

Electronic Supplemental Information

Dess-Martin Periodinane Oxidative Rearrangement for Preparation of α -Keto Thioesters

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General Synthetic Procedures

Reactions involving either air or moisture sensitive reactants were conducted under an atmosphere of argon. All solvents and chemicals were reagent grade and used as supplied from Sigma-Aldrich unless otherwise stated. DMP was sourced from AK Scientific at 95% purity. Anhydrous solvents required were dried according to the procedures outlined in Perrin and Armarego.¹ Removal of solvent was performed under reduced pressure, below 40 °C, using a Büchi rotary evaporator. All reactions and fractions from column chromatography were monitored by thin layer chromatography (TLC). Analytical TLC was done on glass plates (5 × 1.5 cm) pre-coated (0.25 mm) with silica gel (normal SiO₂, Merck 60 F254). Compounds were visualized by exposure to UV light and/ by exposing the plates to KMnO₄ solution, followed by heating. Flash chromatography was performed on silica gel (EM Science, 60Å pore size, 230-400 mesh).

Spectroscopic Analyses

Nuclear magnetic resonance (NMR) spectra were obtained on Varian Inova 500 MHz spectrometer. ¹H NMR chemical shifts are reported in parts per million (ppm) using the residual proton resonance of the solvent as reference: CDCl₃ δ 7.26. ¹³C NMR chemical shifts are reported relative to CDCl₃ δ 77.06. Infrared spectra (IR) were recorded on a Nicolet Magna 750. Cast Film refers to the evaporation of a solution on a NaCl plate. Gas Phase IR-spectra was obtained using a 10 cm gas cell, with KBr window on a Thermo Nicolet 8700 (Madison WI) equipped with a liquid nitrogen cooled MCT/B detector. The spectral resolution was 0.250 wavenumbers from 400 to 4000 wavenumbers with 128 co-added scans for both the sample and background. Mass spectra were recorded on a Kratos IMS-50 (high resolution, electron impact ionization (EI)) or by using an Agilent Technologies 6220 orthogonal acceleration TOF instrument equipped with +ve and –ve ion ESI ionization source, and full-scan MS (high resolution analysis) with two-point lock mass correction operating mode. The instrument inlet was an Agilent Technologies 1200 SL HPLC system. GC-MS analysis of headspace gas was performed using a Bruker Scion 456-GC-TQ GCMS instrument (Billerica, Massachusetts, United States). The column used was a Phenomenex (Zebron ZB-5 fused silica capillary column (30 m x 0.25 mm i.d., 0.25 µm film thickness). The method used was as follows: manual injection of 100 µL headspace gas, Injector at 200 °C, split rate 50:1, constant flow rate at 1 mL/min, helium as carrier gas, isocratic column oven temperature at 50 °C; mass range 10-200 Da, total run time 10 min.

RP-HPLC-HiRes MS Experiment Methods

RP-HPLC-Hi-ResMS was performed using an Agilent 1200 SL HPLC System with a Kinetex C8 reverse-phase analytical column (2.1x50 mm), 100Å pore size, 1.7 µm particle size (Phenomenex, Torrance, CA, USA), thermostated at 50°C followed by mass spectrometric detection. The buffer gradient system was composed of 0.1 % formic acid in water as mobile phase A and 0.1 % formic acid in acetonitrile as mobile phase B.

Methods for Separation of Analytes:

- i. For the separation of analytes an aliquot was loaded onto the column at a flow rate of 0.50 mLmin⁻¹ and an initial buffer composition of 98 % mobile phase A and 2 % mobile phase B. Elution of the analytes was done by use of a linear gradient from 2 % to 95 % mobile phase B over a period of 5 min, held at 95 % mobile phase B for 3 min to remove all analytes from the column and back to 2 % mobile phase B within 1 minute.
- ii. For the separation of analytes an aliquot was loaded onto the column at a flow rate of 0.50 mLmin⁻¹ and an initial buffer composition of 98 % mobile phase A and 2 % mobile phase B. Elution of the analytes was done by using a linear gradient from 2 % to 50 % mobile phase B over a period of 5 min, 50 % to 95 % mobile phase B for 3 min and back to 2 % mobile phase B within 1 minute.

Mass spectra were acquired in positive mode of ionization using an Agilent 6220 Accurate-Mass TOF HPLC/MS system (Santa Clara, CA, USA) equipped with a dual sprayer electrospray ionization source with the second sprayer providing a reference mass solution. Mass correction was performed for every individual spectrum using peaks at m/z 121.0509 and 922.0098 from the reference solution. Mass spectrometric conditions were drying gas 10 L/min at 325°C, nebulizer 35 psi, mass range 100-1100 Da, acquisition rate of ~1.03 spectra/sec, fragmentor 150V, skimmer 65V, capillary 3200V, instrument state 4GHz High Resolution. Data analysis was performed using the Agilent MassHunter Qualitative Analysis software package version B.07.00 SP1.

RP-HPLC-HiRes MS Experiments

➔ **Intermediate Standards:** For each of the proposed intermediates synthesized standards were prepared by diluting 1.0 mg of the respective substrate, into 10 mL of DCM, then further diluting 0.1 mL aliquots to 1.0 mL using dichloromethane (DCM). These standards were then analysed using Method (i) for separation of analytes and the retention time and mass were noted.

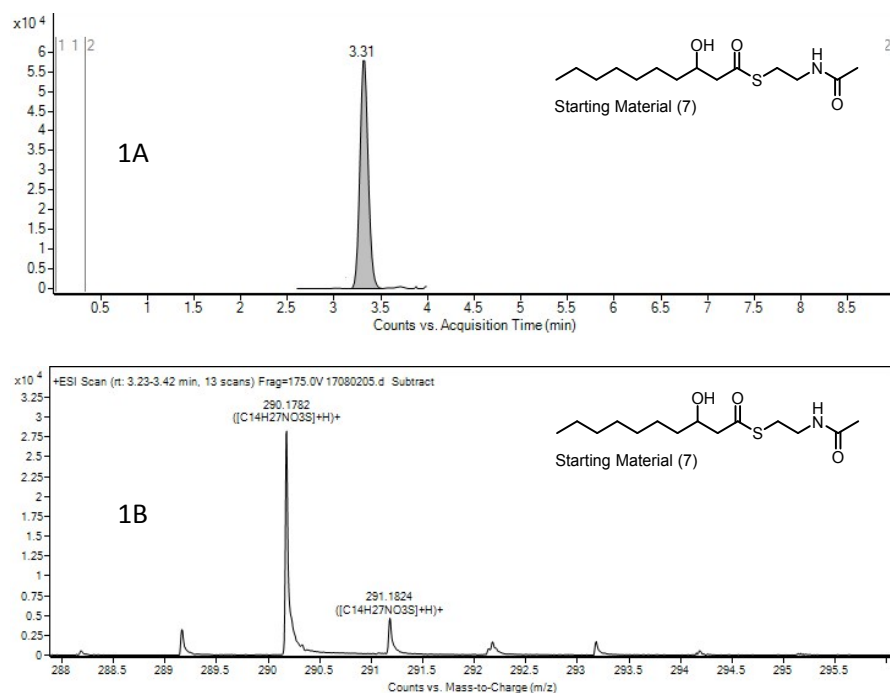
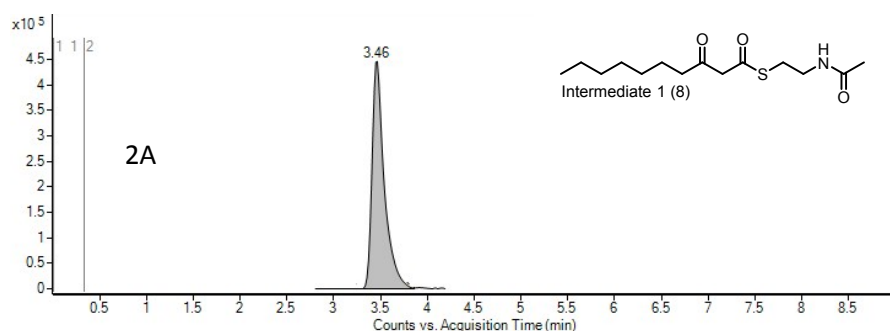


Figure 1 Showing the retention time (1A) and high resolution mass (1B) for the substrate



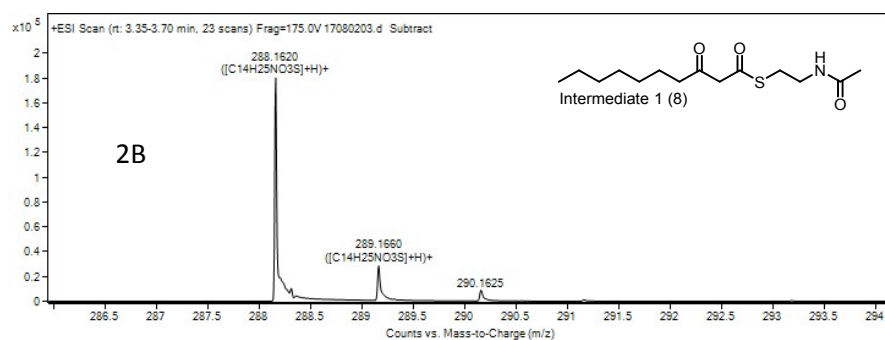


Figure 2 Showing the retention time (2A) and high resolution mass (2B) for the proposed intermediate 1

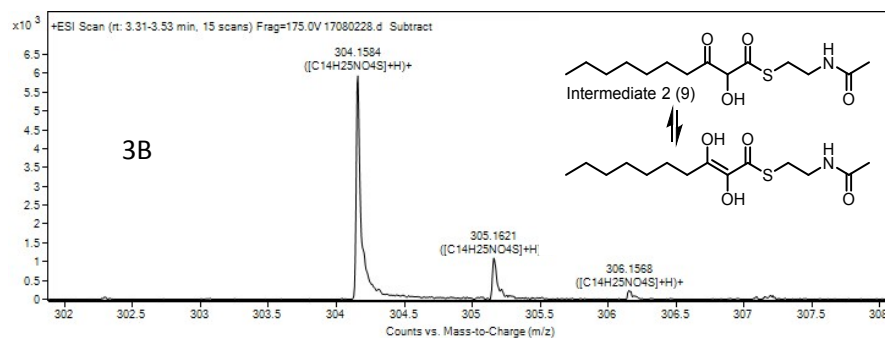
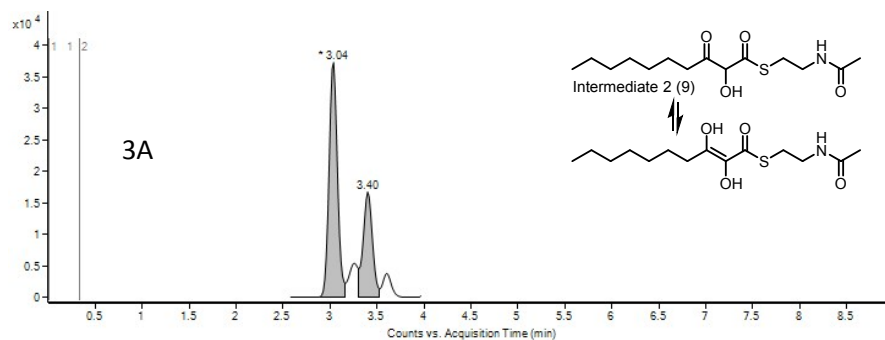
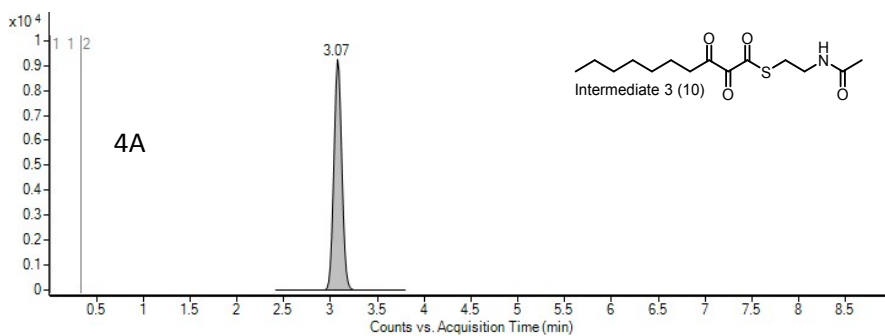


Figure 3 Showing the retention time (3A) and high resolution mass (3B) for the proposed intermediate 2



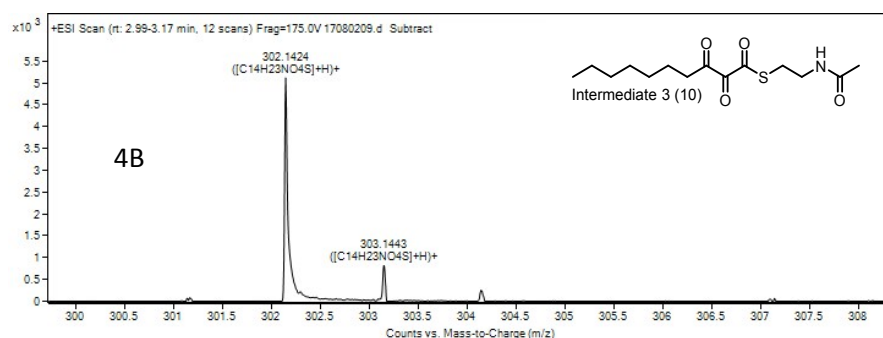


Figure 4 Showing the retention time (4A) and high resolution mass (4B) for the proposed intermediate 3

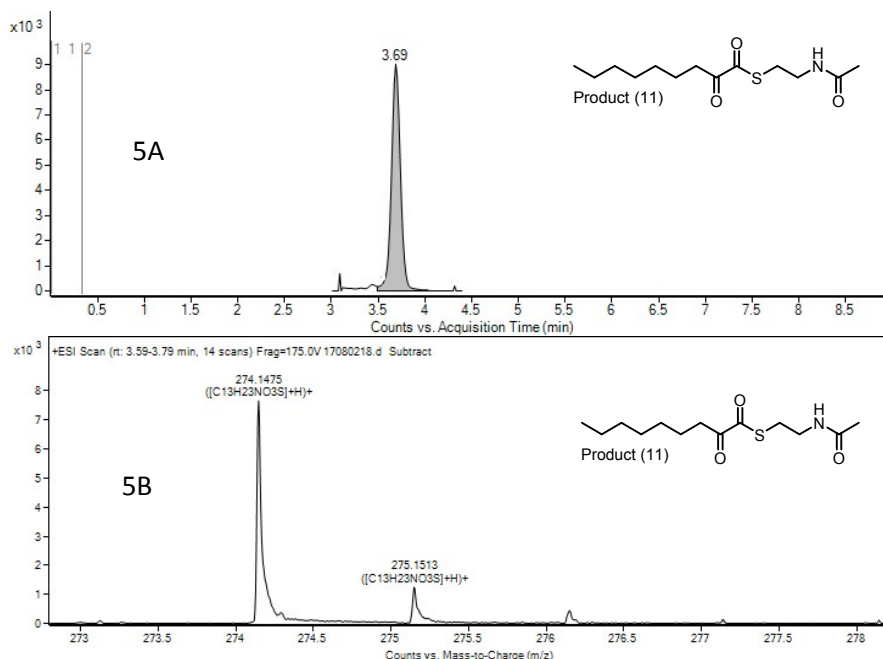
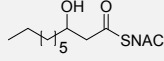
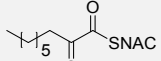
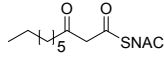
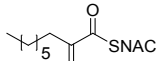
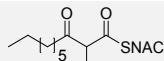
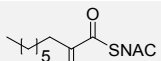
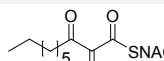
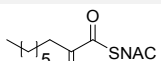


Figure 5 Showing the retention time (5A) and high resolution mass (5B) for the rearranged product

➔ **Rearrangement of Reaction Intermediates:** To four vials containing 10 mL of DCM each, 0.003 mmol of the proposed intermediates was calculated and the mass was weighed out, then added to each vial, followed by the outlined equivalents of DMP. The reaction mixtures were stirred at room temperature for 1 h, before 0.1 mL aliquot was taken and further diluted to 1 mL using DCM, then analysed for the product using Method (i) for the separation of analytes. As outlined in the table all proposed intermediates were found to be converted to the expected rearranged product, with the correct mass and retention time.

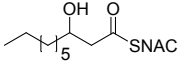
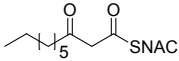
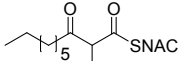
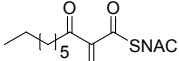
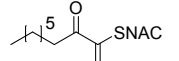
Table 1 Showing a summary of the results from the rearrangement of the reaction intermediates

Substrate	Mass of Substrate/mg	mmol of Substrate	Equiv. of DMP	Product
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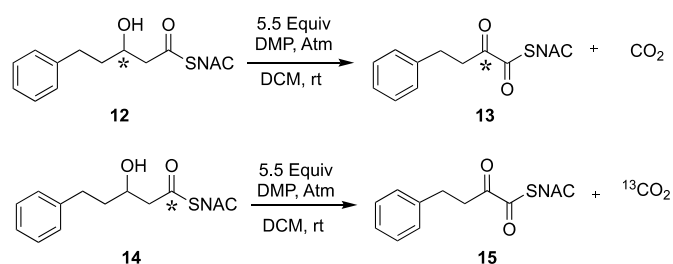
	0.950	0.003	5.5	
7				11
	0.950	0.003	4.4	
8				11
	1.00	0.003	2.2	
9				11
	1.00	0.003	1.1	
10				11

➔ **Effect of DMP Equivalents on the Relative Distribution of Intermediates:** To four vials containing 10 mL of DCM each, compound **7** (6.00 mg, 0.021 mmol) was added to each vial, followed by the outlined equivalents of DMP (1.1, 2.2, 3.3 and 5.5). The DMP sourced from AK Scientific was noted to be 95% pure. As a results a 10% excess of the reagent was used to account for this, leaving a 5% overall excess of the reagent. The reaction mixtures were stirred at room temperature for 1 h, before 0.1 mL aliquot was taken and further diluted to 6 mL using DCM, then analysed for the distribution of intermediates and product using Method (i) for the separation of analytes. The standards were used to confirm the identities of intermediates and products. As outlined in the table, it requires 5.0 equivalents for full conversion, significant amounts of the final product can be observed as early as using 2.2 equivalents of DMP.

Table 2 The effect of DMP equivalents on the relative distribution of products (total equivalents of **7-11** set to 100%)

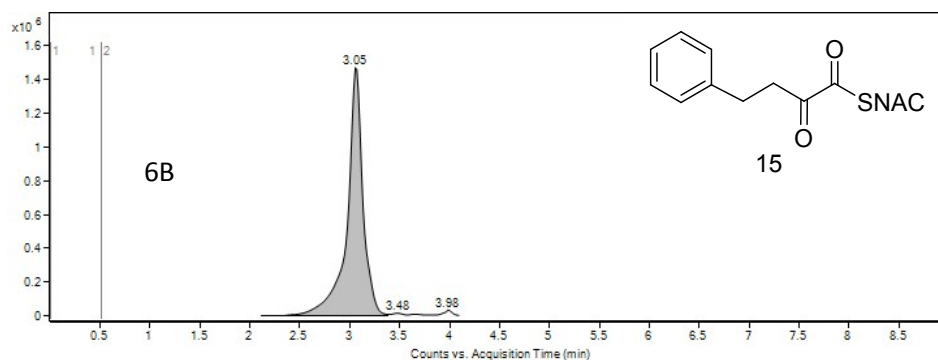
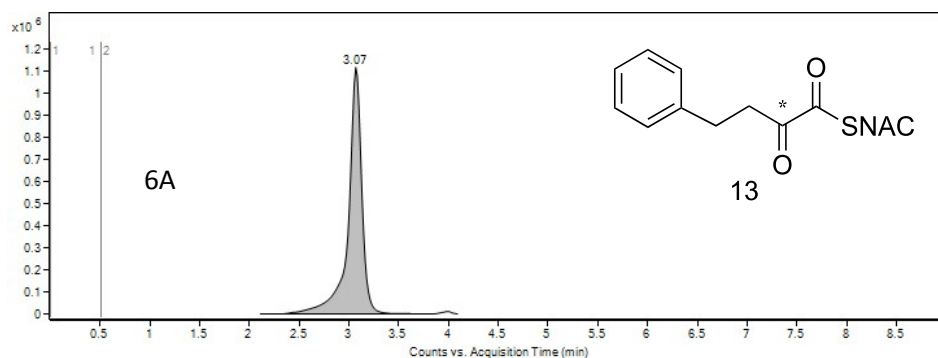
					
7	8	9			
					
10			11		
Equiv. of DMP	% 7	% 8	% 9	% 10	% 11
1.1	0	73	1	1	25
2.2	0	10	0	7	82
3.3	0	1	0	8	91
5.5	0	0	0	1	99

→ ¹³C Labelled Substrate Study



Scheme 1 Showing the transformation of labelled substrates to rearranged products

To a vial containing 10 mL of DCM, labelled compound **12** (6.13 mg, 0.021 mmol) was added, followed by DMP (48.3 mg, 0.114 mmol, 5.5 Equiv). The reaction mixture was stirred at room temperature for 1 h, before 0.1 mL aliquot was taken and further diluted to 6 mL using DCM, then analysed for the product using Method (i) for the separation of analytes. This was then repeated using labelled compound **14**. Based on the results, the label was retained in the product when the ¹³C was at the β-position in the starting material, but was absent in the product when the label was at the thioester carbon in the starting material. This led to the conclusion that the thioester carbon was being extruded in the rearrangement.



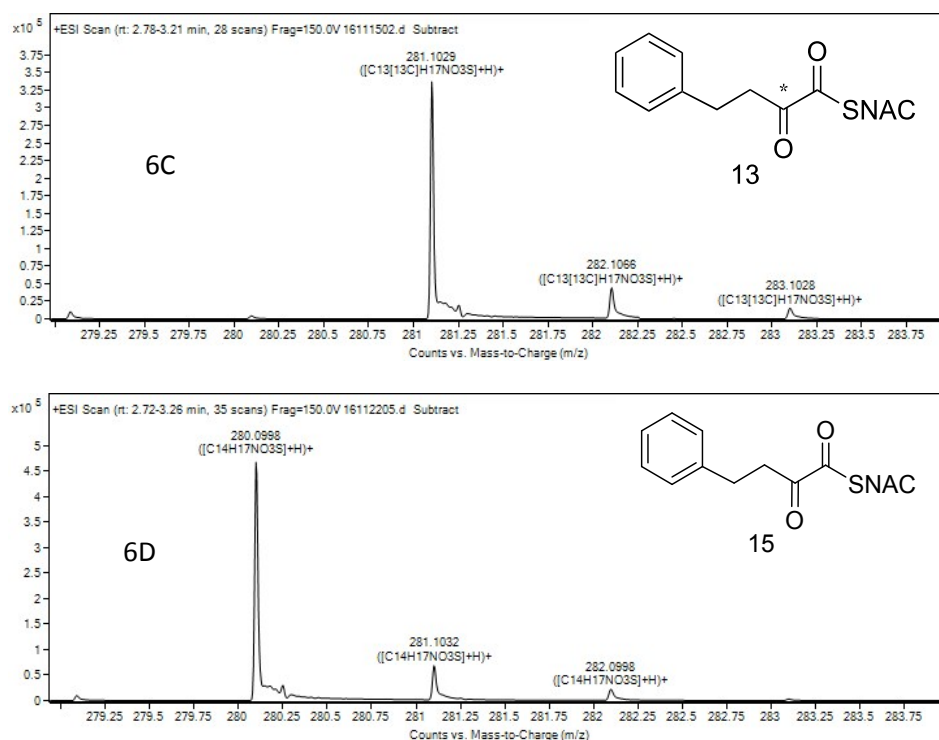
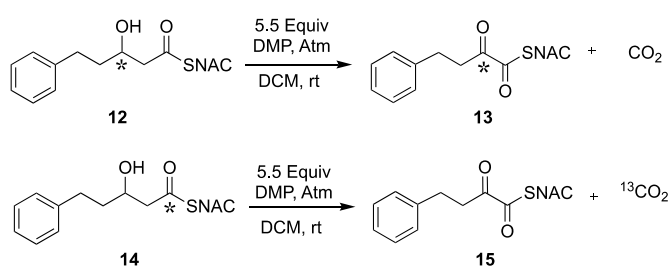


Figure 6 Showing the retention time matching and the mass shift for the labelled and unlabeled products

→ Crossover Experiment with the Labelled Substrates



Scheme 2 Showing the unlabeled and doubly labelled substrates, and corresponding products

To a vial containing 10 mL of DCM, 4.00 mg, 0.014 mmol each of labelled compound **16** and unlabelled **17** was added, followed by 63.0 mg, 0.150 mmol, 5.5 equiv of DMP. The reaction mixture was stirred at room temperature for 1 h, before 0.1 mL aliquot was taken and further diluted to 8 mL using DCM, then analysed for the product using Method (ii) for the separation of analytes. The products observed were singly labelled and doubly labelled as the starting materials were, since there were no scrambling in the labels, this meant that the rearrangement reaction was intramolecular.

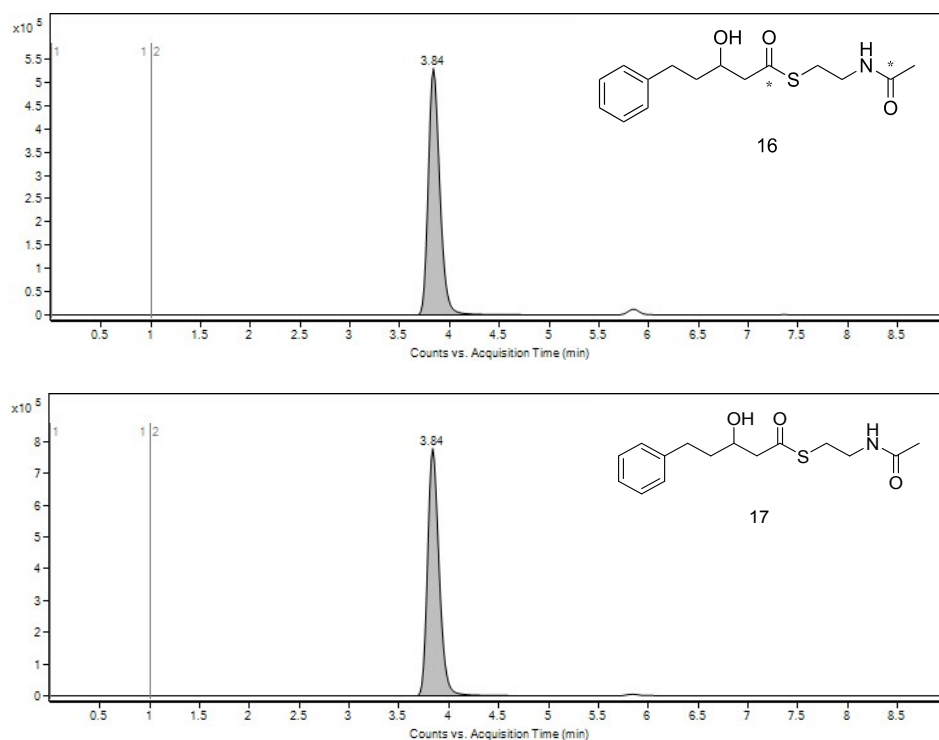


Figure 7 Showing the retention times for the doubly labelled and unlabeled substrates

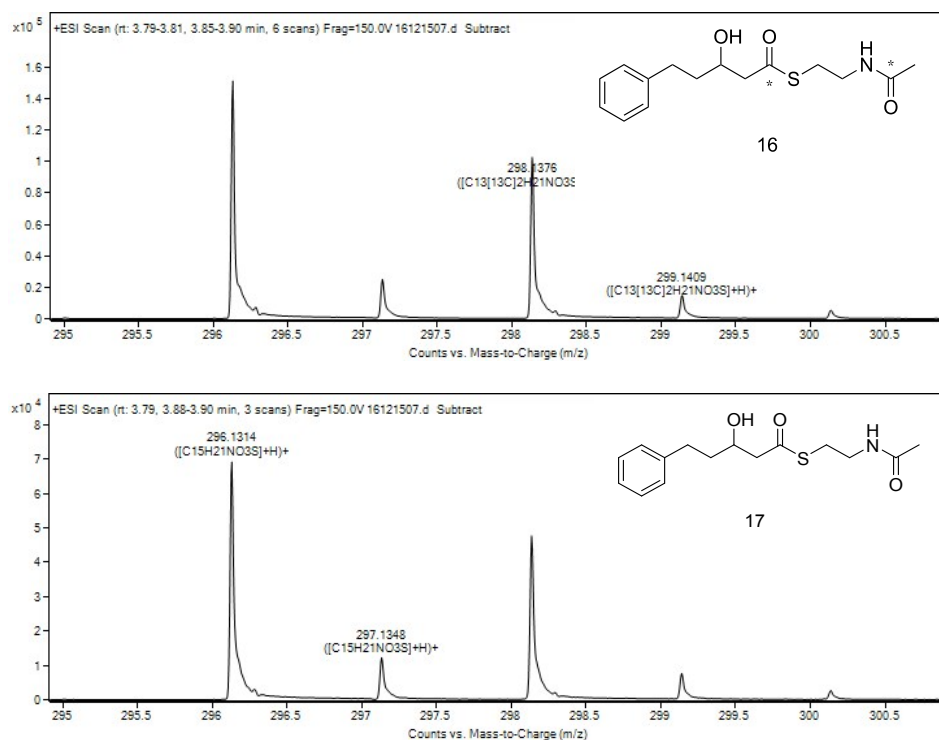


Figure 8 Showing the high resolution mass for the doubly labelled and unlabeled substrates

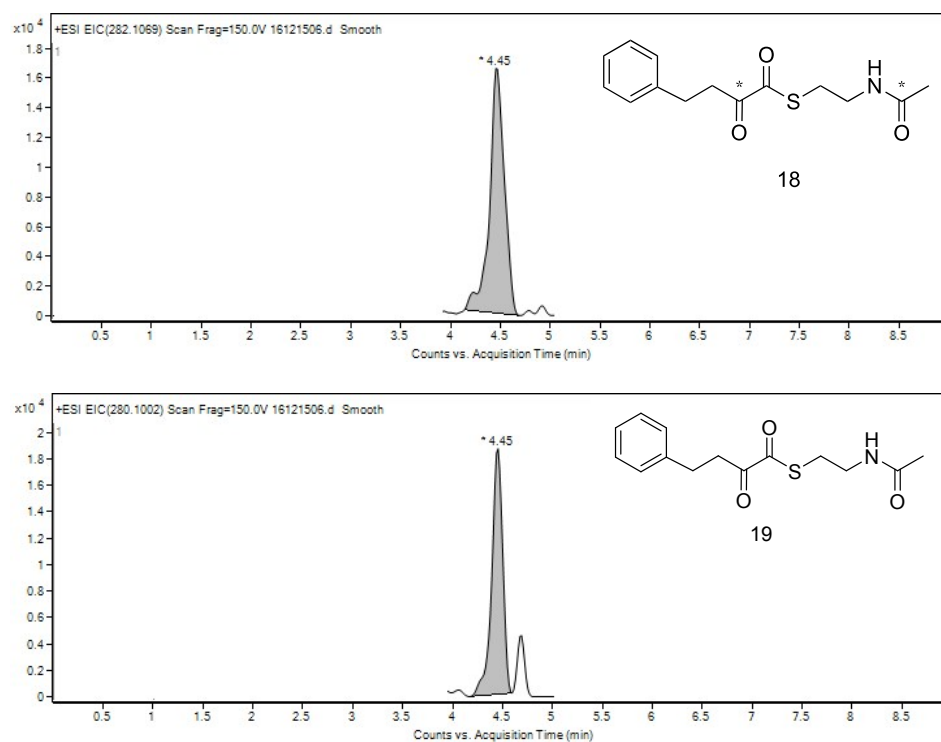


Figure 9 Showing the retention times for the doubly labelled and unlabeled products

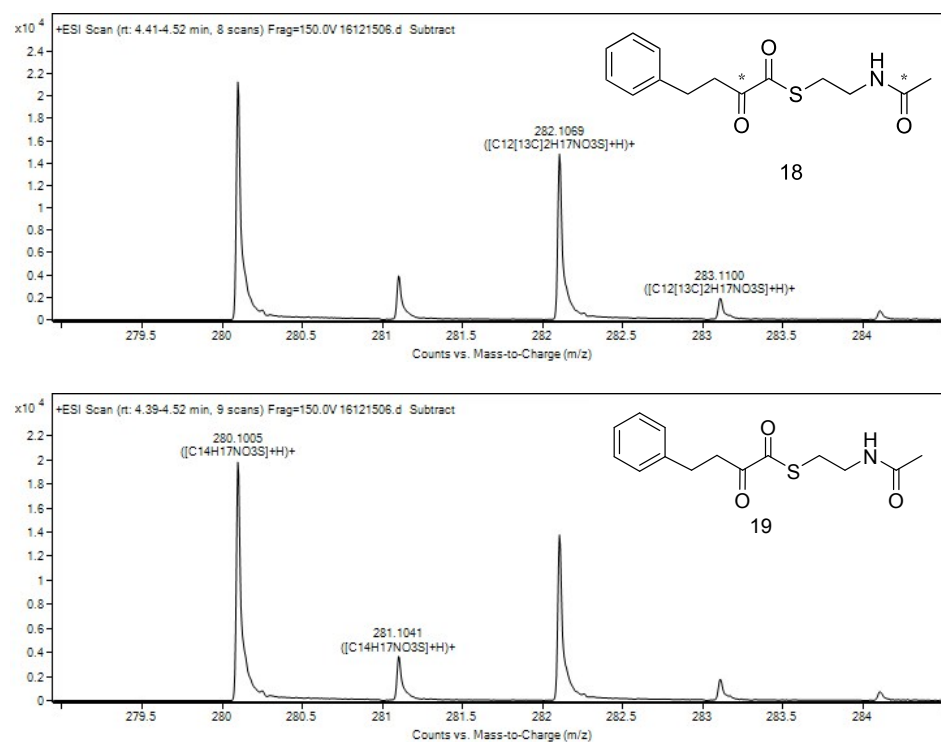


Figure 10 Showing the high resolution mass for the doubly labelled and unlabeled products

➔ Comparison of Thioester vs. Ester vs. Amide, by the Distribution of Intermediates and Product:

To a vial containing 10 mL of DCM, compound **7** (6.0 mg, 0.2 mmol) was added, followed by 5.5 equivalents of DMP. The reaction mixture was stirred at room temperature for 1 h, before 0.1 mL aliquot was taken and further diluted to 6 mL using DCM, then analysed for the distribution of intermediates and products using Method (i) for the separation of analytes. This experiment was repeated using compound **28** and **29** so as to compare the distribution of intermediates and product. It was found that the rearrangement of the esters and amides are much slower than that of the thioester, with the amide being the slowest of the three. Attempts at improving the conversion of the ester and amide to the rearranged product by heating the reaction to 50 °C failed, as no products were found. This may be as a result of thermal degradation of intermediates and product formed.

