was subjected to distillation at 30 mm. In this way any remaining paraldehyde was depolymerized to aldehyde and removed at a relatively low temperature, with minimum loss of acetal. The main fraction distilled at 98–110°, weight 140 g., yield 75%. The product was washed with saturated aqueous potassium carbonate until neutral to litmus, then dried over anhydrous potassium carbonate. It was used without further purification, since any contamination by n-amyl alcohol is not important in the subsequent exchange reaction in which this alcohol is one of the reaction products. However, it is important to remove hydrogen chloride, even though an acid is needed in the exchange reaction, because any volatile acid in the mixture of cis-trans isomers probably would cause isomerization during distillation with resultant complete disappearance of the more volatile isomer. The boiling point of n-amyl acetal,[6] 225°, is so high that it can be easily removed from propylene acetal.

2,4-Dimethyl-1,3-dioxolane.—To a mixture of 110 g. (0.54 mole) of n-amyl acetal and 47.0 g. (0.62 mole) of propylene glycol (b. p., 85.5° at 10 mm.)[7] in a modified Claisen flask having a 7-cm. packing of glass rings[8] was added about 0.5 g. of p-toluenesulfonic acid. After standing for some time (one day) or upon being heated to about 40°, the original two-phase system became a single phase. Product was then taken off as quickly as possible, the flame being adjusted to keep the reflux ratio low so as to minimize refluxing of the propylene acetal and at the same time reflux back n-amyl acetal. It is desirable to distil out the propylene acetal as formed, otherwise a considerable amount of the higher boiling isomer might be converted into the lower boiling one.

The material distilling at 80–102° was collected as the product; weight, 49.5 g. (89%). At least 90% of this is the acetal for when redistilled, 46.5 g. came over without

(6) J. Béduivé, Bull. Soc. Chim. Belg., **34**, 53 (1925).

(7) Kindly supplied by F. W. Mitchell, Jr.

(8) Lucas and Pressman, "Principles and Practice of Organic Chemistry," John Wiley and Sons, New York, N. Y., 1949, Figure 9-4G, page 287.

the temperature rising above 92.8°, where the distillation stopped. The rest was holdup.

Two fractional distillations, in the presence of potassium hydroxide pellets, through a fractionating column rated at 25 theoretical plates and designed to have a small holdup[9] gave two main fractions: I (about 60%), b. p. 90.0–90.2° (745 mm.); n^{25}D 1.3923; II (about 10%) b. p. 92.8–92.9° (745 mm.) n^{25}D 1.3939. These were purified by heating with metallic sodium to remove water and n-amyl alcohol. The constants, as shown in Table I, were essentially unchanged. These compounds represent cis and trans forms, but no decision in regard to further identity can be made without additional data.

TABLE I

CONSTANTS OF ISOMERIC 2,4-DIMETHYL-1,3-DIOXOLANES

	I	II
B. p., °C. (747 mm.)	90.1	93.0
n^{25}D	1.3922	1.3938
d^{25}_4	0.9204	0.9269
MD obs.	26.436	26.345
MD calcd.	26.376	26.376
Carbon, % { Calcd.	58.80	58.80
Found	58.90	58.66
Hydrogen, % { Calcd.	9.87	9.87
Found	9.86	9.96

Summary

2,4-Dimethyl-1,3-dioxolane (propylene acetal) has been prepared by an exchange reaction between propylene glycol and n-amyl acetal. It has been separated into cis and trans forms by fractional distillation.

(9) F. W. Mitchell, Jr., and J. M. O'Gorman, Anal. Chem., **20**, 315 (1948).

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Cyclic Phosphites of Some Aliphatic Glycols

BY H. J. LUCAS, F. W. MITCHELL, JR., AND C. N. SCULLY

The possibility that phosphites of glycols might serve as a means of resolving DL-glycols led to an investigation of cyclic phosphites of some of the lower glycols. The compounds described are principally those related to ethanediol (I, R_1 and R_2 = H), 1,2-propanediol (I, R_1 = CH_3, R_2 = H), 1,3-propanediol (II) and 2,3-butanediol (I, R_1 and R_2 = CH_3), and are glycol chlorophosphites (Y = Cl), glycol hydrogen phosphites (Y = OH), glycol (alkylene) alkyl phosphites (Y = OR), and glycol amidophosphites (Y = NR_2). Also, a few derivatives, III, of pentaerythritol are mentioned.

At the time this investigation was started the only previously described phosphites of dihydroxy compounds were compounds from pyrocatechol, IV (Y = Cl and others),[1] a dimeric product from
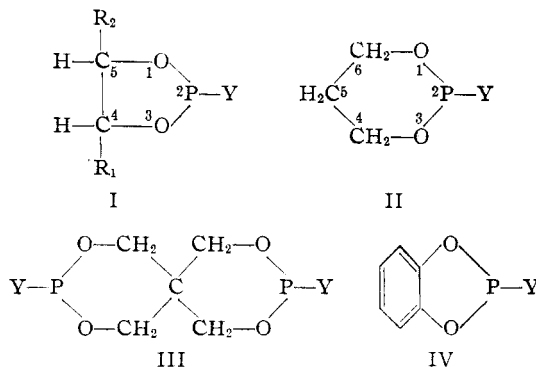
ethylene glycol,[2] and the chlorophosphite ester of meso-2,3-butanediol, on which preliminary studies only had been made.[3] After the work had well

(1) W. Knauer, Ber., **27**, 2565 (1894). The structure of IV (Y = Cl) was first elucidated by L. Anschutz and W. Broeker, ibid., **61**, 1264 (1928), and later prepared in good yield by A. E. Arbuzov and F. G. Valitova, Trans. Kirov Inst. Chem. Tech. Kazan, No. 8, 12 (1940); cf. C. A., **35**, 2485 (1941).

(2) P. Carre, Compt. rend., **136**, 756 (1903).

(3) E. Patterson, Thesis, California Institute of Technology, 1942.

progressed, other publications appeared,[4,5] so that some of the derivatives of ethanediol have now been described.

