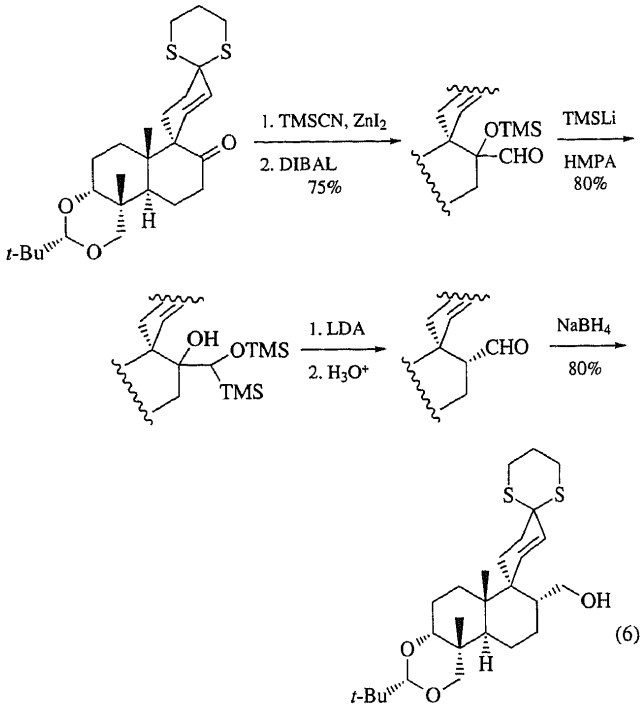
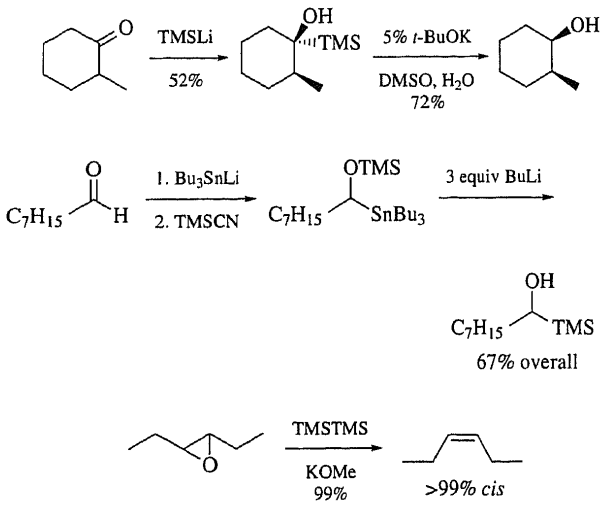


alkene can result in stereospecific inversion of the double bond stereochemistry (eq 9). The epoxidation–deoxygenation sequence has been employed as a method to protect an alkene during catalytic hydrogenation.[16] Allylsilanes may be prepared by the S_N2 displacement of allyl chlorides.[17] The reaction appears to be a direct nucleophilic displacement and does not involve electron transfer processes. TMSLi can also undergo transmetalation to a variety of other organometallic species such as ***Trimethylsilylcopper.*** Vinylsilanes can be obtained by the reaction of an alkyne with TMSLi in the presence of Mn^{II} and methylmagnesium chloride.[18] TMSLi has not been used as extensively as the more readily accessible dimethylphenylsilyllithium for generation of other silyl organometallic reagents.[4,19]



Related Reagents. Dimethyl(phenyl)silane; Hexamethyldisilane; Trimethylsilylpotassium.

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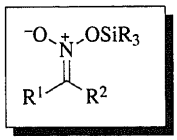
Trimethylsilyl Methanenitronate[1]



($R^1 = R^2 = H$, R_3Si = TMS)
[51146-35-1] $C_4H_{11}NO_2Si$ (MW 133.25)
($R^1 = C_5H_{11}$, $R^2 = H$, R_3Si = TBDMS)
[75157-17-4] $C_{12}H_{27}NO_2Si$ (MW 245.49)
($R^1R^2 = (CH_2)_5$, R_3Si = TBDMS)
[75157-19-6] $C_{12}H_{25}NO_2Si$ (MW 243.47)

