Stereoselective Radical Aryl Migration from Silicon to Carbon†

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Highly diastereoselective radical 1,5 phenyl migration reactions from silicon in diarylsilyl ethers to various C-centered radicals to form the corresponding 3-phenylated alcohols are described. Functionalized aryl groups can also be transferred. The effect of the variation of the attacking radical on the aryl transfer reaction is discussed. Best results are obtained for the phenyl migration to nucleophilic secondary alkyl radicals, where high yields (up to 81%) and high selectivities (up to 95% ds) have been obtained. The mechanism of the process is discussed and a model to explain the stereochemical outcome of the reaction is presented. Finally, stereoselective 1,4 aryl migration reactions from Si to C, including a new method for the α-arylation of esters, are presented.

Introduction

Many natural products and drugs contain aryl groups connected to a C(sp^3)-center. Therefore, the development of methods for the direct C(sp^2)−C(sp^3) bond formation is very important. This bond can be formed by cationic (Friedel−Crafts alkylation), anionic, or radical chemistry. Transition metal catalyzed coupling reactions are also known.[1] However, despite the importance of these C−C bond forming processes, there are only a few examples of stereoselective arylations. Asymmetric Heck[2] and Michael[3] reactions can only formally be regarded as members of this category. Recently, enolate arylations were performed stereoselectively using transition metals as mediators.[4] As an alternative to these methods, we suggest stereoselective radical aryl migrations.[5]

Radical arylations can either be performed by $S_{RN}1$-reactions[6] or by homolytic aromatic substitutions.[7] Minisci et al. have thoroughly studied the intermolecular homolytic aromatic substitution of protonated heteroarenes.[8] Recently, homolytic base-promoted aromatic alkylations by alkylmercury halides[9] or by alkyl halides[10] have been reported. Homolytic aromatic substitutions of pyrroles and indoles with electron-deficient radicals, which occur via initial atom-transfer addition, have been described.[11] Intermolecular radical *ipso* substitutions of aromatic compounds have been reported.[12]

There are many reports on the intramolecular homolytic aromatic substitution under reducing conditions, although its mechanism is not well understood.[13,14] Similar transformations under oxidative conditions have been described.[15] Numerous examples of intramolecular aryl transfers (*ipso* substitutions) from carbon to carbon,[16] nitrogen to carbon,[17] oxygen to carbon,[18] sulfur to car-

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† Dedicated to Professor Dr. Bernd Giese on the occasion of his 60th birthday.

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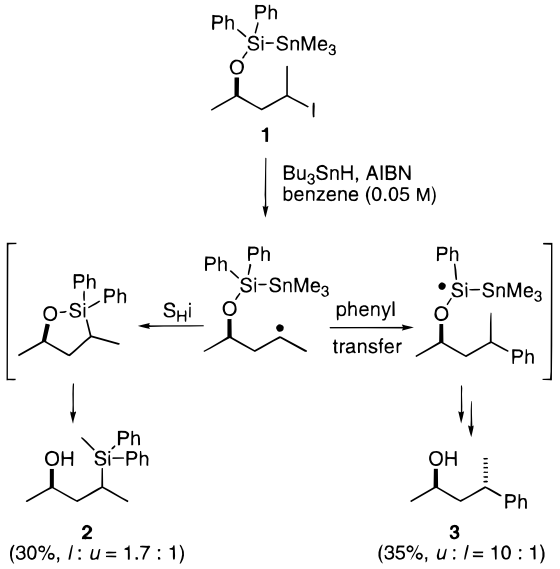
bon,[19] and carbon to silicon[20,21] have been published. Despite many reports on radical aryl transfers to C-centered radicals, there are only a few examples of stereoselective radical aryl migrations.[5,22] In the present paper, highly diastereoselective 1,4 and 1,5 phenyl[5,22b] migration reactions from silicon to differently substituted carbon-centered radicals will be reported. Functionalized aryl groups can also be transferred. A model to explain the stereochemical outcome of the reaction will be presented, and some mechanistic aspects of this important reaction will be discussed.

Results and Discussion

Stereoselective 1,5 Aryl Migration. 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.[23] We found that phenyl migration from silicon to the C-centered radical (*ipso* substitution) began to compete with the S_Hi-reaction in slow cyclizing systems.[5] Slow addition (syringe pump, 7 h) of Bu_3SnH (1.2 equiv) to a solution of iodide **1** in refluxing benzene (0.05 M) afforded, after treatment with methyllithium (MeLi), the alcohols **2** and **3** in 30% and 35% yield, respectively (Scheme 1).[24,25] Alcohol **3**, derived from the 1,5-phenyl migration, was formed with high diastereoselectivity (*u*:*l* = 10:1). The relative configuration of the major isomer of **3** was assigned by comparison of the ^{1}H NMR data with literature values.[26] The S_Hi-derived silylated alcohol **2** was formed with low selectivity (*l*:*u* = 1.7:1).

Scheme 1



Since the C(sp^2)−C(sp^3) bond formation is important (see Introduction), we decided to study the phenyl migration reaction more carefully. From kinetic studies of the S_Hi-reaction, we already knew that the homolytic substitution is fast for stannylated silyl ethers, whereas the corresponding germylated and silylated congeners react about 100−1000 times more slowly.[24] Substitution of the trimethylstannyl group in **1** by a trimethylsilyl or a trimethylgermyl group should therefore suppress the S_Hi-reaction, and higher yields of the desired phenyl migration product should be obtained. In addition, due to the similar electronegativity of germanium, silicon, and tin, the electronics around the oxygen-bound silicon atom of the silyl ether should not be altered too much in going from stannylated to germylated or silylated silyl ethers. Silyl ethers **4** and **5** were prepared from the corresponding chlorosilanes as previously described.[24] Indeed, syringe pump addition of Bu_3SnH to a solution of **4** in benzene (0.05 M) afforded, after desilylation (MeLi), alcohol **3** in 57% yield as a 10:1 (*u*:*l*) mixture of its diastereoisomers (Table 1). With silyl ether **5**, the phenyl migration worked even better, and alcohol **3** was isolated in 70% yield with equal selectivity. As expected, silanylated alcohol **2** was not formed in these reactions (for **4** and **5**). In the desilylation, an excess of MeLi was used in order to transform iodo(tributyl)stannane, formed as a byproduct in the aryl migration, into methyl(tributyl)stannane, which is easily removed by chromatography. Similar strategies to make product purification in tin-mediated radical reactions easier have already been used.[27]

We further tested whether phenyl migration also occurs in silyl ethers derived from commercially available phenylchlorosilanes. *tert*-Butyl(diphenyl)silyl ether **6** and triphenylsilyl ether **7** were readily prepared. Unfortunately, yields and selectivities were lower for the phenyl migration reaction of **6** and **7** (Table 1). The dehalogenation product was determined to be the main product by the ^{1}H NMR analysis of the crude product (for **6** and **7**). We did not isolate the dehalogenation product, since

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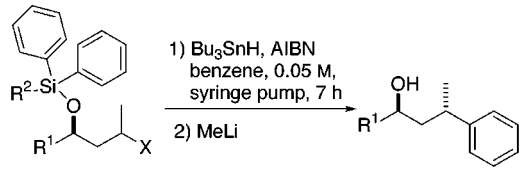
Table 1.



