

Intrazeolite photo-oxygenation of (*R*)-(-)- α -phellandrene[†]

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Thionin-sensitised intrazeolite photo-oxygenation of (*R*)-(-)- α -phellandrene affords (1*S*,5*R*)-5-(1-methylethyl)-2-methylidene-3-cyclohexen-1-yl hydroperoxide as the major ene product. This can be easily reduced with triphenylphosphine to the natural product *trans*-yabunikkeol.

Keywords: intrazeolite photo-oxygenation, (*R*)-(-)- α -phellandrene

Dye-sensitised photo-oxygenation of organic compounds within the confined spaces of zeolite Na-Y have attracted recently considerable attention.¹ It has been found that the regioselectivity² and the diastereoselectivity³ in the ene hydroperoxidation reaction of alkenes can be substantially enhanced within the zeolite compared to the reaction in solution. Furthermore, alkenylarenes that form with singlet oxygen in solution mixtures of ene, [4+2] and [2+2] adducts, afford chemoselectively ene products within Na-Y.⁴ Around 15 years ago it was reported independently by two research groups^{5,6} that reaction of singlet oxygen (¹O₂) with (*R*)-(-)- α -phellandrene (**1**) affords the two diastereoisomeric endoperoxides **2** and **3** as major products, while five other ene adducts (**4–8**) are formed in various amounts. A minor amount of *p*-cymene (**9**) also is formed *via* decomposition of the labile hydroperoxides **4**, **5** and **8** (Scheme 1).

(*R*)-(-)- α -phellandrene is a suitable substrate for study of its intrazeolite photo-oxygenation reaction. The constraint within the zeolite permits the examination of the variation of the [4+2] versus the ene adducts, to the variation of the regioisomers and the diastereoisomers among the ene products. The results in the intrazeolite photo-oxygenation of **1** are found Table 1. It is evident that within the zeolite the relative ratio of the overall ene adducts increases (ene/[4+2] = 34/66 in solution versus ene/[4+2] = 52/48 in the zeolite). Comparing the Diels–Alder adducts, the diastereoisomeric ratio of **2/3** slightly increases in zeolite, while for the ene adducts, for

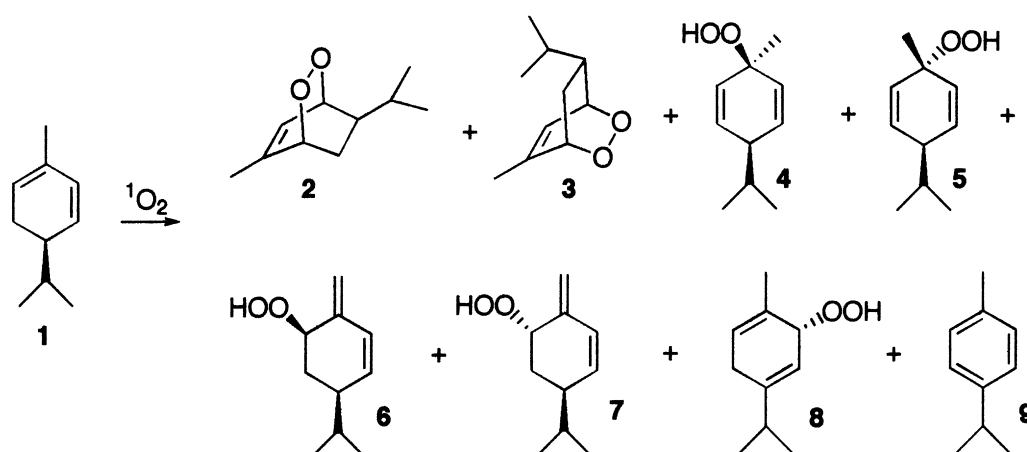
those where the double bond is formed in the interior of the ring, the predominant diastereoisomer in solution is also the predominant one in the zeolite. On the other hand, the amount of the exomethylenic ene adducts **6** and **7** increases substantially within Na-Y (total 35% in zeolite, versus only 3.5% in solution), with a remarkable reverse in the diastereoselectivity. The ratio of **6/7** is 14/86 in zeolite versus 58/42 in solution. To ensure that all adducts had been extracted from the zeolite, the mixture of the oxygenated products from the photo-oxygenation of **1** in solution were supported within thionin/Na-Y pretreated with pyridine (see experimental section), and irradiation was performed under a constant bubbling of oxygen. After extractive workup, the distribution of the products was almost unchanged.

Table 1 Photo-oxygenation of (*R*)-(-)- α -phellandrene in zeolite and in solution^a

Conditions	2 (%)	3 (%)	4 (%)	5 (%)	6 (%)	7 (%)	8 (%)
<i>i</i> -PrOH/RB ^{b,c}	39	26	14	9	2	1.5	3
Thionin/Na-Y	33	15	12	5	5	30	ND

^aRelative percentage of products was measured by ¹H NMR (500 MHz). ^bRB = Rose bengal. ^cPercent values as reported in ref. 6. Photo-oxygenation of **1** in CH₂Cl₂/methylene blue affords similar product distribution to *i*-PrOH/RB.

