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Cyclodehydration of 1,4-Butanediols by Pentaethoxyphosphorane

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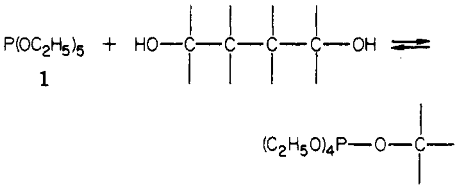
Sometime ago it was reported that pentaethoxyphosphorane and diethoxytriphenylphosphorane can effect the cyclization of various substituted alcohols to heterocycles. These reactions proceeded smoothly at room temperature and required no catalysis or blocking groups.[1] More recently Evans and co-workers[2] have utilized diethoxytriphenylphosphorane to cyclize a variety of diols to cyclic ethers. The major difficulty with using these reagents as synthetic tools has been their general unavailability. The original synthesis involved reaction of a trivalent phosphorus compound with diethyl peroxide. The necessity of working with diethyl peroxide has certainly been a hindrance to the development of these reagents. More recently it has been shown that the same products can be obtained from the reactions of trivalent phosphorus compounds with alkyl benzenesulfenates.[3] The advent of this new synthetic route allows these substances to be obtained in quantity, and thus large quantities of pentamethoxyphosphorane have been prepared and its use as a methylating reagent has been investigated.[4]

In this study pentaethoxyphosphorane has been used to cyclize a variety of 1,4-alkanediols. Pentaethoxyphosphorane was chosen because it can be prepared in high yield, 88%, and in better than 90% purity. For these studies it is more useful than pentamethoxyphosphorane because it undergoes intermolecular alkylation reactions less readily than the methoxy compound. The results of cyclization reactions of seven 1,4-alkanediols are incorporated in Table I. All of the reactions were conducted at room temperature, and the courses of the reactions were monitored by ^{31}P NMR spectroscopy. All of the reactions were conducted at the same concentration except for 2,5-dimethyl-2,5-hexanediol which was conducted at a significantly higher dilution because of its insolubility. The high dilution certainly contributed to the slowness of the reaction. It is gratifying to note that the yield was substantial. The important finding is that the yields in all cases were certainly acceptable, 63% being the lowest. These findings coupled with the other attributes of the cyclization process certainly suggest that the reagent will be of considerable value in synthesis.

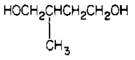
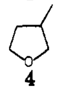
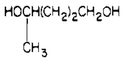
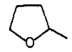
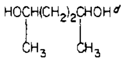
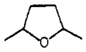
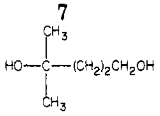
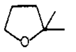
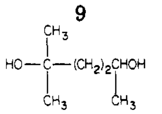
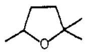
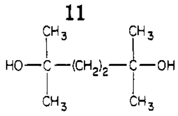
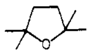
The overall process is of interest, and the relative times required coupled with stereochemical data obtained by Evans et al. suggest that the first reaction involves exchange of one of the hydroxyl groups of the diol to give phosphoranes which then undergo cyclization (eq 1). If cyclization is slow, further exchange can occur that will lead to a diminution in yield; i.e., polymeric phosphoranes will be formed.



$$\mathrm{P(OC_2H_5)_5} + \mathrm{HO{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}OH} \rightleftharpoons \mathrm{(C_2H_5O)_4P{-}O{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}\overset{|}{\underset{|}{C}}{-}OH} \quad (1)$$

