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Synthesis of Biaryls by Intramolecular Radical Aryl Migration from Silicon to Carbon

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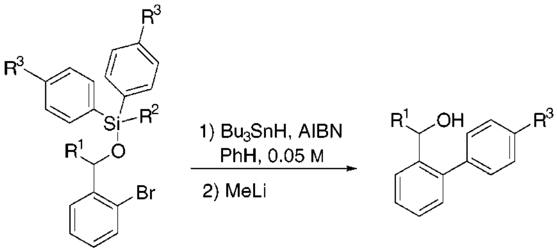
ABSTRACT



A new method for the preparation of biaryls via intramolecular 1,5 aryl migration reaction from silicon in silyl ethers to aryl radicals is presented. Various readily available diphenylsilyl ethers can be used as substrates in this reaction. Functionalized aryl groups can also be transferred. The analogous 1,4 aryl migration reaction is less efficient.

Biaryls are an important class of compounds which occur in many natural products.[1] Moreover, biaryls have found widespread application as ligands in catalytic asymmetric synthesis.[2] They are also found as components in new organic materials, such as electroluminescent conjugated polymers,[3] semiconductors, and liquid crystals.[4]

Most often, biaryls are prepared by transition metal-catalyzed cross-coupling reactions.[5] Radical chemistry has also successfully been used to construct the biaryl unity. Motherwell has shown that biaryls can be prepared under mild conditions by intramolecular radical aryl migration reactions from sulfur in sulfones and sulfonamides to aryl radicals.[6] Similar transformations where aryl migration occurs from oxygen in phenyl ethers to aryl radicals have been disclosed.[7] Amides[8] as well as diazenes[9] have been used as linkers in aryl migration reactions. In these systems, the aryl moiety is transferred from nitrogen to aryl radicals. Biaryls have also been prepared via intramolecular aryl migration from carbon to aryl radicals.[10]

Recently, we presented the phenyl migration reaction from silicon to secondary C-centered radicals as a new method for the stereoselective C(sp^2)−C(sp^3) bond formation (Scheme 1).[11] In this Letter we disclose our first results on the application of this method for the preparation of biaryls.[12]

As in our previous studies, we decided to use the silyl

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[1] Bringmann, G.; Breuning, M.; Tasler, S. *Synthesis* **1999**, 525 and references therein.

[2] Pu, L. *Chem. Rev.* **1998**, *98*, 2405.

[3] Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 402.

[4] Roncali, J. *Chem. Rev.* **1992**, *92*, 711.

[5] Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263.

[6] Motherwell, W. B.; Pennell, A. M. K. *J. Chem. Soc., Chem. Commun.* **1991**, 877. Da Mata, M. L. E. N.; Motherwell, W. B.; Ujjainwalla, F. *Tetrahedron Lett.* **1997**, *38*, 137. Da Mata, M. L. E. N.; Motherwell, W. B.; Ujjainwalla, F. *Tetrahedron Lett.* **1997**, *38*, 141.

[7] Rosa, A. M.; Lobo, A. M.; Branco, P. S.; Prabhakar, S. *Tetrahedron* **1997**, *53*, 285. See also: Crich, D.; Hwang, J.-T. *J. Org. Chem.* **1998**, *63*, 2765.

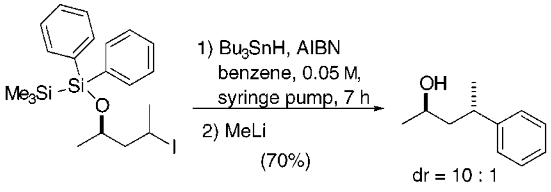
[8] Hey, D. H.; Moynehan, T. M. *J. Chem. Soc.* **1959**, 1563. Grimshaw, J.; Trocha-Grimshaw, J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 799. Grimshaw, J.; Haslett, R. J. *J. Chem. Soc., Perkin Trans. 1* **1980**, 657. Grimshaw, J.; Hamilton, R.; Trocha-Grimshaw, J. *J. Chem. Soc., Perkin Trans. 1* **1982**, 229.

[9] Benati, L.; Spagnolo, P.; Tundo, A.; Zanardi, G. *J. Chem. Soc., Chem. Commun.* **1979**, 141.

