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TETRAHEDRON

The Reaction of Cyclooctatetraene with Dimethyldioxirane[1,2]

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Abstract: The reaction of cyclooctatetraene with dimethyldioxirane leads to the formation of four diepoxides, three triepoxides, and two tetraepoxides. The structures of the triepoxides and tetraepoxides were confirmed by x-ray crystallographic analysis. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Dioxiranes; cycloalkenes; cyclooctenes; epoxidations; epoxides; NMR; oxidations; X-Ray crystal structures.

INTRODUCTION

Cyclooctatetraene **1** is a non-aromatic compound which X-ray[3] and electron diffraction[4,5] studies have shown exists in a non-planar tub form. All of the double bonds in **1** should be amenable to epoxidation. Treatment of **1** with *m*-chloroperbenzoic acid gave a mixture of three diepoxides only[6]. When trifluoroperacetic acid is the oxidant[6] the reaction mixture consists of the same three diepoxides and a single triepoxide. No tetraepoxide was found in either of these oxidations. Dioxiranes have proven to be versatile oxidants which can be used under very mild conditions and usually give high yields of oxidized products[7]. In particular dioxiranes have become the reagents of choice for difficult epoxidations[8]. Based on our experience to date and the results obtained by Anastassiou[6] we felt that dimethyldioxirane was likely to give a more complete oxidation of **1**. We report here the results of our oxidation of **1** using dimethyldioxirane **2** as oxidant.

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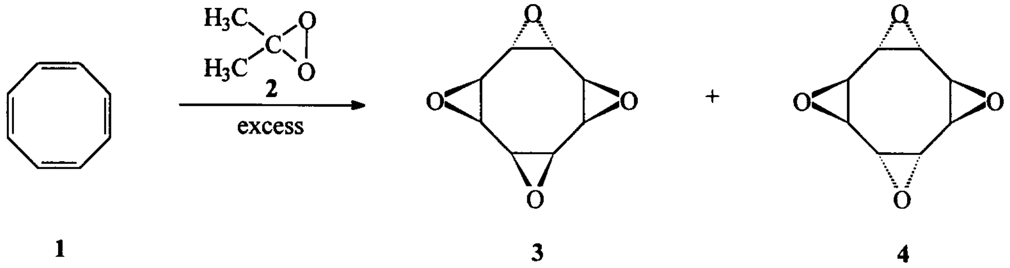
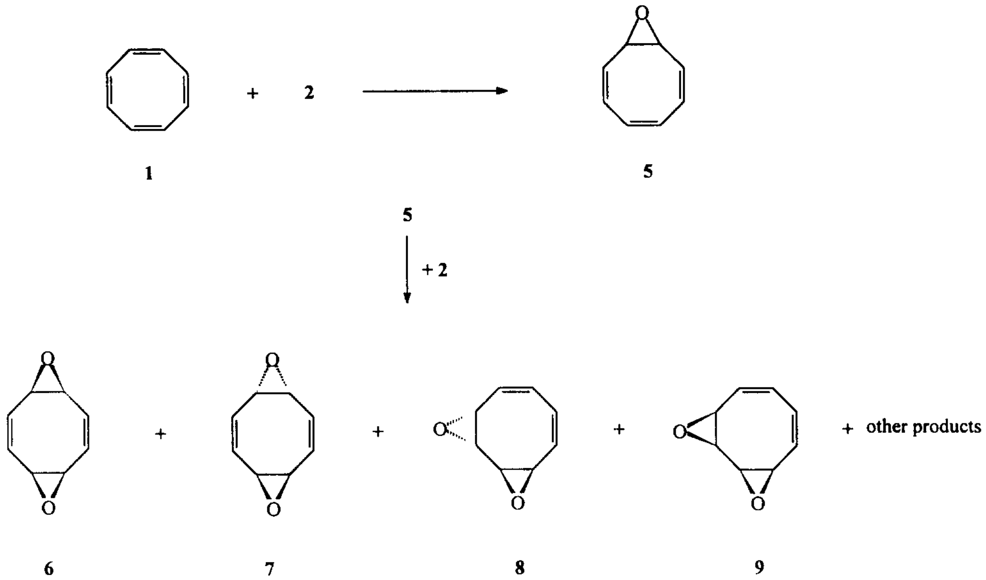
RESULTS AND DISCUSSION

The oxidation of **1** by dioxirane **2** was carried out using various ratios of the oxidants. When **2** is in great excess (> 9 equivalents) and the reaction progress followed by GLC and GC-MS until the complete consumption of **1** then two tetraepoxides are the sole products (Scheme 1).



Scheme 1

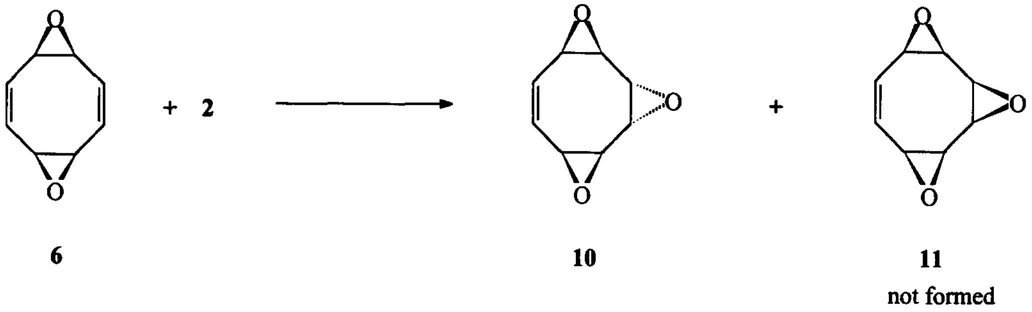
When the reaction is run using a ratio of **1**:**2** of 1:3 then a mixture of eight products is obtained. This mixture consists of four diepoxides, three triepoxides (one in trace amounts), and one tetraepoxide. The product distribution was dioxides **8** (3 %), **6** (5 %), and **7** (4 %) and trioxides **10** (12 %) and **12** (54 %) and tetraepoxide **3** (21 %). This is to be compared with the results using MCPBA[6] which gave dioxides **8** (9 %), **7** (67 %), and **6** (24 %) only. When trifluoroperacetic acid was the oxidant[6] the diepoxides formed were **7** (30 %), **6** (50 %), and **8** (5 %) as well as triepoxide **10** (15 %). Where the same products were obtained in our work and the work of Anastassiou[6] we have confirmed that the stereochemical assignments made in the earlier work are the same as ours. In order to determine the relationships between the various products a number of separate oxidations using intermediate products were studied. First we separately prepared a sample of monoepoxide **5** using **2** as oxidant. Our goal was to react **5** with **2** under reaction conditions where a mixture of diepoxides would be the dominant products. However oxidation of **5** under a variety of conditions always gave a complex mixture of products. We therefore conducted the experiment using a ratio of **1**:**2** of 1:3 and isolated four diepoxides. The four diepoxides are *cis*-cyclooctatetraene-1,5-dioxide, **6**, *trans*-cyclooctatetraene-1,5-dioxide, **7**, *trans*-cyclooctatetraene-1,3-dioxide, **8**, and *cis*- cyclooctatetraene-1,3-dioxide, **9** (Scheme 2). These results are the same as those reported earlier[6] using a peracid as oxidant except that in that case no **9** was observed.



