665. *Internuclear Cyclisation. Part I. Modifications and Extensions of the Pschorr Reaction.*

By D. H. Hey and John M. Osbond.

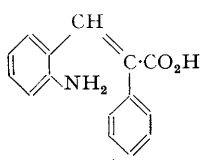
The Pschorr reaction for the synthesis of phenanthrene derivatives has been carried out satisfactorily by a number of modifications of the original procedure by the use of reactions which are known to involve the transient formation of free radicals and which have been previously used for the synthesis of diaryl derivatives. These methods, which constitute a process of homolytic cyclisation, have been extended for the first time to a case in which the internuclear bond is formed between an aromatic carbocyclic nucleus and a heterocyclic nucleus.

The Pschorr reaction (Pschorr, *Ber.*, 1896, **29**, 496) has been used extensively for the synthesis of derivatives of phenanthrene, and more recently of other polycyclic hydrocarbon systems. Pschorr's original method involves the decomposition of the diazonium salt of *o*-amino-α-phenylcinnamic acid (I) in dilute sulphuric acid solution in the presence of copper powder (cf. Gattermann, *Ber.*, 1890, **23**, 1219) at room temperature, which results in ring closure with evolution of nitrogen to give phenanthrene-9-carboxylic acid (II) in 93% yield. In later work (Pschorr and Tapper, *Ber.*, 1906, **39**, 3115; Pschorr *et al.*, *Annalen*, 1912, **391**, 23; Mayer and Balle, *ibid.*, 1914, **403**, 167) the addition of copper powder was often omitted and the diazonium salt was decomposed by warming its aqueous solution on the water-bath. Nylen (*Ber.*, 1920, **53**, 158), who used both methods, obtained an improved yield by the use of copper powder, although this was not the experience of Gulland and Virden (*J.*, 1928, 921). Sharp (*J.*, 1936, 1234), following the procedure of Pschorr and Zeidler (*Annalen*, 1910, **373**, 78), found it advantageous to carry out the diazotisation and ring closure at 50°. There have been further modifications of the original method, particularly for the synthesis of the more complex molecules where there is a tendency for the hydroxy-compound to be formed at the expense of ring closure (cf. Cook, *J.*, 1932, 1472). In one modification diazotisation is carried out in 15% alcoholic hydrochloric acid by the addition of amyl nitrite followed by the addition of copper powder (Pschorr and Quade, *Ber.*, 1906, **39**, 3113, 3119), and using these conditions

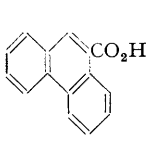
Bogert and Stamatoff (*Rec. Trav. chim.*, 1933, **52**, 584) claimed greatly improved yields. Another procedure which dispenses with copper powder involves the decomposition of the diazonium salt with sodium carbonate (Pschorr and Quade, *Ber.*, 1906, **39**, 3112, 3123), and Hill and Short (*J.*, 1937, 260) observed that the decomposition, although slow in acid solution, was rapid in an alkaline medium. Similarly, it has been shown (Pschorr, Seydel, and Stohrer, *Ber.*, 1902, **35**, 4400; Buchanan, Cook, and Loudon, *J.*, 1944, 325) that, whereas some diazonium salts are comparatively stable in boiling acid solution, ring closure can be readily effected in alkaline solution. Ruggli and Staub (*Helv. Chim. Acta*, 1937, **20**, 37) effected the ring closure of *cis-o*-aminostilbene to phenanthrene by diazotisation (*a*) in aqueous solution with subsequent addition of copper powder (61% yield), (*b*) in alcoholic solution using amyl nitrite and copper (64% yield), and (*c*) in alcoholic solution using amyl nitrite, followed by addition to aqueous sodium hypophosphite and copper (80% yield). Cassaday and Bogert (*J. Amer. Chem. Soc.*, 1939, **61**, 2461, 3058) also used the hypophosphite method but found it essential to employ dioxan as a solvent in order to achieve ring closure rather than phenol formation (cf. Fieser and Kilmer, *ibid.*, 1940, **62**, 1354; Barber and Stickings, *J.*, 1945, 167).

A review of the work of Pschorr and his collaborators, and of the subsequent modified procedures briefly outlined above, suggested that the *intramolecular* reaction which results in the formation of the phenanthrene system has many features in common with the *intermolecular* reactions used to effect the union of dissimilar aromatic nuclei (Hey *et al.*, *J.*, 1934, 1797, 1966; 1938, 108, 113, 699, 1386; 1940, 1284, etc.; Hey and Waters, *Chem. Reviews*, 1937, **21**, 169; Bachmann and Hoffman, *Org. Reactions*, 1944, **2**, 224). These methods include, among others, the decomposition in the presence of neutral aromatic solvents of (*a*) diazohydroxides (Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1924, **46**, 2339; Gomberg and Pernert, *ibid.*, 1926, **48**, 1372; etc.), (*b*) diazoacetates and nitrosoacylarylamines (Elks, Haworth, and Hey, *J.*, 1940, 1285; Grieve and Hey, *J.*, 1934, 1797; France, Heilbron, and Hey, *J.*, 1940, 369; etc.), and (*c*) 1-aryl-3 : 3-dimethyltriazens (Elks and Hey, *J.*, 1943, 441). In these reactions a free aryl radical is formed which reacts with the aromatic solvent. Mention should also be made of the decomposition of dry diazonium chlorides under certain solvents such as acetone or ethyl acetate in the presence of metals such as copper, zinc, mercury, arsenic, or silver (Waters *et al.*, *J.*, 1937, 2007; 1938, 843, 1077; 1939, 864), which reactions frequently provide a convenient source of aryl radicals and might with advantage be applied to the synthesis of phenanthrene derivatives. By means of the above reactions it is also possible, as a consequence of their homolytic character, to prepare aryl-substituted heterocyclic compounds such as aryl-pyridines (Heilbron, Hey, *et al.*, *J.*, 1940, 349, 355, 358, 372, 1279; 1943, 441), -thiophens (Gomberg and Bachmann, *loc. cit.*), -pyrroles (Rinkes, *Rec. Trav. chim.*, 1943, **62**, 116), and -furans (Johnson, *J.*, 1946, 895). The similarity between the Pschorr reaction and the Gomberg reaction has been commented on by Waters (*J.*, 1942, 266; "The Chemistry of Free Radicals," Oxford, 1946, p. 165) and more recently by Schetty (*Helv. Chim. Acta*, 1949, **32**, 24), who has adapted the Pschorr procedure to the preparation of sultones from aryl esters of aniline-*o*-sulphonic acid. An investigation has therefore been initiated into the application of the above reactions to the synthesis of phenanthrene derivatives with particular reference to those cases in which the normal Pschorr reaction gives unsatisfactory results, and to the possible extension of the reaction to include the synthesis of heterocyclic systems.

