Journal of Catalysis **195,** 79–87 (2000)
doi:10.1006/jcat.2000.2975, available online at http://www.idealibrary.com on IDEAL®

Oxidation–Isomerization of an Olefin to Allylic Alcohol Using Titania–Silica and a Base Co-catalyst

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Received March 3, 2000; revised June 22, 2000; accepted June 22, 2000

The potential of a two-step, one-pot synthesis of α,β-unsaturated alcohols from olefins is illustrated on the example of 4-hydroxy-isophorone using titania–silica aerogels and basic co-catalysts. Kinetic analysis of the complex reaction network revealed that titania–silica is efficient in the epoxidation of β-isophorone (3,5,5-trimethyl-3-cyclohexen-1-one) with TBHP at 353 K, whereas the acid/base-catalyzed *in situ* rearrangement to 4-hydroxy-isophorone (4-hydroxy-3,5,5-trimethyl-cyclohex-2-enone) is slow. Addition of solid bases such as CaO, Na_2CO_3, and KF/CaF_2 remarkably accelerated the rearrangement and up to 77.5% selectivity at 83% conversion was achieved in 3 h. Stronger bases (K_2CO_3, BaO, Mg–Al–O-^{t}Bu, guanidine bases) inhibited the epoxidation reaction due to deactivation of the isolated Ti sites, and favored isomerization of β-isophorone to α-isophorone. Hydrophobization of titania–silica by covalently bound surface phenyl groups greatly suppressed oligomerization and isomerization of β-isophorone but did not improve the selectivity to 4-hydroxy-isophorone. © 2000 Academic Press

Key Words: **oxidation; epoxidation; isomerization, isophorone; hydroxy-isophorone; allylic alcohol; titania–silica aerogel, *tert*-butylhydroperoxide; base catalysis.**

1. INTRODUCTION

Allylic oxidation of olefins is an essential process in synthetic organic chemistry affording valuable α,β-unsaturated alcohols and carbonyl compounds. In contrast to epoxidation, allylic oxidation maintains the olefinic functionality in the product, thus allowing further useful transformations. An industrially relevant example is the oxidation of isophorone (3,5,5-trimethyl-cyclohex-2-enone) to ketoisophorone (2,6,6-trimethyl-cyclohex-2-ene-1,4-dione), a cyclic alkenone which is an important intermediate in the synthesis of carotenoids and fragrances (1–4). In general, allylic oxidation involves free radicals and lower oxidation state transition metals, whereas metals with low oxidation activity and high Lewis acidity in their highest oxidation state are the best epoxidation catalysts (5, 6). Allylic oxidation and epoxidation are often competitive processes in the oxidation of (cyclic) olefins, where the nature of the olefin and the stability of the allylic radical intermediate greatly influence the product distribution.

Unfortunately, the choice of truly heterogeneous catalysts for allylic oxidation of complex molecules is rather limited (7). The highly sophisticated Bi–Mo oxides and Fe–Sb oxides, developed for the gas-phase oxidations of propylene to acrolein and isobutylene to methacrolein, do not function in the allylic oxidation of higher olefins (8, 9). Vanadia-containing catalysts are active and selective in the oxidation of α-isophorone to ketoisophorone but the process is complicated by rapid catalyst deactivation at moderate temperatures and background oxidation of isophorone at higher temperatures (10, 11). Heterogenized chromium-based catalysts CrY, Cr–APO-5, and Cr-pillared montmorillonite provide good yields in the liquid-phase oxidation of a variety of alkenes but leaching of the active species and homogeneous catalysis limit the practical application of these catalysts (12–14).

Aiming at circumventing the limitations of heterogeneously catalyzed allylic oxidation, we examined the allylic oxyfunctionalization of cyclic olefins in a two-step, one-pot synthesis involving epoxidation and consecutive base-catalyzed isomerization to the allylic alcohol. The approach is based on our recent observation that epoxidation of β-isophorone with a titania–silica aerogel and *tert*-butylhydroperoxide (TBHP) provides small amounts of 4-hydroxy-isophorone (**2**, Scheme 1) (15, 16). This aerogel is to our knowledge the only heterogeneous catalyst that is able to transform isophorone (**5**) to 4-hydroxy-isophorone (**2**). Apparently, isomerization of the epoxide **1** via ring-opening was catalyzed by the acidic sites in titania–silica. When an inorganic base was added to the reaction mixture to suppress acid-catalyzed side reactions and improve epoxide yield, some of the bases even favored the epoxide ring-opening reaction. For example, $NaHCO_3$ as additive improved the epoxide selectivity from 78 to 93% at 90% conversion, while Na_2CO_3 afforded 65% selectivity to 4-hydroxy-isophorone (**2**) and the epoxide was only a minor product. Another base, $BaCO_3$, catalyzed almost exclusively the isomerization of β-isophorone to

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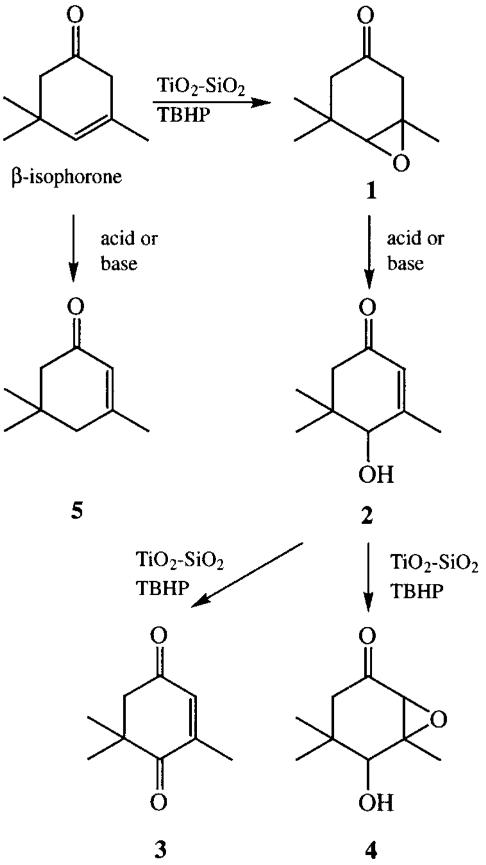


SCHEME 1. Major reactions during the oxidation of β-isophorone to 4-hydroxy-isophorone (**2**); dimerization and oligomerization of reactant and products are not shown.

