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Bullvalene Trisepoxide and Its Stereospecific Rearrangement to 2,8,12-Trioxahexacyclo[8.3.0.0^{3,9}0^{4,6}0^{5,13}0^{7,11}]tridecane: Two New C_3-Symmetrical Oligocycles with Propeller Chirality

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Dedicated to Professor Goverdhan Mehta on the occasion of his birthday

Abstract: Epoxidation of bullvalene (**1**) with a neutralized solution of Oxone gave racemic trisepoxide *rac*-**6** in 93% isolated yield. Its structure was examined by X-ray crystallography. The two enantiomers of **6** were separated by preparative HPLC and exhibited specific rotations of $[\alpha]_D^{25}=+160$, $[\alpha]_{365}^{25}=+567$ ($c=0.946$, $CHCl_3$) for the firstly eluted and $[\alpha]_D^{25}=-157$, $[\alpha]_{365}^{25}=-554$ ($c=0.986$, $CHCl_3$) for the secondly eluted enantiomer of **6**. The geometry of (+)-**6** and the absolute configuration of (−)-**6** were determined by X-ray crystal structure analysis and anomalous diffraction, respectively. According to this, (−)-**6** possesses (3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)- and (+)-**6** has (3*S*,5*R*,7*R*,9*S*,11*S*,13*R*)-configuration. Upon treatment with $BF_3{\cdot}Et_2O$ at −78 °C, trisepoxide *rac*-**6** rearranges with retention of the skeletal three-membered carbocycle to give the cage trisether *rac*-**8**, as proved by X-ray crystal structure analysis, in virtually quantitative yield. Enantiomers of *rac*-**8** were separated by preparative HPLC and exhibited specific rotations of $[\alpha]_D^{25}=+49$, $[\alpha]_{365}^{25}=+170$ ($c=1.01$, $CHCl_3$) (firstly eluting) and $[\alpha]_D^{25}=-46$, $[\alpha]_{365}^{25}=-160$ ($c=1.02$, $CHCl_3$) (secondly eluting enantiomer). The absolute configuration of (−)-**8** was determined by anomalous diffraction to be (1*R*,3*R*,7*R*,9*R*,11*R*,13*R*). DFT computations at the TD-B3LYP/6-31+G(d,p)//B3LYP/6-31+G(d) level of theory for (3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)-**6** and (1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-**8** predicted specific rotations of −206.7 and −83.4, respectively. Acid-catalyzed isomerization of the enantiomerically pure (+)-**6** proceeded without racemization to give exclusively (−)-**8**, and (−)-**6** provided only (+)-**8**. Thus, this isomerization occurs with ring opening of the three C–O bonds in the epoxide moieties in the α-position relative to the three-membered carbocycle rather than in the β-position.

Keywords: bullvalene · chirality · epoxidation · rearrangement · small ring systems · structure elucidation

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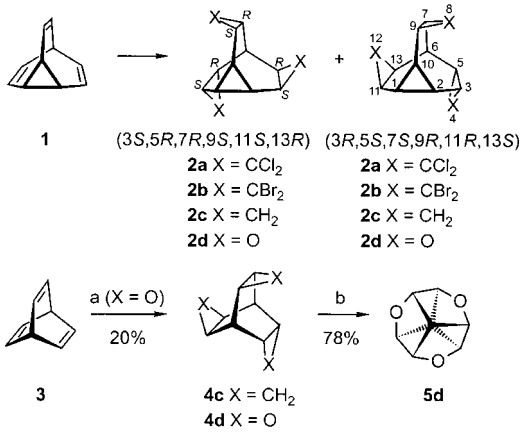
Introduction

The synthesis and chemistry of strained polycyclic aliphatic molecules still deserve considerable interest, and continue to be a challenging objective to organic chemists to probe different concepts of structure and reactivity.[1] Among such structures, the chiral cage-like molecules constitute interesting test cases for the ever advancing theoretical models that computations of chiroptical properties can be based upon.[2] The tricyclic bullvalene **1**, "a compound of 1209600 different faces",[3] is a particularly attractive starting material for the construction of such molecules. Thus, threefold dihalocyclopropanation[4] and threefold methylenation[5] of bullvalene **1** generate rigid C_3-symmetrical propeller-shaped helical molecules **2** which can be left- or right-handed (Scheme 1).[6,7]



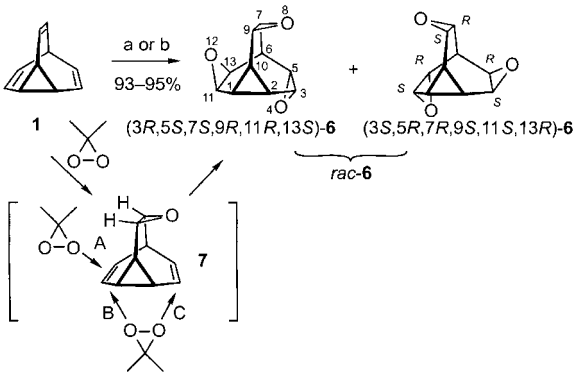
Scheme 1. Propeller-shaped chiral molecules derived from bullvalene **1**[4,5] and from trioxatrishomobarrelene (**4**).[11] a) *m*-chloroperbenzoic acid (MCPBA), $KHCO_3$, CH_2Cl_2, 0→20 °C, 24 h; b) acidic ion-exchange resin Amberlyst 15 or $BF_3{\cdot}Et_2O$, CH_2Cl_2, 20 °C.

