505. *Cinnolines. Part XXI. Further Observations on the Richter Synthesis.*

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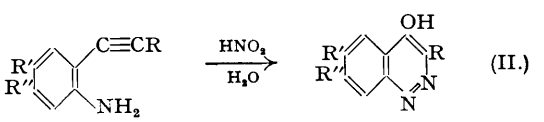
The effect of substituents upon the Richter synthesis of 4-hydroxycinnolines (II) from *o*-aminophenylacetylenes (I) has been further examined. 6-*Chloro-* and 6-*bromo*-4-*hydroxycinnoline*-3-*carboxylic acid*, 4-*hydroxy-* and 6-*methoxy*-4-*hydroxy*-3-*phenylcinnoline* have been prepared. The diazotisation of 2-*amino-* and 5-*chloro*-2-*amino-tolazole*, as well as of 2 : 2′-diaminodiphenyldiacetylene, has been investigated, and the mechanism of the Richter synthesis is discussed in the light of these results.

THE reaction discovered by von Richter, which led to the first authentic cinnoline derivative (*Ber.*, 1883, **16**, 677) and consists in the diazotisation of suitably substituted *o*-aminophenylacetylenes (I) ⟶ (II), has hitherto proved applicable in the cases where R is a hydrogen atom or a carboxyl group (Schofield and Simpson, Part III, *J.*, 1945, 512). Although the reaction is of no practical value as a source of 4-hydroxycinnolines, having been superseded by the Borsche reaction (Part IV, *J.*, 1945, 520, and subsequent papers), the so-called " Richter acids " (II; R = CO_2H) have proved to be compounds of surprising reactivity (Schofield and Simpson, *J.*, 1946, 472). For this reason, and also because of the bearing of the reaction upon modes of addition to acetylenic linkages, we decided to attempt a wider delineation of its scope and mechanism by examining the effect of further variations in R and R′ in (I).



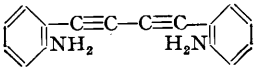
The nature of the substituents present in the benzene ring of *o*-aminoacetophenones affects considerably the Borsche synthesis of 4-hydroxycinnolines, (VII) ⟶ (VIII) (Parts IV and XVIII; *loc. cit.*, and *J.*, 1948, 1170), electron-attracting groups *ortho* or *para* to the amino-group exerting a favouring influence. Since the Richter reaction proceeds when electron-releasing groups are present (R = CO_2H, R′ = MeO, R″ = H, R′R″ = CH_2O_2; Schofield and Simpson, *loc. cit.*), it was of interest to evaluate the effect of electronegative groups. Accordingly, we have worked with compounds containing halogen atoms. 5-Chloro- and 5-bromo-2-nitrocinnamic acids have previously been obtained by a Perkin synthesis (Eichengrün and Einhorn, *Annalen*, 1891, **262**, 133; Eichengrün and Gernheim, *ibid.*, 1895, **284**, 132). The Doebner modification of this reaction (Doebner, *Ber.*, 1900, **33**, 2140; 1902, **35**, 1137) has now given good yields of these compounds. Subsequent bromination provided αβ-*dibromo*-β-(5-*chloro*-2-*nitrophenyl*)- and -β-(5-*bromo*-2-*nitrophenyl*)-*propionic acid*. Attempts to dehydro-

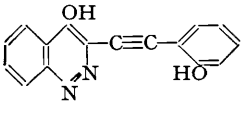
brominate these products led mainly to the regeneration of the original cinnamic acids, but small yields of the desired propiolic acids were obtained. Reduction of the latter, and diazotisation of the resulting amines, without isolation, gave 6-*chloro-* and 6-*bromo*-4-*hydroxycinnoline*-3-*carboxylic acid* (II; R = CO_2H, R″ = H, R′ = Cl or Br). The character of these acids was proved by decarboxylation to the expected 6-chloro- and 6-bromo-4-hydroxycinnoline, identical with authentic specimens. Decarboxylation of the propiolic acids gave 5-*chloro-* and 5-*bromo*-2-*nitrophenylacetylene*, reduction of which, followed by diazotisation of the amines, provided 6-chloro- and 6-bromo-4-hydroxycinnoline.

We next turned our attention to the diazotisation of compounds of the type (I; R = Ph). 2-Aminotolane (I; R = Ph, R′ = R″ = H) has been described by Ruggli and Schind (*Helv. Chim. Acta*, 1935, **18**, 1215). We have effected minor improvements in the route to this compound. To extend the range of aminotolanes available, 2-nitro-5-methoxybenzaldehyde was condensed with phenylacetic acid, giving cis-2-*nitro*-5-*methoxy*-α-*phenylcinnamic acid*. Decarboxylation gave cis-2-*nitro*-5-*methoxystilbene*, which yielded a sticky dichloride from which little or none of the tolane could be obtained. However, isomerisation of this stilbene provided trans-2-*nitro*-5-*methoxystilbene*, of which the *dichloride* yielded 2-*nitro*-5-*methoxytolane* by dehydrochlorination. The allocation of *cis-* and *trans*-structures to these stilbenes is justified by the methods of preparation, and by the similarity of their behaviour to that of the corresponding forms of 2-nitrostilbene (Ruggli, Caspar, and Hegedus, *Helv. Chim. Acta*, 1937, **20**, 250). Diazotisation of 2-aminotolane gave 4-*hydroxy*-3-*phenylcinnoline*, characterised by conversion into 4-*chloro*-3-*phenylcinnoline*. From experiments on the reduction of 2-nitro-5-methoxytolane we were not able to isolate a pure product with the quantities of material available, but diazotisation of the crude reduction product gave 4-*hydroxy*-6-*methoxy*-3-*phenylcinnoline*.

