Highly Enantioselective Copper(I)-Catalyzed Conjugate Addition of 1,3-Diynes to α,β-Unsaturated Trifluoromethyl Ketones

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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. Stock solutions of 1,3-diynes in diethyl ether were prepared as described in the literature, stored in the freezer and a required aliquot concentrated under reduced pressure prior to use. Toluene was distilled from CaH2. 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 non deuterated 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. Chiral GLC analyses were carried out in an chromatograph equipped with a flame ionization detector using nitrogen (1 mL/min) as carrier gas, Tinjector = 220 °C, Tdetector = 220 °C.

Typical procedure for the synthesis of α,β-unsaturated trifluoromethyl ketones 1.

\[
\begin{align*}
\text{Ar-CH=CHOMe} & \quad \xrightarrow{1. \text{CF}_3\text{TMS, TBAF, THF}} \quad \text{Ar-CH=CF}_3 \\
& \quad \xrightarrow{2. 4\text{M HCl, THF}} \\
\end{align*}
\]

Trifluoromethyltrimethylsilane (0.34 mL, 2.31 mmol) was added to a solution of the corresponding α,β-unsaturated methyl ester (1.85 mmol) in pentane (1 mL) at room temperature under nitrogen atmosphere. A 1 M solution of tetrabutylammonium fluoride (TBAF) in THF (5 μL, 0.046 mmol) was added at 0 °C and the reaction mixture was allowed to warm to room temperature and stirred for 18 h. Then, the solvent was removed under reduced pressure. The residue was dissolved in THF (1 mL) and treated with 4 M aqueous HCl (1 mL). After 10 h, the reaction mixture was diluted with diethyl ether (20 mL), washed with brine (10 mL), dried over MgSO4, and concentrated under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:EtOAc (99:01) gave the corresponding enones 1.
(E)-1,1,1-trifluoro-4-phenylbut-3-en-2-one (1a)³

Yellow oil, 90% yield. ¹H NMR (300 MHz, CDCl₃) δ 7.98 (d, J = 16.0 Hz, 1H), 7.68-7.70 (m, 2H), 7.51-7.42 (m, 3H), 7.03 (dd, J = 16.0, 0.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 179.5 (q, J_C-F = 35.1 Hz, C), 146.9 (CH), 139.3 (C), 131.8 (CH), 130.9 (CH), 126.5 (CH), 126.3 (CH), 116.7 (CH), 116.4 (q, J_C-F = 290.9 Hz, CF₃), 18.9 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ −78.3 (s, 3F). Data consistent with the literature.³

(E)-1,1,1-trifluoro-4-(o-tolyl)but-3-en-2-one (1b)⁴

Yellow oil, 85% yield. ¹H NMR (400 MHz, CDCl₃) δ 8.31 (d, J = 15.8 Hz, 1H), 7.70-7.68 (m, 1H), 7.39 (dt, J = 3.9, 1.4 Hz, 1H), 7.29-7.25 (m, 1H), 6.96 (dd, J = 15.8, 0.8 Hz, 1H), 2.50 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 179.5 (q, J_C-F = 35.1 Hz, C), 146.9 (CH), 139.3 (C), 131.8 (CH), 130.9 (CH), 126.5 (CH), 126.3 (CH), 116.7 (CH), 116.4 (q, J_C-F = 290.9 Hz, CF₃), 18.9 (CH₃); ¹⁹F NMR (376 MHz, CDCl₃) δ −78.3 (s, 3F). Data consistent with literature.⁴

(E)-1,1,1-trifluoro-4-(m-tolyl)but-3-en-2-one (1c)⁵

Yellow oil, 60% yield. ¹H NMR (300 MHz, CDCl₃) δ 7.88 (d, J = 16.0 Hz, 1H), 7.39-7.37 (m, 2H), 7.31-7.26 (m, 2H), 6.95 (dd, J = 16.0, 0.8 Hz, 1H), 2.50 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 180.0 (q, J_C-F = 35.3 Hz, C), 150.4 (CH), 139.0 (C), 133.2 (CH), 129.8 (CH), 129.1 (CH), 126.5 (CH), 116.4 (q, J_C-F = 290.8 Hz, CF₃), 116.3 (CH), 21.2 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ −78.1 (s, 3F). Data consistent with literature.⁵

(E)-1,1,1-trifluoro-4-(m-tolyl)but-3-en-2-one (1d)⁶

Yellow oil, 89% yield. ¹H NMR (300 MHz, CDCl₃) δ 7.95 (d, J = 15.9 Hz, 1H), 7.54 (d, J = 8.1 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 6.97 (dd, J = 15.9, 0.7 Hz, 1H), 2.41 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 180.0 (q, J_C-F = 35.3 Hz, C), 150.2 (CH), 143.4 (C), 130.7 (C), 130.0 (2CH), 129.3 (2CH), 116.5 (q, J_C-F = 291.0 Hz, CF₃), 115.6 (CH), 21.7 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ −78.2 (s, 3F). Data consistent with the literature.⁶
(E)-4-(2-bromophenyl)-1,1,1-trifluorobut-3-en-2-one (1e) Yellow oil, 54% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.37 (d, $J$ = 16.0 Hz, 1H), 7.72 (dd, $J$ = 7.6, 1.9 Hz, 1H), 7.67 (dd, $J$ = 7.7, 1.6 Hz, 1H), 7.39-7.30 (m, 2H), 6.99-6.94 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 179.8 (q, $J_{C-F}$ = 35.7 Hz, C), 148.3 (CH), 136.7 (C), 133.9 (CH), 128.1 (CH), 119.1 (CH), 116.3 (q, $J_{C-F}$ = 290.9 Hz, CF$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -78.0 (s, 3F). Data consistent with the literature.\(^3\)

(E)-4-(4-bromophenyl)-1,1,1-trifluorobut-3-en-2-one (1f) Yellow oil, 75% yield.$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.89 (d, $J$ = 16.0 Hz, 1H), 7.65-7.55 (m, 2H), 7.55-7.45 (m, 2H), 7.00 (dd, $J$ = 16.0, 0.8 Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 179.9 (q, $J_{C-F}$ = 35.3 Hz, C), 148.6 (CH), 132.6 (2CH), 132.2 (C), 130.4 (2CH), 127.0 (C), 117.1 (CH), 116.3 (q, $J$ = 290.7 Hz, CF$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -78.1 (s, 3F). Data consistent with literature.\(^3\)

(E)-1,1,1-trifluoro-4-(2-methoxyphenyl)but-3-en-2-one (1g) Yellow oil, 63% yield.$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.29 (d, $J$ = 16.0 Hz, 1H), 7.60 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.46 (ddd, $J$ = 8.5, 7.4, 1.7 Hz, 1H), 7.14 (dd, $J$ = 16.1, 0.9 Hz, 1H), 7.01 (td, $J$ = 7.5, 0.7 Hz, 1H), 6.96 (d, $J$ = 8.4 Hz, 1H), 3.93 (s, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 180.5 (q, $J_{C-F}$ = 34.6 Hz, C), 159.6 (C), 145.8 (CH), 133.7 (CH), 130.3 (CH), 122.4 (C), 120.9 (CH), 117.1 (CH), 116.5 (q, $J$ = 290.9 Hz, CF$_3$), 111.4 (CH), 55.6 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -78.0 (s, 3F). Data consistent with literature.\(^3\)

(E)-1,1,1-trifluoro-4-(4-methoxyphenyl)but-3-en-2-one (1h) Yellow oil, 73% yield.$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.94 (d, $J$ = 15.8 Hz, 1H), 7.60 (dd, $J$ = 7.7, 1.7 Hz, 1H), 7.46 (ddd, $J$ = 8.5, 7.4, 1.7 Hz, 1H), 7.14 (dd, $J$ = 16.1, 0.9 Hz, 1H), 7.01 (td, $J$ = 7.5, 0.7 Hz, 1H), 6.96 (d, $J$ = 8.4 Hz, 1H), 3.88 (s, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 180.5 (q, $J_{C-F}$ = 34.6 Hz, C), 159.6 (C), 145.8 (CH), 133.7 (CH), 130.3 (CH), 122.4 (C), 120.9 (CH), 117.1 (CH), 116.5 (q, $J$ = 290.9 Hz, CF$_3$), 111.4 (CH), 55.5 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -78.0 (s, 3F). Data consistent with literature.\(^3\)

(E)-1,1,1-trifluoro-4-(naphthalen-2-yl)but-3-en-2-one (1i) Yellow solid, mp 63-65 ºC, 70% yield. $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 8.13 (d, $J$ = 15.9 Hz, 1H), 8.06 (s, 1H), 7.92-7.85 (m, 3H), 7.73 (dd, $J$ = 8.7, 1.8 Hz, 1H), 7.62-7.53 (m, 2H), 7.12 (dd, $J$ = 15.9, 0.8 Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 180.0 (q, $J_{C-F}$ = 35.2 Hz, C), 150.2 (CH), 135.1 (C), 133.1 (C), 132.7 (CH), 130.8 (C), 149.9 (CH), 131.4 (2CH), 126.2 (C), 116.4 (q, $J_{C-F}$ = 290.9 Hz, CF$_3$), 114.8 (2CH), 114.1 (CH), 55.5 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ -78.0 (s, 3F). Data consistent with literature.\(^3\)
Synthesis of \((E)-1,1,1\)-trifluoro-6-phenylhex-3-en-2-one \((1j)\) and aliphatic enones \(1k\) and \(1l\).

