



Supporting Information

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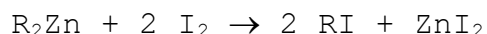
**Nucleophilic Catalysis of the Iodine-Zinc Exchange Reaction. A
new Preparation of Highly Functionalized Diarylzincs**

Florian F. Kneisel, Maximilian Dochnahl, and Paul Knochel

Experimental Section:

General Details:

All NMR spectra were calibrated to the solvent peak.^[1] All experiments were performed under standard *Schlenk* techniques, using dried solvents and argon as inert gas. The concentrations of solutions of dialkylzinc reagents, where stated, were determined by reaction with iodine: the solution of the zinc reagent (1.0 mL) was diluted with dry THF (resulting in an approximately 0.5 mol/L concentrated solution). The concentration of this solution was determined by dropwise addition of a iodine solution (solution of iodine in dry THF, 0.3 mol/L) to the stirred zinc reagent. The concentration of the zinc reagent was then calculated according to the following equation:



The concentrations of solutions of alkyllithium reagents, where stated, were determined by standard procedures.^[2]

General Procedure for the Preparation of $i\text{Pr}_2\text{Zn}$

An ethereal solution of *iPrMgBr* (approx. 1.5 M, 1.0 equiv.) is cooled to 0 °C. A solution of ZnBr_2 in ether (approx. 1.5 M, 0.5 equiv.) is transferred *via cannula* to the cooled solution. After complete addition the solution is allowed to warm to room temperature and stirred overnight. The main part of the ether is removed *in vacuo* at room temperature. $i\text{Pr}_2\text{Zn}$ is distilled from the precipitated MgCl_2 to give an ethereal

solution of $i\text{Pr}_2\text{Zn}$ (5 - 6 M) which is stored under exclusion of light.

General Procedure for the Preparation of $s\text{Bu}_2\text{Zn}$

sec-Butyllithium (ca. 1.4 M in cyclohexane) was filtered through Celite[®]. The concentration of the alkyllithium reagent was determined according to the literature.^[2] The solution was cooled to 0 °C and the volume was reduced in vacuo to 1/10. The orange, highly viscous solution was cooled to -78 °C. An ethereal solution of zinc chloride (1 M, 0.5 equiv.) was slowly added. The solution was allowed to slowly warm up to room temperature and stirred overnight under light exclusion. The precipitated lithium chloride was removed from the solution either by decantation, filtration or by centrifugation. The resulting light sensitive $s\text{Bu}_2\text{Zn}$ solution was approx. 0.6 - 0.8 M (determined by a iodolytic titration as described above).

General Procedure for the Iodine-Zinc Exchange

The aryl iodide (2.0 mmol, 1.0 equiv.) and Li(acac) (0.2 mmol, 0.1 equiv.) were dissolved in dry NMP (1.5 mL). The dialkylzinc reagent ($i\text{Pr}_2\text{Zn}$ or $s\text{Bu}_2\text{Zn}$, as stated in the preparation) (1.1 mmol, 0.55 equiv.) was added at 0 °C. The reaction mixture was stirred at 0 °C or room temperature (as stated in the experiment) and the completion of the iodine-zinc exchange was checked by GC-analysis using tetradecane as internal standard.^[3]

General Procedure for Negishi Cross-Couplings

$\text{Pd}(\text{dba})_2$ (30 mg, 2.5 mol% based on the arylzinc reagent) and tfp (25 mg, 5.0 mol% based on the arylzinc reagent) were dissolved in dry THF (2.0 mL). The mixture was stirred for 5 min at room temperature, and subsequently the electrophilic aryl iodide (1.6 mmol, 0.8 equiv.) was added neat. After the

mixture was stirred for further 5 min, the previously prepared solution of the corresponding bis-arylzinc (1.0 equiv.) reagent was added at room temperature. The consumption of the aryl iodide was checked by GC-analysis using tetradecane as internal standard.^[3] After complete conversion, sat. NH_4Cl solution was added and the mixture was extracted three times with Et_2O . The solvent was evaporated and the product was purified by flash chromatography (SiO_2).

