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Stereoselective Epoxidation of cis-3,4-Disubstituted-(CH_2X)-Cyclobutenes with Dimethyldioxirane and Peroxy Acids. Experimental and Computational Evidence for a Syn-Orienting Electrostatic Effect

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Abstract: The epoxidation reactions of a series of cis-3,4-disustituted-(CH_2X)-cyclobutenes **1-8** with dimethyldioxirane (DMD) and mClPBA have been investigated with both reagents. A remarkable syn diastereoselectivity in the formation of the epoxide has been observed for substrates bearing electron withdrawing substituents. Transition structures for epoxidations of 3,4-dimethylcyclobutene (**1**), diastereoisomeric 3,5-dioxa-4-thia-bicyclo[5.2.0]non-8-ene-4-oxides **7** and **8**, and 3,4-bis(mesyloxymethyl)-1-cyclobutene (**5**) with dioxirane and peroxyformic acid have been located with the B3LYP/6-31G* method. Experimental dominant syn facial selectivity is rationalized mostly as a result of an electrostatic attractive interaction involving the peroxo oxygens of the oxidizing reagents and the positively charged homoallylic hydrogens of the olefins.

Keywords: cycloalkenes, epoxidation, dioxiranes, transition states.

INTRODUCTION

Epoxidations with peroxy acids and dioxiranes have received great attention from both experimental[1-5] and computational[6-14] points of view, due to their important applications for preparative purpose. Diastereoselectivity of such reactions can be controlled by a mix of several factors including steric,[3] H-bonding[3-5] and dipole-dipole interactions.[3, 4]

A great deal of interest has been devoted to hydrogen bonding, i.e. an interaction in which the electrostatic component is strongly dominant. Its importance in the stereocontrol of the epoxidation reactions with both peroxy acids and dioxiranes is supported by convincing experimental evidence[3-5] and it has been recently fully confirmed, for both kind of reagents, by high level calculations in the frame of density functional theory (DFT).[11-14]

Thus, syn epoxidation of allylic and homoallylic alcohols by organic peroxy acids and dioxiranes can be attributed to hydrogen bonding between the alkene's OH hydrogen and reagent peroxo oxygens. Consistent with this explanation, allylic ethers and acetates are epoxidized by dimethyldioxirane (DMD) and m-chloroperoxybenzoic acid (mClPBA) at lower rates and afford mostly the anti isomer, as a result of repulsive steric and/or dipole-dipole interactions.[3, 4, 15]

However, a syn dominant attack has been observed in the epoxidation of allylic carbamates and N,N-dialkyl amides with mClPBA.[16] Alkenes bearing allylic substituents with a lower hydrogen bond acceptor property (RO- and ROCO- groups) show, as well, prevalent syn epoxidation using higher acidic peroxy acids

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than mClPBA such as CF_3COOOH.[1,17,18] These observations were straightforwardly explained by invoking hydrogen bonding in which the peroxy acid acts as hydrogen bond donor and the substituent as hydrogen bond acceptor.[16] However, very recently, such a result has been rationalized by Fehr,[18] on the basis of pure electrostatic interactions due to the fact that "CF_3COOOH possesses a very high electrostatic potential (partial positive charge)". According to the author the peroxy acid approach "is governed by Coulombic attraction with the more electron-rich π face".

Electrostatic interactions, described as repulsive dipole-dipole interactions, were advanced by Curci *et al.*[4] to explain the complete anti stereoselectivity observed in the epoxidation of monoepoxynaphthalene with dimethyldioxirane (DMD). Moreover, more recently, Murray *et al.*[3] rationalized the truly remarkable syn diastereoselectivity of the DMD epoxidation of cyclohexene bearing allylic CH_2X substituents on the basis of attractive dipole-dipole interactions. The above results suggest that electrostatic interactions can give rise to an efficient stereocontrol of the epoxidation of highly polar alkenes with polar reagents. In particular, these effects can open the way to contrasteric facial selectivity.

In fact, Huet *et al.* reported an interesting example of syn facial selectivity in the epoxidation of cis-3,4-bis-(benzyloxymethyl)-1-cyclobutenes with mClPBA, but no convincing explanation was offered by the authors.[19] Our interest in cyclobutene chemistry led us to carry out a systematic investigation of the epoxidation reactions of cis-3,4-bis-(CH_2X)-cyclobutenes with dimethyldioxirane (DMD) and mClPBA. The results described in this paper provide further experimental evidence of a syn orienting effect leading to contrasteric diastereoselectivity.

To support qualitative reasoning which seemed to indicate electrostatic interactions as responsible for such an effect, we performed calculations on some of these reactions at a very good theory level using the B3LYP/6-31G* method. For the largest system the relative TS energies were approximated with a combination of PM3 and B3LYP/6-31G* calculations. The B3LYP/6-31G* theory has already been used to describe computationally epoxidation reactions with both dioxiranes[6,7,10,30] and peroxy acids[8,12,13] and it has been shown to provide good transition structure (TS) geometries as well as accurate reaction energetics. In particular, the B3LYP/6-31G* method reasonably reproduces not only relative but also absolute free activation enthalpies.[10,11,12] Thus, it is considered the most reliable, at a reasonable cost, tool for computational investigations of the mechanism of these reactions. In the field of epoxidation reactions no facial selectivity studies with the B3LYP/6-31G* method have been reported to date, but this theory level has been shown to nicely reproduce the stereochemical outcome of 1,3-dipolar cycloadditions to cis-3,4-dimethylcyclobutene.[20]

As far as we know, the PM3 study of the epoxidation of substituted 1,2-dihydronaphthalene is the only reported [21] computational investigation of face selectivity in the epoxidation of olefins with peroxy acids and no computational study on this problem has been reported so far for dioxirane epoxidations.

RESULTS

Substrates **1, 2, 4-6** (see Scheme 1) were known[19,20,22,23] while **3** was prepared by bis methylation of **2** with CH_3I in THF with a suspension of NaH. Sulfites **7** and **8** (which differ from each other by the sulfur configuration, see Scheme 1) were obtained as a 35 : 65 mixture by reaction of thionyl chloride with **2** in presence of pyridine and separated by column chromatography. They did not convert into each other under epoxidation conditions.

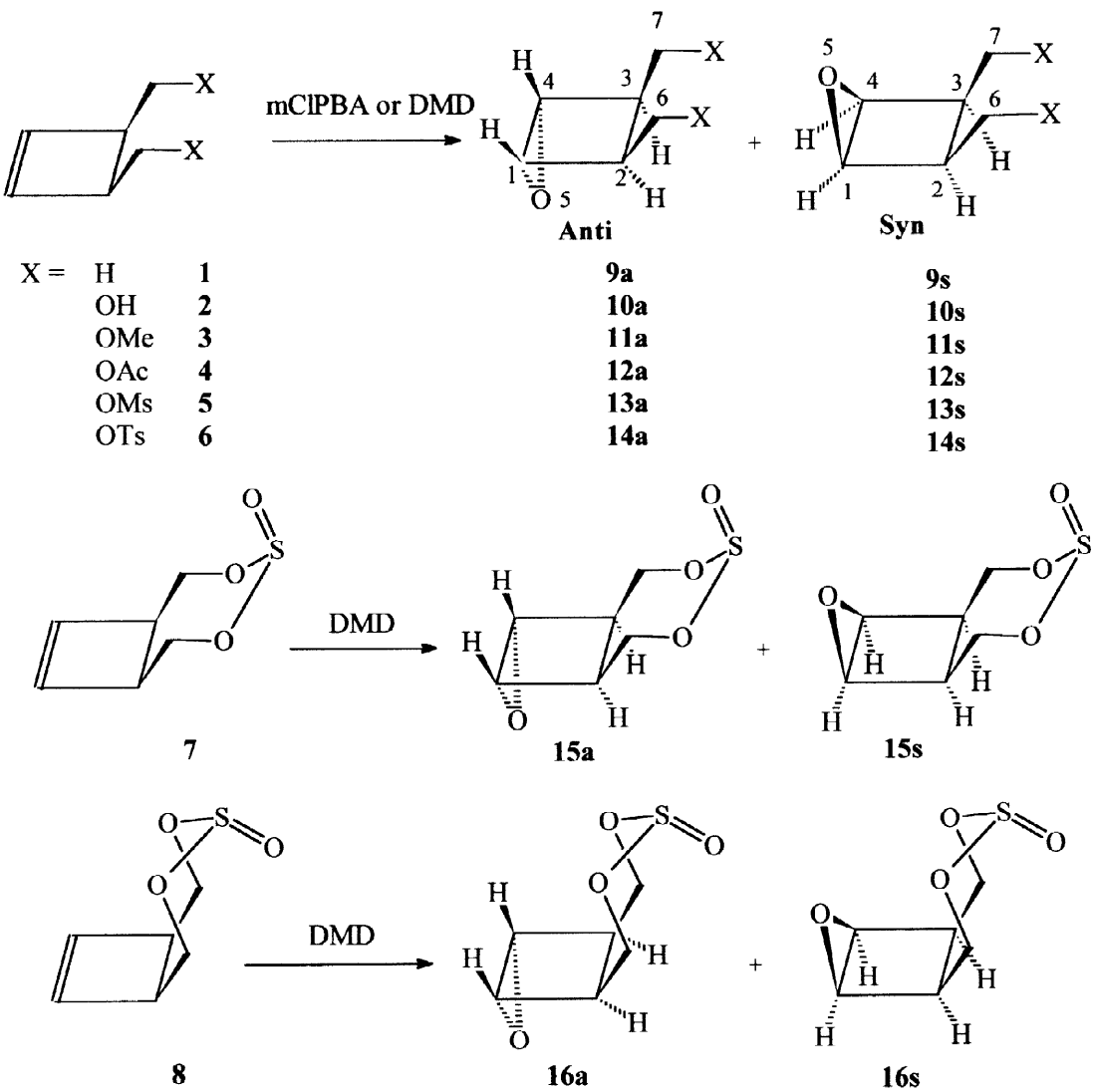
Epoxidations with dimethyldioxirane

Dimethyldioxirane (DMD) was prepared by oxidation of acetone with Oxone® (potassium monoperoxysulfate)[24, 25] and used as 0.08-0.1 M acetone solution or as CCl_4/acetone (9 : 1) solution.[26]

The reactions of a series of cis-3,4-bis-(CH_2X)-cyclobutenes **1-8**, were carried out both in acetone and in CCl_4/acetone (9 : 1) solution, with an excess of DMD at room temperature, to afford high yields of syn/anti epoxide mixtures (> 70 %). In particular, yields were almost quantitative in CCl_4 solution (see Table 1).

The oxidation of substrates **7** and **8** by DMD was chemoselective: only the alkene moiety was epoxidized. No products deriving from competitive oxidation of the sulfite to sulfate groups were detected (by TLC or ^{1}H NMR) in the crude reaction mixture.

On going from acetone to the less polar CCl_4/acetone (9 : 1) solution the decrease (qualitatively, see Reaction Time column in Table 1) in the reaction rate for all cyclobutenes **1-8**, was accompanied by an increase in the syn/anti ratio in all cases but two (that is, in epoxidations of **4** and **7**, Table 1).



X =		Anti	Syn
	H 1	**9a**	**9s**
	OH 2	**10a**	**10s**
	OMe 3	**11a**	**11s**
	OAc 4	**12a**	**12s**
	OMs 5	**13a**	**13s**
	OTs 6	**14a**	**14s**

7 **15a** **15s**

8 **16a** **16s**

Scheme 1

For substrates **3-6**, having electron withdrawing groups in the homoallylic positions, DMD epoxidations were slower (roughly by a factor of 10) than that of cis-3,4-dimethylcyclobutene (**1**) (Table 1). Henbest observed similar effects on the reaction rate for the mClPBA epoxidation of 3-substituted cyclohexenes.[27] Even cyclobutene **2** (X = OH) was much less reactive than **1** indicating that a strong stabilizing hydrogen bonding (a priori possible) interaction is not operative in the transition state of its DMD epoxidation.

