421. *The Structure and Properties of Certain Polycyclic Indolo- and Quinolino-derivatives. Part III.* Derivatives of* 1 : 2 : 2a : 3 : 4 : 5 : 8 : 9 : 10 : 10a-*Decahydro*-5 : 8-*diketo*-2a : 10a-*diazapyrene*.†

By C. Y. Almond and Frederick G. Mann.

Dicyclisation of 1 : 4-bis-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydroquinoxaline gives the diketo-diazapyrene (II) named in the title; the bisphenylhydrazone of this undergoes normal indolisation to the di-indolo-derivative (IV), unlike previous phenylhydrazones in this series which give ψ-indoles. When the diketo-diazapyrene is subjected to the Pfitzinger reaction with isatin, it yields the corresponding bisquinolino-dicarboxylic acid (V), which can be decarboxylated to the bisquinolino-derivative (VI). Both the acid and the decarboxylated derivative undergo ready oxidation, the latter furnishing the diketo-diquinolino-derivative (VII).

In continuation of our studies of the colour and structure of cyclic keto-amines and their quinolino- and indolo-derivatives, we have converted 1 : 2 : 3 : 4-tetrahydroquinoxaline by the action of vinyl cyanide into the colourless crystalline 1 : 4-bis-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydroquinoxaline (I). This compound, when heated in chlorobenzene with aluminium chloride and hydrochloric acid, underwent dicyclisation, and the product on hydrolysis gave 1 : 2 : 2*a* : 3 : 4 : 5 : 8 : 9 : 10 : 10*a*-decahydro-5 : 8-diketo-2*a* : 10*a*-diazapyrene (II). This diketo-diamine formed brilliant deep red crystals, and was apparently too feebly basic to form salts with even strong acids. The reason for the deep colour and feeble basicity is almost certainly the considerable contribution which the polar form (II*A*) must make to the resonance hybrid. A similar explanation was suggested for the properties of 1-ketojulolidine (Mann and Smith, preceding paper), but the duplication of the polar factor in the compound (II) would cause the greater intensity of colour. This receives some support from the fact that solutions of the diketo-diamine in concentrated hydrochloric acid are very deep red, in glacial acetic acid bright red, and in carbon tetrachloride greenish-yellow and fluorescent. It would appear therefore that salt formation with strong acids involves effectively the addition of protons to the negative oxygen atoms in (II*A*), *i.e.*, the formation of a cation identical with (II*A*) except that the oxygen atoms are replaced by hydroxyl groups, and that the consequent marked increase in the proportion of the (II*A*) structure causes the increased intensity of the red colour.

It is noteworthy that the dicyano-compound (I) could be readily hydrolysed to 1 : 4-bis-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydroquinoxaline (III), but attempts to cyclise this acid to the diketone (II) by phosphoric anhydride, phosphorus oxychloride, or sulphuric acid were unsuccessful.

The deep red colour of the diketone (II) is apparently a characteristic property, for the bisphenylhydrazone formed golden crystals. The latter, when indolised by boiling ethanolic hydrogen chloride, ultimately furnished bright yellow crystals of 1 : 2 : 2*a* : 3 : 10 : 10*a*-hexahydrodi-indolo(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2*a* : 10*a*-diazapyrene (IV), m. p. 438—439°. No indication of ψ-indole formation was detected in this indolisation, in which respect it differs markedly from that of the phenylhydrazones of tetrahydro-4-ketoquinoline (Clemo and Perkin, *J.*, 1924, **125**, 1608), of tetrahydro-4-keto-1-phenylquinoline (Mann, *J.*, 1949, 2816), and of 1-ketojulolidine (Mann and Smith, *loc. cit.*).

When the diketone (II) and isatin were boiled together with ethanolic potassium hydroxide solution under nitrogen, acidification ultimately furnished 1 : 2 : 2*a* : 3 : 10 : 10*a*-hexahydrodiquinolino(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2*a* : 10*a*-diazapyrene-4′ : 4″-dicarboxylic acid (V) as dark-green crystals, m. p. 242—246°, which could not be purified but gave a disodium salt as bright red crystals which darkened rapidly on exposure to air, presumably by atmospheric oxidation. It is probable that the marked difference in colour between the acid and its sodium salt is due to the former existing as a zwitterion, the resonance possibilities of which

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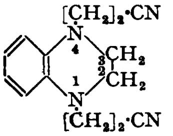
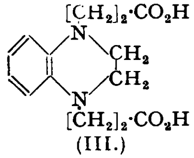
* Part II, preceding paper.