General Procedure for Palladium Catalysed Couplings with Acid Chlorides

$\text{Pd}(\text{dba})_2$ (30 mg, 2.5 mol% based on the arylzinc reagent) and tfp (25 mg, 5.0 mol% based on the arylzinc reagent) was dissolved in dry THF (2.0 mL). The mixture was stirred for 5 min at room temperature, and subsequently the corresponding acid chloride (3.0 mmol, 1.5 equiv.) was added neat. The mixture was stirred for further 5 min and an NMP solution of the corresponding bisarylzinc reagent was added at room temperature. The consumption of the zinc reagent was checked by GC-analysis, using tetradecane as internal standard.^[3] After the reaction was completed, sat. NH_4Cl solution was added and the mixture was extracted three times with Et_2O . The solvent was evaporated and the product was purified by flash chromatography (SiO_2).

General Procedure for Copper Catalysed Allylations

The freshly prepared zinc reagent was cooled to 0 °C and then the corresponding allyl bromide (3.0 mmol, 1.5 equiv.) was added, followed by dropwise addition of $\text{CuCN} \cdot 2 \text{LiCl}$ (a 1.0 M solution in NMP was used, 0.2 mmol, 0.1 equiv.). The mixture was stirred for 5 h at room temperature. The consumption of the zinc reagent was checked by GC-analysis, using tetradecane as internal standard.^[3] After the reaction was completed, sat. NH_4Cl solution was added and the mixture was extracted three

times with Et₂O. The solvent was evaporated and the product was purified by flash chromatography (SiO₂).

General Procedure for Copper Mediated Acylations

The freshly prepared zinc reagent was cooled to 0 °C and then the corresponding acid chloride (3.0 mmol, 1.5 equiv.) was added, followed by dropwise addition of CuCN · 2 LiCl (a 1.0 M solution in NMP was used, catalytic or stoichiometric amounts were used, as indicated in the procedure). The mixture was stirred for 8 h at room temperature. The consumption of the zinc reagent was checked by GC-analysis, using tetradecane as internal standard.^[3] After the reaction was completed, sat. NH₄Cl solution was added and the mixture was extracted three times with Et₂O. The solvent was evaporated and the product was purified by flash chromatography (SiO₂).

4-Benzoylbenzoic acid methyl ester (5a)

Methyl 4-iodobenzoate (525 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange completed after 8 h. The zinc reagent was reacted with benzoyl chloride (420 mg, 3.0 mmol) using CuCN · 2 LiCl (0.4 mL, 0.2 equiv., 20 mol%), as described in the general procedure. The reaction mixture was stirred for 5 h at 55 °C. Flash chromatographical purification (pentane : di-chloromethane = 50 : 50) gave the benzophenone **5a** (394 mg, 82 %, based on 2.0 mmol of the starting iodide) as a white solid (mp.: 105 - 106 °C). Analytical data was found to match literature data.^[4]

2-carboethoxy-4'-nitrobiphenyl (5b)

Ethyl 2-iodobenzoate (552 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using $i\text{Pr}_2\text{Zn}$ (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 8 h. The zinc reagent was reacted with 4-iodo-nitrobenzene (399 mg, 1.6 mmol) using $\text{Pd}(\text{dba})_2$ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 10 h at room temperature. Flash chromatographical purification (pentane : ether = 90 : 10) gave the biphenyl **5b** (385 mg, 71 %, based on 1.6 mmol of the aryl iodide) as a yellow solid (mp.: 66 - 68 °C).

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 8.26 (d, J = 8.7 Hz, 2 H); 7.94 - 7.98 (m, 1 H); 7.44 - 7.63 (m, 4 H); 7.31 - 7.35 (m, 1 H); 4.13 (q, J = 7.2 Hz, 2 H); 1.08 (t, J = 6.9 Hz, 3 H).

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 167.5; 148.7; 147.1; 140.7; 131.8; 130.6; 130.5; 130.5; 129.5; 128.5; 123.3; 61.3; 13.9.

IR (KBr): ν/cm^{-1} = 2989 (w); 1714 (s); 1594 (m); 1517 (s); 1446 (w); 1349 (s); 1286 (s); 1248 (m); 1133 (m); 857 (m); 770 (m); 752 (m); 698 (m).

MS (EI, 70 eV): m/z (%) = 271 (M^+ , 58); 243 (46); 226 (100); 210 (9); 180 (99); 152 (37); 139 (12); 126 (7).

