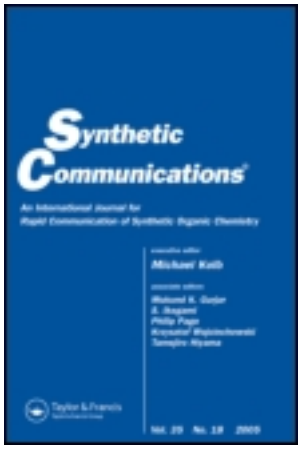


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Simplified Procedure for TEMPO-Catalyzed Oxidation: Selective Oxidation of Alcohols, α-Hydroxy Esters, and Amides Using TEMPO and Calcium Hypochlorite

Sabbasani Rajasekhara Reddy [a] , Selvaraj Stella [a] & Anju Chadha [a b]

[a] Department of Biotechnology, Laboratory of Bioorganic Chemistry, Indian Institute of Technology Madras, Chennai, India

[b] National Center for Catalysis Research, Indian Institute of Technology Madras, Chennai, India

Accepted author version posted online: 12 Jan 2012.Published online: 02 Aug 2012.

To cite this article: Sabbasani Rajasekhara Reddy , Selvaraj Stella & Anju Chadha (2012): Simplified Procedure for TEMPO-Catalyzed Oxidation: Selective Oxidation of Alcohols, α-Hydroxy Esters, and Amides Using TEMPO and Calcium Hypochlorite, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 42:23, 3493-3503

To link to this article: http://dx.doi.org/10.1080/00397911.2011.584650

Synthetic Communications®, 42: 3493–3503, 2012

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2011.584650

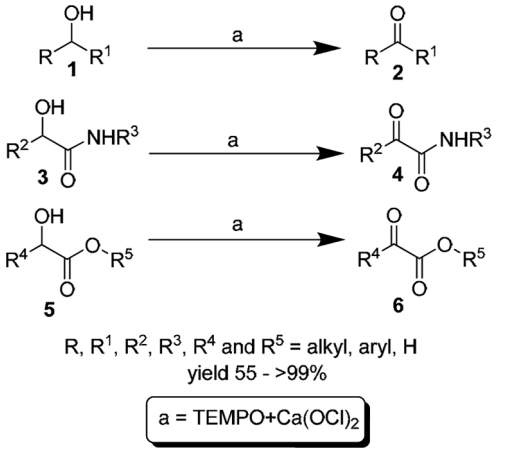
Taylor & Francis
Taylor & Francis Group

SIMPLIFIED PROCEDURE FOR TEMPO-CATALYZED OXIDATION: SELECTIVE OXIDATION OF ALCOHOLS, α-HYDROXY ESTERS, AND AMIDES USING TEMPO AND CALCIUM HYPOCHLORITE

Sabbasani Rajasekhara Reddy,[1] Selvaraj Stella,[1] and Anju Chadha[1,2]

[1]*Department of Biotechnology, Laboratory of Bioorganic Chemistry, Indian Institute of Technology Madras, Chennai, India*
[2]*National Center for Catalysis Research, Indian Institute of Technology Madras, Chennai, India*

GRAPHICAL ABSTRACT



Abstract *A wide range of primary and secondary multifunctional alcohols, α-hydroxyamides, and α-hydroxyesters were oxidized to their corresponding aldehydes, ketones, α-ketoamides, and α-ketoesters under mild reaction conditions using 2,2,6,6-tetramethylpiperidine-1-oxyl as a catalyst with calcium hypochlorite as an oxidant [TEMPO-Ca(OCl)$_2$]. This simplified method does not require any transition metals, acids, or bases and demonstrates controlled and selective oxidation of structurally diverse alcohols, affording moderate to excellent yields at room temperature.*

Keywords Alcohol; calcium hypochlorite; oxidation; TEMPO

Received March 9, 2011.

Address correspondence to Anju Chadha, Laboratory of Bioorganic Chemistry, Department of Biotechnology, Indian Institute of Technology Madras, Chennai 600036, India. E-mail: anjuc@iitm.ac.in

INTRODUCTION

There is a constant need for simple, selective, efficient, mild, and preferably transition metal–free catalysts for the oxidation of alcohols, and this has led to the development of a host of catalytic systems.[1] Many of the metal-based catalyst systems are synthetically useful,[2] and reported literature is dominated by studies screening transition metals and designing new ligands to obtain more efficient processes. Because of this, the advantages of nonmetal catalytic systems[3] have not been fully realized. The use of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) stoichiometrically or catalytically with additional oxidants is well known for the oxidation of alcohols to carbonyl compounds.[4] TEMPO with bleach (sodium hypochlorite, NaOCl) and additives such as a base or phase-transfer catalyst is efficiently used for the oxidation of primary and secondary alcohols.[5] A drawback of the reported TEMPO–bleach procedure is the need for several inorganic salts in the reaction mixture that can be difficult to remove in the workup of large scale oxidations.[4a] In the present work, we sought to simplify the TEMPO–bleach protocol (Anelli's method) by eliminating the use of additives and examined calcium hypochlorite [$Ca(OCl)_2$] as an oxidant that is readily available, stable, solid, inexpensive, and easy to use.[6]

