Model Photostable Compounds

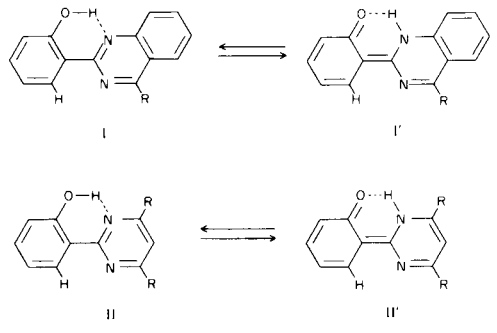
Jan-Erik Anders Otterstedt (1) and Richard Pater

Research and Development Division Contribution No. 482, Jackson Laboratory - Organic Chemicals Department, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19899

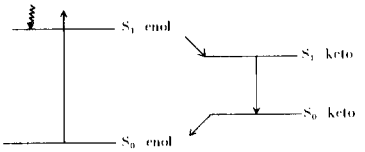
Received August 23, 1971

The photostabilities and syntheses of 2,2′-bis(*o*-hydroxyphenyl)-5,5′-bipyrimidine, 6,6′-bis(*o*-hydroxyphenyl)-3,3′-bipyridine and 3,8-bis(*o*-hydroxyphenyl)-4,7-phenanthroline are discussed. The syntheses of parent compounds lacking the *o*-hydroxy groups are also described.

Steric and resonance effects are important factors in the photostability of 2- and 4-(*o*-hydroxyphenyl)-substituted pyrimidines and quinazolines, since they influence the reversible enol-ketone tautomerism which occurs in these compounds in the lowest excited singlet state (2). The tautomerism is known to account for photostabilization (see below). Steric hinderance to photoketonization lessens photostability, which explains an observation that, of the 2- and 4-(*o*-hydroxyphenyl)-substituted pyrimidines and quinazolines, the 2- isomers are more photostable (2). In the absence of steric effects, as in the case of 2-(*o*-hydroxyphenyl)-substituted quinazolines (I) and pyrimidines (II), the larger the loss in resonance energy accompanying photoketonization, the lower is the photostability. The latter of the two postulates explains an amply demonstrated, higher intrinsic photostability of a 2-(*o*-hydroxyphenyl)quinazoline (I) relative to that of a 2-(*o*-hydroxyphenyl)pyrimidine (II). The loss in resonance energy is smaller on going from I to I′ than on going from II to II′. The formation of II′, in comparison with that of I′, is energetically less favored and is thus retarded, bringing about lower photostability (2).

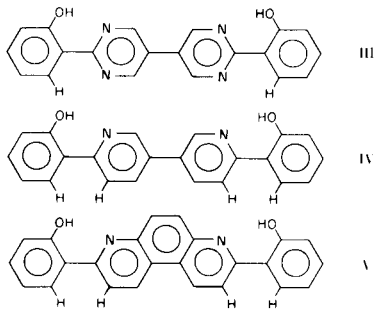


The relationship between reversible ketonization and photostability of chelated molecules of the type I and II appears to be well established. Merrill and Bennett (3) showed that intramolecular hydrogen bonding provides a deactivation mechanism for excited states of *o*-amidophenyl-2*H*-benzotriazoles by increasing internal conversion (a radiationless mode of dissipating the photoexcitation energy in the form of heat within the singlet system) from excited singlet to ground state by a factor of one hundred and considerably decreasing quantum yields for fluorescence and chemical reaction. An increase in the rate of internal conversion had been assumed by Becket and Porter (4) to result from an enol-ketone tautomerism in the lowest excited singlet state of 2,4-dihydroxybenzophenone, although no reason for it had been offered. One of us pointed out (5) that an increase in the rate of internal conversion due to the tautomerism might be possible because of a reversible formation of lower-energy keto form (*e.g.*, I′ or II′) which might have the effect of decreasing the energy gap separating its excited and ground



states, as shown in the diagram. Internal conversion increases exponentially with the decreasing energy gap and becomes, by far, the fastest mode of de-excitation of photoexcited molecules. Photostability, defined as the inverse of the quantum yield of photochemical reaction, is proportional to the rate of internal conversion ($\Phi_R^{-1} \alpha k_{i.c.}$). Calculations of the energy involved and direct observation of a very weak, strongly red-shifted keto fluorescence in *o*-hydroxyphenylsubstituted quinolines, pyrimidines, 2*H*-benzotriazoles, and quinazolines and in 2-hydroxybenzophenone substantiated the theory (5).

The above work (3,5) constitutes a sound theoretical basis for the previous (2) and present correlations of photostabilities with such factors influencing the rate of photoketonization as steric and resonance effects. Present correlations concern a series of three model photostable compounds, III, IV, and V. The photostability data were



III

IV

V

obtained in nylon and polyacrylonitrile (PAN) films and in dimethylformamide (DMF)-acetonitrile solutions and are presented in Table I. A convenient measure of photostability is the inverse of the quantum yield of photochemical reaction (Φ_R^{-1}) which gives the average number of times a molecule must be photoexcited to undergo a chemical reaction (3).