In the case of (I; R = pyridyl), the necessary intermediates as far as 2-nitrotolazole have been described (Ruggli and Cuenin, *Helv. Chim. Acta*, 1944, **27**, 649), but we experienced difficulties in repeating portions of the work described by these authors, and found it necessary to modify their procedures. Again to increase the range of available compounds we prepared 5-*chloro*-2-*nitrostilbazole*, and from the derived *dichloride* obtained by dehydrochlorination 5-*chloro*-2-*nitrotolazole*. The nitrotolazoles were reduced to 2-*aminotolazole* (I; R = pyridyl, R′ = R″ = H), and 5-*chloro*-2-*aminotolazole* (I; R = pyridyl, R′ = Cl, R″ = H), respectively. Diazotisation of these amines gave tarry products from which were isolated, as their *picrates*, what we take to be 2-hydroxy- and 5-chloro-2-hydroxy-tolazole.

From the theoretical standpoint the diazotisation of 2 : 2′-diaminodiphenyldiacetylene (III) promised to be interesting. This compound has been described by Baeyer and Lansberg (*Ber.*, 1882, **15**, 57) who obtained it by oxidising the copper derivative of 2-acetamidophenylacetylene with potassium ferricyanide. In our hands this method gave poor yields, and atmospheric oxidation of the copper compound proved more satisfactory (Salkind and Fundyler, *Ber.*, 1936, **69**, 128). An attempt to prepare the diacetylene through a Grignard reagent (Danehy and Nieuwland, *J. Amer. Chem. Soc.*, 1936, **58**, 1609) failed. Tetrazotisation of 2 : 2′-diaminodiphenyldiacetylene gave a *compound*, m. p. 224—225°, for which analysis suggests the structure (IV). An experiment in more concentrated acid gave a second *product*, m. p. 265—266°, possibly arising from (IV) by hydration of the acetylenic linkage. Whilst there seems no doubt that only one cinnoline ring is formed from this diamine, owing to their inaccessibility the products were not further examined and their structures must be regarded as tentative.

(III.) 

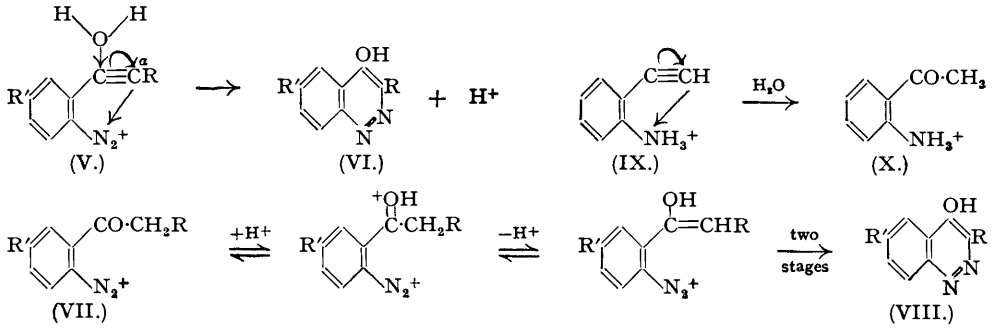


(IV.)

The new examples now available make possible a more complete discussion of the nature of the Richter synthesis, and its relation to certain other reactions, than was originally possible. The facts relating to the reaction may be summarised thus. (*a*) Cinnoline formation is independent of the nature of the substituent at $C_{(5)}$ in the parent phenylacetylene, occurring when this is methoxyl, hydrogen (Part III, *loc. cit.*), or halogen. (*b*) The substituent on $C_{(\alpha)}$ may vary from carboxyl to hydrogen or phenyl, but may not be so strongly electron-attracting as α-pyridinium.

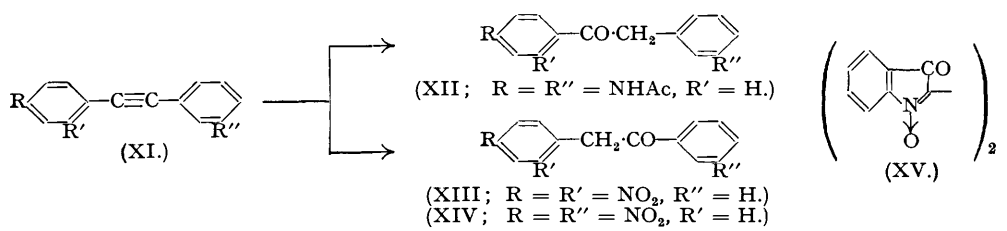
Previously (Part IV, *loc. cit.*) we outlined arguments against a mechanism for the Richter synthesis involving completed hydration of the acetylenic linkage before ring-closure. The