Calcium hypochlorite has been used for ring chlorination of activated benzenoid compounds[6a] and oxidation of aldehydes[6b] alcohols[6c,d] sulfides,[6e] and uronates.[6f] Notably, α-hydroxy carbonyl compounds have been reported to get converted to aldehydes or carboxylic acids in the presence of calcium hypochlorite/acetic acid/acetonitrile[6g] instead of giving α-keto carbonyl compounds. This catalytic system is also known to oxidize α-diketones and α-keto acids to acids. Calcium hypochlorite/acetic acid/acetonitrile has been used for the oxidation of secondary alcohols to ketones,[6c] whereas primary alcohols gave esters under similar conditions. Both the acid and the alcohol portions of the esters were derived from primary alcohols.[6h] On the other hand, excess *tert*-butanol and $NaBrO_3/HBr$[6i] and $Ca(OCl)_2/HCl$[6j] prevented the formation of esters and gave acids in moderate to good yields. Furthermore, $Ca(OCl)_2/Al_2O_3$(microwave and room temperature), when used for the oxidation of benzylic alcohols containing electron-withdrawing groups, gave moderate yields of aldehyde as compared to benzylic alcohols containing electron-donating groups.[6k] Under identical conditions, allylic alcohols gave corresponding acids.[6l] As an alternative to NaOCl in the TEMPO-mediated oxidation of benzylic, aliphatic, and propargylic alcohols, $Ca(OCl)_2/TEMPO/NaHCO_3$ was used under basic conditions as demonstrated by Torii and coworkers.[7] Notably, additives or bases are often needed to increase the catalyst reactivity or to facilitate the turnover process. These systems are synthetically useful but limited in substrate scope. Reportedly, additives are always added when TEMPO is used with oxidants, sodium hypochlorite, or $Ca(OCl)_2$ for the oxidation of alcohols.

This study presents a reinvestigation of the TEMPO-catalyzed oxidation. It turns out that the $TEMPO/Ca(OCl)_2$ catalyst system in acetonitrile can selectively oxidize a variety of alcohols (viz., benzylic, nonbenzylic, heterocyclic, cyclic, acyclic, allylic, α-hydroxy esters, and amides) to the corresponding carbonyl compounds in moderate to excellent yields without any addition of acid or base. This controlled

oxidation reaction is done at room temperature without affecting other existing functionalities.

RESULTS AND DISCUSSION

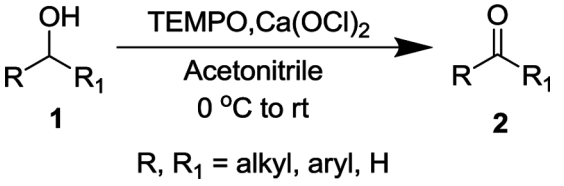
Initial studies of oxidation were done using sodium hypochlorite as an oxidant (1 mmol) and a catalytic amount of TEMPO (0.01 mmol) without additives. At the pH of commercial bleach (12.7), oxidation of *p*-methoxy benzyl alcohol gave the corresponding aldehyde only in 43% yield after 3 h. When calcium hypochlorite was used as an oxidant under identical conditions, to our delight the reaction was complete in 1 h and gave *p*-methoxy benzladehyde in 92% isolated yield. The pH of the oxidation reaction was nearly neutral. Possibly, the generated acid (H^+) [$Ca(OCl)_2$ reacts with water to produce HOCl and ($Ca(OH)_2$); and the available chlorine (65%) in $Ca(OCl)_2$ reacts with water to produce HOCl and HCl] is neutralized by a base ($Ca(OH)_2$ (pK_b–2.43),[8] thereby making the reaction condition mild and suitable for various functional group tolerance. Further, when the oxidation of *p*-methoxy benzyl alcohol was done with oxidant $Ca(OCl)_2$ in the absence of TEMPO, only a trace amount of the product was observed. The catalyst TEMPO is important for the reaction to proceed, and the mechanism of TEMPO in alcohol oxidation has been well discussed in previous papers.[1d,4g,5h]

