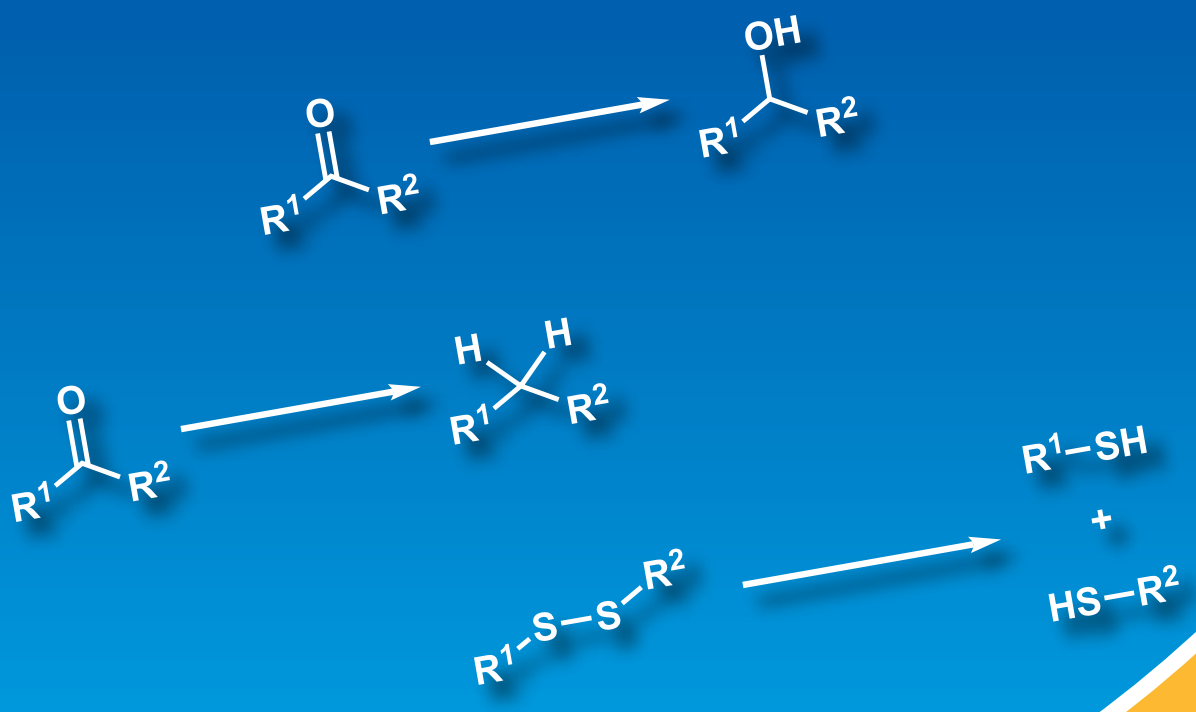
CHEMISTRY

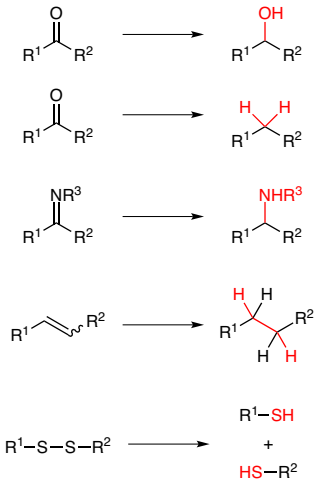
Reducing Agents



- Aluminum Hydrides
- Boranes
- Borohydrides
- Metal Hydrides
- Silanes
- Other Reduction Reagents

Reducing Agents

Reduction is a chemical reaction in which the target substances receive electrons, and is one of the most fundamental reactions in organic chemistry. Reduction reactions include the deoxygenation reaction and the hydrogenation reaction. Well-known reducing agents include metal hydrides[1)] such as lithium aluminum hydride (= $LiAlH_4$) **[L0203]**, boranes for hydride reduction, and hydrazine **[H0172]** used in the Wolff-Kishner reduction. A disconnection reaction of a disulfide moiety into two thiols is also considered a reduction.