1

Table I[a]

diol	product	reaction time, h	% yield
$\mathrm{HOCH_2(CH_2)_2CH_2OH}$ **1a**	 **2**	3.5	94.6[b]
 $\mathrm{HOCH_2\underset{CH_3}{CH}CH_2CH_2OH}$ **3**	 **4**	2.2	66.4[b]
 $\mathrm{HO\underset{CH_3}{CH}(CH_2)_2CH_2OH}$ **5**	 **6**	17.7	69.2[b]
 $\mathrm{HO\underset{CH_3}{CH}(CH_2)_2\underset{CH_3}{CH}OH}$[d] **7**	 **8**	42.0	69.3[c]
 $\mathrm{HO{-}\overset{CH_3}{\underset{CH_3}{C}}{-}(CH_2)_2CH_2OH}$ **9**	 **10**	28.0	78.8[b,c]
 $\mathrm{HO{-}\overset{CH_3}{\underset{CH_3}{C}}{-}(CH_2)_2\underset{CH_3}{CH}OH}$ **11**	 **12**	22.5	62.7[b]
 $\mathrm{HO{-}\overset{CH_3}{\underset{CH_3}{C}}{-}(CH_2)_2{-}\overset{CH_3}{\underset{CH_3}{C}}{-}OH}$ **13**	 **14**	450.0	79.1[b,e]

[a] See Experimental Section for details of experiment. [b] Yield determined by quantitative ^{13}C NMR. [c] Yield determined by GLPC. [d] A mixture of meso and *d,l* isomers was used. [e] Yield determined by isolation.

Experimental Section

^{1}H NMR spectra were run on Varian Model T-60 and FT-80 spectrometers. ^{13}C and ^{31}P NMR spectra were run on a Varian FT-80 spectrometer equipped with a 10-mm, variable-temperature, broad-band probe. ^{13}C chemical shifts are reported in parts per million relative to tetramethylsilane. The qualitative spectra were obtained by using full proton decoupling a 30° flip angle and a 2.05-s repetition rate with no pulse delay.

Quantitative ^{13}C NMR spectra were obtained by inserting a 30-s delay between the acquisition time and the next pulse, i.e., a repetition rate of 32.05 s. The decoupler was gated off during this delay, thus eliminating the Overhauser effect. It was possible to increase the flip angle to 70° for these quantitative spectra.

A standard solution containing tetrahydrofuran, ethanol, and triethyl phosphate (50.0:20.0:30.0) was analyzed by ^{13}C NMR. The results indicated a 49.1:20.8:30.1 mixture.

All manipulations were carried out in an inert atmosphere. All solvents were freshly distilled and scrupulously dried.

Preparation of Pentaethoxyphosphorane, 1. A 1-L three-neck flask, equipped with a pressure equalized dropping funnel and a mechanical stirrer, was charged with 153.7 g (0.997 mol) of freshly distilled ethyl benzenesulfenate[3] and petroleum ether (400 mL) (37-58 °C). The flask was cooled in a dry ice-acetone bath. Over a period of 1.5 h, with vigorous stirring, 74.6 g (0.449 mole) of triethyl phosphite dissolved in petroleum ether (50 mL) was added dropwise. The reaction mixture was allowed to warm to room temperature, and it was stirred for 15 h. The

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(1) (a) Chang, B. C.; Conrad, W.; Denney, D. B.; Denney, D. Z.; Edelman, R.; Powell, R. L.; White, D. W. *J. Am. Chem. Soc.* 1971, *93*, 4004. (b) Denney, D. B.; Powell, R. L.; Taft, A.; Twitchell, D. *Phosphorus Relat. Group V Elem.* 1971, *1*, 151.

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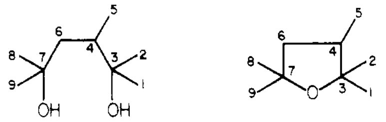
Table II[a]



