Table IV. ^{1}H NMR Spectra of Tricyclo[3.2.0.0^{2,7}]heptan-3-ones 24[a]

compd	CH_3	1-H	2-H	4x-H	4n-H	5-H	6x-H	6n-H	7-H
				Chemical Shifts, δ					
24a		3.00	1.98	2.33	1.87	2.83	2.69	1.23	2.11
24b	1.16	2.76	1.66	2.08	1.72	2.66	2.30	1.23	–
24c	1.12	2.74	–	2.25	1.85	2.67	2.54	1.18	1.81
24d	1.37	–	1.62	2.27	1.79	2.45	2.45	1.03	1.97

compd	1,2	1,5	1,6n	1,7	2,7	4x,4n	4x,5
			Coupling Constants:[b] J, Hz				
24a	3.6	3.6	3.6	3.6	6.8	16.4	5.5
24b	3.6	3.6	3.6	–	–	16.2	5.7
24c	–	3.0	3.0	3.0	–	16.8	5.3
24d	–	–	–	–	6.7	17.5	

compd	4x,6	5,4x	5,6x	5,7	6x,6n	6x,7
			Coupling Constants:[b] J, Hz			
24a	0.9	5.5	8.2	3.6	9.0	3.6
24b		5.7	7.4	–	9.3	–
24c		5.3	8.5	3.0	9.5	3.0
24d					9.2	3.0

[a] $CDCl_3$, 250 MHz. [b] Blanks indicate that coupling constants could not be obtained from first-order analysis of the spectra.

provided pure (96–99%) **26** (isolated yield 12–19%). All new compounds gave satisfactory elemental analyses.

The mass spectra of the isomers were virtually identical, e.g., **26d**: *m/e* 108 (M^+, 1), 93 (14), 91 (24), 81 (8), 80 (100), 79 (53), 77 (26), 53 (12). The ^{1}H NMR spectra consisted of unresolved multiplets, except for the methyl signal. **26b**: δ 1.17 (s, CH_3), 1.0–2.2 (m, 8 H), 2.3–2.6 (m, 1 H). **26c**: δ 1.10 (s + m, CH_3 + 1 H), 1.2–1.3 (m, 1 H), 1.35–2.5 (m, 7 H). **26d**: δ 1.10 (s, CH_3), 1.0–1.2 (m, 1 H), 1.2–1.55 (m, 1 H), 1.6–2.1 (m, 5 H), 2.25 (m, 1 H). Anal. Calcd for C_8H_{12}: C, 88.82; H, 11.18. Found, **26b**: C, 88.75; H, 11.27. Found, **26c**: C, 88.92; H, 11.16. Found, **26d**: C, 88.92; H, 11.18.

Conformational Studies of Annulated 2,2′-Bipyridinium Salts

Carmen Campá, Jaime Camps, José Font,* and Pedro de March

Departamento de Química Orgánica, Universidad Autónoma de Barcelona, Bellaterra, Barcelona, Spain

Received June 17, 1986

The synthesis of several 4,4′-disubstituted 2,2′-bipyridinium bridged diquaternary salts, by reaction of the corresponding 2,2′-bipyridines with several dibromide substrates, is reported. Further sulfonation of two of these salts gives rise to bridged 2,2′-bipyridines with zwitterionic character, **4a,b**. The twist angle between the two pyridine rings can be estimated from spectroscopic data of these salts. In a propane-bridged salt, **9b**, a barrier to conformational mobility of 16.5 kcal mol^{-1} has been obtained by a variable-temperature NMR experiment.

Interest in the chemistry of 2,2′-bipyridine and its derivatives has grown rapidly during recent years due to their applicability in a variety of fields. Derivatives of this biaryl molecule have been extensively used as effective ligands to coordinate a large diversity of metals. The corresponding ruthenium complexes are important photosensitizers in water decomposition studies.[1] Ruthenium complexes of bipyridine have also been attached to a polymer support and used as hydrogenation catalysts.[2] The ruthenium complex of 4-vinyl-4′-methyl-2,2′-bipyridine has been employed in electroactive polymer films, allowing the study of chemically modified electrodes.[3] Moreover, bridged diquaternary 2,2′-bipyridines have potent herbicide properties,[4] and similar or modified diquaternized 2,2′-bipyridinium molecules are being used as mediators or relays for photochemical hydrogen evolution from water.[5]

Ruthenium complexes of bipyridine have been covalently anchored to insoluble polymers, and these photosensitizers have been tried in sacrificial photoreduction of water.[6] Also, we have introduced several relay compounds

(1) (a) Kirch, M.; Lehn, J. M.; Sauvage, J. P. *Helv. Chim. Acta* **1979**, *62*, 1345. (b) Kiwi, J.; Borgarello, E.; Pelizzetti, E.; Visca, M.; Grätzel, M. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 646. (c) Sutin, N.; Creutz, C. *Pure Appl. Chem.* **1980**, *52*, 2717. (d) Keller, P.; Moradpour, A.; Amouyal, E.; Kagan, H. B. *Nouv. J. Chim.* **1980**, *4*, 377. (e) Degani, Y.; Willner, I. *J. Am. Chem. Soc.* **1983**, *105*, 6228. (f) Grätzel, M.; Kalyanasundaran, K.; Kiwi, J. *Solar Energy Materials*; Springer Verlag: Berlin, 1982; pp 37–126.

(2) Drago, R. S.; Nyberg, E. D.; El A'mma, A. G. *Inorg. Chem.* **1981**, *20*, 2461.

