Pergamon

Tetrahedron Letters 40 (1999) 2695–2698

TETRAHEDRON LETTERS

Chromium (VI) Adsorbed on SiO_2/ZrO_2, a New Supported Reagent for Allylic Oxidations

Lúcia H.B.Baptistella*, Ilza M.O.Sousa, Yoshitaka Gushikem, Adriana M.Aleixo
Instituto de Química, Universidade Estadual de Campinas, PO Box 6154, 13083-970, Campinas, SP, Brasil
Received 15 December 1998; revised 4 February 1999; accepted 5 February 1999

Abstracts: Zirconium (IV) oxide coated on the surface of silica gel was used to absorb Cr(VI) from acidic solutions. This material, in conjunction with *t*-butyl hydroperoxide, proved to be very useful for allylic oxidations, promoting very clean reactions, with high regioselectivity.

The concept of utilizing reagents adsorbed on insoluble inorganic supports for organic synthesis has long been known, [1] and applied to a series of reactions. Many systems were studied and some provided a particular environment capable of carry out organic reactions cleanly and in acceptable yields, under very mild conditions.[1,2] Among them, the systems for oxidation reactions always took a special place,[1-3] especially due to the minimization of overoxidation reactions and the safety of handling, owing to the full chemosorption of the toxic byproducts. In this context, a series of Cr(VI) supported reagents were used as efficient oxidants for the transformation of hydroxy compounds to carbonyl compounds,[4] with some few examples related to the oxidation of allylic and benzylic halides,[4b,4i] or the oxidative cleavage of alkenes.[4f]

In recent years, zirconium(IV) oxide coated on a silica gel surface was found to be very effective and selective for the extraction of Cr(VI) from aqueous solutions[5] and it has been considered as an excellent ion-exchanger material for separation and determination of this metal ion.[6] These studies demonstrated that the exchange capacity of the SiO_2/ZrO_2 system increased at lower pH, and the maximum retention of Cr(VI) was achieved at pH 3. The absorption of the metal under these conditions can be represented by the equation bellow:

$$\equiv ZrOH + H^+ + Cr_2O_7^{2-} \rightarrow \equiv ZrOH_2^+\, Cr_2O_7^{2-}$$

where ≡ZrOH denotes the zirconium oxide attached to the silica surface

In this paper, we wish to report that this chemically modified silica with Cr(VI) adsorbed represents a selective allylic oxidant system for organic compounds, promoting very clean reactions, under catalytic conditions, when used in conjunction with *t*-butyl hydroperoxide.

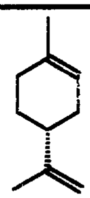
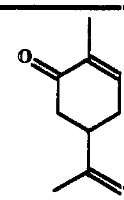
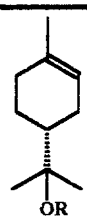
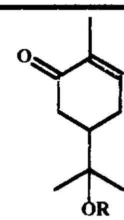
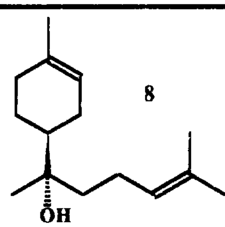
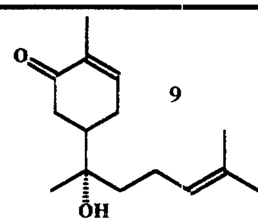
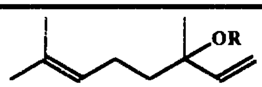
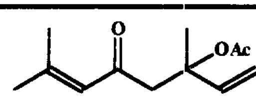
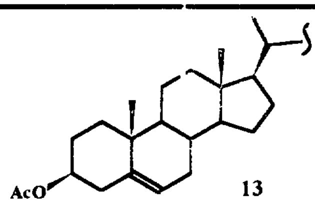
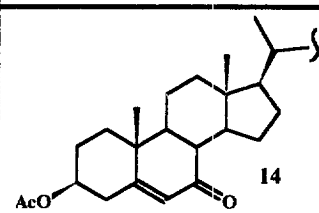
The chemically modified silica was prepared by refluxing activated silica gel (60 Å, 70-230 mesh, specific surface area of 500 m^2g^{-1}) with an ethanolic solution of $ZrCl_4$ (0.06 M, in a proportion of 1g silica/12.5 mL solution), for 8 h and under an argon atmosphere, followed by hydrolytic workup to remove all residues of Cl^-. The amount of Zr attached on the silica surface was determined by X-ray fluorescence, giving 6.2%. Treatment of this support with an acidic aqueous solution of $K_2Cr_2O_7$ (0.001 M, acidification with 0.01M HNO_3 until pH 3) resulted in absorption of the metal ion. The amount of Cr(VI) adsorbed was determined by conventional methodology,[7] and the maximum value obtained was 0.018 mmol g^{-1}.

