Synthesis and Epoxidation of *trans*-5,6-Diacetoxy-1-benzoyloxymethyl-1,3-cyclohexadiene[1]

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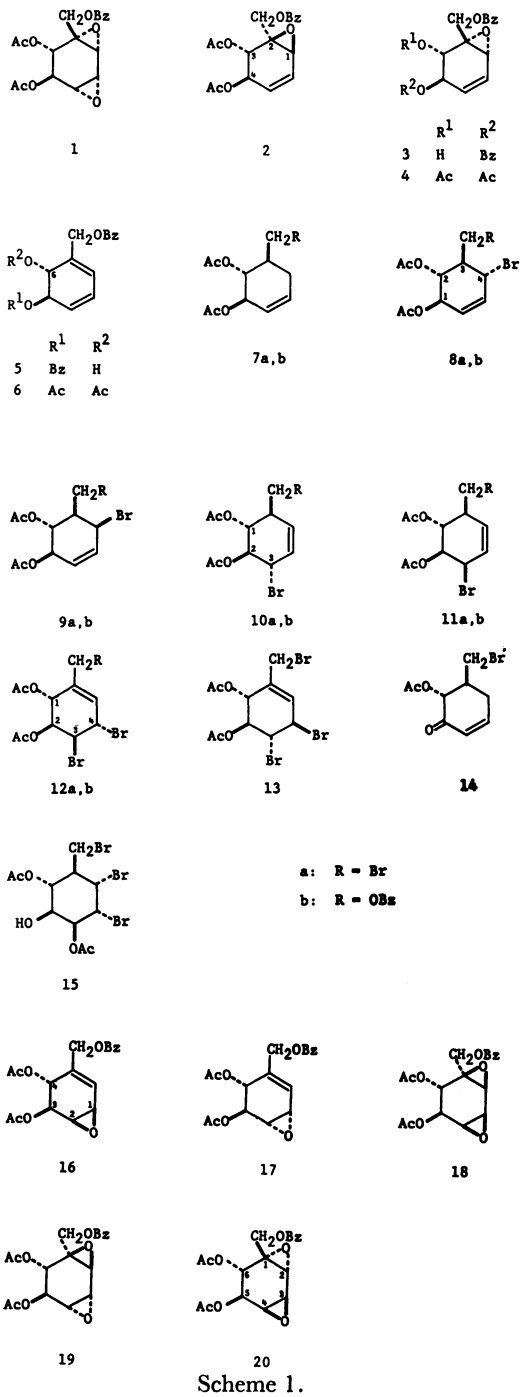
The title substituted 1,3-cyclohexadiene was prepared in three steps from the readily available DL-1,2-di-*O*-acetyl-(1,3/2)-3-bromomethyl-5-cyclohexene-1,2-diol. Epoxidation of it with *m*-chloroperoxybenzoic acid in 1,2-dichloroethane afforded several stereoisomers of the biologically interesting highly oxygenated cyclohexane derivatives.

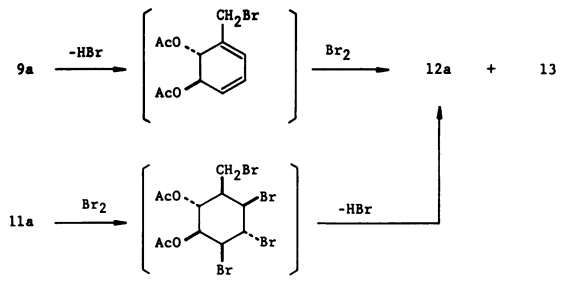
Crotepoxide (**1**),[2] senepoxide (**2**),[3] and pipoxide (**3**)[4] belong to a family of highly oxygenated cyclohexane derivatives which exhibit tumor-inhibitory, antileukemic, or antibiotic activity. Very recently, 1,6-desoxypipoxide (**5**), a key intermediary metabolite of **3**, has been isolated from *Uvaria purpurea*.[5] As a part of a synthetic study of mono- and diepoxycyclohexane compounds of biological interest,[6] several stereoisomeric compounds of this class were synthesized by epoxidation of properly functionalized 1,3-cyclohexadiene **6**.