Nomenclature of the formulas I to III is best made on the basis of the Ring Index[6] since other names are unwieldy and not always definitive. Although these ring systems are not listed in the Ring Index, the parent five-membered ring of I is 1,3,2-dioxaphospholane and the six-membered ring of II is 1,3,2-dioxaphosphorinane.[7] Thus the ethyl ester of the cyclic phosphite of pyrocatechol,[1] IV (Y = OEt), is designated as 2-ethoxy-4,5-benzo-1,3,2-dioxaphospholane.

The glycol chlorophosphites were prepared by the action of phosphorus trichloride on the glycols, as shown in the case of 2-chloro-1,3,2-dioxaphospholane. The reaction was carried out also with 1,2- and 1,3-propanediol, *meso*-2,3-butanediol and

$$CH_2OH \atop CH_2OH \quad + \quad {Cl \atop Cl}\!\!>\!\!P\!-\!Cl \quad \longrightarrow \quad {CH_2O \atop CH_2O}\!\!>\!\!P\!-\!Cl \ + \ 2HCl$$

pentaerythritol. Best results with the glycols were obtained by allowing solutions of the reactants to come together at the upper end of an inclined tube and to react while flowing down before finally entering a flask. This procedure largely eliminated the main side reaction of polymer formation in which PCl forms a link between glycol molecules, as in V, or its obvious isomers. Other necessary conditions are rapid removal of

V

VI

hydrogen chloride from the system and the use of pure materials, in particular, the use of freshly distilled chloroform as a solvent. It was found that by giving attention to these details, the yields could be increased from about 30 to 85%.

A by-product, isolated in about 10% yield from a preparation of 2-chloro-4-methyl-1,3,2-dioxaphospholane, of which the yield was very poor, because of the use of old chloroform as a solvent, is a chlorinated, trialkyl phosphite, VI. The formation of a trialkyl phosphite under the conditions of the reaction was unexpected, since trialkyl phosphites usually are rapidly decomposed by a

hydrogen halide into an alkyl halide and a hydrogen phosphite.

The chlorophosphites, Y = Cl, were colorless, mobile liquids exhibiting the usual chemical characteristics of acyl halides, such as fuming in the air and reacting rapidly with water, alcohols and amines (primary and secondary). They reacted violently with nitric acid, sometimes with a flash of light, and gave immediate precipitates of calomel when dropped into aqueous mercuric chloride. They gave immediate precipitates with silver ion. The pentaerythritol derivative was a solid and although much less reactive, showed the same characteristics.

The chlorine of the chlorophosphites was replaced with ease because of the high reactivity of these compounds. Cyclic hydrogen phosphites, Y = OH, were prepared from the ethanediol and 1,2-propanediol compounds in yields up to 95%, by hydrolysis under carefully controlled conditions; cyclic alkyl alkylene phosphites, Y = OR, were prepared from all the chlorophosphites in yields of 40 to 90% by alcoholysis in the presence of pyridine or N-ethylmorpholine; and a few amido compounds, Y = NR₂, were prepared in yields of 55 to 85% by aminolysis with diethylamine or piperidine. Ammonia or a primary amine gave mixtures from which no pure product could be isolated. The yields and properties of the various compounds[8] are listed in Tables I to IV. The molar refractions given in these tables were calculated according to the Lorentz–Lorenz equation using the atomic factors of Auwers and Eisenlohr.[9]

Compounds in which Y = OR had the typical properties of trialkyl phosphites. They were colorless, mobile liquids (with the exception of spiro derivatives from pentaerythritol, which were solid), readily soluble in organic liquids, and only slightly soluble in water but going into solution in a few minutes on shaking. They rapidly reduced iodine and mercuric chloride and formed solid addition compounds with cuprous chloride.[5]

Compounds with Y = OH reacted like dialkyl phosphites. They reduced mercuric chloride slowly; they were readily soluble in water giving a neutral solution which slowly became acidic, presumable due to hydrolysis to a monoalkyl phosphite. In dilute aqueous alkali at room temperature this hydrolysis was essentially complete in one hour. The ester link of the resulting monoalkyl phosphite was quite resistant toward hydrolysis in neutral solutions, for only about four per cent. was hydrolyzed during forty days standing. In strongly acidic or basic solutions at 100° the phosphites were completely hydrolyzed in a few minutes.

(4) P. A. Rossiiskaya and M. I. Kabachnik, *Bull. acad. sci. U. R. S. S., Classe sci. chim.*, 509 (1947); *cf. C. A.*, **42**, 2924 (1948).

(5) A. E. Arbuzov, V. M. Zoroastrova and N. I. Rizpolozhenskii, *ibid.*, 208 (1948); *cf. C. A.*, **42**, 4932 (1948).

(6) A. M. Patterson and L. T. Capell, "The Ring Index," A. C. S. Monograph No. 84 (1940).

(7) C. A. Decennial Index, 1937–1946, p. 5463.

(8) The first four compounds listed in Table I appear to be less pure than other compounds listed. The spread in boiling points (given in footnotes) is greater and analyses in some cases are not as good.

(9) H. Gilman, "Organic Chemistry," Vol. II, John Wiley and Sons, New York, N. Y., 1938, p. 1739.

TABLE I

YIELDS, PHYSICAL CONSTANTS AND ANALYSES OF 2-SUBSTITUTED 1,3,2-DIOXAPHOSPHOLANES

Substituent	Yield, %	B. p., °C., at 25 mm.	d^{25}_4	n^{25}D	MD (found)	MD (calcd.) w/oP	MD of P	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Phosphorus Calcd.	Phosphorus Found
Methoxy		54[a]	1.2250	1.4406	26.291	19.883	6.41	$C_3H_7PO_3$	29.52	29.20	5.77	5.86	25.38	25.35
Ethoxy		64[b]	1.2259	1.4390	29.198	24.501	4.70	$C_4H_9PO_3$	35.30	35.06	6.66	7.03	22.77	22.60
n-Propoxy		80[c]	1.1684	1.4432	34.072	29.119	4.95	$C_5H_{11}PO_3$	40.00	40.80	7.39	7.38		
Isopropoxy		69[d]	1.1317	1.4347	34.591	29.119	5.47	$C_5H_{11}PO_3$	40.00	40.50	7.39	7.70		
n-Butoxy	88	95.0–95.2	1.0718	1.4432	40.615	33.737	6.88	$C_6H_{13}PO_3$	43.90	43.79	7.98	8.20	18.87	18.15
Isobutoxy	73	87.1–87.2	1.0633	1.4401	40.700	33.737	6.96	$C_6H_{13}PO_3$	43.90	44.11	7.98	8.00	18.87	19.05
s-Butoxy	72	83.1–83.2	1.0765	1.4400	40.185	33.737	6.45	$C_6H_{13}PO_3$	43.90	42.81	7.98	8.08	18.87	18.87
t-Butoxy	87	73.8	1.0593	1.4368	40.579	33.737	6.84	$C_6H_{13}PO_3$	43.90	43.53	7.98	8.17	18.87	19.05
Diethylamino	85	98.7–99.1	1.0556	1.4666	42.858	36.034	6.82	$C_6H_{14}PO_2N$	44.15	43.97	8.65	8.85[g]	18.99	18.88
Piperidyl	55	132[e]	1.1976	1.4971	42.810	38.452	4.36	$C_7H_{14}PO_2N$	47.99	48.23	8.05	8.55[h]		
Chloro	66	56[f]	1.4039	1.4878	25.948	18.504	7.46	$C_2H_4PO_2Cl$	18.44	20.10	3.19	3.24[i]	24.49	24.60

