DOI: 10.1002/ejoc.201100783

Carbon-to-Carbon Anion Relay Chemistry: Facile Generation of Substituted Allyllithium Species

Pinguan Zheng,[a] Zhengxin Cai,[a] Aswinkumar Garimallaprabhakaran,[a]
Parham Rooshenas,[b] Peter R. Schreiner,*[b] and Michael Harmata*[a]

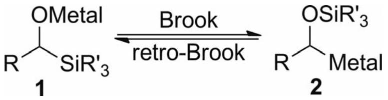
Dedicated to the memory of Professor David Y. Gin

Keywords: Lithium / Metalation / Silicon / Carbanions / Density functional calculations

Treatment of [2-(2-bromophenyl)allyl]trimethylsilane with *t*BuLi in THF at –78 °C resulted in the rapid migration of the trimethylsilyl group to afford an allylic organolithium that can be easily trapped by a wide range of electrophiles. This is a rare example of a synthetically useful and efficient carbon-to-carbon migration of a silicon group and represents a new approach to allylic organolithium species using anion relay chemistry.

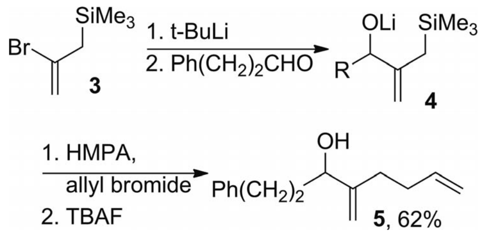
Introduction

The ability to translocate a reactive center from one atom to another is a powerful approach to the generation of reactive intermediates, whether cationic, radical, or anionic in nature. Of the latter, one of the most impressive and one that is still being developed is the Brook rearrangement,[1] the transposition of a silicon atom and its attendant substituents from one atom to another. This generally involves a migration from carbon to oxygen and classically is a 1,2-shift (Scheme 1) although many variations on this basic principle have been developed and used productively in organic synthesis.



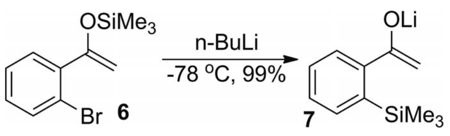
Scheme 1. The Brook rearrangement.

Smith and West have exploited anion relay chemistry (ARC) in which a silicon group migrates from a carbon atom to an oxygen with concomitant generation of a carbanion that can be employed in carbon–carbon bond formation.[2] For example, halogen/metal exchange of **3** with *tert*-butyllithium followed by addition of an aldehyde produced **4**. Subsequent addition of allyl bromide and HMPA afforded **5** in good yield after desilylation (Scheme 2).[3] A shift of the TMS group presumably afforded an allylic anion that reacted with the allyl bromide, but HMPA was necessary for the reaction.



Scheme 2. An example of anion relay chemistry resulting in the formation of an allylic anion.

Another example that is closely related to the work we describe comes from a report by Fallis and co-workers. They described the halogen/metal exchange reaction of **6**, which rapidly led to a silicon migration to form enolate **7** (Scheme 3).[4] This intermediate could be trapped by electrophiles. The driving force for the process is presumably the formation of a more stable enolate anion.



Scheme 3. Generation of a lithium enolate by a silicon migration from oxygen to carbon.

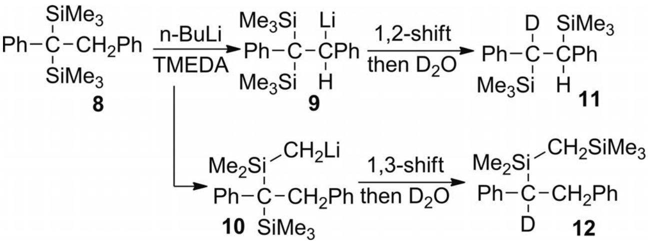
Many other examples of this type of chemistry exist. However, carbon-to-carbon anion relay is much rarer. In an early seminal study, Eisch and Tsai reported this process

---

[a] Department of Chemistry, University of Missouri-Columbia,
601 South College Avenue, Columbia, Missouri 65211, USA
Fax: +1-573-882-2754
E-mail: harmatam@missouri.edu
[b] Institut für Organische Chemie, Justus-Liebig-Universität,
Heinrich-Buff-Ring 58, 35392 Giessen, Germany
Fax: +49-641-99-34309
E-mail: prs@org.chemie.uni-giessen.de