Table 3 Relative distribution of products (total equivalents of starting material-product set to 100%) for thioesters, esters and amides using LC-MS analysis

$7 = X = S$
 $28 = X = O$
 $29 = X = N$

$11 = X = S$

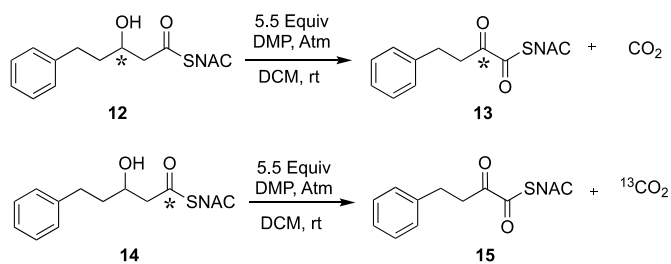
β-keto

α-OH, β-keto

tricarbonyl

X	starting material	B-keto	α-OH-β-keto	tricarbonyl	product
S	0.0	0.0	0.0	0.7	99.3
O	0.0	2.0	34.1	52.3	11.6
NH	2.3	0.0	1.9	95.1	0.7

Analysis on Headspace Gases



Scheme 3 Showing compound (12) producing ¹²CO₂ and retaining the label, while compound (14) produced ¹³CO₂ and extruded the label

To a vial containing 10 mL of DCM, labelled compound **12** (6.13 mg, 0.021 mmol) was added, followed by DMP (48.3 mg, 0.114 mmol, 5.5 Equiv). The reaction mixture was stirred at room temperature for 1 h, before the headspace gas was analysed by Gas Phase IR and GC-MS. This was then repeated using labelled compound **14**. The identity of the gas produce by the reaction was determined to be carbon dioxide. The gas produced from the substrate labelled at the β -position in the starting material showed a gas phase IR pattern consistent with that of $^{12}\text{CO}_2$, however, the gas produced when the label was at the thioester carbon in the starting material had a characteristic shift in its pattern, this shift is consistent with $^{13}\text{CO}_2$. In addition to the gas phase IR analysis, our findings were also supported by the GC-MS analysis of the headspace gas produced by the two reactions to confirm the identity of the gas produced.

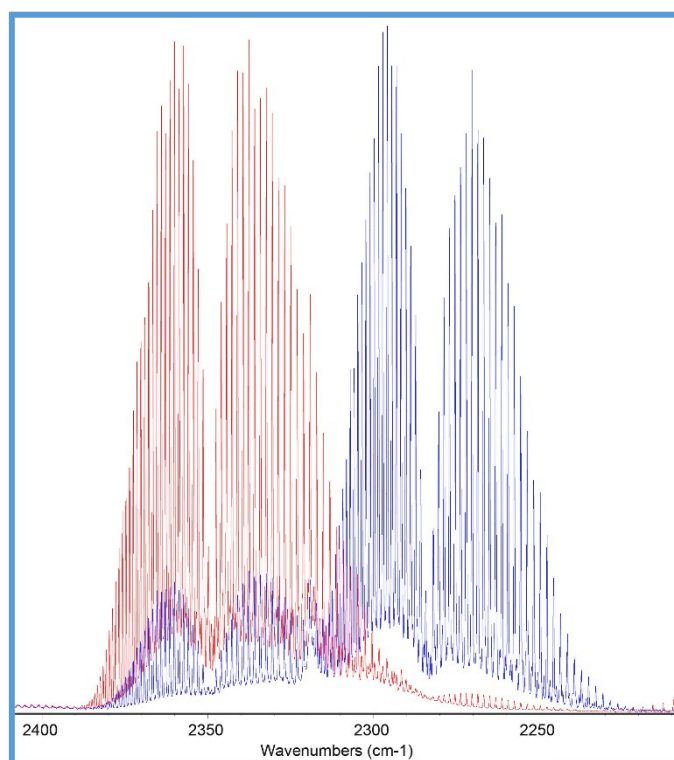


Figure 11 Showing the overlaid results of the gas phase IR for $^{12}\text{CO}_2$ (red trace) vs $^{13}\text{CO}_2$ (blue trace). Residual unlabelled CO_2 in the latter is background from air.

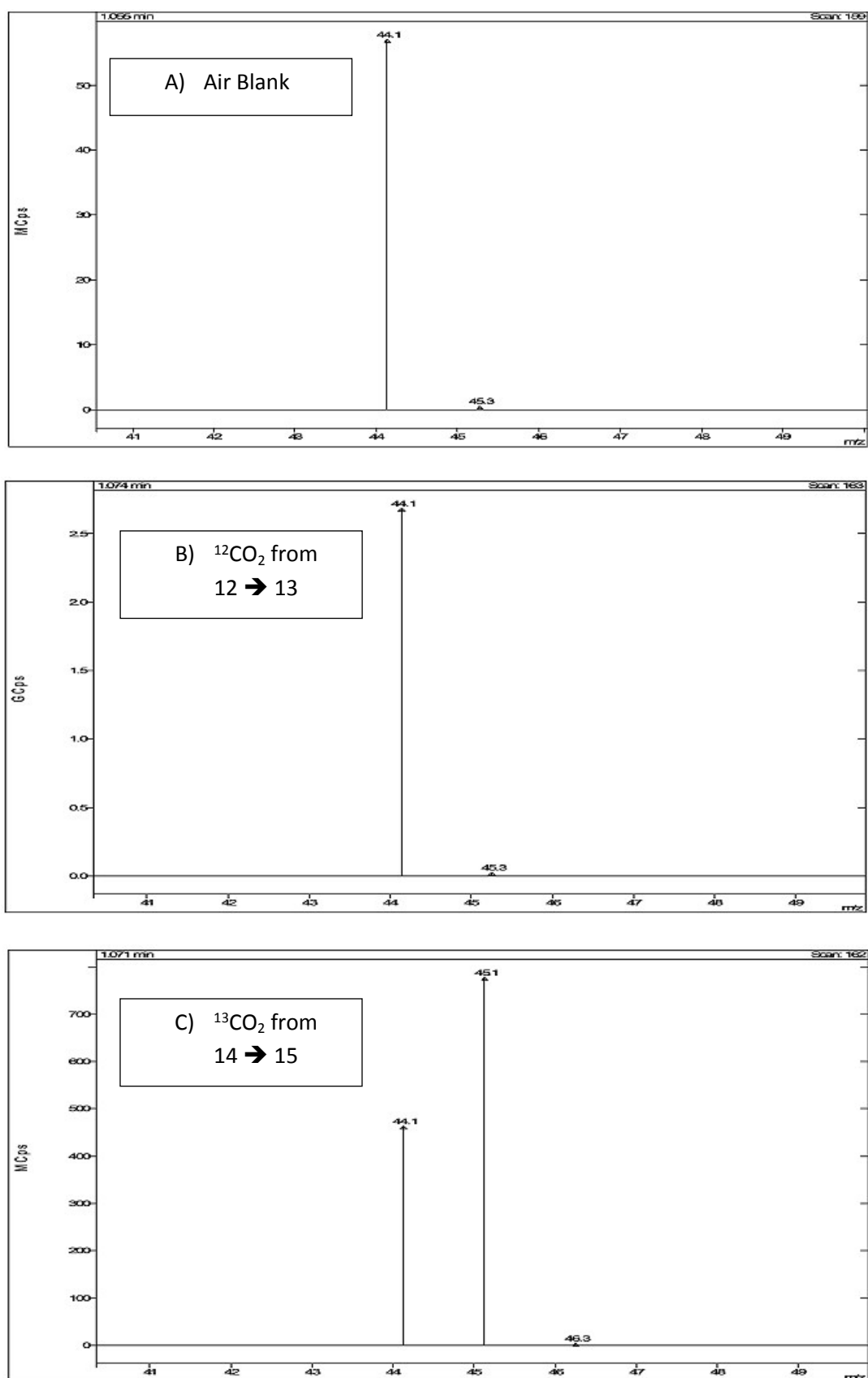
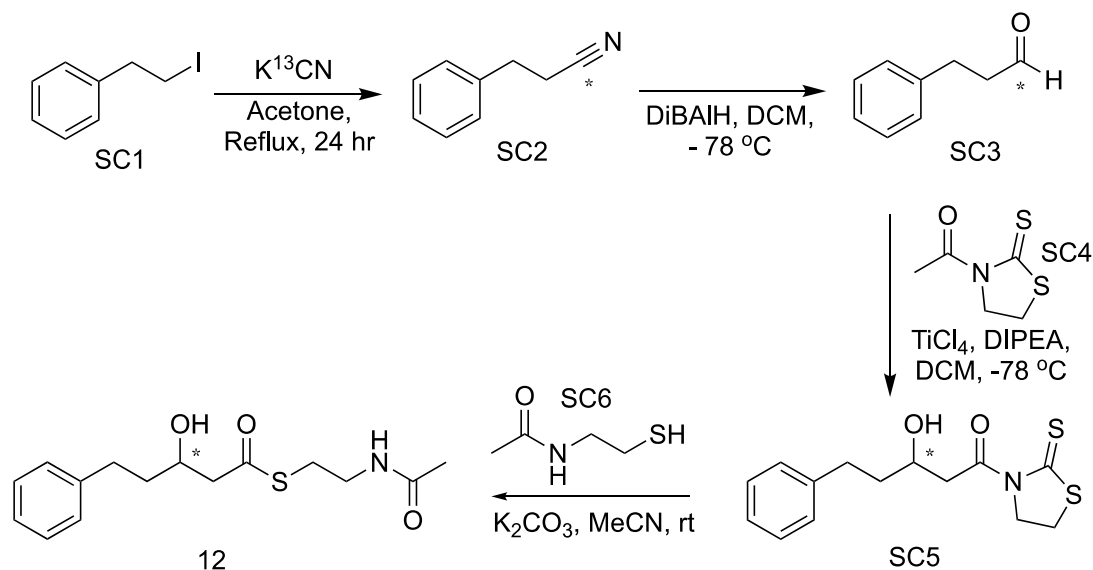


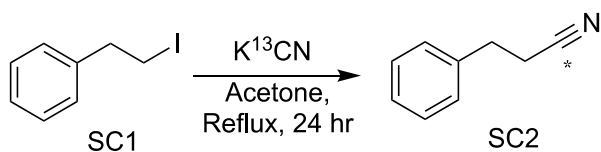
Figure 12 Showing the GCMS results from the analysis of the headspace gases. A) Air Blank, B) $^{12}\text{CO}_2$ from Substrate $12 \rightarrow 13$, C) $^{13}\text{CO}_2$ from substrate $14 \rightarrow 15$

Organic Synthesis

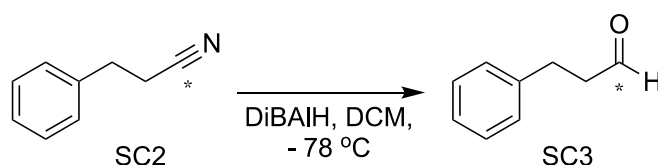
Preparation and Testing of Substrates



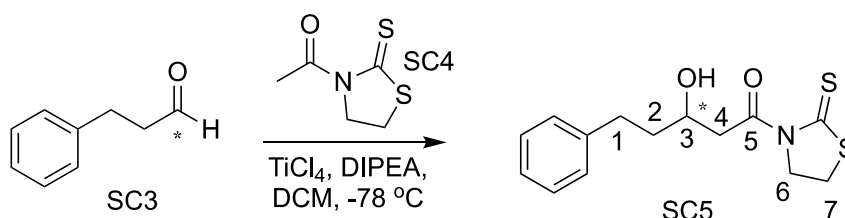
Scheme 4 Showing the preparation of ^{13}C labelled compound 12



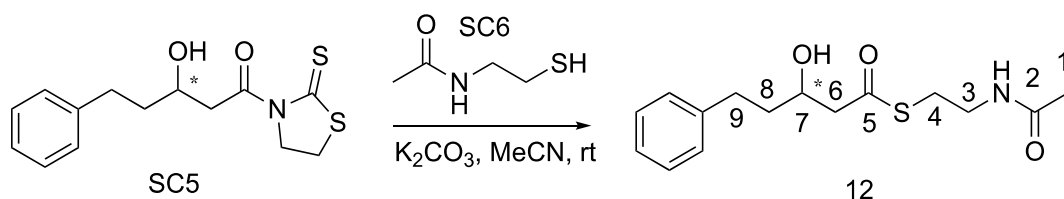
Preparation of SC2. This known compound was prepared by a modified protocol.² In a round bottom flask containing 60 mL of acetone, compound **SC1** (1.87 mL, 12.9 mmol) was added, followed by ^{13}C labelled potassium cyanide (^{13}C , 99%) from Cambridge Isotope Laboratories (0.94 g, 14.2 mmol). The reaction mixture was then refluxed for 24 h then cooled and quenched with saturated sodium bicarbonate (20 mL). The crude reaction mixture was concentrated *in vacuo* then taken up in 20 mL of DCM, then washed with 20 mL of water. The layers were separated and the aqueous layer was extracted with DCM (3 x 15 mL). The combined organic layer was then washed with brine (2 x 15 mL) and dried over sodium sulphate. The solvent was removed *in vacuo*, and the crude product was purified using silica gel (10 % EtOAc in Hexanes (Hex)) to provide compound **SC2** as a yellow oil ($R_f=0.62$, 30 % EtOAc/Hex) 1.45 g, 85 % yield.); IR ($CHCl_3$, cast film) 3064, 3030, 2934, 21.94, 1955, 1874, 1812, 1604, 1496 1455, 1425 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 2H), 7.32 – 7.26 (m, 3H), 2.99 (app q, 2H, $J = 7$ Hz), 2.67 – 2.63 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.1, 128.9, 1.28.3, 129.3, 119.1(^{13}C), 31.6 (d), 19.4 (d); HRMS (EI) calcd for $C_8H_9^{13}CN$ [M^+] 132.0769, found 132.0767.



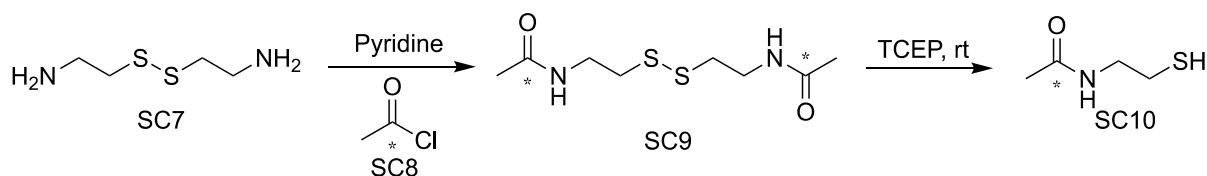
Preparation of SC3. This known compound was prepared by a modified protocol.³ To a flame dried round bottom flask containing 20 mL of dry DCM under argon cooled to $-78\text{ }^\circ\text{C}$, the ^{13}C labelled compound **SC2** (1.00 g, 8.44 mmol) was added followed by DiBAIH(1M) (9.29 mL, 9.29 mmol) then stirred for 2 h. The reaction mixture was then allowed to warm to room temperature then stirred for 4 h, before adding 15 mL of saturated sodium potassium tartrate and allowing to stir for another 30 min. The reaction mixture was diluted with 20 mL of water and the layers were separated. The aqueous layer was extracted with DCM (3 x 15 mL) and the combined organic layer was then washed with brine (2 x 15 mL), then dried over magnesium sulphate. The solvent was removed *in vacuo*, and the crude product was used as is in the following reaction. Crude yield 1.07 g, 94 % ($R_f=0.71$, 30 % EtOAc in Hexanes).



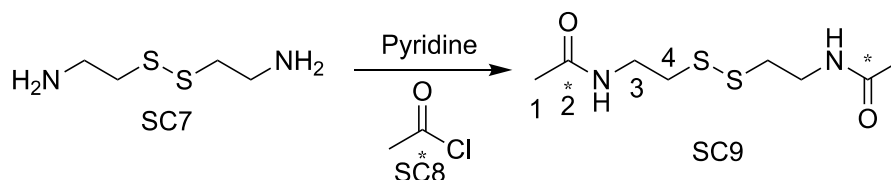
Preparation of SC5. This new compound was synthesized by a method adapted from literature.⁴ To a stirred solution of **SC4** (0.900 g, 5.58 mmol) in dry DCM (25 mL) was added TiCl_4 (1.0 M solution in DCM, 6.14 mL, 6.14 mmol) at $-78\text{ }^\circ\text{C}$ under an argon atmosphere and stirred for 10 min. A solution of diisopropylethylamine (DIPEA) (0.850 g, 6.69 mmol) was added. The reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 1 h. ^{13}C Labelled aldehyde **SC3** (0.830 g, 6.14 mmol) was added to the reaction mixture, which was then stirred for 1.5 h at $-78\text{ }^\circ\text{C}$. The reaction mixture was allowed to warm to room temperature and quenched by the addition of 10 mL saturated ammonium chloride. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4 . The solvent was then removed *in vacuo* and the residue was purified using column chromatography (40 % ethyl acetate in hexanes, R_f value of 0.32 in 50 % ethyl acetate/hexanes) affording the ^{13}C labelled **SC5** as a yellow oil (1.06 g, 64 % yield); IR (CHCl_3 , cast film) 3162, 3023, 2941, 1694, 1495 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.30 – 7.26 (m, 2H, ArH), 7.22 – 7.18 (m, 3H, ArH), 4.60 – 4.56 (m, 2H, H6), 4.24 – 4.21 (m, 1H, H3), 3.53 – 3.50 (m, 1H, H1a), 3.32 – 3.28 (m, 3H, H1b,7), 2.85 – 2.70 (m, 2H, H4), 1.94 – 1.78 (m, 2H, H2); ^{13}C NMR (125 MHz, CDCl_3) δ 201.7 (C8), 174.2 (C5), 141.9 (ArC), 128.5 (ArC), 128.1 (ArC), 126.0 (ArC), 67.4 (^{13}C , C3), 55.8 (C6), 46.1 (d, C4), 38.3 (d, C2), 31.9 (1), 28.5 (C7); HRMS (ESI) calcd for $\text{C}_{13}^{13}\text{CH}_{17}\text{NNaO}_2\text{S}_2$ [$\text{M}+\text{Na}^+$] 319.0626, found 319.0626.



Preparation of 12. This new compound was prepared following a modified literature protocol.⁴ To a flame dried round bottom flask containing 20 mL of dried acetonitrile (ACN) was added **SC5** (0.700 g, 2.36 mmol) followed by K₂CO₃ (1.17 g, 7.09 mmol) at room temperature under an argon atmosphere. Compound **SC6** (0.340 g, 3.07 mmol) was added to the reaction mixture while stirring for 20 min under Argon atmosphere. The solvent was removed *in vacuo*, and the product was taken up in 20 mL of EtOAc and 20 mL of water. The layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting orange residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (35:65) to afford the product **10** as a pale yellow oil (R_f 0.16 EtOAc) 0.44 g, 63 % yield); IR (CHCl₃ Cast Film) 3297, 3085, 2929, 2862, 1687, 1656, 1550 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 7.30 – 7.27 (m, 2H, Ar H), 7.21 – 7.17 (m, 3H, Ar H), 5.73 (br s, 1H, NH), 4.24 – 4.20 (m, 0.5H, H7), 3.94 – 3.92 (m, 0.5H, H7), 3.47 – 3.42 (m, 2H, H3), 3.10 – 3.00 (m, 2H, H4), 2.84 - 2.67 (m, 5H, H6,9, OH), 1.96 (s, 3H, H1), 1.96 – 1.74 (m, 2H, H8); ¹³C NMR (126 MHz CDCl₃) δ 199.4 (C5), 170.6 (C2), 141.6 (ArC), 128.48 (ArC), 128.45 (ArC), 126.0 (ArC), 68.2 (¹³C, C7), 51.1 (d, C6), 39.2 (C9), 38.3 (d, C8), 31.8 (C3), 28.9 (C4), 23.2 (C1); HRMS (ESI) calcd for C₁₄¹³CH₂₁NNaO₃S [M+Na]⁺ 319.1168, found 319.1162.

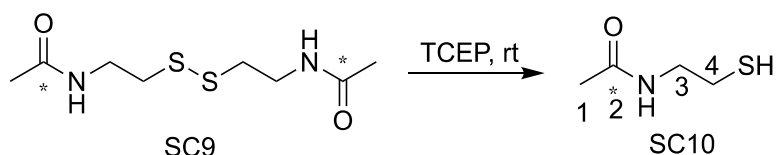


Scheme 5 Showing the preparation of ¹³C labelled compound SC10

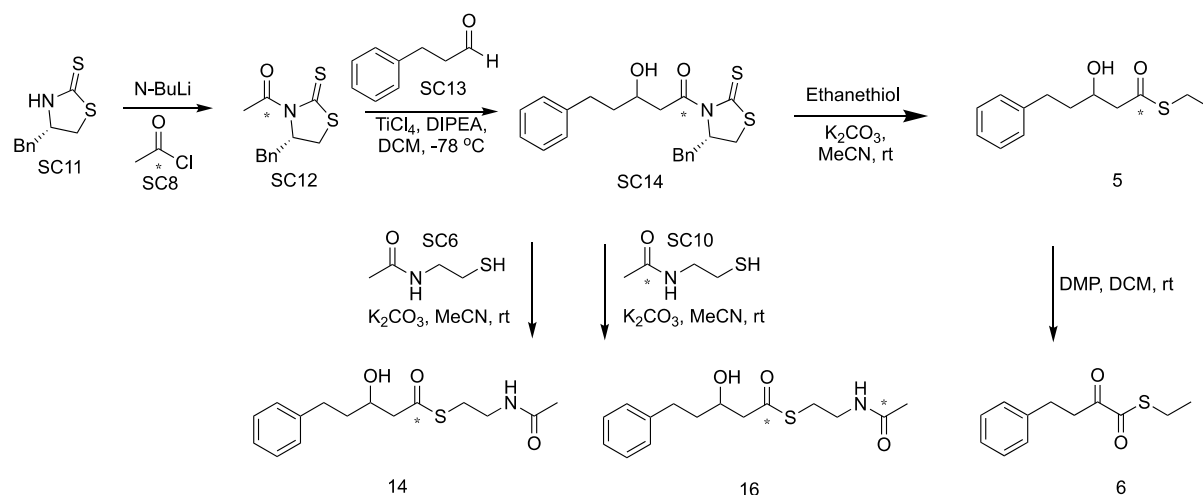


Preparation of SC9. This new compound was prepared by the following protocol. To a flame dried round bottom flask, containing 14 mL of pyridine cooled to 0 °C, **SC7** (0.550 g, 2.45 mmol) was added. After stirring for 5 min ¹³C **SC8** (1.00 g, 12.2 mmol) was added in a dropwise manner to the reaction mixture. The reaction mixture was quenched by addition of 10 mL of water and the 20 mL of DCM. The layers were separated and the aqueous layer was extracted (3 x 20 mL) with DCM. The combined organic layer was then washed with brine (2 x 15 mL) then dried over magnesium

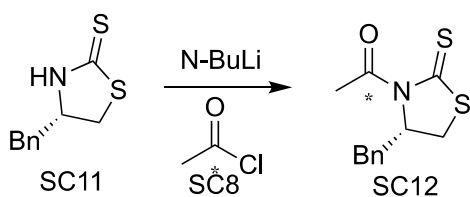
sulphate. The solvent was removed *in vacuo*, and the crude compound was purified on column using a gradient of EtOAc to Acetone, producing a white solid **SC9** ($R_f=0.26$, Acetone) 0.49 g, 83 % yield); IR (CHCl₃ Cast Film) 3292, 3057, 2972, 2864, 1607, 1540 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 6.29 (br s, 2H, NH), 3.59 – 3.55 (m, 4H, H3), 2.83 (t, 4H, J = 6.5 Hz, H4), 2.02 (d, 3H, J = 6 Hz); ¹³C NMR (126 MHz CDCl₃) δ 170.4 (C2), 38.6 (C3), 37.9 (C4), 23.2 (d, C1); HRMS (ESI) calcd for C₆¹³C₂H₁₆N₂NaO₂S₂ [M+Na]⁺ 261.0612, found 261.0614.



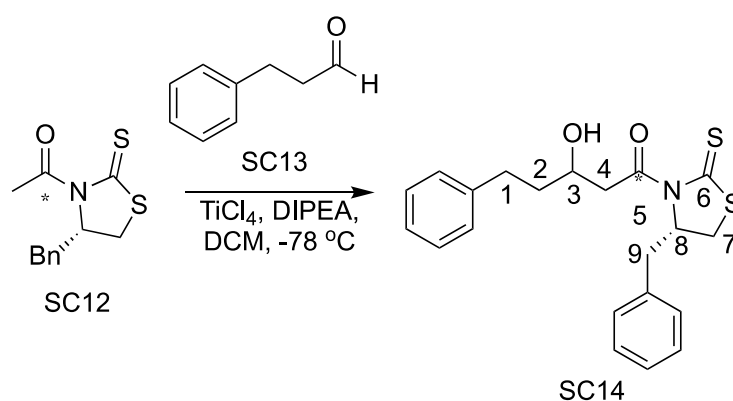
Preparation of SC10. This new compound was prepared by the following protocol. To a round bottom flask compound **SC9** (0.10 g, 0.42 mmol) was added, followed by 20 mL of water, then TCEP (0.24 g, 0.84 mmol) was added under argon. The reaction mixture was stirred for 12 h. The reaction mixture was then extracted with DCM (3 x 20 mL), then combined organic layer was washed with brine (2 x 20 mL) and dried over magnesium sulphate. The solvent was removed *in vacuo* to produce a clear oil which was purified on column using acetone. The product, **SC10** obtained was a clear oil ($R_f=0.88$, acetone) 94.7 mg, 94 % yield); IR (CHCl₃ Cast Film) 3284, 3060, 2979, 2931, 2863, 1607, 1539 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 6.05 (br s, 1H, NH), 3.43 – 3.39 (m, 2H, H3), 2.68 – 2.64 (m, 2H, H4), 1.99 (d, J = 6 Hz, 3H, H1), 1.35 (t, 1H, J = 8.5 Hz, SH); ¹³C NMR (126 MHz CDCl₃) δ 170.1 (C2), 42.5 (C3), 24.7 (C4), 23.2 (d, C1); HRMS (ESI) calcd for C₃¹³CH₉NNaOS [M+Na]⁺ 143.0331, found 143.0331.



Scheme 6 Showing the preparation of ¹³C labelled compound 5, 6, 14 and 16

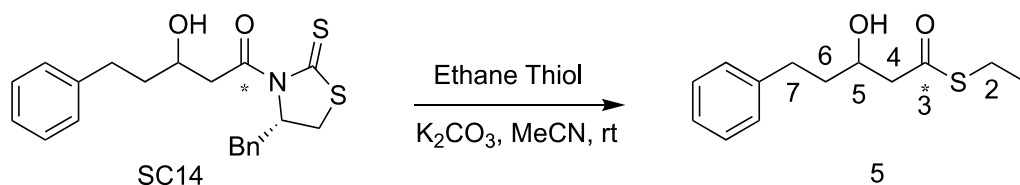


Preparation of SC12. This known compound was prepared by a modified protocol.⁴ To a flame dried round bottom flask compound **SC11** (11.0 g, 57.5 mmol) was dissolved in 250 mL of dry tetrahydrofuran (THF) at 0 °C, under argon. While stirring the mixture, *n*-BuLi (2.5 M in hexane, 25.3 mL, 63.3 mmol) was slowly added and the reaction mixture was allowed to stir for 30 min. The ¹³C labelled **SC8** (4.49 mL, 63.3 mmol) was the slowly added and the reaction mixture was allowed to stir for another hour before quenching with saturated ammonium chloride (40 mL). The layers were separated and the aqueous layer was extracted (3 x 40 mL), then the combined organic layer was washed with water (92 x 40 mL) then brine (2 x 40 mL) and dried over magnesium sulphate. The solvent was removed *in vacuo* and the crude product was purified on column using 10 % EtOAc in Hexanes to provide **SC12** as a yellow solid (*R*_f=0.35, 35 % EtOAc/Hex) 11.52 g, 79 %; IR (CHCl₃, cast film) 3437, 2967, 2932, 1696 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.37 – 7.33 (m, 2H), 7.30 – 7.26 (m, 3H), 5.38 (ddd, *J* = 10.8, 7.0, 3.5 Hz, 1H), 3.38 (dd, *J* = 11.3, 9.5 Hz, 1H), 3.22 (dd, *J* = 13.3, 3.5 Hz, 1H), 3.04 (dd, *J* = 13.5, 10.5 Hz, 1H), 2.89 (d, *J* = 11.5 Hz, 1H), 2.79 (d, *J* = 7.0 Hz); ¹³C NMR (126 MHz, CDCl₃) δ 202.0, 170.7, 136.5, 129.5, 129.0, 127.3, 68.2, 36.7, 31.8 (d), 27.07 (d); [α]_D²⁵ = +248.87 (*c* = 1.0, CHCl₃); HRMS (ESI) calcd for C₁₁¹³CH₁₃NNaOS₂ [M+Na]⁺ 275.0364, found 275.0367.



