of hexane and the remaining solvent removed under reduced pressure. $n\text{-}Bu_4N^+Cl^-$ is exceedingly hygroscopic and should be handled accordingly.

**Preparation of Methyl 4-(Dimethoxymethyl)benzoate.** A solution of 4-carboxybenzaldehyde (6.0 g, 40 mmol) in a 70/30 mixture of diethyl ether/methanol was esterified by treatment with 1.68 g of diazomethane. The resulting solution was concentrated and transferred into a 250-mL flask containing methanol (125 mL), trimethyl orthoformate (4.67 g, 10% excess), *p*-toluenesulfonic acid (0.38 g, 5 mol %), and a Teflon-coated stirring bar. The flask was fitted with a water-cooled condenser and heated at reflux for 24 h. A standard workup followed by microscale distillation afforded 5.75 g (70% yield based on starting acid) of clear colorless liquid, bp 100 °C (0.65 torr).

**Transesterification. Reaction of Methyl Cinnamate with Tetra-*n*-butylammonium Bromide.** Into a 50-mL flask were placed methyl cinnamate (4.00 g), tetra-*n*-butylammonium bromide (15.9 g, 2.00 equiv), and a Teflon-coated stirrer bar. The flask was fitted with a condenser and heated in an oil bath maintained at 140 °C under a static head of nitrogen. After 72 h the reaction was allowed to cool. The resulting semisolid mixture was partitioned between petroleum ether and water. The organic layer was separated and washed with two 250-mL portions of 0.1 M HCl, 200 mL of saturated aqueous sodium bicarbonate, and finally 200 mL of water before being dried ($MgSO_4$) and concentrated in vacuo. Microscale distillation under reduced pressure afforded 4.19 g (83%) of clear, colorless *n*-butyl cinnamate, bp 117 °C (0.7 torr) (lit.[10] bp 288–289 °C).

**Registry No.** $n\text{-}C_7H_{15}CO_2CH_3$, 111-11-5; $2\text{-}CH_3C_7H_{14}CO_2CH_3$, 2177-86-8; $2,2\text{-}(CH_3)_2C_7H_{13}CO_2CH_3$, 14250-74-9; $C_6H_5CH{=}CHCO_2CH_3$, 103-26-4; $C_6H_5CO_2CH_3$, 93-58-3; $p\text{-}(CH_3O)_2CHC_6H_4CO_2CH_3$, 42228-16-0; $(n\text{-}C_4H_9)_4N^+Cl^-$, 1112-67-0; $(n\text{-}C_4H_9)_4N^+Br^-$, 1643-19-2; $(n\text{-}C_4H_9)_4N^+I^-$, 311-28-4; $(n\text{-}C_3H_7)_4N^+Br^-$, 1941-30-6; $n\text{-}C_7H_{15}CO_2\text{-}n\text{-}C_4H_9$, 589-75-3; $2\text{-}CH_3C_7H_{14}CO_2\text{-}n\text{-}C_4H_9$, 79420-98-7; $2,2\text{-}(CH_3)_2C_7H_{13}CO_2\text{-}n\text{-}C_4H_9$, 79420-99-8; $C_6H_5CH{=}CHCO_2\text{-}n\text{-}C_4H_9$, 538-65-8; $C_6H_5CO_2\text{-}n\text{-}C_4H_9$, 136-60-7; $p\text{-}(CH_3O)_2CHC_6H_4CO_2\text{-}n\text{-}C_4H_9$, 79421-00-4; $C_6H_5CH{=}CHCO_2\text{-}n\text{-}C_3H_7$, 7778-83-8; 2-methyloctanoic acid, 3004-93-1; 2-methyloctanoyl chloride, 43152-88-1; 2-octylbromide, 557-35-7; 4-carboxybenzaldehyde, 619-66-9; 4-formylbenzoic acid methyl ester, 1571-08-0.

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(10) Vorländer, D.; Walter, R. *Z. Phys. Chem.* **1925**, *118*, 1.