Synthesis of the Substituted 1,3-Cyclohexadiene. Allylic bromination of DL-1,2-di-*O*-acetyl-(1,3/2)-3-bromomethyl-5-cyclohexene-1,2-diol (**7a**)[7] with molar equiv. of *N*-bromosuccinimide (NBS) in carbon tetrachloride in the presence of α,α'-azobisisobutyronitrile (AIBN) was carried out at 80 °C under nitrogen atmosphere for 0.5 h to give, after crystallization followed by fractionation on a silica-gel column, two dibromides **8a** (23%) and **10a** (7%), and one tribromide **12a** (9%), together with a small proportion of an α,β-unsaturated ketone **14** (3.7%).[8] When the same reaction was quenched after heating for 5 min, the new dibromide **11a** could be isolated in 2.6%, together with **8a** (16%). Under these reaction conditions, four dibromides **8a**—**11a** were expected to be obtainable and to be interconvertible by way of an allylic rearrangement. The results indicated that **8a** and **10a** were comparatively stable among them. When excess NBS (3 molar equiv.) was used in the reaction, **12a** was obtained in a quantitative yield. A small proportion of the isomeric tribromide **13** was shown to be present in a crude **12a** by ^{1}H NMR spectroscopy. Formation of **12a** would be rationalized by a readily dehydrobromination of an unstable dibromide **9a** followed by an addition of bromine generated *in situ* by hydrobromic acid and NBS or an addition of bromine to **9a** and/or **11a** followed by dehydrobromination (Scheme 2).

The structures of the dibromides and tribromide were elucidated on the basis of their ^{1}H NMR spectra. Thus, the spectrum of **8a** showed the coupled signals for H-3 and H-4 as a doublet of doublets of triplets (δ 2.59, J= 3, 3, 9, and 12 Hz) and a doublet of quartets (δ 4.90, J=2.5, 2.5, 2.5, and 9 Hz), indicating the axial–pseudoaxial conformations for H-3 and H-4. In the spectrum of **10a**, two protons attached to the carbon atoms bearing the acetoxyl groups appeared as coupled two doublets of doublets (J=8 and 10 Hz) at δ 5.10 and 5.50, being in accord with the assigned structure.



Scheme 1.



Scheme 2.

In the spectrum of **11a**, one-proton doublet of doublets of doublets (δ 6.10, J=3, 5, and 11 Hz) could be attributed to the C-4 olefinic proton adjacent to the bromo group oriented pseudoaxial conformation. In the spectrum of **12a**, the signals for H-1, H-2, H-3, and H-4 appeared as a doublet (δ 6.04, J=7.5 Hz), a doublet of doublets (δ 5.51, J=3.5 and 7.5 Hz), a triplet (δ 4.63, J=3.5 Hz), and a doublet of doublets (δ 4.96, J=3.5 and 4.5 Hz), respectively, indicating pseudoaxial–axial–equatorial–pseudoequatorial conformations for H-1, H-2, H-3, and H-4. In addition, two doublets of doublets (J=7 and 10 Hz) of small intensity were observed at δ 4.39 and 5.31, which were probably due to C-3 and C-2 protons, respectively, of the isomer **13** contained in crude **12a**.

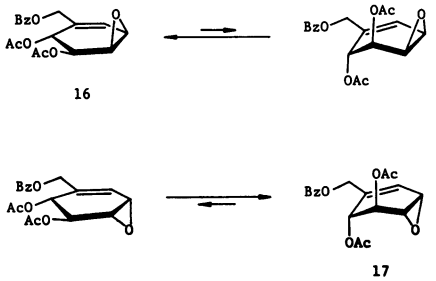
Compound **8a** was converted into the tribromide **15** by treatment with NBS in aqueous acetic acid. The structure of **15** was fully proved by the ^{1}H NMR spectrum, which further confirmed the assigned structure of **8a**.

A similar bromination of the benzoyloxy derivative **7b**[7] with NBS (1.5 molar equiv.) in carbon tetrachloride yielded a mixture of products, from which two monobromides **8b** (20%) and **11b** (10%), and one dibromide **12b** (18%) were isolated. The structures were correlated with those of the corresponding bromo compounds by ^{1}H NMR spectroscopy. In this case, a use of excess NBS did not increase the yield of **12b**. Compounds **8b** and **11b** seemed to be stable under the reaction conditions, probably due to an inductive effect of the benzoyloxyl function. The desired **12b** was conveniently prepared in 42% overall yield from **7a** by direct treatment of crude **12a** with sodium benzoate in 90% aqueous *N*,*N*-dimethylformamide (DMF) at room temperature for 4 h.