Methyl \((E)-5\)-phenylpent-2-enoate\(^7\)

To a stirred solution of 3-phenylpropanal (0.33 mL, 2.49 mmol) in dichloromethane (10 mL), Wittig ylide Ph\(_3\)PCH\(_2\)CO\(_2\)Me (1.0 g, 2.99 mmol) was added at room temperature under nitrogen atmosphere. After 24 h, the solvent was evaporated under reduced pressure and the resulting crude was purified by column chromatography to give methyl \((E)-5\)-phenylpent-2-enoate as a liquid (425 mg, 90%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.38-7.23 (m, 5H), 7.07 (dt, \(J = 15.7, 6.8\) Hz, 1H), 5.91 (dt, \(J = 15.7, 1.6\) Hz, 1H), 3.78 (s, 3H), 2.86-2.81 (m, 2H), 2.62-2.54 (m, 2H). Data consistent with literature.\(^7\)

\((E)-5\)-phenylpent-2-en-1-ol\(^8\)

DIBAL–H (4.2 mL, 4.20 mmol, 1 M in toluene) was added to a solution of \((E)-5\)-phenylpent-2-enoate (400 mg, 2.10 mmol) in tetrahydrofuran (5 mL) at −78 °C under nitrogen atmosphere. After 4 h, saturated aqueous Roche’s salt solution (8 mL) and ethyl acetate (6 mL) were added and stirred for 1h. The organic layer was separated and dried over anhydrous MgSO\(_4\) and evaporated under reduced pressure. The residue was purified by column chromatography to give \((E)-5\)-phenylpent-2-en-1-ol (320 mg, 94%). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.32-7.27 (m, 2H), 7.22-7.18 (m, 3H), 5.78-5.63 (m, 2H), 4.09 (d, \(J = 5.0\) Hz, 2H), 2.75-2.68 (m, 2H), 2.43-2.37 (m, 2H), 1.46 (brs, 1H). Data consistent with literature.\(^8\)
(E)-5-phenylpent-2-enal

To a stirred solution of (E)-5-phenylpent-2-en-1-ol (300 mg, 1.86 mmol) in dichloromethane (16 mL), MnO$_2$ (2.97 g, 34.2 mmol) was added at room temperature under nitrogen atmosphere. After 72 h, dichloromethane was evaporated and the resulting crude was purified by column chromatography to give methyl (E)-5-phenylpent-2-enal as a liquid (278 mg, 93%). $^1$H NMR (300 MHz, CDCl$_3$) δ 9.50 (d, $J = 7.8$ Hz, 1H), 7.34-7.29 (m, 2H), 7.24-7.18 (m, 3H), 6.87 (dt, $J = 15.6, 6.6$ Hz, 1H), 6.14 (ddt, $J = 15.7, 7.9, 1.5$ Hz, 1H), 2.87-2.82 (m, 2H), 2.71-2.63 (m, 2H). Data consistent with literature.$^9$

(E)-1,1,1-trifluoro-6-phenylhex-3-en-2-ol

A 1M solution of TBAF in THF (0.16 mL, 0.156 mmol) was added to a solution of (E)-5-phenylpent-2-enal (250 mg, 1.56 mmol) and TMSCF$_3$ (0.3 mL, 2.06 mmol) in pentane (1 mL) at 0 ºC under nitrogen atmosphere and the resulting mixture was allowed to reach room temperature. After 24 h, pentane was evaporated under reduced pressure. THF (1 mL) and 4M aqueous HCl (1 mL) were added, and the mixture was stirred 24 h. Then, the organic layer was separated, dried over anhydrous MgSO$_4$ and evaporated. Purification by column chromatography gave (E)-1,1,1-trifluoro-6-phenylhex-3-en-2-ol (340 mg, 94%). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.34-7.18 (m, 5H), 6.07-5.98 (m, 1H), 5.55 (dd, $J = 15.5, 6.8$ Hz, 1H), 4.44-4.34 (m, 1H), 2.78-2.73 (m, 2H), 2.49-2.42 (m, 2H), 2.24 (d, $J = 5.6$ Hz, 1H). Data consistent with literature.$^10$

(E)-1,1,1-trifluoro-6-phenylhex-3-en-2-one (1j)

Dess-Martin periodinane (720 mg, 1.70 mmol) was added in one portion to a solution of (E)-1,1,1-trifluoro-6-phenylhex-3-en-2-ol (300 mg, 1.30 mmol) in dichloromethane (2.6 mL) at room temperature under nitrogen atmosphere. After 48 h, the resulting suspension was poured into 3 mL of a 5:1 mixture of saturated aqueous Na$_2$S$_2$O$_3$ solution and saturated aqueous NaHCO$_3$ solution. The organic layer washed with water, dried over MgSO$_4$ and evaporated. The residue was purified by column chromatography to give 1j (200 mg, 67%). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.33-7.11 (m, 6H), 6.36 (dd, $J = 15.8, 1.1$ Hz, 1H), 2.81-2.76 (m, 2H), 2.64-2.56 (m, 2H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) δ 179.7 (q, $J_{C,F} = 35.3$ Hz, C), 155.2 (CH), 139.9 (C), 128.6 (2CH), 128.3 (2CH), 126.5 (CH), 121.9 (CH), 116.4 (q, $J_{C,F} = 290.8$ Hz, CF$_3$), 34.8 (CH$_2$), 33.8 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) δ −78.0 (s, 3F). HRMS (ESI) $m/z$: 228.0754 (M+H)$^+$, C$_{12}$H$_{11}$F$_3$O requires 228.0762.
Methyl (E)-hept-2-enoate\textsuperscript{11}

Prepared from valeraldehyde following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 6.89 (dt, \(J = 15.6, 7.0\) Hz, 1H), 5.74 (dt, \(J = 15.6, 1.6\) Hz, 1H), 3.64 (s, 3H), 2.13 (qd, \(J = 7.2, 1.5\) Hz, 2H), 1.39-1.23 (m, 4H), 0.83 (t, \(J = 7.2\) Hz, 3H). Data consistent with literature.\textsuperscript{11}

(\textit{E})-Hept-2-en-1-ol

Prepared following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 5.72-5.55 (m, 2H), 4.06-4.04 (m, 2H), 2.02 (dd, \(J = 13.1, 6.5\) Hz, 2H), 1.83 (br s, OH), 1.39-1.26 (m, 4H), 0.88 (t, \(J = 7.1\) Hz, 3H).

(\textit{E})-Hept-2-enal\textsuperscript{12}

Prepared following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 9.49 (d, \(J = 7.9\) Hz, 1H), 6.84 (dt, \(J = 15.6, 6.8\) Hz, 1H), 6.11 (ddt, \(J = 15.6, 7.9, 1.5\) Hz, 1H), 2.37-2.29 (m, 2H), 1.54-1.30 (m, 4H), 0.92 (t, \(J = 7.2\) Hz, 3H). Data consistent with literature.\textsuperscript{12}

(\textit{E})-1,1,1-Trifluoroct-3-en-2-ol\textsuperscript{13}

Prepared following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 6.03-5.93 (m, 1H), 5.55-5.48 (m, 1H), 4.41-4.37 (m), 2.21 (br s, OH), 2.15-2.08 (m, 2H), 1.45-1.28 (m, 4H), 0.93-0.86 (m, 3H); \textsuperscript{19}F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta\) -80.0 (s, 3F). Data consistent with literature.\textsuperscript{13}

(\textit{E})-1,1,1-Trifluoroct-3-en-2-one (1k)\textsuperscript{13}

Prepared following the above procedure. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.33 (dt, \(J = 15.3, 7.0\) Hz, 1H), 6.40 (ddd, \(J = 15.8, 2.6, 1.5\) Hz, 1H), 2.34 (ddd, \(J = 14.8, 7.2, 1.6\) Hz, 2H), 1.52-1.46 (m, 2H), 1.41-1.33 (m, 2H), 0.92 (t, \(J = 7.3\) Hz, 3H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 179.8 (q, \(J_{C-F} = 35.1\) Hz, C), 157.0 (CH), 121.3 (CH), 116.2 (q), 32.9 (CH\textsubscript{2}), 29.6 (CH\textsubscript{2}), 22.2 (CH\textsubscript{2}), 15.2 (CH\textsubscript{3}). Data consistent with literature.\textsuperscript{13}

Methyl (\textit{E})-5-methylhex-2-enoate\textsuperscript{14}

Prepared following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 6.95 (dt, \(J = 15.6, 7.0\) Hz, 1H), 5.80 (dt, \(J = 15.6, 1.7\) Hz, 1H), 3.70 (s, 3H), 2.17-2.04 (m, 3H), 0.92 (d, \(J = 6.6\) Hz, 6H). Data consistent with literature.\textsuperscript{14}
(E)-5-Methylhex-2-en-1-ol\textsuperscript{15}

Prepared following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 5.68-5.63 (m, 2H), 4.69 (d, \(J = 4.6\) Hz, 2H), 1.97-1.91 (m, 2H), 1.70-1.56 (m, 1H), 1.42 (br s, OH), 0.89 (d, \(J = 6.6\) Hz, 6H). Data consistent with literature.\textsuperscript{15}

(E)-5-Methylhex-2-enal\textsuperscript{16}

Prepared following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 9.51 (d, \(J = 7.9\) Hz, 1H), 7.11-7.01 (m, 1H), 5.82 (dt, \(J = 15.6, 1.5\) Hz, 1H), 2.26-2.10 (m, 2H), 1.87-1.74 (m, 1H), 0.96 (d, \(J = 6.9\) Hz, 6H). Data consistent with literature.\textsuperscript{16}

(E)-1,1,1-Trifluoro-6-methylhept-3-en-2-ol

Prepared following the above procedure. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 6.00-5.90 (m, 1H), 5.50 (dd, \(J = 15.4, 6.9\) Hz, 1H), 4.44-4.36 (m, 1H), 2.02-1.97 (m, 2H), 1.72-1.63 (m, 1H), 0.90 (dd, \(J = 6.6, 2.2\) Hz, 6H); \textsuperscript{19}F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta\) −80.0 (s, 3F).

