Amine-catalyzed and functional group-controlled chemo- and regioselective synthesis of multi-functionalized CF₃-benzene

via a metal-free process

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1. General methods

- Proton nuclear magnetic resonance (¹H NMR) spectra were recorded with Bruker Avance III 400 MHz spectrometers. Proton chemical shifts are reported in parts per million (δ scale), and are referenced using residual protium in the NMR solvent (CDCl₃: δ 7.26). Data are reported as follows: chemical shift [multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet), coupling constant(s) (Hz), integration].

- Carbon-13 nuclear magnetic resonance (¹³C NMR) spectra were recorded with Bruker Avance 400 MHz spectrometers. Carbon chemical shifts are reported in parts per million (δ scale), and are referenced using the carbon resonances of the solvent (CDCl₃: δ 77.0). Data are reported as follows: chemical shift [multiplicity (if not singlet), assignment (C_q = fully substituted carbon)].

- High resolution mass spectra (HRMS) were recorded on a Waters SYNAPT G2 or Agilent G1969-85000 using an electrospray (ESI) ionization source.

- Column chromatography was performed on silica gel (400-500 mesh) eluting with ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates. UV light and I₂ were used to visualize products.

- Melting points were determined on a Mel-Temp apparatus and are uncorrected.

2. The synthesis of CF₃-functionalized multi-substituted benzenes

2.1 Procedure for 3

The reaction was carried out with 1 (0.20 mmol) and 2 (0.30 mmol), amine catalyst IV (0.05 mmol) and AcOH (0.08 mmol) in toluene (2 mL) under an open atmosphere at 70 °C for 8 h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 80:1) to
give the final CF₃-functionlized tetra-substuted benzenes 3, which was further analyzed by ¹H NMR, ¹³C HMR, HRMS analysis.

**ethyl 2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Diagram of 3a]

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.20 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3a as a white solid with 76% yield (48.6 mg). m.p. 68-70 °C.

**NMR and HRMS data for the product 3a:**

¹H NMR (400 MHz, CDCl₃): δ = 7.80 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.0 Hz, 1H), 7.53-7.50 (m, 5H), 4.44 (q, J = 7.2 Hz, 2H), 1.4 (t, J = 7.2 Hz, 3H) ppm.

¹³C NMR (100 MHz, CDCl₃): δ = 166.4, 149.8, 136.6, 133.4, 132.9 (q, J = 2.0 Hz), 132.2, 131.2 (d, J = 36.0 Hz), 129.8, 129.0, 128.9, 122.1 (d, J = 274.0 Hz), 114.5, 110.3 (d, J = 2.0 Hz), 62.9, 13.9 ppm.

HRMS (ESI): m/z calculated for C₁₇H₁₂F₃NO₂⁺Na 342.0718, found 342.0714.

**ethyl 2'-chloro-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Diagram of 3b]

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.20 mmol) and 2-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3b as a white solid with 73% yield (51.6 mg). m.p. 68-70 °C.
NMR and HRMS data for the product 3b:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.83$ (d, $J = 8.0$ Hz, 1H), 7.69 (d, $J = 8.0$ Hz, 1H), 7.56 (dd, $J = 8.0$, 1.6 Hz, 1H), 7.48-7.40 (m, 2H), 7.34 (dd, $J = 7.6$, 2.0 Hz, 1H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.41 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.3$, 147.2, 135.5, 134.0, 133.6 (q, $J = 2.0$ Hz), 132.8, 132.0, 131.1, 130.8, 130.7 (d, $J = 32.0$ Hz), 130.2, 127.2, 122.0 (d, $J = 274.0$ Hz), 113.7, 112.0 (d, $J = 2.0$ Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$ClF$_3$NO$_2$+Na 376.0328, found 376.0325.

ethyl 3'-chloro-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.20 mmol) and 3-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3c as a white solid with 78% yield (54.9 mg). m.p. 89-91 °C.

NMR and HRMS data for the product 3c:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.82$ (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.0$ Hz, 1H), 7.52-7.45 (m, 3H), 7.42 (dt, $J = 7.2$, 1.6 Hz, 1H), 4.44 (q, $J = 7.2$ Hz, 2H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.2$, 148.1, 138.2, 135.0, 133.5 (d, $J = 3.0$ Hz), 133.2, 132.4, 131.3 (d, $J = 33.0$ Hz), 130.2, 130.0, 129.0, 127.2, 122.0 (d, $J = 274.0$ Hz), 114.1, 110.4 (d, $J = 3.0$ Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$ClF$_3$NO$_2$+Na 376.0328, found 376.0326.
ethyl 4'-chloro-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.20 mmol) and 4-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3d as a white solid with 77% yield (54.2 mg). m.p. 94-96 °C.

NMR and HRMS data for the product 3d:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.81$ (d, $J = 8.0$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 7.53-7.50 (m, 2H), 7.48-7.45 (m, 2H), 4.43 (q, $J = 7.2$ Hz, 2H), 2.43 (s, 3H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm;

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.2$, 148.5, 136.3, 134.9,133.3 (d, $J = 2.0$ Hz), 133.2, 132.4, 131.3 (d, $J = 33.0$ Hz), 130.3, 129.3, 122.0 (d, $J = 275.0$ Hz), 114.3, 110.3 (d, $J = 2.0$ Hz), 63.0, 13.9 ppm;

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$ClF$_3$NO$_2$+Na 376.0328, found 376.0331.

ethyl 2'-bromo-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 2-bromocinnamaldehyde (63.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3e as a white solid with 71% yield (56.5 mg). m.p. 96-98 °C.
NMR and HRMS data for the product 3e:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.83$ (d, $J = 8.0$ Hz, 1H), 7.75 (d, $J = 8.0$, 1.2 Hz, 1H), 7.67 (d, $J = 8.0$ Hz, 1H), 7.47 (td, $J = 7.2$, 1.2 Hz, 1H), 7.40-7.31 (m, 2H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.42 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.3$, 148.8, 137.5, 133.9, 133.6 (q, $J = 2.0$ Hz), 133.4, 132.0, 131.2, 130.7, 130.6 (d, $J = 33.0$ Hz), 127.8, 122.5, 122.0 (, $J = 274.0$ Hz), 113.6, 110.9 (d, $J = 2.0$ Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$BrF$_3$NO$_2$+Na 419.9823, found 419.9819.

ethyl 3'-bromo-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

![Chemical Structure]

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enooate (41.4 mg, 0.2 mmol) and 3-bromocinnamaldehyde (63.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3f as a white solid with 76% yield (60.3 mg). m.p. 102-104 °C.

NMR and HRMS data for the product 3f:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.81$ (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.0$, 1.2 Hz, 1H), 7.67-7.63 (m, 2H), 7.49-7.47 (m, 1H), 7.40 (td, $J = 8.0$, 0.4 Hz, 1H), 4.44 (q, $J = 7.2$ Hz, 2H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.2$, 148.0, 138.4, 133.5 (q, $J = 2.0$ Hz), 133.3, 132.8, 132.4, 131.8, 131.3 (d, $J = 32.0$ Hz), 130.4, 127.7, 123.0, 122.0 (d, $J = 274.0$ Hz), 114.1, 110.4 (d, $J = 2.0$ Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$BrF$_3$NO$_2$+Na 419.9823, found 419.9821.
**ethyl 4'-bromo-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using ethyl \((E)-4\)-cyano-3-(trifluoromethyl)but-3-enolate (41.4 mg, 0.2 mmol) and 4-bromocinnamaldehyde (63.3 mg, 0.3 mmol). Purification of the crude product *via* column chromatography delivered **3g** as a white solid with 78% yield (61.8 mg). m.p. 101-103 °C.

**NMR and HRMS data for the product 3g:**

**1H NMR (400 MHz, CDCl₃):** \(\delta = 7.81 \ (d, J = 8.0 \text{ Hz}, 1\text{H}), 7.70 \ (d, J = 8.0 \text{ Hz}, 1\text{H}), 7.68-7.65 \ (m, 2\text{H}), 7.41-7.38 \ (m, 2\text{H}), 4.43 \ (q, J = 7.2 \text{ Hz}, 2\text{H}), 1.41 \ (t, J = 7.2 \text{ Hz}, 3\text{H}) \text{ ppm.} \)

**13C NMR (100 MHz, CDCl₃):** \(\delta = 166.2, 148.5, 135.4, 133.3 \ (q, J = 2.0 \text{ Hz}), 133.2, 132.4, 132.2, 131.3 \ (d, J = 33.0 \text{ Hz}), 130.5, 124.5, 122.0 \ (, J = 274.0 \text{ Hz}), 114.3, 110.2 \ (d, J = 2.0 \text{ Hz}), 63.0, 13.9 \text{ ppm.} \)

**HRMS (ESI):** m/z calculated for C₁₇H₁₁BrF₃NO₂⁺Na 419.9823, found 419.9826.

**ethyl 2-cyano-2'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using ethyl \((E)-4\)-cyano-3-(trifluoromethyl)but-3-enolate (41.4 mg, 0.2 mmol) and 2-fluorocinnamaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product *via* column chromatography delivered **3h** as a white solid with 72% yield (48.7 mg). m.p. 82-84 °C.
NMR and HRMS data for the product 3h:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.82$ (d, $J = 8.0$ Hz, 1H), 7.73 (d, $J = 8.0$ Hz, 1H), 7.54-7.48 (m, 1H), 7.40 (td, $J = 7.6$, 1.6 Hz, 1H), 7.33-7.28 (m, 1H), 7.24 (d, $J = 8.8$ Hz, 1H), 4.44 (q, $J = 7.2$ Hz, 2H), 1.41 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.2$, 159.3 (d, $J = 248.0$ Hz), 143.9, 134.2, 133.6 (q, $J = 2.0$ Hz), 132.1, 132.0 (d, $J = 8.0$ Hz), 131.1 (d, $J = 2.0$ Hz), 131.0 (d, $J = 33.0$ Hz), 124.7 (d, $J = 4.0$ Hz), 124.3 (d, $J = 15.0$ Hz), 122.0 (d, $J = 274.0$ Hz), 116.4 (d, $J = 21.0$ Hz), 113.9, 111.8 (d, $J = 2.0$ Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$F$_4$NO$_2$+Na 360.0624, found 360.0621.

ethyl 2-cyano-3'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

![Chemical Structure](image)

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-fluorocinnamaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3i as a white solid with 73% yield (49.1 mg). m.p. 95-97 °C.

NMR and HRMS data for the product 3i:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.82$ (d, $J = 8.0$ Hz, 1H), 7.72 (d, $J = 8.0$ Hz, 1H), 7.54-7.48 (m, 1H), 7.33-7.30 (m, 1H), 7.25-7.20 (m, 2H), 4.44 (q, $J = 7.2$ Hz, 2H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.2$, 162.7 (d, $J = 247.0$ Hz), 148.3, 138.4 (d, $J = 7.0$ Hz), 133.5 (q, $J = 2.0$ Hz), 133.3, 132.4, 131.3 (d, $J = 32.0$ Hz), 130.7 (d, $J = 8.0$ Hz), 124.8 (d, $J = 3.0$ Hz), 122.0 (d, $J = 274.0$ Hz), 116.8 (d, $J = 21.0$ Hz), 116.2 (d, $J = 22.0$ Hz), 114.1, 110.4 (d, $J = 2.0$ Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$F$_4$NO$_2$+Na 360.0624, found 360.0625.
**ethyl 2-cyano-4'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Molecular structure](image)

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 4-fluorocinnamaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3j as a white solid with 75% yield (50.7 mg). m.p. 44-46 °C.

**NMR and HRMS data for the product 3j:**

**$^1$H NMR (400 MHz, CDCl$_3$):** δ = 7.80 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.51 (dd, J = 8.4, 5.2 Hz, 2H), 7.24-7.20 (m, 2H), 4.43 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H) ppm.

**$^{13}$C NMR (100 MHz, CDCl$_3$):** δ = 166.3, 163.6 (d, J = 279.0 Hz), 148.7, 133.3, 133.1 (q, J = 2.0 Hz), 132.6 (d, J = 3.0 Hz), 132.3, 131.2 (d, J = 32.0 Hz), 131.0 (d, J = 9.0 Hz), 122.0 (q, J = 274.0 Hz), 116.2 (d, J = 22.0 Hz), 114.4, 110.3 (d, J = 2.0 Hz), 63.0, 13.9 ppm.

**HRMS (ESI):** m/z calculated for C$_{17}$H$_{11}$F$_4$NO$_2$+Na 360.0624, found 360.0627.

**ethyl 2-cyano-2'-nitro-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Molecular structure](image)

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 2-nitrocinamaldehyde (53.2 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered
3k as a white solid with 64% yield (46.3 mg). m.p. 74-76 °C.

NMR and HRMS data for the product 3k:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.29$ (dd, $J = 8.0$, 1.2 Hz, 1H), 7.84 (d, $J = 8.0$ Hz, 1H), 7.80 (td, $J = 7.6$, 1.2 Hz, 1H), 7.73 (td, $J = 8.0$, 1.6 Hz, 1H), 7.61 (d, $J = 8.0$ Hz, 1H), 7.41 (dd, $J = 7.2$, 1.2 Hz, 1H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.42 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.0$, 147.4, 146.9, 134.0, 133.6 (q, $J = 2.0$ Hz), 132.5, 132.1, 132.0, 131.9, 130.9, 130.8 (q, $J = 33.0$ Hz), 125.5, 121.9 (q, $J = 274.0$ Hz), 113.6, 111.1 (d, $J = 2.0$ Hz), 63.1, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{11}$F$_3$N$_2$O$_4$Na 387.0569, found 387.0570.

ethyl 2-cyano-4'-nitro-3-(trifluoromethyl)-meta-biphenyl-4-carboxylate

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 4-nitrocinnamaldehyde (53.2 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3l as a white solid with 68% yield (49.5 mg). m.p. 140-142 °C.