This brochure introduces a variety of reducing agents and catalysts for reduction. We hope that this brochure will be useful for your research in organic synthesis. Catalysts for hydrogenation are introduced in another brochure, “Hydrogenation Catalysts”.

Caution: Many reducing agents may spontaneously ignite on contact with air, or may react violently with water to produce flammable gases. Sufficient safety measures, such as using safety shields, wearing protective equipment, and using extreme caution should be taken when working with these reagents as well as in their disposal.

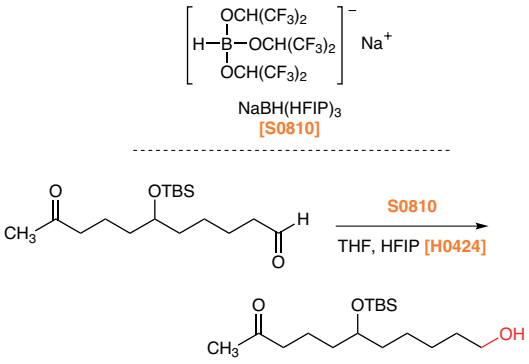
Reduction of Carbonyl Groups and Imino Group

The table below shows the reactivities of each reducing agent toward carbonyl compounds and imines. Please make use of this table as a standard for reactions.

Reagents \ Reactions	Imine → Amine	Aldehyde → Alcohol	Ketone → Alcohol	Ester → Alcohol	Amide → Amine	Carboxylic Acid → Alcohol
$NaBH_3CN$ [S0396]						
$NaBH(OAc)_3$ [S0394]						
$NaBH_4$ [S0480]						
$LiBH_4$ [L0186]						
$LiAlH_4$ [L0170]						
$THF \cdot BH_3$ [T2346]						
$Me_2S \cdot BH_3$ [D1843]						
$PhNEt_2 \cdot BH_3$ [D2581]						

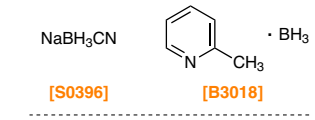
Reactivity : High | Middle | Low

Sodium tris(1,1,1,3,3,3-hexafluoroisopropoxy)borohydride (= $NaBH(HFIP)_3$) **[S0810]** is a selective reducing agent developed by Toshima *et al.* Aldehydes are selectively reduced in the presence of ketones and other reducible functions using **S0810** to afford the corresponding primary alcohols in high yields.[2)]

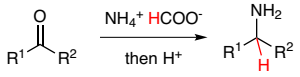


Reductive Amination

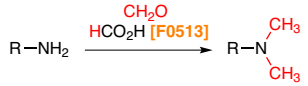
Reductive amination is a synthetic method that converts aldehydes and ketones into an amino group with an amine and a reducing agent. First, carbonyl groups and an amine form imines or iminium salts and subsequent nucleophilic attack by a reducing agent gives the amine moiety. The Leuckart reaction[3)] and Eschweiler-Clarke reaction[4)] are known as classical methods and formic acid **[F0513]** is used as a reducing agent in these reactions. Recently, sodium cyanoborohydride **[S0396]** has been frequently used for reductive amination, in what is called the Borch reaction.[5)] However, this method has a problem in that **S0396** has strong toxicity due to the cyano group. Meanwhile, Kikukawa *et al.* have reported a new method using 2-picoline borane **[B3018]**.[6)] **B3018** is less toxic than **S0396** and can be applied in both aqueous and neat conditions.