α-isophorone (**5**) and hindered any oxidation reaction. No explanation has been found for the strikingly different behaviors of base additives (16).

Rearrangement of epoxides in general affords synthetically useful intermediates such as allylic alcohols, aldehydes, and ketones. Base-catalyzed rearrangements in particular have been known for a long time. In homogeneous catalysis, strong bases such as *t*-BuOK, *t*-BuLi, or lithium dialkylamides are used (17). In heterogeneous catalysis, mainly oxides or phosphates with acid/base properties like MgO, MgO-SiO_2, Al_2O_3, Li_3PO_4, and silicates have been investigated for epoxide ring opening so far (18–20). Typically, these solid bases afford a complex mixture of isomerized products with moderate selectivity for each compound, and the necessary reaction temperature is higher than 100°C. Recently, the catalytic application of a broad range of base catalysts has been reviewed including modified zeolites, alkaline earth oxides, KF on alumina, hydrotalcites, and oxynitrides (21–23). A recent example of acid-catalyzed isomerization of epoxides is the rearrangement of isophorone oxide to a keto-aldehyde catalyzed by zeolites (24).

Despite the tremendous work done on epoxidation of olefins as well as rearrangement of epoxides, only moderate attention has been paid so far to the acid-catalyzed intramolecular rearrangement of epoxides generated *in situ* (25). This idea has been realized recently in the epoxidation and acid-catalyzed rearrangement of open-chain unsaturated alcohols to hydroxytetrahydrofurans and hydroxytetrahydropyrans (26). Both reactions were catalyzed by the acidic sites of TS-1 and Ti-β. Similarly, in the reaction of styrene with H_2O_2 over titanium silicalite the epoxide isomerized *in situ* to phenylacetaldehyde (27, 28).

Intrigued by the importance of allylic oxidation products of isophorone, we chose β-isophorone as a model compound to study the one-pot transformation of olefins to allylic alcohols (Scheme 1). Epoxidation was catalyzed by hydrophilic and hydrophobic titania–silica aerogels, and some inorganic or organic base was added to the reaction mixture to promote epoxide ring-opening. A critical problem in this approach is that epoxide ring-opening requires a strongly basic catalyst, but strong bases are usually detrimental to the epoxidation activity of the Lewis acidic Ti sites and can even lead to complete destruction of the mixed oxide (15, 16).

2. EXPERIMENTAL

2.1. Materials

Analytical grade reagents and ion-exchanged water were used for the preparations. The following basic additives were used as received: Li_2CO_3 (Fluka, 99%), Na_2CO_3 (Fluka, 99.5%), K_2CO_3 (Fluka, 99%), MgO (Fluka, 98%), CaO (Aldrich, 99.9%), SrO (Aldrich, 99.9%), BaO (Riedel-deHaen, 95%), KF/Al_2O_3 (Fluka, ~5.5 mmol F^-/g), Li_3PO_4 (Aldrich), γ-Al_2O_3 (Merck), zeolite 4A (basic form, Fluka), 1,5,7-triazabicyclo[4,4,0]dec-5-ene (Fluka, 98%), 1,1,3,3-tetramethylguanidine (Fluka, 99%), 1,4,5,6-tetrahydropyrimidine (Aldrich, 97%). Preparations of a hydrotalcite exchanged by *t*-BuOK (Mg–Al–O-^{t}Bu) and that of KF supported on CaF_2 (KF/CaF_2) have been published elsewhere (29, 30). β-Isophorone was kindly supplied by Hoffmann-LaRoche, Switzerland (99.5%).

An amorphous mesoporous titania–silica low-temperature aerogel ("LT"aerogel) was prepared on the basis of a former recipe (31). The Si/Ti molar ratio was 12/1, corresponding to ca. 10 wt% TiO_2 for a theoretical catalyst TiO_2–SiO_2. A solution consisting of 6.07 g of titanium bisacetylacetonatediisopropoxide (Aldrich, 75 wt% in *i*-PrOH), 22.83 g of tetramethoxysilane (Fluka, 99%), and 10 ml of *i*-PrOH was prepared. The hydrolysant, consisting of 1.45 g of HNO_3 (65%), 13.01 g of H_2O, and 40 ml of *i*-PrOH was added under vigorous stirring. After 6 h, 6.05 g of trihexylamine in 60 ml of *i*-PrOH was added to the mixture. Gelation occurred within 1 h and the gel was aged for 6 days. The whole procedure was carried out in a glass reactor at room temperature under Ar. The resulting gel was semicontinuously extracted with supercritical CO_2 in an autoclave. A glass liner was used to prevent contamination originating from the steel autoclave. The extraction was completed within 2 h at 313 K and 210 bar with a CO_2 flow of 20 g min^{-1}. Portions of the raw aerogel were ground and heated in a tubular reactor in an upward air flow, at a rate of 5 K min^{-1} up to 673 K and kept at this temperature for 2 h.