NMR and HRMS data for the product 3l:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.41$-8.39 (m, 2H), 7.88 (d, $J = 8.0$ Hz, 1H), 7.76 (d, $J = 8.4$ Hz, 1H), 7.73-7.70 (m, 2H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 165.9$, 148.6, 147.1, 142.6, 134.2 (d, $J = 2.0$ Hz), 133.1, 132.7, 131.5 (d, $J = 33.0$ Hz), 130.2, 124.2, 121.8 (d, $J = 274.0$ Hz), 113.9, 110.4 (d, $J = 2.0$ Hz), 63.2, 13.9 ppm.
HRMS (ESI): m/z calculated for C_{17}H_{11}F_{6}NO_{2}Na 387.0569, found 387.0569.

**ethyl 2-cyano-3,3'-bis(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(trifluoromethyl)cinnamaldehyde (60.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3m as a white solid with 70% yield (53.9 mg). m.p. 58-60 °C.

**NMR and HRMS data for the product 3m:**

**H NMR (400 MHz, CDCl₃):** δ = 7.85 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.76-7.74 (m, 3H), 7.68 (t, J = 8.0 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H) ppm.

**C NMR (100 MHz, CDCl₃):** δ = 166.1, 148.0, 137.3, 133.7 (d, J = 2.0 Hz), 133.3, 132.5, 132.4 (d, J = 1.0 Hz), 131.6 (q, J = 33.0 Hz), 131.4 (q, J = 32.0 Hz), 129.6, 126.5 (q, J = 1.6 Hz), 125.9 (q, J = 1.6 Hz), 123.7 (d, J = 271.0 Hz), 121.9 (d, J = 274.0 Hz), 114.1, 110.5 (d, J = 2.0 Hz), 63.1, 13.9 ppm.

**HRMS (ESI):** m/z calculated for C_{18}H_{11}F_{6}NO_{2}Na 410.0592, found 410.0591.

**ethyl 2-cyano-4'-methyl-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**
Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and trans-4-methylcinnamaldehyde (43.9 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3n as a white solid with 81% yield (53.7 mg). m.p. 62-64 °C.

**NMR and HRMS data for the product 3n:**

$^1$H NMR (400 MHz, CDCl₃): $\delta = 7.78$ (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.0$ Hz, 1H), 7.43-7.41 (m, 2H), 7.34-7.32 (m, 2H), 4.43 (q, $J = 7.2$ Hz, 2H), 2.43 (s, 3H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl₃): $\delta = 166.5$, 149.8, 140.0, 133.7, 133.3, 132.7 (d, $J = 2.0$ Hz), 132.1, 131.1 (d, $J = 32.0$ Hz), 129.6, 129.0, 122.1 (d, $J = 274.0$ Hz), 114.7, 110.1 (d, $J = 3.0$ Hz), 62.9, 21.3, 13.9 ppm.

HRMS (ESI): m/z calculated for C₁₈H₁₄F₃NO₂+Na 356.0874, found 356.0877.

**ethyl 2-cyano-2'-methoxy-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 2-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3o as a white solid with 79% yield (55.4 mg). m.p. 86-87 °C.

**NMR and HRMS data for the product 3o:**

$^1$H NMR (400 MHz, CDCl₃): $\delta = 7.77$ (d, $J = 8.0$ Hz, 1H), 7.67 (d, $J = 8.0$ Hz, 1H), 7.47 (td, $J = 8.4$, 1.6 Hz, 1H), 7.23 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.10-7.03 (m, 2H), 4.43 (q, $J = 7.2$ Hz, 2H), 3.83 (s, 3H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl₃): $\delta = 166.6$, 156.4, 147.1, 134.2, 132.6 (d, $J = 2.0$ Hz), 131.9, 131.4, 130.6, 130.5 (d, $J = 33.0$ Hz), 125.7, 122.2 (d, $J = 274.0$ Hz), 120.9, 114.4,
112.3 (d, $J = 2.0$ Hz), 111.5, 62.8, 55.5, 13.9 ppm.

**HRMS (ESI):** m/z calculated for C$_{18}$H$_{14}$F$_3$NO$_3$+Na 372.0823, found 372.0825.

**ethyl 2-cyano-4'-methoxy-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Chemical structure](image)

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3p as a white solid with 83% yield 57.8 mg). m.p. 101-103 °C.

**NMR and HRMS data for the product 3p:**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.76$ (d, $J = 8.0$ Hz, 1H), 7.70 (d, $J = 8.4$ Hz, 1H), 7.50-7.46 (m, 2H), 7.06-7.02 (m, 2H), 4.42 (q, $J = 7.2$ Hz, 2H), 3.88 (s, 3H), 1.40 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.5$, 160.9, 149.5, 133.3, 132.4 (d, $J = 3.0$ Hz), 132.1, 131.2 (d, $J = 32.0$ Hz), 130.4, 128.8, 122.1 (d, $J = 274.0$ Hz), 114.8, 114.4, 109.9 (d, $J = 2.0$ Hz), 62.9, 55.4, 13.9 ppm.

**HRMS (ESI):** m/z calculated for C$_{18}$H$_{14}$F$_3$NO$_3$+Na 372.0823, found 372.0821.

**ethyl 2',4'-dichloro-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Chemical structure](image)

Prepared according to the general procedure using ethyl (E)-4-cyano-3-
(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(2,4-dichlorophenyl)acrylaldehyde (60.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3q as a white solid with 76% yield (59.1 mg). m.p. 110-112 °C.

**NMR and HRMS data for the product 3q:**

**1H NMR (400 MHz, CDCl₃):** δ = 7.84 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 2.0 Hz, 1H), 7.42 (dd, J = 8.4, 2.0 Hz, 1H), 7.29 (d, J = 8.0 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H) ppm.

**13C NMR (100 MHz, CDCl₃):** δ = 166.1, 146.1, 136.7, 133.9, 133.9, 133.7, 133.3 (d, J = 3.0 Hz), 132.2, 131.6, 130.9 (d, J = 33.0 Hz), 130.2, 127.7, 121.9 (d, J = 274.0 Hz), 113.6, 112.0 (d, J = 2.0 Hz), 63.1, 13.9 ppm.

**HRMS (ESI):** m/z calculated for C₁₇H₁₀Cl₂F₃NO₂Na 409.9938, found 409.9937.

**ethyl 2',5'-dichloro-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(2,5-dichlorophenyl)acrylaldehyde (60.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3r as a white solid with 74% yield (57.2 mg). m.p. 134-136 °C.

**NMR and HRMS data for the product 3r:**

**1H NMR (400 MHz, CDCl₃):** δ = 7.85 (dd, J = 8.0, 0.4 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.44 (dd, J = 8.4, 2.4 Hz, 1H), 7.32 (d, J = 2.8 Hz, 1H), 4.45 (q, J = 7.2 Hz, 2H), 1.42 (t, J = 7.2 Hz, 3H) ppm.
\^{13}C\text{ NMR (100 MHz, CDCl}\_3\text{: }\delta = 166.0, 145.8, 136.8, 134.0 (q, J = 3.0 Hz), 133.7, 133.2, 132.3, 131.3, 131.2, 130.9 (d, J = 33.0 Hz), 130.6, 121.9 (d, J = 274.0 Hz), 113.4, 112.0 (d, J = 2.0 Hz), 63.1, 13.9 ppm.

\textbf{HRMS (ESI): }m/z calculated for \text{C}_{17}\text{H}_{10}\text{Cl}_2\text{F}_3\text{NO}_2\text{+Na} 409.9938, found 409.9940.

\textbf{ethyl 3',4'-dichloro-2-cyano-3-( trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate}

\begin{center}
\begin{tikzpicture}
\end{tikzpicture}
\end{center}

Prepared according to the general procedure using ethyl (\textit{E})-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(3,4-dichlorophenyl)acrylaldehyde (60.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered \textbf{3s} as a white solid with 77\% yield (59.6 mg). m.p. 118-120 °C.

\textbf{NMR and HRMS data for the product \textbf{3s}:}

\textbf{\textit{H} NMR (400 MHz, CDCl}\_3\text{: }\delta = 7.83 (d, J = 8.0 Hz, 1H), 7.70 (d, J = 8.0 Hz, 1H), 7.63-7.59 (m, 2H), 7.39 (dd, J = 8.4, 2.4 Hz, 1H), 4.44 (q, J = 7.2 Hz, 2H), 1.40 (t, J = 7.2 Hz, 3H) ppm.

\textbf{\textit{C} NMR (100 MHz, CDCl}\_3\text{: }\delta = 166.1, 147.0, 136.2, 134.6, 133.7 (d, J = 2.0 Hz), 133.4, 133.1, 132.5, 131.4 (d, J = 33.0 Hz), 131.02, 130.8, 128.2, 121.9 (d, J = 274.0 Hz), 114.0, 110.4 (d, J = 2.0 Hz), 63.1, 13.9 ppm.

\textbf{HRMS (ESI): }m/z calculated for \text{C}_{17}\text{H}_{10}\text{Cl}_2\text{F}_3\text{NO}_2\text{+Na} 409.9938, found 409.9941.

\textbf{ethyl 2'-chloro-2-cyano-5'-fluoro-3-( trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

S15
Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(2-chloro-4-fluorophenyl)acrylaldehyde (55.4 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3t as a white solid with 75% yield (55.4 mg). m.p. 65-67 °C.

**NMR and HRMS data for the product 3t:**

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \text{): } \delta = 7.85 \text{ (dd, } J = 8.0, 0.4 \text{ Hz, 1H}), 7.67 \text{ (d, } J = 8.0 \text{ Hz, 1H}), 7.53 \text{ (dd, } J = 8.8, 4.8 \text{ Hz, 1H}), 7.18 \text{ (ddd, } J = 8.8, 7.6, 3.2 \text{ Hz, 1H}), 7.08 \text{ (dd, } J = 8.0, 2.8 \text{ Hz, 1H}), 4.45 \text{ (q, } J = 7.2 \text{ Hz, 2H}), 1.41 \text{ (t, } J = 7.2 \text{ Hz, 3H) ppm.} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3 \text{): } \delta = 166.1, 161.0 \text{ (d, } J = 248.0 \text{ Hz)}, 146.0, 136.9 \text{ (d, } J = 8.0 \text{ Hz)}, 134.0 \text{ (q, } J = 2.0 \text{ Hz)}, 133.7, 132.3, 131.7 \text{ (d, } J = 8.0 \text{ Hz)}, 130.9 \text{ (d, } J = 33.0 \text{ Hz)}, 128.1 \text{ (d, } J = 4.0 \text{ Hz)}, 121.9 \text{ (q, } J = 274.0 \text{ Hz)}, 118.3 \text{ (d, } J = 23.0 \text{ Hz)}, 118.0 \text{ (d, } J = 24.0 \text{ Hz)}, 113.4, 111.9 \text{ (d, } J = 2.0 \text{ Hz)}, 63.1, 13.9 \text{ ppm.} \]

**HRMS (ESI):** m/z calculated for C\textsubscript{17}H\textsubscript{10}ClF\textsubscript{4}NO\textsubscript{2}\text{Na 394.0234}, found 394.0235.

**ethyl 2''-bromo-4'-chloro-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(2-bromo-4-
chlorophenyl)acrylaldehyde (73.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3u as a white solid with 73% yield (62.8 mg). m.p. 102-104 °C.

NMR and HRMS data for the product 3u:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.84$ (dd, $J = 8.0$, 0.4 Hz, 1H), 7.77 (d, $J = 2.0$ Hz, 1H), 7.65 (d, $J = 8.0$ Hz, 1H), 7.46 (dd, $J = 8.0$, 2.0 Hz, 1H), 7.27 (d, $J = 7.6$ Hz, 1H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.41 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.1$, 147.7, 136.6, 136.0, 133.9, 133.2, 132.2, 131.4, 130.8 (d, $J = 33.0$ Hz), 128.3, 126.0 (d, $J = 4.0$ Hz), 123.1, 121.9 (d, $J = 275.0$ Hz), 113.5, 111.9 (d, $J = 2.0$ Hz), 63.1, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{10}$BrClF$_3$NO$_2$Na 453.9433, found 453.9435.

ethyl 2'-bromo-5'-chloro-2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(2-bromo-5-chlorophenyl)acrylaldehyde (73.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3v as a white solid with 72% yield (62.3 mg). m.p. 156-158 °C.

NMR and HRMS data for the product 3v:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.85$ (dd, $J = 8.0$, 0.4 Hz, 1H), 7.67 (d, $J = 8.4$ Hz, 1H), 7.64 (d, $J = 8.0$ Hz, 1H), 7.36 (dd, $J = 8.4$, 2.8 Hz, 1H), 7.32 (d, $J = 2.8$ Hz, 1H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.42 (t, $J = 7.2$ Hz, 3H) ppm.
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.1$, 147.4, 138.9, 134.5, 134.0 (d, $J = 3.0$ Hz), 134.0, 133.6, 132.3, 131.3, 130.8 (d, $J = 33.0$ Hz), 130.6, 121.9 (d, $J = 274.0$ Hz), 120.6, 113.4, 111.9 (d, $J = 2.0$ Hz), 63.1, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{10}$BrClF$_3$NO$_2$+Na 453.9433, found 453.9431.

**ethyl 4'-bromo-2-cyano-2'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

 Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(4-bromo-2-fluorophenyl)acrylaldehyde (68.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3w as a white solid with 70% yield (58.1 mg). m.p. 98-100 °C.

**NMR and HRMS data for the product 3w:**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.84$ (d, $J = 8.0$ Hz, 1H), 7.71 (d, $J = 8.0$ Hz, 1H), 7.49-7.45 (m, 2H), 7.31-7.27 (m, 1H), 4.44 (q, $J = 7.2$ Hz, 2H), 1.41 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.1$, 159.1 (d, $J = 253.0$ Hz), 142.7, 134.0, 133.9 (q, $J = 2.0$ Hz), 132.3, 132.0 (d, $J = 3.0$ Hz), 131.1 (d, $J = 33.0$ Hz), 128.2 (d, $J = 3.0$ Hz), 124.9 (d, $J = 9.0$ Hz), 123.4, 121.9 (q, $J = 274.0$ Hz), 120.2 (d, $J = 25.0$ Hz), 113.8, 111.7 (d, $J = 1.0$ Hz), 63.1, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{17}$H$_{10}$BrF$_4$NO$_2$+Na 437.9729, found 437.9727.

