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Tetrahedron
Tetrahedron 62 (2006) 10623–10632

Intrazeolite photooxygenation of chiral alkenes. Control of facial selectivity by confinement and cation–π interactions

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Received 27 April 2006; revised 5 July 2006; accepted 5 July 2006
Available online 7 September 2006

Abstract—Depending on the nature of the substituents on the stereogenic carbon atom, the ene reaction of singlet oxygen with several chiral alkenes by confinement within thionin-supported zeolite NaY, may exhibit significant changes on facial selectivity by comparison to their photooxygenation reaction in solution. It is proposed that, apart from the conformational consequences as a result of the alkene confinement within the zeolite cavities, a synergism between Na^+–π interactions and singlet oxygen–Na^+ interactions plays a significant role in the transition states of ene hydroperoxidation. Within NaY, the diastereoselectivity may significantly depend on the site selectivity, as probed through specific deuterium labelling of trisubstituted alkenes bearing a *gem*-dimethyl group. In certain cases, a remote stereogenic centre relative to the reacting double bond may induce enhanced diastereoselection and regioselectivity.

1. Introduction

Mechanistic studies and synthetic applications of singlet oxygen ($^1O_2$) reactions with organic compounds, have attracted the interest of organic chemists for the past 50 years.[1] The singlet oxygen reactions are typically performed in a homogeneous environment in which the dissolved photosensitizing dye is vulnerable to decomposition. In recent years, however, immobilizing the dyes on solid supports has attracted considerable attention, as it contributes to the green character of the oxidation process, while their stability is considerably enhanced, as well.[2] Apart from the practical advantages of using solid materials as singlet oxygen generators, a large number of studies have been focused, on studying the product selectivity of the $^1O_2$ reactions by confining the reacting substrates within supramolecular assemblies as microreactors.[3] Typical examples are zeolites with small pores,[4] Nafion membranes[5] and surfactant vesicles.[6] One of the most practical and efficient systems, which has been studied extensively for the past 10 years is thionin or methylene blue-supported zeolite NaY.[7] In pioneering work, Li and Ramamurthy[8] confined through partial ion exchange dyes, that are organic cations, in the interior of the zeolite NaY supercages, and generated a novel photosensitizing system capable of producing very efficiently $^1O_2$ upon visible light irradiation. Pace and Clennan[9] improved the efficiency of methylene blue-supported NaY as a photosensitizing system, by replacing the solvent hexane with perfluorohexane. The fluorophobicity of the alkenes in perfluorohexane allows their facile migration into the zeolite cavities. Thus, the zeolite medium may be used for preparative scale photooxygenation reactions, without significant changes in product selectivity or loss of the reaction mass balance. In the same study, the upper limit of the $^1O_2$ lifetime within NaY was extrapolated to be around 7.5 μs. More recently, Ramamurthy and co-workers[10] measured directly the $^1O_2$ lifetime within NaY, and found to depend on the alumina content of the zeolite lattice and the intrazeolite water content.

From the early studies, it was clearly evident that a new trend existed for the intrazeolite photooxygenation of trisubstituted alkenes. The reaction is regioselective with predominant or even exclusive formation of the secondary allylic hydroperoxides.[8,11] Moreover, in contrast to the reaction in solution, enhanced reactivity of the less hindered allylic hydrogens was found through specific labelling in the photooxygenation of several *gem*-dimethyl trisubstituted alkenes within NaY.[12] Several models have been postulated to explain the intrazeolite regioselectivity trends,[1,7c] however, none of them is widely acceptable and each specific model is rather considered as a working hypothesis. Yet, the

Keywords: Singlet oxygen; Hydroperoxides; Zeolites; Regioselectivity; Diastereoselection; Cation–π interactions.
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doi:10.1016/j.tet.2006.07.102

majority of them consider a favourable electrostatic interaction between the intrazeolite alkali metal cations and $^1O_2$ in the transition state of the ene hydroperoxidation reaction. Apart from the changes in the regioselectivity for the case of trisubstituted alkenes, it was reported that isobutenylarenes afford within NaY primarily the ene products relative to the Diels–Alder cycloadducts, in a highly chemoselective manner.[13] This selectivity was attributed to the higher destabilization of an open zwitterion (leading to the [4+2] products) relative to a perepoxide intermediate (leading to the ene products) as a consequence of the strong Na^+–arene interactions. Generally, cation–π interactions seem to play a major role in intrazeolite reactions[14] and will be postulated as one of the main driving forces to explain the changes of the diastereoselection trends in the photooxygenation of the chiral alkenes presented throughout this paper.

The study of the diastereoselection in the electrophilic addition of $^1O_2$ to the π face of chiral alkenes is of primary interest in organic synthesis.[15] The confined environment of zeolite and cation–π interactions as well, might be expected to affect significantly the facial selectivity in the intrazeolite photooxygenation of chiral alkenes. One general aspect would be that blocking the less sterically hindered face of a double bond through cation binding within the zeolite, would leave the other face accessible to $^1O_2$ attack. For example, Na^+–π interactions have been postulated to alter the π facial photoreduction of some enone steroids confined within NaY,[16] relative to their reaction in a homogeneous environment. In addition, diastereoselection might be expected even in cases where a stereogenic centre resides at a remote position with respect to the reacting double bond. As a result of 'substrate-coiling' within the zeolite cavities, a remote chiral centre may be brought proximal to the reacting double bond and thus affect the facial selectivity. Ramamurthy and co-workers[17] have elegantly shown this aspect in the photochemical disrotatory electrocyclic reaction of a chiral tropolone ether. Having in mind these possible contributing parameters to the π facial selectivity of the intrazeolite reactions, we focused our interest on the photooxygenation of chiral alkenes bearing a stereogenic centre at the α- or at more remote positions with respect to the reacting double bond. In addition, specific labelling of the less hindered methyl group for the majority of the *gem*-dimethyl trisubstituted alkenes studied herein was accomplished, to examine the interplay of site selectivity on diastereoselection, as abstraction of an allylic hydrogen atom from the two geminal methyls occurs through the participation of two non-equilibrating diastereomeric perepoxide type-intermediates,[12c] which may induce a different degree of diastereoselection.

2. Results and discussion

2.1. Synthesis of chiral alkenes

The chiral alkenes (**1**–**7**) whose photooxygenation was studied are presented in Chart 1. The synthesis of **1**–**7** was accomplished by Wittig coupling of isopropylidenetriphenylphosphorane with the corresponding aldehydes. The necessary aldehydes for the synthesis of substrates **1** and **4** are commercially available, while the rest were prepared according to trivial procedures described in Section 4.

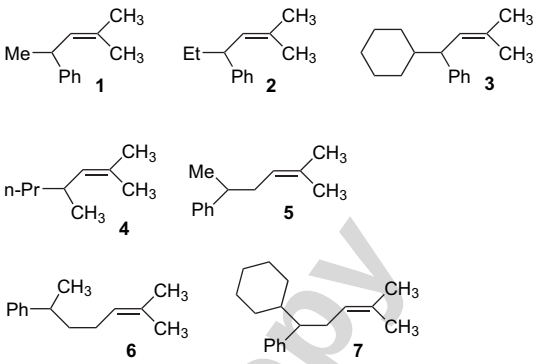


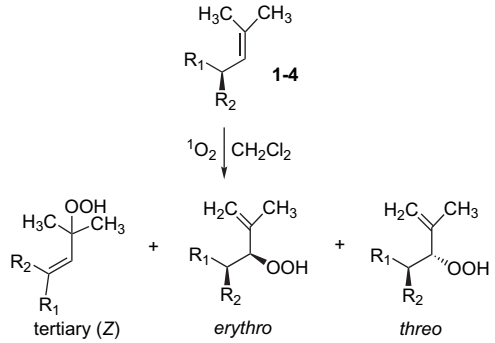
Chart 1. Structures of the chiral alkenes **1**–**7** whose intrazeolite photooxygenation was examined.

