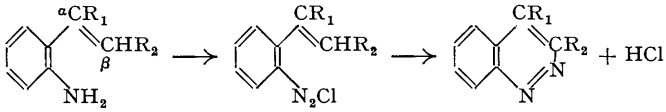
120. *Cinnolines. Part II. The Influence of Substituents on the Widman–Stoermer and the Pschorr Reaction.*

By James C. E. Simpson.

A review of the published evidence respecting cyclisation of diazotised *o*-amino-ethylenes of type (I) leads to the conclusion that the Widman–Stoermer cinnoline synthesis (I ⟶ III) is inhibited when R_1 = H or CO_2H and R_2 = aryl or another negative group such as CO_2H, CO_2Et, or CN. In contrast to these results, it has now been found that the *amino-ethylenes* (IX), (X), and (XI) on diazotisation cyclise with extreme readiness to 3 : 4-*diphenyl*-, 4-*phenyl*-3-*benzyl*-, and 4-*phenyl*-3-(1′-*naphthyl*)-*cinnoline* respectively. In the last reaction 2-*phenylchrysene* (XIII) is formed in small quantity by a concomitant Pschorr reaction, and under suitable conditions the amount can be considerably increased to the exclusion of cinnoline-formation. The attachment of a phenyl group to the α-carbon atom of the amino-ethylene is evidently a dominant factor favouring cinnoline-formation; this is particularly well illustrated in the case of (IX), both geometrical forms of which yield the cinnoline and no 9-phenylphenanthrene, whereas the *cis*- and the *trans*-form of 2-aminostilbene furnish, respectively, phenanthrene and *trans*-stilbene or *trans*-2-hydroxystilbene on diazotisation.

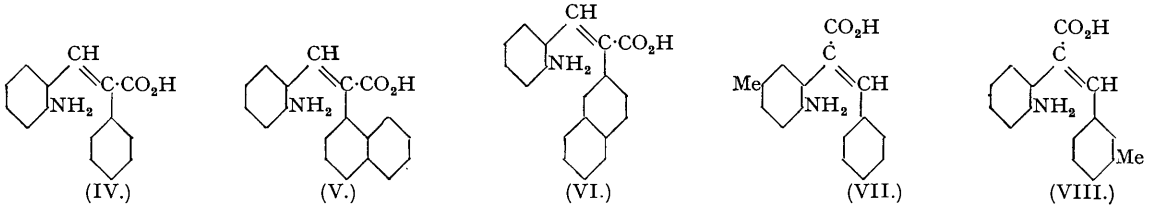
The synthesis of cinnolines by the Widman–Stoermer reaction (Widman, *Ber.*, 1884, **17**, 722; Stoermer and Fincke, *ibid.*, 1909, **42**, 3115; Stoermer and Gaus, *ibid.*, 1912, **45**, 3104; Simpson and Stephenson, J., 1942, 353) involves the diazotisation of *o*-aminoaryl-ethylenes, followed by cyclisation, which usually occurs spontaneously (I ⟶ II ⟶ III) :



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

Little attention has been paid to the question of the influence exerted by substituents R_1 and R_2 on the ease of formation of the hetero-ring, although Stoermer and Gaus (*loc. cit.*) have deduced, from the fact that *o*-amino-cinnamic acid does not yield a cinnoline, that a negative group (R_2) on the β-ethylenic carbon atom of the amino-ethylene inhibits the cyclisation. These authors also state that an increase in the negative character of the substituent (R_1) on the α-carbon atom of the amino-ethylene facilitates cinnoline-formation, but no evidence in support of this assertion has been presented.

There is in fact considerable published evidence to the effect that, when R_2 is negative, particularly aryl, compounds of type (I) do not yield cinnolines on diazotisation. A striking illustration of this point is to be found in certain applications of the Pschorr reaction. In examples such as the synthesis of phenanthrene-9-carboxylic acid from (IV) (Pschorr, *Ber.*, 1896, **29**, 496), of chrysene-1-carboxylic acid from (V) (Weitzenböck and Lieb, *Monatsh.*, 1912, **33**, 549), and of 3 : 4-benzophenanthrene-10-carboxylic acid, mixed with 1 : 2-benzanthracene-4-carboxylic acid, from (VI) (Mayer and Oppenheimer, *Ber.*, 1918, **51**, 510; Cook, J., 1931, 2524), cinnoline-formation is clearly out of the question, owing to the absence of the necessary hydrogen on the β-carbon atom. In compounds (VII) and (VIII), on the other hand, this hydrogen atom is available, and cyclisation to cinnoline derivatives is thus an *a priori* possibility. Mayer and Balle (*Annalen*, 1914, **403**, 167), however, have shown that diazotisation of (VII) and (VIII) leads respectively to 2-methylphenanthrene-10-carboxylic acid and a mixture of 2- and 4-methylphenanthrene-9-carboxylic acids. The non-formation of cinnolines from (VII) and (VIII) is thus apparently attributable either to the aryl residue on the β-carbon atom or to the carboxyl on the α-carbon atom, or to both of these factors.



(IV.) (V.) (VI.) (VII.) (VIII.)

