755. *Internuclear Cyclisation. Part XVII.* The Independent Synthesis of Some* N-*Methylbenzophenanthridones and Their Formation by Internuclear Cyclisation.*

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Unambiguous syntheses of *N*-methyl-1,2-, -2,3-, and -3,4-benzophenanthridones are reported. *N*-Methyl-3,4- and -5,6-benzophenanthridones could be isolated from the appropriate internuclear cyclisations but *N*-methyl-1,2- and -2,3-benzophenanthridones could not. Discrepancies in the literature of these compounds are clarified and mechanisms are suggested for the formation of certain anomalous products of internuclear cyclisation. A convenient preparation of 1-amino-2-naphthoic acid is reported.

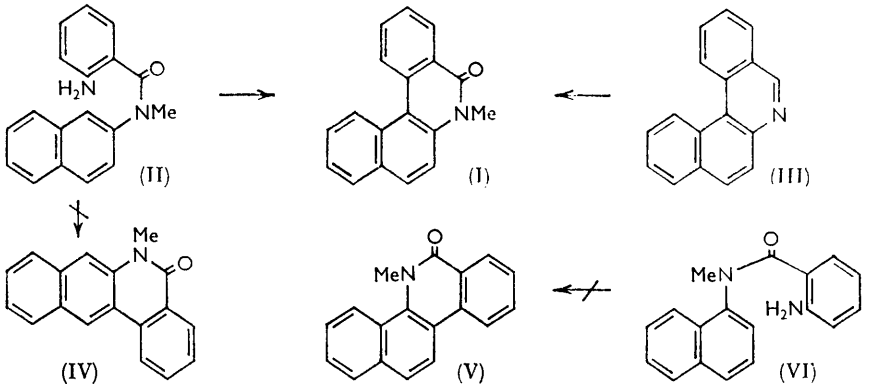
Earlier Parts [1] of this series have described the extension of the Pschorr reaction to the preparation of phenanthridones. Further extension [2,3] to the preparation of benzophenanthridones has led to complex reactions giving a variety of, often isomeric, products. It therefore became desirable to synthesise the expected products of ring closure, the *N*-methylbenzophenanthridones, by independent and unambiguous methods.

N-*Methyl*-3,4-*benzophenanthridone* (I).—Decomposition of the diazonium fluoroborate,

* Part XVI, *J.*, 1961, 232.

[1] Heacock and Hey, *J.*, 1952, 1508, 4059; 1953, 3.
[2] Hey and Turpin, *J.*, 1954, 2471.
[3] Abramovitch, Hey, and Long, *J.*, 1957, 1781.

prepared from 2-amino-*N*-methylbenzo-2′-naphthalide (II), with copper powder in acetone gave a compound, m. p. 198—199°, considered to be *N*-methyl-3,4-benzophenanthridone (I), the product of normal ring-closure.[2] However, this structure was later [4] assigned to another compound, m. p. 120—121°, prepared by methylation of 3,4-benzophenanthridone, a product of the Schmidt reaction on 3,4-benzofluorenone. Reaction with methyl iodide and subsequent oxidation of 3,4-benzophenanthridine (III), under different condi-



tions, was reported to give products with melting points 195—198° [2] and 120—121° [4] identical with the above compounds. Investigation of this anomaly started with an unequivocal synthesis of 3,4-benzophenanthridine (III), since the earlier syntheses contained elements of ambiguity. 2-Nitro-1-naphthylamine was prepared by Saunders and Hamilton's method,[5] that of Meisenheimer and Patzig [6] having failed in our hands. This amine was converted into 2-nitro-1-phenylnaphthalene by a Gomberg reaction [7] and by decomposition of the corresponding diazonium fluoroborate in benzene containing acetone, copper powder, and magnesium sulphate.[8] Reduction of this nitro-compound to the amine and ring closure of the formyl derivative with polyphosphoric acid gave 3,4-benzophenanthridine (III), identical with that previously described.[2,9] Ring closure of the corresponding acetamido-derivative failed. Reaction of the base (III) with methyl iodide and subsequent oxidation by the methods of Hey and Turpin [2] and Keene and Schofield [4] both gave *N*-methyl-3,4-benzophenanthridone with m. p. 119—120°, in agreement with the latter workers. The nature of the isomeric product, m. p. 198—199°, from 2-amino-*N*-methylbenzo-2′-naphthalide (II) is being investigated; this reaction has now been shown [10] to yield the normal cyclisation product, m. p. 119—120°, in addition to the compound, m. p. 198—199°.

