Alkenyl Silanes – Synthesis and Applications

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10th December 2010

Literature Review Presentation

Overview

Introduction

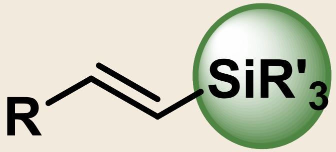
Synthesis of Alkenyl Silanes

- Alkynes
- Silyl Alkynes
- Terminal Vinyl Silanes
- Aldehydes

Applications of Alkenyl Silanes

- Carbon-Oxygen Bond Formations
- Carbon-Carbon Bond Formations

Introduction



Advantages of Alkenyl Silanes

- behaves as latent functional groups unmasked through oxidation
- activated under mild fluoride conditions
- sufficiently stable to acid/base conditions and silica gel to carry through synthesis
- relatively cheap and wide range of silyl precursors commercially available
- organosilanes and reaction by-products are relatively non-toxic

Disadvantages of Alkenyl Silanes

Si-C bond lacks significant dipole and requires activation either by a heteroatom substituent or a fluoride source

Types of Alkenyl Silane Substitution

- all alkyl – TMS, TES, TBDMS etc.
- oxygen – $SiR_n(OR)_{3-n}$, $SiMe_2(OH)$, cyclic siloxanes
- hydrogen
- halides – fluoro, chloro
- ‘safety-catch silanols’ – reveals silanol under fluoride or basic conditions

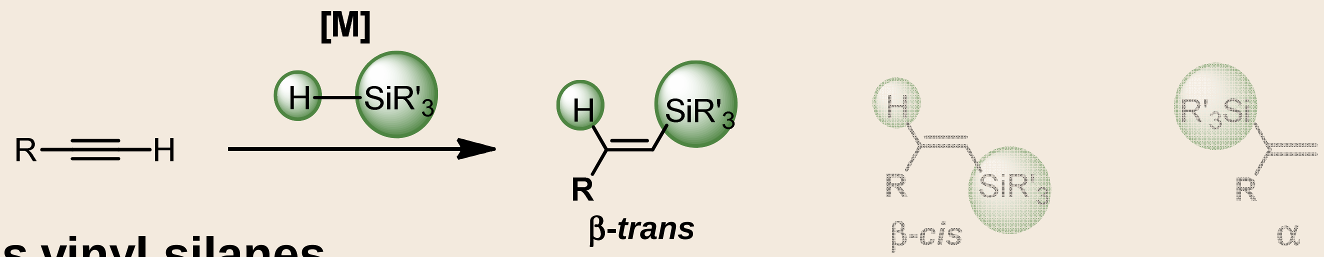
Siletanes; Triallylsilanes; Dimethylbenzyl, phenyl, 2-pyridyl, 2-thienylsilanes

Synthesis of Alkenyl Silanes

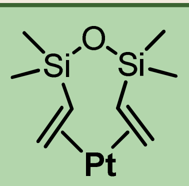
- Alkynes
  - Hydrosilylation
  - Silylformylation
  - (Carbonylative) Silylcarbocyclisation
- Silyl Alkynes
- Terminal Vinyl Silanes
- Aldehydes

Alkynes - Hydrosilylation

Terminal Alkynes



<u>β-*trans* vinyl silanes</u>



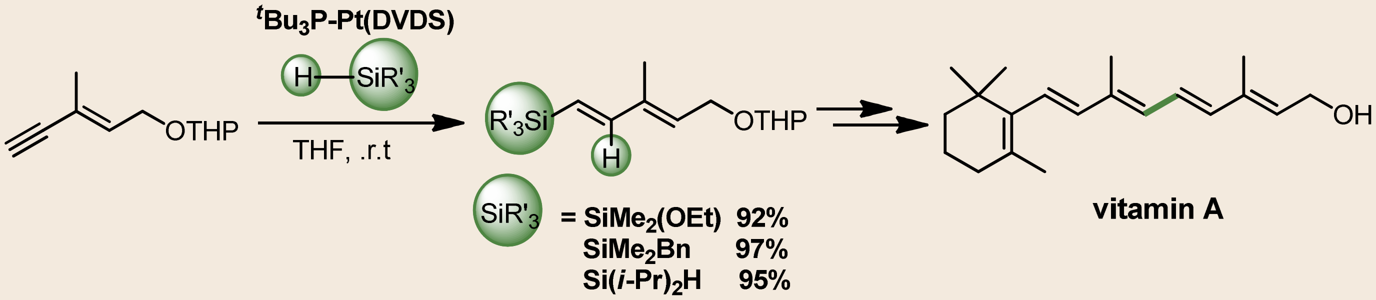
^{t}Bu$_3$P-Pt(DVDS)

Karstedt's catalyst

- Improved reactivity and regioselectivity compared to $H_2(PtCl_6).xH_2O$
- < 1 mol% loading

Platinum-based catalysts (Speier's, $H_2(PtCl_6).6H_2O$ and Karstedt's) effect *syn*-hydrosilylation of terminal alkynes to provide *trans*-vinyl silanes exclusively.

López and co-workers have demonstrated the tolerance of Karstedt's catalyst to a wide variety of Si substituents in the synthesis of silyl dienes.

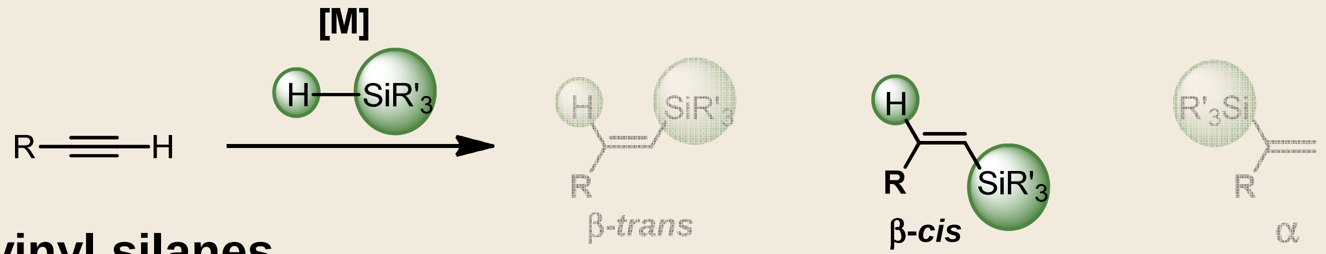


vitamin A

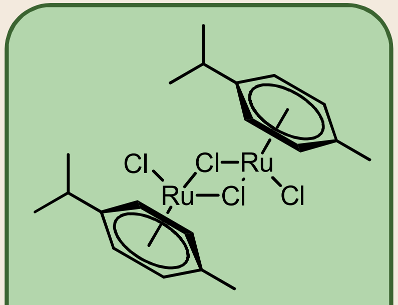
For the synthesis of Karstedt's catalyst: Chandra, G.; Lo, P.Y.; Hitchcock, P.B.; Lappert, M.F. *Organomet.* **1987**, *6*, 191-192.
Montenegro, J.; Bergueiro, J.; Saá, C.; López, S. *Org. Lett.* **2009**, *11*, 141-144.

Alkynes - Hydrosilylation

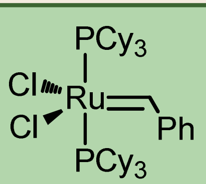
Terminal Alkynes



β-*cis* vinyl silanes

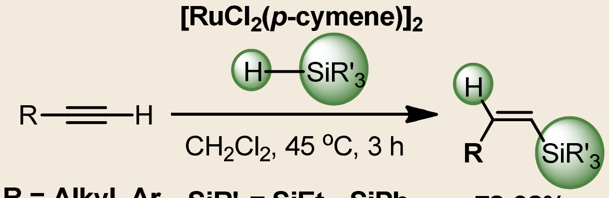


[RuCl$_2$(*p*-cymene)]$_2$
aka magic dust



Grubbs 1st Gen.

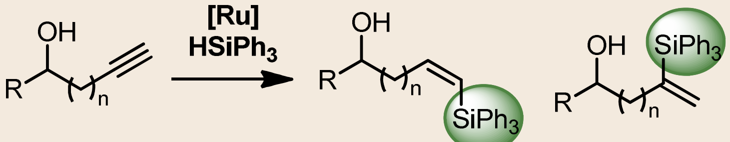
Ruthenium-based catalysts mediate the *anti*-hydrosilylation of terminal alkynes. Regio- and stereoselectivities are influenced by Si substituents and the proximity of free hydroxyl groups.



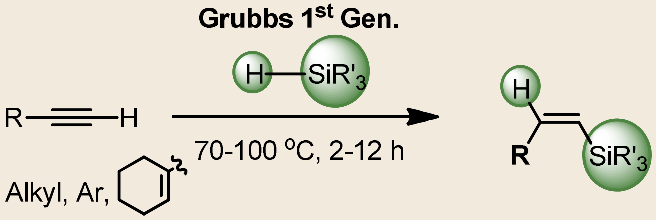
R = Alkyl, Ar,
CH_2OR,
$(CH_2)_2CO_2R$

SiR'_3= $SiEt_3$, $SiPh_3$

78-98%
***Z*:*E* > 96:4**

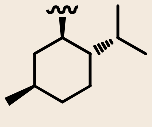


n	yield/%	β-*cis*	:	α
0	60	13	:	87
1	59	2	:	98
2	53	92	:	8
3	61	96	:	4



R = Alkyl, Ar,

SiR'_3	yield/% (*Z*:*E*)
$SiMePh_2$	>75 (>14:1)
$Si(OEt)_3$	40 (1.3:1)
$SiPh_2OR^*$	>95 (>10:1)

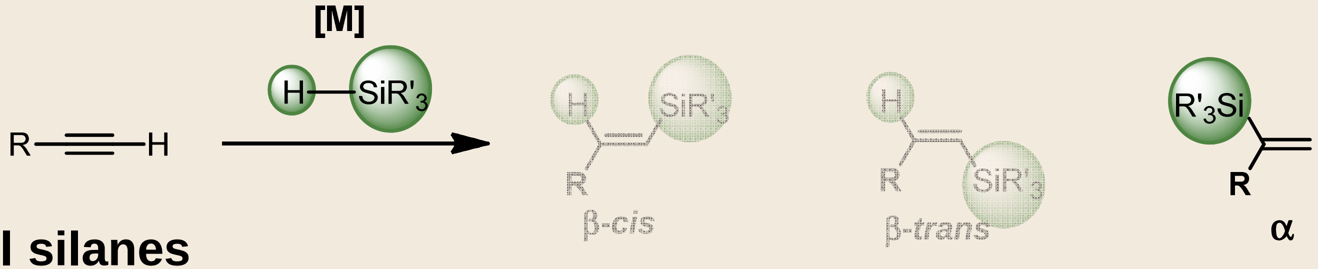


R*

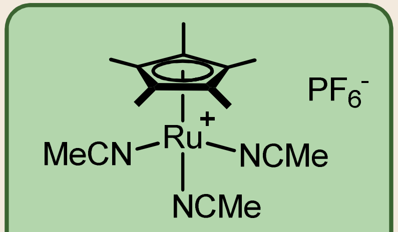
[RuCl$_2$(*p*-cymene)]$_2$ catalyst: Chang, S.; Na, Y. *Org. Lett.* **2000**, *2*, 1887-1889.
Grubbs 1st generation catalyst: Maifield, S.V.; Tran, M.N.; Lee, D. *Tetrahedron Lett.* **2005**, *46*, 105-108.

