dation for Medical Research for a Fellowship awarded to one of us (S.K.D.). The grant from the Alberta Hertiage Foundation to purchase the Bruker AM-300 spectrometer is also gratefully acknowledged.

Registry No. **1a**, 61340-79-2; **1b**, 33707-36-7; **1c**, 35022-78-7; **1d**, 52358-23-3; **2a**, 96212-65-6; **2b**, 96212-66-7; **2c**, 96212-67-8; **2d**, 96212-68-9; **3**, 96212-69-0; **4a**, 96212-70-3; **4b**, 95610-88-1; **4c**, 96212-71-4; **4d**, 96227-28-0; **5a**, 96212-72-5; **5b**, 96212-73-6; **5c**, 96212-74-7; **6**, 96212-75-8; **7a**, 96212-76-9; **7b**, 96212-77-0; **7c**, 96212-78-1; **8a**, 96212-79-2; **8b**, 96212-80-5; **8c**, 96227-29-1; **9**, 96212-81-6; **10**, 96212-82-7; **11**, 96212-83-8; PhCONHOH, 495-18-1; PhOCONHOH, 38064-07-2; *N*-[(benzyloxy)carbonyl]hydroxylamine, 3426-71-9.

Chelate and Macrocycle Effects in the 2,2′-Bipyridine *N*,*N*′-Dioxide Complexation of Alkyltin Trichlorides

Howard Edan Katz

AT&T Bell Laboratories, Murray Hill, New Jersey 07974

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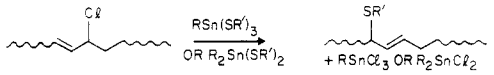
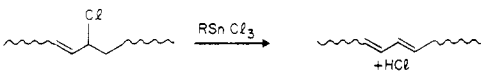
The synthesis of macrocyclic ligands **3**, **4**, and **7** for alkyltin trichloride ($RSnCl_3$) encapsulation is described. Key reactions were the condensation of *p*-$MeOCH_2C_6H_4MgBr$ with 6,6′-dibromo-2,2′-bipyridine, ring closures in dimethylformamide containing Cs_2CO_3, and oxidation of a bipyridyl precursor (**1**) to its *N*,*N*′-dioxide with buffered aqueous H_2O_2 in AcOH. The preparation of 4,4′-di-*tert*-butyl-2,2′-bipyridine 1,1′-dioxide (**8**) is also reported. The affinity of **8** for $MeSnCl_3$ was greater than that of 4-*tert*-butylpyridine 1-oxide, while the affinity of **7** was less than that of **5**. However, **7** was a better inhibitor of the $BuSnCl_3$-catalyzed degradation of *trans*-4-chloro-5-decene than **5**. The ability of the ligands to bind $RSnCl_3$ is evaluated in light of earlier work on organotin chloride–Lewis base interactions, and the relevance of the experiments to the design of additives for alkyltin trithiolate stabilizers for poly(vinyl chloride) is considered.

Monoalkyltin(IV) thiolates ($RSn(SR')_3$) are effective short-term color stabilizers[1] for poly(vinyl chloride) (PVC). This may be attributed to their ability to convert allylic and tertiary chloride moieties at defect sites on the polymer into much more stable alkyl sulfide groups, thereby preventing dehydrochlorination reactions that lead to the unwanted formation of colored polyene chains. Unfortunately, the byproducts of the stabilization process include Lewis acidic monoorganotin trichlorides ($RSnCl_3$), which catalyze[2] the very dehydrochlorinations that are supposed to be prevented by the stabilizers. Because of this serious disadvantage, $RSn(SR')_3$ stabilizers are of limited utility[2] in commercial PVC.

Model reactions for both the stabilization[3] and dehydrochlorination[4] processes have recently been described,



STABILIZATION REACTION



DEHYDROCHLORINATION REACTION

and the mechanisms seem to involve coordination of the chloride leaving group to the tin atom. It was demonstrated[4] that weak Lewis bases, which form complexes with $RSnCl_3$, retard the $RSnCl_3$-promoted elimination of HCl from an allylic chloride in nonpolar media, with a direct correlation between the effectiveness of the base as an inhibitor of dehydrochlorination and the affinity of the base for the tin atom in solution. In addition, the model stabilization reaction was found to occur even in the presence of the Lewis bases. Therefore, it was proposed that a PVC stabilizer formulation containing $RSn(SR')_3$ and a Lewis base might forestall the degradation of PVC over a longer time than would the thiolate alone.

Among the Lewis bases considered, pyridine *N*-oxide was the superior inhibitor of allylic chloride degradation and also the strongest complexing agent for $RSnCl_3$. It was therefore of interest to investigate the $RSnCl_3$-complexing behavior of pyridine *N*-oxide groups when incorporated into chelating and macrocyclic ligands. If chelating ligands were to exhibit stronger $RSnCl_3$ affinities than monodentate ligands, the former would be expected to act as improved dehydrochlorination inhibitors based on previous studies.[4] Macrocyclic ligands might further deactivate $RSnCl_3$ by sterically blocking access of the labile substrate to the catalytically important orbitals on the tin atom.