In the less polar solvent (CCl_4 : acetone = 9 : 1) syn selectivity was higher than 80 % for substrates **5** and **6**. Cyclobutenes **2**, **3**, **4** and **7** showed a lower but not negligible syn selectivity. Epoxidation of cis-3,4-dimethylcyclobutene (**1**) afforded a slight excess of anti epoxide in acetone and a very low excess of syn epoxide in CCl_4 (syn : anti = 44 : 56 and 55 : 45, respectively).

Substrate **8** was the only one to give complete anti (> 99 %) diastereoselectivity. Actually epoxide **16a** (see Scheme 1) was the only isolated product and a careful NMR and GC analysis of the crude reaction mixture did not reveal any signal attributable to epoxide **16s**.

Table 1. Diastereoselectivity in the Epoxidation Reactions with DMD.

Substrate	X	Solvent	Reaction Time [a] (hrs)	Yield (%)	Syn Epoxide (%)	Anti Epoxide (%)
5	MsO-	Acetone	5	85	79	21
		CCl_4:Acetone=9:1	12	99	90	10
4	AcO-	Acetone	2	69	72	28
		CCl_4:Acetone=9:1	6	99	68	32
6	TsO-	Acetone	2	97	63	37
		CCl_4:Acetone=9:1	8	99	82	18
7	OS(O)O-	Acetone	7	88	77	23
		CCl_4:Acetone=9:1	12	85	70	30
2	HO-	Acetone	2	70	57	43
		CCl_4:Acetone=9:1	1	80	67	33
3	MeO-	Acetone	7	99	49	51
		CCl_4:Acetone=9:1	10	99	62	38
1	H	Acetone	0.2	99	44	56
		CCl_4:Acetone=9:1	0.5	99	55	45
8	OS(O)O-	Acetone	2	95	-	100
		CCl_4:Acetone=9:1	5	95	-	100

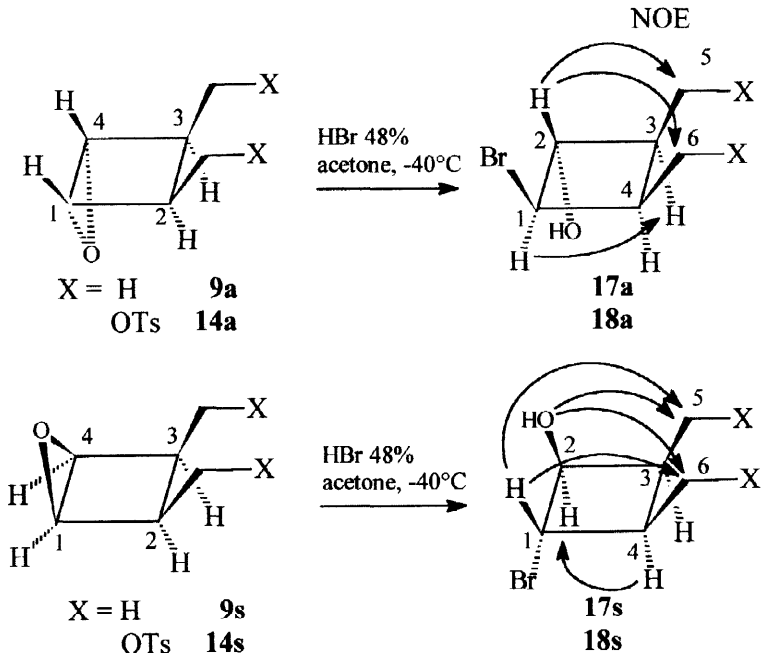
[a] As judged by disappearance of compound **1-8**, upon monitoring the reaction mixture by TLC, ^{1}H NMR or GC analysis.

Anti : syn ratios (**9a-15a** : **9s-15s**) (Table 1) were evaluated by ^{1}H NMR and by GC (for volatile products) or column chromatography. As for stereochemistry assignment, epoxides **9-14** could be grouped in two series, syn and anti, according to the very similar pattern of their NMR spectra. The more noteworthy

NMR features of epoxides **9-14** are as follows: 1) chemical shifts of H-2 and H-3 in anti epoxides are always significantly lower (by at least 0.33 ppm), as a result of shielding effect by the oxirane ring, than those of the corresponding protons in syn epoxides; 2) chemical shift of H-1 and H-4 in anti epoxides are also always lower than those of the corresponding protons in syn epoxides, but in this case the difference is very small (by 0.04 ppm); 3) C-2, C-3 and C-1, C-4 are always more shielded in the syn epoxides than in their anti diastereoisomers.

To substantiate the syn /anti choice we performed NOE experiments for three syn/anti pairs, that is, **9a-9s** (as a mixture), **13a-13s** and **14a-14s** (as pure compounds). Irradiation of H-1 brought about an NOE enhancement of H-2 in all compounds which, however, was substantially higher in those of the syn series (2.2% for **9s**, 2.4 % for **13s** and 2.3 % for **14s**, where H-1 and H-2 bear a cis relationship) than that observed for anti derivatives (1.0 % for **9a**, 1.1 % for **13a**, and 0.9 % for **14a**, where H-1 and H-2 are trans to each other). The difference, although significant, is far from being dramatic. The underlying reason for this small difference can be ascribed to the small syn (in anti epoxides) and anti (in syn epoxides) distortion, with respect to the cyclobutane plane, of H-1 and H-4. Thus, the decrease in the H-1/H-2 distance on passing from syn to anti derivatives is not strong. The stereochemical assignments for **9a-9s**, and **14a-14s** were confirmed by chemical correlation. The 60 : 40 mixture of **9a** + **9s** (obtained by epoxidation of **1** with DMD at - 40° C in acetone) was transformed in high yield (≥ 90 %) to a mixture of trans bromohydrins **17a** + **17s** (62 : 38) by treatment with hydrobromic acid in acetone at - 40 °C.

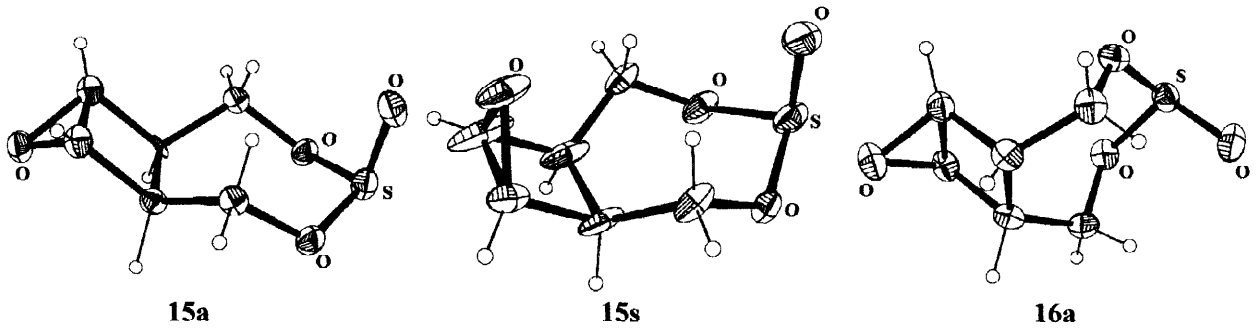
NOE experiments clearly confirmed the anti stereochemistry for the OH group (relative to the methyl groups) in the bromohydrin **17a** (see Scheme 2) and the syn one for the same group in **17s**. In fact, irradiation of H-1 in **17a** brought about increase in the H-3 signal intensity by 2.8 %, while saturation of H-2 induced NOE effect for the signal of the methyl groups (3.0 % for the methyl group at C-5 and 2.5 % for the methyl group at C-6). Irradiation of H-1 in **17s** gave rise to NOE effects for the signal of the methyl groups (2.0 % for the methyl group at C-6 and 1.9 % for the methyl group at C-5), but did not lead to any measurable NOE enhancement for the H-3 signal (see Scheme 2).



Scheme 2

Likewise pure **14s** and pure **14a** were quantitatively transformed into trans bromohydrins **18s** and **18a**, respectively. In **18s** the OH group resonates as a doublet, as confirmed by decoupling experiments as well as D_2O exchange. On saturation of HO proton we observed NOE effect for the signal of the methylene groups (2.3% for the methylene group at C-5 and 1.6 % for the methylene group at C-6) while irradiation of H-4 in **18s** increased the H-2 signal intensity by 3.0 %. In contrast, irradiation of H-4 in **18a** did not give rise any measurable NOE effect for the H-2 signal.

The stereochemistry of the epoxides **15a**, **15s** and **16a** (anti, syn and anti adducts, respectively) were determined by X-ray analysis. The ORTEPs of such structures are reported in Figure 1.[28] Notice that the conformation of the seven membered ring in these products is the same [i.e., the (o) conformation in **15a** and **15s** and the (i) conformation in **16a**] as that in the TSs calculated by us (see later on).



15a **15s** **16a**

Figure 1 ORTEP diagrams of the single crystal X-ray structure of **15a**, **15s**, and **16a**.

Epoxidation with m-Chloroperoxybenzoic acid

The reactions of mClPBA with cyclobutenes **1-6** were carried out in benzene or dichloromethane at room temperature in the presence of solid sodium bicarbonate in order to avoid any acid catalyzed hydrolysis of the epoxides.

For substrates **3–6**, having electron withdrawing groups in the homoallylic positions, epoxidations were much slower (more than 20 times) than that of cis-3,4-dimethylcyclobutene (**1**) (see Reaction Time in Table 2) with the only exception of cyclobutene **2** (X = OH), whose reactivity was similar to that of **1**.

The retarding effect of the X group in mClPBA epoxidations is similar, even if more pronounced, to that observed for DMD reactions. Notice, however, that reactivity of cyclobutene **2** does not represent an exception in the DMD reaction series.

Syn selectivity in the epoxidation reactions with mClPBA was higher than 80 % with substrates **2**, **5** and **6** while also for cyclobutenes **3** and **4**, although lower, it was significant (> 69 %). Epoxidation of cis-3,4-dimethylcyclobutene (**1**) in $CDCl_3$ afforded an equimolar mixture of syn and anti epoxides but in benzene a slight prevalence of syn attack (60 : 40) was observed.

From a synthetic view point it is important to emphasize that:

- the DMD epoxidations were always roughly 10 times faster than the corresponding mClPBA reactions (as evaluated from the time required to achieve similar conversion to products),

- the reaction yields of the DMD epoxidations are always higher than the corresponding peroxyacid reactions. In fact with mClPBA a large amount of unreacted substrate (up to 55 % in the case of cyclobutene **3**) was recovered even using a 50 % excess of peroxy acid.

Table 2. Diastereoselectivity in the Epoxidation Reactions with mClPBA.

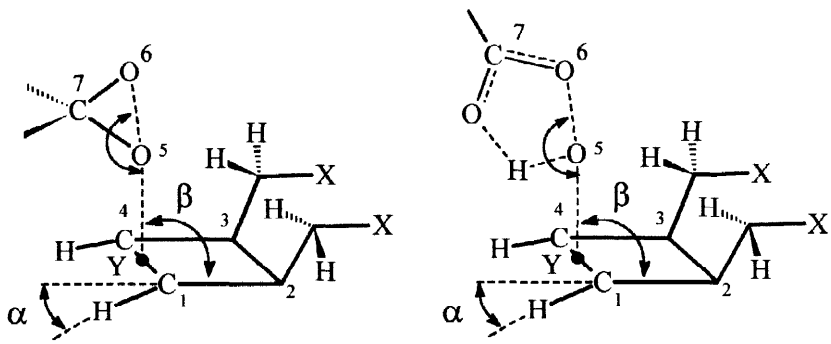
Substrate	X	Solvent	Reaction time[a] (hrs)	Yield (%)	Syn Epoxide (%)	Anti Epoxide (%)
5	MsO-	C_6H_6	91	60	88	12
		CH_2Cl_2	18	69	87	13
2	HO-	CH_2Cl_2	1	55	82	18
		C_6H_6	1	58	81	19
6	TsO-	C_6H_6	18	70	80	20
3	MeO-	C_6H_6	24	45	76	24
4	AcO-	CH_2Cl_2	28	64	69	31
1	H-	C_6D_6	0.75	99	60	40
		$CDCl_3$	0.75	99	49	51

[a] As judged by disappearance of compound **1-6**, upon monitoring the reaction mixture by TLC, ^{1}H NMR or GC analysis.

