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Critical importance of molecular sieves in titanium(IV)–calix[4]arene catalyzed epoxidation of allylic alcohols

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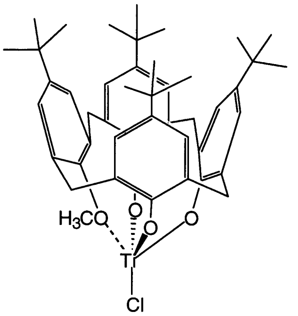
Abstract—The first synthetic application of Ti(IV)–calix[4]arenes as catalysts in regio- and stereoselective epoxidation of allylic alcohols is reported. The catalytic properties of these Ti(IV) complexes are dramatically enhanced in the presence of activated 4 Å molecular sieves. © 2001 Elsevier Science Ltd. All rights reserved.

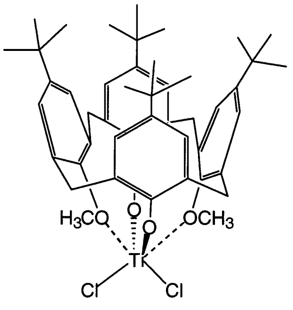
Oxyfunctionalization of organic substrates represents an important industrial process. In recent years particular attention has been paid to the achievement of more effective, selective and benign oxidative procedures based on the use of new catalysts, such as titanium containing zeolites,[1] titanium silicalites,[2] Ti/Si-containing aluminophosphates[3] and titania-silica aerogel,[4] in combination with an appropriate oxygen donor (hydrogen peroxide, urea–hydrogen peroxide adduct, *t*-butyl hydroperoxide).

Very recently Floriani[5] has reported the synthesis and characterization of Ti(IV)–calix[4]arene complexes of type **1** and **2** where the $[TiO_4]$ fragment may be considered as a titanium species anchored on a solid support similar to a zeolite.



$[p\text{-}Bu^t\text{-calix}[4]\text{-}(OMe)(O)_3TiCl]$

1

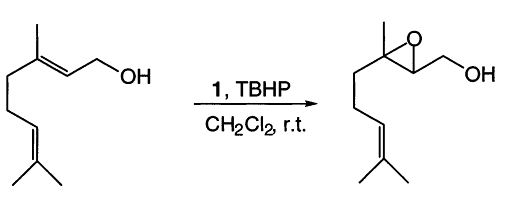


$[p\text{-}Bu^t\text{-calix}[4]\text{-}(OMe)_2(O)_2TiCl_2]$

2

In connection with our previous research,[6] devoted to the elaboration of new and efficient procedures for the epoxidation of allylic alcohols, the catalytic properties of the complexes **1** and **2** were investigated. In preliminary work geraniol **3a**, chosen as a representative allylic alcohol, was submitted to treatment with *t*-butyl hydroperoxide (TBHP) in CH_2Cl_2 (Scheme 1) in the presence of catalytic amounts of compound **1** (Table 1).

The first experiment (entry **a**) showed a rather low activity of catalyst **1** since epoxyalcohol **4a** was obtained as the only product in 25% yield. We suspected that the formation of **4a** could be reasonably explained on the grounds of a Sharpless-type pathway involving coordination both of the allylic alcohol and *t*-butyl hydroperoxide at the metal centre and that the disappointing preparative result could be attributed to the poor tendency of complex **1** to suffer the necessary ligand exchange.[7] Since the rate of ligand exchange of Ti(IV) chlorides and alkoxides can be noticeably increased by molecular sieves,[8] the same experiment was repeated in the presence of activated 4 Å molecular sieves. We found that, under the conditions reported in



3a **4a**

Scheme 1.

Keywords: calixarenes; epoxidation; titanium and compounds; zeolites.

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Table 1. Ti(IV)–calixarene **1**—catalyzed epoxidation of geraniol

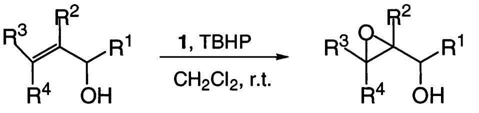
Entry	Reaction time (h)	Catalyst (%)	Yield (%)[a]
a	23	2.5	25
b	2	2.5	95[b]
c	3	1.0	79[b,c]
d	1.5	1.0	75[b]

[a] All the yields refer to isolated, chromatographically pure compounds.

[b] Epoxidation was performed in the presence of 4 Å molecular sieves, previously activated by heating at 250°C for 16 h at 1 mmHg.

