Synthetic Methods

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# Synthesis of Biaryl Compounds through Three-Component Assembly: Ambidentate Effect of the *tert*-Butyldimethylsilyl Group for Regioselective Diels–Alder and Hiyama Coupling Reactions**

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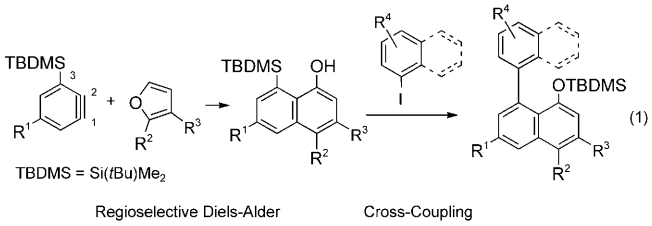
The biaryl moiety is ubiquitous in natural products,[1a–c] pharmaceuticals,[1d,e] polymers,[1f] sensors,[1g] and in ligands for transition-metal catalysts.[1h,i] A number of useful methods for the preparation of these compounds have been developed based on the transition-metal-catalyzed cross-coupling of aryl halides with aryl metal species through Stille, Suzuki, Negishi, and Hiyama reactions.[2]

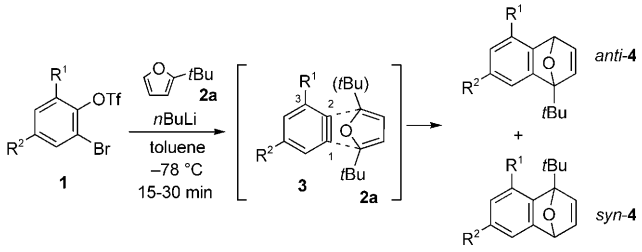
Multicomponent assembly protocols have been recognized as a powerful means for the preparation of molecular complexity and diversity, and are thus particularly suited for combinatorial chemistry and diversity-oriented synthesis.[3] As an approach towards this goal, we now report the novel preparation of multisubstituted unsymmetrical biaryl compounds through the assembly of the following three components: a silylated benzyne, a furan derivative, and an aryl iodide [Eq. (1)]. Thus, this methodology involves the construction of silylnaphthalene derivatives by a regioselective Diels–Alder reaction of 3-*tert*-butyldimethylsilylbenzynes (3-TBDMS-benzynes) with furan derivatives followed by a Hiyama cross-coupling reaction of the generated TBDMS-substituted cycloadducts with aryl iodides.




(1)

We initially examined the Diels–Alder reaction of 3-phenylbenzyne (**3a**, $R^1 = Ph$, $R^2 = H$), generated in situ by treatment of 2-bromo-6-phenylphenyl triflate (**1a**) with *n*BuLi at −78 °C, and 2-*tert*-butylfuran (**2a**) to synthesize a multisubstituted biaryl compound. However, the regioselectivity of the reaction was quite low and afforded a 1:1.3 mixture of the head-to-tail (*anti*) and the head-to-head (*syn*) cycloaddition products **4a** (Table 1, entry 1).[4–6] We devised an alternative method for the synthesis of the biaryl compounds which involved the Diels–Alder reaction of 3-silylbenzyne **3c** or **3d**[7,8] followed by the substitution of the silyl group of the cycloadducts with an aryl group. In this approach the Diels–Alder reaction of 3-(trimethylsilyl)benzyne (3-TMS-benzyne) **3c** with **2a** took place to give *anti*-**4c** with high regioselectivity (Table 1, entry 3). Moreover, the reaction of 3-TBDMS-benzyne **3d** and **2a** exhibited even higher regioselectivity (Table 1, entry 4): *syn*-**4d** was not detected by $^1$H NMR analysis (500 MHz) of the crude reaction mixture. The exclusive *anti* selectivity of the reaction cannot be explained by the simple steric hindrance of the silyl group, because the Diels–Alder reaction of 3-*tert*-butylben-

