An expeditious and efficient bromomethylation of thiols: enabling bromomethyl sulfides as useful building blocks

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5. Distinctive

3. Distinctive

1. General Experimental and Analytical Procedures for the preparation of

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O

NC

for bromoalkyl sulfides (2k1-3, 2a1) and

for bromomethyl sulfides (2i-v) and

selected dithioacetals

(3a-b, f-g, i-m, o-r, v)

dithioacetals 6f and 6k

Information

bromoalkylsulfides (2k1-3, 2a1) from

thiols and selected carbonyl compounds

S

S

2d

2i

2l

N

2r

2j

2n

2o

OMe

S

S

2k3

6k

5k

OH

Ph

S

S

2k

3k3

Br

S

S

3k1

Br

OMe

H-NMR chemical shifts (ppm)

C NMR

F NMR

13

13

1
All reagents and solvents were purchased from commercial sources, and were used as received, unless noted otherwise. Thin layer chromatography (TLC) qualitative analysis were performed using glass or aluminum backed silica gel plates (F<sub>254</sub>). TLC plates were visualized by exposition to a UV light lamp (254 nm) and/or developed with a phosphomolybdic acid solution (20% in ethanol) or iodine. Flash column chromatography was performed on 230-400 mesh silica gel. Rotary chromatography was performed using a Chromatotron™ device, equipped with 1, 2, or 4 mm SiO<sub>2</sub> (high purity, 2-25 μm particle size) layer thickness glass rotors. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were acquired on a Jeol Eclipse 270, Bruker DP300, Bruker Avance III HD 400, and ECA 500 spectrometers. <sup>1</sup>H NMR data is reported as follows: chemical shift, multiplicity (s = singlet, d = doublet or m = multiplet), coupling constants (Hz) and integration. Both reported in parts per million (ppm) on the δ scale. Infrared spectra were recorded on a Varian FT-IR 600IR spectrometer with an ATR sampling accessory. Mass spectra were obtained on an Agilent G1969A ESI-TOF or Jeol AccuTOF JMS-T100LC instruments. Elemental microanalysis was performed on a Thermo Finnigan FLASH EA 1112 series CHNS/O analyzer. Elemental compositions of samples were confirmed by HRMS-ESI-QTOF or HRMS-DART+. Microanalysis confirmed elemental composition of 2o. We couldn’t gather elemental information for molecular ions of samples 2b-c, 2g-j, 2l-n, and 2p-r, and 2t-u albeit [M-Br]<sup>+</sup> base peaks were present (HRMS-ESI-QTOF and/or HRMS-DART+).<sup>1</sup>

2. General procedure for the preparation of bromomethylsulfides from thiols.

To a stirred mixture of the corresponding thiol 1 (1 equiv)<sup>2</sup> and paraformaldehyde (CAS: 30525-89-4) (1.0 equiv), a hydrogen bromide solution 33 wt. % in AcOH (Sigma-Aldrich Cat. No. 248630) (2.0 equiv) was added in one portion. The reaction mixture is stirred at rt<sup>7a</sup> until consumption of starting material (TLC).<sup>3b</sup> The undiluted acetic layer was extracted with hexanes (x3). The combined organic layers were dried over anhy. Na<sub>2</sub>SO<sub>4</sub> and concentrated <i>in vacuo</i>, to afford bromomethylsulfanyl derivative 2 with high purity (usually >95%). Analytical samples can be obtained by bulb-to-bulb vacuum distillation (Kugelrohr). Exceptional

Benzyl[bromomethyl]sulfane (2a) was prepared from benzyl mercaptan (1a) (CAS: 100-53-8) (269 mg, 2.7 mmol), parafomaldehyde (65 mg, 2.2 mmol) and HBr/AcOH (33%) (33%).

The procedure afforded 130 mg of 2a (91%) for all. Spectral data match those previously reported. 2<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.37 – 7.26 (m, SH), 4.43 (s, 2H), 3.89 (s, 2H). 2<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 136.2, 129.4, 128.4, 127.7, 39.9, 25.9 ppm.

1. General Experimental and Analytical Information.
rac(Bromomethyl)((1R,2S)-2-methoxycyclohexyl)sulfane (2b) was prepared from rac(1R,2S)-2-methoxycyclohexanethiol (1b) (223 mg, 1.5 mmol), paraformaldehyde (45.8 mg, 1.5 mmol) and HBr/AcOH (560 µL, 3.1 mmol) in accordance to the general procedure (reaction time 30 min). The procedure affords 311 mg of 2b (85%) as an oil.

1H NMR (400 MHz, CDCl\textsubscript{3}) δ 4.82 (d, J = 10.9 Hz, 1H), 4.71 (d, J = 10.9 Hz, 1H), 3.56 – 3.49 (m, 1H), 3.37 (s, 3H), 3.33 – 3.25 (m, 1H), 1.98 – 1.75 (m, 3H), 1.69 – 1.53 (m, 3H), 1.46 – 1.32 (m, 2H).

13C NMR (100 MHz, CDCl\textsubscript{3}) δ 79.3, 56.4, 48.6, 38.4, 28.7, 28.0, 23.9, 21.5.

(Bromomethyl)(4-(tert-butyl)benzyl)sulfane (2c) was prepared from 4-tert-butylbenzyl mercaptan (1c) (CAS: 49543-63-7) (166.3 mg, 0.92 mmol), paraformaldehyde (27.7 mg, 0.92 mmol) and HBr/AcOH (340 µL, 1.87 mmol), in accordance to the general procedure (45 min reaction time). The procedure affords 253 mg of 2c (quant.) as an oil.

1H NMR (400 MHz, CDCl\textsubscript{3}) δ 7.36 (d, J = 8.3 Hz, 2H), 7.28 (d, J = 8.3 Hz, 2H), 4.46 (s, 2H), 3.87 (s, 2H).

13C NMR (100 MHz, CDCl\textsubscript{3}) δ 150.7, 133.1, 129.1, 125.8, 37.1, 35.5, 34.7, 31.5.

(Bromomethyl)(heptyl)sulfane (2d) was prepared from 1-heptanethiol (1d) (CAS: 1639-09-4) (315 mg, 2.4 mmol), paraformaldehyde (72 mg, 2.4 mmol) and HBr/AcOH (880 µL, 4.9 mmol), in accordance to the general procedure (reaction time 10 min). The procedure affords 533 mg of 2d (99%) as an oil.

