Tetrahedron Letters 55 (2014) 342–345

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

# Oxone/iron(II) sulfate/graphite oxide as a highly effective system for oxidation of alcohols under ultrasonic irradiation

Maryam Mirza-Aghayan[a,*], Mahdieh Molaee Tavana[a], Rabah Boukherroub[b]

[a] *Chemistry and Chemical Engineering Research Center of Iran (CCERCI), PO BOX 14335-186, Tehran, Iran*
[b] *Institut de Recherche Interdisciplinaire (IRI, USR 3078), Université Lille 1, Parc de la Haute Borne, 50 Avenue de Halley-BP70478, 59658 Villeneuve d'Ascq, France*

ARTICLE INFO

*Article history:*
Received 9 July 2013
Revised 14 October 2013
Accepted 7 November 2013
Available online 15 November 2013

*Keywords:*
Oxone
Iron(II) sulfate
Graphite oxide
Alcohols
Oxidation

ABSTRACT

Oxone, in the presence of a catalytic amount of iron(II) sulfate and graphite oxide, oxidizes efficiently alcohols into their corresponding carboxylic acid or ketone compounds at room temperature in short reaction times and in good to quantitative yields under ultrasonic irradiation.

The oxidation of alcohols into their corresponding carbonyl compounds is an important reaction in synthetic organic chemistry and several oxidizing agents are available for this transformation.[1] The oxidation can be achieved using a number of organic and transition metal based reagents.[2] Traditional methods use large amounts of transition metals, involve toxic oxidants such as chromate and permanganate or require harsh reaction conditions.[3,4] Several other systems using aqueous hydrogen peroxide as the oxidant and metal catalysts under phase-transfer catalytic conditions have been reported.[5] Recent efforts have been focused on systems which employ metal compounds only in catalytic amounts together with a stoichiometric oxidant.[6] Several groups have investigated Oxone (potassium hydrogen monopersulfate) as an efficient oxidant of various compounds.[7] For example, Oxone has successfully been used for the oxidation of alcohols into aldehydes and ketones,[7a] and benzaldehyde into benzoic acid.[7b] Oxidation of primary and secondary alcohols into their corresponding oxidized products using 2–6 equiv of Oxone was demonstrated by Parida et al.[8] Wu et al. found that Lewis acids such as $AlCl_3$ play a dominant role in the oxidation of alcohols in the presence of Oxone.[9]

Graphite oxide (GO), prepared by exhaustive oxidation of graphite, has been explored as a heterogeneous catalyst for various organic transformations.[10,11] Recently, GO was applied for the oxidation of alcohols and alkenes, and the hydration of various alkynes into their respective aldehydes and ketones in moderate to high yields.[11b–d] In another report, various alkynes or alcohols were hydrated or oxidized in situ to give the corresponding methyl ketones or aldehydes, respectively, which underwent a subsequent Claisen–Schmidt condensation at 80 or 100 °C after 24 h.[11e]

The use of ultrasound in chemistry offers a method for chemical activation, which has broad applications and uses relatively inexpensive equipment. Ultrasound can generate cavitation within a liquid, which provides a source of energy to enhance a wide range of chemical processes.[12] The application of ultrasound in oxidations of alcohols has been reported.[13] Sonocatalysis is observed during the course of the oxidation of primary hydroxyl groups in homogeneous aqueous medium by the NaOCl/TEMPO system.[13a] Luu et al. have reported acceleration of the oxidation of alcohols by potassium permanganate adsorbed on copper(II) sulfate pentahydrate using ultrasound.[13b] Also, Adams et al. have investigated the conversion of alcohols into carbonyl compounds with a pyridinium chlorochromate/silica gel reagent system by the use of ultrasound technology.[13c]

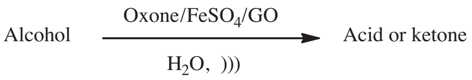
We previously reported the use of GO, a readily available and inexpensive material, as a highly efficient reagent for the synthesis of aldehydes or ketones via the oxidation of various alcohols under ultrasonic irradiation.[14] Herein, we report on the use of Oxone/iron(II) sulfate/GO as a highly efficient system for the oxidation of alcohols to the corresponding carboxylic acid or ketone compounds under ultrasonic irradiation in water as the solvent (Scheme 1).