Among the propeller-like bullvalene derivatives **2**, only the hydrocarbon trishomobullvalene **2c** has been studied thoroughly with respect to its structure[8] and chemistry occurring at the unique bridgehead position.[9] Chiroptical properties of such bridgehead derivatives of **2c** including the bridgehead cation and the hydrocarbon itself as well as bridgehead derivatives of trishomobarrelene **4c** have also been elucidated.[10] Trioxatrishomobarrelene **4d**, the trisepoxide of barrelene **3**, which has also previously been prepared, is an achiral molecule just like the hydrocarbon **4c**, but the rearrangement product of **4d**, D_3-trioxatrishomocubane **5d**, is chiral.[11]

The previously unknown bullvalene trisepoxide **2d** features an intriguing property in that it is chiral itself and would be able to rearrange stereoselectively to the chiral truncated trioxatrishomocubane **8**.[12]

Results and Discussion

Earlier attempts to epoxidize bullvalene with buffered *m*-chloroperbenzoic acid, as successfully applied for the epoxidation of barrelene **3**,[11] and even with the milder *N*-benzoylpercarbamidic acid (PhCN, H_2O_2), which had successfully been used for the epoxidation of benzvalene,[13] only led to decomposition or at best to the rearrangement product *rac*-**8**. Apparently, bullvalene trisepoxide *rac*-**6** is even more sensitive towards acid than barrelene trisepoxide **4d**. Eventually, the racemic trisepoxide *rac*-**6** was obtained in virtually quantitative yield by treatment of **1** with a buffered solution of Oxone in a mixture of acetone, dichloromethane and water. Due to its rather good solubility in water it was isolated in only 93% yield (Scheme 2).



Scheme 2. Preparation of racemic bullvalene trisepoxide *rac*-**6**. a) Oxone, $NaHCO_3$, CH_2Cl_2/acetone/H_2O, 0→20 °C, 3 h; b) dimethyldioxirane, acetone, −78→20 °C, 1.5 h.

Upon treatment of **1** with a 0.1 M solution of dimethyldioxirane in acetone[14a] at −78 to 20 °C, completely pure trisepoxide *rac*-**6** was obtained in 95% yield.

It is remarkable that the trisepoxide *rac*-**6** was formed as a sole product, and that none of a bisepoxide, isomeric to the one leading to *rac*-**6**, could even be detected in the final reaction mixture. Among the three possible directions for attack of the oxidant dimethyldioxirane[14] in the initially formed monoepoxide **7**, the trajectory designated A appears to be less preferable because of the interfering two hydrogen atoms on the already formed oxirane ring. The observed complete preference for direction C among the other two trajectories must be due to an electronic through-space activation of the corresponding double bond by the oxygen of the already formed oxirane, as has also been observed, albeit to a lesser extent, in the epoxidation of barrelene **3**.[11,15]

As the trisepoxide *rac*-**6** formed beautifully looking crystals, an attempt was made to carry out an X-ray crystal structure analysis. However, the crystals turned out to be disordered in that the three epoxy oxygens of each molecule in the crystal appeared in both possible positions, corresponding to a superposition of the two enantiomers (3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)-**6** and (3*S*,5*R*,7*R*,9*S*,11*S*,13*R*)-**6**[17] (Figure 1). Interestingly, this disorder was observed even at 40 K. Further cooling of the crystal by using a Helix open-helium low-temperature device led to fracture of the crystal, probably due to a phase transition. The carbon atoms disclosed rather large thermal parameters. The molecules in the crystal, due to the disorder, occupied special positions

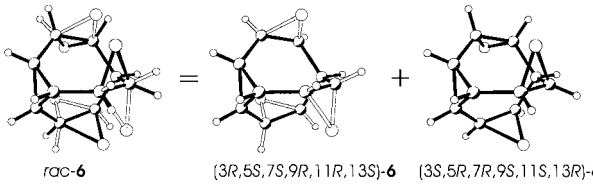


Figure 1. Structure of *rac*-4,8,12-trioxahexacyclo[4.4.3.0^{3,5}0^{7,9}0^{2,10}0^{11,13}]tridecane (trisepoxide *rac*-**6**) in the crystal.[16]

on a mirror plane, however, each enantiomer adopted local C_3 symmetry.

