Regioselective Cobalt-Catalyzed Diels–Alder Reaction towards 1,3-Disubstituted and 1,2,3-Trisubstituted Benzene Derivatives

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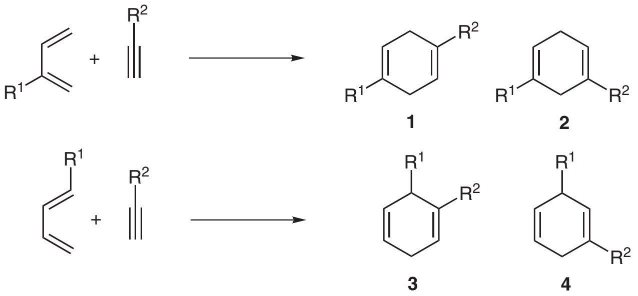
Dedicated to Prof. Dr. Reinhard W. Hoffmann on the occasion of his 75th birthday

Abstract: A straightforward reaction sequence consisting of the Wittig olefination of aldehydes utilizing allyltriphenylphosphonium bromide for the generation of 1-substituted 1,3-dienes, cobalt-catalyzed neutral Diels–Alder reaction with terminal and internal alkynes, and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation of the dihydroaromatic intermediates leads to regiochemically enriched biphenyl, terphenyl, and silyl-functionalized benzene derivatives in good to excellent yields. Starting from a 1,3-diyne and a 1,3-diene, the reaction sequence consisting of cobalt-catalyzed Diels–Alder reaction, DDQ oxidation, and cobalt-catalyzed cyclotrimerization with acetylene gave an axially chiral biphenyl-terphenyl product.

Key words: alkyne, cobalt, Diels–Alder, diene, Wittig olefination

The classical Diels–Alder reaction of unsymmetrical starting materials under thermal conditions gives regioisomers and the regioselectivity of this reaction is controlled by orbital coefficients.[1] The observation of regiochemical preferences in the thermal Diels–Alder reaction is now known as the *ortho*/*para* rule, meaning that the formation of the *meta* products **2** and **4** is unlikely and that the corresponding *para* products of type **1** or *ortho* products of type **3** are formed predominantly (Scheme 1).[2]

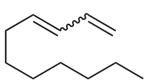
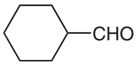
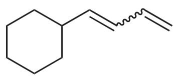
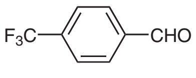
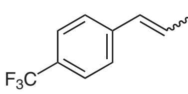
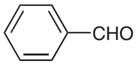
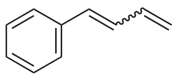
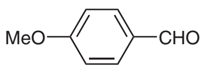
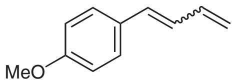


Scheme 1 Regiochemistry of the thermal Diels–Alder reaction

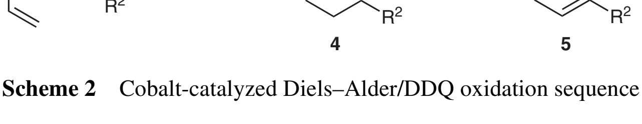
Only recently we were able to describe a simple cobalt catalyst system for the first regioselective formation of the *meta*-substituted products **2** by applying pyridine imine ligands.[3] The results for the alternative approach towards *meta*-substituted Diels–Alder adducts of type **4** generated in the cobalt-catalyzed reaction of a 1-substituted 1,3-diene and a terminal alkyne are described herein.

To this end, a representative selection of 1-substituted 1,3-dienes were synthesized utilizing the Wittig olefination of aldehydes with allyltriphenylphosphonium bromide. The Wittig olefination reactions were performed on a 10–15 mmol scale to give the required 1-substituted 1,3-dienes in reasonable quantities as an *E*/*Z* mixture. The results of the olefination reaction are summarized in Table 1.

Table 1 Results of the Wittig Olefination of Aldehydes with Allyltriphenylphosphonium Bromide

Entry	Aldehyde	Product	Yield (%)
1	n-$H_{15}C_7CHO$		61
2			31
3			63
4			55
5			86

The cobalt-catalyzed Diels–Alder reaction with terminal alkynes was then investigated applying the previously described dibromo[1,2-bis(diphenylphosphino)ethane]cobalt(II) [$CoBr_2$(dppe)] complex as catalyst precursor.[4] The transformation turned out to be highly regioselective and the desired *meta*-substituted aromatic products of type **5** were isolated after 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) oxidation of the dihydroaromatic intermediates **4** (Scheme 2). The results of the reactions are summarized in Table 2.



