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Intramolecular double or triple Suzuki coupling reaction of substituted di- or tribromobenzenes. An easy synthesis of fused tri- or tetracycles with a benzene core

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Abstract

Double or triple intramolecular Suzuki coupling reaction has been developed for the efficient synthesis of tri- or tetracyclic products with a benzene core in good yields. The reaction was realized via a one-pot procedure combining the hydroboration of the C=C bond in the starting aryl halides and the intramolecular Suzuki coupling.

Keywords: Hydroboration; Suzuki coupling; Polycycles; Aryl halides; Alkenes

1. Introduction

Hexahydrobenzodipyrans-based compounds were designed as molecular probes for determining the steric restrictions of the agonist binding site of serotonin 5-HT_{2A} and 5-HT_{2C} receptors and have attracted the attention of chemists and biologists [1]. Over the past decade, the palladium-catalyzed Suzuki coupling reaction of organoboranes with alkenyl or aryl halides has emerged as one of the most powerful methods for the construction of sp^3–sp^3 C–C bonds [2–5]. Recently, an intermolecular double Suzuki coupling protocol has been devised as a practical route to a variety of compounds [6]. To the best of our knowledge, the intramolecular double or triple Suzuki coupling reaction has not been reported so far. Recently, we reported bicyclic carbopalladation [7] and triple cyclic Heck reactions [8] affording fused bicyclic compounds and fused tetracycles with a benzene core, respectively. Here, we wish to report an efficient and versatile general method of the synthesis of hexahydrobenzodipyrans and dodecahydrotriphenylene via a one-pot double or triple intramolecular Suzuki coupling reaction.

2. Results and discussion

2.1. Synthesis of starting materials

1,4-Dibromobenzenes having two equal C=C bond fragments, i.e., **3a** and **3b**, were prepared by the treatment of 2,5-dibromo-1,4-hydroquinone (**1**) [9] with allyl bromide (**2a**) and 2-methylallyl chloride (**2b**), respectively (Scheme 1). Compound with different C=C bond-containing fragments **3c** was obtained from the etherification of compound **4**, which was prepared from the monoetherification of **1** with 2-methylallyl chloride (**2b**), with allyl bromide (**2a**) (Scheme 1).

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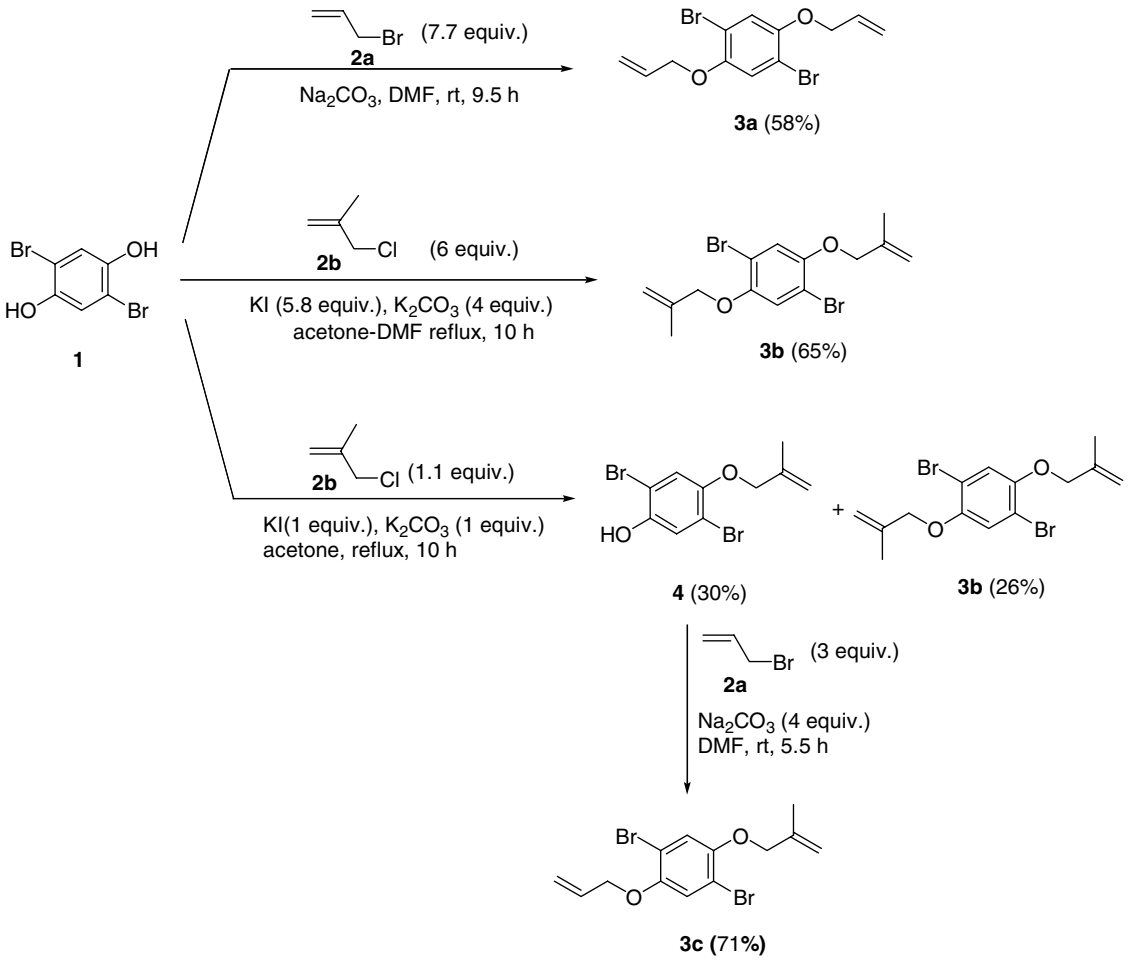
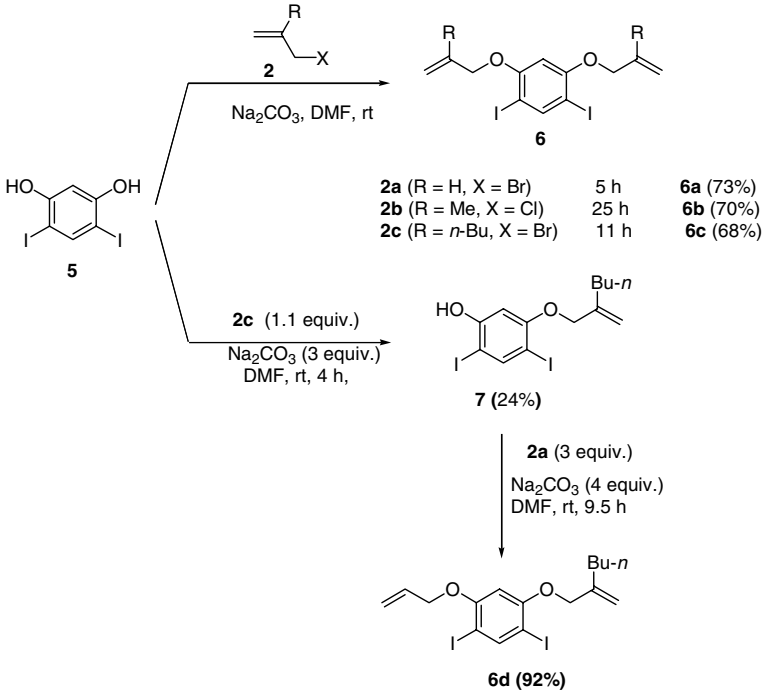


