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Chlorination of Alcohols Using Potassium Chromate-based Chlorotrimethylsilane

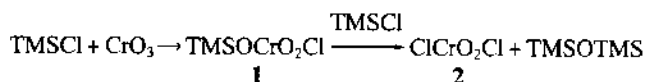
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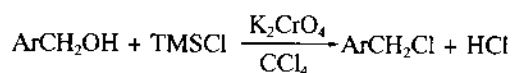
Halogenation¹ is one of the most important functional group transformations in organic chemistry. Recently, halosilanes were found to be useful for halogenation of alcohols. In general, use of chlorotrimethylsilane fails to produce alkyl chlorides. There have been only a few reports² on the use of chlorotrimethylsilane for the preparation of alkyl chlorides. Chlorotrimethylsilane^{2a} alone was known to transform some cyclopropyl alcohols into cyclopropyl chlorides, but it failed to produce chlorides from other alcohols. Potassium carbonate,³ bismuth(III) chloride,⁴ selenium dioxide,⁵ tellurium dioxide,⁶ and manganese dioxide⁷ were known to activate the chlorinating power of chlorotrimethylsilane. Chlorotrimethylsilane⁸ catalyzed by dimethyl sulfoxide was known to convert primary and tertiary alcohols to the corresponding chlorides. Bromotrimethylsilane⁹ needs a higher temperature to react with alcohols to produce alkyl bromides. Iodotrimethylsilane¹⁰ also converts alcohols to alkyl iodides under mild reaction conditions. Silicon tetrachloride¹¹ can convert alcohols to the corresponding chlorides at high temperature, although this is limited to more reactive alcohols. Potassium carbonate^{3a} and manganese dioxide⁷ were known to catalyze chlorination of alcohols using silicon tetrachloride.

In connection with the continued research for the insertion reaction of inorganic compounds to reactive silicon-halogen bond, we reported some valuable reactions for the oxidation of toluenes,¹² alcohols¹³ and olefins¹⁴ and chlorinations of alcohols.^{3a,6,7} Palomo and Aizpurua¹⁵ suggested that there would be formed an insertion product from the reaction of chromic anhydride and chlorotrimethylsilane. That is, a simple insertion of chromic anhydride into reactive silicon-chlorine bond of chlorotrimethylsilane would produce trimethylsilylchlorochromate (1)¹⁵ which Palomo *et al.* proposed as an active oxidant. There is no ground for formation of insertion product, however. We think that Palomo's hypothesis about formation of insertion product is less likely by consideration of our results.¹² We postulated that this very unstable trimethylsilylchlorochromate decomposes rapidly into chromyl chloride (2), along with the formation of hexamethyldisiloxane. Anyway, this reagent¹⁵ was proved to

be efficient for the oxidation of secondary alcohols to ketones, thiols to disulfides, and oximes to the corresponding carbonyl compounds. In the courses of exploring the broad applications of this reagent in organic synthesis, we found that the reagent also appeared to be useful for chlorinations of alcohols. In this paper, we wish to describe another convenient and interesting method which effects such chlorination of alcohols using potassium chromate and chlorotrimethylsilane.¹⁶



Some examples of results of the chlorination using chlorotrimethylsilane are summarized in Table 1. Benzyl alcohol and most of substituted benzyl alcohols such as 4-methylbenzyl alcohol, 2- and 4-methoxybenzyl alcohol, 4-chlorobenzyl alcohol, and 3-nitrobenzyl alcohol were chlorinated efficiently without competing side reactions such as oxidation. 1-Phenyl-1-propanol showed slightly different pattern. Primary alcohols containing 1-octanol and neopentyl alcohol were also chlorinated easily. Neopentyl chloride was obtained in moderate yield from the reaction of neopentyl alcohol without any skeletal rearrangement.



