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Scope and limitations of one-pot multistep reactions with heterogeneous catalysts: The case of alkene epoxidation coupled to epoxide ring-opening

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ABSTRACT

The combination of two reactions in one-pot multistep system requires the compatibility not only between the catalysts of both reactions, but also between all the reaction components and conditions. In the case of the coupling of alkene epoxidation and epoxide ring opening, it has been possible to synthesize cyanohydrin and azidohydrin derivatives through a simple process that involves a one-pot multistep process by using a mixture of two heterogeneous catalysts, a silica-grafted Ti catalyst and ytterbium chloride, whose efficiency depends on the reactivity of the starting alkene. In addition, in some cases the mixture of catalysts can be recovered and reused in several one-pot multistep cycles. However, this system is not possible with electron-deficient alkenes, as the basic catalyst required for epoxidation has shown to be incompatible with the ring-opening process.

1. Introduction

The substitution of conventional stoichiometric methodologies by catalytic processes, combined with the possibility of process intensification by combining several catalytic steps into a one-pot catalytic system, provides a means to improve the economical and environmental aspects of the chemical processes by minimizing the use of chemicals, the waste production and the processing time.

Soluble chemical catalysts can interact, even with mutual destruction in case of incompatible species. For example, acidic catalysts are incompatible with basic catalysts in solution. In this case, heterogeneous catalysis would allow the isolation of the catalytic sites, avoiding their destructive interaction in the so-called "*wolf-and-lamb*" reactions [1]. Furthermore, the use of heterogeneous catalysts allows the easy separation and reuse in other reactions, with the additional advantages that isolation and purification of intermediates are not required. This methodology should constitute a powerful tool in applied chemistry, allowing extremely complex chemical transformations taking place in a one-pot cleaner and more efficient process.

In spite of the interest of this strategy, applications have been scarcely described in the literature. Some examples of use of this methodology are: the sequence of dehydrohalogenation–hydrogenation reactions promoted by modified sol–gel materials [2], acid–base tandem reactions catalyzed by isolated active centers on clay materials [3], base-functionalized magnetically recoverable nanoparticles together with catalytic solids for different tandem reactions [4], a one-pot tandem deacetalization and enantioselective aldol reaction using resin-supported acidic and basic catalysts [5], a sequence of a Michael addition followed by a *N*-acyl iminium cyclization catalyzed by resin supports base and acid catalysts [6], a dehydration–hydrogenation sequence promoted by a supported palladium catalyst on a magnetically separable composite and a cross-linked sulfonic acid polystyrene [7], a condensation–dehydration–reduction reactions using a multifunctional base–acid–metal catalyst [8], or the shift of the coupling of the base-catalyzed transesterification of oil and the acid-catalyzed acetalization of glycerol by use of a zeolitic membrane [9]. One probable reason for the small number of examples might be the need for compatibility between catalysts, solvents, reagents, concomitant products and general conditions of both reactions.

Epoxides are versatile intermediates in organic synthesis because the ring can be easily opened with a large variety of reagents. This reaction is very important in organic synthesis because it leads to the preparation of 1,2-difunctionalized compounds in one step with stereochemical control. In consequence one interesting couple of reactions would be the epoxidation of an alkene and the ring opening of the formed epoxide with a nucleophile (Scheme 1).

Due to environmental considerations, organic hydroperoxides and hydrogen peroxide would be good oxidants for this type of

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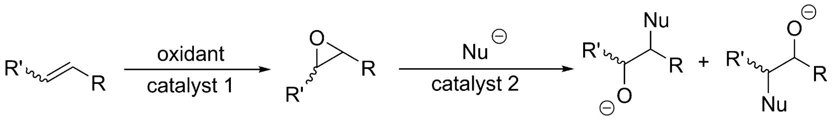


Scheme 1.

reactions [10]. However hydrogen peroxide and concomitant water are good nucleophiles that may open the epoxide in the presence of the second catalyst. Organic hydroperoxides would be then more suitable for one-pot sequential reactions. According to the electronic properties of the substrate different heterogeneous catalysts have to be used. For electron-rich alkenes, metal catalysts (Ti, W, Mo. . .) are more suitable [11]. One simple and efficient catalyst for this type of reaction would be silica modified with Ti(O^{i}Pr) groups [12,13]. In the case of electron-deficient alkenes a basic catalyst would be necessary, and KF/Al_2O_3 has proven to be the most efficient [14].