In the first instance a study was made of the application of the above reactions to *o*-amino-α-phenylcinnamic acid (I), which is known to give phenanthrene-9-carboxylic acid (II) in good yield by the normal Pschorr procedure. Acetylation at room temperature of the acid (I) gave the *acetamido-acid*, whereas acetylation with acetic anhydride at higher temperatures gave 3-phenylcarbostyril (cf. Pschorr, *Ber.*, 1898,



(I.)



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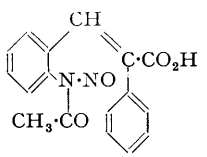

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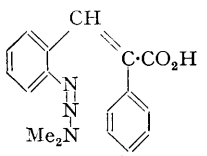
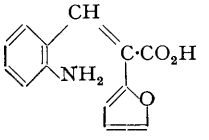


(IV.)

31, 1294). *o*-Nitrosoacetamido-α-phenylcinnamic acid (III) was obtained from the acetyl derivative by treatment with nitrosyl chloride (cf. France, Heilbron, and Hey, *loc. cit.*). 1-*o*-(2-*Carboxy*-2-*phenylvinyl*)*phenyl*-3 : 3-*dimethyltriazen* (IV) was prepared by the method of Elks and Hey (*loc. cit.*) by the addition of an aqueous solution of diazotised *o*-amino-α-phenyl-

cinnamic acid to an alkaline solution of dimethylamine. The preparation of phenanthrene-9-carboxylic acid (II) was then carried out by six methods. The decomposition of the diazonium chloride prepared from *o*-amino-α-phenylcinnamic acid with copper bronze in aqueous solution afforded the acid (II) in 40% yield, whereas with Gattermann's copper powder Pschorr (*Ber.*, 1896, **29**, 496) reported a yield of 93%. On the other hand, decomposition of the dry diazonium chloride under acetone in the presence of copper gave phenanthrene-9-carboxylic acid in 81% yield. For this reaction the diazonium chloride was prepared by the addition of amyl nitrite to an alcoholic hydrogen chloride solution of *o*-amino-α-phenylcinnamic acid, and was sparingly soluble in alcohol and completely precipitated with dry ether. The resulting diazonium salt was kept under AnalaR acetone at room temperature, and appeared to be stable until a trace of copper powder was added, whereupon a vigorous reaction immediately started with evolution of nitrogen and separation of the pure white crystalline acid (II). The reaction was complete in less than a minute, whereas in the normal Pschorr procedure at room temperature it usually takes several hours for completion. In the third modification the aqueous diazonium chloride solution prepared from *o*-amino-α-phenylcinnamic acid was neutralised by the slow addition of an equivalent quantity of aqueous sodium hydroxide with stirring at 0°, which gave phenanthrene-9-carboxylic acid in 75% yield. When an aqueous solution of sodium acetate was added to the diazonium chloride solution in place of the sodium hydroxide, little reaction occurred in the cold, but at room temperature after several hours' stirring phenanthrene-9-carboxylic acid was obtained in 56% yield. Further, when *o*-nitrosoacetamido-α-phenylcinnamic acid (III) was dissolved in warm benzene, nitrogen was evolved and phenanthrene-9-carboxylic acid was afforded in 43% yield. This nitroso-derivative was found to be comparatively stable and it was necessary to boil the solution to ensure completion of the reaction. In boiling ether solution the nitroso-compound (III) decomposed at a slower rate and phenanthrene-9-carboxylic acid was isolated in 37% yield. In the sixth method, dry hydrogen chloride was passed into a boiling solution of the triazen (IV) in benzene, and phenanthrene-9-carboxylic acid was obtained in 58% yield together with some *o-chloro-α-phenylcinnamic acid*. For purposes of comparison the latter acid was prepared by condensation of *o*-chlorobenzaldehyde with sodium phenylacetate in the presence of acetic anhydride and zinc chloride.

As a result of the successful application of the above methods to the preparation of phenanthrene-9-carboxylic acid from *o*-amino-α-phenylcinnamic acid, it seemed possible that the same methods might be applicable to the synthesis of certain heterocylic systems in which the final ring closure involves a pyridine ring. Although several heterocyclic compounds containing nitrogen have been prepared by the Pschorr reaction in the aporphine group (cf. Gadamer, Oberlin, and Schoeler, *Arch. Pharm.*, 1925, **263**, 81; Haworth, Perkin, and Rankin, *J.*, 1925, 2018 etc.), the final ring closure involved in each case two aromatic carbocyclic nuclei. An attempt was made by Amstutz and Spitzmuller (*J. Amer. Chem. Soc.*, 1943, **65**, 367) to effect ring closure in *cis-o*-amino-α-(2-furyl)cinnamic acid (V) by means of the Pschorr procedure or one of its modifications, but only phenolic substances were isolated from the product.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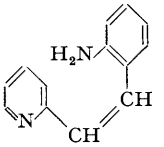
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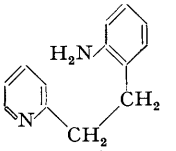
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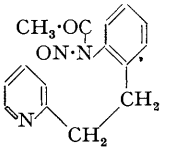
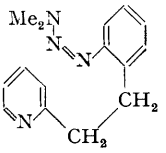

(VIII.)

