SUPPORTING INFORMATION

Thiol-Free Multicomponent Synthesis of Non-racemic β-Acyloxy Thioethers from Biocatalytically Obtained Chiral Halohydrins

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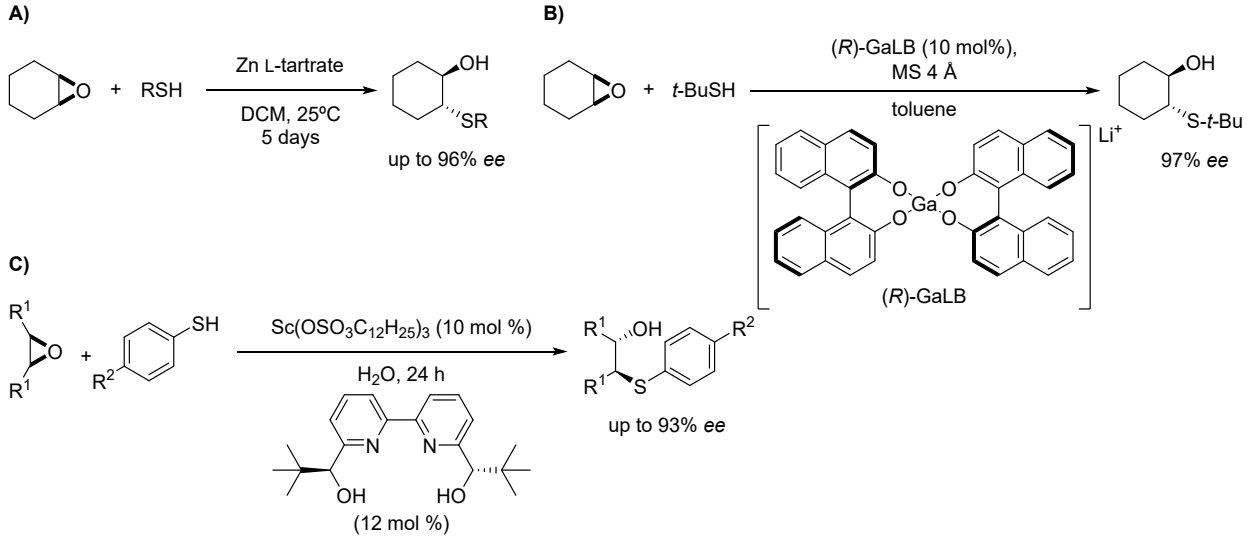
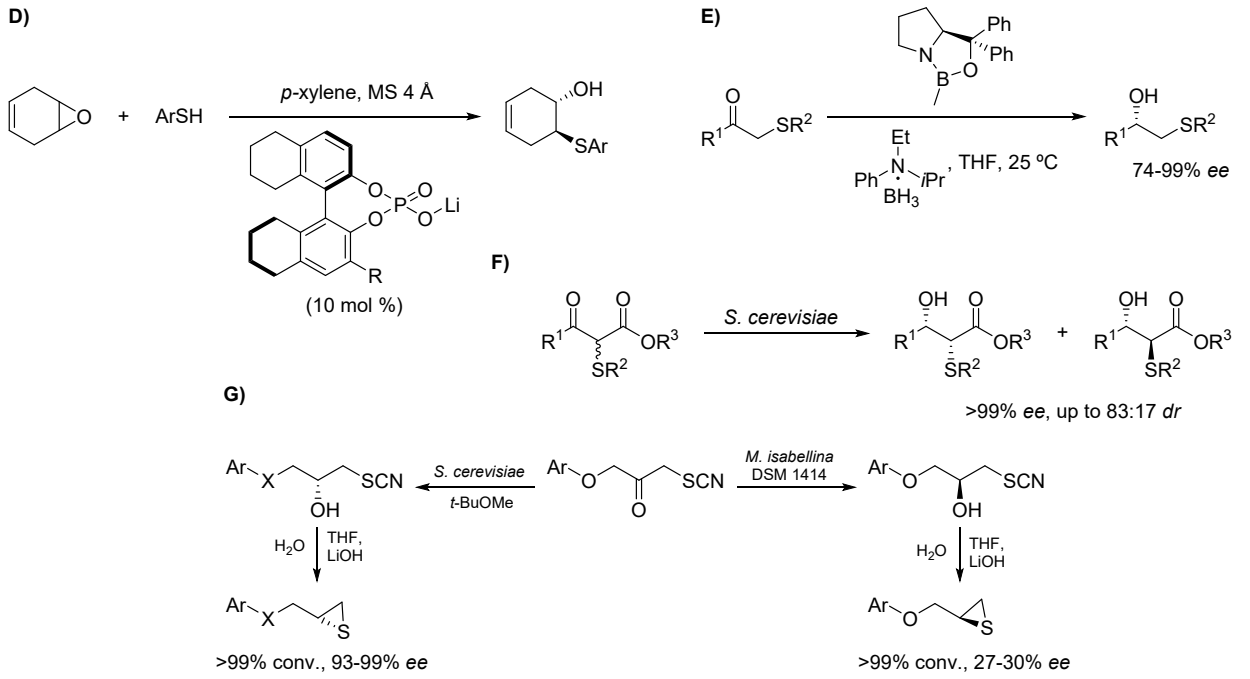
Previous examples of reported asymmetric procedures for the synthesis of ß-oxygenated sulfides



***Scheme S1**. Different strategies for the preparation of enantioenriched ß-hydroxysulfides employing transition metals.*[1–3]



***Scheme S2.** Other methods described towards the synthesis of enantioenriched ß-hydroxysulfides.*[4–9]

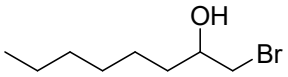
General Information and Procedures

General methods: All haloketones **3** except **3a**, 1-octene, potassium thioacetate, bases and all electrophiles were purchased from commercial sources and used as received. Solvents for chemical reactions were of high purity grade, distilled as received from the supplier, and stored as such. Overexpressed ADHs from *Rhodococcus ruber* (*E. coli*/ADH-A), *Ralstonia* sp. (*E. coli*/RasADH) and *Sphingobium yanoikuyae* (*E. coli*/SyADH), *Thermoanaerobacter* sp. (*E. coli*/ADH-T), *Thermoanaerobacter ethanolicus* (*E. coli*/TeSADH) and *Lactobacillus brevis* (*E. coli*/LBADH) were used as lyophilized cells as described elsewhere.[10]

^{1}H and ^{13}C NMR spectra were recorded at 400.16 and 100.62 MHz, respectively, on a Bruker 400 spectrometer with $CDCl_3$ as a solvent. All spectra were reported in δ (ppm) relative to residual solvent signal [δH ($CHCl_3$) = 7.26 ppm]. Gas chromatographic analyses were performed on an Agilent 6890 with a flame-ionization detector, using a 30 m capillary column of a 0.32 mm × 0.25 μm film thickness, with a 5% phenylpolysiloxane phase. GC-MS analyses were conducted on Shimadzu GCMS-QP2020 employing a 30 m × 0.25 mm × 0.25 μm with a 5% phenylpolysiloxane phase column. For the conversion and *ee* determination, a Chirasil-Dex CB stationary phase column (25 m x 0.25 mm x 0.25 μm, 12.2 psi N_2) was used. HRMS spectra were recorded on a Bruker micrOTOF-Q II mass spectrometer. Ionization was achieved by electrospray and detection set on positive mode. The halohydrins and β-*O*-acyl sulfides displayed spectroscopic data in good agreement with those reported in literature.

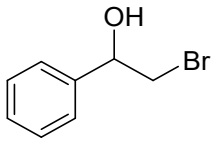
Procedures for the synthesis of racemic halohydrins

Synthesis of ***1-bromooctan-2-ol (1a):***[10] to a solution of 2 g of 1-octene (17.86 mmol) dissolved in a mixture of acetone (23.8 mL) and H_2O (4.2 mL) 137.5 mg ammonium acetate (0.1 equiv., 1.79 mmol) and 3.5 g of N-Bromosuccinimide (19.65 mmol) were added. The reaction was carried out with magnetic stirring at room temperature for 24 h. Then, the organic solvent was evaporated and extracted with CH_2Cl_2 (3x10 mL). The organic fractions were combined and dried with anhydrous Na_2SO_4. The solvent was evaporated at reduced pressure and the crude oil obtained was subjected to column chromatography using a mixture of ethyl acetate/hexane (9:1). 1.646 g was obtained (44% isolated yield).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 – 3.72 (m, 1H), 3.55 (dd, *J* = 10.3, 3.2 Hz, 1H), 3.38 (dd, *J* = 10.3, 7.1 Hz, 1H), 2.09 (d, *J* = 5.0 Hz, 1H), 1.61 – 1.25 (m, 10H), 0.88 (t, *J* = 6.8 Hz, 3H).

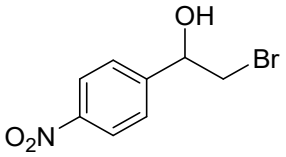
Synthesis of ***2-bromo-1-phenylethan-1-ol (1b):***[11] to a solution of bromoacetophenone (10 mmol) in MeOH (10 mL) at 0°C, $NaBH_4$ was slowly added. When the starting haloketone was completely consumed (TLC), MeOH was evaporated and the crude was extracted with CH_2Cl_2 (3 x 15mL) and H_2O (45 mL). The organic fractions were combined and dried with anhydrous Na_2SO_4. The solvent was evaporated at reduced pressure and the crude oil obtained was subjected to column chromatography using a mixture of CH_2Cl_2/hexane (1:1). 1.216 g was obtained (60% isolated yield).



^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (m, 1H), 4.93 (dt, *J* = 9.0, 3.3 Hz, 1H), 3.65 (dd, *J* = 10.5, 3.3 Hz, 1H), 3.55 (dd, *J* = 10.4, 9.0 Hz, 1H), 2.63 (d, *J* = 3.2 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 140.27 (C), 128.72 (CH), 128.50 (CH), 125.98 (CH), 73.83 (CH), 40.27 (CH_2).

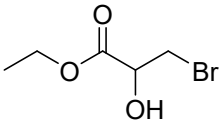
Synthesis of ***2-bromo-1-(4-nitrophenyl)ethan-1-ol (1c):***[12] to a solution of **3c** (5 mmol) in MeOH (5 mL) at 0°C, $NaBH_4$ (1.4 equiv) was slowly added. When the starting haloketone was completely consumed (TLC), MeOH was evaporated and the crude was extracted with CH_2Cl_2 (3 x 10mL) and H_2O (25 mL). The organic fractions were combined and dried with anhydrous Na_2SO_4. The solvent was evaporated at reduced pressure and the crude oil

obtained was subjected to column chromatography using a mixture of CH_2Cl_2/hexane (1:1). 492 mg was obtained (40% isolated yield).



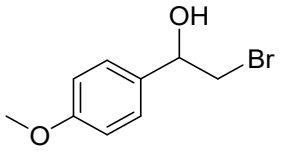
^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 – 8.22 (m, 2H), 7.63 – 7.57 (m, 2H), 5.06 (dt, *J* = 7.8, 3.6 Hz, 1H), 3.69 (dd, *J* = 10.6, 3.4 Hz, 1H), 3.54 (dd, *J* = 10.6, 8.4 Hz, 1H), 2.76 (d, *J* = 3.7 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 147.4 (C), 127.1 (CH), 124.0 (CH), 72.8 (CH), 39.5 (CH_2).

Synthesis of ***ethyl 3-bromo-2-hydroxypropanoate (1d):***[13] to a solution of ethyl 3-bromo-2-oxopropanoate (1.00 g, 5,131 mmol) in MeOH (2.5 mL) at 0°C, $NaBH_4$ was slowly added (1.796 mmol, 67.9 mg). When the starting haloketone was completely consumed (TLC), the MeOH was evaporated and the crude was extracted with CH_2Cl_2 (3 x 10mL) and H_2O (30 mL). The organic fractions were combined and dried with anhydrous Na_2SO_4. The solvent evaporated at reduced pressure and the crude oil obtained was subjected to column chromatography using a mixture of Ethyl Acetate/Hexane (1:3). 570 mg of product was obtained (56% isolated yield).

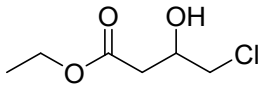


^{1}H NMR (400 MHz, $CDCl_3$):δ= 4.54 – 4.46 (m, 1H), 4.42 – 4.22 (m, 2H), 3.69 (dd, *J* = 7.5, 3.5 Hz, 2H), 3.25 (d, *J* = 6.4 Hz, 1H), 1.64 (s, 1H), 1.33 (t, *J* = 7.1 Hz, 4H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 171.50 (C), 69.75 (CH), 62.55 (CH_2), 35.09 (CH_2), 14.18 (CH_3).

Synthesis of ***2-bromo-1-(4-methoxyphenyl)ethan-1-ol (1e):*** to a solution of 2-bromo-1-(4-methoxyphenyl)ethan-1-one (100 mg, 0.437 mmol) in MeOH (700 µL) at 0°C, $NaBH_4$ was slowly added (0.12 mmol, 4.5 mg). When the starting haloketone was completely consumed (TLC), the MeOH was evaporated and the crude was extracted with CH_2Cl_2 (3 x 5mL) and H_2O (15 mL). The organic fractions were combined and dried with anhydrous Na_2SO_4. Then, the solvent was evaporated at reduced pressure. The product was not isolated, it was used directly in the subsequent multicomponent reaction.



Synthesis of ***ethyl 4-chloro-3-hydroxybutanoate (1f):***[14] to a solution of ethyl 4-chloroacetoacetate (1 g, 6.08 mmol) in MeOH (5 mL) at 0°C, $NaBH_4$ was slowly added (1.672 mmol, 63.2 mg). When the starting haloketone was completely consumed (TLC), the MeOH evaporated and extracted with CH_2Cl_2 (3 x 10mL) and H_2O (30 mL). The organic fractions were combined and dried with anhydrous Na_2SO_4. The solvent evaporated at reduced pressure and the crude oil obtained was subjected to column chromatography using a mixture of CH_2Cl_2/hexane (1:1). 0.538 g of product was obtained (53% isolated yield).

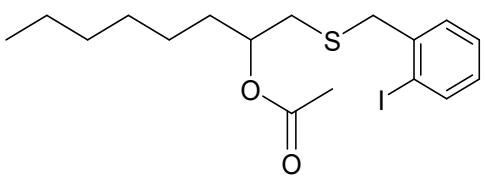


^{1}H NMR (400 MHz, CDCl3): δ = 4.30 – 4.22 (m, 1H), 4.19 (q, *J* = 7.1 Hz, 2H), 3.66 – 3.56 (m, 2H), 3.21 – 3.14 (m, 1H), 2.70 – 2.57 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

MCR general procedure employing racemic or enantioenriched halohydrins

To a solution of the starting halohydrin in 2 mL of DMF, 1.05 equiv. of potassium thioacetate was added. The mixture was stirred at room temperature. When the starting halohydrin was completely consumed (TLC, about 30'), the remaining electrophile (1.1 equiv.) and K_3PO_4 (1.1 equiv.) were added. The reaction remained under agitation for 12 hours. Then, H_2O (5 mL) was added and the reaction was extracted with ethyl acetate (3 x 5 mL). The organic fractions were combined and extracted with H_2O (3 x 15 mL). The organic phase was dried with anhydrous Na_2SO_4. The solvent evaporated at reduced pressure and the crude oil obtained was subjected to column chromatography using an ethyl acetate/hexane mixture.

1-((2-Iodobenzyl)thio)octan-2-yl acetate (2a)

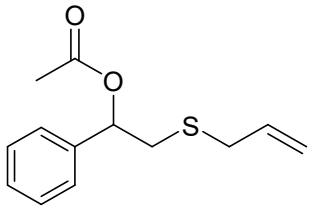


The MCR general procedure was carried out in DMF (0.5 mL) using 1-bromooctan-2-ol (20 mg, 0.11 mmol), potassium thioacetate (14 mg, 0.12 mmol), 1-(chloromethyl)-2-iodobenzene (30 mg, 0.12 mmol) and *t*-BuOK (14

mg, 0.12 mmol). After extraction, the crude was purified by column using silica-gel, employing a mixture of hexane/acetate (9:1) as mobile phase. A yellow oil (20 mg, 45%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.36 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.30 (td, -*J* = 7.5, 1.1 Hz, 1H), 6.93 (td, *J* = 7.7, 1.7 Hz, 1H), 5.0 (m, 1H), 3.85 (s, 2H), 2.63 (dd, *J* = 6.1, 3.3 Hz, 2H), 2.07 (s, 3H), 0.88 (t, *J* = 6.8 Hz). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 170.7 (C), 140.7 (C), 139.9 (CH), 130.1 (CH), 128.8 (CH), 128.3 (CH), 100.6 (C), 72.9 (CH), 41.8 (CH_2), 35.5 (CH_2), 33.2 (CH_2), 31.7 (CH_2), 29.0 (CH_2), 25.2 (CH_2), 22.6 (CH_2), 21.2 (CH_3), 14.1 (CH_3). HRMS (ESI^+, *m/z*): calcd. for $(C_{17}H_{25}INaO_2S)^+$(M+Na)$^+$ 443.0512, found 443.0493. For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -7.4 (c 0.1, $CHCl_3$).

2-(Allylthio)-1-phenylethyl acetate (2b)

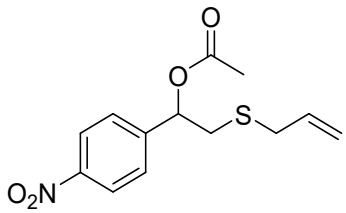


The MCR general procedure was performed using either *t*-BuOK or K_3PO_4, as follows:

Using *t*-BuOK: the reaction was carried out in DMF (0.5 mL) using 2-bromo-1-phenylethan-1-ol (25 mg, 0.13 mmol), potassium thioacetate (16 mg, 0.14 mmol), allyl bromide (18 mg, 0.15 mmol) and *t*-BuOK (17 mg, 0.15 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using CH_2Cl_2 as a mobile phase. A yellow oil (22 mg, 75%) was obtained.

Using K_3PO_4: the reaction was carried out in DMF (0.5 mL) using 2-bromo-1-phenylethan-1-ol (38 mg, 0.19 mmol), potassium thioacetate (24.1 mg, 0.21 mmol), allyl bromide (27.8 mg, 0.23 mmol) and K_3PO_4 (49 mg, 0.23 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using CH_2Cl_2 as a mobile phase. A yellow oil (33 mg, 73%) was obtained. **^{1}H NMR (400 MHz, $CDCl_3$): δ =** 7.33 (m, 6H), 5.85 (dd, *J* = 7.9, 5.7 Hz, 1H), 5.74 (ddt, *J* = 17.1, 10.0, 7.2 Hz, 1H), 5.09 (m, 2H), 3.06 (m, 2H), 2.91 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.81 (dd, *J* = 14.0, 5.7 Hz, 1H), 2.10 (s, 2H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.1 (C), 139.3 (C), 134.1 (CH), 128.5 (CH), 128.3 (CH), 126.6 (CH), 117.6 (CH_2), 74.7 (CH), 36.1 (CH_2), 35.0 (CH_2), 21.2 (CH_3). HRMS (ESI^+, *m/z*): calcd. for $(C_{13}H_{16}NaO_2S)^+$(M+Na)$^+$ 259.0763, found 259.0753. For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -76.6 (c 0.1, $CHCl_3$).

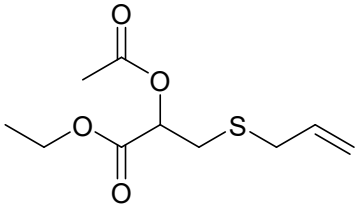
2-(Allylthio)-1-(4-nitrophenyl)ethyl acetate (2c)



The MCR general procedure was carried out in DMF (0.2 mL) using (*S*)-2-bromo-1-(4-nitrophenyl)ethan-1-ol (7 mg, 0.03 mmol), potassium thioacetate (4 mg, 0.033 mmol), allyl bromide (5 mg, 0.036 mmol) and K_3PO_4 (9 mg, 0.04 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using hexane/acetate (9:1) as mobile phase. A green oil (4 mg, 50%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (m, 1H), 7.52 (m, 1H), 5.90 (dd, *J* = 7.5, 5.9 Hz, 1H), 5.74 (m, 1H),5.11 (m, 2H), 3.10 (m, 2H), 2.91 (dd, *J* = 14.1, 7.5 Hz, 1H), 2.81 (dd, *J* = 14.1, 6.0 Hz, 1H), 2.14 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 169.7 (C), 147. 7 (C), 146.5 (C), 134.0 (CH), 127.7 (CH), 123.7 (CH), 118.1 (CH_2), 73.9 (CH), 36.0 (CH_2), 35.4 (CH_2), 21.2 (CH_3). For the (*S*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -11.3 (c 0.2, $CHCl_3$).

Ethyl 2-acetoxy-3-(allylthio)propanoate (2d)

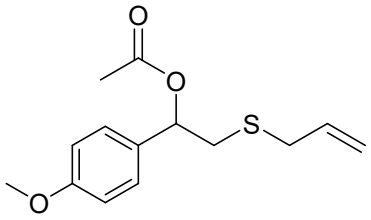


The MCR general procedure was carried out in DMF (0.5 mL) but using ethyl 3-bromo-2-hydroxypropanoate (50 mg, 0.25 mmol), potassium thioacetate (31 mg, 0.27 mmol), allyl bromide (35 mg, 0.29 mmol) and K_3PO_4 (62 mg, 0.29 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using hexane/acetate (3:1) as mobile phase. A yellow oil (32 mg, 54%) was obtained.

