Divergent Pathways in the Reaction of Hexamethylbenzene with Dimethyldioxirane[1,2]

Robert W. Murray,* Megh Singh, and Nigam Rath

Department of Chemistry, University of Missouri−St. Louis, St. Louis, Missouri 63121

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Hexamethylbenzene (**1**) reacts with dimethyldioxirane (**2**) via three separate reaction pathways. In the major pathway the reaction proceeds through an arene oxide which is rapidly transformed to the oxepin valence tautomer. In the first example of the reaction of an oxepin with **2** the oxepin is oxidized to first the *cis*-dioxide and then to the trioxide with the third oxide *trans* to the other two oxide rings. In a second competing pathway a methyl group migrates in the first produced arene oxide to give a hexamethyl-cyclohexadienone. This material then reacts rapidly with **2** to give a *trans*-diepoxide. The third reaction pathway involves the C−H insertion reaction of **2**. This process gives first the derived benzyl alcohol and then the corresponding benzoic acid. Two other minor products are also formed, one is rationalized as arising from reaction of the arene oxide with water. The other is a tricyclic compound of unknown origin.

Introduction

Electron rich hexamethylbenzene (**1**) has been oxidized by a variety of reagents, most notably peracids. Oxidation of **1** with perbenzoic acid gives the ring-opened products, biacetyl and *sym*-dimethyldiacetyl ethylene.[3] Whereas the oxidation of **1** with trifluoroperacetic acid afforded acetic acid only.[4] However, when the trifluoroperacetic acid is used with boron trifluoride, then the product is hexamethyl-2,4-cyclohexadienone.[5] Many natural or nonnatural aromatic compounds including permethylated benzenes have been oxidized by *m*-chloroperbenzoic acid to give quinones or hydroxylated products.[6] Oxidation of **1** with $HOF{\cdot}CH_3CN$ also gave hexamethyl-2,4-cyclohexadienone as an intermediate which then was further oxidized to two keto epoxides.[7] When **1** was photooxidized in methanol a mixture of permethylated benzyl ethers and tetramethylphthalide was obtained.[8] Whereas dye-sensitized photooxidation of **1** in acetonitrile, involving singlet oxygen, afforded epidioxy hydroperoxide via a [4 + 2]-cycloaddition, followed by an ene reaction.[9] Several polyalkylbenzenes, including **1**, have been ozonized in carbon tetrachloride and acetic acid. In the case of **1** the reaction yielded the ring cleaved products, biacetyl and acetic acid.[10] When **1** is oxidized with the Cu(II)−peroxy disulfate system the product is pentamethylbenzyl alcohol.[11] The oxidation of **1**, supported on silica gel or fluorosil, with $O(^3P)$ atoms gave hexamethyl-2,4-cyclohexadienone and its keto epoxide.[12] Oxyfunctionalization of aromatic hydrocarbons, including **1**, as well as methoxybenzenes, with the hydrogen peroxide/methyltrioxorhenium system or with hydrogen peroxide/hexafluoroacetone hydrate, gave the *p*-quinones.[13,14] Acid-catalyzed oxidation of methoxybenzenes by dimethyldioxirane (**2**) afforded the corresponding *p*-quinones in good yields.[15]

Dioxiranes are now recognized as versatile oxygen transfer reagents that can be used under extremely mild conditions.[16] Dioxiranes also show electrophilic character in their chemistry and might be expected to react with **1**. We describe here a study of the reaction of **1** with dioxirane **2**. The resulting chemistry is rich and includes the first example of the reaction of **2** with an oxepin.

Results and Discussion

The reaction of **1** with **2** was studied under a variety of experimental conditions. When the reaction is carried out at room temperature for 24 h using solutions of **1** and **2** in acetone with a ratio of 4:1 (compound **2**:**1**) the ^1H NMR spectrum indicated that a number of products are formed, with the major product being 2,3:4,5:6,7-triepoxy-2,3,4,5,6,7-hexamethyloxepane (**3**). It is accompanied by 2,3:6,7-diepoxy-2,3,4,5,6,7-hexamethyloxepin, **4**, and several minor products. The structures of **3**

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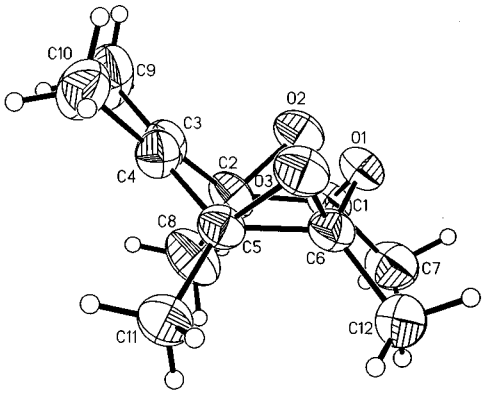


Figure 1. ORTEP drawing of diepoxide **4**.