***Table 1:*** Diels–Alder reactions of 3-substituted benzynes **3**, generated from **1a–d**, and **2a**.[a]




1 3 2a

| Entry | $R^1$ | $R^2$ | **1**, **3** | *anti*-**4**:*syn*-**4**[b] | **4** | Yield [%][c] |
|---|---|---|---|---|---|---|
| 1 | Ph | H | **1a**, **3a** | 1:1.3 | **4a** | 70 |
| 2 | *t*Bu | *t*Bu | **1b**, **3b** | 1.7:1 | **4b** | 53 |
| 3 | TMS | Me | **1c**, **3c** | 39:1 | **4c** | 63 |
| 4 | TBDMS | Me | **1d**, **3d** | >50:1 | **4d** | 69 |

[a] Reaction conditions: 1.0 equiv **1**, 3.0–10 equiv **2a**, 2.0 equiv *n*BuLi in toluene (0.2 M) at −78 °C under nitrogen. [b] Determined by 500 MHz $^1$H NMR spectroscopic analysis of a crude reaction mixture and also by the yield of the isolated product. [c] Total yield of isolated *anti*- and *syn*-**4**. Tf = triflate.

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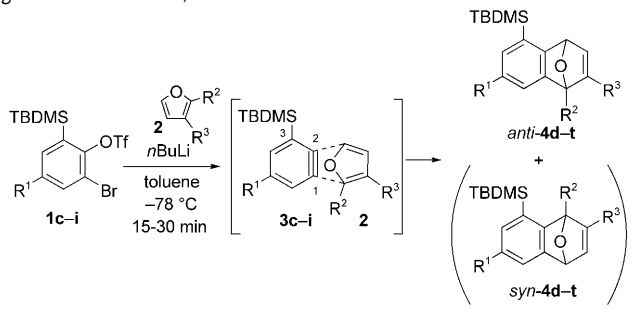
zyne **3b**, generated from **1b** with **2a**, gave **4b** with poor regioselectivity (Table 1, entry 2).

Similar reactions of the 3-TBDMS-benzynes **3d–i** generated from the reactions of **1d–i** and furans **2a–g** were found to give the corresponding *anti*-**4** products (Table 2). The following results are noteworthy: The formation of the *anti*-**4** product invariably predominated and the regioselectivity increased in the order: $R^2 = Me < nBu < tBu \approx SiMe_3 \approx SnBu_3$ (see Table 2). The formation of *syn*-**4** was below the $^1H$ NMR detection limit (500 MHz) for the reactions with 2-*tert*-butylfuran (**2a**; Table 2, entries 4, 10, 12, 15, and 17), 2-TMS-furan (**2e**; Table 2, entries 6 and 13), and 2-(tributylstannyl)furan (**2f**; Table 2, entry 7). However, no regioselectivity was observed in the reaction involving 2-phenylfuran (**2d**; Table 2, entry 5). The use of **2f** provides a solution to this problem [see Eq. (3)]. The reaction of 2,3-dimethylfuran (**2g**) provided *anti*-**4k** (Table 2, entry 8) with a regioselectivity that was much higher than that of 2-methylfuran (**2b**). Although a trimethylsilyl (TMS) group on benzyne **3c** was also as effective as a directing group as the TBDMS group (Table 2, entry 3), the TMS group on the cycloadduct **4g** was not stable enough during the subsequent transformation (see Table 3, entry 2 and Ref. [7]). Substituents $R^1$, such as the fluoro (Table 2, entries 11–13) and silyloxy (Table 2, entry 17) groups, on **3** were tolerated under the stated reaction conditions.

Next, we achieved the regioselective cleavage of the epoxy ring of *anti*-**4f** by using *p*-toluenesulfonic acid ($pTsOH\cdot H_2O$) to give 1-naphthol **5a** almost quantitatively,[9] while the TBDMS group remained intact (Table 3, entry 1).

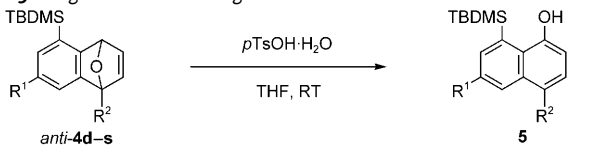
***Table 2:*** Regioselective Diels–Alder reactions of 3-silylbenzynes **3c–i**, generated from **1c–i**, and **2**.[a]




