[1953] Derivatives of Aromatic Primary Amines, etc. Part II. 1817

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

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The cyanoethylation of aniline under the influence of various inorganic catalysts, and that of various aromatic primary amines under the influence of cuprous chloride, has been studied.

Several NN-bis-2-cyanoethylarylamines on cyclisation give the corresponding 2:6-diketojulolidines: others, however, undergo only monocyclisation, forming the corresponding N-2-cyanoethyl-1:2:3:4-tetrahydro-4-ketoquinolines.

p-Phenylenediamine very readily undergoes tetrakiscyanoethylation, and the product on cyclisation gives the red octahydro-1:10-diketophenanthroline (VII), which condenses with hydrazine to form the yellow hexahydrotetra-azapyrene (IX), the deep purple monomethiodide of which constitutes a new type of cyanine dye.

It has been shown (Braunholtz and Mann, Part I *) that several aromatic primary amines, when heated with vinyl cyanide and acetic acid, undergo mono- and/or bis-cyanoethylation, the latter being particularly favoured by acetic acid; *e.g.*, in formic acid, p-toluidine undergoes only monocyanoethylation. The utility of copper acetate, borate, or oleate or of cuprous chloride as additional catalysts for difficult cyanoethylations had already been proved (B.P. 457,621; R. C. Cookson and Mann, J., 1949, 67). Smith and Tung-Yin Yu recently (J. Amer. Chem. Soc., 1952, 74, 1098) emphasised the value of cuprous chloride.

We have consequently investigated the cyanoethylation of aniline when boiled with vinyl cyanide and acetic acid in the presence of various metallic salts under comparable conditions, and find that ferrous sulphate, zinc acetate, and chromium trichloride afford only the monocyanoethyl derivative in 7, 13, and 55% yield, respectively, whereas cuprous cyanide, cobaltous chloride, and cuprous chloride give the biscyanoethyl derivative in 20, 30, and 55% yield, respectively. Smith and Tung-Yin Yu claim a 79% yield in the last case. (Throughout this paper the quoted yields of our cyanoethyl compounds are those of the once-recrystallised material. Our yields, moreover, are also comparable in that they were obtained throughout from one sample of vinyl cyanide : the yields given by different batches of the cyanide may vary according to the age of the cyanide and to the amount of stabiliser present.)

In view of the marked superiority of acetic acid containing cuprous chloride, we have investigated the cyanoethylation of a wider variety of primary aromatic amines when

* J., 1952, 3046, is to be regarded as Part I.

heated under reflux with vinyl cyanide (2-2.5 mols.), acetic acid (2-2.5 mols.), and freshly prepared cuprous chloride (10 g. per mole of amine). The results are summarised in Table 1.

The yields of the biscyanoethyl derivatives, with the exception of that of p-anisidine, are uniformly greater than those recorded by Braunholtz and Mann (*loc. cit.*), who used acetic acid without the cuprous chloride but with heating in an autoclave at 140—145°. The yield of NN-bis-2-cyanoethylaniline claimed by Smith and Tung-Yin Yu (*loc. cit.*) was never achieved, our quoted yield being obtained consistently in several experiments. The preparation of N-2-cyanoethyl-o-toluidine, m. p. 108°, has been claimed (F.P. 47,827), but our product remained persistently as a mobile liquid : it is noteworthy, however, that acet-o-toluidide, m. p. 110°, was the major product in our attempted cyanoethylation of o-toluidine in an autoclave at 145—150° in the absence of cuprous chloride.

The influence in particular of two factors is apparent in Table 1. (a) A substituent ortho to the primary amino-group severely restricts formation of the biscyanoethyl derivative. Indeed, of such amines, only o-toluidine gave the dinitrile : α -naphthylamine, o-aminodiphenyl, m-2-xylidine, and mesidine gave none, and the last two (the only amines having two o-substituents) largely resisted cyanoethylation. This new example of the ortho-effect is presumably due to steric and not electronic causes, in view of the different substituents involved. (b) The low yields of cyanoethyl derivatives from p-chloroaniline and p-nitroaniline may indicate that, in the absence of other factors, cyanoethylation becomes more difficult as the basic strength of the amine falls. This does not accord with Whitmore, Mosher, Adams, Taylor, Chapin, Weisel, and Yanko's suggestion (J. Amer. Chem. Soc., 1944, 66, 725), based chiefly on their studies of aliphatic and heterocyclic amines, that cyanoethylation is governed more by the shape of the reacting molecules than by the basic strength of the amines.