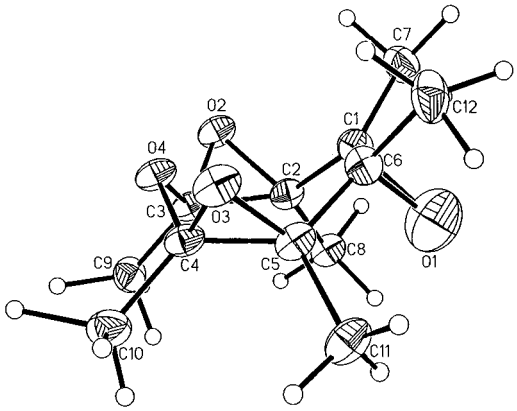


Figure 2. ORTEP drawing of triepoxide **3**.

and **4** were confirmed by X-ray crystallographic analysis. These structures show that the epoxide groups in **4** (Figure 1) are *cis* to each other and that the third epoxide group in **3** (Figure 2) is installed *trans* to the other two epoxide groups. An additional quantity of **2** (10 mL, 0.74 mmol) was added and stirring continued for an additional 24 h. Removal of the solvent on the rotovap and chromatography on the Chromatotron gave samples of the pure products. Oxepane **3** was formed in 51% yield. Oxepin **4**, the presumed precursor to **3**, was no longer in the product mixture. When the reaction is repeated with a lower amount of **2** then **4** becomes the major product, confirming its precursor status. The next most abundant product (19%) was identified as *trans*-3,4:5,6-diepoxy-2,2,3,4,5,6-hexamethylcyclohexanone, **5**. The minor products included the interesting tricyclic compound, *trans*-4,8-dihydroxy-2,6,9-trioxatricyclo[3.3.1.0^1]nonane, **6**. The structure of this unusual product was confirmed by an X-ray structure determination (Figure 3). Other minor products were identified as *trans*-diepoxy-1,2,3,4,5,6-hexamethylcyclohexane-*trans*-1,4-diol, **7**, 2,3,4,5,6-pentamethylbenzyl alcohol, **8** (6.4%), and 2,3,4,5,6-pentamethylbenzoic acid, **9**. Performing the reaction at −20 °C gave almost the same distribution of products. The exceptions being that none of acid **9** or the tricyclic compound **6** were present. This is presumably because the reaction proceeds at a slower rate. When the reaction at room temperature is repeated with a small amount of solid sodium bicarbonate added, then the products are **3**−**5** only. No traces of **6**−**9** were evident. This effect of added bicarbonate turns out to be an important observation. We now routinely use this modification in preparing arene oxides and dioxides and find that formation of side products is suppressed and oxides yields are optimized.

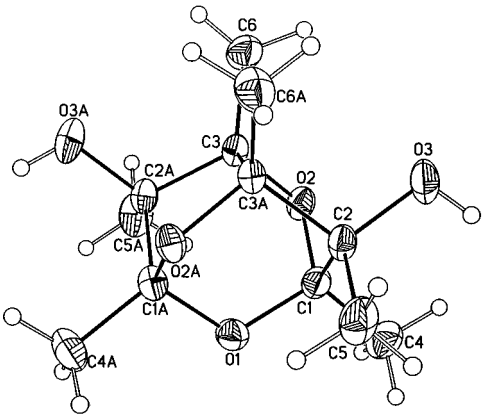
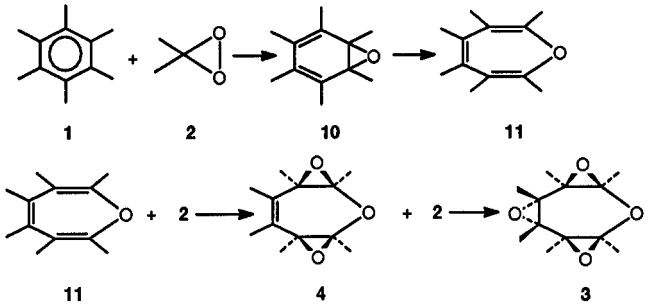
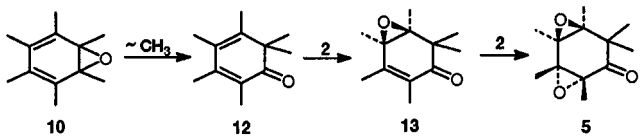


Figure 3. ORTEP drawing of tricyclic compound **6**.

