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Direct Magnesiation of Polyfunctionalized Aromatics and Heterocycles using $(TMP)_2Mg•2LiCl$[**]

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General All reactions were carried out under an argon atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with argon prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen. Yields refer to isolated yields of compounds estimated to be > 95 % pure as determined by ^{1}H-NMR (25 °C) and capillary GC. Column chromatography was performed using SiO_2 (0.040 – 0.063 mm, 230 – 400 mesh ASTM) from Merck if not noted.

Preparation of the reagent $(TMP)_2Mg•2LiCl$ (3a): Method 1.

Magnesium turnings (0.73 g, 15 mmol) were placed in an argon flushed Schlenk-flask and dried for 10-20 min at 150 °C under high vacuum (1 mbar). The flask was evacuated under heating and refilled with argon three times and then cooled under

argon. After the addition of THF (30 mL) 1,2-dichloroethane (1.18 mL, 15 mmol) was added dropwise and the reaction was stirred until all magnesium was consumed (caution, exothermic reaction!), approximately one hour. In another argon flushed Schlenk-flask 2,2,6,6-tetramethylpiperidine (TMPH) (5.07 mL, 30 mmol) and THF (20 mL) were placed. This solution was cooled to –40°C then *n*-BuLi (2.4 M in hexane, 12.5 mL, 30 mmol) was added dropwise. After the addition the reaction mixture was warmed to 0°C and stirred at this temperature for 30 min. Then the previously prepared $MgCl_2$ solution transferred via cannula to the LiTMP solution and the reaction mixture was stirred at 0°C for 30 min, then warmed to 25°C and stirred for an additional hour. The solvents were then removed *in vacuo* affording a pale yellow solid. Freshly distilled THF was then slowly added, under vigorous stirring, until complete dissolution of the salts. The freshly prepared $(TMP)_2Mg•2LiCl$ solution was titrated prior to use at 0°C against benzoic acid using 4-(phenylazo)-diphenylamine as indicator.[1] A concentration of 0.7 M in THF was obtained.

Preparation of the reagent $(TMP)_2Mg•2LiCl$ (3a) from TMPMgCl•LiCl: Method 2.

In an argon flushed Schlenk-flask, 2,2,6,6-tetramethylpiperidine (TMPH) (5.07 mL, 30 mmol) was dissolved in THF (30 mmol). This solution was cooled to –40°C and *n*-BuLi

(2.4 M in hexane, 12.5 mL, 30 mmol) was added dropwise. After the addition was complete, the reaction mixture was warmed to 0°C and stirred at this temperature for 30 min. Freshly titrated TMPMgCl•LiCl[1] (1 M in THF, 30 mL, 30 mmol) was then added dropwise to the LiTMP solution and the reaction mixture was stirred at 0°C for 30 min, warmed to 25°C and stirred for 1 h. The solvents were then removed *in vacuo* affording a yellowish solid. Fresh distilled THF was then slowly added under vigorous stirring, until the complete dissolution of the salts. The fresh $(TMP)_2Mg•2LiCl$ solution was titrated[1] prior to use at 0°C with benzoic acid using 4-(phenylazo)-diphenylamine as indicator. A concentration of 0.7 M in THF was obtained.

Preparation of the reagent [*c*-Hex(*i*-Pr)N]$_2$Mg•2LiCl (3b):

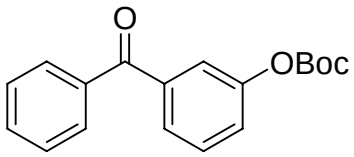
Prepared and titrated as for $(TMP)_2Mg•2LiCl$ (**3a**) (Method 1) from commercially available N-*iso*-propylcyclohexylamine (4.15 mL, 30 mmol), *n*-BuLi ((2.4 M in hexane, 12.5 mL, 30 mmol), magnesium turnings (0.73 g, 15 mmol) and 1,2-dichloroethane (1.18 mL, 15 mmol) in THF. A concentration of 0.55 M in THF was obtained.

Preparation of the reagent [*t*-Bu(*i*-Pr)N]$_2$Mg•2LiCl (3c):

Prepared and titrated as for $(TMP)_2Mg•2LiCl$ (**3a**) (Method 1) from commercially available N-*t*-butylisopropylamine (4.75 mL, 30 mmol), *n*-BuLi (2.4 M in hexane, 12.5 mL, 30 mmol), magnesium turnings (0.73 g, 15 mmol) and 1,2-dichloroethane (1.18 mL, 15 mmol) in THF. A concentration of 0.7 M in THF was obtained.

Preparation of the starting materials:

Synthesis of compound 3-benzoylphenyl *t*-butyl carbonate (5):



A dry 50 mL round-bottomed flask, equipped with a magnetic stirring bar was charged with a solution of the 3-hydroxybenzophenone (1.0 g, 5.05 mmol) in CH_2Cl_2 (20 mL). After cooling to 0 ^oC DMAP, (0.031 g, 0.25 mmol) and Boc_2O (1.3 mL, 6.06 mmol) were added, then the reaction mixture was warmed to 25 ^oC and stirred overnight. The reaction mixture was quenched with saturated aq. NH_4Cl (30 mL), extracted with CH_2Cl_2 (3 x 30 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 9:1) yielded **5** (1.46 g, 97% yield) as a colorless solid.

m.p.: 68.8 – 69.8 °C

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.84 – 7.81 (m, 2 H), 7.70 – 7.60 (m, 3 H), 7.53 – 7.49 (m, 3 H), 7.45 – 7.42 (m, 1 H), 1.58 (s, 9 H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 207.1, 195.7, 151.2, 139.1, 137.4, 132.9, 130.3, 129.6, 128.6, 127.6, 125.6, 123.1, 84.2, 27.9.

MS (70 eV, EI) *m/z* (%): 298 (1) [M^+], 283 (7), 239 (10), 198 (100), 181 (6), 121 (9), 105 (27), 77 (10), 57 (79), 42 (8).

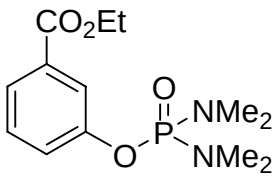
IR (ATR) $\tilde{\nu}$ **(cm^{-1})**: 2981, 1743, 1658, 1285, 1249, 1150, 960, 718, 702.

