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# *The Preparation of Bis-2-cyanoethyl Derivatives of Aromatic Primary Amines, and their Conversion into* 1 : 6-*Diketojulolidines. Part III.**

By JOHN T. BRAUNHOLTZ and FREDERICK G. MANN.

[Reprint Order No. 4740.]

The properties of various nuclear-substituted 1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines have been studied, particularly their hydrolysis to the corresponding 1-2′-carboxyethyl derivatives and the possibility of decarboxylating the latter to the 1-ethyl derivatives. Although this type of decarboxylation has not been achieved, several other reactions have been elucidated.

*NN*-Bis-2-cyanoethylaniline is converted by nitric acid under varying conditions into *NN*-bis-2-cyanoethyl-2 : 4-dinitroaniline, and into *NNN′N′*-tetrakis-2-cyanoethylbenzidine and its 3 : 5 : 3′ : 5′-tetranitro-derivative.

IN Parts I and II (Braunholtz and Mann, *J.*, 1952, 3046; 1953, 1817) we described the cyclisation of nuclear-substituted derivatives of *NN*-bis-2-cyanoethylaniline, $Ph{\cdot}N(C_2H_4{\cdot}CN)_2$, whereby mono- and/or di-cyclisation may occur, to give the corresponding derivatives of 1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (as I) and of 1 : 6-dioxojulolidine (as II). We have now further studied the derivatives of type (I), in order to investigate the possibility (mentioned in Part I) that hydrolysis of the 2-cyanoethyl group followed by decarboxylation might give the corresponding 1-ethyltetrahydro-4-oxoquinolines, and thus provide a synthesis of these 1-alkyl-4-oxo-derivatives alternative to that recently described by Allison, Braunholtz, and Mann (*J.*, 1954, 403). Although these attempts have failed, several noteworthy properties of the intermediate compounds have been revealed.

The ratio of the mono- (I) to di-ketone (II) formed on cyclisation of the bis-2-cyano-

* Part II, *J.*, 1953, 1817.

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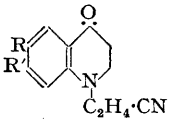
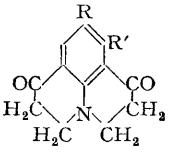
ethylaniline varies considerably with the conditions employed. We have shown (Part II) that *p*-chloro-*NN*-bis-2-cyanoethylaniline when heated with aluminium chloride (8·75 mols.) in chlorobenzene with hydrochloric acid at 155° for 8 hours gives 6-chloro-1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (I; R = Cl, R′ = H) in 40% yield, no diketone being isolated. Repetition of this experiment, but with aluminium chloride


(I)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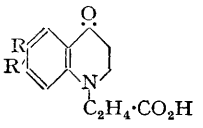
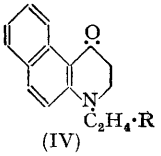
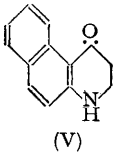

(III)

(6·1 mols.) at 170°, gave this monoketone in 74% yield, and 8-chloro-1 : 6-dioxojulolidine (II; R = Cl, R′ = H) in 6·5% yield. The use of *o*-dichlorobenzene as a solvent, with heating at 190—195° for 3·5 hours, gave solely the diketone in 50% yield.

Bis-2-cyanoethyl-*m*-toluidine, however, when similarly heated with the chloride (6 mols.) in chlorobenzene at 150° for 9 hours, gave 7-methyl-1 : 6-dioxojulolidine (II; R = H, R′ = Me) in *ca.* 40% yield, but when heated at 170° for 8·5 hours gave 1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-7-methyl-4-oxoquinoline (I; R = H, R′ = Me) in 29% yield and the diketone in 19% yield. Reduction in the proportion of aluminium chloride or the use of *o*-dichlorobenzene as a solvent again gave solely the diketone. In this case in particular, the precise conditions which determine the proportion and yield of the mono- and the di-ketone remain uncertain: it is possible however that the nature of the product is determined primarily by the stability of an intermediate aluminium chloride complex, which may vary considerably under different conditions. (It is assumed that the last monocyclisation has occurred to give the 7-methyl compound, since the formation of the 5-methyl isomer would involve cyclisation on to a carbon atom sterically protected by two *ortho* substituents. The product, m. p. 114·5°, showed no indication of being other than homogeneous. It must be emphasised, however, that no decisive evidence for the position of the methyl group is available.)

