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LETTERS

Stereoselective Phenyl Migration from Silicon to Carbon

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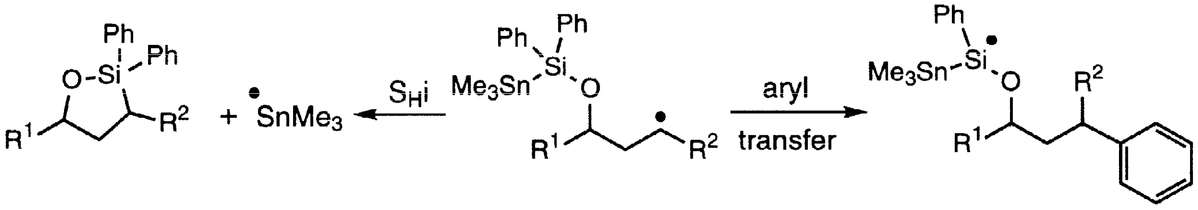
Abstract: In the present letter, the first stereoselective radical 1,5 phenyl transfer from silicon to carbon is reported. Diphenyl(trimethylsilyl)silyl ethers, the corresponding germylated and stannylated derivatives, and also some silyl ethers derived from commercially available silicon protecting groups were tested in this *ipso* substitution reaction. Diastereoselectivities of up to 11:1 were obtained. © 1998 Elsevier Science Ltd. All rights reserved.

During the last fifteen years free radical reactions have received great attention, mainly due to the finding that they can be conducted highly dia- and enantioselective.[1,2] Numerous examples of aryl transfers (*ipso* substitutions) from carbon to carbon,[3] nitrogen to carbon,[4] oxygen to carbon,[5] and sulfur to carbon[6] have been published. However, there are only a few reports on the aryl migration from silicon to carbon.[7,8] In this letter, the first examples of highly diastereoselective radical 1,5 phenyl transfers from silicon to carbon are reported.[9]

We have recently introduced the S_Hi-reaction at silicon using C-centered radicals in the γ-position to diphenyl(trimethylstannyl)silyl ethers as an alternative method for the preparation of cyclic alkoxysilanes.[10] In the meantime, we have found that in systems where the S_Hi-reaction is slow, aryl transfer from silicon to carbon may compete (Scheme 1). We decided to study this 1,5 aryl migration as a method for the stereoselective $C(sp^2)$-$C(sp^3)$ bond formation.



Scheme 1

To this end, iodides **1-5** were prepared from the corresponding chlorosilanes and (*like*)-4-iodo-2-pentanol (THF, NEt_3, DMAP) in high yields (50-96%).[11,12] Treatment of 3-iodo-1-phenylbutanol with the corresponding disilyl chloride under analoguous conditions afforded **6** in 83% yield. Phenyl transfer reactions were performed by slow addition of Bu_3SnH (1.2 equiv) to a 0.05 M solution of the iodide in refluxing benzene.[13] After desilylation (MeLi) the alcohols **7** and **8** were obtained in moderate to good yields with high diastereoselectivities (up to 11:1, Scheme 2, Table). In the case of silyl ether **1**, the aryl transfer product **7** was isolated in 35% yield with high selectivity (*u*:*l* = 10:1, entry 1)[14] besides 30% of the corresponding S_Hi-derived product (see Scheme 1). From our previous studies on the S_Hi-reaction at silicon, we knew that upon replacing the trimethyltin group at

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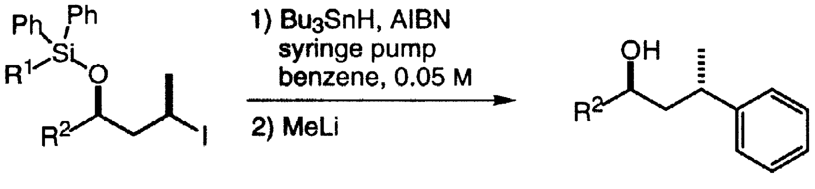
silicon by a trimethylgermyl or a trimethylsilyl group, the rate of the cyclization reaction (→ S_Hi-product) decreases by more than two orders of magnitude.[15] Indeed, the *ipso* substitution product **7** was formed in higher yield (**2** (57%), **3** (70%)) with equal selectivity (10:1, entries 2,3) using the Si and Ge analogs **2** and **3**. In the case of the TBDPS ether **4** and the triphenylsilyl ether **5** a decrease of both the yield and the selectivity was noticed (entries 4,5). The size of the substituent at the stereogenic center has only a small effect on the selectivity. Thus, with the phenyl-substituted silyl ether **6** only a slightly better selectivity (11:1) was obtained for the formation of **8** (entry 6).



