Cobalt-Catalysed Transformations of 1,3,5-Hexatrienes on a Large Scale

Anastasia Schmidt, Elias Maiterth, Gerhard Hilt*

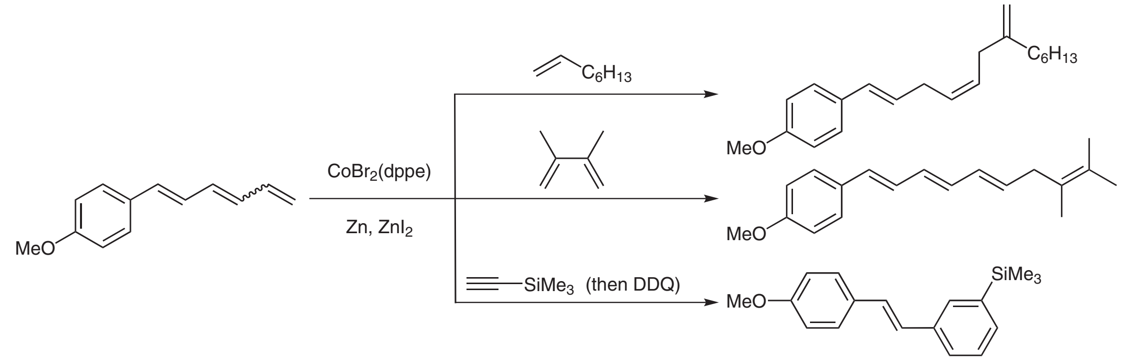
Fachbereich Chemie, Philipps-Universität Marburg, Hans-Meerwein-Straße, 35043 Marburg, Germany
Fax +49(6421)2825677; E-mail: Hilt@chemie.uni-marburg.de

Received: 22.05.2014; Accepted after revision: 12.06.2014

PSP No 276

Abstract: The cobalt-catalysed 1,4-hydrovinylation of an aryl-substituted 1,3,5-hexatriene was investigated on a large scale for the synthesis of a double-skipped 1,4,7-triene product. The reaction proceeds via a regioselective C–H activation of the alkene and the exclusive formation of the 4*Z*-double bond. The cobalt-catalysed 1,4-hexatrienylation of a butadiene derivative led exclusively to the desired all-*E* tetraene product. Finally, the cobalt-catalysed Diels–Alder reaction with trimethylsilyl-substituted alkynes was investigated. The cycloadducts were generated with excellent chemo- and regioselectivity to give the corresponding stilbene derivative.

Key words: alkenes, alkynes, cobalt, 1,3-dienes, Diels–Alder reaction, 1,3,5-hexatrienes, 1,4-hydrovinylation



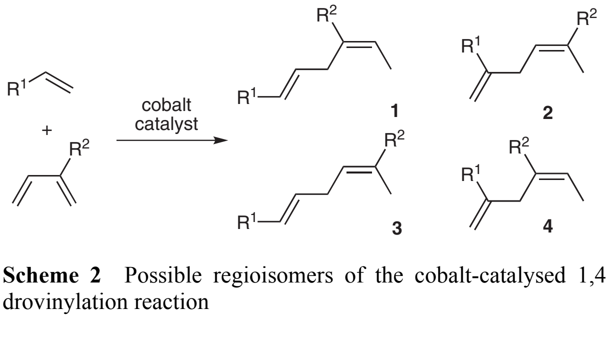
Scheme 1 Cobalt-catalysed transformations of 1,3,5-hexatrienes

Cobalt-catalysed transformations of unsaturated starting materials have been expanded in the last 10 to 15 years to incorporate a vast number of different transformations, other than the well-known cyclotrimerisation of alkynes,[1] the Pauson–Khand reaction,[2] and the Nicholas reaction.[3]

Among these transformations are the cobalt-catalysed Diels–Alder reaction,[4] the Alder–ene reaction[5] as well as the '*reductive*' Alder–ene reaction,[6] and the isomerisation of 1,3-dienes,[7] to name just a few. Another transformation that can be efficiently catalysed by cobalt catalysts is the 1,4-hydrovinylation of 1,3-dienes with terminal alkenes.[7] When unsymmetrical starting materials are applied, up to four isomers of the 1,4-diene products **1**–**4** can be obtained (Scheme 2).