In this paper, we report full experimental details of the synthesis of novel chelating and macrocyclic ligands for $RSnCl_3$. The ability of the ligands to bind $RSnCl_3$ is evaluated in light of earlier work on organotin chloride–Lewis base interactions, and the action of a macrocyclic bipyridine *N*,*N*′-dioxide as an inhibitor of $RSnCl_3$-catalyzed allylic chloride degradation is briefly considered. Some of the synthetic methodology has been reported in a preliminary communication.[5]

Results

The synthesis of the bipyridine cycles is outlined in Schemes I and II. The Grignard reagent[6] from 1-bromo-4-(methoxymethyl)benzene was coupled to 6,6′-dibromo-2,2′-bipyridine[7] with $(PPh_3)_2NiCl_2$ to obtain di-

(1) Brecker, L. R. *Pure Appl. Chem.* **1981**, *53*, 577–82.
(2) Rockett, B. W.; Hadlington, M.; Poyner, W. R. *J. Appl. Polym. Sci.* **1974**, *18*, 745–52. Van Hoang, T.; Michel, A.; Guyot, A. *Polym. Degradation Stab.* **1980–1981**, *3*, 137–44.
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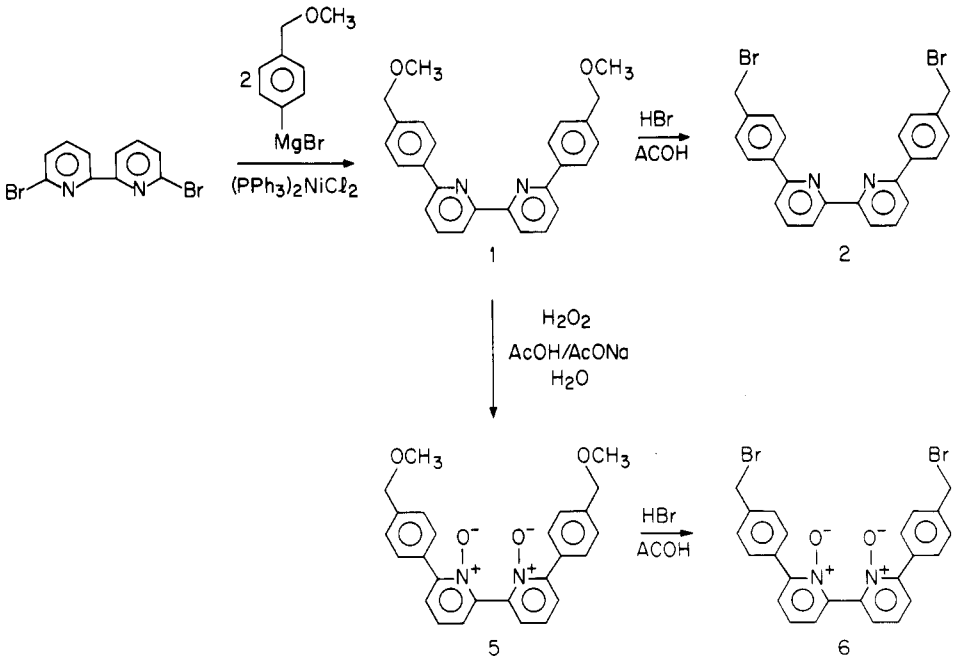
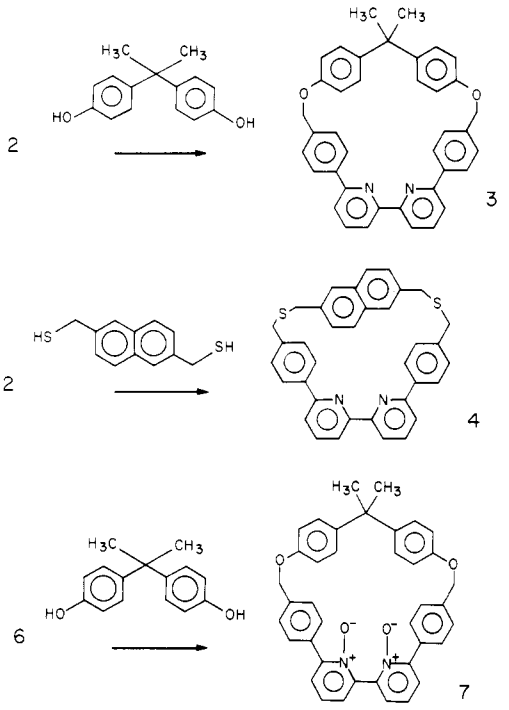
Scheme I



Scheme II



ether **1**. Although the yield was moderate (34% on a 3.2-mmol scale), the only purification required was a trituration. Rigorously dry catalyst and efficient mechanical stirring were essential for the reaction to proceed.

The benzyl methyl ether linkages of **1** were converted to benzyl bromide groups with a saturated solution of HBr in AcOH. An alternative means of preparing **2** was first to synthesize 6,6′-bis(*p*-tolyl)-2,2′-bipyridine from *p*-$CH_3C_6H_4MgBr$ analogous to the synthesis of **1** and then to treat the adduct with *N*-bromosuccinimide in CCl_4 under irradiation. This method proved inferior due to the irreproducibility of the radical bromination and the difficulty in separating **2** from contaminants which contained CH_3 and $CHBr_2$ groups.

Three bridging reagents were employed in attempts to cyclize **2**. One was the commercially available 4,4′-isopropylidenebis(phenol) ("Bisphenol A"). The other two were synthesized from 2,6-naphthalenedicarboxylic acid; reduction of the diacid with $BH_3{\cdot}(CH_2)_4O$ gave 2,6-naphthalenedimethanol,[8] which was converted to the corresponding dithiol[9] by the action[10] of thiourea in 48% aqueous HBr, followed by alkaline hydrolysis in 50% aqueous EtOH (1 h, reflux). The two diols, when caused to react with **2** in $(CH_2)_4O$ at reflux using NaH as base under high dilution conditions, each produced macrocyclic products in ≤1% yields that were not improved when dimethylformamide or *N*-methylpyrrolidinone was present. Gel permeation chromatography suggested that these trace products may have been cyclic dimers (bis[bipyridines]). On the other hand, the diphenol and the dithiol suffered deprotonation by Cs_2CO_3 in dimethylformamide and were cyclized with **2** according to the conditions of Kellogg[11] to obtain **3** and **4** in respectable yields.