The same procedure was conducted in DMF (2 mL), employing 100 mg of the substrate (0.5 mmol), potassium thioacetate (61 mg, 0.53 mmol), allyl bromide (64.5 mg, 0.53 mmol) and K_3PO_4 (113 mg, 0.53 mmol). After work-up and chromatography, a yellow oil (113 mg, 96%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.78 (m, 1H), 5.17 (m, 3H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.21 (d, *J* = 7.2 Hz, 2H), 2.94 (dd, *J* = 14.4, 4.2 Hz, 1H), 2.86 (dd, *J* = 14.4, 7.7 Hz, 1H), 2.17 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.1 (C), 168.7 (C), 133.6 (CH), 117.9 (CH_2), 72.1 (CH), 61.7 (CH_2), 35.3 (CH_2), 31.2 (CH_2), 20.6 (CH_3), 14.1 (CH_3). HRMS (ESI^+, *m/z*): calcd. for $(C_{10}H_{16}NaO_4S)^+$(M+Na)$^+$ 255.0662, found 255.0683. For the (*R*)-enantioenriched compound (98% *ee*), $[\alpha]_D^{20}$ = -53.8 (c 0.1, $CHCl_3$).

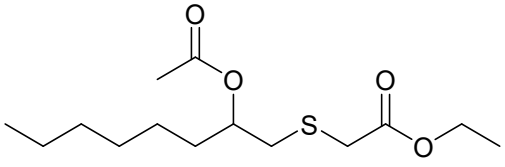
2-(Allylthio)-1-(4-methoxyphenyl)ethyl acetate (2e)



The MCR general procedure was carried out in DMF (0.5 mL) using 2-bromo-1-(4-methoxyphenyl)ethan-1-ol (25 mg, 0.11 mmol), potassium thioacetate (13 mg, 0.114 mmol), allyl bromide (20 mg, 0.12 mmol) and K_3PO_4 (25 mg, 0.12 mmol). After extraction, the crude was purified by silica-gel preparative plate, using hexane/ethyl acetate (3:1) as mobile phase. A colorless oil (16 mg, 56%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.29 (m, 2H), 6.88 (m, 2H), 5.80 (dd, *J* = 7.7, 6.1 Hz, 1H), 5.75 (ddt, *J* = 17.1, 10.0, 7.2 Hz, 1H), 5.14 (bd, , *J* = 10.0), 5.09 (dq, *J* = 16.9, 1.3 Hz, 1H), 3.80 (s, 1H), 3.09 (bdd, *J* = 13.2, 6.5 Hz, 1H), 3.04 (dd, *J* = 13.2, 6.9 Hz, 1H), 2.91 (dd, *J* = 13.9, 7.8 Hz, 1H), 2.79 (dd, *J* = 13.9, 6.0 Hz, 1H), 2.08 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.1 (CH_2),159.6 (CH_2),134.1 (CH_2),131.4 (CH_2), 128.1 (CH_2), 117.6 (CH_2), 113.9 (CH_2), 74.4 (CH_2), 55.3 (CH_2), 35.9 (CH_2), 35.0 (CH_2), 21.3 (CH_2). HRMS (ESI$^+$, *m/z*): calcd. for $(C_{14}H_{18}NaO_3S)^+$(M+Na)$^+$ 289.0869, found 289.0845. For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -59.9 (c 0.5, $CHCl_3$).

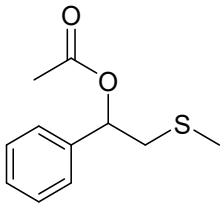
Ethyl 2-((2-acetoxyoctyl)thio)acetate (2g)



The MCR general procedure was carried out in DMF (0.5 mL) using 1-bromooctan-2-ol (50 mg, 0.24 mmol), potassium thioacetate (28 mg, 0.25 mmol), ethyl 2-iodoacetate (56 mg, 0.26 mmol) and potassium phosphate (57 mg, 0.26 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using a mixture of hexane / acetate (3:1) as mobile phase. A yellow oil (47 mg, 68%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.03 (m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.27 (dd, *J* = 35.5, 14.7 Hz, 2H), 2.88 (dd, *J* = 14.0, 4.9 Hz, 1H), 2.75 (dd, *J* = 14.0, 7.0 Hz, 1H), 2.09 (s, 3H), 1.65 (m, 2H), 1.31 (m, 12H), 0.90 (t, *J* = 6.5 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 170.6 (C), 170.2 (C), 72.3 (CH), 61.4 (CH_2), 36.2 (CH_2), 33.8 (CH_2), 33.3 (CH_2), 31.6 (CH_2), 29.0 (CH_2), 25.2 (CH_2), 22.5 (CH_2), 21.1 (CH_3), 14.1 (CH_2), 14.0 (CH_3). HRMS (ESI$^+$, *m/z*): calcd. for $(C_{14}H_{26}NaO_4S)^+$(M+Na)$^+$ 313.1444, found 313.1439. For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = +36.7 (c 0.1, $CHCl_3$).

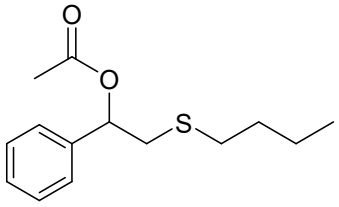
2-(Methylthio)-1-phenylethyl acetate (2h)[15]



The procedure mentioned above was carried out in DMF (0.5 mL) using 2-bromo-1-phenylethan-1-ol (30 mg, 0.15 mmol), potassium thioacetate (19 mg, 0.16 mmol), methyl iodide (24 mg, 0.17 mmol) and *t*-BuOK (19 mg, 0.17 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using a mobile phase of hexane/acetate (9:1). A yellow oil (21 mg, 68%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (m, 1H), 5.89 (dd, *J* = 7.8, 5.8 Hz, 1H), 2.97 (dd, *J* = 13.9, 7.9 Hz, 1H), 2.83 (dd, *J* = 13.9, 5.7 Hz, 1H), 2.11 (s, 1H), 2.08 (s, 1H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.1 (C), 139.3 (C), 128.6 (CH), 128.4 (CH), 126.7 (CH), 74.5 (CH), 40.2 (CH_2), 21.2 (CH_2), 16.3 (CH_3). GC-MS m/z (%) = 150 (81) [(M – AcOH)]$^+$, 107 (100), 77 (54), 103 (39), 78 (37), 104 (36), 79 (36), 61 (30), 121 (23), 62 (22), 91 (21), 105 (21), 135 (15). For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -67.4 (c 0.1, $CHCl_3$).

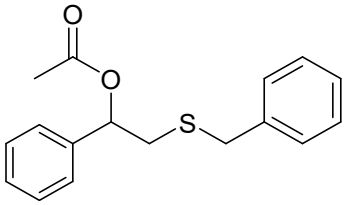
2-(Butylthio)-1-phenylethyl acetate (2i)[16]



The MCR general procedure was carried out in DMF (0.5 mL) using 2-bromo-1-phenylethan-1-ol (30 mg, 0.15 mmol), potassium thioacetate (19 mg, 0.16 mmol), butyl bromide (24 mg, 0.17 mmol) and *t*-BuOK (19 mg, 0.17 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using of hexane/acetate (9:1) as mobile phase. A yellow oil was obtained (20 mg, 53%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34 (m, 1H), 5.85 (dd, *J* = 7.8, 5.9 Hz, 1H), 2.98 (dd, *J* = 13.9, 7.8 Hz, 1H), 2.86 (dd, *J* = 13.9, 5.9 Hz, 1H), 2.48 (t, *J* = 7.4 Hz, 2H), 2.10 (s, 3H), 1.53 (quint, *J* = 7.5 Hz, 2H), 1.37 (sext, *J* = 7.3 Hz, 2H), 0.89 (t, *J* = 7.3 Hz, 1H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.1 (C), 139.4 (C), 128.5 (CH), 128.3 (CH), 126.7 (CH), 75.0 (CH), 37.9 (CH_2), 32.4 (CH_2), 31.6 (CH_2), 21.9 (CH_2), 21.2 (CH_3), 13.6 (CH_3). MS (EI): m/z (%) = 192 (70) $[(M - AcOH)]^+$, 107 (100), 61 (42), 104 (23), 136 (23), 103 (21), 77 (19), 79 (18), 135 (17), 91 (14). For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -56.6 (c 0.1, $CHCl_3$).

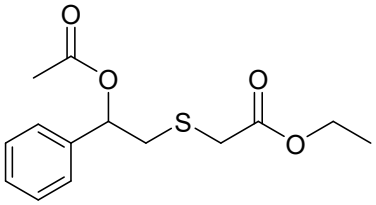
2-(Benzylthio)-1-phenylethyl acetate (2j)[16]



The MCR general procedure was carried out in DMF (0.5 mL) using 2-bromo-1-phenylethan-1-ol (40 mg, 0.2 mmol), potassium thioacetate (24 mg, 0.21 mmol), benzyl bromide (39 mg, 0.23 mmol) and K_3PO_4 (50 mg, 0.23 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using CH_2Cl_2 as mobile phase. A yellow oil (46 mg, 80%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44 – 7.17 (m, 10H), 5.83 (dd, *J* = 7.9, 5.7 Hz, 1H), 3.64 (dd, *J* = 16.0, 13.5 Hz, 2H), 2.86 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.72 (dd, *J* = 14.1, 5.7 Hz, 1H), 2.10 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.1 (C), 139.3 (C), 137.9 (C), 129.1 (CH), 128.6 (CH), 128.4 (CH), 127.2 (CH), 126.7 (CH), 74.6 (CH), 36.8 (CH_2), 36.5 (CH_2), 21.2 (CH_3). MS (EI): m/z (%) = 226 (29) $[(M - AcOH)]^+$, 91 (100), 107 (45), 104 (16), 135 (14), 65 (14), 77 (12), 92 (12), 123 (11), 79 (11). For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -69.6 (c 0.1, $CHCl_3$).

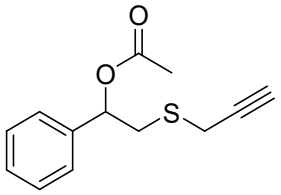
Ethyl 2-((2-acetoxy-2-phenylethyl)thio)acetate (2k)



The MCR general procedure was carried out in DMF (0.5 mL) using 2-bromo-1-phenylethan-1-ol (50 mg, 0.25 mmol), potassium thioacetate (31 mg, 0.27 mmol), ethyl 2-iodoacetate (61 mg, 0.28 mmol) and *t*-BuOK (32 mg, 0.28 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using of hexane/acetate (3:1) as mobile phase. A yellow oil (35 mg, 52%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (m, 5H), 5.93 (dd, *J* = 7.4, 6.1 Hz, 1H), 4.18 (q, *J* = 7.3 Hz, 1H), 3.20 (d, *J* = 14.6 Hz, 1H), 3.15 (d, *J* = 14.7 Hz, 1H), 3.07 (dd, *J* = 14.2, 7.6 Hz, 1H), 3.03 (dd, *J* = 14.1, 5.9 Hz, 1H), 2.11 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 2H. **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.2 (C), 170.1 (C), 139.0 (C), 128.6 (CH), 128.4 (CH), 126.6 (CH), 74.2 (CH), 61.4 (CH_2), 38.0 (CH_2), 33.7 (CH_2), 21.1 (CH_3), 14.2 (CH_3). HRMS (ESI$^+$, *m/z*): calcd. for $(C_{14}H_{18}NaO_4S)^+$(M+Na)$^+$ 305.0802, found 305.0818. For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -78.9 (c 0.1, $CHCl_3$).

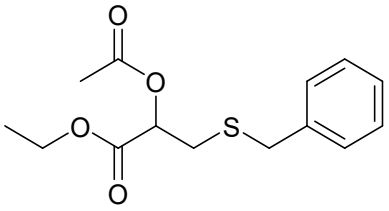
1-Phenyl-2-(prop-2-yn-1-ylthio)ethyl acetate (2l)



The MCR general procedure was carried out in DMF (0.5 mL) using 2-bromo-1-phenylethan-1-ol (50 mg, 0.25 mmol), potassium thioacetate (29 mg, 0.27 mmol), propargyl chloride (21 mg, 0.29 mmol) and *t*-BuOK (32 mg, 0.29 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using hexane/acetate (9:1) as mobile phase. A yellow oil (35 mg, 61%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (m, 5H), 5.94 (dd, *J* = 7.6, 5.9 Hz, 1H), 5.30 (s, 1H), 3.19 (dd, *J* = 7.7, 2.6 Hz, 2H), 3.10 (dd, *J* = 6.7, 3.5 Hz, 2H), 2.27 (t, *J* = 2.6 Hz, 1H), 2.12 (s, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.1 (C), 139.1 (C), 128.6 (CH),128.4 (CH),126.6 (CH), 79.5(C), 74.2 (CH), 71.6 (CH), 37.0 (CH_2), 21.2 (CH_2), 19.6 (CH_3). HRMS (ESI$^+$, *m/z*): calcd. for $(C_{13}H_{14}NaO_2S)^+$(M+Na)$^+$ 257.0607, found 257.0602. For the (*R*)-enantioenriched compound (>99% *ee*), $[\alpha]_D^{20}$ = -7.5 (c 0.2, $CHCl_3$).

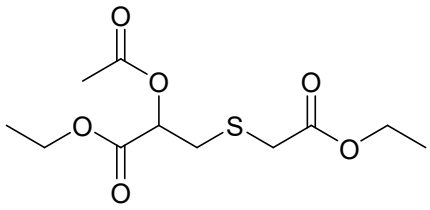
Ethyl 2-acetoxy-3-(benzylthio)propanoate (2m)



The MCR general procedure was carried out in DMF (0.5 mL) but using ethyl 3-bromo-2-hydroxypropanoate (50 mg, 0.25 mmol), potassium thioacetate (31 mg, 0.27 mmol), benzyl bromide (50 mg, 0.29 mmol) and *t*-BuOK (62 mg, 0.29 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using hexane/acetate as mobile phase (3:1). A colorless oil (44 mg, 54%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.30 (m, 5H), 5.19 (dd, *J* = 7.6, 4.3 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 2H), 2.87 (dd, *J* = 14.4, 4.3 Hz, 1H), 2.80 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.17 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 5H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =** 170.2 (C), 168.6 (C), 137.6 (C), 129.0 (CH), 128.6 (CH), 127.3 (CH), 72.1 (CH), 61.7 (CH_2), 36.7 (CH_2), 31.8 (CH_2), 20.7 (CH_3), 14.1 (CH_3). HRMS (ESI$^+$, *m/z*): calcd. for $(C_{14}H_{18}NaO_4S)^+$(M+Na)$^+$ 305.0818, found 305.0829. For the (*R*)-enantioenriched compound (98% *ee*), $[\alpha]_D^{20}$ = -31.3 (c 0.1, $CHCl_3$).

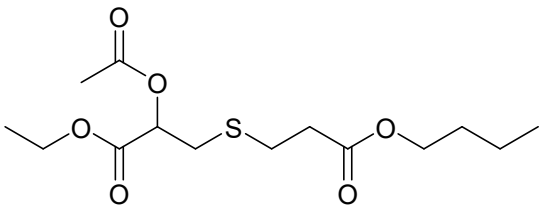
Ethyl 2-acetoxy-3-((2-ethoxy-2-oxoethyl)thio)propanoate (2n)



The MCR general procedure was carried out in DMF (2.5 mL) but using ethyl 3-bromo-2-hydroxypropanoate (300 mg, 1.08 mmol), potassium thioacetate (136 mg, 1.19 mmol), ethyl 2-bromoacetate (217 mg, 1.3 mmol) and K_3PO_4 (276 mg, 1.3 mmol). After extraction, the crude was purified by column with silica-gel, using a mobile phase of hexane/acetate (3:1). A colorless oil (336 mg, 79%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.27 – 4.17 (m, 5H), 3.38 (d, *J* = 15.0 Hz, 1H), 3.28 (d, *J* = 15.0 Hz, 1H), 3.17 (dd, *J* = 14.5, 3.9 Hz, 1H), 3.05 (dd, *J* = 14.5, 7.7 Hz, 1H), 2.17 (s, 3H), 1.30 (td, *J* = 7.1, 1.2 Hz, 6H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =**170.1 (C), 170.0 (C), 168.4 (C), 72.0 (CH), 61.9 (CH_2), 61.5 (CH_2), 34.0 (CH_2), 33.0 (CH_2), 20.6 (CH_3), 14.2 (CH_3), 14.1 (CH_3). For the (*R*)-enantioenriched compound (98% *ee*), $[\alpha]_D^{20}$ = -41.5 (c 0.1, $CHCl_3$).

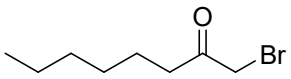
Ethyl 2-acetoxy-3-((3-butoxy-3-oxopropyl)thio)propanoate (2o)



The MCR general procedure was carried out in DMF (0.5 mL) but using ethyl 3-bromo-2-hydroxypropanoate (50 mg, 0.25 mmol), potassium thioacetate (31 mg, 0.27 mmol), butyl acrylate (36 mg, 0.29 mmol) and K_3PO_4 (62 mg, 0.29 mmol). After extraction, the crude was purified by column chromatography with silica-gel, using hexane/acetate (3:1) as mobile phase. A colorless oil (44 mg, 54%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.20 (dd, J = 7.5, 4.1 Hz, 1H), 4.21 (q, J = 7.1, 2H), 4.08 (t, J = 6.7 Hz, 2H), 3.00 (dd, J = 14.4, 4.1 Hz, 1H), 2.93 (dd, J = 14.4, 7.5 Hz, 1H), 2.86 (bt, J = 7.7 Hz, 2H), 2.60 (bt, J = 7.7 Hz, 2H), 2.14 (s, 3H), 1.59 (quint, J = 6.7, 2H), 1.36 (sext, J = 7.6 Hz, 2H), 1.27 (t, J = 7.1 Hz, 3H), 0.91 (t, J = 7.4 Hz, 3H). **^{13}C NMR (100 MHz, $CDCl_3$): δ =**171.7 (C), 170.0 (C), 168.5 (C), 72.4 (CH), 64.6 (CH_2), 61.7 (CH_2), 34.8 (CH_2), 33.1 (CH_2), 30.6 (CH_2), 27.9 (CH_2), 20.6 (CH_3), 19.1 (CH_2), 14.1 (CH_3), 13.6 (CH_3). HRMS (ESI$^+$, *m/z*): calcd. for $(C_{14}H_{24}NaO_4S)^+$(M+Na)$^+$ 343.1186, found 343.1174. For the (*R*)-enantioenriched compound (98% *ee*), $[\alpha]_D^{20}$ = -15.3 (c 0.2, $CHCl_3$).

1-Bromooctan-2-one (3a)[10]



Same protocol for the synthesis of **1a** was carried out, employing 1g of 1-octene. After stirring, Jones reagent was added (CrO_3 aq. H_2SO_4) according to the reported procedure.[17] After extraction, the crude was purified by column chromatography with silica-gel, using hexane/acetate (9:1) as mobile phase. A yellow oil (1215 mg, 62%) was obtained.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.87 (s, 2H), 2.63 (t, *J* = 7.4 Hz, 2H), 1.60 (s, 2H), 1.35 – 1.17 (m, 6H), 0.86 (t, *J* = 6.8 Hz, 3H). **^{13}C NMR (101 MHz, $CDCl_3$): δ =** 202.4 (C), 37.0 (CH_2), 34.4 (CH_2), 31.9 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.2 (CH_2), 24.0 (CH_2), 22.7 (CH_2), 14.2 (CH_3).

Enzymatic protocols and enzyme screening

General procedure for bioreduction using E.coli*/ADH-A.*

In a 1.5 mL Eppendorf tube, to a solution of the corresponding haloketone (20 mM) in Tris-H_2SO_4 buffer 50 mM pH 7.5, 1 mM NADH (570 µL) and 2-PrOH (30 µL), 20 mg of the corresponding enzyme preparation was added. The reaction remained under orbital agitation at 250 rpm and 30°C for 24 h. Then, the crude was extracted with EtOAc (3 x 2 mL) and H_2O (3 x 2mL). The organic fractions were combined and dried over anhydrous Na_2SO_4. The organic solvent was evaporated at reduced pressure and the crude oil obtained was analyzed by GC.

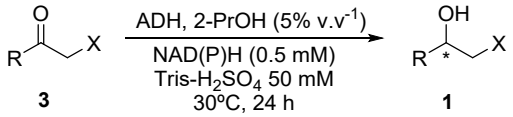
General procedure for bioreduction using E. coli/ADH-A, ADH-T, *SyADH, RasADH or LBADH*

In a 1.5 mL Eppendorf tube, to a solution of the corresponding haloketone (20 mM) in buffer Tris-H_2SO_4 50 mM pH 7.5, 1 mM NADPH (570 µL) and 2-PrOH (30 µL), 20 mg of the corresponding enzyme preparation was added. The reaction remained under orbital agitation at 250 rpm and 30°C for 24 h. Then, the crude was extracted with EtOAc (3 x 2 mL) and H_2O (3 x 2mL). The organic fractions were combined and dried over anhydrous Na_2SO_4. The organic solvent was evaporated at reduced pressure and the crude oil obtained was analyzed by GC.

General procedure for the preparative synthesis of enantiopure halohydrins with lyophilized enzyme preparations of E.coli*/ADH-T, E.coli/SyADH or E.coli/LBADH*

In a 50 mL falcon tube, to a solution of the corresponding haloketone (0.44 mmol, 20 mM) in buffer Tris-H_2SO_4 50 mM pH 7.5 (20.8 mL) and 2-PrOH (1.2 mL), NADPH (0.3 mM) and 500 mg of the corresponding enzyme preparation were added. In the case of **ketone 3c** or **3d**, the addition of 100 µL of DMSO was necessary for a proper solubilization of the substrate. The reaction was kept under orbital agitation at 250 rpm and 30°C for 24 h. Then, the reaction was extracted with EtOAc (3 x 20mL) and H_2O (3x20mL). The organic fractions were combined and dried over anhydrous Na_2SO_4. The organic solvent was evaporated at reduced pressure and the crude oil obtained was purified by column chromatography.