The calcined LT aerogel was further treated in ethylbenzene as follows: 1 g of aerogel was stirred in 50 ml of ethylbenzene for 30 min at 323 K. The solvent was then removed at 333 K and 30 mbar, and the procedure repeated. This procedure was shown to reduce hydrophilicity and improve epoxidation selectivity of titania–silica aerogels (16, 32). The LT aerogel after treatment with ethylbenzene possessed a high BET surface area (816 $m^2 g^{-1}$) and mesoporous structure (mean pore diameter, 8.4 nm; maximum in pore size distribution, 62 nm; total pore volume, 2.3 $cm^3 g^{-1}$; micropore volume, 0.12 $cm^3 g^{-1}$).

In an attempt to clean the surface of the aerogel from organic residue, 1 g of LT aerogel was washed with 80 cm^3 of *i*-PrOH for 5 min at 353 K. After filtration of the catalyst, the procedure was repeated twice. Finally, the aerogel was recalcined according to the standard procedure.

A second, hydrophobic aerogel ("LT-Ph" aerogel) was also prepared in which 20% of the Si atoms was covalently bound to a phenyl group while the Si/Ti = 12/1 atomic ratio was kept constant. At first, 20.25 g of tetramethoxysilane and 6.58 g of phenyltrimethoxysilane (Fluka, 97%) were prehydrolyzed at 343 K for 2 h in a mixture of 50 ml of *i*-PrOH, 6.25 g of H_2O, and 0.35 g of HNO_3. The solution was then heated to 363 K and 6.73 g of titanium bisacetylacetonatediisopropoxide in 15.5 ml of *i*-PrOH was added. Finally, after 6 h, 1.45 g of trihexylamine in 6.25 g of H_2O was dropped into the mixture and the gel was aged for 6 days. After extraction with supercritical CO_2, the raw aerogel was heated at a rate of 5 K min^{-1} to 623 K in a nitrogen flow and kept at this temperature for 1 h. The treatment was repeated in an air flow and the material was kept at 673 K for 2 h. This hydrophobic aerogel LT-Ph possessed a high surface area and mesoporous structure (BET surface area, 688 $m^2 g^{-1}$; mean pore diameter, 9.5 nm; maximum in pore size distribution, 54 nm; total pore volume, 2.0 $cm^3 g^{-1}$; micropore volume, 0.03 $cm^3 g^{-1}$).

2.2. Methods

The epoxidation–isomerization reactions were carried out batchwise in a mechanically stirred, 50-ml thermostated glass reactor equipped with a thermometer, reflux condenser, and septum for withdrawing samples. All epoxidation reactions were performed under Ar (99.99%) to avoid the presence of oxygen and moisture. In a standard procedure, 80 mg of aerogel and 0.2 mmol of solid base additive were predried *in situ* in the reactor at 474 K for 1 h in an Ar flow. After the mixture was cooled to room temperature, ethylbenzene (solvent), 0.5 ml of cumene (internal standard), and alternatively an N-base (0.5 mmol) were added. The mixture was heated to 353 K, 10 mmol of β-isophorone was added, and the reaction was started by introducing 2.7 mmol of *tert*-butyl-hydroperoxide (TBHP, Fluka, ca. 5.5 M in nonane, stored over molecular sieve 4A) to the vigorously stirred slurry. The total reaction volume was 8 ml.

The reaction mixture was analyzed using an HP 5890 gas chromatograph equipped with a cool on-column inlet and an HP-FFAP capillary column. Products were identified by GC–MS and by comparison with authentic samples. The internal standard method was used for quantitative analysis. TBHP conversion was determined by iodometric titration using a Metrohm 686 Titroprocessor. The oxidation selectivity, related to the olefin consumed, is calculated as follows,

$$S_N(\%) = 100\{[N]/([\text{olefin}]_o - [\text{olefin}])\}, \qquad [1]$$

where N represents any product of the reaction (**1**–**5**), the subscript o stands for initial values, and all concentrations are expressed on a molar basis.

The initial rate of β-isophorone oxidation (r_2) was defined as the sum of oxidation products (**1**, **2**, and **3**) formed in the first 2 min, and related to unit amount of catalyst and unit time. Temperature-programmed oxidation experiments were carried out on a Netzsch STA 409 thermoanalyzer. The weight loss of the sample during heat treatment was followed by TG and the evolved gases were analyzed by MS.

Solubilities of alkaline carbonates were measured under reaction conditions but without catalyst and replacing TBHP by an equimolar amount of *tert*-butyl alcohol. The mixture was stirred and heated for 10 min at 353 K. The hot slurry was filtered and the dissolved base was extracted from the filtrate with 2×7.5 ml of H_2O. The combined aqueous solution was cooled to room temperature and the pH was measured with a Metrohm pH meter. The fraction of dissolved base was calculated from the pH shift relative to the pH of distilled water.

3. RESULTS

The influence of various bases and the reaction conditions on the one-pot epoxidation–isomerization of β-isophorone was investigated. Conversion of the substrate and peroxide, and formation of the major products **1**–**5** (Scheme 1), were followed up to 4–5 h. These kinetic curves are characterized in the tables by the initial rate (r_2) and the time required to achieve 50% TBHP conversion ($t_{50\%}$). Olefin and peroxide conversions (X_{olefin}, X_{TBHP}) and selectivities to **1**–**5** are related to the time required to obtain maximum selectivity to 4-hydroxy-isophorone (**2**) (t_{max}).

Oxidation of the OH function of unsaturated alcohols is usually slow over titania–silica, as compared to the rate of the epoxidation reaction (32). Epoxidation of the deactivated C=C bond in **2** and **3** is also slow. Accordingly, the amounts of **3** and **4** were small (with one exception) compared to the amount of **2**. Other minor products, and oligomers, were not determined. A 100% selectivity to **1**–**5** was reached only under special reaction conditions, but in these cases the selectivities to **2** were only 27–41%.