1H NMR (300 MHz, CDCl\textsubscript{3}) δ 4.67 (s, 2H), 2.74 (t, J = 7.4 Hz, 2H), 1.66 (p, J = 7.2 Hz, 2H), 1.43-1.23 (m, 8H), 0.90-0.87 (m, 3H).

13C NMR (75 MHz, CDCl\textsubscript{3}) δ 38.4, 32.9, 31.8, 29.0, 28.9, 28.3, 22.7, 14.2. MS (DART+), m/z 225, 227 (M+H).

(Bromomethyl)(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoroctyl)sulfane (2e) was prepared from 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-1-octanethiol (1e) (CAS: 34451-26-8) (179 mg, 0.47 mmol), paraformaldehyde (14.1 mg, 0.47 mmol) and HBr/AcOH (170 µL, 0.94 mmol), in accordance to the general procedure (reaction time 20 min). The procedure affords 197 mg of 2e (88%) as an oil, after Kugelrohr distillation (70 - 80 °C, 1.0 mmHg). Spectral data match those previously reported.

1H NMR (400 MHz, CDCl\textsubscript{3}) δ 4.64 (s, 2H), 3.03 – 2.98 (m, 2H), 2.59 – 2.42 (m, 2H).

19F NMR (375 MHz, TFA-d) δ -80.2 (tt, J = 10.1, 2.3 Hz, 3F), -113.6-113.8 (m, 2F), -121.2 (bs, 2F), 122.2 (bs, 2H), 122.7 (bs, 2H), 125.4 – 125.5 (m, 2H).

(Bromomethyl)(cyclohexyl)sulfane (2f) was prepared from cyclohexanethiol (1f) (CAS: 1569-69-3) (398 mg, 3.4 mmol), paraformaldehyde (103 mg, 3.4 mmol) and HBr/AcOH (1.26 mL, 7.0 mmol) in accordance to the general procedure (reaction time 10 min). The procedure affords 714 mg of 2f (quant.) as an oil.

1H NMR (300 MHz, CDCl\textsubscript{3}) δ 4.71 (s, 2H), 3.12 - 2.84 (m, 1H), 2.14 - 1.94 (m, 2H), 1.87 - 1.71 (m, 2H), 1.72 - 1.57 (m, 1H), 1.47 – 1.23 (m, 5H).

13C NMR (75 MHz, CDCl\textsubscript{3}) δ 44.2, 36.6, 32.6, 25.9, 25.8. MS (DART+), m/z 225, 227 (M+H).

(Bromomethyl)(isopropyl)sulfane (2g) was prepared from 2-propanethiol (1g) (CAS: 75-33-2) (338 mg, 4.4 mmol), paraformaldehyde (133 mg, 4.4 mmol) and HBr/AcOH (1.63 mL, 9.0 mmol) in accordance to the general procedure (10 min reaction time). The procedure affords 471 mg of 2g (63%) as an oil.

1H NMR (500 MHz, CDCl\textsubscript{3}) δ 4.70 (s, 2H), 3.22 (hept, J = 6.7 Hz, 1H), 1.34 (d, J = 6.7 Hz, 5H).

13C NMR (125 MHz, CDCl\textsubscript{3}) δ 36.8, 35.9, 22.4.

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7 Due to its high volatility, 2f was extracted with pentane.
8 (+)-Neomenthylthiol was prepared from l-menthol (CAS: 2216-51-5) in accordance to: J. M Blanco, O. Caamaño and F. Fernández Tetrahedron 1995, 51, 935-940.
(Bromomethyl)(1S,2S,5R)-2-isopropyl-5-methylcyclohexyl)sulfane (2h) was prepared from (+)-neomenthylthiol (1h) (363 mg, 2.1 mmol), paraformaldehyde (63 mg, 2.1 mmol) and HBr/AcOH (770 μL, 4.3 mmol) in accordance to the general procedure (10 min reaction time). The procedure affords 502 mg of 2h (90%) as an oil. $^1$H NMR (300 MHz, CDCl$_3$) δ 4.71 (s, 2H), 3.48 (bs, 1H), 2.05 (dq, J = 13.9, 3.2 Hz, 1H), 1.95 – 1.69 (m, 3H), 1.57 (m, 1H), 1.32 – 1.04 (m, 2H), 1.13 – 0.89 (m, 4H), 1.00 (d, J = 6.5 Hz, 3H), 0.90 (d, J = 6.5 Hz, 4H), 0.89 (d, J = 6.4 Hz, 3H).

(Bromomethyl)(tert-butyl)sulfane (2i) was prepared with a modification of the general procedure: To a 1 M solution of 2-methyl-2-propanethiol (1i) (CAS: 75-66-1)(473.7 mg, 5.2 mmol) in hexanes, paraformaldehyde (158 mg, 5.2 mmol) was added and the mixture cooled to -20 °C. Subsequently, HBr/AcOH (1.93 mL, 10.7 mmol) was added in one portion and stirred (20 min). Isolation was carried out as described in the general procedure. The procedure affords 728 mg of 2i (76%) as an orange oil. $^1$H NMR (500 MHz, CDCl$_3$) δ 4.78 (s, 2H), 1.42 (s, 9H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 45.1, 34.9, 30.7.

(Bromomethyl)(phenyl)(sulfane) (2j) was prepared from thiophenol (1j) (CAS: 108-98-5)(602 mg, 5.5 mmol), paraformaldehyde (164 mg, 5.5 mmol) and HBr/AcOH (2.0 mL, 11 mmol) in accordance to the general procedure (45 min reaction time). The procedure affords 1.086 g of 2j (98%) as an oil. $^1$H NMR (300 MHz, CDCl$_3$) δ 7.52 – 7.48 (m, 2H), 7.40 – 7.30 (m, 3H), 4.85 (s, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 133.4, 130.6, 129.4, 128.1, 37.8.

(Bromomethyl)(p-tolyl)sulfane (2k) was prepared from 4-methylbenzenethiol (1k) (CAS: 106-45-6)(327 mg, 2.6 mmol), paraformaldehyde (79 mg, 2.6 mmol) and HBr/AcOH (970 μL, 5.4 mmol) in accordance to the general procedure (45 min reaction time). The procedure affords 498 mg of 2k (87%) as a slightly yellow oil after Kugelrohr distillation (60-65 °C, 0.5 mmHg). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.39 (d, J = 8.2 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H), 4.80 (s, 2H), 2.34 (s, 3H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 138.5, 131.4, 130.1, 129.7, 39.0, 21.3. MS (DART+), m/z 217, 219 (M+H).