Scheme 1.



Scheme 2.

Using the same method, 1,3-diiodides **6a–d** were easily synthesized by etherification with the starting precursor **5** [10] as depicted in Scheme 2.

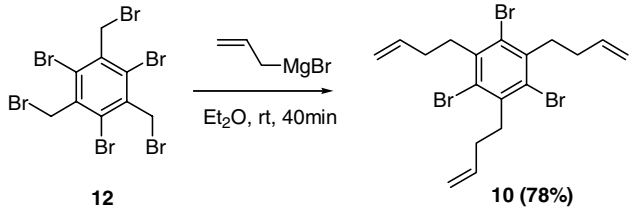
Compound **10** was prepared by the treatment of hexabromide **12** with allylmagnesium bromide as depicted in Scheme 3 as reported [8].

2.2. Hydroboration – intramolecular Suzuki coupling

2,4-Diallyloxy-1,5-diiodobenzene (**6a**) was used as the first substrate to test the double Suzuki coupling reaction under different reaction conditions with the results summarized in Table 1.

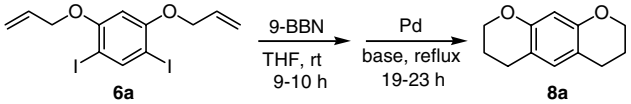
As shown in Table 1, the desired tricyclic compound **8a** was obtained in 33% yield by hydroboration of **6a** with 2.2 equiv. of 9-BBN for 10 h, followed by treatment with 5 mol% $PdCl_2$(dppf) and 3 equiv. of aqueous sodium hydroxide under reflux for 19 h (Table 1, entry 1). However, tricyclic compound **8a** was formed in 55% yield by using 2.4 equiv. of 9-BBN (Table 1, entry 2). Using 10 mol% of $Pd(PPh_3)_4$ as the catalyst and aqueous NaOH or $K_3PO_4 \cdot 3H_2O$ as the base, compound **6a** cyclized to afford tricyclic product **8a** in 42% and 19% yield, respectively (Table 1, entries 3 and 4). The best results were obtained by hydroboration of **6a** with 2.4 equiv. of 9-BBN for 9 h, followed by treatment with 10 mol% $PdCl_2$(dppf) and 3 equiv. of aqueous NaOH under reflux for 23 h affording **8a** in 60% yield (Table 1, entry 5).

Having established the standard reaction conditions for double Suzuki coupling reaction of **6a**, we tried to investigate the scope and cyclization patterns of this reaction. Some typical examples are summarized in Table 2.



