Sulphide as Leaving Group: Highly Stereoselective Bromination of Alkyl Phenyl Sulphides

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1. General remarks

$^1$H, $^{19}$F and $^{13}$C NMR spectra were recorded on a Bruker Avance 400 MHz spectrometer. Low-temperature 1D and 2D NMR spectra were recorded on an Agilent Technologies Ultra High Field (UHF) 800 MHz spectrometer or Agilent 400-MR Long Hold Mag. Res. spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvent signals for $^1$H and $^{13}$C NMR ($^1$H NMR: 7.26 ppm for CDCl$_3$, 1.94 ppm for CD$_3$CN, 5.32 ppm for CD$_2$Cl$_2$; $^{13}$C NMR: 77.00 ppm for CDCl$_3$, 1.32 ppm and 118.26 ppm for CD$_3$CN, 53.84 ppm for CD$_2$Cl$_2$). $^{13}$C NMR spectra were acquired with $^1$H broad band decoupled mode. Coupling constants (J) are in Hz. Melting points were measured using a Stuart scientific melting point apparatus and are uncorrected. Infrared spectra (IR) were recorded using a Nicolet iS 10 FT-IR spectrometer. Low resolution mass spectra were acquired with an Advion Expression CMS instrument. High resolution mass spectra were obtained on a Waters Micromass GCT Premier MS spectrometer or on a Bruker micrOTOF-Q III LC-MS spectrometer (APCI method). Elemental analysis was carried out using an Exeter Analytical CE 440 elemental analyser. Optical rotations were measured on a Perkin-Elmer 343 polarimeter. The enantiomeric excess (ee) was determined by chiral stationary phase HPLC using a Shimadzu SIL-20AHT HPLC instrument.

2. Materials

Analytical grade solvents and commercially available reagents were used as received. Dry CH$_2$Cl$_2$, DCE, toluene, MeCN and Et$_2$O were purchased from commercial sources. Dry THF was obtained from an Inert Pure Solv Micro drying solvent system. Reactions were monitored by TLC analysis (Merck, aluminum plates, silica gel 60 F$_{254}$) and/or $^1$H NMR spectroscopy. Flash column chromatography was performed using silica gel 60 (0.040-0.063 mm, 230-400 mesh). Cinnamate esters,$^1$ 1,1,1,3,3,3-hexafluoropropan-2-yl cinnamates and optically active sulphides (S)-1aa, (S)-1ba, (S)-1da and (S)-1ea were prepared according to published procedures.$^2$ Methyl 3-hydroxy-3-phenylpropanoate and ethyl 3-(4-chlorophenyl)-3-hydroxypropanoate,$^3$ sulphides 1a, 1c, 1d, 1i, 1m, 1s, 1t, 1x, 1za and 1zb,$^4$ 1j and 1k,$^2$ 1l,$^5$ 1n and 1o,$^6$ 1p,$^7$ 1q$^8$ and 1y$^9$ were synthesized according to literature procedures.
3. Reaction of sulphide (1a) with Cl₂ gas

![Chemical structure]

Cl₂ gas was bubbled into a stirred solution of 1a (136 mg, 0.5 mmol) in dry CH₂Cl₂ (3 mL) (ca. 5 bubbles/sec) under N₂ atmosphere. The reaction was stirred for 3 minutes, quenched with styrene (86 μL, 78 mg, 0.75 mmol, 1.5 equiv) and the solvent removed in vacuo. A ¹H NMR spectrum of the residue was recorded to determine the composition of the crude material, which indicated the complete consumption of 1a and the presence of chloride 2a and dehydrochlorinated 3a in a ratio of 70:30.

4. Deoxybromination of β-hydroxy esters

4.1 Dehydroxybromination of methyl 3-hydroxy-3-phenylpropanoate under Appel conditions

![Chemical structure]

Standard conditions for the Appel reaction were followed.¹⁰ A solution of methyl 3-hydroxy-3-phenylpropanoate (90 mg, 0.5 mmol) and tetrabromomethane (166 mg, 0.5 mmol, 1.0 equiv) in dry CH₂Cl₂ (5.0 mL) was cooled to 0 °C, and triphenylphosphine (131 mg, 0.5 mmol, 1.0 equiv) was added portion-wise. The reaction mixture was allowed to reach rt and stirred for 24 h (TLC analysis), then the reaction mixture was evaporated in vacuo. A ¹H NMR spectrum of the residue showed the formation of 4a and 3a in a ratio of 82:18.
4.2 Deoxybromination of ethyl 3-(4-chlorophenyl)-3-hydroxypropanoate with PBr₃

The deoxybromination procedure with PBr₃ was repeated according to A. Sudalai et al.¹¹ In our hands, the ¹H NMR spectrum of the crude material showed the formation of a product mixture containing around 42% of bromide 4da.

\[
\text{Cl} = \text{OEt} \quad \xrightarrow{\text{PBr}_3 \ (1.1 \ \text{equiv})} \quad \text{Br} = \text{OEt} + \text{Cl} = \text{OEt}
\]
5. Preparation of sulphides

5.1 General procedure for the reduction of β-sulphido esters (GP1)

\[
\text{Ar-}S\text{Ph-OEt} \xrightarrow{\text{LiAlH}_4 (0.5 \text{ equiv})} \text{Ar-}S\text{Ph-OH}
\]

To a stirred solution of sulphide (2.0 mmol) in dry THF (4.0 mL) was added dropwise via syringe LiAlH\(_4\) (1.0 mL, 1.0 M solution in Et\(_2\)O, 1.0 mmol, 0.5 equiv) at 0 °C. The reaction mixture was allowed to reach rt and stirred until consumption of the starting material was observed by TLC analysis, then carefully quenched with sat. aq. soln of NH\(_4\)Cl (10 mL) and extracted with Et\(_2\)O (3 x 10 mL). The combined organic layers were dried over Na\(_2\)SO\(_4\) and the solvent removed \textit{in vacuo} to obtain the corresponding alcohol, which was used without further purification.

3-(Phenylthio)-3-(thiophen-2-yl)propan-1-ol

Prepared according to GP1. The reaction was completed in 2 h. The title compound was obtained as a yellow oil (425 mg, 85% yield). IR (neat, cm\(^{-1}\)): \(\nu\) 3331, 3071, 2930, 1473, 1125, 1042, 954. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.79 (br s, 1H), 2.15–2.25 (m, 2H), 3.62–3.68 (m, 1H), 3.80 (dt, \(J = 11.3, 5.8\) Hz, 1H), 4.65 (virt t, \(J = 7.6\) Hz, 1H), 6.75 (d, \(J = 3.5\) Hz, 1H), 6.82 (dd, \(J = 5.1, 3.5\) Hz, 1H), 7.16 (dd, \(J = 5.1, 0.9\) Hz, 1H), 7.19–7.26 (m, 2H), 7.27–7.32 (m, 3H). \(^1\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 39.6, 45.4, 60.1, 124.5, 125.3, 126.3, 127.5, 128.7, 132.8, 134.0, 146.0. HRMS (EI): C\(_{13}\)H\(_{14}\)OS\(_2\)Na [M + Na\(^+\)] calculated: 273.0384, found: 273.0390.

3-(2,4,5-Trifluorophenyl)-3-(phenylthio)propan-1-ol (1u)

Prepared according to GP1. The reaction was completed in 16 h. The title compound was isolated as a pale yellow oil (528 mg, 89% yield). IR (neat, cm\(^{-1}\)): \(\nu\) 3487, 3362, 3100, 2856, 1469, 1123, 978. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.46 (br s, 1H), 2.02–2.10 (m, 1H), 2.16–2.24 (m, 1H), 3.65 (virt dt, \(J = 11.3, 6.3\) Hz, 1H), 3.81 (virt dt, \(J = 11.5, 5.9\) Hz, 1H), 4.69 (virt t, \(J = 7.6\) Hz, 1H), 6.82 (virt dt, \(J = 9.7, 6.6\) Hz, 1H), 7.15 (ddd, \(J = 10.8, 8.7, 6.9\) Hz, 1H), 7.20–7.30 (m, 5H). \(^1\)F NMR (376 MHz, CDCl\(_3\)): \(\delta\) –119.6 (dd, \(J = 15.2, 3.8\) Hz), –134.7 (dd, \(J = 21.7, 3.8\) Hz), –141.9 (dd, \(J = 21.7, 15.1\) Hz). \(^1\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 37.9, 41.8, 60.1,
105.3 (dd, $J = 28.8, 20.7$ Hz), 116.6 (dd, $J = 19.9, 5.2$ Hz), 125.7 (dt, $J = 16.0, 4.6$ Hz), 127.8, 128.9, 132.6, 133.3, 146.9 (ddd, $J = 244.9, 12.6, 3.4$ Hz), 148.8 (ddd, $J = 251.2, 14.5, 12.6$ Hz), 155.2 (ddd, $J = 245.3, 9.3, 2.7$ Hz). HRMS (EI): $\text{C}_{15}\text{H}_{13}\text{F}_3\text{OSNa}$ [M + Na]$^+$ calculated: 321.0537, found: 321.0525.

### 5.2 General procedure for the preparation of β-sulphido mesylates (GP2)$^4$

![Chemical Reaction](attachment:image.png)

To a stirred solution of the sulphido alcohol (2.0 mmol) and methanesulphonyl chloride (260 µL, 321 mg, 2.8 mmol, 1.4 equiv) in CH$_2$Cl$_2$ (5.0 mL) was added dropwise triethylamine (467 µL, 339 mg, 3.4 mmol, 1.4 equiv) at 0 °C. The reaction mixture was allowed to reach rt and stirred until consumption of the starting material was observed by TLC analysis, then diluted with H$_2$O (10 mL) and extracted with CH$_2$Cl$_2$ (3 x 10 mL). The combined organic layers were washed with H$_2$O (3 x 10 mL), brine and dried over Na$_2$SO$_4$. The solvent was removed in vacuo and the crude mixture was purified by flash column chromatography on silica gel to afford the corresponding methanesulphonate.

