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A high-throughput experimentation study of the epoxidation of alkenes with transition-metal-free heterogeneous catalysts

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Abstract

A set of transition-metal-free heterogeneous catalysts for the epoxidation of alkenes with hydrogen peroxide was studied by means of high-throughput experimentation. The catalysts were tested with a range of substrates. Gallium oxide displayed the highest epoxidation activity with all tested alkenes, followed by Ga-MCM-41. The reaction conditions were optimised by investigating the effect of the solvent in which the epoxidation takes place. Considerable improvements in the epoxide yields were obtained in the processes catalysed by Al-MCM-41, Ga-MCM-41 and zeolite USY$_{(2.6)}$. This work confirms the versatility of HTE for studying catalytic systems.

Keywords: Alkenes epoxidation; Transition-metal-free heterogeneous catalysts; High-throughput experimentation; Solvent effects; Hydrogen peroxide

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1. Introduction

Combinatorial and high-throughput experimentation (HTE) techniques represent a very useful and versatile tool in many fields of chemical research. By allowing the rapid preparation, characterisation and testing of a vast number of samples, these techniques offer a large potential for increasing the rate of scientific and technological progress. Since the 1990s, the development of tailored equipment gave impulse to the growth and to the application of HTE to diverse fields, including catalysis [1–9]. Catalysts are generally complex systems. Their synthesis may involve a multi-step mechanism influenced by many parameters. Moreover, it is often difficult to establish an unambiguous relationship between their physicochemical and catalytic properties. This implies that studying a catalytic system can require the investigation of large parameter spaces, for which purpose HTE methods are greatly helpful. HTE can prove useful in all phases of the development of a catalyst, from the discovery of novel catalytic materials to the optimisation of the conditions in which the catalytic reaction takes place. Although these techniques are suitable for research both in homogeneous and heterogeneous catalysis, the application in the latter branch is concentrated on gas-phase reactions while examples of liquid-phase heterogeneous catalysts studied by HTE are far less common [10–12]. This is due to some intrinsic technical difficulties connected to the use of large arrays of miniaturised parallel reactors in liquid-phase heterogeneous processes. The main possible problems are connected to the separation of the catalyst from the liquid phase, both after the catalyst synthesis or in the catalytic test, and to the efficiency of the stirring of the catalyst suspension during the reaction. Various measures can be taken to minimise the effect of these technical issues. This may require an adaptation of the experimental conditions to the HTE equipment available. For example, the filtration of the large numbers of catalysts used in HTE can be very time-consuming and cause relevant losses of solid given the small amount of samples typically employed in HTE. A valid alternative to filtration is the centrifugation of the samples followed by aspiration of the supernatant liquid from the top of the solution using the liquid-detection function available in many liquid-handling HTE workstations. Concerning the stirring, the best results are usually obtained with individual magnetic stirring of each reactor. However, care should be taken to tune the stirring speed for the type of reaction and of catalyst used: the speed should be high enough to provide a good mass transfer but not too high to prevent blocking of the stirrers, which tends to occur at high stirring rates. Moreover, each experimental system might benefit from customised solutions to adapt it to the HTE equipment. Finally, performing a number of experiments in

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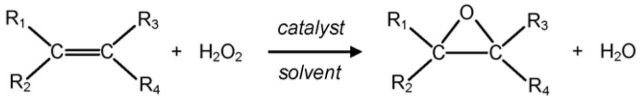
duplicate or in triplicate is a good practice to increase the reliability of the HTE results. Under these conditions, HTE can be employed successfully in liquid-phase heterogeneous catalysis.

Recently, we reported an HTE investigation of transition-metal-free oxides as heterogeneous catalysts for the liquid-phase epoxidation of cyclooctene with aqueous H_2O_2. A large number of boron, aluminium and gallium oxides and of aluminium- and gallium-substituted microporous and mesoporous silicates were prepared and tested as catalysts for the epoxidation of cyclooctene. The best results were obtained with gallium oxide, with aluminium- and gallium-substituted MCM-41 and with zeolite USY with low Si/Al [13,14]. These materials are promising catalysts for the sustainable production of epoxides, a class of compounds with a broad range of applications [15,16].

Here, a further HTE study of selected catalysts from the previous screenings is presented. In order to extend the scope of their application, the epoxidation activity of these catalysts was tested with a series of alkenes. Then, the reaction conditions during the epoxidation were optimised by investigating the effect of the solvent in which the catalytic reaction takes place (Scheme 1). Since the purpose of this study was to gain specific knowledge about the substrate scope and the solvent effect for a set of chosen catalysts, a full factorial HTE approach was used [13].



Scheme 1. Epoxidation of alkenes with hydrogen peroxide.

