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PROTECTION FOR THE ALKYNE –CH

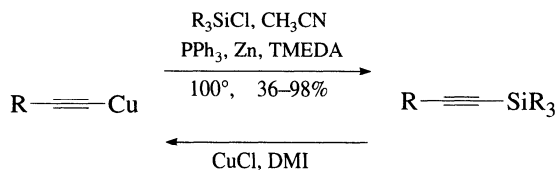
Trimethylsilyl, 655
Triethylsilyl, 656
t-Butyldimethylsilyl, 656
Thexyldimethylsilyl, 656
Dimethyl[1,1-dimethyl-3-(tetrahydro-2*H*-pyran-2-yloxy)propylsilyl, 657
Biphenyldimethylsilyl, 657
Triisopropylsilyl, 657
Biphenyldiisopropylsilyl, 657
2-(2-Hydroxypropyl), 658

Protection of an acetylenic hydrogen is often necessary because of its acidity. The bulk of a silane can protect an acetylene against catalytic hydrogenation because of rate differences between an olefin (primary or secondary) vs. the more hindered protected alkyne.¹ Trialkylsilylacetylenes are often used as a convenient method for introducing an acetylenic unit because they tend to be easily handled liquids or solids, as opposed to gaseous acetylene.

Formation

1. Trialkylsilanes are usually formed by the addition of a lithium or Grignard reagent to the silyl chloride,² and thus, discussions related to the formation of the silyl acetylene bond will be kept to a minimum. Silyl acetylenes are prepared from the alkynylcopper(I) reagents in the presence of PPh₃, Zn or TMEDA in CH₃CN at 100°, 36–98% yield.³ It is interesting to note that the

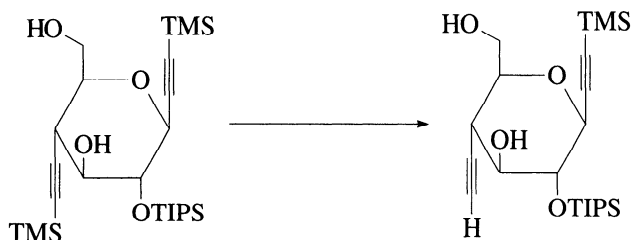
reaction can be reversed to give the alkynylcopper(I) reagent in the presence of CuCl and 1,3-dimethyl-2-imidazolidinone.⁴



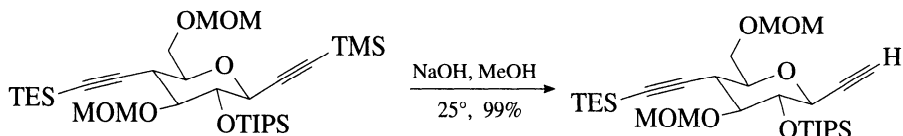
Trimethylsilylalkyne (TMS-alkyne)

Cleavage

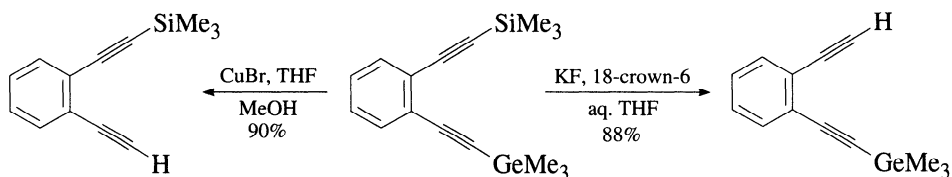
1. KF, MeOH, 50°, 89% yield.^{5,6}
2. AgNO₃, 2,6-lutidine, 90% yield.⁷
3. AgNO₂, MeOH, H₂O, 24°, cool to 0°, add KCN, then HCl, 96% yield.^{8,9}
The reduced electron density of the propargylic alkyne directs the electrophilic silver to the other alkyne and activates it for cleavage.



4. Bu₄N⁺ F⁻, THF, rt, quant.¹⁰
5. K₂CO₃, MeOH¹⁰ or KOH, MeOH, 76%, 99% yield.^{11,12} Under the basic conditions shown in the example, the more electron-deficient silylalkyne will be cleaved faster.¹³