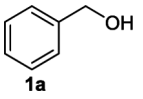
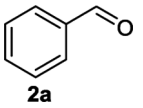
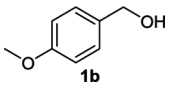
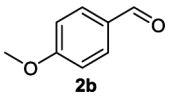
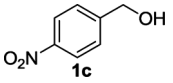
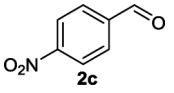
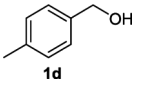
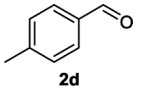
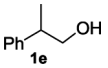
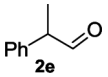
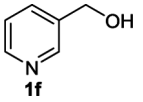
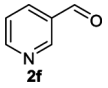
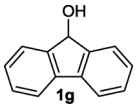
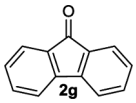
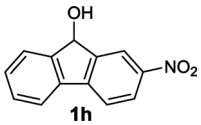
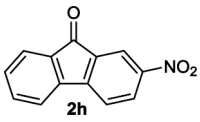
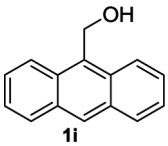
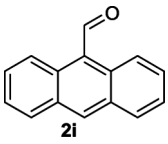
The generality of the TEMPO–calcium hypochlorite catalyst system was examined by the oxidation of a wide range of alcohols. Benzylic alcohols and its derivatives gave excellent yields of the products (85–97%) (Table 1, entries 1–4). Allylic (entry 14), cyclic (entry 10), and nonbenzylic (entry 5) alcohols were also selectively oxidized to the corresponding aldehydes and ketones in moderate to excellent yields (60–85%). In the case of heterocyclic alcohols, only a few metals such as Fe,[1b] Ru,[2e] and Pd[2j] were reportedly used for their oxidation. Significantly, in this study pyridine-3-methanol **1f** was converted to the respective aldehyde in 85% yield without N-oxidized product.[9] Extending the scope of this oxidation system, we examined the oxidation of alcohols using an activated carbon–oxygen system. The first candidate, 9-fluorenol **1 g**, gave 9-fluorenone in quantitative yield. Next, 2-nitro-9-fluorenol **1 h** on oxidation gave 2-nitro-9-fluorenone in quantitative yield. Similarly, secondary alcohols, 1,2,3,4-tetrahydro-1-naphthol **1k**, 1-phenylethanol **1 l**, and benzoin **1 m** could be converted to their respective ketones in good yields (99%, entries 11, 12, and 13). However, unactivated substrate alcohols (entries 5 and 10, Table 1), which are less reactive, require 1.5 equivalent of calcium hypochlorite for the oxidation to give 85% and 60% yields of 2-phenylpropanal **2e** and 2-phenoxycyclohexanone **2j** respectively.

Alkoxycyclohexanones, which are the key intermediates in the preparation of tricyclic β-lactam antibiotics, are generally prepared by the oxidation of the corresponding alcohols.[10] Reported procedures to prepare 2-phenoxy cyclohexanone use 2-chloro cyclohexanone with phenol/base/benzene under reflux conditions, and the yield was 41%.[11] Notably, the oxidation of 2-phenoxy cyclohexanol **1j** using TEMPO/$Ca(OCl)_2$ at room temperature gave 60% yield. No by-products and no oxidative cleavage of the cyclic α-substituted carbonyl compounds were observed.

α-Dicarbonyl compounds are important materials in synthetic organic chemistry.[12] Special reagents and reaction conditions are required to prevent side reactions

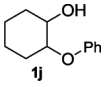
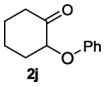
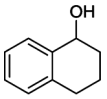
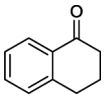
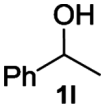
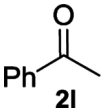
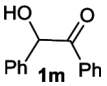
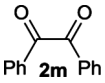
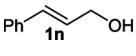
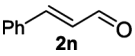
Table 1. Oxidation of alcohols to aldehydes or ketones using catalytic TEMPO and calcium hypochlorite



Entry	Substrate	Time (h)	Product	Isolated yield (%)[a]
1	 **1a**	2.5	 **2a**	85
2	 **1b**	1	 **2b**	92
3	 **1c**	2.5	 **2c**	90
4	 **1d**	1.5	 **2d**	97
5[b]	 **1e**	3	 **2e**	85
6	 **1f**	2	 **2f**	85
7	 **1g**	1	 **2g**	99
8	 **1h**	1.5	 **2h**	99
9	 **1i**	2	 **2i**	85

(*Continued*)

Table 1. Continued

Entry	Substrate	Time (h)	Product	Isolated yield (%)[a]
10[b]	 **1j**	4	 **2j**	60
11	 **1k**	1.5	 **2k**	99
12	 **1l**	1.5	 **2l**	99
13[c]	 **1m**	1.5	 **2m**	99
14	 **1n**	1.5	 **2n**	72

[a]Structures of the products were determined from their spectroscopic (IR, ^{1}H and ^{13}C NMR, and MS) data.

[b]1.5 equiv. calcium hypochlorite was used.