2.2. Diastereoselectivity in the photooxygenation of chiral alkenes bearing a stereogenic centre at the α-position with respect to the double bond (1–4)

Among the chiral alkenes presented in Chart 1, the first four (**1**–**4**) possess a stereogenic centre at the α-position with respect to the reacting double bond. The distribution of the ene products for the photooxygenation of **1**–**4** in solution (dichloromethane, methylene blue as sensitizer, 0 °C) is presented in Table 1. The *erythro* secondary allylic hydroperoxides were primarily formed relative to the *threo* isomers, while the labile tertiary allylic hydroperoxides were formed in up to 14% relative yield, depending on the nature of the substituents R_1 and R_2. Analysis by NOE clearly revealed that they have the *Z* configuration on the newly formed trisubstituted double bond. It is surprising,[18] from the first point of view, that alkene **3** in which the two substituents on the stereogenic carbon atom (phenyl and cyclohexyl) have more or less similar steric demands, affording the highest diastereomeric ratio among **1**–**4**. It is obvious, therefore, that for the phenyl-substituted alkenes **1**–**3**, steric effects cannot explain the stereochemical outcome. The possible reasons will be analyzed below.

Apart from the photooxygenation of **1** for which the relative configuration of the allylic hydroperoxides is known,[20] the

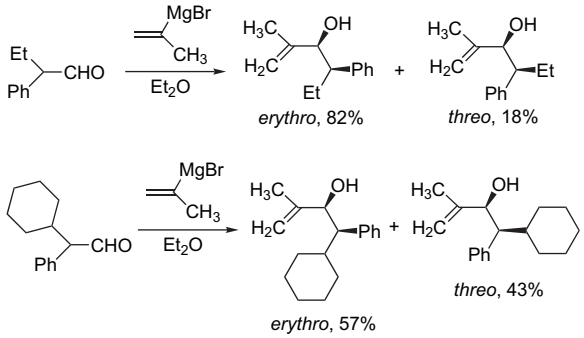
Table 1. Photooxygenation of chiral alkenes **1**–**4** in solution



Alkene	Tertiary (%)[a]	*erythro* (%)[a]	*threo* (%)[a]
R_1=Me, R_2=Ph (**1**)	6	72	22
R_1=Et, R_2=Ph (**2**)	10	70	20
R_1=Cyclohexyl, R_2=Ph (**3**)	14	71	15
R_1=Me, R_2=*n*-Pr (**4**)	—	62	38

[a] Relative percentages.

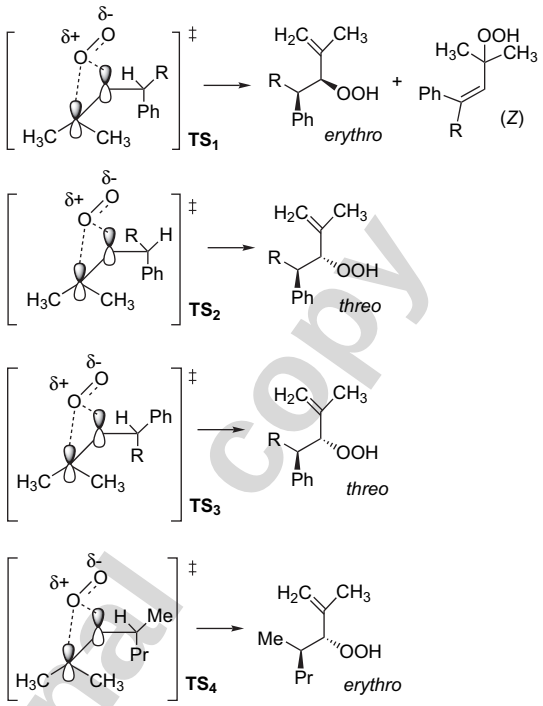
ene products for the case of **2** and **3** were reduced in situ with PPh_3 and the resulting allylic alcohols were compared to the diastereomeric alcohols produced from the reaction of 2-propenylmagnesium bromide with α-ethyl or cyclohexylphenylacetaldehyde (Scheme 1). It is well known[21] that the addition of organolithium or Grignard reagents to α-alkyl substituted phenylacetaldehydes is *erythro* diastereoselective. In our case, reaction of 2-propenylmagnesium bromide with 2-phenylbutyraldehyde afforded the allylic alcohols in a ratio *erythro*/*threo*=4.6/1, while α-cyclohexylphenylacetaldehyde gave a product ratio of *erythro*/*threo*=1.4/1. The predominant formation of the *erythro* allylic hydroperoxide in the photooxygenation of **4**, was reasonably assessed from the photooxygenation results of similar chiral trisubstituted alkenes[20] bearing alkyl substituents on the stereogenic centre.



Scheme 1. Addition of 2-propenylmagnesium bromide to α-substituted phenylacetaldehydes.

The selective formation of the *erythro* stereoisomer in the photooxygenation of **1**–**3** in solution can be explained considering preferential facial approach of $^1O_2$ to the double bond as shown in transition state $\mathbf{TS_1}$ of Scheme 2. The phenyl group is placed to the opposite face of the double bond with respect to the attacking singlet oxygen, due to the unfavourable oxygen–arene electronic repulsions. In addition, for $\mathbf{TS_1}$, the 1,3-allylic strain between the tertiary allylic hydrogen atom and the more hindered allylic methyl group is minimized. Abstraction of the suitably oriented tertiary allylic hydrogen atom leads to the formation of the minor (*Z*)-tertiary allylic hydroperoxides. Transition states $\mathbf{TS_2}$ and $\mathbf{TS_3}$, which lead to the *threo* diastereomers are expected to be less stable compared to $\mathbf{TS_1}$, due to the substantial 1,3-allylic strain between the R group and the proximal allylic methyl for the case of $\mathbf{TS_2}$, or to unfavourable oxygen–arene electronic repulsions for the case of $\mathbf{TS_3}$. By increasing the bulkiness of the alkyl group (R) from methyl to cyclohexyl, enhanced *erythro* diastereoselection is found as reasonably expected ($\mathbf{TS_1}$ vs $\mathbf{TS_2}$). For alkene **4**, the moderate *erythro* selectivity arises through the more favourable transition state $\mathbf{TS_4}$ in which the steric effects (methyl vs *n*-propyl) and the minimum 1,3-allylic strain as well, dictate the facial selectivity.

Photooxygenation of **1**–**4**[22] by confinement within thionin-supported zeolite NaY is highly regioselective, since only the secondary allylic hydroperoxides were obtained, however, with an inverse diastereoselection trend, which is more profound and even remarkable in the case of the cyclohexyl-substituted alkene **3** (Table 2). The *threo* diastereomers were

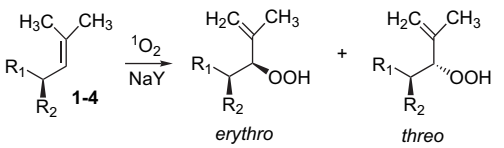


Scheme 2. Possible transition states for the photooxygenation of alkenes **1**–**4** in solution.

predominantly formed, and the ratio *threo*/*erythro* increases with increasing the bulkiness of the R group (for alkenes **1**–**3**).

The predominant formation of the *threo* secondary allylic hydroperoxides by zeolite confinement can be rationalized as follows. Taking into account the strong electrostatic interaction[23] of the phenyl ring to the Na^+ within the NaY supercages, the alkene most likely adopts the conformation shown in Scheme 3. Preferential attack of $^1O_2$ from the less hindered *top* face gives the major *threo* secondary allylic hydroperoxides, while attack from the less accessible *bottom* face gives the minor *erythro* diastereomers. As the bulkiness of the R group increases, the energy difference between the *threo* and *erythro* forming transition states increases as well, in favour of the *threo* isomer. The participation of the *threo*-forming transition state $\mathbf{TS_5}$ (Scheme 3), in which apart from the cation–arene interaction, a favourable $^1O_2$–Na^+ interaction operates cannot be excluded. In the case of alkene **4**, we postulate that preferential interaction of the Na^+ with the less hindered face of the double bond allows the *threo*-forming transition state $\mathbf{TS_6}$ (Scheme 3) to predominate

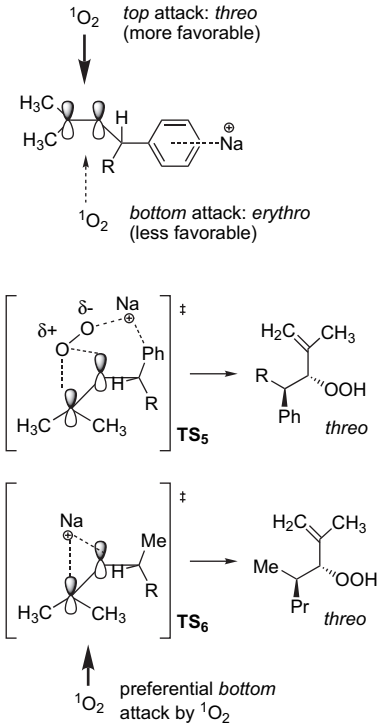
Table 2. Photooxygenation of chiral alkenes **1**–**4** within zeolite NaY



Alkene	*erythro* (%)[a]	*threo* (%)[a]
R_1=Me, R_2=Ph (**1**)	46	54
R_1=Et, R_2=Ph (**2**)	23	77
R_1=Cyclohexyl, R_2=Ph (**3**)	9	91
R_1=Me, R_2=*n*-Pr (**4**)	47	53

[a] Relative percentage.

