

# TMSI

## Product Specification

**TMSI or TMSIM (N-trimethylsilylimidazole)** is the strongest reagent for hydroxyls. It reacts quickly and smoothly with hindered and unhindered hydroxyl and carboxyl groups. TMSI is useful for derivatizing wet sugar samples, hindered hydroxyl groups in steroids and, in conjunction with fluorinated acylation reagents, amino acids. TMSI usually is used without a catalyst. In some cases, however, the silylation rate can be increased by adding a catalyst such as TMCS (for steroids), pyridine hydrochloride (phenols), o-methylhydroxylamine hydrochloride (sterically hindered hydroxyl compounds), piperidine (prostaglandin E methyl esters), or potassium acetate (ecdysterone).

### Features/Benefits

Useful for derivatizing alcohols, hormones, fatty and other organic acids, phenols, prostaglandins, steroids, sulfonic acids, and thiols. Useful in multiderivatization schemes containing hydroxyl and amine groups.

Does not react with aliphatic amines. Less basic amines and amides may react with TMSI.

Derivatizes sugars in the presence of small amounts of water.

TMS derivatives are thermally stable but more susceptible to hydrolysis than their parent compounds.

### 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. TMSI 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 excess silylating reagent. TMSI 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 TMSI to active hydrogen. Not all samples are derivatized by TMSI alone. For moderately hindered or slowly reacting compounds, pyridine is an especially useful solvent because of its ability to act as an HCl acceptor in silylation reactions involving organochlorosilanes. (For information about TMSI+pyridine reagent, refer to Product Specification 496030.)
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.

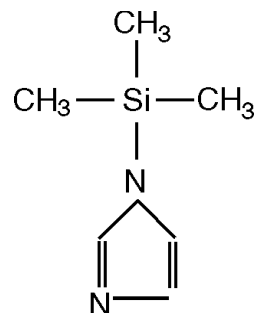
If derivatization is not complete, the addition of a catalyst, use of an appropriate solvent, higher temperature, longer time and/or higher reagent concentration should be evaluated.

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.

TMS derivatives and silylating reagents react with and are sensitive

### Properties

#### Structure:



#### CAS Number:

18156-74-6

#### Molecular Formula:

(CH<sub>3</sub>)<sub>3</sub>SiNCH=NCH=CH

#### Formula Weight: 140.26

#### bp: 93-94°/14mm

#### Flash Point: 42°F (5°C)

#### d: 0.956

#### n<sub>D</sub>: 1.4750 at 20°C

#### Appearance:

clear, colorless to light yellow liquid  
moisture sensitive

796-0260

to active hydrogen atoms. Do not analyze TMSI 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.

### 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



Adapted from Knapp (2).

796-0130

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, -NH<sub>2</sub>, 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 silylating 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.

### Toxicity – Hazards – Storage – Stability

TMSI 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.**

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.

### 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

- A.E. Pierce *Silylation of Organic Compounds* Pierce Chemical Co. (1979).  
 J. Drozd *Chemical Derivatization in Gas Chromatography* Elsevier (1981).  
 R. Piekos, *et al.*, *J. Chromatogr.* 116: 315 (1976).  
 Y. Maruyama and A.E. Takemori, *Biochem. Pharmacol.* 20: 1833 (1971).  
 O.A. Mamer and B.F. Gibbs, *Clin. Chem.* 19: 1006 (1973).  
 T. Aoyama and T. Yashiro, *J. Chromatogr.* 265: 57 (1983).  
 K.E. Rasmussen, *J. Chromatogr.*, 120: 491 (1976).  
 M. Osman, *J. Chromatogr.*, 186: 273 (1979).  
 E.M. Chambaz and E.C. Horning, *Anal. Biochem.*, 30: 7 (1969).  
 T.V. Pokushalova, *et al.*, *Zh. Anal. Khim.*, 41: 721 (1986).  
 C.E. Kientz and A. Verweij, *J. Chromatogr.*, 355: 229 (1986).  
 A.F. Rizzo, *et al.*, *J. Chromatogr.*, 368: 381 (1986).  
 J.P. Thenot and E.C. Horning, *Anal. Lett.*, 5: 21 (1972).  
 A.B. Benkö and V. Mann, *Anal. Lett.*, 13: 735 (1980).  
 K. Uobe, *J. Chromatogr.*, 214: 177 (1981).  
 N. Sakauchi and E.C. Horning, *Anal. Lett.*, 4: 41 (1971).  
 M. Donike, *Chromatographia*, 9: 440 (1976).  
 E. Martinez and E. Gelpi, *J. Chromatogr.*, 167: 77 (1978).  
 R.S. Glass, *J. Organomet. Chem.*, 61: 83 (1973).  
 K.R. Williams and R.A. Anderson, *Anal. Chim. Acta*, 275: 163 (1993).