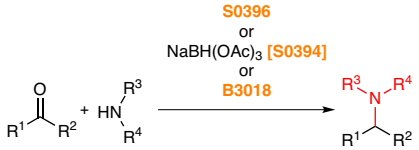
Leuckart reaction



Eschweiler-Clarke reaction

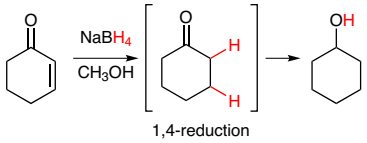


Borch reaction

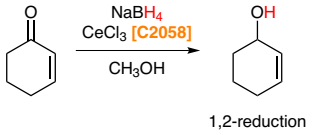


Luche Reduction

When α,β-unsaturated ketones are reduced with sodium borohydride **[B0480]**, 1,4-reduction, not 1,2-reduction, preferentially occurs. However, Luche *et al.* have found that 1,2-reduction preferentially occurred by adding cerium(III) chloride **[C2058]**.[7)] The difference in reactivity can be explained with HSAB theory. A "hard" nucleophile is required for 1,2-reduction, whereas a hydride of **S0480** is originally regarded as a "soft" nucleophile, resulting in 1,4-reduction. However, it is considered that the nucleophile turns "hard" in the presence of **C2058** and alcohol. In addition, since the cerium cation works as a Lewis acid, which promotes the electrophilicity of the carbonyl group, the 1,2-addition preferentially occurs. Incidentally, an aldehyde is not reduced under this method because it forms an acetal, which is inert under these conditions.



1,4-reduction

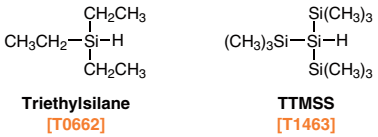


1,2-reduction

Silane Reduction

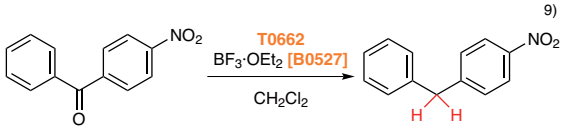
Hydrosilanes are utilized in reduction as a hydride or a hydrogen radical source since the hydrogen atom has lower electronegativity than silicon. For instance, triethylsilane **[T0662]** is known as a reducing agent in the presence of a metal catalyst[8)] and Lewis acid[9)] and can reduce carbonyl groups and hydroxy groups into methylene moieties. **T0662** is also used in the dehalogenation[10)] reaction and in the reduction of olefins.[11)]

Tris(trimethylsilyl)silane (= TTMSS) **[T1463]** is mainly used as a hydrogen radical source in the dehalogenation reaction.[12)] In this manner, hydrosilanes and tin hydrides are currently used complementarily.

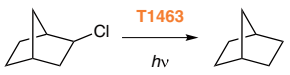


Triethylsilane [T0662] **TTMSS** [T1463]

9)



12)



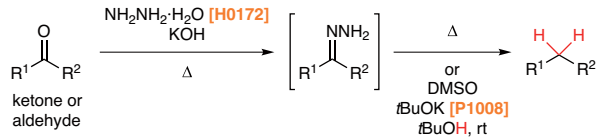
Wolff-Kishner Reduction and Clemensen Reduction

Both Wolff-Kishner reduction[13] and Clemensen reduction[14] are known as reactions to convert carbonyl groups into methylene groups. The Wolff-Kishner reduction can reduce carbonyl groups to methylene moieties in the presence of hydrazine [H0172], strong base, and alcohol. This reaction conventionally requires strong base and intense heat conditions, but an improved method to use a Lewis acid catalyst and a silylhydrazine derivative (Myers modification) has been developed,[15] which proceeds at room temperature.

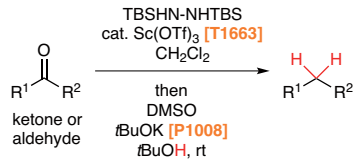
The Clemensen reduction is operated by the treatment of zinc under acidic conditions. Zinc amalgam had been used at first, but a non-aqueous modification using zinc powder and hydrogen chloride in organic solvent has been developed[16] and is utilized widely since mercury in amalgam is highly harmful.