(E)-1,1,1-Trifluoro-6-methylhept-3-en-2-one (1l)

Prepared following the above procedure. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.32-7.24 (m, 1H), 6.38 (dd, \(J = 15.7, 1.1\) Hz, 1H), 2.22-2.18 (m, 2H), 1.87-1.79 (m, 1H), 0.93 (d, \(J = 6.7\) Hz, 6H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 179.6 (q, \(J_{C-F} = 35.1\) Hz, C), 155.7 (CH), 122.4 (CH), 116.2 (q, \(J_{C-F} = 291.0\) Hz, CF\textsubscript{3}), 42.3 (CH\textsubscript{2}), 27.8 (CH), 22.2 (2CH\textsubscript{3}); \textsuperscript{19}F NMR (282 MHz, CDCl\textsubscript{3}) \(\delta\) −78.0 (s, 3F); HRMS (ESI) \textit{m/z}: 181.0844 (M+H\textsuperscript{+}), C\textsubscript{8}H\textsubscript{12}F\textsubscript{3}O requires 181.0840.

Synthesis and characterization of 1,3-diynes 2

1,3-Diynes 2 were synthesized according to the procedure described in the literature.\textsuperscript{1}

4-Bromo-2-methylbut-3-yn-2-ol

Br\textsubscript{2} (3.9 mL, 0.077 mol) was added dropwise via syringe to a stirred solution of KOH (30.1 g, 0.536 mol) in H\textsubscript{2}O (200 mL) at 0 °C. After 15 min, 2-methyl-3-butyn-2-ol (10 mL, 0.103 mol) was added dropwise via an addition funnel. After 1 h, the mixture was warmed to rt and extracted with Et\textsubscript{2}O (3 x 50 mL). The organic phase was dried with MgSO\textsubscript{4}, filtered, concentrated, and purified by column chromatography on silica gel to afford 4-bromo-2-methyl-3-but-3-yn-2-ol in 75% yield. \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 2.51 (br s, 1H), 1.49 (s, 6H). Data consistent with literature.\textsuperscript{17}
Representative procedure: 2-Methyl-6-phenylhexa-3,5-diyn-2-ol

CuCl (23.3 mg, 0.24 mmol) was added to a solution of 30% BuNH₂/H₂O (30 mL). The blue color was quenched by the addition of a spatula of H₂NOH·HCl. Phenylacetylene (2a, 1.29 mL, 11.76 mmol) was added and the reaction mixture was cooled to 0 ºC, becoming a yellow cloudy solution. A solution of 4-bromo-2-methyl-3-but-3-yn-2-ol (2.0 g, 12.35 mmol) in Et₂O (5 mL) was added. Then, a spatula of NH₂(OH)·HCl was added to the reaction mixture. After 5 min, the mixture was warmed to rt and extracted with Et₂O (2 x 25 mL). The organic layer was dried with MgSO₄, filtered, concentrated, and purified by column chromatography on silica gel to afford 2-methyl-6-phenylhexa-3,5-diyn-2-ol (1.93 g, 89%).

2-Methyl-6-phenylhexa-3,5-diyn-2-ol

\[ \text{HO} \quad \text{Me} \quad \text{Me} \quad \text{Me} \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \]

89% yield; ¹H NMR (300 MHz, CDCl₃) δ 7.50-7.47 (m, 2H), 7.37-7.32 (m, 3H), 2.12 (br s, 1H), 1.59 (s, 6H). Data consistent with the literature.¹⁸

6-(3-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol

\[ \text{HO} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \]

71% yield; ¹H NMR (300 MHz, CDCl₃) δ 7.28-7.26 (m, 2H), 7.18-7.14 (m, 1H), 7.10-7.03 (m, 1H), 1.58 (s, 6H). Data consistent with the literature.¹⁸

6-(4-Fluorophenyl)-2-methylhexa-3,5-diyn-2-ol

\[ \text{HO} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \]

80% yield; ¹H NMR (300 MHz, CDCl₃) δ 7.49-7.44 (m, 2H), 7.04-6.98 (m, 2H), 2.06 (br s, 1H), 1.58 (s, 6H). Data consistent with the literature.¹⁹

6-(2-Methoxyphenyl)-2-methylhexa-3,5-diyn-2-ol

\[ \text{HO} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \]

83% yield; ¹H NMR (300 MHz, CDCl₃) δ 7.43 (dd, J = 7.6, 1.7 Hz, 1H), 7.32 (ddd, J = 8.3, 7.6, 1.7 Hz, 1H), 6.92-6.85 (m, 2H), 3.87 (s, 3H), 2.14 (br s, 1H), 1.57 (s, 6H). Data consistent with the literature.²⁰

6-(4-Methoxyphenyl)-2-methylhexa-3,5-diyn-2-ol

\[ \text{HO} \quad \text{Me} \quad \text{Me} \quad \text{Me} \quad \text{Me} \]

78% yield; ¹H NMR (300 MHz, CDCl₃) δ 7.43-7.38 (m, 2H), 6.84-6.79 (m, 2H), 3.79 (s, 3H), 2.60 (br s, 1H), 1.57 (s, 6H). Data consistent with the literature.¹⁹
2-Methyl-6-(thiophen-3-yl)hexa-3,5-diyn-2-ol

\[
\begin{align*}
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{TIPS} \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \\
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{Ph} \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv
\end{align*}
\]

80% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.56 (dd, J = 3.0, 1.2 \text{ Hz}, 1\text{H}), 7.27 (dd, J = 5.0, 3.0 \text{ Hz}, 1\text{H}), 7.13 (dd, J = 5.0, 1.2 \text{ Hz}, 1\text{H}), 2.01 (\text{br s}, 1\text{H}), 1.57 (s, 6\text{H}).\) Data consistent with the literature.\(^{19}\)

2-Methyl-8-phenylocta-3,5-diyn-2-ol

\[
\begin{align*}
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{Ph} \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \\
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{CH}_2\text{CH}_2\text{Ph} \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv
\end{align*}
\]

84% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.35-7.29 (m, 2\text{H}), 7.27-7.20 (m, 3\text{H}), 2.86 (t, J = 7.5 \text{ Hz}, 2\text{H}), 2.59 (t, J = 7.5 \text{ Hz}, 2\text{H}), 2.22 (\text{br s}, 1\text{H}), 1.54 (s, 6\text{H}).\) Data consistent with the literature.\(^{17}\)

11-Chloro-2-methylundeca-3,5-diyn-2-ol

\[
\begin{align*}
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{Cl} \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \\
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{(CH}_2\text{)}_4\text{Cl} \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv
\end{align*}
\]

85% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 3.56 (t, J = 6.5 \text{ Hz}, 2\text{H}), 2.34 (t, J = 6.9 \text{ Hz}, 2\text{H}), 1.93-1.85 (m, 2\text{H}), 1.75-1.65 (m, 2\text{H}), 1.53 (s, 6\text{H}).\)

2-Methyl-6-(triisopropylsilyl)hexa-3,5-diyn-2-ol

\[
\begin{align*}
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{TIPS} \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \\
\text{Me} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \text{CH}_2\text{CH}_2\text{SiMe}_3 \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv
\end{align*}
\]

61% yield; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 1.95 (\text{br s}, 1\text{H}), 1.54 (s, 6\text{H}), 1.08 (s, 21\text{H}).\) Data consistent with the literature.\(^{17}\)

Synthesis of 1,3-diynes 2

A solution of the required diynol (7.71 mmol) in toluene (10 mL) was added to a mixture of K\(_2\)CO\(_3\) (1.07 g, 7.71 mmol) and 18-crown-6 (0.61 g, 2.31 mmol) in toluene (13 mL) under nitrogen atmosphere at room temperature. The reaction mixture was heated at reflux until the reaction was determined to be complete by TLC (1-2 h). Then, the reaction was cooled to room temperature, extracted with EtOAc (2 \(\times\) 50 mL), dried over MgSO\(_4\) and concentrated. The crude oil was purified by column chromatography on silica gel to give the terminal 1,3-diynes 2. The 1,3-diynes were passed through a short plug of alumina and then stored in Et\(_2\)O solution (200 mL) in the freezer. Prior to use they were concentrated via rotary evaporation.

Buta-1,3-diyn-1-ylbenzene (2a)

\[
\begin{align*}
\text{Ph} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad H \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \\
\text{Ph} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad H \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv
\end{align*}
\]

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.54-7.49 (m, 2\text{H}), 7.40-7.28 (m, 3\text{H}), 2.46 (s, 1\text{H}).\) Data consistent with the literature.\(^{17}\)

1-(Buta-1,3-diyn-1-yl)-3-fluorobenzene (2b)

\[
\begin{align*}
\text{Ph} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad H \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv \\
\text{Ph} & \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad H \quad \equiv \quad \equiv \quad \equiv \quad \equiv \quad \equiv
\end{align*}
\]

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.32-7.29 (m, 2\text{H}), 7.23-7.16 (m, 1\text{H}), 7.13-7.06 (m, 1\text{H}), 2.51 (s, 1\text{H}).\)

S-10
1-(Buta-1,3-diyn-1-yl)-4-fluorobenzene (2c)

\[
\text{F} \quad \equiv \equiv \equiv \equiv \equiv \ H
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\) \(\delta 7.53-7.46 \ (m, \ 2H), \ 7.06-6.98 \ (m, \ 2H), \ 2.47 \ (s, \ 1H).\)

1-(Buta-1,3-diyn-1-yl)-2-methoxybenzene (2d)

\[
\text{OMe} \quad \equiv \equiv \equiv \equiv \equiv \ H
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\) \(\delta 7.45 \ (dd, \ J = 7.6, \ 1.7 \ Hz, \ 1H), \ 7.33 \ (ddd, \ J = 8.4, \ 7.5, \ 1.7 \ Hz, \ 1H), \ 6.89 \ (td, \ J = 7.5, \ 1.0 \ Hz, \ 1H), \ 6.87 \ (d, \ J = 8.4 \ Hz, \ 1H), \ 3.87 \ (s, \ 3H), \ 2.52 \ (s, \ 1H). \) Data consistent with the literature.\(^{19}\)