Parida et al.[8] reported that the oxidation of 4-nitrobenzyl alcohol is very slow using Oxone. Thus we investigated the oxidation of

---

[*] Corresponding author. Tel.: +98 21 44580720; fax: +98 2144580777.
*E-mail address:* m.mirzaaghayan@ccerci.ac.ir (M. Mirza-Aghayan).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.11.019



**Scheme 1.** Oxidation of alcohols into carboxylic acid or ketone compounds using the Oxone/$FeSO_4$/GO system under ultrasonic irradiation.

4-nitrobenzyl alcohol (1 mmol) in the presence of Oxone under different conditions to check the efficiency of our method. Various experimental conditions were screened to obtain the maximum yield of product. The results are summarized in Table 1. The oxidation of 4-nitrobenzyl alcohol (1 mmol) in the presence of 5 mmol of Oxone at reflux in water/acetonitrile (1/1) as solvent gave the corresponding 4-nitrobenzoic acid in 72% yield after 24 h. We examined the effect of different Lewis acid catalysts such as $CuSO_4{\cdot}5H_2O$, $COCl_2{\cdot}6H_2O$ and $FeSO_4{\cdot}7H_2O$ on the reaction yield. The results showed that $FeSO_4{\cdot}7H_2O$ was more efficient in comparison with other Lewis acid catalysts (Table 1, entries 2–4). The oxidation occurs in high yield (78%) in the presence of iron(II) sulfate as a Lewis acid in a very short reaction time (2 h) (Table 1, entry 4). In the next step, we investigated the effect of ultrasonic irradiation on the oxidation reaction in water. Ultrasonic irradiation was performed using an ultrasonic homogenizer (Bandelin Sonopuls HD 3100) with probe model MS 73 at 100% power. The results indicate that ultrasonic irradiation accelerates this reaction, has a beneficial effect on the yield and decreases the reaction time. Under ultrasonic irradiation conditions, the reaction time decreased to 30 min and the yield increased to 97% (Table 1, entry 5). The exact role of ultrasonic irradiation in the oxidation process is not clear, but it cannot be excluded that ultrasonic irradiation participates in the oxidation process by generating locally high temperatures.[15] Thus the optimal conditions were attained by using ultrasonic irradiation as the source of energy and water as a green solvent. We next examined the effect of Oxone concentration (2, 1.5 and 1 mmol) and iron(II) sulfate (40, 20, 10 and 5 mol %) (Table 1, entries 5–10). The results indicate that Oxone (1.5 mmol) and iron(II) sulfate (5 mol %) are optimum for this reaction (Table 1, entry 10).

In a previous report, we demonstrated that GO could be applied as a mild and efficient oxidizing agent for the oxidative aromatization of Hantzsch 1,4-dihydropyridine derivatives.[16] More recently, we described the high performance of GO for the synthesis of aldehydes or ketones from various alcohols under ultrasonic irradiation.[14] Finally, we studied the influence of GO on the Oxone oxidation process. We performed this reaction in the presence of 0.1, 0.05 and 0.025 g of GO (Table 1, entries 11–13). The results obtained show that 0.05 g of GO was required for this reaction affording 4-nitrobenzoic acid in 95% yield via the oxidation of 4-nitrobenzyl alcohol with Oxone (1.5 mmol) and iron(II) sulfate (5 mol %) (Table 1, entry 12). In comparison to other examined conditions, the results also indicated that the reaction was cleaner in the presence of GO; purification of the product was easily achieved through simple crystallization. According to the results in Table 1, the optimum conditions for the oxidations are as follows: alcohol (1 mmol) in the presence of Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol %)/GO (0.05 g), water, ultrasonic irradiation. Under these conditions, oxidation of 1-phenylethanol gave acetophenone in 59% yield in the absence of GO, and in 86% in the presence of GO. This result clearly supports the positive effect of GO on the oxidation process.

