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Selective deprotection of silyl ethers



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1. Introduction

Protection/deprotection sequences are common components in modern organic synthesis and methods for protecting and deprotecting hydroxyl groups have become important elements in synthetic strategies.^{1,2} Among the many protecting groups available for rendering hydroxyl groups temporarily inert, silyl groups have earned a place of prominence. Some common silyl protecting groups and their abbreviations are illustrated in Fig. 1.^{3,4}

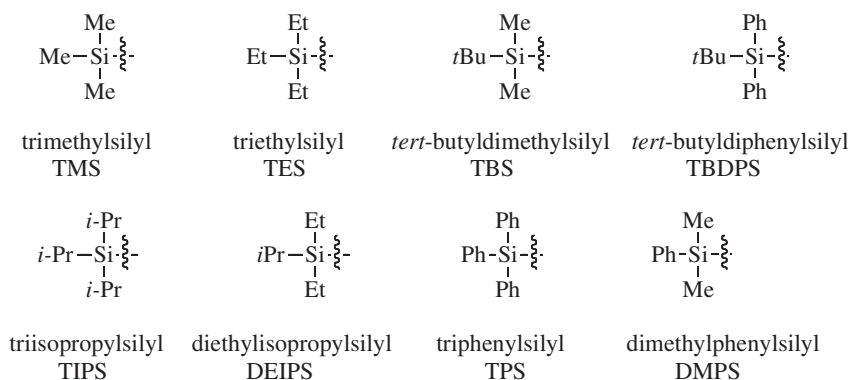


Fig. 1. Some commonly used silyl protecting groups.

As the complexity of synthetic targets has increased, the ability to protect multiple alcohol groups in the same molecule and then sequentially deprotect them allows individual alcohols in a polyhydroxylated compound to be modified. Silyl ether stability—and therefore the ease of deprotection—can be adjusted by altering the substituents on the silicon atom.^{5,6} In most, but not all, cases, the effect is steric.⁷ As a result, multiple hydroxyl groups in a single molecule can be protected as the same functional group but with different reactivities^{3,4} and sequential selective desilylation allows each alcohol group to be released when it needs to be manipulated. This strategy is common in natural product syntheses and, although a comprehensive list of too long to be included here, some recent examples include such diverse natural products as Brevenal,^{8–12} (–)-Sarain A,^{13,14} Amphidinolide H¹⁵ and G,¹⁶ Leucascandrolide A,¹⁷ Psymberin,^{18–21} and Kendomycin.^{22–25}

In recent years, protecting group-free synthetic strategies have been reported with increasing frequency.^{26–34} Although such approaches will undoubtedly become part of the planning of synthetic routes in the future, the development of functional protecting groups such as fluorosilyl^{35,36} and magnetic³⁷ silyl groups that enhance product isolation, improved protocols for desilylation,^{38,39} and enantioselective silylation techniques^{40–45} point toward the continued importance of silyl protecting groups in organic synthesis. And, thus, selective deprotection reactions for silyl-protected polyhydroxy compounds will continue to be important tools in synthetic chemistry.

This paper follows two earlier reviews^{3,4} on selective desilylation reactions and compiles examples from 2004 to the end of 2011. As was the case in the previous reviews, the focus is on reactions that cleave an oxygen–silicon bond and, thus, protection with groups involving a carbon–silicon bond such as the 2-(trimethylsilyl)ethoxymethyl (SEM) group are not included. This review is organized according to the type of silyl-protected alcohol (1°, 2°, etc.) that undergoes deprotection in the presence of another silyl-protected alcohol (1°, 2°, etc.), which remains intact with sub-

categories for acidic, basic, and miscellaneous reaction conditions. The text focuses on new and noteworthy examples with applications of more established methods included in the tabular summary. Although every effort has been made to be comprehensive, many examples of selective desilylation reactions are but one step in a multi-step synthetic scheme and typically not abstracted as a deprotection reaction.

2. Structure and selectivity

In predicting selectivity in silyl deprotection reactions, focus is often on the substituents on the silicon and on the parent alcohol's carbon. The role of steric and electronic effects in silyl deprotection reactions has been described elsewhere.^{1,3–6,46} But, in general, silyl substituents that are bulky tend to slow the rate of silyl ether cleavage under acidic or basic conditions.^{5,46} Similarly, an increase in steric bulk at the parent alcohol carbon decreases reactivity. Electron-withdrawing groups on the silicon atom decrease the rate of hydrolysis of silyl ethers under acidic conditions while electron donating substituents on silicon decrease the rate of base-mediated silyl ether cleavage.

Although this paper is organized according to the type of alcohol being released upon deprotection in the presence of another silyl ether, the entirety of the carbon framework plays a role in determining silyl ether stability and, thus, the rate of deprotection.¹ Through-bond

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