2. Experimental

2.1. The HTE equipment

The catalytic tests were performed using a Tecan Genesis RSP 100 liquid-handling robotic workstation coupled with a personal computer supplied with Gemini software enabling to program the workstation. Dispensing and transferring of the liquids took place using either fixed metal needles or disposable plastic needles. Both types of needle are equipped with a liquid-detecting function, active for conductive liquids. The high accuracy of the operations performed with the needles is ensured by their prior calibration with different liquid classes. The workstation is equipped with a reaction block developed in house, consisting of a heating unit containing 60 wells for 10-ml glass vials (maximum working temperature of 80 °C) and a Variomag plate for the individual magnetic stirring of the 60 parallel reaction vessels (Fig. 1). A stirring speed of 500 rpm was employed in all experiments: this speed was selected since it is high enough to provide a good stirring of the samples and low enough to prevent malfunctioning of some of the stirrers, which was observed at higher stirring rates.

The alkene conversion (X, %), epoxide and by-products yields (Y, %) and selectivities (S, %) were determined by gas chromatography (GC) analysis on a Finnigan Trace GC Ultra from Interscience, equipped with a RTX-5 fused silica column (5 m; 0.1 mm). A short analysis time for each sample (2.25 min) was made possible by the rapid heating and cooling system of the column (Ultra Fast Module). The temperature profile for the analysis of the epoxidation of 1-hexene was: 42 s at 40 °C, 40–250 °C at 200 °C/min, and 30 s at 250 °C. For cyclohexene, the temperature profile was: 45 s at 50 °C, 50–250 °C at 200 °C/min, and 30 s at 250 °C. For all the other alkenes, the temperature profile was: 45 s at 70 °C, 70–250 °C at 180 °C/min, and 30 s at 250 °C. Prior to GC analysis, the samples were centrifuged for 5 min at 3000 rpm to separate the solid catalysts from the reaction mixture. The conversions and yields were calculated by normalising the areas of the GC peaks by means of the area of the internal standard peak (di-*n*-butyl ether).

Fig. 1. The HTE workstation equipped with a 60-wells reaction block.

The identification of the by-products of the epoxidation of the various alkenes was performed by gas chromatography–mass spectrometry (GC–MS) on an Agilent 6890N gas chromatograph coupled to an Agilent 5973 MSD mass spectrometer. The GC was equipped with a WCOT fused silica column (30 m; 0.25 mm) coated with a 0.25 μm thick HP-5 MS film. The temperature programs were analogous to those employed for the GC analyses.

A number of catalytic tests were performed in duplicate or in triplicate: in such case, the average of the obtained values for conversions and yields is reported.

2.2. Materials

Partially hydroxylated gallium oxide was prepared using a similar method to that reported in a previous publication [13]. $GaCl_3$ (20 mmol) was slowly dissolved in 50 ml of 2-butanol. The dissolution is a rapid and exothermic process accompanied by the evolution of HCl gas. A dark brown solution was obtained, to which 3.92 g of deionised H_2O was added dropwise, while stirring. The obtained red-brown, opaque suspension was stirred for 1 h at room temperature and then for 3–24 h at 70 °C in a closed round-bottom flask placed in an oil bath. Next, most of the solvent was removed by evaporation under reduced pressure. The sample was transferred into an oven and calcined according to the following temperature program: 25–100 °C at 10 °C/min; 12 h at 100 °C; 100–200 °C in 30 min; 12 h at 200 °C; 200–300 °C in 30 min; 12 h at 300 °C for the gallium oxide employed in the experiments with different substrates; 25–100 °C at 10 °C/min; 24 h at 100 °C; 100–200 °C in 30 min; 12 h at 200 °C; 200–375 °C in 60 min; 24 h at 375 °C for the gallium oxide used in the experiments with different solvents. A very dark brown solid was obtained in both cases. Prior to the catalytic tests, the solids were reacted for 4 h at 80° with cyclooctene and aqueous H_2O_2 in ethyl acetate (amounts as in the catalytic tests), to remove the chlorine atoms still present in the materials [13]. Then, the solids were washed 3 times with ethanol and dried for 16 h at 90 °C.

Al-MCM-41 and Ga-MCM-41 were prepared with a method reported previously [14]. The two mesoporous materials were calcined at 550 °C for 8 h (from 25 to 550 °C at 2 °C/min). The catalysts were tested and recycled in at least two successive runs before being used in the experiments described in this work [14]. Ultrastable zeolites Y (FAU) were obtained from PQ Zeolites: $USY_{(2.6)}$ (CBV 600, Si/Al = 2.6) and $USY_{(6)}$ (CBV 712, Si/Al = 6). Prior to use, the zeolites were calcined at 550 °C for 2 h (from 25 to 550 °C at 5 °C/min). Then, they were kept for 1 week in a desiccator containing a saturated aqueous solution of NH_4Cl, exposing them to an atmosphere of moisture saturated air. Weighing the zeolites immediately after calcination and again after this procedure allowed determining the amount of H_2O adsorbed into each material at a constant high partial pressure of water vapour. This allowed further handling of the samples in open air without additional precautions.