Many different nucleophiles have been used for epoxide ring-opening, most of them containing heteroatoms, which allows obtaining compounds such as 1,2-azido alcohols [15], 1,2-halohydrins [16], 1,2-hydroxy sulfides [17], or 1,2-diols [18]. Among them α-azido alcohols are important precursors for alternative syntheses of β-aminoalcohols [19]; some of them are part of the structures of pharmaceutical compounds, useful chiral auxiliaries, or intermediates for the synthesis of amino sugars. On the other hand, cyanide is a particularly interesting carbon-based nucleophile for epoxide ring-opening because of its low cost and the synthetic versatility of the nitrile ring-opened products. In view of this, trimethylsilyl azide [20–22] and trimethylsilyl cyanide [23–26] were selected for this study as examples for heteroatom and carbon nucleophiles respectively. Ytterbium derivatives were considered as catalysts for both reactions [27].

The ultimate aim of this work is the combination of the epoxidation-ring opening reactions in the same reaction flask but, as previous step, the conditions for each individual reaction and the compatibility between the different components of both reactions will be studied.

2. Experimental

Reagents were purchased from Aldrich and used as received without further purification. KF/Al_2O_3 catalyst was purchased from Fluka and it was dried at 140 °C under vacuum for 12 h prior to use.

2.1. Catalysts preparation and characterization

SiO_2–Ti(O^{i}Pr)$_2$: This catalyst was prepared by treatment of Merck 60 silica with $Ti(O^iPr)_4$ (2.5 mmol/g) following a procedure reported in the literature [13]. The catalyst was dried at 140 °C under vacuum for 12 h prior to use.

Ytterbium-exchanged laponite: To a solution of $YbCl_3$ (121.6 mg, 0.4 mmol) in methanol (6 mL), laponite (1 g) was slowly added and the suspension was stirred at room temperature for 24 h under argon. The solid was filtered off, thoroughly washed with methanol (10 mL) and then with dichloromethane (20 mL) and dried under vacuum.

Characterization: The surface areas were determined BET nitrogen isotherms at 77 K: SiO_2–$Ti(O^iPr)_2$ 448 m^2/g, Yb-laponite 203 m^2/g. The metal content was determined by ICP: SiO_2–$Ti(O^iPr)_2$ 1.07 mmol Ti/g, Yb-laponite 0.38 mmol Yb/g. SiO_2–$Ti(O^iPr)_2$ was also analyzed after six consecutive cyclohexene epoxidations: 0.95 mmol Ti/g. After the first cyclohexene oxide trimethylsilylcyanation run, the Yb content of Yb-laponite was only 0.12 mmol/g.

2.2. Catalytic test

2.2.1. Epoxidation of alkenes with SiO_2–Ti(O^{i}Pr)$_2$

To a mixture of alkene (2 mmol) and hydroperoxide (1 mmol) in 1.5 mL of solvent under argon, 27.8 mg of dried titanium-silica catalyst were added. In the case of *tert*-butyl hydroperoxide, the anhydrous hydroperoxide form (4 Å MS in decane) was used. The mixture was stirred at 65 °C (at 25 °C in the case of cyclohexene). The reaction was monitored by GC (FID from Hewlett–Packard 5890 II), using a cross-linked methyl silicone column (30 m × 0.25 mm × 0.35 pm), helium as carrier gas (20 psi), injector temperature 230 °C, detector temperature 250 °C and oven temperature program: 45 °C (4 min)–25 °C/min–200 °C (0 min)–40 °C/min–250 °C (5 min). At the end of reaction, the catalyst was removed by filtration and washed with dry dichloromethane.

2.2.2. Epoxidation of α,β-unsaturated ketones

To a mixture of TBHP (178 μL, 5.5 M in decane, 1 mmol) and α,β-unsaturated ketone (2 mmol) in toluene (1.5 mL), dried KF/Al_2O_3 (0.1 mmol) was added. The mixture was stirred at room temperature under argon for 24 h. Yield was determined by ^{1}H-NMR in the crude after filtration of the catalyst.

2.2.3. Epoxide ring-opening with TMSCN/$TMSN_3$

Caution!: TMSCN liberates toxic gas in contact with water. Although the used amounts of TMSCN were very small reactions were carried out under a safety hood, wearing gloves, safety glasses and lab coat, and at the end, all residues were treated with bleach. To a mixture of epoxide (1 mmol) and TMSNu (1.2 mmol), ytterbium catalyst ($YbCl_3$ or ytterbium-exchanged laponite, 0.1 mmol) was added under argon. The mixture was stirred at the corresponding temperature (see Table 3) and the reaction monitored by GC with the method described above. The catalyst was removed by filtration and washed with dry dichloromethane.

