Triazaphenanthrenes. Part VI.* Further Observations on the Widman–Stoermer and Borsche Reactions

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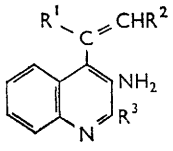
The named reactions have been applied to the synthesis of new 1,2,9-triazaphenanthrenes and 1,2,7- and 1,2,5-triazanaphthalenes. A modified Borsche cyclisation appears to be generally applicable to aminoquinolines but attempts to extend this to simpler aromatic systems have failed.

THE Widman–Stoermer reaction has been used [1] to provide an excellent yield of 4-methylcinnoline by cyclisation in dilute alkaline solution of diazotised *o*-isopropenylaniline. One essential for the success of this reaction is an electron-donating group on the α-carbon atom of the olefinic side-chain, and an α-aryl group has a beneficial effect.[2] The presence of heterocyclic nuclei at the α- or the β-position has been shown to have an inhibiting effect on cinnoline formation, owing to their powerful electron-withdrawing effects, particularly in strong-acid media.[3,4]

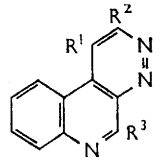
The presence of aryl groups, however, in competition with heterocyclic nuclei, often led to high yields of the cinnoline [3] but when heterocyclic nuclei were present the yield of cinnoline was particularly susceptible to pH because of protonation of the hetero-atom.

This work has now been extended by a study of the cyclisation of a number of amino-ethylenes in the quinoline and pyridine series, and a preliminary study has been made of the resulting new heterocycles.

The ethylenes (I)—(IV) were best prepared by dehydration with boiling sulphuric acid (50%, v/v) of



	R^1	R^2	R^3
(I)	Me	H	Ph
(II)	Ph	H	Ph
(III)	Ph	Me	Ph
(IV)	Me	H	Me



(V)

carbinols obtained by standard Grignard procedures with esters and ketones. Dehydration using iodine in toluene failed, and yields were low when concentrated sulphuric acid was used.

Diazotisation of the amines (I)—(IV) gave yields of triazaphenanthrenes (V) which varied with the substituents, being good for (II), poor for (III), and nil for (I) and (IV). These results are in general agreement with previous investigations of the Widman–Stoermer reaction [2-4] but it is difficult to explain the low yield from (III).

Attempted reduction of 4,10-diphenyl-1,2,9-triazaphenanthrene (V; $R^1 = R^3 = Ph$, $R^2 = H$) to the corresponding pyrroloquinoline (cf. ref. 4) with sodium and ethanol was unsuccessful. Ammonia was not evolved, and the major product appears to be the 1,2,3,4,9,10-hexahydro-derivative. This agrees with the formation of hexahydropyridazines from simple pyridazines,[5] although reduction of 3,6-diphenylpyridazine yields the dihydro-derivative,[6] and pyridazine itself undergoes ring-opening to give a small amount of diamine.[7] Reduction of (V; $R^1 = R^3 = Ph$, $R^2 = H$) with zinc amalgam in 33% acetic acid gave the desired pyrroloquinoline (cf. the reduction of 4-phenylcinnoline to 3-phenylindole [8]). 4,10-Diphenyl-1,2,9-triazaphenanthrene was stable towards prolonged treatment with hot permanganate but readily gave a di-*N*-oxide with hydrogen peroxide–acetic acid; milder conditions gave a mono-*N*-oxide. Neither of the *N*-oxides showed peroxide properties (cf. quinoxaline *N*-oxides [9]).

In the pyridine series the amino-propenes (VI)—(IX) were prepared by dehydration of the appropriate carbinols. During the preparation of 2-(3-amino-2-pyridyl)-propan-2-ol a second product was obtained, often as the major product. This is most probably the pinacol, having regard to the isolation of 2-acetyl-3-aminopyridine after treatment with chromic oxide in acetic acid, and conversion into a pinacolone with hot concentrated hydrochloric acid, but not with iodine in acetic acid.[10] However, the pinacol was stable to sodium periodate, and treatment with lead tetra-acetate gave no identifiable product. Pinacol formation during the reaction between an ester and a Grignard reagent was observed by Boyd and Hatt,[11] and the reduction of ketones to pinacols by magnesium in the presence of a Grignard reagent is well known.[12] Pinacol formation was finally prevented by filtration of the Grignard reagent through kieselguhr.

In all cases diazotisation and cyclisation of the aminopropenes gave 4-methyl derivatives of the respective new triazanaphthalenes (X) [from (VI), (VII), and (VIII)] and (XI) [from (IX)].

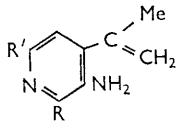
Unfortunately yields were very poor, and in two cases, (VIII) and (IX), the corresponding triazanaphthalenes were isolated only as picrates. Examination of various

* Part V, C. M. Atkinson and A. R. Mattocks, *J. Chem. Soc.*, 1962, 1671.

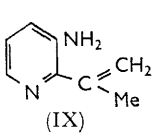
[1] T. L. Jacobs, S. Winstein, R. B. Henderson, E. C. Spaeth, *J. Amer. Chem. Soc.*, 1956, **68**, 1310.
[2] J. C. E. Simpson, *J. Chem. Soc.*, 1943, 449.
[3] J. C. E. Simpson, *J. Chem. Soc.*, 1946, 673.
[4] A. J. Nunn and K. Schofield, *J. Chem. Soc.*, 1953, 3700.
[5] C. Paal and C. Koch, *Ber.*, 1904, **37**, 4382; A. Katzenellenbogen, *ibid.*, 1901, **34**, 3828.
[6] C. Paal and E. Dencks, *Ber.*, 1903, **36**, 491.
[7] M. R. Marquis, *Compt. rend.*, 1903, **136**, 368.
[8] P. W. Neber, G. Knoller, H. Herbst, and A. Trissler, *Annalen*, 1929, **471**, 113.
[9] H. McIlwain, *J. Chem. Soc.*, 1943, 322.
[10] W. E. Bachmann and E. J. H. Chu, *J. Amer. Chem. Soc.*, 1936, **58**, 1118.
[11] D. R. Boyd and H. H. Hatt, *J. Chem. Soc.*, 1927, 898.
[12] M. Gomberg and W. E. Bachmann, *J. Amer. Chem. Soc.*, 1927, **49**, 236.

methods for cyclisation showed that success followed only when the method of Jacobs *et al.*[1] was used.

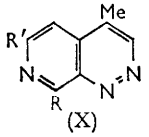
Attempted diazotisation and cyclisation of (IX) in concentrated hydrochloric acid failed, but 3-chloro-2-isopropenylpyridine (picrate) and 2-acetyl-3-hydroxypyridine were isolated, the latter probably formed by



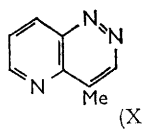
(VI) R = R′ = H
(VII) R = R′ = Me
(VIII) R = Me, R′ = Ph



(IX)



(X)



(XI)

oxidation of the propene with excess of nitrous acid. A third compound, represented as a hydrate of 3-hydroxy-2-isopropenylpyridine, was also isolated. Attempted cyclisation in alkaline solution gave a dark red, high-melting compound which was not identified. These low yields of the desired products seem to indicate that the electron-releasing power of a methyl group at the α-position is insufficient to overcome the effect of the nitrogen atom at the ring α- or γ-positions, in spite of the fact that cyclisation was carried out in the absence of strong acids.