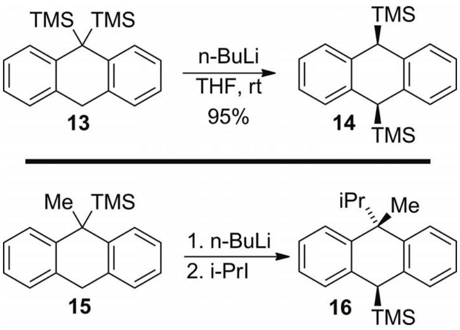
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201100783.

and demonstrated, for example, that the generation of **11** and **12** from **9** and **10**, respectively, occurred through a combination of intramolecular 1,2-, 1,3-, and 1,4-silicon shifts, the driving force being the generation of a more stable carbanion from a less stable carbanion (Scheme 4).[5]



Scheme 4. Carbon-to-carbon anion silicon group shifts.

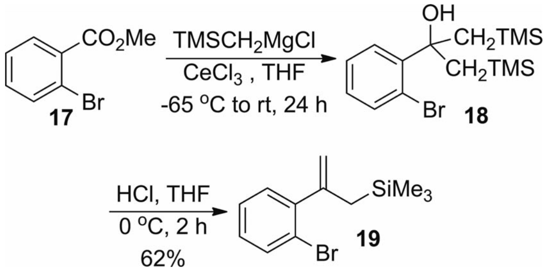
Daney and co-workers reported the 1,4-migration of a trimethylsilyl group in anions derived from dihydroanthracenes. Thus, treatment of **13** with *n*BuLi in THF at room temperature afforded *cis*-**14** in 95% yield (Scheme 5, top).[6] Rabideau and co-workers used this chemistry to synthesize systems such as **16** stereoselectively (Scheme 5, bottom).[7]



Scheme 5. Stereoselective, anionic carbon-to-carbon silicon shifts.

Results and Discussion

We became interested in this process in the course of a study involving the projected generation of **20** for the purpose of further exploration of the electrocyclization chemistry of cyclopentadienones.[8] The substrate needed was prepared by the reaction of methyl *o*-bromobenzoate with trimethylsilylmethylmagnesium chloride in the presence of ceric chloride followed by an acid work-up (Scheme 6).[9]

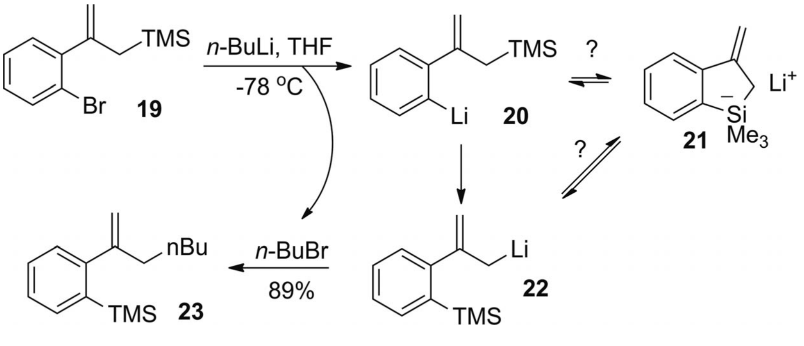


Scheme 6. Preparation of allylic silane **19**.

Treatment of **19** with *n*BuLi in THF at –78 °C initially gave a yellow solution, but this color disappeared by the end of the addition of the organolithium, in less than 15 min. Attempted trapping of the organolithium **20** was unsuccessful as this species reacted, presumably by a carbon-to-carbon 1,4-shift of the silyl group, to give **22**, which reacted with the *n*-butyl bromide formed in the initial halogen/metal exchange to afford **23** in 89% yield (Scheme 7). The potential intermediacy of **21** in the process will receive attention later in this report. Recognizing this process as a rather unusual result, we decided to pursue the reaction as a means of efficiently generating a substituted allyllithium compound.