1-6
(specification of R^1 and R^2 see Table)

7 (R^2 = Me)
8 (R^2 = Ph)

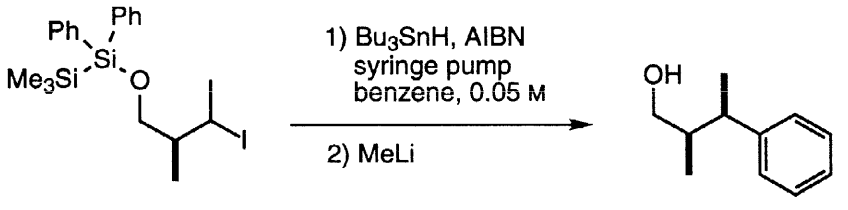
Scheme 2

Table. Diastereoselective phenyl migration from Si to C - variation of the substituents at silicon.

Entry	Compound	R^1	R^2	Product **7** or **8** [%]	Ratio [*u* : *l*][a]
1	**1**[b]	Me_3Sn	Me	35[c]	10 : 1
2	**2**	Me_3Ge	Me	57	10 : 1
3	**3**	Me_3Si	Me	70	10 : 1
4	**4**	*t*-Bu	Me	33	6 : 1
5	**5**	Ph	Me	37	6 : 1
6	**6**[d]	Me_3Si	Ph	62	1 : 11[e]

[a] Determined by GC analysis. [b] Used as a mixture of diastereoisomers (*u* : *l* = 7 : 3). [c] 4-(Methyldiphenylsilyl)-2-pentanol was formed in 30% yield (see text). [d] 1 : 1 Mixture of diastereoisomers. [e] No change of the stereochemical outcome of the reaction. Due to the higher priority of Ph vs. 2-phenylpropyl (according to the CIP convention) the major isomer has to be assigned as *like*-isomer.

We next studied the 1,2 stereoselectivity of the phenyl migration. With silyl ether **9** prepared from the corresponding 3-iodoalcohol (1:1 mixture of diastereoisomers) alcohol **10** was obtained in 17% yield and a diastereoselectivity of 6:1 (Scheme 3).[16]

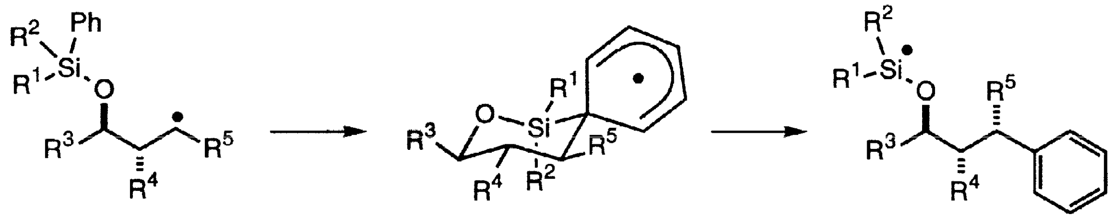


9

10 (*l* : *u* = 6 : 1)