Scheme 1. Oxidation of Hexamethylbenzene by Dimethyldioxirane



Scheme 2. Competing Pathway in the Oxidation of 1 by 2



We believe that the primary reaction proceeds as shown in Scheme 1. The high electron ring density in **1** permits direct oxidation by **2** to give arene oxide **10**. Many arene oxides rearrange to phenols under appropriate conditions. Other arene oxides are in dynamic equilibrium with their valence tautomers. A small number of arene oxides rearrange to stable oxepins.[17] Methyl groups are known[17] to stabilize oxepins leading to the facile conversion of **10** to oxepin **11**. The oxepin is rapidly oxidized by **2** to give the *cis*-diepoxide **4** which is further oxidized to the oxepane **3**. We believe that this is the first example of the oxidation of an oxepin by **2**.

The primary reaction shown in Scheme 1 competes with two other processes. In the first of these a methyl group migrates in arene oxide **10** to give dienone **12** (Scheme 2). This material is then epoxidized by **2** to give the observed *trans* diepoxide **5**, presumably via the mono

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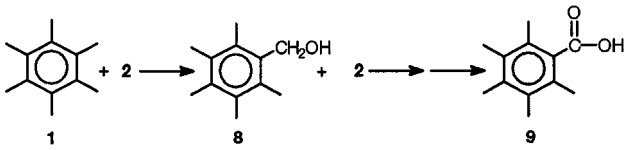
Scheme 3. Competing Insertion Reaction in the Oxidation of 1 by 2



epoxide **13**. This sequence has been verified by synthesizing authentic **12** and oxidizing it with **2** to give first **13** which is then further oxidized to **5**. It is interesting that only *trans*-**5** is formed either in the basic reaction of **1** or in the direct oxidation of **12**. To gain more information on the factors which contribute to the operation of the basic reaction versus the methyl migration route, we have studied several variations of the basic procedure. We speculated that the process shown in Scheme 2 might be acid catalyzed. In the first of the reaction variations we have carried out the basic reaction procedure with a crystal of *p*-toluenesulfonic acid added. Under these conditions only two major products are formed, namely, diepoxide **5** and oxepane **3**. They are formed in the ratio of 85:15 (**5**:**3**). This result is to be compared to the ratio of 25:75 (**5**:**3**) obtained in the basic reaction procedure of **1** with **2**. The reaction sequence given in Scheme 2 is clearly acid catalyzed. This result raised the question of whether the operation of this competing process is also catalyzed by some acid in the basic reaction. Some time ago Baumstark and Vasquez[18] had shown that adding water to the reaction medium increases the rate of some epoxidation reactions of **2**. Suspecting that water could act as an acid catalyst in our current work, we prepared a solution of **2** which was dried with molecular sieves in order to remove traces of water. When the reaction of **1** is performed with this extra dry solution of **2**, then the products **5** and **3** are formed in a ratio of 20:80 (**5**:**3**). In this case the benzoic acid **9** is actually formed in larger yield than is **5**. This result suggests that water provides some acid catalysis.

The formation of alcohol **8** and acid **9** is due to the operation of a second competing process. These products arise from the C−H insertion reaction of **2** (Scheme 3). This most unusual process was first reported by us[19] for **2** in 1986 and was followed by a report[20] by Curci et al. of a similar reaction for trifluoromethylmethyldioxirane. To support this interpretation we have oxidized the benzyl alcohol **8** with **2** and found acid **9** to be the major product. When the oxidation of **1** was performed with an extra dry solution of **2** as described above, the second most abundant product was acid **9**. This is presumably because the removal of water from the reaction medium has slowed the rate of the competing epoxidation reactions and allowed the C−H insertion reaction to assume a more prominent role in the overall reaction.

Some comment is due on the formation of the minor products, diol **7** and the tricyclic compound **6**. We believe that **7** is formed in a concerted opening of arene oxide **10** by water, followed by epoxidation by **2**. Consistent with this suggestion is the absence of this product in the reaction of **1** with extra dry **2**. We suggest that the reaction is concerted since the *trans* diol is accompanied by only a trace of the *cis* isomer. The isomers might be

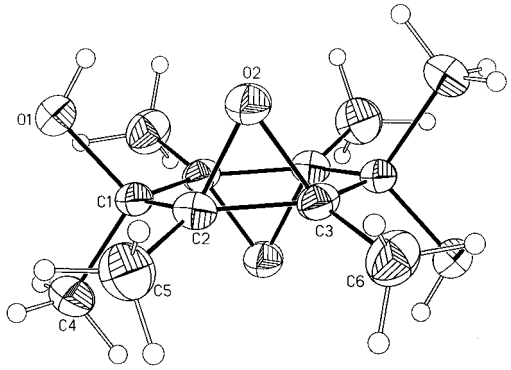


Figure 4. ORTEP drawing of diol **7**.

