of 1-methyl-2-hydroxymethyl piperidine has been detailed in the Experimental Section.

Pharmacology.—The oxa-alkylene analogs of the methonium type compounds herein prepared show interesting dependence of structure on noted hypotensive activity. In contrast to the 1-methyl - 4 - (3 - dialkylaminopropyl) - piperidines[5] which required conversion to the bis-quaternary structure to give hypotensive responses, selected members of the oxa-alkylene series show good activity in the form of the bis-tertiary amines. This effect is noted particularly in the structures I, A_1 = M-methyl-2-piperidyl and Y = $-CH_2O(CH_2)_2-$ which show equal or better activity as the bis-tertiary amine than as the bis-quaternary (compound 1 *vs.* 2, 3 *vs.* 4, 5 *vs.* 6). Equally good activity is obtained when Y is varied as $-CH_2O(CH_2)_3-$ (compounds 9 *vs.* 10, 1 *vs.* 9). On the other hand, the compounds I, Y = $-CH_2OCHCH_3CH_2-$ and $-(CH_2)_2O(CH_2)_2-$ are associated with sharp diminution or disappearance of the hypotensive response (compounds 7, 11 *vs.* 1, 9). In this latter group, hypotensive properties are substantially absent even as bis-quaternaries (compounds 8, 13, with some effect noted with 14).

Variation of I as A = N-methyl-2-pyrrolidyl is associated with a marked diminution in the hypotensive effect when compared to the corresponding active piperidyl derivatives (compounds 15 *vs.* 1, 18 *vs.* 3, 22 *vs.* 10). In only one instance (compound 17) was good hypotensive activity noted with the pyrrolidyl derivatives, and this structure required conversion to the bis-quaternary derivative.

Experimental[7]

2-Hydroxymethyl-1-methylpyridinium Bromide.—A solution of 30.5 g. (0.28 mole) of 2-pyridylcarbinol in 150 ml. of acetonitrile was maintained at 10° during the addition of 54 g. (0.56 mole) of methyl bromide. After standing 20 hours, the product, 54 g. (94%), was separated. A sample recrystallized from ethanol melted at 166–169°.

Anal. Calcd. for $C_7H_{10}BrNO$: C, 41.2; H, 4.9; N, 6.9. Found: C, 40.9; H, 4.9; N, 6.7.

(7) Descriptive data shown in Table I are not reproduced in the Experimental Section.

2-Hydroxymethyl-1-methylpiperidine Hydrochloride.—A solution of 49 g. (0.24 mole) of 2-hydroxymethyl-1-methylpyridinium bromide in 200 ml. of ethanol was hydrogenated over 8 hours in a Parr hydrogenator at 4 atmospheres using 6.0 g.[8] of 5% rhodium-on-carbon as the catalyst. Separation of the catalyst and removal of solvent yielded 50 g. (94%) of product. A sample recrystallized from acetonitrile melted at 154–156°.

Anal. Calcd. for $C_{17}H_{16}BrNO$: C, 40.0; H, 7.7; N, 6.7. Found: C, 39.6; H, 8.0; N, 6.9.

2-(2'-Dimethylaminoethoxymethyl)-1-methylpiperidine (Compound 1).—2-Hydroxymethyl-1-methylpiperidine hydrobromide (16.8 g., 0.08 mole) was dissolved in water, made basic with 40% sodium hydroxide, salted with potassium carbonate and extracted with five 15-ml. portions of toluene. The combined extracts were dried over magnesium sulfate. In a similar manner, 15.8 g. (0.11 mole) of 2-dimethylaminoethyl chloride hydrochloride was converted to a dry toluene solution of the base. Sodium sand was prepared in the usual manner from 1.8 g. (0.08 mole) of sodium in 50 ml. of dry toluene and treated over 3 hours with stirring with the toluene solution of 2-hydroxymethyl-1-methylpiperidine, keeping the temperature below 90°. At the end of this period, the stirred mixture was brought to reflux temperature and the toluene solution of 2-dimethylaminoethyl chloride added dropwise over 1 hour, and then reflux was continued for 7 hours. After removal of sodium chloride, the filtrate concentrated at reduced pressure yielded a residue of 13.8 g. Distillation gave a fraction of 8.1 g. boiling at 58–70° (0.3–0.4 mm.), which on redistillation yielded 5.1 g. (32%) of product boiling at 64–66° (0.25 mm.).

