Generation of Functionalized Aryl and Heteroaryl Aluminum Reagents by Halogen/Lithium Exchange

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Supporting Information
Experimental Details
# Table of Contents

<table>
<thead>
<tr>
<th>Part</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>General considerations</td>
<td>03</td>
</tr>
<tr>
<td>Synthesis of the compounds 5a – 14</td>
<td>04</td>
</tr>
<tr>
<td>Literature</td>
<td>19</td>
</tr>
</tbody>
</table>
General
All reactions were carried out under an argon atmosphere in dried glassware. Syringes and needles were flushed with argon three times before use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under nitrogen and kept over 4 Å molecular sieves. Yields refer to isolated yields of compounds estimated to be of >95 % purity as determined by 1H-NMR and capillary-GC analysis. NMR spectra were recorded in solutions in deuterated chloroform (CDCl₃) with residual chloroform (δ 7.26 ppm for 1H NMR and δ 77.16 ppm for 13C NMR) or deuterated benzene (C₆D₆) with residual benzene (7.16 ppm for 1H NMR and δ 128.06 ppm for 13C NMR). Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Column chromatography was performed using SiO₂ (0.040 – 0.063 mm, 230 – 400 mesh ASTM) from Merck if not indicated otherwise.

General procedures for the preparation of CuCN·2LiCl (1 M solution in THF)
A Schlenk-flask was charged with LiCl (16.96 g, 0.40 mol) and CuCN (17.95 g, 0.20 mol) and dried for 6 h at 150 °C under high vacuum (5·10⁻² mbar; dry stirring). Careful addition of THF (200 mL) and stirring overnight furnishes a slightly yellowish to greenish solution which is kept over molecular sieves (4 Å).

Typical Procedure for the preparation of aryl aluminum reagents (TP1)
A dry and argon-flushed 20 mL Schlenk-tube equipped with a magnetic stirring bar was charged with the aryl halide (1.5 mmol), THF (2.5 mL) and the internal standard (undecane) and cooled to -78 °C. A solution of i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) was added, and the resulting mixture was stirred for 10 min before a solution of n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol) was added dropwise. The reaction mixture was stirred at this temperature for 5 min and then allowed to warm to room temperature. The reaction was monitored by GC-analysis of reaction aliquots, quenched with iodine in dry THF.
Synthesis of Ethyl 3'-cyano-[1,1'-biphenyl]-4-carboxylate (5a)

\[
\text{CN} \quad \text{CO}_2\text{Et}
\]

The aluminum reagent 3a was prepared according to TP1 from 3-bromobenzonitrile (1a, 273 mg, 1.5 mmol), \(i\)-Bu\(_2\)AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and \(n\)-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at \(-78\,^\circ\text{C}\) for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 81% organometallic reagent (3a, 1.21 mmol). A solution of ethyl 4-iodobenzoate (4a, 414 mg, 1.5 mmol), \(\text{Pd}_2\text{dba}_3\) (34 mg, 0.0375 mmol), \(\text{P}(i\)-\(\text{Bu})_3\) (1 M in toluene, 0.15 mL, 0.15 mmol) in THF (1 mL) was added. The resulting mixture was stirred at 50 °C for 12 h. Then, the reaction mixture was quenched with sat. aq. \(\text{NH}_4\text{Cl}\) solution (5 mL), extracted with \(\text{Et}_2\text{O}\) (3 x 15 mL) and dried over \(\text{MgSO}_4\). After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5a as colorless oil (198 mg, 65%).

The analytical data matches the reported one in the literature.¹

Synthesis of 2-(3-Bromobenzoyl)benzonitrile (5b)

\[
\text{CN} \quad \text{O} \quad \text{Br}
\]

The aluminum reagent 3b was prepared according to TP1 from 2-bromobenzonitrile (1b, 273 mg, 1.5 mmol), \(i\)-Bu\(_2\)AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and \(n\)-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at \(-78\,^\circ\text{C}\) for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 64% organometallic reagent (3b, 0.96 mmol). The reaction mixture was cooled to \(-40\,^\circ\text{C}\), then CuCN·2LiCL (1 M in THF, 0.3 mL, 0.3 mmol) and 3-bromobenzoyl chloride (4b, 362 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. \(\text{NH}_4\text{Cl}\) solution (5 mL), extracted with \(\text{Et}_2\text{O}\) (3 x 15 mL) and dried over \(\text{MgSO}_4\). After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5b as a yellowish oil (198 mg, 72%).