Alkynes - Hydrosilylation

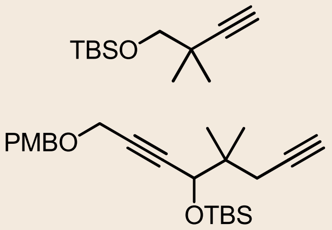
Terminal Alkynes



α vinyl silanes



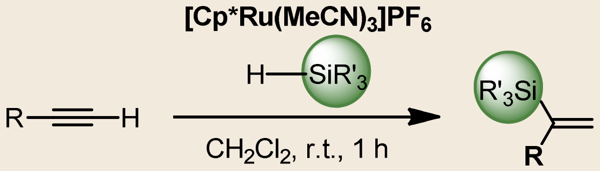
[Cp*Ru(MeCN)$_3$]PF$_6$



no reaction

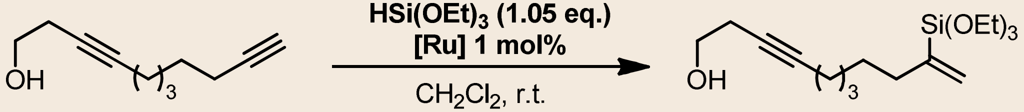
The cyclopentadienylruthenium complex developed by Trost *et al.* provides 1,1-disubstituted vinyl silanes.

The reaction proceeds smoothly in the presence of halides, alkenes, esters, protected amines and free alcohols and carboxylic acids.



SiR'$_3$	yield/%	α : β
SiEt$_3$	88-89	20 : 1
SiMe(OEt)$_2$	86	9 : 1
Si(OEt)$_3$	58-92	>13 : 1
SiMe$_2$Bn	91-99	>14 : 1

Terminal alkynes are significantly more reactive than internal alkynes.



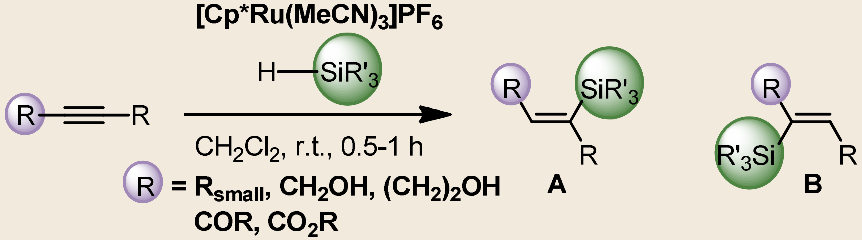
79%, α:β 9:1
no addition over internal alkyne observed

Trost, B.M.; Ball, Z.T. *J. Am. Chem. Soc.* **2005**, *127*, 17644-17655.

Alkynes - Hydrosilylation

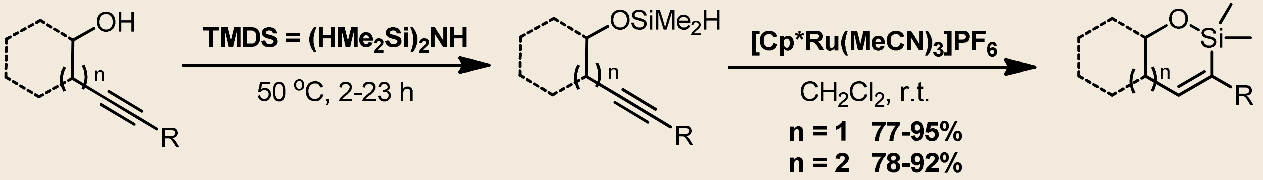
Internal Alkynes

Trost's catalyst also affords tri-substituted silyl alkenes from internal alkynes *via anti* addition. The silyl group preferentially occupies the distal position to small alkyl groups, (homo)propargylic alcohols and carbonyls.

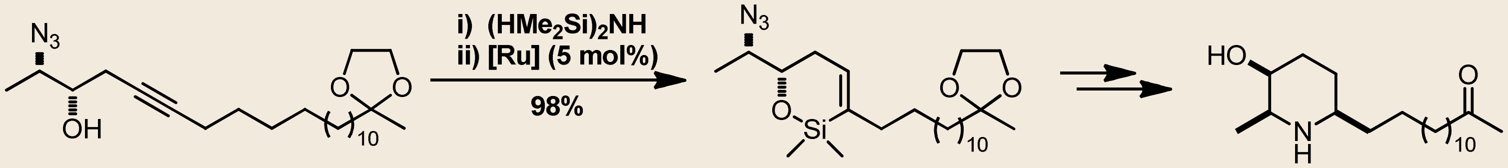


SiR'$_3$	yield/%	A : B
SiEt$_3$	97-99	>13 : 1
BDMS	58-94	>20 : 1
Si(OEt)$_3$	67-99	>5 : 1

When the silane hydride is tethered to the alkyne *via* O-silylation, 6- and 7-membered endocyclic vinyl siloxanes are formed exclusively. A one-pot two-step procedure of O-silylation followed by hydrosilylation has been developed using TMDS.



The total synthesis of (+)-spectaline has been accomplished in 3 steps from the hydroxy alkyne.



(+)-spectaline

Linear alkynes : Trost, B.M.; Ball, Z.T. *J. Am. Chem. Soc.* **2005**, *127*, 17644-17655.
Cyclic silanes: Trost, B.M.; Ball, Z.T. *J. Am. Chem. Soc.* **2003**, *125*, 30-31;(+)-spectaline: *J. Am. Chem. Soc.* **2005**, *127*, 10028-10038.

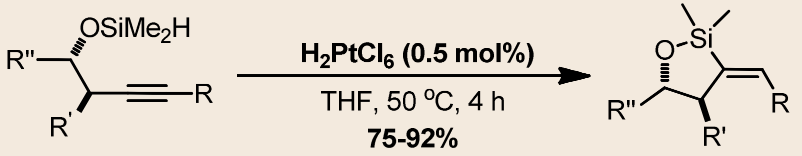
Alkynes - Hydrosilylation

Internal Alkynes

Exocyclic 5-membered siloxanes can be prepared stereoselectively from homopropargylic alcohols utilising a similar O-silylation and hydrosilylation sequence.

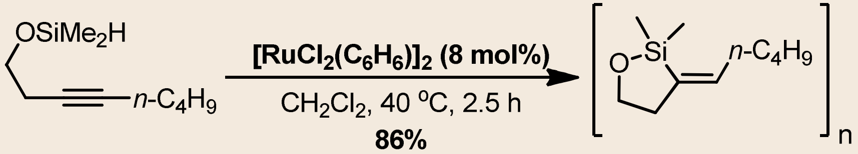
Speier's catalyst yields the *E*- and terminal alkenes while aryl [Ru] catalysts afford the *Z*- product.

***E*-Vinyl Silanes**
Terminal alkenes



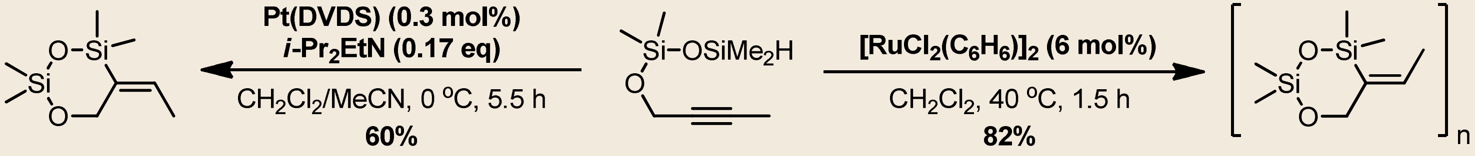
R = H, Me
R' = H, Me
R'' = *c*-C_6H_{11}, Ph

Z-Vinyl Silanes



Propargylic alcohols do not cyclise in this manner. Under similar conditions, polymerisation occurs instead.

A two-atom disiloxane tether, installed with tetramethyldisiloxane and Stryker's catalyst [HCu(PPh_3)]$_6$, allows cyclisation of propargylic alcohols.

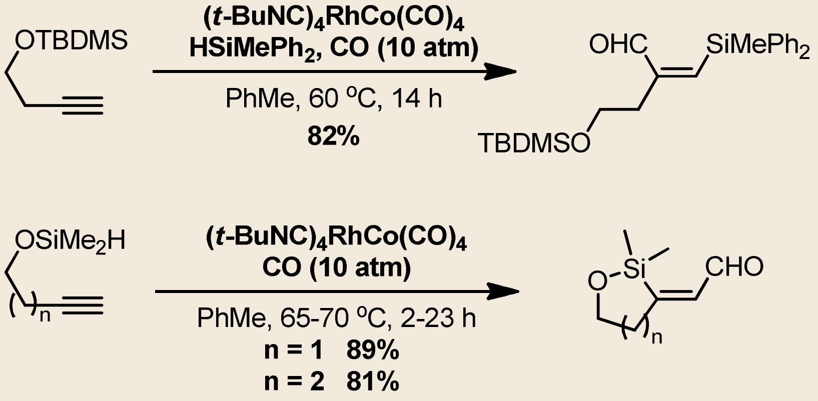


E- and terminal vinyl silanes: Marshall, J.A.; Yanik, M.M. *Org. Lett.* **2000**, *2*, 2173-2175.
Z-Vinyl silanes: Denmark, S.E.; Pan, W. *Org. Lett.* **2002**, *4*, 4163-4166 Propargylic alcohols: Denmark, S.E.; Pan, W. *Org. Lett.* **2003**, *5*, 1119-1122.

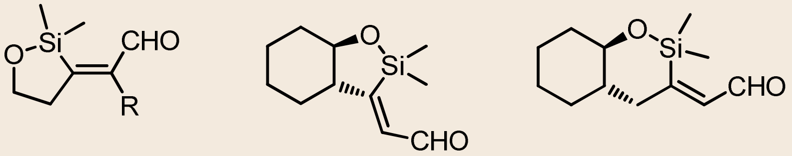
Alkynes - Silylformylation

Terminal and Internal Alkynes

Silylformylation of tethered dimethylsilyl ether-alkynes by Rh and Rh-Co complexes proceeds with opposite regioselectivity to the intermolecular reaction, forming *exo*-oxasilacycles exclusively.

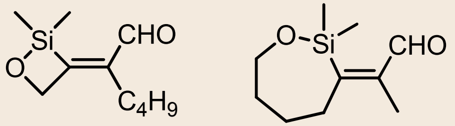


Internal alkynes and cyclic systems are tolerated, affording tetrasubstituted and bicyclic vinyl silanes respectively with complete regio- and stereoselectivity.



51-66% **69%** **73%**

Oxasilacyclobutanes and heptanes could not be prepared by this method.



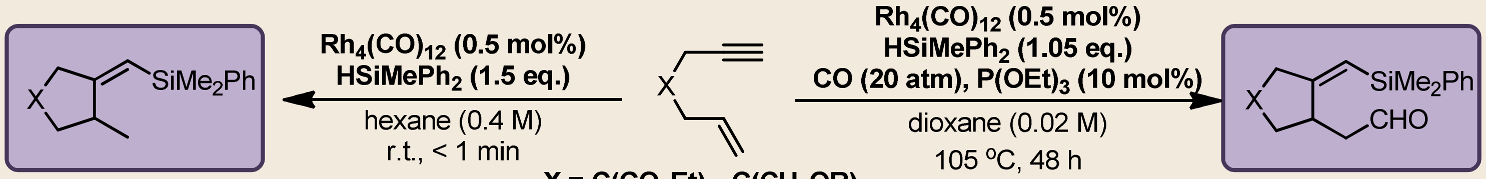
unstable to purification

formed in trace amounts

Ojima, I.; Vidal, E.; Tzamarioudaki, M.; Matsuda, I. *J. Am. Chem. Soc.* **1995**, *117*, 6797-6798.

Alkynes - (Carbonylative) Silylcarbocyclisation

Terminal and Internal Alkynes



X = $C(CO_2Et)_2$, $C(CH_2OR)_2$, NTs, NBn, O

Silylcarbocyclisation (SiCaC) of 1,6-enynes

Ojima and co-workers reported a versatile hydrosilylation-carbocyclisation with Rh catalysts.

- **Esters, ethers, sulfonamides and amines; (free hydroxyls react in lower yields)**
- **Aryl and alkoxysilanes - $HSiMe_2Ph$,$HSiMe(OEt)_2$;**
- **Internal alkynes**

reacted in excellent yields (83-95%).

