Regio- and Chemoselective Synthesis of Fully Substituted Furans

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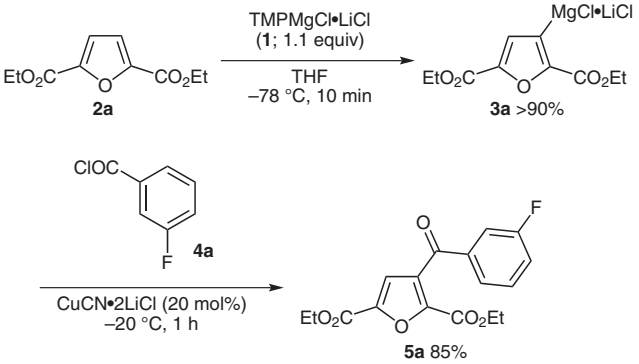
Abstract: Highly functionalized furyl-, indolyl-, and pyrrolylmagnesium reagents are efficiently prepared by direct C–H activation by using regio- and chemoselective magnesium amide bases, such as (tetramethylpiperidyl)magnesium chloride–lithium chloride (TMPMgCl·LiCl) or bis(tetramethylpiperidyl)magnesium–bis(lithium chloride) ($TMP_2Mg·2LiCl$), tolerated by a range of sensitive functional groups. These organometallic reagents readily react with various electrophiles, leading to polyfunctional heterocycles. Furthermore, the full functionalization of the sensitive furan scaffold can be achieved.

Key words: directed metalation, organometallic reagents, metal amides, magnesium, furan

Polyfunctional furans are privileged structures in drug discovery and are present in numerous natural products.[1] Their direct synthesis or functionalization has proven to be highly challenging due to poor tolerance of functional groups and the necessity of activating substituents.[2,3] However, we have recently reported the preparation of highly chemoselective lithium chloride complexed 2,2,6,6-tetramethylpiperidyl (TMP) metal amide bases, such as (tetramethylpiperidyl)magnesium chloride–lithium chloride (TMPMgCl·LiCl; **1**),[4] (tetramethylpiperidyl)zinc chloride–lithium chloride (TMPZnCl·LiCl),[5] bis(tetramethylpiperidyl)zinc–bis(magnesium chloride)–bis(lithium chloride) ($TMP_2Zn·2MgCl_2·2LiCl$),[6] and tris(tetramethylpiperidyl)aluminum–tris(lithium chloride) ($TMP_3Al·3LiCl$),[7] allowing the selective metalation of polyfunctional aromatics and sensitive heterocycles. Moreover, by using these tetramethylpiperidyl-derived metal amides, the full functionalization of the thiophene scaffold was achieved.[8] Herein, we report concise routes to the selective and full functionalization of the more sensitive furan ring. Thus, the disubstituted furan derivative **2a** was smoothly magnesiated by using magnesium complex **1** (1.1 equiv, –78 °C, 10 min), producing the polyfunctional furylmagnesium derivative **3a** (90% yield[9]). A subsequent copper-catalyzed acylation[10] [CuCN·2LiCl (20 mol%), –20 °C, 1 h] with 3-fluorobenzoyl chloride (**4a**) provided the 3-furyl ketone **5a** in 85% yield (Scheme 1).

Furthermore, the metalated diester **3a** efficiently reacted with *S*-methyl benzenethiosulfonate ($MeSSO_2Ph$) to afford the thioether **5b** in 93% yield (Table 1, entry 1).



Scheme 1 Magnesiation of the furan **2a** and subsequent copper(I)-catalyzed acylation

Similarly, **3a** also reacted smoothly with tosyl cyanide (–78 °C, 30 min) to lead to the cyano-substituted furan **5c** in 66% yield (entry 2). In addition, transmetalation of **3a** with zinc chloride (1.1 equiv) gave the corresponding hetarylzinc reagent, providing, after a Negishi cross-coupling[11] [$Pd(PPh_3)_4$ (1 mol%), 25 °C, 3 h] with 3-iodo-1-(trifluoromethyl)benzene (**4b**), the 3-arylfuran **5d** in 79% yield (entry 3). Remarkably, the trimethylsilyl-substituted furan **2b** was regioselectively metalated at the position *ortho* to the carboxyl group when magnesium complex **1** (1.1 equiv, –30 °C, 1 h) was used, generating the hetarylmagnesium reagent **3b** in ca. 90% yield. Chlorination of **3b** with hexachloroethane (–50 °C, 15 h) afforded the 2,3,5-trisubstituted furan **5e** in 48% yield (entry 4). The 3-cyanofuran derivative **5f** was obtained in 52% yield after addition of tosyl cyanide to **3b** (–30 °C, 15 min; entry 5). Moreover, the electron-deficient 5-bromofuran-2-carboxylate **2c** was also regioselectively magnesiated in position 3 with magnesium complex **1** (1.1 equiv) at –78 °C for 30 minutes, generating the 3-furylmagnesium reagent **3c**. Its copper-catalyzed acylation [CuCN·2LiCl (20 mol%), –40 °C, 15 h] with benzoyl chloride provided the expected ketone **5g** in 75% yield (entry 6). Chlorination of **3c** (–78 °C, 30 min, then –78 to 25 °C) with benzenesulfonyl chloride produced ethyl 5-bromo-3-chlorofuran-2-carboxylate (**5h**) in 59% yield (entry 7). Similarly, the reaction of **3c** and tosyl cyanide (–78 °C, 30 min, then –78 to 25 °C) afforded the polyfunctional furan **5i** in 63% yield (entry 8). After transmetalation of **3c** with zinc chloride (1.1 equiv), a palladium-catalyzed cross-coupling[11] [$Pd(PPh_3)_4$ (1 mol%), 25 °C, 6 h] with ethyl 4-iodobenzoate (**4c**) provided the benzoate **5j** in 86% yield (entry 9). Interestingly, the furylzinc reagent obtained after transmetalation of **3c** with zinc chloride (1.1 equiv)

