

The size of the *ortho* to *para* ratios for the halogens would seem to be indicative of a larger polar effect for the halogens from the *ortho* than from the *para* position. It is possible that the *ortho* halogen is bent out of the plane of the ring thus reducing its mesomeric electron release, but this cannot account for all of the effect since in both series an *o*-chloro substituent produces a greater retarding effect than the *m*-chloro (no mesomeric electron release is possible for this latter substituent). It is possible, therefore, that there is a considerable inductive and/or field effect from the *ortho* halogen, greater than that from the *para* halogens. Similarly, other workers¹⁶ have noted that the polar effect of *ortho* halogens seems to be greater than those of the *para* halogens. The *ortho* to *para* ratio for the methyl substituent is

essentially unity, a value to be expected of a substituent that does not have a strong inductive or resonance effect.

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(16) H. C. Brown, Y. Okamoto, and G. Ham, *J. Am. Chem. Soc.*, **79**, 1906 (1957).

4-Hydroxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide and Derived Compounds

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4-Hydroxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-sulfide (II), m.p. 161.0°, has been prepared in 63% yield from pentaerythritol and thiophosphoryl chloride. In an excess of the latter, however, O,O,O-tris(4-methoxy-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-sulfide) phosphorothioate (III) forms. II was converted to the chloromethyl derivative by reaction with a solution of 3,9-dichloro-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane 3,9-dioxide (I) in dimethylformamide; this solution acts as a new type of chlorinating agent. The primary hydroxyl of II is very reactive toward isocyanates, formaldehyde-HCl, and acyl halides, producing several series of hitherto unknown compounds.

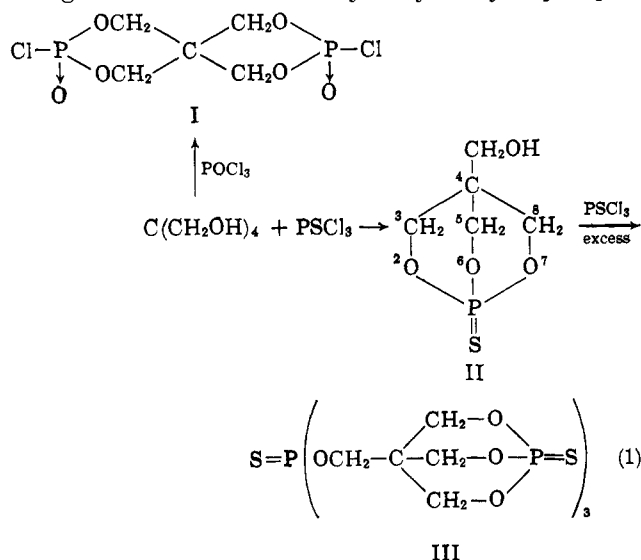
We have previously reported that 3,9-dichloro-2,4,8,10-tetraoxa-3,9-diphosphaspiro[5.5]undecane 3,9-dioxide (I) can be prepared by the interaction of excess phosphoryl chloride and pentaerythritol,¹ and have described some of its reactions.²

In continuation of this work we found that the reaction of pentaerythritol with excess thiophosphoryl chloride gave a chlorine-free product. Further investigation showed that 4-hydroxymethyl-1-phospha-

2,6,7-trioxabicyclo[2.2.2]octane 1-sulfide³ (II) had been first formed followed by conversion to O,O,O-tris(4-methoxy-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-sulfide) phosphorothioate (III). Use of an equal number of moles of reactants permitted isolation of II in 63% yield.

Thus, thiophosphoryl chloride forms with pentaerythritol a bicyclic cage structure readily, while phosphorus oxychloride uses only two phosphorus-chlorine functions to participate in ring formation. We have no entirely satisfactory explanation at present for the completely different behavior of the two phosphorus halides, though the hybridizations of the phosphorus-halogen bonds may be different in the two phosphorus halides. In the case of phosphoryl chloride, reaction might occur through the ionic species $(POCl_2)^+Cl^-$, a form in which its thio analog is not known to exist.⁴ The bicyclic 4-methyl-substituted phosphite has been obtained by condensation of 1,1,1-tris(hydroxymethyl)ethane with phosphorus trichloride in the presence of acid scavengers and in high dilution.^{3,5} The latter condition favored ring closure.

