Polymer-supported Sulfinimidoyl Chloride as a Useful Reagent for Oxidation of Various Alcohols to the Corresponding Carbonyl Compounds

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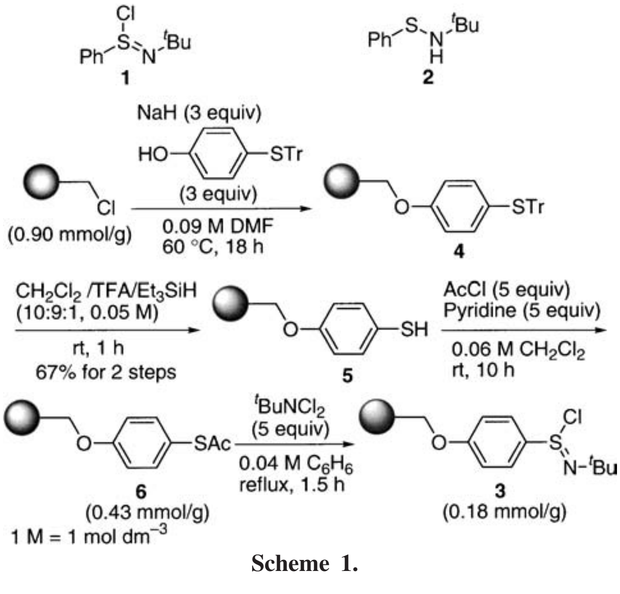
Polymer-supported sulfinimidoyl chloride was prepared in four steps from chloromethyl polystyrene resin. Stoichiometric and catalytic oxidations of various alcohols to the corresponding carbonyl compounds were carried out cleanly by using the prepared polymer-bound oxidant.

Since *N*-*t*-butylbenzenesulfinimidoyl chloride (**1**) was first introduced as an effective oxidizing agent for alcohols to carbonyl compounds,[1] it has been found to be useful also in other oxidation reactions: for example, oxidation of amines to imines,[2] oxidation of hydroxylamines to nitrones,[3] and one-pot dehydrogenation of saturated ketones to α,β-unsaturated ones.[4] However, *N*-*t*-butylbenzenesulfenamide (**2**), a reduced form of **1**, had to be separated by column chromatography after the above-mentioned oxidation reactions of using more than stoichiometric amounts of **1**. Therefore, two approaches were considered to improve the troublesome work-up procedures: one was a development of catalytic oxidation of alcohols by using a catalytic amount of sulfenamide **2**, and the other was that of a polymer-supported sulfinimidoyl chloride. Recently, the former was established by using *N*-chlorosuccinimide (NCS) as a co-oxidant in the presence of potassium carbonate.[5] In this communication, we would like to describe on the latter subject which consisted of i) preparation of polymer-supported sulfinimidoyl chloride **3**, ii) stoichiometric oxidation of various alcohols by using **3**, and iii) **3**-catalyzed oxidation of alcohols with *N*-chlorosuccinimide.

Scheme 1 shows preparation of polymer-supported oxidizing agent[6] **3** which has the sulfinimidoyl chloride group at its termini. Polymer-supported arylthiol **5**[7] was prepared from chloromethyl polystyrene resin[8] according to the reported procedure,[9] and the loading of the arylthiol group was determined by isolation of triphenylmethane formed after deprotection of **4**.[7] The free thiol group of thus prepared **5** was acetylated with acetyl chloride and pyridine to give aryl thioacetate **6**.[7] The loading (0.43 mmol/g) of the thioacetate group was determined by isolation of 0.43 mmol of *N*-benzylacetamide after treating 1 g of **6** with 1.8 mmol of benzylamine in refluxing 1,2-dichloroethane for 6 h. The bright yellow polymer-supported oxidizing agent **3**[7] was obtained by the reaction of **6** and *N*,*N*-dichloro-*t*-butylamine according to the procedure for the preparation of **1**,[1a] followed by washing the resin with dry dichloromethane and drying it in vacuo at 60 °C for 1 h. The substantial loading (0.18 mmol/g) of the sulfinimidoyl chloride group[10] was determined by detecting *p*-methoxybenzylchloride (0.18 mmol) by GC-analysis after treating **3** (1 g) with *p*-methoxybenzylalcohol (0.5 mmol) in dichloromethane at room temperature for 2 h. The polymer-supported oxidizing agent **3** was stable at room temperature in a sealed bottle under an inert gas.[11] Its oxidizing ability did not change after keeping **3** at room temperature for eight days.



