J IRAN CHEM SOC
DOI 10.1007/s13738-013-0235-3

ORIGINAL PAPER

Catalyst-free selective oxidation of alcohols to carbonyls using *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane as an efficient oxidant

Davood Azarifar · Zohreh Najminejad · Kaveh Khosravi

Received: 24 October 2012 / Accepted: 24 January 2013

Abstract A simple and efficient method for the selective oxidation of alcohols to ketones using *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane at room temperature is developed. The reactions were smoothly proceeded under catalyst-free conditions to provide ketones in quantitative yields within short reaction times. Also, this method is compatible with many functional groups including aldehydes, olefins, halogens, amines and esters.

Keywords *Trans*-3, 5-dihydroperoxy-3, 5-dimethyl-1, 2-dioxolane · Alcohols · Oxidation · Catalyst-free

Introduction

Oxidation of alcohols is a well-documented and straightforward method for the synthesis of carbonyl compounds that are important building blocks in a wide variety of organic synthesis [1, 2]. Although several methods for the oxidation of alcohols have been developed [3–6], only few are sufficiently selective in tolerating the presence of other sensitive functional groups [7, 8]. Historically, the most common reagents used for the oxidation of secondary alcohols include the Cr(VI) and Mn(VII) species which environmentally result in considerable amounts of heavy metal wastes [9]. During the last decades, wide varieties of oxidizing agents have been reported throughout the literature for the oxidation of alcohols, but the use of oxygen donors such as H_2O_2, *m*-CPBA, ozone, O_2 and *t*-BuOOH has become increasingly more important in the green context [10–16]. Among these, aqueous H_2O_2 is a high atom-efficiency (47 %) and most attractive in the green context as it is environmentally benign (only generates water as the by-product) and safe in operation [17]. Moreover, it has high solubility in water and many organic solvents that make it attractive in liquid-phase reactions [18, 19]. However, H_2O_2 exhibits lower oxidation power for many purposes including the oxidation of alcohols, and the use of various organic or transition metal-based Lewis acid catalysts for activation of hydrogen peroxide is essential [20–24]. Also, lanthanides [25, 26] such as cerium salts have long been used as catalysts to activate the oxidation of alcohols [27–29]. Many of these reagents and catalysts suffer from certain drawbacks such as toxicity of the transition metals present in these catalysts, long reaction times, low selectivity and yield [14]. As a consequence, the development of more effective and benign methods to overcome these limitations is still an important experimental challenge. In recent years, the obtained *gem*-dihydroperoxides from H_2O_2 [30] have received considerable attention owing to their relevance to peroxidic antimalarial agents [31, 32], which are structurally similar to hydroperoxides. In contrast to H_2O_2, *gem*-dihydroperoxides act more efficiently as high-oxygen content oxidants in various transformations including the oxidation of alcohols [33, 34]. In 1962, Rieche and co-worker [35] reported the preparation and use of *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane in oxidation reactions. Most recently, we have reported the successful use of *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane (DHPDMDO) as a novel oxidant [36], in selective sulfoxidation of sulfides,

D. Azarifar (✉) · Z. Najminejad
Department of Chemistry, Bu-Ali Sina University, Hamedan 5178, Iran
e-mail: dazarifar@gmail.com; azarifar@basu.ac.ir

K. Khosravi
Department of Chemistry, Faculty of Science, Arak University, Arak 38156-8-8349, Iran

Published online: 22 February 2013

the selective halogenation of aromatic compounds and epoxidation of α,β-unsaturated ketones [36–38].

Experimental

Solvents, reagents, and chemical materials were obtained from Aldrich and Merck chemical companies and purified prior to use. Nuclear magnetic resonance spectra were recorded on JEOL FX 90Q using tetramethylsilane (TMS) as an internal standard. Infrared spectra were recorded on a Perkin Elmer GX FT IR spectrometer (KBr pellets).

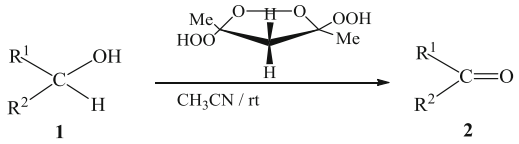
Caution: Although we did not encounter any problem with *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane, it is potentially explosive and should be handled with precautions; all reactions should be carried out behind a safety shield inside a fume hood and transition metal salts or heating should be avoided.