**ethyl 5'-bromo-2-cyano-2'-fluoro-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**
Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(5-bromo-2-fluorophenyl)acrylaldehyde (68.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3x as a white solid with 71% yield (58.7 mg), m.p. 74-76 °C.

_NMR and HRMS data for the product 3x:

1H NMR (400 MHz, CDCl3): δ = 7.85 (dd, J = 8.0, 0.4 Hz, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.62 (ddd, J = 7.6 4.8, 2.8 Hz, 1H), 7.52 (dd, J = 6.4, 2.4 Hz, 1H), 7.16 (t, J = 8.8 Hz, 1H), 4.44 (q, J = 7.2 Hz, 2H), 1.41 (t, J = 7.2 Hz, 3H) ppm.

13C NMR (100 MHz, CDCl3): δ = 166.0, 158.5 (d, J = 249 Hz), 142.3, 134.9 (d, J = 8.0 Hz), 134.1 (q, J = 3.0 Hz), 133.9, 13.6 (d, J = 2.0 Hz), 132.4, 131.1 (d, J = 33.0 Hz), 126.3 (d, J = 16.0 Hz), 121.9 (d, J = 275.0 Hz), 118.2 (d, J = 23.0 Hz), 117.1 (d, J = 3.0 Hz), 113.6, 111.9 (d, J = 1.0 Hz), 63.1, 13.9 ppm.

HRMS (ESI): m/z calculated for C17H10BrF4NO2+Na 437.9729, found 437.9730.

_ethyl 2-cyano-3',4'-dimethoxy-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate_

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(3,4-dimethoxyphenyl)acrylaldehyde (57.7 mg, 0.3 mmol). Purification of the crude product
via column chromatography delivered 3y as a white solid with 79% yield (60.2 mg). m.p. 128-130 °C.

NMR and HRMS data for the product 3y:

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\]: \( \delta = 7.75 \text{ (q, } J = 8.4 \text{ Hz, 2H), 7.11-7.05 \text{ (m, 2H), 7.00 \text{ (d, } J = 8.0 \text{ Hz, 1H), 4.43 \text{ (q, } J = 7.2 \text{ Hz, 2H), 3.95 \text{ (d, } J = 2.0 \text{ Hz, 6H), 1.41 (t, } J = 7.2 \text{ Hz, 3H) ppm.} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3\]: \( \delta = 166.5, 150.4, 149.5, 149.1, 133.3, 132.5, 132.1, 131.2 \text{ (d, } J = 32.0 \text{ Hz), 129.0, 122.1 (d, } J = 274.0 \text{ Hz), 122.0, 114.8, 112.2, 111.4, 110.0 \text{ (d, } J = 2.0 \text{ Hz), 62.9, 56.2, 56.0, 13.9 ppm.} \]

HRMS (ESI): calcd. For C\textsubscript{19}H\textsubscript{16}F\textsubscript{3}NO\textsubscript{4}+Na 402.0929, found 402.0926.

**ethyl 3-cyano-4-(furan-2-yl)-2-(trifluoromethyl)benzoate**

\[
\begin{align*}
\text{NC} & \quad \text{O} \\
\text{F}_3\text{C} & \quad \text{COOEt} \\
\end{align*}
\]

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(furan-2-yl)acrylaldehyde (36.6 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3z as a white solid with 67% yield (41.4 mg). m.p. 86-87 °C.

NMR and HRMS data for the product 3z:

\[ ^1H \text{ NMR (400 MHz, CDCl}_3\]: \( \delta = 8.15 \text{ (d, } J = 8.4 \text{ Hz, 1H), 7.76 \text{ (d, } J = 8.4 \text{ Hz, 1H), 7.63 \text{ (d, } J = 0.4 \text{ Hz, 1H), 7.58 \text{ (d, } J = 3.6 \text{ Hz, 1H), 6.63 (dd, } J = 3.6, 1.2 \text{ Hz, 1H), 4.41 (q, } J = 7.2 \text{ Hz, 2H), 1.39 (t, } J = 7.2 \text{ Hz, 3H) ppm.} \]

\[ ^{13}C \text{ NMR (100 MHz, CDCl}_3\]: \( \delta = 166.4, 147.8, 144.7, 136.8, 132.4, 129.1, 122.1 \text{ (d, } J = 274.0 \text{ Hz), 115.0, 113.8, 112.9, 111.7, 110.5, 105.0 \text{ (d, } J = 2.0 \text{ Hz), 62.9, 13.9 ppm.} \]

HRMS (ESI): calcd. For C\textsubscript{15}H\textsubscript{10}F\textsubscript{3}NO\textsubscript{3}+Na 332.0510, found 332.0515.
ethyl 3-cyano-4-(naphthalen-1-yl)-2-(trifluoromethyl)benzoate

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(naphthalen-1-yl)acrylaldehyde (54.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3aa as a white solid with 71% yield (52.6 mg). m.p. 99-101°C.

NMR and HRMS data for the product 3aa:

$^1$H NMR (400 MHz, CDCl$_3$): δ = 8.00 (d, J = 8.0 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.86 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.61-7.53 (m, 2H), 7.50-7.45 (m, 2H), 7.39 (d, J = 8.4 Hz, 1H), 4.47 (q, J = 7.2 Hz, 2H), 1.43 (t, J = 7.2 Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): δ = 166.4, 148.8, 134.7, 134.1, 133.7, 133.3 (d, J = 2.0 Hz), 131.8, 131.0, 130.9 (d, J = 32.0 Hz), 130.2, 128.8, 127.7, 127.2, 126.5, 125.2, 124.6, 122.1 (d, J = 274.0 Hz), 113.9, 112.3 (d, J = 2.0 Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{21}$H$_{14}$F$_3$NO$_2$+Na 392.0874, found 392.0876.

ethyl 3-cyano-4-(naphthalen-2-yl)-2-(trifluoromethyl)benzoate

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(naphthalen-2-yl)acrylaldehyde (54.7 mg, 0.3 mmol). Purification of the crude product via column chromatography...
chromatography delivered 3ab as a white solid with 73% yield (53.8 mg). m.p. 110-111°C.

NMR and HRMS data for the product 3ab:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ =7.99 (d, $J = 8.8$ Hz, 2H), 7.92 (dd, $J = 8.8$, 5.2 Hz, 2H), 7.85-7.80 (m, 2H), 7.62-7.55 (m, 2H), 4.45 (q, $J = 7.2$ Hz, 2H), 1.41 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ =166.4, 149.8, 133.9, 133.6, 133.5, 133.0, 133.0 (d, $J = 3.0$ Hz), 132.2, 131.3 (d, $J = 32.0$ Hz), 128.9, 128.9, 128.5, 127.8, 127.4, 127.0, 125.9, 122.1 (d, $J = 274.0$ Hz), 114.6, 110.5 (d, $J = 2.0$ Hz), 63.0, 13.9 ppm.

HRMS (ESI): m/z calculated for C$_{21}$H$_{14}$F$_3$NO$_2$+Na 392.0874, found 392.0871.

ethyl 3-cyano-4-(2-methoxynaphthalen-1-yl)-2-(trifluoromethyl)benzoate

![Chemical Structure](image)

Prepared according to the general procedure using ethyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (41.4 mg, 0.2 mmol) and 3-(2-methoxynaphthalen-1-yl)acrylaldehyde (63.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3ac as a white solid with 64% yield (50.9 mg). m.p. 148-149°C.

NMR and HRMS data for the product 3ac:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.01 (d, $J = 9.0$ Hz, 1H), 7.88-7.56 (m, 2H), 7.70 (d, $J = 7.8$ Hz, 1H), 7.42-7.37 (m, 3H), 7.17 (d, $J = 7.8$ Hz, 1H), 4.47 (q, $J = 7.2$ Hz, 2H), 3.92 (s, 3H), 1.44 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): δ =166.7, 154.2, 145.6, 135.5, 132.9, 132.4, 132.0, 131.8, 130.8 (d, $J = 22.0$ Hz), 128.9, 128.5, 127.6, 124.0, 123.3, 122.2 (d, $J = 282.0$ Hz), 118.8, 114.2, 113.7, 112.9, 62.9, 56.4, 13.9 ppm.
HRMS (ESI): m/z calculated for C_{22}H_{16}F_{3}NO_{3}+Na 422.0980, found 422.0982.

**methyl 2-cyano-4'-methoxy-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using methyl \((E)\)-4-cyano-3-(trifluoromethyl)but-3-enoate (38.6 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3ad as a white solid with 74% yield (49.7 mg). m.p. 127-128 °C.

**NMR and HRMS data for the product 3ad:**

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.76\) (d, \(J = 8.0\) Hz, 1H), 7.70 (d, \(J = 8.0\) Hz, 1H), 7.49-7.47 (m, 2H), 7.05-7.03 (m, 2H), 3.97 (s, 3H), 3.88 (s, 3H) ppm.

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 166.1, 160.8, 149.4, 133.2, 132.9\) (d, \(J = 3.0\) Hz), 132.1, 131.0 (d, \(J = 33.0\) Hz) 130.4, 128.8, 122.2 (d, \(J = 274.0\) Hz), 114.8, 114.4, 109.9 (d, \(J = 2.0\) Hz), 71.0, 55.4, 21.5 ppm.

**HRMS (ESI):** m/z calculated for C_{17}H_{12}F_{3}NO_{3}+Na 358.0667, found 358.0665.

**isopropyl 2-cyano-4'-methoxy-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

Prepared according to the general procedure using isopropyl \((E)\)-4-cyano-3-(trifluoromethyl)but-3-enoate (44.2 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography
delivered 3ae as a white solid with 72% yield (52.1 mg). m.p. 82-83 °C.

**NMR and HRMS data for the product 3ae:**

**1H NMR (400 MHz, CDCl3):** \(\delta = 7.75 \text{ (d, } J = 8.4 \text{ Hz, 1H), 7.69 \text{ (d, } J = 8.0 \text{ Hz, 1H), 7.49-7.46 \text{ (m, 2H), 7.06-7.02 \text{ (m, 2H), 5.31-5.25 \text{ (m, 1H), 3.88 (s, 3H), 1.38 (d, } J = 6.4 \text{ Hz, 6H) ppm.}}}

**13C NMR (100 MHz, CDCl3):** \(\delta = 166.1, 160.8, 149.4, 133.2, 132.9 \text{ (d, } J = 2.0 \text{ Hz), 132.1, 131.0 \text{ (d, } J = 32.0 \text{ Hz), 130.4, 128.8, 122.2 \text{ (d, } J = 274.0 \text{ Hz), 114.8, 114.4, 109.9 \text{ (d, } J = 2.0 \text{ Hz), 71.0, 55.4, 21.5 ppm.}}

**HRMS (ESI):** m/z calculated for C_{19}H_{16}F_{3}NO_{3}Na 386.0980, found 386.0975.

**benzyl 2-cyano-3-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Chemical Structure]

Prepared according to the general procedure using benzyl (E)-4-cyano-3-(trifluoromethyl)but-3-enoate (53.8 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3af as a white solid with 73% yield (55.7 mg). m.p. 91-93 °C.

**NMR and HRMS data for the product 3af:**

**1H NMR (600 MHz, CDCl3):** \(\delta = 7.79 \text{ (d, } J = 7.8 \text{ Hz, 1H), 7.71 \text{ (d, } J = 7.8 \text{ Hz, 1H), 7.53-7.49 \text{ (m, 5H), 7.44-7.36 \text{ (m, 5H), 5.38 (s, 2H) ppm.}}

**13C NMR (150 MHz, CDCl3):** \(\delta = 166.2, 149.9, 136.5, 134.5, 133.4, 132.5, 132.2, 131.2 \text{ (q, } J = 31.5 \text{ Hz), 129.8, 128.9, 128.8, 128.74, 128.71, 122.0 \text{ (d, } J = 274.5 \text{ Hz), 114.4, 110.3, 68.7 ppm.}}

**HRMS (ESI):** m/z calculated for C_{22}H_{14}F_{3}O_{2}Na 404.0874, found 404.0870.
ethyl 2-cyano-3-(difluoro-\(\lambda^3\)-methyl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate

Prepared according to the general procedure using ethyl (\(E\))-4-cyano-3-(difluoro-\(\lambda^3\)-methyl)but-3-enoate (37.8 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3ag as a white solid with 78% yield (51.7 mg). m.p. 103-105 °C.

**NMR and HRMS data for the product 3ag:**

\(^1H\) NMR (600 MHz, CDCl\(_3\)): \(\delta = 8.11\) (d, \(J = 8.4\) Hz, 1H), 7.64 (t, \(J = 53.4\) Hz, 1H), 7.64 (d, \(J = 8.4\) Hz, 1H), 7.52-7.49 (m, 2H), 7.05-7.03 (m, 2H), 4.45 (q, \(J = 7.2\) Hz, 2H), 3.88 (s, 3H), 1.43 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^{13}C\) NMR (150 MHz, CDCl\(_3\)): \(\delta = 165.1, 160.8, 150.6, 137.9\) (t, \(J = 22.5\) Hz), 133.7, 132.0, 130.4, 129.7 (d, \(J = 3.0\) Hz), 129.0, 115.5, 114.4, 110.83 (t, \(J = 238.5\) Hz), 110.3, 62.6, 55.4, 14.1 ppm.

\(^{19}F\) NMR (564 MHz, CDCl\(_3\)): \(\delta = -110.24\) (d, \(J = 50.76\) Hz, 2F).

HRMS (ESI): m/z calculated for C\(_{18}\)H\(_{15}\)F\(_2\)NO\(_3\)+Na 354.0918, found 354.0915.

ethyl 2-cyano-4'-methoxy-3-(perfluoroethyl)-[1,1'-biphenyl]-4-carboxylate

Prepared according to the general procedure using ethyl (\(E\))-3-(cyanomethylene)-4,4,5,5,5-pentafluoropentanoate (51.4 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 3ah as a white solid with 66% yield (53.1 mg). m.p. 118-120 °C.
NMR and HRMS data for the product 3ah:

$^1$H NMR (600 MHz, CDCl$_3$): $\delta = 7.72$-$7.69$ (m, 2H), 7.46-$7.44$ (m, 2H), 7.03-$7.02$ (m, 2H), 4.41 (q, $J = 7.2$ Hz, 2H), 3.87 (s, 3H), 1.37 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta = 166.7$, 160.8, 149.9, 134.3 (t, $J = 4.5$ Hz), 133.7, 132.2, 130.5, 128.8, 128.7 (t, $J = 22.5$ Hz), 118.9 (d, $J = 286.5$ Hz), 114.9, 114.4, 113.1 (d, $J = 40.5$ Hz), 111.1, 62.8, 55.4, 13.8 ppm.