The control of the regiochemistry of the products **1** and **2** was accomplished by tuning the ligands on the cobalt catalysts and the electronic nature of the starting materials. While the application of the catalyst precursor CoBr$_2$(dppe) led to products such as **2** in excellent yields and selectivities,[8] the application of the CoBr$_2$(SchmalzPhos) pre-catalyst led to the products of type **3** predominantly.[9] The use of unsymmetrically 2,3-disubstituted 1,3-dienes led to a substrate-based control of the regiochemistry via steric interactions.[10] The optimal conditions for the generation of the sterically more demanding products of type **4**, with the substituents R^1 and R^2 in closest proximity, is an unsolved challenge.

In a recent application, we focussed our attention on the application of 1,3,5-hexatriene derivatives in different cobalt-catalysed reactions.[11] These results inspired us to investigate the possibilities for the stepwise scale-up for such reactions, since a number of interesting products can be generated (Scheme 1).

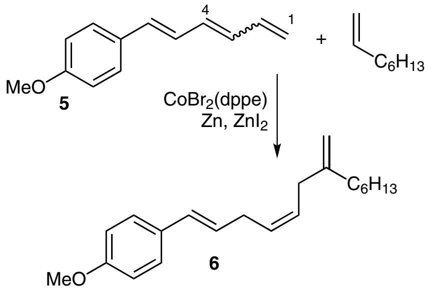


Scheme 2 Possible regioisomers of the cobalt-catalysed 1,4-hydrovinylation reaction

SYNTHESIS 2014, 46, 2040–2044
Advanced online publication: 09.07.2014
DOI: 10.1055/s-0034-1378375; Art ID: ss-2014-z0314-psp

1,4-Hydrovinylation of 1,3,5-Hexatrienes

The 1,4-hydrovinylation of the *E*/*Z*-mixture of 1,3,5-triene **5** with 1-octene was accomplished by cobalt catalysation. We define this process to be a formal regioselective addition of the C–H bond of the alkene (C–H donor) to position 1 and 4 of the 1,3,5-hexatriene (C–H acceptor). This process was catalysed by a cobalt catalyst comprising $CoBr_2$(dppe), zinc powder, and zinc iodide (Scheme 3). An outstanding feature of this cobalt-catalysed process is that the product **6** is formed exclusively. Only the C–H activation of the internal position of the alkene is activated by the cobalt catalyst and also the 1,4-addition to the 1,3,5-hexatriene proceeds exclusively. Although quite a number of other possible C–H activation and addition products (including *E*/*Z* isomers) are possible only the hydrovinylation product **6** could be isolated.



Scheme 3 Cobalt-catalysed 1,4-hydrovinylation of the aryl-substituted 1,3,5-hexatriene **5**

The 1,4-hydrovinylation process led exclusively to the *Z*-configured product **6**, resulting from the postulated mechanism.[8] Also, the product **6** exhibits a challenging double-skipped 1,4-diene subunit. The three different types of double bonds in **6** might be of interest in competition experiments for reactions converting differently substituted and configured double bonds with different rates.

Because of these interesting aspects of this cobalt-catalysed bond formation process, its realisation on a larger scale was investigated. The results of our efforts are summarized in Table 1.

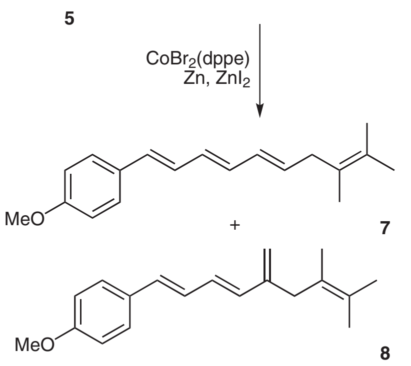
Table 1 Scale-Up of the 1,4-Hydrovinylation of **6** According to Scheme 3

