methoxybenzophenone (22·7 g.) in ether (50 c.c.) and benzene (50 c.c.) were added during ½ hour to 2-pyridylmethyl-lithium [from 1·66 g. of lithium (*Org. Synth.*, **23**, 83)], the red suspension was stirred for 5 hours at room temperature and then for 1 hour under reflux. Decomposition with water, extraction with ether, and concentration of the extract gave the almost pure product (15·6 g.), m. p. (151°) 152—153°. o-*Aminophenyl*-p-*methoxyphenyl*-2-*pyridylmethylcarbinol* separated from methanol in soft white needles, m. p. 152·5—153·5° (Found : C, 75·2; H, 6·2. $C_{20}H_{20}O_2N_2$ requires C, 75·0; H, 6·3%). Acetylation at 95° with pyridine–acetic anhydride gave the *monoacetyl* derivative, crystallising in white needles, m. p. 169—170°, from ethanol (Found : C, 72·95; H, 6·1; N, 7·6. $C_{22}H_{22}O_3N_2$ requires C, 72·9; H, 6·1; N, 7·7%).

Under the same conditions 2-aminobenzophenone (19·7 g. in 100 c.c. of benzene and 50 c.c. of ether) gave 8·7 g. of substantially pure product. *Phenyl*-o-*aminophenyl*-2-*pyridylmethylcarbinol* gave rosettes of white needles, m. p. 164—165°, from ethanol (Found : C, 78·7; H, 6·7. $C_{19}H_{18}ON_2$ requires C, 78·6; H, 6·2%). The *monoacetyl* derivative crystallised from methanol in white needles, m. p. 180—181° (Found : C, 75·5; H, 6·1. $C_{21}H_{20}O_2N_2$ requires C, 75·9; H, 6·1%).

Quinolylmethylcarbinols.—2-Amino-4′-methoxybenzophenone (3 g.) in ether (75 c.c.) was added to 2-quinolylmethyl-lithium (prepared from 0·22 g. of lithium as for 2-pyridylmethyl-lithium) in the same solvent (50 c.c.), and the bright red suspension stirred for 5 hours at room temperature. Worked up as in the above cases this gave the almost pure product (1·7 g.). o-*Aminophenyl*-p-*methoxyphenyl*-2-*quinolylmethylcarbinol* gave soft, dull white needles, m. p. 159—160°, from ethanol (Found : C, 77·4; H, 6·1; N, 7·6. $C_{24}H_{22}O_2N_2$ requires C, 77·8; H, 6·0; N, 7·6%).

In the same way, 2-aminobenzophenone gave the related product in 23% yield. *Phenyl*-o-*aminophenyl*-2-*methylquinolylmethylcarbinol* separated from ethanol as fluffy white needles, m. p. 161—162° (Found : C, 80·85; H, 6·0; N, 8·6. $C_{23}H_{20}ON_2$ requires C, 81·1; H, 5·9; N, 8·2%).

1-*Phenyl*-1-o-*aminophenyl*-2-2′-*pyridyl-* and 1-*Phenyl*-1-o-*aminophenyl*-2-2′-*quinolyl-ethylene.*—Phenyl-*o*-aminophenyl-2-pyridylmethylcarbinol (1 g.) and concentrated sulphuric acid (3 c.c.) were heated at 95° for ¾ hour, and the solution was diluted with ice, made alkaline with aqueous ammonia, and extracted with ether. Concentration of the extract and addition of a little ligroin (b. p. 60—80°) caused the separation of a crystalline yellow solid (0·67 g.), m. p. 137—138°. 1-*Phenyl*-1-o-*aminophenyl*-2-2′-*pyridylethylene* separated from methanol in pale yellow prisms, m. p. 139—140° (Found : C, 83·3; H, 6·0; N, 10·1. $C_{19}H_{16}N_2$ requires C, 83·8; H, 5·9; N, 10·3%). The *picrate* formed small, permanganate-coloured needles from ethanol, m. p. 188—189° (with preliminary shrinking) (Found : C, 60·3; H, 4·1. $C_{19}H_{16}N_2,C_6H_3O_7N_3$ requires C, 59·9; H, 3·8%).

Similar treatment for ½ hour at 95° of the analogous quinolylmethylcarbinol (2 g.) with concentrated sulphuric acid (5 c.c.) gave 1·19 g. of almost pure product. 1-*Phenyl*-1-o-*aminophenyl*-2-2′-*quinolylethylene* separated from methanol as yellow tablets, m. p. 164—165° (Found : C, 85·35; H, 5·5; N, 8·8. $C_{23}H_{18}N_2$ requires C, 85·7; H, 5·6; N, 8·7%).

