Bismuth(III) Oxide Catalyzed Oxidation of Alcohols with *tert*-Butyl Hydroperoxide

Payal Malik, Debashis Chakraborty*

Department of Chemistry, Indian Institute of Technology Madras, Chennai-600 036, Tamil Nadu, India Fax +91(44)22574202; E-mail: dchakraborty@iitm.ac.in *Received 8 July 2010; revised 13 July 2010*

Abstract: A variety of aromatic, aliphatic and conjugated alcohols were transformed into the corresponding carboxylic acids and ketones with aq 70% *t*-BuOOH in the presence of catalytic amounts of bismuth(III) oxide. This method possesses a wide range of capabilities, does not involve cumbersome work-up, exhibits chemoselectivity and proceeds under ambient conditions. The resulting products are obtained in good yields within reasonable time. The overall method is green.

Key words: oxidations, alcohols, Bi2O3, t-BuOOH, reaction rates

The challenge of alcohol oxidation has been of contemporary interest due to its diverse potential in organic synthesis and industrial manufacturing, and it is recognized as a fundamental reaction.¹ The oxidation of primary alcohols results in the formation of aldehydes, which are further oxidized to yield carboxylic acids. Secondary alcohols, on the other hand, give ketones. The most popular and widely used oxidant for such transformations is the Jones reagent.² However, stoichiometric amounts of reagent are required and the reaction is typically performed under highly acidic conditions. Substrates with acid-sensitive functionalities may not tolerate such conditions. In addition, the generation of Cr-based waste products may be considered as a potential environmental hazard.³ Other reagents that have been used successfully include: Oxone,⁴ calcium hypochlorite,⁵ and 2-hydroperoxyhexafluoro-2propanol,⁶ and excellent catalytic methods using metals have been developed using oxidation reactions.⁷ The catalytic oxidation of alcohols employing transition metals such as Ru, Co, Mo, Pd, V, and W have been reported.⁸ In addition, 2,2,6,6-tetramethylpiperidinyl-1-oxyl (TEMPO) together with NaClO has been used as an efficient combination for such oxidations.⁹ However, the above reagents and methods have some limitations, which include the use of superstoichiometric amounts of expensive compounds, highly basic or acidic reaction conditions and/or high temperature. The search for catalytic processes involving environmentally benign reagents will always remain an attractive avenue in this area. Our recent results highlight the oxidation of aldehydes to carboxylic acids using 30% H_2O_2 as the oxidant in the presence of catalytic amounts of AgNO₃.¹⁰ Our continued interest in catalytically active, environmentally benign processes prompted us to investi-

SYNTHESIS 2010, No. 21, pp 3736–3740

Advanced online publication: 17.08.2010

DOI: 10.1055/s-0030-1258221; Art ID: Z17610SS

© Georg Thieme Verlag Stuttgart · New York

gate the application of bismuth(III) reagents to the oxidation of aldehydes.¹¹ It must be noted that bismuth(III) oxide (Bi₂O₃) is reported to catalyze the oxidation of α hydroxy ketones.¹² We were intrigued to carry out the Bi₂O₃-mediated transformation of primary and secondary alcohols into carboxylic acids and ketones, under our previously developed conditions.

Initial attempts to optimize the reaction conditions for the oxidation of primary alcohols to the corresponding carboxylic acids were performed using (2-methoxyphe-nyl)methanol as a suitable substrate in the presence of different solvents, oxidants and 10 mol% bismuth(III) salts (Table 1).