Electronic Supplementary Material (ESI) for Chemical Communications

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**Synthesis of 4-(3-Oxocyclohexyl)benzonitrile (5c)**

The aluminum reagent 3c was prepared according to TPI from 4-bromobenzonitrile (1c, 273 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then warmed to room temperature. Iodolysis indicated a yield of 80 % organometallic reagent (3c, 1.2 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 1.5 mL, 1.5 mmol) was added, followed by a solution of cyclohexenone (4c, 216 mg, 2.25 mmol) and chlorotrimethylsilane (611 mg, 5.63 mmol) and the resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5c as a yellowish oil (122 mg, 51 %).

**¹H-NMR (400 MHz, CDCl₃):** δ / ppm = 7.00 (m, 2 H), 6.44 (m, 2 H), 2.30 - 2.16 (m, 3 H), 1.83 - 1.73 (m, 2 H), 1.49 - 1.43 (m, 1 H), 1.30 - 1.26 (m, 1 H), 1.20 - 1.11 (m, 1 H), 1.05 - 0.97 (m, 1 H).

**¹³C-NMR (100 MHz, CDCl₃):** δ / ppm = 207.1, 149.3, 132.3, 127.4, 118.8, 111.1, 47.9, 44.2, 40.8, 32.0, 25.2.
**IR (Diamond-ATR, neat):** \( \tilde{\nu} / \text{cm}^{-1} = 3045, 2940, 2866, 2225, 1707, 1606, 1505, 1447, 1416, 1345, 1249, 1224, 1177, 1100, 1071, 1056, 1025, 997, 972, 902, 832. \)

**MS (EI, 70 eV):** m/z (%) = 200 (15), 199 (62), 157 (12), 156 (100), 143 (43), 142 (30), 130 (16), 129 (48), 128 (19), 116 (23), 115 (11), 102 (13), 84 (30), 74 (16), 59 (27), 55 (10), 45 (16), 44 (20), 43 (10), 42 (13), 41 (18).

**HRMS (EI) for C\(_{13}\)H\(_{13}\)NO (199.0997):** 199.0991 (M\(^{+}\)).

**Synthesis of \(N,N\)-Dimethyl-1',2',3',4'-tetrahydro-[1,1'-biphenyl]-3-carboxamide (5d)**

The aluminum reagent 3d was prepared according to TP1 from 3-bromo-\(N,N\)-dimethylbenzamide (1d, 342 mg, 1.5 mmol), \(i\)-Bu\(_2\)AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and \(n\)-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 75 % organometallic reagent (3d, 1.13 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 1.5 mL, 1.5 mmol) and 3-bromocyclohexene (4d, 290 mg, 1.8 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH\(_4\)Cl solution (5 mL), extracted with Et\(_2\)O (3 x 15 mL) and dried over MgSO\(_4\). After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5d as a yellowish oil (188 mg, 73 %).

**\(^1\)H-NMR (300 MHz, CDCl\(_3\)):** \( \delta / \text{ppm} = 7.35 - 7.21 \) (m, 4 H), 5.94 - 5.86 (m, 1 H), 5.69 (dq, \( J = 10.2, 2.2 \) Hz, 1 H), 3.46 - 3.38 (m, 1 H), 3.10 (s, 9 H), 2.97 (s, 3 H), 2.11 - 1.97 (m, 3 H), 1.78 - 1.69 (m, 1 H), 1.67 - 1.50 (m, 2 H).

**\(^{13}\)C-NMR (75 MHz, CDCl\(_3\)):** \( \delta / \text{ppm} = 172.1, 147.0, 136.4, 129.7, 129.1, 128.9, 128.3, 126.5, 124.8, 41.8, 39.7, 35.4, 32.6, 25.1, 21.1. \)

**IR (Diamond-ATR, neat):** \( \tilde{\nu} / \text{cm}^{-1} = 3031, 2934, 2860, 2837, 2244, 1624, 1603, 1582, 1503, 1447, 1408, 1398, 1270, 1261, 1174, 1081, 1059, 921, 900, 802, 741, 712, 671. \)

**MS (EI, 70 eV):** m/z (%) = 229 (45), 228 (24), 186 (14), 185 (100), 129 (14), 128 (16), 115 (15).
HRMS (EI) for C_{13}H_{19}NO (229.1467): 229.1451 (M^+).