2.2.4. One-pot reactions

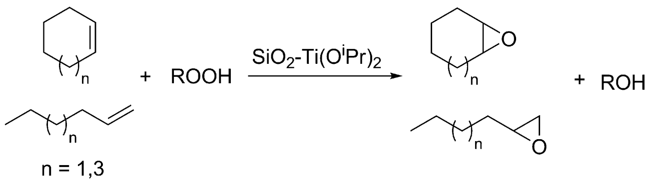
Titanium and ytterbium catalysts were added to a mixture of alkene and hydroperoxide in toluene under conditions described above. The reaction was monitored by GC and at the end of the epoxidation reaction TMSNu (2.4 mmol) was added. The mixture of catalysts was filtered and washed with dry dichloromethane and reactivated under vacuum for 12 h prior to reuse.

3. Results and discussion

3.1. Epoxidation

First, the catalyst for epoxidation of electron-rich alkenes was prepared by treatment of dried silica with $Ti(O^iPr)_4$ in anhydrous toluene under reflux [13,28]. The different commercially available organic hydroperoxides were tested in the epoxidation of several alkenes (Scheme 2).

The results (Table 1) show that the currently available anhydrous *tert*-butyl hydroperoxide (Table 1, entry 1) was less efficient than that the previously available solution in isooctane (87% yield) [13] and the best result (89% yield) was obtained with cumene hydroperoxide (CHP) (Table 1, entry 2). No by-products (diol or 2-alkoxycyclohexanol, allylic oxidation products) were detected,



Scheme 2.

Table 1
Epoxidation of different alkenes with organic hydroperoxides catalyzed by SiO_2–$Ti(O^iPr)_2$[a].

Entry	Alkene	Oxidant	Solvent	*T* (°C)	Yield (%)
1	Cyclohexene	TBHP + MS	DCM	25	71
2	Cyclohexene	CHP	DCM	25	89
3	Cyclooctene	CHP	DCE	65	97
4	1-Octene	CHP	DCE	65	71
5	1-Hexene	CHP	DCE	65	40

[a] Reaction conditions: 1 mmol of oxidant, 2 mmol of alkene, 28 mg of Ti catalyst (7 mol%) activated under vacuum at 140 °C for 12 h, 1.5 mL of solvent, reaction time 24 h. DCM = dichloromethane. DCE = 1,2-dichloroethane.

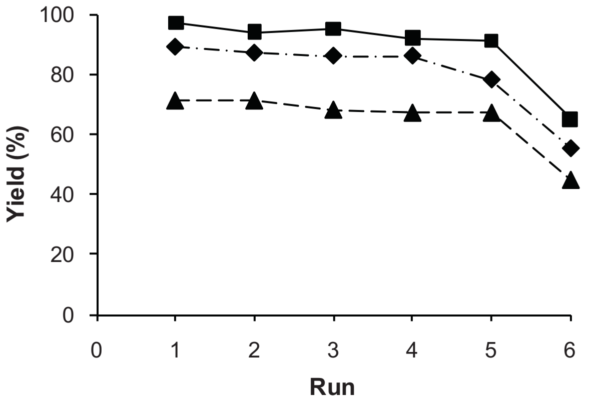
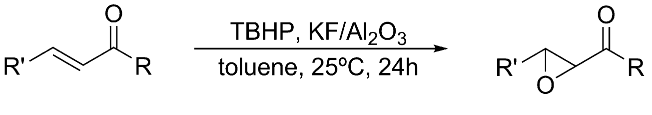


Fig. 1. Recovery of SiO_2–$Ti(O^iPr)_2$ catalyst in the epoxidation reaction with different alkenes: cyclohexene (◆), cyclooctene (■), 1-octene (▲).

and the concomitant alcohol (*tert*-butanol or α,α-dimethylbenzyl alcohol) was not produced in the absence of alkene, showing that the catalyst is not able to decompose the alkyl hydroperoxide.