HRMS (EI) for **$C_{18}H_{18}O_4$** (298.1205): 298.1198.

Synthesis of ethyl 3-[(*t*-butoxycarbonyl)oxy]benzoate (8):

This compound was prepared from commercially available ethyl 3-hydroxybenzoate according to the procedure reported by Knochel *et al*.[2]

Synthesis of ethyl 3-{[bis(dimethylamino)phosphoryl]oxy} benzoate (11):



In a 100 mL round-bottom flask ethyl 3-hydroxybenzoate (3.32 g, 20 mmol), 4-DMAP (0.244 g, 2.0 mmol) were dissolved

in THF (20 mL), then N,N,N´,N´-tetramethyldiamidophosphorochloridate (4.50 g, 3.9 mL, 24 mmol) was carefully added, followed by the addition of triethylamine (2.43 g, 3.33 mL, 24 mmol). The resulting suspension was stirred at room temperature overnight. The mixture was quenched by the addition of a half concentrated aq. NH_4Cl solution. It was extracted with ethyl acetate (3 x 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product (colorless oil) was used without further purification.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.84 – 7.78 (m, 2 H), 7.47 – 7.37 (m, 2 H), 4.38 (q, J = 7.1 Hz, 1 H), 2.75 (d, J = 10.1 Hz, 12 H) 1.40 (t, J = 7.1 Hz, 2 H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 166.1, 151.7, 132.4, 129.8, 125.5, 124.9, 121.5, 61.4, 36.9 (4 C), 14.5.

MS (70 eV, EI) *m/z* (%): 301 (11), 300 (65) [M^+], 255 (20), 226 (13), 192 (36), 135 (100), 92 (16), 44 (32).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 3435, 2997, 1715, 1584, 1483, 1440, 1366, 1268, 1229, 1203, 1097, 1072, 986, 947, 849, 752, 673.

HRMS (EI) for **$C_{13}H_{21}N_2O_4P$** (300.1239): 300.1247.

Synthesis of *t*-butyl 4-bromobenzoate (2d):

This compound was prepared from commercially available 4-bromobenzoyl chloride according to the procedure from the literature.[3]

Synthesis of N,N'-Diethyl-3,5-pyridinedicarboxamide (2g)

This compound was prepared from commercially available pyridine-3,5-dicarboxylic acid according to the literature.[4]

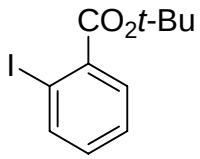
Synthesis of 2,2-dimethyl-1,3-benzodioxan-4-one (12)

This compound was prepared from salicylic acid according to the literature.[5]

Typical procedure for the magnesiation of polyfunctionalized aromatics and heterocycles with $(TMP)_2Mg•2LiCl$, $[c\text{-Hex}(i\text{-Pr})]_2Mg•2LiCl$ and $[t\text{-Bu}(i\text{-Pr})]_2Mg•2LiCl$ (TP 1):

A dry and nitrogen flushed 10 mL Schlenk-flask, equipped with a magnetic stirring bar and a septum, was charged with a solution of the corresponding arene (1.0 mmol) in dry THF (1 mL). After setting the desired temperature (Table 1), the magnesium base (1.1 to 1.2 mmol) was added dropwise and stirred at the same temperature. The completion of the metallation was checked by GC-analysis of reaction aliquots quenched with a solution of I_2 in dry diethyl ether.

Synthesis of *t*-butyl 2-iodobenzoate (4a):



t-Butyl benzoate (**2a**) (0.178 g, 1.0 mmol) was reacted with [*t*-Bu(*i*-Pr)]$_2$Mg•2LiCl (**3c**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at 25 °C for 1 h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at 0 °C, the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 25:1) furnished *t*-butyl 2-iodobenzoate **4a** (0.274 g, 90%) as a pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.72 (dd, J = 7.8 Hz, J = 1.7 Hz, 1 H), 7.70 (dd, J = 7.8 Hz, J = 1.7 Hz, 1 H), 7.40 (dd, J = 7.8 Hz, J = 1.3 Hz, 1 H), 7.12 (td, J = 7.8 Hz, J = 1.8 Hz, 1 H) 1.64 (s, 9 H).

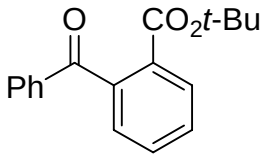
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 166.0, 141.2, 137.7, 132.2, 130.7, 128.1, 93.6, 82.9, 28.4.

MS (70 eV, EI) *m/z* (%): 290 (55) [M^+], 248 (84), 230 (100), 203 (28), 121 (13), 104 (14), 76 (86), 69 (27), 59 (22).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977, 2931, 1712, 1569, 1457, 1366, 1291, 1247, 1168, 1114, 1022, 847, 769.

HRMS (EI) for **$C_{10}H_{11}O_2I$** (303.9960): 302.9887.

Synthesis of *t*-butyl 2-benzoylbenzoate (4b):



t-Butyl benzoate (**2a**) (0.178 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at 25 °C for 1 h, according to **TP 1**. The reaction mixture was cooled to -40 °C, CuCN•2LiCl (1.0 M solution in THF, 0.2 mL, 0.2 mmol) was added and the reaction mixture was stirred for 15 min. Thereafter, benzoyl chloride (0.264 mL, 2.2 mmol) was added at -40 °C and the reaction mixture stirred for 2 h at this temperature. Then the reaction was quenched with sat. aq. NH_4Cl solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 5:1) furnished compound **4b** (0.263 g, 93%) as a colorless solid.

m.p.: 65.2 – 67.3 °C

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.03 (dd, J = 7.4 Hz, J = 1.5 Hz, 1 H), 7.80 (m, 2 H), 7.65 – 7.55 (m, 3 H), 7.48 – 7.38 (m, 3 H), 1.25 (s, 9 H).