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|-------|----|
| ADIC | |
| IADLE | 1. |

| | Time of heating | Mononitrile, NHR∙C₂H₄•CN | | Di NR(C | nitrile, C ₂ H ₄ ·CN) ₂ | Acetamido- compound : | Unchanged amine : | | |
|---|-----------------|-----------------------------|------------------------------|------------|---|--------------------------|----------------------|--|--|
| Amine | (hr.) | Yield, % | M. p.ª | Yield, % | ^ь М. р. ^а | yield, % | yield, °o | | |
| Aniline | 12 | | | 55 | 8384° | | | | |
| o-Toluidine | 12 | 65 | * | 35 | † | Trace | | | |
| m-Toluidine | 6 | | | 50 | 87-88 | | | | |
| ,, | 12 | | | 65 | ,, | | | | |
| ,, | 20 | | | 75 | ,, | | | | |
| p-Toluidine | 12 | | | 50 | 63 - 64 | | | | |
| <i>p</i> -Anisidine | 12 | — | | 40 | 102 - 103 | | | | |
| p-Chloroaniline | 12 | 17 | $74.5 - 75.5^{\circ}$ | 20 | $95 \cdot 5 - 96$ | | | | |
| <i>p</i> -Nitroaniline | 12 | ca. 6 | 128 - 130 | | | | 22 | | |
| α-Naphthylamine | 10 | 80 | 70 - 71 | | | | | | |
| β-Naphthylamine | 12 | | | 25 - 35 | $127 \cdot 5 - 128 \cdot 5$ | | | | |
| o-NH ₂ ·C ₆ H ₄ Ph | 12 | 65 | 86 | | | | | | |
| p-NH, C, H, Ph | 12 | | | 80 | $165 \cdot 5 - 166$ | | | | |
| $1:2:4-C_{6}H_{3}Me_{2}\cdot NH_{2}$ | 12 | | | 11 | 84 | | | | |
| $1:3:2-C_{6}H_{3}Me_{2}\cdot NH_{2}$ | 12 | | | | | ca. 50 | ca. 20 | | |
| $1:3:5:2-C_6H_2Me_3\cdot NH_2$ | 12 | | | | | 30 | | | |
| * Liquid, b. p. 125 | -126°/0 | •2 mm. | † Liquid, b. p. 173°/0·2 mm. | | | | | | |

" Of the pure compounds." Of material once recrystallised.

Other more local factors may affect the yield. Our greater yield of the biscyanoethyl derivative of p-aminodiphenyl than of the analogous derivative of p-toluidine is probably due to the fact that the former derivative (unlike the latter) is almost insoluble in the reaction mixture, and its continuous separation would therefore prevent the attainment of the normal cyanoethylation equilibrium.



We have also investigated the cyanoethylation of certain aromatic diamines. p-Phenylenediamine underwent such ready cyanoethylation that no metallic catalyst was required : the diamine when heated at 120° with vinyl cyanide and acetic acid gave the

tetrakiscyanoethyl compound (I), m. p. 141—142°, in 85% yield, and a similar initial mixture when set aside at room temperature for 12 weeks gave this product in 76% yield. The identification of this compound required care, because the compositions of the diamine and its mono-, bis-, tris- and tetrakis-cyanoethyl derivatives are almost identical, and moreover it has been claimed (B.P. 613,807) that this process gives the *s-p*-biscyanoethyl compound (II), m. p. 140°. Our product, however, shows no NH bands in the 3- μ region of its infra-red spectrum, and its cyclisation (described later) also shows conclusively that it is the tetracyano-derivative. In view of the very ready cyanoethylation of *p*-phenylene-diamine, it is surprising that under similar conditions this diamine did not combine with α -methylacrylonitrile, ethyl acrylate, or ethyl cinnamate.

o-Phenylenediamine, when heated with vinyl cyanide and acetic acid, with or without cuprous chloride, gave only the *s*-o-biscyanoethyl compound (II), which was identified by (a) the presence of an NH band in the 3- μ region of its spectrum, (b) formation of a nitrosamine which readily gave a Liebermann reaction, but no evidence of diazotisation or of green p-nitroso-derivative formation could be obtained. The effect of ortho-substituents in preventing biscyanoethylation of either amino-group is here again pronounced.

Benzidine, either with or without cuprous chloride, also gave solely the biscyanoethyl compound (III), the structure of which was determined by analysis and confirmed by the presence of the NH band at 2.97 μ in its spectrum.

We have further investigated the cyclisation of certain of the above biscyanoethylamino-compounds. The conversion of bis-2-cyanoethylaniline into 1:6-diketojulolidine (IV; R = H) by the action of aluminium chloride in chlorobenzene containing hydrochloric acid has been improved, with the production of the pure diketone in 75% yield. *p*-Chloro-*NN*-bis-2-cyanoethylaniline gave, however, a monoketone, which is undoubtedly 6-chloro-1-2'-cyanoethyl-1:2:3:4-tetrahydro-4-ketoquinoline (V; R = Cl). The evidence for this structure is similar to that previously adduced (Braunholtz and Mann, *loc. cit.*) for the similar monoketone obtained from *NN*-bis-2-cyanoethyl-*p*-anisidine. The infra-red spectrum of the chloro-ketone shows well-defined bands at 4:45 and 6:00 μ corresponding to the -CN and the >CO groups respectively. Its ultra-violet spectrum is closely similar to that of the unsubstituted parent compound, 1:2:3:4-tetrahydro-4ketoquinoline and of the hydroxy- and the methoxy-ketone (V; R = HO and MeO) (cf. p. 1823) (Table 2).