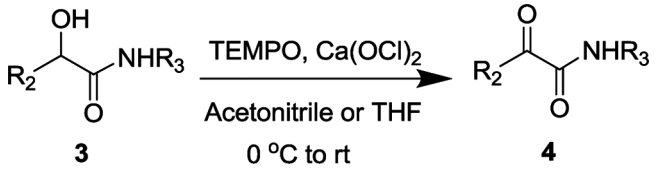
[c]Dichloromethane and acetonitrile in a 1:2 ratio were used as solvent.

during the oxidation of the α-hydroxycarbonyls from which they can be prepared. Significantly, in this study, the oxidation of benzoin (entry 13) quantitatively gave benzil **2m**. The oxidation of cinnamyl alcohol using $Ca(OCl)_2/Al_2O_3$,[6l] NaOCl/KBr/$NaHCO_3$,[5a] and polyethylene glycol (PEG)–supported TEMPO/NaOCl[13] systems gave 40%, 20%, and 28% yield of the aldehyde respectively along with undefined products. In the present study, cinnamyl alcohol **1n** got oxidized to pure cinnamyl aldehyde (72% yield) without the oxidation of the carbon–carbon double bond.

In addition to oxidation of benzylic, allylic, aliphatic and heterocyclic alcohols, the oxidation of α-hydroxyamides was also examined (Table 2). α-Ketoamides, which are electron-deficient compounds and have excellent adducting properties to nucleophiles such as the hydroxyl and thiol groups present in the reactive sites of proteolytic enzymes,[14] play a crucial role in biochemical pathways. Reported methods for the synthesis of α-ketoamides are amidation of α-ketoacids,[15] oxidation of cyano ketones,[16] dicarbonylation of aryl halides using metal complexes (eg., Cu and Pd),[17] acyl halides coupled with isonitriles to form α-ketoimidoyl chloride intermediate followed by hydrolysis,[18] and oxidation of α-hydroxyamides.

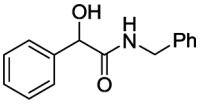
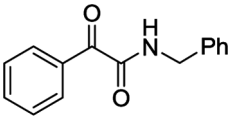
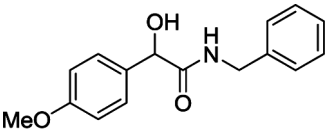
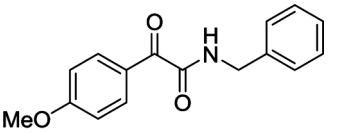
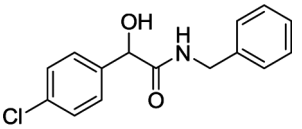
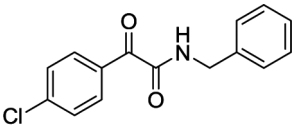
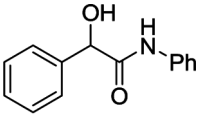
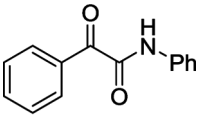
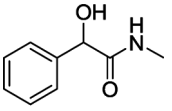
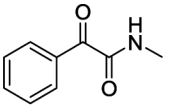
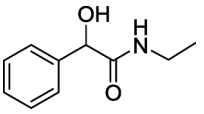
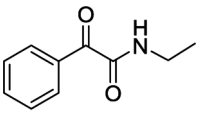
Notably, the oxidation of α-hydroxyamides to α-ketoamides is a key step in the synthesis of norstatine-based HIV-1 protease inhibitors[19] and HCV NS3 protease inhibitors.[20] Asymmetric oxidation of various α-hydroxy-amides using vanadium

Table 2. Oxidation of α-hydroxy amides to α-keto amides using catalytic TEMPO and calcium hypochlorite



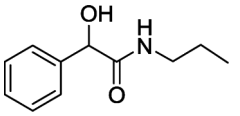
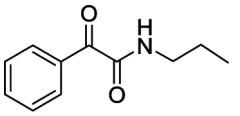
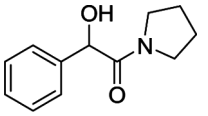
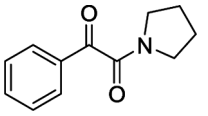
3 4

R_2 = aryl; R_3= CH_2Ph, Ph, Me, Et, Pr, -$(CH_2)_4$-

Entry	Substrate	Time (h)	Product	Isolated yield%[a]
1	 **3a**	0.75	 **4a**	94[b]
2	 **3b**	0.75	 **4b**	92[c]
3	 **3c**	1.5	 **4c**	74[c]
4	 **3d**	0.75	 **4d**	72[c]
5	 **3e**	1.5	 **4e**	55[c]
6	 **3f**	1.0	 **4f**	85[c]

(*Continued*)

Table 2. Continued

Entry	Substrate	Time (h)	Product	Isolated yield%[a]
7	 **3g**	0.5	 **4g**	56[c]
8	 **3h**	1.5	 **4h**	76[c]

[a]Structures of the products were determined from their spectroscopic data (IR, ^{1}H and ^{13}C NMR, and MS).

[b]Acetonitrile was used as solvent.

[c]Tetrahedrofuran was used as solvent.