To demonstrate the potential of this system to promote allylic oxidations, some model compounds were used in a set of experiments, and the best results are shown in table 1.

In all cases, these results were achieved when the combination of the cooxidant[8] *tert*-butyl hydroperoxide (2 equiv.[9]) and the supported chromium-system (3x w/w, corresponding to 0.007-0.02 equiv.) was used in benzene, at room temperature. Variations in solvents (methylene chloride, chlorobenzene), reaction temperatures (until reflux temperatures), molar ratio of the hydroperoxide (0-4 equiv.) and/or weight ratio of the supported catalyst (corresponding to 0.001-0.1 equiv.) did not improve the results. It is known that *tert*-butyl hydroperoxide independently does not effect allylic oxidations,[8h] and in the present study we observed also that the system SiO_2/ZrO_2/Cr(VI) alone is not able to promote any kind of reaction, even when used in a proportion of 0.1 equiv. for a long period.

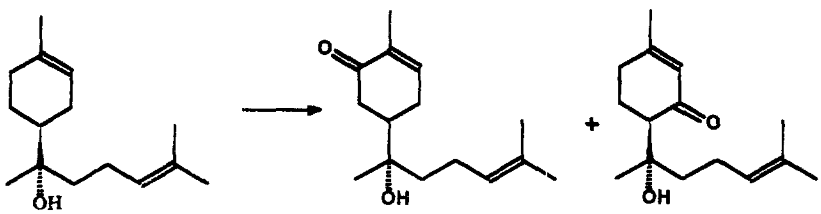
0040-4039/99/$ - see front matter
PII: S0040-4039(99)00335-4

Table 1. Allylic Oxidations with $SiO_2/ZrO_2/Cr(VI)$ – *t*-BuOOH

Entry	Substrate	Product*	Time** (hs)	Yields ***
1	 1	 2	21	50%
2	 3 R=H 4 R=Ac 5 R=TBS	 6 R= Ac 7 R=TBS	 72 36	R = H intractable mixture 6 30% 7 33%
3	 8	 9	40	50%
4	 10 R=H 11 R=Ac	 12	48	R = H intractable mixture 12 15%
5	 13	 14	30	48%

* All products gave satisfactory spectral and physical data.
** At the end of the reaction time, the work-up was restricted to a simple filtration.
*** Yields refer to isolated materials. In all cases, unreacted starting materials (10 to 30%) were recovered.

A very interesting feature in the present methodology is the high regioselectivity observed. In all cases only the secondary allylic carbons reacted. Products indicating oxidations on allylic methyl positions (see entries 1, 2, 3 and 4) or on allylic methine positions (see entry 1) were never detected. If more than one allylic methylene carbon was present, good regioselectivity was also observed. With conformationally flexible molecules, for example with the *p*-menthene compounds **1**, **4**, **5** and **8** (entries 1, 2 and 3), an excellent selectivity was found toward the more reactive position C6, better than those reported with other chromium reagents.[10,11] On the other hand, with conformationally rigid skeletons, exemplified by the reaction on compound **13**, the present method lead to the same degree of selectivity observed with other chromium reagents.[8,11] Additionally, entry 3 also exemplifies another kind of selectivity achieved with this supported oxidant: when cyclic and acyclic secondary carbons are available for oxidations, only the cyclic position reacted. Differences between cyclic and acyclic alkenes *vis a vis* their efficiency on allylic oxidations reactions have been previously reported, and indicate lower rates of conversion, yields, and/or selectivities for the former.[8f,12] Our result with compound **12** was in agreement with those findings, but when both types of alkenes are present in the same molecule, as demonstrated with compound **8**, the reaction occured only on the cyclic position. In order to evaluate this special kind of selectivity, we examined the behaviour of compound **8** with other traditional reagents used for allylic oxidations, including $CrO_3/Ac_2O/AcOH$, *t*-$BuCrO_3/Ac_2O/AcOH/CCl_4$, CrO_3/*t*-$BuOOH/CH_2Cl_2$, *t*-$BuCrO_3$/*t*-$BuOOH/CH_2Cl_2$, $Cr(CO)_6$/*t*-$BuOOH/CH_3CN$, PDC/*t*-$BuOOH/C_6H_6$, PCC/*t*-$BuOOH/C_6H_6$ and CrO_3/3,5-dimethylpyrazol/CH_2Cl_2. In all cases, a mixture of epoxidation products of the double bonds was obtained (even when the acetate derivative of **8** was used), except with CrO_3/3,5-dimethylpyrazol/CH_2Cl_2,[13] that lead to the allylic oxidation products **9** and **15** in 25 and 21% yields, respectively (scheme 1).