Synthesis of (3-(1,3-Dioxolan-2-yl)phenyl)(cyclohexyl)methanone (5e)

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{O} \\
\end{array}
\]

The aluminum reagent 3e was prepared according to TP1 from 2-(3-bromophenyl)-1,3-dioxolane (1e, 344 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 71 % organometallic reagent (3e, 1.07 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 0.3 mL, 0.3 mmol) and cyclohexanecarbonyl chloride (4e, 242 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5e as a yellowish oil (216 mg, 78 %).

\(^1\)H-NMR (400 MHz, C₆D₆): \(\delta / \text{ppm} = 8.32 (t, J = 1.8 \text{ Hz}, 1 \text{ H}), 7.84 (\text{ddd}, J = 7.9, 1.5, 1.4 \text{ Hz}, 1 \text{ H}), 7.60 (\text{ddd}, J = 7.6, 1.4, 1.2 \text{ Hz}, 1 \text{ H}), 7.13 (t, J = 7.7 \text{ Hz}, 1 \text{ H}), 3.63 - 3.55 (m, 2 \text{ H}) 5.69 (s, 1 \text{ H}), 3.50 - 3.42 (m, 2 \text{ H}), 3.03 - 2.96 (m, 1 \text{ H}), 1.79 - 1.74 (m, 2 \text{ H}), 1.63 - 1.57 (m, 2 \text{ H}), 1.54 - 1.46 (m, 3 \text{ H}), 1.15 - 1.05 (m, 3 \text{ H}).

\(^{13}\)C-NMR (100 MHz, C₆D₆): \(\delta / \text{ppm} = 202.3, 139.7, 137.1, 130.9, 129.1, 128.8, 126.9, 103.5, 65.2, 45.6, 29.7, 26.3, 26.0.

IR (Diamond-ATR, neat): \(\tilde{\nu} / \text{cm}^{-1} = 2928, 2853, 1721, 1677, 1604, 1588, 1448, 1373, 1289, 1254, 1241, 1189, 1162, 1132, 1075, 1027, 974, 942, 911, 805, 779, 715, 694, 666.

MS (EI, 70 eV): m/z (%) = 260 (3), 259 (4), 193 (10), 187 (15), 178 (13), 177 (100), 73 (34).

HRMS (EI) for C_{16}H_{20}O₃ (260.1412): 260.1377 (M^+).
Synthesis of (2-(1,3-Dioxolan-2-yl)phenyl)(phenyl)methanone (5f)

The aluminum reagent 3f was prepared according to TP1 from 2-(2-bromophenyl)-1,3-dioxolane (1f, 344 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 83 % organometallic reagent (3f, 1.25 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 0.3 mL, 0.3 mmol) and benzoyl chloride (4f, 232 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5f as a yellowish oil (231 mg, 73 %).

¹H-NMR (400 MHz, C₆D₆): δ / ppm = 7.91 - 7.87 (m, 2 H), 7.76 (dd, J = 7.8, 1.4 Hz, 1 H), 7.15 - 7.06 (m, 3 H), 7.04 - 6.96 (m, 3 H), 6.25 (s, 1 H), 3.41 - 3.36 (m, 2 H), 3.23 - 3.21 (m, 1 H), 3.25 - 3.21 (m, 2 H).

¹³C-NMR (100 MHz, C₆D₆): δ / ppm = 196.8, 139.5, 138.5, 137.9, 132.8, 130.4, 129.7, 128.5, 128.3, 128.2, 127.1, 101.6, 65.0.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3058, 3026, 2960, 2888, 2766, 1663, 1596, 1579, 1473, 1448, 1394, 1313, 1267, 1209, 1151, 1112, 1071, 1025, 970, 926, 848, 804, 764, 758, 700, 687.

MS (EI, 70 eV): m/z (%) = 253 (12), 210 (23), 209 (83), 194 (19), 182 (19), 182 (57), 181 (52), 165 (33), 153 (16), 152 (26), 149 (52), 148 (16), 133 (15), 105 (100), 104 (12), 78 (13), 77 (54), 76 (12), 73 (17), 45 (10).

