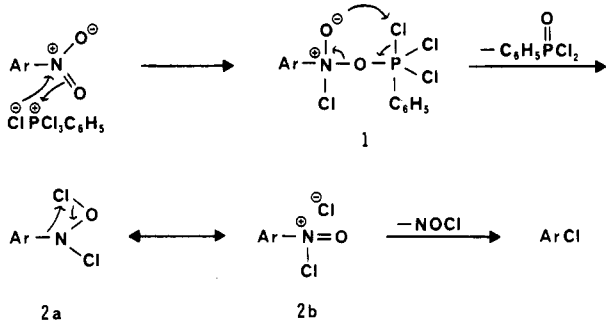
Table I. These data illustrate that substituted benzenes, pyrimidines, pyridines, and anthracenes all undergo this reaction with ease.

From a mechanistic point of view, this conversion could be considered to be the result of a nucleophilic displacement of nitro anion. Although such reactions are unusual, they are not without precedent.[10] However, we are in favor of an alternative reaction pathway with the mechanism proposed below. Initial attack of PTCP on the nitro group gives the zwitterion **1**. Fragmentation of **1** with the loss of phenylphosphonic dichloride could produce the covalent intermediate **2a** or perhaps the ionic form **2b**. The



structure proposed for **2** may be represented by a resonance hybrid of the covalent and ionic forms **2a** and **2b**, respectively. The ionic representation bears a striking resemblance to the aromatic diazo salt intermediates of the Sandmeyer reaction. Since there is clear evidence that the halogenodediazonization step of the Sandmeyer reaction is a radical process,[11] it is also possible that the halogenation of **2** occurs by a radical mechanism.

In order to test our proposed mechanism, we performed an experiment in which we replaced PTCP with freshly generated phosphorus pentachloride. Phosphorus pentachloride was chosen because phosphorus oxychloride would be formed as a byproduct. Using PTCP as the chlorine source produces phenylphosphonic dichloride, which is undetectable in the phenylphosphonic dichloride solvent. Indeed, when nitrobenzene was treated with phosphorus pentachloride in phenylphosphonic dichloride at 110 °C, chlorobenzene and phosphorus oxychloride were the products observed. These data support the first steps of our proposed mechanism.

To gain a better understanding of the second half of our proposed mechanism we carried out the chlorodenitration of nitrobenzene in the presence of copper bromide. Thus, radical decomposition of **2** would be expected to give a product mixture containing bromobenzene and chlorobenzene. Analysis of the reaction mixture revealed only the presence of chlorobenzene. Another test for radical character was carried out by adding hydroquinone to the reaction as a radical trap. No inhibition of product formation was observed. On the basis of these two experiments, we suggest that **2** does not undergo radical decomposition. Rather we feel that **2** gives up nitrosyl chloride via a heterolytic bond-cleavage process to produce aryl chloride products.[13] With this discovery, we feel that we have only scratched the surface with regard to the synthetic potential of PTCP and a host of other little known organophosphorus compounds. We hope that continued work in this area will lead to additional valuable synthetic methodologies.

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(11) Galli, C. *J. Chem. Soc. Perkin Trans. 2* **1984**, 897 and references cited therein.

(12) Phosphorus pentachloride was generated in situ by bubbling chlorine gas into a solution of phosphorus trichloride in phenylphosphonic dichloride.

(13) Although we favor a heterolytic bond cleavage mechanism, fragmentation via a "tight" radical pair is also possible.

Experimental Section

The following procedure for the preparation of 1,2,3-trichlorobenzene is typical. All reaction products were identified by comparison to authentic samples.