Table S1. Enzymatic screening for the preparation of enantioenriched halohydrins by stereoselective α-haloketone reduction.



	1a		**1b**		**1b'**		**1c**		**1d**		**1e**	
E. coli/ADH	conv. (%)	*ee* (%)	conv. (%)	*ee* (%)	conv. (%)	*ee* (%)	conv. (%)	*ee* (%)	conv. (%)	*ee* (%)	conv. (%)	*ee* (%)
ADH-A			>99	46 (*R*)	>99[a]	>99 (*R*)[a]	8	90 (*R*)	>99	98 (*R*)	72	>99 (*R*)
ADH-T	>99[b]	>99 (*R*)[b]	>99	98 (*R*)			80	98 (*R*)	>99	91 (*R*)	90	>99 (*R*)
TesADH			>99	74 (*R*)			97	96 (*R*)	>99	91 (*R*)	19	78 (*R*)
*Sy*ADH			>99	96 (*R*)			>99	<5	>99	98 (*R*)	94	97 (*R*)
*Ras*ADH			>99	<5			77	16 (*R*)	>99	<5	98	8 (*R*)
LBADH	>99[b]	>99 (*S*)[b]	>99	88 (*S*)			>99	>99 (*S*)	>99	90 (*S*)	90	>99 (*S*)

[a] Taken from ref.[18] [b] Taken from ref.[19]

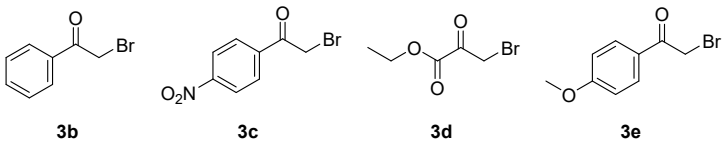
The enzymatic preparations gave good results for selected α-bromoketones **3**. For α-bromoacetophenone **3b**, the enzymatic preparation containing ADH-T afforded (*R*)-**1b** with great selectivity (>99% conv., 98% *ee*). For the α-bromoketone bearing an EWG (4-NO_2) in the aromatic ring, namely α-bromo-*p*-nitroacetophenone **3c**, LBADH-containing biocatalyst displayed high conversion and perfect selectivity, delivering (*S*)-**1c** (>99% conv., >99% *ee*). (*R*)-**1c** (80% conv., 98% *ee*) was also accessible employing ADH-T containing biocatalyst, as already reported.[19] In the case of ketone **3e** bearing an EDG (4-OMe) in the aromatic ring, the best performance was achieved using the enzymatic preparation containing ADH-T. In this case, conversion slightly dropped to 90% but the selectivity was excellent towards the product (*R*)-**1e** (>99% *ee*). The antipode (*S*)-**1e** (>99% *ee*) was also available by using LBADH-containing biocatalyst. The aliphatic ester-containing α-bromoketone **3d** was as well transformed into (*R*)-**1d** either by SyADH or ADH-A-containing enzymatic preparations (>99% conv., 98% *ee*). Either (*R*)- or (*S*)-enantiomers can be prepared by using the proper enzymatic preparation.

Analytics

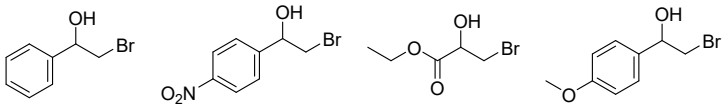
Retention times by Gas Chromatography and chromatograms of enantioenriched halohydrins

GC analyses were carried out in Agilent 6890 GC-FID. For the conversion and *ee* determination, a Chiral ChiralDex CB stationary phase column (25 m x 0.25 mm x 0.25 µm, 12.2 psi N_2) was used.

Table S2. Analytical separation by GC-FID for conversion measurement in the bioreduction of α-haloketones.



3b **3c** **3d** **3e**

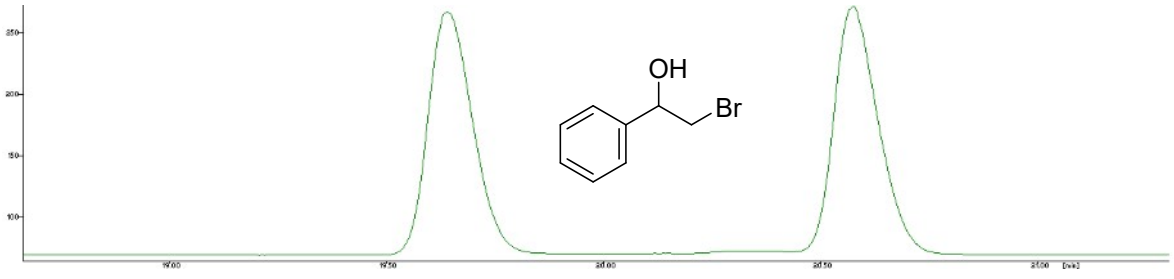


1b **1c** **1d** **1e**

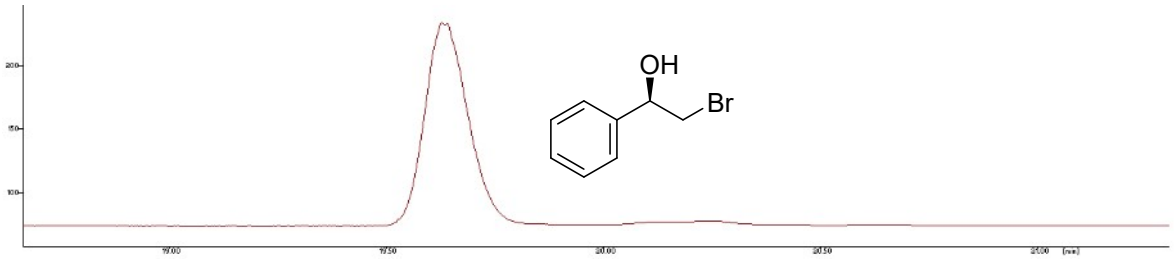
Compound	Temperature program[a]	Time (min)
1b	100/0/2/150/0/20/170/5	18.9
1c	115/7/20/170/7	12.2
1d	70/0/2/100/0/0.5/110/0/20/170/8	24.8
1e	115/0/20/150/20/170/5	23.7
2b	100/0/2/150/0/20/170/5	19.6 (*R*), 20.6 (*S*)
2c	115/7/20/170/7	13.1 (*R*), 13.3 (*S*)
2d	70/0/2/100/0/0.5/110/0/20/170/8	26.8 (*S*), 28.4 (*R*)
2e	115/0/20/150/20/170/5	19.5 (*R*), 20.4 (*S*)

[a] Initial temperature (°C)/ time (min)/ ramp (°C/min)/ final temperature (°C)/ time (min)/ ramp (°C/min)/ final temperature (°C)/ time (min)

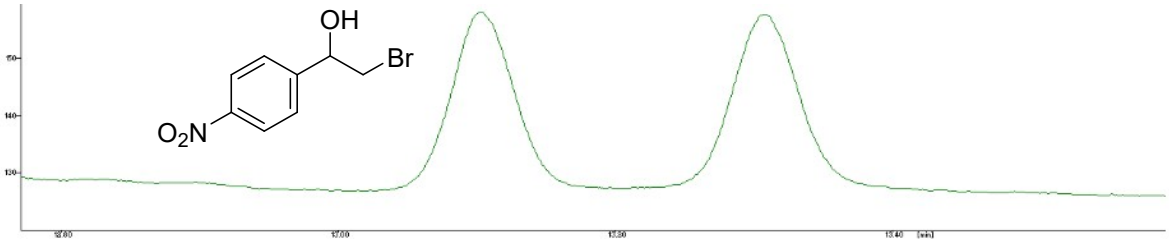
***rac*-1b obtained by chemical reduction**



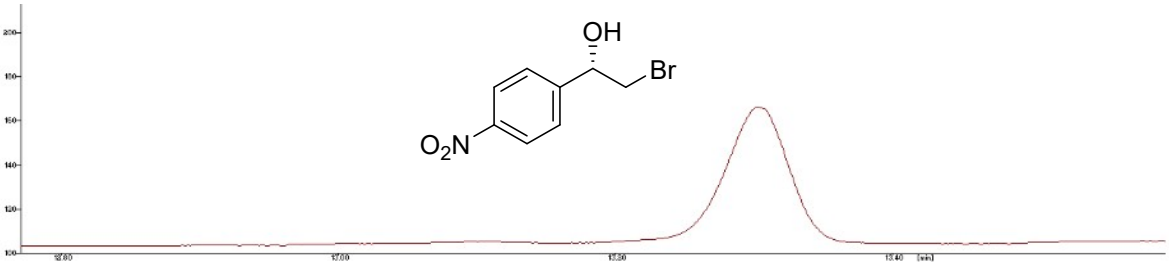
(*R*)-1b obtained by reduction with ADH-T



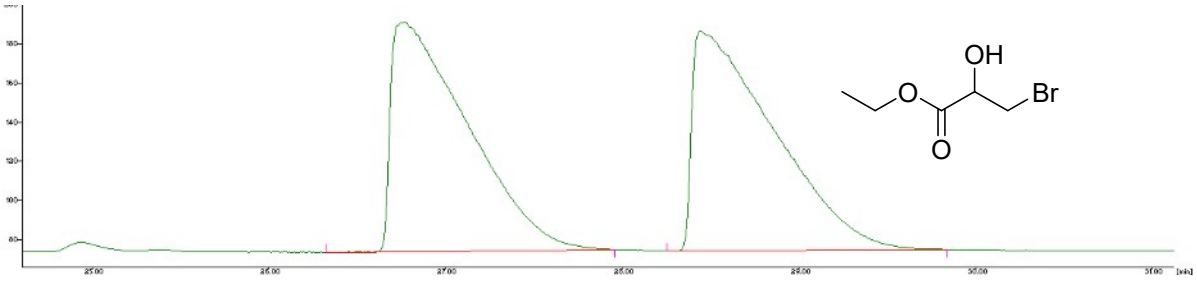
***rac*-2c obtained by chemical reduction**



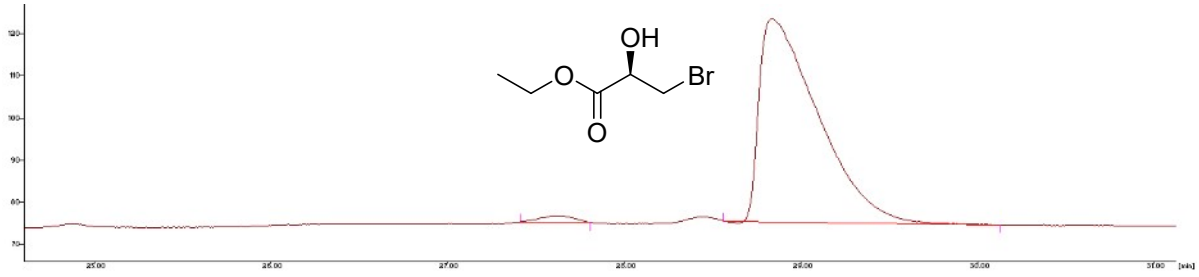
(*S*)-2c obtained by reduction with LBADH



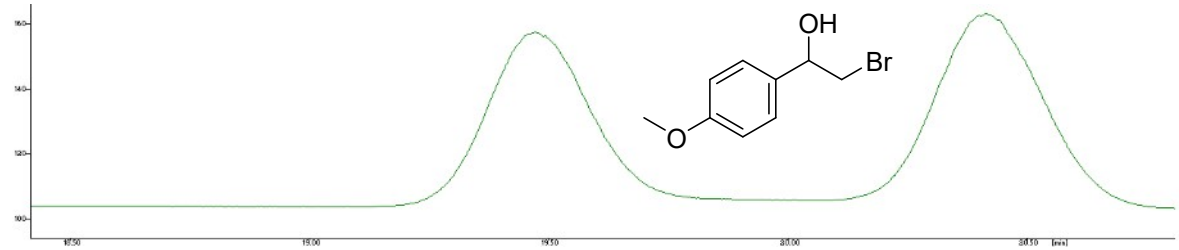
***rac*-2d obtained by chemical reduction**



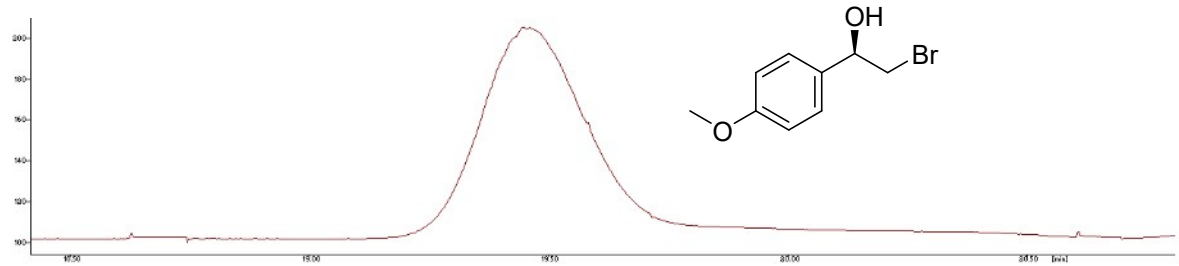
(*R*)-2d obtained by reduction with *SyADH*



***rac*-2e obtained by chemical reduction**

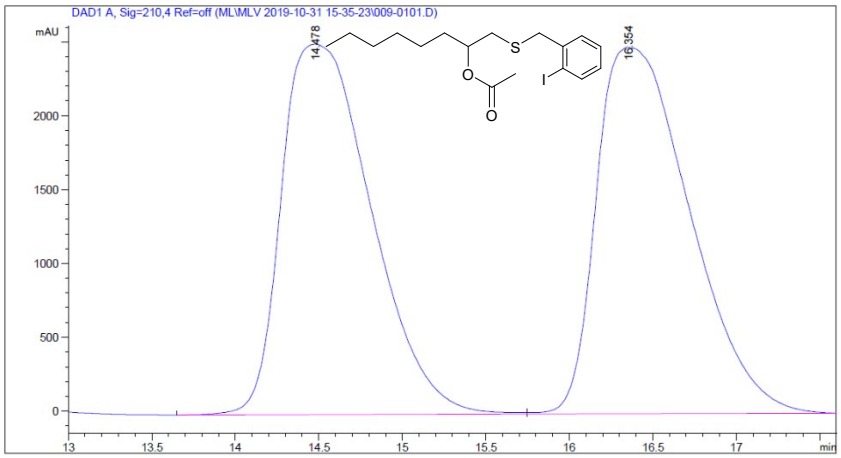


(*R*)-2e obtained by reduction with ADH-T

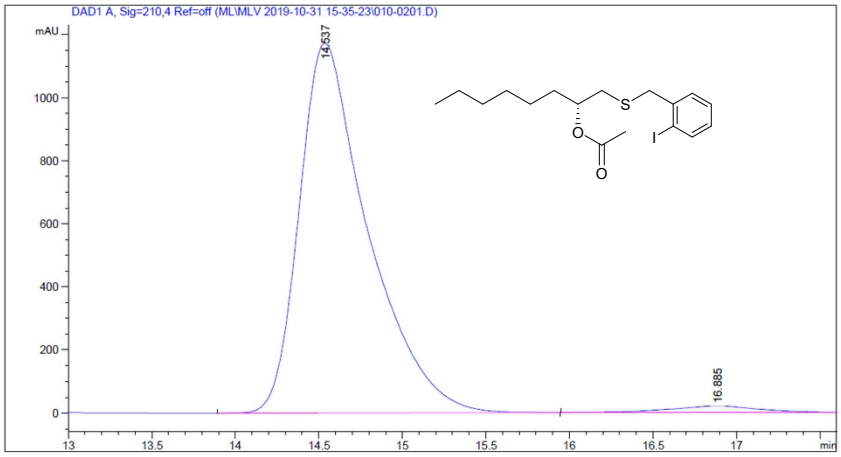


Retention times by HPLC and chromatograms of multicomponent reaction products

The conditions for HPLC analysis of compound **2a** were as follows: Chiralpak OD column (0.46 cm x 25 cm, Daicel Chemical Ind. Ltd.); isocratic elution: *n*-hexane / 2-propanol (99:1), 30 °C, flow 0.3 mL min^{-1}. Retention times: 14.5 (*S*), 16.4 (*R*). 98% *ee.*

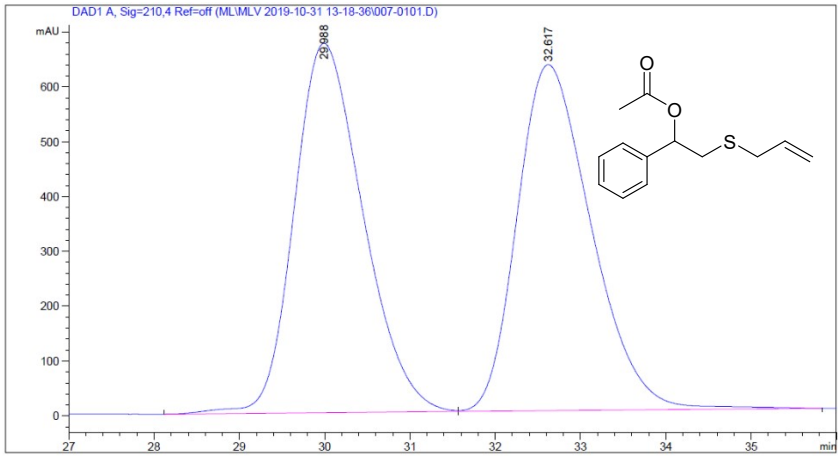


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.478	BV	0.4433	9.40001e4	2507.97095	49.3794
2	16.354	VB	0.4648	9.63630e4	2482.94116	50.6206

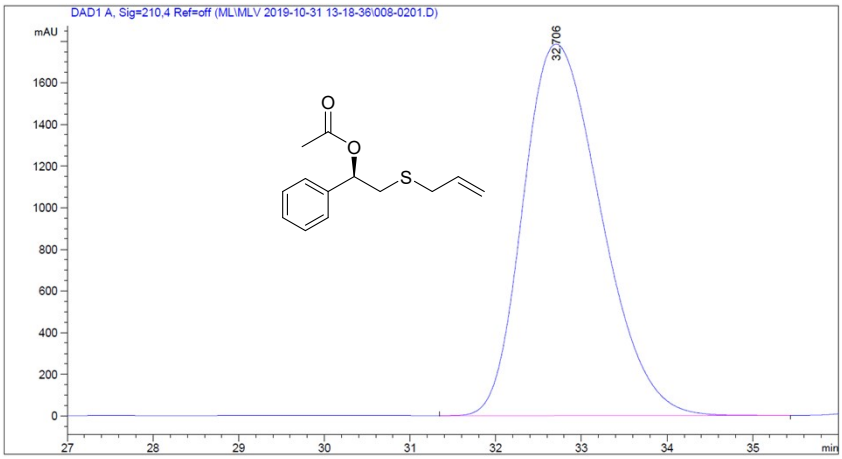


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.537	BB	0.4138	3.35346e4	1172.17883	97.6109
2	16.885	BB	0.5201	820.79468	21.36932	2.3891

The conditions for HPLC analysis of compound **2b** were as follows: Chiralpak OD column (0.46 cm x 25 cm, Daicel Chemical Ind. Ltd.); isocratic elution: *n*-hexane / 2-propanol (99:1), 30 °C, flow 0.3 mL min^{-1}. Retention times: 30.0 (*S*), 32.6 (*R*). >99% *ee.*

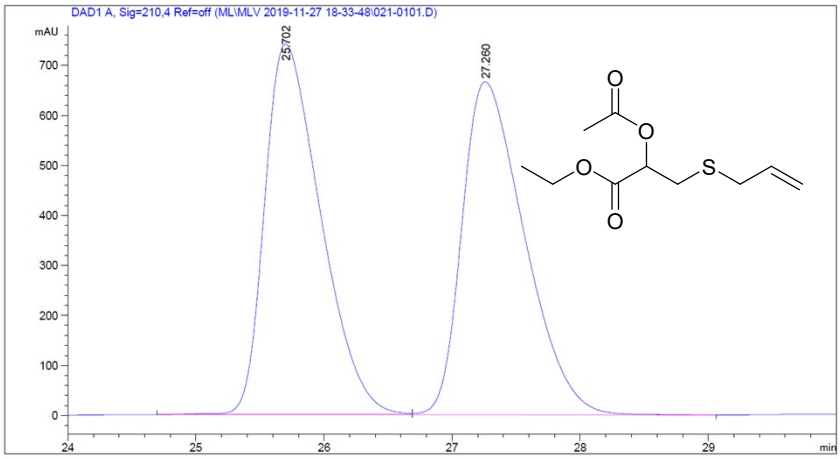


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.988	BV	0.8464	3.77714e4	673.40009	49.7481
2	32.617	VB	0.9195	3.81538e4	630.97540	50.2519

