Tautomeric Pyridines. Part 22.[1] The Effect of Intramolecular Hydrogen Bonding on the Tautomeric Structure of 4-Amino-1,10-phenanthrolines

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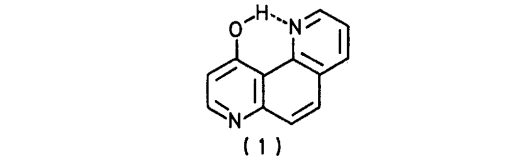
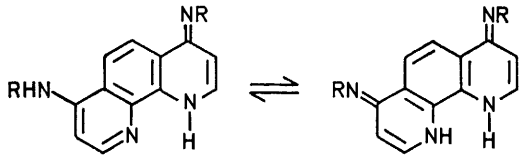
The tautomeric equilibria of 4-amino-1,10-phenanthroline, 4-amino-2,2'-bipyridyl, and certain of their *N*-substituted derivatives are assessed from pK_a and u.v. spectral data. Comparison of pK_T values for 4-amino-, and 4-anilino-1,10-phenanthroline with those for the corresponding pyridine derivatives indicates that in the former series a combination of intramolecular hydrogen bonding and destabilisation by lone pairs in close proximity reduces the predominance of the ' amino ' tautomer by a factor of *ca.* 100.

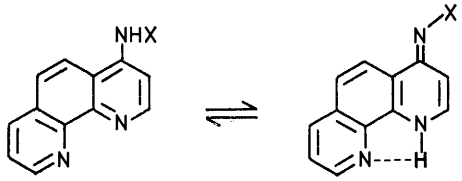
INTRAMOLECULAR hydrogen bonding can significantly influence tautomeric structure [2] and results reported in



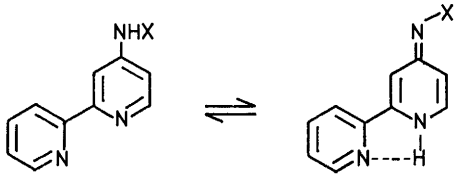
(1)



(2a) (2b)



(3a)	(3b)
(4a) X = Ph	(4b)
(5a) X = C_6H_{11}	(5b)
(6a) X = H	(6b)
(7a) X = COMe	(7b)
(8a) X = $SO_2C_6H_4Me$-*p*	(8b)

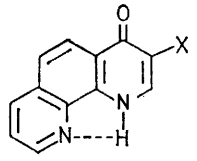


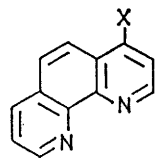
(9a)	(9b)
(10a) X = H	(10b)
(11a) X = COMe	(11b)
(12a) X = $SO_2C_6H_4Me$-*p*	(12b)
(13a) X = Ph	(13b)
(14a) X = Me	(14b)

Part 12 [3] concerned the quantitative effect of such bonding in 10-hydroxy-1,7-phenanthrolines [*cf.* (1)].

Most potential α- and γ-hydroxy-compounds exist in polar solvents predominantly in the oxo-form,[2] and the effect of hydrogen bonding is most marked if it stabilizes the hydroxy-form. For amino-compounds the situation is reversed: they usually exist (in all media) predominantly in the amino-form.[2] Intramolecular hydrogen bond stabilisation of the imino-group has received little attention. U.v. and i.r. data indicate the amino-form for 2-heteroarylaminothiazoles,[4] but the mono- (2a) or bis-imino-structure (2b) has been postulated for 4,7-diamino- and 4,7-bismethylamino-1,10-phenanthrolines on the basis of a negative ferroin test.[5] We now report a study of equilibria of type (3a) ⇌ (3b) within the 1,10-phenanthroline series (4)—(8), as well as an examination of the analogous equilibrium (9a) ⇌ (9b) for the 2,2'-bipyridyls (10)—(14) in which hydrogen bonding is expected to be less effective.

Preparation of Compounds.—8-Aminoquinoline and ethyl ethoxymethylenemalonate gave 8-(β-bisethoxycarbonylvinylamino)quinoline which on refluxing with diphenyl ether gave 3-ethoxycarbonyl-4-hydroxy-1,10-phenanthroline (15), converted by successive treatment with potassium hydroxide and hydrochloric acid into 3-carboxy-4-hydroxy-1,10-phenanthroline (16). At 320 °C, this decarboxylated to give (17) which was chlorinated to 4-chloro-1,10-phenanthroline (18).[6,7]





(15) X = CO_2Et	(18) X = Cl	(22) X = NEt_2
(16) X = CO_2H	(19) X = SPh	(23) X = NMePh
(17) X = H	(20) X = SO_2Ph	(24) X = OPh
	(21) X = piperidino	(25) X = N_3

4,7-Diamino- and 4,7-bismethylamino-1,10-phenanthroline have been prepared from the 4,7-dichloro-compound with ammonia and methylamine [5] and 4-(3-di-

[1] Part 21, C. B. Theissling, N. M. M. Nibbering, M. J. Cook, S. El-Abbady, and A. R. Katritzky, *Tetrahedron Letters*, 1977, 1777.

[2] For a full discussion see J. Elguero, C. Marzin, A. R. Katritzky, and P. Linda, ' The Tautomerism of Heterocycles,' Academic Press, New York, 1976.

[3] G. P. Bean, M. J. Cook, T. M. Dand, A. R. Katritzky, and J. R. Lea, *J. Chem. Soc.* (*B*), 1971, 2339.

[4] Von J. Bödeker, H. Pries, D. Rösch, and G. Malewski, *J. prakt. Chem.*, 1974, **317**, 953.

[5] G. E. Calf and E. L. Samuel, *Austral. J. Chem.*, 1963, **16**, 833.

[6] H. R. Snyder and H. F. Freier, *J. Amer. Chem. Soc.*, 1946, **68**, 1320.

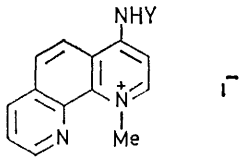
[7] C. J. Hawkins, H. Duewell, and W. F. Pickering, *Analyt. Chim. Acta*, 1961, **25**, 257.

ethylaminopropylamino)-1,10-phenanthroline similarly from (18).[6] However, attempted displacement of the chlorine in (18) by a variety of aliphatic and aromatic amines failed: mild conditions gave back starting material and severe conditions caused extensive decomposition.[8]

The desired compounds were successfully prepared using sequence (18) ⟶ (19) ⟶ (20) in which the potent nucleophile benzenethiolate displaces the halogen atom of (18) and (19) is then oxidised to 4-phenylsulphonyl-1,10-phenanthroline (20). Similar sequences have recently been used in the 3-substituted 2-nitrothiophen [9,10] series. Nucleophilic displacement of the phenylsulphinate anion from 4-phenylsulphonyl-1,10-phenanthroline with amines gave excellent yields of the desired products (4), (5), and (21)—(23).