The Wolff-Kishner reduction and Clemensen reduction are operated under basic and acidic conditions, respectively, so the two reactions can be used complementarily.

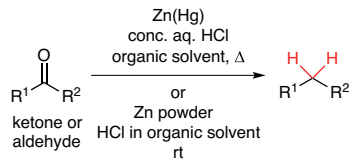
Wolff-Kishner reduction



Myers modification

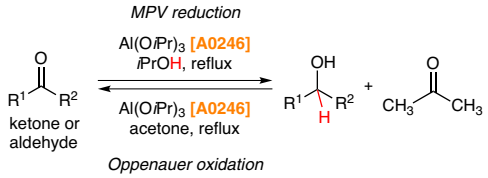


Clemensen reduction



Meerwein-Ponndolf-Verley Reduction

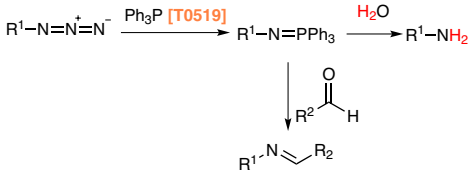
In the Meerwein-Ponndolf-Verley (MPV) reduction, ketones and aldehydes can be reduced to alcohols by the treatment of aluminum isopropoxide [A0246] in isopropyl alcohol [I0163] solvent with heat.[17] This reaction is an equilibrium reaction, so an excess amount of A0246 is needed to bias the reaction toward the desired alcohol. This reaction has an advantage in that it does not affect other functional groups. Following the first report, a modified method using a catalytic amount of samarium(II) iodide[18] [S0494] instead of an excess amount of A0246 and asymmetric MPV reactions[19] was reported. Incidentally, the Oppenauer oxidation[20] is regarded as an opposite reaction of MPV reduction and it proceeds under acetone solvent to oxidize alcohols to carbonyl groups.



SmI_2-catalyzed MPV reduction

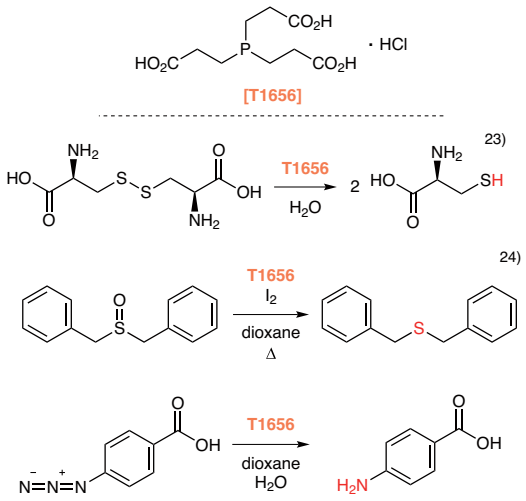
Staudinger Reaction

The Staudinger reaction is utilized to convert an azide to an amine[21] and can be regarded as a reduction in the sense of the addition of a hydrogen atom. When an azide is treated with triphenylphosphine [T0519], an iminophosphorane is formed with the elimination of a nitrogen molecule. The iminophosphorane is hydrolyzed to give the amine moiety. In contrast, the iminophosphorane gives an imine via the aza-Wittig reaction when treated with aldehydes or ketones.[22]



Reducing Agent to Disconnect Disulfide Bond

Tris(2-carboxyethyl)phosphine hydrochloride **[T1656]** can reduce a disulfide bond to give two thiols.[23] In addition, **T1656** can remove the oxygen atom on *N*-oxides and sulfoxides and can be applied to the Staudinger reaction.[24] In this manner, **T1656** shows interesting effects in the reductions of heteroatoms.