### (2,4,5-Trifluorophenyl)-3-(phenylthio)propyl methansulphonate (1v)

Prepared according to GP2. The reaction was completed in 16 h. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 80:20) as a brown oil (568 mg, 91% yield). IR (neat, cm$^{-1}$): ν 3029, 3015, 2659, 1629, 1510, 1353, 1331, 1170, 797, 525. $^1$H NMR (400 MHz, CDCl$_3$): δ 2.21–2.30 (m, 1H), 2.32–2.41 (m, 1H), 2.96 (s, 3H), 4.20 (ddd, $J = 10.3, 6.4, 5.7$ Hz, 1H), 4.39 (ddd, $J = 10.3, 6.7, 5.6$ Hz, 1H), 4.58 (virt t, $J = 7.6, 1$H), 6.86 (virt dt, $J = 9.7, 6.6$ Hz, 1H), 7.09 (ddd, $J = 10.7, 8.6, 6.8$ Hz, 1H), 7.21–7.31 (m, 5H). $^{19}$F NMR (376 MHz, CDCl$_3$): δ −119.1 (dd, $J = 15.2, 3.2$ Hz), −133.8 (dd, $J = 21.6, 2.0$ Hz), −141.4 (dd, $J = 26.3, 10.5$ Hz). $^{13}$C NMR (101 MHz, CDCl$_3$): δ 34.4, 37.3, 41.5, 66.7, 105.6 (dd, $J = 28.7, 20.8$ Hz), 116.5 (dd, $J = 20.0, 5.0$ Hz), 124.6 (dd, $J = 15.8, 4.6$ Hz), 128.2, 129.1, 132.4, 133.1, 146.9 (ddd, $J = 245.6, 12.6, 3.5$ Hz), 149.1 (ddd, $J = 252.0, 14.5, 12.6$ Hz), 155.2 (ddd, $J = 246.0, 9.3, 2.6$ Hz). HRMS (EI): $\text{C}_{16}\text{H}_{15}\text{F}_3\text{O}_3\text{S}_2\text{Na}$ [M + Na]$^+$ calculated: 399.0312, found: 399.0309.
3-(Phenylthio)-3-(thiophen-2-yl)propyl methanesulphonate (1w)

Prepared according to GP-2. The reaction was completed in 3 h. The title compound was isolated by flash column chromatography (silica gel; CH$_2$Cl$_2$) as a yellow oil (636 mg, 97% yield). IR (neat, cm$^{-1}$): $\nu$ 3020, 2935, 1566, 1351, 1169, 961. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.28-2.49 (m, 2H), 2.94 (s, 3H), 4.22 (ddd, $J$ = 10.1, 7.3, 5.2 Hz, 1H), 4.40 (virt dt, $J$ = 10.2, 5.8 Hz, 1H), 4.59 (virt t, $J$ = 7.2 Hz, 1H), 6.78 (d, $J$ = 3.2 Hz, 1H), 6.86 (dd, $J$ = 5.1, 3.5 Hz, 1H), 7.21 (dd, $J$ = 5.1, 0.8 Hz, 1H), 7.23-7.28 (m, 3H), 7.28-7.38 (m, 2H).

5.3 General procedure for the sulpha-Michael addition to cinnamate esters (GP3)

Thiophenol (337 $\mu$L, 364 mg, 3.3 mmol, 1.1 equiv) and triethylamine (42 $\mu$L, 30 mg, 0.3 mmol, 0.1 equiv) were added to the cinnamate ester (3.0 mmol) and the reaction mixture was stirred at rt until complete consumption of the starting material was observed by TLC analysis (9-48 h). The reaction mixture was purified directly by flash column chromatography on silica gel to afford the sulpha-Michael adduct.

Methyl 3-(phenylthio)-3-(o-tolyl)propanoate (1b)

Prepared according GP3. The reaction was completed in 16 h. The title compound was isolated by flash chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a pale yellow oil (566 mg, 66% yield). IR (neat, cm$^{-1}$): $\nu$ 3025, 2925, 2910, 1787, 1599, 1503, 1271, 759, 651. $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 2.40 (s, 3H), 2.98 (m, 2H), 3.55 (s, 3H), 4.87 (virt t, $J$ = 7.7 Hz, 1H), 7.09-7.18 (m, 4H), 7.22-7.27 (m, 3H), 7.28-7.35 (m, 2H). $^{13}$C NMR (101 MHz, CDCl$_3$): $\delta$ 19.4, 40.2, 44.6, 51.8, 126.2, 126.3, 127.4, 128.0, 128.8, 130.5, 133.4, 133.9, 136.1, 138.1, 171.4. HRMS (EI): C$_{17}$H$_{18}$O$_2$SNa [M + Na]$^+$ calculated: 309.0931, found: 309.0925.
Methyl 3-(phenylthio)-3-[4-(trifluoromethyl)phenyl]propanoate (1e)

Prepared according to GP3. Reaction was completed in 16 h. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a white solid (989 mg, 97% yield). Mp: 91–93 °C. IR (neat, cm⁻¹): ν 3019, 2854, 1710, 1564, 1389, 1354, 1015, 758. ¹H NMR (400 MHz, CDCl₃) δ 2.92 (dd, J = 16.0, 8.6 Hz, 1H), 3.00 (dd, J = 16.0, 6.9 Hz, 1H), 3.61 (s, 3H), 4.66 (dd, J = 8.3, 7.2 Hz, 1H), 7.21–7.31 (m, 5H), 7.34 (d, J = 8.2 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 40.3, 48.7, 51.9, 124.0 (q, J = 272.0 Hz), 125.4 (q, J = 3.8 Hz), 128.0, 128.2, 129.0, 129.6 (q, J = 32.4 Hz), 132.7, 133.6, 144.7, 170.8. HRMS (EI): C₁₇H₁₅F₃O₂SNa [M + Na]⁺: calculated: 363.0643, found: 363.0658.

Methyl 3-(4-formylphenyl)-3-(phenylthio)propanoate (1f)

Prepared according to GP3. The reaction was completed in 24 h. The title compound was isolated by flash column chromatography (silica gel; CH₂Cl₂) as a pale yellow oil (792 mg, 88% yield). IR (neat, cm⁻¹): ν 3019, 2979, 2359, 1730, 1211, 1674, 689. ¹H NMR (400 MHz, CDCl₃): δ 2.94 (dd, J = 16.0, 8.5 Hz, 1H), 3.02 (dd, J = 16.0, 7.0 Hz, 1H), 3.61 (s, 3H), 4.67 (dd, J = 8.3, 7.2 Hz, 1H), 7.19–7.31 (m, 5H), 7.37 (d, J = 8.2 Hz, 2H), 7.77 (d, J = 8.2 Hz, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 40.0, 48.9, 51.9, 128.2, 128.3, 128.9, 129.8, 132.5, 133.8, 135.5, 147.5, 170.7, 191.6. HRMS (EI): C₁₇H₁₆O₃SNa [M + Na]⁺: calculated: 323.0718, found: 323.0720.

Methyl 3-(3-nitrophenyl)-3-(phenylthio)propanoate (1g)

Prepared according to GP3. The reaction was completed in 22 h. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc 90:10) as a white solid (718 mg, 84% yield). Mp: 67–69 °C. IR (neat, cm⁻¹): ν 3067, 2961, 2924, 1722, 1578, 1470, 1352, 1218, 1147, 987, 753. ¹H NMR (400 MHz, CDCl₃): δ 2.95 (dd, J = 16.2, 8.8 Hz, 1H), 3.04 (dd, J = 16.2, 6.7 Hz, 1H), 3.62 (s, 3H), 4.70 (dd, J = 8.7, 6.8 Hz, 1H), 7.20–7.34 (m, 5H), 7.41–7.45 (m, 1H), 7.54–7.56 (m, 1H), 8.05–8.10 (m, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 40.1, 48.5, 52.0, 122.5, 128.5, 129.1, 129.3, 132.2, 133.9, 133.9, 142.9, 170.6. HRMS (EI): C₁₆H₁₄NO₄SNa [M + Na]⁺ calculated: 340.0612, found: 340.0619.
Ethyl 3-[(3,5-bis(trifluoromethyl)phenyl)-3-(phenylthio)propanoate (1h)

Prepared according to GP3. Reaction was completed in 48 h. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/CH2Cl2, 80:20) as a pale yellow oil (974 mg, 77% yield). IR (neat, cm⁻¹): ν 3001, 2983, 1732, 1275, 1168, 1125, 681. 1H NMR (400 MHz, CDCl3): δ 1.17 (t, J = 7.1 Hz, 3H), 2.92 (dd, J = 16.0, 8.8 Hz, 1H), 3.04 (dd, J = 16.0, 6.8 Hz, 1H), 4.02–4.13 (m, 2H), 4.68 (dd, J = 8.8, 6.8 Hz, 1H), 7.20–7.34 (m, 5H), 7.57 (s, 2H), 7.71 (s, 1H). 19F NMR (376 MHz, CDCl3): δ –62.9. 13C NMR (101 MHz, CDCl3): δ 13.9, 40.0, 48.6, 61.1, 121.3 (hept, J = 3.7 Hz), 123.1 (q, J = 272.8 Hz), 127.8 (q, J = 2.8 Hz), 128.8, 129.1, 131.5 (q, J = 33.4 Hz), 131.6, 134.4, 143.4, 169.9. HRMS (EI): C19H16F6O2SNa [M + Na]+ calculated: 445.0673, found: 445.0670.