The 1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines of type (I) underwent smooth alkaline hydrolysis to the corresponding crystalline 1-2′-carboxyethyl derivatives of type (III). With one exception, these acids, like the parent nitriles, could be distilled or sublimed without change. When however 1-2′-cyanoethyl- or 1-2′-carboxyethyl-1 : 2 : 3 : 4-tetrahydro-4-oxo-5 : 6-benzoquinoline (IV; R = CN or $CO_2H$) was heated under reduced pressure, loss of the side-chain occurred, with the formation of 1 : 2 : 3 : 4-


(IV)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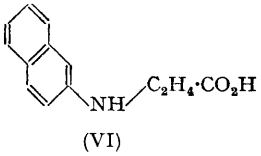
(VI)

tetrahydro-4-oxo-5 : 6-benzoquinoline (V), the identity of which was confirmed by the fact that its infra-red spectrum showed bands at 3·1 and 6·2 μ corresponding to the :NH and :CO groups respectively. The compound (V) in ethanol showed the following ultra-violet spectrum (λ in mμ), which is almost identical with that of the parent nitrile (IV; R = CN) (cf. Part II):

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| $\lambda_{max.}$ ..... | 395—396 | 315 | 258 | 216 | $\lambda_{min.}$ ..... | 340 | 297 | 236 |
| $\varepsilon_{max.}$ ..... | 5700 | 4900 | 36,600 | 25,900 | $\varepsilon_{min.}$ ..... | 1050 | 3700 | 13,700 |

This loss of the side-chain also occurs when the monoketones of type (I) are subjected to acidic hydrolysis. Thus when solutions of the 6-chloro- and the 7-methyl derivative (I; R = Cl, R′ = H; R = H, R′ = Me) in hydrochloric acid were boiled under reflux, the corresponding 6-chloro- and 7-methyl derivatives of tetrahydro-4-oxoquinoline were ultimately isolated. Again the 5 : 6-benzo-analogues formed an exception, for the com-

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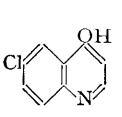
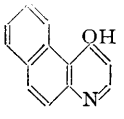
pounds (IV; R = CN and $CO_2H$) when similarly treated furnished β-2-naphthylaminopropionic acid (VI), the hydrogenated keto-pyridine ring having undergone fission. It is clear that the 2-carboxyethyl group in (VI) is derived from this pyridine ring and not from the original 2′-cyanoethyl or 2′-carboxyethyl group in (IV), because the ketone (V) when similarly treated with hydrochloric acid also gave the acid (VI).

The 6-chloro-acid (III; R = Cl, R′ = H), when heated with copper bronze in quinoline at 235—240°, also lost the side-chain to give the 6-chlorotetrahydro-4-oxoquinoline.

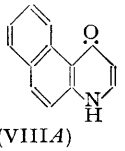
Decarboxylation by pyrolysis of silver salts has been recorded by various authors (cf. Bamberger and Frew, *Ber.*, 1894, **27**, 206; Yu Kanevskaya, Shemyakin, and Bandas, *Ber.*, 1934, **67**, 1518; 1936, **69**, 257, 2152). We found however that the silver salt of the 6-chloro-acid (III; R = Cl, R = H) when heated under reduced pressure gave 6-chloro-4-hydroxyquinoline (VII), and the silver salt of the acid (IV; R = $CO_2H$) similarly gave 4-hydroxy-5 : 6-benzoquinoline (VIII).




(VII)




(VIII)




(VIII*A*)

Attempted decarboxylation of acids of type (III) by heating them with soda-lime or baryta under reduced pressure gave sublimates in minute yield and was therefore unsatisfactory. The acid (IV; R = $CO_2H$) gave 5 : 6-benzoquinoline: it is noteworthy that this acid has thus under various conditions given rise to four degradation products. Attempts to prepare the 1-ethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinolines from monoketones of type (I) were therefore abandoned.

4-Hydroxy-5 : 6-benzoquinoline (VIII) could clearly exist alternatively as the 1 : 4-dihydro-4-oxobenzoquinoline (VIII*A*). Ewing and Steck (*J. Amer. Chem. Soc.*, 1946, **68**, 2181) have found that the ultra-violet absorption spectra of 4-hydroxyquinoline (and several related compounds) in neutral and alkaline solution are almost identical, but differ from that in acid solution: they deduce from this evidence that their compounds in neutral solution exist in the 4-oxoquinoline form (as VIII*A*). The following Table (λ in mμ) shows that the same relation exists between the spectra of the 5 : 6-benzo-derivative in the three media.

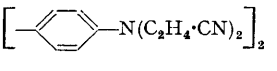
*Spectra of* 4-*hydroxy*-5 : 6-*benzoquinoline.*

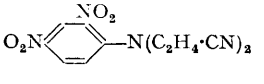
(*A*) in EtOH; (*B*) in aq. 0·1N-NaOH; (*C*) in aq. 0·1N-HCl.

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| (*A*) | $\lambda_{max.}$ | 348 | 332 | 297 | 273 | | $\lambda_{min.}$ | 339 | 324 | 293 | 241 |
| | $\varepsilon_{max.}$ | 4050 | 3840 | 10,000 | 39,400 | | $\varepsilon_{min.}$ | 2250 | 2400 | 9,000 | 9,750 |
| (*B*) | $\lambda_{max}$ | 348 | 331 | 299 | 274 | 255 | $\lambda_{min.}$ | 342 | 326 | 294 | 259 | 238 |
| | $\varepsilon_{max.}$ | 1690 | 2100 | 9,290 | 32,100 | 23,300 | $\varepsilon_{min.}$ | 1170 | 1760 | 8,670 | 22,400 | 14,000 |
| (*C*) | $\lambda_{max.}$ | 344 | 312 | 266 | 237 | 213 | $\lambda_{min.}$ | 388 | 290 | 250 | 224 | |
| | $\varepsilon_{max.}$ | 3470 | 7270 | 27,400 | 25,400 | 33,700 | $\varepsilon_{min.}$ | 2850 | 5450 | 14,600 | 18,900 | |

