Preliminary communication

Addition of dimethylphenylsilyl cuprates to vinyl epoxides: Effect of cuprate stoichiometry on stereochemistry and regiochemistry

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Abstract

The stereochemical and regiochemical outcome of reactions of $PhMe_2SiLi/CuCN$ mixtures with vinyl epoxides depends on the $PhMe_2SiLi/CuCN$ ratio.

Keywords: Silicon; Copper; Lithium; Cuprate; Vinyl epoxide; Stereochemistry

During studies on the degradation of mevinolin (**1a**) and compactin (**1b**) to the enone **2** [1,2], we examined the response of vinyl epoxide **3a** to $(PhMe_2Si)_2CuLi$ [3–5] (prepared from CuI and $PhMe_2SiLi$ [6]), and obtained two isomeric products **4a** and **5a** [7]. The ratio of these isomers was variable and the major product from one experiment could be the minor product in the next run. For this reason we tried $PhMe_2SiLi$ [6] itself. Although the desired allylic silane **4a** was produced [1,8], the yields were erratic [9] (40–91%) and also depended inversely on the scale of the reaction. While our initial experiments had given sufficient quantities of **4a** for our immediate needs, when we later came to examine the compactin series (using **3b** [2]) we obtained a complex mixture with the lithium reagent. We decided, therefore, to try silyl cuprates, but made this time from CuCN [6]. Such reagents [11] gave reproducible results and afforded the isomeric silanes **4b** and **5b**. The ratio of the isomers, which was established without separation, by ^1H NMR measurements, depends on the stoichiometry of the cuprate mixture (Table 1).

The stereochemistry of **4b** and **5b** was established by ^1H NMR measurements, the characteristic features being that $J_{7,8} = 0$ Hz and $J_{6,7} \approx 3.4$ Hz for **4b**, while $J_{7,8} = 5.5$ Hz and $J_{6,7} \approx 0$ Hz for **5b**. Examination of Dreiding models shows that the J-values are entirely

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consistent with the dihedral angles measured on the models.

It is not clear why the different reagent mixtures produce stereoisomeric products. Reaction of carbon organocuprates with vinyl epoxides generally [12,13] proceeds by an *anti* S_N2' pathway [14], but the mechanism [12,13,15] has not been established. In the present case additional considerations are that the effective reagent in each of the $PhMe_2SiLi/CuCN$ equilibrium mixtures [6b] has different steric requirements and offers different opportunities for prior complexation with the epoxide oxygen.

We next reexamined the mevinolin series, but using the CuCN-derived reagents, and found (see Table 1) entirely comparable results. Again, the multiplicity of the vinyl signal in the ^1H NMR spectra was characteristic, being a singlet for **4a** and a doublet ($J = 4.5$ Hz) for **5a**.

We have also treated vinyl epoxides **6a** and **7a** with the three silyl cuprates (Table 2). Once more, the outcome is sensitive to reagent composition, but the results are now complicated by direct epoxide opening (**6a → 6d**, and **7a → 7d**), which was not observed [16] with mevinolin or compactin. Direct epoxide opening, in the case of the simple six-membered ring (**7a → 7d**), is evidently easier than the *syn* S_N2' pathway (**7a → 7c**), which does not appear to be followed. However, for the five-membered ring, at least with the 1 : 1 $PhMe_2SiLi/CuCN$ stoichiometry, some reaction does occur by a *syn* S_N2' mechanism.

1a R = Me
1b R = H

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(1)
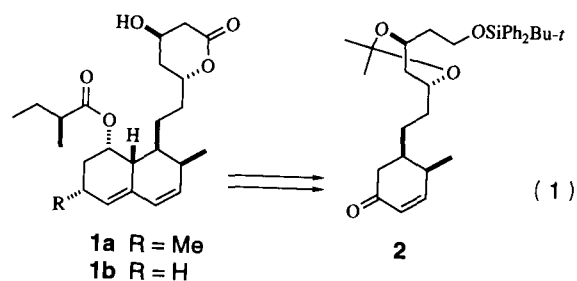
The structure and stereochemistry of the products from **6a** were readily apparent from the ^{13}C and ^{1}H NMR spectra, taken together with mechanistic considerations [17], but the stereochemistry of **7b** and **7d** could be assigned only after hydrogenation to the corresponding cyclohexanols [18].