The low yields of the methyl triazanaphthalenes did not permit full examination of their properties. In the case of 4-methyl-1,2,7-triazanaphthalene, where yields of up to 20% were obtained, the reactivity of the 4-methyl group was established by condensation of the base with benzaldehyde in the presence of zinc chloride, to give 4-styryl-1,2,7-triazanaphthalene. Oxidation of this styryl derivative gave 1,2,7-triazanaphthalene-4-carboxylic acid, but the yield was too low to permit attempted decarboxylation to the parent base.

The Borsche reaction, cyclisation of a diazotised *o*-aminoaryl ketone to form a 4-hydroxycinnoline, is normally best carried out in strong acid.[13] However, cyclisation of diazotised 4-acetyl-3-amino-2-phenylquinoline required [14] an alkaline medium for good results. It was suggested that, in strong acid, salt formation at the ring nitrogen atom inhibited enolisation of the carbonyl group, but that in alkali the diazonium cation coupled with the enolate anion.

In order to test this hypothesis in a simpler system, the ring-closures of diazotised 2-amino-4-dimethylaminoacetophenone, 4-acetyl-3-aminopyridine, and 2-acetyl-3-aminopyridine have been investigated under a variety of conditions. Unfortunately, in all cases a product arising from cyclisation could not be isolated; in acid solution, nitrogen was lost and phenolic compounds formed, while in alkali the only isolable products could not be purified and were probably formed by intermolecular coupling. Of the required starting materials, 2-amino-4-dimethylaminoacetophenone was prepared from 4-amino-2-nitrobenzoic acid through 4-amino-2-nitroacetophenone. Synthesis of the aminopyridyl ketones was extremely difficult and was eventually achieved by ozonolysis of the corresponding benzamidopyridylpropene and subsequent hydrolysis.

Although these results are disappointing, further evidence of the generalised nature of the modified Borsche reaction (in alkali) has been obtained. Cyclisation of 3-amino-2-phenyl-4-propionylquinoline in concentrated hydrochloric acid, rather than in alkali, gave much lower yields of 4-hydroxy-3-methyl-10-phenyl-1,2,9-triazaphenanthrene, and 3-chloro-2-phenyl-4-propionylquinoline was isolated.

This 4-hydroxy-triazaphenanthrene was readily converted into the amino-derivative through the 4-chloro- and 4-phenoxy-compounds, and quaternisation of the amine gave only one methiodide. Methylation of the hydroxy-triazaphenanthrene gave an *N*-methyl derivative, different from the *O*-methyl compound as prepared from the chloro-triazaphenanthrene and sodium methoxide.

EXPERIMENTAL

2-(3-Amino-2-methyl-4-quinolyl)propan-2-ol.— Methyl 3-amino-2-methylquinoline-4-carboxylate [15] (6·0 g.) in dry ether (50 ml.) was added at 0° under nitrogen during 1 hr. to a stirred Grignard reagent prepared from magnesium (4·33 g.) and methyl iodide (11·2 ml.) in dry ether (300 ml.). The mixture was heated under reflux for 6 hr. and set aside overnight, ammonium chloride (60 g.) in ice–water added with stirring, and the organic layer separated. The aqueous layer was made almost neutral with hydrochloric acid, and extracted with ether, and the combined extracts were washed with water, dried, and concentrated. Orange needles (2·85 g.), m. p. 182—186°, separated on cooling and were added to a second crop (1·0 g.), m. p. 180—185°; recrystallisation from ether provided the *carbinol* (3·1 g., 52%), m. p. 191—194° (Found: C, 72·3; H, 7·1; N, 12·8. $C_{13}H_{16}N_2$ requires C, 72·2; H, 7·5; N, 13·0%).

2-(3-Amino-2-methyl-4-quinolyl)propene.— 2-(3-Amino-2-methyl-4-quinolyl)propan-2-ol (1·0 g.) was dissolved in concentrated sulphuric acid (20 ml.) with initial cooling to keep the mixture at room temperature. After 3 hr. the solution was poured on to crushed ice (100 g.) made alkaline with 6N-sodium hydroxide, and extracted thrice with ether; the combined extracts were washed with water, dried, and evaporated, to yield a yellow-orange solid (0·86 g.), m. p. 80—82°. Recrystallisation thrice from n-hexane furnished needles of the *product* (0·56 g., 61·1%), m. p. 85° (Found: C, 78·8; H, 7·2; N, 14·4. $C_{13}H_{14}N_2$ requires C, 78·8; H, 7·1; N, 14·1%).

Methyl 3-Amino-2-phenylquinoline-4-carboxylate.— A stirred suspension of 3-amino-2-phenylquinoline-4-carboxylic acid [16] (44·5 g.) in ether was treated at room temperature with diazomethane prepared from *N*-nitroso-*N*-methylurea (60 g.) in ether (250 ml.). The reaction mixture was worked up as usual, and crystallisation of the residual red oil from light petroleum (b. p. 80—100°) provided long pale yellow

[13] K. Schofield and J. C. E. Simpson, *J. Chem. Soc.*, 1948, 1170.
[14] C. M. Atkinson and A. R. Mattocks, *J. Chem. Soc.*, 1957, 3722.
[15] J. M. Gulland and R. Robinson, *J. Chem. Soc.*, 1925, 1493.
[16] C. M. Atkinson and A. R. Mattocks, *J. Chem. Soc.*, 1957, 3718.

needles of the *product* (23·0 g., 49·1%), m. p. 101—102° (Found: C, 72·8; H, 5·1; N, 10·2. $C_{17}H_{14}N_2O_2$ requires C, 73·4; H, 5·1; N, 10·1%).

2-(3-*Amino*-2-*phenyl*-4-*quinolyl*)*propan*-2-*ol*.—Prepared as described above for the 2-methyl analogue, from 3-amino-2-phenylquinoline-4-carboxylate (20 g.), the pure *carbinol* separated from ether as prisms (10·4 g., 52%), m. p. 188—190° (Found: C, 77·3; H, 6·4; N, 9·9. $C_{18}H_{18}N_2O$ requires C, 77·7; H, 6·5; N, 10·1%).

2-(3-*Amino*-2-*phenyl*-4-*quinolyl*)*propene*.—The carbinol (5·35 g.) was dehydrated as described above with concentrated sulphuric acid (50 ml.). Recrystallisation of the product (4·7 g., 93·9%), m. p. 87—88° from n-hexane provided 2-(3-*amino*-2-*phenyl*-4-*quinolyl*)*propene* as needles, m. p. 88° (Found: C, 82·5; H, 6·2; N, 10·9. $C_{18}H_{16}N_2$ requires C, 83·0; H, 6·2; N, 10·8%).

1-(3-*Amino*-2-*phenyl*-4-*quinolyl*)-1-*phenylethanol*.—4-Acetyl-3-amino-2-phenylquinoline [14] (10 g.) in dry ether (300 ml.) was added during 1 hr. at 0° with stirring to a Grignard reagent prepared from magnesium (3·6 g.) and dry redistilled bromobenzene (16·2 ml.) in dry ether (400 ml.). The mixture was heated under reflux, then worked up as usual, to yield prisms (9·2 g., 71·1%), m. p. 165—169°. Recrystallisation from ether provided the *carbinol*, m. p. 172—173° (Found: C, 81·1; H, 5·9; N, 8·2. $C_{23}H_{20}N_2O$ requires C, 81·2; H, 6·1; N, 8·0%).

1-(3-*Amino*-2-*phenyl*-4-*quinolyl*)-1-*phenylethylene*.— A solution of the foregoing carbinol (8 g.) in concentrated sulphuric acid (40 ml.) and water (35 ml.) was heated under reflux for 1 hr., cooled, and poured on to ice (100 g.). After working up as usual, the resulting brown oil (7 g.) was extracted with boiling n-hexane, and the solution set aside at 0° for 2—3 days to provide crude colourless needles. Recrystallisation from n-hexane gave the pure *olefin* (5·8 g., 76·6%), m. p. 101—102° (Found: C, 86·2; H, 5·5; N, 8·8. $C_{23}H_{18}N_2$ requires C, 85·7; H, 5·6; N, 8·7%).

