192. *New Syntheses of Heterocyclic Compounds. Part VIII. The Schmidt Rearrangement of* 1 : 3-*Dimethyl*-2-*azafluorenones* (*continued*).

By Vladimir A. Petrow.

4-*Amino*-, 4-*benzamido*-, 4-carboxy-, 4-*carbethoxy*-, 7-*nitro*-, 7-*amino*-, 7-*benzamido*-, and 7-methoxy-1 : 3-dimethyl-2-azafluorenones have been submitted to the Schmidt reaction. Only the 4-carbethoxy-derivative (II; R = CO_2Et) underwent rearrangement to give *ethyl* 9-*hydroxy*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene*-

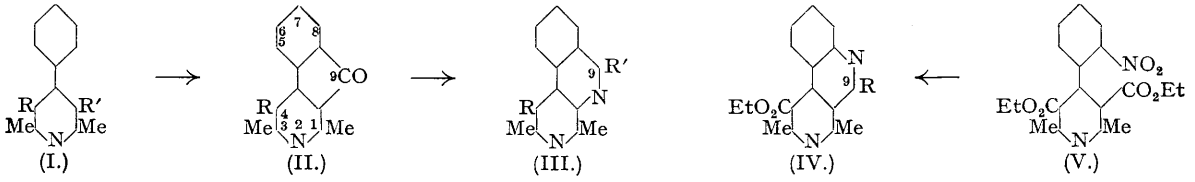
4-*carboxylate* (III; R = CO_2Et; R′ = OH), the constitution of which followed from its non-identity with the isomeric *ethyl* 9-*hydroxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*-5-*carboxylate* (IV; R = OH), obtained by reduction of ethyl 4-*o*-nitrophenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate (V).

(III; R = CO_2Et; R′ = OH) has been converted into the *chloro*-compound (III; R = CO_2Et; R′ = Cl), and thence into *ethyl* 9-*amino*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene*-4-*carboxylate* (III; R = CO_2Et; R′ = NH_2).

In Part V of this series (Petrow, this vol., p. 200) it was reported that the Schmidt rearrangement of 1 : 3-dimethyl-2-azafluorenone (II; R = H) leads to the formation of 9-hydroxy-1 : 3-dimethyl-2 : 10-diazaphenanthrene (III; R = H; R′ = OH) in high yield. The investigation has been continued, and the present communication reports a study of the action of hydrazoic acid on a number of substituted 1 : 3-dimethyl-2-azafluorenones. Some of these have not hitherto been described in the literature, and were prepared as described below.

Nitration of 1 : 3-dimethyl-2-azafluorenone (II; R = H) gave a mono-nitro-derivative in excellent yield. From analogy with the formation of 2-nitrofluorenone from fluorenone by nitration under comparable conditions, this compound has been assigned the constitution of 7-*nitro*-1 : 3-*dimethyl*-2-*azafluorenone*. Reduction gave 7-*amino*-1 : 3-*dimethyl*-2-*azafluorenone*, characterised by its *benzoyl* derivative and *oxime*. The behaviour of this compound showed certain unusual features, perhaps associated with an " imine " type of structure. Thus it generally formed brilliant red micro-needles, m. p. 255°. When this red form was treated with stannous chloride in concentrated hydrochloric acid for 1½ hours on the water-bath, however, an unstable pink form, m. p. 225°, was obtained which gave the same bright yellow benzoyl derivative on benzoylation, and rapidly passed into the bright red form on further crystallisation. Again, it failed to give a positive primary amine test on diazotisation followed by coupling with alkaline β-naphthol. Attempts to prepare a benzylidene derivative gave inconclusive results. Finally, the benzoyl derivative failed to give a methosulphate on heating under reflux with methyl sulphate in nitrobenzene solution.

The isomeric 4-*amino*-1 : 3-*dimethyl*-2-*azafluorenone* (II; R = NH_2) was prepared by application of the new synthetical method described in Part VII (preceding paper). Condensation of benzaldehyde with β-aminocrotononitrile and ethyl β-aminocrotonate led to the formation of *ethyl* 5-*cyano*-4-*phenyl*-2 : 6-*dimethyldihydro*-



pyridine-3-*carboxylate* in 67% yield, smoothly oxidised by dilute nitric acid to *ethyl* 5-*cyano*-4-*phenyl*-2 : 6-*dimethylpyridine*-3-*carboxylate* (I; R = CN; R′ = CO_2Et). Hydrolysis furnished the corresponding *acid* (I; R = CN; R′ = CO_2H), converted by concentrated sulphuric acid into 4-*carbamyl*-1: 3-*dimethyl*-2-*azafluorenone* (II; R = $CO{\cdot}NH_2$). Hypobromite oxidation gave the bright red 4-*amino*-1 : 3-*dimethyl*-2-*azafluorenone* (II; R = NH_2), characterised by its *oxime* and *benzoyl* derivative.

