Facile oxidation of benzyl ethers by the 2-nitrobenzene-sulfonylperoxyl intermediate generated from 2-nitrobenzenesulfonyl chloride and superoxide

Yong Hae Kim,* Yong Il Kim and Joong Young Kim

Department of Chemistry, Korea Advanced Institute of Science and Technology, Taejon, 305-701, Korea

Various benzyl ethers react with a 2-nitrobenzenesulfonyl-peroxyl radical intermediate generated from 2-nitrobenzenesulfonyl chloride and potassium superoxide at −25 °C in acetonitrile to give the corresponding esters in high yields.

Functionalization at the α-C−H bonds of ethers is one of the most useful reactions in organic synthesis, because it provides for the efficient preparation of esters.[1] Ruthenium tetraoxide,[2] chromium trioxide,[3] $PhCN_2N^+Et_3 \cdot MnO_4$[4] and trichloroiso-cyanuric acid[5] oxidize ethers to esters, respectively, but these methods involve the use of poisonous heavy metals and chemicals. Reactions of aryl ethers with ozone[6] and H_2O_2[7] lead to oxidative cleavage of the ether and formation of carboxylic acids. Most recently, a new oxidation system has been described using hypervalent *tert*-butylperoxyiodane which oxidizes benzyl ethers to esters.[8]

In the course of our study on activation of superoxide $(O_2^{\cdot-})$,[9] a 2-nitrobenzenesulfonylperoxyl intermediate (**I**), generated from 2-nitrobenzenesulfonyl chloride and potassium superoxide has been found to have a much stronger oxidizing ability than superoxide itself (Scheme 1).
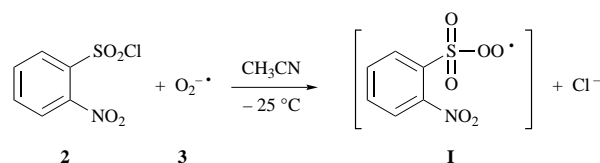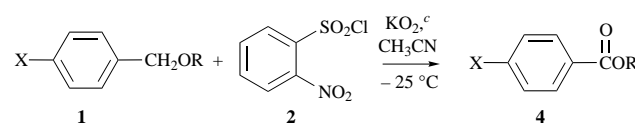
Scheme 1

We have now found that various benzyl ethers react with **I** at −25 °C under mild conditions to give the corresponding esters in excellent yields. The results obtained are summarized in Table 1. In a typical experiment, a solution of 2-nitrobenzene-sulfonyl chloride (666 mg, 3 mmol; CH_3CN, 10 ml) and benzyl ethyl ether (68 mg, 0,5 mmol) was added to a heterogeneous solution of potassium superoxide (639 mg, 9 mmol; CH_3CN, 5 ml) at *ca.* −25 °C. After stirring for 7 h, the reaction mixture was poured into cold water and then extracted with CH_2Cl_2 (25 ml × 3). The CH_2Cl_2 solution was dried over anhydrous magnesium sulfate, filtered and then concentrated under reduced pressure to give the crude product **4b**, which was purified by silica gel chromatography (silica gel: 35–70 mesh, elution: CH_2Cl_2–*n*-hexane = 1 : 1) to afford pure ethyl benzoate (64 mg, 85%) in run 2; δ_H(300 MHz, $CDCl_3$) 1.39 (t, 3H), 4.37 (q, 2H), 7.40–7.56 (m, 3H), 8.05 (d, 2H); δ_C(75 MHz, $CDCl_3$) 14.3, 60.9, 128.3, 129.5, 130.5, 132.7, 166.5; *m/z* (GC–MSD) 150, 122, 106, 105, 77; ν_{max}(neat)/cm^{-1} 1719, 1451, 1367, 1175.

