Conclusions

Predictions of solvent effects on solvolytic reactivity can be achieved using eq 3 and Y_{sim} values for appropriate similarity models (Table VI) to account for solvation effects adjacent to the reaction site. Results fit a consistent pattern (for alkyl, alkenyl, alkynyl, and aryl groups in various aqueous binary mixtures), and larger effects are observed when the number of π-electrons is greater.

Acetonitrile offers useful advantages over organic cosolvents such as acetone and dioxane, previously used extensively in studies of the rates and products of solvolytic reactions in aqueous mixtures.

Experimental Section

Chemicals. 4-Chloropent-2-ene (1),[28] 4-chloro-4-methylpent-2-yne (2),[29] and 2-chloro-2-methylpentane (3)[15b] were prepared by standard methods and were shown to be pure by ^{1}H NMR. Acetone and methanol (Fisons dried-distilled grade) and acetonitrile (Fisons HPLC grade) were used without further purification. Dioxane[30] and ethanol were dried by standard methods.[18]

Kinetics. Conductimetric procedures were as described previously.[10,18]

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Registry No. 1, 1458-99-7; 2, 999-79-1; 3, 4325-48-8; *tert*-butyl chloride, 507-20-0; acetonitrile, 75-05-8; water, 7732-18-5.

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N-Methylated 2,3′-Bipyridinium Ion. First Synthesis of the More Sterically Hindered Isomer

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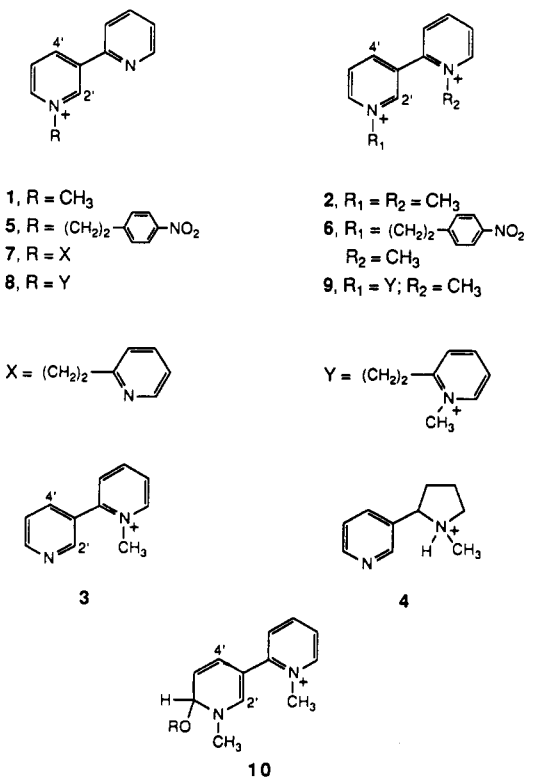
1-Methyl-2,3′-bipyridinium salts can be prepared by deprotection of diquaternized precursors. Protecting groups are eliminated from the 1′-position under basic conditions; they include either *p*-nitrostyrene or 1-methyl-2-vinylpyridinium ion. In DMSO-d_6–CD_3OD a nucleophile adds to 1,1′-dimethyl-2,3′-bipyridinium ion to generate a σ complex having a nucleophile bonded to the 6′-position.

Quaternization of the less reactive nitrogen atom of 2,3′-bipyridine (BIPY) is a challenge. BIPY readily undergoes quaternization with alkylating agents at the sterically less hindered nitrogen atom of the 3-pyridyl ring to give products such as 1.[1] A second alkyl group may be added to the remaining free nitrogen atom to provide a dication such as 2. Strenuous conditions are required[1] to N-alkylate 1 because there is both electronic deactivation and steric hindrance of the free nitrogen atom situated ortho to the adjacent cationic ring. Monoquaternized BIPY having an alkyl group bonded to the less reactive, more hindered nitrogen atom of the 2-pyridyl ring has been unknown.