Scale	Yield (%) of **6** (cobalt catalyst mol%)
2 mmol	72 (10)
5 mmol	60 (20)
10 mmol	53 (20)

While the 1,4-hydrovinylation of **5** led to good yields on a small scale, incomplete conversions were obtained on a 5 mmol scale leading to prolonged reaction times and electrocyclic ring closure reactions of the (*Z*)-**5** eventually resulting in the formation of 4-methoxybiphenyl as the side-product. The low yields could only be partially compensated for by increasing the catalyst loading to 20 mol% on the 5 and 10 mmol scale. Nevertheless, up to 1.57 g of the desired double-skipped product **6** could be obtained from the 10 mmol scale entry as a single regio- and stereoisomer.

1,4-Hexatrienylation of 1,3-Dienes

The cobalt-catalysed 1,4-hexatrienylation of the *E*/*Z*-mixture of 1,3,5-triene **5** with 2,3-dimethyl-1,3-butadiene was also efficiently accomplished (Scheme 4). We define this process to be a formal regioselective addition of a terminal C–H bond of the 1,3,5-hexatriene (C–H donor) to position 1 and 4 of the butadiene derivative (C–H acceptor). Accordingly, a C–H bond of the triene **5** is formally added over the 2,3-dimethyl-1,3-butadiene for the formation of product **7**. As a side-reaction, the cobalt-catalysed C–H activation of the C2 position and its addition over the butadiene derivative was observed for the formation of **8**. In contrast to the 1,4-hydrovinylation, **5** is the C–H donor in this reaction and not the C–H acceptor. The reason for this change in selectivity remains speculative. Although quite a number of other alkenyl C–H bonds of the hexatriene could be activated and also a 1,2-addition to the 1,3-diene is possible, the cobalt catalyst only accounts for the formation of products **7** and **8**.



Scheme 4 Cobalt-catalysed 1,4-hydrohexatrienylation with the aryl-substituted 1,3,5-hexatriene **5**

The reaction was originally performed on a 1.0 mmol scale and we were interested if the reaction can be scaled up to obtain gram quantities of such products. For this purpose the methoxy-substituted hexatriene **5** was reacted on increasing scale with 2,3-dimethyl-1,3-butadiene and in contrast to the previously described hydrovinylation process (Table 1) the yields remained constant (Table 2).

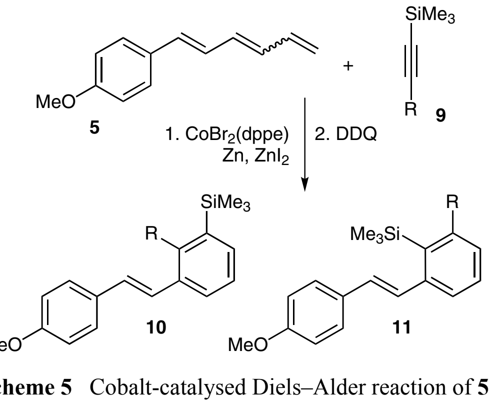
In addition, the ratio of the two products remained identical with the small exception of the reaction on the 2 mmol scale, but we believe that there could have been a mistake during column chromatography so that portions of **8** were lost. Nevertheless, the *E*/*Z*-mixture of **5** was converted into the all-*E* tetraene product **7**, which could be obtained in up to 1.82 g and a good chemoselectivity (**7**/**8** = 7.4:1.0).

Table 2 Scale-Up of the Synthesis of **7** and **8** According to Scheme 4

Scale	Yield (%) of **7** + **8**
1 mmol	73 (7.8:1.0)
2 mmol	66 (9.8:1.0)
5 mmol	68 (7.3:1.0)
10 mmol	68 (7.4:1.0)

Diels–Alder Reaction of 1,3,5-Hexatrienes

Finally, the application of hexatriene **5** as the 1,3-diene part in a Diels–Alder reaction with trimethylsilyl-substituted alkynes **9** was investigated (Scheme 5). The cobalt-catalysed reaction is highly chemoselective and only the 1,3-diene subunit of **5** reacted to form the regioisomers of type **10** exclusively. Accordingly, the cobalt-catalysed Diels–Alder reaction of 1,3,5-hexatrienes is a chemo- and regioselective reaction for the synthesis of stilbene derivatives of type **10**.