2-(3'-Dimethylaminopropoxymethyl)-1-methylpiperidine (compound 9) was prepared by the procedure above from 21 g. (0.1 mole) of 2-hydroxymethyl-1-methylpiperidine bromide, 20.6 g. (0.13 mole) of 3-dimethylaminopropyl chloride hydrochloride and 2.3 g. (0.1 mole) of sodium. Work-up and distillation gave 4.1 g. (19%) of the product boiling at 90–93° (0.6 mm.).

2-(2'-Trimethylammoniumethoxymethyl)-1-dimethylpiperidinium Dibromide (Compound 2).—A solution of 3.0 g. (0.015 mole) of 2-(2-dimethylaminoethoxymethyl)-1-methylpiperidine in 25 ml. of acetonitrile was cooled in a pressure bottle and 3.8 g. (0.04 mole) of methyl bromide added. Precipitation began within an hour. After standing 20 hours, the product was separated; 5.1 g. (86%), m.p. 253–255°.

Acknowledgment.—The authors are indebted to Dr. G. Ungar for the pharmacologic screening of the compounds.

(8) Experience with several runs indicated an optimum proportion of 2.5 g. of the rhodium–carbon catalyst for every 0.1 mole of the pyridinium compound.

YONKERS 1, NEW YORK

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF TEMPLE UNIVERSITY]

The Synthesis of Some 4,4'-Disubstituted 2,2'-Bipyridines[1]

BY GERHARD MAERKER AND FRANCIS H. CASE

RECEIVED OCTOBER 28, 1957

2,2'-Bipyridine-1,1'-dioxide has been utilized for the preparation of several 4,4'-disubstituted 2,2'-bipyridines: dinitro-, diamino-, bis-diethylamino-, dibromo-, dimethoxy-, diethoxy-, diphenoxy-, dicarbethoxy-, dicarboxamido-, hydroxyethoxy-. These derivatives all yield colored complexes with Fe(II).

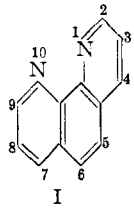
The ability of 1,10-phenanthroline (I) and 2,2'-bipyridine (II) to form highly colored complexes with iron(II) and other metallic ions has long been recognized and has been applied extensively in analytical chemistry for the detection and determination of these cations. In the case of 1,10-phenanthroline, the synthesis of a large number of substituted derivatives of the base has led to the discovery that substitution in the 4- and 7-positions especially has a profound effect upon the stabilities, oxidation–reduction potentials and color intensities of the iron(II) complexes.[2]

The 4- and 4'-positions of 2,2'-bipyridine are situated similarly to the 4- and 7-positions of 1,10-

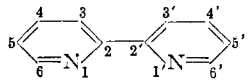
(1) This work was supported by a grant from the Committee on Research and Publications of Temple University.

(2) W. W. Brandt, F. P. Dwyer and E. C. Gyarfas, *Chem. Revs.*, **54**, 959 (1954).

phenanthroline, and thus it was of interest to prepare a series of 4,4′-disubstituted 2,2′-bipyridines whose metal chelates subsequently will be investigated.