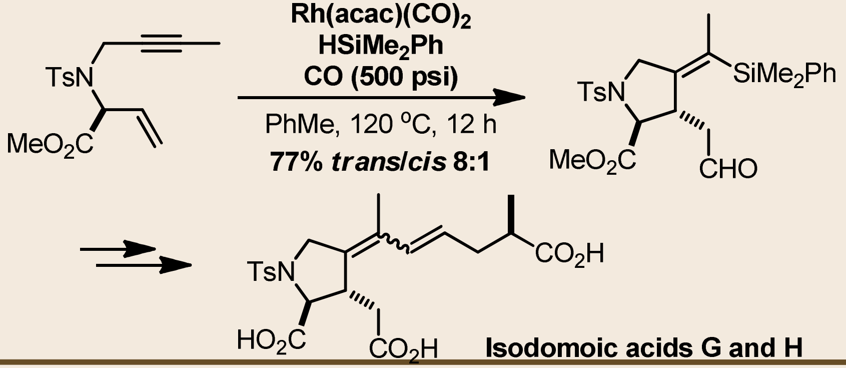
- **Disubstituted alkenes and dienes;**
- **1,7-enynes;**
- **Bulky silanes – $HSiMe_2$(*t*-Bu)**

underwent no or poor conversion.

Carbonylative Silylcarbocyclisation (CO-SiCaC) of 1,6-enynes

High CO concentration, elevated temperature and an external trapping ligand promoted the formation of silylformylated product.

Denmark and co-workers have utilised CO-SiCaC to prepare the pyrrolidine fragment of isodomoic acids G and H.



Isodomoic acids G and H

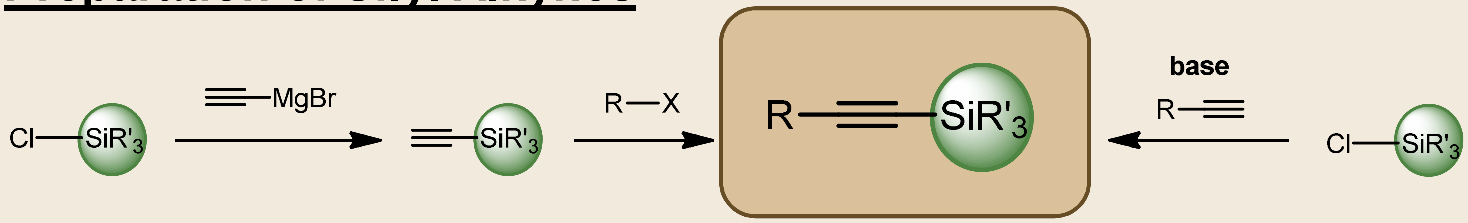
Ojima, I.; Vu. A.T.; Lee, S.-Y.; McCullagh, J.V.; Moralee, A.C.; Fujiwara, M.; Hoang, T.H. *J. Am. Chem. Soc.* **2002**, *124*, 9164-9174.
Isodomoic acids G/H: Denmark, S.E.; Liu, J.H.-C.; Muhuhi, J.M. *J. Am. Chem. Soc.* **2009**, *131*, 14188-14189.

Synthesis of Alkenyl Silanes

- Alkynes
- Silyl Alkynes
  - Hydrogenation
  - Hydrometallation
  - Carbometallation
  - Ring-Closing Metathesis
- Terminal Vinyl Silanes
- Aldehydes

Silyl Alkynes

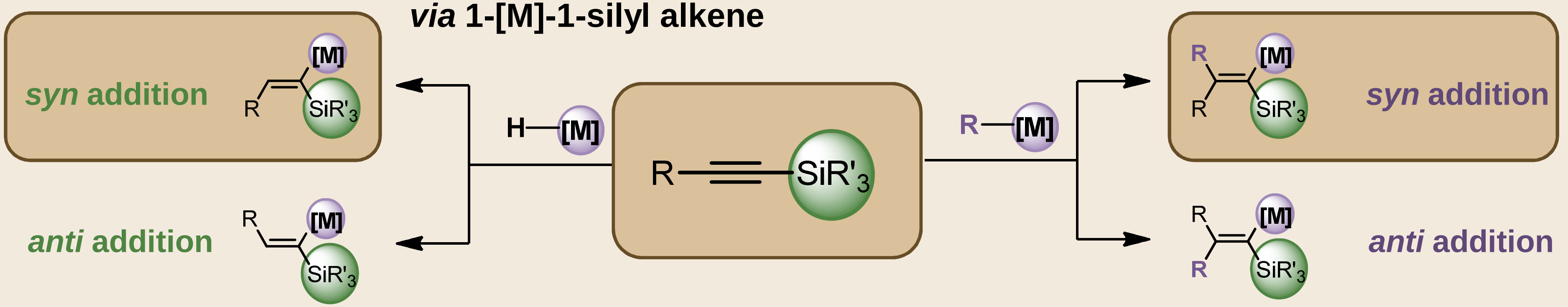
Preparation of Silyl Alkynes



- Wide variety of commercially available chlorosilanes
- Commercially available and readily prepared terminal alkynes
- Double functionalisation from alkynyl Grignard reagent

Hydro- and Carbometallation

via 1-[M]-1-silyl alkene



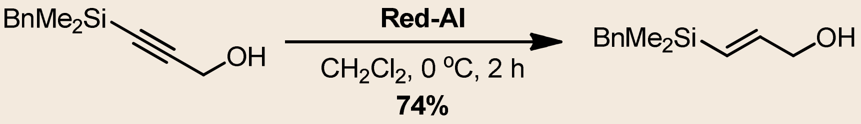
[M] = Alk_2BH, DiBAl-H, *i*-BuMgBr/Cp_2TiCl_2, *t*-$BuZrCp_2Cl$

[M] = MeMgBr, (allyl)ZnBr, Me_2AlCl/Cp_2TiCl_2

Ley, S.V. *Comprehensive Organic Functional Group Transformations Vol.2,* 1st Ed.; Cambridge University Press, 1995.

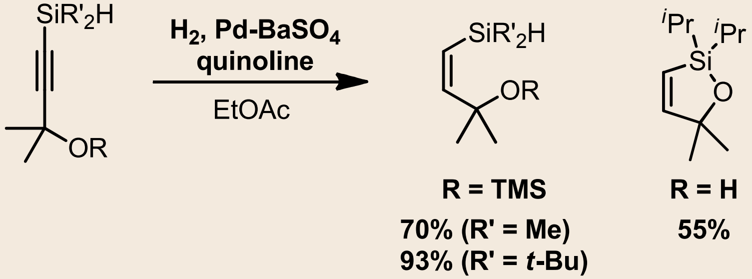
Silyl Alkynes - Hydrogenation

Red-Al Reduction – *trans*-vinyl silanes



Heterogeneous Catalysts – *cis-vinyl silanes*

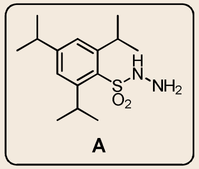
Lindlar's catalyst – tolerates Si-H and Si-O bonds. *Z*-selectivity influenced by concentration and substrate.

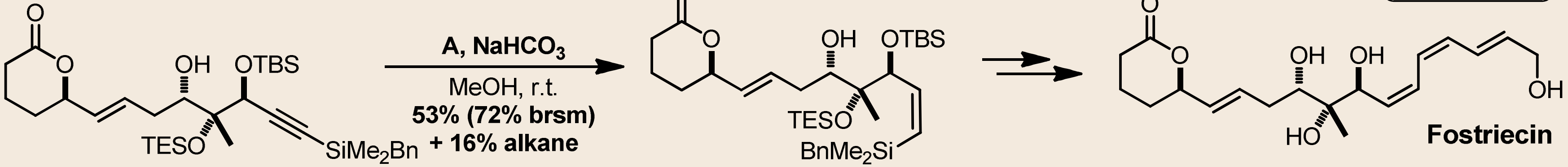


Raney Nickel and P-2Ni

Diimide Reduction

A free hydroxyl group was tolerated in the reduction of a BDMS alkyne using diimide precursor A under mildly basic conditions.





Lindlar's catalyst: Murthi, K.K.; Salomon, R.G. *Tetrahedron Lett.* **1994**, *35*, 517-520. Red-Al: Denmark, S.E.; Fujimori, S. *J. Am. Chem. Soc.* **2005**, *127*, 8971-8973. Diimide: Trost, B.M.; Frederiksen, M.U.; Papillon, J.P.N.; Harrington, P.E.; Shin, S.; Shireman, B.T. *J. Am. Chem. Soc.* **2005**, *127*, 3666-3667.

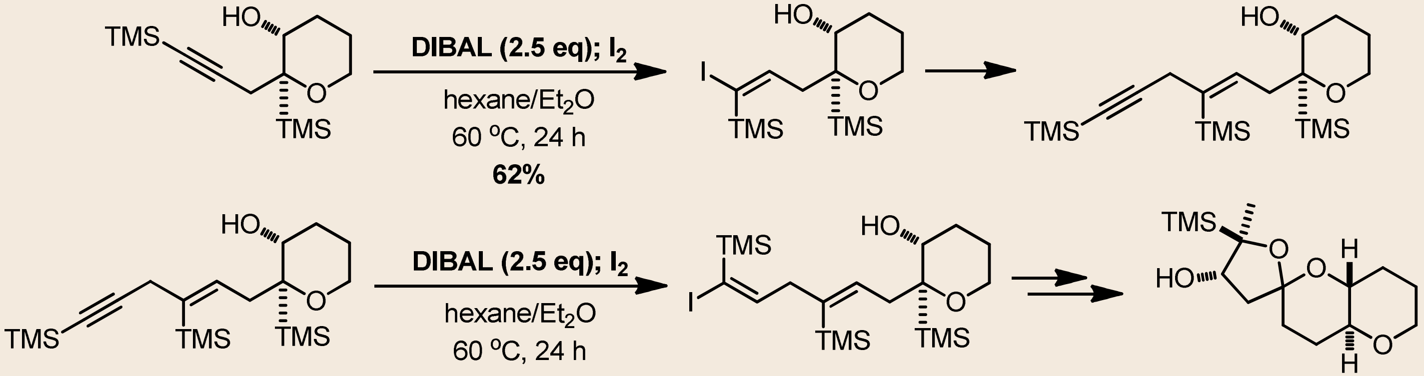
Silyl Alkynes - Hydrometallation

Hydrometallation-Proton Quench

Hydroboration and hydrozirconation of silyl alkynes with dialkylboranes and Schwartz's reagent respectively, followed by protonolysis affords *cis*-vinyl silanes in high stereoselectivities.

Hydrometallation-Halide Quench

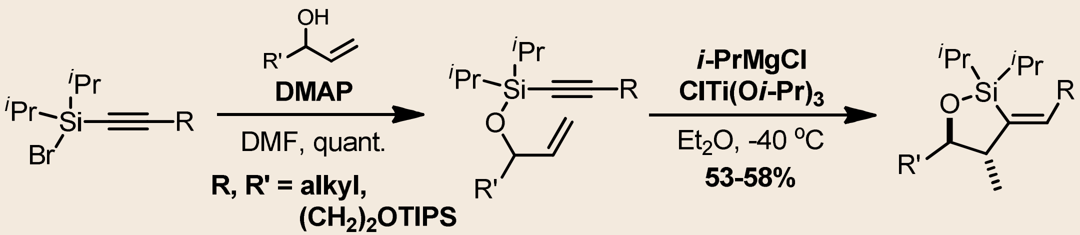
Jamison and co-workers employed a hydroalumination-iodine quench approach to iteratively construct substrates for a ladder polyether cascade synthesis.



Halide: Heffron, T.P.; Simpson, G.L.; Merino, E.; Jamison, T.F. *J. Org. Chem.* **2010**, *75*, 2681-2701.