Because of the poor solubility of **2** in CH_2Cl_2 or AcOH and the tendency of the bipyridine cycles to suffer oxidative degradation, the conversion of the bipyridine unit to the *N*,*N*′-dioxide (for the synthesis of **7**) was best accomplished on **1**. Hydrogen peroxide in buffered aqueous AcOH at 60 °C proved to be a milder and more selective reagent for the conversion of **1** to **5** than H_2O_2/AcOH at 100 °C[12] or *m*-chloroperbenzoic acid[13] in CH_2Cl_2; the latter reagents promoted the decomposition of **1**. The peracid did, however, cleanly convert 4,4′-di-*tert*-butyl-2,2′-bipyridine[14] to its *N*,*N*′-dioxide (**8**). Macrocyclic bipyridine dioxide **7** was obtained from **5** with the same series of reagents and conditions as for the preparation of **3** from **2**, in a yield comparable to the bipyridine cyclizations.

The formation of complexes between the bipyridine dioxides (and 4-*tert*-butylpyridine *N*-oxide) and $MeSnCl_3$

(8) This compound had been synthesized in three steps from 2,6-dimethylnaphthalene. Ando, T.; Nakagawa, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 363–70.
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Table I. Changes in Selected ^1H NMR Chemical Shifts of Ligands and $MeSnCl_3$ upon Complexation at 30 °C

ligand	solv	concn,[a] M	protons	δ(free)	δ(complexed)
8	CD_3CN	0.021	*t*-Bu	1.334	1.435
			H-3	7.48	7.97
			H-6	8.11	8.57
			CH_3Sn	1.73	1.24
9	CD_3CN	0.041[b]	*t*-Bu	1.296	1.356
			H-3,5	7.32	7.69
			H-2,6	8.01	8.51
			CH_3Sn	1.73	1.05
5	50:50 CD_3CN–$CDCl_3$	0.010	OCH_3	3.386	3.354
			CH_2O	4.493	4.501
			pyr-H	7.48[c]	7.95[c]
			CH_3Sn	1.73	0.321[d]
7	50:50 CD_3CN–$CDCl_3$	0.010	$C(CH_3)_2$	1.508	1.476
			CH_2O	5.187[d]	5.26[e]
			ArH[f]	7.53[g]	7.57[d]
			pyr-H	7.5[c]	8.1[e]
			CH_3Sn	1.73	0.5[e]

[a] Concentration of ligand and of $MeSnCl_3$ (for δ(complexed)) in the sample solution. [b] Concentration of $MeSnCl_3$ is 0.021 M. [c] Center of multiplet. [d] Sharp singlet. [e] Very broad. [f] Phenyls adjacent to pyridine rings. [g] AB quartet. The splitting between the two halves of the quartet vs. $MeSnCl_3$ concentration is plotted in Figure 1.

Table II. Chemical Shifts of Ligands (1 Equiv Each) in Competition for 1 Equiv of $MeSnCl_3$[a] at 30 °C

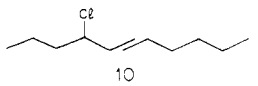
ligands	chem shifts (assignmts)
8 and 9:[b] 8	1.432 (*t*-Bu), 7.97 (H-3)
9[c]	1.304 (*t*-Bu)
5 and 7:[d] 5	3.356 (OCH_3), 4.500 (CH_2O)
7	1.514 ($C(CH_3)_2$), 5.195[e] (CH_2O), 7.54[f] (ArH)

[a] Solvents and concentrations same as Table I. [b] δ(CH_3Sn) is 1.21 ppm. [c] 2 equiv of 9. [d] δ(CH_3Sn) is 0.323 ppm (sharp singlet). [e] Not broadened. [f] AB quartet.

was observed by ^1H NMR. Table I lists the more important chemical shift changes which are observed when 2 equiv of *N*-oxide functionality interact with 1 equiv of tin compound. Since some of these changes were pronounced enough to allow the observation of one complexed oxide in the presence of a different, uncomplexed oxide, it was possible to perform two "competition" experiments (Table II). It appears that 8 has a stronger affinity for the tin compound than does 9 and that 5 forms a more stable complex than 7. The stoichiometry of the complex with 7 (1:1) was verified by titration (Figure 1). The CH_3Sn, CH_3C, and CH_2O ^1H NMR signals in the complex were extremely broad, indicative of a possible isomeric mixture. This broadening was less apparent at 70 °C than at 30 °C.

8

9



10

The inhibitory effect of 5 and 7 upon the $BuSnCl_3$-catalyzed[4] elimination of HCl from *trans*-4-chloro-5-decene (10) in C_6D_5Cl at 100 °C was observed by ^1H NMR. The data, plotted in Figure 2, were calculated from the relative integrals of the chloroallylic and olefinic proton signals in the NMR spectra of the reaction mixtures. Unfortunately, the $BuSnCl_3$ complex of 8 precipitated under these conditions; therefore 8 could not be tested as an inhibitor. Attempts were made to carry out these experiments under the milder conditions of an earlier study,[4] but homogeneous solutions were not obtained.

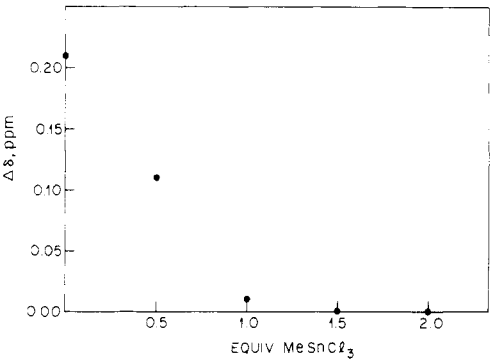


Figure 1. Chemical shift difference between the two pairs of chemically nonequivalent pyridylphenyl protons in 7 (0.013 M in 50:50 CD_3CN–$CDCl_3$, v/v) as a function of the number of equivalents of added $MeSnCl_3$, at 30 °C.