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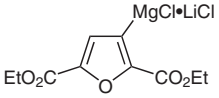
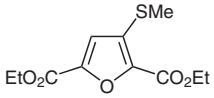
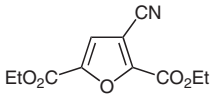
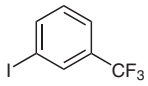
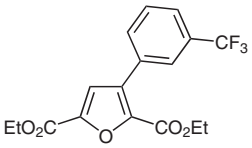
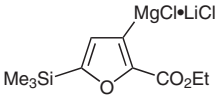
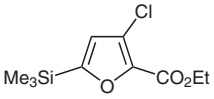
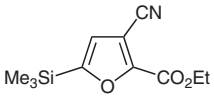
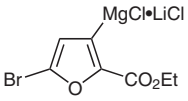
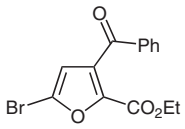
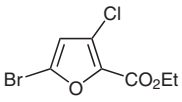
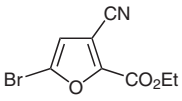
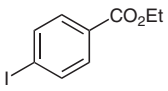
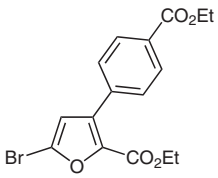
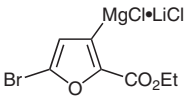
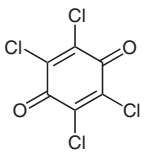
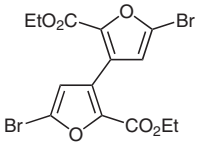
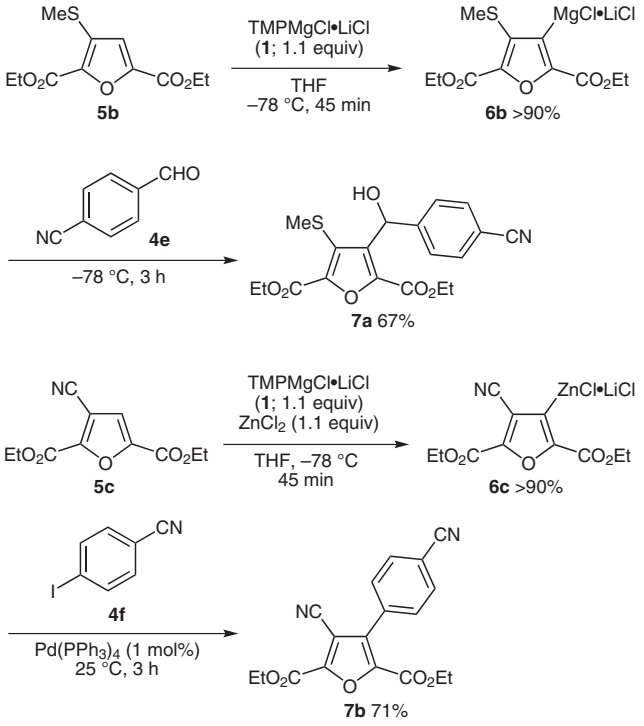
Table 1 Preparation of 2,3,5-Trisubstituted Furans of Type **5**

Entry	Magnesium reagent	Metalation conditions	Electrophile	Product	Yield (%)[a]
1	 **3a**	–78 °C, 10 min	$MeSSO_2Ph$	 **5b**	93
2	**3a**	–78 °C, 10 min	TsCN	 **5c**	66
3	**3a**	–78 °C, 10 min	 **4b**	 **5d**	79[b]
4	 **3b**	–30 °C, 60 min	C_2Cl_6	 **5e**	48
5	**3b**	–30 °C, 60 min	TsCN	 **5f**	52
6	 **3c**	–78 °C, 30 min	PhCOCl	 **5g**	75
7	**3c**	–78 °C, 30 min	$PhSO_2Cl$	 **5h**	59
8	**3c**	–78 °C, 30 min	TsCN	 **5i**	63
9	**3c**	–78 °C, 30 min	 **4c**	 **5j**	86[b]
10	 **3c**	–78 °C, 30 min	 **4d**	 **5k**	80[c]

[a] Isolated yield of analytically pure product.
[b] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv) and a palladium-catalyzed cross-coupling [$Pd(PPh_3)_4$ (1 mol%), 25 °C, 3 h].
[c] Obtained after transmetalation with $ZnCl_2$ (1.1 equiv).

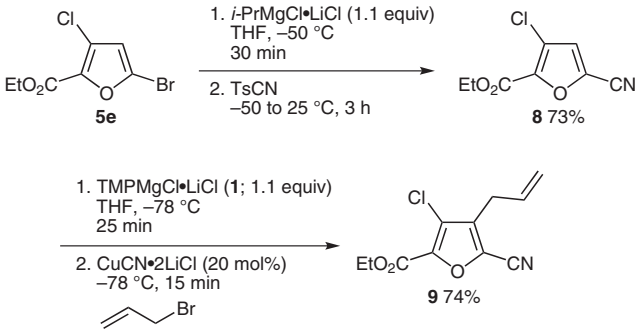
was oxidatively dimerized by addition of chloranil[12] (**4d**; 1.5 equiv, –40 °C, 2 h), leading to the polyfunctional furyl dimer **5k** in 80% yield (entry 10).

Remarkably, the 2,3,5-trisubstituted furan **5b** was efficiently magnesiated with magnesium complex **1** (1.1 equiv, –78 °C, 45 min), leading to the polyfunctional furylmagnesium reagent **6b** (>90% yield[9]). Its addition to 4-cyanobenzaldehyde (**4e**) afforded the fully functionalized furan **7a** in 67% yield (Scheme 2). Similarly, the electron-deficient furan **5c** could be metalated by magnesium complex **1** (1.1 equiv, –78 °C, 45 min) in the presence of zinc chloride (1.1 equiv) to generate the polysubstituted furylzinc chloride **6c** (>90% yield). A Negishi cross-coupling[11] [$Pd(PPh_3)_4$ (1 mol%), 25 °C, 3 h] with 4-iodobenzonitrile (**4f**) provided the fully substituted furan **7b** in 71% yield (Scheme 2).