We now report a convenient synthesis of the heretofore unknown 3 containing only an *N*-methyl group at the sterically hindered 2-pyridyl ring and free of other substituents. Our approach is likely to be useful for the preparation of other compounds having two or more nucleophilic nitrogen atoms, one of which normally does not alkylate owing to deactivation for steric and/or electronic reasons as well as for the synthesis of other derivatives of 3 having different *N*-alkyl groups.

An alternate synthetic pathway has been available for derivatives of 3 having substituents bonded to the 4- and 6-positions of the quaternized ring. They have been prepared by a reaction between a primary amine and the corresponding pyrylium ion precursors in which the charged annular nitrogen atom has been replaced by a positively charged oxygen atom.[2] The pyrylium ions themselves require several steps to prepare,[3] but once the



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compounds are in hand this approach has the advantage that a number of different groups may be attached conveniently to the positively charged nitrogen atom simply by varying the identity of the amine reactant. But **3** lacking substituents at the 4- and 6-positions cannot be prepared by this route.

Our interest in **3** stems from its structural similarity to protonated nicotine **4** and its potential to act as an agonist at nicotinic receptor sites. Under physiological conditions nicotine is protonated at the more basic pyrrolidine nitrogen atom and is believed to bind to receptor sites in this form.[4] An additional component to its binding is hydrogen bonding at the free pyridine nitrogen atom. At physiological pH BIPY exists as the free base. Quaternization as in **3** provides a closer model of protonated nicotine, now containing both the electrostatic and hydrogen bonding sites with a similar spacial relationship.

Results and Discussion

The logic behind our synthetic scheme is straightforward. A protecting group is added first to the more reactive, less hindered nitrogen atom on the 3'-pyridine ring. The more hindered nitrogen atom then is methylated, and finally the protecting group is removed as an alkene in an elimination reaction.

Two different protecting groups were explored. The more useful, the one providing the higher yield of the desired final product **3**, is 2-(4-nitrophenyl)ethyl (NPE). The second is 2-(2-pyridyl)ethyl, which must be N-methylated prior to removal.

***p*-Nitrophenethyl Protecting Group.** The NPE group is attached to BIPY on heating with 2-(4-nitrophenyl)ethyl iodide to give **5**. The protected intermediate then is easily N-methylated with methyl iodide to provide dication **6**.

Removal of the nitrophenethyl protecting group from **6** proved to be troublesome. Weak bases such as pyridine or 4-(dimethylamino)pyridine in methanol would not induce elimination whereas heating a solution of **6** in nitromethane with sodium carbonate resulted in loss of the methyl group to give back **5**. Heating a sample in DMF with quinuclidine led to both elimination and demethylation. Elimination of *p*-nitrostyrene from **6** to give **3** was achieved successfully on heating with 2,2,6,6-tetramethylpiperidine in methanol at reflux for 22 h, affording **3** in 27% yield following workup.

In marked contrast, elimination of the NPE group from aliphatic tertiary amines in 0.1 M NaOH solution is a rapid reaction at 25 °C.[5]

Mechanism of Deprotection. Elimination of the styrene from **6** was followed by ^{1}H NMR in CD_3OD containing about 1 equiv of methoxide ion. After 25 h at room temperature, the reaction mixture contained nearly equal amounts of starting material and elimination product. The elimination was complete after 4 days. Deuterium exchange was observed at positions α to the quaternized nitrogen atoms, likely taking place through base-catalyzed ylide formation.[6]

No deuterium was observed at the α-position of the vinyl group in the nitrostyrene product. Elimination therefore occurs either through a concerted E2 or an $E1cB_{irr}$ mechanism in which carbanion formation is irreversible.[7,8] An E1cB route involving reversible carbanion formation would introduce deuterium.

The signals for both β protons of the styrene showed a minor amount of isotope shifted doublets[9] present in essentially equal amounts consistent with prior isotope exchange at this position next to the activating, quaternized nitrogen atom in starting material **6**, likely by the formation of an ylide intermediate.[6]

The presence of broadened and shielded proton signals[10] suggested that a σ complex resulting from nucleophilic addition to the dication may be present during elimination. An authentic adduct therefore was generated as verification.