Scheme 5 Cobalt-catalysed Diels–Alder reaction of **5** and DDQ oxidation to adducts of type **10**

In a small series of experiments, the application of trimethylsilyl-substituted internal alkynes (R ≠ H) in the cobalt-catalysed process was tested. The results of these experiments are summarized in Table 3.

Table 3 Diels–Alder Reactions of Trimethylsilyl-Substituted Alkynes with **5** According to Scheme 5

Scale	R in **9**	Yield (%) of **10**
1 mmol	H	87
2 mmol	H	89
5 mmol	H	85
10 mmol	H	90
1 mmol	Me	52
1 mmol	*n*-Pr	10

The Diels–Alder reaction of trimethylsilylacetylene **9** (R = H) could be scaled up without problems to a 10 mmol scale yielding the desired product **10** in excellent yields up to 90% so that up to 2.53 g could be generated. Nevertheless, the application of internal alkynes (R = Me and *n*-Pr) was far less successful. In these reactions, it became clear that the steric hindrance of the alkyne reaches its limits when R exceeds the size of a methyl group. It should be mentioned that the application of phenylacetylene in this reaction was not successful as well. The desired product could be detected (GCMS analysis) but because of several side products the corresponding Diels–Alder adduct could not be isolated in pure form.

In summary, we were able to demonstrate that cobalt-catalysed reaction of 1,3,5-hexatriene **5** could be scaled up to 10 mmol scales. While the yields for the 1,4-hexatrienylation and Diels–Alder reaction remained unchanged on a larger scale, the 1,4-hydrovinylation reaction of **5** gave somewhat lower yields on a larger scale. Moreover, the chemo- and regioselectivities of the cobalt-catalysed reactions also remain unchanged so that these reactions can be well applied for the synthesis of various polyene-type products.

All reactions were carried out under an argon atmosphere in heat gun-dried glassware. CH_2Cl_2 was distilled under N_2 from P_4O_{10}. All solvents for chromatography were distilled. Commercially available materials were used without further purification. The starting material **5** was synthesised as reported earlier.[12] Column chromatography was performed on silica gel 60 (Merck 230–400 mesh). ^1H and ^{13}C NMR: Bruker Avance-300 and DRX-500. MS-EI: Hewlett Packard 5973 Mass Selective Detector. HRMS-EI: Finnigan MAT 95. IR: Bruker Alpha P.

Cobalt-Catalysed 1,4-Hydrovinylation for the Synthesis of 6; 10 mmol Scale

Anhydrous ZnI_2 (1.28 g, 4.01 mmol, 40 mol%), Zn powder (260 mg, 4.00 mmol, 40 mol%), and $CoBr_2$(dppe) (1.24 g, 2.00 mmol, 20 mol%) were suspended in anhydrous CH_2Cl_2 (10 mL) under an argon atmosphere in a flame-dried Schlenk tube fitted with a Teflon screw cap. Then **5** (1.86 g, 10.0 mmol) and 1-octene (2.24 g, 20.3 mmol) were added. The mixture was stirred at ambient temperature until no further reaction progress was monitored by GC/MS (24 h). The reaction mixture was filtered over a short pad of silica gel (pentane–Et_2O, 20:1). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (pentane–Et_2O, 20:1). The product **6** was obtained as a colourless oil; yield: 1.57 g (5.27 mmol, 53%).

