Shin-Etsu

Shin-Etsu Silicone

Organosilicon Compounds For Organic Synthesis

Introduction

Recently, the use of organosilicon compounds in organic chemistry has become an increasingly important field. As such, Shin-Etsu Chemical has been a key supplier for many silylating agents currently in use while also searching for and developing new and useful organosilicon compounds. This booklet introduces several newly developed silylating agents and organosilicon compounds, including references for their application.

SILYLATING AGENTS

General Definition

Silylating agents are reagents that are used to replace the active hydrogen of a chemical species with a silyl group (-Si RR'R").
For example,functional groups such as -OH, -COOH, -NH_2, -$CONH_2$, and -SH are converted to -OSiRR'R", -COOSiRR'R", -NHSiRR'R", CONHSiRR'R", and -SSiRR'R",respectively.

Purpose

In general, the replacement of active hydrogens significantly decreases the reactivity of a functional group and dramatically reduces polar interactions such as hydrogen bonding. These replacements can be carried out for many specific reasons, but typically fall under one or more of the following objectives:

(1) Protecting a reactive functional group during one or more chemical reactions
(2) Improving the selectivity of a chemical reaction
(3) Improving stability during distillation
(4) Improving solubility in polar and/or non-polar solvents
(5) Increasing volatility by reducing or eliminating hydrogen-bonding

How To Select?

The most common silylating agents used on an industrial scale are listed in Table I. Reactivity, type of by-product, price, and availability are often important factors that must be considered when the synthetic process is developed.
Another important factor to be considered, the stability of the resultant silylated functional group, is largely determined by the combined steric bulk of the alkyl groups attached to silicon (R, R', and R"). In general, as the steric bulk of the alkyl groups increase, the stability of silylated functional groups also increase.
For convenience, the stability of a silylated functional group can be estimated using Taft's parameters, such as those listed in Table II.
Proper selection may also be influenced by additional reactivity.
For example, CIPS is a bi-functional silylating agent that is effective in the synthesis of nucleosides such as anti-HIV drugs.

How To Eliminate?

Usually, the protective groups are easily removed with water, alcohol or mild acidic or basic condition to yield the original chemical species having an active hydrogen.

Table I

Grade	Formula	Molecular Weight (g/mol)	d	n_D	Boiling Point (°C/mmHg)	Flash Point (°C)
KA-31	Me_3SiCl	108.6	0.85	1.387	57	-15
HMDS	$Me_3SiNHSiMe_3$	161.4	0.77	1.408	126	17
BTSU	$Me_3SiNHCONHSiMe_3$	204.4			(212)*	
BSTFA	$Me_3SiOC(CF_3)=NSiMe_3$	257.4	0.97	1.381	46/17	34
TMST	$Me_3SiOSO_2CF_3$	222.3	1.23	1.363	140	40
TESC	Et_3SiCl	150.7	0.89	1.429	145	39
TIBSC	i-Bu_3SiCl	234.9	0.88	1.446	101/10	87
TBMS	tert-$BuMe_2SiCl$	150.7			125	28
TIPSC	i-Pr_3SiCl	192.8	0.91	1.452	59/8	63
TDSC	$TxMe_2SiCl$**	178.8	0.91	1.449	55/10	49
CIPS	$Cl(i\text{-}Pr)_2SiOSi(i\text{-}Pr)_2Cl$	315.4	1.01	1.453	108/14	110