We have investigated the nitration of bis-2-cyanoethylaniline, in order to insert further substituents into this compound and thus into its cyclised derivatives. This compound, when treated in a sulphuric–acetic acid solution with fuming nitric acid, gives *NNN′N′*-tetrakis-2-cyanoethylbenzidine (IX). With concentrated nitric acid, however, it gives

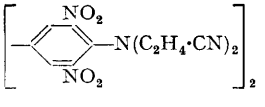
(IX)

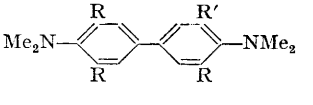



(X)

(XI)




(XII)

*NN*-bis-2-cyanoethyl-2 : 4-dinitroaniline (X) and *NNN′N′*-tetrakis-2-cyanoethyl-3 : 5 : 3′ : 5′-tetranitrobenzidine (XI). This behaviour is analogous to that of dimethyl-

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aniline, which with oxidising agents gives *NNN'N'*-tetramethylbenzidine (cf. Michler and Pattinson, *Ber.*, 1881, **14**, 2161; Willstätter and Kalb, *Ber.*, 1904, **37**, 3765; Rumpf, *Bull. Soc. chim.*, 1940, **7**, 634) and with nitric acid gives 2 : 4-dinitrodimethylaniline and *NNN'N'*-tetramethyl-3 : 5 : 3' : 5'-tetranitrobenzidine (XII; R = R' = $NO_2$) (Hodgson, *J.*, 1942, 584; *J. Soc. Dyers and Colourists*, 1944, **60**, 151).

The identities of (IX) and (X) are confirmed by the fact that the ultra-violet spectrum of (IX) closely resembles those of benzidine and *NN'*-bis-2-cyanoethylbenzidine (cf. Part II), whilst that of (X) resembles that of dimethyl-2 : 4-dinitroaniline :

*Absorption spectra in ethanol* ($\lambda$ *in* m$\mu$).

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Benzidine ..... | $\lambda_{max.}$ | 283—285 | $\varepsilon_{max.}$ | 26,300 | $\lambda_{min.}$ | 240 | $\varepsilon_{min.}$ | 3160 |
| *NN'*-Bis-2-cyanoethylbenzidine | $\lambda_{max.}$ | 296—298 | $\varepsilon_{max.}$ | 26,900 | $\lambda_{min.}$ | 246 | $\varepsilon_{min.}$ | 2690 |
| (IX) ..... | $\lambda_{max.}$ | 303 | $\varepsilon_{max.}$ | 34,380 | $\lambda_{min.}$ | 244 | $\varepsilon_{min.}$ | 1788 |
| Dimethyl-2:4-dinitroaniline*... | $\lambda_{max.}$ | 347 | $\lambda_{min.}$ | 285 | $\lambda_{infl.}$ | *ca.* 270 | | |
| (X) ..... | $\lambda_{max.}$ | 348—349 | $\varepsilon_{max.}$ | 11,300 | $\lambda_{min.}$ | 286 | $\varepsilon_{min.}$ | 2300 |
| | | | $\lambda_{infl.}$ | 268—270 | $\varepsilon_{infl.}$ | 3170 | | |

* Values derived from results of Morgan, Moss, and Porter, *J.*, 1915, **107**, 1296.

The absorption spectrum of the tetranitro-derivative (XI) is unexpectedly simple: this may be due to steric interference between the bis-2-cyanoethylamino- and the nitro-groups, for the dimethylamino-analogue (XII; R = R' = $NO_2$) shows a similar but less marked effect. Whilst preparing the latter, we have also isolated the scarlet *NNN'N'*-tetramethyl-3 : 5 : 3'-trinitrobenzidine (XII; R = $NO_2$, R' = H), which gives an orange-yellow solution in methanol. The absorption spectra of these compounds in methanol are given below, $\varepsilon$ values being inserted in parentheses and $\lambda$ being in m$\mu$ :

| | | |
|---|---|---|
| (XI) ..... | $\lambda_{infl.}$ | 284—293 (13,700) |
| (XII; R = R' = $NO_2$) ..... | $\lambda_{max.}$ | 378 (8170), 365 (8470), 309—310 (23,900) |
| | $\lambda_{min.}$ | 373 (7880), 364 (8330), 266 (9890) |
| | $\lambda_{infl.}$ | 368—372 (8330), 358—360 (8550), 228—232 (21,600) |
| (XII; R = $NO_2$, R' = H) ..... | $\lambda_{max}$ | 418 (5150), 393 (5540), 378 (5770), 315 (25,600) |
| | $\lambda_{min.}$ | 414 (4920), 391 (5190), 374 (5650), 267 (11,000) |
| | $\lambda_{infl.}$ | 426—432 (4540), 380—384 (5600), 370—372 (5730) |

It will be seen that the spectra of the two compounds of type (XII) contain a number of very weak bands, some of which are little more than pronounced inflexions: these two spectra are closely similar in shape, and bear a general resemblance to that of (XI).