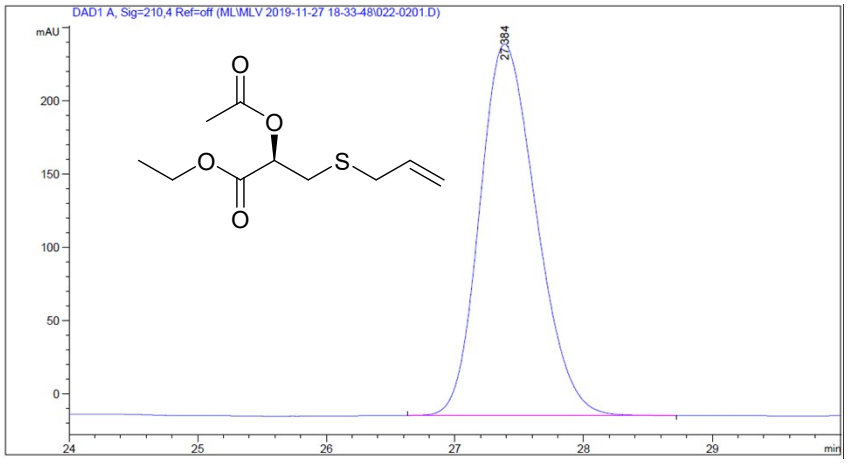


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.706	BB	0.8825	1.12681e5	1784.87292	100.0000

The conditions for HPLC analysis of compound **2d** were as follows: Chiralpak OJ-H column (0.46 cm x 25 cm, Daicel Chemical Ind. Ltd.); isocratic elution: *n*-hexane / 2-propanol (98:2), 30 °C, flow 0.5 mL min^{-1}. Retention times: 14.5 (*S*), 16.4 (*R*). >99% *ee.*

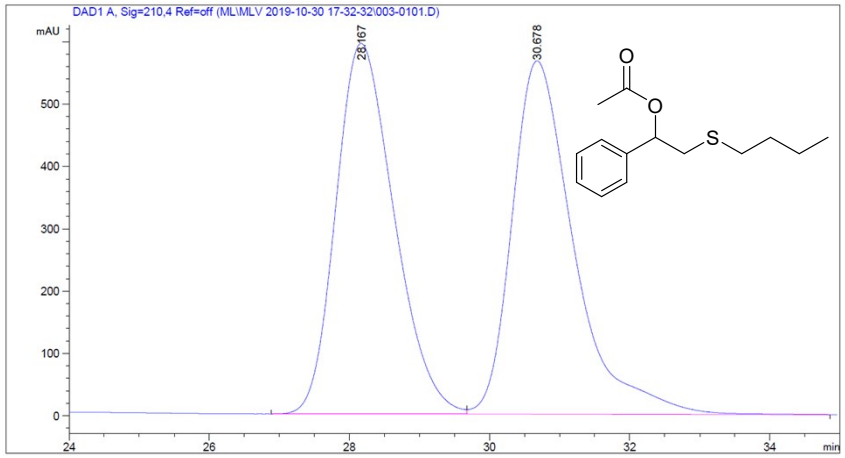


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.702	BV	0.4704	2.25180e4	741.19873	49.9819
2	27.260	VB	0.5228	2.25343e4	665.97443	50.0181

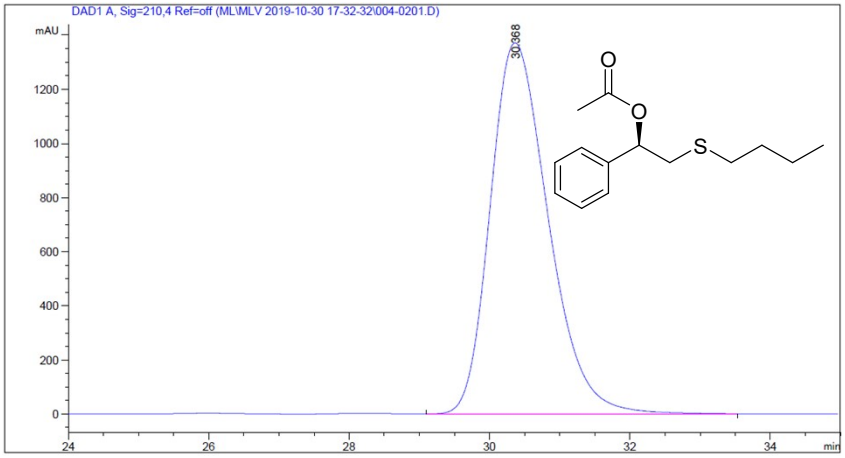


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.384	BB	0.4788	7749.42041	253.38451	100.0000

The conditions for HPLC analysis of compound **2i** were as follows: Chiralpak OD column (0.46 cm x 25 cm, Daicel Chemical Ind. Ltd.); isocratic elution: *n*-hexane / 2-propanol (99:1), 30 °C, flow 0.3 mL min^{-1}. Retention times: 28.2 (*S*), 30.4 (*R*). >99% *ee.*

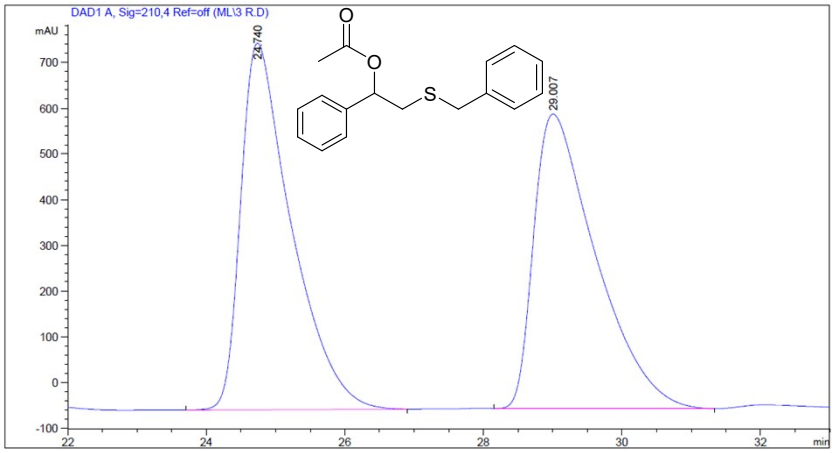


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	28.167	BV	0.8734	3.43303e4	594.77954	49.7568
2	30.678	VB	0.9249	3.46660e4	567.27209	50.2432

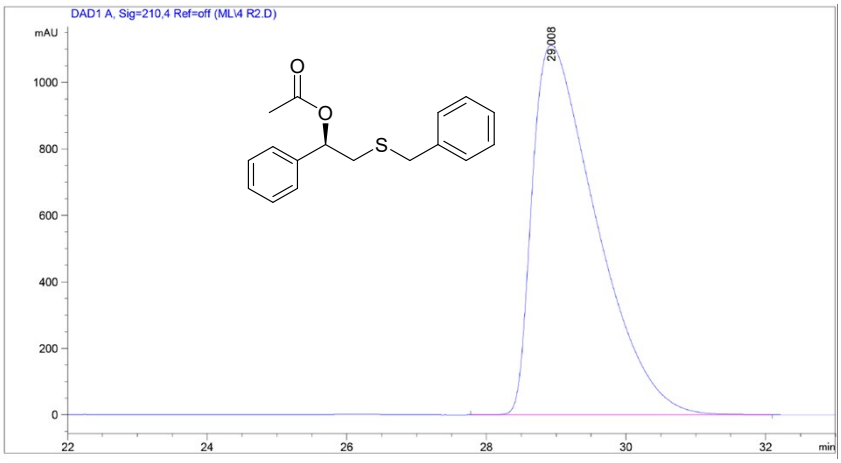


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.368	BB	0.8743	7.87447e4	1370.48230	100.0000

The conditions for HPLC analysis of compound **2j** were as follows: Chiralpak OD column (0.46 cm x 25 cm, Daicel Chemical Ind. Ltd.); isocratic elution: *n*-hexane / 2-propanol (99:1), 30 °C, flow 0.4 mL min^{-1}. Retention times: 24.7 (*S*), 29.0 (*R*). >99% *ee.*



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.740	BB	0.7343	4.07222e4	802.12164	50.3915
2	29.007	BB	0.9162	4.00895e4	644.08331	49.6085

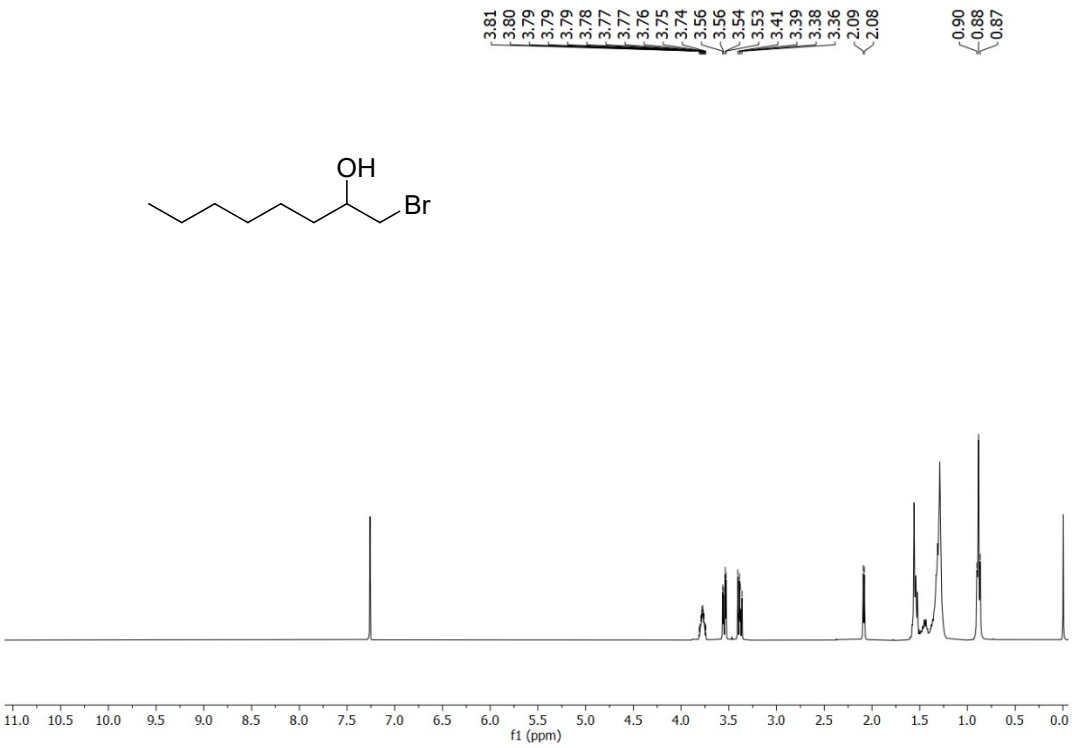


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.008	BB	0.9316	7.07171e4	1112.47583	100.0000

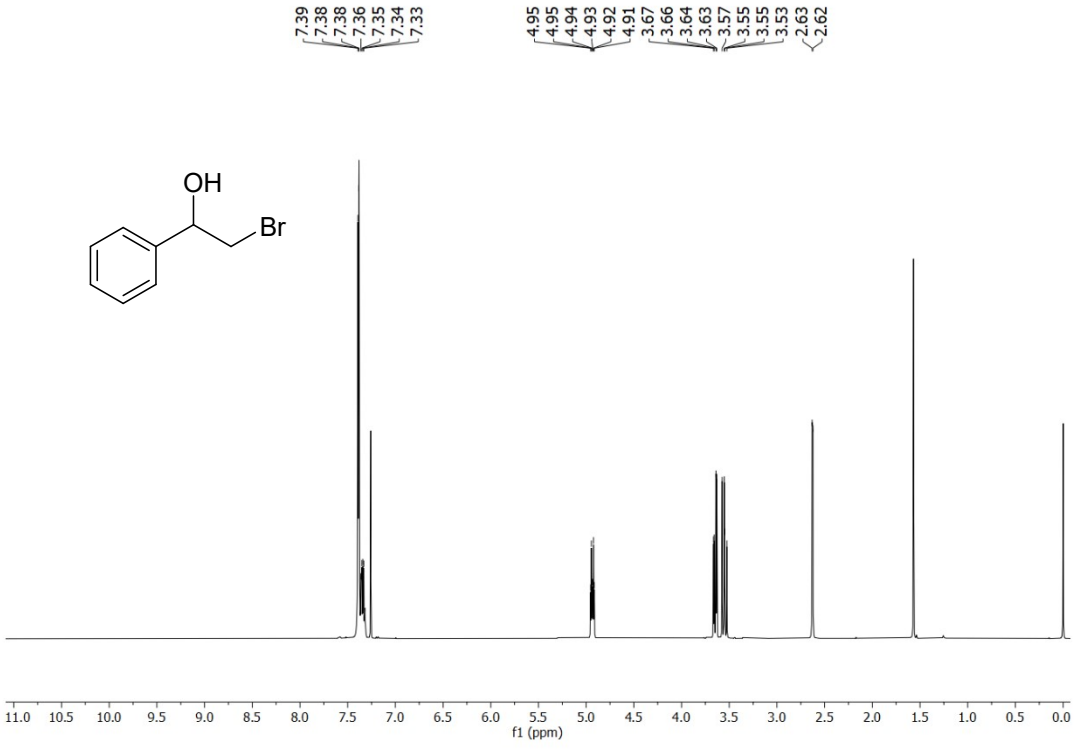
For the remaining compounds, suitable conditions could not be found with the available HPLC columns for enantiomeric excess determination. As enantiopurity is not eroded from the halohydrin to the ß-*O*-acyl sulfide, reported *ee* were taken from the respective starting halohydrin.

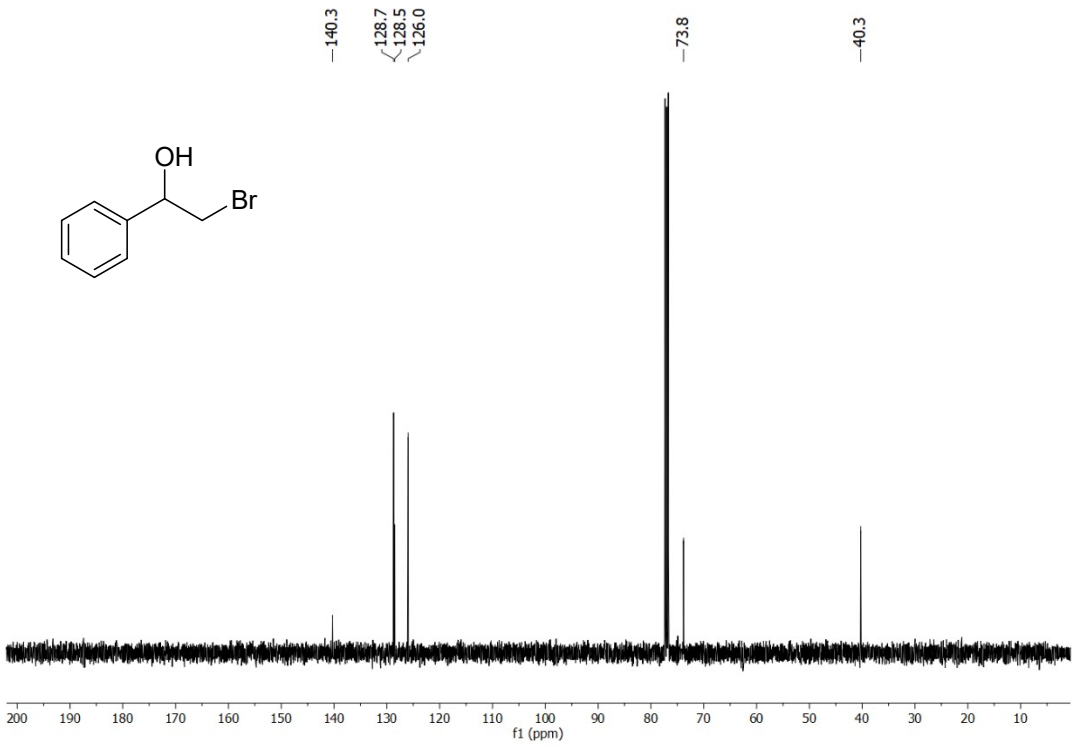
NMR spectra

*1-Bromooctan-2-ol (**1a**)*

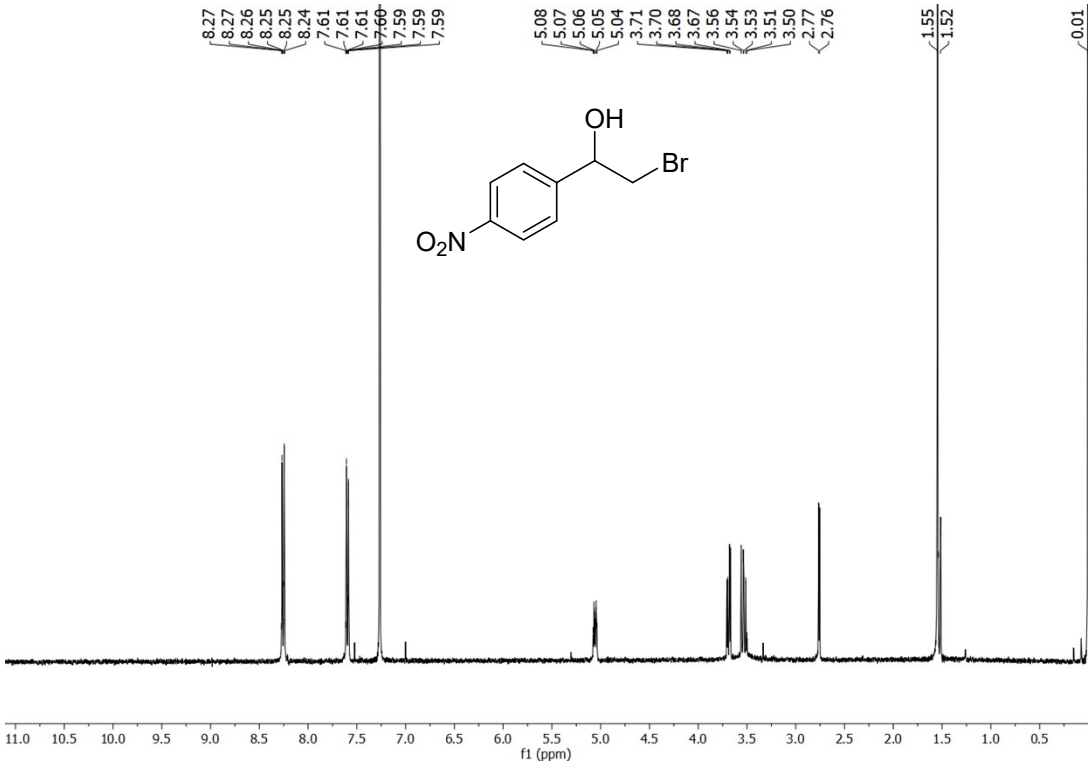


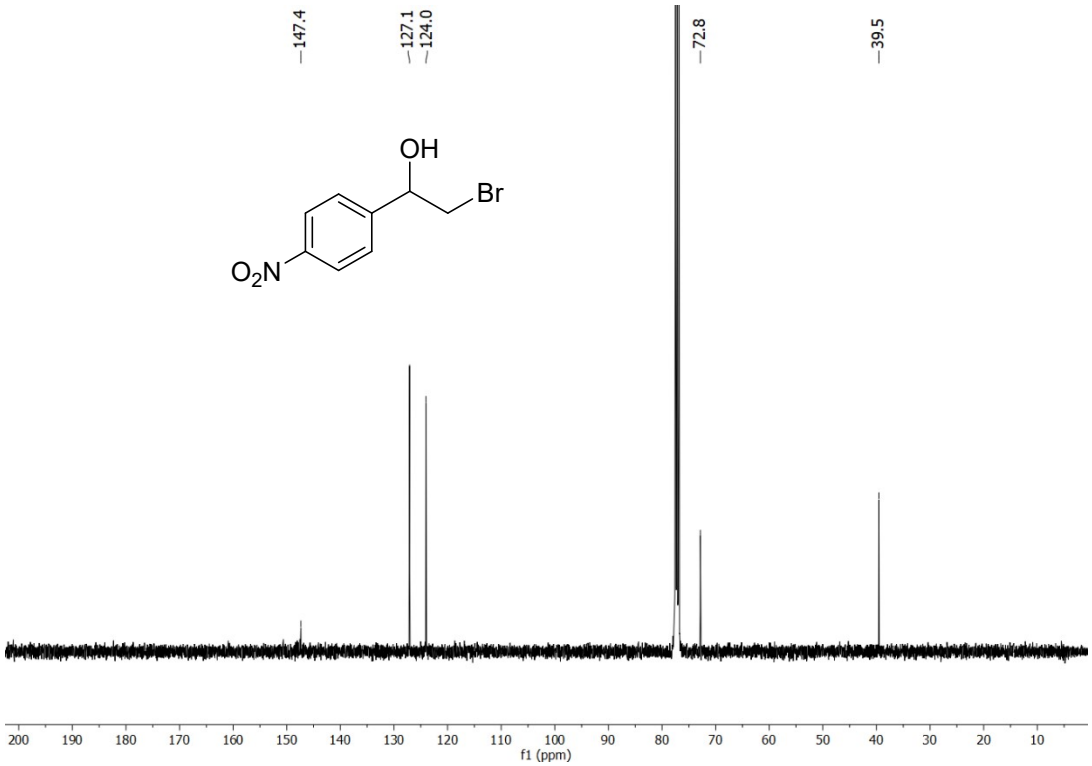
2-Bromo-1-phenylethan-1-ol (**1b**)