| Entry | $R^1$ (**1**) | $R^2$ | $R^3$ | **2** | *anti*-**4**:*syn*-**4**[b] | | Yield [%][c] |
|---|---|---|---|---|---|---|---|
| 1[d] | Me (**1d**) | Me | H | **2b** | 3.9:1 | **4e** | 68 |
| 2[e] | Me (**1d**) | *n*Bu | H | **2c** | 5.9:1 | **4f** | 71 |
| 3[f] | Me (**1c**) | *n*Bu | H | **2c** | 5.0:1 | **4g** | 65 |
| 4[g] | Me (**1d**) | *t*Bu | H | **2a** | >50:1 | **4d** | 69 |
| 5 | Me (**1d**) | Ph | H | **2d** | 1.2:1 | **4h** | 53 |
| 6 | Me (**1d**) | $SiMe_3$ | H | **2e** | >50:1 | **4i** | 40 |
| 7 | Me (**1d**) | $SnBu_3$ | H | **2f** | >50:1 | **4j** | 64 |
| 8 | Me (**1d**) | Me | Me | **2g** | 12:1 | **4k** | 62 |
| 9 | H (**1e**) | *n*Bu | H | **2c** | 7.0:1 | **4l** | 56 |
| 10 | H (**1e**) | *t*Bu | H | **2a** | >50:1 | **4m** | 63 |
| 11[e] | F (**1f**) | *n*Bu | H | **2c** | 10 :1 | **4n** | 58 |
| 12[e] | F (**1f**) | *t*Bu | H | **2a** | >50:1 | **4o** | 63 |
| 13[e] | F (**1f**) | $SiMe_3$ | H | **2e** | >50:1 | **4p** | 49 |
| 14 | Ph (**1g**) | *n*Bu | H | **2c** | 6.2:1 | **4q** | 62 |
| 15 | Ph (**1g**) | *t*Bu | H | **2a** | >50:1 | **4r** | 53 |
| 16[h] | OMe (**1h**) | *n*Bu | H | **2c** | 6.3:1 | **4s** | 43 |
| 17 | $CH_2OTBDMS$ (**1i**) | *t*Bu | H | **2a** | >50:1 | **4t** | 64 |

[a] Reaction conditions: 1.0 equiv **1**, 3.0 equiv **2**, 2.0 equiv *n*BuLi in toluene (0.2 M) at −78 °C under nitrogen. [b] Determined by 500 MHz $^1H$ NMR spectroscopic analysis of a crude reaction mixture and also by the yield of the isolated product. [c] Total yield of the isolated *anti*- and *syn*-**4**. [d] With 15 equiv **2** and 1.5 equiv *n*BuLi. [e] With 10 equiv **2**. [f] With the 3-TMS-benzyne precursor **1c** instead of the 3-TBDMS derivative **1d**. [g] From entry 4 in Table 1. [h] With the corresponding mesylate instead of the triflate.

***Table 3:*** Regioselective cleavage of *anti*-**4**.[a]




| Entry | $R^1$ | $R^2$ | **4** | *t* [h] | **5** | Yield [%][b] |
|---|---|---|---|---|---|---|
| 1 | Me | *n*Bu | *anti*-**4f** | 18 | **5a** | 94 |
| 2[c] | Me | *n*Bu | *anti*-**4g** | 23 | **5b** | 59 |
| 3 | Me | *t*Bu | *anti*-**4d** | 48 | **5c** | 61 |
| 4 | Me | Ph | *anti*-**4h** | 19 | **5d** | 87 |
| 5 | H | *n*Bu | *anti*-**4l** | 19 | **5e** | 87 |
| 6 | F | *n*Bu | *anti*-**4n** | 48 | **5f** | 91 |
| 7 | Ph | *n*Bu | *anti*-**4q** | 60 | **5g** | 97 |
| 8 | OMe | *n*Bu | *anti*-**4s** | 24 | **5h** | 97 |

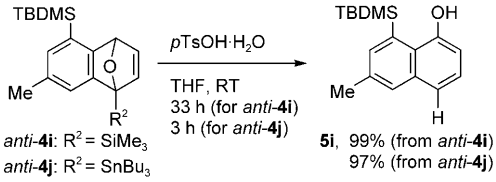
[a] Reaction conditions: 1.0 equiv *anti*-**4**, 1.5–3.0 equiv $pTsOH\cdot H_2O$ in THF (0.15 M) at RT under nitrogen. [b] Yield of isolated **5**. [c] With the 3-TMS-substituted Diels–Alder adduct *anti*-**4g** instead of the 3-TBDMS derivative.

