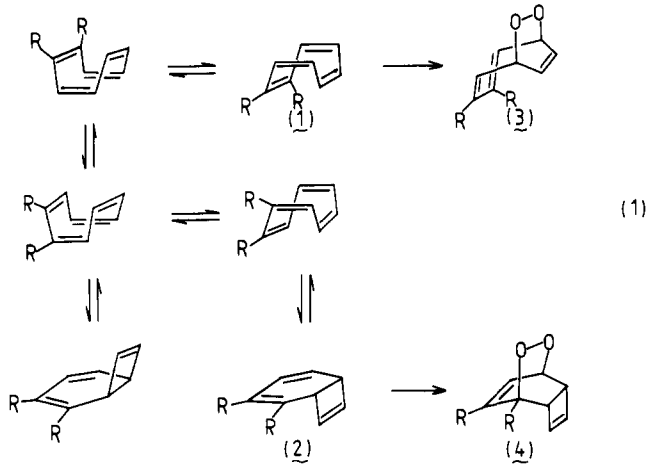
Synthesis of the Endoperoxide *anti*-7,8-Dioxatricyclo[4.2.2.$0^{2,5}$]deca-3,9-diene via Singlet Oxygenation of the Bicyclic Valence Tautomer of Cyclooctatetraene and Its Transformations

Waldemar Adam,*[1a,b] Omar Cueto,[1b] Ottorino De Lucchi,[1b] Karl Peters,[1c] Eva-Maria Peters,[1c] and Hans Georg von Schnering[1c]

Contribution from the Department of Chemistry, University of Puerto Rico, Rio Piedras, Puerto Rico 00931, the Institute of Organic Chemistry, University of Würzburg, Am Hubland, D-8700 Würzburg, West Germany, and the Max-Planck-Institut für Festkörperforschung, D-7000 Stuttgart 80, West Germany. *Received February 17, 1981*

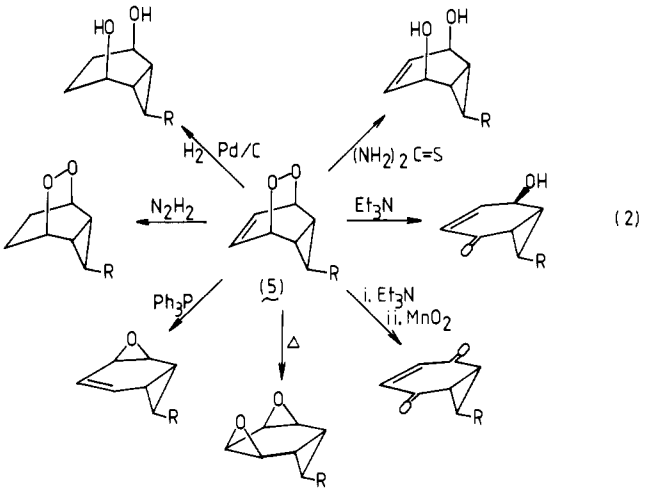
Abstract: The endoperoxide (**4**) of the bicyclic valence isomer of cyclooctatetraene (**2**) is transfromed into a variety of synthetically valuable oxygen-functionalized derivatives. Thus, diimide reduction affords the bicyclic peroxide (**8**), catalytic hydrogenation over Pd/C yields the saturated cis diol (**11**), and thiourea reduction yields the unsaturated cis diol (**12**). Triethylamine-catalyzed isomerization gives the ketol (**13**), which on manganese dioxide oxidation leads to the dione (**14**). Epoxidation of the endoperoxide (**4**) with *m*-CPBA affords the epoxy endoperoxide (**15**), which on thermolysis is converted to the anti,anti,anti triepoxide (**20a**). Triphenylphosphine deoxygenations of **4** and **15** produce respectively epoxides **16** and **17**. On thermolysis **4** is transformed into the diepoxide (**18**). Epoxidation of **18** leads unexpectedly to the anti,anti,syn triepoxide (**20b**), while epoxidation of **17** gives the syn,anti,anti triepoxide (**20c**). X-ray analysis confirms the stereochemical assignments of the isomeric triepoxides (**20a–c**).

Cyclooctatetraene (**1**) has been in the past a favored substrate for cycloaddition reactions.[2] In view of its ability to undergo bicyclization into its valence isomer (**2**) and undergo simultaneously ring inversion, and bond isomerization, a great diversity of products are possible with dienophiles (eq 1). With singlet oxygen



(1)

as reagent, the endoperoxides (**3** and **4**), respectively derived from the monocyclic (**1**) and bicyclic (**2**) valence isomers of cyclooctatetraene (COT), are of particular synthetic interest since they constitute potentially valuable intermediates in the preparation of oxygen-functionalized molecules. For example, recently we showed[3] that the norcaradiene endoperoxides (**5**), obtained in the singlet oxygenation of 7-substituted cycloheptatrienes, provided a convenient synthetic entry into a variety of complex molecules which would have been difficult to prepare by classical preparative methods (eq 2).



(2)

It was, therefore, our interest to apply the synthetic manipulations that are illustrated in eq 2 to the endoperoxides (**3**) and especially **4** in order to provide a supply of valuable oxygen-functionalized COT derivatives. Unfortunately, COT is inert toward dyestuff-sensitized photooxidation.[4] Presumably COT is an efficient quencher of the intermediary triplet state excited dyestuff, so that no singlet oxygen ($^1O_2$) is formed under these conditions. However, even when $^1O_2$ was chemically generated by thermolysis of the anthracene endoperoxide (**6**), an intermediate temperature chemical source of $^1O_2$,[5] no singlet oxygenation of COT was observed indicating that COT is indeed inert toward $^1O_2$.[6] At the elevated temperatures (ca. 120 °C) required for the smooth deoxygenation of **6**, it was argued that an appreciable amount of the bicyclic valence isomer (**2**) should have accumulated,[7] so that some bicyclic endoperoxide (**4**) should have formed (eq 3). Although the planar dienic moiety of **2** should react with $^1O_2$ much faster than with the twisted diene system of **1**, apparently

(1) (a) NIH Career Awardee (1975–1980). Direct correspondence to the Würzburg address. (b) University of Puerto Rico and University of Würzburg. (c) Max-Planck-Institut für Festkörperforschung.

(2) Paquette, L. A. *Tetrahedron* **1975**, *31*, 2855.

(3) (a) Adam, W.; Balci, M. *J. Am. Chem. Soc.* **1979**, *101*, 7537. (b) Adam, W.; Balci, M. *Ibid.* **1979**, *101*, 7542. (c) Adam, W.; Balci, M.; Rivera, J. *Synthesis* **1979**, 807. (d) Adam, W.; Balci, M. *J. Am. Chem. Soc.* **1980**, *102*, 1961. (e) Adam, W.; Balci, M.; Pietrzak, B.; Rebollo, H. *Synthesis* **1980**, 820. (f) Adam, W.; Balci, M.; Pietrzak, B. *J. Am. Chem. Soc.* **1979**, *101*, 6285.

(4) Gollnick, K. *Adv. Photochem.* **1968**, *6*, 1.

(5) Turro, N. J.; Chow, M.-F.; Rigaudy, J. *J. Am. Chem. Soc.* **1979**, *101*, 1300.

(6) Adam, W.; Cueto, O.; De Lucchi, O.; Hill, K.-H., unpublished results.

(7) At 100 °C, the equilibrium concentration of the valence tautomer of COT is 0.01%. CF.: Huisgen, R.; Mietzsch, F.; Boche, F.; Seidl, H. *J. Chem. Soc., Spec. Publ.* **1965**, *19*, 3.

