

Syntheses and Some Reactions of *N,N'*-Diamino-2,2'- and -4,4'-Bipyridinium Salts

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The syntheses and some reactions of *N,N'*-diamino-2,2'- and 4,4'-bipyridinium salts (IV, V and VI) are described. These compounds are prepared by the reaction of bipyridyls (I-III) with *O*-mesitylenesulfonylhydroxylamine in moderate to good yields. Compounds IV and VI were found to give the *N,N'*-diacyl derivatives by the reaction with acyl chlorides and to undergo 1,3-dipolar cycloaddition reaction with an acetylenic compound to give 1:2 adducts. Photoirradiation of *N,N'*-dibenzoylimino-2,2'-bipyridinium betaine (IX) isomerizes to a mono diazepine derivative (XVI).

Recently a general synthetic method of *N*-aminopyridinium salts, precursors of the pyridinium *N*-imines, has been described (1). As part of our continuing interests in the chemistry of pyridinium *N*-imines (2), we have extended our investigations to the bipyridinium derivatives. In particular, it appeared of interest to compare the physical and chemical properties of bipyridinium *N,N'*-diamines with those observed with their pyridine counterparts.

The syntheses of compounds IV, V, and VI were achieved by treating 1 mole equivalent of bipyridyls (I-III) with 2 molar equivalent of *O*-mesitylenesulfonylhydroxylamine (MSH) (3) in methylene chloride at 0°. Thus, 4,4'-bipyridyl (III) afforded 80% yield of *N,N'*-diamine dimesitylenesulfonate (VI), which has already been prepared by the Gösl's procedure using hydroxylamine *O*-sulfonic acid in 34% yield (4). With 4,4'-dimethyl-2,2'-bipyridyl(I), however, a mixture of *N,N'*-diamine salt (IV) and mono *N*-amine salt (VII) was obtained in 77% yield. The ratio of IV and VII was 77:23 (5), as determined from integrated intensities of methyl resonances in its nmr spectrum. The pure *N,N'*-diamine salt (IV) was obtained by fractional recrystallization. Similarly 2,2'-bipyridyl (II) afforded V in 42% yield after repeated recrystallization. It should be noted that hydroxylamine *O*-sulfonic acid has been reported to fail to react with II (4).

We have examined the following three types of reaction: (i) acylation of IV and VI, (ii) 1,3-dipolar cycloaddition of IV and VI, and (iii) photolysis of *N*-acyl derivative (IX). These are considered to be representative reactions reported for pyridinium *N*-imines (6).

Benzoylation of IV and VI was readily accomplished by a Schotten-Baumann reaction to give IX and X (4) in

40 and 90% yields, respectively. Compound X was sparingly soluble in most organic solvents, as previously described (4). *N,N'*-Dicarbethoxyimine (XI) was obtained from VI in 8% yield by refluxing with a large excess of ethyl chloroformate. However, attempts to prepare the *N,N'*-dicarbethoxyimino derivative of IV were unsuccessful under various conditions. We also attempted to react IV with phthaloyl chloride without success. For comparison of spectral properties, the mono *N*-acylimines XII and XIII were also prepared (see Experimental parts). The spectral data of these products are summarized in Table I.

TABLE I
Spectral Data for *N,N'*-Diacyliminobipyridinium Betaines

Compd.	IR (KCl) cm ⁻¹	UV (solvent) nm (ε)
IX	1590	(dioxane) 243 (2.82 x 10 ⁴)
	1540	290 (9.93 x 10 ³)
	1325	353 (1.04 x 10 ⁴)
XII	1590	(dioxane) 247 (1.93 x 10 ⁴)
	1550	278 (1.29 x 10 ⁴)
	1330	357 (4.18 x 10 ³)
X	1590	(dioxane) 221 (a)
	1540	252
	1330	391
XI	1640	(ethanol) 244 (7.55 x 10 ³)
	1615	287 (5.96 x 10 ³)
		389 (1.77 x 10 ⁴)
XIII	1640	(ethanol) 244 (1.13 x 10 ⁴)
	1615	274 (1.13 x 10 ⁴)
		351 (1.22 x 10 ⁴)

(a) The exact intensity was not determined due to low solubility.