[a] B. p. estimated from the observed value of: [a] 60–62° (35 mm.); [b] 60–61° (21 mm.); [c] 84–86° (30 mm.); [d] 64–66° (20 mm.); [e] 108–110° (10 mm.); [f] 46.5° (15 mm.) and 71.3° (50 mm.), m. p. −28°. Previous values[4,5,a] b. p. 60–63° (35 mm.), 55–56° (23 mm.); d^{20}_4 1.2044, d^{20}_0 1.2159; n^{20}D 1.4448, 1.4460. [b] B. p. 61–62.5° (19.5 mm.), 51.5° (15 mm.); d^{20}_4 1.1191, d^{20}_0 1.1317; n^{20}D 1.4397, 1.4395. [f] B. p. 66–68° (47 mm.), 41.5° (10 mm.); d^{20}_0 1.4199, 1.4172; n^{20}D 1.4894, 1.4915. [g] Calcd. N, 8.59; found, N, 7.66. [h] Calcd. N, 8.00; found, N, 8.00. [i] Calcd. Cl, 28.1; found, Cl, 27.9.

TABLE II

YIELDS, PHYSICAL CONSTANTS AND ANALYSES OF 2-SUBSTITUTED 4-METHYL-1,3,2-DIOXAPHOSPHOLANES

Substituent	Yield, %	B. p., °C., at 25 mm.	d^{25}_4	n^{25}D	MD (found)	MD (calcd.) w/o P	MD of P	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Phosphorus Calcd.	Phosphorus Found
Methoxy	50	60.7–60.9	1.1374	1.4354	31.243	24.501	6.74	$C_4H_9PO_3$	35.30	35.33	6.66	6.89	22.77	22.60
Ethoxy	76	70.4–70.7	1.0814	1.4330	36.076	29.119	6.96	$C_5H_{11}PO_3$	40.00	40.26	7.39	7.61	20.64	20.65
n-Propoxy	83	85.6–85.8	1.0540	1.4357	40.690	33.737	6.95	$C_6H_{13}PO_3$	43.90	44.38	7.98	8.12	18.88	18.53
Isopropoxy	84	70.3	1.0380	1.4296	40.143	33.737	6.41	$C_6H_{13}PO_3$	43.90	43.83	7.98	8.41	18.88	18.42
n-Butoxy	79	100.0–100.2	1.0307	1.4380	45.374	38.355	7.02	$C_7H_{15}PO_3$	47.19	47.16	8.49	8.78	17.39	17.42
Isobutoxy	76	91.1–91.3	1.0269	1.4353	45.299	38.355	6.94	$C_7H_{15}PO_3$	47.19	46.85	8.49	8.70	17.39	17.10
s-Butoxy	90	87.9–88.3	1.0249	1.4331	45.188	38.355	6.83	$C_7H_{15}PO_3$	47.19	46.78	8.49	8.48	17.39	17.35
t-Butoxy	54	77.9–78.6	1.0170	1.4307	45.318	38.355	6.96	$C_7H_{15}PO_3$	47.19	47.39	8.49	8.45	17.39	17.47
Diethylamino	79	101.5–101.7	1.0191	1.4594	47.565	40.652	6.91	$C_7H_{16}PO_2N$	47.45	47.12	9.10	9.24[a]	17.48	17.56
Piperidyl	67	132[b]	1.0956	1.4906	49.980	43.070	6.91	$C_8H_{16}PO_2N$	50.78	49.88	8.53	9.09	16.37	16.23
Chloro	86	58[c]	1.2906	1.4707	30.417	23.107	7.31	$C_3H_6PO_2Cl$	25.65	26.82	4.31	4.48[d]	22.05	22.16
D-Bornyl	63	170[e]												

[a] Calcd., N, 7.91; found, N, 7.80. [b] B. p. estimated from the observed value of: 111.5–111.8° (10 mm.)[b]; 75.0–75.8° (50 mm.).[c] [d] Calcd., Cl, 25.22; neut. equiv., 70.4; mol. wt., 140.5; found, Cl, 24.8; neut. equiv., 70.4; mol. wt. (Rast), 136 (average). [e] B. p. estimated from the observed value of 120° (5 mm.).

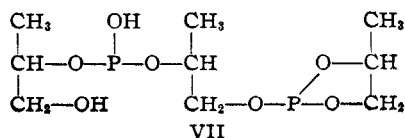## TABLE III

2-SUBSTITUTED 1,3,2-DIOXAPHOSPHORINANES

Substituent	Yield, %	B. p., °C., at 25 mm.	d^{25}_4	n^{25}D	MD (found)	MD (calcd.) w/o P	MD of P	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Phosphorus Calcd.	Phosphorus Found
Ethoxy	86	77.0–77.1	1.1227	1.4498	35.920	29.119	6.80	$C_5H_{11}PO_3$	40.00	39.71	7.39	7.53	20.64	19.74
Diethylamino	86	102.0–102.2	1.0302	1.4679	47.802	40.652	7.15	$C_7H_{16}PO_2N$	47.45	47.12	9.10	9.24[b]	17.48	17.12
Chloro	68	77[a]	1.3489	1.4884	30.034	23.107	6.93	$C_3H_6PO_2Cl$	25.65	25.50	4.31	4.19		

