Catalytic Oxidation of Various Alcohols to the Corresponding Carbonyl Compounds with *N*-Chlorosuccinimide Using a Catalytic Amount of Sulfenamide

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Various primary and secondary alcohols were smoothly oxidized to the corresponding carbonyl compounds with *N*-chlorosuccinimide by using a catalytic amount of *N*-*tert*-butylbenzenesulfenamide (**1**) in the co-existence of potassium carbonate and molecular sieves 4A.

It is an important and challenging topic to explore an efficient method for catalytic oxidation of primary and secondary alcohols to the corresponding carbonyl compounds since more than a stoichiometric amount of hazardous metals such as chromium are used in conventional oxidation reactions. Several catalytic oxidations of alcohols using transition metals have been reported to date, and TPAP-catalyzed oxidation[1] is the most popular one among them. On the other hand, Swern oxidation[2] is a useful stoichiometric oxidation method via an intermediate, chlorodimethylsulfonium chloride ($Me_2SCl^+Cl^-$). However, no catalytic methods for oxidation of alcohols via such sulfonium intermediates were reported. In this communication, we would like to report a novel, highly efficient, and widely applicable method for catalytic oxidation of alcohols to the corresponding carbonyl compounds with *N*-chlorosuccinimide (NCS) by using a catalytic amount of *N*-*tert*-butylbenzenesulfenamide (**1**) in the presence of potassium carbonate and molecular sieves 4A (MS4A).

In previous communications, there was shown that *N*-*tert*-butylphenylsulfinimidoyl chloride (**2**) smoothly oxidized various primary and secondary alcohols to the corresponding carbonyl compounds in the presence of DBU or zinc oxide.[3] The troublesome problem of this oxidation was that *N*-*tert*-butylbenzenesulfenamide (**1**), a reduced product of **2**, should be separated from the desired carbonyl compounds after the oxidation. It was then thought that in situ generation of **2** by oxidation of **1** using an appropriate chlorinating agent would enable **1**-catalyzed oxidation of alcohols, and thus the established catalytic reaction would provide a convenient method for oxidation of alcohols.

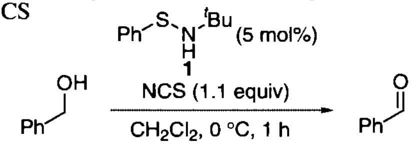
After screening several chlorinating agents such as NCS, *tert*-butyl hypochlorite, and chlorine for regeneration of **2** from **1**, NCS[4] was found to be the most promising chlorinating agent. It was observed that **1**[5] was oxidized with NCS to regenerate **2** along with succinimide by ^{1}H NMR measurement (in $CDCl_3$, rt).[6] Expectedly, benzyl alcohol was oxidized to benzaldehyde in 93% yield in the presence of DBU (2.0 equiv) with **2** generated from more than a stoichiometric amount of **1** (1.4 equiv) and NCS (1.5 equiv).

The above results prompted us to study in detail on the reaction conditions in order to establish catalytic oxidation of alcohols by using **1** and NCS (Table 1). Here, a choice of an appropriate base was very important: that is, the base (i) should be inert to NCS and (ii) can effectively trap HCl formed by the reaction of in situ formed **2** and alcohols. Several bases were examined by taking catalytic oxidation of benzyl alcohol using 5 mol% of **1** in the co-existence of 1.1 equiv of NCS as a model reaction. In the first place, DBU and diisopropylethylamine, which were successfully employed in previously reported oxidation of alcohols using **2**, were examined. Fortunately, DBU was found to work well as a base in the present **1**-catalyzed oxidation, and benzaldehyde was detected in 86% yield while diisopropylethylamine was not effective (Entries 1 and 2). In the above two reactions, slow addition of NCS was necessary since NCS was obviously consumed by the interaction with these amine bases in the reaction media.