Preparation of SC14. This new compound was synthesized by a method adapted from literature.⁴ To a stirred solution of ¹³C labelled compound **SC12** (3.20 g, 12.7 mmol) in dry DCM (100 mL) was added TiCl₄ (1.0 M solution in DCM, 13.9 mL, 13.9 mmol) at –78 °C under argon atmosphere and stirred for 10 min. A solution of diisopropylethylamine (DIPEA) (1.97 g, 15.2 mmol) was added. The reaction mixture was stirred at –78 °C for 1 h. Aldehyde **SC13** (1.87 g, 14.0 mmol) was added to the reaction mixture, which was then stirred for 1.5 h at –78 °C. The reaction mixture was allowed to warm to room temperature and quenched by the addition of 10 mL saturated ammonium chloride. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (20 mL) and dried over Na₂SO₄. The solvent was removed *in vacuo* and the residue was purified using column chromatography (30 % ethyl acetate in hexanes *R*_f value of 0.48) affording the ¹³C labelled **SC14** as a yellow oil (4.16 g, 85 % yield); IR (CHCl₃, cast film) 3462, 3061, 3025, 2927, 1651, 1496 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.36 – 7.18 (m, 10H, ArH), 5.42 – 5.38 (m, 1H, H8), 4.16 (m, 1H, H3), 3.67 (dd, *J* = 19.0, 5.0 Hz, 1H, H4a), 3.42 – 3.28 (m, 1H, H7a), 3.23 – 3.13 (m, 2H, H9a,4b), 3.07 – 3.02 (m, 1H, H9b), 2.91 – 2.82 (m, 2H, H7b,1a), 2.77 – 2.71 (m, 1H, H1b), 1.94 – 1.80 (m, 2H, H2); ¹³C NMR (125 MHz, CDCl₃) δ 201.4 (6), 173.7 (C5), 141.8 (ArC), 136.4 (ArC), 129.3 (ArC), 129.0 (ArC), 128.5 (ArC), 128.4 (ArC), 127.3 (ArC), 125.9 (ArC), 125.8 (ArC),

68.3 (C8), 67.6 (C3), 45.9 (d, C4), 37.9 (C2), 36.8 (C9), 31.8 (C7), 31.7 (C1); HRMS (EI) calcd for $C_{20}^{13}CH_{23}NO_2S_2$ [M^+] 386.1204, found 386.1203.

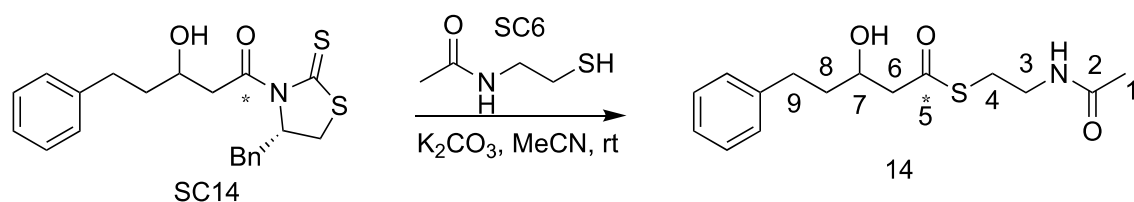


Preparation of 5. This new compound was synthesized by a method adapted from literature.⁴ To a flame dried round bottom flask containing 20 ml of dried ACN was added compound **SC14** (1.50 g, 3.88 mmol) followed by K_2CO_3 (1.61 g, 11.7 mmol) at room temperature under argon atmosphere. Ethanethiol (0.420 mL, 5.83 mmol) was added to the reaction while stirring for 60 min under an argon atmosphere. The solvent was removed in vacuo, and the product was taken up in 20 ml of EtOAc and 20 ml of water. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na_2SO_4 , filtered, and concentrated *in vacuo*. The resulting orange residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (4/1) to afford the product **5** as a pale yellow oil (R_f 0.32 EtOAc) 750 mg, 81 % yield); IR (CHCl₃ Cast Film) 3438, 2930, 2872, 1643 cm^{-1} ; 1H NMR (500 MHz CD₂Cl₂) δ 7.30 – 7.27 (m, 2H, ArH), 7.21 – 7.18 (m, 3H, ArH), 4.09 – 4.04 (m, 1H, H5), 2.93 – 2.88 (m, 2H, H2), 2.84 – 2.67 (m, 5H, H7,4,OH), 1.87 – 1.71 (m, 2H, H6), 1.26 (t, J = 7.5 Hz, 3H, H1); ^{13}C NMR (126 MHz CD₂Cl₂) δ 199.8 ($^{13}C3$), 141.8 (ArC), 128.6 (ArC), 128.5 (ArC), 126.1 (ArC), 68.1 (C5), 50.7 (d, C4), 38.2 (C6), 31.9 (C7), 23.6 (C2), 14.7 (C1); HRMS (ESI) calcd for $C_{12}^{13}CH_{18}NaO_2S$ [$M+Na$]⁺ 262.0953, found 262.0950.

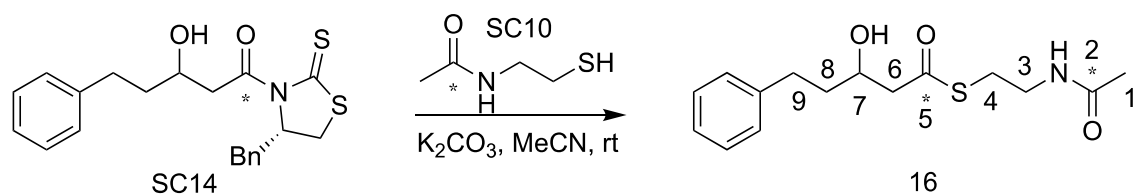


Preparation of 6. This new compound was prepared by the following method. To a round bottom flask was added **5** (70.0 mg, 0.290 mmol) followed by 20 mL of DCM followed by DMP (0.683 mg, 1.61 mmol) while stirring at room temperature for 6 h. The reaction was quenched with 1:1 Na_2SO_3 / $NaHCO_3$ (5 mL). The mixture was extracted with Et₂O (3 x 10 mL), and the combined organic layers were washed with saturated sodium bicarbonate (2 x 5 mL), then dried over brine and Na_2SO_4 , filtered, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (5:1). The product was isolated by flash chromatography to produce **6** as a yellow oil R_f = 0.59 (15 %EtOAc in Hexanes), 45.7 mg, 70 %. IR (CHCl₃ Cast Film) 3086, 3063, 2956, 2926, 2853, 1723, 1667 cm^{-1} ; 1H NMR (700 MHz CDCl₃) δ 7.30 – 7.26 (m, 2H, ArH), 7.22 – 7.20 (m, 3H, ArH), 3.15 (t, J = 7.5 Hz, 2H, H5), 2.97 – 2.91 (m, 4H, H6,2), 1.29 (t, J = 7.5 Hz, 3H, H1); ^{13}C NMR (126 MHz CDCl₃) δ 194.8 (C4), 191.2 (C3), 140.1 (ArC), 128.6 (ArC),

128.4 (ArC), 126.4 (ArC), 38.2 (C5), 29.0 (C6), 23.1 (C2), 14.1 (C1); HRMS (ESI) calcd for $C_{12}H_{14}NaO_2S$ $[M+Na]^+$ 245.0607, found 245.0615.

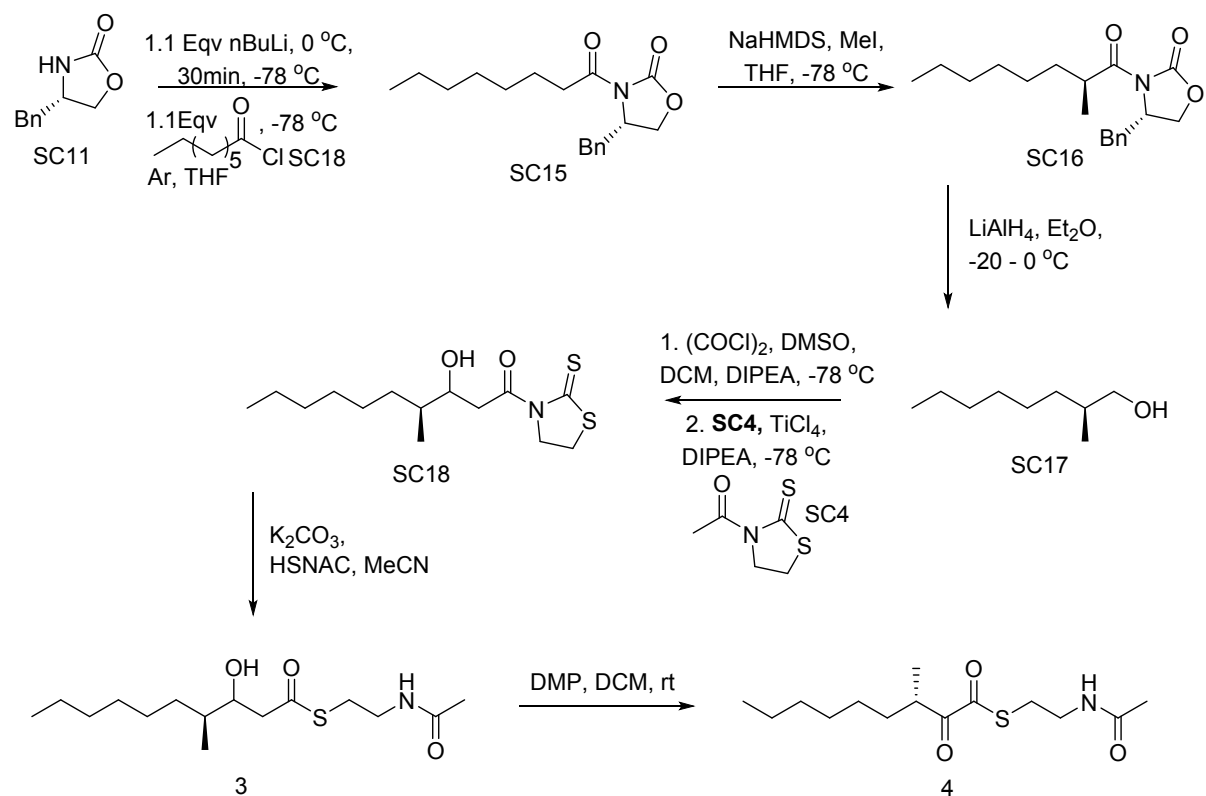


Preparation of 14. This new compound was synthesized by a method adapted from literature.⁴ To a flame dried round bottom flask containing 20 mL of dried ACN was added compound **SC14** (0.600 g, 1.56 mmol) followed by K₂CO₃ (0.650 g, 4.67 mmol) at room temperature under argon atmosphere. Compound **SC6** (0.370 g, 3.11 mmol) was added to the reaction mixture while stirring for 20 min under argon atmosphere. After stirring, the solvent was removed *in vacuo*, and the product was taken up in 20 mL of EtOAc and 20 mL of water. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting orange residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (1:1) to afford the product **14** as a pale yellow oil (*R*_f 0.19 EtOAc) 0.42 g, 90 % yield); IR (CHCl₃ Cast Film) 3294, 3085, 2927, 1652, 1550 cm⁻¹; ¹H NMR (500 MHz CD₂Cl₂) δ 7.29 – 7.26 (m, 2H, ArH), 7.21 – 7.16 (m, 3H, ArH), 5.79 (br s, 1H, NH), 4.05 – 4.03 (m, 1H, H7), 3.43 – 3.39 (m, 2H, H3), 3.03 – 3.00 (m, 2H, H4), 2.79 – 2.67 (m, 5H, H6,H9, OH), 1.91 (s, 3H, H1), 1.80 – 1.73 (m, 2H, H8); ¹³C NMR (126 MHz CD₂Cl₂) δ 199.3 (C5), 170.5 (C2), 142.3 (ArC), 128.8 (ArC), 128.7 (ArC), 126.2 (ArC), 68.4 (C7), 51.8 (d, C6), 39.3 (C9), 38.8 (C8), 32.1 (C3), 29.4 (C4), 23.4 (C1); HRMS (ESI) calcd for $C_{14}^{13}CH_{21}NNaO_3S$ $[M+Na]^+$ 319.1168, found 319.1164.

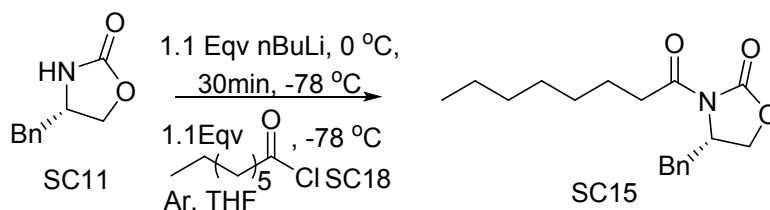


Preparation of 16. This new compound was synthesized by a method adapted from literature.⁴ To a flame dried round bottom flask containing 20 mL of dried ACN was added compound **SC14** (0.15 g, 0.51 mmol) followed by K₂CO₃ (0.21 g, 1.5 mmol) at room temperature under argon atmosphere. Compound **SC10** (0.09 g, 0.76 mmol) was added to the reaction mixture while stirring for 20 min under argon atmosphere. After stirring, the solvent was removed *in vacuo*, and the product was taken up in 20 mL of EtOAc and 20 mL of water. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting orange residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (1:1) to afford the product **16** as a pale yellow oil (*R*_f 0.15 EtOAc) 139 mg, 92 % yield); IR (CHCl₃ Cast Film) 3296, 3061, 2930, 1687, 1612

cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 7.30 – 7.26 (m, 2H, ArH), 7.20 – 7.18 (m, 3H, ArH), 5.77 (br s, 1H, NH), 4.22 (m, 0.5H, H7), 3.93 (m, 0.5H, H7), 3.48 – 3.42 (m, 2H, H3), 3.07 – 3.00 (m, 2H, H4), 2.84 – 2.67 (m, 5H, H6,9,OH), 1.96 (d, *J* = 6.0Hz, 3H, H1), 1.86 – 1.74 (m, 2H, H8); ¹³C NMR (126 MHz CDCl₃) δ 199.4 (C5), 170.5 (C2), 141.6 (ArC), 128.5 (ArC), 128.4 (ArC), 126.0 (ArC), 68.0 (C7), 51.0 (d, C6), 39.3 (C9), 38.5 (d, C8), 32.6 (C3), 28.9 (C4), 23.5 (d, C1); HRMS (ESI) calcd for C₁₃¹³C₂H₂₁NNaO₃S [M+Na]⁺ 320.1201, found 320.1202.

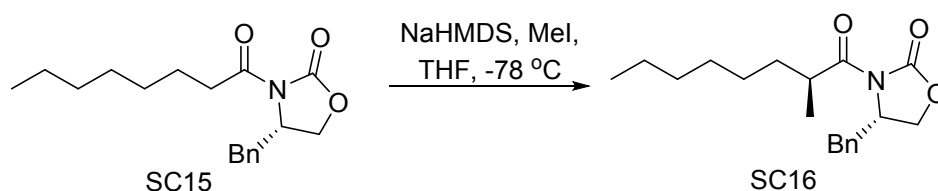


Scheme 7 Showing the preparation of substrate 3 and compound 4

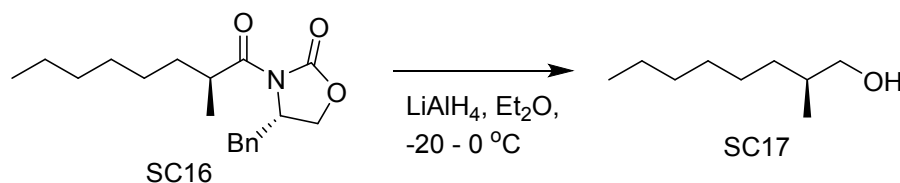


Preparation of SC15. This known compound was synthesized previously in literature and was repeated.⁵ Compound **SC11** (0.500 g, 2.82 mmol) was dissolved in 20 mL of dry THF and cooled to -78 °C using a dry ice/acetone bath. *n*-BuLi (1.32 mL, 2.14 M) was then added dropwise and the reaction mixture was maintained at -78 °C for 15 min. Octanoyl chloride (0.530 mL, 3.10 mmol) was added via syringe and the reaction mixture was allowed to warm over 16 h. The solution was quenched with H₂O (10 mL) and the bulk of the THF was removed *in vacuo*. The aqueous was then extracted with DCM (3 x 10 mL) and the organic layers were pooled, washed with brine and dried

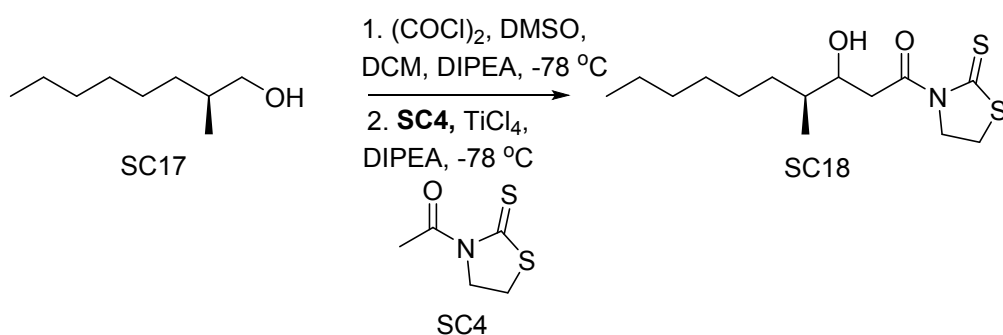
over Na₂SO₄. The crude was concentrated and purified using flash column chromatography (2:1 hexanes/EtOAc), R_f 0.65; to produce **SC15** as a clear oil, yield (0.723 g, 86 %); [α]_D²⁵ = 43.87 (*c* = 1.0, CHCl₃); IR (CHCl₃, cast): 2955, 2928, 2857, 1785, 1703 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.35 – 7.31 (m, 2H), 7.29 – 7.26 (m, 1H), 7.22 – 7.19 (m, 2H), 4.67 (ddt, *J* = 9.7, 7.5, 3.2 Hz, 1H), 4.22 – 4.13 (m, 2H), 3.30 (dd, *J* = 13.4, 3.3 Hz, 1H), 3.01 – 2.85 (m, 2H), 2.77 (dd, *J* = 13.4, 9.6 Hz, 1H), 1.76 – 1.60 (m, 2H), 1.42 – 1.23 (m, 8H), 0.88 (t, *J* = 7.1, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 173.5, 153.5, 135.4, 129.5, 129.0, 127.4, 66.2, 55.2, 38.0, 35.6, 31.7, 29.1, 29.1, 24.8, 22.7, 14.1; HRMS (ES) Calcd for C₁₈N₂O₃ ([M+H]⁺) 304.1907, found 304.1909.



Preparation of SC16. This known compound **SC16** has been synthesized previously and the method was used for this synthesis.⁵ A solution of **SC15** (0.500 g, 1.65 mmol) in 10 mL of dry THF was blanketed with argon and cooled to –78 °C. NaHMDS (1.82 mL, 1 M) was added dropwise via syringe and the reaction mixture was spun at –78 °C for 30 min before methyl iodide (0.31 mL, 4.9 mmol) was added. The reaction mixture warmed to room temperature over 16 h and was quenched with saturated NH₄Cl. The THF was removed *in vacuo* and replaced with 10 mL of EtOAc. The layers were separated and the aqueous was extracted with EtOAc (3 x 10 mL). The organic layers were then pooled, washed with brine and dried over Na₂SO₄. The reaction mixture was concentrated *in vacuo* and purified by column flash chromatography (6:1 Hexanes/EtOAc), R_f 0.45; to produce **SC16** as a pale yellow oil, yield (2.414 g, 92 %); [α]_D²⁵ = 60.77 (*c* = 1.0, CHCl₃); IR (CHCl₃, cast): 2957, 2929, 2858, 1783, 1699, 1455, 1386, 1350 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃) 7.37 – 7.29 (m, 2H), 7.31 – 7.23 (m, 1H), 7.24 – 7.18 (m, 2H), 4.68 (ddt, *J* = 9.6, 7.4, 3.2 Hz, 1H), 4.23 – 4.13 (m, 2H), 3.71 (h, *J* = 6.8 Hz, 1H), 3.27 (dd, *J* = 13.4, 3.3 Hz, 1H), 2.77 (dd, *J* = 13.4, 9.6 Hz, 1H), 1.77 – 1.70 (m, 1H), 1.46 – 1.37 (m, 1H), 1.33 – 1.23 (m, 8H), 1.22 (d, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 1H); ¹³C-NMR (125 MHz, CDCl₃) δ 177.4, 153.1, 135.4, 129.5, 128.9, 127.3, 66.0, 55.4, 38.0, 37.8, 33.5, 31.7, 29.3, 27.3, 22.6, 17.4, 14.1; HRMS (ES) Calcd for C₁₉H₂₇NO₃Na [M+Na]⁺ 340.1883, found 340.1886.

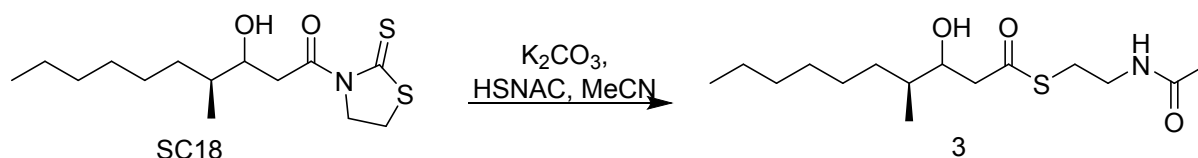


Preparation of SC17. This known compound **SC17** has been synthesized previously.⁵ Absolute EtOH (1.06 mL, 18.2 mmol) and **SC16** (4.12 g, 15.1 mmol) were dissolved in dry diethyl ether (120 mL) and cooled to 0 °C using an ice-water bath. LiBH₄ (9.12 mL, 2.00 M) was added dropwise via syringe and the temperature was maintained at 0 °C for 1.5 h. The reaction mixture was quenched with 1M NaOH (60 mL) and stirred until the solution was clear. The layers were separated and the aqueous was extracted with ether (3 x 60 mL). The organic layers were pooled, washed with brine and dried over anhydrous Na₂SO₄. The organic solvent was removed *in vacuo* to yield a crude colourless oil. Compound **SC17** was then purified by flash chromatography (9:1 Hexanes/EtOAc), R_f 0.20; to produce a clear oil, yield (2.41 g, 92 %); [α]_D²⁵ = −11.14 (c = 1.0, CHCl₃); IR (CHCl₃, cast): 3330, 2957, 2925, 2873, 2857, 1466, 1379 cm^{−1}; ¹H NMR (500 MHz, CDCl₃) δ 3.49 (dd, *J* = 10.5, 5.8 Hz, 1H), 3.40 (dd, *J* = 10.5, 6.6 Hz, 1H), 1.64 – 1.55 (m, 1H), 1.42 – 1.32 (m, 1H), 1.32 – 1.20 (m, 8H), 1.13 – 1.03 (m, 1H) 0.90 (d, *J* = 6.7 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 68.4, 35.8, 33.2, 31.9, 29.6, 27.0, 22.7, 16.6, 14.1; HRMS (ES) Calcd for C₉H₁₈ [M – H₂O]⁺ 126.1409, found 126.1407.

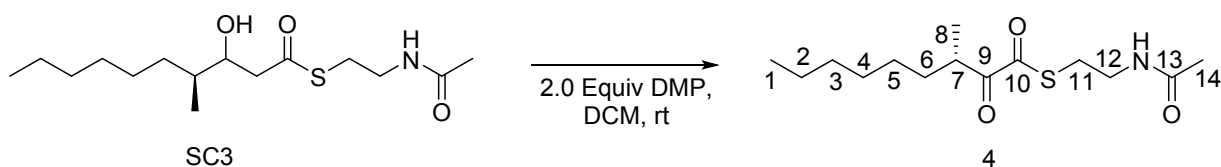


Preparation of SC18. This known compound was prepared following literature protocol.⁵ Oxalyl chloride (2.08 mmol, 0.180 mL) was cooled to −78 °C and a solution of DMSO (dried over 4Å MS, 2.77 mmol, 0.200 mL) in 10 mL dry DCM was added dropwise. After 30 min at −78 °C, a solution of **SC17** (100 mg, 0.692 mmol) in 1.5 mL of DCM was added dropwise and spun at −78 °C for another 20 min. Diisopropylethylamine (DIPEA; dried over 4Å MS, 1.81 mL, 10.4 mmol) was added dropwise and the temperature was maintained for 20 min then warmed to −50 °C for 60 min. The reaction mixture was quenched with 10 mL saturated NH₄Cl and allowed to warm to room temperature. The layers were separated and the organic layer was washed with 10 mL of saturated NaHCO₃ and brine before drying on Na₂SO₄. The solvent was removed and the crude aldehyde was used immediately in the next step. A solution of the freshly prepared crude aldehyde (74.3 mg, 0.461 mmol) in 5 mL of DCM was charged with TiCl₄ (1.0 M, 0.51 mL) at −78 °C. After 30 min at −78 °C, DIPEA (80 μL, 0.46 mmol) was added dropwise and a colour change was noted from bright orange-red to a deep red-brown. After 1 h at −78 °C, the reaction mixture was quenched with 10 mL saturated NH₄Cl and allowed to warm to room temperature. Separation of the layers and extraction of the aqueous layer with DCM (3 x 10 mL) led to the organic layers being pooled, washed with brine and dried on Na₂SO₄. The reaction mixture was concentrated *in vacuo* and subjected to flash column chromatography (3:1 Hexanes/EtOAc), R_f 0.17; to produce **SC18** as a yellow oil, yield (750 mg, 34 % over two steps). IR (CHCl₃, cast film): 3518, 2956, 2926, 1697 cm^{−1}; ¹H-NMR (500 MHz, CDCl₃): Major diastereomer (anti): δ 4.66 – 4.54 (m, 2H), 4.06 – 4.01 (m, 1H), 3.50 – 3.25 (m, 4H), 2.69 (br d, 1H, *J* = 4.0 Hz), 1.70 – 1.60

(m, 1H), 1.52 – 1.11 (m, 10H), 0.93 (d, 3H, J = 6.8 Hz), 0.90 – 0.86 (t, 3H, J = 6.9 Hz); Minor diastereomer (syn): δ 4.66 – 4.54 (m, 2H), 3.98 (m, 1H), 3.50 – 3.25 (m, 2H), 2.82 (br d, 1H, J = 4.0 Hz), 1.70 – 1.60 (m, 1H), 1.52 – 1.11 (m, 10H), 0.93 (d, 3H, J = 6.8 Hz), 0.90 – 0.86 (t, 3H, J = 6.9 Hz); ^{13}C -NMR (125 MHz, CDCl_3): Major diastereomer (anti): δ 201.9, 174.8, 71.4, 55.8, 43.4, 38.2, 32.9, 31.9, 29.6, 28.4, 27.3, 22.7, 14.5, 14.2; Minor diastereomer (syn): δ ; 202.0, 174.9, 72.0, 55.8, 42.4, 38.3, 32.4, 31.9, 29.6, 28.4, 27.2, 22.7, 15.1, 14.2; HRMS (ES) Calcd for $\text{C}_{14}\text{H}_{25}\text{NO}_2\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 326.1219, found 326.1220.

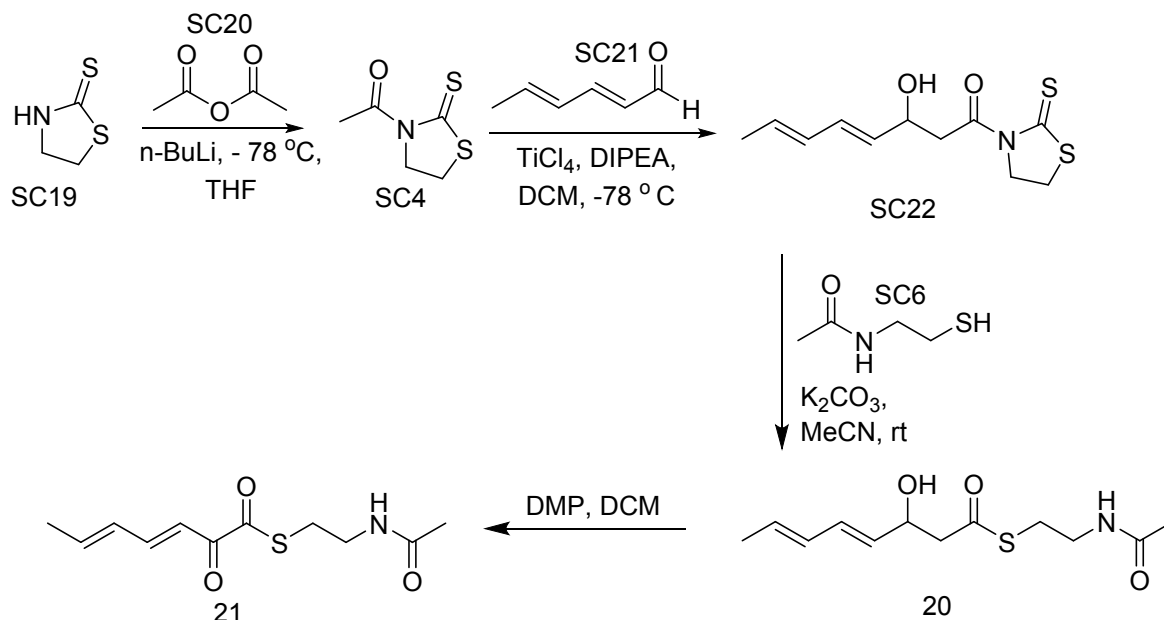


Preparation of 3. This known compound was prepared following a literature protocol.⁵ To a stirred solution of **SC18** (0.400 g, 1.31 mmol) in 10 mL MeCN was added K_2CO_3 (0.760 g, 4.61 mmol) and N-acetylcysteamine (0.190 g, 1.58 mmol). The reaction mixture was stirred until the yellow color disappeared (40 min). The solvent was removed *in vacuo* and the residue was purified using flash column chromatography (50 % ethyl acetate in hexanes), R_f 0.08 (50 % ethyl acetate in hexanes); to produce **3** as a clear oil, yield (0.267 g, 88 %); IR (CHCl_3 , cast): 3302, 2958, 2927, 2857, 1659, 1553 cm^{-1} ; ^1H -NMR (500 MHz, CDCl_3) δ 5.96 – 5.82 (m, 1H), 3.98 (m, J = 8.9, 4.3, 3.5 Hz, 1H, Major Diastereomer), 3.92 (ddd, J = 8.8, 5.5, 3.2 Hz, 1H, Minor Diastereomer), 3.51 – 3.37 (m, 2H), 3.10 – 2.97 (m, 2H), 2.76 – 2.63 (m, 2H), 1.96 (s, 3H), 1.63 – 1.07 (m, 11H), 0.90 – 0.87 (m, 6H, H1); ^{13}C NMR (126 MHz, CDCl_3): Major diastereomer (anti): δ 200.5, 170.5, 72.0, 48.6, 39.4, 38.4, 32.8, 31.9, 29.6, 28.9, 27.2, 23.2, 22.7, 14.2, 14.1; Minor diastereomer (syn): δ 200.0, 170.5, 72.7, 47.7, 39.4, 38.4, 32.8, 32.2, 29.6, 28.9, 27.1, 23.2, 22.7, 15.0, 14.1; HRMS (ES) Calcd for $\text{C}_{15}\text{H}_{29}\text{NO}_3\text{SNa}$ $[\text{M}+\text{Na}]^+$ 326.1760, found 326.1761.

