

N-t-Butyldimethylsilylimidazole

Product Specification

N-t-Butyldimethylsilylimidazole (TBDMSIM) is formed by reacting butyldimethylchlorosilane and imidazole (1:2). Although TBDMSIM is not widely used, the t-butyldimethylsilyl (TBDMS) derivatives it forms enhance thermal stability and increase the inertness of the analyte(s). A weak silylating reagent, TBDMSIM reacts with hydroxyl groups, but is ineffective in silylating thiols, primary or secondary amines, or slightly hindered hydroxyl groups. It is more effective in converting alcohols to TBDMS ethers than is butyldimethylchlorosilane. TBDMSIM is normally used in solution with pyridine or dimethylformamide. The use of imidazole as an acid scavenger can interfere with the quantitative silylation of carboxylic acids. A further problem arises from the poor solubility of some derivatives (e.g., certain steroids) if dimethylformamide is used as the solvent. Precipitates that form can be redissolved by adding another solvent (e.g., dichloromethane) after derivatization. An alternative solution is to use pyridine, rather than dimethylformamide. The addition of TBDMCS (t-butyldimethylchlorosilane) to TBDMSIM greatly increases its reactivity.

Features/Benefits

t-Butyldimethylsilyl (TBDMS) derivatives are more stable to hydrolysis than the corresponding trimethylsilyl (TMS) ethers (the tert-butyldimethylsilyl group is larger than the TMS group). Stability of TBDMS-enol ethers is an advantage in the isolation of ketone enolates from aqueous solution.

Does not release HCl.

Useful for mass spectrometry (tends to provide high-mass ions).

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.

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

1. Weigh 1-10mg sample into a 1mL reaction vessel. Add excess silylating reagent.
2. Allow mixture to stand until silylation is complete. Under extreme conditions compounds may require heating.

To determine when derivatization is complete, analyze aliquots 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 will require heating to drive the reaction to completion. The steric effects of silyl groups of differing bulk and geometry have a major influence on the rate and extent of silylation reactions. Increasing the bulk of substituents on the silicon atom impedes the access of the reagent to functional groups. Silyl derivatives containing bulky substituents will resist chemical degradation by impeding the access of reagents to the reaction center.

Silicones are the most useful phases for TBDMS 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

Properties

Structure:

CC(C)(C)C(C)(C)[Si](C)(C)N1C=CN=C1

CAS Number: 54925-64-3
Molecular Formula: C(CH₃)₃-Si(CH₃)₂ NCH=NCH=CH
Formula Weight: 182.34
bp: 53°/0.2mm
Flash Point: 211°F (99°C)
d: 0.939
n_D: 1.480 at 20°C
Appearance: clear, pale yellow liquid
moisture sensitive

796-0341

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.

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.

Catalysts

1% TBDMCS greatly increases the reactivity of TBDMSIM.

Use pyridinium hydrobromide or O-methylhydroxylamine hydrochloride when silylating hydroxysteroids with TBDMSIM.

Potassium acetate in toluene yields quantitative formation of TBDMS ethers. Alternatively, fewer by-products are formed with sodium formate in hexane at 100°C than with potassium acetate/toluene.



Adapted from Knapp (2).

796-0130,0131

TBDMSIM plus MTBSTFA (N-tert-butyltrimethylsilyl-N-methyltrifluoroacetamide) plus catalytical amounts of TBDMCS, in acetonitrile (5:50:0.5:100) have been used for silylating dihydroxyeicosatetraenoic acids.

Toxicity – Hazards – Storage – Stability

TBDMSIM is a flammable, corrosive liquid. It may irritate eyes, skin, and/or the respiratory system. Store 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. **If you store an opened container or transfer the contents to another container for later reuse, validate that your storage conditions adequately protected the reagent before reusing this product.**

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 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.

Additional Reading

- K. Blau and J. Halket *Handbook of Derivatives for Chromatography* (2nd ed.) John Wiley & Sons, New York, 1993.
D.R. Knapp *Handbook of Analytical Derivatization Reactions* John Wiley & Sons, New York, 1979.
E.J. Corey and T.A. Vendateswarlu, J. Am. Chem. Soc., 94: 6190 (1972).
C. Norsten-Hoog and T. Cronholm, Anal. Biochem., 189: 131-137 (1990).
K. Satouchi and K. Saito, Bio Med.-Mass Spectrom., 6: 396-402 (1979).

Ordering Information

Description	Cat. No.
N-t-Butyldimethylsilylimidazole	
10 x 1mL	33092-U
Microreaction Vessels with Hole Caps and Septa	
1mL, pk. of 12	33293
3mL, pk. of 12	33297
5mL, 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

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.

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), 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 Química 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 Química 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 Química, 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 Química, 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@sig.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.

H

BFF