Catalytic asymmetric conjugate addition of terminal alkynes to β-trifluoromethyl α,β-enones†

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SUPPORTING INFORMATION

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General Experimental Methods

Reactions were carried out under nitrogen in round bottom flasks oven-dried overnight at 120 °C. Commercial reagents were used as purchased. β-Trifluoromethyl-α,β-enones 1 were prepared from the corresponding substituted acetophenones and trifluoroacetaldehyde hemiacetal as described in the literature. Toluene was distilled from CaH2. Tetrahydrofuran (THF) was distilled from Na. Triethylamine was dried and stored on 4 Å molecular sieves. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040-0.063 mm. Melting points were determined in capillary tubes. NMR spectra were run at 300 MHz for 1H and at 75 MHz for 13C NMR using residual nondeuterated solvent (CHCl3) as internal standard (δ 7.26 and 77.0 ppm, respectively), and at 282 MHz for 19F NMR using CFCl3 as internal standard. Chemical shifts are given in ppm. The carbon type was determined by DEPT experiments. High resolution mass spectra (ESI) were recorded on a Q-TOF spectrometer equipped with an electrospray source with a capillary voltage of 3.3 kV (ESI). Specific optical rotations were measured using sodium light (D line 589 nm). Chiral HPLC analyses were performed in a chromatograph equipped with a UV diode-array detector using chiral stationary columns from Daicel.

Typical procedures and characterization data for compounds 3

General procedure for the enantioselective alkynylation reaction

[Cu(CH3CN)4]BF4 (5.7 mg, 0.018 mmol) and L4 (12.4 mg, 0.018 mmol) were placed in a dry round bottom flask which was purged with nitrogen. THF (0.2 mL) was added and the mixture was stirred for 1.5 h at room temperature. Then, a solution of β-trifluoromethyl-α,β-enone 2 (0.090 mmol) in dry THF (1.0 mL) was added via syringe, followed of triethylamine (12.5 µL, 0.090 mmol). The solution was placed in a bath at 40 °C. After 10 min, the alkyne 1 (0.675mmol) was added and the solution was stirred at 40 °C under nitrogen until the reaction was complete (TLC). The reaction mixture was quenched with 20% aqueous NH4Cl (1.0 mL), extracted with CH2Cl2 (2 × 15 mL), washed with brine (15 mL), dried over MgSO4 and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:diethyl ether mixtures afforded compound 3.

(S)-(−)-3-(Trifluoromethyl)-1,5-diphenylpent-4-yn-1-one (3aa)

Purified by flash chromatography eluting with hexane:diethyl ether (99:01). Enantiomeric excess (85%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer tᵣ = 8.1 min, minor enantiomer tᵣ = 10.1 min.

[α]D20 = −34.7 (c 0.81, CHCl3, 85% ee); 1H NMR (300 MHz, CDCl3) δ 8.03-7.99 (m, 2H), 7.62 (ddd, J = 6.6, 1.3 Hz, 2H), 7.40-7.37 (m, 2H), 7.31-7.24 (m, 3H), 4.29-4.16 (m,
1H), 3.60 (dd, \( J = 17.3, 8.9 \) Hz, 1H), 3.42 (dd, \( J = 17.3, 4.2 \) Hz, 1H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)) \( \delta \) 194.5 (C), 136.1 (C), 133.8 (CH), 131.9 (2CH), 128.8 (2CH), 128.6 (CH), 128.2 (2CH), 128.2 (2CH), 125.3 (q, \( J_{C-F} = 263.0 \) Hz, CF\(_3\)), 122.0 (C), 84.3 (C), 81.4 (q, \( J_{C-F} = 6.5 \) Hz, C), 38.3 (CH\(_2\)), 33.7 (q, \( J_{C-F} = 41.2 \) Hz, CH); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \( \delta \) −71.6 (s, 3F); HRMS (ESI) \( m/z \): 303.0893 (M + H), \( C_{18}H_{14}F_{3}O \) requires 303.0991.

\((S)-(S)-3-(Trifluoromethyl)-5-phenyl-1-p-tolympent-4-yn-1-one (3ab)\)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralpak AD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer \( t_r = 8.1 \) min, minor enantiomer \( t_r = 9.1 \) min.

\([\alpha]_D^{20} \approx -28.5 \) (c 0.89, CHCl\(_3\), 80% ee); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.92-7.88 (m, 2H), 7.40-7.36 (m, 2H), 7.31-7.26 (m, 5H), 4.26-4.19 (m, 1H), 3.56 (dd, \( J = 17.2, 8.9 \) Hz, 1H), 3.39 (dd, \( J = 17.2, 4.2 \) Hz, 1H), 2.43 (s, 3H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)) \( \delta \) 194.1 (C), 144.7 (C), 133.6 (C), 131.9 (2CH), 129.5 (2CH), 128.6 (CH), 128.2 (2CH), 127.2 (2CH), 125.4 (q, \( J_{C-F} = 279.3 \) Hz, CF\(_3\)), 122.0 (C), 84.7 (C), 84.2 (C), 38.1 (CH\(_2\)), 33.7 (q, \( J_{C-F} = 31.7 \) Hz, CH), 21.7 (CH\(_3\)); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \( \delta \) −71.6 (s, 3F); HRMS (ESI) \( m/z \): 317.1148 (M + H), \( C_{19}H_{16}F_{3}O \) requires 317.1141.

\((S)-(S)-3-(Trifluoromethyl)-1-(4-methoxyphenyl)-5-phenylpent-4-yn-1-one (3ac)\)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralpak IC), hexane-iPrOH 99:01, 1 mL/min, major enantiomer \( t_r = 9.0 \) min, minor enantiomer \( t_r = 8.0 \) min.