The syn : anti ratio, for the epoxidation reactions with DMD and mClPBA of the same substrate, are almost identical to each other (Tables 1 and 2). This is particularly true when selectivities in solvents with similar dielectric constant [CCl_4 /Acetone (9 : 1) for DMD vs Benzene or CH_2Cl_2 for mClPBA] are compared. The only exception to this parallelism was the alkene **2**, where the peroxyacid reaction showed a higher syn facial selectivity.

COMPUTATIONAL METHOD

Calculations reported in this paper were performed with the Gaussian 94 suite program.[29]



Scheme 3. Schematic depiction of the TSs for dioxiranes and peroxy acids epoxidation of cis-3,4-disubstituted-(CH_2X)-cyclobutenes. The dihedral angle β ($O_5YC_1C_2$) describes the approaching geometry of the reactants to the substrate double bond. Y is a dummy atom placed in the middle of the C=C double bond.

Computational study was carried out using density functional theory with the Becke3LYP method using the 6-31G* basis set (B3LYP/6-31G*). Reagents (DHD, DMD, and HCOOOH), substrates (**1**, **5**, **7**, **8**), and transition structures (TSs) were fully optimized at the B3LYP/6-31G* level. Each transition structure gave only one imaginary harmonic vibrational frequency corresponding to the formation of the new C-O (C_1-O_5 and C_4-O_5) bonds of the forming epoxide and lengthening of the dioxirane O_5-O_6 bond (see Scheme 3 for numbering). Charges cited in the discussion are Mulliken charges. Geometric parameters as well as $\Delta H^{\neq}$ and $\Delta S^{\neq}$ [33] for all the calculated structures are available on request.

COMPUTATIONAL RESULTS AND DISCUSSION

The most noteworthy feature of the epoxidation reactions of substrates **3-7** (with both DMD and mClPBA) is the observation that in all cases the syn isomer is dominant, particularly in low polar solvents (CCl_4 for DMD and benzene for mClPBA). Syn selectivity is at its minimum in the case of the parent **1** and introduction of electron attracting substituents brings about an increase in syn attack. Thus the stereochemical outcome of these reactions is clearly at odds with a steric control of facial selectivity. Therefore, the factors responsible for the observed syn selectivity must be different and should be identified.

We have already shown that the dimethylcyclobutene (**1**) ground state is characterized by a small out-of-plane anti bending of the olefinic hydrogens (α = - 1.2°, for the definition of the α angle see Scheme 3) which favors the syn attack (for example, in 1,3-dipolar cycloadditions)[20] being the effect, which gives rise to this bending, magnified at the TS. However, this factor should play a less important role in dioxirane and peroxy acid epoxidations because out-of-plane distortion of the cyclobutene double bond in the transition structures of these reactions is small (i.e., $|\alpha|$ <10° vs >20° in 1,3-dipolar cycloadditions).[30] Anyway, the anti bending of the olefinic hydrogens in cyclobutenes under study[30] favors the syn attack.

As for steric effect, at first sight it seems that the two cis methyl groups introduce a sizeable steric bias in favor of anti attack. However, is it actually a strong effect or is the peculiar geometry of TSs of these reactions that makes it very weak?

To get a deeper insight into the mechanism of these reactions we located syn and anti TSs in the hope that analysis of their energies, geometries and charges (on those atoms that are close to the reaction center) could help us to explain the observed facial selectivity.

B3LYP/6-31G Transition structures for the epoxidation of cis-3,4-dimethylcyclobutene with DHD and DMD*

First we located the syn and anti transition structures (TSs) of the reactions of dioxirane (DHD) and dimethyldioxirane (DMD), respectively, with cis-3,4-dimethylcyclobutene at a good theory level, i.e., with the B3LYP/6-31G* method. Only exo (i.e., with the dioxirane substituents on the opposite side with respect to the cyclobutene ring) TSs were investigated because endo TSs can hardly compete with their exo counterparts as a result of strong steric interactions (in particular in the DMD reactions).[10]

Geometries of anti (**DHD-1a**) and syn (**DHD-1s**) TSs (see Figure 2) of the DHD epoxidation are very similar to each other. For example, the oxirane forming bonds are only 0.04 Å longer in the syn than in the anti TS (see Table 3). Both TSs have a concerted synchronous spiro butterfly structure, with the plane of the dioxirane ring and the plane of the forming oxirane almost perpendicular to each other. As for this aspect as well as for the YO_5O_6 angle (YO_5O_6 = 166°, see Scheme 3) both TSs closely resemble the TS of the DHD-ethene reaction (YO_5O_6 = 165°).[6,7,10]

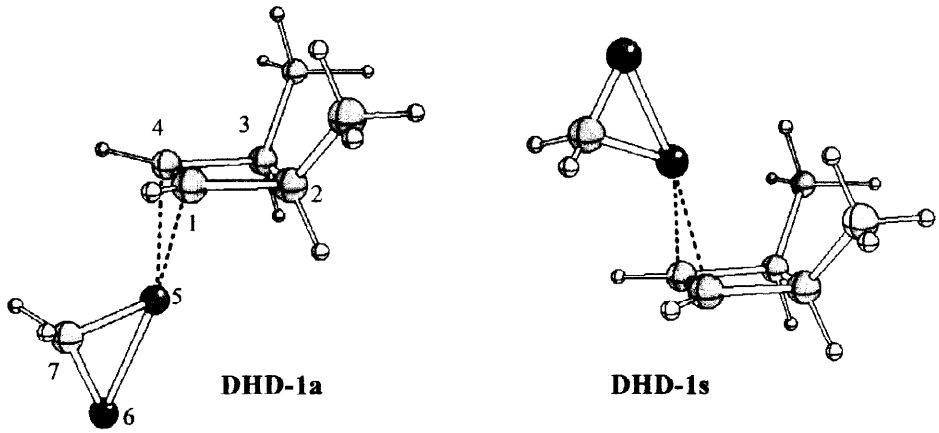


Figure 2. B3LYP/6-31G* anti (**DHD-1a**) and Syn (**DHD-1s**) TSs for the reaction of DHD with **1**.

Introduction of two methyl groups in the dioxirane, (passing from DHD to DMD) does not significantly modify the TS geometries (**DMD-1a** and **DMD-1s**). In particular, it is surprising, as can be easily realized by inspection of the geometry details listed in Table 3, how even the very small geometry variations observed on passing from syn to anti TS of the DHD reaction are almost exactly reproduced in the TSs of the DMD reaction. Also TS dipole moments of the two reactions are similar with the syn TSs less polar by ≈ 0.5 D than the anti ones. Electronic activation energies of the DMD reaction are higher, by ≈ 20 kJ/mol (Table 3), than those of the DHD reaction but relative energies, $E^{\neq}_{rel} = \Delta E^{\neq}_{anti} - \Delta E^{\neq}_{syn}$, are once again similar.

The syn TSs are predicted to be slightly more stable than their anti counterparts ($E^{\neq}_{rel}$ = 3.85 and 5.19 kJ/mol, respectively, for DHD and DMD reaction) even when free activation enthalpies are considered (e.g., $G^{\neq}_{rel} = \Delta G^{\neq}_{anti} - \Delta G^{\neq}_{syn}$ = 3.68 kJ/mol DMD reaction).[35] Thus gas phase computational data overestimate syn selectivity given that experimental results shows that the preference for syn attack in solution should not exceed 0.63 kJ/mol.

The evaluation of the steric effect of the two methyl groups in the epoxidation of the cyclobutene **1** is of interest since the syn face appears to be more crowded than the anti one. We have repeatedly shown that repulsive, either steric or electrostatic interactions are reflected in an increase of the inclination of the trajectory of approach of the attacking reagent to olefin.[20,37] The approaching trajectory is described by the dihedral angle β (i.e., = $O_5YC_1C_2$, see Scheme 3). Thus it was not surprising to find that there is a significant widening of the the β angle on passing from the TS of ethene reaction (≈ 90°) to the syn TSs of dimethylcyclobutene reaction (≈ 99°). However, somewhat unexpectedly, the β angle does not significantly change on going from syn TSs to the corresponding anti TSs (≈ 98°).

The observation of the substantial invariance of the β angle for syn and anti epoxidations is very important because it convincingly demonstrates that the syn and anti faces of cis-3,4-dimethylcyclobutene are sterically almost equivalent for dioxirane attack. The particular geometry of this attack, which takes place at the center of the double bond with an S_N2 like O_6---O_5/π alignment (i.e., YO_5O_6 = 166° and 172° for DHD and DMD, respectively), seems to be best suited to avoid strong steric interactions between the dioxirane oxygens and the hydrogen atoms of the methyl groups of **1**. The distance between O_5 and the nearest methyl hydrogens, 2.48 Å, in syn TSs supports this conclusion and one could even suggest that there is a weak attractive interaction between these atoms.

Table 3. Electronic Energies (E)[a], Electronic Activation Energies ($\Delta E^{\neq}$),[b] Relative Electronic Activation Energies ($E^{\neq}_{rel}$),[c] Bond lengths (O_5-O_6, O_5-O_7, C_7-O_6, C_1-O_5)[d], Plane (YO_5O_6)[e] and Dihedral Angles (β = $O_5YC_1C_2$),[e] Dipole Moments (μ),[f] of Reagents and TSs at B3LYP/6-31G* Level of Theory.

Structure	E[a]	$\Delta E^{\neq}$[b]	$E^{\neq}_{rel}$[c]	O_5-O_6	O_5-C_7	C_7-O_6	C_1-O_5	YO_5O_6	β	μ
DHD[g]	-189.615552	-	-	1.506	1.391	1.391	-	-	-	2.53
DMD[g]	-268.268944	-	-	1.505	1.403	1.403	-	-	-	2.89
HCOOOH[h]	-264.879654	-	-	1.441	-	1.341	-	-	-	1.35
TS-DHDethene[g]	-268.182377	54.14	-	1.873	1.454	1.321	2.012	165.0	90.0	4.86
TS-DMDethene[g]	-346.827906	74.81	-	1.887	1.509	1.321	1.978	172.0	90.0	4.53
1	-234.604048	-	-	-	-	-	-	-	-	0.14
TS **DHD-1a**	-424.203830	41.42	3.85	1.870	1.440	1.327	2.047	165.7	98.5	5.18
TS **DHD-1s**	-424.205307	37.57		1.850	1.436	1.331	2.084	165.8	99.9	4.62
TS **DMD-1a**	-502.849264	62.30	5.19	1.894	1.494	1.324	2.004	171.9	98.2	4.86
TS **DMD-1s**	-502.851242	57.11		1.874	1.486	1.329	2.037	172.3	99.1	4.34
(o)-7	-857.194677	-	-	-	-	-	-	-	-	3.10
TS **DHD-7a**	-1046.789971	53.18	5.69	1.883	1.453	1.322	2.010	166.2	98.5	3.58
TS **DHD-7s**	-1046.792130	47.53		1.867	1.451	1.335	2.044	166.3	99.9	6.41
(i)-**8**	-857.194827	-	-	-	-	-	-	-	-	2.93
TS **DHD-8a**	-1046.793046	45.52	- 23.01	1.878	1.449	1.324	2.028	166.3	97.6	2.54
TS **DHD-8s**	-1046.784280	68.53		1.875	1.451	1.322	2.022	162.6	107.7	6.83
5H'[i]	-1482.140552	-	-	-	-	-	-	-	-	4.46
TS **DHD 5H'a**	-1671.733135	60.29[j]	22.30	1.878	1.451	1.324	1.905 2.122[k]	165.8	97.2	8.65
TS **DHD 5H's**	-1671.741628	37.99[j]	-	1.859	1.450	1.328	2.070 2.046[k]	169.0	97.7	2.06
TS **DHD-5H"a**	-1671.731714	64.02[j]	23.39	1.874	1.458	1.320	1.996	166.4	98.2	8.80
TS **DHD-5H"s**	-1671.740629	40.63[j]	-	1.856	1.449	1.329	2.060	169.4	97.2	2.29
TS **anti, exo-1**	-499.465967	46.61	2.76	1.840	-	1.291	2.070	177.6	98.0	4.08
TS **syn, exo-1**	-499.466980	43.93		1.821	-	1.294	2.103	178.4	99.0	3.54
TS **anti, endo-1**	-499.463802	52.26	6.02	1.849	-	1.289	2.070	178.8	106.1	4.10
TS **syn, endo-1**	-499.466109	46.23		1.843	-	1.287	2.089	178.3	110.8	3.81