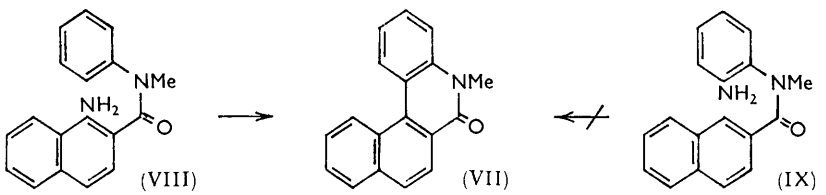
N-*Methyl*-2,3-*benzophenanthridone* (IV).—The compound with m. p. 198—199° obtained by reaction with 2-amino-*N*-methylbenzo-2′-naphthalide (II) could have been *N*-methyl-2,3-benzophenanthridone (IV) resulting from ring closure at the β-position of the naphthalene ring. Neither this compound nor 2,3-benzophenanthridine has been described previously. Unequivocal syntheses from the relatively inaccessible 2,3-disubstituted naphthalenes are now described. 6-Acetamido-1,2,3,4-tetrahydro-7-nitronaphthalene [11] was dehydrogenated by Barnes's method [12] and hydrolysed,[11] and the 3-nitro-2-naphthylamine converted, *via* its diazonium fluoroborate, into 2-nitro-3-phenylnaphthalene and thence into

[4] Keene and Schofield, *J.*, 1958, 2609.
[5] Saunders and Hamilton, *J. Amer. Chem. Soc.*, 1932, **54**, 636.
[6] Meisenheimer and Patzig, *Ber.*, 1906, **39**, 2533.
[7] Hey and Lawton, *J.*, 1940, 374.
[8] Dr. J. I. G. Cadogan, personal communication.
[9] Mills and Schofield, *J.*, 1956, 4213.
[10] Hey, Rees, and Wessels, unpublished work.
[11] Ward and Coulson, *J.*, 1954, 4545.
[12] Barnes, *J. Amer. Chem. Soc.*, 1948, **70**, 145.

3-phenyl-2-naphthylamine. As the overall yield by this method was low a new route was developed. The diazonium fluoroborate prepared from ethyl 3-amino-2-naphthoate [13] was decomposed in benzene to give ethyl 3-phenyl-2-naphthoate, which was hydrolysed to 3-phenyl-2-naphthoic acid, identical with that prepared [14] from 2-fluoronaphthalene, phenyl-lithium, and carbon dioxide. This acid was converted into 3-phenyl-2-naphthylamine *via* the azide by Weisburger and Weisburger's method [15] without the isolation of the intermediates. Formylation of this amine followed by cyclodehydration with polyphosphoric acid gave 2,3-benzophenanthridine, which was treated with methyl iodide and then oxidised, as before, to *N*-methyl-2,3-benzophenanthridone (IV), m. p. 174—175°. This was not identical with the product, m. p. 198—199°, described above.

