Cyclenphosphine Oxide. Anomalous Member of a Homologous Series

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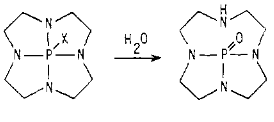
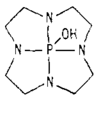
Abstract: Concentration dependence of the ^{31}P NMR chemical shift of cyclenphosphine oxide, **1**, indicates that a monomer–dimer equilibrium is operating in chloroform-*d* solution. This interpretation is supported by infrared spectroscopy. The high-field positions and the ^{31}P NMR chemical shifts of the monomeric and dimeric forms (+10.4 ± 0.5 and −11.2 ± 0.5 ppm, respectively) suggest coordination of the pendent secondary amine group in these structures to the phosphorus center. Among the homologous cyclic phosphoramides, the smallest member, cyclenphosphine oxide, appears to be unique in this tendency for coordination to the phosphorus. Carbon NMR spectra of **1** show exchange of all of the carbon sites presumably through the intermediacy of the hydroxyphosphorane **3**.

In 1974 a Du Pont patent[2] disclosed the synthesis of a compound, $C_8H_{17}N_4PO$, formed by the hydrolysis of a cyclenfluorophosphorane, **2a**. Structure **1** (cyclenphosphine oxide) was proposed for this hydrolysis product based mainly on the proton NMR spectrum which lacks the symmetry expected for the alternative structure **3**.



2 a, X = F
b, X = SCH_3

1



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In this paper we report further investigations of the structure of cyclenphosphine oxide that indicate unique properties for this compound. The higher homologues of **1** with larger peripheral rings (trimethylene, C_3H_6, bridges) behave as simple phosphoramides and exhibit normal ^{31}P NMR chemical shifts.[3] By analogy, the chemical shift of **1** is expected to fall in the range 40 ± 5 ppm[4] This expectation is not realized—the signal for cyclenphosphine oxide appears at much higher field. Furthermore, *the chemical shift of* **1** *is variable* and depends on the solvent, temperature, and concentration of the solutions. Under various conditions, the chemical shift appears throughout the range of +8 to −20 ppm. We offer an explanation for this unusual behavior based on a unique monomer–dimer equilibrium, $\mathbf{4} \rightleftharpoons \mathbf{5}$.

Experimental Section

Instrumentation. Infrared spectra were obtained on a Perkin-Elmer Model 599B grating spectrophotometer with sodium chloride optics.

Nuclear magnetic resonance (NMR) spectra were obtained on a JEOL FX-90Q spectrometer. On this instrument phosphorus spectra are obtained at 36.2 MHz and carbon at 22.5 MHz. All phosphorus spectra were calibrated using external 85% phosphoric acid as the reference with external locking mode. The FT ^{31}P NMR spectra were obtained in the nondecoupled irradiation mode with standard settings as follows: frequence range, 20 kHz; data points, 8192; observation frequency, 72.58 kHz. The resolution inherent in this operation is 4.8 Hz. Signals had an average peak width at half height of 20 Hz. Chemical shifts are expressed with positive values downfield.

Hygroscopic Materials. Cyclenphosphine oxide is an extremely hygroscopic colorless crystalline solid. Samples were sublimed before use and were stored inside a desiccator over Drierite in turn stored within a nitrogen-filled glovebag. Solvents for both NMR and IR experiments were dried to less than 1 ppm of water as determined by Karl Fischer titration and then stored over 3-Å molecular sieves in sealed containers placed in the nitrogen-filled glovebag. All manipulations and sample dilutions were done under nitrogen.

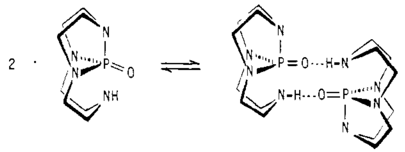
Cyclen(methylthio)phosphorane, 2b. According to an unpublished procedure supplied to us by Dr. T. J. Atkins of E. I. du Pont de Nemours and Company, a solution of 1.9 g of dimethyl disulfide and 4.0 g of cyclenphosphorane[5] in 50 mL of anhydrous methylene chloride was stirred 5 days at 25 °C. The product was concentrated under nitrogen and the solid was recrystallized from hexane giving 3.1 g (63% yield) of hygroscopic colorless crystals of the methylthio derivative, mp 62–65 °C. NMR ($CDCl_3$): 3.2–2.6 (8 H, CH_2) 2.01 ppm (d, J_{PH} = 12.5 Hz, CH_3). ^{31}P NMR (C_6D_6): −21.3 ppm.

