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Silylcupration of allenes followed by reaction with enones. A new strategy for the synthesis of methylenecyclopentanols

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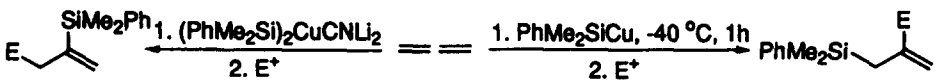
Abstract

Silylcupration of allene using phenyldimethylsilyl-copper followed by conjugated addition to α,β-unsaturated ketones affords oxoallylsilanes with different substitution patterns. When the former oxoallylsilanes are treated with a Lewis acid they undergo highly stereoselective allylsilane terminated cyclization leading to mono-, bi-, and tricyclic methylenecyclopentanols. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: silylcupration; allene; allylsilane; cyclization; methylenecyclopentanol.

Recently, the silylcupration of allenes[1–5] has emerged as a major tool for the synthesis of allyl- and vinylsilanes whose potential as intermediate synthons in organic chemistry is very well known.[6–8] The scope of the reaction and its synthetic applications has recently been reviewed.[9] Addition of the Si-Cu pair occurs *syn*-stereospecifically[10] giving rise to the formation of intermediate cuprates which react with a wide variety of electrophiles leading to vinyl- and allylsilanes with different substitution patterns. The regiochemistry of the addition depends on the nature of the allene,[3] as well as on the steric hindrance of the silyl group attached to copper.[4] Silylcyanocuprates of higher order containing the phenyldimethylsilyl or trimethylsilyl group react with 1,2-propadiene leading, at any temperature between −78°C and 0°C, to vinylsilane-allylcuprate intermediates which are highly reactive toward alkyl halides, halogens, epoxides, oxocompounds, α,β-unsaturated ketones and acid chlorides, thus providing a simple route to attractively functionalized vinylsilanes[1,3] (Scheme 1).



Scheme 1.

More recently, we showed that phenyldimethylsilyl-copper prepared from one equivalent of phenyldimethylsilyl-lithium and copper(I) cyanide reacts with 1,2-propadiene, at −40°C in THF, showing the opposite regiochemistry to that of the corresponding higher order silylcuprate reagent[11]

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(Scheme 1). This route has been profusely used in our work for the preparation of functionalized allylsilanes; in fact, we believe that this methodology is one of the easiest entries to the synthesis of these powerful silicon-synthons. Moreover, allylsilanes are far better carbon nucleophiles than vinylsilanes, and as such have been widely used in synthetic work.[12–14]

We now report that the reaction of phenyldimethylsilyl-copper **1** with 1,2-propadiene (THF, –40°C, 1 h) followed by addition of the α,β-unsaturated ketone **2–8** (–40°C, 1 h then –40°C to 0°C, 0.5 h) in the presence of $BF_3 \cdot Et_2O$ gives the oxoallylsilanes **9–15**, in good yield, after quenching with ammonium chloride solution (Table 1). Conjugate addition is the only reaction observed even in the case of the aldehyde **2**. The use of $BF_3 \cdot Et_2O$ in the reaction mixture increases yields significantly. Compound **13** undergoes isomerization to the *trans*-isomer† in 97% yield, when stirred with a 0.5 M solution of NaOH in H_2O/EtOH/THF.

The bifunctional oxoallylsilanes **9–15**, containing a nucleophilic allylsilane unit and an electrophilic carbonyl moiety, undergo intramolecular reaction when treated with a Lewis acid ($TiCl_4/CH_2Cl_2$, –78°C, 30 min or Et_2AlCl/Tol, 0°C, 1 h). The resulting allylsilane terminated cyclization leads to the formation of 3-methylenecyclopentan-1-ols **16–22** in good yields and with a high degree of stereocontrol. The stereochemistry of the resulting compounds has been assigned on the basis of the observed NMR coupling constants[15] as well as from NOESY experiments. The easy access to exocyclic methylenecyclopentanes is one of the features of this route. Some natural structures containing the 3-methylenecyclopentan-1-ol unit have been found in 5-hydroxymatatabiethers,[16] a family of cyclopentano-monoterpenes isolated from the leaves of *Actinidia polygama* showing strong attracting ability toward male lacewings, *Chrysopa septemunctata* and *Chrysopa japana*.

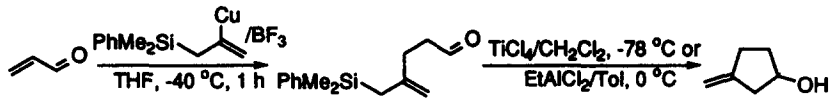
The stereochemistry observed in the cyclization might indicate a preference for the transition state depicted in Scheme 2, where bulky groups (Ph, CO-Lewis acid) attain an equatorial conformation which minimizes steric repulsions.

