A New and Efficient Method for Oxidation of Various Alcohols by Using *N-tert*-Butyl Phenylsulfinimidoyl Chloride

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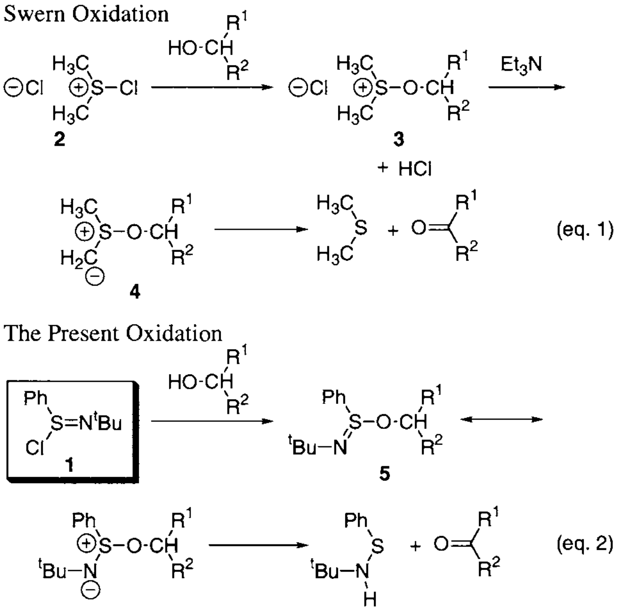
Various primary and secondary alcohols were smoothly oxidized to afford the corresponding aldehydes and ketones in excellent yields by using *N-tert*-butyl phenylsulfinimidoyl chloride (**1**) in the presence of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene). The oxidation of alcohols was carried out in a simple manner by using the isolable oxidizing agent **1** under basic conditions.

Oxidation of alcohols is one of the most fundamental organic transformations and many useful oxidation methods have been developed. Among them, oxidation of alcohols by using activated dimethyl sulfoxides[1] was more frequently employed in the key step of various synthetic strategies. It is generally known that an alcohol reacts with the activated dimethyl sulfoxides to form an alkoxysulfonium salt (**3**), which is in turn deprotonated by bases such as Et_3N to form a dimethylalkoxysulfonium ylide (**4**). Oxidized products are formed by an intramolecular proton transfer of **4** below the temperature of Pummerer rearrangement as shown in Scheme 1, eq 1. Swern et al. demonstrated[2] that a combination of dimethyl sulfoxide and oxalyl chloride proved to be the most useful and practical method among many oxidation methods by using activated dimethyl sulfoxides. However, the control of reaction temperature at each step was crucial for successful oxidation of alcohols because the intermediates formed stepwise in Swern oxidation were quite unstable. For example, it was reported that **2**, an activated intermediate of Swern oxidation, was no longer stable at 20 °C and yields of carbonyl compounds dropped down even at 0 °C.[2] On the other hand, Parikh–Doering oxidation,[1d] in which dimethyl sulfoxide was activated by SO_3–pyridine, could be conducted at room temperature. However, more than 3 equivalents of SO_3–pyridine were generally required in this procedure.

It was considered then that an alkoxysulfilimine (**5**) would behave as a key intermediate to afford oxidation products more conveniently in comparison with the alkoxysulfonium ylide (**4**) (Scheme 1, eq 2) since the reactivity of the sulfilimine (**5**)-nitrogen was lower than that of sulfonium ylide (**4**)-carbon. In addition, it was easily assumed that the intermediate **5** would be more stable than **4** because of its inherent zwitter ionic structure.[3] To the best of our knowledge, however, there are no reports on oxidation reaction of alcohols via **5**. Now, we would like to report here a new and efficient method for oxidation of various alcohols via novel intermediate **5**, which is formed by the reaction of alcohols with *N-tert*-butyl phenylsulfinimidoyl chloride (**1**) in the presence of DBU.

In order to form the key intermediate **5** readily from alcohols, *N-tert*-butyl phenylsulfinimidoyl chloride (**1**), which had already been synthesized by Markovskii et al.,[4] was chosen as an oxidizing agent. In the present experiment, **1** was conveniently prepared by a slight modification of Markovskii's procedure: i.e., a mixture of phenyl thioacetate (5.4 g, 35.5 mmol) and *N*,*N*-dichloro-*tert*-butylamine[5] (5.3 g, 37.3 mmol) in benzene (15 mL) was refluxed for 1 h. The volatiles were evaporated and the crude product was purified by distillation (112–116 °C/0.5 mmHg) to give **1**[6] (4.4 g, 20.3 mmol, 57% as a red-orange liquid). This reagent **1** can be stored for a long time within a sealed bottle at room temperature.



Scheme 1.

In order to find appropriate reaction conditions, an oxidation of benzyl alcohol using **1** was tried as a model, and effects of bases and solvents in the present oxidation reaction were examined (Table 1). When benzyl alcohol and **1** were simply mixed in dichloromethane at –78 °C without using any base, the desired oxidation reaction hardly took place and benzyl chloride was formed in a small amount (entry 1). However, when bases were used for trapping hydrogen chloride generated during the formation of **5**, the desired oxidation smoothly proceeded (entries 2–5). Among the bases examined, the best result was obtained when 2 equivalents of DBU were used (entry 3). It was obvious that 2 equivalents of DBU were necessary for the inhibition of the above mentioned chloride formation as shown in the experiments using 1 or 2 equivalents of DBU (entries 2 and 3). In addition to dichloromethane, toluene, THF, and acetonitrile were tried as solvents in this oxidation reaction. In the cases of using toluene and THF, the reaction mixtures turned to be suspensions and the oxidation reaction proceeded very slowly. Therefore, dichloromethane was found to be the most suitable solvent for the present oxidation reaction.