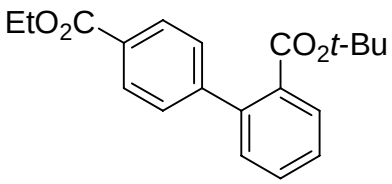
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 196.9, 165.5, 141.2, 137.5, 133.4, 132.2, 131.5, 130.2, 129.9, 128.7, 127.9, 82.9, 27.7.

MS (70 eV, EI) *m/z* (%): 282 (10) [M^+], 227 (67), 209 (100), 181 (48), 152 (25), 149 (17), 105 (32), 77 (15), 57 (12).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2990, 1980, 1703, 1664, 1594, 1450, 1371, 1283, 1247, 1167, 1120, 1037, 932, 844, 805, 778, 720, 700, 665, 635.

HRMS (EI) for **$C_{18}H_{18}O_3$** (282.1255): 282.1232.

Synthesis of 2-*t*-butyl 4'-ethyl biphenyl-2,4'-dicarboxylate (4c):



t-Butyl benzoate (**2a**) (0.178 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at 25 °C for 1 h, according to **TP 1**. The mixture was then cooled to -40 °C and $ZnCl_2$ (1 M in THF, 1.2 mL, 1.2 mmol) was added and the reaction mixture was stirred for 15 min. $Pd(dba)_2$ (11 mg, 2 mol%) and P(*o*-furyl)$_3$ (9 mg, 4 mol%) dissolved in THF (0.5 mL) were then transferred via cannula to the reaction mixture, followed by the addition of ethyl 4-iodobenzoate (0,414 g, 1.5 mmol) dissolved in THF (0.5 mL). The reaction mixture was slowly warmed to 25°C and stirred at this temperature for 12 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution, extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-

pentane/diethyl ether, 10:1) furnished the biphenyl derivative **4c** (0.267 g, 82%) as a colorless oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.11 (d, J = 8.2 Hz, 2 H), 7.86 (dd, J = 7.7 Hz, J = 1.5 Hz, 1 H), 7.54 (dd, J = 7.4 Hz, J = 1.4 Hz, 1 H), 7.46 (dd, J = 7.5 Hz, J = 1.4 Hz, 1 H), 7.42 (d, J = 8.2 Hz, 2 H), 7.33 (dd, J = 7.5 Hz, J = 1.3 Hz, 1 H), 4.43 (q, J = 7.1 Hz, 2 H), 1.45 (t, J = 7.1 Hz, 3 H), 1.29 (s, 9 H).

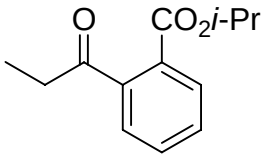
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 167.8, 166.8, 146.9, 141.4, 132.9, 131.1, 130.6, 130.2, 129.4, 128.9, 127.9, 81.8, 61.2, 27.9, 14.6.

MS (70 eV, EI) *m/z* (%): 326 (5) [M^+], 281 (5), 270 (100), 253 (7), 242 (32), 225 (71), 181 (10), 152 (15), 151 (6), 57 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2978, 2933, 1707, 1610, 1367, 1268, 1125, 1098, 847, 752, 703.

HRMS (EI) for **$C_{20}H_{22}O_4$** (326.1518): 326.1500.

Synthesis of *i*-propyl 2-propionylbenzoate (4d):



i-Propyl benzoate (**2b**) (0.164 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at 25 °C for 1 h, according to **TP 1**. The reaction mixture was cooled to -40 °C, CuCN•2LiCl (1.0 M solution in THF, 0.2 mL, 0.2 mmoL) was added and the reaction was stirred for 15 min. Thereafter,

propionyl chloride (0.191 mL, 2.2 mmol) was added at -40 °C, reaction mixture was stirred for 2 h at this temperature. Then the reaction was quenched with sat. aq. NH_4Cl solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 10:1) furnished compound **4d** (0.226 g, 78%) as pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.92 (dd, J = 7.6 Hz, J = 1.8 Hz, 1 H), 7.57 (td, J = 7.5 Hz, J = 1.4 Hz, 1 H), 7.49 (td, J = 7.6 Hz, J = 1.5 Hz, 1 H), 7.34 (dd, J = 7.6 Hz, J = 1.3 Hz, 1 H), 5.24 (sept, J = 6.2 Hz, 1 H), 2.85 (q, J = 7.1 Hz, 2 H), 1.36 (d, J = 6.4 Hz, 6 H), 1.25 (t, J = 7.1 Hz, 3 H).

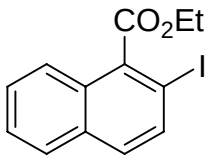
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 206.8, 166.4, 143.7, 132.2, 130.2, 129.7, 129.3, 126.3, 69.6, 36.5, 22.0, 8.4.

MS (70 eV, EI) *m/z* (%): 161 [M^+-*i*-Pr] (12), 160 (100), 131 (18), 104 (60), 77 (12), 76 (21), 66 (8), 50 (8).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2940, 1851, 1771, 1694, 1468, 1336, 1256, 1130, 1057, 995, 899, 760, 712, 693.

HRMS (ESI) for **$C_{13}H_{16}O_3$** (221.1178 $[M+H]^+$): 221.1168 $[M+H]^+$.

Synthesis of ethyl 2-iodonaphthalene-1-carboxylate (4e):



Ethyl 1-naphthoate (**2c**) (0.200 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at 0 °C for 3 h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at 0 °C, the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 25:1) furnished 2-iodonaphthalene-1-carboxylate (**4e**) (0.271 g, 83%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.87 – 7.84 (m, 2 H), 7.79 – 7.76 (m, 1 H), 7.60 (d, J = 8.7 Hz, 1 H), 7.63 – 7.54 (m, 2 H), 4.60 (q, J = 7.1 Hz, 2 H), 1.52 (t, J = 7.1 Hz, 3 H).

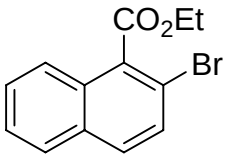
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 169.1, 138.5, 135.4, 132.5, 131.1, 130.8, 128.5, 128.0, 127.2, 124.9, 90.9, 62.4, 14.5.