expected to be formed in approximately equal amounts in a nonconcerted reaction. The stereochemistry in the *trans* diol has been confirmed by X-ray diffraction (Figure 4).[21] We are uncertain as to the origin of tricyclic compound **6**. Its structure has been confirmed by X-ray crystallographic analysis (Figure 3).[21] On the basis of atom composition, we considered the possibility that **6** could arise from **3** by reaction with water. When heated with acetone−water for several days, **3** was recovered unchanged, however. We have also speculated that a small amount of the all *cis* isomer of **3** could have been formed in the basic reaction and that it was converted to **6** by water. We have attempted to synthesize all *cis*-**3** by reacting **4** with a variety of oxidants. When MCPBA, **2**, or trifluoroacetic anhydride/urea hydrogen peroxide adduct (UHP) were reacted with **4**, only **3** was formed. When methyltrioxorhenium/UHP was used as the oxidant, neither **3** nor its all *cis* isomer was produced. Thus to date we have not been able to determine whether the all *cis* isomer of **3** serves as a precursor to **6**.

Experimental Section

Materials and Reagents. Hexamethylbenzene was obtained from Aldrich Chemical and was recrystallized from ethanol prior to use. Silica gel (Merck, 35−70 mesh, 40 Å) was obtained from Aldrich. Oxone (DuPont), $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, was obtained from Aldrich and used as received. Trifluoroacetic anhydride, urea hydrogen peroxide complex (UHP), and methyltrioxorhenium (MTO) were all purchased from Aldrich. *m*-Chloroperbenzoic acid (70−78%) was obtained from Janssen Chimica and used as received. Acetone (Fisher reagent grade) was fractionally distilled over anhydrous potassium carbonate. Methylene chloride and hexane were obtained from Fisher and were distilled from calcium hydride before use. The dimethyldioxirane solution in acetone was prepared according to the literature procedure[22,23] and was assayed for dioxirane content using phenyl methyl sulfide and the GLC method,[23] or concentration was determined using a calibration curve of dioxirane concentration versus UV absorbance at 335 nm.

Instrumentation. ^1H and ^{13}C NMR spectra were recorded on a 300 MHz NMR spectrometer with $CDCl_3$ as solvent. All NMR data are reported in ppm or δ values downfield from TMS. The multiplicities of ^{13}C NMR signals were determined by the attached proton test (APT) pulse sequence. Electron impact and chemical ionization mass spectra were recorded

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(21) A complete list of atomic coordinates, geometric parameters, anisotropic thermal parameters, hydrogen atom coordinates, and structure factors are deposited with the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK and can be obtained on request fron the Director of CCDC.
(22) (a) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847. (b) Singh, M.; Murray, R. W. *J. Org. Chem.* **1992**, *57*, 4263. (c) Adam, W.; Hadjiarapoglou, L.; Bialas, J. *Chem. Ber.* **1991**, *124*, 2377.
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at 70 eV ionizing voltage on a twin EI and CI quadrupole mass spectrometer connected to a gas chromatograph fitted with a 12 m × 0.2 mm × 0.33 μm Ultra-1 (cross-linked methyl silicone) column. Infrared spectra were recorded in KBr pellets on an FT-IR spectrometer. UV−vis spectra were obtained on a UV−vis spectrophotometer. Melting points were determined on a hot stage apparatus and are uncorrected. Chromatographic separations on the Chromatotron were accomplished using 2 mm Kieselgel 60 PF_{254} gypsum coated plates. Gas chromatography was performed on a gas chromatograph using a flame ionization detector, a fused silica capillary column (methyl 5% phenyl silicone liquid phase, 30 mm × 0.25 mm; film thickness 0.5 μm), and He as the carrier gas. The chromatograph was interfaced with an integrator. Elemental analyses were performed by Atlantic Microlab, Inc. (Norcross, GA).

General Procedure for the Reaction of Hexamethylbenzene with Dimethyldioxirane. The reactions of 1 mol equiv of hexamethylbenzene with 1−7 mol equiv of an acetone solution of dimethyldioxirane were carried out by adding the dioxirane solution to a magnetically stirred solution of hexamethylbenzene in acetone at room temperature (20−22 °C) unless otherwise stated. The progress of the reaction was monitored periodically by GLC and GC-MS. Additional amounts of the dioxirane solution were added in several hour intervals until complete consumption of the starting material and/or intermediate products was observed. The relative ratio of the products was determined by GLC and GC-MS analysis of the reaction mixture or by ^{1}H NMR analysis of the crude reaction mixture residue obtained by removal of solvent. The ratios determined by NMR analysis were comparable to those determined by GLC or GC-MS analysis. Solvent was removed on the rotary evaporator and the residue was dissolved in methylene chloride and the solution dried with anhydrous sodium sulfate. The residue obtained by evaporation of the solvent was dried in vacuo. The residue was subjected to radial chromatography on the Chromatotron. The separated products were reanalyzed to ensure purity. The products were characterized using ^{1}H and ^{13}C NMR, X-ray crystallography, and mass spectrometry and by comparison of their spectral and chromatographic properties with those of authentic samples or with literature values.