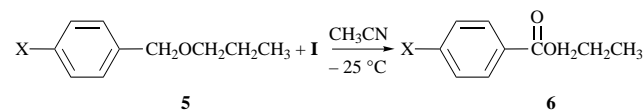In order to establish the effect of *para*-substituted groups for the oxidation of a series of benzyl ethers, competitive oxid-ations of *para*-substituted benzyl propyl ethers with **I** were carried out (Table 2). The Hammett correlation plot for the oxidation of these benzyl propyl ethers showed a better corre-lation of relative rate factors with the σ^+ rather than the σ constants of substituents in the aromatic ring and afforded the reaction constants $\rho^+ = -0.57$ ($r = 0.99$). This ρ^+ value shows **I**

Table 1 Oxidation of benzylic ethers with 2-nitrobenzene peroxy-sulfur intermediate

Run	X	R	Time/h	2:1[a]	Products	Yield (%)[b]
1	H	methyl	7	6	**4a**	83
2	H	ethyl	7	6	**4b**	85
3	H	propyl	7	6	**4c**	87
4	H	cyclo-hexyl	7	6	**4d**	87
5	H	octyl	6	6	**4e**	85
6	Cl	octyl	6	6	**4f**	87
7	OCH_3	octyl	4	4	**4g**	81
8	OCH_3	octyl	4	6	**4g**	93
9	OCH_3	octyl	4	8	**4g**	93
10			4	6	**4h**	84
11			4	6	**4i**	87

[a] Molar ratio. [b] Isolated yields. [c] Molar ratio **3**:**2** = 3.

**Table 2** Competitive oxidations of *para*-substituted benzyl propyl ethers with **I**

X	Relative rate	σ_p^+	ρ^+
OCH_3	2.80	−0.78	−0.573
CH_3	1.51	−0.31	−0.577
H	1	0	—
Cl	0.87	0.11	−0.550
NO_2	0.36	0.79	−0.562

to be an electrophilic species and appears to be comparable to $\rho^+ = -0.65$ for benzylic hydrogen abstraction from dibenzyl ethers by the benzoyloxyl radical.[10]

The possible reaction mechanism of benzyl ethers with **I** can be postulated as shown in Scheme 2. The oxidation can be best

Scheme 2
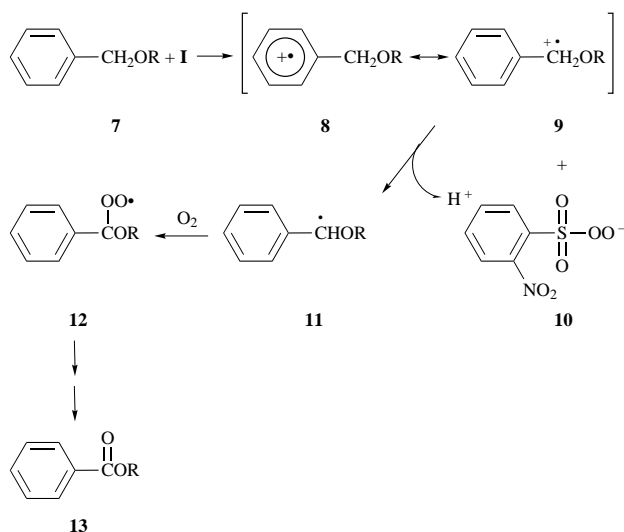
explained by a radical mechanism *via* formation of **I**, which was indirectly observed by a spin trapping study.[11]

One electron transfer from the aromatic ring of **7** to **I** may form a radical cation **8** or **9** whose labile methylene hydrogen is removed to form **11**. Coupling of **11** with molecular oxygen generates the peroxyl radical **12**, which converts to the ester **13**. Formation of a peroxyl radical such as **12** has been well documented in the oxidation of **7** to **13** utilizing hypervalent iodane.[8] The oxidation of benzyl propyl ethers results in higher yields of esters with bubbling in O_2 than with bubbling in N_2.†

Benzyl ethers are commonly used as temporary protecting groups for alcohols, owing to the fact that they are stable to both acids and bases. Despite the numerous methods available for their cleavage,[12] which include catalytic and chemical hydrogenolysis, transfer hydrogenation, bromination hydrolysis, acetolysis, and the use of halosilane reagents or Lewis acid–thiol systems, problems associated with reagent incompatibility or slow debenzylation rates often arise when multiple functionality is present.