[a] Hartree. [b] kJ/mol. [c] $E^{\neq}_{rel} = \Delta E^{\neq}_{anti} - \Delta E^{\neq}_{syn}$, in kJ /mol, positive $E^{\neq}_{rel}$ values means syn facial selectivity. [d] In Å. [e] In degree. [f] In Debye. [g] Data from ref. 10 and 11. [h] Data from ref. 12. [i] **5H** most stable conformation. [j] The activation electronic energies have been calculated relatively to the most stable conformation of **5H**, i.e., **5H'**. [k] C_4-O_5.

Recently, Houk et al. have stressed the role of torsional interactions in governing facial selectivity of the epoxidation.[21] Staggering between the oxirane bonds being formed and the allylic C_2-H and C_3-H bonds in anti TSs (112°) is lower than the corresponding staggering involving the allylic C_2-C and C_3-C (122°) in syn TSs. This effect should slightly favor syn attack.

To conclude, the low steric effect which disfavors the syn attack is compensated by other weak effects (i.e., torsional factors, anti distortion of olefinic hydrogens in the substrate, etc.) which favor this approach thus explaining the almost equimolar mixture of epoxides obtained in the epoxidation of cis-3,4-dimethylcyclobutene.

The very high similarity of geometries, dipole moments and relative electronic energies for TSs of the epoxidation reaction of dimethylcyclobutene with DHD in comparison with that with DMD is noteworthy. Moreover this similarity seems to be the rule in all the epoxidations where substituents on dioxirane are not involved in strong steric interactions. This means that one can locate exo TS structures for the DHD epoxidations of cyclobutenes more complex than **1**, such as **7** and **8**, at good theory level and then use these computational data for meaningfully discuss experimental result obtained with DMD.

Transition structures for the epoxidation of cis-3,4-dimethylcyclobutene with HCOOOH

In the case of HCOOOH epoxidation reaction of **1** we located all the four possible TSs that are reported in Figure 3. They all have a concerted spiro butterfly structure with the breaking O_6---O_5 bond almost co-linear with the π orbital axis (i.e., YO_5O_6 ~ 178-179°). Geometries of the syn,exo and anti,exo TSs (**syn,exo-1** and **anti,exo-1**, that is, the two TSs with the peroxyacid hydroxylic hydrogen pointing away from the cyclobutene ring) are very similar, as far as the core of the reacting system is concerned, to the corresponding TSs of dioxirane epoxidation as illustrated by the β values (99° for **syn,exo-1** and 98° **anti,exo-1** vs 100° and 99° respectively, for syn and anti DHD TSs). Thus, arguments about the facial selectivity reported in the previous section holds also for peroxy acid epoxidation.

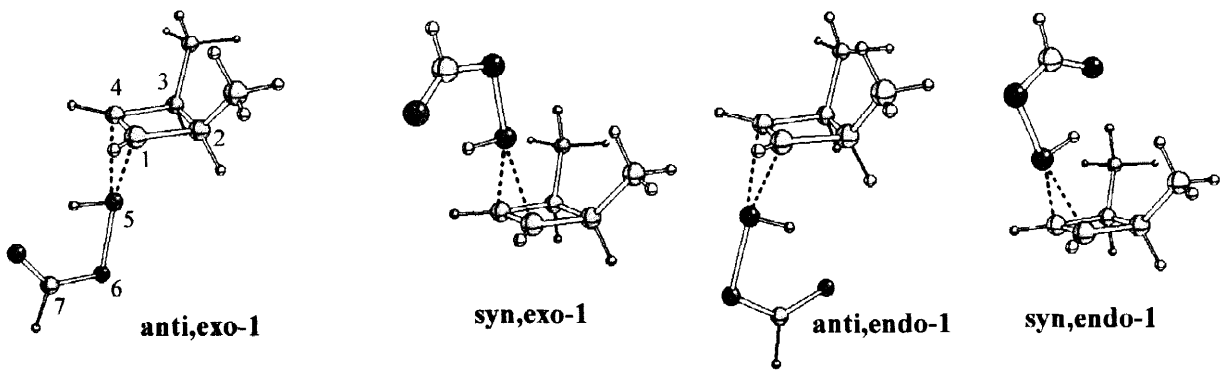


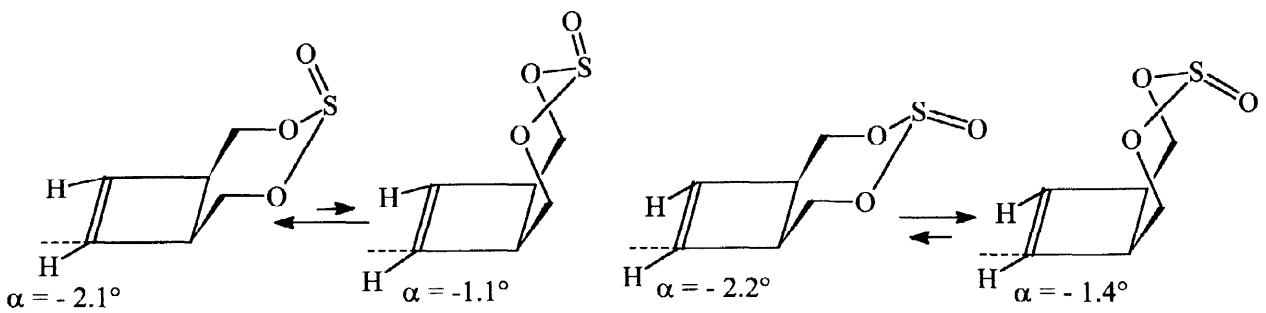
Figure 3. B3LYP/6-31G* TSs for the reaction of peroxyformic acid with **1**.

The two endo TSs (i.e., those ones with the peroxy acid hydroxylic hydrogen facing the methyl groups) are less stable than their exo counterparts (**syn,endo-1** less stable than **syn,exo-1** and **anti,endo-1** less stable than **anti,exo-1**). The lower stability of the endo TSs is the result of their higher steric congestion as convincingly demonstrated by the larger values of the β angle (see Table 3) with respect to exo TSs.

However, it is surprising that the more crowded of the two endo TSs, that is, the syn one (**syn,endo-1**, β = 111°), exhibits a lower activation energy than its anti counterpart (**anti,endo-1**, β = 106°) [$E^{\neq}_{rel}$ = $\Delta E^{\neq}_{anti,endo-1}$ - $\Delta E^{\neq}_{syn,endo-1}$ = 6.02 kJ/mol (Table 3)]. The same observation holds for activation enthalpy ($H^{\neq}_{rel}$ = $\Delta H^{\neq}_{anti,endo-1}$ - $\Delta H^{\neq}_{syn,endo-1}$ = 5.86 kJ/mol)[35] and to a somewhat reduced extent (as syn,endo is disfavored by entropy factors by 11.34 J/mol K)[35] for free activation enthalpy ($G^{\neq}_{rel}$ = $\Delta G^{\neq}_{anti,endo-1}$ - $\Delta G^{\neq}_{syn,endo-1}$ = 2.68 kJ/mol)[35]. Once again one can invoke the syn pyramidalization of the dimethylcyclobutene π bond as a factor that favors syn attack. This effect certainly operates but it is not strong enough to explain the computational observation. In fact, the energy required to deform the dimethylcyclobutene from ground state geometry to geometry it assumes in the **syn,endo-1** and **anti,endo-1** TSs is 3.0 kJ/mol and 6.4 kJ/mol, respectively. Thus, the out-of-plane deformation effect gives rise to an electronic energy stabilization by 3.4 kJ/mol for the **syn,endo-1** over the **anti,endo-1**. This observation demonstrates that a further syn orienting effect (most probably a stabilizing through space interaction between the peroxy acid moiety and the methyl groups) is operative. However we cannot reliably specify the nature (electrostatic, dispersion forces) of such interaction.

Conformers of cyclic sulfites **7** *and* **8**

A conformational search showed that the configurationally stable diastereoisomeric sulfites **7** and **8** exhibit two minima corresponding to conformers with the two oxygens of the seven membered ring pointing inside [(i) conformation] and, respectively, outside [(o) conformation] with respect to the cyclobutene ring (as depicted in Scheme 4). According to B3LYP/6-31G* geometry optimization (o)-**7** is much more stable than (i)-**7** (by 22.45 kJ/mol) while (i)-**8** is much more stable than (o)-**8** (by 24.27 kJ/mol). This large difference (which is certainly present also in the corresponding TSs) led us to assume that the contribution of TSs deriving from the two less stable conformations [(i)-**7** and (o)-**8**, respectively] to the product distribution is negligible. Consequently, we located only the syn and anti TSs arising from conformers (o)-**7** and (i)-**8**. This conformational choice is also consistent with the solid state conformation of the seven membered ring in the final epoxides (see Figure 1).



Scheme 4

Transition structures for the epoxidation of cyclic sulfites **7** *and* **8** *with DHD.*

The four B3LYP/6-31G* transition structures for the reaction of DHD with sulfites (o)-**7** and (i)-**8**, are depicted in Figure 4. All of them exhibit, once again, the well established spiro-butterfly array of atoms at the reaction center.