N-*Methyl*-1,2-*benzophenanthridone* (V).—It has been reported [2] that the diazonium fluoroborate prepared from 2-amino-*N*-methylbenzo-1′-naphthalide (VI) was decomposed by copper powder in acetone to give benzo-1-naphthalide and two unidentified products. The expected product of ring closure is *N*-methyl-1,2-benzophenanthridone, previously unreported in spite of the ready availability of 1,2-benzophenanthridone.[16] Methylation of the latter proved to be unusually difficult, the normal methods, including use of methyl toluene-*p*-sulphonate, failed presumably because of the same steric hindrance which retards the reaction of 1,2-benzophenanthridine with methyl iodide.[17] Prolonged boiling of 1,2-benzophenanthridone with methyl iodide and potassium hydroxide in methyl propyl ketone gave the methylated product, m. p. 98—100°, in small yield. This, however, was not identical with either of the unidentified products from the reaction with 2-amino-*N*-methylbenzo-1′-naphthalide (VI).

N-*Methyl*-5,6-*benzophenanthridone* (VII).—A second product obtained by Keene and Schofield [4] in the Schmidt reaction with 3,4-benzofluorenone mentioned above was methylated to give *N*-methyl-5,6-benzophenanthridone (VII), m. p. 140—141°, which could also result from normal ring closure of the diazonium chloride prepared from 1-amino-*N*-methyl-2-naphthanilide (VIII).[3] This compound was in fact thus obtained with m. p.

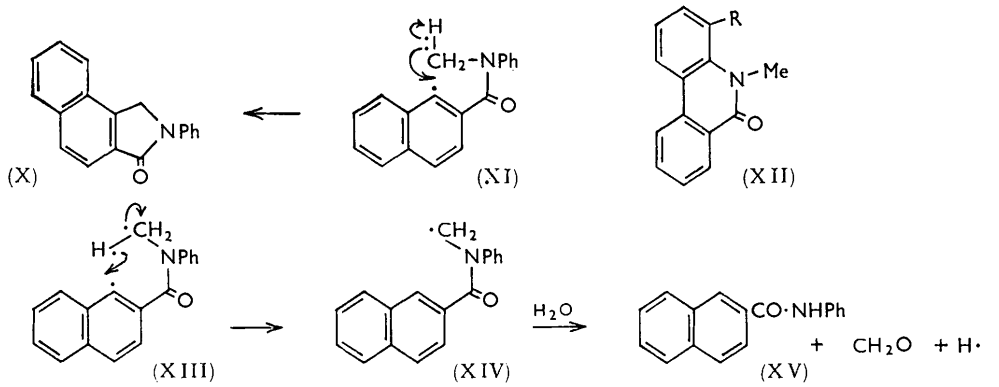


137°, but not identified, and later shown to be identical with the compound, m. p. 140—141°, by a comparison of their infrared spectra. However, this phenanthridone structure was originally assigned [3] to an isomer, m. p. 158—159°, similarly obtained from the closely related *N*-methyl-*N*-2-naphthoyl-*o*-phenylenediamine (IX). The earlier preparation [3] of 1-amino-*N*-methyl-2-naphthanilide (VIII) started from the inaccessible 1-nitro-2-naphthoic acid. In a repetition of the preparation an improved synthesis of 1-amino-2-naphthoic acid was developed from 1-naphthylamine by converting it into α-naphthoxindole,[18] then into hydroxyimino-α-naphthoxindole,[18] and oxidation of the latter with alkaline 30% hydrogen peroxide. The *N*-methyl-anilide (VIII) of this amino-acid gave, on decomposition of its diazonium chloride, the same products as before,[3] namely, 2-naphthanilide and two compounds (probably isomers) with m. p.s 137° and 185°, the former now recognised as *N*-methyl-5,6-benzophenanthridone (VII). The compound of m. p. 185° may, like

[13] Möhlau, *Ber.*, 1895, **28**, 3096.
[14] Huisgen and Rist, *Annalen*, 1955, **594**, 151.
[15] Weisburger and Weisburger, *J. Org. Chem.*, 1958, **23**, 1193.
[16] Caronna, *Gazzetta*, 1941, **71**, 481.
[17] Ritchie, *J. Proc. Roy. Soc. New South Wales*, 1944, **78**, 173.
[18] Hinsberg, *Ber.*, 1888, **21**, 110.

the other similar reaction products, be a phthalimidine, in this case 2-phenyl-4,5-benzophthalimidine (X). This structure has been assigned [19] to a compound of m. p. 177°, formed from 1-naphthaldehyde anil and carbon monoxide at high temperature and pressure.