Scheme 2 Cobalt-catalyzed Diels–Alder/DDQ oxidation sequence

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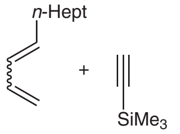
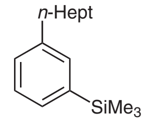
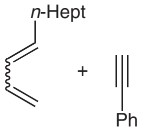
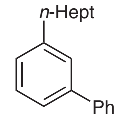
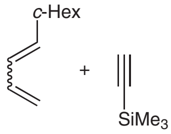
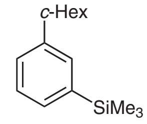
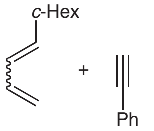
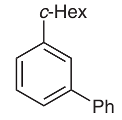
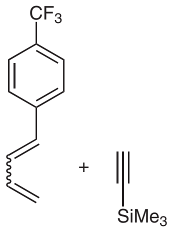
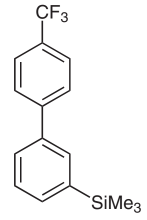
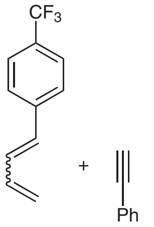
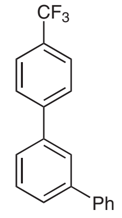
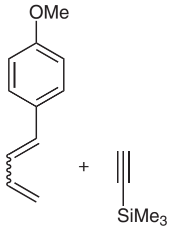
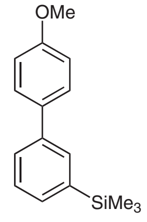
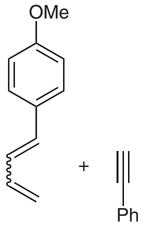
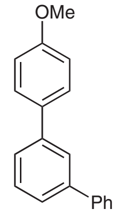
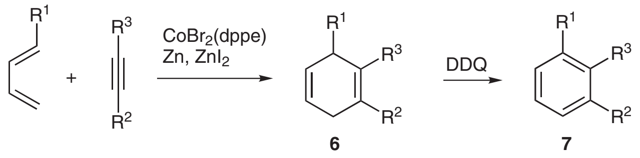
Table 2 Results of the Cobalt-Catalyzed Diels–Alder Reaction Utilizing Terminal Alkynes

Entry	1,3-Diene + alkyne	Product **5**	Yield (%)	Ratio *meta*/*ortho*
1		 **5a**	83	97:3
2		 **5b**	64	81:19
3		 **5c**	93	>99:1
4		 **5d**	56	98:2
5		 **5e**	93	>99:1
6		 **5f**	65	98:2
7		 **5g**	87	>99:1
8		 **5h**	75	98:2

As representative substrates, primary and secondary alkyl-substituted 1,3-dienes such as undeca-1,3-diene and 1-cyclohexylbuta-1,3-diene were chosen. In terms of aryl-substituted 1,3-diene substrates bearing an electron-withdrawing group (CF_3) as well as an electron-donating substituent (OMe) were selected. The results summarized in Table 2 show that the yields for the transformation with (trimethylsilyl)acetylene were in all cases better than in reactions with phenylacetylene. Nevertheless, good to excellent yields were obtained in all examples. The regioselectivities were very high in almost all cases, indicating that the regioselectivity of the reaction is mainly governed by the steric bulk of the substituents.

It seems that electronic effects do not play an important role since the different electronic nature of the substituents of the aryl-substituted 1,3-dienes had little effect on the regioselectivity. Comparable yields were obtained for these transformations (cf. Table 2, entries 5–8). The reaction sequence led to interesting silyl-functionalized products as well as functionalized terphenyl derivatives.

Further investigation on the application of internal alkynes led to the generation of 1,2,3-trisubstituted benzenes following the transformation outlined in Scheme 3. As unsymmetrical internal alkynes 1-(trimethylsilyl)prop-1-yne as well as 1-phenylprop-1-yne were chosen to investigate the regioselectivity when the steric bulk of the alkyne was increased.



Scheme 3 Synthesis of trisubstituted arenes

As before, the dihydroaromatic intermediates **6** were oxidized by DDQ to obtain the corresponding aromatic products **7** to simplify the characterization of the products. The results of these transformations are summarized in Table 3.

Table 3 Results of the Cobalt-Catalyzed Diels–Alder Reaction Utilizing Internal Alkynes