\([\alpha]_D^{20} \approx -40.9 \) (c 0.91, CHCl\(_3\), 80% ee); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.88 (dt, \( J = 9, 3 \) Hz, 2H), 7.29-7.26 (m, 2H), 7.19-7.16 (m, 3H), 6.89-6.84 (dt, \( J = 9, 3 \) Hz, 2H), 4.16-4.09 (m, 1H), 3.70 (s, 3H), 3.43 (dd, \( J = 18, 9 \) Hz, 1H), 3.25 (dd, \( J = 18, 3 \) Hz, 1H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)) \( \delta \) 193.0 (C), 164.0 (C), 131.9 (2CH), 130.6 (2CH), 129.2 (C), 128.6 (CH), 128.2 (2CH), 125.4 (q, \( J_{C-F} = 279.4 \) Hz, CF\(_3\)), 122.1 (C), 114.0 (2CH), 84.3 (C), 82.0 (q, \( J_{C-F} = 3.8 \) Hz, C), 55.5 (CH\(_3\)), 37.9 (CH\(_2\)), 33.8 (q, \( J_{C-F} = 31.6 \) Hz, CH); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \( \delta \) −71.6 (s, 3F); HRMS (ESI) \( m/z \): 333.1088 (M + H), \( C_{19}H_{16}F_{3}O_{2} \) requires 333.1097.
(S)-(−)-1-(4-Chlorophenyl)-3-(trifluoromethyl)-5-phenylpent-4-yn-1-one (3ad)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralcel OD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer $t_r = 7.5$ min, minor enantiomer $t_r = 10.9$ min.

$[\alpha]_D^{20} = -32.7$ (c 0.81, CHCl$_3$, 80% ee); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.95 (dt, $J = 9.0, 3.0$ Hz, 2H), 7.48 (dt, $J = 9.0, 2.4$ Hz, 2H), 7.40-7.36 (m, 2H), 7.31-7.24 (m, 3H), 4.27-4.14 (m, 1H), 3.55 (dd, $J = 17.3, 8.9$ Hz, 1H), 3.38 (dd, $J = 17.3, 4.2$ Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) δ 193.4 (C), 140.4 (C), 134.4 (C), 131.9 (2CH), 129.6 (2CH), 129.2 (2CH), 128.7 (CH), 128.2 (CH), 125.4 (q, $J_{C-F} = 279.3$ Hz, CF$_3$), 121.9 (C), 84.5 (C), 81.6 (q, $J_{C-F} = 3.9$ Hz, C), 38.3 (CH$_2$), 33.7 (q, $J_{C-F} = 31.5$ Hz, CH); $^{19}$F NMR (282 MHz, CDCl$_3$) δ $-71.7$ (s, 3F); HRMS (ESI) $m/z$: 337.0592/339.0564 (M + H$^+$) 100/32.0, C$_{18}$H$_{13}$F$_3$O$_3$Cl requires 337.0607/339.0578.

(3ae)

Purified by flash chromatography eluting with hexane-diethyl ether (95:05). Enantiomeric excess (70%) was determined by chiral HPLC (Chiralcel OD-H), hexane-PrOH 95:05, 1 mL/min, major enantiomer $t_r = 20.1$ min, minor enantiomer $t_r = 31.2$ min.

$[\alpha]_D^{20} = -25.2$ (c 0.60, CHCl$_3$, 70% ee); $^1$H NMR (300 MHz, CDCl$_3$) δ 8.35 (dt, $J = 9.0, 3.0$ Hz, 2H), 8.16 (dt, $J = 9.0, 3.0$ Hz, 2H), 7.40-7.25 (m, 5H), 4.27-4.15 (m, 1H), 3.63 (dd, $J = 17.5, 8.9$ Hz, 1H), 3.47 (dd, $J = 17.5, 4.2$ Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) δ 193.2 (C), 150.7 (C), 140.4 (C), 131.9 (2CH), 129.3 (2CH), 128.9 (CH), 128.3 (2CH), 125.1 (q, $J_{C-F} = 281.3$ Hz, CF$_3$), 124.1 (2CH), 121.7 (C), 84.8 (C), 81.1 (C), 38.9 (CH$_2$), 33.7 (q, $J_{C-F} = 31.9$ Hz, CH); $^{19}$F NMR (282 MHz, CDCl$_3$) δ $-71.6$ (s, 3F); HRMS (ESI) $m/z$: 348.0851 (M + H$^+$), C$_{18}$H$_{13}$F$_3$NO$_3$ requires 348.0848.

(S)-(−)-3-(Trifluoromethyl)-1-(naphthalene-3-yl)-5-phenylpent-4-yn-1-one (3af)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralcel OD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer $t_r = 16.3$ min, minor enantiomer $t_r = 19.1$ min.

$[\alpha]_D^{20} = -118.6$ (c 1.30, CHCl$_3$, 84% ee); $^1$H NMR (300 MHz, CDCl$_3$) δ 8.50 (s, 1H), 8.05 (dd, $J = 8.6, 1.8$ Hz, 1H), 7.98 (d, $J = 7.9$ Hz, 1H), 7.90 (dd, $J = 10.2, 8.6$ Hz, 2H), 7.65-7.54 (m, 2H), 7.38-7.35 (m, 2H), 7.28-7.20 (m, 3H), 4.35-4.22 (m, 1H), 3.73 (dd, $J = 34$ Hz, 1H), 3.47 (dd, $J = 17.5, 8.9$ Hz, 1H), 3.47 (dd, $J = 17.5, 4.2$ Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) δ 193.2 (C), 150.7 (C), 140.4 (C), 131.9 (2CH), 129.3 (2CH), 128.9 (CH), 128.3 (2CH), 125.1 (q, $J_{C-F} = 281.3$ Hz, CF$_3$), 124.1 (2CH), 121.7 (C), 84.8 (C), 81.1 (C), 38.9 (CH$_2$), 33.7 (q, $J_{C-F} = 31.9$ Hz, CH); $^{19}$F NMR (282 MHz, CDCl$_3$) δ $-71.6$ (s, 3F); HRMS (ESI) $m/z$: 348.0851 (M + H$^+$), C$_{18}$H$_{13}$F$_3$NO$_3$ requires 348.0848.
17.2, 8.9 Hz, 1H), 3.54 (dd, J = 17.2, 4.1 Hz, 1H); 13C NMR (75.5 MHz, CDCl₃) δ 194.4 (CH), 135.9 (C), 133.5 (C), 132.4 (C), 131.8 (2CH), 129.64 (CH), 128.9 (CH), 128.7 (CH), 128.6 (CH), 128.2 (2CH), 127.8 (CH), 127.0 (CH), 125.4 (q, J_C-F = 279.4 Hz, CF₃), 123.7 (CH), 122.0 (C), 84.4 (C), 81.9 (q, J_C-F = 3.5 Hz, C), 38.3 (CH₂), 33.8 (q, J_C-F = 31.8 Hz, CH); 19F NMR (282 MHz, CDCl₃) δ −71.5 (s, 3F); HRMS (ESI) m/z: 353.1148 (M + H)+, C₂₂H₁₆F₃O requires 353.1148.

