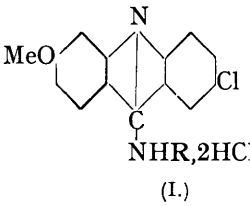
29. *Researches in the Phenanthridine Series. Part III. Meso-substituted Derivatives.*

By Leslie P. Walls.

The chief purpose of this work has been the preparation of compounds likely to possess therapeutic value. With this object, the reactivity of groups ortho to a cyclic tertiary nitrogen atom has been exploited. Phenanthridine resembles its isomeride acridine and quinoline in that the chlorine and the methyl of 9-chloro- and 9-methyl-phenanthridine respectively are reactive, although in the former case to a lesser degree than in the quinoline and acridine analogues. For example, when the chloro-compound was heated with "Naturkupfer" under a variety of conditions no diphenanthridyl could be obtained. Nevertheless this compound is regarded as a useful starting material of preparations, the structures of which might denote the possession of antimalarial properties. The incentive to the preparation of antimalarial drugs supplied by the synthesis in 1926 of plasmoquine has culminated in the synthesis of a series of acridine derivatives (I; R = aliphatic side chain with terminal NEt_2) which are potent antimalarials [the best-known, atebrine, was thought to be (I; R = $CH_2{\cdot}CH_2{\cdot}NEt_2$), but Mauss and Mietzsch, *Klin. Woch.*, 1933, **12**, 1276, have just revealed that R = $CH(CH_3){\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$, which brings it into line with plasmoquine]. The therapeutic significance of each part of the atebrine molecule cannot be gauged, but the close relationship between phenanthridine and acridine suggests that derivatives of this type in the former series might possess valuable properties.

Attempts to alkylate 9-aminophenanthridine (J., 1932, 2225) directly with amines of the type of β-chlorotriethylamine were unsuccessful in that intractable gums were obtained. This failure may be attributable to the peculiar structure of the amine, but similar difficulties are not uncommon with aminoquinolines. The method of the atebrine patent (B.P. 363,392) was too mild for the condensation of aliphatic diamines (II) and 9-chloro(or bromo)-phenanthridine, consistent with its lower reactivity: equivalents of the reactants in hot phenol yield chiefly N-*phenylphenanthridone* (III). However, when the halogen compound is heated with excess of diamine at 120°, substances of the type (IV) are obtained which are colourless oily bases, stronger than quinine in that dihydrochlorides only can be prepared. The latter have p_H 5 in aqueous solution similar to atebrine; their taste is much less bitter than that of quinine, and a local anæsthetic action is suspected.



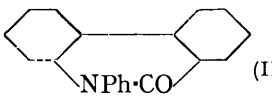
(I.)

$H_2N{\cdot}CH_2{\cdot}CH_2{\cdot}NEt_2$

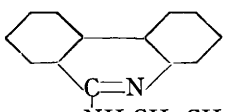
$H_2N{\cdot}CH_2{\cdot}CH_2{\cdot}N<\begin{matrix}CH_2{\cdot}CH_2\\CH_2{\cdot}CH_2\end{matrix}>CH_2$

$H_2N{\cdot}CH_2{\cdot}CH_2{\cdot}N(iso C_4H_9)_2$

(II.)



(III.)



(IV.)

$NH{\cdot}CH_2{\cdot}CH_2$

NEt_2,2HCl

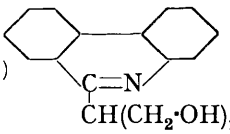
When they were tested in bird malaria by Professor Keilin at the Molteno Institute, Cambridge, they were found to possess no curative properties, and Professor Warrington Yorke has established also that they are of no value in trypanosomiasis. That these derivatives should be useless therapeutically whereas acridine analogues are potent drugs may be due to the absence of substituent chloro- and alkoxy-groups, but a fundamental difference appears to exist between phenanthridine and acridine in their physiological action.