HRMS (EI) for C₁₆H₁₄O₃ (254.0943): 254.0924 (M⁺).
Synthesis of (3-((tert-Butyldimethylsilyl)oxy)phenyl)(o-tolyl)methanone (5g)

The aluminum reagent 3g was prepared according to TP1 from (3-bromophenoxy)(tert-butyl)dimethylsilane (1g, 431 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 81 % organometallic reagent (3g, 1.22 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCL (1 M in THF, 0.3 mL, 0.3 mmol) and 2-methylbenzoyl chloride (4g, 255 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5g as a colorless oil (298 mg, 75 %).

1H-NMR (300 MHz, C₆D₆): δ / ppm = 7.65 - 7.63 (m, 1 H), 7.38 (dt, J = 7.2, 1.5 Hz, 1 H), 7.18 (dd, J = 7.5, 1.4 Hz, 1 H), 7.10 - 7.04 (m, 1 H), 6.99 - 6.89 (m, 4 H), 2.25 (s, 3 H), 0.92 (s, 9 H), 0.07 (s, 6 H).

13C-NMR (75 MHz, C₆D₆): δ / ppm = 197.2, 156.4, 140.1, 139.4, 137.1, 131.2, 130.2, 129.9, 128.8, 125.3, 125.1, 123.9, 121.2, 25.8, 20.0, 18.4, -4.4.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3064, 3023, 2955, 2929, 2891, 2857, 2388, 2279, 2269, 1664, 1595, 1578, 1479, 1472, 1433, 1362, 1330, 1292, 1276, 1253, 1227, 1139, 1106, 1003, 980, 904, 892, 837, 827, 779, 740, 684.

MS (EI, 70 eV): m/z (%) = 326 (37), 270 (31), 269 (100), 119 (56), 91 (23).

HRMS (EI) for C₂₀H₂₆O₂Si (326.1702): 326.1687 (M⁺).

Synthesis of 1-(2-Chloro-5-(trifluoromethyl)phenyl)-2,2-dimethylpropan-1-one (5h)

The aluminum reagent 3h was prepared according to TP1 from 2-bromo-1-chloro-4-(trifluoromethyl)benzene (1h, 389 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65
mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 64 % organometallic reagent (3h, 0.96 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 0.3 mL, 0.3 mmol) and pivaloyl chloride (4h, 199 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5h as a colorless oil (170 mg, 67 %).

**1H-NMR (300 MHz, CD₆₆):** δ / ppm = 7.24 (d, J = 2.2 Hz, 1 H), 6.95 - 6.90 (m, 1 H), 6.83 - 6.78 (m, 1 H), 1.02 - 0.99 (m, 9 H).

**13C-NMR (75 MHz, CD₆₆):** δ / ppm = 208.0, 141.6, 134.0 (q, J = 1 Hz), 130.7, 128.8 (q, J = 32 Hz), 126.6 (q, J = 4 Hz), 124.1 (q, J = 273 Hz), 123.4 (q, J = 4 Hz), 45.1, 26.6.

**19F-NMR (211 MHz, CD₆₆):** δ / ppm = -62.49.

**IR (Diamond-ATR, neat):** ν / cm⁻¹ = 2971, 2907, 2871, 2365, 2330, 2278, 2269, 1704, 1609, 1581, 1479, 1401, 1330, 1286, 1266, 1184, 1173, 1134, 1084, 978, 901, 832, 810, 714.

**MS (EI, 70 eV):** m/z (%) = 264 (1), 209 (22), 207 (43), 57 (100), 41 (32).

**HRMS (EI) for C₁₂H₁₂ClF₃O (264.0529):** 264.0532 (M⁺).

### Synthesis of Ethyl 3-(3-oxocyclohexyl)benzoate (5i)

![Ethyl 3-(3-oxocyclohexyl)benzoate](image)

The aluminum reagent 3i was prepared according to TP1 from ethyl 3-iodobenzoate (1i, 414 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 65 % organometallic reagent (3i, 0.98 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 1.5 mL, 1.5 mmol) was added, followed by a solution of cyclohexenone (4c, 216 mg, 2.25 mmol) and chlorotrimethylsilane (611 mg, 5.63 mmol) and the resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction
mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5i as a yellowish oil (175 mg, 73 %).

