One-pot conversion of citronellal into isopulegol epoxide on mesoporous titanium silicate

Matteo Guidotti,*[a] Giuliano Moretti,[b] Rinaldo Psaro[a] and Nicoletta Ravasio[a]

[a] *Centro CNR "CSSCMTBSO", Dipartimento di Chimica Inorganica, Metallorganica e Analitica, via Venezian 21, 20133 Milano, Italy. Fax: +39-02-2362748; E-mail: labcat@csmtbo.mi.cnr.it*
[b] *Centro CNR "SACSO", Dipartimento di Chimica, p.le Aldo Moro 5, 00185 Roma, Italy*

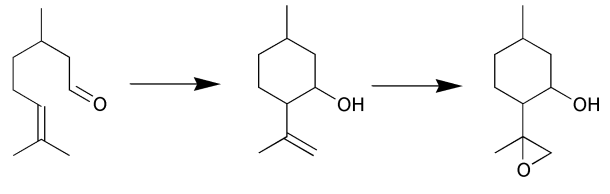
Received (in Liverpool, UK) 26th April 2000, Accepted 4th August 2000
First published as an Advance Article on the web 4th September 2000

Citronellal was converted into isopulegol epoxide in a one-pot two-step reaction achieving a 68% global yield on Ti-MCM-41 and designing a two-solvent catalytic system.

The push of environmental concerns makes bifunctional catalysts the object of growing interest as the tool to reduce the number of steps in a fine chemistry synthesis process.

In a programme aimed at the substitution of homogeneous with heterogeneous Lewis acids in organic synthesis, some of us reported that citronellal **1** (Scheme 1) can be easily cyclized to isopulegol **2** in the presence of acidic mixed oxides.[1] Likewise, we recently reported the epoxidation activity of Ti-containing MCM-41 materials, which easily transform **2** into isopulegol epoxide **3** using *tert*-butylhydroperoxide (TBHP).[2] The high selectivity observed in this reaction, together with the growing interest in isopulegol and related terpenic compounds for uses other than those for the flavour and cosmetic industry (*e.g.* isopulegol derivatives have been claimed to possess a high bactericidal and fungicidal activity[3] and a long-lasting insect repellent action[4]), prompted us to investigate the possibility of obtaining isopulegol epoxide **3** directly from citronellal **1** on the same catalyst.

Preliminary experiments, carried out starting from **1** in the presence of either in-framework or extra-framework Ti-containing MCM-41's, showed that Ti-MCM-41, obtained by grafting an organotitanium precursor onto the MCM-41 surface, leads to better catalytic features than other in-framework Ti-containing solids. This behaviour is also consistent with high conversion values recorded on this mesoporous material, when the epoxidation step is carried out separately (Table 1; tests 5 and 6).



1 **2** **3**

Scheme 1

As in other examples, where an epoxidation reaction is coupled to an acid-catalysed one,[5] the choice of the solvent is not trivial. In fact, while the cyclization reaction is easily carried out in apolar hydrocarbons, *i.e*. n-heptane or toluene (tests 1 and 2), the best results in the epoxidation reactions are achieved in aprotic polar solvents, *i.e.* acetonitrile or ethylacetate, which are bad solvents for the first-step reaction (tests 3 and 4). Therefore, the use of a unique solvent throughout the two-step reaction appeared to be hardly feasible. Moreover, to avoid the oxidation of the non-reacted citronellal **1** by TBHP, it is advisable to add the oxidant after the complete conversion of **1** into **2**. In fact, whenever TBHP is added at the beginning of the cyclization step, a plethora of products is registered, among which is menthone. So, during the first 6 h of reaction the intramolecular cyclization was performed in apolar hydrocarbon. After that time an equal volume of polar solvent was added together with the required TBHP aliquot.