However, direct preparation of 4-amino-1,10-phenanthroline from sulphone (20) and ammonia was not achieved under available conditions. Following Corey,[11] 1,10-phenanthroline 1-oxide was prepared in 65% yield, but the reported [11] nitration in 10% yield to 4-nitro-1,10-phenanthroline 1-oxide could not be repeated: [8] others have failed in this nitration.[12] 4-Phenoxy-1,10-phenanthroline (24) was prepared from (18) and potassium phenate in 68% yield, but fusion of (24) with ammonium acetate failed to produce the amine (6). 4-Phenylsulphonyl-1,10-phenanthroline (20) and sodium azide gave 4-azido-1,10-phenanthroline (25); sodium borohydride reduction then afforded 4-amino-1,10-phenanthroline (6).

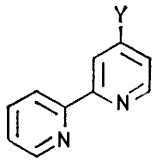
The amine (6) was smoothly acylated by acetic anhydride, and converted by toluene-*p*-sulphonyl chloride into the tosylamide (8). Alkylation of (5) and (4) with methyl iodide yielded the corresponding methiodides (26) and (27).



(26) Y = C_6H_{11}
(27) Y = Ph

4-Nitro-2,2′-bipyridyl 1-oxide was prepared from 2,2′-bipyridyl by peracetic acid oxidation and subsequent nitration.[13] Reduction of the nitro *N*-oxide with sodium borohydride gave 4-amino-2,2′-bipyridyl (10), which reacted with acetic anhydride and tosyl chloride to give (11) and (12), respectively.[13] 4-Nitro-2,2′-bipyridyl with PCl_3–CH_3COCl gave 4-chloro-2,2′-bipyridyl (28).[14] The chloro-compound (28) on heating with dimethylamine and aniline gave 4-dimethylamino- and 4-anilino-2,2′-bipyridyl, respectively. Attempts to prepare 4-*N*-methylanilino-2,2′-bipyridyl either from (31) by refluxing in *N*-methylaniline, or by displacement with benzenethiolate to (30) followed by oxidation to (31) and attempted further displacement, all failed.[8]

Basicity Measurements (*Table* 1).—1,10-Phenanthroline has pK_a 4.90 somewhat lower than pyridine (5.2).[15] The close proximity (*ca.* 2.5 Å) of the two nitrogen atoms in the inflexible fused ring allows the addition of only one proton in moderately weak acidic media; steric and electrostatic factors lead to a much reduced basicity for the addition of the second proton at −1.8.[16] Most substituents affect the basic strengths of phenanthroline and 2,2′-bipyridyl similarly to that of pyridine (this relation has previously been pointed out for 2,2′-bipyridyls [13]). An alkyl group is slightly base strengthening, while chloro-, nitro-, and bromo-substituents are base weakening (Table 1).



(28) Y = Cl
(29) Y = NMe_2
(30) Y = SPh
(31) Y = SO_2Ph

TABLE 1

Comparison of the ionization constants of 4-substituted-1,10-phenanthrolines and corresponding pyridines and 4-substituted-2,2′-bipyridyls

4-Substituent	1,10-Phenanthrolines	Pyridines	2,2′-Bipyridyls
NEt_2	9.10 [a]		
NMe_2			8.30 [a]
NH_2	8.89 [a]	9.2 [c]	8.06 [a,e]
Et	5.44 [b]	6.0 [c]	
Cl	4.29 [a]	3.84 [d]	3.83 [e]
Br	4.30 [b]	3.78 [d]	3.80 [e]
H	4.90 [a,b]	5.2 [c]	4.27 [e]
3-Substituent			
Et	4.98 [b]	5.7 [c]	
Me	5.00 [b]	5.7 [c]	
Cl	3.99 [b]	2.84 [d]	

[a] Present work. [b] See ref. 17. [c] Mean value taken from values given in ref. 15. [d] See ref. 15. [e] See ref. 13.

Depending on the substituents, protonation can occur either at N-1 or -10 in 1,10-phenanthrolines. Ionization constants for the monosubstituted 1,10-phenanthrolines are compared with those of the corresponding pyridines in Table 1. For electron-donating substituents proton-

[8] For full details see S. Nadji, Ph.D. Thesis, University of East Anglia, 1977.
[9] G. Guanti, C. Dell'Erba, and P. Macera, *J. Heterocyclic Chem.*, 1971, **8**, 537.
[10] A. J. Boulton and D. Middleton, *J. Org. Chem.*, 1974, **39**, 2956.
[11] E. J. Corey, A. L. Borror, and T. Foglia, *J. Org. Chem.*, 1965, **30**, 288.
[12] G. Maerker and F. H. Case, *J. Amer. Chem. Soc.*, 1958, **80**, 2745.
[13] R. A. Jones, B. D. Roney, W. H. F. Sasse, and K. O. Wade, *J. Chem. Soc.* (*B*), 1967, 106.
[14] E. Ochiai, *J. Org. Chem.*, 1953, **18**, 534.
[15] D. D. Perrin, 'Dissociation Constants of Organic Bases in Aqueous Solution,' I.U.P.A.C., Butterworths, London, 1965.
[16] A. A. Schilt and W. E. Dunbar, *Tetrahedron*, 1974, **30**, 401.
[17] A. A. Schilt and G. F. Smith, *J. Phys. Chem.*, 1956, **60**, 1546.

ation occurs at the 'substituted' ring but the phenanthrolines are still weaker bases than the corresponding pyridines, a result of the electron-withdrawing effect of the second fused-pyridine ring. However, with electron-withdrawing substituents the phenanthrolines are stronger bases than the corresponding pyridines. For these phenanthrolines protonation occurs on the unsubstituted pyridinoid ring.

The Hammett plot for the pK_a values of 4- and 3-monosubstituted 1,10-phenanthrolines previously measured [17] together with the present additional results shows two separate straight lines (Figure 1). For

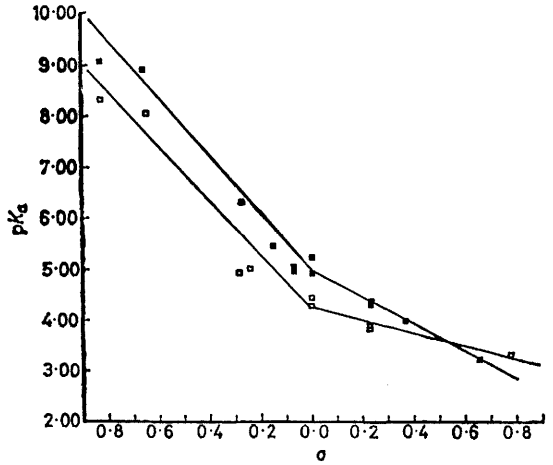


FIGURE 1 ■, pK_a Values of some 4- and 3-monosubstituted 1,10-phenanthrolines *versus* σ and □, pK_a values of some 4-substituted-2,2′-bipyridyls *versus* σ

electron-releasing substituents $\rho = 5.75$; for electron-withdrawing substituents $\rho = 2.40$ illustrating the change of protonation site.