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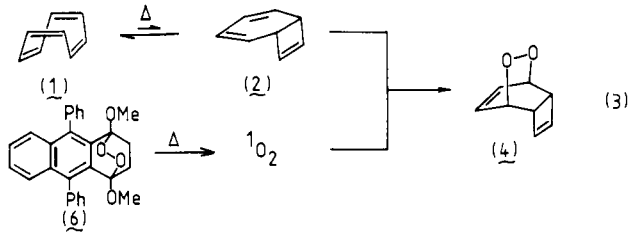
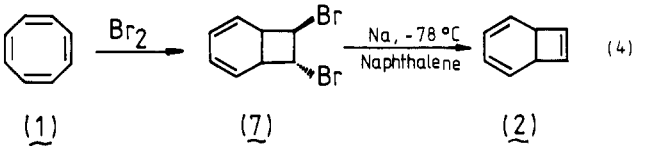


(3)

at the temperatures employed the equilibrium concentration of the bicyclic valence isomer (**2**) was insufficient or singlet oxygen was efficiently deactivated at these temperatures. Clearly, the direct introduction of oxygen functionalities into COT via singlet oxygenation appears to be problematic, unless electron-rich COT derivatives are used.

Fortunately, the bicyclic valence isomer (**2**) can be prepared via the sequence shown in eq 4 and is sufficiently stable at sub-



(4)

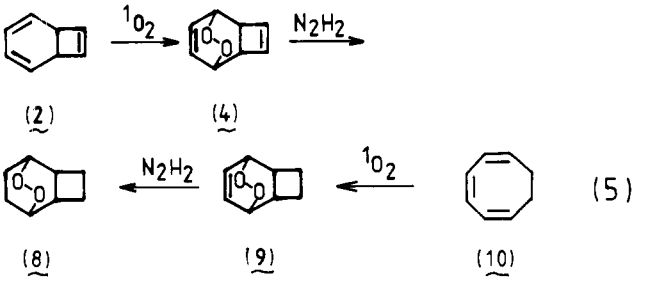
ambient temperatures for synthetic manipulation.[8] Consequently, it was of interest to prepare authentic **2** and explore its reactivity with $^1O_2$. Indeed, should the endoperoxide (**4**) be obtained via this indirect route, the analogous transformations as shown in eq 2 for the norcaradiene endoperoxide (**5**) were to be performed. The preliminary results have already been communicated;[9] however, a recent publication[10] obliges us to report the full experimental details of this investigation.

Results and Discussion

Synthesis and Characterization of Endoperoxide 4. The dibromide (**7**) was prepared according to the literature procedures[11] and debrominated with *n*-BuLi at −78 °C, affording the bicyclic valence tautomer (**2**) in high yields (>90% by NMR). Below −20 °C **2** was sufficiently stable for preparative work. In view of the facile tautomerization into COT, no attempts were made to purify **2**.

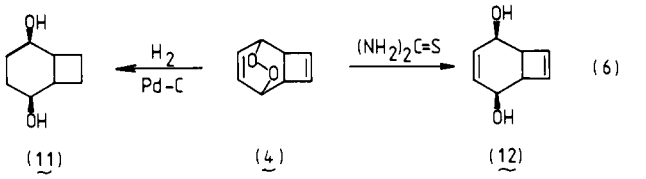
On singlet oxygenation, using a sodium street lamp as the light source and tetraphenylporphyrin as the sensitizer, the endoperoxide (**4**) was obtained in 85% yield, after recrystallization from CH_2Cl_2/*n*-hexane. Elemental analysis and the spectral data (cf. Experimental Section) speak for the proposed bicyclic endoperoxide structure.

Definitive structure proof of **4** derives from the following chemical transformation. On diimide reduction[12] the saturated bicyclic peroxide (**8**) was obtained in 80% yield, mp 123 °C (from hexane). It was not possible to control the selectivity of the diimide reaction to effect the reduction of the more strained cyclobutene double bond by administering stoichiometric amounts of N_2H_2. The cyclohexene double bond was reduced concurrently, leading to a mixture of products that could not be readily separated by MPLC (medium pressure) nor HPLC (high pressure). This reduction product was identical with that prepared via singlet oxygenation of cyclooctatriene (**10**), followed by N_2H_2 reduction (eq 5).[13] From these results it is evident, as expected, that the bicyclic valence tautomer of COT (**2**) readily reacts with $^1O_2$ to produce the endoperoxide (**4**).



(5)

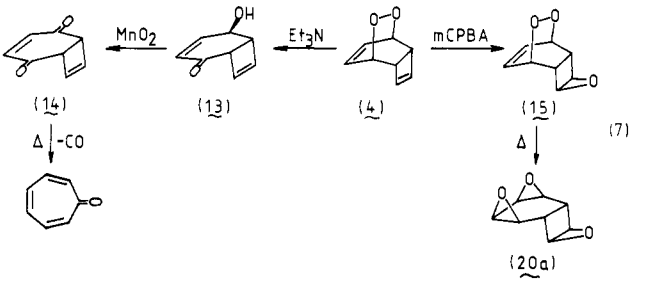
Catalytic and Thiourea Reductions. On catalytic reduction (Pd/C in EtOH) the cis diol (**11**) was obtained in 40% yield. Elemental composition and spectral data (cf. Experimental Section) confirm the 1,4-diol structure (eq 6). The cis stereochemical arrangement is inferred in view of the fixed geometry given in the endoperoxide (**4**).



(6)

Thiourea reduction of **4** affords the unsaturated cis diol (**12**), cf. eq 6, in 65% yield. Although **12** is a labile diol, it could be purified by silica gel column chromatography. Elemental composition and the spectral data (cf. Experimental Section) substantiate the proposed structure, but the cis assignment of the hydroxy substituents is again inferred from the fixed geometry of the endoperoxide (**4**). No further synthetic manipulation of the diols (**11** and **12**) was attempted. It is significant to mention that the unsaturated diol (**12**) can be prepared directly by singlet oxygenation of **2** in the presence of thiourea.[14]

Oxidations. The De La Mare–Kornblum reaction[15] of **4** gave the hydroxy ketone (**13**) in 95% yield, using triethylamine as base (eq 7). Frequently such hydroxy ketones as **13** are base sensitive



(7)

and difficult to handle,[16] but in this particular case **13** could be rigorously purified by silica gel chromatography even at room temperature. Elemental composition and spectral data (cf. Experimental Section) back up the proposed structure.

On oxidation with freshly prepared manganese dioxide, **13** was converted in 90% yield to the known dione (**14**). The latter was prepared by Kitahara et al.[17a] via a more cumbersome route. As observed by these workers, on vacuum flash pyrolysis (VFP) the dione (**14**) decarbonylates into tropone. Presumably **14** first tautomerizes into 1,4-dioxocyclooctatriene, but the latter extrudes CO even faster and does not accumulate.

With *m*-chloroperbenzoic acid (*m*-CPBA) the endoperoxide (**4**) is converted to the epoxyendoperoxide (**15**) in 70% yield (eq 7). Elemental composition and spectral data are consistent with the proposed structure. Although it was expected that the cyclobutene double bond has been epoxidized, i.e., double resonance experiments confirmed that the bridgehead protons were coupled to the cyclohexene olefinic protons, it was not possible to assess

(8) Vogel, E.; Kiefer, H.; Roth, W. R. *Angew. Chem.* **1964**, *76*, 432; *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 442.
(9) Adam, W.; Cueto, O.; De Lucchi, O. *J. Org. Chem.* **1980**, *45*, 5220.
(10) Prinzbach, H.; Maas, M.; Fritz, H.; McMullen, G. *Tetrahedron Lett.* **1980**, 4897.
(11) (a) Huisgen, R.; Boche, G. *Tetrahedron Lett.* **1965**, 1769. (b) Cope, A. C.; Burg, M. *J. Am. Chem. Soc.* **1952**, *74*, 168.
(12) Adam, W.; Eggelte, H. J. *J. Org. Chem.* **1977**, *42*, 3987.
(13) Adam, W.; Erden, I. *Tetrahedron Lett.* **1979**, 2781. Unfortunately the physical constants and spectral data reported for the bicyclic peroxide (**8**) are in error. Cf.: Adam, W.; Erden, I. *Tetrahedron Lett.*, **1980**, 3836.
(14) Kaneko, C.; Suyimoto, A.; Tanaka, S. *Synthesis*, **1974**, 876.
(15) Kornblum, N.; De La Mare, H. E. *J. Am. Chem. Soc.* **1951**, *73*, 880.
(16) Adam, W.; Bakker, B. *Tetrahedron Lett.* **1979**, 4171.
(17) (a) Oda, M.; Kayama, Y.; Kitahara, Y. *Tetrahedron Lett.* **1974**, 2019. (b) Kayama, Y.; Oda, M.; Kitahara, Y. *Ibid.* **1974**, 3293.