† *Note on Nomenclature.* This diketo-compound is regarded as a derivative of pyrene, and the ring system is therefore numbered as in (II).

will differ from those of the acid anion : this explanation is parallel to that given in detail for 1 : 2-dihydro-1-phenylquinolino(3′ : 2′-3 : 4)quinoline-4′-carboxylic acid (Mann, *loc. cit.*), and also for quinolino(2′ : 3′-1 : 2)juloline (Mann and Smith, *loc. cit.*).


(I.)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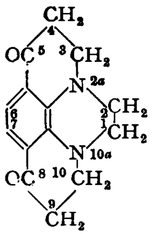
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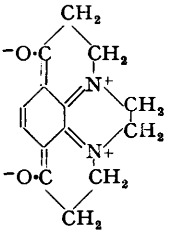
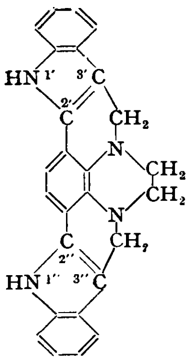
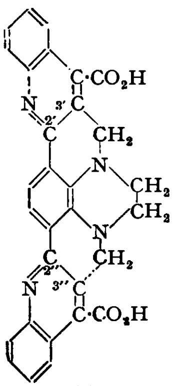

(II*A*.)


(IV.)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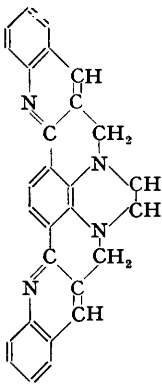
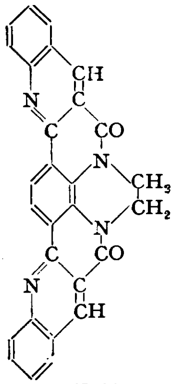

(VI.)


(VII.)

When the acid (V) was heated in a high vacuum, decarboxylation occurred, with sublimation of 1 : 2 : 2*a* : 3 : 10 : 10*a*-hexahydrodiquinolino(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2*a* : 10*a*-diazapyrene (VI) as bright red crystals, m. p. 156—158°. These on exposure to air also darkened apparently with atmospheric oxidation, which however, unlike earlier examples, could not be conveniently taken to completion by these means. When, however, the amine (VI) was treated with potassium permanganate, both reagents in cold acetone, oxidation was rapidly complete, with the formation of the orange crystalline 1 : 2 : 2*a* : 3 : 10 : 10*a*-hexahydro-3 : 10-diketodiquinolino(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2*a* : 10*a*-diazapyrene (VII), m. p. 428—430°. By analogy with similar oxidation products previously studied, there is no reasonable doubt that oxidation has occurred at the methylene groups adjacent to the quinoline rings, *i.e.*, at the 3- and the 10-position, and not at the 1- and the 2-position of the diazapyrene ring.

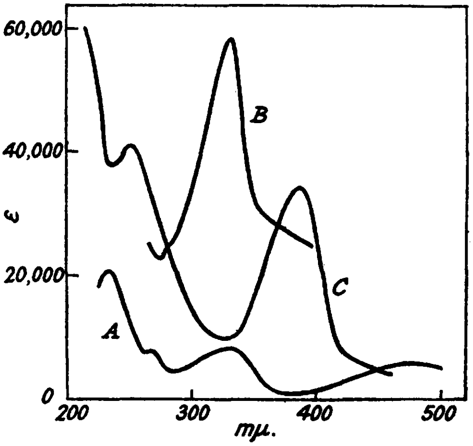
The absorption spectra are shown in the Figure. The compounds (II) and (VI) were measured in ethanolic solution, but the low solubility of (IV) necessitated the use of 2-methoxyethanol, the strong absorption of which severely limits the range of the spectrum. The spectrum (*A*) of (II) has maxima at 232 (ε 20,600), 269 (7300), 330 (7900), and 480 mμ. (5450), and minima at 263 (7000), 285 (4000), and 377 mμ. (320). The spectrum (*B*) of (IV) has mμ.$_{\text{max.}}$ 330 (ε 55,700) and mμ.$_{\text{min.}}$ 272—274 (23,100). The spectrum (*C*) has mμ.$_{\text{max.}}$ 252 (ε 40,400) and 387 (33,800) and mμ.$_{\text{min.}}$ 234 (ε 37,400) and 327 (9100). It is possible that the marked absorption of (IV) at 230 mμ. and of (VI) at 387 mμ. is due in each case to the long conjugated systems and that it is the greater length of this conjugated chain in (VI) which has shifted its absorption to longer wave-lengths than that of (IV).