The enantiomers of *rac*-**6** were eventually separated by preparative HPLC. The firstly eluting (+)-enantiomer had $[\alpha]_D^{25}=+160$ and $[\alpha]_{365}^{25}=+567$ ($c=0.946$, $CHCl_3$); the second had $[\alpha]_D^{25}=-157$ and $[\alpha]_{365}^{25}=-554$ ($c=0.986$, $CHCl_3$). Thus, the specific rotations of the trisepoxides **6** significantly exceed that of the corresponding hydrocarbon trishomobullvalene **2c** ($[\alpha]_D^{20}=117$ in CCl_4[10a]), yet it is much lower than that of the bridgehead carbocation of **2c** with $[\alpha]_D^{20}=-2473$ in CH_2Cl_2.[10a] Single crystals of the enantiomerically pure (+)-**6** and (−)-**6** were also subjected to X-ray structure analysis. In contrast to the racemic compound *rac*-**6**, no disordering was observed in this case, and the molecule displayed almost ideal C_3 symmetry. The skeletal cyclopropane and each of the adjacent oxirane rings adopt a rigidly fixed *gauche* (*synclinal*) conformation, which is similar to that of the predominant conformer of bicyclopropyl in the gas phase[18] with an average torsional angle HCCH of 29(1)°. The cyclopropane C–C bonds in (+)-**6** [av. 1.520(1) Å] are slightly longer than those in unsubstituted cyclopropane [1.499(1) Å in the crystal[19a] or 1.509(3) Å in the gas phase[20]] as well as in hexahydrobullvalene [1.496(7) Å in the gas phase[21]], but shorter than those in bullvalene [1.5352(2) Å].[22]

The C_{sp^2}–C_{sp^2} bonds between the cyclopropane and the oxirane moieties [1.494(1) Å] are significantly shorter than C_{sp^3}–C_{sp^3} single bonds (1.536 Å[20]) and very close to those values found for the central bond in bicyclopropyl [1.4924(4)[19a] vs 1.487(3) Å[19b]]. The two O–C bonds in the oxirane rings are systematically non-equivalent, but the experimental values, within the error limits, are essentially the same [1.461(1) vs 1.454(1) Å]. All these bond length alternations are mostly due to changes of hybridization and incorporation in a polycyclic skeleton[23] rather than to some sort of conjugation between the cyclopropane and oxirane fragments (compare, however, ref. [24]). In the crystal, the molecules of (+)-**6** are linked with each other in a three-dimensional network by a number of weak C-H···O interactions, the shortest one O(4)···H(2) being 2.31(1) Å.

Ab initio computations at a reasonably high level of theory (TD-B3LYP/6-31+G(d,p)//B3LYP/6-31+G(d),[25–30] see Computational studies in the Experimental Section) determined the (3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)-configuration for the enantiomer with negative specific rotations of $[\alpha]_D^{25}=-206.7$ in the gas phase. This prediction has been unequivocally proved by X-ray crystal structure analysis applying $Cu_{K\alpha}$ radiation[31] which, according to the small but significant anomalous diffraction originating from the oxygen atoms, did reveal the absolute (3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)-configuration for this enantiomer (Figure 2). This means at the same time that the (+)-enantiomer possesses (3*S*,5*R*,7*R*,9*S*,11*S*,13*R*)-configuration. The two sets of geometrical parameters determined for (+)-**6** with $Mo_{K\alpha}$ radiation and (−)-**6** with $Cu_{K\alpha}$ radiation are very close to one another (Figure 2).

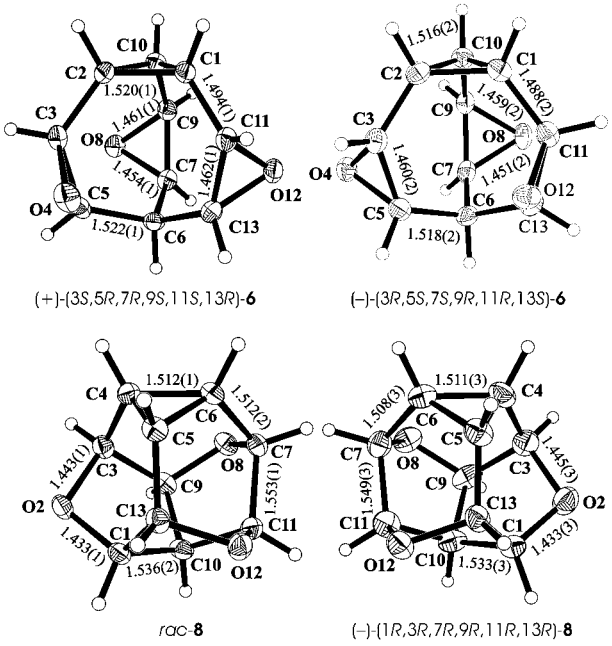
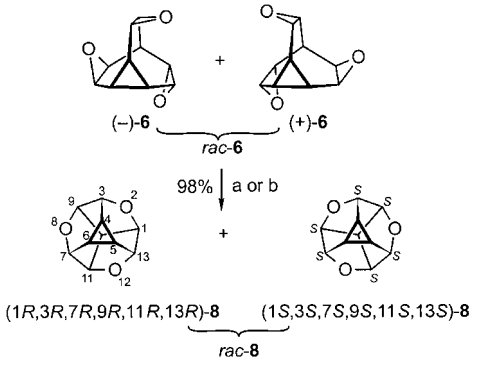


Figure 2. Structure and absolute configuration of (+)- and (−)-4,8,12-trioxahexacyclo[4.4.3.0^{3,5}0^{7,9}0^{2,10}0^{11,13}]tridecanes [(+)-(3*S*,5*R*,7*R*,9*S*,11*S*,13*R*)-**6** and (−)-(3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)-**6**] as well as structure and absolute configuration of *rac*- and (−)-2,8,12-trioxahexacyclo[8.3.0.0^{3,9}0^{4,6}0^{5,13}0^{7,11}]tridecane [*rac*-**8** and (1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-**8**] in the crystal.[16] Bond lengths [Å] represent mean values based on assumed C_3 symmetry; thermal ellipsoids are shown at 50% probability level.

