tone, 0.23 g. of 3β,7β-diacetoxy-5-androsten-17-one, m.p. 161.5–162.5°, $[\alpha]_D$ +105.0°.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 71.32; H, 8.33.

3β,7α-Diacetoxy-5-androsten-17-one (IVa).—Acetylation of 0.20 g. of 7α-hydroxydehydroisoandrosterone (IV) with 3 ml. of acetic anhydride in 3 ml. of pyridine at room temperature overnight yielded, after crystallization from dilute methanol, 0.23 g. of 3β,7α-diacetoxy-5-androsten-17-one, m.p. 168–170°, $[\alpha]_D$ −178.5°.

Anal. Calcd. for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30. Found: C, 70.95; H, 8.53.

3β,7α-Diacetoxy-5-androsten-17-one (IVa) from II.—Acetylation of 0.29 g. of II, m.p. 193–196°, by the method described above yielded, after repeated crystallizations from petroleum ether (b.p. 60–71°), acetone–petroleum ether, and dilute acetone, 103 mg. of 3β,7α-diacetoxy-5-androsten-17-one, m.p. 168.5–170°. This material was identical in all respects, m.p., mixed m.p. and infrared spectrum, with that described above.

Molecular Compound II from IV and V.—A mixture of 100 mg. of 7α-hydroxydehydroisoandrosterone, m.p. 183–184.5°, and 50 mg. of 7β-hydroxydehydroisoandrosterone, m.p. 215–216°, was crystallized twice from dilute acetone. From these crystallizations there was obtained 79 mg. of II, m.p. 196–197.5°, $[\alpha]_D$ −32.0°. The infrared spectrum of this material was identical with that obtained above and was different from that of either of the starting materials.

Anal. Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.78; H, 9.16.

4,6-Androstadiene-3,17-dione (VI) from IV.—A solution of 0.50 g. of 7α-hydroxydehydroisoandrosterone, m.p. 181.5–183.5°, in 20 ml. of toluene and 7.0 ml. of cyclohexanone was evaporated to approximately one-half its volume to free the solution of water. To this was added 4.00 ml. of a toluene solution containing 1.00 g. of aluminum isopropoxide. The resulting solution was heated under reflux for 20 minutes during which time the solution became yellow. The reaction mixture then was poured into 50 ml. of a saturated Rochelle salt solution; the flask was rinsed with benzene and an additional 50 ml. of Rochelle salt solution; then the mixture was distilled with steam. The suspension became brick-red during this steam distillation. The organic material was separated from the suspension by extraction with ether plus a little ethyl acetate. The ether was removed by evaporation and the residue chromatographed on silica gel. The crystalline material eluted with 10% ethyl acetate in benzene weighed 230 mg. and, after being crystallized from acetone–petroleum ether (b.p. 60–71°), yielded 112 mg. of 4,6-androstadiene-3,17-dione,[13] m.p. 170.5–172.5°, $\lambda_{max}^{methanol}$ 283 (ε26,600). This material was identical in all respects (m.p., mixed m.p. and infrared spectrum) with an authentic sample of 4,6-androstadiene-3,17-dione.

4,6-Androstadiene-3,17-dione (VI) from V.—The treatment of 0.40 g. of 7β-hydroxydehydroisoandrosterone (V) by the methods given above yielded, after chromatography and crystallization from acetone–petroleum ether (b.p. 60–71°) and dilute acetone, 37 mg. of 4,6-androstadiene-3,17-dione, m.p. 169.5–171°, $\lambda_{max}^{methanol}$ 282 (ε25,400). The structure was confirmed by mixed m.p. and comparison of infrared spectra.

(13) L. Ruzicka and W. Bosshard, *Helv. Chim Acta*,, **20**, 328 (1937); C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann and J. Pataki, THIS JOURNAL, **72**, 4534 (1950).

CHICAGO 80, ILL.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF TEMPLE UNIVERSITY]

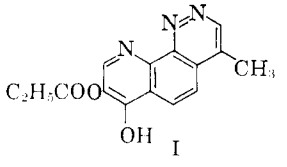
Substituted 1,10-Phenanthrolines. XI. Aza Derivatives[1]

BY FRANCIS H. CASE AND JAMES A. BRENNAN

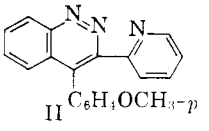
RECEIVED MAY 4, 1959

The syntheses of 2-, 3-, 4- and 5-aza-1,10-phenanthrolines and of 4,7-diaza-1,10-phenanthroline have been described. These compounds are expected to form chelates with Fe(II) and possibly Cu(I).

The compounds 2-aza-8-carbethoxy-7-hydroxy-4-methyl-1,10-phenanthroline[2] (I) and 3-(2-pyridyl)-4-*p*-methoxyphenylcinnoline[3] (II) have been shown by Irving and Williams[4] to have certain advantages over 1,10-phenanthroline as chelating agents.