(Bromomethyl)(p-tolyl)sulfane (2l) was prepared from 2-methylbenzenethiol (1l) (CAS: 137-06-4)(216 mg, 1.74 mmol), paraformaldehyde (52 mg, 1.74 mmol) and HBr/AcOH (640 μL, 3.5 mmol) in accordance to the general procedure (45 min reaction time). The procedure affords 289 mg of 2l (78%) as an oil after Kugelrohr distillation (135-140 °C, 10 mmHg). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.53 – 7.50 (m, 1H), 7.30 – 7.20 (m, 3H), 4.83 (s, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 139.0, 132.8, 130.7, 130.0, 128.0, 126.9, 37.1, 20.5.

(Bromomethyl)(4-chlorophenyl)sulfane (2m) was prepared from 4-chlorothiophenol (1m) (CAS: 106-54-7)(448 mg, 3.1 mmol), paraformaldehyde (93 mg, 3.1 mmol) and HBr/AcOH (970 μL, 5.4 mmol) in accordance to the general procedure (45 min reaction time). The procedure affords 735 mg of 2m (quant) as a yellow solid (mp 29-30 °C). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.44 (d, J = 8.6 Hz, 2H), 7.35 (d, J = 8.6 Hz, 2H), 4.81 (s, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 134.5, 132.2, 131.8, 129.6, 37.5.

(Bromomethyl)(3-chlorophenyl)sulfane (2n) was prepared from 3-chlorothiophenol (1n) (CAS: 2037-31-2)(727 mg, 5.0 mmol), paraformaldehyde (151 mg, 5.0 mmol) and HBr/AcOH (1.85 mL, 10.2 mmol) in accordance to the general procedure (45 min reaction time).
reaction time). The procedure affords 1.064 g of 2n (89%) as a colorless oil. $^1$H NMR (300 MHz, CDCl$_3$) δ 7.47 (s, 1H), 7.39 – 7.32 (m, 1H), 7.34 – 7.24 (m, 2H), 4.83 (s, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) δ 135.4, 135.0, 130.4, 129.8, 128.2, 128.1, 36.4.

(Bromomethyl)(4-bromophenyl)sulfane (2o) was prepared from 4-bromothiophenol (1o) (CAS: 106-53-6) (172.1 mg, 0.9 mmol), paraformaldehyde (27 mg, 0.9 mmol) and HBr/AcOH (330 µL, 1.8 mmol) in accordance to the general procedure (45 min reaction time). The procedure affords 249 mg of 2o (97%) as a solid (mp 72-74 °C). $^1$H NMR (400 MHz, CDCl$_3$) δ 7.51 (d, $J = 8.7$ Hz, 2H), 7.37 (d, $J = 8.7$ Hz, 2H), 4.81 (s, 2H).

$^{13}$C NMR (100 MHz, CDCl$_3$) δ 132.5, 132.3, 129.5, 122.5, 37.2. Found: C, 30.2; H, 2.2; S, 11.2; Br, 56.4. Calc. for C$_7$H$_6$SBr$_2$: C, 29.8; H, 2.1; S, 11.4; Br, 56.7%

(Bromomethyl)(4-fluorophenyl)sulfane (2p) was prepared from 4-fluorothiophenol (1p) (CAS: 371-42-6) (302 mg, 2.4 mmol), paraformaldehyde (71 mg, 2.4 mmol) and HBr/AcOH (870 µL, 4.8 mmol) in accordance to the general procedure (45 min reaction time). The procedure affords 496 mg of 2p (95%) as an oil after Kugelrohr distillation (70-80 °C, 1.0 mmHg).

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.51 (dd, $J = 8.6$, 5.3 Hz, 2H), 7.08 (t, $J = 8.6$ Hz, 2H), 4.78 (s, 2H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 163.06 (d, $J = 248.9$ Hz), 134.02 (d, $J = 8.4$ Hz), 128.36 (d, $J = 3.2$ Hz), 116.57 (d, $J = 22.1$ Hz), 39.07.

(Bromomethyl)(4-methoxyphenyl)sulfane (2q) was prepared from 4-methoxylthiophenol (1q) (CAS: 696-63-9) (328 mg, 2.3 mmol), paraformaldehyde (70 mg, 2.3 mmol) and HBr/AcOH (860 µL, 4.7 mmol) in accordance to the general procedure (60 min reaction time). The procedure affords 437 mg of 2q (80%) as an oil after Kugelrohr distillation (95-100 °C, 1.0 mmHg).

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.48 (d, $J = 8.8$ Hz, 2H), 6.91 (d, $J = 8.8$ Hz, 2H), 4.76 (s, 2H), 3.81 (s, 3H).

$^{13}$C NMR (75 MHz, CDCl$_3$) δ 160.4, 134.5, 123.7, 114.9, 55.5, 40.7.

(Bromomethyl)(2-methoxyphenyl)sulfane (2r) was prepared with a modification of the general procedure: a 2-methoxythiophenol (1r) (CAS: 7217-59-6) (594 mg, 4.2 mmol), and paraformaldehyde (127 mg, 4.2 mmol) mixture was cooled to 0 °C before HBr/AcOH (1.56 mL, 8.6 mmol) addition (45 min reaction time). The procedure affords 514 mg of 2r (52%) as a colourless oil after Kugelrohr distillation (100-105 °C, 3.0 mmHg, decompose).

$^1$H NMR (500 MHz, CDCl$_3$) δ 7.47 (dd, $J = 7.7$, 1.6 Hz, 1H), 7.31 (ddd, $J = 8.2$, 7.5, 1.7 Hz, 1H), 6.99 (td, $J = 7.6$, 1.2 Hz, 1H), 6.90 (dd, $J = 8.2$, 1.1 Hz, 1H), 4.87 (s, 2H), 3.87 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) δ 157.9, 131.5, 129.5, 121.3, 120.9, 111.0, 55.9, 35.8.

4-((bromomethyl)thio)benzonitrile (2s) was prepared from 4-cyanothiophenol (1s) (118.8 mg, 0.87 mmol), paraformaldehyde (26 mg, 0.87 mmol) and HBr/AcOH (320 µL, 1.8 mmol) in accordance to the general procedure (45 min reaction time). The procedure affords 93 mg of 2s (47 %) as a white solid (mp 66-68 °C).