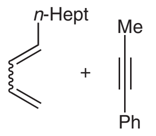
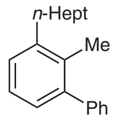
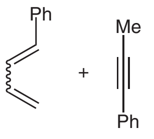
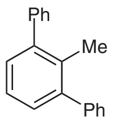
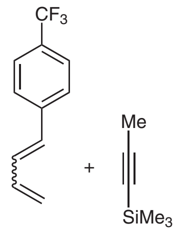
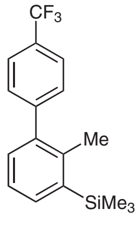
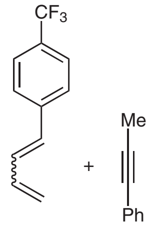
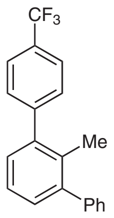
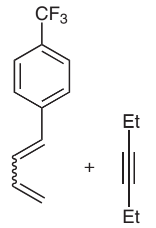
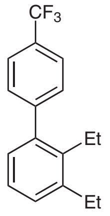
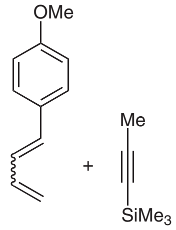
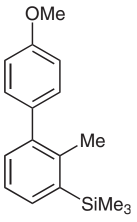
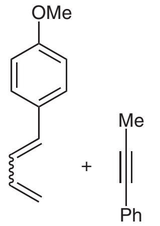
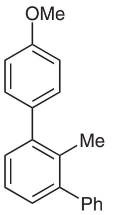
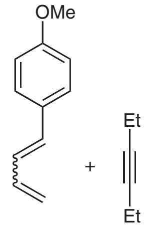
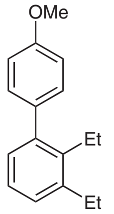
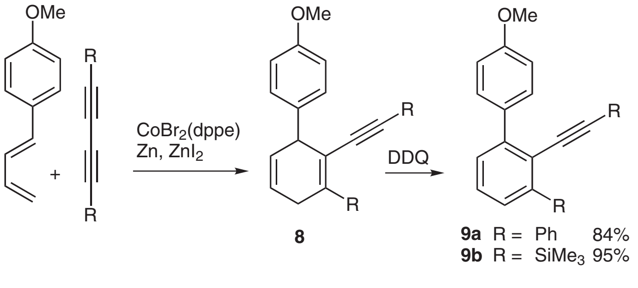
Entry	1,3-Diene + alkyne	Product **7**	Yield (%)	Ratio *meta*/*ortho*
1		 **7a**	56	21:79
2		 **7b**	71	48:52

Table 3 Results of the Cobalt-Catalyzed Diels–Alder Reaction Utilizing Internal Alkynes (continued)

Entry	1,3-Diene + alkyne	Product **7**	Yield (%)	Ratio *meta*/*ortho*
3		 **7c**	72	98:2
4		 **7d**	62	57:43
5		 **7e**	56	
6		 **7f**	72	98:2
7		 **7g**	65	53:47
8		 **7h**	51	

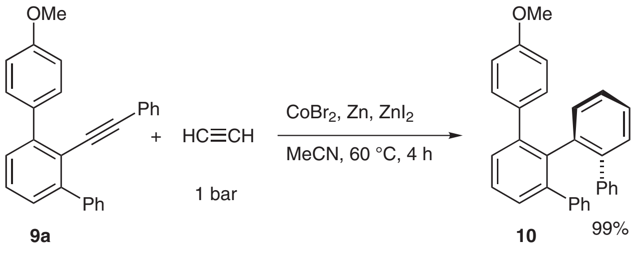
Unlike the earlier results with terminal alkynes, a significant difference between the phenyl and the trimethylsilyl-substituted alkyne could now be observed. While the yields for all transformations were somewhat reduced, the regioselectivities for the silyl-functionalized alkyne were still excellent. On the other hand, the application of 1-phenylprop-1-yne gave mixtures of products close to a 1:1 ratio in all cases with the two aryl groups in a 1,3- (here assigned as the *meta* product) and a 1,2-relation (*ortho* product) to each other. Accordingly, the regioselective cobalt-catalyzed Diels–Alder reaction with internal alkynes is limited with respect to 1-arylalk-1-ynes while 1-silylalk-1-ynes are broadly applicable.

We then turned our attention to the application of 1,3-diynes as substrates.[4b] Although we suspected that the regioselectivity for the phenyl-substituted diyne would be as low as in the previous set of experiments, we were delighted to find that in this reaction product **9a** could be obtained in 84% yield as a single regioisomer (Scheme 4). Obviously the diyne moiety has a positive effect on the regioselectivity based not only on steric demand, but also because of electronic effects. The results for the silyl-functionalized 1,3-diyne were even better, giving the desired product **9b** in an excellent 95% yield as a single regioisomer.



Scheme 4 Application of diynes in cobalt-catalyzed Diels–Alder reactions

In the past we have also investigated the use of simple cobalt catalysts in alkyne cyclotrimerization reactions.[5] In this context **9a** caught our attention, because the conversion of this highly substituted internal diarylacetylene **9a** with acetylene under mild reaction conditions at atmospheric pressure would not only transform the internal alkyne selectively into a 1,2-substituted benzene ring, but also give rise to an axially chiral product (Scheme 5). Therefore, we attempted the conversion of **9a** as a test substrate into the racemic product **10** utilizing a catalyst system consisting of 10 mol% cobalt(II) bromide, 30 mol% zinc powder, and 30 mol% zinc(II) iodide in acetonitrile at elevated temperatures.