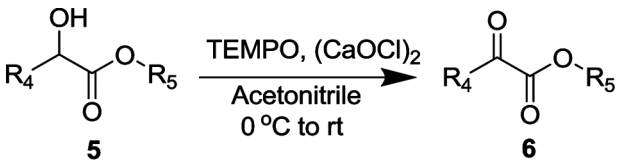
complex (oxidative kinetic resolution) was reported to give up to a maximum of 59% conversion in 8 to 264 h at room temperature.[21]

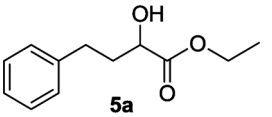
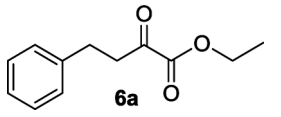
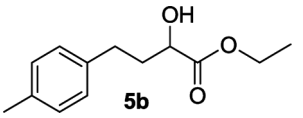
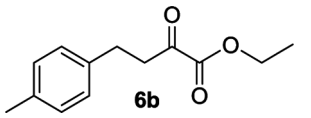
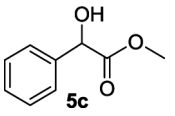
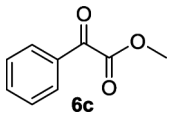
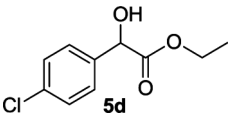
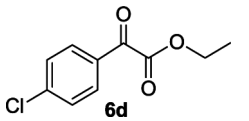
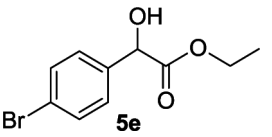
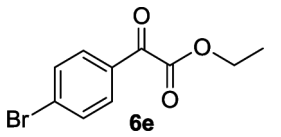
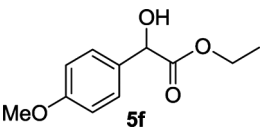
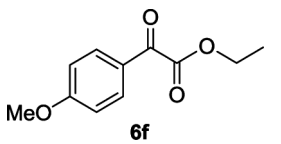
In the present study, oxidation of N-alkyl/aryl α-hydroxyamides to α-ketoamides was done in the presence of TEMPO and $Ca(OCl)_2$ in acetonitrile or tetrahedrofuran (THF) as a solvent at 0 °C to room temperature for 0.5 to 1.5 h (Table 2). Both the N-alkyl and aryl amide groups are tolerated under the present conditions. N-Aryl substituted hydroxyl amides (N-benzyl and N-phenyl) gave excellent yields (72–94%, Table 2, entries 1 to 4), whereas N-alkyl amides gave moderate to good yields (55–85%, Table 2, entries 5–8) of the corresponding keto amides. Oxidation of N-ethyl and N-propyl hydroxyl amides (**3f** and **3 g)** is reported here for the first time. On the other hand, when the oxidation of N-benzyl mandelamide **3a** was done with sodium hypochlorite as an oxidant, only 4% of the oxidized product was formed at 2 h.

The scope of the TEMPO and $Ca(OCl)_2$ oxidation system was further extended to the oxidation of α-hydroxyesters to α-ketoesters (Table 3). Among the numerous reports on the preparation of α-ketocarbonyl compounds,[22] oxidation of α-hydroxycarbonyl compounds is one of the most widely used procedures.[23] Chang et al. have reported a facile method for the synthesis of α-ketocarbonyl compounds from α-hydroxycarbonyl compounds in excellent yields (90–96%) using NaOBr/HCl.[23b] However, the procedure is a little inconvenient as it demands the generation of sodium hypobromite from sodium hydroxide and bromine.

In the present study, the oxidation of α-hydroxyesters was optimized with a catalytic amount of TEMPO and calcium hypochlorite in acetonitrile at 0 °C to room temperature for 1–2 h. Acetonitrile as a solvent provided an almost quantitative yield for the oxidation of α-hydroxy esters (**5a–5e**) to the corresponding α-ketoesters. In the oxidation of ethyl 2-hydroxy-2-(4-methoxyphenyl)acetate **5f**, the electron-donating methoxy group retarded the oxidation reaction and only moderate yield was obtained (55%) (Table 3, entry 6).

Table 3. Oxidation of α-hydroxy esters to α- ketoesters using catalytic TEMPO and calcium hypochlorite



Entry	Substrate	Time (h)	Product	Isolated yield%[a]
1	 **5a**	1	 **6a**	99
2	 **5b**	1	 **6b**	97
3	 **5c**	1	 **6c**	99
4	 **5d**	1.75	 **6d**	90
5	 **5e**	2	 **6e**	92
6	 **5f**	2.5	 **6f**	55

[a]Structures of the products were determined from their spectroscopic (IR, ^{1}H and ^{13}C NMR, and MS) data.

CONCLUSIONS

In summary, calcium hypochlorite with catalytic amount of TEMPO was found to be a versatile terminal oxidant to provide good yields of carbonyl compounds from structurally diverse alcohols. The oxidation is carried out under atmospheric oxygen. This catalyst system works under very mild conditions with no strict

pH control, no additives, more importantly, less effluent. Significantly, this protocol can selectively oxidize primary and secondary alcohols in the presence of sensitive functionalities such as hetero atom, esters, and amides.

