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Review

Alkylsilyl derivatives for gas chromatography

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ABSTRACT

Alkylsilyl reagents are the most widely used reagents for the derivatization of polar compounds containing labile hydrogen atoms for gas chromatography. In this article the reagents and reaction conditions for the formation of trimethylsilyl, alkyldimethylsilyl (particularly *t*-butyldimethylsilyl), cyclic siliconides, haloalkyldimethylsilyl, and flophemesyl (pentafluorophenyldimethylsilyl) derivatives for a wide range of functional groups are reviewed. The importance of steric hindrance on reaction rates and completion, choice of reaction conditions, stability of derivatives, and options for selective detection are described.

Contents

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1. Introduction

Many polar compounds of biomedical or environmental interest are labile at the temperatures required for their separation by gas chromatography. This is particularly true of polar compounds of high molecular mass which require high temperatures to generate sufficient vapor pressure for migration to the gas phase. Here, derivatization is employed to improve the thermal stability of polar compounds and to minimize undesirable interactions with the column and injection liner resulting in poor peak shape or loss of mass through adsorption. Derivatization is also used to facilitate selective detection by the introduction of a molecular fragment into a compound (a tag) that the detector responds to allowing discrimination against matrix components lacking a similar tag or other groups with a strong detector response. Examples of this application are usually to be found in trace analysis or the analysis of complex mixtures, where only information about a series of similar target compounds is required. Derivatization can also be used to reposition peaks in the chromatogram from regions of extensive overlap to regions that are relatively empty of interfering peaks.

Many reagents are used for derivatization but none are as versatile as the trialkysilyl reagents. These reagents have been in use almost from the beginning of gas chromatography [1] for the formation of thermally stable derivatives of polar compounds containing hydrogen atoms bound to electronegative elements, such as oxygen, nitrogen, sulfur or phosphorous (Fig. 1). Trialkylsilyl reagents also form thermally stable derivatives with a wide range of oxyanions (e.g., silicate, carbonate, oxalate, borate, phosphate, phosphite, orthophosphate, arsenite, arsenate, sulfate, vanadate, etc.) that are suitable for separation by gas chromatography [2,3]. The trialkylsilyl derivatives are widely used in organic synthesis as a protecting group where their ability to provide high product yields under mild conditions, and ease of removal under specific conditions (usually by hydrolysis or reaction with the fluoride anion), are highly prized

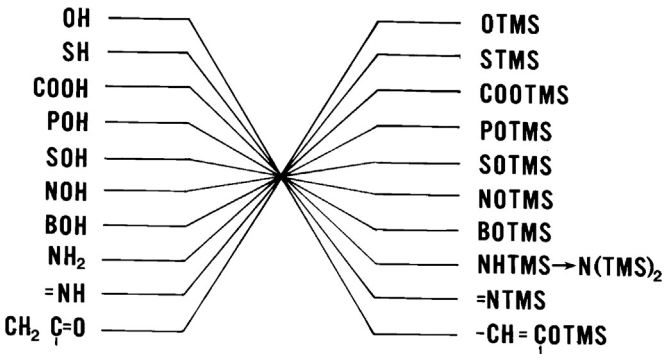

Fig. 1. Reactive functional groups that form trialkylsilyl derivatives.

[4–6]. Reaction conditions for specific functional groups and compounds are compiled elsewhere [1–3,7–10]. This review will focus on broader issues often missed or obscured in compilations of specific recipes of individual reactions with the hope of arriving at a deeper understanding of their reaction chemistry and use.

2. Trialkylsilyl reagents and their reactivity

Numerous reagents have been introduced for the preparation of trialkylsilyl derivatives but only a smaller number have entered into general practice [1–3,7]. These are summarized in Table 1 together with their common abbreviations. Representative structures are shown in Fig. 2. The choice of abbreviations follows common practice except for trimethyliodosilane and trimethysilylimidazole. Typically, TMSI is used for both reagents, but to allow a distinction in this report, TMSI is used for trimethyliodosilane and TMSIm for trimethylsilylimidazole. Higher homologs of the trimethylsilyl derivatives (e.g., triethylsilyl to tri-*n*-hexylsilyl) were described for optimizing the location of target compounds in chromatograms with limited unoccupied space but are little used at present [7,8,11]. Alkyldimethylsilyl and aryldimethylsilyl reagents were explored to find a balance between improving the hydrolytic stability of the trimethylsilyl derivatives and maintaining favorable volatility for gas chromatography and reactivity for hindered functional groups [7,8]. From these studies the *t*-butyldimethylsilyl reagents emerged as the best alternative and these are now the second most important trialkylsilyl reagents after the trimethylsilyl reagents. The *t*-butyldimethylsilyl derivatives are about 1000–10,000 fold more stable to hydrolysis conditions than the trimethylsilyl derivatives. The trimethylsilyl *N*,*N*-dimethylcarbamate [12,13] and *t*-butyldimethylsilyl *N*,*N*-dimethylcarbamate [14] are relatively

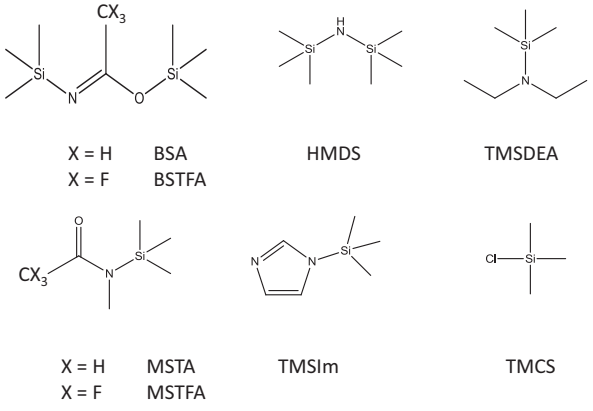

Fig. 2. Structures of some common reagents for the formation of trimethylsilyl derivatives.

Table 1
Common reagents for preparing trialkylsilyl derivatives (TMS = trimethylsilyl and *t*BDMS = *t*-butyldimethylsilyl).

Reagent	Structure	Abbreviation
Trimethylchlorosilane	TMSCl	TMCS
Trimethyliodosilane	TMSI	TMSI
t-Butyldimethylchlorosilane	tBDMSCl	TBDMCS
Hexamethyldisilazane	TMSNHTMS	HMDS
N-Trimethylsilyldiethylamine	$TMSN(C_2H_5)_2$	TMSDEA
N-Trimethylsilylimidazole	$TMSC_3H_3N_2$	TMSIm
N-Methyl-*N*-trimethylsilylacetamide	$CH_3CON(CH_3)TMS$	MSTA
N-Methyl-*N*-trimethylsilyltrifluoroacetamide	$CF_3CON(CH_3)TMS$	MSTFA
N-*t*-Butyldimethylsilyl-*N*-methyltrifluoroacetamide	$CF_3CON(CH_3)$*t*BDMS	MTBSTFA
N,*O*-Bis(trimethylsilyl)acetamide	$CH_3C(OTMS)$=NTMS	BSA
N,*O*-Bis(trimethylsilyl)trifluoroacetamide	$CF_3C(OTMS)$=NTMS	BSTFA
N,*O*-Bis(*t*-butyldimethylsilyl)trifluoroacetamide	$CF_3C(OtBDMS)$=NtBDMS	MTBSTFA
Trimethylsilyl *N*,*N*-dimethylcarbamate	$(CH_3)_2N(CO)OTMS$	TMSDMC