4-10 **3, 11-13**

(specification of R^1, R^2, and X see Table)

compd	R^1	R^2	X	product	yield (%)	dr (*l* : *u*)[a]
4	Me	Me_3Ge	I	**3**	57	1 : 10
5	Me	Me_3Si	I	**3**	70	1 : 10
6	Me	Me_3C	I	**3**	33	1 : 6
7	Me	Ph	I	**3**	37	1 : 6
8	Ph	Me_3Si	I	**11**	62	11 : 1[b]
9	*i*-Pr	Me_3Si	Br	**12**	82	13 : 1
10	*t*-Bu	Me_3Si	Br	**13**	93	10 : 1

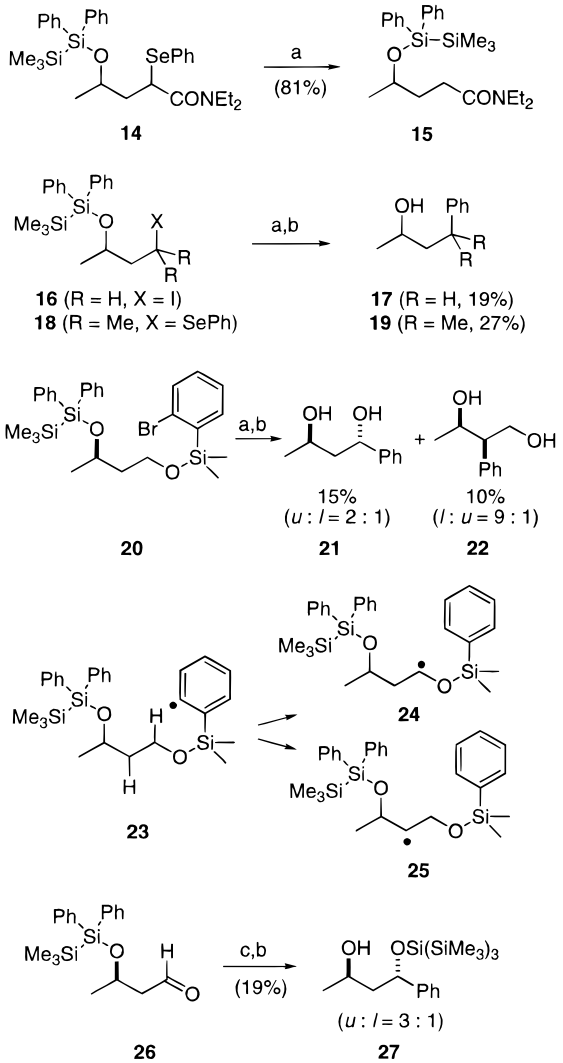
[a] Determined by GC analysis. [b] Determined by ^{1}H NMR spectroscopy.

the 2-pentanol formed after desilylation is rather volatile. An explanation for the decrease of the yield in going from the silylated silyl ether **5** to the *tert*-butyl- or phenyl-substituted derivatives **6** and **7** will be given below. Since the highest yield in this series was obtained for **5**, all of the following studies were conducted with silylated silyl ethers. The synthesis of trimethylsilyl(diphenyl)chlorosilane, necessary for the preparation of the starting materials, is straightforward. The silylated chlorosilane can readily be prepared in large scale (20−30 g), as previously described.[28]

We then studied the effect of the substituent R^1 (see Table 1) on the diastereoselectivity of the phenyl migration reaction. Silyl ethers **8**−**10** were synthesized from the corresponding halo alcohols and trimethylsilyl(diphenyl)chlorosilane. Bromides **9** and **10** were prepared as mixtures (1:1) of their diastereoisomers, whereas iodide **8** was a diastereoisomerically pure compound of unknown relative configuration. Phenyl transfers were performed under the above-mentioned conditions (1.0−1.2 equiv of Bu_3SnH, 10% AIBN, benzene, reflux, 0.05 M, syringe pump, 7 h). The alcohols **11**−**13** were isolated in good to excellent yields with similar selectivities (10−13:1, Table 1). The relative configuration of the major isomer (for **11**−**13**) was assigned in analogy to alcohol **3**. Thus, varying the substituent R^1 has no significant effect on the selectivity. There is no selectivity reversal as might appear from the presentation in the table. Due to the higher priority of Ph, *t*-Bu, and *i*-Pr vs 2-phenylpropyl according to the CIP convention, the major isomer of **11**−**13** has to be assigned as *like*-isomer.[29]

Next, the effect of the nature of the attacking radical on the outcome of the phenyl migration reaction was investigated. To this end, diethylamide **14**, iodide **16**, and selenide **18** were prepared from the corresponding alcohols using standard procedures (NEt_3, DMAP, $Ph_2(Me_3Si)SiCl$, THF). Bis-silyl ether **20**, bearing Curran's radical translocating protecting group,[30] and aldehyde **26** were

Scheme 2



14 **15**

16 (R = H, X = I)
18 (R = Me, X = SePh)

17 (R = H, 19%)
19 (R = Me, 27%)

20 **21** **22**

23 **24** **25**

26 **27**

(a) Bu_3SnH, AIBN, benzene, 0.05 M, syringe pump, 7 h; (b) MeLi; (c) $(TMS)_3SiH$, AIBN, benzene, 0.05 M, syringe pump, 7 h.

synthesized from ethyl β-hydroxybutyrate as described in the Experimental Section. No phenyl migration was observed for selenide **14**. Amide **15**, derived from direct reduction of the intermediate radical, was isolated in 80% yield (Scheme 2). Surprisingly, the reaction with the primary radical, derived from silyl ether **16**, was not efficient, and the corresponding phenylated alcohol **17** was obtained in only 19% yield. A side product (not shown), 1-(methyldiphenylsilanyl)butan-3-ol derived from S_Hi reaction at silicon[24] with subsequent ring opening with MeLi was obtained in 5% yield. Aryl transfer to a tertiary radical is also possible, as illustrated by the transformation of selenide **18** to alcohol **19** (27%). In all cases where low yields of the *ipso* substitution products were obtained, the direct reduction (dehalogenation, deselanation) was the major reaction pathway.