Spectral data for this compound match those of the reported previously.

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2-((Bromomethyl)thio)benzaldehyde (2t) was prepared with a modification of the general procedure: a 2-mercaptobenzaldehyde (1t) (CAS: 29199-11-9) (256 mg, 1.85 mmol) and paraformaldehyde (556 mg, 1.85 mmol) mixture was heated to 30 °C before HBr/AcOH (670 μL, 3.7 mmol) addition (1 h reaction time). The procedure affords 258 mg of 2t (60%) as an orangish solid with ca. 90% purity. An analytical sample can be obtained by partial crystallization from cold hexanes (25% recovered, mp 60 °C [decomp]). 1H NMR (400 MHz, CDCl₃) δ 10.30 (s, 1H), 7.92 (dd, J = 7.6, 1.4 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.48 (ddd, J = 8.3, 6.8, 1.8 Hz, 1H), 4.87 (s, 2H). 13C NMR (100 MHz, CDCl₃) δ 191.56, 137.65, 134.44, 134.40, 133.10, 128.76, 127.12, 34.95. HRMS (ESI-QTOF) m/z: Calculated for C₈H₇OS [M-Br]+ 151.0212; Found 151.0214.

1-(2-((bromomethyl)thio)phenyl)ethan-1-one (2u) was prepared with a modification of the general procedure: a 1-(2-mercaptophenyl)ethan-1-one (1t) (CAS: 29199-11-9) (54.5 mg, 0.36 mmol) and paraformaldehyde (11 mg, 0.36 mmol) mixture was heated to 40 °C before HBr/AcOH (670 μL, 3.7 mmol) addition (1 h reaction time). The procedure affords 35.1 mg of 2u (60%) as a solid (88-90 °C). 1H NMR (400 MHz, CDCl₃) δ 7.90 (dd, J = 7.8, 1.5 Hz, 1H), 7.68 (dd, J = 8.2, 1.2 Hz, 1H), 7.61 (ddd, J = 8.1, 7.2, 1.5 Hz, 1H), 7.34 (ddd, J = 7.8, 7.2, 1.2 Hz, 1H), 4.87 (s, 2H), 2.63 (s, 3H). 13C NMR (100 MHz, CDCl₃) δ 199.21, 137.65, 135.07, 132.86, 131.34, 126.06, 125.43, 34.35, 28.19. HRMS (ESI-QTOF) m/z: Calculated for C₉H₉OS [M-Br]+ 165.0369; Found 165.0368.

Methyl 2-((bromomethyl)thio)benzoate (2v) was prepared from methyl 2-mercaptobenzoate (1v) (CAS: 4892-02-8) (100 mg, 0.6 mmol), paraformaldehyde (18 mg, 0.6 mmol) and HBr/AcOH (220 μL, 1.2 mmol), in accordance to the general procedure (45 min reaction time). The procedure affords 132 mg of 2t (85%) as a slightly yellow solid. mp 114-116 °C. 1H NMR (500 MHz, CDCl₃) δ 8.04 (d, J = 7.8 Hz, 1H), 7.64 (d, J = 7.9 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 4.90 (s, 2H), 3.92 (s, 3H). 13C NMR (125 MHz, CDCl₃) δ 138.3, 133.0, 131.7, 128.0, 125.8, 52.5, 34.0. IR-ATR νmax/cm⁻¹ 1705 (C=O). HRMS (ESI-QTOF) m/z: Calculated for C₉H₁₀O₂SBr [M+H]+ 260.9579, 262.9558; Found 260.9578, 262.9560.

3. Distinctive 1H-NMR chemical shifts (ppm) for bromomethyl sulfides (2i-v) and selected dithioacetals (3a-b, f-g, i-m, o-r, v). Literature reported data is included within parentheses:

|       | S-CH₂-Br  | S-CH₂-S  |
|-------|-----------|----------|
| 2a    | 4.43 (4.33) | 3a (3.37) |
| 2b    | 4.82     | 3b 3.88  |
| 2c    | 4.46     |          |
| 2d    | 4.67     |          |
| 2e    | 4.64 (4.56) |         |

|       | S-CH₂-Br  | S-CH₂-S  |
|-------|-----------|----------|
| 2j    | 4.85     | 3j (4.35) |
| 2k    | 4.80     | 3k 4.24 (4.24) |
| 2l    | 4.83     | 3l 4.29  |
| 2m    | 4.81     | 3m 4.28 (4.28) |
| 2n    | 4.83     |          |
| 2o    | 4.81     | 3o 4.28 (4.28) |

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13 X. Du, H. Liu and D. M. Du, Tetrahedron Asymmetry, 2010, 21, 241–246.
14 K. Ajiki, M. Hirano and K. Tanaka, Org. Lett., 2005, 7, 4193-4195.
4. Procedures for the preparation of bromoalkylsulfides (2k1-3, 2a1) from thiols and selected carbonyl compounds.

Bromoalkylation of thiols were performed following the general procedure for the preparation of bromomethylsulfides from thiols. Dithioacetals (3k1-3, 3a3) were synthesized following a two-fold amount of the thiol reactant following the general bromomethylation procedure. Bromoalkylsulfides (2k1-3, 2a1) could not be purified by either distillation or chromatographic techniques and are reported as mixtures with dithioacetals (3k1-3, 3a3).

(Bromo(4-nitrophenyl)methyl)(p-tolyl)sulfane (2k1) was prepared from 4-methylbenzenethiol (1k) (CAS: 106-45-6) (229.9 mg, 1.85 mmol), 4-nitrobenzaldehyde (279.7 mg, 1.85 mmol) and HBr/AcOH (670 μL, 3.7 mmol) in accordance to the general bromomethylation procedure (16 h reaction time). The procedure affords 537 mg of a mixture consisting on 2k1 (67%) and dithioacetal 3k1 (9%) as a yellow solid.

(1-Bromoethyl)(p-tolyl)sulfane (2k2) was prepared from 4-methylbenzenethiol (1k) (CAS: 106-45-6) (111.6 mg, 0.9 mmol), acetaldehyde (39.5 mg, 0.9 mmol) and HBr/AcOH (330 μL, 1.8 mmol) in accordance to the general procedure (1 h reaction time). The procedure affords 189.3 mg of a mixture consisting on 2k2 (56%) and 3k2 (36%) as a colorless oil.