TABLE IV

2-SUBSTITUTED meso-4,5-DIMETHYL-1,3,2-DIOXAPHOSPHOLANES

Substituent	Yield	B. p.	d^{25}_4	n^{25}D	MD (found)	MD (calcd.) w/oP	MD of P	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Phosphorus Calcd.	Phosphorus Found
Ethoxy	40	77.0–77.6	1.0592	1.4358	40.502	33.737	6.77	$C_6H_{13}PO_3$	43.90	44.05	7.98	7.77	18.88	19.16
Diethylamino	89	109.7–110.3	1.0024	1.4595	52.196	45.270	6.93	$C_8H_{18}PO_2N$	50.25	51.27	9.49	10.04[d]	16.20	16.47
Chloro	72	76[c]	1.2220	1.4696	35.258	20.725	7.53	$C_4H_8PO_2Cl$	31.09	31.40	5.22	5.34	20.05	20.20

[a] B. p. estimated from the observed value of 66.5–67.5° (15 mm.). [b] Calcd., N, 7.90; found, N, 7.39. [c] B. p. estimated from the observed value of 66.0–66.2° (15 mm.). [d] Calcd., N, 7.33; found, N, 7.04.

When alcoholysis was attempted in the absence of a tertiary amine the main reaction products were diethyl phosphites and a high boiling material, probably VII or its obvious isomers where the phosphorus atoms are linked to other oxygen atoms.

```
CH₃    OH    CH₃              CH₃
 |     |      |                |
CH—O—P—O—CH            O—CH
 |                              |
CH₃—OH         CH₂—O—P—O—CH₂
         VII
```

The values for the atomic refraction of phosphorus given in the tables were calculated by taking the difference between the experimentally determined molar refraction and the sum of the atomic refractions of all the atoms in the molecule except phosphorus. There is no significant difference in the values of the atomic refraction of phosphorus in the four series of alkoxy and amino derivatives studied. There is, however, a definite increase in the atomic refraction of phosphorus when it is bonded to chlorine. The

general consistency of the results obtained suggests that where inconsistently low values are listed, as with a few of the compounds in Table I, these inconsistencies might be due to impurities rather than to variations of the molar refractions of the pure materials. It is noted that the deviations were greatest in those cases where there was a considerable range of boiling point (in footnotes). Kabachnik[10] gives a value of 7.04 for P in $P(OR)_3$, $(RO)_2PCl$ and $ROPCl_2$.

The vapors of the alkoxy and amino derivatives of the cyclic phosphites were apparently not toxic to humans in the concentrations encountered in the laboratory and as far as could be determined were non-toxic to mice in concentrations far above those aesthetically tolerable to humans.

At temperatures above 150° the glycol hydrogen phosphites decomposed to give phosphoric acid and phosphine (also probably higher members of the series, P_2H_4, etc.). On one occasion the products of such a decomposition exploded with considerable force as air was being readmitted to the vacuum system in which the reaction had been carried out. The force of the explosion was such as to cause fragments of glass to break other glass vessels as much as ten feet away.

Finally, some resolution of DL-1,2-propanediol was realized by fractional crystallization of the brucine salt of propylene phosphite, prepared by stirring equivalent amounts of brucine and 2-isopropoxy-4-methyl-1,3,2-dioxaphospholane with water until the brucine dissolved. Crystallization was carried out in dioxane solution.

Experimental[11]

2-Chloro-1,3,2-dioxaphospholane.—In a three-necked 1-liter flask fitted with a mechanical stirrer, a dropping funnel and a reflux condenser with a calcium chloride guard tube were placed 500 ml. of anhydrous methylene chloride and 2.5 moles (220 ml.) of recently distilled phosphorus trichloride, b. p. 75.0–75.2°. To this was added with stirring 2.5 moles (139 ml.) of redistilled, anhydrous ethylene glycol at such a rate that gentle refluxing took place. Hydrogen chloride was evolved copiously. At the conclusion of the addition the flask was quickly adapted for distillation and most of the methylene chloride distilled off on a water-bath. The remainder, distilled under reduced pressure, gave 210 g. of a colorless, mobile liquid at 45.5–47.0° (15 mm.). This was soluble in all of the usual unreactive organic solvents, fumed in the air, was violently hydrolyzed by water, and reacted readily with ammonia, primary and secondary amines, and alcohols. It decomposed at temperatures above 130° giving an orange-red solid of carbon, hydrogen and phosphorus. A redistilled sample had the constants shown in Table I.

2-Chloro-4-methyl-1,3,2-dioxaphospholane.—In a 3-liter three-necked flask provided with sealed mechanical stirrer and a wide (16 mm.) addition tube at an angle of about 15° with the horizontal and attached to two identical graduated dropping funnels (Fig. 1) was placed 100 ml. of recently distilled, well dried chloroform. From the dropping funnels 5 moles (360 g.) of anhydrous, redistilled

1,2-propanediol and 5.1 moles (705 g.) of redistilled phosphorus trichloride, each made up to 750 ml. with redistilled, dry chloroform, were allowed to flow at equivalent rates with stirrer running. At the point of mixing considerable heating took place, but further down the tube the liquid was cooler and as it entered the flask was actually below room temperature. The time required was 1.5 hours. Immediately after the last portions ran in the liquid was distilled at atmospheric pressure until the boiler temperature reached 100°. The remainder of the solvent was removed at 200 mm. and the product was distilled rapidly at 50 mm. After discarding a forerun of 50 ml., 604 g. of product was collected at 74.5–80°; yield 86%. There was left 40 g. of viscous, slightly yellow liquid. The main product was a colorless, fuming, highly reactive liquid, sufficiently pure for most subsequent reactions. It can be stored indefinitely in sealed glass ampoules. A redistilled sample had the constants shown in Table II.

The yield of chlorophosphate was lower if proper precautions were not taken. When prepared according to the method described above for 2-chloro-1,3,2-dioxaphospholane the yield was only 64%, probably because there was an excess of one reactant. Delay in distillation was even more serious, for when the reaction mixture was allowed to stand overnight, yields were only 20 to 30%. Use of chloroform which had not been freshly distilled also resulted in low yields (about 40%). In all these cases there was a large residue.