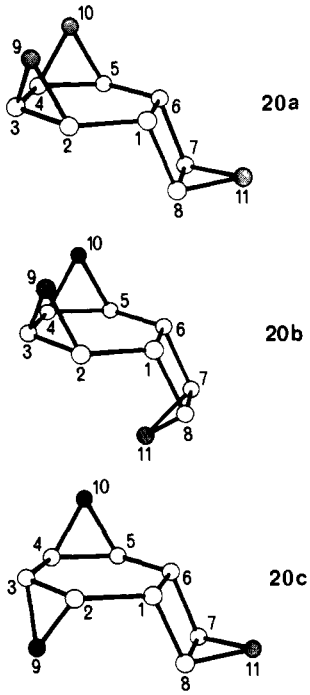
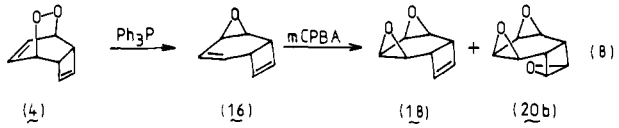
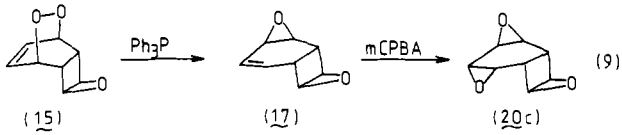


Figure 1. Perspective drawings of the molecules **20a**, **20b**, and **20c** with the labelings of atoms corresponding to Tables II and III.

from the ^{1}H NMR data whether the stereochemical course of the epoxidation was syn or anti. However, as will become clear in the discussion of the stereochemistry of the triepoxides (**20a–c**), **15** has the anti configuration. This would be the expected stereochemical course on the basis of steric arguments. As Dreiding models show, the exo face of the cyclobutene double bond is considerably more accessible than the endo face. In this context it is of interest to mention that the cyclohexene double bond is inert toward epoxidation, even if long reaction times, large excess of peracid, and elevated temperatures are used. Exhaustive epoxidation of epoxydiene (**16**), which was obtained from the endoperoxide (**14**) by triphenylphosphine deoxygenation (eq 8), with

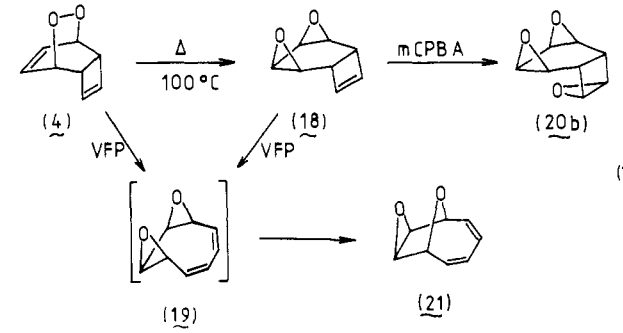


m-CPBA gave the anti,anti,syn triepoxide (**20b**) in 15% yield, together with the diepoxide (**18**) in 80% yield (by H NMR). An X-ray structure determination confirms the proposed stereochemical assignment of these triepoxide isomers (cf. Figure 1). More conveniently, the diepoxide (**17**), which was prepared by triphenylphosphine deoxygenation (eq 9) of the epoxyendoperoxide (**15**), gave on *m*-CPBA epoxidation only the syn,anti,anti triepoxide isomer (**20c**).



Unexpected, however, was the epoxidation of the diepoxide (**18**), which was obtained in the thermolysis (eq 10) of endoperoxide (**4**). The anti,anti,syn triepoxide (**20b**) was obtained in 70% yield. Again an X-ray analysis was necessary to assign unequivocally the stereochemistry of the triepoxide isomer (**20b**) (cf. Figure 1). On the basis of Dreiding models, like in the epoxidation **4** → **15**, steric arguments should favor also exo attack by the peracid in the transformation **18** → **20b**. Presumably deepseated stereoelectronic reasons are responsible for this unusual stereoselectivity.

Triphenylphosphine Deoxygenation. The reaction of **4** with triphenylphosphine proceeded smoothly, leading to the epoxydiene

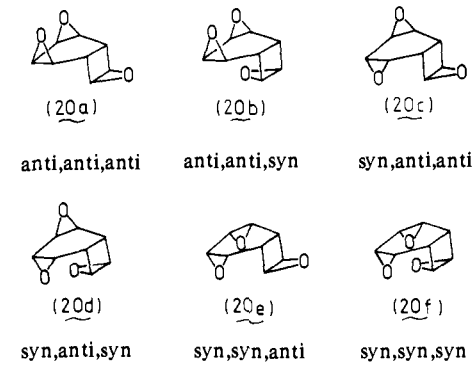


16 (eq 8) in 70% yield. Purification of **16** was difficult, but on silica gel chromatography at −15 °C, eluting with CH_2Cl_2, pure **16** could be obtained. Elemental composition and spectral data confirm the proposed structure. Similarly, the epoxyendoperoxide (**15**) gave on triphenylphosphine reaction the diepoxide (**17**) in 50% yield (eq 9).

Thermolysis. On heating a benzene solution of endoperoxide (**4**) at 100 °C in a sealed tube for 1 h, the diepoxide (**18**) is formed in 80% isolated yield (eq 10). Under vacuum flash pyrolysis (VFP) conditions at ca. 500 °C and 4 torr **18** isomerizes quantitatively into the rearranged product (**21**), whose structure has recently been reported.[10] More directly VFP (500 °C, 10 torr) of endoperoxide **4** affords **21** as the major product. Presumably the intermediary syn diepoxide (**19**) of COT rearranges under the VFP conditions into **21**. Unfortunately this precludes the opportunity of preparing indirectly the syn diepoxide (**19**) of COT via the endoperoxide (**4**), especially since **19** cannot be made by direct epoxidation of COT.[18]

On reflux in benzene the epoxyendoperoxide (**15**) afforded (eq 7) the triepoxide (**20a**) in 60% isolated yield. Elemental analysis and the spectral data (cf. Experimental Section) confirm the structure assignment; however, the anti,anti,anti stereochemistry could only rigorously be assessed by X-ray analysis (Figure 1). Consequently, from the established stereochemistry of **20a** it is clear that the stereochemistry of epoxyendoperoxide (**15**) must also be anti. Thus, as pointed out already in the reaction **4** → **15**, the *m*-CPBA epoxidation takes place as expected from the more accessible exo face of the cyclobutene double bond.

In conclusion, of the six possible triepoxide isomers (**20a–f**)[19]



derived from the bicyclic valence isomer (**2**) of COT, it has been possible to prepare the first three (**20a–c**), starting from the endoperoxide (**4**) as common precursor. The synthetic strategy, quite akin to that employed in the synthesis of the isomeric triepoxides of cycloheptatriene,[3d] is summarized in Scheme I. For example, the anti,anti,anti triepoxide was achieved by the sequence **4** → **15** → **20a**, utilizing *m*-CPBA epoxidation and the thermal endoperoxide–diepoxide rearrangement[20] consecutively. The

(18) Anastassiou, A. G.; Reichmanis, E. *J. Org. Chem.* **1973**, *38*, 2421.
(19) In these stereochemical designations the first syn or anti refers to the configuration of the C_2–C_3 epoxide ring (cf. Fig. 1 for numbering) with respect to the cyclobutane ring and analogously the second syn or anti refers to the configuration of the C_4–C_5 epoxide. The third syn or anti refers to the configuration of the C_7–C_8 epoxide ring with respect to the cyclohexane ring.
(20) Adam, W.; Balci, M. *Tetrahedron*, **1980**, *36*, 833.

