PRELIMINARY COMMUNICATION

An Efficient and Selective Solvent-Free Oxidation of Alcohols

J.-D. LOU* and L.-Z. WANG

College of Life Sciences, China Institute of Metrology, Hangzhou, Zhejiang 310034, China
e-mail: lou@cim.edu.cn

Received 9 December 2002

An oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones by chromium trioxide supported on silica gel at room temperature under solvent-free conditions is described.

Chromium(VI)-based reagents have been extensively used in organic synthesis [1—3], especially in oxidation of alcohols. However, they are not without their problems. For instance, overoxidation can occur, work-up can be problematical, and at all times removal of the product from toxic chromium contamination is a concern, especially with respect to large-scale preparations.

Recently considerable attention has been paid to the solvent-free reactions [4, 5], a number of these studies have focused on the use of microwave technology in organic and organometallic synthesis [6]. In many cases, solvent-free reaction (or solid-state reaction) occurs more efficiently and more selectively than does its solution counterpart, since molecules in a crystal are arranged tightly and regularly. Furthermore, avoiding organic solvents during the reaction in synthesis leads to a clean and economical technology. For example, safety is largely increased, work-up is considerably simplified, cost is reduced, increased amounts of reactants can be used in the same equipment, reactivity and sometimes selectivity are enhanced without dilution. These factors are especially important in industry.

On the other hand, it is well known that the benefits of using solid-supported reagents for organic synthesis are considerable [7], especially as they offer remarkable ease of handling and use; often one can simply weigh the amount of the reagent to be used. At the end of the reaction a filtration suffices to remove the contaminating by-products. Another advantage is reduction in product contamination assured by having the reagent fully bound to a solid support. This is very important for oxidation reactions so that overoxidation can be minimized. Solid-supported oxidants are relatively safe to handle owing to full chemisorption of the toxic chemicals.

On the basis of the previous investigations on advantageous oxidations under solvent-free conditions [8—10] and with solid-supported reagents [11—14], a new, simple, and general procedure for the oxidation of primary and secondary alcohols to the corresponding aldehydes and ketones with chromium trioxide supported on silica gel [11] at room temperature under solvent-free conditions without microwave irradiation has been elaborated.

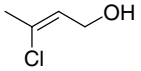
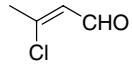
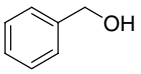
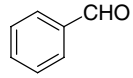
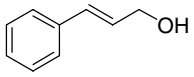
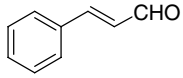
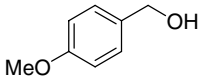
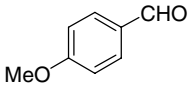
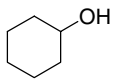
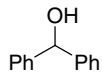
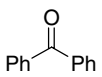
In present reactions, the 1 to 1.2 mole ratio of the oxidant (30 % CrO_3 to silica gel) to substrate is employed. First the oxidant is carefully* added to the substrate and the mixture is stirred magnetically at room temperature. The progress of the reaction is monitored by TLC (plates: aluminium-backed silica gel Merck 60 GF_{254}) using hexane—ethyl acetate (φ_r = 8:2) as eluent. In general, the oxidations are completed within 10 min. The reaction mixture is then extracted with dichloromethane or diethyl ether. Distillation of the solvent affords a product that is of acceptable purity for most purposes.

Mainly, the oxidations are more efficient and selec-

* **Caution**: CrO_3 is a highly toxic agent. The mutagenicity of chromium(VI) compounds is well documented [15]. Special care must always be taken when adding CrO_3 to organic media with respect to the exothermic oxidation.

*The author to whom the correspondence should be addressed.

Table 1. Solvent-Free Oxidation of Alcohols with Chromium Trioxide Supported on Silica Gel

Substrate[a]	Reaction time / min	Product[b]	Yield / %
n-C_4H_9-CH_2-OH	10	n-C_4H_9-CHO	85
n-C_8H_{17}-CH_2-OH	10	n-C_8H_{17}-CHO	79
	7		90
	5		94
	5		95
	5		95
	5		92
	10		81
	10		83
	5		92

a) For solid substrates the reaction temperature should be near or above their melting points; *b*) All the aldehydes and ketones have been described previously in the literature and were identified by their IR spectra or by the IR spectra and melting points of their 2,4-dinitrophenylhydrazones.

tive, the reaction times are shorter, the work-ups are easier, and no overoxidation products are observed. As can be seen in Table 1, this method is generally applicable to a range of alcohols and gives the corresponding aldehydes and ketones in good yields. Therefore, it offers special promise for the oxidation of alcohols to the corresponding carbonyl compounds, and thus can be compared favourably with traditional CrO_3-based oxidation methods [16].

REFERENCES

1. Freeman, F., in *Organic Synthesis by Oxidation with Metal Compounds.* (Mijs, W. J. and de Jonge, C. R. H. I., Editors.) Pp. 68—81. Plenum Press, New York, 1986.
2. Haines, A. H., *Methods for the Oxidation of Organic Compounds, Alcohols, Alcohol Derivatives, Alkyl Halides, Nitroalkanes, Alkyl Azides, Carbonyl Compounds, Hydroxyarenes and Aminoarenes.* Pp. 17—41. Academic Press, London, 1988.
3. Ley, S. V. and Madin, A., in *Comprehensive Organic Synthesis.* Vol. *7.* (Trost, B. M. and Fleming, I., Editors.) Pp. 251—289. Pergamon Press, London, 1991.
4. Metzger, J. D., *Angew. Chem., Int. Ed. 37*, 2975 (1998).
5. Tanaka, K. and Toda, F., *Chem. Rev. 100*, 1025 (2000).
6. Loupy, A., Petit, A., Hamelin, J., Texier-Boullet, F., Jacquault, P., and Mathe, D., *Synthesis 1998,* 1213.
7. Laszlo, P., *Preparative Chemistry Using Supported Reagents.* Academic Press, San Diego, 1987.
8. Lou, J.-D. and Xu, Z.-N., *Tetrahedron Lett. 2002*, 6149.
9. Lou, J.-D. and Xu, Z.-N., *Tetrahedron Lett. 2002*, 6095.
10. Lou, J.-D. and Xu, Z.-N., *Tetrahedron Lett. 2002*, 8843.
11. Lou, J.-D. and Wu, Y.-Y., *Chem. Ind.* (London) *1987,* 531 and references cited therein.
12. Lou, J.-D. and Wu, Y.-Y., *Synth. Commun. 17,* 1717 (1987).
13. Lou, J.-D., *Synth. Commun. 19*, 1841 (1989).
14. Lou, J.-D. and Lou, W.-X., *Synth. Commun. 27*, 3697 (1997).
15. Cupo, D. Y. and Wetterhahn, K. E., *Cancer Res. 45*, 1146 (1985).
16. Fieser, L. F. and Fieser, M., *Reagents for Organic Synthesis.* Vol. *1*, pp. 144—147 and subsequent volumes in the series. Wiley, New York, 1967.