| | | | Таві | LE 2. | | | | | |
|-----------------------------------|------------------------|---|--|---|--------------------|------------------------|---|--|--|
| Compound | | | А | bsorptio | n charac | teristics | | | |
| (V, R = Cl) | λ _{max.} ε | $\begin{array}{c} 393 \\ 4,490 \end{array}$ | $\begin{array}{c} 269 \\ 11,270 \end{array}$ | $2\overline{39} \\ 25,500$ | | $\lambda_{\min.}$ | $\begin{array}{c} 296 \\ 220 \end{array}$ | $252 \\ 6,900$ | |
| Tetrahydro-4-keto- quinoline | λ_{\max} . | 377 4,000 | 259 6,800 | $\begin{array}{r} 235\\ 20,400 \end{array}$ | | λ_{\min} . | $\begin{array}{c} 286 \\ 48 \end{array}$ | $\begin{array}{c} 251 \\ 5,900 \end{array}$ | |
| (V; R = HO) | λ _{max.} ε | $\begin{array}{r} 410 \\ 5.070 \end{array}$ | $\begin{array}{r} 264 \\ 7.760 \end{array}$ | $\begin{array}{r}239\\20,400\end{array}$ | | λ_{\min} . | $\begin{array}{c} 297 \\ 100 \end{array}$ | 259 7,460 | |
| (V; R = MeO) | $\lambda_{max.}$ | $407 \\ 5.100$ | | $\begin{array}{r}238\\28,800\end{array}$ | | λ_{\min} . | $\begin{array}{c} 295 \\ 100 \end{array}$ | $257 \\ 7.400$ | |
| (VI) | λ _{max.} ε | $\begin{array}{c} 400 \\ 6.700 \end{array}$ | 320 5,700 | $258 \\ 36.500$ | $217 \\ 25.200$ | λ_{\min} | $\begin{array}{c} 345 \\ 1.300 \end{array}$ | 299 3,900 | $\begin{array}{r} 237 \\ 13.300 \end{array}$ |
| $[V; R = (CN \cdot C_2 H_4)_2 N]$ | λ_{\max} . | 424-431 3.300 | 277 11.800 | $\begin{array}{c} 247\\ 24.500 \end{array}$ | | λ_{\min} . | 321 180 | $\begin{array}{c} 267 \\ 10.900 \end{array}$ | 216 7.900 |
| (I) | λ_{\max} | 308 - 311 1.860 | $262 \\ 17.600$ | | | λ_{\min} . | $\frac{297}{1.700}$ | $229-23 \\ 4.850$ | 3 |
| Bis-2-cyanoethyl-p- toluidine | λ_{\max} | 300 1.900 | 252 15.800 | | | $\hat{\lambda}_{\min}$ | $\frac{274}{798}$ | $223 \\ 3.600$ | |
| VII) | λ _{max.} ε | $492 - 496 \\ 5.500$ | 248-251 19.400 | | λ_{\min} . | $\frac{382}{177}$ | 220 9.600 | $\lambda_{\text{infl.}} = 27$ | 7—283 8.100 |
| (IV; R = Me) | λ_{\max} . | 414 - 420 5.680 | 305 2.600 | $228 \\ 32.600$ | λ_{\min} . | $341 \\ 314$ | 282 1.050 | $\lambda_{\text{infl.}} = 25$ | 6-260 6.100 |
| (VIII) | λ_{\max} | 478 322 32 | 2— 252 25 | 238 | 215 | $\lambda_{n:in.}$ 37 | 5 288 | 245 247 | 222 224 |
| | ε | 4,500 2,5 | 00 22,000 | 22,900 | 19,400 | ε 40 | 0 1,550 |) 20,700 | 17,200 |
| | - | | | | | | | | |

The above compounds are listed in the order in which they are mentioned in the text. All spectra were determined in ethanolic solution.

NN-Bis-2-cyanoethyl- β -naphthylamine similarly gave 1-2'-cyanoethyl-1 : 2 : 3 : 4-tetrahydro-4-keto-5 : 6-benzoquinoline (VI), the ultra-violet spectrum of which has some close similarities to those of the above three monoketones (Table 2). p-NN-Bis-2-cyanoethylaminodiphenyl, however, gave 1:6-diketo-8-phenyljulolidine (IV; R = Ph). It is



characteristic of all the yellow diketo-juloidines of type (IV) that their ethanolic solutions become deep red on addition of hydrochloric acid. There is little doubt that these diketones exist as a resonance hybrid of (IV) and (IVA), the latter probably making the major contribution to the colour: salt formation involves essentially the addition of a proton to the negative oxygen atom in (IVA), this structure being thus almost exclusively formed (cf. Mann and Smith, J., 1951, 1898).

The cyclisation of NNN'N'-tetrakis-2-cyanoethyl-p-phenylenediamine (I) is of particular interest. Mild conditions afford a brilliant yellow monoketone, which is almost certainly the analogue of our previous monoketones, *i.e.*, it is 1-2'-cyanoethyl-6-NN-bis-2cyanoethylamino-1: 2:3:4-tetrahydro-4-ketoquinoline [V; $R = (CN \cdot C_2H_4)_2N$], m. p. 149—150°, since its ultra-violet spectrum is again similar to that of the unsubstituted tetrahydro-4-ketoquinoline, but markedly different from that of the tetranitrile (I), which in turn closely resembles that of bis-2-cyanoethyl-p-toluidine (Table 2).

