Rhodium-Catalysed Linear-Selective Alkyne Hydroacylation

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I. General Considerations

Chemicals were purchased from Sigma Aldrich, Alfa Aesar, Acros Organics Ltd., or Strem Chemicals Inc. and used as supplied with the exception of 2-methylthiobenzaldehyde 1a which was purified by flash column chromatography on silica gel (5% Et₂O/petrol) and distilled (145 °C, 13 mmHg) prior to use. Anhydrous (where stated), HPLC grade solvents were purchased from Sigma Aldrich, Fisher Scientific or Rathburn and used directly without further purification with the exception of Acetone which was distilled from Drierite®. CH₂Cl₂ was obtained dry from an in-house solvent purification system (Innovative Technology Inc. PS-400-7) having passed through anhydrous alumina columns. ‘Petrol’ refers to the fraction of light petroleum ether boiling in the range 40-60 °C.

Reactions were performed with continuous magnetic stirring, under an atmosphere of nitrogen, unless otherwise stated, using standard Schlenk techniques and all glassware was oven-dried overnight (>200 °C) and allowed to cool under a flow of nitrogen (passed through a Drierite® filled tube) prior to use. Flash column chromatography was performed using Merck Geduran silica gel 60 (particle size 0.040-0.063 nm) with the indicated eluents. Thin Layer Chromatography (TLC) analysis was carried out on Merck Kieselgel 60 PF254 pre-coated aluminium backed sheets and visualised either by UV fluorescence (254 nm) and/or by staining with vanillin or potassium permanganate (KMnO₄).

NMR spectra were recorded at ambient temperature on either Brüker DPX200 (200 MHz), DQX400 (400 MHz) or AVC500 (500 MHz) spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) and referenced relative to the residual solvent peak(s) (as specified). Coupling constants (J) are given in Hertz (Hz) and rounded to the nearest 0.5 Hz. Assignments were made on the basis of chemical shifts, coupling constants, DEPT, COSY, HSQC and comparison with spectra of related compounds. Signal multiplicities are denoted as: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet; br., broad; app., apparent.

Melting points were measured using a Leica Gallen III hot-stage microscope. Low resolution mass spectra were recorded on a Fisons Platform spectrometer (ESI). High resolution mass spectra were measured by the internal service at the University of Oxford using a Bruker Daltronics microTOF spectrometer. m/z ratio values are reported in Daltons; high resolution values are calculated to four decimal places from the molecular formula, all found within a tolerance of 5 ppm. Infrared spectra were determined neat using a Bruker Tensor 27 FT spectrometer with an internal range of 600-4000 cm⁻¹.

Ligand 5b was prepared according to a previously reported procedure. The catalyst [Rh(nbd)₂]BF₄ was synthesized according to literature procedure.²

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I. Preparation of Aldehydes

a. The β-thio-aldehydes 1b–1i were prepared from the corresponding 2-haloaldehydes\(^3\) following General Procedure A (Scheme S-1). Data for aldehydes 1b,\(^1\) 1c,\(^4\) 1d,\(^5\) 1e,\(^1\) and 1h\(^1\) was consistent with the literature. β-Thio-aldehyde 1d was obtained as a side product from the synthesis of aldehyde 1f.

**General Procedure A**

NaSMe (1.2 eq)\(^6\) was added to a DMF solution of the halogenated compound (1.0 eq.) at 0 ºC and the resulting solution stirred at the specified temperature for 18 h. The reaction mixture was allowed to cool to RT, diluted with EtOAc (50 mL), washed with LiCl\(_{aq}\) (2×50 mL), and brine (1×50 mL). The organic layer was dried over MgSO\(_4\), filtered and concentrated *in vacuo*, and the crude residue purified by flash column chromatography.

![Scheme S-1 – General Procedure A for the preparation of aldehydes 1b-1i](image)

3 For the synthesis of the 2-bromo aldehydes used in the preparation of 1g, 1h and 1i, see: M-Y. Lin, A. Das, R-S. Liu, *J. Am. Chem. Soc.*, 2006, 128, 9340.
6 0.8 eq. NaSMe was used in the synthesis of aldehyde 1e.
b. Et₃N (1.50 mL, 11.0 mmol) was added to a solution of ethanethiol (0.65 mL, 8.9 mmol) and bromo-cyclohex-1-enecarbaldehyde (0.50 mL, 4.4 mmol) in CH₂Cl₂ (2.5 mL) at 0 ºC and the resulting solution stirred for 18 h at RT. Volatiles were removed in vacuo and the crude residue purified by flash column chromatography (20% Et₂O/petrol) to afford the title compound 1j⁷ as a colourless oil (467 mg, 62%) as a 9:1 anti:syn mixture of diastereomers.

![Scheme S-2 – Preparation of aldehyde 1j](image)

c. A solution of ethanethiol (2.70 mL, 36.6 mmol) and methacrolein (2.00 mL, 29.2 mmol) in CH₂Cl₂ (7.0 mL) was added dropwise to Et₃N (5.10 mL, 36.6 mmol) at 0 ºC. The resulting reaction mixture was stirred at RT for 48 h before removal of volatiles in vacuo and purification by flash column chromatography to afford the title compound 1k⁸ as a yellow oil (1.40 g, 44%).

![Scheme S-3 – Preparation of aldehyde 1k](image)

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II. Data for Novel Aldehydes 1f, 1h and 1i

2-Chloro-6-(methylthio)benzaldehyde (1f)

![Chemical Structure](image)

Prepared according to General Procedure A using 2,6-dichlorobenzaldehyde (1.00 g, 5.7 mmol), NaSMe (360 mg, 5.1 mmol) and DMF (10 mL) at 90 °C for 18 h. Flash chromatography (20% Et₂O/petrol) afforded β-thio-aldehyde 1f as a pale yellow solid (279 mg, 26%). m.p. (CH₂Cl₂) 85-87 °C; ¹H NMR (400 MHz, CDCl₃) δ 10.65 (1H, s), 7.43-7.38 (1H, m), 7.23-7.17 (2H, m), 2.45 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 192.0, 146.8, 140.3, 133.6, 128.1, 125.6, 123.0, 15.5; LRMS (ESI) m/z 241 (60%, [M+Na+MeOH]+), 209 (65%, [M+Na]+); HRMS (ESI) found m/z 208.9797 ([M+Na]+), C₈H₇ClNaOS requires 208.9797; ν_max (neat)/cm⁻¹ 3097, 3068, 2924, 2987, 2275, 1668, 1571, 1543.