EXPERIMENTAL

TEMPO (2,2,6,6-tetramethylpiperidine-1-oxyl) and calcium hypochlorite ($Ca(OCl)_2$) were obtained from Acros Organics (Belgium), and other starting materials were purchased from Sigma Chemical Co (USA). ^1H and ^{13}C NMR spectra were recorded on Bruker 400 and 500 MHz spectrometers. Chemical shifts are quoted in parts per million (δ) relative to tetramethylsilane (TMS) or $CHCl_3$ (residual chloroform in $CDCl_3$). Infrared (IR) spectra were recorded on a Nicolet 6700 spectrophotometer. Mass spectra were recorded on a Q ToF micromass spectrometer. Flash chromatography was performed on silica gel (100–200 mesh) using hexane and ethylacetate as eluent. Thin-layer chromatography (TLC) was done using Kieselgel 60 F254 aluminium sheets (Merck 1.05554). All reactions were carried out under atmospheric oxygen.

General Procedure for the Oxidation of Alcohols and α-Hydroxyesters

A mixture of TEMPO (1.56 mg, 1 mol%) and alcohol or α-hydroxyester (1 mmol) in acetonitrile (3 mL) was taken in a 25-mL round-bottom flask. Calcium hypochlorite (142 mg, 1 mmol) was added at 0 °C over 10 min and the reaction mixture was allowed to warm to room temperature until completion. The suspension was filtered, and the organic phase was washed with saturated aqueous $NaHCO_3$ (8 mL) followed by brine (8 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, using hexane–ethylacetate as the solvent to give the corresponding carbonyl compound. The structures of the products were confirmed from their spectral (IR, ^1H and ^{13}C NMR, and MS) data, which were similar to those reported in the literature.

General Procedure for the Oxidation of α-Hydroxy Amides

This procedure is the same as before except that amides which are not soluble in acetonitrile at 0 °C, are dissolved in tetrahydrofuran (THF). In the case of N-alkyl amides, aqueous workup was avoided because of the partial solubility of these amides in water. The reaction mass was filtered, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel, using hexane–ethylacetate as the solvent to give the corresponding α-keto amides.

Spectral Data

***N*-Ethyl-2-oxo-2-phenylacetamide (Table 2, 4f).** Colorless liquid. ^1H NMR (500 MHz, $CDCl_3$) δ 8.34–8.32 (m, 2H), 7.63–7.59 (m, 1H), 7.48–7.45 (m, 2H), 7.10 (bs, 1H), 3.46–3.40 (m, 2H), 1.24 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR

(125 MHz, $CDCl_3$) δ 187.9, 161.6, 134.3, 133.4, 131.2, 128.4, 34.3, 14.4. IR (neat) = 3302, 2933, 2103, 1737, 1654, 1524, 1447 cm^{-1}. HRMS $[M+H]^+$: calc. for $C_{10}H_{12}NO_2$ 178.0868; obs. 178.0862.

***N*-Propyl-2-oxo-2-phenylacetamide (Table 2, 4g).** Colorless liquid. ^1H NMR (500 MHz, $CDCl_3$) $\delta_H = 8.34–8.32$ (m, 2H), 7.63–7.60 (m, 1H), 7.49–7.46 (m, 2H), 7.12 (bs, 1H), 3.38–3.34 (m, 2H), 1.67–160 (m, 2H), 0.98 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) $\delta_C = 187.9$, 161.8, 134.3, 133.4, 131.2, 128.4, 41.1, 22.6, 11.3. IR (neat) = 3312, 2965, 1655, 1526, 1449 cm^{-1}. HRMS$[M+H]^+$: calc. for $C_{11}H_{14}NO_2$ 192.1025; obs. 192.1029.

ACKNOWLEDGMENTS

Funding from the Department of Science and Technology (DST), Government of India is gratefully acknowledged. The authors thank the Sophisticated Analytical Instrumentation Facility (SAIF), Indian Institute of Technology Madras, for NMR analysis. One of the authors (S. S.) is grateful to the Council of Scientific and Industrial Research, New Delhi, for the fellowship.