MS (70 eV, EI) *m/z* (%): 326 (100) [M^+], 298 (6), 281 (60), 253 (12), 170 (3), 155 (10), 127 (21), 125 (40), 115 (5), 74 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2978, 1723, 1578, 1501, 1379, 1272, 1230, 1136, 1104, 1030, 806, 740, 664, 560.

HRMS (EI) for **$C_{13}H_{11}O_2{}^{127}I$** (325.9803): 325.9796.

Synthesis of ethyl 2-bromonaphthalene-1-carboxylate (4f):



Ethyl 1-naphthoate (**2c**) (0.200 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at 0 °C for 3 h, according to **TP 1**. $BrCl_2CCCl_2Br$ (0.779 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at 0 °C, the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 25:1) furnished 2-bromonaphthalene-1-carboxylate (**4f**) (0.233 g, 83%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.87 – 7.84 (m, 2 H), 7.79 – 7.76 (m, 1 H), 7.60 (d, J = 8.7 Hz, 1 H), 7.63 – 7.54 (m, 2 H), 4.60 (q, J = 7.1 Hz, 2 H), 1.52 (t, J = 7.1 Hz, 3 H).

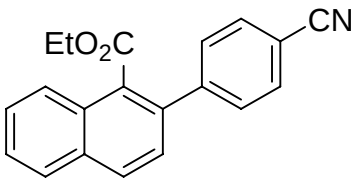
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 169.1, 138.5, 135.4, 132.5, 131.1, 130.8, 128.5, 128.0, 127.2, 124.9, 90.9, 62.4, 14.5.

MS (70 eV, EI) *m/z* (%): 326 (100) [M^+], 298 (6), 281 (60), 253 (12), 170 (3), 155 (10), 127 (21), 125 (40), 115 (5), 74 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2978, 1723, 1578, 1501, 1379, 1272, 1230, 1136, 1104, 1030, 806, 740, 664, 560.

HRMS (EI) for **$C_{13}H_{11}O_2{}^{127}I$** (325.9803): 325.9796.

Synthesis of ethyl 2-(4-cyanophenyl)-1-naphthoate (4g):



Ethyl 1-naphthoate (**2c**) (0.200 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at 0 °C for 3 h, according to **TP 1**. The mixture was then cooled to -40 °C and $ZnCl_2$ (1 M in THF, 1.2 mL, 1.2 mmol) was added and the reaction mixture stirred for 15 min. $Pd(dba)_2$ (11 mg, 2 mol%) and P(*o*-furyl)$_3$ (9 mg, 4 mol%) dissolved in THF (0.5 mL) were then transferred via cannula to the reaction mixture, followed by the addition of 4-iodobenzonitrile (0.342 g, 1.5 mmol) dissolved in THF (1.5 mL). The reaction mixture was slowly warmed to 25°C and stirred at this temperature for 12 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution, extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 4:1) furnished the biphenyl derivative **4g** (0.244 g, 81%) as pale yellow solid.

m.p.: 105.6 – 107.9 °C

^{1}H-NMR (400 MHz, $CDCl_3$) δ : 8.00 (m, 2 H), 7.90 (m, 1 H), 7.72 (ddd, J = 8.4 Hz, J = 1.9 Hz, J = 1.7 Hz, 2 H), 7.58 (m, 4 H), 7.44 (d, J = 8.4 Hz, 1 H), 4.18 (q, J = 7.0 Hz, 2 H), 1.03 (t, J = 7.1 Hz, 3 H).

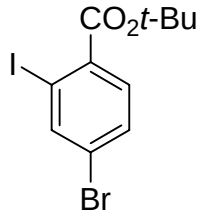
^{13}C-NMR (100 MHz, $CDCl_3$) δ: 169.0, 146.1, 136.3, 133.0, 132.3, 130.7, 130.5, 130.1, 129.7, 128.4, 127.2, 126.7, 125.4, 118.9, 111.7, 61.7, 14.0.

MS (70 eV, EI) *m/z* (%): 302 (17), 301 (77) [M^+], 273 (9),257 (27), 256 (100), 228 (36), 227 (71), 226 (13), 201 (18), 200 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977, 2899, 2223, 1711, 1604, 1593, 1502, 1470, 1429, 1377, 1281, 1233, 1149, 1137, 1033, 1022, 1002, 959, 862, 822, 801, 757, 663.

HRMS (EI) for **$C_{20}H_{15}NO_2$** (301.1103): 301.1084.

Synthesis of *t*-butyl *p*-bromo-2-iodobenzoate (4h):



t-Butyl 4-bromobenzoate (**2d**) (0.178 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3c**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at -20 °C for 1h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at 0 °C, the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-

pentane/diethyl ether, 50:1) furnished **4h** (0.272 g, 71%) as yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.14 (d, J = 1.8 Hz, 1 H), 7.59 (d, J = 8.3 Hz, 1 H), 7.52 (dd, J = 8.3 Hz, J = 1.8 Hz, 1 H), 1.63 (s, 9 H).

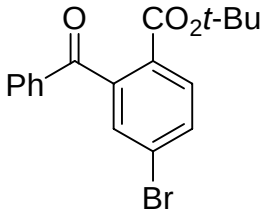
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 165.5, 143.3, 136.2, 131.7, 131.2, 125.9, 94.4, 83.2, 28.4.

MS (70 eV, EI) m/z (%): 382 (10) [M^+], 321 (100), 305 (33), 279 (5), 154 (7), 75 (20).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977, 2931, 1712, 1568, 1456, 1367, 1290, 1247, 1167, 1113, 1021, 847, 768, 724, 677.

HRMS (EI) for **$C_{11}H_{12}O_2BrI$** (381.9065): 381.9089.

Synthesis of *t*-butyl 2-benzoyl-4-bromobenzoate (4i):



t-Butyl 4-bromobenzoate (**2d**) (0.178 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3c**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at -20 °C for 1h, according to **TP 1**. CuCN•2LiCl (1.0 M in THF, 0.2 mL, 0.2 mmoL) was added at -40 °C at and the reaction mixture was stirred for 15 min. Thereafter, benzoyl chloride (0.264 mL, 2.2 mmol) was added at -40 °C and the reaction mixture was stirred for 2 h at this temperature. Then the reaction was

quenched with sat. aq. NH_4Cl solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 5:1) furnished **4i** (0.278 g, 77%) as yellow solid.

m.p.: 71.1 – 73.3 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ : 7.90 (d, J = 8.4 Hz, 1H), 7.80 – 7.78 (m, 2 H), 7.70 (dd, J = 8.4 Hz, J = 2.1 Hz, 1 H), 7.62 – 7.57 (m, 1 H), 7.53 – 7.44 (m, 3 H), 1.24 (s, 9 H).