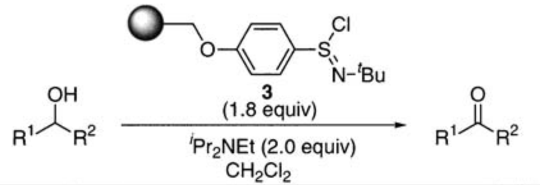
Scheme 1.

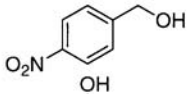
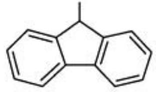
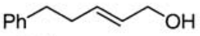
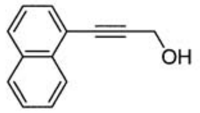
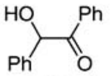
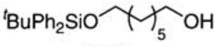
Stoichiometric oxidation of various primary and secondary alcohols to the corresponding aldehydes and ketones was performed by using **3** and ethyldiisopropylamine[12] (Table 1). Oxidation of benzylic and allylic alcohols proceeded smoothly at −78 °C within 30 min by adding the mixture of alcohol and ethyldiisopropylamine to the oxidizing agent **3** (Table 1, entries 1–4, Method A). On the other hand, for the efficient oxidation of aliphatic primary and secondary alcohols, it was necessary to add ethyldiisopropylamine to the premixed slurry of alcohol and **3** at −78 °C (Table 1, entries 6–8, Method B). In the above oxidation of using **3**, undesirable co-products were not detected after the reaction and it obviously simplified the work-up procedures.

Typical experimental procedure for the stoichiometric oxidation of alcohol with **3** is as follows (Table 1, entry 1): to a slurry of **3** (0.18 mmol/g, 1.0 g, 0.18 mmol) in CH_2Cl_2 (10 mL) was added a mixture of *p*-nitrobenzylalcohol (15.3 mg, 0.10 mmol) and ethyldiisopropylamine (25.8 mg, 0.20 mmol) in CH_2Cl_2 (2 mL) at −78 °C. The reaction mixture was stirred at −78 °C for 30 min, and the reaction was quenched by adding H_2O (2 mL). The mixture was filtered through Celite pad, and filtrate was extracted with CH_2Cl_2. The combined organic extracts were washed with H_2O and brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The crude product was purified by preparative TLC to afford *p*-nitrobenzaldehyde (14.8 mg, 98%).

Two successive synthetic reactions composed of alcohol-oxidation and carbon-carbon bond formation, which were often operated in organic synthesis, were efficiently carried out by the **3**-mediated oxidation because an oxidation product was obtained just by filtering the reaction mixture. Indeed, oxidation of *p*-nitrobenzylalcohol and BF_3-catalyzed aldol reaction of thus

Table 1. Oxidation of various alcohols to the corresponding carbonyl compounds by using polymer-supported sulfinimidoyl chloride **3**



Entry	Alcohol	Conditions[a]	Yield/%[b]
1		A, –78 °C, 30 min	98
2		A, –78 °C, 30 min	89
3		A, –78 °C, 30 min	84[c]
4		A, –78 °C, 30 min	80
5		A, –78 °C, 30 min	90
6		B, –78 °C ~ rt, 30 min	89
7		B, –78 °C ~ rt, 30 min	85
8		B, –78 °C ~ rt, 30 min	81

[a] Method A: a mixture of alcohol and ^{i}Pr$_2$NEt was added to the swelled polymer **3** in CH$_2$Cl$_2$ at –78 °C. Method B: alcohol was added to the swelled polymer **3** in CH$_2$Cl$_2$ at 0 °C then ^{i}Pr$_2$NEt was added at –78 °C. [b] Isolated yield. [c] The stereo isomeric ratio (E/Z = 96/4) did not change by the present oxidation.

obtained aldehyde with trimethylsilyl enol ether of acetophenone were conveniently carried to give the desired aldol product in 86% isolated yield for two steps.