(Bromo(phenyl)methyl)(p-tolyl)sulfane (2k3) was prepared with a modification of the general procedure: a mixture of 4-methylbenzenethiol (1k) (CAS: 106-45-6)
(158.1 mg, 1.27 mmol) and benzaldehyde (135 mg, 1.27 mmol) was heated to 30°C, before HBr/AcOH (460 μL, 2.5 mmol) was added (16 h reaction time). The procedure affords 325 mg of a mixture consisting on 2k3 (46%) and 3k2 (29%) as a yellow solid. 2k3H NMR (400 MHz, CDCl3) δ 7.51 (d, J = 8.0, 1.7 Hz, 2H), 7.45 (d, J = 8.0 Hz, 2H), 7.33 – 7.31 (m, 3H), 7.17 (d, J = 7.7 Hz, 2H), 6.25 (s, 1H), 2.34 (s, 3H). 13C NMR (100 MHz, CDCl3) δ 139.9, 139.3, 133.4, 130.1, 129.2, 129.1, 128.8, 127.1, 62.2, 21.4. (Phenylmethylene)bis(p-tolylsulfane) (3k3) 1H NMR (400 MHz, CDCl3) δ 7.32 (dd, J = 8.0, 1.5 Hz, 2H), 7.27 – 7.20 (m, 7H), 7.04 (d, J = 8.0 Hz, 4H), 5.31 (s, 1H), 2.29 (s, 6H). 13C NMR (100 MHz, CDCl3) 140.1, 138.1, 133.3, 131.0, 129.7, 128.5, 128.0, 61.4, 21.3.

Benzyl(bromo(phenyl)methyl)sulfane (2a3) was prepared with a modification of the general procedure: a mixture of benzyl mercaptan (1a) (CAS: 100-53-8) (141.3 mg, 1.14 mmol) and benzaldehyde (120.7 mg, 1.14 mmol) was heated to 30°C, before HBr/AcOH (410 μL, 2.28 mmol) was added (1 h reaction time). The procedure affords 343 mg of a mixture consisting on 2a3 (61 %) and 3a2 (19 %) as an orange oil. 2a3H NMR (400 MHz, CDCl3) δ 7.44 – 7.28 (m, 10H), 5.87 (s, 1H), 4.01 (s, 2H) 13C NMR (100 MHz, CDCl3) δ 139.5, 136.4, 129.4, 129.3, 129.1, 128.85, 127.7, 127.2, 60.4, 39.0. (Phenylmethylene)bis(benzylsulfane) (3a3) δ 7.33 – 7.22 (m, 11H), 7.17 – 7.12 (m, 4H), 4.47 (s, 1H), 3.77 (d, J = 13.4 Hz, 2H), 3.55 (d, J = 13.4 Hz, 2H). 13C NMR (100 MHz, CDCl3) δ 139.7, 137.9, 129.1, 128.7, 128.6, 128.13, 128.0, 127.1, 51.0, 36.7.

5. Distinctive 1H-NMR chemical shifts (ppm) for bromoalkyl sulfides (2k1-3, 2a1) and selected dithioacetals (3k1-3, 3a3). Literature reported data is included within parentheses:

| R1     | R2     | -S-CHR-S- |
|--------|--------|-----------|
| 2k1    | p-Tol  | 6.22      |
| 2k2    | p-Tol  | 5.43      |
| 2k3    | p-Tol  | 6.25      |
| 2a3    | Ph     | 5.87      |
| 3k1    |        | 5.33 (5.34) |
| 3k2    |        | 4.42 (4.42) |
| 3k3    |        | 5.31 (5.31) |
| 3a3    |        | 3.77, 3.55 (3.7) |

6. Procedures for bromo-lithium exchange / functionalization.

I. Preparation of β-hydroxysulfides (5): Under an argon atmosphere, a 1.6 M solution of BuLi (1.1 eq) was added dropwise to a cold (-78 °C) THF solution (0.6 M) of the

18 HSQC and HMBC were used for assignment.
19 S. Kumar, R. Kadu and S. Kumar, Org. Biomol. Chem., 2016, 14, 9210–9214.
20 H. Xi, E. Ma and Z. Li, Tetrahedron, 2016, 72, 4111–4116.
21 H. Zhang, H. Wang, H. Yang and H. Fu, Org. Biomol. Chem., 2015, 13, 6149–6153.
22 M. Kakimoto, T. Seri and Y. Imai, Synthesis, 1987, 1987, 164–166.
corresponding bromomethyl sulfide (2f, 2h or 2k) (1 eq). After 15 min, a THF solution of benzaldehyde (CAS: 100-52-7) (1.1 M, 0.95 eq) was added in one portion via syringe and stirred for 1 h at the same temperature (-78 °C). Subsequently, the reaction mixture was diluted with MeOH followed by half-saturated NH₄Cl solution and extracted with Et₂O (x4). The organic extracts were dried over Na₂SO₄, and the solvent removed in vacuo (no heating). The crude material was purified by radial chromatography using mixtures of hexanes/acetone or hexane/EtOAc.

2-(cyclohexylthio)-1-phenylethan-1-ol (5f) was prepared from 2f (259 mg, 1.2 mmol), BuLi 1.6 M (850 µL, 1.4 mmol) and benzaldehyde (125 mg, 1.2 mmol), in accordance to the general procedure for the preparation of β-hydroxysulfides. The procedure affords 208 mg of 5f (71%) as a colorless liquid. ¹H NMR (400 MHz, CDCl₃) δ 7.39 – 7.30 (m, 4H), 7.31 – 7.21 (m, 1H), 4.68 (ddd, J = 9.3, 3.7, 2.6 Hz, 1H), 3.16 (d, J = 2.5 Hz, 1H), 2.95 (dd, J = 13.7, 3.8 Hz, 1H), 2.70 (dd, J = 13.7, 9.3 Hz, 1H), 2.66 – 2.59 (m, 1H), 2.02 – 1.90 (m, 2H), 1.81 – 1.70 (m, 2H), 1.65 – 1.54 (m, 1H), 1.41 – 1.17 (m, 5H). ¹³C NMR (100 MHz, CDCl₃) δ 142.8, 128.5, 127.8, 125.8, 72.1, 43.7, 40.2, 33.9, 33.7, 26.1, 25.8. HRMS (ESI-QTOF) m/z: Calculated for C₁₄H₂₀OSNa [M+Na]⁺ 259.1127; Found 259.1128.