(3) (a) Gosh, P. K.; Spiro, T. G. *J. Am. Chem. Soc.* **1980**, *102*, 5543. (b) Abruña, H. D.; Denisevich, P.; Umaña, M.; Meyer, T. J.; Murray, R. W. *J. Am. Chem. Soc.* **1981**, *103*, 1. (c) Abruña, H. D.; Breiks, A. I.; Collum, D. B. *Inorg. Chem.* **1985**, *24*, 988.

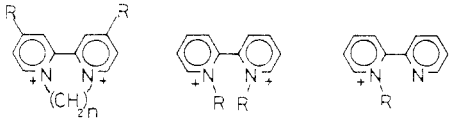
(4) Summers, L. A. *The Bipyridinium Herbicides*; Academic: New York, 1980.

(5) (a) Amouyal, E.; Zidler, B.; Keller, P.; Moradpour, A. *Chem. Phys. Lett.* **1980**, *74*, 314. (b) Keller, P.; Moradpour, A.; Amouyal, E.; Zidler, B. *J. Mol. Catal.* **1981**, *12*, 261. (c) Bourdelande, J. L.; Camps, J.; Font, J.; de March, P.; Brillas, E. *J. Photochem.* **1985**, *30*, 437.

(6) Bosch, P.; Campá, C.; Camps, J.; Font, J.; de March, P.; Virgili, A. *An. Quim., Ser. C* **1985**, *81*, 162.

0022-3263/87/1952-0521$01.50/0

that more effectively induce electron transport from the excited photosensitizer to the platinum catalyst, where water is reduced.[5c] These compounds are bridged diquaternary salts of type 1 and nonbridged diquaternized 2,2′-bipyridinium salts of type 2, with either sulfonic acid groups covalently bound to the R groups or bromide being the counteranions. We have also synthesized a monoquaternized compound of type 3.



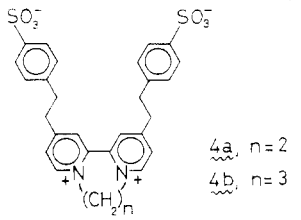
1 2 3

The conformation of these molecules, mainly the dihedral angle between both aromatic rings, has received much attention in the last years. Rebeck and co-workers[7] and Thummel et al.[8] have recently demonstrated the effect of annulation on the shape of these biaryl systems.

We report here not only the synthesis of new 2,2′-bipyridinium derivatives but also our conformational studies on these molecules, especially the ones that are of zwitterionic nature.

Synthesis

For photoreduction of water using colloidal SiO_2 as negative charged interface,[1e] zwitterionic neutral relay compounds with high negative redox potential are needed. We therefore set out to prepare **4a,b** from 4,4′-dimethyl-2,2′-bipyridine, **5**.[9] Thus, the dianion prepared from re-



4a, n = 2
4b, n = 3

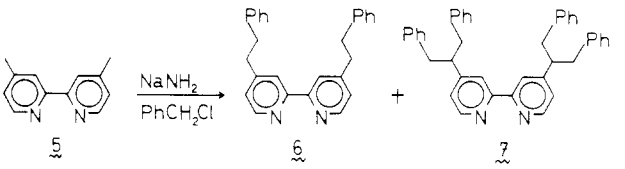
action of **5** with sodium amide was treated with benzyl chloride. This reaction gave a mixture of two benzylated products: the dibenzylated[10] and the tetrabenzylated bipyridines **6** (14%) and **7** (7%), respectively (Scheme I).

Two more steps were needed to obtain **4a,b** from **6**: sulfonation of the benzene rings and quaternization of the nitrogen atoms by annulation. Due to the conditions of the sulfonation reaction, we attempted it first and obtained 4,4′-bis(4-sulfonatophenethyl)-2,2′-bipyridinium, **8**, in 72% yield. However, all attempts to bridge the disodium salt of **8** with 1,2-dibromoethane or 1,3-dibromopropane failed (Scheme II).

Alternatively, when bipyridine **6** was refluxed in 1,2-dibromoethane, the 1,1′-ethano-bridged diquaternary bromide salt **9a** was isolated in 91% yield. This compound is water soluble, and in the absence of oxygen, addition of zinc gives a green color, demonstrating the formation of the corresponding radical cation. Similarly, **9b** was obtained in high yield from **6** and 1,3-dibromopropane, and its radical cation has a violet color.

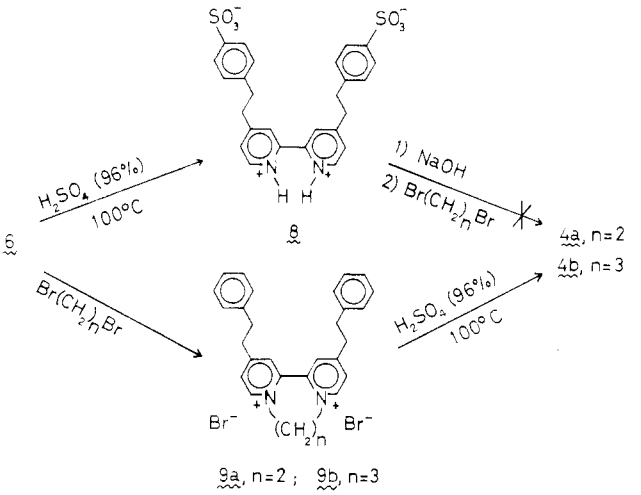
Both derivatives, **9a** and **9b**, were sulfonated under