Now 2-aminostilbenes in which both the α- and the β-ethylenic carbon atom carry hydrogen atoms also show a characteristic behaviour on diazotisation. Although the reaction has not been studied with every known 2-aminostilbene of this type, it has been shown in several instances that the diazonium salt decomposes on warming with production of benzaldehyde. Examples of this are the diazotisations of 2-amino- and 4-nitro-2-amino-stilbene (Sachs and Hilpert, *Ber.*, 1906, **39**, 899), and of 2-amino-4-cyanostilbene (Ullmann and Gschwind, *ibid.*, 1908, **41**, 2291), although the second compound behaves normally in that its diazonium salt yields a diazoamino-compound with aniline. The failure of these stilbenes to undergo the expected Pschorr cyclisation is due to the fact that they are *trans*-derivatives, for Ruggli and Staub (*Helv. Chim. Acta*, 1937, **20**, 37) and Taylor and Hobson (J., 1936, 181) have shown that *cis*-2-aminostilbene furnishes phenanthrene after diazotisation, the former authors isolating the hydrocarbon in yields as high as 80%. More recently, an 18% yield of phenanthrene has been obtained from tetrazotised *cis*-2 : 4′-diaminostilbene by Ruggli and Dinger

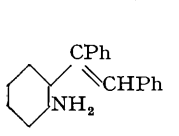
(*Helv. Chim. Acta*, 1941, **24**, 173), whereas the *trans*-diamine gave stilbene (13%) as the sole isolable product. Similarly, a re-investigation of the diazotisation of *trans*-2-aminostilbene by Ruggli and Staub (*loc. cit.*) showed that, according to the conditions used, *trans*-stilbene (62%) or *trans*-2-hydroxystilbene and a little benzaldehyde are produced.

The essential point which emerges from these considerations is that *cis*-2-aminostilbenes, in which both the α- and the β-carbon atom carry hydrogen atoms, behave normally in the Pschorr reaction, but that neither they nor their *trans*-isomers undergo cinnoline cyclisation.

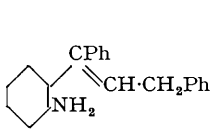
A third category of substances of type (I) in which R_2 is negative comprises *o*-aminocinnamic acid and its simple derivatives. Here again, no instance of cinnoline-formation has been recorded. Diazotisation of the free acid leads to the formation of coumarin, coumaric acid, or cinnamic acid according to the experimental conditions (Fischer, *Ber.*, 1881, **14**, 479; Stoermer and Heymann, *ibid.*, 1912, **45**, 3099); *o*-aminocinnamic ester furnishes the *o*-cyano-ester in the Sandmeyer reaction (Komppa, Öf. Finska Vetenskaps-Societetens Förhandlingar, **36**, 121; Linstead and Noble, J., 1937, 936); and *o*-aminocinnamonitrile gives an inconclusive result (production of an alkali-soluble dark oil; Pschorr, *Ber.*, 1898, **31**, 1296).

The available data thus lead to the conclusion that the formation of cinnolines from compounds of type (I) does not occur in cases where R_2 is aryl or another negative group and R_1 is either hydrogen or carboxyl.

In this paper are recorded the results of diazotisation of some new *o*-amino-ethylenes of type (I) in which R_1 = phenyl. The *compounds* (IX), (X), and (XI) were prepared by the Grignard reaction between *o*-amino-benzophenone and the appropriate aryl halide, followed by dehydration of the resultant dl-*carbinols*. Diazotisation of (IX) and (X) yielded **3 : 4-*diphenylcinnoline*** (XII; R = Ph) and **4-*phenyl*-3-*benzylcinnoline*** (XII; R = CH_2Ph) respectively in almost quantitative yields. Similar treatment of (XI), on the other hand, furnished **4-*phenyl*-3-(1′-*naphthyl*)*cinnoline*** (XII; R = 1′-naphthyl) as major product, accompanied by small amounts of a *hydrocarbon*, $C_{24}H_{16}$, which is regarded as 2-phenylchrysene (XIII), and further investigation showed that these two types of cyclisation may become virtually mutually exclusive under suitable experimental conditions. It is thus clear that cinnoline-formation is to be regarded as a reaction which is potentially alternative to, and in competition with, any Pschorr-cyclisation arising from the diazotisation of a substance of general formula (I; R_2 = aryl).



(IX.)



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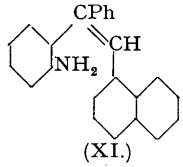

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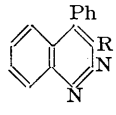

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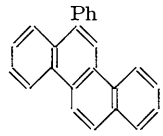

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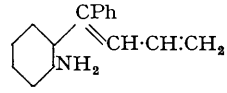


(XIV.)