I



II

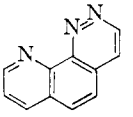
The difference in absorptive power of the chelates of these substances is ascribed to the presence of the third nuclear nitrogen atom in the 2-position. It seemed desirable to us to prepare the parent substance, 2-aza-1,10-phenanthroline (III) and in addition the other three isomeric monaza derivatives of 1,10-phenanthroline, *i.e.*, the 3- (IV), 4- (V) and 5- (VI). These can be considered as pyrido derivatives of cinnoline, quinazoline, quinoxaline and 1,5-naphthyridine, respectively.

(1) This work was supported by a grant from the Committee on Research and Publications of Temple University.

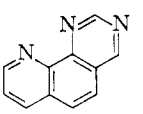
(2) L. McKenzie and C. S. Hamilton, *J. Org. Chem.*, **16**, 1414 (1951).

(3) K. Schofield, *J. Chem. Soc.*, 2408 (1949).

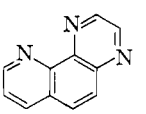
(4) H. Irving and R. Williams, *Analyst*, **77**, 813 (1952).



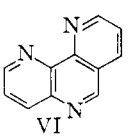
III



IV



V



VI

The synthesis of III was accomplished in the following manner: 8-amino-4-methylcinnoline[2,5] was converted to 4-methyl-2-aza-1,10-phenanthroline by a modified Skraup reaction[6] involving acrolein. The methyl group then was removed by conversion to the styryl derivative, oxidation to the acid and decarboxylation.

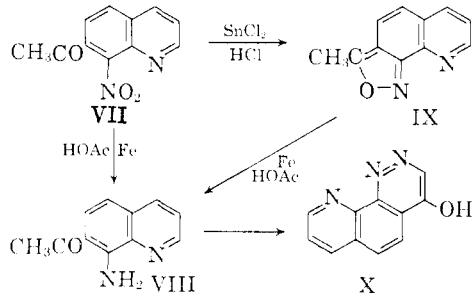
The 4-hydroxy derivative of 2-aza-1,10-phenanthroline (X) also was prepared, but by an entirely different procedure. 3-Acetamido-2-nitroacetophenone[7] was converted in a modified Skraup reaction to 7-acetyl-8-nitroquinoline (VII). Reduction by iron and acetic acid yielded the corresponding amine VIII, but stannous chloride and hydrochloric acid produced 3-methyl-(pyrido-(3,2-g)-anthranil) (IX). It was found that the anthranil then could be reduced further to VIII by iron and acetic acid. Reduction of VII using

(5) K. Schofield and T. Swain, *J. Chem. Soc.*, 1367 (1949).

(6) H. L. Yale and J. Bernstein, THIS JOURNAL, **70**, 254 (1948).

(7) N. Leonard and S. Boyd, *J. Org. Chem.*, **11**, 405 (1946).

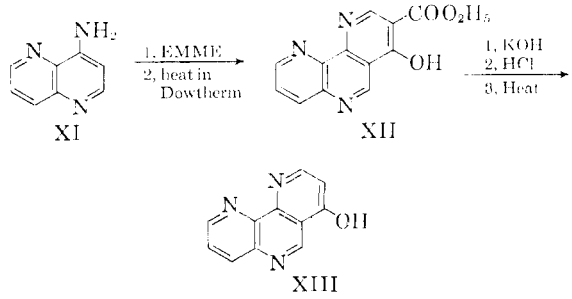
Adams catalyst yielded a mixture of amine and anthranil, but continued treatment of this type did not further change the anthranil. This is at variance with the results obtained by Nord[8] in the reduction of *o*-nitrobenzaldehyde and *o*-nitroacetophenone.



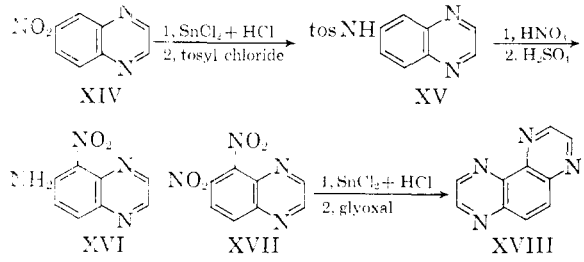
Diazotization of VIII in sulfuric and acetic acid yielded 4-hydroxy-2-aza-1,10-phenanthroline (X). The use of hydrochloric acid yielded, in addition, some 7-acetyl-8-chloroquinoline. The procedure of Atkinson and Mattocks,[9] in which the diazotized amine was made alkaline, was unsuccessful.

The preparation of 3-aza-1,10-phenanthroline (IV) in small yield was effected by subjecting 8-aminoquinazoline[10] to a modified Skraup reaction. A similar reaction with 5-acetamidoquinoxaline[11] yielded 4-aza-1,10-phenanthroline (V). An earlier attempt by Linsker and Evans[12] to prepare V by the action of glyoxal on 7,8-diaminoquinoline was unsuccessful.

The preparation of 5-aza-1,10-phenanthroline (VI) was attempted by way of a Skraup reaction on 4-amino-1,5-naphthyridine (XI) but, this failing, it was effected by reaction of XI with ethyl ethoxymethylenemalonate to yield XII, cyclization, hydrolysis, decarboxylation and conversion of the resulting 4-hydroxy-6-aza-1,10-phenanthroline (XIII) to the chloro derivative, which was catalytically reduced in the presence of palladium. In another attempt at synthesis of VI, 3,4-diaminopyridine was condensed with two moles of ethyl ethoxymethylenemalonate, but the resulting compound failed to cyclize.