1-(Buta-1,3-diyn-1-yl)-4-methoxybenzene (2e)

\[
\text{MeO} \quad \equiv \equiv \equiv \equiv \equiv \ H
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\) \(\delta 7.47-7.42 \ (m, \ 2H), \ 6.85-6.81 \ (m, \ 2H), \ 3.81 \ (s, \ 3H), \ 2.45 \ (s, \ 1H). \) Data consistent with the literature.\(^{19}\)

3-(Buta-1,3-diyn-1-yl)thiophene (2f)

\[
\text{S} \quad \equiv \equiv \equiv \equiv \equiv \ H
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\) \(\delta 7.60 \ (dd, \ J = 3.0, \ 1.2 \ Hz, \ 1H), \ 7.27 \ (dd, \ J = 5.0, \ 3.0 \ Hz, \ 1H), \ 7.15 \ (dd, \ J = 5.0, \ 1.2 \ Hz, \ 1H), \ 2.46 \ (s, \ 1H).\)

Hexa-3,5-diyn-1-ylbenzene (2g)

\[
\equiv \equiv \equiv \equiv \equiv \equiv \equiv \ H
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\) \(\delta 7.33-7.19 \ (m, \ 5H), \ 2.85 \ (t, \ J = 7.5 \ Hz, \ 2H), \ 2.55 \ (d, \ J = 7.5 \ Hz, \ 2H), \ 1.97 \ (t, \ J = 1.2 \ Hz, \ 1H). \) Data consistent with the literature.\(^{17}\)

9-Chloronona-1,3-diyn (2h)

\[
\text{Cl} \quad \equiv \equiv \equiv \equiv \equiv \equiv \equiv \ H
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\) \(\delta 3.54 \ (t, \ J = 6.4 \ Hz, \ 2H), \ 2.31 \ (td, \ J = 7.0, \ 1.2 \ Hz, \ 2H), \ 1.97 \ (t, \ J = 1.2 \ Hz, \ 1H), \ 1.93-1.84 \ (m, \ 2H), \ 1.77-1.64 \ (m, \ 2H).\)

Buta-1,3-diyn-1-yltriisopropylsilane (2i)

\[
\text{TIPS} \quad \equiv \equiv \equiv \equiv \equiv \equiv \equiv \ H
\]

\(^1\text{H} \text{NMR (300 MHz, CDCl}_3\) \(\delta 2.07 \ (s, \ 1H), \ 1.09 \ (s, \ 21H).\)

Typical procedures and characterization data for compounds 3

**General procedure for the enantioselective conjugate diynylation reaction**

[Cu(CH\(_3\)CN\(_4\)]BF\(_4\) (1.1 mg, 0.0034 mmol) and (R)-L1 (4.1 mg, 0.0034 mmol) were added to a dried round bottom flask which was purged with nitrogen. Toluene (0.2 mL) was added via syringe and the mixture was stirred for 1.5 h at room temperature under nitrogen atmosphere. Then, a solution of \(\alpha,\beta\)-unsaturated trifluoromethyl ketone 1 (0.144 mmol) in toluene (1.0 mL) was added via syringe, followed of triethylamine (2 µL, 0.0144 mmol). The solution was stirred for 10 min at room temperature. Then a solution of 1,3-diyn 2 (0.188 mmol) in toluene (1.0 mL) was added via syringe and the solution
was stirred at room temperature until the reaction was complete (TLC). 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:ethyl acetate mixtures afforded compound 3.

(R)-1,1,1-trifluoro-4,8-diphenylocta-5,7-diyne-2-one (3aa)

Purified by flash chromatography eluting with hexane:ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-PrOH 95:05, 1 mL/min, major enantiomer tᵣ = 4.96 min, minor enantiomer tᵣ = 4.61 min.

[α]D²⁰ = 29.3 (c 1.05, CHCl₃) (93% ee); ¹H NMR (300 MHz, CDCl₃) δ 7.51-7.48 (m, 2H), 7.42-7.29 (m, 8H), 4.41 (dd, J = 7.9, 6.2 Hz, 1H), 3.37 (ddd, J = 18.7, 7.9, 0.5 Hz, 1H), 3.19 (ddd, J = 18.7, 6.2, 0.5 Hz, 1H); ¹³C NMR (75.5 MHz, CDCl₃) δ 188.1 (q, JCF = 36.2 Hz, C), 138.3 (C), 132.6 (2CH), 129.2 (CH), 129.1 (2CH), 128.4 (2CH), 127.9 (CH), 127.4 (2CH), 121.5 (C), 115.3 (q, JCF = 291.8 Hz, CF₃), 82.2 (C), 77.3 (C), 73.5 (C), 68.4 (C), 44.4 (CH₂), 32.6 (CH); ¹⁹F NMR (282 MHz, CDCl₃) δ −79.7 (s, 3F); HRMS (ESI) m/z: 327.0982 (M+ H)⁺, C₂₀H₁₄F₃O requires 327.0997.

(S)-1,1,1-trifluoro-8-phenyl-4-(o-tolyl)octa-5,7-diyne-2-one (3ba)

Purified by flash chromatography eluting with hexane:ethyl acetate (99:01). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralcel OD-H), hexane-PrOH 95:05, 1 mL/min, major enantiomer tᵣ = 16.0 min, minor enantiomer tᵣ = 11.8 min.

[α]D²⁰ = 35.2 (c 1.02, CHCl₃) (94% ee); ¹H NMR (300 MHz, CDCl₃) δ 7.49-7.45 (m, 3H), 7.36-7.31 (m, 3H), 7.25-7.19 (m, 3H), 4.59 (dd, J = 8.7, 5.4 Hz, 1H), 3.37 (ddd, J = 18.7, 8.7, 0.5 Hz, 1H), 3.16 (ddd, J = 18.7, 5.4, 0.5 Hz, 1H), 2.42 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 188.7 (q, JCF = 36.2 Hz, C), 136.8 (C), 135.5 (C), 133.0 (2CH), 131.5 (CH), 129.6 (CH), 128.3 (2CH), 127.5 (CH), 127.3 (CH), 121.9 (C), 115.7 (q, JCF = 291.6 Hz, CF₃), 82.8 (C), 77.9 (C), 74.0 (C), 68.3 (C), 43.4 (CH₂), 29.4 (CH), 19.7 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ −79.6 (s, 3F); HRMS (ESI) m/z: 341.1160 (M+ H)⁺, C₂₁H₁₆F₃O requires 341.1153.
(S)-1,1,1-trifluoro-8-phenyl-4-(m-tolyl)octa-5,7-diyn-2-one (3ca)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.1 min, minor enantiomer t_r = 4.6 min.

[α]_D<sup>20</sup> = −18.9 (c 1.00, CHCl_3) (93% ee); <sup>1</sup>H NMR (300 MHz, CDCl_3) δ 7.50-7.47 (m, 2H), 7.36-7.31 (m, 3H), 7.23-7.11 (m, 4H), 4.37 (dd, J = 8.0, 6.0 Hz, 1H), 3.36 (ddd, J = 18.7, 6.1, 0.5 Hz, 1H), 2.38 (s, 3H); <sup>13</sup>C NMR (75.5 MHz, CDCl_3) δ 188.1 (q, J_C-F = 36.4 Hz, C), 138.9 (C), 138.2 (C), 132.6 (2CH), 129.2 (CH), 128.8 (CH), 128.4 (2CH), 128.0 (CH), 124.4 (CH), 121.5 (C), 115.3 (q, J_C-F = 291.9 Hz, CF_3), 82.3 (C), 77.2 (C), 73.6 (C), 68.3 (C), 44.4 (CH_2), 32.5 (CH_2), 21.4 (CH_2); <sup>19</sup>F NMR (282 MHz, CDCl_3) δ −79.7 (s, 3F); HRMS (ESI) m/z: 341.1164 (M+ H)<sup>+</sup>, C_21H_16F_3O requires 341.1153.

(R)-1,1,1-trifluoro-8-phenyl-4-(p-tolyl)octa-5,7-diyn-2-one (3da)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.4 min, minor enantiomer t_r = 4.9 min.

[α]_D<sup>20</sup> = −25.8 (c 0.84, CHCl_3) (92% ee); <sup>1</sup>H NMR (300 MHz, CDCl_3) δ 7.50-7.47 (m, 2H), 7.36-7.26 (m, 5H), 7.19-7.16 (m, 2H), 4.37 (dd, J = 7.7, 6.4 Hz, 1H), 3.35 (ddd, J = 18.7, 7.7, 0.5 Hz, 1H), 3.17 (ddd, J = 18.7, 6.4, 0.5 Hz, 1H), 2.35 (s, 3H); <sup>13</sup>C NMR (75.5 MHz, CDCl_3) δ 188.1 (q, J_C-F = 36.2 Hz, C), 137.7 (C), 135.3 (C), 132.6 (2CH), 129.7 (2CH), 129.2 (CH), 128.4 (2CH), 127.2 (2CH), 121.5 (C), 115.3 (q, J_C-F = 291.8 Hz, CF_3), 82.5 (C), 77.2 (C), 73.6 (C), 68.3 (C), 44.4 (CH_2), 32.2 (CH), 21.0 (CH_2); <sup>19</sup>F NMR (282 MHz, CDCl_3) δ −79.7 (s, 3F); HRMS (ESI) m/z: 341.1150 (M+ H)<sup>+</sup>, C_21H_16F_3O requires 341.1153.

(S)-4-(2-bromophenyl)-1,1,1-trifluoro-8-phenylocta-5,7-diyn-2-one (3ea)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AS-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer t_r = 5.2 min, minor enantiomer t_r = 4.8 min.