A preliminary attempt was made to bring about a ring closure of 2-(2-aminostyryl)pyridine (VI) to 5 : 6-benzoquinoline (X), but this was unsuccessful owing to the *trans*-configuration of the molecule (cf. Rath and Lehmann, *Ber.*, 1925, **58**, 342) determined initially by the high temperature required for the condensation of *o*-nitrobenzaldehyde and α-picoline. This amine was also used by Simpson (*J.*, 1946, 673) in the Widman–Stoermer reaction, but no appreciable tendency to any well-defined ring-closure was observed. As was shown by Ruggli *et al.* (*Helv. Chim. Acta*, 1936, **19**, 1288; 1937, **20**, 37; 1941, **24**, 173), the success of the Pschorr reaction is dependent on the utilisation of the appropriate *cis*-form of the substituted ethylene employed. Fortunately, in the condensation between a substituted *o*-nitrobenzaldehyde and phenylacetic acid, the *cis*-isomer is preferentially formed owing to the influence of the carboxyl group, although mixtures of *cis*- and *trans*-acids are sometimes obtained (Amstutz and Spitzmuller,

loc. cit.; Buchanan, Cook, and Loudon, *loc. cit.*). For these reasons it was therefore not surprising that the only product obtained from the application of the Pschorr procedure to 2-(2-aminostyryl)pyridine (VI) in dilute hydrochloric acid was 2-(2-chlorostyryl)pyridine, isolated as the *picrate*. An authentic specimen of this pyridine was prepared by condensation of *o*-chlorobenzaldehyde with α-picoline in acetic anhydride (cf. Simpson, *loc. cit.*). Similarly, decomposition of the 3 : 3-dimethyltriazen derived from 2-(2-aminostyryl)pyridine (VI) also gave on decomposition with hydrogen chloride in benzene solution 2-(2-chlorostyryl)pyridine. Acetylation of 2-(2-aminostyryl)pyridine gave a diacetyl derivative, and attempts to prepare a nitroso-derivative from this were unsuccessful.

In order to overcome the difficulty arising from the geometrical isomerism of the styrylpyridine, 2-(2-*o*-aminophenylethyl)pyridine (VII) was prepared by reduction of 2-nitrostilbazole (Shaw and Wagstaff, *J.*, 1933, 79) or its alkine with phosphorus and hydrogen iodide, and when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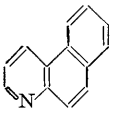
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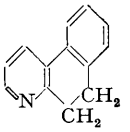
(XI.)

this base was submitted to the normal Pschorr procedure in dilute acid solution with use of copper powder a small yield of 5 : 6-benzoquinoline (X), isolated as the picrate, was obtained. The intermediate 7 : 8-*dihydro*-5 : 6-*benzoquinoline* (XI) had presumably been oxidised by the excess of nitrous acid present to give (X).

In a second reaction with 2-2′-*o*-aminophenylethylpyridine, dioxan containing sulphuric acid was used as the solvent and diazotisation was attempted with amyl nitrite (cf. Cassaday and Bogert, *loc. cit.*). The diazotisation, however, proceeded only in the presence of a small quantity of water, and the resulting diazonium chloride solution was decomposed by the addition of copper powder with subsequent warming. From this reaction three products were isolated, namely, 7 : 8-dihydro-5 : 6-benzoquinoline (XI) and 2-2′-phenylethylpyridine as picrates in small yield, together with 2-(2′-*o*-hydroxyphenylethyl)pyridine as the major product. As far as the authors are aware, these two reactions provide the first known examples of the application of a Pschorr-type reaction to a case in which the final ring-closure is effected on to a pyridine nucleus. In the latter reaction it is suggested that 7 : 8-dihydro-5 : 6-benzoquinoline and 2-2′-phenylethylpyridine result from the decomposition of the covalent diazonium chloride to a free aryl radical with elimination of nitrogen, and that the radical then reacts either intramolecularly with the pyridine nucleus in close proximity or intermolecularly with the solvent molecules from which it abstracts a hydrogen atom. It is not surprising that low yields of the benzoquinoline were obtained in these reactions, because Ruggli and Staub (*loc. cit.*) in an analogous reaction with carbocyclic nuclei obtained only a trace of 9 : 10-dihydrophenanthrene from *o*-2′-phenylethylaniline, although better yields were obtained in alcoholic solution. In an attempt to increase the yields of the benzoquinoline in these reactions, recourse was made to the use of 2-(2-*o*-nitrosoacetamidophenylethyl)pyridine (VIII) which was obtained by the action of nitrosyl chloride on either the *acetyl* or the *diacetyl* derivative of 2-(2-*o*-aminophenylethyl)pyridine (VII). 2-(2-*o*-Nitrosoacetamidophenylethyl)pyridine (VIII) decomposed in solution in benzene with evolution of nitrogen to give 7 : 8-dihydro-5 : 6-benzoquinoline (XI) in 41% yield as a pale yellow oil together with a small amount of 2-(2-*o*-acetamidophenylethyl)-pyridine, characterised by its *picrate* and by hydrolysis to the base (VII). By heating the dihydrobenzoquinoline (XI) with selenium at 300°, 5 : 6-benzoquinoline (X) was obtained, identical with an authentic specimen.

The preparation of a nitrosoacylarylamine by the action of nitrosyl chloride on the diacetyl derivative of an amine had not been previously reported, but the general character of the reaction was confirmed by showing that nitrosation of *NN*-diacetylaniline under similar conditions proceeded in a similar manner, and acetanilide and diphenyl were isolated from the decomposition of the product in benzene solution.

The triazen (IX) was prepared as a pale yellow oil by the addition of the diazonium chloride solution prepared from 2-(2-*o*-aminophenylethyl)pyridine (VII) to an alkaline solution of dimethylamine (cf. Elks and Hey, *loc. cit.*). The triazen was decomposed in solution in benzene with dry hydrogen chloride to give in 58% yield 2-(2-*o*-chlorophenylethyl)pyridine, characterised as the *picrate*. The presence of 5 : 6-benzoquinoline was not detected in the products of this

reaction, or in those from the action of aqueous sodium hydroxide on the diazonium sulphate prepared from 2-(2-*o*-aminophenylethyl)pyridine. The only product isolated from the latter reaction was 2-(2-*o*-hydroxyphenylethyl)pyridine, which was obtained in 40% yield.