The preparation of II has been reported in a recent patent,⁶ by the transesterification of pentaerythritol with triethyl phosphite followed by sulfuration of the trivalent phosphorus under free-radical conditions with the use of octyl mercaptan. We have been unable to repeat the second step of this synthesis according to the description given, but have found that the bicyclic



(1) R. Rätz and O. J. Sweeting, *J. Org. Chem.*, **28**, 1608 (1963).

(2) R. Rätz and O. J. Sweeting, *ibid.*, **28**, 1612 (1963).

(3) An alternate system of numbering this ring system has been used [J. G. Verkade and L. T. Reynolds, *ibid.*, **25**, 663 (1960)]. According to that system, compound II would be 1-hydroxymethyl-4-phospha-3,5,8-trioxabicyclo[2.2.2]octane 4-sulfide.

(4) J. R. Van Wazer, "Phosphorus and Its Compounds," Vol. 1, Interscience Publishers, Inc., New York, N. Y., 1958, pp. 255, 258.

(5) O. Neunhoeffer and W. Maiwald, *Ber.*, **95**, 108 (1962).

(6) W. S. Wadsworth, Jr., and W. D. Emmons, U. S. Patent 3,038,001 (June 5, 1962); *Chem. Abstr.*, **67**, 12322 (1962).

TABLE I
 4-(N-SUBSTITUTED CARBAMOYLOXYMETHYL)-1-PHOSPHA-2,6,7-TRIOXABICYCLO[2.2.2]OCTANE 1-SULFIDES (VI)

R	Recrystn. solvent	M.p., °C.	Yield, %	Formula	Calcd., %					Found, %				
					C	H	N	P	S	C	H	N	P	S
CH ₃	Methanol	170-172	94.2	C ₇ H ₁₂ NO ₃ PS	33.20	4.75	5.54	12.23		33.22	4.76	5.30	11.99	
C ₂ H ₅	Ethanol	124	90.0	C ₈ H ₁₄ NO ₃ PS	35.95	5.28	5.24	11.59		36.15	5.26	5.48	11.44	
<i>n</i> -C ₄ H ₉	Needles from ethanol	102	93.5	C ₁₀ H ₁₈ NO ₃ PS	40.67	6.14	4.74	10.49		40.47	6.21	4.88	10.34	
C ₆ H ₅	Concd. CH ₃ COOH	184-185	98	C ₁₂ H ₁₄ NO ₃ PS	45.71	4.45	4.45	9.85	10.15	45.43	4.95	4.70	9.95	10.62
<i>p</i> -C ₆ H ₄ NO ₂	Concd. CH ₃ COOH or dimethylformamide ^a	259.5-261.5	96.5	C ₁₂ H ₁₃ N ₂ O ₇ PS	40.00	3.62	7.77			39.99	4.13	7.71		
<i>p</i> -C ₆ H ₄ Cl	Small needles from concd. CH ₃ COOH	249-250	94.0	C ₁₂ H ₁₃ ClNO ₃ PS	41.22	3.72	4.00			41.04	3.83	4.10		
<i>p</i> -CH ₃ C ₆ H ₄ SO ₂ ^b	Small needles from concd. CH ₃ COOH	188-187	96.0	C ₁₃ H ₁₆ NO ₃ PS ₂	39.69	4.08	3.56			39.75	4.40	3.60		

^a Heated 2 hr. at 180° (2 mm.) to remove solvated dimethylformamide. ^b *p*-Toluenesulfonyl isocyanate and II reacted at room temperature.

 TABLE II
 O,O-DIALKYL S-(4-METHOXYMETHYL-1-PHOSPHA-2,6,7-TRIOXABICYCLO[2.2.2]OCTANE 1-SULFIDE) PHOSPHORODITHIOATES AND PHOSPHOROTHIOATES (VIII)