Next, some solid bases were examined. Zinc oxide, a useful solid base in the stoichiometric oxidation using **2**, was found not to be effective in the present catalytic oxidation (Entry 3). On the other hand, dried potassium carbonate[7] gave a good result (90%) while other carbonate salts such as sodium and cesium carbonates did not (Entries 4–6). This catalytic oxidation of using potassium carbonate as a base was performed by a simple operation since the slow addition of NCS was not necessary in this case.

Further, the addition of dehydrating agents[7] such as molecular sieves or Drierite® improved the yield of benzaldehyde up to 98% when potassium carbonate was used as a base (Entries 7–10). The use of anhydrous sodium sulfate or magnesium sulfate did not affect the **1**-catalyzed oxidation (Entry 11 and 12).

Table 1. Catalytic oxidation of benzyl alcohol by using **1** and NCS



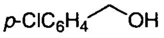
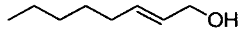
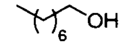
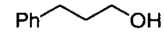
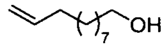
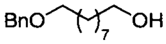
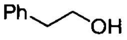
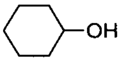
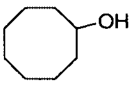
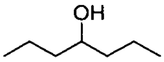
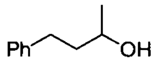
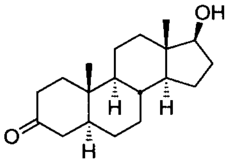
Entry	Base (equiv)	Dehydrating agent	Yield/%[a]
1[b]	DBU (1.1)	–	86
2[b]	^{i}Pr$_2$NEt (1.1)	–	35
3	ZnO (5)	–	24
4	Na_2CO_3 (10)	–	56
5	K_2CO_3 (10)	–	90
6	Cs_2CO_3 (10)	–	44
7	K_2CO_3 (10)	MS3A (1 g/mmol)	97
8	K_2CO_3 (10)	MS4A (1 g/mmol)	98 (<1)[c]
9	K_2CO_3 (10)	MS5A (1 g/mmol)	95
10	K_2CO_3 (10)	Drierite® (1 g/mmol)	94
11[d]	K_2CO_3 (10)	Na_2SO_4 (10 equiv)	91
12[d]	K_2CO_3 (10)	$MgSO_4$ (10 equiv)	88

[a] Determined by GC-analysis using an internal standard. [b] A solution of NCS in CH_2Cl_2 was added during 15 min. [c] In the absence of **1**. [d] The reaction time was 2 h.

It was shown that the catalyst **1** played a very important role in this oxidation since only less than 1% of benzaldehyde was detected in the absence of **1** (Entry 8).

Various primary and secondary alcohols were smoothly oxidized to the corresponding carbonyl compounds in high yields with NCS by using 5 mol% of **1** in the coexistence of potassium carbonate and MS4A as shown in Table 2. It is noted that the present catalytic oxidation proceeded under rather mild conditions because 2-phenylethanol was quantitatively oxidized to phenylacetaldehyde (Entry 7).[3b] Moreover, formed carbonyl compounds were easily isolated by preparative thin-layer chromatography (Entries 6 and 12).

Table 2. Catalytic oxidation of various alcohols[a]

Entry	Alcohol	Conditions	Yield/%[b]
1		0 °C, 1 h	93
2		0 °C, 1 h	>99
3		rt, 1 h	94
4		rt, 1 h	95
5		rt, 30 min	>99
6		rt, 1 h	93[c]
7		0 °C, 1 h	>99
8		rt, 1 h	93
9		rt, 1 h	99
10		rt, 1 h	>99
11		rt, 1 h	96
12		rt, 1 h	96[c]

[a] **1** (5 mol%), NCS (1.1 equiv), K_2CO_3 (10 equiv), MS4A (1 g/mmol) in CH_2Cl_2. [b] Determined by GC-analysis using an internal standard unless otherwise noted. [c] Isolated yield.