Recently Dewar and Maitlis[13] reported the preparation of 5,6-dinitroquinoxaline (XVII) by nitration of quinoxaline, although their proof of structure was not complete. We have now confirmed this structure as follows: 6-nitroquinoxaline (XIV) was reduced to the amine, which then was tosylated to yield XV and nitrated. Hydrolysis afforded a nitroaminoquinoxaline (XVI) which on reductive acetylation yielded the same diacetyl derivative as the dinitro compound.[13] Reduction of the dinitroquinoxaline and then treatment with sodium glyoxal bisulfite yielded 4,7-diaza-1,10-phenanthroline (XVIII).



Experimental

4-Methyl-2-aza-1,10-phenanthroline.—A mixture of 8.4 g. of 8-amino-4-methylcinnoline,[2,5] 15.8 g. of arsenic acid and 56 ml. of phosphoric acid (85%) was warmed to 100° and 5.3 ml. of freshly distilled acrolein was added with vigorous stirring at such a rate that the temperature remained at 100 ± 2°. The reaction mixture was stirred for an additional 30 minutes at 100°. The blue solution was poured on ice and made alkaline with dilute ammonium hydroxide. The tarry solid that separated was removed by filtration and the filtrate was extracted with chloroform which was then used to extract the phenanthroline from the solid material. The solvent was removed in a stream of nitrogen and the residue crystallized from benzene–petroleum ether. In this manner 4.7 g. (43.9%) of crude 4-methyl-2-aza-1,10-phenanthroline, m.p. 185–188°, was obtained. Repeated crystallization from this same solvent raised the melting point to 189–190°. An analytical sample was prepared by sublimation at 170° (1–2 mm.) followed by recrystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{12}H_9N_3$: C, 73.84; H, 4.61. Found: C, 74.16; H, 4.59.

4-Styryl-2-aza-1,10-phenanthroline.—A mixture of 4.7 g. of 4-methyl-2-aza-1,10-phenanthroline, 35 ml. of purified benzaldehyde and 2 g. of anhydrous zinc chloride was refluxed for five hours, cooled in an ice-bath and treated with 45 ml. of benzene and 45 ml. of 2 *N* hydrochloric acid. A solid was precipitated and the mixture was heated to boiling for one hour, cooled in ice and filtered. The crude solid hydrochloride was washed thoroughly with benzene, then dried in a vacuum desiccator overnight. The base was obtained by addition of the pulverized hydrochloride, in small portions, to a stirred, concentrated solution of potassium hydroxide which was then extracted with chloroform. The solvent was removed in a stream of nitrogen and the residue crystallized from benzene. There was obtained 4.76 g. (70%) of faintly yellow, crystalline material melting at 216–217°. An analytical sample was prepared by sublimation at 190° (1–2 mm.) and recrystallization from benzene.

Anal. Calcd. for $C_{19}H_{13}N_3$: C, 80.56; H, 4.59. Found: C, 80.35; H, 4.71.

2-Aza-1,10-phenanthroline-4-carboxylic Acid.—A solution of 1.84 g. of 4-styryl-1,10-phenanthroline in a mixture of 16 ml. of pyridine and 16 ml. of water was cooled to 0° and treated with 2.62 g. (0.0165 mole) of potassium permanganate. The addition of oxidant was such that the temperature did not rise above 2°. The mixture was stirred 15 minutes with cooling, three hours at room temperature, filtered, using a filter aid, and the manganese dioxide shaken twice with 15-ml. portions of 0.1 *N* sodium hydroxide solution. The combined filtrate and washings were concentrated to 15 ml. at 50° (40 mm.) using an antifoam agent. The concentrate was filtered, acidified with 6 *N* hydrochloric acid and the solid that formed was removed by

(8) F. Nord, *Ber.*, **52B**, 1705 (1919).
(9) C. Atkinson and A. Mattocks, *J. Chem. Soc.*, 3722 (1957).
(10) R. Elderfield, *et al.*, *J. Org. Chem.*, **12**, 405 (1947).
(11) F. J. Wolf, R. H. Beutel and J. R. Stevens, THIS JOURNAL, **70**, 2572 (1948).
(12) F. Linsker and R. Evans, *ibid.*, **68**, 874 (1946).
(13) M. Dewar and P. Maitlis, *J. Chem. Soc.*, 2518 (1957).

filtration and washed well with ether. It was purified by decolorizing in sodium carbonate solution and acidifying with dilute acetic acid. The yield of 2-aza-1,10-phenanthroline-4-carboxylic acid, m.p. 196–197° dec., was 1.1 g. or 75.4%. The acid can also be crystallized from water.

Anal. Calcd. for $C_{12}H_7N_3O_2$: C, 64.00; H, 3.11. Found: C, 63.64; H, 2.94.