(S)-(−)-3-(Trifluoromethyl)-5-phenyl-1-(thiophen-2-yl)pent-4-yn-1-one (3ag)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (90%) was determined by chiral HPLC (Chiralcel OD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer tᵣ = 10.5 min, minor enantiomer tᵣ = 15.2 min.

[α]D²⁰ −6.1 (c 1.09, CHCl₃, 90% ee); ¹H NMR (300 MHz, CDCl₃) δ 7.77 (dd, J = 3.8, 1.1 Hz, 1H), 7.68 (dd, J = 5, 1.1 Hz, 1H), 7.36–7.33 (m, 2H), 7.28–7.22 (m, 3H), 7.14 (dd, J = 5, 3.8 Hz, 1H), 4.23–4.10 (m, 1H), 3.47 (dd, J = 16.6, 8.9 Hz, 1H), 3.32 (dd, J = 16.6, 4.5 Hz, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 187.4 (C), 143.2 (C), 134.7 (CH), 132.7 (CH), 131.9 (2CH), 128.7 (CH), 128.3 (CH), 128.2 (2CH), 125.2 (q, J_C-F = 278.7 Hz, CF₃), 121.9 (C), 84.7 (C), 81.5 (C), 38.7 (CH₂), 33.8 (q, J_C-F = 31.7 Hz, CH); ¹⁹F NMR (282 MHz, CDCl₃) δ −71.7 (s, 3F); HRMS (ESI) m/z: 309.0550 (M + H)+, C₁₆H₁₂F₃OS requires 309.0555.

(S)-(−)-3-(Trifluoromethyl)-5-(4-methoxyphenyl)-1-phenylpent-4-yn-1-one (3ba)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (83%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer tᵣ = 15.9 min, minor enantiomer tᵣ = 14.4 min.

[α]D²⁰ −20.3 (c 0.93, CHCl₃, 83% ee); ¹H NMR (300 MHz, CDCl₃) δ 8.02–7.99 (m, 2H), 7.64–7.59 (m, 1H), 7.53–7.47 (m, 2H), 7.31 (dt, J = 9, 3 Hz, 2H), 6.79 (dt, J = 9, 3 Hz, 2H), 4.27–4.14 (m, 1H), 3.79 (s, 3H), 3.58 (dd, J = 17.2, 8.9 Hz, 1H), 3.41 (dd, J = 17.2, 4.2 Hz, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 194.7 (C), 159.8 (C), 136.1 (C), 133.7 (CH), 133.3 (2CH), 128.8 (2CH), 128.2 (2CH), 125.4 (q, J_C-F = 279.1 Hz, CF₃), 114.1 (C), 113.8 (2CH), 84.2 (C), 80.4 (q, J_C-F = 3.5 Hz, C), 55.3 (CH₃), 38.3 (CH₂), 33.7 (q, J_C-F = 31.7 Hz, CH); ¹⁹F NMR (282 MHz, CDCl₃) δ −71.7 (s, 3F); HRMS (ESI) m/z: 333.1088 (M + H)+ C₁₉H₁₆F₃O₂ requires 333.1097.
(S)-(−)-3-(Trifluoromethyl)-5-(4-fluorophenyl)-1-phenylpent-4-yn-1-one (3ca)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer t<sub>r</sub> = 8.8 min, minor enantiomer t<sub>r</sub> = 10.8 min.

[α]<sub>D</sub><sup>20</sup> −15.7 (c 1.15, CHCl<sub>3</sub>, 80% ee); 1H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.02-7.99 (m, 2H), 7.65-7.60 (m, 1H), 7.53-7.48 (m, 2H), 7.39-7.34 (m, 2H), 7.00-6.93 (m, 2H), 4.24-4.17 (m, 1H), 3.59 (dd, <i>J</i> = 17.3, 9 Hz, 1H), 3.42 (dd, <i>J</i> = 17.3, 4.1 Hz, 1H); 13C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 194.5 (C), 162.7 (d, <i>J</i> = 249.9 Hz, C), 136.0 (C), 133.9 (CH), 133.8 (d, <i>J</i> = 8.5 Hz, 2CH), 128.8 (2CH), 128.2 (2CH), 125.3 (q, <i>J</i> = 279.2 Hz, CF<sub>3</sub>), 115.1 (d, <i>J</i> = 3.5 Hz, C), 115.5 (d, <i>J</i><sub>CF</sub> = 22.1 Hz, 2CH), 83.3 (C), 81.6 (q, <i>J</i><sub>CF</sub> = 5.1 Hz, C), 38.2 (CH<sub>2</sub>), 33.6 (q, <i>J</i><sub>CF</sub> = 31.6 Hz, CH); 19F NMR (282 MHz, CDCl<sub>3</sub>) δ −71.6 (s, 3F), −110.7 (s, 1F); HRMS (ESI) <i>m/z</i>: 321.0892 (M + H)+, C<sub>18</sub>H<sub>13</sub>F<sub>4</sub>O requires 321.0897.

(5)-(−)-3-(Trifluoromethyl)-5-(4-Chlorophenyl)-1-phenylpent-4-yn-1-one (3da)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (77%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer t<sub>r</sub> = 10.5 min, minor enantiomer t<sub>r</sub> = 11.5 min.