CHP was also used for the epoxidation of another cyclic alkene, cyclooctene, and two linear alkenes, 1-octene and 1-hexene (Scheme 2). All these alkenes are less reactive than cyclohexene, and the yield did not exceed 10% at 25 °C. Thus, the reaction temperature was increased to 65 °C. Under such conditions, yields ranged from moderate to excellent in the order cyclooctene > 1-octene > 1-hexene. In addition, in the reactions with the most reactive alkenes the catalyst was recovered and reused under the same conditions. As can be seen in Fig. 1, the activity of the catalyst remains almost constant in 5 consecutive runs with a slight drop in the sixth run.

On the other hand, KF/Al_2O_3, in combination with TBHP as an oxidant, was the method of choice for epoxidation of electrophilic alkenes since previous results with CHP showed that this oxidant was not as effective as TBHP. The reactions in toluene were tested with different α,β-unsaturated ketones (Scheme 3) bearing both aliphatic and aromatic substituents. In all cases α,β-epoxy ketones were obtained with excellent yields (Table 2). Results were also similar in chlorinated solvents (dichloromethane and 1,2-dichloroethane).



Scheme 3.

Table 2
Epoxidation of different alkenes with TBHP catalyzed by KF/Al_2O_3[a].

Entry	R	R′	Run	Yield (%)
1	Et	Me	1	93
2	Me	Ph	1	100
3	Ph	Ph	1	100
4			2	92
5			3	87
6			4	57
7	Et	H	1	100

[a] Reaction conditions: 1 mmol of TBHP, 2 mmol of alkene, 0.1 mmol of KF catalyst activated under vacuum at 140 °C for 12 h, 1.5 mL of toluene, reaction time 24 h.

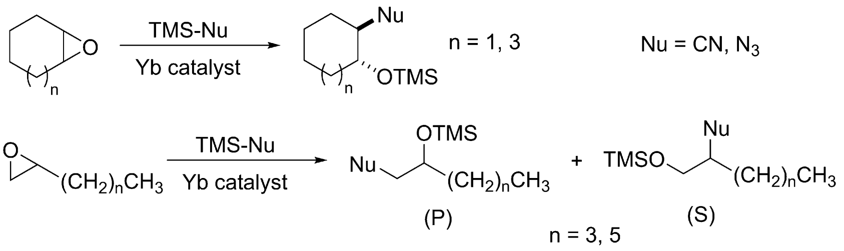
In addition, the KF/Al_2O_3 catalyst was recovered after the epoxidation reaction of *trans*-chalcone (Table 2, entry 3) and could be reused in two additional consecutive reaction cycles with high yield, with a drop only in the fourth run (Table 2, entries 4–6).

3.2. *Epoxide ring-opening*

As previously commented, two different nucleophiles were chosen to open the epoxides: cyanide and azide (Scheme 4). When cyclohexene and cyclooctene oxides were used as substrates *trans*-products were obtained in both cases. In the case of the linear epoxides, two regioisomers can be obtained depending on the position attacked by the nucleophile, leading to the product with the nucleophile in the primary (P) or in the secondary (S) carbon atom (Scheme 4). Ytterbium chloride was chosen as catalyst given that it is insoluble under the reaction conditions and so, it behaves as a heterogeneous catalyst. In such case the products resulting from the chloride addition (Nu=Cl) were also detected [20]. Alternatively, laponite was exchanged with ytterbium (Lap-Yb, 0.38 mmol Yb/g) and also tested as heterogeneous catalyst in order to compare the behavior of both catalysts. The results of the epoxide ring-opening reaction are gathered in Table 3.

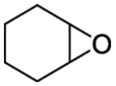
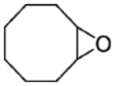
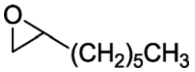
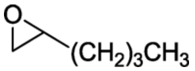
It can be observed (Table 3) that epoxides from cyclic alkenes were efficiently opened using ytterbium chloride as a catalyst. Cyclohexene oxide was able to react with both nucleophiles at room temperature with total conversion, although the product of addition of chloride was also observed in variable amount (20–35%) (Table 3, entries 1 and 3). Cyclooctene oxide was less reactive and good yields were only reached when the reaction was carried out at 85 °C. Regarding to the laponite-exchanged catalysts, it can be postulated that the displacement of the chloride counterion by the support prevents the formation of chlorinated products (Table 3, entries 2, 4, 6 and 8). The most relevant example was the opening of cyclohexene oxide with TMSCN, in which 98% of the desired product was obtained. However, with less reactive epoxides and/or nucleophiles, several unidentified products were also detected, decreasing in this way the selectivity of the reaction. Moreover, extensive Yb leaching was detected after reaction with cyclohexene oxide, probably due to the formation of soluble $Yb(CN)_3$ species. In view of those results, ring-opening reactions of 1,2-epoxyoctane and 1,2-epoxyhexane were tested only with $YbCl_3$. Reactions took place at 65 °C with high conversion values (Table 3, entries 9–12). In all cases, even for chloride addition, the selectivity towards the product resulting from the nucleophilic attack to the primary position of the epoxide was very high.