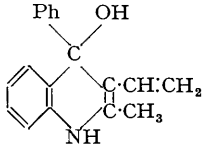
In the case of (IX) the Pschorr-cyclisation seems to be inhibited completely, because the amino-ethylene has been obtained in both the possible geometrical forms; the isomers show a strong depression of the melting point on admixture, and each of them gives 3 : 4-diphenylcinnoline in high yield under identical conditions; on the other hand, 9-phenylphenanthrene (Koelsch, *J. Amer. Chem. Soc.*, 1934, **56**, 480; Bradsher and Schneider, *ibid.*, 1938, **60**, 2960) could not be isolated from either isomer, conditions being used under which (XI) was cyclised to 2-phenylchrysene, the only recognisable product being, in each case, 3 : 4-diphenylcinnoline (in much diminished yield). This result stands in interesting contrast to that of the diazotisation of *cis*- and of *trans*-2-aminostilbene, to which reference has already been made. A further matter of interest is that each of the isomers (IX) is unaffected sterically by hot alcoholic hydrochloric acid, so there can be no doubt that the cinnoline is produced directly from two different stereoisomeric entities, and therefore, in this case at least, the cyclisation must be independent of spatial configuration. Unfortunately this point could not be established in the case of (XI), because, although two stereoisomeric amino-ethylenes, m. p.'s 145° and 183°, were again obtained, the latter was unreactive; it could not be acetylated under normal conditions, neither could it be diazotised. Although no detailed study of the actual configurations of these pairs of amino-ethylenes has been made (*e.g.*, by the nitrobenzene–iodine method of Ruggli and Dinger, *loc. cit.*), the production of 2-phenyl-chrysene from the diazotisable amine (XI), m. p. 145°, makes it clear that the α-naphthyl and *o*-aminophenyl nuclei occupy *cis*-positions in the latter substance.

It is obvious that the attachment of a phenyl group to the α-carbon atom of the amino-ethylene exerts an enormously powerful effect in favour of cinnoline formation, and that it overcomes the inhibitory action of an aryl group on the β-carbon atom, which is itself far from weak, as is shown by the behaviour of the 2-amino-stilbenes. It is therefore surprising that no cinnoline derivatives were obtained by Mayer and Balle (*loc. cit.*) on diazotisation of (VII) and (VIII); even after allowance has been made for possible activation of the *o*- and *p*-positions by the methyl group in (VIII), the complete inhibition of cinnoline formation would scarcely be anticipated as the result of the replacement of phenyl by carboxyl on the α-carbon atom. [The work of Ruggli and his associates (*Helv. Chim. Acta*, 1936, **19**, 1288 and *loc. cit.*) has shown that a carboxyl on either the α- or the β-carbon atom has no direct effect in promoting the phenanthrene cyclisation, but that it merely directs the aryl nuclei into the necessary *cis*-positions during the synthesis of the stilbene]. It is possibly of significance that Mayer and Balle obtained the phenanthrene acid from (VII) in a yield of only 3%, in contrast to yields of the order of 75% secured in many other cases in the literature where cinnoline formation is not theoretically possible. Unfortunately the authors do not record the yield of mixed phenanthrene acids from (VIII).

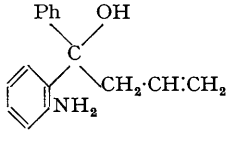
The observations recorded above show that the formation of 3 : 4-diphenyl- and of 4-phenyl-3-(1′-naphthyl)-cinnoline does not occur spontaneously. The diazotisations were carried out in strongly acid solution, followed by dilution, in contrast to the aqueous acid media employed in previous cases (Stoermer and Fincke; Simpson and Stephenson, *locc. cit.*), in which cyclisation appeared to be spontaneous. The effect of acid concentration, and of varying the group attached to the α-carbon atom of the amino-ethylene, are problems which it is hoped to investigate.

The carbinols from which (IX) and (X) were derived were prepared in high yield by the Grignard method, but the condensation of *o*-aminobenzophenone with the Grignard compound of α-chloromethylnaphthalene did not proceed smoothly, doubtless owing to the fact that considerable amounts of *s*-1 : 1′-dinaphthylethane were formed during the reaction. This hydrocarbon has previously been prepared by reduction of the amide of α-thionaphthoic acid (Bamberger and Lodter, *Ber.*, 1888, **21**, 54), and by dehydrogenation of α-methylnaphthalene with sulphur (Friedmann, *ibid.*, 1916, **49**, 277). The crude Grignard-product, after removal of hydrocarbons, yielded the unreactive amino-ethylene (XI), m. p. 183°, together with the *acetamido-carbinol*, m. p. 175°, on treatment with acetic anhydride in pyridine at 100°. The aforesaid amino-ethylene was converted into the diazotisable isomer, m. p. 145°, by means of hot alcoholic hydrochloric acid.

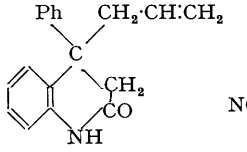
In the hope of obtaining the butadiene (XIV), *o*-aminobenzophenone was condensed with allylmagnesium bromide. An *amino-carbinol*, m. p. 72°, of the expected composition $C_{16}H_{17}ON$, was isolated in high yield, which resinified on treatment with hot dilute sulphuric acid; the resin gave an amorphous adduct with maleic anhydride. Treatment of the crude Grignard reaction product with pyridine–acetic anhydride yielded some of the neutral *acetamido-carbinol*, $C_{18}H_{19}O_2N$, but the main product was a basic *substance*, m. p. 80°, $C_{18}H_{17}ON$, which readily rearranged in hot dilute sulphuric acid to an *isomeride*, m. p. 130°. The basic character of the substance, m. p. 80°, excludes its formulation as an acetamido-ethylene; it must therefore be bicyclic, and if the *amino-carbinol* has the normal structure (XV) it can be represented either by the 3 : 4-dihydro-2-quinolone structure (XVI) or by the expression (XVII). The isomerisation to the substance, m. p. 130°, could then consist in a shift of side-chain unsaturation on the basis of (XVI), or in cyclisation of (XVII) to a tetrahydrofuran.