TABLE I

Photostabilities of Model Compounds (a)

Compound	Matrix	Φ_R^{-1}
2,2′-Bis(*o*-hydroxyphenyl)-5,5′-bipyrimidine (III)	Nylon	7.1×10^6
	PAN (b)	6.9×10^6
	DMF-CH_3CN (1:12)	3.1×10^7
6,6′-Bis(*o*-hydroxyphenyl)-3,3′-bipyridine (IV)	Nylon	4.5×10^5
	PAN (b)	1.8×10^5
	DMF-CH_3CN (1:12)	3.5×10^5
3,8-Bis(*o*-hydroxyphenyl)-4,7-phenanthroline (V)	Nylon	5.6×10^6
	PAN (b)	1.6×10^6
	DMF-CH_3CN (1:8)	1.1×10^6

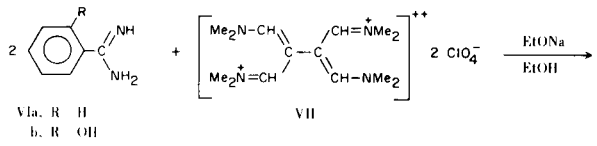
(a) Determined as described in ref. 3. (b) Polyacrylonitrile.

The bipyrimidine (III) must be counted among the most photostable organic compounds. A sharp decrease in the photostability is observed on going from III to the bipyridine (IV). We believe that this pronounced effect is due to two distinct factors responsible for retarding the photoketonization of the model compound IV. The two factors, each of which has an adverse effect on photostability, are (a) an increase in resonance energy on going from the bipyrimidine (III) to the bipyridine (IV), and (b) the appearance in IV of a steric hindrance to planarity of the biphenyl type between *o*-hydroxyphenyl groups and pyridine rings. Compound III is free of an analogous steric effect between *o*-hydroxyphenyl groups and the bipyrimidine moiety. The amount of steric hindrance to planarity and the attendant decrease in photostability on going from III to IV and from a 2- to a 4-(*o*-hydroxyphenyl)-pyrimidine, which was discussed in the previous paper (2), should be similar. The decrease in photostability on going from III to IV is more than tenfold (Table I) and is due to the compounding of the steric and resonance effects. The decrease on going from a 2- to a 4-(*o*-hydroxyphenyl)pyrimidine, attributable entirely to the steric effect, is markedly smaller. This indicates that there is a significant contribution of the resonance effect to the decrease in photostability observed on going from III to IV. The importance of resonance effects is convincingly demonstrated by comparing photostabilities of the phenanthroline (V) and bipyridine (IV) compounds, the former being a bridged version of the latter. The bridging allows the steric conditions prevailing in IV to be retained in V and provides for a more extensively conjugated heterocyclic system. Whereas the destruction of aromaticity as a result of photoketonization is total in IV, it is only partial in V, owing to an aromatic character retained by the middle benzene ring. The loss in resonance energy accompanying photoketonization is thus smaller in the case of V than in the case of IV. Consequently, photoketonization of V should be favored relative to that of IV resulting in higher photostability. The data of Table I show that the phenanthroline compound V is significantly more photostable than the bipyridine compound IV, in agreement with the theory (5).

Syntheses.

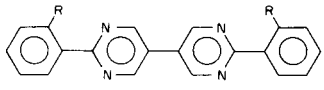
Model photostable compounds III, IV and V were prepared by unequivocal methods. Their analogs lacking the OH groups (IIIa, IVc, and Vb) were synthesized by the same methods to verify the course of the reactions and to demonstrate that the novel syntheses have a wider scope and thus may be used broadly.

2,2′-Diphenyl-5,5′-bipyrimidine (IIIa) and 2,2′-bis(*o*-hydroxyphenyl)-5,5′-bipyrimidine (III) were prepared *via* a one-step condensation involving a precursor (VII) (6) of 1,1,2,2-ethanetetracarboxaldehyde and benzamidine (VIa) or *o*-hydroxybenzamidine (VIb), respectively:



VIa, R = H
b, R = OH

VII

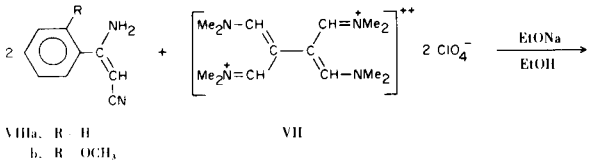


IIIa, R = H
III, R = OH

Compound IIIa was recently prepared by an Ullmann reaction of 5-bromo-2-phenylpyrimidine-4-carboxylic acid and by a Busch reaction of 5-bromo-2-phenylpyrimidine (7). Condensation of VII with the benzamidine VIa or

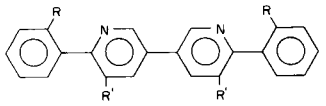
VIb thus parallels that of VII with guanidine or *S*-methylisothiourea which also provides a route to 2,2′-substituted 5,5′-bipyrimidines (8).