Preparation of DHPDMDO [35]

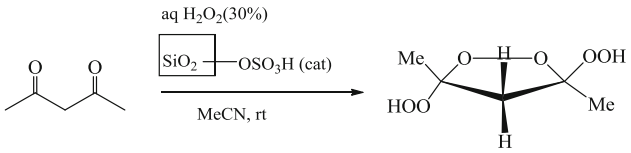
To a stirred solution of acetylacetone (100 mg, 1 mmol) in CH_3CN (4 mL) was added silica sulfuric acid (SSA) (100 mg) and stirring of the reaction mixture was continued for 5 min at room temperature. Then, aqueous 30 % H_2O_2 (5 mmol) was added to the reaction mixture and was allowed to stir for 30 min at room temperature. After completion of the reaction as monitored by TLC, the resulting mixture was filtered and washed with EtOAc (2 × 5 mL) to separate the solid catalyst. The combined filtrates were diluted with water (5 mL) and extracted with EtOAc (3 × 5 mL). The organic layer was separated, dried over anhydrous Mg_2SO_4 and evaporated under reduced pressure to give almost pure white crystalline product 1 (Scheme 2).

General experimental procedure for oxidation of alcohols

To a solution of alcohol 1 (1 mmol) in MeCN (5 mL) was added *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane (166 mg, 1 mmol). The mixture was stirred at room temperature for an appropriate time (Table 2). After completion of the reaction as monitored by TLC, the remaining peroxide was neutralized with saturated aqueous Na_2SO_3 solution (3 mL). The resulting mixture was diluted with water (15 mL) and then extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layer was washed with water and dried over anhydrous $MgSO_4$. Then, the solvent was removed under reduced pressure to leave almost the pure product. The known products were characterized on the basis of their physical and spectroscopic (IR, ^{1}H NMR, and ^{13}C NMR) data that were consistent with the previously reported data [3b].



Scheme 1 Oxidation of secondary alcohols to ketones by *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane



Scheme 2 Silica sulfuric acid-catalyzed synthesis of *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane using aqueous H_2O_2 (30 %)

Results and discussion

As a result of our continued interest in the synthesis of *gem*-dihydroperoxides [39, 40] and their applications in various transformations [37, 38], herein, we are encouraged to examine the oxidative capacity of *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane (DHPDMDO) in oxidation of variously substituted secondary alcohols 1 to respective ketones 2 at room temperature in high yields as shown in Scheme 1.

DHPDMDO has been prepared from silica sulfuric acid (SSA)-catalyzed reaction of acetylacetone with aqueous H_2O_2 (30 %) following our reported procedure (Scheme 2) [36].

To the best of our knowledge, the present study represents the first example, wherein *trans*-3,5-dihydroperoxy-

Table 1 Screening the reaction parameters in model oxidation of cyclohexanol with the oxidant DHPDMDO at room temperature[a]

Entry	Solvent	DHPDMDO (mmol)	Time (min)	Catalyst	Yield (%)[b]
1	EtOH	1	200	None	Trace
2	CH_3CN	1	35	None	94
3	AcOH	1	100	None	30
4	THF	1	80	None	30
5	PhMe	1	200	None	Trace
6	CH_2Cl_2	1	80	None	50
7	CH_3CN	0.5	200	None	45
8	CH_3CN	0.35	250	None	30
9	CH_3CN	0.25	350	None	15
10	CH_3CN	0.5	60	TiO_2	50
11	CH_3CN	0.35	80	TiO_2	35
12	CH_3CN	0.5	55	CuCl	30
13	CH_3CN	0.5	80	Silica sulfuric acid	60

[a] Conditions: cyclohexanol (1 mmol), solvent (5 mL), catalyst (0.001 mmol)

[b] Isolated yield

Table 2 Catalyst-free oxidation of the secondary alcohols with DHPDMDO in CH_3CN at room temperature[a]