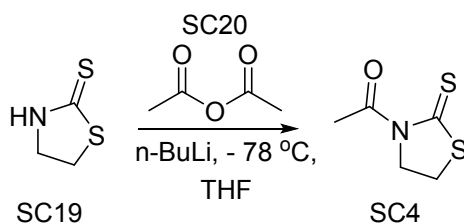


Preparation of Compound 4: This new compound was prepared by the following method. To a stirred solution of **SC3** (0.10 g, 0.33 mmol) in 20 mL of DCM exposed to air, Dess-Martin periodinane (DMP) (0.28 g, 0.66 mmol) was added and the reaction mixture was stirred for 2 h. The reaction mixture was quenched by addition of 10 mL of 1:1 mixture of saturated NaHCO_3 : $\text{Na}_2\text{S}_2\text{O}_3$ and stirred for 5 min. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with saturated sodium bicarbonate (2 x 20 mL), then brine (20 mL) and dried over Na_2SO_4 . The solvent was removed *in vacuo* and the residue was purified using column chromatography (50 % ethyl acetate in hexanes, R_f value of 0.21) affording the product as a yellow oil, (0.039 g, 41 % yield); $[\alpha]_{\text{D}}^{25}$ = 9.10 (c = 1.0, CHCl_3); IR (CHCl_3 , cast film) 3288, 3079,

2957, 2930, 2858, 1720, 1676, 1552 cm^{-1} ; ^1H NMR (700 MHz, CDCl_3) δ 5.81 (br s, 1H, NH), 3.46 (q, 2H, $J = 6.3$ Hz, H12), 3.28 (q, 1H, $J = 7.0$ Hz, H7), 3.11 (t, 2H, $J = 6.3$ Hz, H11), 1.97 (s, 3H, H14), 1.70 – 1.25 (m, 10H, H2,3,4,5,6) 1.12 (d, 3H, $J = 7$ Hz, H8), 0.86 (t, 3H, $J = 7.0$ Hz, H1); ^{13}C NMR (175 MHz, CDCl_3) δ 198.4 (C9), 191.6 (C10), 170.3 (C13), 39.6 (C7), 39.0 (C12), 32.3 (C6), 31.6 (C5), 29.2 (C4), 28.5 (C3), 27.1 (C11), 23.2 (C2), 22.6 (C14), 15.4 (C8), 14.1 (C1); HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{26}\text{NO}_3\text{S}$ $[\text{M}+\text{H}^+]$ 288.1628, found 288.1628.

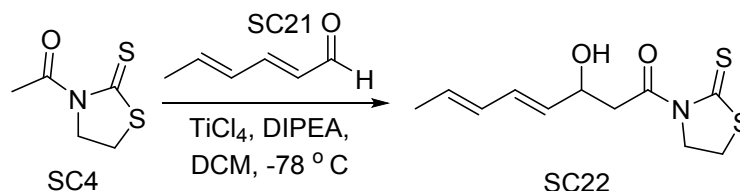


Scheme 8 Showing the preparation of substrate 20 and compound 21

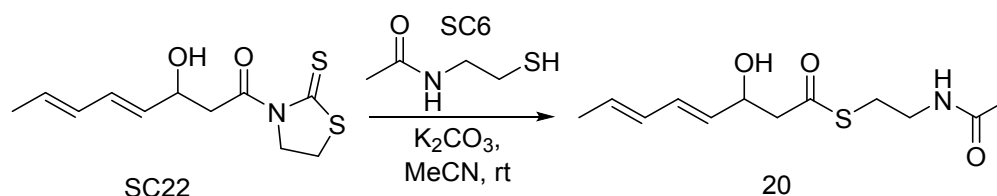


Preparation of SC4. This known compound was prepared following literature protocol.⁵ To a flame dried round bottom flask was added **SC19** (15.0 g, 126 mmol) along with 60 mL dry THF at -78°C under argon atmosphere. $n\text{-BuLi}$ (55.4 mL, 138 mmol, 2.5 M) was added to the solution in the round bottom flask and stirred for 30 min. The temperature was then reduced to 0°C and stirred for a further 15 min. Compound **SC20** (15.5 mL, 164 mmol) was slowly added to the reaction mixture maintaining 0°C , and stirred for 2 h. The reaction mixture was quenched with saturated NH_4Cl (20 mL), then extracted with Et_2O (3 x 10 mL), and the combined organic layers were dried over brine and Na_2SO_4 , filtered, and concentrated *in vacuo*. The resulting orange oil was purified by column chromatography using an eluent system of hexane/ethyl acetate (70:30) to afford the product **SC4** as a yellow oil of R_f 0.39 (30 % Ethyl Acetate in hexanes) (18.2 g, 90 % yield); IR (CHCl_3 Cast Film) 3004, 2942, 2890, 1696 cm^{-1} ; ^1H NMR (500 MHz CDCl_3) δ 4.58 (t, $J = 7.5$ Hz, 2H), 3.288 (t, $J = 7.5$ Hz, 2H),

2.783 (s, 3H); ^{13}C NMR (126 MHz CDCl_3) δ 202.0, 171.5, 55.7, 28.2, 27.0; HRMS (EI) calcd for $\text{C}_5\text{H}_7\text{NOS}_2$ [M^+] 160.9969, found 160.9968.

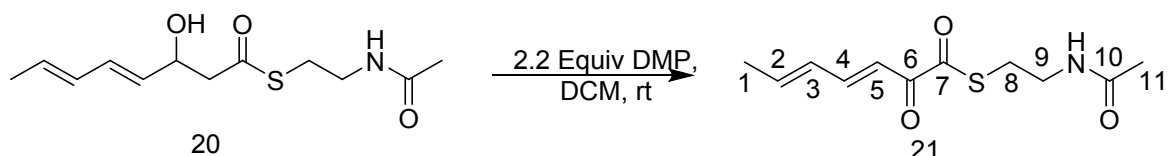


Preparation of SC22. This known compound was synthesized following literature protocol.⁵ To a stirred solution of **SC4** (0.80 g, 5.0 mmol) in dry DCM (25 mL) was added TiCl_4 (1.0 M solution in DCM, 5.5 mL, 5.5 mmol) at -78°C under argon atmosphere and stirred for 10 min. A solution of diisopropylethylamine (DIPEA) (0.83 g, 6.5 mmol) was added. The reaction mixture was stirred at -78°C for 1 h. Aldehyde **SC21** (0.48 g, 5.0 mmol) was added to the reaction mixture, which was then stirred for 1 h at -78°C . The reaction mixture was allowed to warm to room temperature and quenched by the addition of 10 mL saturated ammonium chloride. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4 . The solvent was removed *in vacuo* and the residue was purified using column chromatography (20 % ethyl acetate in hexanes) affording the product **SC22** as a yellow oil, R_f values of 0.39 (50 % ethyl acetate in hexanes), (0.828 g, 65 % yield): IR (CHCl_3 , cast film) 3442, 3017, 2928, 1697 cm^{-1} ; ^1H NMR (700 MHz, CDCl_3) δ 6.25 (dd, $J = 15.3, 10.4$ Hz, 1H), 6.07 – 5.97 (m, 1H), 5.81 – 5.69 (m, 1H), 5.64 – 5.51 (m, 1H), 4.76 – 4.64 (m, 1H), 4.65 – 4.54 (m, 2H), 3.60 – 3.42 (m, 2H), 3.30 (m, 2H), 2.90 (br s, 1H), 2.84 (br s, 1H), 1.76 (m, 3H); ^{13}C NMR (176 MHz, CDCl_3) δ 201.8, 173.4, 131.3, 130.7, 130.7, 130.6, 127.6, 68.7, 55.7, 45.8, 28.4, 18.2; HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{15}\text{NNaO}_2\text{S}_2$ [$\text{M}+\text{Na}$] $^+$ 280.0436, found 280.0437.

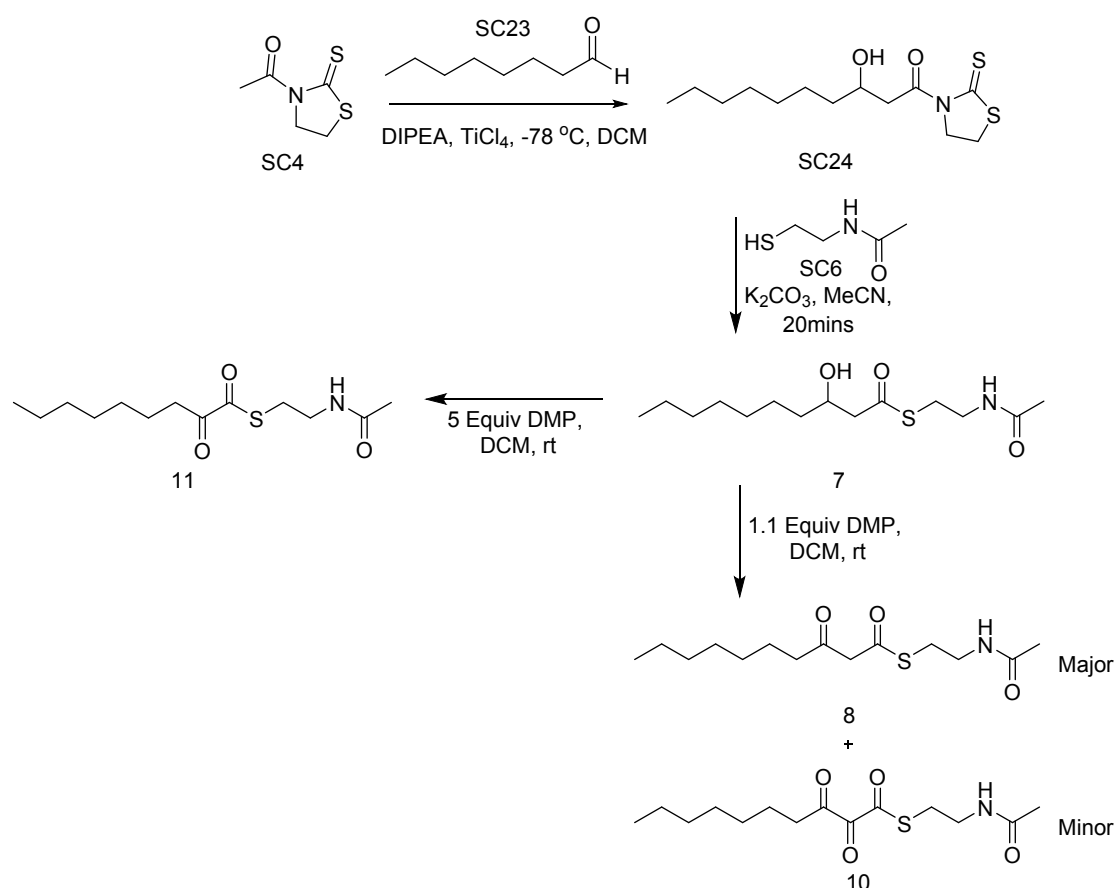


Preparation of 20. This known compound was synthesized by literature protocol.⁵ To a stirred solution of **SC22** (0.60 g, 2.3 mmol) in 10 mL ACN was added K_2CO_3 (1.15 g, 7.00 mmol) and **SC6** (0.33 g, 2.8 mmol). The reaction mixture was stirred until the yellow color disappeared (40 min). The solvent was removed *in vacuo* and the residue was purified using flash column chromatography (50

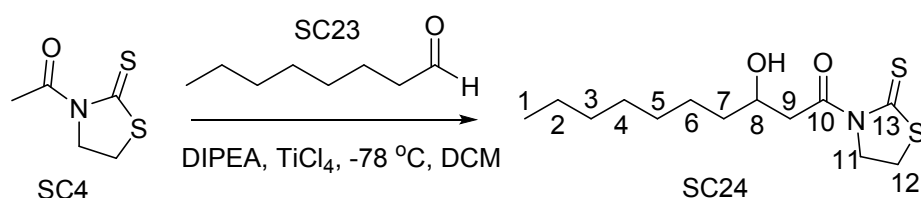
% ethyl acetate in hexanes) to give **20** as a clear oil (0.38 g, 63 % yield): IR (CHCl₃, cast film) 3298, 3090, 3019, 2932, 2878, 1658, 1551 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 6.23 (dd, *J* = 15.3, 10.4 Hz, 1H), 6.05 – 5.95 (m, 1H), 5.90 (br s, 1H), 5.73 (dq, *J* = 13.8, 6.7 Hz, 1H), 5.59 – 5.51 (m, 1H), 4.67 – 4.61 (m, 1H), 3.50 – 3.38 (m, 2H), 3.11 – 2.99 (m, 2H), 2.87 – 2.74 (m, 2H), 2.70 (br s, 1H), 1.95 (s, 3H), 1.77 – 1.73 (m, 3H); ¹³C NMR (176 MHz, CDCl₃) δ 198.5, 170.5, 131.6, 131.1, 130.4, 130.4, 69.4, 51.0, 39.3, 28.9, 23.2, 18.2; HRMS (ESI) calcd for C₁₂H₁₉NNaO₃S [M+Na]⁺ 280.0978, found 280.0980.



Preparation of Compound 21: This new compound was prepared by the following method. To a stirred solution of **20** (0.28 g, 1.1 mmol) in 20 mL of DCM exposed to air, Dess-Martin periodinane (DMP) (0.91 g, 2.4 mmol) was added and the reaction mixture was stirred for 2 h. The reaction mixture was quenched by addition of 10 mL of 1:1 mixture of saturated NaHCO₃:Na₂S₂O₃ and stirred for 5 min. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed saturated sodium bicarbonate (2 x 15 mL), then with brine (20 mL) and dried over Na₂SO₄. The solvent was removed *in vacuo* and the residue was purified using column chromatography (50 % ethyl acetate in hexanes, R_f value of 0.41(EtOAc)) affording the product **21** as a yellow oil, (0.171 g, 66 % yield); IR (CHCl₃, cast film) 3299, 3085, 2927, 2855, 1718, 1666, 1549 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.57 (dd, 1H, *J* = 15.5, 11.0 Hz, H5), 6.68 (d, 1H, *J* = 16.0 Hz, H4), 6.44 – 6.30 (m, 2H, H2,3), 5.77 (br s, 1H, NH), 3.48 (q, 2H, *J* = 6.5 Hz, H9), 3.12 (t, 2H, *J* = 6.5 Hz, H8), 1.97 (s, 3H, H11), 1.93 (d, 3H, *J* = 6.5 Hz, H1); ¹³C NMR (125 MHz, CDCl₃) δ 192.8 (C6), 183.0 (C7), 170.3 (C10), 150.0 (C5), 145.4 (C3), 131.0 (C2), 118.9 (C4), 39.0 (C9), 28.6 (C8), 23.3 (C11), 19.2 (C1); HRMS (ESI) calcd for C₁₁H₁₆NO₃S [M+H]⁺ 242.0845, found 242.0848.

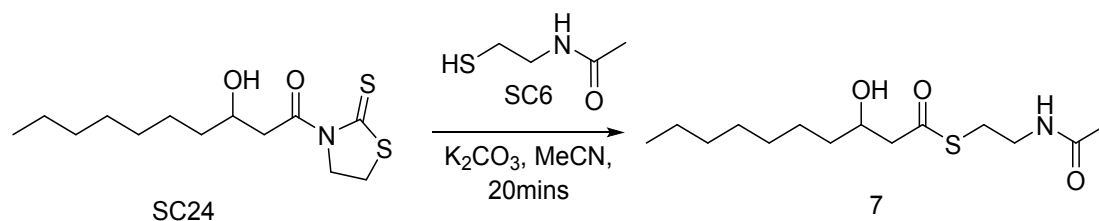


Scheme 9 Showing the preparation of substrate 7, compound 11, and intermediates 8 and 10

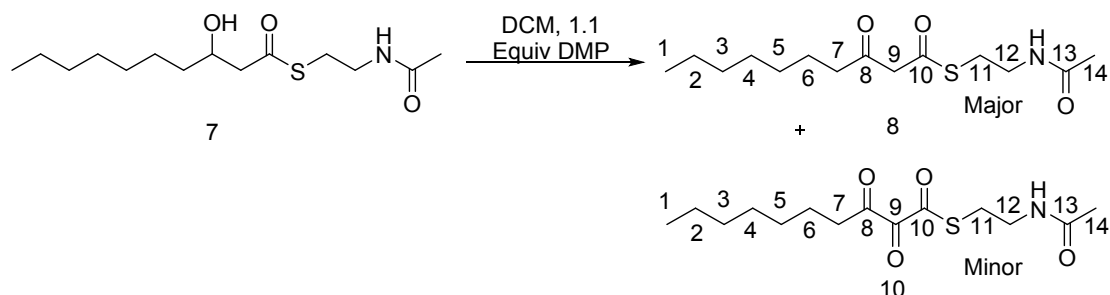


Preparation of SC24. This new compound was prepared following a modified literature protocol.⁴ To a flame dried round bottom flask was added **SC4** (3.50 g, 21.7 mmol) along with 100 mL DCM at -78°C under an argon atmosphere. TiCl_4 (23.9 mL, 23.9 mmol) was added to the solution in the round bottom flask and the mixture stirred for 10 min. DIPEA (3.58 mL, 28.2 mmol) was added to the round bottom flask and stirred for 1 h. Aldehyde **SC23** (3.72 mL, 23.88 mmol) was added to the reaction mixture and stirred for 1 h at -78°C . The reaction mixture was allowed to warm to room temperature while stirred, then quenched with saturated NH_4Cl (20 mL). The reaction mixture was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and MgSO_4 , filtered, and concentrated *in vacuo*. The resulting yellow oil was purified by column chromatography using an eluent system of hexane/ethyl acetate (70:30) to afford the product **SC24** as a yellow oil of R_f 0.42 (50 % Ethyl Acetate in hexanes), 4.44 g, 71 % yield; IR (CHCl_3 Cast Film) 3509, 3423, 2927, 2855, 1697 cm^{-1} ; ^1H NMR (500 MHz CDCl_3) δ 4.64 – 4.55 (m, 2H, H11), 4.09 (m, 1H, H8), 3.53 – 3.49 (dd, J = 18.0, 2.0 Hz, 1H, H9a), 3.32 – 3.25 (m, 3H, H12,9b), 2.88 (s, 1H, OH), 1.58 – 1.44 (m, 2H, H7), 1.36 – 1.28 (m, 10H, H2,3,4,5,6) 0.89 – 0.86 (t, J = 7.0 Hz, 3H, H1); ^{13}C NMR (126 MHz

CDCl₃) δ 201.9 (C13), 174.3 (C10), 68.2 (C8), 55.7 (C11), 45.8 (C9), 36.6 (C7), 31.8 (C6), 29.5 (C5), 29.3 (C4), 28.4 (C12), 25.5 (C3), 22.7 (C2), 14.1 (C1); HRMS (EI) calcd for C₁₃H₂₃NO₂S₂ [M⁺] 289.1170, found 289.1177.



Preparation of 7. This known compound was prepared following a modified literature protocol.⁴ To a round bottom flask containing 20 mL of dry ACN, was added **SC24** (3.35 g, 11.6 mmol) followed by K₂CO₃ (6.69 g, 40.5 mmol) at room temperature under an argon atmosphere. Compound **SC6** (1.66 g, 11.9 mmol) was then added to the reaction mixture, and the mixture was stirred for 20 min. The solvent was then removed *in vacuo* and the residue was taken up in 20 mL EtOAc and 20 mL water. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting orange residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (40:60) to afford the product **5** as a yellow oil of R_f 0.21 (Ethyl Acetate), 2.58 g, 77 % yield); IR (CHCl₃ Cast Film) 3303, 3078, 2953, 2921, 2871, 2849, 1696, 1687, 1642 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 5.85 (s, 1H), 4.05 (s, 1H), 3.50 – 3.37 (m, 2H), 3.09 – 3.00 (m, 2H), 2.77 – 2.66 (m, 3H), 1.97 (s, 3H), 1.54 – 1.27 (m, 12H), 0.89 – 0.86 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (126 MHz CDCl₃) δ 199.6, 170.5, 51.1, 51.1, 39.3, 36.8, 31.8, 29.5, 29.2, 28.9, 25.5, 23.3, 22.7, 14.1; HRMS (ESI) calcd for C₁₄H₂₇NNaO₃S [M+Na]⁺ 312.1604, found 312.1602.

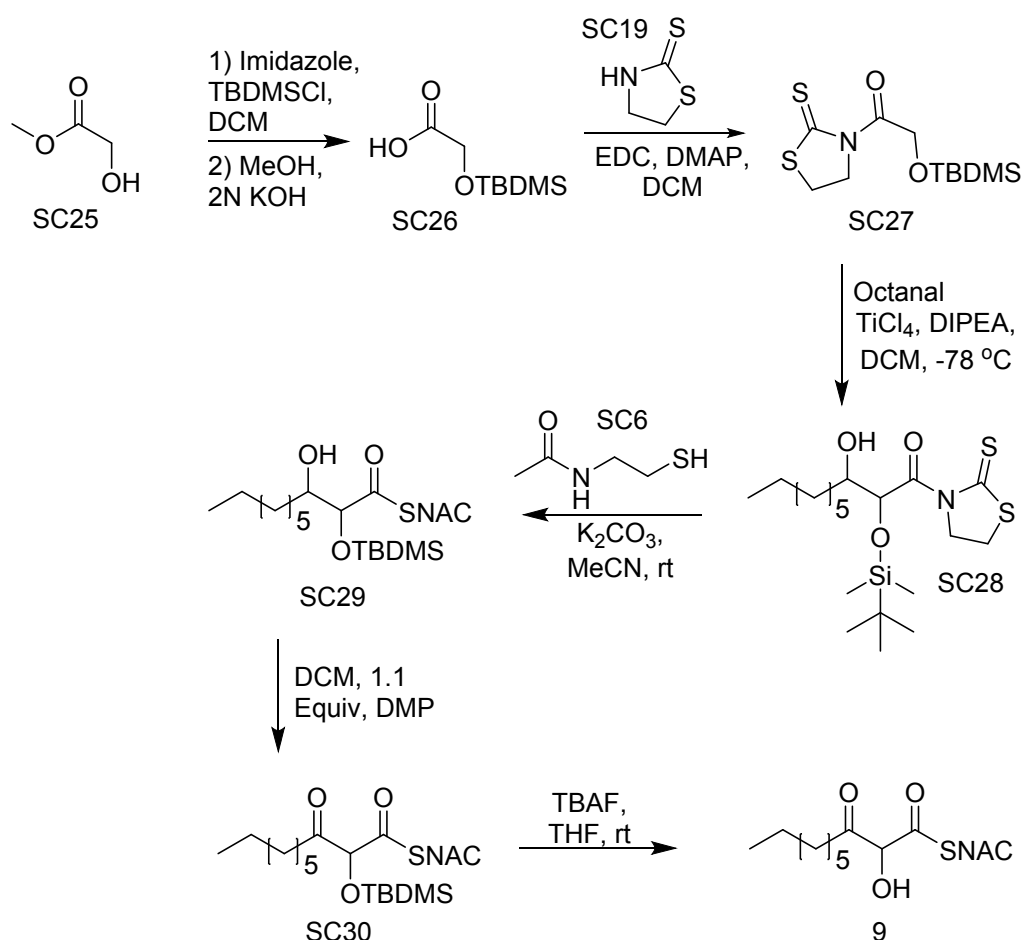


Preparation of 8 and 10. This new compound was prepared by the following method. To a round bottom flask was added **SC31** (1.50 g, 5.19 mmol) followed by 20 mL of DCM. DMP (2.31 g, 5.45 mmol) was added and stirred for 30 min at room temperature, then quenched with 1:3 Na₂SO₃ / NaHCO₃ (10 mL). The mixture was extracted with EtOAc (3 x 10 mL), and the combined organic layers were washed with saturated sodium bicarbonate (2 x 10 mL), then dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography

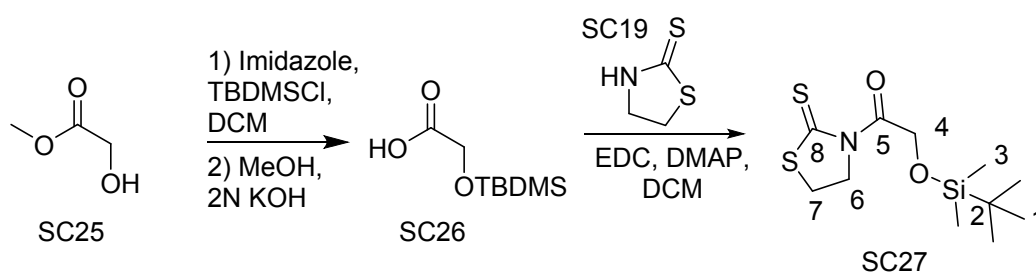
using an eluent system of hexane/ethyl acetate (1:1) to afford the product as a white solid of R_f 0.11 (50 % Ethyl Acetate in hexanes) (1.14 g, 76 % yield); Major; IR (CHCl₃ Cast Film) 3281, 2949, 2923, 2856, 1717, 1687, 1637 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 5.87 (br s, 1H, NH), 3.69 (s, 2H, H₉), 3.46 (q, J = 6.5 Hz, 2H, H₁₂), 3.09 (q, J = 6.0 Hz, 2H, H₁₁), 2.52 (t, J = 7.5 Hz, 2H, H₇), 1.97 (s, 3H, H₁₄), 1.60 – 1.59 (m, 2H, H₆), 1.28 (br s, 8H, H_{2,3,4,5}), 0.88 (t, J = 7.0 Hz, 3H, H₁); ¹³C NMR (126 MHz CDCl₃) δ 202.4 (C₈), 192.6 (C₁₀), 170.5 (C₁₃), 57.3 (C₉), 43.6 (C₇), 39.4 (C₁₂), 31.8 (C₅), 29.4 (C₄), 29.1 (C₆), 28.0 (C₁₄), 26.4 (C₃), 23.6 (C₂), 14.2(C₁); HRMS (ESI) calcd for C₁₃H₂₃NNaO₃S [M+Na]⁺ 310.1447, found 310.1444. Minor; ¹H NMR (500 MHz CDCl₃) δ 5.83 (br s, 1H, NH), 3.51 – 3.46 (m, 2H, H₁₂), 3.20 – 3.11 (m, 2H, H₁₁), 2.58 – 2.54 (m, 2H, H₇), 1.97 (s, 3H, H₁₄), 1.60 – 1.59 (m, 10H, H_{6,5,4,3,2}), 0.92 (t, J = 7.0 Hz, 3H, H₁); ¹³C NMR (126 MHz CDCl₃) δ 207.8 (C₈), 190.3(C₁₀), 184.7 (9), 170.5 (C₁₃), 43.0 (C₇), 39.4 (C₁₂), 31.6 (C₅), 29.1 (C₄), 28.9 (C₆), 27.9 (C₁₄), 26.5 (C₃), 23.3 (C₂), 14.1(C₁); HRMS (ESI) calcd for C₁₄H₂₄NO₄S [M+Na]⁺ 302.1426, found 302.1426.



Preparation of 11. This new compound was prepared by the following method. To a round bottom flask was added **7** (0.400 g, 1.38 mmol) followed by 25 mL of DCM, opened to air. DMP (2.93 g, 6.91 mmol) was added to the solution and stirred for 5 h. The reaction mixture was then quenched with 1:1 Na₂SO₃ /NaHCO₃ (10 mL). The mixture was extracted with Et₂O (3 x 10 mL), and the combined organic layers were washed with saturated sodium bicarbonate (3 x 10 mL), then dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting yellow residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (50:50) to afford the product **11** as a yellow oil of R_f 0.14 (50 % Ethyl Acetate in hexanes), 279 mg, 74 % yield; IR (CHCl₃ Cast Film) 3287, 3092, 2954, 2929, 2857, 1724, 1674 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 5.75 (s, 1H, NH), 3.49 – 3.45 (q, J = 12.5, 6.5 Hz, 2H, H₁₁), 3.12 – 3.09 (t, J = 6.5 Hz, 2H, H₁₀), 2.81 – 2.78 (t, J = 7.5 Hz, 2H, H₇), 1.97 (s, 3H, H₁₃), 1.66 – 1.59 (m, 2H, H₆), 1.32 – 1.29 (m, 8H, H_{2,3,4,5}), 0.89 – 0.86 (t, J = 6.5 Hz, 3H, H₁); ¹³C NMR (126 MHz CDCl₃) δ 195.3 (C₈), 191.5 (C₉), 170.4 (C₁₂), 38.9 (C₁₁), 36.5 (C₇), 31.6 (C₅), 29.0 (C₁₀), 28.9 (C₄), 28.5 (C₃), 23.3 (C₁₃), 23.1 (C₆), 22.6 (C₂), 14.1 (C₁); HRMS (ESI) calcd for C₁₃H₂₃NNaO₃S [M+Na]⁺ 296.1291, found 296.1291.

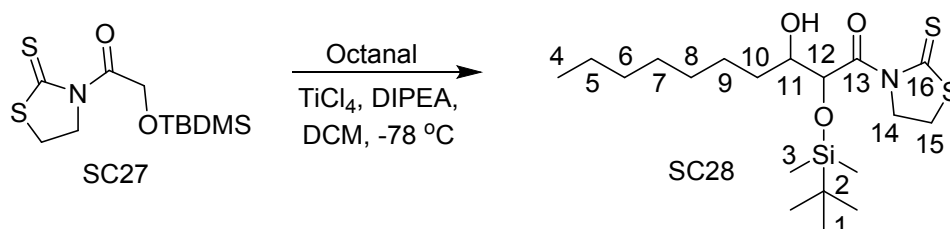


Scheme 10 Showing the preparation of intermediate 9

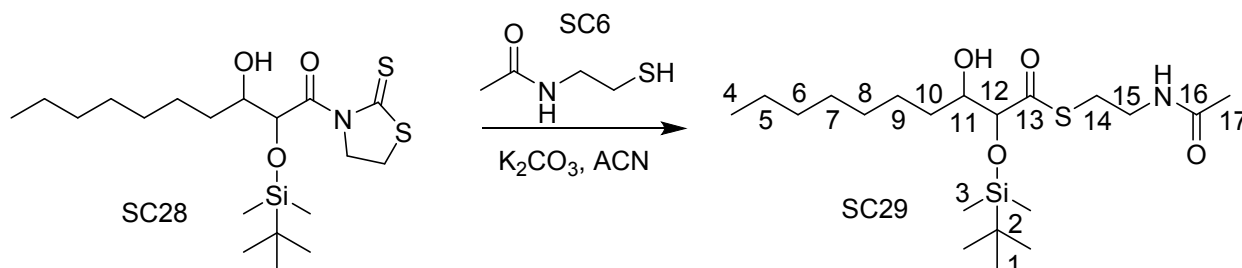


Preparation of SC27. This new compound was prepared by a modified method.⁶ In 25 mL of dry DCM, methyl glycolate **SC25** (1.20 g, 13.3 mmol) was dissolved, followed by imidazole (1.81 g, 26.6 mmol), then TBDMSCl (2.41 g, 16.0 mmol). The reaction mixture was stirred for 24 h at room temperature, then quenched by addition of 20 mL of saturated sodium bicarbonate. The mixture was extracted with DCM (3 x 20 mL), and the combined organic layers were dried over brine and magnesium sulphate, filtered, and concentrated *in vacuo*. This crude product **SC26** was used as is in the next step. In 50 mL of dry DCM, compound **SC26** from the previous step was dissolved, followed by EDC (3.78 g, 19.7 mmol), then 4-DMAP (0.320 g, 2.63 mmol), and **SC19** (1.72 g, 14.5 mmol) and stirred at 0 °C for 30 min, then allowed to warm to room temperature and stirred for 24 h. The reaction mixture was partitioned in 40 mL Et₂O and 40 mL of 0.5 M HCl. The organic layer was washed with brine (2 x 20 mL) and dried over magnesium sulphate, then concentrated *in vacuo*. The

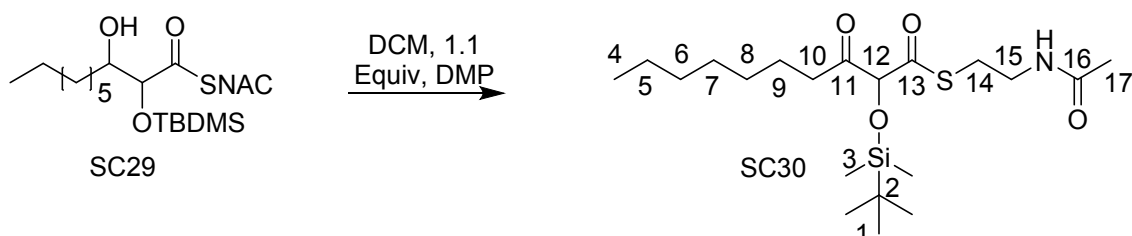
crude product was then purified on column (50 % EtOAc in Hexanes) to yield **SC27** as a yellow solid $R_f = 0.85$ (50 % EtOAc in Hexanes), 2.42 g, 63 % yield over three steps); IR (CHCl₃ Cast Film) 2952, 2929, 2856, 1714 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 5.12 (s, 2H, H4), 4.61 (t, $J = 8.0$ Hz, 2H, H6), 3.37 (t, $J = 8.0$ Hz, 2H, H7), 0.93 (s, 9H, H1), 0.12 (s, 6H, H3); ¹³C NMR (126 MHz CDCl₃) δ 201.0 (C8), 173.7 (C5), 67.0 (C4), 55.8 (C6), 29.5 (C7), 25.8 (C1), 18.6 (C2), -5.3 (C3); HRMS (ESI) calcd for C₁₁H₂₁NNaO₂S₂Si [M+Na]⁺ 314.0675, found 314.0674.