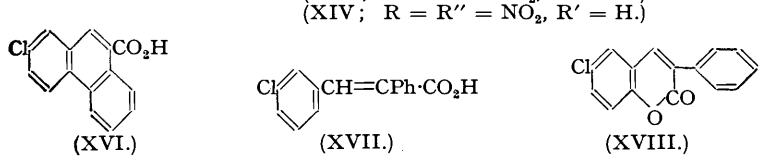
mechanism suggested for the reaction, (V) ⟶ (VI), involves intramolecular co-ordination of the diazonium group with $C_{(\alpha)}$ of the side-chain, together with simultaneous addition of the



elements of hydroxyl to $C_{(\beta)}$. The facts mentioned in (*a*) above provide support for this argument. This is seen by comparison with the Borsche reaction, (VII) ⟶ (VIII), which, in dilute acid, depends for its success upon the presence of an electron-attracting substituent *para* (or *ortho*) to the diazonium group (R′ in VII), it being essential under these conditions to stabilise the latter to accommodate the true rate-controlling step which is the enolisation of the ketone group (Part XVIII, *loc. cit.*). If initial completed hydration of the triple bond occurred in the Richter reaction, a similar state of affairs would arise, but the synthesis is in fact independent of such enolisation, and hence of the character of the substituent R′ in (V). As shown by the facts (*b*), the Richter reaction can tolerate fairly wide variations in the $C_{(\alpha)}$ substituent (R in V), failing to give a cinnoline only in the cases where R absorbs electronic charge accruing at $C_{(\alpha)}$ by polarisation of the acetylene group (V) and essential there for co-ordination with the diazonium cation if cinnoline formation is to occur. Thus the reaction fails in the case of (V; R = pyridyl), for the pyridyl group will become strongly electron-attracting in acid solution (cf. Part VII for a similar effect in the Widman–Stoermer synthesis, *J.*, 1946, 673).

The examples of cinnoline formation from tolane derivatives are especially interesting in relation to the hydration of acetylenic compounds. Cinnoline formation from *o*-aminophenylacetylene was anticipated because this compound on hydration gives *o*-aminoacetophenone, (IX) ⟶ (X) (Part III, *loc. cit.*). Here the protonised amino-group appears not to exert its expected electron-attracting effect through the aromatic nucleus. Now in other cases, in the tolane field, substituents in the aromatic nuclei effectively control the direction of hydration exactly as predicted from electronic theory [*e.g.*, (XI) ⟶ (XIII), *Chem. Reviews*, 1938, **23**, 247; (XI) ⟶ (XII), and (XI) ⟶ (XIV), Harrison, *J.*, 1926, 1232]. Thus the hydration of *o*-aminophenylacetylene, and cinnoline formation from diazotised 2-aminotolanes, appear to be anomalous, unless it is granted that in both cases the substituent group exerts itself across space rather than through the aromatic nucleus [as in (V) and (IX)]. The necessity for this kind of polarisation, leading to incipient hydration in the required direction is stressed by the fact that tolanes are linear molecules (Robertson and Woodward, *Proc. Roy. Soc.*, 1938, *A*, **164**, 436) and could not otherwise form the non-linear transition state leading to cyclisation.





The probable formation of only one cinnoline ring from tetrazotised 2 : 2′-diaminodiphenyldiacetylene contrasts with the production of di-isatogen (XV) from the related dinitro-compound.

The difference is understandable if isatogen formation is a free-radical process as suggested by Ruggli, Caspar, and Hegedus (*loc. cit.*).

In connection with the work described above on tolane derivatives, we prepared *5-chloro-2-nitro-α-phenylcinnamic acid*, hoping to proceed thence by the usual steps to the related tolane. However, attempts to decarboxylate this acid gave small amounts of a nitrogen-free *compound*, m. p. 198—199°, apparently $C_{15}H_9O_2Cl$ or $C_{15}H_{11}O_2Cl$. (XVI) and (XVII) appeared to be possible structures. The first of these, *2-chlorophenanthrene-9-carboxylic acid*, m. p. 233—234°, was obtained from a Pschorr reaction with *5-chloro-2-amino-α-phenylcinnamic acid*, formed by reduction of the nitro-acid. Both it and *3-chloro-α-phenylcinnamic acid* (XVII), m. p. 163—164°, differed from the unknown product which, indeed, did not manifest acidic properties and seems to be best represented by the structure (XVIII).

Experimental.

M.p.s are uncorrected. Unless otherwise stated, ethereal extracts were dried with sodium sulphate.

5-Chloro-2-nitrocinnamic Acid.—5-Chloro-2-nitrobenzaldehyde (50 g.) (obtained in quantitative yield by the method of Mettler, *Ber.*, 1905, **38**, 2807), malonic acid (56 g.), pyridine (100 c.c.), and piperidine (2 c.c.) were heated for 2 hours at 95°, the solution was boiled for ¼ hour and poured into 2N-hydrochloric acid (750 c.c.), giving a substantially pure product (44 g.). The acid formed white micro-crystals, m. p. 174°, from dilute alcohol. The *methyl* ester gave white needles, m. p. 130—131°, from ether–ligroin (b. p. 40—60°) (Found: C, 49·9; H, 3·0. $C_{10}H_8O_4NCl$ requires C, 49·7; H, 3·3%).