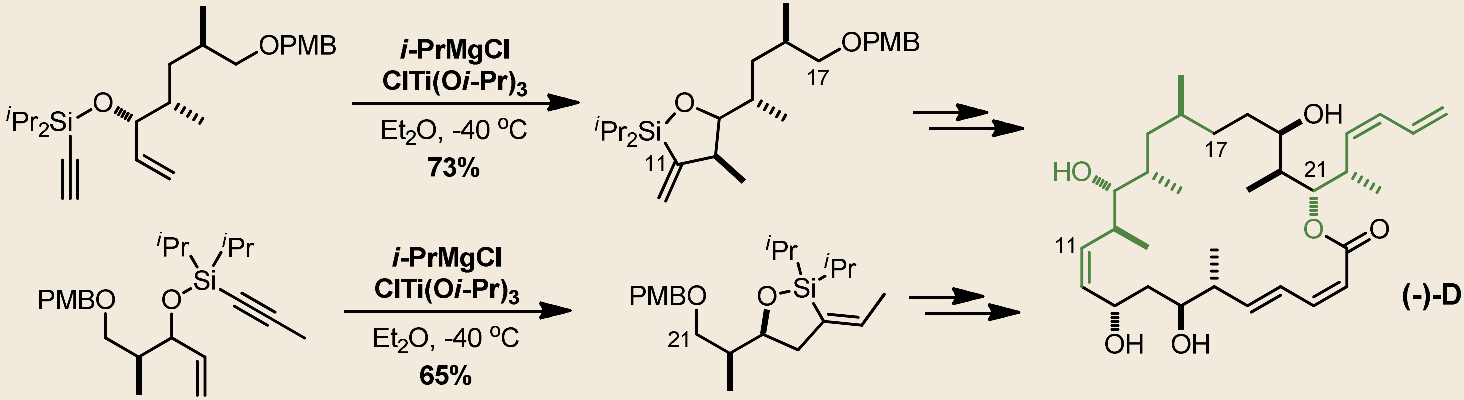
Silyl Alkynes - Hydrometallation

Hydrotitanation-Cyclisation



Phillips and co-workers have developed a (η^2-propene)Ti(Oi-Pr)$_2$ effected cyclisation of 1,5 silyl enynes. The *anti* diastereoisomer was produced exclusively.

This methodology was used to prepare the C11-C17 and C21-C26 fragments of (-)-dictyostatin.



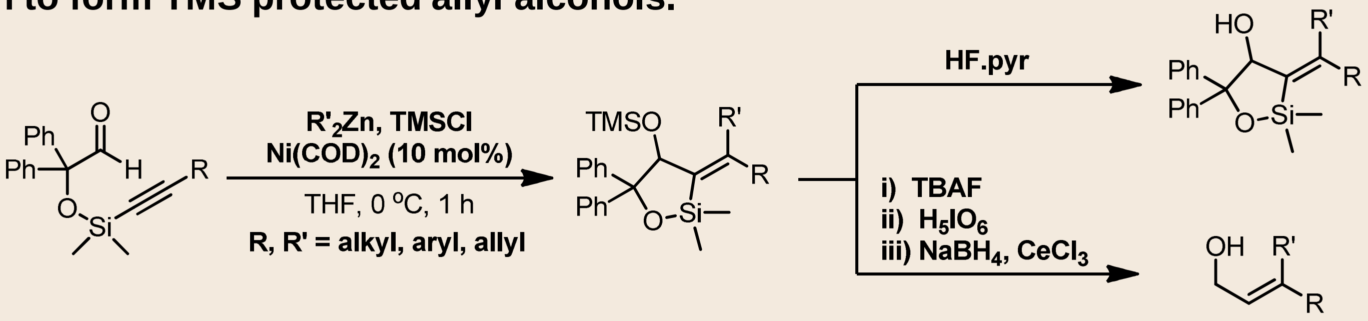
(-)-Dictyostatin

O'Neil, G.W.; Phillips. A.J. *Tetrahedron Lett*. **2004**, *45*, 4253-4256.
(-)-Dictyostatin: O'Neil, G.W.; Phillips, A.J. *J. Am. Chem. Soc*. **2006**, *128*, 5340-5341..

Silyl Alkynes - Carbometallation

Alkylative Cyclisation

Organozinc reagents have been added over alkynyl silyl ethers followed by nickel-catalysed cyclisation to form TMS protected allyl alcohols.



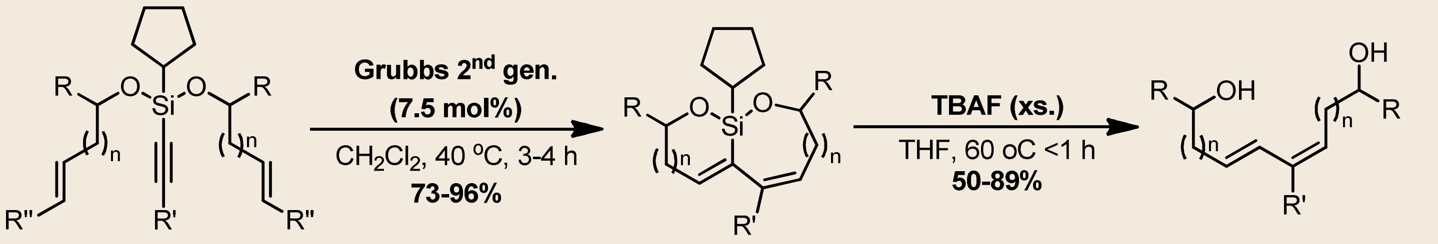
The oxasilacylic products can undergo selective TMS deprotection or global desilylation to yield trisubstituted allylic alcohols in good yields (58-63% over 4 steps).

Poor yields (< 30%) were observed when R = R' = aryl.

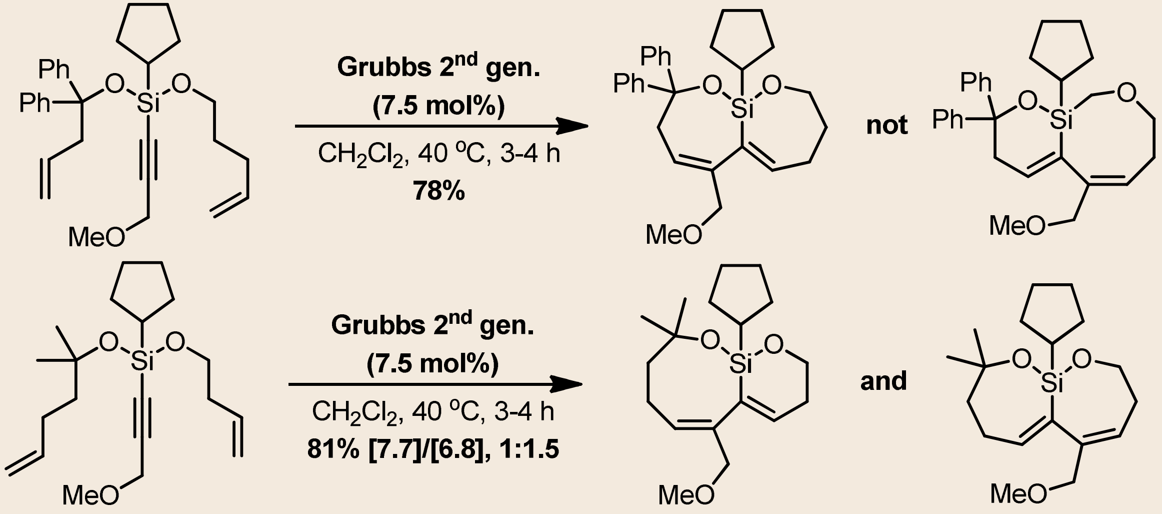
Lozanov, M.; Montgomery, J. *Tetrahedron Lett*. **2001**, *42*, 3259-3261.
Oblinger, E.; Montgomery, J. *J. Am. Chem. Soc*. **1997**, *119, 9065-9066.*

Silyl Alkynes - RCM

Double Cyclisations of Alkynyl Silaketals



Internal and terminal dienes underwent cyclisation with Grubbs 2nd generation catalyst in good yields. Longer tether lengths (n=1,2) and internal and terminal dienes (R''=H, Me) gave comparable results.

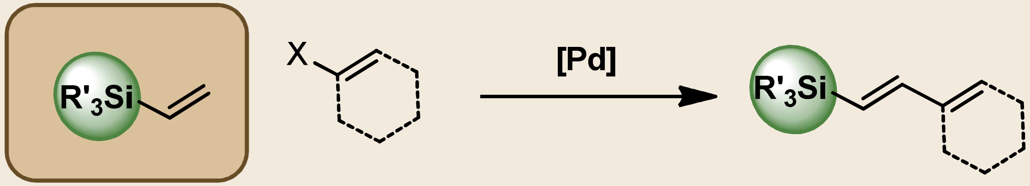


Grimm. J.B.; Otte, R.D.; Lee, D. *J. Organomet. Chem.* **2005**, 690, 5508-5516.

Synthesis of Alkenyl Silanes

- Alkynes
- Silyl Alkynes
- Terminal Vinyl Silanes
  - Heck Coupling
  - Ring-Closing Metathesis
- Aldehydes

Terminal Vinyl Silanes – Heck Coupling

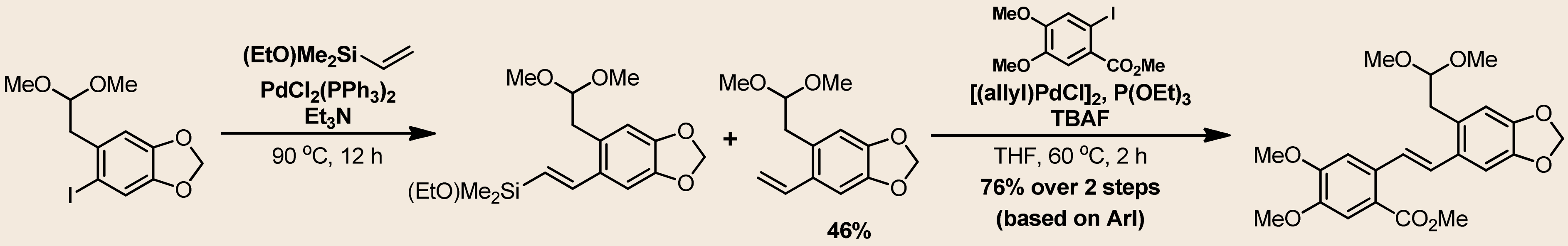


Non-alkyl Si-substituents are required to

- **Activate the vinyl silane to Heck cross-coupling**
- **Subsequent functionalisation of the silyl diene**

Alkoxysilanes generally require forcing conditions, and even then react only in poor yields with significant protodesilylated products recovered.

This trend is observed in Hanaoka's synthesis of nitidine. Recovered protodesilylated styrene could be converted to the desired styrylbenzoate by a Heck reaction.

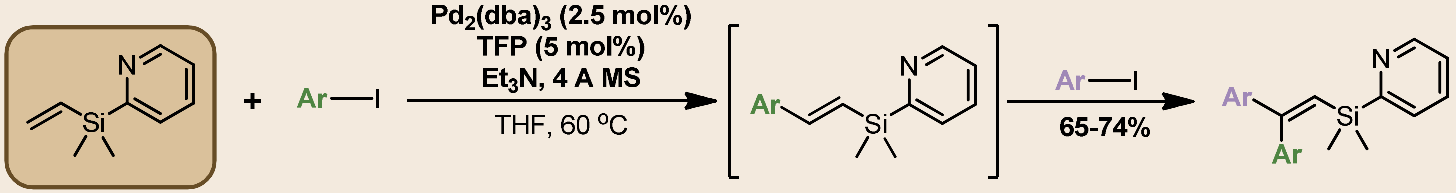


Minami, T.; Nishimoto, A.; Hanaoka, M. *Tetrahedron Lett.* **1995**, *36*, 9505-9508.

Terminal Vinyl Silanes – Heck Coupling

2-Pyridylsilanes

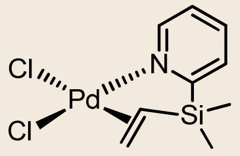
2-pyridylsilanes undergo single or double Heck couplings with aryl iodides and are more reactive than methyl acrylate and styrene under these coupling conditions.