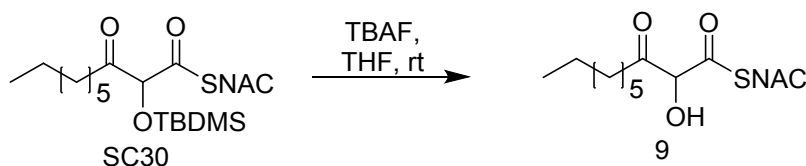
Preparation of SC28. This new compound was synthesized by a modified protocol.⁴ To a stirred solution of **SC27** (0.500 g, 1.72 mmol) in dry DCM (50 mL) was added TiCl₄ (1.0 M solution in DCM, 1.89 mL, 1.89 mmol) at -78 °C under argon atmosphere and stirred for 10 min. A solution of diisopropylethylamine (DIPEA) (0.280 g, 2.23 mmol) was added. The reaction mixture was stirred at -78 °C for 1 h. Octanal (0.240 g, 1.89 mmol) was added to the reaction mixture, which was then stirred for 1 h at -78 °C. The reaction mixture was allowed to warm to room temperature and quenched by the addition of 10 mL saturated ammonium chloride. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 15 mL). The combined organic layers were washed with brine (20 mL) and dried over Na₂SO₄. The solvent was removed *in vacuo* and the residue was purified using column chromatography (50 % ethyl acetate in hexanes) affording the product **SC28** as a yellow oil, R_f values of 0.74 (50 % ethyl acetate in hexanes), (0.51 g, 71 % yield): IR (CHCl₃, cast film) 3448, 2953, 2928, 2856, 1717 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.28 (s 1H, H12), 4.62 – 4.47 (m, 2H, H14), 3.97 (m, 1H H11), 3.50 – 3.42 (m, 1H, H15a), 3.25 – 3.19 (m, 1H, H15b), 1.56 (m, 1H, H10a), 1.55 – 1.24 (m, 11H, H10a,5,6,7,8,9), 0.95 (s, 9H, H1), 0.88 (t, $J = 7.2$ Hz, 3H, H4), 0.11 (s, 3H, H3a), 0.07 (s, 3H, H3b); ¹³C NMR (100 MHz, CDCl₃) δ 201.9 (C13), 174.7 (C16), 75.7 (C12), 73.3 (C11), 57.1 (C14), 35.0 (C10), 31.9 (C9), 29.6 (C15), 29.4 (C8), 29.2 (C7), 26.0 (C6), 25.9 (C1), 22.8 (C5), 18.5 (C4), 14.2 (C2), -4.4 (C3a), -5.0 (C3b); HRMS (ESI) calcd for C₁₉H₃₇NNaO₃S₂Si [M+Na]⁺ 442.1876, found 442.1871.



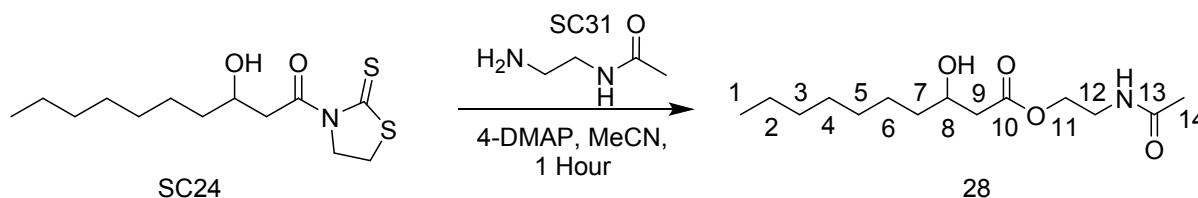
Preparation of SC29. This new compound was synthesized by a method adapted from the literature.⁴ To a stirred solution of **SC28** (0.450 g, 1.07 mmol) in 20 mL MeCN was added K₂CO₃ (0.260 g, 2.14 mmol) and **SC6** (0.440 g, 3.22 mmol). The reaction mixture was stirred until the yellow color disappeared (30 min). The solvent was removed *in vacuo* and the residue was purified using flash column chromatography (50 % ethyl acetate in hexanes), R_f = 0.22 (50 % EtOAc in Hexanes) to give **SC29** as a clear oil (0.32 g, 70 % yield): IR (CHCl₃, cast film) 3287, 3080, 2954, 2929, 2856, 1685 cm⁻¹; ¹H NMR (700 MHz, CDCl₃) δ 5.75 (br s, 1H, NH), 4.12 (dd, *J* = 6.0, 3.5 Hz, 1H, H11), 4.01 (d, *J* = 7.0 Hz, 1H, H12), 3.45 – 3.43 (m, 2H, H14), 3.07 – 3.05 (m, 1H, H15a), 2.96 – 2.94 (m, 1H, H15b), 1.97 (s, 3H, H17), 1.78 – 1.70 (m, 1H, H10a), 1.50 – 1.48 (m, 1H, H10b), 1.48 – 1.27 (m, 10H, H5,6,7,8,9), 0.89 – 0.86 (m, 12H, H4,1), 0.6 (s, 3H, H3a), 0.04 (s, 3H, H3b); ¹³C NMR (176 MHz, CDCl₃) δ 205.7 (C13), 170.1 (C16), 78.8 (C12), 73.0 (C11), 40.2 (C15), 39.3 (C10), 34.4 (C9), 31.7 (C8), 29.5 (C14), 29.2 (C7), 28.2 (C6), 25.8 (C5), 25.4 (C1), 22.7 (C17), 18.1 (C2), 14.1 (C4), –4.3 (C3a), –5.0 (C3b); HRMS (ESI) calcd for C₂₀H₄₁NNaO₄SSi [M+Na]⁺ 442.2418, found 442.2418.



Preparation of SC30. This new compound was prepared following a modified literature protocol.⁵ To a round bottom flask was added **SC29** (0.20 g, 0.47 mmol) followed by 20 mL dry DCM. DMP (0.440 g, 1.03 mmol) was added and stirred for 3 h at room temperature, then quenched with 1:3 Na₂SO₃ / NaHCO₃ (10 mL). The mixture was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (1:1) to afford the product **SC30** as a white solid of R_f 0.21 (50 % Ethyl Acetate in hexanes) (161.2 mg, 82 % yield); IR (CHCl₃ Cast Film) 3289, 2956, 2929, 2857, 1733, 1658 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 5.80 (br s, 1H, NH), 4.83 (s, 1H, H12), 3.50 – 3.44 (m, 2H, H15), 3.14 – 3.11 (m, 2H, H14), 1.98 (s, 3H, H17), 1.75 – 1.26 (m, 12H, H5,6,7,8,9,10), 0.90 – 0.87 (m, 12H, H1,4), 0.5 – 0.4 (m, 6H, H3); ¹³C NMR (126 MHz CDCl₃) δ 195.2 (C13), 191.9 (C11), 170.2 (C16), 74.1 (C12), 39.0 (C15), 33.7 (C10), 31.8 (C9), 29.3 (C8), 29.1 (C15), 28.5 (C1), 25.7 (C7), 25.2 (C17), 23.3 (C6), 22.6 (C5), 18.3 (C2), 14.1 (C4), –4.7 (C3a), –5.1 (C3b); HRMS (ESI) calcd for C₂₀H₃₉NNaO₄SSi [M+Na]⁺ 440.2261, found 440.2256.

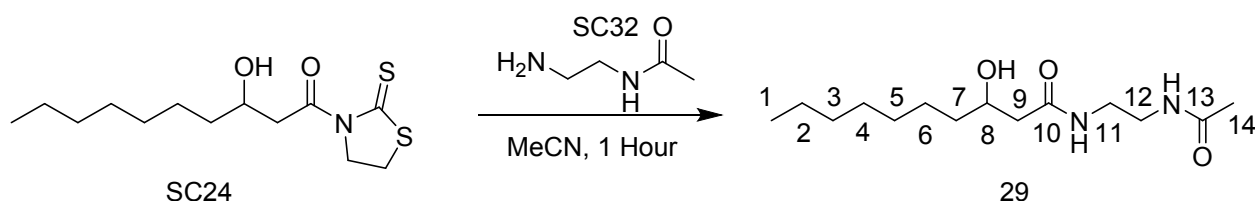


Preparation of 9. This new compound was prepared following a modified protocol.⁷ To a flame dried vial containing 10 mL dry THF, **SC30** (10 mg, 0.02 mmol) was added followed by TBAF (1.0 M, 0.03 mL, 0.03 mmol) and stirred for 30 min. Due to the unstable nature of the compound no purification was possible, and this sample was used as is for the HiRes LCMS assay. HRMS (ESI) calcd for C₁₄H₂₆NO₄S [M+H]⁺ 304.1577, found 304.1584.



Scheme 11 Showing the preparation of substrate 28

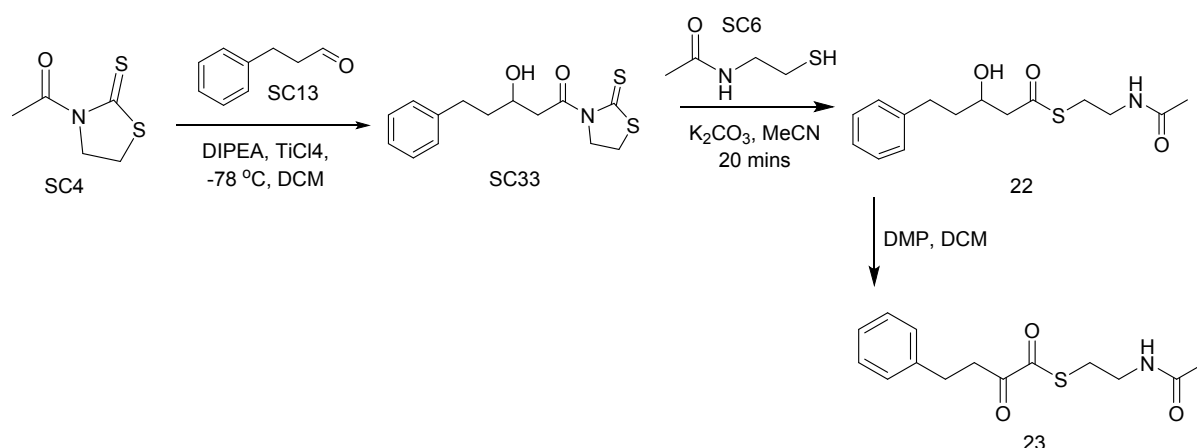
Preparation of 28. This new compound was prepared following a modified protocol.⁴ To a round bottom flask was added **SC24** (1.00 g, 3.45 mmol) followed by 4-DMAP (0.210 g, 1.72 mmol) and 100 mL of dry DCM at room temperature. N-acetyl ethanolamine **SC31** (1.43 g, 13.8 mmol) was added while stirring for 24 h. The layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting residue was purified by column chromatography to yield the product **28** as a white solid R_f 0.19 (EtOAc), 0.87 g, 92 % yield); IR (CHCl₃ Cast Film) 3552, 3289, 3094, 2923, 2850, 1718, 1640 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 5.92 (br s, 1H, NH), 4.25 – 4.17 (m, 2H, H11), 4.02 (m, 1H, H8), 3.53 (q, *J* = 5.5 Hz, 2H, H12), 2.83 (d, *J* = 3.5 Hz, 1H, OH), 2.52 (dd, *J* = 16.0, 3.0 Hz, 1H, H9a), 2.41 (dd, *J* = 16.0, 9.5 Hz, 1H, H9b), 1.98 (s, 3H, H14), 1.54 – 1.27 (m, 12H, H2,3,4,5,6,7), 0.88 (t, *J* = 7.5 Hz, 3H, H1); ¹³C NMR (126 MHz CDCl₃) δ 172.8 (C10), 170.5 (C13), 68.3 (C8), 63.5 (C11), 41.8 (C9), 38.7 (C12), 36.8 (C7), 31.8 (C6), 29.5 (C5), 29.3 (C4), 25.5 (C3), 23.3 (C14), 22.7 (C2), 14.1 (C1); HRMS (ESI) calcd for C₁₄H₂₇NNaO₄ [M+Na]⁺ 296.1832, found 296.1829.



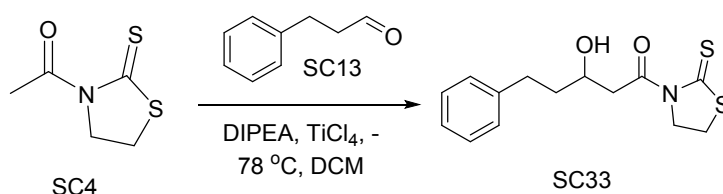
Scheme 12 Showing the preparation of substrate 29

Preparation of 29. This new compound was prepared following a modified literature protocol.⁴ To a round bottom flask was added **SC24** (1.00 g, 3.45 mmol) followed by 100 mL of dry DCM at room temperature, then **SC32** (1.40 g, 13.82 mmol) was added to the reaction mixture, then stirred for 60 min. The reaction mixture was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting residue was purified by recrystallization from Et₂O to yield the product **29** as a white solid R_f 0.29 (Acetone), 0.88 g, 93 % yield); IR (CHCl₃ Cast Film) 3299, 3095, 2919, 2851, 1630, 1567 cm⁻¹; ¹H NMR (500 MHz CDCl₃)

δ 6.61, (br s, 1H, NH10), 6.19 (br s, 1H, NH13), 3.95 (m, 1H, H8), 3.60 (br s, 1H, OH), 3.43 – 3.35 (m, 2H, H11,12), 2.36 (dd, J = 15.0, 2.5 Hz, 1H, H9a), 2.25 (dd, J = 15.0, 9.0 Hz, 1H, H9b), 1.99 (s, 3H, H14), 1.52 – 1.24 (m, 12H, H2,3,4,5,6,7), 0.88 (t, J = 7.0 Hz, 3H, H1); ^{13}C NMR (126 MHz CDCl_3) δ 173.6 (C10), 171.6 (C13), 68.8 (C8), 42.8 (C9), 40.2 (C11), 40.1 (C12), 37.1 (C7), 31.8 (C6), 29.5 (C5), 29.3 (C4), 25.5 (C3), 23.3 (C14), 22.7 (C2), 14.1 (C1); HRMS (ESI) calcd for $\text{C}_{14}\text{H}_{28}\text{N}_2\text{NaO}_3$ $[\text{M}+\text{Na}]^+$ 295.1992, found 295.1993.

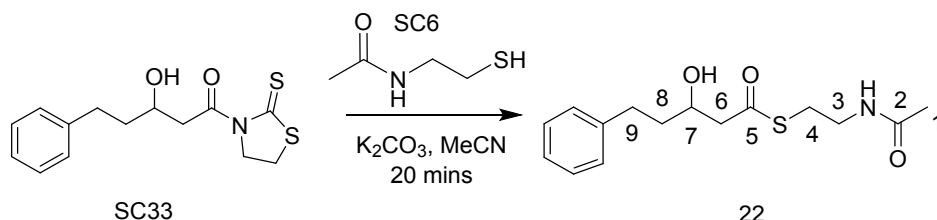


Scheme 13 Showing the preparation of substrate 22 and compound 23

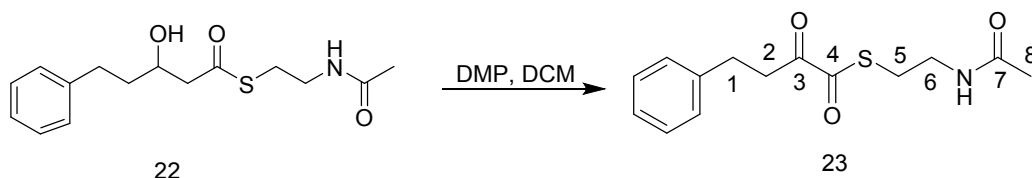


Preparation of SC33. This known compound was synthesized by a method adapted from literature.⁸ To a stirred solution of **SC4** (0.50 g, 3.1 mmol) in dry DCM (25 mL) was added TiCl_4 (1.0 M solution in DCM, 3.4 mL, 3.4 mmol) at -78°C under argon atmosphere and stirred for 10 min. A solution of diisopropylethylamine (DIPEA) (0.480 g, 3.72 mmol) was added. The reaction mixture was stirred at -78°C for 1 h. 3-phenyl propanal **SC13** (0.46 g, 3.4 mmol) was added to the reaction mixture, which was then stirred for 1.5 h at -78°C . The reaction mixture was allowed to warm to room temperature and quenched by the addition of 10 mL saturated ammonium chloride. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic layers were washed with brine (20 mL) and dried over Na_2SO_4 . The solvent was removed *in vacuo* and the residue was purified using column chromatography (40 % ethyl acetate in hexanes R_f value of 0.32 (50 % ethyl acetate in hexanes)) affording the product **SC33** as a yellow oil (0.60 g, 66 % yield); IR

(CHCl₃, cast film) 3306, 3083, 3059, 3024, 2940, 1695 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.30 – 7.26 (m, 2H), 7.21 – 7.18 (m, 3H), 4.61 – 4.57 (m, 2H), 4.13 – 4.11 (m, 1H), 3.52 (dd, 1H, *J* = 18.0, 2.5 Hz), 3.36 – 3.28 (m, 3H), 3.02 (d, 1H, *J* = 3.5 Hz), 2.84 – 2.70 (m, 2H), 1.92 – 1.80 (m, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 201.9, 174.1, 141.8, 128.5, 128.4, 125.9, 67.4, 55.7, 45.8, 38.1, 31.8, 28.4; HRMS (EI) calcd for C₁₄H₁₇NO₂S₂ [M⁺]: 295.0701, found 295.0700.

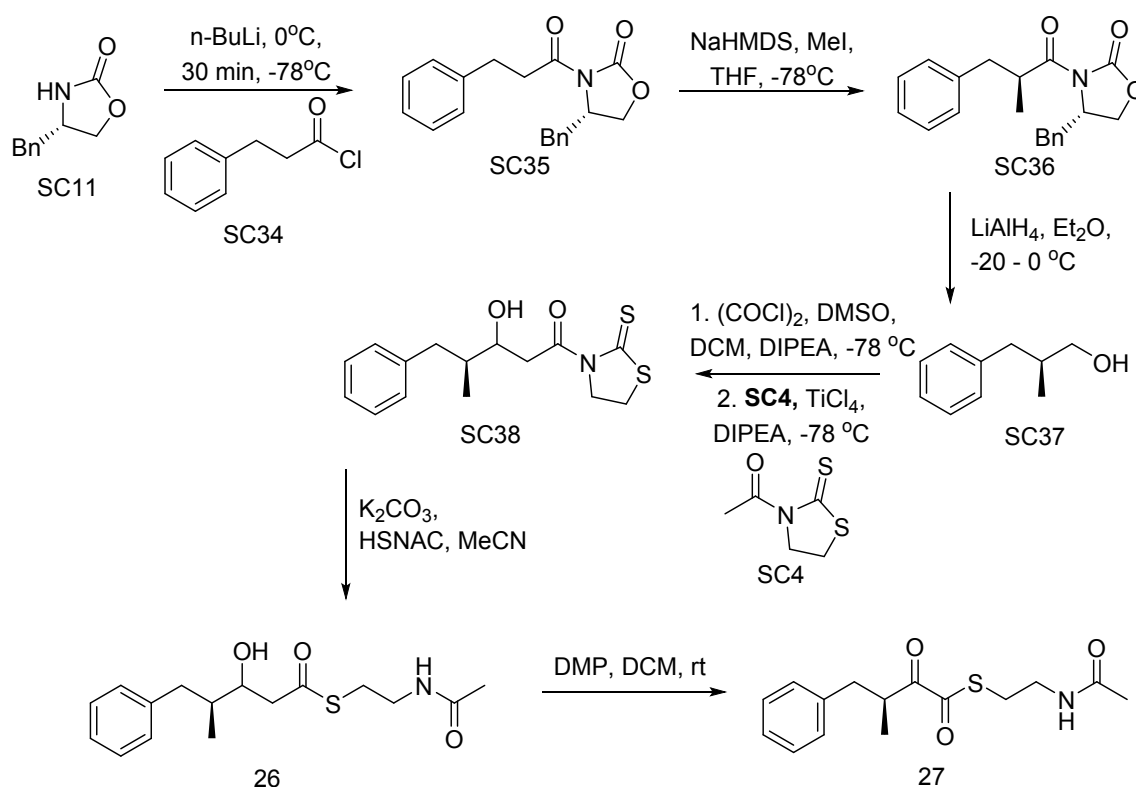


Preparation of 22. This new compound was prepared following a modified literature protocol.⁴ To a round bottom flask containing 20 mL of dry ACN, was added **SC33** (0.25 g, 0.85 mmol) followed by K₂CO₃ (0.420 g, 2.54 mmol) at room temperature, under argon atmosphere. HSNAC (0.130 g, 1.10 mmol) was then added to the reaction mixture, which was then stirred for 20 min under an argon atmosphere. The solvent was then removed *in vacuo* and the residue was taken up in 20 mL EtOAc and 20 mL water. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 10 mL), and the combined organic layers were dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting orange residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (35:65) to afford the product **22** as a yellow oil of R_f 0.23 (Ethyl Acetate) (142.6 mg, 57 % yield); IR (CHCl₃ Cast Film) 3289, 3084, 3061, 3025.19, 2936, 2864, 1655 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 7.30 – 7.27 (m, 2H, ArH), 7.21 – 7.18 (m, 3H, ArH), 5.90 (s, 1H, NH), 4.09 – 4.06 (m, 1H, H7), 3.48 – 3.42 (m, 2H, H3), 3.08 – 3.01 (m, 2H, H4), 2.84 – 2.67 (m, 4H, H6,9), 1.96 (s, 3H, H1), 1.86 – 1.75 (m, 2H, H8); ¹³C NMR (126 MHz CDCl₃) δ 199.5 (C5), 170.5 (C2), 141.6 (ArC), 128.5 (ArC), 128.5 (ArC), 126.1 (ArC), 68.1 (C7), 51.1 (C9), 39.3 (C3), 38.3 (C8), 31.8 (C6), 29.0 (C4), 23.3 (C1); HRMS (ESI) calcd for C₁₅H₂₁NNaO₃S [M+Na]⁺ 318.1134, found 318.1137.

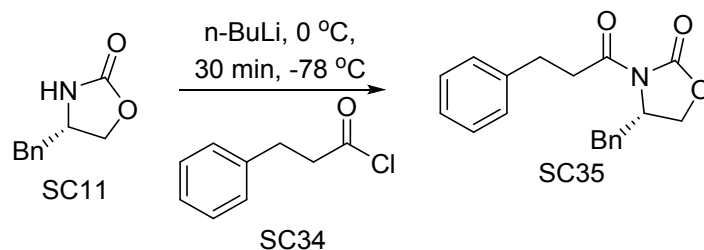


Preparation of 23. This new compound was prepared by the following method. To a round bottom flask containing 20 mL DCM was added **22** (138 mg, 0.470 mmol) followed by DMP (991 mg, 2.34 mmol) while stirring at room temperature, the reaction mixture was then allowed to stir for 6 hour. The reaction mixture was quenched with 1:1 Na₂SO₃ / NaHCO₃ (10 mL) then extracted with Et₂O (3 x 10 mL), and the combined organic layers were washed with saturated sodium bicarbonate (2 x 10

mL, then dried over brine and Na₂SO₄, filtered, and concentrated *in vacuo*. The resulting residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (60:40). The product was isolated by flash chromatography to produce **23** as a yellow oil *R*_f = 0.09 (50 %EtOAc in Hexanes), 81.9 mg, 63 %. IR (CHCl₃ Cast Film) 3330, 3063, 2932, 1722, 1672 cm⁻¹; ¹H NMR (700 MHz CDCl₃) δ 7.30 – 7.26 (m, 2H, ArH), 7.22 – 7.17 (m, 3H, ArH), 5.78 (s, 1H, NH), 3.47 – 3.43 (m, 2H, H6), 3.17 – 3.14 (m, 2H, H2), 3.11 – 3.08 (m, 2H, H5), 2.98 – 2.95 (m, 2H, H1), 1.98 (s, 3H, H8) ¹³C NMR (126 MHz CDCl₃) δ 194.3 (C3), 191.3 (C4), 170.6 (C7), 141.9 (ArC), 131.8 (ArC), 128.1 (ArC), 126.6 (ArC), 39.0 (C6), 38.3 (C2), 29.1 (C1), 28.6 (C5), 23.3 (C8); HRMS (ESI) calcd for C₁₄H₁₇NNaO₃S [M+Na]⁺ 302.0821, found 302.0824.

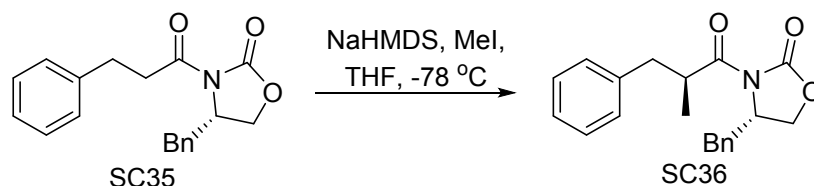


Scheme 14 Showing the preparation of substrate **26** and compound **27**

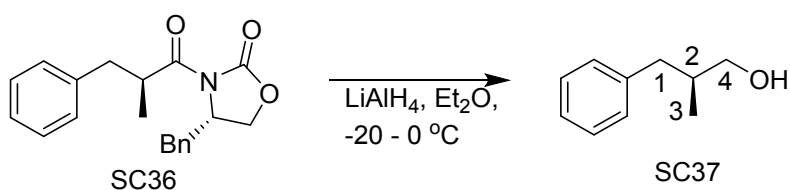


Preparation of SC35. This known compound was prepared following a modified literature protocol.⁹ Compound **SC11** (2.50 g, 14.1 mmol) was dissolved in 100 mL of dry THF and cooled to -78 °C using a dry ice/acetone bath. *n*-BuLi (6.21 mL, 15.5 M) was then added dropwise and the reaction mixture

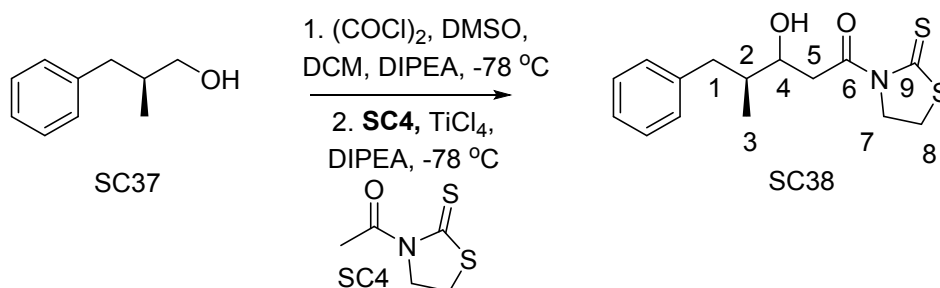
was maintained at $-78\text{ }^{\circ}\text{C}$ for 15 min. Compound **SC34** (2.31 mL, 15.5 mmol) was added via syringe and the reaction mixture was allowed to warm to room temperature over 16 h. The reaction mixture was quenched with saturated ammonium chloride (10 mL) and the bulk of the THF was removed *in vacuo*. The aqueous layer was then extracted with DCM (3 x 20 mL) and the organic layers were pooled, washed with brine and dried over Na_2SO_4 . The crude was concentrated and purified using flash column chromatography (20 % EtOAc in Hexanes), R_f 0.44 (30 % EtOAc in Hexanes); to produce the product **SC35** as a white solid, yield (4.16 g, 95 %); $[\alpha]_D^{25} = 57.33$ ($c = 1.0$, CHCl_3); IR (CHCl_3 , cast): 3086, 3028, 2922, 2857, 1954, 1778, 1699 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.34 – 7.26 (m, 7H), 7.23 – 7.17 (m, 3H), 4.69 – 4.64 (m, 1H), 4.20 – 4.14 (m, 2H), 3.34 – 3.22 (m, 3H), 3.05 – 3.01 (m, 2H), 2.74 (dd, $J = 13.5, 9.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.4, 153.4, 140.5, 135.2, 129.4, 129.0, 128.6, 128.5, 127.4, 126.3, 66.2, 55.1, 37.9, 37.1, 30.3; HRMS (ES) Calcd for $\text{C}_{19}\text{N}_2\text{O}_3$ ($[\text{M}+\text{H}]^+$) 310.1438, found 310.1434.



Preparation of SC36. This known compound was prepared following a modified literature protocol.¹⁰ To a solution of **SC35** (3.00 g, 9.72 mmol) in 80 mL of dry THF was blanketed with argon and cooled to $-78\text{ }^{\circ}\text{C}$. NaHMDS (12.7 mL, 12.7 mmol) was added dropwise via syringe and the reaction mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min before methyl iodide (0.930 mL, 10.7 mmol) was added. The reaction mixture was allowed to warm to room temperature over 16 h and was quenched with saturated NH_4Cl . The THF was removed *in vacuo* and replaced with 20 mL of EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The organic layers were then pooled, washed with brine and dried over Na_2SO_4 . The reaction mixture was concentrated *in vacuo* and purified by column chromatography (5 % EtOAc/Hexanes), R_f 0.5 (20 % EtOAc/Hexanes); to produce the product **SC36** as a pale yellow oil, yield (2.52 g, 80 %); $[\alpha]_D^{25} = 104.74$ ($c = 1.0$, CHCl_3); IR (CHCl_3 , cast): 3062, 3028, 2975, 2930, 1780, 1698 cm^{-1} ; ^1H -NMR (500 MHz, CDCl_3) 7.34 – 7.31 (m, 2H), 7.29 – 7.22 (m, 3H), 7.24 – 7.18 (m, 5H), 4.55 – 4.50 (m, 1H), 4.15 – 4.07 (m, 2H), 3.96 (t, $J = 8.5$ Hz, 1H), 3.25 (dd, $J = 13.5, 3.5$ Hz, 1H), 3.04 (dd, $J = 13.5, 8.0$ Hz, 1H), 2.78 – 2.70 (m, 2H), 1.26 (d, $J = 6.5$ Hz, 3H); ^{13}C -NMR (125 MHz, CDCl_3): ^{13}C NMR (126 MHz, CDCl_3) δ 176.5, 153.0, 139.2, 135.3, 129.5, 129.2, 128.9, 128.3, 127.3, 126.4, 66.0, 55.4, 39.9, 39.5, 37.9, 17.1; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 346.1414, found 346.1417.