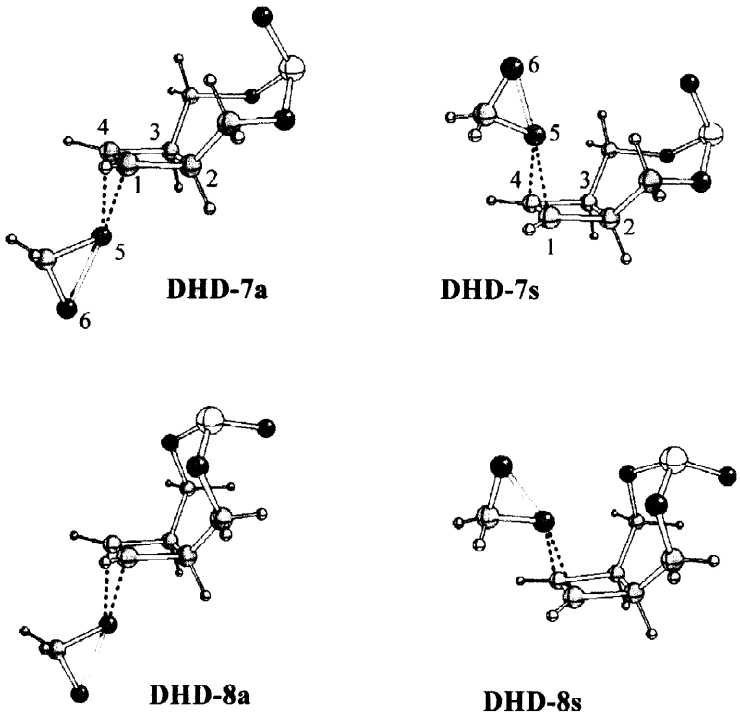


Figure 4. B3LYP/6-31G* TSs for the reaction of DHD with sulfites (o)-**7** and (i)-**8**

The syn and anti TSs for the reaction of (o)-**7** (**DHD-7s** and **DHD-7a**) feature the very same DHD trajectory inclinations (β = 100° and 99°, respectively) as those of the syn and anti TSs of the DHD reaction with dimethylcyclobutene. Thus, also the steric shielding of the syn face of (o)-**7** is very small. Computational data satisfactorily reproduce the observed facial selectivity of **7**, by predicting the syn TS more stable by 5.69 kJ/mol [as compared to the experimental (CCl_4/acetone) $G^{\neq}_{rel}$ value of 2.97 kJ/mol)] than the anti one, as well as the lower reactivity of **7** in comparison to **1** (calculated electronic activation energy for the epoxidation of **1** is 6.3 kJ/mol lower than that of **7**). However, it should be emphasized that calculated data are gas phase data. Thus, given that the syn TS **DHD-7s** has a higher dipole moment than that of the anti TS **DHD-7a** an increase in syn selectivity should be anticipated on going from gas phase to solution. That is, calculations actually overestimate syn facial selectivity for compound **7**.

A complete reversal of facial selectivity of the DHD epoxidation was experimentally observed on passing from **7** to **8**, only the anti epoxide was detected with the latter cyclobutene. Consistently, the syn transition structure (**DHD-8s**) has a much higher electronic activation energy (23.01 kJ/mol) than the anti transition structure (**DHD-8a**). The strong repulsions present in the syn TS **DHD-8s** (whose electrostatic origin will be commented later on) are clearly reflected in the widening of the β angle (108° in **DHD-8s** vs 98° in **DHD-8a**) and narrowing of the YO_5O_6 angle (163° in **DHD-8s** vs 166° in **DHD-8a**).

Transition structures for the epoxidation of **5** *with DHD.*

At this point we were ready to address the problem of face selectivity in the dioxirane epoxidation of cis-3,4-bis(mesyloxymethyl)-1-cyclobutene (**5**), the most facially selective of the cyclobutenes used. However, the size of this system is too large to be amenable to good level calculations also considering the conformational freedom of this derivative with acyclic substituents.

Thus to simplify the problem, we replaced both the methyl groups attached to the sulfur atoms in **5** with hydrogen atoms. The PM3 potential energy surface of such substrate (**5H**), exhibits ten local minima within 7.95 kJ/mol. These isomers differ from each other for the conformation of both the $CH_2OS(H)O_2$ branches. Similar conformers (**5H'**, **5H''** etc.) have been located at the B3LYP/6-31G* level.

The syn and anti transition structures of DHD epoxidation of **5H** were then built with a procedure similar to the "rigid TS model" used in transition state modeling with empirical force-field:[34] the position of the atoms of the dioxirane and cyclobutene ring (which are involved in bonding changes) were fixed at the geometry of the B3LYP/6-31G* syn and anti TSs for DHD epoxidation of cis-3,4-dimethylcyclobutene while the geometries of the $CH_2OS(H)O_2$ branches were optimized with the semiempirical PM3 method.[32]

We will refer to these transition structures as *pseudo* TSs in order to avoid confusion with the B3LYP/6-31G* TSs (true first order saddle points).[6]

Using the above procedure we located seven *pseudo* syn and eight *pseudo* anti TSs whose energies were then calculated at the B3LYP/6-31G* level by single point calculations. We found that all the pseudo syn TSs are more stable than all the pseudo anti TSs and that in the syn-anti pairs the syn derivative is always much more stable (by > 14.77 kJ/mol) than the anti isomer. For example, the electronic energy difference between the most stable syn TS and the most stable anti TS is 23.43 kJ/mol. This energy difference corresponds to higher face selectivity than that observed by experiment.

A weak point of the above approach is that the "reaction core" is also fixed at a synchronous bond forming geometry for the cyclobutene conformers which lack a symmetry plane. In order to evaluate reliability of this approach and to assess whether it leads to an overestimation of syn selectivity, we located two (out of seven) couples of true syn-anti TSs,[38] using the B3LYP/6-31G* method (see Figure 5), starting from the first and second most stable syn-anti pairs of *pseudo* TS geometries.

The most stable couple of the DFT syn-anti TSs (**DHD-5H's** and **DHD-5H'a**, respectively) features a concerted asynchronous attack while the other couple (**DHD-5H''s** and **DHD-5H''a**) show a synchronous approach. It is gratifying that the relative stabilities of DFT TSs substantially reproduce those of *pseudo* TSs, i.e., syn TSs are still much more stable than their anti counterpart (≤ 22.30 kJ/mol, Table 3).

Thus, computational data (gas phase) predict higher syn selectivity in comparison to the solution experiment [$G^{\neq}_{rel} = \Delta G^{\neq}_{anti} - \Delta G^{\neq}_{syn}$ = 5.44 kJ/mol (CCl_4/acetone)]. Such difference can be explained, at least in part, by solvation effects. The more polar (see dipole moments in Table 3) anti TSs (**DHD-5H'a** and **DHD-5H''a**, μ = 8.65 and 8.80 Debye, respectively) should be more stabilized than syn TSs (**DHD-5H's** and **DHD-5H''s**, μ = 2.06 and 2.29 Debye, respectively) in solution with a reduction of syn facial selectivity with respect to gas phase.

The experimetal results concerning the solvent effect on syn/anti ratios (Table 1) support this hypothesis. In fact, syn selectivity decreases, for the epoxidation of substrates **5** and **6**, when polarity of the solvent is increased. The syn epoxides drop from 90 to 79 % and from 82 to 63 %, passing from a CCl_4 to an acetone solution for **5** and **6** respectively. On the other hand the solvent effect is opposite for substrate **7**, which shows higher syn facial selectivity in acetone (77 %) than in CCl_4 solution (70 %). It is gratifying that the computed dipolar moments for anti TSs **DHD-7a** (μ = 3.58 D) is lower than the syn TSs **DHD-7s** (μ = 6.83 D). Computational studies concerning the solvent effect on the epoxidation reactions of the above (and related) substrates are in progress in our group.[36]

The ability of the "pseudo TS approach" descrided above, in reproducing B3LYP/6-31G* TSs is interesting as it opens the way to a reliable study of reasonably large systems. The potential of this method is under active investigation in our laboratory.

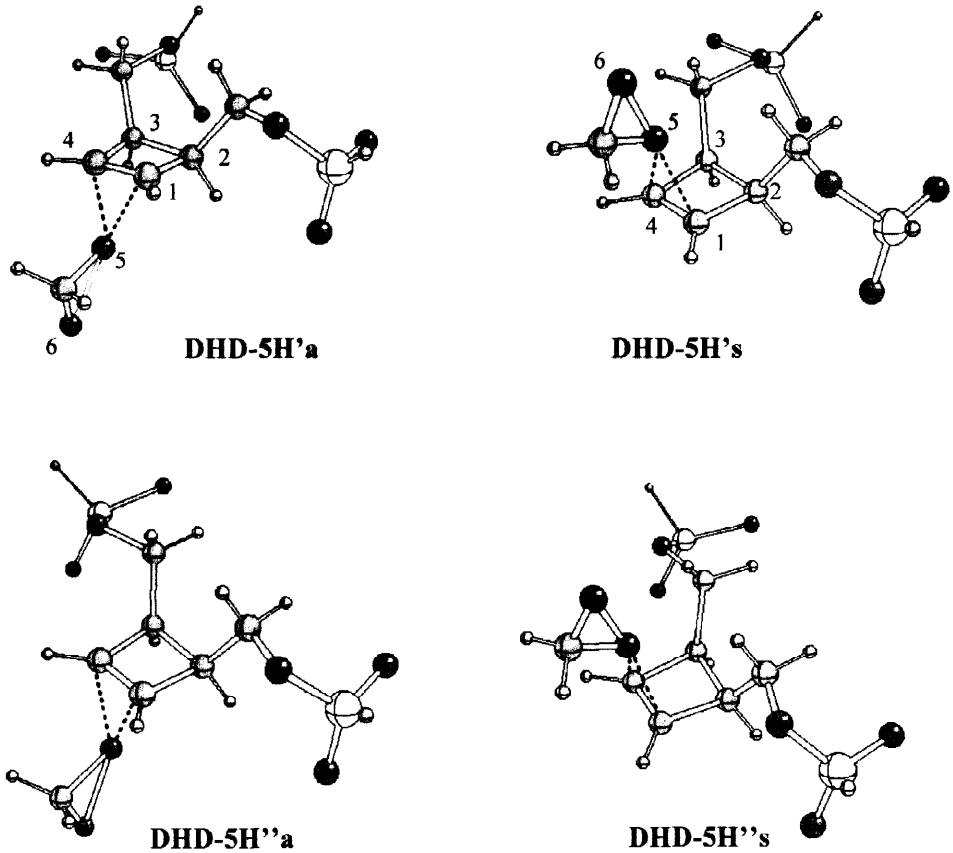


Figure 5. B3LYP/6-31G* TSs for the reaction of DHD with the first (**5H'**) and the second (**5H"**) most stable conformers of **5H**.

The origin of the syn selectivity in the epoxidation reactions

Syn attack by dioxirane and peroxy acids is certainly favored by syn pyramidalization (anti bending of the olefinic hydrogens, $\alpha < 0°$) of the olefinic carbons in cyclobutenes.[30,39] However, the key factor that we propose as the controlling effect of facial distereoselectivity is a Coloumbic interaction involving dioxirane peroxo oxygens, in particular the proximal O_5, and, the homoallylic hydrogens, of the allylic CH_2X (or the two homoallylic oxygen atoms in the case of **8**), group pointing towards the reaction center (see Scheme 3).

Initially, we will consider the facial selectivity exhibited by cyclic derivatives **7** and **8**. Dioxiranes are polarized reagents (μ = 2.53 D, for DHD)[10] having a net negative charge (- 0.21, for DHD)[11] localised on both the oxygen atoms. Negative charge on these oxygen atoms is larger in the transition structures than in the dioxirane itself (- 0.33 on O_5 and - 0.42 on O_6, in **DHD-7s**) as a result of electron transfer (> 0.3 electrons) from the nucleophilic double bond to the electrophilic dioxirane.

Moreover, due to the spiro butterfly array of the TS, the oxygen O_5 faces both the CH_2 groups (total net charge = + 0.26) in **DHD-7s**. In particular, O_5 is very close to one of the homoallylic hydrogen atoms (2.38 Å) which has a net positive charge of + 0.22. Therefore, an attractive (stabilizing) Coulombic interaction between the dioxirane oxygen and the hydrogens at the homoallylic position is certainly operative in **DHD-7s** . Such an interaction is absent in **DHD-7a**.

In the syn TS **DHD-8s** the two homoallylic oxygen atoms (net charge = - 0.52) of the sulfite moiety face the dioxirane oxygens O_5 and O_6 thus leading to a strong repulsive (destabilizing) Coulombic interaction which is missing in the anti TS **DHD-8a**.

The electrostatic hypothesis works well also for the epoxidation with cyclobutenes that bear acyclic substituents as shown by the TS located for the DHD epoxidation of **5H**. In the syn TSs (**DHD-5H's** and **DHD-5H"s**), like in the syn-TS **DHD-7s**, a couple of homoallylic hydrogen atoms (net charge + 0.24) point towards the proximal dioxirane oxygen atom (O_5, net charge = - 0.34). In both these TSs both the CH_2 groups are more positively charged (total net charge = + 0.32) than in the sulfite TS, due to the higher electron withdrawing character of the $OS(H)O_2$ group in comparison with that of the sulfite group.

