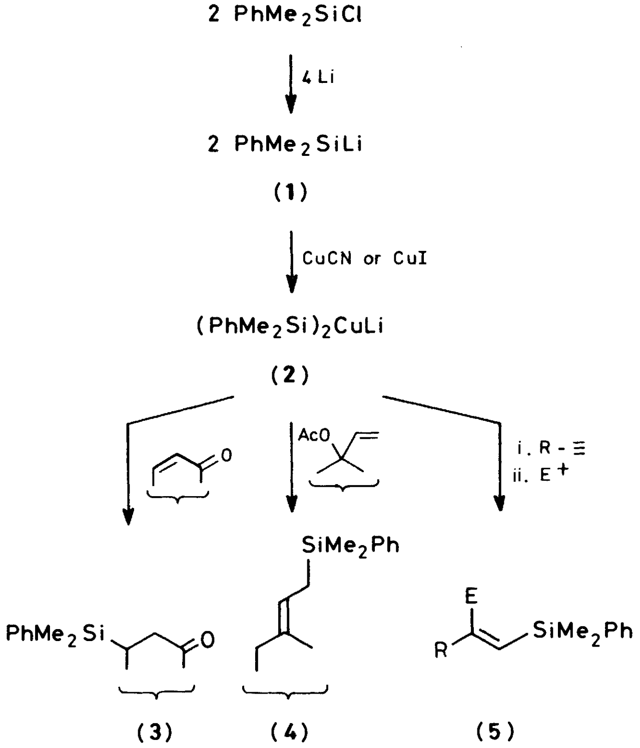
Observations on Various Silyl-cuprate Reagents†

Ian Fleming * and Trevor W. Newton
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW

The mixed silyl-cuprate reagent (**6**), made from 1 equiv. of methyl-lithium, 1 equiv. of phenyldimethylsilyl-lithium, and 1 equiv. of copper(I) cyanide, reacts with 3-methylcyclohexenone (**7**), with methyl cinnamate (**9**), with 1-vinylcyclohexyl acetate (**11**), and with hex-1-yne (**13**) to transfer, in each case, the silyl group, and to give the β-silylcarbonyl compounds (**8**) and (**10**), the allylsilane (**12**), and the vinylsilane (**14**), without the concomitant formation of involatile silicon-containing by-products. The silyl-cuprate reagent (**15**), prepared from trimethylsilyl-lithium and copper(I) cyanide, reacts with similar substrates, in the same way, even though hexamethylphosphoric triamide (HMPA) is present in the reaction medium.

We have reported three types of reaction of the silyl-cuprate reagent (**2**). As shown in Scheme 1, these are (i) the conjugate addition of the silyl group to αβ-unsaturated carbonyl compounds (**2**)→(**3**),[1] (ii) the conjugate displacement of a tertiary allylic acetate, giving allylsilanes, (**2**)→(**4**),[2] and (iii) the silyl-cupration of acetylenes leading to vinylsilanes (**2**)→(**5**).[3] These are powerful methods for making carbon–silicon bonds in relatively complex molecules, since they allow the silyl group to be introduced as a nucleophile. The more usual method for making carbon–silicon bonds uses a silyl halide and an organometallic carbon nucleophile, and is consequently restricted to relatively simple, and usually small, carbon units.



Scheme 1.

In almost all this work we have used the phenyldimethylsilyl group, rather than the more usual trimethylsilyl group, because phenyldimethylsilyl-lithium (**1**) is much easier to make than trimethylsilyl-lithium. The former is available simply by stirring phenyldimethylsilyl chloride and two equivalents of lithium in tetrahydrofuran,[4] whereas the latter is usually made either from hexamethyldisilane and methyl-lithium in hexamethylphosphoric triamide (HMPA)[5] (a solvent to be avoided, if possible), or from bis(trimethylsilyl)mercury[6] (an inconvenient starting material to say the least[7]). We have therefore found it convenient to stick to the phenyldimethylsilyl reagent, since the presence of the phenyl group is unlikely to interfere seriously with any of the chemistry one might want to do with the products (**3**), (**4**), and (**5**). Indeed, insofar as we have used these compounds, they are very little different from their trimethylsilyl counterparts.[8] Furthermore, for one part of our work, the phenyl group is an essential feature, which has allowed us to replace the silyl group in an organic molecule with a hydroxy group.[9]