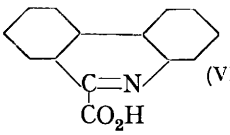
The newly discovered importance of the aliphatic diamines (II) rendered desirable an investigation of their facile preparation. The early method (Gabriel, *Ber.*, 1891, **24**, 1121; Ristenpart, *Ber.*, 1896, **29**, 2526) of condensation of phthalo-β-bromoethylimide with the appropriate dialkylamine is improved by isolating the phthalodialkylaminoethylimide

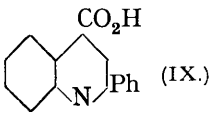
(compare VI). For the diethyl derivative, however, (VI) is best prepared from commercially available β-hydroxytriethylamine (V), a novocaine intermediate, according to the scheme :

$$\underset{\text{(V.)}}{Et_2N{\cdot}CH_2{\cdot}CH_2{\cdot}OH} \longrightarrow Et_2N{\cdot}CH_2{\cdot}CH_2Cl \xrightarrow{C_6H_4(CO)_2NK} Et_2N{\cdot}CH_2{\cdot}CH_2{\cdot}N\langle CO,CO\rangle \text{ (VI.)}$$

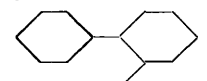
9-Methylphenanthridine condenses readily with two equivalents of formaldehyde to yield 9-ββ′-*dihydroxy*iso*propylphenanthridine* (VII), but a monohydroxy-compound could not be isolated although 9-methylacridine is readily converted into 9-β-hydroxyethylacridine (Homberger and Jensen, *J. Amer. Chem. Soc.*, 1926, **48**, 800). The dihydroxy-compound was oxidised smoothly by Kiliani's mixture to *phenanthridine-9-carboxylic acid* (VIII) together with some phenanthridone. 9-ω-Chloromethylphenanthridine which might have been used for this purpose gave very little (VIII) but chiefly phenanthridone. The carboxylic acid forms with hydrochloric acid a yellow crystalline complex which slowly loses hydrogen chloride and water on exposure. Phenanthridine-9-carboxylic acid bears some structural analogy to " cincophen " or " atophan " (IX), a well-known uric acid eliminant and gout remedy. Through the kindness of the Therapeutic Trials Committee of the Medical Research Council toxicity tests were carried out at the National Institute which showed that in common with cincophen derivatives and certain other drugs (*e.g.*, salvarsan) it frequently causes fatty degeneration of the liver, and its pharmacology has not been investigated further.

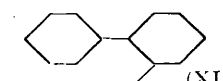
(VII.) 

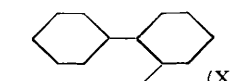
(VIII.) 

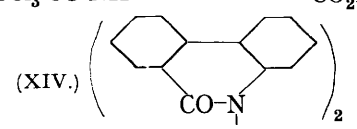
(IX.) 

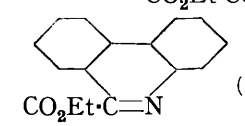
Various applications of the process of conversion of acyl-*o*-xenylamines into phenanthridines have been described (J., 1931, 2447; 1932, 2225). That the method failed in the case of formyl derivatives led to the investigation of other routes to phenanthridines unsubstituted in the meso(9)-position. Pyrolysis of phenanthridine-9-carboxylic acid proceeds smoothly and almost quantitatively at a low temperature to give phenanthridine, and accordingly, since the same would probably apply to its derivatives, the action of phosphorus oxychloride on the likeliest precursors of the carboxylic acid, *trichloroacet-o-xenylamide* (X), o-*xenyloxamic acid* (XI), and its *ethyl* ester (XII), has been studied. The first-named was, however, recovered quantitatively, and a similar non-reactivity was found for *dichloroacet*-o-*xenylamide* in contrast to the facile conversion of chloroacet-*o*-xenylamide into 9-ω-chloromethylphenanthridine (J., 1931, 2447). From (XII) only a small quantity of the desired ester (XIII) was obtained, which was identified with the product of esterification of (VIII). In the case of (XI) a violent reaction occurred, but the carboxylic acid was not among the products. Owing to its sparing solubility, (XIV) was most readily isolated, and its distillation over zinc dust gave a good yield of phenanthridine. It is unlikely that a diphenyl derivative would be converted into phenanthridine by this process, and therefore the formula indicated is tentatively advanced which has been allotted by Graebe and Wander (*Annalen*, 1893, **276**, 245) to a difficultly fusible substance obtained by alkaline reduction of *o*-nitrodiphenyl-*o*′-carboxylic acid. In addition were isolated phenanthridone and s.-*di*-o-*xenyloxamide*, and a substance which gave *o*-xenylamine and carbazole by the Baeyer reduction process, the latter doubtlessly being formed pyrogenically from the former (compare Blank, *Ber.*, 1891, **24**, 306).