Ethyl 3-(phenythio)-3-(thiophen-2-yl)propanoate

Prepared according to GP3. The reaction was completed in 9 h. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a yellow oil (900 mg, 56% yield). IR (neat, cm⁻¹): ν 3010, 2979, 1730, 1211, 1146, 1024, 689. 1H NMR (400 MHz, CDCl3): δ 1.20 (t, J = 7.1 Hz, 3H), 2.94 (dd, J = 16.2, 8.0 Hz, 1H), 2.98 (dd, J = 16.5, 7.6 Hz, 1H), 4.01-4.19 (m, 2H), 4.92 (virt t, J = 7.6 Hz, 1H), 6.78 (d, J = 3.3 Hz, 1H), 6.83–6.85 (m, 1H), 7.18 (dd, J = 5.1, 1.0 Hz, 1H), 7.23–7.30 (m, 3H), 7.31–7.39 (m, 2H). 13C NMR (101 MHz, CDCl3): δ 14.1, 42.0, 44.6, 60.9, 124.7, 125.3, 126.4, 128.1, 128.9, 133.1, 133.6, 144.6, 170.4. HRMS (EI): C15H16O2S2Na [M + Na]+ calculated: 315.0481, found: 315.0489.

5.4 Synthesis of 3-(4-chlorophenyl)-3-(phenythio)propanenitrile (1r)

Thiophenol (919 μL, 990 mg, 9.0 mmol, 3.0 equiv) and DIPEA (52 μL, 39 mg, 0.3 mmol, 0.1 equiv) were added to 3-(4-chlorophenyl)acrylonitrile (489 mg, 3.0 mmol) and the reaction mixture was stirred at 120 °C until complete consumption of the starting material was observed by TLC analysis (24 h). The reaction mixture was directly purified by flash chromatography (silica gel; petroleum ether/EtOAc 95:5) to afford the title compound as a white solid (779 mg,
95% yield). Mp: 80–81 °C. IR (neat, cm⁻¹): ν 2979, 1730, 1489, 1211, 1146, 1024, 689. \(^1\)H NMR (400 MHz, CDCl₃) δ 2.84 (dd, \(J = 16.6, 8.1\) Hz, 1H), 2.90 (dd, \(J = 16.6, 5.9\) Hz, 1H), 4.38 (dd, \(J = 8.1, 5.9\) Hz, 1H), 7.24–7.39 (m, 9H). \(^{13}\)C NMR (101 MHz, CDCl₃) δ 24.9, 48.6, 116.9, 128.8, 128.9, 129.1, 129.3, 131.9, 133.9, 134.3, 136.8. HRMS (EI): C₁₅H₁₂ClINSNa [M + Na]+ calculated: 296.0277, found: 296.0275.

6. Bromination of sulphides with Br₂

6.1 General procedure for bromination of sulphides

To a stirred solution of sulphide 1 (0.5 mmol) in dry CH₂Cl₂ (3.0 mL) was added Br₂ (500 µL, 1.0 M in CH₂Cl₂, 0.5 mmol, 1.0 equiv) at rt under N₂ atmosphere and the reaction progress was monitored by \(^1\)H NMR analysis using a stock solution of styrene in CDCl₃ (0.03 M). After the consumption of the starting material (4 min-48 h), the reaction mixture was quenched by either the addition of styrene (68 µL, 0.6 mmol, 1.2 equiv) or a sat. aq. soln of Na₂S₂O₃, which led to an immediate fading of the red colour. After the evaporation of the solvents or aqueous work up, the residue was purified by flash column chromatography to afford the corresponding bromide.

Products that precipitated from the reaction mixture were purified by either recrystallization or trituration.

An analogous procedure was followed for slow-reacting substrates (sulphides 1g-i, 1o) using a 1.0 M Br₂ solution in DCE, DCE as solvent and a reaction temperature of 50 °C.

Methyl 3-bromo-3-phenylpropanoate (4a)

4a

Reaction was quenched with styrene after 25 min. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc 95:5) as a yellow oil (115 mg, 95% yield). All analytical data are consistent with those reported in the literature.\(^{12}\)
**Methyl 3-bromo-3-(o-tolyl)propanoate (4b)**

Reaction was quenched with styrene after 25 min. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 96:4) as a yellow oil (112 mg, 87% yield). IR (neat, cm\(^{-1}\)): \(\nu\) 3011, 2951, 1736, 1435, 1200, 761, 627. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 2.45 (s, 3H), 3.26 (dd, \(J = 16.4, 6.0\) Hz, 1H), 3.43 (dd, \(J = 16.4, 9.0\) Hz, 1H), 3.70 (s, 3H), 5.64 (dd, \(J = 9.0, 6.0\) Hz, 1H), 7.13–7.27 (m, 3H), 7.39–7.45 (m, 1H). \(^13\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 19.1, 43.5, 44.3, 52.1, 126.1, 126.7, 128.6, 130.8, 135.7, 138.5, 170.3. HRMS (APCI): \(C_{11}H_{14}BrO_2\) [M + H]\(^+\) calculated: 257.0177, found: 257.0179. Anal. Calcd for \(C_{11}H_{13}BrO_2\): C, 51.38; H, 5.10. Found: C, 51.31; H, 5.13.

**Ethyl 3-bromo-3-(p-tolyl)propanoate (4c)**

Reaction was quenched with styrene after 25 min. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 97:3) as a yellow oil (115 mg, 84% yield). IR (neat, cm\(^{-1}\)): \(\nu\) 2924, 1734, 1374, 1184, 1018, 734, 515. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 1.24 (t, \(J = 7.1\) Hz, 3H), 2.34 (s, 3H), 3.19 (dd, \(J = 16.1, 6.2\) Hz, 1H), 3.34 (dd, \(J = 16.1, 9.0\) Hz, 1H), 4.06–4.25 (m, 2H), 5.41 (dd, \(J = 9.0, 6.2\) Hz, 1H), 7.16 (d, \(J = 8.1\) Hz, 2H), 7.32 (d, \(J = 8.1\) Hz, 2H). \(^13\)C NMR (101 MHz, CDCl\(_3\)): \(\delta\) 14.1, 21.1, 44.8, 48.2, 60.1, 127.0, 129.4, 137.8, 138.7, 169.7. HRMS (APCI): \(C_{12}H_{16}BrO_2\) [M + H]\(^+\) calculated: 271.0334, found: 271.0347. Anal. Calcd for \(C_{12}H_{15}BrO_2\): C, 53.16; H, 5.58. Found: C, 53.11; H, 5.50.

**Methyl 3-bromo-3-(4-chlorophenyl)propanoate (4d)**

Reaction was quenched with styrene after 25 min. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 96:4) as a yellow oil (135 mg, 97% yield). All analytical data are consistent with those reported in the literature.\(^13\)

**Methyl 3-bromo-3-(4-(trifluoromethyl)phenyl)propanoate (4e)**

The reaction was performed at double concentration (1.5 mL of dry CH\(_2\)Cl\(_2\)) and quenched with styrene after 48 h. The title compound was isolated by flash chromatography (silica gel; petroleum ether/CH\(_2\)Cl\(_2\), 60:40) as a yellow oil (148 mg, 95% yield). IR (neat,


Methyl 3-bromo-3-(4-formylphenyl)propanoate (4f)

The reaction was performed at double concentration (1.5 mL of dry CH₂Cl₂) and quenched with styrene after 4 h. The title compound was isolated by flash column chromatography (silica gel; CH₂Cl₂) as a yellow oil (123 mg, 90% yield). IR (neat, cm⁻¹):υ 3012, 2953, 1732, 1527, 1347, 1024, 683. ¹H NMR (400 MHz, CDCl₃): δ 3.25 (dd, J = 16.4, 6.7 Hz, 1H), 3.36 (dd, J = 16.4, 8.5 Hz, 1H), 3.70 (s, 3H), 5.42 (dd, J = 8.3, 6.9 Hz, 1H), 7.60 (d, J = 8.2 Hz, 2H), 7.87 (d, J = 8.2 Hz, 2H), 10.01 (s, 1H). ¹³C NMR (101 MHz, CDCl₃): δ 44.1, 46.1, 52.1, 127.9, 130.1, 136.3, 146.9, 169.6, 191.3. HRMS (APCI): C₁₁H₁₁⁷⁹BrO₃ [M + H]+ calculated: 270.9972, found: 270.9964. Anal. Calcd for C₁₁H₁₁BrO₃: C, 48.73; H, 4.22. Found: C, 48.60; H, 4.05.