2-Aza-1,10-phenanthroline.—A mixture of 0.6 g. of 2-aza-1,10-phenanthroline-4-carboxylic acid and 3 g. of benzophenone was heated at 155° in a stream of nitrogen for 1.5 hr., cooled and extracted with two 50-ml. portions of ether. The combined ether extracts were extracted with 3 *N* hydrochloric acid. The combined acid extracts were made basic with reagent ammonium hydroxide, then extracted with chloroform. The solvent was removed in a stream of nitrogen and the residue crystallized from *n*-heptane. There was obtained 0.11 g. (22.4%) of 2-aza-1,10-phenanthroline, m.p. 170.5–171.5°. An analytical sample was sublimed at 145° (1–2 mm.) and then crystallized from *n*-heptane.

Anal. Calcd. for $C_{11}H_7N_3$: C, 72.90; H, 3.87. Found: C, 72.76; H, 3.98.

7-Acetyl-8-nitroquinoline.—The procedure for this preparation was entirely similar to that for 4-methyl-2-aza-1,10-phenanthroline above, with the substitution of an equivalent amount of 3-acetamido-2-nitroacetophenone for 8-amino-4-methylcinnoline. From 44.4 g. of 3-acetamido-2-nitroacetophenone[7] and proportional amounts of the other ingredients there was obtained, by extraction of the filter cake with butanone, crystallization from this same solvent and recrystallization from alcohol, 19.5 g. (46.1%) of material melting at 210–211°. An analytical sample was prepared by sublimation at 190° (1–2 mm.).

Anal. Calcd. for $C_{11}H_8N_2O_3$: C, 61.11; H, 3.73. Found: C, 61.11; H, 3.82.

Reduction of 7-Acetyl-8-nitroquinoline. Method A.—To a stirred solution of 6.6 g. of 7-acetyl-8-nitroquinoline in 40 ml. of acetic acid at 90–95° there was added 6.8 g. of iron filings in 10–12 portions during 75 minutes. Ten milliliters of water was added at the start of the reaction and again after 45 minutes. After 1.75 hr. the mixture was diluted with water and extracted with ether. The combined extracts were washed with water, with dilute sodium carbonate solution, again with water, dried with anhydrous sodium sulfate and evaporated. The residue on crystallization from *n*-heptane yielded 4.45 g. or 79.9% of golden, crystalline material melting at 108–109°. An analytical sample was sublimed at 90° (1–2 mm.).

Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 71.00; H, 5.38. Found: C, 70.96; H, 5.37.

Method B.—A mixture of 10 g. of 7-acetyl-8-nitroquinoline and 176 ml. of 6 *N* hydrochloric acid was warmed to 50°. A solution of 31.4 g. of stannous chloride dihydrate in 32 ml. of concentrated hydrochloric acid was added with vigorous stirring, at a rate sufficient to maintain the temperature at 50°. The mixture was stirred an additional 15 min. at 50°, allowed to come to room temperature, cooled, filtered and the filter cake air-dried (melting point > 220°). The solid was dissolved in 200 ml. of water, made strongly basic with concentrated potassium hydroxide, filtered and the separated solid air-dried. The yield of crude 3-methyl-(pyrido[3,2-g]anthranil), m.p. 160–163°, was 7.91 g. or 93%. Recrystallization from benzene–petroleum ether (b.p. 30–60°) after using decolorizing carbon raised the melting point to 165–166°. An analytical sample was prepared by sublimation at 145° (1–2 mm.).

Anal. Calcd. for $C_{11}H_8N_2O$: C, 71.74; H, 4.34. Found: C, 71.65; H, 4.26.

Reduction of the anthranil by iron and acetic acid yielded 7-acetyl-8-aminoquinoline (77.1%). Reduction by Adams catalyst was unsuccessful.

Method C.—A suspension of 2.8 g. of 7-acetyl-8-nitroquinoline and 30 mg. of Adams platinum catalyst in 100 ml. of absolute ethanol was shaken at 2–3 atmospheres pressure of hydrogen until three equivalents of hydrogen had been absorbed. The catalyst was removed by filtration and the alcohol evaporated under diminished pressure. The residue was extracted with *n*-heptane which after treatment with decolorizing carbon gave 0.98 g. (40.6%) of 7-acetyl-8-aminoquinoline, m.p. 107–108°. The *n*-heptane-insoluble portion was crystallized from benzene–petroleum ether after treatment with decolorizing carbon, and yielded 1.0 g. (42%) of 3-methyl-(pyrido[3,2-g]anthranil), m.p. 165–166°.

4-Hydroxy-2-aza-1,10-phenanthroline. Method A.—A solution of 1.1 g. of sodium nitrite in 21 ml. of water was added at 0–5° to a stirred solution of 3.0 g. of 7-acetyl-8-aminoquinoline in 240 ml. of 9 *N* hydrochloric acid. The resulting solution was stirred an additional 0.5 hour at 0°, allowed to stand at room temperature for 12 hours and then heated on a steam-bath at 60° until a small aliquot gave a negative coupling reaction with alkaline β-naphthol solution. The mixture was concentrated to one-fifth its volume by distillation at the water-pump, made basic with solid sodium carbonate and extracted with benzene. The residue, obtained after evaporation of the solvent, was crystallized from petroleum ether (b.p. 30–60°) and gave 1.74 g. (53%) of a colorless substance, m.p. 49–50°, presumed to be 8-chloro-7-acetylquinoline.