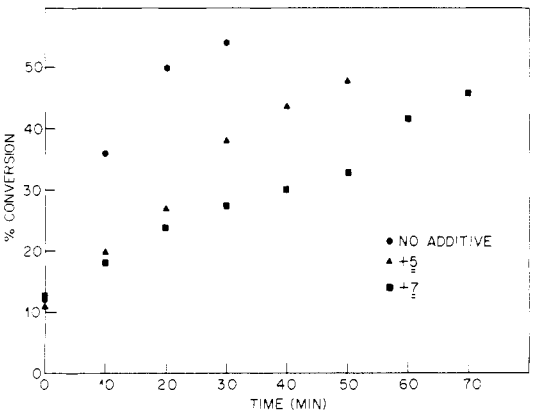


Figure 2. Percent conversion to diene of *trans*-4-chloro-5-decene catalyzed by $BuSnCl_3$ in C_6D_5Cl at 100 °C as a function of time.

Discussion

The synthesis of macrocycles incorporating 6,6′-disubstituted 2,2′-bipyridines has been the subject of several recent reports.[15] Two issues which arise in planning syntheses of these macrocycles are the functionalization of the bipyridines at the 6,6′-positions and the actual closure of the rings. The method described here for in-

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troducing aryl substituents onto the 6,6′-positions of the bipyridine starting material is related to the procedure of Dietrich-Buchecker et al.,[16] who employed PhLi and 2,2′-bipyridine in a direct condensation reaction. In their case, 6,6′-diphenyl-2,2′-bipyridine was obtained in 35% yield on a 2-mmol scale following oxidation and chromatography of the reaction mixture. The present method requires the prior preparation[7] of 6,6′-dibromo-2,2′-bipyridine but gives the desired product in a comparable yield with an extremely simple workup. When the aryllithium methodology was employed with 1,10-phenanthroline, macrocycle precursors were obtained which functioned as bis nucleophiles in the subsequent ring closures.[17] Compound **2**, on the other hand, is a bis electrophile.

It is not clear why the attempted cyclizations of the diols with **2** using NaH in $(CH_2)_4O$ were unsuccessful. Perhaps the dianions of the diols were aggregated or insoluble under the reaction conditions. It is also possible that the lack of a polyether or polyamine structure in the target macrocycles prevented Na^+ from acting as a template. Cesium(+) in dimethylformamide is often a more effective counterion than Na^+ in promoting macrocyclization reactions,[11] and **3**, **4**, and **7** were successfully synthesized by using Cs_2CO_3 in dimethylformamide. These cycles are much more rigid than previously reported[15] macrocyclic bipyridines. Analogous macrocyclic bipyridine dioxides have not yet been studied.

It would have been desirable to synthesize **7** directly from **3** by oxidation. Unfortunately, despite the successful employment of $H_2O_2/AcOH/H_2O$ at 100 °C[12] and of *m*-chloroperbenzoic acid[13] in $CHCl_3$ in the preparation of unhindered bipyridine *N*,*N*′-dioxides, neither reagent cleanly oxidized **3** to its dioxide. Indeed, the bis *N*-oxide **7** could only be obtained via **5** by using unusually mild oxidation conditions to prepare **5** from **1**.

The complexation of organotin chlorides by Lewis bases, including pyridine *N*-oxides, has been thoroughly explored.[18] The chelation of di- and triorganotin species with 2,2′-bipyridine *N*,*N*′-dioxide has been postulated,[19] though not proven. The present investigation marks the first observation of the interaction of a monoorganotin trichloride with bipyridine dioxides. This interaction is responsible for the chemical shift changes listed in Table I. The resonances of the pyridyl protons are moved 0.4–0.7 ppm downfield upon complexation, reflecting the reduced electron density in the heterocyclic rings upon coordination of the *N*-oxide groups to $MeSnCl_3$. The small downfield shifts of the *tert*-butyl protons in **8** and **9** are probably due to this change in electron density as well. Electron donation to the tin compound is also reflected in the upfield shifts of the CH_3Sn protons. Shielding of the complexed CH_3Sn group by aromatic residues in the binders may contribute to this upfield shift as well. On the other hand, the smaller changes in the proton shifts of the more remote groups in **5** and **7** are more likely caused by conformational changes induced by the methyl and chloro groups on the tin.

Table II lists chemical shifts for the assignable protons in two experiments where 1 equiv of $MeSnCl_3$ was mixed with a stoichiometric amount of each of two competing ligands. The data, when compared with those of Table I, indicate which of the ligands in each pair is complexed and which is not, consequently pointing out which ligand has a greater affinity for the tin compound. Bidentate ligand **8** forms a more stable complex than does **9**; the free energy difference is at least 2 kcal/mol.[20] This is simple but strong evidence for **8** acting as a chelating agent rather than as a bridging ligand, since one would not expect a polymeric, bridged complex to be thermodynamically favored over a monomeric complex with two unhindered pyridine *N*-oxide ligands. Although this experimental result may seem predictable, an earlier experiment[21] revealed that Bu_2SnCl_2 formed a bridged, polymeric complex with the potentially chelating 1,2-bis(diphenylphosphino)ethane.