Cyclenphosphine Oxide, 1. A 0.25-g sample of cyclen(methylthio)phosphorane, **2b**, was stirred in 2 mL of water at 100 °C for 30–40 min until all of the melted droplets dissolved. The solvent was removed by freeze-drying (0.1 mm) and the residue sublimed at 170 °C/0.1 mm giving 0.19 g (87% yield) of **1**, mp 210–214 °C, under nitrogen. Crystals of **1** that are exposed to air are hydrated without melting: the hydrated crystals melt with partial decomposition at less than 180 °C. The ^1H NMR and IR spectra of **1** prepared by this route are identical with the spectra of cyclenphosphine oxide prepared by the hydrolysis of cyclenfluorophosphorane, **2a**.[2] ^{31}P NMR: see Table I (in Supplementary Material) for chemical shifts of the singlet. ^{13}C NMR (CD_3OD): 56 °C, 44.6 ppm (d, J_{PC} = 9 Hz); −35 °C, 44.0, 43.8, 43.4, and 42.9 ppm; ($CDCl_3$): 52 °C, 47.0 ppm (d, J_{PC} = 6 Hz); −39 °C, see Figure 2.

Cyclenmethoxyphosphorane, 6. A solution of 74 mg of cyclen(methylthio)phosphorane in 10 mL of anhydrous methanol was refluxed 10 h. This solution was concentrated and the residue was distilled bulb-to-bulb at 70 °C/0.1 mm giving 63 mg (91% yield) of clear colorless oil shown by NMR to be pure **6**. ^1H NMR ($CDCl_3$, 60 MHz): 3.51 (d, J_{PH} = 12.4 Hz, CH_3) and 2.6–3.2 ppm (14 lines, CH_2). ^{31}P NMR ($CDCl_3$): −20.4 ppm. This chemical shift varies only slightly (less than 0.5 ppm) with changes in concentration and temperature of the sample. ^{13}C NMR ($CDCl_3$): 45.7 ppm (d, J_{PC} = 11.7 Hz, CH_2).

Results

Qualitative. The chemical shifts of cyclenphosphine oxide, **1**, in chloroform-*d* and acetonitrile-d_3 solutions appear at progressively lower field on dilution (see Figure 3). Concentration dependence of the chemical shift of **1** suggests that association equilibria are involved.[6] We believe that a rapid monomer–dimer equilibrium ($\mathbf{4} \rightleftharpoons \mathbf{5}$) is occurring with cyclenphosphine oxide and



4 5 (1)

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[1] 3M Center, 201-2W-17, St. Paul, MN 55144.

[2] Richman, J. E. U.S. Patent 3 987 128, 1976.

[3] Richman, J. E.; Flay, R. B.; Gupta, O. D. *ACS Symp. Ser.* **1981**, *No. 171*, 271–275.

[4] This prediction is based on the sizes of the two smaller fused rings in these structures.[3] Phosphoramides with 5,5-fused rings show ^{31}P NMR shifts of about +40 ppm; 5,6 about +25, and 6,6 about +12 ppm.

[5] Richman, J. E.; Atkins, T. J. *Tetrahedron Lett.* **1978**, 4333–4336.

[6] Dimerization of cyclophosphazene oxides has been observed in both the crystalline state and in solution: (a) Bullen, G. J.; Dann, P. E.; Evans, M. L.; Hursthouse, M. B.; Shaw, R. A.; Wait, K.; Woods, M.; Yu, H. S. *Z. Naturforsch.* **1976**, *31b*, 995–996; (b) Dhathathreyan, K. S.; Krishnamurthy, S. S.; Murthy, A. R. V.; Cameron, T. S.; Chan, C.; Shaw, R. A.; Woods, M. *J. Chem. Soc. Chem. Commun.* **1980**, 231–233.

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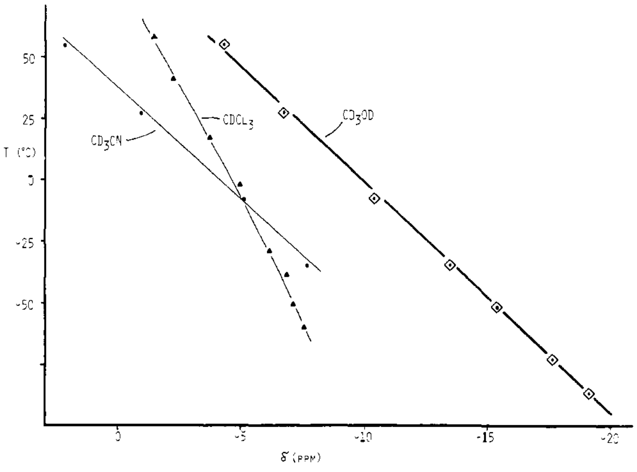


Figure 1. Temperature dependence of ^{31}P NMR chemical shifts of **1** in various solvents.

