Zinc-Mediated Regiodiverse Synthesis of Vinyl Bromide Derivatives and Their in situ Palladium-Catalysed Cross-Coupling Reactions

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Dedicated to Prof. Dr. Reinhard W. Hoffmann on the occasion of his 80th birthday. Many thanks for the fruitful and entertaining discussions.

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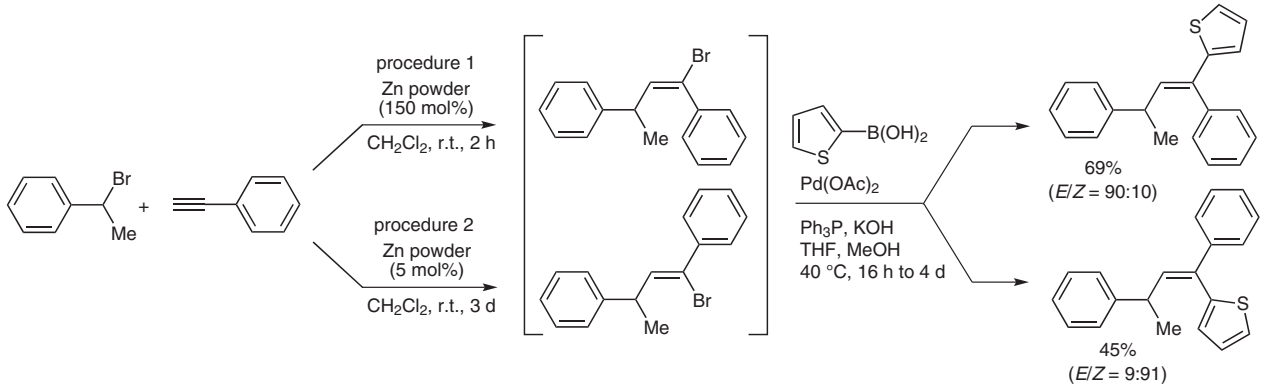
Abstract: The synthesis of vinyl bromide derivatives was realised by a zinc-mediated addition of a benzylic bromide to a terminal alkyne. The geometry of the C=C bond is dependent on the amount of zinc powder applied. When 5 mol% of Zn is used, the *Z*-configured vinyl bromide is generated while with 150 mol% the *E*-geometry is obtained predominantly. In a three-component one-pot reaction, the in situ generated vinyl bromides were reacted further in a palladium-catalysed Suzuki cross-coupling reaction utilizing aromatic boronic acids to obtain trisubstituted double bonds in good overall yields. The reactions were conducted on a 5–20 mmol scale to visualise that the reactions are also capable of generating larger amounts of products.

Key words: alkynes, cross coupling, palladium, vinyl bromides, zinc



Scheme 1 Zinc-mediated regiodiverse synthesis of vinyl bromide derivatives followed by a Suzuki cross-coupling reaction

The synthesis of double bonds has been a key issue in organic synthesis for a long time and many excellent examples are known to generate double bonds regio- and stereoselectively.[1] One general example for such a transformation is the regioselective addition of organometallic species to triple bonds to generate vinylic organometallic intermediates, which can be utilised for a number of follow-up transformations.[2] For the synthesis of vinyl bromides such vinylic organometallic intermediates are generated in stoichiometric amounts and mostly have to be quenched with bromine or other sources of the halide atom.[3]

Recently, we reported a stereodiverse method for the synthesis of vinyl bromide derivatives from an alkyne and a benzyl bromide addressing both double bond geometries (Scheme 1).[4] The selectivity of the reactions depended greatly on the amount of zinc powder added acting as initiator for the transformation. The initial reaction conditions for the formation of the *E*-isomer **3** on a 1.0 mmol scale were: alkyne **1** 1.0 mmol, benzyl bromide **2** 1.5 mmol, Zn powder 150 mol% in dichloromethane at ambient temperature (Scheme 2). Utilizing this protocol, product **3** could be isolated in 95% yield and the ratio of the stereoisomer **3** and **4** were in the range of *E*/*Z* = 87:13 (Scheme 2). On the other hand, the *Z*-isomer **4** was generated as the major stereoisomer (70%, *E*/*Z* = 7:93) when the reaction conditions were altered in the way that zinc powder was applied in 5 mol% keeping the other reaction conditions unchanged.