Reaction of Hexamethylbenzene with Dimethyldioxirane. 1. At Room Temperature. To a magnetically stirred solution of hexamethylbenzene, **1** (0.1135 g, 0.7 mmol), in 3 mL of acetone was added 38 mL (2.8 mmol) of an 0.074 M solution of dimethyldioxirane, **2**, in acetone. The reaction mixture was stirred at room temperature for 24 h to give an orange-yellow solution. The solvent was removed and an ^{1}H NMR spectrum of the residue recorded. The spectrum indicated the presence of 2,3:4,5:6,7-triepoxy-2,3,4,5,6,7-hexamethyloxepane, **3**, 2,3:6,7-diepoxy-2,3,4,5,6,7-hexamethyloxepin, **4**, 3,4:5,6-diepoxy-2,2,3,4,5,6-hexamethylcyclohexanone, **5**, 4,5-epoxy-2,3,4,5,6,6-hexamethyl-2-cyclohexen-1-one, **13**, and several other products, but no starting material. An additional quantity of **2** (10 mL) was added and the reaction mixture was stirred for an additional 24 h. Solvent was removed on the rotovap to give a colorless residue (0.1484 g). GLC and ^{1}H NMR analysis of the residue indicated the presence of the triepoxide, **3**, as the major product and the diepoxy ketone, **5**, as the minor product, in the ratio 75:25. Other minor products present were identified as *trans*-4,8-dihydroxy-2,6,9-trioxatricyclo[3.3.1.0^1]nonane, **6**, *trans*-2,3:5,6-diepoxy-1,2,3,4,5,6-hexamethylcyclohexane-*trans*-1,4-diol, **7**, 2,3,4,5,6-pentamethylbenzyl alcohol, **8**, and 2,3,4,5,6-pentamethylbenzoic acid, **9**.

Purification of the residue on the Chromatotron using acetone (5−10%) in hexane as eluent gave the triepoxide, **3**, as a colorless crystalline solid (0.081 g, 51%); mp 137−138 °C; IR (KBr) 3009, 2945, 1459, 1387, 1195, 1135, 1090, 996, 891, 872, 802, 738, 679 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.39 (s, 6H), 1.44 (s, 6H), 1.66 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.80, 15.71, 19, 74, 65.78, 66.54, 88.38; MS (EI, 70 eV): *m/z* (relative intensity) 183 (M^+-CH_3CO,1), 169 (4), 141 (45), 123 (10), 113 (8), 99 (20), 88 (83), 83 (20), 55 (12), 43 (100); MS (CI, methane) 227 (M + 1, 5); Calcd for $C_{12}H_{18}O_4$: 226.28. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.70; H, 8.01. The first minor product was isolated as a colorless viscous liquid (0.278 g, 19%) and was identified as the *trans*-diepoxyketone, **5**, by comparing its ^{1}H and ^{13}C NMR and mass spectral data with those of an authentic sample.[7,9] The second minor product was identified as the tricyclic diol **6** (0.0045 g, 3%) on the basis of its X-ray crystallographic structure and the following data: mp 120−122 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.32 (s, 6H), 1.33 (s, 12H), 1.81 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 13.76, 14.84, 15.23, 78.98, 88.26, 107.60; MS (EI, 70 eV): *m/z* (relative intensity) 201(0.1), 183(3), 157(3), 141(21), 115(100), 99(12), 88(19), 43(20); Calcd for $C_{12}H_{20}O_5$: 244.28. The third minor product was isolated as a colorless crystalline solid (0.012 g, 7.5%) and was identified as *trans*-2,3:5,6-diepoxy-1,2,3,4,5,6-hexamethylcyclohexane-*trans*-1,4-diol, **7**, on the basis of the following data: mp 130−135 °C (dec); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.34 (s, 6H), 1.37 (s, 6H), 1.41 (s, 6H), 2.10 (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.80, 16.11, 20.75, 67.11, 68.84, 72.08; MS (EI, 70 eV): *m/z* (relative intensity) 167(1), 153(9), 141(62), 125(97), 115(15), 99(29), 83(27), 81(9), 55(15), 43(100); Calcd for $C_{12}H_{20}O_4$: 228.28. Another minor product was isolated as a colorless crystalline solid (0.008 g, 6.4%) and was identified as 2,3,4,5,6-pentamethylbenzyl alcohol, **8**; mp 160−162 °C, lit.[8,24] mp 160−161 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (br s, 1H), 2.22 (s, 6H), 2.24 (s, 3H), 2.35 (s, 6H), 4.76 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.26, 16.74, 17.06, 60.18, 132.78, 132.83, 133.93, 135.04; MS (EI, 70 EV): *m/z* (relative intensity) 179(M + 1, 7), 178 (M^+, 58), 161(22), 160(100), 145(57), 135(17), 119(24), 105(15),91(19), 77(11); Calcd for $C_{12}H_{18}O$: 178.28. The final minor product was isolated as a colorless crystalline solid (0.007 g, 5%) and was identified as 2,3,4,5,6-pentamethylbenzoic acid, **9**, mp 210−211 °C, lit.[25] mp 211 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.20 (s, 6H), 2.23 (s, 3H), 2.27 (s, 6H), 11.2 (br s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.13, 16.76, 17.68, 128.94, 132.01, 132.88, 136.49, 177.13; MS (EI, 70 eV): *m/z* (relative intensity) 193 (M + 1, 13), 192 (M^+, 100), 177(33), 174(57), 147(70), 131(52), 115(16), 105(14), 91(25), 77(12); Calcd for $C_{12}H_{16}O_2$: 192.26.