3-*Amino*-2-*phenyl*-4-*propionylquinoline*.— 3-Amino-2-phenylquinoline-4-carboxyamide [11] (20 g.) was added with stirring during 15 min. to a Grignard reagent prepared from magnesium (10·3 g.) and ethyl iodide (34 ml.) in ether (150 ml.) and benzene (400 ml.). The mixture was heated under reflux for 4 hr., cooled, and stirred with ice (500 g.) and concentrated hydrochloric acid (200 g.) for 15 min. Extraction in the usual way yielded a sticky solid (16·8 g.) which on recrystallisation from benzene–light petroleum gave the *ketimide* as colourless crystals, m. p. 191° (Found: C, 78·4; H, 5·5; N, 16·1. $C_{18}H_{17}N_3$ requires C, 78·5; H, 6·2; N, 15·3%). This (10 g.) was heated under reflux with water (50 ml.) and concentrated hydrochloric acid (25 ml.) for 1 hr. The reaction mixture was basified (sodium hydroxide), extracted thrice with ether, and the residue from evaporation of the dried extract was recrystallised from n-hexane, to yield the *ketone* (8·5 g., 40·5%) as pale yellow needles, m. p. 78° (Found: C, 78·0; H, 6·0; N, 10·6. $C_{18}H_{16}N_2O$ requires C, 78·3; H, 5·7; N, 10·2%).

1-(3-*Amino*-2-*phenylquinolyl*)-1-*phenylpropan*-1-*ol*.—To a Grignard solution prepared from magnesium (3·6 g.) and bromobenzene (17 ml.) in dry ether (200 ml.) was added a solution of 3-amino-2-phenyl-4-propionylquinoline (9·0 g.) in ether (200 ml.). The mixture was refluxed in an atmosphere of dry nitrogen for 3 hr. then worked up in the usual manner, to yield needles (8·5 g., 73·1%) of the *carbinol*, m. p. 153° (from ether) (Found: C, 80·6; H, 6·7; N, 7·6. $C_{24}H_{23}N_2O$ requires C, 81·3; H, 6·3; N, 7·9%).

1-(3-*Amino*-2-*phenyl*-4-*quinolyl*)-1-*phenylpropene*.— The foregoing carbinol (8·0 g.) was dehydrated in boiling concentrated sulphuric acid (25 ml.) and water (30 ml.) as usual, to yield the olefin (6·4 g.) as a pale yellow uncrystallisable oil; *picrate*, needles (from ethanol), m. p. 196—197° (Found: C, 63·9; H, 4·3; N, 11·7. $C_{30}H_{22}N_8O_7$ requires C, 63·7; H, 4·1; N, 12·4%).

4,10-*Diphenyl*-1,2,9-*triazaphenanthrene*.— 1-(3-Amino-2-phenyl-4-quinolyl)-1-phenylethylene (8 g.) in glacial acetic acid (15 ml.) and concentrated sulphuric acid (2 ml.) was treated dropwise during ½ hr. with sodium nitrite (1·8 g.) in water (10 ml.). The resulting dark red solution was allowed to stand at room temperature for 2 hr. and poured into water (150 ml.). The solid (7·5 g.) which precipitated was washed with water and recrystallised from methanol, to yield the *triazaphenanthrene* as pale yellow needles (6·4 g., 77·1%), m. p. 185—186° (Found: C, 82·0; H, 4·5; N, 13·1. $C_{23}H_{15}N_3$ requires C, 82·9; H, 4·5; N, 12·6%); *methiodide*, prepared under reflux in nitromethane, crystallised as orange-yellow needles, m. p. 259° (Found: C, 60·5; H, 3·9; I, 25·8; N, 8·8. $C_{24}H_{18}IN_3$ requires C, 60·6; H, 3·8; I, 26·7; N, 8·9%).

N-*Oxides of* 4,10-*Diphenyl*-1,2,9-*triazaphenanthrene*.—(*a*) The base (400 mg.) in glacial acetic acid (10 ml.) was treated with 30% hydrogen peroxide (2 ml.) and set aside for 24 hr. The mixture was poured into water and the solid was collected and dried at 80°; extraction with methanol (2 × 20 ml.) gave pale yellow needles of the starting material (150 mg.), m. p. 185—186°. Recrystallisation of the residue from 50% aqueous acetic acid gave the required N-*oxide* as yellow needles, m. p. 198—199° (Found: C, 79·7; H, 4·6; N, 12·4. $C_{23}H_{15}N_3O$ requires C, 79·1; H, 4·3; N, 12·0%).

(*b*) The base (200 mg.) in glacial acetic acid (3 ml.) was heated at 90—95° for 1 hr. with 30% hydrogen peroxide (1·2 ml.). The crystalline solid (190 mg.) which separated on cooling was recrystallised from 50% aqueous acetic acid, to yield the *di*-N-*oxide* as pale yellow needles, m. p. 293° (Found: C, 75·2; H, 3·9; N, 11·5. $C_{23}H_{16}N_3O_2$ requires C, 75·6; H, 4·1; N, 11·5%).

Reduction of 4,10-*Diphenyl*-1,2,9-*triazaphenanthrene*.—(*a*) The base (900 mg.) in ethanol (25 ml.) was heated under reflux and treated with sodium (2·5 g.; *ca.* 20 pieces) during ½ hr. The solution was poured into water (200 ml.), and the buff coloured precipitate (700 mg.) was collected, dried, and extracted with cold methanol (10 ml.) to remove starting material (150 mg.), m.p. and mixed m. p. 185—186°. The methanol solution was evaporated to an oily solid which, on recrystallisation from light petroleum (b. p. 60—80°), gave colourless needles of 1,2,3,4,9,10-*hexahydro*-4,10-*diphenyl*-1,2,9-*triazaphenanthrene*, m. p. 81—82° (Found: C, 80·4; H, 6·6; N, 12·0. $C_{23}H_{21}N_3$ requires C, 81·4; H, 6·2; N, 12·4%).

(*b*) The base (500 mg.) was dissolved in 33% aqueous acetic acid (3 ml.) and heated under reflux for 2 hr. with zinc amalgam (1 g.), cooled, treated with water (20 ml.), made alkaline with 4N-sodium hydroxide, extracted thrice with ether, and the extract concentrated to a pale yellow oil (320 mg.) which crystallised to an oily solid on standing. Recrystallisation from 50% benzene–light petroleum (b. p. 60—80°) gave plates of 1,4-*diphenylpyrrolo*[2,3-c]-*quinoline*, m. p. 75—76° (Found: C, 85·2; H, 5·3; N, 8·9. $C_{23}H_{16}N_2$ requires C, 86·2; H, 5·0; N, 8·8%).