1-o-*Aminophenyl*-1-p-*methoxyphenyl*-2-2′-*pyridyl-* and 1-o-*Aminophenyl*-1-p-*methoxyphenyl*-2-2′-

quinolyl-ethylene.—The pyridylcarbinol (3 g.) and sulphuric acid (60 c.c.; 20% v/v) were heated 1 hour at 95°, the solution was made alkaline with aqueous ammonia and extracted with ether, and the solvent was removed *in vacuo*, leaving a creamy froth (2·8 g.). This did not crystallise but provided a *picrate*, forming beautiful crimson needles, m. p. 168—169°, from ethanol (Found: C, 58·5; H, 3·8; N, 13·8. $C_{20}H_{18}ON_2,C_6H_3O_7N_3$ requires C, 58·8; H, 4·0; N, 13·2%).

The 2-quinolylmethylcarbinol (1 g.), treated similarly with sulphuric acid (30 c.c.; 20% v/v) for 1 hour at 95°, gave the almost pure product (0·67 g.) after one crystallisation from methanol. 1-o-*Aminophenyl*-1-p-*methoxylphenyl*-2-2′-*quinolylethylene* formed crisp, pale yellow prisms, m. p. 154·5—155·5°, from methanol (Found: C, 82·0; H, 5·9; N, 7·5. $C_{24}H_{20}ON_2$ requires C, 81·8; H, 5·7; N, 7·9%).

Diazotisation of the Ethylenes.—(i) The methoxyphenylpyridylethylene, prepared as above from the carbinol (4 g.), in acetic acid (26 c.c.) and concentrated hydrochloric acid (16 c.c.), was diazotised with aqueous sodium nitrite (5%), water was added (30 c.c.), and the solution set aside for 4 days at room temperature. Neutralisation with solid sodium carbonate gave a granular precipitate (4·23 g.), which after two crystallisations from aqueous methanol (charcoal) gave the almost pure product (2·7 g.), m. p. 156—157°. 4-p-*Methoxyphenyl*-3-2′-*pyridylcinnoline* formed pale yellow tablets, m. p. 157—158°, from aqueous methanol (Found: C, 76·5; H, 5·0. $C_{20}H_{15}ON_3$ requires C, 76·7; H, 4·8%).

(ii) The phenylpyridylethylene (0·3 g.) was diazotised in the same way, and the solution set aside for 14 days at room temperature and neutralised with solid sodium carbonate. The aqueous layer was decanted from a precipitated tar, and the latter dissolved in methanol (charcoal) and treated with picric acid in the same solvent. Several crystallisations of the crude picrate from methanol gave a fairly pure product (0·14 g.), m. p. 188—191°. 4-*Phenyl*-3-2′-*pyridylcinnoline picrate*, on further crystallisation, formed yellow leaflets, m. p. 194—196° (with some preliminary softening) (Found: C, 57·6; H, 3·4. $C_{19}H_{13}N_3,C_6H_3O_7N_3,CH_3OH$ requires C, 57·35; H, 3·7%).

(iii) The methoxyphenylquinolylethylene (0·6 g.) was diazotised as in (i), the solution set aside for 14 days at room temperature and worked up as above. From methanol (charcoal) the crude product gave almost pure material (0·48 g.), m. p. 149—151°. 4-p-*Methoxyphenyl*-3-2′-*quinolylcinnoline* separated from methanol as glistening, pale yellow tablets, m. p. 151—152° (Found: C, 78·6; H, 4·7; N, 11·0. $C_{24}H_{17}ON_3$ requires C, 79·3; H, 4·7; N, 12·7%).

Under these conditions the phenylquinolylethylene has not yielded a homogeneous product.

2-p-*Nitrobenzylpyridine*.—2-Benzylpyridine (20 g.) in concentrated sulphuric acid (28 c.c.) was added during ½ hour to a stirred mixture of nitric acid (11 c.c.; *d* 1·42) and concentrated sulphuric acid (14 c.c.) at −5° to 0°. The solution was kept for 4 hours at room temperature, poured on to ice, and neutralised with solid sodium carbonate, and the precipitate collected after a short time. The crude material from 5 such experiments (77 g.) was decolorised in ethanol (250 c.c.), and the solution concentrated to half volume, giving white needles (50 g.), m. p. 79—80° (Tschitschibabin *et al.*, *loc. cit.*, give m. p. 81°). Further concentration gave a second crop (10 g.) (total yield, 47%). Nitrations on the 50-g. scale gave similar yields.