The analytical data matches the reported one in the literature.²

**Synthesis of Ethyl 2-(3-chlorobenzoyl)benzoate (5j)**

The aluminum reagent 3j was prepared according to TP1 from ethyl 2-iodobenzoate (1j, 414 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 72 % organometallic reagent (3j, 1.08 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 0.3 mL, 0.3 mmol) and 3-chlorobenzoyl chloride (4j, 289 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5j as a colorless oil (253 mg, 81 %).

¹H-NMR (300 MHz, C₆D₆): δ / ppm = 7.98 (t, J = 1.8 Hz, 1 H), 7.94 - 7.89 (m, 1 H), 7.49 (dt, J = 7.7, 1.4 Hz, 1 H), 7.09 (ddd, J = 8.0, 2.2, 1.1 Hz, 1 H), 7.05 - 7.00 (m, 3 H), 6.75 (t, J = 7.9 Hz, 1 H), 3.78 (q, J = 7.1 Hz, 2 H), 0.72 (t, J = 7.2 Hz, 3 H).

¹³C-NMR (75 MHz, C₆D₆): δ / ppm = 194.7, 165.6, 141.6, 139.8, 135.1, 132.7, 132.3, 130.3, 130.1, 129.7, 129.7, 127.9, 127.7, 61.5, 13.6.

IR (Diamond-ATR, neat): \( v \) / cm⁻¹ = 3068, 2982, 2936, 2903, 2872, 1713, 1675, 1596, 1571, 1466, 1445, 1424, 1366, 1275, 1253, 1153, 1126, 1079, 1041, 1014, 957, 944, 896, 854, 771, 763, 735, 709, 685, 673.

MS (EI, 70 eV): m/z (%) = 288 (15), 245 (11), 243 (34), 177 (53), 152 (19), 149 (100), 139 (22), 111 (14).

HRMS (EI) for C₁₆H₁₃ClO₃ (288.0553): 288.0552 (M⁺).
Synthesis of Ethyl 5-(2-(ethoxycarbonyl)allyl)furan-2-carboxylate (9a)

The aluminum reagent 7a was prepared according to TP1 from ethyl 5-bromofuran-2-carboxylate (6a, 329 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 82 % organometallic reagent (7a, 1.23 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCL (1 M in THF, 1.5 mL, 1.5 mmol) and ethyl 2-(bromomethyl)acrylate (8a, 347 mg, 1.8 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 9a as a yellowish oil (258 mg, 83 %).

The analytical data matches the reported one in the literature.³

Synthesis of Ethyl 5-(thiophene-2-carbonyl)thiophene-2-carboxylate (9b)

The aluminum reagent 7b was prepared according to TP1 from ethyl 5-bromo thiophene-2-carboxylate (6b, 353 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 72 % organometallic reagent (7b, 1.08 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCL (1 M in THF, 0.3 mL, 0.3 mmol) and thiophene-2-carbonyl chloride (8b, 242 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 9b as a yellow solid (196 mg, 68 %).
m.p. (°C): 73-75.

$^1$H-NMR (400 MHz, C$_6$D$_6$): $\delta$ / ppm = 7.54 (d, $J = 3.9$ Hz, 1 H), 7.39 (dd, $J = 3.8$, 1.1 Hz, 1 H), 7.26 (d, $J = 4.3$ Hz, 1 H), 6.91 - 6.86 (m, 1 H), 6.54 - 6.51 (m, 1 H), 4.03 - 3.97 (m, 2 H), 0.94 (t, $J = 7.1$ Hz, 3 H).

$^{13}$C-NMR (100 MHz, C$_6$D$_6$): $\delta$ / ppm = 178.1, 161.4, 147.5, 143.1, 139.9, 134.0, 133.5, 133.1, 132.4, 128.0, 61.6, 14.1.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm$^{-1}$ = 3078, 2979, 2945, 1712, 1603, 1584, 1524, 1520, 1412, 1346, 1288, 1247, 1230, 1212, 1172, 1092, 1084, 1052, 1039, 1003, 865, 834, 790, 751, 743, 726, 703.