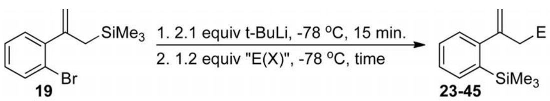
To avoid alkylation with *n*-butyl bromide, halogen/metal exchange of **19** was conducted with *t*BuLi at –78 °C in THF. This resulted in the efficient generation of the allyllithium **22**, as evidenced by various trapping experiments summarized in Table 1. In general, the alkylation process was completed rapidly, although some reactions were allowed to proceed for 1 h.

Primary alkyl bromides and iodides functioned as excellent electrophiles in this reaction (Table 1, entries 1–4 and 8). Allyl bromide, benzyl chloride, and 2-naphthylmethyl bromide also produced alkylation products in high yields (Table 1, entries 5–7). Ketones could also be used as electrophiles, although the yield was only fair for cyclopentanone, perhaps because of its enhanced acidity, and pinacolone gave a good yield of the adduct (Table 1, entries 9–11). Butadiene monoxide reacted at the less substituted carbon to give a good yield of the 1,6-diene **34** (Table 1, entry 12).

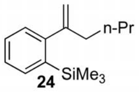
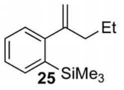
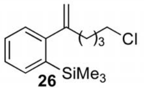
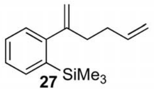
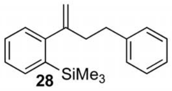
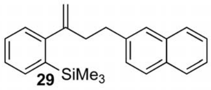
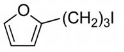
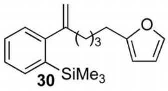
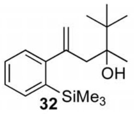
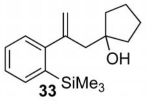
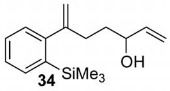
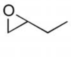
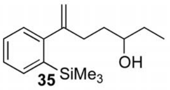
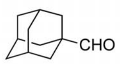
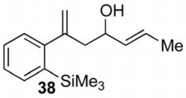
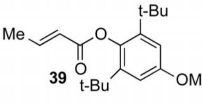
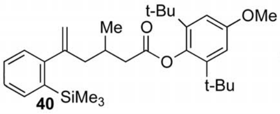
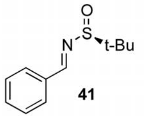
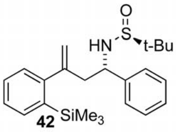
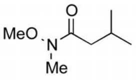
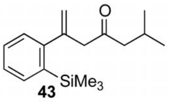
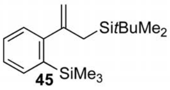
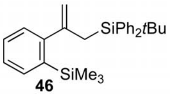


Scheme 7. Halogen/metal exchange of **19** followed by silicon group migration and electrophilic trapping.

Table 1. Generation and trapping of allyllithium **22**.



19 → **23-45**

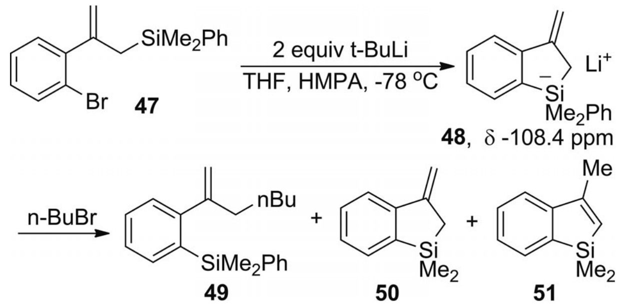
Entry	Electrophile	Product	Time	% Yield
1	*n*-BuBr	 **23**	30 min	94[a]
2	*n*-PrBr	 **24**	30 min	83[a]
3	EtBr	 **25**	30 min	89[a]
4	Br(CH$_2$)$_3$Cl	 **26**	30 min	58[a]
5	allyl bromide	 **27**	30 min	74[a]
6	PhCH$_2$Cl	 **28**	30 min	94[a]
7	2-bromomethylnaphthalene	 **29**	20 min	63[b]
8		 **30**	15 min	77[b]
9	cyclohexanone	 **31**	30 min	75[b]
10	pinacolone	 **32**	30 min	70[b]
11	cyclopentanone	 **33**	30 min	44[b]
12	butadiene monoxide	 **34**	1 h	52[b]
13		 **35**	30 min	70[b]
14	PhCHO	 **36**	30 min	68[b]
15		 **37**	10 min	72[b]
16	crotonaldehyde	 **38**	10 min	86[b]
17	 **39**	 **40**	10 min	67[b]
18	 **41**	 **42**	10 min	71[b]
19		 **43**	30 min	67[b]
20	(CyS)$_2$	 **44**	30 min	62[b]
21	TBSCl	 **45**	30 min	68[b]
22	TBDPSCl	 **46**	30 min	75[b]

[a] Yield based on NMR analysis in the presence of an internal standard. [b] Isolated yield.