Scheme I



5 6 7

Scheme II

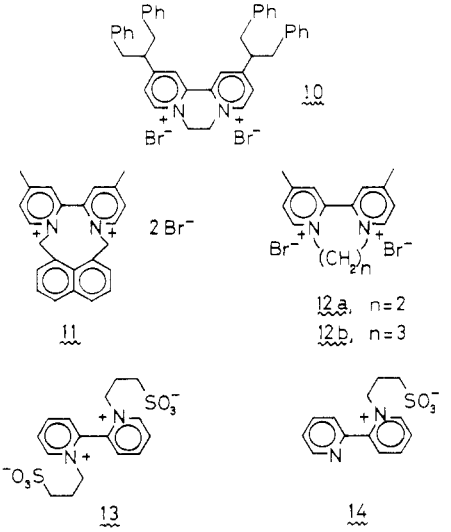


9a, n = 2 ; 9b, n = 3

standard conditions, affording the zwitterionic compounds **4a** and **4b**.[5c] These betaines were slightly soluble in water, but their solubility increased in the presence of electrolytes or in acidic media. The corresponding radical anions were also green and violet, respectively.

Compound **7** was also treated with 1,2-dibromoethane to provide the 1,1′-ethano-bridged diquaternary salt **10**. However, all attempts to obtain a tetrasulfonated derivative of **10**, which would open up the possibility of having a 2,2′-bipyridine relay with two formal negative charges in its oxidized form, proved unsuccessful.

Sulfonic acid groups could also be attached to the bridge, provided that it possessed aromatic character. For this purpose, we reacted **5** with 1,8-bis(bromomethyl)-naphthalene.[11] The bridged bipyridine **11** was isolated in 46% yield from this reaction, but all attempts to disulfonate the naphthalene nucleus were unsuccessful.



10 11 12a, n = 2 12b, n = 3 13 14

(7) (a) Rebeck, J., Jr.; Costello, T.; Wattley, R. *J. Am. Chem. Soc.* **1985**, *107*, 7487. (b) Rebeck, J., Jr.; Trend, J. E. *J. Am. Chem. Soc.* **1978**, *100*, 4315.

(8) Thummel, R. P.; Lefoulon, F.; Mahadevan, R. *J. Org. Chem.* **1985**, *50*, 3824.

(9) Sasse, W. H. F.; Whittle, C. P. *J. Chem. Soc.* **1961**, 1347.

(10) Bos, K. D.; Kraaijkamp, J. G.; Noltes, J. G. *Synth. Commun.* **1979**, *9*, 497.

(11) Vögtle, F.; Brombach, D. *Chem. Ber.* **1975**, *108*, 1682.

We also synthesized two known quaternized bridged bipyridines, namely, **12a**[12] and **12b**.[5a]

During the course of our work, the synthesis of a nonbridged zwitterionic bipyridine **13** was reported.[1e] Heating 2,2′-bipyridine and 1,3-propanesultone in *N,N*-dimethylformamide at 120 °C gave us the analogous monoquaternized **14** in 90% yield, while **13** was isolated in 55% yield only under reflux conditions.

Conformational Analysis

One can relate the dihedral angle between the aromatic rings of 2,2′-bipyridines with their spectroscopic properties. Early work by Homer et al.[12] correlated this angle with the ultraviolet absorption maxima of some diquaternized salts. Proton NMR spectra have also been related to the dihedral angle. Vögtle and Brombach[11] observed differences in the chemical shift of H_3 and H_5 of 2,2′-bipyridines, while Thummel et al.[8] analyzed the conformational mobility of the biaryl system by the multiplicity and coupling constants of the bridge protons.

A comparison study of the ultraviolet absorption maxima for our compounds and earlier reported values for some other bipyridinium salts indicates that when both rings are nearly coplanar, the absorption maxima are shifted to longer wavelengths: compare **12a** (305 nm) with our bridged compounds **4a**, **9a**, and **10** (310, 310, and 311 nm). Bridging the nitrogen atoms with a longer chain causes a larger dihedral angle, and the system loses conjugation: compare **12b** (284 nm) with **4b**, **9b**, and **11** (286, 286, and 280 nm). The nonbridged 2,2′-bipyridinium ions can attain an orthogonal conformation, thus minimizing the steric and electrostatic repulsive effects causing the absorption maxima to be hypsochromically shifted. Diquat (**2**, R = Me) is the most representative example, with λ_{max} = 269 nm. The zwitterionic compounds **13** and **14** (272 and 273 nm) have absorption maxima very similar to **2**, R = Me, therefore showing a twist angle close to 90°. Intermediate situations are found in 2,2′-bipyridine itself (284 nm) and **8** in basic medium (282 nm).