The residues remaining from a typical preparation were fairly viscous, yellowish liquids from which a small amount of intensely colored orange flocculent precipitate settled out after 24 hours, leaving the liquid almost colorless. The orange solid was removed by suction filtration and washed with water. It could be stored indefinitely under water but if allowed to dry it would inflame spontaneously in air.

Saponification of 2-Chloro-4-methyl-1,3,2-dioxaphospholane.—Water was added dropwise to 0.132 mole (18.5 g.) of the chlorophosphate until the vigorous reaction had ceased. The liquid was then heated on a steam-bath for 72 hours with several-fold excess of 8 N NaOH. The liquid was extracted continuously with ethyl ether for 48 hours, and from the ether extract there was obtained 3.7 g. (0.049 mole) of 1,2-propanediol, b. p. 80–84° (10 mm.), characterized by conversion to bis-N,N-diphenyl-carbamide, m. p. 143.5–144.5° (no depression of mixed melting point with an authentic sample).

2-(2-Chloroisopropoxy)-4-methyl-1,3,2-dioxaphospholane (VI).—The large residue from a preparation using old chloroform, and therefore not a typical experiment, gave 80 g. of colorless distillate, b. p. 94.5° (10 mm.). It differed from chlorophosphites in not fuming in moist air, not giving an immediate precipitate with silver ion, in reducing mercuric chloride instantly and in not being miscible with water. However, it dissolved rapidly, owing to hydrolysis, and the resulting solution was acidic and like typical cyclic phosphite compounds, reduced mercuric chloride, iodine or silver ion slowly. Hydrolysis with dilute sulfuric acid in the presence of paraformaldehyde[12] gave 1 mole of 1,2-propanediol per atom of phosphorus, along with an almost equivalent amount of 1-chloro-2-propanol.

Anal. Calcd. for $C_6H_{12}O_3ClP$: P, 15.5; sapon. equiv., 198. Found: P, 15.75; sapon. equiv., 224.

2-Chloro-1,3,2-dioxaphosphorinane.—From 1.0 mole (76 g.) of 1,3-propanediol, b. p. 105–107° (20 mm.), and 1.0 mole (137.4 g.) of redistilled phosphorus trichloride, following the procedure used with ethanediol, was obtained 96 g. of a colorless, mobile liquid, crude yield, 68%. This was redistilled (see Table III). This is much less reactive than the ethanediol compound.

2-Chloro-4,5-dimethyl-1,3,2-dioxaphospholane.—From 0.825 mole (74.3 g.) of *meso*-2,3-butanediol, m. p. 34.6°, and 0.825 mole (113.4 g.) of phosphorus trichloride, following the procedure used with ethanediol except that

(10) M. I. Kabachnik, *Bull. acad. sci. U. R. S. S., Classe sci. chim.*, 219 (1948); *cf. C. A.*, **42**, 5736 (1948).

(11) Microanalyses for carbon, hydrogen, chlorine and nitrogen by G. Oppenheimer and G. A. Swinehart. Phosphorus was determined by the wet combustion method of Niederl and Niederl, "Micromethods of Qualitative Organic Microanalysis," John Wiley and Sons, Inc., New York, N. Y., 1942, p. 200.

(12) M. Senkus, *Ind. Eng. Chem.*, **38**, 913 (1946), recovered 2,3-butanediol from dilute aqueous solutions by conversion to the formal.

here the glycol was dissolved in warm, anhydrous ether, there was obtained 92 g. (72%) of colorless, mobile, fuming liquid. It was less reactive than the chlorophosphites of ethanediol and 1,2-propanediol, more reactive that that of 1,3-propanediol. This would indicate that the six-membered phosphorinane ring is more stable than the five-membered phospholane ring.

3,9-Dichloro-2,4,8,10,3,9-tetraoxadiphospho-spiro(5,5)-hendecane.—To 1.0 mole (137.4 g.) of phosphorus trichloride in 750 ml. of methylene chloride was added with stirring 0.5 mole (68.1 g.) of pentaerythritol, m. p. 257–259°. The reaction was initiated with difficulty after one hour of refluxing, following which it proceeded smoothly. Refluxing was continued for one hour after the last of the pentaerythritol had disappeared. Following removal of the solvent the residue was twice recrystallized from chloroform; weight of colorless crystalline product, 53.5 g. (yield 40%), m. p. 121–123°; fairly stable in moist air.

Anal. Calcd. for $C_5H_8O_4P_2Cl_2$; C, 22.65; H, 3.04. Found: C, 22.62; H, 3.37.

2-Hydroxy-1,3,2-dioxaphospholane.—A solution of 1 mole (18.0 g.) of water in 50 ml. of dioxane was added slowly to 1 mole (126.8 g.) of 2-chloro-1,3,2-dioxaphospholane in 250 ml. of anhydrous dioxane. Following removal of solvent from the resulting two-phase liquid by distillation at 40 mm., at 1 mm. a slightly viscous liquid distilled at 220–225°. At this point the liquid in the boiler began to decompose and an odor resembling phosphine was noted. The bath was dropped immediately and air was admitted into the system. When the pressure had risen to 20 mm. a violent explosion shattered the apparatus.

Redistillation of the product through a short-path apparatus was accomplished with bath at 125°, to give a very viscous, water-soluble liquid, insoluble or only slightly soluble in non-polar organic solvents, $n^{25}D$ 1.4862, d^{25} 1.52, molecular weight, 420 (cryoscopic in succinonitrile), 576 (cryoscopic in water). Its highly viscous nature and high molecular weight indicate association. It slowly reduced silver and mercuric ion.

2-Hydroxy-4-methyl-1,3,2-dioxaphospholane.—A solution of 0.63 mole (11.25 g.) of water in 100 ml. of anhydrous dioxane was added, in five separate portions and with cooling between additions, to 0.625 mole (87.8 g.) of 2-chloro-4-methyl-1,3,2-dioxaphospholane dissolved in 100 ml. of anhydrous dioxane in a 500-ml. flask. The pressure was lowered to 40 mm., the contents were held at room temperature to remove as much hydrogen chloride as possible, then dioxane was removed with bath at 90°. At 0.6 mm. and with bath at 120–125° a colorless liquid with viscosity similar to that of 1,2-propanediol distilled at 76–82°, weight 73 g., yield 96%. The yield was much lower if water was added undiluted to either the chlorophosphite alone or in solution, or if hydrogen chloride was not rapidly removed. The amount of non-distillable residue was larger in such cases.