Experimental.

o-Amino-α-phenylcinnamic Acid (I).—Hydrogen sulphide was passed into a solution of *o*-nitro-α-phenylcinnamic acid (8 g.) in aqueous ammonia (40 c.c., *d* 0·88) and water (80 c.c.) for 6 hours at 0°. The reaction mixture was then heated until the excess of ammonia and hydrogen sulphide had been expelled, and the sulphur which had been deposited was filtered off. The filtrate was made just acid with dilute acetic acid, and the yellow precipitate was dissolved in boiling dilute hydrochloric acid and the solution filtered hot. The filtrate was made just alkaline with dilute ammonia and re-acidification with dilute acetic gave the pure amino-acid, which crystallised from toluene in yellow rod-like needles (7·17 g.), m. p. 184—185°. Pschorr (*Ber.*, 1896, **29**, 496) gives m. p. 185—186°.

Action of Acetic Anhydride on o-Amino-α-phenylcinnamic Acid.—(*a*) The amino-acid (2 g.) was boiled under reflux with acetic anhydride (20 c.c.) and concentrated sulphuric acid (2 drops) for 2 hours. The reaction mixture was poured on ice and water (200 c.c.) and the oil, which separated, solidified. 3-Phenylcarbostyril separated from alcohol in colourless needles (1·3 g.), m. p. 228°. Wislicenus and Erbe (*Annalen*, 1920, **421**, 147) give m. p. 227—228°; Pschorr (*Ber.*, 1898, **31**, 1294) gives m. p. 234° (corr.). (*b*) The amino-acid (3 g.) was added to glacial acetic acid (40 c.c.), acetic anhydride (15 c.c.), and concentrated sulphuric acid (2 drops), and the solution was left at room temperature for 3 hours. The reaction mixture was poured into water (400 c.c.) and cooled to 0°. *o-Acetamido-α-phenylcinnamic acid* was collected and crystallised from aqueous alcohol in colourless plates (2·89 g.), m. p. 225—226° (Found: C, 72·9; H, 5·3. $C_{17}H_{15}O_3N$ requires C, 72·6; H, 5·4%). A mixed m. p. with 3-phenylcarbostyril gave a marked depression to 185—187°.

o-Nitrosoacetamido-α-phenylcinnamic Acid (III) (cf. France, Heilbron, and Hey, *loc. cit.*).—A mixture of *o*-acetamido-α-phenylcinnamic acid (5 g.), freshly fused potassium acetate (5 g.), phosphoric oxide (0·5 g.), glacial acetic acid (35 c.c.), and acetic anhydride (15 c.c.) was cooled to 0° and nitrosyl chloride (3·44 g.) dissolved in glacial acetic acid (6·88 g.) was added dropwise with stirring. After the addition the solution, which had become orange in colour, was stirred for a further 30 minutes and was filtered from a small amount of unchanged acetamido-acid. The filtrate was added to ice-cold water (400 c.c.) in portions with stirring. The nitroso-compound separated as a yellowish-white precipitate which tended to coagulate to a gum. It was collected and dried over concentrated sulphuric acid at 0°. The yellow, dry, brittle mass was extracted with cold dry ether and a small amount of insoluble *o*-acetamido-α-phenylcinnamic acid (0·16 g.) was separated. Evaporation of the ethereal extract at room temperature under reduced pressure gave *o*-nitrosoacetamido-α-phenylcinnamic acid as a yellow amorphous solid (4·47 g.), m. p. 89° (decomp.). When heated on a spatula in a bare flame it gave the characteristic "flash" of nitroso-derivatives of this type.

1-*o*-(2-*Carboxy*-2-*phenylvinyl*)*phenyl*-3 : 3-*dimethyltriazen* (IV) (cf. Elks and Hey, *loc. cit.*).—*o*-Amino-α-phenylcinnamic acid (4·8 g.) was dissolved in concentrated hydrochloric acid (6·6 g.) and water (40 c.c.) by warming. After being cooled to 0°, the suspended hydrochloride was diazotised by the addition of sodium nitrite (1·4 g.) in water (15 c.c.). A further quantity of water (125 c.c.) was then added to dissolve the sparingly soluble diazonium chloride, which separated in yellow needles. The filtered diazonium solution was added dropwise at 0°, with stirring, to a solution of sodium carbonate (13·4 g.) in water (100 c.c.) and aqueous dimethylamine (3·2 g., 33%) cooled to 0°. White silky needles soon separated, and after the addition the reaction mixture was stirred at room temperature for a further half hour. The mixture was acidified by the addition of glacial acetic acid and the 1-*o*-(2-*carboxy*-2-*phenylvinyl*)*phenyl*-3 : 3-*dimethyltriazen* was collected; it crystallised from benzene–light petroleum (b. p. 60—80°) in colourless needles (4·75 g.), m. p. 154—155° (decomp.) (Found: C, 69·3; H, 5·8. $C_{17}H_{17}O_2N_3$ requires C, 69·1; H, 5·8%).

Phenanthrene-9-carboxylic Acid (II).—This was prepared by the following six methods: (*a*) *o*-Amino-phenylcinnamic acid (1·45 g.) was dissolved in concentrated hydrochloric acid (3·3 g.) and water (100 c.c.) by warming. The solution was cooled to 0° and a solution of sodium nitrite (0·7 g.) in water (10 c.c.) was added dropwise. When copper bronze (1 g.) was added to the diazonium solution, nitrogen was evolved, and after an hour the solution was warmed on the water-bath to complete the reaction, as shown by a negative coupling reaction with alkaline β-naphthol. The white solid which had separated was collected, dissolved in dilute ammonia solution, and filtered to remove copper bronze. Acidification of the alkaline filtrate gave phenanthrene-9-carboxylic acid, which separated from glacial acetic acid in colourless needles (0·53 g., 40%), m. p. 250—252°. Using copper powder, Pschorr (*Ber.*, 1896, **29**, 496) records a yield of 93%, which has been corroborated by Hey and Mulley (unpublished work).

(*b*) *o*-Amino-α-phenylcinnamic acid (4·8 g.) was diazotised, as described above, in a mixture of concentrated hydrochloric acid (7·6 c.c.) and water (60 c.c.) by the addition at 0° of sodium nitrite (1·5 g.) in water (17 c.c.). Aqueous sodium hydroxide (10%) was added dropwise to the filtered diazonium solution with stirring at 0° until the solution was neutral to litmus. After the first few drops of alkali had been added, nitrogen was evolved briskly and the reddish-brown solution was stirred overnight at room temperature. The filtered solution was acidified, and the white precipitate (4·5 g.) collected. Crystallisation from glacial acetic acid gave phenanthrene-9-carboxylic acid (3·3 g., 75%), m. p. 246—249°.