1,2,3-Trichlorobenzene. Chlorine gas (400 mg, 5.61 mM) was bubbled into a solution of dichlorophenyl phosphine (789 μL, 5.73 mM) in phenylphosphonic dichloride (10 mL) at room temperature. The reaction warmed slightly but did not rise above 30 °C. The initially clear, colorless solution turned pale yellow but remained clear. To this mixture was added 1,2-dichloro-3-nitrobenzene (1.0 g, 5.23 mM), and the reaction was heated to 170 °C for 5 h. The cooled reaction was then poured onto crushed ice/water (100 mL) and neutralized with 50% aqueous sodium hydroxide. After extraction with ether, (100 mL) the ether extracts were washed with brine and dried over anhydrous magnesium sulfate. Concentration in vacuo gives 1,2,3-trichlorobenzene (880 mg, 93%).

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Free Radicals in Organic Synthesis. A Novel Synthesis of Glycerol Based on Ethylene Glycol and Formaldehyde

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Introduction

The free-radical addition of alcohols,[1] amines,[2] and carboxylic acids[3,4] and derivatives[5] to olefins is well known as a synthetic method for the formation of carbon–carbon bonds. The formation of carbon–carbon bonds by the free-radical addition of various substrates to formaldehyde is less well known.[6,7] This type of reaction is, however, quite useful synthetically.[8]

Although cyclic formals undergo reaction with formaldehyde in the presence of free radicals, the yield is reduced due to β-scission of the initially formed radical[9] (eq

(1) Urry, W. H.; Stacey, F. W.; Huyser, E. S.; Juveland, O. O. *J. Am. Chem. Soc.* **1953**, *75*, 250.

(2) Urry, W. H.; Juveland, O. O. *J. Am. Chem. Soc.* **1958**, *80*, 3322.

(3) Vogel, H. H. *Synthesis* **1970**, 99.

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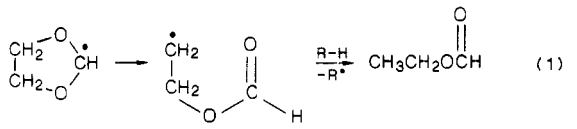
Table I. Reaction of 2,2-Dimethyl-1,3-dioxolane with Formaldehyde in the Presence of Free-Radical Initiators[a]

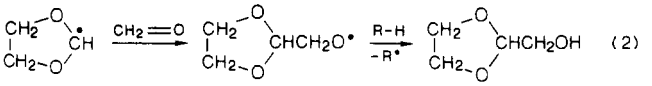
expt no.	1 (g)	$(CH_2{=}O)_x$[b]	initiator[b]	(g)	time (h)	temp (°C)	conv. 1 (%)	select. 2 (%)
1	25	5	DTBP	(5)	6	145	11.4	86
2	25	5	DTBP	(5)	4	160	12.5	71
3	25	5	DTBP	(2)	6	145	18.0	83
4	25	5	DTBP	(2)	6	145	11.5	80
5	25	5	TBPB	(3)	6	120	12.1	85
6	25	5	TBCP	(3)	6	150	20.8	75

[a] Procedure given in Experimental Section. [b] DTBP = di-*tert*-butyl peroxide, TBPB = *tert*-butyl perbenzoate, TBCP = *tert*-butyl cumyl peroxide, $(CH_2{=}O)_x$ = paraformaldehyde.

1). Formates are obtained as a major byproduct along with the hydroxymethyl derivative (eq 2).



(1)



(2)

Because cyclic ketals would not undergo this β-scission, we investigated the reaction of 2,2-dimethyl-1,3-dioxolane with formaldehyde under various conditions. The product 2,2-dimethyl-4-(hydroxymethyl)-1,3-dioxolane is an important synthetic intermediate and glycerol precursor.