In short the electron deficiency of the CH_2 groups, facing the reaction center, can be held responsible of the observed syn selectivity. The observed solvent effect on the syn facial selectivity provides experimental evidence that these interactions are operative.

We conclude that, in general, dioxiranes have the tendency to epoxidize the face which brings the homoallylic hydrogens of a CH_2X (with X electron attracting) group closer to the proximal dioxirane oxygen.

Our rationalization can also be applied to the DMD epoxidation reactions with homoallylic substituted cyclohexenes, already investigated by Murray *et al.*, bearing electron withdrawing substituents (Br, OC(O)Me, COOMe, and NHC(O)Ph).[3] It is simply a quantitative restatement on a computational basis of the stabilizing dipole-dipole interaction advanced by these authors.

The same electrostatic interaction that favors the syn epoxidation with dioxiranes, can also be active in the peroxy acid epoxidation of cyclobutenes **3-6**. Similarity of "reaction core" geometries of peroxy acid as compared to dioxirane epoxidations has already been stressed above. Moreover, electron transfer from the cyclobutene double bond to the peroxy acid is once again of ≈ 0.3 electrons and the negative net charge on the proximal peroxy acid oxygen (O_5) is $\approx$ -0.44. Consistently, the experimental syn : anti ratio listed in Tables 1 and 2 do not show, as a rule, any significant difference for the two types of epoxidising reagents. 3,4-Bis(hydroxymethyl)-cyclobutene **2** is the only exception (not only for face selectivity but also for reaction rate) suggesting that stabilizing hydrogen bonding effects in the mClPBA reaction are responsible for the different behavior of this derivative.

CONCLUSIONS

The syn facial selectivity observed in the dioxirane as well as peroxy acid epoxidations of cyclobutenes bearing a CH_2X substituent (when X is an electron withdrawing group) has been explained on the basis of deformation effect and of electrostatic interactions, in the transition state, involving the methylene hydrogens and the proximal peroxo oxygen of the epoxidising agent.

The experimental facial selectivity trends could be fairly well reproduced by B3LYP/6-31G* calculations thus confirming that this method provides a reliable tool to investigate selectivity and reaction rates of alkenes epoxidation reactions.

EXPERIMENTAL

Melting points are uncorrected. Elemental analyses were made on a Carlo Erba CNSH analyzer, model 1106. Infrared spectra were recorded as KBr discs, nujol or films on a Perkin-Elmer FT1000 spectrophotometer. ^1H and ^{13}C-NMR spectra were recorded in $CDCl_3$ solutions (unless otherwise stated) on a

Bruker AE 300 spectrometer with Me_4Si as internal standard. Protons were correlated by decoupling and COSY experiments, while protons were correlated to carbons by ^1H-^{13}C heterocorrelated spectra. GC analyses were performed with a DANI 6500, PTV injector, CP-Sil 19CB (25 m) capillary column using H_2 as a carrier. Preparative column chromatography was performed on Merk Silica gel 60 (79-230 mesh) using cyclohexane : ethyl acetate mixtures (from 95 : 5 to 60 : 40) unless otherwise stated. cis-3,4-Dimethyl-1-cyclobutene (**1**),[19,20] cis-1,2-dihydroxymethyl-3-cyclobutene (**2**),[23] cis-3,4-bis(acetoxymethyl)-1-cyclobutene (**4**),[33] cis-3,4-bis(mesyloxymethyl)-1-cyclobutene (**5**)[19] and cis-3,4-bis(tosyloxymethyl)-1-cyclobutene (**6**)[23] were prepared according to published procedures.

cis-3,4-Bis(methoxymethyl)-1-cyclobutene (3).

A solution of **2** (510 mg, 4.0 mmol) in dry THF (1 ml) was added dropwise to a stirring suspension of NaH in dry THF (5 ml), cooled under nitrogen to 0 °C. Methyl iodide (1.5 ml, 10.7 mmol) was added dropwise to the mixture, which was further stirred for 22 hrs at 0 °C under nitrogen. After that time, 18 ml of water was added dropwise to the reaction mixture under stirring (one hour) at room temperature. After adding other 10 ml of water the suspension was extracted ten times with diethylether (50 ml) and the organic solution was dried over $MgSO_4$. Evaporation left 637 mg (99%) of product **3** as a colorless oil. ^1H NMR ($CDCl_3$): δ 3.2 (m, 2 H, H-3 and H-4), 3.35 (s, 6 H, CH_3), 3.52 (m, 4 H, CH_2), 6.17 (s, 2 H, H-1 and H-2); ^{13}C NMR ($CDCl_3$) δ: 45.5 (C-3 and C-4), 58.7 (CH_3), 72.2 (C-5 and C-6), 138.4 (C-1 and C-2); IR (cm^{-1}): 3049, 2950, 1451, 1112. Anal. Calc. for $C_8H_{14}O_2$: C, 67.57; H, 9.92; O, 22.50. Found: C, 67.46; H, 9.94.

(1r,4c,7c)-3,5-dioxa-4-thia-bicyclo[5.2.0]non-8-ene-4-oxide (7) and (1r,4t,7c)-3,5-dioxa-4-thia-bicyclo[5.2.0]non-8-ene-4-oxide (8)

A solution of thionyl chloride (0.63 ml, 1.25 g, 11.0 mmol) in $CHCl_3$ (10 ml) was added dropwise to a solution of cyclobutene **2** (1.00 g, 8.8 mmol) and pyridine (1.8 ml, 21.9 mmol, distilled over KOH) in $CHCl_3$ (40 ml) keeping the temperature at 0 °C. After 1 hr a 5% $NaHCO_3/H_2O$ solution was added. The organic phase was extracted twice with 5 % HCl (2 x 50 ml), washed three times with H_2O and dried over $MgSO_4$. The solvent was evaporated and column chromatography of the red oily residue (using cyclohexane : ethyl acetate = 9 : 1 as eluent) afforded compound **7** (448 mg, 32 %) and **8** (827 mg, 59 %) in that order.

(1r,4c,7c)-3,5-dioxa-4-thia-bicyclo[5.2.0]non-8-ene-4-oxide (7). Colorless oil; ^1H NMR ($CDCl_3$): δ 3.41-3.44 (m, 2 H, H-3 and H-4), 3.80-3.84 (dd, 2 H, H-5, H-6, $J_{6,6'} = J_{5,5'} = 12.5$ Hz, $J_{4,5} = J_{3,6} = 5.1$ Hz), 4.90-5.00 (dd, 2 H, H-5', H-6', $J_{6,6'} = J_{5,5'} = 12.5$ Hz, $J_{4,5'} = J_{3,6'} \sim 12.5$ Hz), 6.13 (s, 2 H, H-1 and H-2); ^{13}C NMR ($CDCl_3$) 47.4 (CH), 60.0 (CH_2), 135.9 (CH). IR (cm^{-1}): 3045, 2944, 1438, 1369, 1230, 1180, 980. Anal. Calc. for $C_6H_8O_3S$: C, 44.99; H, 5.03; O, 29.96; S, 20.01. Found: C, 45.02; H, 5.01; S, 20.11.

(1r,4t,7c)-3,5-dioxa-4-thia-bicyclo[5.2.0]non-8-ene-4-oxide (8). Colorless oil; ^1H NMR ($CDCl_3$): δ 3.28 (s, 2 H, broad H-3 e H-4), 3.86-3.94 (dd, 2 H, H-5, H-6, $J_{6,6'} = J_{5,5'} = 13.3$ Hz, $J_{4,5} = J_{3,6} \sim 1$ Hz), 4.90-5.00 (dd, 2 H, H-5', H-6', $J_{6,6'} = J_{5,5'} = 12.5$ Hz, $J_{4,5'} = J_{3,6'} < 0.5$ Hz), 6.05 (s, 2 H, H-1 e H-2); ^{13}C NMR ($CDCl_3$) 49.0 (CH), 58.9 (CH_2), 136.3 (CH). IR (cm^{-1}): 3043, 2951, 1436, 1374, 1231, 1186, 946. Anal. Calc. for $C_6H_8O_3S$: C, 44.99; H, 5.03; O, 29.96; S, 20.01. Found: C, 45.05; H, 5.04; S, 20.07.

Epoxidation with DMD

A solution of DMD in CCl_4 : acetone = 9 : 1 (1 ml, 0.3 M, 3 mmol) prepared as described in ref. 26 was added at room temperature to sulfite **7** (100 mg, 0.625 mmol) and left at r.t. for 12 hrs. The solvent and DMD

in excess were evaporated to leave a colourless oil (109 mg). Using column chromatography (eluent: cyclohexane : ethyl acetate = 7 : 3) we obtained three fractions: the first one contained pure **15a** (15 mg, 0.08 mmol,), the second one a mixture of **15a** + **15s** (70 mg, 0.39 mmol), and the third one pure **15s** (10 mg 0.06 mmol) with a 85 % overall yield .

(1r,4c,7c,8t,10t)-3,5,9-Trioxa-4-thia -tricyclo[5.3.0.0^{8,10}]decane-4-oxide (15a). Colorless crystals m.p. = 109.8-110.0 °C (from cyclohexane : ethyl acetate = 9 : 1); ^{1}H NMR ($CDCl_3$) δ: 2.70-2.80 (m, 2 H, H-2, H-3); 3.75 (d, 2 H, H-1, H-4, $J_{1,2} = J_{3,4}$ ~1 Hz,), 3.76-3.83 (dd, 2 H, H-6, H-7, $J_{6,6'} = J_{7,7'} = 13.1$ Hz, $J_{2,6} = J_{3,7} = 5.5$ Hz), 5.05-5.15 (dd, 2 H, H-6', H-7', $J_{6,6'} = J_{7,7'} = 13.1$ Hz, $J_{2,6'} = J_{3,7'} \sim 13$ Hz), ^{13}C NMR ($CDCl_3$) δ: 46.0 (C-2 and C-3), 53.0 (C-1 and C-4), 56.9 (CH_2-O). IR (cm^{-1}): 2960, 1440, 1372, 1230, 1180, 980. Anal. Calc. for $C_6H_8O_4S$: C, 40.90; H, 4.58; O, 36.32; S, 18.20. Found: C, 40.79; H, 4.49; S, 18.16.

(1r,4c,7c,8c,10c)-3,5,9-Trioxa-4-thia -tricyclo[5.3.0.0^{8,10}]decane-4-oxide (15s). Colorless crystals, m.p. = 108.8 - 109.0 °C (from cyclohexane : ethyl acetate = 9 : 1); ^{1}H NMR ($CDCl_3$) δ: 3.05-3.12 (m, 2 H, H-2, H-3); 3.72-3.78 (dd, 2 H, H-6, H-7, $J_{6,6'} = J_{7,7'} = 12.6$ Hz, $J_{2,6} = J_{3,7} = 4.6$ Hz), 3.85 (s, 2 H, H-1, H-4), 5.10-5.20 (dd, 2 H, H-6', H-7', $J_{6,6'} = J_{7,7'} = 12.6$ Hz, $J_{2,6'} = J_{3,7'} \sim 13$ Hz), ^{13}C NMR ($CDCl_3$) δ: 44.7 (C-2 and C-3), 48.9 (C-1 and C-4), 58.1 (CH_2-O). IR (cm^{-1}): 2965, 1450, 1380, 1236, 1182, 985. Anal. Calc. for $C_6H_8O_4S$: C, 40.90; H, 4.58; O, 36.32; S, 18.20. Found: C, 40.80; H, 4.50; S, 18.27.

Likewise, **8** was epoxidised with DMD to give high yield (95 %) of **16a**.