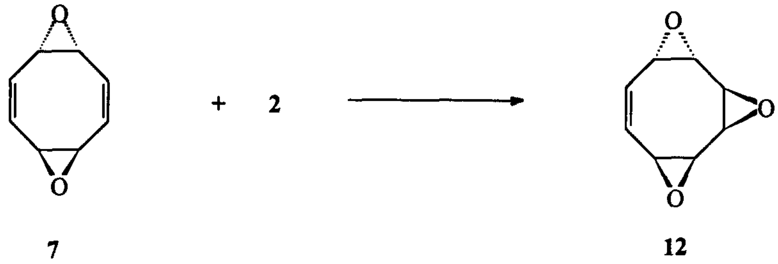
Scheme 2

In order to determine the reaction fate of each of the four diepoxides we separately prepared samples of each using the peracid route[6]. Oxidation of the *cis*-1,5-diepoxide **6** with **2** gave only the *cis,trans,cis*-triepoxide **10**. While the all *cis*-triepoxide,**11**, is also a possible product it is not formed (Scheme 3). Similarly, oxidation of the *trans*-1,5-diepoxide **7** with **2** gave the only possible triepoxide, *cis,cis,trans*-cyclooctatetraene-triepoxide **12** (Scheme 4). Oxidation of a sample of the *trans*-1,3-diepoxide **8** with **2** gave the two triepoxides **10** and **12** with **10** as the major product (Scheme 5). The triepoxides **10** and **12** are in turn further transformed into the two tetraepoxides **4** and **3**, respectively. In this latter transformation tetraepoxide **3** is the major product. Finally, oxidation of the *cis*-1,3-diepoxide **9** with **2** gave triepoxide **12** as the major product along with the all *cis* triepoxide **11** as a minor product (Scheme 6).

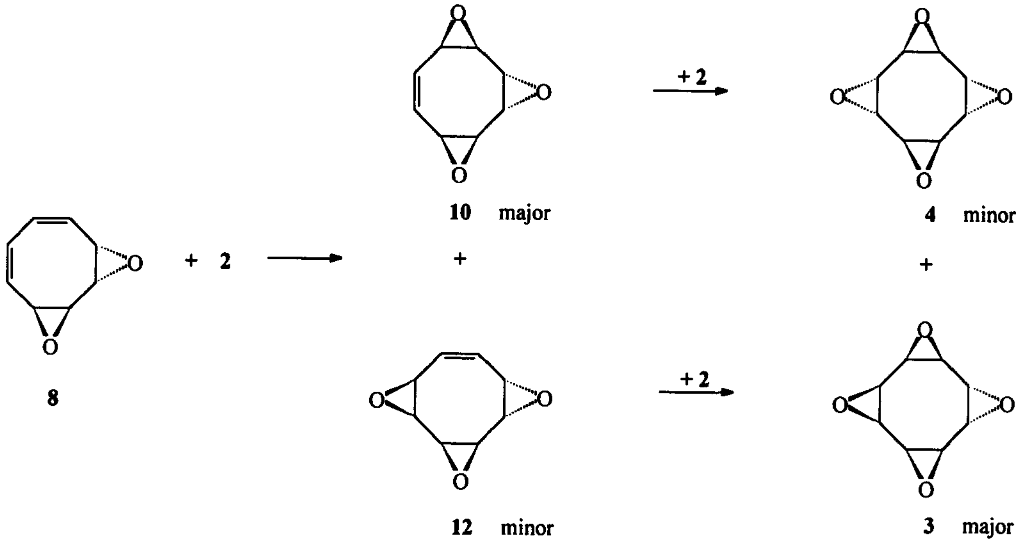
As seen subsequently (Scheme 7) triepoxide **10** also gives some **3** when reacted with **2**. Thus the tetraepoxide **3** observed in the reaction of dioxide **8** actually has two sources, namely triepoxides **10** and **12**. By following the reaction of **8** with **2** by periodic GLC analysis it was possible to observe that the reaction of **12** with **2** was much faster than the reaction of **10** with **2**.