[α]_D<sup>20</sup> = −95.3 (c 0.55, CHCl_3) (94% ee); <sup>1</sup>H NMR (300 MHz, CDCl_3) δ 7.71 (dd, J = 7.8, 1.7 Hz, 1H), 7.58 (dd, J = 7.9, 1.2 Hz, 1H), 7.52-7.48 (m, 2H), 7.39-7.32 (m, 4H), 7.22-7.16 (m, 1H), 4.85 (dd, J = 7.8, 5.8 Hz, 1H), 3.25 (m, 1H), 3.23 (s, 1H); <sup>13</sup>C NMR (75.5 MHz, CDCl_3) δ 188.2 (q, J_C-F = 36.4 Hz, C), 137.7 (C), 133.7 (CH), 133.0 (2CH),...
130.0 (CH), 129.9 (CH), 129.7 (CH), 128.8 (2CH), 128.6 (CH), 123.3 (C), 121.8 (C), 115.7 (q, $J_{C-F} = 291.7$ Hz, CF$_3$), 81.4 (C), 77.8 (C), 73.9 (C), 69.5 (C), 43.2 (CH$_2$), 33.1 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ $-79.5$ (s, 3F); HRMS (ESI) $m/z$: 405.0096/407.0075 (M+ H)$^+$ 98.8/100.0, C$_{20}$H$_{13}$BrF$_3$O requires 405.0102/407.0081.

**(R)-4-(4-bromophenyl)-1,1,1-trifluoro-8-phenylocta-5,7-diyn-2-one (3fa)**

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-$^3$PrOH 99:01, 1 mL/min, major enantiomer $t_r = 7.5$ min, minor enantiomer $t_r = 6.9$ min.

$[\alpha]_D^{20} - 19.9$ (c 0.78, CHCl$_3$) (92% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.51-7.47 (m, 4H), 7.37-7.27 (m, 5H), 4.37 (t, $J = 7.0$ Hz, 1H), 3.35 (ddd, $J = 18.8$, 7.5, 0.4 Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 187.8 (q, $J_{C-F} = 36.6$ Hz, C), 137.3 (C), 132.6 (2CH), 132.2 (2CH), 129.3 (CH), 129.1 (2CH), 128.4 (2CH), 121.9 (C), 121.3 (C), 115.2 (q, $J_{C-F} = 291.6$ Hz, CF$_3$), 81.4 (C), 77.6 (C), 73.3 (C), 68.8 (C), 44.2 (CH$_2$), 32.1 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ $-79.7$ (s, 3F); HRMS (ESI) $m/z$: 405.0099/407.0078 (M+ H)$^+$ 98.8/100.0, C$_{20}$H$_{13}$BrF$_3$O requires 405.0102/407.0081.

**(S)-1,1,1-trifluoro-4-(2-methoxyphenyl)-8-phenylocta-5,7-diyn-2-one (3ga)**

Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AS-H), hexane-$^3$PrOH 95:05, 1 mL/min, major enantiomer $t_r = 4.8$ min, minor enantiomer $t_r = 4.6$ min.

$[\alpha]_D^{20} - 23.5$ (c 1.01, CHCl$_3$) (94% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.58 (dd, $J = 7.6$, 1.7 Hz, 1H), 7.51-7.48 (m, 2H), 7.36-7.27 (m, 4H), 7.01 (td, $J = 7.5$, 1.1 Hz, 1H), 6.89 (dd, $J = 8.3$, 0.9 Hz, 1H), 4.75 (dd, $J = 7.8$, 5.7 Hz, 1H), 3.85 (s, 3H), 3.21 (dd, $J = 6.6$, 2.5 Hz, 2H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.5 (q, $J_{C-F} = 35.6$ Hz, C), 156.9 (C), 132.6 (2CH), 129.1 (CH), 128.7 (CH), 128.4 (2CH), 126.1 (C), 121.7 (C), 121.0 (CH), 115.4 (q, $J_{C-F} = 292.1$ Hz, CF$_3$), 110.6 (CH), 82.4 (C), 76.6 (C), 73.8 (C), 68.1 (C), 55.4 (CH$_3$), 42.6 (CH$_2$), 27.4 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ $-79.7$ (s, 3F); HRMS (ESI) $m/z$: 357.1107 (M+ H)$^+$, C$_{21}$H$_{16}$F$_3$O$_2$ requires 357.1102.
(R)-1,1,1-trifluoro-4-(4-methoxyphenyl)-8-phenylocta-5,7-diyn-2-one (3ha)

Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer $t_r = 9.6$ min, minor enantiomer $t_r = 8.3$ min.

$[\alpha]_D^{20} = -31.6$ (c 0.70, CHCl$_3$) (92% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.48 (dd, $J = 7.9, 1.7$ Hz, 2H), 7.36-7.26 (m, 5H), 6.92-6.87 (m, 2H), 4.38-4.31 (m, 1H), 3.80 (s, 3H), 3.33 (ddd, $J = 18.6, 7.6, 0.5$ Hz, 1H), 3.20-3.12 (m, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.2 (q, $J_{C-F} = 36.4$ Hz, C), 159.2 (C), 132.5 (2CH), 130.3 (C), 129.2 (CH), 128.5 (2CH), 128.4 (2CH), 121.5 (C), 115.2 (q, $J_{C-F} = 297.6$ Hz, CF$_3$), 114.4 (2CH), 82.5 (C), 77.2 (C), 73.5 (C), 68.2 (C), 55.3 (CH$_3$), 44.5 (CH$_2$), 31.8 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ $-79.8$ (s, 3F); HRMS (ESI) $m/z$: 357.1112 (M+ H)$^+$, C$_{21}$H$_{16}$F$_3$O$_2$ requires 357.1102.

(R)-1,1,1-trifluoro-4-(naphthalene-2-yl)-8-phenylocta-5,7-diyn-2-one (3ia)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer $t_r = 8.3$ min, minor enantiomer $t_r = 7.3$ min.

$[\alpha]_D^{20} = -38.8$ (c 1.00, CHCl$_3$) (92% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.88-7.83 (m, 4H), 7.54-7.48 (m, 5H), 7.37-7.29 (m, 3H), 4.59 (dd, $J = 7.8, 6.2$ Hz, 1H), 3.45 (dd, $J = 18.4, 7.8$ Hz, 1H), 3.29 (dd, $J = 18.4, 6.2$ Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.1 (q, $J_{C-F} = 36.4$ Hz, C), 135.5 (C), 133.4 (C), 132.8 (C), 132.6 (2CH), 129.3 (CH), 129.1 (CH), 128.4 (2CH), 127.9 (CH), 127.7 (CH), 126.6 (CH), 126.4 (CH), 126.3 (CH), 125.0 (CH), 121.5 (C), 115.3 (q, $J_{C-F} = 291.9$ Hz, CF$_3$), 82.1 (C), 77.4 (C), 73.5 (C), 68.7 (C), 44.3 (CH$_2$), 32.7 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ $-79.7$ (s, 3F); HRMS (ESI) $m/z$: 377.1158 (M+ H)$^+$, C$_{24}$H$_{16}$F$_3$O requires 377.1153.

(S)-1,1,1-trifluoro-4-phenethyl-8-phenylocta-5,7-diyn-2-one (3ja)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (84%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer $t_r = 5.1$ min, minor enantiomer $t_r = 4.8$ min.

$[\alpha]_D^{20} = -44.5$ (c 0.44, CHCl$_3$) (84% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.52-7.49 (m, 2H), 7.37-7.29 (m, 5H), 7.24-7.21 (m, 3H), 3.15-3.02 (m, 2H), 2.95-2.73 (m, 3H), 1.91-1.83 (m, 2H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.6 (q, $J_{C-F} = 36.1$ Hz, C), 140.6 (C), 5-15.
132.6 (2CH), 129.2 (CH), 128.6 (2CH), 128.5 (2CH), 128.4 (2CH), 121.6 (C), 115.3 (q, $J_{C-F} = 292.0$ Hz, CF$_3$), 83.5 (C), 77.2 (C), 73.6 (C), 67.7 (C), 41.4 (CH$_2$), 35.8 (CH$_2$), 33.3 (CH), 26.5 (CH$_2$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −79.8 (s, 3F); HRMS (ESI) $m/z$: 355.1329 (M+ H$^+$), C$_{22}$H$_{18}$F$_3$O requires 355.1310.

(S)-4-Butyl-1,1,1-trifluoro-8-phenylocta-5,7-diyn-2-one (3ka)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (87%) was determined by chiral HPLC (Chiralcel OD-H), hexane-$^t$PrOH 99:01, 1 mL/min, major enantiomer $t_r = 14.0$ min, minor enantiomer $t_r = 9.5$ min.

$[\alpha]_D^{20} = 3.8$ (c 0.63, CHCl$_3$) (87% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.50-7.46 (m, 2H), 7.36-7.28 (m, 3H), 3.15-3.00 (m, 2H), 2.88 (dd, $J = 18.3$, 6.0 Hz, 1H), 1.55-1.49 (m, 2H), 1.43-1.34 (m, 4H), 0.93 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 188.9 (q, $J_{C-F} = 35.8$ Hz, C), 132.5 (2CH), 129.1 (CH), 128.4 (2CH), 121.7 (C), 115.4 (q, $J_{C-F} = 291.9$ Hz, CF$_3$), 84.2 (C), 76.3 (C), 73.7 (C), 67.0 (C), 41.5 (CH$_2$), 33.9 (CH$_2$), 29.2 (CH), 26.9 (CH$_2$), 22.3 (CH$_2$)13.9 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −79.8 (s, 3F); HRMS (ESI) $m/z$: 307.1312 (M+ H$^+$), C$_{18}$H$_{18}$F$_3$O requires 307.1310.

(S)-1,1,1-Trifluoro-4-isobutyl-8-phenylocta-5,7-diyn-2-one (3la)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (88%) was determined by chiral HPLC (Chiralcel OD-H), hexane-$^t$PrOH 99:01, 1 mL/min, major enantiomer $t_r = 10.9$ min, minor enantiomer $t_r = 9.1$ min.

