Kulinkovich-type reactions of thioamides: similar to those of carboxylic amides?

Ewelina Augustowska, Antoine Boiron, Jérôme Deffit and Yvan Six*

Laboratoire de Synthèse Organique DCSO, UMR 7652 CNRS/Ecole Polytechnique, 91128 Palaiseau Cedex, France.
Fax: +33(0)1 6933 5972; Tel: +33(0)1 6933 5979; E-mail: six@dcso.polytechnique.fr

Supplementary Information – Part 1

Experimental procedures and characterisation data for compounds **1aO**, **1aS**, **1bO**, **1bS**, **1cO**, **1cS**, **1dS**, **1eS**, **1fS**, **1gS**.

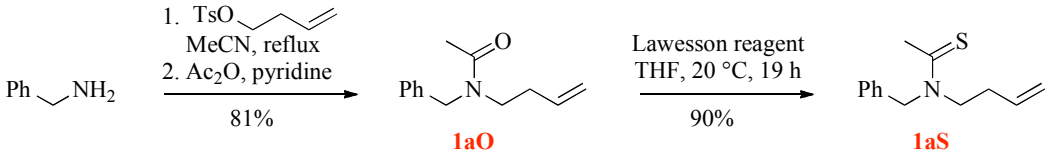
I. General remarks

Titanium(IV) *iso*-propoxide (VERTEC® TIPT) was purchased from Alfa Aesar, distilled under reduced pressure and stored under argon for several months. Other commercial reagents were used as received, without purification. The Grignard reagents were purchased from Sigma-Aldrich or Acros and titrated once a month according to a method described in the literature.[1] All reactions were carried out under nitrogen. Tetrahydrofuran, diethyl ether, dichloromethane, toluene and methanol were purified using a MB SPS-800 solvent purification system (MBRAUN). The temperatures mentioned are the temperatures of the cold baths or the oil baths used. Flash column chromatography was performed on Merck silica gel 60 (40–63 μm). Concentration under reduced pressure was carried out using rotary evaporators at 40°C. NMR spectra were recorded with AM 400 and AVANCE 400 Bruker spectrometers (^{1}H at 400 MHz, ^{13}C at 100.6 MHz. Chemical shifts δ are given in ppm, referenced to the peak of tetramethylsilane, defined at $\delta = 0.00$ (^{1}H NMR), or the solvent peak of $CDCl_3$, defined at $\delta = 77.0$ (^{13}C NMR). Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, sext = sextuplet, sept = septuplet, m = multiplet, br = broad. Coupling constants J are given in Hz. Infrared spectra were recorded with a Perkin-Elmer 2000 FT-IR spectrometer. Melting points were determined using a Büchi 535 apparatus and were not corrected. Low-resolution mass spectra were recorded on a Hewlett-Packard Quad GC-MS engine spectrometer *via* direct injection. High-resolution mass spectrometry was performed on a JEOL GC-mate II spectrometer.

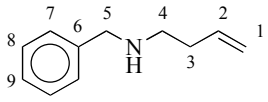
1– H.-S. Lin, L. A. Paquette, *Synth. Comm.* **1994**, *24*, 2503–2506.

II. Syntheses of amides and thioamides 1

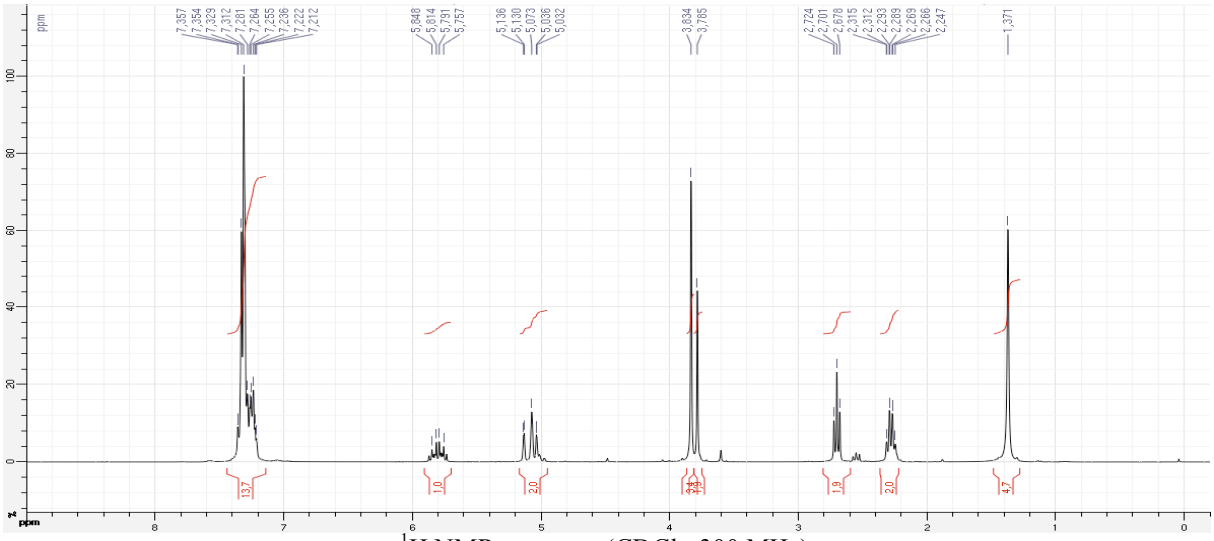
■ Amide **1aO** and thioamide **1aS**.



a) But-3-en-1-yl 4-methylbenzenesulfonate[2] (1.00 equiv, 4.42 mmol, 1.00 g) was added to a solution of benzylamine (3.00 equiv, 13.3 mmol, 1.45 mL) in MeCN (4.5 mL). The mixture was stirred at reflux for 2 h 40 min. After cooling, the mixture was concentrated. 1N NaOH aq. solution (25 mL) and Et_2O (25 mL) were added to the residue. The organic layer was separated, and the aqueous phase was extracted with Et_2O (25 mL). The combined organic phases were dried over Na_2SO_4, filtered and concentrated to afford a yellow oil (1.36 g) that was used in the next step without further purification.

N-Benzylbut-3-en-1-amine 

Yellow oil. R_f 0.25 (EtOAc/heptane 30%, PMA). ^{1}H NMR ($CDCl_3$, 300 MHz) 1.37 (1 H, br s, NH), 2.28 (2 H, qt, J 7.0, 1.5, H3), 2.70 (2 H, t, J 7.0, H4), 3.78 (2 H, s, H5), 5.05 (1 H, dq, J 10.0, 1.5, H1a), 5.10 (1 H, dq, J 17.5, 1.5, H1b), 5.80 (1 H, ddt, J 17.5, 10.0, 7.0, H2), 7.14–7.44 (5 H, m, H7–H9). ^{13}C NMR ($CDCl_3$, 75.5 MHz) 34.2 (C3), 48.2 (C4), 53.8 (C5), 116.3 (C12), 126.8 (C9), 128.0, 128.3 (C7, C8), 136.4 (C2), 140.4 (C6).



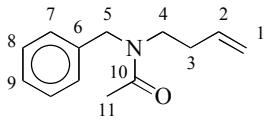
^{1}H NMR spectrum ($CDCl_3$, 300 MHz).

b) Acetic anhydride (4.00 equiv, 17.7 mmol, 1.81 g) was added dropwise to a solution of the crude product obtained above (1.36 g), in pyridine (10 mL) at 0°C. The cooling bath was removed, and the solution was stirred at 20°C for 1 h 30 min. CH_2Cl_2 (0.10 L) was then added. The mixture was washed successively with 1M NaOH aq. solution (0.10 L), H_2O

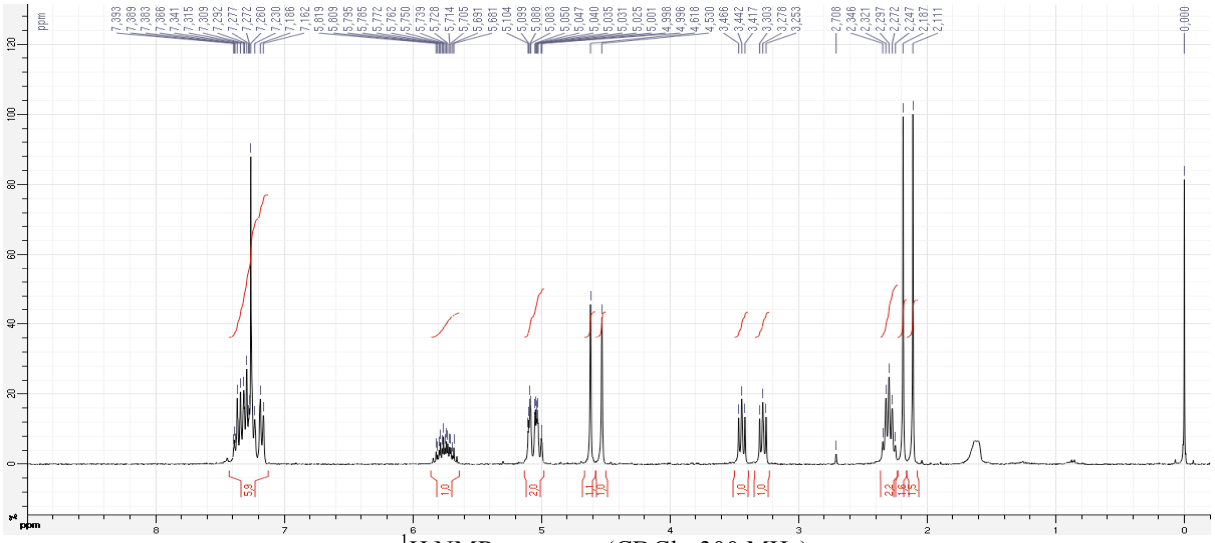
2– E. Falb, A. Nudelman, H. E. Gottlieb, A. Hassner, *Eur. J. Org. Chem.* **2000**, 645–655.

(0.10 L), 1N HCl aq. solution (2 × 0.10 L) and H_2O (0.10 L). The organic phase was dried over Na_2SO_4, filtered and concentrated to afford a yellow oil (1.38 g). Purification by flash column chromatography on silica gel, (EtOAc/heptane, gradient from 10% to 100%) yielded pure *N*-benzyl-*N*-(but-3-en-1-yl)acetamide **1aO** (731 mg, 3.60 mmol, 81% over the two steps).

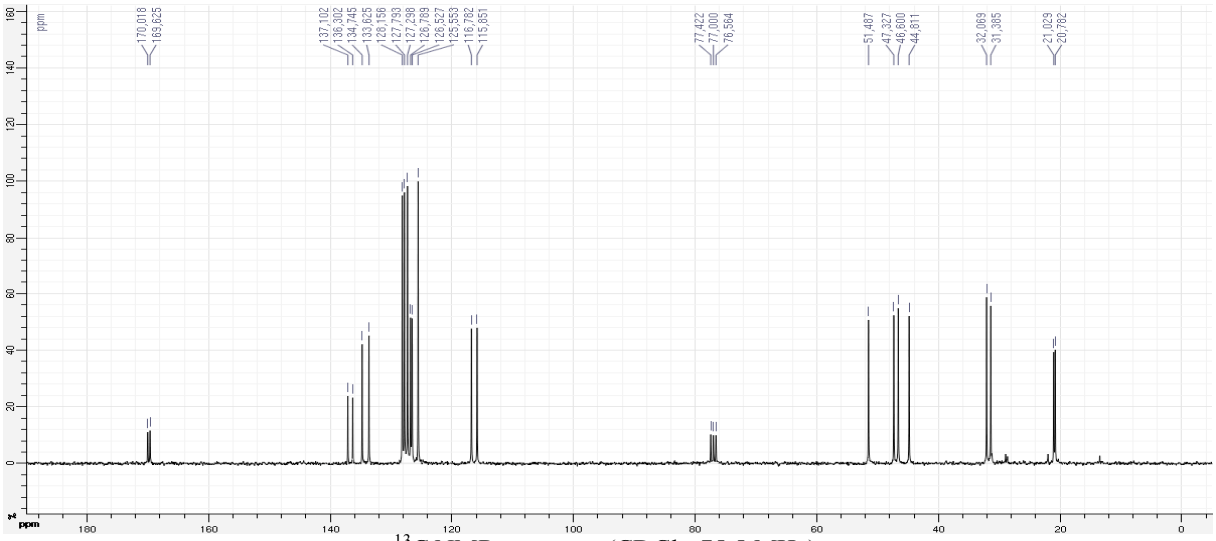
N-Benzyl-*N*-(but-3-en-1-yl)acetamide **1aO**



Colourless oil. R_f 0.35 (EtOAc/heptane 40%, PMA). IR ν 2977, 2928, 1634, 1474, 1446, 1417, 1360, 1239, 1226, 999, 985, 914, 728, 697 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) (50 : 50 mixture of two rotamers) First rotamer (slightly major) 2.31 (2 H, tdt, J 7.5, 7.0, 1.0, H3), 2.19 (3 H, s, H11), 3.44 (2 H, t, J 7.5, H4), 4.62 (2 H, s, H5), 4.98–5.13 (2 H, m, H1), 5.73 (1 H, ddt, J 17.5, 10.0, 7.0, H2), 7.12–7.43 (5 H, m, H7–H9). Other rotamer 2.28 (2 H, qt, J 7.5, 1.0, H3), 2.11 (3 H, s, H11), 3.28 (2 H, t, J 7.5, H4), 4.53 (2 H, s, H5), 4.98–5.13 (2 H, m, H1), 5.77 (1 H, ddt, J 17.0, 10.0, 7.0, H2), 7.12–7.43 (5 H, m, H7–H9). ^{13}C NMR ($CDCl_3$, 75.5 MHz) (50 : 50 mixture of two rotamers) 20.8 and 21.0 (C11); 31.4 and 32.1 (C3); 44.8, 46.6, 47.3 and 51.5 (C4, C5), 115.9 and 116.8 (C1); 126.5 and 126.8 (C9); 125.6, 127.3, 127.8 and 128.2 (C7, C8); 133.6 and 134.7 (C2); 136.3 and 137.1 (C6); 169.6 and 170.0 C10). MS *m/z* (ES^+) 204 (MH^+), 223, 226 (MNa^+), 227, 243. HRMS *m/z* (ES^+) 226.1226 (MNa^+ $C_{13}H_{17}NNaO$ requires 226.1208).



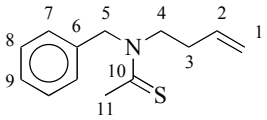
^1H NMR spectrum ($CDCl_3$, 300 MHz).



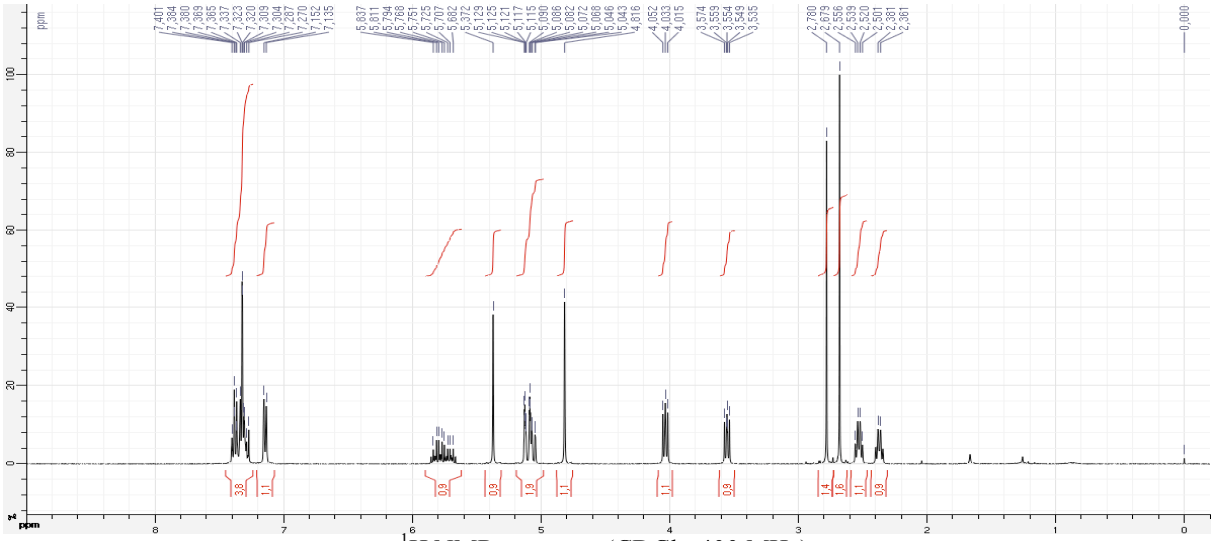
^{13}C NMR spectrum ($CDCl_3$, 75.5 MHz).

c) Lawesson reagent (0.550 equiv, 3.30 mmol, 1.33 g) was added to a solution of *N*-benzyl-*N*-(but-3-en-1-yl)acetamide **1aO** (1.00 equiv, 6.00 mmol, 1.22 g) in THF (6.0 mL) at 20 °C. The mixture was then stirred at 20°C for 19 h, by which time the starting material had been entirely consumed (the reaction was nearly complete after 1 h as revealed by TLC analysis). The reaction mixture was filtered through a short pad of celite, that was then rinsed with EtOAc. The resulting clear solution was concentrated to afford a pale yellow oil. Purification of the crude product by flash column chromatography on silica gel, (EtOAc/pet. ether, gradient from 0% to 50%) yielded pure *N*-benzyl-*N*-(but-3-en-1-yl)ethanethioamide **1aS** (1.19 g, 5.43 mmol, 90%).