The rational for the change of stereoselectivity is believed to be HBr as the accompanying side-product formed from **2** and zinc powder leading to the isomerisation of the intermediate. When an excess of 150 mmol% of zinc powder is applied, the HBr is quenched and no isomerisation can take place.

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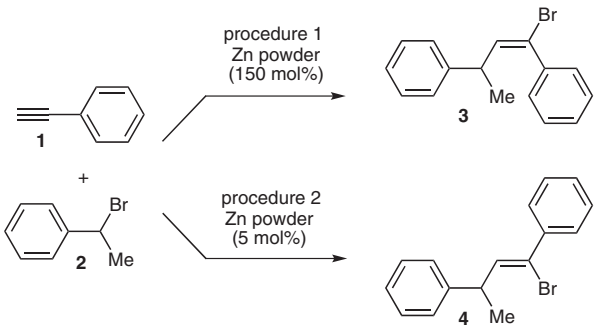


Scheme 2 Stereodiverse synthesis of the *E*-vinyl bromide **3** and the corresponding *Z*-isomer **4** by altering the amount of Zn powder

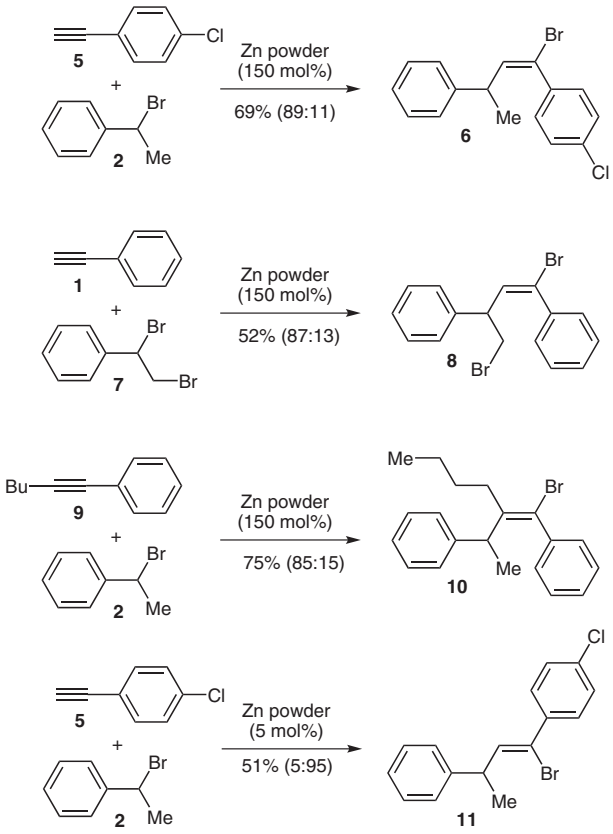
Starting from the initial reaction conditions and having achieved good yields and selectivities, the scale for the formation of **3** was increased successively (see Table 1). At the beginning, we were expecting an exothermic reaction when applying 150 mol% zinc powder on a larger scale, but until the end of this series of experiments, eventually ending with a 20 mmol scale reaction, the conversions led only to a moderate evolution of heat, which could be easily controlled with an ice bath, if necessary. The reduction of the excess zinc powder was not advisable. The in situ generated HBr, responsible for the isomerisation of the double bond geometry for the synthesis of **4**, can only be efficiently quenched with the excess of zinc powder applied. Also, the upscaling of the reaction for the synthesis of **3** utilizing 1.5 equivalents of **2** on a 10 mmol scale led to an increasing amount of the Wurtz coupling product from **2** resulting in an increasingly tedious work-up. However, when the excess of **2** was reduced to 1.2 equivalents, the amount of accompanying Wurtz coupling product was largely reduced. On a 10 mmol scale the desired product **3** could be isolated in 81% yield and the *E*/*Z* ratio was still in an acceptable range of 88:12. When the scale was doubled to 20 mmol **3** was still obtained in 79% with an *E*/*Z* ratio of 88:12. At this scope it was also possible to obtain **3** after distillative purification from the crude product in 78% yield with *E*/*Z* = 86:14.

