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Oxidative Deprotection of Benzylic Silyl Ethers to Their Corresponding Carbonyl Compounds Using Nitrogen Dioxide Gas

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Abstract

Oxidative deprotection of benzylic silyl ethers has been carried out using nitrogen dioxide gas to the corresponding aldehydes and ketones in quantitative yields.

Introduction

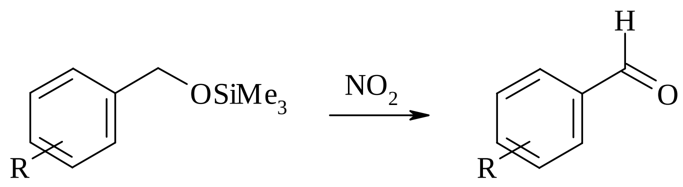
Selective protection and deprotection of functional groups is important in organic synthesis. Hydroxy group is one of the most abundant functional groups in organic molecules and its protection is important in multi-step synthesis. As a consequence, conversion of the hydroxy group to silyl ether is one of the most useful and convenient methods for the protection of this functional group.[1,2] Direct oxidation of silyl ethers to the corresponding carbonyl compounds has found considerable attention during recent years. The reported methods include $Fe(NO_3)_3.3/2N_2O_4$ and $Cu(NO_3)_2.N_2O_4$,[3] 2,3-dicholoro-5,6-dicyanoquinone (DDQ),[4,5] strontium manganate ($SrMnO_4$) in the presence of $AlCl_3$,[6] tetrabutylammonium periodate (TBAPI) in the presence of $AlCl_3$ and BF_3,[7] Bis[trinitratocerium(IV)]chromate[$(NO_3)_3Ce]_2CrO_4$,[8] ceric ammonium nitrate (CAN),[9] N-bromosuccinimide (NBS),[10] potassium permanganate ($KMnO_4$) and barium manganate ($BaMnO_4$) in the presence of Lewis acids,[11] Jones reagent (CrO_3/H_2SO_4/acetone),[12-14] Collins reagent (CrO_3.2py),[15] pyridinium chlorochromate (PCC),[16,17] $[PhCH_2NMe_2Ph]_2S_2O_8$,[18] Magtrieve™ (CrO_2),[19] dinitrogen tetroxide-impregnated activated charcoal (N_2O_4/Charcoal),[20] cetyltrimethylammonium peroxodisulfate $(CTA)_2S_2O_8$,[21] trinitratocerium(IV) bromate (TNCB) supported on $NaHSO_4$,[22] 4-aminobenzoic acid supported on silica gel,[23] and silica gel supported on Dess-Martin periodinane.[24] However, some of the reported methods show limitations such as the use of expensive reagents or dangerous procedure for their preparation,[8] long reaction times,[15] low yields of the products, and tedious work-up.[15-17] Therefore, the introduction of new methods and inexpensiv reagents for the transformation of this functional group is still in demand.

A solvent-free process at ambient pressure with the gaseous NO_2 to give high yield of the product and with easy separation of the products for further use is certainly superior. We report herein the specific oxidations of benzylic silyl ethers which gives high yield of the corresponding carbonyl compounds in quantitative yields.

Results and Discussion

a) Oxidative deprotection of silyl ethers to carbonyl compounds

Gaseous NO_2/N_2O_4 is a new, rapid and efficient reagent that can be used for the oxidative deprotection of benzylic silyl ethers to the corresponding aldehydes under ambient temperature (**Scheme 1**).



1 **2**

Scheme 1

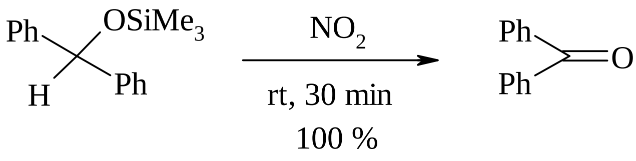
No particular precautions were necessary if 1 mmol of **1a–f** was exposed to 0.6 bar NO_2/N_2O_4 gas in an evacuated 100 mL flask (about 5.8 mmol calculated for NO_2) at room temperature with occasional shaking. The initial liquids took up the brown gas and changed their colors rapidly. The pure benzaldehydes were produced within 5 to 60 min depending on the substitution pattern, which determines the reactivity, viscosity, and rate of dissolution of NO_2 in **1**. After evacuation of the reaction gas mixture, all solid benzaldehydes afforded pure crystals. The purity of the aldehydes **2** was verified by thin layer chromatography (TLC) and by melting-point determinations of the solid aldehydes (Table 1). Furthermore, FT-IR and ^1H NMR spectroscopy revealed no traces of the corresponding benzoic acids or aromatic nitro compounds.[25] The results have been summarized in **Table 1**.

Substrates **1a–c,** and **1e** are highly reactive, but the marked decrease in the reactivity of the methoxy derivatives such as **1d** has to be attributed to the well-known complexing ability of the anisoyl group that weakens the reactivity of NO_2. The decreased reactivity of **1e** may be due to steric reasons.

Table 1. Oxidation of benzylic silyl ethers **1** with NO_2/N_2O_4 to give benzaldehydes **2**.

Entry	R	t (min)	Temp. (°C)	Yield (%)	m.p. (°C)
1a	H	5	25	100	liq.
1b	*o*-Me	5	25	100	liq.
1c	*p*-Me	5	25	100	liq.
1d	3,4-dimethoxy	10	25	100	45
1e	*o*-Cl	60	25	100	12
1f	*p*-Cl	5	25	100	47

Also the protected secondary alcohols such as benzhydrol were oxidized by NO_2 to give the corresponding ketone (**Scheme 2**).

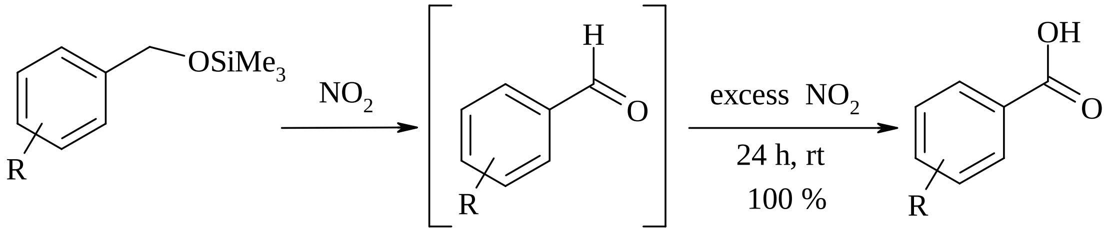


3 **4**

Scheme 2

b) Oxidative deprotection of silyl ethers to benzoic acids

The reasons quoted for further oxidations require further scrutiny by experiments with the silyl ethers. It is indeed possible to quantitatively oxidize the silyl ethers directly to benzoic acids with excess NO_2 gas within 24 h and at room temperature (**Scheme 3**).



Scheme 3. Quantitative oxidation of silyl ethers with excess NO_2 gas.

All of the benzylic silyl ethers **1a-f** as in Table 1 were successfully transformed to their carboxylic acids with quantitative yields.

Conclusion

We have acheived a green and sustainable method for the producing of carbonyl compounds from their silyl ether derivatives. There are no residues from the oxidant in the solvent-free chemospecific process, and the quantitatively obtained products are immediately pure upon vacuum treatment. No solvents or adsorbents are required for waste-producing purification procedures of the products.

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