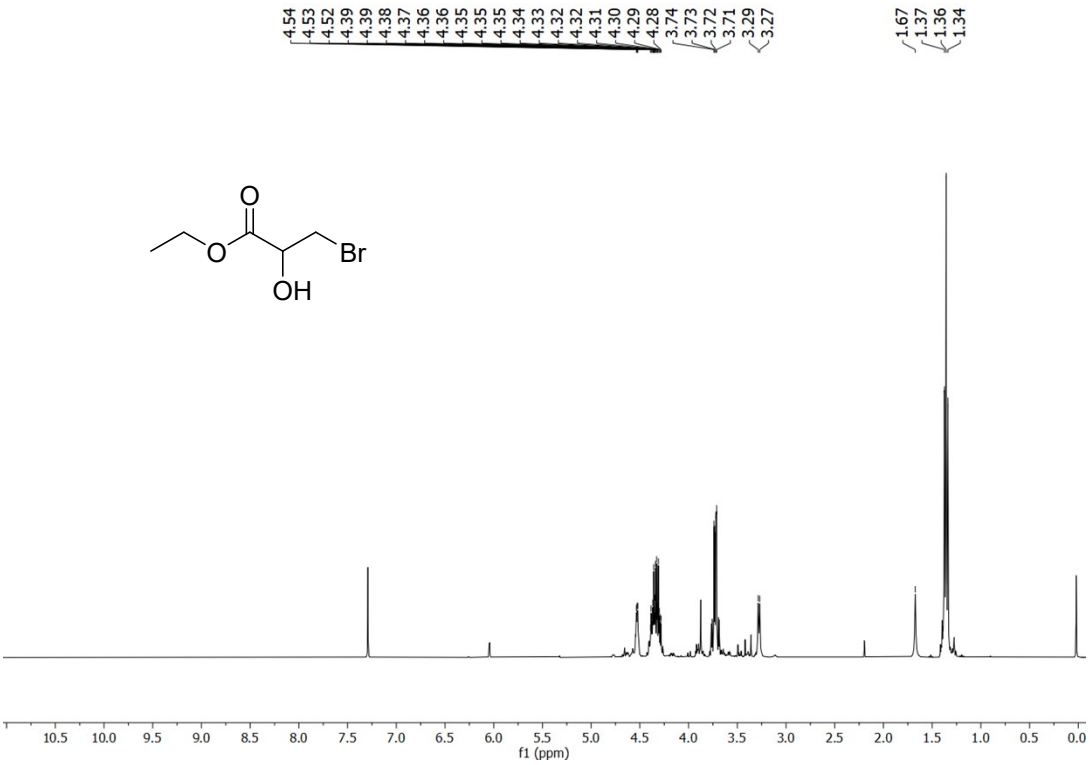

140.3
128.7
128.5
126.0
73.8
40.3
OH
Br
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

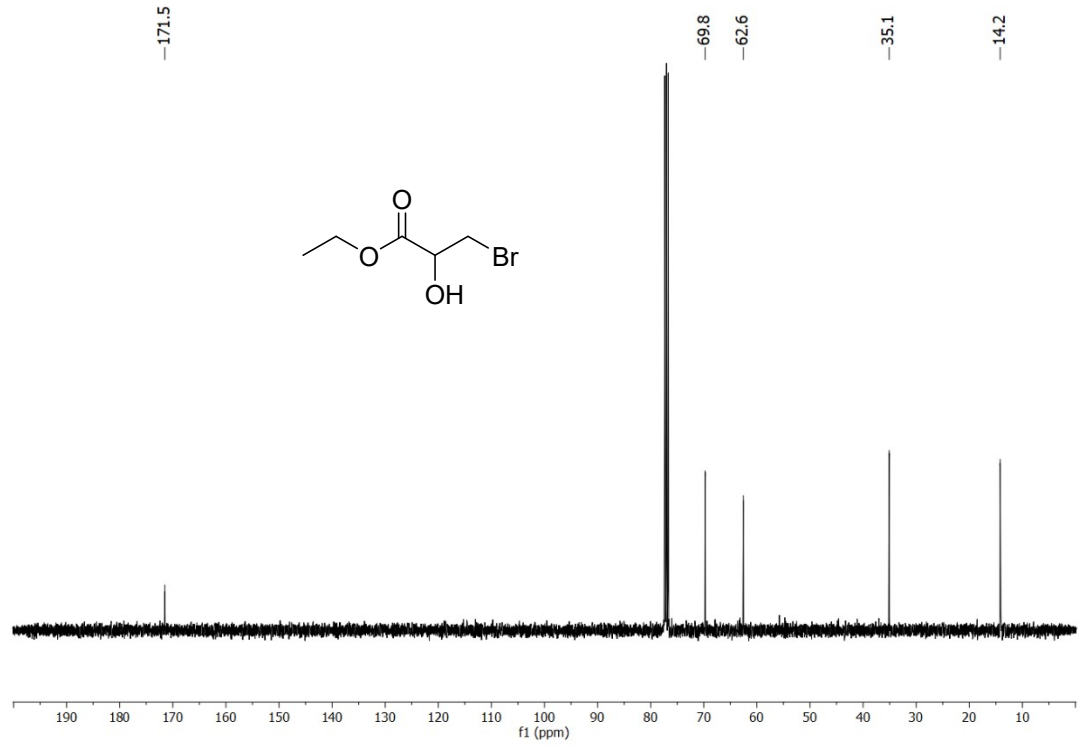
*2-Bromo-1-(4-nitrophenyl)ethan-1-ol (**1c**)*



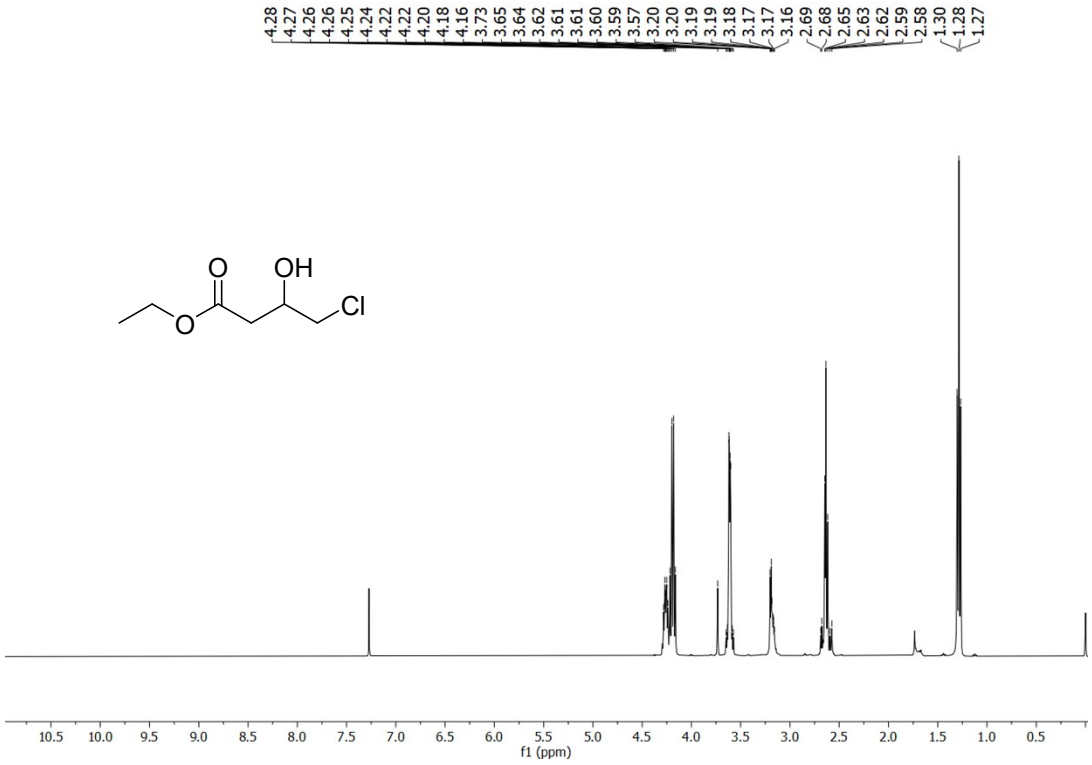


*Ethyl 3-bromo-2-hydroxypropanoate (**1d**)*

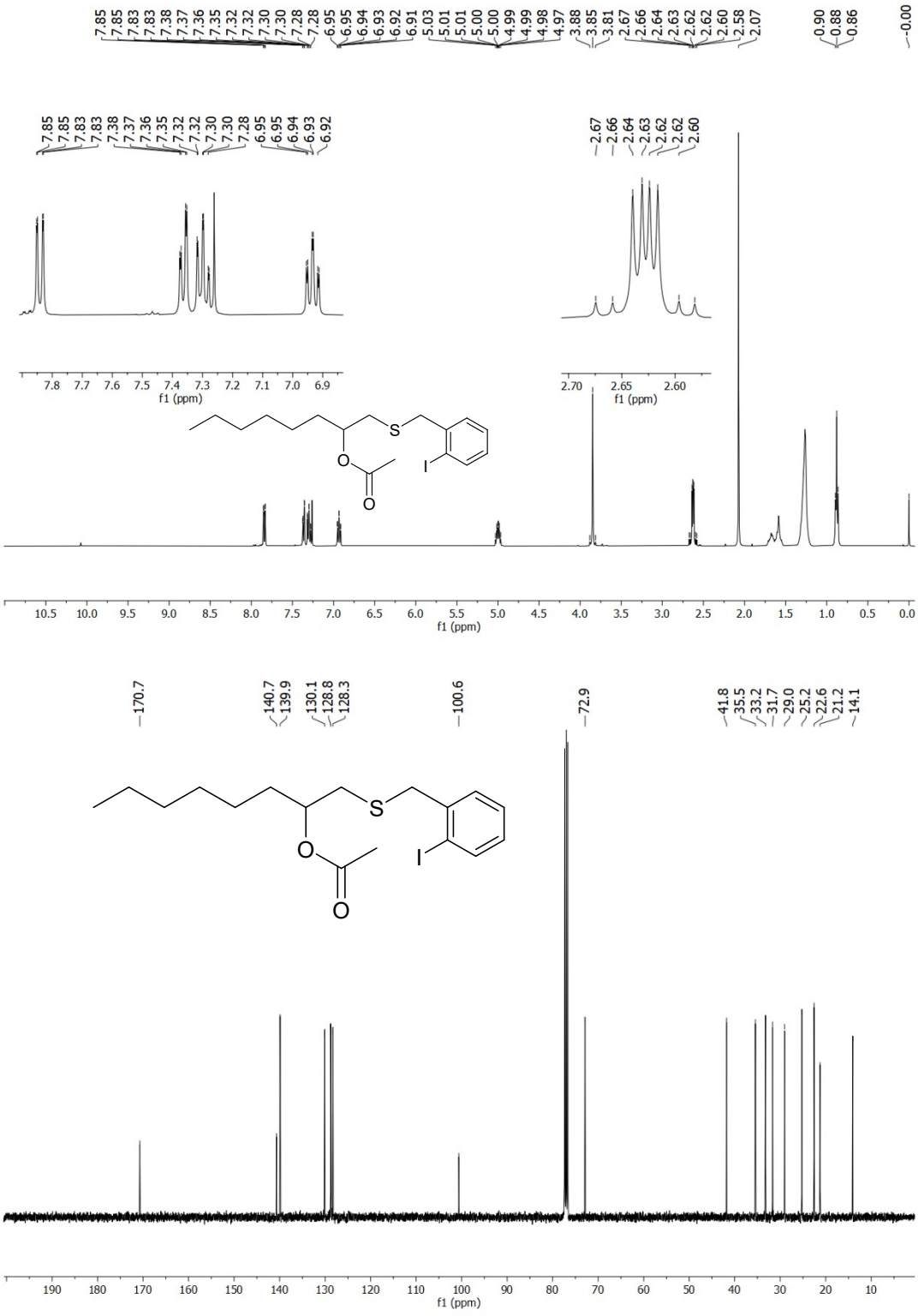




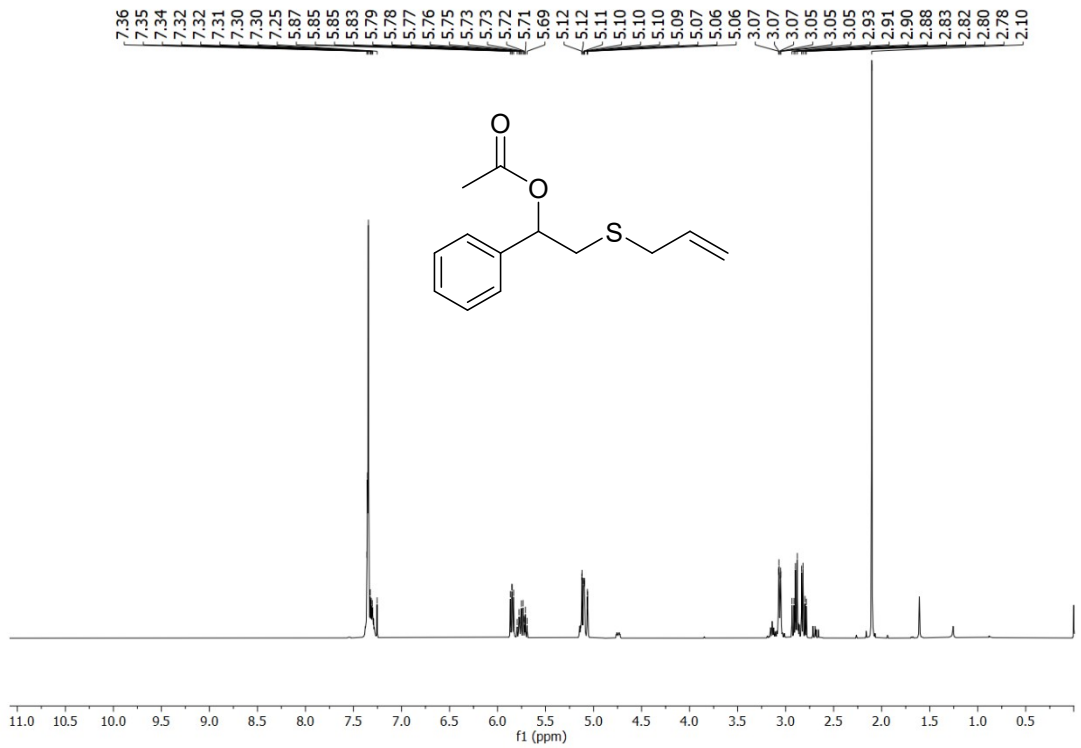
*Ethyl 4-chloro-3-hydroxybutanoate (**1f**)*

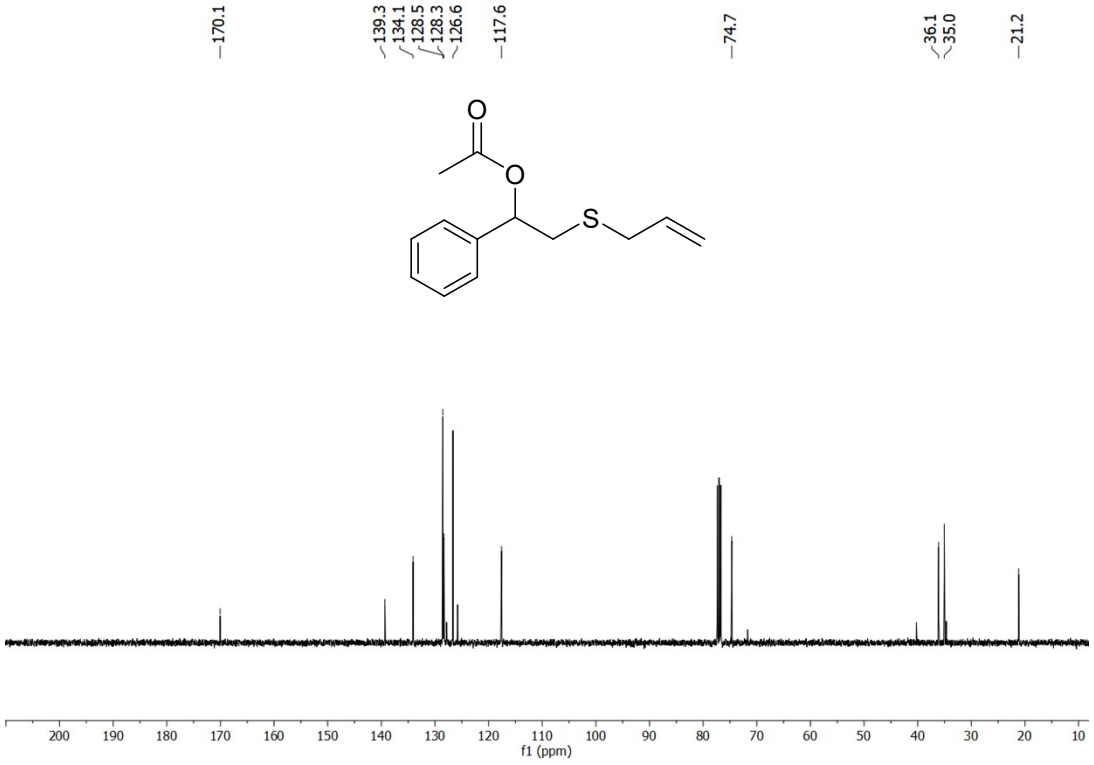


*1-((2-Iodobenzyl)thio)octan-2-yl acetate (**2a**)*

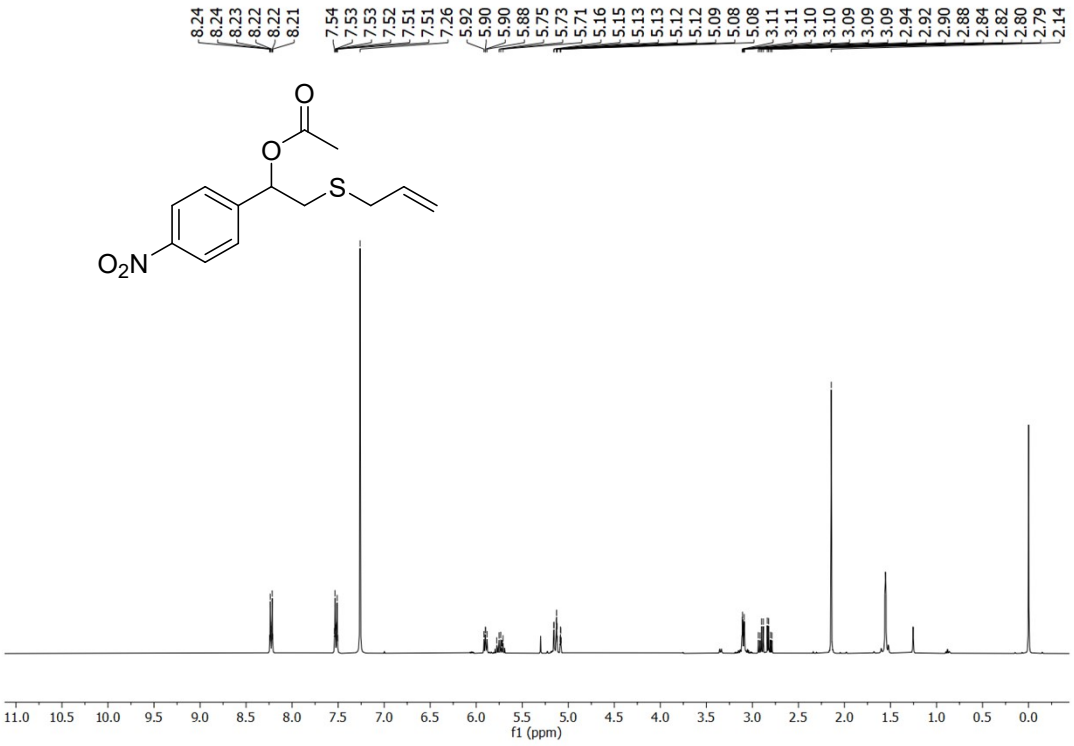


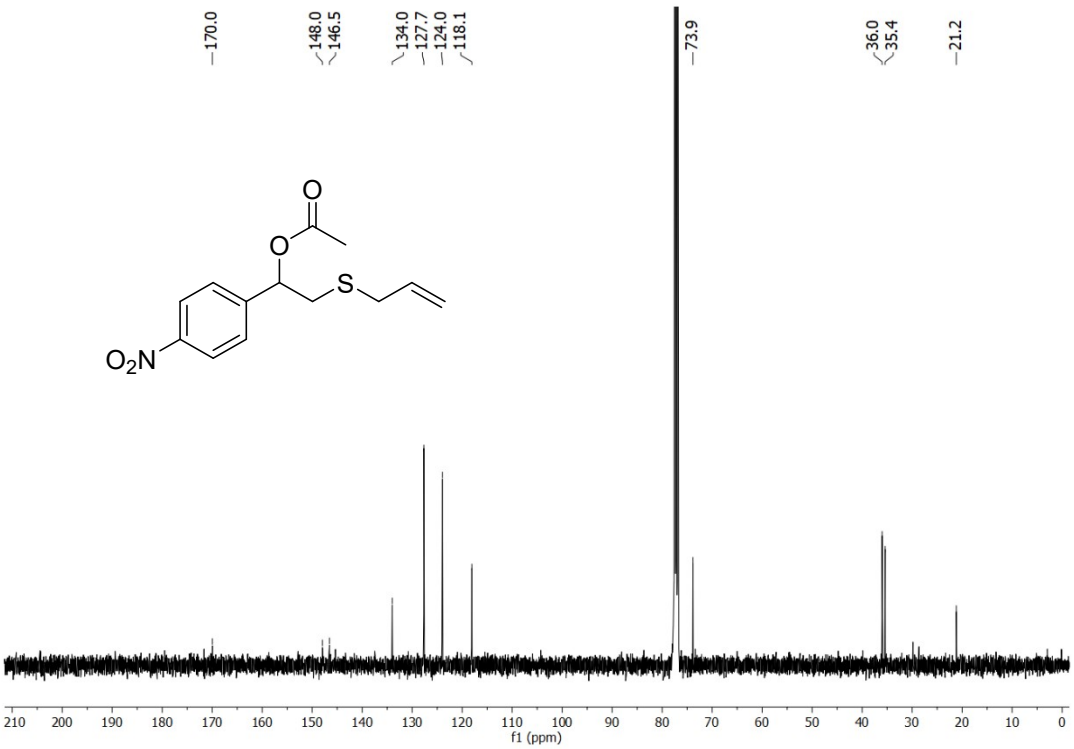
*2-(Allylthio)-1-phenylethyl acetate (**2b**)*