Table 1 Upscaling of the Synthesis of **3** and **4** According to Scheme 2

Scale	Yield (%) **3** (*E*/*Z*)	Yield (%) **4** (*E*/*Z*)
1 mmol	95 (87:13)	70 (7:93)
2 mmol	90 (86:14)	65 (9:91)
5 mmol	96 (88:12)	58 (9:91)
10 mmol	87 (86:14)	69 (12:88)
10 mmol[a]	81 (88:12)[a]	76 (56:44)[a]
20 mmol	79 (88:12)[a]	62 (11:89)

[a] Reduced excess of **2** (1.2 equiv).

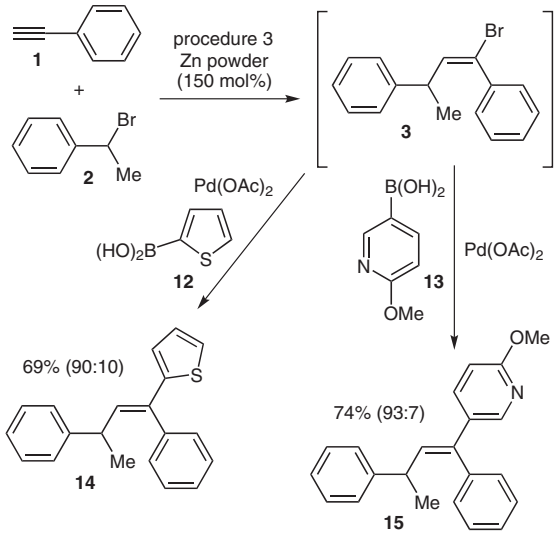
For the synthesis of **4**, 5 mol% of zinc powder were applied (Scheme 2). On a 10 mmol scale **4** could be generated in 69% yield (*E*/*Z* = 12:88). The yield only dropped slightly to 62%, with remaining good *E*/*Z* selectivity of 11:89, when the reaction was performed on a 20 mmol scale but the result is still acceptable yielding as much as 3.6 g of **4**. The reduction of the excess of **2** from 1.5 to 1.2 equivalents led to a 56:44 mixture of **3** and **4** on a 10 mmol scale, indicating that this process is only applicable for the *E*-isomer. For other substrates the maximum scale of the conversions were reduced to 10 mmol mostly for economic reasons. Nevertheless, three parameters were altered in the substrate to evaluate the feasibility of the reaction when modifications of **2** and **3** were applied (Scheme 3). The use of 1-chloro-4-ethynylbenzene (**5**) under the reaction conditions led to **6** in acceptable yield of 69% and a good *E*/*Z* ratio of 89:11. More complex benzylic halides, such as **7** could also be applied. For this dibromo derivative only the benzylic halide reacts leaving the alkyl bromide untouched. The application of (1,2-dibromoethyl)benzene (**7**) generated **8** in 52% yield in a good *E*/*Z* ratio of 87:13, but required a longer reaction time of 48 hours and warming to 40 °C. The reduced yield can be attributed to an E1cB-type elimination of the in situ generated benzylic zinc organic species. Accordingly, the yield of 52% for the synthesis of **8** is quite remarkable. In addition internal alkyne **9** could be used with more suc-



Scheme 3 Synthesis of *E*-configured vinyl bromides **6**, **8**, and **10** and the *Z*-configured vinyl bromide **11**

cess yielding product **10** in 75% (*E*/*Z* = 85:15) with no changes in the reaction conditions. The synthesis of the *Z*-configured vinyl bromide **11** was realised utilizing the reaction conditions applying only 5 mol% of zinc powder in acceptable yield and with a good *E*/*Z* ratio of 5:95.