Phenyl migration to secondary α-oxy-radicals is less selective. Reaction of silyl ether **20** under the optimized conditions afforded after desilylation the desired diol **21** in 15% yield as a 2 to 1 (*u*:*l*) diastereoisomeric mixture.[31]

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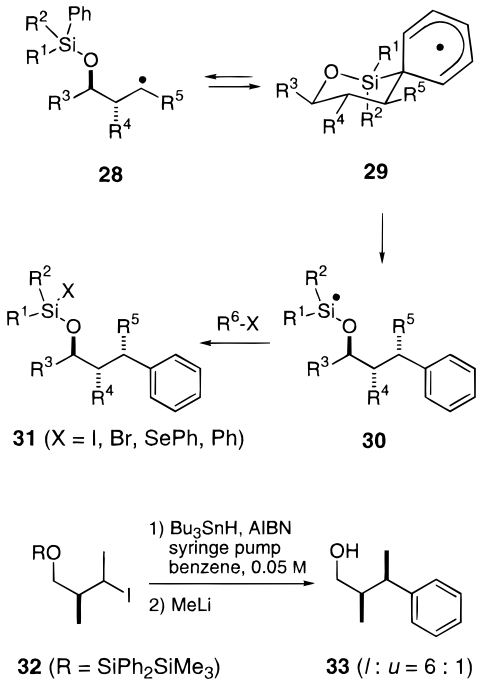
A side product, diol **22** was isolated in 10% yield with high selectivity (*l*:*u* = 9:1). Radical **23** undergoes the expected 1,5 hydrogen transfer to form radical **24**, which eventually leads after phenyl migration and subsequent desilylation to alcohol **21**. The byproduct **22** derives from initial 1,6 hydrogen transfer in **23** to generate radical **25,** which after stereoselective 1,4 phenyl migration[32] and desilylation affords diol **22**. 1,6 Hydrogen transfers in similar systems have previously been described.[30a] The formation of 1,3-butandiol, the major observed product (^{1}H NMR spectroscopy, not isolated) can be explained by four possible pathways. Reduction of aryl radical **23**, α-oxy radical **24**, or secondary radical **25** will all give 1,3-butanediol after desilylation. In addition, Curran reported 1,7 hydrogen transfers using *o*-bromophenyl-(dimethyl)silyl ethers as radical translocating groups.[30a] 1,7-Hydrogen transfer and subsequent reduction would also afford 1,3-butanediol after desilylation. Since we were not interested in the hydrogen transfer step, we did not further study the reaction mechanism leading to 1,3-butanediol.

An alternative way to generate radicals in the α position of an oxygen atom is addition of silyl radicals to aldehydes.[33,34] Thus, reaction of **26** with tris(trimethylsilyl)silyl radicals, followed by subsequent 1,5 phenyl migration and selective monodesilylation[35] afforded alcohol **27** in 19% yield. As for **20**, moderate selectivity was observed (*u*:*l* = 3:1). In general, aryl migration to a stabilized secondary radical is less efficient and less selective than the analogous reaction with secondary alkyl radicals.

From the experimental results, we suggest the following mechanism for the phenyl migration reaction: Radical **28**, generated after initial halogen abstraction (or S_H2 reaction at selenium) by a tin radical, undergoes intramolecular *ipso* attack at the migrating phenyl group to form cyclohexadienyl radical **29** (Scheme 3). The addition is probably reversible, especially for stabilized radicals (see below). Spirocyclic cyclohexadienyl radicals with silyl substituents at the spiro position have already been characterized by ESR spectroscopy.[36] Rearomatization will then lead to silyl radical **30**. The rearomatization step (**29** → **30**) is probably not reversible, since halogen abstraction[37] (from starting halide) should be faster under the reaction conditions than intramolecular addition of the silyl radical to the phenyl group. Furthermore, silyl radical **30** can also undergo homolytic aromatic substitution with the solvent benzene (**30** → **31**).[38] Indeed, Crich already reported that intramolecular

Scheme 3



homolytic aromatic substitution on benzene can compete with intramolecular *ipso*-attack in radical biaryl synthesis.[18f] The reason is that the intramolecular process requires *ipso*-attack, which is sterically hindered. However, we cannot exclude reversibility in the rearomatization process. In fact, Sakurai reported radical phenyl migrations from carbon to silicon under drastic conditions.[21] So far, all experiments to address the reversibility in the rearomatization step (**29** → **30**) in our system failed.

The efficiency of the rearomatization process (formation of **30**) should be altered upon varying the substituents at the Si-atom. Thus, radical stabilizing substituents at silicon, such as trimethylgermyl or trimethylsilyl, should lead to faster rearomatization and therefore to higher concentration of silyl radical **30** and eventually to higher yields in the reaction, as observed in the experiment. Since halogen abstraction,[37] as well as homolytic aromatic substitution (see above)[38] with silyl radicals are fast, reduction of silyl radical **30** by Bu_3SnH should not compete with halogen abstraction or homolytic aromatic substitution (→ **31**). We looked at the ^{1}H NMR spectrum of the crude product in the reaction of iodide **5** (prior to the MeLi treatment). Indeed, no Si−H resonance was observed.

To explain the stereochemical outcome of the phenyl migration, we suggest the following model: We assume that the low-energy transition state for the formation of **29** resembles a chair with the substituents R^3−R^5 in equatorial positions. According to this model, the observed 1,3 selectivity can readily be understood. The similar selectivities obtained for **6** and **7** (*u*:*l* = 6:1, see Table 1) are compatible with the model, since in the cyclohexadienyl radical **29** derived from TBDPS ether **6**, the bulky *tert*-butyl group is expected to occupy the equatorial position (R^1 in **29**), placing the phenyl group axial (R^2 in **29**). Thus, the transition state in the formation of **29** derived from **6** should resemble the transition state derived from **7** with respect to the 1,3 diaxial interaction in the chair (R^2 = phenyl in both

(31) The relative configuration of the major isomer of **21** was assigned by comparison of the ^{1}H NMR data with literature values: Barbero, A.; Blackmore, D. C.; Fleming, I.; Wesley, R. N. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1329.