[10] Giraud, L.; Lacôte, E.; Renaud, P. *Helv. Chim. Acta* **1997**, *80*, 2148. Alcaide, B.; Rodríguez-Vicente, A. *Tetrahedron Lett.* **1998**, *39*, 6589.

10.1021/ol005661f CCC: $19.00

Scheme 1. Stereoselective Radical Phenyl Migration from Silicon to Carbon

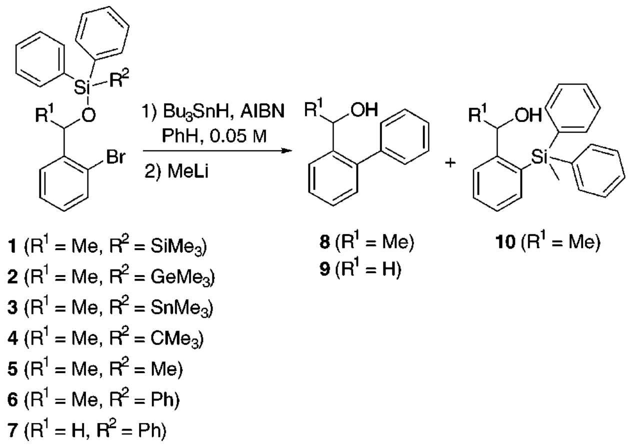


ether functionality to link the attacking aryl radical with the migrating aryl group. Silicon tethers have often been used to transform an *inter*molecular reaction to an *intra*molecular process, a concept often called the Stork[13] temporary silicon connection.[14] However, in the aryl migration reactions from Si to aryl radicals discussed herein, the tether is cleaved during the reaction as will be discussed in the mechanistic section of the paper. Differently substituted diphenylsilyl ethers **1**−**7** were readily prepared from the corresponding chlorosilanes and benzyl alcohols using standard conditions.[15−17] Phenyl migrations were performed by slow addition (syringe pump, 7 h) of Bu_3SnH and AIBN to a solution of the silyl ether in benzene (0.05 M). After complete addition, stirring was continued for 30 min and the reaction mixture was then allowed to cool to room temperature. Desilylation using methyllithium[18] afforded after chromatography (SiO_2) the desired biphenyl derivatives **8** or **9** in moderate to good yields (Scheme 2, Table 1) along with silylated benzyl alcohol **10** (for **1**−**3**). The side product **10** derives from intramolecular homolytic substitution at silicon (S_Hi)[17,19] and subsequent ring opening of the intermediate cyclic silyl ether with MeLi (see Scheme 3).

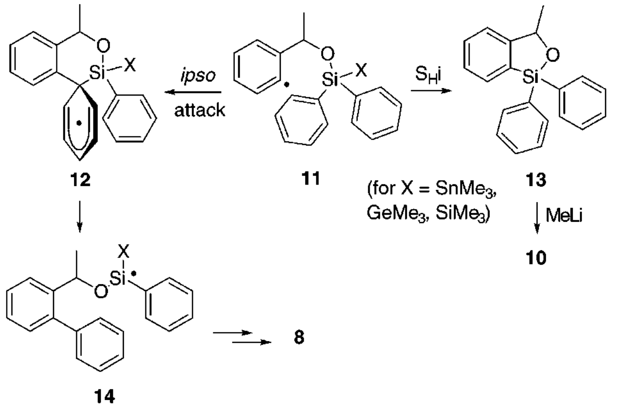
Table 1. Optimization of the Phenyl Migration from Silicon to Aryl Radicals by Varying the Silyl Ether

entry	silyl ether	**8** (%)	**10** (%)
1	**1**	55	28
2	**2**	52	39
3	**3**		84
4	**4**	56	
5	**5**	52	
6	**6**	71	

Scheme 2. Radical Phenyl Migration from Silicon to Aryl Radicals



Scheme 3. Mechanism



As expected from our previous studies on the S_Hi reaction at silicon,[17,19] no biphenyl **8** was formed in the reaction of stannylated silyl ether **3** and the S_Hi-derived alcohol **10** was isolated in 84% yield (Table 1, entry 3). Phenyl migration to the aryl radical generated from **3** is too slow to compete with the S_Hi reaction. For germylated or silylated silyl ethers, the S_Hi reaction with primary alkyl radicals is about 100−1000 times slower than the corresponding reaction with stannylated silyl ethers.[17] Similar kinetics may also be expected for the S_Hi reaction at silicon with aryl radicals;