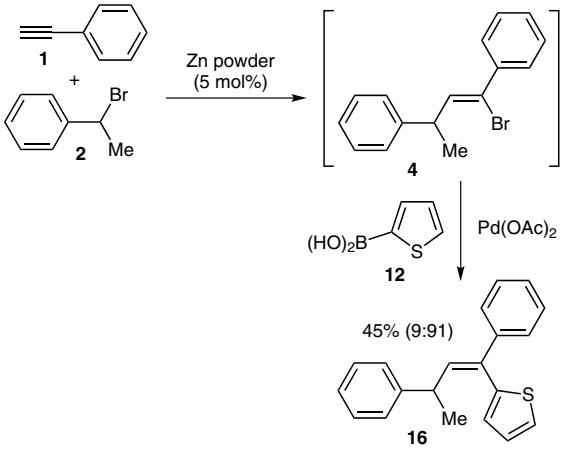
The vinyl bromides generated by the herein discussed protocol can be modified directly applying palladium-based Suzuki cross-coupling conditions.[5] Therefore, the formation of the intermediates was monitored by TLC and GCMS analysis and after completion of the reaction, the intermediates of type **3** were directly converted with boronic acids such as **12** and **13** to the corresponding trisubstituted alkene derivatives **14** and **15** (Scheme 4).



Scheme 4 Zinc-mediated synthesis of *E*-configured vinyl bromides and their Suzuki cross-coupling with boronic acids

These three-component one-pot reactions were performed on a 5 mmol scale and product **14** was obtained in 69% yield as a mixture (*E*/*Z* = 90:10). The increased *E*/*Z* selectivity can be rationalised by a slower rate of the *Z*-configured intermediate in the Suzuki cross-coupling step based on steric hindrance. A similar effect was observed for the formation of **15**, which was obtained in 74% yield as a mixture (*E*/*Z* = 93:7).

Similarly, the conversion of intermediate **4** in such a three-component one-pot reaction utilizing the same boronic acid **12** as coupling partner led to the corresponding product **16** (Scheme 5). On a 5 mmol scale the product was obtained in an acceptable yield of 45%, with similar *E*/*Z* ratio of 9:91 in favour of the desired *Z*-product. To achieve this result, the reaction protocol had to be adjusted to a longer reaction time of four days. The Suzuki cross-coupling gave low yields, which was ascribed to the significant amounts of accruing HBr generated in the first reaction step eventually leading to proto-deboration of the boronic acid. Unfortunately, the HBr could not be removed efficiently by bubbling nitrogen through the solution to increase the yield of **16**.



Scheme 5 Zinc-mediated synthesis of *Z*-configured vinyl bromide **4** and its Suzuki cross-coupling with boronic acid **12**

Nevertheless, only slight adaptions in the reaction procedure are necessary during the scaling-up and it seems to be possible to further enlarge the reaction scope due to its mild and easy to handle reaction conditions.

In summary, we have presented the multigram scale-up for the zinc-mediated synthesis of vinyl bromides whereas the stereoselectivity of the obtained double bond can be directed with the amount of zinc applied. The presented three-component sequence implying a Suzuki cross-coupling with boronic acids enable the synthesis of high functionalised alkenes in good yields and *E*/*Z* ratios.

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} and THF from Na. MeOH was distilled and dried over molecular sieves. All solvents for chromatography were distilled. Commercially available materials were used without further purification. Column chromatography was performed on silica gel 60 (Merck 230–400 mesh). ^1H and ^{13}C NMR: Bruker Avance-300. MS-EI: Hewlett Packard 5973 Mass Selective Detector. HRMS-EI: Finnigan MAT 95. IR: Bruker Alpha P.