Anal. Calcd. for $C_{11}H_8NOCl$: C, 64.23; H, 3.89; N, 6.82; Cl, 17.3. Found: C, 64.10; H, 3.92; N, 6.90; Cl, 16.9.

The aqueous solution, after benzene extraction, was acidified with acetic acid and again extracted with benzene. The solvent was evaporated in a stream of nitrogen and the residue crystallized from this same solvent to give 0.4 g. (12.7%), of 4-hydroxy-2-aza-1,10-phenanthroline melting at 263° (sealed tube). An analytical sample was sublimed at 200° (1–2 mm.).

Anal. Calcd. for $C_{11}H_7N_3O$: C, 67.00; H, 3.55. Found: C, 66.97; H, 3.60.

Method B.—Diazotization in 5 *N* hydrochloric acid (20 ml. for 3.0 g. of amine) yielded 13% of hydroxyazaphenanthroline and 30% of 7-acetyl-8-chloroquinoline.

Method C.—A solution of 1.1 g. of sodium nitrite in 4 ml. of water was added at 0–5° to a stirred suspension of 3.0 g. of 7-acetyl-8-aminoquinoline in 16 ml. of acetic acid and 16 ml. of 10 *N* sulfuric acid. The resulting solution after stirring an additional 0.5 hour at 0° was allowed to stand in the dark for two days or until a small aliquot failed to couple with alkaline β-naphthol solution. The reaction mixture was made alkaline with solid sodium carbonate. Extraction of this mixture with benzene failed to yield any product. The mixture was acidified with acetic acid and some solid, largely inorganic salts, was precipitated. The solid was removed by filtration, dried, pulverized and extracted with benzene as was also the filtrate. The combined extracts were evaporated to dryness and the residue after several crystallizations from benzene gave 0.70 g. (22%) of crude 4-hydroxy-2-aza-1,10-phenanthroline, m.p. 255–8°. A sublimation of this material at 200° (1–2 mm.) raised the m.p. to 261°.

3-Aza-1,10-phenanthroline.—The procedure for this preparation was entirely similar to that for 4-methyl-2-aza-1,10-phenanthroline above, with the substitution of an equivalent amount of 8-aminoquinazoline[10] for 8-amino-4-methylcinnoline. From 5.74 g. of 8-aminoquinazoline and proportional amounts of the other ingredients, there was obtained 1.92 g. of crude reaction product which was crystallized several times from water, after treatment with decolorizing carbon, yielding 0.8 g. (10.0%) of colorless feathers, m.p. 144–145°. The infrared spectrum for this compound indicates a hydroxyl group (2.95 μ), a secondary amine group (3.05 μ), a cycloalkane ring (3.47 μ). This substance has been provisionally assigned the structure 7-hydroxy-7,8,9,10-tetrahydro-3-aza-1,10-phenanthroline. An analytical sample was recrystallized from water and from chloroform and then sublimed at 125° (1–2 mm.).

Anal. Calcd. for $C_{11}H_{11}N_3O$: C, 65.67; H, 5.47. Found: C, 65.18; H, 5.28.

The combined aqueous filtrates from the above crystallizations were made basic with ammonium hydroxide and extracted with chloroform. The solvent was removed and the residue crystallized from *n*-heptane to give 0.96 g. of crude 3-azaphenanthroline, m.p. 155–160°. This was dissolved in benzene and percolated over alumina which had been wet previously with *n*-heptane. The column was developed with benzene and produced two distinct bands, one dark in color near the top of the column and another bright yellow farther down the column. The yellow band was eluted with a large volume of benzene. After all of the yellow material had been removed, ether was used to elute the 3-azaphenanthroline. The red color given by this substance with acidic ferrous sulfate solution was used to follow its

progress off the column. The yield of pure 3-aza-1,10-phenanthroline obtained, m.p. 171.5–172.5°, was 0.62 g. or 8.7%. An analytical sample was sublimed at 150° (1–2 mm.) and then crystallized from *n*-heptane.

Anal. Calcd. for $C_{11}H_7N_3$: C, 72.90; H, 3.87. Found: C, 73.04; H, 3.85.

4-Aza-1,10-phenanthroline.—The procedure for this preparation was entirely similar to that for 4-methyl-2-aza-1,10-phenanthroline above, with the substitution of an equivalent amount of 5-acetamidoquinoxaline[11] for 8-amino-4-methylcinnoline. From 6.2 g. of 5-acetamidoquinoxaline and proportional amounts of the other ingredients, there was obtained 1.1 g. or 18.4% of material crystallized from benzene–petroleum ether melting at 146.5–147.5°. An analytical sample was prepared by sublimation at 125° (1–2 mm.).

Anal. Calcd. for $C_{11}H_7N_3$: C, 72.92; H, 3.87; N, 23.2. Found: C, 72.81; H, 3.82; N, 23.2.