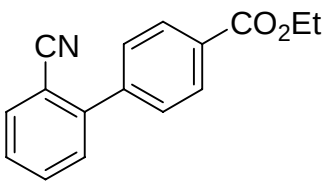
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 195.2, 164.7, 142.8, 136.9, 133.7, 132.9, 131.8, 130.8, 130.2, 129.9, 128.8, 127.1, 83.4, 27.7.

MS (70 eV, EI) *m/z* (%): 360 (7) [M^+-H], 307 (89), 305 (39), 287 (65), 227 (11), 181 (100), 152 (39), 105 (80), 77 (35), 57 (43).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2979, 2933, 1713, 1674, 1538, 1449, 1392, 1368, 1299, 1289, 1128, 1093, 946, 848, 696.

HRMS (EI) for **$C_{18}H_{17}BrO_3$** (360.0361): 360.0343.

Synthesis of ethyl 2'-cyanobiphenyl-4-carboxylate (4j):



Benzonitrile (**2e**) (0.104 mL, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at

-30 °C for 3 h, according to **TP 1**. The mixture was then cooled to -40 °C and $ZnCl_2$ (1 M solution in THF, 1.2 mL, 1.2 mmol) was added and the reaction mixture stirred for 15 min. $Pd(dba)_2$ (11 mg, 2 mol%) and P(*o*-furyl)$_3$ (9 mg, 4 mol%) dissolved in THF (0.5 mL) were then transferred via cannula to the reaction mixture, followed by the addition of ethyl 4-iodobenzoate (0.414 g, 1.5 mmol) dissolved in THF (0.5 mL). The reaction mixture was slowly warmed to 25°C and stirred at this temperature for 12 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution, extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 4:1) furnished the biphenyl derivative **4j** (0.176 g, 70%) as colorless solid.

m.p.: 115.0 – 117.3 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ : 8.19 (d, J = 8.2 Hz, 2 H), 7.81 (d, J = 8.2 Hz, 1 H), 7.67 (m, 3 H), 7.54 (m, 2 H), 4.44 (q, J = 7.3 Hz, 2 H), 1.44 (t, J = 7.1 Hz, 3 H).

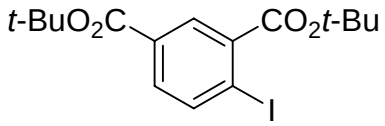
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 166.4, 144.7, 142.6, 134.1, 133.2, 131.1, 130.3, 130.2, 129.1, 128.4, 118.6, 11.6, 61.4, 14.6.

MS (70 eV, EI) *m/z* (%): 251 (30) [M^+], 223 (33), 207 (17), 206 (100), 179 (26), 178 (32), 177 (30), 152 (11), 151 (39), 150 (15), 75 (9).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2908, 2224, 1708, 1607, 1594, 1559, 1478, 1406, 1366, 1315, 1272, 1184, 1110, 1097, 1030, 860, 763, 740, 721, 704.

HRMS (EI) for **$C_{16}H_{13}NO_2$** (251.0946): 251.0960.

Synthesis of Di-*t*-butyl 4-iodobenzene-1,3-dioate (4k):



Di-*t*-butyl isophthalate (**2f**) (0.278 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at 0 °C for 1 h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at 0 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 9:1) furnished the 4-iodobenzene-1,3-dioate **4k** (0.380 g, 94%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.21 (d, J = 2.1 Hz, 1 H), 7.99 (d, J = 8.4 Hz, 1 H), 7.66 (dd, J = 8.4 Hz, J = 2.1 Hz, 1 H), 1.63 (s, 9 H), 1.59 (s, 9 H).

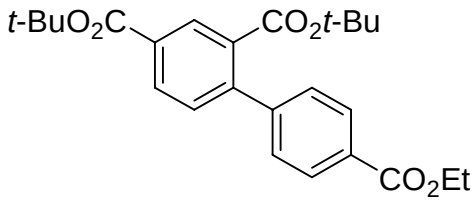
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 165.6, 165.5, 141.0, 137.66, 132.1, 131.9, 130.9, 98.9, 83.1, 81.9, 28.1.

MS (70 eV, EI) *m/z* (%): 404 (8), 348 (27), 292 (15), 275 (28), 165 (2), 127 (2), 103 (2), 75 (3), 57 (10), 41 (2).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977, 2932, 1713, 1590, 1367, 1245, 1154, 1140, 1014, 842, 758, 732.

HRMS (EI) for **$C_{16}H_{29}O_4I$** (404.0485): 404.0498.

Synthesis of 2,4-di-*t*-butyl 4'-ethyl biphenyl-2,4,4'-tricarboxylate (4l):



Di-*t*-butyl isophthalate (**2f**) (0.278 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at 0 °C for 1 h, according to **TP 1**. The mixture was then cooled to -40 °C and $ZnCl_2$ (1 M solution in THF, 1.2 mL, 1.2 mmol) was added and the reaction mixture stirred for 15 min. $Pd(dba)_2$ (11 mg, 2 mol%) and P(*o*-furyl)$_3$ (9 mg, 4 mol%) dissolved in THF (0.5 mL) were then transferred via cannula to the reaction mixture, followed by the addition of ethyl 4-iodobenzoate (0.414 g, 1.5 mmol) dissolved in THF (0.5 mL). The reaction mixture was slowly warmed to 25°C and stirred at this temperature for 12 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution, extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 8:1) furnished the biphenyl derivative **4l** (0.375 g, 88%) as yellow oil.

^{1}H-NMR (600 MHz, $CDCl_3$) δ: 8.39 (d, J = 1.3 Hz, 1 H), 8.08 (m, 3 H), 7.36 (m, 3 H), 4.39 (q, J = 7.1 Hz, 2 H), 1.60 (s, 9 H), 1.40 (t, J = 7.1 Hz, 3 H), 1.26 (s, 9 H).