Procedure 1; *E*-Vinyl Bromides

In a Schlenk flask, the corresponding alkyne (1–20 mmol, 1.0 equiv) and bromoethylbenzene (1.2–1.5 equiv) were added via syringe and dissolved under an argon atmosphere in CH_2Cl_2 (1–20 mL). Zn powder (150 mol%) was added and if necessary the reaction temperature was controlled using an ice bath. The mixture was stirred for 2 h at r.t. and filtered over silica gel (pentane–Et_2O, 20:1). The solvent was removed and the residue was purified by column chromatography on silica gel (eluent as indicated) yielding the *E*-vinyl bromides **3**, **6**, **8**, and **10**.

(*E*)-(1-Bromobut-1-ene-1,3-diyl)dibenzene (3)

Reaction scale, 5 mmol: The product was prepared using phenylacetylene (**1**; 511 mg, 5.0 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 1.39 g, 7.5 mmol, 1.5 equiv), and Zn powder (490 mg, 7.5 mmol, 150 mol%) in CH_2Cl_2 (5.0 mL). After column chromatography (pentane–CH_2Cl_2, 200:1), product **3** was obtained as a colourless oil (1.38 g, 4.79 mmol, 96%, *E*/*Z* = 88:12).

IR (film): 3059, 3027, 2966, 2926, 2869, 1601, 1491, 1444, 1373, 1015, 872, 764, 699, 543 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.18 (m, 7 H), 7.16–7.12 (m, 1 H), 7.11–7.04 (m, 2 H), 6.27 (d, *J* = 10.7 Hz, 1 H), 3.43 (dq, *J* = 10.7, 6.9 Hz, 1 H), 1.26 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.6, 138.5, 128.8, 128.7, 128.6, 128.3, 127.7, 126.8, 126.4, 119.8, 40.7, 22.0.

MS (EI): *m*/*z* (%) = 286 ([M^+], 5), 207 (83), 191 (54), 129 (100), 105 (31), 77 (27).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}Br$: 286.0357; found: 286.0348.

(*E*)-1-(1-Bromo-3-phenylbut-1-enyl)-4-chlorobenzene (6)
Reaction scale, 10 mmol: The product was prepared using 1-chloro-4-ethynylbenzene (**5**; 1.36 g, 10.0 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 2.22 g, 12.0 mmol, 1.2 equiv), and Zn powder (981 mg, 15.0 mmol, 150 mol%) in CH_2Cl_2 (10.0 mL). After column chromatography (pentane–CH_2Cl_2, 100:1), product **6** was obtained as a colourless oil (2.22 g, 6.94 mmol, 69%, *E*/*Z* = 89:11).

IR (film): 3028, 2968, 2927, 1596, 1487, 1450, 1257, 1090, 1012, 873, 823, 738, 697, 554 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.31–7.21 (m, 5 H), 7.20–7.14 (m, 2 H), 7.08 (d, *J* = 8.2 Hz, 2 H), 6.31 (d, *J* = 10.7 Hz, 1 H), 3.50–3.32 (m, 1 H), 1.28 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.5, 139.3, 137.3, 134.7, 130.3, 128.9, 128.7, 126.8, 126.7, 118.5, 41.0, 22.3.

MS (EI): *m*/*z* (%) = 322 ([M^+], 9), 241 (100), 225 (36), 206 (27), 191 (31), 163 (28), 129 (42), 105 (27).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}BrCl$: 321.9947; found: 321.9959.

(*E*)-(1,4-Dibromobut-1-ene-1,3-diyl)dibenzene (8)
Reaction scale, 10 mmol: The product was prepared using phenylacetylene (**1**; 1.02 g, 10.0 mmol, 1.0 equiv), 1,2-dibromoethylbenzene (**7**; 3.96 g, 15.0 mmol, 1.5 equiv), and Zn powder (981 mg, 15.0 mmol, 150 mol%) in CH_2Cl_2 (10.0 mL). The reaction mixture was stirred at 40 °C for 48 h. After column chromatography (pentane–CH_2Cl_2, 100:1), product **8** was obtained as a colourless oil (1.90 g, 5.19 mmol, 52%, *E*/*Z* = 87:13).