The hydroxy compound acted somewhat as a monobasic pseudo acid. A freshly made solution was essentially neutral, but on the addition of base the end-point faded. An hour was required to reach a permanent end-point. However, an aqueous solution after standing for 8 to 10 hours gave a sharp, permanent end-point immediately. This may be interpreted as indicating either that the phosphite ring may have opened through hydrolysis or that a pseudo acid changes slowly to a true acid when in contact with water. Neutralization equivalents varied from 122 to 145 (calcd. 122). No increase was noted after standing for 45 days.

The viscosity of the liquid changed in an interesting fashion. On standing overnight it increased somewhat and after 5 days so much that the liquid would hardly flow. This liquid distilled at 76.5° (0.65 mm.) leaving very little residue. The distillate was as mobile as the original. After a week this had thickened enough to be immobile. On redistillation at 0.65 mm. the temperature rose to 90° and the distillate was much more viscous than
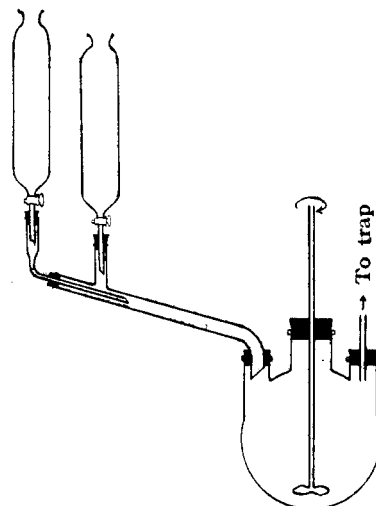

Fig. 1.—Apparatus for preparation of glycol chlorophosphites.

the two previous ones. The change in viscosity on standing did not significantly alter the neutralization equivalent. In one case the neutralization equivalent was 145 one day after preparation and was 143 after 40 days.

Further evidence for the structure proposed, in addition to the neutralization equivalent, was obtained from results of hydrolysis. When heated with a two-fold excess of 3 N base, 20.0 g. of 1,2-propanediol was recovered from 0.3 mole (36.6 g.) of the hydroxy compound, yield 88%. Also, a 95% yield of formal was obtained in both acidic and basic hydrolysis, by the procedure of Senkus.[12]

Non-volatile Residue from 2-Hydroxy-4-methyl-1,3,2-dioxaphospholane Preparation.—Unlike the volatile compound, the aqueous solution of this gave an immediate sharp end-point when neutralized. Values of the neutralization equivalent varied from 67 to 96. The residue became more viscous on standing, but there was little change in neutralization equivalent; in one case, after standing for 40 days it increased from 94 to 96. Hydrolysis of 5.42 g. which had a saponification equivalent of 96, gave 1.5 ml. of formal, only 36% of the amount to be expected from an equal weight of the volatile compound.

2-Alkoxy Derivatives, Y = OR.—Cyclic alkyl alkylene phosphites of ethanediol, 1,2-propanediol, 1,3-propanediol and 2,3-butanediol were prepared as follows: In a 100-ml. two-necked flask, fitted with a dropping funnel and a calcium chloride guard tube, was placed 30 ml. of ligroin and 0.1 mole of the chlorophosphite. With the flask immersed in ice-water and the contents cooled to about 5°, 0.15 mole of redistilled pyridine or N-ethylmorpholine was added. N-Ethylmorpholine was preferred since its hydrochloride was easier to remove from the product. Then 0.1 mole of a pure anhydrous alcohol, diluted with about 10 ml. of ligroin, was added to the mixture dropwise, with cooling and agitation. After standing at room temperature for one or two hours the liquid was removed from the solid amine hydrochloride by means of a filter stick, so as to exclude moisture, and washed with at least three 15-ml. portions of ligroin. After filtrate and washings had stood for about fifteen hours, to allow further separation of the solid, the liquid was distilled through a 40 cm. column packed with a continuous wire helix. Foaming was troublesome. Some amine hydrochloride crystallized out of most of the fractions of the first distillation. Usually two or more distillations were necessary. Data are given in Tables I to IV.

2-Amino Derivatives, Y = NR₂.—The piperidyl and diethylamino derivatives were prepared by the same procedure as the alkoxy derivatives except that two moles of the secondary amine were used per mole of chlorophos-

phite and the tertiary amine was omitted. The products were liquids with a somewhat disagreeable odor. They underwent hydrolysis only slightly more readily than the corresponding alkoxy derivatives. Yields, physical constants and analyses of the products are in the tables.

Derivatives of the Cyclic Phosphite of Pentaerythritol. —The ethoxy derivative, 3,9-diethoxy-2,4,8,10,3,9-tetra-oxadiphosphospiro(5,5)hendecane, was prepared in the following manner: to a clear, filtered solution of 0.1 mole (26.5 g.) of the solid chlorophosphite dissolved in 50 ml. of chloroform was added with cooling: first, 0.24 mole (27.5 g.) of N-ethylmorpholine, next, 0.2 mole (9.2 g.) of absolute ethanol in three portions. After standing overnight at 5° the well-formed tabular crystals of N-ethylmorpholine hydrochloride were removed, and two more crops were precipitated by addition of 80 ml. of ligroin in two portions. Additional ligroin brought down an oil instead of the crystals. After removal of solvents *in vacuo* on a water-bath the residue solidified into a mass of soft white crystals, weight 19.7 g. (70% yield). It was rapidly hydrolyzed by atmospheric moisture. A sample stored in a desiccator over calcium chloride for 20 hours turned to a liquid. No solvent or mixture of solvents could be found which was satisfactory for recrystallization of the product. Sublimation at 0.4 mm. pressure gave long colorless needles, m. p. 80-82°.