HR-MS: ($\text{C}_{15}\text{H}_{13}\text{NO}_4$) calculated 271.0845 found 271.0838

4'-Fluoro-6-methoxy-biphenyl-3-carboxylic acid methyl ester (5c)

Methyl 3-iodo-4-methoxybenzoate (584 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using $i\text{Pr}_2\text{Zn}$ (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed

after 8 h. The zinc reagent was reacted with 4-fluoroiodobenzene (355 mg, 1.6 mmol) using Pd(dba)₂ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 10 h at room temperature. Flash chromatographical purification (pentane : ether = 90 : 10) gave the biphenyl **5c** (432 mg, 83 %, based on 1.6 mmol of the aryl iodide) as a white solid (mp.: 106 - 107 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 7.94 - 8.08 (m, 2 H); 7.45 - 7.52 (m, 2 H); 7.06 - 7.14 (m, 2 H); 7.00 (d, *J* = 8.7 Hz, 1 H); 3.90 (s, 3 H); 3.88 (s, 3 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 166.9; 162.3 (*J* = 245 Hz); 160.2; 133.5 (*J* = 3 Hz); 132.4; 131.3 (*J* = 8 Hz); 130.9; 129.6; 122.8; 115.4 (*J* = 23 Hz); 110.7; 55.9; 52.0.

IR (KBr): ν/cm⁻¹ = 3020 (w); 2999 (w); 2955 (w); 1893 (w); 1723 (s); 1604 (s); 1518 (s); 1499 (s); 1439 (s); 1302 (s); 1280 (s); 1243 (s); 1161 (s); 1116 (m); 1039 (m); 1020 (m); 979 (w); 829 (s); 766 (m).

MS (EI, 70 eV): m/z (%) = 260 (M⁺, 93); 229 (100); 213 (4); 201 (5); 186 (26); 170 (7); 157 (20); 146 (2); 138 (2); 114 (2).

HR-MS: (C₁₅H₁₃FO₃) calculated 260.0849 found 260.0850

4-Isothiocyanato-3-trimethylstannylbenzoic acid ethyl ester (5d)

Ethyl 3-iodo-4-isothiocyanatobenzoate (666 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (2.0 mL). A solution of s-Bu₂Zn in ether (2.2 mL, 1.1 mmol) was added at 0 °C. The ether was immediately removed in vacuo to accelerate the reaction. The solution was stirred 30 minutes at 0 °C and then allowed to warm to room temperature. The I-Zn exchange was completed within 3 h. The zinc reagent was reacted with Me₃SnCl (1.0 M in THF, 3.0 mL, 3.0 mmol) at room temperature and furthermore stirred for 4 h at room temperature. Flash

chromatographical purification (pentane : ether = 50 : 50) gave the arylstannane **5d** (497 mg, 66 %, based on 2.0 mmol of the aryl iodide) as a pale solid (mp.: 64 - 65 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 8.02 (d, J = 1.8 Hz, 1 H), 7.88 (dd, J_A = 8.4 Hz, J_B = 1.8 Hz, 1 H), 7.22 (d, J = 8.4 Hz, 1 H), 4.29 (q, J = 7.1 Hz, 2 H), 1.30 (t, J = 6.9 Hz, 3 H), 0.34 (s, 9 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 165.8, 141.6, 137.8, 137.6, 134.9, 131.0, 130.9, 128.1, 126.1, 125.5, 61.1, 14.2, -8.9.

IR (KBr): ν/cm^{-1} = 3430 (brw), 2982 (m), 2920 (w), 2171 (m), 2102 (brs), 1718 (s), 1602 (w), 1583 (s), 1463 (m), 1366 (m), 1275 (s), 1250 (s), 1232 (m), 1171 (w), 1109 (s), 1055 (w), 1021 (w), 936 (s), 856 (w), 767 (s), 700 (w), 532 (m), 513 (w), 431 (w).

MS (EI, 70 eV): m/z (%) = 371 (M⁺, 0.1), 360 (17), 358 (19), 357 (17), 356 (100), 355 (37), 354 (73), 353 (25), 352 (44), 328 (16), 326 (22), 324 (17).