The fact that for all ene and [4+2] adducts, when the photo-oxygenation is carried out in solution, the major diastereoisomer



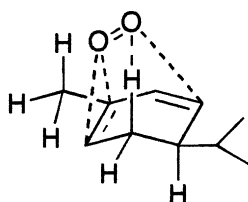
Scheme 1

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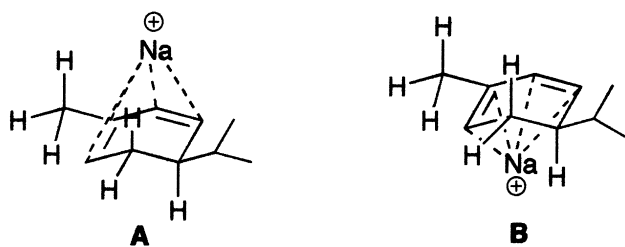
[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.

mer is always that in which the new C–O bond is *cis* to the isopropyl group (for example **2** is predominant over **3**, or **4** over **5**) was rationalised in terms of a common perepoxide-type intermediate shown in Scheme 2. In that intermediate, singlet oxygen attacks the more reactive trisubstituted double bond of the more stable conformation of **1** from the top phase. The “positive” interaction⁷ of oxygen with the axially oriented allylic hydrogen results in significant stabilisation.

To explain the photo-oxygenation results within the zeolite, we take into account the interaction of a Na⁺ (there is one charge compensating Na⁺ per Al atom in the zeolite lattice) with the conjugated system. In the more stable conformation of phellandrene where the isopropyl group is equatorial, the Na⁺ has two binding sites on the two diastereotopic phases of the diene. In complex **A**, the cation is placed on top of the diene, and in complex **B** on to the bottom (Scheme 3). In complex **B**, ¹O₂ can approach only from the top phase and can form two possible perepoxide-type intermediates. One in which oxygen is oriented towards the less substituted side of the trisubstituted double bond (**B_{exo}**), and one where orientation is towards the more substituted side (**B_{endo}**).



Scheme 2 Favourable attack of ¹O₂ to (*R*)-(-)- α -phellandrene in solution

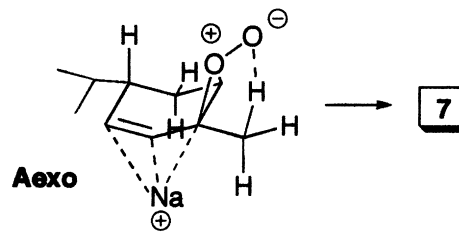


Scheme 3 Possible complexes of the Na⁺ interaction to (*R*)-(-)- α -phellandrene within Na–Y

For **B_{endo}**, oxygen can interact with the axial allylic hydrogen, while for **B_{exo}** this interaction is less pronounced due to the fast rotation of the methyl group. It is well established that interaction of ¹O₂ with axially-oriented allylic hydrogens in cycloalkenes stabilises the transition state of perepoxide formation.⁷ Therefore, the transition state for the formation of **B_{endo}** is expected to be lower in energy compared to the transition state for the formation of **B_{exo}**. In complex **A**, singlet oxygen can approach only from the bottom phase and can form the two possible perepoxide-type intermediates, **A_{endo}** and **A_{exo}**. For the **A_{endo}** where ¹O₂ is placed towards the more substituted side of the double bond, oxygen cannot interact with an allylic hydrogen, since it resides at the equatorial position. Thus, the transition state for the formation of **A_{endo}** increases in energy and formation of the perepoxide **A_{exo}** where oxygen is placed towards the methyl group (Scheme 4)

is expected to compete substantially. Indeed, **A_{exo}** leads to the major ene product **7**. Similarly, **B_{endo}** which is expected to predominate over **B_{exo}**, is the precursor of the major endoperoxide **2** and the major tertiary hydroperoxide **4**.

In conclusion, we have shown that cation – π interactions within the confined environment of zeolite Na–Y can affect the diastereoselection of the ene pathway in the photo-oxygenation of (*R*)-(-)- α -phellandrene. The major ene product is the optically active (1*S*,5*R*)-5-(1-methylethyl)-2-methylidene-3-cyclohexen-1-yl hydroperoxide (**7**) which can be easily reduced with PPh₃ to the natural product *trans*-yabunikkeol, that is found in the essential oils of *cinnamomum japonicum*⁸ and *piper nigrum*.⁹



Scheme 4

Experimental

Product analysis was performed by ¹H NMR on a AMX 500 MHz Bruker instrument. Complete characterisation data of products **2–9** are described in ref. 6b. Thionin-supported zeolite Na–Y was prepared as described in ref. 2a.

To dry thionin/Na–Y (1 g) were added hexane (5 ml) containing pyridine (15 ml). After 5 minutes, hexane (5 ml) containing (*R*)-(-)- α -phellandrene (15 ml) were added and irradiation was performed immediately with a 300 W Xenon lamp under a constant bubbling of oxygen for 2–3 minutes. At the time, the phellandrene had been completely consumed. Moistened tetrahydrofuran (10 ml) was added and the slurry was stirred for 3 hours and then filtered. The solvents were removed and the ¹H NMR was recorded. In the absence of pyridine, substantial isomerisation of **1** to α -terpinene occurs, and eventually various amounts of the endoperoxide ascaridole are also formed by the reaction with singlet oxygen. Furthermore, the labile hydroperoxides **4** and **5** vanish and transform to *p*-cymene. However, the ratio of the diastereoisomeric products **2/3** and **6/7** remains almost unchanged. The mass balance of the photo-oxygenation reaction as measured by using 2-phenylethanol as external standard was >85%.

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