# Reaction of Epoxides with 2,6-Di-*tert*-butylphenol

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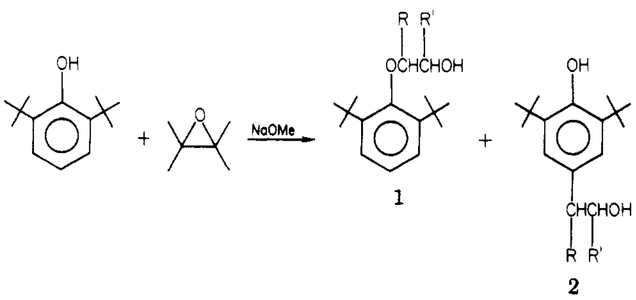
The alkylation of phenols with epoxides under basic conditions is known to give the 2-hydroxyethyl ethers of the phenols and their hydroxyethyl oligomers.[1] Since it is well-known that 2,6-di-*tert*-butylphenol, in many cases, is alkylated at the 4-position rather than on the oxygen,[2] we investigated the reaction of this phenol with epoxides. We now report that both carbon and oxygen alkylation occur when epoxides react with 2,6-di-*tert*-butylphenol and that the relative amount of carbon alkylation increases with an increase in the number of substituents on the epoxide.

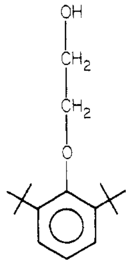
When equimolar amounts of 2,6-di-*tert*-butylphenol and ethylene oxide are heated with a small amount of sodium methoxide for 4 h at 220 °C, the primary product is the 2-hydroxyethyl ether of the phenol **1a** along with a smaller amount of 4-(2-hydroxyethyl)-2,6-di-*tert*-butylphenol (**2a**). GC analysis shows that the hydroxyethyl oligomers of these alcohols are also formed during the reaction. It is important to note that these oligomers are formed in the same ratio as their parent compounds from which they are derived. Thus, the ratio of **1a**:**2a** depends soley on their relative rates of formation rather than on subsequent reactions. Distillation of the crude product gives up to 44% yields of a mixture of 1 and 2.

Table I. Formation of 1 and 2[b]

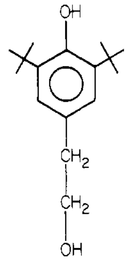


| reaction | R | R′ | 2:1[d] | bp, °C (mm)[c] | % yield |
|---|---|---|---|---|---|
| a | H | H | 4 | 125-127 (0.7) | 44 |
| b | H | $CH_3$ | 1.2 | 110-120 (0.5) | 39 |
| c | H | $C_2H_5$ | 0.97 | 122-137 (1.0) | 43 |
| d | H | $n\text{-}C_8H_{17}$ | 1 | 221-268 (1.4) | 49 |
| e | H | Ph | 1.13[a] | 134-165 (0.9) | 19 |
| f | H | $CH_2OPh$ | 1.22[a] | 194-229 (1.0) | 31 |
| g | | $C_4H_8$ | all 2 | 150-170 (0.2) | 28 |
| h | | $C_3H_6$ | all 2 | 146-151 (0.7) | 14 |

[a] From $^1H$ NMR ratios of $PhCH_2$ to $PhOCH_2$ areas. [b] All were analyzed by field desorption, atomic composition mass spectroscopy and found to have accurate masses with 3 ppm of the calculated values. [c] The boiling point range of the products, 1 and 2, used to establish the yield and product ratio. [d] From GC peak areas.



1a



2a

It can be seen from Table I that ethylene oxide alkylates the oxygen 4 times more readily than the carbon. When the more bulky propylene oxide, or other epoxides of terminal olefins, are used in this reaction, the relative amount of carbon alkylated products increases. With these epoxides, the oxygen and carbon are alkylated at equal rates. As would be expected under base-catalyzed conditions, the phenol reacts only at the least substituted (methylene) carbon of the epoxide to give a primary alkyl attachment.[3] Epoxides of cyclic olefins give only the carbon alkylation products. In these cases, the phenol

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(1) Miller, S. A.; Bann, B.; Thrower, R. D. *J. Chem. Soc.* **1950**, 3623.
(2) Starnes, W. H., Jr.; Patton, T. L. U.S. Patent 3526668 (1970); *Chem. Abstr.* **1970**, *73*, 98589d.
(3) Chitwood, H. C.; Freure, B. T. *J. Am. Chem. Soc.* **1946**, *68*, 680.

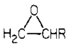
0022-3263/81/1946-5224$01.25/0

Table II. Effect of the Catalyst on the Cis to Trans Ratio[a] of 4-(2-Hydroxycyclohexyl)-2,6-di-*tert*-butylphenol

| metal alkoxide | solvent | cis/trans | % yield |
|---|---|---|---|
| LiOMe | | 0.75 | 22 |
| NaOMe | | 0.11 | 28 |
| NaOMe | $Me_2SO$ | all trans | 30 |
| K-*t*-OBu | $Me_2SO$ | all trans | 51 |

[a] Assumed assignment of isomers.[4,5]