The above reactions of bis-2-cyanoethylaniline with nitric acid are of value because the direct dicyanoethylation of nitroanilines or the tetracyanoethylation of benzidine has not yet been achieved.

When this investigation was almost complete, a brief record of the monocyclisation of bis-2-cyanoethylaniline was published by Johnson and DeAcetis (*J. Amer. Chem. Soc.*, 1953, **75**, 2766).

## Experimental

*Cyanoethylation.*—(1) A mixture of *m*-nitroaniline (27 g.), vinyl cyanide (26 c.c., 2·04 mols.), acetic acid (25 c.c., 2·1 mols.), and cuprous chloride (2 g.) was boiled under reflux for 13 hr., allowed to cool, and then poured with stirring into an excess of aqueous ammonia (*d* 0·88). The semi-solid deposit, when recrystallised from ethanol, gave orange N-2-*cyanoethyl*-m-*nitroaniline*, m. p. 97·5° (26 g., 70%) (Found: C, 56·45; H, 4·9; N, 22·0. $C_9H_9O_2N_3$ requires C, 56·5; H, 4·8; N, 22·0%).

(2) β-Naphthylamine (5 g.), similarly treated with vinyl cyanide (2·4 c.c., 1·04 mols.), acetic acid (2·1 c.c., 0·95 mol.), and cuprous chloride (0·2 g.) but with 4 hours' heating, gave *N*-2-cyanoethyl-β-naphthylamine, m. p. 99—100° (from ethanol) (Found: N, 14·3. Calc. for $C_{13}H_{12}N_2$: N, 14·3%). Bauer, Cymerman, and Sheldon (*J.*, 1951, 3312) give m. p. 102°.

(3) *p*-Chloroaniline, when cyanoethylated as described in Part II but with 18 hours' heating, gave *p*-chloro-*NN*-bis-2-cyanoethylaniline, m. p. 91—92° (from ethanol), without intermediate distillation, and in 27% yield.

*Cyclisation.*—(1) p-*Chloro*-NN-*bis*-2-*cyanoethylaniline*. A mixture of the dinitrile (11·5 g.), aluminium chloride (40 g., 6·1 mols.), chlorobenzene (30 c.c.), and concentrated hydrochloric acid (1·5 c.c.) was heated at 170° for 8 hr. Working up as previously described (Part II) gave a yellowish-brown oil which rapidly solidified and on fractional crystallisation from ethanol

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furnished 6-chloro-1-2′-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (I; R = Cl, R′ = H), pale yellow plates, m. p. 136—137° (8·5 g., 74%), and 8-*chloro*-1 : 6-*dioxojulolidine* (II; R = Cl; R′ = H), brilliant yellow plates, m. p. 200—201° (0·75 g., 6·5%) (Found: C, 60·8; H, 4·2; N, 6·2. $C_{12}H_{10}O_2NCl$ requires C, 61·1; H, 4·25; N, 5·95%); the latter gave a *bis-phenylhydrazone*, bright yellow, m. p. 283° (decomp.; in sealed tube) (Found: C, 69·4; H, 5·6; N, 16·6. $C_{24}H_{22}N_5Cl$ requires C, 69·35; H, 5·35; N, 16·85%).

Repetition of the cyclisation using *o*-dichlorobenzene, with heating at 190—195° for 3·5 hours, gave solely the diketone, m. p. 195—197° after one recrystallisation (5·75 g., 50%).

(2) NN-*Bis*-2-*cyanoethyl*-m-*toluidine*. The cyclisation with aluminium chloride (6 mols.) and 9 hours' heating at 150° to 7-methyl-1 : 6-dioxojulolidine (II; R = H; R′ = Me) in 35—45% yield has been described (Part I). Repetition of this experiment, with the dinitrile (10·5 g.) and aluminium chloride (40 g., 6·2 mols.) in chlorobenzene (30 c.c.) containing concentrated hydrochloric acid (1·5 c.c.), and heating at 170° for 8·5 hr., gave a crude product which on fractional crystallisation from ethanol gave the less soluble 1-2′-*cyanoethyl*-1 : 2 : 3 : 4-*tetrahydro*-7-*methyl*-4-*oxoquinoline* (I; R = H, R′ = Me) (3 g., 29%), very pale yellow, m. p. 114·5° (Found: C, 72·9; H, 6·9; N, 13·15. $C_{13}H_{14}ON_2$ requires C, 72·9; H, 6·6; N, 13·1%). This gave a *semicarbazone*, colourless needles, m. p. 207°, from aqueous ethanol (Found: C, 62·1; H, 6·0; N, 26·0. $C_{14}H_{17}ON_5$ requires C, 62·0; H, 6·3; N, 25·8%). The ethanolic mother-liquors from the cyclisation ultimately gave the above diketone, m. p. 116—118° (2 g., 19%). When this experiment was modified by using (*a*) treble the above quantities, (*b*) the above quantities but with the chloride reduced to 20 g. (3 mols.), and (*c*) the above quantities with *o*-dichlorobenzene as solvent and with heating at 190—195° for 4 hr., only the diketone was isolated, in yields of 46, 45, and 70% respectively.