When the same procedure was performed with a reduced amount of **2**, the intermediate diepoxyoxepin **4** could be isolated as the major product. To a magnetically stirred solution of **1** (0.110 g, 0.678 mmol) in 2 mL of acetone was added 20 mL (1.36 mmol) of 0.069 M **2** in acetone. The reaction mixture was stirred at room temperature for 5 h to give an orange solution. No trace of **2** was observed (KI/starch). The solvent was removed on the rotovap to give a colorless residue (0.1206 g). ^{1}H NMR and GLC analysis of the residue indicated the presence of unreacted **1** (62%), diepoxide **4** (29%), triepoxide **3** (5%), epoxy ketone **13** (5%), and traces of diepoxy ketone **5**. Purification of the residue on the Chromatotron using acetone (5−10%) in hexane afforded diepoxide **4** as a colorless solid (0.036 g, 25%); mp 115−117 °C; IR (KBr): 2938, 1477, 1379, 1252, 1188, 1139, 1112, 991, 902, 884, 806, 722, 632 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.37 (s, 6H), 1.75 (s, 6H), 1.79 (s, 6H); ^{13}C NMR ($CDCl_3$), 75 MHz): δ 14.68, 17.36, 20.57, 66.10, 90.71, 127.89; MS (EI, 70 eV): *m/z* (relative intensity) 194(1), 167(M^+ − CH_3CO,2), 153(40), 151(66), 125(58), 111(18), 91(12), 55(8), 43(100); MS (CI, methane) did not show the M + H or M peak; Calcd for $C_{12}H_{18}O_3$: 210.28. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.64; H, 8.69.

2. At −25 °C. The general procedure was followed using 0.082 g (0.5052 mmol) of **1** in 3 mL of acetone and 46 mL (3.03 mmol) of an 0.066 M solution of **2** in acetone. The reaction mixture was stirred at −25 °C (CCl_4/dry ice bath) and monitored periodically by GLC and GC/MS. The reaction mixture was stirred for 72 h to give a pale yellow solution. Solvent was removed on the rotovap to give a colorless residue (0.1082 g). GLC, GC/MS, and ^{1}H NMR analysis of the residue indicated the presence of the triepoxide **3**, diepoxide **4** (major

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Table 1. Crystal Data and Structure Refinement for Compound 3

empirical formula	$C_{12}H_{18}O_4$
formula weight	226.26
temperature	193(2) K
crystal system	monoclinic
space group	$P2_1/c$
unit cell dimensions	$a = 14.6110(7)$ Å, $\alpha = 90°$ $b = 8.3409(5)$ Å, $\beta = 99.188(2)°$ $c = 9.8061(4)$ Å, $\gamma = 90°$
volume, z	1179.73(10) Å^3, 4
density (calculated)	1.274 mg/m^3
absorption coefficient	0.095 mm^{-1}
crystal size	0.10 × 0.20 × 0.33 mm
θ range for data collection	1.41 to 22.50°
reflections collected	5337
independent reflections	1537 ($R_{int} = 0.0860$)
data/restraints/parameters	1519/0/145
goodness-of-fit on F^2	1.080
final R indices [$I > 2\sigma(I)$]	$R1 = 0.0926$, $wR2 = 0.2622$
R indices (all data)	$R1 = 0.1113$, $wR2 = 0.2917$
largest diff peak and hole	0.346 and −0.687 e Å^{-3}

