N-Hydroxysuccinimide-promoted Oxidation of Primary Alcohols and Aldehydes to Form Active Esters with Hypervalent(III) Iodine

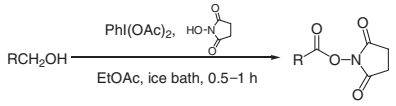
Naiwei Wang,[1,2] Renhua Liu,*[1] Qing Xu,[1] and Xinmiao Liang*[1]
[1]*Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian 116023, P. R. China*
[2]*Graduate School of the Chinese Academy of Sciences, Beijing 100039, P. R. China*

(Received March 13, 2006; CL-060299; E-mail: liangxm@dicp.ac.cn)

A simple, mild, and efficient method for the conversion of primary alcohols and aldehydes to *N*-hydroxysuccinimide esters with (diacetoxyiodo)benzene in high yield is developed. *N*-Hydroxysuccinimide acts not only as an esterification partner but also as an activator of $PhI(OAc)_2$ in this reaction.

In the past decade, the use of hypervalent iodine reagents for performing a wide range of chemical transformations, especially for oxidation reactions has become an increasing popularity in organic syntheses.[1] Oxidation methods based on pentavalent iodine reagents such as the Dess–Martin periodinane[2] and *o*-iodoxybenzoic acid[3] have been common and extensively developed. However, despite their utility, iodine(v)[4] reagents are potentially explosive, cannot be stocked, and the generated iodine(III) species are largely not utilized. In contrast, iodine(III) reagents such as iodosobenzene and (diacetoxyiodo)benzene (DIB) are low toxicity, safe, ready availability, and easy handling hypervalent iodine reagents. But, despite their advantages, iodine(III) reagents, until now, are relatively underrepresented as a result of their low reactivity especially toward alcohols comparing with pentavalent iodine reagents. Therefore, a facile and efficient use of the readily available and relatively stable iodine(III) reagents in place of iodine(V) reagents especially for the oxidation of alcohols seems highly desirable. Only few selective catalytic oxidations of alcohols to carbonyl products with $PhI(OAc)_2$ are reported.

In one early report, it was shown ruthenium catalyzes the oxidation of alcohols by $PhI(OAc)_2$, as demonstrated for saturated aliphatic and benzylic alcohols.[5] The activation of 2,2,6,6-tetramethyl-1-piperidinyloxyl (TEMPO) by $PhI(OAc)_2$ was used in the oxidation of alcohols.[6] The catalytic oxidation of secondary allylic alcohols with $PhI(OAc)_2$ mediated by chromium(III)(salen) complexes to afford the respective enones, has been reported.[7] Polymer-supported $PhI(OAc)_2$ in combination with KBr in aqueous media can also effectively and conveniently oxidize alcohols but primary alcohols were further oxidized to carboxylic acids.[8] In addition, molecular iodine as efficient catalyst for the oxidation of alcohols with $PhI(OAc)_2$ has been reported.[9] Recently, Giannis et al. firstly reported an efficient method for direct oxidation of primary alcohols and aldehydes to form active esters with 1-hydroxy-1,2-benziodoxole-3(1*H*)-one-1-oxide (IBX).[3e,3h] The active esters are valuable intermediates, especially in peptide synthesis since their reaction with various amines could lead to the corresponding amides. Although this method is efficient for the conversion of alcohols to active esters, development of improved synthetic methods for the conversion of alcohols to active esters with $PhI(OAc)_2$ is still desired. Herein, we present our results in the development of the oxidation of primary alcohols and aldehydes to form *N*-hydroxysuccinimide esters with (diacetoxyiodo)benzene (Scheme 1).



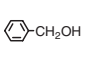
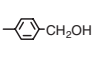
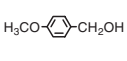
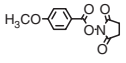
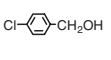
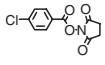
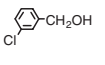
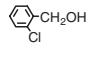
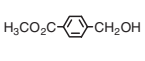
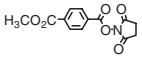
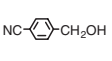
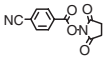
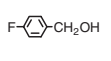
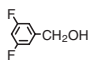
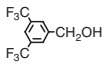
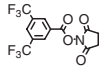
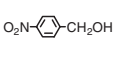
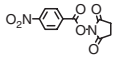
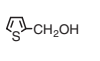
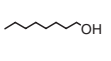
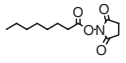
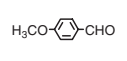
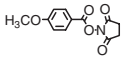
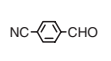
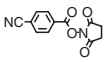
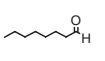
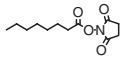
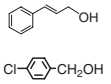
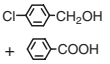
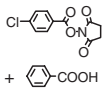
Scheme 1.