Table I. Special Dihedral Angles of 20a, 20b, and 20c[a]

	20a	20b	20c
TMR/FMR	71.8	71.2	72.1
FMR/SMR	64.9	60.7	62.8
2/3 TMR/SMR	76.8	75.4	77.3
4/5 TMR/SMR	73.9	74.4	75.4

[a] TMR = three-membered ring. FMR = four-membered ring. SMR = six-membered ring.

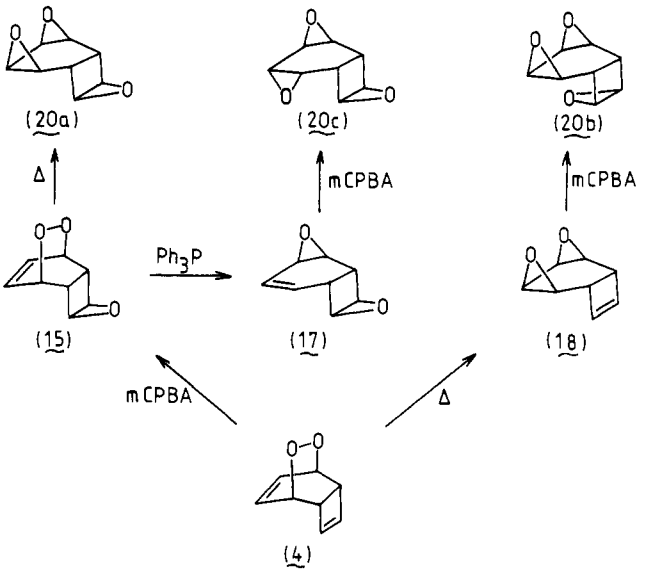
syn,anti,anti triepoxide could be obtained via the sequence **4** → **15** → **17** → **20c**, utilizing *m*-CPBA epoxidation, triphenylphosphine deoxygenation, and again *m*-CPBA epoxidation. Finally, the anti,anti,syn triepoxide was prepared via the sequence **4** → **18** → **20b**, engaging first the endoperoxide–diepoxide rearrangement[20] and subsequently *m*-CPBA epoxidation. Here the surprising result was the endo attack by the peracid on the diepoxide (**18**), an unusual epoxidation stereochemistry which required structure confirmation by X-ray analysis (Figure 1). The results of the X-ray structure determinations of the triepoxides (**20a–c**) are given in the next section.

Description of the X-ray Structures of 20a, 20b, and 20c

X-ray structure determinations of single crystals of the anti,anti,anti (**20a**), anti,anti,syn (**20b**), and syn,anti,anti (**20c**) triepoxide isomers have been completed. A perspective drawing of these three molecules is shown in Figure 1. Crystal parameters, bond lengths, and angles are given in Table II and III.

The mean C–C bond length of the three-membered rings is 146.3 pm and is nearly comparable with that of aromatic systems. The C–C distance common to the four- and six-menbered ring is extended to 157 pm. The mean C–C distance of the six-membered ring is 150 pm and that of the four-membered ring 152.5 pm.

Scheme I



In all molecules the four-membered ring has a planar geometry and is nearly a square. The mean bond angle at the C atoms common to the six-membered ring is 88° and that common to the three-membered ring 92°.

Dihedral angles between the rings of all molecules are given in Table I.

Experimental Section

Boiling points and melting points are uncorrected. Infrared spectra were taken on a Beckman Acculab 4 or on a Perkin-Elmer 157 G spec-

Table II. Positional (×10^4) and Thermal Parameters of the Atoms of 20a, 20b, and 20c[a]

atom	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
				20a					
C(1)	7580 (7)	1581 (2)	1230 (10)	43 (2)	32 (2)	30 (2)	−5 (2)	8 (2)	5 (2)
C(2)	9648 (7)	1431 (2)	570 (10)	34 (2)	34 (2)	37 (2)	−7 (2)	8 (2)	−4 (2)
C(3)	9946 (7)	896 (2)	−1045 (9)	33 (2)	35 (2)	29 (2)	2 (2)	9 (2)	3 (2)
C(4)	8154 (7)	498 (2)	−2202 (9)	46 (2)	24 (2)	35 (2)	2 (2)	13 (2)	3 (2)
C(5)	6048 (7)	631 (2)	−1790 (10)	44 (2)	23 (2)	43 (2)	−1 (2)	14 (2)	−2 (2)
C(6)	5663 (7)	1160 (2)	−80 (10)	35 (2)	28 (2)	38 (2)	4 (2)	16 (2)	3 (3)
C(7)	4603 (7)	1654 (2)	−2200 (10)	42 (3)	36 (2)	41 (2)	2 (2)	1 (2)	13 (2)
C(8)	6391 (8)	2044 (2)	−970 (10)	51 (3)	25 (2)	50 (3)	3 (2)	14 (2)	8 (2)
O(9)	777 (5)	945 (1)	2230 (7)	43 (2)	57 (2)	33 (2)	−2 (1)	2 (1)	12 (2)
O(10)	7366 (5)	195 (1)	82 (8)	61 (2)	27 (2)	68 (2)	12 (2)	34 (2)	6 (1)
O(11)	4388 (6)	2135 (1)	−249 (9)	63 (2)	42 (2)	64 (2)	−4 (2)	21 (2)	21 (2)
				20b					
C(1)	1973 (4)	1527 (7)	19 (5)	23 (2)	20 (2)	35 (2)	2 (2)	3 (2)	4 (2)
C(2)	3080 (4)	2830 (7)	−175 (5)	32 (2)	21 (2)	24 (2)	0 (2)	3 (2)	−3 (2)
C(3)	4446 (4)	2393 (7)	674 (5)	26 (2)	27 (2)	30 (2)	−8 (2)	10 (2)	−5 (2)
C(4)	4781 (4)	604 (7)	1708 (5)	26 (2)	26 (2)	27 (2)	−8 (2)	3 (2)	3 (2)
C(5)	3740 (5)	9241 (7)	1885 (4)	35 (2)	19 (2)	22 (2)	−1 (2)	3 (2)	2 (2)
C(6)	2327 (4)	9637 (7)	1078 (4)	27 (2)	22 (2)	25 (2)	1 (2)	10 (2)	−2 (2)
C(7)	1690 (4)	8144 (7)	−156 (5)	26 (2)	25 (2)	34 (2)	1 (2)	9 (2)	−4 (2)
C(8)	1355 (5)	9909 (8)	−1138 (5)	26 (2)	30 (2)	35 (2)	3 (2)	−5 (2)	−2 (2)
O(9)	3762 (3)	4186 (5)	990 (3)	40 (2)	18 (2)	36 (2)	−6 (1)	6 (1)	−2 (1)
O(10)	4375 (3)	815 (5)	2924 (3)	44 (2)	30 (2)	20 (2)	−6 (1)	3 (1)	0 (2)
O(11)	2387 (3)	8430 (6)	−1144 (3)	34 (2)	35 (2)	29 (2)	−7 (1)	10 (1)	−5 (2)
				20c					
C(1)	2824 (5)	2095 (4)	4488 (5)	43 (2)	35 (2)	28 (1)	−8 (1)	8 (1)	0 (1)
C(2)	4635 (5)	2710 (5)	4148 (5)	42 (2)	42 (2)	36 (2)	−10 (1)	7 (1)	−7 (1)
C(3)	4906 (5)	2762 (5)	2116 (6)	45 (2)	47 (2)	53 (2)	−15 (2)	22 (2)	−7 (2)
C(4)	3334 (5)	2273 (5)	219 (6)	57 (2)	45 (2)	44 (2)	−14 (2)	25 (2)	−9 (2)
C(5)	1543 (5)	1717 (4)	423 (5)	46 (2)	39 (2)	38 (2)	−16 (1)	14 (1)	−6 (1)
C(6)	1178 (5)	1563 (4)	2511 (5)	44 (2)	35 (2)	37 (2)	−14 (1)	15 (1)	−12 (1)
C(7)	−105 (5)	3180 (5)	2270 (6)	43 (2)	48 (2)	41 (2)	−10 (2)	19 (2)	−5 (2)
C(8)	1413 (5)	3667 (5)	4121 (6)	49 (2)	40 (2)	45 (2)	−17 (1)	22 (2)	−10 (1)
O(9)	4442 (4)	4452 (3)	2428 (4)	56 (2)	43 (1)	53 (1)	−13 (1)	21 (1)	−17 (1)
O(10)	2958 (4)	360 (3)	658 (4)	71 (2)	47 (1)	61 (2)	−25 (1)	30 (1)	−6 (1)
O(11)	−239 (4)	2833 (4)	4437 (4)	59 (2)	58 (2)	56 (2)	−16 (1)	36 (1)	−8 (1)