3-*Methyl*-4-*phenyl*-1,2,9-*triazaphenanthrene*.— 1-(3-Amino-2-phenyl-4-quinolyl)-1-phenylpropene (1 g.) was dissolved in glacial acetic acid (4 ml.) and concentrated sulphuric acid (1·0 ml.), cooled, and treated dropwise at

0° with sodium nitrite (200 mg.) in water (2 ml.). The solution was allowed to stand until no coupling reaction was evident, and poured into water (20 ml.). The precipitate (850 mg.) was collected, washed with water, and treated with 2N-sodium hydroxide (20 ml.). The insoluble material (70 mg.) was filtered off, washed with water, and recrystallised from ethanol, to give yellow needles of the *triazaphenanthrene*, m. p. 192° (Found: C, 82·4; H, 5·0; N, 12·2. $C_{24}H_{17}N_3$ requires C, 83·0; H, 4·9; N, 12·1%). Neutralisation of the alkaline filtrate with 2N-hydrochloric acid gave a precipitate (600 mg.) which was collected, washed well with water, and recrystallised from methanol (charcoal), to yield needles of 1-(3-*hydroxy*-2-*phenyl*-4-*quinolyl*)-1-*phenylpropene*, m. p. 131—132° (Found: C, 84·7; H, 5·3; N, 5·2. $C_{24}H_{19}NO$ requires C, 85·4; H, 5·7; N, 4·2%).

Ethyl 3-*Aminoisonicotinate*.—A mixture of 3-amino-isonicotinic acid [17] (80 g.), ethanol (160 ml.), and concentrated sulphuric acid (80 ml.) was heated under reflux on a steam-bath for 30 hr., and the resulting solution poured into water (1 l.). Ether extraction of the basified (Na_2CO_3) mixture, and recrystallisation of the residue from light petroleum (b. p. 60—80°), yielded pale yellow needles (67 g., 69%) of the *ester*, m. p. 65° (Found: C, 57·2; H, 6·1; N, 16·8. $C_8H_{10}N_2O_2$ requires C, 57·7; H, 6·1; N, 17·3%).

2-(3-*Amino*-4-*pyridyl*)*propan*-2-*ol*.—A solution of the foregoing ester (66 g.) in dry benzene (1 l.) was added, with stirring during ½ hr., to a Grignard solution prepared from magnesium (38 g.) and methyl iodide (80 g.) in dry ether (1200 ml.). The mixture was heated under reflux for 4 hr., cooled, and worked up as usual. Continuous extraction with ether for 10 hr., and concentration of the ether solution to 100 ml., gave the *carbinol* (40·5 g., 61·4%) as long needles, m. p. 160—161° (from benzene) (Found: C, 62·3; H, 7·8; N, 18·6. $C_8H_{12}N_2O$ requires C, 63·1; H, 8·0; N, 18·4%).

2-(3-*Amino*-4-*pyridyl*)*propene*.—The carbinol (42 g.) was dissolved, with cooling, in concentrated sulphuric acid (300 ml.) and set aside at room temperature for 6 hr. The reaction mixture was worked up as usual, to give a pale yellow oil (32 g.). Attempts to crystallise this propene from light petroleum (b. p. 60—80°) failed but the *benzoyl derivative* (benzoyl chloride in pyridine) crystallised with difficulty from light petroleum (b. p. 60—80°) as prisms, m. p. 104° (Found: C, 75·4; H, 5·6. $C_{18}H_{14}N_2O$ requires C, 75·6; H, 5·9%); *picrate* small needles, m. p. 133° (Found: C, 45·4; H, 3·8; N, 18·8. $C_{14}H_{13}N_5O$ requires C, 46·3; H, 3·6; N, 19·3%).

Ethyl 3-*Amino*-2,6-*dimethylisonicotinate*.—A solution of 3-amino-2,6-dimethylisonicotinic acid hydrochloride [15] (15 g.) in ethanol (30 ml.) and concentrated sulphuric acid (15 ml.) was heated under reflux on a steam-bath for 15 hr. and worked up as usual. The ester (10·5 g., 61·4%) crystallised from light petroleum (b. p. 60—80°) as needles, m. p. 47—48° (Found: C, 62·5; H, 7·3; N, 14·0. $C_{10}H_{14}N_2O_2$ requires C, 61·8; H, 7·3; N, 14·4%).

2-(3-*Amino*-2,6-*dimethylpyridyl*)*propan*-2-*ol*.—This was prepared as usual from the foregoing ester (19 g.), magnesium (9·5 g.), methyl iodide (57 g.), and ether (350 ml.); the carbinol formed prisms (11 g., 57·3%), m. p. 113° [from 50% benzene–light petroleum (b. p. 60—80°)] (Found: C, 66·6; H, 9·2; N, 16·0. $C_{10}H_{16}N_2O$ requires C, 66·6; H, 8·95; N, 15·6%).

4-(3-*Amino*-2,6-*dimethylpyridyl*)*propene*.—Dehydration of the carbinol with boiling 50% v/v sulphuric acid formed a yellow oil which could not be made to crystallise; the *benzoyl derivative* (prepared in pyridine with benzoyl chloride) crystallised as small prisms, m. p. 155° (Found: C, 76·7; H, 7·0; N, 10·3. $C_{17}H_{18}N_2O$ requires C, 76·7; H, 6·8; N, 10·5%).

2-*Methyl*-6-*phenylcinchomeronimide*.—2-Methyl-6-phenylcinchomeronic acid [18] (50 g.) was heated on a steam-bath for 5 hr. with acetic anhydride (300 ml.), and the mixture concentrated to about 150 ml. under reduced pressure. The anhydride (39 g.), needles, m. p. 195—196° (lit.,[19] 196°) was mixed with acetamide (50 g.) and acetic anhydride (10 ml.), and heated to 125—130° (oil bath) under reflux, and retained at this temperature for 6 hr. The *imide* (24 g., 51·8%), which was washed with acetic acid and then water, formed needles, m. p. 163° (from acetone) (Found: C, 70·6; H, 4·2; N, 11·8. $C_{14}H_{10}N_2O_2$ requires C, 70·9; H, 4·5; N, 11·6%).

3-*Amino*-2-*methyl*-6-*phenylisonicotinic Acid*.—The well powdered imide (10 g.) was added at 0° to a stirred solution of bromine (7·4 g.) in sodium hydroxide (9·5 g. in 100 ml. of water). After 15 min. the mixture was heated at 70—80° for 1 hr., cooled, and acidified to Congo Red with concentrated hydrochloric acid. The solution was evaporated to dryness under reduced pressure and the residue extracted with ethanol (3 × 150 ml.). The combined extracts were treated with 5N-hydrochloric acid (10 ml.), and the solution was evaporated to about 30 ml. and cooled. The solid (17 g.) was collected and recrystallised from 2N-hydrochloric acid (charcoal), to provide pale yellow needles, m. p. 241—242°, of 3-*amino*-2-*methyl*-6-*phenylisonicotinic acid hydrochloride* (Found: C, 54·9; H, 5·9; Cl, 12·4; N, 9·9. $C_{13}H_{13}ClN_2O_2,H_2O$ requires C, 55·1; H, 5·3; Cl, 12·5; N, 9·9%). Attempts to obtain the free acid by neutralisation of aqueous solutions of the hydrochloride gave only gelatinous material.

Ethyl 3-*Amino*-2-*methyl*-6-*phenylisonicotinate*.—Prepared as usual from the amino-acid hydrochloride (50 g.), the *ester* (33 g., 63·2%) crystallised from light petroleum (b. p. 60—80°) as pale yellow needles, m. p. 90—91° (Found: C, 70·1; H, 6·5; N, 11·0. $C_{15}H_{18}N_2O_2$ requires C, 70·3; H, 6·3; N, 10·9%).

2-(3-*Amino*-2-*methyl*-6-*phenyl*-4-*pyridyl*)*propan*-2-*ol*.—Prepared as usual from the above ester (5·2 g.), magnesium (1·9 g.), and methyl iodide (11·5 g.) in ether (100 ml.) and benzene (100 ml.), the *carbinol* formed plates (2·6 g., 52·9%), m. p. 107° [from 50% benzene–light petroleum (b. p. 60—80°)] (Found: C, 74·3; H, 7·4; N, 11·6. $C_{15}H_{18}N_2O$ requires C, 74·4; H, 7·5; N, 11·6%).