However, a similar reaction of the TMS analogue *anti*-**4g** suffered partial cleavage of its TMS group, thus resulting in a significant decrease in the yield of the 1-naphthol **5b** (Table 3, entry 2). To study the generality of this reaction several *anti*-**4** derivatives were isomerized to 1-naphthols **5** by using $pTsOH\cdot H_2O$ (Table 3). The presence of electron-withdrawing and electron-donating $R^1$ groups on the benzene ring and the presence of substituents $R^2$ at the ring junction of *anti*-**4** did not affect the cleavage reactions, with **5** being obtained in good to excellent yields (Table 3, entries 4–8). The presence of a bulky *t*Bu substituent as $R^2$ resulted in the reaction being slower and only a moderate yield of the product (Table 3, entry 3). In all cases, the epoxy ring was opened regioselectively.

Cleavage of the epoxy ring of *anti*-**4i** and *anti*-**4j** took place with similar perfect regioselectivy, although complete protodesilylation and protodestannylation occurred simultaneously. These reactions are useful as a selective method for the synthesis of 8-TBDMS-1-naphthols such as **5i** [Eq. (2)].

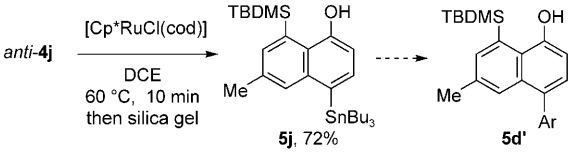
Ruthenium-catalyzed isomerization[10] was found to be effective as an alternative method for the chemoselective cleavage of the epoxy ring of *anti*-**4** derivatives with acid-sensitive functional groups. Thus, *anti*-**4j** was selectively converted into 8-TBDMS-4-stannyl-1-naphthol **5j** in the presence of [Cp*RuCl(cod)] (0.15 equiv; $Cp^* = C_5Me_5$, cod = 1,5-cyclooctadiene). The tributylstannyl group, which can be replaced with various aryl groups by Stille coupling




(2)

reactions, remained intact.[11] Although the Diels–Alder reaction of 2-phenylfuran (**2d**) exhibited little selectivity (Table 2, entry 5), the series of a regioselective Diels–Alder reaction with 2-stannylfuran (**2f**), a ring-opening reaction, and a Stille coupling is a highly reliable method for the regioselective synthesis of 8-TBDMS-4-aryl-1-naphthols **5d′** [Eq. (3)].

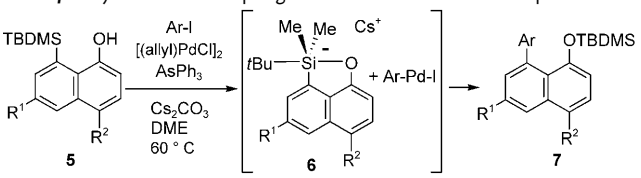



(3)

Another highly intriguing, but difficult task was the substitution of the TBDMS group of **5** with an aryl group. Although Hiyama cross-coupling reactions of aryl silanes are widely used,[2,12] there is no precedent, to the best of our knowledge, of such a reaction with the robust TBDMS group. After intensive screening of various palladium sources, ligands, bases, and solvents, we finally found that the coupling reaction between **5a** and iodobenzene could be effected by the use of [{(allyl)PdCl}$_2$], $AsPh_3$, and $Cs_2CO_3$ in 1,2-dimethoxyethane (DME) to provide the 8-phenyl-1-naphthyl TBDMS ether (**7a**) in 77% yield (Table 4, entry 1). Moderate to good yields of the biaryl products **7** were obtained from electron-rich (Table 4, entries 4 and 5) and electron-poor aryl iodides (Table 4, entries 6–9) as well as from 1-naphthyl iodide (Table 4, entry 10). This conversion protocol was found to be tolerant of a number of functional groups, including ester (Table 4, entry 6), nitrile (Table 4, entry 7), carbonyl (Table 4, entry 8), and nitro groups (Table 4, entry 9).