2-(Methylthio)cyclohept-1-enecarbaldehyde (1h)

![Chemical Structure](image)

Prepared according to General Procedure A using 2-bromocyclohept-1-enecarbaldehyde (700 mg, 3.5 mmol), NaSMe (293 mg, 4.2 mmol) and DMF (15 mL) at RT for 24 h. Flash chromatography (15% Et₂O/petrol) afforded β-thio-aldehyde 1h as a yellow oil (412 mg, 69%). ¹H NMR (400 MHz, CDCl₃) δ 10.23 (1H, s), 2.75-2.69 (2H, m), 2.56-2.50 (2H, m), 2.33 (3H, s), 1.83-1.76 (2H, m), 1.65-1.57 (2H, m), 1.46-1.39 (2H, m); ¹³C NMR (101 MHz, CDCl₃) δ 193.0, 163.0, 142.5, 34.7, 32.0, 26.0, 25.8, 25.7, 15.4; LRMS (ESI) m/z 241 (55%, [M+K+MeOH]+), 209 (50%, [M+K]+), 193 (30%, [M+Na]+); HRMS (ESI) found m/z 193.0661 ([M+Na]+), C₉H₁₄NaOS requires 193.0658; ν_max (film)/cm⁻¹ 2922, 2850, 2729, 1654, 1567.
4-(Methylthio)-5,6-dihydro-2H-pyran-3-carbaldehyde (1i)

Prepared according to General Procedure A using 4-bromo-5,6-dihydro-2H-pyran-3-carbaldehyde (2.00 g, 10.6 mmol), NaSMe (890 mg, 12.7 mmol) and DMF (40 mL) at RT for 18 h. Flash chromatography (30% Et$_2$O/petrol) afforded $\beta$-thio-aldehyde 1i as an off-white solid (646 mg, 39%). m.p. (CH$_2$Cl$_2$) 48-52 $^\circ$C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.14 (1H, s), 4.33 (2H, t, $J$ 2.0), 3.84 (2H, t, $J$ 5.5), 2.58 (2H, tt, $J$ 5.5, 2.0), 2.36 (3H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 187.1, 154.4, 132.7, 65.0, 64.1, 29.6, 13.3; LRMS (ESI) m/z 213 (65%, [M+Na+MeOH]$^+$), 181 (65%, [M+Na]$^+$); HRMS (ESI) found m/z 181.0303 ([M+Na]$^+$), $C_7H_{10}NaO_2S^+$ requires 181.0294; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3004, 2987, 2941, 2904, 2863, 2850, 2827, 2740, 1641, 1572.
III. General Procedures for Rh-Catalysed Hydroacylation

General procedure B (Ligand screen, Table 1)

[Rh(nbd)$_2$]BF$_4$ and the appropriate ligand were dissolved in acetone (2.0 mL)$^9$ and stirred at RT for 5 min. H$_2$(g) was bubbled through the pre-catalyst solution for 2 min, then the solution purged with N$_2$(g). 2-methylthiobenzaldehyde (39 µL 0.30 mmol) and 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol) were added and the reaction mixture was stirred at RT for 2 h. The reaction mixture was diluted with Et$_2$O, filtered through a short plug of celite and the filtrate concentrated in vacuo.

A sample of the crude residue was analysed by $^1$H NMR in CDCl$_3$, to determine conversion and the regioselectivity of the reaction.

General procedure C (Reaction scope, Tables 2 and 3)

[Rh(nbd)$_2$]BF$_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) were dissolved in acetone (1.5 mL) and stirred at RT for 5 min. H$_2$(g) was bubbled through the pre-catalyst solution for 2 min, then the solution purged with N$_2$(g). Aldehyde (0.30 mmol) and alkyne (0.45 mmol) were added as a solution in acetone (0.5 mL) and the reaction mixture was stirred at RT for 1-2.5 h. The reaction mixture was diluted with Et$_2$O, filtered through a short plug of celite and the filtrate concentrated in vacuo. The crude residue was purified by flash column chromatography.

A sample of the crude residue was analysed by $^1$H NMR in CDCl$_3$ to determine the regioselectivity of the reaction.

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$^9$ Table 1, Entry 9, only 1.0 mL of acetone used.
IV. Data for Enones 3a-3u

\((E)-3-(3,5\text{-bis(Trifluoromethyl)phenyl})-1-(2\text{-methylthio)phenyl})\text{prop-2-en-1-one} (3a)\)

![Chemical Structure](image)

Prepared according to General Procedure C using 2\text{-}(methylthio)benzaldehyde (39 µL, 0.30 mmol) and 1-ethynyl-3,5\text{-bis(trifluoromethyl)benzene} (80 µL, 0.45 mmol), [Rh(nbd)\text{2}]BF\text{4} (5.6 mg, 0.015 mmol), dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (20% Et\text{2}O/petrol) afforded the title compound 3a as a bright yellow solid (109 mg, 93%). m.p. (CH\text{2}Cl\text{2}) 99-100 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\text{3}) δ 8.01 (2H, s), 7.89 (1H, s), 7.77 (1H, dd, \textit{J} 8.0, 1.5), 7.68 (1H, d, \textit{J} 16.0), 7.55-7.50 (1H, m), 7.47 (1H, d, \textit{J} 16.0), 7.41 (1H, app. d, \textit{J} 8.0), 7.30-7.25 (1H, m), 2.48 (3H, s); \textsuperscript{13}C NMR (101 MHz, CDCl\text{3}) δ 191.4, 141.3, 140.85, 137.0, 136.2, 132.5 (2C, q, \textit{J}_{C-F} 33.5), 132.2, 129.8, 127.9 (2C, br. s), 127.8, 126.2, 124.2, 123.5-123.2 (m), 123.0 (2C, q, \textit{J}_{C-F} 273.0), 16.4; \textsuperscript{19}F NMR (376 MHz, CDCl\text{3}) δ -63.0 (6F, s); LRMS (ESI) \textit{m}/\textit{z} 803 (100%, [2M+H]\textsuperscript{+}), 413 (10%, [M+Na]\textsuperscript{+}); HRMS (ESI) found \textit{m}/\textit{z} 413.0411 ([M+Na]\textsuperscript{+}), \textit{C}_{18}\text{H}_{12}\text{F}_{6}\text{NaOS}\textsuperscript{+} requires 413.0411; \textit{v}_{\text{max}} (neat)/cm\textsuperscript{-1} 3099, 2927, 2851, 1653, 1603, 1588.