[α]<sub>D</sub><sup>20</sup> −20.4 (c 0.90, CHCl<sub>3</sub>, 77% ee); 1H NMR (300 MHz, CDCl<sub>3</sub>) δ 8.02-7.99 (m, 2H), 7.62 (ddd, <i>J</i> = 6.6, 3.9, 1.3 Hz, 1H), 7.54-7.48 (m, 2H), 7.33-7.22 (m, 4H), 4.26-4.15 (m, 1H), 3.59 (dd, <i>J</i> = 17.3, 9 Hz, 1H), 3.42 (dd, <i>J</i> = 17.3, 4.1 Hz, 1H); 13C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 194.4 (C), 136.0 (C), 134.7 (C), 133.8 (CH), 133.1 (2CH), 128.8 (2CH), 128.6 (2CH), 128.2 (2CH), 125.3 (q, <i>J</i><sub>CF</sub> = 279.4 Hz, CF<sub>3</sub>), 120.5 (C), 83.2 (C), 80.9 (C), 38.2 (CH<sub>2</sub>), 33.7 (q, <i>J</i><sub>CF</sub> = 31.7 Hz, CH); 19F NMR (282 MHz, CDCl<sub>3</sub>) δ −71.5 (s, 3F); HRMS (ESI) <i>m/z</i>: 337.0594 / 339.0553 (M + H)+ 100 / 28.9 C<sub>18</sub>H<sub>13</sub>ClF<sub>3</sub>O requires 337.0607 / 339.0578.

(S)-(−)-3-(Trifluoromethyl)-5-(4-methoxyphenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3bg)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AY-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer t<sub>r</sub> = 25.3 min, minor enantiomer t<sub>r</sub> = 16.8 min.

[α]<sub>D</sub><sup>20</sup> −7.3 (c 0.98, CHCl<sub>3</sub>, 93% ee); 1H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.79 (dd, <i>J</i> = 3.8, 1.1 Hz, 1H), 7.72-7.70 (m, 1H), 7.32-7.28 (m, 2H), 7.17 (dd, <i>J</i> = 5, 3.8 Hz, 1H), 6.81-
6.77 (m, 2H), 4.23-4.11 (m, 1H), 3.79 (s, 3H), 3.48 (dd, \( J = 16.6, 8.9 \) Hz, 1H), 3.33 (dd, \( J = 16.6, 4.5 \) Hz, 1H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)) \( \delta \) 187.5 (C), 159.8 (C), 143.3 (C), 134.7 (CH), 133.3 (2CH), 132.6 (CH), 128.3 (CH), 125.2 (q, \( J_{C-F} = 279.3 \) Hz, CF\(_3\)), 114.0 (C), 113.8 (2CH), 84.6 (C), 80.0 (q, \( J_{C-F} = 3.3 \) Hz, C), 55.3 (CH\(_3\)), 38.8 (CH\(_2\)), 33.8 (q, \( J_{C-F} = 31.7 \) Hz, CH); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \( \delta \) –71.8 (s, 3F); HRMS (ESI) \( m/z \): 338.0592 (M + H)

\( (S)-(\cdash)\)-3-(Trifluoromethyl)-5-(4-fluorophenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3cg)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (90%) was determined by chiral HPLC (Chiralcel OD-H), hexane-\( ^1\)PrOH 99:01, 1 mL/min, major enantiomer \( t_r = 12.6 \) min, minor enantiomer \( t_r = 14.9 \) min.

\([\alpha]_D^{20}\) –6.4 (c 1.03, CHCl\(_3\), 90% ee); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.79 (dd, \( J = 3.9, 1.1 \) Hz, 1H), 7.72 (dd, \( J = 5, 1.1 \) Hz, 1H), 7.38-7.32 (m, 2H), 7.18 (dd, \( J = 5, 3.9 \) Hz, 1H), 7.00-6.93 (m, 2H), 4.23-4.08 (m, 1H), 3.49 (dd, \( J = 16.7, 9 \) Hz, 1H), 3.35 (dd, \( J = 16.7, 4.4 \) Hz, 1H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)) \( \delta \) 187.3 (C), 143.2 (C), 134.8 (CH), 133.8 (d, \( J = 8.5 \) Hz, 2CH), 132.7 (CH), 128.3 (CH), 125.0 (q, \( J_{C-F} = 279.5 \) Hz, CF\(_3\)), 118.0 (C), 115.5 (d, \( J = 22.1 \) Hz, 2CH), 83.6 (C), 81.2 (q, \( J_{C-F} = 3.6 \) Hz, C), 38.7 (CH\(_2\)), 33.8 (q, \( J_{C-F} = 31.9 \) Hz, CH); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \( \delta \) –71.6 (s, 3F), –110.7 (s, 1F); HRMS (ESI) \( m/z \): 327.0455 (M + H)

\( (S)-(\cdash)\)-5-(4-Chlorophenyl)-3-(trifluoromethyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3dg)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralpak IC), hexane-\( ^1\)PrOH 99:01, 1 mL/min, major enantiomer \( t_r = 6.5 \) min, minor enantiomer \( t_r = 7.0 \) min.

\([\alpha]_D^{20}\) –6.9 (c 1.06, CHCl\(_3\), 84% ee); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \( \delta \) 7.79 (dd, \( J = 3.9, 1.0 \) Hz, 1H), 7.22 (dd, \( J = 4.9, 1.0 \) Hz, 1H), 7.31-7.23 (m, 4H), 7.18 (dd, \( J = 4.9, 3.9 \) Hz, 1H), 4.21-4.14 (m, 1H), 3.49 (dd, \( J = 16.7, 9.0 \) Hz, 1H), 3.35 (dd, \( J = 16.7, 4.4 \) Hz, 1H); \(^{13}\)C NMR (75.5 MHz, CDCl\(_3\)) \( \delta \) 187.3 (C), 143.1 (C), 134.8 (C), 134.8 (CH), 133.1 (2CH), 132.6 (CH), 128.6 (2CH), 128.4 (CH), 125.1 (q, \( J_{C-F} = 279.6 \) Hz, CF\(_3\)), 120.4 (C), 83.6 (C), 82.5 (C), 38.6 (CH\(_2\)), 33.9 (q, \( J_{C-F} = 31.9 \) Hz, CH); \(^{19}\)F NMR (282 MHz, CDCl\(_3\)) \( \delta \) –71.5 (s, 3F); HRMS (ESI) \( m/z \): 343.0158 / 345.0128 (M + H)

\( C_{16}H_{11}ClF_3OS \) requires 343.0171 / 345.0142.
(S)-(−)-3-(Trifluoromethyl)-5-(2-methoxyphenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3eg)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (98%) was determined by chiral HPLC (Chiralcel OD-H), hexane-PrOH 95:05, 1 mL/min, major enantiomer $t_r = 10.7$ min, minor enantiomer $t_r = 13.2$ min.