Synthetically useful 1,3-cyclohexadiene **6** was prepared by treatment of **12b** with zinc dust in ethanol at 70 °C for 0.5 h. The product was purified by chromatography on silica gel to give **6** as an oil in 62% yield. The structure of **6** was established by the ^{1}H NMR spectrum, which showed a doublet of doublets (δ 5.25, J=4 and 5 Hz) and a doublet (δ 5.53, J=5 Hz) attributable to two olefinic protons H-3 and H-4, respectively. These data were in good accord with those of the corresponding 1-benzyloxyl derivative reported by White *et al.*[9]

Epoxidation of **6**. Compound **6** was treated with *m*-chloroperoxybenzoic acid (*m*CPBA) in 1,2-dichloroethane at room temperature or at reflux temperature with a radical inhibitor.[10] When an equimolar *m*CPBA was used at room temperature, **6** was consumed within 15 h and three monoepoxides were formed. They were fractionated by use of a silica-gel column to give **4** (14%), **16** (8.4%), and **17** (13%). The structure of **4** was deduced by comparison of the ^{1}H NMR spectrum with those of **2** and **3**. Thus, the signals due to H-3 and H-4 appeared as a two-proton narrow multiplet at δ 5.53 in contrast with those of **2** [H-3 (δ 5.57) and H-4 (δ 5.17)].[3] The C-4 proton of **4** was apparently deshielded by the proximate 1,2-epoxide ring in the half-chair conformation with two acetoxyl groups being diequatorially situated. It was further supported by the spectrum of **3** which revealed the C-4 proton attached to the carbon atom bearing the benzoyloxyl group at δ 5.68.[4b]

The ^{1}H NMR spectra of **16** and **17** showed two epoxide and one olefinic protons, respectively, indicating that they were an epimeric pair of the 3,4-epoxide of **6**. In the spectrum of **16**, the signals due to H-3 and H-4 appeared as a doublet (J=8.2 Hz) at δ 5.28 and 5.79, respectively, being in consistent with the proposed structure in which two acetoxyl groups were oriented diequatorially and the C-4 proton was deshielded by the epoxide group. Whereas, in the spectrum of **17**, two narrow triplets (J=2 Hz) appeared δ 5.30 and 5.46, which could be attributed to H-3 and H-4, respectively, in the preferred conformation with two acetoxyl groups in diaxial disposition.[11] The above data suggested that the conformational preference of these compounds might be due to the configurational relationship between trans-vicinal substituents and epoxide group independent of the steric and polar effect of benzoyloxymethyl group.[12]



Scheme 3.

When the similar reaction was carried out under forcing conditions[10] (2,6-di-*t*-butyl-*p*-cresol, reflux, 1.5 h), a sole crystalline diepoxide **20** was isolated, after chromatography on silica gel, in 12% yield, along with **4** (3.5%), **16** (1.3%), and **17** (2.6%). The ^{1}H NMR spectrum of **20** showed two coupled sharp doublets (J=8 Hz) at δ 5.28 and 5.65, attributable to H-5 and H-6, respectively. The spectral data were in accord with the proposed structure where the C-5 and C-6 protons adopted the diaxial conformation and the former was deshielded by the proximate 1,2-epoxide group.[13]

The structure was further confirmed by epoxidation of the monoepoxides obtained. Epoxidation of **16** with *m*CPBA occurred smoothly to give **20** selectively. While, **4** did not react with *m*CPBA at room temperature, however, under forcing conditions, formation of **20** was detected by TLC. On the other hand, although **17** was expected to give **1** and/or **19**, it was not oxidized,

but underwent decomposition on prolonged reaction time. The reactivity of **17** may be explained by the steric and electronic effects exerted by diaxial arrangement of two acetoxyl groups.

Accordingly, it was noted that the 1,2-double bond of **6** was deactivated by the inductive effect of the C-1 benzoyloxymethyl group, comparing with that of the corresponding diene with the C-1 benzyloxymethyl group.[9] Stereospecificity of the epoxidation of *trans*-5,6-diacetoxy-1,3-cyclohexadienyl system seems to depend rather on an interaction of the neighboring group than on the spacial steric effect,[14] *e.g.* a conformational requirement of the molecule in the transition state of epoxidation, leading predominantly to the epoxide with two acetoxyl groups in equatorial orientation.

Experimental

Unless otherwise noted, melting points were determined on a Mitamura Riken micro hot stage and are uncorrected. ^{1}H NMR spectra were taken on a Varian EM-360 (60 MHz), EM-390 (90 MHz), or HA-100D (100 MHz) spectrometer in chloroform-*d* ($CDCl_3$) with reference to tetramethylsilane as an internal standard. The peak positions are given in terms of δ-values and values given for coupling constants are of first-order. Mass spectrum was recorded on a Hitachi M-80 mass spectrometer at 70 eV. TLC was performed on silica gel (Wakogel B-10, Wako Pure Chemical Ind., Ltd.). The silica gel used for a column chromatography was Wakogel C-300. Organic solutions were dried over anhydrous sodium sulfate and concentrated below 50 °C under reduced pressure.