4-Amino-1,5-naphthyridine.—Anhydrous ammonia was passed into a mixture of 19.7 g. of 4-chloro-1,5-naphthyridine,[14] 80 g. of phenol and 20 g. of acetamide at 170° for 6 hr. After making strongly alkaline with sodium hydroxide solution the precipitate was removed by filtration and crystallized from water. The yield of product melting at 200° was 15 g. (86.2%). The pure amine melts at 202–203°.

Anal. Calcd. for $C_8H_7N_3$: C, 66.19; H, 4.86. Found: C, 66.61; H, 4.79.

4-(β-Dicarbethoxyvinylamino)-1,5-naphthyridine.—A mixture of 10.5 g. of 4-amino-1,5-naphthyridine and 16.5 g. of ethyl ethoxymethylenemalonate was heated for three hours at 140–150° and the cooled mixture (solid) crystallized from ethanol, yielding 20 g. (87.7%) of pure product, m.p. 134–135°.

Anal. Calcd. for $C_{16}H_{17}O_4N_3$: C, 60.94; H, 5.43. Found: C, 60.89; H, 5.57.

3-Carbethoxy-4-hydroxy-6-aza-1,10-phenanthroline.—To 100 ml. of refluxing Dowtherm A was added 5 g. of 4-(β-dicarbethoxyvinylamino)-1,5-naphthyridine, the refluxing being continued for one hour. After cooling, the precipitated solid was removed by filtration, and washed, first with petroleum ether and then with warm ethanol. The yield of crude ester was 3.8 g. (89.0%). A sample, crystallized from dimethylformamide, melted at 290–291° dec.

Anal. Calcd. for $C_{14}H_{11}O_3N_3$: C, 62.45; H, 4.12. Found: C, 62.59; H, 4.15.

4-Hydroxy-6-aza-1,10-phenanthroline.—Twenty-four grams of crude 3-carbethoxy-4-hydroxy-6-aza-1,10-phenanthroline was refluxed with 250 ml. of 4% sodium hydroxide for six hours. The solution then was made faintly acid, and the resulting precipitate removed by filtration and dried (19.5 g.). A suspension of this crude product in 450 ml. of mineral oil was heated with stirring at 320–330° for 1.25 hr. After cooling, the insoluble material was removed by filtration and washed with petroleum ether. Crystallization from ethanol yielded 11.5 g. (59.9%) of pure hydrated product, m.p. 304–305°.

Anal. Calcd. for $C_{11}H_7ON_3 \cdot H_2O$: C, 61.37; H, 4.22. Found: C, 61.51; H, 4.11.

4-Chloro-6-aza-1,10-phenanthroline.—A mixture of 5.4 g. of 4-hydroxy-6-aza-1,10-phenanthroline (dried at 110°) and 120 ml. of phosphorus oxychloride was heated at reflux for 5–6 hr. After removal of the excess of phosphorus oxychloride by distillation *in vacuo*, the mixture was poured on ice and made alkaline with ammonium hydroxide. Extraction with benzene and then removal of solvent left a residue which yielded, after crystallization from benzene, 3.9 g. (66.1%) of chloro compound, m.p. 211–212°.

Anal. Calcd. for $C_{11}H_6N_3Cl$: C, 61.25; H, 2.78. Found: C, 61.55; H, 2.68.

5-Aza-1,10-phenanthroline.—A mixture of 1.5 g. of 4-chloro-6-aza-1,10-phenanthroline, 1 g. of 10% palladium-on-carbon, 5 ml. of 10% potassium hydroxide solution and 70 ml. of absolute ethanol was shaken under 40 lb. pressure of hydrogen for 2 hr., after which the contents of the flask was evaporated to dryness, taken up in a minimum of water and extracted with chloroform. Removal of the solvent yielded 0.7 g. (55.6%) of 5-aza-1,10-phenanthroline, m.p. 150–151°. The pure product melts at 152–153°.

Anal. Calcd. for $C_{11}H_7N_3$: C, 72.90; H, 3.87. Found: C, 72.91; H, 3.91.

3,4-Bis-(β-dicarbethoxyvinylamino)-pyridine.—A mixture of 15.3 g. of 3,4-diaminopyridine and 61.2 g. of ethyl ethoxymethylenemalonate was heated on the steam-bath for 5 hr. The insoluble material obtained after warming with benzene was separated by filtration and crystallized from ethanol. The yield of pure material was 19 g. (30.2%), m.p. 170–171°.

Anal. Calcd. for $C_{21}H_{27}O_8N_3$: C, 56.12; H, 6.06. Found: C, 56.05; H, 6.21.

Attempts to cyclize this compound were unsuccessful.

5,6-Dinitroquinoxaline.—This preparation differed from that given by Dewar and Maitlis[13] only in the isolation of the product. Extraction with ether, rather than chloroform–acetone, was continued until an extract was only faintly colored. Methanol (125 ml. when 19.4 g. of quinoxaline was used in the nitration) was added to the combined extracts and the ether removed by distillation. The cooled residue deposited crude 5,6-dinitroquinoxaline, and concentration of the filtrate after removal of the solid yielded additional material. Repeated crystallizations from methanol gave 5,6-dinitroquinoxaline, m.p. 168–170°, in a 22% yield.