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(11) Studer, A.; Bossart, M.; Steen, H. *Tetrahedron Lett.* **1998**, *39*, 8829. Amrein, S.; Bossart, M.; Vasella, T.; Studer, A. Submitted for publication. For stereoselective radical aryl migrations from sulfur to C-centered radicals, see: Studer, A.; Bossart, M. *Chem. Commun.* **1998**, 2127.

(12) To the best of our knowledge, radical aryl migrations from silicon to aryl radicals are unknown. For early reports on the aryl migration from Si to primary C-centered radicals, see: Wilt, J. W.; Dockus, C. F. *J. Am. Chem. Soc.* **1970**, *92*, 5813. Wilt, J. W.; Chwang, W. K. *J. Am. Chem. Soc.* **1974**, *96*, 6194. Wilt, J. W.; Chwang, W. K.; Dockus, C. F.; Tomiuk, N. M. *J. Am. Chem. Soc.* **1978**, *100*, 5534. Sakurai, H.; Hosomi, A. *J. Am. Chem. Soc.* **1970**, *92*, 7507.

(13) Stork, G.; Suh, H. S.; Kim, G. *J. Am. Chem. Soc.* **1991**, *113*, 7054.

(14) For reviews, see: Bols, M.; Skrydstrup, T. *Chem. Rev.* **1995**, *95*, 1253. Fensterbank, L.; Malacria, M.; Sieburth, S. McN. *Synthesis* **1997**, 813.

(15) **1** from $ClSiPh_2SiMe_3$[16] and 1-(2-bromophenyl)ethanol (NEt_3, DMAP, THF, 92%); **2** in analogy from $ClSiPh_2GeMe_3$[17] (71%); **3** in analogy from $ClSiPh_2SnMe_3$[16] (60%); **4** in analogy from $ClSiPh_2$-*t*-Bu (74%); **5** in analogy from $ClSiPh_2Me$ (84%); **6** from $ClSiPh_3$ and imidazole in DMF (37%); **8** from benzyl alcohol and $ClSiPh_3$ in pyridine/toluene (1:1, 64%).

(16) Tamao, K.; Kawachi, A.; Ito, Y. *J. Am. Chem. Soc.* **1992**, *114*, 3989. Murakami, M.; Suginome, M.; Fujimoto, K.; Nakamura, H.; Andersson, P. G.; Ito, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6487. Kawachi, A.; Doi, N.; Tamao, K. *J. Am. Chem. Soc.* **1997**, *119*, 233.

(17) Studer, A.; Steen, H. *Chem. Eur. J.* **1999**, *5*, 759.

(18) In the desilylation, an excess of MeLi was used in order to transform the tributyltin bromide formed as a byproduct in the aryl migration to methyltributylstannane, which is easily removed by chromatography. See also: Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 7200. Renaud, P.; Lacôte, E.; Quaranta, L. *Tetrahedron Lett.* **1998**, *39*, 2123.

(19) Studer, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 462.

thus, the S_Hi reaction should be supressed for silylated as well as for germylated silyl ethers, and the desired phenyl migration should be the major reaction pathway. Indeed, the phenyl migration product **8** is the main product in the reaction of **1** (55%) and the S_Hi-derived alcohol **10** was isolated in only 28% yield (entry 1). Similar results were obtained for the germylated silyl ether **2**, where biphenyl **8** was isolated in 52% yield along with 39% of the side product **10** (entry 2).