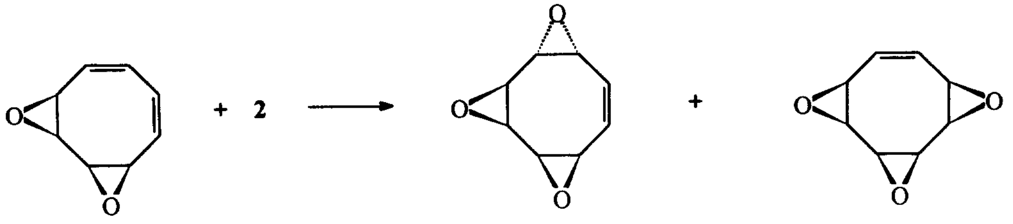
Scheme 3



Scheme 4



Scheme 5

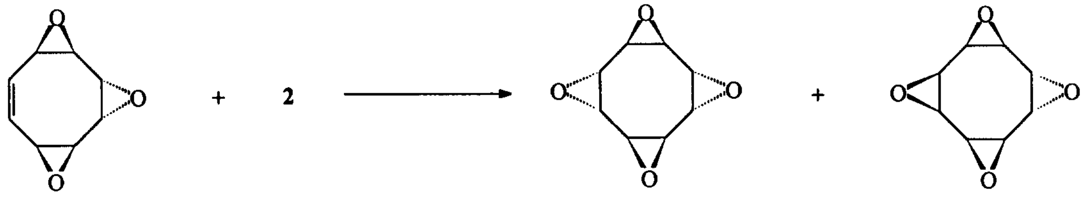


9 **12** major **11** minor

Scheme 6

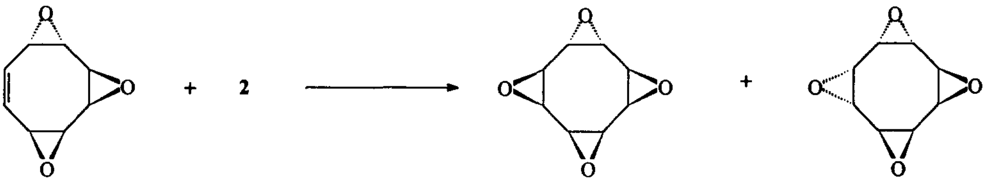
Finally we examined the oxidation of the triepoxides produced from the diepoxide oxidations. A sample of the *cis, trans,cis*-trioxide **10** obtained from the oxidation of the *cis*-1,5-dioxide **6** was oxidized by **2** to give tetraepoxide **4** which was accompanied by a trace of tetraepoxide **3** (Scheme 7). The trioxide, *cis,cis,trans*-cyclooctatatraene-1,3,5-trioxide **12,** was isolated from the reaction of **1** with **2** (1:3 ratio) and then reacted with **2**. This reaction gave tetraepoxide **3** in 100 % yield. A possible third tetraepoxide **13** was not formed (Scheme 8). The all *cis* triepoxide **11** is oxidized by **2** to tetraepoxide **3**. While the all *cis* tetraepoxide **14** is also a possible product it was not found (Scheme 9).

The reaction workups used to obtain tetraepoxide **3** always also contained another solid material. This colorless solid is insoluble in almost all of the common solvents. It is high melting (>320° C) and has an elemental analysis which is only slightly different than that for tetraepoxide **3**. We have not characterized this material further, but conclude that it is likely to be a polymer derived from **3**.



10 **4** **3** (trace)

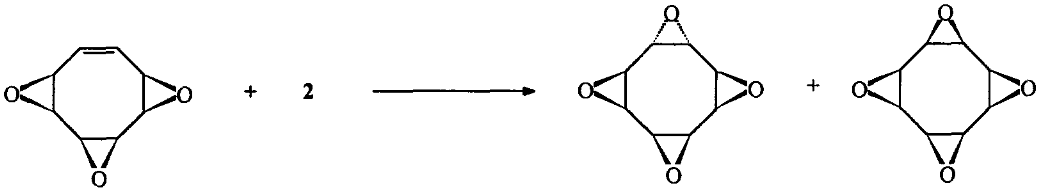
Scheme 7



12 **3** **13**

not formed

Scheme 8



11 **3** **14**

not formed

Scheme 9

In the earlier report[6] on the oxidation of **1** Anastassiou found that diepoxide **7** undergoes conformational isomerization as revealed by a variable temperature NMR study. He also concludes that diepoxide **6** and triepoxide **10** are conformationally rigid. We have confirmed the observation with respect to **10** and also have studied the variable temperature spectrum of triepoxides **11** and **12** and found no evidence for conformational isomerization. In our earlier report[2] we indicated that the tetraepoxides **3** and **4** are also conformationally rigid.

The structures of tetraepoxides **3** and **4** as well as the triepoxides **10, 11** and **12** were established using X-ray crystallography. The structure of tetraepoxide **3** is shown in Figure 1 and clearly shows the *cis,cis,cis,trans* arrangement of the epoxide oxygens. The isomeric tetraepoxide **4** has a *cis,trans,cis,trans* arrangement of the epoxide oxygens as shown in the X-ray structure (Figure 2). Likewise the structure of triepoxide **10** is seen as having a *cis,trans,cis* arrangement of the oxygen atoms (Figure 3). Triepoxide **12** has the epoxide oygen atoms arranged in a *cis,cis,trans* manner as shown in Figure 4. Finally, we were able to obtain crystals of the all *cis* triepoxide, **11**, whose structure is shown in Figure 5. While good crystals were readily obtained for **3,4, 10** and **11,** triepoxide **12** was first isolated as a viscous liquid which resisted several attempts at crystallization. Low melting (44-45° C) crystals of **12** were finally obtained by storing the triepoxide in pentane at -25° C for several days.

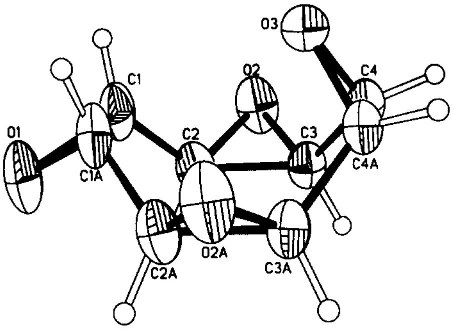


Figure 1. X-ray Crystal Structure of **3**.

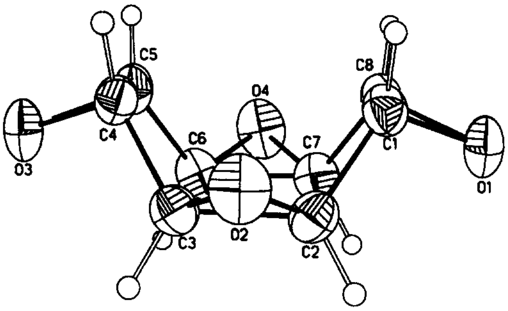


Figure 2. X-ray Crystal Structure of **4**.

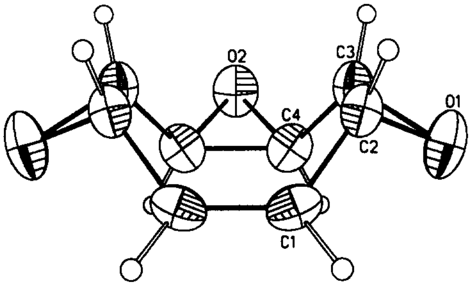


Figure 3. X-ray Crystal Structure of **10**.

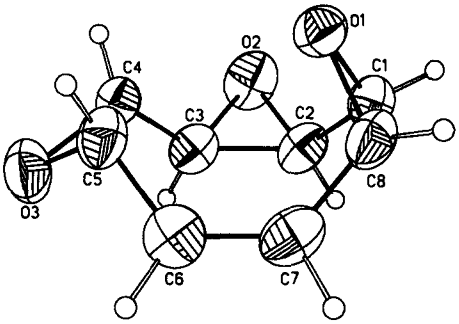


Figure 4. X-ray Crystal Structure of **12**.