$[\alpha]_D^{20} -7.8 \ (c 0.90, \text{CHCl}_3, 98\% \text{ ee}); ^1\text{H NMR} \ (300 \text{ MHz, CDCl}_3) \ \delta 7.80 \ (dd, J = 3.9, 1.1 \text{ Hz, 1H}), 7.70 \ (dd, J = 5.0, 1.1 \text{ Hz, 1H}), 7.34-7.24 \ (m, 2H), 7.17 \ (dd, J = 4.9, 3.8 \text{ Hz, 1H}), 6.91-6.77 \ (m, 2H), 4.29-4.21 \ (m, 1H), 3.78 \ (s, 3H), 3.52 \ (dd, J = 16.6, 8.5 \text{ Hz, 1H}), 3.36 \ (dd, J = 16.6, 4.8 \text{ Hz, 1H}); ^{13}\text{C NMR} \ (75.5 \text{ MHz, CDCl}_3) \ \delta 187.5 \ (C), 160.4 \ (C), 143.4 \ (C), 134.5 \ (CH), 133.7 \ (CH), 132.6 \ (CH), 130.1 \ (CH), 128.3 \ (CH), 125.2 \ (q, J_{\text{C-F}} = 279.5 \text{ Hz, CF}_3), 120.3 \ (CH), 111.3 \ (C), 110.8 \ (CH), 85.5 \ (C), 81.1 \ (C), 55.7 \ (CH_3), 38.9 \ (\text{CH}_2), 34.1 \ (q, J_{\text{C-F}} = 31.8 \text{ Hz, CH}); ^{19}\text{F NMR} \ (282 \text{ MHz, CDCl}_3) \ \delta -71.6 \ (s, 3\text{ F}); \text{HRMS (ESI) } m/z: \ 338.0590 \ (M + H)^+ \text{ C}_{17}\text{H}_{14}\text{F}_3\text{O}_2\text{S requires 338.0588.}

(S)-(−)-3-(Trifluoromethyl)-5-(3-fluorophenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3fg)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (99%) was determined by chiral HPLC (Chiralcel OD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer $t_r = 13.7$ min, minor enantiomer $t_r = 10.9$ min.

$[\alpha]_D^{20} -8.3 \ (c 0.87, \text{CHCl}_3, 99\% \text{ ee}); ^1\text{H NMR} \ (300 \text{ MHz, CDCl}_3) \ \delta 7.79 \ (dd, J = 2.7, 1.3 \text{ Hz, 1H}), 7.74 \ (ddd, J = 9.7, 4.9, 1.1 \text{ Hz, 1H}), 7.28-7.14 \ (m, 3H), 7.08-6.98 \ (m, 2H), 4.25-4.13 \ (m, 1H), 3.50 \ (dd, J = 16.7, 9.0 \text{ Hz, 1H}), 3.36 \ (dd, J = 16.7, 4.4 \text{ Hz, 1H}); ^{13}\text{C NMR} \ (75.5 \text{ MHz, CDCl}_3) \ \delta 187.2 \ (C), 162.2 \ (d, J_{\text{C-F}} = 246.7 \text{ Hz, C}), 143.1 \ (C), 134.8 \ (CH), 132.7 \ (CH), 129.8 \ (d, J_{\text{C-F}} = 8.6 \text{ Hz, CH}), 128.4 \ (CH), 127.8 \ (d, J_{\text{C-F}} = 3.1 \text{ Hz, CH}), 125.1 \ (q, J_{\text{C-F}} = 279.4 \text{ Hz, CF}_3), 123.7 \ (d, J_{\text{C-F}} = 9.4 \text{ Hz, C}), 118.7 \ (d, J_{\text{C-F}} = 23.0 \text{ Hz, CH}), 116.1 \ (d, J = 21.2 \text{ Hz, CH}), 83.4 \ (q, J_{\text{C-F}} = 3.4 \text{ Hz, C}), 82.5 \ (d, J_{\text{C-F}} = 3.5 \text{ Hz, C}), 38.6 \ (\text{CH}_2), 33.8 \ (q, J_{\text{C-F}} = 31.9 \text{ Hz, CH}); ^{19}\text{F NMR} \ (282 \text{ MHz, CDCl}_3) \ \delta -71.6 \ (s, 3\text{ F}), -113.4 \ (s, 1\text{ F}); \text{HRMS (ESI) } m/z: \ 327.0457 \ (M + H)^+ \text{ C}_{16}\text{H}_{14}\text{F}_4\text{OS requires 327.0459.}

(S)-(−)-3-(trifluoromethyl)-5-(3,5-dimethoxyphenyl)-1-(thiophen-2-yl)pent-4-yn-1-one (3gg)

Purified by flash chromatography eluting with hexane-diethyl ether (95:05). Enantiomeric excess (86%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 95:05, 1 mL/min, major
enantiomer $t_r = 11.2$ min, minor enantiomer $t_r = 12.5$ min.