Initial investigation of the oxidation of alcohols was carried out using benzyl alcohol as substrate with 10% *N*-hydroxysuccinimide (NHS) and 1.2 equiv. of $PhI(OAc)_2$ for 1 h. The preliminary result (91% yield of benzaldehyde) clearly indicated the role of *N*-hydroxysuccinimide as an activator of $PhI(OAc)_2$. Inspired by the preliminary result, further experiments were carried out with 1.1 equiv. of NHS. In a typical experiment, to a mixture of 5.0 mmol of benzyl alcohol and 11 mmol of $PhI(OAc)_2$ in 10 mL of MeCN, 5.5 mmol of NHS was added and the reaction mixture was stirred in an open vessel with ice bath for 0.5 h. The corresponding ester was detected as the exclusive product as judged by GC. Further experiments showed that $CHCl_3$, CH_2Cl_2, DMSO, and EtOAc are also equally efficient for the reaction. The major product was benzoic acid using THF as the solvent, whereas the reaction was incomplete using $PhCH_3$ as the solvent.

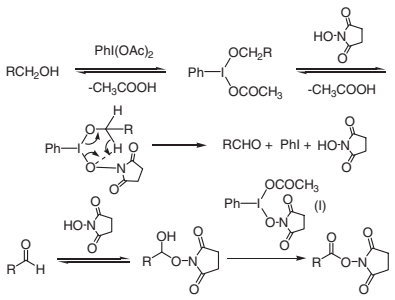
To demonstrate the scope and efficiency of the present method, the typically experimental conditions were applied to the oxidation of a variety of alcohols and aldehydes (Table 1). As shown in Table 1, both electron-deficient and electron-rich benzylic alcohols were quantitatively converted into their corresponding active esters in high yield within 0.5 h (Entries 1–12). Additionally, steric hindrance effect had relatively minor influence on the oxidation of alcohols (Entries 4–6). Sulfur-containing benzylic alcohol also underwent smooth oxidation to provide corresponding active ester (Entry 13). Aliphatic alcohol can also be oxidized to the corresponding active ester with a modest decrease in the selectivity (Entry 14). Aldehydes just as alcohols can be oxidized to form corresponding active esters with high efficiency and yields (Entries 15–17). However, this protocol was not successful in the case of cinnamyl alcohol (Entry 18). No corresponding active ester was detected and the major product of oxidation was benzaldehyde. It is noteworthy that 4-chlorobenzyl alcohol was completely converted into active ester whereas benzoic acid remained unreacted for the mixture of 4-chlorobenzyl alcohol and benzoic acid (Entry 19).

A plausible mechanism is depicted in Scheme 2. After a ligand exchange around the iodine atom,[11] alcohols are oxidized to form aldehydes with NHS as a catalyst. The NHS anion might act as a hydrogen acceptor during the conversion of alcohols to aldehydes. The successful oxidation of aldehydes benefits from the presence of DIB–NHS (I) adduct which might be the actual oxidizing agent. Analogous adduct has been recently report-

Table 1. Oxidation of primary alcohols and aldehydes[10,13]

Entry	Substrate	Product	Time/h	Yield[a]
1			0.5	92
2			0.5	95
3			0.5	92
4			0.5	95
5			0.5	93
6			0.5	92
7			0.5	90
8			0.5	92
9			0.5	91
10			0.5	93
11			0.5	87
12			0.5	82
13			0.5	90
14			1	74[b]
15			0.5	91[c]
16			0.5	91[c]
17			1	70[b,c]
18		—	0.5	0
19			0.5	100/0

[a]Isolated yield. [b]The solvent is MeCN. [c]5.5 mmol of $PhI(OAc)_2$ is added.



Scheme 2. Plausible reaction mechanism.

ed.[3h,12] Reaction of this putative adduct with an aldehyde–NHS adduct would finally afford the corresponding NHS esters. As an alternative mechanism, oxidation by *N*-oxoammonium generated from NHS by the oxidation with DIB may be involved.

In conclusion, we have demonstrated a simple and effective for the direct oxidative conversion of alcohols and aldehydes to the corresponding NHS esters with $PhI(OAc)_2$ in high yield. The present method is mild, facile, efficient, and fast. Moreover, it is noteworthy that the oxidation ability of $PhI(OAc)_2$ towards alcohols is promoted by NHS.

References and Notes

1 a) V. V. Zhdankin, P. J. Stang, *Chem. Rev.* **2002**, *102*, 2523. b) H. Tohma, Y. Kita, *Adv. Synth. Catal.* **2004**, *346*, 111. c) T. Wirth, *Angew. Chem., Int. Ed.* **2005**, *44*, 3656.