(32) Stereoselective 1,4 phenyl migration reactions will be discussed below. The relative configuration of the major isomer of **22** was assigned in analogy to the compounds obtained in those studies (see below).

(33) Chatgilialoglu, C. *Chem. Rev.* **1995**, *95*, 1229.

(34) Damm, W.; Dickhaut, J.; Wetterich, F.; Giese, B. *Tetrahedron Lett.* **1993**, *34*, 431.

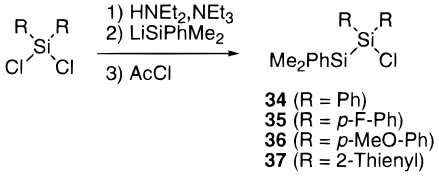
(35) Brook, M. A.; Gottardo, C.; Balduzzi, S.; Mohamed, M. *Tetrahedron Lett.* **1997**, *38*, 6997. Brook, M. A.; Balduzzi, S.; Mohamed, M.; Gottardo, C. *Tetrahedron* **1999**, *55*, 10027.

(36) Sakurai, H.; Nozue, I.; Hosomi, A. *J. Am. Chem. Soc.* **1976**, *98*, 8279. Kira, M.; Sugiyama, H.; Sakurai, H. *J. Am. Chem. Soc.* **1983**, *105*, 6436.

(37) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5123.

(38) Chatgilialoglu, C.; Ingold, K. U.; Scaiano, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 3292.

Scheme 4



34 (R = Ph)
35 (R = *p*-F-Ph)
36 (R = *p*-MeO-Ph)
37 (R = 2-Thienyl)

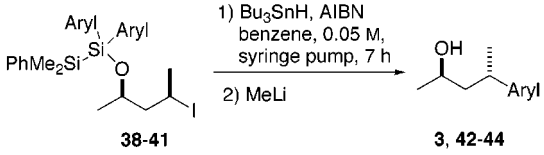
systems). To further corroborate our model, we also studied the 1,2 stereoselectivity. In agreement with the model, transformation of iodide **32** under the standard conditions afforded alcohol **33** with *like* selectivity (6:1). The relative configuration of the major isomer was assigned after Swern oxidation of alcohol **33** to the corresponding known[39] aldehyde.

We believe that cyclohexadienyl radical **29**, bearing a radical-stabilizing group R[5], can also rearomatize to form the corresponding stabilized C-centered radical, making the initial *ipso* attack reversible. The reversibility should lead to lower yields as observed for the α-oxygen-stabilized radicals. However, we are not sure whether for the α-amido-stabilized radical derived from **14**, where only reduced product **15** was observed, initial *ipso* attack is too slow (for steric reasons), or whether the equilibrium in the reversible addition lies too far to the side of the C-centered radical. Reversibility of the initial *ipso* attack should also lower the selectivity if product control under thermodynamic conditions is less selective. Indeed, lower selectivities were obtained for the α-oxygen-stabilized radicals. Equilibrium will probably never be reached under the reaction conditions.

According to the mechanism, the silyl radical formed after rearomatization (**29** → **30**, Scheme 3) can either abstract the halogen atom from unreacted starting material (or S_H2 at selenium) or react with benzene (S_HAr). The S_HAr should occur at higher conversion, when most of the starting halide (selenide) is consumed. Halogen abstraction is a chain propagation step, and substoichiometric amounts of Bu_3SnH (for initiation) should be sufficient to run the reaction. The phenyl migration can therefore be considered as an Unimolecular Chain Transfer Reaction (UMCT).[23,24,40] With 0.2 equiv of Bu_3SnH, under otherwise identical conditions, phenyl migration product **3** was obtained in only 35% yield (*u*:*l* = 10:1) along with unreacted starting material. It turned out, that 0.4 equiv of Bu_3SnH are necessary to get yields as high as those obtained for the reaction conducted with 1.2 equiv Bu_3SnH. Thus, the reaction is catalytic in tin hydride, but the chains are short and a large amount of initiator is necessary. This is probably due to the fact that the silyl radicals formed after rearomatization can add to benzene and thus prevent propagation of the chain.[41]

To further explore the scope of the reaction, phenyl migrations of functionalized arenes were studied. To this end, chlorosilanes **34**−**37** were prepared from known diaryldichlorosilanes in three steps as shown in Scheme 4. The silylating reagents were isolated with moderate to high purity (75−95%). For synthetic reasons, the trimethylsilyl group, normally used as the silyl substituent in the disilyl ethers, was replaced by the dimethylphenylsilyl group. The silyl ethers **38**−**41** were prepared under standard conditions (NEt_3, DMAP, THF) from the corresponding alcohol in 48−81% yield, as specified in the Experimental Section.

Table 2.



38-41 **3, 42-44**

(specification of R see Table)

compd	Aryl	product	yield (%)	dr (*u* : *l*)[a]
38	Ph	**3**	71	9 : **1**
39	*p*-F-Ph	**42**	36	10 : 1
40	*p*-MeO-Ph	**43**	30	9 : **1**
41[b]	2-Thienyl	**44**	–	–

[a] Determined by GC analysis. [b] Mixture of Diastereoisomers (1:1).

To test whether the additional phenyl group in the disilane has an effect on the phenyl migration, we first studied the phenyl migration of silyl ether **38** (Table 2). Alcohol **3** was isolated in similar yield (71%; 70% for **5**, see Table 1) and with similar selectivity (*u*:*l* = 9:1; 10:1 for **5**), showing that the replacement of the trimethylsilyl group by the dimethylphenylsilyl group has no significant effect on the reaction. With the electron-poor *p*-fluorophenyl derivative **39**, a decrease in the yield was observed (36%); however, selectivity remained high. Alcohol **42** was formed as a 10 to 1 mixture of diastereoisomers. Similar results were obtained with the *p*-methoxyphenyl compound **40**, where the migration product was isolated in 30% yield. The relative configuration of the major isomer of **42** and **43** was assigned in analogy to alcohol **3**. 1,5 Thienyl migration failed, and alcohol **44** was not formed. These results suggest that polar effects do not play an important role in the aryl migration to nucleophilic secondary alkyl radicals. For electron-rich as well as for electron-poor arenes, lower yields of the corresponding aryl transfer product were obtained as compared to the phenyl migration. So far, it is not clear, why functionalized aryl groups are transferred less efficiently. Since the substituents are in the *para* position, steric effects should only play minor roles.