(*c*) *o*-Amino-α-phenylcinnamic acid (2·4 g.) was diazotised, as described above, in a mixture of concentrated hydrochloric acid (4 c.c.) and water (30 c.c.) at 0° by the addition of sodium nitrite (0·8 g.) in water (10 c.c.). An equivalent amount of sodium acetate in water (50 c.c.) was added dropwise at 0° to the filtered diazonium chloride solution with vigorous stirring. The yellow solution became deeper in colour, and no evolution of nitrogen was observed during 3 hours at 0°, but when the solution was allowed to come to room temperature gassing occurred. The solution was stirred at room temperature

for 24 hours, nitrogen being slowly evolved. The brown insoluble material was collected (1·65 g.), and crystallisation from aqueous acetic acid gave phenanthrene-9-carboxylic acid (1·25 g., 56%), m. p. 246—250°. A mixed m. p. with an authentic specimen showed no depression.

(*d*) *o*-Amino-α-phenylcinnamic acid (4·8 g.) was dissolved in ethyl alcohol (25 c.c.) with warming. Dry hydrogen chloride was then passed into the solution until the hydrochloride of the base was precipitated. The resulting suspension was cooled to 0° and *iso*amyl nitrite (3·5 c.c.) was added dropwise with shaking. The yellow diazonium salt which formed was sparingly soluble in alcohol, and after it had stood for ½ hour dry ether (200 c.c.) was added to ensure complete precipitation of the diazonium salt, which was filtered on a sintered-glass crucible and washed well with AnalaR acetone (3 × 100 c.c.), care being taken to keep the solid covered by the solvent. The diazonium salt was then transferred to a conical flask and AnalaR acetone (100 c.c.) was added at room temperature. No reaction occurred until a small amount of copper powder was added, whereupon an immediate reaction commenced, which became very vigorous with evolution of nitrogen. The reaction was complete in one minute and a crystalline solid separated (2·8 g.), m. p. 250—251°. From the mother-liquor a further crop was obtained (1·15 g.), m. p. 246—248°. Crystallisation from glacial acetic acid gave the pure phenanthrene-9-carboxylic acid (3·65 g., 81%), m. p. 252—253°, which separated in stout needles or colourless feathery needles. A mixed m. p. with an authentic specimen showed no depression. When this experiment was repeated with *cyclo*hexane in place of acetone as the solvent, no reaction occurred when copper powder was added (cf. Makin and Waters, *J.*, 1938, 843). Decomposition, however, took place when the mixture was warmed on the water-bath, to give phenanthrene-9-carboxylic acid.

(*e*) (i) A solution of *o*-nitrosoacetamido-α-phenylcinnamic acid (4·47 g.) in sodium-dried benzene (100 c.c.) was left at room temperature for several hours, but no decomposition appeared to take place. When the yellowish-orange solution was warmed gently to 50° on the water-bath nitrogen was evolved slowly. The rate of decomposition became brisk, however, only at 60°, and the solution was finally boiled under reflux for 4 hours to ensure complete decomposition. After 15 minutes' heating a solid began to crystallise on the side of the flask, and on cooling some whitish-cream material separated in a crystalline form. The cold mixture was shaken with dilute aqueous ammonia, and the crystalline material dissolved into the alkaline layer. Acidification of the alkaline extract precipitated a white solid (2·45 g.), m. p. 230—250°, and crystallisation from glacial acetic acid gave phenanthrene-9-carboxylic acid (1·4 g., 43·4%), m. p. 249—251°. A mixed m. p. with an authentic specimen showed no depression. From the benzene extract a reddish-brown gum (0·3 g.) was obtained, from which a white solid (0·05 g.), m. p. 120—130°, was isolated but not identified. (ii) A solution of *o*-nitrosoacetamido-α-phenylcinnamic acid (2 g.) in sodium-dried ether (100 c.c.) was boiled under reflux for 2 hours. The yellow solution gradually became orange in colour and nitrogen was evolved. After 15 minutes the solution became cloudy and a crystalline solid separated on the side of the flask. The solid (0·56 g.) was collected, and after two crystallisations from acetic acid phenanthrene-9-carboxylic acid (0·1 g.), m. p. 249°, was obtained. The ethereal filtrate was extracted with dilute ammonia solution, which gave on acidification a further quantity of the acid. After crystallisation from acetic acid of the combined fractions phenanthrene-9-carboxylic acid (0·52 g., 37%), m. p. 250—251°, was obtained.

(*f*) 1-*o*-(2-Carboxy-2-phenylvinyl)phenyl-3 : 3-dimethyltriazen (4·45 g.) was dissolved in sodium-dried benzene (100 c.c.) by warming, and when the solution was boiling steadily under reflux a stream of dry hydrogen chloride was passed through it for ½ hour. Nitrogen was evolved and dimethylamine hydrochloride separated from the solution, which became dark red. The reaction mixture was extracted first with warm water to remove the dimethylamine hydrochloride and then with dilute ammonia solution. The solid, which was obtained on acidification of the alkaline extract, was crystallised from glacial acetic acid and gave phenanthrene-9-carboxylic acid (1·95 g., 58%), m. p. 247—250°. A mixed m. p. with an authentic specimen showed no depression. Concentration of the acetic acid mother-liquor gave a second compound, which after crystallisation from aqueous alcohol gave *o-chloro-α-phenylcinnamic acid* (0·35 g., 9%) in long colourless needles, m. p. 172° (Found : C, 69·2; H, 4·15. $C_{15}H_{11}O_2Cl$ requires C, 69·6; H, 4·3%). A mixed m. p. with an authentic specimen, prepared as described below, showed no depression.

o-Chloro-α-phenylcinnamic Acid.—A mixture of *o*-chlorobenzaldehyde (3·5 g.) and sodium phenylacetate (4 g.) was heated with acetic anhydride (50 c.c.) in an oil-bath at 130—150° for 8 hours. When cold, the reaction mixture was poured into water (400 c.c.) with stirring, and the mixture was warmed until the acetic anhydride had decomposed. The product was extracted with ether and shaken with dilute aqueous ammonia. Acidification of the ammoniacal extract deposited a white precipitate. Crystallisation from aqueous alcohol gave *o*-chloro-α-phenylcinnamic acid in colourless needles, m. p. 170—171°.