Formation of a phthalimidine in this reaction would result from attack (see XI) of the *N*-methyl instead of the *N*-phenyl group by the diazonium centre, reacting either as a free radical or as a carbonium ion, depending on experimental conditions, with loss of nitrogen and a hydrogen atom or proton, respectively. This mechanism is similar to that thought to be responsible for the abnormal deamination and dealkylation which occur when ring closure on to an anilide ring bearing an *ortho*-substituent, to form (XII), is attempted.[2] Formation of the new intramolecular bond is prevented, regardless of the electronic character of the *ortho*-substituent (*e.g.*, R = Me, Et, Cl, NO_2, CO_2H), presumably because of the strong repulsion between this substituent and the *N*-alkyl group as the planar configuration of the product is approached (see XII). In accordance with this view, normal ring closure occurs once more when the *ortho*- and *N*-substituents form part of a five-membered ring where this steric repulsion is absent.[20] The deamination and dealkylation, which always occur together, would result from attack of the diazonium centre, again either as a free radical, as shown in (XIII) ⟶ (XIV) ⟶ (XV), or carbonium ion, on a hydrogen of the *N*-methyl group.



Evidence for this mechanism is provided by the isolation of benzaldehyde after decomposition of the diazonium sulphate prepared from 2-amino-*N*-benzyl-*o*-benzotoluidide.[21] It is difficult to predict whether reaction *via* the five-membered cyclic transition state (XI) or the six-membered cyclic transition state (XIII) will predominate. Closely related mechanisms, in the ionic form, have been suggested independently by Cohen, Moran, and Sowinski,[22] conversions of the type (XIII) ⟶ (XIV), for example, being regarded as a 1,5-shift of a hydride ion.

Experimental

Light petroleum refers to the fraction of b. p. 40—60°.

2-Nitro-1-phenylnaphthalene.—(*a*) A solution of 2-nitronaphthalene-1-diazonium sulphate was prepared from 2-nitro-1-naphthylamine [5] (5·6 g.) in glacial acetic acid (30 ml.) and sodium nitrite (2·5 g.) in concentrated sulphuric acid (25 ml.) at 0—5°. Benzene (125 ml.) was added, followed by sodium hydroxide solution until the aqueous layer was alkaline. Stirring was continued overnight, the benzene layer was separated, and the aqueous layer extracted with more benzene. The combined benzene solution was dried (Na_2SO_4), the solvent removed, the dark residue was dissolved in ethanol and treated with charcoal, and the ethanol was removed. The residue, in benzene, was thoroughly washed with 5N-hydrochloric acid, followed

[19] Murahashi, *J. Amer. Chem. Soc.*, 1955, **77**, 6403.
[20] See Plant and Tomlinson, *J.*, 1932, 2188; Humber *et al.*, *J.*, 1954, 4622.
[21] Turpin, Ph.D. Thesis, Univ. of London, 1955.
[22] Cohen, Moran, and Sowinski, *J. Org. Chem.*, 1961, **26**, 1.

by water. The dried (Na_2SO_4) benzene solution was reduced in volume and passed over alumina which was then eluted with benzene to yield a solid (0·48 g.), m. p. 111—113°. Crystallisation from light petroleum gave 2-*nitro*-1-*phenylnaphthalene* in pale yellow needles (0·44 g.), m. p. 128—130° (Found: C, 77·1; H, 4·4. $C_{16}H_{11}NO_2$ requires C, 77·1; H, 4·5%).