6-Aminoquinoxaline.—A mixture of 41 g. of 6-nitroquinoxaline, 161 g. of stannous chloride dihydrate and 800 ml. of ethanol was refluxed for 5 hr. on a steam-bath. After removal of most of the ethanol, the mixture was made strongly alkaline and extracted with ether. Removal of ether and crystallization from benzene yielded 24 g. (70.6%) of amine, m.p. 157–158° (Hinsberg[15] records m.p. 159–160° for a product prepared from 1,2,4-triaminobenzene and glyoxal).

6-*p*-Toluenesulfonamidoquinoxaline.—To a cold (0°) solution of 29 g. of 6-aminoquinoxaline dissolved in 202 ml. of dry pyridine there was added slowly 38 g. of *p*-toluenesulfonyl chloride. The mixture was heated then for 30 min. on a steam-bath under reflux and poured into ice-water. The precipitate was removed by filtration, washed with water and dried in air. Crystallization from benzene yielded 44.6 g. (74.6%), m.p. 182–183°.

Anal. Calcd. for $C_{15}H_{13}N_3O_2S$: C, 60.18; H, 4.38. Found: C, 60.15; H, 4.24.

5-Nitro-6-*p*-toluenesulfonamidoquinoxaline.—To a solution of 4.3 g. of 6-*p*-toluenesulfonamidoquinoxaline in 11 ml. of glacial acetic acid at 60° was added a mixture of 1 ml. of nitric acid (d.1.5) and 2 ml. of glacial acetic acid at such a rate that the temperature of the reaction mixture did not exceed 85°. The temperature was maintained at 85° for 30 min. The mixture was then poured on ice, the resulting precipitate removed by filtration and crystallized from methanol, yielding 2.7 g. (54.5%) of a product melting at 197–198°.

Anal. Calcd. for $C_{15}H_{12}N_4O_4S$: C, 52.32; H, 3.51. Found: C, 52.44; H, 3.65.

6-Amino-5-nitroquinoxaline.—A mixture of 5 g. of 5-nitro-6-*p*-toluenesulfonamidoquinoxaline and 25 ml. of concentrated sulfuric acid was heated for one hr. on the steam-bath. It was then poured on ice and made alkaline with ammonium hydroxide. The resulting precipitate was dried and crystallized from ethanol, yielding 2 g. of pure product melting at 226–227°.

Anal. Calcd. for $C_8H_6N_4O_2$: C, 50.52; H, 3.13. Found: C, 50.19; H, 2.90.

On deamination with hypophosphorous acid, 5-nitroquinoxaline[16] was obtained.

Reductive acetylation of 6-amino-5-nitroquinoxaline using zinc and a mixture of acetic anhydride and glacial acetic acid yielded a diacetate, m.p. 231–232°, identical with that obtained by a similar treatment of 5,6-dinitroquinoxaline.

4,7-Diaza-1,10-phenanthroline.—To a stirred suspension of 4.0 g. (0.018 mole) of 5,6-dinitroquinoxaline in 100 ml. of 6 *N* hydrochloric acid at 50° there was added 24.6 g. (0.109 mole) of stannous chloride dihydrate in 25 ml. of concentrated hydrochloric acid. The mixture was stirred an additional 15 minutes at 50°, cooled and made strongly basic with concentrated potassium hydroxide. It then was extracted with ether and the combined extracts, after drying with anhydrous sodium sulfate, were concentrated to one-third of the initial volume by distillation. This solution was added

(14) J. T. Adams, C. K. Bradsher, D. S. Breslow, S. T. Amore and C. R. Hauser, THIS JOURNAL, **68**, 1317 (1946).

(15) O. Hinsberg, *Ann.*, **237**, 345 (1887).

(16) H. Schultz, THIS JOURNAL, **72**, 3824 (1950).

to a stirred solution of 4.84 g. (0.018 mole) of glyoxal–sodium bisulfite in 80 ml. of water at 40°. After removal of the ether the temperature was raised to 100° and maintained there for one hour. The mixture was cooled, made basic with 50% potassium hydroxide and the solid that separated was extracted with chloroform. The solvent was removed in a stream of nitrogen and the residue crystallized from benzene–petroleum ether, after decolorizing, to give 1.70 g. (51.3%) of 4,7-diaza-1,10-phenanthroline, m.p. 242° (sealed tube). An analytical sample was prepared by sublimation at 190° (1–2 mm.) and then recrystallization from benzene–petroleum ether.

Anal. Calcd. for $C_{10}H_6N_4$: C, 65.93; H, 3.29. Found: C, 66.19; H, 3.22.

PHILADELPHIA 22, PENNA.