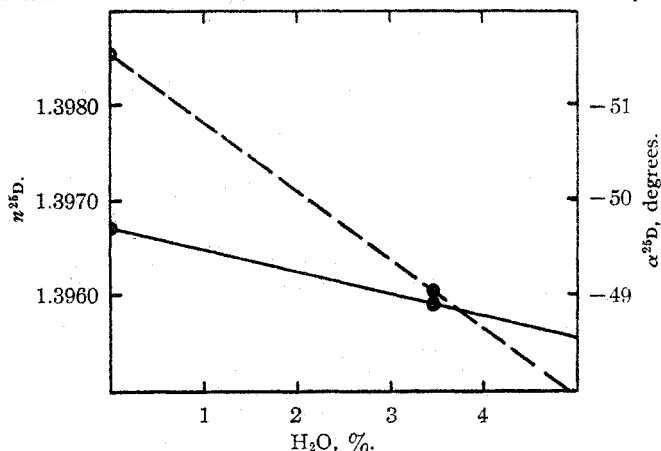*Anal.* Calcd. for $C_9H_{18}P_2O_6$: P, 21.80. Found: P, 21.50.

Fig. 2.—Effect of water on the refractive index and optical rotation of the cyclic formal of 1,2-propanediol: $n^{25}D$ ————; $\alpha^{25}D$ — — —.

Ethanolysis of 2-Chloro-4-methyl-1,3,2-dioxaphospholane in the Absence of Base.—The reactants were combined, both diluted and undiluted, under the conditions shown in Table V. Distillation was done at 10 mm. Two main products were obtained in combined yields varying between 75 and 90%, but neither of these was the desired chlorophosphite ester. The more volatile compound, b. p. 68-71° at 10 mm., had $n^{25}D$ ranging from 1.4070 to 1.4100 and the other, b. p. 120-130° at 10 mm., had $n^{25}D$ 1.46. The lower boiling compound was diethyl phosphite (DEP).[13] Two moles of ethanol were obtained per atom of phosphorus.

Anal. Calcd. for $C_4H_{11}PO_3$: C, 34.78; H, 8.03; P, 22.43; sapn. equiv., 69; mol. wt., 138.1. Found: C, 34.95; H, 8.02; P, 21.58; sapn. equiv., 75; mol. wt. (Rast), 141.

The higher boiling compound was an ester which appeared to contain 3 glycol units and 2 phosphite units (appropriated to TGDP). Structure VII has been assigned it. Saponification yielded 1.2 moles of glycol per atom of phosphorus.

(13) B. p. 76° (14 mm.), $n^{20}D$ 1.40823; A. E. Arbuzov and A. Ivanov, *J. Russ. Phys. Chem. Soc.*, **47**, 2019 (1915); *Chem. Zentr.*, **87**, II, 308 (1916).

TABLE V

ETHANOL (A) AND PROPYLENE CHLOROPHOSPHITE (B)

A moles	B moles	Order of adding	Temp., °C.	Product, % DEP	TGDP	Over-all yield, %
1	1	Simul.	*ca.* 25	20	80	90
2	1	A to B	*ca.* 25	60[a]	40	80
2[b]	1	B to A	*ca.* 25	45	55	80
2	1	B to A	0	65	35	90
1.2[c]	1[c]	Simul.	−70	40	60	75

[a] Small amount of ethyl chloride was recovered. [b] In $CHCl_3$. [c] In equal volume of CH_2Cl_2.

Anal. Calcd. for $C_9H_{20}P_2O_7$: C, 35.77; H, 6.67; P, 20.50; sapn. equiv., 75.5. Found: C, 35.44; H, 6.54; P, 20.28; sapn. equiv., 70.

DL-4-Methyl-1,3-dioxolane.—This was prepared from 1,2-propanediol and paraformaldehyde by the method of Senkus[12] and recovered as the azeotrope with water, b. p. 74° (745 mm.), through a small column of about 15 theoretical plates. It was salted out with potassium carbonate, dried with anhydrous copper sulfate and distilled, b. p. 84.2° (745 mm.), weight 8.4 g. (95% yield from 0.1 mole, 7.6 g., of glycol); $n^{25}D$ 1.3966; dn/dt −0.0004; d^{25}_4 0.9834.

D(−)-4-Methyl-1,3-dioxolane.—This was prepared from D(−)-1,2-propanediol,[14] $\alpha^{25}D$ −16.03°, in the same manner and with the same yields as the inactive formal; b. p. 84.2° (745 mm.); $n^{25}D$ 1.3971°, dn/dt −0.0004, $\alpha^{25}D$ −51.33°; $[\alpha]^{25}D$ −52.4° (undiluted).

Usefulness of Formal.—The recovery of formal from dilute aqueous solutions of the glycol is essentially quantitative (≠10%) down to amounts as small as 3 g. In addition, the rotation of the formal of the optically active glycol is very high. Thus the formal should prove to be of value in analysis of 1,2-propanediol possessing low activity. Analysis is facilitated by knowing how the refractive index and the rotation of the active formal change as water is added. This is shown in Fig. 2.

Partial Resolution of 1,2-Propanediol.—To a solution of 0.1 mole (16.4 g.) of 2-isopropoxy-4-methyl-1,3,2-dioxaphospholane in 100 ml. of water was added 0.1 mole (39.5 g.) of anhydrous brucine. The mixture was stirred until the brucine dissolved, which required 1 to 2 hours. Water was removed at 25 mm. The first half of the distillate was redistilled to give the water–isopropyl alcohol azeotrope, b. p. 80° (87% yield). Dioxane was added and the dioxane–water azeotrope removed at 25 mm. A crop of crystals was obtained. These were removed from the liquid by suction filtration and the operation repeated until 54.8 g. (98% yield) of brucine salt was obtained. This was systematically recrystallized from dioxane. There were two types of crystals: prisms, m. p. 187-188°, and needles, growing in rosettes, m. p. 133-138°. Those have not been investigated.

The least soluble fraction of salts, crystallized three times from dioxane, was converted to the formal, $\alpha^{25}D$

(14) The active glycol was produced by phyto reduction of acetal with yeast, following the procedure of P. A. Levene and A. Walti, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 545. The recovery of the glycol was effected without laborious distillation, first, by a ten-fold concentration by freezing in a deep freeze unit, then by converion to and recovery of the formal. Hydrolysis of this gave the glycol, b. p. 84.2-84.5° (10 mm.), $\alpha^{25}D$ (observed) −16.03° (undiluted), previous value, $\alpha^{18}D$ −16.3°, E. Färber and F. F. Nord, *Biochem. Z.*, **112**, 316 (1920). This glycol has been shown to be related configurationally to (−)-lactic acid by P. A. Levene and H. L. Haller, *J. Biol. Chem.*, **67**, 329 (1926), and thus to have the D configuration, K. Freudenberg and Fr. Brauns, *Ber.*, **55**, 1339 (1922).