$[\alpha]_D^{20} = 7.0$ (c 0.93, CHCl$_3$, 86% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.80 (dd, $J = 3.8, 1.1$ Hz, 1H), 7.71 (dd, $J = 4.9, 1.1$ Hz, 1H), 7.17 (dd, $J = 4.9, 3.8$ Hz, 1H), 6.51 (d, $J = 2.3$ Hz, 2H), 6.42 (t, $J = 2.3$ Hz, 1H), 4.22-4.15 (m, 1H), 3.75 (s, 6H), 3.49 (dd, $J = 16.6, 8.9$ Hz, 1H), 3.35 (dd, $J = 16.6, 4.5$ Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 187.4 (C), 160.4 (2C), 143.2 (C), 134.7 (CH), 132.7 (CH), 130.7 (CH), 125.2 (q, $J_{C-F} = 279.3$ Hz, CF$_3$), 123.2 (C), 109.6 (2CH), 102.3 (CH), 84.7 (C), 80.0 (q, $J_{C-F} = 3.4$ Hz, C), 55.4 (2CH$_3$), 38.7 (CH$_2$), 33.8 (q, $J_{C-F} = 31.8$ Hz, CH); 19F NMR (282 MHz, CDCl$_3$) $\delta$ $-71.6$ (s, 3F); HRMS (ESI) $m/z$: 368.0690 (M + H)$^+$ C$_{18}$H$_{15}$F$_3$O$_3$S requires 368.0694.

$(S)-(\pm)-3$-(Trifluoromethyl)-1-(thiophen-2-yl)-5-(thiophen-3-yl)pent-4-yn-1-one (3hg)

Purified by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (88%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer $t_r = 11.1$ min, minor enantiomer $t_r = 15.5$ min.

$[\alpha]_D^{20} = 5.4$ (c 0.86, CHCl$_3$, 88% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.79 (dd, $J = 3.9, 1.1$ Hz, 1H), 7.71 (dd, $J = 4.9, 1.1$ Hz, 1H), 7.40 (dd, $J = 3.0, 1.2$ Hz, 1H), 7.22 (dd, $J = 5.0, 3.0$ Hz, 1H), 7.04 (dd, $J = 5.0, 1.2$ Hz, 1H), 4.22-4.11 (m, 1H), 3.49 (dd, $J = 16.7, 8.9$ Hz, 1H), 3.34 (dd, $J = 16.7, 4.4$ Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 187.3 (C), 134.7 (CH), 132.6 (CH), 129.9 (CH), 129.7 (CH), 125.3 (CH), 125.1 (q, $J_{C-F} = 279.5$ Hz, CF$_3$), 120.9 (C), 81.1 (q, $J_{C-F} = 3.5$ Hz, C), 79.9 (C), 38.7 (CH$_2$), 33.8 (q, $J_{C-F} = 31.7$ Hz, CH); 19F NMR (282 MHz, CDCl$_3$) $\delta$ $-71.6$ (s, 3F); HRMS (ESI) $m/z$: 314.0043 (M + H)$^+$ C$_{14}$H$_{9}$F$_3$OS requires 314.0047.

$(S)-(\pm)-7$-phenyl-1-(thiophen-2-yl)-3-(trifluoromethyl)hept-4-yn-1-one (3ig)

Purification by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralcel AD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer $t_r = 9.7$ min, minor enantiomer $t_r = 10.8$ min.

$[\alpha]_D^{20} = 1.2$ (c 0.73, CHCl$_3$, 92% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.71 (td, $J = 4.7, 1.2$ Hz, 2H), 7.26-7.12 (m, 6H), 4.05 (m, 1H), 3.31 (dd, $J = 16.6, 9.0$ Hz, 1H), 3.19 (dd, $J = 16.6, 4.5$ Hz, 1H), 2.74 (t, $J = 7.2$ Hz, 2H), 2.42 (td, $J = 7.5, 2.4$ Hz, 2H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 187.6 (C), 143.4 (C), 140.3 (C), 134.5 (CH), 132.5 (CH), 128.5 (2CH), 128.3 (3CH), 126.2 (CH), 125.5 (q, $J_{C-F} = 277.5$ Hz, CF$_3$), 84.6 (C), 73.3 (C), 38.9 (CH$_2$), 34.6 (CH$_2$), 33.3 (q, $J_{C-F} = 30.8$ Hz, CH), 20.8 (CH$_2$); 19F NMR (282 MHz, CDCl$_3$) $\delta$ $-72.1$ (s, 3F); HRMS (ESI) $m/z$: 337.0854 (M + H)$^+$ C$_{18}$H$_{16}$F$_3$OS requires 337.0868.
**((S)-(+)−5-(Trifluoromethyl)-1,7-diphenylhept-6-yn-3-one (3ah))**

Purification by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (79%) was determined by chiral HPLC (Chiralcel AD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer $t_r = 6.6$ min, minor enantiomer $t_r = 9.6$ min.

$\left[\alpha\right]_D^{20} +6.1$ (c 0.8, CHCl$_3$, 79% ee); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.42-7.36 (m, 2H), 7.35-7.22 (m, 5H), 7.24-7.14 (m, 2H), 3.99 (m, 1H), 3.01-2.78 (m, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) δ 204.3 (C), 140.4 (C), 131.9 (CH), 128.7 (CH), 128.6 (CH), 128.3 (CH), 126.3 (CH), 125.1 (q, $J_{C-F} = 277.1$ Hz, CF$_3$), 121.9 (C), 84.4 (C), 81.5 (q, $J_{C-F} = 3.6$ Hz, C), 44.7 (CH$_2$), 42.1 (CH$_2$), 33.4 (q, $J_{C-F} = 31.7$ Hz, CH), 29.5 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) δ −71.8 (s, 3F); HRMS (ESI) $m/z$: 331.1306 (M + H)$^+$ C$_{20}$H$_{18}$F$_3$O requires 331.1304.

**((S)-(+)−5-(Trifluoromethyl)-7-(4-methoxyphenyl)-1-phenylhept-6-yn-3-one (3bh))**

Purification by flash chromatography eluting with hexane-diethyl ether (99:01). Enantiomeric excess (82%) was determined by chiral HPLC (Chiralcel AD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer $t_r = 11.3$ min, minor enantiomer $t_r = 17.4$ min.