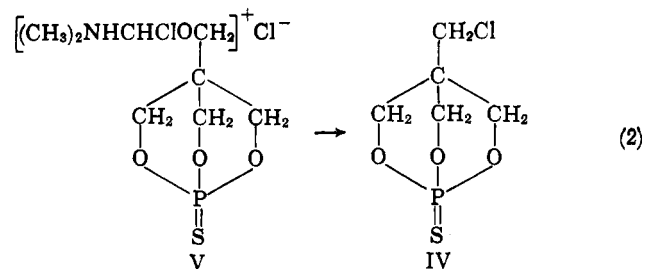
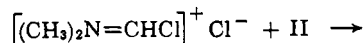
Z	Y	Solvent	Recrystn. solvent	M.p., °C.	Yield, %	Formula	Calcd., %				Found, %			
							C	H	P	S	C	H	P	S
S	CH ₃	Acetonitrile	Methanol	94.5	97.5	C ₈ H ₁₆ O ₆ P ₂ S ₃	26.22	4.38	16.91	26.22	26.62	4.47	16.90	26.22
S	C ₂ H ₅	Acetonitrile	CCl ₄	69	97.7	C ₁₀ H ₂₀ O ₆ P ₂ S ₃	30.45	5.11	15.72	24.41	30.38	5.51	15.67	24.90
S	<i>i</i> -C ₃ H ₇	Acetonitrile	2-Propanol	116.5-117	97.0	C ₁₂ H ₂₄ O ₆ P ₂ S ₃	34.30	5.69	14.71	22.75	34.32	5.80	14.70	22.60
O	C ₂ H ₅	Acetonitrile	Ethanol	95	98.0	C ₁₀ H ₂₀ O ₇ P ₂ S ₂	31.75	5.28	16.36	16.95	31.65	5.21	16.40	16.83

phosphite that forms in the first step can react with elemental sulfur at 140° to give II, in low yield.

Chemistry of 4-Hydroxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide (II).—The reactivity of the hydroxyl group was investigated under conditions which did not disrupt the phosphorus-containing cycle. The types of reaction and the new compounds obtained are discussed below.

A. Chlorination.—The classical agents for replacing aliphatic hydroxyl groups with chlorine, such as thionyl chloride and phosphorus pentachloride, did not react satisfactorily. The former failed completely to produce the desired 4-chloromethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-sulfide (IV), and phosphorus pentachloride gave this compound in very low yield, apparently because of desulfuration.

IV can be obtained, however, in good yield and high purity by an unusual chlorination method found recently in our laboratory for aliphatic glycols.¹ This



method consists in the use of solutions of I in dimethylformamide, to form a Vilsmeier-Haak adduct¹ which readily loses the amide chloride, $(CH_3)_2N=CHCl + Cl^-$,⁷ giving IV, as indicated in eq. 2. The unstable intermediate V decomposes to form IV and dimethylformamide.

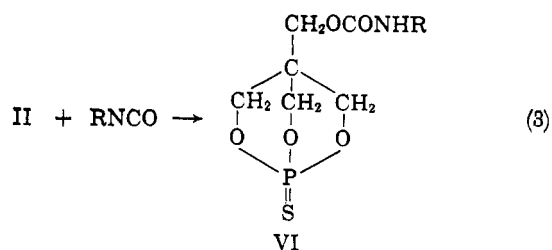
This new chlorination procedure seems to be of general application and can be used for molecules which

(7) H. Elingsfeld, M. Seefelder, and H. Weidinger, *Angew. Chem.*, **72**, 836 (1960).

decompose when treated with more vigorous reagents such as thionyl chloride or phosphorus pentachloride. Since dimethylformamide is recovered, it is likely that only catalytic amounts of dimethylformamide are required for the successful chlorination of II or other similar compounds containing hydroxyl groups. The use of dimethylformamide as a solvent in this particular reaction, however, has several advantages. The reaction can be conducted in a homogeneous solution, from which the corresponding acid to I precursor separates as the insoluble acidic dimethylammonium salt,⁸ as a result of attack of this acid on the solvent. This salt can be filtered, leaving IV to be recovered from the filtrate. The procedure can be simplified by adding water to the reaction mixture to dissolve the salt and to precipitate IV in satisfactory yield and high purity.

IV was subjected to the Arbusov-Michaelis reaction with excess triethyl phosphite at reflux temperature with the expectation of replacing $-Cl$ with $-P(O)(OC_2H_5)_2$, but most of the starting material was recovered unchanged.

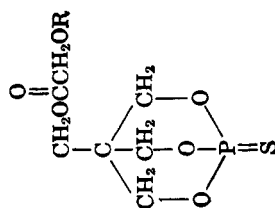
B. Reactions with Isocyanates.—It has been found that the primary hydroxyl in II reacts with mono- and polyfunctional isocyanates to form a hitherto unknown type of carbamate, as illustrated in eq. 3.