More vigorous conditions of cyclisation, however, give a beautiful vermilion diketone of composition $C_{18}H_{18}O_2N_4$ and m. p. 250–251°. This might be 4:7-bis-2'-cyanoethyl-1:2:3:4:7:8:9:10-octahydro-1:10-diketo-4:7-phenanthroline (VII), the similar anthracene compound (VIII), or 8-NN'-di-(2-cyanoethyl)amino-1:6-diketojulolidine [IV; $R = (CN \cdot C_2H_4)_2N$]. Its identification as (VII) rests on the following evidence. (a) Its ultra-violet spectrum is entirely different from that of 1:6-diketo-8-methyljulolidine (IV; R = Me), which might reasonably be assumed to have a spectrum similar to that of [IV; $R = (CN \cdot C_2H_4)_2N$], particularly as the spectra of the p-toluidine dinitrile and tetranitrile (I) are so closely related. (b) The diketone reacts rapidly with hydrazine in hot methanolic solution to give the brilliant yellow 1:8-bis-2'-cyanoethyl-1:2:3:6:7:8-hexa-hydro-1:4:5:8-tetra-azapyrene (IX), a type of reaction which the two isomeric diketones could not give.



We have attempted to prepare a compound analogous to (IX) by using *o*-phenylenediamine, but the only derivative isolated was the di-*o*-amino-anil (X): apparently the large-ring system which the condensation of one molecule of the diketone (VII) with one of the diamine would entail is too unstable for ready formation.

On one occasion the cyclisation of the tetranitrile (I) gave a brilliant orange diketone, m. p. 195—196°, isomeric with (VII). The minute yield precluded a detailed investigation, but its ultra-violet spectrum is entirely different from that of (VII), and, for example, from that of (IV; R = Me), and its infra-red spectrum shows the CN band at 4.44 μ and the >CO band at 5.95 μ , but the >NH band is absent from the 3- μ region : it is almost certain therefore that this diketone is the diaza-anthracenedione (VIII).

The colour of the red and of the orange diketone also supports the structures (VII) and (VIII), respectively. It is significant that in the red diketone (VII) charge separation can occur in either or in both amino-ketone rings as in (VIIA), but in the orange diketone (VIII), although this separation can occur in either amino-ketone ring, it cannot occur simultaneously in both : the greater degree of resonance in (VII) thus accounts for its deeper and more intense colour. In the monoketone [V; $R = (CN \cdot C_2H_4)_2N$] only one amino-ketone ring is involved, and the compound is thus yellow. It is probably not a coincidence that the m. p.s of the monoketone and of (VIII) and (VII) increase in this order, *i.e.*, as the possible proportion of polar component increases.

The yellow diazine (IX) is a compound of considerable interest. When added even to a large excess of methanolic picric acid solution, it formed a beautiful deep maroon, crystalline monopicrate, and a higher picrate could not be isolated. Similarly, even prolonged boiling of a mixture of (IX) with methyl iodide gave only a deep purple (almost black) crystalline monomethiodide, which gave a deep red ethanolic solution and also formed a reddish-purple methopicrate. It is clear therefore that the methyl iodide has caused quaternisation on the $N_{(4)}$ atom (XIA) and not the $N_{(1)}$ atom. Quaternisation on the $N_{(1)}$ atom should cause no significant change in the colour of the diazine, whereas that on the $N_{(4)}$ atom gives a cation which will exist as a resonance hybrid of (XIA) and (XIB). This explains the deep colour of the monopicrate and the monomethiodide, and the latter clearly represents an entirely new type of cyanine dye.

EXPERIMENTAL

Consistent m. p.s for certain compounds could only be obtained when determined in evacuated sealed tubes : these are denoted as " (E. T.)."

Cyanoethylation.—(A) Aniline with inorganic catalysts. In a series of experiments, mixtures of aniline (3.6 c.c.), vinyl cyanide (5.2 c.c., 2 mol.), acetic acid (2 c.c., 0.8 mol.), and various anhydrous inorganic catalysts (0.4 g.) were heated under reflux for 10 hr., and the mixture then cooled, made alkaline with saturated sodium carbonate solution, and extracted with chloroform. Evaporation of the extract and recrystallisation of the residue afforded mono-2-cyanoethylaniline from $FeSO_4$ (7% yield), $Zn(OAc)_2$ (15%), $CrCl_3$ (55%), and bis-2-cyanoethylaniline from $Cu_2(CN)_2$ (20%), $CoCl_2$ (30%), and Cu_2Cl_2 (55%). The yield in the last experiment was unchanged when the acetic acid was increased to 2.1 mol. The use of aluminium chloride led to a vigorous reaction in the cold solution, with production of a white aluminium derivative.

(B) Various amines, with use of cuprous chloride. In the experiments summarised in Table 1, a mixture of the amine, vinyl cyanide (2 mol.), acetic acid (2 mol.), and freshly prepared dry cuprous chloride (10 g. per g.-mol. of amine) was boiled under reflux for the time stated, cooled, and then vigorously stirred whilst an excess of concentrated ammonia solution was added. The precipitated oily nitrile usually slowly solidified and was then recrystallised: in the rare cases when solidification did not occur, the heavy oil was distilled. (Experimental details are given only when distillation was necessary.)