3.1. *Influence of Inorganic Bases*

Oxidation of β-isophorone at 80°C over the LT aerogel without any additive is illustrated in Fig. 1 and Table 1 (entry 1). Epoxide **1** formation was fast, but rearrangement to 4-hydroxy-isophorone (**2**) proceeded slowly and no maximum in the amount of **2** was reached within 5 h. Rearrangement of **1** can occur on the acidic sites of titania–silica. It has been reported that titania–silica is an efficient catalyst for isomerization of cyclohexene oxide, pinene oxide, and 3-carene oxide, but the selectivities to the corresponding allylic alcohols were moderate to low (0–26%) (18).

Addition of alkali carbonates as basic co-catalysts remarkably influenced the relative rate of epoxidation and isomerization reactions, and thus the product distribution. The kinetic curves in Fig. 2 can be interpreted by evaluating the base strength and solubilities of the co-catalysts in the organic reaction medium. Spectrophotometric measurements revealed increasing solid state basicity of carbonates with ascending ionic radius of the alkali metal (33). Solubility measurements, carried out under the conditions of the epoxidation reaction, showed that the fraction of dissolved base varied significantly: 2.6% for Li_2CO_3, 13.9% for Na_2CO_3, and 10.9% in the case of K_2CO_3. As both the dissolved and undissolved solid base can catalyze isomerization, the estimated order of basicity under reaction conditions is $K_2CO_3 > Na_2CO_3 \gg Li_2CO_3$.

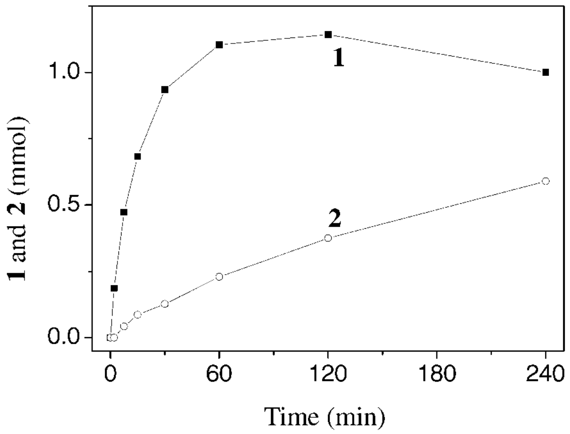


FIG. 1. Formation of β-isophorone oxide (**1**) and 4-hydroxy-isophorone (**2**) in the epoxidation of β-isophorone over the LT aerogel without any additive; standard conditions, given in Experimental part.

TABLE 1

Influence of Solid Base Additives in the Oxidation of β-Isophorone According to Scheme 1 (Standard Conditions)

Additives	r_2[a] (mmol/g min)	$t_{50\%}$[b] (min)	t_{max} (min)	X_{olefin}[c] (%)	X_{TBHP}[d] (%)	Selectivity (%) 1	2	3	4	5
			Alkali Carbonates							
No additive	1.16	12.5	300[e]	99.5	99.5	37.5	28	1	3	9
Li_2CO_3	0.71	30	240[e]	67.5	83.5	41	41	0	3	5
Na_2CO_3	1.33	12	120	74	84	0	71.5	2.5	3	8
K_2CO_3	0.96	>240	2	20.5	6	1	10	18	2.5	19
			Alkaline-Earth Oxides							
MgO	1.57	15	300[e]	100	100	40	31	4.5	3.5	7
CaO	1.19	15	180	83	89.5	1.5	77.5	1.5	3.5	12.5
SrO	1.21	23.5	300[e]	93.5	100	39.5	31	1	3	9.5
BaO	0.12	>300	300[e]	56.5	48	0	31	2	0	61.5
			Other Catalysts							
Li_3PO_4	0.5	57	240[e]	73	77.5	42.5	30.5	1	3	7.5
Mg–Al–O-^{t}Bu	0.35	>360	2	17	4	0	13	0	0	80.5
KF/Al_2O_3	1.8	68	15	67.5	30.5	2	31.5	5	1.5	42.5
KF/CaF_2	0.66	120	300[e]	59	60.5	2.5	74	4	7.5	11
γ-Al_2O_3	2.45	14	240[e]	96.5	100	20	59	2.5	6.5	7.5
Zeolite 4 A	1.23	24	240[e]	83	100	37	33	2	3	5

[a] Initial rate of formation of (**1** + **2** + **3**).

[b] Reaction time necessary for 50% TBHP conversion.

[c] Olefin (β-isophorone) conversion.

[d] TBHP conversion.

[e] Reaction was stopped, though the maximum in the formation of **2** was not yet reached.