REFERENCES

1. (a) Sheldon, R. A.; Arends, I. W. C. E.; Dijksman, A. *Catal. Today* **2000**, *57*, 157; (b) Wang, N.; Liu, R.; Chen, J.; Liang, X. *Chem. Commun.* **2005**, *5322*; (c) Tojo, G.; Fernandez, G. M. Oxidation of Alcohols to Aldehydes and Ketones; Springer: New York, **2006**; (d) Wang, X.; Liu, R.; Jin, Y.; Liang, X. *Chem. Eur. J.* **2008**, *14*, 2679.
2. (a) ten Brink, G. J.; Arends, I. W. C. E.; Sheldon, R. A. *Science* **2000**, *287*, 1636; (b) Stahl, S. S.; Thorman, J. L.; Nelson, R. C.; Kozee, M. A. *J. Am. Chem. Soc.* **2001**, *123*, 7188; (c) Steinhoff, B. A.; Fix, S. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2002**, *124*, 766; (d) Muldoon, J.; Brown, S. N. *Org. Lett.* **2002**, *4*, 1043; (e) Yamaguchi, K.; Mizuno, N. *Angew. Chem. Int. Ed.* **2002**, *41*, 4538; (f) Schultz, M. J.; Park. C. C.; Sigman, M. S. *Chem. Commun.* **2002**, 3034; (g) Uozumi, Y.; Nakao, R. *Angew. Chem. Int. Ed.* **2003**, *42*, 194; (h) Zhan, B.-Z.; White, M. A.; Sham, T.-K.; Pincock, J. A.; Doucet, R. J.; Ramana Rao, K. V.; Robertson, K. N.; Cameron, T. S. *J. Am. Chem. Soc.* **2003**, *125*, 2195; (i) Jensen, D. R.; Schultz, M. J.; Mueller, J. A.; Sigman, M. S. *Angew. Chem. Int. Ed.* **2003**, *42*, 3810; (j) Marko, I. E.; Gautier, A.; Dumeunier, R.; Doda, K.; Philippart, F.; Brown, S. M.; Urch, C. J. *Angew. Chem. Int. Ed.* **2004**, *43*, 1588; (k) Mori, K.; Hara, T.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Am. Chem. Soc.* **2004**, *126*, 10657; (l) Genet, J. P.; Pons, D.; Juge, S. *Synth. Commun.* **1989**, *19*, 1721.
3. (a) Liu, R.; Liang, X.; Dong, C.; Hu, X. *J. Am. Chem. Soc.* **2004**, *126*, 4112; (b) Bjørsvik, H. R.; Liguori, L.; Costantino, F.; Minisci, F. *Org. Process Res. Dev.* **2002**, *6*, 197; (c) Miller, R. A.; Hoerrner, R. S. *Org. Lett.* **2003**, *5*, 285.
4. (a) de Nooy, A. E. J.; Besemer, A. C.; Bekkum, H. V. *Synthesis* **1996**, 1153; (b) Bobbit, J. M.; Flores, M. C. L. *Heterocycles* **1988**, *27*, 509; (c) Adam, W.; Saha-Moller, C. R.; Ganeshpure, P. A. *Chem. Rev.* **2001**, *101*, 3499; (d) Sheldon, R. A.; Arends, I. W. C. E.; ten Brink G. J.; Dijksman, A. *Acc. Chem. Res.* **2002**, *35*, 774; (e) Sheldon, R. A.; Arends, I. W. C. E. *Adv. Synth. Cat.* **2004**, *346*, 1051; (f) Luca, L. D.; Giacomelli, G.; Porcheddu, A. *Org. Lett.* **2001**, *3*, 3041; (g) Luca, L. D.; Giacomelli, G.; Masala, S.; Porcheddu, A. *J. Org. Chem.* **2003**, *68*, 4999.