IR (film): 3007, 2924, 2855, 1677, 1645, 1605, 1510, 1459, 1298, 1247, 1174, 1108, 1033, 966, 889, 834, 757, 726, 530 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.25 (m, 2 H), 6.86–6.81 (m, 2 H), 6.35 (d, J = 15.8 Hz, 1 H), 6.05 (dt, J = 15.8, 6.5 Hz, 1 H), 5.54 (m, 2 H), 4.77–4.74 (m, 2 H), 3.80 (s, 3 H), 2.95 (t, J = 6.4 Hz, 2 H), 2.80 (d, J = 6.5 Hz, 2 H), 2.07–1.99 (m, 2 H), 1.47–1.41 (m, 2 H), 1.36–1.23 (m, 6 H), 0.88 (t, J = 6.8 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 158.9, 148.9, 130.8, 129.7, 128.6, 128.5, 127.2, 126.7, 114.1, 109.5, 55.4, 36.5, 34.2, 31.9, 30.8, 29.3, 27.9, 22.8, 14.3.

MS (EI): m/z (%) = 298 (M^+, 10), 213 (10), 185 (10), 136 (15), 134 (100), 121 (50), 91 (15), 79 (10), 77 (15), 41 (10).

HRMS (EI): m/z calcd for $C_{21}H_{30}O$: 298.2297; found: 298.2294.

Cobalt-Catalysed 1,4-Hexatrienylation for the Synthesis of 7; 10 mmol Scale[11]

Anhydrous ZnI_2 (638 mg, 2.00 mmol, 20 mol%), Zn powder (130 mg, 2.00 mmol, 20 mol%), and $CoBr_2$(dppe) (619 mg, 1.00 mmol, 10 mol%) were suspended in anhydrous CH_2Cl_2 (10 mL) under an argon atmosphere in a flame-dried Schlenk tube fitted with a Teflon screw cap. Then, **5** (1.86 g, 10.0 mmol) and 2,3-dimethyl-1,3-butadiene (2.3 mL, 20.3 mmol) were added and the mixture was stirred at r.t. until no further reaction progress was monitored by GC/MS (24 h). The reaction mixture was filtered over a short pad of silica gel (pentane–Et_2O, 20:1). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (pentane–Et_2O, 20:1). The product **7** + **8** was obtained as a colourless oil; yield: 1.82 g (6.80 mmol, 68%, **7**/**8** = 7.4:1).

Analytical Data for **7**

IR (film): 2915, 2857, 1599, 1510, 1460, 1440, 1374, 1299, 1252, 1174, 1109, 1027, 993, 844, 824, 536 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.34–7.31 (m, 2 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 6.71–6.65 (m, 1 H), 6.47 (d, *J* = 15.5 Hz, 1 H), 6.30–6.27 (m, 2 H), 6.11 (dd, *J* = 15.0, 9.9 Hz, 1 H), 5.71–5.64 (m, 1 H), 3.81 (s, 3 H), 2.84 (d, *J* = 6.8 Hz, 2 H), 1.68 (s, 6 H), 1.65 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.2, 132.9, 132.8, 131.3, 131.2, 130.8, 130.6, 127.7, 127.6, 127.5, 125.6, 114.2, 55.4, 38.1, 20.8, 20.4, 18.6.MS (EI): *m*/*z* (%) = 268 (M^+, 100), 253 (7), 225 (20), 207 (29), 197 (9), 185 (61), 173 (25), 159 (23), 145 (29), 128 (28), 121 (56), 115 (27).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{24}O$: 268.1827; found: 268.1842.

Cobalt-Catalysed Diels–Alder Reaction for the Synthesis of 10 (R = H); 10 mmol Scale[11]

Anhydrous ZnI_2 (640 mg, 2.01 mmol, 20 mol%), Zn powder (130 mg, 2.00 mmol, 20 mol%), and $CoBr_2$(dppe) (620 mg, 1.00 mmol, 10 mol%) were suspended in anhydrous CH_2Cl_2 (10 mL) under an argon atmosphere in a flame-dried Schlenk tube fitted with a Teflon screw cap. Then, **5** (1.86 g, 10.0 mmol) and trimethylsilylacetylene (1.29 g, 13.0 mmol) were added and the mixture was stirred at r.t. until no further reaction progress was monitored by GC/MS (20 h). The reaction mixture was filtered through a small pad of silica gel (pentane–Et_2O, 50:1), and the solvent was removed under reduced pressure. The residual dihydroaromatic intermediate was oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 2.51 g, 11.1 mmol, 1.1 equiv) in toluene. After 1 h at r.t., the mixture was filtered through a short pad of deactivated silica gel (pentane–Et_2O, 50:1), and the solvent was removed under reduced pressure. The product **10** (R = H) was obtained as a yellow solid; yield: 2.53 g (8.98 mmol, 90%); mp 89–90 °C.