More striking information can be obtained from the difference in chemical shift between the H_3 and H_5 protons of the 2,2′-bipyridine system, as Vögtle and Brombach[11] have already pointed out. We have compared $\Delta\delta(H_3-H_5)$ values among some known compounds and the substances synthesized in this work. Compound **1** (R = H, n = 4), having noncoplanar pyridine rings, shows similar values for the chemical shifts of those protons: δ 8.41 and 8.46, respectively[11] ($\Delta\delta$ = −0.05 ppm). These values approximate the value for the corresponding protons in the pyridinium cation (δ 8.50).[13] Nevertheless, in compounds **1** (R = H, n = 3 and n = 2), H_3 is downfield shifted due to the anisotropic effect of the vicinal nearly coplanar aromatic ring: the differences $\Delta\delta$, 0.12 and 0.62 ppm, are thus an indirect measure of the dihedral angle.[11]

In most of our compounds, the $\Delta\delta(H_3-H_5)$ values can be easily obtained due to the absence of H_4. Compounds **9b**, **11**, and **12b**, having dihedral angles between 45 and 60° (molecular models), show small $\Delta\delta$ values (0.33, 0.14, and 0.09 ppm) as does the propano-bridged **1** (R = H, n = 3). On the other hand, **9a**, **10**, and **12a**, where an ethano bridge forces the rings to an almost coplanar situation, have higher values of $\Delta\delta$ (0 8, 0.5, and 0.6 ppm, respectively), similarly to compound **1** (R = H, n = 2). Nonbridged compounds **13** and **14** with rings in orthogonal disposition present a zero $\Delta\delta$ value.

Zwitterionic compounds **4a** and **4b** show unusual behavior, since the benzenesulfonate groups introduce an additional anisotropic effect. Proton H_3 (δ 7.58 and 7.95, respectively) is shielded in comparison with the nonsulfonated **9a** and **9b** (δ 7.58 and 8.66 ppm, respectively). This shielding is due to the folding of the sulfonated phenethyl moiety by charge electrostatic attraction between alternate sulfonate and pyridinium groups: protons H_3 lie, then, one below and the other above the benzene rings and are therefore clearly under their positive anisotropic cones. Molecular models indicate that this folding is more pronounced in **4a** than in **4b**, and the observed shielding is higher for **4a** since the latter is less planar.

Moreover, when the ^{1}H NMR spectrum of **4a** was run in D_2O/CF_3COOH, the resonance of H_3 shifted downfield to 8.27 ppm due to the more extended conformation required by protonation of the sulfonate group.

In all the 1,1′-ethano-bridged salts (**4a**, **9a**, **10**, and **12a**), the methylene protons appear as a sharp singlet in the range δ 5.1–5.3, indicating that for those quasi-planar systems all four protons are equivalent. A similar situation was observed by Thummel et al.[8] for 3,3′-ethano-bridged 2,2′-bipyridines.

The ^{1}H NMR spectrum of **11** in Me_2SO-d_6 at room temperature presents an AB system (δ 5.36 and 5.88 with J = 14.5 Hz) for the methylene protons, indicating the rigidity of the molecule. No modification of the spectrum was observed upon heating the solution up to 100 °C.

In the ^{1}H NMR spectrum of **12b** in D_2O at 27 °C, the central methylene protons appear as a broad multiplet (δ 2.6–3.1), while the protons of the other two methylene groups appear as complex absorptions in two well-defined zones (δ 4.3–4.7 and 4.8–5.2), indicating that this molecule is conformationally rigid on the NMR time scale. Comparing these absorptions with those observed for the 1,1′-ethano-bridged compounds, an upfield shift for one of the protons is noticed. This shift is explained by examination of a molecular model, which indicates that one of the α-protons points toward the shielding region of the adjacent pyridine and hence is shifted upfield to 4.3–4.7 ppm.

The spectrum of **12b** in Me_2SO-d_6 run at 27 °C is completely similar to that in water, but when the spectrum is obtained at 100 °C, the α-nitrogen methylene protons collapse to a well-defined triplet centered at 4.74 ppm, J = 6.7 Hz.

Compound **9b** has a similar behavior. At 27 °C (Me_2SO-d_6), it presents complex absorptions at 2.6–3.0 (central methylene), 4.3–4.8 (α-methylene proton pointing toward the pyridine ring), and 4.9–5.3 ppm (the other α-methylene proton). When the temperature was raised in 5 °C increments, the coalescence temperature was determined to be 335 K. Assuming a value of J = 14 Hz for the geminal coupling constant, $\Delta G^{\ddagger}$ was calculated by the Gutowsky equation to be 16.5 kcal/mol. This value is somewhat higher than the one found for a similar trimethylene-bridged biphenyl system[7a] ($\Delta G^{\ddagger}$ = 14.6 kcal/mol) and in excellent agreement with the $\Delta G^{\ddagger}$ value (16.8 kcal/mol) determined for a diprotonated 2,2′-bipyridine.[7b]

This conformational rigidity of 1,1′-propano-bridged bipyridinium salts at 27 °C has also to be contrasted with the mobility shown by 3,3′-propano-bridged bipyridines reported by Thummel et al.[8] In our case, the presence of the two quaternary nitrogens should cause the higher barrier for conformational inversion, as was already pointed out by Rebeck and Trend.[7b] MNDO and MM2 energy calculations for these compounds are being performed in our laboratory and will be reported elsewhere.

(12) Homer, R. F.; Tomlinson, T. E. *J. Chem. Soc.* **1960**, 2498.

(13) Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden*, Springer Verlag: Berlin, 1976.

Experimental Section

^1H NMR and ^{13}C NMR were recorded on a Bruker WP80SY spectrometer. Infrared spectra were recorded on a Perkin-Elmer 1310 spectrometer and ultraviolet spectra on a Perkin-Elmer 550 spectrometer. Mass spectra were obtained on a Hewlett-Packard 5985-B GC-MS system.