* Melting point °C
** Tx : Thexyl

Table II. Steric Parameter E_s^{Si}, Taft's parameter

R	E_s^{Si}
Methyl	0
Ethyl	-0.261
n-Propyl	-0.315
n-Butyl	-0.348
iso-Butyl	-0.400
iso-Propyl	-0.677
sec-Butyl	-0.704
Cyclohexyl	-0.757
Me_3CCH_2	-0.589
Et_2CH	-0.816
tert-Butyl	-1.670
Tx	-1.899

$$RMe_2SiCl \xrightarrow[\text{acridine}]{\text{aq. dioxane}} RMe_2SiOH$$

R : aliphatic group

$$(\log k_{rel}) / 2.1 = E_s^{Si}$$

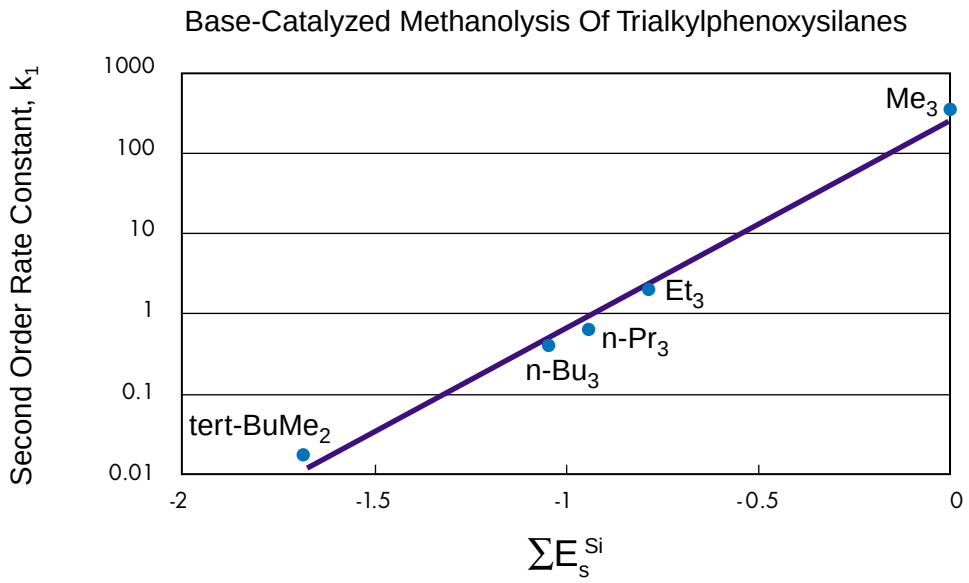
N. Shimizu, et al. Chem. Lett., 1263-1266 (1992)

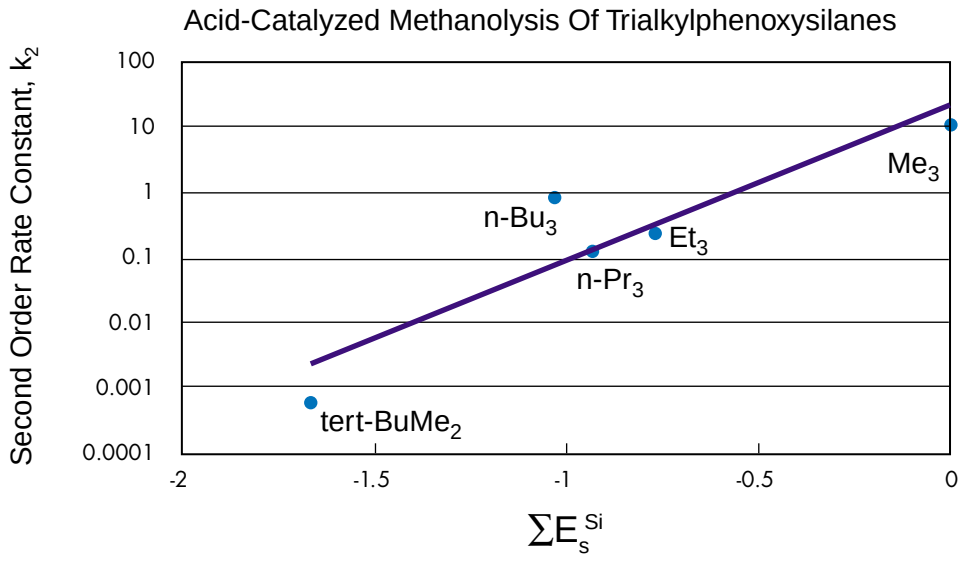
Application of Taft's Parameter

$(\sum E_s^{Si} = E_s^{Si}(R_1) + E_s^{Si}(R_2) + E_s^{Si}(R_3))$

Since the plots of log(k) vs. $\sum E_s^{si}$ show linear relationships, the relative stability of silylated compounds can be conveniently estimated.