Methyl 3-bromo-3-(3-nitrophenyl)propanoate (4g)

The reaction was performed in dry DCE (3.0 mL) at 50 °C, using Br₂ (0.5 mL, 1.0 M in DCE, 0.5 mmol, 1.0 equiv) and quenched with styrene after 2 h. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/CH₂Cl₂, 70:30) as a yellow solid (129 mg, 90% yield). Mp: 84-86 °C. IR (neat, cm⁻¹): υ 3012, 2953, 1732, 1347, 1024, 683. ¹H NMR (400 MHz, CDCl₃): δ 3.26 (dd, J = 16.5, 7.0 Hz, 1H), 3.38 (dd, J = 16.5, 8.2 Hz, 1H), 3.71 (s, 3H), 5.43 (dd, J = 8.2, 7.0 Hz, 1H), 7.55 (t, J = 8.0 Hz, 1H), 7.76 (d, J = 7.8 Hz, 1H), 8.10–8.21 (m, 1H), 8.29 (t, J = 1.8 Hz, 1H). ¹³C NMR (101 MHz, CDCl₃): δ 44.2, 45.1, 52.3, 122.2, 123.6, 129.9, 133.4, 142.8, 148.3, 169.5. HRMS (APCI): C₁₀H₁₀⁷⁹BrNO₄ [M + H]+ calculated: 287.9874, found: 287.9866. Anal. Calcd for C₁₀H₁₀BrNO₄: C, 41.69; H, 3.53; N, 4.86. Found: C, 41.54; H, 3.53; N, 4.53.
Ethyl 3-[3,5-bis(trifluoromethyl)phenyl]-3-bromopropanoate (4h)

The reaction was performed in dry DCE (3.0 mL) at 50 °C, using Br₂ (1.0 mL, 1.0 M in DCE, 1.0 mmol, 2.0 equiv) and quenched with styrene after 2 h. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/CH₂Cl₂ 70:30) as a colourless oil (175 mg, 89% yield). IR (neat, cm⁻¹): ν 3011, 2958, 2545, 1734, 1373, 1275, 1066, 727, 591. ¹H NMR (400 MHz, CDCl₃): δ 1.23 (t, J = 7.1 Hz, 3H), 3.23 (dd, J = 16.4, 7.1 Hz, 1H), 3.36 (dd, J = 16.4, 8.2 Hz, 1H), 4.08–4.23 (m, 2H), 5.43 (virt t, J = 7.6 Hz, 1H), 7.83 (s, 1H), 7.88 (s, 2H). ¹³C NMR (101 MHz, CDCl₃): δ 14.0, 44.5, 44.7, 61.4, 122.6 (hept, J = 3.7 Hz), 122.9 (q, J = 27.29 Hz), 127.6, 132.3 (q, J = 33.6 Hz), 143.3, 168.8. LRMS (ESI): m/z (%) 393 (100) [M]⁺. Anal. Calcd for C₁₃H₁₁BrF₆O₂: C, 39.72; H, 2.82. Found: C, 39.68; H, 2.89.

Ethyl bromo-3-(2,4,5-trifluorophenyl)propanoate (4i)

The reaction was performed in dry DCE (3.0 mL) at 50 °C, using Br₂ (0.6 mL, 1.0 M in DCE, 0.6 mmol, 1.2 equiv), stirred for 16 h and then quenched with styrene. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/CH₂Cl₂ 70:30) as a pale yellow oil (578 mg, 93% yield). IR (neat, cm⁻¹): ν 2921, 2852, 1734, 1514, 1336, 1110, 887, 527. ¹H NMR (400 MHz, CDCl₃): δ 1.24 (t, J = 7.1 Hz, 3H), 3.19 (dd, J = 16.4, 7.0 Hz, 1H), 3.31 (dd, J = 16.4, 8.3 Hz, 1H), 4.10–4.23 (m, 2H), 5.56 (virt t, J = 7.7 Hz, 1H), 6.94 (virt dt, J = 9.7, 6.5 Hz, 1H), 7.29 (ddt, J = 10.3, 8.4, 6.8 Hz, 1H). ¹⁹F NMR (376 MHz, CDCl₃): δ –117.1 (dd, J = 15.1, 4.8 Hz), –131.8 (dd, J = 21.4, 4.8 Hz), –140.9 (dd, J = 21.4, 15.1 Hz). ¹³C NMR (101 MHz, CDCl₃): δ 14.0, 38.1 (d, J = 2.9 Hz), 43.6, 61.3, 106.1 (dd, J = 28.0, 20.9 Hz), 116.6 (ddd, J = 20.2, 4.4, 1.5 Hz), 124.6 (ddd, J = 15.2, 7.1, 2.5 Hz), 146.9 (ddd, J = 246.3, 12.8, 3.6 Hz), 150.1 (ddd, J = 253.9, 14.3, 12.5 Hz), 154.6 (ddd, J = 249.2, 9.4, 2.7 Hz), 169.0. LRMS (ESI): m/z (%) 311 (50) [M]⁺. Anal. Calcd for C₁₁H₁₀BrF₃O₂: C, 42.47; H, 3.24. Found: C, 42.39; H, 3.20.

1,1,1,3,3,3-Hexafluoropropan-2-yl 3-bromo-3-phenylpropanoate (4j)

Reaction was quenched with styrene after 90 min. The title compound was isolated as an inseparable mixture with 1,1,1,3,3,3-hexafluoropropan-2-yl cinnamate (8%) by flash column chromatography (silica gel; petroleum ether/CH₂Cl₂ 90:10) as a pale
yellow oil (174 mg, 90%). $^1$H NMR (400 MHz, CDCl$_3$): δ 3.44 (dd, $J = 16.5$, 6.3 Hz, 1H), 3.56 (dd, $J = 16.5$, 9.0 Hz, 1H), 5.38 (dd, $J = 9.0$, 6.3 Hz, 1H), 5.74 (hept, $J = 6.0$ Hz, 1H), 7.31–7.39 (m, 3H), 7.40–7.46 (m, 2H). $^{19}$F NMR (376 MHz, CDCl$_3$): δ –73.2.

$^{13}$C NMR (101 MHz, CDCl$_3$): δ 43.9, 45.9, 66.7 (hept, $J = 34.9$ Hz), 120.2 (q, $J = 281.9$ Hz), 127.0, 129.0, 129.2, 139.7, 166.5.

$N$-Benzyl-3-bromo-3-phenylpropanamide (4k)

[N-Benzyl-3-bromo-3-phenylpropanamide (4k)]

Reaction was quenched with styrene after 30 min. The title compound was isolated by flash column chromatography (silica gel; CH$_2$Cl$_2$/EtOAc, 90:10) as a white solid (130 mg, 81% yield). Mp: 127–129 °C. IR (neat, cm$^{-1}$): ν 3263, 3089, 2965, 1635, 1567, 691, 582.

$^1$H NMR (400 MHz, CDCl$_3$): δ 3.07 (dd, $J = 14.7$, 5.9 Hz, 1H), 3.16 (dd, $J = 14.7$, 8.9 Hz, 1H), 4.43 (d, $J = 5.7$ Hz, 2H), 5.52 (dd, $J = 8.9$, 5.9 Hz, 1H), 5.81 (br s, 1H), 7.12–7.19 (m, 2H), 7.29–7.38 (m, 6H), 7.39–7.47 (m, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$): δ 43.7, 47.4, 49.4, 127.2, 127.6, 127.7, 128.7, 128.9, 129.0, 137.7, 141.0, 168.7. HRMS (APCI): C$_{16}$H$_{17}$BrNO [M + H]$^+$ calculated: 318.0483, found: 318.0488. Anal. Calcd for C$_{16}$H$_{16}$BrNO: C, 60.39; H, 5.07; N, 4.40. Found: C, 60.41; H, 5.00; N, 4.38.

3-Bromo-3-phenyl-1-(pyrrolidin-1-yl)propan-1-one (4l)

[3-Bromo-3-phenyl-1-(pyrrolidin-1-yl)propan-1-one (4l)]

Reaction was quenched with styrene after 30 min. The title compound was isolated by flash column chromatography (silica gel; CH$_2$Cl$_2$/EtOAc, 80:20) as a white solid (129 mg, 91% yield). Mp: 93–95 °C. IR (neat, cm$^{-1}$): ν 2989, 2870, 1626, 1440, 713, 605, 529.

$^1$H NMR (400 MHz, CDCl$_3$): δ 1.78–2.02 (m, 4H), 3.08 (dd, $J = 15.7$, 5.6 Hz, 1H), 3.36 (dd, $J = 15.5$, 8.8 Hz, 2H), 3.33–3.46 (m, 3H), 3.47–3.56 (m, 1H), 3.58 (dt, $J = 9.9$, 6.8 Hz, 1H), 5.58 (dd, $J = 8.7$, 5.6 Hz, 1H), 7.24–7.31 (m, 1H), 7.32–7.36 (m, 2H), 7.46 (d, $J = 7.3$ Hz, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$): δ 24.3, 26.0, 44.9, 45.8, 46.7, 49.7, 127.3, 128.4, 128.7, 141.6, 167.4. HRMS (APCI): C$_{13}$H$_{17}$BrNO [M + H]$^+$ calculated: 282.0493, found: 282.0488.

$S$-Phenyl 3-bromo-3-phenylpropanethioate (4m)

[S-Phenyl 3-bromo-3-phenylpropanethioate (4m)]

Reaction was quenched with styrene after 40 min. The title compound was isolated by flash chromatography column (silica gel; petroleum ether/CH$_2$Cl$_2$ 70:30) as a colourless oil (100 mg, 61% yield). IR (neat, cm$^{-1}$): ν 3189, 1856, 1667, 1485, 1423, 1148, 978, 699, 587. $^1$H NMR
(400 MHz, CDCl₃): δ 3.49 (dd, J = 15.9, 6.4 Hz, 1H), 3.66 (dd, J = 15.9, 8.6 Hz, 1H), 5.44 (dd, J = 8.5, 6.4 Hz, 1H), 7.28–7.46 (m, 10H). ¹³C (101 MHz, CDCl₃) δ 47.3, 52.6, 126.8, 127.3, 128.9, 128.9, 129.3, 129.7, 134.4, 140.3, 193.7. LRMS (ESI): m/z (%) 263 (15) [M + Na - Br]⁺. Anal. Calcd for C₁₅H₁₃BrOS: C, 56.09; H, 4.08. Found: C, 56.01; H, 4.05.

