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Reaction of Hexamethylbenzene with Dimethyldioxirane[1]

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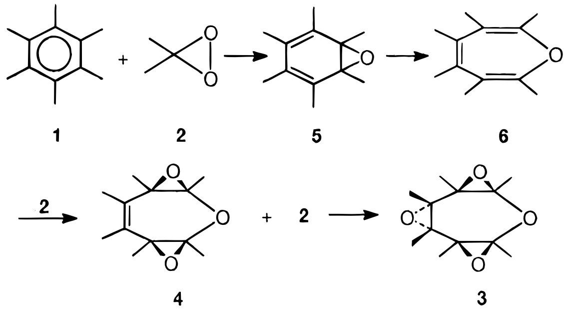
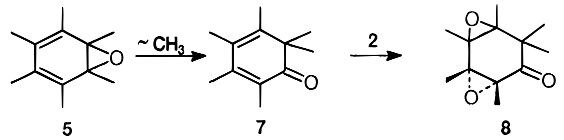
Hexamethylbenzene (**1**) has been oxidized by a variety of methods. Peracid methods have been used most frequently. Oxidation of **1** by perbenzoic acid leads to the ring-opened products, biacetyl and *sym*-dimethyldiacetyl ethylene.[2] When trifluoroperacetic acid is the oxidant, only acetic acid is formed.[3] However when trifluoroperacetic acid is used with boron trifluoride, then the product is hexamethyl-2,4-cyclohexadienone.[4] Oxidation of some naturally occurring aromatic terpenoids as well as some nonnatural aromatic compounds, some of which were polymethylated, by *m*-chloroperbenzoic acid gave quinones or hydroxylated products.[5] Oxidation of **1** with the HOF·CH_3CN system gives two keto epoxides which are presumed to arise from an intermediate cyclohexadienone.[6] Photooxidation of **1** gives a mixture of permethylated benzyl ethers and tetramethylphthalide.[7] When the Cu(II)-peroxydisulfate system is used to oxidize **1** the product is pentamethylbenzyl alcohol.[8] Supported on silica gel or Florisil, **1** was oxidized with $O(^3P)$ atoms to yield hexamethyl-2,4-cyclohexadienone and the derived keto diepoxide.[9] In related work methoxybenzenes have been oxidized by the methyltrioxorhenium−hydrogen peroxide system to afford the derived *p*-benzoquinones.[10] Similarly, methoxybenzenes have been oxidized by dimethyldioxirane and strong acid to give *p*-benzoquinones.[11] Some polymethylated arenes have been oxidized to the *p*-quinones with the hexafluoroacetone hydrate−hydrogen peroxide system.[12]

In the current work we have oxidized[13] **1** with dimethyldioxirane (**2**) which produced the interesting triepoxide 2,3:4,5:6,7-triepoxy-2,3,4,5,6,7-hexamethyloxepane (**3**) (51% yield) as the major product and a number of other reaction products[15] including 2,3:6,7-diepoxy-2,3,4,5,6,7-hexamethyloxepin (**4**).[16] The reaction is believed to proceed through oxide **5** (Scheme 1). In contrast to other oxidations of **1**, in this case oxide **5** is readily converted to its valence tautomer, 2,3,4,5,6,7-hexamethyloxepin (**6**). In a minor reaction pathway oxide **5** also undergoes a previously observed[6] methyl shift to give cyclohexadienone **7** which is easily oxidized by **2** to the known[6,9] *trans*-diepoxy compound **8** (Scheme 2).

Scheme 1. Oxidation of Hexamethylbenzene with Dimethyldioxirane



Scheme 2. Competing Pathway in the Oxidation of Hexamethylbenzene by Dimethyldioxirane



Methyl groups are known to stabilize oxepins.[17−21] Oxepins are nonaromatic and have boat conformations. Access to oxepin **6** permits dioxirane **2** to engage in its

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[13] Sample experimental details: To a magnetically stirred solution of **1** (0.114 g, 0.7 mmol) in 3 mL of acetone was added 38 mL (2.8 mmol) of 0.074 M **2** in acetone solution.[14] The reaction mixture was stirred at room temperature for 24 h to give an orange-yellow solution. The solvent was removed and an ^1H NMR spectrum taken of the residue. The spectrum indicated the presence of **3**, **4**, and **8** and several other products, but no starting material. An additional aliquot (10 mL) of the solution of **2** was added and stirring continued for an additional 24 h. Solvent was removed to give a colorless residue (0.148 g). GLC and ^1H NMR analysis of the residue indicated the presence of **3** as the major product and **8** as a minor product in the ratio 75:25. Purification of the residue on the Chromatotron using acetone (5−10%) in hexane as eluent afforded **3** as a colorless crystalline solid (0.081 g): mp 137−138 °C; IR (KBr) 3009, 2945, 1459, 1387, 1195, 1135, 1090, 996, 891, 872, 802, 738, 679 cm^{-1}; ^1H 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 second product was isolated as a colorless, viscous liquid and was identified as *trans*-3,4:5,6-diepoxy-2,2,3,4,5,6-hexamethylcyclohexanone by comparing its ^1H and ^{13}C NMR and mass spectrum with those of an authentic sample.[6,9]

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[15] Details concerning the minor products will be provided in the full paper.