HR-MS: (C₁₃H₁₇NO₂SSn) calculated 371.0002 found: 370.9986

3'-Methoxy-biphenyl-4-carboxylic acid methyl ester (5e)

3-Iodo-4-methoxybenzene (468 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 8 h. The zinc reagent was reacted with methyl 4-iodobenzoate (420 mg, 1.6 mmol) using Pd(dba)₂ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 8 h at room temperature. Flash chromatographical purification (pentane : ether = 90 : 10) gave the biphenyl **5e** (417 mg, 86 %, based on 1.6 mmol of the aryl iodide) as a yellow solid (mp.: 53 - 55 °C).

Analytical data was found to match literature data.^[5]

2'-Nitro-biphenyl-3-carbonitrile (5f)

3-Iodobenzonitrile (458 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using $i\text{Pr}_2\text{Zn}$ (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 10 h. The zinc reagent was reacted with 2-iodo-nitrobenzene (399 mg, 1.6 mmol) using $\text{Pd}(\text{dba})_2$ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 6 h at room temperature. Flash chromatographical purification (pentane : ether = 70 : 30) gave the biphenyl **5f** (376 mg, 84 %, based on 1.6 mmol of the aryl iodide) as a colourless oil.

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 7.94 – 8.02 (m, 1 H); 7.50 – 7.87 (m, 6 H); 7.36 – 7.43 (m, 1 H).

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 139.1; 134.4; 133.0; 132.5; 131.8; 131.6; 130.7; 130.1; 129.5; 129.4; 124.7; 118.4; 113.1.

IR (film): ν/cm^{-1} = 3090 (w); 2924 (w); 2860 (w); 1659 (s); 1570 (w); 1519 (s); 1482 (w); 1446 (s); 1350 (m); 1281 (s); 928 (w); 854 (w); 809 (m); 780 (w); 745 (m); 715 (w); 595 (m).

MS (EI, 70 eV): m/z (%) = 224 (M^+ , 43); 207 (54); 196 (84); 177 (100); 168 (53); 151 (69); 140 (43); 117 (9).

HR-MS: ($\text{C}_{13}\text{H}_8\text{N}_2\text{O}_2$) calculated 224.0586 found 224.0599

3-(6-Chloro-pyridine-3-carbonyl) benzonitrile (5g)

3-Iodobenzonitrile (458 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using $i\text{Pr}_2\text{Zn}$ (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after

10 h. The zinc reagent was transmetallated by dropwise addition of $\text{CuCN} \cdot 2 \text{LiCl}$ (2.2 mL, 2.2 mmol, 1.1 equiv.) at 0 °C, as described in the general procedure. The copper species was subsequently reacted with 6-chloro-nicotinyl chloride (282 mg, 1.6 mmol) for 2 h at room temperature. Flash chromatographical purification (pentane : ether = 50 : 50) gave the ketone **5g** (373 mg, 77 %, based on 1.6 mmol of the acid chloride) as a yellow solid (mp.: 101 - 102 °C).

$^1\text{H-NMR}$ (CDCl_3 , 300 MHz): δ = 8.75 (dd, J_A = 2.4 Hz, J_B = 0.6 Hz, 1 H); 8.06 - 8.11 (m, 2 H); 8.01 (dt, J_A = 8.1 Hz, J_B = 1.5 Hz, 1 H); 7.93 (dt, J_A = 7.8 Hz, J_B = 1.2 Hz, 1 H); 7.68 (td, J_A = 7.8 Hz, J_B = 0.6 Hz, 1 H); 7.52 (dd, J_A = 8.4 Hz, J_B = 0.6 Hz, 1 H).

$^{13}\text{C-NMR}$ (CDCl_3 , 75 MHz): δ = 191.5; 156.0; 151.1; 139.7; 137.5; 136.3; 133.6; 133.3; 130.9; 129.9; 124.8; 117.6; 113.6.

IR (film): ν/cm^{-1} = 3079 (w); 3064 (w); 2230 (m); 1661 (s); 1572 (s); 1554 (m); 1456 (w); 1442 (m); 1357 (m); 1295 (m); 1283 (s); 1201 (w); 1173 (w); 1136 (m); 1104 (m); 973 (m); 923 (w); 848 (w); 806 (m); 761 (m).

MS (EI, 70 eV): m/z (%) = 242 (M^+ , 26); 214 (3); 207 (100); 179 (4); 151 (2); 142 (14); 140 (40); 130 (37); 102 (27).