Fig. 2 shows the results obtained in several consecutive cycles of the ring-opening reaction of cyclohexene oxide and cyclooctene oxide with TMSCN after the recovery of $YbCl_3$ catalyst. It could be recovered up to four times without noticeable yield drop. Inter-



Scheme 4.

Table 3
Results of epoxide ring-opening with Yb catalysts[a].

Entry	Epoxide	Catalyst	Nu	T (°C)	Solvent	Conv. (%)	Yield (%)	
							Nu	Cl
1		$YbCl_3$	CN	25	DCM	100	80	20
2		Lap-Yb	CN	25	DCM	100	98	0
3		$YbCl_3$	N_3	25	DCM	100	65	35
4		Lap-Yb	N_3	25	DCE	100	30	0
5		$YbCl_3$	CN	85	DCE	87	74	13
6		Lap-Yb	CN	85	DCE	100	77	0
7		$YbCl_3$	N_3	85	DCE	76	25	31
8		Lap-Yb	N_3	85	DCE	77	19	0
9		$YbCl_3$	CN	65	DCE	100	86/7[b]	5/2[b]
10		$YbCl_3$	N_3	65	DCE	100	58/15[b]	24/3[b]
11		$YbCl_3$	CN	65	DCE	100	88/7[b]	4/1[b]
12		$YbCl_3$	N_3	65	DCE	98	89/4[b]	4/1[b]

[a] Reaction conditions: 1 mmol of epoxide, 1.2 mmol of TMSNu, 0.1 mmol of Yb catalyst, 1.5 mL of solvent, reaction time 24 h. DCM = dichloromethane. DCE = 1,2-dichloroethane.

[b] Yields of the reaction on the primary and secondary carbon atoms (P/S).

estingly, in both cases, the yield in the desired product increased after the first recovery at the expense that chlorinated product does not form, probably due to the substitution of the active chloride by cyanide in the recovered catalyst. A possible explanation to this behavior might be the replacement of the labile chloride atoms by cyanide in the ytterbium catalyst in the first reaction and therefore, no more chloride ions would be available for an attack to the epoxide in a new reaction.

It is worth noting that the ring-opening of α,β-epoxy ketones with TMSCN or $TMSN_3$ promoted by $YbCl_3$ in toluene at 25 °C led to very good results as well. For instance, 98% conversion was obtained with chalcone epoxide and TMSCN. The two possible regioisomers were obtained in 71/29 ratio (Fig. 3) and the major product was that coming from the *anti* attack of cyanide in the β-position. Despite of these results, preliminary compatibility studies proved the impossibility in carrying out the tandem epoxidation-ring opening reactions with electron-deficient alkenes. For this reason, ring-opening of α,β-epoxy ketones was not studied as deeply as that of the other epoxides.

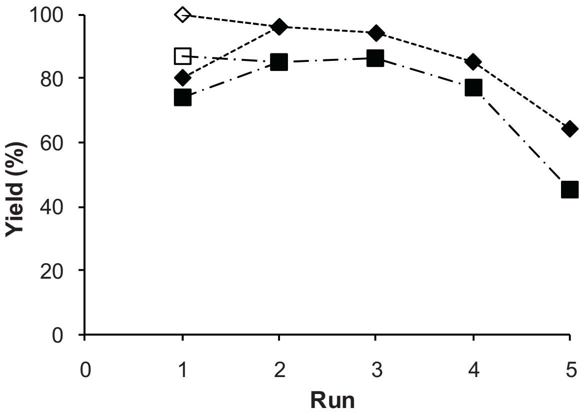


Fig. 2. Recovery of $YbCl_3$ in the epoxide ring-opening reaction with TMSCN with different alkenes: cyclohexene oxide (◆), cyclooctene oxide (■). Filled symbols are for cyanohydrins yield and open symbols represent total yield (including chlorhydrins).