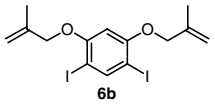
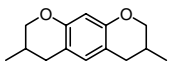
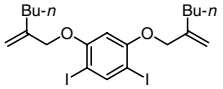
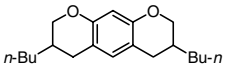
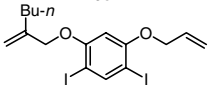
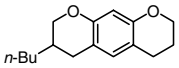
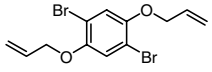
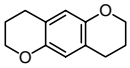
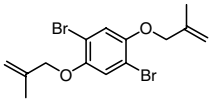
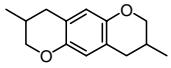
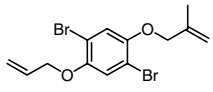
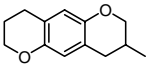
Scheme 3.

Table 1
Cyclization of **6a** under different reaction conditions



Entry	9-BBN (equiv.)	Pd (mol%)	Base	Yield (%)
1	2.2	$PdCl_2$(dppf) (5)	NaOH	33
2	2.4	$PdCl_2$(dppf) (5)	NaOH	55
3	2.4	$Pd(PPh_3)_4$ (10)	NaOH	42
4	2.4	$Pd(PPh_3)_4$ (10)	$K_3PO_4 \cdot 3H_2O$	19
5	2.4	$PdCl_2$(dppf) (10)	NaOH	60

Table 2
Cyclization of **3** and **6** via intramolecular double Suzuki coupling reaction

Entry	Substrates	Products	Yields (%)
1	 **6b**	 **8b**	68%
2	 **6c**	 **8c**	62%
3	 **6d**	 **8d**	66%
4	 **3a**	 **9a**	50%
5	 **3b**	 **9b**	51%
6	 **3c**	 **9c**	45%

From Table 2, it is obvious that a series of tricyclic compounds **8b–d** can be efficiently prepared from their corresponding precursors, i.e., diiodides **6b–d** in 68%, 62%, and 66% yield, respectively (Table 2, entries 1–3). Compounds **9a–c** were prepared in moderate yields from dibromides **3a–c** under the standard conditions (Table 2, entries 4–6).

Furthermore, when 1,3,5-tribromo-2,4,6-tri(3-butenyl)benzene (**10**) [8] was hydroborated with 3.5 equiv. of 9-BBN at r.t. for 10 h, followed by the treatment with 10 mol% $PdCl_2$(dppf) and 3 equiv. of aqueous NaOH under for 24 h tetracyclic product **11** was afforded in 35% yield (Scheme 4).

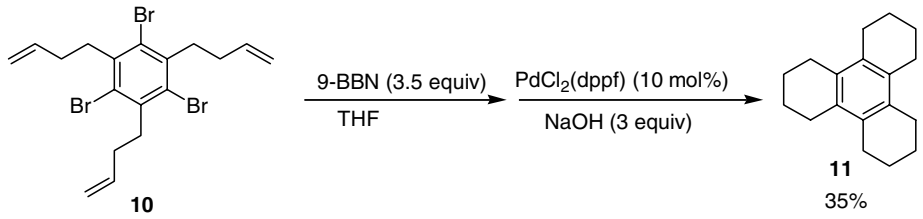
In conclusion, a new and convenient synthesis of tricycles or tetracycles with a benzene core was developed via double or triple intramolecular Suzuki coupling reactions. Further studies in this area are being conducted in our laboratory.

3. Experimental

3.1. Synthesis of starting materials

3.1.1. 1,3,5-Tribromo-2,4,6-tri(but-3′-enyl)benzene (*10*)

Compound **10** was prepared according to the literature [8].



Scheme 4.

*3.1.2. Synthesis of 1,4-dibromo-2,5-di(allyloxy)benzene (**3a**) (typical procedure A)*

To a solution of **1** (2.0 g, 7.5 mmol), allyl bromide (**2a**) (7.0 g, 58 mmol), and Na_2CO_3 (6.0 g, 57 mmol) in DMF (30 mL) was stirred at r.t. for 9.5 h, the reaction mixture was quenched with water (15 mL), extracted with Et_2O (20 mL × 3), washed with brine, and dried over $MgSO_4$. Evaporation and flash column chromatography on silica gel (petroleum ether/ethyl acetate = 20:1) gave **3a** (1.52 g, 58%) as a white solid; m.p.: 91 °C (dichloromethane–petroleum ether). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (s, 2H), 6.12–5.90 (m, 2H), 5.45 (dd, $J = 17.25$ and 1.27 Hz, 2H), 5.32 (dd, $J = 10.64$ and 1.18 Hz, 2H), 4.53 (dd, $J = 3.66$ and 1.32 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.7, 132.3, 118.8, 118.0, 111.2, 70.7; IR (KBr) $\nu = 1648$, 1492, 1359, 1211, 1066 cm^{-1}; MS (EI) *m/z* (%): 350 (M^+, $2 \times {}^{81}$Br, 10.5), 348 (M^+, $1 \times {}^{81}$Br, $1 \times {}^{79}$Br, 20.9), 346 (M^+, $2 \times {}^{79}$Br, 10.7), 41 (100.0). Anal. Calc. for $C_{12}H_{12}Br_2O_2$: C, 41.41; H, 3.48. Found: C, 41.44; H, 3.42.