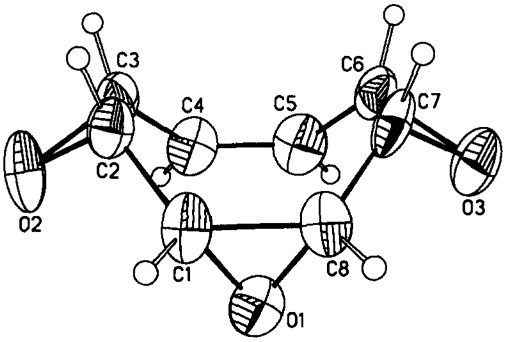


Figure 5. X-ray Crystal Structure of **11**.

EXPERIMENTAL

Instrumentation and General Methods. ^{1}H and ^{13}C were recorded on a Varian XL-300 (^{1}H, 300 MHz and ^{13}C, 75 MHz), a Varian UNITY-*plus* (^{1}H, 300 MHz and ^{13}C, 75.4 MHz) or a Bruker ARX-500 (^{1}H, 500.13 MHz and ^{13}C, 125.76 MHz) spectrometer in $CDCl_3$ with tetramethylsilane (TMS, $\delta = 0.00$) as an internal reference. All NMR data are reported in ppm or δ values downfield from TMS and coupling constants, *J*, are reported in Hz. ^{13}C NMR spectra were proton decoupled and recorded in $CDCl_3$. The center peak of the solvent $CDCl_3$ at 77.00 ppm was used as an internal reference. The multiplicities of the ^{13}C NMR signals were determined by the attached proton test (APT) pulse sequence. Where necessary COSY and HETCOR experiments were performed on a Bruker ARX-500 spectrometer (^1H, 500.13 MHz and ^{13}C, 125.76 MHz). The low temperature solution NMR spectra of the tetraepoxides were performed at 500.13 MHz for ^1H or 125.76 MHz for ^{13}C. The samples were prepared by dissolving the epoxides in THF-d_8. The samples were then introduced into the precooled probe of the spectrometer. The ^{13}C NMR solid state CP-MAS spectrum of the polymeric material from *cis,cis,cis,trans*-cyclooctatetraene tetraepoxide was recorded at 75.4 MHz on a Varian UNITY-*plus* spectrometer. The solid sample was finely ground and packed into a 7 mm zirconia rotor that was spun at the magic angle with a spinning rate of about 3-4 kHz. ^1H pulse duration for a 90° flip angle was 4 μs which was also the value for ^{13}C as set by Hartmann-Hahn conditions[9]. For the cross polarization a contact time of 2 ms was employed, while the recycle delay for CP experiments was typically 5 s. The number of transients was varied in order to achieve good signal-to-noise ratios. Spinning side bands were eliminated by using a basic TOSS sequence[10,11]. Chemical shifts of the polymeric solid were measured with respect to the aromatic signal for hexamethylbenzene at 132.1 ppm. Electron impact (EI) and chemical ionization (CI) mass spectra were recorded, at 70 eV ionizing voltage, on a Hewlett-Packard 5988A twin EI and CI quadrupole mass spectrometer connected to a Hewlett-Packard 5890A gas chromatograph fitted with a Hewlett-Packard 12 m X 0.33 μm Ultra-1 (cross-linked methyl silicone) column. Solutions were evaporated under reduced pressure with a rotary evaporator, and the residues were flash chromatographed on a silica gel or neutral alumina column using an ethyl acetate/hexane or diethyl ether/hexane mixture as the eluent unless specified otherwise. UV-VIS spectra were obtained on a Hitachi U-3110 UV-VIS spectrophotometer. Infrared spectra were recorded from KBr pellets on a Perkin-Elmer Model 1600 FT-IR spectrometer. Melting points were determined on a Dynamics Optics AHT 713921 hot-stage apparatus and are uncorrected. Microanalyses were performed by Atlantic Microlab, Inc., Norcross, GA.

Materials and Reagents. 1,3,5,7-Cyclooctatetraene and Oxone (DuPont), $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$, were obtained from Aldrich and used as such. Sodium bicarbonate, neutral alumina (Brockman Activity 1, 80-200 mesh) and potassium iodide-starch paper were obtained from Fisher. Acetone (Fisher reagent grade) was fractionally distilled over anhydrous potassium carbonate. Methylene chloride and hexane were obtained from Fisher and distilled from calcium hydride before use. The dimethyldioxirane was prepared according to the literature procedure[8,12] and was assayed for dioxirane content using phenyl methyl sulfide and the GLC method[12] or concentration was determined using a calibration curve of dioxirane concentration versus UV absorbance at 335 nm. Analytical thin-layer chromatography (TLC) analyses were performed on EM silica gel plates, $60PF_{254}$. Visualization was accomplished with UV light, iodine, $KMn0_4$ solution and/or vanillin/sulfuric acid solution.

Preparation, Purification and Characterization of the Intermediate Substrates/Products.

Cyclooctatetraene Oxide (5): Cyclooctatetraene oxide[13] was prepared by the oxidation of cyclooctatetraene with dimethyldioxirane solution at room temperature. To a magnetically stirred solution of cyclooctatetraene (0.432 g, 4.14 mmol) in acetone (5 mL) was added 90 mL (6.22 mmol) of 0.069 M dimethyldioxirane solution in acetone. The reaction mixture was stirred at room temperature in the dark. The progress of the reaction was monitored periodically by GLC. After 60 min the GLC analysis indicated the presence of cyclooctatetraene oxide and unreacted cyclooctatetraene in the ratio of 90:10. Traces of four stereoisomeric dioxides and three stereoisomeric trioxides were also present. After 75 min no trace of **2** was observed. The solvent was removed on the rotary evaporator to give a pale yellow liquid which was dissolved in pentane and the solution dried with anhydrous Na_2SO_4. Evaporation of the solvent *in vacuo* gave a viscous liquid (0.537 g). A pure sample of the oxide was isolated by Kugelrohr distillation as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.49 (s, 2H), 5.93 (br s, 2H), 6.04 (br s, 2H), 6.10 (br s, 2H); 13C NMR (75.4 MHz, $CDCl_3$): δ 55.33, 125.73, 126.43, 128.03; MS (EI, 70 eV): m/z (relative intensity) 120(M^+,4), 119(8), 92(10), 91(100), 65(16); Calcd for C_8H_8O 120.15.