Upon treatment with boron trifluoride etherate at −78°C, trisepoxide *rac*-**6** rearranged with retention of the skeletal three-membered carbocycle to give the hexacyclic trisether *rac*-**8** in virtually quantitative yield (Scheme 3).



Scheme 3. Rearrangement of bullvalene trisepoxide *rac*-**6** to the cage trisether *rac*-**8** and its possible stereochemistry. a) $BF_3{\cdot}Et_2O$, CH_2Cl_2, −78°C, 15 min; b) $MgSO_4$, CH_2Cl_2, 20°C, 15 min.

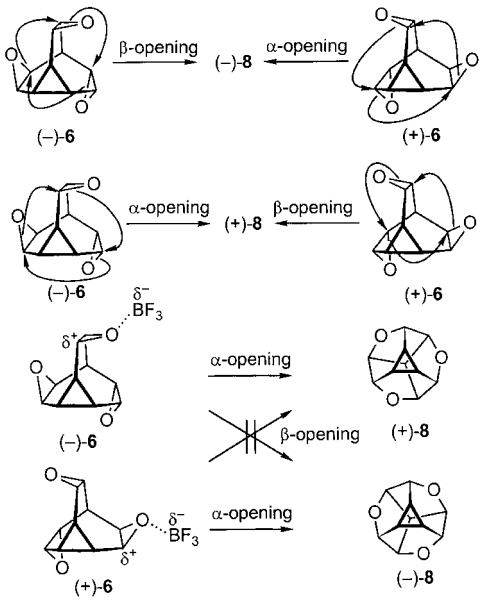
However, the same quantitative rearrangement to *rac*-**8** was observed upon simply stirring a solution of *rac*-**6** in dichloromethane with anhydrous magnesium sulfate at ambient temperature for 15 min. This was accidentally found when anhydrous magnesium instead of sodium sulfate was used to dry the organic extracts in a repeated preparation of *rac*-**6**.

An X-ray crystal structure analysis of the trisether *rac*-**8** (Figure 2) disclosed almost ideal C_3 symmetry for this molecule. The three cyclopropane C–C bonds [1.512(1) Å] are exactly of the same length as the three C–C bonds adjacent to the cyclopropane [1.512(2) Å], that is, while the cyclopropane bonds are slightly lengthened as compared to the normal length in cyclopropane [1.499(1) Å in the crystal[19] or 1.509(3) Å in the gas phase[20]], the ones adjacent to the cyclopropane are essentially shorter than the bonds C3–C9, C7–C11 and C1–C13 [1.553(1) Å]. The latter are closer to the normal C_{sp^3}–C_{sp^3} bond length (1.536 Å[20]) which is exactly the same as the three C–C bonds adjacent to the unique bridgehead [1.536(2) Å]. In the crystal, molecules are linked with each other by weak cyclopropane C-H···O contacts; the distances H···O (2.50–2.60 Å) are well in the standard range for similar contacts.[32]

These enantiomeric trisethers **8**[17] were separated by preparative HPLC and exhibited specific rotations of $[\alpha]_D^{25} = +49$ and $[\alpha]_{365}^{25} = +170$ ($c = 1.01$, $CHCl_3$) for the firstly as well as $[\alpha]_D^{25} = -46$ and $[\alpha]_{365}^{25} = -160$ ($c = 1.02$, $CHCl_3$) for the secondly eluted enantiomer. The ab initio computed (see Computational studies) specific rotation for the trisether (1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-**8** was $[\alpha]_D^{25} = -83.4$, and X-ray crystal structure analysis applying $Cu_{K\alpha}$ radiation[31] did reveal this absolute configuration for the enantiomer (−)-**8** (Figure 2, one of the three independent molecules has been shown). Thus, this computation for the gas phase predicts the sign of the rotation of the compound correctly, but somewhat overestimates the absolute value. The two sets of geometrical parameters determined for *rac*-**8** with $Mo_{K\alpha}$ radiation and (−)-**8** with $Cu_{K\alpha}$ radiation differ from one another insignificantly (Figure 2), in spite of their different crystal systems (triclinic and orthorhombic, respectively).

At first glance, the rearrangement of (−)-**6** or (+)-**6** may each produce a pair of enantiomers (−)-**8** and (+)-**8** (Scheme 4).