2-(((1S,2S,5R)-2-isopropyl-5-methylcyclohexyl)thio)-1-phenylethan-1-ol (5h) was prepared from 2h (351 mg, 1.3 mmol), BuLi 1.6 M (910 µL, 1.4 mmol) and benzaldehyde (154 mg, 1.4 mmol), in accordance to the general procedure for the preparation of β-hydroxysulfides. The procedure affords 299.3 mg of the diastereoisomeric mixture of 5h (dr 1.4 : 1 as determined by ¹H-NMR, 77%) as a slightly yellow liquid. HRMS (ESI-QTOF) m/z: Calculated for C₁₈H₂₈OSNa [M+Na]⁺ 315.1753; Found 315.1752. Mixture of diastereoisomers: ¹H NMR (500 MHz, CDCl₃) δ 7.40 – 7.31 (m, 8H), 7.31 – 7.26 (m, 2H), 4.74 – 4.67 (m, 1H), 3.28 – 3.24 (m, 1H), 3.22 – 3.18 (m, 1H), 3.15 (d, J = 1.9 Hz, 1H), 3.10 (d, J = 2.3 Hz, 1H), 2.95 (dd, J = 10.3, 3.5 Hz), 2.91 (dd, J = 10.3, 3.2 Hz), 2.71 (dd, J = 13.3, 9.6 Hz), 2.66 (dd, J = 13.7, 10.0 Hz, 1H), 2.02 – 1.87 (mz, 4H), 1.78 – 1.63 (m, 7H), 1.31 – 1.03 (m, 7H), 0.96 (d, J = 6.6 Hz, 6H), 0.95 (d, J = 6.7 Hz, 6H), 0.91 (d, J = 6.6 Hz, 6H). ¹³C NMR (125 MHz, CDCl₃) δ 142.80, 142.66, 128.60, 128.00, 126.00, 72.42, 71.13, 49.28, 48.79, 48.57, 45.91, 43.13, 42.14, 41.31, 40.06, 35.46, 35.39, 30.11, 30.04, 26.76, 26.32, 25.95, 25.90, 22.34, 22.31, 21.21, 21.15, 21.12, 20.88.

1-Phenyl-2-(p-tolylthio)ethan-1-ol (5k) was prepared from 2k (144 mg, 0.66 mmol), BuLi 1.6 M (460 µL, 0.73 mmol) and benzaldehyde (67 mg, 0.63 mmol), in accordance to the general procedure for the preparation of β-hydroxysulfides. The procedure affords 125 mg of 5k (77%) as a colorless liquid. Spectral data for this compound match those of the reported previously. ¹H NMR (400 MHz, CDCl₃) δ 7.36 – 7.31 (m, 6H), 7.33 – 7.24 (m, 1H), 7.13 (d, J = 7.8 Hz, 2H), 4.67 (d, J = 9.5 Hz, 1H), 3.27 (dd, J = 13.8, 3.3 Hz, 1H), 3.02 (dd, J = 13.8, 9.7 Hz, 1H), 2.91 (s, 1H), 2.33 (s, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 142.3, 137.3, 131.2, 131.0, 130.1, 128.7, 128.0, 126.0, 71.6, 45.0, 21.2.

II. Preparation of unsymmetrical dithioacetals (6): Under an argon atmosphere, a 1.6 M solution of BuLi (1.1 eq) was added dropwise to a cold (-78 °C) THF solution (0.6 M) of the corresponding bromomethyl sulfide (2f or 2k) (1 eq). After 15 min, a THF solution of phenyl disulfide (CAS: 882-33-7)(1.1 M, 0.95 eq) was added in one portion via

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²⁴ 1.1 eq (1.1 M solution in THF) of benzaldehyde for the electrophilic quench in the case of 2h.
²⁵ C. Huo, Y. Wang, Y. Yuan, F. Chen and J. Tang, Chem. Commun. 2016, 52, 7233-7236.
syringe and stirred for 1 h at the same temperature (-78 °C). Subsequently, the reaction mixture was diluted with MeOH and a half-saturated NH₄Cl solution, and extracted with Et₂O (x4). The organic extracts were dried over Na₂SO₄, and the solvent removed in vacuo. The crude material was purified by radial chromatography using mixtures of hexanes/acetone (99:1 to 98:2). In all cases, butyl(phenyl)sulfane was obtained as a by-product (from the condensation between butyl bromide and thiophenolate), which spectral data matching those previously reported.

Cyclohexyl((phenylthio)methyl)sulfane (6f) was prepared from 2f (291 mg, 1.4 mmol), BuLi 1.6 M (960 µL, 1.5 mmol) and phenyl disulfide (289 mg, 1.3 mmol). The procedure affords 188 mg of 6f (60% yield) as a syrup. Spectral data for this compound match those of the reported previously.¹⁷

¹H NMR (400 MHz, CDCl₃) δ 7.41 (d, J = 8.0 Hz, 2H), 7.31 (t, J = 7.6 Hz, 2H), 7.25 – 7.20 (m, 1H), 4.05 (s, 2H), 3.03 – 2.83 (m, 1H), 2.06 – 1.90 (m, 2H), 1.87 – 1.70 (m, 2H), 1.69 – 1.54 (m, 1H), 1.48 – 1.15 (m, 5H).

¹³C NMR (100 MHz, CDCl₃) δ 135.9, 130.4, 129.1, 126.9, 43.4, 36.3, 33.4, 26.1, 25.9.

Phenyl((p-tolylthio)methyl)sulfane (6k) was prepared from 2k (203 mg, 0.93 mmol), BuLi 1.6 M (640 µL, 1.03 mmol) and 1,2-diphenyldisulfane (194 mg, 0.89 mmol). The procedure affords 126 mg of 6k (58% yield) as a syrup. ¹H NMR (400 MHz, CDCl₃) δ 7.42 (d, J = 8.1 Hz, 2H), 7.36 – 7.28 (m, 4H), 7.23 (t, J = 7.1 Hz, 1H), 7.13 (d, J = 8.1 Hz, 2H), 4.30 (s, 2H), 2.34 (s, 3H).

¹³C NMR (100 MHz, CDCl₃) δ 137.7, 135.3, 131.8, 131.3, 130.7, 129.9, 129.1, 129.1, 127.2, 41.5, 21.3.