Reaction between 4,4′-Dimethyl-2,2′-bipyridine (5) and Benzyl Chloride. The reaction between **5**[9] (2.76 g, 15 mmol) and benzyl chloride (4 mL, 35 mmol) was performed according to Bos et al.[10] A flash column chromatography with chloroform/ethanol (99:1) afforded two main products: 4,4′-bis(1-benzylphenethyl)-2,2′-bipyridine, **7** (mp 198–200 °C), and 4,4′-bis(phenethyl)-2,2′-bipyridine, **6** (mp 148–149 °C, lit.[10] mp 147–149 °C). Spectral data for **7**: ^1H NMR ($CDCl_3$) δ 3.0 (d, 8 H, J = 6 Hz), 6.88 (dd, 2 H, J = 6 Hz, J' = 2 Hz), 7.1 (m, 20 H), 8.26 (d, 2 H, J = 2 Hz), 8.44 (d, 2 H, J = 6 Hz); ^{13}C NMR ($CDCl_3$) δ 41.6, 49.5, 120.4, 123.6, 126.1, 128.2, 129.0, 139.6, 148.8, 154.4, 156.1.

Spectral data for **6**: ^1H NMR coincident with data reported by Bos et al.;[10] ^{13}C NMR ($CDCl_3$) δ 36.5, 37.2, 121.2, 123.8, 126.1, 128.3, 128.35, 140.8, 148.9, 151.5, 156.2; UV (ethanol) λ_{max} 284 and 241 nm.

4,4′-Bis(4-sulfonatophenethyl)-2,2′-bipyridinium (8). A solution of **6** (109 mg, 0.3 mmol) in 1.5 mL of concentrated sulfuric acid (96%) was heated at 100 °C for 25 min. The cooled solution was poured over 5 g of ice–water, and the white precipitate formed was filtered off and washed with cold water, ether, and pentane, affording **8** (113 mg, 72%): ^1H NMR (D_2O) δ 3.1 (m, 8 H), 7.13 (d, 4 H, J = 8 Hz), 7.33 (d, 2 H, J = 2 Hz), 7.55 (dd, 2 H, J = 6 Hz, J' = 2 Hz), 7.63 (d, 4 H, J = 8 Hz), 8.51 (d, 2 H, J = 6 Hz); ^1H NMR (CD_3OD/Na_2CO_3) δ 3.1 (s, 8 H), 7.21 (d, 4 H, J = 8 Hz), 7.33 (dd, 2 H, J = 6 Hz, J' = 2 Hz), 7.7 (d, 4 H, J = 8 Hz), 8.12 (d, 2 H, J = 2 Hz), 8.15 (d, 2 H, J = 6 Hz); UV (ethanol/HCl) λ_{max} 299 nm; UV (ethanol/Na_2CO_3) λ_{max} 282 nm.

Anal. Calcd for $C_{26}H_{24}N_2S_2O_6 \cdot 2H_2O$: C, 55.71; H, 5.00; N, 5.00. Found: C, 55.89; H, 4.56; N, 4.96.

2,11-Diphenethyl-6,7-dihydrodipyrido[1,2-*a*:2′,1′-*c*]pyrazinium Dibromide (9a). A mixture of **6** (250 mg, 0.68 mmol) and 4 mL of 1,2-dibromoethane was refluxed for 24 h, and a precipitate was formed. After cooling, the precipitate was filtered off and washed with pentane, affording 344 mg of a white solid identified as **9a** (91% yield): ^1H NMR (CD_3OD) δ 3.05–3.6 (m, 8 H), 5.3 (s, 4 H), 7.3 (m, 10 H), 8.14 (dd, 2 H, J = 6 Hz, J' = 2 Hz), 8.94 (d, 2 H, J = 2 Hz), 9.07 (d, 2 H, J = 6 Hz); ^{13}C NMR (D_2O) δ 35.8, 38.2, 52.8, 127.9, 129.0, 130.0, 130.1, 131.4, 139.4, 140.5, 147.0, 166.5; UV (water) λ_{max} 310 and 231 nm.

Anal. Calcd for $C_{28}H_{28}N_2Br_2 \cdot H_2O$: C, 58.94; H, 5.26; N, 4.91. Found: C, 58.70; H, 5.05; N, 4.74.

2,11-Bis(4-sulfonatophenethyl)-6,7-dihydrodipyrido[1,2-*a*:2′,1′-*c*]pyrazinium (4a). To 130 mg (0.36 mmol) of **9a** was added 2 mL of concentrated sulfuric acid (96%), and immediate evolution of hydrogen bromide was observed. When this evolution stopped, the solid was completely dissolved and the solution was heated for 25 min at 100 °C. The solution was cooled and poured over 10 g of ice–water, and $NaHCO_3$ was added to reach pH 2–3. A precipitate was formed, and it was filtered off and washed with cold water, yielding 50 mg (38% yield) of a white solid that was identified as **4a**. The solid was insoluble in methanol and slightly soluble in water, and its solubility increased in the presence of electrolytes: ^1H NMR (D_2O) δ 3.0–3.6 (m, 4 H), 5.1 (s, 4 H), 7.18 (d, 4 H, J = 8 Hz), 7.58 (d, 2 H, J = 2 Hz), 7.63 (d, 4 H, J = 8 Hz), 8.02 (dd, 2 H, J = 6 Hz, J' = 2 Hz), 8.9 (d, 2 H, J = 6 Hz); ^1H NMR (D_2O/CF_3COOH) δ 3.0–3.6 (m, 4 H), 5.13 (s, 4 H), 7.24 (d, 4 H, J = 8 Hz), 7.64 (d, 4 H, J = 8 Hz), 8.0 (dd, 2 H, J = 6 Hz, J' = 2 Hz), 8.27 (d, 2 H, J = 2 Hz), 8.92 (d, 2 H, J = 6 Hz); UV (water) λ_{max} 310 nm.