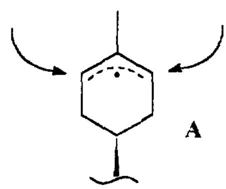


8 **9** **15**[14]

Reaction conditions: CrO_3 (10 equiv.), 3,5-dimethylpyrazol. CH_2Cl_2. −20°C to room temperature. 20 hs

Scheme 1

It must be noted that, in all allylic oxidation reactions carried with *p*-menthene structures (entries 1, 2 and 3 in table 1 and scheme 1), independently of the Cr(VI) reagent used – supported or not, the enones resulting from attack at the C5 ring positions were isolated as a racemic mixture (**2**, **6** and **7**) or as a epimeric mixture at C4 (**8**). This fact is best understood by considering the proposed mechanism in these allylic oxidations,[11] which must have the intermediancy of a radical (or a carbocation) as **A**. Similar remarks appear in the literature for this type of reaction on limonene.[10]



A

Finally, another feature that must be noted on the present reactions with the supported Cr(VI) catalyst refers to the presence of tertiary alcohols on the substrates. Compounds containing a tertiary allylic alcohol, as represented by **10**, gave an intractable mixture of products, probably due to the expected oxidative rearrangement of this group. On the other hand, the results obtained with compounds containing a simple tertiary alcohol, as shown on entries 2 and 3 of table 1, indicate that competing rections on these centers depends on the steric effects around them. Thus, with compound **3**, the steric acessibility of the tertiary alcohol probably facilitated interations with the modified silica and promoted competing reactions, while with compound **8** the steric hindrance around this group prevented this kind of interactions, and the desired allylic oxidation reaction ocurred without interference.

In summary, the system SiO_2/ZrO_2/Cr(VI), in conjunction with *t*-butyl hydroperoxide, proved to be very useful for allylic oxidations, permitting the direct preparation of enones with high selectivity. The reactions were carried out under very mild conditions, proceeded cleanly, and gave moderate yields of important and versatile compounds for organic synthesis.

Acknowledgements: This work was supported financially by the Fundação de Amparo à Pesquisa do Estado de São Paulo. L.H.B.B. is also grateful to Dr. P.M.Imamura for his helpfull discussions.