3.3. Compatibility studies and one-pot reactions

As previously commented, the final aim of this work was the combination of alkene epoxidation and epoxide ring-opening reactions in one-pot with the simultaneous presence of both catalysts (Scheme 5). This process is far from evident given that the compatibility of a high number of parameters has to be taken into account in each reaction. Consequently, before the coupling between both reactions, several compatibility studies between catalysts, reaction conditions and reagents were carried out. Cyclohexene was chosen as reference substrate and TMSCN as reagent in the ring-opening reaction.

It had been reported in the literature that $Ti(O^iPr)_4$, which is the precursor of the titanium catalyst, was able to accomplish the epoxide ring-opening reaction with TMSCN [24]. Then, it was necessary

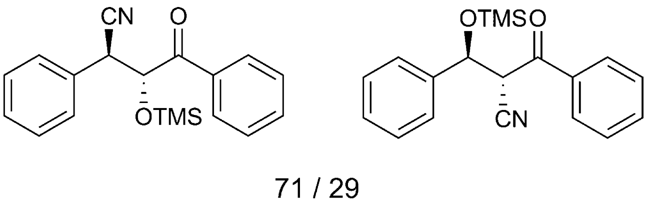
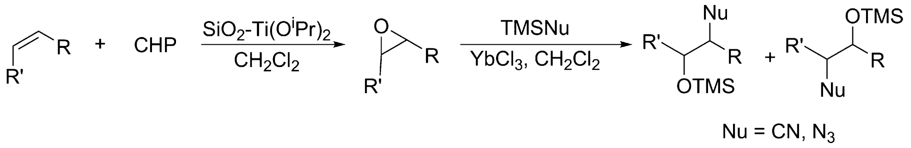


Fig. 3. Opening products of 2,3-epoxychalcone with TMSCN.



Scheme 5.

Table 4
Tandem epoxidation-ring opening reactions using TMSCN[a].

Entry	Alkene	Solvent	*T* (°C)[b]	Run	Yield (%)		
					Epoxidation	Ring-Opening	Global
1	Cyclohexene	DCM	25	1	89	80[d]	71
2				2	87	79	69
3				3	87	75	65
4				4	85	45	38
5	Cyclooctene	DCE	65[c]	1	97	70[e]	68
6				2	95	66	63
7				3	94	65	61
8				4	94	26	24
9	1-Octene	DCE	65	1	71	56[f]	40
10	1-Hexene	DCE	65	1	40	<5[g]	–

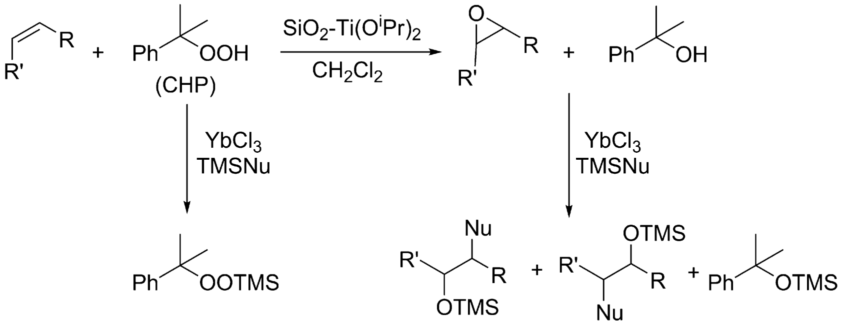
[a] Reaction conditions: 1 mmol of CHP, 2 mmol of alkene, 2.4 mmol of TMSCN, 28 mg of Ti catalyst, 0.1 mmol of $YbCl_3$.
[b] Epoxidation and ring-opening were carried out at the same temperature.
[c] Ring-opening was carried out at 85 °C.
[d] Total conversion of epoxide. 20% yield of chlorhydrin.
[e] 84% conversion of epoxide. 14% yield of chlorhydrin.
[f] Yield to cyanohydrin product (primary 47%; secondary 9%). In addition, 29% yield of chlorhydrins was obtained.
[g] Other unidentified products were obtained.

to check if SiO_2–Ti(O^{i}Pr)$_2$ was also able to promote that reaction. It was found that this solid did not catalyze the epoxide ring-opening reaction and that a different catalyst was required to complete the sequence. Next step was to check the compatibility between the catalysts of both reactions. For this task, the epoxidation reaction was carried out in the presence of the ytterbium catalyst. It was confirmed that the yield of the reaction was exactly the same as that found with only SiO_2–Ti(O^{i}Pr)$_2$ as catalyst. The opposite experiment was also carried out, that is, the ring-opening reaction was performed in the presence of SiO_2–Ti(O^{i}Pr)$_2$ and here again, the yield was not affected. These results indicate that both catalysts did not interfere with each other to give different by-products and, in addition, no mutual deactivation was detected.