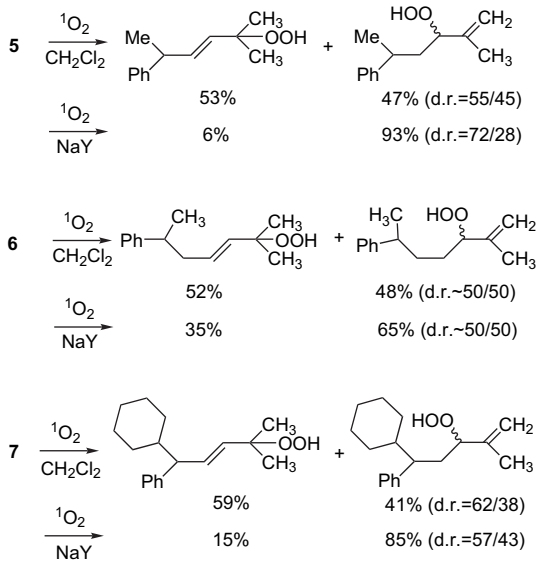
slightly. Furthermore, for alkene **4**, the change of the diastereoselection trend on going from the reaction in solution to the confined zeolite environment, is not as impressive as in the case of **1**–**3**. We postulate that since the electrostatic interaction between **4** and an Na^+ is not expected to be as strong[24] as with the phenyl-substituted alkenes **1**–**3**, reaction of $^1O_2$ with non-Na^+ bound alkene **4** conformers within NaY[25] may also occur.



Scheme 3. Possible *threo*-forming transition states for the photooxygenation of **1**–**4** within NaY.

2.3. Diastereoselectivity in the photooxygenation of chiral alkenes bearing a stereogenic centre at a remote position with respect to the double bond (5–7)

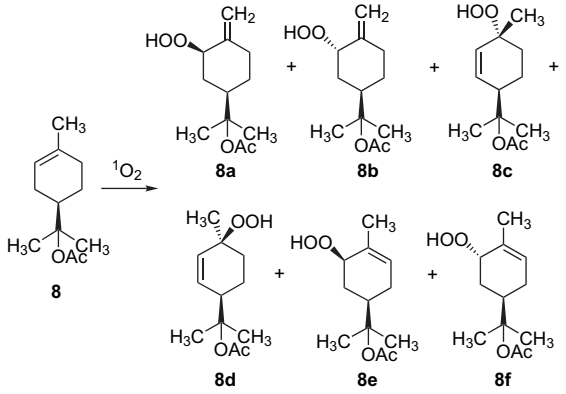
As we discussed earlier, due to the adsorption of the reactant alkenes in the confined environment, increased diastereoselectivity might be expected in cases where a chiral centre resides at a remote position with respect to the reacting double bond, as a consequence of 'substrate-coiling' in the limited space of zeolite cavities. To examine this interesting aspect we performed the photooxygenation of alkenes **5**,[26] **6**, and **7**, which possess a stereogenic centre at the β- or γ-position with respect to the double bond. Reaction of **5** with $^1O_2$ in solution gave the expected ene product distribution (secondary vs tertiary allylic hydroperoxides=47/53), while for the secondary hydroperoxides a low diastereomeric ratio was found (~10% dr, not specified). By NaY confinement, however, the reaction is 94% regioselective in favour of the secondary hydroperoxides (Scheme 4), and the diastereomeric ratio enhances significantly (dr=72/28). We postulate that, upon interaction of the alkene with the Na^+ within the cages, the substrate folds, and the chirality is 'transferred' close to the reaction centre (double bond). Consequently, the facial selectivity of $^1O_2$ to the double bond is significantly affected. For a further examination of this enhanced diastereoselection, we prepared alkene **7**,[27] in which the more bulky cyclohexyl group has replaced the methyl group on the stereogenic centre of **5**. Photooxygenation of **7** in solution gave a mixture of tertiary and secondary allylic hydroperoxides in a ratio 59/41, and a relatively enhanced diastereomeric ratio for the case of the secondary allylic hydroperoxides (dr=62/38, not specified). While the reaction by zeolite confinement is 85% regioselective in favour of the formation of the secondary allylic hydroperoxides, the diastereoselection was not enhanced, as in the case of **5**, but essentially slightly decreased to 57/43 (Scheme 4). We assume that the bulkiness of the cyclohexyl ring may force **7** at NaY to adopt a conformation in which the stereogenic centre may not become proximal to the reacting double bond, and thus, affect substantially the facial selectivity. We next studied the photooxygenation of the chiral alkene **6** (Scheme 4), which bears the same substituents on the stereogenic centre as alkene **5**, however, situated at the more remote γ-position with respect to the double bond. In solution, the expected regioselectivity trend was found, while the diastereomeric ratio for the secondary allylic hydroperoxides was negligible (by GC and ^1H NMR). Photooxygenation of **6** within NaY gave predominantly the secondary allylic hydroperoxides (65% relative ratio), yet, the diastereoselection, as for the reaction in solution, was negligible. We would like to point out the significant difference in the regioselectivity on going from **5** to **7** within NaY. The relative ratio of the tertiary allylic hydroperoxide in the case of **5** is remarkably low (6%) and increases to 35% for **7**. Similar regioselectivity changes had been reported by our group[12c] on studying the regioselectivity in the photooxygenation of structurally analogous phenyl-substituted alkenes and had been explained in terms of different substrate conformations within NaY which allow methylene allylic hydrogen abstraction to occur with different energetic consequences. From the above results we conclude that it is difficult to predict an enhancement of facial selectivity for the case of alkenes bearing remote stereogenic centres, since the relative bulkiness of the substituents in the interior of the zeolite cage, may or may not provide suitable proximity of the pre-existing chirality to the reacting double bond.



Scheme 4. Photooxygenation of chiral alkenes **5**–**7** in solution and within zeolite NaY.

A dramatic change in regioselectivity and diastereoselection was found in the photooxygenation of α-terpinyl acetate (**8**), by zeolite confinement relative to reaction in solution (Table 3), and exemplifies the role of the zeolite confinement as a powerful medium to control product selectivity, even if a stereogenic centre resides at a remote position with respect to the reacting double bond. In contrast to the photooxygenation of **8** in solution, which gives the expected ene product distribution based on the already published results of similar cycloalkenes such as limonene,[29] the intrazeolite photooxygenation of **8**[30] gave mainly one regioisomeric adduct (**8d**) in >90% dr. It is worthy to emphasize here, the predominant formation of a tertiary allylic hydroperoxide (**8d**), which is unique for an intrazeolite reaction, since trisubstituted alkenes afford within NaY primarily it is the secondary allylic hydroperoxides.

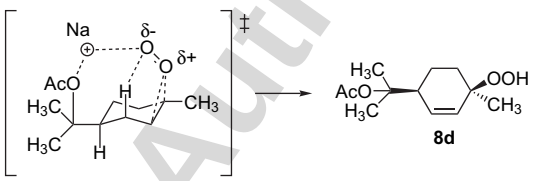
Table 3. Photooxygenation of α-terpinyl acetate (**8**) in solution and within NaY



	8a (%)[a]	**8b** (%)[a]	**8c** (%)[a]	**8d** (%)[a]	**8e/8f** (%)[a]
In solution	27	17	7	40	9
Within NaY	5	4	2	87	2

[a] Relative percentage.