Ti-MCM-41 has been prepared in the following way: MCM-41 was synthesized according to procedures developed by Mobil researchers.[6] Titanium was grafted onto the MCM-41 surface using titanocene dichloride as precursor following the procedure described by Maschmeyer *et al.*[7] Details about the preparation of the samples are reported in ref. 2. The Ti content, determined by ICP-atomic emission spectroscopy, of the Ti-MCM-41 sample was 1.88 wt.%. The specific surface area (BET), the total pore volume and the effective mean pore diameter of the solid were 860 m^2g^{-1}, 0.52 cm^3g^{-1} and 2.3 nm, respectively. The mesoporous solid was pretreated by heating at 773 K for 1 h in air. The catalytic reactions were carried out in a glass batch reactor at 363 K under anhydrous nitrogen using acetonitrile and toluene or n-heptane and ethyl acetate as solvents, anhydrous TBHP as oxidant (oxidant : substrate molar ratio = 1.1) and 15 wt.% catalyst with respect to the substrate citronellal **1**. The solvent : citronellal volume ratio is 25. The samples taken during the 24 h reaction were analysed by gas chromatography (FID detector; mesitylene as internal standard). The products were identified by GC-MS and NMR spectroscopy.

It is worth noting that pure MCM-41 (without titanium) was completely inactive, while some amorphous silica is able to catalyse the cyclization reaction.[1,8] This confirms that the Ti-

Table 1 Catalytic tests on Ti-MCM-41 (1.88% Ti)

Test no.	$Solv_1$[a]	$Solv_2$[b]	$Conv_1$[c] (%)	Sel_1[d] (%)	$Conv_2$[e] (%)	Sel_2[f] (%)
1	$PhCH_3$	$PhCH_3$	> 98	> 98	9	—[g]
2	n-C_7H_{16}	n-C_7H_{16}	> 98	> 98	5	—[g]
3	CH_3CN	—	47	90	—[h]	—[h]
4	AcOEt	—	74	95	—[h]	—[h]
5	—	CH_3CN	—[h]	—[h]	73[i]	80[i]
6	—	AcOEt	—[h]	—[h]	78[i]	41[i]
7	$PhCH_3$	$PhCH_3$ + CH_3CN	> 98	> 98	76	90
8	n-C_7H_{16}	n-C_7H_{16} + AcOEt	> 98	> 98	58	75

[a] Cyclisation: 5 ml solvent; 15 wt.% catalyst; 358 K under reflux; 6 h. [b] Epoxidation: 5 + 5 ml solvent; 15 wt.% catalyst; TBHP:isopulegol molar ratio = 1.1; 358 K under reflux; 18 h. [c] Conversion based on consumption of **1**. [d] Selectivity to **2**. [e] Conversion based on consumption of **2**. [f] Selectivity to **3**. [g] Under detection limit. [h] Step not run. [i] From Ref. 2.

DOI: 10.1039/b003397i

This journal is © The Royal Society of Chemistry 2000

free mesoporous material is lacking in acidic sites and also that the presence of titanium(IV) in a siliceous matrix gives rise by itself to a material containing both redox and acidic properties.[9] Besides, the introduction of trivalent metal ion, although widely used in bifunctional catalysts,[10,11] appears to be redundant. The use of a MCM-41 sample containing both titanium (1.91 wt.% grafted from titanocene) and aluminium (0.59 wt.% inserted by isomorphous substitution for Si) did not lead to a remarkable improvement in catalytic features: the Al insertion shortens the first-step reaction time (cyclization is complete after 2 h), leaving the second-step reaction time and selectivity (74% conversion of **2** and 88% selectivity to **3** after 18 h in toluene + acetonitrile) practically unaffected.

Both toluene and n-heptane exhibit a complete and selective conversion of **1** into **2** within 6 h and this is consistent with the results obtained on amorphous mixed-oxide TiO_2–SiO_2.[1] The reaction time is rather longer, but is necessary to avoid the presence of unreacted citronellal in the second step.

In the epoxidation step, as in the tests on other terpenic unsaturated alcohols,[2] acetonitrile (test 7) showed better performances than ethyl acetate (test 8). This behaviour might be attributed to the weakly basic character of acetonitrile that inhibits the formation of acid-catalysed secondary products from isopulegol epoxide **3**.[12] The main by-product formed in the second-step reaction is isopulegone, *i.e.* 5-methyl-2-(1-methylethenyl)cyclohexanone.