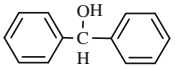
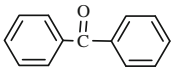
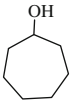
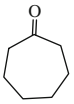
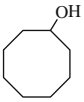
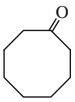
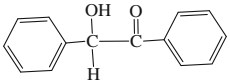
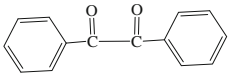
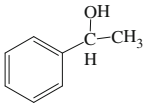
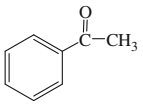
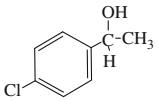
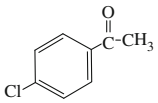
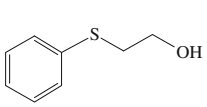
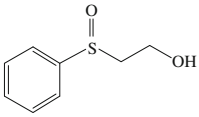
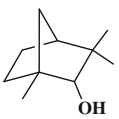
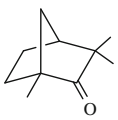
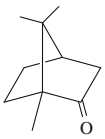
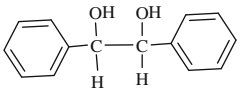
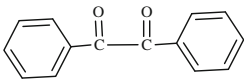
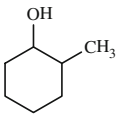
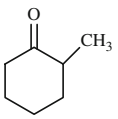
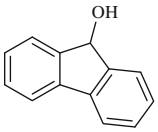
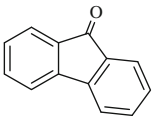
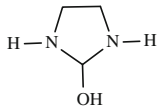
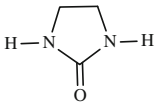
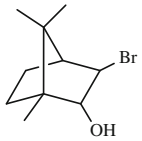
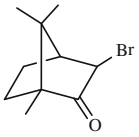
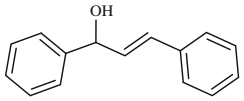
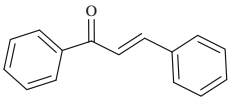
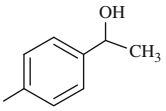
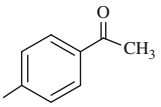
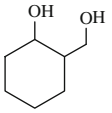
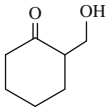
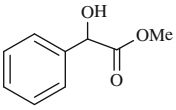
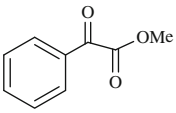
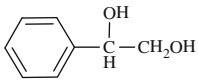
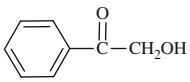
Entry	Substrate	Product 2	Time (min)	Yield (%)[b]
1			30	90
2			35	94
3			35	88
4			35	86
5			30	92
6			25	96
7			30	97
8			30	96
9			30	96
10			28	92
11			28	94
12			30	85
13			30	92
14			20	90

Table 2 continued[a]

Entry	Substrate	Product 2	Time (min)	Yield (%)[b]
15			35	80
16			28	85
17			25	86
18			40	90
19			40	80
20			20	86
21			25	92

[a] Conditions: alcohol 1 (1 mmol), DHPDMDO (1 mmol), CH_3CN (5 mL), room temperature

[b] Isolated yield

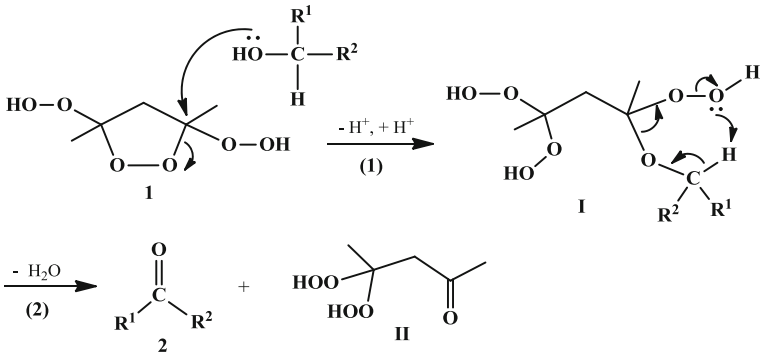
[a] Conditions: alcohol 1 (1 mmol), DHPDMDO (1 mmol), CH_3CN (5 mL), room temperature.
[b] Isolated yield.