***cis*-Cyclooctatetraene-1,5-dioxide (6)** was prepared by the reaction of cyclooctatetraene oxide and trifluoroperacetic acid[6,14]. Recrystallization of the residue from ether/hexane afforded a colorless crystalline solid: mp 166-167° C; lit[6,14] mp 165-167° C;^{1}H NMR (300 MHz, $CDCl_3$): δ 3.66 (s, 4H). 5.76 (s, 4H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 54.89, 126.87; MS (EI, 70 eV): m/z (relative intensity) 136(M^+, 2), 107(97), 91(12), 81(47), 79(82), 77(100), 68(36), 51(40); Calcd for $C_8H_8O_2$ 136.15.

***trans*-Cyclooctatetraene-1,3-dioxide (8)** was prepared by the literature procedure[6]. ^{1}H NMR (500.13 MHz, $CDCl_3$): 3.17 (d, J = 3.60 Hz, 2H) 3.58 (d, J = 3.60 Hz, 2H), 5.63 (d, J = 10.0 Hz, 2H), 5.99 (d, J = 10.0 Hz, 2H); ^{13}C NMR (125.76 MHz, $CDCl_3$): δ 54.39, 54.60, 124.48, 130.05; MS (EI, 70 eV): m/z (relative intensity) 136(M^+,5), 107(45), 91(8), 81(28), 79(81), 78(64), 77(100), 68(10), 65(14), 53(25), 51(38); Calcd for $C_8H_8O_2$ 136.15.

***cis*-Cyclooctatetrane-1,3-dioxide (9)** was prepared by the literature procedure[14]. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.33 (d, *J* = 3.88 Hz, 1H), 3.42 (dd, *J* = 3.82, 1.53 Hz, 1H), 3.73 (app t or dd, *J* = 4.09 Hz, 1H), 3.81 (dd, *J* = 4.30, 1.08 Hz, 1H), 5.62 (dd, *J* = 12.0, 3.83 Hz, 1H), 5.77 (d, *J* = 11.20 Hz, 1H), 6.02 (ddd, *J* = 12.0, 11.14, 3.88 Hz, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 52.72, 54.66, 54.86, 55.30, 123.00, 124.79, 127.78, 128.29; MS (EI, 70 eV): m/z (relative intensity) 136(M^+,2) 107(62), 91(13), 81(27), 79(73), 78 (30), 77(100), 68(19), 63(10), 51(30); Calcd for $C_8H_8O_2$ 136.15.

***trans*-Cyclooctatetraene-1,5-dioxide (7)** was also prepared by the literature procedure[7]. A fairly pure sample of the dioxide was isolated by bulb to bulb kugelrohr distillation. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.62 (s, 2H), 3.80 (d, *J* = 1.90 Hz, 2H), 5.59 (dd, 2H), 6.06 (d, *J* = 11.60 Hz, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 55.98, 58.68, 124.14, 127.82; MS(EI, 70 eV): m/z (relative intensity) 136(M^+,4), 107(87), 91(6), 81(34), 79(68), 77(100), 68(36), 51(37); Calcd for $C_8H_8O_2$ 136.15. Dioxide **7** decomposes slowly even at -25° in the freezer.

General Procedure for the reaction of 1 with 2. Reactions of an equivalent of **1** with various equivalents (1-8) of a solution of **2** in acetone were performed. The reaction mixture was stirred at room temperature in the dark. The progress of the reaction was monitored by GLC, GC/MS, ^{1}H NMR, TLC analysis (silica gel) and KI/starch at regular intervals. When all of the **2** was consumed, the solvent was removed *in vacuo*. The residue was redissolved in acetone and, where necessary, a fresh batch of **2** was added. The administration of **2** was continued until complete consumption of starting material and/or the intermediate products. The solvent was removed on the rotovap and the residue was dissolved in methylene chloride, the solution dried with anhydrous sodium sulfate, and filtered. The residue obtained by evaporation of the solvent was dried *in vacuo*. Products in the residue were separated and characterized using ^{1}H and ^{13}C NMR, elemental analysis, and infrared and mass spectroscopy. Known products were characterized by comparison of their spectral and chromatographic properties with those of authentic samples or literature values.

Reaction of Cyclooctatetraene Oxide (5) with 2 (1:1) The general procedure was followed using **5** (0.031 g, 0.258 mmol) in acetone (1mL) and 4.2 mL (0.258 mmol) of an 0.062 M solution of **2** in acetone. After 1 h all of the **2** had reacted. The solvent was removed on the rotovap to give a colorless liquid which was dissolved in methylene chloride and the solution dried with anhydrous sodium sulfate. The drying agent was filtered off and the solvent evaporated *in vacuo* to give a colorless liquid (0.0236 g). GLC and ^{1}H NMR analysis of the reaction mixture indicated the presence of several products including dioxides **6-9**, trioxides **10-12**, and tetraoxide **3** along with unreacted **5**.