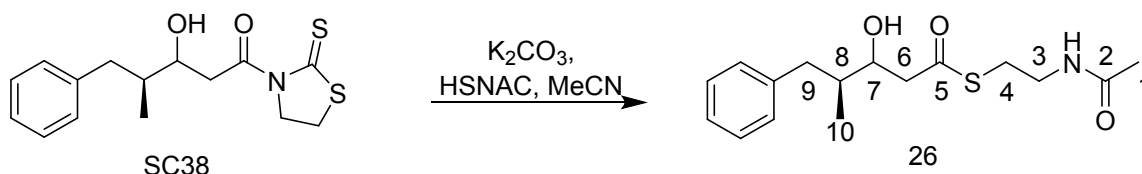


Preparation of SC37. This new compound was prepared following a modified literature protocol.⁴ In 100 mL of dry Et₂O compound **SC36** (2.40 g, 7.42 mmol) was dissolved and cooled to 0 °C using an ice-water bath. LiAlH₄ (22.3 mL, 22.3 mmol) was added dropwise via syringe and the temperature was maintained at 0 °C for 1.5 h. The reaction mixture was quenched with 1 M NaOH (60 mL) and stirred until the solution was clear. The layers were separated and the aqueous was extracted with ether (3 x 60 mL). The organic layers were pooled, washed with brine and dried over anhydrous Na₂SO₄. The organic solvent was removed *in vacuo* to yield a crude colourless oil. Compound **SC37** was then purified by flash chromatography (20 % EtOAc in Hexanes), R_f 0.66 (50 % EtOAc in Hexanes); to produce a pale yellow oil, yield (1.06 g, 95%); [α]_D²⁵ = -10.92 (*c* = 1.0, CHCl₃); IR (CHCl₃, cast): 3348, 2955, 2921, 2873, 1495, 1455 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.29 – 7.26 (m, 2H, ArH), 7.21 – 7.16 (m, 3H, ArH), 3.53 – 3.43 (m, 2H, H4), 2.76 (dd, *J* = 13.5, 6.0 Hz, 1H, H1a), 2.41 (dd, *J* = 13.5, 8.0 Hz, 1H, H1b), 1.96 – 1.92 (m, 2H, H2,OH), 0.91 (d, *J* = 7.0 Hz, 3H, H3); ¹³C NMR (125 MHz, CDCl₃) δ 140.6 (ArC), 129.1 (ArC), 128.2 (ArC), 125.8 (ArC), 67.5 (C4), 39.7 (C1), 37.7 (C2), 16.4 (C3); HRMS (EI) Calcd for C₁₀H₁₄O [M⁺] 150.1045, found 150.1045.

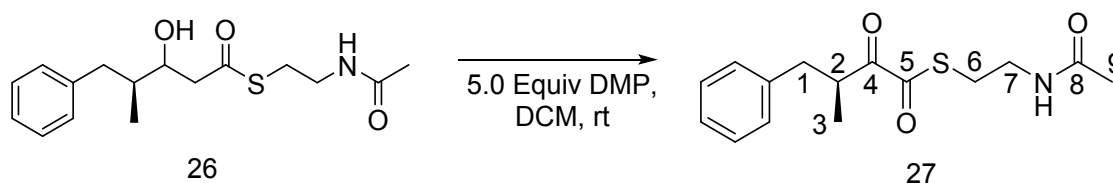


Preparation of SC38. This new compound was prepared following a modified literature protocol.⁴ Oxalyl chloride (1.35 mL, 16.0 mmol) in 50 mL of dry DCM was cooled to -78 °C and a solution of DMSO (dried over 4Å MS, 1.51 mL, 21.3 mmol) in 20 mL dry DCM was added dropwise. After 30 min at -78 °C, a solution of **SC37** (0.800 g, 5.32 mmol) in 5 mL of DCM was added dropwise and stirred at -78 °C for another 20 min. Diisopropylethylamine (DIPEA; dried over 4Å MS, 10.12 mL, 78.88 mmol) was added dropwise and the temperature was maintained for 20 min then warmed to -50 °C for 60 min. The reaction mixture was quenched with 10 mL of saturated NH₄Cl and allowed to warm to room temperature. The layers were separated and the organic layers were washed with 10 mL of saturated NaHCO₃ and brine before drying on Na₂SO₄. The solvent was removed and the crude aldehyde was used immediately in the next step. A solution of the compound **x** (0.70 g, 4.34 mmol) in 50 mL of dry DCM was charged with TiCl₄ (4.78 mL, 4.78 mmol) at -78 °C. After 15 min at -78 °C, DIPEA (0.670 mL, 5.21 mmol) was added dropwise and a colour change was noted from bright orange-red to a deep red-brown. The reaction mixture was allowed to stir for 1 h then a solution of the crude aldehyde (0.64 g, 4.77 mmol) in 5 mL of dry DCM was added dropwise. After 1 h at -78 °C, the reaction mixture was quenched with 10 mL of saturated NH₄Cl and allowed to warm to room temperature. Separation of the layers and extraction of the aqueous layer with DCM (3 x 10 mL) led to the organic layers being pooled, washed with brine and dried on Na₂SO₄. The reaction mixture was concentrated *in vacuo* and subjected to flash column chromatography (30 % EtOAc/Hexanes), R_f 0.44 (50 % EtOAc in Hexanes); to produce the product **SC38** as a yellow oil, yield (1.04 g, 77 % over two steps). IR (CHCl₃, cast film): 3537, 3060, 2963, 2932, 1692 cm⁻¹; ¹H-NMR (500 MHz, CDCl₃): δ 7.31 – 7.27 (m, 2H, ArH), 7.21 – 7.19 (m, 3H, ArH), 4.60 – 4.56 (m, 2H, H7), 4.09 – 4.06 (m, 1H, H4), 3.44 –

3.43 (m, 2H, H5), 3.30 – 3.26 (m, 2H, H8), 2.90 – 2.86 (m, 1H, H1a), 2.51 – 2.46 (m, 1H, H1b), 1.91 – 1.88 (m, 1H, H2), 0.94 (d, J = 6.5 Hz, 3H, H3); ^{13}C -NMR (125 MHz, CDCl_3): δ 201.9 (C9), 174.6 (C6), 140.8 (ArC), 129.2 (ArC), 128.2 (ArC), 125.8 (ArC), 71.5 (C4), 55.7 (C7), 43.6 (C5), 40.3 (C2), 39.5 (C1), 28.3 (C8), 14.1 (C3); HRMS (ESI) Calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_2\text{S}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ 332.0749, found 332.0757.

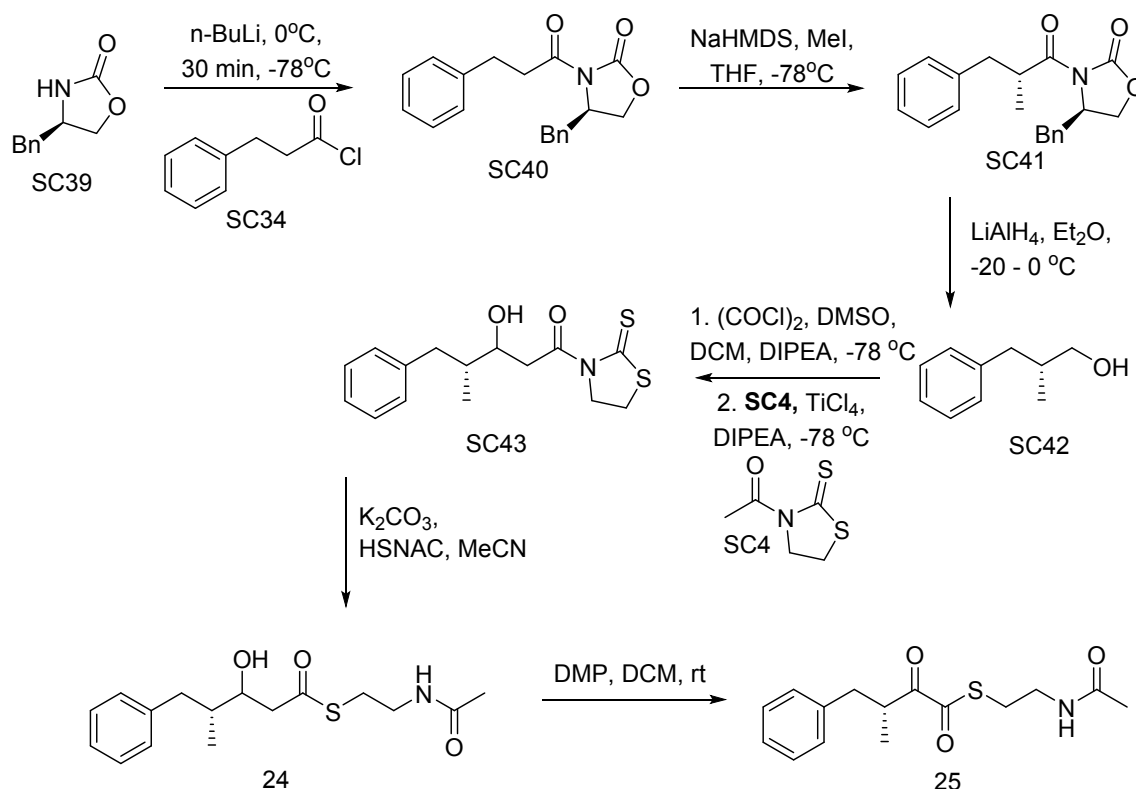


Preparation of 26. This new compound was prepared following a modified literature protocol.⁵ To a stirred solution of **SC38** (0.900 g, 2.91 mmol) in 20 mL ACN was added K_2CO_3 (1.44 g, 8.73 mmol) and N-acetylcysteamine (0.450 g, 3.78 mmol). The reaction mixture was stirred until the yellow color disappeared 30 min. The solvent was removed *in vacuo* and the residue was purified using flash column chromatography (50 % ethyl acetate in hexanes), R_f = 0.06 (50 % EtOAc in Hexanes) to give **24** as a pale yellow oil (0.79 g, 88 % yield): IR (CHCl_3 , cast film) 3303, 3084, 2966, 2932, 1687, 1558 cm^{-1} ; ^1H NMR (700 MHz, CDCl_3) δ 7.29 – 7.26 (m, 2H, ArH), 7.20 – 7.16 (m, 3H, ArH), 5.95 (br s, 1H, NH), 4.05 – 4.02 (m, 1H, H7), 3.46 – 3.42 (m, 2H, H3), 3.07 – 3.00 (m, 2H, H4), 2.87 – 2.67 (m, 4H, H6,9a,OH), 2.46 – 2.41 (m, 1H, H9b), 1.96 (s, 3H, H1), 1.83 – 1.81 (m, 1H, H8), 0.89 (d, J = 7.0 Hz, H10); ^{13}C NMR (176 MHz, CDCl_3) δ 199.9 (C5), 170.6 (C2), 140.6, 129.2 (ArC), 128.4 (ArC), 126.0 (ArC), 70.8 (C7), 48.8 (C6), 40.6 (C8), 39.5 (C3), 29.0 (C9), 28.9 (C3), 23.2 (C1), 13.6 (C10); HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{23}\text{NNaO}_3\text{S}$ $[\text{M}+\text{Na}]^+$ 332.1291, found 332.1286.

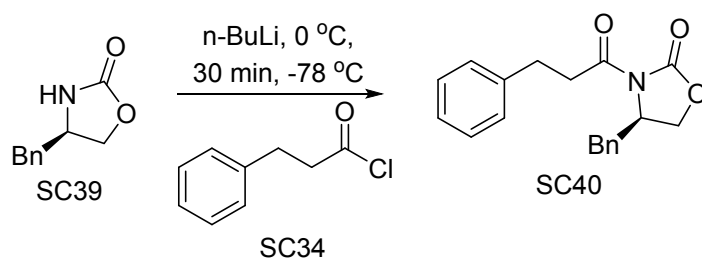


Preparation of 27. This new compound was prepared by the following method. To a round bottom flask was added **26** (10.0 mg, 0.030 mmol) followed by 20 mL of DCM. The DMP (68.5 mg, 0.160 mmol) was added then stirred for 3 h at room temperature. The reaction was then quenched with 1:1 Na_2SO_3 / NaHCO_3 (10 mL). The mixture was extracted with Et_2O (3 x 10 mL), and the combined organic layers were washed with saturated sodium bicarbonate (3 x 10 mL), then dried over brine and Na_2SO_4 , filtered, and concentrated *in vacuo*. The resulting yellow residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (60:40) to afford the product **25** as a yellow oil of R_f 0.09 (40 % Ethyl Acetate in hexanes) (5.9 mg, 62 % yield); $[\alpha]_D^{25}$ = 28.09 (c = 0.603, CHCl_3); IR (CHCl_3 Cast Film) 3413.37, 3287, 3086, 3064, 3028, 2966, 2930, 2875, 2855, 1720, 1676 cm^{-1} ; ^1H NMR (500 MHz CDCl_3) δ 7.29 – 7.24 (m, 2H, ArH), 7.22 – 7.14 (m, 3H, ArH), 5.70 (s, 1H, NH), 3.60 (m, 1H, H2), 3.46 – 3.41 (m, 2H, H7), 3.08 – 3.06 (m, 2H, H6), 3.04 – 3.02 (dd, J = 10.0, 5.0, 1H, H1a), 2.64 – 2.61 (dd, J = 9.5, 5.5 Hz, 1H, H1b), 1.98 (s, 3H, H9), 1.40 – 1.30 (dd, J = 5 Hz, 3H, H3); ^{13}C NMR (126 MHz CDCl_3) δ 197.7 (C4), 191.2 (C5), 170.4 (C8), 129.2 (ArC), 128.0 (ArC), 126.6 (ArC), 41.6

(C2), 38.9 (C7), 38.4 (C1), 28.6 (C6), 23.2 (C9), 15.5 (C3); HRMS (ESI) calcd for $C_{15}H_{19}NNaO_3S$ $[M+Na]^+$ 316.0978, found 316.0983.

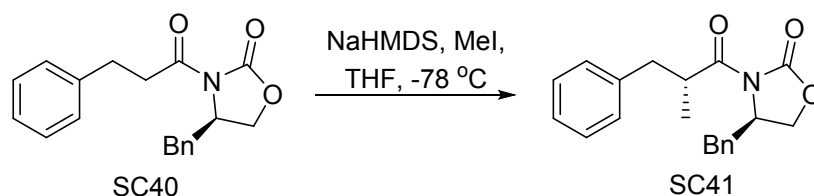


Scheme 15 Showing the preparation of substrate 24 and compound 25

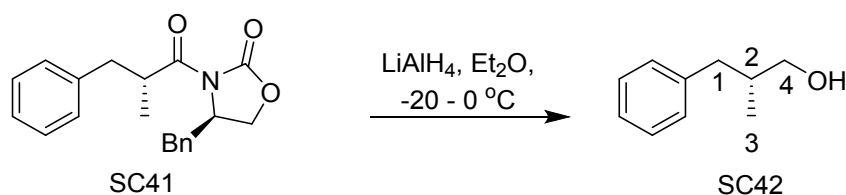


Preparation of SC40. This known compound was prepared following a modified literature protocol.¹¹ Compound **SC39** (2.50 g, 14.1 mmol) was dissolved in 100 mL of dry THF and cooled to $-78\text{ }^{\circ}\text{C}$ using a dry ice/acetone bath. $n\text{-BuLi}$ (6.21 mL, 15.5 mmol) was then added dropwise and the reaction mixture was maintained at $-78\text{ }^{\circ}\text{C}$ for 15 min. Compound **SC34** (2.31 mL, 15.5 mmol) was added via syringe and the reaction mixture was allowed to warm over 16 h. The solution was quenched with saturated ammonium chloride (10 mL) and the bulk of the THF was removed *in vacuo*. The aqueous layer was then extracted with DCM (3 x 20 mL) and the organic layer was pooled, washed with brine and dried over Na_2SO_4 . The crude was concentrated and purified using flash column chromatography (20 % EtOAc in Hexanes), R_f 0.44 (30 % EtOAc in Hexanes); to produce the product **SC40** as a white solid, yield (4.01 g, 92 %); $[\alpha]_D^{25} = -60.19$ ($c = 1.0$, CHCl_3); IR (CHCl_3 , cast): 3062, 3028, 2921, 1782,

1699 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.36 – 7.29 (m, 7H), 7.25 – 7.19 (m, 3H), 4.71 – 4.68 (m, 1H), 4.22 – 4.17 (m, 2H), 3.3 – 3.25 (m, 3H), 3.08 – 3.04 (m, 2H), 2.79 (dd, J = 13.0, 9.5 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.4, 153.4, 140.5, 135.2, 129.5, 129.0, 128.6, 128.5, 127.4, 126.3, 66.2, 55.1, 37.9, 37.2, 30.3; HRMS (ES) Calcd for $\text{C}_{19}\text{N}_1\text{NNaO}_3$ $[\text{M}+\text{Na}]^+$ 332.1257, found 332.1257.

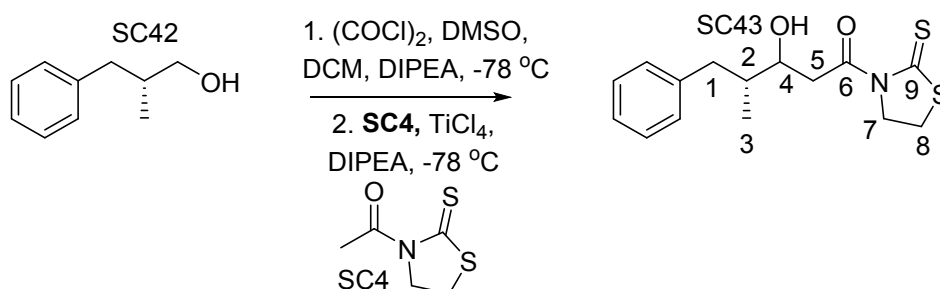


Preparation of SC41. This known compound was prepared following a modified literature protocol.¹² A solution of **SC40** (3.90 g, 12.7 mmol) in 80 mL of dry THF was blanketed with argon and cooled to $-78\text{ }^\circ\text{C}$. NaHMDS (13.91 mL, 13.91 mmol) was added dropwise via syringe and the reaction mixture was stirred at $-78\text{ }^\circ\text{C}$ for 30 min before methyl iodide (1.02 mL, 16.4 mmol) was added. The reaction mixture was allowed to warm to room temperature over 16 h and was quenched with saturated NH_4Cl . The THF was removed *in vacuo* and replaced with 20 mL of EtOAc. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The organic layers were then pooled, washed with brine and dried over Na_2SO_4 . The reaction mixture was concentrated *in vacuo* and purified by column chromatography (5 % EtOAc/Hexanes), R_f 0.5 (20 % EtOAc/Hexanes); to produce the product **SC41** as a pale yellow oil, yield (3.31 g, 81 %); $[\alpha]_{\text{D}}^{25} = -100.00$ (c = 1.0, CHCl_3); IR (CHCl_3 , cast): 3062, 3028, 2975, 2931, 1780, 1698 cm^{-1} ; ^1H -NMR (500 MHz, CDCl_3) 7.35 – 7.32 (m, 2H), 7.29 – 7.26 (m, 3H), 7.24 – 7.18 (m, 5H), 4.54 – 4.51 (m, 1H), 4.15 – 4.07 (m, 2H), 3.96 (t, J = 8.5 Hz, 1H), 3.25 (dd, J = 13.5, 3.5 Hz, 1H), 3.04 (dd, J = 13.5, 8.0 Hz, 1H), 2.78 – 2.70 (m, 2H), 1.26 (d, J = 7.0 Hz, 3H); ^{13}C -NMR (125 MHz, CDCl_3): ^{13}C NMR (126 MHz, CDCl_3) δ 176.5, 153.0, 139.2, 135.3, 129.5, 129.2, 128.9, 128.3, 127.3, 126.4, 66.0, 55.4, 39.9, 39.5, 37.9, 17.1; HRMS (ESI) Calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 346.1414, found 346.1410.

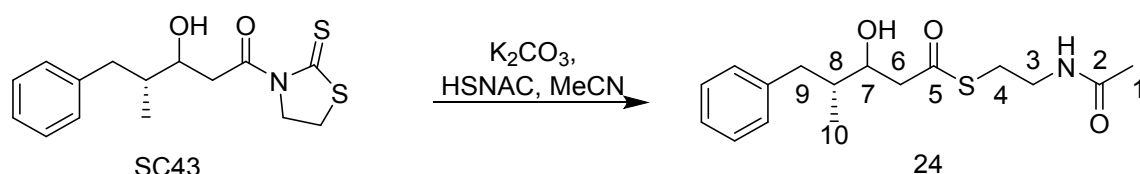


Preparation of SC42. This new compound was prepared following a modified literature protocol.⁴ In 100 mL of dry Et_2O compound **SC41** (2.70 g, 8.35 mmol) was dissolved and cooled to $0\text{ }^\circ\text{C}$ using an ice-water bath. LiAlH_4 (25.05 mL, 25.05 mmol) was added dropwise via syringe and the temperature was maintained at $0\text{ }^\circ\text{C}$ for 1.5 h. The reaction mixture was quenched with 1M NaOH (60 mL) and stirred until the solution was clear. The layers were separated and the aqueous was extracted with ether (3 x 60 mL). The organic layers were pooled, washed with brine and dried over anhydrous Na_2SO_4 . The organic solvent was removed *in vacuo* to yield a crude colourless oil. Compound **SC42** was then purified by flash chromatography (20 % EtOAc in Hexanes), R_f 0.66 (50 % EtOAc in Hexanes); to produce a pale yellow oil, yield (1.08 g, 86 %); $[\alpha]_{\text{D}}^{25} = 11.62$ (c = 1.0, CHCl_3); IR (CHCl_3 ,

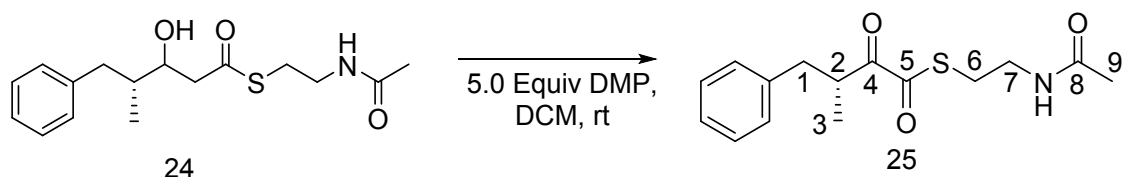
cast): 3337, 2955, 2925, 2872, 1495, 1453 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.32 – 7.30 (m, 2H, ArH), 7.22 – 7.20 (m, 3H, ArH), 3.57 – 3.47 (m, 2H, H4), 2.79 (dd, J = 13.0, 6.0 Hz, 1H, H1a), 2.45 (dd, J = 13.3, 8.0 Hz, 1H, H1b), 1.99 – 1.95 (m, 1H, H2), 1.83 (br s, 1H, OH), 0.94 (d, J = 7.0 Hz, 3H, H3); ^{13}C NMR (125 MHz, CDCl_3) δ 140.6 (ArC), 129.1 (ArC), 128.2 (ArC), 125.9 (ArC), 67.6 (C4), 39.7 (C1), 37.8 (C2), 16.4 (C3); HRMS (EI) Calcd for $\text{C}_{10}\text{H}_{14}\text{O}$ [M^+] 150.1045, found 150.1045.



Preparation of SC43. This new compound was prepared following a modified literature protocol.⁵ Oxalyl chloride (1.01 mL, 12.0 mmol) in 50 mL of dry DCM was cooled to $-78\text{ }^\circ\text{C}$ and a solution of DMSO (dried over 4 \AA MS, 1.13 mL, 16.0 mmol) in 20 mL dry DCM was added dropwise. After 30 min at $-78\text{ }^\circ\text{C}$, a solution of **SC42** (0.600 g, 3.99 mmol) in 5 mL of DCM was added dropwise and stirred at $-78\text{ }^\circ\text{C}$ for another 20 min. Diisopropylethylamine (DIPEA; dried over 4 \AA MS, 7.59 mL, 59.9 mmol) was added dropwise and the temperature was maintained for 20 min then warmed to $-50\text{ }^\circ\text{C}$ for 60 min. The reaction mixture was quenched with 10 mL of saturated NH_4Cl and allowed to warm to room temperature. The layers were separated and the organic was washed with 10 mL of saturated NaHCO_3 and brine before drying on Na_2SO_4 . The solvent was removed and the crude aldehyde was used immediately in the next step. A solution of the compound **SC4** (0.500 g, 3.10 mmol) in 50 mL of dry DCM was charged with TiCl_4 (3.41 mL, 3.41 mmol) at $-78\text{ }^\circ\text{C}$. After 15 min at $-78\text{ }^\circ\text{C}$, DIPEA (0.470 mL, 3.72 mmol) was added dropwise and a colour change was noted from bright orange-red to a deep red-brown. The reaction mixture was allowed to stir for 1 h then a solution of the crude aldehyde (0.460 g, 3.41 mmol) in 5 mL of dry DCM was added dropwise. After 1 h at $-78\text{ }^\circ\text{C}$, the reaction mixture was quenched with 10 mL of saturated NH_4Cl and allowed to warm to room temperature. Separation of the layers and extraction of the aqueous layer with DCM (3 x 10 mL) led to the organic layers being pooled, washed with brine and dried on Na_2SO_4 . The reaction mixture was concentrated *in vacuo* and subjected to flash column chromatography (30 % EtOAc/Hexanes), R_f 0.40 (50 % EtOAc in Hexanes); to produce the product **SC43** as a yellow oil, yield (0.64 g, 66 % over two steps). IR (CHCl_3 , cast film): 3529, 3024, 2963, 2931, 1694 cm^{-1} ; ^1H -NMR (500 MHz, CDCl_3): δ 7.29 – 7.26 (m, 2H, ArH), 7.20 – 7.17 (m, 3H, ArH), 4.62 – 4.56 (m, 2H, H7), 4.06 – 3.98 (m, 1H, H4), 3.59 – 3.27 (m, 4H, H5,8), 3.03 – 2.85 (m, 2H, H1a,OH), 2.50 – 2.38 (m, 1H, H1b), 1.99 – 1.87 (m, 1H, H2), 0.94 – 0.87 (m, 3H, H3); ^{13}C -NMR (125 MHz, CDCl_3): δ 201.9 (C9), 174.6 (C6), 140.8 (ArC), 129.3 (ArC), 128.3 (ArC), 125.9 (ArC), 71.5 (C4), 55.7 (C7), 43.6 (C5), 40.3 (C2), 39.6 (C1), 28.4 (C8), 14.0 (C3); HRMS (ES) Calcd for $\text{C}_{15}\text{H}_{19}\text{NO}_2\text{S}_2\text{Na}$ [$\text{M}+\text{Na}$] $^+$ 332.0749, found 332.0752.

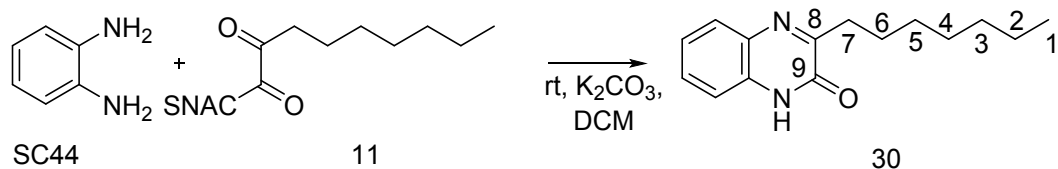


Preparation of 24. This new compound was synthesized by a modified literature protocol.⁴ To a stirred solution of **SC43** (0.600 g, 1.94 mmol) in 20 mL ACN was added K_2CO_3 (0.960 g, 5.82 mmol) and N-acetylcysteamine (0.300 g, 2.52 mmol). The reaction mixture was stirred until the yellow color disappeared 30 min. The solvent was removed *in vacuo* and the residue was purified using flash column chromatography (50 % ethyl acetate in hexanes), R_f = 0.06 (50 % EtOAc in Hexanes) to give **24** as a pale yellow oil (0.42 g, 70 % yield): IR (CHCl_3 , cast film) 3301, 3084, 2965, 2932, 1687, 1557 cm^{-1} ; ^1H NMR (700 MHz, CDCl_3) δ 7.31 – 7.28 (m, 2H, ArH), 7.22 – 7.18 (m, 3H, ArH), 6.16 (br s, 1H, NH), 4.06 – 4.04 (m, 1H, H7), 3.47 – 3.43 (m, 2H, H3), 3.10 – 3.00 (m, 3H, H4, OH), 2.94 – 2.68 (m, 3H, H6,9a), 2.47 – 2.37 (m, 1H, H9b), 1.97 (s, 3H, H1), 1.87 – 1.82 (m, 1H, H8), 0.90 (d, J = 7.0 Hz, 3H, H10); ^{13}C NMR (176 MHz, CDCl_3) δ 199.7 (C5), 170.6 (C2), 140.6 (ArC), 129.2 (ArC), 128.3 (ArC), 125.9 (ArC), 70.8 (C7), 48.8 (C6), 40.6 (C8), 39.2 (C3), 38.6 (C9), 28.9 (C4), 23.1 (C1), 13.5 (C10); HRMS (ESI) calcd for $\text{C}_{16}\text{H}_{23}\text{NNaO}_3\text{S}$ $[\text{M}+\text{Na}]^+$ 332.1291, found 332.1286.



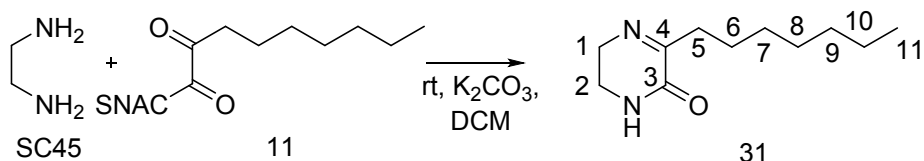
Preparation of 25. This new compound was prepared by the following method. To a round bottom flask was added **24** (10.0 mg, 0.030 mmol) followed by 20 mL of DCM. The DMP (68.5 mg, 0.160 mmol) was then added then stirred for 4 h. The reaction was quenched with 1:1 Na_2SO_3 / NaHCO_3 (10 mL). The mixture was extracted with Et_2O (3 x 10 mL), and the combined organic layers were washed with saturated sodium bicarbonate (3 x 10 mL), then dried over brine and Na_2SO_4 , filtered, and concentrated *in vacuo*. The resulting yellow residue was purified by flash chromatography using an eluent system of hexane/ethyl acetate (50:50) to afford the product **25** as a yellow oil of R_f 0.11 (50 % Ethyl Acetate in hexanes) (5.71 mg, 60 % yield); $[\alpha]_{\text{D}}^{25}$ = -26.90 (c = 0.633, CHCl_3); IR (CHCl_3 Cast Film) 3411.96, 3295.36, 3085.62, 3064.09, 3028.14, 2972.65, 2934.37, 2876.66, 1719.99, 1676.13 cm^{-1} ; ^1H NMR (500 MHz CDCl_3) δ 7.29 – 7.28 (m, 2H, ArH), 7.21 – 7.15 (m, 3H, ArH), 5.74 (s, 1H, NH), 3.65 – 3.60 (sextet, J = 5 Hz, 1H, H2), 3.44–3.40 (m, 2H, H7), 3.08 – 3.06 (m, 2H, H6), 3.04 – 3.01 (dd, J = 9.5, 5.5 Hz, 1H, H1a), 2.64 – 2.61 (dd, J = 9.5, 5 Hz, 1H, H1b), 1.96 (s, 3H, H9), 1.14 – 1.1 (d, J = 5 Hz, 3H, H3); ^{13}C NMR (126 MHz CDCl_3) δ 197.7 (C4), 191.2 (C5), 171.0 (C8), 129.2 (ArC), 128.5 (ArC), 126.6 (ArC), 41.6 (C2), 38.9 (C7), 38.4 (C1), 31.6 (C9), 28.2 (C6), 15.5 (C3); HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{19}\text{NNaO}_3\text{S}$ $[\text{M}+\text{Na}]^+$ 316.0978, found 316.0977.