MS (EI, 70 eV): m/z (%) = 266 (41), 238 (13), 221 (49), 111 (100), 97 (11), 85 (18), 83 (11), 83 (10), 71 (28), 69 (14), 57 (46), 56 (10), 55 (18), 43 (40), 42 (10), 41 (18).

HRMS (EI) for C$_{12}$H$_{10}$O$_3$S$_2$: 266.0071 (M$^+$).

**Synthesis of Cyclopropyl(5-(4-methoxyphenyl)-3-(phenylthio)thiophen-2-yl)methanone (9c)**

The aluminum reagent 7c was prepared according to TPI from 2-bromo-5-(4-methoxyphenyl)-3-(phenylthio)thiophene (6c, 566 mg, 1.5 mmol), i-Bu$_2$AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 93 % organometallic reagent (7c, 1.40 mmol). The reaction mixture was cooled to -40 °C, then CuCN$\cdot$2LiCl (1 M in THF, 0.3 mL, 0.3 mmol) and cyclopropanecarbonyl chloride (8c, 172 mg, 1.65 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH$_4$Cl solution (5 mL), extracted with Et$_2$O (3 x 15 mL) and dried over MgSO$_4$. After filtration, the solvents were evaporated *in vacuo*. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 9c as a yellow solid (435 mg, 85 %).

**1H-NMR (400 MHz, C6D6):** δ / ppm = 7.50 - 7.47 (m, 2 H), 7.18 - 7.14 (m, 3 H), 7.03 - 6.95 (m, 3 H), 6.69 - 6.62 (m, 2 H), 3.26 (s, 3 H), 2.28 - 2.22 (m, 1 H), 1.36 - 1.30 (m, 2 H), 0.65 - 0.60 (m, 2 H).

**13C-NMR (100 MHz, C6D6):** δ / ppm = 194.3, 160.0, 147.2, 142.3, 138.4, 135.0, 133.9, 129.9, 129.3, 127.1, 126.6, 123.2, 114.7, 54.9, 19.2, 11.3.

**IR (Diamond-ATR, neat):** ν / cm⁻¹ = 3087, 3070, 3017, 3005, 2969, 2935, 2841, 1627, 1606, 1538, 1501, 1438, 1427, 1411, 1293, 1254, 1217, 1176, 1111, 1084, 1031, 1019, 998, 993, 951, 897, 833, 821, 808, 751, 708, 704, 695, 673.

**MS (EI, 70 eV):** m/z (%) = 368 (13), 367 (25), 366 (100), 325 (23), 309 (14), 221 (11), 151 (10), 69 (14), 41 (13).

**HRMS (EI) for C21H18O2S2 (366.0748):** 366.0747 (M⁺).

**Synthesis of 4-(Quinolin-3-yl)benzonitrile (9d)**

The aluminum reagent 7d was prepared according to TP1 from 3-bromoquinoline (1a, 312 mg, 1.5 mmol), i-Bu₂AlCl (1 M in THF, 1.65 mL, 1.65 mmol) and n-BuLi (2.5 M in hexane, 0.66 mL, 1.65 mmol). The reaction was carried out in THF (2.5 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 63 % organometallic reagent (7d, 0.95 mmol). A solution of 4-iodobenzonitrile (8d, 344 mg, 1.5 mmol), Pd₂dba₃ (34 mg, 0.0375 mmol), P(t-Bu)₃ (1 M in toluene, 0.15 mL, 0.15 mmol) in NMP (2 mL) was added. The resulting mixture was stirred at 50 °C for 12 h. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (5 mL), extracted with Et₂O (3 x 15 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 5a as a yellow solid (159 mg, 73 %).

The analytical data matches the reported one in the literature.¹
Synthesis of (2-(1,3-dioxolan-2-yl)phenyl)(4-chlorophenyl)methanone (10)

The aluminum reagent 3f was prepared according to an upscaled TP1 from 2-(2-bromophenyl)-1,3-dioxolane (1f, 2.29 g, 10 mmol), i-Bu₂AlCl (1 M in THF, 11 mL, 11 mmol) and n-BuLi (2.5 M in hexane, 4.4 mL, 11 mmol). The reaction was carried out in THF (10 mL) at -78 °C for 10 min and was then allowed to warm to room temperature. Iodolysis indicated a yield of 84% organometallic reagent (3f, 8.4 mmol). The reaction mixture was cooled to -40 °C, then CuCN·2LiCl (1 M in THF, 2 mL, 2 mmol) and 4-chlorobenzoyl chloride (4f, 1.93 g, 11 mmol) were added. The resulting mixture was allowed to warm to 25 °C and stirred overnight. Then, the reaction mixture was quenched with sat. aq. NH₄Cl solution (35 mL), extracted with Et₂O (3 x 100 mL) and dried over MgSO₄. After filtration, the solvents were evaporated in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 10 as a yellowish solid (1.82 g, 75%).

m.p. (°C): 86.