(XVII.)



(XV.)



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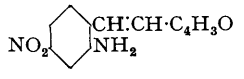
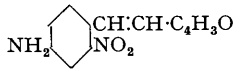


(XVIII.)



(XIX.)

Various other modes of isomerisation, however, may be envisaged by analogy with the work of Bogert and his school (*J. Amer. Chem. Soc.*, 1934, **56**, 185, 248, 959; 1935, **57**, 151) on the cyclisation of aryl-olefins, and the constitution of the substance, m. p. 130°, must be left in abeyance until further data are available.

This work, as originally planned, included the synthesis of a number of 2-aminostilbenes with a view to varying the group on the β-ethylenic carbon atom as widely as possible. Thiele and Escales (*Ber.*, 1901, **34**, 2842) have prepared 2 : 4-dinitrostilbene by condensation of 2 : 4-dinitrotoluene with benzaldehyde in presence of piperidine, and Pfeiffer (*ibid.*, 1915, **48**, 1777) has shown that this method is of general applicability. In the present work 2 : 4-dinitrotoluene was condensed with furfural, vanillin, and piperonal. The furfurylidene *derivative* was reduced to each of the isomeric *nitro-amines* (XVIII) and (XIX); neither amine gave any crystalline product on diazotisation. In view of the results discussed above, reduction of the condensation *products* from the other aldehydes was not studied, except for a single unsuccessful experiment with the piperonylidene compound. From the method used in their formation, the amines (XVIII) and (XIX) may safely be regarded as *trans*-derivatives.

Addendum.—In Part I (Simpson and Stephenson, *loc. cit.*) it was stated that no crystalline carbinol could be obtained by the action of methylmagnesium iodide on either 5-chloro-2-amino-4′-hydroxybenzophenone or 5-chloro-2-amino-2′-hydroxy-5′-methylbenzophenone. The pure crystalline *carbinols* have now been prepared, and their properties are described in the experimental section. Each carbinol was readily dehydrated to the corresponding ethylene previously described (*loc. cit.*).

Experimental.

(Melting points are uncorrected.)

α-Phenyl-α-(2-aminophenyl)-β-(1′-naphthyl)ethylenes (XI).—A Grignard solution was prepared from magnesium (2·2 g.), ether (50 c.c.), and a solution of α-chloromethylnaphthalene (Fieser and Gates, *J. Amer. Chem. Soc.*, 1940, **62**, 2335) (14·5 c.c.) in ether (40 c.c.), which was added during 20 minutes with gentle refluxing. A solution of *o*-aminobenzophenone (4 g.) in ether (120 c.c.) was added at room temperature, and the product, after being refluxed for 1 hour, was decomposed with ice-cold ammoniacal ammonium chloride. *s*-1 : 1′-Dinaphthylethane (usually about 2 g.) crystallised from the dried and concentrated ethereal solution, and was recrystallised from benzene–alcohol, forming rosettes of colourless needles, m. p. 161—161·5° (Found: C, 93·1; H, 6·4. Calc. for $C_{22}H_{18}$: C, 93·6; H, 6·4%). The hydrocarbon is described by Bamberger and Lodter and by Friedmann (*locc. cit.*) as greenish-yellow tablets, m. p. 160°.

The filtrate from the dinaphthylethane was diluted with ether, and the amino-carbinol removed as an insoluble oily hydrochloride by extraction with 2N-hydrochloric acid. The base, liberated with ammonia and collected with ether, was a viscous resin which could not be crystallised. It was heated at 100° for 2 hours with its own weights of acetic anhydride and pyridine, and the *amino-ethylene* precipitated by slight dilution with water and scratching. The crude product was

washed with a little methanol, yielding 1·8 g. of nearly pure material, which crystallised from acetone in almost colourless glassy prisms, m. p. 182—183° (Found: C, 89·4; H, 5·85; N, 4·3. $C_{24}H_{19}N$ requires C, 89·7; H, 5·95; N, 4·4%). The amine, dissolved in a mixture of acetic and hydrochloric acids, was treated with sodium nitrite, but was recovered unchanged after addition of ammonia. As was anticipated from its method of isolation, the pure substance also failed to react with acetic anhydride in pyridine at 100°. It can be precipitated as a smeary hydrochloride by addition of hydrochloric acid to its ethereal or chloroform solution, but the strength of acid necessary for the extraction appears to depend on several factors. Thus 2N-acid will remove it readily from an ethereal solution of the crude product formed by the reaction with acetic anhydride, but repeated shaking with concentrated acid was necessary to remove the base from a mixture of it and *s*-1 : 1′-dinaphthylethane dissolved in chloroform.