Most of secondary alcohols such as 2-hexanol, 4-heptanol and 2-octanol and cyclic alcohols such as cyclohexanol and menthol were also converted into the corresponding alkyl chlorides smoothly without side reactions such as skeletal migration or elimination. For example, 2-chlorooctane and menthyl chloride were obtained from 2-octanol and menthol in moderate yield. These results were different from that of reactions of thionyl chloride which is known to produce 2-chlorooctane in very low yield due to the competing elimination or migration.¹⁷ In addition to, borneol, which is very prone to skeletal migration, was found to be chlorinated

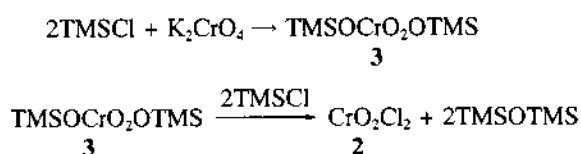
Table 1. Potassium Chromate-Based Chlorination of Alcohols with Chlorotrimethylsilane at Room Temperature

Reactant	Reaction Time (hr.)	Product	Yield ^a (%)
Benzyl alcohol	2	Benzyl chloride	97
4-Methylbenzyl alcohol	3.3	4-Methylbenzyl chloride	98
2-Methoxybenzyl alcohol	2	2-Methoxybenzyl chloride	92
4-Methoxybenzyl alcohol	2	4-Methoxybenzyl chloride	97
4-Chlorobenzyl alcohol	3.3	4-Chlorobenzyl chloride	97
3-Nitrobenzyl alcohol	2.7	3-Nitrobenzyl chloride	90
1-Phenyl-1-propanol	3.3	1-Phenyl-1-chloropropane	60
1-Octanol	2.7	1-Chlorooctane	60
Neopentyl alcohol	2.3	Neopentyl chloride	76
2-Hexanol	3.3	2-Chlorohexane	70
4-Heptanol	2.7	4-Chloroheptane	75
2-Octanol	3	2-Chlorooctane	75
Menthol	2.7	Menthyl chloride	60
Cyclohexanol	2.3	Chlorocyclohexane	65
Cinnamyl alcohol	2	Cinnamyl chloride	97
Borneol	3.3	Bornyl chloride	80
tert-Butyl alcohol	2.7	tert-Butyl chloride	86

^a Isolated yields.

without any skeletal migration.¹⁸ Conversion of tertiary alcohols into corresponding chlorides was appeared to have some problems due to competing elimination. Few examples of chlorinations using thionyl chloride have been reported. Allylic alcohol such as *trans*-cinnamyl alcohol also produced effectively allylic chloride at room temperature without any side reactions.

The chemical reaction between chlorotrimethylsilane and potassium chromate leading to the effective chlorinating agent is not clear yet. The first step of the reaction could be the formation of bistrimethylsilylchromate(3)¹⁹ in an equilibrium concentration from the reaction of two equivalents of chlorotrimethylsilane and potassium chromate. Further reaction of bistrimethylsilylchromate with another two equivalents of chlorotrimethylsilane would remove the trimethylsiloxy group of bistrimethylsilylchromate as hexamethyldisiloxane. This could result in temporarily formation of chromyl chloride(2). However, the exact pattern of this decomposition has not been completely understood yet.



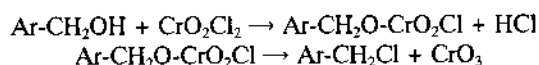
This type of replacement of trimethylsiloxy group¹² with chlorine atom to form chlorine-heteroatom bonds were observed for the reactions of TMS esters of chromate,²² and chlorochromate,¹² selenite,⁵ nitrite and nitrate,²⁰ and chlorate.²¹ From these reactions, corresponding chromyl chloride, selenium oxychloride, nitrosyl and nityl chloride, dichlorine dioxide were postulated to be formed, respectively.

The crude NMR spectrum of this reagent prepared *in situ* after stirring for 2 hours at room temperature showed only two types of singlet due to the methyl protons of excess chlorotrimethylsilane and hexamethyldisiloxane. No NMR peak other than these two types of protons was observed.