Both aromatic and aliphatic aldehydes reacted with the organolithium species to give the expected adducts in good yields (Table 1, entries 14–16).[10] Michael addition with the hindered crotonic ester **39** was possible, with the yield being lowered by the repeated chromatography necessary to obtain the product free of the starting material (Table 1, entry 17). The chiral imine **41** afforded the adduct **42** in diastereomerically pure form in agreement with expectations based on literature precedent (Table 1 entry 18).[11]

The Weinreb amide of 3-methylbutanoic acid trapped **22** in 67% yield (Table 1, entry 19). Dicyclohexyl disulfide afforded sulfide **44** in 62% yield (Table 1, entry 20). Finally, the silicon electrophiles TBSCl and TBDPSCl afforded good yields of the corresponding allylsilanes **45** and **46** (Table 1, entries 21 and 22). Some reactions had yields lower than expected due to the formation of the alkene derived from the protonation of **22**.

We believed that the reaction takes place via a pentaorganosilicate species that serves as an intermediate in the transfer of the trimethylsilyl group. Finding evidence for such an intermediate has not yet been possible with **20**. However, treatment of **47** with *t*BuLi in a mixture of THF and HMPA at –78 °C gave several products by ^{29}Si NMR spectroscopy. The dominant species has a signal at δ = –108.4 ppm, which is consistent with values determined for other putative pentaorganosilicate species.[12] HMPA was needed to observe the organosilicate species, which is consistent with the results of others.[13] Finally, treatment of the reaction mixture with *n*-butyl bromide afforded **49**, **50**, and **51** in 63, 16, and 3% yields, respectively (Scheme 8). The siloles **50** and **51** presumably result from the ejection of phenyllithium from **48**, a reaction that is well documented and useful for the synthesis of siloles.[14]



Scheme 8. NMR evidence for the formation of a pentaorganosilicate intermediate.

To address mechanistic questions associated with this process, we also conducted density functional theory (DFT) computational studies. As the computational approach for the system under consideration we employed the B3PW91[15] combination of functionals utilizing a correlation-consistent double-ζ basis set[16] (cc-pVDZ). All stationary points were characterized as minima or transition-state structures by computing analytical second derivatives; the zero-point vibrational energies (ZPVE) were used to correct the electronic energies. To approximate solvent effects, we applied the recently developed universal solvation model, SMD.[17] The corresponding structures were reoptimized in water (ε_r = 78.39; strictly as an upper bound for a very polar solvent) and THF (ε_r = 7.32). All computations were performed with the Gaussian 09 program package.[18] The data are summarized in Figure 1 and Table 2.

We first modeled the rearrangement of **20** to **22** with the two free anions **C1$_\mathbf{A}$** and **C2$_\mathbf{A}$**, the latter being slightly more stable by 0.4 kcal mol^{-1}. A structure analogous to **21** is not a minimum but rather a very low-lying transition-state structure **TS$_\mathbf{A}$** ($\Delta H^{\ddagger}$ = +2.9 kcal mol^{-1}, cf. Figure 1 and Table 2) with a square-pyramidal central structure with a methyl group in the apical position. The carbon atoms involved occupy the basal positions within the transition-state structure and display similar distances to the silicon center (about 2 Å). Hence, this process is reminiscent of a Berry pseudo-rotation typical of pentacoordinate silicon.[19] The activation barrier is also in the range of reported values for Berry pseudo-rotations.[20] Although this appears to be at odds with the formation of **48** and related pentaorganosilicates, it is likely that the electron-withdrawing nature of the Si-bound phenyl group in **48** plays a role in the stabilization of that species.