Scheme 3

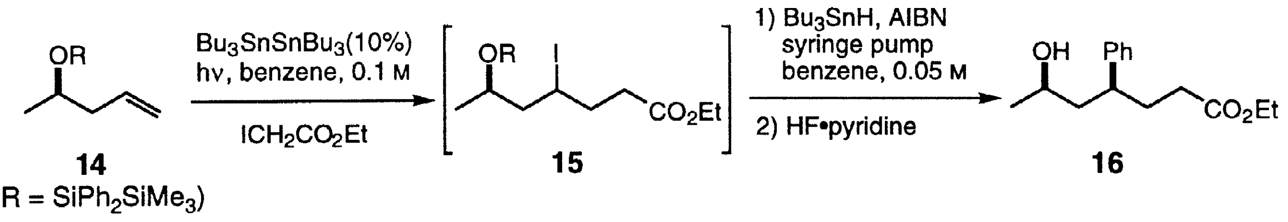
From the selectivities observed in the systems studied so far we suggest the following model to explain the stereochemical outcome of the phenyl migration: Radical **11**, generated after initial iodine abstraction, undergoes intramolecular *ipso* attack at the silylated phenyl group to form cyclohexadienyl radical **12** (Scheme 4).[17] We assume that the low energy transition state for the formation of **12** resembles a chair with the substituents in equatorial positions. Rearomatization then affords silyl radical **13** which eventually leads to the corresponding alcohol. According to this model, the observed 1,3- (→ *unlike* products) and 1,2 selectivity (→ *like* product) can be readily understood (see Scheme 4). The similar selectivities obtained for **4** and **5** are compatible with the model since in the cyclohexadienyl radical **12** derived from TBDPS ether **4** the bulky *tert*-butyl group is expected to occupy the equatorial position (R^1 in **12**) placing the phenyl group axial (R^2 in **12**). Thus, the transition state in the formation of **12** derived from **4** should resemble the transition state derived from **5** with respect to the 1,3 diaxial interaction in the chair (R^2 = phenyl in both systems).



11 **12** **13**

Scheme 4

We next studied a reaction sequence comprising a radical addition reaction with a subsequent aryl migration in one pot. Silylether **14** was first allowed to react with ethyl iodoacetate under atom transfer conditions[18] to afford the intermediate iodide **15**, which after dilution was directly transformed to **16** under the conditions specified above (Scheme 5). Hydroxyester **16** was isolated in 39% yield as a 11:1 (*u*:*l*) mixture of diastereoisomers.[19]



14 ($R = SiPh_2SiMe_3$) **15** **16**

Scheme 5

In summary, we have shown that the intramolecular *ipso* substitution in diphenyl(trimethylsilyl)silyl ethers is an efficient method for the stereoselective C(sp^3)–phenyl bond formation. High 1,2- and 1,3 diastereoslectivities were obtained in the 1,5 phenyl migration reaction.

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References and Notes

[1] D. P. Curran, N. A. Porter, B. Giese, Stereochemistry of Radical Reactions, VCH, Weinheim, 1995.

[2] Enantioselective reactions: M. Murakata, T. Jono, Y. Mizuno, O. Hoshino, *J. Am. Chem. Soc.* **1997**, *119*, 11713 and references cited therein; M. P. Sibi, J. J. Shay, J. Ji, *Tetrahedron Lett.* **1997**, *38*, 5955; N. A. Porter, J. H. Wu, G. Zhang, A. D. Reed, *J. Org. Chem.* **1997**, *62*, 6702; K. Schwarzkopf, M. Blumenstein, A. Hayen, J. O. Metzger, *Eur. J. Org. Chem.* **1998**, 177.

[3] L. Giraud, E. Lacôte, P. Renaud, *Helv. Chim. Acta*, **1997**, *80*, 2148 and references cited therein.

[4] E. Lee, H. S. Whang, C. K. Chung, *Tetrahedron Lett.* **1995**, *36*, 913.

[5] E. Lee, C. Lee, J. S. Tae, H. S. Wang, K. S. Li, *Tetrahedron Lett.* **1993**, *34*, 2343 and references cited therein; R. Leardini, H. McNab, D. Nanni, *Tetrahedron* **1995**, *51*, 12143; A. M. Rosa, A. M. Lobo, P. S. Branco, S. Prabhakar, *Tetrahedron* **1997**, *53*, 285; D. Crich, J.-T. Hwang, *J. Org. Chem.* **1998**, *63*, 2765.

[6] a) S. Caddick, K. Aboutayab, K. Jenkins, R. I. West, *J. Chem. Soc. Perkin Trans 1* **1996**, 675; F. Aldabbagh, W. R. Bowmann, *Tetrahedron Lett.* **1997**, *38*, 3793; b) M. L. E. N. da Mata, W. B. Motherwell, F. Ujjainwalla, *ibid.* **1997**, *38*, 137; c) M. L. E. N. da Mata, W. B. Motherwell, F. Ujjainwalla, *ibid.* **1997**, *38*, 141; E. Bonfand, W. B. Motherwell, A. M. K. Pennell, M. K. Uddin, F. Ujjainwalla, *Heterocycles*, **1997**, *46*, 523.