Further, catalytic oxidation of alcohols was performed by using 20 mol% of the polymer-supported oxidizing agent **3** and two equivalents of NCS. As shown in Table 2, benzylic alcohols and primary and secondary aliphatic alcohols were readily oxidized to the corresponding aldehydes and ketones. It was found there that ethyldiisopropylamine was a suitable base for the catalytic oxidation of benzylic alcohols[13] while potassium carbonate was preferred for that of aliphatic primary and secondary alcohols.[14] Even when the amount of the catalyst **3** was reduced to 10 mol%, the catalytic oxidation of benzylalcohol proceeded smoothly and benzaldehyde was detected in 91% yield by GC-analysis (Table 2, entry 1).

Thus, it was noted that the new polymer-supported sulfinimidoyl chloride **3** was a convenient reagent for oxidation of alcohols, and can be applied to other oxidation reactions which were successfully conducted by **1**, and in flow-through organic synthesis systems.

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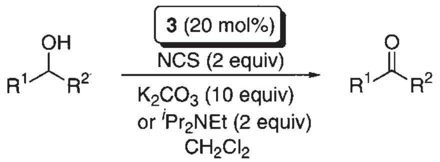
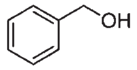
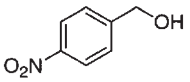
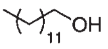
Table 2. The **3**-catalyzed oxidation of various alcohols to the corresponding carbonyl compounds with NCS



Entry	Alcohol	Reaction conditions[a]	Yield/%[b]
1[c]		^{i}Pr$_2$NEt (2 equiv), 0 °C, 1 h	94, 91[d]
2		^{i}Pr$_2$NEt (2 equiv), rt, 1 h	92
3		K$_2$CO$_3$ (10 equiv), MS4A (1 g/mmol), rt, 5 h	85
4		K$_2$CO$_3$ (10 equiv), MS4A (1 g/mmol), rt, 20 h	83

[a] Base, (dehydrating agent), temperature, reaction time. [b] Isolated yield except entry 1. [c] Yields were determined by GC-analysis by using an internal standard. [d] 10 mol% of **3** was used and the reaction time was 2 h.

References and Notes

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5 T. Mukaiyama, J. Matsuo, D. Iida, and H. Kitagawa, *Chem. Lett.*, **2001**, 846.

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7 IR (KBr, cm^{-1}) **3**: 1203, 1108, 687; **4**: 1227, 687; **5**: 2561, 1200, 687; **6**: 1759, 1705, 1195, 687.

8 The resin used (cross-linked with 1% divinylbenzene) was purchased from Tokyo Kasei Kogyo.

9 J. R. Horton, L. M. Stamp, and A. Routledge, *Tetrahedron Lett.*, **41**, 9181 (2000).

10 Treatment of **1** with *p*-methoxybenzylalcohol under the same reaction conditions gave *p*-methoxybenzylchloride in 75% yield. Neither chloride-titration nor elemental analysis of **3** gave a reliable loading of the sulfinimidoyl chloride group.

11 The resin **3** should be handled under strictly anhydrous conditions because of its low loading.

12 In addition to benzaldehyde, a little amount of benzylchloride was detected when DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) or potassium carbonate was used as a base in the oxidation of benzylalcohol.

13 The mixture of the alcohol and ethyldiisopropylamine in CH$_2$Cl$_2$ was added to the slurry of **3** in CH$_2$Cl$_2$ at −78 °C, followed by the rapid addition of NCS in CH$_2$Cl$_2$ at 0 °C.

14 Alcohol was added to the suspension of **3**, K$_2$CO$_3$, and MS4A in CH$_2$Cl$_2$ at room temperature.