I

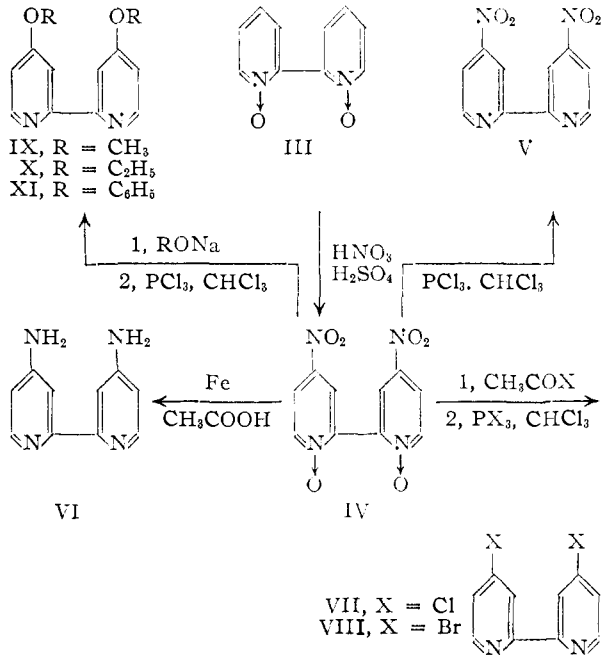


II

Until recently, only a few 4,4′-disubstituted derivatives of 2,2′-bipyridine had been reported[3] and these were prepared by the rather tedious methods of Ullman[4] or of Hein and co-workers.[5,6] A more suitable and versatile method was suggested to us by the work of Ochiai and co-workers[7] who prepared a number of 4-substituted pyridine derivatives by utilization of the reactions of pyridine-1-oxides. It was hoped that if the 1,1′-dioxide of 2,2′-bipyridine could be prepared, its reactions would be analogous to those reported by Ochiai for pyridine-1-oxide. When the investigations to be described were nearly completed, an abstract of an article by Haginiwa[8] appeared which indicated that a portion of our work (preparation of 2,2′-bipyridine-1,1′-dioxide, 4,4′-dinitro- and 4,4′-dichloro-2,2′-bipyridine-1,1′-dioxides, and 4,4′-dichloro-2,2′-bipyridine) had simultaneously been carried out elsewhere. Our preparation of these compounds, which agrees in essential details with those of the Japanese author, consequently is not given in this article.

Although the N-oxide groups of aromatic heterocyclic N-oxides generally are more resistant to reduction than nitro substituents on the ring, Hamana[9] has shown that the former groupings can be reduced selectively in 4-nitropyridine-1-oxide and 4-nitroquinoline-1-oxide by the action of phosphorus trichloride. This reagent was also found by us to produce 4,4′-dinitro-2,2′-bipyridine (V) from 4,4′-dinitro-2,2′-bipyridine-1,1′-dioxide (IV), although the yields were poor due to the low solubility of IV in the chloroform solvent.

Reduction of IV to 4,4′-diamino-2,2′-bipyridine (VI) was carried out by the use of iron powder in glacial acetic acid according to the method of den Hertog and Overhoff.[10] Haginiwa also attempted the preparation of VI but was unsuccessful when catalytic reduction in acid medium failed to give the desired product. In order to provide positive evidence that the diamine VI and hence the preceding dinitro dioxide IV is the 4,4′-derivative, VI was prepared by an independent synthesis. 4,4′-Dimethyl-2,2′-bipyridine was oxidized, as previously described,[3] to the corresponding dicarboxylic acid. The latter was then converted to the diamide and this in turn to the diamine using the procedure of Teague and Roe[11] for isoquinoline 3-carboxamide. This product proved to be identical with the diamine obtained by reduction of the dinitro derivative. Conversion of the dinitro dioxide IV to the dichloro dioxide was carried out essentially according to the method of Haginiwa.[8] It was found that the oxide was unstable at the boiling point of the crystallizing solvent, dimethylformamide, and decomposed slowly on repeated recrystallizations. The impure material was therefore reduced directly to 4,4′-dichloro-2,2′-bipyridine (VII) m.p. 131–132° (Haginiwa reports 143°).



4,4′ - Dibromo - 2,2′ - bipyridine - 1,1′ - dioxide (VIII) was prepared in a manner similar to that of the corresponding dichloro derivative,[8] by the action of acetyl bromide on IV. Again the dioxide was unstable, partially decomposing on recrystallization to 4,4′-dibromo-2,2′-bipyridine (VIII). The latter was prepared by treatment of the dioxide with phosphorus tribromide in chloroform.

The chlorine substituents of VII were easily displaced by diethylamino groups when VII was treated with aqueous diethylamine in a sealed tube at 130–140°. The oxide was converted, without purification, to 4,4′-bis-(diethylamino)-2,2′-bipyridine by the action of phosphorus trichloride. Direct displacement of the nitro groups of IV with alkoxy and phenoxy groups was carried out by reaction of IV with sodium methoxide, sodium ethoxide and sodium phenoxide, respectively. In the case of the alkoxide reactions an excess of the respective alcohol was used as solvent, but the reaction of sodium phenoxide with IV gave better results in nitrobenzene than in excess phenol. The resulting 4,4′-dimethoxy-2,2′-bipyridine-1,1′-dioxide and its 4,4′-diethoxy and 4,4′-diphenoxy analogs were difficult to purify. They were therefore deoxygenated, without complete purification,