2-(3-*Amino*-2-*methyl*-6-*phenyl*-4-*pyridyl*)*propene*.—Dehydration of the above carbinol (10 g.) by heating under reflux for 1 hr. with 18N-sulphuric acid (60 ml.), and isolation as usual, provided the propene (8·5 g.) as an uncrystallisable yellow oil; the *dibenzoyl deriative* (from benzoyl chloride in pyridine) formed small needles, m. p. 224—225° (from ethanol) (Found: C, 79·9; H, 5·9; N, 6·9. $C_{29}H_{24}N_2O_2$ requires C, 80·5; H, 5·6; N, 6·5%).

4-*Methyl*-1,2,7-*triazanaphthalene*.—(*a*) A solution of 2-(3-amino-4-pyridyl)propene (15 g.) in sulphuric acid (*d* 1·84; 8·5 ml.) and water (80 ml.) was treated with sodium nitrite (7·5 g.) in water (25 ml.), added during 15 min. at 0°. The solution was then poured into ice–water (300 g.) and set aside for 3 days in the dark at room temperature.

[17] S. Gabriel and J. Colman, *Ber.*, 1902, **35**, 2831.
[18] Y.-S. Kao and R. Robinson, *J. Chem. Soc.*, 1955, 2865.
[19] O. Mumm and R. Neumann, *Ber.*, 1926, **59**, 1616.

After 2 days (the solution no longer coupled with alkaline 2-naphthol) the solution was made alkaline with 4N-sodium hydroxide and continuously extracted with benzene (600 ml.) for 6 hr. The benzene solution was evaporated under reduced pressure, to yield a red oily product (4·4 g.) which solidified on standing. Chromatography on alumina 1 : 1 (v/v) benzene–light petroleum (b. p. 60—80°) gave 4-*methyl*-1,2,7-*triazanaphthalene* (2·8 g., 17·3%) as leaflets, m. p. 125° [from light petroleum (b. p. 60—80°)] (Found: C, 68·2; H, 4·8; N, 29·8. $C_8H_7N_3$ requires C, 68·2; H, 4·9; N, 28·9%); *picrate*, m. p. 255°, needles (from benzene) (Found: C, 44·0; H, 3·0; N, 22·4. $C_{14}H_{10}N_6O$ requires C, 44·9; H, 2·7; N, 22·5%); *methiodide*, red needles, m. p. 163—164° (Found: C, 38·1; H, 3·3; I, 43·9; N, 15·0. $C_9H_{10}IN_2$ requires C, 37·6; H, 3·5; I, 44·3; N, 14·6%).

(*b*) The propene (6·5 g.) in concentrated hydrochloric acid (32 ml.) and water (70 ml.) was diazotised with sodium nitrite (80 ml. of 5% solution) at 0°, set aside at 0° for 15 min., and treated at 0° with 4N-sodium hydroxide (120 ml.). After 24 hr. at room temperature the solution was continuously extracted with ether for 8 hr., to yield an oil (2·1 g.) from which 4-methyl-1,2,7-triazanaphthalene (0·8 g., 11·3%), m. p. 125°, was obtained by chromatography on alumina.

4-*Styryl*-1,2,7-*triazanapthalene*.—The base (500 mg.) was heated under reflux for 3 hr. with benzaldehyde (2 g.) and anhydrous zinc chloride (150 mg.). The mixture was cooled and treated with ether (25 ml.) and 2N-hydrochloric acid (10 ml.); the hydrochloride, in water (25 ml.), was basified with 2N-sodium hydroxide, and the dark solid filtered off, washed thoroughly with water, and recrystallised from methanol (charcoal), to provide the *product* (230 mg., 29%) as yellow plates, m. p. 95—96° (Found: C, 76·7; H, 4·5; N, 18·8. $C_{15}H_{11}N_3$ requires C, 77·2; H, 4·8; N, 18·0%).

1,2,7-*Triazanaphthalene*-4-*carboxylic Acid*.—The styryl derivative (250 mg.) was suspended in water and stirred at room temperature with potassium permanganate (500 mg.) added in small portions during about 15 min. The mixture was then heated at 35—40° for 15 min., cooled, filtered, and the precipitate washed with 2N-sodium hydroxide (10 ml.). The combined filtrates were evaporated to *ca.* 5 ml., neutralised with 4N-hydrochloric acid, and the solid (90 mg.) was collected and purified by precipitation from solution in sodium carbonate solution after decolorisation with charcoal. The *product* (60 mg., 31·7%) was obtained as buff coloured micro-crystals, m. p. 202—203° (Found: C, 54·5; H, 2·4; N, 23·0. $C_8H_5N_3O_2$ requires C, 54·9; H, 2·8; N, 24·0%).

4,6,8-*Trimethyl*-1,2,7-*triazanaphthalene*.—A solution of 2-(3-amino-2,6-dimethyl-4-pyridyl)propene (4·8 g.) in sulphuric acid (*d* 1·84; 3 ml.) and water (25 ml.) was diazotised at 0° with sodium nitrite (2·1 g.) in water (10 ml.). The solution was poured into ice and water (350 g.) and set aside in the dark at room temperature for 3 days. The solution was basified with 4N-sodium hydroxide and continuously extracted with benzene (600 ml.). Removal of the benzene under reduced pressure gave tarry material (1·4 g.) from which the *product* (750 mg., 14·6%), leaflets, m. p. 142—143° [from light petroleum (b. p. 40—60°)], was obtained by chromatography on alumina in 1 : 1 (v/v) benzene–light petroleum (b. p. 60—80°) (Found: C, 69·7; H, 6·7; N, 23·7. $C_{10}H_{11}N_3$ requires C, 69·3; H, 6·4; N, 24·3%). The *picrate* separated from ethanol as clusters of green needles, m. p. 181—182° (Found: C, 48·1; H, 3·6; N, 20·4. $C_{16}H_{14}N_6O_7$ requires C, 47·8; H, 3·5; N, 20·9%).

4,8-*Dimethyl*-6-*phenyl*-1,2,7-*triazanaphthalene*.—A solution of 2-(3-amino-2-methyl-6-phenyl-4-pyridyl)propene (4·5 g.) in sulphuric acid (*d* 1·84; 3 ml.) and water (25 ml.) was treated at 0° with sodium nitrite (1·4 g.) in water (10 ml.) and set aside at 0° for 10 min. The solution was diluted to about 400 ml. with ice–water and left at room temperature for 5 days. Alkali-insoluble products were obtained as in previous experiments by basification and continuous extraction with benzene. The resulting tar (350 mg.) was treated with ether (10 ml.), and the dark insoluble solid (120 mg.; m. p. 360°) removed. The ether-soluble fraction was dissolved in benzene (5 ml.) and treated with picric acid, to yield greenish yellow needles of the picrate, m. p. 217—218° (Found: C, 55·4; H, 3·1; N, 17·9. $C_{22}H_{17}N_6O_7$ requires C, 55·3; H, 3·6; N, 17·6%).

Ethyl 3-*Aminopicolinate*.—The method used was essentially that of Oakes, Pascoe, and Rydon,[20] but heating under reflux for 36 hr. was necessary for a good yield of the ester.