$^{19}$F NMR (564 MHz, CDCl$_3$): $\delta = -81.0$ (s, 3F), -105.2 (s, 2F).

HRMS (ESI): m/z calculated for C$_{19}$H$_{14}$F$_5$NO$_3$+Na 422.0792, found 422.0788.

2.2 Procedure for 5

The reaction was carried out with 4 (0.20 mmol) and 2 (0.30 mmol), amine catalyst IV (0.05 mmol) and AcOH (0.08 mmol) in toluene (2 mL) under an open atmosphere at 70 °C for 12 h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 100:1) to give the final CF$_3$-functionlized penta-substituted benzenes 5, which was further analyzed by $^1$H NMR, $^{13}$C NMR, HRMS analysis.

ethyl 2'-formyl-5'-{(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5a as a white solid with 75% yield (59.4 mg). m.p. 84-86 °C.
NMR and HRMS data for the product 5a:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.82$ (s, 1H), 7.75 (s, 1H), 7.48-7.45 (m, 3H), 7.42-7.40 (m, 3H), 7.35-7.33 (m, 2H), 7.31-7.28 (m, 2H), 4.00 (q, $J = 7.2$ Hz, 2H), 0.99 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 192.0$, 165.9, 144.7, 142.1, 137.5, 136.9, 135.1, 133.0 (d, $J = 2.0$ Hz), 129.8, 129.5, 129.4 (d, $J = 32.0$ Hz), 128.7, 128.64, 128.62, 128.1, 128.0 (d, $J = 4.0$ Hz), 122.9 (d, $J = 273.0$ Hz), 62.0, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{17}$F$_3$O$_3$+Na 421.1027, found 421.1025.

ethyl 3''-chboro-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enolate (57.3 mg, 0.2 mmol) and 3-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5b as a white solid with 74% yield (63.7 mg). m.p. 130-132 °C.

NMR and HRMS data for the product 5b:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.83$ (s, 1H), 7.79 (s, 1H), 7.50-7.47 (m, 3H), 7.41-7.38 (m, 1H), 7.36-7.32 (m, 3H), 7.31 (t, $J = 1.6$ Hz, 1H), 7.19-7.17 (m, 1H), 4.06 (q, $J = 7.2$ Hz, 2H), 1.06 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 191.6$, 165.6, 145.3, 140.1, 137.1, 136.9, 136.5, 134.0, 133.1 (d, $J = 2.0$ Hz), 129.7, 129.8 (d, $J = 32.0$ Hz), 129.6, 129.3, 129.0, 128.8, 128.7, 128.4 (q, $J = 5.0$ Hz), 128.1, 122.8 (q, $J = 273.0$ Hz), 62.2, 13.6 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{16}$ClF$_3$O$_3$+Na 455.0638, found 455.0641.
ethyl 4''-chloro-2'-formyl-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-
carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 4-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5c as a white solid with 79% yield (68.6 mg). m.p. 96-98 °C.

NMR and HRMS data for the product 5c:

$^1$H NMR (400 MHz, CDCl$_3$): δ = 9.81 (s, 1H), 7.78 (s, 1H), 7.48-7.47 (m, 3H), 7.40-7.38 (m, 2H), 7.36-7.34 (m, 2H), 7.24-7.22 (s, 2H), 4.04 (q, $J = 7.2$ Hz, 2H), 1.05 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): δ = 191.7, 165.7, 145.2, 140.4, 136.9, 136.7, 134.8, 133.8, 133.1 (d, $J = 2.0$ Hz), 131.1, 129.6 (d, $J = 32.0$ Hz), 129.5, 129.0, 128.8, 128.3, 128.2 (q, $J = 5.0$ Hz), 122.8 (q, $J = 273.0$ Hz), 62.2, 13.6 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{16}$ClF$_3$O$_3$Na 455.0638, found 455.0635.

ethyl 2''-bromo-2'-formyl-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-
carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 2-bromocinnamaldehyde (63.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5d as a white solid with 70% yield (67.1 mg). m.p. 86-88 °C.
NMR and HRMS data for the product 5d:

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 9.83\) (s, 1H), 7.83 (s, 1H), 7.55 (dd, \(J = 8.0, 0.8\) Hz, 1H), 7.53-7.49 (m, 3H), 7.40-7.36 (m, 3H), 7.34-7.28 (m, 2H), 4.00 (q, \(J = 7.2\) Hz, 2H), 1.01 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 190.8, 165.4, 145.4, 140.1, 136.8, 136.7, 136.2, 132.7\) (d, \(J = 2.0\) Hz), 132.3, 131.2, 130.1 (d, \(J = 32.0\) Hz), 130.0, 129.7, 129.1, 128.9, 128.6 (q, \(J = 4.0\) Hz), 127.0, 123.6, 122.8 (d, \(J = 273.0\) Hz), 62.0, 13.5 ppm.

HRMS (ESI): m/z calculated for C\(_{23}\)H\(_{16}\)BrF\(_3\)O\(_3\)+Na 499.0133, found 499.0116.

**ethyl 3''-bromo-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate**

![ethyl 3''-bromo-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate](image)

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-bromocinnamaldehyde (63.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5e as a white solid with 75% yield (71.3 mg). m.p. 134-136 °C.

NMR and HRMS data for the product 5e:

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 9.82\) (s, 1H), 7.79 (s, 1H), 7.55 (ddd, \(J = 8.0, 2.0, 1.2\) Hz, 1H), 7.50-7.46 (m, 4H), 7.36-7.34 (m, 2H), 7.28 (t, \(J = 7.6\) Hz, 1H), 7.22 (d, \(J = 7.6, 1.2\) Hz, 1H), 4.06 (q, \(J = 7.2\) Hz, 2H), 1.07 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 191.5, 165.6, 145.3, 140.0, 137.3, 136.9, 136.4, 133.1\) (d, \(J = 2.0\) Hz), 132.5, 131.6, 129.7 (d, \(J = 32.0\) Hz), 129.6, 129.5, 129.0, 128.8, 128.5, 128.4 (q, \(J = 4.0\) Hz), 122.8 (d, \(J = 273.0\) Hz), 122.1, 62.2, 13.6 ppm.

HRMS (ESI): m/z calculated for C\(_{23}\)H\(_{16}\)BrF\(_3\)O\(_3\)+Na 499.0133, found 499.0140.
ethyl 4''-bromo-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-
carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 4-bromocinnaldehyde (63.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5f as a white solid with 80% yield (76.2 mg). m.p. 102-104 °C.

NMR and HRMS data for the product 5f:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.81$ (s, 1H), 7.78 (s, 1H), 7.54 (d, $J = 8.4$ Hz, 2H), 7.50-7.47 (m, 3H), 7.36-7.34 (m, 2H), 7.16 (d, $J = 8.4$ Hz, 2H), 4.04 (q, $J = 7.2$ Hz, 2H), 1.05 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 191.7$, 165.7, 145.3, 140.4, 136.9, 136.6, 134.3, 133.0 (d, $J = 1.0$ Hz), 131.3, 131.2, 129.6 (q, $J = 33.0$ Hz), 129.6, 129.0, 128.8, 128.3 (q, $J = 4.0$ Hz), 123.0, 122.8 (q, $J = 273.0$ Hz), 62.2, 13.6 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{16}$BrF$_3$O$_3$+Na 499.0133, found 499.0130.

ethyl 2''-fluoro-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-
carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 2-fluorocinnaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5g as a white solid with 71% yield (58.9 mg). m.p. 100-102 °C.
NMR and HRMS data for the product 5g:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.84$ (s, 1H), 7.83 (s, 1H), 7.52-7.48 (m, 3H), 7.42-7.37 (m, 3H), 7.27 (td, $J = 7.6$, 2.0 Hz, 1H), 7.19 (td, $J = 7.6$, 1.2 Hz, 1H), 7.14-7.09 (m, 1H), 4.06-3.98 (m, 2H), 1.01 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 191.2$, 165.6, 159.6 (d, $J = 246.0$ Hz), 145.6, 136.6, 136.5, 134.9, 133.6 (d, $J = 2.0$ Hz), 131.1 (d, $J = 3.0$ Hz), 130.7 (d, $J = 8.0$ Hz), 130.1 (d, $J = 32.0$ Hz), 129.8, 129.1, 128.6 (q, $J = 5.0$ Hz), 123.8 (d, $J = 4.0$ Hz), 123.6 (d, $J = 17.0$ Hz), 122.8 (q, $J = 273.0$ Hz), 115.2 (d, $J = 21.0$ Hz), 62.1, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{16}$F$_4$O$_3$+Na 439.0933, found 439.0930.

ethyl 3''-fluoro-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-fluorocinnamaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5h as a white solid with 76% yield (63.4 mg). m.p. 102-104 °C.

NMR and HRMS data for the product 5h:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.82$ (s, 1H), 7.79 (s, 1H), 7.51-7.46 (m, 3H), 7.40-7.34 (m, 3H), 7.14-7.02 (m, 2H), 4.05 (q, $J = 7.2$ Hz, 2H), 1.05 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 191.6$, 165.6, 162.2 (d, $J = 246.0$ Hz), 145.2, 140.3, 137.4 (d, $J = 8.0$ Hz), 137.0, 136.6, 133.0 (d, $J = 1.0$ Hz), 129.7 (d, $J = 8.0$ Hz), 129.6, 128.9, 128.8, 128.4 (q, $J = 5.0$ Hz), 125.7 (d, $J = 3.0$ Hz), 122.8 (q, $J = 273.0$ Hz), 117.1 (d, $J = 22.0$ Hz), 115.6 (d, $J = 21.0$ Hz), 62.1, 13.6 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{16}$F$_4$O$_3$+Na 439.0933, found 439.0932.
ethyl 4''-fluoro-2'-formyl-5'-{(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 4-fluorocinnamaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5i as a white solid with 82% yield (68.5 mg). m.p. 98-100 °C.

NMR and HRMS data for the product 5i:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.81$ (s, 1H), 7.78 (s, 1H), 7.49-7.47 (m, 3H), 7.36-7.34 (m, 2H), 7.29-7.25 (m, 2H), 7.13-7.07 (m, 2H), 4.04 (q, $J = 7.2$ Hz, 2H), 1.05 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 191.9, 165.8, 162.8$ (d, $J = 247.0$ Hz), 145.1, 140.7, 137.1, 136.9, 133.3, 131.6 (d, $J = 9.0$ Hz), 131.1 (d, $J = 4.0$ Hz), 129.6, 129.5 (d, $J = 32.0$ Hz), 128.9, 128.8, 128.2 (q, $J = 5.0$ Hz), 122.8 (q, $J = 273.0$ Hz), 115.1 (d, $J = 21.0$ Hz), 62.1, 13.6 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{16}$F$_4$O$_3$Na 439.0933, found 439.0934.

ethyl 2''-formyl-2''-nitro-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 2-nitrocinamaldehyde (53.2
mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5j as a white solid with 72% yield (63.7 mg). m.p. 80-81 °C.

**NMR and HRMS data for the product 5j:**

\(^1H\) NMR (400 MHz, CDCl\(_3\)): \(\delta = 9.80\) (s, 1H), 8.24 (dd, \(J = 8.0, 1.2\) Hz, 1H), 7.87 (s, 1H), 7.66 (dd, \(J = 7.6, 1.6\) Hz, 1H), 7.60 (dd, \(J = 8.0, 1.6\) Hz, 1H), 7.54-7.50 (m, 3H), 7.45-7.42 (m, 2H), 7.32 (dd, \(J = 7.6, 1.6\) Hz, 1H), 4.01-3.85 (m, 2H), 0.99 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \(\delta = 190.9, 165.4, 148.0, 146.8, 137.9, 136.1, 134.9\) (d, \(J = 1.0\) Hz), 133.0, 132.2, 131.8, 133.4 (d, \(J = 2.0\) Hz), 130.4 (d, \(J = 33.0\) Hz), 130.0, 129.5, 129.4, 129.0, 128.5 (q, \(J = 5.0\) Hz), 124.5, 122.7 (q, \(J = 273.0\) Hz), 62.2, 13.5 ppm.

HRMS (ESI): m/z calculated for C\(_{23}H_{16}F_3NO_5\)+Na 466.0878, found 466.0879.

**ethyl 2'-formyl-4''-nitro-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 4-nitrocinnamaldehyde (53.2 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5k as a white solid with 75% yield (66.2 mg). m.p. 150-152 °C.

**NMR and HRMS data for the product 5k:**

\(^1H\) NMR (400 MHz, CDCl\(_3\)): \(\delta = 9.82\) (s, 1H), 8.28-8.26 (m, 2H), 7.88 (s, 1H), 7.53-7.51 (m, 3H), 7.47-7.44 (m, 2H), 7.40-7.38 (m, 2H), 4.02 (q, \(J = 7.2\) Hz, 2H), 1.05 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^{13}C\) NMR (100 MHz, CDCl\(_3\)): \(\delta = 190.9, 165.4, 148.0, 146.8, 137.9, 136.1, 134.9\) (d,
\( J = 1.0 \text{ Hz}, 133.0, 132.2, 131.8, 133.4 \ (d, \ J = 2.0 \text{ Hz}), 130.4 \ (d, \ J = 33.0 \text{ Hz}), 130.0, 129.5, 129.4, 129.0, 128.5 \ (q, \ J = 5.0 \text{ Hz}), 124.5, 122.7 \ (q, \ J = 273.0 \text{ Hz}), 62.2, 13.5 \text{ ppm.}

HRMS (ESI): m/z calculated for C_{23}\text{H}_{16}\text{F}_{3}\text{NO}_{5}+\text{Na} 466.0878, \text{ found } 466.0881.

ethyl 2'-formyl-3''',5'-bis(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

![Chemical structure](image)

Prepared according to the general procedure using ethyl ethyl (\( E \))-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-trifluoromethylenecinnamaldehyde (60.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5I as a white solid with 69% yield (64.8 mg). m.p. 142-144 °C.