\((E)-1\text{-}(2\text{-Methylthio)phenyl)-3-(4\text{-trifluoromethyl)phenyl})\text{prop-2-en-1-one} (3b)\)

![Chemical Structure](image)

Prepared according to General Procedure C using 2\text{-}(methylthio)benzaldehyde (39 µL, 0.30 mmol) and 1-ethynyl-4\text{-}(trifluoromethyl)benzene (73 µL, 0.45 mmol), [Rh(nbd)\text{2}]BF\text{4} (5.6 mg, 0.015 mmol), dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et\text{2}O/petrol) afforded the title compound 3b as a yellow solid (80 mg, 83%). m.p. (CH\text{2}Cl\text{2}) 102-104 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\text{3}) δ 7.76-7.62 (6H, m), 7.53-7.47 (1H, m), 7.44-7.37 (1H d, \textit{J} 16.0 overlapping 1H, m), 7.29-7.22 (1H, m), 2.47 (3H, s); \textsuperscript{13}C NMR (101 MHz, CDCl\text{3}) δ 192.1, 142.8, 141.1, 138.2, 136.6, 131.9, 131.8 (q, \textit{J}_{C-F} 33.0), 129.7, 128.5 (2C), 126.7, 126.2, 125.9 (2C, q, \textit{J}_{C-F} 4.0), 124.2,
123.8 (q, $J_{C-F}$ 272.5), 16.4; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -63.8, (3F, s); LRMS (ESI) $m/z$ 667 (100%, [2M+Na$^+$]), 345 (70%, [M+Na$^+$]), 323 (25%, [M+H$^+$]); HRMS (ESI) found $m/z$ 345.0527 ([M+Na$^+$]), C$_{17}$H$_{13}$F$_3$NaOS$^+$ requires 345.0531; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 2961, 2923, 1658, 1599, 1585, 1577, 1556.

(E)-3-(3,5-Difluorophenyl)-1-(2-(methylthio)phenyl)prop-2-en-1-one (3c)

![Chemical structure of 3c]

Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol), 1-ethynyl-4-fluorobenzene (52 µL, 0.45 mmol), [Rh(nbd)$_2$]BF$_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et$_2$O/petrol) afforded the title compound 3c as a yellow solid (74 mg, 91%). m.p. (CH$_2$Cl$_2$) 82-84 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.75-7.71 (1H, m), 7.57-7.46 (2H, m), 7.39 (1H, app. d, $J_{H-F}$ 8.0), 7.32 (1H, d, $J_{H-F}$ 15.5), 7.28-7.22 (1H, m), 7.14-7.07 (2H, m), 6.85 (1H, app. t, $J_{H-F}$ 8.5, 2.0), 2.48 (3H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 191.8, 163.2 (2C, dd, $J_{C-F}$ 249.0, 12.8), 142.0 (t, $J_{C-F}$ 3.0), 141.1, 138.1 (t, $J_{C-F}$ 9.5), 136.5, 132.0, 129.7, 126.7, 126.2, 124.2, 110.0 (2C, dd, $J_{C-F}$ 18.5, 7.0), 105.5 (t, $J_{C-F}$ 25.0), 16.4; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -109.9 (2F, s); LRMS (ESI) $m/z$ 603 (100%, [2M+Na$^+$]), 329 (45%, [M+K$^+$]), 313 (60%, [M+Na$^+$]), 291 (20%, [M+H$^+$]); HRMS (ESI) found $m/z$ 313.0466 ([M+Na$^+$]), C$_{16}$H$_{12}$F$_2$NaOS$^+$ requires 313.0469; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3083, 2922, 1663, 1620, 1606, 1588.

(E)-3-(4-Fluorophenyl)-1-(2-(methylthio)phenyl)prop-2-en-1-one (3d)

![Chemical structure of 3d]

Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol), 1-ethynyl-4-fluorobenzene (52 µL, 0.45 mmol), [Rh(nbd)$_2$]BF$_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) for 2 h at RT. Purification by flash chromatography (30% Et$_2$O/petrol) afforded the title compound 3d as a yellow solid (74 mg, 91%). m.p. (CH$_2$Cl$_2$) 54-56 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.93-7.75 (1H, m), 7.57-7.46 (2H, m), 7.39 (1H, app. d, $J_{H-F}$ 8.0), 7.32 (1H, d, $J_{H-F}$ 15.5), 7.28-7.22 (1H, m), 7.14-7.07 (2H, m), 6.85 (1H, app. t, $J_{H-F}$ 8.5, 2.0), 2.48 (3H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 191.8, 163.2 (2C, dd, $J_{C-F}$ 249.0, 12.8), 142.0 (t, $J_{C-F}$ 3.0), 141.1, 138.1 (t, $J_{C-F}$ 9.5), 136.5, 132.0, 129.7, 126.7, 126.2, 124.2, 110.0 (2C, dd, $J_{C-F}$ 18.5, 7.0), 105.5 (t, $J_{C-F}$ 25.0), 16.4; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -109.9 (2F, s); LRMS (ESI) $m/z$ 603 (100%, [2M+Na$^+$]), 329 (45%, [M+K$^+$]), 313 (60%, [M+Na$^+$]), 291 (20%, [M+H$^+$]); HRMS (ESI) found $m/z$ 313.0466 ([M+Na$^+$]), C$_{16}$H$_{12}$F$_2$NaOS$^+$ requires 313.0469; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3083, 2922, 1663, 1620, 1606, 1588.
MHz, CDCl\textsubscript{3}) \(\delta\) 7.70 (1H, app. d, \(J\) 7.5), 7.64-7.53 (3H, m), 7.51-7.44 (1H, m), 7.38 (1H, app. d, \(J\) 8.0), 7.29-7.20 (2H, m), 7.09 (2H, app. t, \(J\) 8.5), 2.46 (3H, s); \(^{13}\)C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 192.6, 164.0 (d, \(J\) C-F 252.0), 143.9, 140.6, 137.1, 131.6, 131.0 (d, \(J\) C-F 3.0), 130.4 (2C, d, \(J\) C-F 8.0), 129.4, 126.2, 124.4 (2C), 116.1 (2C, d, \(J\) C-F 22.5), 16.4; \(^{19}\)F NMR (376 MHz, CDCl\textsubscript{3}) \(\delta\) -110.0 (1F, s); LRMS ESI m/z 567 (100%, [2M+Na]\(^{+}\)), 295 (65%, [M+Na]\(^{+}\)); HRMS (ESI) found m/z 295.0561 ([M+Na]\(^{+}\)), \(\text{C}_{16}\text{H}_{13}\text{FNaOS}\(^{+}\) requires 295.0563; \(\nu_{\text{max}}\) (neat)/cm\(^{-1}\) 3066, 2977, 2920, 1650, 1595, 1586, 1554, 1504.