Authentic σ Complex. Dication **2** was used to model **6** because it has fewer protons and cannot undergo elimination. The addition of DMSO-d_6 to the methanol provided a dramatic change.[14] In 4:1 DMSO-d_6–CD_3OD the addition of 2 equiv of 2,2,6,6-tetramethylpiperidine quickly gave a 3:1 mixture of dication **2** and a single σ adduct **10**. No change was observed after $1^3/_4$ hrs, suggesting a reaction at completion. When another proton spectrum was recorded 10 min after the addition of 2 equiv of DCl, adduct was found to be converted back to **2**, thereby showing that σ complex formation can be reversed.

All of the proton signals of the adduct and starting material are sharp, indicative of slow ligand exchange between the two components. Adduct signals are shielded with respect to starting material. The 4'-, 5'-, and 6'-protons of the 3-pyridyl ring form a coupled three spin system whereas the 3-, 4-, 5-, and 6-protons on the 2-pyridyl ring form a four spin system, making assignments easy. The former three are shifted farther upfield than the latter four, indicating that they are bonded to the ring with the added nucleophile. Nucleophile addition must take place to the 6'-position of the 3-pyridyl ring because the signal for this site, now sp^3 hybridized, shows the largest change, moving from 9.3 to 5.74 ppm with an allylic coupling of 4.5 Hz.

A spectrum of **10** recorded $1^3/_4$ h after addition of the piperidine showed 73% deuteriation at the 2'-position of **2** and 68% deuteriation at the 2'-position of **10**, the same within experimental error, indicating that the starting material and adduct are in equilibrium. The adduct therefore may be the thermodynamic product, consistent with its considerable resonance stabilization.

One reason for the slow deprotection step then is σ adduct formation, an adduct possessing a more basic and therefore a poorer leaving group that likely does not participate in elimination.

Pyridylethyl Protecting Group. When 2-vinylpyridine and BIPY·2HCl were heated at reflux in methanol, monoquaternized **7** was obtained after 2 days. This

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(10) 1,1'-Dimethyl-4,4'-bipyridinium ion[11] (paraquat) reacts with methanol to give a radical cation that shows broadened NMR signals. Nitroarenes form charge-transfer complexes with anions that undergo electron exchange with uncomplexed material leading to broadened lines.[12,13]
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outcome stands in contrast to the reported facile diquaternization.[15] The acid salt of the nucleophile presumably serves to bring about N-protonation of the vinylpyridine alkylating agent thereby turning it into a more reactive Michael-type substrate while at the same time providing a nucleophilic site on the BIPY.

The major limitation to the use of this protecting group is found with the next step, N-methylation. Both pyridine rings in **7** are nucleophilic; that belonging to the protecting group is more reactive because it is more basic. N-Methylation of this ring gives **8**, which now contains a more acidic methylene side chain and therefore a more easily removable protecting group, 1-methyl-2-vinylpyridinium ion.[16] Unfortunately, due to the large increase in carbon acidity of the methylene unit, deprotection of **8** is so facile[16] that it takes place in competition with the desired methylation of the pyridine ring of the protected BIPY to give **9**. The reaction mixture becomes contaminated with unprotected BIPY that, in turn, rapidly undergoes N-methylation to give **1**. However, pure **9** readily undergoes elimination to give **3** simply by the action of the basic resin poly 4-vinylpyridine suspended in methanol–water at room temperature. This unfortunate competition caused us to limit the development of this route.

Identification of *N*-Methyl Isomers by NMR and Their Conformations. Isomeric monomethylated BIPYs **1** and **3** in D_2O have very different proton NMR spectra that serve to distinguish them easily. Among the signals of the annular protons the one at lowest field, an apparent singlet of H-2′ at 9.37 ppm, serves as a characteristic and unique peak of **1**. The signal for H-2′ of dication **2** also is located at about the same position, at 9.30 ppm. But the lowest field signal of **3** is not that for H-2′ found at 8.78 ppm; instead, it is an apparent doublet at 8.96 ppm due to H-6. The deshielding of H-2′ in **1** is likely to be is due to a combination of the magnetic anisotropy of the neighboring ring and the electrostatic field effect of the nitrogen lone pair in this same ring.[17]