(3) NN-*Bis*-2′-*cyanoethyl*-3 : 4-*dimethylaniline*. A mixture of this dinitrile (2 g.), aluminium chloride (7 g., 6 mols.), chlorobenzene (5·5 c.c.), and hydrochloric acid (0·5 c.c.) was heated at 170° for 8·5 hr. The product, worked up as usual, furnished 1-2′-*cyanoethyl*-1 : 2 : 3 : 4-*tetrahydro*-6 : 7-*dimethyl*-4-*oxoquinoline* (I; R = R′ = Me), very pale, yellow plates, m. p. 144·5—145° (from ethanol) (Found: C, 73·6; H, 7·0; N, 12·1. $C_{14}H_{16}ON_2$ requires C, 73·7; H, 7·05; N, 12·3%): 0·7 g., 35%. It gave a colourless *semicarbazone*, m. p. 216·5°, from aqueous ethanol (Found: C, 63·1; H, 6·7; N, 24·3. $C_{15}H_{19}ON_5$ requires C, 63·1; H, 6·7; N, 24·5%). It is again assumed that the methyl groups are in the 6 : 7- and not the 5 : 6-positions.

*Hydrolysis of Nitriles* (I) *to Acids* (III).—(1) A solution of the 6-chloro-ketone (I; R = Cl, R′ = H) (8 g.) and potassium hydroxide (10 g.) in aqueous ethanol (50 c.c.) was boiled under reflux for 4 hr., cooled, diluted with water (50 c.c.), filtered, and acidified. The 1-2′-*carboxyethyl*-6-*chloro*-1 : 2 : 3 : 4-*tetrahydro*-4-*oxoquinoline* (III; R = Cl, R′ = H) (7 g., 81%) which separated formed pale yellow crystals, m. p. 154—155°, after repeated recrystallisation from aqueous ethanol (Found: C, 57·0; H, 4·9; N, 5·7. $C_{12}H_{12}O_3NCl$ requires C, 56·8; H, 4·8; N, 5·5%). More concentrated alkali, or longer heating, caused contamination of the acid by a brown tar. The acid gave a pale yellow *silver* salt, m. p. 135° (decomp.) (Found: N, 4·4. $C_{12}H_{11}O_3NClAg$ requires N, 3·9%).

(2) The 7-*methyl* analogue (III; R = H, R′ = Me) was similarly prepared and purified, and furnished almost colourless crystals (77%), m. p. 140·5—142·5° (Found: C, 67·2; H, 6·8; N, 5·9. $C_{13}H_{15}O_3N$ requires C, 66·95; H, 6·5; N, 6·0%).

(3) The 5 : 6-*benzo*-analogue (IV; R = $CO_2H$), similarly prepared, formed yellow crystals (93%), m. p. 161—161·5° (Found: C, 71·4; H, 5·7; N, 5·15. $C_{16}H_{15}O_3N$ requires C, 71·4; H, 5·6; N, 5·2°). It gave a pale yellow *silver* salt, m. p. 158·5° (decomp.) (Found: N, 3·9. $C_{16}H_{14}O_3NAg$ requires N, 3·7%).

*Action of Heat.*—(1) The keto-nitriles (I; R = Cl, R′ = H; R = MeO, R′ = H; and R = H, R′ = Me), when heated at 0·1 mm. above their m. p.s, distilled or sublimed unchanged. (2) The keto-acids (III; R = Cl, R′ = H) and (I; R = H, R′ = Me) behaved similarly. (3) The benzo-nitrile (IV; R = CN) when heated at 250°/0·1 mm. gave a viscous yellow distillate which solidified, and when recrystallised from aqueous ethanol furnished 1 : 2 : 3 : 4-*tetrahydro*-4-*oxo*-5 : 6-*benzoquinoline* (V), pale yellow needles, m. p. 138°, in almost theoretical yield (Found: C, 78·9; H, 5·8; N, 7·0. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·65; N, 7·1%). The benzo-acid (IV; R = $CO_2H$) behaved similarly.

The compound (V) gave a 2 : 4-dinitrophenylhydrazone, bright orange needles, m. p. 247° (decomp.), which could not be obtained pure. Neither a semicarbazone nor a benzoyl derivative could be isolated, and cyanoethylation in acetic acid with cuprous chloride could not be achieved.

When dry hydrogen chloride was passed into an acetone solution of (V), the hydrochloride was rapidly precipitated as bright yellow plates; these were unstable to water and to even

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mild heating, having in consequence an indefinite m. p. Consistent analytical values could not be obtained. In contrast, 1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline when similarly treated gave the *hydrochloride* as hygroscopic cream-coloured crystals, m. p. 145° (Found: C, 59·1; H, 5·8; N, 7·6. $C_9H_9ON$,HCl requires C, 58·85; H, 5·5; N, 7·6%): this hydrochloride, although decomposed by water and hot solvents, is thus appreciably more stable than that of (V).