The foregoing basicity data already provide considerable evidence for the existence of 4-amino-1,10-phenanthroline predominantly in the amino-form (6a), *viz.* (a) the close correspondence of its pK_a with that of 4-aminopyridine (Table 1) and (b) the fact that the pK_a of (6) lies on the Hammett line (Figure 1). Further evidence is provided by a consideration of the effect of *N*-alkylation (Table 2). In 4-aminopyridine, alkylation at the amino-group increases the pK_a by *ca.* 0.6 units.[15] In the 4-amino-1,10-phenanthroline series substitution of a cyclohexyl at the amino-group, *i.e.* (5), increases the pK_a value by *ca.* 0.17 units and substitution by two ethyl groups (22), raises the pK_a by 0.21 units. Both the tautomerically mobile compounds (5) and (6) are considerably less basic than the conjugate base of (26), the model for the imino-tautomer, and the full significance of this is discussed below. Relative to (5), (6), and (22), the 4-piperidino-derivative (21) shows a large depression of basic strength (>1.2 units); that this is a steric effect twisting the piperidino-group out of the molecular plane is supported by the u.v. spectra (*vide infra*). A similar, though smaller effect is apparent from the pK_a value of 4-*N*-methylanilino-1,10-phenanthroline (23), 0.59 units lower than that of the 4-anilino-derivative (4) (Table 2). As for (5), (6), and (22) the compounds are significantly less basic than the model for the corresponding imino-tautomer, *viz.* the conjugate base of (27). 4-Acetamido-1,10-phenanthroline (pK_a 5.20) gives a slightly higher pK_a value (0.2 units) than that which can be predicted from the Hammett substituent constant (σ_{NHCOCH_3} *ca.* 0), but nevertheless falls within experimental error. The low pK_a for the *N*-tosylamido-derivative is indicative that the compound exists to a large extent as the imino-tautomer (see below).

TABLE 2

pK_a Values of some 4-substituted-1,10-phenanthrolines

1,10-Phenanthroline derivative	pK_a	Standard deviation	10^5 Concentration (M)	λ/nm
1,10-Phenanthroline	4.90	0.13	6.2	310
4-Chloro	4.29	0.08	9.3	305
4-Amino	8.89	0.11	6.7	285
4-Diethylamino	9.10	0.07	4.1	320
4-Cyclohexylamino	9.06	0.05	3.6	335
4-Piperidino	7.65	0.07	3.8	350
4-Acetamido	5.20	0.08	8.1	325
4-Tosylamido	4.70	0.11	6.0	350
4-Anilino	8.10	0.07	6.2	246
4-*N*-Methylanilino	7.51	0.11	8.1	300
4-Cyclohexylamino-1-methyl-1,10-phenanthrolinium iodide	13.82	0.10	4.2	340
4-Anilino-1-methyl-1,10-phenanthrolinium iodide	10.49	0.12	2.49	305

TABLE 3

pK_a Values of some 4-substituted-2,2′-bipyridyls

2,2′-Bipyridyl derivative	pK_a	Standard deviation	10^5 Concentration (M)	λ/nm
4-Amino	8.06	0.05	0.02	270
4-Methylamino	8.14	0.07	8.5	265
4-Dimethylamino	8.30	0.06	9.1	280
4-Anilino	7.20	0.09	4·02	330
4-Acetamido	4.41	0.11	7.50	310
4-Tosylamido	3.85	0.09	6.90	320

Basicity of 2,2′-Bipyridyls (*Tables* 1 *and* 3).—Bipyridyl is a weaker base, pK_a 4.27, than 1,10-phenanthroline. The intrinsic base-weakening effect of the second nitrogen atom is offset in 1,10-phenanthroline because planarity causes lone pair–lone pair repulsions in the free base, which cannot be relieved by twisting to the *trans*-form. Just as for the 1,10-phenanthrolines, bipyridyls with electron-donor substituents are weaker bases than the corresponding pyridines, while those with electron-withdrawing substituents are stronger. The site of protonation of bipyridyls also depends upon the electronic effect of the substituent and the Hammett plot (Figure 1) clearly shows the change in this site. For the 2,2′-bipyridyls with an electron-withdrawing substituent at the 4-position $\rho = 1.25$; for those with an electron-donating group $\rho = 5.59$. The latter value is close to that for pyridines, 6.01,[18] indicating (a) protonation occurs at N-1 and (b) strong interaction between the substituents and the positive nitrogen atom within

[18] C. D. Johnson, 'The Hammett Equation,' Cambridge University Press, Cambridge, 1973, p. 45.

the ring itself. The low ρ of 1.25 reflects the small effect of electron-withdrawing substituents on the reaction site in the far ring.

Tautomerism of 4-Amino- and 4-Cyclohexylamino-1,10-phenanthroline and 4-Amino-2,2′-bipyridyl.—The u.v. spectra (aqueous media) of the neutral forms of 4-amino-1,10-phenanthroline (6), 4-cyclohexylamino-1,10-phenanthroline (5), and the dialkylated derivative 4-diethylamino-1,10-phenanthroline (22) are similar to one another but dissimilar from that of 4-*N*-cyclohexylimino-1-methyl-1,10-phenanthroline (32) (Table 4 and Figure 2). This confirms that the two tautomeric compounds exist predominantly in the ' amino '-form (3a) in the aqueous phase. The spectrum of 4-piperidino-1,10-phenanthroline (21) differs somewhat from those of (5), (6), and (22) in that there are no major bands at wavelengths longer than *ca.* 295 nm (Table 4, Figure 2).