The following compounds were prepared according to procedure A.

*3.1.3. Synthesis of 1,4-dibromo-2,5-di(2′-methylallyloxy)-benzene (**3b**)*

The reaction of **1** (0.5 g, 1.87 mmol), K_2CO_3 (1.05 g, 7.61 mmol), KI (1.80 g, 10.9 mmol), and **2b** (1.01 g, 11.2 mmol) in acetone–DMF (20 mL/5mL) under reflux for 10 h afforded **3b** (458 mg, 65%) as a white solid; m.p.: 93–94 °C (ethyl acetate–petroleum ether). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (s, 2H), 5.15 (s, 2H), 5.02 (s, 2H), 4.44 (s, 4H), 1.85 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.6, 139.9, 118.4, 113.1, 110.9, 73.3, 19.3; IR (KBr) $\nu = 1654$, 1496, 1215, 1075, 1048 cm^{-1}; MS (EI) *m/z* (%): 378 (M^+, $2 \times {}^{81}$Br, 6.2), 376 (M^+, $1 \times {}^{81}$Br, $1 \times {}^{79}$Br, 12.5), 374 (M^+, $2 \times {}^{79}$Br, 6.4), 55 (100.0). Anal. Calc. for $C_{14}H_{16}Br_2O_2$: C, 44.71; H, 4.29. Found: C, 44.71; H, 4.55.

*3.1.4. Synthesis of 2,5-dibromo-4-(2′-methylallyloxy)-phenol (**4**)*

The reaction of **1** (0.5 g, 1.87 mmol), K_2CO_3 (0.26 g, 1.87 mmol), KI (0.31 g, 1.87mmol) and, **2b** (0.19 g, 2.10 mmol) in acetone (15 mL) under reflux was complete after 10 h as monitored by TLC analysis. Then the mixture was diluted with water (10 mL), acidified with concentrated HCl, extracted with ethyl acetate (20 mL × 3), and dried over $MgSO_4$. Evaporation and flash column chromatography on silica gel (petroleum ether/ethyl acetate = 10:1) afforded **3b** (180 mg, 26%) and **4** (180 mg, 30%) as a white solid; m.p.: 96–97 °C (dichloromethane–petroleum ether). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (s, 1H), 6.98 (s, 1H), 5.20 (s, 1H), 5.14 (s, 1H), 5.02 (s, 1H), 4.41 (s, 2H), 1.84 (s, 3H); IR (KBr) $\nu = 3275$, 1659, 1501, 1419, 1211, 1064 cm^{-1}; MS (EI) *m/z* (%): 324 (M^+, $2 \times {}^{81}$Br, 6.5), 322 (M^+, $1 \times {}^{81}$Br, $1 \times {}^{79}$Br, 13.4), 320 (M^+, $2 \times {}^{79}$Br, 7.1), 55 (100.0). Anal. Calc. for $C_{10}H_{10}Br_2O_2$: C, 37.30; H, 3.13. Found: C, 37.40; H, 3.25.

*3.1.5. Synthesis of 1,4-dibromo-2-(2′-methylallyloxy)-5-(allyloxy)benzene (**3c**)*

The reaction of **4** (0.717 g, 2.23 mmol), Na_2CO_3 (0.95 g, 8.92 mmol), and allylic bromide (**2a**) (0.81 g, 6.68 mmol) in DMF (15 mL) afforded **3c** (572 mg, 71%) as a white solid; m.p.: 53–54 °C (ethyl ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (s, 1H), 7.09 (s, 1H), 6.10-5.96 (m, 1H), 5.50 (dd, $J = 17.10$ and 1.50 Hz, 1H), 5.32 (dd, $J = 10.50$ and 1.50 Hz, 1H), 5.14 (s, 1H), 5.01 (s, 1H), 4.54 (d, $J = 7.50$ Hz, 2H), 4.43 (s, 2H), 1.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.8, 149.6, 140.0, 132.4, 118.9, 118.5, 118.0, 113.2, 111.1, 111.0, 73.4, 70.7, 19.3; IR (KBr) $\nu = 1653$, 1494, 1213, 1063, 1012 cm^{-1}; MS (EI) *m/z* (%): 364 (M^+, $2 \times {}^{81}$Br, 5.2), 362 (M^+, $1 \times {}^{81}$Br, $1 \times {}^{79}$Br, 10.8), 360 (M^+, $2 \times {}^{79}$Br, 5.9), 55 (100.0). Anal. Calc. for $C_{13}H_{14}Br_2O_2$: C, 43.13; H, 3.90. Found: C, 43.23; H, 3.97.