However, there are two disadvantages to working with the phenyldimethylsilyl group. Because we usually use one equivalent of the silyl-cuprate reagent (**2**) for each equivalent of substrate, one silyl group is left unused. After work-up this appears as a relatively involatile by-product, which has to be separated from the product, (**3**), (**4**) or (**5**), that we are interested in. Secondly, if the silanes (**3**), (**4**), and (**5**) are later to be used in syntheses in any of the usual ways, the phenyldimethylsilyl group will be taken off the organic molecule and will again appear as a relatively involatile by-product. These problems do not arise with the trimethylsilyl group, because the by-product, usually hexamethyldisiloxane, is volatile, and effectively disappears during the work-up. For this reason we have now investigated some silyl-cuprate reagents which avoid one or both of these problems.

Results and Discussion

One reagent (**6**) solves only the first problem, but still allows us to introduce the phenyldimethylsilyl group when we specifically want it.[9] This reagent is a mixed cuprate made from 1 equiv. of phenyldimethylsilyl-lithium[4] and 1 equiv. of methyl-lithium. We find that this reagent transfers specifically the silyl group, and not the methyl group, to each of our three types of substrate, as shown by the examples in Scheme 2. In each case, the silicon-containing by-products were significantly less abundant, and purification was, therefore, easier.

Our second reagent (**15**) simply uses 2 equiv. of trimethylsilyl-lithium, prepared in HMPA by Still's method.[5] What we were concerned with here was to demonstrate that the HMPA did not interfere with any of the cuprate chemistry. As shown by the examples in Scheme 3, it does not present any problems, except