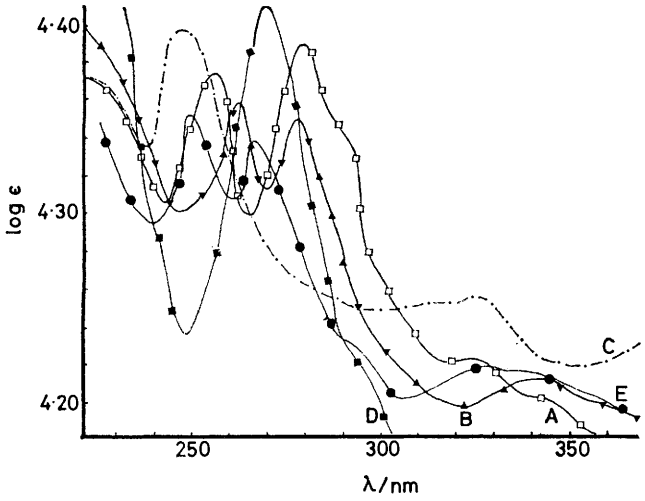


FIGURE 2 A, 4-Diethylamino-1,10-phenanthroline (neutral); B, 4-amino-1,10-phenanthroline (neutral); C, 4-cyclohexylimino-1-methyl-1,10-phenanthroline; D, 4-piperidino-1,10-phenanthroline; E, 4-cyclohexylamino-1,10-phenanthroline. Data refer to aqueous solution

This difference coupled with the low pK_a value supports the view that the piperidino-group is twisted out of plane by steric interaction between the α-equatorial proton and 5-H. The spectrum of the cation of (21) resembles closely that of 1,10-phenanthroline itself [8] which is also consistent with this conclusion.

The spectra of the cations of the mobile compounds (5) and (6) and of the two fixed models (22) and (32) are similar (Table 4, Figure 3), indicating that cations of similar structure are produced. Accordingly the equation $pK_T = pK_{a_1} - pK_{a_2}$ [19] can be applied. The pK_a of the imino-compound (32) is far higher (13.82) than those for 4-amino-1,10-phenanthroline (8.89), 4-cyclohexylamino-1,10-phenanthroline (9.06), and the 4-diethylamino-derivative (9.10) indicating pK_T *ca.* 4.7 for the mobile compounds. The preference for the amino-form is significantly smaller than that for 4-aminopyridine, pK_T 8.7.[20]

[19] A. R. Katritzky and J. M. Lagowski, *Adv. Heterocyclic Chem.*, 1963, **1**, 311.

The u.v. absorptions of the neutral forms of the 4-amino- (10), 4-methylamino- (14), and 4-dimethylamino-2,2′-bipyridyl (29) are similar, demonstrating that the

TABLE 4

U.v. spectral data for 4-substituted 1,10-phenanthrolines in aqueous solution

4-Substituted-1,10-phenanthroline	Neutral species λ/nm (log ε)	Monocation λ/nm (log ε)
4-Amino-1,10-phenanthroline	210 (4.01)	212 (3.80)
	242 (4.30)	240 (4.00)
	265 (4.35)	268 (4.42)
	318 (4.13)	284s (4.24)
	357s (4.06)	320 (4.16)
		347s (4.09)
4-Diethylamino-1,10-phenanthroline	213 (4.38)	208 (4.36)
	240 (4.00)	225 (4.34)
	263 (4.42)	256 (4.37)
	284s (4.35)	278 (4.41)
	320 (4.10)	291 (4.24)
	340s (4.14)	320 (4.14)
	352 (4.16)	355 (4.11)
4-Cyclohexylamino-1-methyl-1,10-phenanthrolinium iodide	232 (4.37)	218 (4.3)
	248 (4.40)	251 (4.32)
	314s (4.26)	275 (4.31)
	370 (4.23)	300s (4.26)
	376 (4.26)	332 (4.24)
		350 (4.26)
4-Piperidino-1,10-phenanthroline	212 (4.41)	222 (4.38)
	230 (4.42)	268 (4.36)
	268 (4.41)	305s (4.17)
	315s (4.10)	352 (4.10)
4-Cyclohexylamino-1,10-phenanthroline		210 (4.42)
	225 (4.38)	250 (4.32)
	248 (4.35)	270 (4.33)
	271 (4.33)	290 (4.24)
	290s (4.23)	332 (4.17)
	329 (4.22)	
	348s (4.21)	
4-Anilino-1,10-phenanthroline	213 (4.38)	218 (4.33)
	295s (4.33)	241 (4.42)
	268 (4.60)	271 (4.02)
	290s (4.29)	337 (4.22)
	335 (4.28)	
4-*N*-Methylanilino-1,10-phenanthroline	220 (4.35)	246 (4.36)
	245 (4.41)	268 (4.40)
	277 (4.33)	285 (4.35)
	330 (4.25)	325 (4.30)
	347s (4.21)	
4-Anilino-1-methyl-1,10-phenanthroline	225 (4.36)	217 (4.40)
	305 (3.85)	247 (4.38)
	375 (3.98)	268 (4.40)
		283s (4.36)
		337 (4.28)
4-Tosylamido-1,10-phenanthroline	220 (4.40)	215 (4.41)
	238 (4.46)	240s (4.10)
	269 (4.37)	275 (4.31)
	305 (4.28)	302 (4.17
		327s (4.07)
		393s (4.00)
4-Acetamido-1,10-phenanthroline	212 (3.81)	218 (4.43)
	251 (4.20)	240 (4.38)
	291 (3.15)	265 (4.41)
	310s (3.10)	283 (4.20)
		317 (4.15)
		348 (4.07)

former two compounds exist predominantly in the amino-forms (10a) and (14a) in aqueous solution (Table 5). Since the absorptions of these compounds do not change significantly in ethanol and cyclohexane,[8] the amino-form is also preferred in non-polar media. As expected, cationic spectra for 4-amino-, 4-methylamino-, and 4-

[20] M. J. Cook, A. R. Katritzky, P. Linda, and R. D. Tack, *J.C.S. Perkin II*, 1973, 1080.

dimethylamino-2,2′-bipyridyl are also similar (Table 5). However the absence of basicity data for the other fixed model precludes a quantitative treatment.

TABLE 5

U.v. spectral data for 4-substituted-2,2′-bipyridyls in aqueous solution

	Neutral species λ/nm ($10^3 \times \varepsilon$)	Monocation λ/nm ($10^3 \times \varepsilon$)
4-Amino	232 (18.4)	240 (17.1)
	275 (9.6)	275 (12.2)
4-Methylamino	228 (22.1)	235 (21.1)
	272 (15.8)	263 (17.6)
4-Dimethylamino	239 (14.3)	242 (16.1)
	275 (15.5)	277 (11.0)
		315s (7.6)
4-Anilino	220 (8.3)	245 (8.2)
	282 (12.9)	283 (11.19)
4-Acetamido	230 (21.5)	230 (31.3)
	280 (18.5)	285 (14.0)
	304 (16.2)	327s (5.8)
		341s (5.06)
4-Tosylamido	229 (19.1)	229 (21.2)
	281 (15.1)	248 (16.8)
	308 (10.05)	280 (24.0)
		306 (11.20)

Tautomerism of 4-Anilino-1,10-phenanthroline and 4-Anilino-2,2′-bipyridyl.—The u.v. spectra of the cations