\((E)-3-(4\text{-Bromophenyl})-1-(2-(\text{methylthio})phenyl)prop-2-en-1-one (3e)\)

\begin{center}
\includegraphics[width=0.2\textwidth]{image}
\end{center}

Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol), 1-ethyl-4-bromobenzene (81 mg, 0.45 mmol), [Rh(nbd)\(_2\)]BF\(_4\) (5.6 mg, 0.015 mmol) and dcepe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (20% Et\(_2\)O/petrol) afforded the title compound 3e as a yellow solid (93 mg, 93%). m.p. (CH\(_2\)Cl\(_2\)) 77-80 °C; \(^{1}\)H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 7.70 (1H, dd, \(J\) 7.5, 1.5), 7.64-7.44 (1H, d, \(J\) 16.0 overlapping 5H, m), 7.39 (1H, app. d, \(J\) 8.0), 7.31 (1H, d, \(J\) 16.0), 7.28-7.22 (1H, m), 2.46 (3H, s); \(^{13}\)C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 192.5, 143.7, 140.7, 136.9, 133.7, 132.2 (2C), 131.7, 129.8 (2C), 129.5, 126.2, 125.1, 124.8, 124.1, 16.4; LRMS (ESI) m/z 689 (100%, [2M(\(^{79}\)Br)+Na]\(^{+}\)), 357 (40%, [M+Na]\(^{+}\)); HRMS (ESI) found m/z 354.9757 ([M(\(^{79}\)Br)+Na]\(^{+}\)), \(\text{C}_{16}\text{H}_{13}\text{BrNaOS}\(^{+}\) requires 354.9763; \(\nu_{\text{max}}\) (neat)/cm\(^{-1}\) 3096, 2955, 2920, 2853, 1655, 1592, 1562.

\((E)-3-(2\text{-Chlorophenyl})-1-(2-(\text{methylthio})phenyl)prop-2-en-1-one (3f)\)

\begin{center}
\includegraphics[width=0.2\textwidth]{image}
\end{center}

Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol), 1-chloro-2-ethylbenzene (54 µL, 0.45 mmol), [Rh(nbd)\(_2\)]BF\(_4\) (5.6 mg, 0.015 mmol) and depe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (30% Et\(_2\)O/petrol)
afforded the title compound 3f as a yellow solid (76 mg, 88%). m.p. (CH₂Cl₂) 59-62 °C; ¹H NMR (400 MHz, CD₂Cl₂) δ 8.01 (1H, d, J 16.0), 7.82-7.73 (2H, m), 7.56-7.50 (1H, m), 7.50-7.42 (2H, m), 7.41-7.26 (1H, d, J 16.0 overlapping 3H, m), 2.49 (3H, s); ¹³C NMR (101 MHz, CD₂Cl₂) δ 192.5, 141.3, 140.7, 137.1, 135.6, 133.5, 132.1, 131.7, 130.6, 130.0, 128.2, 127.7, 127.6, 126.6, 124.4, 16.6; LRMS (ESI) m/z 599 (100%, [2M(³⁵Cl)+Na]⁺), 311 (40%, [M(³⁵Cl)+Na]⁺), 289 (15%, [M(³⁵Cl)+H]⁺); HRMS (ESI) found m/z 311.0265 ([M(³⁵Cl)+Na]⁺), C₁₆H₁₃³⁵ClNaOS⁺ requires 311.0268; νmax (neat)/cm⁻¹ 3065, 2961, 2919, 1650, 1592, 1556.

(E)-Methyl 4-(3-(2-(methylthio)phenyl)-3-oxoprop-1-en-1-yl)benzoate (3g)

Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol), methyl 4-ethynylbenzoate (66 mg, 0.45 mmol), [Rh(nbd)₂]BF₄ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et₂O/petrol) afforded the title compound 3g as a bright yellow solid (69 mg, 74%). m.p. (CH₂Cl₂) 119-120 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.06 (2H, app. d, J 8.5), 7.73 (1H, dd, J 7.5, 1.5), 7.69-7.62 (3H, m), 7.52-7.46 (1H, m), 7.43-7.37 (2H, m), 7.28-7.22 (1H, m), 3.93 (3H, s), 2.77 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 192.2, 166.4, 143.3, 140.9, 139.0, 136.7, 131.8, 131.5, 130.1 (2C), 129.6, 128.3 (2C), 126.6, 126.2, 124.1, 52.3, 16.4; LRMS (ESI) m/z 647 (100%, [2M+Na]⁺), 335 (45%, [M+Na]⁺), 313 (30%, [M+H]⁺); HRMS (ESI) found m/z 335.0707 ([M+Na]⁺), C₁₈H₁₆NaO₃S⁺ requires 335.0712; νmax (neat)/cm⁻¹ 3067, 2954, 2913, 1655, 1603, 1564.