Table III. Bond Lengths (pm) and Angles (deg) for the Molecules 20a, 20b, and 20c

	20a	20b	20c
	Bond Lengths		
C(1)-C(2)	150.5 (7)	151.7 (7)	150.9 (5)
C(1)-C(6)	158.0 (6)	157.0 (6)	156.2 (4)
C(1)-C(8)	153.3 (6)	153.6 (6)	152.7 (5)
C(3)-C(2)	147.8 (6)	146.4 (6)	144.7 (6)
C(3)-C(4)	147.9 (6)	150.6 (6)	148.8 (5)
C(5)-C(4)	147.6 (7)	147.4 (7)	144.7 (6)
C(5)-C(6)	150.8 (6)	149.2 (6)	150.5 (6)
C(7)-C(6)	154.1 (6)	154.0 (7)	152.2 (5)
C(7)-C(8)	147.1 (6)	146.2 (7)	145.1 (5)
O(9)-C(2)	144.7 (5)	145.1 (6)	144.9 (4)
O(9)-C(3)	145.2 (5)	144.6 (6)	143.6 (5)
O(10)-C(4)	145.6 (5)	145.3 (6)	143.8 (4)
O(10)-C(5)	145.2 (5)	144.8 (5)	144.1 (5)
O(11)-C(7)	145.4 (6)	145.6 (7)	144.5 (5)
O(11)-C(8)	145.2 (7)	145.6 (6)	144.1 (5)
	Angles		
C(2)-C(1)-C(6)	117.1 (4)	118.8 (3)	117.6 (3)
C(2)-C(1)-C(8)	111.4 (3)	114.9 (4)	114.6 (3)
C(6)-C(1)-C(8)	87.9 (3)	88.0 (3)	87.8 (2)
C(1)-C(2)-C(3)	122.3 (4)	120.0 (4)	122.5 (3)
O(9)-C(2)-C(3)	59.5 (3)	59.5 (3)	59.4 (2)
O(9)-C(2)-C(1)	116.2 (4)	114.9 (4)	116.9 (3)
C(2)-C(3)-C(4)	120.2 (4)	121.0 (4)	120.1 (4)
C(2)-C(3)-O(9)	59.2 (3)	59.8 (3)	60.3 (3)
C(4)-C(3)-O(9)	117.8 (4)	117.1 (4)	113.6 (3)
C(3)-C(4)-C(5)	120.7 (4)	120.7 (4)	119.9 (4)
O(10)-C(4)-C(3)	116.3 (3)	117.2 (4)	115.9 (2)
O(10)-C(4)-C(5)	59.4 (3)	59.3 (3)	59.9 (2)
C(4)-C(5)-C(6)	121.5 (4)	120.9 (4)	123.2 (3)
O(10)-C(5)-C(4)	59.6 (3)	59.6 (3)	59.7 (2)
O(10)-C(5)-C(6)	114.6 (3)	115.8 (4)	116.3 (2)
C(1)-C(6)-C(5)	118.0 (4)	118.4 (4)	116.7 (3)
C(1)-C(6)-C(7)	88.0 (3)	88.0 (3)	88.0 (3)
C(5)-C(6)-C(7)	112.8 (4)	116.3 (4)	114.0 (2)
C(6)-C(7)-C(8)	91.7 (3)	91.8 (4)	92.2 (3)
O(11)-C(7)-C(6)	106.5 (3)	107.3 (4)	106.3 (2)
O(11)-C(7)-C(8)	59.5 (3)	59.8 (3)	59.7 (2)
C(1)-C(8)-C(7)	92.4 (3)	92.2 (3)	92.0 (3)
O(11)-C(8)-C(1)	107.0 (4)	107.2 (3)	106.8 (3)
O(11)-C(8)-C(7)	59.6 (3)	59.9 (3)	60.0 (2)
C(2)-O(9)-C(3)	61.3 (4)	60.7 (3)	60.2 (3)
C(4)-O(10)-C(5)	61.0 (3)	61.1 (3)	60.4 (2)
C(7)-O(11)-C(8)	60.8 (3)	60.3 (3)	60.3 (2)

trophotometer and ^{1}H NMR spectra on a Varian T-60, Hitachi Perkin-Elmer R-24B or on a 90 MHz Bruker HFX 10 spectrometer. The elemental analyses of all new substances were within accepted limits, i.e., ±0.3% for C and H, and were performed in-house. The ^{13}C NMR spectra were kindly run by Professor H. Hopf (University of Braunschweig) and Professor R. Neidlein (University of Heidelberg). Commerical reagents and solvents were purified to match reported physical and spectral data. Known compounds used in this research were either purchased from standard suppliers or prepared according to the literature procedures and purified to match the reported physical and spectral data.

Endoperoxide 4 from Triene 2. (a) Preparation of Triene 2. A 100-mL, two-necked, round-bottomed flask, provided with a magnetic spinbar, a rubber septum, and a three-way stopcock, was connected to a nitrogen manifold. After flame drying under a nitrogen atmosphere, 3.8 mmol of **7** in 40 mL of anhydrous ether (freshly distilled from the benzophenone ketyl radical) was introduced through the septum by means of a syringe. The contents were cooled to -60 °C and while magnetic stirring continued a stoichiometric amount of standardized *n*-butyllithium in *n*-hexane was added dropwise by means of a calibrated syringe and then the mixture was allowed to stir at -50 °C for 120 min. The ^{1}H NMR at low temperature (<0 °C) showed essentially pure triene **2**, together with small amounts of cyclooctatetraene and unreacted **7**. This solution was used directly for the singlet oxygenation.

(b) Endoperoxide 4 via Singlet Oxygenation of Triene 2. To the above solution of triene **2** was added ca. 2 mg of tetraphenylporphyrin (TPP) in 2 mL of Et_2O by means of a syringe. The solution was irradiated with a General Electric 150-W sodium street lamp at -30 °C for 120 min while oxygen gas was continuously bubbled through it. After completion of the singlet oxygenation (monitored by ^{1}H NMR) the reaction mixture was washed with 3 × 10 mL of cold water and dried over anhydrous $MgSO_4$ and the solvent was roto-evaporated (20 °C at 15 torr) to afford the crude endoperoxide. Column chromatography on silica gel at -10 °C with use of CH_2Cl_2 as eluant, and subsequent recrystallization from CH_2Cl_2/*n*-hexane, afforded pure endoperoxide in 85% yield; mp 75-76 °C, correct combustion analysis for the $C_8H_8O_2$ elemental composition. Spectral data; ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.20 (m, 2 H), 4.59 (m, 2 H), 5.91 (s, 2 H), 6.20 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.4 (d), 76.2 (d), 127.2 (d), 140.1 (d); IR (CCl_4) ν 3120, 3060, 2970, 1375, 1300, 950, 920 cm^{-1}.