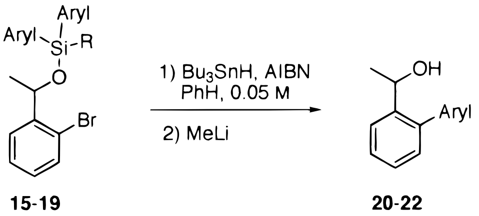
To completely supress the S_Hi reaction, the heavier group 14 substituent (R^2 in Scheme 2) was replaced by an alkyl or a phenyl group. For all these diphenylsilyl ethers (**4**−**6**), phenyl migration worked well, and biphenyl **8** was isolated in good yields (52−71%, entries 4−6). An additional advantage of **4**−**6** over their silylated or germylated congeners besides suppression of the undesired S_Hi reaction is the fact that they are derived from commercially available chlorosilanes. To illustrate that issue, we prepared biphenyl **9** from commercially available 2-bromobenzyl alcohol and triphenylchlorosilane in two steps via silylation (pyridine/toluene, → **7**, 64%, unoptimized) and subsequent phenyl transfer reaction (52%). As a side product, benzyl alcohol, derived from direct reduction of the initially formed aryl radical (dehalogenation) and subsequent removal of the triphenylsilyl group, was formed in 17%.

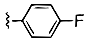
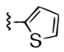
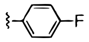
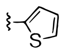
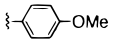
For the phenyl migration, we suggest the following mechanism (Scheme 3). Depending on the substituent X, aryl radical **11** either undergoes S_Hi reaction at silicon to form cyclic silyl ether **13** or it reacts with one of the two phenyl groups to form radical **12**, which then rearomatizes to form silyl radical **14**. Radical **14** can either abstract a halogen atom from the starting bromide[20] or it can react with benzene in a homolytic aromatic substitution.[21] Desilylation (MeLi) then affords biphenyl **8**. In the other reaction pathway, ring opening of **13** with MeLi eventually leads to alcohol **10**.

We also tried to run the phenyl migration reaction using catalytic amounts of tin hydride. Reaction of **6** with 18% Bu_3SnH and 4% AIBN under otherwise identical conditions (benzene, 0.05 M, syringe pump, 7 h) afforded after desilylation alcohol **8** in only 21% along with 72% of 1-(2-bromophenyl)ethanol derived from unreacted starting material. Thus, halogen abstraction of silyl radical **14** does not seem to be the major reaction pathway.

We next tested whether it is possible to transfer functionalized aryl groups from silicon to aryl radicals. To this end, silyl ethers **15**−**19** were prepared from the corresponding chlorosilanes.[22]

Table 2. 1,5-Migration of Functionalized Aryl Groups



entry	bromide	R	aryl	yield (%)
1	**15**	$SiMe_2Ph$		49 (**20**)[a]
2	**16**	$SiMe_2Ph$		–[b]
3	**17**	*t*-Bu		35 (**20**)
4	**18**	*t*-Bu		–[c]
5	**19**	Me		77 (**22**)

[a] The corresponding S_Hi product was formed as a side product. [b] Various inseparable products were formed. [c] Various inseparable products were formed. In addition, 46% of **18** were recovered.

For the *p*-fluoro derivative **15**, the aryl migration product **20** was formed in 49% (Table 2, entry 1). Reaction with thienyl derivative **16** afforded an inseparable product mixture. Compound **21** could not be clearly identified (entry 2). With *tert*-butylated silyl ethers **17** and **18**, the results obtained were similar to those for the corresponding disilyl ethers **15** and **16** (entries 3 and 4). The best result was obtained for the transfer of the *p*-methoxyphenyl group (→ **22** (77%), entry 5).

We then studied the 1,5 phenyl migration to vinyl radicals. The aryl migration reactions were conducted under the above-mentioned conditions. Unfortunately, neither for **23** nor for **24** (Figure 1) did phenyl migration occurr. To our surprise, no reduction product (dehalogenation) was formed in the reaction of **23** and the starting bromide was recovered. For **24** only 28% of the dehalogenation product was observed along with unreacted bromide as determined by ^1H NMR spectroscopy. We also tried to reduce bromide **24** under radical dehalogenation conditions (addition of tin hydride in one portion at higher concentration). However, even under these conditions only 45−50% of the dehalogenation product was formed (^1H NMR) and no phenyl migration was observed.

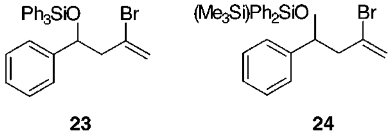


Figure 1.