(X.) 

(XI.) 

(XII.) 

(XIV.) 

(XIII.) 

The results obtained reveal certain apparent anomalies in the general synthetic process which consists essentially in the removal of H^X. The course of the reaction must depend on the nature of R, and of nuclear substituents, particularly in the heteronucleus.

Although the reaction proceeds smoothly when $R = CH_2Cl$, it fails completely for $R = CHCl_2$ and CCl_3, which suggests that, as the negative character of R is increased, enolisation, the most probable preliminary to ring closure, is inhibited. The electronic character of R has, however, no consistent influence, for CH_2Cl gives a better result than CH_3, but CO_2Et gives a very poor yield and $CHCl_2$ fails; *o*- exceeds *m*- and *p*-$C_6H_4{\cdot}NO_2$ and equals C_6H_5.

Experimental.

9-Bromophenanthridine was prepared by the method used by Graebe and Wander (*loc. cit.*) for the chloro-compound. Phenanthridone, required in considerable quantity, was best prepared by treating 9-ω-chloromethylphenanthridine (4·5 g.) in hot glacial acetic acid with powdered sodium dichromate (9 g.; 1·5 equivs.), added portionwise, and refluxing the mixture for 1 hour and then allowing it to cool. The product crystallised from nitrobenzene in characteristic white needles (3·5 g.).

Phenanthridone (4 g.), phosphorus oxybromide (4 g.), and phosphorus tribromide (4 g.) were heated for 5 hours at 200°. On cautious addition of water to decompose phosphorus halides, a dark solid was liberated which was extracted repeatedly with boiling petroleum (b. p. 80—100°). From the extract, small white prisms crystallised, m. p. 123—124° (Found: N, 5·4; Br, 30·7. $C_{13}H_8NBr$ requires N, 5·45; Br, 31·0%).

Phthalo-β-diethylaminoethylimide.—β-Chlorotriethylamine, freshly prepared from the hydrochloride (5 g.) (Gough and King, J., 1928, 2437), was heated in intimate admixture with finely powdered potassium phthalimide (4·5 g.) for 2 hours at 130°, vigorous effervescence occurring. The melt was extracted repeatedly with hot alcohol, which left potassium chloride undissolved. The residue on evaporation of alcohol was extracted with petroleum (b. p. 60—80°), in which most of it dissolved. Evaporation of petroleum left a white crystalline solid, which was further purified by extraction with petroleum (b. p. 40—60°) to yield large transparent prisms (5 g.), m. p. 46—47° (Found: N, 11·45. $C_{14}H_{18}O_2N_2$ requires N, 11·4%). This *phthalimide* is moderately easily soluble in water, but extremely soluble in all organic solvents. It was readily hydrolysed by heating under reflux with 20% hydrochloric acid for 2 hours. On cooling, phthalic acid separated; the filtrate on addition of potash sticks gave a basic oil, which was distilled. The fraction collected at 140—150° consisted chiefly of β-aminotriethylamine (Ristenpart, *loc. cit.*).

Phthalo-β-diisobutylaminoethylimide.—Phthalo-β-bromoethylimide (14 g.) and di*iso*butylamine (14 g.; 2 equivs.) were heated together at 130—140° for 4 hours. Anhydrous powdered potassium carbonate (8 g.) was then added, and the excess of di*iso*butylamine (7—8 g.) recovered by evaporation under reduced pressure. The residue was extracted with methylene dichloride, the extract washed with water, dried over potassium carbonate, and evaporated, leaving an oil which dissolved almost completely on extraction with dilute hydrochloric acid. Neutralisation of the extract liberated *phthalo-β-diisobutylaminoethylimide*, which crystallised on cooling (12 g.). It separated from alcohol or petroleum (b. p. 40—60°) in large colourless plates, m. p. 52° (Found: N, 9·4. $C_{18}H_{26}O_2N_2$ requires N, 9·25%).