The solvent used for recrystallisation of the product was ethanol unless otherwise stated: the identity of known products was checked by mixed m. p. determinations. Aniline gave the dinitrile, m. p. 83—84°. o-Toluidine gave an oil which on distillation at 0.2 mm. gave fractions: (a) B. p. 67—75°, in very small amount: this was the acet-o-toluidide, and crystallised immediately after distillation. (b) B. p. 135—160°: this fraction when redistilled gave N-2'-cyanoethyl-o-toluidine, b. p. 125—126°/0.2 mm. (Found: C, 75.3; H, 7.3; N, 17.3; C₁₀H₁₂N₂ requires C, 75.0; H, 7.5; N, 17.5%). (c) B. p. 173°, which when redistilled gave NN-bis-2'-cyanoethyl-o-toluidine, b. p. 182°/0.4 mm. (Found: C, 72.9; H, 7.1; N, 19.5; C₁₃H₁₅N₃ requires C, 73.2; H, 7.0; N, 19.7%). These two nitriles were colourless liquids which could not be induced to crystallise. m-Toluidine gave the dinitrile, m. p. 86—87°: the increase in yield with time of heating is shown in Table 1. p-Toluidine gave a product which

after recrystallisation was still a mixture, but on distillation at 0.5 mm. gave fractions: (a) b. p. 150—170°; (b) b. p. 170—195°; (c) b. p. 225°. Fractions (a) and (b) on recrystallisation gave p-chloro-N-2'-cyanoethylaniline, m. p. 74.5—75.5° (Found: N, 15.7. Calc. for $C_9H_9N_2Cl$: N, 15.5%): Bauer, Cymerman, and Sheldon (J., 1951, 3312) give m. p. 76°. Fraction (c) gave the dinitrile, m. p. 95.5—96°. p-Nitroaniline gave a product which on cooling deposited the unchanged amine (22%). Treatment of the filtrate with ammonia then gave N-2'-cyanoethyl-p-nitroaniline, pale yellow needles (from ethanol or benzene), m. p. 128—130° (Found: C, 57.0, 57.0; H, 4.9, 4.9; N, 22.3. $C_9H_9O_2N_3$ requires C, 56.5; H, 4.8; N, 22.0%). The infra-red spectrum showed the following significant groups: —NH at 3.04; -CN at 4.43; -NO₂ as a complex band at approx. 7.5 μ .

α-Naphthylamine gave a product which on distillation gave a fraction, b. p. $180-194^{\circ}/0.2$ mm.; this when recrystallised gave N-2'-cyanoethyl-α-naphthylamine, m. p. 70-71° (Found: C, 79.8; H, 6.5; N, 14.3. C₁₃H₁₂N₂ requires C, 79.6; H, 6.2; N, 14.3%). β-Naphthylamine gave NN-bis-2'-cyanoethyl-β-naphthylamine, m. p. 127.5-128.5° (Found: C, 77.1; H, 5.8; N, 16.9. C₁₆H₁₅N₃ requires C, 77.1; H, 6.0; N, 16.9%).

o-Aminodiphenyl gave o-N-2''-cyanoethylaminodiphenyl, m. p. 86° (from methanol) (Found: C, 81·0; H, 6·6; N, 12·7. $C_{15}H_{14}N_2$ requires C, 81·0; H, 6·4; N, 12·6%). *p*-Aminodiphenyl gave p-NN-bis-2''-cyanoethylaminodiphenyl, m. p. 165·5—166° (from acetone) (Found: C, 78·8; H, 6·5; N, 15·5. $C_{18}H_{17}N_3$ requires C, 78·6; H, 6·2; N, 15·3%).

o-4-Xylidine gave the NN-bis-2-cyanoethyl derivative, m. p. 84° (Found : C, 74·1; H, 7·3; N, 18·7. $C_{14}H_{17}N_3$ requires C, 74·0; H, 7·5; N, 18·5%). m-2-Xylidine gave an oily product which on distillation at 0·3 mm. afforded the fractions : (a) b. p. 60—70°, mainly unchanged amine; (b) 125—130°, which solidified and gave the acetoxylidide, m. p. 177—178° (Found : N, 8·9. Calc. for $C_{10}H_{13}ON$: N, 8·6%); (c) b. p. 165—170°; the small amount precluded purification, but this fraction was apparently the 2-cyanoethyl derivative. Mesidine gave a product which on distillation afforded the acetyl derivative, m. p. 217·5—219·5° (Found : N, 8·0. Calc. for $C_{11}H_{15}ON$: N, 7·9%), most of the product forming an intractable gum in the distilling-flask.

In an earlier series of experiments in which cuprous chloride was not used, a mixture of p-aminobenzoic acid (19 g.), vinyl cyanide (27 c.c., 3 mol.), and acetic acid (22.5 c.c., 2.6 mol.) was heated in an autoclave at 150° for 7 hr., and on cooling deposited a pale yellow, granular solid (23 g.), which on fractional recrystallisation from ethanol yielded colourless crystals of p-(2-cyanoethylamino)benzoic acid (9.2 g., 35%), m. p. 221.5—222.5° (Found : C, 63.1; H, 5.1; N, 14.8. C₁₀H₁₀O₂N₂ requires C, 63.1; H, 5.3; N, 14.7%). The more soluble fractions yielded only p-acetamidobenzoic acid, m. p. 255—256° (decomp.) (Found : N, 8.0. Calc. for C₉H₉O₃N : N, 7.8%). This result again exemplifies the fact that weak bases undergo cyanoethylation with difficulty and seldom beyond the mononitrile stage.

o-Toluidine, when treated under the same conditions as the above acid, gave acet-o-toluidide, m. p. 111—112° (Found : N, 9.35. Calc. for $C_9H_{11}ON$: N, 9.4%), with a trace of a higherboiling liquid fraction.