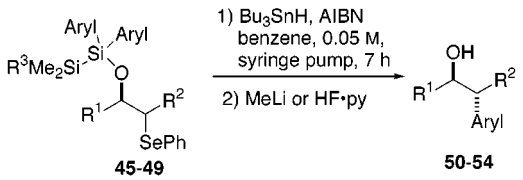
Stereoselective 1,4 Aryl Migration. Our next series of experiments was used to determine if 1,4-aryl migration to secondary C-centered radicals is also possible. Radical precursors **45**−**49** were prepared from the corresponding alcohols and chlorosilanes using standard silylation conditions (NEt_3, DMAP, THF, or DMF, imidazole). Aryl migrations were conducted by slow addition (syringe pump) of Bu_3SnH (1.2 equiv) to a solution of the corresponding radical precursor in benzene. In the reaction of silyl ethers **45** and **46**, desilylation was performed with MeLi. For the esters (**47**−**49**), HF·pyridine was used to remove the remainder of the initial silyl group after aryl migration.

(39) Fleming, I.; Lewis, J. J. *J. Chem. Soc., Perkin Trans. 1* **1992**, *24*, 3257.

(40) Curran, D. P.; Xu, J.; Lazzarini, E. *J. Chem. Soc., Perkin Trans 1* **1995**, 3049. Curran, D. P.; Xu, J. *Ibid.* **1995**, 3061. Martinez-Grau, A.; Curran, D. P. *J. Org. Chem.* **1995**, *60*, 8332. Curran, D. P.; Xu, J.; Lazzarini, E. *J. Am. Chem. Soc.* **1995**, *117*, 6603. Martinez-Grau, A.; Curran, D. P. *Tetrahedron* **1997**, *53*, 5679. Curran, D. P.; Xu, J. *Synlett* **1997**, 1102. For other UMCT reactions see: Keck, G. E.; Enholm, E. J.; Yates, J. B.; Wiley, M. R. *Tetrahedron* **1985**, *41*, 4079. Kim, S.; Koh, J. S. *J. Chem. Soc., Chem. Commun.* **1992**, 1377. Boivin, J.; Camara, J.; Zard, S. Z. *J. Am. Chem. Soc.* **1992**, *114*, 7909.

(41) Cole, S. J.; Kirwan, J. N.; Roberts, B. P.; Willis, C. R. *J. Chem. Soc., Perkin Trans. 1* **1991**, 103.

Table 3.

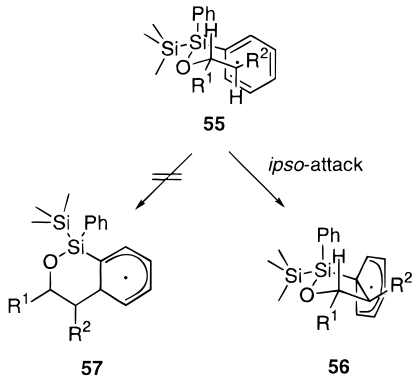


(specification of R^1 and R^2 see Table)

compd	R^1	R^2	R^3	Aryl	product	yield (%)	dr (*l* : *u*)
45[a]	Me	Me	Me	Ph	**50**	81	1 : 14[b]
46	Ph	Me	Me	Ph	**51**	74	18 : 1[b]
47	Me	CO_2t-Bu	Me	Ph	**52**	57	> 98 : < 2[c]
48	Me	CO_2t-Bu	Ph	*p*-MeO-Ph	**53**	47	> 98 : < 2[c]
49	Me	CO_2t-Bu	Ph	*p*-F-Ph	**54**	35	> 98 : < 2[c]

[a] Bromide was used instead of phenylselanide. [b] Determined by GC analysis. [c] Determined by ^{1}H NMR spectroscopy.

Scheme 5



We were pleased to find that 1,4 phenyl migration works even better than in the homologuous system. Thus, alcohol **50**[26] was isolated in 81% yield with high selectivity (*u*:*l* = 14:1, Table 3). Even higher selectivity (18:1) was obtained for the phenyl migration of benzylic silyl ether **46** (→ **51**, 74%). α-Arylation of an ester can also be done by using the radical aryl migration strategy. Radical phenylation of selanide **47** afforded, after desilylation, *β*-hydroxy ester **52** in 57% yield with excellent selectivity. In the ^{1}H NMR spectrum, no signals of the corresponding diastereoisomer were observed. A slightly lower yield was obtained for the migration of the *p*-MeO-phenyl group. Ester **53** was isolated in 47% yield as a diastereoisomerically pure compound. The electron poor fluorinated phenyl group was transferred with excellent selectivity, and hydroxy ester **54** was obtained in 35% yield.

The mechanism of the 1,4 phenyl migration is probably very similar to the homologuous 1,5 phenyl transfer (see discussion above). The stereochemical outcome of the aryl transfer reaction can be explained by assuming a transition state which resembles a chair (**55** → **56**), with the substituents R^1 and R^2 in pseudoequatorial positions, very similar to the ubiquitous 5-*exo* hexenyl radical cyclization reaction (Scheme 5).[42] The higher selectivity (as compared to the 1,5 phenyl migration) is not unexpected, since the transition state must be more rigid and the stereoinducing center is closer (1,2 stereoinduction).

(42) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinheim, 1996.

Interestingly, no products derived from *ortho* attack of radical **55** (→ **57**) were observed. *Ortho*-attack is the major reaction pathway in similar 1,4 phenyl migrations from sulfur in sulfonates to aryl radicals.[19c]

As in the 1,5 aryl migration to nucleophilic secondary radicals, polar effects are not important in the 1,4 aryl migration to electrophilic radicals. Only slightly higher yields were obtained for the transfer of an electron-rich (→ **53**, 47%) versus the analoguous reaction of an electron-poor aryl group (→ **54**, 35%). Once again, the best yields were obtained for the migration of the unfunctionalized phenyl group.