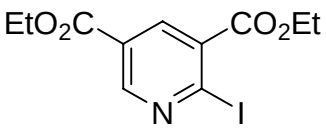
^{13}C-NMR (150 MHz, $CDCl_3$) δ: 167.0, 166.6, 165.0, 145.9, 133.1, 131.8, 131.7, 131.1, 130.7, 129.8, 129.6, 128.7, 82.2, 81.9, 61.3, 28.4, 27.8, 14.5.

MS (70 eV, EI) m/z (%): 426 (1) [M^+], 371 (14), 370 (48), 353 (15), 315 (14), 314 (59),297 (19), 286 (61), 269 (75), 225 (16), 179 (15), 151 (26), 141 (13), 57 (100).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2977, 2931, 1710, 1605, 1476, 1392, 1366, 1310, 1269, 1251, 1158, 1140, 1099, 1025, 1005, 933, 843, 762, 701.

HRMS (EI) for **$C_{25}H_{30}O_6$** (426.2042): 426.2041.

Synthesis of diethyl 2-iodopyridine-3,5-dicarboxylate (4m):



Diethyl pyridine-3,5-dicarboxylate (**2g**) (0.129 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at -40 ^{o}C for 3 h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at -40 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 ×

15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 9:1) furnished 2-iodopyridine-3,5-dicarboxylate **4m** (0.269 g, 77%) as a pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.98 (d, J = 2.3 Hz, 1 H), 8.49 (d, J = 2.3 Hz, 1 H), 4.48 (q, J = 7.2 Hz, 2 H), 4.46 (q, J = 7.2 Hz, 2 H), 1.47 (t, J = 7.2 Hz, 3 H), 1.44 (t, J = 7.2 Hz, 3 H).

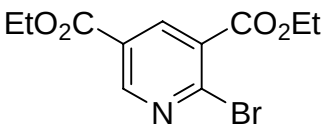
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 165.2, 164.4, 152.7, 138.7, 133.7, 125.6, 122.5, 62.8, 62.5, 14.5, 14.1.

MS (70 eV, EI) *m/z* (%): 349 (100) [M^+], 304 (24), 276 (8), 222 (28), 193 (32), 178 (13), 165 (14), 138 (4), 122 (3), 104 (4), 93 (3), 76 (6).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2989, 2938, 1728, 1714, 1584, 1377, 1238, 1210, 1102, 1018, 760.

HRMS (EI) for **$C_{11}H_{12}O_4NI$** (348.9811): 348.9891.

Synthesis of diethyl 2-bromopyridine-3,5-dicarboxylate (4n):



Diethyl pyridine-3,5-dicarboxylate (**2g**) (0.129 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at -40 °C for 3 h, according to **TP 1**. $BrCl_2CCCl_2Br$

(0.779 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at -40 °C, the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 9:1) furnished diethyl 2-bromopyridine-3,5-dicarboxylate **4n** (0.211 g, 70%) as a pale yellow solid.

m.p.: 40.2 – 41.8 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 8.95 (d, J = 2.3 Hz, 1 H), 8.52 (d, J = 2.3 Hz, 1 H), 4.39 (q, J = 7.1 Hz, 2 H), 4.38 (q, J = 7.1 Hz, 2 H), 1.37 (t, J = 7.1 Hz, 3 H), 1.36 (t, J = 7.1 Hz, 3 H).

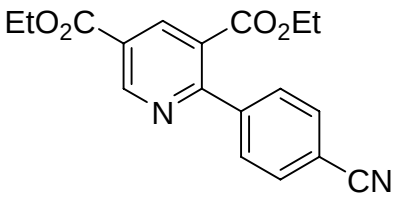
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 164.6, 164.0, 152.7, 140.3, 130.2, 125.6, 63.3, 62.8, 14.4, 14.3.

MS (70 eV, EI) *m/z* (%): 301 (40) [M^+], 275 (28), 273 (30), 258 (100), 255 (94), 230 (37), 228 (39), 202 (11), 194 (27), 166 (15), 76 (15), 45 (10).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2996, 1733, 1717, 1588, 1551, 1380, 1243, 1229, 1109, 1049, 1017, 762.

HRMS (EI) for **$C_{11}H_{12}O_4NBr$** (300.9949): 300.9952.

Synthesis of diethyl 2-(4-cyanophenyl)pyridine-3,5-dicarboxylate (4o):



Diethyl pyridine-3,5-dicarboxylate (**2g**) (0.129 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at -40 °C for 3 h, according to **TP 1**. Then $ZnCl_2$ (1 M solution in THF, 1.2 mL, 1.2 mmol) was added and the reaction mixture stirred for 15 min. $Pd(dba)_2$ (11 mg, 2 mol%) and P(*o*-furyl)$_3$ (9 mg, 4 mol%) dissolved in THF (0.5 mL) were then transferred via cannula to the reaction mixture, followed by the addition of 4-iodobenzonitrile (0.342 g, 1.5 mmol) dissolved in THF (1.5 mL). The reaction mixture was slowly warmed to 25°C and stirred at this temperature for 12 h. The reaction mixture was quenched with sat. aq. NH_4Cl solution, extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 3:1) furnished the biphenyl derivative **4o** (0.237 g, 73%) as colorless solid.

m.p.: 119.0 – 113.9 °C.

^{1}H-NMR (600 MHz, $CDCl_3$) δ: 9.32 (d, J = 2.0 Hz, 1 H), 8.73 (d, J = 2.2 Hz, 1 H), 7.73 (d, J = 8.6 Hz, 2 H), 7.64 (d, J = 8.6 Hz, 2 H), 4.55 (d, J = 7.1 Hz, 2 H), 4.21 (d, J = 7.1 Hz, 2 H), 1.43 (t, J = 7.1 Hz, 3 H), 1.13 (t, J = 7.1 Hz, 3 H).