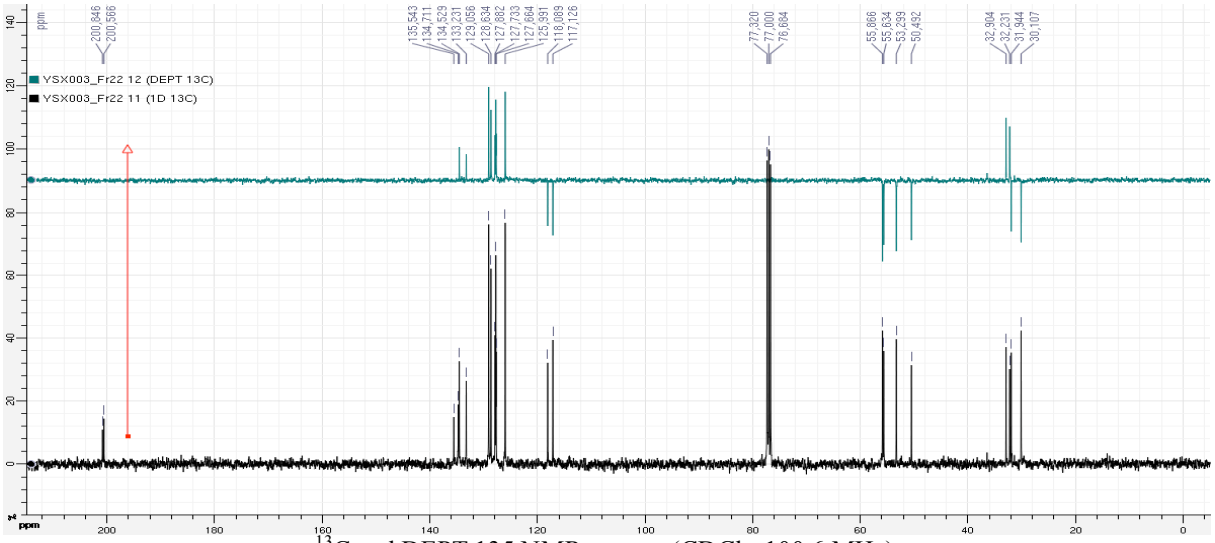
N-Benzyl-*N*-(but-3-en-1-yl)ethanethioamide **1aS**



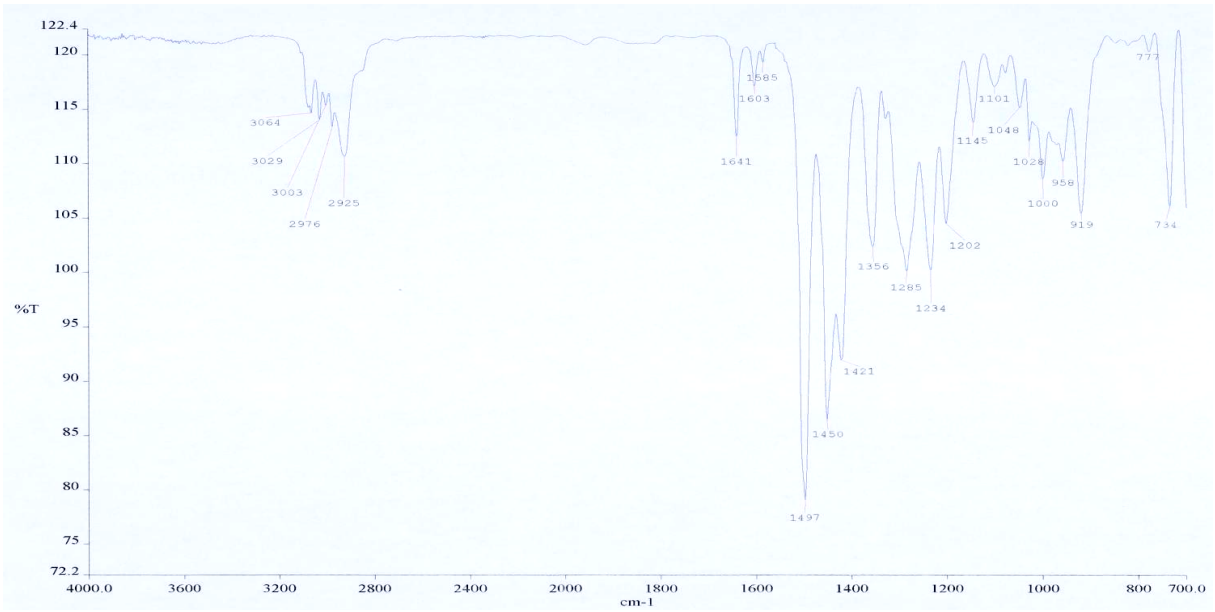
Pale yellow oil with an unpleasant smell. R_f 0.2 (AcOEt/Pet. ether 10%, anisaldehyde [pink spot] or PMA). IR (neat) ν 3064, 3029, 3003, 2976, 2925, 1641 (w), 1497 (s), 1450 (s), 1421, 1356, 1285, 1234, 1202, 1000, 958, 919, 734 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) 55 : 45 mixture of two rotamers. Major rotamer 2.53 (2 H, tdt, J 7.5, 7.0, 1.5, H3), 2.68 (3 H, s, H11), 4.03 (2 H, t, J 7.5, H4), 4.82 (2 H, s, H5), 5.02–5.16 (2 H, m, H1), 5.80 (1 H, ddt, J 17.0, 10.0, 7.0, H2), 7.14 (2 H, d, J 7.5, H7), 7.24–7.43 (3 H, m, H8, H9). Minor rotamer 2.37 (2 H, tdt, J 8.0, 7.0, 1.5, H3), 2.78 (3 H, s, H11), 3.55 (2 H, t, J 8.0, H4), 5.02–5.16 (2 H, m, H1), 5.37 (2 H, s, H5), 5.72 (1 H, ddt, J 17.0, 10.0, 7.0, H2), 7.24–7.43 (5 H, m, H7, H8, H9). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 55 : 45 mixture of two rotamers 30.1 (C3), 31.9 (C3), 32.2 (C11), 32.9 (C11), 50.5 (C4), 53.3 (C4), 55.6 (C5), 55.9 (C5), 117.1 (C1), 118.1 (C1), 126.0 (C7), 127.7 (C9), 127.7 (C7), 127.9 (C9), 128.6 (C8), 129.1 (C8), 133.2 (C2), 134.5 (C2), 134.7 (C6), 135.5 (C6), 200.6 (C10), 200.8 (C10). MS *m/z* (positive CI, NH_3) 186, 190, 220 (MH^+), 221, 222. HRMS *m/z* (EI) 219.1087 ($M^{+\bullet}$ $C_{13}H_{17}NS$ requires 219.1082).



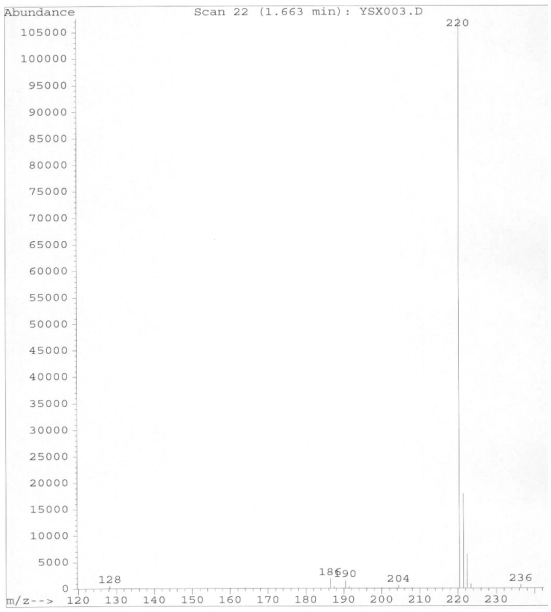
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C and DEPT 135 NMR spectra ($CDCl_3$, 100.6 MHz).

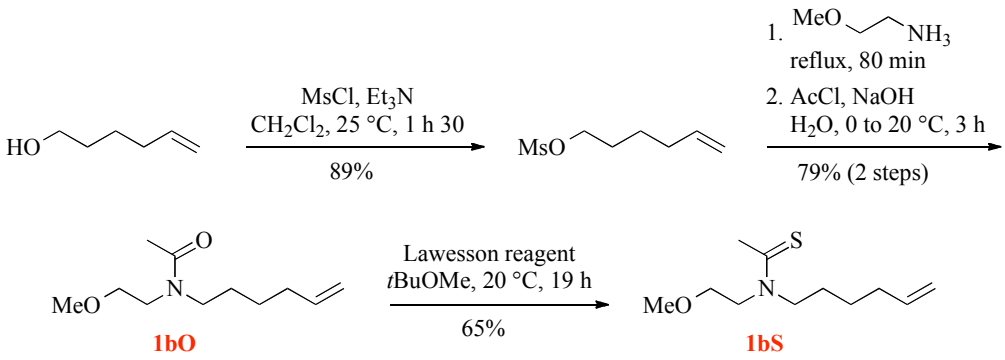


IR spectrum.



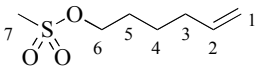
MS spectrum (positive CI, NH_3).

■ Amide **1bO** and thioamide **1bS**.



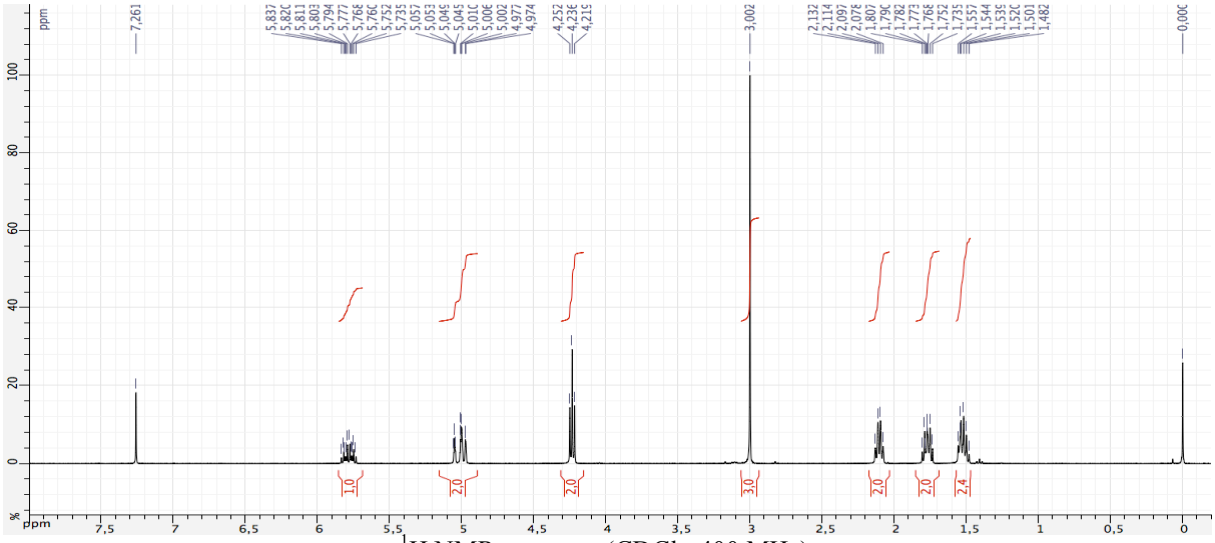
a) Methanesulfonyl chloride (1.10 equiv, 8.24 mmol, 638 µL) was added dropwise to a solution of 5-hexen-1-ol (1.00 equiv, 7.49 mmol, 900 µL) and triethylamine (1.10 equiv, 8.24 mmol, 1.15 mL) in CH_2Cl_2 (50 mL) at 0 °C. The cold bath was removed after 5 minutes, and the mixture was stirred at 25 °C for 90 minutes, then washed with saturated $NaHCO_3$ aqueous solution (25 mL), H_2O (25 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford pure 5-hexenyl methanesulfonate (1.19 g, 6.68 mmol, 89%).

Hex-5-en-1-yl methanesulfonate[3]



Colourless oil. R_f 0.45 (AcOEt/Pet. ether 30%, PMA). ^{1}H NMR ($CDCl_3$, 400 MHz) 1.52 (2 H, m, H4 or H5), 1.77 (2 H, m, H4 or H5), 2.11 (2 H, qt, J 7.0, 1.5, H3), 3.00 (3 H, s, H7), 4.24 (2 H, t, J 6.5, H6), 4.99 (1 H, dq, J 10.0, 1.5, H1 *cis* to H2), 5.03 (1 H, dq, J 17.0, 1.5, H1 *trans* to H2), 5.79 (1 H, ddt, J 17.0, 10.0, 7.0, H2).

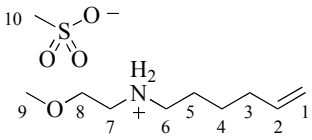
3– M. C. Marcotullio, V. Campagna, S. Sternativo, F. Costantino, M. Curini, *Synthesis* **2006**, *11*, 2760–2766.



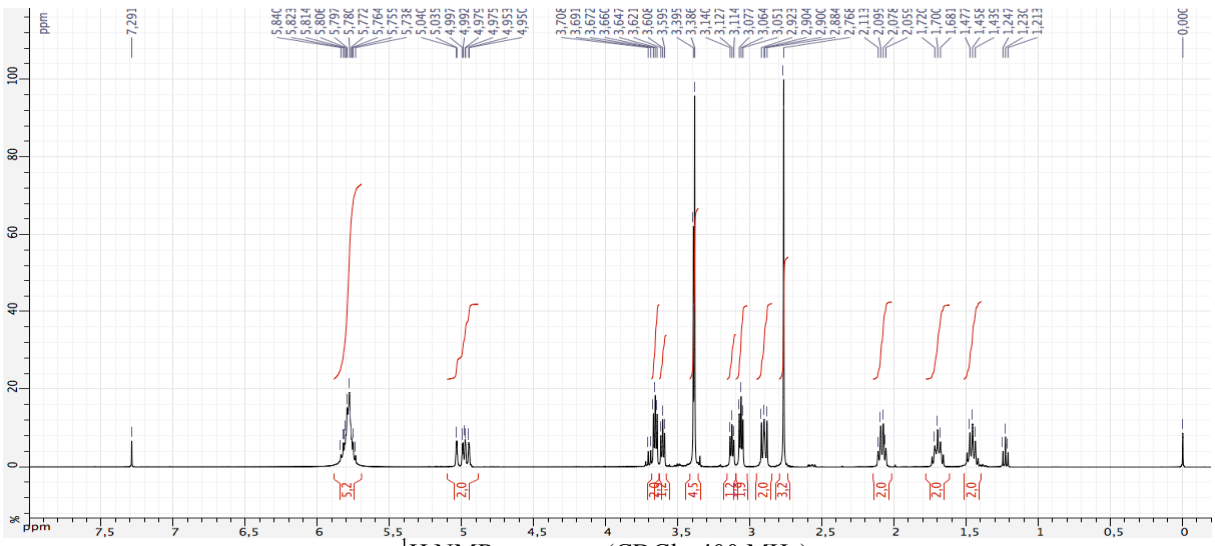
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

b) A solution of 5-hexenyl methanesulfonate (1.00 equiv, 6.68 mmol, 1.19 g) in 2-methoxyethylamine (5.00 equiv, 33.4 mmol, 2.90 mL) was stirred at reflux for 80 minutes. After cooling, the mixture was concentrated under reduced pressure to afford a yellow oil that was engaged in the next step without purification (1.80 g).

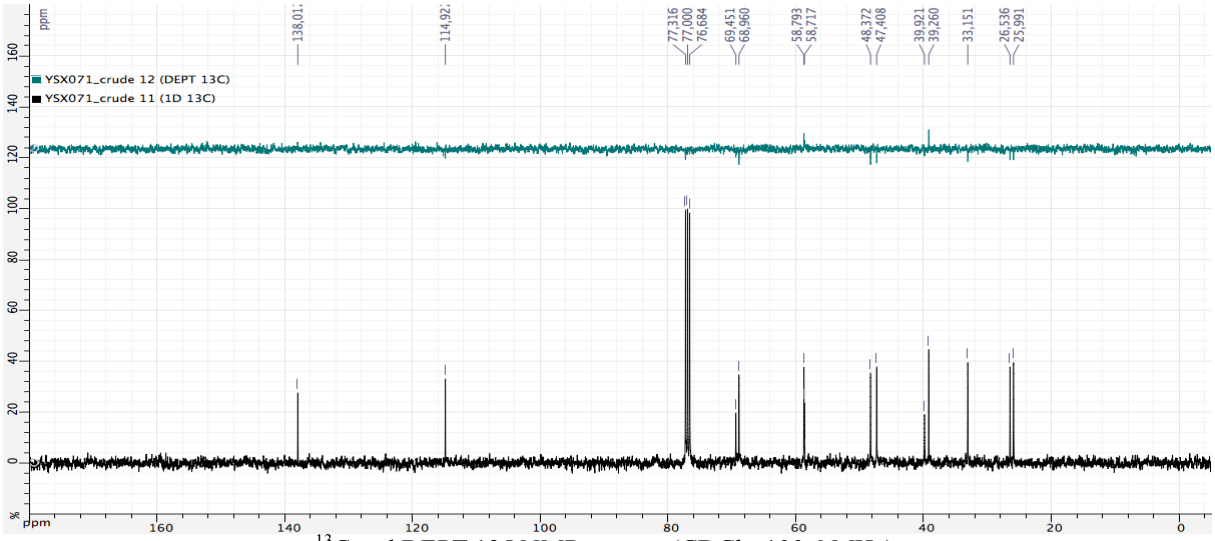
(Hex-5-en-1-yl) (2-methoxyethyl) azanium methanesulfonate



Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz) ^{1}H NMR ($CDCl_3$, 400 MHz) 1.46 (2 H, m, H4 or H5), 1.70 (2 H, m, H4 or H5), 2.09 (2 H, qt, J 7.0, 1.5, H3), 2.77 (3 H, s, H10), 2.90 (2 H, t, J 8.0, H6), 3.06 (2 H, t, J 5.0, H7), 3.39 (3 H, s, H9), 3.66 (2 H, t, J 5.0, H8), 4.96 (1 H, dq, J 10.0, 1.5, H1 *cis* to H2), 5.02 (1 H, dq, J 17.0, 1.5, H1 *trans* to H2), 5.78 (2 H, br s, NH_2^+), 5.79 (1 H, ddt, J 17.0, 10.0, 7.0, H2). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 26.0, 26.5 (C4, C5), 33.2 (C3), 39.3 (C10), 47.4, 48.4 (C6, C7), 58.8 (C9), 69.0 (C8), 114.9 (C1), 138.0 (C2).