NMR and HRMS data for the product 5I:

\(^1\text{H NMR (400 MHz, CDCl}_3\)): \( \delta = 9.82 \ (s, 1\text{H}), 7.83 \ (s, 1\text{H}), 7.83 \ (d, \ J = 7.6 \text{ Hz}, 1\text{H}), 7.58-7.47 \ (m, 6\text{H}), 7.39-7.36 \ (m, 2\text{H}), 4.05-3.95 \ (m, 2\text{H}), 1.01 \ (t, \ J = 7.2 \text{ Hz}, 3\text{H}) \text{ ppm.}

\(^{13}\text{C NMR (100 MHz, CDCl}_3\)): \( \delta = 191.4, 165.5, 145.8, 139.9, 136.6, 136.4, 136.3 \ (d, \ J = 1.0 \text{ Hz}), 133.3 \ (d, \ J = 2.0 \text{ Hz}), 133.2 \ (d, \ J = 1.0 \text{ Hz}), 130.4 \ (d, \ J = 33.0 \text{ Hz}), 130.0, 129.7, 129.2, 128.9, 128.5 \ (d, \ J = 4.0 \text{ Hz}), 128.4, 126.4 \ (q, \ J = 3.0 \text{ Hz}), 125.2 \ (q, \ J = 4.0 \text{ Hz}), 122.7 \ (d, \ J = 273.0 \text{ Hz}), 122.5, 62.2, 13.4 \text{ ppm.}

HRMS (ESI): m/z calculated for C_{24}\text{H}_{16}\text{F}_{6}\text{O}_{3}+\text{Na} 489.0901, \text{ found } 489.0906.

ethyl 2'-formyl-4''-methyl-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate
Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 4-methylcinnamaldehyde (43.9 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5m as a white solid with 83% yield (68.6 mg). m.p. 101-103 °C.

**NMR and HRMS data for the product 5m:**

1H NMR (400 MHz, CDCl3): δ = 9.81 (s, 1H), 7.73 (s, 1H), 7.46-7.42 (m, 3H), 7.34-7.32 (m, 2H), 7.23-7.17 (m, 4H), 4.03 (q, J = 7.2 Hz, 2H), 2.39 (s, 3H), 1.02 (t, J = 7.2 Hz, 3H) ppm.

13C NMR (100 MHz, CDCl3): δ = 192.2, 166.0, 144.5, 142.3, 138.6, 137.7, 137.1, 133.1 (d, J = 2.0 Hz), 132.0, 129.7, 129.4, 129.3 (d, J = 32.0 Hz), 128.8, 128.6, 127.9 (q, J = 5.0 Hz), 122.7 (q, J = 273.0 Hz), 62.0, 21.3, 13.6 ppm.

HRMS (ESI): m/z calculated for C24H19F3O3+Na 435.1184, found 435.1188.

**ethyl2''-formyl-2''-methoxy-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 2-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5n as a white solid with 80% yield (68.2 mg). m.p. 108-110 °C.

**NMR and HRMS data for the product 5n:**
$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.78$ (s, 1H), 7.74 (s, 1H), 7.48-7.44 (m, 3H), 7.41-7.7.35 (m, 3H), 7.23 (dd, $J = 7.6$, 1.6 Hz, 1H), 7.02 (td, $J = 7.6$, 0.8 Hz, 1H), 6.92 (d, $J = 8.0$ Hz, 1H), 4.00 (q, $J = 7.2$ Hz, 2H), 3.72 (s, 3H), 0.99 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 191.6$, 166.0, 156.2, 144.2, 138.4, 137.5, 137.2, 133.0 (d, $J = 2.0$ Hz), 130.7, 130.4, 129.9 (d, $J = 33.0$ Hz), 129.6, 128.7, 127.9 (q, $J = 5.0$ Hz), 124.5, 123.0 (d, $J = 273.0$ Hz), 120.5, 110.7, 61.8, 55.6, 13.6 ppm.

HRMS (ESI): m/z calculated for C$_{24}$H$_{19}$F$_3$O$_4$+Na 451.1133, found 451.1135.

\[
\text{ethyl } 2'\text{-formyl-4''-methoxy-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate}
\]

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5o as a white solid with 84% yield (72.3 mg). m.p. 88-90 °C.

NMR and HRMS data for the product 5o:

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 9.81$ (s, 1H), 7.72 (s, 1H), 7.48-7.44 (m, 3H), 7.34-7.32 (m, 2H), 7.24-7.20 (m, 2H), 6.95-6.93 (m, 2H), 4.05 (q, $J = 7.2$ Hz, 2H), 3.84 (s, 3H), 1.05 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 192.3$, 166.0, 159.9, 144.5, 142.0, 137.7, 137.3, 133.2 (d, $J = 2.0$ Hz), 131.1, 129.4, 129.3 (d, $J = 32.0$ Hz), 128.6, 127.8 (d, $J = 4.0$ Hz), 127.0, 122.9 (q, $J = 273.0$ Hz), 113.6, 62.0, 55.3, 13.7 ppm.

HRMS (ESI): m/z calculated for C$_{24}$H$_{19}$F$_3$O$_4$+Na 451.1133, found 451.1131.

\[
\text{ethyl } 2'',4''\text{-dichloro-2'-formyl-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate}
\]
Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-(2,4-dichlorophenyl)acrylaldehyde (60.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5p as a white solid with 71% yield (66.4 mg). m.p. 172-174 °C.

**NMR and HRMS data for the product 5p:**

**1H NMR (400 MHz, CDCl3):** δ = 9.81 (s, 1H), 7.86 (s, 1H), 7.52-7.49 (m, 3H), 7.46 (d, J = 2.0 Hz, 1H), 7.39 (dd, J = 7.6, 4.0 Hz, 2H), 7.32 (dd, J = 8.0, 2.0 Hz, 1H), 7.23 (d, J = 8.4 Hz, 2H), 4.05 (q, J = 7.2 Hz, 2H), 1.07 (t, J = 7.2 Hz, 3H) ppm.

**13C NMR (100 MHz, CDCl3):** δ = 190.6, 165.3, 146.0, 137.1, 136.3, 136.1, 135.2, 134.2, 133.6, 131.7, 130.3 (d, J = 33.0 Hz), 129.8, 129.3, 129.1, 129.0, 128.9, 128.8 (d, J = 4.0 Hz), 126.8, 122.7 (d, J = 273.0 Hz), 62.2, 13.6 ppm.

**HRMS (ESI):** m/z calculated for C_{23}H_{15}Cl_{2}F_{3}O_{3}Na 489.0248, found 489.0246.

**ethyl 2''-5''-dichloro-2'-formyl-5'-((trifluoromethyl))-1,1'';3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-(2,5-dichlorophenyl)acrylaldehyde (60.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5q as a white solid with 71% yield (66.4 mg). m.p. 172-174 °C.
**NMR and HRMS data for the product 5q:**

**$^1$H NMR (400 MHz, CDCl$_3$):** $\delta$ = 9.82 (s, 1H), 7.86 (s, 1H), 7.53-7.50 (m, 3H), 7.41-7.37 (m, 2H), 7.36-7.34 (m, 2H), 7.32-7.31 (m, 1H), 4.08 (qd, $J$ = 7.2, 2.8 Hz, 2H), 1.08 (t, $J$ = 7.2 Hz, 3H) ppm.

**$^{13}$C NMR (100 MHz, CDCl$_3$):** $\delta$ = 190.5, 165.2, 146.0, 136.9, 136.6, 136.2, 135.9, 132.8 (d, $J$ = 2.0 Hz), 132.4, 131.8, 130.8, 130.5, 130.2, 129.9, 129.8, 129.3, 129.0, 128.9 (d, $J$ = 5.0 Hz), 122.7 (d, $J$ = 273.0 Hz), 62.2, 13.6 ppm.

**HRMS (ESI):** m/z calculated for C$_{23}$H$_{15}$Cl$_2$F$_3$O$_3$+Na 489.0248, found 489.0247.

**ethyl 3''',4''''-dichloro-2''-formyl-5'''-(trifluoromethyl)-[1,1''':3',1'''-terphenyl]-4'''-carboxylate**

![Structure of the product 5q](image)

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-(3,4-dichlorophenyl)acrylaldehyde (60.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5r as a white solid with 74% yield (69.1 mg). m.p. 146-148 °C.

**NMR and HRMS data for the product 5r:**

**$^1$H NMR (400 MHz, CDCl$_3$):** $\delta$ = 9.82 (s, 1H), 7.82 (s, 1H), 7.51-7.47 (m, 4H), 7.40 (d, $J$ = 2.0 Hz, 1H), 7.37-7.35 (m, 2H), 7.13 (dd, $J$ = 8.0, 2.0 Hz, 1H), 4.08 (qd, $J$ = 7.2, 2.4 Hz, 2H), 1.10 (t, $J$ = 7.2 Hz, 3H) ppm.

**$^{13}$C NMR (100 MHz, CDCl$_3$):** $\delta$ = 191.4, 165.5, 145.8, 138.8, 136.5, 136.3, 135.4, 133.1 (d, $J$ = 2.0 Hz), 132.9, 132.3, 131.4, 129.9, 129.7, 129.2, 128.9, 128.6 (q, $J$ = 5.0 Hz), 122.7 (d, $J$ = 273.0 Hz), 62.3, 13.6 ppm.

**HRMS (ESI):** m/z calculated for C$_{23}$H$_{15}$Cl$_2$F$_3$O$_3$+Na 489.0248, found 489.0250.
ethyl 4''-bromo-2''-fluoro-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-(4-bromo-2-fluorophenyl)acrylaldehyde (68.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5s as a white solid with 76% yield (75.2 mg). m.p. 136-137 °C.

NMR and HRMS data for the product 5s:

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 9.82\) (s, 1H), 7.86 (s, 1H), 7.53-7.49 (m, 3H), 7.40-7.33 (m, 3H), 7.13 (dd, \(J = 8.8, 1.6\) Hz, 1H) , 7.13 (t, \(J = 7.6\) Hz, 3H), 4.07 (q, \(J = 7.2\) Hz, 2H), 1.08 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^13\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 190.9, 165.4, 159.5\) (d, \(J = 249.0\) Hz), 146.1, 136.2, 133.7, 133.5 (d, \(J = 1.0\) Hz), 131.9 (d, \(J = 4.0\) Hz), 130.3 (d, \(J = 32.0\) Hz), 129.8, 129.3, 129.0, 128.9 (d, \(J = 5.0\) Hz), 127.2 (d, \(J = 3.0\) Hz), 126.0, 123.3 (d, \(J = 9.0\) Hz), 123.0 (d, \(J = 17.0\) Hz), 122.7 (d, \(J = 273.0\) Hz), 118.9 (d, \(J = 25.0\) Hz), 62.3, 13.6 ppm.

HRMS (ESI): m/z calculated for C\(_{23}\)H\(_{15}\)BrF\(_4\)O\(_3\)+Na 517.0038, found 517.0041.

ethyl 5''-bromo-2''-fluoro-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-
(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-(5-bromo-2-fluorophenyl)acrylaldehyde (68.7 mg, 0.3 mmol). Purification of the crude product \textit{via} column chromatography delivered 5t as a white solid with 73% yield (71.9 mg). m.p. 140-142 °C.

\textit{NMR and HRMS data for the product 5t:}

\textbf{1H NMR (400 MHz, CDCl$_3$):} $\delta = 9.83$ (s, 1H), 7.86 (s, 1H), 7.53-7.49 (m, 4H), 7.41-7.38 (m, 3H), 7.01 (t, $J = 8.8$ Hz, 1H), 4.15-4.07 (m, 2H), 1.11 (t, $J = 7.2$ Hz, 3H) ppm.

\textbf{13C NMR (100 MHz, CDCl$_3$):} $\delta = 190.8, 165.3, 158.8$ (d, $J = 246.0$ Hz), 146.2, 136.12, 136.09, 133.54 (d, $J = 2.0$ Hz), 133.47, 133.41 (d, $J = 6.0$ Hz), 133.2, 130.4 (d, $J = 33.0$ Hz), 129.8, 129.3, 129.1 (d, $J = 4.0$ Hz), 129.0, 125.9 (d, $J = 18.0$ Hz), 122.7 (d, $J = 273.0$ Hz), 116.9 (d, $J = 24.0$ Hz), 116.2 (d, $J = 4.0$ Hz), 62.3, 13.6 ppm.

\textbf{HRMS (ESI):} m/z calculated for C$_{23}$H$_{15}$BrF$_4$O$_3$+Na 517.0038, found 517.0043.

\textit{ethyl 2'-formyl-3'',4''-dimethoxy-5''-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate}

\begin{center}
\includegraphics[width=0.3\textwidth]{5u.png}
\end{center}

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-(3,4-dimethoxyphenyl)acrylaldehyde (57.7 mg, 0.3 mmol). Purification of the crude product \textit{via} column chromatography delivered 5u as a white solid with 78% yield (71.3 mg). m.p. 110-111 °C.

\textit{NMR and HRMS data for the product 5u:}

\textbf{1H NMR (400 MHz, CDCl$_3$):} $\delta = 9.82$ (s, 1H), 7.72 (s, 1H), 7.47-7.44 (m, 3H), 7.34-7.32 (m, 2H), 6.92-6.90 (m, 1H), 6.86-6.84 (m, 2H), 4.10-4.04 (m, 2H), 3.92 (s, 3H), 3.86 (s, 3H), 1.07 (t, $J = 7.2$ Hz, 3H) ppm.
\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 192.3, 166.1, 149.4, 148.6, 144.3, 142.0, 137.7, 137.4, 133.0 (d, J = 2.0 Hz), 129.4, 129.3 (d, J = 33.0 Hz), 128.6, 127.9 (q, J = 4.0 Hz), 127.1, 122.9 (d, J = 273.0 Hz), 122.8, 113.2, 110.7, 62.1, 56.0, 55.9, 13.7 ppm.