The competition experiment involving **5** and **7** showed that **5** is a decidedly stronger ligand for $MeSnCl_3$ than is **7**. Examination of CPK models reveals little or no difference in strain or entropy loss between **5** and **7** forming bridged complexes with $MeSnCl_3$, whereas the chelated complex of **7** is somewhat strained and rigidified relative to the chelate complex of **5**, due to the snug fit of $MeSnCl_3$ inside the enforced cavity of **7**. It is not surprising, therefore, that **7** shows weaker affinity for $MeSnCl_3$ than does **5** (Table II). The fact that **7**·$MeSnCl_3$ is a 1:1 complex which is soluble[19] in CD_3CN is further evidence for a nonbridged structure. Except for the complexes of **3** and **4** with $MeSnCl_3$, the encapsulation of tin compounds by macrocyclic ligands had never been demonstrated, although bridged complexes of tin chlorides have been reported[22] where the ligands happened to be attached to macrocycles.

Despite the demonstrated[4] correlation between the affinity of a ligand for $RSnCl_3$ and its effectiveness as an inhibitor of tin-catalyzed dehydrochlorination of allylic chlorides, **7** is actually a slightly better inhibitor of the $BuSnCl_3$-promoted[23] dehydrochlorination of **10** than is **5** (Figure 2). The time needed to reach 40% degradation increased from 12 min to 33 min to 55 min in the presence of no additive, **5**, and **7**, respectively. The lesser accessibility of the tin atom in **7**·$BuSnCl_3$ to the allylic chloride outweighs the presumed lower stability of **7**·$BuSnCl_3$ compared to **5**·$BuSnCl_3$. Unfortunately, the actual differences in degradation rates are small and might have appeared larger if the reaction could have been run under milder conditions. However, the observation of any benefit at all from **7** vs. **5** is further evidence of a nonbridged, encapsulated structure for **7**·$RSnCl_3$ complexes and raises the possibility of designing more practical dehydrochlorination inhibitors (PVC stabilizer additives) which operate by blocking access of labile chloride groups to electrophilic tin atoms, as well as by neutralizing the tin catalysts through Lewis base–Lewis acid interactions.

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(19) Das, V. G. K. *Inorg. Nucl. Chem. Lett.* **1973**, *9*, 155–60. The complexes under study were too insoluble to characterize spectroscopically in solution.

(20) The differences between corresponding data in Tables I and II are of the same order as the experimental error. Although these differences may be used to calculate an equilibrium constant for the reaction $MeSnCl_3$·(**9**)$_2$ + **8** ⇌ $MeSnCl_3$·(**8**) + 2(**9**) of ~20, the resulting $\Delta G°$ is a lower limit at best.

(21) Harrison, P. G.; Sharpe, N. W.; Pelizzi, C.; Pelizzi, G.; Tarasconi, P. *J. Chem. Soc., Dalton Trans.* **1983**, 921–6.

(22) Valle, G.; Cassol, A.; Russo, U. *Inorg. Chim. Acta* **1984**, *82*, 81–4. Cusack, P. A.; Patel, B. N.; Smith, P. J.; Allen, D. W.; Nowell, I. W. *J. Chem. Soc., Dalton Trans.* **1984**, 1239–43. Smith, P. J.; Patel, B. N. *J. Organomet. Chem.* **1983**, *243*, C73–4. Martin, J.; Robert, J. B. *Nouv. J. Chim.* **1980**, *4*, 515–21.

(23) Under the reaction conditions, it is possible that some of the $RSnCl_3$ disproportionates to other catalytically active tin species, which also may be complexed and deactivated by **5** and **7**.

Macrocycles **3**, **4**, and **7** were designed with a narrow purpose in mind, namely, to illustrate a concept in the formulation of additives to PVC stabilizers (though not as actual additives themselves). However, the structure of the cycles deserves more general comment. Compounds **3**, **4**, and **7** are among the more rigid of a small class of macrocycles whose ligating groups lie on one side of a well-defined cavity which can accommodate a chelated metal atom and also several additional ligands attached to the metal. It is possible to construct analogs of **3**, **4**, and **7** that are binders of metal complexes in which the ligands accompanying the metal are forced to interact with groups on the framework of the binder. Thus, the compounds discussed here might lead to the design and synthesis of new organometallic compounds in which both the metals and the ligands display unusual reactivity.

Experimental Section

General Data. Ethyl ether and $(CH_2)_4O$ were distilled from Na–benzophenone ketyl. Dimethylformamide (Burdick and Jackson "high purity") was stored over molecular sieves. The routine alkylation of 4-bromobenzyl alcohol (MeI/NaH/$(CH_2)_4O$) was carried out to obtain 1-bromo-4-(methoxymethyl)benzene in quantitative yield. The starting material 6,6′-dibromo-2,2′-bipyridine was prepared by Michigan State University Synthesis Laboratory; other starting materials were commercially available reagent grade. Solutions of crude organic products were dried with $MgSO_4$ during workup procedures. Silica gel for column chromatography was E. Merck, particle size 63–200 μm; TLC plates were E. Merck silica gel 60 F-254. Values of R_f are approximate and were obtained in solvent mixtures prepared on a v/v basis by observation of TLC plates under a UV lamp. Melting points are uncorrected.

Nuclear magnetic resonance spectra were obtained on a JEOL FX90Q FT spectrometer containing a variable-temperature probe and are reported in parts per million vs. Me_4Si. The positions of some AB quartets were assigned by homonuclear decoupling. Deuteriochloroform was dried over K_2CO_3, and CD_3CN was distilled from P_2O_5. Mass spectra (MS) are listed as *m/e* (relative intensity). Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN; samples for analysis were dried at 110 °C under vacuum. Macrocyclic compounds were analyzed by gel permeation chromatography (Altex μ-spherogel column, 10-μm pore size, 8-mm inner diameter, 30 cm long) and gave single peaks in positions that were consistent with the assigned structures of the compounds.