Conclusions

In this work, a new method for the stereoselective $C(sp^2)-C(sp^3)$ bond formation was presented. Since aryl groups occur in many natural products and in many drugs, methods for the introduction of aryl groups are very important. However, there are only few methods for the stereoselective $C(sp^2)-C(sp^3)$ bond formation. Here, we showed that the radical aryl migration from silicon in diaryldisilyl ethers to various C-centered radicals is an efficient route for the stereoselective introduction of aryl groups. To the best of our knowledge, there are only very few stereoselective radical aryl migrations reported in the literature.[22]

Our starting materials are readily prepared from chiral secondary alcohols. Many methods for the preparation of enantiomerically pure secondary alcohols are known. Thus, the application of this chemistry for the preparation of optically pure compounds is obvious. The synthesis of the diphenyldisilylchlorosilanes used for the preparation of the starting silyl ethers is straightforward and large amounts are readily available.

In general, 1,3 stereocontrol in intermolecular free radical C−C-bond forming reactions is difficult. We formally applied the Stork[43] temporary silicon connection to transform an *inter*molecular reaction to an *intra*molecular process.[44] In our chemistry, however, silicon is detached from the reacting group during the reaction. In the transition state, the connection still exists, thus ensuring highly selective radical aryl migrations.

We showed that 1,4 and 1,5 phenyl group transfers to various types of C-centered radicals are possible. Best results were obtained for aryl migrations to nucleophilic secondary radicals, where high yields and high selectivities were observed. Polar effects seem to play only minor roles in these processes. Finally, we have to point out, that α-arylations of esters can be performed with excellent stereoselectivities by using this new method.

Experimental Section

General. All reactions were carried out in oven-dried glassware under an argon atmosphere. Tetrahydrofuran (THF) and benzene (PhH) were freshly distilled from sodium/benzophenone under argon. Melting points are uncorrected. IR spectra were recorded using an FTIR apparatus. Mass spectra were obtained by EI or ESI methods. Flash column chromatography was performed using Fluka silica gel 60 (40−63 *μ*m).

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

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

Elemental analyses were performed by the Microanalytical Laboratory of the Laboratorium für Organische Chemie, ETH-Zürich.

General Procedure (GP 1) for the Silylation of Secondary Alcohols. The chlorosilane was dissolved under Ar in Et_2O, THF, or CH_2Cl_2. The solution was cooled to 0 °C, and NEt_3 was added. A solution of the alcohol in Et_2O, THF, or CH_2Cl_2 was added over 3 min. DMAP was added, and the suspension formed was allowed to warm to rt and stirred for 3−12 h. Addition of hexane or pentane and filtration of the solid gave after evaporation of the solvent the crude product which was purified either by distillation or flash chromatography.

General Procedure (GP 2) for the Aryl Migration Reaction. The silyl ether was dissolved in benzene under argon and heated to reflux followed by slow addition of Bu_3SnH and AIBN in benzene over 7 h. After complete addition of the tin hydride solution, stirring was continued at that temperature for 30 min. The solution was then allowed to warm to rt, and MeLi was added. This was followed by stirring at rt for 12 h and then slow addition of H_2O and Et_2O. The reaction mixture was washed with saturated aqueous NH_4Cl and brine. The organic phase was dried ($MgSO_4$) and evaporated to yield the crude product.

Representative Example for the Synthesis of Silyl Ethers Bearing Unfunctionalized Phenyl Groups: *l*-[(4-Iodopentan-2-oxy)diphenylsilyl]trimethylsilane (5). According to GP 1 with 1-chloro-2,2,2-trimethyl-1,1-diphenyldisilane[28] (870 mg, 3.0 mmol), THF (13 mL + 3 mL), *l*-4-iodopentan-2-ol (700 mg, 3.30 mmol), NEt_3 (0.49 mL, 3.35 mmol), and DMAP (cat.), and a reaction time of 12 h at rt. Purification by FC (Et_2O/pentane 1:100) afforded **5**: 1.13 g (80%). IR ($CHCl_3$) 3068 s, 2966 s, 1958 w, 1888w, 1824 w, 1774 w, 1428 s, 1144 s, 1106 s, 1056 s cm^{-1}; ^1H NMR (400 MHz) 7.64−7.54 (m, 4H), 7.42−7.34 (m, 6H), 4.35−4.26 (m, 1H), 4.08−4.00 (m, 1H), 1.95−1.87 (m, 1H), 1.89 (d, 3H, J = 6.9 Hz), 1.73−1.66 (m, 1H), 1.14 (d, 3H, J = 6.1 Hz), 0.21 (d, 9H, J = 0.4 Hz); ^{13}C NMR (100 MHz) 137.3, 137.1, 135.0, 134.8, 129.5, 129.4, 127.8, 127.7, 70.5, 52.9, 29.6, 27.7, 24.1, −1.0; MS (EI) 469.1 (<1, $[M + H]^+$), 453.1 (<1, $[M - CH_3]^+$), 309.0 (100). Anal. Calcd for $C_{20}H_{29}IOSi_2$ (468.52): C, 51.27; H, 6.24. Found: C, 51.40; H 6.35.

Representative Example of a 1,5 Phenyl Migration: 4-Phenylpentan-2-ol (3). According to GP 2 with silyl ether **5** (114 mg, 0.24 mmol), benzene (5 mL), Bu_3SnH (65 μL, 0.24 mmol), AIBN (8 mg, 0.04 mmol) in benzene (0.5 mL), and MeLi (2.3 mL, 3.7 mmol). Purification by FC (Et_2O/pentane 1:4) afforded **3**: 28 mg (70%). The physical data are in agreement with the values reported in the literature.[26] The diastereoisomer ratio (*u*:*l* = 10:1) was determined by GC-analysis.