Results and Discussion

The reaction of 2,2-dimethyl-1,3-dioxolane (**1**) with formaldehyde in the presence of free-radical initiators such as di-*tert*-butyl peroxide was found to give good yields of 2,2-dimethyl-4-(hydroxymethyl)-1,3-dioxolane (**2**). In an example 1 (25 g), paraformaldehyde (5 g), and di-*tert*-butyl peroxide (5 g) were heated in an autoclave equipped with a glass liner at 145 °C for 6 h. The liquid effluent from this reactor showed 11.4% conversion of **1**. **2** was formed in 86% selectivity based on products derived from **1**. (The products were identified by GC/FTIR and GC/MS.[10])

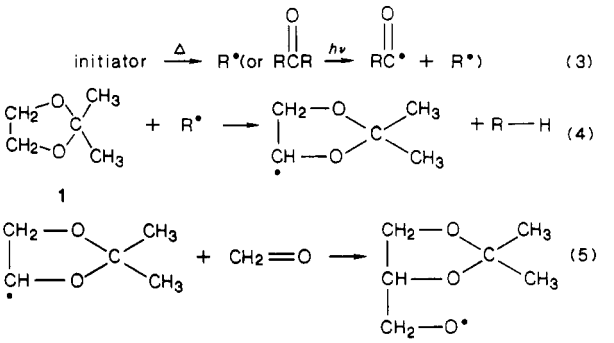
The major products from di-*tert*-butyl peroxide were acetone and *tert*-butyl alcohol. Small quantities of methane and ethane were observed in the gaseous products from the reaction. Ethanol was formed in small amounts.

Various substituted dioxolanes **4** were present but in usually less than 0.5% of the reaction mixture. 4,4′-Bi-(2,2-dimethyl-1,3-dioxolane) (**3**) formed by dimerization of the radicals derived from **1** was observed in 0.8% concentration. Ethylene glycol and glycerol formed by hydrolysis of **1** and **2**, respectively, were present in less than 0.5% concentration.

The reaction was conducted successfully at 120 °C to 160 °C in the presence of several different initiators. Selectivity to **2** of 80–86% was obtained. At 160 °C, the selectivity dropped to 71%. Table I contains a summary of the data.

The reaction of **1** with formaldehyde could also be catalyzed by UV light. Paraformaldehyde or formalin could be used as the formaldehyde source. A higher conversion of **1** was obtained with formalin in spite of the fact that the product **2** as well as the reactant **1** was hydrolyzed to a significant extent. Sensitizers such as acetone or initiators such as *tert*-butyl perbenzoate did not accelerate the reaction greatly. This is not surprising since small amounts of acetone were always present in **1** (due to hydrolysis). The results are summarized in Table II.

The reaction may be explained in terms of a free-radical chain reaction.[11] Free radicals generated by thermal decomposition of a free-radical initiator such as di-*tert*-butyl peroxide or photolysis of a carbonyl compound such as acetone (eq 3) abstract a hydrogen from the 4 position of the dioxolane ring (eq 4). This radical adds to formaldehyde to produce an alkoxy radical (eq 5). The alkoxy radical then reacts with **1** at the 4 position to produce **2** (eq 6). The radical formed in eq 6 is then available for reaction with more formaldehyde in a chain reaction. The chain reaction is terminated when any two radicals react to form nonradical products. Two possibilities for termination are shown in eq 7 and 8.



(3)

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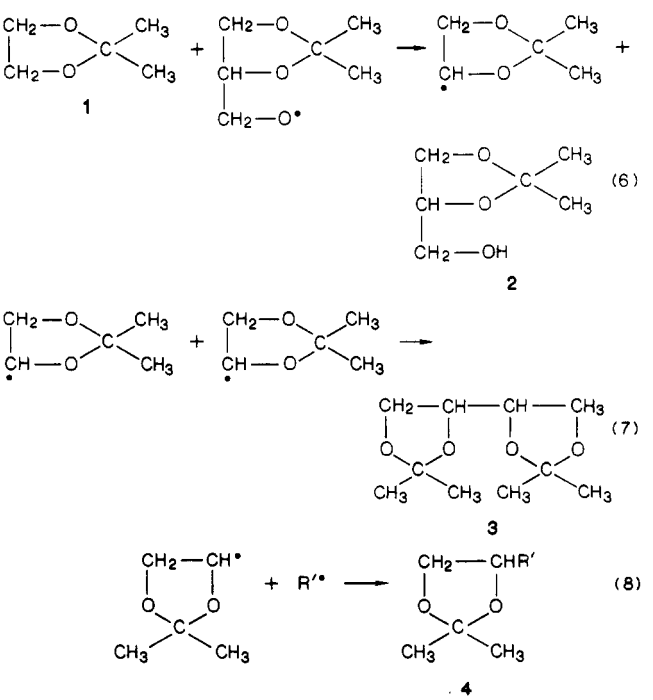