IR (film): 3058, 3026, 2957, 1597, 1489, 1446, 1258, 842, 761, 697, 544, 514 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.47–7.28 (m, 8 H), 7.15 (d, *J* = 7.1 Hz, 2 H), 6.46 (d, *J* = 8.6 Hz, 1 H), 3.78–3.73 (m, 1 H), 3.56 (d, *J* = 7.1 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.7, 138.3, 129.0, 128.8, 128.7, 128.4, 128.3, 127.5, 127.2, 123.3, 48.5, 36.3.

MS (EI): *m*/*z* (%) = 366 ([M^+], 4), 271 (60), 205 (43), 191 (100), 128 (27), 103 (31), 77 (26).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}Br_2$: 365.9442; found: 365.9446.

(*E*)-(1-Bromo-2-butylbut-1-ene-1,3-diyl)dibenzene (10)
Reaction scale, 10 mmol: The product was prepared using hex-1-ynylbenzene (**9**; 1.58 g, 10.0 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 2,75 g, 15.0 mmol, 1.5 equiv), and Zn powder (981 mg, 15.0 mmol, 150 mol%) in CH_2Cl_2 (10.0 mL). After column chromatography (pentane–CH_2Cl_2, 200:1), product **10** was obtained as a colourless oil (2.57 g, 7.51 mmol, 75%, *E*/*Z* = 85:15).

IR (film): 3060, 3027, 2958, 2871, 1601, 1494, 1452, 1374, 1101, 1027, 840, 761, 699, 549 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.39 (m, 4 H), 7.36–7.28 (m, 3 H), 7.24–7.14 (m, 3 H), 3.92 (q, *J* = 7.2 Hz, 1 H), 2.24–2.01 (m, 2 H), 1.40 (d, *J* = 7.2 Hz, 3 H), 1.34–1.17 (m, 2 H), 1.16–1.03 (m, 2 H), 0.84 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.1, 142.9, 141.5, 129.0, 128.5, 128.1, 127.9, 127.4, 126.3, 119.4, 41.9, 32.5, 30.6, 23.2, 17.5, 13.7.

MS (EI): *m*/*z* (%) = 342 ([M^+], 10), 263 (100), 219 (16), 205 (68), 143 (24), 115 (33), 105 (70).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{23}Br$: 342.0983; found: 342.0977.

Procedure 2; *Z*-Vinyl Bromides
In a Schlenk flask, the corresponding alkyne (1–20 mmol, 1.0 equiv) and bromoethylbenzene **2** (1.5 equiv) were added via syringe and dissolved in CH_2Cl_2 (1–20 mL) under an argon atmosphere. Zn powder (5 mol%) was added and if necessary the reaction temperature was controlled using an ice bath. The mixture was stirred for 48 h to 4 d at r.t. and filtered over silica gel (pentane–Et_2O, 20:1). The solvent was removed and the residue was purified by column chromatography on silica gel (eluent as indicated) yielding the *Z*-vinyl bromides **4** and **11**.

(*Z*)-(1-Bromobut-1-ene-1,3-diyl)dibenzene (4)
Reaction scale, 10 mmol: The product was prepared using phenylacetylene (**1**; 1.02 g, 10.0 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 2.78 g, 15.0 mmol, 1.5 equiv), and Zn powder (33 mg, 0.5 mmol, 5 mol%) in CH_2Cl_2 (10.0 mL) at r.t. and stirring for 3 d. After column chromatography (pentane–CH_2Cl_2, 100:1), product **4** was obtained as a colourless oil (1.97 g, 6.87 mmol, 69%, *E*/*Z* = 12:88).

IR (film): 3058, 3027, 2966, 2926, 2869, 1601, 1493, 1444, 1372, 1014, 870, 760, 699 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 7.3 Hz, 2 H), 7.40–7.27 (m, 8 H), 6.36 (d, *J* = 9.1 Hz, 1 H), 4.22–4.13 (m, 1 H), 1.53 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.8, 138.7, 136.3, 128.7, 128.8, 128.4, 127.8, 127.2, 126.6, 124.4, 42.7, 20.8.