The dehydration of the amino-carbinol with acetic anhydride was not always complete. In an experiment using 8 g. of *o*-aminobenzophenone, the total basic material was treated as above with pyridine and acetic anhydride, and then separated into neutral and basic fractions with ether and hydrochloric acid. The neutral fraction gave about 3·3 g. of the *acetamido-carbinol*, which formed colourless needles, m. p. 175—176°, from aqueous alcohol (Found: C, 82·0; H, 6·15; N, 4·1. $C_{26}H_{23}O_2N$ requires C, 81·9; H, 6·1; N, 3·7%). The basic fraction was almost pure amino-ethylene (3·2 g.).

The foregoing amino-ethylene was refluxed for 1¼ hours with 40 vols. of a mixture of equal parts of concentrated hydrochloric acid and alcohol; the *isomeride*, then precipitated by addition of ammonia, separated from aqueous alcohol in small soft needles, m. p. 144—145° (yield, 60—65%) (Found: C, 89·3; H, 6·0; N, 4·8. $C_{24}H_{19}N$ requires C, 89·7; H, 5·95; N, 4·4%).

2-*Phenylchrysene* (XIII).—(*a*) A solution of the amino-ethylene, m. p. 144°, (0·5 g.) in acetic acid (5 c.c.) and concentrated hydrochloric acid (3·5 c.c.) was treated at 0° with 2½% aqueous sodium nitrite (8 c.c.). (A brownish-red solution of the diazonium salt was formed, which gave a red insoluble product when a few drops of the solution were added to alkaline β-naphthol solution.) The clear diazonium solution was diluted with water (20 c.c.), and on slight warming of the resulting turbid solution a solid was gradually precipitated, which was recrystallised from slightly aqueous methanol–acetone. The product (330 mg.) was digested with a little hot aqueous alcohol, and the small insoluble fraction crystallised from a large volume of alcohol, yielding slightly discoloured leaflets of 2-*phenylchrysene*, m. p. 192—192·5° (Found: C, 94·7; H, 5·8. $C_{24}H_{16}$ requires C, 94·7; H, 5·3%).

(*b*) A solution of the diazonium salt (from 1 g. of amine) was divided into two equal parts. One portion was poured slowly (5 mins.) into excess of a slightly warm solution of sodium acetate in which was suspended 0·2 g. of copper powder. After a few minutes the precipitate was collected, washed, dried, and extracted with hot ethyl acetate–alcohol (charcoal). The filtered extract, on concentration to a small volume, deposited 0·19 g. of 2-phenylchrysene, m. p. 180—185°, which after two crystallisations from ethyl acetate formed discoloured leaflets, m. p. 192—193° alone and when mixed with the specimen described in (*a*). No other compound was isolated from the mother-liquors; an exhaustive search was not made, but it is certain that the corresponding cinnoline (*q.v.*) could not have been present in appreciable quantity.

4-*Phenyl*-3-(1′-*naphthyl*)*cinnoline* (XII, R = α-$C_{10}H_7$).—The second portion of the diazonium solution mentioned above was diluted with water (1½ vols.) and left for a few hours at room temperature. The precipitate that had gradually formed was collected, washed, and crystallised from aqueous alcohol after removal of a few mg. of insoluble material, presumably 2-phenylchrysene; one further crystallisation yielded the *cinnoline* (270 mg.) in almost pure condition, m. p. 174—176°. The same substance was also obtained from the first alcoholic filtrate from the 2-phenylchrysene described in (*a*) above; comparison of the two experiments showed that warming the diazonium solution after dilution diminished slightly the yield of cinnoline in favour of hydrocarbon. The pure cinnoline separated from aqueous alcohol in brittle yellow polyhedra, m. p. 178—179° (Found: C, 87·2; H, 4·4; N, 8·3. $C_{24}H_{16}N_2$ requires C, 86·75; H, 4·85; N, 8·4%).

Phenylbenzyl-2-*aminophenylcarbinol*.—A solution of *o*-aminobenzophenone (2 g.) in ether (60 c.c.) was added to a Grignard solution prepared from magnesium (1·1 g.), benzyl chloride (5·5 g.), and ether (30 c.c.). After being refluxed for ¾ hour, the reaction product was decomposed as already described. On concentration of the washed and dried ethereal solution, the almost pure *carbinol* rapidly crystallised (2·2 g.), and after recrystallisation from methanol formed faintly yellow, glassy prisms, m. p. 150—150·5° (Found: C, 83·0; H, 6·75; N, 5·4. $C_{20}H_{19}ON$ requires C, 83·0; H, 6·6; N, 4·8%).

α-(2-*Aminophenyl*)-αβ-*diphenylethylenes* (IX).—The above carbinol (750 mg.) was heated at 100° with 25 c.c. of aqueous sulphuric acid (20% by volume), the originally clear solution soon becoming turbid. After ¾ hour the reaction mixture was made alkaline with ammonia, and the product, which solidified on scratching, crystallised from aqueous alcohol, yielding 0·42 g. of fairly pure *amino-ethylene*; after several crystallisations the base formed clusters of cream-coloured prismatic needles, m. p. 113—114° (Found: C, 88·75; H, 6·2; N, 5·4. $C_{20}H_{17}N$ requires C, 88·5; H, 6·3; N, 5·2%).