Partial hydrolysis of ethyl 4-phenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate (I; R = R′ = CO_2Et) gave the mono-ester (I; R = CO_2Et; R′ = CO_2H) (Hantzsch, *Ber.*, 1884, **17**, 2910), converted by concentrated sulphuric acid into *ethyl* 1 : 3-*dimethyl*-2-*azafluorenone*-4-*carboxylate* (II; R = CO_2Et) in yields not exceeding 20%. This ester was better prepared when required in quantity by direct esterification of the readily accessible 1 : 3-dimethyl-2-azafluorenone-4-carboxylic acid (Mills, Palmer, and Tomkinson, *J.*, 1924, **125**, 2366) by the silver salt method. The remaining compound examined, 7-methoxy-1 : 3-dimethyl-2-azafluorenone, has been described by Borsche and Hahn (*Annalen*, 1939, **537**, 230).

The above derivatives of 1 : 3-dimethyl-2-azafluorenone failed to undergo the Schmidt rearrangement, with the exception of (II; R = CO_2Et), which gave an *ethyl* 9-*hydroxydiazaphenanthrenecarboxylate* in 35% yield. Although two structures (III; R = CO_2Et; R′ = OH) and (IV; R = OH) are clearly possible for this compound, the former is preferred from analogy with the Schmidt rearrangement of the parent ring system (II; R = H), which was shown in Part V (*loc. cit.*) to lead to the 2 : 10-diazaphenanthrene (III; R = H; R′ = OH). In contrast to (III; R = H; R′ = OH) this new carbethoxy-derivative was readily soluble in sodium hydroxide solution, from which it was precipitated by carbon dioxide. It formed a sparingly soluble bright yellow potassium salt, and failed to give a coloration with ferric chloride. Its formulation as *ethyl* 9-*hydroxy*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene*-4-*carboxylate* (III; R = CO_2Et; R′ = OH) followed, however, from its non-identity with authentic *ethyl* 9-*hydroxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*-5-*carboxylate* (IV; R = OH), obtained by reduction of ethyl 4-*o*-nitrophenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate (V) with stannous chloride.

Now Kenner and Stubbings (*J.*, 1921, **119**, 602) have observed that although reduction of ethyl *oo*′-dinitrodiphenate leads to the formation of the corresponding dilactam, yet combustion analyses of this compound give figures consistently low for carbon and more in accord with its formulation as the corresponding diaminodiacid. Similar observations have been recorded by Bell (*J.*, 1934, 837) for the reduction product of ethyl *o*-nitrodiphenate. Although this anomalous behaviour has now been observed with the ethyl *o*-nitrodiphenate analogue (V), yet the chemical properties of the reduction product clearly indicated the *lactam* structure (IV;

R = OH). Thus this compound gave a crimson coloration with ferric chloride, a behaviour often associated with an α-hydroxypyridine residue (cf. Köenigs and Geigy, *Ber.*, 1884, **17**, 591). It was insoluble in potassium carbonate solution, but formed bright yellow crystalline salts on treatment with sodium or potassium hydroxide. It failed to give a positive primary amine test on diazotisation followed by coupling with alkaline β-naphthol. Acetylation led to the formation of an unstable *acetyl* derivative (IV; R = OAc), which no longer gave a coloration with ferric chloride and underwent rapid hydrolysis to the original compound on crystallisation from aqueous alcohol (cf. the acetylation of α-hydroxypyridine, Tschitschibabin and Szokow, *Ber.*, 1925, **58**, 2650).

Ethyl 9-*chloro*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene*-4-*carboxylate* (III; R = CO_2Et; R′ = Cl) was readily obtained from the corresponding hydroxy-compound, and passed smoothly into *ethyl* 9-*amino*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene*-4-*carboxylate* (III; R = CO_2Et; R′ = NH_2) on heating with alcoholic ammonia at 200°. The constitution assigned to this compound followed from its reconversion into (III; R = CO_2Et; R′ = OH) by nitrous acid.