$\left[\alpha\right]_D^{20} +3.0$ (c 0.5, CHCl$_3$, 82% ee); $^1$H NMR (300 MHz, CDCl$_3$) δ 7.33 (d, $J = 9.0$ Hz, 2H), 7.31-7.12 (m, 6H), 6.82 (d, $J = 9.0$ Hz, 2H), 3.98 (m, 1H), 3.81 (s, 3H), 3.00-2.78 (m, 6H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) δ 204.4 (C), 159.9 (C), 140.5 (C), 140.5 (CH), 133.4 (CH), 128.6 (CH), 128.3 (CH), 126.3 (CH), 125.1 (q, $J_{C-F} = 278.3$ Hz, CF$_3$), 114.0 (C), 113.9 (CH), 84.3 (C), 80.1 (q, $J_{C-F} = 1.6$ Hz, C), 55.3 (CH$_3$), 44.8 (CH$_2$), 42.1 (CH$_2$), 33.4 (q, $J_{C-F} = 31.5$ Hz, CH), 29.5 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) δ −71.9 (s, 3F); HRMS (ESI) $m/z$: 361.1415 (M + H)$^+$ C$_{21}$H$_{20}$F$_3$O$_2$ requires 361.1410.
Determination of the absolute configuration of (S)-(−)-3aa

\[
\begin{align*}
\text{Ph} & \quad \text{CF}_3 \quad \text{O} \\
\text{Ph} & \quad \text{LiAlH}_4 \\
\text{THF}, 75 \, ^\circ \text{C} & \quad \text{Ph} \quad \text{CF}_3 \quad \text{OH} \\
PCC, \text{4Å MS} & \quad \text{silica gel, CH}_2\text{Cl}_2 \\
\text{Ph} & \quad \text{CF}_3 \quad \text{O} \\
\end{align*}
\]

\((E,S)-3-(\text{Trifluoromethyl})-1,5\text{-diphenylpent-4-en-1-ol (4)}\)

Lithium aluminium hydride (12.1 mg, 0.320 mmol) was added to a solution of 3aa (16.1 mg, 0.053 mmol, 80% ee) in dry THF (1.5 mL) at room temperature, and the solution was stirred overnight at 75 °C. The reaction mixture was quenched with 20% aqueous NH₄Cl (1.0 mL), extracted with CH₂Cl₂ (2 x 15 mL), washed with brine (15 mL), dried over MgSO₄ and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:EtOAc (98:02) afforded compound 4 (16.2 mg, 99%) as a mixture of diastereomers.

\((E,S)-3-(\text{Trifluoromethyl})-1,5\text{-diphenylpent-4-en-1-one (5)}\)

To a 25 mL round-bottom flask equipped with a magnetic stirring bar was added PCC (137 mg, 0.64 mmol), 4Å MS (300 mg), silica gel (300 mg) and CH₂Cl₂ (10 mL). The mixture was cooled to 0 °C and the mixture of alcohols 4 (16.2 mg, 0.05 mmol) in CH₂Cl₂ (1 mL) was added dropwise. The reaction was warmed up to room temperature and was stirred for 3 h. The mixture was filtered through a pad of silica gel eluting with CH₂Cl₂. The solvent was removed under reduced pressure. The residual crude product was purified by flash column chromatography eluting with hexane:Et₂O (99:01) to afford the ketone 5 (10.5 mg, 66%).

Enantiomeric excess (78%) was determined by chiral HPLC (Chiralpak AD-H), hexane-
PrOH 99:01, 1 mL/min, major enantiomer \( t_r = 9.6 \) min, minor enantiomer \( t_r = 10.8 \) min. (lit\(^2\), Chiralpak AD-H, hexane-
PrOH 99.6:0.4, flow = 0.7 mL/min, \( R \)-enantiomer \( t_r = 19.3 \) min, \( S \)-enantiomer \( t_r = 16.3 \) min ); \([\alpha]^{D}_{20} = +4.9 \) (c 0.57, CCl₄, 78% ee) (lit\(^2\,^3\,\alpha]^{D}_{20} = -16.5 \) (0.95, CCl₄, 40% ee) for the \( R \)-isomer);\(^1\)H NMR (300 MHz, CDCl₃) \( \delta \) 7.98-7.95 (m, 2H), 7.62-7.57 (m, 1H), 7.51-7.46 (m, 2H), 7.37-7.24 (m, 5H), 6.70 (d, \( J = 15.9 \) Hz, 1H), 6.04 (dd, \( J = 15.9, 8.6 \) Hz, 1H), 3.93-3.83 (m, 1H), 3.40-3.38 (m, 2H); \(^13\)C NMR (75.5 MHz, CDCl₃) \( \delta \) 195.4 (C), 136.4 (C), 136.3 (CH), 136.1 (C), 133.6 (CH), 128.8 (2CH), 128.5 (2CH), 128.1 (CH), 128.1 (2CH), 126.9 (q, \( J = 274.7 \) Hz, CF₃), 121.5 (q, \( J = 2.4 \) Hz, CH), 42.6 (q, \( J = 27.7 \) Hz, CH), 37.4 (s, CH₂); \(^19\)F NMR (282 MHz, CDCl₃) \( \delta \) -71.2 (s, 3F); HRMS (ESI) \( m/z \): 305.1158 (M + H)\(^+\) \( C_{18}H_{16}F_{3}O \) requires 305.1153.
Synthetic transformations of compound 3aa. Synthesis of compounds 6 and 7

(Z,S)-(−)-1,5-Diphenyl-3-(trifluoromethyl)pent-4-en-1-one (6)

A solution of (S)-3aa (10.6 mg, 0.035 mmol, 80% ee) in benzene (0.5 mL) was stirred in the presence of Lindlar’s catalyst (2.5 mg) under hydrogen atmosphere (balloon) for 1 h. Then, the reaction mixture was filtered through a pad of Celite® eluting with EtOAc. The solvent was removed under reduced pressure to give 5 (9.4 mg, 88%). Enantiomeric excess (80%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer tᵣ = 7.7 min, minor enantiomer tᵣ = 7.3 min.