The carbamates listed in Table I were prepared by interaction of II with equimolar amounts of the isocyanate in most cases at elevated temperature. The reaction products were colorless crystalline solids, easily recrystallized, obtained in all cases in over 90% yield.

(8) See ref. 1.

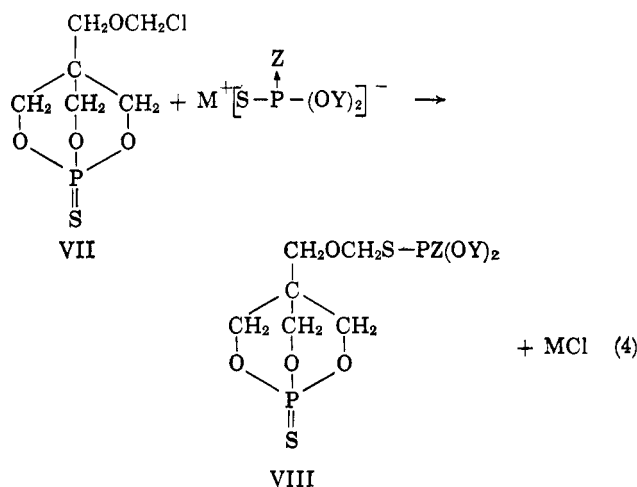
TABLE III
 SUBSTITUTED 4-HALOPHENOXACETONYLMETHYL-1-PROSPA-2,6,7-TRIOXABICYCLO[2.2.2]OCTANE 1-SULFIDES (X)



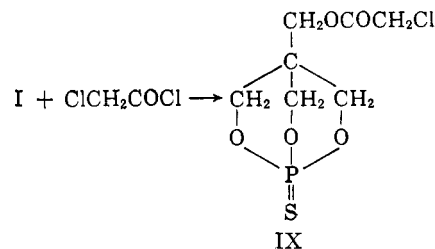
R	Solvent	Recrystn. solvent	M.p., °C.	Yield, %	Formula	Calcd., %					Found, %				
						C	H	Cl	P	S	C	H	Cl	P	S
C ₆ H ₅ -	Dimethylformamide	<i>o</i> -Dichlorobenzene	202	94.0	C ₁₃ H ₁₅ O ₄ P ₂ S	47.27	4.58		9.38		47.80	4.85		9.54	
2,4-Cl ₂ C ₆ H ₃ -	Acetonitrile	<i>o</i> -Dichlorobenzene	187-187.5	98.9	C ₁₃ H ₁₃ Cl ₂ O ₄ P ₂ S	39.11	3.28	17.76	7.76	8.03	38.91	3.20	18.2	7.61	7.85
4-FC ₆ H ₄ -	Acetonitrile	<i>o</i> -Dichlorobenzene	146-148	67.0	C ₁₃ H ₁₄ FO ₄ P ₂ S	44.83	4.05		8.89		43.72	3.70		9.07	
2,4-ClFC ₆ H ₃ -	Dimethylformamide	<i>o</i> -Dichlorobenzene	159-160	80.0	C ₁₃ H ₁₃ ClFO ₄ P ₂ S	40.80	3.42	9.26	8.09		40.40	3.44	10.10	7.90	
2,4,5-Cl ₃ C ₆ H ₂ -	Dimethylformamide	Acetone-petr. ether ^a	205	82.0	C ₁₃ H ₁₁ Cl ₃ O ₄ P ₂ S	36.01	2.79	24.53	7.14		36.68	2.90	24.20	7.30	
C ₆ Cl ₅ -	Dimethylformamide	Acetonitrile	228	99.5	C ₁₃ H ₁₀ Cl ₅ O ₄ P ₂ S	31.07	2.01	35.28	6.16		31.15	2.21	34.91	6.28	

^a The crude product was dissolved in a minimum amount of acetone and to the clear solution petroleum ether was added until turbidity occurred.