Two novel, double pyridine-ring closures were accomplished by using the precursor (VII) (6) of 1,1,2,2-ethanetetracarboxaldehyde and β-aminocinnamonitriles (VIIIa or VIIIb). Compound VII and β-aminocinnamonitrile (VIIIa)



VIIIa, R = H
b, R = OCH_3

VII

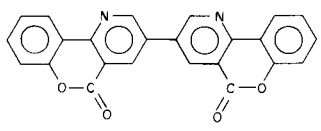


IVa, R = H; R′ = CN
b, R = H; R′ = COOH
c, R = H; R′ = H
d, R = OCH_3; R′ = CN
e, R = OCH_3; R′ = COOH
f, R = OCH_3; R′ = H
IV, R = OH; R′ = H

gave 5,5′-dicyano-6,6′-diphenyl-3,3′-bipyridine (IVa). An analogous condensation involving VII and *o*-methoxy-β-aminocinnamonitrile (VIIIb) produced 5,5′-dicyano-6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVd). These double cyclizations resulted in only modest yields (~ 20%) of the dicyano compounds IVa and IVd under optimum conditions. The products, however, were readily isolated. The low yields obtained might be due to dimethylamine which is liberated when VII is heated with sodium ethoxide. Dimethylamine may react with the other substrates (VIa-b, VIIIa-b) to give products which cannot participate in the desired condensations. A possible remedy, then, would be to remove dimethylamine with, *e.g.*, ethyl acetate prior to adding the other substrates. Attempts at condensing VII with two molar equivalents of the ethyl ester of β-aminocinnamic acid in the presence of sodium ethoxide were unsuccessful.

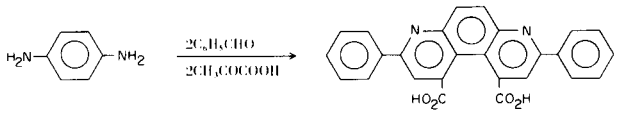
Hydrolysis of 5,5′-dicyano-6,6′-diphenyl-3,3′-bipyridine (IVa) under acidic conditions (concentrated hydrochloric acid) proceeded readily to give a high yield of 6,6′-diphenyl-3,3′-bipyridine-5,5′-dicarboxylic acid (IVb) which was decarboxylated, also in a high yield, to 6,6′-diphenyl-3,3′-bipyridine (IVc).

Hydrolysis of 5,5′-dicyano-6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVd) under acidic conditions (concentrated hydrochloric acid) led only to a high-melting dilactone of 6,6′-bis(*o*-hydroxyphenyl)-3,3′-bipyridine-5,5′-dicarboxylic acid (IX) which resisted decarboxylation. Compound IX dissolved in a dilute, aqueous sodium hydroxide solution after being heated, but was precipitated by acidification and, in this respect, behaved like a lactone of 2-(*o*-hydroxyphenyl)benzoic acid (9). For this reason, hydrolysis of IVd was carried out in a basic medium to give a high yield of 6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine-5,5′-dicarboxylic acid (IVe) which was decarboxylated to 6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVf). The latter underwent demethylation in the presence of refluxing 48% aqueous hydrobromic acid to give 6,6′-bis(*o*-hydroxyphenyl)-3,3′-bipyridine (IV).



IX

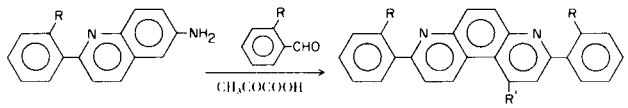
An attractive route to 3,8-diaryl-4,7-phenanthrolines appeared to be through 3,8-diaryl-4,7-phenanthroline-1,10-dicarboxylic acids. Woodruff and Adams (10) claimed to have prepared 3,8-diphenyl-4,7-phenanthroline-1,10-dicarboxylic acid (X) in one step from *p*-phenylenediamine and two molar equivalents each of benzaldehyde and pyruvic acid (Doebner's pyruvic acid synthesis). We have



X

repeated this synthesis and conclude that X does not form as claimed (10). Properties of the product (red-brick color and solubility in ethanol) appear to be inconsistent with the structure (X). Moreover, a decarboxylation followed by a vacuum sublimation of the decarboxylated material produced a relatively high yield (*ca.* 50%) of 6-amino-2-phenylquinoline (XIa) which could only arise by decarboxylation of 6-amino-2-phenylquinoline-4-carboxylic acid, a reaction we eventually employed. In addition, we have failed to obtain X after having condensed 6-amino-2-phenylquinoline-4-carboxylic acid with benzaldehyde and pyruvic acid. The formation of X appears also unlikely in the light of investigations of Bodforss (11) and of Skita and Wulff (12), neither of which was quoted by Woodruff and Adams (10).

Unequivocal methods of preparing derivatives of V involved condensing 6-amino-2-phenylquinoline (XIa) with benzaldehyde and pyruvic acid to give 3,8-diphenyl-4,7-phenanthroline-1-carboxylic acid (Va) and 6-amino-2-(*o*-methoxyphenyl)quinoline (XIb) with *o*-methoxybenzaldehyde and pyruvic acid to give 3,8-bis(*o*-methoxyphenyl)-4,7-phenanthroline-1-carboxylic acid (Vc). The course of



XIa, R = H
b, R = OCH_3

Va, R = H; R′ = COOH
b, R = H; R′ = H
c, R = OCH_3; R′ = COOH
d, R = OCH_3; R′ = H
V, R = OH; R′ = H

these reactions predictably paralleled that of a Skraup synthesis (13) and that of two Doebner's pyruvic acid syntheses (14,15), all of which involved 6-aminoquinoline and yielded 4,7-phenanthrolines.