MS (EI): *m*/*z* (%) = 286 ([M^+], 10), 207 (95), 191 (65), 129 (100), 105 (22), 77 (22).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}Br$: 286.0357; found: 286.0348.

(*Z*)-1-(1-Bromo-3-phenylbut-1-enyl)-4-chlorobenzene (11)
Reaction scale, 7.4 mmol: The product was prepared using 1-chloro-4-ethynylbenzene (**5**; 1.01 g, 7.4 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 2.06 g, 11.0 mmol, 1.5 equiv), and Zn powder (24 mg, 0.37 mmol, 5 mol%) in CH_2Cl_2 (8.0 mL) at r.t. and stirring for 3 d. After column chromatography (pentane–CH_2Cl_2, 200:1), product **11** was obtained as a colourless oil (1.20 g, 3.74 mmol, 51%, *E*/*Z* = 5:95).

IR (film): 3026, 2969, 2922, 1592, 1487, 1453, 1258, 1091, 1014, 873, 825, 738, 697, 553 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53–7.43 (m, 2 H), 7.39–7.24 (m, 7 H), 6.31 (d, *J* = 9.1 Hz, 1 H), 4.17–4.06 (m, 1 H), 1.49 (dd, *J* = 7.0, 4.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.2, 138.3, 136.7, 134.3, 128.9, 128.7, 128.3, 127.0, 126.5, 122.9, 42.6, 20.5.

MS (EI): *m*/*z* (%) = 322 ([M^+], 10), 241 (100), 225 (51), 206 (25), 191 (33), 163 (26), 129 (27).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{14}BrCl$: 321.9947; found: 321.9959.

Procedure 3; Trisubstituted Alkenes 14–16
For the synthesis of trisubstituted alkenes **14**–**16**, the corresponding vinyl bromides were prepared in situ as before on a 5 mmol scale (procedure 1 or 2). After complete conversion of the starting material THF (5.0 mL), MeOH (5.0 mL), KOH (561 mg, 10 mmol, 2.0 equiv), Ph_3P (52 mg, 0.2 mmol, 4 mol%), $Pd(OAc)_2$ (22 mg, 0.1 mmol, 2 mol%), and the corresponding boronic acid (6.5 mmol, 1.3 equiv) were added. The reaction mixture was stirred at 40 °C until complete conversion was detected and filtered over silica gel (pentane–Et_2O, 1:1). The solvent was removed and the residue was purified by column chromatography on silica gel (eluent as indicated), yielding the products **14**–**16**.

(*E*)-2-(1,3-Diphenylbut-1-enyl)thiophene (14)
The intermediate was prepared in situ using phenylacetylene (**1**; 510 mg, 5.0 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 1.11 g, 6.0 mmol, 1.2 equiv), and Zn powder (489 mg, 7.5 mmol, 150 mol%)

in CH_2Cl_2 (5.0 mL) (procedure 1). After complete conversion, procedure 3 was realised using 2-thiopheneboronic acid (**12**; 832 mg, 6.5 mmol, 1.3 equiv); reaction time 16 h. After column chromatography (pentane–CH_2Cl_2, 100:1), product **14** was obtained as a colourless oil (1.03 g, 3.55 mmol, 71%, *E*/*Z* = 90:10).

IR (film): 3024, 2963, 1598, 1491, 1491, 1446, 1349, 1230, 1016, 912, 869, 829, 768, 692, 548 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.49–7.36 (m, 3 H), 7.36–7.27 (m, 4 H), 7.24–7.17 (m, 3 H), 7.14 (d, *J* = 5.1 Hz, 1 H), 6.88 (dd, *J* = 5.1, 3.6 Hz, 1 H), 6.58 (d, *J* = 3.6 Hz, 1 H), 6.27 (d, *J* = 10.2 Hz, 1 H), 3.50 (dq, *J* = 10.5, 6.9 Hz, 1 H), 1.38 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 147.0, 145.8, 139.1, 134.5, 132.8, 128.5, 128.3, 127.5, 127.2, 126.9, 126.0, 125.3, 123.9, 39.0, 22.1.