2.3. Catalytic tests

The reaction conditions for the epoxidation of the selected alkenes (1-hexene (97%), 1-octene (99%), 1-decene (95%), *R*-(+)-limonene (97%), cyclohexene (99%) and *cis*-cyclooctene (95%)) were derived from the methods used previously with gallium oxide [13] and with the alumino- and gallosilicates [14]. For the reactions with gallium oxide, 1.25 mmol of alkene, 0.625 mmol of di-*n*-butyl ether, 1.36 ml of ethyl acetate and 2.50 mmol of hydrogen peroxide (H_2O_2) as a 50 wt.% aqueous solution were added to 0.074 g of the catalyst. For the reactions with Al-MCM-41, Ga-MCM-41 and with the USY zeolites, 0.625 mmol of alkene, 0.313 mmol of di-*n*-butyl ether, 1.50 ml of ethyl acetate and 6.25 mmol of H_2O_2 as a 50 wt.% aqueous solution were added to the catalyst (0.156 g of Al-MCM-41, 0.166 g of Ga-MCM-41, 0.065 g of $USY_{(2.6)}$ or 0.123 g of $USY_{(6)}$). First, ethyl acetate and the solution containing the alkene and di-*n*-butyl ether were added to the solid catalyst while stirring. Then, the aqueous solution of hydrogen peroxide was added. All solutions were dispensed using the HTE workstation. The reaction mixture was stirred for 1 h at 500 rpm and 80 °C in capped vials placed in the 60-wells reaction block.

The reaction conditions for the epoxidation of *cis*-cyclooctene in different solvents (ethyl acetate, toluene, 2-propanol, ethanol, acetonitrile, formamide, *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO) and 1:1 (in volume) mixtures of each of the mentioned solvents with ethyl acetate) were similar to those used for the catalytic tests with different alkenes (*vide supra*). For the reactions with gallium oxide, 1.25 mmol of *cis*-cyclooctene, 0.625 mmol of di-*n*-butyl ether, 1.36 ml of solvent (or 0.68 ml of each of the two solvents employed) and 2.50 mmol of H_2O_2 as a 50 wt.% aqueous solution were added to 0.047 g of the catalyst. For the reactions with the alumino- and gallosilicates, 0.625 mmol of *cis*-cyclooctene, 0.313 mmol of di-*n*-butyl ether, 1.50 ml of solvent (or 0.75 ml of each of the two solvents employed) and 6.25 mmol of H_2O_2 as a 50 wt.% aqueous solution were added to the catalyst (0.156 g of Al-MCM-41, 0.166 g of Ga-MCM-41, 0.065 g of $USY_{(2.6)}$ or 0.123 g of $USY_{(6)}$). First, the solvent(s) and the solution containing *cis*-cyclooctene and di-*n*-butyl ether were added to the solid catalyst while stirring. Next, the aqueous solution of hydrogen peroxide was added. All solutions were dispensed by means of the HTE workstation. The reaction mixture was stirred for 4 h at 500 rpm and 80 °C in capped vials placed in the 60-wells reaction block. The rubber septum of the caps was pierced with a sharp needle to prevent building up of pressure in the reactors during the catalytic test.

3. Results and discussion

3.1. Study of the epoxidation activity with different alkenes

Gallium oxide, Al-MCM-41, Ga-MCM-41 and zeolite $USY_{(2.6)}$ (Si/Al = 2.6) were identified as active catalysts for the epoxidation of cyclooctene with aqueous hydrogen peroxide [13,14]. A crucial feature of a good catalyst is the ability to work with different substrates. Therefore, in this work, the scope of application of these materials is extended to the epoxidation of a variety of alkenes (Tables 1–7). Zeolite $USY_{(6)}$ (Si/Al = 6) is tested together with the catalysts mentioned above. In previous tests, this catalyst displayed high conversion of cyclooctene but low epoxide selectivity, due to the presence of strong Brønsted acid sites [14]. However, the type of sites present in this zeolite may prove suitable in the epoxidation of other substrates. The activity of the various catalysts is measured in the first phase of the epoxidation process (1 h at 80 °C), when the differences between the reaction rates are more evident. All the catalysts show activity with the selected substrates, although the level of alkene conversion and the epoxide selectivity vary conspicuously as a function of the catalyst and of the substrate employed (Tables 1–7).