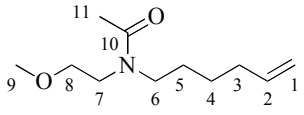
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



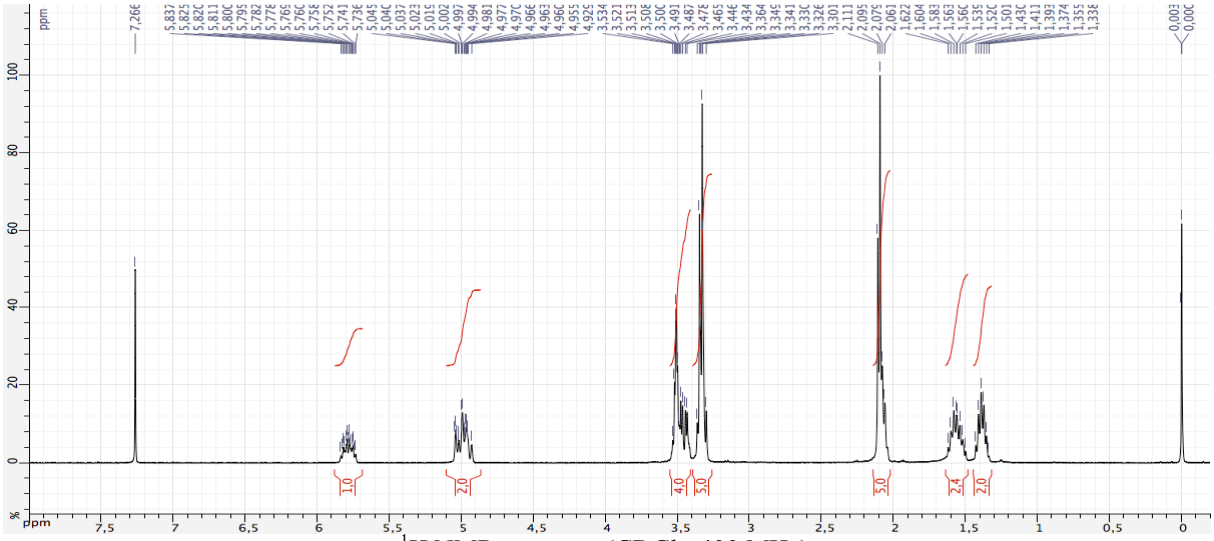
^{13}C and DEPT 135 NMR spectra ($CDCl_3$, 100.6 MHz).

c) Acetyl chloride (2.00 equiv, 4.46 mmol, 318 µL) was added dropwise to a vigorously stirred mixture of the crude (hex-5-en-1-yl) (2-methoxyethyl) azanium methanesulfonate (1.00 equiv, assumed 2.23 mmol, 599 mg) and 2.0 M aqueous NaOH solution (4.5 mL) at 0 °C. The cold bath was removed after 30 minutes, and the mixture was stirred at 20 °C for a further 2 h 30. EtOAc (20 mL) was then added, and the aqueous layer was separated. The organic layer was washed with H_2O (20 mL) and brine (5.0 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford pure *N*-(hex-5-en-1-yl)-*N*-(2-methoxyethyl)acetamide **1bO** (351 mg, 1.76 mmol, 79% over 2 steps).

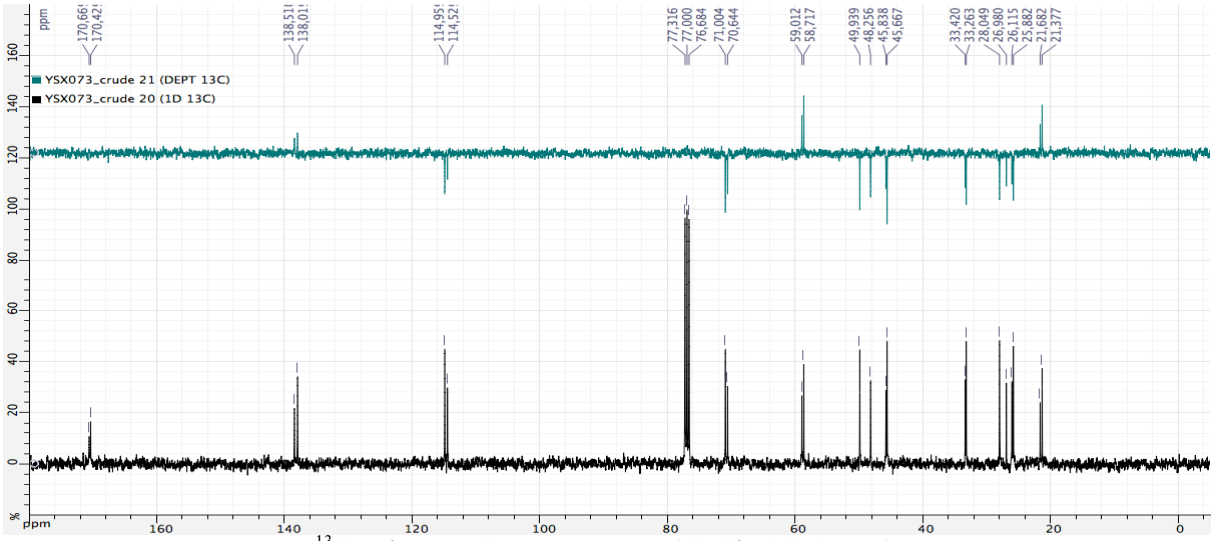
N-(Hex-5-en-1-yl)-*N*-(2-methoxyethyl)acetamide **1bO**



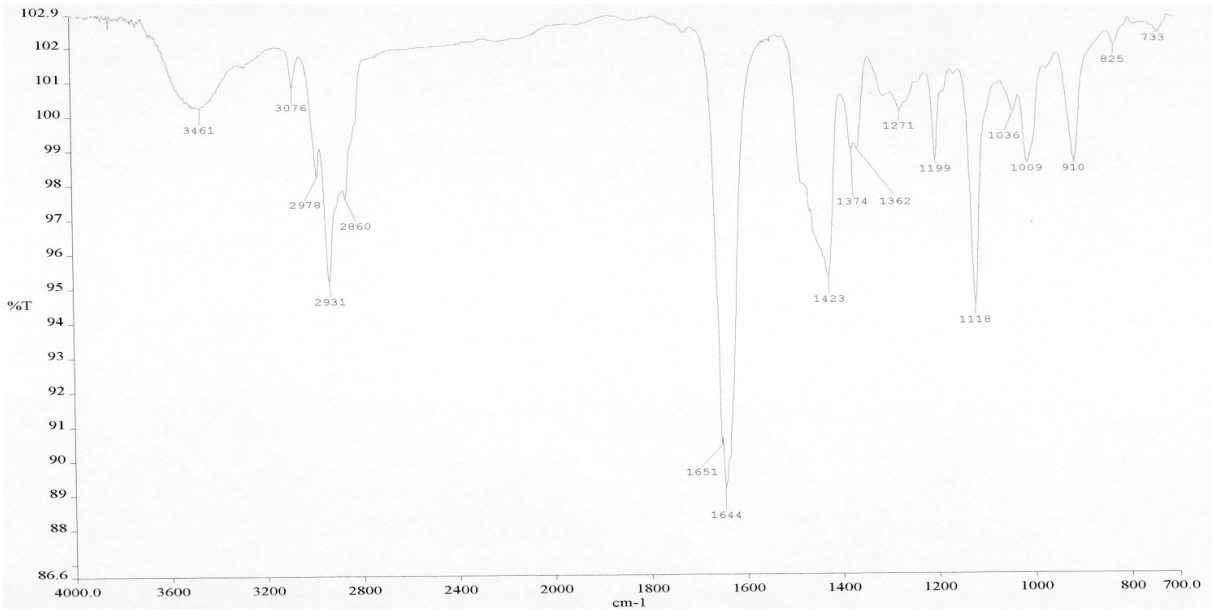
Pale yellow oil. R_f 0.15 (AcOEt/Pet. ether 50%, PMA). IR (neat) ν 3461 (br, w), 2978 (m), 2931 (m), 2860 (m), 1651 (s), 1644 (s), 1423 (m), 1364 (w), 1362 (w), 1199 (w), 1118 (m), 1009 (w), 910 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) 60 : 40 mixture of two rotamers. Major rotamer 1.39 (2 H, quint, J 7.5, H4), 1.58 (2 H, m, H5), 2.03–2.13 (2 H, m, H3), 2.09 (3 H, s, H11), 3.28–3.55 (6 H, m, H6–H8), 3.33 (3 H, s, H9), 4.90–5.07 (2 H, m, H1), 5.78 (1 H, ddt, J 17.0, 10.0, 7.0, H2). Minor rotamer 1.38 (2 H, quint, J 7.5, H4), 1.54 (2 H, m, H5), 2.03–2.13 (2 H, m, H3), 2.11 (3 H, s, H11), 3.28–3.55 (6 H, m, H6–H8), 3.35 (3 H, s, H9), 4.90–5.07 (2 H, m, H1), 5.79 (1 H, ddt, J 17.0, 10.0, 7.0, H2). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 60 : 40 mixture of two rotamers. Major rotamer 21.4 (C11), 25.9, 28.0 (C4, C5), 33.3 (C3), 45.7, 49.9 (C6, C7), 58.7 (C9), 71.0 (C8), 115.0 (C1), 138.0 (C2), 170.4 (C10). Minor rotamer 21.7 (C11), 26.1, 27.0 (C4, C5), 33.4 (C3), 45.8, 48.3 (C6, C7), 59.0 (C9), 70.6 (C8), 114.5 (C1), 138.5 (C2), 170.7 (C10). MS *m/z* (positive CI, NH_3) 200 (MH^+), 201. HRMS *m/z* (EI) 199.1572 ($M^{+\bullet}$ $C_{11}H_{21}NO_2$ requires 199.1572).



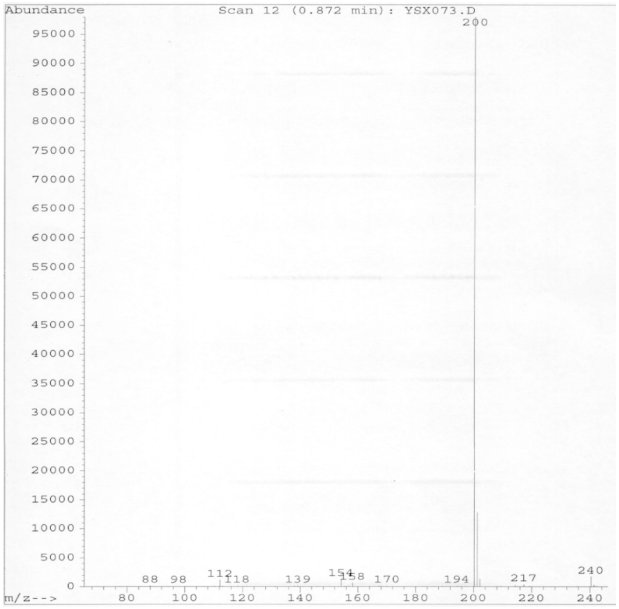
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C and DEPT 135 NMR spectra ($CDCl_3$, 100.6 MHz).



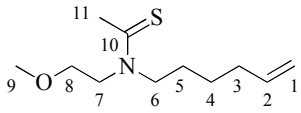
IR spectrum.



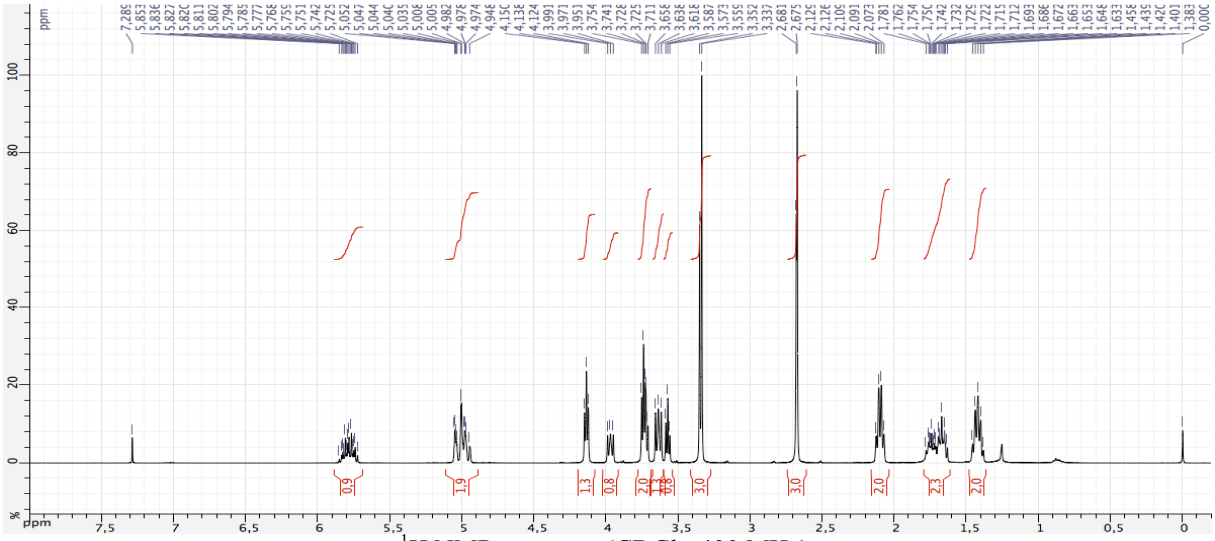
MS spectrum (positive CI, NH_3).

d) Lawesson reagent (0.500 equiv, 753 µmol, 305 mg) was added to a solution of *N*-(hex-5-en-1-yl)-*N*-(2-methoxyethyl)acetamide **1bO** (1.00 equiv, 1.51 mmol, 300 mg) in *t*BuOMe (2.0 mL) at 20 °C. The mixture was stirred at 20 °C for 19 h, then filtered through a short pad of celite, that was then rinsed with Et_2O (10 mL). The resulting clear solution was concentrated to afford a colourless oil (410 mg). Purification by flash column chromatography on silica gel (EtOAc/heptane, gradient from 5 to 50%) yielded pure *N*-(hex-5-en-1-yl)-*N*-(2-methoxyethyl)ethanethioamide **1bS** (212 mg, 984 µmol, 65%).

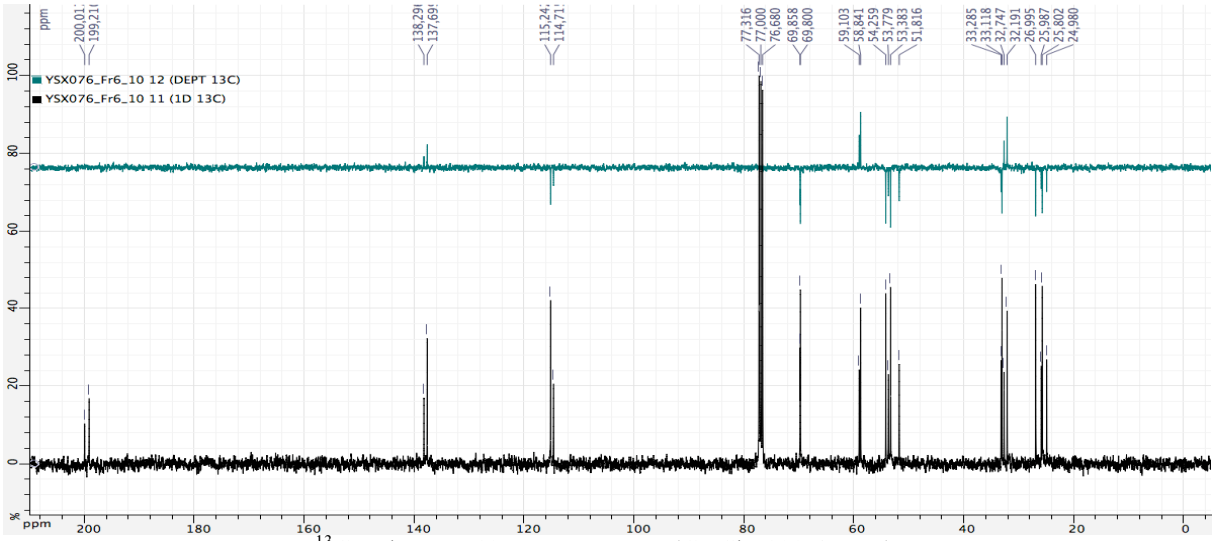
N-(Hex-5-en-1-yl)-*N*-(2-methoxyethyl)ethanethioamide **1bS**