Experimental.

M. ps. are corrected. Microanalyses are by Drs. Weiler and Strauss, Oxford.

7-*Nitro*-1 : 3-*dimethyl*-2-*azafluorenone*.—1 : 3-Dimethyl-2-azafluorenone (2 g.) dissolved in concentrated sulphuric acid (10 ml.) was treated at 0° with potassium nitrate (1 g.) added slowly in portions. Reaction was completed by heating on the water-bath for 1 hour; the mixture was then poured on ice and made alkaline with ammonia, and the precipitated product collected and extracted with spirit. The *compound* separated from amyl alcohol in needles, m.p. 230·5° (Found: C, 66·2; H, 4·0; N, 11·0. $C_{14}H_{10}O_3N_2$ requires C, 66·2; H, 4·0; N, 11·0%). Yield, nearly quantitative.

7-*Amino*-1 : 3-*dimethyl*-2-*azafluorenone*.—(*a*) The corresponding nitro-compound (2·1 g.) dissolved in concentrated hydrochloric acid (35 ml.) was treated with stannous chloride (5·5 g.) for 30 minutes on the water-bath. After standing overnight at 0° the product was collected, decomposed with sodium hydroxide, and the precipitated *base* crystallised from spirit (charcoal). If formed brilliant red needles, m. p. 255° (Found: C, 74·3; H, 5·6; N, 12·2. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·4; N, 12·5%). The *benzoyl* derivative, bright yellow needles from spirit, m. p. 254° (Found: C, 76·9; H, 5·2; N, 8·8. $C_{21}H_{16}O_2N_2$ requires C, 76·9; H, 4·9; N, 8·5%), was obtained by treating the base (1·1 g.) in pyridine (10 ml.) with benzoyl chloride (900 mg.) for 30 minutes on the water-bath. The *oxime*, orange needles from aqueous pyridine, m. p. 280° (decomp.) (Found: N, 17·3. $C_{14}H_{13}ON_3$ requires N, 17·6%), was obtained by heating the base (4·5 g.), hydroxylamine hydrochloride (4·5 g.), and pyridine (40 ml.) for 30 minutes under reflux, followed by precipitation with ammonia.

(*b*) The amino-derivative [m. p. 255°; prep. by method (*a*)] (4·2 g.) in concentrated hydrochloric acid (50 ml.) was treated with stannous chloride (11 g.) for 1½ hours on the water-bath. After 12 hours at 0° the product was collected and dissolved in water, and sodium hydroxide added in excess. The precipitated 7-amino-1 : 3-dimethyl-2-azafluorenone separated from aqueous spirit as a felted mass of pink needles, m. p. 224—225°, not depressed in admixture with the bright red form, m. p. 255°.

(*c*) The nitro-compound (2 g.) in excess of concentrated hydrochloric acid was reduced with tin (5 g.). After dilution and removal of the tin as sulphide, the filtrate was evaporated to small bulk, and the base precipitated by addition of ammonia. The *product*, which may have been a ?-chloro-7-amino derivative, separated from a large volume of spirit as octahedra, m. p. 303° (Found: C, 63·6; H, 5·9; N, 10·6; Cl, 13·8. $C_{14}H_{11}ON_2Cl$ requires C, 65·0; H, 4·3; N, 10·8; Cl, 13·7%).

Ethyl 5-*Cyano*-4-*phenyl*-2 : 6-*dimethyldihydropyridine*-3-*carboxylate*.—Benzaldehyde (32 g.), β-aminocrotononitrile (25 g.), ethyl β-aminocrotonate (39 g.), and absolute alcohol (50 ml.) were heated under reflux for several days. The solid product was crystallised from aqueous alcohol giving the *ester* in rectangular plates, m. p. 171—172·5° (Found: C, 72·1; H, 6·3; N, 10·0. $C_{17}H_{18}O_2N_2$ requires C, 72·3; H, 6·4; N, 9·9%). Yield, 57 g.