(*b*) 2-Nitro-1-naphthylamine (2 g.) in sulphuric acid (10 ml.) and water (20 ml.) was diazotised with sodium nitrite (1 g.) in water (10 ml.), and the solution was stirred at 0° for 1 hr., filtered, and diluted with water (10 ml.). Sodium fluoroborate (2·5 g.) in water (10 ml.) was then added slowly at 0° with stirring and after 15 min. the precipitate was collected, washed with ice-water, ice-cold ethanol, and ether, and dried *in vacuo*. Crystallisation from acetone–ether gave 2-*nitronaphthalene*-1-*diazonium fluoroborate* (0·6 g.), m. p. 127° (Found: C, 41·5; H, 3·0. $C_{10}H_6BF_4N_3O_2$ requires C, 41·8; H, 2·1%). This fluoroborate (1 g.) was added to a vigorously stirred suspension of magnesium sulphate (7 g.) and copper powder (2·5 g.) in benzene (50 ml.) and acetone (5 ml.).[8] The mixture was stirred for 5 hr., set aside overnight, and filtered, and the solid was extracted with hot benzene (5 × 50 ml.). The combined solutions were reduced in volume and passed over alumina; elution with benzene yielded a solid which crystallised from light petroleum to give 2-nitro-1-phenylnaphthalene (0·2 g.), m. p. 128—130°, identical with the product prepared by method (*a*).

1-*Phenyl*-2-*naphthylamine*.—To a hot solution of this nitro-compound (0·4 g.) and hydrazine hydrate (1 ml.) in ethanol (80 ml.) enough Raney nickel was added to decompose the hydrazine completely. After 1 hr. the solution was boiled and filtered, the filtrate was evaporated, and the residual gum was dried *in vacuo* over sulphuric acid. Crystallisation from light petroleum gave the amine (0·3 g.), m. p. 93—94°, as recorded in the literature.[9,23]

3,4-*Benzophenanthridine*.—2-Formamido-1-phenylnaphthalene [9] was stirred with an excess of polyphosphoric acid at 150° for 2 hr. The mixture was allowed to cool to 60° and poured with stirring on ice. An excess of aqueous ammonia was added and the precipitate crystallised from light petroleum in colourless needles of 3,4-benzophenanthridine, m. p. 108—110°, identical with that prepared by Hey and Turpin.[2] No crystalline solid could be isolated from similar treatment of the corresponding acetyl derivative.

2-*Acetamido*-3-*nitronaphthalene* (cf. ref. 12).—6-Acetamido-1,2,3,4-tetrahydro-7-nitronaphthalene [11] (0·44 g.) was boiled under reflux with *N*-bromosuccinimide (0·68 g.) and benzoyl peroxide (0·02 g.) in carbon tetrachloride (60 ml.) for 1 hr. Acetic acid (1 ml.) and fused potassium acetate (3 g.) were then added and boiling was continued for a further hour. The mixture was cooled and poured on ice and sodium hydroxide (2 g.) with stirring. The product was extracted with ether, and the extracts were dried (Na_2SO_4) and evaporated. Crystallisation of the residue from light petroleum gave the yellow nitro-amide (0·17 g.), m. p. 130—131°, in agreement with Ward and Coulson.[11]

2-*Nitro*-3-*phenylnaphthalene*.—3-Nitro-2-naphthylamine [11] (0·5 g.) in sulphuric acid (2·5 ml.) and water (5 ml.) was diazotised with sodium nitrite (0·5 g.) in water (2·5 ml.) and then treated with sodium fluoroborate (1 g.) in water (5 ml.) as described above. Crystallisation from acetone–ether gave 3-*nitronaphthalene*-2-*diazonium fluoroborate* (0·44 g.), m. p. 130—132° (decomp.) (Found: C, 42·6; H, 2·35. $C_{10}H_6BF_4N_3O_2$ requires C, 41·8; H, 2·1%). The fluoroborate (0·8 g.) was decomposed in benzene (80 ml.) containing acetone (8 ml.), magnesium sulphate (8 g.), and copper powder (3 g.) as described above. The product was similarly purified by chromatography on alumina, followed by several crystallisations from light-petroleum, to give yellow 2-*nitro*-3-*phenylnaphthalene* (0·11 g.), m. p. 99—101° (Found: C, 76·8; H, 4·6. $C_{16}H_{11}NO_2$ requires C, 77·1; H, 4·5%).