(3) F. H. Case, THIS JOURNAL, **68**, 2574 (1946).
(4) P. E. Fanta, *Chem. Revs.*, **38**, 139 (1946).
(5) F. Hein and W. Retter, *Ber.*, **61**, 1790 (1928).
(6) F. Hein and H. Schwedler, *ibid.*, **68**, 681 (1935).
(7) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).
(8) J. Haginiwa, *J. Pharm. Soc. Japan*, **75**, 731 (1955); *C. A.*, **50**, 3435 (1956).
(9) M. Hamana, *J. Pharm. Soc. Japan*, **71**, 263 (1951); *C. A.*, **46**, 4542c (1952).
(10) H. J. den Hertog and J. Overhoff, *Rec. trav. chim.*, **69**, 468 (1950).
(11) C. A. Teague, Jr., and A. Roe, THIS JOURNAL, **73**, 688 (1951).

to the corresponding bases (IX–XI) by reaction with phosphorus trichloride in refluxing chloroform.

The attempted synthesis of 4,4'-dihydroxy-2,2'-bipyridine by treatment of X with 48% HBr has thus far yielded only 4-hydroxy-4'-ethoxy-2,2'-bipyridine instead of the desired product. Haginiwa attempted the preparation of the dihydroxy bipyridine by treatment of IV with 30% sulfuric acid and obtained the dihydroxy dioxide, but attempted deoxygenation with phosphorus trichloride in chloroform resulted in the displacement of the hydroxy groups with chlorine atoms, giving the dichloro derivative VII as the only product.

In view of the successful results attending the preparation of 2,2'-bipyridine-1,1'-dioxide and its 4,4'-derivatives it was considered desirable to ascertain whether similar procedures were applicable to the synthesis of 4,7-disubstituted 1,10-phenanthrolines. Linsker and Evans[12] have already reported the formation of 1,10-phenanthroline-1,10-dioxide in aqueous solution and the preparation of its picrate. We have been unable, however, to repeat this work, but were able to isolate the monoxide in small yield. Nitration of this substance, however, yielded no isolable product.

Experimental

4,4'-Dinitro-2,2'-bipyridine (V).—A suspension of 1.5 g. (0.0054 mole) of 4,4'-dinitro-2,2'-bipyridine-1,1'-dioxide[8] in 23 ml. of anhydrous chloroform was cooled to 0°, and 3 ml. (0.034 mole) of phosphorus trichloride was added. The mixture was heated at reflux over a water-bath for 1 hr., cooled to room temperature, and poured into a mixture of ice and water. The resulting suspension was made alkaline with aqueous sodium hydroxide and 1.3 g. of unchanged starting material recovered by filtration. The aqueous layer of the filtrate was extracted with several portions of fresh chloroform and discarded. The combined chloroform portions were evaporated to a crystalline residue (0.2 g., m.p. 182–185°) which was recrystallized from 95% ethanol to yield 0.12 g. of orange needles, m.p. 191.5–194.5°. Repeated recrystallizations from the same solvent raised the melting point to 195–197°.

Anal. Calcd. for $C_{10}H_6O_4N_4$: C, 48.79; H, 2.46. Found: C, 48.64; H, 2.43.

2,2'-Bipyridine-4,4'-dicarboxylic Acid.—The procedure of Case,[3] involving the oxidation of 4,4'-dimethyl-2,2'-bipyridine in neutral potassium permanganate solution, followed by acidification with hydrochloric acid, was repeated. A 44.6% yield of the dicarboxylic acid (m.p. >360°) was obtained.

Diethyl 2,2'-Bipyridine-4,4'-dicarboxylate.—A solution of 1.9 g. (0.0078 mole) of 2,2'-bipyridine-4,4'-dicarboxylic acid in a mixture of 21 ml. of concentrated sulfuric acid and 45 ml. of absolute ethanol was refluxed for 10 hr. and was then cooled and poured on ice. Neutralization with 25% aqueous sodium hydroxide caused precipitation of a white solid. The latter was collected by filtration, washed thoroughly with water and allowed to dry. The product was crystallized twice from 95% ethanol yielding 1.0 g. (42.7%) of white needles melting at 159–160.5°.

Anal. Calcd. for $C_{16}H_{16}O_4N_2$: C, 63.99; H, 5.37. Found: C, 64.14; H, 5.51.

2,2'-Bipyridine-4,4'-dicarboxamide.—A suspension of 0.9 g. (0.0030 mole) of diethyl 2,2'-bipyridine-4,4'-dicarboxylate in 50 ml. of absolute ethanol saturated with anhydrous ammonia at 0° was heated in a sealed tube for 11 hr. at 90°. After cooling, the contents of the tube were filtered, and the solid thus obtained was washed with absolute ethanol and dried to obtain 0.6 g. (83.3%) of white crystals, m.p. 340° dec. The pure product, crystallized from ethylene glycol, melted at 351° dec. It gave a positive ferroin reaction.