*3.1.6. Synthesis of 1,3-diiodo-4,6-di(allyloxy)benzene (**6a**)*

The reaction of **5** (1.0 g, 2.76 mmol), Na_2CO_3 (2.34 g, 22.08 mmol), and allylic bromide (**2a**) (2.67 g, 22.08 mmol) in DMF (15 mL) afforded **6a** (855 mg, 73%) as a white solid; m.p.: 72–73 °C (ethyl ether–petroleum ether). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 6.36 (s, 1H), 6.11–5.96 (m, 2H), 5.50 (dq, $J = 17.25$ and 1.60 Hz, 2H), 5.33 (dq, $J = 10.50$ and 1.60 Hz, 2H), 4.57 (dt, $J = 4.88$ and 1.60 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.4, 146.8, 132.1, 118.0, 98.8, 76.5, 70.0; IR (KBr) $\nu = 1650$, 1351, 1270, 1035 cm^{-1}; MS (EI) *m/z* (%): 442 (M^+, 47.9), 41 (100.0). Anal. Calc.

for $C_{12}H_{12}I_2O_2$: C, 32.61; H, 2.74. Found: C, 32.71; H, 2.88.

3.1.7. Synthesis of 1,3-diiodo-4,6-di(2′-methylallyloxy)-benzene (6b)

The reaction of **5** (3.0 g, 8.29 mmol), Na_2CO_3 (7.03 g, 66.30 mmol), and **2b** (6.00 g, 66.30 mmol) in DMF (15 mL) afforded **6b** (2.173 g, 70%) as a white solid; m.p.: 101–102 °C (ethyl ether-petroleum ether). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1H), 6.35 (s, 1H), 5.17 (s, 2H), 5.03 (s, 2H), 4.46 (s, 4H), 1.85 (s, 6H); ^{13}C NMR(75 MHz, $CDCl_3$) δ 158.4, 146.7, 139.9, 113.3, 98.4, 76.2, 72.9, 19.4; IR (KBr) $v = 1655$, 1201, 1056 cm^{-1}; MS (EI) *m/z* (%): 470 (M^+, 26.2), 55 (100.0). Anal. Calc. for $C_{14}H_{16}I_2O_2$: C, 35.77; H, 3.43. Found: C, 35.92; H, 3.56.

3.1.8. Synthesis of 1,3-diiodo-4,6-di(2′-butylallyloxy)-benzene (6c)

The reaction of **5** (1.0 g, 2.76 mmol), Na_2CO_3 (2.34 g, 22.08 mmol), and **2c** (1.467 g, 8.29 mmol) in DMF (15 mL) afforded **6c** (1.032 g, 68%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (s, 1H), 6.35 (s, 1H), 5.19 (s, 2H), 5.03 (s, 2H), 4.48 (s, 4H), 2.16 (t, $J = 7.65$ Hz, 4H), 1.55–1.27 (m, 8H), 0.93 (t, $J = 7.35$ Hz, 6H); ^{13}C NMR(75 MHz, $CDCl_3$) δ 158.5, 146.7, 144.0, 112.3, 98.5, 76.1, 72.0, 32.7, 29.7, 22.5, 13.9; IR (KBr) $v = 2930$, 1654, 1449, 1275, 1191, 1039 cm^{-1}; MS (EI) *m/z* (%): 555 ($M + 1$, 10.7), 554 (M^+, 15.3), 55 (100.0). Anal. Calc. for $C_{20}H_{28}I_2O_2$: C, 43.34; H, 5.09. Found: C, 43.64; H, 5.14.

3.1.9. Synthesis of 2,4-diiodo-5-(2′-butylallyloxy)phenol (7)

The reaction of **5** (1.0 g, 2.76 mmol), Na_2CO_3 (878 mg, 8.29 mmol), and **2c** (538 mg, 3.04 mmol) in DMF (10 mL) afforded **7** (308 mg, 24%) and **6c** (233 mg, 15%) as a colorless oil; The data for **7**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (s, 1H), 6.53 (s, 1H), 5.28 (s, 1H), 5.20 (s, 1H), 5.03 (s, 1H), 4.46 (s, 2H), 2.16 (t, $J = 7.50$ Hz, 2H), 1.55–1.28 (m, 4H), 0.92 (t, $J = 7.20$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0, 156.1, 145.5, 143.7, 112.3, 99.8, 76.1, 75.1, 71.8, 32.8, 29.7, 22.5, 13.9; IR (KBr) $v = 3482$, 2956, 1652, 1456, 1175, 1034 cm^{-1}; MS (EI) *m/z* (%): 459 ($M^+ + 1$, 31.3), 458 (M^+, 44.6), 362 (100.0). This compound was submitted to next step without further characterization.

3.1.10. Synthesis of 1,3-diiodo-4-(allyloxy)-6-(2′-butylallyloxy)benzene (6d)

The reaction of **7** (0.611 g, 1.33 mmol), Na_2CO_3 (0.57 g, 5.32 mmol), and allyl bromide (**2a**) (0.46 mL, 0.65 g, 5.34 mmol) in DMF (15 mL) afforded **6d** (606 mg, 92%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (s, 1H), 6.35 (s, 1H), 6.10–5.94 (m, 1H), 5.50 (dq, $J = 17.25$ and 3.20 Hz, 1H), 5.32 (dq, $J = 10.55$ and 3.20 Hz, 1H), 5.19 (s, 1H), 5.03 (S, 1H), 4.60–4.53 (m, 2H), 4.49 (s, 2H), 2.15 (t, $J = 7.65$ Hz, 2H), 1.55–1.29 (m, 4H), 0.92 (t, $J = 7.05$ Hz, 3H); ^{13}C NMR(75 MHz, $CDCl_3$) δ 158.5, 158.4, 146.8, 144.0, 132.1, 117.9, 112.4, 98.7, 76.4, 76.2, 72.0, 70.0, 32.7, 29.7, 22.5, 13.9; IR (KBr) $v = 2929$, 1650, 1274, 1038 cm^{-1}; MS (EI) *m/z* (%): 498 (M^+, 29.2), 55 (100.0). Anal. Calc. for $C_{16}H_{20}I_2O_2$: C, 38.58; H, 4.05. Found: C, 38.77; H, 4.13.