Among the explored catalysts, gallium oxide gives the highest epoxide yield with each of the substrates. The alkene conversions and epoxide yields obtained with this catalyst are reported in Fig. 2. The highest conversion among the studied alkenes is obtained with limonene (42%), with a selectivity of 91% towards the totality of the epoxide products, i.e. the ring epoxide (**a**), the side-chain epoxide (**b**) and the diepoxide (**c**) [17,18]. On the basis of electronic effects, the more substituted double bond located on the ring of limonene is expected to be more reactive towards epoxidation compared to the side-chain

Table 1
Epoxidation of limonene with different transition-metal-free catalysts (1 h at 80 °C).

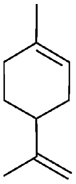
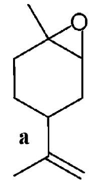
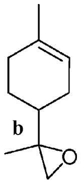
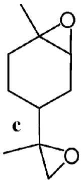
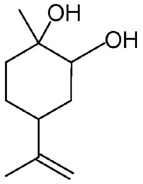
Catalyst		 a	 b	 c	
	X_{limonene} (%)	$S_{\text{limonene epoxides}}$ (%)		Epoxide distribution (**a**:**b**:**c**)	$S_{\text{1,2-limonene diol}}$ (%)
Gallium oxide	42	91		0.8:0.1:0.1	6.8
Al-MCM-41	14	68		0.6:0.2:0.2	25
Ga-MCM-41	21	56		0.7:0.2:0.1	36
USY$_{(2.6)}$	5.1	19		0.4:0.4:0.2	50
USY$_{(6)}$	55	23		0.0:0.6:0.4	43

Table 2
Epoxidation of cyclooctene with different transition-metal-free catalysts (1 h at 80 °C)

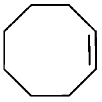
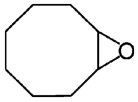
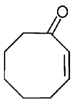
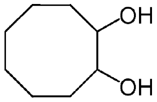
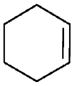
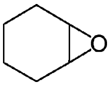
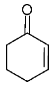
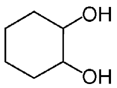
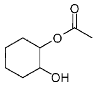
Catalyst				
	$X_{\text{cyclooctene}}$ (%)	$S_{\text{epoxycyclooctane}}$ (%)	$S_{\text{2-cycloocten-1-one}}$ (%)	$S_{\text{1,2-cyclooctanediol}}$ (%)
Gallium oxide	36	>99	0.3	0.2
Al-MCM-41	4.9	94	0.0	5.5
Ga-MCM-41	7.6	94	0.0	2.6
USY$_{(2.6)}$	4.6	98	1.8	0.0
USY$_{(6)}$	23	88	0.0	2.1

Table 3
Epoxidation of cyclohexene with different transition-metal-free catalysts (1 h at 80 °C)

Catalyst					
	$X_{\text{cyclohexene}}$ (%)	$S_{\text{epoxycyclohexane}}$ (%)	$S_{\text{2-cyclohexen-1-one}}$ (%)	$S_{\text{1,2-cyclohexanediol}}$ (%)	$S_{\text{1,2-cyclohexanediol acetate}}$ (%)
Gallium oxide	19	76	13	5.9	2.3
Al-MCM-41	4.0	30	26	23	18
Ga-MCM-41	4.7	43	39	17	0.9
USY$_{(2.6)}$	4.5	19	4.4	28	36
USY$_{(6)}$	29	2.0	1.4	23	28

double bond [19,20]. Indeed, epoxide **a** is the major product (Table 1, entry 1), with an almost identical amount of *cis* and *trans* isomers. The main by-product is the diol formed by the hydrolysis of the epoxide function of **a**. High conversion (36%) and very high epoxide selectivity (>99%) is obtained with cyclooctene, in line with previous reports [13]. The conversion of cyclohexene is lower (19%), though still acceptable. Besides epoxycyclohexane (76% selectivity), the major products are

Table 4
Epoxidation of styrene with different transition-metal-free catalysts (1 h at 80 °C)

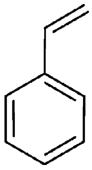
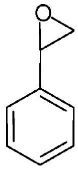
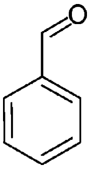
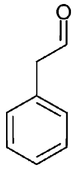
Catalyst				
	X_{styrene} (%)	$S_{\text{styrene oxide}}$ (%)	$S_{\text{benzaldehyde}}$ (%)	$S_{\text{phenylacetaldehyde}}$ (%)
Gallium oxide	6.0	76	15	5.3
Al-MCM-41	2.6	0.0	81	0.0
Ga-MCM-41	4.0	4.5	64	6.3
USY$_{(2.6)}$	16	0.0	70	12
USY$_{(6)}$	24	0.0	86	11

Table 5
Epoxidation of 1-hexene with different transition-metal-free catalysts (1 h at 80 °C)