(1r,4t,7c,8t,10t)-3,5,9-Trioxa-4-thia -tricyclo[5.3.0.0^{8,10}]decane-4-oxide (16a). Colorless crystals, m.p. = 83.9 - 85.0 °C (from cyclohexane : ethyl acetate = 9 : 1); ^{1}H NMR ($CDCl_3$) δ: 2.50 (s, 2 H, H-2, H-3); 3.95-4.01 (m, 2 H, H-6, H-7, $J_{6,6'} = J_{7,7'} = 13.6$ Hz), 3.99 (s, 2 H, H-1, H-4), 5.02-5.09 (d, 2 H, H-6', H-7', $J_{6,6'} = J_{7,7'} = 13.6$ Hz), ^{13}C NMR ($CDCl_3$) δ: 46.9 (C-2 e C-3), 56.3 (C-1 e C-4), 57.1 (CH_2-O). IR (cm^{-1}): 2949, 1456, 1380, 1229, 1170, 930. Anal. Calc. for $C_6H_8O_4S$: C, 40.90; H, 4.58; O, 36.32; S, 18.20. Found: C, 40.82; H, 4.55; S, 18.25.

Cis-3,4-dimethylcyclobutene as well as its epoxides are highly volatile compounds. Thus the epoxidation reaction with mClPBA for such a substrate has been performed in deuterated solvent ($CDCl_3$ and C_6D_6). Syn : anti ratio was evaluated by ^{1}H NMR and GC analysis on the reaction mixture.

9a ^{1}H NMR ($CDCl_3$) δ: 1.00 (d, 6 H, Me, $J_{2,Me} = J_{3,Me} = 7.3$ Hz), 2.15 (q, 2 H, H-2 and H-3 $J_{2,Me} = J_{3,Me} = 7.3$ Hz) 3.63 (s broad, 2 H, H-1 and H-4). ^{1}H NMR (C_6D_6) δ: 0.62 (d, 6 H, Me, $J_{2,Me} = J_{3,Me} = 7.3$ Hz), 2.00 (m, 2H, H-2 and H-3) 3.40 (s, 2 H, H-1 and H-4). ^{13}C NMR ($CDCl_3$) δ: 12.8 (CH_3), 43.3 (C-2 and C-3), 61.7 (C-1 and C-4).

9s ^{1}H NMR ($CDCl_3$) δ: ^{1}H NMR ($CDCl_3$) δ: 0.85 (d, 6 H, Me, $J_{2,Me} = J_{3,Me} = 6.6$ Hz), 2.48 (q, 2 H, H-2 and H-3, $J_{2,Me} = J_{3,Me} = 6.6$ Hz) 3.75 (s, 2 H, H-1 and H-4). ^{1}H NMR (C_6D_6) δ: 0.80 (d, 6 H, Me, $J_{2,Me} = J_{3,Me} = 7.3$ Hz), 2.00 (m, 2H, H-2 and H-3) 3.40 (s, 2 H, H-1 and H-4). ^{13}C NMR ($CDCl_3$) δ: 12.2 (CH_3), 42.2 (C-2 and C-3), 58.6 (C-1 and C-4).

We followed an identical procedure to that one described for **7** in the epoxidation of cyclobutenes **2-6**.

Epoxides **10a** and **10s** were characterised as a mixture.

10a; ^{1}H NMR (CD_3COCD_3) δ: 2.25 (m, 2 H, H-2 and H-3); 3.55-3.70 (m, 4 H, CH_2-O), 3.76 (s, 2 H, H-1 and H-4); ^{13}C NMR δ: 50.8 (C-2 and C-3), 60.1 (C-1 and C-4), 63.0 (CH_2-O).

10s; ^{1}H NMR (CD_3COCD_3) δ: 2.66 (m, 2 H, H-2 and H-3); 3.55-3.70 (m, 4 H, CH_2-O), 3.88 (d, 2 H, H-1 and H-4, $J_{1,2} = 1.7$ Hz); ^{13}C NMR δ: 49.5 (C-2 and C-3), 56.8 (C-1 and C-4), 63.2 (CH_2-O); IR (**10a** + **10s**) cm^{-1}: 3344, 2970, 1027. Anal. Calc. for $C_6H_{10}O_3$: C, 55.37; H, 7.74; O, 36.88. Found (**10a** + **10s**): C, 55.30; H, 7.71.

11a, colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.35 (m, 2 H, H-2, H-3); 3.29 (s, 6 H, MeO), 3.41-3.58 (m, 4 H, CH_2-O), 3.78 (d, 2 H, H-1, H-4, $J_{1,2}$ = 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ: 42.9 (C-2 and C-3), 56.3 (C-1 and C-4), 58.8 (OCH_3), 69.0 (CH_2-O); IR cm^{-1}: 2921, 2849, 1458, 1099. Anal. Calc. for $C_8H_{14}O_3$: C, 60.74; H, 8.92; O, 30.34. Found: C, 60.66; H, 8.96.

11s, colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.74 (m, 2 H, H-2, H-3); 3.2 (s, 6 H, CH_3O), 3.24 (m, 2 H, CH_2-O), 3.48 (m, 2 H, CH_2-O), 3.90 (s, 2 H, H-1, H-4); ^{13}C NMR ($CDCl_3$) δ: 41.8 (C-2 and C-3), 53.0 (C-1 and C-4), 58.9 (CH_3), 68.4 (CH_2); IR cm^{-1}: 2918, 2849, 1458, 1101. Anal. Calc. for $C_8H_{14}O_3$: C, 60.74; H, 8.92; O, 30.34. Found: C, 60.69; H, 8.90.

12a, colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.02 (s, 6 H, CH_3), 2.52 (m, 2 H, H-2 e H-3), 3.87 (d, 2 H, H-1 and H-3, $J_{1,2}$ = 1.7 Hz), 4.30 (m, 4 H, CH_2-O); ^{13}C NMR ($CDCl_3$) δ: 19.8 (CH_3), 41.2 (C-2 e C-3), 54.8 (C-1 and C-4), 59.6 (CH_2-O), 169.8 (C); IR (Nujol) cm^{-1} : 1736 , 1035. Anal. Calc. for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59; O, 37.34. Found: C, 56.01; H, 6.61.

12s, colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.05 (s, 6 H, CH_3), 2.80 (m, 2 H, H-2 and H-3), 3.91 (s, 2 H, H-1 and H-4), 4.00 (m, 2 H, CH_2-O), 4.17 (m, 2 H, CH_2-O); ^{13}C NMR ($CDCl_3$) δ: 20.9 (CH_3), 40.7 (C-2 and C-3), 52.4 (C-1 and C-4), 60.4 (C-6 and C-7), 170.8 (C); IR (Nujol) cm^{-1}: 1733, 1037. Anal. Calc. for $C_{10}H_{14}O_5$: C, 56.07; H, 6.59; O, 37.34. Found: C, 55.96; H, 6.63.

13a colorless oil; ^{1}H NMR (CD_3COCD_3) δ: 2.55 (m, 2 H, H-2 and H-3), 3.18 (s, 6 H, CH_3), 4.00 (d, 2 H, H-1 and H-4, $J_{1,2}$ = 1.7 Hz), 4.55 (m, 4 H, CH_2-O); ^{13}C NMR ($CDCl_3$) δ: 37.6 (CH_3), 43.7 (C-2 and C-3), 56.1 (C-1 and C-4), 67.6 (CH_2-O); IR (Nujol) cm^{-1}; 1349, 1169. Anal. Calc. for $C_8H_{14}O_7S_2$: C, 33.56; H, 4.93; O, 39.12; S, 22.39. Found: C, 33.69; H, 4.98; S, 22.44.

13s white crystals m.p. = 98 - 99 °C; ^{1}H NMR (CD_3COCD_3) δ: 3.05 (m, 2 H, H-2 and H-3), 3.12 (s, 6 H, CH_3), 4.05 (s, 2 H, H-1 and H-4), 4.15 (m, 2 H, CH_2-O), 4.35 (m, 2 H, CH_2-O); ^{13}C NMR ($CDCl_3$) δ: 37.4 (CH_3), 42.4 (C-2 and C-3), 52.9 (C-1 and C-4), 67.2 (CH_2-O); IR (Nujol) cm^{-1}: 1311, 1167. Anal. Calc. for $C_8H_{14}O_7S_2$: C, 33.56; H, 4.93; O, 39.12; S, 22.39. Found: C, 33.62; H, 4.95; S, 22.48.

Epoxidation with mClPBA

mClPBA (210 mg , 50 %, 0.61 mmol) was added portionwise to a stirred solution of **6** (154 mg, 0.36 mmol) in CH_2Cl_2 (5 ml) in the presence of solid $NaHCO_3$ (23 mg, 0.27 mmol) at 0 °C. The reaction mixture was stirred for 18 hrs at room temperature, then the suspension was washed twice with a saturated solution of $NaHCO_3$ and dried over $MgSO_4$. Evaporation of the solvent led to a crude product which consisted of unreacted **6** (46 mg, 30 %) and a mixture of syn : anti epoxides (**14s** : **14a** = 80 : 20). Purification by chromatography on silica gel (cyclohexane : ethyl acetate = 7 : 3) firstly led to **14a** (19 mg) then to **14s** (85 mg).

14a, colorless oil. ^{1}H NMR (C_6D_6) δ: 1.80 (s, 6 H, CH_3), 1.97 (m, 2 H, H-2 and H-3), 3.19 (d, 2 H, H-1 and H-4, $J_{1,2}$ = 1.83 Hz), 3.68 (m, 4 H, CH_2-O), 6.79 (m, 2 H, aromatics), 7.76 (m, 3 H, aromatics); ^{1}H NMR ($CDCl_3$) δ: 2.45 (m, 2 H, CH_3, H-2 and H-3), 3.79 (d, 2 H, H-1 and H-4, $J_{1,2}$ = 1.70 Hz), 4.14 (m, 4 H, CH_2-O), 7.38 (m, 4 H, aromatics), 7.76 (m, 4 H, aromatics); ^{13}C NMR (C_6D_6) δ: 21.2 (CH_3), 42.4 (C-2 and C-3), 54.8 (C-1 and C-4), 66.2 (CH_2-O), 128.2 (CH), 130.0 (C), 130.1 (CH), 144.8 (C); IR cm^{-1}: 2955, 2923, 1600, 1361, 1175, 1096, 968, 950. Anal. Calc. for $C_{20}H_{22}O_7S_2$: C, 54.78, H, 5.06; O, 25.54; S, 14.62. Found: C, 54.70, H, 5.09; S, 14.66.

14s, white crystals; m.p. = 76.5 - 77.3 °C; ^{1}H NMR (C_6D_6) δ: 1.80 (s, 6 H, CH_3), 2.12 (m, 2 H, H-2 and H-3), 3.07 (s, 2 H, H-1 and H-4), 3.70 (m, AB system 2 H, CH_2-O), 3.87 (m, AB system 2 H, CH_2-O), 6.71

(m, 4 H, aromatics), 7.74 (m, 4 H, aromatics); ^{1}H NMR ($CDCl_3$) δ: 2.45 (s, 6 H, CH_3), 2.84 (m, 2 H, H-2 and H-3), 3.76 (m, AB system, 2 H, CH_2-O), 3.79 (s, 2 H, H-1 and H-4), 4.00 (m, AB system 2 H, CH_2-O), 7.35 (m, 4 H, aromatics), 7.75 (m, 4 H, aromatics). ^{13}C NMR (C_6D_6) δ: 21.8 (CH_3), 41.8 (C-2 and C-3), 52.2 (C-1 and C-4), 66.5 (CH_2-O), 128.8, 130.6 (CH), 134.6, 145.2 (C); IR (Nujol) cm^{-1}: 1599, 1361, 1189, 1096, 967, 954. Anal. Calc. for $C_{20}H_{22}O_7S_2$: C, 54.78, H, 5.06; O, 25.54; S, 14.62. Found: C, 54.73, H, 5.04; S, 14.58.