IR (film, ATR): 3010, 2955, 2843, 1602, 1578, 1510, 1500, 1011, 1282, 1248, 1175, 1114, 1031, 963, 894, 832, 754 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.63 (s, 1 H), 7.51 (dd, *J* = 7.7, 0.7 Hz, 1 H), 7.48 (d, *J* = 8.7 Hz, 2 H), 7.41 (d, *J* = 7.2 Hz, 1 H), 7.35 (t, *J* = 7.4 Hz, 1 H), 7.09 (d, *J* = 16.3 Hz, 1 H), 7.02 (d, *J* = 16.1 Hz, 1 H), 6.92 (d, *J* = 8.6 Hz, 2 H), 3.84 (s, 3 H), 0.32 (dd, *J* = 1.7, 0.7 Hz, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 140.9, 137.0, 132.4, 131.6, 130.4, 128.3, 128.2, 127.9, 127.1, 126.6, 11.3, 55.5, 1.0.

MS (EI): *m*/*z* (%) = 282 (M^+, 100), 267 (74), 252 (4), 235 (5), 219 (5), 178 (13), 165 (17).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{22}OSi$: 282.1440; found: 282.1436.

Cobalt-Catalysed Diels–Alder Reaction for the Synthesis of 10 (R = Me); 1 mmol Scale

Anhydrous ZnI_2 (128 mg, 0.40 mmol, 40 mol%), Zn powder (26 mg, 0.40 mmol, 40 mol%), and $CoBr_2$(dppe) (123 mg, 0.20 mmol, 20 mol%) were suspended in anhydrous CH_2Cl_2 (1 mL) under an argon atmosphere in a flame-dried Schlenk tube fitted with a Teflon screw cap. Then, **5** (186 mg, 1.00 mmol) and 1-trimethylsilyl-1-propyne (149 mg, 1.33 mmol) were added and the mixture was stirred at r.t. until no further reaction progress was monitored by GC/MS (26 h). The reaction mixture was filtered through a small pad of silica gel (pentane–Et_2O, 10:1), and the solvent was removed under reduced pressure. The residual dihydroaromatic intermediate was oxidized with DDQ (250 mg, 1.10 mmol, 1.1 equiv) in toluene. After 1 h at r.t., the mixture was filtered through a short pad of deactivated silica gel (pentane–Et_2O, 10:1), and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (pentane–Et_2O, 10:1) The product **10** (R = Me) was obtained as a white solid; yield: 154 mg (0.52 mmol, 52%); mp 87–88 °C.

IR (film): 3056, 2998, 2951, 2835, 1604, 1576, 1508, 1462, 1440, 1421, 1410, 1303, 1284, 1247, 1200, 1172, 1141, 1108, 1033, 963, 881, 856, 834, 821, 752, 724, 687, 638, 620, 533, 513, 465, 415, 381 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.56 (dd, *J* = 7.6, 1.0 Hz, 1 H), 7.49–7.44 (m, 2 H), 7.40 (dd, *J* = 7.4, 1.3 Hz, 1 H), 7.25 (d, *J* = 16.0 Hz, 1 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 6.93–6.87 (m, 3 H), 3.84 (s, 3 H), 2.52 (s, 3 H), 0.36–0.35 (m, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 159.4, 141.0, 139.4, 137.2, 133.7, 130.8, 130.2, 127.9, 127.0, 125.6, 125.6, 114.3, 55.5, 20.3, 0.4.

HRMS (EI): *m*/*z* calcd for $C_{19}H_{24}OSi$: 296.1596; found: 296.1596.