While opening of the three C–O bonds in the epoxide moieties adjacent to the skeletal three-membered ring in (−)-**6** and (+)-**6** (α-opening)[33a–d] would yield (+)-**8** and (−)-**8**, respectively, opening of the C–O bonds in the β-position[33e–h] of the cyclopropane core in (−)-**6** and (+)-**6** (β-opening) would give (−)-**8** and (+)-**8**, respectively. Taking into account that the Lewis acid, for example, boron trifluoride, activates one epoxide moiety in such a way that it will be attacked in a nucleophilic fashion by the appropriately oriented neighboring oxirane oxygen atom, the carbon atom in the α-position of the skeletal cyclopropyl group ought to be more prone to be attacked, as cyclopropyl substituents are well known to stabilize an adjacent positive charge efficiently.[34] If this concept was correct, the rearrangement should be stereospecific and produce (−)-**8** only from (+)-**6** as well as (+)-**8** from (−)-**6**, respectively. In fact, the enantiomerically pure (+)-**6** isomerized without racemization to give exclusively (−)-**8**, and (−)-**6** produced only (+)-**8** (a very small fraction of an unidentified impurity with $t_R =$ 40 min was detected in both cases). Thus, according to the assignment of the absolute configuration based on computations and on anomalous diffraction, (−)-**8** was formed exclusively from (+)-**6** and (+)-**8** from (−)-**6**. This can only occur with ring opening of the three C–O bonds in the epoxide moieties in the α-position to the skeletal three-membered carbocycle (Scheme 4).



Scheme 4. Stereochemical aspects of the rearrangement of enantiomeric bullvalene trisepoxides **6** to the hexacyclic cage trisethers **8**.

Experimental Section

General aspects: Starting materials: bullvalene (tricyclo[3.3.2.0^{2,8}]deca-3,6,9-triene) (**1**)[35] and a solution of dimethyldioxirane[14a] were prepared according to previously published procedures. All operations in anhydrous solvents were performed under an argon atmosphere in flame-dried glassware. Dichloromethane was dried by distillation from P_4O_{10}. All other chemicals were used as commercially available. Organic extracts were dried over Na_2SO_4. IR spectra were recorded on a Bruker IFS 66 (FT-IR) spectrophotometer as KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 250 (250 MHz for ^{1}H and 62.9 MHz for ^{13}C NMR) instrument in $CDCl_3$. Multiplicities were determined by DEPT (distortionless enhancement by polarization transfer), chemical shifts refer to $\delta_{TMS} = 0.00$ according to the chemical shifts of residual $CHCl_3$ signals. Mass spectra (EI, 70 eV) were measured with a Finnigan MAT 95 spectrometer. Chiral HPLC analyses were performed on a JASCO PU-986 chromatograph equipped with both a refractive index (JASCO RI-2031) and a polarimetric (JASCO OR-990) detector, using a 25 × 0.46 cm column with Chiralcel OD, hexane/2-propanol (90:10 *v*/*v*), 0.5 mL min^{-1}; preparative separations of enantiomers were performed on the same instrument using a 25 × 2.0 cm column with Chiralcel OD, hexane/2-propanol, 9.0 mL min^{-1}. Optical rotations were measured on a JASCO P-1030 digital polarimeter in a 2 cm cell. Melting points were de-

termined on a Büchi 510 capillary melting point apparatus, values are uncorrected.

4,8,12-Trioxahexacyclo[4.4.3.0^{3,5}0^{7,9}0^{2,10}0^{11,13}]tridecane (bullvalene trisepoxide, *rac*-6): a) To a vigorously stirred solution of bullvalene (**1**)[35] (1.20 g, 9.22 mmol) in a mixture of acetone (35 mL) and dichloromethane (20 mL) was added a neutralized solution of Oxone [prepared from $2KHSO_5{\cdot}KHSO_4{\cdot}K_2SO_4$ (Oxone, 28.29 g, 92.0 mmol SO_5^{2-}), $NaHCO_3$ (11.59 g, 138.0 mmol) in H_2O (150 mL)][36] at 0 °C over a period of 10 min. After stirring at ambient temp. for an additional 3 h, the reaction mixture was diluted with water (80 mL) and extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried and concentrated under reduced pressure (20 Torr) at 30 °C to give essentially pure bullvalene trisepoxide *rac*-**6** (1.53 g, 93 %). An analytical sample was obtained by recrystallization from hexane/CH_2Cl_2 and had m.p. 237 °C (decomp.). ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.49 (q, J = 6.8 Hz, 1H; CH), 3.39–3.35 (m, 3H; 3OCH), 3.04 (dd, J = 4.8, 6.8 Hz, 3H; 3OCH), 1.74 ppm (p, J = 2.0 Hz, 3H; *c*Pr-H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 53.5 (3CH), 51.0 (3CH), 30.7 (CH), 18.9 ppm (3CH); MS (EI): *m*/*z* (%): 178 (18) $[M]^+$, 169 (16), 131 (25), 121 (26), 103 (96), 91 (60), 81 (100), 77 (64); HRMS: *m*/*z*: calcd for $C_{10}H_{10}O_3$: 178.0629; found: 178.0629. The structure of *rac*-**6** was also confirmed by X-ray crystal structure analysis. HPLC analysis proved it to be a 1:1 mixture of two enantiomers with t_R = 45 and 60 min, respectively, and they were separated by preparative HPLC. The firstly eluted enantiomer had m.p. 245–246 °C (decomp.), $[\alpha]_D^{25}$ = +160 and $[\alpha]_{365}^{25}$ = +567 (c = 0.946, $CHCl_3$); the second one had m.p. 244–245 °C (decomp.), $[\alpha]_D^{25}$ = −157 and $[\alpha]_{365}^{25}$ = −554 (c = 0.986, $CHCl_3$). The structures of (+)-(3*S*,5*R*,7*R*,9*S*,11*S*,13*R*)- and (−)-(3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)-4,8,12-trioxahexacyclo-[4.4.3.0^{3,5}0^{7,9}0^{2,10}0^{11,13}]tridecanes [(+)-**6** and (−)-**6**] as well as the absolute configuration of (−)-**6** were also proved by an X-ray crystal structure analysis applying $Cu_{K\alpha}$ radiation in the latter case.

