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CHLORINATION AND CYCLODEHYDRATION OF 1,2-DIOLS WITH THE "TRIPHENYLPHOSPHINE-TETRACHLOROMETHANE-POTASSIUM CARBONATE" REAGENT

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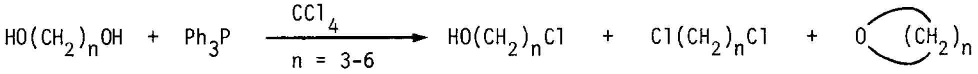
Summary: The yields of the epoxides obtained from the reaction of 1,2-diols with the "triphenylphosphine-tetrachloromethane-potassium carbonate reagent" range from 27-85% depending on the relative concentration of triphenylphosphine and diol. In the absence of heterogeneous potassium carbonate, reactions of 1,2-diols with triphenylphosphine-tetrachloromethane give largely 1,2-chlorohydrins.

The chlorination of primary and secondary alcohols with triphenylphosphine (TPP) and tetrachloromethane (CCl_4) is rapidly becoming a useful synthetic tool.[1] Quite recently, we reported that a series of acyclic, aliphatic diols [e.g., $HO(CH_2)_nOH$, where n = 3, 5, and 6] undergoes preferential chlorination to chlorohydrins and dichlorides with TPP-CCl_4. The exceptions (n=4) are 1,4-diols [e.g., 1,4-butanediol, <u>cis</u>-2-butene-1,4-diol, and <u>cis</u>-1,2-bis(hydroxymethyl)cyclohexane] where cyclodehydration to the appropriate tetrahydrofuran is preferred[2] (Eq. 1). It was

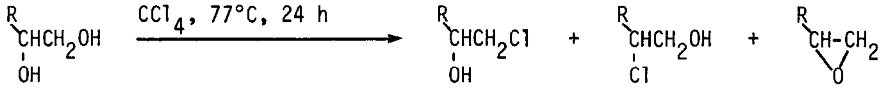


$$HO(CH_2)_nOH + Ph_3P \xrightarrow[n\,=\,3\text{-}6]{CCl_4} HO(CH_2)_nCl + Cl(CH_2)_nCl + O\,(CH_2)_n \qquad (1)$$

also inferred that 1,2-diols may be susceptible to "controlled cyclodehydration" rather than chlorination with TPP-CCl_4 in the presence of heterogeneous potassium carbonate (K_2CO_3). Here, we report our preliminary findings on the synthetic potential of the "TPP-CCl_4-K_2CO_3" reagent as a preparative method for epoxides from 1,2-diols.

We have examined the reactions of several diols with both "TPP-CCl_4" and "TPP-CCl_4-K_2CO_3" reagents. The general experimental procedure[3] involves addition of the diol (5 mmol) to a mixture of TPP (1.97 g, 7.5 mmol) and anhydrous K_2CO_3 (1.38 g, 10 mmol) in anhydrous tetrachloromethane (15 mL) with stirring at reflux for 24 h. After cooling to ambient temperature (ca. 25°), the composition of the reaction mixture was determined by ^{13}C and ^{1}H NMR analyses[3] as well as gas-liquid chromatography (GLC)[3] comparisons with retention times of authentic materials. Isolation and purification of the products can be achieved by removal of K_2CO_3 (KCl) by filtration, followed by washing the CCl_4 solution with water (2 x 100 mL), drying (over Na_2SO_4) and concentrating to dryness (rotary evaporator). Distillation of the oily residue at reduced pressure gives the product(s).[4]