Reaction of 1 with 2 (1:3) (Preparation and Isolation of Trioxide 12) The general procedure was followed using 0.120 g (1.152 mmol) of **1** in acetone (2 mL) and 63 ml (3.465 mmol) of an 0.055 M solution of **2** in acetone. After 17 h reaction time the solvent was removed on the rotovap to give a colorless liquid which was dissolved in methylene chloride and the solution dried with anhydrous Na_2SO_4. Evaporation of the solvent *in vacuo* gave a colorless, pasty solid (0.1758 g). GLC and NMR analysis of the reaction mixture showed the presence of the dioxides **8** (3 %), **6** (5 %), and **7** (4 %) as well as the trioxides **10** (12 %) and **12** (54 %), and the tetraoxide **3** (21 %). The residue was extracted with dry pentane to remove most of the minor products. Evaporation of the pentane gave a fairly pure sample of **12** (82 % pure). Repetitive sublimation and distillation of the residue gave an analytically pure sample of **12** (0.068 g, 39 %) which was isolated as a colorless viscous liquid: IR(neat): 2989(s), 1665(mw), 1435(s), 1364(w), 1311(w), 1250(ms), 1079(m), 986(s), 930(ms), 821(vs), 763(m), 701(s) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.08 (dq, *J* = 3.84, 0.74 Hz, 1H), 3.28 (dt, J = 3.88, 0.74 Hz, 1H), 3.46 (dq, *J* = 4.05, 0.68 Hz, 1H), 3.56-3.64 (m, 2H), 3.69 (dt, *J* = 4.15, 0.87 Hz, 1H), 5.80 (ddd, *J* = 11.68, 2.53, 1,12 Hz, 1H), 5.86 (ddd, *J* = 11.68, 1.12,1.12 Hz, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 53.71, 54.05, 54.42, 54,61, 55.67, 55.72, 125.59, 126.97; MS (EI, 70 eV): m/z (relative intensity) 153(M+1,0.2), 152 M$^+$,3), 123(16), 95(65), 94(50), 81(100), 78(15), 77(38), 71(29), 69(17), 68(78), 67(62), 66(71), 65(79), 55(41), 51(41), 41(40), Calcd for $C_8H_8O_3$152.15. Anal. Calcd for $C_8H_8O_3$: C, 63.15; H, 5.30; Found: C, 63.80; H, 5.40. In an attempt to observe any conformational isomerization the variable temperature ^{1}H NMR spectrum of **12** was measured. The room temperature (+27° C) spectrum consists of eight signals as reported above. The low temperature (-60° C) spectrum shows only seven signals. Two olefinic proton signals which appear at δ 5.80 and 5.86 ppm at room temperature become a singlet at δ 5.90 ppm at the low temperature. Also two epoxy protons which appear as two multiplets at 3.56-3.64 ppm at room temperature become two symmetrical doublets at low temperature. At high temperature (+ 49° C) the spectrum shows eight signals which are sharper than those observed at room temperature. We conclude that there is no evidence for conformational isomerization. After several days storage at - 25° C a pentane solution of **12** afforded colorless cubes/rods, mp 44-45° C. The spectroscopic data for this material are identical to those obtained on the liquid sample and reported above. The single crystal X-ray structure of solid **12** unambiguously proved the *cis,cis,trans* arrangement of the epoxide groups (Figure 3).

***cis,trans,cis*-Cyclooctatetraene-1,3,5-trioxide (10).** The general procedure was followed using 0.032 g (0.235 mmol) of **6** in acetone (2 mL) and 14 mL (0.94 mmol) of an acetone solution of **2** (0.067 M). GLC analysis of thr reaction mixture after 24 h indicated the presence of **10** and unreacted **6** in the ratio of 59:41. No other trioxide was formed in the reaction, but there were traces of the two tetroxides. The reaction mixture was stirred at room temperature for an additional 4 days. The solvent was removed on the rotovap to give a colorless solid. GLC analysis of the solid indicated the presence of unreacted **6** as well as **10** and **4** in the ratio of 9:81:10. An additional 10 mL of the solution of **2** was added and stirring continued for an additional 5 days. The solvent was removed on the rotovap to give a colorless crystalline solid which wa dissolved in methylene chloride and the solution dried with anhydrous Na_2SO_4. Evaporation of the solvent *in vacuo* gave a colorless crystalline solid (0.037 g). GLC and NMR analysis of the solid indicated the presence of **10** and **4** in a ratio of 72:28. Traces of **3** were also present. The separation of **10** was accomplished by silica gel column chromatography using ethyl acetate/hexane (5-20 %) as eluent to give the trioxide as colorless cubes (0.0254 g, 71 %), mp 150-152° C, lit[6] mp 145-146° C; IR (KBr) 3002(w), 2937(w), 1420(m). 1242(m), 1094(w), 1041(ms), 957(m), 837(ms), 795(vs), 716(m), 626(m) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.10 (s, 2H), 3.38 (d, $J = 3.36$ Hz, 2H), 3.53 (d, $J = 3.36$ Hz, 2H), 5.95 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 52.76, 53.38, 54.23, 128.12, MS (EI, 70 eV): m/z (relative intensity) 152 (M^+,2), 123(8), 95(45), 94(29), 81(100), 77(37), 69(17), 68(79), 67(57), 66(65), 65(68), 55(54), 41(45), Calcd for $C_8H_8O_3$ 152.15. The single crystal X-ray structure clearly shows the *cis,trans,cis* arrangement of the oxide groups in **10.**

***cis,cis,cis*-Cyclooctatetraene-1,3,5-trioxide (11).** Reaction of **1** or **5** with dioxirane **2** always gives trioxide **11** in trace amounts (see experimental). The residues from several different reactions were combined and used for the isolation of **11**. The separation of **11** was accomplished by column chromatography on neutral alumina (Brockman Activity 1, 80-200 mesh) using diethyl ether/hexane (10-50 %) as eluent to afford **11** as a colorless solid which was recrystallized with acetone/hexane to give colorless rods, mp 220° C (dec); IR(KBr) 3005(mw), 2980(m), 1449(s), 1283(m), 1095(m), 1025(s), 958(s), 839(s), 891(m), 836(s), 813(m), 796(s), 748(vs), 664(s), 554(s), cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.48 (d, J = 3.50 Hz, 2H), 3.52 (d, J = 3.50 Hz, 2H), 3.71 (s, 2H), 5.96 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 52.94, 53.25, 55.0, 126.19; MS(EI, 70 eV): m/z (relative intensity) 152 (M$^+$,4), 123(4), 95(14), 81(100), 77(23), 69(17), 68(62), 67(23), 66(19), 65(25), 55(25), 55(33), 41(19), Calcd for $C_8H_8O_3$ 152.15. Anal. Calcd for $C_8H_8O_3$: C, 63.15; H, 5.30; Found: C, 62.86; H, 5.34. The variable temperature ^{1}H NMR spectra of **11** in $CDCl_3$ were recorded. The spectrum of **11** remained invariant in the temperature range of - 60°C to + 49°C. We conclude that no conformational isomerization was occurring in this temperature range. The single crystal X-ray analysis supports the assigned structure of **11** (Figure 5).