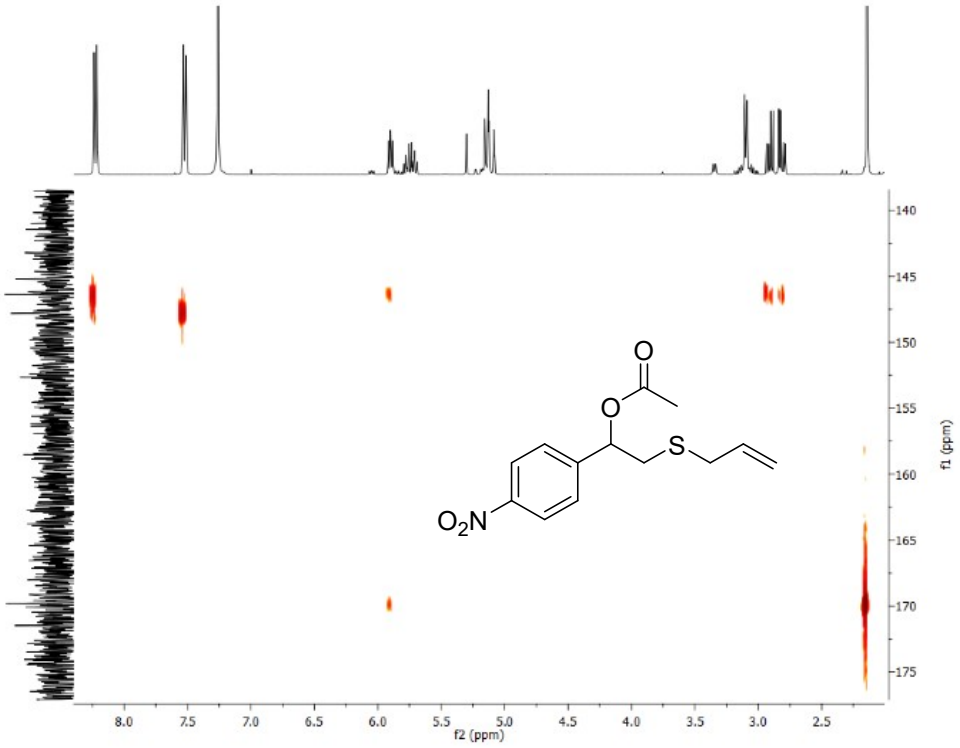




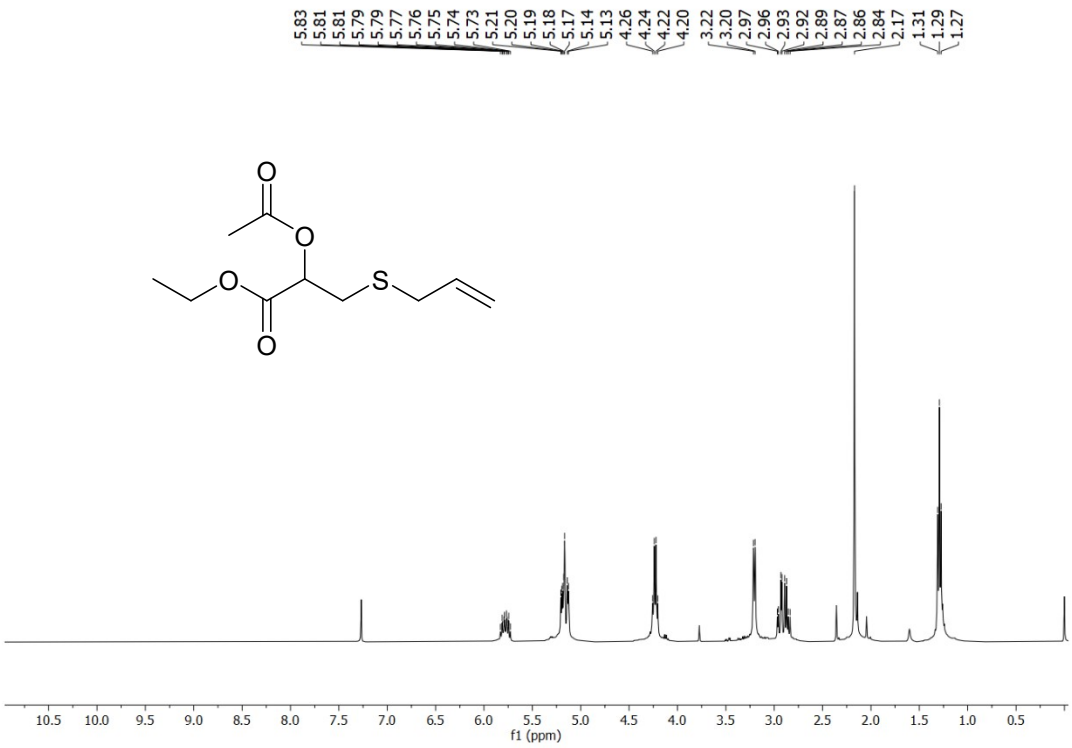
*2-(Allylthio)-1-(4-nitrophenyl)ethyl acetate (**2c**)*

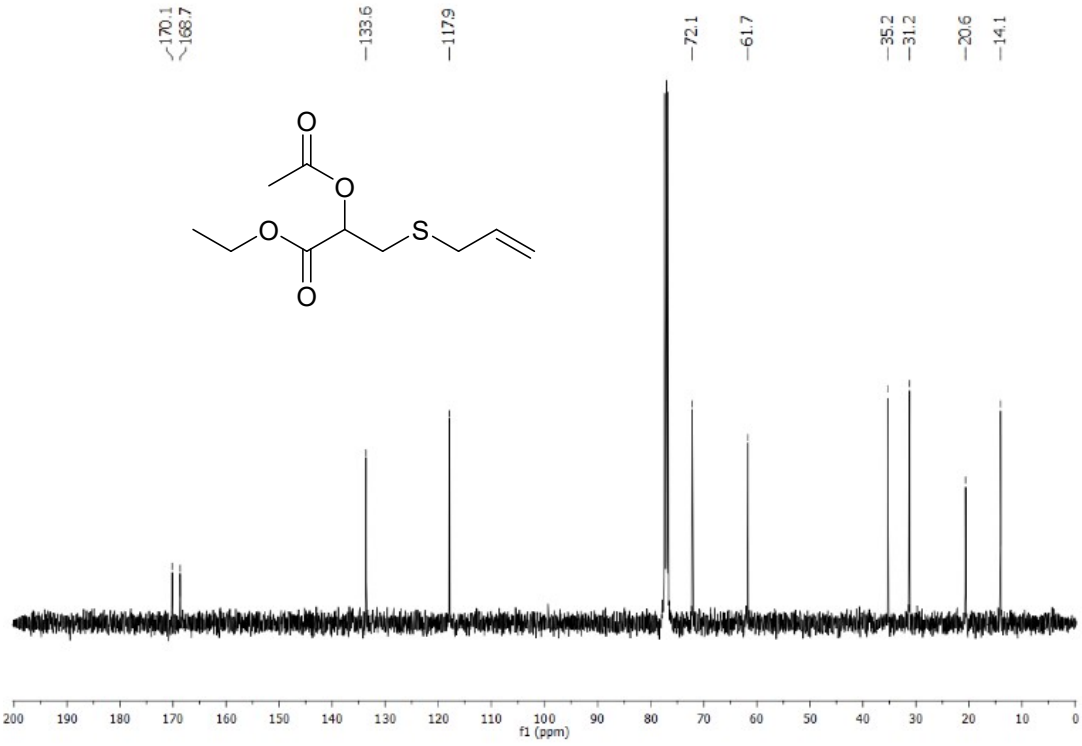




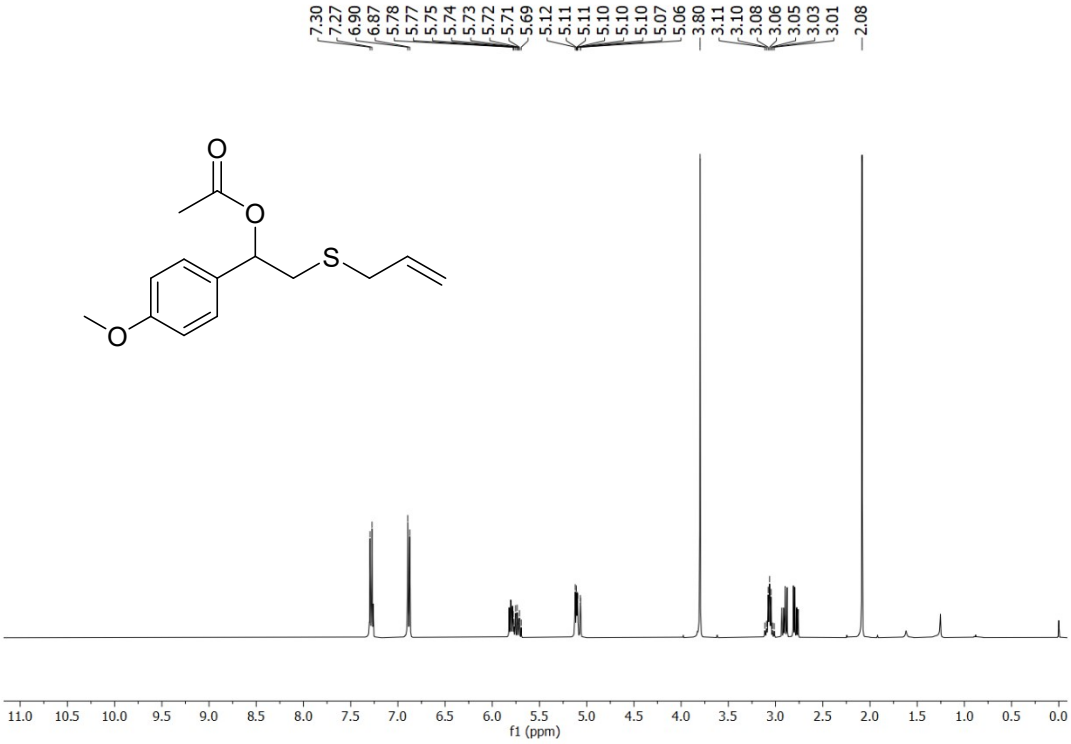

O
O
S
O_2N
140
145
150
155
160
165
170
175
f1 (ppm)
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
f2 (ppm)

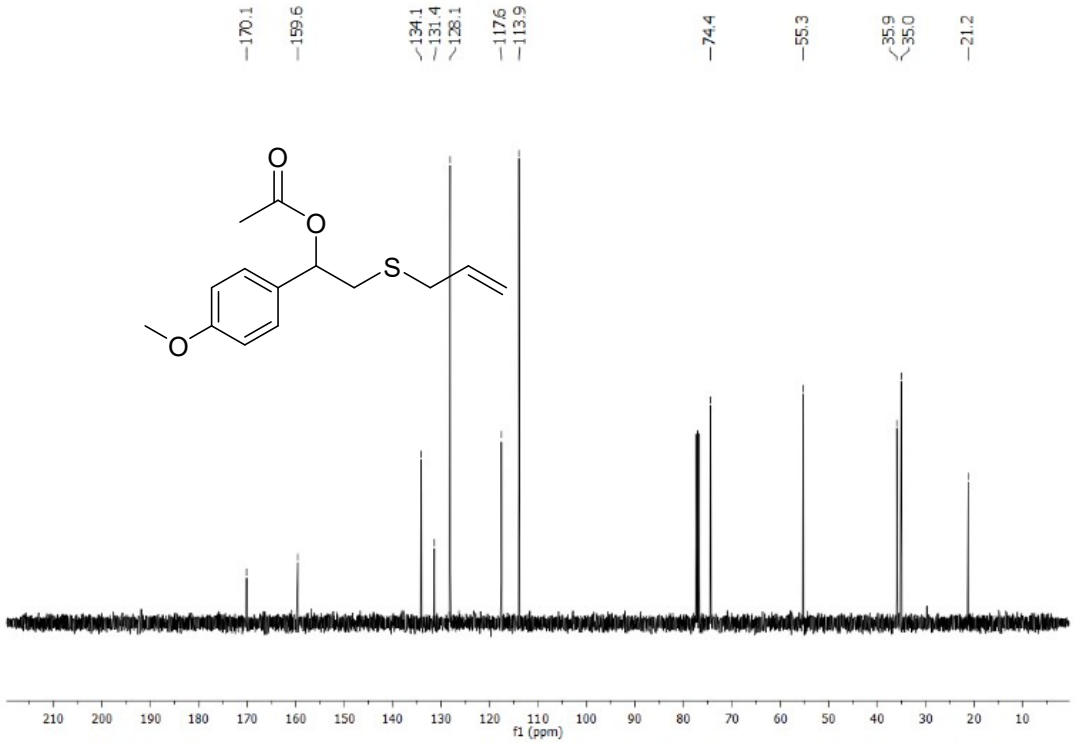
*Ethyl 2-acetoxy-3-(allylthio)propanoate (**2d**)*



