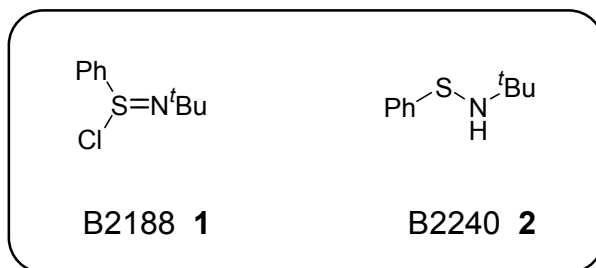
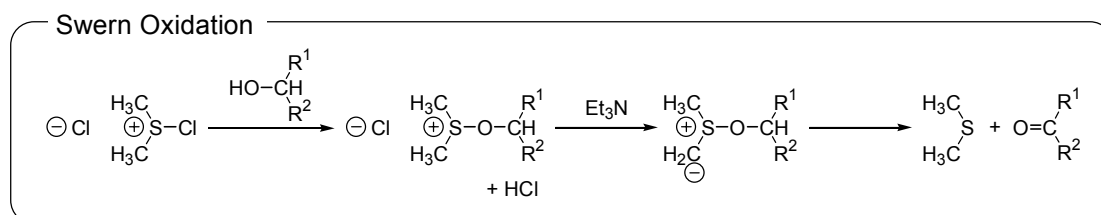


New Oxidation of Primary & Secondary Alcohols



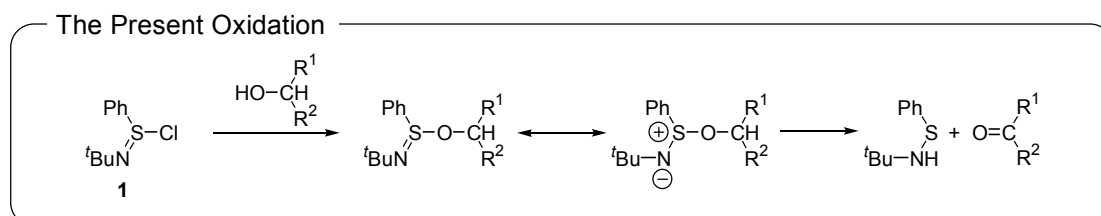
Mukaiyama and co-workers have reported the oxidation of alcohols to aldehydes or ketones, using *N*-*tert*-butylbenzenesulfinimidoyl chloride and *N*-*tert*-butylbenzenesulfenamide. The former is used as a stoichiometric oxidizing agent and the latter is used as an oxidizing catalyst. Both compounds yield aldehydes or ketones with high chemical selectivity and high yield.

Oxidation reactions of primary and secondary alcohols to their corresponding aldehydes and ketones are one of the most important reactions in organic synthesis. Many oxidizing agents utilizing chromium oxides such as Jones reagent, Sarett reagent, and Collins reagent, as well as those utilizing hypervalent organoiodane, such as the Dess-Martin periodinane have been developed. In addition to these oxidizing agents, the Swern oxidation, which uses DMSO activated with oxalyl chloride, is widely used and considered one of the most practical oxidation procedures.



The Swern oxidation is known as an excellent oxidation method since highly toxic chromium oxides and explosive hypervalent organoiodanes are not used. However, the reaction temperature must be strictly controlled below -20°C , due to the thermal instability of the activated intermediates formed by the reaction of DMSO and oxalyl chloride. Furthermore, because the byproduct, dimethyl sulfide, has a stench, it is considered to be unsuitable for mass production.

In 2000, Mukaiyama and co-workers reported the oxidation of alcohols using sulfinimidoyl compound **1**. According to that, **1**, having similar structure to activated DMSO, oxidized primary or secondary alcohols to the corresponding aldehydes or ketones almost quantitatively under mild conditions in the presence of a base.¹⁾ Significantly, the reaction with primary alcohols affords only aldehydes, and does not produce carboxylic acids as byproducts.