Reaction of 1 with Excess 2 (Preparation of Tetraoxides 3 and 4). The general procedure was followed using 0.065 g (0.624 mmol) of **1** in acetone (2 mL) and 55 mL (3.85 mmol) of an 0.07 M solution of **2** in acetone. GLC and GC-MS analysis of the reaction mixture after 2 h indicated the presence of several products including **5** as well as stereoisomeric dioxides and trioxides and traces of stereoisomeric tetroxides. GLC analysis of the reaction mixture after 72 h indicated the presence of three products: trioxide **10** and tetroxides **3** and **4** in a 9:7:84 ratio. After 240 h GLC analysis of the reaction mixture indicated that the major products were a mixture of **3** and **4** with just a trace of **10**. The solvent was removed on the rotovap and an additional quantity of **2** (25 mL) was added and the reaction mixture was stirred for an additional 164 h. The solvent was removed on the rotovap to give a colorless crystalline solid which was dissolved in methylene chloride and the solution dried with anhydrous Na_2SO_4. Evaporation of the solvent *in vacuo* gave a colorless crystalline solid (0.1056 g, 100 %). GLC and ^{1}H NMR of the residue indicated the presence of an analytically pure mixture of **3** and **4** in an 87:13 ratio. The separation of the isomers was accomplished by repeated fractional crystallization from acetone. Tetraepoxide **3** was obtained as a colorless crystalline solid, mp > 320° C (dec); ^{1}H NMR (300MHz, $CDCl_3$): δ 3.11 (d, J = 2.66 Hz, 2H), 3.28 (s, 2H), 3.35 (d, J = 3.66 Hz, 2H), 3.76 (s, 2H); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 52.64, 53.06, 53.13, 54.11; MS(EI, 70 eV): m/z (relative intensity) 150 (M$^+$-18, 0.05), 139(1), 121(3), 110(5), 97(9) 81(71), 71(100), 69(16), 55(28), 53(32), Calcd for $C_8H_8O_4$ 168.15; Anal. Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80; Found: C, 56.79; H, 4.81. The single crystal X-ray structure (Figure 1) unambiguously demonstrated the *cis,cis,cis,trans* arrangement of the oxide groups in

3. A variable temperature study of the ^{1}H and ^{13}C NMR spectra of **3** in the range of -107° C to + 27° C showed that the spectra were invariant with the exception of some line broadening at the lower temperature. We conclude that no conformational isomerization is occurring in **3**. Tetraoxide **4** was isolated as a colorless crystalline solid, mp 180-185° C (dec); ^{1}H NMR (300 MHz, CDCl$_3$): δ 3.17 (s, 8H); ^{13}C NMR (75.4 MHz, CDCl$_3$): δ 52.71; MS (EI, 70 eV): m/z (relative intensity) 168 (M$^+$, 2), 139(0.4), 110(3), 97(5), 81(51), 71(100), 68(31), 55(32), 53(23), Calcd for $C_8H_8O_4$ 168.15. Anal. Calcd for $C_8H_8O_4$: C, 57.14; H, 4.80; Found: C, 56.53; H, 4.72. The single crystal X-ray structure (Figure 2) shows the *cis,trans, cis,trans* arrangement of the oxide groups in **4**. A variable temperature ^{1}H and ^{13}C NMR spectral study indicated that these spectra remained invariant in the range of -107° to + 27° C. Thus there was no evidence for any conformational isomerization. In separate experiments it was found that running the oxidation with sodium bicarbonate present or using an extra dry solution of **2** gave essentially the same results as described above.

Reaction of Diepoxide 8 with 2. The general procedure was used using 0.0172 g (0.1263 mmol) of **8** in acetone (1 mL) and 2.1 mL (0.145 mmol) of an 0.069 M solution of **2** in acetone. GLC analysis of the reaction mixture after 48 h indicated the presence of triepoxides **10** and **12** as well as tetraepoxide **3** and unreacted **8**.

Reaction of Diepoxide 9 with 2 The general procedure was followed using 0.096 g (0.0705 mmol) of **9** in acetone (1 mL) and 1.5 mL (0.084 mmol) of an 0.056 M solution of **2** in acetone. After 18 h the solvent was removed on th rotovap to give a colorless waxy solid (0.0115 g). ^{1}H NMR, GC-MS, and GLC analysis indicated the presence of triepoxides **10** and **11** along with tetraepoxide **3** and unreacted **9**.

Reaction of Diepoxide 6 with 2 The general procedure was followed using 0.014 g (0.1028 mmol) of **6** in acetone (1 mL) and 12 mL (0.066 mmol) of an 0.055 M solution of **2** in acetone. GLC analysis of the reaction mixture after 30 h indicated the presence of triepoxide **10** and tetraepoxide **4**. The solvent was removed on the rotovap to give a colorless solid (0.0161 g).

Reaction of Diepoxide 7 with 2 The general procedure was followed using 0.015 g (0.1101 mmol) of **7** in acetone (1 mL) and 5 mL (0.335 mmol) of an 0.067 M solution of **2** in acetone. GLC analysis of the reaction mixture after 4 h indicated the presence of triepoxide **12** and unreacted **7** as well as traces of tetraepoxide **3**.

An additional quantity of the solution of **2** (5 mL) was added and stirring at room temperature continued. After 4 days no trace of **7** was evident. The solvent was removed on the rotovap to give a colorless solid (0.0176 g). GLC and ^{1}H NMR analysis of the residue indicated the presence of triepoxide **12** and tetraepoxide **3** in the ratio of 54:46.

Reaction of Triepoxide 10 with 2 The general procedure was followed using 0.0174 g (0.1143 mmol) of **10** in acetone (2 mL) and 10.3 mL (0.69 mmol) of an 0.067 M solution of **2** in acetone. After 4 days an additional quantity (5 mL) of dioxirane solution was added. After 7 days the solvent was evaporated on the rotovap to give a colorless crystalline solid (0.0195 g, 100 %). GLC, GC-MS, and ^{1}H NMR analyses indicated the presence of tetraepoxide **4** (>99%) and a trace of tetraepoxide **3**.

Reaction of Triepoxide 12 with 2 The general procedure was followed using 0.062 g (0.4074 mmol) of **12** in acetone (2 mL) and 13.5 mL (0.815 mmol) of an 0.061 M solution of **2** in acetone. After the reaction was complete (36 h) the solvent was removed on the rotovap to afford a colorless crystalline solid (0.0693 g, 100 %). The product was identified as tetraepoxide **3** by comparing its ^{1}H, ^{13}C NMR and GC-MS data with those of an authentic sample of **3**.

Reaction of Triepoxide 11 with 2 The general procedure was followed using 0.0162 g (0.1064 mmol) of **11** in methylene chloride (1 mL) and 3.8 mL (0.2128 mmol) of an 0.056 M solution of **2** in acetone. After reaction was complete (6 h) the solvent was evaporated on the rotovap to afford a colorless crystalline solid (0.018 g, 100%). GLC, GC-MS, and ^{1}H NMR analysis of the product indicated that only tetraepoxide **3** was present.