Finally, we investigated the 1,4 phenyl migration from silicon to aryl radicals. Silyl ethers **25**−**27** were prepared from *o*-bromophenol using $ClSiPh_2SiMe_3$[16] or $ClSiPh_2Me$ and NEt_3/DMAP in THF (for **25**, **27**) or $ClSiPh_3$ and NEt_3/

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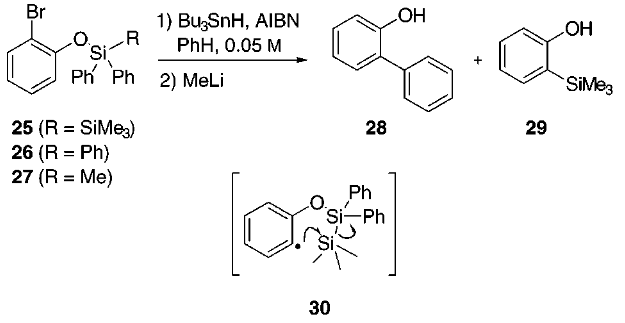
[20] Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5123.

[21] Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 3292.

[22] The chlorosilanes were prepared according to known procedures (see ref 16) starting from the corresponding di(aryl)dichlorosilanes, see Supporting Information.

Scheme 4. 1,4 Phenyl Migration from Silicon to Aryl Radicals



DMAP in CH_2Cl_2 (**26**) (Scheme 4). The aryl migrations were performed under our standard aryl transfer conditions. Interestingly, transformation of **25** afforded silylated phenol **29** as the major product in 50% yield along with the desired biphenyl derivative **28** (38%). Phenol **29** is formed via initial S_Hi reaction at silicon (see **30**). This is the first time in our studies on the homolytic substitution at silicon[17,19] that a trimethylsilyl group migration was observed. Obviously, the transition state of the 4-*exo* attack at the silicon next to the oxygen atom is too strained and 5-*endo* attack at the silicon atom on the periphery occurs in addition to *ipso* attack (minor pathway). Trimethylsilyl group migrations to heteroatom-centered radicals are well-known;[23] however, similar migrations to C-centered radicals have not been observed so far.[24] Interestingly, no products derived from *ortho* attack at the phenyl group were observed.[6]

To suppress the S_Hi reaction, the trimethylsilyl group in **25** was replaced by a phenyl group (**26**). However, neither phenyl migration nor dehalogenation was observed in the reaction of **26**. After desilylation, *o*-bromophenol was recovered in 71% yield. It turned out that even upon adding Bu_3SnH in one portion to the bromide, no reaction occurred. Since silyl ether **26** was carefully purified by chromatography followed by recrystallization, we do not believe that phenol impurities are the reason for the failure of the radical reaction. Neither with tris(trimethylsilyl)silane[25] nor with tin chloride in *t*-BuOH in the presence of cyanoborohydride[26] was any reaction observed. Even SmI_2 in THF (HMPA) did not lead to any aryl migration. It seems that the triphenylsilyl group completely blocks the bromide. We also obtained an X-ray structure of **26**. Surprisingly, in the solid state the bromide is not protected by the silyl group and reaction with tin radicals seems to be feasible. Also for **27** bearing the smaller methyl substituent, no radical reaction was observed. Although the X-ray structure of **26** did not offer the final answer, we believe that in solution the bulky silyl group protects the bromide toward any attack.

In conclusion, we present a new method for the preparation of biaryls by intramolecular aryl migration from silicon to aryl radicals. The starting materials are readily prepared from commercially available silicon protecting groups and experiments are very easy to conduct.

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Supporting Information Available: Full experimental details, spectroscopic and analytical data for all new compounds, and X-ray structural data for **26** (CCDC-141621). This material is available free of charge via the Internet at http://pubs.acs.org.

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(23) Schiesser, C. H.; Wild, L. M. *Tetrahedron* **1996**, *52*, 13265.

(24) For a 1,2 silyl migration to C-centered radicals, see: Sugimoto, I.; Shuto, S.; Matsuda, A. *Synlett* **1999**, 1766 and references therein.

(25) Chatgilialoglu, C. *Acc. Chem. Res.* **1992**, *25*, 188.

(26) Stork, G.; Sher, P. M. *J. Am. Chem. Soc.* **1986**, *108*, 303.