The starting 6-amino-2-arylquinolines (XIa, b) were obtained most conveniently by condensing *p*-aminoacetanilide with pyruvic acid and benzaldehyde or *o*-methoxybenzaldehyde to give the corresponding *N*-acetyl derivatives of 6-amino-2-arylquinoline-4-carboxylic acids (16), saponifying the above (16) and decarboxylating the resulting 6-amino-2-arylquinoline-4-carboxylic acids (17).

Decarboxylation of 3,8-diphenyl-4,7-phenanthroline-1-carboxylic acid (Va) was carried out in bulk to furnish 3,8-diphenyl-4,7-phenanthroline (Vb). The compound had been prepared by a shorter route involving 4,7-phenanthroline and phenyl lithium (18). Decarboxylation of 3,8-bis-(*o*-methoxyphenyl)-4,7-phenanthroline-1-carboxylic acid (Vc) was carried out in quinoline in the presence of copper to give 3,8-bis(*o*-methoxyphenyl)-4,7-phenanthroline (Vd) which was demethylated in the presence of 48% hydrobromic acid to 3,8-bis(*o*-hydroxyphenyl)-4,7-phenanthroline (V).

EXPERIMENTAL

2,2′-Diphenyl-5,5′-bipyrimidine (IIIa).

A sodium ethoxide solution, prepared from 1.15 g. (0.05 g.-atom) of sodium and 20 ml. of absolute ethanol, was added dropwise to a suspension of 4.51 g. (0.01 mole) of [2,3-bis-(dimethylaminomethylene)-1,4-butanediylidene]bis[dimethylammonium perchlorate] (VII) (6) and 3.15 g. (0.02 mole) of benzamidine hydrochloride in 50 ml. of refluxing absolute ethanol. The mixture was heated under reflux for 1-½ hours and filtered while still hot. The cake was washed with ethanol and dried in the air to give 1.43 g. (46% of theory) of a solid, m.p. 331-332°. The crude product was purified by sublimation (250-260° at 0.25 mm Hg) and crystallization from acetic acid, m.p. 333°; lit. m.p. 333-335° and 335-337.5° (7). The ir spectrum was consistent with the structure: it showed no O-H, N-H, and C=O stretching bands; uv spectrum supported the structure: λ max 311 nm, ε max 37,200 (in acetic acid) which was similar to that of *p*-quaterphenyl in chloroform (λ max 300 nm, ε max 39,000). Compound IIIa and *p*-quaterphenyl showed an absorption maximum in ethanol at the same wavelength (300 nm).

Anal. Calcd. for $C_{20}H_{14}N_4$: C, 77.39; H, 4.54; N, 18.05. Found: C, 77.14; H, 4.85; N, 18.39.

2,2′-Bis(*o*-hydroxyphenyl)-5,5′-bipyrimidine (III).

A sodium ethoxide solution, prepared from 1.15 g. (0.05 g.-atom) of sodium and 60 ml. of absolute ethanol, and 10.4 g. (0.023 mole) of [2,3-bis(dimethylaminomethylene)-1,4-butanediylidene]bis[dimethylammonium perchlorate] (VII) (6) was heated under reflux for 35 minutes. To the hot mixture was added, all in one portion, 8.33 g. (0.045 mole) of *o*-hydroxybenzamidine sulfate (19). The condensation was allowed to proceed under reflux for 40 minutes. The reaction mixture was filtered hot, the cake washed with ethanol and slurried in 75 ml. of hot water containing 1 ml. of acetic acid. The slurry was filtered, the cake washed with water and dried (2.79 g.). The crude product was sublimed at 280-300° (0.25 mm Hg) and the sublimate crystallized from acetic acid to give 1.33 g. (17% theory) of the title compound, m.p. 315°, uv spectrum (in acetic acid): λ max 357 nm (ε max 30,700) and λ max 302 nm (ε max 27,600).

Anal. Calcd. for $C_{20}H_{14}N_4O_2$: C, 70.16; H, 4.12; N, 16.37. Found: C, 70.32; H, 4.07; N, 16.19.

5,5′-Dicyano-6,6′-diphenyl-3,3′-bipyridine (IVa).