¹H-NMR (400 MHz, C₆D₆): δ / ppm = 7.71 (d, J = 8.4 Hz, 1 H), 7.62 - 7.58 (m, 2 H), 7.16 - 7.12 (m, 1 H), 7.02 - 6.96 (m, 4 H), 6.15 (s, 1 H), 3.39 - 3.33 (m, 2 H), 3.30 - 3.23 (m, 2 H).

¹³C-NMR (100 MHz, C₆D₆): δ / ppm = 195.5, 139.2, 138.9, 137.8, 136.7, 131.7, 129.9, 128.8, 128.4, 128.1, 127.2, 101.6, 65.0.

IR (Diamond-ATR, neat): ν / cm⁻¹ = 3085, 3062, 3036, 2989, 2961, 2895, 2859, 2758, 1671, 1662, 1584, 1569, 1482, 1470, 1446, 1396, 1305, 1287, 1267, 1211, 1177, 1150, 1112, 1087, 1075, 1064, 1011, 972, 954, 940, 927, 852, 781, 773, 758, 744, 671.

MS (EI, 70 eV): m/z (%) = 289 (22), 288 (14), 287 (61), 246 (14), 245 (39), 244 (38), 243 (100), 209 (20), 181 (50), 165 (11), 153 (11), 152 (42), 149 (40), 148 (13), 139 (60), 111 (27), 105 (16), 104 (11), 77 (12), 76 (15), 75 (12), 73 (10).

HRMS (EI) for C₁₆H₁₃ClO₃ (288.0553): 288.0522 (M⁺).
Synthesis of 1-(4-chlorophenyl)phthalazine (11)

(2-(1,3-Dioxolan-2-yl)phenyl)(4-chlorophenyl)methanone (10, 577 mg, 2 mmol) was dissolved in MeOH (20 mL). Hydrazine hydrate (801 mg, 16 mmol) and p-toluenesulfonic acid monohydrate (38 mg, 0.2 mmol) were added and the resulting mixture was stirred under reflux. After stirring for 14 h, the reaction mixture was concentrated in vacuo. The crude product obtained was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 11 greenish solid (361 mg, 75%).


$^1$H-NMR (400 MHz, CDCl$_3$): δ / ppm = 9.54 (s, 1 H), 8.06 - 8.01 (m, 2 H), 7.95 - 7.86 (m, 2 H), 7.71 - 7.67 (m, 2 H), 7.56 - 7.50 (m, 2 H).

$^{13}$C-NMR (100 MHz, CDCl$_3$): δ / ppm = 159.0, 150.7, 135.9, 134.5, 133.1, 132.6, 131.4, 128.9, 127.1, 127.0, 125.9, 125.3.

IR (Diamond-ATR, neat): $\tilde{\nu}$ / cm$^{-1}$ = 3074, 3059, 3032, 2976, 1615, 1591, 1540, 1485, 1408, 1379, 1352, 1292, 1267, 1225, 1180, 1132, 1105, 1085, 1015, 993, 952, 945, 880, 834, 812, 797, 762, 733, 716, 667, 662.

MS (EI, 70 eV): m/z (%) = 242 (18), 241 (39), 240 (51), 239 (100), 206 (12), 205 (74), 177 (16), 176 (21), 88 (13), 75 (13).

HRMS (EI) for C$_{14}$H$_9$ClN$_2$ (240.0454): 240.0418 (M$^+$).