Oxidation of alkyl benzyl ethers to the benzoate esters provides a convenient method for the deprotection of benzyl ether protecting groups, because alkyl benzoates are readily hydrolyzed to the corresponding alcohols under basic conditions.[12] Without purification of the crude intermediate 3-menthyl benzoate **15**, hydrolysis gives the alcohol **16** directly. After general work-up, the crude 3-menthyl benzoate **15** was treated

with KOH in aqueous methanol at room temperature, leading to menthol **16** in 85% yield without any racemization (Scheme 3).

Scheme 3
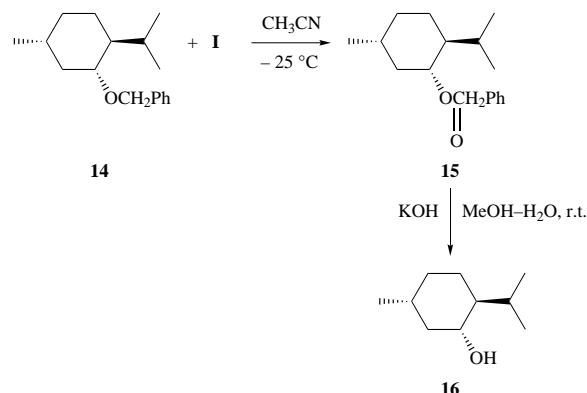
The present method may be utilized to oxidize ethers to esters effectively under mild conditions and also to deprotect benzylic ethers to alcohols.

References

1 C. A. Godfrey, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Flemming, Pergamon, Oxford, 1991, vol. 7, p. 235.
2 P. F. Schuda, B. M. Cichowicz and M. R. Heimann, *Tetrahedron Lett.*, 1983, **24**, 3829.
3 B. S. Bal, K. S. Kochhar and H. W. Pinnick, *J. Org. Chem.*, 1981, **46**, 1492.
4 H.-J. Schmidt and H. J. Schafer, *Angew Chem.*, *Int. Ed. Engl.*, 1979, **18**, 69.
5 E. C. Juenge and D. A. Beal, *Tetrahedron Lett.*, 1968, 5819.
6 P. Angibeaud, J. Defaye, A. Gadelle and J.-P. Utille, *Synthesis*, 1985, 1123.
7 M. Sasidharan, S. Suresh and A. Sudalai, *Tetrahedron Lett.*, 1995, **36**, 9071.
8 M. Ochiai, T. Ito, H. Takahashi, A. Nakanishi, M. Toyonari, T. Sueda, S. Goto and M. Shiro, *J. Am. Chem. Soc.*, 1996, **118**, 7716.
9 Y. H. Kim and B. C. Chung, *J. Org. Chem.*, 1983, **48**, 1562; Y. H. Kim, B. C. Chung and H. S. Chang, *Tetrahedron Lett.*, 1985, **26**, 1079; Y. H. Kim, H. K. Lee and H. S. Chang, *Tetrahedron Lett.*, 1987, **28**, 4285; Y. H. Kim, K. S. Kim and H. K. Lee, *Tetrahedron Lett.*, 1989, **30**, 6357.
10 G. A. Russel and R. C. Williamson, *J. Am. Chem. Soc.*, 1964, **86**, 2357; R. L. Huang, H. H. Lee and S. H. Song, *J. Chem. Soc.*, 1962, 3336.
11 Y. H. Kim, S. C. Lim, M. Hoshino, Y. Ohtsuka and T. Ohishi, *Chem. Lett.*, 1989, 167.
12 T. W. Greene and P. G. M. Wuts, *Protective Groups in Organic Synthesis*, Wiley, New York, 1991, ch. 2.

† The oxidations of benzyl propyl ether were compared with bubbling in O_2 and N_2 for 1 h respectively: with O_2; product 56%, starting material was recovered in 43%, with N_2; product 34%, starting material was recovered in 64% yield.