EXPERIMENTAL.

1 : 2 : 3 : 4-*Tetrahydroquinoxaline.*—Catechol (48 g.) and ethylenediamine hydrate (50 g.) were heated together at 200—210° for 15 hours in an autoclave, and the cold product, when washed with water, dried, and recrystallised from light petroleum (b. p. 80—100°), furnished the quinoxaline as golden yellow plates, m. p. 96—97° (cf. Merz and von Ris, *Ber.*, 1887, **20**, 1191).

1 : 4-*Bis-2′-cyanoethyl-*1 : 2 : 3 : 4-*tetrahydroquinoxaline* (I).—A solution of the quinoxaline (20 g.) in acetic acid (45 g.) was boiled under reflux whilst vinyl cyanide (32 g.) was added during 30 minutes. The mixture was then boiled for 7 hours, cooled, neutralised with saturated sodium carbonate solution, and extracted with chloroform. Evaporation of the dried extract gave a residue of the 2′-*cyanoethyl* compound (I), which after recrystallisation from ethanol (charcoal) gave colourless crystals (27·9 g., 80%), m. p. 88·5—89° (Found : C, 69·9; H, 6·6; N, 23·3. $C_{14}H_{16}N_4$ requires C, 69·8; H, 6·7; N, 23·4%).

1 : 4-*Bis-2′-carboxyethyl-*1 : 2 : 3 : 4-*tetrahydroquinoxaline* (III).—A mixture of the cyanoethyl compound (I) (30 g.), potassium hydroxide (60 g.), and water (400 c.c.) was boiled under reflux for 3 hours, cooled, and acidified with hydrochloric acid. The 2′-*carboxyethyl* compound (III) was precipitated at pH 4, collected, and recrystallised from aqueous ethanol; it formed pale pink (almost white) crystals (24 g., 71%), m. p. 136—137° (Found : C, 60·0; H, 6·3; N, 10·2. $C_{14}H_{18}O_4N_2$ requires C, 60·4; H, 6·5; N, 10·1%).



(*A*) *The diketo-diamine* (II) *in ethanolic solution.*
(*B*) *The di-indolo-derivative* (IV) *in 2-methoxyethanol solution.*
(*C*) *The diquinolino-derivative* (VI) *in ethanolic solution.*

1 : 2 : 2a : 3 : 4 : 5 : 8 : 9 : 10 : 10a-*Decahydro-*5 : 8-*diketo-*2a : 10a-*diazapyrene* (II).—The 2′-cyanoethyl compound (I) (20 g.) was added to a mixture of powdered anhydrous aluminium chloride (60 g.), chlorobenzene (250 c.c.), and concentrated hydrochloric acid (3 c.c.), which was then heated with stirring at 140—160° for 6 hours. The product was then mixed with ice-water and distilled with steam to remove the chlorobenzene. The *diketone* (II) separated from the cold residue, and when collected, washed, dried, and recrystallised from ethanol gave brilliant red crystals (12·5 g., 63%), m. p. 245—246° (Found : C, 69·1; H, 5·7; N, 11·55. $C_{14}H_{14}O_2N_2$ requires C, 69·4; H, 5·8; N, 11·6%).

When pure phenylhydrazine (20 c.c.) and acetic acid (2 c.c.) were added to a solution of the diketone (II) (3 g.) in boiling ethanol (350 c.c.), and the mixture was then heated under reflux for 1 hour, the *bisphenylhydrazone* separated as golden plates (4 g., 77%), m. p. 242—244°, the low solubility of which prevented recrystallisation (Found : C, 74·0; H, 5·9; N, 20·9. $C_{26}H_{26}N_6$ requires C, 73·9; H, 6·2; N, 19·9%).