5-Bromo-2-nitrocinnamic Acid.—5-Bromo-2-nitrobenzaldehyde (20 g.) (Mettler, *loc. cit.*) gave in the same way 5-bromo-2-nitrocinnamic acid (19·8 g.), forming cream-coloured needles, m. p. 170—171°, from ethanol. The *methyl* ester gave white needles, m. p. 150—151°, from ether–ligroin (b. p. 40—60°) (Found: C, 42·5; H, 2·7. $C_{10}H_8O_4NBr$ requires C, 42·0; H, 2·8%).

αβ-Dibromo-β-(5-chloro-2-nitrophenyl)- and αβ-Dibromo-β-(5-bromo-2-nitrophenyl)-propionic Acid.—The chlorocinnamic acid (20 g.) was heated for ½ hour at 95° with bromine in acetic acid (72 c.c.; 30% by weight), the solution was diluted with water (105 c.c.), and the massive yellow crystals were collected (27·6 g.). *αβ-Dibromo-β-(5-chloro-2-nitrophenyl)propionic acid* formed white micro-crystals, m. p. 179·5—180°, from dilute alcohol (Found: C, 28·5; H, 1·9. $C_9H_6O_4NClBr_2$ requires C, 27·9; H, 1·6%).

Prepared by this method, in equal yield, *αβ-dibromo-β-(5-bromo-2-nitrophenyl)propionic acid* separated from dilute alcohol in yellow crystals, m. p. 194° (slight decomp.) (Found: C, 25·6; H, 1·8. $C_9H_6O_4NBr_3$ requires C, 25·0; H, 1·4%).

5-Chloro- and 5-Bromo-2-nitrophenylpropiolic Acid.—The chloro-dibromide (40 g.) in alcohol (200 c.c.) and 10% aqueous sodium hydroxide (260 c.c.) were set aside for 6 hours at room temperature, and the mixture was poured into 2N-nitric acid (250 c.c.). The decarboxylation experiments below indicate that the crude product (18·6 g.) contained about 50% of the original cinnamic acid. Exhaustive crystallisation from water gave small buff-coloured crystals of 5-chloro-2-nitrophenylpropiolic acid, m. p. 138° (decomp.). The behaviour of the bromo-dibromide was similar, and 5-bromo-2-nitrophenylpropiolic acid gave colourless crystals, m. p. 136—137° (decomp.). Satisfactory analyses of these compounds were not obtained, perhaps owing to decarboxylation during drying.

5-Chloro- and 5-Bromo-2-nitrophenylacetylene.—In each case the crude mixture obtained as above (10 g.) was heated under reflux for 22 hours with water (1·6 l.) and then steam-distilled. The reaction liquor, on cooling, deposited the parent cinnamic acid (*ca.* 5 g.). Ether-extraction of the distillate (1·5 l.) gave the arylacetylene (*ca.* 45%, allowing for recovered cinnamic acid). *5-Chloro-2-nitrophenylacetylene* formed long white needles, m. p. 78—79°, from dilute alcohol (Found: C, 53·5; H, 2·6. $C_8H_4O_2NCl$ requires C, 52·9; H, 2·2%), and *5-bromo-2-nitrophenylacetylene* was obtained in the same form, m. p. 92—93°, from this solvent (Found: C. 42·5; H, 1·7. $C_8H_4O_2NBr$ requires C, 42·5; H, 1·8%).

6-Chloro- and 6-Bromo-4-hydroxycinnoline-3-carboxylic Acid.—To a mixture prepared from ferrous sulphate (30 g. in 60 c.c. of water) and aqueous ammonia (15 c.c., *d* 0·88) at 50°, recrystallised 5-chloro-2-nitrophenylpropiolic acid (3 g.) in aqueous ammonia (5 c.c., *d* 0·88, in 5 c.c. of water) was added during ¼ hour with shaking. The whole was shaken at 50° for a further ¼ hour, set aside for ¾ hour at room temperature, and filtered, the filtrate cooled to 5°, acidified with sulphuric acid (25 c.c.; 8N.), and diazotised at 0—5° with aqueous sodium nitrite (25%). After 7 days at room temperature the product (1·97 g., 66%) was collected. *6-Chloro-4-hydroxycinnoline-3-carboxylic acid* formed silvery-white plates, m. p. 263—264° (decomp.), from acetic acid (Found: C, 48·3; H, 2·5. $C_9H_5O_3N_2Cl$ requires C, 48·1; H, 2·3%). *6-Bromo-4-hydroxycinnoline-3-carboxylic acid*, obtained in similar yield by the same method, gave white needles, m. p. 264° (decomp.), from acetic acid (Found: C, 40·0; H, 2·0. $C_9H_5O_3N_2Br$ requires C, 40·1; H, 1·9%). Experiments in which cyclisation was effected at 70° gave somewhat lower yields (60%) of these products. An attempt to esterify the chloro-acid (Simpson, *J.*, 1946, 1035) failed. These acids were decarboxylated in benzophenone (Schofield and Simpson, *loc. cit.*) to give 6-chloro- and 6-bromo-4-hydroxycinnoline, identical with authentic specimens.