References

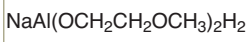
1) Review: J. Málek, M. Černý, *Synthesis* **1972**, 217.
2) Y. Kuroiwa, S. Matsumura, K. Toshima, *Synlett* **2008**, *16*, 2523.
3) R. Leuckart, *Ber.* **1885**, *18*, 2341.
4) a) W. Eschweiler, *Ber.* **1905**, *38*, 880.
   b) H. T. Clarke, H. B. Gillespie, S. Z. Weisshaus, *J. Am. Chem. Soc.* **1933**, *55*, 4571.
5) a) R. F. Borch, M. D. Bernstein, H. D. Durst, *J. Am. Chem. Soc.* **1971**, *93*, 2897.
   b) R. F. Borch, A. I. Hassid, *J. Org. Chem.* **1972**, *37*, 1673.
6) S. Sato, T. Sakamoto, E. Miyazawa, Y. Kikugawa, *Tetrahedron* **2004**, *60*, 7899.
7) a) J. L. Luche, *J. Am. Chem. Soc.* **1978**, *100*, 2226.
   b) J.-L. Luche, L. Rodriguez-Hahn, P. Crabbé, *J. Chem. Soc., Chem. Commun.* **1978**, 601.
8) M. Mirza-Aghayan, M. Kalantari, R. Boukherroub, *Appl. Organomet. Chem.* **2019**, *33*, e4837.
9) I. Smonou, *Synth. Commun.* **1994**, *24*, 1999.
10) R. P. Allen, B. P. Roberts, C. R. Willis, *J. Chem. Soc., Chem. Commun.* **1989**, 1387.
11) A. R. Jesus, A. P. Marques, A. P. Rauter, *Pure Appl. Chem.* **2016**, *88*, 349.
12) C. Chatgilialoglu, D. Griller, M. Lesage, *J. Org. Chem.* **1988**, *53*, 3641.
13) a) Kishner, *N. J. Russ. Phys. Chem. Soc.* **1911**, *43*, 582.
   b) L. Wolff, *Ann.* **1912**, *394*, 86.
14) a) E. Clemmensen, *Ber.* **1913**, *46*, 1837.
   b) E. Clemmensen, *Ber.* **1914**, *47*, 51.
   c) E. Clemmensen, *Ber.* **1914**, *47*, 681.
15) M. E. Furrow, A. G. Myers, *J. Am. Chem. Soc.* **2004**, *126*, 5436.
16) a) S. Yamamura, S. Ueda, Y. Hirata, *Chem. Commun.* **1967**, 1049.
   b) S. Yamamura, Y. Hirata, *J. Chem. Soc. C* **1968**, 2887.
   c) M. Toda, M. Hayashi, Y. Hirata, S. Yamamura, *Bull. Chem. Soc. Jpn.* **1972**, *45*, 264.
17) a) H. Meerwein, R. Schmidt, *Ann.* **1925**, *444*, 221.
   b) A. Verley, *Bull. Soc. Chim. Fr.* **1925**, *37*, 537.
   c) W. Ponndorf, *Angew. Chem.* **1926**, *39*, 138.
18) J. L. Namy, J. Souppe, J. Collin, H. B. Kagan, *J. Org. Chem.* **1984**, *49*, 2045.
19) D. A. Evans. S. G. Nelson, M. R. Gagne, A. R. Muci, *J. Am. Chem. Soc.* **1993**, *115*, 9800.
20) R. V. Oppenauer, *Rec. Trav. Chim. Pays-Bas* **1937**, *56*, 137.
21 H. Staudinger, J. Meyer, *Helv. Chim. Acta* **1919**, *2*, 635.
22) T. Sasaki, S. Eguchi, T. Okano, *J. Am. Chem. Soc.* **1983**, *105*, 5912.
23) J. A. Burns, J. C. Butler, J. Moran, G. M. Whitesides, *J. Org. Chem.* ***1991***, *56*, 2648.
24) A. M. Faucher, C. Grand-Maître, *Synth. Commun.* **2003**, *33*, 3503.