b) To a vigorously stirred solution of dimethyldioxirane (ca. 6 mmol, 60 mL of a ca. 0.1 M solution in acetone) was added in one portion bullvalene **1** (156 mg, 1.2 mmol) at −78 °C. The reaction mixture was allowed to warm up to ambient temperature over a period of 0.5 h, stirred at this temperature for an additional 1 h, and concentrated under reduced pressure. The residue was taken up with dichloromethane (40 mL), the solution was dried and concentrated again to give essentially pure bullvalene trisepoxide *rac*-**6** (203 mg, 95 %).

2,8,12-Trioxahexacyclo[8.3.0.0^{3,9}0^{4,6}0^{5,13}0^{7,11}]tridecane (*rac*-8): a) To a stirred solution of bullvalene trisepoxide (*rac*-**6**) (150 mg, 0.84 mmol) in anhydrous dichloromethane (5 mL) were added at −78 °C under argon two drops of boron trifluoride etherate. After stirring at this temperature for an additional 15 min, the still cold mixture was poured into a vigorously stirred aqueous saturated $NaHCO_3$ solution (20 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL), the combined organic extracts were dried and concentrated under reduced pressure to give *rac*-**8** (147 mg, 98 %) as a colorless powder in essentially pure form. An analytical sample was obtained by recrystallization from CH_2Cl_2/hexane. M.p. 298–299 °C (decomp.); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.54–4.44 (m, 6H; 6OCH), 3.08 (q, J = 7.3 Hz, 1H; CH), 1.69 ppm (p, J = 1.9 Hz, 3H; *c*Pr-H); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 77.4 (3CH), 67.3 (3CH), 47.5 (CH), 13.1 ppm (3CH); IR (KBr): $\tilde{\nu}$ = 3055, 2995, 2973, 1358, 1095, 1060, 1024, 937, 859, 840 cm^{-1}; MS (EI): *m*/*z* (%): 178 (92) $[M]^+$, 149 (50), 131 (28), 121 (25), 103 (18), 91 (22), 81 (100), 77 (24); HRMS: calcd for $C_{10}H_{10}O_3$: 178.0629; found: 178.0629. HPLC analysis proved it to be a 1:1 mixture of two enantiomers with t_R = 27 and 32 min, respectively, and they were separated by preparative HPLC. The firstly eluted enantiomer (1*S*,3*S*,7*S*,9*S*,11*S*,13*S*)-**8** had m.p. 287–289 °C (decomp.), $[\alpha]_D^{25}$ = +49 and $[\alpha]_{365}^{25}$ = +170 (c = 1.01, $CHCl_3$); the second one (1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-**8** had m.p. 285–287 °C (decomp.), $[\alpha]_D^{25}$ = −46 and $[\alpha]_{365}^{25}$ = −160 (c = 1.02, $CHCl_3$). Isomerization of the enantiomerically pure (+)-**6** proceeded without racemization to give exclusively (−)-**8**, and (−)-**6** produced only (+)-**8** (a very minor unidentified impurity with t_R = 40 min was detected in both cases). The structures of *rac*- and (−)-(1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-2,8,12-trioxahexacyclo[8.3.0.0^{3,9}0^{4,6}0^{5,13}0^{7,11}]tridecanes [rac-**8** and (−)-(1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-**8**] as well as the absolute configuration of (−)-**8** were also proved by an X-ray crystal structure analysis applying $Cu_{K\alpha}$ radiation in the latter case.

b) A solution of *rac*-**6** (499 mg, 2.8 mmol) in CH_2Cl_2 (40 mL) was vigorously stirred with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure to give 489 mg (98 %) of *rac*-**8**.

Computational studies: Geometries were optimized by using density functional theory (DFT) employing Becke's three-parameter functional with the Lee-Yang-Parr correlation functional (B3LYP)[27–30] utilizing the 6-31+G(d) basis set[30,37] as implemented in Gaussian 98.[26] All optimized structures were characterized as minima by computing analytical second energy derivatives.[38]

The root mean square (RMS) deviation of the computed geometries from the experimental ones for the C–C and C–O bond lengths were 0.009(0) and 0.008(5) Å for (−)-**6** and (−)-**8**, respectively. The maximum deviations were 0.010(4) and 0.012(0) Å, respectively. Hence, the computed and experimentally determined geometries are in good agreement. The optical rotations were computed via the sum-over-states method from the circular dichroism data:

$$\beta = \frac{c}{3\pi h}\,\mathrm{Im}\sum_{n\neq 0}\frac{\langle 0|\mu|n\rangle\langle n|\mathbf{m}|0\rangle}{\omega_{n_0}^2-\omega^2}$$

where μ and **m** are the electric dipole and magnetic dipole operators, respectively; the summation runs over all excitations and β is the trace of the frequency-dependent electric–dipole magnetic–dipole polarizability tensor.[39]