−6.9°. This is only about 13% of the rotation of the optically pure formal. Brucine does not seem to be a satisfactory alkaloid for the resolution.[15]

Summary

A number of glycols have been shown to react with phosphorus trichloride. The products are highly reactive chlorophosphite esters. From

(15) It is planned to continue this investigation with other alkaloids.

these, by reaction with alcohols, are formed mixed glycol alkyl phosphites, which undergo hydrolysis slowly. Addition of brucine to the resulting solutions yields brucine salts. These have some promise as a means of resolving DL-glycols.

Propylene formal is useful in recovering 1,2-propanediol from dilute aqueous solution.

Preparation and Hydrolysis of Some Acetals and Esters of D(—)-2,3-Butanediol

BY H. K. GARNER* AND H. J. LUCAS

The value of formals in the recovery of the lower glycols from dilute aqueous solutions[1] and the possibility that phosphite esters may serve as intermediates in resolving glycols[2] makes desirable a study of the stereochemistry of formation and hydrolysis of cyclic acetals and cyclic esters of glycols. D(−)-2,3-Butanediol was used since it is the most readily available active glycol.[3] The structures, configurations and names of the compounds studied are shown in Fig. 1.

Nomenclature.—The names shown in Fig. 1 are based on the parent ring systems of the Ring Index.[4] Thus I, II and III are derivatives of 1,3-dioxalane, and IV and V of 1,3,2-dioxathiolane, but the ring systems of VI to X are not found in the Index. The nomenclature of compounds VI to IX as derivatives of 1,3,2-dioxaphospholane follows that of *Chemical Abstracts*.[5] The system of X is more complex. It seems better to use only the common name.

In Table I, in which are listed properties and the analytical data, are given also the common names, which indicate better the chemical nature of the acetal or ester.

Hydrolysis.—In Table II are shown the conditions for hydrolysis of the compounds of Table I and the properties of the resulting glycol, in the case of the formal, or of the resulting formal, in all the other cases. In the first case the glycol recovered had $\alpha^{25}D$ −12.96°. Since the initial glycol had $\alpha^{25}D$ −13.00° it is evident that during the changes glycol → formal → glycol the maximum loss of optical activity is only 0.3%. Thus the

* U. S. Rubber Co., Passaic, N. J.

(1) M. Senkus, *Ind. Eng. Chem.*, **38**, 913 (1946).

(2) H. J. Lucas, F. W. Mitchell, Jr., and C. N. Scully, THIS JOURNAL, **72**, 5491 (1950).

(3) About the time these investigations were started, publications began to appear by Neish and co-workers in the *Canadian Journal of Research* on various derivatives of this glycol, including cyclic acetals and esters. Pertinent work of theirs is referred to later.

(4) A. M. Patterson and L. T. Capell, "The Ring Index," Reinhold Publishing Corp., New York, N. Y., 1940.

(5) *C. A. Decennial Index*, 1937-1946, pp. 3553, 5463.

method of converting the glycol to the formal, for the purpose of removing it from a dilute aqueous solution, followed by hydrolysis of the formal to the glycol, does not cause any appreciable change in configuration at either asymmetric carbon atom, for the over-all change. In other cases, therefore, it was necessary only to recover the formal from reaction mixtures and to deter-
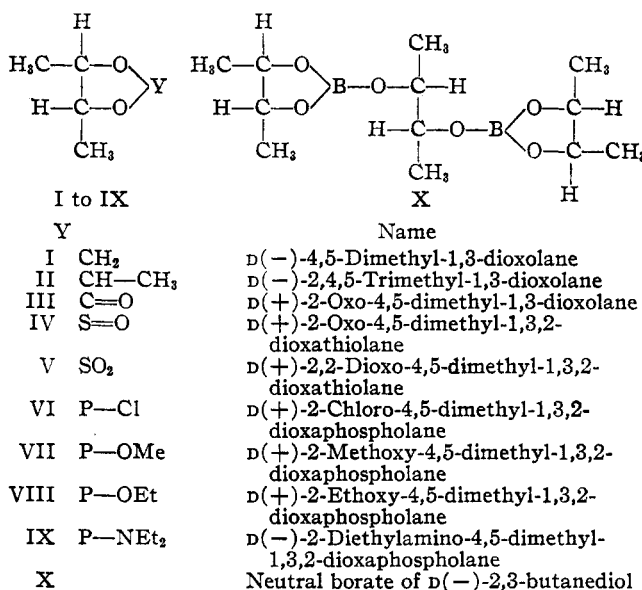

Fig. 1.—Configurations and names of some cyclic acetals and esters of D(−)-2,3-butanediol.

	Y	Name
I	CH₂	D(−)-4,5-Dimethyl-1,3-dioxolane
II	CH—CH₃	D(−)-2,4,5-Trimethyl-1,3-dioxolane
III	C=O	D(+)-2-Oxo-4,5-dimethyl-1,3-dioxolane
IV	S=O	D(+)-2-Oxo-4,5-dimethyl-1,3,2-dioxathiolane
V	SO₂	D(+)-2,2-Dioxo-4,5-dimethyl-1,3,2-dioxathiolane
VI	P—Cl	D(+)-2-Chloro-4,5-dimethyl-1,3,2-dioxaphospholane
VII	P—OMe	D(+)-2-Methoxy-4,5-dimethyl-1,3,2-dioxaphospholane
VIII	P—OEt	D(+)-2-Ethoxy-4,5-dimethyl-1,3,2-dioxaphospholane
IX	P—NEt₂	D(−)-2-Diethylamino-4,5-dimethyl-1,3,2-dioxaphospholane
X		Neutral borate of D(−)-2,3-butanediol

mine its physical properties. By comparison of the resulting data with the properties of the active formal or with those of the *meso* formal, the properties of which are known,[1] conclusions could be drawn as to configurational changes. Hydrolysis of acetal, carbonate, sulfite and chlorophosphite yield formal of high rotation, thus showing that formation and hydrolysis of these compounds does not involve any significant change in configuration.

The results with the formal and acetal indicate