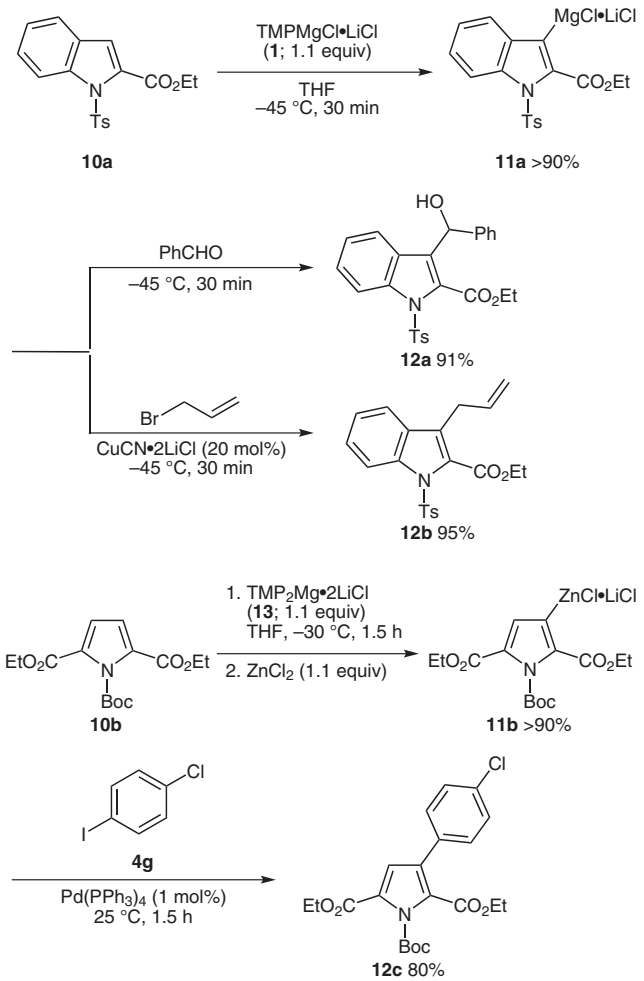
Scheme 2 Preparation of the fully functionalized furans **7a** and **7b**

Interestingly, attempted metalation of **5e** with magnesium complex **1** merely produced regioisomeric furylmagnesium reagents at positions 4 and 5 due to halogen-dance side reactions.[13] However, a chemoselective bromine–magnesium exchange reaction of the furan-2-carboxylate **5e** when using isopropylmagnesium chloride–lithium chloride[14] (1.1 equiv, –50 °C, 30 min) efficiently produced the expected 5-furylmagnesium derivative, which reacted smoothly with tosyl cyanide (–50 to 25 °C, 3 h), leading to the functionalized furan **8** in 73% yield (Scheme 3). A subsequent metalation of **8** with magnesium complex **1** (1.1 equiv, –78 °C, 25 min) followed by a copper-catalyzed allylation [CuCN·2LiCl (20 mol%), –78 °C, 15 min] afforded the fully substituted furan-2-carboxylate **9** in 74% yield (Scheme 3).



Scheme 3 Preparation of the fully functionalized furan derivative **9**

Furthermore, we could also apply this methodology to the selective functionalization of more sensitive heterocycles such as electron-deficient pyrrole and indole derivatives. Thus, the 2-(ethoxycarbonyl)indole **10a** was regioselectively magnesiated by magnesium complex **1** (1.1 equiv, –45 °C, 30 min), providing the functionalized hetarylmagnesium derivative **11a** (Scheme 4). Its addition to benzaldehyde (–45 °C, 30 min) or a copper-catalyzed allylation [CuCN·2LiCl (20 mol%), –45 °C, 30 min] led to the 2,3-disubstituted indole derivatives **12a** and **12b** in 91 and 95% yield, respectively (Scheme 4). Similarly, the



Scheme 4 Preparation of the polyfunctional N-heterocycles of type **12**

tert-butoxycarbonyl-protected ester-substituted pyrrole **10b** smoothly reacted with a bis-amide base such as bis(tetramethylpiperidyl)magnesium–bis(lithium chloride)[15] ($TMP_2Mg{\cdot}2LiCl$; **13**; 1.1 equiv, –30 °C, 1.5 h), producing, after transmetalation with zinc chloride (1.1 equiv), the polysubstituted pyrrol-3-ylzinc reagent **11b**. A subsequent palladium-catalyzed cross-coupling[11] [$Pd(PPh_3)_4$ (1 mol%), 25 °C, 1.5 h] with 1-chloro-4-iodobenzene (**4g**) provided the tetrasubstituted pyrrole **12c** in 80% yield (Scheme 4).

In summary, we presented regio- and chemoselective magnesiations for the efficient functionalization of sensitive heterocycles, such as electron-deficient furans, pyrroles, or indoles. When selective (tetramethylpiperidyl)magnesium bases such as (tetramethylpiperidyl)magnesium chloride–lithium chloride (TMPMgCl·LiCl) or bis(tetramethylpiperidyl)magnesium–bis(lithium chloride) ($TMP_2Mg{\cdot}2LiCl$) are used, a range of functional groups can be tolerated, such as esters or nitriles. Moreover, we showed the applicability of this method in the selective functionalization of the furan scaffold at all positions. Further extension of this methodology towards the synthesis of furan-containing natural products is currently underway in our laboratories.