Ar, Ar = Ph, 2- and 3-thiophene

Complex-induced proximity effect (CIPE):

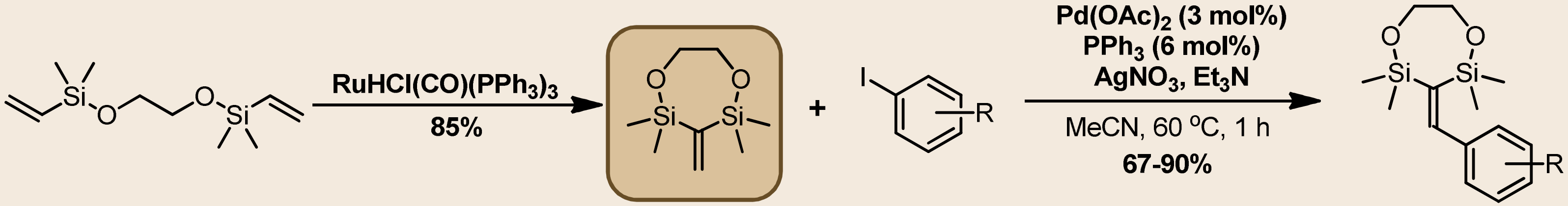
Coordination of the vinyl silane to palladium *via* the pyridyl group makes carbopalladation kinetically and/or thermodynamically more favourable.



isolated
X-ray crystal structure

Cyclic 1,1-bis(silyl)ethenes

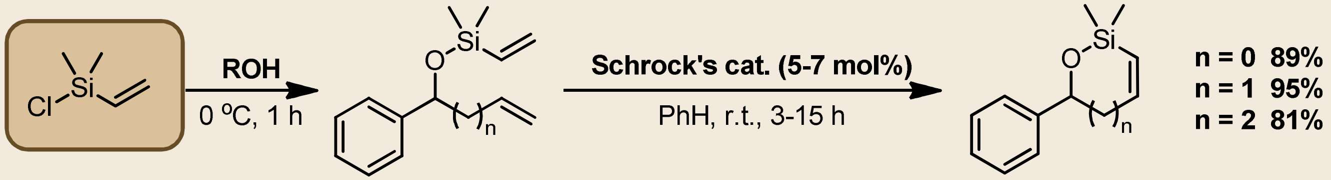
Marciniec and co-workers have reported a vinyl silane which couples with a variety of electronically diverse aryl halides. No desilylation products were observed.



2-Pyridyl silanes: Itama, K.; Nokami, T.; Ishimura, Y.; Mitsudo, K.; Kamei, T.; Yoshida, J. *J. Am. Chem. Soc.* **2001**, *123*, 11577-11585.
Bis(silyl)ethenes: Pawluc, P.; Hreczycho, G.; Suchecki, A.; Kubicki, M.; Marciniec, B. *Tetrahedron*, **2009**, *65*, 5497-5502.

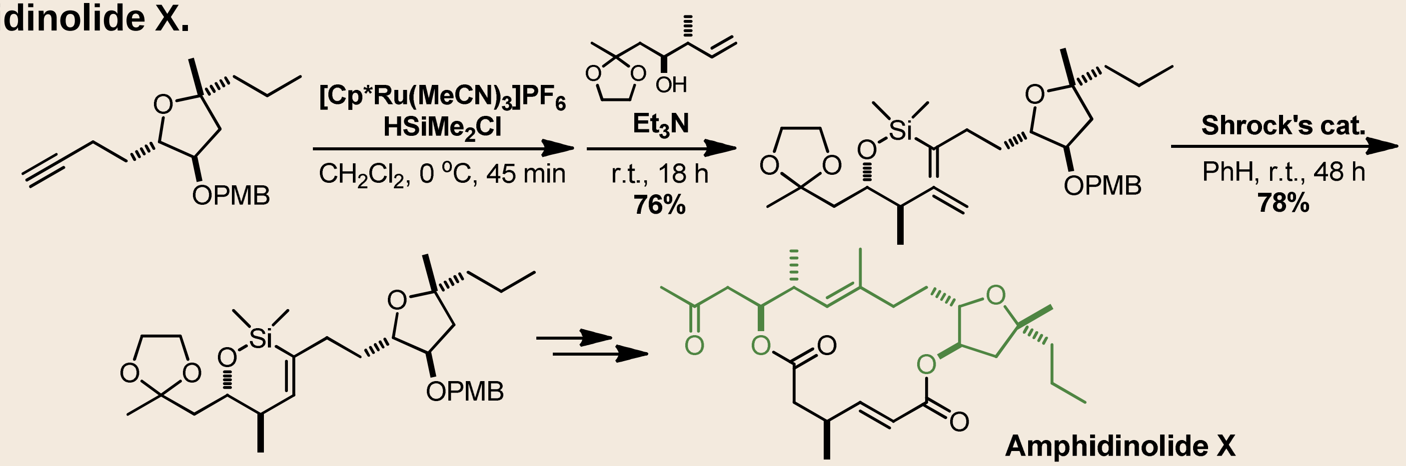
Terminal Vinyl Silanes - RCM

Cyclic Siloxanes



Denmark and co-workers utilised Schrock's catalyst to effect RCM on vinyl silanes forming medium sized cyclic siloxanes. The reaction tolerates substitution on either the vinyl silane or alkane, but not when both are substituted. No product formed with Grubbs I catalyst.

The Vilarassa group has applied a hydrosilylation-RCM sequence to the total synthesis of amphidinolide X.



Amphidinolide X

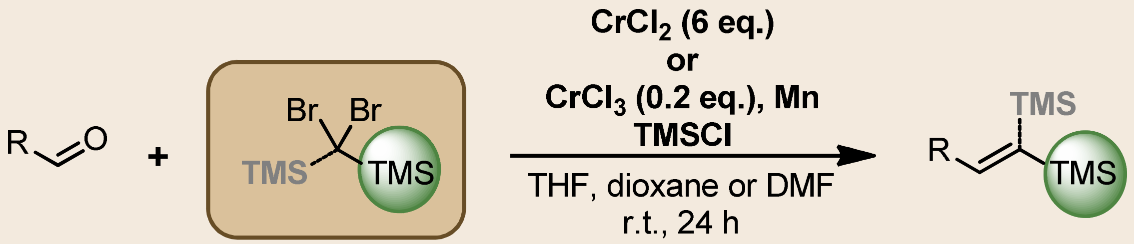
Denmark, S.E.; Yang, S.-M. *Org. Lett.* **2001**, *3*, 1749-1752.
Amphidinolide X: Rodriguez-Escrich, C.; Urpi, F.; Vilarrasa, J. *Org. Lett.* **2008**, *10*, 5191-5194.

Synthesis of Alkenyl Silanes

- Alkynes
- Silyl Alkynes
- Terminal Vinyl Silanes
- Aldehydes
  - Takai Olefination
  - Peterson-Type Olefination

Aldehyes – Takai Olefinations

Takai and co-workers broadened the chormium(II) mediated vinyl iodide synthesis to form vinyl TMS silanes with a dibromomethylsilane reagent *via* Cr(II) insertion into the both C-Br bonds facilitating addition to the aldehyde and elimination.



Alkyl, aryl and conjugated aldehydes undergo olefination in good to excellent yields (77-88%). Ketones do not react under these conditions.

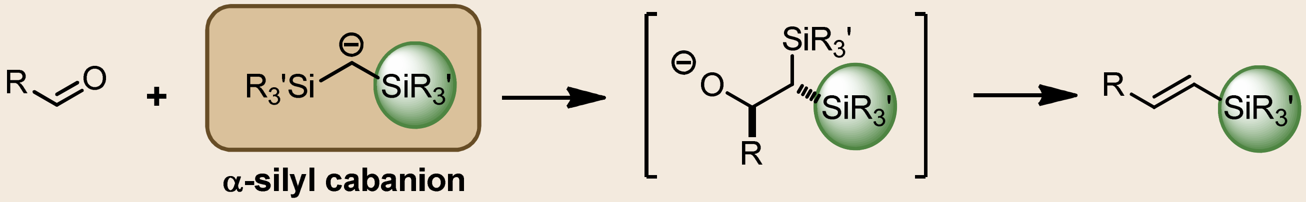
Stoichiometric Cr(II) – *trans*-vinyl silanes formed exclusively

Catalytic Cr(III) – Mn or Zn employed as metal co-reductant
Slight drop in selectivity (*trans*/*cis* > 91:9)

Hodgson and co-workers extended this reaction to dibromodisilylmethanes, preparing 1,1-bis(silyl) trisubstituted alkenes.

Takai, K.; Kataoka, Y.; Okazoe, T.; Utimoto, K. *Tetrahedron Lett.* **1987**, *28*, 1443-1446. Catalytic: *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1581-1586. Bis(silyl)alkenes: Hodgson, D.M.; Comina, P.J. *Tetrahedron Lett.* **1994**, *35*, 9469-9470.

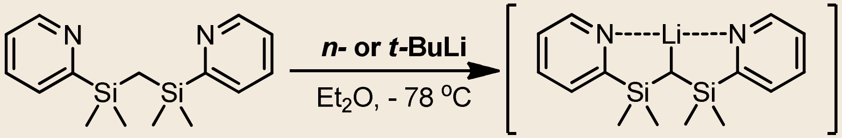
Aldehyes - Peterson-Type Olefinations



α-silyl cabanion

Deprotonation

Bis(2-pyridyldimethylsilyl)methane readily deprotonates when treated with BuLi to provide the pyridyl-stabilised lithium complex.

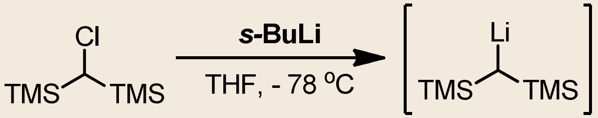


These undergo a Peterson olefination with alkyl, aryl, heteroaryl and conjugated aldehydes and ketones in good to excellents yields and exclusive *E* stereoselectivity (56-100%, > 99% *E*).

Aldehydes with α-quarternary centres and *ortho*-substitution react in excellent yields (> 94%).

Lithium-Halide Exchange

Bis(trimethylsilyl)chloromethane undergoes lithium-chlorine exchange with *s*-BuLi.



***n*- or *t*-BuLi problematic**

When treated with aldehydes, the β-hydroxysilanes eliminate *via* a concerted *syn*-periplanar pathway under basic conditions to afford the *trans*-vinyl silanes in excellent yields and good selectivity (65-93%, *cis*/*trans* > 9:1).

Alkyl, aryl and heteroaryl aldehydes are well tolerated.

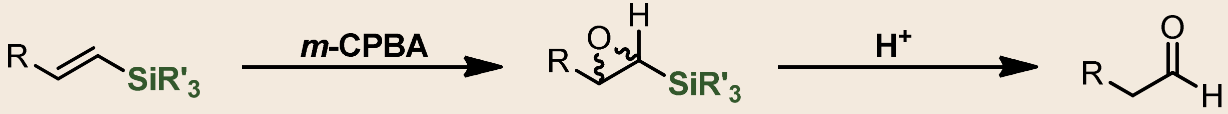
Deprotonation: Itami, K.; Nokami, T.; Yoshida, J. *Org. Lett.* **2000**, *2*, 1299-1302.
Lithium-halide exchange: McNulty, J.; Das, P. *Chem. Commun.* **2008**, 1244-1245.