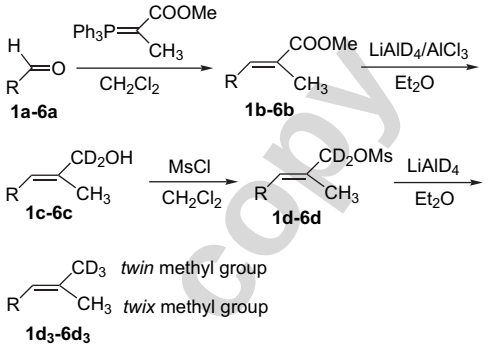
The enhanced regioselectivity/diastereoselectivity within NaY can be explained considering a synergism of $^1O_2$–Na^+ and Na^+–acetate interactions. Essentially, an Na^+ bound to the –OAc functionality directs singlet oxygen to abstract a pseudoaxially oriented allylic hydrogen atom at the more substituted side of the alkene (Scheme 5).



Scheme 5. Transition state for the selective formation of the hydroperoxide **8d** in the intrazeolite photooxygenation of α-terpinyl acetate.

2.4. Interplay of regioselectivity and diastereoselectivity in the photooxygenation of the chiral alkenes 1–6, through specific methyl group labelling

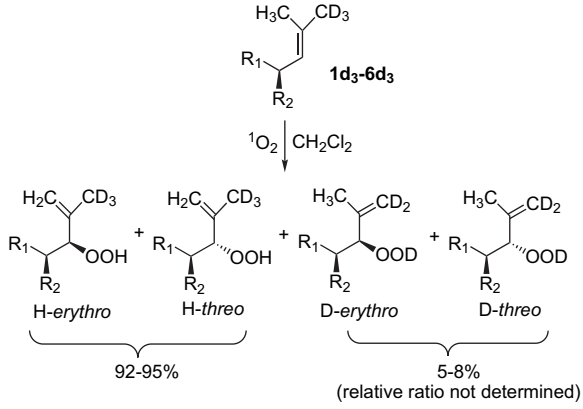
To determine the ratio of the *threo*/*erythro* stereoisomers induced by abstraction of an allylic hydrogen atom either from the more (*twix* CH_3)[31] or from the less (*twin* CH_3)[31] substituted side of the double bond, we prepared stereoselectively the deuterium labelled at the *twin* position chiral alkenes **1d$_3$–6d$_3$**. The synthesis was accomplished in >95% purity for the (*E*)-isomer as shown in Scheme 6, applying an already well known methodology.[12c]



Scheme 6. Synthesis of the chiral labelled alkenes **1d$_3$–6d$_3$**.

Photooxygenation of **1d$_3$–6d$_3$** in solution (Table 4) afforded the mixture of tertiary and secondary allylic hydroperoxides, as shown in Table 1 and in Scheme 4 for their perprotio analogues. For clarity purposes, since photooxygenation of **1d$_3$–6d$_3$** in solution is around 92–95% regioselective for allylic hydrogen atom abstraction from the more substituted side of the alkene (cis effect selectivity),[32] we will analyze below the diastereoselectivity arising only from the reaction of the *twix* methyl group. We define H-*threo* or H-*erythro* as the diastereomeric secondary allylic hydroperoxides resulting from allylic hydrogen atom abstraction from the *twix* methyl group (CH_3), and D-*threo* and D-*erythro* as the hydroperoxides resulting from allylic deuterium atom abstraction from the labelled *twin* methyl group (CD_3). The ratio of secondary H-*threo*/H-*erythro* allylic hydroperoxides was assessed by integration of the terminal olefinic hydrogen atoms in the region of 5 ppm.

Table 4. Stereochemistry in the photooxygenation of **1d$_3$–6d$_3$** in solution

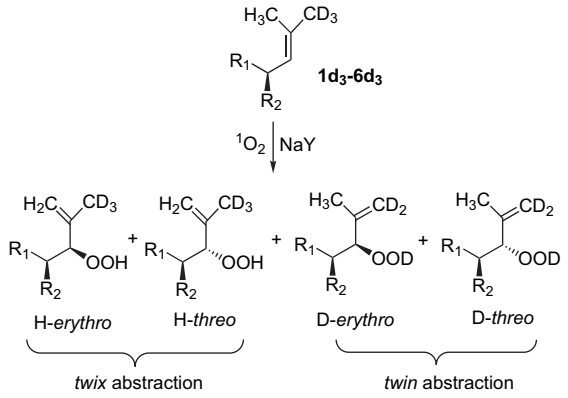


Alkene	H-*erythro*/H-*threo* (%)
R_1=Me, R_2=Ph (**1d$_3$**)	77/23
R_1=Et, R_2=Ph (**2d$_3$**)	78/22
R_1=Cyclohexyl, R_2=Ph (**3d$_3$**)	83/17
R_1=Me, R_2=*n*-Pr (**4d$_3$**)	62/38
5d$_3$	55/45[a]
6d$_3$	~50/50[a]

[a] The relative configuration of the major and minor *erythro* or *threo* diastereomers in the photooxygenation of **5d$_3$** and **6d$_3$** was not assessed.

The intrazeolite photooxygenation of **1d$_3$–6d$_3$** afforded the mixture of tertiary and secondary allylic hydroperoxides, with the latest being predominant or only products. For discussion purposes we will emphasize only to the stereochemical analysis of the secondary allylic hydroperoxides (Table 5). Enhanced *twin* selectivity was found, in accordance with the previously reported studies on other labelled trisubstituted alkenes,[7c] and therefore, analysis of the diastereoselectivity obtained from allylic hydrogen abstraction either from the labelled *twin* (CD_3) or from the *twix* methyl group became possible.

Table 5. Stereochemistry in the photooxygenation of **1d$_3$–6d$_3$** within NaY



Alkene	*twin*/*twix* (%)	H-*erythro*/H-*threo* (%)	H-*erythro*/H-*threo* (%)
R_1=Me, R_2=Ph (**1d$_3$**)	62/38	52/48	44/56
R_1=Et, R_2=Ph (**2d$_3$**)	60/40	23/77	22/78
R_1=Cyclohexyl, R_2=Ph (**3d$_3$**)	55/45	11/89	08/92
R_1=Me, R_2=*n*-Pr (**4d$_3$**)	52/48	44/56	50/50
5d$_3$	30/70	77/23[a]	58/42[a]
6d$_3$	47/54	~50/50[a]	~50/50[a]

[a] The relative configuration of the major and minor *erythro* or *threo* diastereomers in the photooxygenation of **5d$_3$** and **6d$_3$** was not assessed.

The ratio of secondary H-*threo*/H-*erythro* allylic hydroperoxides was assessed by integration of the terminal olefinic hydrogen atoms in the region of 5 ppm. On the other hand, the ratio D-*threo*/D-*erythro*, formed by abstraction of an allylic deuterium atom from the *twin* methyl group (CD_3), was assessed either by integration of the diastereotopic allylic methyls, or extrapolated, taking into account the total ratio of *threo*/*erythro* hydroperoxides and the ratio H-*threo*/H-*erythro*, as well. The typical ^{1}H NMR spectra, based on which the H-*threo*/H-*erythro* and D-*threo*/D-*erythro* ratios were calculated, for the photooxygenation of **3d$_3$** in solution and within NaY are shown in Figure 1.

The intrazeolite results present in Table 5 indicate that for alkenes **1d$_3$–4d$_3$** the diastereoselection arisen from abstraction of an allylic H or D atom (from the *twix* or the *twin* methyl group, respectively), is more or less very similar. The only significant change was found in the intrazeolite photooxygenation of **5d$_3$**, where the diastereoselectivity depends significantly on the orientation of singlet oxygen to form the perepoxide intermediates, either towards the more or towards the less substituted side of the double bond. Thus, abstraction of a D atom from the *twin* methyl group proceeds with moderate diastereoselection (18% dr), while H atom abstraction from the *twix* methyl group proceeds with significantly higher facial selectivity (54% dr). The significant dependence of diastereoselectivity on site selectivity, most probably indicates that upon folding of the alkene within NaY cages, the stereogenic centre is more proximal to the more substituted side of the double bond, and therefore, control of the facial approach in the case of the *twix*-oriented perepoxide intermediate is more profound.