Cobalt-Catalysed Diels–Alder Reaction for the Synthesis of 10 (R = *n*-Pr); 1 mmol Scale

Anhydrous ZnI_2 (64 mg, 0.20 mmol, 20 mol%), Zn powder (13 mg, 0.20 mmol, 20 mol%), and $CoBr_2$(dppe) (62 mg, 0.10 mmol, 10 mol%) were suspended in anhydrous CH_2Cl_2 (1 mL) under an argon atmosphere in a flame-dried Schlenk tube fitted with a Teflon screw cap. Then, **5** (186 mg, 1.00 mmol) and 1-trimethylsilyl-1-pentyne (182 mg, 1.30 mmol) were added and the mixture was stirred at r.t. until no further reaction progress was monitored by GC/MS (24 h). The reaction mixture was filtered through a small pad of silica gel (pentane–Et_2O, 10:1), and the solvent was removed under reduced pressure. The residual dihydroaromatic intermediate was oxidized with DDQ (250 mg, 1.10 mmol, 1.1 equiv) in toluene. After 1 h at r.t., the mixture was filtered through a short pad of deactivated silica gel (pentane–Et_2O, 10:1), and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography on silica gel (pentane–Et_2O, 10:1). The product **10** (R = *n*-Pr) was obtained as a colourless oil; yield: 33 mg (0.10 mmol, 10%).

IR (film): 3050, 2955, 2872, 2835, 1604, 1574, 1508, 1460, 1411, 1298, 1245, 1173, 1140, 1109, 1034, 960, 902, 830, 754, 724, 684, 620, 533, 393 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.62 (dd, *J* = 7.7, 1.0 Hz, 1 H), 7.50–7.44 (m, 2 H), 7.42 (dd, *J* = 7.4, 1.3 Hz, 1 H), 7.28 (d, *J* = 16.1 Hz, 1 H), 7.22 (t, *J* = 7.6 Hz, 1 H), 6.98–6.90 (m, 3 H), 3.85 (s, 3 H), 2.92–2.72 (m, 2 H), 1.68–1.47 (m, 2 H), 1.06 (t, *J* = 7.3 Hz, 3 H), 0.37–0.35 (m, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.4, 146.3, 138.9, 136.5, 134.2, 130.9, 129.8, 127.8, 127.3, 125.8, 125.3, 114.3, 55.5, 36.6, 25.3, 14.7, 0.91.

HRMS (EI): *m*/*z* calcd for $C_{21}H_{28}OSi$: 324.1909; found: 324.1913.

References

(1) For reviews, see: (a) Broere, D. L. J.; Ruijter, E. *Synthesis* **2012**, *44*, 2639. (b) Shibata, Y.; Tanaka, K. *Synthesis* **2012**, *44*, 323. (c) Dominguez, G.; Perez-Castells, J. *Chem. Soc. Rev.* **2011**, *40*, 3430. (d) Hua, R.; Abrenica, M. V. A.; Wang, P. *Curr. Org. Chem.* **2011**, *5*, 712. (e) Shaaban, M. R.; El-Sayed, R.; Elwahy, A. H. M. *Tetrahedron* **2011**, *67*, 6095. (f) Pla-Quintana, A.; Roglans, A. *Molecules* **2010**, *15*, 9230. (g) Inglesby, P. A.; Evans, P. A. *Chem. Soc. Rev.* **2010**, *39*, 2791. (h) Galan, B. R.; Rovis, T. *Angew. Chem. Int. Ed.* **2009**, *48*, 2830. (i) Tanaka, K. *Chem. Asian J.* **2009**, *4*, 508. (j) Shibata, T.; Tsuchikama, K. *Org. Biomol. Chem.* **2008**, *6*, 1317. (k) Agenet, N.; Busine, O.; Slowinski, F.; Gandon, V.; Aubert, C.; Malacria, M. *Org. React.* **2007**, *68*, 1. (l) Gandon, V.; Aubert, C.; Malacria, M. *Chem. Commun.* **2006**, 2209. (m) Chopade, P. R.; Louie, J. *Adv. Synth. Catal.* **2006**, *348*, 2307.