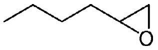
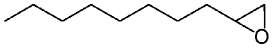
Catalyst	 $X_{1\text{-hexene}}$ (%)	 $S_{1,2\text{-epoxyhexane}}$ (%)
Gallium oxide	2.7	97
Al-MCM-41	0.2	>99
Ga-MCM-41	0.4	>99
$USY_{(2.6)}$	0.4	>99
$USY_{(6)}$	0.1	>99

Table 7
Epoxidation of 1-decene with different transition-metal-free catalysts (1 h at 80 °C)

Catalyst	 $X_{1\text{-decene}}$ (%)	 $S_{1,2\text{-epoxydecane}}$ (%)
Gallium oxide	3.5	98
Al-MCM-41	0.3	>99
Ga-MCM-41	2.0	77
$USY_{(2.6)}$	0.2	53
$USY_{(6)}$	0.5	13

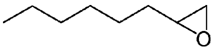
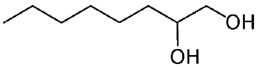
1,2-cyclohexanediol, formed by the hydrolysis of the epoxide ring, and 2-cyclohexen-1-one, obtained by the allylic oxidation of cyclohexene taking place in the presence of O_2 formed by the decomposition of H_2O_2 [21]. For the three linear, terminal alkenes the conversion is highly selective towards the epoxide but proceeds more slowly than with cyclic alkenes, as expected on the basis of electronic effects [12,22,23]. Styrene is converted with moderate yield and with an epoxide selectivity of 76%. In summary, gallium oxide shows relevant conversion of all the tested alkenes, with selectivity towards the epoxide ranging from 76% to 100%. These results point to the versatility of this material as epoxidation catalyst with aqueous hydrogen peroxide. When the activities in the epoxidation of different substrates are compared [19,24,25], gallium oxide confirms to be superior to aluminium oxide [13].

The catalytic behaviour of the other catalysts differs substantially from that of gallium oxide (Tables 1–7). Al-MCM-41 and Ga-MCM-41 follow similar trends, with the gallium-containing material displaying higher catalytic activities with all substrates [14]. Good conversions of limonene are observed with these two catalysts, although the epoxide selectivity is lower than with gallium oxide. The decrease in selectivity is due to the further reaction of the limonene epoxide **a**, as proven by the lower ratio of this compound among the epoxide products and by the increased selectivity towards the diol. Cyclooctene conversion proceeds with high epoxide selectivity reaching 4.9% with Al-MCM-41 and 7.6% with Ga-MCM-41, in agreement with previous reports [14]. Cyclohexene conversion is similar, showing reduced selectivity, due to consecutive reaction of the epoxide and to allylic oxidation of the substrate (*vide supra*). The conversion of styrene is in the same range of that obtained with gallium oxide but almost no epoxide is formed. The main product is benzaldehyde. This compound is often observed as a major product of the oxidation of styrene and has been proposed to form by the further reaction of styrene oxide with H_2O_2 [26–28]. Finally, the epoxidation of the three linear alkenes is selective but takes place slowly, in line with what observed with gallium oxide.

Zeolite $USY_{(2.6)}$ and $USY_{(6)}$ show low epoxide yields with all alkenes except cyclooctene and limonene. $USY_{(2.6)}$ gives lower conversions than $USY_{(6)}$, with in general a higher epoxide selectivity (Tables 1–7). $USY_{(6)}$ displays very high conversion of limonene (55%) with low epoxide selectivity. With both zeolites, the major product is 1,2-limonene diol. The fraction of epoxide **a** is much lower than with gallium oxide or with the MCM-41 materials. With $USY_{(6)}$, only the side-chain epoxide **b** and the diepoxide **c** are present, while any epoxide **a** that formed reacted further on the strong Brønsted acid sites of this zeolite. The epoxidation of cyclooctene follows the trend expected from previous studies [14]. $USY_{(6)}$ is very active in catalysing the conversion of cyclohexene to 1,2-cyclohexanediol and related products. $USY_{(2.6)}$ is less active but shows higher selectivity towards epoxycyclohexane. Both zeolites display high styrene conversion leading to the formation of benzaldehyde and, in lower amount, of phenylacetaldehyde, while no styrene oxide is obtained. With the three linear alkenes, low epoxide yields are obtained with the USY zeolites. 1-Octene is converted in higher amounts particularly with $USY_{(6)}$, with 1,2-octanediol being the main product. In the reactions for which higher conversions are observed, viz. for limonene, cyclohexene and styrene with $USY_{(6)}$ and styrene with $USY_{(2.6)}$, the mass balance is between 85% and 89%. This effect was already noticed with cyclooctene and is attributed to the formation of bulky molecules that tend to block the zeolite pores [14].