3. Conclusions

As a conclusion, we have shown that the confined environment of zeolite NaY may in certain cases remarkably alter

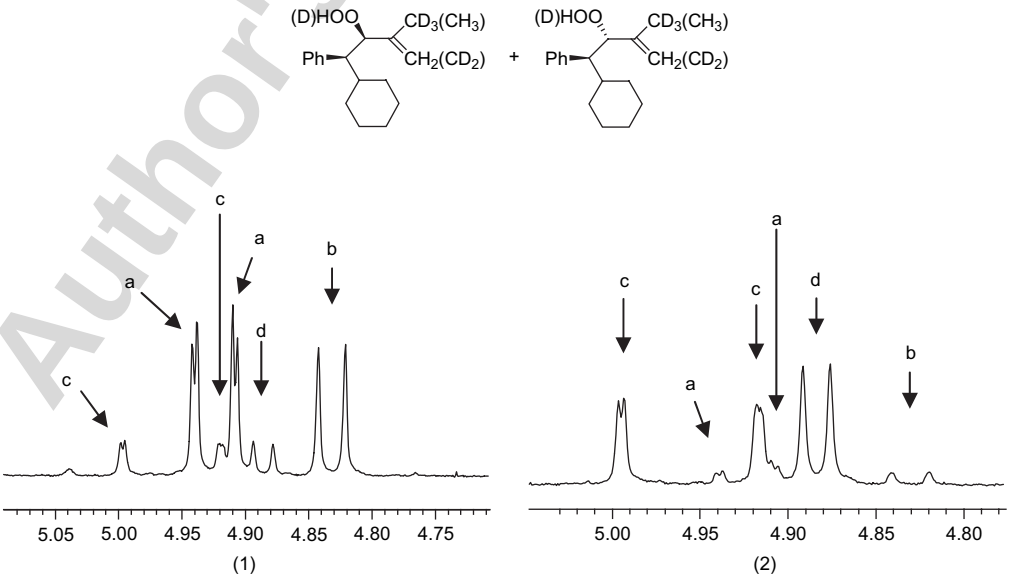


Figure 1. Part of the crude ^{1}H NMR spectrum in the region 4.7–5.1 ppm for the photooxygenation of **3d$_3$** in solution (1) and within NaY (2). *Abbreviations*: (a) terminal olefinic hydrogen (H-*erythro*); (b) allylic hydrogen on the carbon bearing the –OOH(D) functionality (H-*erythro*+D-*erythro*); (c) terminal olefinic hydrogen (H-*threo*); (d) allylic hydrogen on the carbon bearing the –OOH(D) functionality (H-*threo*+D-*threo*).

the facial selectivity in the photooxygenation of some chiral alkenes compared to their reaction in solution. It is postulated that within zeolite, a synergism between cation–π and singlet oxygen–cation interactions as well, are the main driving forces for the facial selectivity changes. In certain cases, enhanced regioselectivity and diastereoselection can be induced by a remote stereogenic centre relative to the reacting double bond, as a consequence of substrate confinement within the limited space of a cavity. We believe that the current results may provide a basis for the development of models with predictive capability in order to tune the behaviour of $^1O_2$ reactions by zeolite confinement.

4. Experimental

4.1. General

Nuclear magnetic resonance spectra were obtained on a 300 and 500 MHz instruments. Isomeric purities were determined by ^{1}H NMR and by GC analysis on a 60 m HP-5 capillary column. All spectra reported herein were taken in $CDCl_3$. Since, in addition to the synthesis of **1**–**6**, the stereoselectively labelled at the *twin* position analogous substrates **1d$_3$**–**6d$_3$** were prepared, we will describe below the synthesis of the labelled alkenes only. The only chiral alkene, which was not prepared in its labelled form was (1-cyclohexyl-4-methylpent-3-enyl)benzene (**7**) and the details of its synthesis are presented separately below.

4.2. Synthesis of (1-cyclohexyl-4-methylpent-3-enyl)-benzene (7)

4.2.1. Methyl 3-cyclohexyl-3-hydroxy-3-phenylpropanoate. In a flame-dried flask were added 2-bromoacetate (55 mmol), cyclohexylphenyl ketone (30 mmol), 2 g of activated Zn, and as a solvent was used a mixture of 100 mL dry benzene and 50 mL of dry ether. The slurry was refluxed for 1 day and then it was poured into 100 mL 2 N H_2SO_4. After extraction, the organic layer was dried and the solvent was removed under vacuum to produce methyl 3-cyclohexyl-3-hydroxy-3-phenylpropanoate in 75% yield as a white solid. The starting material cyclohexylphenyl ketone, was obtained in two steps by phenylmagnesium bromide addition to cyclohexanecarboxaldehyde, followed by oxidation of the resulting alcohol with Jone's reagent (70% yield over two steps). ^{1}H NMR of the hydroxyl ester: 7.19–7.35 (m, 5H), 4.30 (br s, 1H), 3.49 (s, 3H), 3.02 (d, 1H, J=16 Hz), 2.84 (d, 1H, J=16 Hz), 0.96–1.75 (m, 11H).

4.2.2. 1-Cyclohexyl-1-phenylpropane-1,3-diol. The methyl 3-cyclohexyl-3-hydroxy-3-phenylpropanoate was reduced into 95% yield by reacting for 8 h at ambient temperature and under inert atmosphere, with 1 mol equiv of $LiAlH_4$ in dry ether. ^{1}H NMR: 7.21–7.36 (m, 5H), 3.70 (m, 2H), 3.47 (t, 2H, J=7.5 Hz), 0.86–1.97 (m, 11H).

4.2.3. 3-Cyclohexyl-3-phenylpropan-1-ol. In a flame-dried flask were placed 0.99 g of 1-cyclohexyl-1-phenylpropane-1,3-diol (4 mmol) and 15 mL dry dichloromethane. At 0 °C were added by syringe 10 mmol (1.5 mL) of BF_3 etherated and then 0.73 mL of triethylsilane.[28] After 24 h the reduction of the benzylic hydroxyl was complete by TLC. The reaction mixture was washed with saturated solution of $NaHCO_3$, the organic layer was dried and the solvent was evaporated to yield after column chromatography (hexane/ethyl acetate=6/1) 0.62 g of 3-cyclohexyl-3-phenylpropan-1-ol (70%). ^{1}H NMR: 7.11–7.29 (m, 5H), 3.45 (m, 1H), 3.36 (m, 1H,), 3.36 (m, 1H), 0.75–2.10 (m, 13H).

4.2.4. 3-Cyclohexyl-3-phenylpropanal. The alcohol was oxidized to the corresponding aldehyde (3-cyclohexyl-3-phenylpropanal) in 75% isolated yield by PCC oxidation of 3-cyclohexyl-3-phenylpropan-1-ol in dry dichloromethane. ^{1}H NMR: 9.70 (s, 1H), 7.13–7.29 (m, 5H), 2.97 (t, 1H, J=6.0 Hz), 2.78 (m, 2H), 0.82–1.81 (m, 11H).

4.2.5. (1-Cyclohexyl-4-methylpent-3-enyl)benzene (7). The aldehyde reacted with the ylide obtained from the reaction of triphenylphosphoniumisopropyl iodide with *n*-BuLi in dry THF, to obtain after column chromatography (hexane as eluent) the desired alkene **7** in 59% isolated yield. ^{1}H NMR: 7.09–7.27 (m, 5H), 4.94 (t, 1H, J=7.0 Hz), 2.52 (m, 2H), 2.34 (m, 1H), 2.24 (m, 1H), 1.59 (s, 3H), 1.53 (s, 3H), 0.77–1.91 (m, 10H). ^{13}C NMR: 144.5, 131.7, 128.7, 127.7, 125.6, 123.2, 52.4, 42.5, 31.5, 31.1, 30.7, 26.7, 25.7, 17.7.