(react with alkenes in a 1,3-dipolar cycloaddition reaction;[1c,3-5] undergo Bu_4NF-mediated diastereoselective carbonyl addition to aldehydes;[6-12] react with alkyllithium reagents to give oximes;[13] oxidative coupling leads to 1,2-dinitro alkanes;[14,15] cross coupling with silyl enol ethers or enamines gives β-nitro carbonyl derivatives;[15] conversion of thiocarbonyl to carbonyl groups;[1c,16] can be converted into carbonyl compounds (cf. Nef reaction)[17])

Alternate Name: [(trimethylsilyl)-*aci*-nitro]methane.
Physical Data: $R^1 = C_5H_{11}$, $R^2 = H$, R_3Si = TBDMS: bp 80–90 °C/0.02 mmHg. $R^1R^2 = (CH_2)_5$, R_3Si = TBDMS: bp

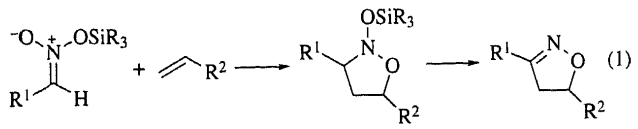
150 °C/0.01 mmHg. A more complete list of silyl nitronates is given by Torssell.[1c]

Solubility: sol pentane and in all nonprotic common organic solvents.

Preparative Methods: a large number of silylation conditions can be applied to primary or secondary nitroalkanes,[1,2] including: R_3SiCl/Et_3N (or Ag^+ or Li_2S), R_3SiOTf, LDA/R_3SiCl, R_3SiCl/DBU,[17a] silylated amides, etc. The first reports were published by Ioffe, Tartakovskii, and their colleagues in the early 1970s.[1] The silyl nitronates are isolated by nonaqueous workup and purified by bulb-to-bulb distillation, with the TBDMS derivatives being much more thermally stable than the TMS derivatives.[2] From crystal structure analyses and NMR studies it is concluded that the silyl group migrates rapidly from one nitronate oxygen to the other and that the more stable configuration of silyl nitronates derived from primary nitroalkanes is (*E*).[2,8]

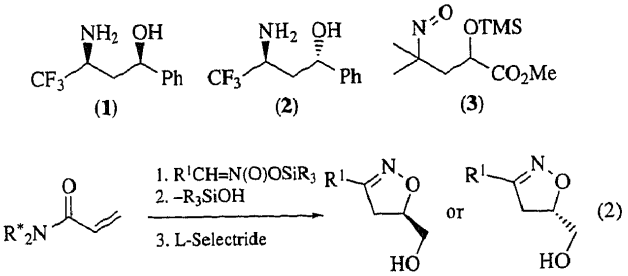
Handling, Storage, and Precautions: although there are indications that some trimethylsilyl nitronates are thermally unstable,[1c] there have been no reports of violent decompositions. Silyl nitronates are, of course, extremely sensitive to moisture, and they are more resistant to base than to acid. All silyl nitronates should be kept under an inert atmosphere and stored in a freezer.

Reactions of Silyl Nitronates with C–C Bond Formation. Silyl nitronates are synthetically equivalent to nitrile oxides in [3 + 2] cycloadditions. The [3 + 2] adducts shown in eq 1 lose trialkylsilanol very readily, with formation of Δ^2-isoxazolines.[1c,3–5] Silyl nitronates are somewhat less reactive than nitrile oxides, which is not a disadvantage in intramolecular cycloadditions.[3] The reaction is also applicable to the CF_3-substituted silyl nitronate ($R^1 = CF_3$, $R^2 = H$).[18] Depending upon the method of reduction, either the amino alcohol (**1**) or its epimer (**2**) can be obtained with a diastereoselectivity of ca. 4:1. When the silyl nitronate is derived from a secondary nitroalkane, no silanol elimination can occur; the corresponding isoxazolidines undergo a rearrangement to nitroso silyl ethers such as (**3**).[1d,19] The isoxazolidines derived from primary nitroalkanes are not only precursors to amino alcohols but also to β-hydroxy ketones. Thus the nitrile oxide/silyl nitronate [3 + 2] cycloaddition route constitutes an alternative access to aldols.[1c,20,21] This method becomes especially attractive when rendered enantioselective. Addition of a silyl nitronate from a primary nitroalkane to a chiral acrylamide (such as ***10,2-Camphorsultam***,[4] ***trans-2,5-Dimethylpyrrolidine***,[22] or Kemp–Rebek acid derivatives[5]), silanol elimination, and reductive removal of the auxiliary gives 3-substituted Δ^2-isoxazoline-5-methanols in either enantiomeric form (eq 2).