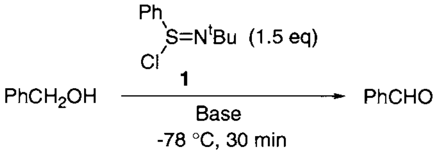


Table 1. Effect of bases and solvents in oxidation of benzyl alcohol to benzaldehyde by using **1**

Entry	Base (eq)	Solvent	Yield/%[a]
1	none	CH_2Cl_2	2 (21)
2	DBU (1.0)	CH_2Cl_2	65 (26)
3	DBU (2.0)	CH_2Cl_2	98 (-)
4	Et_3N (2.0)	CH_2Cl_2	57 (3)
5	pyridine (2.0)	CH_2Cl_2	6 (25)
6[b]	DBU (2.0)	toluene	76 (trace)
7[b]	DBU (2.0)	THF	69 (trace)
8[b]	DBU (2.0)	CH_3CN	88 (5)

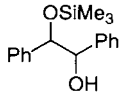
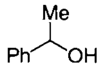
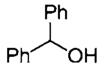
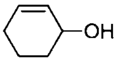
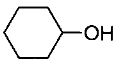
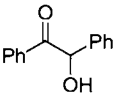
[a] Determined by GC analyses using an internal standard. Numbers in parentheses were yields of benzyl chloride. [b] The reaction temperature was 0 °C.

Oxidation of various alcohols other than benzyl alcohol was performed in excellent yields by using **1** and DBU in dichloromethane (Table 2). Benzylic and allylic alcohols were oxidized even at –78 °C and normal primary alcohols and secondary alcohols were oxidized at temperatures ranging from 0 °C to room temperature. Overoxidation to form carboxylic acids was not observed when primary alcohols were converted to aldehydes by using **1**. It is noted that in the present oxidation reaction, the reaction temperature is not necesssarily kept below –20 °C, because **1** is quite stable and no other competing reactions such as rearrangements occurred during the oxidation reaction. Interestingly enough, trimetylsilyloxy group was not cleaved under the present oxidation condition (entry 6) whereas dioxidized product was obtained by Swern oxidation, presumably because of the deprotection of the trimetylsilyloxy group with hydrogen chloride before the addition of triethylamine (cf., Scheme 1, eq 1). This result shows that the combination of **1** and DBU would also be useful for oxidation of acid-labile compounds.

Typical experimental procedure (Table 1, entry 3) is as follows: under an argon atmosphere, a solution of **1** (266 mg, 1.23 mmol) in CH_2Cl_2 (1.5 mL) was added to a mixture of benzyl alcohol (103 mg, 0.82 mmol), DBU (251 mg, 1.65 mmol) and CH_2Cl_2 (1.5 mL) at –78 °C. The yellow color of **1** disappeared immediately after the addition of **1**. The resulted colorless reaction mixture was stirred for 30 min at the same temperature and the reaction was quenched by adding 1% aqueous HCl (5 mL). The mixture was extracted with CH_2Cl_2 and the yield of benzaldehyde was determined by GC analysis using an internal standard (0.80 mmol, 98%).[7]

Thus, a novel and efficient method for oxidation of various kinds of alcohols by using **1** in the presence of DBU was explored. The oxidation reaction of alcohols would proceed via a mechanistically new intermediate, alkoxysulfilimine (**5**).[8] Further, this oxidation method has some advantages over Swern oxidation. (i) The oxidizing agent **1** is quite stable and can be used directly without any treatment. (ii) The reaction conditions are not required to be strictly controlled and the oxidation reaction can be conducted even at room temperature. (iii) The oxidation reaction is applicable to the oxidation of acid-labile compounds since the present reaction can be conducted under basic conditions.

Table 2. Oxidation of various alcohols to the corresponding carbonyl compounds by using **1** and DBU[a]

Entry	Alcohol	Conditions	Yield/%[b]
1	$PhCH_2OH$	-78 °C, 30 min	98
2	p-$MeOC_6H_4CH_2OH$	-78 °C, 30 min	90
3	$Ph(CH_2)_3OH$	0 °C, 30 min	94[c]
4	$CH_3(CH_2)_7OH$	rt, 30 min	98[c]
5	$BnO(CH_2)_{10}OH$	0 °C, 1 h	92[d]
6[e]		-78 °C, 30 min	91[d]
7		-78 °C, 30 min	93
8		-78 °C, 30 min	99[d]
9		-78 °C, 30 min	94
10		rt, 30 min	91
11		-78 °C, 30 min	92[d]

[a] Reaction conditions: **1** (1.5 eq), DBU (2.0 eq), in CH_2Cl_2. For details, see text. [b] Yields were determined by GC analyses unless otherwise noted. [c] Yields were determined after the derivatization to 2,4-dinitrophenylhydrazones. [d] Isolated yield. [e] The reaction was quenched with saturated aqueous $NaHCO_3$.

Further investigations on preparing more suitable *N*-alkyl sulfinimidoyl chlorides together with their application to the oxidation reaction are now in progress.

References and Notes

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6 ^1H NMR (270 MHz, $CDCl_3$, TMS) δ 1.58 (9H, s), 7.5–7.7 (3H, m), 8.1–8.2 (2H, m). ^{13}C NMR (67.5 MHz, $CDCl_3$) δ 29.53, 64.15, 125.91, 129.19, 133.17, 142.63. The sulfinimidoyl chloride **1** was decomposed at ca. above 160 °C. Markovskii et al. described that **1** was purified by crystallization in petroleum ether and ether (3 : 1) at –50 °C.[4]

7 The carbonyl compounds were isolated by silica gel-column chromatography. The major co-product was diphenyl disulfide.

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