4.3. Synthesis of the labelled chiral alkenes 1d$_3$–6d$_3$

4.3.1. Chiral aldehydes 1a–6a. The aldehydes **1a** and **4a** are commercially available. The rest were prepared as follows. Aldehyde **2a**: it was prepared in 71% isolated yield by oxidation of 2-phenyl-1-butanol with PCC in dichloromethane. ^{1}H NMR: 9.69 (br s, 1H), 7.20–7.47 (m, 5H), 3.43 (t, 1H, J=7.0 Hz), 2.13 (m, 1H), 1.78 (m, 1H), 0.92 (t, 3H, J=7.5 Hz). Aldehyde **3a**: it was prepared in two steps from reduction of α-cyclohexylphenylacetic acid with $LiAlH_4$, followed by PCC oxidation of the resulting alcohol (60% yield, over two steps). ^{1}H NMR: 9.71 (d, 1H, J=3.5 Hz), 7.18–7.38 (m, 5H), 3.25 (dd, 1H, J_1=9.5 Hz, J_2=3.5 Hz), 2.12 (m, 1H), 0.80–1.86 (m, 10H). Aldehyde **6a**: it was prepared in two steps as follows: 3-phenyl-1-butanol was transformed to corresponding bromide in 96% yield by reacting with the PPh_3–Br_2 complex. ^{1}H NMR of the bromide: 7.19–7.35 (m, 5H), 3.32 (m, 1H), 3.18 (m, 1H), 2.96 (m, 1H), 2.11 (q, 2H, J=7.5 Hz), 1.29 (d, 3H, J=7.0 Hz). The bromide was transformed to the organomagnesium reagent in the presence of 1.4 mol equiv of Mg turnings, and then the Grignard reagent reacted with *N*-formylpiperidine[33] at 0 °C for 30 min. Acidic work up (3 N HCl) and extraction of the crude reaction mixture afforded the crude aldehyde **6a**, which was purified by flash column chromatography using hexane as eluent (56% isolated yield). ^{1}H NMR: 9.69 (t, 1H, J=1.5 Hz), 7.16–7.33 (m, 5H), 2.72 (m, 2H), 2.32 (m, 2H), 1.90 (m, 2H), 1.29 (d, 3H, J=7.0 Hz).

4.3.2. α,β-Unsaturated esters 1b–6b. In a one-necked flask were placed 60 mL of dry CH_2Cl_2, and 40 mmol of the stabilized ylide methyl(triphenylphosphoranylidene)propionate and 25 mmol of the aldehydes **1a**–**6a**. The solution was refluxed until consumption of the aldehyde (normally 2–6 h is necessary). For the case of the bulkiest aldehyde **6c**, the reaction time was 2 days. Most of the solvent was removed by evaporation and then 50 mL of hexane were added. The

solid residue was washed with hexane (4×50 mL), the solvent was evaporated and the oily residue was chromatographed or distilled at reduced pressure (for volatile derivative **4b**). The α,β-unsaturated esters were isolated in 50–75% yield and in >95% purity for the (*E*)-isomer. ^{1}H NMR data: compound **1b**: 7.22–7.35 (m, 5H), 6.87 (d, 1H, *J*=11.0 Hz), 3.77 (m, 1H), 3.72 (s, 3H), 1.91 (s, 3H), 1.39 (d, 3H, *J*=7.0 Hz). Compound **2b**: 7.19–7.35 (m, 5H), 6.88 (d, 1H, *J*=10.0 Hz), 3.73 (s, 3H), 3.50 (m, 1H), 1.90 (s, 3H), 1.78 (m, 2H), 0.88 (t, 3H, *J*=7.5 Hz). Compound **3b**: 7.16–7.31 (m, 5H), 6.97 (dd, 1H, J_1=10.5 Hz, J_2=1.5 Hz), 3.72 (s, 3H), 3.28 (t, 1H, *J*=10.0 Hz), 1.86 (d, 3H, *J*=1.5 Hz), 0.80–1.85 (m, 11H). Compound **4b**: 6.51 (d, 1H, *J*=8.0 Hz), 3.72 (s, 3H), 2.50 (m, 1H), 1.83 (s, 3H), 1.25 (m, 4H), 0.97 (d, 3H, *J*=7.0 Hz), 0.87 (t, 3H, *J*=7.0 Hz). Compound **5b**: 7.19–7.32 (m, 5H), 6.73 (t, 1H, *J*=6.5 Hz), 3.71 (s, 3H), 2.87 (m, 1H), 2.44 (m, 2H), 1.77 (s, 3H), 1.28 (d, 3H, *J*=6.5 Hz). Compound **6b**: 7.19–7.34 (m, 5H), 6.76 (t, 1H, *J*=7.0 Hz), 3.75 (s, 3H), 2.74 (m, 1H), 2.08 (m, 2H), 1.76 (m, 2H), 1.75 (s, 3H), 1.29 (d, 3H, *J*=7.0 Hz).

4.3.3. Allylic alcohols-d_2, 1c–6c. In a flame-dried two-necked flask were placed 12 mmol of $LiAlD_4$ and 15 mL of dry ether. The flask was cooled to 0 °C and subsequently 4 mmol of anhydrous $AlCl_3$ were added in portions. The resulting slurry was stirred for an additional 20 min, followed by the dropwise addition of the α,β-unsaturated ester **1b**–**6b** (15 mmol). The reaction mixture was stirred for 1–2 h and then treated with 1 mL of water. After extraction with diethyl ether, the deuterated allylic alcohols **1c**–**6c** were isolated in 85–95% yield. ^{1}H NMR: compound **1c**: 7.18–7.34 (m, 5H), 5.58 (d, 1H, *J*=9.5 Hz), 3.73 (m, 1H), 1.75 (s, 3H), 1.58 (br s, 1H), 1.29 (t, 3H, *J*=7.0 Hz). Compound **2c**: 7.17–7.36 (m, 5H), 5.57 (dd, 1H, J_1=9.5 Hz, J_2=1.0 Hz), 3.41 (m, 1H), 1.73 (d, 3H, *J*=1.0 Hz), 1.62–1.78 (m, 2H), 1.49 (br s, 1H), 0.87 (t, 3H, *J*=7.0 Hz). Compound **3c**: 7.15–7.30 (m, 5H), 5.63 (d, 1H, *J*=9.5 Hz), 3.19 (t, 1H, *J*=9.5 Hz), 1.87 (m, 1H), 1.69 (s, 3H), 0.78–1.74 (m, 10H). Compound **4c**: 5.11 (d, 1H, *J*=8.0 Hz), 2.37 (m, 1H), 1.66 (s, 3H), 1.54 (br s, 1H), 1.17–1.30 (m, 4H), 0.92 (d, 3H, *J*=7.0 Hz), 0.87 (t, 3H, *J*=7.0 Hz). Compound **5c**: 7.18–7.32 (m, 5H), 5.37 (t, 1H, *J*=7.5 Hz), 2.73 (m, 1H), 2.31 (m, 2H), 1.60 (s, 3H), 1.56 (br s, 1H), 1.25 (d, 3H, *J*=7.0 Hz). Compound **6c**: 7.20–7.33 (m, 5H), 5.39 (t, 1H, *J*=7.0 Hz), 2.73 (m, 1H), 1.97 (m, 2H), 1.68 (m, 2H), 1.60 (s, 3H), 1.28 (d, 3H, *J*=7.0 Hz), 1.29 (br s, 1H).

4.3.4. Mesylates of the allylic alcohols-d_2, 1d–6d. The allylic alcohols-d_2, **1c**–**6c** (10 mmol) were placed into a flask charged with 30 mmol of dry triethylamine and 30 mL of dry dichloromethane. Subsequently, 11 mmol of methanesulfonyl chloride were added dropwise at 0 °C. After 25 min the reaction was complete (by TLC). The solids were removed by filtration and the organic layer was washed with 5% HCl (until pH was acidic), then with saturated solution of $NaHCO_3$, and finally with 50 mL of brine. The allylic mesylates do not persist and were used immediately in the next step without purification.