Aluminum Hydrides

L0203 25g 100g

Lithium Aluminum Hydride
(Powder)
CAS RN: 16853-85-3

S0467 25g 100g 500g



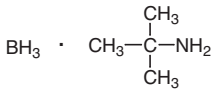
Sodium Dihydridobis(2-methoxyethoxy)aluminate
(70% in Toluene, *ca.* 3.6mol/L)
CAS RN: 22722-98-1

Boranes

B5082 5g 25g

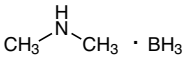
Borane - Ammonia Complex
CAS RN: 13774-81-7

B1264 25g 100g



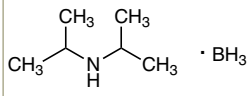
Borane - *tert*-Butylamine Complex
CAS RN: 7337-45-3

D1842 25g 100g 500g



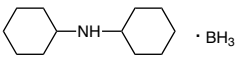
Dimethylamine Borane
CAS RN: 74-94-2

B5544 25g



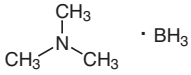
Borane - Diisopropylamine Complex
CAS RN: 55124-35-1

B5545 5g 25g



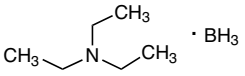
Dicyclohexylamine Borane
CAS RN: 131765-96-3

T1181 25g



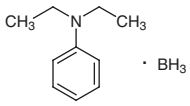
Trimethylamine Borane
CAS RN: 75-22-9

T1180 25g



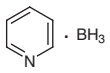
Triethylamine Borane
CAS RN: 1722-26-5

D2581 25g 100g



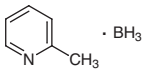
N,N-Diethylaniline Borane
CAS RN: 13289-97-9

B1569 25mL



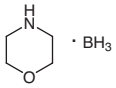
Borane - Pyridine Complex
CAS RN: 110-51-0

B3018 5g 25g



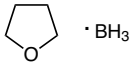
Borane - 2-Methylpyridine Complex
CAS RN: 3999-38-0

M0898 5g 25g



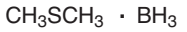
Borane - Morpholine Complex
CAS RN: 4856-95-5

T2346 100mL 500mL



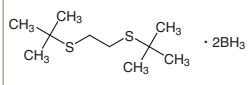
Borane - Tetrahydrofuran Complex (8.5% in Tetrahydrofuran, *ca.* 0.9mol/L)
CAS RN: 14044-65-6

D1843 25mL 100mL



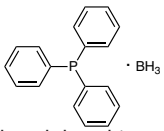
Dimethyl Sulfide Borane
CAS RN: 13292-87-0

B1827 1g



1,2-Bis(*tert*-butylthio)-ethane Borane
CAS RN: 71522-78-6

T1789 25g



Triphenylphosphine Borane
CAS RN: 2049-55-0

Borohydrides

S0480 25g 100g 500g

Sodium Borohydride
CAS RN: 16940-66-2

L0186 100mL

Lithium Borohydride
(*ca.* 4mol/L in Tetrahydrofuran)
CAS RN: 16949-15-8

P1681 25g 100g

Potassium Borohydride
CAS RN: 13762-51-1

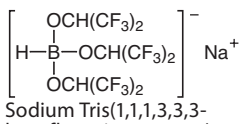
S0394 25g 100g

Sodium Triacetoxyborohydride
CAS RN: 56553-60-7

S0396 5g 25g 250g

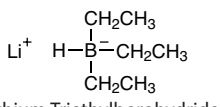
Sodium Cyanoborohydride
CAS RN: 25895-60-7

S0810 5g



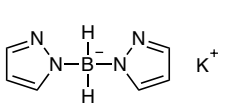
Sodium Tris(1,1,1,3,3,3-hexafluoroisopropoxy)-borohydride
CAS RN: 139494-68-1

L0190 100mL 500mL



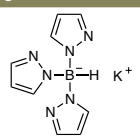
Lithium Triethylborohydride
(*ca.* 12% in Tetrahydrofuran, *ca.* 1.0mol/L)
CAS RN: 22560-16-3