In a similar fashion, various alcohols were oxidized smoothly using Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol %)/GO (0.05 g) in water under ultrasonic irradiation to give the corresponding carboxylic acid or ketone compounds. The results are summarized in Table 2. Under these experimental conditions, the reactions of benzyl alcohol, 2-hydroxybenzyl alcohol and 4-nitrobenzyl alcohol gave the corresponding acids in 98%, 92% and 90% yields, respectively, (Table 2, entries 1–3). Oxidation of substrates containing electron-donating groups such as 4-methoxybenzyl alcohol resulted in the formation of the corresponding acid derivative in moderate yield 67% (Table 2, entry 4). The oxidation of 4-chlorocinnamyl alcohol gave 4-chlorocinnamic acid in 94% yield (Table 2, entry 5). We also investigated the oxidation of heterocyclic alcohols such as thiophene-2-methanol and 3-pyridine-3-methanol. Oxidation of thiophene-2-methanol gave only the corresponding aldehyde in 96% yield even after 60 min, while oxidation of 3-pyridine-3-methanol afforded the corresponding nicotinic acid in 94% yield after 30 min (Table 2, entries 6 and 7).

Oxidation of secondary alcohols such as 1-phenylethanol, 1-phenylpropanol, benzhydrol and 1-indanol yielded acetophenone, propiophenone, benzophenone and 1-indanone in 86%, 81%, 81% and 83% yields, respectively, (Table 2, entries 8–11). Similarly, oxidation of an aliphatic alcohol, cyclohexanol, using this method, afforded cyclohexanone in 95% yield (Table 2, entry 12). It should be noted that under these experimental conditions, no reaction occurred with the tertiary alcohol, 2-(4-biphenylyl)-2-propanol

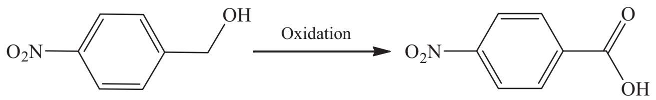


**Table 1**
Effect of the Lewis acid, solvent and ultrasonic irradiation on the oxidation of 4-nitrobenzyl alcohol

| Entry | Conditions | Time | Yield[a,b] (%) |
|---|---|---|---|
| 1 | Oxone (5 mmol), reflux, $H_2O$–MeCN (1:1) | 24 h | 72 |
| 2 | Oxone (2 mmol)/$CuSO_4{\cdot}5H_2O$ (40 mol %), reflux, $H_2O$–MeCN (1:1) | 4 h | 79 |
| 3 | Oxone (2 mmol)/$COCl_2{\cdot}6H_2O$ (40 mol %), reflux, $H_2O$–MeCN (1:1) | 4 h | 43 |
| 4 | Oxone (2 mmol)/$FeSO_4{\cdot}7H_2O$ (40 mol %), reflux, $H_2O$–MeCN (1:1) | 2 h | 78 |
| 5 | Oxone (2 mmol)/$FeSO_4{\cdot}7H_2O$ (40 mol%), $H_2O$,))) | 30 min | 97 |
| 6 | Oxone (1 mmol)/$FeSO_4{\cdot}7H_2O$ (40 mol%), $H_2O$,))) | 30 min | 59 |
| 7 | Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (40 mol %), $H_2O$,))) | 30 min | 95 |
| 8 | Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (20 mol %), $H_2O$,))) | 30 min | 91 |
| 9 | Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (10 mol %), $H_2O$,))) | 30 min | 89 |
| 10 | Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol %), $H_2O$,))) | 30 min | 86 |
| 11 | Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol%)/GO (0.1 g), $H_2O$,))) | 30 min | 98 |
| 12 | Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol %)/GO (0.05 g), $H_2O$,))) | 30 min | 96 |
| 13 | Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol%)/GO (0.025 g), $H_2O$,))) | 30 min | 87 |

[a] Reaction conditions: 4-nitrobenzyl alcohol (1 mmol) in 10 ml of solvent.
[b] Isolated yield.