3-Bromo-3-phenylpropanoic acid (4n)

Reaction was quenched with styrene after 1 h. The title compound was obtained by trituration with cold n-hexane (2 x 5 mL) as an off-white solid (101 mg, 88% yield). All analytical data are consistent with those reported in the literature.¹⁴

3-Bromo-3-(4-nitrophenyl)propanoic acid (4o)

The reaction was performed in dry DCE (3.0 mL) at 50 °C, using Br₂ (1.0 mL, 1.0 M in DCE, 1.0 mmol, 2.0 equiv) and stirred for 7 h. Then the solvent was removed in vacuo. The title compound was obtained by trituration with n-hexane (2 x 5 mL) as an off-white solid (110 mg, 64% yield). Compound has been previously described in the literature without NMR data. Mp: 167-169 °C; lit.¹⁵: 169-171 °C. ¹H NMR (400 MHz, CD₃CN): δ 3.27–3.43 (m, 2H), 5.50 (vrit t, J = 7.4 Hz, 1H), 7.71 (d, J = 8.5 Hz, 2H), 8.20 (d, J = 8.4 Hz, 2H), 9.42 (s, 1H). ¹³C NMR (101 MHz, CD₃CN): δ 43.8, 46.9, 124.8, 129.4, 148.6, 149.1, 170.9.

3-Bromo-1,3-diphenyl-1-propanone (4p)

Reaction was quenched with sat. aq. soln of Na₂S₂O₃ (ca. 4 mL) after 4 min and stirred for a further 5 min. The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic phases were washed with H₂O, brine, dried over Na₂SO₄ and the solvent removed in vacuo. The title compound was obtained by recrystallization from Et₂O (ca. 6 mL) as a white solid (96 mg, 67% yield). All analytical data are consistent with those reported in the literature.¹⁶
3-Bromo-3-phenylpropanenitrile (4q)

The reaction was performed at double concentration (1.5 mL in dry CH₂Cl₂), using Br₂ (0.6 mL, 1.0 M in CH₂Cl₂, 0.6 mmol, 1.2 equiv), quenched with sat. aq. soln of Na₂S₂O₃ (ca. 4 mL) after 9 h and stirred for a further 5 min. The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic phases were washed with H₂O, brine, dried over Na₂SO₄ and the solvent removed in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether/EtOAc 95:5) to give the title compound as a pale yellow oil (60 mg, 57% yield). IR (neat, cm⁻¹): ν 3011, 2984, 2564, 1495, 1410, 1157, 942, 525. ¹H NMR (400 MHz, CDCl₃): δ 3.24 (dd, J = 16.7, 6.6 Hz, 1H), 3.30 (dd, J = 16.7, 7.0, 1H), 5.15 (virt t, J = 7.1, 1H), 7.32-7.49 (m, 5H). ¹³C NMR (101 MHz, CDCl₃): δ 29.4, 45.3, 116.5, 127.0, 129.1, 129.5, 138.7. HRMS (APCI): C₉H₇BrN [M + H]⁺ calculated: 209.9912, found: 209.9913. Anal. Calcd for C₉H₈BrN: C, 51.46; H, 3.86; N, 6.67. Found: C, 51.46; H, 3.84; N, 6.67.

3-Bromo-3-(4-chlorophenyl)propanenitrile (4r)

The reaction was performed at double concentration (1.5 mL in dry CH₂Cl₂), using Br₂ (0.6 mL, 1.0 M in CH₂Cl₂, 0.6 mmol, 1.2 equiv), quenched with sat. aq. soln of Na₂S₂O₃ (ca. 4 mL) after 18 h and stirred for a further 5 min. The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic phases were washed with H₂O, brine, dried over Na₂SO₄ and the solvent removed in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether/EtOAc 90:10) to give the title compound as a brown oil (101 mg, 80% yield). IR (neat, cm⁻¹): ν 3001, 2974, 2442, 1589, 1321, 1010, 950, 501. ¹H NMR (400 MHz, CDCl₃): δ 3.22 (dd, J = 16.3, 6.5 Hz, 1H), 3.28 (dd, J = 16.3, 6.4 Hz, 1H), 5.11 (virt t, J = 7.1 Hz, 1H), 7.33–7.44 (m, 4H). ¹³C NMR (101 MHz, CDCl₃): δ 29.4, 44.1, 116.2, 128.3, 129.4, 135.5, 137.2. LRMS (ESI): m/z (%) 279 (20) [M + Cl]⁺. Anal. Calcd for C₉H₇BrClN: C, 44.21; H, 2.89; N 5.73. Found: C, 44.18; H, 2.91; N, 2.80.

(1-Bromo-3-chloropropyl)benzene (4s)

Reaction was quenched with sat. aq. soln of Na₂S₂O₃ (ca. 4 mL) after 5 min and stirred for a further 5 min. The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic phases were washed with H₂O, brine, dried over Na₂SO₄ and the solvent removed in vacuo. The title compound was isolated by flash column chromatography (silica gel; petroleum ether) as
a colourless oil (63 mg, 54% yield). All analytical data are consistent with those reported in the literature.  

3-Bromo-3-phenylpropan-1-ol (4t)

Reaction was stirred for 5 min and then directly evaporated in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether/EtOAc 80:20) to afford the title compound as a colourless oil (91 mg, 85% yield). All analytical data are consistent with those reported in the literature. The title compound was stored at –20 °C as it was prone to degradation.

3-Bromo-3-(2,4,5-trifluorophenyl)propan-1-ol (4u)

Reaction was quenched with styrene after 90 min. The title compound was isolated by flash chromatography (silica gel; n-hexane/Et2O 70:30) as a colourless oil (63 mg, 48% yield). The title compound was stored at –20 °C as it was prone to degradation.

IR (neat, cm⁻¹): ν 3015, 2824, 1789, 1535, 1125, 1115, 984, 568. ¹H NMR (400 MHz, CDCl₃): δ 1.55 (br s, 1H), 2.22–2.32 (m, 1H), 2.44 (virt ddt, J = 14.5, 9.7, 4.9 Hz, 1H), 3.79 (virt dt, J = 10.8, 5.3 Hz, 1H), 3.87 (ddd, J = 11.0, 8.0, 4.6 Hz, 1H), 5.43 (dd, J = 9.5, 5.4 Hz, 1H), 6.93 (virt dt, J = 9.7, 6.5 Hz, 1H), 7.31 (ddd, J = 10.5, 8.5, 6.8 Hz, 1H). ¹⁹F NMR (376 MHz, CDCl₃): δ –117.9 (dd, J = 15.1, 4.6 Hz), –132.5 (dd, J = 21.6, 4.6 Hz), –141.1 (dd, J = 21.5, 15.1 Hz). ¹³C NMR (101 MHz, CDCl₃): δ 40.9, 41.7 (d, J = 2.9 Hz), 60.1, 105.9 (dd, J = 28.2, 20.9 Hz), 116.8 (dd, J = 20.1, 4.5, 1.4 Hz), 125.6 (dd, J = 15.4, 5.1, 4.5 Hz), 147.0 (ddd, J = 245.9, 12.8, 3.6 Hz), 149.9 (ddd, J = 253.4, 14.5, 12.5 Hz), 154.5 (ddd, J = 248.3, 9.4, 2.7 Hz). LRMS (ESI): m/z (%) 535 (61) [2 M⁺]. Anal. Caled for C₉H₈BrF₃O: C, 40.18; H, 3.00. Found: C, 40.14; H, 2.97.

3-Bromo-3-(2,4,5-trifluorophenyl)propyl methanesulphonate (4v)

Reaction was quenched with sat. aq. soln of Na₂S₂O₃ (ca. 4 mL) after 1 h and stirred for a further 5 min. The aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic phases were washed with H₂O, brine, dried over Na₂SO₄ and the solvent removed in vacuo. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc 80:20) as a pale yellow oil (169 mg, 97% yield). IR (neat, cm⁻¹): ν 2921, 1513, 1353, 1134, 1170, 992, 575. ¹H NMR (400 MHz, CDCl₃): δ 2.44–2.55 (m, 1H),
2.61 (virt ddt, J = 14.6, 9.6, 4.7 Hz, 1H), 3.06 (s, 3H), 4.32–4.49 (m, 2H), 5.31 (dd, 8.9, 5.0 Hz, 1H), 6.97 (virt dt, J = 9.7, 6.5 Hz, 1H), 7.30 (ddd, J = 10.3, 8.4, 6.9 Hz, 1H). 19F NMR (376 MHz, CDCl3): δ –117.4 (dd, J = 15.1, 4.8 Hz), –131.4 (dd, J = 21.5, 4.9 Hz), –140.5 (dd, J = 21.6, 15.1 Hz). 13C NMR (101 MHz, CDCl3): δ 37.4, 37.9, 40.3 (d, J = 2.8 Hz), 66.9, 106.2 (dd, J = 28.1, 21.0 Hz), 116.7 (ddd, J = 20.2, 4.3, 1.4 Hz), 124.5 (ddd, J = 15.1, 4.8, 4.4 Hz), 147.0 (ddd, J = 246.6, 12.8, 3.6 Hz), 150.2 (ddd, J = 254.3, 14.4, 12.5 Hz), 154.6 (ddd, J = 248.9, 9.5, 2.7 Hz). HMRS (APCI): C10H10BrF3O3S [M + H]+ calculated: 345.9502, found: 345.9492.