Ethyl 5-*cyano*-4-*phenyl*-2 : 6-*dimethylpyridine*-3-*carboxylate* (I; R = CN; R′ = CO_2Et), large octahedra from light petroleum (b. p. 60—80°), m. p. 101—102° (Found: C, 72·8; H, 5·7; N, 9·8. $C_{17}H_{16}O_2N_2$ requires C, 72·9; H, 5·7; N, 10·0%), was obtained by oxidising the above dihydro-ester with four parts of dilute nitric acid (from 1 vol. conc. acid and 7 vols. water) on the water-bath. Yield, 72%.

5-*Cyano*-4-*phenyl*-2 : 6-*dimethylpyridine*-3-*carboxylic Acid* (I; R = CN, R′ = CO_2H).—The above ester (41 g.), potassium hydroxide (9 g.), and absolute alcohol (90 ml.) were heated under reflux for 100 hours. The alcohol was removed on the water-bath, the residue taken up in a little water, and the filtered solution acidified with concentrated sulphuric acid (9 g.) in water. The precipitated acid was crystallised once (charcoal) from aqueous alcohol. The *acid* formed needles, m. p. 236—237° (Found: C, 71·4; H, 4·8; N, 11·1. $C_{15}H_{12}O_2N_2$ requires C, 71·4; H, 4·8; N, 11·1%). Yield, 27·5 g. (73%).

4-*Carbamyl*-1 : 3-*dimethyl*-2-*azafluorenone* (II; R = CO·NH_2).—A 40% yield was obtained by adhering to the following conditions. The above cyano-acid (20 g.) in concentrated sulphuric acid (80 ml.) was heated in a water-bath for 75 minutes. The *well-cooled* mixture was *slowly* poured with vigorous stirring on a large excess of crushed ice. Ammonia was added in excess and the precipitated *amide* collected and crystallised once (charcoal) from glacial acetic acid. It formed long needles, m. p. 288° (Found: C, 71·2; H, 4·8; N, 10·7. $C_{15}H_{12}O_2N_2$ requires C, 71·4; H, 4·8; N, 11·1%).

4-*Amino*-1 : 3-*dimethyl*-2-*azafluorenone* (II; R = NH_2).—Finely powdered 4-carbamyl-1 : 3-dimethyl-2-azafluorenone (20 g.) was added in one portion to a mechanically stirred cooled solution of bromine (15 g.) in 10% potassium hydroxide (250 ml.). The compound rapidly went into solution. After 30 minutes, a further quantity of 10% potassium hydroxide (150 ml.) was added, and the mixture heated on the water-bath for 30 minutes. The product was transferred to an evaporating dish and taken down to dryness on the water-bath. The finely powdered red residual solids were thoroughly extracted with benzene, and the bulked liquors concentrated until crystallisation commenced. The *base* formed squat coral-red needles, m. p. 186·5—187·5° (Found: C, 75·0; H, 5·4; N, 12·3. $C_{14}H_{12}ON_2$ requires C, 75·0; H, 5·4; N, 12·5%). Yield, 50%. The *benzoyl* derivative, faintly yellow silky needles from aqueous methyl alcohol, m. p. 245—246° (Found: C, 76·7; H, 5·0; N, 8·8. $C_{21}H_{16}O_2N_2$ requires C, 76·8; H, 4·9; N, 8·5%), was prepared by treating the base with benzoyl chloride in pyridine solution at 100°. The *oxime* formed golden-yellow needles from aqueous pyridine, m. p. >300° (Found: N, 17·8. $C_{14}H_{13}ON_3$ requires N, 17·6%).

Ethyl 1 : 3-*Dimethyl*-2-*azafluorenone*-4-*carboxylate* (II; R = CO_2Et).—5-Carbethoxy-4-phenyl-2 : 6-dimethylpyridine-3-carboxylic acid (3·5 g.) (Hantzsch, *loc. cit.*) and concentrated sulphuric acid (7 ml.) were heated on the water-bath for 45 minutes. The cooled mixture was poured on crushed ice and made alkaline with ammonia, and the precipitated *ester* collected and crystallised from aqueous methyl alcohol. It formed silky needles, m. p. 115·5—116·5° (Found: C, 72·4; H, 5·2; N, 4·9. $C_{17}H_{15}O_3N$ requires C, 72·6; H, 5·3; N, 5·0%). Alternatively, the silver salt of 1 : 3-di-

methyl-2-azafluorenone-4-carboxylic acid was heated under reflux with excess of ethyl iodide in absolute alcoholic solution for several hours.