Scheme 5 Cobalt-catalyzed cyclotrimerization utilizing acetylene

The transformation to the biphenyl-terphenyl derivative **10** was complete within four hours and a single product was isolated in almost quantitative yield. Accordingly, approaches towards chiral derivatives of this type with functional groups replacing the phenyl groups on the diyne substrate (R ≠ Ph, Scheme 4) can be envisaged utilizing chiral ligands such as Norphos [1,2-bis(diphenylphoshino)bicyclo[2.2.1]hept-5-ene] in the cyclotrimerization reaction with acetylene. These investigations are currently in progress in our laboratory.

In conclusion we have presented a facile synthesis of regioselectively substituted 1,3-di- and 1,2,3-trisubstituted benzene derivatives in a short reaction sequence. Interesting silyl-functionalized benzene and biphenyl products as well as regiochemically enriched terphenyl products are accessible. The application of internal alkynes gave excellent results utilizing silyl-functionalized alkynes and the application of 1,3-diynes in combination with a cobalt-catalyzed cyclotrimerization using acetylene under atmospheric pressure gave a very interesting chiral biphenyl-terphenyl product.

NMR spectra were recorded on a 300 MHz instrument. Electron impact mass (EI) spectra were recorded on a Varian MAT CH 7A. High resolution mass spectra were recorded on a Finnigan MAT95Q instrument. GC and GCMS were recorded on Hewlett Packard 5890 and on an Agilent 6890N gaschromatograph with a mass detector Agilent 5973. IR data were recorded on a Bruker IFS 88 interferometer as a film or a KBr pellet. All reagents were of commercial quality, zinc iodide was dried in vacuo at 150 °C before use.

1,3-Dienes by Wittig Olefination; General Procedure

Allyltriphenylphosphonium bromide (1.2 equiv) and *t*-BuOK were suspended in THF at 0 °C. After 15 min the aldehyde (1.0 equiv) was added and the reaction was monitored by TLC control. The reaction was quenched by addition of sat. aq NH_4Cl and extracted with MTBE (3 ×). The organic phases were dried ($MgSO_4$), the solvent was removed from the residue, and the residue was purified by column chromatography (silica gel, pentane–MTBE mixtures).

1,3-Disubstituted and 1,2,3-Trisubstituted Benzene Derivatives by the Diels–Alder Reaction; General Procedure

A suspension of $CoBr_2$(dppe) (10 mol%), Zn powder (10 mol%), and ZnI_2 (20 mol%) in CH_2Cl_2 (0.5 mL) was charged with the 1,3-diene (1.2 mmol) and the alkyne (1 mmol). After complete conversion (up to 2 d), the mixture was filtered through a small pad of silica gel (MTBE), the solvent was removed and the residual dihydroaromatic intermediate was oxidized with DDQ (1.1 equiv) in benzene or toluene (10–20 mL) to give the corresponding aromatic product. The solvent was removed and the residue was purified by column chromatography (silica gel). The ratios of regioisomers were determined by integration of GC/GC-MS and ^{1}H NMR signals.

1-Heptyl-3-(trimethylsilyl)benzene (5a)

Light yellow oil; yield: 83%; R_f = 0.46 (pentane). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 0.31 (*meta*) and 0.38 (*ortho*).

IR: 2956, 2927, 2856, 1466, 1405, 1248, 1122 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.37 (m, 2 H), 7.32 (t, *J* = 7.3 Hz, 1 H), 7.24–7.20 (m, 1 H), 2.65 (t, *J* = 7.8 Hz, 2 H), 1.67 (quint, *J* = 7.3 Hz, 2 H), 1.45–1.27 (m, 8 H), 0.94 (t, *J* = 6.7 Hz, 3 H), 0.31 (s, 9 H)

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.0, 140.2, 133.3, 130.5, 128.8, 127.6, 36.1, 31.8, 31.6, 29.4, 29.1, 22.6, 14.0, –1.0.

MS (EI): *m*/*z* = 248 (M$^+$, 12), 233 (100), 161 (5), 148 (6), 131 (5), 73 (5).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{16}H_{28}Si$: 248.1960; found: 248.1957.

3-Heptyl-1,1′-biphenyl (5b)

Colorless oil; yield: 64%; R_f = 0.27 (pentane). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 2.68 (*meta*) and 2.57 (*ortho*).

IR: 2927, 2855, 1600, 1479, 1455, 1075 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63–7.58 (m, 2 H, H_{Ar}), 7.47–7.28 (m, 6 H, H_{Ar}), 7.22–7.15 (m, 1 H, H_{Ar}), 2.68 (t, *J* = 7.8 Hz, 2 H, CH_2), 1.68 (quint, *J* = 7.4 Hz, 2 H, CH_2), 1.42–1.16 (m, 8 H, CH_2), 0.93–0.83 (m, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.4, 141.4, 141.1, 128.6, 128.6, 127.3, 127.3, 127.1, 127.0, 124.4, 36.1, 31.8, 31.5, 29.3, 29.2, 22.6, 14.0.