Action of Copper Powder on the Diazonium Solution prepared from the Dihydrochloride of 2-(2-Aminostyryl)pyridine (VI).—A solution of 2-(2-aminostyryl)pyridine dihydrochloride (5·2 g.) (Simpson, *loc. cit.*) in concentrated hydrochloric acid (2 c.c.) and water (25 c.c.) was diazotised by the addition at 0° of a solution of sodium nitrite (1·7 g.) in water (10 c.c.). To the filtered diazonium chloride solution, copper powder (5 g.) was added, and immediate decomposition occurred with evolution of nitrogen and the formation of a thick yellowish foam. The mixture was shaken at room temperature for 3 hours, after which the solution no longer gave a red precipitate with alkaline β-naphthol. The reaction mixture was warmed on the water-bath, and the solid material dissolved, leaving the copper powder, which was filtered off. The filtrate was made alkaline and the mixture was extracted with ether. After filtration from some insoluble material the ether was evaporated and the residual red gum (0·6 g.) was converted into a *picrate*, which separated from alcohol in yellow plates, m. p. 205—206°, both alone and on admixture with 2-(2-chlorostyryl)pyridine picrate, prepared as described below (Found : C, 51·0; H, 2·6. $C_{13}H_{10}NCl,C_6H_3O_7N_3$ requires C, 51·3; H, 2·9%).

2-(2-*Chlorostyryl*)*pyridine.*—*o*-Chlorobenzaldehyde (5·6 g.) and α-picoline (3·72 g.) were heated with acetic anhydride (5 g.) for 9 hours in an oil bath at 155—160°. The mixture was distilled with steam to remove unchanged material and the residue was made alkaline by addition of 10% aqueous sodium hydroxide. The solid which separated crystallised from aqueous ammoniacal alcohol to give 2-(2-chlorostyryl)pyridine (5 g.), m. p. 75—77°. Simpson (*loc. cit.*) gives m. p. 77—78°. The picrate of this base separated from alcohol in yellow plates, m. p. 205—206°.

1-o-(2-2′-*Pyridylvinyl*)*phenyl*-3 : 3-*dimethyltriazen* (cf. Elks and Hey, *loc. cit.*).—A solution of 2-(2-aminostyryl)pyridine (4·9 g.) in water (40 c.c.) and concentrated hydrochloric acid (11 c.c.) was diazotised at 0° by the addition of a solution of sodium nitrite (1·75 g.) in water (10 c.c.). The diazonium solution was added dropwise with stirring to a mixture of aqueous dimethylamine (4 g., 33% solution) and aqueous sodium carbonate (15 g., in 150 c.c.). A red gum separated, and after a further ½ hour's stirring the mixture was extracted with ether. The ethereal extract afforded on distillation the triazen (4 g.), b. p. 220°/3·2 mm., as a red glass, which could not be induced to crystallise. A small portion when dissolved in hydrochloric acid gave a red precipitate with alkaline β-naphthol.

Decomposition of 1-o-(2-2′-*Pyridylvinyl*)*phenyl*-3 : 3-*dimethyltriazen in Benzene*.—Dry hydrogen chloride was passed into a solution of the triazen (4 g.) in dry benzene (75 c.c.) maintained at the boil under reflux. Decomposition began at once and a red oily tar was deposited. After ½ hour the mixture was washed with aqueous sodium hydroxide, and the benzene extract was dried. Distillation of the solvent left a red glass (3·25 g.), which on treatment with alcoholic picric acid (3·5 g.) gave three picrates. The major product was 2-(2-chlorostyryl)pyridine picrate, m. p. and mixed m. p. 204—205°. The other two picrates, which separated in long red needles, m. p. 190—192°, and in yellowish-orange needles, m. p. 182—185°, were not identified.

2-(2-*Hydroxy*-2-o-*nitrophenylethyl*)*pyridine* (cf. Shaw and Wagstaff, *loc. cit.*).—A mixture of *o*-nitrobenzaldehyde (7·5 g.) and α-picoline (4·6 g.) was boiled under reflux with water (3·6 c.c.) and glacial acetic acid (1 c.c.) for 30 hours. The reaction mixture was made alkaline and the precipitated alkine was collected and washed with water. Crystallisation from alcohol gave 2-(2-hydroxy-2-*o*-nitrophenylethyl)pyridine in colourless crystals (4·3 g.), m. p. 137°. Roth (*Ber.*, 1900, **33**, 3476) gives m. p. 137—138°.

2-(2-o-*Aminophenylethyl*)*pyridine* (VII).—This was prepared from *o*-nitrostilbazole by the method of Shaw and Wagstaff (*loc. cit.*) or by reduction of the above alkine. 2-(2-Hydroxy-2-*o*-nitrophenylethyl)-pyridine (4·1 g.) was heated with red phosphorus (2·5 g.) and hydriodic acid (22 c.c.; *d* 1·7) for 5 hours in an oil-bath at 160°. The filtered solution was made alkaline and extracted with ether, which on evaporation yielded a yellow solid. Crystallisation from light petroleum (b. p. 40—60°) gave 2-(2-*o*-aminophenylethyl)pyridine (1·5 g.) in long colourless needles, m. p. 58—60°.