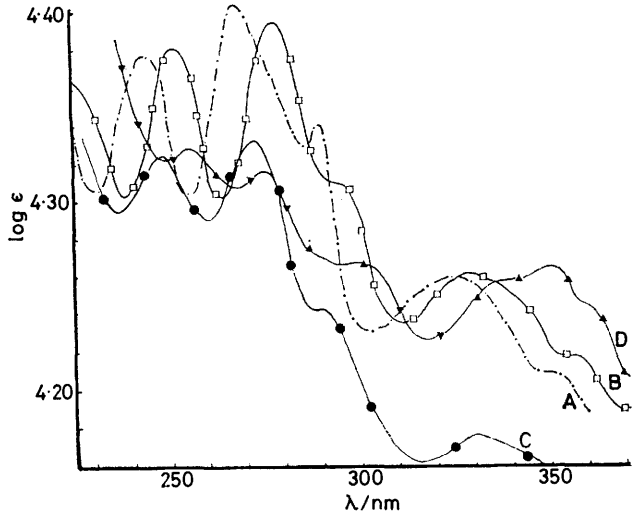
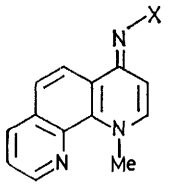
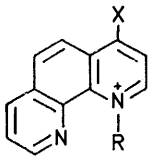


FIGURE 3 A, 4-Diethylamino-1,10-phenanthrolinium cation; B, 4-amino-1,10-phenanthrolinium cation; C, 4-cyclohexylamino-1,10-phenanthrolinium cation; D, 4-cyclohexylamino-1-methyl-1,10-phenanthrolinium cation. Data refer to aqueous solution

(37)—(39) derived respectively from 4-anilino- (4), 4-*N*-methylanilino-1,10-phenanthroline (23), and 1,4-dihydro-1-methyl-4-phenylimino-1,10-phenanthroline (33) validate their similar structures (Figure 4, Table 4). However, for the neutral species the tautomeric compound (4) shows a spectrum close to that for (23) but unlike that of (33) (Figure 5, Table 4): hence 4-anilino-1,10-phenanthroline (4) exists predominantly in the amino-form (4a). The pK_a measurements confirm and quantify this conclusion, indicating a pK_T of *ca.* 2—3. Since the absorption of the mobile compound (4) is the



(32) X = C_6H_{11}
(33) X = Ph



(34) R = H, X = NH_2
(35) R = H, X = NHC_6H_{11}
(36) R = H, X = NEt_2
(37) R = Me, X = NHC_6H_{11}
(38) R = H, X = NHPh
(39) R = H, X = NMePh
(40) R = Me, X = NHPh

same in both ethanol and cyclohexane, it exists predominantly in the amino-form (4a), also in non-polar media.

The u.v. spectrum of 4-anilino-2,2′-bipyridyl (13) is similar in water (Table 5), ethanol, and cyclohexane,[8] demonstrating that this compound exists predominantly as the same tautomer, presumably the amino-form (13a), in both polar and non-polar solvents. However, no quantitative estimate of the pK_T for this equilibrium is available.

Tautomerism of 4-Acetamido-1,10-phenanthroline and 4-Acetamido-2,2′-bipyridyl.—Results from previous

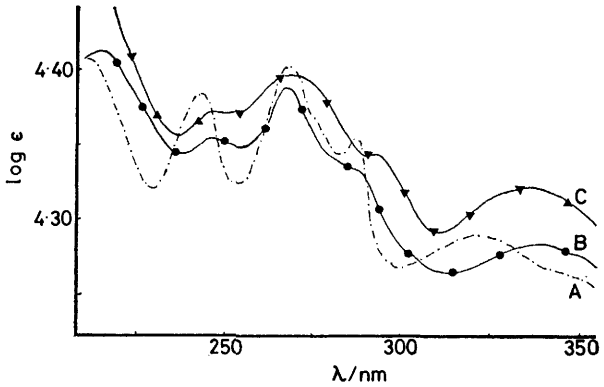


FIGURE 4 A, 4-*N*-Methylanilino-1,10-phenanthrolinium cation; B, 4-anilino-1-methyl-1,10-phenanthrolinium iodide; C, 4-anilino-1,10-phenanthrolinium cation. Data refer to aqueous solution

work * indicate that tautomeric equilibria of acetamido-compounds should resemble those of their amino-analogues. The basicity of the 4-acetamido-1,10-phenanthroline (7) (pK_a 5.20) lies on the Hammett plot

* For 4-aminopyridine see ref. 20; 4-anilinopyridine see extrapolation given below; 4-methylsulphonamidopyridine see ref. 21; for 4-acetamidopyridine see R. A. Jones and A. R. Katritzky, *J. Chem. Soc.*, 1959, 1317.

(Figure 1) indicating the predominance of the amino-form (7a). The spectrum of (7) does not vary with the solvent for water (Table 5), ethanol, cyclohexane, and dioxan,[8] indicating that the amino-form (7a) also dominates in these media.

4-Acetamido-2,2′-bipyridyl (11) also has a pK_a value (4.17) close to that which can be predicted from the Hammett equation, 4.37 (see Figure 1). The u.v. spectra of the material in water (Table 5), ethanol, cyclohexane, and dioxan [8] are similar indicating a predominance for (11a) in each solvent.

Tautomerism of 4-Tosylamido-1,10-phenanthroline and 4-Tosylamido-2,2′-bipyridyl.—For 4-methylsulphonamidopyridine in aqueous solution, K_{imino}/K_{amino} = *ca.* 30 [21] and the 4-phenylsulphonamido-derivative also exists predominantly as the imino-form in alcohol, but not in dioxan.[22] Thus, 4-tosylamido-1,10-phenanthroline may exist in the ' imino '-form. The spectra in 95% ethanol dioxan, and cyclohexane (Figure 6) unfortunately give little further information as the influence of

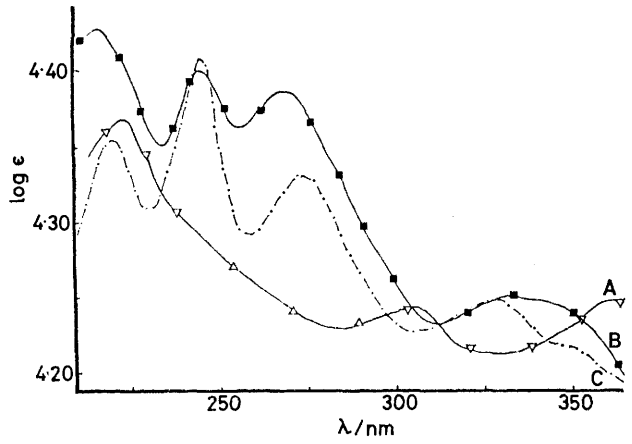


FIGURE 5 A, 1-Methyl-4-phenylimino-1,10-phenanthroline; B, 4-anilino-1,10-phenanthroline; C, 4-*N*-methylanilino-1,10-phenanthroline. Data refer to aqueous solution

solvent on the equilibrium appears to be slight, although in dioxan and cyclohexane, new peaks at 302 and 249 nm were observed, which may be due to the amino-tautomer. It is probable that 4-tosylamido-1,10-phenanthroline exists predominantly as the imino-tautomer in all solvents studied, but small amounts of the amino-tautomer may be present in cyclohexane and dioxan.