Tetraepoxide 3 Polymer During the workup of the reaction mixture giving **3** a colorless insoluble solid was always found to be present. This solid was insoluble in all of the common solvents. The solid (mp > 320° C) was characterized by IR, MS, and CP-MAS spectra; IR(KBr) 3500 (br s), 3004 (w), 2936 (m), 1636 (br m), 1430 (m), 1364 (m), 1298 (m), 1240 (m), 1100 (vs), 1019 (m), 874 (ms), 852 (ms), 803 (s), 697 (m), 635 (w) cm^{-1}; ^{13}C NMR (75.4 MHz, CP-MAS): δ 48.98, 54.32, 65.73; MS(EI, 70 eV): m/z (relative intensity) 169 (M+1, 86), 168 (M^+, 91), Calcd for $C_8H_8O_4$ 168.15, Anal Calcd for $C_8H_8O_4$ C, 57.14; H, 4.80; Found: C, 55.80; H, 5.01. Our tentative conclusion is that this material is a polymer derived from **3**.

X-Ray Crystallographic Analyses of Compounds 3, 4, 10, 11, and 12 Crystals of appropriate dimensions were mounted on glass fibers in random orientations. Preliminary examination and data collection were performed using a Siemens SMART Charge Coupled Device (CCD) Detector system single crystal x-ray diffractometer using graphite monochromated Mo Kα radiation (λ=0.7103 Å) equipped with a sealed tube x-ray source at 25° C for **3** and -50°C for **4, 10, 11**, and **12.** Preliminary unit cell constants were determined with a set of 45 narrow frames (0.3° in ϖ) scans. A typical data set collected consists of 4028 frames of intensity data collected wth a frame width of 0.3° in ϖ and counting time of 15 secs/frame at a crystal to detector distance of 4.930 cm. The double pass method of scanning was used to exclude any noise. The collected frames were integrated using an orientation matrix determined from the narrow frame scans. SMART and SAINT software packages (Bruker Analytical x-ray, Madison, WI, 1997) were used for data collection and data integration. Analysis of the integrated data did not show any decay. Final cell constants were determined by a global refinement of xyz centroids of 8192 reflections ($\theta < 25.0°$). Collected data were corrected for systematic errors using SADABS (Blessing, R.H., Acta Cryst. (1995), A51, 33-38) based upon the Laue symmetry.

Structure solution and refinement were carried out using the SHELXTL-PLUS software package (Sheldrick, G.M., Bruker Analytical X-Ray Division, Madison, WI, 1997). The structures were solved by direct methods and refined successfully in the monoclinic space groups as listed below. Full matrix least-squares refinement was carried out by minimizing $\Sigma w (F_o^2-F_c^2)^2$. The non-hydrogen atoms were refined anisotropically to convergence. The hydrogen atoms were treated using the appropriate riding model (AFIX m3). Projection views of the molecules with non-hydrogen atoms represented by 50 % probability ellipsoids, and showing the atom labeling are presented in Figures 1-5.

A complete list of positional and isotropic displacement coefficients, geometrical parameters, anisotropic displacement coefficients for the non-hydrogen atoms, hydrogen atom parameters is submitted as Tables 1-5 in the supplementary material. Lists of calculated and observed structure factors are available in electronic media from the authors.

Crystal Data for 3: $C_8H_8O_4$. M = 168.14, a = 4.8544(2) Å, b = 11.7404(5) Å, c = 6.2339(2) Å, β = 96.642(2)° V = 352.90(2) Å^3, space group Im, Z = 2, D_c = 1.582 mg/m^3, μ = 0.129 mm^{-1}, crystal size 0.32 x 0.16 x 0.08 mm^3, θ range for data collection = 3.47 to 26.97°, number of collected/ independent reflections =

2980/794, R1[I>2σ(I)] = 0.069, wR2 = 0.169, absolute structure parameter Flack X = 9(4) absolute structure undetermined, largest diff. peak and hole = 0.32 and -0.23 e.Å^{-3}.

Crystal Data for 4: $C_8H_8O_4$, M = 168.14, a = 12.0182(1) Å, b = 6.3924(1) Å, c = 10.2734(1) Å, β = 105.059(1)°, V = 762.15(2) Å^3, space group Cc, Z = 4, D_c = 1.465 mg/m^3, μ = 0.119 mm^{-1}, crystal size 0.40 x 0.22 x 0.20 mm^3, θ range for data collection = 3.51 to 28.27°, number of collected/independent reflections = 7428/1870, R1[I>2σ(I)] = 0.031, wR2 = 0/083, absolute structure parameter Flack X = 0/6(7) absolute structure undetermined, largest diff. peak and hole = 0.20 and -0.15 e.Å^{-3}.

Crystal Data for 10: $C_8H_8O_3$, M = 152.14, a = 4.8256(1) Å, b = 11.5796(3) Å, c = 6.1152(1) Å, β = 94.784(2)°, V = 340.1518(13) Å^3, space group Im, Z = 2, D_c = 1.484 mg/m^3, μ = 0.114 mm^{-1}, crystal size 0.40 x 0.33 x 0.28 mm^3, θ range for data collection = 3.52 to 28.17°, number of collected/independent reflections = 4790/822, R1[I>2σ(I)] = 0.028, wR2 = 0.070, absolute structure parameter Flack X = 0(1), largest diff. peak and hole = 0.16 and -0.11 e.Å^{-3}.

Crystal Data for 11: $C_8H_8O_3$, M = 152.14, a = 6.8672(2) Å, b = 12.0553(2) Å. c = 8.2430(2) Å, β = 104.463(2)°, V = 660.78(3) Å^3, space group Cc, Z = 4, D_c = 1.529 mg/m3, μ = 0.118 mm^{-1}, crystal size 0.40 x 0.33 x 0.20 mm^3, θ range for data collection = 3.38 to 24.97°, number of collected/independent reflections = 4355/1163, R1[I>2σ(I)] = 0.062, wR2 = 0.140, absolute structure parameter Flack X = 0(2), largest diff. peak and hole = 0.31 and -0.32 e.Å^{-3}.

Crystal Data for 12: $C_8H_8O_3$ M = 152.14, a = 9.2160(2) Å, b = 6.4227(1) Å, c = 12.0651(2) Å, β = 101.643(1)°, V = 699.46(2) Å^3, space group $P2_1c$, Z = 4, D_c = 1.445 mg/m^3, μ = 0.111 mm^{-1}, crystal size 0.40 x 0.33 x 0.11 mm^3, θ range for data collection = 2.26 to 26.00°, number of collected/independent reflections = 11694/1371, R1[I>2σ(I)] = 0.049, wR2 = 0.1436, largest diff. peak and hole = 0.31 and -0.20 e.Å^{-3}.

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