[16] When the reaction of **1** with **2** is performed with a reduced amount of **2**, then the diepoxy compound **4** is the major product. The reaction residue was purified on the Chromatotron using acetone (5−10%) in hexane as eluent to give **4** as a colorless crystalline solid: mp 115−117 °C; IR (KBr) 2938, 1477, 1379, 1252, 1188, 1139, 1112, 991, 902, 884, 806, 722, 632 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 1.37 (s, 6H), 1.75 (s, 6H), 1.79 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) 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.

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well known propensity to epoxidize alkenes.[22] Since **2** is used in neutral solution and under very mild conditions, its use minimizes the cation chemistry (e.g., **5** → **7**) associated with some of the other oxidants used to oxidize **1**. Under these latter conditions methyl migration dominates the chemistry and forecloses routes to the oxepin and the type of interesting products observed here. When the reaction of **1** with **2** is performed with a reduced amount of **2**, then the diepoxide **4** is the major product, indicating that **4** is the precursor to **3**.

X-ray crystallographic analysis[23] of diepoxide **4**[24] (Figure 1) shows that the 2,3 and 6,7 epoxy groups are *cis* to each other. A similar structure determination for **3**[24] (Figure 2) indicates that the 4,5 epoxy group is *trans* to those at the 2,3 and 6,7 positions. The figures clearly show the boat conformation in both structures. The placement of the 4,5 epoxy group *trans* to the other two epoxy groups in **3** is presumably due to the more hindered approach to the *cis* isomer suggested by Figure 1.

Dimethyldioxirane has been used to synthesize other polyoxides in ring structures. A particularly interesting example is the conversion *of exo,exo,exo*-3,6,9-tri[[(4-methylphenylsulfonyl)oxy]methyl]-*cis,cis*-cyclonona-1,4,7-triene to its all *exo* trioxide.[25] We believe, however, that the oxidation of **1** to the polyoxides **3** and **4** is the first example to show that dimethyldioxirane can oxidize an aromatic compound to such products *via* an oxepin.

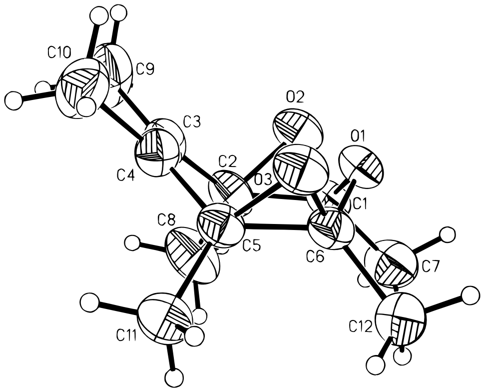

Figure 1. ORTEP drawing of diepoxide **4**.

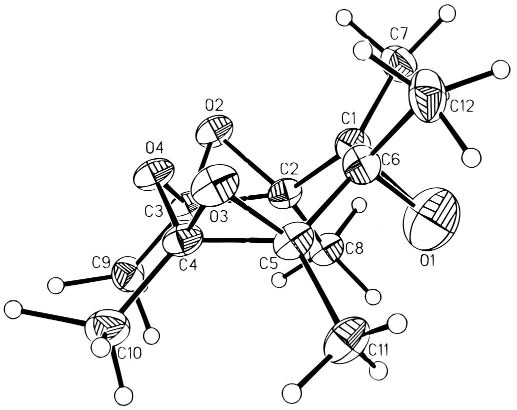

Figure 2. ORTEP drawing of triepoxide **3**.

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[24] Single crystal X-ray diffraction data for compounds **3** and **4** were collected using a Siemens SMART CCD diffractometer equipped with graphite monochromated Mo Kα radiation. Both compounds crystallize in the monoclinic space group $P2_1/c$. Figures 1 and 2 show the molecular projection views. Crystal data for **3** at 193 K: a = 14.6610(7), b = 8.3409(5), c = 9.8061(4) Å, β = 99.188(2)°, V = 1179.7(1) Å^3; Z = 4, 5537 reflections collected of which 1537 unique and 1211 $F_0 > 4\sigma(F_0)$, least squares refinement based on F^2, $R(F)$ = 9.3%, $wR(F^2)$ = 29.2%. Higher residual values are due to poor crystal quality. Crystal data for **4** at 298 K: a = 14.6871(9), b = 8.3848(5), c = 9.9452(4) Å, β = 99.289(2)°, V = 1208.7(1) Å^3; Z = 4, 5512 reflections collected of which 1567 unique and 1198 $F_0 > 4\sigma(F_0)$, least squares refinement based on F^2, $R(F)$ = 7.1%, $wR(F^2)$ = 22.8%.

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