All reactions were carried out under argon atmosphere in dried glassware. All starting materials were purchased from commercial suppliers and used without further purification, unless stated otherwise. The reagents CuCN·2LiCl,[4] TMPMgCl·LiCl (**1**),[4] and $TMP_2Mg{\cdot}2LiCl$ (**13**)[15] were prepared according to literature procedures. Tetramethylpiperidine, liquid acid chlorides, aldehydes, and allyl bromide were distilled prior to use. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under N_2. Purification by flash column chromatography was performed on silica gel (0.040–0.063 mm, 230–400 mesh ASTM) from Merck, unless indicated otherwise. Yields refer to isolated compounds that are estimated to be >95% pure as determined by ^1H NMR spectroscopy and capillary GC analysis. NMR spectra of samples in $CDCl_3$ (unless stated otherwise) were recorded on a Bruker AC 300 spectrometer, and NMR chemical shifts are referenced with respect to the residual solvent signal of $CHCl_3$ (^1H: $\delta = 7.25$; ^{13}C: $\delta = 77.0$). Melting points were determined on a Büchi B-540 apparatus and are uncorrected. IR spectra were recorded on a Perkin 281 infrared spectrophotometer. MS (EI) and HRMS measurements were carried out on a Finnigan MAT 95Q or a Finnigan MAT 90 mass spectrometer.

Magnesiation of Functionalized Furans by TMPMgCl·LiCl (1); General Procedure

A dry and argon-flushed Schlenk flask, equipped with a magnetic stirrer and a septum was charged with the functionalized furan derivative as a 1 M soln in THF and cooled to the given temperature. Subsequently, 1.1 M TMPMgCl·LiCl in THF (**1**; 1.1 equiv) was added dropwise and the reaction mixture was stirred for the indicated time. Complete conversion of the magnesiation was checked by GC analysis of an iodolyzed reaction aliquot.

Diethyl 3-(3-Fluorobenzoyl)furan-2,5-dicarboxylate (5a)

According to the general procedure, the metalation of diethyl furan-2,5-dicarboxylate (**2a**; 212 mg, 1.0 mmol) in THF (1 mL) was complete within 10 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 1 mL, 1.1 mmol) was used, followed by the addition of 1 M CuCN·2LiCl in THF (0.2 mL, 20 mol%) at –78 °C and further stirring for 15 min. At –20 °C, 3-fluorobenzoyl chloride (**4a**; 174 mg, 1.1 mmol) was added and the mixture was stirred for 1 h, and then quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–Et_2O, 4:1); this afforded **5a** as a colorless solid.

Yield: 285 mg (85%); mp 73–75 °C.

IR (ATR): 2908, 2880, 1796, 1480, 1444, 1384, 1168, 1148, 968, 780 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.59–7.53$ (m, 2 H), 7.48–7.41 (m, 1 H), 7.34–7.27 (m, 2 H), 4.42 (q, $J = 7.1$ Hz, 2 H), 4.18 (q, $J = 7.1$ Hz, 2 H), 1.40 (t, $J = 7.1$ Hz, 3 H), 1.07 (t, $J = 7.1$ Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 188.3$, 164.5, 161.2, 157.2 (d, $J = 36$ Hz), 146.5, 143.9, 138.7 (d, $J = 7$ Hz), 130.8, 130.4 (d, $J = 8$ Hz), 125.4, 121.0 (d, $J = 22$ Hz), 118.2, 115.7 (d, $J = 23$ Hz), 62.1, 62.1, 14.2, 13.7.

MS (EI, 70 eV): *m*/*z* (%) = 334 (100) [M^+], 289 (34), 262 (34), 239 (30), 210 (79), 187 (37), 122 (76).

HRMS (EI): *m*/*z* $[M]^+$ calcd for $C_{17}H_{15}O_6F$: 334.0853; found: 334.0857.

Diethyl 3-(Methylsulfanyl)furan-2,5-dicarboxylate (5b)

According to the general procedure, the metalation of diethyl furan-2,5-dicarboxylate (**2a**; 2.0 mmol, 424 mg) in THF (2 mL) was complete within 10 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 2 mL, 2.2 mmol) was used, followed by the addition of $PhSO_2SMe$ (471 mg, 2.5 mmol). After warming to –50 °C, the reaction mixture was continuously stirred for 3 h, and then quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; CH_2Cl_2); this afforded **5b** as a pale yellow solid.

Yield: 481 mg (93%); mp 69–70 °C.

IR (ATR): 2872, 1728, 1560, 1432, 1392, 1168, 1012, 972, 768 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.14$ (s, 1 H), 4.41 (q, $J = 7.1$ Hz, 2 H), 4.40 (q, $J = 7.1$ Hz, 2 H), 2.47 (s, 3 H), 1.39 (t, $J = 7.1$ Hz, 3 H), 1.38 (t, $J = 7.1$ Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 158.4$, 157.8 145.9, 139.3, 133.6, 118.2, 116.5, 61.8, 61.4, 15.6, 14.3.

MS (EI, 70 eV): *m*/*z* (%) = 258 (100) [M^+], 228 (7) 212 (17), 196 (20).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{14}N_5S$: 258.0562; found: 258.0555.

Diethyl 3-Cyanofuran-2,5-dicarboxylate (5c)

According to the general procedure, the metalation of diethyl furan-2,5-dicarboxylate (**2a**; 5.0 mmol, 1.06 g) in THF (5 mL) was complete within 10 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 5 mL, 5.5 mmol) was used, followed by the addition of tosyl cyanide (1.09 g, 6.0 mmol) and further stirring for 30 min, and then the reaction mixture was quenched with sat. aq NH_4Cl (15 mL). The aqueous layer was extracted with Et_2O (3 × 30 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–Et_2O, 5:1); this afforded **5c** as a colorless solid.

Yield: 781 mg (66%); mp 93–95 °C.

IR (ATR): 2948, 2248, 1724, 1584, 1524, 1496, 820, 780, 736 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.37 (s, 1 H), 4.48 (q, *J* = 7.3 Hz, 2 H), 4.41 (q, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.3 Hz, 3 H), 1.38 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.6, 155.6, 150.2, 147.0, 119.2, 110.8, 104.1, 63.0, 62.4, 14.1, 14.0.