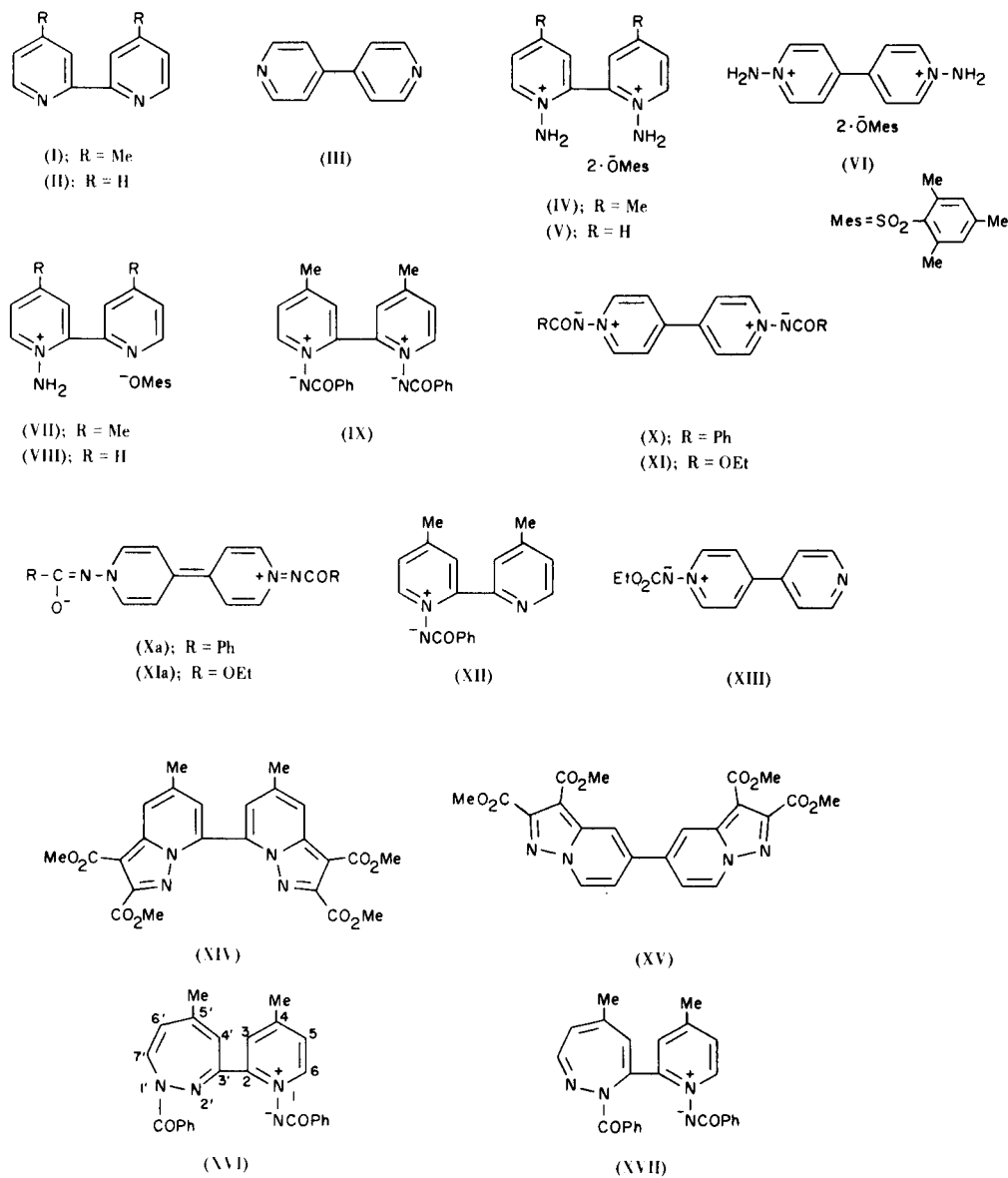


TABLE II

Spectral Data for 1,3-Dipolarcycloaddition Products

Compd.	IR (KCl) cm ⁻¹	UV (ethanol) nm	NMR (CDCl ₃) τ	mol. wt. (Mass spectrometry)
XIV	1745	230	1.91 (brs 2H H-4, H-4')	494
	1700	294	2.80 (d 2H H-6, H-6' J = 3 Hz)	
		316	6.14 (s 12H -COOCH ₃) 7.54 (s 6H -CH ₃)	
XV	1745	253	1.36 (d 2H H-7, H-7' J = 7.5 Hz)	466
	1720	297	1.52 (d 2H H-4, H-4' J = 3 Hz)	
		340	2.62 (dd 2H H-6, H-6' J = 7.5 Hz, J = 3 Hz)	
			5.95 (s 6H -COOCH ₃) 6.03 (s 6H -COOCH ₃)	

The observed spectral data of IX are in good agreement with those of the mono benzoyl derivative (XII) and reported values for *N*-benzoyliminopyridinium betaines (6,7). On the other hand, X and XI exhibited a large bathochromic shifts of the long wave-length uv absorption maxima. This fact suggests considerable contribution of canonical forms such as Xa and XIa to the resonance hybrids.

Compounds IV and VI were found to undergo 1,3-dipolar cycloadditions to dimethyl acetylenedicarboxylate (DAC) to give 1:2 adducts. The structural assignment of these adducts was based on elemental analyses and spectral evidence (Table II). The uv absorption maxima of XIV and XV were observed to be shifted to longer wavelengths when compared with 2,3-dicarbethoxypyrazolo[1,5-*a*]pyridines (8), suggesting the existing of an appreciable electronic interaction between the adjacent pyrazolo-[1,5-*a*]pyridine nuclei. This reaction is completely analogous to the behavior of pyridinium *N*-imines (8).

TABLE III
NMR Data for Compound XVI

	NMR (CDCl ₃) τ	
XVI	1.26	(d 1H H-6 J = 7 Hz)
	1.75-2.75	(m 12H H-3, H-5 -COC ₆ H ₅)
	3.35	(d 1H H-7' J = 7.5 Hz)
	3.57	(brs 1H H-4')
	4.29	(dd 1H H-6' J = 7.5 Hz, J = 1.5 Hz)
	7.57	(s 3H -CH ₃)
	8.31	(s 3H -CH ₃)