Preparation of Quinoxalinones



Scheme 16 Showing the preparation of quinoxalinone **30**

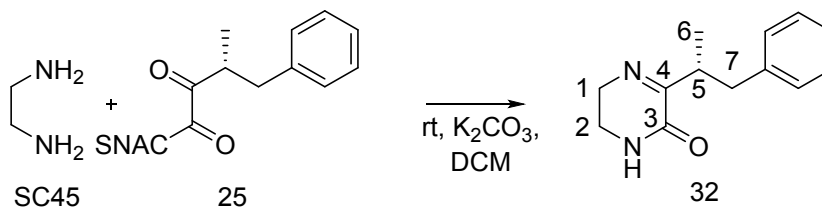
Preparation of 30. This new compound was prepared by the following method. To a vial containing 5 mL of dry DCM was added **11** (20.0 mg, 0.069 mmol), followed by **SC44** (14.9 mg, 0.138 mmol), then potassium carbonate (28.7 mg, 0.207 mmol). The reaction mixture was then stirred at room temperature for 12 h. The reaction mixture was quenched by addition of 1 M HCl to pH 5. The layers were separated and the aqueous layers was washed with DCM (2 x 5 mL). The organic layers were pooled and washed with water, then brine, then dried over magnesium sulphate. The solvent was removed *in vacuo* to produce **30** as an orange/brown solid of R_f 0.76 (80 % Ethyl Acetate in hexanes) (14.3 mg, 85 % yield); IR (CHCl₃ Cast Film) 3011.52, 2955.84, 2914.99, 2884.26, 1667.68 cm⁻¹; ¹H NMR (500 MHz CDCl₃) δ 7.84 – 7.82 (d, J = 8 Hz, 1H, ArH), 7.48 – 7.45 (t, J = 7 Hz, 1H, ArH), 7.34 – 7.31 (t, J = 7 Hz, 1H, ArH), 7.22 – 7.21 (d, J = 8 Hz, 1H, ArH), 2.97 – 2.94 (t, J = 8 Hz, 2H, H7), 1.85 – 1.79 (p, J = 15, 7.5 Hz, 2H, H6), 1.49 – 1.43 (m, 2H, H5), 1.42 – 1.35 (m, 2H, H4), 1.33 – 1.27, (m, 4H, H2,3), 0.90 – 0.84 (t, J = 7 Hz, 3H, H1); ¹³C NMR (126 MHz CDCl₃) δ 162.3 (C9), 155.8 (C8), 132.8 (ArC), 130.8 (ArC), 129.6 (ArC), 128.9 (ArC), 124.1 (ArC), 115.1 (ArC), 33.7 (C7), 31.8 (C5), 29.6 (C4), 29.2 (C3), 26.9 (C2), 22.8 (C6), 14.1 (C1); HRMS (ESI) calcd for C₁₅H₁₉N₂O 243.1503 [M-H]⁻, found 243.1503.



Scheme 17 Showing the preparation of quinoxalinone **31**

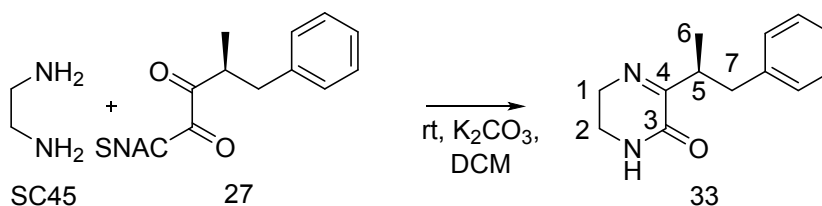
Preparation of 31. This new compound was prepared by the following method. To a vial containing 5 mL of dry DCM was added **11** (50.0 mg, 0.173 mmol), followed by **SC45** (20.8 mg, 0.346 mmol), then potassium carbonate (71.6 mg, 0.518 mmol). The reaction mixture was then stirred at room temperature for 12 h. The reaction mixture was quenched by addition of 1 M HCl to pH 5. The layers were separated and the aqueous layers was washed with DCM (2 x 5 mL). The organic layers were pooled and washed with water, then brine, then dried over magnesium sulphate. The solvent was removed *in vacuo* to produce **31** as a yellow oil of R_f 0.10 (50 % Ethyl Acetate in hexanes) (30.2 mg, 89 % yield); IR (CHCl₃ Cast Film) 3219, 3076, 2955, 2926, 2855, 1689, 1632 cm⁻¹; ¹H NMR (700 MHz

CDCl₃) δ 3.75 (t, J = 6.3 Hz, 2H, H1), 3.44 – 3.41 (m, 2H, H2), 2.59 (t, J = 7.7 Hz, 2H, H5), 1.60 – 1.55 (m, 2H, H6), 1.36 – 1.25 (m, 8H, H7,8,9,10), 0.86 (t, J = 13.3 Hz, 3H, H11); ¹³C NMR (126 MHz CDCl₃) δ 166.7 (C3), 157.8 (C4), 47.8 (C1), 39.4 (C2), 33.9 (C5), 31.9 (C7), 29.9 (C8), 29.5 (C9), 26.4 (C6), 22.8 (C10), 14.2 (C11); HRMS (ESI) calcd for C₁₁H₂₁N₂O 197.1648 [M+H]⁺, found 197.1648.



Scheme 18 Showing the preparation of quinoxalinone 32

Preparation of 32. This new compound was prepared by the following method. To a vial containing 5 mL of dry DCM was added **25** (16.0 mg, 0.055 mmol), followed by **SC45** (6.57 mg, 0.109 mmol), then potassium carbonate (22.6 mg, 0.164 mmol). The reaction mixture was then stirred at room temperature for 12 h. The reaction mixture was quenched by addition of 1 M HCl to pH 5. The layers were separated and the aqueous layers was washed with DCM (2 x 5 mL). The organic layers were pooled and washed with water, then brine, then dried over magnesium sulphate. The solvent was removed *in vacuo* to produce **32** as an yellow oil of R_f 0.12 (50 % Ethyl Acetate in hexanes) (10.7 g, 91 % yield); [α]_D²⁵ = -4.62 (c = 0.75, CHCl₃); IR (CHCl₃ Cast Film) 3226, 3062, 2967, 2930, 2871, 1686, 1632 cm⁻¹; ¹H NMR (700 MHz CDCl₃) δ 7.17 – 7.15 (m, 2H, ArH), 7.10 – 7.06 (m, 3H, ArH), 6.20 (br s, 1H, NH), 3.67 – 3.63 (m, 2H, H1), 3.41 – 3.39 (m, 1H, H5), 3.27 – 3.24 (m, 2H, H2), 2.92 (dd, J = 13.3, 5.6 Hz, 1H, H7a), 2.51 (dd, J = 13.3, 8.4 Hz, 1H, H7b), 0.99 (d, J = 7.0 Hz, 3H, H6); ¹³C NMR (126 MHz CDCl₃) δ 169.5 (C3), 157.6 (C4), 140.5 (ArC), 129.4 (ArC), 128.3 (ArC), 126.1 (ArC), 47.8 (C1), 40.6 (C7), 39.1 (C2), 37.6 (C5), 17.7 (C6); HRMS (ESI) calcd for C₁₃H₁₇N₂O 217.1335 [M+H]⁺, found 217.1332.



Scheme 19 Showing the preparation of quinoxalinone 33

Preparation of 33. This new compound was prepared by the following method. To a vial containing 5 mL of dry DCM was added **27** (12.0 mg, 0.041 mmol), followed by **SC45** (4.93 mg, 0.082 mmol), then potassium carbonate (17.0 mg, 0.123 mmol). The reaction mixture was then stirred at room temperature for 12 h. The reaction mixture was quenched by addition of 1 M HCl to pH 5. The layers were separated and the aqueous layers was washed with DCM (2 x 5 mL). The organic layers were pooled and washed with water, then brine, then dried over magnesium sulphate. The solvent was removed *in vacuo* to produce **33** as an yellow oil of R_f 0.12 (50 % Ethyl Acetate in hexanes) (7.5 mg, 85 % yield); [α]_D²⁵ = 2.32 (c = 0.75, CHCl₃); IR (CHCl₃ Cast Film) 3289, 3083, 3063, 2966, 2928, 1685, 1631 cm⁻¹; ¹H NMR (700 MHz CDCl₃) δ 7.18 – 7.15 (m, 2H, ArH), 7.10 – 7.06 (m, 3H, ArH), 5.95 (br s,

¹H, NH), 3.67 – 3.63 (m, 2H, H1), 3.41 – 3.39 (m, 1H, H5), 3.26 – 3.23 (m, 2H, H2), 2.92 (dd, *J* = 13.3, 5.6 Hz, 1H, H7a), 2.51 (dd, *J* = 13.3, 8.4 Hz, 1H, H7b), 0.99 (d, *J* = 7.0 Hz, 3H, H6); ¹³C NMR (126 MHz CDCl₃) δ 169.5 (C3), 157.4 (C4), 140.5 (ArC), 129.4 (ArC), 128.3 (ArC), 126.1 (ArC), 47.8 (C1), 40.6 (C7), 39.2 (C2), 37.6 (C5), 17.7 (C6); HRMS (ESI) calcd for C₁₃H₁₇N₂O 217.1335 [M+H]⁺, found 217.1332.

¹H and ¹³C NMR Spectra of all Products and New Compounds



Agilent Technologies

Department of Chemistry, University of Alberta

Recorded on: **u500, Jan 20 2016**
Pulse Sequence: **PRESAT**

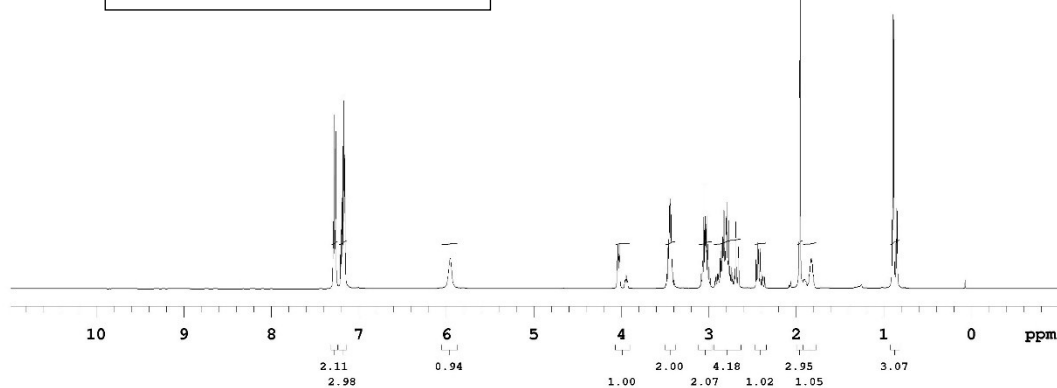
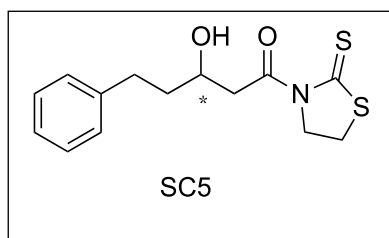
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Digital Res (Hz/pp): **0.18**

Acquisition Time(s): **5**
Hz per mm(Hz/mm): **25.04**

Relaxation Delay(s): **0.1**
Completed Scans: **16**

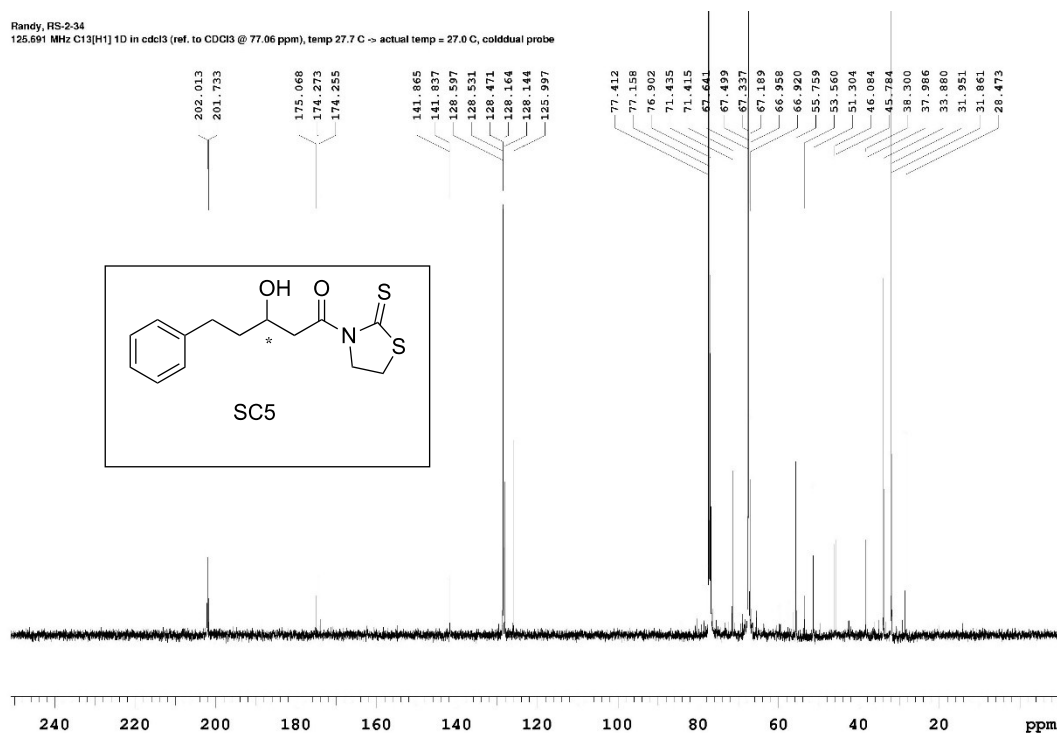
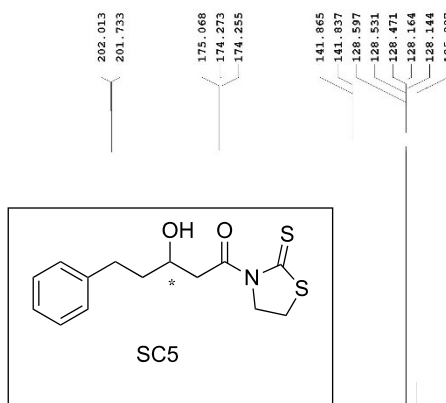
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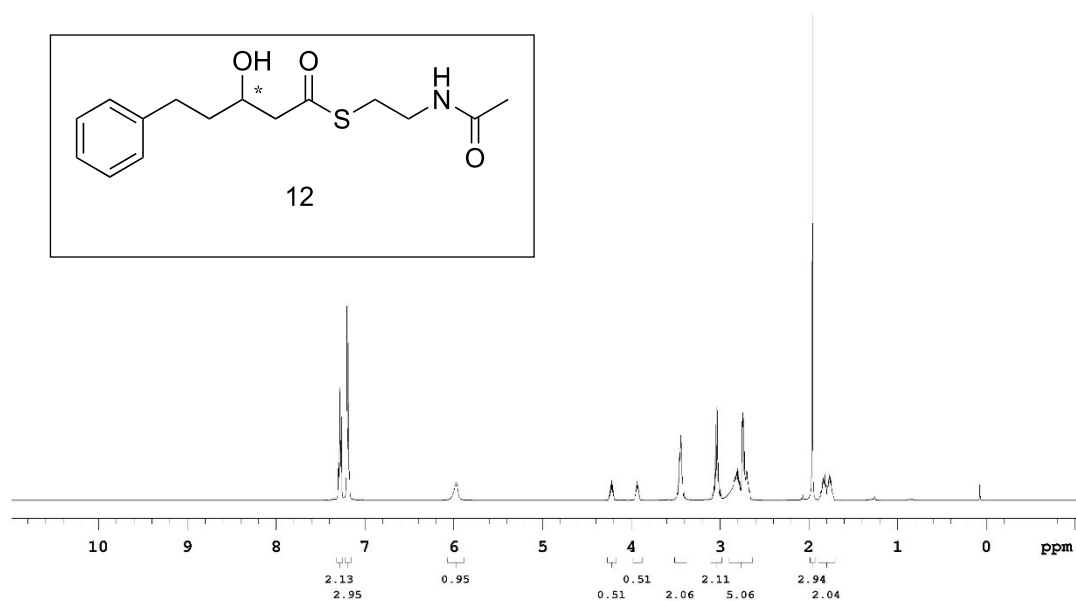