6-Chloro- and 6-Bromo-4-hydroxycinnoline.—5-Chloro-2-nitrophenylacetylene (0·5 g.) and aqueous ammonia (1·5 c.c., *d* 0·88, and 4 c.c. of water) were treated with zinc dust (1·5 g.), added in one portion. After being stirred for ¼ hour, the mixture was kept 1 hour at room temperature with occasional shaking, and then extracted with ether, and the amine removed from the ether with hydrochloric acid (20 c.c.; 2N.). The acid solution was diazotised at 0° with aqueous sodium nitrite (10%) and heated at 70° for ½ hour, giving 6-chloro-4-hydroxycinnoline, m. p. 287—288° (20%, based on the nitro-compound). An experiment in which the amine was isolated as a pale yellow solid, m. p. 51°, indicated that it was formed in 32% yield in the reduction. 6-Bromo-4-hydroxycinnoline was formed in similar yield from 5-bromo-2-nitrophenylacetylene.

2-Nitrotolane.—(*a*) The chlorination of *trans*-2-nitrostilbene by the method of Ruggli, Caspar, and Hegedus (*loc. cit.*) gave the dichloride, m. p. 87—88°, in 87·5% yield.

(*b*) The dichloride (4 g.) in alcohol (15 c.c.) was treated dropwise with sodium hydroxide (5·7 g. in 15 c.c. each of water and alcohol) during ¼ hour at 95°, the mixture heated for a further 1¾ hours and poured into water (200 c.c.). Ether removed a sticky solid which on trituration with methanol provided pale yellow crystals of 2-nitrotolane, m. p. 53—54° (2·52 g., 84%).

2-Aminotolane.—The nitro-compound (0·2 g.) in acetic acid (8 c.c.) and concentrated hydrochloric acid (2 c.c.) was treated with stannous chloride (1 g.) in concentrated hydrochloric acid (2 c.c.), the mixture heated at 40° for ¼ hour, cooled, poured into ice-cold sodium hydroxide solution, and the product extracted with ether. Removal of the ether gave the amine (0·15 g.), forming pale yellow needles, m. p. 88—89°, from methanol.

4-Hydroxy-3-phenylcinnoline.—2-Aminotolane (0·04 g.) was diazotised at 0° in concentrated hydrochloric acid (1 c.c.) with aqueous sodium nitrite (1·5%), the solution set aside overnight, warmed at 95° for ½ hour, and diluted, and the product collected (0·025 g.). Recrystallisation from acohol gave white leaflets of *4-hydroxy-3-phenylcinnoline*, m. p. 260—261° (Found: C, 75·7; H, 4·8. $C_{14}H_{10}ON_2$ requires C, 76·65; H, 4·5%).

4-Chloro-3-phenylcinnoline.—4-Hydroxy-3-phenylcinnoline (0·1 g.), phosphorus oxychloride (2 c.c.), and phosphorus pentachloride (0·2 g.) were heated for 1 hour at 95°, and the mixture decomposed with ice, basified, and extracted with ether. Removal of the solvent gave a red solid (0·09 g.), which separated from ether–ligroin (b. p. 40—60°) as orange micro-crystals of *4-chloro-3-phenylcinnoline*, m. p. 119—120° (Found: C, 69·85; H, 3·6; N, 11·4. $C_{14}H_9N_2Cl$ requires C, 69·85; H, 3·8; N, 11·6%).

2-Nitro-5-methoxy-α-phenylcinnamic Acid.—2-Nitro-5-methoxybenzaldehyde (27·3 g.), phenylacetic acid (20·4 g.), potassium acetate (14·7 g.), and acetic anhydride (45·8 g.), were heated for 14 hours at 95° in a stream of nitrogen, and the mixture was diluted and made alkaline with sodium hydroxide solution. The solution was washed with ether and acidified with hydrochloric acid, and the product collected (32 g.). *2-Nitro-5-methoxy-α-phenylcinnamic acid* gave pale buff-coloured prisms, m. p. 158—159°, from dilute alcohol (Found: C, 64·3; H, 4·4. $C_{16}H_{13}O_5N$ requires C, 64·2; H, 4·4%).

cis-2-*Nitro-5-methoxystilbene.*—The cinnamic acid (5 g.) was added during 5 minutes to quinoline (25 c.c.) containing copper chromite catalyst (0·2 g.) at 225—230°, the temperature maintained for 20 minutes, and the mixture poured into hydrochloric acid (150 c.c.; 2N.), and extracted with ether. The sticky product left after removal of the ether, on trituration with methanol, gave a pale yellow solid (3·17 g.). cis-2-*Nitro-5-methoxystilbene* formed pale yellow rhombs from ether–ligroin (b. p. 40—60°), m. p. 55—56° (Found: C, 70·7; H, 5·1. $C_{15}H_{13}O_3N$ requires C, 70·6; H, 5·1%).