β-Di*iso*butylaminoethylamine, obtained in good yield by hydrolysis of the foregoing phthalimide with 20% hydrochloric acid as for the diethylamino-compound, distilled at 200° under atmospheric pressure as a fuming liquid of faintly ammoniacal odour; unlike the β-diethylamino- and the β-piperidino-ethylamine, it was not completely miscible with water. When it was heated with aqueous picric acid (2 equivs.), a yellow crystalline powder separated which was sparingly soluble in water. It crystallised from hot methylated spirit in transparent flat yellow prisms which disintegrated on cooling; m. p. 190—192° (decomp.), but dependent on the rate of heating (Found: N, 18·1. $C_{10}H_{24}N_2,2C_6H_3O_7N_3$ requires N, 17·7%).

Reaction between 9-Bromophenanthridine and β-Aminotriethylamine.—β-Aminotriethylamine (2·3 g.; 1 equiv.) was added to a solution of 9-bromophenanthridine (5·2 g.) in phenol (20 g.)

at 100°, and the mixture heated for 2 hours, with occasional stirring; dilute caustic soda solution was then added in excess to dissolve phenol. From the residual light-coloured gum, when stirred with alcohol, a white powder (2·5 g.) separated, which crystallised from alcohol in colourless needles containing no bromine, m. p. 118—119°, depressed on admixture with 9-bromophenanthridine (Found: N, 5·3. *N-Phenylphenanthridone*, $C_{19}H_{13}ON$, requires N, 5·15%).

The alcoholic mother-liquor contained basic substances, but these could not be isolated in a pure condition.

9-β-*Diethylaminoethylaminophenanthridine*.—9-Bromophenanthridine (2 g.) or 9-chlorophenanthridine and excess of β-aminotriethylamine (2·5 g.) were heated at 120°. After 2 hours, excess of dilute hydrochloric acid was added (charcoal), which effected almost complete dissolution. Addition of alkali precipitated a light-coloured gum (2·2 g.), which would not solidify; when a solution in alcohol was treated with concentrated hydrochloric acid, white glistening needles of solvated 9-β-*diethylaminoethylaminophenanthridine dihydrochloride* crystallised (Found: Cl, 16·85; loss at 110°, 11·2. $C_{19}H_{23}N_3,2HCl,EtOH$ requires Cl, 17·25; EtOH, 11·15%). The salt crystallised from a small volume of water in minute white hydrated needles (Found: Cl, 16·7; loss at 100°, 13·1. $C_{19}H_{23}N_3,2HCl,3H_2O$ requires Cl, 16·9; H_2O, 12·85%). Solvent of crystallisation was readily lost without further decomposition of the salt at 100° under reduced pressure. The anhydrous salt melted at 238—243° after sintering much lower; it was sparingly soluble in alcohol, but slight hydration of the solvent caused a great increase in solubility; a 2% aqueous solution had p_H 4 (Found for anhydrous salt: N, 11·7; Cl, 19·25. $C_{19}H_{23}N_3,2HCl$ requires N, 11·5; Cl, 19·4%). When the base was evaporated to dryness with hydrochloric acid (1 equiv.), a gum was obtained which could not be crystallised; addition of more hydrochloric acid converted it readily into the dihydrochloride.

A *dipicrate*, prepared in the usual way, was almost insoluble in water, and only slightly soluble in alcohol, from which it crystallised in transparent yellow prisms, m. p. 208—211° (Found: N, 16·95. $C_{19}H_{23}N_3,2C_6H_3O_7N_3$ requires N, 16·8%).