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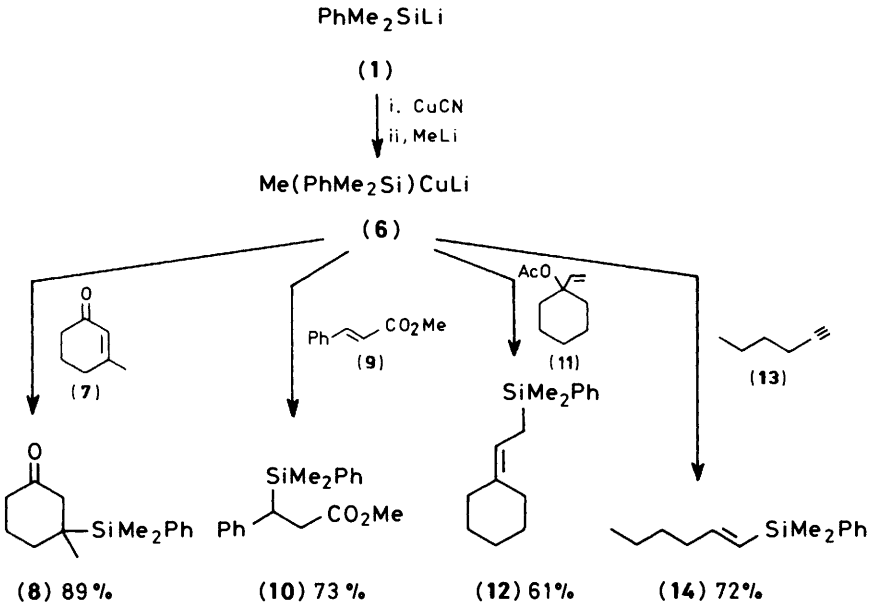
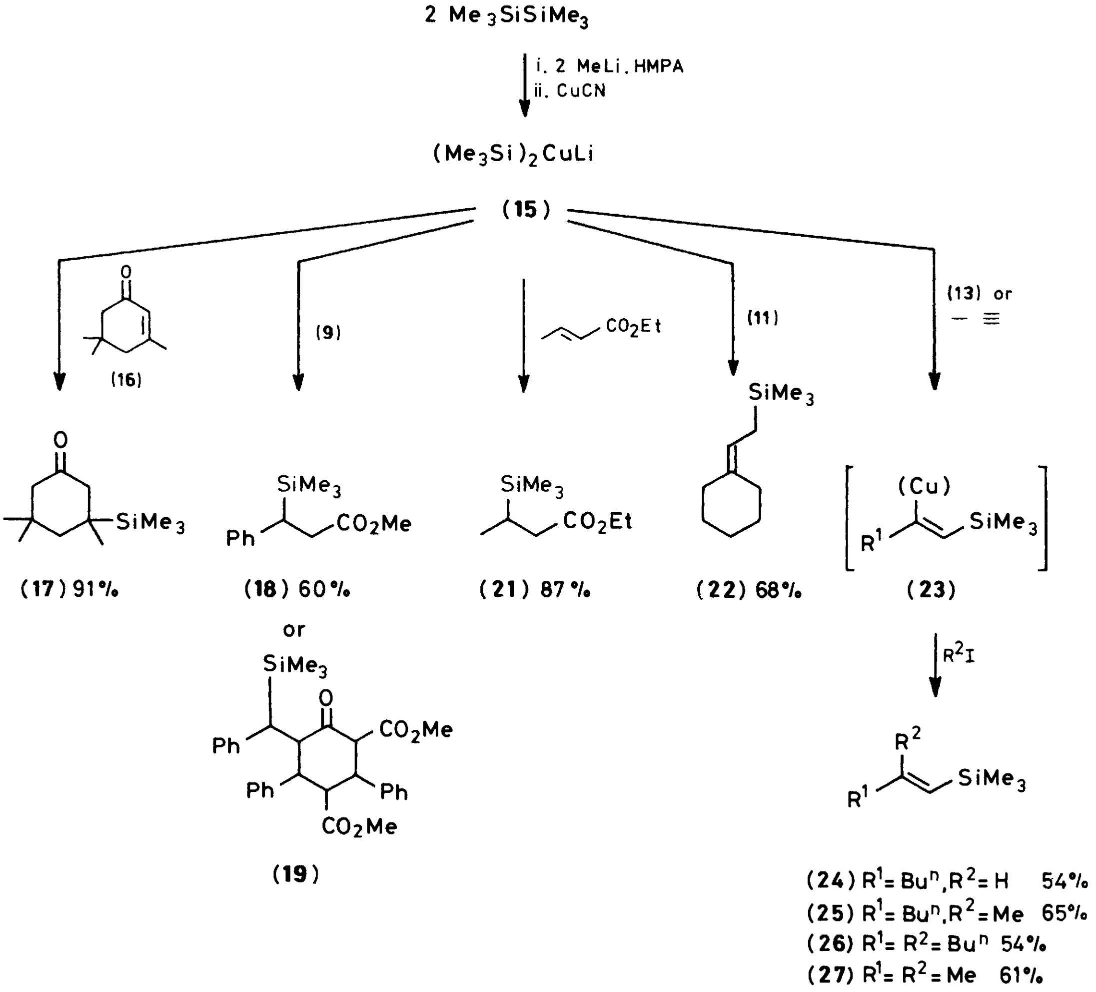


Scheme 2.



Scheme 3.

that the conjugate addition to the unsaturated ester **(9)** + **(15)**$\rightarrow$**(18)** had to be carried out at low temperature (−78 °C) if further reaction of the first-formed enolate was to be avoided. Thus, we found a product which probably has the structure **(19)**, when we carried out the reaction at −23 °C, in the way that worked for the phenyldimethylsilyl-cuprate reagent **(2)** or **(6)**. The presence of HMPA is actually an advantage in one respect: judging by our experience with the phenyldimethylsilyl reagent,[3] vinyl-copper species like **(23)** react with the less-reactive alkyl halides like n-butyl iodide only when HMPA is present. Certainly in this case, the vinyl-copper species **(23)** did react cleanly with n-butyl iodide to give the 2,2-disubstituted vinylsilane **(26)**. None of the reactions in Scheme 3 takes place when trimethylsilyl-lithium is used in the absence of a copper(I) salt.