Applications of Alkenyl Silanes

- Carbon-Oxygen Bond Formations
  - Epoxidation-Oxidation
  - Tamao-Fleming Oxidation
- Carbon-Carbon Bond Formations

Carbon-Oxygen Bond Formations

Epoxidation-Oxidation

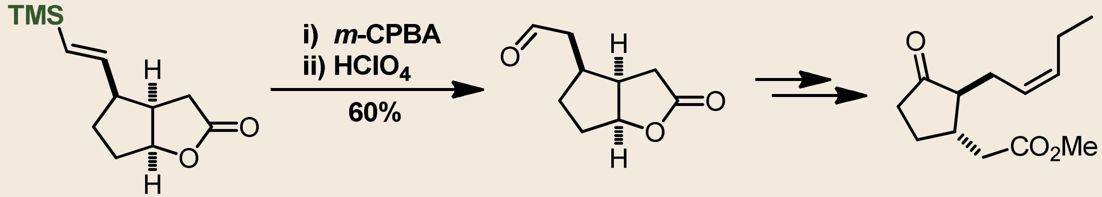


SiR'_3 = all carbon substituents
TMS, TBDMS, DMPS

H^+ = $HClO_4$, HCO_2H, TFA etc

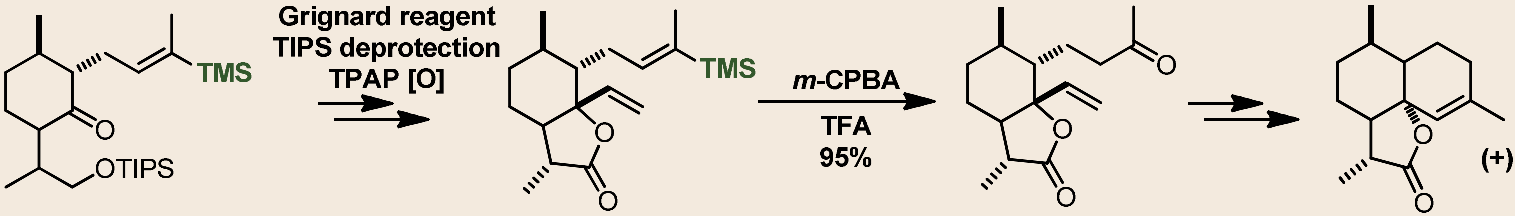
Unactivated vinyl silanes can undergo oxidation to the corresponding aldehyde *via* the silyl epoxide through a 2-step epoxidation-oxidation sequence.

Inomata's synthesis of (+)-methyl jasmonate



(+)-methyl jasmonate

1-silyl-1,2-trisubstituted alkenes form ketones. Dudley and co-workers exploited the stability of vinyl TMS silanes to a number of reagents and conditions, unmasking the ketone at a later stage of the synthesis

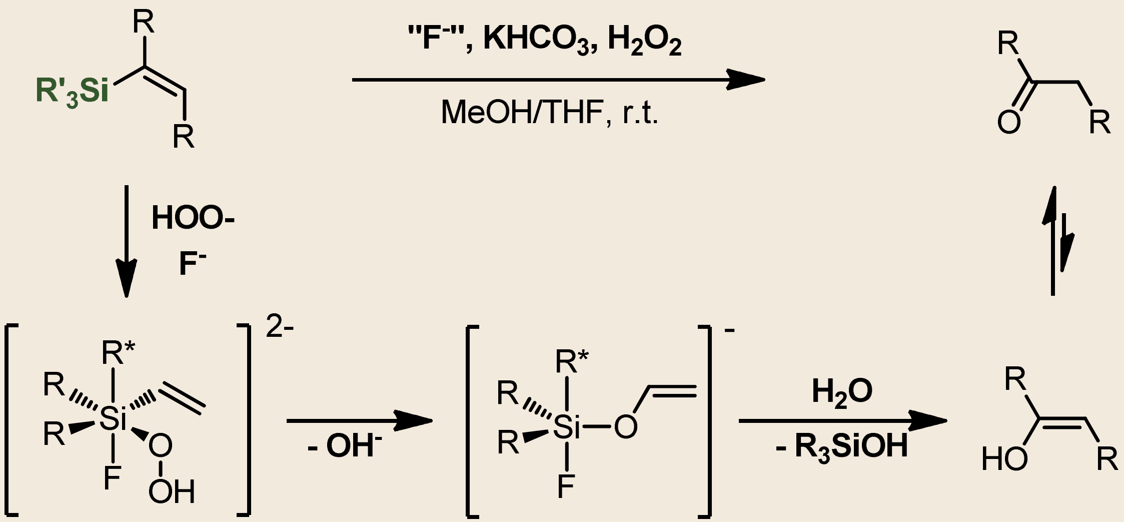


(+)-Dihydro-*epi*-deoxy-arteannuin B

(+)-Methyl jasmonate: Suzuki, K.; Inomata, K.; Endo, Y. *Org. Lett*. **2004,** *6*, 409-411.
(+)-Dihydro-*epi*-deoxyarteannuin B: Dudley, G.B.; Engel, D.A.; Ghiviriga, I.; Lam, H.; Poon, K.W.C.; Singletary, J.A. *Org. Lett.* **2007**, *9,* 2839-2842.

Carbon-Oxygen Bond Formations

Tamao-Fleming Oxidations



Activated silanes undergo direct oxidation to aldehydes and ketones when treated with a F^- source, H_2O_2 and base. The reaction is thought to proceed through hexa- and penta-fluorosilicate intermediates.

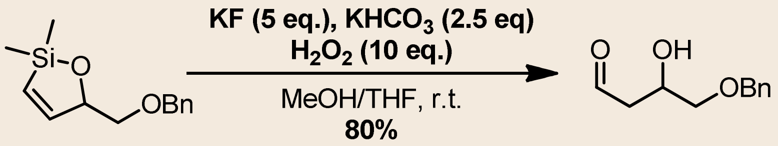
Activating groups: Benzyldimethylsilanes (BDMS) – a 'safety-catch silanol'
Dimethylsilyl ethers
Allyldimethylsilanes (ADMS) – *via* fluorodimethylsilane

Vinyl BDMS: Trost, B.M.; Ball, Z.T.; Joge, T. *Angew. Chem. Int. Ed.* **2003**, *42*, 3415-3418.
Vinyl ADMS: Magar, S.S.; Fuchs, P.L. *Tetrahedron Lett.* **1991**, *32*, 7513-7516.

Carbon-Oxygen Bond Formations

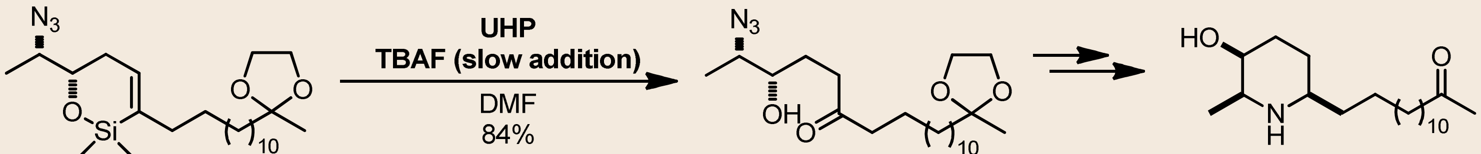
Tamao-Fleming Oxidations

Cyclic Vinyl Siloxanes



The oxidation of cyclic siloxanes reveals β- and γ-hydroxyaldehydes or ketones.
Di- and trisubstituted silyl alkenes either *endo-* or *exo-* to the ring can be oxidised efficiently.

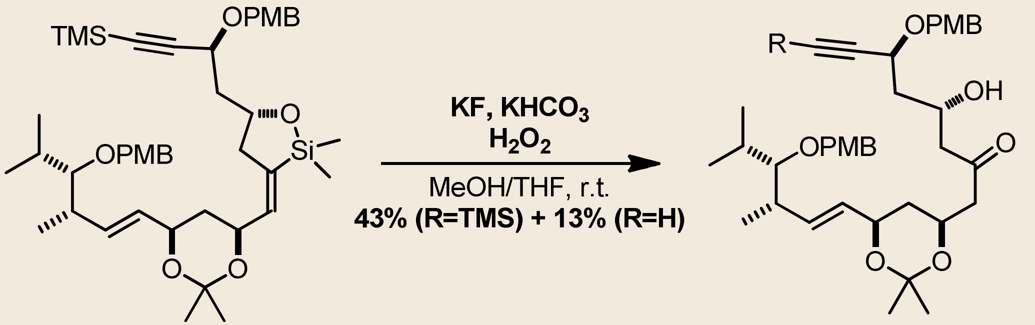
Endocyclic Vinyl Siloxanes



(+)-spectaline

Oxidation in the presence of an azide.
UHP = urea-H$_2$O$_2$ adduct.

Exocyclic Vinyl Siloxanes



Oxidation in the presence of a TMS-acetylene in McDonald's synthesis of RK-397.

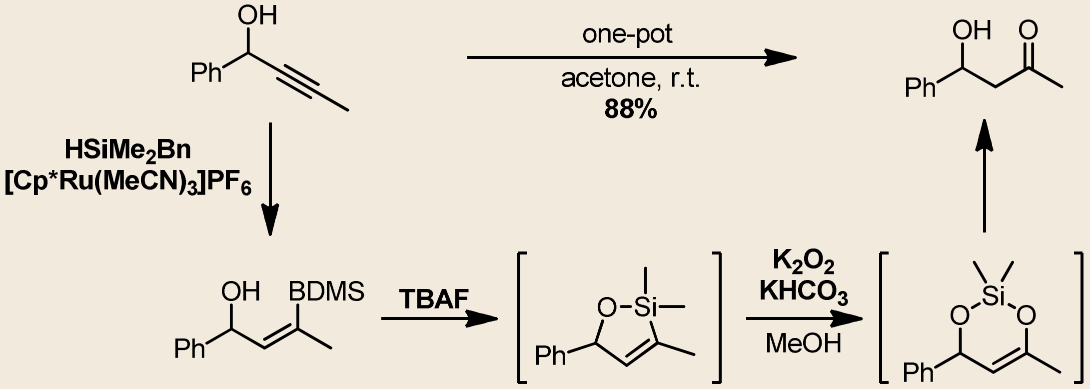
Aldehyde: Chang, S.; Grubbs, R.H. *Tetrahedron Lett.* **1997**, *38*, 4757-4760. RK-397: Burova, S.A.; McDonald, F.E. *J. Am. Chem. Soc.* **2004**, *126*, 2495-2400.
(+)-Spectaline: Trost, B.M.; Ball, Z.T.; Laemmerhold, K.M. *J. Am. Chem. Soc.* **2005**, *127*, 10028-10038.

Carbon-Oxygen Bond Formations

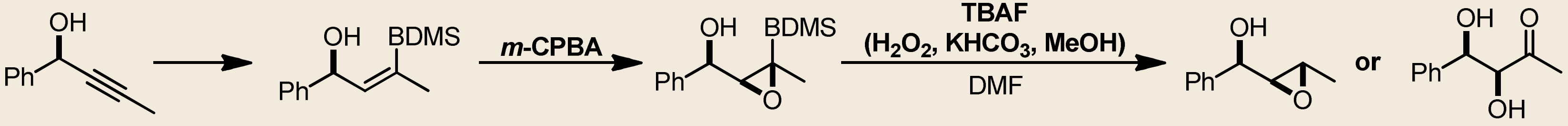
Tamao-Fleming Oxidations

One-Pot Hydrosilylation-Oxidation

The Trost group has developed a one-pot conversion of propargylic alcohols to β-hydroxy-ketones. BDMS readily forms the silanol when treated with TBAF. Intramolecular trapping with the free alcohol is believed to form an endocyclic vinyl siloxane intermediate.



Elaboration of this methodology and use of enantiomerically-enriched propargylic alcohols provides an entry point to stereochemically well-defined α,β-hydroxylketones and epoxy alcohols.