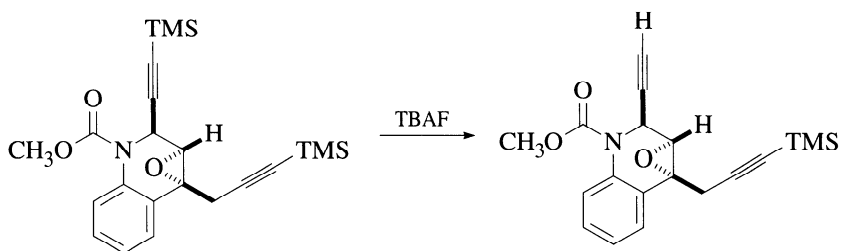


6. KF, 18-crown-6, aq. THF, 88% yield.¹⁴

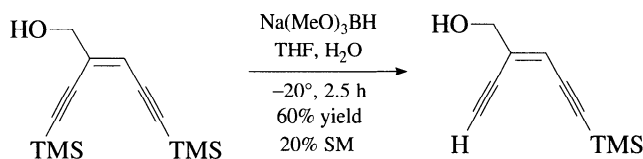


In a similar example, a trimethylsilyl group was cleaved with NaOH, MeOH, H₂O in the presence of a triethylgermyl group.¹⁵ The latter group can also be cleaved with methanolic HClO₄; the rate increases with increasing electron density.¹⁶

7. Bu₄N⁺ F⁻, 0.4 eq., THF, MeOH, -20° to -10°, 98% yield.¹⁷



8. Na(MeO)₃BH, THF, H₂O, -20°, 2.5 h, 60% yield + 20% starting material (SM).⁶



9. MeLi/LiBr.¹⁸
 10. Amberlyst basic resin, MeOH, 80–98% yield.¹⁹
 11. LiOH, THF, H₂O, 1 h, 98% yield. A TIPS-alkyne is stable to these conditions.²⁰

Triethylsilylalkyne (TES-alkyne)

The relative rates of cleavage in aqueous, methanolic alkali at 29.4° for the following silanes are PhC≡CSiMe₃/PhC≡CSiEtMe₂/PhC≡CSiEt₂Me/PhC≡CSiEt₃/PhC≡CSiPh₃, 277:49:7.4:1:11.8.²¹ A TES group can be cleaved selectively in the presence of a TBDMS group (*t*-BuOK, MeOH, 40°, 65%).⁸

t-Butyldimethylsilylalkyne and Thexyldimethylsilylalkyne (TBDMS- and TDS-alkyne)

Formation

For the TBDMS group, KHMDS, THF, TBDMSOTf, -78°, 98% yield.⁸ The TDS group behaves similarly, except that it is slightly more hindered.

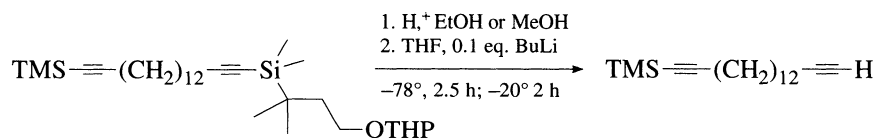
Cleavage

$\text{Bu}_4\text{N}^+ \text{F}^-$, THF, -23° , 75% yield.^{22,23}

Dimethyl[1,1-dimethyl-3-(tetrahydro-2H-pyran-2-yloxy)propylsilylalkyne]
(DOPS-alkyne)

Cleavage

THF, 0.1 eq. BuLi, -78° , 2.5 h; -20° , 2 h.¹⁰



Protection of the OH with an alcohol-protective group gives this approach considerable versatility

Biphenyldimethylsilylalkyne (BDMS-alkyne)

Formation

BuLi, BDMSCl, THF, 75–98% yield. The advantage of this group is that many of the derivatives tend to be crystalline and thus provide a safe alternative for purification. Some smaller silylalkynes have been reported to explode upon distillation.²⁴

Cleavage

K_2CO_3 , MeOH, 72–98% yield. Cleavage occurs selectively in the presence of biphenyldiisopropylalkyne.²⁴

Triisopropylsilylalkyne (TIPS-alkyne)

Cleavage

TBAF, THF, H_2O , 20° , 99% yield.²⁵

Biphenyldiisopropylsilylalkyne (BDIPS-alkyne)

Formation

BuLi, BDIPSCl, THF, 81% yield.²⁴

Cleavage

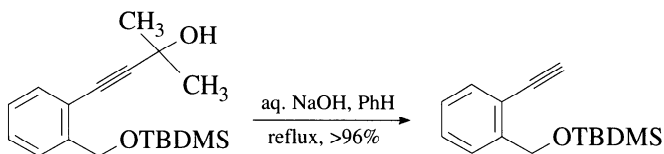
The cleavage of this group is reported to be similar to that of the triisopropylsilyl analogue.²⁴

2-(2-Hydroxypropyl)alkyne [(Me₂C(OH)-alkyne)]**Formation**

In this case, the low-cost 2-methyl-2-hydroxy-3-butyne is used as a convenient source of acetylene.

Cleavage

NaOH, benzene, reflux, > 96% yield.²⁶⁻²⁸



Ref. 26

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