3-*Phenyl*-2-*naphthoic Acid*.—Ethyl 3-amino-2-naphthoate [13] (2 g.) was diazotised in hydrochloric acid and converted, as described above, into 3-ethoxycarbonylnaphthalene-2-diazonium fluoroborate (2·33 g.), m. p. 140—142° (decomp.) (from acetone–ether) (Found: C, 50·4; H, 3·5. $C_{13}H_{11}BF_4N_2O_2$ requires C, 49·7; H, 3·5%). This was decomposed in benzene as in the previous example. Evaporation of the combined benzene solutions left a gum which was hydrolysed with aqueous-ethanolic potassium hydroxide. After removal of the ethanol, alkali-insoluble material was extracted with ether, and the aqueous solution was acidified. The dried precipitate crystallised from light petroleum to give 3-phenyl-2-naphthoic acid (1·5 g.), m. p. 165—166°, converted by concentrated sulphuric acid into 2,3-benzofluorenone, m. p. 150—151°. Huisgen and Rist [14] record m. p.s 163—166° and 150—151°, respectively, for these two compounds.

[23] Zaugg, Freifelder, and Horrom, *J. Org. Chem.*, 1950, **15**, 1197.

Methyl anthranilate was similarly converted into *o-methoxycarbonylbenzenediazonium fluoroborate* (41%), m. p. 99—101° (decomp.) (Found: C, 39·3; H, 2·9. $C_8H_7BF_4N_2O_2$ requires C, 38·4; H, 2·8%), which decomposed in benzene under the above conditions to yield methyl biphenyl-2-carboxylate (21%), b. p. 308°.

3-Phenyl-2-naphthylamine (cf. ref. 15).—3-Phenyl-2-naphthoic acid (0·7 g.) was converted with thionyl chloride into its acid chloride. To a stirred solution of the latter in acetone (25 ml.), sodium azide (0·3 g.) in water (2 ml.) was added in the cold and the stirring continued for 3 hr., then water (36 ml.) was added and the solution extracted with ether. The dried (Na_2SO_4) ethereal solution was evaporated and the residual gum was heated under reflux with acetic anhydride (5 ml.) for 3 hr. Acetic anhydride was removed *in vacuo* and the residue hydrolysed during 3 hr. by boiling ethanolic hydrochloric acid. The mixture was filtered hot, boiled to remove ethanol, and basified at 0° with aqueous ammonia. A buff solid, obtained by extraction with ether, crystallised from light petroleum to give *3-phenyl-2-naphthylamine* (0·2 g.), m. p. 96—97° (Found: C, 87·3; H, 6·0. $C_{16}H_{13}N$ requires C, 87·6; H, 5·9%). This amine was identical with that obtained by reduction of 2-nitro-3-phenylnaphthalene with hydrazine and Raney nickel. Heating under reflux with anhydrous formic acid gave the *formyl derivative*, m. p. 125—126° (Found: C, 81·3; H, 5·6. $C_{17}H_{13}NO$ requires C, 81·7; H, 5·3%).

2,3-Benzophenanthridine.—2-Formamido-3-phenylnaphthalene (0·3 g.) was stirred with an excess of polyphosphoric acid at 150° for 2 hr. The mixture was allowed to cool to 60° and poured with stirring on ice. An excess of aqueous ammonia was added and the precipitate was crystallised twice from light petroleum to give needles of *2,3-benzophenanthridine* (0·14 g.), m. p. 146—147° (Found: C, 89·6; H, 4·85. $C_{17}H_{11}N$ requires C, 89·1; H, 4·8%).