On a larger scale, 6·7 g. of the amino-carbinol gave 2·4 g. of amino-ethylene, m. p. 113—114°. The earlier recrystallisation liquors were combined and concentrated. On standing, a further crop (2·1 g.), m. p. 85—95°, separated; after several crystallisations from methyl alcohol the isomeric *amino-ethylene* was obtained in clusters of hard short prisms, m. p. 102—104°, and 85—90° when mixed with its geometrical isomeride (Found: C, 88·35; H, 6·2; N, 5·55%).

Each of the amino-ethylenes, after being refluxed for 2 hours in alcohol and concentrated hydrochloric acid (1 : 1, 40 parts), was recovered unchanged on addition of ammonia. The hydrochloride of the amine, m. p. 113—114°, was easily soluble in alcohol; that of the isomer, m. p. 102—104°, was sparingly soluble.

3 : 4-*Diphenylcinnoline* (XII, R = Ph).—(*a*) Each of the foregoing compounds was diazotised under the conditions already described for the amino-ethylene (XI), m. p. 145°. Dilution with water caused an immediate precipitation of 3 : 4-*diphenylcinnoline*. The crude product, which was formed in virtually quantitative yield, had m. p. 148—150°, and on recrystallisation from aqueous methanol formed dense yellow rhombs, m. p. 149—150° (Found: C, 85·2; H, 5·4; N, 9·8. $C_{20}H_{14}N_2$ requires C, 85·1; H, 5·0; N, 9·9%).

(*b*) In attempts to effect cyclisation to 9-phenylphenanthrene, each of the isomers, m. p. 113° and 102°, was diazotised as rapidly as possible under the same conditions as before, and the solutions were then poured into excess of aqueous sodium acetate at *ca.* 80°, containing *ca.* 0·2 g. of copper powder in suspension. After being warmed for a few minutes, the suspensions were set aside for some hours, filtered, and extracted with chloroform–ether. The extracts, which contained no phenolic material, yielded respectively 40% and 35% of 3 : 4-diphenylcinnoline, m. p. and mixed m. p. 149—150°; no other crystalline substance could be isolated from the oily mother-liquors.

Phenyl-2-*aminophenyl*-β-*phenylethylcarbinol*.—β-Phenylethylmagnesium bromide [from 3·3 g. of magnesium, 21 c.c. of β-phenylethyl bromide (Norris, Watt, and Thomas, *J. Amer. Chem. Soc.*, 1916, **38**, 1071), and 100 c.c. of ether] and *o*-aminobenzophenone (6 g. in 160 c.c. of ether) yielded a gummy product, which was isolated by the method already described. When an ethereal solution of it was shaken with 2N-hydrochloric acid, an oily hydrochloride was thrown out, which was basified with ammonia and extracted with ether. The residue (8·9 g.) from the dried and evaporated solution crystallised on standing, and after several crystallisations from aqueous alcohol the *carbinol* (5 g.) was obtained in short prismatic needles, m. p. 97—98° to an opaque liquid which cleared at 102° (Found: C, 82·4; H, 6·8; N, 5·1. $C_{21}H_{21}ON$ requires C, 83·1; H, 7·0; N, 4·6%).

Treatment of the crude resinous product from the Grignard reaction with pyridine–acetic anhydride yielded the N-*acetyl* derivative of the carbinol, which crystallised from benzene–acetone in clusters of fine colourless needles, m. p. 168—168·5° (Found : C, 80·0; H, 6·8; N, 4·15. $C_{23}H_{23}O_2N$ requires C, 79·95; H, 6·7; N, 4·1%).

α-Phenyl-α-(2-aminophenyl)-β-benzylethylene (X).—Dehydration of the carbinol was effected with 10% sulphuric acid (20 vols.) at 100° for ¾ hour. The *amine* crystallised from aqueous alcohol in clusters of needles, m. p. 108—109° (yield, 33%) (Found : C, 88·3; H, 6·9; N, 5·1. $C_{21}H_{19}N$ requires C, 88·4; H, 6·7; N, 4·9%).

4-Phenyl-3-benzylcinnoline (XII, R = CH_2Ph).—A solution of the amino-ethylene (X) (0·5 g.) in glacial acetic acid (5 c.c.) and concentrated hydrochloric acid (4 c.c.) was diazotised with 2½% aqueous sodium nitrite at 0°. After 10 minutes, water (10 c.c.) was added, and the solution warmed to 40—50°. Unlike previous analogues, this *cinnoline* showed markedly basic properties, as it was not precipitated until the solution was made alkaline with ammonia. It formed pale yellow, prismatic needles (yield, almost quantitative), m. p. 116·5—118°, from alcohol (Found : C, 85·1; H, 5·25; N, 9·65. $C_{21}H_{16}N_2$ requires C, 85·1; H, 5·4; N, 9·5%).