(C) Diamines. (i) p-Phenylenediamine. (a) A series of experiments showed that the highest yield of the tetranitrile was obtained when the diamine was heated with vinyl cyanide (5.4 mol.) and acetic acid (4.2 mol.) in a sealed tube at 120° for 14 hr. On cooling, NNN'N'-tetrakis-2'-cyanoethyl-p-phenylenediamine (I) (83%) crystallised in colourless needles, m. p. 132-136°, raised to 141-142° by recrystallisation from ethanol (Found : C, 67.2; H, 6.3; N, 26.1. $C_{18}H_{20}N_6$ requires C, 67.5; H, 6.3; N, 26.2%). (b) When a mixture of the amine, vinyl cyanide (7.7 mol.), and acetic acid (4.2 mol.) was boiled under reflux for 24 hr., the yield of (I) was 70%. (c) When a mixture identical with that in (b) was first gently warmed to give a clear solution and then set aside in a securely closed flask for 12 weeks, the yield of (I) was 76%.

An acetone solution of (I) was saturated with hydrogen chloride, and the precipitated white *dihydrochloride*, m. p. 160—161°, then collected, washed with acetone, and dried in desiccator (Found : C, 54.5; H, 5.9; N, 21.0. $C_{18}H_{20}N_{6.2}$ HCl requires C, 54.9; H, 5.6; N, 21.3%). The salt is unstable in moist air and readily deposits the free base.

When a mixture of the diamine and acetic acid was heated with α -methylacrylonitrile (with or without cuprous chloride) or with ethyl cinnamate, the chief product was NN'-diacetyl-*p*-phenylenediamine, whereas use of ethyl acrylate gave a brown gum.

(ii) o-Phenylenediamine. A mixture of the diamine, vinyl cyanide (8 mol.), and acetic acid (4.2 mol.) was boiled under reflux for 24 hr., and the cold reaction mixture made alkaline and then extracted with ether. After evaporation of the solvent, the residue when recrystal-lised from methanol gave NN'-bis-2'-cyanoethyl-o-phenylenediamine (II) as colourless crystals,

m. p. 118.5—119° (Found : C, 67.4; H, 6.3; N, 26.4. $C_{12}H_{14}N_4$ requires C, 67.3; H, 6.6; N, 26.2%). In all subsequent preparations, the dinitrile (II) crystallised as the reaction mixture cooled.

(iii) Benzidine. When a mixture of benzidine, vinyl cyanide (8 mol.), and acetic acid (4.5 mol.) was boiled under reflux for 8 hr., NN'-bis-2''-cyanoethylbenzidine (III) separated in quantitative yield from the hot mixture : after cooling, it was collected and recrystallised from 2-methoxyethanol, giving colourless crystals, m. p. $245-245\cdot5^{\circ}$ (Found : C, $74\cdot4$; H, $6\cdot3$; N, $19\cdot2$. C₁₈H₁₈N₄ requires C, $74\cdot4$; H, $6\cdot3$; N, $19\cdot3\%$). Attempts further to cyanoethylate the dinitrile (III) gave intractable gums.

Cyclisation.—Bis-2'-cyanoethylaniline. Consistent yields of pure 1:6-diketojulolidine, m. p. 145—146° (75%), are obtained by the method previously described (Braunholtz and Mann, loc. cit.) if the reaction mixture is heated to 170° (oil-bath temp.) for 8.5 hr., allowed to cool, then poured cautiously into ice-water and worked up as before. The diketone readily gives a bisdiphenylhydrazone, intensely yellow crystals (after washing with methanol), m. p. 210—211° (Found : C, 81.2; H, 5.8; N, 12.9. $C_{36}H_{31}N_5$ requires C, 81.0; H, 5.9; N, 13.1%).

p-Chloro-NN-bis-2'-cyanoethylaniline. This dinitrile (5 g.) was added to a mixture of chlorobenzene (15 c.c.), aluminium chloride (25 g., 8.75 mol.), and concentrated hydrochloric acid (1 c.c.), which was heated with stirring at 155° for 8 hr. After cooling, hydrolysis by ice-water, and removal of chlorobenzene by steam-distillation, a viscous reddish-brown tar slowly separated in the residue. An ethanolic solution of this tar deposited the crystalline yellow 6-chloro-1-2'cyanoethyl-1: 2: 3: 4-tetrahydro-4-ketoquinoline (V; R = Cl) (2 g., 40%), m. p. 136—137° (from ethanol) (Found: C, 61·3; H, 4·9; N, 12·2. $C_{12}H_{11}ON_2Cl$ requires C, 61·3; H, 4·7; N, 11·9%). It formed a semicarbazone, yellow needles (from aqueous ethanol), m. p. 173—175° (Found: C, 53·4; H, 5·1; N, 23·8. $C_{13}H_{14}ON_5Cl$ requires C, 53·5; H, 4·8; N, 24·0%).