The conversion of (2-methoxyphenyl)methanol into 2methoxybenzoic acid is extremely facile in ethyl acetate in the presence of 10 mol% Bi_2O_3 and five equivalents of aqueous 70% *t*-BuOOH as the oxidant (Table 1, entry 1)

Table 1	Optimization of the Conversion of (2-Methoxyphe-
nyl)metha	nol into 2-Methoxybenzoic Acida

OMe	OH Bi salt, t-E solvent,	BuOOH	OMe O OH	
Entry	Catalyst	Solvent	Time (h) ^b	Yield (%)
1	Bi ₂ O ₃	EtOAc	24	96
2	Bi ₂ O ₃	MeCN	29	88
3	Bi ₂ O ₃	toluene	48	85
4	Bi ₂ O ₃	CH_2Cl_2	42	87
5	Bi ₂ O ₃	DMF	36	89
6	Bi ₂ O ₃	DMSO	39	85
7	Bi ₂ O ₃	THF	40	82
8	Bi ₂ O ₃	EtOH	35	83
9	Bi ₂ O ₃	MeNO ₂	32	80
10	BiCl ₃	EtOAc	35	85
11	BiBr ₃	EtOAc	41	84
12	Bi(NO ₃) ₃ •5H ₂ O	EtOAc	57	50

^a Reaction conditions: aq 70% *t*-BuOOH (5 equiv), bismuth(III) salt (10 mol%).

^b Reaction monitored by TLC until all the alcohol was consumed.

^c Isolated yield after column chromatography.

when heated to reflux. Oxidation with aqueous t-BuOOH alone in ethyl acetate was found to be negligible (<5%). In the presence of 5 mol% Bi₂O₃ and five equivalents of aqueous 70% t-BuOOH as the oxidant in ethyl acetate, the reaction required 36 hours to reach completion with 75% isolated yield of the product. In ethyl acetate, with 10 mol% Bi₂O₃ and five equivalents of aqueous 70% t-BuOOH as the oxidant, the reaction went to completion in a much shorter time. With five equivalents of 5 M t-BuOOH in decane, the reaction was found to reach completion in 30 hours with 90% isolated yield. The reaction took much longer to reach completion (39 h) when performed with five equivalents of aqueous 30% H₂O₂ in ethyl acetate, and yielded 86% of product. Ethyl acetate yielded the best results among the different solvents used for optimization (Table 1, entries 1–9). Other bismuth(III) salts (Table 1, entries 10-12) were not as effective as Bi_2O_3 .

Having established the optimal conditions for oxidation, we continued our studies with a variety of aromatic and al-

iphatic substrates (Table 2). The scope of our catalytic system was applicable to a wide range of aromatic, conjugated, and aliphatic substrates. The primary alcohols were converted into the corresponding carboxylic acids in good isolated yields in reasonable times (Table 2, entries 1–16). It is pertinent to mention here that mild halogenic oxidants such as hypochlorites,¹³ chlorites,¹⁴ and N-bromosuccinimide (NBS)¹⁵ are not suitable for use with substrates with electron-rich aromatic rings, olefinic bonds, or secondary hydroxy groups. Substitutions at different positions on the phenyl ring did not hinder the reaction, although the reaction time was affected. The catalytic system developed here is mild and showed sufficient selectivity to enable the expected oxidation to take place without affecting other functionalities such as phenol and amine groups (Table 2, entries 7 and 8). Oxidation of α , β -unsaturated derivatives (Table 2, entry 15) resulted in the formation of the expected acid in very good yield. In addition, the transformation of secondary alcohols into ketones was also extremely facile, as indicated by entries 17-20 of Table 2.

Table 2 Bi₂O₃-Catalyzed Oxidation of Alcohols^a

R¹∕_ОН —	Bi ₂ O ₃ (10 mol%) aq 70% <i>t</i> ·BuOOH (5 equiv) EtOAc	4		
$R^1 \xrightarrow{OH} R^2$ –	$ Bi_2O_3 (10 \text{ mol\%}) aq 70\% tBuOOH (5 equiv) EtOAc R1 R1 R$	2		
Entry	Alcohol	Product	Time (h) ^b	Yield (%) ^c
1	СН ₂ ОН	Соон	18	88
2	MeO-CH ₂ OH	МеО-СООН	23	90
3	CH ₂ OH OMe	ОМе	24	96
4	MeO CH ₂ OH	мео	29	87
5	MeO CH ₂ OH	Мео-Соон	31	89
6	MeO MeO MeO	ОМе МеО-СООН МеО	25	90
7	HO CH ₂ OH	но-Соон	27	87
8	Me ₂ N-CH ₂ OH	Me ₂ N-COOH	33	85

Synthesis 2010, No. 21, 3736–3740 © Thieme Stuttgart · New York

 Table 2
 Bi₂O₃-Catalyzed Oxidation of Alcohols^a (continued)



^a Reactions performed in EtOAc with 10 mol% Bi_2O_3 and aq 70% *t*-BuOOH (5 equiv), reflux.