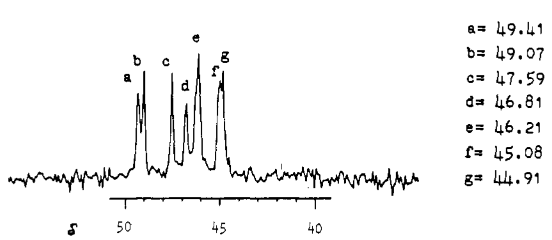


Figure 2. ^{13}C NMR spectrum of **1** in $CDCl_3$ at -39 °C.

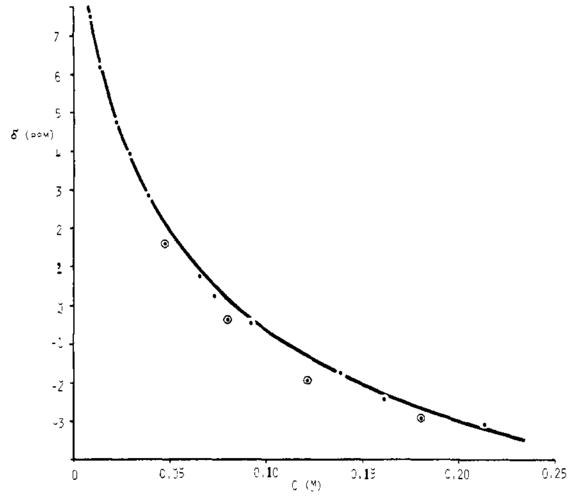


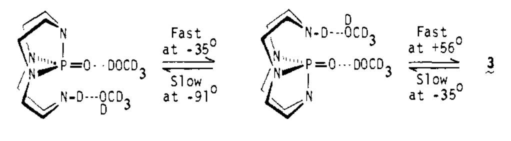
Figure 3. Observed ^{31}P chemical shifts of **1** as a function of concentration in $CDCl_3$ at 28 °C. The curve is calculated from eq 3 with $\delta_D = -11.2$, $\delta_M = 10.4$, and $K = 10.75$. Circled points represent preliminary data not included in calculations. See the footnote for Table I in Supplementary Material.

that the ^{31}P chemical shifts of these two forms differ by more than 20 ppm (vide infra).

Temperature also affects the equilibrium between **4** and **5**: an increase in temperature should shift the equilibrium to favor the monomer.[7] Consistent with this, the ^{31}P signal of cyclenphosphine oxide shows a pronounced shift to lower field with an increase in temperature (see Figure 1).[8] This is the same direction as the effect of dilution which also increases monomer:dimer.

Further evidence in support of an equilibrium between **4** and **5** was obtained from a study of the effects of dilution on the infrared spectrum of this compound in chloroform-*d*.[9] In the solid state (Nujol or KBr) cyclenphosphine oxide shows only one band at 3090 cm^{-1} assigned to the hydrogen-bonded NH stretching mode of dimeric structure **5**.[10] In chloroform-*d* solution the oxide shows an additional band at 3330 cm^{-1} consistent with a free NH stretching mode of monomeric structure **4**. On dilution the ratio of the 3330 to 3090-cm^{-1} band increases as would be expected for a shift in the monomer–dimer equilibrium.

Scheme I



(2)

Whereas ^{31}P NMR spectroscopy shows evidence for rapid equilibrium 1, ^{13}C NMR shows another somewhat slower equilibrium. Under conditions where equilibrium 1 is operating rapidly, the ^{13}C NMR spectrum of cyclenphosphine oxide should show four distinct carbons variously coupled to phosphorus. At -39 °C in chloroform-*d* the carbon NMR spectrum (Figure 2) consists of seven lines presumably due to three doublets and one broad singlet. On warming to 52 °C this solution exhibits a doublet at 47.0 ppm ($J_{PC} = 6$ Hz). At intermediate temperatures the collapse of the seven-line pattern to the doublet is observed. This temperature dependence of the carbon spectrum is consistent with a slow scrambling process that exchanges the four unique carbon positions of the rapidly equilibrating monomeric and dimeric structures **4** and **5**. We suggest the intermediacy of hydroxyphosphorane **3** for the carbon scrambling process.[11] Hydroxyphosphoranes have recently been characterized as stable structures in closely related compounds.[12]

$$(\mathbf{4} \overset{\text{fast}}{\rightleftharpoons} \mathbf{5}) \overset{\text{intermediate rate}}{\rightleftharpoons} \mathbf{3}$$