2-(3-*Amino*-2-*pyridyl*)*propan*-2-*ol*.—(*a*) A solution of ethyl 3-aminopicolinate (12 g.) in dry benzene (250 ml.) was added, with stirring during ½ hr., to a Grignard solution prepared from magnesium (5·2 g.) and methyl iodide (33 g.) in dry ether (250 ml.) and previously filtered through kieselguhr in an atmosphere of dry nitrogen. After heating under reflux for 4 hr. the mixture was worked up as usual and yielded an oily carbinol (8·5 g.). Benzoylation with benzoyl chloride in pyridine gave the *product* as plates, m. p. 129—130° (Found: C, 69·7; H, 6·2; N, 11·4. $C_{15}H_{16}N_2O_2$ requires C, 70·3; H, 6·2; N, 11·0%).

(*b*) The above reaction between the ester (20·5 g.) was repeated but without filtration of the Grignard solution, prepared from magnesium (9·0 g.) and methyl iodide (53 g.) in ether (400 ml.). Treatment of the reaction mixture as described above gave an oily product which, on treatment with ether (50 ml.), gave the carbinol (10 g.) and the *pinacol* (3·4 g.) which crystallised from benzene as yellow needles, m. p. 156° (Found: C, 61·6; H, 5·7; N, 20·9. $C_{14}H_{18}N_4O_2$ requires C, 61·4; H, 6·5; N, 20·5%). The pinacol (300 mg.), in concentrated hydrochloric acid (10 ml.), was heated under reflux for 1 hr., poured into water (10 ml.), and neutralised with sodium carbonate. The pale yellow oily product (230 mg.) was dissolved in benzene (5 ml.), filtered from a small amount of inorganic material, and the product (180 mg.) recrystallised from 1 : 1 benzene–light petroleum (b. p. 60—80°), to yield the *pinacolone* as needes, m. p. 154° (Found: C, 66·4; H, 5·7; N, 21·4. $C_{14}H_{16}N_4O$ requires C, 65·6; H, 6·3; N, 21·9%).

2-*Acetyl*-3-*aminopyridine*.—The pinacol (800 mg.) was dissolved in glacial acetic acid (12 ml.), treated with chromium trioxide (250 mg.), and heated on a steam-bath for 45 min. The solution was poured into water (50 ml.), neutralised with sodium carbonate, extracted thrice with ether, and the dried ($MgSO_4$) extract was evaporated to dryness. The oil (220 mg.) solidified after several hours at 0°, and crystallised from light petroleum (b. p. 40—60°) as yellow *plates*, m. p. 63—64° (Found: C, 61·3; H, 5·6; N, 20·4. $C_7H_8N_2O$ requires C, 61·7; H, 5·9; N, 20·6%). The 2,4-*dinitrophenylhydrazone hydrochloride* formed needles, m. p. 276—277° (from glacial acetic acid) (Found: C, 44·1; H, 3·9; Cl, 10·6; N, 25·7. $C_{13}H_{13}ClN_6O_4$ requires C, 44·2; H, 3·7; Cl, 10·1; N, 23·8%).

[20] V. Oakes, R. Pascoe, and H. N. Rydon, *J. Chem. Soc.*, 1956, 1045.

2-(3-*Benzamido*-2-*pyridyl*)*propene*.—The oily carbinol (12·0 g.) was dissolved in 18N-sulphuric acid (100 ml.), heated under reflux for 45 min., and the mixture worked up as usual. Treatment of the oily propene with benzoyl chloride in pyridine gave the *product* as polyhedra, m. p. 85—86° [from light petroleum (b. p. 60—80°)] (Found: C, 75·7; H, 6·0; N, 11·45. $C_{15}H_{14}N_2O$ requires C, 75·6; H, 5·95; N, 11·75%); *picrate*, needles (from ethanol), m. p. 185—186° (Found: C, 45·3; H, 3·3; N, 18·8. $C_{14}H_{13}N_5O_7$ requires C, 46·3; H, 3·6; N, 19·3%). Attempted dehydration of the carbinol using iodine in boiling toluene failed.

4-*Methyl*-1,2,5-*triazanaphthalene*.—(*a*) The crude propene (6 g.) was dissolved in concentrated hydrochloric acid (25 ml.) and water (50 ml.), cooled to below 0°, and treated with solid sodium nitrite (2·5 g.). The clear solution was set aside for a further 10 min. at 0°, then warmed to 50—60°, when the solution darkened, much effervescence occurred, and the coupling reaction was negative after 10 min. The solution was basified with 4N-sodium hydroxide, extracted continuously with ether for 6 hr., and the uncrystallisable oil (600 mg.) converted into 2-(3-*chloro*-2-*pyridyl*)-*propene picrate* (350 mg.), a microcrystalline solid, m. p. 145° (from ethanol) (Found: C, 42·4; H, 3·45; Cl, 8·6; N, 14·7. $C_{14}H_{11}N_4O_7Cl,H_2O$ requires C, 41·9; H, 3·3; Cl, 8·9; N, 14·0%). Neutralisation of the mother-liquor gave an oily emulsion from which was extracted with ether (3 × 50 ml.) a pale yellow oil (3·5 g.). Vacuum-sublimation yielded 2-*acetyl*-3-*hydroxypyridine* (200 mg.) as long needles, m. p. 55—56° (Found: C, 60·4; H, 5·5; N, 10·1. $C_7H_7NO_2$ requires C, 61·3; H, 5·1; N, 10·2%). The residual oil solidified, and recrystallisation from light petroleum (b. p. 40—60°) gave needles, m. p. 52—53° of 2-(3-*hydroxy*-2-*pyridyl*)*propene* (Found: C, 63·2; H, 7·2; N, 8·9. C_8H_9NO,H_2O requires C, 62·8; H, 7·2; N, 9·2%).

(*b*) The propene (2 g.) was diazotised in hydrochloric acid (10 ml.; conc.) and water (40 ml.) with sodium nitrite (26 ml. of 5% solution). After 10 min. at 0° the solution was poured into water (300 ml.) and set aside for 5 days in the dark. The solution was basified with 4N-sodium hydroxide and continuously extracted with benzene, to yield, on evaporation, an oil (120 mg.) which could not be recrystallised from n-hexane, but gave 4-*methyl*-1,2,5-*triazanaphthalene picrate* (170 mg.), m. p. 228°, needles (from benzene) (Found: C, 44·1; H, 2·9; N, 22·4. $C_{14}H_{10}N_6O_7$ requires C, 44·9; H, 2·7; N, 22·5%).

4-*Amino*-2-*nitroacetophenone*.— 4-Amino-2-nitrobenzoic acid [21] (45 g.) was heated under reflux with thionyl chloride (125 ml.) for 15 min., the excess of thionyl chloride was removed, and the crude acid chloride was dissolved in dioxan (100 ml.) and added to a solution of magnesium (5·4 g.) in a mixture of diethyl malonate (35·5 g.), ethanol (20 ml.), and ether (25 ml.). The mixture was refluxed for 30 min., and shaken with sulphuric acid (250 ml.; 10% v/v) until all solid material had dissolved. The organic layer was removed, the mixture extracted with ether (2 × 100 ml.), and the combined extracts were washed with water, dried, and evaporated. The crude product was dissolved in a mixture of acetic acid (75 ml.), concentrated sulphuric acid (10 ml.), and water (50 ml.), and refluxed for 3 hr. The cooled mixture was basified with ammonia and the precipitate was collected, dried, and recrystallised from benzene. Recrystallisation from water gave 4-*amino*-2-*nitroacetophenone* as yellow needles (12 g., 26·7%), m. p. 133—134° (Found: C, 52·9; H, 4·45; N, 14·6. $C_8H_8N_2O_3$ requires C, 53·3; H, 4·8; N, 15·55%); 2,4-*dinitrophenylhydrazone*, red leaflets, m. p. 237° (from acetic acid) (Found: C, 47·4; H, 3·8. $C_{14}H_{14}N_4O_2$ requires C, 46·7; H, 3·4).