A general recipe is as follows: A solution of phenyldimethylsilyl-lithium[3] (3 mmol) prepared in THF (3 ml) was added by syringe to a stirred suspension of copper(I) cyanide (269 mg, 3 mmol) in THF (5 ml) at 0°C. The resulting black mixture was stirred at this temperature for an additional period of 30 min, and then used immediately. The solution of phenyldimethylsilyl-copper **1** (3 mmol) in THF (8 ml) was cooled at –40°C and a slight excess of allene was added from a balloon. After 1 h at this temperature 3 mmol of $BF_3 \cdot Et_2O$ (0.38 ml) were added, at –78°C and the mixture stirred for 10 min more, then 3.6 mmol of **3** (526 mg) in THF (5 ml) were added dropwise at –40°C and the resulting solution was kept at this temperature for 1 h. After gentle warming to 0°C (over 0.5 h) the mixture was quenched with saturated ammonium chloride solution and extracted twice with Et_2O. The organic phase was dried over $MgSO_4$ and rotoevaporated. By flash chromatography (EtOAc:hexanes, 1:20) **10** (860 mg, 2.67 mmol) was isolated in 89% yield as a colorless oil. IR (neat): 1720, 1640, 840. ^1H NMR ($CDCl_3$): 7.53–7.06 (m, 10H), 4.74 (br s, 1H), 4.71 (br s, 1H), 3.56 (t, J=7.4, 1H), 2.85 (dd, J=7.4, 16.3, 1H), 2.67 (dd, J=7.4, 16.3, 1H), 1.95 (s, 3H), 1.71 (d, J=14.1, 1H), 1.53 (d, J=14.1, 1H), 0.35 (s, 3H), 0.28 (s, 3H). ^{13}C NMR ($CDCl_3$): 207.1, 148.2, 142.5, 139.1, 133.7, 129.1, 128.4, 128.1, 127.7, 126.6, 107.7, 48.8, 47.2, 30.4, 25.8, –2.8, –3.1. MS-CI: 323 (M+1), 135 (base).

$TiCl_4$ (1.2 mmol, 0.13 ml) was added slowly to a solution of **10** (2 mmol, 644 mg) in CH_2Cl_2 (8 ml) at –78°C. After stirring for 30 min at this temperature, 2 ml of MeOH were added at once and the mixture was allowed to warm up to 0°C. The reaction mixture was washed with a saturated solution of

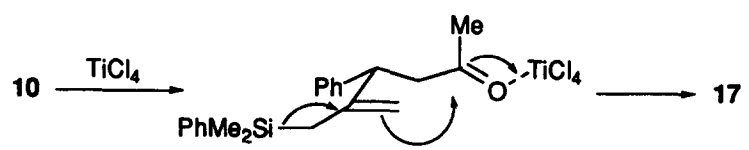
† All attempts to cyclize the *trans*-isomer resulted in formation of low yields of the *trans*-fused bicyclic analogue to **20**, along with much desilylated starting material and other by-products.

Table 1



ENONE	OXOALLYLSILANE[a]	METHYLENECYCLOPENTANOL[a]
Ph, O, H — 2	Ph, O, H; PhMe2Si — 9 (92%)	Ph, H, H, OH — 16 (87%)
Ph, O — 3	Ph, O; PhMe2Si — 10 (89%)	Ph, H, CH3, OH — 17 (83%) Z:E/16:1[b]
O — 4	O; SiMe2Ph — 11 (88%)	OH — 18 (92%)
O — 5	O; SiMe2Ph — 12 (73%)	OH — 19 (81%)
O — 6	H, O; SiMe2Ph — 13 (77%)	H, OH — 20 (79%)[c]
Ph, O — 7	Ph, O; SiMe2Ph — 14 (84%) trans:cis/18:1[b]	OH; Ph; H — 21 (70%)
O — 8	H, O; SiMe2Ph; H — 15 (82%)	H, OH; H, H — 22 (68%)

[a] Isolated yield. All compounds gave satisfactory physicochemical data. [b] *Z/E* ratio determined by NMR and GLC. [c] Yield of epimeric alcohols (3:1 ratio).



Scheme 2.

sodium bicarbonate, extracted with diethyl ether, dried over $MgSO_4$ and rotoevaporated. NMR and GLC of the crude product showed that **17** was accompanied by a small amount of the respective *trans*-isomer (*cis*:*trans* ratio 16:1). Purification by flash-chromatography (EtOAc:hexanes, 1:10) gave **17** (312 mg, 1.66 mmol) in 83% yield as a colorless oil. IR (neat): 3350, 1651, 882. ^1H NMR ($CDCl_3$): 7.35–7.18 (m, 5H), 5.02 (m, 1H), 4.63 (m, 1H), 3.73 (t with fine couplings, J=9.5, 1H), 2.65 (d with fine couplings,

J=15.8, 1H), 2.61 (d with fine couplings, J=15.8, 1H), 2.28 (dd, J=9.5, 13.1, 1H), 2.06 (dd, J=9,5, 13.1, 1H), 1.75 (br s, 1H), 1.43 (s, 3H). ^{13}C NMR ($CDCl_3$): 153.9, 144.4, 128.4, 128.2, 126.2, 109.5, 77.1, 50.2, 49.2, 49.1, 27.7. MS-EI: 188 (M), 145 (98%), 129 (base).

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