(E)-1-(2-(Methylthio)phenyl)-3-(4-nitrophenyl)prop-2-en-1-one (3h)
Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol), 1-ethynyl-4-nitrobenzene (54 µL, 0.45 mmol), [Rh(nbd)$_2$]BF$_4$ (5.6 mg, 0.015 mmol) and depe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (100% CH$_2$Cl$_2$), followed by recrystallisation from CH$_2$Cl$_2$/petrol, afforded the title compound 3h as a dark yellow crystalline solid (60 mg, 67%). m.p. (CH$_2$Cl$_2$) 148-150 °C; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.26 (2H, d, $J$ 8.5), 7.78-7.75 (3H, m), 7.68 (1H, d, $J$ 16.0), 7.54-7.38 (1H, d, $J$ 16.0 overlapping 2H, m), 7.30-7.23 (1H, m), 2.48 (3H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 191.5, 148.5, 141.5, 141.3, 141.0, 136.3, 132.1, 129.8 (2C), 128.9 (2C), 128.1, 126.2, 124.2 (2C), 16.4; LRMS (ESI) $m/z$ 354 (20%, [M+H$^+$]), 322 (100%, [M+Na$^+$]); HRMS (ESI) found $m/z$ 322.0507 ([M+Na$^+$]), C$_{16}$H$_{13}$NNaO$_3$S$^+$ requires 322.0508; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 2917, 2850, 1651, 1586, 1513, 1338.

(E)-1-(2-(Methylthio)phenyl)-3-(thiophen-3-yl)prop-2-en-1-one (3i)

Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol) and 3-ethynylthiophene (42 µL, 0.45 mmol), [Rh(nbd)$_2$]BF$_4$ (5.6 mg, 0.015 mmol), depe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (35% Et$_2$O/petrol) afforded the title compound 3i as a brown oil (75 mg, 96%). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.66 (1H, dd, $J$ 8.0, 1.5), 7.60 (1H, d, $J$ 16.0), 7.57-7.54 (1H, m), 7.49-7.43 (1H, m), 7.40-7.34 (3H, m), 7.23 (1H, m), 7.12 (1H, d, $J$ 16.0), 2.46 (3H, s); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 193.3, 140.3, 138.8, 138.1, 138.3, 137.3, 131.4, 129.3, 129.1, 127.1, 126.3, 125.3, 124.7, 124.2, 16.5; LRMS (ESI) $m/z$ 543 (100%, [2M+Na$^+$]), 299 (35%, [M+K$^+$]), 283 (45%, [M+Na$^+$]), 261 (10%, [M+H$^+$]); HRMS (ESI) found $m/z$ 283.0219 ([M+Na$^+$]), C$_{14}$H$_{12}$NaOS$_2^+$ requires 283.0222; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 2980, 2919, 1650, 1616, 1590, 1558, 1516.

(E)-1-(2-(Methylthio)phenyl)non-2-en-1-one (3j)
Prepared according to General Procedure C using 2-(methylthio)benzaldehyde (39 µL, 0.30 mmol) and 1-octyne (66 µL, 0.45 mmol), [Rh(nbd)₂]BF₄ (5.6 mg, 0.015 mmol), dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (20% Et₂O/petrol) afforded the title compound 3j as a green oil (66 mg, 84%). ¹H NMR (400 MHz, CDCl₃) δ 7.57 (1H, dd, J 7.5, 1.5), 7.46-7.41 (1H, m), 7.34 (1H, app. d, J 7.5), 7.19 (1H, app. td, J 7.5, 1.0), 6.87 (1H, dt, J 15.5, 7.0), 6.64 (1H, dt, J 15.5, 1.5), 2.43 (3H, s), 2.32-2.24 (2H, m), 1.54-1.42 (2H, m), 1.37-1.25 (6H, m), 0.92-0.83 (3H, m); ¹³C NMR (101 MHz, CDCl₃) δ 193.5, 151.2, 140.2, 137.1, 131.2, 129.3, 128.6, 126.2, 124.0, 32.8, 31.6, 28.9, 28.0, 22.5, 16.4, 14.0; LRMS (ESI) m/z 547 (100%, [2M+Na]+), 285 (50%, [M+Na]+), 263 (20%, [M+H]+); HRMS (ESI) found m/z 285.1277 ([M+Na]+), C₁₆H₂₂NaOS⁺ requires 285.1284; ν max (neat)/cm⁻¹ 2924, 2855, 1658, 1614.

(E)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(3,4-dimethoxy-2-(methylthio)phenyl)prop-2-en-1-one (3k)

Prepared according to General Procedure C using 3,4-dimethoxy-2-(methylthio)benzaldehyde (64 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)₂]BF₄ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (30% Et₂O/petrol), followed by recrystallisation from petrol, afforded the title compound 3k as a pale yellow solid (82 mg, 61%). m.p. (CH₂Cl₂) 123-124 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.97 (2H, s), 7.87 (1H, s), 7.50 (1H, d, J 16.0), 7.32 (1H, d, J 16.0), 7.27 (1H, d, J 8.5), 6.96 (1H, d, J 8.5), 3.95 (6H, s), 2.43 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 190.1, 155.3, 150.4, 138.8, 137.2, 136.4, 132.4, (2C, q, J_C-F 33.5), 130.4, 129.8, 127.8 (2C, br. s) 124.8, 123.0 (2C, q, J_C-F 273.0), 123.4-123.1 (m), 111.7, 60.5, 58.0, 19.4; ¹⁹F NMR (376 MHz, CDCl₃) δ -61.3 (6F, s); LRMS (ESI) m/z 923 (100%, [2M+Na]+), 473 (20%, [M+Na]+); HRMS (ESI) found m/z 473.0601 ([M+Na]+), C₂₀H₁₆F₆NaO₃S⁺ requires 473.0617; ν max (neat)/cm⁻¹ 3013, 2978, 2943, 2923, 1647, 1585.

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(E)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(4,5-dimethoxy-2-(methylthio)phenyl)prop-2-en-1-one (3l)

Prepared according to General Procedure C using 4,5-dimethoxy-2-(methylthio)benzaldehyde (64 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)₂]BF₄ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (20% Et₂O/petrol) afforded the title compound 3l as a yellow solid (93 mg, 73%).

m.p. (CH₂Cl₂) 140-142 °C; ¹H NMR (400 MHz, CDCl₃) δ 8.00 (2H, s), 7.88 (1H, s), 7.69 (1H, d, J 15.5), 7.49 (1H, d, J 15.5), 7.26 (1H, s), 6.96 (1H, s), 3.98 (3H, s), 3.94 (3H, s), 3.47 (3H, s); ¹³C NMR (101 MHz, CDCl₃) δ 190.4, 152.3, 146.5, 139.5, 137.3, 133.7, 132.4 (2C, q, J_C-F 34.5), 130.5, 128.3, 127.8 (2C), 123.2 (app. quin, J_C-F 4.0), 123.0 (2C, q, J_C-F 273.0), 112.9, 111.0, 54.4, 56.1, 19.0; ¹⁹F NMR (376 MHz, CDCl₃) δ -63.0 (6F, s); LRMS (ESI) m/z 923 (100%, [2M+Na]⁺), 473 (20%, [M+Na]⁺), 451 (10%, [M+H]⁺); HRMS (ESI) found m/z 473.0613 ([M+Na]⁺), C₂₀H₁₆F₆NaO₃S⁺ requires 473.0617; νmax (neat)/cm⁻¹ 3025, 2967, 2914, 2853, 1651, 1547.