HRMS (ESI): m/z calculated for C\(_{25}\)H\(_{21}\)F\(_3\)O\(_5\)+Na: 481.1239, found 481.1236

ethyl 2-formyl-3-(furan-2-yl)-5-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

[Chemical structure image]

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (57.3 mg, 0.2 mmol) and 3-(furan-2-yl)acrylaldehyde (36.6 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5v as a white solid with 64% yield (49.8 mg). m.p. 76-77 °C.

NMR and HRMS data for the product 5v:

\(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 9.91 (s, 1H), 7.76 (s, 1H), 7.55 (dd, J = 2.0, 0.8 Hz, 1H), 7.49-7.45 (m, 3H), 7.35-7.32 (m, 2H), 6.58 (dd, J = 3.2, 0.8 Hz, 1H), 6.53 (dd, J = 3.2, 1.6 Hz, 1H), 4.26 (q, J = 7.2, 2.4 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H) ppm.

\(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 191.5, 165.9, 146.9, 144.8, 144.0, 137.5, 137.0, 132.8 (d, J = 2.0 Hz), 130.5, 129.8 (d, J = 32.0 Hz), 129.5, 128.9 (d, J = 4.0 Hz), 128.8, 128.7, 122.7 (d, J = 273.0 Hz), 113.0, 111.6, 62.4, 13.8 ppm.

HRMS (ESI): m/z calculated for C\(_{21}\)H\(_{15}\)F\(_3\)O\(_4\)+Na 411.0820, found 411.0822.

ethyl 2-formyl-3-(naphthalen-1-yl)-5-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate

[Chemical structure image]
Prepared according to the general procedure using ethyl ethyl \((E)-5\text{-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate}\) (57.3 mg, 0.2 mmol) and 3-(naphthalen-1-yl)acrylaldehyde (54.7 mg, 0.3 mmol). Purification of the crude product \textit{via} column chromatography delivered 5w as a white solid with 69\% yield (61.7 mg). m.p. 110-112 °C.

\textit{NMR and HRMS data for the product 5w:}

\( ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \): \( \delta = 9.67 \ (s, \ 1H), 7.90 \ (dd, J = 12.8, 8.4 \text{ Hz, } 1H), 7.85 \ (s, \ 1H), 7.53-7.45 \ (m, \ 5H), 7.43-7.38 \ (m, \ 5H), 3.77-3.68 \ (m, \ 2H), 0.55 \ (t, J = 7.2 \text{ Hz, } 3H) \) ppm.

\( ^{13}\text{C NMR} \ (100 \text{ MHz, CDCl}_3) \): \( \delta = 191.4, 165.6, 144.8, 140.8, 137.5, 137.3, 133.7 \ (d, \ J = 2.0 \text{ Hz}), 133.1, 132.5, 132.4, 129.9 \ (d, J = 33.0 \text{ Hz}), 129.5, 129.2, 128.7, 128.6, 128.5 \ (d, J = 5.0 \text{ Hz}), 128.3, 128.2, 126.8, 126.2, 125.7, 124.8, 122.9 \ (d, J = 273.0 \text{ Hz}), 62.6, 13.0 \) ppm.

\textit{HRMS (ESI):} m/z calculated for C\textsubscript{27}H\textsubscript{19}F\textsubscript{3}O\textsubscript{3}Na 471.1184, found 471.1182.

\textit{ethyl 2-formyl-3-(naphthalen-2-yl)-5-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate}

Prepared according to the general procedure using ethyl ethyl \((E)-5\text{-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate}\) (57.3 mg, 0.2 mmol) and 3-(naphthalen-2-yl)acrylaldehyde (54.7 mg, 0.3 mmol). Purification of the crude product \textit{via} column chromatography delivered 5x as a white solid with 72\% yield (64.5 mg). m.p. 116-118 °C.

\textit{NMR and HRMS data for the product 5x:}

\( ^1\text{H NMR} \ (400 \text{ MHz, CDCl}_3) \): \( \delta = 9.83 \ (s, \ 1H), 7.89-7.87 \ (m, \ 2H), 7.83-7.81 \ (m, \ 1H), \)
7.79 (s, 1H), 7.77-7.76 (m, 1H), 7.54-7.52 (m, 2H), 7.49-7.45 (m, 3H), 7.42 (dd, J = 8.4, 1.6 Hz, 1H), 7.38-7.35 (m, 2H), 3.96-3.87 (m, 2H), 0.86 (t, J = 7.2 Hz, 3H) ppm.

**13C NMR (100 MHz, CDCl3):** δ = 191.9, 165.9, 144.8, 142.1, 137.5, 137.0, 133.2 (d, J = 2.0 Hz), 132.9, 132.7, 132.6, 129.5 (d, J = 32.0 Hz), 129.4, 129.3, 129.1, 128.7, 128.6, 128.1, 128.0 (d, J = 4.0 Hz), 127.8, 127.7, 127.5, 126.8, 126.7, 122.9 (d, J = 273.0 Hz), 62.0, 13.5 ppm.

**HRMS (ESI):** m/z calculated for C27H19F3O3Na 471.1184, found 471.1181.

**ethyl 2-formyl-3-(2-methoxynaphthalen-1-yl)-5-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate**

![Chemical Structure](image)

Prepared according to the general procedure using ethyl ethyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enolate (57.3 mg, 0.2 mmol) and 3-(2-methoxynaphthalen-1-yl)acrylaldehyde (63.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5y as a white solid with 61% yield (58.6 mg). m.p. 119-121°C.

**NMR and HRMS data for the product 5y:**

**1H NMR (400 MHz, CDCl3):** δ = 9.69 (s, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.83 (s, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.47-7.46 (m, 3H), 7.42-7.31 (m, 5H), 7.21 (d, J = 8.4 Hz, 1H), 3.86 (s, 3H), 3.73-3.64 (m, 2H), 0.55 (t, J = 7.2 Hz, 3H) ppm.

**13C NMR (100 MHz, CDCl3):** δ = 191.6, 165.6, 154.6, 144.8, 137.8, 137.7, 137.6, 133.9 (d, J = 2.0 Hz), 133.4, 131.0, 130.1 (d, J = 32.0 Hz), 129.5, 128.6, 128.5, 128.4 (d, J = 4.0 Hz), 127.9, 127.0, 124.7, 123.8, 123.0 (d, J = 273.0 Hz), 117.5, 112.7, 100.0, 61.4, 56.5, 13.0 ppm.

**HRMS (ESI):** m/z calculated for C28H21F3O4Na 501.1290, found 501.1287.
ethyl 4-bromo-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-(4-bromophenyl)-5-oxo-3-(trifluoromethyl)pent-3-enoate (73.0 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5z as a white solid with 76% yield (72.2 mg). m.p. 135-136 °C.

NMR and HRMS data for the product 5z:

$^1$H NMR (600 MHz, CDCl$_3$): $\delta = 9.78$ (s, 1H), 7.70 (s, 1H), 7.60-7.58 (m, 2H), 7.44-7.42 (m, 3H), 7.31-7.29 (m, 2H), 7.22-7.20 (m, 2H), 4.01 (q, $J = 7.2$ Hz, 2H), 0.99 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta = 191.8$, 165.7, 143.1, 142.8, 136.7, 136.6, 134.6, 133.2, 131.7, 130.9, 129.8, 129.6 (d, $J = 33.0$ Hz), 128.9, 128.2, 127.9 (d, $J = 4.5$ Hz), 123.1, 122.7 (d, $J = 273.0$ Hz), 62.1, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{23}$H$_{16}$BrF$_3$O$_3$+Na 499.0133, found 499.0129.

ethyl 4-fluoro-2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-5-(4-fluorophenyl)-5-oxo-3-(trifluoromethyl)pent-3-enoate (60.9 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5aa as a white solid with 74% yield (61.4 mg). m.p. 107-109 °C.

NMR and HRMS data for the product 5aa:


**1H NMR (600 MHz, CDCl₃):** δ = 9.79 (s, 1H), 7.71 (s, 1H), 7.43-7.41 (m, 3H), 7.33-7.30 (m, 4H), 7.17-7.14 (m, 2H), 4.01 (q, J = 7.2 Hz, 2H), 0.99 (t, J = 7.2 Hz, 3H) ppm.

**13C NMR (150 MHz, CDCl₃):** δ = 191.9, 165.8, 162.9 (d, J = 247.5 Hz), 143.3, 142.6, 136.8, 134.7, 133.6 (d, J = 1.5 Hz), 133.1, 131 (d, J = 7.5 Hz), 129.8, 129.5 (d, J = 31.5 Hz), 128.8, 128.2, 128.1 (d, J = 4.5 Hz), 122.8 (d, J = 273.0 Hz), 115.7 (d, J = 22.5 Hz), 62.1, 13.5 ppm.

**HRMS (ESI):** m/z calculated for C₂₃H₁₆F₄O₃Na 439.0933, found 439.0930.

**ethyl 2'-formyl-4-methoxy-5'- (trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate**

![Chemical Structure](image_url)

Prepared according to the general procedure using ethyl ethyl (E)-5-(4-methoxyphenyl)-5-oxo-3-(trifluoromethyl)pent-3-enoate (63.3 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered **5ab** as a white solid with 77% yield (66.3 mg). m.p. 77-79 °C.

**NMR and HRMS data for the product 5ab:**

**1H NMR (600 MHz, CDCl₃):** δ = 9.81 (s, 1H), 7.75 (s, 1H), 7.41-7.40 (m, 3H), 7.29-7.28 (m, 4H), 7.01-6.98 (m, 2H), 3.99 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 0.98 (t, J = 7.2 Hz, 3H) ppm.

**13C NMR (150 MHz, CDCl₃):** δ = 192.3, 166.0, 160.1, 144.4, 141.9, 136.8, 135.2, 132.5, 130.9, 129.3, 129.4, 129.2 (d, J = 10.5 Hz), 128.5, 128.0, 127.9, 122.9 (d, J = 273.0 Hz), 114.2, 61.9, 55.4, 13.5 ppm.

**HRMS (ESI):** m/z calculated for C₂₄H₁₉F₃O₄Na 451.4133, found 451.1134.

**ethyl 3,4-dichloro-2'-formyl-5'- (trifluoromethyl)- [1,1':3',1''-terphenyl]-4'-carboxylate**
Prepared according to the general procedure using ethyl (E)-5-(3,4-dichlorophenyl)-5-oxo-3-(trifluoromethyl)pent-3-enoate (71.0 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered \( \text{5ac} \) as a white solid with 72% yield (67.1 mg). m.p. 123-124 °C.

**NMR and HRMS data for the product \( \text{5ac} \):**

\(^1\text{H NMR (600 MHz, CDCl}_3\): \( \delta = 9.78 \) (s, 1H), 7.67 (s, 1H), 7.52 (d, \( J = 8.4 \) Hz, 1H), 7.46-7.43 (m, 4H), 7.32-7.30 (m, 2H), 7.15 (dd, \( J = 8.4, 2.4 \) Hz, 1H), 4.02 (q, \( J = 7.2 \) Hz, 2H), 0.99 (t, \( J = 7.2 \) Hz, 3H) ppm.

\(^1\text{C NMR (150 MHz, CDCl}_3\): \( \delta = 191.4, 165.5, 143.3, 141.6, 138.0, 136.4, 134.2, 133.6, 133.0, 132.8, 130.9, 130.4, 129.9, 129.7, 129.1, 128.6, 128.3, 128.0 \) (d, \( J = 4.5 \) Hz), 122.6 (d, \( J = 273.0 \) Hz), 62.2, 13.5 ppm.

**HRMS (ESI):** m/z calculated for \( \text{C}_{23}\text{H}_{15}\text{Cl}_2\text{F}_3\text{O}_3\text{Na} \) 521.0510, found 521.0509.

**ethyl 6-formyl-5-(naphthalen-1-yl)-3-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate**

Prepared according to the general procedure using ethyl (\( E \))-5-(naphthalen-1-yl)-5-oxo-3-(trifluoromethyl)pent-3-enolate (67.3 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered \( \text{5ad} \) as a white solid with 70% yield (54.7 mg). m.p. 96-97 °C.

**NMR and HRMS data for the product \( \text{5ad} \):**

\(^1\text{H NMR (600 MHz, CDCl}_3\): \( \delta = 9.85 \) (s, 1H), 7.93-7.51 (m, 5H), 7.57-7.53 (m, 2H), 7.43-7.41 (m, 4H), 7.35-7.31 (m, 2H), 4.02 (q, \( J = 7.2 \) Hz, 2H), 1.00 (t, \( J = 7.2 \) Hz, 3H) ppm.
ppm.

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 192.0, 165.9, 144.7, 142.3, 136.9, 135.1, 135.0, 133.0, 132.9, 129.8, 129.5 (d, $J$ = 33.0 Hz), 128.9, 128.6, 128.4, 128.3, 128.1, 127.8, 127.0, 126.9, 122.9 (d, $J$ = 273.0 Hz), 62.0, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{27}$H$_{19}$F$_3$O$_3$+Na 471.1184, found 471.1186.

**methyl 2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using methyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (54.4 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5ae as a white solid with 71% yield (54.7 mg). m.p. 119-121 °C.

**NMR and HRMS data for the product 5ae:**

$^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 9.82 (s, 1H), 7.76 (s, 1H), 7.48-7.46 (m, 3H), 7.43-7.42 (m, 3H), 7.36-7.34 (m, 2H), 7.29-7.28 (m, 2H), 3.54 (s, 3H) ppm.

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 192.0, 166.4, 144.8, 142.2, 137.4, 136.8, 135.0, 132.7, 129.6, 129.4, 128.7, 128.6, 128.1, 128.0 (d, $J$ = 4.5 Hz), 122.8 (d, $J$ = 273.0 Hz), 52.6 ppm.

HRMS (ESI): m/z calculated for C$_{22}$H$_{15}$F$_3$O$_3$+Na 407.0871, found 407.0872.