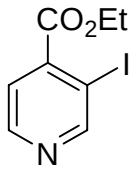
^{13}C-NMR (150 MHz, $CDCl_3$) δ: 166.5, 164.4, 160.5, 152.4, 144.0, 139.6, 132.1, 129.7, 127.2, 125.5, 118.8, 113.2, 62.3, 62.2, 14.5, 14.0.

MS (70 eV, EI) *m/z* (%): 324 (9) [M^+], 296 (17), 295 (100), 179 (24), 267 (59), 251 (11), 223 (10), 152 (10),140 (7), 102 (4).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2979, 2911, 2224, 1721, 1596, 1448, 1398, 1319, 1244, 1227, 1148, 1091, 1018, 149, 852, 798, 775, 743, 646.

HRMS (EI) for **$C_{18}H_{16}N_2O_4$** (324.1110): 324.1111.

Synthesis of ethyl 3-iodopyridine-4-carboxylate (4p):



Ethyl isonicotinate (**2h**) (0.151 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.71 mL, 1.2 mmol) at -40 °C for 12 h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at -40 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-

pentane/diethyl ether, 7:3) furnished ethyl 3-iodopyridine-4-carboxylate **4p** (0.152 g, 66%) as a light brown oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 9.12 (s, 1 H), 8.62 (d, J = 4.9 Hz, 1 H), 7.65 (d, J = 4.9 Hz, 1 H), 4.45 (q, J = 7.1 Hz, 2 H), 1.45 (t, J = 7.1 Hz, 3 H).

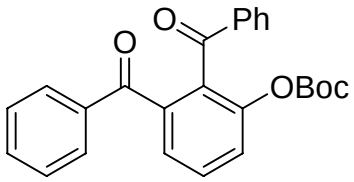
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 165.2, 159.8, 149.3, 142.7, 124.6, 92.6, 62.7, 14.4.

MS (70 eV, EI) m/z (%): 277 (100) [M^+], 248 (47), 232 (57), 204 (24), 177 (23), 127 (5), 122 (10), 94 (7), 78 (4), 50 (1).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2980, 1727, 1464, 1260, 1078, 1010, 776, 700, 662.

HRMS (EI) for **$C_8H_8INO_2$** (276.9599): found 276.9590.

Synthesis of *t*-butyl 2,3-dibenzoylphenyl carbonate (7):



3-Benzoylphenyl t-butyl carbonate (**5**) (0.298 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at -20 °C for 4 h, according to **TP 1**. CuCN•2LiCl (1.0 M solution in THF, 1.1 mL, 1.1 mmoL) was added at -20 °C at and the reaction mixture was stirred for 15 min. Thereafter, benzoyl chloride (0.264 mL, 2.2 mmol) was added at -20 °C and the reaction mixture was stirred for 2 h. Then the reaction

was quenched with sat. aq. NH_4Cl solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 4:1) furnished **7** (0.305 g, 72%) as a colorless solid.

m.p.: 138.6 - 140.1 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.82 – 7.76 (m, 4 H), 7.62 – 7.51 (m, 4 H), 7.49 – 7.39 (m, 5 H), 1.34 (s, 9 H).

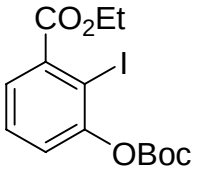
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 195.6, 194.5, 151.1, 148.9, 140.0, 137.7, 134.5, 133.4, 130.5, 130.0, 129.5, 128, 6, 128.5, 128.0, 126.3, 84.3, 27.6.

MS (70 eV, EI) *m/z* (%): 303 (18), 302 (100), 301 (63) [M^+-Boc], 225 (56), 77 (34), 57 (45), 44 (13), 41 (19).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2984, 1765, 1672, 1658, 1596, 1446, 1250, 1223, 1151, 1132, 927, 836, 700.

HRMS (ESI) for **$C_{25}H_{22}O_5$** (403.11545 [M^++H]): 403.1548 [M^++H].

Synthesis of *t*-butyl 3-[(*t*-butoxycarbonyl)oxy]-2-iodobenzoate (10):



Ethyl 3-[(*t*-butoxycarbonyl)oxy]benzoate (**8**) (0.266 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57

mL, 1.1 mmol) at 0 °C for 2 h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at -40 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/diethyl ether, 8:1) furnished iodide **10** (0.152 g, 78%) as a pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.61 (dd, J = 7.61 Hz, J = 1.6 Hz, 1 H), 7.41 (t, J = 7.8 Hz, 1 H), 7.31 (dd, J = 7.8 Hz, J = 1.6 Hz, 1 H), 4.43 (q, J = 7.2 Hz, 2 H), 1.6 (s, 9 H), 1.43 (t, J = 7.2 Hz, 3 H).

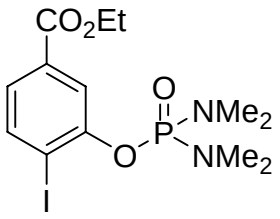
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 166.6, 152.2, 151.0, 138.6, 129.4, 125.5, 92.1, 84.7, 62.2, 27.9, 14.4.

MS (70 eV, EI) *m/z* (%): 392 (2) [M^+], 318 (10), 291 (100), 246 (31), 91 (5), 57 (69).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2976, 1767, 1756, 1724, 1225, 1137, 1023, 871, 739.

HRMS (EI) for **$C_{14}H_{18}O_5$** (392.0120): 392.0126.

Synthesis of ethyl 3-{[bis(dimethylamino)phosphoryl]oxy} 4-iodobenzoate (13):



Ethyl 3-{[bis(dimethylamino)phosphoryl]oxy}benzoate (**11**) (0.300 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at 0 °C for 1 h, according to **TP 1**. I_2 (0.609 g, 2.4 mmol) dissolved in dry THF (2 mL) was then added dropwise at -40 °C and the resulting mixture was warmed to 25 °C and stirred for 1 h. The reaction mixture was quenched with sat. aq. $Na_2S_2O_3$ solution (5 mL), extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvent was evaporated *in vacuo*. Purification by flash-chromatography (ethyl acetate) furnished iodide **13** (0.388 g, 91%) as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.98 (dd, J = 1.7 Hz, J = 1.2 Hz, 1 H), 7.85 (dd, J = 8.2 Hz, J = 0.9 Hz, 1 H), 7.52 (dd, J = 8.3 Hz, J = 1.4 Hz, 1 H) , 4.3 (q, J = 7.1 Hz, 2 H) , 2.8 (d, J = 10.1 Hz, 12 H) , 1.4 (t, J = 7.2 Hz, 3 H).