3.2. Intramolecular double or triple Suzuki coupling reaction

3.2.1. Synthesis of 2,3,4,6,7,8-hexahydrobenzo[1,2b:5,4b′]dipyran (8a) (typical procedure B)

To a solution of **6a** (147 mg, 0.333 mmol) in anhydrous THF (2 mL) was added a solution of 9-BBN (2.5 mL, 0.32 M solution in THF, 0.799 mmol) at room temperature under N_2. The reaction mixture was stirred at this temperature for 12 h. To the borane solution thus obtained were added $PdCl_2$(dppf) (24 mg, 10 mol%) and aqueous NaOH (0.34 mL of 3 M solution, 1.02 mmol) at room temperature. The mixture was stirred under reflux for 24 h and then cooled to r.t., H_2O_2 (0.5 mL, 30%) was added. The mixture was extracted with ether, the organic layer was washed with brine and dried over $MgSO_4$. Concentration and purification by flash column chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) gave **8a** (38 mg, 60%) as a white solid, m.p.: 81 °C (petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.69 (s, 1H), 6.26 (s, 1H), 4.12 (t, $J = 5.05$ Hz, 4H), 2.68 (t, $J = 6.50$ Hz, 4H), 2.01–1.90 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 130.2, 114.4, 103.8, 66.4, 24.2, 22.6; IR (KBr) $v = 2965$, 1627, 1490, 1156, 1056 cm^{-1}; MS (EI) *m/z* (%): 191 ($M^+ + 1$, 13.3), 190 (M^+, 100.0). Anal. Calc. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.73; H, 7.39.

The following compounds were prepared according to procedure B.

3.2.2. Synthesis of 3,7-dimethyl-2,3,4,6,7,8-hexahydrobenzo[1,2b:5,4b′]dipyran (8b)

A solution of **6b** (145 mg, 0.309 mmol) and 9-BBN (2.3 mL, 0.32 M solution in THF, 0.742 mmol) in THF (2 mL) was stirred at r.t. for 11 h. Then the mixture was treated with $PdCl_2$(dppf) (23 mg, 10 mol%) and aqueous NaOH (0.31 mL of 3 M solution, 0.93 mmol) and stirred under reflux for 23 h to give **8b** (46 mg, 68%) as a white solid, m.p.: 106 °C (petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.67 (s, 1H), 6.28 (s, 1H), 4.16–4.07 (m, 2H), 3.62 (t, $J = 9.90$ Hz, 2H), 2.72 (dd, $J = 15.75$ and 3.55 Hz, 2H), 2.40–2.26 (m, 2H), 2.19–2.02 (m, 2H), 1.02 (d, $J = 6.80$ Hz, 6H); IR (KBr) $v = 2959$, 1625, 1505, 1159, 1126 cm^{-1}; MS (EI) *m/z* (%): 219 ($M^+ + 1$, 26.0), 218 (M^+, 100.0). Anal. Calc. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.98; H, 8.28.

*3.2.3. Synthesis of 3,7-dibutyl-2,3,4,6,7,8-hexahydrobenzo[1,2b:5,4b′]dipyran (**8c**)*

A solution of **6c** (160 mg, 0.289 mmol) and 9-BBN (2.2 mL, 0.32 M solution in THF, 0.694 mmol) in THF (2 mL) was stirred at r.t. for 9 h. Then the mixture was treated with $PdCl_2$(dppf) (21 mg, 10 mol%) and aqueous NaOH (0.29 mL of 3 M solution, 0.87 mmol) and stirred under reflux for 23 h to give **8c** (54 mg, 62%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.68 (s, 1H), 6.27 (s, 1H), 4.20–4.09 (m, 2H), 3.72–3.61 (m, 2H), 2.80–2.70 (m, 2H), 2.40–2.26 (m, 2H), 2.04–1.86 (m, 2H), 1.47–1.18 (m, 12H), 0.98–0.80 (m, 6H); IR (KBr) $v = 2958$, 1627, 1494, 1162, 1131 cm^{-1}; MS (EI) *m/z* (%): 303 ($M^+ + 1$, 28.3), 302 (M^+, 100.0); HRMS Calc. for $C_{20}H_{30}O_2$: 302.22458. Found: 302.22187.