*Action of Hydrochloric Acid.*—In the following experiments, a mixture of equal volumes of concentrated acid and water was used throughout. (1) A solution of tetrahydro-4-oxoquinoline (1 g.) in the acid (25 c.c.) was boiled under reflux for 4 hr., and then cooled, neutralised to pH 7, and extracted with ether, 80% of the unchanged ketone being recovered.

(2) When 1 : 6-dioxojulolidine was similarly treated, extraction with chloroform furnished unchanged diketone in 60% yield. When the boiling was extended to 17 hr., only a reddish-brown intractable tar was obtained.

(3) The 7-methyl keto-nitrile (I; R = H, R′ = Me) (1 g.) was treated as in (1), the cold acid solution being however basified and extracted with ether. The extract after removal of the solvent gave a residue which, when recrystallised from aqueous ethanol, furnished tetrahydro-7-methyl-4-oxoquinoline, pale yellow, m. p. 100—101° (Found: C, 74·1; H, 6·7. Calc. for $C_{10}H_{11}ON$: C, 74·5; H, 6·9%): 0·45 g., 60%. The position of the methyl group in this compound, as in the parent nitrile, is uncertain: Clemo and Perkin (*J.*, 1925, 2297) prepared a compound, m. p. 109°, which they considered to be this 7-methyl isomer.

The alkaline solution from the ether-extraction was then acidified and extracted with chloroform. Evaporation of the extract gave a residue which, after recrystallisation from aqueous ethanol, gave the carboxy-ketone (III; R = H, R′ = Me) (0·15 g., 14%), m. p. 138—140°, raised to 140—141·5° on admixture with an authentic sample. It is thus reasonably certain that hydrolysis of the nitrile (as I) to the acid (as III) precedes the complete loss of the side-chain. (4) The 6-chloro-keto-nitrile (I; R = Cl; R′ = H) (1 g.) was treated as in (1), and the cold acid solution then brought to pH 4. The yellow-brown solid deposited (0·7 g., 91%), after recrystallisation from aqueous ethanol and then benzene–*cyclo*hexane, gave 6-chloro-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline, pale yellow needles, m. p. 125·5—126° (Found: C, 59·3; H, 4·6; N, 7·8. Calc. for $C_9H_8ONCl$: C, 59·5; H, 4·45; N, 7·7%). Extending the time of boiling from 4 to 14 hr. gave identical results.

Since however Elderfield and Maggiolo (*J. Amer. Chem. Soc.*, 1949, **71**, 1906) give m. p. 112° (corr.) for this compound and m. p. 125° (corr.) for β-*p*-chloroanilinopropionic acid, which clearly could also arise under the above conditions, the following confirmation of the identity of the ketoquinoline was obtained. (*a*) It formed a 2 : 4-*dinitrophenylhydrazone*, deep red plates, m. p. 282° (decomp.) (Found: N, 19·6. $C_{15}H_{12}O_4N_5Cl$ requires N, 19·4%). (*b*) Its ultra-violet spectrum (*A*) is almost identical with that of the parent keto-nitrile (*B*) (cf. Part II), both determined in ethanol.

| | | | | | | |
|---|---|---|---|---|---|---|
| (*A*) $\lambda_{max.}$ | 392 | 263 | 237 | $\lambda_{min.}$ | 292 | 252 |
| $\varepsilon_{max.}$ | 3990 | 8790 | 22,800 | $\varepsilon_{min.}$ | 61 | 6530 |
| (*B*) $\lambda_{max.}$ | 392—394 | 268—269 | 239 | $\lambda_{min.}$ | 296 | 252 |
| $\varepsilon_{max.}$ | 4490 | 11,270 | 25,000 | $\varepsilon_{min.}$ | 220 | 6900 |

(*c*) *p*-Chloro-*N*-2-cyanoethylaniline was subjected to alkaline hydrolysis (cf. p. 655), and the clear cold solution then brought to pH 5; the highly crystalline β-*p*-chloroanilinopropionic acid separated, having m. p. 121·5° after recrystallisation from aqueous ethanol (Found: C, 53·9; H, 5·1; N, 6·85. Calc. for $C_9H_{10}O_2NCl$: C, 54·1; H, 5·05; N, 7·0%). This m. p. was markedly depressed when the acid was mixed with the above ketoquinoline.

(5) The 5 : 6-benzo-keto-nitrile (IV; R = CN) (0·5 g.) was similarly treated, with 6·5 hours' boiling. The cold reaction mixture, when neutralised to pH 7, deposited a buff-coloured solid (0·28 g., 75%) which, when recrystallised from benzene and then from aqueous ethanol, gave β-2-*naphthylaminopropionic acid* (VI), cream-coloured plates, m. p. 128—128·5° (Found: C, 72·2; H, 5·8; N, 6·4. $C_{13}H_{13}O_2N$ requires C, 72·5; H, 6·1; N, 6·5%). The acid (VI), in almost the same yield, was obtained by similar treatment of the keto-acid (IV; R = $CO_2H$) and of the unsubstituted ketone (V).