Bicyclic Peroxide 8 via Diimide Reduction of Endoperoxide 4. A 100-mL, two-necked, round-bottomed flask, provided with magnetic spinbar and a 20-mL pressure-equalizing addition funnel, was charged with 10 mmol of potassium azodicarboxylate in 30 mL of CH_2Cl_2. The slurry was cooled to 0 °C and a solution of 4.5 mmol of endoperoxide **4** in 10 mL of CH_2Cl_2 was added. While the mixture was being cooled and stirred a solution of 18 mmol of HOAc in 5 mL of CH_2Cl_2 was added dropwise within 15 min. The mixture was stirred at 25 °C for 4 h and 15 mL of H_2O was added slowly. The organic layer was extracted with 3 × 10 mL of aqueous 5% $NaHCO_3$ and washed with H_2O. After being dried over anhydrous $MgSO_4$, the solvent was roto-evaporated (25 °C at 15 torr) and the solid residue recrystallized from hexane, affording the pure substance in 80% yield; mp 123 °C, correct combustion analysis for the $C_8H_{12}O_2$ elemental composition. Spectral data: ^{1}H NMR (CCl_4, Me_4Si) δ 2.18 (m, 8 H), 3.03 (m, 2 H), 3.93 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 20.2 (t), 20.7 (t), 33.7 (d), and 73.7 (d); IR (CCl_4) ν 2960, 2880, 1475, 1455, 1040, 945 cm^{-1}.

Bicyclic Peroxide 8 by Diimide Reduction of Endoperoxide 9. (a) Preparation of Endoperoxide 9 by Photooxygenation of Cyclooctatriene (10). A solution of 10 mmol of cyclooctatriene (**10**) and 2 mg of tetraphenylporphyrin (TPP) in 10 mL of CCl_4 was irradiated with a General Electric 150-W sodium street lamp at 10 °C, while oxygen gas was continuously bubbled through it. The reaction was complete after 20 h, as monitored by ^{1}H NMR, affording the [4.2.2] cycloadduct and [2.2.2] cycloadduct (**9**) in an 80% and 20% yield, respectively (by NMR analysis). The [2.2.2] cycloadduct (**9**) was isolated by low-temperature (-10 °C) column chromatography on silica gel eluting with CH_2Cl_2 and recrystallized from CH_2Cl_2/hexane, mp 85–86 °C. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 1.20–2.40 (m, 2 H), 3.00 (m, 2 H), 4.46 (m, 2 H), and 6.72 (m, 2 H); IR (CCl_4) ν 3025, 2960, 1615, 1370, 1250, 945 cm^{-1}.

(b) Diimide Reduction of Endoperoxide 9. A 50-mL, two-necked, round-bottomed flask, provided with a magnetic spinbar and a 10-mL pressure-equalizing addition funnel, was charged with 2 mmol of potassium azodicarboxylate in 15 mL of CH_2Cl_2. The slurry was cooled to 0 °C and a solution of 0.3 mmol of endoperoxide **9** in 5 mL of CH_2Cl_2 was added. While the solution was being cooled and stirred, a solution of 3.8 mmol of HOAc in 3 mL of CH_2Cl_2 was added dropwise. The mixture was stirred at room temperature (25 °C) for 4 h and 10 mL of H_2O was added slowly. The organic layer was extracted with 3 × 5 mL of aqueous 5% $NaHCO_3$ and washed with H_2O. After being dried over anhydrous $MgSO_4$, the solvent was roto-evaporated (25 °C at 15 torr) affording the saturated endoperoxide (**8**), mp 120–121 °C (from CH_2Cl_2/hexane). Its spectral data matched perfectly with those obtained for a sample of bicyclic peroxide **8** prepared by exhaustive diimide reduction of endoperoxide **4**.

Diol 11 via Catalytic Hydrogenation of Endoperoxide 4. A sample of 2.57 mmol of endoperoxide **4** was dissolved in 10 mL of EtOH and stirred in the presence of 10% Pd–C under hydrogen atmosphere for 7 h. After filtration, the solvent was roto-evaporated (25 °C at 15 torr) and the residue recrystallized from CH_2Cl_2 affording the pure material in 80% yield; mp 91–93 °C, correct combustion analysis for the $C_8H_{14}O_2$ elemental composition. Spectral data: ^{1}H NMR (CD_3COCD_3, Me_4Si) δ 0.70–3.20 (complex m, 10 H), 3.30–4.00 (complex m, 4 H); IR ($CHCl_3$) ν 3600, 3580–3100, 3000, 2970, 2940, 2880, 1450, 1045, 990, 950 cm^{-1}.

Dienediol 12 via Reduction of Endoperoxide 4 with Thiourea. A solution of 2.7 mmol of endoperoxide **4** and 2.7 mmol of thiourea in 20 mL of MeOH was stirred at 25 °C for 3 h. After filtration the solvent was roto-evaporated (25 °C at 15 torr) and the residue chromatographed on silica gel at 25 °C eluting with a 9:1 CH_2Cl_2/MeOH mixture. Subsequent recrystallization from ether afforded the pure diol in 65% yield; mp 45–46 °C, correct combustion analysis for the $C_8H_{10}O_2$ elemental composition. Spectral data: ^{1}H NMR (CD_3COCD_3, Me_4Si) δ 3.26 (broad s, 2 H), 3.75 (broad s, 2 H), 4.28 (broad s, 2 H), 6.07 (m, 4H);

^{13}C NMR ($CDCl_3$, Me_4Si) δ 47.4 (d), 66.3 (d), 131.0 (d), 139.2 (d); IR ($CHCl_3$) ν 3100–3600, 3040, 3000, 2910, 1420, 1250, 990, 810 cm^{-1}.

Keto Alcohol 13 via Base-Catalyzed Isomerization of Endoperoxide 4. A 50-mL, round-bottomed flask, provided with a magnetic spinbar and a 20-mL pressure-equalizing funnel, was charged with 4.56 mmol of endoperoxide **4** in 20 mL of CH_2Cl_2. After the solution was cooled to 0 °C, 9.12 mmol of Et_3N in 10 mL of CH_2Cl_2 were added slowly and stirred at 25 °C for 4 h. The solvent was roto-evaporated (25 °C at 15 torr) and the residue chromatographed on silica gel at 25 °C, eluting with a 9:1 $CHCl_3$/MeOH mixture to remove the Et_3N. Subsequent "Kugelrohr" distillation (120–125 °C at 0.01 torr) gave the pure keto alcohol (**13**) in 95% yield; correct combustion analysis for the $C_8H_8O_2$ elemental composition. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.48 (m, 1 H), 3.62 (broad d, 1 H, J = 3.6 Hz), 3.77 (broad s, 1 H), 4.40 (broad s, 1 H), 5.97 (d, 1 H, 10.2 Hz), 6.15 (m, 1 H), 6.32 (dd, 1 H), 6.78 (q split into d, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 48.6, 51.8, 64.3, 128.0, 139.0, 141.1, 144.7; IR ($CHCl_3$) ν 3600, 3400, 3040, 3020, 3000, 1675, 1015 cm^{-1}.

Dienedione 14 via MnO_2 Oxidation of Keto Alcohol 13. A 50-mL, round-bottomed flask, provided with a magnetic spinbar, was charged with 4.56 mmol of keto alcohol **13** in 30 mL of CH_2Cl_2. Then, 52 mmol of freshly prepared MnO_2 was added and the mixture stirred at 25 °C for 12 h. The MnO_2 was removed by filtration, the solvent roto-evaporated (25 °C at 15 torr), and the residue chromatographed on silica gel at 25 °C, eluting with CH_2Cl_2. The pure material was obtained in 90% yield; mp 50–51 °C (lit.[17] mp 51–52 °C). ^{1}H NMR and IR matched the reported data.