Ethyl 9-*Hydroxy*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene* 4-*carboxylate* (III; R = CO_2Et; R′ = OH).—To a solution of ethyl 1 : 3-dimethyl-2-azafluorenone-4-carboxylate (160 g.) in concentrated sulphuric acid (750 ml.) was added, below 10° with mechanical stirring over a period of 4 hours, a solution of sodium azide (68 g.) in water (190 ml.). After a further 4 hours' stirring and cooling, the mixture was left overnight at room temperature. The product was poured on crushed ice and ammonia added in excess. The precipitated sulphate was collected and dissolved in the minimum amount of hot dilute 5% sodium hydroxide solution, and the mixture filtered, cooled, and saturated with carbon dioxide. The precipitated *base* was collected and crystallised three times from spirit. It separated in a felted mass of silky needles, m. p. 255—256° (Found: C, 69·4; H, 5·6; N, 9·7. $C_{17}H_{16}O_3N_2$ requires C, 69·0; H, 5·4; N, 9·5%). Yield, 35%.

Ethyl 9-*Chloro*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene*-4-*carboxylate* (III; R = CO_2Et; R′ = Cl).—The above hydroxy-compound (3 g.), phosphorus pentachloride (2·2 g.), and phosphorus oxychloride (15 ml.) were heated under reflux at 150—160° until all the solid had reacted and gone into solution. Excess of phosphorus halides was removed under reduced pressure on the water-bath, the residue was ground with dilute ammonia, and, after 12 hours at room temperature, the solid was collected. The *product* was extracted once with a little hot spirit and crystallised (charcoal) from benzene–light petroleum. It formed faintly pink octahedra, m. p. 186—187° (Found: Cl, 11·1. $C_{17}H_{15}O_2N_2Cl$ requires Cl, 11·3%). Yield, 55%.

Ethyl 9-*Amino*-1 : 3-*dimethyl*-2 : 10-*diazaphenanthrene*-4-*carboxylate* (III; R = CO_2Et; R′ = NH_2).—The above chloro-compound (2 g.), saturated alcoholic ammonia (20 ml.), and a trace of copper salt were heated at 180° for 8 hours in a sealed tube. The product was taken to dryness, decomposed by sodium hydroxide solution, and the liberated *base* crystallised once from aqueous acetone and once from benzene–alcohol. It formed flat pale yellow needles, m. p. 200—201° (Found: C, 68·7; H, 5·9; N, 14·1. $C_{17}H_{17}O_2N_3$ requires C, 69·2; H, 5·8; N, 14·2%). Yield, 40%. The constitution assigned to this compound followed from its reconversion by nitrous acid in dilute hydrochloric acid into (III; R = CO_2Et; R′ = OH), identified by m. p. and mixed m. p. with an authentic specimen.

Ethyl 9-*Hydroxy*-6 : 8-*dimethyl*-7 : 10-*diazaphenanthrene*-5-*carboxylate* (IV; R = OH).—Ethyl 4-*o*-nitrophenyl-2 : 6-dimethylpyridine-3 : 5-dicarboxylate (1·5 g.), glacial acetic acid (12·5 ml.), concentrated hydrochloric acid (9 ml.), and stannous chloride (3·25 g.) were heated under reflux for 35 minutes. After 12 hours at 0° the product was collected, dissolved in water (5 ml.), and treated with 10% sodium hydroxide (25 ml.). The yellow sodium salt was collected and dissolved in water (10 ml.), and the *base* liberated by addition of 2N-sulphuric acid (25 ml.). It formed glancing needles, m. p. 184—185° (Found for samples dried in a vacuum at 100° to constant weight: C, 65·7, 65·3; H, 5·3, 5·1; N, 9·2, 9·0. $C_{17}H_{16}O_2N_2$ requires C, 69·0; H, 5·4; N, 9·5%). Yield, 400 mg. On acetylation, an unstable *acetyl* derivative (IV; R = Ac) was obtained, m. p. 171°, which was analysed without purification (Found: C, 65·7; H, 5·2; N, 7·8. $C_{19}H_{18}O_4N_2$ requires C, 67·5; H, 5·3; N, 8·3%). Although this product failed to give a coloration with ferric chloride, recrystallisation from aqueous alcohol led to a substance of indefinite m. p. which gave a crimson coloration. Two crystallisations were sufficient to convert the acetyl derivative back into (IV; R = OH), m. p. 185°.

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