Only the single excitations of the valence electrons were computed at the time-dependent (TD) DFT level of theory by using the B3LYP functional at the respective optimized geometries with the 6-31+G(d,p) basis set[30,37] as implemented in Gaussian 03. The ORs thus obtained apply to the gas phase while the experimental ORs are measured in solution. In general computations of the gas-phase overshoot the solvated values[40] due to interactions with the solvent, sometimes considerably so. Currently the solvent cannot be taken into account explicitly, but for non-interacting or weakly interacting solvents (i.e., van der Waals and small dipole interactions only) the gas phase computations are a decent approximation.

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[16] Crystals suitable for X-ray structure analysis were obtained by slow evaporation of their solution in heptane/THF [*rac*-**6**, (+)-(3*S*,5*R*,7*R*,9*S*,11*S*,13*R*)-**6**, and (−)-(3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)-**6**], hexane/Et_2O/CH_2Cl_2 (*rac*-**8**) or hexane/Et_2O [(−)-(1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-**8**]. The X-ray data were collected on a Bruker SMART CCD 6000 diffractometer at 120.0 K [*rac*-**6**, (+)-**6** and *rac*-**8**, $Mo_{K\alpha}$ (λ = 0.71073 Å), graphite monochromator, ω scan, 0.3°/frame, equipped with an Oxford Cryostream LT-device] or at 100.0 K [(−)-**6** and (−)-**8**, $Cu_{K\alpha}$ (λ = 1.54178 Å), ϕ and ω scan, 0.5°/frame]. Structures were solved by direct methods and refined by full-matrix least squares on F^2 for all data. Non-hydrogen atoms (except the disordered ones) were refined with anisotropic displacement parameters, H atoms in the molecule of *rac*-**6**, (−)-**6** and (−)-**8** were placed in calculated positions and refined using a "riding model", H atoms in the molecule of *rac*-**8** were located in the difference Fourier map and refined isotropically. Disordered atoms were refined with equal site occupation factors of 0.5. Attempts to refine the structure of *rac*-**6** in space groups of lower symmetry (even as triclinic) still led to the disordered model, and so did the refinement of the data collected at lower temperature (see above). *rac*-**6** ($C_{10}H_{10}O_3$, M = 178.18, crystal size 0.44 × 0.07 × 0.07 mm^3) crystallized in the orthorhombic space group *P*nma, a = 13.2410(8), b = 9.3870(6), c = 6.3534(4) Å, $\alpha = \beta = \gamma = 90°$, V = 789.68(9) Å^3, Z = 4, ρ = 1.499 mg mm^{-3}, μ = 0.111 mm^{-1}. At 120.0(2) K 7077 intensities were measured: ($\theta_{max} = 29.00°$, 1106 independent reflections, R_{int} = 0.0771). Final R_1 = 0.0848 for 87 refined parameters and 1106 reflections with $I \geq 2\sigma(I)$, wR_2 (all data) = 0.2219, GOF = 1.085, maximum and minimum residual electron density 0.420 and −0.501 e Å^{-3}. (+)-**6** ($C_{10}H_{10}O_3$, M = 178.18, crystal size 0.41 × 0.35 × 0.24 mm^3) crystallized in the orthorhombic space group $P2_12_12_1$, a = 6.3592(5), b = 9.2747(8), c = 13.216(1) Å, $\alpha = \beta = \gamma = 90°$, V = 779.5(1) Å^3, Z = 4, ρ = 1.518 mg mm^{-3}, μ = 0.112 mm^{-1}. At 120.0(2) K 9088 intensities were measured: (θ_{max} = 28.99°, 2058 independent reflections, R_{int} = 0.0293). Final R_1 = 0.0279 for 158 refined parameters and 2058 reflections with $I \geq 2\sigma(I)$, wR_2 (all data) = 0.0797, GOF = 1.179, maximum and minimum residual electron density 0.218 and −0.201 e Å^{-3}. (−)-**6** ($C_{10}H_{10}O_3$, M = 178.18, crystal size 0.20 × 0.10 × 0.10 mm^3) crystallized in the orthorhombic space group $P2_12_12_1$, a = 6.336(2), b = 9.250(2), c = 13.171(2) Å, $\alpha = \beta = \gamma = 90°$, V = 771.9(3) Å^3, Z = 4, ρ = 1.533 mg mm^{-3}, μ = 0.942 mm^{-1}. At 100.0(2) K 14311 intensities were measured: (θ_{max} = 58.95°, 1100 independent reflections, R_{int} = 0.0303). Final R_1 = 0.0226 for 119 refined parameters and 1100 reflections with $I \geq 2\sigma(I)$, wR_2 (all data) = 0.0572, GOF = 1.103, maximum and minimum residual electron density 0.116 and −0.152 e Å^{-3}, absolute structure parameter 0.01(19). A refinement of the inverted structure of (−)-**6** gave the following data: R_1 ($I \geq 2\sigma(I)$) = 0.0230, wR_2 (all data) = 0.0578, GOF = 1.106, absolute structure parameter = 1.0(2), maximum and minimum residual electron density 0.116 and −0.152 e Å^{-3}. *rac*-**8** ($C_{10}H_{10}O_3$, M = 178.18, crystal size 0.35 × 0.28 × 0.22 mm^3) crystallized in the triclinic space group $P\bar{1}$, a = 6.3954(2), b = 6.7956(2), c = 9.6558(2) Å, α = 80.57(1), β = 80.51(1), γ = 63.61(1)°, V = 368.80(2) Å^3, Z = 2, ρ = 1.605 mg mm^{-3}, μ = 0.119 mm^{-1}. At 120.0(2) K 3782 intensities were measured: (θ_{max} = 28.99°, 1929 independent reflections, R_{int} = 0.0506). Final R_1 = 0.0395 for 158 refined parameters and 1929 reflections with $I \geq 2\sigma(I)$, wR_2 (all data) = 0.1127, GOF = 1.017, maximum and minimum residual electron density 0.479 and −0.211 e Å^{-3}. (−)-**8** ($C_{10}H_{10}O_3$, M = 178.18, crystal size 0.22 × 0.15 × 0.08 mm^3) crystallized in the orthorhombic space group $P2_12_12_1$, a = 6.744(2), b = 10.414(2), c = 32.347(2) Å, $\alpha = \beta = \gamma = 90°$, V = 2271.8(8) Å^3, Z = 12, ρ = 1.563 mg mm^{-3}, μ = 0.960 mm^{-1}. At 100(2) K 37570 intensities were measured: (θ_{max} = 58.88°, 3242 independent reflections, R_{int} = 0.0325). Final R_1 = 0.0247 for 353 refined parameters and 3242 reflections with $I \geq 2\sigma(I)$, wR_2 (all data) = 0.0615, GOF = 1.103, maximum and minimum residual electron density 0.130 and −0.148 e Å^{-3}, absolute structure parameter 0.01(14). A refinement of the inverted structure of (−)-**8** gave the following data: R_1 ($I \geq 2\sigma(I)$) = 0.0250, wR_2 (all data) = 0.0620, GOF = 1.113, absolute structure parameter = 0.98(14), maximum and minimum residual electron density 0.130 and −0.148 e Å^{-3}. CCDC-252650 (*rac*-**6**), -252651 [(+)-**6**], -252113 [(−)-**6**], -252652 (*rac*-**8**) and -252114 [(−)-**8**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