P1439 1g 5g



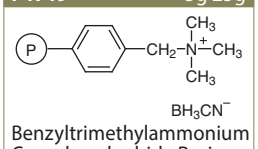
Potassium Bis(1-pyrazolyl)-borohydride
CAS RN: 18583-59-0

P1440 1g 5g



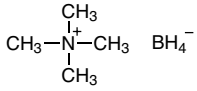
Potassium Tris(1-pyrazolyl)-borohydride
CAS RN: 18583-60-3

P1719 5g 25g



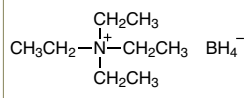
Benzyltrimethylammonium Cyanoborohydride Resin cross-linked with 10% DVB
(30-50mesh) (2.6-3.0mmol/g)

T0852 5g 25g



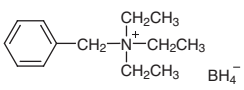
Tetramethylammonium Borohydride
CAS RN: 16883-45-7

T0837 5g 25g



Tetraethylammonium Borohydride
CAS RN: 17083-85-1

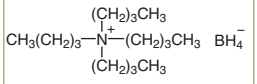
B3128 5g 25g



Benzyltriethylammonium Borohydride
CAS RN: 85874-45-9

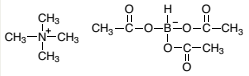
Please inquire for pricing and availability of listed products to our local sales representatives.

T0917 5g 25g



Tetrabutylammonium Borohydride
CAS RN: 33725-74-5

T1553 5g 25g



Tetramethylammonium Triacetoxyborohydride
CAS RN: 109704-53-2

Metal Hydrides

S0481 100g 500g

NaH

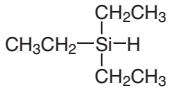
Sodium Hydride (60%, dispersion in Paraffin Liquid)
CAS RN: 7646-69-7

Z0010 1g 5g 25g

Zirconocene Chloride Hydride
CAS RN: 37342-97-5

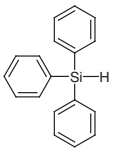
Silanes

T0662 25mL 250mL



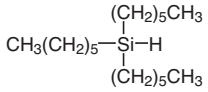
Triethylsilane
CAS RN: 617-86-7

T0661 5g 25g



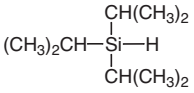
Triphenylsilane
CAS RN: 789-25-3

T1334 10g



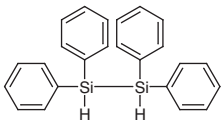
Trihexylsilane
CAS RN: 2929-52-4

T1533 5mL 25mL 100mL



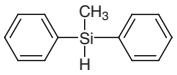
Triisopropylsilane
CAS RN: 6485-79-6

T1896 1g 5g



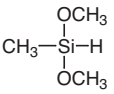
1,1,2,2-Tetraphenyldisilane
CAS RN: 16343-18-3

D1825 25mL



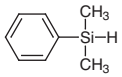
Methyldiphenylsilane
CAS RN: 776-76-1

D2100 25mL 100mL



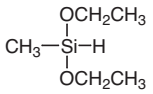
Dimethoxy(methyl)silane
CAS RN: 16881-77-9

D2196 5mL 25mL



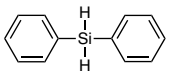
Dimethylphenylsilane
CAS RN: 766-77-8

D2403 25mL



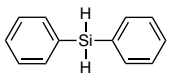
Diethoxymethylsilane
CAS RN: 2031-62-1

D2406 5g 25g



Diphenylsilane (>97.0%)
CAS RN: 775-12-2

D2820 5g 25g



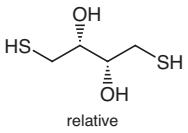
Diphenylsilane (>98.0%)
CAS RN: 775-12-2