$\left[\alpha\right]_D^{20} = 70.2$ (c 0.45, CHCl₃, 80% ee); $^1$H NMR (300 MHz, CDCl₃) δ 7.79 (dd, J = 3.9, 1.1 Hz, 1H), 7.71 (dd, J = 4.9, 1.1 Hz, 1H), 7.40 (dd, J = 3.0, 1.2 Hz, 1H), 7.22 (dd, J = 5.0, 3.0 Hz, 1H), 7.17 (dd, J = 5.0, 3.9 Hz, 1H), 7.04 (dd, J = 5.0, 1.2 Hz, 1H), 4.22-4.11 (m, 1H), 3.49 (dd, J = 16.7, 8.9 Hz, 1H), 3.34 (dd, J = 16.7, 4.4 Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl₃) δ 195.5 (C), 136.3 (C), 135.9 (C), 135.7 (CH), 133.4 (CH), 128.7 (2CH), 128.4 (2CH), 128.3 (2CH), 128.1 (2CH), 127.5 (CH), 125.1 (q, J = 279.5 Hz, CF₃), 123.8 (q, J = 2.3 Hz, CH), 38.3 (q, J = 27.4 Hz, CH), 38.0 (q, J = 1.8 Hz, CH₂); $^{19}$F NMR (282 MHz, CDCl₃) δ −71.0 (s, 3F); HRMS (ESI) m/z: 305.1159 (M + H)⁺ C₁₈H₁₆F₃O requires 305.1153.

(R)-(−)-3-Iodo-2,6-diphenyl-4-(trifluoromethyl)-4H-pyran (7)

A solution of I₂ (30.1 mg, 0.119 mmol) in CH₂Cl₂ (2 mL) was added to a mixture of (S)-3aa (18 mg, 0.060 mmol 85% ee) and NaHCO₃ (10 mg, 0.119 mmol) under nitrogen atmosphere. The solution was stirred overnight at 40 ºC (reflux). The reaction mixture was quenched with saturated aqueous Na₂S₂O₃ (1.0 mL), extracted with CH₂Cl₂ (2 × 15 mL), washed with brine (15 mL), dried over MgSO₄ and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:Et₂O (98:02) gave compound 7 (19.9 mg, 77%). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralpak AD-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer tᵣ = 6.5 min, minor enantiomer tᵣ = 4.7 min.

$\left[\alpha\right]_D^{20} = 7.0$ (c 0.45, CHCl₃, 84% ee); $^1$H NMR (300 MHz, CDCl₃) δ 7.69-7.58 (m, 4H), 7.54-7.42 (m, 3H), 7.42-7.34 (m, 3H), 5.29 (d, J = 5.8 Hz, 1H), 4.16-4.02 (m, 1H); $^{13}$C NMR (75.5 MHz, CDCl₃) δ 155.1 (C), 153.1 (C), 135.9 (C), 132.3 (C), 129.9 (CH), 129.7 (2CH), 129.6 (CH), 128.7 (C), 128.5 (2CH), 128.2 (2CH), 125.4 (q, J = 223.7 Hz, CF₃), 125.0 (2CH), 90.4 (q, J = 1.8 Hz, CH), 49.5 (q, J = 22.7 Hz, CH); $^{19}$F NMR (282 MHz, CDCl₃) δ −74.4 (s, 3F); HRMS (ESI) m/z: 428.9961 (M + H)⁺ C₁₈H₁₃F₃IO requires 428.9958.


3. We thank Professor Tsutomu Konno, Kyoto Institute of Technology, for sending us complete characterization data of compound (E,R)-5.
**Electronic Supplementary Material (ESI) for Chemical Communications**

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![NMR Spectrum](image)

**3aa**

$^{13}$C NMR, 75.5 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
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$^{1}$H NMR, 300 MHz, CDCl$_3$
3ab

$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}\text{F NMR, 282 MHz, CDCl}_3$
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$^{1}$HNMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$

**3ac**

![Chemical Structure](image)
$^{19}$F NMR, 282 MHz, CDCl$_3$
3ad

$^1$HNMR, 300 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$\text{CF}_3$

$\text{NO}_2$

$\text{3ae}$

$^1\text{H NMR, 300 MHz, CDCl}_3$
$^{13}\text{C NMR, 75.5 MHz, CDCl}_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
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$^{1}$H NMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$\text{ESI for Chemical Communications}$

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$\text{1H NMR, 300 MHz, CDCl}_3$

$3\text{ag}$

$\text{Chemical Structure}$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}F$ NMR, 282 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
\begin{align*}
\text{HNMR, 300 MHz, CDCl}_3
\end{align*}
3da

$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
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\[ \text{MeO} \]

\[ \text{CF}_3 \]

\[ \text{O} \]

\[ \text{S} \]

$^{1}$H NMR, 300 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
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$^1$HNMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
Electronic Supplementary Material (ESI) for Chemical Communications
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^1^H NMR, 300 MHz, CDCl₃
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
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$\text{CF}_3\ O$

$\text{F}$

3fg

$^1\text{H}NMR$, 300 MHz, CDCl$_3$

f1 (ppm)
$^1$H NMR, 300 MHz, CDCl$_3$
3eg

$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$^1$HNMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}\text{F NMR, 282 MHz, CDCl}_3$
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Electronic Supplementary Material (ESI) for Chemical Communications

$^1$H NMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$1^\text{H} \text{NMR, 300MHz, CDCl}_3$
3ig

$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
3ah
$^1$H NMR, 300 MHz, CDCl$_3$
$^\text{13}C$ NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
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$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$^1$H NMR, 300 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
$^1$HNMR, 300 MHz, CDCl$_3$
$^13$C NMR, 75 MHz, CDCl$_3$
$^{19}$F NMR, 282 MHz, CDCl$_3$
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$\overset{1}{\text{H}}$NMR, 300 MHz, CDCl$_3$
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$^{19}$F NMR, 282 MHz, CDCl$_3$
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**Diagram 1:**

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**Diagram 2:**

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**Combined Area:** 100.000
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**Total Area %:** 100.000

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3ca

Retention Time (min)

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S92
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![Chemical structure of 3lg]

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S104