^b Reaction monitored by TLC until all the alcohol was consumed.

^c Isolated yield after column chromatography.

Kinetic studies on the oxidation of (2-methoxyphenyl)methanol, 3-phenylprop-2-en-1-ol, (4-nitrophenyl)methanol, butanol, and di-4-tolylmethanol were explored next. High-pressure liquid chromatography (HPLC) was used to determine the various starting materials, products and aldehyde intermediates (for primary alcohols) formed during the alcohol oxidation as a function of time. The concentration of reactant, intermediate and product for the oxidation of butanol is shown in Figure 1. The concentration of the alcohol decreases steadily, while that of the carboxylic acid increases. The concentration of the intermediate aldehyde increases, achieves a steady state, and is then progressively converted into the acid. We have calculated the rate of such reactions. As an example let us consider the conversion of butanol into butyric acid, using the Van't Hoff differential method to determine the order (n) and rate constant (k) (Figure 2).



Figure 1 Concentration versus time plot for the oxidation of butanol with 10 mol% Bi_2O_3 and aq 70% *t*-BuOOH (5 equiv) in EtOAc under reflux

From Figure 1, the rate of the reaction at different concentrations can be estimated by evaluating the slope of the tangent at each point on the curve corresponding to that of butanol. With these data, $\log_{10}(\text{rate})$ versus $\log_{10}(\text{concentration})$ is plotted (Figure 2). The order (*n*) and rate constant (*k*) is given by the slope of the line and its intercept on the $\log_{10}(\text{rate})$ axis, respectively. From Figure 2, it is clear that this reaction proceeds with second-order kinetics (*n* = 2.08) and the rate constant *k* = 0.7006 L·mol⁻¹h⁻¹. For the other substrates, namely (2-methoxyphenyl)methanol, 3-phenylprop-2-en-1-ol, (4-nitrophenyl)methanol, and di-4-tolylmethanol, the order of the reactions are also $n \approx 2$, with rate constants (*k*) of 0.9174, 0.8874, 0.7105, and 1.293 L·mol⁻¹h⁻¹, respectively (see the Supporting Information for details).



Figure 2 Van't Hoff differential plot for the oxidation of butanol with $10 \text{ mol}\% \text{ Bi}_2\text{O}_3$ and 70% aq *t*-BuOOH (5 equiv) in EtOAc under reflux

In summary, we have developed a simple, efficient, chemoselective and inexpensive catalytic method for the oxidation of primary alcohols to carboxylic acids and secondary alcohols to ketones using the bench-top reagent Bi_2O_3 . The overall method is green. It is noteworthy that this method does not depend upon elaborate ligands or other additives.

All substrates used in this study were purchased from Aldrich and used as received. Solvents were purchased from Ranchem, India and purified using standard methods. ¹H and ¹³C NMR spectra of samples in CDCl₃ were recorded with a Bruker Avance 400 instrument. Chemical shifts (δ) were referenced to residual solvent resonances and are reported as parts per million (ppm) relative to TMS. HPLC analysis was performed with a Waters HPLC instrument fitted with a Waters 515 pump and Waters 2487 dual λ absorbance detector.

General Procedure

To a stirred suspension of Bi_2O_3 (46 mg, 0.1 mmol) and alcohol (1 mmol) in EtOAc (2.5 mL) was added aq 70% *t*-BuOOH (0.95 mL, 5 mmol). The reaction mixture was heated to reflux and the progress of the reaction was monitored by TLC until all the alcohol was consumed. All the volatiles were removed and the crude product was treated with sat. aq NaHCO₃ (2 × 1 mL) and extracted with EtOAc (2 mL). The aqueous layer was acidified with 2 M HCl and extracted and subjected to column chromatography. The spectral data for all compounds were identical to those reported in the literature.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

Acknowledgment

This work was supported by the Department of Science and Technology, New Delhi. The services from the NMR facility, purchased under the FIST program and sponsored by the Department of Science and Technology, New Delhi, is gratefully acknowledged.