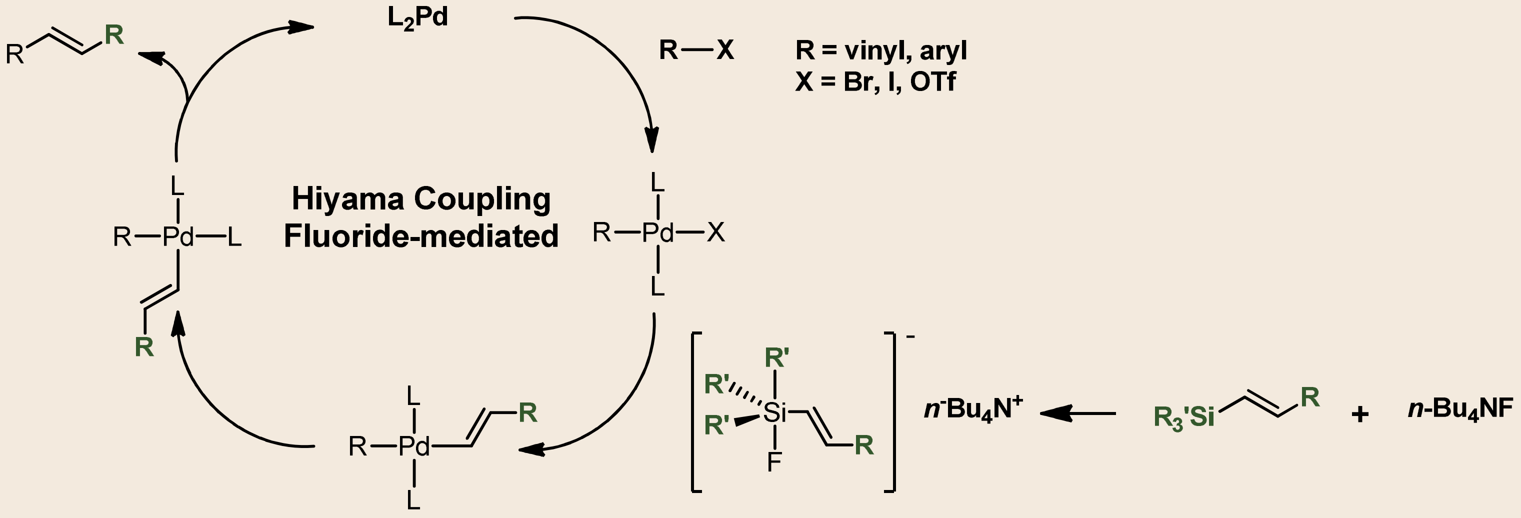
One-Pot: Trost, B.M.; Ball, Z.T.; Joge, T. *Angew. Chem. Int. Ed.* **2003**, *42*, 3415-3418.
Epoxidation & Elaboration: Trost, B.M.; Ball, Z.T.; Laemmerhold, K.M. *J. Am. Chem. Soc.* **2005**, *127*, 10028-10038.

Applications of Alkenyl Silanes

- Carbon-Oxygen Bond Formations
- Carbon-Carbon Bond Formations
  - Hiyama Cross-Coupling
  - Hiyama-Denmark Cross-Coupling
  - Other Fluoride-Free Couplings
  - Cu(I) Alkenyl-C-to-O Silyl Migration

Carbon-Carbon Bond Formations

Hiyama Cross-Coupling



Suitably functionalised silanes are activated by TBAF, forming the pentacoordinate silicate complex which undergoes transmetallation with palladium.

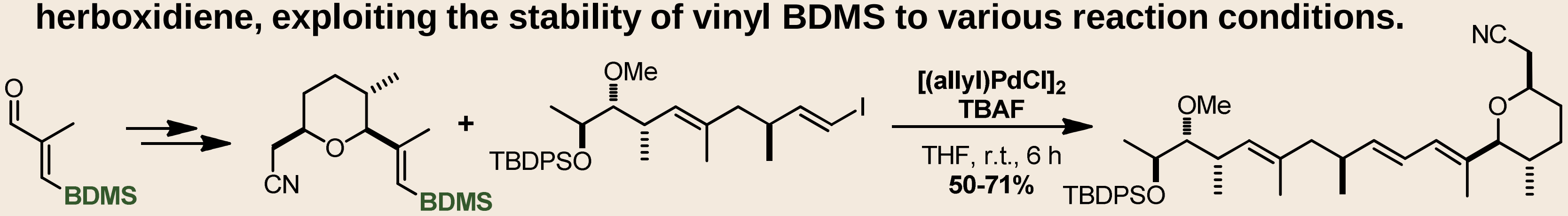
Activating groups: Chloro- and fluorodimethylsilanes
(Exo- and endoyclic) dimethylsilyl ethers, disiloxanes and silanols
Isopropylsilyl hydrides
'Safety-catch silanols' – BDMS; siletanes; isopropylsilyl hydrides;
triallyl silanes; dimethylphenyl, 2-pyridyl,
2-thienylsilanes,

Carbon-Carbon Bond Formations

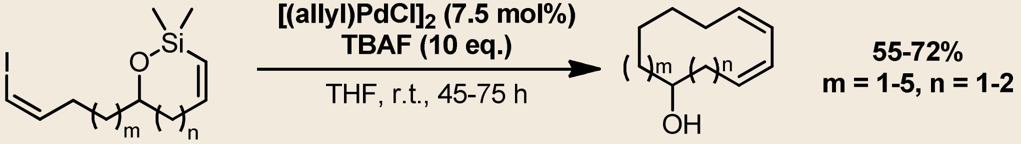
Hiyama Cross-Coupling

Intermolecular-Cross Coupling

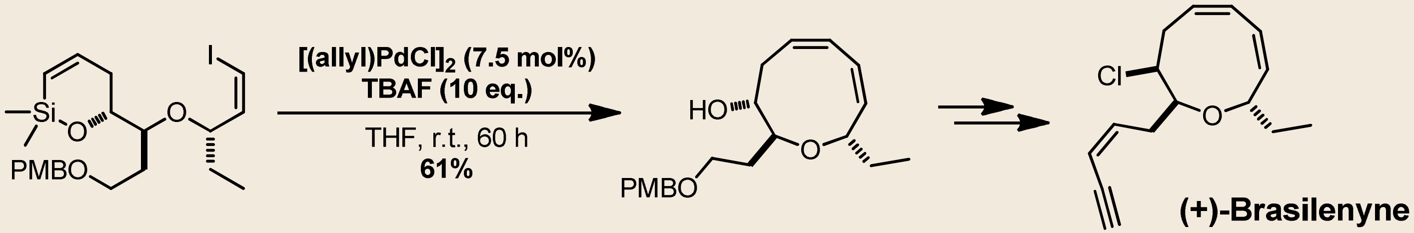
Panek and co-workers incorporated a Hiyama coupling in their end-game strategy towards herboxidiene, exploiting the stability of vinyl BDMS to various reaction conditions.



Intramolecular Cross-Coupling



The Denmark group has combined RCM and intramolecular Hiyama coupling to access 8 to 12-membered ring systems, controlling the relative position of the alcohol and diene.



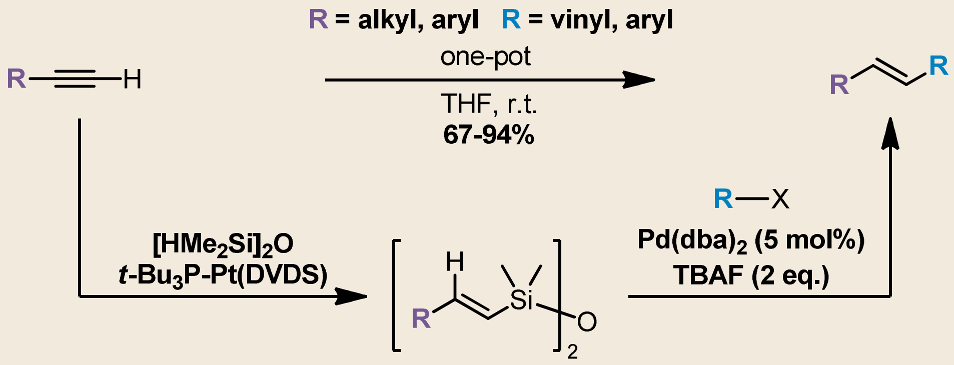
Herboxidiene: Zhang, Y.; Panek, J.S. *Org. Lett.* **2007**, *9*, 3141-3143.
Intramolecular: Denmark, S.E.; Yang, S.-M. *J. Am. Chem. Soc.* **2002**, *124*, 2102-2103; (+)-Brasilenyne: *J. Am. Chem. Soc.* **2004**, *126*, 12432-12440.

Carbon-Carbon Bond Formations

Hiyama Cross-Coupling

One-Pot Hydrosilylation-Coupling

Denmark and Wang have illustrated the possibility of combining hydrosilylation followed by cross-coupling, amounting to an overall *syn*-hydrocarbation of carbon-carbon triple bonds.



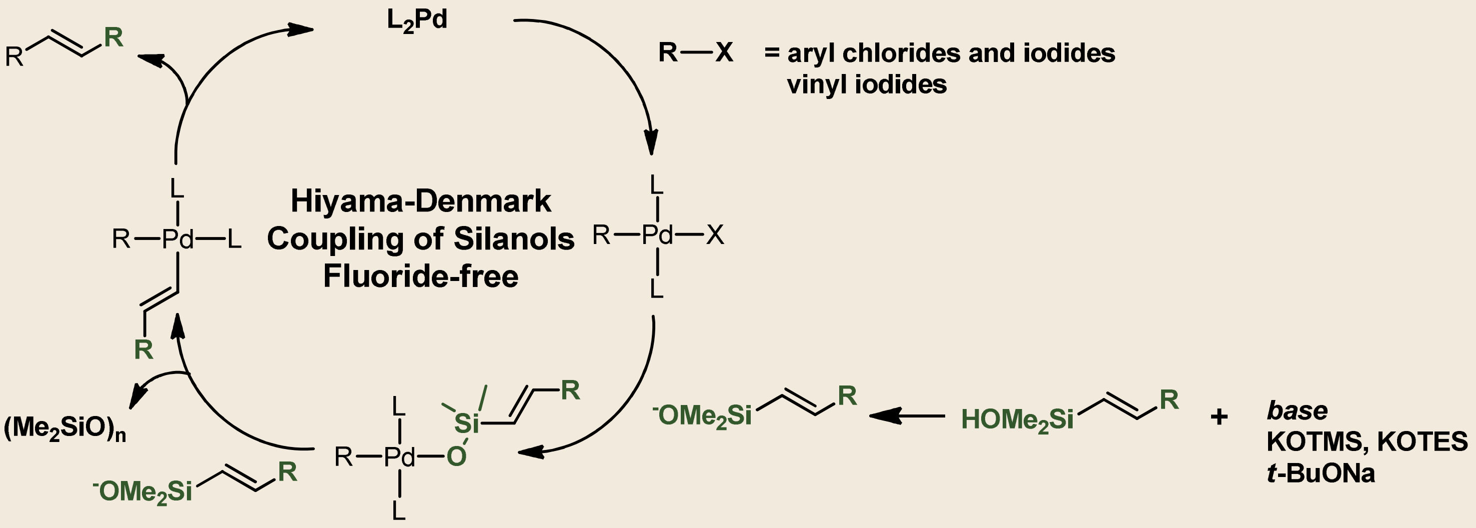
The platinum catalysed hydrosilylation of terminal alkynes forms β-*trans*-vinyldisiloxanes which are activated by fluoride to cross-couple with aryl iodides and vinyl bromides and iodides with good conservation of double bond stereochemistry (*E*/*Z* > 92:8).

The *cine*-1,1-disubstituted product is formed in appreciable amounts (5-9%) when (*E*)-vinyl halides are used as coupling partners.

Denmark, S.E.; Wang, Z. *Org. Lett.* **2001**, *3*, 1073-1076.

Carbon-Carbon Bond Formations

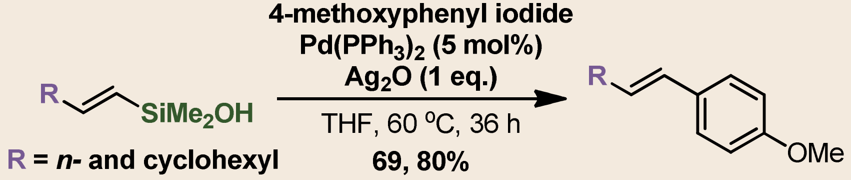
Hiyama-Denmark Cross Coupling



The fluoride-free Hiyama-Denmark coupling eschews the conventional pentacoordinate silicate, proceeding instead by a Si-O-Pd linkage which facilities Si to Pd transmetallation.