Alternative preparation of unsymmetrical dithioacetals 6f and 6k

To a cold (0 °C) suspension of NaH (60% in mineral oil, 1 eq) in dry THF (0.5 M), thiophenol (1.0 eq) was added dropwise via syringe. After 30 min, bromomethyl sulfide 2f or 2k (1.1 eq) solution in dry THF (0.5 M) was added in one portion and stirred for 1 h at the same temperature. Afterwards, the reaction mixture was diluted with cold water and extracted with EtOAc (x4). The organic extracts were dried over Na₂SO₄, and the solvent removed in vacuo. Dithioacetals 6f or 6k were purified by column chromatography using mixtures of hexanes/EtOAc. Yields: 6f 97%, 6k 85%.

Procedures for free radical reactions

I. Reduction – Preparation of thioether methyl(p-tolyl)sulfane (8j): a degassed solution of bromomethylsulfide (2j) (112 mg, 0.52 mmol), tris(trimethylsilyl)silane (CAS: 1873-77-4) (154 mg, 0.62 mmol), and 1,1'-azobis(cyclohexanecarbonitrile) (ABCN, CAS: 2094-98-6) (12.6 mg, 0.05 mmol) in dry benzene (5 mL), was refluxed for 30 min. After this, the reaction mixture was cooled down (rt), and concentrated in vacuo. The crude mixture

26 A. M. Thomas, S. Asha, K. S. Sindhu and G. Anilkumar, Tetrahedron Lett., 2015, 56, 6560–6564.
27 K. Sipilä, T. Hase, J. Koskimies, J. Matikainen and J. Kansikas, Phosphorus, Sulfur Silicon Relat. Elem., 2002, 177, 709–727.
was directly analyzed by $^1$H-NMR using mesitylene as an internal standard to estimate a 85% yield.²⁸

\[
\begin{align*}
\text{R} & \equiv \text{Cy, } 2f \\
\text{R} & \equiv \text{p-tol, } 2k \\
\text{Br} & \\
\text{EtB} / O_2 \\
\text{Bu} & \text{SnH} \\
\text{DCM, } 0 \degree C
\end{align*}
\]

II. Radical additions - Preparation of γ-sulfenylnitriles (9f, 9k) and ethyl γ-sulfenylbutyrates (10f, 10k): to a dry, cold (0 °C) solution of the corresponding bromomethylsulfide 2f or 2k (1 eq), acrylonitrile (CAS: 107-13-1) or methyl acrylate (CAS: 96-33-3) (2 equiv) in DCM (0.01 M), a 1 M Et$_3$B solution in hexanes (0.2 eq) was added using a syringe and air was bubbled simultaneously. After this, a freshly prepared solution of Bu$_3$SnH (1.25 eq) in dry benzene (0.2 M) were added through a 2 h lapse (syringe pump), at 0 °C. Through the Bu$_3$SnH addition, additional Et$_3$B (0.2 eq) was added every 20 min with additional air bubbling (1.4 eq total). Afterwards, the reaction mixture was allowed to warm until rt and stirred for 1 h. Next, solvent was removed (no vacuum), and the resulting material was filtered on silica gel and purified by radial chromatography using mixtures of hexanes : EtOAc.

4-(Cyclohexythio)butanenitrile (9f) was prepared from 2f (190 mg, 0.91 mmol), acrylonitrile (120 µL, 1.82 mmol), Bu$_3$SnH 0.2 M in dry benzene (5.7 mL, 1.14 mmol), and Et$_3$B 1M in hexanes (1.27 mL, 1.27 mmol). The procedure affords 84.2 mg of 9f (51%) as an oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 2.69 – 2.61 (m, 3H), 2.51 (td, J = 7.1, 1.4 Hz, 2H), 1.99 – 1.87 (m, 4H), 1.80 – 1.72 (m, 2H), 1.66 – 1.59 (m, 1H), 1.38 – 1.19 (m, 5H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 119.2, 43.5, 33.6, 28.5, 26.0, 25.7, 25.6, 16.0. IR-ATR $\nu_{\text{max}}$ (cm$^{-1}$) 2246 (CN). HRMS (DART) m/z: Calculated for C$_{10}$H$_{18}$NS [M+H]$^+$ 184.1160; Found 184.1164.

4-(p-Tolylthio)butanenitrile (9k) was prepared from 2k (206 mg, 0.95 mmol), acrylonitrile (130 µL, 1.90 mmol), Bu$_3$SnH 0.2 M in dry benzene (1.19 mmol, 5.9 mL), and Et$_3$B 1M in hexanes (1.33 mL, 1.33 mmol). The procedure affords 145.4 mg of 9k (80%) as a clear oil. $^1$H NMR (400 MHz, CDCl$_3$) δ 7.26 (dd, J = 8.2, 2.3 Hz, 2H), 7.10 (dd, J = 8.2, 2.2 Hz, 2H), 3.0 – 2.90 (m, 2H), 2.5 – 2.43 (m, 2H), 2.31 (s, 3H), 2.28 (s, 3H).

²⁸ Reaction profiles featured clean conversions. Yield estimation using an internal standard was needed due a high volatility of the product and similar polarity of (TMS)$_3$SiBr. Spectral data of the product match those already reported in the literature: T. H. Chuo, R. Boobalan and C. Chen, ChemistrySelect, 2016, 1, 2174–2180.
1.89 (qd, J = 7.0, 1.7 Hz, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 137.0, 130.93, 130.85, 129.9, 119.2, 33.2, 24.9, 21.0, 15.8. IR-ATR $\nu_{\text{max}}$ (cm$^{-1}$) 2246 (CN). HRMS (ESI-QTOF) m/z: Calculated for C$_{11}$H$_{14}$NS [M+H]$^+$ 192.0847; Found 192.0828.

**Methyl 4-(cyclohexylthio)butanoate (10f)** was prepared from 2f (171.3 mg, 0.82 mmol), methyl acrylate (150 $\mu$L, 1.64 mmol), Bu$_3$SnH 0.2 M in dry benzene (5.1 mL), and Et$_3$B 1M in hexanes (1.15 mL, 1.15 mmol). The procedure affords 64 mg of 10f (36%) as an oil. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 3.68 (s, 3H), 2.68 – 2.61 (m, 1H), 2.57 (t, J = 7.3 Hz, 2H), 2.44 (t, J = 7.4 Hz, 2H), 2.00 – 1.86 (m, 4H), 1.80 – 1.71 (m, 2H), 1.65 – 1.57 (m, 1H), 1.37 – 1.19 (m, 5H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 173.7, 51.6, 43.4, 33.8, 33.00, 29.4, 26.2, 25.9, 25.2. IR-ATR $\nu_{\text{max}}$ (cm$^{-1}$) 1737 (C=O). HRMS (DART+) m/z: Calculated for C$_{11}$H$_{22}$O$_2$S [M+H]$^+$ 217.1262; Found 217.1275.

