

TMCS

Product Specification

TMCS (trimethylchlorosilane) is a silylation catalyst, rarely used alone in analytical applications but typically mixed with other silylation reagents to increase their reactivity (e.g., HMDS/TMCS/pyridine, BSTFA/TMCS, BSA/TMCS) in derivatization of alcohols, alkaloids, amines, biogenic amines, carboxylic acids, phenols, and steroids. Compounds derivatized with BSTFA/TMCS include opiates, PPC (PCP metabolite) and THC metabolites.

Features/Benefits

TMCS increases the reactivity of other silylation reagents. Amides and many secondary amines and hindered hydroxyls, incompletely derivatized by BSTFA alone, can be derivatized by adding 1-20% TMCS to BSTFA.

Typical Procedure

This procedure is intended to be a guideline and may be adapted as necessary to meet the needs of a specific application. Always take proper safety precautions when using a silylating reagent – consult MSDS for specific handling information. TMCS is extremely sensitive to moisture and should be handled under dry conditions.

Prepare a reagent blank (all components, solvents, etc., *except sample*), following the same procedure as used for the sample.

1. Weigh 1-10mg of sample into a 5mL reaction vessel. If appropriate, dissolve sample in solvent (see below). If sample is in aqueous solution, evaporate to dryness, then use neat or add solvent.
2. Add silylating reagent + TMCS (e.g., BSTFA plus 1% TMCS). The reagent can be used at full strength or with a solvent.* In most applications it is advisable to use an excess of the silylating reagent – at least a 2:1 molar ratio of reagent to active hydrogen. In most cases 1% TMCS and silyl reagent is sufficient to achieve the desired derivatization. If after using this mixture under rugged conditions it appears the derivatization is not complete, additional TMCS may be added, up to a final concentration of about 30%.
3. Allow the mixture to stand until silylation is complete. To determine when derivatization is complete, analyze aliquots of the sample at selected time intervals until no further increase in product peak(s) is observed.

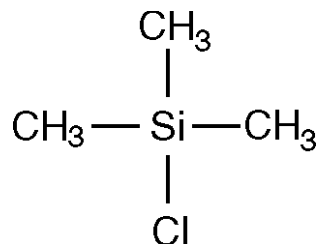
Derivatization times vary widely, depending upon the specific compound(s) being derivatized. Many compounds are completely derivatized as soon as they dissolve in the reagent. Compounds with poor solubility may require warming. A few compounds will require heating at 70°C for 20-30 minutes. Under extreme conditions compounds may require heating for up to 16 hours to drive the reaction to completion.

If derivatization is not complete, the addition of a catalyst, use of an appropriate solvent, higher temperature, longer time and/or higher reagent concentration should be evaluated.

Use a glass injection port liner or direct on column injection when working with silylating reagents. Erratic and irreproducible results are more common when stainless steel injection ports are used.

Properties

Structure:



CAS Number:

75-77-4

Molecular Formula:

$\text{ClSi}(\text{CH}_3)_3$

Formula Weight: 108.66

bp: 57°C

Flash Point: -18°F (-27°C)

d: 0.856

n_D : 1.3870 at 20°C

Appearance:

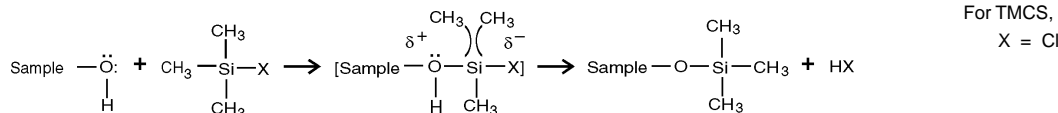
clear, colorless liquid with a pungent odor
moisture sensitive

796-0259

TMS derivatives and silylating reagents react with and are sensitive to active hydrogen atoms. Do not analyze TMS derivatives on stationary phases with these functional groups (e.g., polyethylene glycol phases). Silicones are the most useful phases for TMS derivatives – they combine inertness and stability with excellent separating characteristics for these derivatives. Nonpolar silicone phases include SPB™-1 and SPB-5. Normal hydrocarbons (carbon-hydrogen analytes with single bonds) are separated by these phases. More polar phases, SPB-1701 and SP™-2250, separate carbon-hydrogen analytes that also contain Br, Cl, F, N, O, P, or S atoms or groups. A highly polar cyanopropylphenylsiloxane phase, SP-2330, is useful for separating fatty acid methyl esters or aromatics.

*Nonpolar organic solvents such as hexane, ether, benzene, and toluene are excellent solvents for the reagent and the reaction products; they do not accelerate the rate of reaction. Polar solvents such as pyridine, dimethylformamide (DMF), dimethylsulfoxide (DMSO), tetrahydrofuran (THF), and acetonitrile are more often used because they can facilitate the reaction. Pyridine is an especially useful solvent because it can act as an HCl acceptor in silylation reactions involving organochlorosilanes.

Contact our Technical Service Department (phone 800-359-3041 or 814-359-3041, FAX 800-359-3044 or 814-359-5468) for expert answers to your questions.



Adapted from Knapp (2).