1-Bromoadamantane (4y)

Reaction was quenched with sat. aq. soln of Na2S2O3 (ca. 4 mL) after 1 h and stirred for further 5 min. The aqueous layer was extracted with CH2Cl2 (3 x 10 mL) and the combined organic phases were washed with H2O, brine, dried over Na2SO4 and the solvent removed in vacuo. The title compound was obtained by flash column chromatography (silica gel; petroleum ether) as a white solid (76 mg, 68% yield). All analytical data are consistent with those reported in the literature.19

(3-Bromo-3-methylbutyl)benzene (4za)

Reaction was stirred for 30 min and then directly evaporated in vacuo. The 1H NMR yield (51%) was determined by adding dibromomethane (35 μL, 87 mg, 0.5 mmol, 1.0 equiv) as internal standard to the crude product re-dissolved in CDCl3. All analytical data are consistent with those reported in the literature.20

3-Bromo-3-methylbutyl 4-methylbenzenesulfonate (4zb)

Reaction was quenched with styrene after 24 h. The title compound was isolated as an inseparable 3:1 mixture with 3,4-dibromo-3-methylbutyl 4-methylbenzenesulfonate by flash column chromatography (silica gel; petroleum ether 100%) as a colourless oil (48 mg, 30% yield). All analytical data are consistent with those reported in the literature.21
6.2 Bromination followed by solvolysis with 2,2,2-trifluoroethanol

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\text{Ar} - \text{R} \xrightarrow{1)} \text{Br}_2 (1.0 \text{ equiv}) \text{CH}_2\text{Cl}_2, \text{rt} \quad \text{To a stirred solution of the sulphide (0.5 mmol) in dry CH}_2\text{Cl}_2 (3.0 \text{ mL}) was added Br}_2 (0.5 \text{ mL, 1.0 M solution in CH}_2\text{Cl}_2, 0.5 \text{ mmol, 1.0 equiv}) under N}_2\text{ atmosphere. The reaction was stirred at rt for 25 min and then quenched by the addition of sat. aq. soln of Na}_2\text{S}_2\text{O}_3 (ca. 4 mL) and stirred for a further 5 min. The aqueous layer was extracted with CH}_2\text{Cl}_2 (3 x 10 mL) and the combined organic phases were washed with H}_2\text{O, brine, dried over Na}_2\text{SO}_4 and the solvent removed } in \text{ vacuo. The residue was re-dissolved in TFE (5.0 mL) and 2,6-lutidine (175 \text{ lL, 161 mg, 3.0 equiv}) was added at 0 \text{ C. The mixture was stirred for 2 h, then 1.0 M HCl (5 mL) and petroleum ether (20 mL) were added. The aqueous layer was extracted with petroleum ether (2 x 20 mL) and the combined organic layers were washed with 1.0 M HCl (2 x 5 mL), brine, dried over Na}_2\text{SO}_4 and concentrated } in \text{ vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether/CH}_2\text{Cl}_2, 70:30 \rightarrow 0:100) to afford the title compound as a yellow oil (80 mg, 50% yield). IR (neat, cm}\text{–}^1\text{): v 2938, 1353, 1158, 964, 526. }^1\text{H NMR (400 MHz, CDCl}_3\text{):} \delta 2.22 (\text{ddd, J = 19.6, 9.3, 5.0 Hz, 1H}, 2.36 (\text{ddd, J = 19.1, 9.4, 4.8 Hz, 1H}), 3.02 (\text{s, 3H}), 3.64–3.82 (\text{m, 2H}), 4.29 (\text{virt dt, J = 10.2, 5.2 Hz, 1H}), 4.45 (\text{ddd, J = 9.8, 8.8, 4.5 Hz, 1H}), 4.91 (\text{dd, J = 9.1, 4.6 Hz, 1H}), 7.01 (\text{dd, J = 5.0, 3.5 Hz, 1H}), 7.06 (\text{d, J = 2.8 Hz, 1H}), 7.36 (\text{d, J = 4.7 Hz, 1H}). }^19\text{F NMR (376 MHz, CDCl}_3\text{):} \delta –77.2. }^{13}\text{C NMR (101 MHz, CDCl}_3\text{):} \delta 37.1, 37.8, 65.4 (\text{q, J = 34.3 Hz}), 66.3, 74.6, 122.5, 125.3, 126.5, 126.9, 142.3. HMRS (EI): C\text{10H13F3O4S}_2\text{Na [M + Na]}^+ \text{calculated: 341.0105, found: 341.0089.}

1-Bromo-4-[phenyl(2,2,2-trifluoroethoxy)methyl]benzene (4xa)

\[
\text{Br} \quad \text{4xa} \quad \text{The procedure was similar to 4wa. The reaction was stirred at rt for 1 h and concentrated } in \text{ vacuo without any quench before solvolysis step. The title compound was obtained by flash column chromatography (silica gel; petroleum ether/EtOAc 98:2) as a pale yellow oil (134 mg, 78% yield). All analytical data are consistent with those reported in the literature.}
\]
6.3 Bromination followed by mesylation with sulphide (1u)

To a stirred solution of sulphide 1u (144 mg, 0.5 mmol) in dry CH₂Cl₂ (3.0 mL) was added Br₂ (500 µL, 1.0 M in CH₂Cl₂, 0.5 mmol, 1.0 equiv) at rt under N₂ atmosphere and stirred for 90 min. The reaction mixture was quenched by the addition of styrene (68 µL, 62 mg, 0.6 mmol, 1.2 equiv). To the resulting colourless solution were added dropwise methanesulphonyl chloride (54 µL, 79 mg, 0.7 mmol, 1.4 equiv) and triethylamine (97 µL, 70 mg, 0.7 mmol, 1.4 equiv) at 0 °C. The reaction mixture was allowed to reach rt and stirred for 16 h, then diluted with H₂O (10 mL) and extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with H₂O, brine and dried over Na₂SO₄. The solvent was removed in vacuo and the crude mixture was purified by flash column chromatography (silica gel; petroleum ether/EtOAc, 90:10) to afford bromide 4v as a brown oil (65 mg, 45% yield).

6.4 Large scale bromination of β-sulphido ester (1f)

To a stirred solution of sulphide 1f (1.50 g, 5.0 mmol) in dry CH₂Cl₂ (15.0 mL) was added via syringe Br₂ (5.0 mL, 1.0 M in CH₂Cl₂, 5.0 mmol, 1.0 equiv) under N₂ atmosphere. The reaction was stirred at rt for 8 h, then quenched by the addition of styrene (743 µL, 676 mg, 6.5 mmol, 1.3 equiv). The mixture was concentrated in vacuo and the residue was purified by flash column chromatography (silica gel; CH₂Cl₂/petroleum ether 90:10) to afford the corresponding bromide (1.29 g, 95% yield).
7. General procedure for the transesterification of enantiomERICALLY enriched hexafluoroisopropyl esters to cinnamate methyl esters (GP4)

To a solution of (S)-1,1,1,3,3,3-hexafluoropropan-2-yl 3-aryl-3-(phenylthio)propanoate (1.0 mmol) in methanol (7.0 mL) was added a few drops of concentrated HCl and the resulting mixture was stirred under reflux for 120 h. After the completion of the reaction, as judged by TLC analysis, the solvent was removed in vacuo and the residue was purified by flash column chromatography on silica gel to give the corresponding (S)-methyl 3-aryl-3-(phenylthio)propanoate.

(--)-(S)-Methyl-3-phenyl-3-(phenylthio)propanoate (--)-(S)-1a

Prepared according to GP4. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a colourless oil (253 mg, 93% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1.0 mL/min, 210 nm): \( t_r \) (minor) = 8.6 min; \( t_r \) (major) = 11.3 min: 97% ee. \([\alpha]_D^{20} = -150.2 \) (c 1.27, CHCl₃). Enantioenriched (--)-(S)-1a has previously been described.²

(--)-(S)-Methyl-3-(phenylthio)-3-(o-tolyl)propanoate (--)-(S)-1b

Prepared according to GP4. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a colourless oil (255 mg, 89% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK OD-H, n-hexane/i-PrOH, 95:5, 1.0 mL/min, 210 nm): \( t_r \) (minor) = 6.0 min; \( t_r \) (major) = 10.4 min: 78% ee. \([\alpha]_D^{20} = -62.3 \) (c 1.41, CHCl₃).
(--)-(S)-Methyl-3-(4-chlorophenyl)-3-(phenylthio)propanoate (--)-(S)-1d

Prepared according to GP4. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a yellow oil (288 mg, 94% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK OD-H, n-hexane/i-PrOH, 95:5, 0.5 mL/min, 210 nm): t_r (major) = 10.9 min; t_r (minor) = 14.0 min: 99% ee. [α]_D^{20} = -169.0 (c 1.18, CHCl_3).

(--)-(S)-Methyl-3-(phenylthio)-3-(4-(trifluoromethyl)phenyl)propanoate (--)-(S)-1e

Prepared according to GP4. The title compound was isolated by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) as a white solid (316 mg, 93% yield). Mp: 91–93 °C. Enantiomeric excess was determined by HPLC analysis (CHIRALPAK OD-H, n-hexane/i-PrOH, 95:5, 0.5 mL/min, 210 nm): t_r (major) = 10.2 min; t_r (minor) = 13.0 min: 98% ee. [α]_D^{20} = -139.0 (c 1.51, CHCl_3).

8. Optically active bromides

8.1. Bromination of enantiomerically enriched sulphides

To an oven-dried 10 mL Schlenk tube containing a stirred solution of sulphide (--)-(S)-1a (68 mg, 0.25 mmol, 97% ee) in dry CH_2Cl_2 (1.5 mL) cooled to −40 °C was added via syringe Br_2 (250 μL, 1M in CH_2Cl_2, 0.25 mmol, 1.0 equiv) under N_2 atmosphere. The reaction mixture was quenched via syringe with styrene (34 μL, 31 mg, 0.3 mmol, 1.3 equiv) after 15 h, which led to an immediate fading of the red colour. Evaporation of the solvent in vacuo and purification by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) gave the title compound as a yellow oil (54 mg, 89% yield). Enantiomeric excess was determined by HPLC...
analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 95:5, 0.75 mL/min, 210 nm): $t_r$ (major) = 7.3 min; $t_r$ (minor) = 9.3 min: 93% ee. $[\alpha]_D^{20} = +114.9$ (c 1.01, CHCl$_3$).