6,6′-Bis(4-(methoxymethyl)phenyl)-2,2′-bipyridine (1). A slurry of 6,6′-dibromo-2,2′-dipyridine[7] (5.3 g, 17 mmol) and $(PPh_3)_2NiCl_2$ (1.1 g) in 700 mL of Et_2O was mechanically stirred and heated at reflux for 15 min under Ar. The Grignard reagent[6] formed from 1-bromo-4-(methoxymethyl)benzene (10.3 g, 51 mmol) and excess Mg (Alfa resublimed chips) in 50 mL of $(CH_2)_4O$, and 50 mL of Et_2O was added to the heated slurry over 10 min. The mixture was stirred and heated for an additional 75 min, allowed to cool, and then decanted into 150 mL of dilute aqueous NH_4Cl. The organic layer was washed with 150 mL of concentrated aqueous NaCl, dried, filtered, and concentrated to a solid. The solid was suspended in 50 mL of MeOH, and the suspension heated to reflux and then cooled to −15 °C, yielding 1.6 g (24%) of yellow crystals: mp 166–169 °C; R_f 0.1 (CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 3.39 (*s*, 6, OCH_3), 4.50 (*s*, 4, CH_2O), 7.45 (*d*, 4, *J* = 8.5 Hz, Ph-H), 7.78 (*m*, 4, pyr-H), 8.12 (*d*, 4, *J* = 8.5 Hz, Ph-H), 8.55 (*d* of *d*, 2, J_1 = 7 Hz, J_2 = 1.8 Hz, pyr-H); ^{13}C NMR δ 58.08, 74.35, 119.49, 120.17, 126.92, 127.95, 137.54, 138.72, 139.02, 155.87, 155.94; MS, *m/e* (relative intensity) 396 (98, M^+), 381 (48), 365 (100). Anal. Calcd for $C_{26}H_{12}N_2O_2$: C, 78.76; H, 6.10; N, 7.07. Found: C, 78.58; H, 6.12; N, 6.90. A run utilizing 3.2 mmol of dibromide resulted in a yield of 34%.

6,6′-Bis(4-(bromomethyl)phenyl)-2,2′-bipyridine (2). A solution of **1** (0.58 g) in 35 mL of AcOH was saturated with gaseous HBr with ice-bath cooling. The solution was capped with a $CaCl_2$-filled drying tube and stirred 48 h at ambient temperature. The solution was cautiously poured into a 2-L flask containing 300 mL of H_2O and 200 mL of CH_2Cl_2. The aqueous layer was made basic (pH 9) by the *careful* addition of Na_2CO_3 in *small portions* with swirling. The contents of the flask were transferred to a separatory funnel, and the suspension that comprised the lower layer was removed and concentrated, leaving solid, crude product in nearly quantitative recovery. Recrystallization of the solid from 25 mL of $ClCH_2CH_2Cl$ gave 0.48 g (66%) of **2** as white plates: mp 237–238 °C; ^1H NMR ($CDCl_3$ dilute) δ 4.58 (*s*, 4, CH_2Br), 7.54 (*d*, 4, *J* = 8.4 Hz, Ph-H), 7.85 (*m*, 4, pyr-H), 8.15 (*d*, 4, *J* = 8.4 Hz, Ph-H), 8.59 (*d*, 2, *J* = 8 Hz, pyr-H); ^{13}C NMR (50 °C) 33.1, 119.8, 120.4, 127.4, 129.5, 137.7, 138.6, 139.7, 155.8, 156.1; MS (^{79}Br), *m/e* (relative intensity) 492 (10, M^+), 413 (100), 334 (55), 167 (35). Anal. Calcd for $C_{24}H_{18}Br_2N_2$: C, 58.32; H, 3.67; Br, 32.34; N, 5.67. Found: C, 58.44; H, 3.73; N, 5.57; Br, 32.10.

22,22-Dimethyl-17,27-dioxa-40,41-diazaheptacyclo[27.2.2.2^{12,15}.2^{18,21}.2^{23,26}.1^{2,6}.1^{7,11}]hentetraconta-2,4,6(41),7,9,11-(40),12,14,18,20,23,25,29,31,32,34,36,38-octadecaene (3). A mixture of **2** (200 mg, 0.40 mmol) and 4,4′-(2-propylidene)bis(phenol) (92 mg, 0.40 mmol) was dissolved in 15 mL of $(CH_2)_4O$ and 85 mL of dimethylformamide with gentle heating. This solution was added by syringe pump over 40 h to a suspension of Cs_2CO_3 (530 mg) in 400 mL of dimethylformamide at 60 °C with stirring under Ar. After 48 h of additional stirring and heating, the solvents were distilled at 55 °C/0.7 kPa, leaving a residue which was taken up in 150 mL of CH_2Cl_2 and 50 mL of H_2O. The organic layer was washed with 2 × 100 mL of H_2O and 100 mL of concentrated aqueous NaCl, dried, filtered, and concentrated to a semisolid. This was dissolved in a minimal amount of hot $ClCH_2CH_2Cl$ and chromatographed on 5 g of silica gel, eluting with CH_2Cl_2, to yield 82 mg (36%) of **3** as a hard white foam: R_f 0.4 (10:90 EtOAc/CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.64 (*s*, 6, CH_3), 5.26 (*s*, 4, CH_2O), 6.75 and 7.11 (AB *q*, 8, *J* = 8.8 Hz, PhCPh), 7.35 and 7.83 (AB *q*, 8, *J* = 8.0 Hz, pyr-Ph-H), 7.8 (*m*, 6, pyr-H); ^{13}C NMR δ 30.2, 41.1, 69.5, 115.1, 120.0, 120.2, 126.5, 127.3, 127.8, 137.3, 138.3, 139.4, 143.0, 155.9, 156.3, 158.5; MS, *m/e* (relative intensity) 560 (23, M^+), 545 (50), 426 (28), 334 (66), 167 (100). Anal. Calcd for $C_{39}H_{32}N_2O_2$: C, 83.54; H, 5.75; N, 5.00. Found: C, 83.84; H, 6.00; N, 4.82.