NN-Bis-2'-cyanoethyl-p-anisidine. This dinitrile, when treated as the above bis-2'-cyanoethylaniline, gave, after removal of the chlorobenzene, a heavy oil which separated from the cold mixture and slowly solidified. Recrystallisation from ethanol gave 6-hydroxy-1-2'-cyanoethyl-1: 2:3:4-tetrahydro-4-ketoquinoline (V; R = HO) (18%), bright orange crystals, m. p. 176-177° (Found: C, 66.5; H, 5.5; N, 12.9. $C_{12}H_{12}O_2N_2$ requires C, 66.65; H, 5.6; N, 12.95%); this gave a 2:4-dinitrophenylhydrazone, dark purple crystals, m. p. 250° (decomp.) (Found: C, 53.5; H, 4.4; N, 20.7. $C_{18}H_{16}O_5N_{6.2}H_2O$ requires C, 53.3; H, 4.2; N, 20.7%), which became anhydrous at 75°/0.1 mm. (Found: C, 54.5; H, 3.9. $C_{18}H_{16}O_5N_6$ requires C, 54.55; H, 4.05%).

The ketone (V; R = HO) readily gave a bright red solution in 10% aqueous sodium hydroxide, and its aqueous ethanolic solution gave a purple-brown colour with ferric chloride.

That demethylation had accompanied the above cyclisation was confirmed as follows: (a) the ketone in alkaline solution with methyl sulphate gave 6-methoxy-1-2'-cyanoethyl-1:2:3:4-tetrahydro-4-ketoquinoline (V; R = MeO), yellow crystals (from ethanol), m. p. 122-123° (Found: C, 67.75; H, 6.4; N, 12.1. $C_{13}H_{14}O_2N_2$ requires C, 67.8; H, 6.15; N, 12.15%) [2:4-dinitrophenylhydrazone, deep purple, m. p. 231° (decomp.) (Found: N, 20.3. $C_{19}H_{18}O_5N_6$ requires N, 20.45%); (b) the ketone when similarly treated with benzoyl chloride gave 6-benzoyloxy-1-2'-cyanoethyl-1:2:3:4-tetrahydro-4-ketoquinoline (V; R = BzO), pale yellow (from ethanol), m. p. 149-150° (Found: C, 71.6; H, 5.2; N, 8.8. $C_{19}H_{16}O_3N_2$ requires C, 71.3; H, 5.05; N, 8.75%).

In Part I (*loc. cit.*), the above hydroxy-compound, m. p. $176-177^{\circ}$, was isolated in very small quantity and erroneously identified as the methoxy-compound. The compound prepared above has the same m. p. (mixed and unmixed) and the same absorption spectrum as our earlier compound, and its identity is now certain. This mistaken identity does not affect the validity of our earlier evidence for the structure of the monoketone ring.

NN-Bis-2'-cyanoethyl-β-naphthylamine. This dinitrile, treated at 170° as above, gave a heavy brown oil which slowly solidified. An extract in boiling benzene on cooling deposited 1-2'-cyanoethyl-1: 2:3:4-tetrahydro-4-keto-5:6-benzoquinoline (VI) (82%), which, recrystallised from ethanol, gave bright yellow crystals, m. p. 121·5—123·5° (Found: C, 76·6; H, 5·5; N, 11·1. $C_{16}H_{14}ON_2$ requires C, 76·8; H, 5·6; N, 11·2%). It gave a semicarbazone, pale yellow needles (from aqueous ethanol), m. p. 233° (Found: C, 66·7; H, 5·8; N, 22·7. $C_{17}H_{17}ON_5$ requires C, 66·5; H, 5·6; N, 22·8%).

p-NN-Bis-2"-cyanoethylaminodiphenyl. This dinitrile, treated as above, gave on hydrolysis a brilliant scarlet suspension, which, however, when steam-distilled to remove chlorobenzene, changed colour and deposited the solid granular 1: 6-diketo-8-phenyljulolidine (IV; R = Ph) (85%); after recrystallisation from methanolic acetone, this afforded lustrous yellow crystals, m. p. 228·5—229·5° (Found : C, 77·8; H, 5·4; N, 5·1. $C_{18}H_{15}O_2N$ requires C, 78·0; H, 5·45; N, 5·1%). It gave a *bisphenylhydrazone*, m. p. 239—240° (E.T.), after being washed with warm methanol and dried at 50°/0·1 mm. (Found : C, 78·5; H, 6·0; N, 15·0. $C_{30}H_{27}N_5$ requires C, 78·75; H, 5·95; N, 15·3%).

NNN'N'-Tetrakis-2'-cyanoethyl-p-phenylenediamine (I). A considerable variation in the conditions employed for this cyclisation was studied, and the following are apparently the optimum conditions for the formation of the mono- and the di-ketone. The course of the reaction is apparently determined less by the time of heating and proportion of aluminium chloride than by the temperature: oil-bath temperatures of 160—165° favour monoketone formation, but those of ca. 175° give solely the diketone.