*Synthesis of bromohydrins **17a** and **17s** from the corresponding epoxides*

HBr (48 % solution in water) was added to a solution of a 60 : 40 mixture of **9a** + **9s** (obtained by epoxidation of 91 mg of **1** [1.11 mmol] with DMD in acetone at - 40 °C for 6 hrs) in acetone (10 ml) at - 40°C. Reaction was allowed to proceed at - 40 °C. After 12 hrs the reaction mixture, allowed to warm up to room temperature, was neutralized with a saturated solution of $NaHCO_3$ and the acetone was evaporated. Residue was extracted twice with methylene chloride (4 ml). The combined organic phase were dried over $MgSO_4$ and evaporated to yield 129 mg (99 % yield) **17a** : **17s** mixture (60 : 40). Purification by flash chromatography on silica gel (cyclohexane : ethyl acetate = 8 : 2) yielded pure **17a** and **17s**.

17a, colorless oil; ^{1}H NMR ($CDCl_3$) δ: 1.05 (d, 3 H, Me-5, $J_{Me,\,H\text{-}3}$ = 7.6 Hz), 1.09 (d, 3 H, Me-6, $J_{Me\text{-}6,\,H\text{-}4}$ = 6.8 Hz), 2.10-2.25 (m, 1 H, H-3), 2.39-2.54 (m, 1 H, H-4), 2.58 (s, 1 H, broad, OH), 3.95 (ddd, 1 H, H-2, $J_{2,3}$= 8.3, $J_{1,2}$=7.3 $J_{2,4}$=1.2 Hz), 4.24 (dd, 1 H, H-1, $J_{1,4}$ = 8.5, $J_{1,2}$ = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ: 12.8 (CH_3), 13.3 (CH_3), 30.5 (C-4), 38.7 (C-3), 52.8 (C-1), 81.2 (C-2). IR cm^{-1}: 3421 (broad), 2943, 1458, 1035. Anal. Calc. for $C_6H_{11}OBr$: C, 40.25, H, 6.19; O, 8.94; Br, 44.62. Found: C, 40.37, H, 6.18.

17s, colorless oil; ^{1}H NMR ($CDCl_3$) δ: 0.98 (d, 3 H, Me-5, $J_{Me\text{-}5,\,H\text{-}3}$ =7.8 Hz), 1.03 (d, 3H, Me-6, $J_{Me\text{-}6,\,H\text{-}4}$ = 6.8 Hz), 2.20-2.30 (m, 1 H, H-4), 2.25 (s, 1 H, broad, OH), 2.65-2.80 (m, 1 H, H-3), 3.84 (dd, H-1, $J_{2,3}$ = 9.5, $J_{1,2}$ =7.6, $J_{2,4}$ = 1.2 Hz), 4.30 (dd, 1 H, H-2, $J_{1,4}$ = 8.5, $J_{1,2}$ = 7.3 Hz); ^{13}C NMR ($CDCl_3$) δ: 7.5 (CH_3), 11.7 (CH_3), 36.2 (C-4), 36.8 (C-3), 55.4 (C-1), 74.2 (C-2). IR cm^{-1}: 3429 (broad), 2939, 1450, 1043. Anal. Calc. for $C_6H_{11}OBr$: C, 40.25, H, 6.19; O, 8.94; Br, 44.62. Found: C, 40.30, H, 6.12.

*Synthesis of bromohydris **18a** and **18s***

HBr (48 % solution in water, 0.1 ml) was added to a solution of **14a** (20 mg, 0.045 mmol) in acetone (0.5 ml). Reaction was allowed to proceed at room temperature. After 4 hrs the reaction mixture was neutralized with a saturated solution of $NaHCO_3$ and the acetone was evaporated. Residue was extracted twice with methylene chloride (2 ml). The combined organic phase were dried over $MgSO_4$ and evaporated to give quantitatively **18a** (23 mg, 0.044 mmol) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ: 2.39 (s, 6 H), 2.42-2.55 (m, 1 H, H-3), 2.68-2.80 (m, 1 H, H-4), 3.15 (s, broad, 1 H, OH), 4.00-4.05 (dd, 1 H, H-1, $J_{1,4}$ = 10.4, $J_{1,2}$ = 8.2, $J_{1,3}$ < 0.5 Hz), 4.11-4.19 (m, 4 H, CH_2,) 4.20-4.26 (m, 1 H, H-2), 7.30-7-40 (m, 4 H, aromatics), 7.70-7.80 (m, 4 H, aromatics). ^{13}C NMR ($CDCl_3$) δ: 21.6 (CH_3), 29.1 (CH), 43.2 (CH), 45.8 (CH), 67.8 (CH_2), 68.5 (CH_2), 76.5 (CH), 127.9 (CH), 127.8 (CH), 129.88 (CH), 129.95 (CH), 132.2 (C), 132.4 (C), 154.2 (C). IR (Nujol) cm^{-1}: 3433 (broad), 3042, 2943, 1602, 1365, 1160, 1075, 960. Anal. Calc. for $C_{20}H_{23}O_7BrS_2$: C, 46.25; H, 4.46; O, 21.56; Br, 15.38; S, 12.34. Found: C, 46.18; H, 4.43; S, 12.40.

In a similar fashion **18s** has been prepared staring from **14s** as a colorless oil; ^{1}H NMR ($CDCl_3$) δ: 2.47 (s, 6 H), 2.52 (d, 1 H, OH, $J_{OH,\,H\text{-}2}$ = 6.5 Hz), 2.53-2.62 (m, 1 H, H-4), 2.96-3.06 (m, 1 H, H-3), 3.98-4.05 (dd, 1 H, H-1, $J_{1,4}$ = 9.5, $J_{1,2}$ = 7.0, $J_{1,3}$ < 0.5 Hz), 4.07-4.14 (m, 2 H, CH_2,) 4.16-4.23 (m, 1 H), 4.27-4.33 (m, 1 H), 4.37-4.45 (ddd, 1 H, H-2, $J_{2,3}$ = 14.0, $J_{1,2}$ = 7.0, $J_{2,OH}$ ~ 6.5 Hz); ^{1}H NMR (CD_3COCD_3) δ: 2.45 (s, 6 H), 2.55-2.65 (m, 1 H, H-4,), 2.96-3.06 (m, 1 H, H-3), 4.10-4.30 (m, 5 H), 4.45 (ddd, 1 H, H-2, $J_{2,3}$ = 8.5, $J_{2,3}$ =

7.3, $J_{2,OH}$ ~ 5.8 Hz), 5.15 (d, OH, 1 H, $J_{H\text{-}2,\ OH}$ = 5.8 Hz), 7.45 (m, 4 H, aromatics), 7.80 (m, 4 H, aromatics). ^{13}C NMR ($CDCl_3$) δ: 21.5 (CH_3), 39.3 (CH), 41.0 (CH), 47.1 (CH), 63.9 (CH_2), 65.5 (CH_2), 73.2 (CH), 127.82 (CH), 127.85 (CH), 129.90 (CH), 129.93 (CH), 132.1 (C), 132.3 (C), 145.09 (C), 145.16 (CH). IR (Nujol) cm^{-1}: 3388 (broad), 3038, 2940, 1599, 1360, 1165, 1080, 957. Anal. Calc. for $C_{20}H_{23}O_7BrS_2$: C, 46.25; H, 4.46; O, 21.56; Br, 15.38; S, 12.34. Found: C, 46.22; H, 4.44; S, 12.30.

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30. Cyclic sulfites **7**, **8** and **5H** show a syn pyramidalization of the olefinic carbon (anti bending of the olefinic hydrogens) higher than **1**. For conformers (o)-7, (i)-7, (o)-**8** and (i)-**8** the α angles (B3LYP/6-31G*) are -2.1, -1.2, -2.2 and -1.4° respectively. The two most stable conformation of **5H** (**5H'** and **5H''**) show an even higher pyramidalization with α angles of -2.3° and -3.0°. The α values in the calculated TSs (B3LYP/6-31G*) are as follows: **DHD-1a** +6.4°, **DHD-1s** -7.9°, **DHD-1a** +7.2°, **DHD-1s** -8.2°, **DHD-7a** +6.7°, **DHD-7s** -9.0°, **DHD-8a** +7.7°, **DHD-8s** -11.1°, **DHD-5H'a** +14.5°, +1.0°, **DHD-5H's** -8.4°, -8.1° (two different α values are reported because the TSs **DHD-5H'a** and **DHD-5H's** are asynchronous), **DHD-5H''a** +8.0°, **DHD-5H''s** -9.1°, **anti,exo-1** +6.7°, **syn,exo-1** -8.4°, **anti,endo-1** +7.8°, **syn,endo-1** -10.45°.
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35. Activation thermodynamic parameters are as follows: **DHD-1a**, $\Delta H^{\neq}$ = 44.89 kJ/mol , $\Delta S^{\neq}$ = -116.06 J/mol K, $\Delta G^{\neq}$ = 79.45 kJ/mol; **DHD-1s**, $\Delta H^{\neq}$ = 41.00 kJ /mol , $\Delta S^{\neq}$ = -119.75 J/mol K, $\Delta G^{\neq}$ = 76.69 kJ/mol; **DMD-1a**, $\Delta H^{\neq}$ = 65.22 kJ/mol, $\Delta S^{\neq}$ = -40.29 J/mol K, $\Delta G^{\neq}$ = 101.38 kJ/mol; **DMD-1s**, $\Delta H^{\neq}$ = 60.08 kJ/mol, $\Delta S^{\neq}$ = -129.03 J/mol K, $\Delta G^{\neq}$ = 98.58 kJ/mol; **DHD-7a**, $\Delta H^{\neq}$ = 56.11 kJ/mol, $\Delta S^{\neq}$ = -113.72 J/mol K, $\Delta G^{\neq}$ = 90.00 kJ/mol; **DHD-7s**; $\Delta H^{\neq}$ = 50.67 kJ/mol , $\Delta S^{\neq}$ = -120.58 J/mol K, $\Delta G^{\neq}$ = 88.49 kJ/mol; **DHD-8a**, $\Delta H^{\neq}$ = 48.49 kJ/mol, $\Delta S^{\neq}$ = -114.22 J/mol K, $\Delta G^{\neq}$ = 82.51 kJ/mol; **DHD-8s**, $\Delta H^{\neq}$ = 72.97 kJ/mol, $\Delta S^{\neq}$ = -104.52 J/mol K, $\Delta G^{\neq}$ = 106.57 kJ/mol; **anti, exo-1**, $\Delta H^{\neq}$ = 49.04 kJ /mol , $\Delta S^{\neq}$ = -121.80 J/mol K, $\Delta G^{\neq}$ = 85.35 kJ/mol; **syn,exo-1**, $\Delta H^{\neq}$ = 47.86 kJ /mol , $\Delta S^{\neq}$ = -122.84 J/mol K, $\Delta G^{\neq}$ = 82.84 kJ/mol; **anti endo-1**, $\Delta H^{\neq}$ = 54.77 kJ /mol , $\Delta S^{\neq}$ = -120.96 J/mol K, $\Delta G^{\neq}$= 90.88 kJ/mol; **syn, endo-1**, $\Delta H^{\neq}$= 48.74 kJ /mol , $\Delta S^{\neq}$= -132.26 J/mol K, $\Delta G^{\neq}$= 88.20 kJ/mol.
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38. Owing to excessive CPU time requirement, frequencies were not calculated for the Tss
39. For example, the energy required to deform the cyclic sulfite (o)-**7** from ground state geometry to geometry it assumes in the **DHD-7s** and **DHD-7a** TSs is 6.98 kJ/mol and 7.88 kJ/mol, respectively. Thus, the out-of-plane deformation effect gives rise to an electronic energy stabilization by 0.9 kJ/mol for the **DHD-7s** over the **DHD-7a**.