2,6-(Methanothiomethano[1,4]benzeno[2,6]pyridino[2,6]-pyridino[1,4]benzenomethanothiomethano)naphthalene (4). Separate solutions of **2** (185 mg, 0.38 mmol) in 10 mL of $(CH_2)_4O$ and 40 mL of dimethylformamide and 2,6-bis(mercaptomethyl)naphthalene[9] (82 mg, 0.37 mmol) in 50 mL of dimethylformamide were added simultaneously by syringe pump to a stirred suspension of Cs_2CO_3 (490 mg) in 200 mL of dimethylformamide at 40–45 °C under Ar over 1.2 h. After 1.5 h of additional stirring and heating, the cloudy white suspension was concentrated at reduced pressure. The residual solids were taken up in 100 mL each of H_2O and CH_2Cl_2, dried, filtered, and concentrated to a semisolid that was dissolved in a small amount of hot $ClCH_2CH_2Cl$ and loaded onto a column of 3 g of silica gel. The column was eluted with 25 mL of CH_2Cl_2 followed by 1% EtOAc in CH_2Cl_2. The band from 10 to 36 mL total elution gave **4** (62 mg, 30%) as a white solid. This nearly pure product was recrystallized from $ClCH_2CH_2Cl$ to obtain analytically pure **4** (45 mg, 22%): mp 240 °C (with prior darkening); R_f 0.8 (10:90 EtOAc/CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 3.831, 3.861 (2 *s*, 8, CH_2SCH_2), 7.03 (*d*, 4, *J* = 8.2 Hz, Ph-H), 7.2 (*m*, 2, β-Np-H), 7.6 (*m*, 6, pyr-H), 7.81 (*s*, 2, α-Np-H), 7.81 (*m*, 2, α-Np-H), 8.10 (*d*, 4, *J* = 8.2 Hz, Ph-H); ^{13}C NMR δ 36.14, 36.83, 119.3, 119.6, 127.1, 127.2, 127.4, 128.0, 129.4, 132.2, 135.8, 137.5, 138.0, 139.5, 155.6, 157.0; MS, *m/e* (relative intensity) 552 (24, M^+), 519 (38), 398 (75), 155 (100). Anal. Calcd for $C_{36}H_{28}N_2S_2$: C, 78.22; H, 5.11; N, 5.07; S, 11.60. Found: C, 77.87; H, 5.12; N, 4.95; S, 11.54.

6,6′-Bis(4-(methoxymethyl)phenyl)-2,2′-bipyridine 1,1′-Dioxide (5). Compound **1** (500 mg) was stirred with 25 mL of AcOH, 5 mL of 30% aqueous H_2O_2, and $NaOAc{\cdot}3H_2O$ (4 *g*) for 48 h at 60 °C. The mixture was poured into 100 mL of CH_2Cl_2 and 100 mL of H_2O and brought to pH 9 with Na_2CO_3. The organic layer was dried, filtered, and concentrated. Chromatography of the residue on 15 g of silica gel, loading in CH_2Cl_2, and then eluting with 100 mL of EtOAc followed by 200 mL of 10:90 EtOH/EtOAc gave **5** (220 mg, 41%) from the latter eluate as a light yellow amorphous material: R_f 0.06 (EtOAc); ^1H NMR ($CDCl_3$) δ 3.40 (*s*, 6, OCH_3), 4.51 (*s*, 4, CH_2O), 7.42 and 7.85 (AB *q*, 8, *J* = 8.1 Hz, Ph-H), 7.5 (*m*, 6, pyr-H); MS, *m/e* (relative

intensity) 428 (50, M^+), 412 (99), 411 (100), 396 (75), 381 (85), 365 (80). Anal. Calcd for $C_{26}H_{24}N_2O_4$: C, 72.88; H, 5.65; N, 6.54. Found: C, 72.79; H, 5.66; N, 6.29.

22,22-Dimethyl-17,27-dioxa-40,41-diazaheptacyclo-[27.2.2.2^{12,15}.2^{18,21}.2^{23,26}.1^{2,6}.1^{7,11}]hentetraconta-2,4,6(41),7,9,11-(40),12,14,18,20,23,25,29,31,32,34,36,38-octadecaene 40,41-Dioxide (7). Diether dioxide **5** was converted to the dibromide **6** by using the procedure described for **2**. The crude product, isolated in 94% yield, was used without purification. The cyclization of **6** to form **7** was carried out in a manner analogous to the preparation of **3**, except the dibromide–bis(phenol) solution did not contain $(CH_2)_4O$. Chromatographic purification was accomplished by eluting the product from the silica gel column with 0–10% EtOH in EtOAc. The yield from 225 mg of **6** was 59 mg (23%) of light yellow solid, which was the monohydrate of **7**: mp 160–290 °C (gradual decomposition); ^{1}H NMR (50:50 CD_3CN–$CDCl_3$, v/v) δ 1.51 (s, 6, CH_3), 5.18 (s, 4, CH_2O), 6.67 and 7.01 (AB q, 8, J = 8.8 Hz, PhCPh), 7.5 (m, 14, ArH); MS, m/e (relative intensity) 592 (25, M^+), 577 (30) , 545 (45), 320 (100), 212 (55), 166 (95). Anal. Calcd for $C_{39}H_{32}N_2O_4{\cdot}H_2O$: C, 76.70; H, 5.61; N, 4.59. Found: C, 76.92; H, 5.60; N, 4.62. The ^{1}H NMR spectrum recorded in $CDCl_3$ displayed an AB quartet at 5.12 and 5.20 ppm (J = 14 Hz) for the CH_2 protons.