MS (EI, 70 eV): *m*/*z* (%) = 237 (36) [M$^+$], 209 (37), 192 (59), 181 (100), 164 (53), 137 (23).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{11}NO_5$: 237.0637; found: 237.0624.

Diethyl 3-[3-(Trifluoromethyl)phenyl]furan-2,5-dicarboxylate (5d)

According to the general procedure, the metalation of diethyl furan-2,5-dicarboxylate (**2a**; 1.0 mmol, 212 mg) in THF (1 mL) was complete within 10 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 1 mL, 1.1 mmol) was used, followed by addition of 1 M $ZnCl_2$ in THF (1.1 mL, 1.1 mmol) at –78 °C and further stirring for 15 min. $Pd(PPh_3)_4$ (12 mg, 1 mol%) and **4b** (299 mg, 1.1 mmol) were added and the reaction mixture was allowed to warm to 25 °C. After stirring for 3 h, the mixture was quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; CH_2Cl_2); this afforded **5d** as a colorless solid.

Yield: 281 mg (79%); mp 78–79 °C.

IR (ATR): 1484, 1456, 1380, 1368, 1272, 1224, 972, 900, 872 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82 (s, 1 H), 7.75 (d, *J* = 7.7 Hz, 1 H), 7.65 (d, *J* = 8.6 Hz, 1 H), 7.54 (t, *J* = 7.7 Hz, 1 H), 7.30 (s, 1 H), 4.42 (q, *J* = 7.3 Hz, 2 H), 4.34 (q, *J* = 7.3 Hz, 2 H), 1.41 (t, *J* = 7.3 Hz, 3 H), 1.30 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.3, 157.9, 145.8, 141.4, 133.2, 132.6, 131.7, 128.7, 126.3, 125.4, 123.0, 119.8, 61.8, 61.7, 14.3, 14.0.

MS (EI, 70 eV): *m*/*z* (%) = 356 (100) [M$^+$], 311 (32), 283 (34), 256 (17).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{15}O_5F_3$: 356.0872; found: 356.0862.

Ethyl 3-Chloro-5-(trimethylsilyl)furan-2-carboxylate (5e)

According to the general procedure, the metalation of ethyl 5-(trimethylsilyl)furan-2-carboxylate (**2b**, 414 mg, 2.0 mmol) in THF (2 mL) was complete within 1 h at –30 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 2 mL, 2.2 mmol) was used, followed by addition of hexachloroethane (710 mg, 3 mmol) in THF (3 mL) at –50 °C and further stirring for 15 h. The mixture was then quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 2:1); this afforded **5e** as a colorless oil.

Yield: 237 mg (48%).

IR (ATR): 2962, 1370, 1342, 1276, 1252, 1176, 1038, 932, 838 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.64 (s, 1 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H), 0.29 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.3, 158.2, 143.0, 123.6, 123.1, 61.0, 14.3, –2.0.

MS (EI, 70 eV): *m*/*z* (%) = 246 (53) [M$^+$], 231 (100), 203 (33), 174 (6), 103 (28), 75 (41).

HRMS (EI): *m*/*z* calcd for $C_{10}H_{15}ClO_3Si$: 246.0479; found 246.0454.

Ethyl 3-Cyano-5-(trimethylsilyl)furan-2-carboxylate (5f)

According to the general procedure, the metalation of ethyl 5-(trimethylsilyl)furan-2-carboxylate (**2b**, 212 mg, 1.0 mmol) in THF (1 mL) was complete within 1 h at –30 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 1 mL, 1.1 mmol) was used, followed by addition of TsCN (217 mg, 1.2 mmol) in THF (1 mL) and further stirring for 15 min at –30 °C. The mixture was then quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 1:1); this afforded **5f** as a colorless solid.

Yield: 141 mg (52%); mp 100–102 °C.

IR (ATR): 3118, 2246, 1722, 1576, 1476, 1376, 1296, 1016, 838 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.84 (s, 1 H), 4.44 (q, *J* = 7.1 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H), 0.32 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.3, 156.7, 152.4, 122.3, 112.3, 103.0, 62.2, 14.1, –2.1.

MS (EI, 70 eV): *m*/*z* (%) = 237 (21) [M$^+$], 222 (100), 194 (47), 43 (9).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{15}NO_3Si$: 237.0821; found: 237.0828.

Ethyl 3-Benzoyl-5-bromofuran-2-carboxylate (5g)

According to the general procedure, the metalation of ethyl 5-bromofuran-2-carboxylate (**2c**; 219 mg, 1.0 mmol) in THF (1 mL) was complete within 30 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 1 mL, 1.1 mmol) was used, followed by addition of 1 M CuCN·2LiCl in THF (0.2 mL, 20 mol%) at –78 °C and further stirring for 15 min. At –40 °C, BzCl (1.2 mmol, 169 mg) was added; the mixture was stirred for 15 h, and then quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 5:4); this afforded **5g** as a colorless solid.

Yield: 242 mg (75%); mp 95–96 °C.

IR (ATR): 3066, 2982, 1574, 1478, 1176, 1100, 934, 716, 686 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 7.0 Hz, 2 H), 7.60 (t, *J* = 7.5 Hz, 1 H), 7.46 (t, *J* = 7.5 Hz, 2 H), 6.61 (s, 1 H), 4.09 (q, *J* = 7.1 Hz, 2 H), 0.96 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.5, 156.7, 143.3, 136.7, 134.0, 132.8, 129.5, 128.6, 127.8, 114.4, 61.6, 13.5.

MS (EI, 70 eV): *m*/*z* (%) = 324 (98) [M$^+$, ^{81}Br], 322 (100) [M$^+$, ^{79}Br], 278 (25), 250 (45), 219 (37), 217 (36), 170 (18), 143 (15), 105 (46), 77 (36).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}BrO_4$: 321.9841; found: 321.9834.