Bromination of DL-*1,2-Di-O-acetyl-(1,3/2)-3-bromomethyl-5-cyclohexene-1,2-diol (7a) with NBS in Carbon Tetrachloride.* *a)*: To a solution of **7a**[7] (1.46 g) in carbon tetrachloride (15 ml) was added NBS (0.89 g, molar equiv.) and AIBN (10 mg), and the mixture was stirred at 80 °C under nitrogen stream for 0.5 h. After the reaction mixture was cooled to room temperature, succinimide formed was removed by filtration and washed with carbon tetrachloride. The filtrate and washings were combined and concentrated. The oily residue was crystallized from ethanol to give 0.34 g (20%) of DL-1,2-di-*O*-acetyl-(1,3/2,4)-4-bromo-3-bromomethyl-5-cyclohexene-1,2-diol (**8a**) as needles: mp 103—105 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.03 (3H, s) and 2.08 (3H, s) (OAc), 2.59 (1H, tdd, $J_{2,3}$=12 Hz, $J_{3,4}$=9 Hz, $J_{3,7}$=$J_{3,7'}$=3 Hz, H-3), 3.73 (1H, dd) and 3.90 (1H, dd) (J_{gem}=12 Hz, H-7 and H-7'), 4.90 (1H, dq, $J_{1,4}$=$J_{4,5}$=$J_{4,6}$=2.5 Hz, H-4), 5.19 (1H, dd, $J_{1,2}$=9 Hz, H-2), 5.42—5.71 (2H, H-1 and H-5) and 6.05 (1H, dt, $J_{5,6}$=10.5 Hz, $J_{1,6}$=2.5 Hz, H-6).

Found: C, 35.43; H, 3.83; Br, 42.96%. Calcd for $C_{11}H_{14}Br_2O_4$: C, 35.70; H, 3.81; Br, 43.19%.

The mother liquor of **8a** was concentrated and the residue was chromatographed on a silica-gel column (65 g) with 2-butanone–toluene (1 : 20) as an eluent. The first fraction [R_f 0.71, 2-butanone–toluene (1 : 8)] gave 0.20 g (9%) of DL-1,2-di-*O*-acetyl-(1,4/2,3)-3,4-dibromo-6-bromomethyl-5-cyclohexene-1,2-diol (**12a**) as an oil: ^{1}H NMR ($CDCl_3$, 100 MHz) δ=2.10 (6H, s, OAc), 3.93 (2H, AB q, J=12 Hz, C$\underline{H}_2$Br), 4.63 (1H, t, $J_{2,3}$=$J_{3,4}$=3.5 Hz, H-3), 4.96 (1H, dd, $J_{4,5}$=4.5 Hz, H-4), 5.51 (1H, dd, $J_{1,2}$=7.5 Hz, H-2), 6.04 (1H, d, H-1) and 6.16 (1H, br d, H-5). Traces of the ^{1}H NMR signals due to the isomer **13** were observed: δ=4.39 (1H, dd, $J_{2,3}$=10 Hz, $J_{3,4}$=7.5 Hz, H-3), 5.31 (1H, dd, $J_{1,2}$=7 Hz, H-2), 5.84 (1H, br d, H-1).

Found: C, 29.82; H, 3.07%. Calcd for $C_{11}H_{13}Br_3O_4$: C, 29.42; H, 2.92%.

The second fraction (R_f 0.58) gave an another crop (90 mg) of **8a** and the combined yield was 23%.

The third fraction (R_f 0.49) gave 0.13 g (7%) of DL-1,2-di-*O*-acetyl-(1,3/2,6)-3-bromo-6-bromomethyl-4-cyclohexene-1,2-diol (**10a**) as prisms: mp 126—128 °C; ^{1}H NMR ($CDCl_3$, 60 MHz) δ=2.06 (3H, s) and 2.09 (3H, s) (OAc), 2.75—3.10 (1H, m, H-6), 4.62 (1H. br d, $J_{2,3}$=8 Hz, H-3), 5.10 (1H, dd, $J_{1,2}$=10 Hz, $J_{1,6}$=8 Hz, H-1), 5.50 (1H, dd, H-2), 5.62 (1H, dt, $J_{3,5}$=$J_{5,6}$=2 Hz, $J_{4,5}$=10 Hz, H-5) and 5.99 (1H, dt, $J_{3,4}$=$J_{4,6}$=2.5 Hz, H-4).