4.3.5. Chiral alkenes-d_3, 1d$_3$–6d$_3$. To a flame-dried flask charged with 20 mL of dry ether were suspended 4 mmol of $LiAlD_4$. The crude mesylates **1d**–**6d** (10 mmol) were added dropwise at 0 °C. The reaction mixture was stirred overnight. After treatment with 2 mL of water and extraction with ether, the resulting crude alkenes **1d$_3$**–**6d$_3$** were purified by flash silica gel chromatography using hexane as eluent. The geometric purity of the (*E*)-alkenes was >95% and was estimated by comparison with the spectra of their corresponding perprotio alkenes. ^{1}H NMR of **1d$_3$**: 7.17–7.33 (m, 5H), 5.29 (dq, 1H, J_1=9.5 Hz, J_2=1.0 Hz), 3.67 (m, 1H), 1.69 (d, 3H, *J*=1.0 Hz), 1.30 (t, 3H, *J*=7.5 Hz); ^{13}C NMR of **1d$_3$**: 147.3, 130.4, 130.2, 128.3, 126.9, 125.7, 38.1, 25.1 (septet, J_{C-D}=19 Hz), 22.4, 17.9; MS, *m*/*z*=163 (100%, *m*/*z*=148). ^{1}H NMR of **2d$_3$**: 7.14–7.32 (m, 5H), 5.28 (dq, 1H, J_1=9.5 Hz, J_2=1.0 Hz), 3.36 (m, 1H), 1.57–1.76 (m, 2H), 1.67 (d, 3H, *J*=1.0 Hz), 0.86 (t, 3H, *J*=7.5 Hz); ^{13}C NMR of **2d$_3$**: 146.2, 131.2, 128.9, 128.3, 127.3, 125.7, 46.1, 30.1, 25.0 (septet, J_{C-D}=19 Hz), 18.0, 12.2; MS, *m*/*z*=177 (100%, *m*/*z*=148); HRMS calcd for $C_{13}H_{15}D_3$: 177.1597, found: 177.1597. ^{1}H NMR of **3d$_3$**: 7.15–7.29 (m, 5H), 5.35 (dq, 1H, J_1=10.0 Hz, J_2=1.0 Hz), 3.14 (t, 1H, *J*=10.0 Hz), 0.77–1.89 (m, 11H), 1.63 (d, 3H, *J*=1.0 Hz); ^{13}C NMR of **3d$_3$**: 145.3, 131.3, 128.2, 127.9, 125.5, 51.16, 43.6, 31.5, 31.1, 26.6, 26.5, 26.4, 25.1 (septet, J_{C-D}=19 Hz), 18.1; HRMS calcd for $C_{17}H_{21}D_3$: 231.2066, found: 231.2064. ^{1}H NMR of **4d$_3$**: 4.90 (d, 1H, *J*=9.0 Hz), 2.34 (m, 1H), 1.62 (s, 3H), 1.17–1.30 (m, 4H), 0.92 (d, 3H, *J*=7.0 Hz), 0.89 (t, 3H, *J*=7.0 Hz). ^{13}C NMR of **4d$_3$**: 131.6, 129.3, 40.1, 32.1, 24.8 (septet, J_{C-D}=19 Hz), 21.2, 20.5, 17.8, 14.2. ^{1}H NMR of **5d$_3$**: 7.19–7.32 (m, 5H), 5.10 (t, 1H, *J*=6.5 Hz), 2.72 (m, 1H), 2.25 (m, 2H), 1.56 (s, 3H), 1.24 (d, 3H, *J*=7.0 Hz). ^{1}H NMR of **6d$_3$**: 7.19–7.33 (m, 5H), 5.12 (t, 1H, *J*=7.0 Hz), 2.73 (m, 1H), 1.91 (m, 2H), 1.59–1.68 (m, 2H), 1.55 (s, 3H), 1.27 (d, 3H, *J*=7.0 Hz).

4.4. Photooxygenation of chiral alkenes 1–7 and their labelled analogues

The photooxygenation of the alkenes in solution was accomplished by dissolving 10 mg of each alkene in a solution of 10^{-4} M methylene blue in dichloromethane (5 mL). The solution was bubbled with oxygen gas and then irradiated with a 300 W Xenon lamp until the alkene was consumed (by TLC). The intrazeolite reactions were carried as follows. In a test tube were added 1 g of freshly dried thionin-supported zeolite NaY and 5 mL of dry hexane, which contained 10 μL of pyridine. After 5 min, a hexane solution (5 mL) containing each alkenes-d_3 or their perprotio analogues (10 mg) was added. The tube was immediately photolyzed at 0 °C under a constant slow stream of oxygen gas for 1–2 min, followed by immediate addition of 10 mL of moistened tetrahydrofuran. The slurry was stirred for 3 h and then the solid was removed by filtration. The solvent was removed by rotary evaporation and the ^{1}H NMR spectrum was taken directly on the crude reaction mixture. The spectroscopic data for the ene allylic hydroperoxides obtained from the photooxygenation of **1** have been reported (see Ref. 19). Photooxygenation of **2** (or **2d$_3$**): tertiary hydroperoxide {7.10–7.35 (m, 5H), 5.56 (s, 1H), 2.31 (q, 2H, *J*=7.5 Hz), 1.16 (s, 6H), 0.98 (t, 3H, *J*=7.5 Hz)}; *erythro* secondary hydroperoxide {7.83 (br s, 1H), 7.10–7.35 (m, 5H), 4.89 (br s, 1H), 4.87 (br s, 1H), 4.51 (d, 1H, *J*=9.5 Hz), 2.60 (m, 1H), 2.12 (m, 1H), 1.57 (s, 3H), 1.62 (m, 1H), 0.73 (t, 3H, *J*=7.0 Hz)}; *threo* secondary

hydroperoxide {7.65 (br s, 1H), 7.10–7.35 (m, 5H), 5.11 (br s, 1H), 5.06 (br s, 1H), 4.51 (d, 1H, J=9.5 Hz), 2.58 (m, 1H), 1.78 (s, 3H), 1.64 (m, 1H), 1.52 (m, 1H), 0.71 (t, 3H, J=7.0 Hz)}. Photooxygenation of **3** (or **3d$_3$**): tertiary hydroperoxide {7.05–7.30 (m, 5H), 5.55 (s, 1H), 2.09 (br t, 1H, J=11.0 Hz), 1.12 (s, 6H), 0.80–1.85 (m, 10H)}; *erythro* secondary hydroperoxide {7.75 (br s, 1H), 7.05–7.30 (m, 5H), 4.94 (br s, 1H), 4.91 (br s, 1H), 4.83 (d, 1H, J=10.5 Hz), 2.70 (dd, 1H, J_1=10.5 Hz, J_2=4.5 Hz), 1.61 (s, 3H), 0.80–1.85 (m, 10H)}; *threo* secondary hydroperoxide {7.60 (br s, 1H), 7.05–7.30 (m, 5H), 4.99 (br s, 1H) 4.92 (br s, 1H), 4.88 (d, 1H, J=7.5 Hz), 2.55 (t, 1H, J=7.0 Hz), 1.68 (s, 3H), 0.80–1.85 (m, 10H)}. Photooxygenation of **4** (or **4d$_3$**): *erythro* secondary hydroperoxide (as alcohol obtained after reduction with PPh_3, characteristic absorptions) {4.97 (br s, 1H) 4.90 (br s, 1H), 3.88 (d, 1H, J=6.5 Hz), 1.72 (s, 3H)}; *threo* secondary hydroperoxide (as alcohol obtained after reduction with PPh_3, characteristic absorptions) {4.93 (br s, 1H), 4.88 (br s, 1H), 3.79 (d, 1H, J=6.5 Hz), 1.73 (s, 3H)}. Photooxygenation of **5** (or **5d$_3$**): tertiary hydroperoxide (as alcohol obtained after reduction with PPh_3, characteristic absorptions) {5.85 (dd, 1H, J_1=16.0 Hz, J_2=7.0 Hz), 5.61 (d, 1H, J=16.0 Hz), 3.45 (m, 1H), 1.46 (s, 6H), 1.41 (d, 3H, J=7.5 Hz)}; main diastereomeric secondary hydroperoxide (as alcohol obtained after reduction with PPh_3, characteristic absorptions) {4.90 (d, 1H, J=1.5 Hz) 4.80 (d, 1H, J=1.5 Hz), 3.84 (dd, 1H, J_1=8.5 Hz, J_2=4.5 Hz), 2.99 (m, 1H), 1.78–1.90 (m, 2H), 1.70 (s, 3H), 1.29 (d, 3H, J=7.0 Hz)}; minor diastereomeric secondary hydroperoxide (as alcohol obtained after reduction with PPh_3, characteristic absorptions) {4.88 (d, 1H, J=1.5 Hz), 4.86 (d, 1H, J=1.5 Hz), 4.04 (t, 1H, J=8.5 Hz), 2.85 (m, 1H), 1.78–1.90 (m, 2H), 1.76 (s, 3H), 1.29 (d, 3H, J=7.0 Hz)}. Photooxygenation of **6** (or **6d$_3$**): tertiary hydroperoxide (characteristic absorptions) {5.62 (dt, 1H, J_1=16 Hz, J_2=7.5 Hz), 5.41 (d, 1H, J=16.0 Hz), 2.85 (m, 1H), 2.37 (m, 2H), 1.27 (s, 6H)}; secondary hydroperoxides (characteristic absorptions) {5.03 (br s, 1H), 5.00 (br s, 1H), 4.31 (t, 1H, J=7.5 Hz) corresponding to the one diastereomer, 4.30 (t, 1H, J=7.5 Hz) corresponding to the other diastereomer, 2.72 (m, 2H), 1.70 (s, 3H) corresponding to the one diastereomer, 1.66 (s, 3H) corresponding to the other diastereomer}. Photooxygenation of **7**: tertiary hydroperoxide (characteristic absorptions) {5.87 (dd, 1H, J_1=16 Hz, J_2=7.5 Hz), 5.53 (d, 1H, J=16.0 Hz), 2.94 (t, 1H, J=9.0 Hz), 1.34 (s, 3H), 1.31 (s, 3H)}; major secondary hydroperoxide (characteristic absorptions) {7.65 (s, 1H, –OOH), 4.90 (br s, 1H), 4.85 (br s, 1H), 3.98 (m, 1H), 2.60 (m, 1H), 1.62 (s, 3H)}; minor secondary hydroperoxide (characteristic absorptions) {7.56 (s, 1H, –OOH), 5.05 (br s, 1H), 4.79 (br s, 1H), 4.00 (m, 1H), 2.21 (m, 1H), 1.73 (s, 3H)}.