compd	carbon number—^{13}C, δ 1	2	3	4	5	6	7	8	9
1a			63.2	30.3		30.3	63.2		
2			68.2	26.2		26.2	68.2		
3			67.6	36.9	16.8	33.5	60.3		
4			75.0	34.0	17.8	34.6	68.0		
5	23.8		68.1	36.5		29.5	62.9		
6	20.9		75.6	33.5		26.2	67.8		
7[b]	24.0		68.5	36.4		36.4	68.5	24.0	
	23.6		67.9	35.2		35.2	67.9	23.6	
8[c]	21.7		75.9	34.7		34.7	75.9	21.7	
			75.0	33.6		33.6	75.0		
9	29.0	29.0	70.0	40.1		27.4	62.2		
10	27.3	27.3	80.1	38.0		25.7	66.5		
11	28.8	28.8	69.7	39.5		33.6	67.1	22.9	
12	28.6	29.9	81.5	39.5		34.5	75.3	22.3	
13	29.9	29.9	71.0	38.3		38.3	71.0	29.9	29.9
14	31.5	31.5	82.6	40.7		40.7	82.6	31.5	31.5

[a] See Experimental Section for details of NMR experiment. [b] A mixture of the meso and *d,l* isomers. [c] A mixture of cis and trans isomers.

mixture was cooled to −78 °C, and the solution was separated from the solid diphenyl disulfide by forcing it with nitrogen through a sintered glass plug. The precipitate was washed, at −78 °C, with an additional 250 mL of petroleum ether. The petroleum ether fractions were combined and concentrated at reduced pressure. The residual oil was distilled through a 6-in. Vigreaux column, bp 58–64 °C (0.55 mm), to yield 100.6 g (87.6%) of 1. ^{31}P NMR spectroscopy indicated this material was contaminated with 8% of triethyl phosphate.

Preparation of 2-Methyl-2,5-pentanediol. This material was prepared according to the method of Colonge and Macey[5] using methylmagnesium iodide and γ-butyrolactone to yield 8.85 g (46.8%) of product, bp 77 °C (0.15 mm) [lit.[6] bp 107 °C (5.5 mm)].

Preparation of 2-Methyl-2,5-hexanediol. This substance was prepared in a similar fashion as above using methylmagnesium iodide and γ-valerolactone to yield 13.0 g (61.5%) of product, bp 67 °C (0.20 mm) [lit.[7] bp 107 °C (4 mm)].

Reactions of Diols with 1. In a representative experiment, 1 (0.033 mol) dissolved in dichloromethane (5 mL) was added, at 0 °C, to a stirred solution of the diol (0.033 mol) in dichloromethane (15 mL). The reaction mixture was allowed to warm to room temperature. The progress of the reaction was monitored by observing changes in the ^{31}P NMR spectra of the mixture. When it was established that the reaction was complete, the mixture was distilled at atmospheric pressure. All fractions were subjected to ^{13}C NMR analysis both qualitative and quantitative.

Reaction of 2,5-Dimethyl-2,5-hexanediol with 1. Compound 1, 8.92 g (0.35 mol), was dissolved in dichloromethane (10 mL). It was then added, at room temperature, to a stirred solution of 2,5-dimethyl-2,5-hexanediol, 5.08 g (0.035 mol) in dichloromethane (100 mL). The progress of the reaction was monitored by observing changes in the ^{31}P NMR spectra of the mixture. When it was established that the reaction was complete, the mixture was distilled to give 3.53 g (79.1%) of a colorless liquid, bp 115 °C (760 mm) [lit.[8] bp 115.5–116.5 °C (760 mm)]. The residue consisted of the higher boiling triethyl phosphate.

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Registry No. 1, 7735-87-7; 2, 109-99-9; 3, 2938-98-9; 4, 13423-15-9; 5, 626-95-9; 6, 96-47-9; 7, 2935-44-6; 8, 1003-38-9; 9, 1462-10-8; 10, 1003-17-4; 11, 29044-06-2; 12, 82004-72-6; 13, 110-03-2; 14, 15045-43-9; PhSOEt, 54815-45-1; P(OEt)$_3$, 122-52-1; 1,4-butanediol, 110-63-4; γ-butyrolactone, 96-48-0; γ-valerolactone, 108-29-2.

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