Found: C, 35.87; H, 3.81; Br, 43.05%. Calcd for $C_{11}H_{14}Br_2O_4$: C, 35.70; H, 3.81; Br, 43.19%.

The fourth fraction (R_f 0.42) gave 45 mg (3.7%) of DL-*trans*-6-acetoxy-5-bromomethyl-2-cyclohexen-1-one (**14**) as a glass: ^{1}H NMR ($CDCl_3$, 60 MHz) δ=2.21 (3H, s, OAc), 2.60 (2H, m, H-4 and H-4'), 3.52 (2H, d, $J_{3,5}$=3.5 Hz, C$\underline{H}_2$Br), 5.32 (1H, d, $J_{5,6}$=12 Hz, H-6), 6.03 (1H, dt, $J_{2,3}$=10 Hz, $J_{2,4}$=$J_{2,4'}$=1.5 Hz, H-2) and 6.95 (1H, dt, $J_{3,4}$=$J_{3,4'}$=3.5 Hz, H-3).

Found: C, 43.77; H, 4.44; Br, 32.26%. Calcd for $C_9H_{10}BrO_3$: C, 43.93; H, 4.10; Br, 32.47%.

b): The similar reaction of **7a** (1.46 g) with NBS (0.89 g) was quenched after heating at 80 °C for 5 min, and the reaction mixture was processed similarly as described in a. The product was fractionally crystallized from ethanol to give 0.30 g (16%) of **8a** and 49 mg (2.6%) of DL-1,2-di-*O*-acetyl-(1/2,3,-6)-3-bromo-6-bromomethyl-4-cyclohexene-1,2-diol (**11a**) as cubic crystals: mp 105—108 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.08 (3H, s) and 2.10 (3H, s) (OAc), 2.78—3.13 (1H, m, H-6), 3.33 (1H, dd, $J_{6,7}$=6.5 Hz, J_{gem}=10 Hz, H-7), 3.51 (1H, dd, $J_{6,7'}$=4.5 Hz, H-7'), 4.75—4.98 (2H, m, H-2 and H-3), 5.49 (1H, dd, $J_{1,2}$=10.5 Hz, $J_{1,6}$=9 Hz, H-1), 5.56 (1H, dd, $J_{4,5}$=11 Hz, $J_{5,6}$=3 Hz, H-5) and 6.01 (1H, ddd, $J_{3,4}$=5 Hz, $J_{4,6}$=3 Hz, H-4).

Found: C, 35.53; H, 3.88; Br, 43.27%. Calcd for $C_{11}H_{14}Br_2O_4$: C, 35.70; H, 3.81; Br, 43.19%.

c): A mixture of **7a** (2.0 g), NBS (2.45 g, 2 molar equiv.), and AIBN (5 mg) in carbon tetrachloride (20 ml) was heated at reflux under nitrogen atmosphere for 2 h. Succinimide formed was removed by filtration and the filtrate was concentrated to give 3.1 g (100%) of **12a** as an oil.

DL-*1,3-Di-O-acetyl-(1,2,4/3,5,6)-5,6-dibromo-4-bromomethyl-1,-2,3-cyclohexanetriol (15).* To a mixture of **8a** (90 mg) in 50% aqueous acetic acid (12 ml) was added NBS (43 mg, molar equiv.) and the reaction mixture was allowed to stand at room temperature for 2 d. Precipitates were collected to give 17 mg (11%) of **15**: mp 198—200 °C; ^{1}H NMR (dimethyl-d_6 sulfoxide, 60 MHz) δ=2.09 (6H, s, OAc), 3.68 (2H, d, J=2 Hz, C$\underline{H}_2$Br), 4.31 (1H, dd, $J_{4,5}$=3.5 Hz, $J_{5,6}$=10 Hz, H-5), 4.71 (1H, t, $J_{3,4}$=3.5 Hz, H-4), 5.07 (1H, t, $J_{1,2}$=$J_{1,6}$=10.5 Hz, H-1) and 5.22 (1H, t, $J_{2,3}$=3.5 Hz, H-3).

Found: C, 28.44; H, 3.24; Br, 51.25%. Calcd for $C_{11}H_{15}Br_3O_5$: C, 28.29; H, 3.24; Br, 51.34%.