(-)-(R)-Methyl 3-bromo-3-(o-tolyl)propanoate (-)-(R)-4b

To an oven-dried 10 mL Schlenk tube containing a stirred solution of sulphide (-)-(S)-1b (72 mg, 0.25 mmol, 78% ee) in dry CH$_2$Cl$_2$ (1.5 mL) cooled to −40 °C was added via syringe Br$_2$ (250 μL, 1M in CH$_2$Cl$_2$, 0.25 mmol, 1 equiv) under N$_2$ atmosphere. The reaction mixture was quenched via syringe with styrene (34 μL, 31 mg, 0.3 mmol, 1.3 equiv) after 15 h, which led to an immediate fading of the red colour. Evaporation of the solvent in vacuo and purification by flash column chromatography (silica gel; petroleum ether/EtOAc, 97:3) gave the title compound as a yellow oil (64 mg, 99% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 95:5, 0.75 mL/min, 210 nm): $t_r$ (major) = 6.9 min; $t_r$ (minor) = 10.5 min: 66% ee. $[\alpha]_D^{20} = –13.6$ (c 1.03, CHCl$_3$).

(+)-(R)-Methyl 3-bromo-3-(4-chlorophenyl)propanoate (+)-(R)-4d

To an oven-dried 10 mL Schlenk tube containing a stirred solution of sulphide (+)-(S)-1d (77 mg, 0.25 mmol, 99% ee) in dry CH$_2$Cl$_2$ (1.5 mL) cooled to −40 °C was added via syringe Br$_2$ (250 μL, 1M in CH$_2$Cl$_2$, 0.25 mmol, 1.0 equiv) under N$_2$ atmosphere. The reaction mixture was quenched via syringe with styrene (34 μL, 31 mg, 0.3 mmol, 1.3 equiv) after 24 h, which led to an immediate fading of the red colour. Evaporation of the solvent in vacuo and purification by flash column chromatography (silica gel; petroleum ether/EtOAc, 95:5) gave the title compound as a yellow oil (67 mg, 97% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 0.5 mL/min, 210 nm): $t_r$ (major) = 14.8 min; $t_r$ (minor) = 15.6 min: 93% ee. $[\alpha]_D^{20} = +85.2$ (c 1.09, CHCl$_3$).

(+)-(R)-Methyl 3-bromo-3-(4-(trifluoromethyl)phenyl)propanoate (+)-(R)-4e

To an oven-dried 10 mL Schlenk tube containing a stirred solution of sulphide (+)-(S)-1e (85 mg, 0.25 mmol, 98% ee) in dry CH$_2$Cl$_2$ (750 μL) was added via syringe Br$_2$ (275 μL, 1M in CH$_2$Cl$_2$, 0.275 mmol, 1.1 equiv) at rt under N$_2$ atmosphere. The reaction mixture was quenched via syringe with styrene (34 μL, 31 mg, 0.3 mmol, 1.3 equiv) after 48 h at rt, which led to an immediate fading of the red colour. Evaporation of the solvent in vacuo and
purification by flash column chromatography (silica gel; petroleum ether/CH$_2$Cl$_2$, 70:30) gave the title compound as a yellow oil (74 mg, 95% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 0.5 mL/min, 210 nm): $t_r$ (major) = 14.3 min; $t_r$ (minor) = 15.3 min; 86% ee. [$\alpha$]$_{D}^{20}$ = +73.9 (c 1.68, CHCl$_3$).

8.2. Monitoring the racemisation of bromide (R)-4a

Enantiomeric excess of β-bromo ester (R)-4a (93% ee), stored at –20 °C or rt, was measured over a 14-week period.

9. Synthesis of (–)-(S)-3-azido-3-phenylpropan-1-ol

9.1 Two-pot procedure

To a stirred solution of (+)-(R)-4a (61 mg, 0.25 mmol) in dry CH$_2$Cl$_2$ (2.0 mL) was added via syringe DIBAL-H (0.4 mL, 1.0 M in CH$_2$Cl$_2$, 0.4 mmol, 2.0 equiv) at 0 °C under N$_2$ atmosphere. After stirring for 30 min (TLC analysis), the mixture was carefully quenched with H$_2$O, filtered over a Celite pad, which was washed with CH$_2$Cl$_2$ (3 x 10 mL). The combined
organic layers were washed with H₂O, brine, dried over Na₂SO₄ and concentrated in vacuo to give the corresponding alcohol (R)-4t as a brown oil (50 mg, 93% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 90:10, 0.75 mL/min, 210 nm): tᵣ (major) = 9.3 min; tᵣ (minor) = 10.3 min: 83% ee. All analytical data are consistent with those reported in the literature.²²

Alcohol (R)-4t was dissolved in DMF (1.0 mL) and sodium azide (23 mg, 0.35 mmol, 1.5 equiv) was added at 0 °C under N₂ atmosphere. The reaction was allowed to reach rt and stirred overnight. H₂O (3 mL) was added and the aqueous layer was extracted with Et₂O (3 x 10 mL) and the combined organic layers were washed with H₂O, brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether/EtOAc, 80:20) to afford the azido alcohol (–)-(S)-5 as a colourless oil (35 mg, 86% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 90:10, 0.75 mL/min, 210 nm): tᵣ (minor) = 8.6 min; tᵣ (major) = 9.4 min: 83% ee. The enantiomerically enriched (+)-(R)-5 enantiomer has been previously described.²³

9.2 One-pot procedure

To a stirred solution of (+)-(R)-4a (61 mg, 0.25 mmol) in dry CH₂Cl₂ (2.0 mL) was added via syringe DIBAL-H (0.4 mL, 1.0 M in CH₂Cl₂, 0.4 mmol, 2.0 equiv) at 0 °C under N₂ atmosphere. After stirring for 30 min (TLC analysis), dry DMF (2.0 mL) was added, followed by sodium azide (25 mg, 0.38 mmol, 1.5 equiv) and the reaction was allowed to reach rt and stirred overnight. The mixture was carefully quenched with H₂O and filtered over a Celite pad, which was washed with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with H₂O, brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash column chromatography (silica gel; petroleum ether/EtOAc, 80:20) to afford the title compound as a colourless oil (27 mg, 62% yield). Enantiomeric excess was determined by HPLC analysis (CHIRALPAK IB-H, n-hexane/i-PrOH, 90:10, 0.75 mL/min, 210 nm): tᵣ (minor) = 8.6 min; tᵣ (major) = 9.4 min: 90% ee. [α]D²⁰ = –186.9 (c 1.0, CHCl₃); lit.²³: (+)-(R)-5: [α]D²⁰ = +192.7 (c 0.95, CHCl₃). No literature ee value was disclosed, however, an ee of >90% is deduced based on the synthetic sequence.
10. NMR studies

10.1. NMR monitoring of the bromination of (1e)

10.1.1. Low-temperature NMR spectroscopic characterization of adduct (1e·Br₂)

A solution of sulphide 1e (34 mg, 0.1 mmol) in CD₂Cl₂ (0.6 mL), containing 1,1,2,2-tetrachloroethane (11 µL, 17 mg, 0.1 mmol, 1.0 equiv) as internal standard, was prepared under N₂ atmosphere. The solution was transferred via syringe to a 5 mm NMR tube placed in a sub-seal capped Schlenk tube. The NMR tube was sealed with a precision seal rubber septum, which was covered with parafilm. The NMR tube was allowed to equilibrate to –20 °C in the NMR spectrometer, before a Br₂ solution (100 µL, 1.0 M in CD₂Cl₂, 0.1 mmol, 1.0 equiv), precooled to ca –20 °C in a freezer, was added via syringe. The NMR tube was placed immediately back into the NMR spectrometer and a series of 1D and 2D NMR experiments were recorded.

¹H NMR (800 MHz, CD₂Cl₂, –20 °C): δ 3.05 (dd, J = 16.5, 10.1 Hz, 1H, H7), 3.14 (dd, J = 16.6, 4.8 Hz, 1H, H7), 3.55 (s, 3H, H9), 4.82 (dd, J = 9.8, 5.0 Hz, 1H, H6), 7.33-7.35 (m, 4H, H4, H12), 7.40 (t, J = 7.2 Hz, 1H, H13), 7.43 (d, J = 7.5 Hz, 2H, H11), 7.53 (d, J = 7.8 Hz, 2H, H3).

¹⁹F NMR (376 MHz, CD₂Cl₂, 20 °C): δ –62.9.