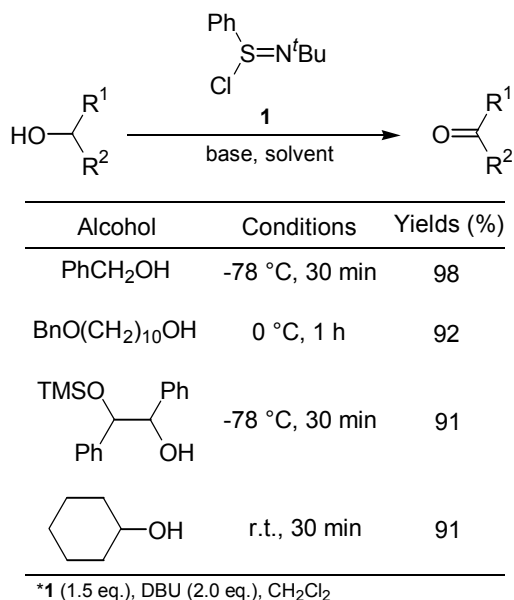


Keywords : oxidizing agents, oxidation of primary & secondary alcohols

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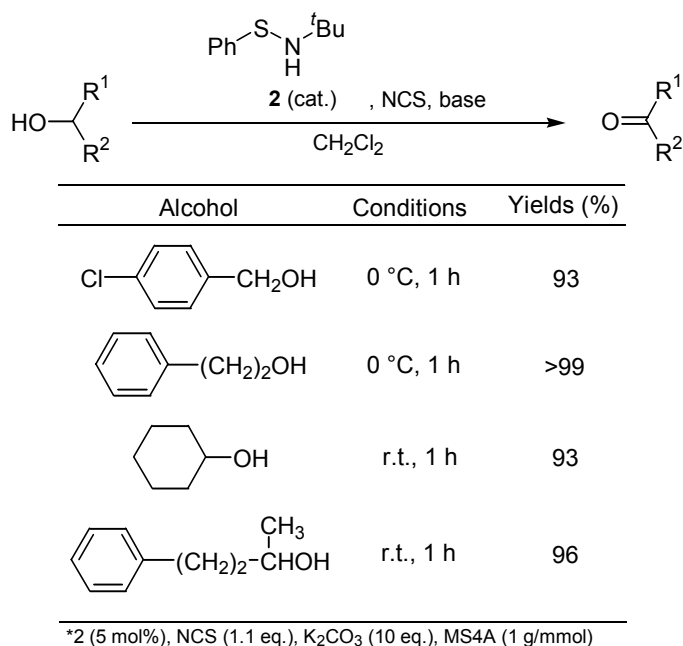
Unlike the Swern oxidation, the oxidations using **1** do not require activation or strict control of reaction temperature. Solvents such as toluene, THF, acetonitrile, DMF, and dichloromethane can also be used for oxidations using **1**. This oxidation reaction is also applicable to the oxidation of acid labile compounds, since the reaction proceeds under basic conditions. A typical reaction example is shown below.

Table 1. Stoichiometric oxidation of various alcohols by using **1**.



The catalytic oxidation of alcohols to aldehydes or ketones has also been explored. To date, oxidation methods using tetrapropylammonium perruthenate (TPAP) and 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO) as a catalyst have been reported and put into practical use. The oxidation of alcohols reported in 2001 by Mukaiyama and co-workers using catalytic amounts of sulfenamide **2** is a new catalytic oxidation method. In this method, *N*-chlorosuccinimide (NCS) is used as a co-oxidant to yield the corresponding aldehydes and ketones from primary and secondary alcohols.²⁾ Compared with TPAP, which has been reported as an explosion hazard, and TEMPO, which requires strict temperature control, this procedure is a safe and convenient method for the catalytic oxidation of alcohols. An example of this method is shown below.

Table 2. Catalytic oxidation of various alcohols by using **2**.