Table III. Effect of the Catalyst on the Ratio of 1 to 2

| metal alkoxide |  | solvent | 2/1 | % yield |
|---|---|---|---|---|
| LiOMe | H | | 1.33 | 30 |
| NaOMe | H | | 4.0 | 44 |
| K-*t*-OBu | H | $Me_2SO$ | 6.7 | 54 |
| LiOMe | $CH_3$ | | 0.43 | 32 |
| LiOMe | $CH_3$ | $Me_2SO$ | 0.5 | 23 |
| NaOMe | $CH_3$ | | 1.16 | 40 |
| K-*t*-OBu | $CH_3$ | $Me_2SO$ | 4.8 | 44 |

must attack at a position which results in a product with a secondary alkyl group attachment. Since this represents a significant increase in steric requirements, alkylation occurs only at the more accessible 4-position of the phenol. Using the same rationale, it would be expected that the linear 1,2-disubstituted epoxides would give only carbon alkylated products. Cyclohexene oxide reacts with 2,6-di-*tert*-butylphenol to give a mixture of cis and trans isomers. However, only one isomer is formed when dimethyl sulfoxide is used as a solvent. This isomer is assumed to be the more stable trans isomer since this product predominates under all reaction conditions (Table II).[4,5]

Since the relative amounts of carbon to oxygen alkylation changed with different epoxides, it seemed likely that different alkali metal salts could also affect this ratio. Indeed, there is a relationship between the alkali metal used to catalyze the reaction and the ratio of carbon to oxygen alkylation. Table III shows that the ratio of carbon to oxygen alkylation decreases in the order Li > Na > K when either ethylene oxide or propylene oxide is used in the reaction. Similarly there is evidence that the presence of dimethyl sulfoxide in the reaction favors ether formation. These facts are consistent with the increasing ability to form free ions as one goes from lithium to sodium to potassium and with the fact that ion pairing is thought to be absent in dimethyl sulfoxide.[6]

Finally, it was found that a temperature of about 160 °C is required to effect the reaction, using sodium methoxide as the catalyst. Higher temperatures of ~220 °C are required for the reaction to proceed at an appreciable rate.

## Experimental Section

$^1H$ NMR spectra were obtained on a Bruker WH200, using quadrature detection, spectrum frequency 200.132, sweep width 3401.361, filter width 4300 Hz, acquisition time 4.819 s, relaxation delay 20 s, pulse width 2.5 $\mu s$ (40°), line broadening 0.4 Hz, number of scans 16, data points 32K, 0.2 g/0.5 mL of $CDCl_3$ solutions with $Me_4Si$ as standard in deuterium locks; IR, Perkin-Elmer 467 (KBr pellet); mass spectra, Varian MAT 311A. Boiling points are uncorrected. Melting points were obtained on a Fisher-Johns melting point apparatus and are uncorrected. Microanalyses were performed by the Huffman Laboratories, Wheatridge, CO. A Hewlett Packard Model 5710A gas chromatograph with 91.4 × 0.476 cm, 10% UCW98 columns was used for GC work. The GC was temperature programmed from 80 to 280 °C at 16 °C/min, using a helium flow of 20 mL/min.

**Reaction of Epoxides with 2,6-Di-*tert*-butylphenol.** In general, 2,6-di-*tert*-butylphenol (103 g, 0.5 mol), epoxide (0.5 mol), and 2–5 g of the alkali-metal alkoxide were heated in a 300-mL rocking bomb at 220 °C for 4 h. The reaction product was taken up in toluene, washed with water, rotovapped to remove the toluene, the crude product distilled to collect the ether and the carbon alkylated phenol, and the product analyzed by IR, GC, MS, and $^1H$ NMR.

**4-(2-Hydroxycyclohexyl)-2,6-di-*tert*-butylphenol.** 2,6-Di-*tert*-butylphenol (103 g, 0.5 mol), 50 g (0.5 mol) of cyclohexene oxide, and 3 g of sodium methoxide was reacted and worked up according to the general procedure to give 43 g (28% yield) of a mixture of the cis and trans isomers of **2g**, 4-(2-hydroxycyclohexyl)-2,6-di-*tert*-butylphenol, bp 150–170 °C (0.2 mm). The major isomer (assumed to be trans) was obtained by recrystallization from 2-propanol: mp 119–121 °C; IR 3620 (hindered OH), 3400 (broad band, unhindered OH), 860 $cm^{-1}$ (1,2,3,5-substituted aromatic); mass spectrum, *m/e* 304; NMR $\delta$ 1.436 (s, 18 H, $CCH_3$), 1.335–1.832 (m, 9 H, CH, $CH_2$), 3.70 (m, 1 H, CH), 5.044 (s, 1 H, OH), 7.01 (s, 2 H, ArH). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.60. Found C, 78.56; H, 10.65.