Ethyl 5-Bromo-3-chlorofuran-2-carboxylate (5h)

According to the general procedure, the metalation of ethyl 5-bromofuran-2-carboxylate (**2c**; 1.09 g, 5.0 mmol) in THF (5 mL) was complete within 30 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 5 mL, 5.5 mmol) was used, followed by addition of $PhSO_2Cl$ (7.5 mmol, 1.32 g). After 3 h at –78 °C, the reaction mixture was allowed to warm to 25 °C, and then quenched with sat. aq NH_4Cl (15 mL). The aqueous layer was extracted with Et_2O (3 × 30 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 8:1); this afforded **5h** as a colorless solid.

Yield: 748 mg (59%); mp 98–100 °C.

IR (ATR): 2984, 2360, 1698, 1466, 1376, 1290, 1170, 1098, 932 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.48 (s, 1 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 1.38 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.8, 141.7, 127.2, 125.3, 116.1, 61.5, 14.3.

MS (EI, 70 eV): *m*/*z* (%) = 256 (14) [M^+, ^{37}Cl ^{81}Br], 254 (53) [M^+, ^{37}Cl ^{79}Br, ^{35}Cl ^{81}Br], 252 (43) [M^+, ^{35}Cl ^{79}Br], 226 (93), 209 (100), 182 (64), 153 (24), 129 (23), 72 (21).

HRMS (EI): *m*/*z* calcd for $C_7H_6BrClO_3$: 251.9189; found: 251.9185.

Ethyl 5-Bromo-3-cyanofuran-2-carboxylate (5i)

According to the general procedure, the metalation of ethyl 5-bromofuran-2-carboxylate (**2c**; 1.09 g, 5.0 mmol) in THF (5 mL) was complete within 30 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 5 mL, 5.5 mmol) was used, followed by addition of TsCN (5.5 mmol, 997 mg) in THF (6 mL). After stirring for 30 min at –78 °C, the reaction mixture was allowed to warm to 25 °C, and then quenched with sat. aq NH_4Cl (15 mL). The aqueous layer was extracted with Et_2O (3 × 30 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 3:1); this afforded **5i** as a colorless solid.

Yield: 765 mg (63%); mp 103–105 °C.

IR (ATR): 2982, 1720, 1668, 1596, 1478, 1400, 1304, 1016, 934 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.69 (s, 1 H), 4.45 (q, *J* = 7.1 Hz, 2 H), 1.42 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.3, 150.2, 128.7, 115.3, 110.6, 105.2, 62.7, 14.1.

MS (EI, 70 eV): *m*/*z* (%) = 245 (30), [M^+, ^{81}Br], 243 (34) [M^+, ^{79}Br], 217 (96), 215 (100), 200 (54), 198 (55), 173 (34), 171 (34), 144 (16), 142 (18), 108 (9), 63 (18).

HRMS (EI): *m*/*z* calcd for $C_8H_6BrNO_3$: 242.9531; found: 242.9521.

Ethyl 5-Bromo-3-[4-(ethoxycarbonyl)phenyl]furan-2-carboxylate (5j)

According to the general procedure, the metalation of ethyl 5-bromofuran-2-carboxylate (**2c**; 219 mg, 1.0 mmol) in THF (1 mL) was complete within 30 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 1 mL, 1.1 mmol) was used, followed by addition of 1 M $ZnCl_2$ in THF (1.1 mL, 1.1 mmol) at –78 °C and further stirring for 15 min. $Pd(PPh_3)_4$ (12 mg, 1 mol%) and ethyl 4-iodobenzoate (**4c**; 1.1 mmol, 304 mg) were added and the reaction mixture was allowed to warm to 25 °C. After stirring for 6 h, the reaction mixture was quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–Et_2O, 8:1); this afforded **5j** as a colorless solid.

Yield: 314 mg (86%); mp 71–72 °C.

IR (ATR): 2988, 2532, 1980, 1664, 1568, 1476, 1280, 1108, 1080, 1020 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.4 Hz, 2 H), 7.60 (d, *J* = 8.4 Hz, 2 H), 6.57 (s, 1 H), 4.39 (q, *J* = 7.1 Hz, 2 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 1.39 (t, *J* = 7.1 Hz, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1, 157.8, 142.2, 135.5, 135.3, 130.6, 129.3, 129.2, 127.0, 115.9, 61.3, 61.1, 14.3, 14.1.

MS (EI, 70 eV): *m*/*z* (%) = 368 (100), [M^+, ^{81}Br], 366 (99) [M^+, ^{79}Br], 233 (54), 295 (33).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}BrO_5$: 368.0082; found: 368.0062.

Diethyl 5,5′-Dibromo-3,3′-bifuran-2,2′-dicarboxylate (5k)

According to the general procedure, the metalation of ethyl 5-bromofuran-2-carboxylate (**2c**; 219 mg, 1.0 mmol) in THF (1 mL) was complete within 30 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 1 mL, 1.1 mmol) was used, followed by addition of 1 M $ZnCl_2$ in THF (1.1 mL, 1.1 mmol) at –78 °C and further stirring for 15 min. Subsequently, chloranil (**4d**; 369 mg, 1.5 mmol) in THF (7 mL) was slowly added. After stirring for 15 min, the reaction mixture was allowed to warm to –40 °C and stirred for 2 h. The reaction mixture was quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude residue was purified by flash column chromatography (silica gel; CH_2Cl_2); this afforded **5j** as a pale brown solid.

Yield: 174 mg (80%); mp 168–170 °C.

IR (ATR): 2904, 2112, 1628, 1596, 1448, 1148, 1088, 1020, 940, 684 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 6.61 (s, 2 H), 4.29 (q, *J* = 7.1 Hz, 4 H), 1.30 (t, *J* = 7.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 157.8, 142.8, 126.7, 125.6, 116.9, 61.6, 14.4.

MS (EI, 70 eV): *m*/*z* (%) = 438 (26) [M^+, ^{81}Br, ^{81}Br], 436 (53) [M^+, ^{79}Br, ^{81}Br], 434 ([M^+, ^{79}Br, ^{79}Br], 357 (83), 327 (100), 299 (30), 227 (27).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{12}Br_2O_6$: 435.8980; found: 435.8980.