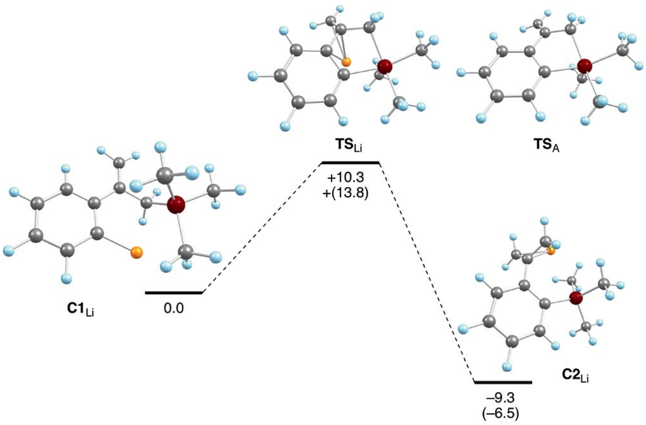


Figure 1. Potential energy hypersurface for the rearrangement of **C1$_\mathbf{Li}$** to **C2$_\mathbf{Li}$** computed at the B3PW91/cc-pVDZ level with relative enthalpies [$\Delta H_{0(\mathrm{sol})}$] in kcal mol^{-1} in an aqueous solution (Li = orange, Si = red, C = grey, H = light blue). The corresponding values for THF as solvent are shown in parentheses. ZPVE corrections are taken from gas-phase optimizations also at the B3PW91/cc-pVDZ level. The optimized structure of the free anion **TS$_\mathbf{A}$** is shown for comparison.

Table 2. Energies of the calculated structures.

Entry	Structure	Energy [kcal mol^{-1}]
1	**C1$_\mathbf{A}$**	0.0
2	**C2$_\mathbf{A}$**	–0.4[a]
3	**TS$_\mathbf{A}$**	2.9[a]
4	**C1$_\mathbf{Li}$**	0.0
5	**C2$_\mathbf{Li}$**	–11.7[b]
6	**Ts$_\mathbf{Li}$**	8.6[b]
7	**Ts$_\mathbf{Li}$(H$_2$O)**	10.3[b]
8	**Ts$_\mathbf{Li}$(THF)**	13.8[b]
9	**C1$_\mathbf{Na}$**	0.0
10	**C2$_\mathbf{Na}$**	–7.3[c]
11	**TS$_\mathbf{Na}$**	5.3[c]

[a] Relative to **C1$_\mathbf{A}$**. [b] Relative to **C1$_\mathbf{Li}$** or the solvated analogue. [c] Relative to **C1$_\mathbf{Na}$**.

To determine the effect of the counterion, we studied this rearrangement in the presence of Li$^+$ (Figure 1). Structure **C1$_\mathbf{Li}$** reacts to give **C2$_\mathbf{Li}$** exothermically (ΔH = –11.7 kcal mol^{-1}). In contrast to the free anions, these two minima display only tetracoordinate Si atoms. In **C1$_\mathbf{Li}$**, lithium is attached to the phenyl ring, but **C2$_\mathbf{Li}$** displays an η^3-allyllithium, which represents a sizeable driving force for the forward reaction through transition-state structure **TS$_\mathbf{Li}$** ($\Delta H^{\ddagger}$ = +8.6 kcal mol^{-1}). The counterion apparently stabilizes the negative charge in the reactant and thus increases the activation barrier. To probe this hypothesis, we modeled the same reaction with a less electronegative sodium cation as the counterion. The rearrangement barrier for **C1$_\mathbf{Na}$** to **C2$_\mathbf{Na}$** (ΔH = –7.3 kcal mol^{-1}) is reduced to +5.3 kcal mol^{-1}.

Our investigations were refined by using the SMD solvent model at the same level of theory to approximate the influence of solvent effects on the reaction of **C1$_\mathbf{Li}$** to **C2$_\mathbf{Li}$**. Both in an aqueous solution and THF, the activation barriers increase significantly to 10.3 and 13.8 kcal mol^{-1}, respectively. Nevertheless, these barriers are low from the perspective of reaction rate and rearrangement is expected to be rapid, even at –78 °C.

The computational studies along with our experimental work strongly support the idea that pentaorganosilicates need not be invoked as intermediates in this reaction. Full silicon transfer and a real allylic organolithium best describe what becomes of **19** after halogen/metal exchange. Although this picture may be subject to modification as we explore other systems, it appears that for **19** the structure most resembling a pentaorganosilicate is a transition state and not an intermediate.