Reagents for both reactions (CHP and TMSCN) could also hinder the progress of the reactions if they were not compatible. In order to verify this possibility, every reaction was carried out in the presence of the other reagent in the reaction medium. It was found that the yield of the epoxidation reaction decreased to around 50% when TMSCN was present. On the other hand ring-opening reaction did not take place in the presence of CHP since it consumed all the TMSCN in a side reaction. Similar compatibilities studies were carried out using $TMSN_3$. The explanation for the incompatibility of ring-opening in the presence of CHP is the formation of by-products coming from the reaction of CHP with TMSNu (Scheme 6). A similar reaction occurs with 2-phenyl-2-propanol, the concomitant product of the epoxidation reaction (Scheme 6). All these by-product were detected by gas chromatography and characterized by NMR and mass spectrometry. In view of those results TMSNu was added at the end of the epoxidation reaction to prevent reaction with CHP, and an excess of nucleophile was also required in order to compensate the amount consumed by the reaction with the concomitant alcohol.

Finally, compatibility studies carried out between catalysts in the tandem epoxidation-ring opening with electron-deficient alkenes showed that the presence of ytterbium chloride in the reaction of epoxidation with KF–Al_2O_3 did not affect the yield of this reaction. On the contrary, the presence of KF–Al_2O_3 in the second reaction prevented the formation of any ring opening product. It seems that there is some close contact between acid and basic sites, and that the effective base is in excess over the acid in spite of using equimolecular amounts of fluoride and ytterbium.

Due to the results in these compatibility studies, the tests of tandem reactions were restricted to those shown in Scheme 5. The results obtained in the tandem epoxidation-ring opening reactions under the appropriate conditions are shown in Table 4 (TMSCN) and Table 5 ($TMSN_3$). As can be seen, the global yield was moderately



Scheme 6.

Table 5
Tandem epoxidation-ring opening reactions using $TMSN_3$[a].

Entry	Alkene	Solvent	T (°C)[b]	Yield (%)		
				Epoxidation	Ring-Opening	Global
1	Cyclohexene	DCM	25	89	80	71
2	Cyclooctene	DCE	65[c]	97	46	45
3	1-Octene	DCE	65	71	<5	–
4	1-Hexene	DCE	65	40	<5	–

[a] Reaction conditions: 1 mmol of CHP, 2 mmol of alkene, 2.4 mmol of $TMSN_3$, 28 mg of Ti catalyst and 0.1 mmol of $YbCl_3$.
[b] Epoxidation and ring-opening were carried out at the same temperature.
[c] Ring-opening was carried out at 85 °C.

high when cyclic alkenes were used (Table 4, entries 1 and 5). In addition, the mixture of catalysts can be recovered and reused up to three times with only a slight decrease in global yield. The results in table below show that this drop in the global yield is due to the epoxide ring-opening step. We observed that in this precise step, there was a decrease in the conversion as well as a formation of by-products as the catalyst was recovered and used in a new run. Unfortunately, the efficiency of the one-pot method is much lower when linear alkenes are used.

As in the case of using TMSCN, relatively high global yields of azidohydrins (Table 5) were obtained with cyclic olefins, above all for cyclohexene (71%). However, epoxides from linear alkenes were not able to give the ring-opening reaction, showing again that the success of this type of combined systems is far from evident and important limitations can be found depending on the substrate, reagents, catalysts, and reaction conditions.

4. Conclusions

The combination of alkene epoxidation and epoxide ring opening is possible by the use a silica-supported titanium catalyst and ytterbium chloride. The main problem is the uncatalyzed reaction of hydroperoxides and concomitant alcohols with the nucleophile used in the ring opening reaction, which forces to use an excess of nucleophile to compensate its consumption in these side reactions.

The best results are obtained with highly reactive cycloalkenes, cyclohexene and cyclooctene, as substrates, whereas linear alkenes lead to lower yields. Furthermore, this heterogeneous system can be recovered and reused up to three times with only a slight loss in global yield.

However this combination is not possible in the case of electron-deficient alkenes, as ytterbium chloride is poisoned by the presence of the basic catalyst needed to perform the epoxidation reaction.