Diethyl 3-[(4-Cyanophenyl)(hydroxy)methyl]-4-(methylsulfanyl)furan-2,5-dicarboxylate (7a)

According to the general procedure, the metalation of **5b** (253 mg, 1.0 mmol) in THF (4 mL) was complete within 45 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 1 mL, 1.1 mmol) was used, followed by addition of 4-cyanobenzaldehyde (197 mg, 1.5 mmol) and further stirring for 3 h. Subsequently, the reaction mixture was allowed to warm to 25 °C. The reaction mixture was quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude residue was purified by flash column chromatography (silica gel; CH_2Cl_2); this afforded **7a** as a pale yellow oil.

Yield: 262 mg (67%).

IR (ATR): 2908, 2872, 1780, 1608, 1368, 1284, 1180, 1016, 904, 696 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.6 Hz, 2 H), 7.47 (d, *J* = 8.6 Hz, 2 H), 6.26 (d, *J* = 11.9 Hz, 1 H), 5.50 (d, *J* = 11.9 Hz, 1 H), 4.48–4.36 (m, 4 H), 2.39 (s, 3 H), 1.43 (t, *J* = 7.3 Hz, 3 H), 1.38 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 157.5, 147.9, 146.2, 140.7, 140.5, 132.5, 128.0, 126.8, 118.9, 111.7, 67.7, 63.1, 62.3, 19.6, 14.5, 14.3.

MS (EI, 70 eV): *m*/*z* (%) = 389 (98) [M^+], 360 (52), 341 (37), 313 (100), 297 (20), 131 (55).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{19}NO_6S$: 389.0933; found: 389.0934.

Diethyl 3-Cyano-4-(4-cyanophenyl)furan-2,5-dicarboxylate (7b)

Diethyl 3-cyanofuran-2,5-dicarboxylate (**5c**; 237 mg, 1 mmol) was dissolved in THF (4 mL), and 1 M $ZnCl_2$ in THF (1.1 mL, 1.1 mmol) was added. After the mixture had been cooled to –78 °C, TMPMgCl·LiCl (1.2 mmol, 1.1 mL, 1.1 M in THF) was added and

the mixture was continuously stirred for 20 min. $Pd(PPh_3)_4$ (12 mg, 1 mol%) and 4-iodobenzonitrile (**4f**; 275 mg, 1.2 mmol) were added at –78 °C, and the reaction mixture was allowed to warm to 25 °C. After stirring for 3 h, the mixture was quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; CH_2Cl_2); this afforded **7b** as a pale brown solid.

Yield: 239 mg (71%); mp 156–158 °C.

IR (ATR): 2988, 1504, 1452, 1324, 1180, 1080, 1012, 844, 776, cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.6 Hz, 2 H), 7.64 (d, *J* = 8.6 Hz, 2 H), 4.52 (q, *J* = 7.1 Hz, 2 H), 4.35 (q, *J* = 7.1 Hz, 2 H), 1.46 (t, *J* = 7.1 Hz, 3 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.8, 155.5, 149.6, 142.1, 133.1, 132.1, 130.5, 118.0, 113.8, 110.2, 105.3, 63.3, 62.6, 14.1, 14.0.

MS (EI, 70 eV): *m*/*z* (%) = 338 (100) [M^+], 310 (34), 293 (24), 281 (34), 264 (33).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{14}N_2O_5$: 338.0903; found: 338.0888.

Ethyl 3-Chloro-5-cyanofuran-2-carboxylate (8)

After ethyl 5-bromo-3-chlorofuran-2-carboxylate (**5e**; 748 mg, 3.0 mmol) in THF (5 mL) had been cooled to –50 °C, 1.36 M *i*-PrMgCl·LiCl in THF (2.4 mL, 3.3 mmol) was added dropwise. After the mixture had stirred for 30 min, TsCN (181 mg, 1.1 mmol) in THF (1.5 mL) was added and the reaction mixture was allowed to warm to 25 °C. After further stirring for 3 h, the mixture was quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 1:1); this afforded **8** as a colorless solid.

Yield: 440 mg (73%); mp 80–81 °C.

IR (ATR): 2986, 2238, 1718, 1547, 1516, 1114, 1052, 1012, 856 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.12 (s, 1 H), 4.42 (q, *J* = 7.0 Hz, 2 H), 1.40 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.2, 142.9, 127.3, 124.0, 123.4, 109.5, 62.3, 14.1.

MS (EI, 70 eV): *m*/*z* (%) = 199 (25) [M^+], 171 (82), 154 (100), 127 (20), 98 (15).

HRMS (EI): *m*/*z* calcd for $C_8H_6ClNO_3$: 199.0036; found: 199.0020.

Ethyl 4-Allyl-3-chloro-5-cyanofuran-2-carboxylate (9)

According to the general procedure, the metalation of **8** (136 mg, 0.68 mmol) in THF (1.4 mL) was complete within 25 min at –78 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 0.7 mL, 0.75 mmol) was used, followed by addition of 1 M CuCN·2LiCl in THF (0.14 mL, 20 mol%) at –78 °C and further stirring for 15 min. Allyl bromide (121 mg, 1.0 mmol) was added to the mixture at –78 °C and the mixture was continuously stirred for 15 min, and then quenched with sat. aq NH_4Cl (3 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 1:1); this afforded **9** as a colorless oil.

Yield: 120 mg (74%).

IR (ATR): 2986, 1532, 1406, 1286, 1184, 1032, 992, 768 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 5.93–5.80 (m, 1 H), 5.22–5.13 (m, 2 H), 4.42 (q, *J* = 7.1 Hz, 2 H), 3.37–3.34 (m, 2 H), 1.40 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.4, 142.8, 136.1, 131.3, 125.6, 124.4, 119.0, 109.9, 62.4, 27.9, 14.4.