Acetylation of 2-(2-o-*Aminophenylethyl*)*pyridine*.—(*a*) A solution of the above amine (0·5 g.) in acetic anhydride (2 c.c.) was kept at room temperature for 2 hours. Water was added, and the solution made alkaline with aqueous sodium carbonate. The acetyl derivative, which was extracted with ether, crystallised from light petroleum (b. p. 40—60°) in transparent flat cubes, m. p. 62—67°. Further crystallisation from the same solvent raised the m. p. to 66—68° when the crystals were air-dried, but when dried *in vacuo* over concentrated sulphuric acid the solid tended to collapse, soften, and become brittle and then had m. p. 60—62°. A correct analysis of the base could not be obtained, but the *picrate* separated from alcohol in yellow needles, m. p. 159—160° (Found: C, 54·1; H, 4·2. $C_{15}H_{16}ON_2,C_6H_3O_7N_3$ requires C, 53·7; H, 4·1%). (*b*) A solution of 2-(2-*o*-aminophenylethyl)-pyridine in acetic anhydride (10 c.c.) was boiled under reflux for 12 hours. The solution was poured into water, made alkaline with aqueous sodium carbonate, and extracted with ether. Removal of the ether gave 2-(2-o-*diacetylaminophenylethyl*)*pyridine*, which separated from light petroleum (b. p. 40—60°) in colourless needles, m. p. 45° (Found: C, 72·6; H, 6·2. $C_{17}H_{18}O_2N_2$ requires C, 72·6; H, 6·1%). The *picrate* separated from alcohol in yellow needles, m. p. 170—171° (Found: C, 54·2; H, 4·1. $C_{17}H_{18}O_2N_2,C_6H_3O_7N_3$ requires C, 54·0; H, 4·1%).

Action of Copper Powder on the Diazonium Sulphate prepared from 2-(2-o-*Aminophenylethyl*)*pyridine* (VII).—(*a*) A warm solution of the amine (5 g.) in a mixture of concentrated sulphuric acid (3·5 c.c.) and water (40 c.c.) was cooled to 0° and the suspended sulphate was diazotised by addition of a solution of sodium nitrite (2 g.) in water (20 c.c.). When copper powder (5 g.) was added a vigorous reaction ensued. After ¾ hour the solution was made alkaline by addition of aqueous sodium hydroxide (10%) and extracted with ether. This extract afforded a red gum (0·6 g.), which was treated with alcoholic picric acid. A small amount of picrate was finally obtained in yellow needles, m. p. 249—250°, by repeated crystallisation from benzene. A mixed m. p. with 5 : 6-benzoquinoline picrate (m. p. 251—252°) gave no depression. (*b*) A mixture of concentrated sulphuric acid (8 c.c.) and water (10 c.c.) was added to a solution of the amine (5·9 g.) in dioxan (50 c.c.). *iso*Amyl nitrite (5 g.) was added to the stirred suspension of the sulphate at 25—30° and the mixture was stirred for 2 hours with the addition of water (20 c.c.) to facilitate diazotisation. Some unchanged amine sulphate was removed by filtration and copper powder (5 g.) was added to the thick red filtrate. Nitrogen was evolved and the reaction was completed by warming on the water-bath for 15 minutes. The reaction mixture was made alkaline by addition of aqueous sodium carbonate and extracted with ether. After distillation of the ether, dioxan, and amyl alcohol, a red oil remained, which on distillation gave two main fractions: (i) a pale yellow oil, b. p. 90—120°/10^{-2} mm. (0·4 g.), and (ii) a thick yellow oil, b. p. 130—150°/10^{-2} mm. (1·5 g.). Picric acid (0·5 g.) in alcohol was added to the first fraction, and a mixture of two picrates separated which was purified by fractional crystallisation from alcohol. The two picrates were obtained in approximately equal quantities. The *picrate* of 7 : 8-dihydro-5 : 6-benzoquinoline separated from alcohol in yellow needles, m. p. 204—205° (Found: C, 55·85; H, 3·3. $C_{13}H_{11}N,C_6H_3O_7N_3$ requires C, 55·6; H, 3·4%). The second picrate, which separated from benzene–light petroleum (b. p. 60—80°) in yellow plates, m. p. 125—125·5°, was considered to be 2-2′-phenylethylpyridine picrate (Found: C, 55·0; H, 4·0. Calc. for $C_{13}H_{13}N,C_6H_3O_7N_3$: C, 55·4; H, 3·9%). Bergstrom, Norton, and Seibert (*J. Org. Chem.*, 1945, **10**, 454) give m. p. 125·5—127° for this picrate. The second fraction solidified when scratched with light petroleum (b. p. 40—60°) and crystallisation from light petroleum (b. p. 60—80°) gave 2-(2-*o*-hydroxyphenylethyl)pyridine in colourless needles, m. p. 91—92° (Found: C, 78·4; H, 6·7. Calc. for $C_{13}H_{13}ON$: C, 78·35; H, 6·6%). Chiang and Hartung (*J. Org. Chem.*, 1945, **10**, 21) give m. p. 92—93° for this compound. The *picrate* separated from benzene in needles, m. p. 147—148° (Found: C, 53·5; H, 3·9. $C_{13}H_{13}ON,C_6H_3O_7N_3$ requires C, 53·3; H, 3·8%).

Conversion of 2-(2-o-*Nitrosoacetamidophenylethyl*)*pyridine into* 7 : 8-*Dihydro*-5 : 6-*benzoquinoline* (XI).—(*a*) A solution of nitrosyl chloride (0·65 g.) in acetic anhydride (2·4 c.c.) was added at 0° dropwise to a