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References

[1] B.J. Cohen, M.A. Kraus, A. Patchornik, J. Am. Chem. Soc. 103 (1981) 7620–7629.
[2] F. Gelman, J. Blum, D. Avnir, J. Am. Chem. Soc. 122 (2000) 11999–12000.
[3] K. Motokura, N. Fujita, K. Mori, T. Mizugaki, K. Ebitani, K. Kaneda, J. Am. Chem. Soc. 127 (2005) 9674–9675.
[4] N.T.S. Phan, C.S. Gill, J.V. Nguyen, Z.J. Zhang, C.W. Jones, Angew. Chem. Int. Ed. 45 (2006) 2209–2212.
[5] K.K. Akagawa, S. Sakamoto, K. Kudo, Tetrahedron Lett. 48 (2007) 985–987.
[6] A.W. Pilling, J. Boehmer, D.J. Dixon, Angew. Chem. Int. Ed. 46 (2007) 5428–5430.
[7] R. Abu-Reziq, D. Wang, M. Post, H. Alper, Chem. Mater. 20 (2008) 2544–2550.
[8] M.J. Climent, A. Corma, S. Iborra, M. Mifsud, A. Velty, Green Chem. 12 (2010) 99–107.
[9] J.M. Fraile, R. Mallada, J.A. Mayoral, M. Menéndez, L. Roldán, Chem. Eur. J. 16 (2010) 3296–3299.
[10] R.A. Sheldon, M.C.A. van Vliet, Oxidation, in: R.A. Sheldon, H. van Bekkum (Eds.), Fine Chemicals through Heterogeneous Catalysis, Wiley-VCH, Weinheim, 2001, pp. 473–490.
[11] R.A. Sheldon, J.A. Van Doorn, J. Catal. 31 (1973) 427–437.
[12] J.M. Fraile, J.I. García, J.A. Mayoral, L.C. de Mènorval, F. Rachdi, J. Chem Soc., Chem. Commun. (1995) 539–540.
[13] C. Cativiela, J.M. Fraile, J.I. García, J.A. Mayoral, J. Mol. Catal. A 112 (1996) 259–267.
[14] J.M. Fraile, J.I. García, J.A. Mayoral, F. Figueras, Tetrahedron Lett. 37 (1996) 5995–5996.
[15] K. Arai, M.M. Salter, Y. Yamashira, S. Kobayashi, Angew. Chem. Int. Ed. 46 (2007) 955–957.
[16] E. Tokuoka, S. Kotani, H. Matsunaga, T. Ishizuka, S. Hashimoto, M. Kakaijama, Tetrahedron: Asymmetry 16 (2005) 2391–2392.
[17] Y.J. Chen, C. Chen, Tetrahedron: Asymmetry 18 (2007) 1313–1319.
[18] S. Matsunaga, J. Das, J. Roels, E.M. Vogl, M. Yamamoto, I. Iada, K. Yamaguchi, M. Shibasaki, J. Am. Chem. Soc. 122 (2000) 2252–2260.
[19] E.J. Corey, R.K. Bakshi, S. Shibata, C.P. Chen, V.K. Singh, J. Am. Chem. Soc. 109 (1987) 925–926.
[20] L.E. Martinez, J.L. Leighton, D.H. Carsten, E.N. Jacobsen, J. Am. Chem. Soc. 117 (1995) 5897–5898.
[21] B.M.L. Dioos, P.A. Jacobs, Appl. Catal. A 281 (2005) 181–188.
[22] B.M.L. Dioos, W.A. Geurts, P.A. Jacobs, Catal. Lett. 97 (2004) 125–129.
[23] A.E. Vougiokas, H.B. Kagan, Tetrahedron Lett. 28 (1987) 5513–5516.
[24] M.B. Cole, K.D. Shimizu, C.A. Krueger, J.P.A. Harrity, M.L. Snapper, A.H. Hoveyda, Angew. Chem. Int. Ed. 35 (1996) 1668–1671.
[25] K.D. Shimizu, M.B. Cole, C.A. Krueger, K.W. Kuntz, M.L. Snapper, A.H. Hoveyda, Angew. Chem. Int. Ed. 36 (1997) 1704–1707.
[26] N. Oguni, Y. Miyagi, K. Ito, Tetrahedron Lett. 39 (1998) 9023–9026.
[27] S.E. Schaus, E.N. Jacobsen, Org. Lett. 2 (2000) 1001–1004.
[28] J.M. Fraile, J.I. García, J.A. Mayoral, E. Vispe, J. Catal. 189 (2000) 40–51.