HR-MS: ($\text{C}_{13}\text{H}_7\text{ClN}_2\text{O}$) calculated 242.0247 found 242.0266

3-Acetyl-4-methylbenzotrile (5h)

3-Iodo-4-methylbenzotrile (486 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 10 h. The zinc reagent was reacted with acetyl chloride (237 mg, 3.0 mmol) using Pd(dba)₂ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 4 h at room temperature. Flash chromatographical purification (pentane : ether = 70 : 30) gave the ketone **5h** (277 mg, 87 %, based on 2.0 mmol of the starting iodide) as a yellow solid (mp.: 101 -102 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 7.69 (d, *J* = 7.8 Hz, 1 H); 7.51 - 7.58 (m, 2 H); 2.58 (s, 3 H); 2.51 (s, 3 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 200.8; 141.6; 139.0; 135.3; 129.6; 129.1; 118.1; 114.8; 29.8; 21.0.

IR (film): ν/cm⁻¹ = 3115 (w); 3080 (w); 3045 (w); 2971 (w); 2931 (w); 2228 (s); 1687 (s); 1557 (m); 1494 (w); 1443 (s); 1379 (s); 1362 (s); 1291 (m); 1250 (s); 1141 (w); 1060 (w); 1034 (w); 972 (m); 960 (w); 918 (w); 897 (m); 827 (s); 656 (m); 615 (m); 545 (m); 516 (m); 446 (m).

MS (EI, 70 eV): m/z (%) = 159 (M⁺, 29); 144 (100); 128 (1); 116 (31); 103 (1); 89 (11); 75 (1); 63 (5).

HR-MS: (C₁₀H₉NO) calculated 159.0684 found 159.0698

2'-Benzoyl-4-biphenylcarboxylic acid methyl ester (5i)

2-Iodobenzophenone (616 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange completed after 10 h. The zinc reagent was reacted with methyl 4-iodobenzoate

(420 mg, 1.6 mmol) using Pd(dba)₂ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 6 h at room temperature. Flash chromatographical purification (pentane : dichloromethane = 80 : 20) gave the biphenyl **5i** (512 mg, 81 %, based on 1.6 mmol of the aryl iodide) as a white solid (mp.: 97 - 99 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 7.78 - 7.83 (m, 2 H); 7.18 - 7.64 (m, 11 H); 3.79 (s, 3 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 189.3; 166.8; 140.2; 139.1; 137.3; 133.2; 130.6; 130.3; 130.1; 130.0; 129.6; 129.1; 129.0; 128.3; 127.8; 127.3; 52.1.

IR (KBr): ν/cm⁻¹ = 3115 (w); 3074 (w); 2950 (w); 1720 (s); 1663 (s); 1608 (m); 1596 (m); 1580 (w); 1479 (w); 1448 (m); 1433 (m); 1406 (w); 1396 (w); 1313 (m); 1277 (s); 1250 (s); 1185 (m); 1150 (w); 1114 (m); 1102 (m); 1021 (w); 1004 (w); 927 (m); 860 (m); 772 (m); 759 (s); 749 (s); 715 (s); 700 (m); 649 (m); 638 (m); 639 (m).

MS (EI, 70 eV): m/z (%) = 316 (M⁺, 100); 301 (39); 285 (25); 257 (73); 239 (36); 217 (10); 195 (31); 180 (26); 165 (9); 152 (48); 126 (6); 105 (33).

HR-MS: (C₂₁H₁₆O₃) calculated 316.1099 found 316.1125

4-(5-Acetyl-2-thiophenyl)benzoic acid methyl ester (5j)

5-Acetyl-2-iodothiophene (504 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at 0°C as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 5 h. The zinc reagent was reacted with methyl 4-iodo-benzoate (420 mg, 1.6 mmol) using Pd(dba)₂ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 5 h at room temperature.

Flash chromatographical purification (toluene : ether = 95 : 5) gave the thiophene **5j** (270 mg, 52 %, based on 1.6 mmol of the aryl iodide) as a yellow solid (mp.: 178 - 180 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 8.07 (d, *J* = 8.7 Hz, 2 H); 7.70 (d, *J* = 8.4 Hz, 2 H); 7.67 (d, *J* = 4.2 Hz, 1 H); 7.42 (d, *J* = 4.2 Hz, 1 H); 3.93 (s, 3 H); 2.57 (s, 3 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 190.9; 166.8; 151.3; 144.7; 137.8; 133.7; 130.8; 130.7; 126.4; 125.5; 52.6; 27.0.