MS (EI): *m*/*z* = 252 (M$^+$, 75), 209 (6), 181 (9), 168 (100), 152 (25).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{19}H_{24}$: 252.1878; found: 252.1879.

1-Cyclohexyl-3-(trimethylsilyl)benzene (5c)

Colorless oil; yield: 93%; R_f = 0.38 (pentane).

IR: 2925, 2851, 1448, 1408, 1247, 1115, 849, 836, 752 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.36 (m, 2 H), 7.31 (t, *J* = 7.5 Hz, 1 H), 7.23 (d, *J* = 7.7 Hz, 1 H), 2.56–2.50 (m, 1 H), 1.95–1.84 (m, 4 H), 1.78 (d, *J* = 6.8 Hz, 1 H), 1.53–1.37 (m, 4 H), 1.34–1.25 (m, 1 H), 0.30 (s, 9 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.1, 140.2, 131.9, 130.8, 127.6, 127.1, 44.7, 34.5, 26.9, 26.1, –1.0.

MS (EI): *m*/*z* = 232 (M$^+$, 10), 217 (100), 161 (5), 73 (5).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{15}H_{24}Si$: 232.1647; found: 232.1644.

3-Cyclohexyl-1,1′-biphenyl (5d)

Colorless oil; yield: 56%; R_f = 0.18 (pentane).

IR: 3057, 3031, 2924, 2850, 1599, 1478, 1447, 798, 756, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62–7.59 (m, 2 H), 7.47–7.41 (m, 4 H), 7.40–7.33 (m, 2 H), 7.20 (d, *J* = 7.5 Hz, 1 H), 2.56–2.50 (tt, *J* = 11.5, 3.3 Hz, 1 H), 1.98–1.93 (m, 2 H), 1.91–1.85 (m, 2 H), 1.81–1.76 (m, 1 H), 1.55–1.39 (m, 4 H), 1.29 (tq, *J* = 12.5, 3.4 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 148.5, 141.6, 141.2, 128.6, 128.6, 127.2, 127.0, 125.8, 125.7, 124.6, 44.7, 34.5, 26.9, 26.1.

MS (EI): *m*/*z* = 236 (M$^+$, 100), 193 (45), 180 (81), 165 (67).

HRMS (EI): *m*/*z* [M]$^+$ calcd for $C_{18}H_{20}$: 236.1565; found: 236.1560.

4-(Trifluoromethyl)-3′-(trimethylsilyl)-1,1′-biphenyl (5e)

Colorless oil; yield: 93%; R_f = 0.45 (pentane).

IR: 2957, 1617, 1327, 1250, 1166, 1126, 1072, 1016 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76–7.71 (m, 5 H), 7.62–7.58 (m, 2 H), 7.52–7.46 (m, 1 H), 0.35 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.2, 141.5, 139.2, 133.2, 132.2, 129.3 (q, *J* = 32 Hz), 128.3, 127.8, 127.6, 125.7 (q, *J* = 4 Hz), 124.4 (q, *J* = 272 Hz), –1.1.

MS (EI): *m/z* = 294 (M^+, 18), 279 (100), 263 (9), 214 (5), 165 (5), 139 (5).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{16}H_{17}F_3Si$: 294.1052; found: 294.1056.

4-(Trifluoromethyl)-1,1′:3′,1″-terphenyl (5f)

Colorless solid; yield: 65%; R_f = 0.22 (pentane). The ratio of regioisomers was determined by integration of GC signals.

IR: 2925, 1614, 1571, 1393, 1335, 1159, 1112, 1073 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85–7.82 (m, 1 H), 7.81–7.71 (m, 4 H), 7.71–7.63 (m, 3 H), 7.65–7.55 (m, 2 H), 7.55–7.46 (m, 2 H), 7.45–7.38 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.7, 142.1, 140.9, 140.3, 129.5 (q, *J* = 32 Hz), 129.4, 128.9, 127.6, 127.2, 127.0, 126.2, 126.2, 125.7 (q, *J* = 4 Hz), 124.3 (q, *J* = 272 Hz).

MS (EI): *m/z* = 298 (M^+, 100), 279 (7), 238 (6), 228 (24), 152 (14), 139 (9), 113 (7), 101 (8).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{13}F_3$: 298.0969; found: 298.0962.

4-Methoxy-3′-(trimethylsilyl)-1,1′-biphenyl (5g)

Colorless oil; yield: 87%; R_f = 0.59 (pentane–MTBE, 10:1).

IR: 2940, 1695, 1508, 1282, 1243, 1178, 1121, 1023 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.68 (m, 1 H), 7.57–7.52 (m, 3 H), 7.51–7.47 (m, 1 H), 7.45–7.39 (m, 1 H), 7.03–6.97 (m, 2 H), 3.87 (s, 3 H), 0.32 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 140.9, 140.1, 134.2, 131.7, 131.7, 128.3, 128.1, 127.4, 114.2, 55.3, –1.1.