[c] Solvent: *n*-hexane.

entry **b**, epoxidation took place in a very rapid and efficient way to afford **4a**, again as the sole product. In fact, as confirmed by ^{1}H NMR analysis (400 MHz) on the crude reaction mixture, no evidence for the formation of either citrale or 6,7-epoxygeraniol could be detected.

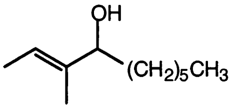
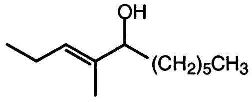
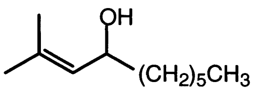
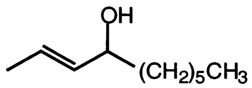
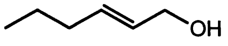


Scheme 2.

A satisfactory degree of generality was confirmed by a set of experiments performed on primary and secondary allylic alcohols (Table 2), which pointed out the high efficiency of the Ti(IV) complex **1**/molecular sieve system. The typical diastereoselectivity of Ti(IV) alkoxides was usually observed (entries **a**–**d**) and very good stereochemical results were obtained in entry **c**, as expected (Scheme 2).

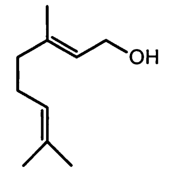
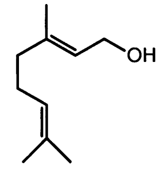
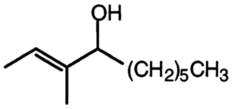
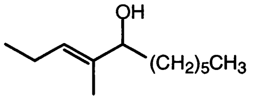
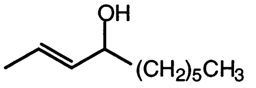
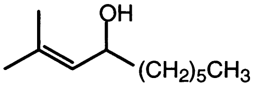
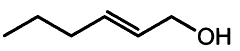
Very interestingly, comparable efficiency was obtained by performing the epoxidation in the presence of Ti(IV)–calixarene complex **2**, although higher amounts of catalyst were occasionally required (Table 3).

Table 2. Epoxidation of secondary allylic alcohols promoted by the Ti(IV) catalyst **1**/m.s. system

Entry	Substrate	Catalyst (%)	Reac. Time (h)	Yield (%)a)
a		1.0	0.5	95 (27/73)
b		1.0	0.5	87 (22/78)
c		2.5	2.0	95 (95/5)
d		1.0	3.0	82 (64/36)
e		1.0	6.0	78
f		1.0	16.0	64

a) All the yields refer to isolated, chromatographically pure compounds, whose structures were confirmed by spectroscopic data (^{1}H, ^{13}C-NMR, IR). Values in parentheses refer to *threo / erythro* diastereoisomeric ratios, determined by ^{1}H-NMR analysis on crude products.

Table 3. Epoxidation of allylic alcohols promoted by the Ti(IV) complex **2**/m.s. system

Entry	Substrate	Catalyst (%)	Reac. Time (h)	Yield (%)[a]
a		2.5	1.0	91
b		1.0	1.5	77
c		3.0	0.5	95 (27/73)
d		1.0	1.0	75 (37/63)
e		2.5	3.0	90 (61/39)
f		2.5	1.0	95 (93/7)
g		2.5	6.0	87
h		1.0	16.0	95

[a] All the yields refer to isolated, chromatographically pure compounds, whose structures were confirmed by spectroscopic data (^{1}H, ^{13}C-NMR, IR). Values in parentheses refer to *threo / erythro* diastereoisomeric ratios, determined by ^{1}H-NMR analysis on crude products.

In conclusion, we have reported the first synthetic applications of titanium(IV)–calix[4]arene complexes **1** and **2** whose catalytic properties in the epoxidation of allylic alcohols are remarkably enhanced in the presence of activated molecular sieves. It is noteworthy that the procedure is efficient, selective and simple and no work up is required.[9]

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8. Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807.
9. In a typical experimental procedure a mixture of allylic alcohol (2 mmol), TBHP (5–6 M decane solution, 0.54 ml), catalyst **1** (or **2**) and activated molecular sieves in CH_2Cl_2 (10 ml) was stirred at room temperature under the conditions reported in Tables 1–3 and monitored by TLC. After the completion of the reaction, the mixture was directly poured into the top of a silica gel chromatographic column. Elution with light petroleum/diethyl ether mixtures afforded pure epoxyalcohols **4**.