**isopropyl 2'-formyl-5'-(trifluoromethyl)-[1,1':3',1''-terphenyl]-4'-carboxylate**
Prepared according to the general procedure using isopropyl (E)-5-oxo-5-phenyl-3-(trifluoromethyl)pent-3-enoate (60.1 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 5af as a white solid with 67% yield (55.2 mg). m.p. 102-103 °C.

**NMR and HRMS data for the product 5af:**

**1H NMR (600 MHz, CDCl₃):** δ = 9.81 (s, 1H), 7.75 (s, 1H), 7.47 (m, 3H), 7.42-7.70 (m, 3H), 7.35-7.33 (m, 2H), 7.32-7.30 (m, 2H), 4.92-4.88 (m, 1H), 0.98 (d, J = 6.0 Hz, 6H) ppm.

**13C NMR (150 MHz, CDCl₃):** δ = 192.11, 165.33, 144.5, 141.9, 137.5, 136.8, 135.0, 133.2, 129.9, 129.4, 129.2 (d, J = 10.5 Hz), 128.6, 128.6, 128.1, 128.0 (d, J = 4.5 Hz), 122.9 (d, J = 273.0 Hz), 70.0, 29.7, 21.1 ppm.

**HRMS (ESI):** m/z calculated for C₂₄H₁₉F₃O₃Na 435.1184, found 435.1186.

### 2.3 Procedure for 7

The reaction was carried out with 6 (0.20 mmol) and 2 (0.30 mmol), amine catalyst IV (0.05 mmol) and AcOH (0.08 mmol) in toluene (2 mL) under an open atmosphere at 70 °C for 72 h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 80:1) to give the final diaryl substituted benzenes 7, which was further analyzed by ¹H NMR, ¹³C HNR, HRMS analysis.

**ethyl 2’-cyano-[1,1’:3’,1”-terphenyl]-4’-carboxylate**
Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and cinnamaldehyde (39.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7a as a white solid with 68% yield (44.3 mg). m.p. 78-79 °C.

**NMR and HRMS data for the product 7a:**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.08$ (d, $J = 8.0$ Hz, 1H), 7.59 (dd, $J = 12.0$, 3.0 Hz, 2H), 7.59 (d, $J = 8.0$ Hz, 1H), 7.53-7.41 (m, 6H), 7.38-7.36 (m, 2H), 4.04 (q, $J = 7.2$ Hz, 2H), 0.94 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.8$, 148.9, 147.0, 137.8, 137.7, 133.3, 131.6, 129.2, 129.0, 128.9, 128.8, 128.7, 128.6, 128.2, 116.8, 113.3, 61.4, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{22}$H$_{17}$NO$_2$+Na 350.1157, found 350.1160.

**ethyl 2-chloro-2'-cyano-[1,1':3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 2-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7b as a white solid with 61% yield (43.8 mg). m.p. 108-109 °C.

**NMR and HRMS data for the product 7b:**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta = 8.08$ (d, $J = 8.0$ Hz, 1H), 7.55-7.52 (m, 1H), 7.50 (d, $J = 8.0$ Hz, 1H), 7.46-7.43 (m, 3H), 7.42-7.38 (m, 5H), 4.06 (q, $J = 7.2$ Hz, 2H), 0.95 ppm.
(t, J = 7.2 Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 166.8, 146.4, 146.3, 137.4, 136.7, 132.9, 132.8, 132.4, 130.9, 130.5, 130.1, 129.6, 129.0, 128.7, 128.3, 127.1, 126.1, 116.1, 61.6, 13.6 ppm.

HRMS (ESI): m/z calculated for C$_{22}$H$_{16}$ClNO$_2$+Na 384.0767, found 384.0770.

**ethyl 3-chloro-2'-cyano-[1,1':3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 3-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7c as a white solid with 63% yield (45.6 mg). m.p. 126-128 °C.

**NMR and HRMS data for the product 7c:**

$^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 8.08 (d, $J = 8.0$ Hz, 1H), 7.56-7.55 (m, 1H), 7.53 (d, $J = 8.4$ Hz, 1H), 7.51-7.44 (m, 6H), 7.37-7.35 (m, 2H), 4.05 (q, $J = 7.2$ Hz, 2H), 0.94 (t, $J = 7.2$ Hz, 3H) ppm.

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 166.6, 147.3, 147.1, 139.4, 137.5, 134.7, 133.4, 132.2, 130.1, 129.4, 129.0, 128.9, 128.7, 128.6, 128.3, 127.2, 116.5, 113.4, 61.5, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{22}$H$_{16}$ClNO$_2$+Na 384.0767, found 384.0768.

**ethyl 4-chloro-2'-cyano-[1,1':3',1''-terphenyl]-4'-carboxylate**
Prepared according to the general procedure using ethyl ethyl \((E)-4\)-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 4-chlorocinnamaldehyde (50.0 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered \(7d\) as a white solid with 66\% yield (47.5 mg). m.p. 104-106 \(^\circ\)C.

**NMR and HRMS data for the product \(7d\):**

\(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 8.09\) (d, \(J = 8.4\) Hz, 1H), 7.55-7.52 (m, 3H), 7.49-7.46 (m, 5H), 7.37-7.35 (m, 2H), 4.05 (q, \(J = 7.2\) Hz, 2H), 0.94 (t, \(J = 7.2\) Hz, 3H) ppm.

\(^13\)C NMR (150 MHz, CDCl\(_3\)): \(\delta = 166.7, 147.6, 147.1, 137.5, 136.0, 135.6, 133.4, 131.9, 130.2, 129.1, 128.8, 128.7, 128.6, 128.3, 116.7, 113.2, 61.5, 13.5\) ppm.

HRMS (ESI): m/z calculated for C\(_{22}\)H\(_{16}\)ClNO\(_2\)+Na 384.0767, found 384.0771.

**ethyl 4-bromo-2'-cyano-[1,1':3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using ethyl ethyl \((E)-4\)-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 4-bromocinnamaldehyde (63.3 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered \(7e\) as a white solid with 67\% yield (54.3 mg). m.p. 118-120 \(^\circ\)C.

**NMR and HRMS data for the product \(7e\):**

\(^1\)H NMR (600 MHz, CDCl\(_3\)): \(\delta = 8.09\) (d, \(J = 7.8\) Hz, 1H), 7.66-7.64 (m, 2H), 7.53 (d,
$J = 8.4 \text{ Hz, 1H}$, 7.48-7.46 (m, 5H), 7.37-7.35 (m, 2H), 4.05 (q, $J = 7.2 \text{ Hz, 2H}$), 0.94 (t, $J = 7.2 \text{ Hz, 3H}$) ppm.

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta = 166.7$, 147.6, 147.1, 137.5, 136.5, 133.4, 132.0, 132.0, 130.5, 128.8, 128.7, 128.6, 128.3, 123.9, 116.7, 113.2, 61.5, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{22}$H$_{16}$BrNO$_2$+Na 428.0262, found 428.0262.

**ethyl 2'-cyano-3-fluoro-[1,1':3',1''-terphenyl]-4'-carboxylate**

![Structural formula](image)

Prepared according to the general procedure using ethyl ethyl ($E$)-4-cyano-3-phenylbut-3-enate (43.1 mg, 0.2 mmol) and 3-fluorcinnaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7f as a white solid with 65% yield (44.7 mg). m.p. 72-74 °C.

**NMR and HRMS data for the product 7f.**

$^1$H NMR (600 MHz, CDCl$_3$): $\delta = 8.09$ (d, $J = 7.8 \text{ Hz, 1H}$), 7.55 (d, $J = 7.8 \text{ Hz, 1H}$), 7.49-7.47 (m, 4H), 7.38-7.36 (m, 3H), 7.30-7.28 (m, 1H), 7.20-7.17 (m, 1H), 4.05 (q, $J = 7.2 \text{ Hz, 2H}$), 0.94 (t, $J = 7.2 \text{ Hz, 3H}$) ppm.

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta = 166.7$, 162.6 (d, $J = 246.0 \text{ Hz}$), 147.4 (d, $J = 1.5 \text{ Hz}$), 147.1, 139.7 (d, $J = 7.5 \text{ Hz}$), 137.5, 133.4, 132.1, 130.5 (d, $J = 9.0 \text{ Hz}$), 128.8 (d, $J = 33.0 \text{ Hz}$), 128.7, 128.3, 124.8 (d, $J = 3.0 \text{ Hz}$), 116.5, 116.3, 116.2 (d, $J = 3.0 \text{ Hz}$), 116.0, 113.3, 61.6, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{22}$H$_{16}$FNO$_2$+Na 368.1063, found 368.1064.

**ethyl 2'-cyano-4-fluoro-[1,1':3',1''-terphenyl]-4'-carboxylate**

S52
Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 4-fluorocinnamaldehyde (45.1 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7g as a white solid with 64% yield (44.1 mg). m.p. 70-72 °C.

NMR and HRMS data for the product 7g:

$^1$H NMR (600 MHz, CDCl$_3$): $\delta$ = 8.08 (d, $J$ = 7.8 Hz, 1H), 7.58 (dd, $J$ = 9.0, 4.8 Hz, 2H), 7.54 (d, $J$ = 8.4 Hz, 1H), 7.47-7.46 (m, 3H), 7.37-7.36 (m, 2H), 7.22-7.19 (m, 2H), 4.05 (q, $J$ = 7.2 Hz, 2H), 0.94 (t, $J$ = 7.2 Hz, 3H) ppm.

$^{13}$C NMR (150 MHz, CDCl$_3$): $\delta$ = 166.7, 163.4 (d, $J$ = 247.5 Hz), 147.8, 147.1, 137.6, 133.7 (d, $J$ = 3.0 Hz), 133.4, 131.7, 130.9, 130.8, 128.9, 128.7, 128.6, 128.3, 116.8, 116.0, 115.9, 113.3, 61.5, 13.5 ppm.

HRMS (ESI): m/z calculated for C$_{22}$H$_{16}$FNO$_2$+Na 368.1063, found 368.1060.

deethyl 2'-cyano-4-methyl-[1,1':3',1''-terphenyl]-4'-carboxylate

Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 4-methylcinnamaldehyde (43.9 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7h as a white solid with 72% yield (49.2 mg). m.p. 81-82 °C.
NMR and HRMS data for the product 7h:

\(^1^H \text{NMR (400 MHz, CDCl}_3\):} \, \delta = 8.06 \, (d, \, J = 8.0 \, Hz, \, 1H), \, 7.54 \, (d, \, J = 8.4 \, Hz, \, 1H), \, 7.50-7.48 \, (m, \, 2H), \, 7.46-7.43 \, (m, \, 3H), \, 7.37-7.35 \, (m, \, 2H), \, 7.31-7.29 \, (m, \, 2H), \, 4.04 \, (q, \, J = 7.2 \, Hz, \, 2H), \, 2.42 \, (s, \, 3H), \, 0.93 \, (t, \, J = 7.2 \, Hz, \, 3H) \, ppm.

\(^{13}\text{C NMR (100 MHz, CDCl}_3\):} \, \delta = 166.8, \, 149.0, \, 147.0, \, 139.3, \, 137.9, \, 134.8, \, 133.2, \, 131.3, \, 129.5, \, 128.9, \, 128.8, \, 128.7, \, 128.6, \, 117.0, \, 113.2, \, 61.4, \, 21.3, \, 13.5 \, ppm.

HRMS (ESI): \, m/z \, \text{calculated for C}_{23}\text{H}_{19}\text{NO}_2^{+}\text{Na} \, 364.1313, \, \text{found} \, 364.1313

\textit{ethyl 2'-cyano-2-methoxy-[1,1':3',1''-terphenyl]-4'-carboxylate}

\[\text{\includegraphics[width=5cm]{terphenyl}}\]

Prepared according to the general procedure using ethyl ethyl ($E$)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 2-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7i as a white solid with 70% yield (50.3 mg). m.p. 158-160 °C.

NMR and HRMS data for the product 7i:

\(^1^H \text{NMR (600 MHz, CDCl}_3\):} \, \delta = 8.06 \, (d, \, J = 8.4 \, Hz, \, 1H), \, 7.51 \, (d, \, J = 8.4 \, Hz, \, 1H), \, 7.47-7.42 \, (m, \, 4H), \, 7.38 \, (d, \, J = 7.2 \, Hz, \, 1H), \, 7.30 \, (dd, \, J = 7.8, \, 1.2 \, Hz, \, 1H), \, 7.07 \, (t, \, J = 7.2 \, Hz, \, 1H), \, 7.03 \, (d, \, J = 7.2 \, Hz, \, 1H), \, 4.04 \, (q, \, J = 7.2 \, Hz, \, 2H), \, 3.85 \, (s, \, 3H), \, 0.94 \, (t, \, J = 7.8 \, Hz, \, 3H) \, ppm.

\(^{13}\text{C NMR (150 MHz, CDCl}_3\):} \, \delta = 167.0, \, 156.4, \, 146.2, \, 146.0, \, 137.8, \, 132.9, \, 131.4, \, 130.8, \, 130.7, \, 129.8, \, 128.8, \, 128.5, \, 128.2, \, 126.8, \, 120.8, \, 116.8, \, 115.2, \, 111.3, \, 61.4, \, 55.5, \, 13.5 \, ppm.

HRMS (ESI): \, m/z \, \text{calculated for C}_{23}\text{H}_{19}\text{NO}_3^{+}\text{Na} \, 380.1263, \, \text{found} \, 380.1261.

\textit{ethyl 2'-cyano-4-methoxy-[1,1':3',1''-terphenyl]-4'-carboxylate}
Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7j as a white solid with 74% yield (52.6 mg). m.p. 98-100 °C.

**NMR and HRMS data for the product 7j:**

1H NMR (400 MHz, CDCl3): δ = 8.06 (d, J = 8.4 Hz, 1H), 7.57-7.52 (m, 3H), 7.49-7.43 (m, 3H), 7.38-7.35 (m, 2H), 7.05-7.00 (m, 2H), 4.04 (q, J = 7.2 Hz, 2H), 3.86 (s, 3H), 0.94 (t, J = 7.2 Hz, 3H) ppm.