(E)-1-(2,6-bis(Methylthio)phenyl)-3-(3,5-bis(trifluoromethyl)phenyl)prop-2-en-1-one (3m)

Prepared according to General Procedure C using 2,6-bis(methylthio)benzaldehyde (59 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)₂]BF₄ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (15% Et₂O/petrol) afforded the title compound 3m as a yellow solid (94 mg, 70%). m.p. (CH₂Cl₂) 116-117 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.96 (2H, s), 7.87 (1H, s), 7.43-7.37 (1H, m), 7.34 (1H, d, J 16.0), 7.27 (2H, d, J 8.0), 7.09 (1H, d, J 16.0), 2.44 (6H, s); ¹³C NMR (101 MHz, CDCl₃) δ 195.1, 141.2,
140.3 (2C), 136.8, 135.9, 132.4 (2C, q, \( J_{C-F} \) 33.5), 130.5, 130.2, 128.0 (2C, app. d, \( J_{C-F} \) 3.5'), 126.1 (2C), 123.5 (app. quin, \( J_{C-F} \) 4.0'), 123.0 (2C, q, \( J_{C-F} \) 273.0), 17.7 (2C); \( \delta \) (2C); \( \delta \) (376 MHz, CDCl\(_3\)) \( \delta \) -63.0 (6F, s); LRMS (ESI) \( m/z \) 895 (100%, [2M+Na]\(^+\)), 459 (35%, [M+Na]\(^+\)), 437 (15%, [M+H]\(^+\)); HRMS (ESI) found 459.0275 ([M+Na]\(^+\)), \( C_{19}H_{14}F_{6}NaOS_{2} \) requires 459.0282; \( \nu_{max} \) (neat)/cm\(^{-1}\) 3048, 2963, 2924, 1648, 1558.

\((E)-3-(3,5\text{-bis(Trifluoromethyl)phenyl})-1-(2\text{-methylthio})-3\text{-trifluoromethyl)phenyl})\text{-prop-2-en-1-one} (3n)\)

Prepared according to General Procedure C using 2-(methylthio)-3-(trifluoromethyl)benzaldehyde (66 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)]\(_2\)BF\(_4\) (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1.5 h. Purification by flash chromatography (10% Et\(_2\)O/petrol) afforded the title compound 3n as an off-white solid (129 mg, 94%). m.p. (CH\(_2\)Cl\(_2\)) 97-100 °C; \( ^1H \) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.98 (2H, s), 7.92-7.85 (2H, m), 7.63-7.52 (2H, m), 7.43 (1H, d, \( J \) 16.0), 7.27 (1H, d, \( J \) 16.0), 2.34 (3H, s); \( ^{13}C \) NMR (101 MHz, CDCl\(_3\)) \( \delta \) 194.2, 148.6, 140.6, 136.5, 135.2 (q, \( J_{C-F} \) 36.5), 132.5 (2C, q, \( J_{C-F} \) 33.5), 132.3, 131.0, 130.0, 129.2, 128.4 (app. q, \( J_{C-F} \) 5.5), 128.0 (2C, br. s), 123.3 (q, \( J_{C-F} \) 74.0), 122.9 (2C, q, \( J_{C-F} \) 273.0), 123.7 (app. quin, \( J_{C-F} \) 4.0), 22.1; \( ^{19}F \) NMR (376 MHz, CDCl\(_3\)) \( \delta \) -59.7 (3F, s), -63.1 (6F, s); LRMS (ESI) \( m/z \) 939 (100%, [2M+Na]\(^+\)), 481 (80%, [M+Na]\(^+\)); HRMS (ESI) found \( m/z \) 481.0276 ([M+Na]\(^+\)), \( C_{19}H_{11}F_{6}NaOS^+ \) requires 481.0279; \( \nu_{max} \) (neat)/cm\(^{-1}\) 2961, 2925, 2854, 1649, 1632, 1579.

\((E)-3-(3,5\text{-bis(Trifluoromethyl)phenyl})-1-(2\text{-chloro-6-(methylthio)phenyl})\text{-prop-2-en-1-one} (3o)\)

Electronic Supplementary Material (ESI) for Chemical Communications
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Prepared according to General Procedure C using 2-chloro-6-(methylthio)benzaldehyde (56 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)\textsubscript{2}]BF\textsubscript{4} (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at 50 °C for 18 h. Purification by flash chromatography (25% Et\textsubscript{2}O/petrol) afforded the title compound 3o as a yellow solid (100 mg, 78%). m.p. (CH\textsubscript{2}Cl\textsubscript{2}) 96-100 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) 7.97 (2H, s), 7.89 (1H, s), 7.42-7.24 (4H, m), 7.33 (1H, d, \( J \) 16.5), 2.46 (3H, s); \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) \( \delta \) 193.5, 142.2, 138.3, 137.8, 136.5, 132.5 (2C, q, \( J_{C\text{-}F} \) 33.5), 130.9, 130.7, 129.9, 128.1 (2C, br. s), 127.0, 126.5, 123.9-123.7 (m), 122.9 (2C, q, \( J_{C\text{-}F} \) 273.0), 17.5; \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) -63.0 (6F, s); LRMS (ESI) \( m/z \) 811 (100%, [2M(\textsuperscript{35}Cl)+Na\textsuperscript{+}]), 417 (50%, [M(\textsuperscript{35}Cl)+Na\textsuperscript{+}]), 395 (80%, [M+H\textsuperscript{+}]); HRMS (ESI) found \( m/z \) 417.0007 ([M(\textsuperscript{35}Cl)+Na\textsuperscript{+}]), \( C_{18}H_{11}\textsuperscript{35}ClNaO\textsuperscript{+} \) requires 417.0016; \( \nu_{\text{max}} \) (neat)/cm\textsuperscript{-1} 3055, 2960, 2927, 1652, 1632, 1573, 1557.