$[\alpha]_D^{20} = 5.6$ (c 0.51, CHCl$_3$) (88% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.50-7.46 (m, 2H), 7.36-7.28 (m, 3H), 3.15-3.00 (m, 2H), 2.88 (dd, $J = 18.3$, 6.0 Hz, 1H), 1.55-1.49 (m, 2H), 1.43-1.34 (m, 4H), 0.93 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.8 (q, $J_{C-F} = 35.9$ Hz, C), 132.5 (2CH), 129.1 (CH), 128.4 (2CH), 121.7 (C), 115.3 (q, $J_{C-F} = 291.9$ Hz, CF$_3$), 84.0 (C), 76.3 (C), 73.7 (C), 67.0 (C), 43.3 (CH$_2$), 41.9 (CH$_2$), 26.1 (CH), 25.2 (CH), 23.2 (CH$_3$), 21.2 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −79.8 (s, 3F); HRMS (ESI) $m/z$: 307.1317 (M+ H$^+$), C$_{18}$H$_{18}$F$_3$O requires 307.1310.

(R)-1,1,1-trifluoro-8-(3-fluorophenyl)-4-phenylocta-5,7-diyn-2-one (3ab)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (90%) was determined by chiral HPLC (Chiralpak AS-H), hexane-$^t$PrOH 99:01, 1 mL/min, major enantiomer $t_r = 5.9$ min, minor enantiomer $t_r = 5.3$ min.
$[\alpha]_{D}^{20} -15.7$ (c 0.60, CHCl$_3$) (90% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.42-7.26 (m, 7H), 7.19-7.15 (m, 1H), 7.10-7.06 (m, 1H), 4.41 (dd, J = 7.9, 6.1 Hz, 1H), 3.37 (ddd, J = 18.7, 8.0, 0.5 Hz, 1H), 3.18 (dd, J = 18.7, 6.1 Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.0 (q, J$_{C-F}$ = 36.3 Hz, C), 162.2 (d, J$_{C-F}$ = 247.3 Hz, C), 138.1 (C), 130.1 (d, J = 8.5 Hz, CH), 129.1 (2CH), 128.5 (d, J = 3.2 Hz, CH), 128.0 (CH), 127.4 (2CH), 123.4 (d, J = 9.5 Hz, C), 119.3 (d, J = 22.9 Hz, CH), 116.8 (d, J$_{C-F}$ = 21.3 Hz, CH), 115.3 (q, J = 291.7 Hz, CF$_3$), 82.9 (C), 77.5 (C), 75.8 (q, J$_{C-F}$ = 3.4 Hz, C), 68.1 (C), 44.4 (CH$_2$), 32.6 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −79.7 (s, 3F), −112.8 (s, 1F); HRMS (ESI) m/z: 345.0910 (M+ H)$^+$, C$_{20}$H$_{13}$F$_4$O requires 345.0903.

(R)-1,1,1-trifluoro-8-(4-fluorophenyl)-4-phenylocta-5,7-diyn-2-one (3ac)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer $t_r$ = 8.9 min, minor enantiomer $t_r$ = 6.5 min.

$[\alpha]_{D}^{20} -14.5$ (c 0.67, CHCl$_3$) (92% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.49-7.45 (m, 2H), 7.41-7.29 (m, 5H), 7.04-6.98 (m, 2H), 4.40 (dd, J = 8.0, 6.1 Hz, 1H), 3.36 (ddd, J = 18.7, 8.0 Hz, 1H), 3.18 (dd, J = 18.7, 6.1 Hz, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.0 (q, J$_{C-F}$ = 36.4 Hz, C), 163.0 (d, J$_{C-F}$ = 251.6 Hz, C), 138.2 (C), 134.6 (d, J$_{C-F}$ = 8.5 Hz, 2CH), 129.1 (2CH), 128.0 (CH), 127.4 (2CH), 115.9 (d, J = 3.7 Hz, C), 115.3 (d, J$_{C-F}$ = 22.3 Hz, 2CH), 115.3 (q, J$_{C-F}$ = 291.8 Hz, CF$_3$), 82.2 (C), 76.2 (C), 73.3 (C), 68.3 (C), 44.4 (CH$_2$), 32.6 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −79.7 (s, 3F), −109.0 (s, 1F); HRMS (ESI) m/z: 345.0913 (M+ H)$^+$, C$_{20}$H$_{13}$F$_4$O requires 345.0903.

(R)-1,1,1-trifluoro-8-(2-methoxyphenyl)-4-phenylocta-5,7-diyn-2-one (3ad)

Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralpak AS-H), hexane-PrOH 95:05, 1 mL/min, major enantiomer $t_r$ = 6.6 min, minor enantiomer $t_r$ = 6.3 min.

$[\alpha]_{D}^{20} -17.0$ (c 0.91, CHCl$_3$) (92% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.46-7.29 (m, 7H), 6.90 (dd, J = 7.5, 1.0 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 4.41 (dd, J = 7.7, 6.3 Hz, 1H), 3.88 (s, 3H), 3.41-3.32 (m, 1H), 3.23-3.14 (m, 1H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 188.0 (q, J$_{C-F}$ = 36.4 Hz, C), 161.5 (C), 138.4 (C), 134.5 (CH), 130.7 (CH), 129.0 (2CH), 127.9 (CH), 127.4 (2CH), 120.5 (CH), 115.3 (q, J$_{C-F}$ = 291.8 Hz, CF$_3$), 110.7 (CH), 110.6 (CH), 82.7 (C), 77.3 (C), 73.8 (C), 68.7 (C), 55.8 (CH$_3$), 44.4 (CH$_2$), 32.6 (CH); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ −79.7 (s, 3F); HRMS (ESI) m/z: 357.1109 (M+ H)$^+$, C$_{21}$H$_{14}$F$_3$O$_2$ requires 357.1102.
(R)-1,1,1-trifluoro-8-(4-methoxyphenyl)-4-phenylocta-5,7-diyn-2-one (3ae)

Purified by flash chromatography eluting with hexane-ethyl acetate (95:05). Enantiomeric excess (91%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 80.20, 1 mL/min, major enantiomer t<sub>r</sub> = 11.7 min, minor enantiomer t<sub>r</sub> = 8.0 min.

[α]<sub>D</sub><sup>20</sup> = −32.7 (c 0.75, CHCl<sub>3</sub>) (91% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.44-7.30 (m, 7H), 6.86-6.81 (m, 2H), 4.40 (dd, J = 7.9, 6.2 Hz, 1H), 3.81 (s, 3H), 3.36 (ddd, J = 18.6, 7.9, 0.5 Hz, 1H), 3.18 (ddd, J = 18.6, 6.2, 0.5 Hz, 1H); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 188.1 (q, J<sub>CF</sub> = 36.7 Hz, C), 160.4 (C), 138.5 (C), 134.2 (2CH), 129.0 (2CH), 127.9 (CH), 127.4 (2CH), 115.3 (q, J<sub>CF</sub> = 291.6 Hz, CF<sub>3</sub>), 114.1 (2CH), 113.4 (C), 81.6 (C), 77.5 (C), 72.4 (C), 68.7 (C), 55.3 (CH<sub>3</sub>), 44.5 (CH<sub>2</sub>), 32.6 (CH); <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ −79.8 (s, 3F); HRMS (ESI) m/z: 357.1115 (M+ H)<sup>+</sup>, C<sub>21</sub>H<sub>16</sub>F<sub>3</sub>O<sub>2</sub> requires 357.1102.

(R)-1,1,1-trifluoro-4-phenyl-8-(thiophen-3-yl)octa-5,7-diyn-2-one (3af)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (94%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer t<sub>r</sub> = 8.4 min, minor enantiomer t<sub>r</sub> = 7.1 min.

[α]<sub>D</sub><sup>20</sup> = −26.6 (c 0.86, CHCl<sub>3</sub>) (94% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.56 (dd, J = 3.0, 1.2 Hz, 1H), 7.41-7.25 (m, 5H), 7.26 (dd, J = 5.0, 3.0 Hz, 1H), 7.13 (dd, J = 5.0, 1.2 Hz, 1H), 4.40 (dd, J = 7.9, 1.6 Hz, 1H), 3.36 (ddd, J = 18.6, 7.9, 0.5 Hz, 1H), 3.18 (ddd, J = 18.6, 6.1, 0.5 Hz, 1H); <sup>13</sup>C NMR (75.5 MHz, CDCl<sub>3</sub>) δ 188.0 (q, J = 36.7 Hz, C), 131.4 (CH), 130.2 (CH), 129.1 (2CH), 127.9 (CH), 127.4 (2CH), 125.6 (CH), 120.6 (C), 115.3 (q, J = 291.7 Hz, CF<sub>3</sub>), 82.0 (C), 73.2 (C), 72.5 (C), 68.4 (C), 44.4 (CH<sub>2</sub>), 32.6 (CH); <sup>19</sup>F NMR (282 MHz, CDCl<sub>3</sub>) δ −79.8 (s, 3F); HRMS (ESI) m/z: 333.0569 (M+ H)<sup>+</sup>, C<sub>18</sub>H<sub>12</sub>F<sub>3</sub>OS requires 333.0561.

(R)-1,1,1-trifluoro-4,10-diphenyldeca-5,7-diyn-2-one (3ag)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer t<sub>r</sub> = 6.4 min, minor enantiomer t<sub>r</sub> = 5.7 min.

[α]<sub>D</sub><sup>20</sup> = −14.2 (c 0.90, CHCl<sub>3</sub>) (93% ee); <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ 7.37-7.19 (m, 10H), 4.31 (dd, J = 7.6, 6.5 Hz, 1H), 3.31 (ddd, J = 18.6, 7.9, 0.5 Hz, 1H), 3.13 (ddd, J = 18.6, 6.2, 0.4 Hz, 1H), 2.85 (t, J = 7.5 Hz, 2H), 2.57 (t, J = 7.5 Hz, 2H); <sup>13</sup>C NMR
(75.5 MHz, CDCl₃) δ 188.1 (q, J_C-F = 36.3 Hz, C), 140.0 (C), 138.5 (C), 129.0 (2CH), 128.5 (2CH), 128.3 (2CH), 127.8 (CH), 127.3 (2CH), 126.5 (CH), 115.2 (q, J_C-F = 291.6 Hz, CF₃), 79.3 (C), 75.6 (C), 68.7 (C), 65.3 (C), 44.5 (CH₂), 34.5 (CH₂), 32.3 (CH), 21.4 (CH₂); ¹⁹F NMR (282 MHz, CDCl₃) δ −79.8 (s, 3F); HRMS (ESI) m/z: 355.1317 (M+ H)⁺, C₂₂H₁₈F₃O requires 355.1310.