**Table 2**
Oxidation of various alcohols using Oxone/$FeSO_4{\cdot}7H_2O$ (5 mol %)/GO (0.05 g)

| Entry | Substrate | Product[17,18] | Time (min) | Yield[a] (%) |
|---|---|---|---|---|
| 1 | Benzyl alcohol | Benzoic acid | 30 | 98 |
| 2 | 2-Hydroxybenzyl alcohol | 2-Hydroxybenzoic acid | 30 | 92 |
| 3 | 4-Nitrobenzyl alcohol | 4-Nitrobenzoic acid | 30 | 90 |
| 4 | 4-Methoxybenzyl alcohol | 4-Methoxybenzoic acid | 60 | 67 |
| 5 | 4-Chlorocinnamyl alcohol | 4-Chlorocinnamic acid | 45 | 94 |
| 6 | Thiophene-2-methanol | Thiophene-2-carbaldehyde | 60 | 96 |
| 7 | 3-Pyridinylmethanol | Nicotinic acid | 30 | 94 |
| 8 | 1-Phenylethanol | Acetophenone | 20 | 86 |
| 9 | 1-Phenylpropanol | Propiophenone | 30 | 81 |
| 10 | Benzhydrol | Benzophenone | 30 | 81 |
| 11 | 1-Indanol | 1-Indanone | 30 | 83 |
| 12 | Cyclohexanol | Cyclohexanone | 30 | 95 |
| 13 | 2-(4-Biphenylyl)-2-propanol | No reaction | 30 | – |

[a] Isolated product.

(Table 2, entry 13). Only the starting compound was recovered, even after 180 min and the dehydration product was not observed.

A comparison of the present system (Oxone/$FeSO_4{\cdot}7H_2O$/GO) with our previous results using GO system[14] for the oxidation of secondary alcohols clearly indicates that the present system is more active and gives better yields. Indeed, the oxidation of cyclohexanol, benzhydrol and thiophene-2-methanol using GO afforded cyclohexanone, benzophenone and thiophene-2-carbaldehyde in 98%, 35% and 10% yields after 120, 60 and 90 min, respectively,[14] as compared to 95%, 81% and 96% yields obtained after 30, 30, and 60 min, respectively, using Oxone/$FeSO_4{\cdot}7H_2O$/GO.

The mechanism of oxidation using the Oxone/$FeSO_4{\cdot}7H_2O$/GO system under ultrasonic irradiation is not clear. Different conditions were tested to clarify the role of ultrasonic irradiation. We first investigated the influence of ultrasound on the GO properties. It is well known that ultrasound irradiation of graphite oxide allows its exfoliation to graphene oxide. Graphite oxide (0.05 g) was irradiated in water by ultrasound for 3 h and then 4-nitrobenzyl alcohol (1 mmol)/Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol %) was added. The obtained results indicated that the oxidation was very slow even at reflux of water. We concluded that the transformation of graphite oxide to graphene oxide under ultrasonic irradiation is not important for this reaction. In the next test, we investigated the influence of microwave irradiation on the reaction of 4-nitrobenzyl alcohol (1 mmol)/Oxone (1.5 mmol)/$FeSO_4{\cdot}7H_2O$ (5 mol %)/graphite oxide (0.05 g) in water. After 3 min of microwave irradiation, 4-nitrobenzoic acid was obtained only in 37% yield. We concluded that a high temperature can assist in the oxidation process, but it is not enough for this reaction.