IR (KBr): ν/cm⁻¹ = 3436 (m); 2958 (w); 1723 (vs); 1659 (vs); 1605 (w); 1436 (s); 1360 (m); 1276 (vs); 1189 (m); 1115 (m); 958 (w); 856 (w); 808 (m); 770 (m); 604 (w).

MS (EI, 70 eV): m/z (%) = 260 (M⁺; 100); 247 (10); 245 (173); 229 (21); 173 (30).

HR-MS: (C₁₄H₁₂O₃S) calculated 260.0507 found 260.0516

4-Allyl-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-one (5k)

Iodoantipyrene (628 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 10 h. The zinc reagent was reacted with allyl bromide (363 mg, 3.0 mmol) using CuCN · 2 LiCl (0.2 mL, 0.2 mmol, 0.1 equiv.), as described in the general procedure. The reaction mixture was stirred for 3 h at room temperature. Flash chromatographical purification (ether) gave the heterocycle **5k** (384 mg, 84 %, based on 2.0 mmol of the starting iodide) as a yellow oil.

Analytical data was found to match literature date.^[6]

Acetic acid 2-cyclohexanecarbonyl-4-formyl-6-methoxyphenyl ester (51)

Acetic acid 4-formyl-2-iodo-6-methoxyphenyl ester (640 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at 0 °C as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 2 h. The zinc reagent was reacted with cyclohexanecarbonyl chloride (440 mg, 3.0 mmol) using Pd(dba)₂ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 5 h at room temperature. Flash chromatographical purification (dichloromethane) gave the aldehyde **51** (456 mg, 75 %, based on 2.0 mmol of the starting aryl iodide) as a yellow solid (mp.: 95 -96 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 9.96 - 9.98 (m, 1 H); 7.68 -7.70 (m, 1 H); 7.56 - 7.58 (m, 1 H); 3.92 (s, 3 H); 3.00 (tt, *J*_A = 5.7 Hz, *J*_B = 1.8 Hz, 1 H); 2.34 (s, 3 H); 1.64 -1.93 (m, 5 H); 1.20 - 1.46 (m, 5 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 203.3; 190.5; 168.0; 152.9; 143.2; 134.5; 133.6; 123.8; 112.9; 56.6; 49.3; 28.8; 25.9; 25.7; 20.6.

IR (KBr): ν/cm⁻¹ = 3074 (w); 2942 (m); 2853 (m); 1761 (s); 1707 (s); 1682 (s); 1589 (m); 1472 (m); 1450 (m); 1431 (s); 1386 (s); 1374 (m); 1337 (m); 1289 (s); 1249 (m); 1202 (s); 1187 (s); 1148 (s); 1136 (s); 1057 (m); 1004 (m); 970 (m); 887 (m); 754 (m); 727 (m); 674 (m).

MS (EI, 70 eV): m/z (%) = 304 (M⁺, 1); 262 (36); 233 (17); 194 (7); 179 (100); 150 (2); 136 (5); 83 (2).

HR-MS: (C₁₇H₂₀O₅) calculated 304.1311 found 304.1282

3-Allyl-4,5-dimethoxybenzaldehyde (5m)

4,5-Dimethoxy-3-iodobenzaldehyde (584 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL).

The iodine-zinc exchange was performed at 0°C to room temperature as described in the general procedure, using *sec*-Bu₂Zn (1.4 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 2 h. The zinc reagent was reacted with allyl bromide (363 mg, 3.0 mmol) using CuCN · 2 LiCl (0.2 mL, 0.2 mmol, 0.1 equiv.), as described in the general procedure. The reaction mixture was stirred for 2 h at room temperature. Flash chromatographical purification (pentane : ether = 80 : 20) gave the aldehyde **5m** (317 mg, 77 %, based on 2.0 mmol of the starting aryl iodide) as a colourless oil.

¹H-NMR (CDCl₃, 300 MHz): δ = 9.86 (s, 1 H); 7.32 (d, *J* = 1.5 Hz, 1 H); 7.30 (d, *J* = 2.1 Hz, 1 H); 5.87 – 6.03 (m, 1 H); 5.01 – 5.14 (m, 2 H); 3.91 (s, 3 H); 3.89 (s, 3 H); 3.43 – 3.47 (m, 2 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 191.3; 153.3; 152.6; 136.4; 134.4; 132.3; 126.6; 116.4; 109.1; 60.8; 55.9; 34.0.