More noteworthy is that this reaction was achieved without using any fluoride activator. The fact that the TBDMS group was transferred to the neighboring oxygen atom during the reaction indicated the formation of the pentacoordinate silicate **6** as an intermediate.[13] Although fluoride-free coupling reactions of aryl silanes through intramolecular activation have been reported, all the examples are limited to the use of flexible aliphatic alcohols.[14,15] Our examples present the possible additional activation of the Si–C bond by an intramolecular phenolic hydroxy group for cross-coupling reactions. Furthermore, our results are of particular interest because the equatorial Si–C bond of **6** was cleaved (Figure 1), whereas in the previously reported cases the axial substituents of **8** were exclusively cleaved, as observed in common palladium-catalyzed cross-coupling reactions.

***Table 4:*** Hiyama cross-coupling reactions of 8-TBDMS-1-naphthols **5**.[a]




| Entry | $R^1$ | $R^2$ | **5** | Ar | *t* [h] | **7** | Yield [%][b] |
|---|---|---|---|---|---|---|---|
| 1 | Me | *n*Bu | **5a** | Ph | 2 | **7a** | 77 |
| 2 | Me | H | **5i** | Ph | 2.5 | **7b** | 72 |
| 3 | H | *n*Bu | **5e** | Ph | 12 | **7c** | 61 |
| 4 | Me | *n*Bu | **5a** | 2-$MeOC_6H_4$ | 2 | **7d** | 55[c] |
| 5 | Me | *n*Bu | **5a** | 4-$MeOC_6H_4$ | 8 | **7e** | 60 |
| 6 | Me | *n*Bu | **5a** | 4-$EtOCOC_6H_4$ | 2 | **7f** | 80[c] |
| 7 | Me | *n*Bu | **5a** | 4-$NCC_6H_4$ | 2 | **7g** | 81 |
| 8 | Me | *n*Bu | **5a** | 4-$MeCOC_6H_4$ | 2 | **7h** | 68 |
| 9 | Me | *n*Bu | **5a** | 4-$O_2NC_6H_4$ | 7 | **7i** | 55 |
| 10 | Me | *n*Bu | **5a** | 1-naphthyl | 1.5 | **7j** | 46 |

[a] Reaction conditions: 1.0 equiv ArI, 1.2 equiv **5**, 0.06 equiv [{(allyl)PdCl}$_2$], 0.24 equiv $AsPh_3$, 1.5 equiv $Cs_2CO_3$ in DME (0.1 M) at 60 °C under argon. [b] Yield of isolated **7**. [c] Yield determined by NMR spectroscopy. Pure product was isolated after desilylation.

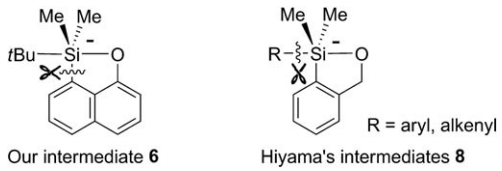



***Figure 1.*** Contrasting cleavage sites of two types of intermediates.

In summary, we have developed a new method for the synthesis of biaryl compounds by assembling three components, namely, silylated benzyne precursors **1**, furan derivatives **2**, and aryl iodides. This method features the use of the robust *tert*-butyldimethylsilyl (TBDMS) group for two different purposes, namely, the silicon-directing Diels–Alder reactions of 3-TBDMS-benzynes and the Hiyama coupling of the TBDMS-substituted cycloadducts. The Diels–Alder reactions of the 3-TBDMS-benzynes and the 2-substituted furans possibly take place through a nonsynchronous concerted mechanism[5a] that reflects the regioselectivity of the reaction. Further investigations into the detailed mechanism and expansion of the scope of the reaction are now underway.

## *Experimental Section*

General procedure for the regioselective Diels–Alder reactions of 3-TBDMS-benzynes **3d–i** (Table 2): An oven-dried pear-shaped flask was charged with **1d–i** (1.0 equiv), capped with an inlet adapter with a three-way stopcock, and then evacuated and back-filled with nitrogen (this process was repeated twice). An azeotropic dehydration using toluene was then carried out (this process was repeated twice). Anhydrous toluene (0.2 M) and furan **2a–g** (3.0 equiv) were added by syringe, followed by the slow addition of a 1.6 M solution of *n*BuLi in hexane (2.0 equiv) over 10 min at −78 °C. After 10–30 min, a saturated aqueous $NH_4Cl$ solution was added and the reaction mixture then extracted with EtOAc (this process was repeated three times). The combined organic layers were dried over $MgSO_4$ and

concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel.