The catalytic cycle of **2** using NCS as a co-oxidant is considered to be as follows. First, catalyst **2** is oxidized by NCS and generates **1** in the reaction system. Next, **1** reacts with alcohols and generates carbonyl compounds, via the intermediate **3**. Catalyst **2** is regenerated at the same time and the catalytic cycle continues.

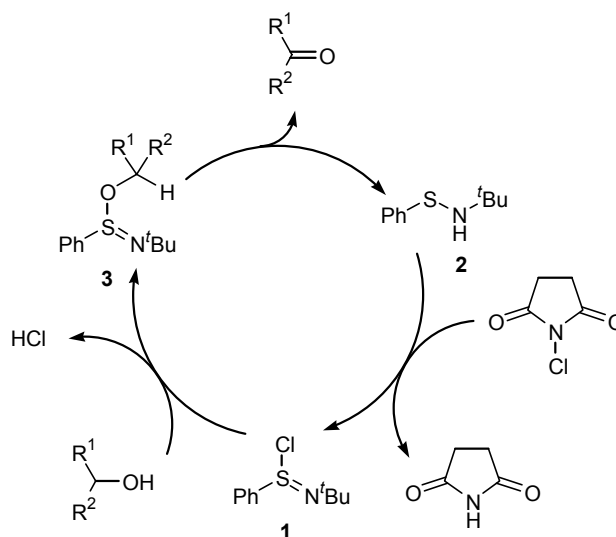
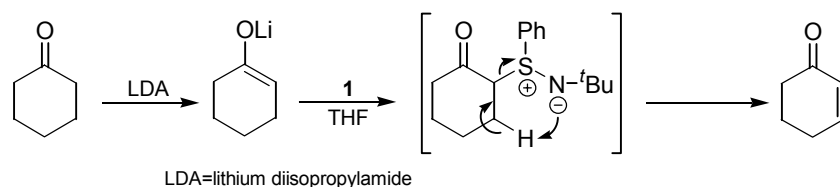


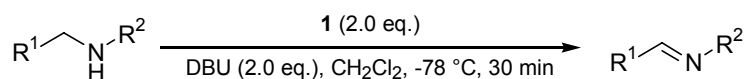
Fig. 1 Catalytic cycle of **2**.

Many applications have been reported using **1** other than the oxidation of alcohols. For example, **1** reacts with ketones and carboxylates treated with LDA to produce the corresponding α,β -unsaturated ketones and carbonyl compounds.³⁾ When the reaction is run with acyclic ketones, only the (*E*)-form is produced.



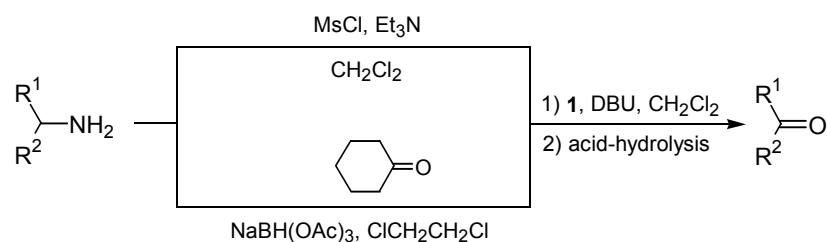
Scheme 1

In addition, **1** reacts with secondary amines to afford the corresponding imines under the same reaction conditions as the oxidation of alcohols.⁴⁾



Scheme 2

The reaction of **1** with primary amines affords aldehydes or ketones. After *N*-mesylation or *N*-cyclohexylation, **1** can react with primary amines. After an acidic hydrolysis, the corresponding carbonyl compounds are obtained.⁵⁾



Scheme 3

As mentioned above, reactions using **1** and **2** do not require the use of highly toxic chromium oxides or explosive hypervalent organoiodanes. Reactions using **1** and **2** are safe, easy, and environmentally friendly oxidation methods, and their broad future application is expected.

B2188	<i>N-tert</i> -Butylbenzenesulfinimidoyl Chloride	(1)	5g	1g
B2240	<i>N-tert</i> -Butylbenzenesulfenamide	(2)	25g	5g

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