From these results, we believe that under ultrasonic irradiation potassium persulfate in the presence of Fe(II) can produce sulfate ion radicals, Fe(III) and hydroxyl radicals, which are responsible for the oxidation reaction (Scheme 2). Indeed, sonolysis of organic compounds is mainly ascribed to the sonochemical generation of radicals and thermal decomposition in the cavitation microbubbles.[19] GO most likely participates in the oxidation process through the generation of sulfate and hydroxyl radicals or as an oxidant itself.[14]

In conclusion, we have investigated the oxidation of aromatic, heterocyclic and aliphatic alcohol derivatives using Oxone/iron(II)/graphite oxide under ultrasonic irradiation. Primary and secondary alcohols were converted into the corresponding acids and ketones, respectively, under these conditions. This protocol is advantageous as the oxidation takes place under mild conditions, in short reaction times and in good to high yields with a very simple work-up procedure. Further investigations using GO for other chemical transformations (synthesis of pyridine and xanthene derivatives) are currently in progress.

$$KHSO_5 + Fe(II) \xrightarrow{)))} SO_4^{-\cdot} + Fe(III) + OH^{\cdot}$$

**Scheme 2.** A plausible reaction mechanism.

## References and notes

1. Hudlicky, M. *Oxidation in Organic Chemistry*; American Chemical Society: Washington, DC, 1990. pp 114–163.
2. Tojo, G.; Fernandez, M. In *Oxidation of Alcohols to Aldehydes and Ketones*; Tojo, G., Ed.; Springer Science & Business Media: New York, 2006.
3. Mijs, W. J.; de Jonge, C. R. H. *Organic Synthesis by Oxidation with Metal Compounds*; Plenum: New York, 1986.
4. Enache, D. I.; Edwards, J. K.; Landon, P.; Solsona-Espriu, B.; Carley, A. F.; Herzing, A. A.; Watanabe, M.; Kiely, C. J.; Knight, D. W.; Hutchings, G. J. *Science* **2006**, *311*, 362.
5. (a) Barak, G.; Dakka, J.; Sasson, Y. *J. Org. Chem.* **1988**, *53*, 3553; (b) Schrader, S.; Dehmlow, E. V. *Org. Prep. Proced. Int.* **2000**, *32*, 123; (c) Hulce, M.; Marks, D. W. *J. Chem. Educ.* **2001**, *78*, 66.
6. (a) Zondervan, C.; Hage, R.; Feringa, B. L. *Chem. Commun.* **1997**, 419; (b) Coleman, K. S.; Lorber, C. Y.; Osborn, J. A. *Eur. J. Inorg. Chem.* **1998**, *1*, 1673; (c) Moody, C. J.; Palmer, F. N. *Tetrahedron Lett.* **2002**, *43*, 139; (d) Dijksman, A.; Marino-Gonzales, A.; Payeras, A. M. I.; Arends, I. W. C. E.; Sheldon, R. A. *J. Am. Chem. Soc.* **2001**, *123*, 6826.
7. (a) Koo, B. S.; Lee, K. L.; Lee, K. J. *Synth. Commun.* **2002**, *32*, 2115; (b) Webb, K. S.; Ruszkay, S. J. *Tetrahedron* **1998**, *54*, 401; (c) Brik, M. E. *Tetrahedron Lett.* **1995**, *36*, 5519; (d) Trost, B. M.; Curran, D. P. *Tetrahedron Lett.* **1981**, *22*, 1287; (e) Evans, T. L.; Grade, M. M. *Synth. Commun.* **1986**, *16*, 1207; (f) Trost, B. M.; Braslau, R. *J. Org. Chem.* **1988**, *53*, 532; (g) De Poorter, B.; Ricci, M.; Meunier, B. *Tetrahedron Lett.* **1985**, *26*, 4459; (h) Bolm, C.; Magnus, A. S.; Hilderbrand, J. P. *Org. Lett.* **2000**, *2*, 1173; (i) Zolfigol, M. A.; Bagherzadeh, M.; Chehardoli, G.; Malakpour, S. E. *Synth. Commun.* **2001**, *31*, 1149.
8. Parida, K. N.; Jhulki, S.; Mandal, S.; Moorthy, J. N. *Tetrahedron* **2012**, *68*, 9763.
9. Wu, S.; Ma, H.; Lei, Z. *Tetrahedron* **2010**, *66*, 8641.
10. Spiro, M. *Catal. Today* **1990**, *7*, 167.
11. (a) Vijay Kumar, A.; Rama Rao, K. *Tetrahedron Lett.* **2011**, *52*, 5188; (b) Dreyer, D. R.; Jia, H.-P.; Bielawski, C. W. *Angew. Chem., Int. Ed.* **2010**, *49*, 6813; (c) Dreyer, D. R.; Bielawski, C. W. *Chem. Sci.* **2011**, *2*, 1233; (d) Jia, H.-P.; Dreyer, D. R.; Bielawski, C. W. *Tetrahedron* **2011**, *67*, 4431; (e) Jia, H.-P.; Dreyer, D. R.; Bielawski, C. W. *Adv. Synth. Catal.* **2011**, *353*, 528; (f) Dreyer, D. R.; Jia, H.-P.; Todd, A. D.; Geng, J.; Bielawski, C. W. *Org. Biomol. Chem.* **2011**, *9*, 7292; (g) Dreyer, D. R.; Jarvis, K. A.; Ferreira, P. J.; Bielawski, C. W. *Polym. Chem.* **2012**, *3*, 757; (h) Dreyer, D. R.; Jarvis, K. A.; Ferreira, P. J.; Bielawski, C. W. *Macromolecules* **2011**, *44*, 7659.
12. (a) Mason, T. J. *Chem. Soc. Rev.* **1997**, *26*, 443; (b) Cravotto, G.; Cintas, P. *Chem. Soc. Rev.* **2006**, *35*, 180; (c) Singh, V.; Preet Kaur, K.; Khurana, A.; Kad, G. L. *Resonance* **1998**, *3*, 56; (d) Entezari, M. H.; Kruus, P. *Ultrason. Sonochem.* **1994**, *1*, S75.
13. (a) Brochette-Lemoine, S.; Trombotto, S.; Joannard, D.; Descotes, G.; Bouchu, A.; Queneau, Y. *Ultrason. Sonochem.* **2000**, *7*, 157; (b) Luu, T. X. T.; Christensen, P.; Duus, F.; Le, T. N. *Synth. Commun.* **2008**, *38*, 2011; (c) Adams, L. L.; Luzzio, F. A. *J. Org. Chem.* **1989**, *54*, 5387.
14. Mirza-Aghayan, M.; Kashef-Azar, E.; Boukherroub, R. *Tetrahedron Lett.* **2012**, *53*, 4962.
15. Suslick, K. S.; Dokytcz, S. J.; Flint, E. B. *Ultrasonics* **1990**, *28*, 280.
16. Mirza-Aghayan, M.; Boukherroub, R.; Nemati, M.; Rahimifard, M. *Tetrahedron Lett.* **2012**, *53*, 2473.