MS (EI): *m/z* = 256 (M^+, 49), 241 (100), 225 (6), 198 (6), 181 (5), 120 (8).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{16}H_{20}OSi$: 256.1283; found: 256.1277.

4-Methoxy-1,1′:3′,1″-terphenyl (5h)

Colorless solid; yield: 75%; R_f = 0.38 (pentane–MTBE, 20:1). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 3.87 (*meta*) and 3.86 (*ortho*).

IR: 2954, 2835, 1606, 1515, 1474, 1286, 1240, 1181, 1028 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.78–7.76 (m, 1 H), 7.67–7.44 (m, 9 H), 7.40–7.34 (m, 1 H), 7.03–6.98 (m, 2 H), 3.87 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.3, 141.8, 141.4, 141.3, 133.7, 129.1, 128.8, 128.3, 127.3, 127.3, 125.7, 125.7, 125.5, 114.3, 55.4.

MS (EI): *m/z* = 260 (M^+, 100), 245 (25), 215 (18), 202 (12), 189 (6), 130 (8).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{16}O$: 260.1201; found: 260.1209.

3-Heptyl-2-methyl-1,1′-biphenyl (7a) and 2-Heptyl-6-methyl-1,1′-biphenyl (7a′)

Colorless oil; yield: 56%; R_f = 0.31 (pentane). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 2.35 (*ortho*) and 2.58 (*meta*).

***ortho*-Isomer**

IR: 3058, 2926, 2856, 1601, 1581, 1491, 1462, 1378, 1071, 1010 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.10 (m, 8 H, H_{Ar}), 2.35 (t, *J* = 7.8 Hz, 2 H, CH_2), 2.05 (s, 9 H, CH_3), 1.48–1.10 (m, 10 H, CH_2), 0.88 (t, *J* = 7.0 Hz, 3 H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.9, 140.7, 136.1, 131.4, 129.3, 128.1, 127.0, 127.0, 126.5, 126.3, 33.5, 31.6, 31.2, 29.3, 28.9, 22.6, 20.9, 14.0.

MS (EI): *m/z* = 266 (M^+, 54), 181 (100), 165 (56), 152 (6).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{20}H_{26}$: 266.2035; found: 266.2041.

2′-Methyl-1,1′:3′,1″-terphenyl (7b) and 3′-Methyl-1,1′:2′,1″-terphenyl (7b′)

Colorless oil; yield: 71%; R_f = 0.14 (pentane). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 2.20 (*ortho*) and 2.13 (*meta*).

The analytical data for the mixture are:

IR: 3056, 3023, 1600, 1574, 1496, 1460, 1441, 1426, 1071 cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.46–7.42 (m, 4 H), 7.40–7.35 (m, 6 H), 7.33 (d, *J* = 7.4 Hz, 1 H), 7.32–7.25 (m, 5 H), 7.24–7.21 (m, 2 H), 7.19–7.10 (m, 4 H,), 7.08–7.04 (m, 4 H), 2.20 (s, 3 H), 2.13 (s, 3 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 142.8, 142.4, 141.9, 141.5, 140.4, 140.2, 136.4, 132.9, 130.3, 129.8, 129.3, 129.1, 128.9, 128.0, 127.7, 127.6, 127.3, 127.1, 126.7, 126.2, 126.0, 125.2, 21.1, 18.6.

MS (EI): *m/z* = 244 (M^+, 100), 229 (79), 202 (14), 165 (15), 152 (6), 113 (9).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{19}H_{16}$: 244.1252; found: 244.1243.

2-Methyl-4′-(trifluoromethyl)-3-(trimethylsilyl)-1,1′-biphenyl (7c)

Colorless solid; yield: 72%; R_f = 0.41 (pentane). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 0.43 (*meta*) and 0.49 (*ortho*).

IR: 2965, 1614, 1326, 1247, 1157, 1127, 1106, 1070 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.1 Hz, 2 H), 7.59 (dd, *J* = 7.1, 1.6 Hz, 1 H), 7.47 (d, *J* = 8.0 Hz, 2 H), 7.34–7.23 (m, 2 H), 2.38 (s, 3 H), 0.43 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.4, 140.8, 140.4, 139.8, 134.2, 130.7, 129.7, 129.0 (q, *J* = 32 Hz), 125.1, 125.0 (q, *J* = 4 Hz), 124.4 (q, *J* = 272 Hz), 21.0, 0.1.

MS (EI): *m/z* = 308 (M^+, 34), 293 (100), 215 (53), 195 (5), 165 (20), 73 (22).

HRMS (EI): *m/z* $[M]^+$ calcd for $C_{17}H_{19}F_3Si$: 308.1208; found: 308.1203.

2-Methyl-4′-(trifluoromethyl)-1,1′:3′,1″-terphenyl (7d) and 3-Methyl-4′-(trifluoromethyl)-1,1′:2′,1″-terphenyl (7d′)

Colorless oil; yield: 62%; R_f = 0.20 (pentane). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 2.14 (*meta*) and 2.23 (*ortho*).