9-β-*Piperidinoethylaminophenanthridine*.—9-Bromophenanthridine (3·3 g.) and β-piperidinoethylamine (3 g.) were condensed together as for the previous preparation. The oily triamine gave a *dihydrochloride* in prismatic needles (4·1 g.) from alcohol. The salt crystallised from water in colourless prismatic hydrated needles, which lost solvent without decomposition at 100° under reduced pressure (Found: Cl, 17·15; loss, 8·6, 8·7. $C_{20}H_{23}N_3,2HCl,2H_2O$ requires Cl, 17·15; H_2O, 8·7%). The anhydrous dihydrochloride had m. p. *ca.* 265—270° and was sparingly soluble in anhydrous but readily soluble in aqueous alcohol (Found: N, 11·2; Cl, 18·55. $C_{20}H_{23}N_3,2HCl$ requires N, 11·1; Cl, 18·8%); p_H of 2% aqueous solution, 5.

A solution of the base in 2*N*-nitric acid deposited, on cooling, glistening yellow needles of a *dinitrate*, m. p. 130—135° (decomp.), dependent on the rate of heating (Found for salt dried at 100° under reduced pressure: N, 16·25. $C_{20}H_{23}N_3,2HNO_3$ requires N, 16·25%).

9-β-*Diisobutylaminoethylaminophenanthridine*.—This compound, prepared from 9-chlorophenanthridine and β-di*iso*butylaminoethylamine, also could not be obtained crystalline. The *dihydrochloride* did not crystallise well from alcohol, but white glistening plates were obtained from water. Water of crystallisation was lost with partial melting at *ca.* 110°; complete fusion occurred at 142—144° (Found for hydrated salt: Cl, 14·45; loss, 14·2. $C_{23}H_{31}N_3,2HCl,4H_2O$ requires Cl, 14·4; H_2O, 14·6%. Found for anhydrous salt: N, 10·1; Cl, 16·3. $C_{23}H_{31}N_3,2HCl$ requires N, 9·95; Cl, 16·8%).

9-ββ′-*Dihydroxyisopropylphenanthridine*.—This was prepared in good yield when 9-methylphenanthridine (15 g.), 40% aqueous formaldehyde (15 c.c.), and alcohol (15 c.c.), forming a homogeneous solution, were heated under reflux for 5 hours. More formaldehyde solution was then added (5 c.c.) and after a further 5 hours' heating the solution was poured into a large volume of ether. The ethereal solution was washed repeatedly with water to remove alcohol and formaldehyde, dried over anhydrous potassium carbonate, and cooled to 0°. Ether was decanted and the residue was leached with water to leave the crude product (16·5 g.), which crystallised from benzene in colourless flat prismatic needles (14·5 g.), m. p. 129·5°—sometimes lustrous plates separated from the hot liquor (Found: C, 76·05; H, 6·35; N, 5·65. $C_{16}H_{15}O_2N$ requires C, 75·9; H, 5·95; N, 5·55%). The *base* dissolved readily in dilute mineral acid; it was very soluble in alcohol, but much less so in benzene and ether. Heated with acetic anhydride in pyridine, it gave a *diacetyl* derivative, which crystallised from methyl alcohol in white needles, m. p. 93°, quite soluble in hot petroleum (b. p. 60—80°) (Found: C, 71·3; H, 5·75; N, 4·15. $C_{20}H_{19}O_4N$ requires C, 71·2; H, 5·65; N, 4·15%).

Phenanthridine-9-carboxylic Acid.—In a typical experiment 9-ββ′-dihydroxy*iso*propylphenanthridine (5·5 g.) was dissolved in hot 2*N*-sulphuric acid (20 c.c.) and treated dropwise

with Kiliani's dichromate mixture (88 g.) during 30 minutes; after 2 hours the product was diluted with water and filtered, and the residue extracted repeatedly with hot dilute caustic soda solution. On evaporation of the alkaline extract and cooling, *sodium phenanthridine-9-carboxylate* (4 g.) separated in glistening white flaky crystals, which were recrystallised from hot water (charcoal) (Found: loss on heating in a vacuum, 17·6. $C_{14}H_8O_2NNa,3H_2O$ requires H_2O, 18·05%. Found for the anhydrous salt: Na, 9·25. $C_{14}H_8O_2NNa$ requires Na, 9·4%). The anhydrous salt was hygroscopic.

The residue from the above extraction with caustic soda was heated with hot dilute sulphuric acid to remove chromium compounds; the greyish-white residue (1 g.) sublimed at 250°/6 mm. in white needles, which, recrystallised from nitrobenzene, had m. p. 293°, alone or in admixture with phenanthridone.