3,5-dimethyl-1,2-dioxolane (DHPDMDO) is effectively used for selective conversion of secondary alcohols to ketones. Initially, we used cyclohexanol as the test compound for the oxidation using DHPDMDO at room temperature. The effects of various reaction parameters on the model reaction were investigated (Table 1). To study the effect of solvent, different solvents such as EtOH, H_2O, CH_3CN, AcOH, THF, PhMe and CH_2Cl_2 were examined using the oxidant DHPDMDO (1 mmol) in the absence of any catalyst. CH_3CN proved to be a superior solvent among all the solvents screened in this transformation (entry 2). It was noted that the oxidant *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane, apparently with high atom-efficiency for containing three peroxide units, reacted most efficiently only when used in one equimolar amount in the reaction, reducing its amount resulted in higher reaction times and lower yields (entries 7–9). In order to improve the efficiency of the oxidant, various catalysts such as TiO_2, CuCl, and silica sulfuric acid were examined in the reaction which did not have any significant improving effect on the yield, although the reaction time was reduced considerably (entries 10–13). Finally, we achieved an optimized reaction condition using stoichiometric amount of DHPDMDO as the oxidant in CH_3CN at room temperature without any catalyst.

To establish the generality of the reagent and also to extend the scope of the reaction, a series of secondary alcohols carrying different functional groups were subjected to oxidation under the optimized conditions. The results summarized in Table 2 indicate that all the reactions proceed with high yields and also with high compatibility with the functional groups present in the reactions within short reaction times. The results of Table 2 (entries 15–17) demonstrate that the reaction is chemo selective and the other functional groups like double bond, amino group, and ester group are not oxidized under these reaction conditions. Interestingly, it was noticed that the substrates containing two or more hydroxyl groups undergo mono-oxidation so that the cyclic and benzylic hydroxyl groups react preferentially (entries 19, 21).

A plausible mechanism to explain the transformation of the secondary alcohols into corresponding carbonyl compounds using *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane as the oxidant is depicted in Scheme 3. It is more likely that a nucleophilic attack by the oxygen atom of

Scheme 3 Possible passway for oxidation of alcohols with DHPDMDO



hydroxyl group to the C-3 position of dioxolane ring of the oxidant takes place (step 1). The driving force for such attack comes from the strong electron affinity of C-3 carbon atoms bearing two strong electron withdrawing peroxy groups. In addition, opening the dioxolane ring as a result of this attack relieves the ring strain and yields the more stable open chain intermediate I. As shown in Scheme 3, the intermediate I undergoes α-hydrogen abstraction by hydroperoxy group along with C–O and O–O bond cleavages through a 6-membered transition state (step 2) to yield the product 2 together with water and a *gem*-dihydroperoxy ketone II.

Conclusions

In summary, *trans*-3,5-dihydroperoxy-3,5-dimethyl-1,2-dioxolane (DHPDMDO) has been conveniently used as an effective and high oxygen-content oxidant in selective oxidation of variously substituted secondary alcohols. The simplicity of the procedure, the mildness of the reaction conditions, high yields and chemo selectivity, and the absence of any expensive or toxic catalyst in the reaction demonstrate the advantages of this method.

Acknowledgments The authors wish to thank the Buali Sina University research council for the financial support.