Conclusions

We have discovered a convenient and novel way to synthesize 2-aryl-substituted allyllithium species by a carbon-to-carbon silicon 1,4-shift.[21] The efficiency of this process is surprising given that benzene and propene have been estimated to have the same pK_a values, but calculations suggest that the reaction is just sufficiently exothermic (and perhaps more exergonic) to proceed to completion.[22] The scope of this reaction with respect to metal,[23] substituents on silicon and the remaining organic fragment, as well as its potential use in synthesis remain to be explored. In addition, the subtleties of group transfers or exchanges between the same elements in a given structure remain to be fully elucidated. Work in these areas is in progress and the results will be reported in due course.

Experimental Section

A flame-dried 25 mL round-bottomed flask was charged with bromoalkene **19** (400 mg, 1.48 mmol), 4-*tert*-butylanisole (260 µL, 1.48 mmol, internal standard), and THF (7.5 mL). The solution was cooled to –78 °C before *t*BuLi (1.06 м, 2.9 mL) was added dropwise. After this, the clear orange solution was stirred for 15 min at –78 °C and the reaction was quenched by the slow addition of *n*BuBr (190 µL, 1.77 mmol). The reaction was monitored by GC–MS. After being stirred for 30 min, it was diluted with diethyl ether, washed with water, and dried with $MgSO_4$. The solvent was concentrated in vacuo to provide 342 mg of the crude product. NMR analysis of the crude showed the ratio of the product **23** and *tert*-butylanisole was 1:1. The NMR yield was calculated to be 94% based on the NMR ratio of the product and internal standard and corrected based on recovered mass. Analytical samples were obtained by careful column chromatography (SiO_2, hexanes). For **23**: IR: $\tilde{\nu}$ = 2953, 2925, 1462, 1246, 1115, 898, 837, 727 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58, (dd, *J* = 7.1, 1.4 Hz, 1 H); 7.26–7.35 (m, 2 H), 7.14 (dd, *J* = 7.5, 1.0 Hz), 5.16 (q, *J* = 1.7 Hz, 1 H), 4.93 (m, 1 H), 2.34 (t, *J* = 7.9 Hz, 2 H), 1.55–1.58 (m, 2 H), 1.36–1.40 (m, 4 H), 0.93–0.96 (m, 3 H), 0.31 (s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.1, 150.8, 137.1, 134.8, 128.3, 127.9, 125.8, 113.3, 38.7, 31.7, 27.0, 22.5, 14.0. 0.9 ppm.

Supporting Information (see footnote on the first page of this article): Experimental procedures and characterization data for new compounds.

Acknowledgments

This work was supported by a grant from the National Science Foundation to whom we are grateful. Thanks to Advanced Asymmetrics, Inc. for a gift of the chiral sulfinamide precursor to **41**.

---

[1] a) W. H. Moser, *Tetrahedron* **2001**, *57*, 2065; b) A. G. Brook, A. R. Bassindale in *Rearrangements in Ground and Excited States* (Ed.: P. de Mayo), Academic Press, New York, **1980**, vol. 2, pp. 149–227; c) M. A. Brook, *Silicon in Organic, Organometallic, and Polymer Chemistry*, Wiley, New York, **2000**; d) K. Tomooka in *The Chemistry of Functional Groups Volume 104: The Chemistry of Organic Lithium Compounds* (Eds.: Z. Rappoport, I. Marek), Wiley-VCH, Chichester, **2004**, ch. 12, pp. 749–828; for recent examples of the application of the Brook rearrangement, see: e) C. Wang, Z.-B. Gan, J. Lu, X. Wu, Z.-L. Song, *Tetrahedron Lett.* **2011**, *52*, 2462; f) B. Liu, C.-D. Lu, *J. Org. Chem.* **2011**, *76*, 4205; g) Z. Song, Z. Lei, L. Gao, X. Wu, L. Li, *Org. Lett.* **2010**, *12*, 5298; h) D. C. Schmitt, J. S. Johnson, *Org. Lett.* **2010**, *12*, 944; i) M. Sasaki, H. Ikemoto, K. Takeda, *Heterocycles* **2009**, *78*, 2919.

[2] A. B. Smith III, W. M. West, *Chem. Commun.* **2008**, 5883.