(6)

(7)

(8)

Under the optimum conditions for formation of **2** from formaldehyde and **1**, only a trace (<1%) of glycerol was obtained from ethylene glycol and paraformaldehyde. The

(10) The product had spectra identical with the commerical material.

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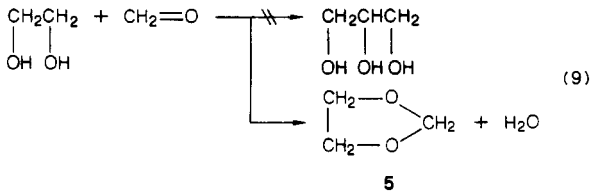
Table II. Reaction of 2,2-Dimethyl-1,3-dioxolane with Formaldehyde in the Presence of UV Light[a]

expt no.	1 (mL)	$(CH_2=O)_x$[b] (g)	formalin (mL)	acetone (mL)	TBPB[b] (g)	conv. 1 (%)	select. 2 (%)	select. EG (%)	select. glycerol (%)
7	3.0	0.3				7.5	70.7	<1	<1
8	3.0	0.3		1.0		8.6	52.3	<1	1.5
9	3.0	0.3			0.05	10.8	58.4	<1	<1
10	3.0		1.0			21.5	52.5	39.7	1.0
11	3.0		1.0	1.0		22.9	46.9	41.3	2.6
12	3.0		1.0		0.05	24.5	39.9	48.0	2.1

[a] Procedure given in Experimental Section. [b] $(CH_2=O)_x$ = paraformaldehyde, TBPB = *tert*-butyl perbenzoate, EG = ethylene glycol.

main product from this reaction was 1,3-dioxolane (**5**) (eq 9).



(9)

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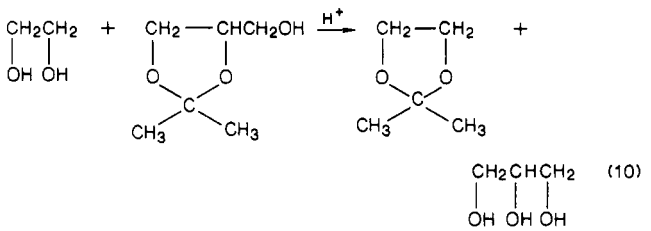
The hydromethyl derivative **2** was used to prepare glycerol and **1** by reaction with ethylene glycol (eq 10). A



(10)

variety of acids and acidic resins could be used for this reaction but phosphoric acid appeared to give the highest yield and purity (80% distilled yield of **1**, 97% purity). Glycerol could also be obtained in high yield. Details may be found in the Experimental Section.

Conclusion

The reaction of **1** with formaldehyde to produce **2** and the reaction of **2** with ethylene glycol to produce **1** and glycerol offers a route to glycerol based on ethylene glycol and formaldehyde. The direct reaction of formaldehyde and ethylene glycol does not produce significant quantities of glycerol.

Experimental Section

Materials. Di-*tert*-butyl peroxide, *tert*-butyl perbenzoate, and paraformaldehyde were obtained from Aldrich Chemical Co. *tert*-Butyl cumyl peroxide was Trigonox T from Noury Chemical. 2,2-Dimethyl-1,3-dioxolane, 2,2-dimethyl-4-(hydroxymethyl)-1,3-dioxolane, and phosphoric acid (85%) were obtained from Alfa Chemicals.