$$R_1R_2R_3SiOPh \xrightarrow[MeOH]{\text{Acid}(k_2) \text{ or base}(k_1)} R_1R_2R_3SiOMe + PhOH$$



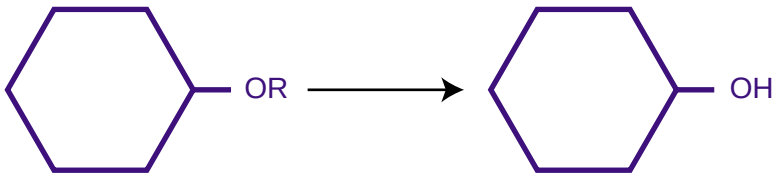


The Half-Life Of Silylethers Under Elimination Conditions

$CH_3CH_2CH_2CH_2OR \longrightarrow CH_3CH_2CH_2CH_2OH$

R	H^+	OH^-
TBDMS	<1min	1hour
TIPS	18min	14hour
TBDPS*	244min	<4hour

* TBDPS : tert-Butyldiphenylsilyl



R	H^+	OH^-	F^-
TBDMS	<1min	1hour	76min
TIPS	18min	14hour	137min
TBDPS	244min	<4hour	-

Conditions

H^+ : 1% HCl in 95% EtOH at 22.5°C

OH^- : 5% NaOH in 95% EtOH at 90°C

F^- : 2 eq. TBAF in THF at 22.5°C

J.M.Muchowski, et al., Tetrahedron Lett.,24,2865(1983)
R.F.Cunico, et al.J.Org.Chem.,45,4797(1980)
K.K.Ogilvie,et al.,Tetrahedron Lett.,24,2865(1974)

ORGANOSILICON COMPOUNDS

Other Organosilicon Compounds

Additional applications for silylating agents, such as reducing agents or alkylating agents, have increased recently.

Organosilicon compounds for these applications are listed in Table III.

CMTMS, TMSA, ATMS and TMVS are used as alkylating agents for preparation of silicon containing organic compounds.

TES and HBS are used as reducing agents.

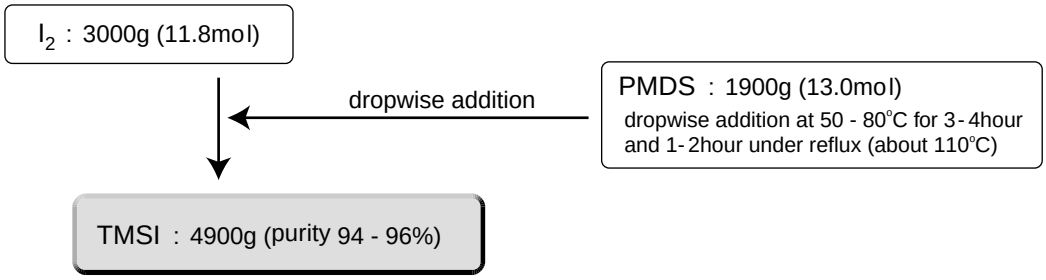
PMDS is a precursor of trimethylsilyliodide, which is used in ether and ester bond cleavage reactions under neutral conditions.