This means that bistrimethylsilylchromate can exist only as a transient species in this reaction condition. The ratio of methyl protons of chlorotrimethylsilane and hexamethyldisiloxane did not vary on standing for 2-3 days or on heating the mixture for several hours. All these steps are believed to be reversible and are in equilibrium. Thus actual chlorinating species is likely chromyl chloride, although chlorinations using chromyl chloride could not find in literature as we know.

Chromyl chloride²² itself is a powerful oxidant for converting alkenes to aldehydes, oxiranes, ketones, chlorohydrins, α -chloroketones, vicinal-chloroacetates, and α -hydroxy ketones, and for oxidizing alkylaromatics to alcohols, aldehydes (Etard reaction), and ketones. Chromyl chloride oxidizes phenols to quinones and coupling products. Chromyl chloride is used to prepare di-*tert*-butyl chromate, *tert*-butyl chromate-tri-pyridine, and 2,4-(2,4-dimethylpentyl) chromate, which are useful oxidants. However, owing to the poor selectivity and the low yields, this reaction does not appear to be particularly useful for organic synthesis. The recent applications of chromyl chloride are oxidation of olefins and enol ethers.

The reaction might proceed through the initial attack of alcoholic oxygen to the positive chromium atom to form a very unstable transient intermediate followed by the subsequent decomposition by chlorine atom. The chromic anhydride can be regenerated from the reaction of chromyl chloride with alcohols.



In conclusion, in the presence of phase transfer catalyst, reagent generated *in situ* from chlorotrimethylsilane and potassium chromate can serve as an efficient chlorinating agent for a wide variety of alcohols. This *in situ* generated agent was found to be very effective for the chlorination of a wide variety of alcohols to the corresponding chlorides. Primary, secondary and substituted benzyl alcohols were converted into corresponding chlorides when treated with potassium chromate and chlorotrimethylsilane at room temperature. Although, much work remains to be done to understand detailed aspects of this reaction, this reagent generated *in situ* will be a valuable addition to the lists of chlorinating agents for alcohols to the corresponding chlorides. We are currently investigating the nature of actual chlorinating species, mechanisms and other applications of this reagent system.

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16. The reaction of benzyl alcohol is representative. A well-dried, 100 mL two-necked flask equipped with a reflux condenser and an oil bubbler was placed 0.048 mole of chlorotrimethylsilane and 0.012 mole of potassium chromate with a catalytic amount of phase transfer catalyst, benzyltriethylammonium chloride in 15 mL of carbon tetrachloride. After stirring for several minutes at room temperature, the mixture changed into a heterogeneous pale yellow solution. And 0.01 mole of benzyl alcohol diluted in 10 mL carbon tetrachloride was added dropwise to the above mixture, and the resulting reaction mixture was stirred for 2 hours at room temperature. The crude reaction mixture was checked by TLC (eluent: methylene chloride/carbon tetrachloride, V/V=50:50) and NMR spectra. The TLC observation and NMR spectrum of the crude reaction mixture showed complete conversion to benzyl chloride. The reaction mixture was filtrated through a silica gel (70-230 mesh) column and the solvent was removed using a rotary evaporator. The product was identical in all respects with the authentic benzyl chloride.
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19. Bistrimethylsilylchromate is one of the trimethylsilyl derivative of chromic acid. Although its preparation from chromic anhydride and hexamethyldisiloxane has been known for a long time, reports on the application as an oxidant are scarce. With water it hydrolyzes to chromic acid and silanol. Synthesis in greater scale, distillation leads, on occasion, to an explosion. According to literature (Schmidt, M.; Schmidbaur, H. *Chem. Ber.* **1959**, *92*, 2667), bistrimethylsilylchromate can be prepared from the insertion reaction of chromic anhydride into hexamethyldisiloxane. That is, chromic anhydride dissolves in refluxing anhydrous hexamethyldisiloxane at 100 °C developing orange color. Vacuum distillation gives bistrimethylsilylchromate, TMSO-CrO₂-OTMS as an orange red oil (bp 75 °C/1.0 mmHg). It dissolves well in benzene and carbon tetrachloride forming an orange solution.
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