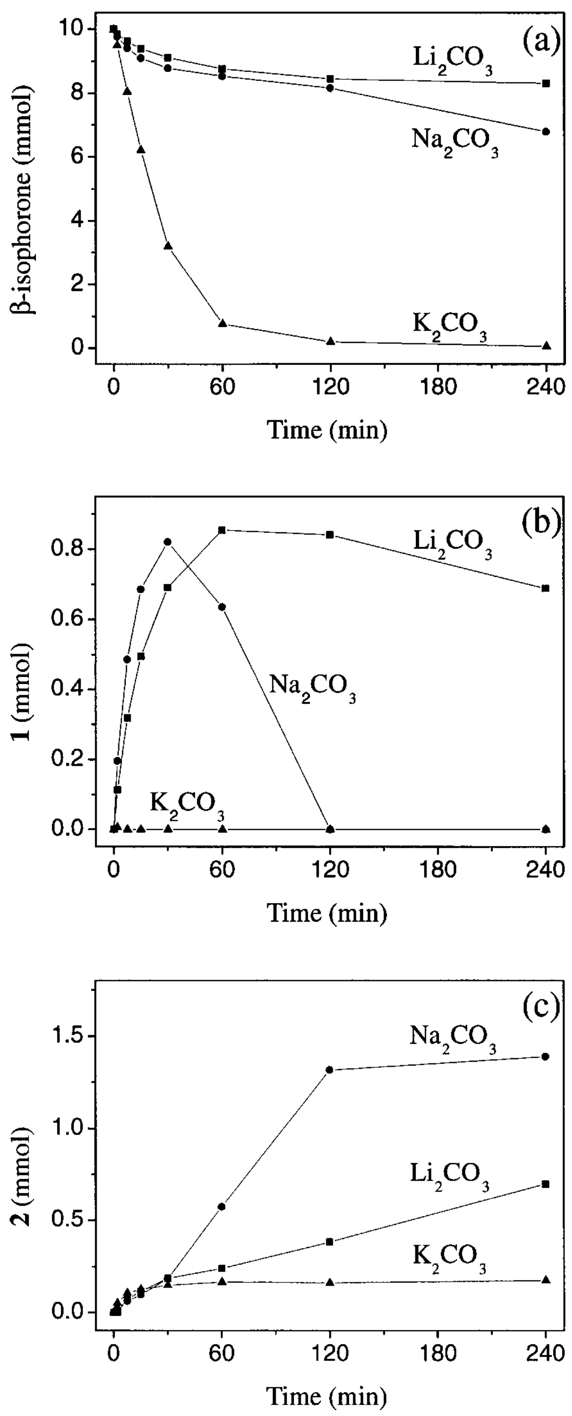


FIG. 2. Influence of alkali carbonates as additives on β-isophorone consumption (a), the formation of epoxide (**1**) (b), and 4-hydroxy-isophorone (**2**) (c); standard conditions.

It is clear from Fig. 2 that Na_2CO_3 was the best co-catalyst: both the epoxide **1** formation and its isomerization to **2** were fast, affording 71.5% selectivity to **2** in the optimum (in 2 h, Table 1). Apparently, the basicity of Li_2CO_3 was too weak to catalyze ring-opening, and the improvement compared to the reference reaction was small. On the other hand, the strongly basic K_2CO_3 catalyzed the rapid nonoxidative conversion of β-isophorone to α-isophorone (**5**) and to oligomers. After only 2 min the selectivity to nonvolatile products (undetectable by GC analysis) approached 50%. Besides, K_2CO_3 was highly efficient in the isomerization of epoxide **1** to hydroxy-isophorone (**2**) and in the further oxidation of **2** to keto-isophorone (**3**). These observations confirm that a strong base—though advantageous for epoxide ring-opening—can be detrimental to the formation of epoxide (16).

Alkaline-earth oxides show the same trend as alkali carbonates, that is increasing basicity with increasing ionic radius (22). Good performance of alkaline-earth oxides as base catalysts usually requires a high reaction temperature (ca. 800 K (22)) in order to remove water and carbon dioxide from the catalyst. Consequently, under the standard conditions applied here (353 K) the presence of surface carbonate and hydroxide species cannot be excluded. In addition, CaO partly dissolved during reaction, which was indicated by the significant pH shift of 1.02 observed in the solubility measurements (see Section 2.2). For comparison, Na_2CO_3 caused a pH shift of 0.83 under the same conditions.

Among the alkaline-earth oxides, CaO afforded the highest selectivity of 77.5% to the allylic alcohol **2** (Table 1). MgO and SrO barely affected the product distribution, as compared to that for the reaction without additive. BaO, being the strongest base, suppressed the epoxidation reaction and catalyzed the isomerization of β- to α-isophorone (**5**). Note that $BaCO_3$ is an even more efficient catalyst for the isomerization of β- to α-isophorone (16).

To separate the catalytic effect of the surface of solid CaO from that of dissolved species in epoxide rearrangement, the reaction was repeated with different amounts of CaO (Fig. 3). With small amounts of base (1 mol% or less, relative to β-isophorone) the isomerization of epoxide was too slow, while too high amounts (4 mol% or more) accelerated also the nonoxidative conversion (isomerization) of β-isophorone. The latter effect is seen in Fig. 3a, above 1 h reaction time (ca. 90% peroxide conversion). These experiments indicate that the surface sites of undissolved base are also involved in the isomerization reactions. Unfortunately, a quantitative determination of the amount of dissolved CaO was hindered by the presence of surface hydroxide and carbonate species.

Several other bases, which had been suggested for various base-catalyzed reactions, were also tested in β-isophorone oxidation (Table 1). Li_3PO_4, which has been used for propene oxide isomerization at 245°C (34), was not efficient under our conditions. *tert*-Butoxy-exchanged hydrotalcites showed high activity in aldol condensation (29). Here, this strongly basic material catalyzed the immediate rearrangement of epoxide **1** to hydroxy-isophorone (**2**) only in the first minutes of the reaction, while isomerization from β- to α-isophorone (**5**) dominated at higher conversions. KF/Al_2O_3