IR: 3059, 1618, 1403, 1326, 1165, 1068, 1019 cm^{-1}.

***meta*-Isomer 7d**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.2 Hz, 2 H), 7.55–7.15 (m, 10 H), 2.14 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.1, 143.2, 142.1, 141.5, 132.8, 129.7, 129.7, 129.3, 129.1 (q, *J* = 33 Hz) 128.2, 127.4 127.0, 125.5, 125.1 (q, *J* = 4 Hz), 124.3 (q, *J* = 272 Hz), 18.6.

***ortho*-Isomer 7d′**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.15 (m, 10 H), 7.07 (dd, *J* = 7.7, 1.8 Hz, 2 H), 2.23 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$) resolved signals: δ = 145.7, 140.4, 140.1, 139.6, 136.8, 130.2, 130.0, 129.8, 128.7, 127.9, 127.5, 126.6, 124.4 (q, *J* = 4 Hz), 124.3 (q, *J* = 272 Hz), 21.1.

MS (EI): *m/z* = 312 (M$^+$, 100), 297 (10), 281 (6), 271 (7), 243 (9), 228 (7), 165 (20), 146 (5).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{20}H_{15}F_3$: 312.1126; found: 312.1129.

2,3-Diethyl-4′-(trifluoromethyl)-1,1′-biphenyl (7e)

Colorless oil; yield: 56%; R_f = 0.34 (pentane).

IR: 2970, 2876, 1618, 1464, 1403, 1326, 1165, 1127, 1069, 1017 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.1 Hz, 2 H), 7.49 (d, *J* = 8.1 Hz, 2 H), 7.31–7.23 (m, 2 H), 7.05 (dd, *J* = 7.3, 1.5 Hz, 1 H), 2.82 (q, *J* = 7.5 Hz, 2 H), 2.64 (q, *J* = 7.5 Hz, 2 H), 1.36 (t, *J* = 7.5 Hz, 3 H), 1.05 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.7, 142.5, 141.0, 139.3, 129.6, 128.9 (q, *J* = 32 Hz), 128.4, 127.6, 125.6, 124.8 (q, *J* = 4 Hz), 124.4 (q, *J* = 272 Hz), 25.6, 22.4, 15.7, 15.4.

MS (EI): *m/z* = 278 (M$^+$, 100), 263 (48), 249 (64), 235 (67), 215 (15), 178 (22), 165 (42).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{17}H_{17}F_3$: 278.1282; found: 278.1278.

4-Methoxy-2′-methyl-3′-(trimethylsilyl)-1,1′-biphenyl (7f)

Colorless solid; yield: 72%; R_f = 0.50 (pentane–MTBE, 10:1). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 0.41 (*meta*) and 0.34 (*ortho*).

IR: 3055, 2954, 2834, 1610, 1513, 1458, 1283, 1246, 1176, 1036 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.54–7.49 (m, 1 H), 7.30–7.25 (m, 4 H), 7.02–6.97 (m, 2 H), 3.90 (s, 3 H), 2.39 (s, 3 H), 0.41 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 141.8, 140.9, 139.3, 135.0, 133.4, 131.2, 124.9, 113.5, 55.3, 21.1, 0.2.

MS (EI): *m/z* = 270 (M$^+$, 99), 255 (65), 240 (100), 195 (17), 181 (9), 165 (34), 152 (18), 127 (17), 73 (22).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{17}H_{22}OSi$: 270.1440; found: 270.1435.

4-Methoxy-2′-methyl-1,1′:3′,1″-terphenyl (7g) and 4-Methoxy-3′-methyl-1,1′:2′,1″-terphenyl (7g′)

Colorless oil; yield: 65%; R_f = 0.41 (pentane–MTBE, 20:1). The ratio of isomers was determined by integration of ^{1}H NMR signals: δ = 2.20 (*meta*) and 2.16 (*ortho*).

IR: 3056, 2955, 2834, 1610, 1514, 1462, 1290, 1247, 1178, 1034 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48–7.19 (m, 16 H), 7.10–7.06 (m, 2 H), 7.03–6.97 (m, 4 H), 6.73–6.67 (m, 2 H), 3.89 (s, 3 H), 3.75 (s, 3 H), 2.20 (s, 3 H), 2.16 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.5, 157.9, 142.9, 142.5, 142.5, 141.1, 140.5, 136.5, 134.8, 134.4, 133.1, 131.6, 130.8, 130.4, 130.4, 129.3, 129.1, 128.8, 128.7, 128.0, 127.7, 127.6, 127.1, 126.7, 126.2, 125.3, 113.5, 112.9, 55.3, 55.0, 21.2, 18.7.

MS (EI): *m/z* = 274 (M$^+$, 100), 259 (14), 244 (10), 228 (10), 215 (34), 202 (9), 189 (8).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{20}H_{18}O$: 274.1358; found: 274.1348.