With the purpose of obtaining a deeper insight about the heterogeneity of the system,[13] the reaction mixture was carefully filtered at *ca*. 50% conversion (2 h reaction) in the second step. Testing the colourless filtered solution for further reaction, no activity of the liquid mixture was observed. From this behaviour, the observed catalyst is presumably heterogeneous. Because of the intrinsic low chemical and mechanical stability of MCM-41-based materials,[14] work is in progress to verify whether or not the catalyst is stable and recyclable.

In summary, the best result for the one-pot conversion of citronellal into isopulegol epoxide with a *ca*. 68% global yield was achieved on Ti-MCM-41 as follows. Toluene was used as the solvent for the 6 h long cyclization step during which all the citronellal **1** was completely and selectively converted into isopulegol **2**. Then, after the addition of TBHP and acetonitrile, over the following 18 h isopulegol **2** was epoxidised to **3** with a 76% conversion and a 90% selectivity (test 7).

In this reaction, employing Ti-MCM-41 obviates the use of homogeneous catalysts in both steps, namely zinc halides in the first and transition metal complexes or peroxy acids in the second, thereby limiting the waste production to the work-up phase, when the TBHP in excess has to be quenched. Such bifunctional behaviour is to be attributed to the high dispersion of Ti^{IV} onto the surface of the mesoporous solid, which brings acidity into the silica matrix and causes the excellent activity in the epoxidation step.

The authors gratefully acknowledge the CNR-MURST for financial support through the 'Program Chemistry Law 95/95-I year'.

Notes and references

1 N. Ravasio, M. Antenori, F. Babudri and M. Gargano, *Stud. Surf. Sci. Catal.*, 1997, **108**, 625.
2 C. Berlini, M. Guidotti, G. Moretti, R. Psaro and N. Ravasio, *Catal. Today*, 2000, **60**, 219.
3 P. Kalck, R. Naigre and S. Sirol, *Fr. Pat.* 2,721,926, 1996.
4 S. Okura, A. Amano, T. Yamamoto and H. Ota, *Jpn. Pat.* 10 36,201, 1998.
5 M. van Klaveren and R. A. Sheldon in: *3rd World Congress on Oxidation Catalysis*, ed. R. K. Grasselli, S. T. Oyama, A. M. Gaffney and J. E. Lyons, Elsevier, 1997, p. 567
6 J. S. Beck, J. C. Vartuli, W. J. Roth, M. E. Leonowicz, C. T. Kresge, K. D. Schmitt, C. T.-W. Chu, D. H. Olson, E. W. Sheppard, S. B. McCullen, J. B. Higgins and J. L. Schlenker, *J. Am. Chem. Soc.*, 1992, **114**, 10 834.
7 T. Maschmeyer, F. Rey, G. Sankar and J. M. Thomas, *Nature*, 1995, **378**, 159; R. D. Oldroyd, G. Sankar, J. M. Thomas and D. Özkaya, *J. Phys. Chem. B*, 1998, **102**, 1849.
8 P. J. Kropp, G. W. Breton, S. L. Craig, S. D. Crawford, W. F. Durland, J. E. Jones and J. S. Raleigh, *J. Org. Chem.*, 1995, **60**, 4146.
9 J. C. van der Waal, P. Lin, M. S. Rigutto and H. van Bekkum, *Stud. Surf. Sci. Catal.*, 1997, **105**, 1093; A. Bhaumik and T. Tatsumi, *J. Catal.*, 1999, **182**, 349.
10 D. Trong On, M. P. Kapoor, P. N. Joshi, L. Bonneviot and S. Kaliaguine, *Catal. Lett.*, 1997, **44**, 171.
11 A. Corma, M. Iglesias and F. Sànchez, *J. Chem. Soc., Chem. Commun.*, 1995, 1635.
12 A. Corma, P. Esteve and A. Martìnez, *J. Catal.*, 1996, **161**, 11.
13 R. A. Sheldon, M. Wallau, I. W. C. E. Arends and U. Schuchardt, *Acc. Chem. Res.*, 1998, **31**, 485.
14 N. Igarashi, Y. Tanaka, S.-I. Nakata and T. Tatsumi, *Chem. Lett.*, 1999, 1.