trans-2-*Nitro-5-methoxystilbene.*—The *cis*-compound (3·85 g.) was heated for 10 minutes at 210—215° in nitrobenzene (20 c.c.) containing a crystal of iodine, and the nitrobenzene removed under reduced pressure at 95°. trans-2-*Nitro-5-methoxystilbene* (3·80 g.) crystallised in pale yellow rhombs, m. p. 70—71°, from dilute methanol, (Found: C, 70·65; H, 5·0%). In one decarboxylation experiment carried out under conditions apparently identical with those above, a 60% yield of the *trans*-isomer was obtained directly.

trans-2-*Nitro-5-methoxystilbene Dichloride.*—The *trans*-stilbene (1 g.) in carbon disulphide (10 c.c.) was treated with dry chlorine for 1 hour, the solvent removed *in vacuo*, and the residue triturated with methanol, yielding a yellow solid (0·75 g.). The *dichloride* crystallised in white prisms, m. p. 114—116°, from methanol (Found: C, 55·4; H, 3·95. $C_{15}H_{13}O_3NCl_2$ requires C, 55·2; H, 4·0%).

2-Nitro-5-methoxytolane.—The dichloride (1 g.) in ethanol (20 c.c.) was dehydrochlorinated as described above, with use of sodium hydroxide (1·1 g. in 5 c.c. each of water and alcohol). The product was poured into water (150 c.c.), and the precipitate collected (0·28 g.). Ether extraction of the liquor gave a further small amount (0·06 g.). Crystallisation from dilute methanol gave lustreless buff-coloured aggregates of *2-nitro-5-methoxytolane*, m. p. 64·5—65·5° (Found: C, 70·6; H, 4·5. $C_{15}H_{11}O_3N$ requires C, 71·1; H, 4·4%).

4-Hydroxy-6-methoxy-3-phenylcinnoline.—The nitro-compound (0·1 g.) in acetic acid (8 c.c.) and concentrated hydrochloric acid (2 c.c.) was treated with stannous chloride (0·5 g.) in concentrated hydrochloric acid (2 c.c.) and heated for 2 hours at 95°. The crude amine (0·08 g. of oily solid) was isolated as described above. We were unable to obtain crystalline derivatives with picric acid or acetic anhydride.

The crude amine (0·04 g.) in concentrated hydrochloric acid (2 c.c.) was diazotised at 0° with aqueous sodium nitrite (10%), and the solution warmed at 95° for ½ hour. The solid precipitated by dilution crystallised from dilute acetic acid in white micro-crystals of *4-hydroxy-6-methoxy-3-phenylcinnoline*, m. p. 318—319° (Found: C, 71·4; H, 5·05; N, 10·8. $C_{15}H_{12}O_2N_2$ requires C, 71·4; H, 4·8; N, 11·1%).

2-Nitrostilbazole Dichloride.—2-Nitrostilbazole (15 g.) in boiling carbon disulphide (50 c.c.) was treated with dry chlorine for ½ hour, and the product collected and ground with sodium carbonate solution (2N.), yielding 16·6 g. of the dichloride, m. p. 134—135°. When chlorination was carried out as described by Ruggli and Cuenin (*loc. cit.*), the dichloride appeared to be contaminated with a high-melting by-product which was unaffected by sodium carbonate and only removed by repeated crystallisation, giving the pure product in only 47% yield.

2-Nitrotolazole.—The dichloride (2 g.) in alcohol (7 c.c.) was heated at 95° and treated dropwise during 1 hour with potassium hydroxide (0·76 g. in 6 c.c. each of alcohol and water), and the mixture heated under reflux for a further hour, poured into water (100 c.c.), and extracted with ether. The dark brown solid remaining after removal of the ether was dried on a porous plate, giving 2-nitrotolazole (1·20 g.), m. p. 51—53°. The conditions of Ruggli and Cuenin (*loc. cit.*) gave only poor yields in our hands.

2-Aminotolazole.—2-Nitrotolazole (1 g.) in hydrochloric acid (10 c.c.; 6N.) was treated with stannous chloride (5 g.) in concentrated hydrochloric acid (5 c.c.) at 45—50° for ½ hour, and the solution cooled, added to aqueous potassium hydroxide, and extracted with ether. Removal of the ether gave a pale yellow solid (0·78 g.). *2-Aminotolazole* formed yellow leaflets, m. p. 104—105°, from dilute methanol (Found: C, 79·1; H, 5·05. $C_{13}H_{10}N_2$ requires C, 80·4; H, 5·2%).

Diazotisation of 2-Aminotolazole.—The solution obtained when the amine (0·2 g.) was diazotised at 0° with aqueous sodium nitrite (10%) was set aside for 16 days at room temperature, heated to 70° for 10 minutes, neutralised with sodium acetate, and extracted with ether. Removal of the solvent and treatment of the residue in alcohol (10 c.c.) with picric acid (0·2 g. in 5 c.c. of alcohol) gave a yellow solid

(0·10 g.). Crystallisation from alcohol gave yellow micro-crystals of *2-hydroxytolazole picrate*, m. p. 204—205° (Found: C, 49·9; H, 2·9. $C_{13}H_9ON,C_6H_3O_7N_3,2H_2O$ requires C, 49·6; H, 3·5%).