5. (a) Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. *J. Org. Chem.* **1987**, *52*, 2559; (b) Anelli, P. L.; Banfi, S.; Montanari, F.; Quici, S. *J. Org. Chem.* **1989**, *54*, 2970; (c) Bolm, C.; Fey, T. *Chem. Commun.* **1999**, 1795; (d) Leanna, M. R.; Sowin, T. J.; Morton, H. E. *Tetrahedron Lett.* **1992**, *33*, 5029; (e) Zhao, M.; Li, J.; Mano, E.; Song, Z.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. *J. Org. Chem.* **1999**, *64*, 2564; (f) Gheorghe, A.; Chinnusamy, T.; Cuevas-Yañez, E.; Hilgers, P.; Reiser, O. *Org. Lett.* **2008**, *10*, 4171; (g) Janssen, M. H. A.; Castellana, J. F. C.; Jackman, H.; Dunn, P. J.; Sheldon, R. A. *Green Chem.* **2011**, *13*, 905; (h) Ciriminna, R.; Pagliaro, M. *Tetrahedron Lett.* **2004**, *45*, 6381–6383
6. (a) Nwauka, S. O.; Keehn, P. M. *Synth. Commun.* **1989**, *19*, 799; (b) Nwauka, S. O.; Keehn, P. M. *Tetrahedron Lett.* **1982**, *23*, 3131; (c) Nwauka, S. O.; Keehn, P. M. *Tetrahedron Lett.* **1982**, *23*, 35; (d) Ravichandran, R.; Divakar, S. *J. Mol. Cat.* **1994**, *88*, 117; (e) Waber, J. V.; Schneider, M.; Salami, B.; Paquer, D. *Recl. Trav. Chim. Pay-Bas.* **1986**, *105*, 99; (f) Lin, F.; Peng, W.; Xu, W.; Han, X.; Yu, B. *Carbohydr. Res.* **2004**, *339*, 1219; (g) Nwauka, S. O.; Keehn, P. M. *Tetrahedron Lett.* **1982**, *23*, 3135; (h) McDonald, C. E.; Nice, L. E.; Shaw, A. W.; Nestor, N. B. *Tetrahedron Lett.* **1993**, *34*, 2741; (i) Veeraiah, T.; Periasamy, M. *Synth. Commun.* **1989**, *19*, 2151; (j) Kabalka, G. W.; Chatla, N.; Wadgaonkar, P. P.; Deshpande, S. M. *Synth. Commun.* **1990**, *20*, 1617; (k) Mojtahedi, M.; Saidi, M. R.; Bolourtchain, M.; Shirzi, J. S. *Monatsh. Chem.* **2001**, *132*, 655; (l) Kim, K. S.; Song, Y. H.; Hahn, C. S. *Bull. Korean Chem. Soc.* **1988**, *9*, 60.
7. Inokuchi, T.; Matsumoto, S.; Nishiyama, T.; Torii, S. *J. Org. Chem.* **1990**, *55*, 462.
8. (a) Jain, P. C.; Jain, M. *Engineering Chemistry*, 12th ed.; Dhanapat Rai: India, 1998; (b) http://wwdmag.com/Calcium-Hypochloritearticle2463.
9. Jana, N. K.; Verkade, J. G. *Org. Lett.* **2003**, *5*, 3787
10. Matsumoto, T.; Murayama, T.; Mitsuhashi, S.; Miura, T. *Tetrahedron Lett.* **1999**, *40*, 5043.
11. Lauktien, G.; Volk, F.-J.; Frahm, A. W. *Tetrahedron: Asymmetry* **1997**, *8*, 3457
12. Kirihara, M.; Ochiai, Y.; Takizawa, S.; Nemoto, H. *Chem. Commun.* **1999**, 1387.
13. Pozzi, G.; Cavazzini, M.; Quici, S.; Benaglia, M.; Anna, G. D. *Org. Lett.* **2004**, *6*, 441
14. Mehdi, S. *Biorg. Chem.* **1993**, *21*, 249.
15. (a) Papanikos, A.; Meldal, M. *J. Am. Chem. Soc.* **2001**, *123*, 2176; (b) Nakamura, M.; Inoue, J.; Yamada, T. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2807; (c) Ocain, T. D.; Rich, D. H. *J. Med. Chem.* **1992**, *35*, 451.
16. (a) Takahashi, K.; Shibasaki, K.; Ogura, K.; Iida, H. *Chem. Lett.* **1983**, *12*, 859; (b) Yang, Z.; Zhang, Z.; Meanwell, N. A.; Kadow, J. F.; Wang, T. A. *Org. Lett.* **2002**, *4*, 1103.
17. (a) Tsukada, N.; Ohba, Y.; Inoue, Y. *J. Organomet. Chem.* **2003**, *687*, 436; (b) Liu, J.; Zhang, R.; Wang, S.; Sun, W.; Xia, C. A. *Org. Lett.* **2009**, *11*, 1321.
18. Chen, J. J.; Deshpande, S. V. *Tetrahedron Lett.* **2003**, *44*, 8873–8876
19. Sheha, M. M.; Mahfouz, N. M.; Hassan, H. Y.; Youssef, A. F.; Mimoto, T.; Kiso, Y. *Eur. J. Med. Chem.* **2000**, *35*, 887
20. Han, W.; Hu, Z.; Jiang, X.; Wasserman, Z. R.; Decicco, C. P. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 1111
21. (a) Weng, S.-S.; Shen, M.-W.; Kao, J.-Q.; Munot, Y. S.; Chen, C. -T. *Proc. Natl. Acad. Sci. USA* **2006**, *103*, 3522; (b) Chen, C.-T.; Bettigeri, S.; Weng, S.-S.; Pawar, V. D.; Lin, Y. H.; Liu, C.-Y.; Lee, W.-Z. *J. Org. Chem.* **2007**, *72*, 8175.
22. (a) Coopper, A. J. L.; Ginos, J. Z.; Meister, A. *Chem. Rev.* **1983**, *83*, 321; (b) Kim, S.; Yoon, J. I.; Lee, Y. I. *Synlett.* **1997**, 475; (c) Galobardes, M. R.; Pinnick, H. W. *Tetrahedron Lett.* **1981**, *22*, 5235; (d) Wright, J. B. *J. Am. Chem. Soc.* **1955**, *77*, 4883.
23. (a) Burkhart, J. P.; Peet, N. P.; Bey, P. *Tetrahedron Lett.* **1988**, *29*, 3433; (b) Chang, H. S.; Woo, J. C.; Lee, K. M.; Ko, Y. K.; Moon, S.-S.; Kim, D.-W. *Synth. Commun.* **2002**, *32*, 31, and references cited therein.