Bromination of DL-*1,2-Di-O-acetyl-(1,3/2)-3-benzoyloxymethyl-5-cyclohexene-1,2-diol (7b) with NBS in Carbon Tetrachloride.* To a solution of **7b**[7] (0.664 g) in carbon tetrachloride (20 ml) was added NBS (0.356 g, molar equiv.) and AIBN (10 mg), and the mixture was heated at reflux under nitrogen stream for 1 h. An additional amount of NBS (0.18 g) and AIBN (5 mg) was added and heating was continued for 1 h. At this time, **7b** was almost consumed and the formation of four components were detected by TLC [R_f 0.67, 0.60, 0.49, and 0.42 in 2-butanone–toluene (1 : 9)]. An insoluble material was removed by filtration and the filtrate was concentrated to an oil (0.60 g), which was chromatographed on a silica-gel column (30 g) with 2-butanone–toluene (1 : 20) as an eluent. The

first fraction (R_f 0.67) gave, after recrystallization from ethanol, 0.172 g (17.6%) of DL-1,2-di-*O*-acetyl-(1,6/2,5)-3-benzoyloxymethyl-5,6-dibromo-3-cyclohexene-1,2-diol (**12b**) as prisms: mp 132—134 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ= 2.03 (3H, s) and 2.07 (3H, s) (OAc), 4.63 (1H, t, $J_{5,6}=J_{1,6}=$ 3 Hz, H-6), 4.78 (2H, br s, C$\underline{H}_2$OBz), 4.93 (1H, br dd, $J_{4,5}=$ 4.5 Hz, H-5), 5.49 (1H, dd, $J_{1,2}=7.3$ Hz, H-1), 6.01 (1H, br d, H-2), 6.11 (1H, br d, H-4), and 7.29—7.68 (3H, m) and 7.91—8.10 (2H, m) (phenyl).

Found: C, 44.29; H, 3.87; Br, 32.85%. Calcd for $C_{18}H_{18}Br_2O_6$: C, 44.12; H, 3.71; Br, 32.60%.

The second fraction (R_f 0.60) gave 0.163 g (20%) of DL-1,2-di-*O*-acetyl-(1,3/2,4)-3-benzoyloxymethyl-4-bromo-5-cyclohexene-1,2-diol (**8b**) as an oil: ^{1}H NMR ($CDCl_3$, 60 MHz) δ= 2.03 (3H, s) and 2.07 (3H, s) (OAc), 2.50—3.20 (1H, m, H-6), 4.30—4.72 (2H, m, C$\underline{H}_2$OBz), 4.91 (1H, ddd, $J_{4,5}=J_{4,6}=2.8$ Hz, $J_{3,4}=9$ Hz, H-4), 5.33 (1H, dd, $J_{1,2}=9.7$ Hz, $J_{2,3}=11.3$ Hz, H-2), 5.59 (1H, ddd, $J_{1,5}=J_{1,6}=2.7$ Hz, H-1), 5.69 (1H, ddd, $J_{5,6}=10.3$ Hz, H-6), 6.09 (1H, ddd, H-5), and 7.30—7.70 (3H, m) and 7.90—8.20 (2H, m) (phenyl).

Compound **8b** was not stable enough to give a satisfactory analytical data.

The third fraction (R_f 0.49) gave 82 mg (10%) of DL-1,2-di-*O*-acetyl-(1,3/2,6)-3-benzoyloxymethyl-6-bromo-4-cyclohexene-1,2-diol (**11b**) as crystals: mp 90—92 °C; ^{1}H NMR ($CDCl_3$, 60 MHz) δ=2.06 (3H, s) and 2.14 (3H, s) (OAc), 2.79—3.22 (1H, m, H-3), 4.22 (1H, dd, $J_{3,7}=5$ Hz, $J_{gem}=11$ Hz, H-7), 4.50 (1H, dd, $J_{3,7'}=4.5$ Hz, H-7'), 4.73—5.03 (2H, m, H-1 and H-6), 5.66 (1H, dd, $J_{3,4}=2$ Hz, $J_{4,5}=10.5$ Hz, H-4), 6.00 (1H, ddd, $J_{3,5}=2.5$ Hz, $J_{5,6}=5$ Hz, H-5), and 7.30—7.60 (3H, m) and 7.90—8.20 (2H, m) (phenyl).

Found: C, 52.72; H, 4.70; Br, 19.43%. Calcd for $C_{18}H_{19}BrO_6$: C, 52.56; H, 4.62; Br, 19.43%.