¹³C NMR (201 MHz, CD₂Cl₂, –20 °C): δ 38.4 (C7), 52.4 (C9), 52.9 (br s, C6), 124.0 (q, J = 272.3 Hz, C1), 125.7 (q, J = 3.5 Hz, C3), 128.7 (C4), 129.0 (br s, C10), 129.8 (C12), 130.1 (q, J = 32.4 Hz, C2), 130.6 (C13), 133.1 (C11), 141.2 (br s, C5), 169.9 (C8).
$^1$H NMR (800 MHz, CD$_2$Cl$_2$, –20 °C) of 1e vs 1e·Br$_2$ (2 min after Br$_2$ addition)
$^{13}$C NMR (201 MHz, CD$_2$Cl$_2$, $-20$ °C) of 1e vs 1e·Br$_2$ (15 min after Br$_2$ addition)
HSQC (800 MHz, CDCl$_3$, –20 °C)
HMB (800 MHz, CD2Cl2, –20 °C)
$^1$H NMR monitoring of the conversion of (1e·Br$_2$) to bromide (4e) after raising the temperature to 20 °C

$^1$H NMR spectra (Fig. 4 in the manuscript) were recorded at 15 min intervals over a period of 14.5 h. The first $^1$H NMR spectrum was recorded after monitoring the reaction at –20 °C for 4 h. The conditioning of the NMR spectrometer to reach 20 °C took around 30 min.
10.1.2. $^1$H NMR monitoring (400 MHz) of the bromination of (1e) at –20 °C

$^1$H NMR spectra were recorded at 5 min intervals over a period of 650 min. The reaction was performed in an NMR tube as described in section 10.1.1.
10.1.3. Monitoring the bromination of (1e) by quantitative $^1$H NMR at 20 °C

Dibromomethane (17 mg, 0.1 mmol, 1.0 equiv) as internal standard was added as a stock solution (0.6 mL, 0.17 M in CD$_2$Cl$_2$) to sulphide 1e (34 mg, 0.1 mmol) under N$_2$ atmosphere. The solution was transferred via syringe to a 5 mm NMR tube placed in a suba-seal capped Schlenk tube. The NMR tube was sealed with a precision seal rubber septum, which was covered with parafilm. A Br$_2$ solution (100 µL, 1.0 M in CD$_2$Cl$_2$, 0.1 mmol, 1.0 equiv) was added via syringe and a series of 1D NMR spectra (400 MHz, 20 °C) were recorded over a period of 60 hours.

Acquisition parameters for the NMR experiment were as follows: pulse sequence = zg, D1 = 60 sec, AQ = 8.17 sec, TD = 131072, SW = 20 ppm, DS = 0, NS = 16, RG = 64.
10.2. NMR monitoring of the bromination of sulphide (1eb)

10.2.1. Preparation of sulphide (1eb)

4-Bromothiophenol (1.70 g, 9.0 mmol, 3.0 equiv) and triethylamine (125 μL, 91 mg, 0.9 mmol, 0.3 equiv) were added to methyl 3-(4-(trifluoromethyl)phenyl)cinnamate (690 mg, 3.0 mmol) and the reaction mixture was stirred at 50 °C for 4 h. The reaction mixture was directly purified by flash column chromatography (silica gel; petroleum ether/CH$_2$Cl$_2$, 70:30 → 0:100) to afford the title compound as a yellow solid (1.19 g, 95% yield). Mp: 99–100 °C. IR (neat, cm$^{-1}$): $\nu$ 3129, 3084, 2761, 1623, 1572, 1251, 1289, 1020, 764. Full assignments were made based on HMBC and HSQC experiments. $^1$H NMR (400 MHz, CD$_2$Cl$_2$): $\delta$ 2.83 (dd, $J$ = 16.2, 8.7 Hz, 1H, H7), 2.89 (dd, $J$ = 16.2, 7.3 Hz, 1H, H7), 3.50 (s, 3H, H9), 4.57 (virt, $J$ = 8.0 Hz, 1H, H6), 7.06 (d, $J$ = 8.4 Hz, 2H, H11), 7.27–7.31 (m, 4H, H4, H12), 7.45 (d, $J$ = 8.2 Hz, 2H, H3). $^{19}$F NMR (376 MHz, CD$_2$Cl$_2$) $\delta$ -62.8. $^{13}$C NMR (101 MHz, CD$_2$Cl$_2$): $\delta$ 40.4 (C7), 49.1 (C6), 52.2 (C9), 122.8 (C13), 124.5 (q, $J =$ 272.3 Hz, C1), 125.7 (q, $J =$ 3.8, C3), 128.4 (C4), 129.8 (q, $J$ = 32.4 Hz, C2), 132.4 (C12), 132.4 (C10), 135.4 (C11), 145.1 (C5), 170.8 (C8). HRMS (EI): C$_{17}$H$_{14}$F$_3$O$_2$S [M – Br]$^+$ calculated: 339.0667, found: 339.0666.
10.2.2. Monitoring the bromination of sulphide (1eb) by NMR and characterisation of adduct (1eb·Br₂)

Dibromomethane solution (0.6 mL, 0.17 M in CD₂Cl₂, 0.1 mmol, 1.0 equiv), as internal standard, was added to a sulphide 1eb (42 mg, 0.1 mmol) under N₂ atmosphere. The solution was transferred via syringe in a 5 mm NMR tube placed in a suba-seal capped Schlenk tube. The NMR tube was sealed with a precision seal rubber septum and covered with parafilm. A Br₂ solution (100 µL, 1.0 M in CD₂Cl₂, 0.1 mmol, 1.0 equiv) was added via syringe and a series of 1D NMR (400 MHz, 20 °C) spectra were recorded over a period of 60 hours. Full NMR spectroscopic characterization of adduct 1eb·Br₂ was achieved within the first hour.

¹H NMR (400 MHz, CD₂Cl₂): δ 2.96 (dd, J = 16.2, 8.7 Hz, 1H, H7), 3.03 (dd, J = 16.2, 6.7 Hz, 1H, H7), 3.59 (s, 3H, H9), 4.70 (virt t, J = 7.6 Hz, 1H, H6), 7.20 (d, J = 8.3 Hz, 2H, H11), 7.36 (d, J = 8.1 Hz, 2H, H4), 7.42 (d, J = 8.3 Hz, 2H, H12), 7.55 (d, J = 8.1 Hz, 2H, H3).

¹⁹F NMR (376 MHz, CD₂Cl₂) δ -62.9.

¹³C NMR (101 MHz, CD₂Cl₂): δ 39.9 (C7), 50.2 (C6), 52.3 (C9), 123.6 (br s, C13), 124.1 (q, J = 271.6 Hz, C1), 125.8 (q, J = 3.8, C3), 128.6 (C4), 130.4 (q, J = 32.4 Hz, C2), 131.3 (br s, C10), 132.6 (C12), 135.3 (C11), 143.3 (br s, C5), 170.5 (C8).
$\text{CH}_2\text{Br}_2$

$\text{Br}_2\text{S}--\text{O}$

$\text{F}_3\text{C}$

$1\text{eb}\cdot\text{Br}_2$

$(400 \text{ MHz, } \text{CD}_2\text{Cl}_2, 20 ^\circ\text{C}, 5 \text{ min after } \text{Br}_2 \text{ addition})$

$\text{Br}_2\text{S}--\text{O}$

$\text{F}_3\text{C}$

$1\text{eb}\cdot\text{Br}_2$

$(101 \text{ MHz, } \text{CD}_2\text{Cl}_2, 20 ^\circ\text{C}, 30 \text{ min after } \text{Br}_2 \text{ addition})$
10.2.3. NMR monitoring of the bromination of (1eb) at 20 °C
11. References


12. HPLC traces of optically active compounds

12.1 HPLC traces of (±)-1a and (−)-(S)-1a

CHIRALPAK IB-H, n-hexane/i-PrOH, 99:1, 1 mL/min, 210 nm

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12.2 HPLC traces of (±)-1b and (−)-(S)-1b

CHIRALPAK OD-H, n-hexane/i-PrOH, 95:5, 1.0 mL/min, 210 nm

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12.3 HPLC traces of (±)-1d and (−)-(S)-1d

CHIRALPAK OD-H, n-hexane/i-PrOH, 95:5, 0.5 mL/min, 210 nm

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12.4 HPLC traces of (±)-1e and (−)-(S)-1e

CHIRALPAK OD-H, n-hexane/i-PrOH, 95:5, 0.5 mL/min, 210 nm

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12.5 HPLC traces of (±)-4a and (+)-(R)-4a

CHIRALPAK IB-H, $n$-hexane/$i$-PrOH, 95:5, 0.75 mL/min, 210 nm

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12.6 HPLC traces of (±)-4b and (−)-(R)-4b

CHIRALPAK IB-H, n-hexane/i-PrOH, 95:5, 0.75 mL/min, 210 nm

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12.7 HPLC traces of (±)-4d and (+)-(R)-4d

CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 0.5 mL/min, 210 nm

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12.8 HPLC traces of (±)-4e and (+)-(R)-4e

CHIRALPAK IB-H, n-hexane/i-PrOH, 98:2, 0.5 mL/min, 210 nm

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12.9 HPLC traces of (±)-5 and (−)-(S)-5

CHIRALPAK IB-H, \(n\)-hexane/\(i\)-PrOH, 90:10, 0.75 mL/min, 210 nm

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12.10 HPLC traces of (±)-4t and (R)-4t

CHIRALPAK IB-H, n-hexane/i-PrOH, 90:10, 0.75 mL/min, 210 nm

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13. Copies of $^1$H NMR and $^{13}$C NMR spectra
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(CDCl₃, 400 MHz)

4a
(CDCl₃, 101 MHz)
4e
(CDCl₃, 400 MHz)

4e
(CDCl₃, 101 MHz)
$\text{Br}\begin{array}{c}O\end{array}CF_3$

4j

(CDC$_3$, 400 MHz)

$\text{Br}\begin{array}{c}O\end{array}CF_3$

4j

(CDC$_3$, 101 MHz)
4za
(CDCl₃, 400 MHz)

$\text{CH}_2\text{Br}_2$
Br\_\text{O-SO}\_\text{phen}

4zb

(CDC\textsubscript{3}, 400 MHz)

Br\_\text{O-SO}\_\text{phen}

4zb

(CDC\textsubscript{3}, 101 MHz)