The *N*-methyl shifts are characteristic and therefore especially diagnostic. They along with the annular proton shifts[18] suggest that **2** and **3** have a conformation different from that in **1**. The 1′-methyl of **1** and **2** fall at 4.54 and 4.56 ppm, respectively, which is unexceptional and similar to the shift at 4.46 ppm of the methyl of 1-methyl-4,4′-bipyridinium ion.[19] However, the 1-methyl groups of **2** and **3** are at much higher field, 4.29 and 4.25 ppm, respectively, and are located in a shielding region of the adjacent aromatic ring just as in the cases of the methyl substituents in bridged *o,o*-dimethylbiphenyls[20] and diquaternized 3,3′-dimethyl-2,2′-bipyridinium ions.[21] The preferred conformation of **2** and **3** therefore is likely to be distinctly nonplanar.[22]

Experimental Section

Shift standards include tetramethylsilane (TMS), sodium 3-(trimethylsilyl)-1-propanesulfonate (DSS), or sodium 3-(trimethylsilyl)propionate-2,2,3,3-d_4 (TSP). Melting points are uncorrected.

1′-Methyl-2,3′-bipyridinium Iodide (1). 2,3′-Bipyridine and excess methyl iodide in acetone gave crystals of **1** after standing overnight at room temperature. Recrystallization from water–isopropyl alcohol yielded pale yellow crystals: mp 166.5–168.5 °C (lit.[1] mp 167–168 °C); ^{1}H NMR (D_2O, TSP) δ 9.37 (H2′, 1 H, s), 9.01 (H4′, 1 H, d, $J_{4',5'}$ = 8.2 Hz), 8.88 (H6′, 1 H, d, $J_{5',6'}$ = 6.1 Hz), 8.76 (H6, 1 H, ddd, $J_{5,6}$ = 5.0 Hz, $J_{4,6}$ = 1.7 Hz, $J_{3,6}$ = 0.95 Hz), 8.20 (H5′, 1 H, dd), 8.11 (H4, 1 H, unsymmetrical td, $J_{3,4} \approx J_{4,5}$ = 7.7 Hz), 8.05 (H3, 1 H, dt, $J_{3,5}$ = 1.1 Hz), 7.64 (H5, 1 H, ddd), 4.54 (NCH_3, s).

1,1′-Dimethyl-2,3′-bipyridinium Diiodide (2). 2,3′-Bipyridine and excess methyl iodide in acetonitrile when heated in a sealed vial on a steam bath for 4 h gave a red-orange oil that crystallized on standing. Repeated recrystallization from water–ethanol gave the analytical sample: mp 210–214 °C dec (lit.[1] mp 196–197 °C); ^{1}H NMR (D_2O, TSP, peaks are broad and no fine coupling is present) δ 9.30 (H2′, 1 H, s), 9.17 (H6 or H6′, 1 H, d, $J_{5,6}$ = 6.2 Hz), 9.10 (H6 or H6′, 1 H, d, $J_{5,6}$ or $J_{5',6'}$ = 6.2 Hz), 8.89 (H4′, 1 H, d, $J_{4',5'}$ = 8.3 Hz), 8.75 (H4, 1 H, t, $J_{3,4} = J_{4,5}$ = 7.7 Hz), 8.39 (H5 or H5′, 1 H, dd), 8.27 (H5 or H5′, 1 H, dd), 8.22 (H3, 1 H, d), 4.56 (1′-NCH_3), 4.29 (1-NCH_3). Anal. Calcd for $C_{12}H_{14}N_2I_2$: C, 32.75; H, 3.21; N, 6.37. Found: C, 32.70; H, 3.11; N, 6.27.