*3.2.4. Synthesis of 3-butyl-2,3,4,6,7,8-hexahydrobenzo[1,2b:5,4b′]dipyran (**8d**)*

A solution of **6d** (154 mg, 0.309 mmol) and 9-BBN (2.3 mL, 0.32 M solution in THF, 0.742 mmol) in THF (2 mL) was stirred at r.t. for 9 h. Then the mixture was treated with $PdCl_2$(dppf) (23 mg, 10 mol%) and aqueous NaOH (0.31 mL of 3 M solution, 0.93 mmol) and stirred under reflux for 23 h to give **8d** (50 mg, 66%) as a colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.69 (s, 1H), 6.27 (s, 1H), 4.19–4.08 (m, 3H), 3.68 (t, $J = 9.60$ Hz, 1H), 2.81–2.63 (m, 3H), 2.40–2.26 (m, 1H), 2.02–1.90 (m, 3H), 1.43–1.20 (m, 6H), 0.97–0.85 (m, 3H); IR (KBr) $v = 2961$, 1630, 1159, 1094 cm^{-1}; MS (EI) *m/z* (%): 247 ($M^+ + 1$, 20.4), 246 (M^+, 100.0); HRMS Calc. for $C_{16}H_{22}O_2$: 246.16198. Found: 246.16481.

*3.2.5. Synthesis of 2,3,4,7,8,9-hexahydrobenzo[1,2b:4,5b′]dipyran (**9a**)*

A solution of **3a** (110 mg, 0.316 mmol) and 9-BBN (2.4 mL, 0.32 M solution in THF, 0.758 mmol) in THF (2 mL) was stirred at r.t. for 9 h. Then the mixture was treated with $PdCl_2$(dppf) (22 mg, 10 mol%) and aqueous NaOH (0.32 mL of 3 M solution, 0.96 mmol) and stirred under reflux for 24 h to give **9a** (30 mg, 50%) as a white solid; m.p.: 101–102 °C (petroleum ether) (lit. [1] m.p.: 104–106 °C (ethyl acetate)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.47 (s, 2H), 4.10 (t, $J = 4.91$ Hz, 4H), 2.70 (t, $J = 6.40$ Hz, 4H), 2.10–1.80 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 121.2, 116.6, 66.3, 24.7, 22.6; IR (KBr) $v = 1504$, 1262, 1062, 801 cm^{-1}; MS (EI) *m/z* (%): 191 ($M^+ + 1$, 13.3), 190 (M^+, 100.0); Anal. Calc. for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.68; H, 7.24.

*3.2.6. Synthesis of 3,8-dimethyl-2,3,4,7,8,9-hexahydrobenzo[1,2b:4,5b′]dipyran (**9b**)*

A solution of **3b** (105 mg, 0.279 mmol) and 9-BBN (2.1 mL, 0.32 M solution in THF, 0.672 mmol) in THF (2 mL) was stirred at r.t. for 11 h. Then the mixture was treated with $PdCl_2$(dppf) (21 mg, 10 mol%) and aqueous NaOH (0.28 mL of 3 M solution, 0.84 mmol) and stirred under reflux for 23 h to give **9b** (31 mg, 51%) as a white solid; m.p.: 165 °C (petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48 (s, 2H), 4.15–4.06 (m, 2H), 3.61 (t, $J = 9.65$ Hz, 2H), 2.82–2.70 (m, 2H), 2.43–2.30 (m, 2H), 2.19–2.02 (m, 2H), 1.00 (d, $J = 6.70$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.9, 120.8, 116.3, 71.7, 33.1, 27.3, 17.0; IR (KBr) $v = 2957$, 1504, 1422, 1035 cm^{-1}; MS (EI) *m/z* (%): 219 ($M^+ + 1$, 16.8), 218 (M^+, 100.0). Anal. Calc. for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.76; H, 8.20.

*3.2.7. Synthesis of 3-methyl-2,3,4,7,8,9-hexahydrobenzo[1,2b:4,5b′]dipyran (**9c**)*

A solution of **3c** (120 mg, 0.331 mmol) and 9-BBN (2.5 mL, 0.32 M solution in THF, 0.80 mmol) in THF (2 mL) was stirred at r.t. for 11 h. Then the mixture was treated with $PdCl_2$(dppf) (24 mg, 10 mol%) and aqueous NaOH (0.33 mL of 3 M solution, 0.99 mmol) and stirred under reflux for 23 h to give **9c** (30 mg, 45%) as a white solid; m.p.: 114 °C (petroleum ether); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.48 (d, $J = 5.90$ Hz, 2H), 4.18–4.06 (m, 3H), 3.61 (t, $J = 10.0$ Hz, 1H), 2.83–2.68 (m, 3H), 2.37 (dd, $J = 15.90$ and 9.60 Hz, 1H), 2.19–2.03 (m, 1H), 2.00–1.90 (m, 2H), 1.01 (d, $J = 6.70$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 148.0, 121.4, 121.1, 116.9, 116.6, 72.0, 66.6, 33.4, 27.5, 24.9, 22.8, 17.2; IR (KBr) $v = 2934$, 1504, 1422, 1059, 1028 cm^{-1}; MS (EI) *m/z* (%): 205 ($M^+ + 1$, 17.4), 204 (M^+, 100.0). HRMS Calc. for $C_{13}H_{16}O_2$: 204.11503. Found: 204.11127.