**Methyl 4-(p-tolylthio)butanoate (10k)** was prepared from 2k (181 mg, 0.83 mmol), methyl acrylate (150 $\mu$L, 1.67 mmol), Bu$_3$SnH 0.2 M in dry benzene (5.2 mL), and Et$_3$B 1M in hexanes (1.17 mL). The procedure affords 104.2 mg of 10k (56%) as an oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.25 (d, J = 10.5 Hz, 2H), 7.09 (d, J = 8.3 Hz, 2H), 3.66 (s, 3H), 2.91 (t, J = 7.1 Hz, 2H), 2.46 (dd, J = 7.3 Hz, 2H), 2.31 (s, 3H), 1.92 (p, J = 7.2 Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 173.6, 136.4, 132.2, 130.4, 129.8, 51.7, 33.8, 32.7, 24.5, 21.1. IR-ATR $\nu_{\text{max}}$ (cm$^{-1}$) 1734 (C=O). HRMS (DART) m/z: Calculated for C$_{12}$H$_{17}$O$_2$S [M+H]$^+$ 225.0949; Found 225.0964.
Benzyl[bromomethyl]sulfane (2a)
rac(Bromomethyl)((1R,2S)-2-methoxycyclohexyl)sulfane (2b)

\[
\begin{align*}
\text{f1 (ppm)} & : 0.0, 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0 \\
\text{S} & \quad \text{Br} \\
\text{O} & \quad \text{Me}
\end{align*}
\]
(Bromomethyl)(4-(tert-butyl)benzyl)sulfane (2c)
(Bromomethyl)(heptyl)sulfane (2d)
(Bromomethyl)(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoroctyl)sulfane (2e)
(Bromomethyl)(cyclohexyl)sulfane (2f)
(Bromomethyl)(isopropyl)sulfane (2g)
(Bromomethyl)((1R, 2S, 5R)-2-isopropyl-5-methylcyclohexyl)sulfane (2h)
(Bromomethyl)(tert-butyl)sulfane (2i)
(Bromomethyl)(phenyl)(sulfane) (2j)
1-[(bromomethyl)thio]-4-methylbenzene (2k)

\[
\begin{array}{c}
\text{S} \\
\text{Br}
\end{array}
\]
(Bromomethyl)(o-tolyl)sulfane (2l)
(Bromomethyl)(4-chlorophenyl)sulfane (2m)
(Bromomethyl)(3-chlorophenyl)sulfane (2n)

\[
\begin{array}{c}
\text{Cl} \\
\text{S} \\
\text{Br}
\end{array}
\]
(Bromomethyl)(4-bromophenyl)sulfane (2o)
(Bromomethyl)(4-fluorophenyl)sulfane (2p)
(Bromomethyl)(4-methoxyphenyl)sulfane (2q)
4-((bromomethyl)thio)benzonitrile (2s)
2-((Bromomethyl)thio)benzaldehyde (2t)

\[
\begin{align*}
\text{O} & \text{H} \\
\text{S} & \text{Br}
\end{align*}
\]
1-(2-((bromomethyl)thio)phenyl)ethan-1-one (2u)
Methyl 2-((bromomethyl)thio)benzoate (2v)
(Bromo(4-nitrophenyl)methyl)(p-tolyl)sulfane (2k1)

A - 2k1
B - 3k2
C - 4-Nitrobenzaldehyde

A
B
C

S
Br
N\text{O}_2
((4-Nitrophenyl)methylene)bis(p-tolylsulfane) (3k1)
(1-Bromoethyl)(p-toly)sulfane (2k2)
Ethane-1,1-diylbis(p-tolylsulfane) (3k2)
(Bromo(phenyl)methyl)(p-tolyl)sulfane (2k3)

A- 2k3
B- 3k3
C- Benzaldehyde
(Phenylmethylene)bis(p-tolylsulfane) (3k3)
Benzyl(bromo(phenyl)methyl)sulfane (2a3)

A - 2a3
B - 3a3
C - Benzaldehyde
### 2-(Cyclohexylthio)-1-phenylethanol (5f)

![Structure of 2-(Cyclohexylthio)-1-phenylethanol (5f)](image)

#### NMR Spectra

**1H NMR Spectra:**
- **4.70 - 4.65 ppm:**
- **3.10 - 3.05 ppm:**
- **2.90 - 2.85 ppm:**
- **2.59 - 2.55 ppm:**

**13C NMR Spectra:**
- **25.76 ppm:**
- **33.68 ppm:**
- **33.89 ppm:**
- **40.15 ppm:**
- **43.72 ppm:**
- **72.05 ppm:**
- **125.82 ppm:**
- **127.77 ppm:**
- **128.47 ppm:**
- **142.77 ppm:**

**Assignments:**
- **OH:** 3.60 ppm
- **SCH2:** 3.70 ppm
- **Ph:** 7.24 ppm

---

| 1H (ppm) | 13C (ppm) |
|----------|-----------|
| 0.99     | 72.05     |
| 1.22     | 25.76     |
| 1.32     | 33.68     |
| 1.87     | 33.89     |
| 2.12     | 40.15     |
| 2.42     | 43.72     |
| 2.52     | 125.82    |
| 2.72     | 127.77    |
| 2.92     | 128.47    |
| 3.16     | 142.77    |
2-(((1S,2S,5R)-2-Isopropyl-5-methylcyclohexyl)thio)-1-phenylethanol (5h)
1-Phenyl-2-(p-tolylthio)ethan-1-ol (5k)
Cyclohexyl((phenylthio)methyl)sulfane (6f):
Phenyl((p-tolylthio)methyl)sulfane (6k)
4-(Cyclohexylthio)butanenitrile (9f):
4-(p-Tolythio)butanenitrile (9k)

![Chemical Structure](image)

**Graphical Representation**

- **f1 (ppm)**
  - 7.5 to 0.0
  - 1.840 to 1.914
  - 2.309 to 2.492

- **f1 (δ)**
  - 100 to 0
  - 119.18 to 136.96

**Additional Details**

- **Formula**: S-CN
Methyl 4-(cyclohexylthio)butanoate (10f)
Methyl 4-(p-tolylthio)butanoate (10k)