Table III

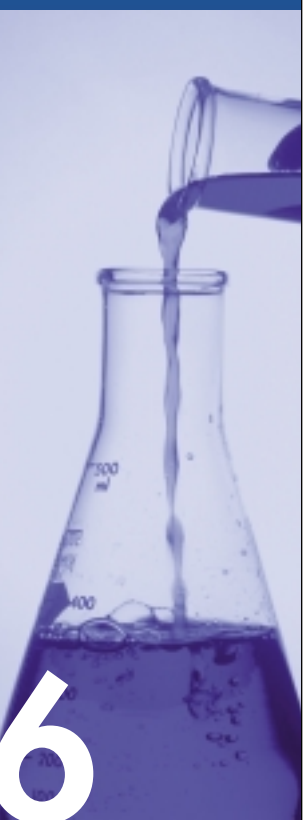
Grade	Formula	Mol Wt. (g/mol)	d	n_D	Boiling Point (°C)	Melting Point (°C)	Flash Point (°C)	Reference (F&F)
CMTMS	$ClCH_2SiMe_3$	122.7	0.886	1.418	97	-	<-2	5:724, 12:118
TES	Et_3SiH	116.3	0.731	1.412	107	-	-1	1:1218, 2:433 4:530, 5:694
HBS	tert-$BuMe_2SiH$	116.3	0.702	1.398	86	-	-14	
TMSA	$HC{\equiv}CSiMe_3$	98.2	0.695	1.388	53	-	-34	
PMDS	$Me_3SiSiMe_3$	146.4	0.758	1.374	112	14	-9	11:253
ATMS	$CH_2{=}CHCH_2SiMe_3$	114.3	0.712	1.405	86	-	7	10:6, 11:16, 12:23
TMVS	$CH_2{=}CHSiMe_3$	100.2	0.687	1.388	54	-	-34	9:498, 10:444, 12:566

Example Of TMSI Preparation

Using a reaction vessel equipped with a condenser, a thermometer and a stirrer



A. Hosomi, et al Journal of Synthetic Organic Chemistry Japan 40, 545-553 (1982)
W. C. Groutase, et al Synthesis, 861 (1980)



Regulatory Status Of Organosilicon Compounds

The CAS number and regulatory status of each organosilicon compound is listed in Table IV.

Table IV

Grade	Chemical Name	CAS No.	JECS	TSCA No.	EINECS
KA-31	Trimethylsilylchloride	75-77-4	2-2041	75-77-4	2009005
HMDS	1,1,1, 3,3,3-Hexamethyldisilazane	999-97-3	9-1324	999-97-3	2136685
BTSU	N, N'-bis(Trimethylsilyl)urea	18297-63-7	2-3250	18297-63-7	2421779
BSTFA	N,O-bis(Trimethylsilyl)trifluoroacetoamide	25561-30-2	REGISTERED	-	2471039
TMST	Trimethylsilyltrifluoromethanesulfonate	27607-77-8	REGISTERED	27607-77-8	2485654
TESC	Triethylsilylchloride	994-30-9	2-2041	994-30-9	2136156
TBMS	tert-Butyldimethylsilylchloride	18162-48-6	2-2041	18162-48-6	2420424
TIBSC	Triisobutylsilylchloride	13154-25-1	2-2041	-	-
TIPSC	Triisopropylsilylchloride	13154-24-0	2-2041	-	-
TDSC	Thexyldimethylsilylchloride	67373-56-2	2-2041	-	-
CIPS	1,3-Dichloro-1,1,3,3-Tetraisopropyldisiloxane	69304-37-6	REGISTERED	-	-
CMTMS	Chloromethyltrimethylsilane	2344-80-1	-	2344-80-1	2190585
TES	Triethylsilane	617-86-7	-	617-86-7	2105353
HBS	tert-Butyldimethylsilane	29681-57-0	REGISTERED	-	-
TMSA	Trimethylsilylacetylene	1066-54-2	REGISTERED	1066-54-2	2139199
PMDS	Hexamethyldisilane	1450-14-2	REGISTERED	1450-14-2	2159110
ATMS	Allyltrimethylsilane	762-72-1	-	762-72-1	2121045
TMVS	Trimethylvinylsilane	754-05-2	-	754-05-2	2120429

REFERENCES

Silylating Agents, General and Kinetics

1 : E.Colvin, Silicon Reagents In Organic Synthesis, Academic Press (1988).
2 : M.Lalonde, Synthesis, 817 (1985).
3 : E. Akerman, Acta Chem. Scand., 11, 373-381 (1957).
4 : H.Wetter, et al., Tetrahedron Lett., 26, 5515 (1985).