Analytical. ^1H NMR spectra were recorded on a Varian EM-390 spectrometer. The GC/FTIR work was done on a Digilab FTS 15E. Other GC work was done on a Hewlett-Packard 5890 with a 3392A integrator. The column was a 15-m capillary (fused silica) with 5% crosslinked phenyl methyl silicone.

Photochemical Reactor. The photochemical reactor was a RMR 500 Rayonet chamber reactor. A RMA 400 Rayonet merry-go-round was used. Four RPR 2537-Å lamps or four RPR 3500-Å lamps were used.

Procedure (Thermal). 2,2-Dimethyl-1,3-dioxolane, paraformaldehyde, and initiator were charged to a 300-mL stainless steel autoclave equipped with a cooling coil, electric heater, Magne-Drive stirrer, and glass liner. The autoclave was sealed and heated to the desired temperature for the required time. The autoclave was then cooled to ambient temperature and vented slowly, and the liquid was filtered from a small amount of solid and analyzed by GC or GC/FTIR.

Procedure (Photochemical). Pyrex test tubes (100 × 13 mm) equipped with screw caps were charged with 2,2-dimethyl-1,3-dioxolane, paraformaldehyde (or formalin), and initiators (or sensitizers) and then placed in the photochemical reactor for a week. Analysis was by GC or GC/FTIR as above.

Reaction of 2,2-Dimethyl-4-(hydroxymethyl)-1,3-dioxolane with Ethylene Glycol. Best yields of **1** were obtained when the reaction was run in the following manner: Ethylene glycol and 85% H_3PO_4 were charged to a flask equipped with a stirrer, a thermometer, a heating mantle, a small Vigereaux column, and distilling head (water-cooled condenser). The mixture was heated to 100–110 °C and a stream of nitrogen passed over the reaction mixture to aid in the removal of water. After removal of the water, the reaction mixture was cooled to 40–50 °C and 2,2-dimethyl-4-(hydroxymethyl)-1,3-dioxolane added. The mixture was heated over several hours to a pot temperature of 150 °C. Pure (>97%) 2,2-dimethyl-1,3-dioxolane was found to distill at 93–97 °C. Identifiction was by ^1H NMR. Pure glycerol was obtained from the pot residue by vacuum distillation.

An Efficient and Catalytically Enantioselective Route to (*S*)-(−)-Phenyloxirane

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Chiral oxiranes are often useful starting materials in enantiospecific synthesis. We describe herein a practical method for the synthesis of (*S*)-(−)-phenyloxirane (styrene oxide, **1**) which illustrates an approach that is potentially applicable to the enantioselective preparation of numerous chiral 1-substituted oxiranes. A key step in the process is the catalytic reduction of an achiral chloromethyl ketone by means of a chiral oxazaborolidine as catalyst and borane as stoichiometric reductant, a method recently developed in these laboratories.[1,2] This paper describes in detail the preparation of the chiral catalyst starting from proline, the enantioselective catalytic reduction, and the further conversion to epoxide.

N-(Benzyloxycarbonyl)-(*S*)-proline[3] was synthesized from proline by reaction with benzyl chloroformate in aqueous solution at 0–5 °C in 96% yield and esterified in methanol with boron trifluoride etherate as catalyst[4] to give the oily methyl ester in essentially quantitative crude yield. Reaction of this unpurified product with phenylmagnesium chloride in tetrahydrofuran (THF) provided directly (*S*)-(−)-2-(diphenylhydroxymethyl)pyrrolidine (**2**)

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(3) Grassmann, W.; Wünsch, E. *Chem. Ber.* **1958**, *91*, 462–465.
(4) Yamada, T.; Isono, N.; Inui, A.; Miyazawa, T.; Kuwata, S.; Watanabe, H. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1897–1898.

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