Our third reagent combines the virtues of the other two, and uses 1 equiv. of trimethylsilyl-lithium and 1 equiv. of methyl-lithium with 1 equiv. of copper(I) cyanide. This reacted cleanly with the cyclohexenone **(7)**, transferring again only the silyl group to give 3-methyl-3-trimethylsilylcyclohexanone (**8**; Me for Ph) in 61% yield. We did not pursue this reagent with the other substrates, but we certainly expect it to work with each of them.

In summary, it is possible to transfer a phenyldimethylsilyl group to each of our standard substrates, without creating phenyldimethylsilyl by-products, by using the mixed cuprate reagent **(6)**, and it is also possible to transfer the trimethylsilyl group to the same substrates in the presence of HMPA. Trost and Chan[10] have successfully treated an allyl bromide with the same trimethylsilyl cuprate reagent in HMPA; we imagine that the HMPA in all these reactions could be replaced by the more expensive but perhaps less dangerous dipolar aprotic solvent *N,N'*-dimethyl-*N,N'*-propyleneurea.[11]

Experimental

Light petroleum refers to the fraction of b.p. 40—60 °C. Work-up means the addition of saturated ammonium chloride solution (1.0 ml), dilution with light petroleum, filtration through glass wool, washing with saturated aqueous ammonium chloride (3 × 20 ml), drying ($MgSO_4$), and evaporation under reduced pressure.

The Mixed Dimethyl(phenyl)silyl(methyl)cuprate Reagent **(6)**.—A solution of dimethyl(phenyl)silyl-lithium **(2)**[3] (1.0 mmol) in THF was added to copper(I) cyanide (89.4 mg, 1.0 mmol) under argon at 0 °C. After 10 min, methyl-lithium (0.8 ml; 1.25M solution in ether) was added dropwise and the mixture was stirred for a further 10 min at 0 °C before use.

3-*Dimethyl(phenyl)silyl*-3-*methylcyclohexanone* **(8)**.—3-Methylcyclohex-2-enone[12] (0.29 ml, 2.5 mmol) was added to a stirred solution of the mixed cuprate reagent **(6)** (3.0 mmol) under argon at −23 °C. The mixture was stirred for 1 h at −23 °C and for 2 h at 0 °C and then quenched by addition of saturated aqueous ammonium chloride (1.0 ml). Work-up followed by column chromatography (light petroleum–ether, 7:3 v/v) gave the ketone **(8)** (545 mg, 89%) as prisms, m.p. 66—67 °C (from ethanol), identical with an authentic sample.[1] No peak at δ 0.98 (authentic[13] 3,3-dimethylcyclohexanone absorbs there) was visible in the ^1H n.m.r. spectrum of the crude products, and the amount of methyl transfer was therefore estimated to be less than 2%.

Methyl 3-*Dimethyl(phenyl)silyl*-3-*phenylpropanoate* **(10)**.—Methyl cinnamate (454 mg, 2.8 mmol) was added dropwise to a stirred solution of the mixed cuprate reagent **(6)** (3.0 mmol) under argon at −23 °C. The mixture was stirred for 1 h at −23 °C and for 1 h at 0 °C. Work-up followed by column chromatography (light petroleum–ether, 7:3 v/v) gave the *ester* **(10)** (610 mg, 73%) as an oil, R_F (light petroleum–ether, 7:3 v/v) 0.70, $\nu_{max.}(CCl_4)$ 1 740 (CO), 1 600 (Ph), 1 424 and 1 160 (SiPh), and 1 248 cm^{1} (SiMe); $\delta(CCl_4)$ 7.7—7.0 (10 H, m, Ph), 3.59 (3 H, s, OMe), 3.2—2.7 (3 H, m, $CHCH_2CO_2Me$) and 0.40 and 0.35 (6 H, 2 s, $SiMe_2$) (Found: M^+, 298.1382. $C_{18}H_{22}O_2Si$ requires *M*, 298.1389), *m/z* 298 (20%, M^+) and 135 (100, Me_2PhSi).