General procedure for the regioselective cleavage of *anti*-**4** (Table 3): A round-bottom flask was charged with *anti*-**4** (1.0 equiv) and *p*TsOH·$H_2O$ (0.5 equiv), then evacuated, and back-filled with nitrogen. Anhydrous THF (0.15 M) was added by syringe and the mixture stirred at room temperature. After a few hours, a second portion of *p*TsOH·$H_2O$ (0.5–2.0 equiv) was added and the reaction mixture stirred for several hours (this portion-wise addition was repeated until *anti*-**4** was consumed, as judged by TLC analysis). The reaction mixture was extracted with EtOAc (this process was repeated three times). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel.

General procedure for the Hiyama coupling reactions of **5** with aryl iodides (Table 4): An oven-dried reaction tube was charged with **5** (1.2 equiv), $AsPh_3$ (0.24 equiv), and $Cs_2CO_3$ (1.5 equiv). The reaction tube was capped with a rubber septum and then evacuated and back-filled with argon (this process was repeated twice). Anhydrous DME (0.1 M) was added by syringe, through the septum, followed by the addition of the aryl iodide (1.0 equiv; solid aryl halides were added with other reagents before the evacuation) and [{(allyl)PdCl}$_2$] (0.06 equiv). The reaction mixture was heated to 60 °C until **5** was completely consumed, as determined by TLC analysis. At this point the reaction mixture was cooled to room temperature, filtered through a thin pad of celite (eluting with EtOAc), and the eluent was concentrated under reduced pressure. The crude product purified by flash column chromatography on silica gel.

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**Keywords:** arynes · biaryls · C–C coupling · cycloaddition · synthetic methods

[1] a) K. B. G. Torssell, *Natural Product Chemistry*, Wiley, Chichester, **1983**; b) R. H. Thomson, *The Chemistry of Natural Products*, Blackie and Son, Glasgow, **1985**; c) O. Baudoin, F. Guéritte, *Stud. Nat. Prod. Chem.* **2003**, *29*, 355–417; d) A. V. R. Rao, M. K. Gurjar, K. L. Reddy, A. S. Rao, *Chem. Rev.* **1995**, *95*, 2135–2167; e) K. C. Nicolaou, C. N. C. Boddy, S. Bräse, N. Winssinger, *Angew. Chem.* **1999**, *111*, 2230–2287; *Angew. Chem. Int. Ed.* **1999**, *38*, 2096–2152; f) J. Roncali, *Chem. Rev.* **1992**, *92*, 711–738; g) X. Mei, C. Wolf, *J. Am. Chem. Soc.* **2006**, *128*, 13326–13327; h) J. M. Brunel, *Chem. Rev.* **2005**, *105*, 857–897; i) M. Berthod, G. Mignani, G. Woodward, M. Lemaire, *Chem. Rev.* **2005**, *105*, 1801–1836.

[2] a) *Handbook of Organopalladium Chemistry for Organic Synthesis* (Eds.: E. Negishi, A. De Meijere), Wiley Interscience, New York, **2002**; b) *Metal-Catalyzed Cross-Coupling Reactions, Vols. 1 and 2* (Eds.: A. De Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**.

[3] For recent examples, see: a) K. Tonogaki, K. Itami, J. Yoshida, *J. Am. Chem. Soc.* **2006**, *128*, 1464–1465; b) S.-X. Wang, M.-X. Wang, D.-X. Wang, J. Zhu, *Angew. Chem.* **2008**, *120*, 394–397; *Angew. Chem. Int. Ed.* **2008**, *47*, 388–391.

[4] For recent reviews on benzynes, see: a) H. Pellissier, M. Santelli, *Tetrahedron* **2003**, *59*, 701–730; b) H. H. Wenk, M. Winkler, W. Sander, *Angew. Chem.* **2003**, *115*, 518–546; *Angew. Chem. Int. Ed.* **2003**, *42*, 502–528; c) A. M. Dyke, A. J. Hester, G. C. Lloyd-Jones, *Synthesis* **2006**, 4093–4112.