Solvent polarity has profound influence on the spectrum of 4-tosylamido-2,2′-bipyridyl: the spectra in water (Table 5) and ethanol are similar, but dramatically different spectra were observed in dioxan and cyclohexane (Figure 7) indicating considerable amounts of the amino-tautomer.

General Conclusions.—Qualitative comparison of the tautomeric equilibria of the parent compounds and acylated derivatives of the aminophenanthrolines anp aminobipyridyls with the corresponding 4-aminopyridine derivatives,* shows that in aqueous media the predominant tautomer of each derivative does not vary from one series to another. However, in dioxan and

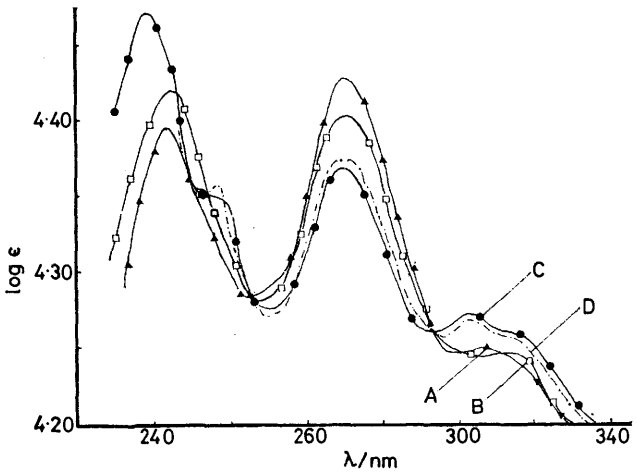


FIGURE 6 4-Tosylamido-1,10-phenanthroline in A, H_2O; B, EtOH; C, dioxan; D, cyclohexane

cyclohexane the *p*-tolylsulphonyl derivative of aminophenanthroline probably exists predominantly as the imino-tautomer whereas 4-phenylsulphonamidopyridine in dioxan exists predominantly as the amino-form.[22]

Quantitative comparison is limited to the 4-amino- and 4-anilino-phenanthrolines and -pyridines. 4-Amino-1,10-phenanthroline, pK_T 4.7, compares with 4-aminopyridine, pK_T 8.7.[20] 4-Anilinophenanthroline pK_T *ca.* 2—3 compares with an estimated value of 6—7 for 4-anilinopyridine (from data for the 2-derivative, pK_T 4.3,[23] and the difference in pK_T for 2-amino- and 4-amino-pyridine, 6.2 [24] and 8.7 [20] respectively). Thus the value for ΔpK_T between the pyridine and phenanthroline series is *ca.* 4 units. This difference presumably reflects the summation of a number of factors of which the following would seem to be the most important: (i)

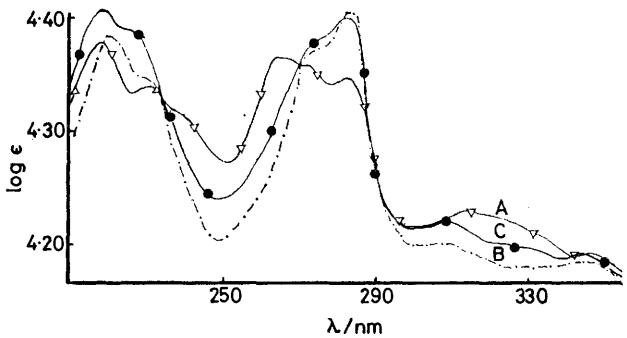


FIGURE 7 4-Tosylamido-2,2′-bipyridyl in A, EtOH; B, dioxan; C, cyclohexane

benzoannelation, (ii) 1,10-lone pair–lone pair interactions in the amino-form, (iii) intramolecular hydrogen bond stabilisation of the imino-form.

* See footnote on p. 1219.

[21] R. A. Jones and A. R. Katritzky, *J. Chem. Soc.*, 1961, 378.

[22] Yu. N. Sheinker, E. M. Peresleni, N. P. Zosimova, and Yu. I. Pomerantsev, *Russ. J. Phys. Chem.*, 1959, **33**, 303.

[23] S.-O. Chua, M. J. Cook, and A. R. Katritzky, *J.C.S. Perkin II*, 1973, 2111; *cf.* also Y. Takahashi, S. Otsuka, H. Masuda, M. Hirota, Y. Ito, and Y. Hamada, *Bull. Chem. Soc. Japan*, 1976, **49**, 2770.

Benzoannelation is known to increase the proportion of the NH · · · C=X tautomer at the expense of the N · · · C–XH tautomer in hydroxy ⇌ keto, mercapto ⇌ thione, methyl ⇌ methide equilibria * as well as in amino ⇌ imino equilibria. The reduction in the preference of the amino-tautomer is illustrated by data for 2-aminoquinoline, pK_T 4.3,[20] and 2-aminopyridine, pK_T 6.2.[24] It can be assumed that this factor may similarly contribute *ca.* 2 units to the 4 units difference in pK_T between the pyridine and phenanthroline series.

The remaining 2 units of ΔpK_T arise from a combination of the other two effects. It is not easy to estimate quantitatively the individual contributions of either, although qualitatively it is expected that they reinforce rather than oppose each other. Thus two nitrogen lone electron pairs in close proximity should serve to destabilise the amino-form and intramolecular hydrogen bonding should specifically stabilise the imino-form.

EXPERIMENTAL

M.p.s are uncorrected. The purity of the products was determined by t.l.c. on silica gel G (E. Merck, Darmstadt). Column chromatography was performed on silica gel, powder, 60—200 mesh (J. T. Baker Chemical Co.).

U.v. and Basicity Measurements.—U.v. spectra were recorded using a Unicam SP 800 spectrophotometer and pK_a values were calculated from spectrophotometric data obtained from a Unicam SP 500 series 2 spectrophotometer. For compounds insufficiently soluble in water, dissolution was achieved by addition of a little ethanol but in no instance did the ethanol concentration exceed 5% by volume. Solutions for various pH ranges were prepared using hydrochloric acid (0.6—3.3), acetic acid–sodium hydroxide (3.6—5.6), potassium dihydrogen phosphate–sodium hydroxide (5.2—7.8), boric acid–sodium hydroxide (8.0—10.3), and sodium hydroxide (11.0—12.6).