In view of the well-known photoisomerization of *N*-acyliminopyridinium betaines to 1,2-diazepines (9), it appeared to be of interest to examine the photochemical behavior of IX. Preliminary study revealed that only the half of the molecule isomerizes to a diazepine and the further reaction is extremely slow.

Thus, irradiation of an ethanolic solution of IX with a 300 w high-pressure mercury lamp in a Pyrex tube led to the isolation of a yellow compound XVI in 64% yield. The structure of XVI was elucidated by its uv, ir and nmr spectra. The uv ($\lambda_{\text{max}}^{\text{dioxane}}$ 240 and 356 nm) and ir spectra (ν_{max} (chloroform) 1645 and 1590 cm^{-1}) of this photoisomer showed absorption bands characteristic of both *N*-benzoyl-1(1H)2-diazepine (9) and *N*-benzoyliminopyridinium betaine (7). The nmr spectrum (Table III) not only excluded the alternative structure (XVII), but also confirmed the assigned structure XVI unambiguously. The signal assignments are based on those derived from a number of earlier studies (10).

Upon prolonged irradiation (more than 60 hours) in ethanol, most of XVI was recovered unchanged, although the formation of a small amount of many unidentified products was detected by tlc.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were recorded on a Hitachi EPI G-2 spectrophotometer, uv spectra on a Hitachi 124 spectrophotometer, nmr spectra on a Hitachi R-20A spectrometer and mass spectra on a Hitachi RMU-6D mass spectrometer operating at 70 eV.

N,N'-Diamino-4,4'-bipyridinium Dimesitylenesulfonate (VI).

To an ice-cooled solution of 4,4'-bipyridyl (III) (3.12 g.) in methylene chloride (30 ml.) was added dropwise a solution of MSH (12.90 g.) in methylene chloride (20 ml.). The reaction mixture was allowed to stand at room temperature for 10 minutes. After addition of ether, the precipitated crystals were collected and recrystallized from methanol-ethyl acetate to give white needles of VI, m.p. 238-239°, yield, 9.37 g. (80%).