(S)-1,1,1-trifluoro-10-phenyl-4-(o-tolyl)deca-5,7-diyn-2-one (3bg)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (95%) was determined by chiral HPLC (Chiralpak AS-H), hexane-PrOH 99:01, 1 mL/min, major enantiomer tᵣ = 5.4 min, minor enantiomer tᵣ = 5.1 min.

[α]D²⁰ −6.1 (c 1.15, CHCl₃) (95% ee); ¹H NMR (300 MHz, CDCl₃) δ 7.43-7.41 (m, 1H), 7.33-7.17 (m, 8H), 4.49 (dd, J = 8.7, 5.4 Hz, 1H), 3.30 (dd, J = 18.5, 8.7 Hz, 1H), 3.09 (dd, J = 18.5, 5.4 Hz, 1H), 2.84 (t, J = 7.5 Hz, 2H), 2.55 (t, J = 7.5 Hz, 2H), 2.38 (s, 3H); ¹³C NMR (75.5 MHz, CDCl₃) δ 188.3 (q, J_C-F = 36.5 Hz, C), 140.0 (C), 136.6 (C), 135.0 (C), 131.0 (CH), 128.5 (2CH), 128.3 (2CH), 127.8 (CH), 127.1 (CH), 126.8 (CH), 126.5 (CH), 115.3 (q, J_C-F = 291.9 Hz, CF₃), 79.0 (C), 75.8 (C), 68.1 (C), 65.4 (C), 43.0 (CH₂), 34.5 (CH₂), 28.7 (CH), 21.4 (CH₂), 19.2 (CH₃); ¹⁹F NMR (282 MHz, CDCl₃) δ −79.7 (s, 3F); HRMS (ESI) m/z: 369.1470 (M+ H)⁺, C₂₃H₂₀F₃O requires 369.1466.
(R)-12-chloro-1,1,1-trifluoro-4-phenylundeca-5,7-diyn-2-one (3ah)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (93%) was determined by chiral HPLC (Chiralpak AS-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer \( t_r = 7.5 \) min, minor

\[ [\alpha]_D^{20} -11.7 \ (c \ 0.89, \ CHCl_3) \ (93\% \ ee); \]
\[ ^1H \ NMR \ (300 \ MHz, \ CDCl_3) \ \delta \ 7.38-7.26 \ (m, 5H), \ 4.30 \ (dd, \ J = 7.5, 6.5 Hz, 1H), \ 3.55 \ (t, \ J = 6.4 Hz, 2H), \ 3.30 \ (ddd, \ J = 18.6, 7.9, 0.5 Hz, 1H), \ 3.12 \ (ddd, \ J = 18.6, 6.9, 0.5 Hz, 1H), \ 2.33 \ (td, \ J = 6.9, 1.0 Hz, 1H), \ 1.94-1.84 \ (m, 2H), \ 1.74-1.64 \ (m, 2H); \]
\[ ^13C \ NMR \ (75.5 \ MHz, \ CDCl_3) \ \delta \ 188.1 \ (q, \ J_{CF} = 36.2 \ Hz, \ C), \ 138.5 \ (C), \ 129.0 \ (2CH), \ 127.8 \ (CH), \ 127.3 \ (2CH), \ 115.2 \ (q, \ J_{CF} = 291.8 \ Hz, \ CF_3), \ 79.2 \ (C), \ 75.5 \ (C), \ 68.6 \ (C), \ 65.3 \ (C), \ 44.5 \ (CH_2), \ 44.3 \ (CH_2), \ 32.2 \ (CH), \ 31.4 \ (CH_2), \ 25.3 \ (CH_2), \ 18.5 \ (CH_2); \]
\[ ^19F \ NMR \ (282 \ MHz, \ CDCl_3) \ \delta \ -79.8 \ (s, 3F); \]
HRMS (ESI) \( m/z: \)
341.0930/343.0899 \( (M+H)^+ \) 100.0/31.7, \( \text{C}_{18}\text{H}_{17}\text{ClF}_3\text{O} \) requires 341.0920/343.0891.

(R)-1,1,1-trifluoro-4-phenyl-(triisopropylsilyl)octa-5,7-diyn-2-one (3ai)

Purified by flash chromatography eluting with hexane-ethyl acetate (99:01). Enantiomeric excess (85%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer \( t_r = 8.6 \) min, minor

\[ [\alpha]_D^{20} -14.5 \ (c \ 0.77, \ CHCl_3) \ (85\% \ ee); \]
\[ ^1H \ NMR \ (300 \ MHz, \ CDCl_3) \ \delta \ 7.37-7.29 \ (m, 5H), \ 4.33 \ (t, \ J = 6.0 \ Hz, 1H), \ 3.34 \ (ddd, \ J = 18.8, 7.5, 0.5 \ Hz, 1H), \ 3.16 \ (ddd, \ J = 18.8, 6.5, 0.5 \ Hz, 1H), \ 1.08 \ (s, 21H); \]
\[ ^13C \ NMR \ (75.5 \ MHz, \ CDCl_3) \ \delta \ 188.0 \ (q, \ J_{CF} = 36.3 \ Hz, \ C), \ 138.2 \ (C), \ 129.0 \ (2CH), \ 127.9 \ (CH), \ 127.4 \ (2CH), \ 115.2 \ (q, \ J_{CF} = 291.9 \ Hz, \ CF_3), \ 89.1 \ (C), \ 83.3 \ (C), \ 76.3 \ (C), \ 69.0 \ (C), \ 44.3 \ (CH_2), \ 32.2 \ (CH), \ 18.5 \ (6CH_3), \ 11.2 \ (3CH); \]
\[ ^19F \ NMR \ (282 \ MHz, \ CDCl_3) \ \delta \ -79.8 \ (s, 3F); \]
HRMS (ESI) \( m/z: \)
407.2024 \( (M+H)^+ \), \( \text{C}_{23}\text{H}_{30}\text{ClF}_3\text{OSi} \) requires 407.2018.
Synthetic transformations of compounds 3

(R)-1,1,1-trifluoro-4,8-diphenyloctan-2-one (4)

A solution of compound 3aa (10 mg, 0.031 mmol, 93% ee) in EtOAc (0.4 mL) was stirred under hydrogen atmosphere in the presence of 10% Pd/C (3 mg) for 30 min at room temperature. Then, the reaction mixture was filtered through a short pad of silica gel, which was washed with EtOAc, and the solvent was removed under reduced pressure. Purification by flash chromatography on silica gel eluting with hexane:EtOAc (99:01) gave compound 4 (9.2 mg, 89%). Enantiomeric excess (92%) was determined by chiral HPLC, Chiralcel OD-H, hexane-IPA 99:01, 1mL/min, major enantiomer t_r = 10.8 min, minor enantiomer t_r = 7.6 min. 

[α]_D^20 = -2.3 (c 0.78, CHCl_3) (92% ee); ^1H NMR (300 MHz, CDCl_3) δ 7.33-7.21 (m, 5H), 7.20-7.09 (m, 5H), 3.26-3.16 (m, 1H), 3.02-2.99 (m, 2H), 2.56-2.50 (m, 2H), 1.70-1.48 (m, 4H), 1.28-1.17 (m, 2H); ^13C NMR (75.5 MHz, CDCl_3) δ 190.2 (q, J_C-F = 35.1 Hz, C), 143.0 (C), 142.4 (C), 128.7 (2CH), 128.3 (2CH), 128.3 (2CH), 127.3 (2CH), 126.8 (CH), 125.7 (CH), 115.4 (q, J_C-F = 292.2 Hz, CF_3), 43.5 (CH_2), 39.7 (CH), 35.9 (CH_2), 35.6 (CH_2), 31.2 (CH_2), 26.8 (CH_2); ^19F NMR (282 MHz, CDCl_3) δ −80.0 (s, 3F); HRMS (ESI) m/z: 335.1631 (M+ H)^+ , C_{20}H_{22}F_3O requires 335.1623.

(4R)-1,1,1-trifluoro-2-methyl-4,8-diphenylocta-5,7-diyne-2-ol (5)

A commercial 3 M solution of MeMgCl in THF (77 µL, 0.230 mmol) was diluted with diethyl ether (0.3 mL) and cooled to 0 ºC under nitrogen. A solution of compound 3aa (50 mg, 0.153 mmol) in dry diethyl ether (0.5 mL) was added dropwise via syringe and the reaction mixture was allowed to reach room temperature. After 2 h, the reaction was quenched with a solution of citric acid (1 mL). The aqueous layer was extracted with diethyl ether (3 x 15 mL) and the organic layer was dried over MgSO_4. Removal of the solvent under reduced pressure followed by flash chromatography eluting with hexane:EtOAc (99:01) gave 5 (40.8 mg, 78%) as a ca. 4.5:1 mixture of two diastereomeric alcohols. Enantiomeric excess (91%) was determined by chiral HPLC, Chiralpak AY-H, hexane-IPA 99:01, 1 mL/min, major diastereomer: major enantiomer t_r = 23.2 min, minor enantiomer t_r = 16.1 min.