Reagent made using 2 : 1 PhMe$_2$SiLi/CuCN has been reported [19] to convert **7a** into the *trans* disubstituted cyclohexene **7b**, but the dependence of the stereochemical outcome with silyl cuprate reagents—in the present case, using vinyl epoxides **3a**, **3b**, and **6a**—has not been observed before.

The three silyllithium / copper cyanide mixtures have been examined by NMR techniques [6b], which established the nature of the main species that are formed, and the behavior of the mixtures towards 2-cyclohexenone and 1-octyne [6] has also been studied. In each case the enone is converted [6b] into the same product—the result of conjugate delivery of the
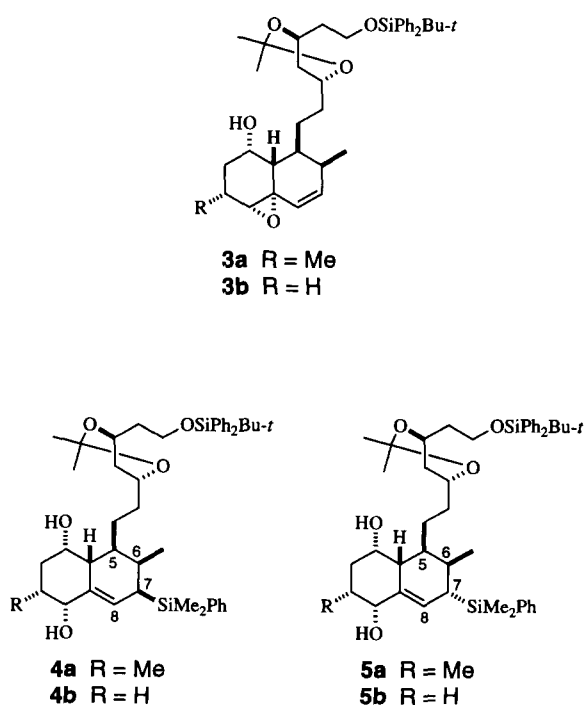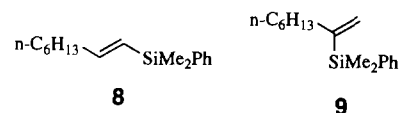
Table 1

Vinyl epoxide	PhMe$_2$SiLi:CuCN	Overall yield (%)	Products
3b	1:1	93	**4b:5b** 1:6
3b	2:1	95	**4b:5b** 11:1
3b	3:1	97	**4b:5b** 15:1
3a	1:1	98	**4a:5a** 1:8
3a	2:1	97	**4a:5a** 7:1
3a	3:1	96	**4a:5a** 7:1

PhMe$_2$Si unit—but, with the acetylene, the 1:1 ratio leads to a mixture (60:40) of terminal (**8**) and internal (**9**) silanes (after quenching with water), while the 2:1 and 3:1 ratios lead almost exclusively to **8**.

8

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In summary, our results show that the course of reactions of dimethylphenylsilyl cuprates with vinyl epoxides is sensitive to the stoichiometry of the reagent and, in favorable cases, significant stereochemical con-

3a R = Me
3b R = H

4a R = Me
4b R = H

5a R = Me
5b R = H

Table 2 [a]

	6b		**6c**		**6d**	Total yield
6a						
PhMe$_2$SiLi	–	:	–	:	1	(27%)
1 PhMe$_2$SiLi 1 CuCN	5.6	:	1	:	–	(72%)
2 PhMe$_2$SiLi 1 CuCN	1.14	:	–	:	1	(79%)
3 PhMe$_2$SiLi 1 CuCN	1	:	–	:	1.5	(70%)

	7b		**7c**		**7d**	
7a						
PhMe$_2$SiLi	–	:	–	:	1	(40%)
1 PhMe$_2$SiLi 1 CuCN	1	:	–	:	–	(70%)
2 PhMe$_2$SiLi 1 CuCN	4.9	:	–	:	1	(94%)
3 PhMe$_2$SiLi 1 CuCN	1.5	:	–	:	1	(90%)

[a] Yields and ratios determined by isolation.

trol is possible in preparatively useful S_N2' experiments.

All new compounds were characterized by spectroscopic measurements and either combustion analysis or mass measurement.

References and notes

[1] D.L.J. Clive and C. Zhang, J. Chem. Soc., Chem. Commun. (1993) 647.