[5] Regioselective Diels–Alder reactions of benzynes controlled by their C3 substituents have been limited to the 3-fluoro-[5a] and 3-alkoxybenzynes,[5b,c] which produced cycloadducts with a good to excellent *syn* regioselectivity: a) G. W. Gribble, D. J. Keavy, S. E. Branz, W. J. Kelly, M. A. Pals, *Tetrahedron Lett.* **1988**, *29*, 6227–6230; b) T. Matsumoto, T. Hosoya, M. Katsuki, K. Suzuki, *Tetrahedron Lett.* **1991**, *32*, 6735–6736; c) R. G. F. Giles, A. B. Hughes, M. V. Sargent, *J. Chem. Soc. Perkin Trans. 1* **1991**, 1581–1587.

[6] The Diels–Alder reactions of the 3-alkyl- or 3-aryl benzynes provided mixtures of the *syn* and *anti* adducts in various ratios, the regioselectivity of which could not be predicted, see: a) J. E. Anderson, R. W. Franck, W. L. Mandella, *J. Am. Chem. Soc.* **1972**, *94*, 4608–4614; b) M. S. Newman, R. Kannan, *J. Org. Chem.* **1976**, *41*, 3356–3359.

[7] The Diels–Alder reaction between 3-fluoro-6-(trimethylsilyl)-benzyne and 2-(trimethylsilyl)furan (**2e**) has been reported to give exclusively the 1,5-bis(trimethylsilyl)-1,4-epoxy-8-fluoro-1,4-dihydronaphthalene. However, the Diels–Alder reaction of the simple 3-(trimethylsilyl)benzyne was not examined. It was also reported that the trimethylsilyl group was cleaved during the acid-catalyzed opening of the 1,4-epoxide of another Diels–Alder product, see: E. Masson, M. Schlosser, *Eur. J. Org. Chem.* **2005**, 4401–4405.

[8] For the regioselective dipolar [2+3] cycloaddition reactions of 3-silylated benzynes with nitrones, see: T. Matsumoto, T. Sohma, S. Hatazaki, K. Suzuki, *Synlett* **1993**, 843–846.

[9] For some examples of acid-catalyzed opening of 1,4-epoxy-1,4-dihydronaphthalenes, see: a) D. G. Batt, D. G. Jones, S. La Greca, *J. Org. Chem.* **1991**, *56*, 6704–6708; b) M. Schlosser, E. Castagnetti, *Eur. J. Org. Chem.* **2001**, 3991–3997; c) D. E. Kaelin, S. M. Sparks, H. R. Plake, S. F. Martin, *J. Am. Chem. Soc.* **2003**, *125*, 12994–12995; d) S. Sörgel, C. Azap, H.-U. Reißig, *Eur. J. Org. Chem.* **2006**, 4405–4418.

[10] K. Villeneuve, W. Tam, *J. Am. Chem. Soc.* **2006**, *128*, 3514–3515.

[11] For examples, see: G. Bringmann, R. Götz, S. Harmsen, J. Holenz, R. Walter, *Liebigs Ann.* **1996**, 2045–2058.

[12] a) T. Hiyama, *J. Organomet. Chem.* **2002**, *653*, 58–61; b) S. E. Denmark, M. H. Ober, *Aldrichimica Acta* **2003**, *36*, 75–85.

[13] No reaction took place with the methyl ether of **5a** under the same reaction conditions, which strongly suggests that the formation of the silicate **6** is crucial for this coupling reaction.

[14] a) H. Taguchi, K. Ghoroku, M. Tadaki, A. Tsubouchi, T. Takeda, *J. Org. Chem.* **2002**, *67*, 8450–8456; b) Y. Nakao, H. Imanaka, A. K. Sahoo, A. Yada, T. Hiyama, *J. Am. Chem. Soc.* **2005**, *127*, 6952–6953; c) Y. Nakao, J. Chen, M. Tanaka, T. Hiyama, *J. Am. Chem. Soc.* **2007**, *129*, 11694–11695; for the activation of vinylsilanes by an intramolecular carboxyl group, see: d) M. Shindo, K. Matsumoto, K. Shishido, *Synlett* **2005**, 176–178.

[15] For examples of intermolecular fluoride-free Hiyama reactions, see: E. Alacid, C. Nájera, *Adv. Synth. Catal.* **2006**, *348*, 2085–2091.

  