Summarising, Ga-MCM-41 gives the best results among the microporous and mesoporous silicates. However, the epoxide yields are markedly lower than those obtained with gallium

Table 6
Epoxidation of 1-octene with different transition-metal-free catalysts (1 h at 80 °C)

Catalyst	 $X_{1\text{-octene}}$ (%)	 $S_{1,2\text{-epoxyoctane}}$ (%)	 $S_{1,2\text{-octanediol}}$ (%)
Gallium oxide	4.3	99	0.0
Al-MCM-41	0.8	>99	0.0
Ga-MCM-41	1.4	>99	0.0
$USY_{(2.6)}$	1.4	33	38
$USY_{(6)}$	5.0	4.0	53

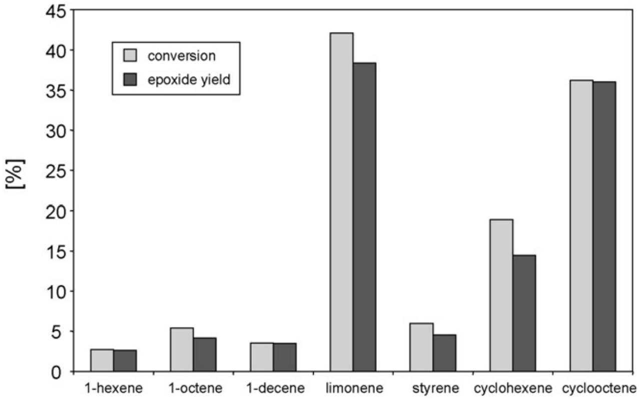


Fig. 2. Epoxidation of various alkenes with H_2O_2 catalysed by gallium oxide (1 h at 80 °C).

oxide and low epoxide selectivities are observed in the epoxidation of limonene, styrene and cyclohexene. Such low selectivites can be ascribed to consecutive reactions of the epoxide ring catalysed by the Brønsted acidity of these materials and to reactions of the substrate with O_2 formed in the disproportionation of H_2O_2, which was used in higher concentration with these catalysts than with gallium oxide. The effect of the Brønsted acidity is particularly evident with the two USY zeolites, for which the conversion is directly proportional and the epoxide selectivity is inversely proportional to the strength of the Brønsted acid sites.

3.2. *Study of the epoxidation activity with different solvents*

The catalytic epoxidation of cyclooctene with gallium oxide, aluminium- and gallium-substituted MCM-41 and zeolite $USY_{(2.6)}$ was optimised by exploring the effect of the solvent in which the reaction takes place. The nature of the solvent of a liquid-phase catalytic process can play a strong role in determining the outcome of the reaction. The solvent can influence the access of the reagents to the catalytic sites, facilitate their coordination to the active centres but also poison the active sites by competitive coordination. Moreover, the solvent can display catalytic activity on its own.

Table 8
Boiling points and electric properties of the employed solvents

	Boiling point (°C)	Dipole moment (D)	Dielectric constant (at 25 °C)
Ethyl acetate	77	1.78	6.0
Toluene	111	0.37	2.4
Ethanol	78	1.69	24
2-Propanol	82	1.66	18
Acetonitrile	82	3.92	38[a]
DMF	153	3.86	37
DMSO	189	3.96	48[a]

[a] at 20 °C.

A set of high-boiling point solvents with different levels of polarity were explored (Table 8). Each solvent was tested alone or as a 1:1 mixture with ethyl acetate, i.e. the solvent used in the previous studies with transition-metal-free catalysts [13,14]. Formamide was excluded from the set of solvents after a preliminary experiment in which overpressure was built in the reaction vials due to O_2 generated by the reaction of formamide with H_2O_2 [29]. The epoxide yields as a function of the solvent employed are reported in Fig. 3, while a more detailed overview of the catalytic results can be found in Table 9.

For gallium oxide, the highest epoxide yields are obtained with ethyl acetate, i.e. the solvent that was used in the previous