TIPSC

1 : Ohwa, et al., Chem. Lett. 41 (1987).
2 : A.P.Kozikowski, et al., J. Org. Chem., 49, 3239 (1984).
3 : S.V.Frye, et al., Tetrahedron Lett., 27, 3223 (1986).

TDSC

1 : H.Wetter, et al., Tetrahedron Lett., 26, 5515 (1985).
2 : B.Loubinoux, et al., Tetrahedron, 50, 2047 (1994).
3 : R.D.Walkup, et al., Tetrahedron Lett., 28, 4019 (1987).
4 : R.N.Mosra, et al., J. Med. Chem., 34, 2882 (1991).
5 : G.Confalonieri, et al., Tetrahedron, 50, 3235 (1994).

TMST

1 : S.Murata, et al., J. Am. Chem. Soc., 101, 2738-2739 (1979).
2 : S.Murata, et al., J. Am. Chem. Soc., 102, 3248-3249 (1980).
3 : H.Vorbruggen, et al., Chem. Ber., 114, 1234-1255 (1981).

CIPS

1 : A.Matsuda, et al., Chem. Pharma. Bull., 36, 945-953 (1988).

HBS

1 : K.Yamamoto, et al., Bull. Chem. Soc. Jpn., 62, 2111-2113 (1989).
2 : Y.Tanabe, et al., Tetrahedron Lett., 35, 8413-8415 (1994).
3 : H.Vorbruggen, et al., Chem. Ber., 114, 1234-1255 (1981).

Shin-Etsu

Shin-Etsu Chemical Co.,Ltd.

Silicone Division Sales and Marketing Department Ⅱ < Silanes and Resins >
6-1, Ohtemachi 2-chome, Chiyoda-ku, Tokyo, Japan
Phone : +81-(0)3-3246-5131 Fax : +81-(0)3-3246-5361

Shin-Etsu Silicones of America, Inc.
1150 Damar Drive, Akron, OH 44305, U.S.A.
Phone : +1-330-630-9860 Fax : +1-330-630-9855

Shin-Etsu Silicones Europe B. V.
Bolderweg 32, 1332 AV, Almere, The Netherlands
Phone : +31-(0)36-5493170 Fax : +31-(0)36-5326459

Shin-Etsu Silicone Taiwan Co., Ltd.
Hung Kuo Bldg. 11F-D, No. 167, Tun Hua N. Rd.,
Taipei, 10549 Taiwan, R.O.C.
Phone : +886-(0)2-2715-0055 Fax : +886-(0)2-2715-0066

Shin-Etsu Silicone Korea Co., Ltd.
Danam Bldg., 9F, 120, Namdaemunno5(o)-ga,
Jung-gu, Seoul 100-704, Korea
Phone : +82-(0)2-775-9691 Fax : +82-(0)2-775-9690

Shin-Etsu Singapore Pte. Ltd.
4 Shenton Way, #10-03/06, SGX Centre Ⅱ, Singapore 068807
Phone : +65-6743-7277 Fax : +65-6743-7477

Shin-Etsu Silicones (Thailand) Ltd.
7th Floor, Harindhorn Tower, 54 North Sathorn Road,
Bangkok 10500, Thailand
Phone : +66-(0)2-632-2941 Fax : +66-(0)2-632-2945

Shin-Etsu Silicone International Trading (Shanghai) Co., Ltd.
29F Junyao International Plaza, No.789,
Zhao Jia Bang Road, Shanghai
Phone : +86-(0)21-6443-5550 Fax : +86-(0)21-6443-5868

The Development and Manufacture of Shin-Etsu Silicones are based on the following registered international quality and environmental management standards.

Gunma Complex	ISO 9001	ISO 14001
Naoetsu Plant	ISO 9001	ISO 14001
Takefu Plant	ISO 9001	ISO 14001

http://www.silicone.jp/