stirred mixture of 2-(2-*o*-acetamidophenylethyl)pyridine (1·2 g.) in acetic acid (15 c.c.) and acetic anhydride (5 c.c.) containing freshly fused potassium acetate (1·2 g.) and phosphoric oxide (0·5 g.). After 10 minutes the mixture was poured into ice-water, and the solution made alkaline by addition of aqueous sodium carbonate. The solution was extracted with ether, and the extract dried (Na_2SO_4). The red gum obtained on removal of the solvent was dissolved in benzene and warmed on the water-bath for 2 hours, after which the benzene was removed under reduced pressure. The residual gum (0·47 g.), which could not be induced to crystallise, was dissolved in benzene and added to picric acid (0·5 g.) in benzene. The resulting picrate was purified by further crystallisation and 7 : 8-dihydro-5 : 6-benzoquinoline picrate separated in long yellow needles; m. p. and mixed m. p. with the product prepared above, 205—206°. (*b*) 2-(2-*o*-Aminophenylethyl)pyridine (6 g.) was heated with acetic anhydride (20 c.c.) for 15 hours on a boiling water-bath. The diacetyl derivative, which formed, was not isolated, but fused potassium acetate (8 g.) and phosphoric oxide (1 g.) were added directly to the solution at 0°, followed by a nitrosyl chloride solution (16 c.c. of 25% w/v in acetic anhydride) added dropwise with stirring. The reaction mixture was kept for ½ hour and was then poured on a suspension of sodium carbonate (60 g., anhydrous) in crushed ice and water (100 g.) with vigorous stirring. The solution was extracted with benzene (350 c.c.), which was subsequently shaken with aqueous sodium carbonate solution. The dried benzene extract was heated under reflux for 1 hour, after which the reaction was complete. The benzene was removed under reduced pressure and the residual red gum was extracted with ether, shaken with aqueous sodium carbonate, and dried ($CaCl_2$). The red oil which remained after removal of the ether gave two fractions on vacuum distillation: (i) b. p. 94—108°/4 × 10^{-3} mm. (1·75 g.), and (ii) b. p. 140—142°/1 × 10^{-2} mm. (1·3 g.). A portion of the first fraction gave a picrate which separated from alcohol in long yellow glistening needles, m. p. and mixed m. p. with 7 : 8-dihydro-5 : 6-benzoquinoline picrate 204—207°. The remainder of the first fraction was redistilled twice (b. p. 80—85°/4 × 10^{-4} mm. and b. p. 112—114°/1·6 × 10^{-2} mm.) to give 7 : 8-*dihydro*-5 : 6-*benzoquinoline* as a pale yellow mobile oil (Found: C, 85·6; H, 6·3. $C_{13}H_{11}N$ requires C, 86·1; H, 6·1%). The second fraction, a red viscous oil, could not be induced to crystallise, but a portion was converted into the picrate, which separated from alcohol in yellow needles, m. p. and mixed m. p. with 2-(2-*o*-acetamidophenylethyl)pyridine picrate 159—160°. A second portion of the second fraction was boiled under reflux with 20% sulphuric acid for 2 hours. The solution was made alkaline, and ether extracted 2-(2-*o*-aminophenylethyl)pyridine, m. p. and mixed m. p. 58—59°, in colourless needles from light petroleum (b. p. 40—60°).

5 : 6-*Benzoquinoline* (X) —7 : 8-Dihydro-5 : 6-benzoquinoline picrate (0·75 g.) was decomposed with aqueous sodium hydroxide, and the free base was extracted with ether. The base was heated with selenium powder (1 g.) at 300° for 5 hours. A crystalline deposit of 5 : 6-benzoquinoline formed on the side of the tube after a short time. The reaction mixture was extracted with light petroleum (b. p. 40—60°), from which 5 : 6-benzoquinoline (0·25 g.) separated in colourless plates, m. p. and mixed m. p. with an authentic specimen 90—91°.

Decomposition of 1-o-(2-2′-*Pyridylethyl*)*phenyl*-3 : 3-*dimethyltriazen* (IX).—A solution of 2-(2-*o*-aminophenylethyl)pyridine (6 g.) in concentrated hydrochloric acid (15 c.c.) and water (20 c.c.) was diazotised at 0° with a solution of sodium nitrite (2·5 g.) in water (20 c.c.). The diazonium chloride solution was added at 0° to a solution of dimethylamine (4·8 g.; 33% w/v in water) and sodium carbonate (10 g., anhydrous) in water (150 c.c.) with vigorous stirring. The oil which separated was extracted with ether and dried ($CaCl_2$). The triazen (6 g.) was collected at 165—167°/7 × 10^{-2} mm. as a pale yellow oil. It was dissolved in benzene (100 c.c.), and dry hydrogen chloride was passed through the boiling solution until no more nitrogen was evolved. The black tarry solution was shaken with aqueous sodium hydroxide, and the benzene extract was dried. Removal of the solvent left a black viscous oil, which was collected at 105—115°/8 × 10^{-3} mm. as a pale yellow oil. The base was converted in alcoholic solution into the picrate, which separated in orange-yellow crystals (5·5 g.), m. p. 130—134°. Further crystallisation from benzene gave 2-(2-o-*chlorophenylethyl*)*pyridine picrate*, m. p. 134—135° (Found: C, 51·2; H, 3·2. $C_{13}H_{12}NCl,C_6H_3O_7N_3$ requires C, 51·1; H, 3·4%).

Action of Aqueous Sodium Hydroxide on the Diazonium Sulphate prepared from 2-(2-o-*Aminophenylethyl*)*pyridine*.—A solution of sodium nitrite (2 g.) in water (20 c.c.) was added dropwise at 0° to 2-(2-*o*-aminophenylethyl)pyridine (5 g.) in concentrated sulphuric acid (3·5 g.) and water (40 c.c.). The diazonium sulphate solution was stirred for 20 minutes at 0° and aqueous sodium hydroxide was added until the mixture was just alkaline. Nitrogen was evolved and a tar which separated gradually dissolved to give a deep red solution. Stirring was continued at room temperature for 15 hours. The dark mixture was extracted with ether and distillation of the extract gave 2-(2-*o*-hydroxyphenylethyl)pyridine as a pale yellow viscous oil (1·9 g.), b. p. 140—145°/7 × 10^{-2} mm., which gradually solidified. Crystallisation from light petroleum (b. p. 60—80°) afforded colourless needles, m. p. 91—92°.

Nitrosation of NN-*Diacetylaniline*.—A solution of nitrosyl chloride (0·65 g. of 25% w/v acetic acid solution) was added dropwise at 0° to a mixture of diacetylaniline (1·7 g.) in acetic anhydride (5 c.c.) and acetic acid (5 c.c.) containing anhydrous sodium acetate (1·4 g.) and phosphoric oxide (0·25 g.). After 0·5 hour the mixture was poured into ice-cold water, and aqueous sodium carbonate was added to the clear yellow solution. The alkaline solution was ether-extracted, and removal of the solvent under reduced pressure gave a solid residue which was dissolved in benzene and warmed on the water-bath. The benzene was removed and the resulting gum was distilled with steam. Extraction of the aqueous distillate with ether afforded a residue which on crystallisation from light petroleum (b. p. 40—60°) gave acetanilide, m. p. and mixed m. p. 114°. Further concentration of the mother-liquor gave a small quantity of diphenyl, m. p. and mixed m. p. 70°.

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