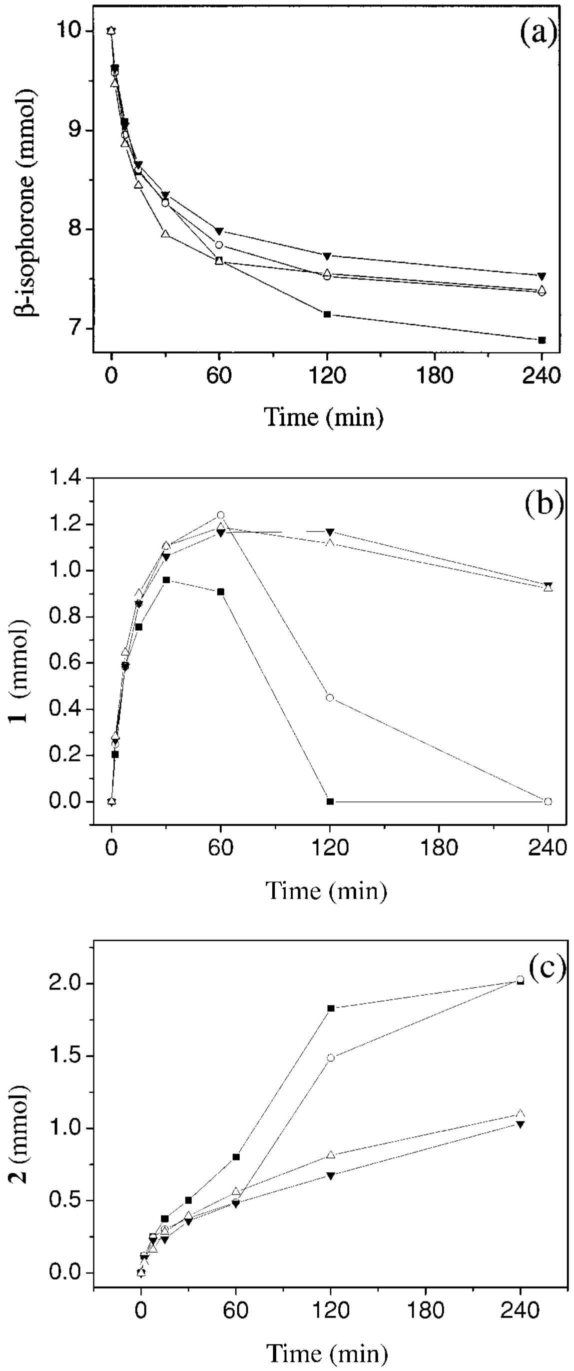


FIG. 3. Influence of the amount of CaO on β-isophorone consumption (a), formation of epoxide (**1**) (b), and 4-hydroxy-isophorone (**2**) (c); (■) 4 mol%, (○) 2 mol% (standard conditions), (▼) 1 mol%, (△) 0.5 mol% (mol% related to β-isophorone).

had a similar but less pronounced effect on the product distribution (Table 1).

The basicity of KF/CaF$_2$ was found to be weak in 1-butene isomerization, as compared to that of KF/Al$_2$O$_3$ (35). Interestingly, among all tested basic co-catalysts, KF/CaF$_2$ showed one of the highest selectivities to **2**. Due to the weak basicity, the reaction rate was low compared to the rates achieved with Na$_2$CO$_3$ and CaO additives.

γ-Alumina is known to catalyze isomerization of various epoxides including limonene oxide (36). The weaker basicity as compared to that of KF/Al$_2$O$_3$ is evident from the slow isomerization of **1** to **2** (high t_{max}), but the cumulative selectivity to oxidation products **1**–**4** is high (88%, Table 1).

In the epoxidation of (E)-2-hexen-1-ol with titania–silica aerogels, zeolite 4A revealed a beneficial effect on conversion and epoxide selectivity, which was attributed to the basicity and drying ability of the Na-exchanged molecular sieve (32). Here, in the epoxidation of β-isophorone, the product distribution was barely affected by this material.

3.2. Influence of Strong Nitrogen Bases

It was shown that various amines and N-heteroaromatic compounds enhanced the selectivities in the epoxidation of allylic alcohols (37). We assumed that strong N-bases which dissolve well in the reaction medium may be better co-catalysts for *in situ* epoxide rearrangement than the partly soluble inorganic bases. 1,5,7-Triazabicyclo[4, 4, 0]dec-5-ene (TBD) is a prototype of strong guanidine base catalysts (38). Due to their strong basicity (pK_{B} around 25 (39)), we tested TBD and two other amines, 1,1,3,3-tetramethylguanidine and 1,4,5,6-tetrahydropyrimidine, as potential base catalysts. Unfortunately, all three strong bases lowered the rate of oxidation and the selectivity to epoxide **1**, and—unexpectedly—did not catalyze epoxide ring-opening and formation of **2**. No improvement could be achieved by variation of the amount of base.

3.3. Influence of the Hydrophilic–Hydrophobic Nature of the Aerogel

Temperature-programmed oxidation of the calcined LT aerogel indicated the presence of significant amount of organic residue (3.5 wt% expressed as carbon content). To remove this polar residue, originating from catalyst precursors and only partially eliminated by extraction with the apolar supercritical CO$_2$, the LT aerogel was washed with the polar protic solvent i-PrOH. After recalcination at 673 K the carbon content was only 2.1 wt%. After hydrophobisation in ethylbenzene, this catalyst was tested in isophorone oxidation with and without Na$_2$CO$_3$ as additive. Unfortunately, no positive effect could be achieved by catalyst purification: the cleaner catalyst was less active and in the presence of base the maximum selectivity to **2** dropped from 71.5% to 36.5%.