The identity of the acid (VI) was confirmed by its preparation from *N*-2-cyanoethyl-β-naphthylamine, which on alkaline hydrolysis (cf. p. 655) also furnished (VI), m. p. 125°, unchanged by admixture with the previous sample (Found: C, 72·6; H, 6·3%). The acid did not give a benzoyl or toluene-*p*-sulphonyl derivative under the usual Schotten–Baumann conditions.

The infra-red spectrum of (VI) includes bands at 2·98 and 3·77 μ consistent with its structure

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as an amino-acid. Furthermore, its ultra-violet spectrum is closely akin to that of β-naphthylamine :

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| $C_{10}H_7 \cdot NH_2$ | $\lambda_{max.}$ | 340 | 290 | 280 | 237 | 213 | $\lambda_{min.}$ | 304 | 288 | 258 | 217 |
| | $\varepsilon_{max.}$ | 2120 | 4690 | 6290 | 55,000 | 24,000 | $\varepsilon_{min.}$ | 560 | 4520 | 3520 | 18,700 |
| (VI) ..... | $\lambda_{max.}$ | 346—8 | 292 | 282 | 244 | 214 | $\lambda_{min.}$ | 309 | 288 | 263 | 221 |
| | $\varepsilon_{max.}$ | 2460 | 7940 | 9290 | 48,000 | 29,900 | $\varepsilon_{min.}$ | 800 | 7590 | 5300 | 14,900 |

*Pyrolysis of Silver Salts.*—(1) The silver salt (3·5 g.) of the 6-chloro-acid (III; R = Cl, R′ = H) was heated at 220—225°/0·1 mm. in a wide-bore sublimation tube for 1 hr., a highly crystalline sublimate being deposited. This sublimate (1·2 g., 69%), when recrystallised from aqueous ethanol, gave the colourless hemihydrate of 6-chloro-4-hydroxyquinoline (VII), m. p. 261—262° (Found : C, 57·4; H, 3·5; N, 7·65. Calc. for $C_9H_6ONCl,\frac{1}{2}H_2O$ : C, 57·4; H, 3·7; N, 7·4%). The compound in aqueous ethanol gave a blood-red colour with ferric chloride, but an attempted preparation of the 2 : 4-dinitrophenylhydrazone failed. Bachmann and and Cooper (*J. Org. Chem.*, 1944, **9**, 302) give m. p. 269° (corr.) for the anhydrous base.

(2) The silver salt (2 g.) of the acid (IV; R = $CO_2H$) was similarly treated, the temperature rising to 250°/0·1 mm. The crystalline pale yellow sublimate (0·7 g., 67%) when recrystallised from ethanol gave 4-hydroxy-5 : 6-benzoquinoline (VIII), colourless, m. p. 272—273° (in a sealed tube, bath-temp. rising from 255°) (Found : C, 80·0; H, 4·75; N, 7·3. Calc. for $C_{13}H_9ON$ : C, 80·0; H, 4·65; N, 7·2%). Mueller and Hamilton (*J. Amer. Chem. Soc.*, 1943, **65**, 1017) give m. p. 286—288°. It gave a *hydrochloride* which separated in colourless needles of indefinite m. p. when a warm methanolic solution was saturated with hydrogen chloride (Found : N, 5·8. $C_{13}H_9ON,HCl$ requires N, 6·0%).

Attempts to prepare the acetyl and toluene-*p*-sulphonyl derivatives failed, but treatment with boiling phosphorus oxychloride gave colourless 4-chloro-5 : 6-benzoquinoline, m. p. 58—60° (from aqueous ethanol) (Found : N, 6·6. Calc. for $C_{13}H_8NCl$ : N, 6·55%). Mueller and Hamilton (*loc. cit.*) give m. p. 62—63°.

*Action of Barium Hydroxide.*—An intimate mixture of the 5 : 6-benzo-acid (IV; R = $CO_2H$) and a large excess of the hydroxide was heated at 300—320°/0·03 mm. for 5 hr. The very small pale yellow sublimate, m. p. 68—78°, was treated in ethanolic solution with picric acid, and gave 5 : 6-benzoquinoline picrate, yellow crystals (from methanolic acetone), m. p. 250° alone and when mixed with the sample described below (Found : C, 56·1; H, 2·9; N, 13·4. Calc. for $C_{13}H_9N,C_6H_3O_7N_3$ : C, 55·9; H, 3·0; N, 13·7%).

To confirm this identification, β-naphthylamine was converted by the Skraup reaction into 5 : 6-benzoquinoline (60% yield), which gave a picrate, m. p. 251—252° (Found : C, 56·2; H, 3·2; N, 13·5%). It also gave a *hydrochloride*, colourless hygroscopic needles, m. p. 230° (decomp.), from ethanolic acetone (Found : C, 72·3; H, 5·1; N, 6·4. $C_{13}H_9N,HCl$ requires C, 72·4; H, 4·7; N, 6·5%). Skraup and Cobenzl (*Monatsh.*, 1883, **4**, 436) record the picrate, m. p. 251—252°, and the hydrochloride dihydrate, the m. p. of which is not stated.