C. Chloromethylation of II and Utilization of the Resultant Chloromethyl Ether.—The conversion of II into the corresponding chloromethyl ether (VII) was achieved in high yield by the treatment of a solution of II in benzene with paraformaldehyde and gaseous hydrogen chloride. In contrast with the behavior of IV, the chlorine atom of the chloromethyl ether undergoes various nucleophilic exchange reactions. Here we report only a few typical reactions such as that with the sodium or ammonium salts of dialkyl dithiophosphoric and dialkyl thiophosphoric acids. Novel structures of the general formula VIII were obtained according to eq. 4 (summarized in Table II).



D. Reaction with Acid Halides and Utilization of the Reaction Products.—Chloroacetyl chloride and II reacted smoothly in a mole ratio of 1:1 or 2:1 and in the absence of any acid scavenger at 100° with release of HCl to give IX in high yield. Compound IX can be



utilized for various reactions, since it contains a reactive chlorine atom. Condensations with various substituted phenoxides in polar solvents have been thoroughly investigated and some of the reaction products (X) are listed in Table III. Surprisingly it was found that several of the halogenated sodium phenoxides, such as sodium 2,4-dichlorophenoxide, 2,4,5-trichlorophenoxide, and 2-chloro-4-fluorophenoxide, are readily soluble in ether, while the sodium 4-fluorophenoxide and pentachlorophenoxide are completely insoluble in this solvent. The ether solubility of certain halophenoxides was advantageously exploited for their purification.

E. Reaction with Carbamyl Chlorides.—N,N-disubstituted carbamates should be capable of formation by reaction of II with N,N-disubstituted carbamyl chlorides. The latter, however, reacted very slowly, in contrast with the reaction of isocyanates (*cf.* section B above). Whereas the latter reacted immediately at about 100° to give the desired urethans in an almost quantitative yield, N,N-diethylcarbamyl chloride

reacted with II very slowly at 145° to give a yield of only 42%, and N,N-diphenylcarbonyl chloride required more rigorous conditions to give even trace amounts of the desired carbamate. The latter was always obtained in contaminated form accompanied by unidentified colored materials. This lack of reactivity toward carbonyl chlorides is surprising when compared with the high reactivity of II toward chloroacetyl chloride.

Experimental⁹

4-Hydroxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide (II).—A mixture of 99.0 g. (0.73 mole) of pentaerythritol and 123.5 g. (0.73 mole) of thiophosphoryl chloride was heated at 145° in a 500-ml. round-bottomed flask equipped for reflux and protected from atmospheric moisture. Evolution of hydrogen chloride ceased after 5 hr. The resulting cake was crushed at room temperature and washed with ether; the crude product (143 g.) was extracted with 750 ml. of boiling water, from which II crystallized in colorless needles, m.p. 156–158°. Once recrystallized from xylene, II was obtained in 63% yield, 89.5 g., shiny needles, m.p. 161°.

Anal. Calcd. for C₈H₉O₇PS: C, 30.61; H, 4.62; P, 15.79; S, 16.35. Found: C, 30.70; H, 5.10; P, 15.70; S, 16.32.

The infrared spectrum of II showed very strong absorptions at 2.8 (OH stretching), 9.4 (OH deformation), 6.8 (CH₂ deformation), 9.9 (P—O—C), 8.7 (P—O—C vibration?), 11.5 and 12.2 (probably ring vibrations), 14.5 (P=S), and somewhat weaker absorptions at 3.4 and 3.5 μ (CH₂ stretching). Bands at 7.25 and 7.6 μ were assumed to result from CH deformation frequencies, probably of the twisting and wagging vibrations. The spectrum was consistent with structure II illustrated.

O,O,O-Tris(4-methoxy-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-sulfide) Phosphorothioate (III).—II, 3.0 g., was suspended in 30 g. of thiophosphoryl chloride and the mixture was refluxed for 30 hr. until hydrogen chloride evolution had ceased. The mixture was cooled to room temperature and the solid which separated was filtered, washed several times with ether, powdered, and finally washed with three 20-ml. portions of acetone. The product, 3.2 g. (97%), a fine crystalline powder, melted at 270° with complete decomposition; it was slightly soluble in acetone, and readily soluble in dimethylformamide.

Anal. Calcd. for C₁₈H₂₄O₁₂P₃S₄: C, 27.81; H, 3.71; P, 19.11; S, 19.75. Found: C, 27.60, 27.90; H, 4.38, 4.22; P, 18.69, 18.75; S, 20.20.