[2] Experimental details of the compactin degradation will be reported elsewhere.

[3] We imply by this formulation only the stoichiometry: 2 moles PhMe$_2$SiLi per mole CuI.

[4] (a) I. Fleming and D. Marchi Jr., Synthesis (1981) 560; (b) D.J. Ager, I. Fleming and S.K. Patel, J. Chem. Soc., Perkin Trans., 1 (1981) 2520.

[5] Cf. S. Sharma and A.C. Oehlschlager, J. Org. Chem., 54 (1989) 5383.

[6] (a) I. Fleming, T.W. Newton and F. Roessler, J. Chem. Soc., Perkin Trans, 1 (1981) 2527; (b) S. Sharma and A.C. Oehlschlager, Tetrahedron, 45 (1989) 557; (c) we made PhMe$_2$SiLi according to the experimental procedure of Sharma and Oehlschlager.

[7] Tetrahydrofuran was used for all experiments.

[8] In principle, either stereochemistry at C(6) would have been suitable for us.

[9] This variation was discovered some months after our preliminary communication (Ref. [1]). We were unable to identify the cause, despite extensive experimentation, including deliberate addition of lithium salts. Cf. Ref. [10].

[10] (a) J.P. Marino and M.G. Kelly, J. Org. Chem., 46 (1981) 4389; (b) J.P. Marino, R. Fernández de la Pradilla and E. Laborde, J. Org. Chem., 52 (1987) 4898.

[11] Mole ratio of CuCN to epoxide $\geq 2:1$ for 3a,b and ca. 1:1 for 6a, 7a. We used CuCN from Fluka (purum p.a.) and purified it using the method of J.A. Marshall, J.D. Trometer and D.G. Cleary, Tetrahedron, 45 (1989) 391.

[12] J.A. Marshall, Chem. Rev., 89 (1989) 1503.

[13] (a) G. Teutsch, Tetrahedron Lett. (1979) 2051; (b) G. Teutsch, Tetrahedron Lett., 23 (1982) 4697.

[14] A competing pathway is opening of the allylic epoxide C–O bond (see Ref. [12]).

[15] E.J. Corey and N.W. Boaz, Tetrahedron Lett., 25 (1984) 3063.

[16] If this pathway is followed at all in these cases it must be to a very minor extent, judged by the high total yields of 4a,b and 5a,b.

[17] We assume that direct epoxide opening of 8a with PhMe$_2$SiLi occurs by the normal trans pathway. Assignment of cis and trans stereochemistry was guided by the characteristic chemical shift difference (see Ref. [10b]) between the two methylene protons, the cis isomer having the larger different (0.57 ppm for cis (6c) and 0.26 ppm for trans (6b) isomers).

[18] Trans 4-(dimethylphenylsilyl)cyclohexanol from 7b: ^{13}C NMR (75.47 MHz, C$_6$D$_6$) δ −5.02 (CH$_3$Si), 24.67 (CHSi), 26.23 (CH$_2$), 37.53 (CH$_2$), 70.73 (CHOH), 128.00 (aryl CH), 129.11 (aryl CH), 134.17 (aryl CH), 138.24 aryl CSi). ^{1}H NMR (300 MHz, C$_6$D$_6$) δ 0.49 (tt, $J = 12.75$, 3.0 Hz), 3.2 (tt, $J = 10.75$, 3.8 Hz). Cis and trans 4-t-butylcyclohexanol have δ CHOH at 3.75 and 3.24, respectively in C$_6$D$_6$.
Trans 2-(dimethylphenylsilyl)cyclohexanol from 7d: ^{13}C NMR (75.47 MHz, C$_6$D$_6$) δ −3.24 (CH$_3$Si), −2.78 (CH$_3$Si), 25.41 (CH$_2$), 27.04 (CH$_2$, two overlapping signals), 34.80 (CHSi), 38.34 (CH$_2$), 72.86 (CHOH), 127.93 (aryl CH), 128.99 (aryl CH), 134.52 (aryl CH), 139.23 aryl CSi). ^{1}H NMR (300 MHz, C$_6$D$_6$) δ 0.75 (t, $J = 2.9$, 11.5 Hz).

[19] B. Laycock, W. Kitching and G. Wickham, Tetrahedron Lett., 24 (1983) 5785.