2 a) D. B. Dess, J. C. Martin, *J. Org. Chem.* **1983**, *48*, 4155. b) D. B. Dess, J. C. Martin, *J. Am. Chem. Soc.* **1991**, *113*, 7277. c) S. D. Meyer, S. L. Schreiber, *J. Org. Chem.* **1994**, *59*, 7549. d) A. G. M. Barrett, D. Hamprecht, M. Ohkubo, *J. Org. Chem.* **1997**, *62*, 9376. e) A. G. Myers, B. Zhong, M. Movassaghi, D. W. Kung, B. A. Lanman, S. Kwon, *Tetrahedron Lett.* **2000**, *41*, 1359. f) J. I. C. Lena, J. I. M. Hernando, M. D. R. Ferreira, E. Altinel, S. Arseniyadis, *Synlett* **2001**, 597.

3 a) M. Frigerio, M. Santagostino, S. Sputore, G. Palmisano, *J. Org. Chem.* **1995**, *60*, 7272. b) E. J. Corey, A. Palani, *Tetrahedron Lett.* **1995**, *36*, 3485. c) D. Crich, X. S. Mo, *Synlett* **1999**, 67. d) K. C. Nicolaou, T. Montagnon, P. S. Baran, Y. L. Zhong, *J. Am. Chem. Soc.* **2002**, *124*, 2245. e) R. Mazitschek, M. Mulbaier, A. Giannis, *Angew. Chem., Int. Ed.* **2002**, *41*, 4059. f) J. D. More, N. S. Finney, *Org. Lett.* **2002**, *4*, 3001. g) A. Ozanne, L. Pouysegu, D. Depernet, B. Francois, S. Quideau, *Org. Lett.* **2003**, *5*, 2903. h) A. Schulze, A. Giannis, *Adv. Synth. Catal.* **2004**, *346*, 252.

4 a) V. Gert, *Chem. Eng. News* **1989**, *30*, 2. b) A. R. Katritzky, G. P. Savage, J. K. Gallos, H. D. Durst, *Org. Prep. Proced. Int.* **1989**, *21*, 157. c) A. Varvoglis, in *Hypervalent Iodine in Organic Synthesis*, Academic Press, London, **1997**, pp. 16–17.

5 P. Muller, J. Godoy, *Tetrahedron Lett.* **1981**, *22*, 2361.

6 A. D. Mico, R. Margarita, L. Parlanti, A. Vescovi, G. Piancatelli, *J. Org. Chem.* **1997**, *62*, 6974.

7 W. Adam, S. Hajra, M. Herderich, C. R. Saha-Moller, *Org. Lett.* **2000**, *2*, 2773.

8 a) H. Tohma, S. Takizawa, T. Maegawa, Y. Kita, *Angew. Chem., Int. Ed.* **2000**, *39*, 1306. b) H. Tohma, T. Maegawa, Y. Kita, *Synlett* **2003**, 723.

9 N. N. Karade, G. B. Tiwari, D. B. Huple, *Synlett* **2005**, 2039.

10 A typical experimental procedure is as follows (Table 1, Entry 1): To a mixture of 5.0 mmol of benzyl alcohol and 11 mmol of $PhI(OAc)_2$ in 10 mL of EtOAc, 5.5 mmol of NHS was added and the reaction mixture was stirred in an open vessel with ice bath for 0.5 h. After completion of reaction, a yellow solution was formed. The solvent was removed under reduced pressure and pure product was obtained by column chromatography (silica gel, petroleum ether/EtOAc, 4/1) in 92% yield as colorless crystal. mp: 137–138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, 2H, $J = 8.0$ Hz), 7.68 (t, 1H, $J = 8.0$ Hz), 7.51 (t, 2H, $J = 8.0$ Hz), 2.90 (s, 4H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 25.8, 125.2, 129.0, 130.7, 135.1, 162.0, 169.5; IR: 3070, 2952, 1794, 1768, 1733, 1598, 1208, 744, 705 cm^{-1}; HRAPCIMS m/z: calcd for $(M + H)^+$, 220.0610; found, 220.0616.

11 a) A. Seveno, G. Morel, A. Foucaud, E. Marchand, *Tetrahedron Lett.* **1977**, *18*, 3349. b) B. C. Schardt, C. L. Hill, *Inorg. Chem.* **1983**, *22*, 1563.

12 K. C. Nicolaou, T. Montagnon, P. S. Baran, *Angew. Chem., Int. Ed.* **2002**, *41*, 993.

13 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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