References

1. R.A. Sheldon, J.K. Kochi, *Metal Catalyzed Oxidations of Organic Compounds* (Academic Press, London, 1981)
2. M. Hudlicky, *Oxidation in Organic Chemistry* (Am. Chem. Soc., Washington, DC, 1990)
3. J. Muzart, Tetrahedron **59**, 5789 (2003)
4. S. Pääkkönen, J. Pursiainen, M. Lajunen, Tetrahedron Lett. **51**, 6695 (2010)
5. V.B. Sharma, S.L. Jain, B. Sain, J. Mol. Cat. A: Chem. **212**, 55 (2004)
6. V.B. Sharma, S.L. Jain, B. Sain, J. Mol. Cat. A: Chem. **227**, 47 (2005)
7. C. Kuhakarn, K. Kittigowittana, M. Pohmakotr, V. Reutrakul, Tetrahedron **61**, 8995 (2005)
8. S.L. Jain, V.B. Sharma, B. Sain, Tetrahedron **62**, 6841 (2006)
9. S.V. Ley, A. Madin, in *Comprehensive Organic Synthesis, 7*, ed. by B.M. Trost, I. Fleming (Pergamon, Oxford, 1991), pp. 305–327
10. K. Kaczorowska, Z. Kolarska, K. Mitka, P. Kowalski, Tetrahedron **61**, 8315 (2005). and references cited therein
11. M. Patek, B. Drake, M. Lebel, Tetrahedron Lett. **36**, 2227 (1995)
12. S. Sylvian, A. Wanger, C. Mioskowosky, Tetrahedron Lett. **38**, 1043 (1997)
13. R. Noyori, M. Aoki, K. Sato, Chem. Commun. **16**, 1977 (2003)
14. B.S. Lane, K. Burgess, Chem. Rev. **103**, 2457 (2003)
15. A.J. Catino, R.E. Forslund, H.R. Yao, K.M. Frank, D.A. Bennet, J. Am. Chem. Soc. **122**, 1729 (2000)
16. B.S. Lane, K. Burgess, Chem. Rev. **103**, 2456 (2003)
17. K. Sato, M. Hyodo, M. Aoki, X.-Q. Zheng, R. Noyori, Tetrahedron **57**, 2469 (2001)
18. C.W. Jones, *Applications of Hydrogen Peroxides and Derivatives* (Royal Society of Chemistry, Cambridge, 1999)
19. G. Srukul, *Catalytic Oxidations with Hydrogen Peroxides as Oxidant* (Kluwer Academic, Dordreecht, 1992)
20. M. Matteucci, G. Bhalay, M. Bradley, Org. Lett. **5**, 235 (2003)
21. O. Bortolini, D.F. Furia, G. Modena, R. Seraglia, J. Org. Chem. **50**, 2688 (1985)
22. M.R. Berenguer, O.J. Campon, L. Coppi, Chem. Abstr. **135**, 242230 (2003)
23. H. Hashimoto, T. Ural, EP Patent 1277752A1
24. H. Hashimoto, T. Ural, Chem. Abstr. **135**, 357923 (2003)
25. B. Kagan, Chem. Rev. **102**, 19805 (2002)
26. S. Kobayashi, *Lanthanides: Chemistry and Use in Organic Synthesis* (Springer, Berlin, 1999)
27. L.B. Young, W.S. Trahanovsky, J. Org. Chem. **32**, 2349 (1967)
28. Ho, T.-L. Synthesis. **12**, 936 (1978)
29. N. Al-Haq, A.C. Sullivan, J.R.H. Wilson, Tetrahedron Lett. **44**, 769 (2003)
30. For a review, see: T. Kratz, W. Zeiss, In *Peroxide Chemistry*; Adam, W., Ed.; Wiley-VCH: Weinheim, (2000); pp 41–59
31. For leading examples, see: J. Iskara, D. Bonnet-Delpon, J. P. Begue, Tetrahedron Lett. **44**, 6309 (2003)
32. K. Tsuchiya, Y. Hamada, A. Masuyama, M. Nojima, K.J. McCullough, H.-S. Kim, Y. Shibata, Y. Wataya, Tetrahedron Lett. **40**, 4077 (1999)
33. J.J.P. Selvam, V. Suresh, K. Rajesh, D.C. Babu, N. Suryakiran, Y. Venkateswalu, Tetrahedron Lett. **49**, 3463 (2008)
34. K. Zmitek, M. Zupan, S. Stavber, J. Iskra, Org. Lett. **8**, 2491 (2006)
35. A. Rieche, C. Bischoff, Chem. Ber. **95**, 77 (1962)
36. D. Azarifar, Z. Najminejad, K. Khosravi, Synth. Commun. (2013), In press, DOI 101080/00397911.2011.610549
37. D. Azarifar, K. Khosravi, Synlett. **18**, 2755 (2010)
38. D. Azarifar, K. Khosravi, Z. Najminejad, K. Soleimani, Heterocycles **81**, 2855 (2010)
39. D. Azarifar, K. Khosravi, F. Soleimani, Synthesis 2553 (2009)
40. D. Azarifar, K. Khosravi, F. Soleimanei, F. Molecules **15**, 1433 (2010)