2,3-Diethyl-4′-methoxy-1,1′-biphenyl (7h)

Colorless oil; yield: 51%; R_f = 0.36 (pentane–MTBE, 20:1).

IR: 2966, 2933, 2874, 2834, 1610, 1513, 1463, 1289, 1245, 1176, 1043, 1027 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.26–7.14 (m, 4 H), 7.03 (dd, *J* = 6.9, 2.0 Hz, 1 H), 6.97–6.92 (m, 2 H), 3.86 (s, 3 H), 2.75 (q, *J* = 7.5 Hz, 2 H), 2.62 (q, *J* = 7.5 Hz, 2 H), 1.30 (t, *J* = 7.5 Hz, 3 H), 1.00 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.4, 142.2, 142.1, 139.8, 135.3, 130.2, 128.1, 127.6, 125.4, 113.2, 55.2, 25.7, 22.4, 15.7, 15.4.

MS (EI): *m/z* = 240 (M$^+$, 100), 225 (38), 211 (15), 196 (43), 181 (20), 165 (28), 152 (21), 139 (6), 128 (5), 115 (9).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{17}H_{20}O$: 240.1514; found: 240.1516.

4-Methoxy-2′-(phenylethynyl)-1,1′:3′,1″-terphenyl (9a)

Colorless solid; yield: 84%; R_f = 0.42 (pentane–MTBE, 20:1).

IR: 3056, 2834, 1609, 1513, 1456, 1248, 1177, 1030, 835, 803, 759, 732, 700 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.64 (m, 4 H), 7.51–7.36 (m, 6 H), 7.23–7.19 (m, 3 H), 7.07–7.01 (m, 4 H), 3.90 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.1, 145.0, 144.4, 141.1, 133.5, 131.0, 130.8, 129.6, 128.3, 128.1, 128.1, 128.0, 127.8, 127.7, 127.3, 123.6, 120.1, 113.2, 95.7, 89.1, 55.3.

MS (EI): *m/z* = 360 (M$^+$, 100), 344 (18), 329 (80), 313 (34), 283 (59), 268 (24), 252 (21), 239 (61), 156 (28), 143 (15).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{27}H_{20}O$: 360.1514; found: 360.1513.

4-Methoxy-3′-(trimethylsilyl)-2′-[(trimethylsilyl)ethynyl]-1,1′-biphenyl (9b)

Colorless solid; yield: 95%; R_f = 0.58 (pentane–MTBE, 10:1).

IR: 2957, 2898, 2834, 2148, 1610, 1514, 1290, 1251, 1177, 1147, 1027 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.57–7.53 (m, 2 H), 7.45 (dd, *J* = 5.8, 2.9 Hz, 1 H), 7.37–7.32 (m, 2 H), 6.97–6.92 (m, 2 H), 3.86 (s, 3 H), 0.42 (s, 9 H), 0.15 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 159.0, 144.4, 143.6, 133.3, 132.4, 130.8, 130.0, 127.6, 126.3, 113.0, 106.1, 101.2, 55.3, –0.6, –0.9.

MS (EI): *m/z* = 352 (M$^+$, 53), 337 (10), 321 (17), 264 (13), 249 (55), 225 (17), 205 (10), 189 (6), 73 (100).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{21}H_{28}OSi_2$: 352.1679; found: 352.1667.

4-Methoxy-3′-phenyl-1,1′:2′,1″:2″,1‴-quaterphenyl (10)

A suspension of $CoBr_2$ (10 mol%), Zn powder (10 mol%), and ZnI_2 (20 mol%) in MeCN (1.5 mL) under an atmosphere of acetylene (1 bar) was charged with **9a** (0.2 mmol) and then heated to 60 °C. After 4 h the mixture was purified by column chromatography (pentane) to give **10** as a colorless solid; yield: 99%; R_f = 0.48 (pentane–MTBE, 20:1).

IR: 3050, 2918, 1610, 1514, 1455, 1248, 1177, 809, 752, 697 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41 (dd, *J* = 8.5, 6.9 Hz, 1 H), 7.30–7.26 (m, 2 H), 7.20–6.96 (m, 10 H), 6.86–6.81 (m, 2 H), 6.76 (dt, *J* = 8.9, 2.6 Hz, 2 H), 6.73–6.68 (m, 2 H), 6.61 (dt, *J* = 8.8, 2.5 Hz, 2 H), 3.76 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.9, 141.9, 141.7, 141.4, 141.1, 140.8, 137.8, 137.6, 134.1, 133.3, 130.6, 129.7, 129.6, 129.5, 129.3, 128.8, 127.5, 127.4, 127.3, 127.1, 126.3, 126.0, 125.9, 112.8, 55.1.

MS (EI): *m/z* = 412 (M$^+$, 100), 365 (4), 302 (8), 289 (10).

HRMS (EI): *m/z* [M]$^+$ calcd for $C_{31}H_{24}O$: 412.1827; found: 412.1828.

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