4-*Dimethylamino*-2-*nitroacetophenone*.— 4-Amino-2-nitroacetophenone (1·8 g.) was stirred under reflux with a solution of sodium carbonate (anhydrous; 14 g.) in water (35 ml.) and treated dropwise during 1 hr. with dimethyl sulphate (15 g.). After heating under reflux for a further ½ hr. the mixture was cooled. The solid (1·5 g., 72·4%) was recrystallised from ethanol, to give the *ketone* as pale yellow needles, m. p. 155—156° (Found: C, 57·6; H, 6·1; N, 13·7. $C_{10}H_{12}N_2O_2$ requires C, 57·7; H, 5·8; N, 13·5%).

2-*Amino*-4-*dimethylaminoacetophenone*.—To a solution of the nitro-compound (2·5 g.) in concentrated hydrochloric acid (25 ml.) was added, portionwise, stannous chloride dihydrate (10 g.). The mixture was heated under reflux for 5 min., cooled, and made alkaline with 4N-sodium hydroxide. The crude product (1·5 g.) obtained by extraction with ether, was recrystallised from isopropyl alcohol to give needles, m. p. 114—115°, of the *product* (Found: C, 66·9; H, 8·0; N, 15·9. $C_{10}H_{14}N_2O$ requires C, 67·4; H, 7·9; N, 15·7%).

Reaction of 2-*Amino*-4-*dimethylaminoacetophenone with Nitrous Acid*.—(*a*) A solution of the amine (0·8 g.) in glacial acetic acid (5 ml.) and 10N-sulphuric acid (5 ml.) was cooled to 0° and treated with sodium nitrite (0·2 g.) in small portions. This solution (1 ml.) coupled with 2-naphthol in alkaline solution to give the azo-compound which formed red crystals, m. p. 276—277° (from ethanol). The remainder of the solution was allowed to attain room temperature slowly (evolution of nitrogen was noted) and set aside for several days. It was heated to 75° for 15 min., cooled, diluted with water (25 ml.), and the solid (0·5 g.) was collected, washed, and dried. Recrystallisation from ethanol gave 4-dimethylamino-2-hydroxyacetophenone as needles, m. p. 121·5—122·5° (lit.,[22] 120°) (Found: C, 67·0; H, 7·60; N, 7·9. Calc. for $C_{10}H_{13}NO_2$: C, 67·0; H, 7·3; N, 7·8%). Further attempts to cyclise the diazonium salt in other acid media at both room temperature and at 70° gave the same hydroxy-ketone.

(*b*) To a solution of the amine (0·4 g.) in 5N-sulphuric acid (5 ml.) was added solid sodium nitrite (0·1 g.) the temperature being kept below 5°. After 5 min. the solution was treated with excess of 5N-sodium hydroxide (*ca.* 6 ml.). The mixture rapidly darkened and the solid (200 mg.) was collected, but no useful material could be obtained from this product.

The alkaline filtrate was neutralised with 2N-sulphuric acid but yielded only 4-dimethylamino-2-hydroxyacetophenone.

4-*Acetyl*-3-*aminopyridine*.— 2-(3-Benzamido-4-pyridyl) propene (5 g.) in acetic acid (100 ml.) was treated with ozonized oxygen (containing 5—6% ozone) at about 7 l. per hr. for 6 hr. at 15—20°. Hydrogen peroxide (100 vol.; 10 ml.) was added, and the solution heated on a steam-bath for 1 hr. After pouring into ice–water (100 g.), the mixture was partially neutralised with 4N-sodium hydroxide (50 ml.), and the colourless crystalline product (3·4 g.) was collected, washed with water, and dried at 60°. Recrystallisation from 50% aqueous ethanol gave 4-*acetyl*-3-*benzamidopyridine* as needles, m. p. 121—122° (Found: C, 69·3; H, 4·9; N, 11·4. $C_{14}H_{12}N_2O_2$ requires C, 70·0; H, 5·0; N,

[21] J. J. Blanksma and D. Hoegen, *Rec. Trav. chim.*, 1946, **65**, 333.

[22] H. V. Peckmann and M. Schall, *Ber.*, 1899, **32**, 3690.

11·7%). This (2 g.) was heated with concentrated hydrochloric acid (25 ml.) under reflux for 2 hr., to provide 4-*acetyl*-3-*aminopyridine* (0·9 g.) as yellow plates, m. p. 87° [from light petroleum (b. p. 80—100°)] (Found: C, 62·2; H, 6·15; N, 20·45. $C_7H_8N_2O$ requires C, 61·7; H, 5·9; N, 20·6%); 2,4-*dinitrophenylhydrazone hydrochloride*, pale yellow needles, m. p. 287—288° (decomp.) (from acetic acid) (Found: C, 44·5; H, 3·9; Cl, 9·8; N, 26·2. $C_{13}H_{13}ClN_8O_4$ requires C, 44·2; H, 3·7; Cl, 10·1; N, 23·8%).

2-*Acetyl*-3-*aminopyridine*.—Prepared as for the 4-acetyl derivative using 2-(3-benzamido-4-pyridyl)propene (5 g.), the crude product (4·1 g.) was recrystallised from 50% aqueous alcohol, to give needles of the *ketone* (3·7 g.), m. p. 89—90° (Found: C, 70·1; H, 4·8; N, 11·7. $C_{14}H_{22}N_2O_2$ requires C, 70·0; H, 5·0; N, 11·7%). Hydrolysis of the benzamido-compound (3 g.) as before gave the *amino-ketone* as yellow plates, m. p. 63—64° [from light petroleum (b. p. 40—60°)]. The acetyl compound was identical (mixed m. p.) with the product obtained by chromium trioxide oxidation of the pinacol (described above) from a Grignard reaction between ethyl 3-aminopicolinate and methylmagnesium iodide.

Action of Nitrous Acid on 4-*Acetyl*-3-*aminopyridine*.—(*a*) A solution of the ketone (250 mg.) in acetic acid (3 ml.) and concentrated sulphuric acid (1 ml.) was treated with solid sodium nitrite (100 mg.) at 0°, set aside for 5 min., and then slowly heated to 50—60° on a water-bath. After the vigorous effervescence subsided the solution was cooled, poured into water (10 ml.), and neutralised with 4N-sodium hydroxide. Extraction of the yellow solution with chloroform (2 × 50 ml.) and evaporation of the dried chloroform extract gave 4-acetyl-3-hydroxypyridine as an uncrystallisable oil (190 mg.); 2,4-*dinitrophenylhydrazone*, needles, m. p. 248—249° (from acetic acid) (Found: C, 49·5; H, 3·8; N, 21·6. $C_{13}H_{11}N_5O_5$ requires C, 49·2; H, 3·5; N, 22·1%).

(*b*) The ketone (250 mg.) was dissolved in concentrated hydrochloric acid (2 ml.) and water (8 ml.), and the clear solution treated at 0° with solid sodium nitrite (100 mg.). The solution was allowed to stand for 5 min. and was then treated with excess of 5N-sodium hydroxide (about 10 ml.) below 0°. The mixture rapidly darkened, with much frothing, and the dark solid (130 mg.) was collected after 1 hr. at room temperature. Attempted recrystallisation of this material did not afford any well defined compound but solid which separated from 50% acetic acid had m. p. 360°.

Neutralisation of the alkaline filtrate with 4N-hydrochloric acid gave more brown intractable material (40 mg.) of high m. p.