MS (EI, 70 eV): *m*/*z* (%) = 239 (68) [M^+], 211 (30), 194 (100), 167 (21), 136 (27), 102 (29).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{10}ClNO_3$: 239.0349; found: 239.0357.

Ethyl 3-[Hydroxy(phenyl)methyl]-1-tosylindole-2-carboxylate (12a)

According to the general procedure, the metalation of **10a** (172 mg, 0.5 mol) in THF (2.5 mL) was complete within 30 min at –45 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 0.5 mL, 0.55 mmol) was used, followed by addition of benzaldehyde (0.6 mol, 64 mg) at –45 °C. Stirring continued for 30 min, and then the mixture was quenched with sat. aq NH_4Cl (3 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; CH_2Cl_2); this afforded **12a** as a colorless solid.

Yield: 205 mg (91%); mp 51–52 °C.

IR (ATR): 3526, 1596, 1448, 1368, 1258, 1174, 1016, 748, 668 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.7 Hz, 1 H), 7.75 (d, *J* = 8.4 Hz, 2 H), 7.44–7.12 (m, 10 H), 6.15 (d, *J* = 5.2 Hz, 1 H), 4.45 (q, *J* = 7.0 Hz, 2 H), 2.82 (d, *J* = 5.2 Hz, 1 H), 2.32 (s, 3 H) 1.37 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 163.2, 145.1, 141.5, 136.9, 134.2, 129.9, 129.6, 128.7, 128.3, 127.9, 127.6, 127.2, 126.7, 126.1, 124.3, 121.9, 115.4, 68.9, 62.7, 21.6, 13.9.

MS (EI, 70 eV): *m*/*z* (%) = 449 (4) [M^+], 294 (54), 248 (100), 220 (14), 204 (9), 165 (6), 105 (12), 91 (13), 77 (6).

HRMS (EI): *m*/*z* calcd for $C_{25}H_{23}NO_5S$: 449.1297; found: 449.1281.

Ethyl 3-Allyl-1-tosylindole-2-carboxylate (12b)

According to the general procedure, the metalation of **10a** (172 mg, 0.5 mol) in THF (2.5 mL) was complete within 30 min at –45 °C when 1.1 M TMPMgCl·LiCl in THF (**1**; 0.5 mL, 0.55 mmol) was used, followed by addition of 1 M CuCN·2LiCl in THF (0.12 mL, 20 mol%) at –45 °C and further stirring for 15 min. Allyl bromide (0.6 mmol, 73 mg) was added to the mixture at –45 °C, and stirring continued for 30 min, after which the mixture was quenched with sat. aq NH_4Cl (3 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; pentane–CH_2Cl_2, 5:4); this afforded **12b** as a colorless solid.

Yield: 182 mg (95%); mp 66–68 °C.

IR (ATR): 1640, 1598, 1440, 1308, 1260, 1180, 1146, 810, 750 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.3 Hz, 1 H), 7.76 (d, *J* = 6.6 Hz, 2 H), 7.47 (d, *J* = 7.9 Hz, 1 H), 7.37 (t, *J* = 5.9 Hz, 1 H), 7.23 (t, *J* = 7.0 Hz, 1 H), 7.17 (d, *J* = 6.8 Hz, 2 H), 5.93–5.80 (m, 1 H), 5.03–4.93 (m, 2 H), 4.45 (q, *J* = 7.1 Hz, 2 H), 3.51 (td, *J* = 6.2, 1.7 Hz, 2 H), 2.31 (s, 3 H), 1.41 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.4, 144.8, 137.1, 134.6, 134.5, 129.8, 129.4, 128.8, 127.2, 126.7, 126.5, 124.0, 120.7, 116.3, 115.6, 62.1, 28.7, 21.6, 14.1.

MS (EI, 70 eV): *m*/*z* (%) = 383 (33) [M^+], 338 (8), 228 (100), 200 (16), 183 (27), 154 (77), 128 (28), 91 (34).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{21}NO_4S$: 383.1191; found: 383.1186.

1-*tert*-Butyl 2,5-Diethyl 3-(4-Chlorophenyl)pyrrole-1,2,5-tricarboxylate (12c)

According to the general procedure, the metalation of **10b** (311 mg, 1.0 mmol) in THF (1 mL) by 0.58 M $TMP_2Mg{\cdot}2LiCl$ in THF (**13**; 1.9 mL, 1.1 mmol) was complete within 1.5 h at –30 °C; 1 M $ZnCl_2$ in THF (1.1 mL, 1.1 mmol) was added to the mixture at –30 °C and stirring continued for 15 min. $Pd(PPh_3)_4$ (12 mg, 1 mol%) and 1-chloro-4-iodobenzene (**4g**; 358 mg, 1.5 mmol) were added and the reaction mixture was allowed to warm to 25 °C. After stirring for 1.5 h, the reaction mixture was quenched with sat. aq NH_4Cl (5 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL) and the combined organic phases were dried (Na_2SO_4) and concentrated in vacuo. The crude product was purified by flash column chromatography (silica gel; CH_2Cl_2); this afforded **12c** as a colorless solid.

Yield: 339 mg (80%); mp 80–81 °C.

IR (ATR): 2984, 1724, 1548, 1440, 1384, 1296, 1152, 1124, 928, 784 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.31 (m, 4 H), 6.82 (s, 1 H), 4.34 (q, *J* = 7.1 Hz, 2 H), 4.21 (q, *J* = 7.1 Hz, 2 H), 1.65 (s, 9 H), 1.35 (t, *J* = 7.1 Hz, 3 H), 1.13 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 160.1, 159.5, 148.5, 133.5, 132.6, 130.9, 129.9, 127.9, 125.9, 123.2, 117.3, 86.3, 61.2, 61.2, 27.4, 14.3, 13.9.

MS (EI, 70 eV): *m*/*z* (%) = 421 (4) [M^+], 321 (100), 274 (14), 202 (13).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{24}ClNO_6$: 421.1292; found: 421.1270.

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