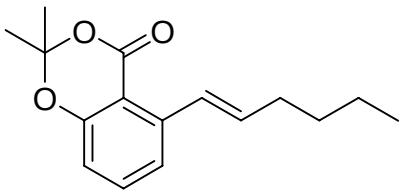
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 165.7, 151.8, 151.7, 139.8, 132.5, 126.3, 120.4, 120.3, 95.1, 61.5, 37.1, 14.5.

MS (70 eV, EI) *m/z* (%): 426 (18) [M^+], 381 (5), 300 (13), 299 (100), 135 (60), 44 (15).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2930, 2900, 1716, 1469, 1400, 1289, 1208, 1102, 98, 953, 850, 754, 677.

HRMS (EI) for **$C_{13}H_{20}O_4N_2IP$** (426.0205): 426.0221.

Synthesis of 5-[(1*E*)-hex-1-en-1-yl]-2,2-dimethyl-4*H*-1,3-benzodioxin-4-one (17):



Dimethyl-1,3-benzodioan-4-one **14** (0.178 g, 1.0 mmol) was reacted with $(TMP)_2Mg•2LiCl$ (**3a**) (0.7 M in THF, 1.57 mL, 1.1 mmol) at -40 °C for 10 min, according to **TP 1**. $ZnCl_2$ (1 M solution in THF, 1.2 mL, 1.2 mmol) was added at -40 °C, the reaction was stirred for 15 min and then $Pd(PPh_3)_4$ (29 mg, 5 mol%) in THF (0.5 mL) and *E*-hexenyl iodide[6] **16** (0,414 g, 1.5 mmol) dissolved in THF (0.5 mL) were added. The reaction mixture was slowly warmed to 25°C and stirred at this temperature for 12 h. Reaction was quenched with sat. aq. NH_4Cl solution extracted with diethyl ether (3 × 15 mL) and dried over anhydrous Na_2SO_4. After filtration, the solvents were evaporated *in vacuo*. Purification by chromatography on alumina (Grade III, *n*-pentane/diethyl ether, 10:1) furnished compound **17** (0.200 g, 77%) as a pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.49 – 7.39 (m, 2 H), 7.24 (d, J = 7.8 Hz, 1 H), 6.82 (dd, J = 8.1, J = 1.1 Hz, 1 H), 6.24 (dt, J = 15.7 Hz, J = 6.9 Hz, 1 H), 2.29 (qd, J = 6.9 Hz, J = 1.4 Hz, 1 H), 1.7 (s, 6 H), 1.53 – 1.36 (m, 4 H), 0.05 (t, J = 7.1 Hz, 3 H).

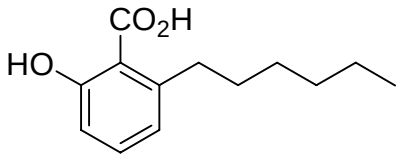
^{13}C-NMR (75 MHz, $CDCl_3$) δ: 160.6, 157.0, 142.9, 135.9, 135.2, 128.2, 121.4, 115.7, 110.8, 105.3, 33.1, 25.9, 22.5, 14.2.

MS (70 eV, EI) *m/z* (%): 260 (36) [M^+], 202 (100), 187 (19), 173 (9), 160 (31), 147 (57), 132 (17), 115 (17), 103 (30), 91 (6), 77 (14), 63 (6), 51 (5).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2997, 2950, 2920, 1723, 1597, 1573, 1470, 1375, 1310, 1258, 1201, 1091, 964, 775, 690.

HRMS (EI) for **$C_{16}H_{20}O_3$** (260.1412): 260.1414.

Synthesis of 6-hexyl salicylic acid (18):



To a solution of **17** (0.260 g, 1.0 mmol) in methanol (30 mL) Pd/C (0.050 g, 5 mol%) was added. The mixture was hydrogenated at 25 ^oC under 1 atm of H_2 for 24 h. The catalyst was removed by filtration through Celite® by using a short-pad column. The solvents were evaporated *in vacuo* and the crude material dissolved in a mixture of THF (10 mL) and H_2O (10 mL). KOH (0.273 g, 4.9 mmol) was added and the mixture refluxed for 12 h. The mixture was cooled to 25 ^oC and concentrated HCl was added dropwise until pH 1. The reaction mixture was then extracted with ethyl acetate (3 × 30 mL) and the solvent was dried over anhydrous Na_2SO_4. After filtration, the solvents

were evaporated *in vacuo*. Purification by flash-chromatography (*n*-pentane/ethyl acetate/acetic acid, 20:2:1) furnished the 6-hexyl salicylic acid (**18**) (0.198 g, 89%) as colorless solid.

m.p.: 94.7 – 94.4 °C.

^{1}H-NMR (300 MHz, $CDCl_3$) δ: 7.40 (t, J = 8.0 Hz, 1 H), 6.93 (d, J = 7.5 Hz, 1 H), 6.80 (dd, J = 8.1 Hz, J = 0.9 Hz, 1 H), 3.1 (t, J = 7.6 Hz, 2 H), 1.7 (s, 6 H), 1.65 – 1.55 (m, 2 H), 1.44 – 1.29 (m, 6 H), 0.90 (t, J = 6.9 Hz, 3 H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ: 160.4, 157.4, 148.8, 135.2, 125.3, 115.3, 112.3, 105.2, 34.6, 31.9, 31.4, 29.6, 25.9, 22.8, 22.8, 14.3.

MS (70 eV, EI) *m/z* (%): 262 (15) [M^+], 204 (100), 162 (22), 147 (17), 134 (32), 105 (2), 91 (7), 77 (7), 51 (3).

IR (ATR) $\tilde{\nu}$ (cm^{-1}): 2925, 2855, 1724, 1604, 1580, 1476, 1307, 1267, 1207, 1040, 922, 775, 695.

HRMS (EI) for **$C_{16}H_{22}O_3$** (262.1568): 262.1550.

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