1′-(2-(4-Nitrophenyl)ethyl)-2,3′-bipyridinium Iodide (5). A solution of 1.52 g (6.61 mmol) of 4-(2-bromoethyl)-1-nitrobenzene and 3 g (20 mmol) of sodium iodide in 10 mL of acetone was stirred overnight at room temperature. The precipitate was discarded, the solution was concentrated, ethyl acetate (20 mL) was added, and the insoluble sodium iodide was removed. To the filtrate was added 0.993 g (6.35 mmol) of 2,3′-bipyridine, and the solution was heated at reflux for 2 days. The precipitated product was collected to yield 1.84 g of solid. The volume of the filtrate was reduced and then heated again at reflux for an additional day. A second crop of 0.478 g was collected. Both crops were recrystallized from acetonitrile and ethyl acetate to give 1.87 g (4.32 mmol, 68% yield) of bright yellow needlelike crystals: mp 177–179 °C dec; ^{1}H NMR (DMSO-d_6, DSS) δ 9.86 (H2′, 1 H, s), 9.30 (H4′, 1 H, d, $J_{4',5'}$ = 8.5 Hz), 9.16 (H6′, 1 H, d, $J_{5',6'}$ = 6.1 Hz), 8.87 (H6, 1 H, ddd, $J_{5,6}$ = 4.8, $J_{4,6}$ = 1.7, $J_{3,6}$ = 0.91 Hz), 8.25–8.40 (H3, H5′, Ph, 4 H, m), 8.17 (H4, 1 H, td, $J_{3,4} \approx J_{4,5}$ = 7.8), 7.65–7.71 (H5, Ph, 3 H, m), 5.10 (CH_2, t, J = 7.7 Hz), 3.59 (CH_2, t, J = 7.6 Hz); ^{13}C NMR (DMSO-d_6) δ 150.2, 149.7, 146.6, 144.4, 144.3, 143.2, 142.4, 138.2, 138.1, 130.5, 128.0, 125.2, 123.7, 121.9, 61.1, 36.1.

A sample was converted to the perchlorate salt by heating 92 mg (0.21 mmol) of the iodide of **5** in aqueous sodium perchlorate followed by cooling. Recrystallization from water and ethanol gave 53 mg (62% yield) of flaky white crystals (mp 153–154.5 °C). The ^{1}H NMR of the perchlorate was consistent with that of the iodide. Anal. Calcd for $C_{18}H_{16}N_3O_2{\cdot}ClO_4$: C, 53.28; H, 3.97; N, 10.35. Found: C, 53.07; H, 3.87; N, 10.22.

1-Methyl-1′-(2-(4-nitrophenyl)ethyl)-2,3′-bipyridinium Diiodide (6). To 1.73 g (3.99 mmol) of the iodide of **5** divided among four screw-top tubes was added 4 mL of acetonitrile, previously dried over 3A molecular sieves, and 5 mL of methyl iodide. After heating on a steam bath for 6.5 h a very viscous dark red oil appeared and crystallized on cooling to give 2.06 g of solid. Recrystallization from water and isopropyl alcohol gave 1.87 g (79% yield) of dark red crystals (mp 176–180 °C dec), which after drying under vacuum turned lighter in color: ^{1}H NMR (DMSO-d_6, TSP) δ 9.56 (H2′, 1 H, s), 9.26–9.34 (H6, H6′, 2 H, overlapping d), 8.98 (H4′, 1 H, d, $J_{4',5'}$ = 8.3 Hz), 8.84 (H4, 1 H, td, $J_{3,4} \approx J_{4,5}$ = 7.9, $J_{4,6}$ = 1.2 Hz), 8.45 (H5′, 1 H, $J_{5',6'}$ = 6.4), 8.37 (H5, 1 H, ddd, $J_{5,6}$ = 6.2, $J_{3,5}$ = 1.2 Hz), 8.30 (H3, 1 H, dd), 8.24 (Ph, d, J = 8.7 Hz), 7.61 (Ph, d), 5.03 (CH_2, t, J = 7.8 Hz), 4.20 (NCH_3, s), 3.54 (CH_2, t). Anal. Calcd for $C_{19}H_{19}N_3O_2I_2{\cdot}H_2O$: C, 38.47; H, 3.57; N, 7.08. Found: C, 38.19; H, 3.47; N, 6.92.