13C NMR (100 MHz, CDCl3): δ = 166.8, 160.5, 148.6, 147.1, 137.9, 133.3, 131.1, 130.3, 130.0, 128.8, 128.7, 128.6, 128.2, 117.1, 114.3, 113.1, 61.4, 55.4, 13.5 ppm.

HRMS (ESI): m/z calculated for C23H19NO3+Na 380.1263, found 380.1264.

**ethyl 2-chloro-2'-cyano-5-fluoro-[1,1':3',1''-terphenyl]-4'-carboxylate**

Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-phenylbut-3-enoate (43.1 mg, 0.2 mmol) and 3-(2-chloro-5-fluorophenyl)acrylaldehyde (55.4 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered 7k as a white solid with 62% yield (47.4 mg). m.p. 132-134 °C.
**NMR and HRMS data for the product 7k:**

**$^1$H NMR (600 MHz, CDCl$_3$):** $\delta = 8.10$ (d, $J = 7.8$ Hz, 1H), 7.50-7.45 (m, 5H), 7.38-7.33 (m, 2H), 7.14-7.11 (m, 2H), 4.07 (q, $J = 7.2$ Hz, 2H), 0.95 (t, $J = 7.2$ Hz, 3H) ppm.

**$^{13}$C NMR (100 MHz, CDCl$_3$):** $\delta = 166.7$, 161.0 (d, $J = 165.0$ Hz), 146.4, 145.1, 138.1 (d, $J = 5.0$ Hz), 137.2, 133.1, 132.8, 131.5 (d, $J = 5.0$ Hz), 129.3, 128.8, 128.7 (d, $J = 5.0$ Hz), 128.3, 128.0 (d, $J = 2.0$ Hz), 118.0 (d, $J = 16.0$ Hz), 117.7 (d, $J = 14.0$ Hz), 115.8, 114.8, 61.6, 13.5 ppm.

**HRMS (ESI):** m/z calculated for C$_{22}$H$_{15}$ClFNO$_2$+Na 402.0673, found 402.0674.

**ethyl 2'-cyano-4''-fluoro-4'-methoxy-[1,1':3',1''-terphenyl]-4'-carboxylate**

![Chemical Structure](image)

Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-(4-fluorophenyl)but-3-enoate (46.7 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product *via* column chromatography delivered 7l as a white solid with 71% yield (53.5 mg). m.p. 127-128 °C.

**NMR and HRMS data for the product 7l:**

**$^1$H NMR (600 MHz, CDCl$_3$):** $\delta = 8.08$ (d, $J = 7.8$ Hz, 1H), 7.55-7.53 (m, 3H), 7.36-7.33 (m, 2H), 7.18-7.15 (m, 2H), 7.04-7.02 (m, 2H), 4.08 (q, $J = 7.2$ Hz, 2H), 3.87 (s, 3H), 1.02 (t, $J = 7.2$ Hz, 3H) ppm.

**$^{13}$C NMR (150 MHz, CDCl$_3$):** $\delta = 166.5$, 162.9 (d, $J = 247.5$ Hz), 160.5, 148.7, 146.1, 133.9, 133.5, 130.9, 130.5 (d, $J = 7.5$ Hz), 130.3, 129.8, 129.1, 117.1, 115.4 (d, $J = 7.5$ Hz), 114.3, 113.2, 61.5, 55.4, 13.7 ppm.

**HRMS (ESI):** m/z calculated for C$_{22}$H$_{16}$FNO$_2$+Na 398.1168, found 398.1165.
**ethyl 2'-cyano-4''-nitro-[1,1':3',1''-terphenyl]-4'-carboxylate**

![Structure of ethyl 2'-cyano-4''-nitro-[1,1':3',1''-terphenyl]-4'-carboxylate](image)

Prepared according to the general procedure using ethyl ethyl (E)-4-cyano-3-(4-nitrophenyl)but-3-enolate (52.1 mg, 0.2 mmol) and 4-methoxycinnamaldehyde (48.7 mg, 0.3 mmol). Purification of the crude product via column chromatography delivered **7m** as a white solid with 69% yield (52.1 mg). m.p. 162-163 °C.

**NMR and HRMS data for the product 7m:**

**1H NMR (600 MHz, CDCl₃):** \(\delta = 8.36-8.34\) (m, 2H), 8.23 (d, \(J = 7.8\) Hz, 1H), 7.64 (d, \(J = 7.8\) Hz, 1H), 7.57-7.53 (m, 5H), 7.05-7.03 (m, 2H), 4.11 (q, \(J = 7.2\) Hz, 2H), 3.88 (s, 3H), 1.06 (t, \(J = 7.2\) Hz, 3H) ppm.

**13C NMR (150 MHz, CDCl₃):** \(\delta = 165.4\), 160.8, 149.2, 147.8, 145.3, 144.9, 134.1, 130.3, 129.9, 129.6, 129.3, 123.5, 116.6, 114.4, 112.8, 61.7, 55.4, 13.7 ppm.

HRMS (ESI): m/z calculated for C₂₂H₁₆FNO₂⁺Na 425.1113, found 425.1118.

**3. Synthetic transformations of 5a**

**3.1 Procedure of terminal alkyne 8**

![Procedure of terminal alkyne 8](image)

To a solution of **5a** (39.8 mg, 0.10 mmol) in ethyl alcohol (2 mL) was added BOR (48.0 mg, 0.2 mmol) and Cs₂CO₃ (97.7 mg, 0.30 mmol). The mixture was stirred at room temperature. When the reaction was complete (based on TLC monitoring), the reaction mixture was concentrated and the residue was purified by flash...
chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to give 8 as a white solid in 83% yield (32.7 mg). m.p. 78-79 °C.

**NMR and HRMS data for the product 8:**

**1H NMR (600 MHz, CDCl3):** \( \delta = 7.69 \) (s, 1H), 7.59-7.58 (m, 2H), 7.48-7.43 (m, 3H), 7.41-7.37 (m, 5H), 4.00 (q, \( J = 7.2 \) Hz, 2H), 2.99 (s, 1H), 0.97 (t, \( J = 7.2 \) Hz, 3H) ppm.

**13C NMR (100 MHz, CDCl3):** \( \delta = 166.3, 146.4, 144.8, 138.8, 137.3, 131.5, 129.5, 129.2, 128.5, 128.3, 128.2, 127.8, 126.7 \) (d, \( J = 33.0 \) Hz), 129.3 (d, \( J = 4.5 \) Hz), 124.6, 123.2 \( d, J = 271.5 \) Hz), 87.5, 80.0, 61.8, 13.5 ppm.

**HRMS (ESI):** \( m/z \) calculated for C\(_{23}\)H\(_{17}\)F\(_3\)O\(_3\)+Na 417.1078, found 417.1079.

**3.2 Procedure of CF\(_3\)-functionalized multi-substituted benzene-bridged Zidovudine 9**

To a solution of 8 (39.4 mg, 0.10 mmol) in THF (1.0 mL) was added Zidovudine (26.7 mg, 0.10 mmol), a freshly prepared solution of CuSO\(_4\)•5H\(_2\)O (25.0 mg, 0.10 mmol) and sodium ascorbate (19.8 mg, 0.10 mmol) in H\(_2\)O (1.0 mL). When the reaction was complete (based on TLC monitoring), the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to give 9 as a white solid in 81% yield (53.6 mg). m.p. 153-154 °C.

**NMR and HRMS data for the product 9:**

**1H NMR (400 MHz, CDCl3):** \( \delta = 8.81 \) (s, 1H), 7.79 (s, 1H), 7.25-7.16 (m, 10H), 7.11-7.09 (m, 1H), 6.83 (s, 1H), 5.97 (t, \( J = 6.8 \) Hz, 1H), 5.11-5.06 (m, 1H), 4.00 (q, \( J = 7.2 \) Hz, 2H), 3.87-3.85 (m, 1H), 3.78 (dd, \( J = 12.4, 2.0 \) Hz, 1H), 3.33 (dd, \( J = 12.4, 2.0 \) Hz, 1H), 2.96 (br, 1H), 2.81-2.64 (m, 2H), 1.89 (s, 3H), 0.96 (t, \( J = 7.2 \) Hz, 3H) ppm.
$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta = 166.5, 163.4, 150.2, 144.4, 144.0, 142.1, 139.5,$
$137.9, 137.2, 132.8, 132.0, 130.0 (d, $J = 6.0$ Hz), 129.4, 128.1, 127.7 (d, $J = 2.0$ Hz),
127.6 (d, $J = 3.0$ Hz), 127.0 (d, $J = 4.0$ Hz), 123.7, 123.4 (d, $J = 273.0$ Hz), 111.3, 89.1,
85.3, 61.8, 61.2, 58.6, 36.7, 31.6, 22.7, 14.1, 13.5, 12.4 ppm.

**HRMS (ESI):** m/z calculated for $\text{C}_{34}\text{H}_{30}\text{F}_3\text{N}_5\text{O}_6+\text{Na}$ 684.2046, found 684.2047.
4. Crystal data of 3a

Empirical formula \( \text{C}_{17}\text{H}_{12}\text{F}_{3}\text{NO}_{2} \)
Formula weight 319.28
Temperature/K 293(2)
Crystal system triclinic
Space group P-1
a/Å 7.9917(5)
b/Å 8.3050(6)
c/Å 11.8750(7)
α/° 107.623(6)
β/° 97.098(5)
γ/° 91.682(5)
Volume/Å\(^3\) 743.55(9)
Z 2
\( \rho_{\text{calc}} \)/g/cm\(^3\) 1.426
\( \mu \)/mm\(^{-1}\) 1.025
F(000) 328.0
Crystal size/mm\(^3\) 0.8 \times 0.6 \times 0.5
Radiation CuK\(\alpha\) (\(\lambda = 1.54184\))
2\(\Theta\) range for data collection/° 11.186 to 145.5
Index ranges \(-9 \leq h \leq 9, -10 \leq k \leq 10, -9 \leq l \leq 14\)
Reflections collected 6956
Independent reflections 2880 [\(R_{\text{int}} = 0.0222, R_{\text{sigma}} = 0.0211\)]
Data/restraints/parameters 2880/0/209
Goodness-of-fit on F\(^2\) 1.038
Final R indexes [\(I \geq 2\sigma(I)\)] \(R_1 = 0.0570, wR_2 = 0.1626\)
Final R indexes [all data] \(R_1 = 0.0624, wR_2 = 0.1702\)
Largest diff. peak/hole / e Å\(^3\) 0.27/-0.32
5. Crystal data of 5a

Empirical formula: \( \text{C}_{23}\text{H}_{17}\text{F}_{3}\text{O}_{3} \)

Formula weight: 398.36

Temperature/K: 293.8(2)

Crystal system: orthorhombic

Space group: Pbca

\( a/\text{Å} \): 17.2218(6)

\( b/\text{Å} \): 13.2420(4)

\( c/\text{Å} \): 17.2998(5)

\( \alpha/^{\circ} \): 90

\( \beta/^{\circ} \): 90

\( \gamma/^{\circ} \): 90

Volume/\( \text{Å}^3 \): 3945.3(2)

\( Z \): 8

\( \rho_{\text{calc}}/\text{g/cm}^3 \): 1.341

\( \mu/\text{mm}^{-1} \): 0.909

\( F(000) \): 1648.0

Crystal size/mm\(^3\): \( 0.75 \times 0.6 \times 0.5 \)

Radiation: CuK\( \alpha \) (\( \lambda = 1.54184 \))

2\( \Theta \) range for data collection/\( ^{\circ} \): 9.856 to 144.854

Index ranges: \(-21 \leq h \leq 13, -10 \leq k \leq 16, -13 \leq l \leq 21 \)

Reflections collected: 11346

Independent reflections: 3809 [\( R_{\text{int}} = 0.0276, R_{\text{sigma}} = 0.0225 \)]

Data/restraints/parameters: 3809/0/263

Goodness-of-fit on \( F^2 \): 1.085

Final R indexes [\( I \geq 2\sigma (I) \)]: \( R_1 = 0.0650, wR_2 = 0.1607 \)

Final R indexes [all data]: \( R_1 = 0.0739, wR_2 = 0.1709 \)

Largest diff. peak/hole / e \( \text{Å}^3 \): 0.30/-0.53
6. Crystal data of 7e

Empirical formula \( \text{C}_{22}\text{H}_{13}\text{BrNO}_2 \)
Formula weight \( 405.26 \)
Temperature/K \( 292.4(5) \)
Crystal system monoclinic
Space group \( \text{I2/a} \)
\( a/\text{Å} \) \( 15.8840(6) \)
\( b/\text{Å} \) \( 7.2300(2) \)
\( c/\text{Å} \) \( 32.8613(11) \)
\( \alpha/° \) \( 90 \)
\( \beta/° \) \( 90.675(3) \)
\( \gamma/° \) \( 90 \)
Volume/\( \text{Å}^3 \) \( 3773.5(2) \)
\( Z \) \( 8 \)
\( \rho_{\text{calc}} \text{g/cm}^3 \) \( 1.427 \)
\( \mu/\text{mm}^{-1} \) \( 3.089 \)
\( F(000) \) \( 1640.0 \)
Crystal size/mm\(^3\) \( 0.6 \times 0.4 \times 0.3 \)
Radiation \( \text{CuK\(\alpha \)} \ (\lambda = 1.54184) \)
2\(\Theta\) range for data collection/° \( 10.77 \) to 145.068
Index ranges \(-19 \leq h \leq 16, -5 \leq k \leq 8, -36 \leq l \leq 40 \)
Reflections collected \( 10640 \)
Independent reflections \( 3658 \) [\( \text{R}_{\text{int}} = 0.0337, \text{R}_{\text{sigma}} = 0.0270 \)]
Data/restraints/parameters \( 3658/0/236 \)
Goodness-of-fit on \( F^2 \) \( 1.022 \)
Final R indexes [\( I \geq 2\sigma (I) \)] \( R_1 = 0.0582, \text{wR}_2 = 0.1593 \)
Final R indexes [all data] \( R_1 = 0.0641, \text{wR}_2 = 0.1688 \)
Largest diff. peak/hole / e Å\(^3\) \( 0.47/-0.75 \)
7. NMR spectra
S105
S134
8. HRMS spectra
**5ac**

**5ad**
9. Control experiments results