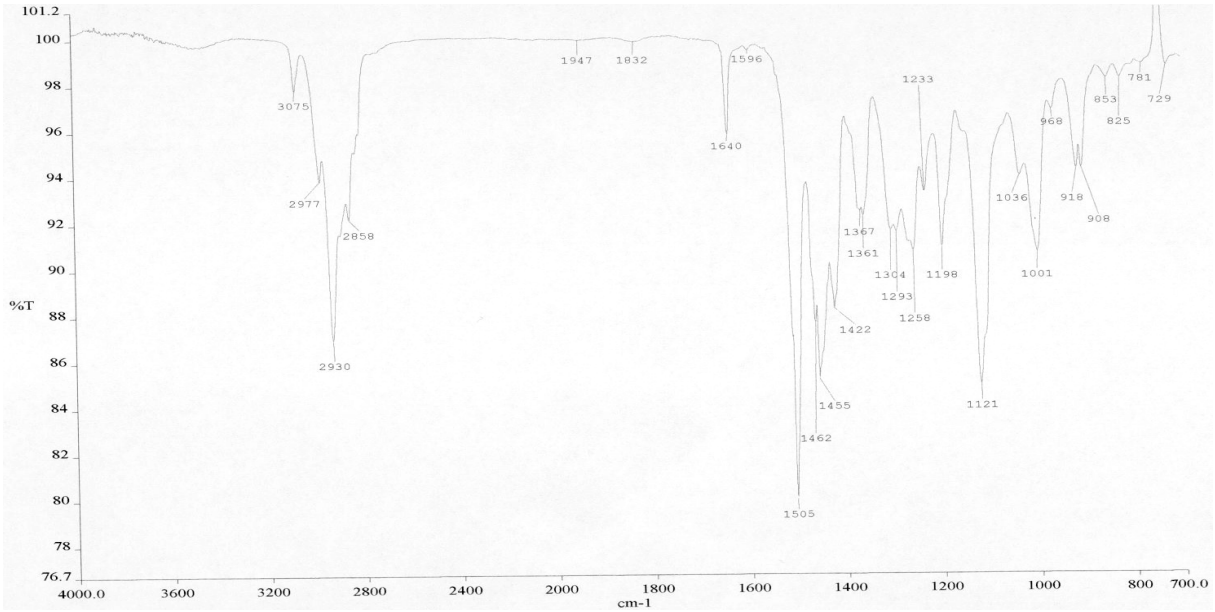
Pale yellow oil. R_f 0.15 and 0.3 (2 spots) (AcOEt/Pet. ether 20%, PMA). IR (neat) ν 2977 (m), 2930 (s), 2858 (m), 1505 (s), 1462 (m), 1455 (s), 1422 (m), 1367 (m), 1361 (m), 1304 (m), 1293 (m), 1258 (m), 1198 (m), 1121 (s), 1001 (m), 918 (w), 908 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) 63 : 37 mixture of two rotamers. Major rotamer 1.42 (2 H, quint, J 7.5, H4), 1.67 (2 H, m, H5), 2.10 (2 H, m, H3), 2.67 (3 H, s, H11), 3.34 (3 H, s, H9), 3.64 (2 H, m, H6), 3.74 (2 H, t, J 5.0, H7 or H8), 4.14 (2 H, t, J 5.0, H7 or H8), 4.92–5.08 (2 H, m, H1), 5.78 (1 H, ddt, J 17.0, 10.0, 6.5, H2). Minor rotamer 1.42 (2 H, quint, J 7.5, H4), 1.74 (2 H, m, H5), 2.10 (2 H, m, H3), 2.68 (3 H, s, H11), 3.35 (3 H, s, H9), 3.57 (2 H, t, J 5.5, H7 or H8), 3.72 (2 H, t, J 5.5, H7 or H8), 3.97 (2 H, m, H6), 4.92–5.08 (2 H, m, H1), 5.80 (1 H, ddt, J 17.0, 10.0, 6.5, H2). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 63 : 37 mixture of two rotamers. Major rotamer 25.8, 27.0 (C4, C5), 32.2 (C11), 33.1 (C3), 53.4, 54.3 (C6, C7), 58.8 (C9), 69.8 (C8), 115.2 (C1), 137.7 (C2), 199.2 (C10). Minor rotamer 25.0, 26.0 (C4, C5), 32.7 (C11), 33.3 (C3), 51.8, 53.8 (C6, C7), 59.1 (C9), 69.9 (C8), 114.7 (C1), 138.3 (C2), 200.0 (C10). MS *m/z* (positive CI, NH_3) 124, 156, 182, 216 (MH^+), 217, 218. HRMS *m/z* (EI) 215.1344 ($M^{+\bullet}$ $C_{11}H_{21}NOS$ requires 215.1344).



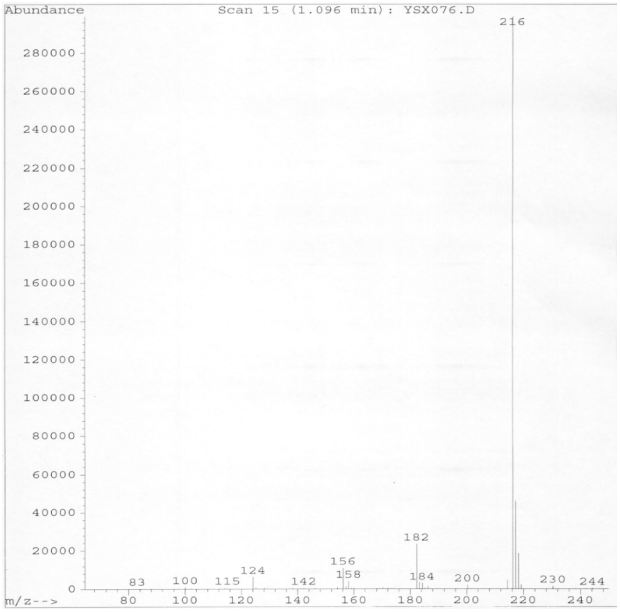
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C and DEPT 135 NMR spectra ($CDCl_3$, 100.6 MHz).

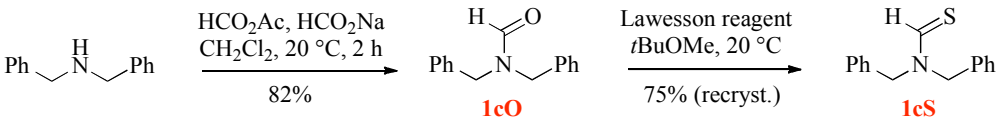


IR spectrum.



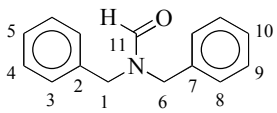
MS spectrum (positive CI, NH_3).

■ Amide **1cO** and thioamide **1cS**.



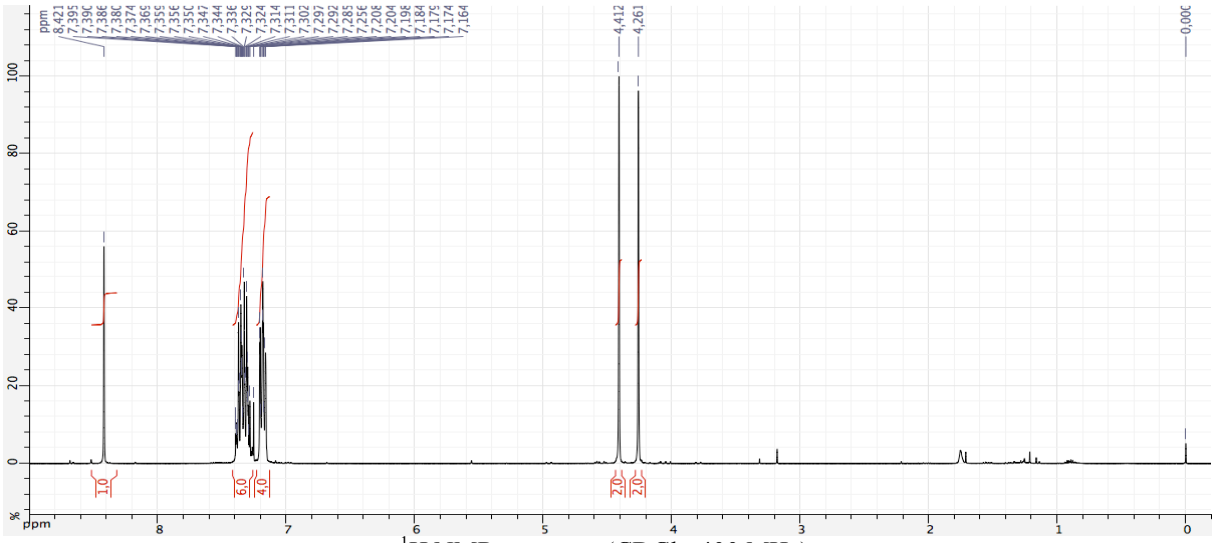
a) A mixture of formic acid (5.00 equiv, 100 mmol, 3.77 mL) and acetic anhydride (5.00 equiv, 100 mmol, 9.45 mL) was stirred at 50°C for 30 min. After cooling, sodium formate (1.50 equiv, 30.0 mmol, 2.04 g) was added, followed by a solution of dibenzylamine (1.00 equiv, 20.0 mmol, 3.84 mL) in CH_2Cl_2 (40 mL). The resulting white suspension was stirred at 20°C for 2 h. Saturated $NaHCO_3$ aqueous solution (50 mL) was then carefully added. The organic phase was separated, and the aqueous layer extracted with CH_2Cl_2 (2 × 40 mL). The combined organic phases were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a pale yellow oil (6.51 g). This oil was dissolved in CH_2Cl_2 (50 mL), washed with 1 M NaOH aqueous solution (50 mL) and H_2O (50 mL), then dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a pale yellow oil that solidified on standing (4.59 g). Purification by flash column chromatography on silica gel (EtOAc/petroleum ether, gradient from 5% to 30%) yielded pure *N*,*N*-dibenzylformamide **1cO** (3.72 g, 16.5 mmol, 82%).

N,*N*-Dibenzylformamide **1cO**[4]

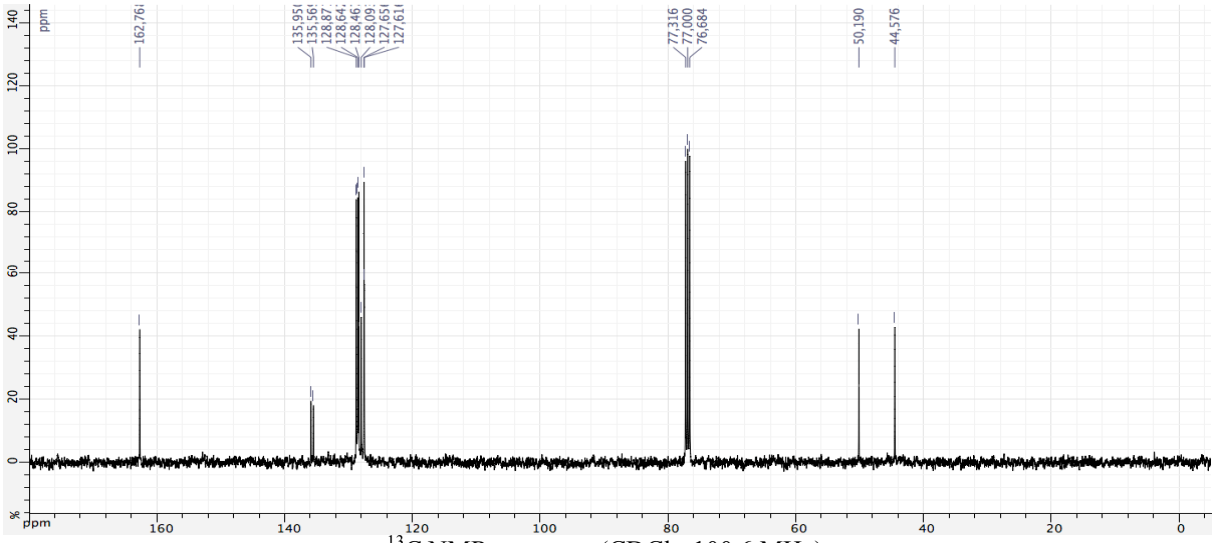


Colourless crystals. R_f 0.2 [AcOEt/Pet. ether 30%, PMA]. ^{1}H NMR ($CDCl_3$, 400 MHz) 4.26 (2 H, s, H1 or H6), 4.41 (2 H, s, H1 or H6), 7.14–7.23 (4 H, m, Ar), 7.27–7.41 (6 H, m, Ar), 8.42 (1 H, s, H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 44.6, 50.2 (C1, C6), 127.6, 128.1 (C5, C10), 127.7, 128.5, 128.6, 128.9 (C3, C4, C8, C9), 135.6, 135.9 (C2, C7), 162.8 (C11).

4– H.-L. Lee, J. Aubé, *Tetrahedron* **2007**, *63*, 9007–9015.



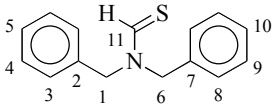
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR spectrum ($CDCl_3$, 100.6 MHz).

b) Lawesson reagent (0.500 equiv, 6.00 mmol, 2.43 g) was added to a solution of *N*,*N*-dibenzylformamide (1.00 equiv, 12.0 mmol, 2.75 g) in *t*BuOMe (12 mL) at 20°C. The mixture was stirred at 20°C for 18 h, then filtered through a short pad of celite, that was then rinsed with EtOAc. The resulting clear solution was concentrated to afford a yellow oil (4.92 g) that solidified on standing. Purification of the crude product by three successive crystallisations in MeOH (5.0 mL) afforded pure *N*,*N*-dibenzylmethanethioamide **1cS** (2.16 g, 8.95 mmol, 75%).

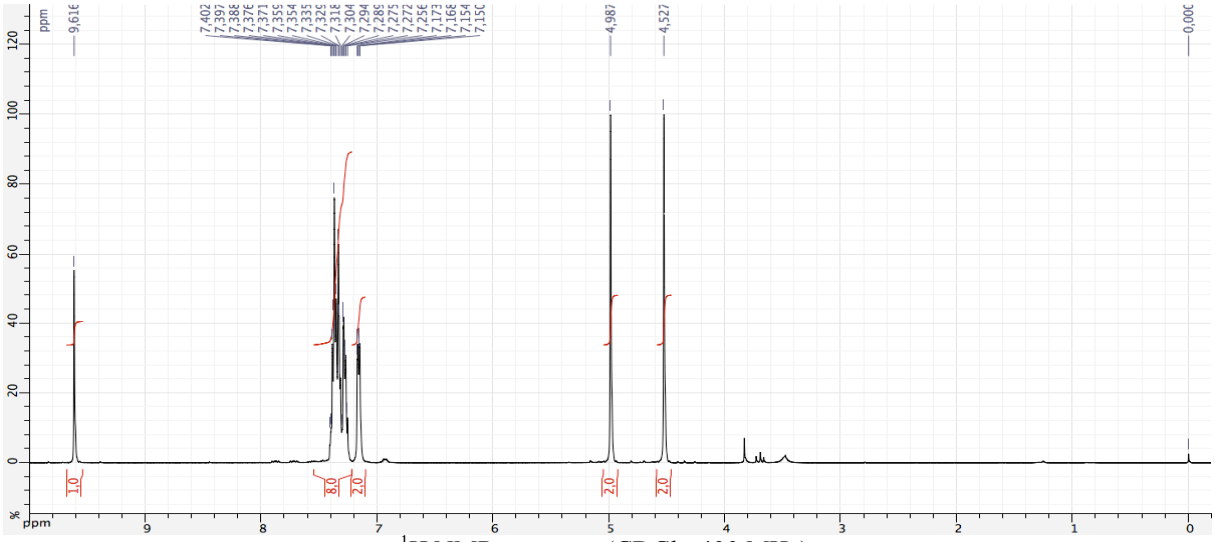
N,*N*-Dibenzylmethanethioamide **1cS**[5]



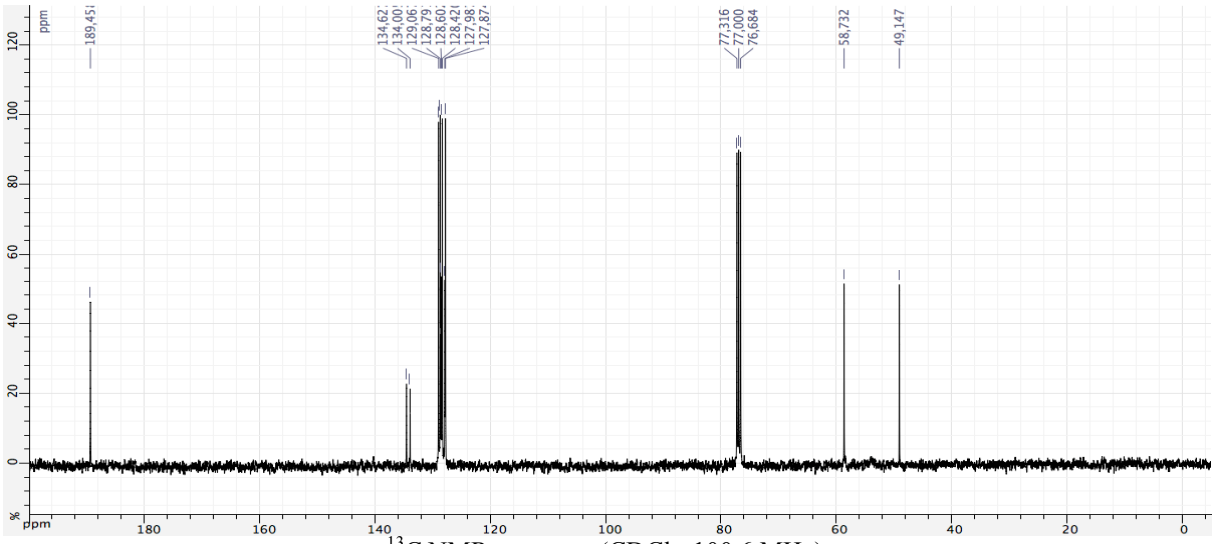
Colourless crystals. R_f 0.5 (AcOEt/Pet. ether 30%, anisaldehyde). ^{1}H NMR ($CDCl_3$, 400 MHz) 4.53 (2 H, s, H1 or H6), 4.99 (2 H, s, H1 or H6), 7.16 (2 H, br d, J 7.0, H3 or H8),

5– F. Shibahara, R. Sugiura, T. Murai, *Org. Lett.* **2009**, *11*, 3064–3067, supporting information.

7.24–7.42 (8 H, m, Ar), 9.62 (1 H, s, H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 49.1, 58.7 (C1, C6), 127.9, 128.4, 128.8, 129.1 (C3, C4, C8, C9), 128.0, 128.6 (C5, C10), 134.0, 134.6 (C2, C7), 189.5 (C11).

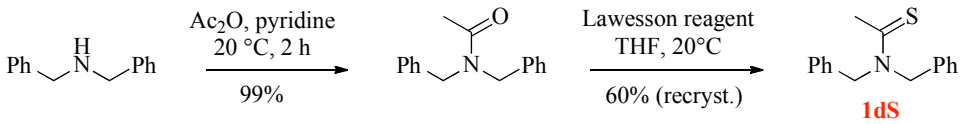


^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



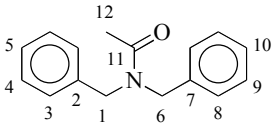
^{13}C NMR spectrum ($CDCl_3$, 100.6 MHz).

■ Thioamide **1dS**.