In methanol-d_4 at -35 °C the ^{13}C NMR spectrum of cyclenphosphine oxide shows two doublets ($J_{PC} = 12.8$ and 5.8 Hz) which on further cooling to -91 °C collapse to a single broad peak. On warming the sample to 56 °C the spectrum evolves to a single doublet ($J_{PC} = 8.8$ Hz). The high-temperature doublet is consistent with rapid carbon site exchange through the hydroxyphosphorane intermediate. The coalescence at -91 °C suggests that the low-temperature limiting spectrum similar to the seven-line pattern observed in chloroform-*d* has not been reached. What then is the intermediate spectrum, the pair of doublets observed at -35 °C? For this symmetry we suggest a rapid prototropy that exchanges carbon sites while maintaining the uniqueness of sites adjacent to axial and equatorial nitrogen positions. A mechanism for such an exchange is shown in Scheme I.

Quantitative. We have quantitatively analyzed the data on the concentration dependences of ^{31}P NMR chemical shifts of cyclenphosphine oxide. We assume that equilibrium 1 is operating. The calculations give values for the equilibrium constant, *K*, and the chemical shifts δ_M and δ_D, respectively, of the monomer and dimer.

Two different mathematical approaches are discussed in the Supplementary Material. The more useful approach applies a linear regression analysis of eq 3 derived from the equilibrium expression and the expression for the averaged chemical shift, δ, of the monomer and dimer.[13]

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[7] Jowsten, M. D.; Schaad, L. J., "Hydrogen Bonding"; Marcel Dekker, Inc.: New York, 1974; p 42.

[8] The slope of Figure 1 shows a temperature sensitivity of the ^{31}P chemical shift that is nearly triple that of the triphenylphosphine and triphenylphosphine oxide system suggested for phosphorus temperature calibration: Dickert, F. L.; Hellmann, S. W. *Anal. Chem.* **1980**, *52*, 996.

[9] An attempted determination of the molecular weight of cyclenphosphine oxide by chloroform solution osmometry apparently failed due to the extremely hygroscopic nature of this compound.

[10] A close model for the bonding in structure **5** is not available. The free and bonded (dimeric?) N-H stretching bands of $Cl_2PONHCH_3$ appear at 3408 and 3195 cm^{-1}, respectively; Nyquist, R. A. *Spectrochim. Acta* **1963**, *19*, 713–729. Free secondary amines in general fall in the range 3310–3360 cm^{-1}: Russell, R. A.; Thompson, H. W. *J. Chem. Soc.* **1955**, 483–486.

[11] Pseudorotation between the distorted trigonal bipyramidal forms of **3** is expected to very rapid, analogous to **6**.

[12] (a) Segall, Y.; Granoth, I. *J. Am. Chem. Soc.* **1978**, *100*, 5130–5134. (b) Segall, Y.; Granoth, I. *Ibid.* **1979**, *101*, 3687–3688. (c) Granoth, I.; Martin, J. C. *Ibid.* **1978**, *100*, 5229–5230. (d) Granoth, I.; Martin, J. C. *Ibid.* **1979**, *101*, 4618–4622. (e) Munoz, A.; Garrigues, B.; Koenig, M. *Tetrahedron* **1980**, *36*, 2467–2482.

$$\delta = \delta_D + (\delta_D - \delta_M)x \tag{3}$$

where

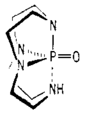
$$x = \frac{1 - (1 + 8\,KC)^{1/2}}{4KC}$$

Constant C represents the total gram-atom concentration of phosphorus nuclei.

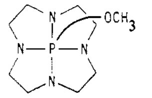
Linear regression analysis of δ as a function of x gives the value of K that is the best fit for the data. Values of δ_D and δ_M are determined from the slope and intercept of this plot. The results are $\delta_D = -11.2 \pm 0.5$ ppm, $\delta_M = 10.4 \pm 0.5$ ppm, and $K = 10.7 \pm 2$ M^{-1}. Figure 3 shows a plot of the observed data vs. the theoretical curve calculated from these values.