II from 4-Hydroxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane¹⁰ and Elemental Sulfur.—A mixture of 1.64 g. of the phosphite and 0.676 g. of flowers of sulfur (100% excess over the calculated amount) was placed in a small flask and heated for 30 min. to 140° with shaking. Cooling to room temperature gave a glassy product which was ground and extracted thrice with 7-ml. portions of hot water. On filtering and cooling, white crystals separated from the filtrate: 0.20 g., m.p. 142–160°. One recrystallization from xylene gave shiny needles, m.p. 161°, which showed no melting point depression when mixed with authentic II.

4-Chloromethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide (IV) by Treatment of II with Phosphorus Pentachloride.—In a 50-ml. round-bottomed flask, 5.0 g. of II was mixed with 5.31 g. of phosphorus pentachloride. Exothermic reaction occurred, and, after standing 1 hr. at room temperature, the volatile products were removed at 145° at 14 mm. The residue (6.3 g.) was treated with 30 ml. of cold water to give after drying over phosphorus pentoxide 5.6 g. of a yellowish powder (extraction with 30 ml. of ethyl acetate removed the color almost completely). No suitable solvent for recrystallization was found and the powder was therefore dissolved in acetone and reprecipitated by addition of water. After filtration and drying, the product was dissolved again in acetone and the solvent was evaporated to a very small volume until turbidity occurred. Standing at 0° for several days resulted in 1.0 g. of white crystals, m.p. 209–212°. Vacuum sublimation at 180° at 0.1 mm. gave long white needles, m.p. 216°.

Anal. Calcd. for C₈H₈ClO₇PS: C, 27.95; H, 3.73; Cl, 16.51; P, 14.40. Found: C, 28.25; H, 4.14; Cl, 16.56; P, 14.50.

Evaporation of the yellow ethyl acetate solution resulted in 2.5 g. of a yellow sticky product which was converted to a dry powder by ether treatment. Vacuum sublimation resulted in a small amount of needles, m.p. 216°, identical with the analyzed product (a considerable amount of nonvolatile, sticky, brown material remained). A small amount of IV, m.p. 216°, was also obtained when the solid obtained from ethyl acetate extraction was subjected to recrystallization from water.

4-Chloromethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide (IV) from I and II in Dimethylformamide.—To a solution of 2.2 g. (0.011 mole) of II in 6 ml. of anhydrous dimethylformamide was added a solution of I (1.8 g., 0.0061 mole) in 7 ml. of the same solvent. The mixture was refluxed for 30 min. and allowed to cool to room temperature, whereupon separation of the acidic salt, m.p. 262–263°, occurred; after standing overnight, 1.4 g. had precipitated. Water was added to the clear yellow filtrate to cause separation of small needles of IV; 1.5 g. (58%), m.p. 210–214°. Vacuum sublimation at 190° at 1 mm. resulted in long white needles, m.p. 216°.

Reaction of II with Phosgene.—Phosgene (70 g.) was condensed in a 500-ml. three-necked flask and diluted with 100 ml. of chilled dry toluene. To this was added dropwise a solution of 10 g. of II in 30 ml. of dry pyridine at –30°. Separation of an oil was observed. After the addition was complete, the mixture was allowed to stand at room temperature. After 2 hr. the oily product had become solid. Standing overnight did not appreciably increase the amount, 51.2 g. The hygroscopic product was treated with ice-water to give 9.6 g. of a brown solid (a water treatment was selected since pyridine hydrochloride could not be removed by solvent treatment). No unchanged starting material was extractable by means of hot xylene. The product showed a C=O absorption at approximately 5.8 μ and was found to be free of chlorine. It did not melt below 250°, but decomposed above this temperature, and was not identified.

Formation of Urethans of II.—Several urethans were synthesized by treatment of equimolar amounts of II and the appropriate isocyanate. The ingredients were mixed in a round-bottomed flask suitably protected from atmospheric moisture, and heated with an oil bath. All of the urethans were well-characterized crystalline solids (Table I). Two representative examples are given.

A. 4-(N-Phenylcarbamyloxymethyl)-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide.—II (9.8 g.) and 5.5 g. of phenyl isocyanate were heated to 170°; after five min., the mixture was cooled to room temperature, whereupon formation of a transparent glass took place. This glass was transformed into a crystalline powder upon being stirred with a small amount of ether and, when dried, weighed 14.2 g.; recrystallized from glacial acetic acid in 98% yield, it melted at 184–185°.