Synthesis of 1-(4-chlorophenyl)-3-phenylisobenzofuran (13)

(2-(1,3-Dioxolan-2-yl)phenyl)(4-chlorophenyl)methanone (10, 577 mg, 2 mmol) was dissolved in acetone (10 mL) and p-toluenesulfonic acid monohydrate (38 mg, 0.2 mmol) was added at room temperature. After stirring for 1 h, the reaction mixture was quenched with sat. aq. NH$_4$Cl solution (15 mL), extracted with Et$_2$O (3 x 50 mL) and dried over MgSO$_4$. After filtration, the solvents were removed in vacuo and the crude aldehyde 12 was obtained as a colorless oil (465 mg, 1.9 mmol). A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirrer, was charged with 12 (465 mg, 1.9 mmol) in anhydrous THF (15 mL). A
solution of anisyl Grignard (1.1 M in THF, 1.73 mL, 1.9 mmol) was added dropwise at 0 °C and the resulting mixture was stirred at 0 °C for 30 min. Then, an aqueous solution of HCl (4 M, 10 mL) was slowly added at 0 °C. The mixture (still under argon) was warmed to room temperature and stirred for 1 h, then extracted with ether (3 x 50 mL). The combined organic extracts were washed with a saturated solution of NaHCO₃, brine and dried over Na₂SO₄. After filtration, the solvent was removed in vacuo. The crude product was purified by flash column chromatography (dichloromethane:ethyl acetate = 1:1) to give 13 as a yellow solid (527 mg, 91 %).

The analytical data matches the reported one in the literature.⁵

**Synthesis of (2-(4-chlorobenzoyl)phenyl)(4-methoxyphenyl)methanone (14)**

(2-(1,3-Dioxolan-2-yl)phenyl)(4-chlorophenyl)methanone (10, 577 mg, 2 mmol) was dissolved in acetone (10 mL) and p-toluenesulfonic acid monohydrate (38 mg, 0.2 mmol) was added at room temperature. After stirring for 1 h, the reaction mixture was quenched with sat. aq. NH₄Cl solution (15 mL), extracted with Et₂O (3 x 50 mL) and dried over MgSO₄. After filtration, the solvents were removed in vacuo and the crude aldehyde 12 was obtained as a colorless oil (465 mg, 1.9 mmol). A dry and argon-flushed Schlenk-flask, equipped with a magnetic stirrer, was charged with 12 (465 mg, 1.9 mmol) in anhydrous THF (15 mL). A solution of PhMgCl (1.7 M in THF, 1.1 mL, 1.9 mmol) was added dropwise at 0 °C and the resulting mixture was stirred at 0 °C for 30 min. Then, an aqueous solution of HCl (4 M, 10 mL) was slowly added at 0 °C. The mixture (still under argon) was warmed to room temperature and stirred for 1 h, then extracted with ether (3 x 50 mL). The combined organic extracts were washed with a saturated solution of NaHCO₃, brine and dried over Na₂SO₄. After filtration, the solvent was removed in vacuo. The crude product was purified by flash column chromatography (pentane:diethyl ether = 9:1) to give 14 as a yellowish solid (447 mg, 67 %).

m.p. (°C): 138-140.

¹H-NMR (400 MHz, CDCl₃): δ / ppm = 7.66 (m, 4 H), 7.61 - 7.55 (m, 4 H), 7.33 (d, J = 9.0 Hz, 2 H), 6.85 (d, J = 9.0 Hz, 2 H), 3.82 (s, 3 H).
$^{13}$C-NMR (100 MHz, CDCl$_3$): $\delta$ / ppm = 195.6, 195.1, 163.7, 140.2, 139.6, 139.5, 135.7, 132.4, 131.2, 130.5, 130.3, 130.0, 129.6, 129.4, 128.7, 113.7, 55.6.

**IR (Diamond-ATR, neat):** $\tilde{\nu}$ / cm$^{-1}$ = 3059, 2961, 2926, 2836, 1770, 1742, 1665, 1655, 1596, 1584, 1567, 1509, 1459, 1438, 1397, 1313, 1282, 1254, 1173, 1150, 1088, 1033, 1013, 936, 923, 839, 831, 787, 782, 748, 734, 684, 679.

**MS (EI, 70 eV):** m/z (%) = 352 (28), 351 (18), 350 (71), 243 (21), 240 (11), 239 (64), 211 (10), 152 (14), 139 (13), 136 (10), 135 (100), 111 (12), 92 (10), 77 (17).

**HRMS (EI) for C$_{21}$H$_{15}$ClO$_3$ (350.0710):** 350.0707 (M$^+$).
Literature