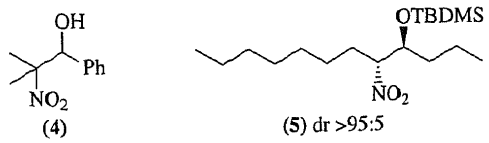
(1)

R^2 = alkyl, vinyl, phenyl, COR, $CONR_2$, CO_2R

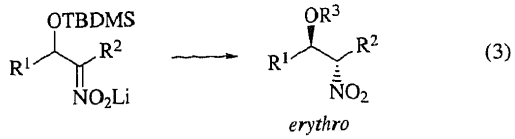


(2)

The second most important synthetic application of silyl nitronates in C–C bond-forming reactions is their fluoride-mediated addition to aldehydes.[6–12] Silyl nitronates from secondary nitroalkanes lead to free nitro aldols such as (**4**),[8] while those from primary nitro alkanes give silylated products. In contrast to the classical Henry reaction, the silyl variant is highly diastereoselective with aldehydes, furnishing *erythro-O*-silylated nitro aldols (e.g. **5**).[9] It is important that the reaction temperature does not rise above 0 °C, otherwise *threo*/*erythro* equilibration takes place. The same *erythro*-nitro aldol derivatives are available by diastereoselective protonation of silyloxy nitronates (eq 3) (usually the dr is >20:1), while the nonsilylated *threo*-epimers (R^3 = H, dr = 7:3–20:1) are formed by kinetic protonation of lithioxy lithio nitronates in THF/DMPU (eq 4).[9] Other recent modifications of the nitroaldol addition using titanium nitronates[23] or $ClSiR_3$ in situ[24] are less selective. It should also be mentioned that there are recent reports[25] about the enantioselective addition of nitromethane to aldehydes in the presence of rare earth binaphthol complexes.

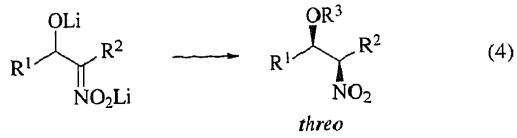


(4) (5) dr >95:5



(3)

erythro

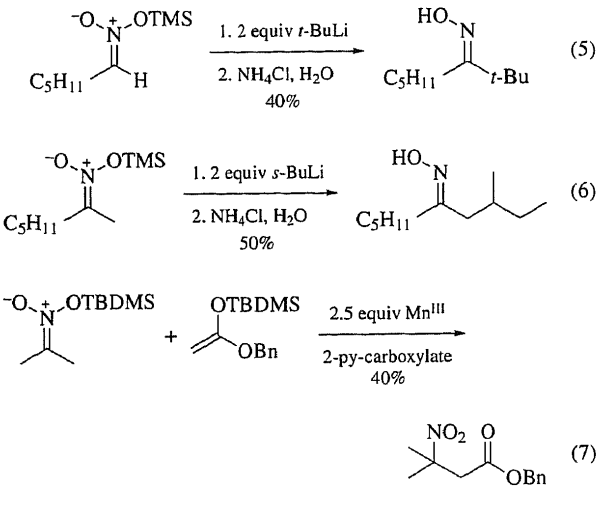


(4)

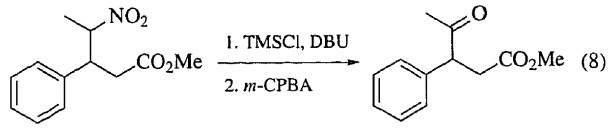
threo

Reactions of Silyl Nitronates with Strong Base.[13] With 2 equiv of an alkyllithium, the nitronates from primary nitroalkanes give oximes with the newly introduced alkyl group attached to the oxime carbon (eq 5). The analogous reaction of silyl nitronates from secondary nitroalkanes produces oximes in which chain extension has occurred in the α-position (eq 6). These reactions take place when alkyllithium is added to 0.1 molar silyl nitronate in THF at dry-ice temperature, with subsequent warming to room temperature before aqueous workup. Probably a nitrile oxide is the intermediate in the first case and a nitroso alkene in the second case. Finally, oxidative cross couplings of silyl nitronates with silyl enol ethers, ketene acet-