The influence of the hydrophilic or hydrophobic nature of the catalyst surface on the product distribution and oxidation activity was investigated by comparing LT and LT-Ph aerogels. In both catalysts the Si/Ti atomic ratio was 12, but in LT-Ph phenyl groups were covalently bound to 20% of the Si atoms (40). The hydrophobicity of a phenyl-modified aerogel has been proved earlier (41). In general,

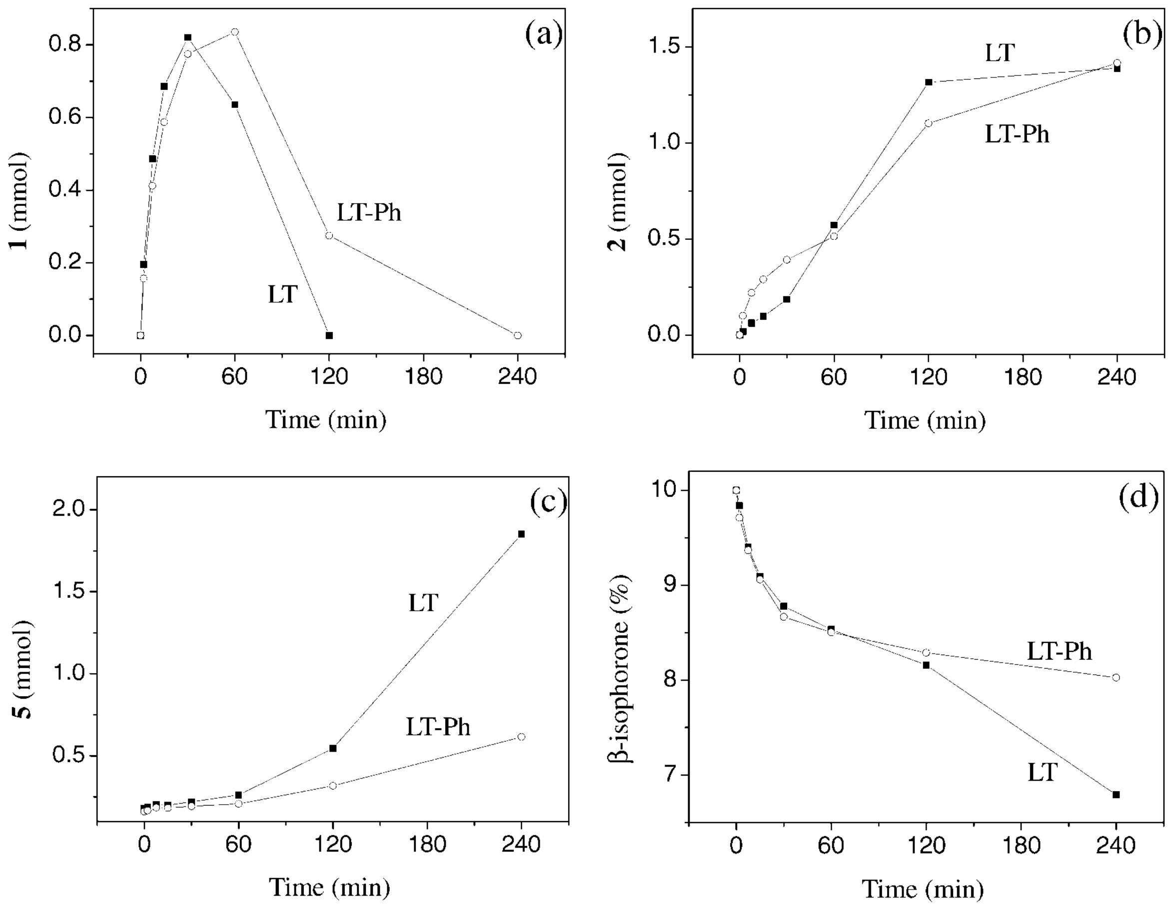


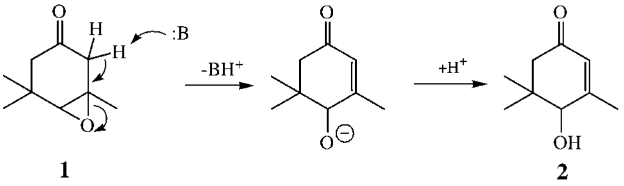
FIG. 4. Comparison of LT and LT-Ph aerogels in the epoxidation and isomerization of β-isophorone in the presence of Na_2CO_3: formation and consumption of epoxide (**1**) (a), 4-hydroxy-isophorone (**2**) (b), α-isophorone (**5**) (c), and β-isophorone (d); (■) LT (standard conditions), (○) LT-Ph.

the organically modified aerogel was less active for epoxidation, but oligomerization of reactant and products was also suppressed. In the best case, in the presence of Na_2CO_3, the selectivity to **2** was 72% at 79% olefin conversion and only 1.5% oligomers formed, compared to 15% with the LT aerogel in the optimum.

The different behavior of hydrophilic LT and hydrophobic LT-Ph, in the presence of Na_2CO_3 as co-catalyst, is illustrated in Fig. 4. In the early stage of the reaction the rates of epoxide **1** formation are almost identical on both catalysts but consumption of **1** by isomerization to **2** is significantly slower on LT-Ph (Fig. 4a). The likely explanation for this difference is the suppressed acidity (31) and hence isomerization activity of the LT-Ph aerogel. The isomerization activity of LT-Ph is lower also in other acid/base-catalyzed transformations, such as the formation of α- from β-isophorone (Fig. 4c), and in general in the nonoxidative consumption of β-isophorone (Fig. 4d, decay after 120 min). It was shown independently that isomerization of β- to α-isophorone (**5**) over LT-Ph was negligible in the absence of Na_2CO_3. For example, after 4 h the amount of **5** was 22.5% in the presence and only 3.5% in the absence of Na_2CO_3, while the olefin conversions were comparable (74–84%). Interestingly, the time-resolved formation of the key product 4-hydroxy-isophorone (**2**) is rather similar on both catalysts in the presence of Na_2CO_3 (Fig. 4b). This indicates that hydrophobization of titania–silica does not lead to significant improvement in the production of **2**. This result can be understood when considering the complex network of acid/base-catalyzed and oxidation reactions shown in Scheme 1.