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE]

Unsaturated Macrocyclic Compounds. X.[1] Poly-oxygenated Macrocyclic Compounds from Hepta-1,6-diyn-4-ol

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RECEIVED MAY 28, 1959

The oxidative coupling of the readily available hepta-1,6-diyn-4-ol (dipropargylcarbinol) (Ia) with oxygen in the presence of cuprous chloride and ammonium chloride has been studied. Acetylation followed by direct crystallization yielded a pure stereoisomer of the cyclic dimer II, while chromatography gave a mixture of the two possible stereoisomers of II, the cyclic trimer V and the cyclic tetramer VIII. Successive hydrogenation, saponification and oxidation of II, V and VIII yielded cyclotetradecane-1,8-dione (IV), cycloheneicosane-1,8,15-trione (VI) and cycloöctacosane-1,8,15,22-tetrone (IX), respectively. The structures of VI and IX were confirmed through their conversion *via* the thioketals to cycloheneicosane (VII) and cycloöctacosane (X), respectively. The coupling of hepta-1,6-diyn-4-ol acetate (Ib) by the oxygen, cuprous chloride, ammonium chloride method yielded the cyclic dimers II as sole cyclic products, whereas oxidation with cupric acetate in pyridine led only to the cyclic trimer V. The ultraviolet spectra of the cyclic poly-acetylenes are discussed and it is shown that the spectra of both isomers of the cyclic dimer II are anomalous.

It has been found recently that macrocyclic poly-acetylenes can be prepared simply by the oxidative coupling of linear terminal diacetylenes under either of two types of reaction conditions.[2] Oxidation with oxygen in the presence of cuprous chloride and ammonium chloride in aqueous ethanol yielded the cyclic dimers besides linear products.[2a,b] On the other hand when the oxidation was carried out with cupric acetate in pyridine (without using a high dilution technique, *cf.*[2c]), the reaction was more complex and cyclic trimers, tetramers, etc., were obtained besides (in some cases) the cyclic dimers.[2d]

When we undertook the work described below, the only carbocyclic poly-acetylenes obtained by either of the above techniques were hydrocarbons. In order to determine whether acetylenic carbocycles containing functional groups could be prepared, we decided to study the oxidative coupling of hepta-1,6-diyn-4-ol (Ia). The corresponding hydrocarbon, hepta-1,6-diyne, had given the cyclic dimer by the oxygen–cuprous chloride method[2b] and the cyclic trimer and tetramer by the cupric acetate–pyridine technique.[2d] It has now been found that poly-oxygenated poly-acetylenic macrocycles can in fact be obtained from the carbinol Ia, as described in the present paper.

Hepta-1,6-diyn-4-ol (dipropargylcarbinol) (Ia) was prepared readily in quantity by the condensation between propargyl aluminum bromide and ethyl formate.[3] The coupling of the carbinol Ia was carried out by means of oxygen in the presence of cuprous chloride and ammonium chloride in aqueous ethanol acidified with hydrochloric acid.[2a,b] The total reaction mixture then was acetylated.

A highly crystalline insoluble substance (explosion point *ca.* 235°) could be obtained by direct crystallization in *ca.* 1% yield. It was clearly cyclic in view of the empirical formula $[(C_9H_8O_2)_n]$ and since the infrared spectrum showed it to contain α-diacetylene but no terminal acetylene groupings. This substance proved to be one of the two possible stereoisomers of the cyclic dimer, cyclotetradeca-1,3,8,10-tetrayne-6,13-diol diacetate (II), as evidenced by the abnormal ultraviolet spectrum (see below) and by the full hydrogenation results. Thus, the corresponding saturated compound (cyclotetradecane-1,8-diol diacetate) (III) on saponification and oxidation yielded cyclotetradecane-1,8-dione (IV), the melting point of which (148°) agreed well with that reported.[4] The corresponding dioxime also exhibited the expected melting point.[4] It is of interest to note that the saturated diol diacetate III appeared to be homogeneous and showed a sharp melting point at 109–110°. This fact gives support that the acetylenic diacetate II from which it was derived is one pure stereoisomer, although it has not been determined whether it is the *cis*- or the *trans*-glycol diacetate.

Chromatography on alumina of the total acetylated material after removal of the above-described cyclic dimer II gave three different crystalline products. The first of these in order of polarity was obtained in *ca.* 1.5% yield and showed an explosion point at *ca.* 195°. The infrared spectrum was similar to that of the insoluble cyclic dimer II, but showed several new bands in the 10–14 μ

(1) For Part IX, see F. Sondheimer and R. Wolovsky, *Tetrahedron Letters*, No. 3, 3 (1959).

(2) (a) F. Sondheimer and Y. Amiel, THIS JOURNAL, **78**, 4178 (1956); **79**, 5817 (1957); (b) F. Sondheimer, Y. Amiel and R. Wolovsky, *Proc. Chem. Soc.*, 22 (1957); THIS JOURNAL, **79**, 6263 (1957); (c) G. Eglinton and A. R. Galbraith, *Chemistry & Industry*, 737 (1956); *J. Chem. Soc.*, 889 (1959); (d) F. Sondheimer, Y. Amiel and R. Wolovsky, THIS JOURNAL, **79**, 4247 (1957); **81**, 4600 (1959); (e) G. Eglinton and A. R. Galbraith, *Proc. Chem. Soc.*, 350 (1957).

(3) M. Gaudemar, *Compt. rend.*, **239**, 1303 (1954); *Ann. chim. (Paris)*, [1] **13**, 205 (1956).

(4) A. T. Blomquist and R. D. Spencer, THIS JOURNAL, **70**, 30 (1948). Prof. Blomquist informed us that unfortunately he no longer possessed a sample for comparison.