1-Methyl-2,3′-bipyridinium Perchlorate (3·ClO_4) from 6. A suspension of 1.77 g (2.99 mmol) of the diiodide of **6** in 0.849 g (6.01 mmol) of 2,2,6,6-tetramethylpiperidine and 25 mL of methanol was heated at reflux with stirring for 22 h. Dilution with 200 mL of ethyl acetate and cooling in a refrigerator overnight produced a dark brown precipitate that was discarded. The concentrated filtrate gave a black tar that was extracted with ethanol (10–15 mL) and then with acetone. Both extracts were diluted with ethyl acetate and cyclohexane and chilled with

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stirring. The ethanol portion yielded 0.351 g of light brown product (mp 142–147 °C). A second crop of 0.189 g of dark brown solid was precipitated by further dilution and cooling. The acetone extract yielded 31 mg of dark brown precipitate. The precipitates consisted of a mixture of **3**·I and 2,2,6,6-tetramethylpiperidine hydroiodide, which could not be easily separated.

The iodide was converted to the perchlorate by dissolving 0.499 g of precipitate in 10 mL of 4/1 methanol/ethanol and doubling the volume by the addition of 8/5/36 ethanol/70% $HClO_4$/ethyl acetate to give 0.410 g of brown-orange solid (mp >240 °C). The free base was prepared by stirring for a few hours a solution of this salt in 40 mL of methanol and 2 mL of water with a suspension of poly-4-vinylpyridine. The polymer was removed, the orange filtrate was decolorized with charcoal and evaporated to yield a solid. Recrystallization from ethanol gave 0.221 g (27% yield) of the perchlorate salt as light yellow crystals (mp 132–134 °C). An analytical sample was prepared by recrystallization once from a solution of ethanol and sodium perchlorate and once from ethanol: mp 132–134 °C dec; ^1H NMR (D_2O, TSP) δ 8.96 (H6, 1 H, d, $J_{5,6}$ = 6.1 Hz), 8.84 (H6′, 1 H, dd, $J_{5',6'}$ = 5.0 Hz, $J_{4',6'}$ = 1.5 Hz), 8.78 (H2′, 1 H, dd, $J_{2',4'}$ = 2.3 Hz, $J_{2',5'}$ = 0.92 Hz), 8.66 (H4, 1 H, t, $J_{3,4} \approx J_{4,5}$ = 8.0 Hz), 8.04–8.19 (H4′, H3, H5, 3 H, m), 7.77 (H5′, 1 H, $J_{4',5'}$ = 8.0 Hz, dd), 4.25 (NCH_3, s); ^{13}C NMR (D_2O, TSP) δ 155.2, 154.1, 151.00, 149.6, 148.7, 140.9, 133.3, 131.3, 130.4, 127.3, 50.0. Anal. Calcd for $C_{11}H_{11}N_2 \cdot ClO_4$: C, 48.81; H, 4.10; N, 10.35. Found: C, 49.00; H, 4.03; N, 10.29.

In an alternate preparation 60 mg (0.10 mmol) of the diiodide of **6** suspended in a mixture of 10 mL of methanol and 35 μL (0.2 mmol) of 2,2,6,6-tetramethylpiperidine was heated at reflux for 2 days. After the mixture was cooled and a small amount of precipitate removed, 4 mL of $CHCl_3$ was added dropwise. The precipitated brown solid was removed and the mother liquor was concentrated to about one-third of its volume, and ethyl ether was added until a new precipitate appeared. The supernatant liquid was removed, and the collected solid, contaminated with peperidine salt, was then added to 8/5/36 ethanol/70% $HClO_4$/ethyl acetate to give 24 mg (64%) of product as its diperchlorate salt.