REFERENCES AND NOTES

1. McKillop, A.; Young, D.W. *Synthesis* **1979**, 401-422 and 481-500.
2. a) *Preparative Chemistry Using Supportd Reagents*; Lazlo, P., Ed.; Academic Press: San Diego, **1987**; b) *Solid Supports and Catalysis in Organic Synthesis*; Smith, K., Ed.; Ellis-Horwood: Chichester, **1992**; c) Clark, J.H. *Catalysis of Organic Reactions by Supported Inorganic Reagents*; VCH: New York, **1994**.
3. Lazlo, P. Solid-supported oxidants. In *Comprehensive Organic Synthesis*; Trost, B.M., Ed.; Pergamon Press: Oxford; vol. 7, **1991**; pp. 839-848.
4. a) Cheng, Y. S.; Liu, W. L.; Chen, S. *Synthesis* **1980**, 223-224; b) Santaniello, E.; Ferraboschi, P. *Nouv. J. Chim.* **1980**, *4*, 279-281 ; c) Santaniello, E.; Ponti, F.; Manzocchi, A. *Synthesis* **1978**, 534-535; d) Singh, R. P.; Subbarao, H. N.; Dev, S. *Tetrahedron* **1979**, *35*, 1789-1793; e) Brunelet, T.; Jouitteau, C.; Gelbard, G. *J.Org.Chem.* **1986**, *51*, 4016-4022; f) San Filippo Jr., J.; Chern, C. I. *J.Org.Chem.* **1977**, *42*, 2182-2183 ; g) Adams, L. L.; Luzzio, F. A. *J.Org.Chem.* **1989**, *54*, 5387-5390; h) Basiuk, V. A. *Russian Chem. Rev.* **1995**, *64*, 1003-1019; i) Kabalka, G. W.; Pagni, R. M. *Tetrahedron* **1997**, *53*, 7999-8065 and ref. cited therein.
5. Gushikem, Y.; Peixoto, C. R. M.; Kubota, L. K. Exchange property of Ti(IV) and Zr(IV) oxides grafted on silica gel surface. Sorption of Cr(VI) from an acid solution. In *New Developments in Ion Exchange. Fundamentals and Applications*; Abe, M.; Kataoka, T.; Suzuki, T., Eds.; Elsevier-Kodansha: Tokyo, **1991**; pp. 607-612.
6. Peixoto, C. R. M.; Gushikem, Y.; Baccan, N. *Analyst* **1992**, *117*, 1029-1032.
7. *Standard Methods for the Examination of Water and Wastwater*, 18th ed.; Amer.Public Health Assoc.: Washington DC, **1992**; pp. 3.58-3.60.
8. For some examples of catalytic chromium(VI) oxidations using *t*-butyl hydroperoxide as cooxidant, see: a) Pearson, A. J.; Chen, Y. S.; Hsu, S. Y.; Ray, T. *Tetrahedron Lett.* **1984**, *25*, 1235-1238; b) Pearson, A. J.; Chen, Y. S.; Han, G. R.; Hsu, S. Y.; Ray, T. *J.Chem.Soc Perkin Trans. I* **1985**, 267-273; c) Muzart, J. *Tetrahedron Lett.* **1986**, *27*, 3139-3142; d) Muzart, J. *Tetrahedron Lett.* **1987**, *28*, 2133-2134 and 4665-4668. For a general use of *t*-butyl hydroperoxide on allylic oxidations, see: e) Umbreit, M. A.; Sharpless, K. B. *J.Am.Chem.Soc.* **1977**. *99*, 5526-5528; f) Muzart, J. *Bull. Soc. Chim. Fr.* **1986**, 65-77; g) Page, P. C. B.; McCarthy, T. J. Oxidation Adjacent to C=C Bonds. In *Comprehensive Organic Synthesis*; Trost, B.M., Ed.; Pergamon Press: Oxford; vol. 7, **1991**; pp. 83-117; h) Chidambaram, N.; Chandrasekaran, S. *J.Org.Chem.* **1987**, *52*, 5048-5051; i) Salvador, J. A. R.; Melo, M. L. S.; Neves, A. S. C. *Tetrahedron Lett.* **1997**, *38*, 119-122.
9. The *t*-butyl hydroperoxide used was commercial grade, 70% aqueous solution.
10. Actually, reports on the literature concerning allylic oxidations on limonene **1** show either a slight selectivity toward the carbon C6 (references 8b, 8g and 11) or a great selectivity toward carbon 3 (reference 8h. It is noteworthy that this selectivity was contested by A. F. Thomas and Y. Bessière in *Nat.Prod.Rep.* **1989**, *6*, 291-309)
11. a) Dauben, W. G.; Lorber, M.; Fullerton, D. S. *J.Org.Chem.* **1969**, *34*, 3587-3592; b) Fujita, K. *Nippon Kagaku Zasshi*, **1960**, 1676.
12. Cainelli, G.; Cardillo, G. *Chromium Oxidations in Organic Chemistry*; Springer-Verlag: Berlin, **1984**; p. 41 and 65.
13. Corey, E. J.; Fleet, G. W. *Tetrahedron Lett.* **1973**, 4499-4501.
14. Compound **15** presented spectral and physical data in agreement with those reported in the literature for the (6R,1'S)-*epi*-hernandulcin. See Mori, K.; Kato, M. *Tetrahedron* **1986**, *42*, 5895-5900.