(2-*Cyclohexylidene-ethyl)dimethyl(phenyl)silane* **(12)**.—1-Vinylcyclohexyl acetate **(11)**[14] (420 mg, 2.8 mmol) was added to a stirred solution of the mixed cuprate reagent **(6)** (3.00 mmol) under argon at −23 °C. The mixture was stirred for 1 h at −23 °C and for 1 h at 0 °C. Work-up followed by column chromatography (light petroleum–ether, 19:1 v/v) gave the allylsilane **(12)** (473 mg, 61%) as an oil, identical with an authentic sample.[2]

(E)-1-*Dimethyl(phenyl)silylhex*-1-*ene* **(14)**.—Hex-1-yne (0.48 ml, 4.35 mmol) was added dropwise to a stirred solution of the mixed cuprate reagent **(6)** (4.35 mmol) under argon at 0 °C and the mixture was stirred for 20 min. Work-up followed by column chromatography (light petroleum) gave the vinylsilane **(14)** (680 mg, 72%) identical with an authentic sample.[3]

Lithium Bis(trimethylsilyl)cuprate **(15)**.—A solution of trimethylsilyl-lithium **(6)** (10.0 mmol) prepared[5,15] in HMPA (5 ml) and ether (10 ml, from the methyl-lithium) was diluted with THF (20 ml) at 0 °C. Copper(I) cyanide (447 mg, 5.0 mmol) was added in one portion and the resulting black mixture was stirred for 20 min at 0 °C before use.

3,3,5-*Trimethyl*-3-*trimethylsilylcyclohexanone* **(17)**.—3,5,5-Trimethylcyclohex-2-enone **(16)** (0.45 ml, 3.0 mmol) was added to a stirred solution of the bis(trimethylsilyl)cuprate **(15)** (5.0 mmol) under argon at −23 °C. The mixture was stirred for 1 h at −23 °C and for 30 min at 0 °C. Work-up followed by column chromatography (light petroleum–ether, 7:3 v/v) gave the ketone **(17)**[16] (748 mg, 91%) as an oil, R_F(light petroleum–ether, 7:3 v/v) 0.56, $\nu_{max.}(CCl_4)$ 1 712 (CO) and 1 247 cm^{1} (SiMe), $\delta(CCl_4)$ 2.30—1.30 (6 H, m, 3 CH_2's), 0.95 (9 H, s, br, 3 ring CH_3's), and −0.11 (9 H, s, $SiMe_3$) (Found: M^+, 212.1610. $C_{12}H_{24}OSi$ requires *M*, 212.1597), *m/z* 212 (5%, M^+), 197 (63 *M* − Me), and 73 (100, Me_3Si).

Methyl 3-*Trimethylsilyl*-3-*phenylpropanoate* **(18)**.—A solution of methyl cinnamate (243 mg, 1.5 mmol) in THF (5 ml) was added dropwise slowly to a stirred solution of the bis(trimethylsilyl)cuprate **(15)** (2.5 mmol) under argon at −78 °C. The mixture was stirred for 1 h at −78 °C and for 1 h at −23 °C and then quenched by addition of methanol (1.0 ml) and allowed to warm gradually to room temperature. Work-up followed by column chromatography (light petroleum–ether, 4:1 v/v) gave the *ester* **(18)** (353 mg, 60%) as an oil, R_F (light petroleum–ether, 4:1 v/v) 0.47, $\nu_{max.}(CCl_4)$ 1 742 (CO), 1 603, 1 583, and 1 498 (Ph), and 1 252 cm^{-1} (SiMe); $\delta(CCl_4)$ 7.58—7.05 (5 H, m, Ph), 3.63 (3 H, s, OMe), 3.00—2.57 (3 H, m, CH_2CHSi), and 0.03 (3 H, s, $SiMe_3$) (Found: M^+, 236.1224, $C_{13}H_{20}O_2Si$ requires *M*, 236.1232), *m/z* 236 (4%, M^+), 221 (2, *M* − Me), and 73 (100, Me_3Si).