Materials.—All solvents were dried over molecular sieves. 2,2′-Bipyridyl was generously donated by I.C.I. Ltd. Reagents were obtained as commercial samples and were used without further purification unless otherwise stated. The following materials were prepared following literature routes: 4-chloro-1,10-phenanthroline,[6] m.p. 163—165 °C, picrate, m.p. 204—207 °C (lit.,[6] 203—206 °C); 4-amino-2,2′-bipyridyl,[13] m.p. 124—125 °C (lit.,[13] 128—129 °C); 4-acetamido-2,2′-bipyridyl,[13] m.p. 186—187 °C (lit.,[13] 187 °C); 4-chloro-2,2′-bipyridyl,[13] m.p. 84 °C (lit.,[13] 84—85 °C); 4-dimethylamino-2,2′-bipyridyl,[13] m.p. 102 °C (lit.,[13] 100 °C).

4-*Thiophenoxy*-1,10-*phenanthroline* (19).—A mixture of 4-chloro-1,10-phenanthroline (2.15 g), thiophenol (1.1 g), and KOH (2.0 g) was heated on a steam-bath for 10 h. The mixture was digested with 30% aqueous KOH solution (35 ml) and the solution was decanted. The residue was washed with water and crystallised from aqueous MeOH (1 : 3) to afford the *thiophenoxy-derivative* as plates (1.6 g, 55%), m.p. 180—182 °C (Found: C, 74.6; H, 4.0; N, 9.5. $C_{18}H_{12}N_2S$ requires C, 75.0; H, 4.2; N, 9.7%).

4-*Phenylsulphonyl*-1,10-*phenanthroline* (20).—The thiophenoxy-compound (0.5 g) in MeOH (10 ml) was treated with an aqueous solution of sodium periodate (0.65 g in 5 ml) and the mixture refluxed for 2 h. The solvent was removed under reduced pressure and the residue extracted with $CHCl_3$. $CHCl_3$ was removed and the solid crystallised from MeOH to afford the *sulphone* (0.32 g, 57%) as pale yellow needles, m.p. 96—100 °C (Found: C, 66.9; H, 3.6; N, 8.5. $C_{18}H_{12}N_2O_2S$ requires C, 67.5; H, 3.75; N, 8.7%).

4-*Anilino*-1,10-*phenanthroline* (4).—A mixture of 4-phenylsulphonyl-1,10-phenanthroline (1.0 g) and freshly distilled aniline (10 ml) was refluxed for 3 h and cooled. AnalaR grade Me_2CO (30 ml) was added, and the solid collected by filtration and recrystallised from aqueous MeOH (1 : 5) to afford 4-*anilino*-1,10-*phenanthroline* as yellow needles (0.26 g, 31%), m.p. 295—300 °C (Found: C, 79.5; H, 4.9; N, 15.2. $C_{18}H_{13}N_3$ requires C, 79.7; H, 4.8; N, 15.5%).

4-(N-*Methylanilino*)-1,10-*phenanthroline* (23).—The sulphone (1.0 g) was treated with freshly distilled *N*-methylaniline (10 ml), and the mixture was refluxed for 3 h. The mixture was cooled to room temperature and light petroleum (b.p. 80—100 °C) (30 ml) added. The solid was separated and recrystallised from aqueous MeOH (1 : 6) to afford the 4-(N-*methyl*-N-*phenylamino*)-*derivative* (0.37 g, 42%) as yellow plates, m.p. 310—313 °C (Found: C, 80.4; H, 5.3; N, 14.4. $C_{19}H_{15}N_3$ requires C, 80.4; H, 5.3; N, 14.7%).

4-*Cyclohexylamino*-1,10-*phenanthroline* (5).—A mixture of sulphone (1.0 g) and cyclohexylamine (15 ml) was refluxed for 5 h. The mixture was cooled to room temperature, and unchanged cyclohexylamine was removed under reduced pressure. The residue, 4-*cyclohexylamino*-1,10-*phenanthroline* (0.54 g, 63%), was collected as needles, m.p. 260—263 °C (from benzene) (Found: C, 77.9; H, 7.2; N, 14.6. $C_{18}H_{19}N_3$ requires C, 78.0; H, 6.9; N, 15.2%).

4-*Piperidino*-1,10-*phenanthroline* (21).—A mixture of sulphone (1.0 g) in piperidine (15 ml) by the procedure described above, afforded 4-*piperidino*-1,10-*phenanthroline* (0.58 g, 71%) as yellow needles, m.p. 251—254 °C (from benzene) (Found: C, 78.2; H, 7.0; N, 15.4. $C_{17}H_{19}N_3$ requires C, 78.0; H, 6.9; N, 15.2%).

4-*Phenoxy*-1,10-*phenanthroline* (24).—4-Chloro-1,10-phenanthroline (2.1 g), KOH (2.26 g), and phenol (2.82 g) were heated for 2 h at 100—110 °C. The mixture was cooled, diluted, basified with aqueous NaOH, and extracted with Et_2O. The extract was dried and evaporated. Crude 4-*phenoxy*-1,10-*phenanthroline* (24) was obtained as yellow oily crystals which by chromatography on alumina (type H) (elution with $CHCl_3$) gave pure material (2.18 g, 81%) as yellow needles, m.p. 196—197 °C (Found: C, 79.7; H, 4.4; N, 10.2. $C_{18}H_{12}N_2O$ requires C, 79.4; H, 4.4; N, 10.3%).

Attempted Preparation of 4-*Amino*-1,10-*phenanthroline* (6).—The phenoxy-compound (1.36 g) and ammonium acetate (20 g) were heated at 170—180 °C (bath temperature) for 90 min. The mixture was cooled, diluted with water, and basified. The insoluble solid was collected by filtration and dissolved in 10% aqueous HOAc (50 ml). The solution was filtered, basified, and extracted with $CHCl_3$ (3 × 50 ml). Removal of the $CHCl_3$ gave a residue which on crystallisation from cyclohexane was shown to be unchanged starting material.

4-*Azido*-1,10-*phenanthroline* (25).—The sulphone (2 g) was stirred at 20 °C in Me_2SO (20 ml) for 4 h with sodium azide (0.6 g). Water (150 ml) was added, and the mixture was extracted with Et_2O (3 × 50 ml). After drying ($MgSO_4$), the extracts were passed down a short alumina column.

* See *e.g.* data tabulated in refs. 20 and 24.

[24] M. J. Cook, A. R. Katritzky P. Linda, and R. D. Tack, *J.C.S. Perkin II*, 1972, 1295.

The eluate was concentrated and warmed. Hexane was added and, on cooling, the mixture afforded the *azide* as a yellow solid (0.8 g, 58%), m.p. 171—186 °C (decomp.); $\nu_{max.}$ (Nujol) 2 120, 2 105, 1 530, and 980 cm^{-1}. A satisfactory elemental analysis could not be obtained for this compound, owing to its ready decomposition.