Anal. Calcd. for $C_{12}H_{10}O_2N_4$: C, 59.50; H, 4.16. Found: C, 59.21; H, 4.45.

4,4'-Diamino-2,2'-bipyridine. A. From 4,4'-Dinitro-2,2'-bipyridine-1,1'-dioxide.—To a solution of 4.0 g. (0.014 mole) of 4,4'-dinitro-2,2'-bipyridine-1,1'-dioxide in 160 ml. of glacial acetic acid at 100° was added 8.8 g. of iron powder (100 mesh). The mixture was heated at 114° with stirring for 70 min. and was then cooled to room temperature and added to 100 ml. of water. It was made alkaline with 25% sodium hydroxide and brought to a volume of 600 ml. with water. Filtration afforded a black, tarry precipitate which was dried in the oven at 65° and then extracted with 95% ethanol until further extraction no longer gave a purple alcohol solution. The combined extracts were filtered and then acidified, with cooling, with concentrated hydrochloric acid. The resulting suspension was filtered, the white precipitate washed with 95% ethanol and discarded, and the alcoholic wash solution combined with the filtrate. The alcoholic solution was concentrated to a volume of 250 ml. On standing, long needles deposited in the concentrate and were collected by filtration (4.8 g.). The filtrate, after further concentration, yielded a second crop of crystals (0.8 g.). The solids were combined and recrystallized from aqueous ethanol (125 ml. of 95% ethanol and 8 ml. of water) to give 2.4 g. of the hydrochloride of the product. The latter material was dissolved in water and the free base precipitated by addition of dilute sodium hydroxide solution. The white precipitate, after filtration and drying, weighed 1.1 g. (41.0%) (m.p. 277–278°). Crystallization from water did not raise this melting point.

Anal. Calcd. for $C_{10}H_{10}N_4$: C, 64.50; H, 5.41. Found: C, 64.62; H, 5.24.

B. From 2,2'-Bipyridine-4,4'-dicarboxamide.—To 20 ml. of a 15% aqueous sodium hydroxide solution at −4° was added 1.2 g. (0.005 mole) of crude 2,2'-bipyridine-4,4'-dicarboxamide. The suspension was stirred (at −4 to 1°) while 55 ml. of bromine was added slowly. The resulting reaction mixture was a thick paste. After addition of 10 ml. of water, the mixture was heated on the steam-bath at 83° for 70 min. The resulting solution was cooled and filtered. The precipitate, after washing with water and drying, weighed 0.1 g. (10.9%). It was crystallized from water and gave a white crystalline product which did not depress the melting point of the 4,4'-diamino-2,2'-bipyridine prepared by method A.

4,4'-Dibromo-2,2'-bipyridine-1,1'-dioxide.—To a suspension of 1.0 g. (0.0036 mole) of 4,4'-dinitro-2,2'-bipyridine-1,1'-dioxide in 15 ml. of glacial acetic acid at 60° was added 7.8 ml. of acetyl bromide[13] and the mixture refluxed for two hours on the water-bath. The solution was cooled to room temperature, poured on 150 g. of crushed ice, and neutralized with 15% sodium carbonate solution yielding 1.1 g. of dried precipitate (88.4%), m.p. 227–230° dec. This material was difficultly soluble in most organic solvents, and was partially deoxygenated on crystallization from aqueous dimethylformamide. Use of aqueous methanol as solvent gave better results, but the compound still could not be purified sufficiently for analysis. Attempts to precipitate the picrate from aqueous solutions failed.

4,4'-Dibromo-2,2'-bipyridine (VIII).—A suspension of 1.0 g. (0.0029 mole) of crude 4,4'-dibromo-2,2'-bipyridine-1,1'-dioxide in 25 ml. of anhydrous chloroform was cooled to −3°, and 4.0 ml. (0.042 mole) of phosphorus tribromide was added. After the mixture had been allowed to reflux for 75 min., it was cooled and poured into a mixture of ice and water. After phase separation, the chloroform layer was extracted repeatedly with distilled water, and the aqueous extracts were combined with the water layer from the reaction mixture. Neutralization of the aqueous solution with 25% sodium hydroxide caused separation of a voluminous white precipitate which, after cooling of the mixture, was isolated by filtration and washed thoroughly with water. The crude solid (m.p. 135–136°), which gave a strong ferroin reaction, was obtained in 77.1% yield. Recrystallization from petroleum ether (b.p. 60–70°) gave white needles melting at 141–142°.