P1291 5mL 25mL

Phenylsilane
CAS RN: 694-53-1

Other Reduction Reagents

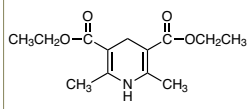
D1071 1g 5g 25g



relative

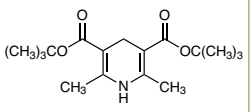
DL-Dithiothreitol
CAS RN: 3483-12-3

D3775 1g 5g 25g



Hantzsch Ester
CAS RN: 1149-23-1

D4311 1g 5g



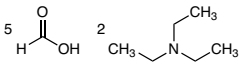
Di-*tert*-butyl 1,4-Dihydro-2,6-dimethyl-3,5-pyridinedicarboxylate
CAS RN: 55536-71-5

D5792 5g 25g 100g

Na

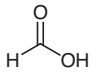
SD Super Fine™ (Sodium 25wt% dispersion in mineral oil)
CAS RN: 7440-23-5

F1202 25mL 100mL



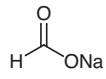
TEAF
CAS RN: 15077-13-1

F0513 300mL



Formic Acid
CAS RN: 64-18-6

S0807 500g



Sodium Formate
CAS RN: 141-53-7

H0172 25mL 500mL

$H_2NNH_2 \cdot H_2O$

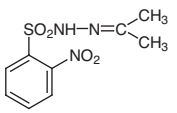
Hydrazine Monohydrate
CAS RN: 7803-57-8

H1221 300mL

HI

Hydriodic Acid (57%)
CAS RN: 10034-85-2

I0777 1g 5g



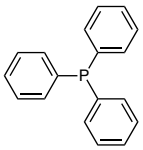
IPNBSH
CAS RN: 6655-27-2

S0494 25mL 100mL

SmI_2

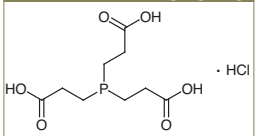
Samarium(II) Iodide (*ca.* 0.1mol/L in Tetrahydrofuran)
CAS RN: 32248-43-4

T0519 25g 100g 500g



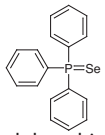
Triphenylphosphine
CAS RN: 603-35-0

T1656 1g 5g 25g



Tris(2-carboxyethyl)-phosphine Hydrochloride
CAS RN: 51805-45-9

T1819 5g



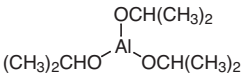
Triphenylphosphine Selenide
CAS RN: 3878-44-2

C2058 5g 25g

$CeCl_3$

Cerium(III) Chloride Anhydrous
CAS RN: 7790-86-5

A0246 100g 500g



Aluminum Isopropoxide
CAS RN: 555-31-7

Ordering and Customer Service

TCI AMERICA
Tel : 800-423-8616 / 503-283-1681
Fax : 888-520-1075 / 503-283-1987
E-mail : Sales-US@TCIchemicals.com

TCI EUROPE N.V.
Tel : +32 (0)3 735 07 00
Fax : +32 (0)3 735 07 01
E-mail : Sales-EU@TCIchemicals.com

TCI Deutschland GmbH
Tel : +49 (0)6196 64053-00
Fax : +49 (0)6196 64053-01
E-mail : Sales-DE@TCIchemicals.com

Tokyo Chemical Industry UK Ltd.
Tel : +44 (0)1865 784560
Fax : +44 (0)1865 784561
E-mail : Sales-UK@TCIchemicals.com

TCI Chemicals (India) Pvt. Ltd.
Tel : 1800 425 7889 / 044-2262 0909
Fax : 044-2262 8902
E-mail : Sales-IN@TCIchemicals.com

梯希爱(上海)化成工业发展有限公司
Tel : 800-988-0390 / 021-67121386
Fax : 021-6712-1385
E-mail : Sales-CN@TCIchemicals.com

TOKYO CHEMICAL INDUSTRY CO., LTD.
Tel : +81 (0)3-5640-8878
Fax : +81 (0)3-5640-8902
E-mail : globalbusiness@TCIchemicals.com