4,4′-Bis(1,1-dimethylethyl)-2,2′-bipyridine 1,1′-Dioxide (8). A solution of 4,4′-di-*tert*-butyl-2,2′-bipyridine[14] (1.0 g, 3.7 mmol) and *m*-chloroperbenzoic acid (2.6 g, 15 mmol) in 30 mL of CH_2Cl_2 was stirred for 48 h at ambient temperature, diluted to 50 mL with CH_2Cl_2 and washed with 50 mL of aqueous Na_2CO_3. The washings were extracted with 50 mL of CH_2Cl_2, and the combined organic layers were washed with 50 mL of additional Na_2CO_3 solution, dried, filtered, and concentrated to a yellow foam. This foam was chromatographed on 20 g of neutral alumina (Fisher, activity 1, 80–200 mesh), eluting with 0–5% MeOH in CH_2Cl_2, to yield 0.88 g (78%) of **8** as a foam: ^{1}H NMR ($CDCl_3$) δ 1.38 (s, 18, CH_3), 7.29 (d of d, 2, J_1 = 3 Hz, J_2 = 7 Hz, H-5,5′), 7.60 (d, 2, J_1 = 3 Hz, H-3,3′), 8.20 (d, 2, J_2 = 7 Hz, H-6,6′). Anal. Calcd for $C_{18}H_{24}N_2O_2$: C, 71.97; H, 8.05; N, 9.33. Found: C, 72.01; H, 8.03; N, 9.28.

$MeSnCl_3$ Complex Formation with 5, 7, 8, and 9. Stock solutions of 2.00-mL total volume were prepared of each of the ligands and also of $MeSnCl_3$ (handled in an N_2-filled glovebag), in CD_3CN or 50:50 $CDCl_3$–CD_3CN (v/v). Aliquots of the stock solutions were combined to obtain experimental solutions of the compositions listed in Table I. The 90-MHz ^{1}H NMR spectra of the experimental solutions were recorded and were independent of the order in which the component stock solutions were introduced. No solid precipitation was observed.

Dehydrochlorination of 10 in the Presence of 5 and 7. Reactant solutions consisting of **10** (14.0 μL, 12.7 mg, 0.073 mmol), $BuSnCl_3$ (2.7 μL, 4.5 mg, 0.016 mmol), and C_6D_5Cl (0.40 mL) were prepared. Some of the solutions also contained **5** (7.4 mg, 0.017 mmol) or **7** (10.3 mg, 0.017 mmol), and these solutions were made homogeneous by gentle heating before the addition of **10** or $BuSnCl_3$. The reactant solutions were heated to 100 °C as quickly as possible (<5 min) in the probe of the NMR spectrometer, after which spectra were recorded at 10-min intervals. Conversion of the allylic chloride (2 olefinic H, 1 chloroallylic H) to a conjugated diene (4 olefinic H) was monitored by the increase in the ratio of olefinic to chloroallylic protons. Compounds **5** and **7** did not appear to decompose during the experiments.

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Registry No. **1**, 95601-80-2; **2**, 95601-81-3; **3**, 95601-82-4; **4**, 95628-38-9; **5**, 96259-23-3; **5**·$MeSnCl_3$, 96292-57-8; **6**, 96259-25-5; **7**, 96259-24-4; **7**·$MeSnCl_3$, 96292-54-5; **8**, 96259-26-6; **8**·$MeSnCl_3$, 96292-55-6; **9**, 23569-17-7; **9**·2$MeSnCl_3$, 96292-56-7; **10**, 90370-35-7; $MeOCH_2$-*p*-C_6H_4MgBr, 96259-22-2; *p*-$BrC_6H_4CH_2OMe$, 1515-88-4; $(p\text{-}HOC_6H_4)_2C(CH_3)_2$, 80-05-7; $MeSnCl_3$, 993-16-8; (*E*,*E*)-$CH_3CH_2CH{=}CHCH{=}CH(CH_2)_3CH_3$, 92260-75-8; 6,6′-dibromo-2,2′-bipyridine, 49669-22-9; 2,6-bis(mercaptomethyl)naphthalene, 43012-09-5; 4,4′-di-*tert*-butyl-2,2′-bipyridine, 72914-19-3.

Intramolecular Nitrogen–Phosphorus Interactions of Phosphate Esters

Dean F. Bushey,* Brenda F. Johnson, and Jamin Huang

Union Carbide Agricultural Products Company, Research Triangle Park, North Carolina 27709

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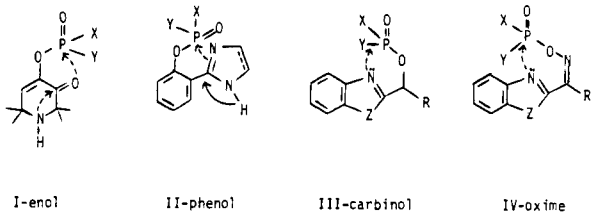
Four different classes of phosphate esters derived from enols, phenols, carbinols, and oximes have been shown to undergo intramolecular rearrangements assisted by a neighboring nitrogen. The unexpected products from these rearrangements have been characterized by spectral methods, especially ^{13}C NMR. Rearrangements involving the *O*-ethyl *S*-propyl thiophosphate group have led to particularly interesting results.

The reaction of phosphate esters with acetylcholinesterase is an important biological process in insect control. In this process, the imidazole group of histidine is assumed to be responsible for activation of the serine hydroxyl, which in turn displaces a ligand of the phosphate insecticide.[1a] An analogous rate acceleration by neighboring amide or amine functionalities in phosphate ester hydrolysis has been documented by several investigators.[1b–f] The implications of this type of intramolecular interaction on the preparation, stability, and biological activity of potential organophosphate insecticides containing a distal nitrogen have not been addressed.

Scheme I



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