Anal. Calcd. for C₁₂H₁₄NO₈PS: C, 45.71; H, 4.45; N, 4.45; P, 9.85; S, 10.15. Found: C, 45.43; H, 4.95; N, 4.70; P, 9.95; S, 10.62.

B. 4-(N-p-Nitrophenylcarbamyloxymethyl)-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide.—II (5.9 g.) and 4.98 g. of p-nitrophenyl isocyanate were heated at 145°, forming a yellow cake, which was pulverized, extracted with 30 ml. of ether, and dried to yield 10.5 g. of crystalline material (96.5%). Recrystallization from refluxing glacial acetic acid gave yellow needles, melting at 255° with decomposition. Recrystallization from dimethylformamide gave a yellow crystalline powder which partly melted at approximately 150°, resolidified, and finally melted at 259.5–261.5° (partial melting at 150° was the result of solvation with one molecule of dimethylformamide; a sample, recrystallized from dimethylformamide and heated for 2 hr. at 180° at 0.1 mm. lost the solvated dimethylformamide entirely).

Anal. Calcd. for C₁₂H₁₃N₂O₇PS: C, 40.00; H, 3.62; N, 7.77. Found: C, 39.99; H, 4.13; N, 7.71.

The infrared spectrum of this compound showed N—H absorption at 2.95, C=O at 5.72, and the C—O bond at 8.3 μ. The nitro group could be clearly recognized at 6.5 and 7.5 μ.

4-(N-Diethylcarbamyloxymethyl)-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide.—A mixture of 3.0 g. (0.15 mole) of II and an excess of diethyl carbonyl chloride heated in an oil bath evolved hydrogen chloride at 135°. After heating 2 hr. at 145°, gas evolution had ceased and the clear, slightly brown reaction mixture was allowed to stand overnight. A semisolid product was obtained. This material was filtered on a sintered-glass Büchner funnel, and 2.0 g. of shiny, colorless crystals were iso-

(9) All melting points were taken on a Fisher-Johns apparatus and are uncorrected.

(10) W. S. Wadsworth, Jr., and W. D. Emmons, *J. Am. Chem. Soc.*, **84**, 610 (1962).

lated, which were washed with cold water to remove a very small amount of diethylamine hydrochloride. The residue was then recrystallized from dioxane to give colorless, prismatic crystals melting at 177.5–178.0° in 42.2% yield.

Anal. Calcd. for $C_{10}H_{18}NPSO_2$: N, 4.74; P, 10.51. Found: N, 5.00; P, 10.63.

4-Chloromethoxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide (VII).—In a flask equipped with stirrer was placed 49.5 g. of II; 1 l. of benzene was added, followed by 8.6 g. of paraformaldehyde. A stream of hydrogen chloride was passed into the reaction mixture with stirring at room temperature until most of the solid had dissolved. A very small amount of greasy residue that remained was removed from the reaction mixture by filtration. The clear solution was allowed to stand and, after 2 hr., crystallization began to occur. Filtration gave 11.5 g. of a crystalline material melting at 155–157°. The filtrate was then allowed to stand for 2 days, and a second crop of 16.7 g. of colorless crystals, m.p. 156–158°, was isolated. A third crop of 23.4 g. of colorless crystals was collected by evaporation of the benzene to dryness. The three crops were combined and recrystallized from xylene to yield VII as colorless plates melting at 157.5–158.0° (83.3% yield).

Anal. Calcd. for $C_8H_{10}ClO_4PS$: C, 29.44; H, 4.12; Cl, 14.50; P, 12.68. Found: C, 29.75; H, 4.24; Cl, 13.96; P, 12.51.

One representative example is given for compounds of the general structure VIII (Table II).

O,O-Dimethyl S-(4-methoxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide) Phosphorodithioate.—To a solution of 4.43 g. (0.0182 mole) of VII in 40 ml. of acetonitrile was added a solution of 3.21 g. (0.0182 mole) of ammonium O,O-dimethyldithiophosphate in 80 ml. of acetonitrile at room temperature within 10 min. After 15 hr. at room temperature 1.2 g. of ammonium chloride was removed by filtration and the filtrate was evaporated to dryness, giving a colorless, oily residue which solidified to a crystalline cake. A yield of 97.5%, 6.45 g., was obtained, which upon recrystallization from methanol gave colorless small crystals, m.p. 94.5°.