Anal. Calcd. for C₂₈H₃₄N₄O₆S₂: C, 57.33; H, 5.84; N, 9.55. Found: C, 57.60; H, 5.76; N, 9.64.

After treatment of VI with 1*N* sodium hydroxide solution, the uv spectrum had two strong absorption maxima at 421 and 429 nm. The absorptions disappeared upon addition of one drop of 1*N* hydrochloric acid solution (6).

N,N'-Diamino-4,4'-dimethyl-2,2'-bipyridinium Dimesitylenesulfonate (IV).

Using a similar procedure as described for VI, a mixture (11.72 g.) of IV and VII were obtained from I (3.68 g.) and MSH (12.90 g.). Repeated recrystallization from methanol-ethyl acetate gave white needles of IV, m.p. 237-238°, yield, 5.70 g. (43%).

Anal. Calcd. for C₃₀H₃₈N₄O₆S₂: C, 58.62; H, 6.32; N, 9.12. Found: C, 58.79; H, 6.10; N, 9.08.

After treatment of IV with 1*N* sodium hydroxide solution, the uv spectrum showed a strong absorption maximum at 328 nm, which disappeared upon addition of one drop of 1*N* hydrochloric acid.

N,N'-Diamino-2,2'-bipyridinium Dimesitylenesulfonate (V).

In a similar manner as described for IV, II (234 mg.) gave white cubics of V, m.p. 224-226° (from methanol-ethyl acetate), yield, 234 mg. (42%).

Anal. Calcd. for C₂₈H₃₄N₄O₆S₂: C, 57.33; H, 5.84; N, 9.64. Found: C, 57.16; H, 5.99; N, 9.55.

N,N'-Diethoxycarbonylimino-4,4'-bipyridinium Betaine (XI).

A mixture of VI (586 mg.) and ethyl chloroformate (10 ml.) was heated at 70-90° for 12 hours. The excess ethyl chloroformate was evaporated and water was added to the residue. After the aqueous solution was made alkaline with potassium carbonate, the solution was extracted with chloroform. The dried extract was concentrated to give greenish yellow crystals of XI, m.p. 268-269° (from ethanol), yield, 25 mg. (8%). The mass spectrum showed the parent *m/e* at 330 (calcd. 330).

Anal. Calcd. for C₁₆H₁₈N₄O₄: C, 58.17; H, 5.49; N, 16.96. Found: C, 58.34; H, 5.78; N, 16.79.

N-Ethoxycarbonylimino-4-(4'-pyridyl)pyridinium Betaine (XIII).

A crude reaction product (680 mg.) obtained from III and

MSH was heated in ethyl chloroformate (10 ml.) at 80° for 6 hours. After working-up as described for XI, the residue was purified by chromatography (alumina, benzene-chloroform) and recrystallized from benzene to give XIII, m.p. 210-212°, yield, 60 mg. The mass spectrum showed the parent m/e at 243 (calcd. 243).

Anal. Calcd. for C₁₃H₁₃N₃O₂: C, 64.18; H, 5.39; N, 17.28. Found: C, 64.21; H, 5.21; N, 17.12.

N,N'-Dibenzoylimino-4,4'-dimethyl-2,2'-bipyridinium Betaine (IX).

To an ice-cooled solution of IV (0.68 g.) in water (5 ml.) was added dropwise concurrently benzoyl chloride (0.64 g.) and 20% sodium hydroxide solution (20 ml.) with stirring. The reaction mixture was stirred for 12 hours under ice cooling and extracted with chloroform. The dried extract was concentrated and the residual solid was purified by chromatography (alumina, chloroform) and recrystallized from ethanol to give IX, m.p. 248-249°, yield, 410 mg. (90%); nmr (deuteriochloroform) τ 1.26 (d, 2H, H-6, H-6', J = 7 Hz), 2.05-2.82 (m, 14H, H-3, H-3', H-5, H-5', -COC₆H₅), 7.52 (s, 6H, 2 x CH₃). The mass spectrum showed no parent peak. The highest peak was m/e 303.