Action of Nitrous Acid on 2-*Acetyl*-3-*aminopyridine*.—(*a*) A solution of the amino-ketone (250 mg.) in concentrated hydrochloric acid (4 ml.) was treated at 0° with sodium nitrite (100 mg.). More concentrated hydrochloric acid (6 ml.) was added and the solution was heated to 60° on a water-bath for about 1 hr. (effervescence and coupling ceased after 10 min.). The solution was concentrated to about 2 ml. under reduced pressure, make alkaline with ammonia, and the oil was extracted with ether, to provide material (40 mg.) which contained chlorine and was probably 2-acetyl-3-chloropyridine. The aqueous solution was neutralised with 2N-hydrochloric acid, and extracted with ether, to provide a yellow oil (130 mg.) which solidified on standing. Vacuum-sublimation provided 2-acetyl-3-hydroxypyridine, m. p. 55—56°, identical with material obtained (above) during the diazotisation of 2-(3-amino-2-pyridyl)propene; 2,4-*dinitrophenylhydrazone*, orange-yellow needles, m. p. 261—262° (from acetic acid) (Found: C, 49·5; H, 3·6; N, 21·5. $C_{13}H_{11}N_5O_6$ requires C, 49·2; H, 3·5; N, 22·1%).

(*b*) The amino-ketone (100 mg.) was diazotised in concentrated hydrochloric acid (1 ml.) and water (5 ml.) with solid sodium nitrite (40 mg.) below 0°, and after 5 min. 2N-sodium hydroxide (10 ml.) was added. The solution darkened rapidly, gas was evolved, and a dark brown precipitate (55 mg.), m. p. 300°, separated; this would not crystallise. Neutralisation of the alkaline filtrate with 2N-hydrochloric acid yielded a red-brown solid (20 mg.), m. p. 320—340°.

4-*Hydroxy*-3-*methyl*-10-*phenyl*-1,2,9-*triazaphenanthrene*.—(*a*) A hot solution of 3-amino-2-phenyl-4-propionylquinoline (1·0 g.) in concentrated hydrochloric acid (2·5 ml.) and water (10 ml.) was cooled to −5°, and the finely divided suspension treated below 0° with sodium nitrite (250 mg.) in water (5 ml.) during 5 min. The solution was then treated with 6N-sodium hydroxide (10 ml.) and allowed to warm to room temperature during 2 hr. A small amount of precipitate was filtered off and the orange-yellow solution was neutralised with 5N-hydrochloric acid. The precipitate (900 mg.) was collected, dried, and recrystallised from ethanol, to give leaflets, m. p. 202°, of the *product* (Found: C, 75·2; H, 4·6; N, 14·6. $C_{18}H_{13}N_3O$ requires C, 76·0; H, 5·0; N, 14·7%).

(*b*) The amino-ketone (500 mg.) was dissolved in concentrated hydrochloric acid (1·5 ml.) and treated at 0° with sodium nitrite (150 mg.) in water (1 ml.). After a few minutes, concentrated hydrochloric acid (10 ml.) was added and the mixture heated at 60° for 2 hr. (nitrogen evolved). Excess of hydrochloric acid was removed under reduced pressure and the residue neutralised with a concentrated solution of sodium acetate. The oily solid (400 mg.) was collected, dried, and digested with n-hexane, to yield an insoluble fraction [80 mg.; m. p. and mixed m. p. with the product from (*a*) 195—197°] and a soluble fraction, m. p. 83—84°, identified as *ethyl*-3-*chloro*-2-*phenyl*-4-*quinolyl ketone* (Found: C, 72·6; H, 4·6; Cl, 11·6; N, 4·5. $C_{18}H_{14}ClNO$ requires C, 73·1; H, 4·8; Cl, 12·0; N, 4·7%).

4-*Chloro*-3-*methyl*-10-*phenyl*-1,2,9-*triazaphenanthrene*.—The hydroxy-compound (600 mg.), phosphorus pentachloride (900 mg.), and phosphoryl chloride (4·5 ml.) were heated together under reflux for 2 hr. The excess of phosphoryl chloride was distilled under reduced pressure and the residue was shaken with benzene (25 ml.), ice (20 g.), and 3N-sodium hydroxide (10 ml.). The benzene layer was collected, the aqueous layer extracted twice with further benzene, and the combined benzene extracts were dried ($MgSO_4$) and evaporated, to yield a solid (550 mg.), m. p. 180—183°. The *chloro-compound*, m. p. 186°, crystallised from ethyl acetate as blades (Found: C, 71·0; H, 4·3; Cl, 12·1; N, 12·6. $C_{18}H_{12}ClN_3$ requires C, 70·7; H, 4·0; Cl, 11·6; N, 13·7%).

3-*Methyl*-4-*phenoxy*-10-*phenyl*-1,2,9-*triazaphenanthrene*.—The chloro-compound (300 mg.) was heated on a steam-bath for 2 hr. with potassium hydroxide (100 mg.) in phenol (1·5 g.). The product was cooled, digested with warm 2N-sodium hydroxide (25 ml.), and the solid (300 mg.) recrystallised from methyl acetate, from which the pure phenoxy-compound separated as needles, m. p. 159—160° (Found: C, 79·3; H, 4·8; N, 11·3. $C_{24}H_{17}N_3O$ requires C, 79·3; H, 4·7; N, 11·6%).

4-*Amino*-3-*methyl*-10-*phenyl*-1,2,9-*triazaphenanthrene*.—(*a*) The phenoxy-compound (200 mg.) was heated in an open tube with ammonium acetate (2 g.) at 180—200°

in an oil-bath for 3 hr., the ammonium acetate being renewed when necessary. The cold mixture was digested with 2N-sodium hydroxide, and the well washed crude product (110 mg.) was recrystallised from nitromethane, to provide pale brown needles of the *amine*, m. p. 245—246° (Found: C, 72·6; H, 5·0; N, 17·6. $C_{18}H_{14}N_4,H_2O$ requires C, 71·1; H, 5·3; N, 18·4%); *methiodide*, needles (from methanol), m. p. 263° (decomp.) (Found: C, 52·9; H, 3·75; I, 29·2; N, 12·8. $C_{19}H_{17}IN_4$ requires C, 53·2; H, 4·0; I, 29·7; N, 13·1%).

(*b*) A stream of dry ammonia was passed for ½ hr. through a solution of the phenoxy-compound (100 mg.) in acetamide (1 g.) at 175° ± 5°. The mixture was cooled, diluted with water, and the precipitate (65 mg.), m. p. 225—230°, washed and dried. Recrystallisation from nitromethane gave the amine, m. p. 245—246°.

4-*Methoxy*-3-*methyl*-10-*phenyl*-1,2,9-*triazaphenanthrene*.—The chloro-compound (100 mg.) was heated under reflux for 2 hr. with methanolic sodium methoxide prepared from sodium (0·25 g.) and methanol (15 ml.). The *methoxy-compound* formed needles, m. p. 201—202° (from ethyl alcohol) (Found: C, 76·2; H, 5·1; N, 14·4. $C_{19}H_{18}N_3O$ requires C, 75·7; H, 5·0; N, 14·0%).

N-*Methyl*-3-*methyl*-4-*oxo*-10-*phenyl*-1,2,9-*triazaphenanthrene*.—A cold solution of the hydroxy-compound (100 mg.) in 3N-sodium hydroxide (2 ml.) was treated with dimethyl sulphate and the suspension was heated at *ca.* 50° for 5 min. The *derivative*, m. p. 243—244°, crystallised from ethyl alcohol as leaflets (Found: C, 75·6; H, 5·0; N, 13·9. $C_{19}H_{15}N_3O$ requires C, 75·7; H, 5·0; N, 14·0%).

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