\[(E)-3\text{(3,5-bis(Trifluoromethyl)phenyl)-1-(2-(methylthio)cyclohex-1-en-1-yl)prop-2-en-1-one (3p)}\]

Prepared according to General Procedure C using 2-(methylthio)cyclohex-1-enecarbaldehyde (47 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)\textsubscript{2}]BF\textsubscript{4} (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2 h. Purification by flash chromatography (10-15% EtOAc/petrol) afforded the title compound 3p as a bright yellow solid (100 mg, 85%). m.p. (CH\textsubscript{2}Cl\textsubscript{2}) 96-99 °C; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) 7.95 (2H, s), 7.85 (1H, s), 7.63 (1H, d, \( J \) 15.5), 7.31 (1H, d, \( J \) 15.5), 2.57-2.49 (4H, m), 2.31 (3H, s), 1.83-1.70 (4H, m); \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) \( \delta \) 190.9, 148.8, 138.4, 137.6, 132.3 (2C, q, \( J_{C\text{-}F} \) 33.5), 131.8, 128.0, 127.7 (2C, br. s), 123.1 (2C, q, \( J_{C\text{-}F} \) 277.0), 123.0-122.7 (m), 30.1, 28.2, 23.0, 21.9, 15.0; \textsuperscript{19}F NMR (376 MHz, CDCl\textsubscript{3}) \( \delta \) -63.0 (6F, s); LRMS (ESI) \( m/z \) 814 (100%, [2M+Na\textsuperscript{+}]), 417 (50%, [M+Na\textsuperscript{+}]), 395 (80%, [M+H\textsuperscript{+}]); HRMS (ESI) found \( m/z \) 417.0071 ([M+Na\textsuperscript{+}]), \( C_{18}H_{16}F_6NaO\textsuperscript{+} \) requires 417.0078; \( \nu_{\text{max}} \) (neat)/cm\textsuperscript{-1} 3055, 2960, 2927, 1652, 1632, 1573, 1557.
(E)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(2-(methylthio)cyclohept-1-en-1-yl)prop-2-en-1-one (3q)

Prepared according to General Procedure C using 2-(methylthio)cyclohept-1-enecarbaldehyde (51 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)₂]BF₄ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1 h. Purification by flash chromatography (15% Et₂O/petrol) afforded the title compound 3q as a bright yellow solid (77 mg, 63%). m.p. (CH₂Cl₂) 76-78 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.95 (2H, s), 7.85 (1H, s), 7.56 (1H, d, J 16.0), 7.14 (1H, d, J 16.0), 2.71-2.65 (2H, m), 2.60-2.53 (2H, m), 2.28 (3H, s), 1.85-1.80 (2H, m), 1.66 (4H, m); ¹³C NMR (101 MHz, CDCl₃) δ 193.1, 149.4 (2C), 141.8, 137.5, 132.3 (2C, q, J₇-F 33.0), 129.6, 127.6 (2C, br. s), 123.0 (2C, q, J₇-F 273.0), 122.9-122.7 (m), 33.8, 31.8, 31.1, 26.6, 25.8, 16.2; ¹⁹F NMR (376 MHz, CDCl₃) δ -63.0 (6F, s); LRMS (ESI) m/z 839 (100%, [2M+Na]⁺), 447 (50%, [M+K]⁺), 409 (85%, [M+H]⁺); HRMS (ESI) found m/z 431.0871 ([M+Na]⁺), C₁₉H₁₈F₆NaOS⁺ requires 431.0875; νmax (neat)/cm⁻¹ 2924, 2855, 1663, 1602.

(E)-3-(3,5-bis(Trifluoromethyl)phenyl)-1-(4-(methylthio)-5,6-dihydro-2H-pyran-3-yl)prop-2-en-1-one (3r)

Prepared according to General Procedure C using 4-(methylthio)-5,6-dihydro-2H-pyran-3-carbaldehyde (47 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)₂]BF₄ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1.5 h. Recrystallisation from CH₂Cl₂ afforded the title compound 3r as a bright yellow crystalline solid (100 mg, 84%). m.p. (CH₂Cl₂) 189-192 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.95 (2H, s), 7.87 (1H, s), 7.69 (1H, d, J 15.5), 7.07 (1H, d, J 15.5), 4.62 (2H, s), 3.91 (2H, t, J 5.5), 2.68-2.61 (2H, m), 2.37 (3H,
s; $^{13}$C NMR (126 MHz, $d_6$-DMSO) $\delta$ 185.9, 151.8, 138.7, 137.8, 130.8 (2C), 129.0 (br. s), 127.2, 127.0, 123.2 (2C, q, $J_{C-F}$ 272.0), 123.0-122.7 (m), 66.5, 63.6, 28.9, 13.4; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -63.0 (6F, s); LRMS (ESI) m/z 815 (100%, [2M+Na]$^+$), 419 (20%, [M+Na]$^+$), 397 (30%, [M+H]$^+$); HRMS (ESI) found m/z 419.0513 ([M+Na]$^+$), C$_{17}$H$_{14}$F$_6$NaOS$^+$ requires 419.0511; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3093, 2961, 2921, 2851, 1650, 1597, 1514.

(E)-3,5-bis(Trifluoromethyl)phenyl)-1-(2-ethylthio)cyclohexyl)prop-2-en-1-one (3s)

Prepared according to General Procedure C using 2-(ethylthio)cyclohexanecarbaldehyde (77 mg, 0.30 mmol, 9:1 anti:syn), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)$_2$]BF$_4$ (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 1.5 h. Purification by flash chromatography (5% Et$_2$O/petrol) afforded the title compound 3s as an off-white solid (95 mg, 80%). This was obtained as an inseparable mixture of diastereomers (9:1 anti:syn). m.p. (CH$_2$Cl$_2$) 66-68 °C; LRMS (ESI) m/z 843 (100%, [2M+Na]$^+$), 433 (40%, [M+Na]$^+$), 411 (30%, [M+H]$^+$); HRMS (ESI) found m/z 433.1027 ([M+Na]$^+$), C$_{19}$H$_{20}$F$_6$NaOS$^+$ requires 433.1031; $\nu_{\text{max}}$ (neat)/cm$^{-1}$ 3049, 2935, 2859, 1689, 1664, 1609.