References

- (a) Hollingworth, G. J. In *Comprehensive Organic Functional Group Transformations*, Vol. 5; Katritzky, A. R.; Meth-Cohn, O.; Rees, C. W.; Pattenden, G., Eds.; Elsevier Science: Oxford, **1995**, 23. (b) Hudlicky, M. In *Oxidations in Organic Chemistry*, *ACS Monograph Series 186*; American Chemical Society: Washington DC, **1990**, 174.
 (c) Larock, R. C. In *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*, 2nd ed.; Wiley: New York, **1999**, 1653.
 (d) Smith, M. B.; March, J. *Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*, 5th ed.; Wiley-Interscience: New York, **2001**, 917–919. (e) Sheldon, R. A.; Van Bekkum, H. *Fine Chemicals through Heterogeneous Catalysis*; Wiley-VCH: Weinheim, **2001**.
- (2) (a) Bowden, K.; Heilbron, I. M.; Jones, E. R. H.; Weedon, B. C. L. J. Chem. Soc. 1946, 39. (b) Heilbron, I.; Jones, E. R. H.; Sondheimer, F. J. Chem. Soc. 1949, 604. (c) Bladon, P.; Fabian, J. M.; Henbest, H. B.; Koch, H. P.; Wood, G. W. J. Chem. Soc. 1951, 2402. (d) Curtis, R. G.; Heilbron, I.; Jones, E. R. H.; Woods, G. F. J. Chem. Soc. 1953, 457. (e) Bowers, A.; Halsall, T. G.; Jones, E. R. H.; Lemin, A. J. J. Chem. Soc. 1953, 2548. (f) Djerassi, C.; Engle, R. R.;

Synthesis 2010, No. 21, 3736-3740 © Thieme Stuttgart · New York

Bowers, A. J. Org. Chem. 1956, 21, 1547.

- (3) Cainelli, G.; Cardillo, G. *Chromium Oxidations in Organic Chemistry*; Springer: Berlin, **1984**.
- (4) Benjamin, R. T.; Sivakumar, M.; Hollist, G. O.; Borhan, B. Org. Lett. 2003, 5, 1031.
- (5) Nwaukwa, S. O.; Keehn, P. M. *Tetrahedron Lett.* **1982**, *23*, 3131.
- (6) Ganem, B.; Heggs, R. P.; Biloski, A. J.; Schwartz, D. R. *Tetrahedron Lett.* **1980**, *21*, 685.
- (7) (a) Yamada, T.; Rhode, O.; Takai, T.; Mukaiyama, T. Chem. Lett. 1991, 5. (b) Bhatia, B.; Punniyamurthy, T.; Iqbal, J. J. Org. Chem. 1993, 58, 5518. (c) Heaney, H. Top. Curr. Chem. 1993, 1, 1. (d) Kharata, A. N.; Pendleton, P.; Badalyan, A.; Abedini, M.; Amini, M. M. J. Mol. Catal. A: Chem. 2001, 175, 277. (e) Biella, S.; Prati, L.; Rossi, M. J. Mol. Catal. A: Chem. 2003, 197, 207. (f) Grill, J. M.; Ogle, J. W.; Miller, S. A. J. Org. Chem. 2006, 71, 9291. (g) Joseph, J. K.; Jain, S. L.; Sain, J. B. Catal. Commun. 2007, 8, 83. (h) Lim, M.; Yoon, C. M.; An, G.; Rhee, H. Tetrahedron Lett. 2007, 48, 3835. (i) Zhou, X. T.; Ji, H. B.; Yuan, Q. L.; Xu, J. C.; Pei, L. X.; Wang, L. F. Chin. Chem. Lett. 2007, 18, 926. (j) Sloboda-Rozner, D.; Neimann, K.; Neumann, R. J. Mol. Catal. A: Chem. 2007, 262, 109. (k) Mukhopadhyay, C.; Datta, A. Catal. Commun. 2008, 9, 2588. (l) Uyanik, M.; Ishihara, K. Chem. Commun. 2009, 2086.
- (8) (a) Noureldin, N. A.; Donald, G. L. J. Org. Chem. 1982, 47, 2790. (b) Murahashi, S. I.; Naota, T.; Hirai, N. J. Org. Chem. 1993, 58, 7318. (c) Sato, K.; Aoki, M.; Takagi, J.; Noyori, R. J. Am. Chem. Soc. 1997, 119, 12386. (d) Sato, K.; Takagi, J.; Aoki, M.; Noyori, R. Tetrahedron Lett. 1998, 39, 7549. (e) Betzemeier, B.; Cavazzini, M.; Quici, S.; Knochel, P. Tetrahedron Lett. 2000, 41, 4343. (f) Hongbing, J.; Mizugaki, T.; Ebitani, K.; Kaneda, K. Tetrahedron Lett.