(a) The tetranitrile (5 g.) was added to a mixture of chlorobenzene (70 c.c.), aluminium chloride (70 g., 25 mol.), and concentrated hydrochloric acid (3 c.c.), which was then kept at 160° with vigorous stirring for 20 hr. It was cooled, hydrolysed with ice-water, and steam-distilled to remove chlorobenzene as before The cold residual liquid contained a small amount of dark tar, from which no pure component could be isolated. The dark red supernatant aqueous layer was therefore extracted with chloroform, and the dried extract (which was deep red with an orange fluorescence) on evaporation left a red gum. The latter on recrystallisation from methanol gave brilliant yellow crystals of 1-2'-cyanoethyl-6-NN-bis-(2-cyanoethyl)amino-1:2:3:4-tetrahydro-4-ketoquinoline [V; $R = (CN \cdot C_2H_4)_2N$], m. p. $149-150^{\circ}$ (0.5 g., 10°) (Found: C, $67 \cdot 4$; H, $6 \cdot 0$; N, $22 \cdot 0$. $C_{18}H_{19}ON_5$ requires C, $67 \cdot 3$; H, $6 \cdot 0$; N, $21 \cdot 8^{\circ}$). It formed a semicarbazone, yellow crystals (from aqueous ethanol), m. p. $206-207^{\circ}$ (Found: N, $29 \cdot 6$. $C_{19}H_{22}ON_8$ requires N, $29 \cdot 6^{\circ}$).

(b) A mixture of the tetranitrile (5 g.) with chlorobenzene (40 c.c.), aluminium chloride (41 g., 14.5 mol.), and concentrated hydrochloric acid (2 c.c.) was heated at 175° for 10 hr. and then treated as above. Evaporation of the chloroform gave a red gum which on recrystallisation from methanol afforded vermilion needles of 4:7-bis-2'-cyanoethyl-1:2:3:4:7:8:9:10-octahydro-1:10-diketo-4:7-phenanthroline (VII), m. p. 250—251° (E.T.) (0.25 g., 5%) (Found: C, 67.3; H, 5.7; N, 17.6, 17.5. $C_{18}H_{18}O_2N_4$ requires C, 67.1; H, 5.6; N, 17.4%).

(c) On one occasion when the tetranitrile (10 g.) was heated with chlorobenzene (100 c.c.), aluminium chloride (125 g., 22 mol.), and hydrochloric acid (3 c.c.) at 160-165° for 30 hr., and then worked up as before, repeated recrystallisation of the residual gum from methanolic acetone gave brilliant orange plates, m. p. 195-196°, of the isomeric diketone, presumably 1: 5-bis-2'-cyanoethyl-1: 2: 3: 4: 5: 6: 7: 8-octahydro-1: 5-diaza-anthracene-4: 8-dione (VIII) (Found: C, 67.5; H, 5.9; N, 17.0. $C_{18}H_{18}O_2N_4$ requires C, 67.1; H, 5.6; N, 17.4%): mixed m. p. with (VII), 185.5-199.5°. In solution this compound gave a 2: 4-dinitrophenylhydrazone. All attempts to cyclise the tetranitrile (I) by means of aluminium chloride in ethylene dichloride or in nitrobenzene, or of ferric or stannic chloride failed.

Derivatives of the diketone (VII). (a) When an excess of hydrazine hydrate was added to a hot methanolic solution of (VII), the bright red colour changed immediately to bright yellow, and 1: 8-bis-2'-cyanoethyl-1: 2: 3: 6: 7: 8-hexahydro-1: 4: 5: 8-tetra-azapyrene (IX) separated in almost theoretical yield as yellow needles, m. p. 271-272° (E.T.) (from methanol) (Found: C, 67.85; H, 5.6; N, 26.6. $C_{18}H_{18}N_6$ requires C, 67.8; H, 5.7; N, 26.4%). It formed from ethanol a deep maroon monopicrate, m. p. 223.5° (decomp., E.T.) (Found: C, 52.6; H, 4.0; N, 22.7. $C_{18}H_{18}N_6, C_6H_3O_7N_3$ requires C, 52.6; H, 3.9; N, 23.0%).

When a fine suspension of (VII) in methyl iodide was boiled under reflux for 6 hr., the deep purple monomethiodide (XIA or B) separated, m. p. 190—191° (decomp.) after recrystallisation from ethanol (Found : C, 49.6; H, 4.7; N, 18.25. $C_{19}H_{21}N_{g}I$ requires C, 49.6; H, 4.6; N, 18.25%). It formed a monomethopicrate, reddish-purple plates, m. p. 130.5—131.5° (decomp.) (Found : C, 53.5; H, 3.95; N, 22.2. $C_{25}H_{23}O_7N_9$ requires C, 53.5; H, 4.1; N, 22.45%).

(b) A solution of the diketone (VII) (0.075 g.) and o-phenylenediamine (0.075 g., 3 mol.) in acetic acid (5 c.c.) was boiled under reflux for 1.5 hr., becoming almost colourless. The cold solution was poured into water, which when basified deposited in small yield the *di-o-amino-anil* (X) of the diketone : repeated recrystallisation from benzene-cyclohexane gave colourless crystals, m. p. 175.5—176.5° (Found : C, 71.7; H, 5.8; N, 22.2. $C_{30}H_{30}N_8$ requires C, 71.7; H, 6.0; N, 22.3%). When the above condensation was repeated with the diamine (1 mol.) and 4 hours' heating, no definite product could be isolated.

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