Anal. Calcd. for C₂₆H₂₂N₄O₂: C, 73.91; H, 5.29; N, 13.26. Found: C, 73.71; H, 5.31; N, 13.28.

N-Benzoylimino-4-methyl-2-(4'-methyl-2'-pyridyl)pyridinium Betaine (XII).

To an ice-cooled solution of a mixture (624 mg.) of IV and VII (a ratio = 77:23) in water (5 ml.) was added dropwise concurrently benzoyl chloride (564 mg.) and 20% sodium hydroxide solution (20 ml.) with stirring. The reaction mixture was stirred for 12 hours. Working-up as described for IX, the residue was submitted to column chromatography on alumina. Elution with benzene gave yellow crystals of XII (80 mg.), m.p. 192-194° [from benzene-petroleum ether (b.p. 60-80°)], in addition to IX (210 mg.); nmr (deuteriochloroform) τ 1.43 (d, 1H, H-6, J = 7 Hz), 1.43 (d, 1H, H-6', J = 6 Hz), 1.85-3.00 (m, 9H, H-3, H-3', H-5, H-5', -COC₆H₅), 7.46 (s, 3H, CH₃), 7.78 (s, 3H, CH₃). The mass spectrum showed the parent m/e at 303 (calcd. 303).

Anal. Calcd. for C₁₉H₁₇N₃O: C, 75.22; H, 5.65; N, 13.85. Found: C, 75.20; H, 5.63; N, 13.98.

2,2',3,3'-Tetramethoxycarbonyl-5,5'-dimethyl-7,7'-bipyrazolo[1,5-*a*]pyridine (XIV).

A mixture of IV (1.23 g.) and potassium carbonate (0.83 g.) in DMF (20 ml.) was stirred for 10 minutes at room temperature. To the stirring solution was added dropwise a solution of dimethyl acetylene dicarboxylate (1.00 g.) in DMF (2 ml.) and the mixture was stirred for 3 days at room temperature. The reaction mixture was concentrated to dryness under reduced pressure and the residue was extracted with chloroform. The dried extract was concentrated, and the residue was purified by chromatography (alumina, benzene) and recrystallization from acetone to give XIV, m.p. above 295°, yield, 80 mg. (8%).

Anal. Calcd. for C₂₄H₂₂N₄O₈: C, 58.30; H, 4.48; N, 11.33. Found: C, 58.47; H, 4.37; N, 11.25.

2,2',3,3'-Tetramethoxycarbonyl-5,5'-bipyrazolo[1,5-*a*]pyridine (XV).

Using a similar procedure described for XIV, XV was obtained from VI (1.17 g.) and dimethyl acetylenedicarboxylate (1.00 g.) as a white powder. Recrystallization from chloroform-methanol gave XV, m.p. above 295°, yield, 209 mg. (22%).

Anal. Calcd. for C₂₂H₁₈N₄O₈: C, 56.65; H, 3.89; N, 12.01. Found: C, 56.17; H, 4.07; N, 11.64.

N-Benzoylimino-4-methyl-2-(1'-benzoyl-5'-methyl-1'(1'*H*)2'-diazepin-3-yl)pyridinium Betaine (XVI).

A solution of IX (116 mg.) in ethanol (50 ml.) was irradiated using a 300 w high pressure mercury lamp for 8 hours in a Pyrex vessel. The solvent was removed *in vacuo* and the residue was purified by preparative tlc (alumina-chloroform) and recrystallized from acetone-petroleum ether (b.p. 30-60°) to give yellow crystals of XVI, m.p. 235-236°, yield, 74 mg. (64%); ir (potassium chloride) cm⁻¹ 1650, 1590, 1550, 1330; uv λ max (dioxane) 240 nm (ϵ 27000), 356 (7700). The mass spectrum showed no parent peak and the highest peak was m/e 303.

Anal. Calcd. for C₂₆H₂₂N₄O₂: C, 73.91; H, 5.25; N, 13.26. Found: C, 73.67; H, 5.28; N, 13.04.

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