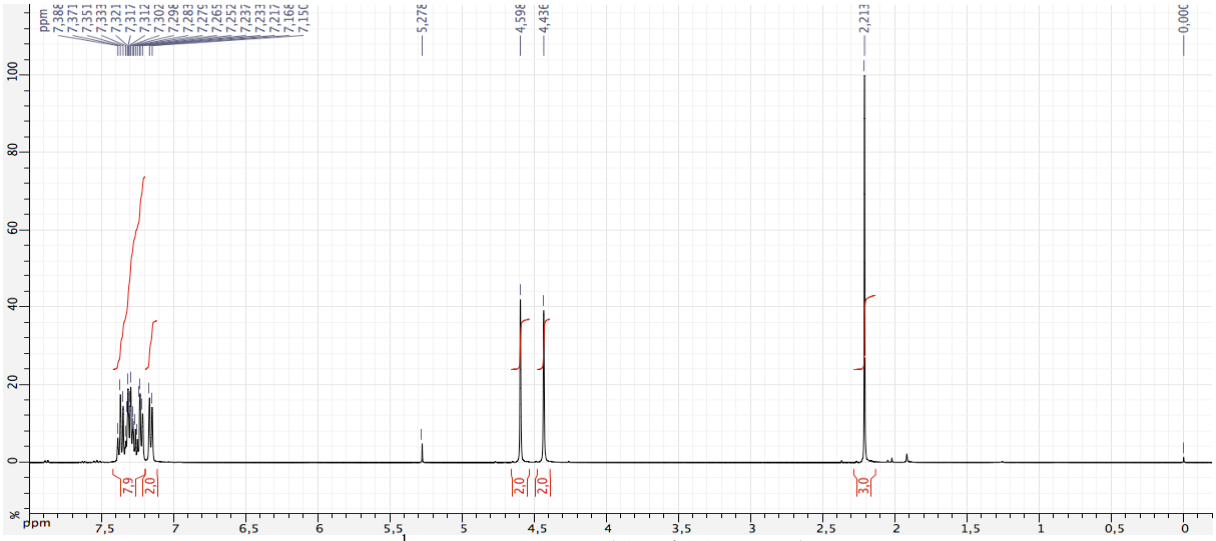


a) Acetic anhydride (1.10 equiv, 11.1 mmol, 1.05 mL) was added dropwise to a solution of dibenzylamine (1.00 equiv, 10.1 mmol, 1.95 mL) in pyridine (5.0 mL) at 0°C. The cold bath was removed after 5 min, and the mixture was stirred at 20 °C for 135 min. CH_2Cl_2 (50 mL) was added, then the solution was washed with 1 M NaOH aqueous solution (50 mL), H_2O (50 mL), 2 M HCl aqueous solution (2 × 50 mL) and H_2O (50 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford pure *N*,*N*-dibenzylacetamide (2.40 g, 10.0 mmol, 99%).

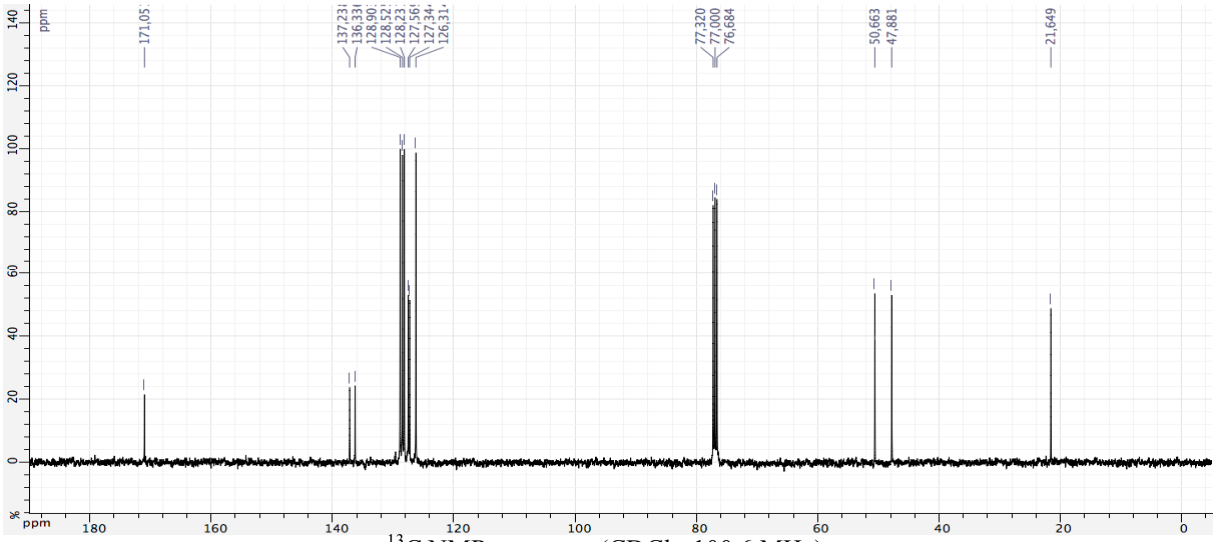
N,*N*-Dibenzylacetamide[6]



Pale yellow oil. R_f 0.2 [AcOEt/Pet. ether 30%, anisaldehyde (white colour)]. ^{1}H NMR ($CDCl_3$, 400 MHz) 2.21 (3 H, s, H12), 4.44 (2 H, s, H1 or H6), 4.60 (2 H, s, H1 or H6), 7.16 (2 H, br d, J 7.5, H3 or H8), 7.20–7.40 (8 H, m, Ar). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 21.6 (C12), 47.9, 50.7 (C1, C6), 126.3, 128.2, 128.5, 128.9 (C3, C4, C8, C9), 127.3, 127.6 (C5, C10), 136.3, 137.2 (C2, C7), 171.1 (C11).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



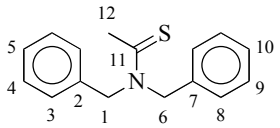
^{13}C NMR spectrum ($CDCl_3$, 100.6 MHz).

b) Lawesson reagent (0.500 equiv, 4.03 mmol, 1.63 g) was added to a solution of *N*,*N*-dibenzylacetamide (1.00 equiv, 8.07 mmol, 1.93 g) in THF (8.0 mL) at 20°C. The mixture was then stirred at 20°C for 7 h 30 min, by which time the starting material had been entirely consumed. The reaction mixture was filtered through a short pad of celite, that was then

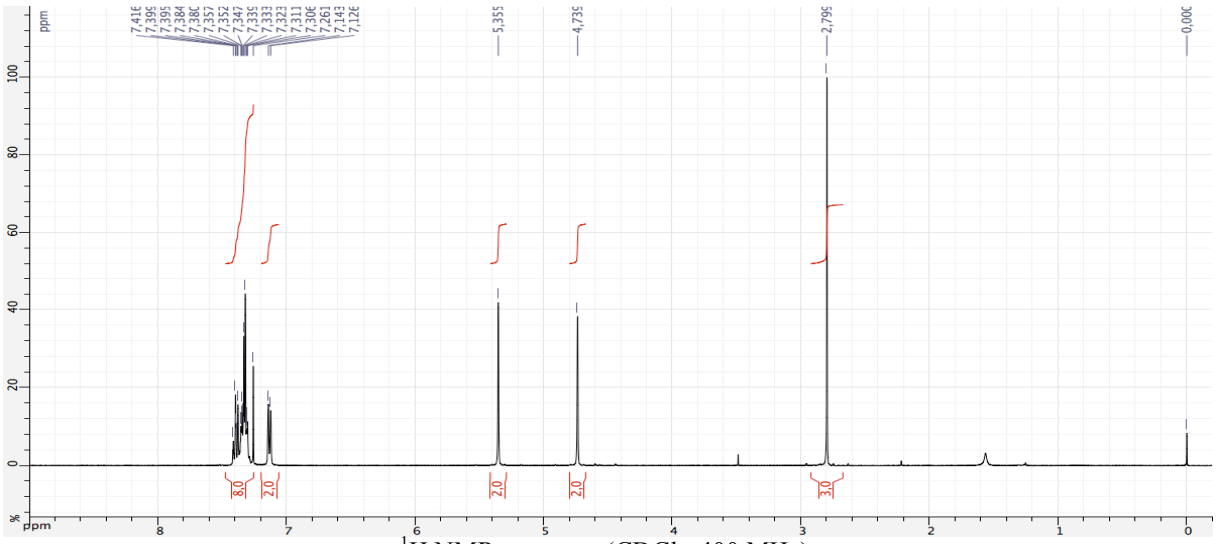
6– S. Zhou, K. Junge, D. Addis, S. Das, M. Beller, *Angew. Chem.* **2009**, *121*, 9671–9674; *Angew. Chem. Int. Ed.* **2009**, *48*, 9507–9510, supporting information.

rinsed with EtOAc. The resulting clear solution was concentrated to afford light yellow crystals (3.59 g). Purification of the crude product by two successive crystallisations in MeOH (6.0 mL and 10 mL) afforded pure *N*,*N*-dibenzylethanethioamide **1dS** (1.25 g, 4.89 mmol, 60%).

N,*N*-Dibenzylethanethioamide **1dS**

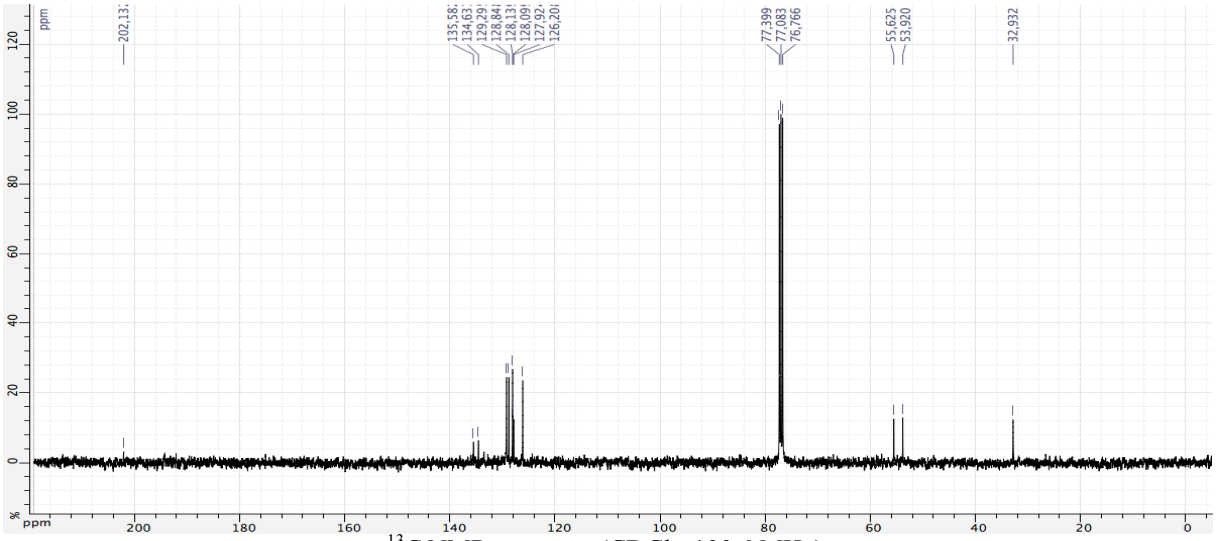


Colourless crystals. M.p. 85.9–87.2°C (MeOH) (litt.[7] m.p. 87–89°C). R_f 0.5 [AcOEt/Pet. ether 30%, anisaldehyde (pale white colour)]. IR (neat) ν 3060 (w), 3024 (w), 2955 (w), 2928 (w), 1494 (m), 1483 (s), 1453 (m), 1446 (m), 1420 (m), 1266 (m), 1231 (s), 1200 (m), 960 (s), 932 (m), 752 (m), 739 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) 2.80 (3 H, s, H12), 4.74 (2 H, s, H1 or H6), 5.35 (2 H, s, H1 or H6), 7.13 (2 H, br d, J 7.0, H3 or H8), 7.28–7.43 (8 H, m, Ar). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 32.9 (C12), 53.9, 55.6 (C1, C6), 126.2, 128.1, 128.8, 129.3 (C3, C4, C8, C9), 127.9, 128.1 (C5, C10), 134.6, 135.6 (C2, C7), 202.1 (C11). MS *m/z* (positive CI, NH_3) 240, 256 (MH^+), 257, 272, 273 ($MH^+..NH_3$), 274. HRMS *m/z* (EI) 255.1085 ($M^{+\bullet}$ $C_{16}H_{17}NS$ requires 255.1082).

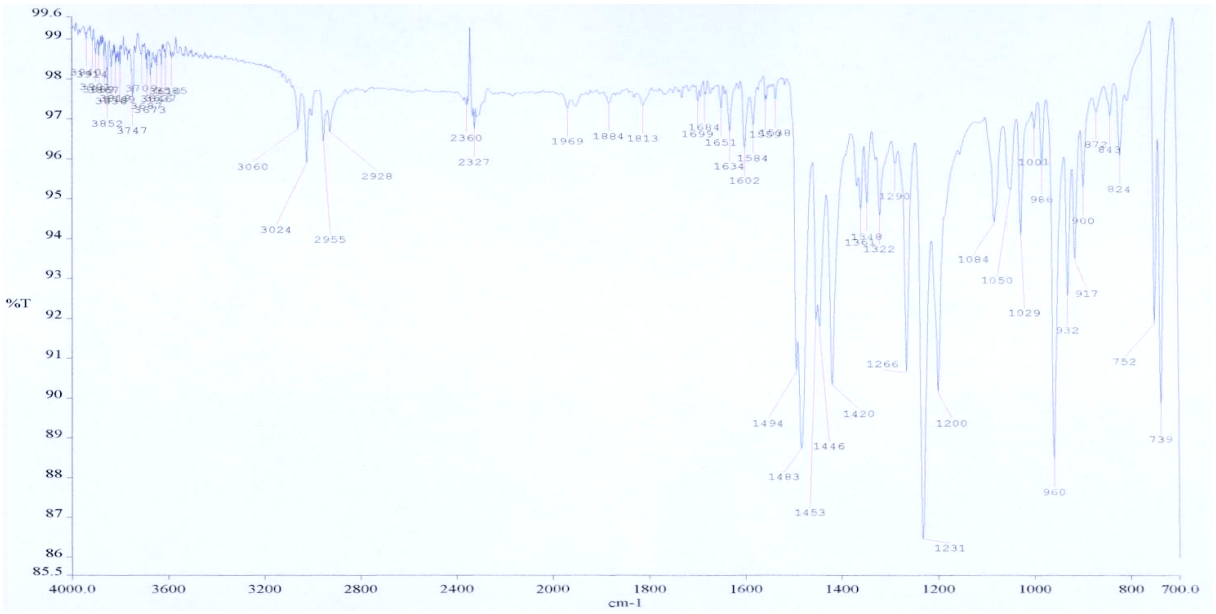


^1H NMR spectrum ($CDCl_3$, 400 MHz).

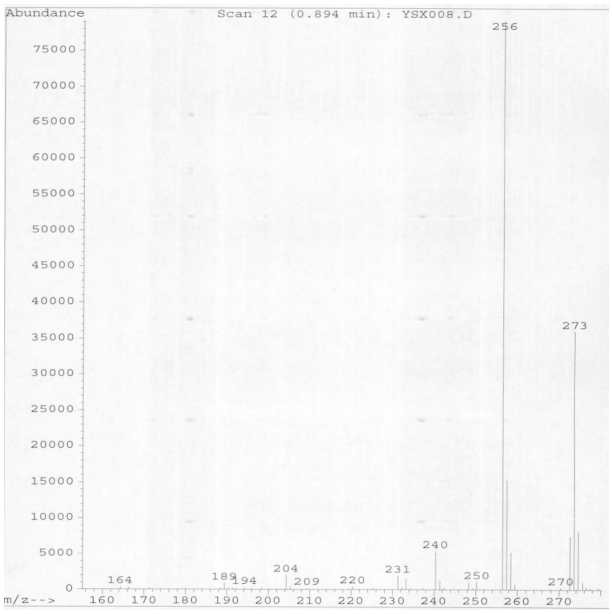
7– U. Berg, M. Grimaud, J. Sandström, *Nouv. J. Chim.* **1979**, *3*, 175.



^{13}C NMR spectrum ($CDCl_3$, 100.6 MHz).

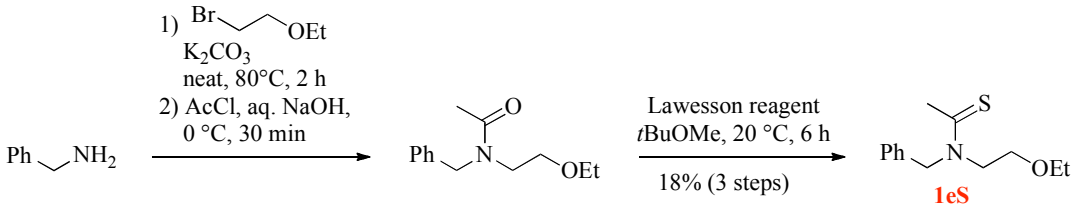


IR spectrum.

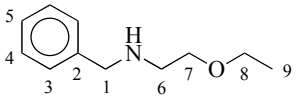


MS spectrum (positive CI, NH_3).

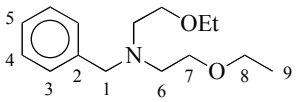
■ Thioamide **1eS**.



a) 2-Bromoethyl ethyl ether (1.00 equiv, 10.0 mmol, 1.13 mL) was added in four equal fractions (at t = 0, 20, 40 and 60 min) to a stirred, hot (80 °C), mixture of benzylamine (2.00 equiv, 20.0 mmol, 2.18 mL) and K_2CO_3 (1.00 equiv, 10.0 mmol, 1.38 g). After a further 1 h of stirring at 80 °C, the reaction mixture was allowed to cool to room temperature. *t*BuOMe (5.0 mL) was added. The suspension was filtered through a short pad of sand and celite (from bottom to top), that was then rinsed thoroughly with *t*BuOMe (20 mL). The resulting clear solution was concentrated under reduced pressure to afford a light brown oil (1.97 g). Analysis of the crude product by ^{1}H NMR spectroscopy gave an estimation of 53 : 41 : 6 for the ratio of benzylamine, *N*-benzyl-2-ethoxyethanamine and *N*-benzyl-2-ethoxy-*N*-(2-ethoxyethyl)ethanamine.