N-Methyl-2,3-benzophenanthridone (cf. ref. 4).—2,3-Benzophenanthridine (0·2 g.) was boiled under reflux with an excess of methyl iodide for 1 hr. and the methyl iodide removed. The resulting methiodide was dissolved in hot dioxan (5 ml.) and water (5 ml.), and a solution of potassium hydroxide (0·3 g.) in water (1 ml.) was added, followed by potassium ferricyanide (0·46 g.) in water (4 ml.). The mixture was heated on the water bath for 30 min. with occasional shaking, allowed to cool, diluted with water (20 ml.), and extracted with chloroform. Evaporation of the dried (Na_2SO_4) extracts gave an oil, which solidified on trituration with light petroleum. Recrystallisation from the same solvent gave *N-methyl-2,3-benzophananthridone* in colourless needles, m. p. 174—175° (Found: C, 82·9; H, 5·3. $C_{18}H_{13}NO$ requires C, 83·4; H, 5·0%).

N-Methyl-1,2-benzophenanthridone (cf. ref. 24).—1,2-Benzophenanthridone [16] (0·86 g.), powdered potassium hydroxide (0·6 g.), and methyl propyl ketone (10 ml.) were boiled under reflux and methyl iodide (1 ml.) was added. Similar quantities of methyl iodide were added after approximately every 10 hr. during 50 hr. The mixture was filtered, the residue was washed with acetone, and the combined solutions gave, on evaporation, a red tar, which was dissolved in ethanol and treated with a saturated ethanolic solution of picric acid. Recrystallisation of the precipitate from ethanol gave *N-methyl-1,2-benzophenanthridone picrate* in orange needles, m. p. 136—137° (Found: C, 59·0; H, 3·5. $C_{18}H_{13}NO,C_6H_3N_3O_7$ requires C, 59·0; H, 3·3%). This picrate in ethanol was adsorbed on alumina; elution with ethanol gave an oil which crystallised from light petroleum in pale yellow prisms of *N-methyl-1,2-benzophenanthridone* (5%), m. p. 98—100° (Found: C, 83·8; H, 5·1. $C_{18}H_{13}NO$ requires C, 83·4; H, 5·0%).

1-Amino-2-naphthoic Acid.—To hydroxyimino-α-naphthoxindole [18] (5 g.) in 10% aqueous sodium hydroxide, 30% aqueous hydrogen peroxide (10 ml.) was added dropwise with stirring. Stirring was continued until effervescence ceased. The solution was then heated with charcoal, filtered, cooled to 0°, and made acid to Congo Red with 2N-hydrochloric acid. The gelatinous precipitate was collected, redissolved in 10% aqueous sodium hydroxide, and reprecipitated at 0° with 2N-hydrochloric acid to give 1-amino-2-naphthoic acid (3·0 g.), m. p. 205°.

1-Amino-N-methyl-2-naphthanilide Hydrochloride.—This acid (3 g.) and phosphorus tri-(*N*-methylanilide) (2 g.) in dry toluene (100 ml.) was heated under reflux for 2 hr. The mixture was filtered, the filtrate evaporated to dryness, and the residue extracted with chloroform. The gummy solid, which was insoluble in the toluene, was extracted with 10% aqueous sodium hydroxide and then with chloroform. The combined chloroform solutions were dried (Na_2SO_4) and the solvent was removed. The residue was extracted with anhydrous ether and to this

[24] Pachter and Kloetzel, *J. Amer. Chem. Soc.*, 1952, **74**, 1321.

solution saturated dry ethereal hydrogen chloride was added. The amine hydrochloride (1·8 g.) had m. p. 167—170° after recrystallisation from ethanol–ether saturated with hydrogen chloride. Abramovitch, Hey, and Long [3] record m. p. 170—171°. The diazonium chloride prepared from this amine hydrochloride (1·5 g.) was decomposed by copper powder in water as described previously,[3] the crystalline products isolated being 2-naphthanilide (0·12 g.), m. p. and mixed m. p. 166—168°, *N*-methyl-5,6-benzophenanthridone (0·1 g.), m. p. and mixed m. p. 137°, and a very small amount of a yellow solid, m. p. 180—183°, in agreement with the earlier work.[3]

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