Epoxyendoperoxide 15 via Epoxidation of Endoperoxide 4. A solution of 1.98 mmol of endoperoxide **4** and 3.97 mmol of *m*-chloroperbenzoic acid in 60 mL of CH_2Cl_2 was stirred for 36 h at 25 °C in the presence of solid $NaHCO_3$. The solvent was roto-evaporated (25 °C at 15 torr) and the residue chromatographed on silica gel at −10 °C, eluting with CH_2Cl_2. Subsequent recrystallization from CH_2Cl_2/hexane afforded the pure epoxyendoperoxide (**15**) in 70% yield; mp 85–86 °C, correct combustion analysis for the $C_8H_8O_3$ elemental composition. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.89 (m, 2 H), 3.58 (m, 2 H), 4.77 (m, 2 H), 6.73 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.8 (d), 55.5 (d), 70.7 (d), 130.8 (d); IR (KBr) ν 3020, 2940, 1610, 1410, 1360, 1250, 1170, 970, 930, 890, 700 cm^{-1}.

Epoxydiene 16 via Triphenylphosphine Deoxygenation of Endoperoxide 4. A 25-mL, one-necked, round-bottomed flask, provided with a magnetic spinbar, was charged with 1.83 mmol of endoperoxide **4** in 15 mL of $CHCl_3$. After the solution was cooled to 0 °C, 1.83 mmol of triphenylphosphine was added in small portions over a period of 30 min and stirring at 25 °C was continued for 30 min. The solvent was roto-evaporated (25 °C at 15 torr) and the residue chromatographed on silica gel at 15 °C, eluting with CH_2Cl_2. Subsequent recrystallization from CH_2Cl_2/*n*-hexane afforded the pure material in 70% yield; mp 81–82 °C, correct combustion analysis for the C_8H_8O elemental composition. spectral data: ^{1}H NMR (CCl_4, Me_4Si) δ 2.96–3.73 (m, 4 H), 5.92 (m, 2 H), 6.23 (m, 2 H); IR (CCl_4) ν 3120, 3080, 3060, 2900, 1580, 1470, 1080, 830 cm^{-1}.

Epoxidation of Epoxydiene 16. A solution of 1.67 mmol of epoxydiene **16** and 5 mmol of *m*-chloroperbenzoic acid in 60 mL of CH_2Cl_2 was stirred for 36 h at 25 °C in the presence of solid $NaHCO_3$. The solvent was roto-evaporated (25 °C at 15 torr). The residue was submitted to medium pressure liquid chromatography on silica gel eluting with CH_2Cl_2, affording the syn diepoxide (**18**) and the anti,anti,syn triepoxide (**20b**) in 85% and 15% yield, respectively. The physical and spectral data of these products matched those obtained in the transformations **4** → **18** → **20b**.

Diepoxide 17 via Triphenylphosphine Deoxygenation of Epoxyendoperoxide 15. A 50-mL, one-necked, round-bottomed flask, provided with a magnetic spinbar, was charged with 5.88 mmol of epoxyendoperoxide **15** in 30 mL of $CHCl_3$. After the solution was cooled to 0 °C, 5.88 mmol of triphenylphosphine was added in portions over a period of 30 min and stirring at 25 °C was continued for 60 min. The solvent was roto-evaporated (25 °C at 15 torr). The residue was chromatographed on silylated silica gel at −10 °C, eluting with CH_2Cl_2, affording the pure material in 50% yield; correct combustion analysis for the $C_8H_8O_2$ elemental composition. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.52 (m, 1 H), 2.83 (broad d, 1 H, J = 5.7 Hz), 3.22 (m, 2 H), 3.70 (t, 1 H, J = 2.3 Hz), 3.92 (t, 1 H, J = 2.4 Hz), 5.70 (A part of AB system split in d of d, 1 H, J_{AB} = 9.9 Hz, J_{dd} = 3.6 Hz), 6.12 (B part of AB system split in d of d, J_{dd} = 1.5 Hz); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.2 (d), 39.8 (d), 46.5 (d), 51.6 (d), 54.3 (d), 57.2 (d), 125.0 (d), 128.9 (d); IR (CCl_4) ν 3040, 3010, 2970, 2940, 1440, 1330, 1200, 1015, 940, 840, 825 cm^{-1}.

Syn Dioxide 18 via Thermolysis of Endoperoxide 4. A solution of 2.65 mmol of endoperoxide **4** in 4 mL of benzene was heated in a sealed tube for 1 h at 100 °C. Roto-evaporation of the solvent (25 °C at 15 torr) gave the crude product. Recrystallization from CH_2Cl_2/*n*-hexane and subsequent sublimation (80 °C at 2 torr) afforded the pure material in 80% yield; mp 105–107 °C, correct combustion analysis for the $C_8H_8O_2$ elemental composition. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 3.10 (broad d, 2 H, J = 3 Hz), 3.30 (s, 2 H) 3.45 (broad d, 2 H, J = 3 Hz), 6.20 (s, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 39.4 (d), 48.2 (d), 49.9 (d) and 137.3 (d); IR (KBr) ν 3130, 3000, 2915, 1580, 1420, 1060, 950, 860 cm^{-1}.

Table IV. X-ray Operations and Results of **20a**, **20b**, and **20c**

	20a	20b	20c
crystal size, mm	0.1 × 0.1 × 2.5	0.3 × 0.3 × 1.2	0.1 × 0.1 × 0.2
no. of measd intensities	1735	1750	1570
no. of obsd reflections	1170	1427	1193
no. of struct factors of direct phase determination	82	85	132
R_{aniso}	0.075	0.087	0.070
space group	$P2_1/n$	$P2_1/n$	$P\bar{1}$
a, pm	656.8 (3)	1078.7 (4)	754.6 (2)
b, pm	2313.6 (8)	632.5 (2)	759.6 (2)
c, pm	454.9 (2)	1019.8 (2)	671.4 (2)
α, deg			73.10 (2)
β, deg	105.03 (3)	109.48 (2)	113.32 (2)
γ, deg			92.05 (2)
no. of formula units/cell	4	4	2
calcd density, g cm^{-3}	1.513	1.540	1.500

Vacuum Flash Pyrolysis (VFP) of Diepoxide 18 and Endoperoxide 4. A sample of 1 mmol of diepoxide **18** was pyrolyzed at 500 °C and 4 torr, affording **21** as a major product; mp 51–52 °C from hexane, correct combustion analysis for the $C_8H_8O_2$ elemental composition. Spectral data: ^{1}H NMR (CCl_4, Me_4Si) δ 3.73 (s, 2 H), 4.70 (m, 2 H), 5.95 (m, 4 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 58.7 (d), 76.4 (d), 127.5 (d), 133.6 (d); IR (neat) ν 3040, 3950, 1430, 1400, 1290, 1210, 1080, 1040, 990, 910, 860, 800, 700 cm^{-1}. Similarly, 1 mmol of endoperoxide **4** gave **21** as the major product directly when pyrolyzed at 500 °C and 10 torr.

Anti,Anti,Anti Triepoxide 20a via Thermolysis of Epoxyendoperoxide 15. A solution of 0.66 mmol of epoxyendoperoxide **15** in 5 mL of benzene was refluxed for 12 h. The solvent was roto-evaporated (ca. 25 °C at 15 torr) and the residue chromatographed on silica gel at 25 °C, eluting with CH_2Cl_2. Subsequent recrystallization from CH_2Cl_2/*n*-hexane afforded the pure substance in 60% yield; mp 160–161 °C, correct combustion analysis for the $C_8H_8O_3$ elemental composition. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.60 (m, 2 H), 3.00 (m, 2 H), 3.58 (m, 2 H), 3.87 (m, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 38.0 (d), 47.4 (d), 48.1 (d), 54.5 (d); IR (KBr) ν 2980, 2940, 1430, 1330, 1270, 1200, 1065, 950, 940, 860, 820 cm^{-1}. Unequivocal confirmation of the anti,anti,anti stereochemistry of triepoxide **20a** rests on X-ray analysis (Figure 1).