[3] A. B. Smith III, M. O. Duffey, *Synlett* **2004**, 1363.

[4] B. M. Comanita, S. Woo, A. G. Fallis, *Tetrahedron Lett.* **1999**, *40*, 5283.

[5] a) J. J. Eisch, M. R. Tsai, *J. Organomet. Chem.* **1982**, *225*, 5; b) J. J. Eisch, M. R. Tsai, *J. Am. Chem. Soc.* **1973**, *95*, 4065.

[6] a) M. Daney, R. Lapouyade, H. Bouas-Laurent, *J. Org. Chem.* **1983**, *48*, 5055; b) M. Daney, B. Labrande, R. Lapouyade, H. Bouas-Laurent, *J. Organomet. Chem.* **1978**, *159*, 385.

[7] R. K. Dhar, D. K. Clawson, F. R. Fronczek, P. W. Rabideau, *J. Org. Chem.* **1992**, *57*, 2917.

[8] a) M. Harmata, P. Zheng, P. R. Schreiner, A. Navarro-Vázquez, *Angew. Chem. Int. Ed.* **2006**, *45*, 1966; b) M. Harmata, P. Zheng, P. R. Schreiner, A. Navarro-Vázquez, *Tetrahedron Lett.* **2007**, *48*, 5919.

[9] B. A. Narayanan, W. H. Bunnelle, *Tetrahedron Lett.* **1987**, *28*, 6261.

[10] In principle, ketone and aldehyde adducts of **22** could engage in further silyl transfer to oxygen. No evidence for such a process was observed, but no attempt has yet been made to drive the reaction.

[11] a) S. Kobayashi, Y. Mori, J. S. Fossey, M. M. Salter, *Chem. Rev.* **2011**, *111*, 2626; b) M. T. Robak, M. A. Herbage, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 3600; c) F. Ferreira, C. Botuha, F. Chemla, A. Perez-Luna, *Chem. Soc. Rev.* **2009**, *38*, 1162.

[12] E. P. A. Couzijn, J. C. Slootweg, A. W. Ehlers, K. Lammertsma, *Z. Anorg. Allg. Chem.* **2009**, *635*, 1273. Note that the same basic experiment with **19** revealed no evidence of a hypervalent silicon species as assessed by ^{29}Si NMR analysis.

[13] A. H. J. F. de Keijzer, F. J. J. de Kanter, M. Schakel, R. F. Schmitz, G. W. Klumpp, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1127.

[14] a) P. F. Hudrlik, D. Dai, A. M. Hudrlik, *J. Organomet. Chem.* **2006**, *691*, 1257; b) Z. Wang, H. Fang, Z. Xi, *Tetrahedron Lett.* **2005**, *46*, 499.

[15] J. P. Perdew, Y. Wang, *Phys. Rev. B* **1992**, *23*, 12947.

[16] T. H. Dunning, *J. Chem. Phys.* **1989**, *90*, 1007.

[17] A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2009**, *113*, 6378.

[18] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell,

J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, *Gaussian 09, Revision B.2*, Gaussian, Inc., Wallingford, CT, **2009**.

[19] E. P. A. Couzijn, J. C. Slootweg, A. W. Ehlers, K. Lammertsma, *J. Am. Chem. Soc.* **2010**, *132*, 18127.

[20] R. R. Holmes, *Chem. Rev.* **1990**, *90*, 17.

[21] O. Desponds, M. Schlosser, *J. Organomet. Chem.* **1991**, *409*, 93.

[22] a) D. W. Boerth, A. Streitwieser Jr., *J. Am. Chem. Soc.* **1981**, *103*, 6443; b) A. Streitwieser Jr., P. J. Scannon, H. M. Niemeyer, *J. Am. Chem. Soc.* **1972**, *94*, 7936; for silicon migration rationalized on the basis of differences in carbanion stability, see: L. Bonnafoux, R. Scopelliti, F. R. Leroux, F. Colobert, *Tetrahedron Lett.* **2007**, *48*, 8768.

[23] For leading examples and references, see: a) J. J. Eshelby, P. C. Crowley, P. J. Parsons, *Synlett* **1993**, 277; b) T. Seiser, N. Cramer, *Angew. Chem. Int. Ed.* **2010**, *49*, 10163.

Received: June 1, 2011