5-Chloro-2-nitrostilbazole.—5-Chloro-2-nitrobenzaldehyde (5 g.), α-picoline (2·6 g.), and acetic anhydride (4·2 g.), were heated for 10 hours at 165—170° in a stream of nitrogen, and the mixture was steam-distilled. The non-volatile tar was dissolved in hydrochloric acid (100 c.c.; 6N.) (charcoal), yielding a white hydrochloride (7·3 g.), m. p. 221—222° (decomp.), which when decomposed with sodium hydroxide gave the substantially pure product (4·62 g.). Recrystallised from dilute alcohol *5-chloro-2-nitrostilbazole* formed pale yellow needles, m. p. 92° (Found: C, 60·3; H, 3·6. $C_{13}H_9O_2N_2Cl$ requires C, 59·9; H, 3·5%).

5-Chloro-2-nitrostilbazole Dichloride.—The stilbazole (10 g.) in carbon disulphide (20 c.c.) was chlorinated as before, yielding the almost pure *dichloride* (10·3 g.), which formed cream-coloured leaflets, m. p. 163—164°, from alcohol (Found: C, 47·6; H, 2·75. $C_{13}H_9O_2N_2Cl_3$ requires C, 47·1; H, 2·7%).

5-Chloro-2-nitrotolazole.—The above dichloride (2 g.) in alcohol (13 c.c.) was dehydrochlorinated with potassium hydroxide (0·68 g. in 6 c.c. each of alcohol and water) as for 2-nitrostilbazole dichloride, yielding the substantially pure product as a white solid (1·36 g.) which turned purple when kept. *5-Chloro-2-nitrotolazole* formed thin white needles, m. p. 128—129°, from alcohol (Found: C, 59·8; H, 3·3; N, 10·4. $C_{13}H_7O_2N_2Cl$ requires C, 60·3; H, 2·7; N, 10·8%).

5-Chloro-2-aminotolazole.—The nitro-compound (1 g.) in hydrochloric acid (20 c.c., 6N.) was treated with stannous chloride (5 g.) in concentrated hydrochloric acid (5 c.c.), heated for 20 minutes at 40°, and worked up as before, yielding a yellow solid (0·62 g.). *5-Chloro-2-aminotolazole* crystallised from dilute alcohol in glistening yellow leaflets, m. p. 130—131° (Found: C, 65·25; H, 3·9. $C_{13}H_9N_2Cl,\frac{1}{2}H_2O$ requires C, 65·7; H, 4·2%).

Diazotisation of 5-Chloro-2-aminotolazole.—The amine (0·2 g.) in concentrated hydrochloric acid (10 c.c.) was diazotised at 0° with aqueous sodium nitrite (10%), the solution set aside for 10 days at room temperature, warmed to 70° for 3 hours, and worked up as described previously, yielding a picrate (0·17 g.). *5-Chloro-2-hydroxytolazole picrate* separated from alcohol in light brown micro-crystals, m. p. 194—195° (Found: C, 48·3; H, 2·6. $C_{13}H_8ONCl,C_6H_3O_7N_3,\frac{1}{2}H_2O$ requires C, 48·8; H, 2·6%).

2 : 2′-Diaminodiphenyldiacetylene.—(i) The decarboxylation of 2-nitrophenylpropiolic acid was carried out as described by Schofield and Simpson (*loc. cit.*), and 2-nitrophenylacetylene, m. p. 81—82°, was isolated in 68% yield by steam-distillation.

(ii) The nitro-compound (5 g.), covered with aqueous ammonia (1·5 c.c., *d* 0·88, and 4 c.c. of water), was treated with zinc dust (15 g.) in one portion, and the whole stirred for 1½ hours, the temperature being allowed to rise freely. After 1 hour at room temperature the mixture was worked up as before, giving a brown oil (3·7 g.). Distillation gave 2-aminophenylacetylene as a colourless oil, b. p. 98—100°/12 mm. (2·68 g.). The amine (1·48 g.) reacted vigorously with acetic anhydride (1·8 c.c.), giving 2-acetamidophenylacetylene (1·95 g.), which formed thin white leaflets from water, m. p. 84° (Baeyer and Lansberg, *loc. cit.*, give m. p. 75°) (Found: C, 74·95; H, 5·8. Calc. for $C_{10}H_9ON$: C, 75·4; H, 5·7%).

(iii) A solution containing 2-acetamidophenylacetylene (0·5 g.), alcohol (10 c.c.), cuprous chloride (from 4 g. of copper sulphate), and ammonia (15 c.c.; *d* 0·88), was aerated for 24 hours, ammonia being added from time to time to maintain the volume. The mixture was extracted with chloroform, and the solvent removed *in vacuo*, yielding 2 : 2′-diaminodiphenyldiacetylene (0·33 g.), which formed white needles (turning purple when kept), m. p. 225°, from alcohol (Baeyer and Lansberg, *loc. cit.*, give m. p. 231°) (Found: C, 75·2; H, 5·2; N, 8·85. Calc. for $C_{20}H_{16}O_2N_2$: C, 75·9; H, 5·1; N, 8·85%). The bisacetamido-compound (2·18 g.), heated for ½ hour at 95° with concentrated sulphuric acid, water, and alcohol (35 c.c. of each), gave on basification the substantially pure amine (1·52 g.) as yellow needles, m. p. 127—128°, from alcohol (Baeyer and Lansberg, *loc. cit.*, give m. p. 128°) (Found: C, 80·7; H, 5·55. Calc. for $C_{16}H_{12}N_2,\frac{1}{2}H_2O$: C, 79·7; H, 5·4%).