Anal. Calcd. for $C_{10}H_6Br_2N_2$: C, 38.25; H, 1.93. Found: C, 38.59; H, 2.01.

4,4'-Diethoxy-2,2'-bipyridine-1,1'-dioxide.—To a solution of sodium ethoxide in ethanol, prepared from 0.3 g. (0.013 mole) of sodium metal and 40 ml. of absolute ethanol,

(12) F. Linsker and R. L. Evans, THIS JOURNAL, **68**, 403 (1946).

(13) T. M. Burton and E. F. Degering, *ibid.*, **62**, 227 (1940).

was added 1.0 g. (0.0036 mole) of 4,4'-dinitro-2,2'-bipyridine-1,1'-dioxide. The mixture was agitated on a water-bath at 60–65° for 3.5 hr., cooled to room temperature, and neutralized by dropwise addition of concentrated hydrochloric acid. The resulting mixture was filtered, the inorganic filter cake washed with ethanol and the alcohol washings combined. Evaporation of the ethanol solution on the steam-bath yielded an oily residue which changed to an amorphous solid on standing overnight. The solid was extracted with 50 ml. of boiling 1,2-dichloroethane, the extract treated with decolorizing carbon and the resulting orange solution allowed to cool slowly. The solid (0.65 g., 65.5%), which precipitated, melted at 195–199°. Recrystallization from 1,2-dichloroethane gave impure crystals (m.p. 197.5–199°). The monopicrate was prepared for analysis.

Anal. Calcd. for $C_{20}H_{19}O_{11}N_5$: C, 47.53; H, 3.79. Found: C, 47.53; H, 3.95.

4,4'-Diethoxy-2,2'-bipyridine (X).—Deoxygenation of 4,4'-diethoxy-2,2'-bipyridine-1,1'-dioxide with phosphorus trichloride in chloroform by a method similar to that described for 4,4'-dibromo-2,2'-bipyridine-1,1'-dioxide gave a 67.9% yield of white needles (from petroleum ether), m.p. 122–124°.

Anal. Calcd. for $C_{14}H_{16}O_2N_2$: C, 68.83; H, 6.60. Found: C, 69.01; H, 6.89.

4,4'-Dimethoxy-2,2'-bipyridine-1,1'-dioxide.—To a solution of sodium methoxide in methanol, prepared from 0.9 g. (0.039 mole) of metallic sodium and 120 ml. of methanol, was added 3.0 g. (0.011 mole) of 4,4'-dinitro-2,2'-bipyridine-1,1'-dioxide. The suspension was stirred for 3.25 hr. at 30–35°, cooled to 3°, and then neutralized with concentrated sulfuric acid and filtered. The white inorganic filter cake was discarded and the yellow methanol solution was evaporated on the steam-bath to a solid residue. The latter was extracted with three 100-ml. portions of boiling chloroform. The chloroform extracts were combined, treated with decolorizing carbon and condensed to a volume of 175 ml. To the hot solution, 100 ml. of petroleum ether (b.p. 60–70°) was added, producing a yellow precipitate (2.4 g., 88.9%) which melted at 224–225° dec. Two recrystallizations from a mixture of propanol-1 and petroleum ether raised the melting point of the product to 229° dec. The monopicrate of this compound (m.p. 190.5–192.0°) was prepared for analysis.

Anal. Calcd. for $C_{18}H_{15}O_{11}N_5$: C, 45.29; H, 3.17. Found: C, 45.45; H, 3.18.

4,4'-Dimethoxy-2,2'-bipyridine (IX).—Reduction of 4,4'-dimethoxy-2,2'-bipyridine-1,1'-dioxide with phosphorus trichloride in chloroform by the method described above gave a 69.0% yield of white crystals (from absolute ethanol), m.p. 170–172°.

Anal. Calcd. for $C_{12}H_{12}O_2N_2$: C, 66.65; H, 5.59. Found: C, 66.90; H, 5.47.