4. DISCUSSION

The results in Table 1 and Figs. 1–4 demonstrate that good selectivity in the one-pot oxidation–isomerization of β-isophorone to 4-hydroxy-isophorone (**2**, Scheme 1) can only be obtained when the rates of epoxide formation and its rearrangement to hydroxy-isophorone are considerably higher than the rates of other oxidation, isomerization, and dimerization type side reactions. At best, 77.5% selectivity to **2** was achieved at 83% β-isophorone conversion and almost 90% TBHP conversion. In this reaction the oxidation step was catalyzed by a hydrophilic titania–silica aerogel



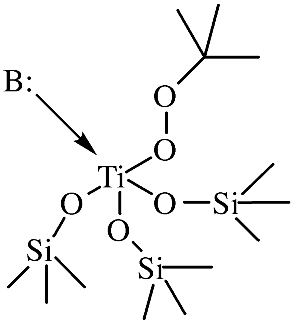
SCHEME 2. Base-catalyzed rearrangement of **1** to **2**.

and isomerization was accelerated by CaO as basic co-catalyst. Testing of a broad range of inorganic and organic bases revealed that the appropriate choice of the amount and the basic strength of co-catalyst is crucial for achieving good yields to **2**.

Earlier mechanistic studies proved that both acid and base catalyze the epoxide ring-opening and the formation of allylic alcohols. In the course of "β-elimination" a proton is abstracted by the base from the least substituted carbon atom and a C–O bond is cleaved (20, 42) (Scheme 2). A similar mechanism has been suggested for solids possessing acidic and basic sites, but in the presence of strong acidic sites the cleavage of the C–O bond precedes the abstraction of hydrogen and the main product is a ketone (18).

The titania-silica aerogel (LT) is active in both the epoxidation and isomerization reactions but the isomerization is slow and incomplete, as shown in Fig. 1. Titania–silica contains both Brønsted sites and Lewis acidic sites (43, 44). It is also known that formation of the peroxo complex during epoxidation enhances the acidity of the Lewis acidic Ti site (45–47). Very recently, we have demonstrated that the surface Brønsted sites are poor catalysts for the rearrangement of epoxides (48). Accordingly, the same active sites of the aerogel catalyze the epoxide formation and its isomerization to **2**.

Upon addition of a solid inorganic base to the reaction mixture, partial solvation in the apolar medium takes place. The dissolved basic species can neutralize the Brønsted acid sites of the catalyst, but also interact with the active Ti sites by coordination at these sites as illustrated in Scheme 3 (37). This interaction lowers the Lewis acidity of Ti and therefore diminishes its oxidation and isomerization activity. The product distribution strongly depends on the basic strength of the co-catalyst. Weak bases, such as Li_2CO_3, Li_3PO_4, and MgO, have only a small deactivating effect on Ti and they themselves are too weak for efficient catalysis of epoxide rearrangement. As a result, the influence of weak bases on the product distribution is minor. With medium strong bases (e.g., Na_2CO_3, CaO, and KF-CaF_2) the rate of epoxidation is acceptably high and these bases are efficient in epoxide rearrangement, leading to good yields to hydroxy-isophorone (**2**). When the base co-catalyst is too strong, such as K_2CO_3, BaO, and guanidine bases, epoxidation is suppressed and undesired side reactions (isomerization of β- to α-isophorone, dimerization, and oligomerization) are accelerated. It is expected that large, slowly diffusing oligomers can block the catalyst pores and also contribute to the observed loss of epoxidation activity.



SCHEME 3. Interaction of the base co-catalyst with the Ti peroxo complex (simplified drawing, further possible interaction to obtain the favored octahedral coordination of Ti is not shown).

The fraction of inorganic base dissolved in the apolar medium is small. As expected, the surface of undissolved base is also efficient in the epoxide rearrangement (Fig. 3). The amount of added base has a strong influence on the formation of **2**; this effect is comparable to that of the basic strength of the co-catalyst.

Hydrophobization of titania–silica with ethylbenzene by azeotropic distillation has been shown to suppress the acid-catalyzed side reactions and enhance the epoxide selectivity (16). This effect was attributed to the formation of Si–O–Si bonds from surface Si–OH functions by elimination of water, but dehydration of the Ti site should also be considered (43). The process is reversible and water formed in the side reactions can regenerate the acidic sites. A more efficient hydrophobization is the introduction of surface phenyl groups in the aerogel (49). Figure 4 illustrates the suppressed activity of LT-Ph aerogel in the isomerization of β- to α-isophorone while the efficiency in the epoxidation reaction was barely influenced. Unfortunately, the overall performance of titania–silica in the production of hydroxy-isophorone (**2**) in the presence of Na_2CO_3 co-catalyst could not be improved by hydrophobization.

Clearly, the one-pot oxidation of an olefin to the corresponding allylic alcohol is a demanding task as the two major steps, the epoxidation and the subsequent rearrangement, require different conditions. No base or only a weak base additive in apolar medium is the best for the fast and selective epoxidation over titania–silica (32, 50), while epoxide rearrangement is facile with strong bases in polar and apolar solvents (18, 42, 51).

5. CONCLUSIONS

The successful oxidation of β-isophorone to 4-hydroxy-isophorone illustrates the potential of the two-step, one-pot transformation of an olefin to allylic alcohol. The best results were achieved using a 10 wt% TiO_2–90 wt% SiO_2 aerogel and TBHP for epoxidation, and CaO as basic co-catalyst for the *in situ* rearrangement of epoxide. Simultaneous application of the two solid catalysts under mild conditions afforded good yields to 4-hydroxy-isophorone in only 3 h. This study focused on the proper selection and pretreatment of the two catalysts. Future investigations should uncover the applicability of this method for the transformation of other olefins.

ACKNOWLEDGMENTS

The authors are grateful to M. Maciejewski for the thermal analytical investigations, and to M. Schneider (Hoffmann-LaRoche, Switzerland) for valuable discussions.

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