1′-(2-(2-Pyridyl)ethyl)-2,3′-bipyridinium Chloride Hydrochloride (7·HCl). A solution of 4.18 g (18.2 mmol) of 2,3′-bipyridine dihydrochloride[24] and 4.0 mL (37 mmol) of 2-vinylpyridine in 120 mL of methanol was heated at reflux for 2 days. The solvent was evaporated to leave a yellow liquid and solid residue. Two recrystallizations of this residue from 20% ethanol–80% isopropyl alcohol gave 4.34 g of a white solid (mp 185–188 °C). A second crop of 0.256 g of pale yellow solid (mp 181–186.5 °C) was collected (72% total yield). An analytical sample was prepared by recrystallization from isopropyl alcohol (mp 188–189 °C dec). Anal. Calcd for $C_{17}H_{16}N_3Cl \cdot HCl \cdot H_2O$: C, 57.96; H, 5.44; N, 11.93. Found: C, 58.66; H, 5.47; N, 12.08.

1′-(2-(2-Pyridyl)ethyl)-2,3′-bipyridinium Chloride (7). A solution of 4.15 g (11.8 mmol) of the hydrochloride of **7** in 100 mL of methanol was stirred overnight with a suspension of 5.2 g (about 4 equiv) of poly-4-vinylpyridine resin. After filtration the methanol was evaporated to a yellow oil. Addition of hexanes to a solution of the oil in isopropyl alcohol produced 2.45 g of a white precipitate. The mother liquor was evaporated to an oil which solidifed on standing and was recrystallized from acetonitrile and ethyl acetate to yield 1.07 g of white solid. Recrystallization of both crops from acetonitrile and ethyl acetate yielded 2.80 g of white solid (mp 64.5–66.5 °C, 75% yield). An analytical sample was prepared by recrystallization from acetonitrile and ethyl acetate: mp 66–67 °C; ^1H NMR (DMSO-d_6, TMS) [the nonquaternized 2-pyridyl ring is indicated with double primed numbers] δ 9.84 (H2′, 1 H, t, $J_{2',4'} \approx J_{2',6'}$ = 1.3 Hz), 9.22 (H4′, 1 H, ddd, $J_{4',5'}$ = 8.2 Hz, $J_{4',6'}$ = 1.5 Hz), 9.15 (H6′, 1 H, dt, $J_{5',6'}$ = 6.1 Hz), 8.81 (H6, 1 H, ddd, $J_{5,6}$ = 4.8 Hz, $J_{4,6}$ = 1.8 Hz, $J_{3,6}$ = 0.9 Hz), 8.50 (H6″, 1 H, ddd, $J_{4'',6''}$ = 1.8 Hz, $J_{3'',6''}$ = 0.9 Hz), 8.29 (H3, 1 H, dt, $J_{3,4}$ = 8.0 Hz, $J_{3,5} \approx$ 1.0 Hz), 8.24 (H5′, 1 H, dd), 8.10 (H4, 1 H, td, $J_{4,5}$ = 7.8 Hz), 7.79 (H4″, 1 H, td, $J_{3'',4''} \approx J_{4'',5''}$ = 7.7 Hz), 7.60 (H5, 1 H, ddd), 7.40 (H3″, 1 H, dt, $J_{3'',5''} \approx$ 1.1 Hz), 7.30 (H5″, 1 H, ddd, $J_{5'',6''}$ = 4.9 Hz), 5.18 (NCH_2, t, J = 7.2 Hz), 3.59 (CCH_2, 2 H, t). Anal. Calcd for $C_{17}H_{16}N_3Cl \cdot H_2O$: C, 64.66; H, 5.74; N, 13.31. Found: C, 64.27; H, 5.93; N, 13.25.