Table 2. Crystal Data and Structure Refinement for Compound 4

empirical formula	$C_{12}H_{18}O_3$
formula weight	210.26
temperature	298(2) K
crystal system	monoclinic
space group	$P2_1/c$
unit cell dimensions	$a = 14.6871(9)$ Å, $\alpha = 90°$ $b = 8.3848(5)$ Å, $\beta = 99.289(2)°$ $c = 9.9452(6)$ Å, $\gamma = 90°$
volume, z	1208.68(13) Å^3, 4
density (calculated)	1.155 mg/m^3
absorption coefficient	0.082 mm^{-1}
crystal size	0.55 × 1.15 × 0.10 mm
θ range for data collection	1.40 to 22.50°
reflections collected	5512
independent reflections	1567 ($R_{int} = 0.0862$)
data/restraints/parameters	1542/0/137
goodness-of-fit on F^2	1.082
final R indices [$I > 2\sigma(I)$]	$R1 = 0.0714$, $wR2 = 0.1985$
R indices (all data)	$R1 = 0.0952$, $wR2 = 0.2278$
largest diff peak and hole	0.333 and −0.199 e Å^{-3}

product), epoxy ketone **13**, and diepoxy diol **7**. Unreacted **1** was also present as were traces of diepoxy ketone **5** and benzyl alcohol **8**.

3. With Added Sodium Bicarbonate. The general procedure was followed using 0.122 g (0.752 mmol) of **1** in 2 mL of acetone, sodium bicarbonate (0.50 g), and 75 mL (4.5 mmol) of an 0.064 M solution of **2** in acetone. The reaction mixture was stirred at room temperature in the dark. The progress of the reaction was monitored periodically by GLC and GC/MS. Analysis of the reaction mixture after 64 h indicated the presence of oxepane **3**, oxepin **4**, and diepoxy ketone **5** in the ratio of 58:27:15. No starting material was present. An additional quantity of **2** was added, and the reaction mixture was stirred overnight. GLC and ^{1}H NMR analysis of the reaction mixture showed only the presence of oxepane **3** and diepoxy ketone **5** in the ratio 90:10. None of the other previously observed minor products were present.

4. Using An Extra Dry Solution of 2. To a magnetically stirred solution of **1** (0.044 g, 0.272 mmol) in 3 mL of acetone was added 21 mL (1.64 mmol) of an 0.0785 M solution of **2** which had been dried with molecular sieves. The reaction mixture was stirred at room temperature, and the progress of the reaction was monitored by GLC and GC/MS. After 96 h the solvent was removed on the rotovap to give a colorless residue (0.0575 g). GLC and ^{1}H NMR analysis of the residue indicated the presence of oxepane **3** as the major product accompanied by diepoxy ketone **5** and acid **9** as minor products in the ratio 58:16:27. The oxepane-to-diepoxy ketone ratio (**3**:**5**) was found to be 80:20. None of the other minor products were found to be present.

5. With a Trace of *P*-toluenesulfonic Acid Added. To a magnetically stirred solution of **1** (0.022 g, 0.135 mmol) and a small crystal of *p*-toluenesulfonic acid in 3 mL of acetone was added 11 mL (0.813 mmol) of an 0.074 M solution of **2** in acetone. the reaction mixture was stirred at room temperature, and the progress of the reaction was monitored periodically by GLC and GC/MS. After 96 h the solvent was removed on the rotovap to give a colorless viscous liquid (0.032 g). GLC and ^{1}H NMR analysis of the residue indicated the presence of the diepoxy ketone **5** and oxepane **3** in the ratio of 85:15. The residue also contained traces of the diol **7** and acid **9**.

Table 3. Crystal Data and Structure Refinement for Compound 6

empirical formula	$C_{12}H_{20}O_5$
formula weight	244.28
temperature	298(2) K
crystal system	orthorhombic
space group	$C222_1$
unit cell dimensions	$a = 10.8553(2)$ Å, $\alpha = 90°$ $b = 13.4006(2)$ Å, $\beta = 90°$ $c = 8.5790(2)$ Å, $\gamma = 90°$
volume, z	1247.97(4) Å^3, 4
density (calculated)	1.300 mg/m^3
absorption coefficient	0.100 mm^{-1}
crystal size	0.33 × 0.33 × 0.09 mm
θ range for data collection	2.41 to 28.00°
reflections collected	6580
independent reflections	1516 ($R_{int} = 0.0578$)
data/restraints/parameters	1507/0/78
goodness-of-fit on F^2	1.093
final R indices [$I > 2\sigma(I)$]	$R1 = 0.0502$, $wR2 = 0.1258$
R indices (all data)	$R1 = 0.0615$, $wR2 = 0.1359$
largest diff peak and hole	0.298 and −0.230 e Å^{-3}