796-0130

Mechanism (1,2)

Silylation is the most widely used derivatization procedure for GC analysis. In silylation, an active hydrogen is replaced by an alkylsilyl group, most often trimethylsilyl (TMS). Compared to their parent compounds, silyl derivatives generally are more volatile, less polar, and more thermally stable.

Silyl derivatives are formed by the displacement of the active proton in -OH, -COOH, =NH, -NH₂, and -SH groups. The general reaction for the formation of trialkylsilyl derivatives is shown above.

The reaction is viewed as a nucleophilic attack upon the silicon atom of the silyl donor, producing a bimolecular transition state. The silyl compound leaving group (X) must possess low basicity, the ability to stabilize a negative charge in the transition state, and little or no tendency for π (p-d) back bonding between itself and the silicon atom.

The ideal silyl compound leaving group (X) must be such that it is readily lost from the transition state during reaction, but possesses sufficient chemical stability in combination with the alkyl silyl group to allow long term storage of the derivatizing agent for use as required. As the formation of the transition state is reversible, the derivatization will only proceed to completion if the basicity of the leaving group X exceeds that of the group it replaces. The ease of derivatization of various functional groups for a given silyating agent follows this order: alcohol > phenol > carboxylic acid > amine > amide. Within this sequence reactivity towards a particular silylating reagent will also be influenced by steric hindrance, hence the ease of reactivity for alcohols follows the order: primary > secondary > tertiary, and for amines: primary > secondary.

The addition of TMCS, which is a relatively weak silyl donor, to a silyl reagent (e.g., BSTFA) will enhance the donor strength of the stronger donor. The byproduct of TMCS reactions is HCl.

Toxicity – Hazards – Storage – Stability

TMCS is a flammable, moisture-sensitive liquid. It may irritate eyes, skin, and/or the respiratory system. Store in a brown bottle or amber ampul at room temperature, in a dry, well ventilated area away from ignition sources. Use only in a well ventilated area and keep away from ignition sources.

Properly stored, this reagent is stable indefinitely. Recommended storage conditions for the unopened product are stated on the label. Moisture will decompose both TMS reagents and derivatives. To exclude moisture, Supelco packages this product under nitrogen. If you store an opened container or transfer the contents to another container for later reuse, add desiccant. **Before reuse, validate that your storage conditions adequately protected the reagent.**

References

1. K. Blau and J. Halket *Handbook of Derivatives for Chromatography* (2nd ed.) John Wiley & Sons, New York, 1993.
2. D.R. Knapp *Handbook of Analytical Derivatization Reactions* John Wiley & Sons, New York, 1979.

Additional Reading

- K. Grob, *et al.*, *Recognition of Adulterated Oils by Direct Analysis of the Minor Components* *Fett-wiss.-Technol.*, 96 (8), 286-290 (1994).
- W. G. Taylor, *et al.*, *Rapid Identification of 4-hydroxy-2-alkylquinolines Produced by Pseudomonas aeruginosa, Using Gas Chromatography* *J. Chromatogr. B, Biomed. Appl.*, 664 (2), 458-462 (1995).
- J. M. Bennett, *et al.*, *Tiglylglycine Excreted in Urine in Disorders of Isoleucine Metabolism and the Respiratory Chain Measured by Stable Isotope Dilution GC-MS* *Clin. Chem.*, 40 (10), 1879-1883 (1994).
- C. Cocito and C. Delfino *Simultaneous Determination By GC of Free and Combined Fatty Acids and Sterols in Grape Musts and Yeasts as Silylated Compounds* *Food-Chem.*, 50 (3), 297-305 (1994).
- D.A. Black, *et al.*, *Analysis of Urinary Benzodiazepines, Using Solid-Phase Extraction and Gas Chromatography-Mass Spectrometry* *J. Anal. Toxicol.*, 18 (4), 185-188 (1994).
- M.J. Bennett, *et al.*, *Population Screening for Medium-chain Acyl-CoA Dehydrogenase Deficiency: Analysis of Medium-chain Fatty Acids and Acylglycines in Blood Spots* *Ann. Clin. Biochem.*, 31 (1), 72-77 (1994).

Ordering Information

Description	Cat. No.
TMCS, 100mL	33014
BSTFA + TMCS, 99:1	
144 ampuls x 0.1 mL	33154-U
20 ampuls x 1 mL	33148
25 mL	33155-U
50 mL	33149-U
BSA + TMCS, 5:1	
20 ampuls x 1 mL	33018
25 mL	33019-U
BSA + TMCS + TMSI, 3:2:3	
144 ampuls x 1 mL	33151
20 ampuls x 1 mL	33030
25 mL	33031-U
HMDS + TMCS, 3:1	
20 ampuls x 1 mL	33046
HMDS + TMCS + Pyridine, 3:1:9	
20 ampuls x 1 mL	33038
25 mL	33039

For information about BSTFA + TMCS, refer to Product Specification 496021 (BSA + TMCS: 496018; HMDS + TMCS: 496025; HMDS + TMCS + Pyridine: 496026).

Microreaction Vessels with Hole Caps and Septa

1 mL, pk. of 12	33293
3 mL, pk. of 12	33297
5 mL, pk. of 12	33299

Books

<i>Handbook of Derivatives for Chromatography</i> , K. Blau and J. Halket	Z246220
<i>Handbook of Analytical Derivatization Reactions</i> , D.R. Knapp	23561

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