(2) (a) Pellissier, H.; Clavier, H. *Chem. Rev.* **2014**, *114*, 2775. (b) Aitken, D. J.; Eijsberg, H.; Frongia, A.; Ollivier, J.; Piras, P. P. *Synthesis* **2014**, *46*, 1. (c) Lee, H.-W.; Kwong, F.-Y. *Eur. J. Org. Chem.* **2010**, 789. (d) Laschat, S.; Becheanu, A.; Bell, T.; Baro, A. *Synlett* **2005**, 2547. (e) Blanco-Urgoiti, J.; Añorbe, L.; Pérez-Serrano, L.; Domínguez, G.; Pérez-Castells, J. *Chem. Soc. Rev.* **2004**, *33*, 32.

(3) (a) Nishibayashi, Y. *Synthesis* **2012**, *44*, 489. (b) Miyake, Y.; Uemura, S.; Nishibayashi, Y. *ChemCatChem* **2009**, *1*, 342. (c) Omae, I. *Appl. Organomet. Chem.* **2007**, *21*, 318. (d) Diaz, D. D.; Betancort, J. M.; Martin, V. S. *Synlett* **2007**, 343.

(4) Leading references: (a) Fiebig, L.; Kuttner, J.; Hilt, G.; Schwarzer, M.; Frenking, G.; Schmalz, H.-G.; Schäfer, M. *J. Org. Chem.* **2013**, *78*, 10485. (b) Erver, F.; Kuttner, J. R.; Hilt, G. *J. Org. Chem.* **2012**, *77*, 8375. (c) Arndt, M.; Hilt, G.; Khlebnikov, A. F.; Kozhushkov, S. I.; de Meijere, A. *Eur. J. Org. Chem.* **2012**, 3112. (d) Hilt, G.; Janikowski, J. *Org. Lett.* **2009**, *11*, 773.

(5) (a) Erver, F.; Hilt, G. *J. Org. Chem.* **2012**, *77*, 5216. (b) Hilt, G.; Erver, F.; Harms, K. *Org. Lett.* **2011**, *13*, 304. (c) Hilt, G.; Paul, A.; Treutwein, J. *Org. Lett.* **2010**, *12*, 1536. (d) Hilt, G.; Treutwein, J. *Angew. Chem. Int. Ed.* **2007**, *46*, 8500.

(6) (a) Wang, C.-C.; Lin, P.-S.; Cheng, C.-H. *J. Am. Chem. Soc.* **2002**, *124*, 9696. (b) Chang, H.-T.; Jayanth, T. T.; Wang, C.-C.; Cheng, C.-H. *J. Am. Chem. Soc.* **2007**, *129*, 12032.

(7) (a) Timsina, Y. N.; Biswas, S.; RajanBabu, T. V. *J. Am. Chem. Soc.* **2014**, *136*, 6215. (b) Schmidt A.; Hilt, G. *Chem. Asian J.* **2014**, in press; DOI: 10.1002/asia.201402323. (c) Clark, J. R.; Griffith, J. R.; Diver, S. T. *J. Am. Chem. Soc.* **2013**, *135*, 3327. (d) Pünner, F.; Schmidt, A.; Hilt, G. *Angew. Chem. Int. Ed.* **2012**, *51*, 1270.

(8) (a) Hilt, G. *Eur. J. Org. Chem.* **2012**, 4441. (b) Kersten, L.; Hilt, G. *Adv. Synth. Catal.* **2012**, *354*, 863.

(9) (a) Arndt, M.; Dindaroğlu, M.; Schmalz, H.-G.; Hilt, G. *Synthesis* **2012**, *44*, 3534. (b) Arndt, M.; Dindaroğlu, M.; Schmalz, H.-G.; Hilt, G. *Org. Lett.* **2011**, *13*, 6236. (c) Erver, F.; Hilt, G. *Org. Lett.* **2011**, *13*, 5700.

(10) Hilt, G.; Roesner, S. *Synthesis* **2011**, 662.

(11) Schmidt, A.; Hilt, G. *Org. Lett.* **2013**, *15*, 2708.

(12) Hilt, G.; Danz, M. *Synthesis* **2008**, 2257.