1-Methyl-1′-(2-(1-methyl-2-pyridinio)ethyl)-2,3′-bipyridinium Triiodide (9). To a solution of 212 mg (0.602 mmol) of **7** in 2.5 mL of acetonitrile that was dried over molecular sieves for 2 days was added 1.5 mL (24 mmol) of methyl iodide. Following heating at about 100 °C in a sealed tube for 2 h and then cooling, a viscous red-orange oil appeared. After the solvent was decanted, the oil was crystallized from hot methanol with stirring and cooling. Recrystallization from water–isopropyl alcohol gave 113 mg of light yellow crystals: mp 175–178 °C dec; 24% yield; ^1H NMR (DMSO-d_6, TMS) [the protecting group is indicated by double primed numbers] δ 9.69 (H2′, 1 H, s), 9.42 (H6′, 1 H, d, $J_{5',6'}$ = 6.3 Hz), 9.33 (H6, 1 H, d, $J_{5,6}$ = 6.0 Hz), 9.10 (H6″, 1 H, d, $J_{5'',6''}$ = 6.0 Hz), 9.04 (H4′, 1 H, d, $J_{4',5'}$ = 8.4 Hz), 8.87 (H4, 1 H, t, $J_{3,4} \approx J_{4,5}$ = 8.0 Hz), 8.58 (H4″, 1 H, t, $J_{3'',4''} \approx J_{4'',5''}$ = 7.8 Hz), 8.52 (H5′, 1 H, dd), 8.39 (H5, 1 H, unresolved dd), 8.35 (H3, 1 H, partially overlaps 8.39, d), 8.09 (H5″, 1 H, unresolved dd), 8.05 (H3″, 1 H, d), 5.16 (NCH_2, t, J = 7.6 Hz), 4.43 (NCH_3, s), 4.28 (1-NCH_3, s), 3.961 (CCH_2, t, J = 7.5 Hz). Anal. Calcd for $C_{19}H_{22}N_3I_3 \cdot H_2O$: C, 33.02; H, 3.50; N, 6.08. Found: C, 33.19; H, 3.43; N, 6.17.

1-Methyl-2,3′-bipyridinium Iodide (3·I) from 9. Water was added dropwise to a mixture of 20 mg (0.029 mmol) of **9** in 3 mL of methanol until the solid dissolved. To the solution was added 40 mg of poly-4-vinylpyridine, and the resulting suspension was stirred overnight. The resin was removed and the solvent was evaporated to yield a yellow solid that was extracted with ethanol. The ethanol was evaporated and an orange solid crystallized on standing (mp 144–146 °C). The ^1H NMR of this orange solid is consistent with authentic **3** prepared from **6**.

Adduct 10 of 1,1′-Dimethyl-2,3′-bipyridinium Diiodide (2) in 4/1 DMSO-d_6/Methanol-d_4. To 22 mg (0.050 mmol) of **2** in an NMR tube was added 0.40 mL of DMSO-d_6 and 0.1 mL of methanol-d_4. After recording the proton spectrum, 16.9 μL (0.100 mmol) of 2,2,6,6-tetramethylpiperidine was added. The same proton NMR spectra were recorded 15 min and $1^3/_4$ h after the addition of the piperidine, showing a stable mixture of **2** and σ adduct **10**. A proton spectrum recorded 10 min after the addition of 13.7 μL (0.1 mmol) of 20% DCl in D_2O indicated the presence of almost completely regenerated **2**, leaving only a trace of the σ adduct: ^1H NMR of adduct **10** δ 8.80 (H6, d, $J_{5,6}$ = 6.3 Hz), 8.30–8.43 (H4 part of multiplet for H3, H5 and H5′ of **2**), 7.95 (H3, d, $J_{3,4}$ = 8.2 Hz), 7.74 (H5, t, $J_{4,5} \approx$ 7.1 Hz), 7.68 (H2′, s, 68% D incorporation) 6.88 (H4′, d, $J_{4',5'}$ = 9.8 Hz), 5.74 (H6′, d, $J_{5',6'}$ = 4.5 Hz), 5.46 (H5′, dd), 4.22 (1-NCH_3, s), 3.32 (1′-NCH_3, s).

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Registry No. 1, 110462-46-9; 2, 63095-08-9; 3·I, 134529-10-5; 3·ClO_4, 134529-12-7; 5·I, 134529-13-8; 5·ClO_4, 134529-21-8; 6, 134529-14-9; 7, 134529-15-0; 7·HCl, 134529-19-4; 8, 134529-16-1; 9, 134529-17-2; 10, 134529-18-3; 2,3′-bipyridine, 581-50-0; 4-(2-bromoethyl)-1-nitrobenzene, 5339-26-4; 2,3′-bipyridine dihydrochloride, 42907-60-8; 2-vinylpyridine, 100-69-6.

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