17. Ultrasonic irradiation was performed in an ultrasonic homogenizer (Bandelin Sonopuls HD 3100) with probe model MS 73 at 100% power. The GO utilized in this work was synthesized using graphite according to a modified Hummers method. The prepared GO was characterized using powder XRD, UV/vis spectroscopy and FT-IR spectroscopy to establish its authenticity.[14] *Typical procedure for the oxidation of alcohols:* To a solution of alcohol (0.1 mmol) in 10 ml of solvent were added Oxone (1.5 mmol), $FeSO_4{\cdot}7H_2O$ (5 mol %) and GO (0.05 g). The resulting mixture was irradiated with an ultrasonic probe for the time indicated in Table 2. The mixture was filtered through a sintered funnel and extracted with EtOAc. The organic layer was dried over $Na_2SO_4$, filtered and evaporated under reduced pressure. Purification was achieved by recrystallization from EtOAc/*n*-hexane or by column chromatography using *n*-hexane/EtOAc: 9:1 as eluent (for entries 2, 4 and 11). The spectroscopic data of the obtained acids were compared with authentic samples.[18]

18. *The Aldrich Library of 13C and 1H FT NMR Spectra*; Pouchert, C. J., Behnke, J., Eds., 1st ed., 1993; Vol. 1–3,.

19. Wu, T. N.; Shi, M.-C. *Sustain. Environ. Res.* **2010**, *20*, 245.