Major (1S,4R)-diastereomer: ^1H NMR (300 MHz, CDCl_3) δ 7.50-7.45 (m, 2H), 7.39-7.31 (m, 8H), 4.04 (dd, J = 9.8, 4.9 Hz, 1H), 2.53 (s, OH), 2.38 (dd, J = 14.5, 9.8 Hz, 1H), 2.10 (dd, J = 14.5, 4.9 Hz, 1H), 1.46 (s, 3H); ^13C NMR (75.5 MHz, CDCl_3) δ 140.2 (C), 132.5 (2CH), 129.2 (CH), 129.1 (2CH), 128.4 (2CH), 127.6 (CH), 127.4 (2CH), 121.5 (C), 84.1 (C), 77.2 (C), 73.7 (q, J_C-F = 28.5 Hz, C), 73.5 (C), 69.1 (C), 42.6 (CH_2), 33.3 (CH), 20.3 (CH_3); ^19F NMR (282 MHz, CDCl_3) δ −84.0 (s, 3F).
Minor (1R,4R)-diastereomer (representative peaks taken from the diastereomeric mixture): $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 4.13 (dd, $J$ = 9.8, 4.3 Hz, 1H), 2.54 (s, 1H), 2.23-2.17 (m, 2H), 1.58 (s, 3H); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –83.1 (s, 3F).

(2S,4R,Z)-2-methyl-4-phenyl-5-(3-phenylpro-2-yn-1-ylidene)-2-(trifluoromethyl)tetrahydrofuran (6)

AgOTf (10.0 mg, 0.038 mmol) was added to a solution of the diastereomeric mixture of 5 (26 mg, 0.076 mmol) in THF (0.5 mL) at rt under nitrogen atmosphere and the mixtures was stirred overnight. Then, removal of the solvent under reduced pressure followed by flash chromatography eluting with hexane:EtOAc (99:01) allowed to obtain furan 6 as the major product (15.6 mg, 60%). Enantiomeric excess (92%) was determined by chiral HPLC (Chiralcel OD-H), hexane-iPrOH 99:01, 1 mL/min, major enantiomer $t_r$ = 13.3 min, minor enantiomer $t_r$ = 27.4 min. The cyclization product resulting from the minor diastereomer of 5 could not be obtained pure in sufficient amount.

$[\alpha]_D^{20}$ –5.9 (c1.00, CHCl$_3$) (92% ee); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.43-7.25 (m, 10H), 4.30 (d, $J$ = 2.2 Hz, 1H), 4.18 (dddd, $J$ = 11.5, 9.3, 2.2 Hz, 1H), 2.50 (dd, $J$ = 12.9, 11.5 Hz, 1H), 2.40 (dd, $J$ = 12.9, 9.3 Hz, 1H), 1.63 (s, 3H); $^{13}$C NMR (75.5 MHz, CDCl$_3$) $\delta$ 168.5 (C), 138.5 (C), 131.3 (2CH), 129.0 (2CH), 128.5 (2CH), 128.1 (2CH), 127.8 (CH), 127.5 (CH), 125.2 (q, $J_{C-F}$ = 254.4 Hz, CF$_3$), 124.1 (C), 93.1 (C), 84.8 (C), 84.2 (C), 81.0 (CH), 47.3 (CH), 40.0 (CH$_2$), 20.3 (CH$_3$); $^{19}$F NMR (282 MHz, CDCl$_3$) $\delta$ –82.2 (s, 3F); HRMS (ESI) $m/z$: 343.1300 (M+ H)$^+$, C$_{21}$H$_{18}$F$_3$O requires 343.1310.

The stereochemistry of compound 6 was determined by NOESY experiments (See figure S1 and NOESY experiment in the NMR spectra section). A relevant interaction was observed between the CH$_3$ group at C2 ($\delta$ 1.63) and H4 ($\delta$ 4.18) which indicated the **trans** disposition between the Me group at C2 and the phenyl group at C4. NOE was also observed between one of the hydrogens of the phenyl group at C4 ($\delta$ 7.30) and the olefinic hydrogen H1’ ($\delta$ 4.30) which indicated the Z geometry of the exocyclic double bond. Other spatial interactions detected in the NOESY experiment are shown in figure S1.

The cyclization product resulting from the minor diastereomer of 5 could not be obtained pure in sufficient amount.
\(\delta\) 137.9 (C), 129.1 (2CH), 128.0 (CH), 127.3 (2CH), 115.2 (q, \(J = 291.6\) Hz, CF3), 76.1 (C), 68.0 (C), 67.6 (C), 67.1 (CH), 44.2 (CH2), 32.1 (CH); \(^{19}\)F NMR (CDCl3, 282 MHz) \(\delta -79.8\) (s, 3F). HRMS (ESI) \(m/z\): 250.0601 (M+ H)+, \(C_{13}H_9F_3O\) requires 250.0605.

**Figure S1.** Interactions observed in NOESY experiment with compound 6.

(R)-1,1,1-trifluoro-4-phenylocta-5,7-diyn-2-one (7)

AcOH (4 \(\mu\)L, 0.096 mmol) and 1M TBAF in THF (68 \(\mu\)L, 0.068 mmol) were added to a solution of 3aa (35.4 mg, 0.087 mmol) in THF (1 mL) at 0 °C under \(N_2\) atmosphere. After 4 h, the reaction was quenched with H2O (1 mL). The aqueous layer was extracted with diethyl ether (3 x 15 mL). The organic layer was washed with saturated aqueous NaHCO3 and dried over MgSO4. Removal of the solvent under reduced pressure followed by flash chromatography eluting with hexane:EtOAc (99:01) gave 7 (15 mg, 70%). Enantiomeric excess (85%) was determined by GLC (Supelco \(\beta\)-dex-225, \(T_{column}\) = 100 °C (5 min) to 150 °C at 5 °C/min), major enantiomer \(t_r = 20.2\) min, minor enantiomer \(t_r = 19.9\) min.

\([\alpha]_D^{20}\) −6.0 (c 0.80, CHCl3) (85%); \(^1\)H NMR (CDCl3, 300 MHz) \(\delta 7.38-7.30\) (m, 5H), 4.31 (t, \(J = 7.0\) Hz, 1H), 3.33 (dd, \(J = 18.7, 7.9\) Hz, 1H), 3.15 (dd, \(J = 18.7, 6.2\) Hz, 1H), 2.10 (d, \(J = 1.1\) Hz, 1H); \(^{13}\)C NMR (CDCl3, 75.5 MHz) \(\delta 187.9\) (q, \(J = 36.1\) Hz, C), 137.9 (C), 129.1 (2CH), 128.0 (CH), 127.3 (2CH), 115.2 (q, \(J = 291.6\) Hz, CF3), 76.1 (C), 68.0 (C), 67.6 (C), 67.1 (CH), 44.2 (CH2), 32.1 (CH); \(^{19}\)F NMR (CDCl3, 282 MHz) \(\delta -79.8\) (s, 3F). HRMS (ESI) \(m/z\): 250.0601 (M+ H)+, \(C_{13}H_9F_3O\) requires 250.0605.
References:


$^1$H NMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^{1}$H NMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
^1H NMR, 300 MHz, CDC$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
$^1$H NMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
1H NMR, 300 MHz, CDCl₃
$^{13}$C NMR, 75 MHz, CDCl$_3$
Br

3fa

Ph\(^{-}\)

\(^1\)H NMR, 300 MHz, CDCl\(_3\)
$^{13}$C NMR, 75 MHz, CDCl$_3$
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$^1$H NMR, 300 MHz, CDCl$_3$
$^{13}$C NMR, 75 MHz, CDCl$_3$
\textsuperscript{1}H NMR, 300 MHz, CDCl\textsubscript{3}
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$\text{O}$

$\text{CF}_3$

$3\text{ac}$

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$\text{C NMR, 75 MHz, CDCl}_3$

$3\text{ae}$

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$^1$H NMR, 300 MHz, CDCl$_3$
$^1$H NMR, CDCl$_3$, 300 MHz

![NMR spectrum](image-url)

**Compound 7**
$^{13}$C NMR, CDCl$_3$, 75 MHz
### Table 1: Retention Time and Area Analysis

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**Note:** The data represents the peaks observed in the chromatograms with their respective retention times (RT) and areas. The Area % indicates the percentage contribution of each peak to the total area.
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S-78
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### Note

- The first table represents the first set of data with peaks at 5.06 and 5.02 minutes, with areas of 47.64% and 61.52% respectively.
- The second table represents the second set of data with peaks at 5.28 and 5.91 minutes, with areas of 4.891% and 95.105% respectively.
- The peak areas and retention times are consistent across both tables, indicating reliability in the data collection process.

---

*Figure 1: Chromatogram showing the separation of compounds.*

*Figure 2: Additional chromatogram with peak identification.*
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**Total Area:** 24367614 **(100.00%)**

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**Total Area:** 15317000 **(100.00%)**
### Table 1: Retention Time and Area Analysis

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Total: 3389040

### Table 2: Retention Time and Area Analysis

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Total: 3125800

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X-ray data for compound 3af: crystallized from dichloromethane/n-hexane at -20 °C; C_{18}H_{11}F_{3}O_{3}S_{1}; M_r=332.33; monoclinic; space group = P2_1; a = 5.5930(1), b = 8.1070(3); c = 17.5700(5) Å; α = 90.00, β = 95.029(2), γ = 90.00°; V = 793.60(4) Å³; Z = 2; ρ_{calcd} = 1.391 Mg m⁻³; μ = 0.235 mm⁻¹; F(000) = 240. A colourless crystal of 0.04x0.08x0.10 mm³ was used; 2709 [R(int) = 0.0399] independent reflections were collected on a Enraf Nonius CCD diffractometer by using graphite-monochromated MoKα radiation (λ = 0.71073 Å) operating at 50 kV and 30 mA. The cell parameters were determined and refined by a least-squares fit of all reflections. The structure was solved by direct methods and Fourier synthesis. It was refined by full-matrix least-squares procedures on \( F^2 \) (SHELXL-97). All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included in calculated positions and refined riding on the respective carbon atoms. Final R(\( R_\text{w} \)) values were R = 0.0689 and \( R_\text{w} \) = 0.1968. CCDC-1046444 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

**Figure S2.** ORTEP plot for the X-ray structure of compound 3af. The thermal ellipsoids are drawn at the 50% probability level.