Anal. Calcd. for $C_8H_{16}O_6P_2S_3$: C, 26.22; H, 4.38; P, 16.91; S, 26.22. Found: C, 26.62; H, 4.47; P, 16.90; S, 26.22.

4-(Chloroacetoxymethyl)-1-phospha-2,7,8-trioxabicyclo[2.2.2]octane 1-Sulfide (IX).—In a 250-ml. round-bottomed flask suitably protected from moisture was placed 78.4 g. (0.40 mole) of II and 86 g. (0.76 mole) of chloroacetyl chloride and the mixture was heated to 90°; at this temperature, evolution of hydrogen chloride began. The bath temperature was slowly raised to 130° and held for a period of 4 hr. The reaction mixture was allowed to cool to room temperature. The semicrystalline product was placed on a Büchner funnel, and a brown oil of repugnant odor was removed. Final storage of the solid product on a clay plate gave 95.0 g. of ester (87% yield) in the form of gray crystals. A further small amount of an oily by-product was removed by washing the product in a beaker with 200 ml. of meth-

anol (the ester is almost insoluble in methanol). After filtration, 82.0 g. of product was obtained, which was much lighter in color and also nearly odorless. This material was recrystallized from 400 ml. of *o*-dichlorobenzene and 67.0 g. of colorless, odorless crystals melting at 142° was obtained. A second crop of 11 g. was recovered by storage of the mother liquor in a refrigerator for several days.

Anal. Calcd. for $C_7H_{10}ClO_6PS$: C, 30.84; H, 3.70; Cl, 13.00; P, 11.36. Found: C, 30.38; H, 3.61; Cl, 13.6; P, 11.69.

Two representative examples are given for the preparation of 4-halophenoxyacetoxymethyl-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-sulfides (Table III).

4-(2-Chloro-4-fluorophenoxyacetoxymethyl)-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide.—A solution of 3.37 g. (0.0201 mole) of sodium 2-chloro-4-fluorophenoxide (purified by dissolving the crude salt in diethyl ether, filtering, and evaporating to dryness) in 10 ml. of dimethylformamide was combined with a solution of 5.45 g. of IX (0.0201 mole) in 10 ml. of dimethylformamide and allowed to stand for 3.5 hr. The sodium chloride formed was not filtered but was dissolved by addition of 100 ml. of water which caused to separate simultaneously a colorless semisolid (upon scratching, the latter became completely powdery). After filtration, and washing the crystals with ethanol and finally with ether, the yield was 6.1 g. (80%). Recrystallization from *o*-dichlorobenzene resulted in colorless, prismatic crystals melting at 159.5–160°.

Anal. Calcd. for $C_{13}H_{13}ClFO_6PS$: C, 40.80; H, 3.42; Cl, 9.26; P, 8.09. Found: C, 40.40; H, 3.44; Cl, 10.1; P, 7.90.

4-(2,4,5-Trichlorophenoxyacetoxymethyl)-1-phospha-2,6,7-trioxabicyclo[2.2.2]octane 1-Sulfide.—A solution of 2.58 g. (0.0118 mole) of sodium 2,4,5-trichlorophenoxide (purified by dissolving the crude salt in diethyl ether, filtering, and adding ligroin to the filtrate for crystallization) in 10 ml. of dimethylformamide was combined with a solution of 3.2 g. (0.012 mole) of IX in 10 ml. of the same solvent, and the mixture was allowed to stand overnight. The sodium chloride formed was dissolved by the addition of 100 ml. of water which also precipitated the desired trichlorophenoxyacetic acid ester. Purification was possible by dissolving the crude in just enough acetone to effect solution and adding petroleum ether to the clear solution until turbidity occurred. Upon standing, prismatic crystals separated. An 82% yield was obtained, m.p. 204.5–205.5°.

Anal. Calcd. for $C_{13}H_{12}Cl_3O_6PS$: C, 36.01; H, 2.79; Cl, 24.53; P, 7.14. Found: C, 36.68; H, 2.90; Cl, 24.20; P, 7.30.

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