2002, 43, 7179. (g) Steinhoff, B. A.; Stahl, S. S. Org. Lett.
2002, 4, 4179. (h) Ten Brink, G. J.; Arends, I. C. W. E.;
Sheldon, R. A. Adv. Synth. Catal. 2002, 344, 355.
(i) Maeda, Y.; Kakiuchi, N.; Matsumura, S.; Nishimura, T.;
Kawamura, T.; Uemura, S. J. Org. Chem. 2002, 67, 6718.
(j) Yamaguchi, K.; Mizuno, N. Chem. Eur. J. 2003, 9, 4353.
(k) Sharma, V. B.; Jain, S. L.; Sain, B. Tetrahedron Lett.
2003, 44, 383. (l) Jeyakumar, K.; Chand, D. K. Appl.
Organomet. Chem. 2006, 20, 840.

- (9) (a) Miyazawa, T.; Endo, T.; Shiihashi, S.; Okawara, M. J. Org. Chem. 1985, 50, 1332. (b) Anelli, P. L.; Biffi, C.; Montanari, F.; Quici, S. J. Org. Chem. 1987, 52, 2559. (c) Nooy, A.; De E, J.; Besemer, A. C.; Bekkum, H. V. Synthesis 1996, 1153. (d) Rychnovsky, S. D.; Vaidyanathan, R. J. Org. Chem. 1999, 64, 310. (e) Zhao, M.; Li, J.; Song, Z.; Desmond, R.; Tschaen, D. M.; Grabowski, E. J. J.; Reider, P. J. J. Org. Chem. 1999, 64, 2564. (f) Tashino, Y.; Togo, H. Synlett 2004, 2010.
- (10) Chakraborty, D.; Gowda, R. R.; Malik, P. *Tetrahedron Lett.* 2009, 50, 6553.
- (11) Malik, P.; Chakraborty, D. *Tetrahedron Lett.* **2010**, *51*, 3521.
- (12) Encyclopedia of Reagents for Organic Synthesis, Vol. 1; Wiley, **2001**, 538.
- (13) (a) Stevens, R. V.; Chapman, K. T.; Stubbs, C. A.; Tam, W. W.; Albizati, K. F. *Tetrahedron Lett.* **1982**, *23*, 4647.
 (b) Wilson, S. R.; Tofigh, S.; Misra, R. N. J. Org. Chem. **1982**, *47*, 1360.
- (14) (a) Bal, B. S.; Childers, W. E. Jr.; Pinnick, H. W. *Tetrahedron* **1981**, *37*, 2091. (b) Dalcanale, E.; Montanari, F. J. Org. Chem. **1986**, *51*, 567.
- (15) (a) Ogawa, T.; Matsui, M. J. Am. Chem. Soc. 1976, 98, 1629. (b) Cheung, Y.-F. Tetrahedron Lett. 1979, 3809.