Phenyl-2-aminophenylallylcarbinol (XV) *and Derivatives.*—(*a*) Allylmagnesium bromide (from 2·2 g. of magnesium, 10 c.c. of allyl bromide, and 50 c.c. of ether) and *o*-aminobenzophenone (4 g. in 90 c.c. of ether) gave a red suspension; in similar reactions, this generally indicated incomplete reaction with the amino-ketone, and addition of a further 3 c.c. of allyl bromide and 0·5 g. of magnesium produced the usual pale yellow suspension. This was worked up in the usual manner and yielded a viscous resin (5 g.), which was heated for 2 hours at 100° with 3 c.c. each of pyridine and acetic anhydride; water was then added, the product extracted with ether, and the extract was washed, first with water, and then with 2N-hydrochloric acid. Basification of the acid washings with ammonia gave an oil (3·13 g.), which was collected with ether; it crystallised almost completely from slightly aqueous alcohol, yielding the *substance* (XVI) or (XVII) as cream-coloured rods, m. p. 79—80° after several crystallisations (Found : C, 81·65, 82·1; H, 6·65, 6·7; N, 5·55, 5·6. $C_{18}H_{17}ON$ requires C, 82·1; H, 6·5; N, 5·3%).

(*b*) The original ethereal solution, from which the foregoing substance was removed with hydrochloric acid, was washed with aqueous sodium carbonate and water, dried, and evaporated. A solution of the residue in ether–ligroin deposited the N-*acetyl* derivative (0·7 g.) of the amino-carbinol (XV) in clusters of prisms, m. p. 129—130° after crystallisation from benzene–ligroin (Found : C, 76·9; H, 6·7; N, 5·2. $C_{18}H_{19}O_2N$ requires C, 76·85; H, 6·8; N, 5·0%). After being refluxed for 3 hours with 10% alcoholic potassium hydroxide, it yielded the amino-carbinol (XV), m. p. 67—69° from ether–ligroin (yield, 50%), identified by mixed m. p. with the specimen described in (*c*).

(*c*) An ethereal solution of the crude resinous carbinol from 6 g. of *o*-aminobenzophenone was shaken with 2N-hydrochloric acid, and the base, liberated from the acid washings with ammonia, was extracted with ether. A solution of it in benzene–ligroin deposited dense prisms (4·5 g.) of the *amino-carbinol*, m. p. 70—72° after recrystallisation [45—50° when mixed with the substance, m. p. 80°, described in (*a*)] (Found : C, 80·6; H, 6·75; N, 6·05. $C_{18}H_{17}ON$ requires C, 80·3; H, 7·15; N, 5·85%).

(*d*) A solution of the compound (1·2 g.), m. p. 80°, in aqueous sulphuric acid (5% by volume; 24 c.c.) was heated at 100° for ¼ hour, the originally clear solution becoming oily almost immediately. The *isomeride* was liberated by addition of ammonia, and separated from aqueous alcohol in short well-formed needles (0·8 g.), m. p. 129·5—130·5° (Found : C, 82·0; H, 6·35; N, 5·5. $C_{18}H_{17}ON$ requires C, 82·1; H, 6·5; N, 5·3%).

(*e*) A solution of the amino-carbinol (XV) (300 mg.) in 5% aqueous sulphuric acid (6 c.c.) was kept at 100° for 25 minutes, after which ammonia was added to the still clear solution, and the precipitated oil collected with ether. Benzoylation of this material in pyridine gave a resin, from which *ca.* 50 mg. of the N-*benzoyl* derivative of the amino-carbinol were isolated (needles), m. p. (after crystallisation from aqueous alcohol) 173—174° alone and mixed with an authentic specimen (m. p. 173·5—175°) (Found : C, 80·75; H, 6·0; N, 4·25. $C_{23}H_{21}O_2N$ requires C, 80·4; H, 6·15; N, 4·1%).

Condensations of 2 : 4-*Dinitrotoluene with Aldehydes.*—Freshly-distilled furfural (50 c.c.), 2 : 4-dinitrotoluene (100 g.), and piperidine (5 c.c.) were heated under an air-condenser at 120—130° (bath temp.) for 1 hour, and then at 130—140° for a further hour. The mass was digested with a mixture of equal volumes of ethyl acetate and alcohol, filtered cold, and the product crystallised from ethyl acetate, from which the *furfurylidene* compound (47 g.) separated in orange-brown prismatic needles, m. p. 135—136°, easily soluble in acetone and hot acetic acid, and almost insoluble in alcohol (Found : C, 55·5; H, 3·2; N, 11·25. $C_{12}H_8O_5N_2$ requires C, 55·4; H, 3·1; N, 10·8%). The reaction was incomplete, the crude product smelling strongly of furfural; increasing the length of time or the temperature of the reaction, however, produced considerable decomposition. On the other hand, analogous condensations with piperonal and vanillin proceeded smoothly, and yielded *products* which crystallised respectively in lustrous, brick-red, brittle prisms, m. p. 179·5—180·5°, sparingly soluble in alcohol, acetone, chloroform, acetic acid, and ethyl acetate, but easily soluble in hot *cyclo*hexanone (Found : C, 57·55; H, 3·3; N, 9·05. $C_{15}H_{10}O_6N_2$ requires C, 57·3; H, 3·2; N, 8·9%), and small scarlet prisms, m. p. 191—191·5°, moderately soluble in hot ethyl acetate (Found : C, 57·0; H, 4·1; N, 9·0. $C_{15}H_{12}O_6N_2$ requires C, 57·0; H, 3·8; N, 8·9%).