Discussion

Our data give a reasonably accurate determination of the values of δ_D and δ_M, the ^{31}P NMR chemical shifts of the dimer, **5**, and monomer **4**, in chloroform-*d* solutions. The chemical shifts of the monomeric form (+10.4 ± 0.5 ppm) is surprising in view of the prediction from homologous model compounds[3,4] of a chemical shift of 40 ± 5 ppm for this oxide. We interpret the unusually high field shift of **4** to indicate that the amine group in the pendent bridge is coordinated to the phosphorus in chloroform solutions (cf. structure **4a**).[14]



4a



6

Our data show that the dimeric form **5**, (δ −11.2 ± 0.5 ppm in chloroform) appears at considerably higher field than the monomer. The shift of **5** approaches the shift of cyclenmethoxyphosphorane, **6**,[2] (−20.0 ppm) a closely analogous compound that is fully pentacoordinated. Apparently, the dimer **5** has electronic and geometric demands that bring the pendent nitrogen into even closer coordination with the phosphorus than in the structure of the monomer. This is consistent with the expectations implied in structure **5** since H-bonding should increase both the electron density at the nitrogen and the nucleophilic character of the phosphorus at the same time locking the molecule in a geometry that facilitates the bonding of nitrogen to the phosphorus. This accounts for the large difference in chemical shifts of the monomeric and dimeric forms of cyclenphosphine oxide.

In methanol and water solutions, ^{31}P NMR indicates yet another behavior for the oxide. In these solvents there is no concentration dependence for the chemical shift. In strongly hydrogen-bonding solvents the monomer–dimer equilibrium (1) is displaced completely to the monomer by the formation of strong H bonds between the monomer and the solvent (see Scheme I). The absence of concentration dependence for the chemical shift of the oxide in these solvents is evidence that there is no monomer–dimer equilibrium; however, a pronounced temperature dependence of the ^{31}P chemical shifts (Figure 1) shows that monomer–solvent equilbria are still operating. At low temperatures an upfield shift to nearly −20 ppm is observed for the oxide in methanol-d_4 suggesting that the phosphorus of the H-bonded form resembles the fully pentacoordinated phosphorus of **6**. Carbon NMR results (vide supra), however, rule out the fully symmetrical structure **3**, in methanol except as an intermediate. The structures in Scheme I apparently represent the stable form of cyclenphosphine oxide in methanol solution.

Conclusions

These results can be compared with previous work done on structures of phosphatranes. Verkade and co-workers[15] have concluded that the phosphate derivative of the tetradentate ligand triethanolamine (phosphatrane oxide) shows no transannular P–N bonding.[16] Our results suggest that cyclenphosphine oxide in the free monomeric form does show transannular P–N bonding. Apparently the 12-membered ligand, cyclen, is better able to accommodate the geometry of pentavalent phosphorus than is triethanolamine. Surprisingly, the higher homologues of cyclenphosphine oxide do not show transannular P–N bonding: this property appears to be unique to the cyclen derivative. In spite of this tendency, it is noteworthy that cyclenphosphine oxide is stable with respect to its tautomeric form, the symmetrical hydroxyphosphorane. This probably is the result of an electronic effect rather than a geometric effect: recent results suggest that more electronegative groups stabilize hydroxyphosphoranes.[12c]

Registry No. 1, 61754-96-9; **2a**, 61754-87-8; **2b**, 84195-30-2; **6**, 61754-92-5; dimethyl disulfide, 624-92-0; cyclenphosphorane, 64317-97-1.

Supplementary Material Available: The derivation of eq 3, tables of data used to plot Figures 1, 3, and 4, a table of ^{31}P NMR chemical shifts of **1** in several solvents, and infrared intensities of the 3330- and 3090-cm^{-1} bands at different concentrations (8 pages). Ordering information is given on any current masthead page.

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(13) The derivation of eq 3 is given in the Supplementary Material.

(14) In previous papers in this series we have also observed a unique tendency for phosphorus toward pentavalence in the twelve-membered cyclen derivatives. See ref 5 and Richman, J. E. *Tetrahedron Lett.* **1977**, 559–562.

(15) Milbrath, D. S.; Verkade, J. G. *J. Am. Chem. Soc.* **1977**, *99*, 6607–6613.

(16) Stronger polarization of the phosphorus does induce transannular coordination in phosphatranes: Van Aken, D.; Merkelbach, I. I.; Koster, A. S.; Buck, H. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1045–1046.