Acknowledgements

This work was supported by the community initiative INTERREG IIIB, MEDOCC programme (Aquatex project). This European programme supports projects aimed at translational co-operation in the field of territorial development of Mediterranean countries. The authors are indebted to Professors Michael Orfanopoulos and Georgios Vassilikogiannakis for fruitful discussions and productive collaboration in the field of singlet oxygen chemistry for the past 15–20 years.

References and notes

1. (a) Wasserman, H. H.; Murray, R. W. *Singlet Oxygen*; Academic: New York, NY, 1979; (b) For a recent review article, see: Clennan, E. L.; Pace, A. *Tetrahedron* **2005**, *61*, 6665–6691.
2. Wahlen, J.; de Vos, D. E.; Jacobs, P. A.; Alsters, P. L. *Adv. Synth. Catal.* **2004**, *346*, 152–164.
3. Tung, C.-H.; Wu, L.-Z.; Zhang, L.-P.; Chen, B. *Acc. Chem. Res.* **2003**, *36*, 39–47.
4. (a) Tung, C.-H.; Wang, H.; Ying, Y.-M. *J. Am. Chem. Soc.* **1998**, *120*, 5179–5186; (b) Chen, Y.-Z.; Wu, L.-Z.; Zhang, L.-P.; Tung, C.-H. *J. Org. Chem.* **2005**, *70*, 4676–4681.
5. Tung, C.-H.; Guan, J.-Q. *J. Am. Chem. Soc.* **1998**, *120*, 11874–11879.
6. Tung, C.-H.; Wu, L. Z.; Zhang, L. P.; Li, H. R.; Yi, X. Y.; Ming, K. S.; Yuan, Z. Y.; Guan, J. Q.; Wang, H. W.; Ying, Y. M.; Xu, X. H. *Pure Appl. Chem.* **2000**, *72*, 2289–2298.
7. (a) Ramamurthy, V.; Lakshminarasimhan, P.; Grey, C. P.; Johnston, L. J. *Chem. Commun.* **1998**, 2411–2424; (b) Sen, S. E.; Smith, S. M.; Sullivan, K. A. *Tetrahedron* **1999**, *55*, 12657–12698; (c) Stratakis, M. *Curr. Org. Synth.* **2005**, *2*, 281–299.
8. Li, X.; Ramamurthy, V. *J. Am. Chem. Soc.* **1996**, *118*, 10666–10667.
9. Pace, A.; Clennan, E. L. *J. Am. Chem. Soc.* **2002**, *124*, 11236–11237.
10. Jockusch, S.; Sivaguru, J.; Turro, N. J.; Ramamurthy, V. *Photochem. Photobiol. Sci.* **2005**, *4*, 403–405.
11. Robbins, R. J.; Ramamurthy, V. *Chem. Commun.* **1997**, 1071–1072.
12. (a) Stratakis, M.; Froudakis, G. *Org. Lett.* **2000**, *2*, 1369–1372; (b) Clennan, E. L.; Sram, J. P. *Tetrahedron* **2000**, *56*, 6945–6950; (c) Stratakis, M.; Nencka, R.; Rabalakos, C.; Adam, W.; Krebs, O. *J. Org. Chem.* **2002**, *67*, 8758–8763.
13. Stratakis, M.; Rabalakos, C.; Mpourmpakis, G.; Froudakis, G. E. *J. Org. Chem.* **2003**, *68*, 2839–2843.
14. Ramamurthy, V.; Shailaja, J.; Kaanumalle, L. S.; Sunoj, R. B.; Chandrasekhar, J. *Chem. Commun.* **2003**, 1987–1999.
15. Prein, M.; Adam, W. *Angew. Chem., Int. Ed.* **1996**, *35*, 477–494.
16. Rao, V. J.; Uppili, S. R.; Corbin, D. R.; Schwarz, S.; Lustig, S. R.; Ramamurthy, V. *J. Am. Chem. Soc.* **1998**, *120*, 2480–2481.
17. Joy, A.; Uppili, S.; Netherthon, M. R.; Scheffer, J. R.; Ramamurthy, V. *J. Am. Chem. Soc.* **2000**, *122*, 728–729.
18. The relevant to the **1–4** chiral alkene, for which R_1=methyl and R_2=*tert*-butyl(2,4,5,5-tetramethyl-2-hexene) affords a ratio *erythro*/*threo* secondary allylic hydroperoxides=71/29 (see Ref. 19). This diastereomeric ratio is lower compared to the *erythro*/*threo* ratio obtained from the photooxygenation of **3**.
19. Adam, W.; Nestler, B. *Liebigs Ann. Chem.* **1990**, 1051–1053.
20. Adam, W.; Brunker, H.-G.; Kumar, A. S.; Peters, E.-M.; Peters, K.; Schneider, U.; von Schnering, H. G. *J. Am. Chem. Soc.* **1996**, *118*, 1899–1905.
21. Karabatsos, G. J. *J. Am. Chem. Soc.* **1967**, *89*, 1367–1371 and references cited therein.
22. A preliminary account for the intrazeolite photooxygenation of the phenyl-substituted alkenes **1–3** has been published: Stratakis, M.; Kalaitzakis, D.; Stavroulakis, D.; Kosmas, G.; Tsangarakis, C. *Org. Lett.* **2003**, *5*, 3471–3474.
23. Feller, D. *Chem. Phys. Lett.* **2000**, *322*, 543–548.

24. The interaction of an isolated double bond to the Na^+ is at least 10 kcal/mol less exothermic compared to the Na^+–benzene interaction. Ma, J. C.; Dougherty, D. A. *Chem. Rev.* **1997**, *97*, 1303–1324.
25. Clennan, E. L.; Sram, J. P.; Pace, A.; Vincer, K.; White, S. *J. Org. Chem.* **2002**, *67*, 3975–3978.
26. Stratakis, M.; Kosmas, G. *Tetrahedron Lett.* **2001**, *42*, 6007–6009.
27. Alkene **7** was prepared as follows. Reformatsky coupling of 2-bromoacetate with phenyl cyclohexyl ketone in the presence of activated Zn, afforded methyl 3-cyclohexyl-3-hydroxy-3-phenylpropanoate, which was reduced to 1-cyclohexyl-1-phenylpropane-1,3-diol by $LiAlH_4$. Selective reduction[28] of the tertiary benzylic hydroxyl with Et_3SiH/BF_3 yielded 3-cyclohexyl-3-phenylpropan-1-ol, which was oxidized with PCC to form 3-cyclohexyl-3-phenylpropanal. Finally, Wittig coupling of the aldehyde with isopropylidenetriphenylphosphorane afforded **7**.
28. Orfanopoulos, M.; Smonou, I. *Synth. Commun.* **1988**, *18*, 833–839.
29. Gollnick, K.; Schade, G. *Tetrahedron Lett.* **1973**, *11*, 857–860.
30. Stratakis, M.; Sofikiti, N.; Baskakis, C.; Raptis, C. *Tetrahedron Lett.* **2004**, *45*, 5433–5436.
31. For the definition of the terminology *twin* and *twix*, see: Adam, W.; Bottke, N.; Krebs, O. *J. Am. Chem. Soc.* **2000**, *122*, 6791–6792.
32. Stratakis, M.; Orfanopoulos, M. *Tetrahedron* **2000**, *56*, 1595–1615.
33. Olah, G. A.; Arvanaghi, M. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 878–879.