[7] J. W. Wilt, C. F. Dockus, *J. Am. Chem. Soc.* **1970**, *92*, 5813; J. W. Wilt, W. K. Chwang, *ibid.* **1974**, *96*, 6194; J. W. Wilt, W. K. Chwang, C. F. Dockus, N. M. Tomiuk, *ibid.* **1978**, *100*, 5534.

[8] H. Sakurai, A. Hosomi, *J. Am. Chem. Soc.* **1970**, *92*, 7507.

[9] For diastereoselective radical phenyl migrations from sulfur to carbon see: H. J. Köhler, W. N. Speckamp, *J. Chem. Soc. Chem. Commun.* **1980**, 142; D. L. Clive, T. L. B. Boivin, *J. Org. Chem.* **1989**, *54*, 1997; P. C. Montevecchi, M. L. Navacchia, *J. Org. Chem.* **1998**, *63*, 537; A. Studer, M. Bossart, *J. Chem. Soc., Chem. Commun*, in press. See also: J. Aubé, X. Peng, Y. Wang, F. Takusagawa, *J. Am. Chem. Soc.* **1992**, *114*, 5466;

[10] A. Studer, *Angew. Chem.* **1998**, *110*, 507; *Angew. Chem. Int. Ed.* **1998**, *37*, 462.

[11] (Chlorodiphenylsilyl)trimethyl stannane was prepared according to known procedures.[12] The germylated and silylated chlorosilanes were prepared analogously. Triphenyl- and *t*-butyldiphenylsilyl chloride (TBDPSCl) are commercially available. The TBDPS ether **4** was prepared in DMF using imidazole as base. In the formation of **1** partial epimerization (30%) occurred during silylation. All the compounds described in the present communication were prepared as racemic mixtures. In the equations only one enantiomer is shown.

[12] A. Kawachi, N. Doi, K. Tamao, *J. Am. Chem. Soc.* **1997**, *119*, 233.

[13] Experimental procedure: Bu_3SnH (64 μL, 0.24 mmol) and AIBN (8 mg, 0.05 mmol) in benzene (0.5 mL) were added over 7 h (syringe pump) to a refluxing solution of iodide **3** (114 mg, 0.24 mmol) in benzene (5 mL). After complete addition the reaction mixture was stirred under reflux for additional 30 min. The mixture was then allowed to cool to room temperature and MeLi (15 equiv, 3.65 mmol) was slowly added. After stirring for 12 h the reaction mixture was hydrolyzed with sat. aq. NH_4Cl. Extraction with ether and washing of the organic phase with brine afforded after drying ($MgSO_4$) and purification by flash column chromatography (SiO_2, pentane/Et_2O 4/1) the known alcohol **7**[14] as a colorless oil: 28 mg (70%).

[14] The relative configuration of **7** has previously been assigned: J. M. Brown, R. G. Naik, *J. Chem. Soc. Chem. Commun.* **1982**, 348. As an additional side product 1-methylbutanol (not quantified due to its volatility) was formed. 1-Methylbutanol is derived from the direct reduction product. In all the other systems investigated (entries 2-6) the reduction product was also observed.

[15] A. Studer, H. Steen, *Chem. Eur. J.*, accepted for publication.

[16] The relative configuration of the major isomer was assigned after oxidation (Swern) to the corresponding known aldehyde: I. Fleming, J. J. Lewis, *J. Chem. Soc. Perkin Trans 1* **1992**, 3257.

[17] Spirocyclic cyclohexadienyl radicals with two silyl substituents at the spiro position have been characterized by EPR spectroscopy. A 6-membered chair conformation was suggested for the non spin carrying ring: H. Sakurai, I. Nozue, A. Hosomi, *J. Am. Chem. Soc.* **1976**, *98*, 8279.

[18] D. P. Curran, M-H. Chen, D. Kim, *J. Am. Chem. Soc.* **1989**, *111*, 6265.

[19] The relative configuration was assigned by analogy.