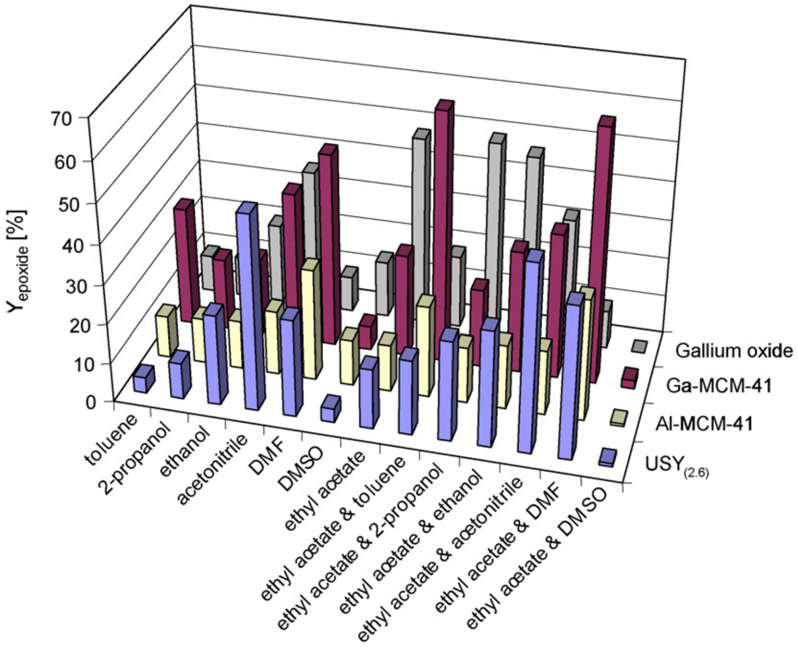


Fig. 3. Effect of the solvent on the epoxidation of cyclooctene with H_2O_2 using different transition-metal-free catalysts ($Y_{epoxide}$ = epoxycyclooctane yield after 4 h at 80 °C).

studies, and with the 1:1 mixtures of ethyl acetate with ethanol and 2-propanol. All other solvents give lower conversions of cyclooctene. It can be concluded that ethyl acetate, alone or in combination with a co-solvent with similar physicochemical properties (Table 8), presents the optimal features for the epoxidation of cyclooctene with gallium oxide.

For Al-MCM-41, Ga-MCM-41 and $USY_{(2.6)}$, remarkable improvements in the catalytic activity are obtained with various solvents. The epoxidation of cyclooctene with Ga-MCM-41 gives much higher conversion when performed in a 1:1 mixture of ethyl acetate with toluene, acetonitrile or DMF or with acetonitrile and DMF alone. With toluene and DMF the very high

Table 9
Effect of the solvent on the epoxidation of cyclooctene with 50 wt.% aqueous H_2O_2 using different transition-metal-free catalysts

Catalyst	Solvent(s)	X (%)	$Y_{epoxide}$ (%)	$S_{epoxide}$ (%)
Gallium oxide	Toluene	10	10	97
	2-Propanol	11	10	94
	Ethanol	21	20	98
	Acetonitrile	38	36	95
	DMF	10	9.1	94
	DMSO	14	14	>99
	Ethyl acetate	48	48	>99
	Ethyl acetate and toluene	19	19	99
	Ethyl acetate and 2-propanol	49	49	>99
	Ethyl acetate and ethanol	47	47	99
	Ethyl acetate and acetonitrile	33	32	97
	Ethyl acetate and DMF	11	9.7	90
	Ethyl acetate and DMSO	0.0	0.0	0.0
Al-MCM-41	Toluene	11	11	99
	2-Propanol	12	11	98
	Ethanol	13	12	98
	Acetonitrile	25	16	65
	DMF	30	28	95
	DMSO	12	12	>99
	Ethyl acetate	12	12	97
	Ethyl acetate and toluene	24	23	99
	Ethyl acetate and 2-propanol	15	14	98
	Ethyl acetate and ethanol	17	16	99
	Ethyl acetate and acetonitrile	25	16	67
	Ethyl acetate and DMF	31	31	99
	Ethyl acetate and DMSO	0.7	0.7	>99
Ga-MCM-41	Toluene	30	30	>99
	2-Propanol	19	18	99
	Ethanol	20	20	>99
	Acetonitrile	65	38	59
	DMF	50	49	98
	DMSO	13	6.1	48
	Ethyl acetate	26	26	99
	Ethyl acetate and toluene	64	63	>99
	Ethyl acetate and 2-propanol	20	20	>99
	Ethyl acetate and ethanol	31	31	>99
	Ethyl acetate and acetonitrile	56	37	66
	Ethyl acetate and DMF	65	64	98
	Ethyl acetate and DMSO	4.0	2.1	53
$USY_{(2.6)}$	Toluene	6.3	4.0	63
	2-Propanol	9.5	9.3	98
	Ethanol	23	23	99
	Acetonitrile	61	49	82
	DMF	25	25	99
	DMSO	5.5	3.5	64
	Ethyl acetate	17	15	91
	Ethyl acetate and toluene	19	19	99
	Ethyl acetate and 2-propanol	35	25	72
	Ethyl acetate and ethanol	44	29	68
	Ethyl acetate and acetonitrile	50	47	95
	Ethyl acetate and DMF	39	38	99
	Ethyl acetate and DMSO	0.8	0.8	>99

4 h at 80 °C; X = cyclooctene conversion; $Y_{epoxide}$ = epoxycyclooctane yield; $S_{epoxide}$ = epoxycyclooctane selectivity.