Reaction of Lithium Bis(trimethylsilyl)cuprate **(15)** *with Methyl Cinnamate*.—When the reaction was carried out at −23 °C for 1 h and 0 °C for 1 h, followed by column chromatography a compound, probably **(19)**, was isolated, $\nu_{max.}$ 1 755 (CO_2Me), 1 740 (CO_2Me), and 1 710 cm^{-1} (CO); $\delta(CD_2Cl_2)$ 7.75—7.0 (11 H, m, ArH) 7.7—6.7 (4 H, m, ArH), 4.3—

3.3 (5 H, m, CH's), 3.7 and 3.2 (3 H, s, 2 × OMe's), 2.3 (1 H, d, C*H*Si), and −0.1 (9 H, s, $SiMe_3$); *m/z* 528 (40%, M^+), 513 (20, *M* − Me), 476 (25, *M* − MeOH), 469 (30, *M* − CO_2Me), 437 (30, *M* − CO_2Me − MeOH), 365 (75, *M* − PhCH=$CHCO_2Me$ − H or *M* − $PhCHSiMe_3$), and 307 (100, *M* − PhCH=$CHCO_2Me$ − CO_2Me).

Ethyl 3-*Trimethylsilylbutanoate* (**21**).—Ethyl crotonate (**20**) (342 mg, 3.0 mmol) was added dropwise to a stirred solution of the bis(trimethylsilyl)cuprate (**15**) (5.0 mmol) under argon at −23 °C. The mixture was stirred for 2 h at −23 °C and for 1 h at 0 °C. Work-up followed by column chromatography (light petroleum–ether, 19:1 v/v) gave the *ester* (**21**) (492 mg, 87%) as an oil, R_F (light petroleum–ether, 19:1 v/v) 0.12, $\nu_{max.}(CCl_4)$ 1 738 (CO) and 1 251 cm ^{1} (SiMe); $\delta(CCl_4)$ 4.13 (2 H, m, OCH_2CH_3), 2.65—2.10 (2 H, m, CH_2CO_2OEt), 1.40—1.10 (3 H, t br, *J* 7 Hz, OCH_2CH_3), 1.05—0.60 (1 H, m, C*H*Si), 0.85 (3 H, d, *J* 7 Hz, CH_3CHSi), and −0.08 (9 H, s, $SiMe_3$) (Found: *m/z* 187.1151, $C_9H_{19}O_2Si$ requires *M* − H, 187.1154), *m/z* 188 (5%, M^+), 187 (18, *M* − H), 143 (4, *M* − OEt), 73 (52, Me_3Si), and 69 (100, *M* − H − Me_3SiOH − CH_2=CH_2).

(2-*Cyclohexylidene-ethyl*)*trimethylsilane* (**22**).—1-Vinylcyclohexyl acetate (**11**)[14] (670 mg, 4.0 mmol) was added to a stirred solution of the bis(trimethylsilyl)cuprate reagent (**15**) (5.0 mmol) under argon at −23 °C and kept for 1 h at 0 °C. Work-up followed by column chromatography (light petroleum–ether, 19:1 v/v) gave the allylsilane (**22**)[17] (4.8 mg, 68%) as an oil identical with an authentic sample.

The Silylcupration of Hex-1-*yne*.—Hex-1-yne (0.22 ml, 2.0 mmol) was added to a stirred solution of the bis(trimethylsilyl)-cuprate reagent (**15**) (2.5 mmol) under argon at 0 °C and the mixture was stirred for 20 min to give the vinyl-copper species (**23**).

(E)-1-*Trimethylsilylhex*-1-*ene* (**24**).—The vinyl-copper species (**23**) (0.5 mmol) was quenched with water (1.0 ml). Work-up followed by column chromatography (light petroleum–ether, 19:1 v/v) gave the vinylsilane (**24**)[18] (42 mg, 54%) as an oil, R_F (light petroleum–ether, 19:1 v/v) 0.76, $\nu_{max.}(CCl_4)$ 1 620 (C=C), 1 250 (SiMe), and 990 cm^{-1} (*trans*-CH=CH). The n.m.r. spectrum was closely similar to that reported[19] (Found: *m/z* 141.1104. $C_8H_{17}Si$ requires *M* − Me, 141.1099), *m/z* 141 (4%, *M* − Me) and 73 (100, Me_3Si).