Tetrazotisation of 2 : 2′-Diaminodiphenyldiacetylene.—The diamine (0·93 g.) in sulphuric acid (50 c.c.; 4N.) was tetrazotised at 0° with aqueous sodium nitrite (5·6 c.c.; 10%). After 5 weeks at room temperature the solution was warmed at 70° for 1 hour and then diluted, and the product collected (0·74 g.; m. p. 190—195°). Recrystallisation from dilute alcohol gave pale green needles of a *compound*, m. p. 224—225° (Found: C, 72·7; H, 4·15. $C_{16}H_{10}O_2N_2$ requires C, 73·3; H, 3·8%). An experiment in 8N-sulphuric acid gave a second *product*, forming pale buff-coloured micro-crystals, m. p. 265—266°, from alcohol (Found: N, 10·0. $C_{16}H_{12}O_3N_2$ requires N, 10·0%).

5-Chloro-2-nitro-α-phenylcinnamic Acid.—5-Chloro-2-nitrobenzaldehyde (18·5 g.), phenylacetic acid (13·6 g.), fused potassium acetate (9·8 g.), and acetic anhydride (30·6 g.), were heated under nitrogen for 10 hours, and the mixture was worked up as described in the similar case above, yielding a pale brown solid (24·7 g.). Crystallisation from dilute alcohol provided cream prisms of *5-chloro-2-nitro-α-phenylcinnamic acid*, m. p. 183—184° (Found: C, 59·3; H, 3·4. $C_{15}H_{10}O_4NCl$ requires C, 59·3; H, 3·3%).

Attempted Decarboxylation of 5-Chloro-2-nitro-α-phenylcinnamic Acid.—The acid (15 g.) was added during 4 minutes to quinoline (75 c.c.) containing copper chromite catalyst (0·5 g.) at 230°, heated for 4 minutes further, cooled, and poured into hydrochloric acid. The mixture was extracted with ether, and removal of the solvent left a sticky *product* which on trituration with methanol gave a yellow solid (1·10 g.). Crystallisation from ethanol gave white needles, m. p. 198—199° [Found: C, 69·9; H, 3·7; *M* (Rast), 260. $C_{15}H_9O_2Cl$ requires C, 70·2; H, 3·5%; *M*, 267·5].

2-Chlorophenanthrene-9-carboxylic Acid.—To a mixture prepared from ferrous sulphate (18·4 g.), water (25 c.c.), and ammonia (22 c.c.; *d* 0·88), was added, in one portion, a solution of 5-chloro-2-nitro-α-phenylcinnamic acid (3·0 g.) in warm dilute aqueous ammonia (10 c.c.; 2N.). After 1 hour at 95° the mixture was filtered, the filtrate neutralised with acetic acid, and the product collected (2·63 g.). *5-Chloro-2-amino-α-phenylcinnamic acid* formed yellow cubes, m. p. 221—222°, from dilute alcohol (Found: C, 66·9; H, 4·45. $C_{15}H_{12}O_2NCl$ requires C, 65·85; H, 4·4%).

The sodium salt of the amino-acid (from 1 g. of acid and 0·15 g. of sodium hydroxide in 10 c.c. of water) was added to sodium nitrite (0·25 g.) in water (2 c.c.), and the solution added dropwise with stirring during 20 minutes to sulphuric acid (15 c.c.; 5N.) at 0—5°. After a further ½ hour's stirring the pre-

cipitate was collected, suspended in water (10 c.c.), and treated with copper powder (0·2 g.) at 100° for ½ hour, the mixture made alkaline with ammonia and filtered, and the product precipitated with mineral acid (0·59 g.). *2-Chlorophenanthrene-9-carboxylic acid* gave white leaflets, m. p. 233—234°, from dilute alcohol (Found: C, 70·2; H, 3·6. $C_{15}H_9O_2Cl$ requires C, 70·2; H, 3·5%).

3-Chloro-α-phenylcinnamic Acid.—*m*-Chlorobenzaldehyde (5 g.), phenylacetic acid (4·8 g.), potassium acetate (3·5 g.), and acetic anhydride (11 g.) were treated as in previous cases, giving 7·80 g. of product. *3-Chloro-α-phenylcinnamic acid* formed stout white cubes, m. p. 163·4—164°, from dilute alcohol (Found: C, 69·3; H, 4·3. $C_{15}H_{11}O_2Cl$ requires C, 69·6; H, 4·3%).

The authors are indebted to the Chemical Society for a grant from the Research Fund, and to I.C.I. Ltd. and the Council of University College, Exeter, for other financial aid.

WASHINGTON SINGER LABORATORIES,
UNIVERSITY COLLEGE OF THE SOUTH WEST, EXETER. [*Received, March 29th,* 1949.]