*Action of Quinoline.*—A suspension of the 6-chloro-acid (III; R = Cl, R′ = H) (2 g.) in quinoline (25 c.c.) containing copper-bronze (0·1 g.) was heated under reflux (bath-temp., 235—240°) for 2 hr. The cold product was poured into water, the quinoline removed by steam-distillation, and the supernatant yellow aqueous layer decanted from a brown tar. From the aqueous layer 6-chloro-1 : 2 : 3 : 4-tetrahydro-4-oxoquinoline (0·1 g., 7%) slowly crystallised, and after recrystallisation from aqueous ethanol formed yellow crystals, m. p. and mixed m. p. 124—125°. Ethanolic extraction (charcoal) of the tarry residue also gave the keto-quinoline (0·5 g., 35%, estimated as the 2 : 4-dinitrophenylhydrazone).

*Nitration of* NN-*Bis*-2-*cyanoethylaniline.*—(*a*) A solution of the dinitrile (10 g.) in acetic acid (10 c.c.) containing concentrated sulphuric acid (20 c.c.) was cooled to 0—5°, and vigorously stirred whilst fuming nitric acid (2·5 c.c., 1·2 mols.) was added dropwise so that the temperature did not rise above 25°. The mixture was then stirred at room temperature for 30 min. and poured on ice. The deep blackish-green tarry precipitate, when repeatedly recrystallised from acetone–benzene and then from acetone, gave NNN′N′-*tetrakis*-2-*cyanoethylbenzidine* (IX), pale yellow crystals, m. p. 180° (Found : C, 72·9; H, 6·1; N, 21·1. $C_{24}H_{24}N_6$ requires C, 72·8; H, 6·1; N, 21·2%), in small yield. Its low solubility in boiling solvents precluded reliable molecular-weight determinations. Very slight changes in the above conditions produced heavy tars from which the pure (IV) could not be isolated.

(*b*) The powdered dinitrile (10 g.) was slowly added to vigorously stirred concentrated nitric acid (50 c.c.) at room temperature : the mixture, which had become slightly warm, was stirred for 1·5 hr. and then poured on ice-water (*ca.* 25 c.c.). The dark green precipitate was collected,

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washed, dried, and extracted first with boiling benzene and then with boiling acetone–benzene. Each extract, when diluted with *cyclo*hexane, deposited an orange-yellow product, m. p. 127—129° (total yield, 8 g., 55%), which after repeated recrystallisation from acetone–benzene gave NN-*bis*-2-*cyanoethyl*-2 : 4-*dinitroaniline* (X), bright orange-yellow, m. p. 134—135° (Found : C, 49·6; H, 3·8; N, 24·0%; *M*, ebullioscopic in acetone, 288. $C_{12}H_{11}O_4N_5$ requires C, 49·8; H, 3·8; N, 24·2%; *M*, 289). It dissolved readily in aqueous sodium hydroxide to give a red solution.

The undissolved residue from the above extraction when recrystallised from acetone gave NNN'N'-*tetrakis*-2-*cyanoethyl*-3 : 5 : 3' : 5'-*tetranitrobenzidine* (XI) (2 g., 28%), bright orange, m. p. 225·5° (decomp.) (Found : C, 50·25; H, 3·5; N, 24·1%; *M*, ebullioscopic in acetone, 612. $C_{24}H_{20}O_8N_{10}$ requires C, 50·0; H, 3·5; N, 24·3%; *M*, 576). The low solubility of this compound also precluded more accurate molecular-weight determinations.

*Nitration of Dimethylaniline.*—(*a*) The amine (8·5 g.) was added slowly with vigorous stirring to dilute nitric acid (250 c.c.; *d* 1·11) at −5°. The mixture was kept at −5° for 30 min. and then set aside overnight at room temperature. The brown semi-crystalline product was washed with much boiling ethanol, and the residue (3 g., 20%) when recrystallised from dioxan gave bright orange *NNN'N'*-tetramethyl-3 : 5 : 3' : 5'-tetranitrobenzidine (XII; R = R' = $NO_2$), m. p. 271° (decomp.) (Found : C, 46·0; H, 3·6. Calc. for $C_{16}H_{16}O_8N_6$ : C, 45·75; H, 3·8%). The ethanolic extract deposited dimethyl-2 : 4-dinitroaniline on cooling. This method is based on that of van Romburgh (*Rec. Trav. chim.*, 1922, **41**, 38) who gives m. p. 272° for the tetranitro-compound.

(*b*) When however the amine (5 g.) was added slowly to dilute nitric acid (100 c.c.; *d* 1·13) at 5—10° and this temperature was maintained for 2 hr., the mixture being then poured on ice, the product when repeatedly recrystallised from ethanolic–acetone gave NNN'N'-*tetramethyl*-3 : 5 : 3'-*trinitrobenzidine* (XII; R = $NO_2$, R' = H), scarlet needles, m. p. 198·5° (Found : C, 51·3; H, 4·5; N, 18·7%; *M*, ebullioscopic in acetone, 355. $C_{16}H_{17}O_6N_5$ requires C, 51·2; H, 4·55; N, 18·7%; *M*, 375), in small yield. Dimethyl-2 : 4-dinitroaniline was also isolated.

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