4,4'-Diphenoxy-2,2'-bipyridine (XI).—Sodium phenoxide was prepared by adding 0.2 g. (0.0087 mole) of sodium metal to 3.0 g. (0.032 mole) of melted phenol. After all of the sodium had reacted, the mixture was cooled and the solid crushed and added to a suspension of 1.0 g. (0.0036 mole) of 4,4'-dinitro-2,2'-bipyridine-1,1'-dioxide in 50 ml. of nitrobenzene. The mixture was heated with agitation at 40–50° for 3.5 hr. and, after cooling, was poured into 700 ml. of ether. After acidification with 4.0 ml. of glacial acetic acid and cooling, filtration afforded 1.6 g. of an ether-insoluble solid. A suspension of the latter in 50 ml. of water had a *p*H of 8. Addition of 4 drops of concentrated sulfuric acid lowered the *p*H to 4. The suspension was filtered and the solid washed with water and dried. The yield of product, m.p. 273.5–274°, was 1.0 g. (74.6%). A small amount of this solid, treated with phosphorus trichloride in chloroform by the method described above gave a 58.3% yield of white crystals (from absolute ethanol), m.p. 156.5–157.5°.

Anal. Calcd. for $C_{22}H_{16}O_2N_2$: C, 77.63; H, 4.74. Found: C, 77.88; H, 4.65.

4,4'-Bis-(diethylamino)-2,2'-bipyridine.—A suspension of 3.0 g. (0.012 mole) of 4,4'-dichloro-2,2'-bipyridine-1,1'-dioxide in 12 ml. (0.12 mole) of diethylamine and 12 ml. of water was heated in a sealed tube for 8 hours at 130–140°. After cooling to room temperature, diethylamine and water were removed by distillation *in vacuo* (aspirator). The residue was cooled and extracted with acetone. The acetone extract was evaporated to dryness and the oily residue was washed with ether, causing solidification. In this manner 2.2 g. (57.3%) of crude product (m.p. 225–229°) was obtained. A portion of the crude dioxide, treated with phosphorus trichloride in chloroform in the manner previously described, yielded a crystalline product melting at 156–157° after crystallization from aqueous ethanol; yield 50.0%.

Anal. Calcd. for $C_{18}H_{26}N_4$: C, 72.44; H, 8.78. Found: C, 72.56; H, 8.80.

4-Hydroxy-4'-ethoxy-2,2'-bipyridine.—A solution of 2.5 g. (0.010 mole) of 4,4'-diethoxy-2,2'-bipyridine in 100 ml. of 48% hydrobromic acid was refluxed for 4 hr. At the end of this period, the volume of hydrobromic acid was reduced by distillation *in vacuo* (aspirator) to 40 ml. The residue was neutralized with solid sodium carbonate, and the resulting suspension was filtered. The solid thus obtained was refluxed with 300 ml. of benzene, using a Dean–Stark tube to trap the water removed from the solid as the benzene–water azeotrope. The benzene solution was then filtered and condensed to a volume of about 70 ml. by distillation. To the hot residue, 7 ml. of petroleum ether (b.p. 60–70°) was added. On cooling, 0.81 g. of crude product melting at 161–165° separated. Recrystallization of the solid from benzene–petroleum ether (b.p. 60–70°) yielded white crystals, m.p. 164–166°.

Anal. Calcd. for $C_{12}H_{12}O_2N_2$: C, 66.65; H, 5.59. Found: C, 66.77; H, 5.55.

1,10-Phenanthroline-1-oxide.—To a solution of 3 g. (0.015 mole) of 1,10-phenanthroline monohydrate in 25 ml. of glacial acetic acid was added 4 ml. (0.13 mole) of 30% hydrogen peroxide and the solution agitated at 70–80° for 3 hr. After addition of 2 ml. (0.065 mole) of hydrogen peroxide, heating and stirring were continued for 2 hr. and the solution was then evaporated *in vacuo* to a volume of 10 ml. After addition of 10 ml. of water, concentration to a total volume of 10 ml. was repeated. The resulting solution, made alkaline with aqueous ammonia, was continuously extracted with chloroform for 72 hr. Addition of carbon tetrachloride to the boiling chloroform solution precipitated a small amount of resinous material which was removed by filtration. Addition of ether to the filtrate precipitated a brown solid (0.7 g., m.p. 170–174°) which was collected by filtration. After washing with boiling ether, the residue was crystallized from toluene, yielding the pure mono-oxide, m.p. 179–180°.

Anal. Calcd. for $C_{12}H_8ON_2$: C, 73.46; H, 4.11. Found: C, 73.36; H, 3.78.

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