A suspension of 36.1 g. (0.08 mole) of [2,3-bis(dimethylaminomethylene)-1,4-butanediylidene]bis[dimethylammonium perchlorate] (VII) (6) in a solution of sodium ethoxide prepared from 4.14 g. (0.18 g.-atom) of sodium and 200 ml. of absolute ethanol was heated under reflux for 30 minutes. To the reaction mixture was added dropwise a solution of 25.76 g. (0.178 mole) of β-aminocinnamonitrile (VIIIa) (20) in 120 ml. of absolute ethanol during 40 minutes. The refluxing was then continued for 45 minutes. The precipitate was filtered, washed with ethanol and slurried in 150 ml. of hot water. The insoluble portion was filtered, washed thoroughly with water and dried. The solid was suspended in 100 ml. of boiling acetone, stirred for 15 minutes and filtered to give 6.32 g. (22% of theory) of a crude product. A small portion of the material (0.5 g.) was crystallized from 300 ml. of acetone, the crystallized product sublimed at 260-270° (0.25 mm Hg) and the sublimate crystallized from acetone to give a pure sample of the title compound, m.p. 277-278°. The ir spectrum showed no N-H, O-H and C=O stretching bands. A band due to a C≡N stretch appeared at 2,230 cm^{-1}.

Anal. Calcd. for $C_{24}H_{14}N_4$: C, 80.42; H, 3.94; N, 15.63. Found: C, 80.22; H, 4.07; N, 15.86.

6,6′-Diphenyl-3,3′-bipyridine-5,5′-dicarboxylic Acid (IVb).

Crude 5,5′-dicyano-6,6′-diphenyl-3,3′-bipyridine (IVa), 2.64 g. (0.0073 mole), and concentrated hydrochloric acid (15 ml.) were heated in a sealed, heavy-walled Pyrex glass tube, which was immersed partially in an oil bath maintained at 200°, for 4-½ hours. Most of the dicyano compound went into solution at the end of the heating period. A precipitate appeared after the tube was cooled to 0°. The tube was opened, the reaction mixture filtered and the cake washed with a 15% aqueous sodium chloride solution. The solid was dissolved in 50 ml. of a 5% aqueous sodium hydroxide solution, the solution heated to boiling with charcoal and filtered. A colorless product was recovered from the hot filtrate after addition of an excess acetic acid, filtration, washing with water and drying (2.44 g. or 84% of theory). The title compound was found to melt at 313-314° with gas evolution. Strong ir bands were found at 1,705, 1,443, 1,255, 1,220, 742 and 697 cm^{-1}.

Anal. Calcd. for $C_{24}H_{16}N_2O_4$: C, 72.69; H, 4.07; N, 7.07; O, 16.14. Found: C, 72.54; H, 4.28; N, 6.97; O, 16.23.

6,6′-Diphenyl-3,3′-bipyridine (IVc).

6,6′-Diphenyl-3,3′-bipyridine-5,5′-dicarboxylic acid (IVb), 1.0 g. (0.00252 mole), was heated in the well of a sublimation apparatus at 315-320° under nitrogen until the evolution of carbon dioxide was complete. The residue was sublimed at 190-250° (0.02 mm Hg) to give 0.61 g. (78% of theory) of a somewhat yellow sublimate which was crystallized twice from acetone (0.3 g. of the product from 125 ml. of acetone). A pure sample of the title compound melted at 221-222°. Strong ir bands were observed at 1,588, 1,540, 1,467, 1,017, 997, 835, 776, 735 and 694 cm^{-1}; uv spectrum: λ max 312 nm, ε max 44,400 (in ethanol) and λ max 330 nm, ε max 45,700 (in acetic acid); nmr spectrum at 60 Mc. (in deuterated DMSO at 100° with TMS as external standard) showed three broad peaks centered around

7.48, 8.11 and 9.06 ppm (relative peak areas 3:4:1). The lowest-field signal (at 9.06 ppm) is assigned to α-pyridine protons).

Anal. Calcd. for $C_{22}H_{16}N_2$: C, 85.68; H, 5.23; N, 9.08. Found: C, 85.64; H, 5.20; N, 9.16.

o-Methoxy-β-aminocinnamonitrile (VIIIb).

A mixture of *o*-methoxybenzonitrile, 68.59 g. (0.515 mole), acetonitrile, 42.6 g. (1.03 mole), and sodium hydride, 42.0 g. (1.03 mole) of a 59% mineral-oil dispersion, in dry tetrahydrofuran (500 ml.) was heated in the atmosphere of nitrogen under reflux with magnetic stirring for 6 hours. Unreacted sodium hydride was separated from the hot reaction solution by filtration and washed thoroughly with boiling tetrahydrofuran. The filtrate was concentrated to a thick syrup under reduced pressure and triturated in ether. The crystalline material was filtered and washed with ice-cold ether. The solid was gradually added to a mixture of ice and water with vigorous stirring and cooling. The precipitate was filtered, washed thoroughly with water and dried. The product was dissolved in 500 ml. of hot ethyl acetate and the solution filtered. To the filtrate was added 450 ml. of boiling petroleum ether (boiling range 36-52°) and the product was allowed to crystallize at 10°. The crystallized material was filtered, washed with an ice-cold mixture of ethyl acetate/petroleum ether (1:1) and dried to give 33.7 g. (38% of theory) of a product melting at 137-138°. A small amount of the product was recrystallized from an ethyl acetate/petroleum ether mixture to give an analytical sample of the title compound, m.p. 137-138.5°. The ir spectrum showed N-H stretching bands at 2.9, 3.0 and 3.1 μ, a C≡N stretching band at 4.58 μ and peaks at 6.12, 6.3 and 6.41 μ.