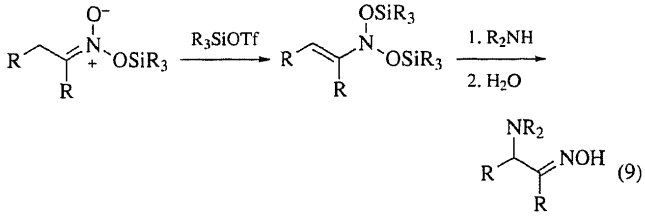
als, or enamines produce β-nitro carbonyl compounds (eq 7) or, by HNO_2 elimination, α,β-unsaturated ketones and esters.[15]



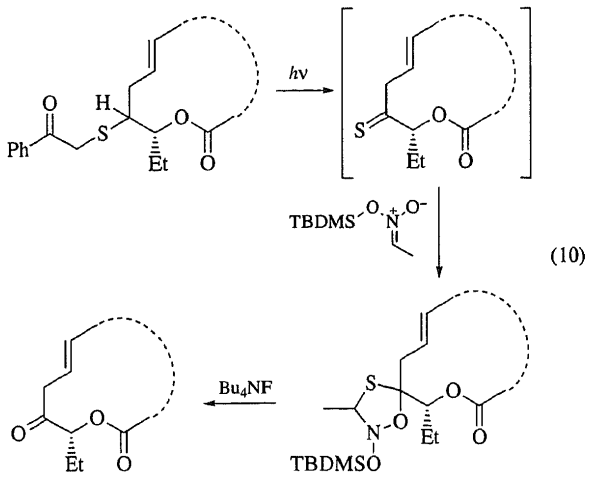
Functionalization Reactions of Silyl Nitronates. Silyl nitronates can be used for a number of transformations in which the carbon skeleton is not changed. Thus they are intermediates en route from nitroalkanes to ketones (the transform[26] of the Nef reaction). Peroxy acid treatment converts silyl nitronates, which would not survive the classical conditions of the Nef reaction, to ketones[17a] (eq 8). Aldehydes can be obtained analogously, using stannyl nitronates.[17b]



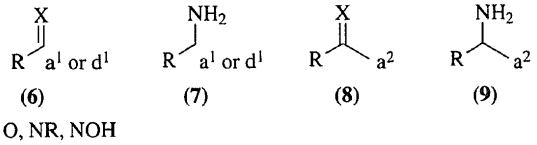
Silyl nitronates can also be further silylated to the interesting *N,N*-bis(silyloxy)enamines (eq 9).[27] In contrast to the *N,N*-bis-(lithioxy)enamines, the double bond in the bis-(silyloxy)enamines appears to have electrophilic rather than nucleophilic reactivity. With primary and secondary amines, α-amino oximes are produced (eq 9)[27] in a kind of S_N' substitution, followed by hydrolytic desilylation. In this manner, the bis-(silyloxy)enamine is reacting as a nitroso alkene.



Conversion of Thioketones to Ketones.[16] Thioketones generated by a Norrish-type photofragmentation of a sulfenyl acetophenone are trapped in situ by [3 + 2] dipolar cycloaddition with a silyl nitronate (eq 10). Fluoride treatment of the resulting heterocycle produces the ketone.[16b] This transformation is compatible with a variety of functional groups and has been used as part of a synthetic manipulation in which an α-acyl cyclic thioether is converted stereoselectively, with ring enlargement, to a ketolactone (methynolide synthesis).[16a]



Silyl Nitronate Reactivity Pattern. As illustrated by the examples described above, silyl nitronates provide a^1 and d^1 acyl and aminoalkyl synthons (**6** and **7**), as well as a^2 α-carbonyl and aminoalkyl synthetic building blocks (**8** and **9**).[1e,28]



Related Reagents. Lithium α-Lithiomethanenitronate; Nitroethane; Nitromethane; 1-Nitropropane; Phenylsulfonylnitromethane.