2-2′ : 4′-*Dinitrobenzylpyridine*.—The mononitro-compound (40 g.) was added during ¼ hour to a stirred mixture of concentrated sulphuric acid (80 c.c.) and nitric acid (22·4 c.c.; *d* 1·42) at −5° to 0°. After being stirred for a further 20 minutes at this temperature and ½ hour without a freezing mixture and kept for 2 hours at room temperature, the solution was heated for 1 hour at 95° and poured on ice. The sulphate of the base separated and was collected after a short time, suspended in water (400 c.c.), and made alkaline with aqueous ammonia, and the base extracted with a large volume of ether [the base is only sparingly soluble, but extraction gave a purer product than filtration; in nitrations where larger amounts of nitric acid were used, small quantities of an ether-insoluble solid, m. p. 144°, presumably 2-2′ : 4′-dinitrobenzoylpyridine (Tschitschibabin *et al.*, *loc. cit.*, give m. p. 148°), were isolated]. Concentration of the extract gave large yellow prisms of practically pure 2-2′ : 4′-dinitrobenzylpyridine [40·5 g. (83%); m. p. 92—93° (Tschitschibabin *et al.*, *loc. cit.*, give m. p. 93°)], unmistakably recognised by its striking behaviour on exposure to light.

2-2′-*Nitro*-4′-*aminobenzylpyridine*.—Reduction of the dinitro-compound by Wilson's method (*loc. cit.*) on the small scale (5—10 g.) gave 75—80% of the amine, but in larger runs (30 g.) yields fell to 65—70%.

2-o-*Nitrobenzylpyridine*.—The amine (30 g.) in hydrochloric acid (90 c.c.; 6N.) was diazotised with aqueous sodium nitrite (10%), ice-cold hypophosphorous acid (from 210 g. of sodium hypophosphite, 150 c.c. of water, and 450 c.c. of 6N-hydrochloric acid) was added, and the solution was kept for 24 hours at 0°. The oil obtained by adding an excess of sodium hydroxide (5N.), followed by ether extraction, was treated in alcohol (100 c.c.) with warm alcoholic picric acid (21 g. in 180 c.c.), giving a yellow crystalline product (35·3 g.), m. p. 149—151°. This was extracted with benzene (2 portions of 500 c.c., each for 4—5 hours) in a Sohxlet apparatus. The extract (charcoal) gave yellow needles on cooling. Half of the benzene was distilled from the filtrate and used further to extract the remaining crude picrate. In this way 28·5 g. (48%) of substantially pure picrate, m. p. 155—156°, were obtained. 2-o-*Nitrobenzylpyridine picrate* crystallised from benzene in rosettes of bright yellow needles, m. p. 157—158° (Found: C, 48·8; H, 3·0; N, 14·8. $C_{12}H_{10}O_2N_2,C_6H_3O_7N_3$ requires C, 48·8; H, 3·0; N, 15·8%).

2-o-*Nitrobenzoylpyridine*.—The picrate (10 g.) was warmed for ¼ hour on the steam-bath with sodium hydroxide (2·3 g. in 200 c.c. of water), water added (100 c.c.), the mixture extracted with ether, and the solvent removed. The residual oil was heated at 95° with potassium permanganate (10 g. in 800 c.c. of water), further amounts of the latter (10 g. and 2 g.) were added after ¾ hour and 2 hours, and the mixture was then evaporated to dryness. The residue was digested with alcohol (250 c.c. in all) and the extract (charcoal) concentrated, giving white needles (3·8 g., 71%), m. p. 115—117°, suitable for use in the next stage. 2-o-*Nitrobenzoylpyridine picrate* formed yellow needles, m. p. 147—148°, from alcohol (Found: C, 47·4; H, 2·6. $C_{12}H_8O_3N_2,C_6H_3O_7N_3$ requires C, 47·3; H, 2·4%).

2-o-*Aminobenzoylpyridine*.—The nitro-compound (5 g.) in concentrated hydrochloric acid (5 c.c.) was treated with a solution of stannous chloride (15 g.) in concentrated hydrochloric acid (20 c.c.) during 5 minutes, and the mixture heated for 1 hour at 95° and set aside for 5 hours at room temperature. Making alkaline with concentrated aqueous sodium hydroxide, extraction with ether, removal of the

solvent, and one crystallisation from methanol (charcoal) gave crisp yellow needles of almost pure amine (3·8 g.), m. p. 145—146°. 2-o-*Aminobenzoylpyridine* separated from methanol in clusters of yellow blades, m. p. 145—146° (Found: C, 72·5; H, 5·3. $C_{12}H_{10}ON_2$ requires C, 72·7; H, 5·1%). With a small amount of hydrochloric acid the base gave an orange solution, turning yellow with excess of acid. The *picrate* of the base formed beautiful orange needles from ethanol, softening characteristically at 156—158°, and melting to a dark red liquid at 164—165° (Found: C, 50·6; H, 3·3. $C_{12}H_{10}ON_2,C_6H_3O_7N_3$ requires C, 50·6; H, 3·1%).