α-Nitroaminophenyl-β-(2-furyl)ethylenes (XVIII and XIX).—(*a*) The foregoing dinitrophenylfurylethylene (6 g.) was dissolved in acetic acid (90 c.c.) and treated at 95—100° with iron filings (4·5 g.), added in 10 portions during 20 minutes with frequent shaking; two additions of 10 c.c. portions of water were made at intervals of 5 and 10 minutes from the start of the experiment. Reduction was rapid, and an iron oxide sludge was formed. The solution was diluted with water (2 vols.), and the sludge and the decanted liquid extracted separately with ether. The combined extracts were washed with very dilute hydrochloric acid, sodium carbonate solution, and water, dried, and evaporated, and the residue taken up in methyl alcohol. The *nitroamine* (1·2 g.) rapidly separated in crimson needles, m. p. 130·5—131·5° after recrystallisation; it dissolved in benzene to a yellow, and in methanol to an intensely red, solution (Found : C, 62·3; H, 4·75; N, 12·6. $C_{12}H_{10}O_3N_2$ requires C, 62·6; H, 4·4; N, 12·2%). The N-*acetyl* derivative, prepared with acetic anhydride–pyridine at 100°, crystallised from aqueous acetone in sheaves of yellow silky needles, m. p. 214—215° (Found : C, 61·5; H, 4·95; N, 10·75. $C_{14}H_{12}O_4N_2$ requires C, 61·7; H, 4·45; N, 10·3%).

Diazotisation of the nitroamine was carried out under the conditions already described, but in this case the hydrochloride was insoluble in the mixed acid medium. Gradual addition of excess of aqueous sodium nitrite did not bring about solution; instead, a brown amorphous product was formed, which, after some hours, was collected, suspended in benzene–ether, and separated by means of aqueous ammonia into a small neutral fraction and a dark amorphous fraction partly soluble in alkali. The neutral ether-soluble fraction, after chromatographic purification, yielded undiazotised nitroamine (0·1 g. from 0·65 g.); the aqueous suspension, after slight concentration in presence of sodium hydroxide, was acidified, but the precipitated material could not be crystallised either from solvents or by the use of the chromatographic method.

(*b*) Hydrogen sulphide was passed for ½ hour, with shaking, into a warm suspension of the dinitro-compound (10 g.) in alcohol (150 c.c.) and concentrated aqueous ammonia (15 c.c.), and the red solution set aside overnight. It was then concentrated somewhat and filtered from inorganic matter. On evaporation to a small volume, followed by cautious addition of water, the *nitroamine* (yield, 50—55%) separated in purple-red blades or deep scarlet needles, m. p. 86—88° after recrystallisation (aqueous methanol); amorphous matter was removed if necessary by extracting the crude product with ether, in which the nitroamine is soluble (Found : C, 62·4; H, 4·75; N, 12·45. $C_{12}H_{10}O_3N_2$ requires C, 62·6; H, 4·4;

N, 12·2%). The N-*acetyl* derivative, prepared by the usual method, separated from aqueous methanol in long, brittle, orange-brown needles, m. p. 168·5—169·5° (Found : C, 61·25; H, 4·7; N, 10·35. $C_{14}H_{12}O_4N_2$ requires C, 61·7; H, 4·45; N, 10·3%).

A solution of the nitroamine in 10 parts of acetic acid gave, like its isomer, an insoluble yellow hydrochloride on addition of 6 parts of concentrated hydrochloric acid. Diazotisation yielded a soluble diazonium salt (dark red solution), which did not form a cinnoline, because the solution (i) evolved nitrogen on warming alone or with copper powder, and (ii) gave a purple precipitate and a red solution on pouring into alkaline β-naphthol and sodium phenoxide solution respectively.

Carbinols from Methylmagnesium Iodide and Chloroaminohydroxybenzophenones.—The condensations of methylmagnesium iodide with (*a*) 5-chloro-2-amino-4′-hydroxybenzophenone and (*b*) 5-chloro-2-amino-2′-hydroxy-5′-methylbenzophenone were carried out substantially as previously described (*loc. cit.*), but the products were isolated by pouring into iced ammoniacal ammonium chloride. The ethereal extracts were washed with water, dried, and evaporated, and the residues crystallised respectively from aqueous alcohol and ether–ligroin. The *carbinol* from (*a*) formed large dense prisms (4·1 g. from 6 g. of amino-ketone), m. p. 173—174° (Found : C, 63·8; H, 5·1; N, 5·6. $C_{14}H_{14}O_2NCl$ requires C, 63·7; H, 5·35; N, 5·3%). Reaction (*b*) yielded a *carbinol* (9·3 g. from 11·5 g. of amino-ketone) which separated from aqueous alcohol in small, very pale yellow prisms, m. p. 117—118·5° (Found : C, 65·65; H, 6·05; N, 5·3. $C_{15}H_{16}O_2NCl$ requires C, 64·9; H, 5·8; N, 5·0%), and 90—100° when mixed with the related ethylene (m. p. 108°). Each carbinol was dehydrated by aqueous sulphuric acid at 100° to the corresponding amino-ethylene (yields, 75% and 50% respectively).

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