Practical Synthesis of ***12b***. A mixture of crude **12a** (1.13 g), sodium benzoate (0.40 g), and 90% aqueous DMF (20 ml) was stirred at room temperature for 1 d. TLC indicated the formation of one major (R_f 0.64) and one minor components (R_f 0.35) in 2-butanone–toluene (1 : 8). The reaction mixture was partitioned between ethyl acetate (30 ml) and water (20 ml). The organic layer was washed with water thoroughly, dried, and concentrated. The residue was crystallized from ethanol to give 0.58 g (47% based on **7a** used) of **12b**: mp 129—130 °C.

DL-trans-*5,6-Diacetoxy-1-benzoyloxymethyl-1,3-cyclohexadiene (****6****).* To a stirred solution of **12b** (2.0 g) in ethanol (45 ml) was added zinc dust (1.06 g, 4 atomic equiv.) in portions at 70 °C. The suspension was stirred vigorously at this temperature for 20 min. At this time, **12b** disappeared and one main component (R_f 0.51) and two minor components (R_f 0.16 and 0.12) were formed [TLC: 2-butanone–toluene (1 : 15)]. An insoluble material was removed by filtration and the filtrate was concentrated to give a pale yellow oil (1.2 g), which was chromatographed on a silica-gel column (30 g) with 2-butanone–toluene (1 : 15) as an eluent. The major fraction gave 0.83 g (62%) of **6** as a homogeneous oil: ^{1}H NMR ($CDCl_3$, 60 MHz) δ=1.98 (3H, s) and 2.00 (3H, s) (OAc), 4.74 (2H, s, C$\underline{H}_2$OBz), 5.25 (1H, dd, $J_{4,5}=4$ Hz, $J_{5,6}=5$ Hz, H-5), 5.53 (1H, d, H-6), 5.61—6.20 (3H, br m, H-2, H-3, and H-4) and 6.71—7.92 (5H, m, phenyl).

Found: *m/e* 330.1097. Calcd for $C_{18}H_{18}O_6$: M, 330.1102.[15]

Epoxidation of ***6****. a)*: To a solution of **6** (0.83 g) in 1,2-dichloroethane (20 ml) was added dropwise a solution of *m*CPBA (0.62 g, one molar equiv., purity 70%) in 1,2-dichloroethane (8 ml) at room temperature for 10 min. The reaction mixture was stirred at room temperature for 15 h. At this time, disappearance of **6** and formation of three major components were shown by TLC [R_f 0.51, 0.39, and 0.35 2-butanone–toluene (1 : 8)]. Then the mixture was washed successively with 10% aqueous sodium sulfite, saturated aqueous sodium hydrogencarbonate, and water, and dried. Evaporation of the solvent gave a clear oil which was chromatographed on a silica-gel column (50 g) with 2-butanone–toluene (1 : 15) as an eluent. The first fraction gave an oil which crystallized on standing to give 81 mg (14%) of DL-3,4-di-*O*-acetyl-1,2-anhydro-(1,2,3/4)-2-*C*-benzoyloxymethyl-5-cyclohexene-1,2,3,4-tetrol (**4**) as prisms: mp 112—113 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.02 (3H, s) and 2.10 (3H, s) (OAc), 3.51 (1H, dd, $J_{1,5}=1.5$ Hz, $J_{1,6}=3.8$ Hz, H-1), 4.26 (1H, d) and 4.56 (1H, d) ($J_{gem}=12.5$ Hz, C$\underline{H}_2$OBz), 5.53 (2H, m, H-3 and H-4), 5.71 (1H, dt, $J_{4,5}=1.5$ Hz, $J_{5,6}=9.5$ Hz, H-5), 6.00 (1H, ddd, $J_{4,6}=1.5$ Hz, H-6), and 7.47—7.99 (5H, m, phenyl).

The second fraction gave 50 mg (8.4%) of DL-3,4-di-*O*-acetyl-1,2-anhydro-(1,2,3/4)-5-benzoyloxymethyl-5-cyclohexene-1,2,3,4-tetrol (**16**) as a homogeneous oil: ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.00 (3H, s) and 2.10 (3H, s) (OAc), 3.44 (1H, t, $J_{1,2}=J_{1,6}=4$ Hz, H-1), 3.58 (1H, dd, $J_{2,3}=1.3$ Hz, H-2), 4.73 (2H, s, C$\underline{H}_2$OBz), 5.28 (1H, dd, $J_{3,4}=8.2$ Hz, H-3), 5.79 (1H, br d, H-4), 6.16 (1H, br s, H-6), and 7.43—7.96 (5H, m, phenyl).