Anti diastereomer: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.98 (2H, s), 7.87 (1H, s), 7.63 (1H, d, J 16.0), 6.93 (1H, d, J 16.0), 2.95-2.82 (2H, m), 2.60-2.51 (2H, m), 2.26-2.16 (1H, m), 1.92-1.87 (1H, m) 1.86-1.75 (2H, m), 1.53-1.23 (4H, m), 1.20 (3H, t, J 7.5); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 201.5, 138.8, 136.9, 132.4 (2C, q, $J_{C-F}$ 33.5), 129.1, 127.9 (2C. app. d, $J_{C-F}$ 3.0), 123.2 (app. quin, $J_{C-F}$ 4.0), 123.0 (2C, q, $J_{C-F}$ 273.0), 58.8, 44.1, 34.3, 30.5, 26.0, 25.5, 24.9, 14.9; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -63.1 (6F, s.).

The following NMR signals are consistent with the syn diastereomer: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.96 (2H, s), 7.64 (1H, d, J 16.0), 7.05 (1H, d, J 16.0), 2.39-2.32 (1H, m), 2.10-2.03 (1H, m), 1.69-1.64 (1H, m), 1.17 (3H, t, J 7.5); $^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 199.2, 138.4, 137.0, 127.7 (2C, d, $J_{C-F}$ 5.0), 126.8, 123.2 (app. quin, $J_{C-F}$ 4.0), 53.1, 44.6, 31.9, 29.7, 26.4, 24.2, 23.0, 14.8; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -63.1 (6F, s).
(E)-1-(3,5-bis(Trifluoromethyl)phenyl)-5-(ethylthio)-4-methylpent-1-en-3-one (3t)

 Prepared according to General Procedure C using 3-(ethylthio)-2-methylpropanal (33 mg, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)2]BF4 (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 4 h. Purification by flash chromatography (5% Et2O/petrol) afforded the title compound 3t as a pale yellow oily solid (60 mg, 54%).

\[
\begin{align*}
\text{MeS} & \quad \text{O} \\
& \quad \text{CF}\_3 \\
& \quad \text{CF}\_3
\end{align*}
\]

\[\delta 7.98 (2H, s), 7.89 (1H, s), 7.65 (1H, d, J 16.0), 6.94 (1H, d, J 16.0), 3.15-3.04 (1H, m), 2.95 (1H, dd, J 13.0, 7.5), 2.66-2.53 (3H, m), 1.32-1.23 (6H, m); \]

\[\text{^1}^3\text{C NMR (101 MHz, CDCl}_3\delta 201.2, 139.2, 136.7, 133.5 (2C, q, J_{C-F} 33.5), 127.9 (2C, br. s), 127.8, 123.5 (app. quin, J_{C-F} 3.0), 123.0 (2C, q, J_{C-F} 273.0), 45.6, 34.3, 26.9, 19.6, 14.7; \]

\[\text{^19}\text{F NMR (376 MHz, CDCl}_3\delta -63.0 (6F, s); LRMS (ESI) m/z 763 (95%, [2M+Na]^{+}), 409 (100%, [M+K]^{+}), 393 (40%, [M+Na]^{+}), 371 (25%, [M+H]^{+}); HRMS (ESI) found m/z 393.1710 [M+Na]^{+}, C_{16}H_{16}F_{6}NaOS^{+} requires 393.0718; \]

\[\nu_{\text{max}} \text{(neat)/cm}^{-1} 2975, 2931, 1694, 1688, 1614.\]

(E)-1-(3,5-bis(Trifluoromethyl)phenyl)-5-(methylthio)pent-1-en-3-one (3u)

 Prepared according to General Procedure C using 3-(methylthio)propionaldehyde (30 µL, 0.30 mmol), 1-ethynyl-3,5-bis(trifluoromethyl)benzene (80 µL, 0.45 mmol), [Rh(nbd)2]BF4 (5.6 mg, 0.015 mmol) and dcpe (6.3 mg, 0.015 mmol) in acetone (2.0 mL) at RT for 2.5 h. Purification by flash chromatography (5% EtOAc/petrol) afforded the title compound 3u as an off-white solid (85 mg, 82%).

\[
\begin{align*}
\text{MeS} & \quad \text{O} \\
& \quad \text{CF}\_3 \\
& \quad \text{CF}\_3
\end{align*}
\]

\[\delta 7.97 (2H, s), 7.89 (1H, s), 7.61 (1H, d, J 16.0), 6.88 (1H, d, J 16.0), 3.05-2.99 (2H, m), 2.88-2.82 (2H, m), 2.16 (3H, s); \]

\[\text{^1}^3\text{C NMR (101 MHz, CDCl}_3\delta 197.4, 139.0, \]

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136.6, 132.5 (2C, q, $J_{CF}$ 33.5), 128.7, 127.8 (2C, app. d, $J_{CF}$ 2.0), 123.5 (app. quin, $J_{CF}$ 3.0), 122.8 (2C, q, $J_{CF}$ 272.5), 40.3, 27.5, 14.7; $^{19}$F NMR (376 MHz, CDCl$_3$) $\delta$ -63.1 (6F, s); LRMS (ESI) $m/z$ 365 (100%, [M+Na]$^+$); HRMS (ESI) found $m/z$ 365.0401 ([M+Na]$^+$), C$_{14}$H$_{12}$F$_6$NaOS requires 365.0405; $\nu_{max}$ (neat)/cm$^{-1}$ 3044, 2961, 2934, 2888, 1697, 1612.
V. Spectral Data for Novel Compounds

$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
\( ^1H \) NMR (400 MHz, CDCl\(_3\))

\( ^{13}C \) NMR (101 MHz, CDCl\(_3\))
H NMR (400 MHz, CDCl₃)

13C NMR (101 MHz, CDCl₃)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)

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$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (377 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CD$_2$Cl$_2$)

$^{13}$C NMR (101 MHz, CD$_2$Cl$_2$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)

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$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)
$^{1}H$ NMR (400 MHz, CDCl$_3$)

$^{13}C$ NMR (126 MHz, $d_{6}$-DMSO)

$^{19}F$ NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)
$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)

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$^1$H NMR (400 MHz, CDCl$_3$)

$^{13}$C NMR (101 MHz, CDCl$_3$)

$^{19}$F NMR (376 MHz, CDCl$_3$)