Representative Example for the Synthesis of the Chlorosilanes Bearing Functionalized Phenyl Groups: 1-Chloro-2,2-dimethyl-1,1-bis(4-fluorophenyl)-2-phenyldisilane (35). Bis(4-fluorophenyl)dichlorosilane (18.8 g, 65 mmol) was dissolved under Ar in THF (48 mL) and cooled to 0 °C. NEt_3 (10.4 mL, 75 mmol) and $HNEt_2$ (6.75 mL, 65 mmol) were added according to a literature procedure.[45] After stirring for 4 h at 0 °C, hexane was added, and the suspension was filtered and distilled (0.01 Torr, 80−95 °C) to afford (chlorobis(4-fluorophenyl)silanyl)diethylamide (17.9 g, 84%). ^1H NMR (200 MHz, $CDCl_3$) 7.79−7.68 (m, 4H), 7.22−7.06 (m, 4H), 2.93 (q, 4H, J = 7.1 Hz), 1.06 (t, 6H, J = 7.1 Hz). Dimethylphenylchlorosilane (2.9 mL, 17.5 mmol) and Li-wire (0.43 g, 62 mmol) were reacted in THF (35 mL) at 0 °C according to ref 28. The Li-silanide solution formed was slowly added to a solution of (chlorobis(4-fluorophenyl)silanyl)diethylamide (5.70 g, 17.5 mmol) in THF (13 mL) at 0 °C.[46] After stirring for 1 h at 0 °C, hexane (90 mL) was added, and the salts were filtered off under Ar. Distillation (0.02 Torr, 115−135 °C afforded bis(4-fluorophenyl)(*N*,*N*-diethylamino)(dimethylphenylsilyl)silane (3.20 g, 43%). ^1H NMR (200 MHz, $CDCl_3$) 7.48−7.02 (m, 13H), 2.95 (q, 4H, J = 13.6 Hz), 0.93 (t, 6H, J = 13.6 Hz), 0.43 (s, 6H). Bis(4-fluorophenyl)(*N*,*N*-diethylamino)(dimethylphenylsilyl)silane (3.20 g, 7.5 mmol) was dissolved in CH_2Cl_2 (7 mL) at 0 °C, and acetyl chloride (0.54 mL, 7.5 mmol) was added.[47] After 2 h, the solvent was removed and the residue distilled (0.02 Torr, 100−120 °C) to afford **35**: 2.39 g (82%) in about 90% purity. ^1H NMR (300 MHz, $CDCl_3$) 7.47−7.02 (m, 13H), 0.53 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) 164.7 (d, J_{C-F} = 251.4 Hz), 136.9 (d, J_{C-F} = 7.3 Hz), 134.5, 129.7, 128.3, 116.2, 115.7 (d, J_{C-F} = 19.5 Hz), −4.0.

Representative Example for the Synthesis of Silyl Ethers Bearing Functionalized Phenyl Groups: *l*-[(4-Iodopentan-2-oxy)bis(4-fluorophenyl)silyl]dimethylphenylsilane (39). According to GP 1 with **35** (445 mg, 1.1 mmol), THF (6 mL + 2 mL), *l*-4-iodopentan-2-ol (237 mg, 1.10 mmol), NEt_3 (0.15 mL, 1.10 mmol), and DMAP (cat.), and a reaction time of 4 h at 0 °C. Purification by FC (Et_2O/pentane 1:200) afforded **39**: 180 mg (29%). IR ($CHCl_3$) 2964 w, 1587 s, 1498 s, 1160 m, 1054 m cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) 7.51−7.43 (m, 4H), 7.37−7.25 (m, 5H), 7.07−7.02 (m, 4H), 4.18−4.10 (m, 1H), 4.00−3.93 (m, 1H), 1.92−1.81 (m, 1H), 1.85 (d, 3H, J = 6.9 Hz), 1.65−1.58 (m, 1H), 1.02 (d, 3H, J = 6.1 Hz), 0.48 (s, 3H), 0.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) 164.1 (d, J_{C-F} = 249.4 Hz), 164.0 (d, J_{C-F} = 249.0 Hz), 137.7, 137.2 (d, J_{C-F} = 7.6 Hz), 136.9 (d, J_{C-F} = 7.5 Hz), 134.3, 132.3 (d, J_{C-F} = 3.8 Hz), 131.7 (d, J_{C-F} = 3.8 Hz), 128.9, 127.8, 115.1 (d, J_{C-F} = 19.8 Hz), 115.1 (d, J_{C-F} = 19.8 Hz), 70.8, 52.7, 29.5, 27.5, 24.0, −2.7, −2.8. MS (EI) 431.1 (14, $[M - Si(CH_3)_2(C_6H_5)]^+$), 345.0 (100). HRMS calcd for ($[M - Si(CH_3)_2Ph]^+$) $C_{17}H_{18}F_2IOSi$: 431.0140; found: 431.0143.

Representative Example of a 1,5 Aryl Migration with Functionalized Phenyl Groups: *l*-4-(4-Fluorophenyl)-pentan-2-ol (42). According to GP 2 with silyl ether **39** (208 mg, 0.36 mmol), benzene (7 mL), Bu_3SnH (103 μL, 0.39 mmol), AIBN (7 mg, 0.04 mmol) in benzene (0.9 mL), and MeLi (3.4 mL, 5.44 mmol). Purification by FC (Et_2O/pentane 1:6) afforded **42**: 24 mg (36%). The diastereoisomer ratio (*u*:*l* = 10:1) was determined by GC-analysis. IR ($CHCl_3$) 3609 m, 2967 s, 1604 m, 1509 s, 1158 m, 1093 m cm^{-1}. ^1H NMR (400 MHz) 7.19−7.13 (m, 2H), 7.01−6.95 (m, 2H), 3.79−3.71 (m, 1H), 2.87 (qt, 1H, $J_1 = J_2$ = 7.1 Hz), 1.82−1.74 (m, 1H), 1.65−1.58 (m, 1H), 1.24 (d, 3H, J = 6.9 Hz), 1.19 (d, 3H, J = 6.2 Hz). ^{13}C NMR (100 MHz) 161.3 (d, J_{CF} = 243.8 Hz), 143.0 (d, J_{CF} = 3.0 Hz), 128.1 (d, J_{CF} = 7.7 Hz), 115.2 (d, J_{CF} = 20.9 Hz), 66.3, 47.9, 36.1, 23.8, 22.4. MS (EI) 182.2 (3, $[M]^+$), 123.2 (100). HRMS calcd for ($[M]^+$) $C_{11}H_{15}FO$: 182.1103; found: 182.1106.