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18. Originally, we had problems reproducing the preparation of $F_3CCH{=}N(O)OTBDMS$ (Beck, A. K.; Seebach, D. *CB* **1991**, *124*, 2897; *CA* **1992**, *116*, 40 553c); using Torsell's procedure we are able to prepare this silyl nitronate: Marti, R. E.; Heiner, J.; Seebach, D. *LA* **1995**, in press.
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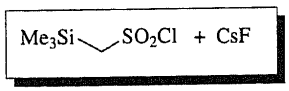
(Trimethylsilyl)methanesulfonyl Chloride–Cesium Fluoride



($Me_3SiCH_2SO_2Cl$)		
[18143-34-5]	$C_4H_{11}ClO_2SSi$	(MW 186.76)
(CsF)		
[13400-13-0]	CsF	(MW 151.91)

(source of 'free' sulfene in solution;[1] source of silylated sulfene[8])

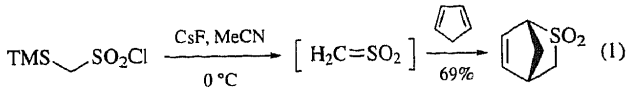
Physical Data: $Me_3SiCH_2SO_2Cl$ is a colorless liquid, bp 50–52 °C/0.6 mmHg, 57 °C/1 mmHg; mp 18 °C, n_D^{20} 1.4700,[3] 1.4680.[7a] See also ***Cesium Fluoride***.

Solubility: acetonitrile is the preferred solvent due to solubility of CsF and absence of hydrogen bonding; $Me_3SiCH_2SO_2Cl$ is soluble in most organic solvents.

Preparative Methods: $Me_3SiCH_2SO_2Cl$ is: (1) formed in 58% isolated yield via reaction of ***(Chloromethyl)trimethylsilane*** with ***Thiourea*** in ethanol followed by concentration and chlorination in water, extraction, and distillation;[2] (2) formed in 63% isolated yield by ***Peracetic Acid*** oxidation of (trimethylsilyl)methanethiol followed by treatment with ***Phosphorus(V) Chloride***;[2] (3) formed in 84% yield through reaction of Me_3SiCH_2Cl with ***Magnesium*** followed by sequential reaction of the Grignard reagent with ***Sulfur Dioxide*** followed by ***Chlorine***;[3] and (4) formed in 53% yield through reaction of tetramethylsilane with ***Sulfuryl Chloride***.[7a]

Handling, Storage, and Precautions: like most sulfonyl chlorides, the title compound hydrolyzes slowly to produce HCl and therefore should be kept dry. The byproduct of hydrolysis is hexamethyldisiloxane. Hydrolysis is very rapid with 5% NaOH solution.[7a]

Formation of Sulfene Adducts. A widely used procedure for the generation of sulfene involves the treatment of ***Methanesulfonyl Chloride*** with ***Triethylamine***. While adducts of sulfene, generated by this route, can usually be isolated in satisfactory yield, the amine or its acid salt may isomerize or decompose base- or acid-sensitive reaction partners. Furthermore, the interpretation of reaction mechanisms can sometimes be complicated by the presence of the amine. Thus the amine may form a complex with sulfene prior to its reaction with other substrates. In the presence of a fluoride ion source such as CsF, $Me_3SiCH_2SO_2Cl$ undergoes fluorodesilylation to give sulfene which can be trapped with ***Cyclopentadiene*** giving the Diels–Alder adduct 2-thiabicyclo[2.2.1]hept-5-ene 2,2-dioxide in 69% yield (eq 1). The same reaction fails when mesyl chloride–triethylamine is used as a sulfene source. Additional examples of sulfene adducts, including a number of thietane *S,S*-dioxides, formed from $Me_3SiCH_2SO_2Cl$ are given in Table 1.[1,2,5,8] This procedure can also be used with homologs of $Me_3SiCH_2SO_2Cl$ such as $Me_3SiCHRSO_2Cl$, $(Me_3SiCH_2SO_2)_2O$, $(Me_3SiCHRSO_2)_2O$, $Me_3SiCH_2S(O)Cl$,[4] and 1-(trimethylsilyl)-cyclopropanesulfonyl chloride.[5,6] If $Me_3SiCH_2SO_2Cl$ is treated with triethylamine in the presence of the electron-rich alkene ***Ketene Diethyl Acetal***, then the silylated sulfene trimethylsilylthioformaldehyde *S,S*-dioxide ($Me_3SiCH{=}SO_2$) is trapped.[8] The mechanism of hydrolysis of $Me_3SiCH_2SO_2Cl$ in the presence of KF has been studied.[3]



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