### Ordering Information

Description	Cat. No.
<b>TMSI</b>	
25mL	<b>33068-U</b>
For information about TMSI+pyridine reagent, refer to Publication 496030. For information about TMSI+BSA+TMCS, refer to Publication 496019.	
<b>Microreaction Vessels with Hole Caps and Septa</b>	
1mL, pk. of 12	<b>33293</b>
3mL, pk. of 12	<b>33297</b>
5mL, pk. of 12	<b>33299</b>

### Books

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

For more information, or current prices, contact your nearest Supelco subsidiary listed below. To obtain further contact information, visit our website ([www.sigma-aldrich.com](http://www.sigma-aldrich.com)), see the Supelco catalog, or contact Supelco, Bellefonte, PA 16823-0048 USA.

ARGENTINA · Sigma-Aldrich de Argentina, S.A. · Buenos Aires 1119 AUSTRALIA · Sigma-Aldrich Pty. Ltd. · Castle Hill NSW 2154 AUSTRIA · Sigma-Aldrich Handels GmbH · A-1110 Wien  
 BELGIUM · Sigma-Aldrich N.V./S.A. · B-2880 Bornem BRAZIL · Sigma-Aldrich Quimica Brasil Ltda. · 01239-010 São Paulo, SP CANADA · Sigma-Aldrich Canada, Ltd. · 2149 Winston Park Dr., Oakville, ON L6H 6J8  
 CZECH REPUBLIC · Sigma-Aldrich s.r.o. · 186 00 Praha 8 DENMARK · Sigma-Aldrich Denmark A/S · DK-2665 Vallensbaek Strand FINLAND · Sigma-Aldrich Finland/YA-Kemia Oy · FIN-00700 Helsinki  
 FRANCE · Sigma-Aldrich Chimie · 38297 Saint-Quentin-Fallavier Cedex GERMANY · Sigma-Aldrich Chemie GmbH · D-82041 Deisenhofen GREECE · Sigma-Aldrich (o.m.) Ltd. · Ilioupoli 16346, Athens  
 HUNGARY · Sigma-Aldrich Kft. · H-1067 Budapest INDIA · Sigma-Aldrich Co. · Bangalore 560 048 IRELAND · Sigma-Aldrich Ireland Ltd. · Dublin 24 ISRAEL · Sigma Israel Chemicals Ltd. · Rehovot 76100  
 ITALY · Sigma-Aldrich s.r.l. · 20151 Milano JAPAN · Sigma-Aldrich Japan K.K. · Chuo-ku, Tokyo 103 KOREA · Sigma-Aldrich Korea · Seoul MALAYSIA · Sigma-Aldrich (M) Sdn. Bhd. · 58200 Kuala Lumpur  
 MEXICO · Sigma-Aldrich Quimica S.A. de C.V. · 50200 Toluca NETHERLANDS · Sigma-Aldrich Chemie BV · 3330 AA Zwijndrecht NORWAY · Sigma-Aldrich Norway · Torshov · N-0401 Oslo  
 POLAND · Sigma-Aldrich Sp. z o.o. · 61-663 Poznań PORTUGAL · Sigma-Aldrich Quimica, S.A. · Sintra 2710 RUSSIA · Sigma-Aldrich Russia · Moscow 103062 SINGAPORE · Sigma-Aldrich Pte. Ltd.  
 SOUTH AFRICA · Sigma-Aldrich (pty) Ltd. · Jet Park 1459 SPAIN · Sigma-Aldrich Quimica, S.A. · 28100 Alcobendas, Madrid SWEDEN · Sigma-Aldrich Sweden AB · 135 70 Stockholm  
 SWITZERLAND · Supelco · CH-9471 Buchs UNITED KINGDOM · Sigma-Aldrich Company Ltd. · Poole, Dorset BH12 4QH  
 UNITED STATES · Supelco · Supelco Park · Bellefonte, PA 16823-0048 · Phone 800-247-6628 or 814-359-3441 · Fax 800-447-3044 or 814-359-3044 · email: [supelco@sial.com](mailto:supelco@sial.com)

Supelco is a member of the Sigma-Aldrich family. Supelco products are sold through Sigma-Aldrich, Inc. Sigma-Aldrich warrants that its products conform to the information contained in this and other Sigma-Aldrich publications. Purchaser must determine the suitability of the product for a particular use. Additional terms and conditions may apply. Please see the reverse side of the invoice or packing slip.