Anal. Calcd. for $C_{10}H_{10}N_2O$: C, 68.94; H, 5.78; N, 16.08. Found: C, 68.88; H, 5.69; N, 16.06.

5,5′-Dicyano-6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVd).

A sodium ethoxide solution was prepared from 4.20 g. (0.18 g.-atom) of sodium and 450 ml. of absolute ethanol in a 2-l., 3-neck flask equipped with reflux condenser, drying tube, dropping funnel and magnetic stirring bar. To the solution were added 100 ml. of dry dimethylsulfoxide and 40.6 g. (0.09 mole) of [2,3-bis(dimethylaminomethylene)-1,4-butanediylidene]bis[dimethylammonium perchlorate] (VII) (6). The mixture was heated under reflux for 25 minutes. A warm solution of 31.3 g. (0.18 mole) of *o*-methoxy-β-aminocinnamonitrile (VIIIb) in 450 ml. of absolute ethanol was added dropwise to the reaction flask during 1-½ hours. The reflux was maintained for 2 hours after the addition was complete. The reaction mixture was cooled in ice, filtered and the cake washed with ice-cold ethanol. The solid was slurried in hot water and stirred for 15 minutes. The residue was filtered, washed with water and dried to give 6.57 g. (20% of theory) of the title compound, m.p. 279-281°. A small portion of this material was sublimed at 280° (0.02 mm Hg) and the sublimate crystallized from acetone, m.p. 280-281°. The ir spectrum showed main bands at 2,227 (C≡N stretch), 1,596, 1,490, 1,456, 1,432, 1,273, 1,252, 1,241, 1,020, 1,013, 899, and 751 cm^{-1}.

Anal. Calcd. for $C_{26}H_{18}N_4O_2$: C, 74.63; H, 4.33; N, 13.38; O, 7.65. Found: C, 74.43; H, 4.56; N, 13.17; O, 7.69.

Dilactone of 6,6′-bis(*o*-hydroxyphenyl)-3,3′-bipyridine-5,5′-dicarboxylic Acid (IX).

5,5′-Dicyano-6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVd), 1.11 g. (0.00265 mole), and concentrated hydrochloric acid (10 ml.) were heated in a sealed heavy-walled Pyrex glass tube at 160° for 3 hours. The tube was cooled in ice and opened. The reaction mixture was filtered and the cake washed with a 15% aqueous sodium chloride solution. The product was dissolved in a hot, 5% aqueous sodium hydroxide solution and the solution filtered. The dilactone was recovered from the filtrate following an acidification with acetic acid. A high yield (0.97 g. or 95% of theory) of the title compound, m.p. 381-382° was obtained. The product showed a m.p. of 382-383° after a vacuum sublimation. The ir spectrum showed main bands at 3,067, 1,760, 1,730, 1,605, 1,598, 1,444, 1,254, 1,171, 1,108, 1,050, and 755 cm^{-1}.

Anal. Calcd. for $C_{24}H_{12}N_2O_4$: C, 73.46; H, 3.08; N, 7.14; O, 16.31. Found: C, 73.30; H, 3.21; N, 7.15; O, 16.52.

6,6′-Bis(*o*-methoxyphenyl)-3,3′-bipyridine-5,5′-dicarboxylic Acid (IVe).

A mixture of 3.44 g. (0.0082 mole) of 5,5′-dicyano-6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVd), 14.0 g. of sodium hydroxide, 50 ml. of water and 100 ml. of ethanol was heated in a 400 ml. stainless-steel autoclave at 160° for 5 hours. The reaction solution was filtered to remove mechanical impurities and the filtrate was neutralized with a dilute hydrochloric acid solution. The precipitate was isolated by filtration, washed thoroughly with water and dried at 100° *in vacuo* to give 3.48 g. (93% of theory) of the title compound, m.p. 290-291° with gas evolution. The ir spectrum showed main bands at 1,715, 1,600, 1,492, 1,460, 1,436, 1,270, 1,242, and 750 cm^{-1}.

Anal. Calcd. for $C_{26}H_{20}N_2O_6$: C, 68.42; H, 4.41; N, 6.13; O, 21.03. Found: C, 68.33; H, 4.43; N, 6.28; O, 20.96.

6,6′-Bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVf).