Table 4. Crystal Data and Structure Refinement for Compound 7

empirical formula	$C_{12}H_{22}O_4$
formula weight	230.30
temperature	298(2) K
wavelength	0.71073 Å
crystal system	triclinic
space group	$P\bar{1}$
unit cell dimensions	$a = 7.6039(3)$ Å, $\alpha = 73.117(2)°$ $b = 8.3499(2)$ Å, $\beta = 80.608(2)°$ $c = 12.1530(4)$ Å, $\gamma = 66.424(2)°$
volume, z	675.76(4) Å^3, 2
density (calculated)	1.201 mg/m^3
absorption coefficient	0.093 mm^{-1}
F (000)	268
crystal size	0.15 × 0.10 × 0.10 mm
θ range for data collection	3.51 to 24.78°
limiting indices	$-8 \le h \le 8$, $-9 \le k \le 9$, $0 \le l \le 14$
reflections collected	6051
independent reflections	2257 ($R_{int} = 0.078$)
adsorption correction	none
refinement method	full-matrix least-squares on F^2
data/restraints/parameters	2213/0/154
goodness-of-fit on F^2	1.025
final R indices [$I > 2\sigma(I)$]	$R1 = 0.0697$, $wR2 = 0.1675$
R indices (all data)	$R1 = 0.1637$, $wR2 = 0.2195$
largest diff peak and hole	0.256 and −0.253 e Å^{-3}

Reaction of 2,3,4,5,6,6-Hexamethyl-2,4-cyclohexadiene-1-one, 12, with 2. A sample of **12** was synthesized following the literature procedure.[5,26] To a magnetically stirred solution of **12** (0.0446 g, 0.25 mmol) in acetone (2 mL) was added 11 mL (0.75 mmol) of 0.07 M **2** in acetone. The reaction mixture was stirred at room temperature and was monitored periodically by ^{1}H NMR, GLC, and GC/MS. ^{1}H NMR analysis of the reaction mixture after 27 h showed the presence of monoepoxide **13** and diepoxide **5** in a 20:80 ratio. The reaction mixture was treated with a fresh solution of **2** in acetone and stirring continued at room temperature for another 20 h. Solvent was removed on the rotary evaporator to give diepoxide **5** as a colorless viscous liquid (0.0472 g, 90%). The product was identified by comparing its ^{1}H and ^{13}C NMR data with those in the literature.

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Reaction of 2,3,4,5,6-Pentamethylbenzyl Alcohol, 8, with 2. To a magnetically stirred solution of **8** (0.051 g, 0.286 mmol) in acetone (2 mL) was added a solution of 0.066 M **2** in acetone (13 mL, 0.858 mmol) at room temperature. The reaction mixture was stirred at room temperature and monitored periodically by GLC and GC/MS. After 3 days reaction was complete. The solvent was removed on the rotary evaporator to afford a colorless crystalline solid (0.0628 g). Purification of the residue by neutralization with sodium bicarbonate solution, extraction with methylene chloride, and acidification of the aqueous solution with dilute HCl afforded a colorless crystalline solid which was identified as 2,3,4,5,6-pentamethylbenzoic acid. The ^{1}H and ^{13}C NMR and mass spectral data of this compound were identical with those of an authentic sample of **9**.

Attempted Reaction of Oxepane 3 with Water. A solution of **3** (5 mg) in 2 mL of acetone containing a drop of water was stirred at room temperature and then at acetone reflux. After 10 days the oxepane was unchanged, and no other products were formed.

X-ray Diffraction Studies. Single-crystal X-ray diffraction analyses of the compounds **3**, **4**, **6**, and **7** were undertaken to elucidate their solid-state structures unambiguously. Crystals of appropriate dimensions were mounted on glass fibers in random orientations. Data were collected using a Siemens SMART CCD area detector system (Mo Kα, λ = 0.71073 Å). Intensity data were collected with frame width of 0.3° in ω and counting time of 10 s/frame at a crystal to detector distance of 4.930 cm. The double pass method of scanning was used to exclude any noise. A SMART software package (Siemen's Analytical X-ray, Madison, WI, 1995) was used for data collection and SAINT was used for frame integration (Siemen's Analytical X-ray, Madison, WI, 1995). Structure solution and refinement were carried out using the SHELXTL-PLUS (5.03) software package (Sheldrick, G. M., Siemen's Analytical X-ray, Madison, WI, 1995). The structures were solved by direct methods and full matrix least-squares refinement was carried out by minimizing $\Sigma w(F_o^2 - F_c^2)^2$ to convergence. A summary of crystal data and structure refinement parameters is given in Tables 1−4.

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