The carboxylic acid as liberated from its sodium salt could not be crystallised conveniently from solvents, but was purified as follows. The salt (2·8 g.) was dissolved in hot water and treated dropwise with concentrated hydrochloric acid. At first the carboxylic acid separated as a white powder, but addition of further acid caused redissolution to a pale yellow liquid, from which, on cooling, yellow silky needles of a hydrochloric acid complex (2·8 g.) crystallised, containing less than one equivalent of hydrogen chloride [Found: loss at 100°/25 mm. (HCl + H_2O), 23·6; N, 4·85, 4·9; Cl, 8·25, 8·05%]. When the complex was heated with water, *phenanthridine-9-carboxylic acid* was liberated as a white microcrystalline powder (Found: C, 75·05; H, 4·4; N, 6·15. $C_{14}H_9O_2N$ requires C, 75·35; H, 4·05; N, 6·3%). The acid is insoluble in water and petroleum, sparingly soluble in benzene, and moderately easily in alcohol or acetone. Pyridine, which has been used successfully as a solvent for acridine-9-carboxylic acid (Homberger and Jensen, *loc. cit.*), proved unsatisfactory here: large colourless prisms, presumably of a complex, separated slowly when the hot solution was cooled, but on exposure to the atmosphere, or on boiling with petroleum, they effloresced and powdered.

When the acid (1 g.) was heated for 30 minutes at 155°, it melted with effervescence; the melt sublimed at 120°/5 mm. in white glistening crystals (0·6 g.), m. p. 105—107° alone or in admixture with phenanthridine.

Ethyl Phenanthridine-9-carboxylate.—None of the methods tried gave a good yield, but the following was most successful. Dry hydrogen chloride was led for 1 hour into a solution of the hydrochloride of the acid (2·5 g.) in alcohol (25 c.c.). The solution was heated gently under reflux for 1½ hours and then evaporated to dryness. Dilute caustic soda solution was added in excess and the product was extracted with ether. The ethereal solution was washed with dilute alkali and then with water, dried over anhydrous sodium sulphate, and evaporated to dryness. The residue (1·5 g.) set to a crystalline mass, which was extracted with petroleum (b. p. 40—60°). On partial evaporation and cooling, glistening white needles of the *ethyl* ester separated, m. p. 57—58° (Found: C, 76·4; H, 5·05. $C_{16}H_{13}O_2N$ requires C, 76·5; H, 5·2%).

Ethyl o-*Xenyloxamate and* s.-*Di*-o-*xenyloxamide.*—*o*-Xenylamine (9 g.) and ethyl oxalate (7·5 g.) were heated at 140° (oil-bath) for 4·5 hours, ethyl alcohol distilling during the reaction (compare Klinger, *Annalen*, 1877, **184**, 263). The solid product was ground and boiled with methylated spirit, to leave a white crystalline powder (1·2 g.), which separated from benzene in colourless needles, m. p. 233—235°, presumably of s.-*di*-o-*xenyloxamide* (Found: C, 79·7; H, 5·15. $C_{26}H_{20}O_2N_2$ requires C, 79·6; H, 5·1%). The filtrate deposited, on cooling, colourless prisms (11 g.) of *ethyl* o-*xenyloxamate*, m. p. 112—113° (Found: N, 5·25. $C_{16}H_{15}O_3N$ requires N, 5·2%).

When the foregoing ester (5 g.) was refluxed for 2 hours with phosphorus oxychloride (10 g.), there was a slight evolution of hydrogen chloride, but on decomposition of the excess of acid chloride with water, ethyl *o*-xenyloxamate (4 g.) was recovered unchanged. Neutralisation of the acid filtrate precipitated a light yellow oil (<1 g.) which solidified on standing, and on crystallisation twice from methyl alcohol occurred in very small yield in crystals characteristic of ethyl phenanthridine-9-carboxylate, m. p. 57—58°, alone or in admixture with it.