A solution of 2.72 g. (0.00595 mole) of 6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine-5,5′-dicarboxylic acid (IVe) in 70 ml. of quinoline was heated under nitrogen in the presence of 2.7 g. of a copper powder in an oil bath maintained at 220-230° for 4 hours and at 235° for 2 hours. Quinoline was distilled in vacuum, the residue extracted several times with hot benzene and the combined benzene extracts filtered. The filtrate was concentrated and to the concentrate was added hot cyclohexane. The product was allowed to crystallize at 5°. The precipitate was filtered, washed with a mixture of benzene and cyclohexane and slurried in a boiling solution of 2 g. of sodium hydroxide in 50 ml. of water. The slurry was filtered hot and the cake washed first with a dilute aqueous sodium hydroxide solution and then with water. The ir spectrum of the dried material (2.27 g.) showed neither N-H nor C=O stretching bands. The product, however, still appeared to be impure. It was sublimed at 225° (0.03 mm Hg) to give 1.76 g. of a green-yellow sublimate, m.p. 153-157°. The sublimed material was chromatographed on a neutral-alumina column using a 1:1 mixture of benzene and acetone as eluent. Crystallization from a mixture of benzene and cyclohexane provided a colorless sample of the title compound, m.p. 163-164°. The uv spectrum (in ethanol); λ max 316 nm, ε max 33,500; the nmr spectrum (at 60 Mc. in deuterochloroform with TMS as internal standard) supported the structure. Signals due to 6 protons of the methoxy groups were observed at 3.90 ppm. Aromatic protons gave rise to signals falling in 3 groups at 6.9-7.5 ppm (6 protons), 7.8-8.0 ppm (6 protons) and 8.67 ppm (2 protons), the latter being assigned to α-protons of the pyridine rings.

Anal. Calcd. for $C_{24}H_{20}N_2O_2$: C, 78.24; H, 5.47; N, 7.60. Found: C, 78.62; H, 5.48; N, 7.82.

6,6′-Bis(*o*-hydroxyphenyl)-3,3′-bipyridine (IV).

A solution of 1.56 g. (0.00423 mole) of 6,6′-bis(*o*-methoxyphenyl)-3,3′-bipyridine (IVf) in 35 ml. of 48% aqueous hydrobromic acid was heated under reflux for 4 hours. The reaction mixture was cooled to room temperature, the precipitate filtered

and washed with a cold 48% hydrobromic acid. The cake was slurried in water, the slurry stirred for 15 minutes and filtered. The cake was washed with water, dried and crystallized from dimethylformamide to give 0.98 g. (68% of theory) of the title compound, m.p. 311-313°. The uv spectrum (in acetic acid): λ max 350 and 302 nm; ε max 36,000 and 26,000, respectively.

Anal. Calcd. for $C_{22}H_{16}N_2O_2$: C, 77.63; H, 4.73; N, 8.23; O, 9.40. Found: C, 77.72; H, 4.72; N, 8.28; O, 9.45.

3,8-Diphenyl-4,7-phenanthroline-1-carboxylic Acid (Va).

To a solution of 5.02 g. (0.023 mole) of 6-amino-2-phenylquinoline (17) and 2.42 g. (0.023 mole) of benzaldehyde in 75 ml. of ethanol was added dropwise 2.00 g. (0.023 mole) of pyruvic acid dissolved in 10 ml. of ethanol. The mixture was heated under reflux for 3-½ hours, cooled and filtered. The cake was washed with ethanol and dried to give 3.51 g. (41% of theory) of a crude product. The material was added to 100 ml. of a 15% aqueous sodium carbonate solution and the mixture heated under reflux for 30 minutes. It was cooled to room temperature, an insoluble yellow sodium salt filtered and washed with a 15% aqueous sodium carbonate solution. The cake was dissolved in 125 ml. of boiling water, the hot solution filtered through a fine sintered-glass funnel and the filtrate treated with an excess of acetic acid. The precipitate was filtered, washed thoroughly with water and dried *in vacuo* to give 3.42 g. of the title compound, m.p. 276-278° gas evolution.

Anal. Calcd. for $C_{25}H_{16}N_2O_2$: C, 79.77; H, 4.28; N, 7.44. Found: C, 79.39; H, 4.21; N, 7.36.

3,8-Diphenyl-4,7-phenanthroline (Vb).

An intimate mixture of 2.09 g. (0.00555 mole) of 3,8-diphenyl-4,7-phenanthroline-1-carboxylic acid (Va) and 2.1 g. of a copper powder was placed in the well of a sublimation apparatus and heated at 285° under nitrogen until the evolution of carbon dioxide was complete. The decarboxylated material was sublimed *in vacuo* (280°/0.05 mm Hg) to give 1.52 g. (83% of theory) of a pale yellow sublimate, m.p. 272-273°. The crude product was crystallized first from acetic acid and then from toluene to give a colorless sample of the title compound, m.p. 274°, lit. (18), m.p. 278°. The uv spectrum (in dimethylformamide): λ max 324 and 304 nm; ε max 46,000 and 41,900, respectively.

Anal. Calcd. for $C_{24}H_{16}N_2$: C, 86.72; H, 4.85; N, 8.42. Found: C, 86.46; H, 4.96; N, 8.55.

3,8-Bis(*o*-methoxyphenyl)-4,7-phenanthroline-1-carboxylic Acid (Vc).

A mixture of 18.5 g. of 6-amino-2-(*o*-methoxyphenyl)quinoline (17), 10.0 g. of *o*-methoxybenzaldehyde and 7.0 g. of pyruvic acid in 500 ml. of absolute ethanol was heated under reflux for 18 hours. The precipitate was filtered and washed with boiling ethanol. The product was dissolved in 100 ml. of a 5% aqueous sodium hydroxide solution, the solution filtered and the filtrate neutralized with dilute aqueous hydrochloric acid. The precipitate was filtered, washed thoroughly with water and dried *in vacuo* to give 4.51 g. of the title compound, m.p. 278° with gas evolution.