The reaction of 4-methyl-1,2-pentanediol (1) with a molar equiv of TPP in CCl_4 solvent gave 4-methyl-1-chloro-2-pentanol (26%), 4-methyl-2-chloro-1-pentanol (32%), and unreacted diol 1 (42%). Similarly, 1,2-decanediol (2) gave 1-chloro-2-decanol (17%), 2-chloro-1-decanol (44%), and unreacted diol 2 (39%). The ratios of the regioisomeric chlorohydrins (*2-Cℓ/1-Cℓ*) strongly suggest that they are formed largely from an "*A1*" type reaction of the epoxide with hydrochloric acid.[5] It is anticipated that a regioselective chlorination of 1 or 2 with TPP-CCl_4[6] should favor the primary hydroxyl group over the secondary hydroxyl.[7] The presence of epoxides as intermediates was easily proven by treating diols 1 and 2 with a 1.1 molar equiv of TPP in CCl_4 over K_2CO_3 (an HCl scavenger)[2] affording 4-methyl-1,2-epoxypentane (45%) and 1,2-epoxydecane (49%), respectively.



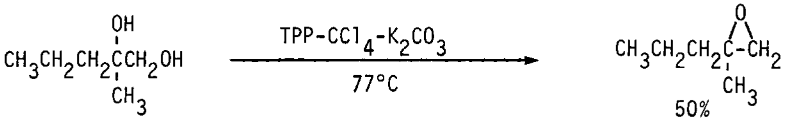
					2-Cℓ/1-Cℓ
	R = $CH_2CH(CH_3)_2$ (1)				
(42%)	TPP-CCl_4	26%	32%	0%	1.22
(49%)[a]	TPP-CCl_4-K_2CO_3	0	0	45	
	R = n-C_8H_{17} (2)				
(39%)	TPP-CCl_4	17	44	0	2.59
(25%)[b]	TPP-CCl_4-K_2CO_3	0	0	49	

[a] Analysis of a sample of the reaction mixture by ^{13}C NMR indicated the presence of an unidentified substance (6%). [b] The ^{13}C NMR spectrum ($CDCl_3$) of a sample of the reaction mixture indicates the presence of a substance (26%) with ^{13}C signals at δ 64.5 and 71.1 (this region is characteristic of alkyl carbonates).

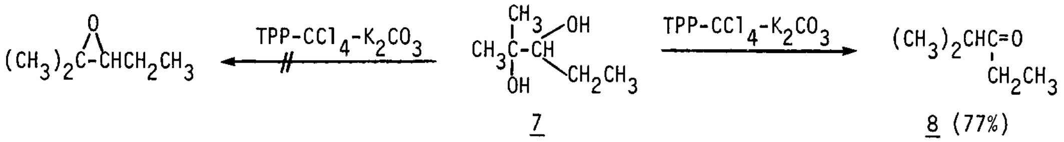
The yields of some of the monosubstituted epoxides depend on the relative concentration of TPP in the "TPP-CCl_4-K_2CO_3" reagent and diol. For example, reaction of 1,2-propanediol (3) with 1.25 (2.0) molar equiv of TPP gave 1,2-epoxypropane in 33% (85%) by ^{1}H NMR analyses. A similar trend is observed when phenyl-1,2-ethanediol (4) is subjected to analogous reaction conditions. Treatment of diol 4 with 1.25 (1.50) molar equiv of TPP afforded 39% (69%) yield of phenyl-1,2-epoxyethane. Generally, attempts to improve the yields of the epoxides by increasing the molar concentration of TPP much beyond 2 molar equiv were unsuccessful. In fact, a diminution in the overall yield of epoxide was observed with higher TPP concentrations perhaps resulting from competitive reactions between the epoxide and "phosphorus reagents" (i.e., $Ph_3P\text{-}Cl_2$,[8] TPP[9])

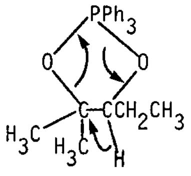
The only cyclic diol examined here, trans-1,2-cyclohexanediol (5) is readily converted into trans-2-chlorocyclohexanol (88%) with TPP-CCl_4; however, the presence of K_2CO_3 effectively scavenges the hydrochloric acid formed in the reaction to afford 86% cyclohexene oxide.