The third fraction gave 76 mg (13%) of DL-3,4-di-*O*-acetyl-1,2-anhydro-(1,2,4/3)-5-benzoyloxymethyl-5-cyclohexene-1,2,-3,4-tetrol (**17**) as prisms: mp 116—117.5 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.00 (3H, s) and 2.03 (3H, s) (OAc), 3.38 (1H, t, $J_{1,2}=J_{1,6}=4$ Hz, H-1), 3.55 (1H, m, H-2), 4.74 (2H, s, C$\underline{H}_2$OBz), 5.30 (1H, t, $J_{2,3}=J_{3,4}=2$ Hz, H-3), 5.46 (1H, t, $J_{4,6}=2$ Hz, H-4), 6.43 (1H, br d, H-6), and 7.41—7.98 (5H, m, phenyl).

Found for **4**: C, 62.24; H, 5.33%, for **16**: C, 62.17; H, 5.32%, and for **17**: C, 62.50; H, 5.27%. Calcd for $C_{18}H_{18}O_7$: C, 62.42; H, 5.24%.

b): When the similar reaction was carried out in dichloromethane in the presence of phosphate buffer solution (pH 8) under vigorous stirring, **4** (11%); **16** (14%), and **17** (13%) were isolated by chromatography.

c): To a solution of crude **6** prepared from **12b** (0.30 g) were added *m*CPBA (0.20 g, 1.2 molar equiv.) and 2,6-di-*t*-butyl-*p*-cresol (3 mg), and the mixture was refluxed for 90 min. After having been cooled, the reaction mixture was filtered to remove *m*-chlorobenzoic acid and the filtrate was processed similarly as described in a. The mixture of products was chromatographed on silica gel (30 g) with 2-butanone–toluene (1 : 15) as an eluent. The first fraction [R_f 0.51, 2-butanone–toluene (1 : 8)] gave 8 mg (3.5%) of **4** as an oil.

The second fraction (R_f 0.38) gave an oil which crystallized on standing to give 30 mg (12%) of DL-5,6-di-*O*-acetyl-1,2 : 3,4-dianhydro-(1,2,6/3,4,5)-1-*C*-benzoyloxymethyl-1,2,3,4,5,6-cyclohexanehexol (**20**): mp 128—129 °C; ^{1}H NMR ($CDCl_3$, 90 MHz) δ=2.06 (6H, s, OAc), 3.35 (1H, d, $J_{3,4}=4.5$ Hz, $J_{4,5}=1.2$ Hz, H-4), 3.56 (1H, dd, $J_{2,3}=2.5$ Hz, H-3), 3.69 (1H, d, H-2), 4.13 (1H, d) and 4.42 (1H, d) ($J_{gem}=12$ Hz, C$\underline{H}_2$OBz), 5.28 (1H, dd, $J_{5,6}=8$ Hz, H-5), 5.65 (1H, d, H-6), and 7.36—7.98 (5H, m, phenyl).

Found: C, 59.81; H, 5.11%. Calcd for $C_{18}H_{18}O_8$: C, 59.67; H, 5.11%.

The third fraction (R_f 0.37) gave 3 mg (1.3%) of **16**.

The fourth fraction (R_f 0.35) gave 6 mg (2.6%) of **17**.

d): When **6** was treated with excess *m*CPBA (3 molar equiv.) similarly as described in c, **20** was obtained in 20% yield after chromatography, along with a trace of monoepoxides.

Epoxidation of ***4****.* A solution of **4** (0.14 g) and *m*CPBA (0.19 g, 2 molar equiv.) in 1,2-dichloroethane (3.5 ml) was allowed to stand at room temperature for 2 d. At this time,

TLC indicated that **4** remained almost unchanged.

Treatment of **4** (58 mg) with *m*CPBA (42 mg, equimolar) in 1,2-dichloroethane in the presence of 2,6-di-*t*-butyl-*p*-cresol (3 mg) at reflux temperature for 7 h, followed by the conventional acetylation, gave many products, one of which was identified with **20** by TLC. There was no product present, which was identical with **1**.[16]

*Epoxidation of **16**.* Compound **16** (5 mg) was treated with *m*CPBA (7 mg, 2 molar equiv.) in 1,2-dichloroethane (0.6 ml) at room temperature for 3 d. About half of **16** was found to be converted into **20** by TLC.

*Epoxidation of **17**.* Compound **17** (20 mg) was recovered unchanged, after having been treated with *m*CPBA (28 mg, 2 molar equiv.) in 1,2-dichloroethane (2 ml) at room temperature for 2 d. Under the forcing conditions,[10] **17** (62 mg) gave several products, but there was no product identical with **1**. Furthermore, the ^{1}H NMR spectrum of the mixture of products did not show any signals due to epoxide protons.

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