MS (EI): *m*/*z* (%) = 290 ([M^+], 100), 275 (72), 241 (16), 191 (39), 171 (20), 129 (19), 91 (18), 77 (9).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{18}S$: 220.1129; found: 290.1127.

(*E*)-5-(1,3-Diphenylbut-1-enyl)-2-methoxypyridine (15)
The intermediate was prepared in situ using phenylacetylene (**1**; 510 mg, 5.0 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 1.11 g, 6.0 mmol, 1.2 equiv), and Zn powder (489 mg, 7.5 mmol, 150 mol%) in CH_2Cl_2 (5.0 mL) (procedure 1). After complete conversion, procedure 3 was realised using 6-methoxypyridine-3-boronic acid (**13**; 995 mg, 6.5 mmol, 1.3 equiv); reaction time 16 h. After column chromatography (pentane–EtOAc, 50:1), product **15** was obtained as a colourless oil (1.17 g, 3.70 mmol, 74%, *E*/*Z* = 93:7).

IR (film): 3023, 2966, 1599, 1491, 1451, 1381, 1348, 1285, 1251, 1127, 1024, 830, 766, 700, 627 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.98 (dd, *J* = 2.5, 0.6 Hz, 1 H), 7.45 (dd, *J* = 8.7, 2.5 Hz, 1 H), 7.42–7.35 (m, 2 H), 7.33–7.27 (m, 3 H), 7.25–7.14 (m, 5 H), 6.63 (dd, *J* = 8.7, 0.7 Hz, 1 H), 6.14 (d, *J* = 10.3 Hz, 1 H), 3.91 (s, 3 H), 3.61 (dq, *J* = 10.4, 6.9 Hz, 1 H), 1.39 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2, 146.1, 145.5, 139.4, 137.3, 137.0, 133.5, 131.5, 129.6, 128.5, 128.4, 127.3, 126.9, 126.1, 110.1, 53.4, 39.2, 22.4.

MS (EI): *m*/*z* (%) = 315 ([M^+], 60), 300 (100), 284 (7), 238 (7), 222 (18), 191 (9), 165 (8), 91 (11), 77 (5).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{21}NO$: 315.1623; found: 315.1624.

(*Z*)-2-(1,3-Diphenylbut-1-enyl)thiophene (16)
The intermediate was prepared in situ using phenylacetylene (**1**; 510 mg, 5.0 mmol, 1.0 equiv), 1-bromoethylbenzene (**2**; 1.39 g, 7.5 mmol, 1.5 equiv), and Zn powder (16 mg, 0.25 mmol, 5 mol%) in CH_2Cl_2 (5.0 mL) (procedure 2). After complete conversion (3 d), procedure 3 was realised using 2-thiopheneboronic acid (**12**; 832 mg, 6.5 mmol, 1.3 equiv); reaction time 4 d. After column chromatography (pentane–CH_2Cl_2, 100:1), product **16** was obtained as a colourless oil (653 mg, 2.25 mmol, 45%, *E*/*Z* = 9:91).

IR (film): 3023, 2963, 1596, 1491, 1490, 1439, 1349, 1233, 1016, 912, 869, 825, 767, 695, 549 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.28 (m, 2 H), 7.28–7.21 (m, 7 H), 7.21–7.13 (m, 2 H), 7.02 (dd, *J* = 5.1, 3.5 Hz, 1 H), 6.89 (dd, *J* = 3.5, 1.2 Hz, 1 H), 6.16 (d, *J* = 10.3 Hz, 1 H), 3.90 (dq, *J* = 10.3, 6.9 Hz, 1 H), 1.41 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.9, 142.7, 141.2, 137.1, 133.3, 128.6, 128.1, 127.8, 127.5, 127.4, 127.1, 126.8, 126.2, 125.7, 39.5, 22.4.

MS (EI): *m*/*z* (%) = 290 ([M^+], 100), 275 (74), 241 (16), 191 (47), 171 (26), 129 (15), 91 (24), 77 (15).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{18}S$: 220.1129; found: 290.1127.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

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