1-o-*Aminophenyl*-1-2′-*pyridylethanol*.—The foregoing amino-ketone (5 g.) in ether (400 c.c.) and benzene (100 c.c.) was added quickly at room temperature to a stirred Grignard reagent [from magnesium (2·7 g.), methyl iodide (16·1 g.), and ether (200 c.c.)], and the pinkish grey suspension was heated under reflux for 1¾ hours. Decomposition with ice and ammonium chloride, extraction with ether, removal of the solvent, and recrystallisation from ether–ligroin (b. p. 40—60°) gave the almost pure carbinol (3·7 g.), m. p. 95—97°. 1-o-*Aminophenyl*-1-2′-*pyridylethanol* separated from ether–ligroin (b. p. 40—60°) as fawn prisms, m. p. 97·5—98° (Found: C, 72·7; H, 6·8. $C_{13}H_{14}ON_2$ requires C, 72·8; H, 6·6%). The *picrate* formed crisp, yellowish-orange needles, m. p. (153°) 156—157° (decomp.), from benzene (Found: C, 52·5; H, 4·2. $C_{13}H_{14}ON_2,C_6H_3O_7N_3$ requires C, 51·5; H, 3·9%).

o-*Aminophenyl*-2-*pyridylbenzylcarbinol*.—The amino-ketone (1 g.) in ether (250 c.c.) was added rapidly at room temperature to a stirred Grignard reagent [from benzyl chloride (2·56 g.), magnesium (0·5 g.), and ether (60 c.c.)], and the suspension heated under reflux for 4 hours. Worked up as above, the product (0·8 g., m. p. 131—132°) was obtained almost pure from the ether extract. o-*Aminophenyl*-2-*pyridylbenzylcarbinol* separated from methanol in large colourless prisms, m. p. 131·5—132° (Found: C, 78·3; H, 6·3; N, 9·7. $C_{19}H_{18}ON_2$ requires C, 78·6; H, 6·25; N, 9·6%).

4-2′-*Pyridylcinnoline*.—(i) The powdered 1-pyridylethanol (0·15 g.) was added to concentrated sulphuric acid (0·6 c.c.) at 95° during ¼ hour, with shaking, the temperature maintained for a further hour, and the solution diluted with ice, made alkaline with sodium hydroxide solution, and extracted with ether. The oil left after removal of the ether gave, with picric acid in ethanol, an almost pure product (0·27 g.), m. p. (138°) 141—142°. 1-o-*Aminophenyl*-1-2′-*pyridylethylene picrate* separated from ethanol in soft yellow needles, m. p. 141—142° (Found: C, 53·6; H, 3·8. $C_{13}H_{12}N_2,C_6H_3O_7N_3$ requires C, 53·6; H, 3·6%).

(ii) The oil (1·03 g.), obtained by dehydrating the carbinol (1·2 g.) as above, was diazotised in 2N-hydrochloric acid (12 c.c.) with 10% aqueous sodium nitrite. After 3 weeks at room temperature the solution was made alkaline with solid sodium carbonate, giving a tarry precipitate which became granular after a short time and was then collected, dissolved in warm methanol (charcoal), and treated with picric acid (0·9 g.) in the same solvent. Two crystallisations of the crude product from methanol gave fairly pure material (0·65 g.), m. p. (188°) 196—199°. 4-2′-*Pyridylcinnoline picrate* separated from methanol as beautiful, felted, mustard-yellow needles, m. p. (198°) 201—203° (Found: C, 51·3, 51·5; H, 2·8, 3·0; N, 19·7, 19·8. $C_{13}H_9N_3,C_6H_3O_7N_3$ requires C, 52·3; H, 2·8; N, 19·3%). It strongly depressed the m. p. (207—208°) of the picrate of the "$C_{13}H_9N_3$ base" (Part V, *loc. cit.*).

The picrate (0·25 g.) was warmed at 95° with sodium hydroxide (0·25 g. in 10 c.c. of water) for ½ hour, the mixture extracted with ether, and the solvent removed. The crude base (0·1 g.) was readily soluble in the usual solvents and was purified by crystallisation from ligroin (b. p. 40—60°) containing a small proportion of ethyl acetate. In this way 4-2′-*pyridylcinnoline* was obtained as stout, crisp, almost colourless prisms, m. p. 128—129° (Found: C, 73·8, 73·9; H, 4·75, 5·0; N, 20·5, 20·8. $C_{13}H_9O_3$ requires C, 75·3; H, 4·4; N, 20·3. $C_{13}H_9N_3,\frac{1}{2}H_2O$ requires C, 72·2; H, 4·7; N, 19·4%). It strongly depressed the m. p. (148—149°) of the "$C_{13}H_9N_3$ base" (Part V, *loc. cit.*) (the m. p. of the latter compound depends on its degree of hydration and falls a little with ageing).

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