[17] According to the systematic stereochemical nomenclature, these two enantiomers of bullvalene trisepoxide **6** have to be designated (3*R*,5*S*,7*S*,9*R*,11*R*,13*S*)- and (3*S*,5*R*,7*R*,9*S*,11*S*,13*R*)-4,8,12-trioxahexacyclo[4.4.3.$0^{3,5}0^{7,9}0^{2,10}0^{11,13}$]tridecane. The systematic names of enantiomers of **8** are (1*S*,3*S*,7*S*,9*S*,11*S*,13*S*)- and (1*R*,3*R*,7*R*,9*R*,11*R*,13*R*)-2,8,12-trioxahexacyclo[8.3.0.$0^{3,9}0^{4,6}0^{5,13}0^{7,11}$]tridecane. For simplicity, these C_3-symmetrical propeller-shaped helical molecules might also be called (*P*) and (*M*) enantiomers applying the stereochemical descriptors for helicenes [see a) K. P. Meurer, F. Vögtle, *Top. Curr. Chem.* **1985**, *127*, 1–76]. In these cases an additional convention has

to be applied in that the molecules would, for example, be viewed along the axis pointing from the center of the cyclopropane ring towards the opposite bridgehead carbon atom. However, due to this arbitrary choice of directionality, the compounds designated as (*P*)-**6** and (*M*)-**6** would have negative and positive signs of specific rotations, which are opposite to those for (*P*)- and (*M*)-π- and σ-helicenes, compare b) V. Buss, K. Kolster, *Chem. Phys.* **1996**, *203*, 309–316; c) A. Ferrarini, G. Gottarelli, P. L. Nordio, G. P. Spada, *J. Chem. Soc. Perkin Trans. 2* **1999**, 411–417; d) A. de Meijere, A. F. Khlebnikov, R. R. Kostikov, S. I. Kozhushkov, P. R. Schreiner, A. Wittkopp, D. S. Yufit, *Angew. Chem.* **1999**, *111*, 3682–3685; *Angew. Chem. Int. Ed.* **1999**, *38*, 3474–3477; e) A. de Meijere, A. F. Khlebnikov, S. I. Kozhushkov, R. R. Kostikov, P. R. Schreiner, A. Wittkopp, C. Rinderspacher, D. S. Yufit, J. A. K. Howard, *Chem. Eur. J.* **2002**, *8*, 828–842; f) A. de Meijere, A. F. Khlebnikov, S. I. Kozhushkov, K. Miyazawa, D. Frank, P. R. Schreiner, C. Rinderspacher, D. S. Yufit, J. A. K. Howard, *Angew. Chem.* **2004**, *116*, 6715–6719; *Angew. Chem. Int. Ed.* **2004**, *43*, 6553–6557.

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