The lithium methoxide catalyzed reaction gave 33.3 g (22% yield) of an oil, bp 179–188 °C (1.1 mm), which consisted of two isomers by GC. Its IR and $^1H$ NMR data were essentially the same as the above.

The potassium *tert*-butoxide catalyzed reaction which contained 100 mL of dimethyl sulfoxide gave 78.7 g (51.4% yield) of an oil, bp 156–162 °C (1.0 mm), which contained only one isomer (trans) by GC, *m/e* 304, its IR and $^1H$ NMR data the same as the above, and mp 119–121 °C (from 2-propanol).

**4-(2-Hydroxypropyl)-2,6-di-*tert*-butylphenol.** 2,6-Di-*tert*-butylphenol (103 g, 0.5 mol), 29 g (0.5 mol) of propylene oxide, and 5 g of sodium methoxide gave 52 g (39% yield) of **2b** as an oil, bp 110–120 °C (0.5 mm), which by GC was 1.2:1 ratio of carbon to oxygen alkylated phenol. This was redistilled to give 6 g of an oil, bp 131–136 °C (0.7 mm), which was proven to be the carbon alkylated product by IR and $^1H$ NMR: IR 3620 (hindered OH), 860 $cm^{-1}$ (1,2,3,5-substituted aromatic); NMR $\delta$ 1.21 and 1.24 (d, 3 H, $HCCH_3$), 1.43 (s, 18 H, $CCH_3$), 2.59–2.72 (m, 2 H, $ArCH_2$), 3.93–3.96 (m, 1 H, CH), 5.12 (s, 1 H, OH), 7.01 (s, 2 H, ArH).

The oxygen alkylated product was isolated as the primary product when potassium *tert*-butoxide was used as the catalyst in the presence of 100 mL of $Me_2SO$. The product [67 g (44% yield), bp 122–137 °C (1.0 mm)] consisted of a 4.8:1 ratio of oxygen to carbon alkylated products. Redistillation gave 10.5 g of the pure ether: bp 119–120 °C (1.0 mm); IR 3400 (broad band, unhindered OH), 760 $cm^{-1}$ (1,2,3-substituted aromatic); NMR $\delta$ 1.23 and 1.27 (d, 3 H, $HCCH_3$), 1.43 (s, 18 H, $CCH_3$), 2.53 (s, 1 H, COH), 3.60–3.85 (m, 2 H, $ArOCH_2$), 4.38 (m, 1 H, OCH), 6.93–7.26 (m, 3 H, ArH).

Oligomer formation was detected by GC for both the oxygen and carbon alkylated products in most of the reactions. It was proven in the sodium methoxide catalyzed reaction of 1,2-epoxybutane by field desorption mass spectroscopy where *m/e* 206, 278, 350, 422, 494, and 566 were found. GC analysis of the crude reaction mixture showed that these oligomers were formed in the same ratio as the oxygen and carbon alkylated products.

**Acknowledgment.** I thank Mr. P. C. Jacobs for much of this laboratory work and Dr. J. C. Westfahl and Dr. R. P. Lattimer for their spectroscopic work.

**Registry No. 1a**, 79618-25-0; **1b**, 79618-26-1; **1c**, 79631-81-5; **1d**, 79618-27-2; **1e**, 79618-28-3; **1f**, 79631-82-6; **2a**, 3673-68-5; **2b**, 18734-98-0; **2c**, 18734-99-1; **2d**, 79618-29-4; **2e**, 18735-01-8; **2f**, 79618-30-7; *trans*-**2g**, 79618-31-8; *cis*-**2g**, 79618-33-0; **2h**, 79618-32-9; 2,6-di-*tert*-butyl phenol, 128-39-2; cyclohexene oxide, 286-20-4; propylene oxide, 75-56-9; ethylene oxide, 75-21-8; ethyloxirane, 106-88-7; octyloxirane, 2404-44-6; phenyloxirane, 96-09-3; (phenoxymethyl)oxirane, 122-60-1; cyclopentene oxide, 285-67-6.

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[4] Bartlett, P. D.; Berry, C. M. *J. Am. Chem. Soc.* **1934**, *56*, 2683.

[5] Huitric, A. C.; Carr, J. B. *J. Org. Chem.* **1961**, *26*, 2648.

[6] Block, E. "Reactions of Organosulfur Compounds"; Academic Press: New York, 1978; p 37.