Representative Example for the Synthesis of the Silyl Ethers for the 1,4 Aryl Migration: [(3-Bromobutan-2-oxy)diphenylsilyl]trimethylsilane (45). According to GP 1 with 1-chloro-2,2,2-trimethyl-1,1-diphenyldisilane[28] (156 mg, 0.52 mmol), Et_2O (5 mL + 2 mL), 3-bromobutan-2-ol (79 mg, 0.52 mmol), NEt_3 (0.08 mL, 0.52 mmol), and DMAP (cat.), and a reaction time of 12 h at rt. Purification by FC (Et_2O/pentane 1:100) afforded **45**: 100 mg (47%). IR ($CHCl_3$) 2955 m, 1588 w, 1428 s, 1107 s, 856 s cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) isomer A: 7.65−7.49 (m, 4H), 7.47−7.28 (m, 6H), 4.06−3.97 (m, 1H), 3.90−3.84 (m, 1H), 1.60 (d, 3H, J = 6.8 Hz), 1.19 (d, 3H, J = 6.1 Hz), 0.20 (s, 9H). Isomer B: 7.65−7.49 (m, 4H), 7.47−7.28 (m, 6H), 4.06−3.97 (m, 1H), 3.90−3.84 (m, 1H), 1.63 (d, 3H, J = 6.7 Hz), 1.21 (d, 3H, J = 6.3 Hz), 0.20 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) isomer A: 136.8, 136.6, 135.0, 134.8, 129.6, 129.5, 127.9, 127.8, 73.7, 56.2, 21.5, 20.7, −1.3. Isomer B: 136.8, 136.6, 134.8, 134.7, 129.6, 129.6, 127.9, 127.8, 72.9, 54.0, 19.9, 18.9, −1.3. MS (EI) 333.1 (36, $[M - Si(CH_3)_3]^+$), 261.0 (100). HRMS calcd for ($[M - Si(CH_3)_3]^+$) $C_{16}H_{18}{}^{79}BrOSi$: 333.0310; found: 333.0303.

Representative Example for the Synthesis of the Silylated Esters: 3-(Diphenyl(trimethylsilyl)siloxy)-2-(phenylselanyl)butyric Acid *tert*-Butyl Ester (47). According to GP 1 with 1-chloro-2,2,2-trimethyl-1,1-diphenyldisilane[28] (222 mg, 0.76 mmol), THF (4 mL + 2 mL), 3-hydroxy-

(45) Tamao, K.; Nakajo, E.; Ito, Y. *Tetrahedron* **1988**, *44*, 3997.

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2-(phenylselanyl)butyric acid *tert*-butyl ester (264 mg, 0.84 mmol), NEt_3 (0.12 mL, 0.84 mmol), and DMAP (cat.), and a reaction time of 14 h at rt. Purification by FC (Et_2O/pentane 1:100) afforded **47**: 398 mg (83%, mixture of isomers). IR ($CHCl_3$) 2979 s, 1716 s, 1579 m, 1428 s, 1369 s, 991 s cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) isomer A: 7.60−7.54 (m, 4H), 7.52−7.46 (m, 2H), 7.42−7.18 (m, 9H), 4.32−4.21 (m, 1H), 3.57 (d, 1H, J = 8.4 Hz), 1.36 (s, 9H), 1.30 (d, 3H, J = 6.2 Hz), 0.16 (s, 9H). Isomer B: 7.60−7.54 (m, 4H), 7.52−7.46 (m, 2H), 7.42−7.18 (m, 9H), 4.32−4.21 (m, 1H), 3.71 (d, 1H, J = 7.1 Hz), 1.32 (s, 9H), 1.29 (d, 3H, J = 6.2 Hz), 0.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) both isomers: 170.8, 170.4, 137.3, 136.8, 136.7, 136.7, 135.0, 134.9, 134.8, 134.5, 129.5, 129.4, 129.4, 129.3, 129.0, 128.9, 128.8, 128.0, 127.8, 127.8, 127.7, 81.1, 81.0, 70.8, 70.7, 53.8, 53.3, 27.9, 27.8, 22.1, 21.3, −1.2, −1.2. MS (EI) 497.3 (<1, $[M(^{80}Se) - Si(CH_3)_3]^+$), 49.0 (100). Anal. Calcd for $C_{29}H_{38}O_3SeSi_2$ (569.75): C, 61.14; H, 6.72. Found: C, 61.30; H, 6.75.

Representative Example of a 1,4 Phenyl Migration: *u*-2-Hydroxy-3-phenylbutan-2-ol (50). According to GP 2 with silyl ether **45** (98 mg, 0.24 mmol), benzene (7 mL), Bu_3SnH (69 μL, 0.26 mmol), AIBN (5 mg, 0.03 mmol) in benzene (0.6 mL), and MeLi (2.3 mL, 3.7 mmol). Purification by FC (Et_2O/pentane 1:6) afforded **50**: 29 mg (81%). The diastereoisomer ratio (*u*:*l* = 14:1) was determined by GC-analysis. The physical data are in agreement with the values reported in the literature.[26,48]

Representative Example of a 1,4 Aryl Migration to a α-Carbonyl C-Radical: *l*-3-Hydroxy-2-phenylbutyric Acid *tert*-Butyl Ester (52). According to GP 2 with silyl ether **47** (119 mg, 0.21 mmol), benzene (4.2 mL), Bu_3SnH (67 μL, 0.25 mmol), AIBN (3 mg, 0.02 mmol) in benzene (0.5 mL). After removal of the solvent, the residue was dissolved in CH_2Cl_2 (6 mL), and HF·pyridine (0.06 mL) was added. After stirring for 30 min at 0 °C, the mixture was worked up as described in GP 2 using CH_2Cl_2 as solvent. Purification by FC (Et_2O/pentane 1:5) afforded **52**: 28 mg (57%). In the ^1H NMR spectrum no signals of the *unlike* isomer were observed. IR ($CHCl_3$) 3587 w br, 2981 m, 1716 s, 1369 s cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) 7.37−7.27 (m, 5H), 4.38−4.26 (m, 1H), 3.41 (d, 1H, J = 6.6 Hz), 2.38 (s, 1H), 1.42 (s, 9H), 1.21 (d, 3H, J = 6.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) 172.7, 135.9, 129.3, 128.8, 127.8, 81.5, 68.8, 59.8, 28.0, 20.5. MS (EI) 237.2 (<1, $[M + H]^+$), 136.1 (100). Anal. Calcd for $C_{14}H_{20}O_3$ (236.31): C, 71.16; H, 8.53. Found: C, 71.11; H, 8.58.

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Supporting Information Available: Full experimental details for the preparation and the corresponding analytical data of **3**, **4**, **6**−**22**, **26**−**27**, **32**−**33**, **36**−**38**, **40**−**41**, **43**, **46**, **48**−**49**, **51**, **53**−**54**. This material is available free of charge via the Internet at http://pubs.acs.org.

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