IR (film): ν/cm⁻¹ = 3079 (w); 3005 (w); 2978 (m); 2941 (m); 2837 (m); 2739 (w); 1694 (s); 1639 (m); 1586 (s); 1487 (s); 1464 (s); 1427 (s); 1388 (s); 1333 (m); 1299 (s); 1232 (m); 1140 (s); 1074 (m); 1003 (s); 915 (m); 858 (m).

MS (EI, 70 eV): m/z (%) = 206 (M⁺, 100); 191 (4); 177 (14); 163 (9); 147 (7); 135 (11); 131 (13); 103 (22); 91 (14).

HR-MS: (C₁₂H₁₄O₃) calculated 206.0943 found 206.0944

5'-Formyl-2',3'-dimethoxy-4-biphenylcarboxylic acid methyl ester (5n)

4,5-Dimethoxy-3-iodobenzaldehyde (584 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at 0 °C as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange completed after 2 h. The zinc reagent was reacted with methyl 4-iodobenzoate

(420 mg, 1.6 mmol) using Pd(dba)₂ (30 mg, 2.5 mol%) and tfp (25 mg, 5.0 mol%), as described in the general procedure. The reaction mixture was stirred for 6 h at room temperature. Flash chromatographical purification (dichloromethane) gave the biphenyl **5n** (360 mg, 60 %, based on 1.6 mmol of the aryl iodide) as a white solid (mp. 118 - 119 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 9.87 (s, 1 H); 8.02 - 8.05 (d, *J* = 8.1 Hz, 2 H); 7.53 - 7.56 (d, *J* = 8.7 Hz, 2 H); 7.41 (s, 2 H); 3.91 (s, 3 H); 3.87 (s, 3 H); 3.63 (s, 3 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 191.3; 167.3; 154.2; 152.4; 142.1; 135.4; 132.9; 130.0; 129.8; 129.6; 127.2; 110.7; 61.3; 56.5; 52.6.

IR (film): ν/cm⁻¹ = 2950 (w); 2848 (w); 1722 (s); 1698 (vs); 1612 (m); 1584 (s); 1455 (s); 1387 (s); 1292 (s); 1251 (m); 1187 (m); 1141 (s); 1024 (m); 976 (m); 852 (m); 773 (m); 710 (s); 619 (m); 495 (w).

MS (EI, 70 eV): m/z (%) = 300 (M⁺, 519); 269 (19); 241 (8); 226 (18); 198 (13); 155 (5); 135 (12); 99 (4).

HR-MS: (C₁₇H₁₆O₅) calculated 300.0998 found 300.0992

2-(2-Acetoxy-5-formyl-3-iodobenzyl)acrylic acid ethyl ester (5o)

Acetic acid 4-formyl-2,6-diiodophenyl ester (832 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at 0 °C as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 2 h. The zinc reagent was reacted with ethyl (2-bromomethyl)acrylate (570 mg, 3.0 mmol) using CuCN · 2 LiCl (0.2 mL, 0.2 mmol, 0.1 equiv.), as described in the general procedure. The reaction mixture was stirred for 3 h at room temperature. Flash chromatographical purification (toluene : ethyl acetate = 95 : 5) gave the aldehyde **5o**

(241 mg, 60 %, based on 2.0 mmol of the starting aryl iodide) as a colourless oil.

¹H-NMR (CDCl₃, 300 MHz): δ = 9.82 (s, 1 H); 8.14 (d, *J* = 2.1 Hz, 1 H); 7.66 (d, *J* = 1.8 Hz, 1 H); 6.26 (d, *J* = 0.9 Hz, 1 H); 5.44 (d, *J* = 1.2 Hz, 1 H); 4.10 – 4.13 (d, *J* = 7.2 Hz, 2 H); 3.56 (s, 2 H); 2.32 (s, 3 H); 1.17 – 1.22 (t, *J* = 7.2 Hz, 3 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 190.0; 167.9; 166.6; 154.9; 139.5; 137.9; 135.9; 134.8; 132.4; 128.0; 93.3; 61.5; 33.7; 21.6; 14.5.