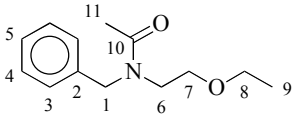
N-Benzyl-2-ethoxyethanamine 

^{1}H NMR ($CDCl_3$, 400 MHz) 1.20 (3 H, t, J 7.0, H9), 1.56 (1 H, br s, NH), 2.81 (2 H, t, J 5.0, H6), 3.49 (2 H, q, J 7.0, H8), 3.55 (2 H, t, J 5.0, H7), 3.82 (2 H, s, H1), 7.20–7.38 (5 H, m). ^{13}C NMR ($CDCl_3$, 100.6 MHz) characteristic signals: 15.2 (C9), 48.9 (C6), 54.0. (C1), 66.4 (C8), 69.8 (C7), 126.8 (C5), 128.1, 128.3 (C3, C4), 140.3 (C2).

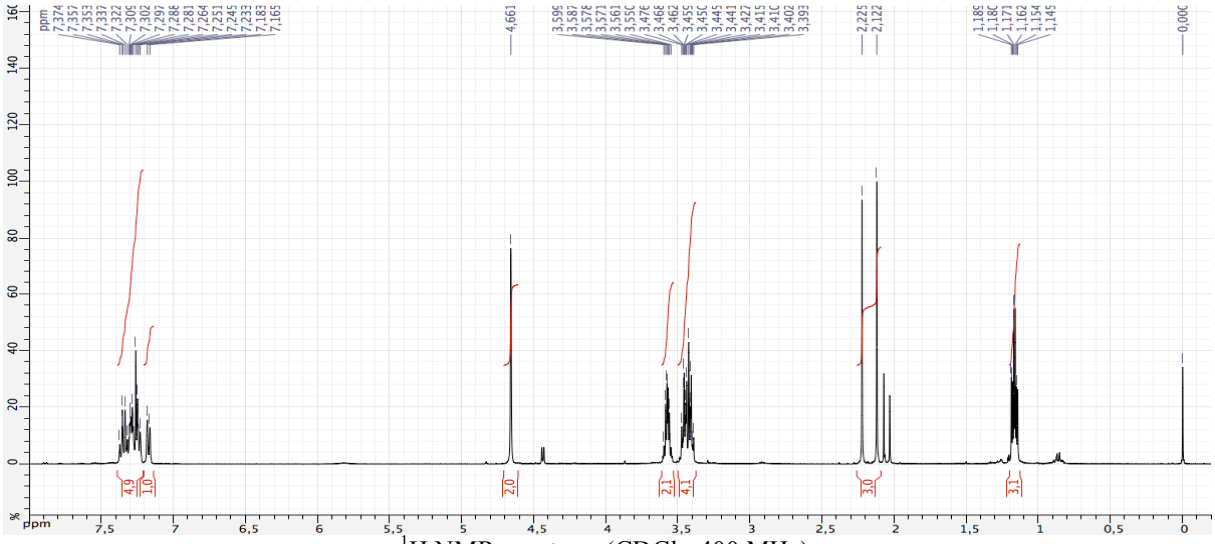
N-Benzyl-2-ethoxy-*N*-(2-ethoxyethyl)ethanamine 

^{1}H NMR ($CDCl_3$, 400 MHz) characteristic signals: 1.17 (6 H, t, J 7.0, H9), 2.75 (4 H, t, J 6.5, H6), 3.45 (4 H, q, J 7.0, H8), 3.51 (4 H, t, J 6.5, H7).

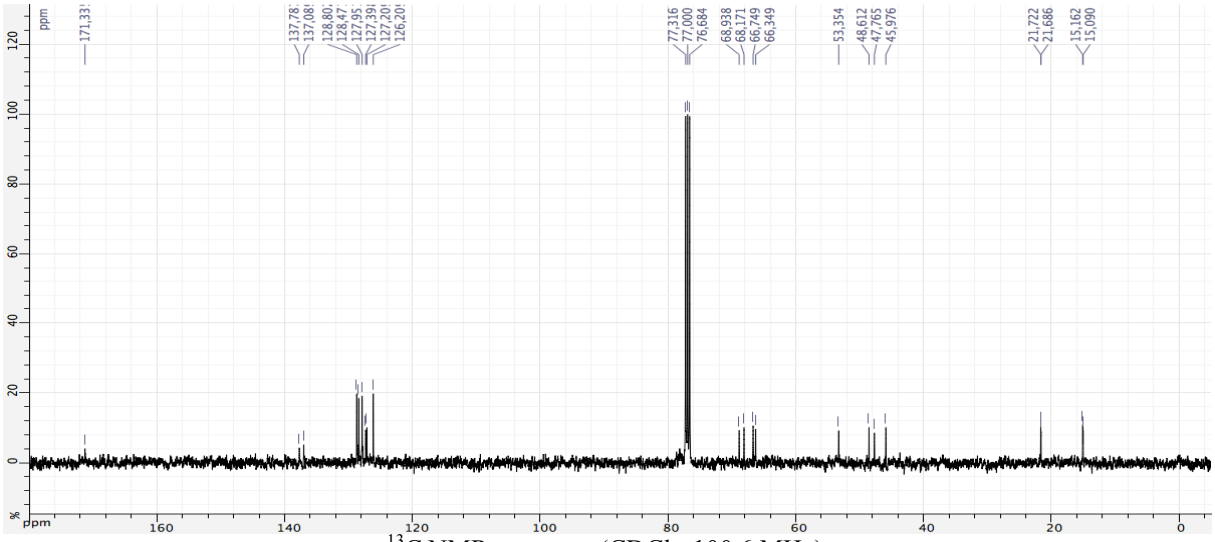
b) Acetyl chloride (1.00 equiv, 20.0 mmol, 1.48 mL) was added dropwise to a cold (0 °C) slurry of the mixture of amines obtained as above (1.00 equiv, assumed 20.0 mmol, 1.97 g) in 2 M NaOH aqueous solution (12 mL). After 30 min of stirring at 0 °C, the mixture was extracted with petroleum ether (6 × 25 mL) was added. The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a colourless oil (974 mg). Analysis of the crude product by ^{1}H and ^{13}C NMR spectroscopy assessed that it contained fairly pure *N*-benzyl-*N*-(2-ethoxyethyl)acetamide and it was engaged in the next step without further purification.

N-Benzyl-*N*-(2-ethoxyethyl)acetamide 

Colourless oil. R_f 0.25 (UV-active, AcOEt/Pet. ether 50%, anisaldehyde or PMA). ^{1}H NMR ($CDCl_3$, 400 MHz) 50 : 50 mixture of two rotamers: 1.16 and 1.17 (3 H, t, J 7.0, H9), 2.12 and 2.22 (3 H, s, H11), 3.38–3.50 (2 H, m, H6), 3.42 and 3.45 (2 H, q, J 7.0, H8), 3.53–3.62 (2 H, m, H7), 4.66 (2 H, s, H1), 7.14–7.39 (5 H, m, H3, H4, H5). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 50 : 50 mixture of two rotamers: 15.1 and 15.2 (C9), 21.7 and 21.7 (C11), 46.0, 47.8, 48.6, 53.4 (C1, C6), 66.3 and 66.7 (C8), 68.2 and 68.9 (C7), 126.2, 128.0, 128.5 and 128.8 (C3, C4), 127.2 and 127.4 (C5), 137.1 and 137.8 (C2), 171.3 (C10).



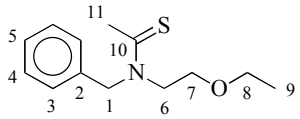
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



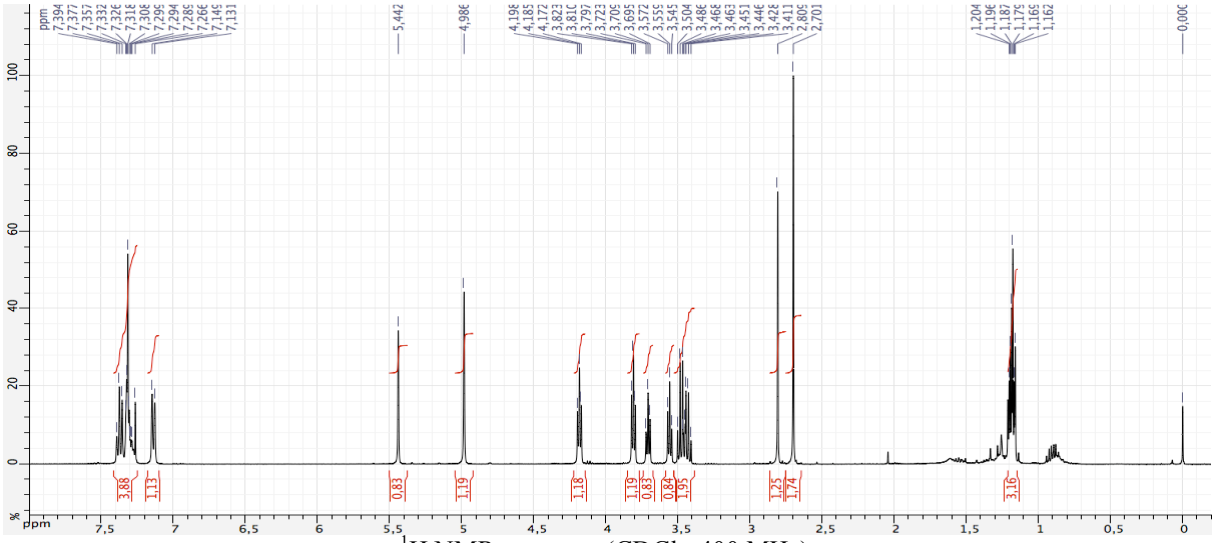
^{13}C NMR spectrum ($CDCl_3$, 100.6 MHz).

c) Lawesson reagent (0.550 equiv, 2.42 mmol, 979 mg) was added to a solution of *N*-benzyl-*N*-(2-ethoxyethyl)acetamide (1.00 equiv, assumed 4.40 mmol, 974 mg) in *t*BuOMe (4.0 mL) at 20°C. The mixture was then stirred at 20°C for 6 h. 0.1 M HCl aqueous solution (20 mL) and petroleum ether (20 mL) were added. The organic layer was separated and the aqueous phase extracted with petroleum ether (2 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a colourless oil (610 mg). Purification by flash column chromatography on silica gel (EtOAc/petroleum ether, gradient from 0% to 30%) yielded pure *N*-benzyl-*N*-(2-ethoxyethyl)ethanethioamide (426 mg, 1.79 mmol, 18% over 3 steps based on the starting 2-bromoethyl ethyl ether).

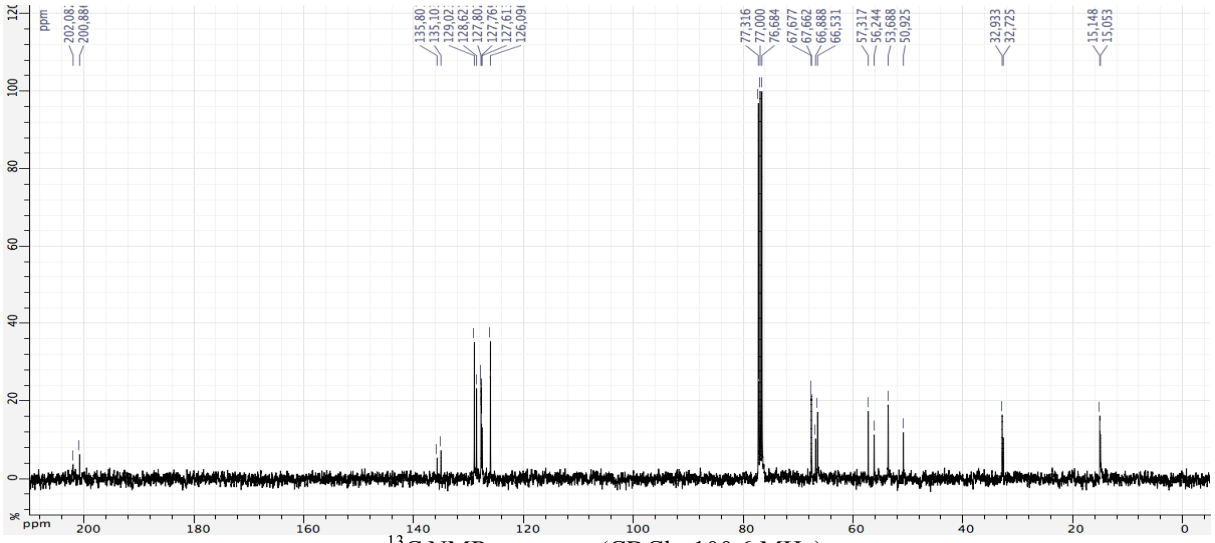
N-Benzyl-*N*-(2-ethoxyethyl)ethanethioamide



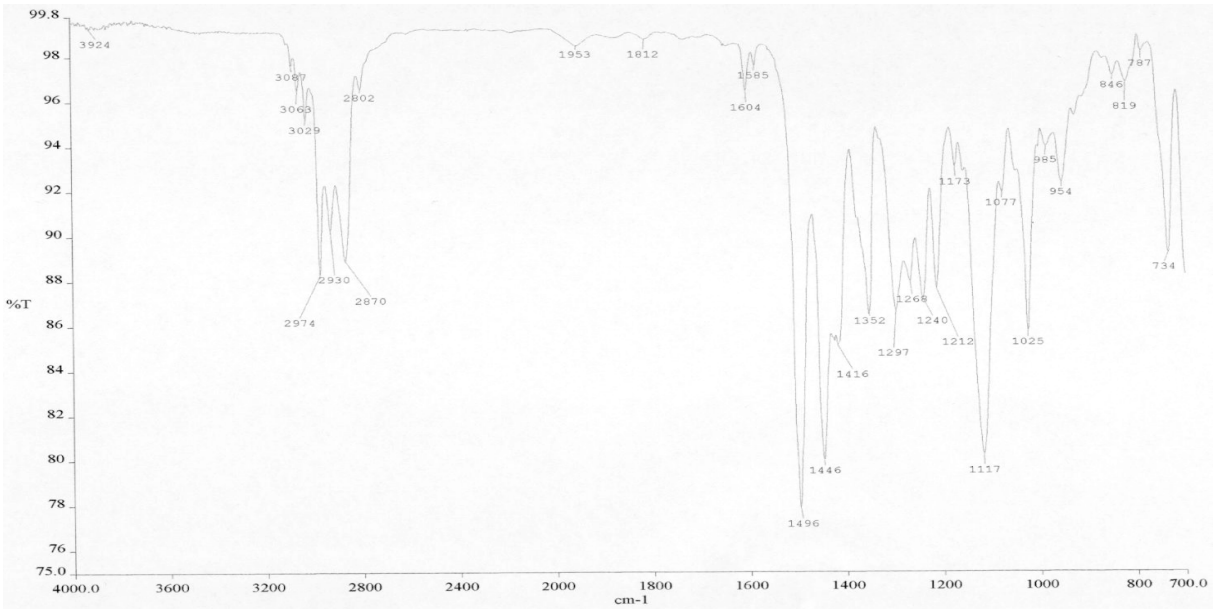
Colourless oil. R_f 0.2–0.3 (UV-active, AcOEt/Pet. ether 20%, anisaldehyde or PMA). IR (neat) ν 2974 (m), 2930 (m), 2870 (m), 1496 (s), 1446 (s), 1416 (m), 1352 (m), 1297 (m), 1268 (m), 1240 (m), 1212 (m), 1117 (s), 1025 (m), 734 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) 58 : 42 mixture of two rotamers. Major rotamer 1.18 (3 H, t, J 7.0, H9), 2.70 (3 H, s, H11), 3.48 (2 H, q, J 7.0, H8), 3.81 (2 H, t, J 5.0, H6 or H7), 4.19 (2 H, t, J 5.0, H6 or H7), 4.99 (2 H, s, H1), 7.14 (2 H, br d, J 7.5, H3), 7.25–7.42 (3 H, m, H4, H5). Minor rotamer 1.19 (3 H, t, J 7.0, H9), 2.81 (3 H, s, H11), 3.44 (2 H, q, J 7.0, H8), 3.56 (2 H, t, J 5.5, H6 or H7), 3.71 (2 H, t, J 5.5, H6 or H7), 5.44 (2 H, s, H1), 7.25–7.42 (5 H, m, H3–H5). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 58 : 42 mixture of two rotamers: 15.1 (C9), 15.1 (C9), 32.7 (C11), 32.9 (C11), 50.9 (C6), 53.7 (C6), 56.2 (C1), 57.3 (C1), 66.5 (C8), 66.9 (C8), 67.7 (C7), 67.7 (C7), 126.1 (C3), 127.6 (C5), 127.8 (C5), 127.8 (C3), 128.6 (C4), 129.0 (C4), 135.1 (C2), 135.8 (C2), 200.9 (C10), 202.1 (C10). MS *m/z* (positive CI, NH_3) 204, 222, 238 (MH^+), 239, 240. HRMS *m/z* (EI) 237.1186 ($M^{+\bullet}$ $C_{13}H_{19}NOS$ requires 237.1187).



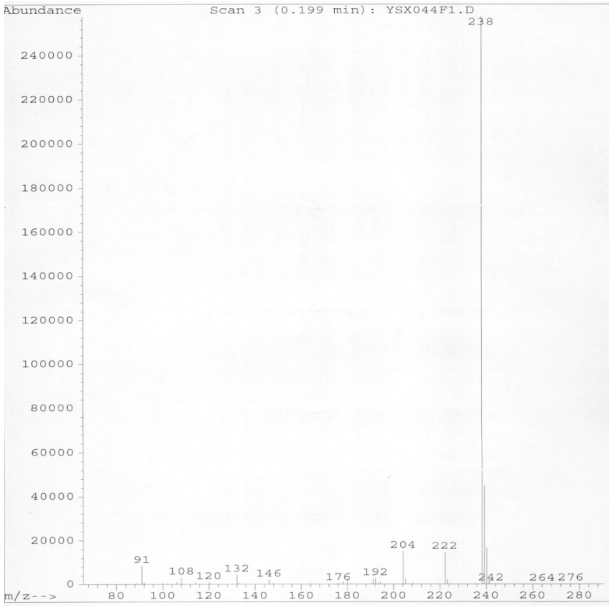
^1H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR spectrum ($CDCl_3$, 100.6 MHz).