4-Amino-1,10-phenanthroline (6).—Sodium borohydride (0.5 g) in MeOH (30 ml) was added to the azide (1 g), cooled in an ice-bath to maintain the temperature below 20 °C. After the initially vigorous reaction had ceased (20 min) MeOH was removed *in vacuo*. Water (10 ml) was added, and the mixture was extracted with Et_2O (3 × 30 ml). After drying ($MgSO_4$) and removal of solvent from the extract, the yellow residue was crystallised from cyclohexane to give the *amine* as yellow prisms (0.27 g, 31%), m.p. 124—125 °C (Found: C, 74.1; H, 4.9; N, 21.8. $C_{12}H_9N_3$ requires C, 73.8; H, 4.6; N, 21.5%).

4-Acetamido-1,10-phenanthroline (7).—4-Amino-1,10-phenanthroline (0.5 g), Ac_2O (0.3 g), glacial HOAc (1 ml), and zinc dust (0.05 g) were refluxed for 0.5 h, and then poured into cold water (10 ml) and stirred for 15 min. The solid was filtered off and washed with cold water. Recrystallisation from hot water yielded the *acetamide* as needles (0.48 g, 90%), m.p. 161—162 °C (Found: C, 70.6; H, 4.8; N, 17.5. $C_{14}H_{11}N_3O$ requires C, 70.9; H, 4.7; N, 17.7%).

4-Tosylamido-1,10-phenanthroline (8).—4-Amino-1,10-phenanthroline (0.3 g) and toluene-*p*-sulphonyl chloride (3 g) were added to 5% aqueous NaOH (20 ml). The mixture was shaken vigorously for 0.5 h, cooled, and acidified. The mixture was extracted four times with Et_2O and the extract dried over $MgSO_4$. Et_2O was finally removed and the *tosylamido-derivative* crystallized from EtOH as needles (0.53 g, 94%), m.p. 151—152 °C (Found: C, 65.5; H, 4.6; N, 12.3. $C_{19}H_{15}N_3O_2S$ requires C, 65.3; H, 4.6; N, 12.0%).

4-Cyclohexylamino-1-methyl-1,10-phenanthrolinium Iodide (26).—4-Cyclohexylamino-1,10-phenanthroline (0.5 g) and MeI (15 ml) were heated under reflux for 20 min. The excess of MeI was removed at reduced pressure, and the resultant yellow solid (0.54 g, 72%) was recrystallised from EtOH to give the *methiodide* as yellow needles, m.p. 276 °C (Found: C, 54.0; H, 5.4; N, 9.8. $C_{19}H_{22}IN_3$ requires C, 54.4; H, 5.3; N, 10.0%).

4-Anilino-1-methyl-1,10-phenanthrolinium Iodide (27).—4-Anilino-1,10-phenanthroline (0.4 g) and MeI (15 ml) were refluxed for 0.5 h, and the excess of MeI was evaporated. The resultant yellow solid (0.45 g, 75%) was recrystallized from EtOH to give the *methiodide* as yellow needles, m.p. 248—250 °C (Found: C, 55.0; H, 4.0; N, 9.8. $C_{19}H_{13}N_3$ requires C, 55.2; H, 3.9; N, 10.2%).

4-Tosylamido-2,2′-bipyridyl (12).—4-Amino-2,2′-bipyridyl (1.7 g) and toluene-*p*-sulphonyl chloride (6 g) in 10% aqueous NaOH (20 ml) were refluxed for 20 min. The mixture was cooled, acidified, and extracted with $CHCl_3$ (3 × 40 ml). The extract was evaporated and the residual solid (2.56 g, 29%) was recrystallized from aqueous EtOH to afford *4-tosylamido-2,2′-bipyridyl* as needles, m.p. 125—126 °C (Found: C, 62.4; H, 4.4; N, 13.0. $C_{17}H_{15}N_3O_2S$ requires C, 62.8; H, 4.6; N, 12.9%).

4-Anilino-2,2′-bipyridyl (13).—4-Chloro-2,2′-bipyridyl (2 g) and aniline (10 ml) were heated at 160 °C for 6 h. The mixture was cooled and the residual solid filtered off and washed three times with Et_2O (30 ml). The brown solid was purified on preparative t.l.c. (chloroform eluant) and the *anilino-derivative* obtained as needles (0.8 g, 31%), m.p. 220—223 °C (Found: C, 77.5; H, 5.5; N, 17.1. $C_{16}H_{13}N_3$ requires C, 77.7; H, 5.3; N, 17.0%).

4-Thiophenoxy-2,2′-bipyridyl (30).—4-Chloro-2,2′-bipyridyl (4 g), KOH (10 g), and thiophenol (15 ml) were heated at 150 °C for 15 h. The mixture was then dissolved in H_2O and stirred with 30% aqueous KOH for 1 h. The mixture was filtered and *4-thiophenoxy-2,2′-bipyridyl* (2.75 g, 50%) recrystallized from cyclohexane to afford yellow needles, m.p. 88—90 °C (Found: C, 72.6; H, 4.8; N, 10.5. $C_{16}H_{12}N_2S$ requires C, 72.7; H, 4.5; N, 10.6%).

4-Phenylsulphonyl-2,2′-bipyridyl.—4-Thiophenoxy-2,2′-bipyridyl (2.5 g) in MeOH was treated with aqueous sodium periodate solution (2.5 g in 20 ml), and the mixture refluxed for 2 h. The mixture was filtered and the solvent removed under reduced pressure. The residue was dissolved in water and extracted with $CHCl_3$. Evaporation of the $CHCl_3$ afforded the sulphone as yellow needles (1.76 g, 63%), m.p. 101—104 °C (Found: C, 64.7; H, 4.3; N, 9.7. $C_{16}H_{12}N_2O_2S$ requires C, 64.8; H, 4.1; N, 9.5%).

4-Methylamino-2,2′-bipyridyl.—4-Chloro-2,2′-bipyridyl (1 g) and $MeNH_2$ (5 ml) were heated in a sealed tube at 40 °C for 7 h. $MeNH_2$ was evaporated and the residue dissolved in aqueous 5% NaOH (10 ml). The solution was extracted with $CHCl_3$ and the extract dried and evaporated to afford *4-methylamino-2,2′-bipyridyl* which on crystallisation from MeOH gave microcrystals (0.17 g, 18%), m.p. 118—119 °C (Found: C, 71.7; H, 5.7; N, 22.8. $C_{11}H_{11}N_3$ requires C, 71.4; H, 5.9; N, 22.7%).

We thank Dr. A. Nayak for help with some of the experimental work.

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