epoxide selectivity displayed in ethyl acetate is retained, while with acetonitrile the selectivity drops due to the formation of other products of the oxidation of cyclooctene (2-cycloocten-1-one, cyclooctanol-2-one, 5-hydroxyepoxycyclooctane). The epoxide yields obtained in the 1:1 mixture of ethyl acetate with either toluene (63%) or DMF (64%) represent a big improvement compared to the 26% yield displayed in ethyl acetate. Among the two options, the use of a 1:1 mixture of ethyl acetate and toluene is preferable over that with DMF for health, environmental and economical reasons. Under these conditions, Ga-MCM-41 becomes a very attractive, stable heterogeneous catalyst for the epoxidation of alkenes with hydrogen peroxide. The solvent effects observed with Al-MCM-41 are very similar to those described for Ga-MCM-41, although all the yields are at a lower level in agreement with the differences in activity between the two MCM-41 catalysts already discussed [14]. For the epoxidation with $USY_{(2.6)}$, acetonitrile is the most favourable solvent both alone or in combination with ethyl acetate, reaching up to 49% epoxide yield. This is a considerable improvement compared to the 15% yield found in ethyl acetate. However, the epoxide selectivity is lower than with ethyl acetate, particularly when acetonitrile is used alone. This drop in selectivity and the nature of the by-products formed are similar to what is observed with Al-MCM-41 and Ga-MCM-41. Improved epoxide yields are also obtained with DMF, particularly when used in combination with ethyl acetate, and with the mixtures of ethyl acetate with ethanol or 2-propanol, although the epoxide selectivity with the two alcohols is noticeably lower.

The increased epoxidation activity of Al-MCM-41, Ga-MCM-41 and $USY_{(2.6)}$ with acetonitrile and DMF can be explained by the high polarity of these solvents. In the catalytic tests with ethyl acetate as solvent and with high concentration of hydrogen peroxide, a biphasic liquid system is formed [14]. A polar (co-)solvent like acetonitrile or DMF can be used to improve the miscibility of H_2O_2 in the reaction mixture and, thus, to favour the access of the oxidant to the active sites. However, the polarity of the solvent should not be so high as to cause phase separation of the rather apolar alkene, which would be detrimental to the access of the substrate to the catalytic active sites. Another contribution of acetonitrile and DMF to the epoxidation activity stems from their ability to react with H_2O_2 to give peroxide species that favour the transfer of oxygen to the alkenes [29,30]. The catalytic effect of these solvents was checked by running the epoxidation of cyclooctene under the same experimental conditions used with the alumino- and gallosilicates but without the solid catalysts. The blank samples with acetonitrile and a 1:1 mixture of ethyl acetate and acetonitrile give a slightly higher epoxide yield compared to that in the ethyl acetate blank (4% against 3%). On the other hand, the blank with DMF shows 7% of epoxide yield and that with a 1:1 mixture of ethyl acetate and DMF reaches 20% of epoxide yield, indicating that DMF contributes significantly to the final catalytic activity. The lower epoxide yield of the blank with only DMF compared to that with ethyl acetate and DMF is ascribed to the low miscibility of DMF with cyclooctene.

The large improvement in the epoxidation activity of Al-MCM-41 and Ga-MCM-41 when toluene is used in combination with ethyl acetate cannot be explained in terms of improved miscibility of the reaction mixture. On the contrary, the low polarity of toluene causes an even more pronounced phase separation. Toluene is not expected to react with H_2O_2 as it is confirmed by the analogous, low epoxide yields observed with blank samples containing either ethyl acetate or a 1:1 mixture of toluene and ethyl acetate. The positive effect of toluene seems rather to be related to an interaction with the catalyst, since the effect is observed only with the two MCM-41 materials. The low polarity of the solvent might favour the access of the alkenes into the relatively hydrophobic channels of the two mesoporous catalysts. Another possible explanation involves the low tendency of toluene, compared to ethyl acetate or other polar solvents, to coordinate to the active surface sites of the catalyst and, thus, to limit their availability for the catalytic reaction [31].

While the positive effect of polar solvents was predictable, the identification of toluene and ethyl acetate as a very suitable combination of solvents for epoxidation with Al-MCM-41 and Ga-MCM-41 was unexpected. Its discovery is directly related to the screening of large parameter spaces typical of HTE.

4. Conclusions

The epoxidation of alkenes with a set of novel transition-metal-free catalysts was studied using HTE. Gallium-containing catalysts showed the highest activities in the epoxidation of the selected alkenes. The optimisation of the solvent used in the catalytic reaction led to a very large improvement in the epoxide yields with Al-MCM-41, Ga-MCM-41 and $USY_{(2.6)}$. Particularly, an increase from 26% to 63% was observed in the reaction catalysed by Ga-MCM-41 when using toluene as a co-solvent with ethyl acetate. These results, together with those from previous work [13,14], demonstrate that HTE is a very useful tool in all stages of the development of novel heterogeneous catalysts for liquid-phase reactions: from the synthesis and testing of large libraries of catalysts to a detailed study and optimisation of the catalytic properties of the most promising of these materials.

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