*3.2.8. Synthesis of dodecahydrotriphenylene (**11**)*

A solution of **10** (120 mg, 0.252 mmol) and 9-BBN (2.8 mL, 0.32 M solution in THF, 0.896 mmol) in THF (2 mL) was stirred at r.t. for 11 h. Then the mixture was treated with $PdCl_2$(dppf) (20 mg, 10 mol%) and aqueous NaOH (0.3 mL of 3 M solution, 0.90 mmol) and stirred under reflux for 23 h to give **11** (21 mg, 35%) as a white solid; m.p.: 231–232 °C (petroleum ether) (lit. [11], m.p.: 232 °C (petroleum ether)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.80–2.50 (m, 12H), 2.00–1.70 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 132.6, 26.8, 23.0; IR (KBr) $v = 2917$, 1432 cm^{-1}; MS (EI) *m/z* (%): 241 ($M^+ + 1$, 12.0), 240 (M^+, 100.00). Anal. Calc. for $C_{18}H_{24}$: C, 89.94; H, 10.06. Found: C, 89.60; H, 10.05.

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References

[1] M.S. Whiteside, D. Kurrasch-Orbaugh, D. Marona-Lewicka, D.E. Nichols, A. Monte, Bioorg. Med. Chem. 10 (2002) 3301, and references therein.
[2] N. Miyaura, A. Suzuki, Chem. Rev. 95 (1995) 2457.
[3] (a) M. Sabat, C.R. Johnson, Org. Lett. 2 (2000) 1089;
(b) A. Kamatani, L.E. Overman, J. Org. Chem. 64 (1999) 8743;
(c) M. Sasaki, H. Fuwa, M. Inoue, K. Tachibana, Tetrahedron Lett. 39 (1998) 9027.
[4] (a) B.M. Trost, C.B. Lee, J. Am. Chem. Soc. 120 (1998) 6818;
(b) D. Meng, S.J. Danishefsky, Angew. Chem. Int. Ed. 38 (1999) 1485;
(c) D. Meng, Q. Tan, S.J. Danishefsky, Angew. Chem. Int. Ed. 38 (1999) 3197;
(d) A. Fürstner, I. Konetzki, J. Org. Chem. 63 (1998) 3072.
[5] For the recent intramolecular Suzuki coupling reactions, see (a) M. Kaiser, C. Siciliano, I. Assfalg-Machleidt, M. Groll, A.G. Milbradt, L. Moroder, Org. Lett. 5 (2003) 3435;
(b) M. Bauer, M.E. Maier, Org. Lett. 4 (2002) 2205;
(c) M.C. Willis, C.K. Claverie, M.F. Mahon, Chem. Commun. (2002) 832;
(d) M. Relbøll, A.J. Edwards, A.D. Rae, A.C. Willis, M.A. Bennett, E. Wenger, J. Am. Chem. Soc. 124 (2002) 8348;
(e) V. Lobrégat, G. Alcaraz, H. Bienaymé, M. Vaultier, Chem. Commun. (2001) 817;
(f) A.-C. Carbonnelle, J. Zhu, Org. Lett. 2 (2000) 3477;
(g) S.R. Chemler, S.J. Danishefsky, Org. Lett. 2 (2000) 2695.
[6] (a) N. Saygili, A.S. Batsanov, M.R. Bryce, Org. Biomol. Chem. 2 (2004) 852;
(b) D. Simoni, G. Giannini, P.G. Baraldi, R. Romagnoli, M. Roberti, R. Rondanin, R. Baruchello, G. Grisolia, M. Rossi, D. Mirizzi, F.P. Invidiata, S. Grimaudo, M. Tolomeo, Tetrahedron Lett. 44 (2003) 3005;
(c) S. Langle, M. Abarbri, A. Duchêne, Tetrahedron Lett. 44 (2003) 9255;
(d) B.A. Johns, C.R. Johnson, Tetrahedron Lett. 39 (1998) 749;
(e) J.A. Soderquist, G. León, J.C. Colberg, I. Martinez, Tetrahedron Lett. 36 (1995) 3119;
(f) S.D. Mandolesi, S.E. Vaillard, J.C. Podestá, R.A. Rossi, Organometallics 21 (2002) 4886;
(g) S.R. Piettre, C. André, M.C. Chanal, J.B. Ducep, B. Lesur, F. Piriou, P. Raboisson, J.M. Rondeau, C. Schelcher, P. Zimmermann, A.J. Ganzhorn, J. Med. Chem. 40 (1997) 4208;
(h) F-J. Zhang, C. Cortez, R.G. Harvey, J. Org. Chem. 65 (2000) 3952.
[7] (a) S. Ma, B. Xu, J. Org. Chem. 63 (1998) 9156;
(b) S. Ma, B. Xu, B. Ni, J. Org. Chem. 65 (2000) 8532.
[8] S. Ma, B. Ni, J. Org. Chem. 67 (2002) 8280.
[9] M. Dingjan, J. Eames, Bull. Chem. Soc. Jpn. 74 (2001) 179.
[10] I. Thomsen, K.B.G. Torssell, Acta. Chem. Scand. 45 (1991) 539.
[11] D.P. Chakraborty, S.K. Roy, U.P. Jana, T. Karmakar, J. Indian Chem. Soc. 61 (1984) 975.