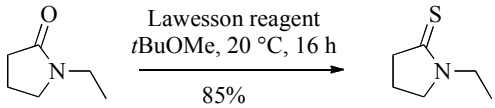


IR spectrum.



MS spectrum (positive CI, NH_3).

■ Thioamide **1fS**.

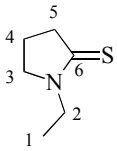


1fS

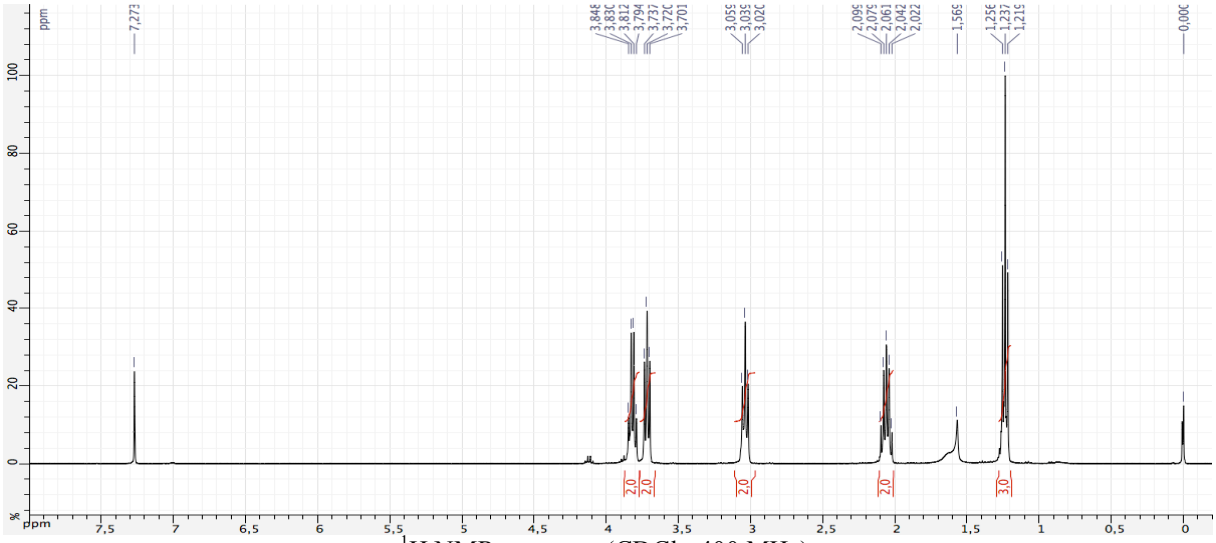
Lawesson reagent (0.500 equiv, 10.0 mmol, 4.04 g) was added to a solution of 1-ethylpyrrolidin-2-one (1.00 equiv, 20.0 mmol, 2.28 mL) in *t*BuOMe (20 mL) at 20°C. The mixture was then stirred at 20°C for 16 h, then filtered through a short pad of SiO_2, that was then rinsed with *t*BuOMe (20 mL). The resulting clear solution was concentrated to afford a colourless oil with an unpleasant smell (4.08 g). Purification by flash column chromatography

on silica gel (EtOAc/heptane, gradient from 5 to 30%) yielded pure 1-ethylpyrrolidin-2-thione **1fS** (2.20 g, 17.1 mmol, 85%).

1-Ethylpyrrolidin-2-thione[8]

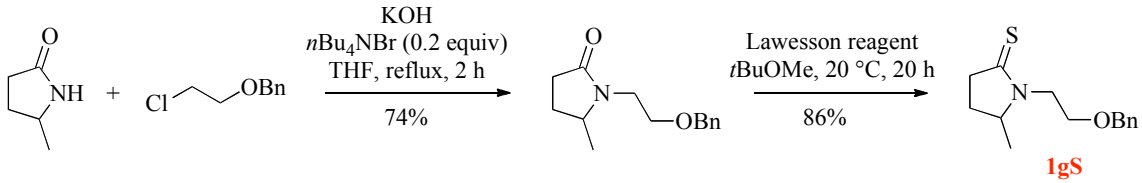


Colourless oil. R_f 0.15 (UV-active, AcOEt/Pet. ether 20%, PMA). ^{1}H NMR ($CDCl_3$, 400 MHz) 1.24 (3 H, t, J 7.0, H1), 2.06 (2 H, tt, J 8.0, 7.0, H4), 3.04 (2 H, t, J 8.0, H5), 3.72 (2 H, t, J 7.0, H3), 3.82 (2 H, q, J 7.0, H2).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

■ Thioamide **1gS**.

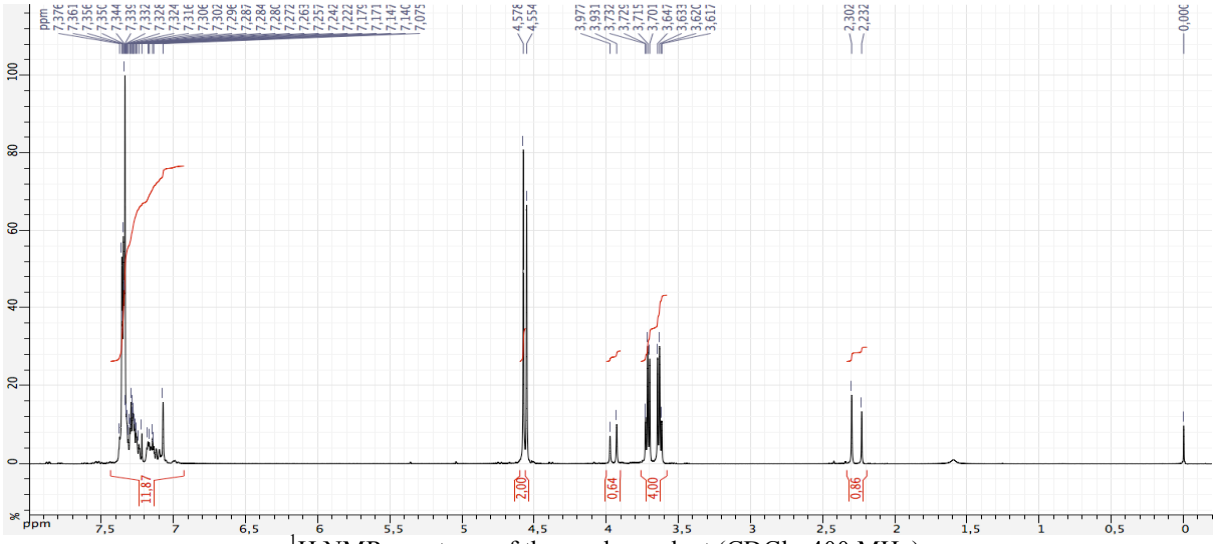


1gS

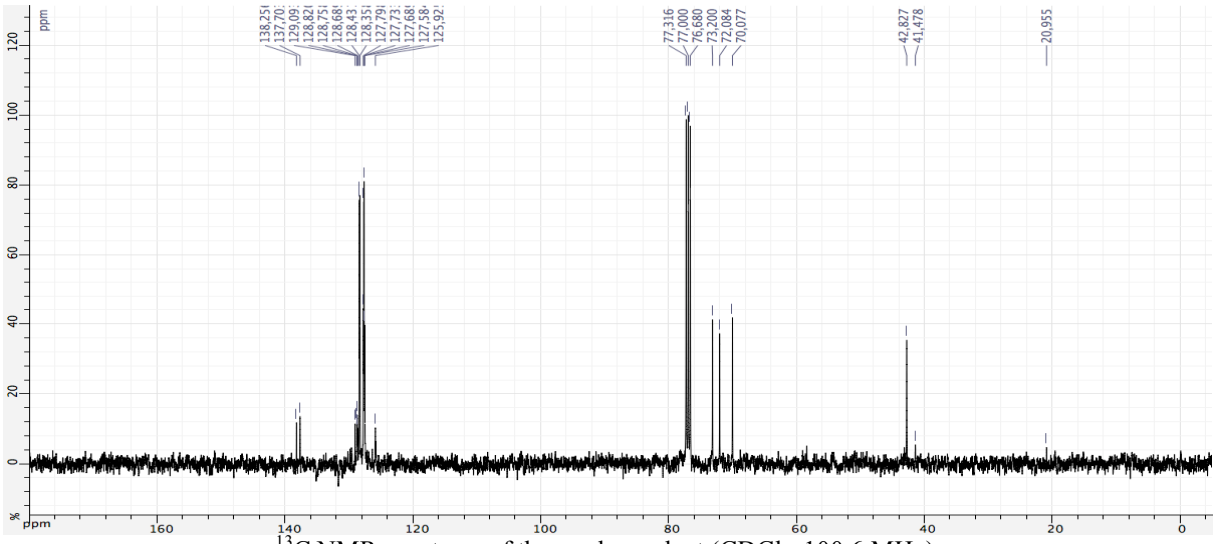
a) Synthesis of 2-chloroethoxymethylbenzene:[9] *p*TSA.H_2O (5.00% equiv, 2.50 mmol, 476 mg) was added to a solution of benzyl alcohol (1.00 equiv, 50.0 mmol, 5.17 mL) and 2-chloroethanol (2.00 equiv, 100 mmol, 6.70 mL) in toluene (50 mL). The mixture was heated at reflux for 30 h with a Dean-Stark apparatus and the production of H_2O (about 0.9 mL, 50 mmol) was observed. After cooling, the solution was washed with H_2O (50 mL), 0.1 M NaOH aqueous solution (2 × 25 mL) and H_2O (25 mL). The organic layer was then dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford a pale brown oil (7.03 g). Analysis by ^{1}H and ^{13}C NMR spectroscopy revealed that the main components were 2-chloroethoxymethylbenzene, dibenzyl ether, 1-benzyl-4-methylbenzene and 1-benzyl-2-

8– D. C. Smith, S. W. Lee, P. L. Fuchs, *J. Org. Chem.* **1994**, *59*, 348–354.
9– Procedure adapted from A. Buzas, A. Champagnac, A. Dehnel, G. Lavielle, M. Pommier, *J. Med. Chem.* **1980**, *23*, 149–153.

methylbenzenewere (56 : 26 : 14 : 10): the ratio of 2-chloroethoxymethylbenzene and dibenzyl ether was estimated to be 68 : 32 by ^{13}C NMR spectroscopy; the ratio of 1-benzyl-4-methylbenzene and 1-benzyl-2-methylbenzene, resulting of Friedel-Crafts type alkylation of toluene, was estimated to be 60 : 40 by ^{1}H NMR spectroscopy; the ratio of the latter two products and 2-chloroethoxymethylbenzene was estimated to be 24 : 76 by ^{1}H NMR spectroscopy. The amount of 2-chloroethoxymethylbenzene produced is thus estimated to be 21.9 mmol (44%).

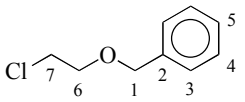


^{1}H NMR spectrum of the crude product ($CDCl_3$, 400 MHz).



^{13}C NMR spectrum of the crude product ($CDCl_3$, 100.6 MHz).

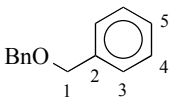
2-Chloroethoxymethylbenzene[10]



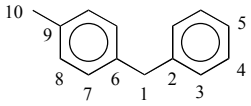
^{1}H NMR ($CDCl_3$, 400 MHz) 3.67 (4 H, AA'BB' system,[11] δ_A 3.64, δ_B 3.71, *N* 12.0 (*K*, *L* and *M* could not be measured accurately), H6, H7), 4.58 (2 H, s, H1), 7.04–7.40 (5 H, m, H3–H5).

10– S. M. Ludeman, D. L. Bartlett, G. Zon, *J. Org. Chem.* **1979**, *44*, 1163–1166.
11– H. Günther, *Angew. Chem.* **1972**, *84*, 907–920; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 861–948.

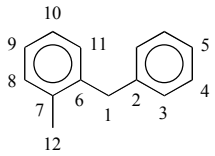
^{13}C NMR ($CDCl_3$, 100.6 MHz) 42.8 (C7), 70.1 (C6), 73.2 (C1), 127.7 (C3), 127.8 (C5), 128.4 (C4), 137.7 (C2).

Dibenzyl ether[12] 

^{1}H NMR ($CDCl_3$, 400 MHz) characteristic signal: 4.55 (2 H, s, H1). ^{13}C NMR ($CDCl_3$, 100.6 MHz) characteristic signals: 72.1 (C1), 127.6 (C5), 127.7 (C3), 128.4 (C4), 138.3 (C2).

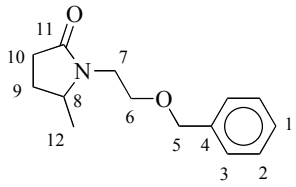
1-Benzyl-4-methylbenzene[13] 

^{1}H NMR ($CDCl_3$, 400 MHz) characteristic signals: 2.30 (3 H, s, H10), 3.93 (2 H, s, H1). ^{13}C NMR ($CDCl_3$, 100.6 MHz) characteristic signals: 21.0 (C10), 41.5 (C1).

1-Benzyl-2-methylbenzene[13] 

^{1}H NMR ($CDCl_3$, 400 MHz) characteristic signals: 2.23 (3 H, s, H10), 3.98 (2 H, s, H1).

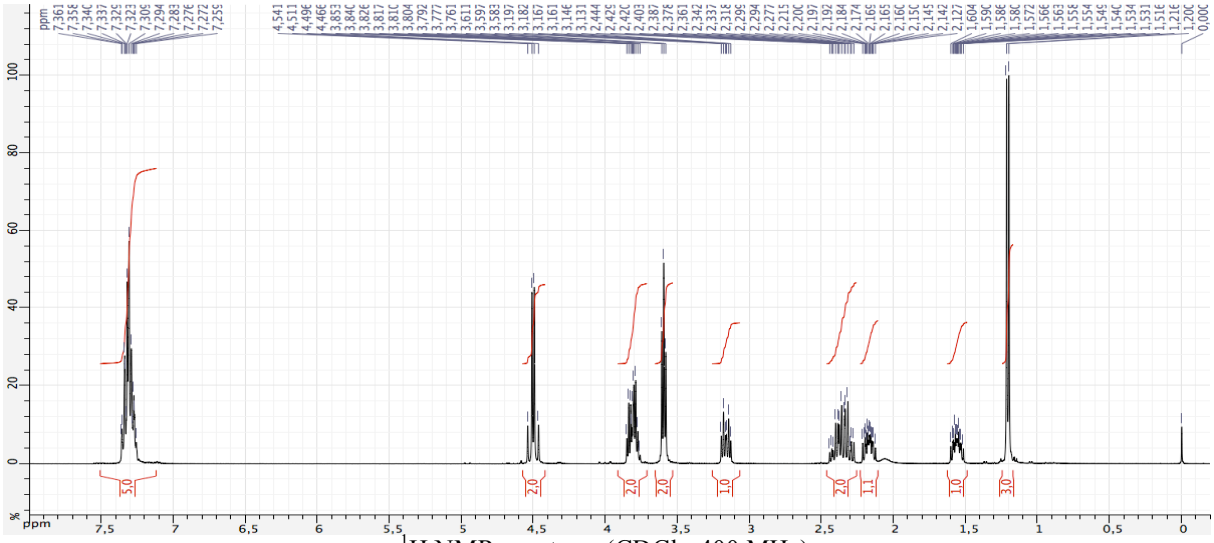
b) A solution of 5-methylpyrrolidin-2-one (1.00 equiv, 12.5 mmol, 1.24 g) and 2-chloroethoxymethylbenzene (3.51 g of crude product of the experiment described above, i.e. 0.87 equiv, 10.9 mmol) in THF (5.0 mL) was added dropwise, over 30 min, to a suspension of KOH (powder, 1.10 equiv, 13.7 mmol, 772 mg) and nBu$_4$NBr (20.0% equiv, 2.50 mmol, 806 mg) in THF (12.5 mL). The mixture was heated at reflux for 2 h. After cooling, the solution was filtered (rinsing: EtOAc) and concentrated under reduced pressure to afford a black oil. Purification by flash column chromatography on silica gel, (EtOAc/pet. ether, gradient from 20 to 100%) yielded pure 1-(2-benzyloxyethyl)-5-methyl-pyrrolidin-2-one (2.15 g, 9.20 mmol, 74%).[14]

1-(2-Benzyloxyethyl)-5-methyl-pyrrolidin-2-one 

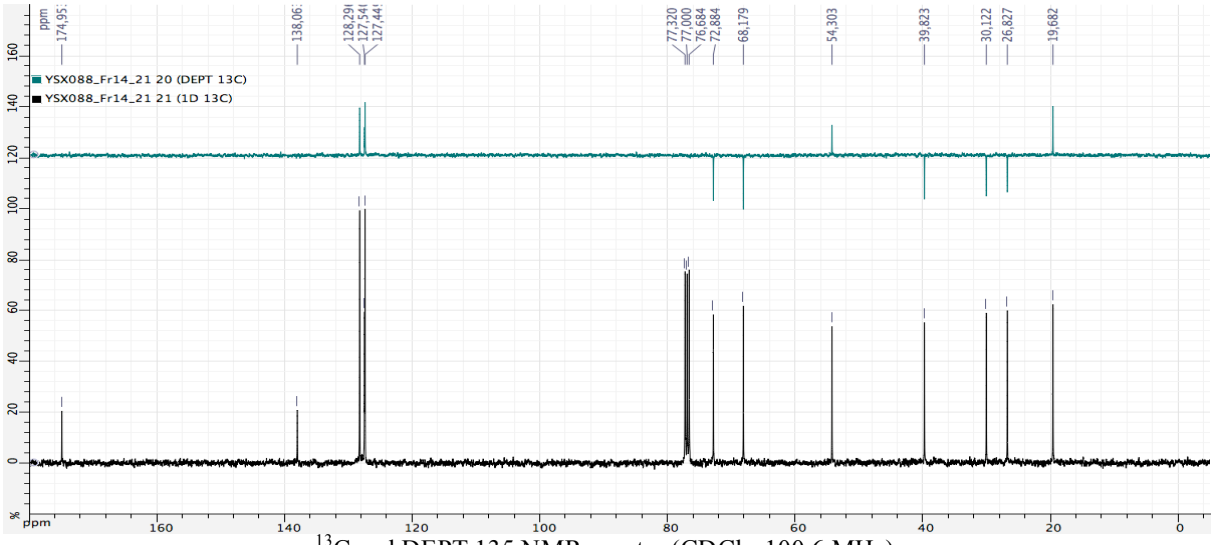
Amber oil. R_f 0.05 (UV-active, AcOEt/Pet. ether 50%, anisaldehyde [yellow spot]). IR (neat) ν 3480 (br, w), 3031 (w), 2968 (m), 2932 (m), 2867 (m), 1694 (s), 1688 (s), 1682 (s), 1674 (s), 1668 (s), 1496 (w), 1455 (m), 1435 (m), 1417 (m), 1377 (m), 1360 (m), 1312 (m), 1278

12– SDBSWeb; http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology, date of access: 14 October 2011).
13– D. Srimani, A. Bej, A. Sarkar, *J. Org. Chem.* **2010**, *75*, 4296–4299 (supporting information).
14– Procedure adapted from H. Takahata, H. Okajima, T. Yamazaki, *Chem. Pharm. Bull.* **1980**, *28*, 3632–3638.