2,12-Diphenethyl-7,8-dihydro-6*H*-dipyrido[1,2-*a*:2′,1′-*c*][1,4]diazepinium Dibromide (9b). The synthesis and spectroscopic data of this compound have been described elsewhere.[5c]

2,12-Bis(4-sulfonatophenethyl)-7,8-dihydro-6*H*-dipyrido[1,2-*a*:2′,1′-*c*][1,4]diazepinium (4b). This compound has also been described.[5c]

2,11-Bis(1-benzylphenethyl)-6,7-dihydrodipyrido[1,2-*a*:2′,1′-*c*]pyrazinium Dibromide (10). A solution of **7** (160 mg, 0.29 mmol) in 3 mL of 1,2-dibromoethane was refluxed for 16 h, during which time a precipitate was formed. The mixture was cooled and filtered, and the solid was washed with chloroform and pentane, affording 207 mg of a white solid identified as **10** (94% yield). This compound was very soluble in methanol and slightly soluble in water: ^1H NMR (CD_3OD) δ 3.3 (m, 8 H), 4.0 (m, 2 H), 5.21 (s, 4 H), 7.25 (m, 20 H), 8.20 (dd, 2 H, J = 6 Hz, J' = 2 Hz), 8.67 (d, 2 H, J = 2 Hz), 9.03 (d, 2 H, J = 6 Hz); UV (ethanol) λ_{max} 311 nm.

Anal. Calcd for $C_{42}H_{40}N_2Br_2 \cdot 3/2H_2O$: C, 66.40; H, 5.73; N, 3.69. Found: C, 66.16; H, 5.59; N, 3.72.

2,17-Dimethyl-6*H*,13*H*-naphtho[*fg*]dipyrido[1,2-*a*:2′,1′-*c*][1,4]diazonium Dibromide (11). Compounds **5** and 1,8-bis(bromomethyl)naphthalene were allowed to react, following the procedure described by Vögtle and Brombach[11] (46% yield): ^1H NMR (D_2O) δ 2.8 (s, 6 H), 5.0 (d, 2 H, J = 16 Hz), 5.6 (d, 2 H, J = 16 Hz), 7.4 (dd, 2 H, J = 10 Hz, J' = 8 Hz), 7.9 (m, 4 H), 8.22 (d, 2 H, J = 6 Hz), 8.36 (br s, 2 H), 9.4 (d, 2 H, J = 6 Hz); ^1H NMR (Me_2SO-d_6) δ 2.75 (s, 6 H), 5.36 (d, 2 H, J = 14.5 Hz), 5.88 (d, 2 H, J = 14.5 Hz), 7.68 (dd, 2 H, J = 10 Hz, J' = 8 Hz), 8.20 (d, 2 H, J = 10 Hz), 8.27–8.51 (m, 4 H), 8.57 (br s, 2 H), 9.62 (d, 2 H, J = 6 Hz); ^{13}C NMR (D_2O/dioxane) δ 23.2, 62.5, 127.15, 127.26, 132.5, 133.1, 133.9, 136.3, 136.6, 138.2, 144.2, 146.3, 165.3; IR (KBr) 3410, 3340, 3080–2900, 1640 cm^{-1}; UV (water) λ_{max} 280 nm.

Anal. Calcd for $C_{24}H_{22}N_2Br_2 \cdot 3/2H_2O$: C, 54.87; H, 4.79; N, 5.33. Found: C, 54.76; H, 4.69; N, 5.35.

2,11-Dimethyl-6,7-dihydrodipyrido[1,2-*a*:2′,1′-*c*]pyrazinium Dibromide (12a). The procedure of Homer and Tomlinson[12] was modified. A solution of 184 mg (1 mmol) of 4,4′-dimethyl-2,2′-bipyridine in 5 mL of 1,2-dibromoethane was refluxed for 24 h, during which time a precipitate was formed. The mixture was cooled and filtered, and the precipitate was washed with acetone and pentane to afford 370 mg (95% yield) of a white crystalline solid identified as **12a**: ^1H NMR (D_2O) δ 2.85 (s, 6 H), 5.27 (s, 4 H), 8.18 (d, 2 H, J = 6 Hz), 8.78 (s, 2 H), 8.98 (d, 2 H, J = 6 Hz); ^{13}C NMR (D_2O) δ 24.6, 54.3, 131.2, 133.3, 141.1, 148.1, 165.9; UV (water) λ_{max} 305 nm.

2,12-Dimethyl-7,8-dihydro-6*H*-dipyrido[1,2-*a*:2′,1′-*c*][1,4]diazepinium Dibromide (12b).[5a] A mixture of 368 mg (2 mmol) of 4,4′-dimethyl-2,2′-bipyridine in 1,3-dibromopropane (5 mL) was heated at 125 °C for 24 h. After filtration, the solid was washed with acetone and pentane to give **12b** (733 mg, 95% yield): ^1H NMR (D_2O) δ 2.66 (s, 6 H), 2.6–3.1 (m, 2 H), 4.3–4.7 (m, 2 H), 5.0 (dt, 2 H, J = 14 Hz, J' = 4.5 Hz), 8.21 (d, 2 H, J = 6 Hz), 8.30 (s, 2 H), 9.0 (d, 2 H, J = 6 Hz); ^1H NMR (Me_2SO-d_6, 100 °C) δ 2.7 (s, 6 H), 2.6–3.1 (m, 2 H), 4.74 (t, 4 H, J = 6.7 Hz), 8.3 (d, 2 H, J = 6 Hz), 8.45 (s, 2 H), 9.25 (d, 2 H, J = 6 Hz); ^{13}C NMR (D_2O) δ 24.4, 32.5, 57.8, 133.7, 134.6, 145.3, 148.6, 165.8; UV (water) λ_{max} 284 nm.