Anal. Calcd. for $C_{27}H_{20}N_2O_4$: C, 74.29; H, 4.62; N, 6.42; O, 14.66. Found: C, 73.95; H, 4.49; N, 6.57; O, 14.51.

3,8-Bis(*o*-methoxyphenyl)-4,7-phenanthroline (Vd).

A solution of 4.0 g. of 3,8-bis(*o*-methoxyphenyl)-4,7-phenanthroline-1-carboxylic acid (Vc) in 140 ml. of quinoline was heated under nitrogen in the presence of 6.0 g. of a copper powder at 230° for 3-½ hours. The hot reaction mixture was filtered. Quinoline was removed from the filtrate by vacuum distillation. The residue was extracted twice with boiling benzene, the combined hot benzene extracts filtered and the product allowed to crystallize from the filtrate. Recrystallization from benzene produced a colorless sample of the title compound, m.p. 239-241°.

Anal. Calcd. for $C_{26}H_{20}N_2O_2$: C, 79.57; H, 5.13; N, 7.14. Found: C, 79.45; H, 4.95; N, 7.30.

3,8-Bis(*o*-hydroxyphenyl)-4,7-phenanthroline (V).

A solution of 1.5 g. of 3,8-bis(*o*-methoxyphenyl)-4,7-phenanthroline (Vd) in 15 ml. of a 48% aqueous hydrobromic acid solution was heated in a sealed, heavy-walled Pyrex glass tube which was partially immersed in an oil bath maintained at 200° for 5-½ hours. The reaction mixture was removed from the tube at 0° and filtered. The cake was washed first with 48% aqueous hydrobromic acid and then with water. The product was slurried in a boiling, 5% aqueous sodium hydroxide solution, the slurry filtered and the cake washed in succession with hot, 5% aqueous sodium hydroxide solution, water and boiling acetic acid. The residue was dried and sublimed *in vacuo* (0.02 mm Hg) at 350° (sand bath) to give 0.75 g. of a sublimate which was crystallized from 500 ml. of dimethylformamide. The title compound (0.55 g.) was found to melt sharply at 383°. The uv spectra: λ max 363, 353, 306 nm (ε max 31,500, 31,300, 21,600) in acetic acid and λ max 367, 356, 304 nm (ε max 36,600, 36,600, 28,300) in dimethylformamide.

Anal. Calcd. for $C_{24}H_{16}N_2O_2$: C, 79.10; H, 4.42; N, 7.69; O, 8.78. Found: C, 78.90; H, 4.59; N, 8.05; O, 8.61.

REFERENCES

(1) Present address Tumatorpsvägen I. D., S-27200 Simrishamn, Sweden.

(2) R. Pater, *J. Heterocyclic Chem.*, 7, 1113 (1970).

(3) J. R. Merrill and R. G. Bennett, *J. Chem. Phys.*, 43, 1410 (1965).

(4) A. Beckett and G. Porter, *Trans. Faraday Soc.*, 59, 2051 (1963).

(5) J.-E. A. Otterstedt, submitted to *J. Chem. Phys.*

(6) Z. Arnold, *Collect. Czech. Chem. Commun.*, 27, 2993 (1962); see S. Trofimenko, *J. Org. Chem.*, 29, 3046 (1964), for an alternative synthesis of 1,1,2,2-ethanetetracarboxaldehyde.

(7) M. P. L. Caton, D. T. Hurst, J. F. W. McOmie and R. R. Hunt, *J. Chem. Soc.* (C), 1204 (1967).

(8) R. Pater, *J. Heterocyclic Chem.*, 8, 743 (1971).

(9) C. Graebe and P. Schestakov, *Ann. Chem.*, 284, 319 (1895).

(10) E. H. Woodruff and R. Adams, *J. Am. Chem. Soc.*, 54, 1977 (1932).

(11) S. Bodforss, *Ann. Chem.*, 455, 41 (1927).

(12) A. Skita and C. Wulff, *ibid.*, 455, 17 (1927).

(13) R. H. F. Manske and M. Kulka, "Organic Reactions", Vol. VII, John Wiley and Sons, Inc., New York, 1953, p. 59.

(14) C. Willgerodt and S. Jablonski, *Ber.*, 33, 2918 (1900).

(15) W. Borsche and M. Wagner-Roemmick, *Ann. Chem.*, 544, 280 (1940).

(16) Friedlaender, "Fortschritte der Tierfarbenfabrikation," J. Springer, *Berlin*, 13, 824; *Chem. Zentralbl.*, 1916, II, 707.

(17) *Ibid.*, 13, 832; *Ibid.*, 1919, II, 852.

(18) R. H. Wiley, C. H. Jarboe, Jr., and F. N. Hayes, *J. Org. Chem.*, 23, 268 (1958).

(19) A. P. T. Easson and F. U. Pyman, *J. Chem. Soc.*, 2999 (1931).

(20) E. v. Meyer, *J. Prakt. Chem.*, [2], 52, 110 (1895).