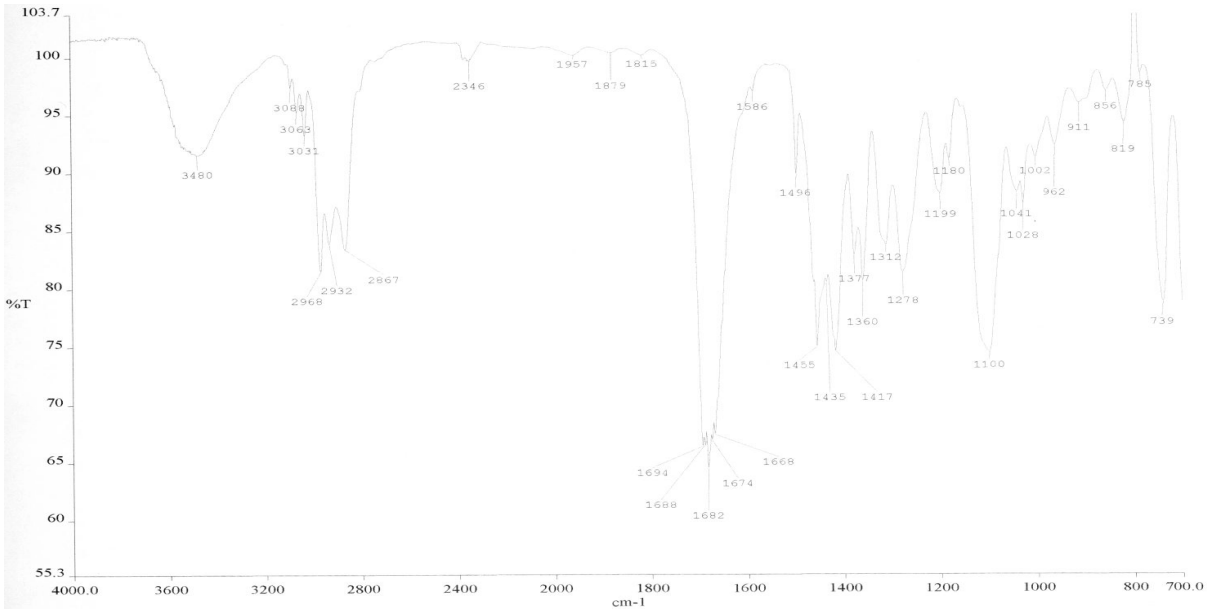
(m), 1199 (w), 1100 (m), 1041 (w), 1028 (w), 739 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) 1.21 (3 H, d, J 6.5, H12), 1.56 (1 H, dddd, J 12.5, 9.5, 7.0, 6.0, H9a), 2.17 (1 H, dddd, J 12.5, 9.0, 7.5, 6.0, H9b), 2.36 (2 H, AB part of an ABXY system, δ_A 2.32, δ_B 2.40, J_{AB} 17.0, J_{AX} 7.0, J_{AY} 9.0, J_{BX} 9.5, J_{BY} 6.0, H10), 3.16 (1 H, dt, J 14.0, 6.0, H7a), 3.60 (2 H, m looking like t, J 6.5, H6), 3.80 (1 H, dqd, J 7.5, 6.5, 6.0, H8), 3.82 (1 H, dt, J 14.0, 5.5, H7b), 4.50 (2 H, AB system, δ_A 4.49, δ_B 4.52, J_{AB} 12.0, H5), 7.23–7.38 (5 H, m, H1–H3). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 19.7 (C12), 26.8 (C9), 30.1 (C10), 39.8 (C7), 54.3 (C8), 68.2 (C6), 72.9 (C5), 127.4 (C3), 127.5 (C1), 128.5 (C2), 138.1 (C4), 175.0 (C11). MS *m/z* (positive CI, NH_3) 112, 234 (MH^+), 235. HRMS *m/z* (EI) 233.1409 ($M^{+\bullet}$ $C_{14}H_{19}NO_2$ requires 233.1416).



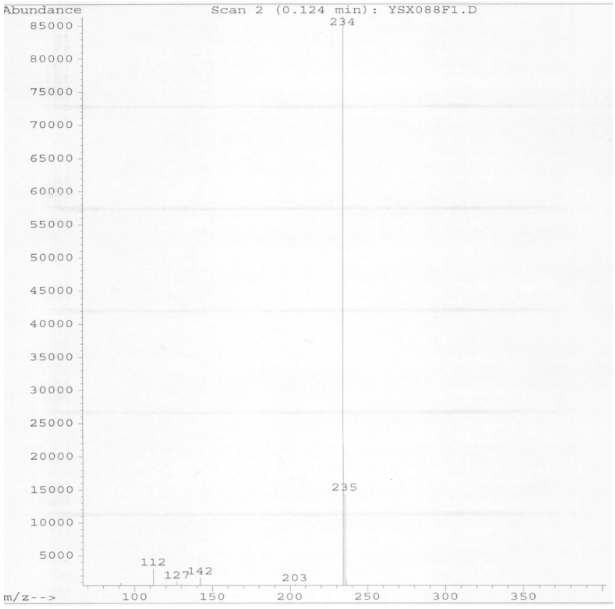
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C and DEPT 135 NMR spectra ($CDCl_3$, 100.6 MHz).



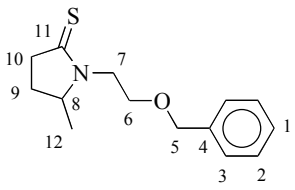
IR spectrum.



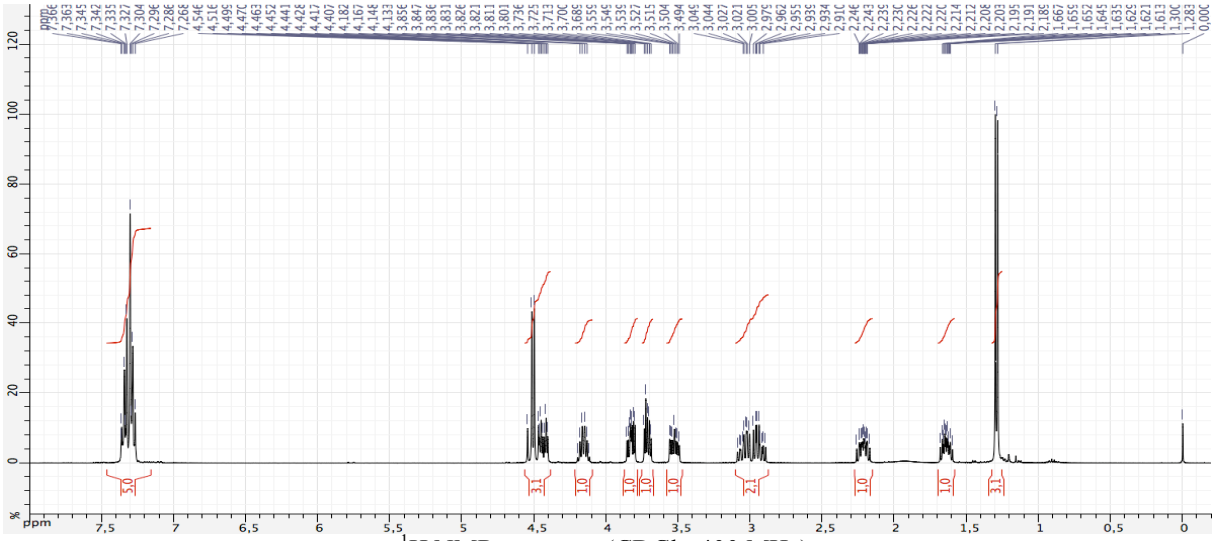
MS spectrum (positive CI, NH_3).

c) Lawesson reagent (0.550 equiv, 5.06 mmol, 2.05 g) was added to a solution of 1-(2-benzyloxyethyl)-5-methyl-pyrrolidin-2-one (1.00 equiv, 9.20 mmol, 2.15 g) in *t*BuOMe (9.0 mL) at 20 °C. The mixture was then stirred at 20 °C for 20 h. The reaction mixture consisted in a clear solution with a white precipitate stuck on the walls of the flask. The clear solution was transferred into another flask and the reaction flask was rinsed with *t*BuOMe (3 × 8.0 mL). The combined organic phases were concentrated under reduced pressure to afford a pale orange oil (3.08 g). Purification by flash column chromatography on silica gel, (EtOAc/pet. ether, gradient from 10% to 50%) yielded pure 1-(2-benzyloxyethyl)-5-methyl-pyrrolidin-2-thione **1gS** (1.97 g, 7.91 mmol, 86%).

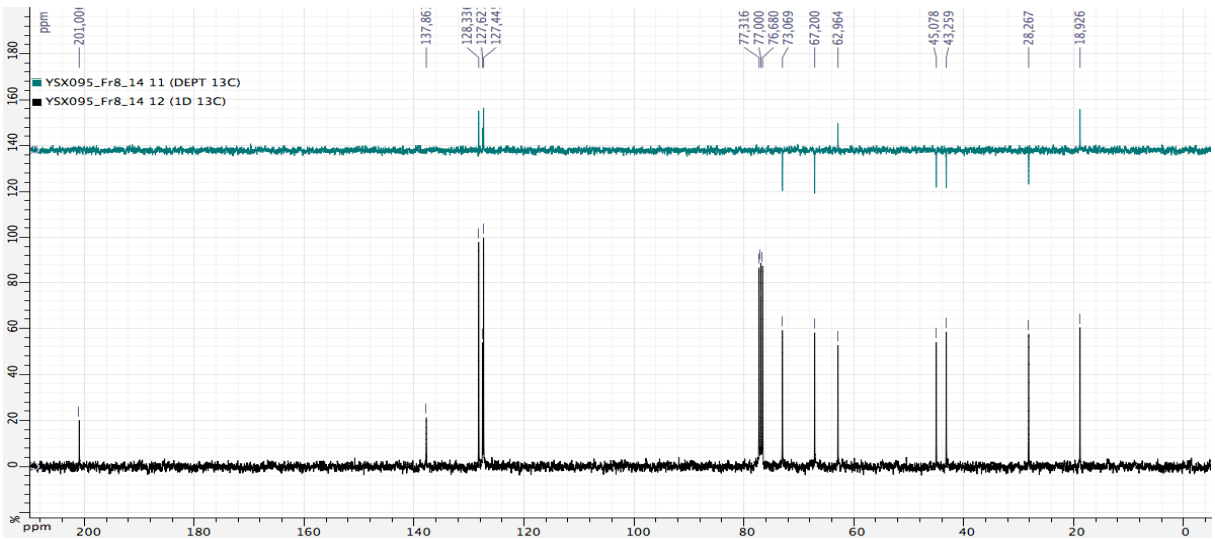
1-(2-Benzyloxyethyl)-5-methyl-pyrrolidin-2-thione **1gS**



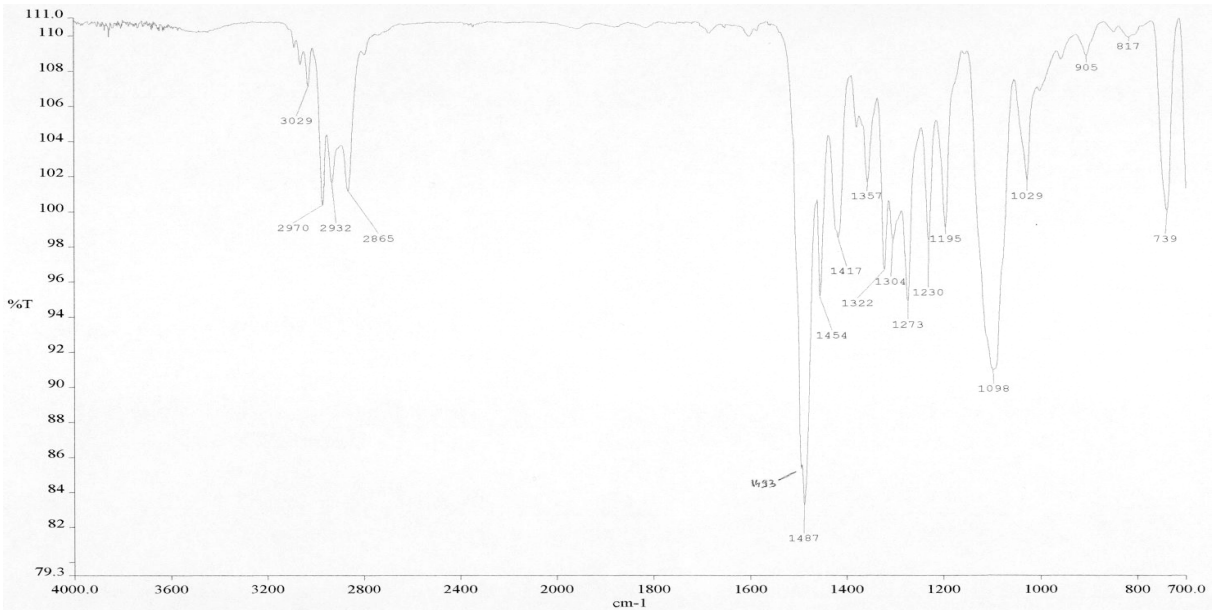
Pale yellow oil. R_f 0.25 (UV-active, AcOEt/Pet. ether 30%, anisaldehyde [white spot]). IR (neat) ν 3029 (w), 2970 (m), 2932 (m), 2865 (m), 1493 (s), 1487 (s), 1454 (m), 1417 (m), 1357 (m), 1322 (m), 1304 (m), 1273 (m), 1230 (m), 1195 (m), 1098 (m), 1029 (m), 739 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) 1.29 (3 H, d, J 6.5, H12), 1.64 (1 H, dddd, J 12.5, 9.0, 6.5, 5.5, H9a), 2.22 (1 H, dddd, J 12.5, 9.5, 7.5, 6.5, H9b), 2.99 (2 H, AB part of an ABXY system, δ_A 2.94, δ_B 3.04, J_{AB} 18.0, J_{AX} 6.5, J_{AY} 9.5, J_{BX} 9.0, J_{BY} 6.5, H10), 3.53 (1 H, ddd, J 14.0, 8.0, 4.5, H7a), 3.77 (2 H, AB part of an ABXY system, δ_A 3.71, δ_B 3.83, J_{AB} 10.0, J_{AX} 4.5, J_{AY} 4.5, J_{BX} 8.0, J_{BY} 4.0, H6), 4.16 (1 H, dqd, J 7.5, 6.5, 5.5, H8), 4.43 (1 H, ddd, J 14.0, 4.5, 4.0, H7b), 4.51 (2 H, AB system, δ_A 4.49, δ_B 4.53, J_{AB} 12.0, H5), 7.24–7.39 (5 H, m, H1–H3). ^{13}C NMR ($CDCl_3$, 100.6 MHz) 18.9 (C12), 28.3 (C9), 43.3, 45.1 (C7, C10), 63.0 (C8), 67.2 (C6), 73.1 (C5), 127.4 (C3), 127.6 (C1), 128.3 (C2), 137.9 (C4), 201.0 (C11). MS *m/z* (positive CI, NH_3) 158, 216, 250 (MH^+), 251, 252. HRMS *m/z* (EI) 249.1196 ($M^{+\bullet}$ $C_{14}H_{19}NOS$ requires 249.1187).



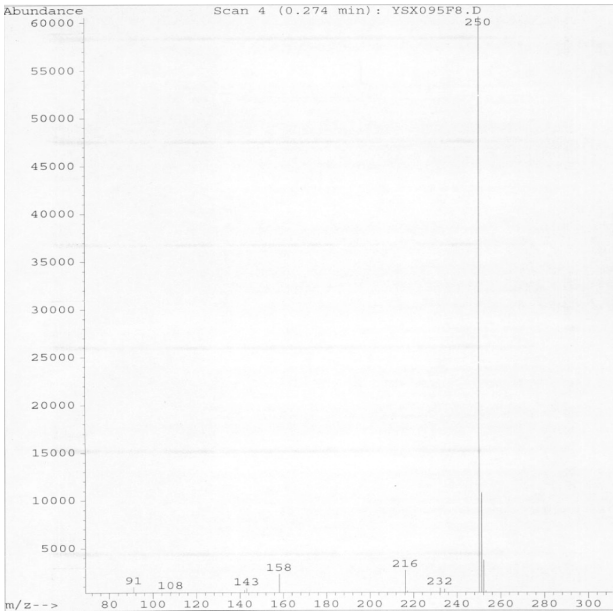
^1H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C and DEPT 135 NMR spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (positive CI, NH_3).