A proposed catalytic cycle is shown in Figure 1. The catalyst **1** was oxidized with NCS to generate sulfinimidoyl chloride **2** and succinimide as described above. The formed oxidizing agent **2** reacted with alcohols in the presence of potassium carbonate to afford alkoxysulfilimine (**3**), a key intermediate of oxidation, which decomposed to carbonyl compounds along with the catalyst **1**. Thus, a catalytic cycle was effectively established.

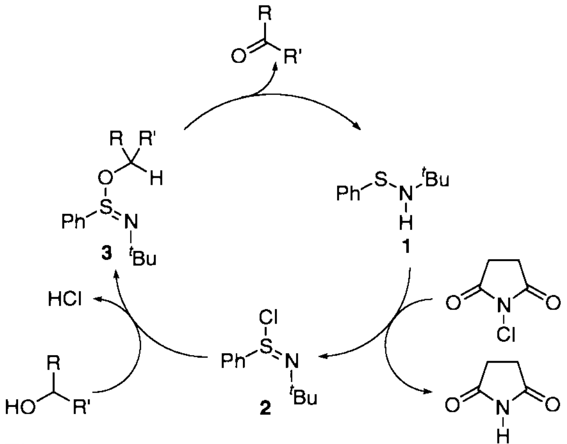


Figure 1.

General experimental procedure (Table 1, Entry 8) is as follows: to a stirred suspension of MS4A[7] (500 mg), K_2CO_3[7] (691 mg, 5.0 mmol), and NCS (73.4 mg, 0.55 mmol) in CH_2Cl_2 (1 mL) were successively added a solution of benzyl alcohol (54.1 mg, 0.50 mmol) in CH_2Cl_2 (1.5 mL) and a solution of **1**[5] (4.5 mg, 25 μmol) in CH_2Cl_2 (1.5 mL) at 0 °C. After the reaction mixture was kept stirring at the same temperature for an additional hour, it was quenched by adding H_2O. The resulting mixture was filtered through Celite-pad, and the filtrate was extracted with CH_2Cl_2. The yield of benzaldehyde (98%) was determined by GC-analysis using naphthalene as an internal standard.

Reaction conditions presented here were not yet sufficiently optimized, and studies on scope and limitations of the **1**-catalyzed oxidation are now in progress.

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References and Notes

1 TPAP: tetrapropylammonium perruthenate. W. P. Griffith, S. V. Ley, G. P. Whitcombe, and A. D. White, *J. Chem. Soc., Chem. Commun.*, **1987**, 1625.

2 A. J. Mancuso and D. Swern, *Synthesis*, **1981**, 165.

3 a) T. Mukaiyama, J. Matsuo, and M. Yanagisawa, *Chem. Lett.*, **2000**, 1072. b) J. Matsuo, H. Kitagawa, D. Iida, and T. Mukaiyama, *Chem. Lett.*, **2001**, 150.

4 a) E. J. Corey and C. U. Kim, *J. Am. Chem. Soc.*, **94**, 7586 (1972). b) T. Mukaiyama, M. Tsunoda, and K. Saigo, *Chem. Lett.*, **1975**, 691.

5 The catalyst, *N*-*tert*-butylbenzenesulfenamide (**1**),[5a] was prepared from benzenesulfenyl chloride[5b] and *tert*-butylamine. See: a) Y. Miura, H. Asada, and M. Kinoshita, *Bull. Chem. Soc. Jpn.*, **50**, 1855 (1977). b) A. G. M. Barrett, D. Dhanak, G. G. Graboski, and S. J. Taylor, *Org. Synth.*, **68**, 8 (1990).

6 In the case of *N*,*N*-dialkylsulfenamides, alkylamino-succinimidosulfonium chlorides were obtained on treatment with NCS. See: M. Haake and H. Benack, *Synthesis*, **1976**, 308.

7 Powdered potassium carbonate was dried *in vacuo* by heating it with a heat-gun. Molecular sieves and Drierite® were also dried *in vacuo* at 250 °C for 12 h.