Attempts to improve the yield by reaction at a higher temperature (160°) and by heating a xylene solution of the oxamic ester with excess of phosphoric oxide were unsuccessful.

o-*Xenyloxamic Acid.*—*o*-Xenylamine (18 g.) and crystalline oxalic acid (18 g.) were heated for 1 hour at 130—140°; evolution of water then occurred (compare Aschan, *Ber.*, 1890, **23**, 1820). The white crystalline aggregate was ground with boiling dilute sulphuric acid; the mass of white prismatic needles left undissolved (23 g.) was recrystallised from benzene; m. p. 155—158° (decomp.). The *acid* was moderately easily soluble in alcohol or benzene, or aqueous caustic potash solution, but only slightly soluble in hot water (Found: N, 5·85. $C_{14}H_{11}O_3N$ requires N, 5·8%).

o-*Xenyloxamic Acid and Phosphorus Oxychloride.*—The following is typical of several experiments. *o*-Xenyloxamic acid (13 g.) and phosphorus oxychloride (25 g.) reacted vigorously with rapid darkening of the solution and separation of purplish crystals. On addition of water, a dark brown mass was obtained insoluble in acid or alkali. On boiling with methylated spirit most of the tar dissolved; the extract deposited, on evaporation and cooling, a greyish-white powder (*ca.* 2·5 g.), a sublimate from which at 250°/6 mm. crystallised from nitrobenzene in needles characteristic of phenanthridone.

The residue from the extraction with spirit was heated with boiling glacial acetic acid (*ca.* 100 c.c.) and from the extract were obtained by fractional crystallisation, *s.*-di-*o*-xenyloxamide, and a substance A in colourless acicular prisms, m. p. >310° (*M*, by Rast's method, *ca.* 370). Insoluble in glacial acetic acid was (XIV) (1 g.), which crystallised from a large volume of boiling nitrobenzene in hard glass-like cubes, insoluble in molten camphor, m. p. >310° [Found by micro-analysis: C, 80·0; H, 4·3; N, 7·6. $(C_{13}H_8ON)_2$ requires C, 80·4; H, 4·15; N, 7·2%].

Zinc Dust Distillation of the Products.—The substance was mixed with zinc dust and placed in the rear end of a hard glass tube, the front end of which was packed with zinc dust–pumice mixture. A stream of hydrogen was passed through the tube, which was heated strongly, starting from the extremities.

From A a greenish-yellow semi-solid fluorescent distillate collected rapidly and in good yield. It was extracted with dilute hydrochloric acid to leave a crystalline residue, which gave glistening white plates from alcohol, m. p. *ca.* 237° alone or in admixture with carbazole, and had also the characteristic colour reactions of this substance. The base liberated from the hydrochloric acid extract on neutralisation, yielded with acetic anhydride acet-*o*-xenylamide as sole product.

From (XIV) a good yield of distillate was obtained which set to a light brown solid, completely soluble in dilute acid. It was purified by crystallisation of its sulphate from alcohol, and finally by sublimation under reduced pressure. The base thus obtained in glistening white crystals melted at 105° alone or in admixture with phenanthridine. *Di-* and *tri-chloroacet-*o*-xenylamide* were prepared by treating an ethereal solution of *o*-xenylamine (2 equivs.) with the appropriate acid chloride, added slowly with stirring. *o*-Xenylamine hydrochloride was separated, and the combined ethereal filtrate and washings were dried over anhydrous potassium carbonate and evaporated. The acetyl derivatives were crystallised from petroleum (b. p. 60—80°); for the *dichloro*-compound, white needles, m. p. 104—106° (Found: N, 5·0; Cl, 25·05. $C_{14}H_{11}ONCl_2$ requires N, 5·0; Cl, 25·35%), and for the *trichloro*-compound, glistening white plates, m. p. 92—94° (Found: N, 4·45; Cl, 33·6. $C_{14}H_{10}ONCl_3$ requires N, 4·15; Cl, 33·85%).

When these acetyl derivatives were refluxed with phosphorus oxychloride in various proportions, and under various conditions, they were recovered quantitatively. Addition of phosphorus pentachloride did not promote reaction, and when phosphoryl chloride was replaced by thionyl chloride no reaction occurred: fusion with zinc chloride caused charring.

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