1,1′-Bis(3-sulfonatopropyl)-2,2′-bipyridinium (13). Although this product has been described,[1e] it was prepared by a modified procedure. A solution of 2,2′-bipyridine (0.78 g, 5 mmol) and propanesultone (1.83 g, 15 mmol) in *N*,*N*-dimethylformamide was refluxed for 24 h, and a precipitate was formed. After cooling, the crude was filtered and washed with methanol (to dissolve the monoreaction product) to afford 1.1 g (55% yield) of **13**: ^1H NMR (D_2O) δ 2.0–2.6 (m, 4 H), 2.8 (t, 4 H, J = 7 Hz), 4.0–5.0 (m, 4 H), 8.25–8.55 (m, 4 H), 8.85 (t, 2 H, J = 7 Hz), 9.3 (d, 2 H, J = 5 Hz); ^{13}C NMR (D_2O) δ 26.9, 48.0, 59.1, 132.6, 132.8, 143.3, 149.1, 149.3; UV (water) λ_{max} 272 nm.

Anal. Calcd for $C_{16}H_{20}N_2S_2O_6 \cdot 3/2H_2O$: C, 44.96; H, 5.38; N, 6.56. Found: C, 44.90; H, 5.03; N, 6.62.

1-(Sulfonatopropyl)-2-(2-pyridyl)pyridinium (14). A solution of 2,2′-bipyridine (1.56 g, 10 mmol) and propanesultone (2.68 g, 22 mmol) in 12 mL of *N*,*N*-dimethylformamide was heated for 24 h at 120 °C. The formed precipitate was filtered after cooling and washed with acetone and pentane to give 2.52 g of crude **14** (90% yield). This solid contained 5% of the product of double alkylation, **13**. The compound was purified by dissolving it in methanol, filtration of the insoluble material, and recrystallization of the monosulfonate in acetone. The desired **14** was obtained as a solid (2.16 g, 77% yield): ^1H NMR (D_2O) δ 2.27 (m, 2 H), 2.76 (t, 2 H, J = 7 Hz), 4.73 (t, 2 H, J = 7 Hz), 7.6–8.3

(m, 5 H), 8.61 (dd, 1 H, J = 8 Hz, J' = 2 Hz), 8.75 (m, 1 H), 9.05 (d, 1 H, J = 7 Hz); ^{13}C NMR (D_2O) δ 26.9, 48.3, 58.5, 127.0, 127.5, 129.3, 131.4, 140.2, 147.1, 147.6, 149.8, 150.9, 153.2; UV (water) λ_{max} 273 nm.

Anal. Calcd for $C_{13}H_{14}N_2SO_3$: C, 56.11; H, 5.04; N, 10.07. Found: C, 55.90; H, 5.13; N, 9.90.

Supplementary Material Available: IR spectra for compounds **4a** and **6** and mass spectra for compounds **6** and **7** (1 page). Ordering information is given on any current masthead page.

Synthesis of Substituted 1,4-Oxathianes. Mechanistic Details of Diethoxytriphenylphosphorane- and Triphenylphosphine/Tetrachloromethane-Promoted Cyclodehydrations and ^{13}C NMR Spectroscopy

William T. Murray, Jeffery W. Kelly, and Slayton A. Evans, Jr.*

William Rand Kenan, Jr., Laboratories of Chemistry, University of North Carolina, Chapel Hill, North Carolina 27514

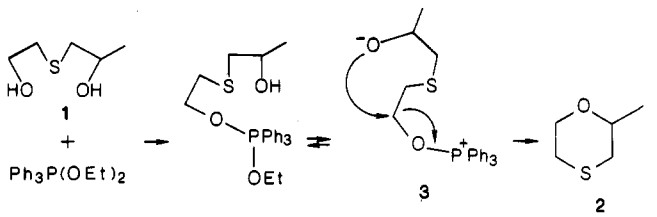
Received June 6, 1986

Diethoxytriphenylphosphorane (DTPP) initiates stereospecific cyclodehydrations of 2,2′-bis(hydroxyethyl) sulfides to the corresponding 1,4-oxathianes in a single step (70–85%) by GLC and ^{13}C NMR analyses. The mechanistic details of Ph_3P/CCl_4- and $Ph_3P(OEt)_2$-promoted cyclodehydrations are probed by specific deuterium labeling in combination with ^{1}H and ^{13}C NMR spectroscopy. Carbon-13 NMR shift correlations, which are valuable for stereochemical and conformational assignments of substituted 1,4-oxathianes, are also reported.