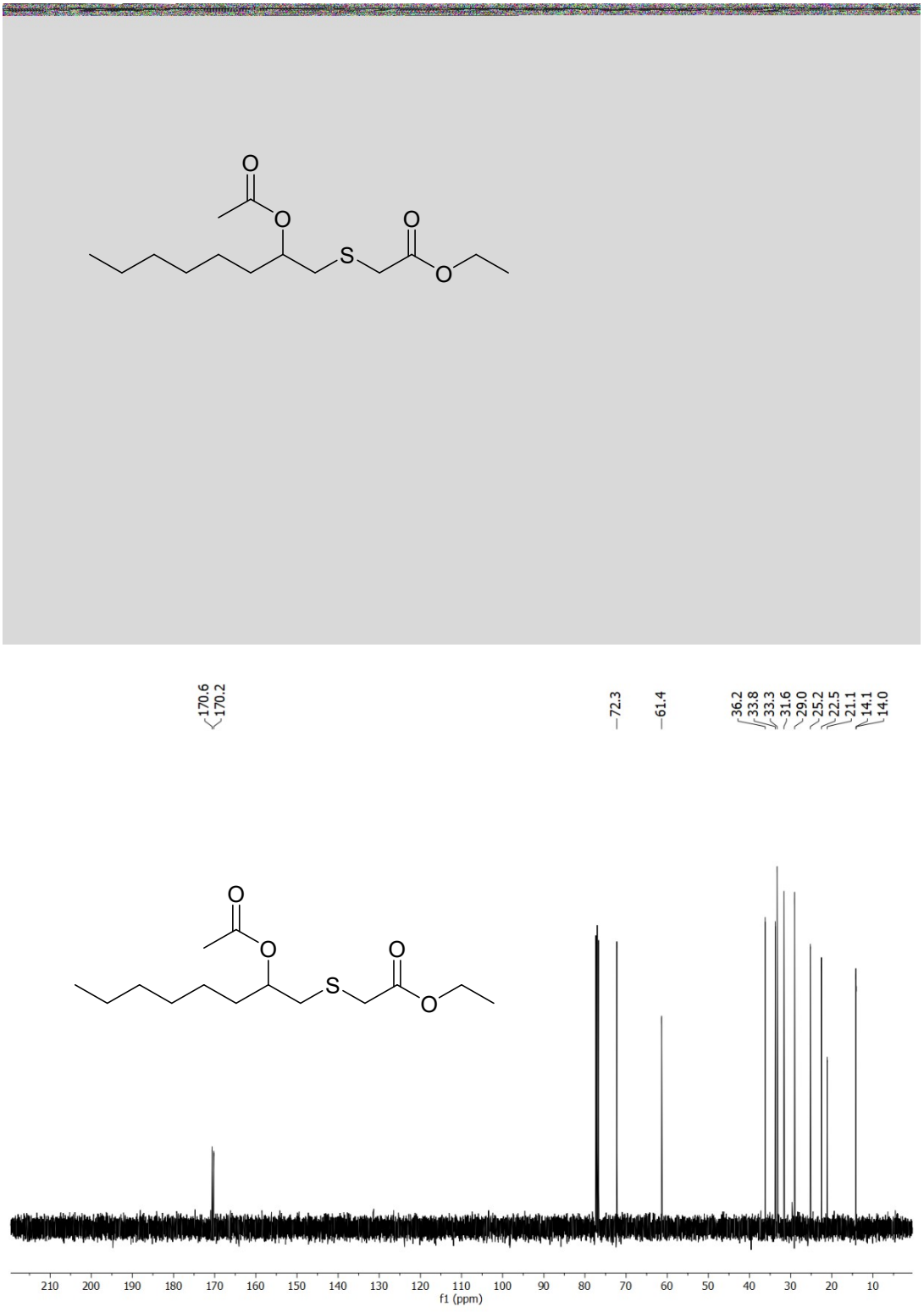


*2-(Allylthio)-1-(4-methoxyphenyl)ethyl acetate (**2e**)*

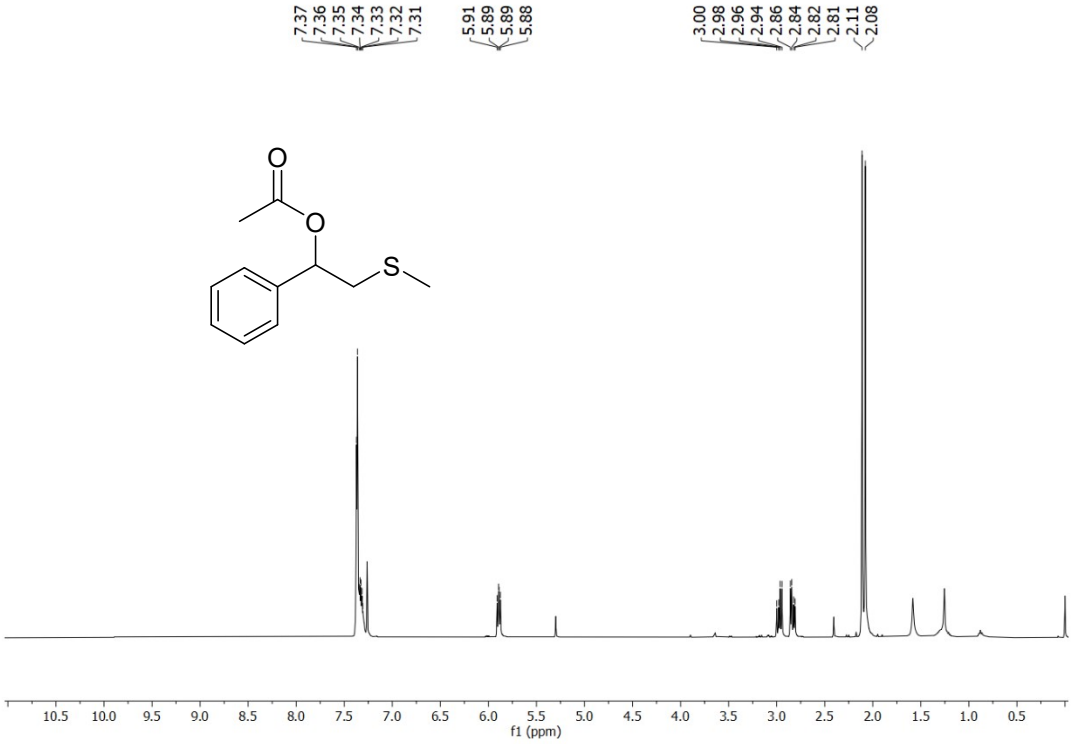


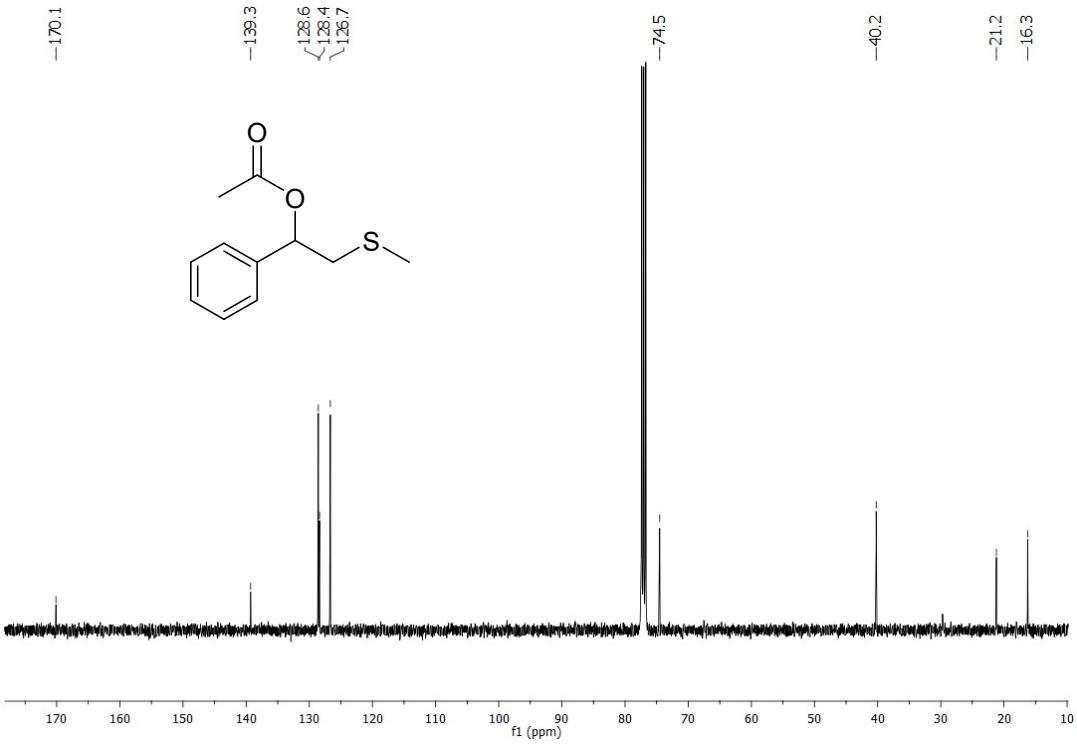


*Ethyl 2-((2-acetoxyoctyl)thio)acetate (**2g**)*

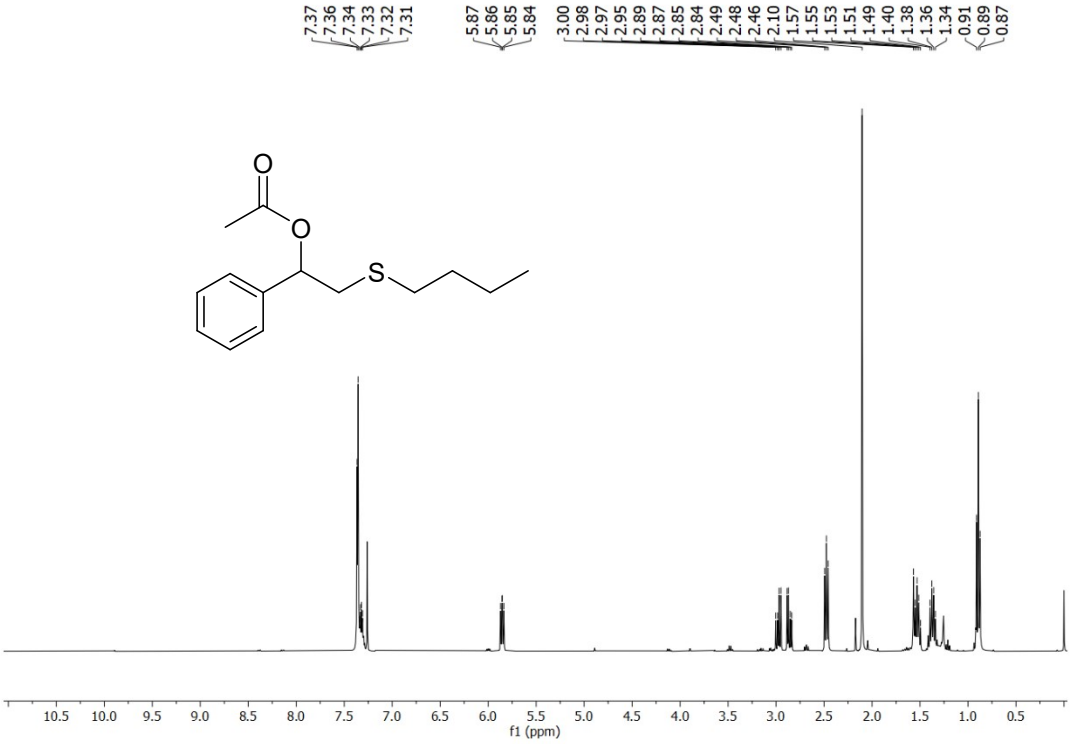


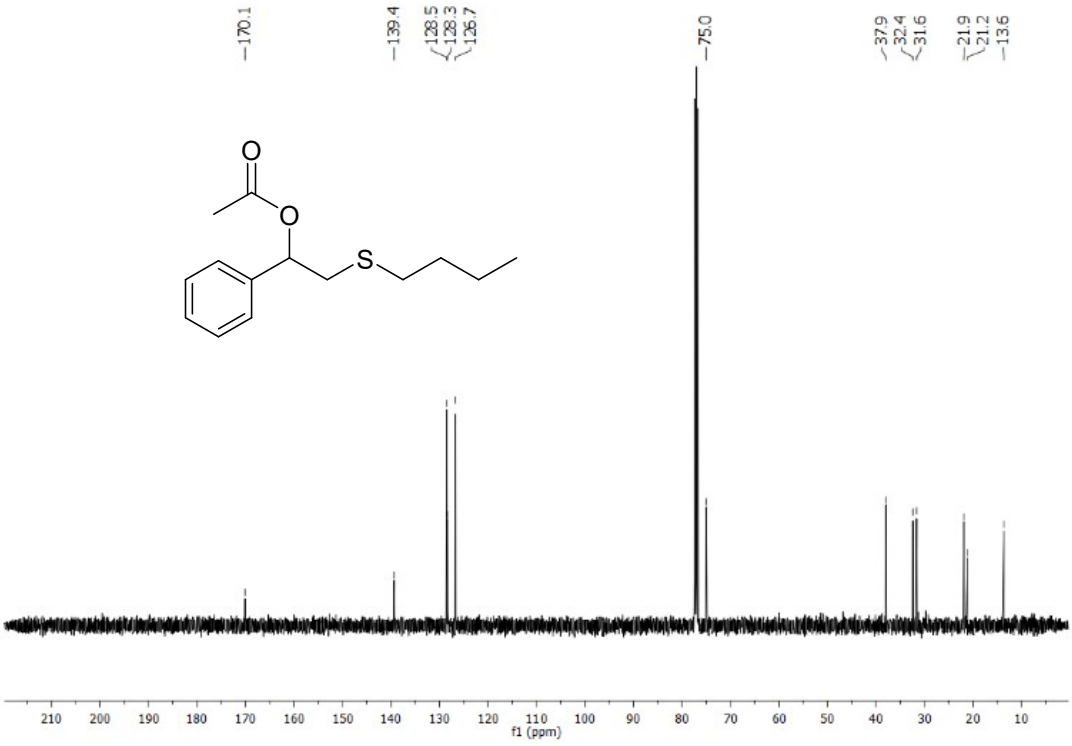
*2-(Methylthio)-1-phenylethyl acetate (**2h**)*



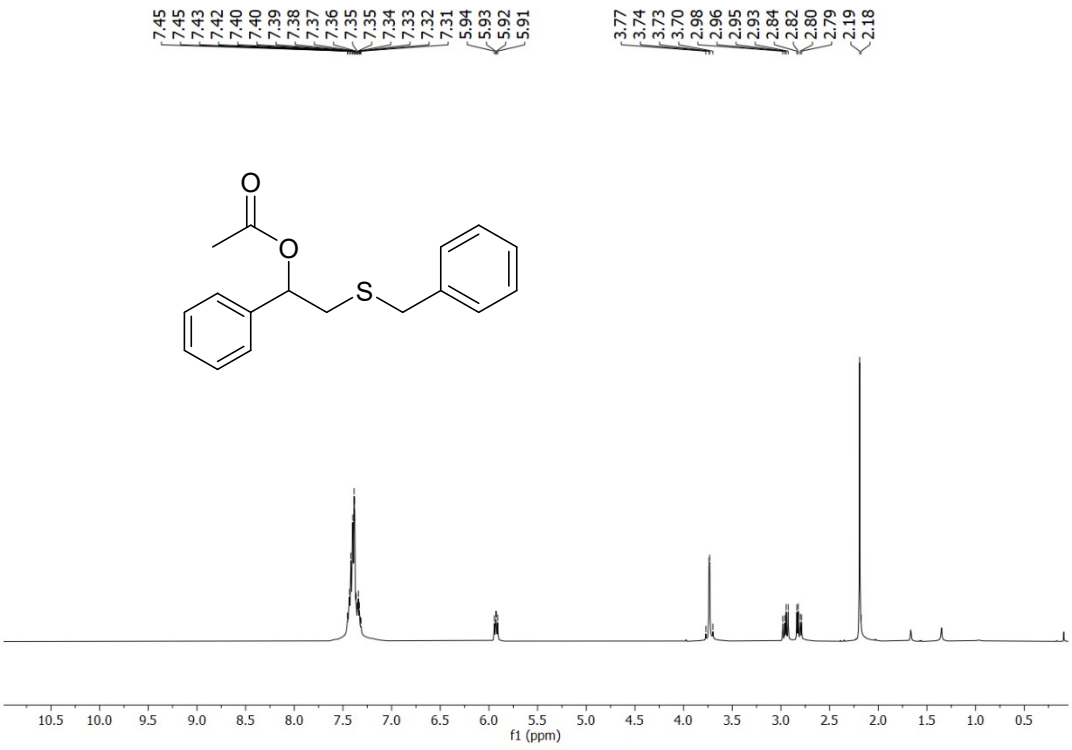


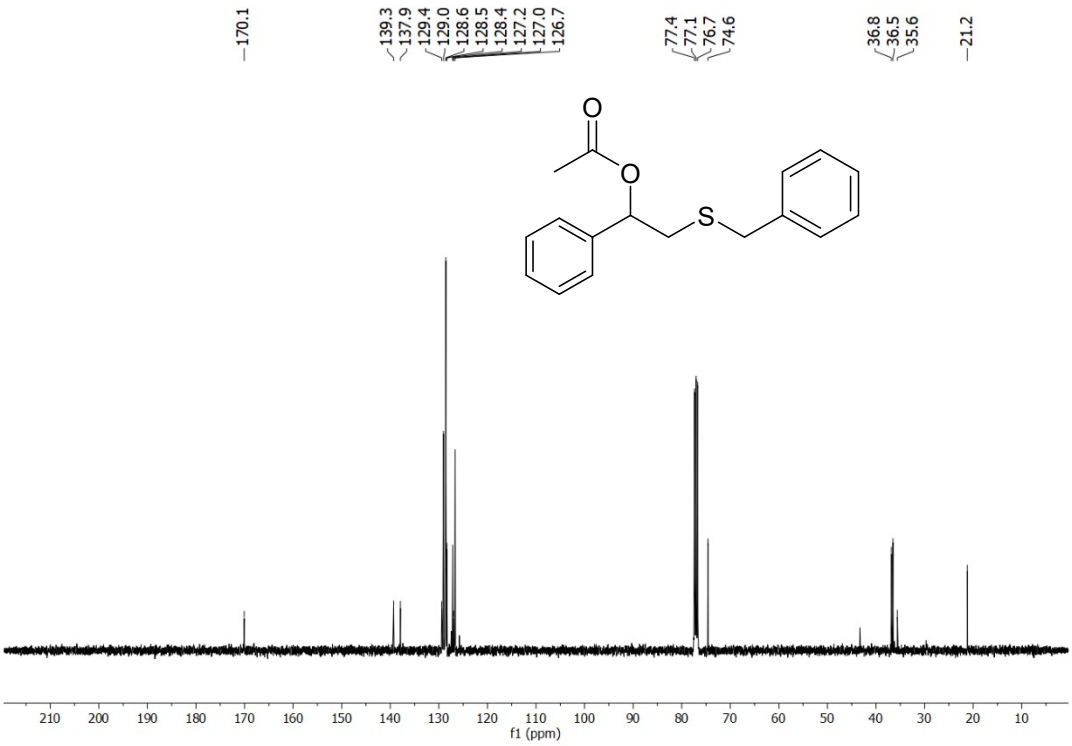
*2-(Butylthio)-1-phenylethyl acetate (**2i**)*



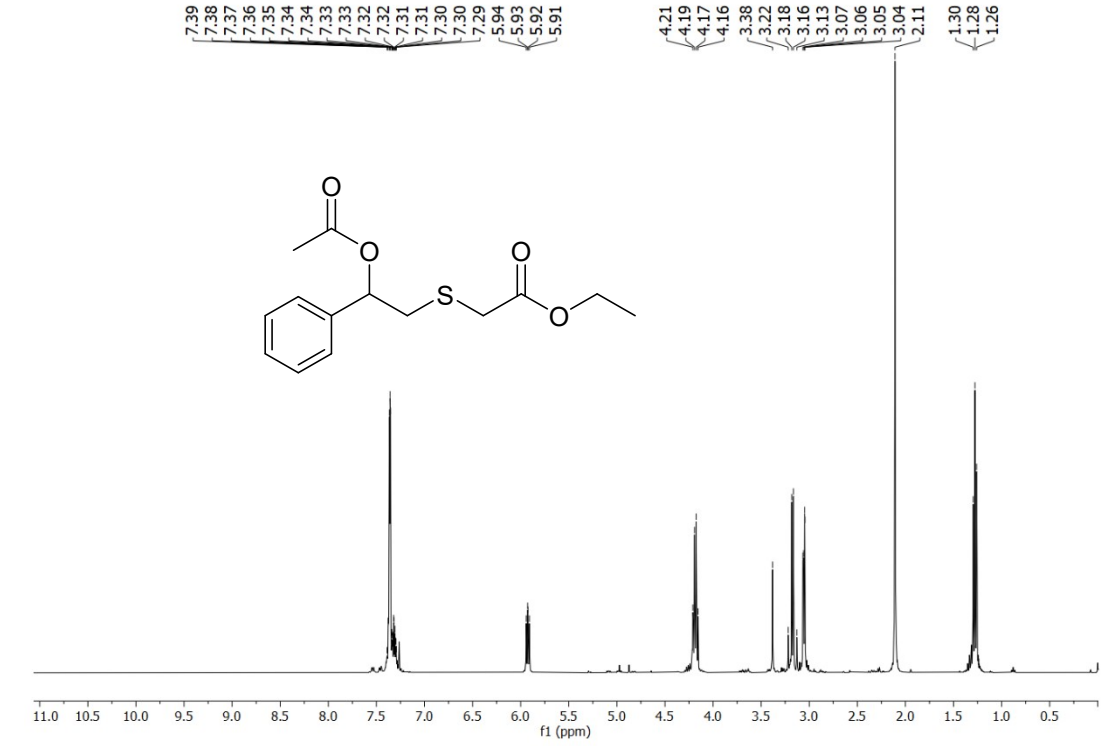


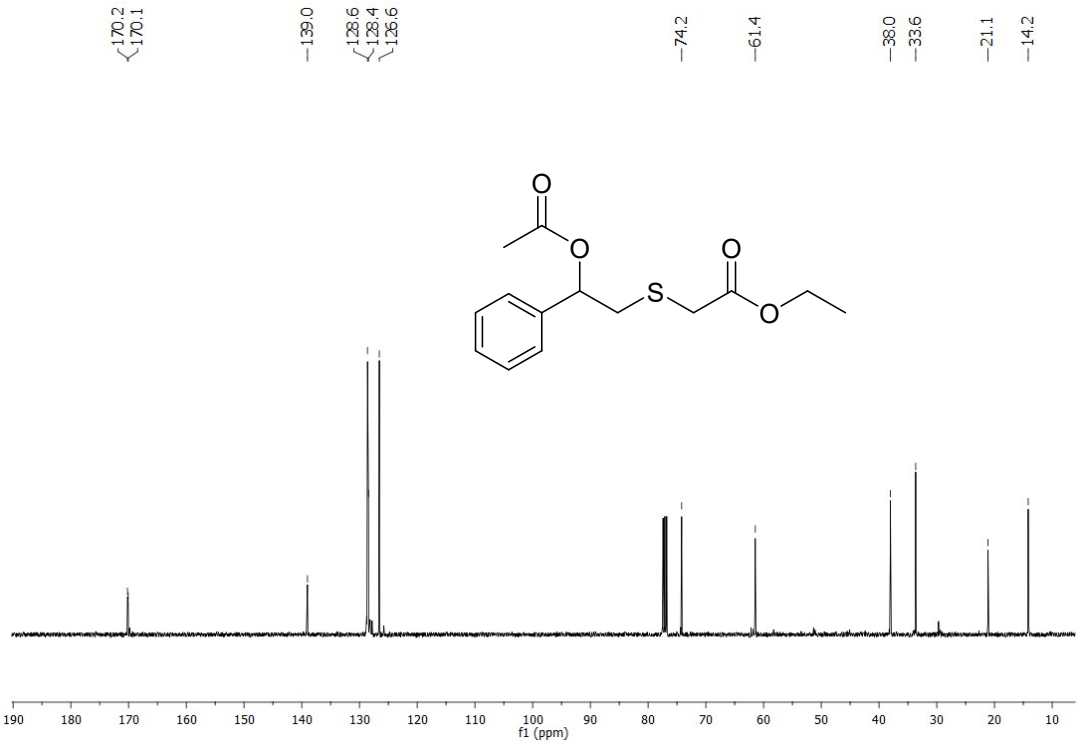
*2-(Benzylthio)-1-phenylethyl acetate (**2j**)*



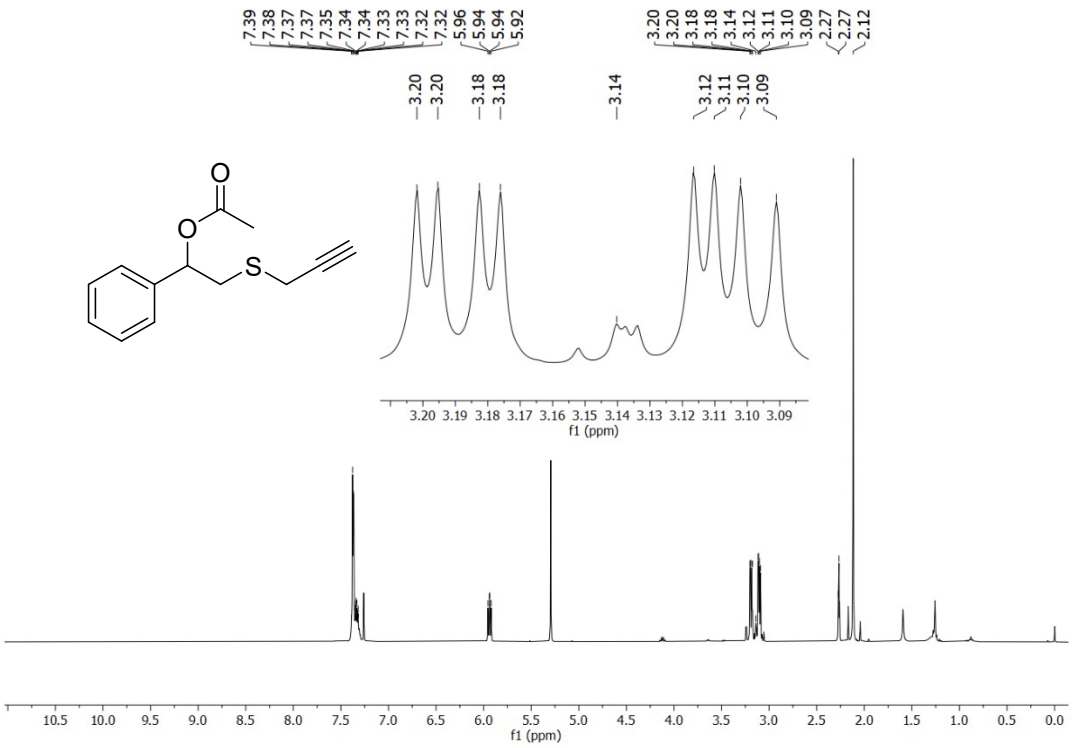


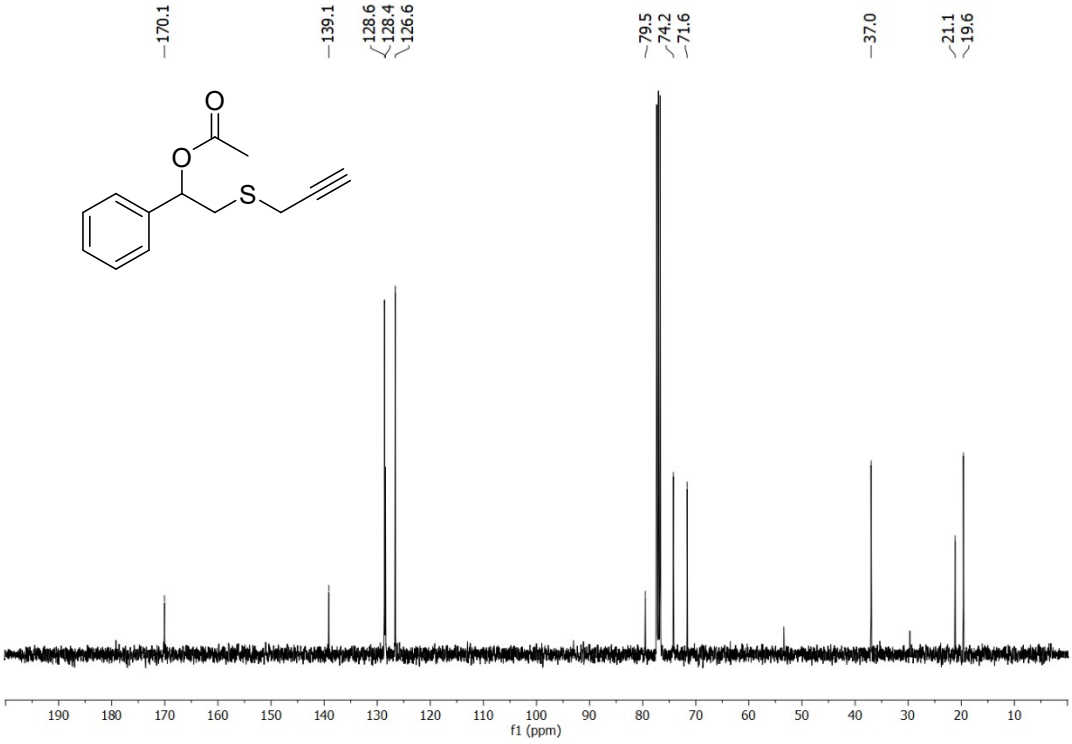
*Ethyl 2-((2-acetoxy-2-phenylethyl)thio)acetate (**2k**)*