Anti,Anti,Syn Triepoxide 20b via Epoxidation of Diepoxide 18. A solution of 6.03 mmol of epoxide **18** and 15.6 mmol of *m*-chloroperbenzoic acid in 200 mL of CH_2Cl_2 was stirred for 48 h at 25 °C in the presence of solid $NaHCO_3$. The *m*-chlorobenzoic acid was extracted with 4 × 10 mL of aqueous 5% NaOH, the organic layer dried over anhydrous $MgSO_4$, and the solvent roto-evaporated (25 °C at 15 torr). The residue was chromatographed on silica gel at 25 °C, eluting with CH_2Cl_2. Recrystallization from CH_2Cl_2/*n*-pentane gave the pure substance in 70% yield; mp 209–210 °C, correct combustion analysis for the $C_8H_8O_3$ elemental composition. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.81 (s, 2 H), 3.13 (m, 2 H), 3.45 (m, 2 H), 4.10 (s, 2 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 35.7 (d), 47.9 (d), 48.4 (d) and 52.1 (d); IR (KBr) ν 3000, 2980, 2940, 980, 940, 860 cm^{-1}. Unequivocal confirmation of the anti,anti,syn stereochemistry rests on X-ray analysis (Figure 1).

Syn,Anti,Anti Triepoxide 20c via Epoxidation of Diepoxide 17. A solution of 3.7 mmol of diepoxide **17** and 10 mmol of *m*-chloroperbenzoic acid in 40 mL of CH_2Cl_2 was stirred for 40 h at 25 °C in the presence of solid $NaHCO_3$. The *m*-chlorobenzoic acid was extracted with 2 × 20 mL of aqueous 5% NaOH, the organic layer dried over anhydrous $MgSO_4$, and the solvent roto-evaporated (25 °C at 15 torr). The residue was chromatographed on silica gel at 25 °C, eluting with CH_2Cl_2. Recrystallization from *n*-hexane/CH_2Cl_2 afforded the pure substance in 60% yield; mp 83–84 °C, correct combustion analysis for the $C_8H_8O_3$ elemental composition. Spectral data: ^{1}H NMR ($CDCl_3$, Me_4Si) δ 2.51 (m, 2 H), 3.04–3.65 (m, 4 H), 3.78 (m, 1 H), 4.00 (m, 1 H); IR ($CHCl_3$) ν 3000, 2940, 1450, 1330, 1240, 1200, 1020, 950, 860, 825 cm^{-1}. Unequivocal confirmation of the syn,anti,anti stereochemistry rests on X-ray analysis (Figure 1).

X-ray Crystallography. Clear, colorless crystals were optically centered on a Syntex PI four circle diffractometer. The intensities of all

reflections were measured according to the ω technique (Mo Kα, graphite monochromator), using a scan range of 1° and a scan speed between 0.5 and 24.0 deg min^{-1} as a function of the intensities of the reflections. In the range between $3.0° \leq 2\theta \leq 55.0°$ all reflections hkl with $F > 3\sigma(F)$ were applied for the structure determination. For the evaluation the SHELXTL System on an Eclipse S250 at the Max-Planck-Institut für Festkörperforschung was employed. All structures were solved by the direct phase determination. The parameters of the complete structures could be refined by anisotropic least-squares cycles to the given R values. The positions of the hydrogen atoms were calculated geometrically and considered isotropically in all refinements. Special X-ray operations and results are listed in Table IV. We have omitted the presentation of the structure factors, which can be obtained upon request.

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Mechanisms of the π-Electron Steric Effect

Joseph B. Lambert*[1a] and Kalulu M. Taba[1b]

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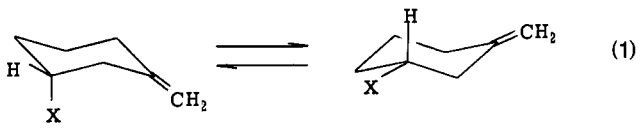
Abstract: Replacement of a β-CH_2 in methoxycyclohexane by $C{=}CH_2$ produces an increased proportion of the equatorial conformer in a nonpolar medium. We previously suggested that this change resulted from an electrostatic repulsion between the axial 3-methoxy group and the exocyclic $C{=}CH_2$ structure. We now observe that exocyclic $C{=}C(CH_3)_2$ yields the opposite result, an increased proportion of the axial 3-methoxy conformer. The presence of methyl on the exocyclic double bond reduces or eliminates the $C{=}CX_2$ dipole. These observations are consistent with the earlier suggestion that this π-electron steric effect results from dipole–dipole interactions. The corresponding 3-methoxy $C{=}CCl_2$ and $C{=}CBr_2$ systems, however, also exhibit an increased proportion of the axial conformer. In the halogen systems, either the dipolar interaction has changed sign as the result of an unexpected alteration of intervector angles or an alternative attractive mechanism such as an n–π^* orbital interaction has become important. The orbital interaction would be favored by the lower LUMO's of the halogenated double bond.

We recently reported the functional equivalent of a π-electron steric effect on the conformational equilibria of 3-substituted 1-(*exo*-methylene)cyclohexanes (eq 1).[2] In this system, one of



(1)

the cyclohexane CH_2 groups, with its axial proton, has been replaced by $C{=}CH_2$. Because the mutual repulsion between the axial substitutent X and the syn-axial ring protons is a substantial factor in determining axial/equatorial equilibrium constants in cyclohexane, one might expect that removal of one such axial proton would increase the proportion of the axial conformer. The 3-alkyl ketone effect in 3-substituted cyclohexanones has been interpreted in these terms.[3] We found that 3-alkyl-1-methylenecyclohexanes behave in a similar fashion.[2] Replacement of a CH_2 group of cyclohexane with $C{=}O$ or $C{=}CH_2$ increases the proportion of the axial alkyl conformer.

The cyclohexanone studies did not examine polar substituents at the 3-position.[3] In our methylenecyclohexane study, we were able to examine OH, OCH_3, and SCH_3, among others. Surprisingly, the effect of the exo-methylene group on these substituents was opposite to that on the alkyl groups. Replacement of the CH_2 of cyclohexane by $C{=}CH_2$ brought about a large decrease in the proportion of the 3-axial isomer. These observations were made in the almost nonpolar solvent CF_2Cl_2, in which intramolecular interactions should achieve the greatest importance. We attributed the decreased axial population to a repulsive interaction between the 3-axial substituent and the 1-$C{=}CH_2$ group.[2] Through-bond orbital interactions should have caused the opposite result (increased axial population), so we attributed our observations to electrostatic rather than orbital interactions. These interactions could involve the dipole of the 3 substituent and either the dipole or the quadrupole of the $C{=}CH_2$ group. Calculations suggested that both mechanisms could contribute.[2]

Examination of the same equilibrium in a polar, hydrogen-bonding solvent ($CHFCl_2$) showed an appreciable increase in the axial population. Solvation partially insulates the 3 substituent from the $C{=}CH_2$ group, thereby decreasing the repulsive electrostatic interaction that had served to disfavor the axial conformer. With this effect substantially reduced, the proportion of axial conformer is actually larger than in cyclohexyl, as in the 3-alkyl ketone effect. Thus in a polar solvent, the effect originally expected is realized, although it does not reflect the true intramolecular interactions. Solvent effects on conformational equilibria have been thoroughly studied.[4a] In cyclohexyl systems such as methoxycyclohexane solvent effects are opposite to what we observed in the *exo*-methylenecyclohexanes, since polar solvents decrease the proportion of the axial cyclohexyl conformer.[4b]

The exact nature of the intramolecular effects observed in CF_2Cl_2 was not clear.[2] Although we favored simple electrostatic interactions, they were not fully defined. Because electrostatic calculations are fraught with uncertainties in these systems, we

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