IR (film): ν/cm⁻¹ = 2982 (m); 2851 (w); 1769 (s); 1704 (s); 1632 (m); 1593 (m); 1566 (m); 1427 (m); 1370 (s); 1300 (m); 1257 (s); 1211 (s); 1143 (s); 1099 (s); 1010 (m); 952 (w); 896 (m); 816 (w); 709 (w); 675 (w).

MS (EI, 70 eV): *m/z* (%) = 402 (M⁺, 2); 360 (45); 314 (77); 285 (17); 257 (4); 207 (2); 187 (5); 159 (11); 103 (10); 77 (6); 43 (100).

HR-MS: (C₁₅H₁₅IO₅) calculated 401.9964 found 401.9977

2-(2-Indan-1-ylidene-2-phenylethyl)acrylic acid ethyl ester **(8)**

1-Phenyl-4-(2-iodophenyl)-1-butyne (664 mg, 2.0 mmol) and Li(acac) (21 mg, 0.2 mmol) were dissolved in dry NMP (1.5 mL). The iodine-zinc exchange was performed at room temperature as described in the general procedure, using *i*Pr₂Zn (0.2 mL, 1.1 mmol, 0.55 equiv.). The iodine-zinc exchange was completed after 12 h. The zinc reagent was transmetallated by addition of stoichiometric amount of CuCN · 2 LiCl (2.2 mL, 2.2 mmol, 1.1 equiv.). Heating the mixture for 8 h at 60 °C resulted in a carbocupration reaction as checked by GC-analysis.^[3] Subsequent treatment with ethyl (2-bromomethyl)acrylate (570 mg, 3.0 mmol) at 0 °C, followed by stirring for 5 h at room temperature gave the carbocycle **8**. Flash

chromatographical purification (pentane : ether = 98 : 2) gave pure **8** (343 mg, 54 %, based on 2.0 mmol of the starting aryl iodide) as a white solid (mp.: 62 - 63 °C).

¹H-NMR (CDCl₃, 300 MHz): δ = 7.04 - 7.39 (m, 9 H); 6.18 (m, 1 H); 5.69 (m, 1 H); 4.14 (q, J = 7.2 Hz, 2 H); 3.73 (s, 2 H); 2.74 - 2.83 (m, 2 H); 2.61 - 2.70 (m, 2 H); 1.22 (t, J = 6.9 Hz, 3 H).

¹³C-NMR (CDCl₃, 75 MHz): δ = 167.4; 147.7; 144.1; 142.3; 140.8; 137.3; 130.3; 128.5; 128.3; 127.9; 126.7; 126.5; 125.5; 125.2; 124.3; 60.9; 36.8; 34.0; 30.5; 14.3.

IR (film): ν/cm^{-1} = 3066 (w); 3027 (w); 2980 (w); 2950 (w); 1720 (s); 1636 (m); 1598 (w); 1492 (m); 1470 (m); 1443 (m); 1387 (m); 1259 (s); 1163 (s); 1112 (w); 1027 (m); 946 (m); 756 (s); 704 (m).

MS (EI, 70 eV): m/z (%) = 318 (M⁺, 65); 289 (16); 272 (16); 243 (25); 227 (42); 205 (100); 165 (12); 153 (9); 129 (16); 115 (27); 91 (22).

HR-MS: (C₂₂H₂₂O₂) calculated 318.1620 found 318.1620

References and Notes:

- [1] H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* **1997**, *62*, 7512.
- [2] H.-S. Lin, L. Paquette, *Synth. Commun.* **1994**, *24*, 2503.
- [3] An aliquot of the reaction mixture was hydrolysed with sat. NH₄Cl solution and the organic compounds were extracted with Et₂O. The organic layer was subsequently subjected to GC-analysis.
- [4] L. J. Goossen, K. Gosh, *Eur. J. Org. Chem.* **2002**, *19*, 3254.

- [5] C. G. Blettner, W. A. Koenig, W. Stenzel, T. Schotten, *J. Org. Chem.* **1999**, *64*, 3885.
- [6] M. Abarbri, J. Thibonnet, L. Bérillon, F. Dehmel, M. Rottländer, P. Knochel, *J. Org. Chem.* **2000**, *65*, 4618.