Substituted 1,4-oxathianes are important precursors in the synthesis of biologically significant 1,4-oxathiins, which are themselves useful as fungicides and pesticides.[1] In addition, stereochemical and conformational descriptions of substituted 1,4-oxathianes and their *S*-oxides have attracted considerable attention.[2] While several preparative methods are available for their construction, few exhibit the synthetic versatility suitable for strategic placement of various substituents within the basic heterocycle.[3]

Results of recent studies from our laboratories have demonstrated that diethoxytriphenylphosphorane (DTPP) is useful for converting diols to cyclic ethers,[4] α,ω-mercapto alcohols to cyclic sulfides,[5] and β-amino alcohols to aziridines.[6] Therefore, we envisioned that DTPP would efficiently convert substituted 2,2′-bis(hydroxyethyl) sulfides to 1,4-oxathianes. It seemed reasonable that this objective could also be accomplished with high regio- and stereospecificity since the mechanism of cyclodehydration of diols with DTPP does not involve steps that would compromise the stereochemical integrity of critical stereocenters.[4]

Scheme I



Cyclodehydration. The specific formulation described in Scheme I represents the synthetic format as well as the mechanistic rationale for DTPP-promoted cyclodehydration of 1,5-diols. Specifically, reaction of 2-hydroxypropyl 2-hydroxyethyl sulfide (1) [prepared by regiospecific mercaptide (i.e., $^-SCH_2CH_2OH$) ring opening of propylene oxide][7] with DTPP (40 °C, 48 h) affords 2-methyl-1,4-oxathiane (**2**; 80% by GLC and ^{13}C NMR).

From Scheme I, cyclodehydration of diol **1** with DTPP requires initial phosphoranylation of the primary hydroxyl group[8] followed by loss of ethanol to afford betaine **3**, the quintessential intermediate governing cyclization. In fact, the stereospecific syntheses of *trans*- and *cis*-2,3-dimethyl-1,4-oxathiane (*trans*-**4**, *cis*-**4**) from reaction of *threo*- and *erythro*-2-hydroxy-3-[(2-hydroxyethyl)thio]-butane (*threo*-**5**, *erythro*-**5**) with DTPP (see Table I) strongly support initial phosphoranylation of the primary hydroxyl and subsequent intramolecular displacement of triphenylphosphine oxide (TPPO) by secondary alkoxide ion from an intermediate synonymous to **3** (vide infra).

Generally, the cyclodehydration of 2,2′-bis(hydroxyethyl) sulfides with DTPP gives substituted 1,4-oxathianes in yields ranging from 66 to 85% by GLC and ^{13}C NMR analyses (Table I). These results are especially significant when comparisons are made with other popular prepara-

(1) (a) von Schmeling, B.; Kulka, M. *Science (Washington, D.C.)* **1960**, *152*, 659. (b) King, R. R.; Greenhalgh, R.; Marshall, D. D. *J. Org. Chem.* **1978**, *43*, 1262. (c) Rooney, R. P.; Dyer, J. C.; Evans, S. A., Jr. *Org. Magn. Reson.* **1981**, *16*, 266–272.

(2) (a) Frieze, D. M.; Evans, S. A., Jr. *J. Org. Chem.* **1975**, *40*, 2690. (b) Frieze, D. M.; Hughes, P. H.; Merrill, R. L.; Evans, S. A., Jr. *J. Org. Chem.* **1977**, *42*, 2206. (c) Rooney, R. P. Ph.D. Thesis, University of North Carolina, 1980. (d) Carretero, J. C.; Garcia Ruano, J. L.; Radriquez, J. H. *Tetrahedron Lett.* **1984**, *25*, 3029–3032. (e) Lee, D.; Keifer, J. C.; Rooney, R. P.; Garner, T. B.; Evans, S. A., Jr. *J. Org. Chem.* **1979**, *44*, 2580. (f) Evans, S. A., Jr.; Goldsmith, B.; Merrill, R. L., Jr.; Williams, R. E. *J. Org. Chem.* **1977**, *42*, 438. (g) Zefirov, N. S.; Balgoveshchensky, U. S.; Kazimirchik, I. V.; Surova, N. S. *Tetrahedron* **1971**, *27*, 3111. (h) Hronowski, J. J.; Szarek, W. A. *J. Med. Chem.* **1982**, *25*, 522–526. (i) Lopez Aparicio, F. J.; Zorrilla Benitez, F.; Santoyo Gonzalez, F. *Carbohydr. Res.* **1982**, *110*, 195–205. (j) Trost, B. M.; Vladuchick, W. C.; Bridges, A. J. *J. Am. Chem. Soc.* **1980**, *102*, 3554–3572. (k) Mattay, J.; Dittmer, C. *J. Org. Chem.* **1986**, *51*, 1894–1897.

(3) Pihlaja, K.; Pasaner, P. In *The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups, and Their Sulfur Analogs*; Patai, S., Ed.; Wiley: Chichester, 1980; p 845.

(4) Robinson, P. L.; Barry, C. N.; Kelly, J. W.; Evans, S. A., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 5210–5219.

(5) Robinson, P. L.; Kelly, J. W.; Evans, S. A., Jr. *Phosphorus Sulfur*, in press.

(6) Kelly, J. W.; Eskew, N. L.; Evans, S. A., Jr. *J. Org. Chem.* **1986**, *51*, 95.97.

(7) (a) Owen, L. N.; Smith, P. N. *J. Chem. Soc.* **1951**, 2973. (b) Rooney, R. P.; Evans, S. A., Jr. *J. Org. Chem.* **1980**, *45*, 180–183.

(8) Kelly, J. W.; Evans, S. A., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7681–7685.

0022-3263/87/1952-0525$01.50/0