1 : 2 : 2a : 3 : 10 : 10a-*Hexahydrodi-indolo*(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2a : 10a-*diazapyrene* (IV).—A mixture of the bisphenylhydrazone (2 g.), ethanol (125 c.c.), and saturated ethanolic hydrogen chloride (125 c.c.) was boiled under reflux for 3 hours. The pale brown precipitate which had separated was collected, washed with ethanol, and dissolved in hot water. Basification then precipitated the *di-indolo*-compound (IV), which was insoluble in almost all the common organic solvents, but recrystallised from 2-methoxyethanol as hygroscopic bright yellow crystals (0·9 g., 50%), m. p. 438—439° (Found : C, 79·6; H, 5·4; N, 13·9. $C_{26}H_{22}N_4$ requires C, 79·8; H, 5·7; N, 14·3%). The very high m. p. raised a doubt as to whether, in spite of the above analysis, this compound was actually a ψ-indole. An examination of the infra-red spectrum of the thoroughly dried material, kindly under taken by Dr. R. N. Haszeldine, shows the –NH– band in the 3-μ. region, and the compound cannot therefore be the bis-ψ-indole. The intermediate possibility, namely, that one of these groups is a true indole and the other a ψ-indole, is so improbable that it can reasonably be ignored.

1 : 2 : 2a : 3 : 10 : 10a-*Hexahydrodiquinolino*(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2a : 10a-*diazapyrene*-4′ : 4″-*dicarboxylic Acid* (V).—A mixture of the diketone (II) (4 g.), isatin (8 g.), 30% aqueous potassium hyroxide (48 c.c.), and ethanol (80 c.c.) was boiled under reflux under nitrogen for 18 hours. The cold solution

was poured into air-free water, and the acid (V) then precipitated with acetic acid, all these operations being performed under nitrogen. The minute dark green crystals of the acid (V), when collected, washed with ethanol, and dried, had m. p. 242—246° (evacuated tube); the yield was 7 g. (85%).

No satisfactory solvent for recrystallisation of the acid was found. The *disodium* salt was therefore prepared by dissolving the acid in boiling 20% aqueous sodium hydroxide; on cooling, the red sodium salt separated, and was recrystallised from 10% air-free sodium hydroxide solution as bright red crystals which darkened rapidly on exposure to air (Found: N, 10·5. $C_{30}H_{18}O_4N_4Na_2$ requires N, 10·3%).

1 : 2 : 2a : 3 : 10 : 10a-*Hexahydrodiquinolino*(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2a : 10a-*diazapyrene* (VI).—The acid, when heated in a sublimation apparatus at 300°/0·01 mm., underwent decarboxylation and the dark red *amine* (VI) sublimed; it was purified by sublimation at 210—220°/5 × 10^{-6} mm. and obtained as a bright red crystalline powder, m. p. 156—158° (evacuated tube), which darkened on exposure to air (Found: C, 81·9; H, 5·3; N, 13·4. $C_{28}H_{20}N_4$ requires C, 81·5; H, 4·9; N, 13·6%).

1 : 2 : 2a : 3 : 10 : 10a-*Hexahydro*-3 : 10-*diketodiquinolino*(3′ : 2′-4 : 5)(2″ : 3″-8 : 9)-2a : 10a-*diazapyrene* (VII).—A cold saturated acetone solution of potassium permanganate was added with stirring to a solution of the amine (3 g.) in acetone (500 c.c.) until a faint pink colour remained. The precipitated manganese dioxide was collected, and evaporation of the filtrate left a residue of the diketo-compound. The major portion of the latter had however been adsorbed by the manganese dioxide from which it was removed by repeated extraction with acetone. The united residues from the acetone evaporation were recrystallised from dry freshly-distilled pyridine, and the *diketo*-compound (VII) obtained as fine orange crystals (1·3 g., 41%), m. p. 428—430° (Found: C, 76·1; H, 4·0; N, 13·0. $C_{28}H_{16}O_2N_4$ requires C, 76·35; H, 3·7; N, 12·7%).

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