Increased alkyl substitution about the carbinol carbons of the diol has a pronounced effect on the yield of the epoxide. Specifically, 2-methyl-1,2-pentanediol (6) gives slightly more epoxide (50% yield) than diols 3 and 4 under comparable reaction conditions (1.25 equiv of TPP).



By contrast, the diastereoisomeric 2-methyl-2,3-pentanediol (7) reacts with 2.0 equiv of TPP in CCl_4 solvent containing K_2CO_3 to afford 77% of 2-methyl-3-pentanone (8), but no epoxide. Ketone 8 apparently arises via a 1,2-hydride shift from either the dioxyphosphorane A or perhaps more likely, the oxyphosphonium salt B. Surprisingly, the reaction of 2,3-dimethyl-2,3-butanediol (9) with 1.1 (2.2) equiv of TPP in CCl_4 solvent with K_2CO_3 did not afford 3,3-dimethyl-2-butanone via a methyl migration but gives instead 27% (36%) of 2,3-dimethyl-2,3-epoxybutane (10)





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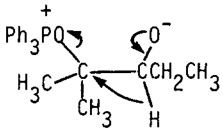

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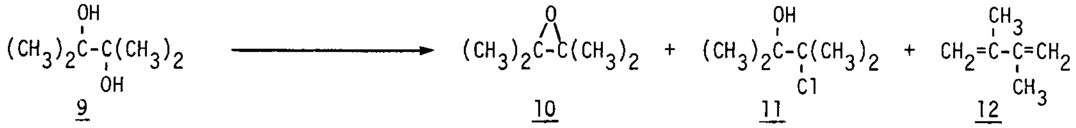

(50-63%)	TPP-CCl_4-K_2CO_3	27-36%	10-14%	0%
(2%)	TPP-CCl_4-CH_3CN	0%	80%	18%

and 10% (14%) of 2,3-dimethyl-3-chloro-2-butanol (11). In the absence of K_2CO_3 and in the mixed solvent system (CCl_4-CH_3CN), a good yield of chlorohydrin 11 (80%) and 18% of 2,3-dimethylbuta-1,3-diene (12) can be realized. It has been previously reported that the reaction of diol 9 with TPP-CCl_4 in acetonitrile solvent gave diene 12 in 88%.[10] Chlorohydrin 11 probably comes from the reaction between 2,3-dimethyl-2,3-epoxybutane and HCl while diene 12 may originate from sequential dehydration of diol 9 or elimination-dehydration of chlorohydrin 11.

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2. C. N. Barry and S. A. Evans, Jr., J. Org. Chem., 46, 3361-3364 (1981).
3. Triphenylphosphine [recrystallized from a mixture of methanol and petroleum ether (boiling range 30-60°C)] was obtained from M & T Chemicals, Inc. (TPP-VWVAH-27k) and the Aldrich Chemical Co. Tetrachloromethane was dried and distilled over phosphorus pentoxide (See A. J. Gordon and R. A. Ford, "The Chemist's Companion", John Wiley & Sons: New York, 1972, p 432). Potassium carbonate (Fisher Scientific Co.) was carefully ground and filtered through a 120 U.S. Standard Sieve (0.125 mm opening). Gas chromatographic analyses were obtained on a Hewlett-Packard Model 5754B gas chromatograph using a stainless steel column [0.125 in. (i.d.) x 6 ft packed with 20% Carbowax 20M on Chromosorb W-HP-AW-DMCS (100-120 mesh). Preparative HPLC was performed on a Waters LC500A HPLC using two Teflon columns (Waters Prepak-500/Silica). ^{1}H NMR were recorded on the Varian Model XL-100-12 and Perkin-Elmer Model R24B NMR spectrometers. The ^{13}C NMR FT spectra were recorded on the Varian XL-100 and the Bruker Model WM-250 NMR spectrometer at 30° with noise decoupling.
4. The more volatile epoxides (e.g., 1,2-epoxypropane) may be distilled (atmospheric pressure) directly from the reaction mixture along with CCl_4 and $CHCl_3$.

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