(E)-2-*Methyl*-1-*trimethylsilylhex*-1-*ene* (**25**).—Methyl iodide (1.0 ml) was added to a stirred solution of the vinyl-copper species (**23**) (2.0 mmol) under argon at 0 °C and the mixture was stirred for 20 min. Work-up followed by column chromatography (light petroleum–ether, 19:1 v/v) gave the *vinylsilane* (**25**) (110 mg, 65%) as an oil, R_F (light petroleum–ether, 19:1 v/v) 0.75, $\nu_{max.}(CCl_4)$ 1 620 (C=C) and 1 250 cm^{-1} (SiMe); $\delta(CCl_4)$ 5.14 (1 H, s br, CCHSi), 2.02 (2 H, t, *J* 7 Hz, CH_2C=C), 1.68 (3 H, s, CH_3C=C), 1.6—1.1 (4 H, m, other CH_2's), 1.83 (3 H, t, *J* Hz, CH_3CH_2), and 0.02 (9 H, s, $SiMe_3$) (Found: *m/z* 155.1253. $C_9H_{19}Si$ requires *M* − Me, 155.1256), *m/z* 155 (6%, *M* − Me) and 73 (100, Me_3Si). This compound has been obtained before only as a component of a mixture.[18]

2-*Butyl*-1-*trimethylsilylhex*-1-*ene* (**26**).—n-Butyl iodide (1.0 ml) was added to a stirred solution of the vinyl-copper species (**23**) (2.0 mmol) under argon at 0 °C and the mixture was stirred for 2 h. Work-up followed by column chromatography (light petroleum–ether, 19:1 v/v) gave the *vinylsilane* (**26**) (230 mg, 54%) as an oil, R_F (light petroleum–ether, 19:1 v/v) 0.75, $\nu_{max.}(CCl_4)$ 1.620 (C=C) and 1 250 cm^{-1} (SiMe); $\delta(CCl_4)$ 5.08 (1 H, s br, C=CHSi), 2.4—0.7 (18 H, m, 2 × Bu^n), and 0.10 (9 H, s, $SiMe_3$) (Found: M^+, 212.1964. $C_{13}H_{28}Si$ requires *M*, 212.1960), *m/z* 212 (11%, M^+), 197 (9, *M* − Me), and 73 (100, Me_3Si).

2-*Methyl*-1-*trimethylsilylprop*-1-*ene* (**27**).—Propyne gas (96 ml, 4.0 mmol) was injected over a stirred solution of the bis(trimethylsilyl)cuprate (**15**) (5.0 mmol) at 0 °C and the mixture was stirred for 20 min at 0 °C. Methyl iodide (1.0 ml) was added to the vinyl-copper intermediate and the mixture was stirred for a further 20 min. Work-up followed by column chromatography (light petroleum–ether, 19:1 v/v) gave the *vinylsilane* (**27**)[20] (312 mg, 61%) as an oil, R_F (light petroleum–ether, 19:1 v/v) 0.80, $\nu_{max.}(CCl_4)$ 1 620 (C=C) and 1 250 cm^{-1} (SiMe); $\delta(CCl_4)$ 5.12 (1 H, s br, C=CHSi), 1.85 (3 H, s, Me *trans* to Si), 1.68 (3 H, s, Me *cis* to Si), and 0.05 (9 H, s, $SiMe_3$) (Found: M^+, 128.1023. $C_7H_{16}Si$ requires *M*, 128.1022), *m/z* 128 (4%, M^+), 113 (31, *M* − Me), and 73 (100, Me_3Si).

3-*Methyl*-3-*trimethylsilylcyclohexanone*.—A solution of trimethylsilyl-lithium (5.0 mmol) in HMPA (3 ml) and ether was diluted with THF (10 ml) at 0 °C. Copper(I) cyanide (497 mg, 5.0 mmol) was added in one portion and the mixture was stirred for 10 min. Methyl-lithium (4.0 ml of a 1.25M solution in ether) was added dropwise and the mixture was stirred for a further 10 min. 3-Methylcyclohex-2-enone[12] (0.45 ml, 4.0 mmol) was added under argon at −23 °C, the mixture stirred for 1 h at −23 °C and for 2 h at 0 °C. Work-up followed by column chromatography (light petroleum–ether, 7:3 v/v) gave the ketone[1] (449 mg, 61%) as an oil, identical with an authentic sample.

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