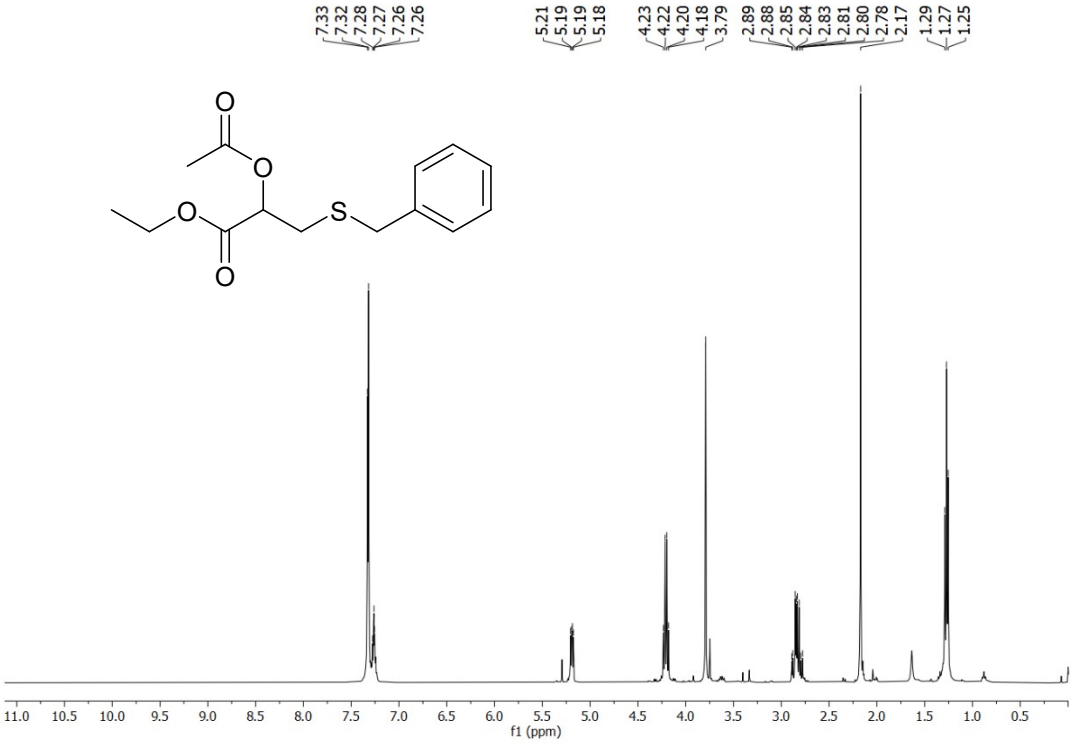


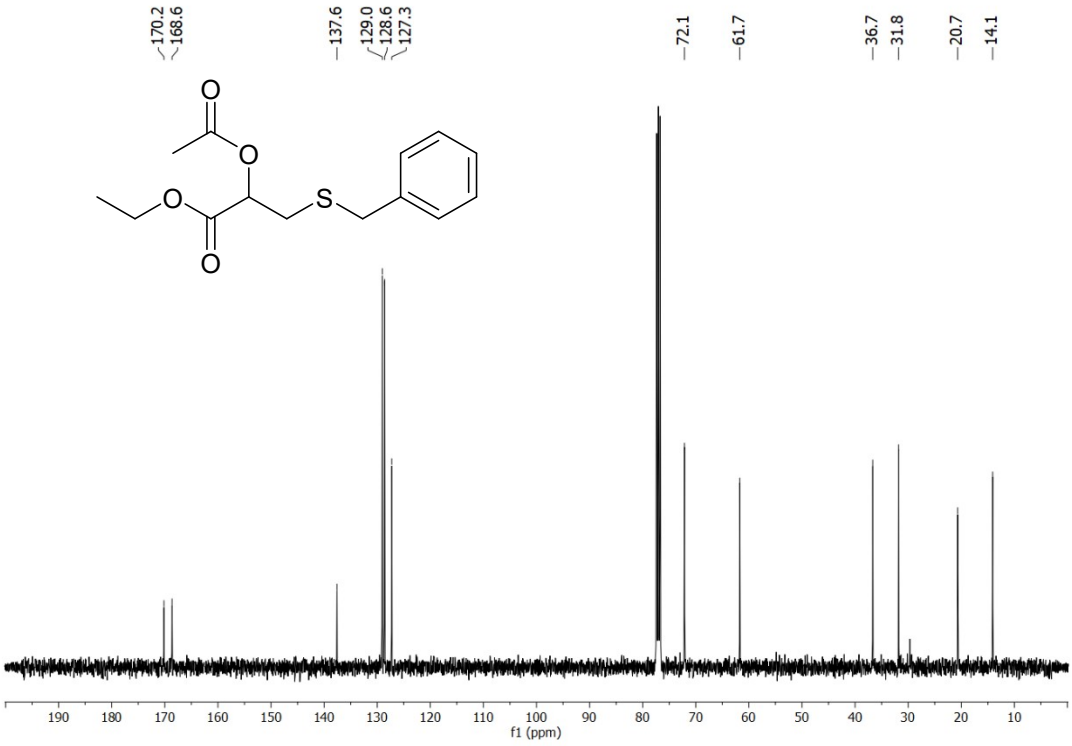
*1-Phenyl-2-(prop-2-yn-1-ylthio)ethyl acetate (**2l**)*



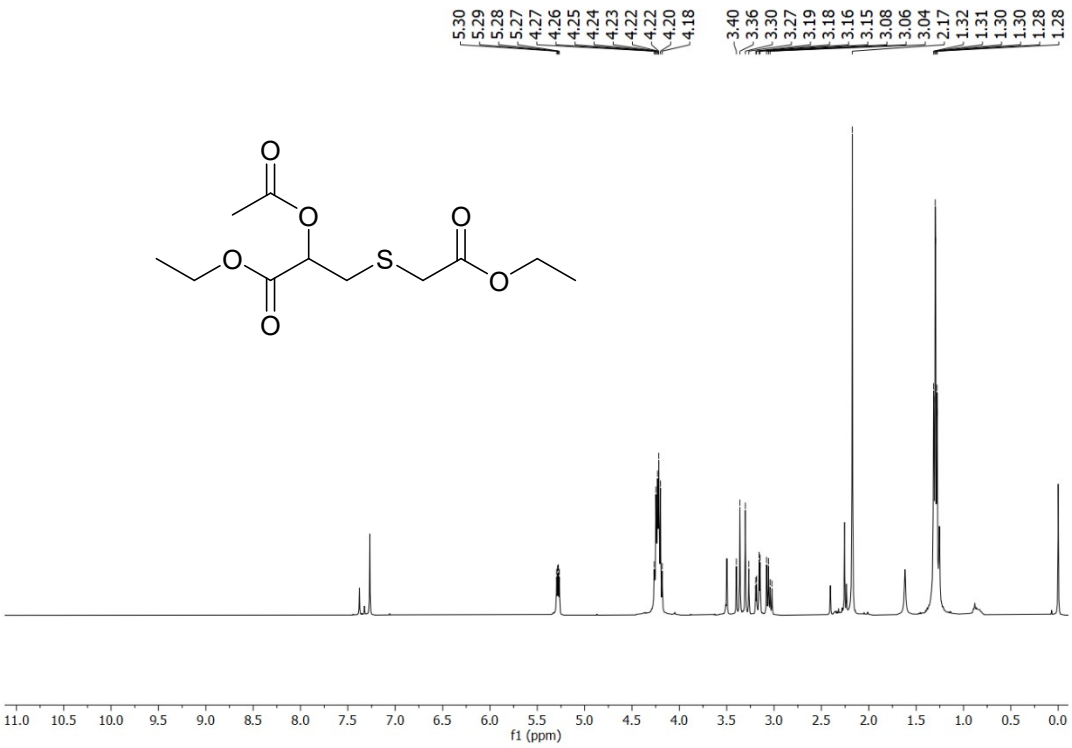


*Ethyl 2-acetoxy-3-(benzylthio)propanoate (**2m**)*

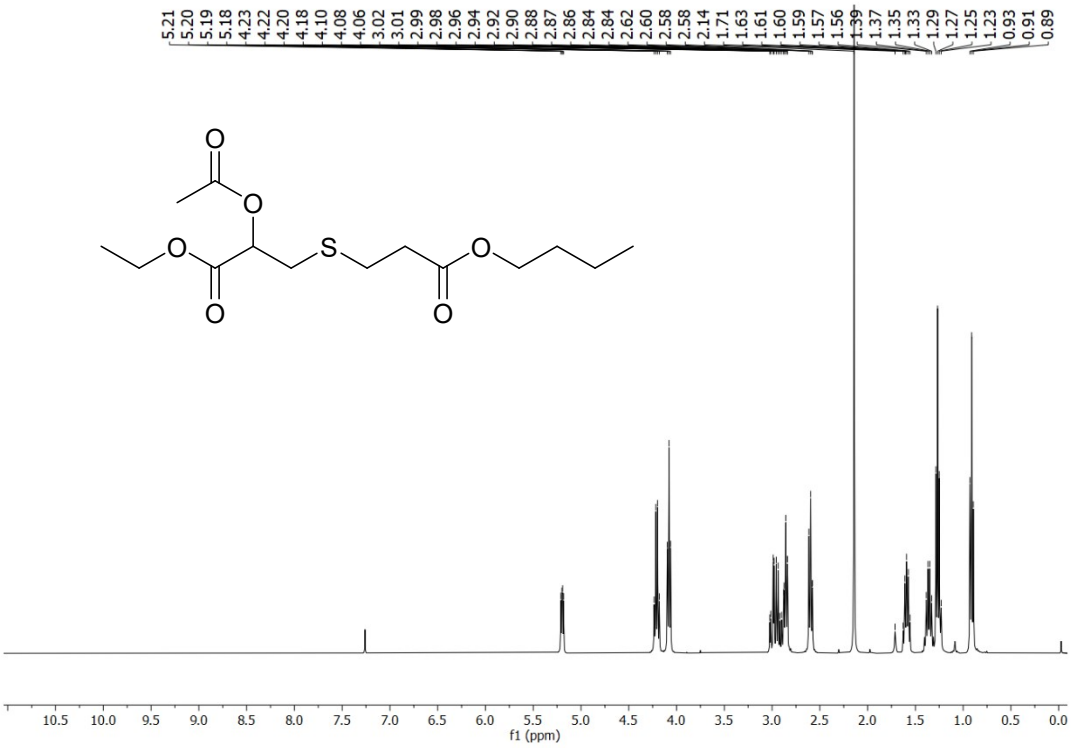


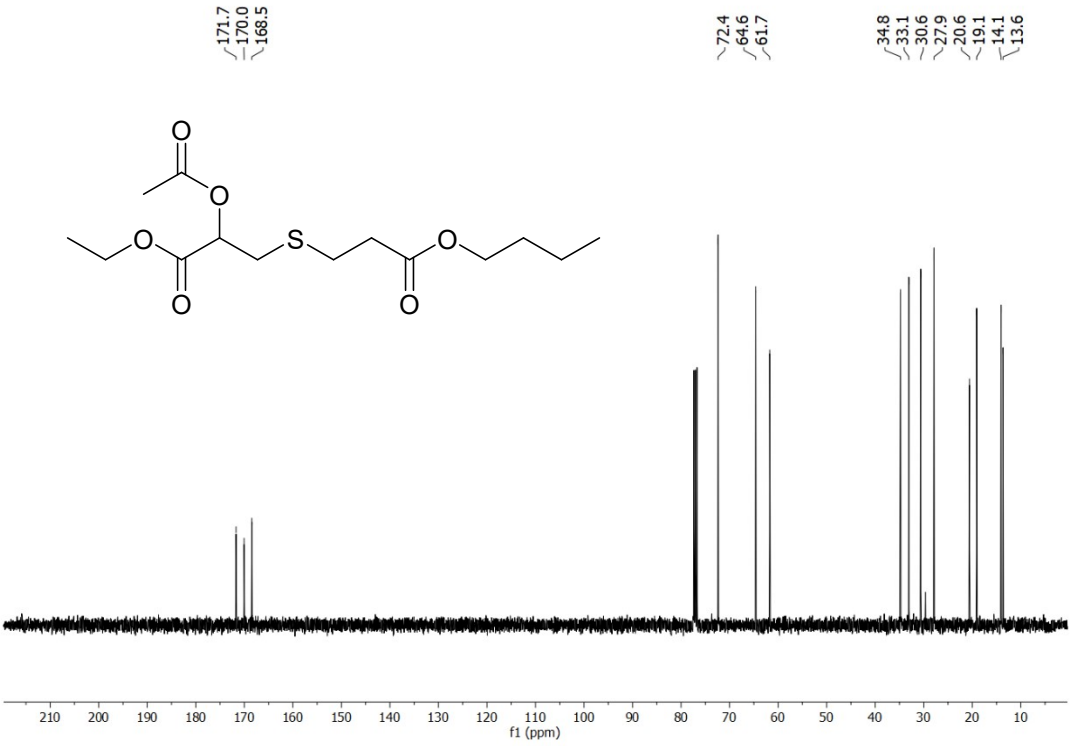


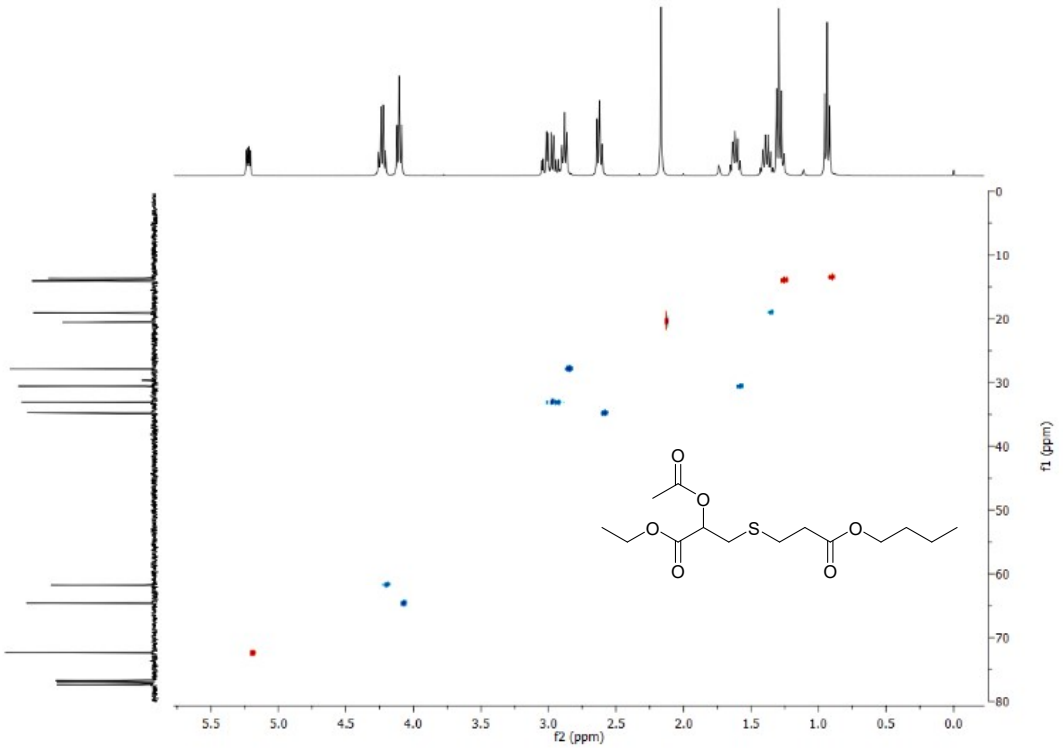
*Ethyl 2-acetoxy-3-((2-ethoxy-2-oxoethyl)thio)propanoate (**2n**)*



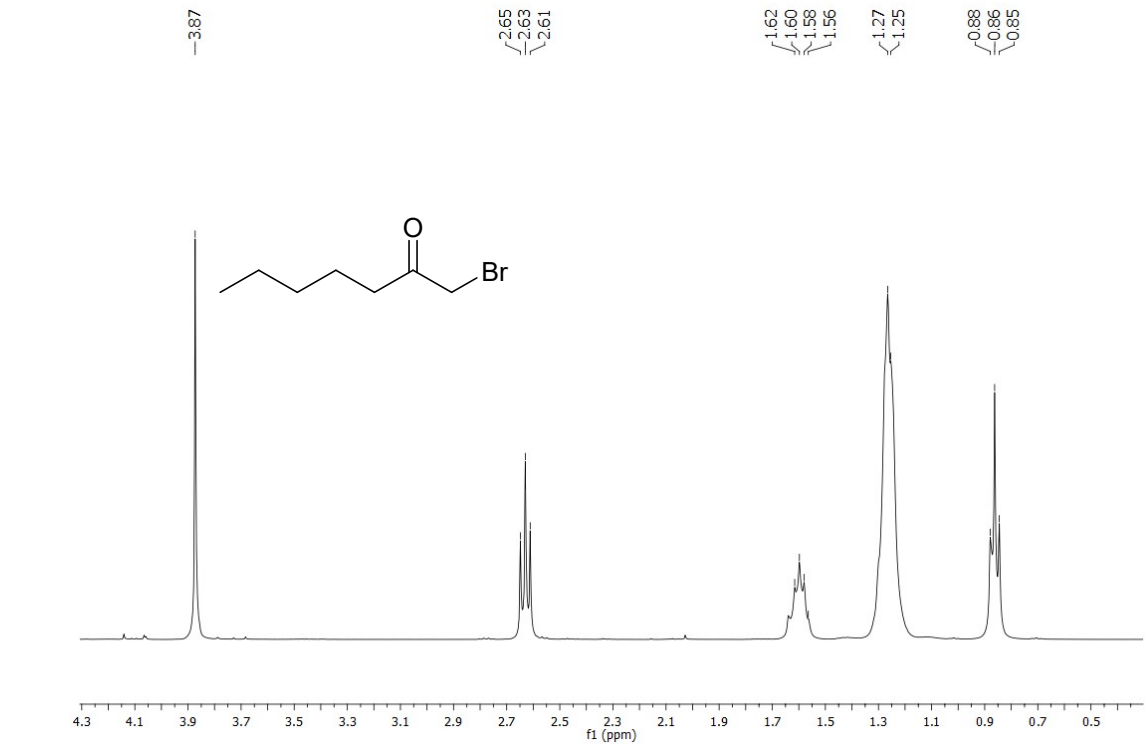
*Ethyl 2-acetoxy-3-((3-butoxy-3-oxopropyl)thio)propanoate (**2o**)*

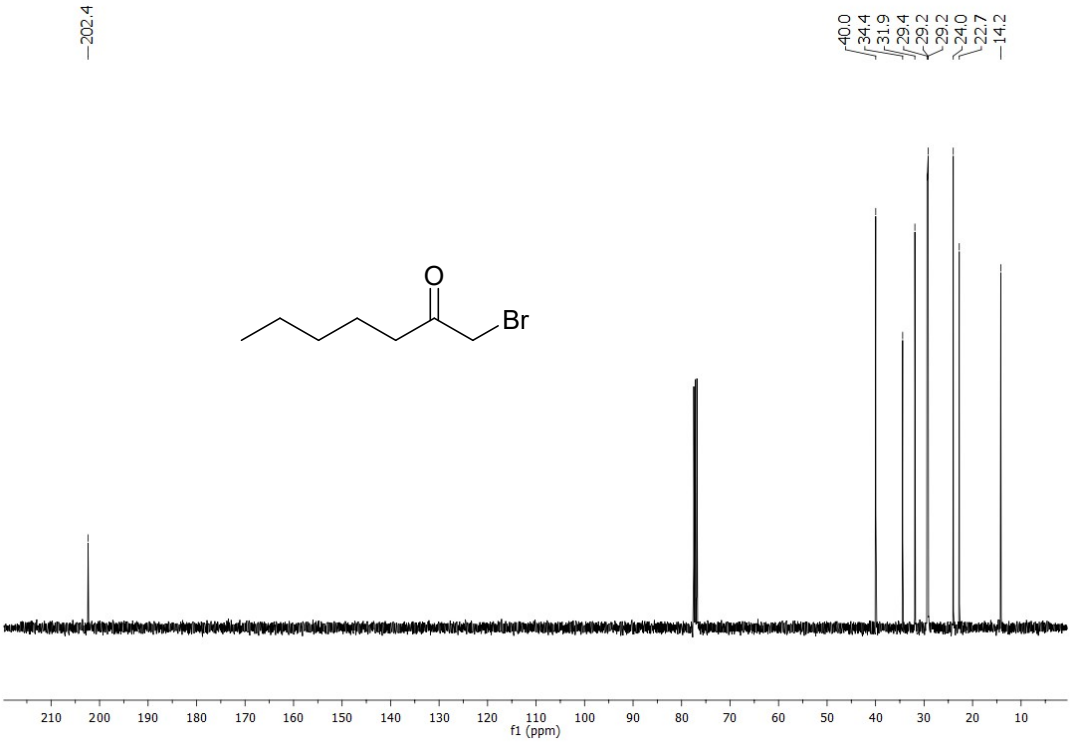





f2 (ppm)
f1 (ppm)
O
O
O
S
O
O
O

*1-Bromooctan-2-one (**3a**)*





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