Divinyltetramethyldisiloxane (DVDS) is used in place of terminal vinyl silanols.

Hiyama and co-workers have reported silver(I) oxide activated vinyl silanol couplings with an aryl iodide.



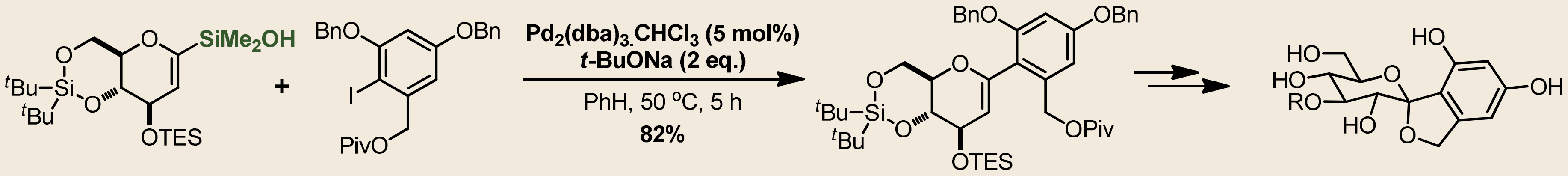
Mechanism: Denmark, S.E.; Regens, C.S. *Acc. Chem. Res.* **2008**, *41*, 1486-1499.
Silver(I) oxide: Hirabayashi, K.; Kawashima, J.; Nishihara, Y.; Mori, A.; Hiyama, T. *Org. Lett.* **1999**, *1*, 299-301.

Carbon-Carbon Bond Formations

Hiyama-Denmark Cross Coupling

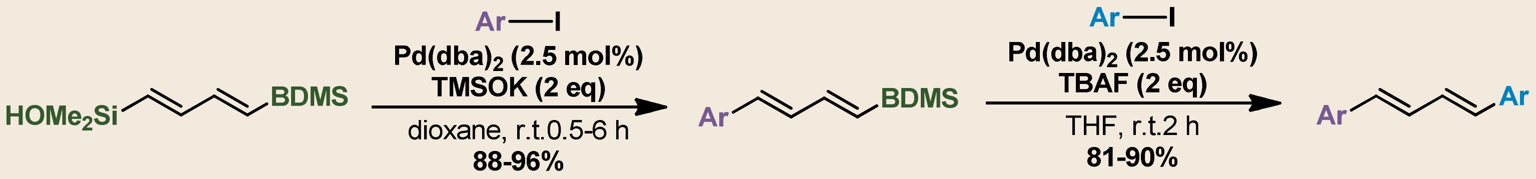
(+)-Papulacandin D Spiroketal Synthesis

Denmark has applied the fluoride-free cross coupling to the challenging coupling of a base-sensitive protected glucal silanol and a sterically hindered aryl iodide. The coupling assembled the entire carbon skeleton of the spiroketal.



Orthogonal Silicon Cross-Coupling

Combining both silicon cross-coupling conditions, Denmark has devised a synthetic sequence that differentiates functionalised1,4-bissilylbutadienes on the basis of the silane's reactivity in the absence of fluoride.



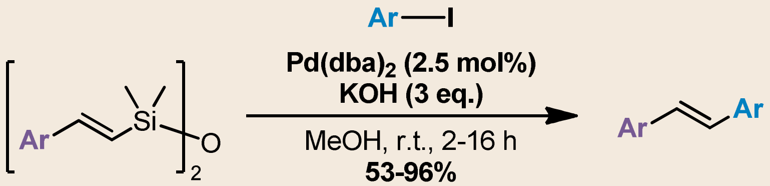
(+)-Papulacandin D: Denmark, S.E.; Regens, C.S.; Kobayashi, T. *J. Am. Chem. Soc.* **2007**, *129*, 2774-2776.
Orthogonal coupling: Denmark, S.E.; Tymonko, S.A. *J. Am. Chem. Soc.* **2005**, *127,* 8004-8005.

Carbon-Carbon Bond Formations

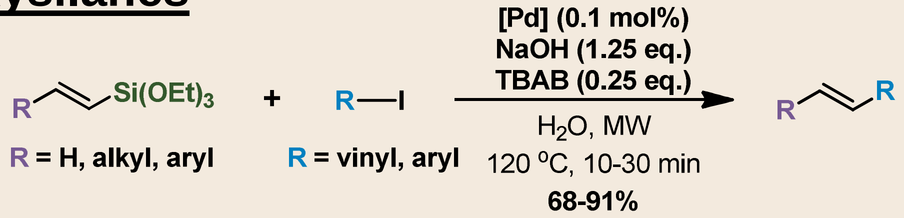
Other Fluoride-Free Cross Coupling

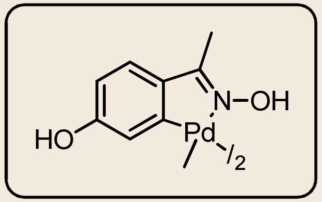
A number of 'safety-catch silanols' have been developed in which a base, instead of fluoride, is used to unmask the reactive silanol.

Disiloxanes

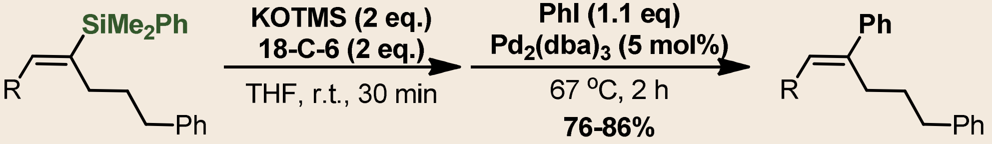


Triethoxysilanes





Dimethylphenylsilanes



R = H, Me or (CH$_2$)$_3$Ph

Other substitution patterns recover significant amounts (33-50%) of desilylated starting material.

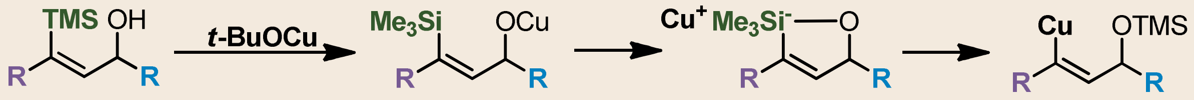
Disiloxanes: Sore, H.F.; Boehner, C.M.; MacDonald, S.J.F.; Norton, D.; Fox, D.J.; Spring, D.R. *Org. Biomol. Chem.* **2009**, *7*, 1068-1071.
Triethoxysilanes: Alacid, E.; Najera, C. *J. Org. Chem.* **2008**, *73*, 2315-2322. DMPS: Anderson, J.C.; Munday, R.H. *J. Org. Chem.* **2004**, *69*, 8971-8974.

Carbon-Carbon Bond Formations

Cu(I) Alkenyl-C-to-O Silyl Migration

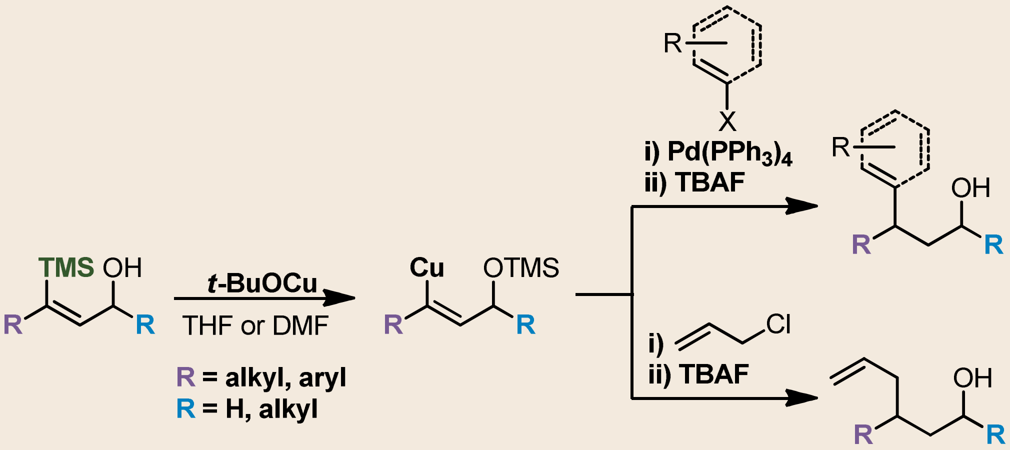
1,4-Migrations

Takeda reported a *t*-BuOCu mediated a 1,4 C-to-O silyl migration in (*Z*)-γ-TMS allylic alcohols. The pentacoordinate silicate performs a Brook-type rearrangement to form vinyl copper species.



The vinylcopper can undergo:

- **Pd-catalysed cross couplings with aryl iodides and vinyl bromides**
- **Cu(I)-promoted cross coupling with allylic chlorides**



No reaction in the absence of Pd
Stereochemically defined dienes

aryl iodides: 63-77%
vinyl bromides: 61-71%

73-88%

Allylation with complete retention of configuration

Taguchi, H.; Ghoroku, K.; Tadaki, M.; Tsubouchi, A.; Takeda, T. *Org. Lett.* **2001**, *3*, 3811-3814; *J. Org. Chem.* **2002**, *67*, 8450-8456.

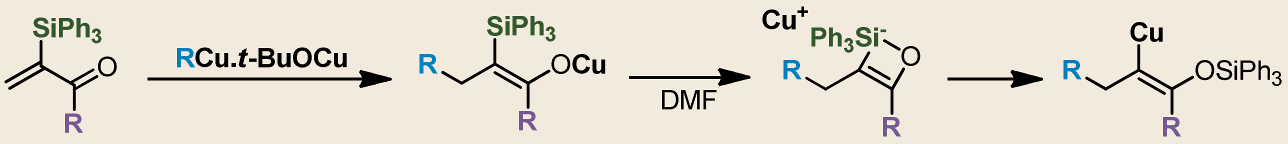
Carbon-Carbon Bond Formations

Cu(I) Alkenyl-C-to-O Silyl Migration

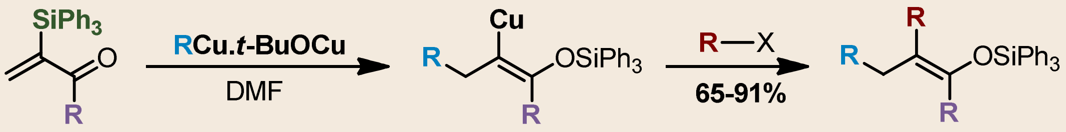
1,3-Migrations

α-Silyl-α,β-unsaturated ketones first undergo 1,4-addition with organocopper reagents. The resultant enolate suffers 1,3-silyl migration, forming vinyl copper species.

Only the *Z*-alkenylcopper species is formed as migration occurs *via* the cyclic silicate.



The vinylcopper reacts with allylic and benzyl chlorides, methyl iodide and dimethylphenylsilane chlorides to afford regio- and stereodefined trisubstituted silyl enol ethers in good to excellent yields with perfect stereoselectivity.



R = 1° and 2° alkyl, aryl

R = alkyl, allyl   R = allyl, benzyl, methyl, silyl

Tsubouchi, A.; Enatsu, S.; Kanno, R.; Takeda, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 7089-7091.

Summary

Synthesis of Alkenyl Silanes

Alkynes	Terminal Vinyl Silanes
Silyl Alkynes	Aldehydes

Applications of Alkenyl Silanes

- Carbon-Oxygen Bond Formations
  - Epoxidation-Oxidation
  - Tamao-Fleming Oxidation
- Carbon-Carbon Bond Formations
  - Hiyama Cross-Coupling
  - Hiyama-Denmark Cross-Coupling
  - Other Fluoride-Free Couplings
  - Cu(I) Alkenyl-C-to-O Silyl Migration

Thank you!