Randy, RS-2-34

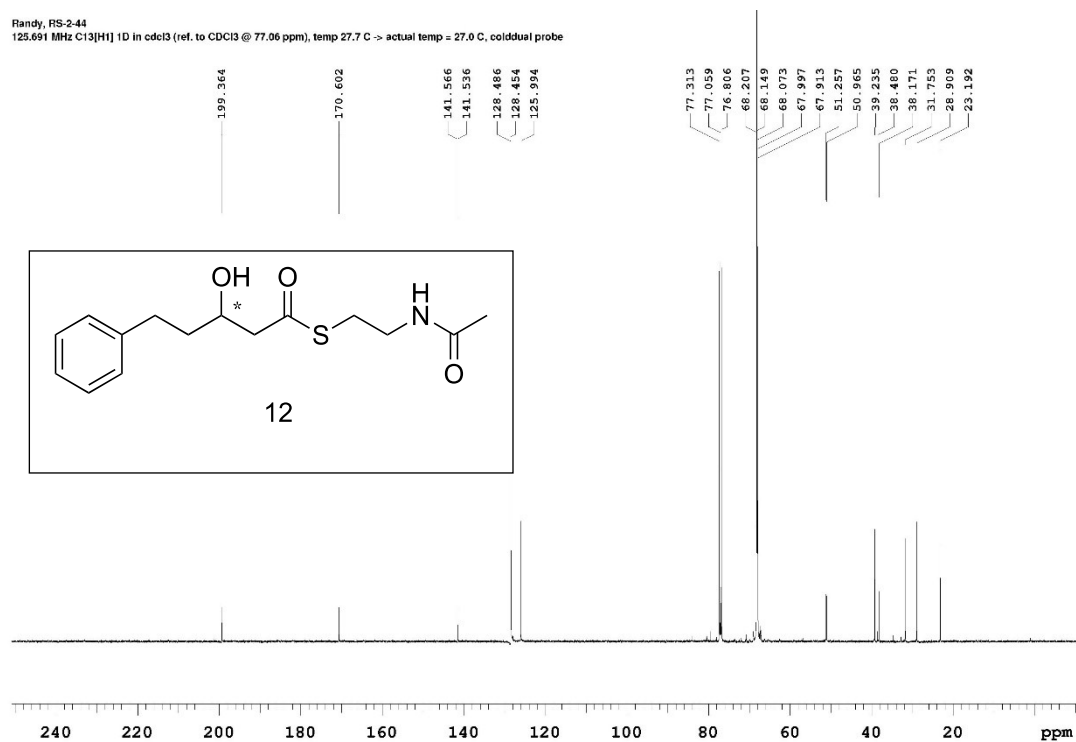
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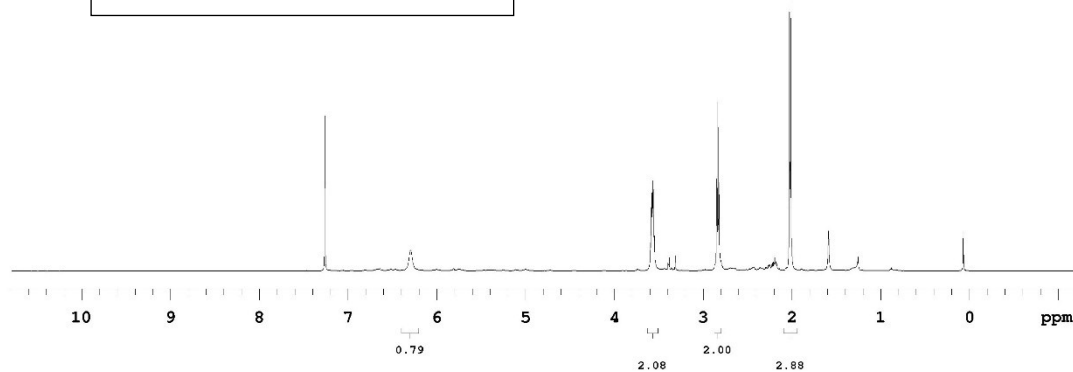
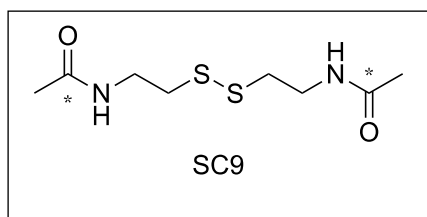
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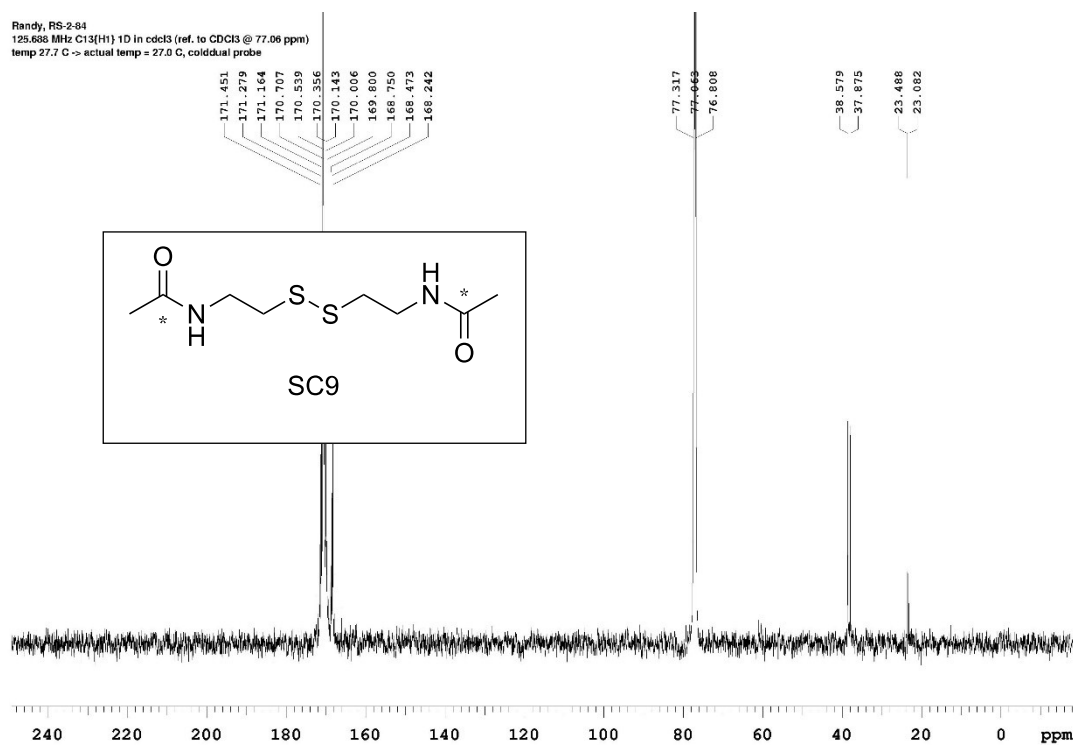
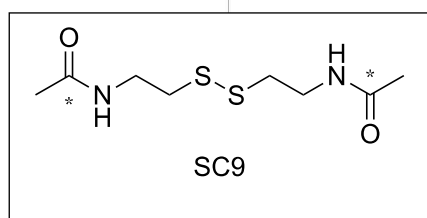
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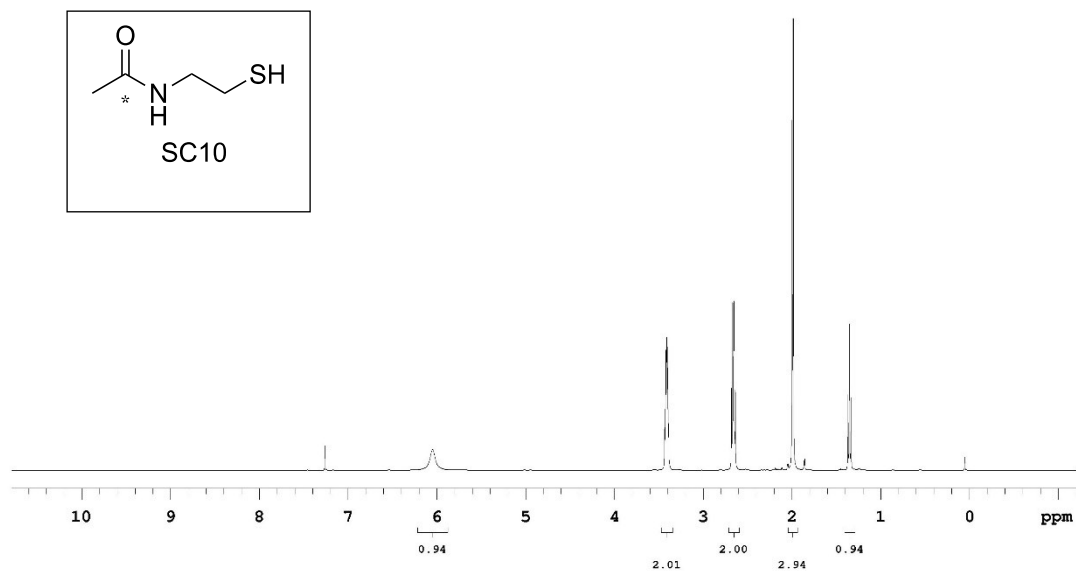
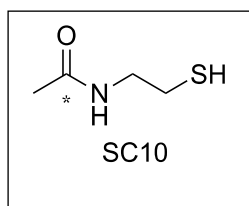
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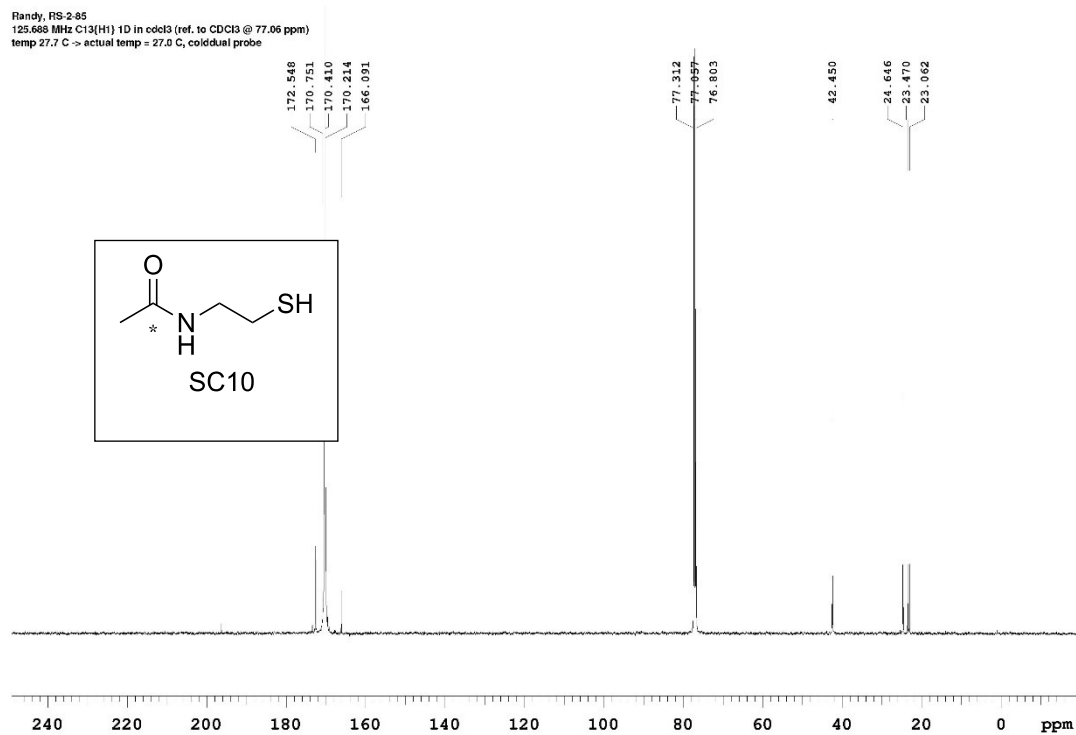
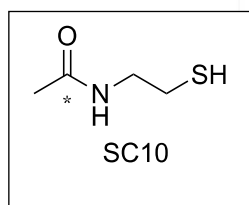
Randy, RS-2-84
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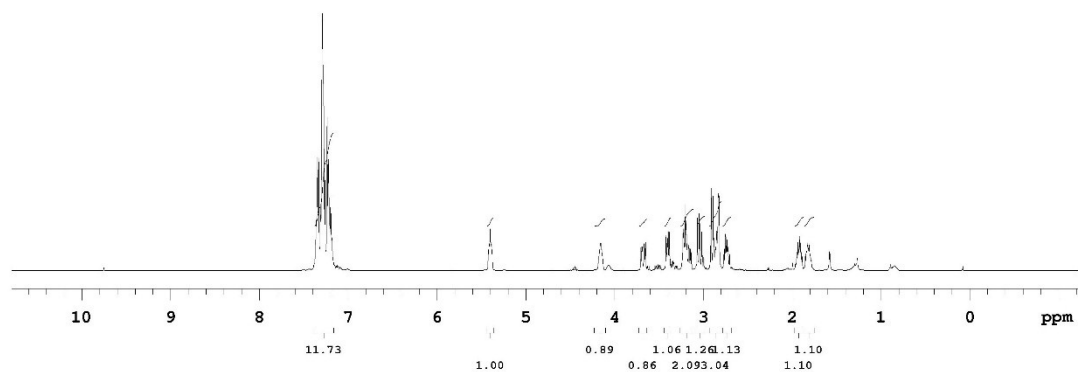
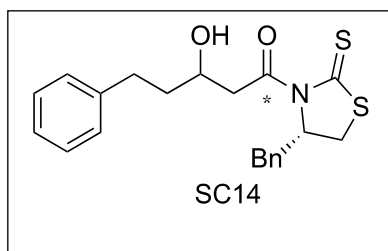
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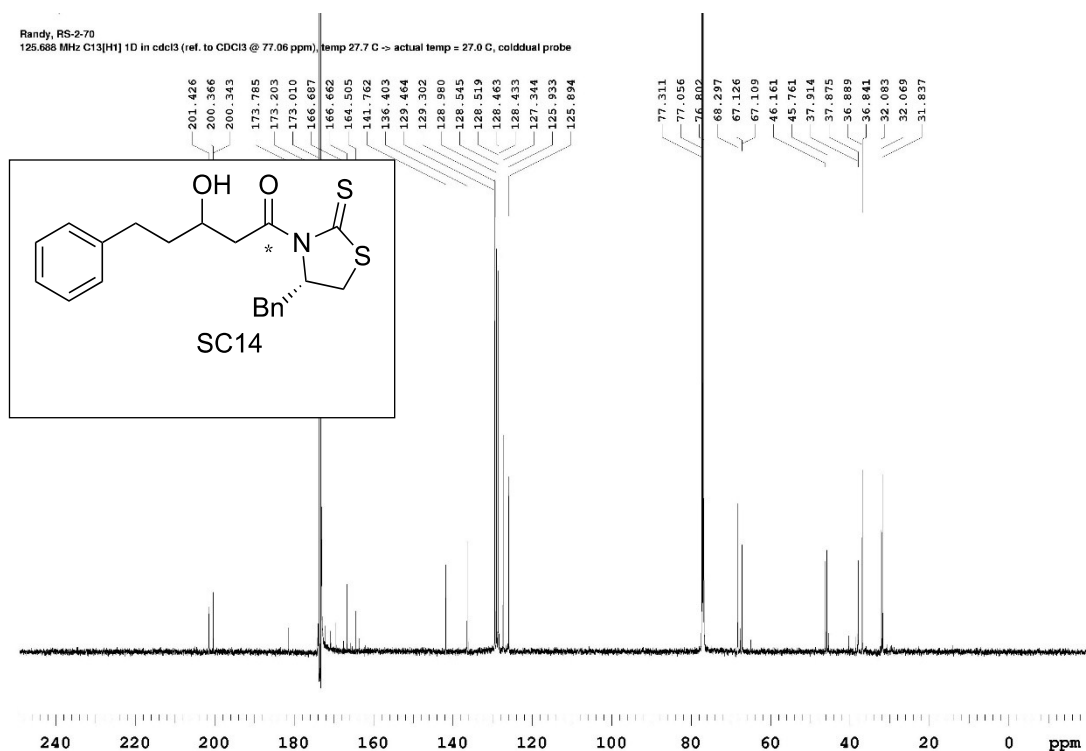
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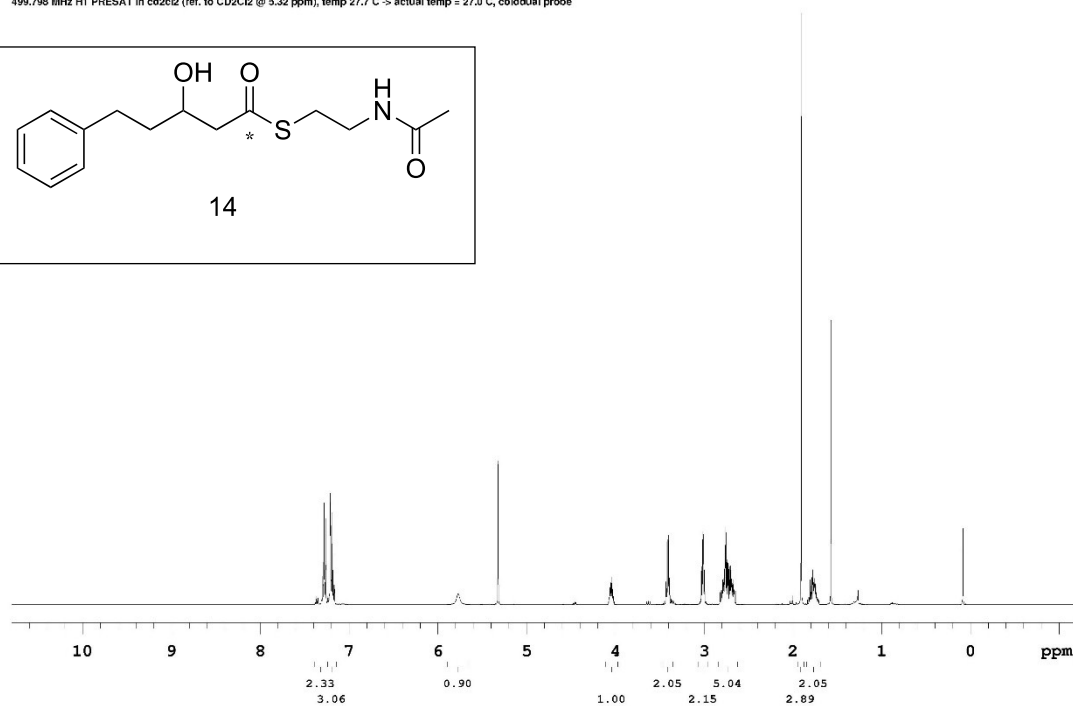
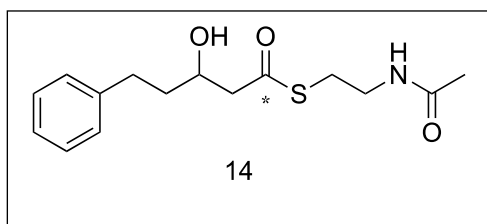
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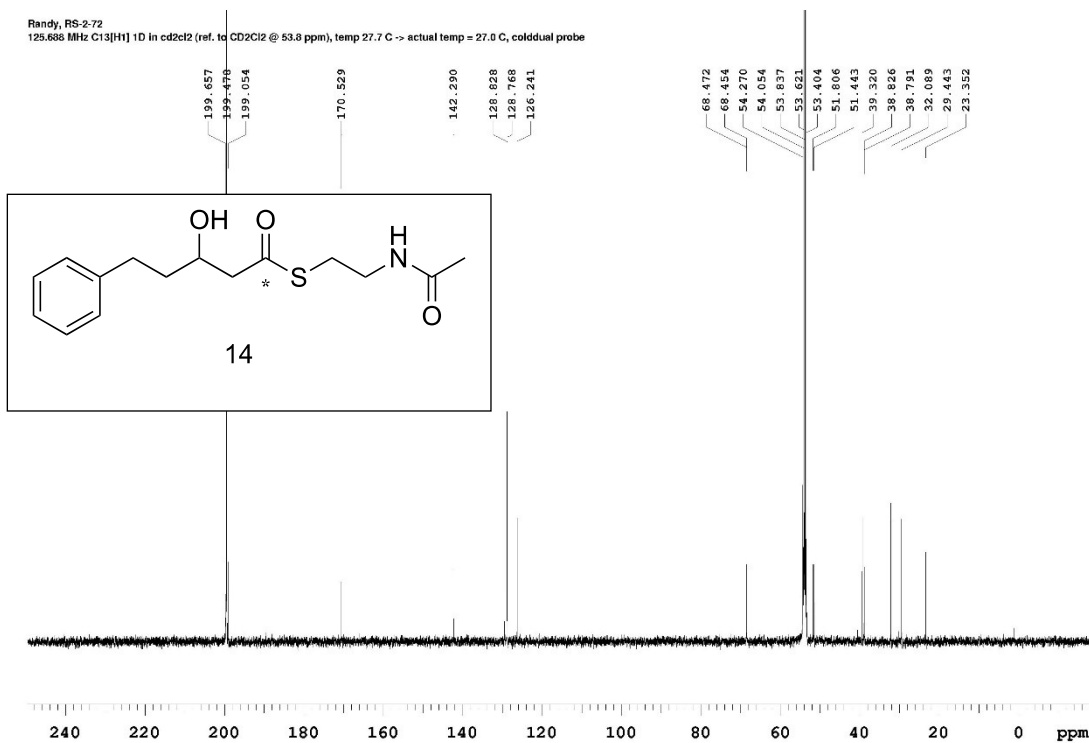
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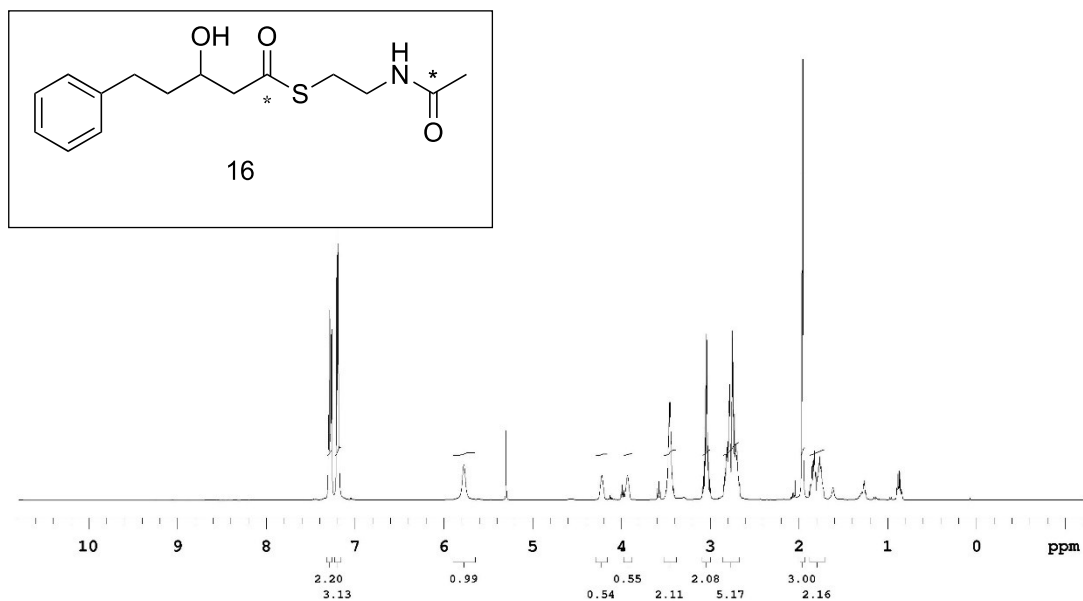
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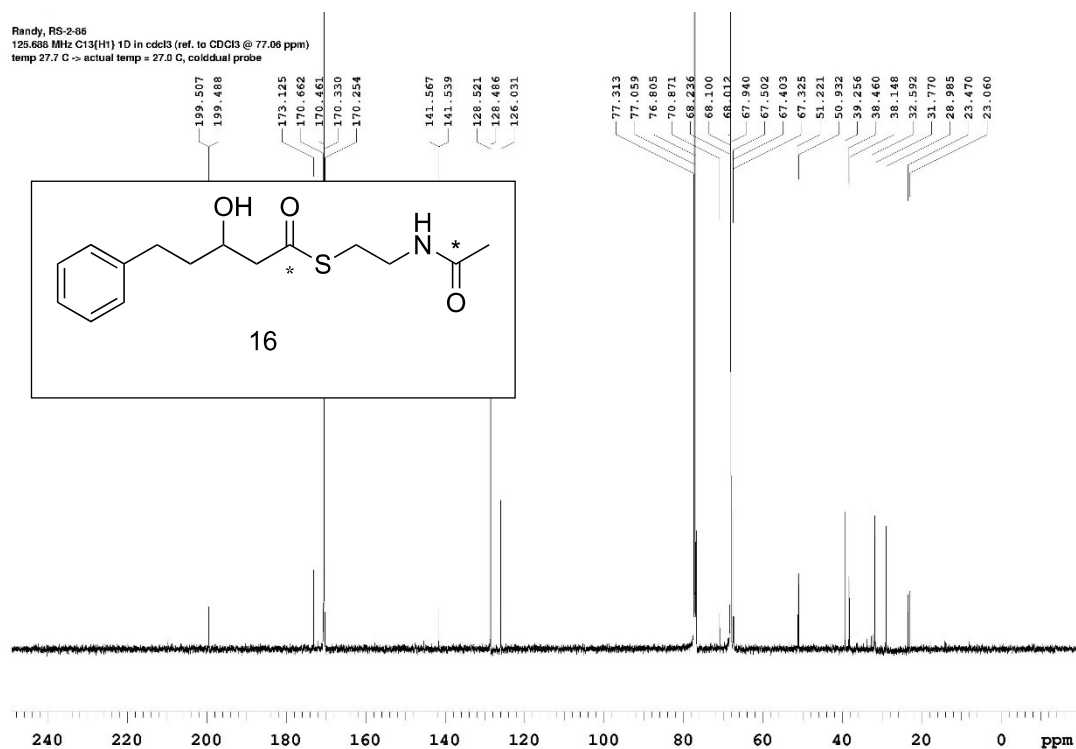
Randy, RS-2-72
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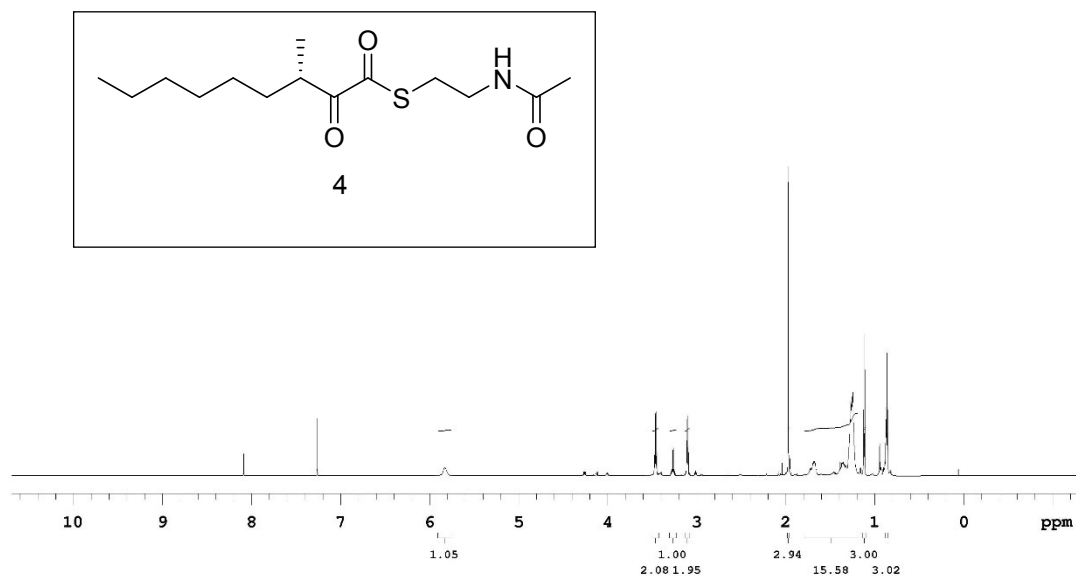
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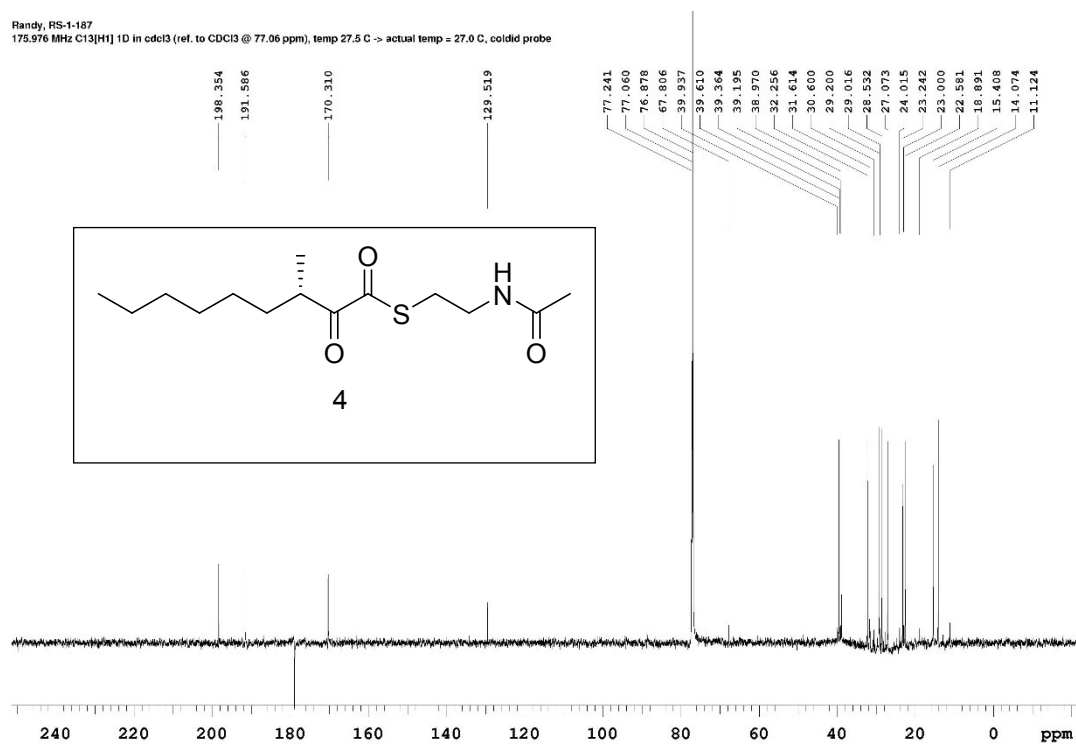
Randy, RS-2-88
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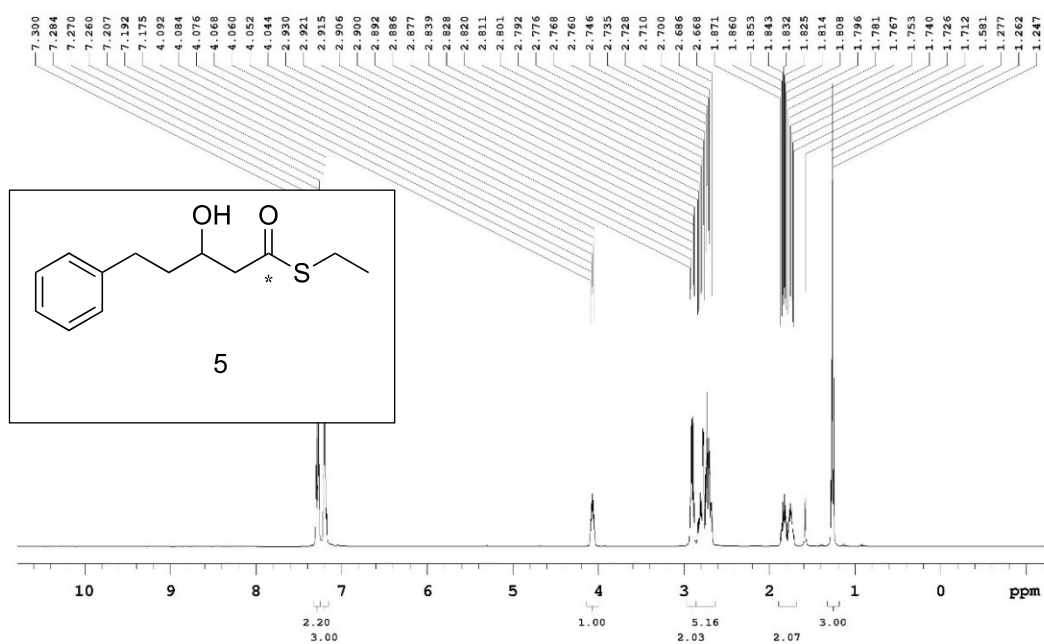
Randy, RS-1-187
 699.769 MHz ¹H PRESAT in cdCl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.5 C -> actual temp = 27.0 C, coldid probe



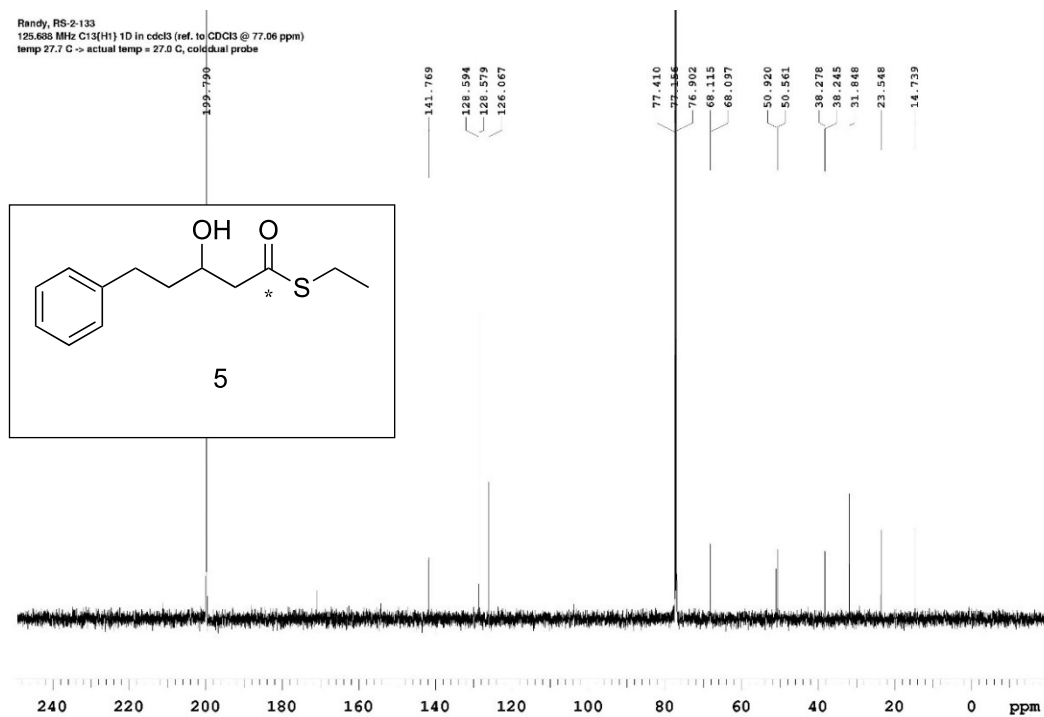
Randy, RS-1-187
 175.976 MHz ¹³C[¹H] 1D in cdCl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.5 C -> actual temp = 27.0 C, coldid probe



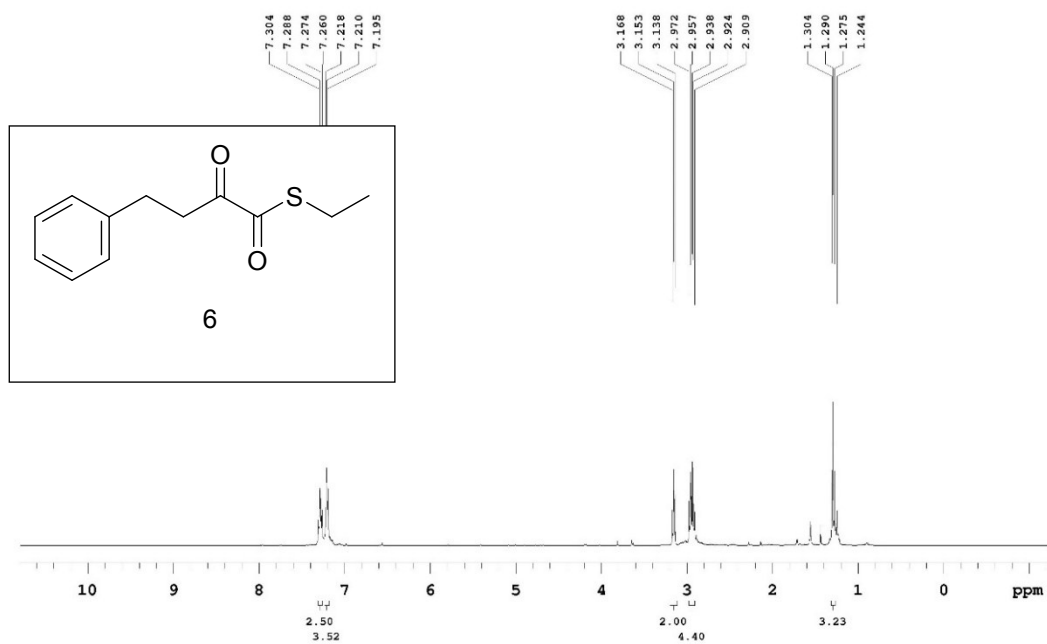
Randy, RS-2-133
499.797 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldlual probe



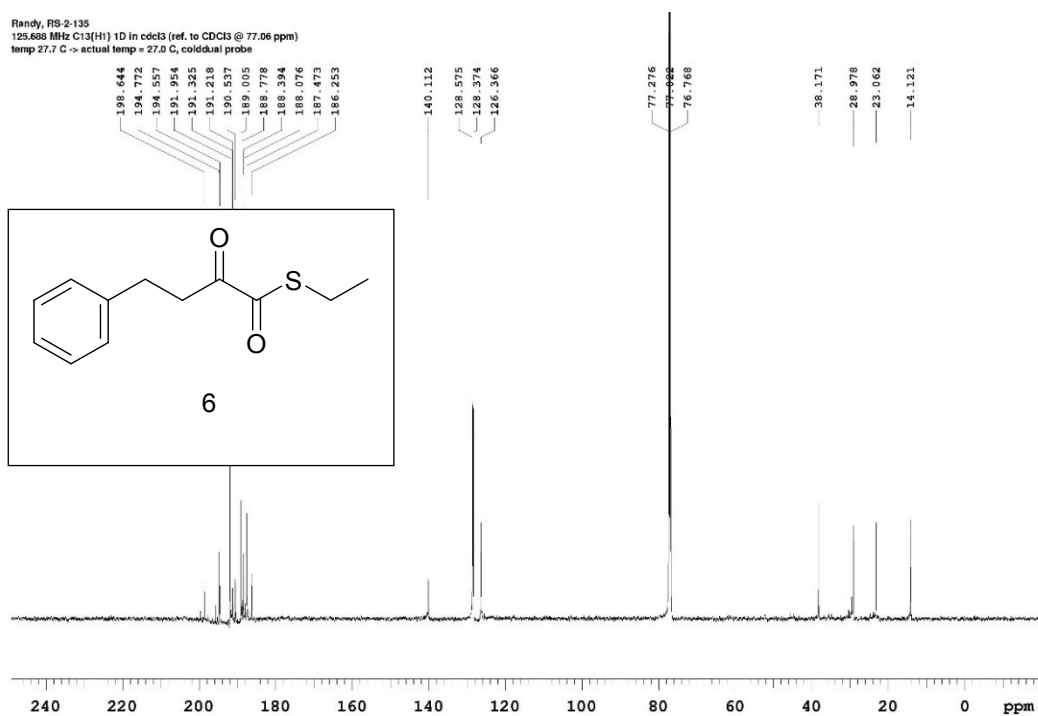
Randy, RS-2-133
125.688 MHz ¹³C 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldlual probe



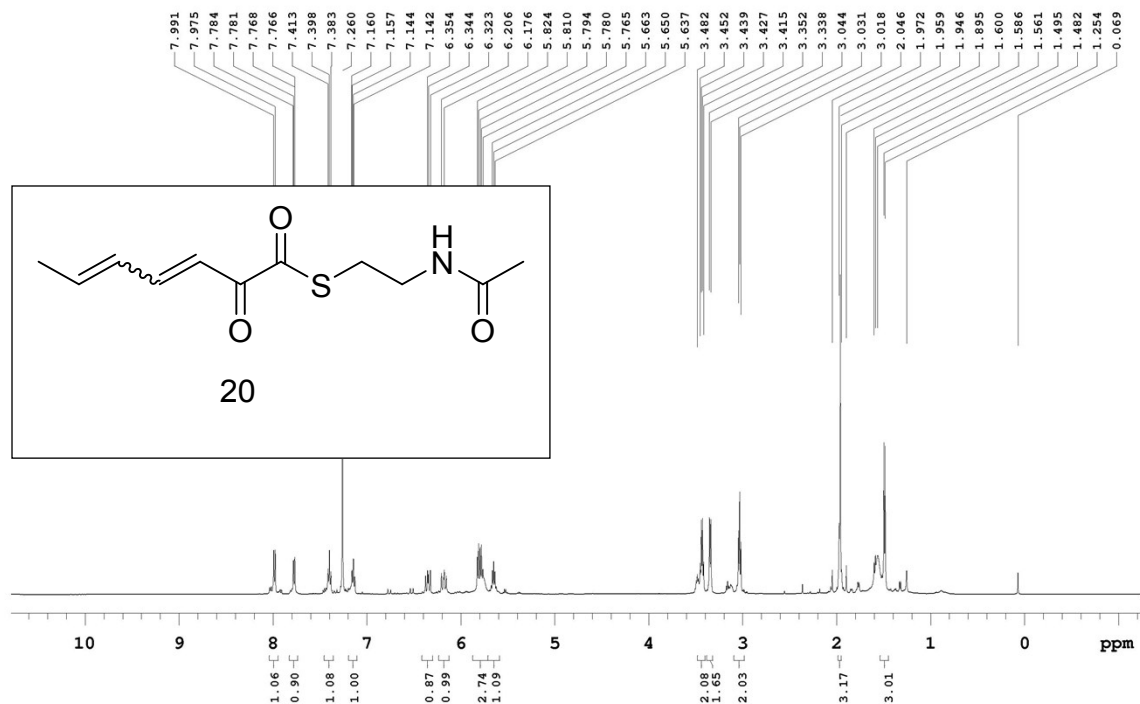
Randy, RS-2-135
499.797 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldchual probe



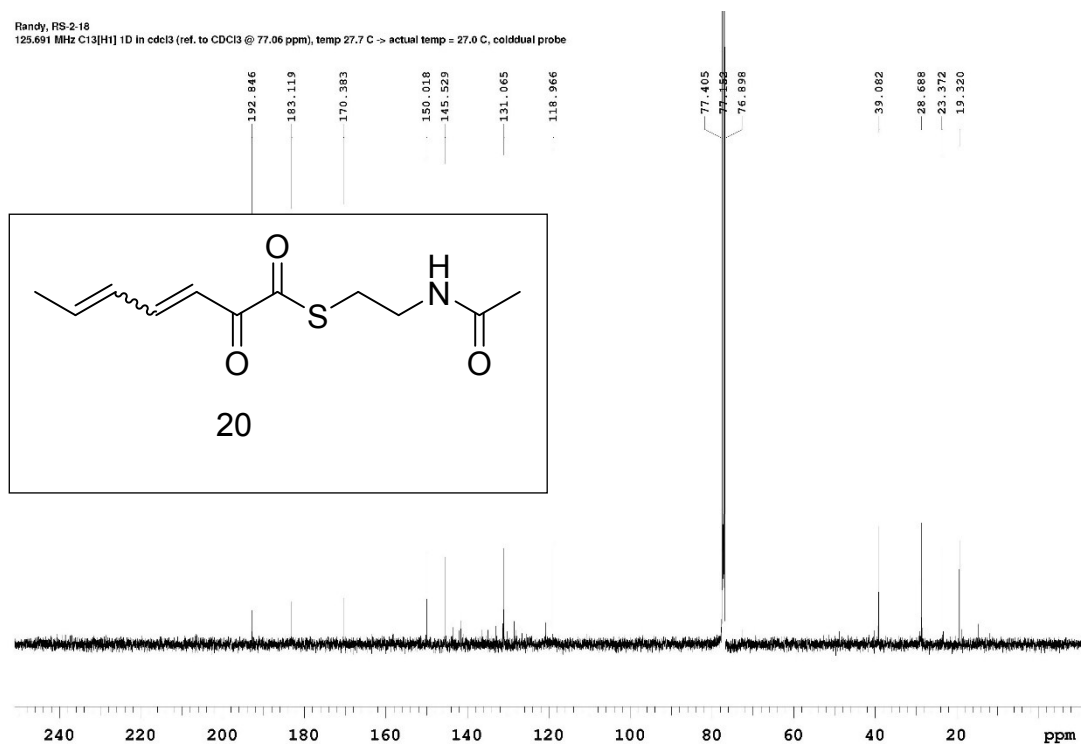
Randy, RS-2-135
125.668 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldchual probe



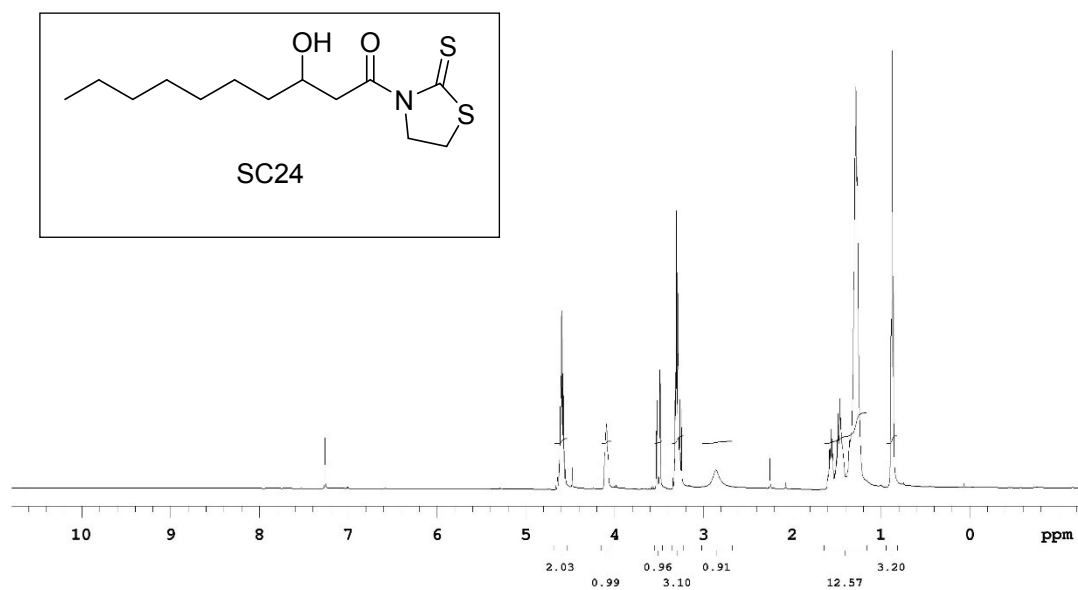
Randy, RS-2-18
499.797 MHz H1 1D in cdcl3 (ref. to CDCl3 @ 7.26 ppm)
temp 27.7 C -> actual temp = 27.0 C, cold dual probe



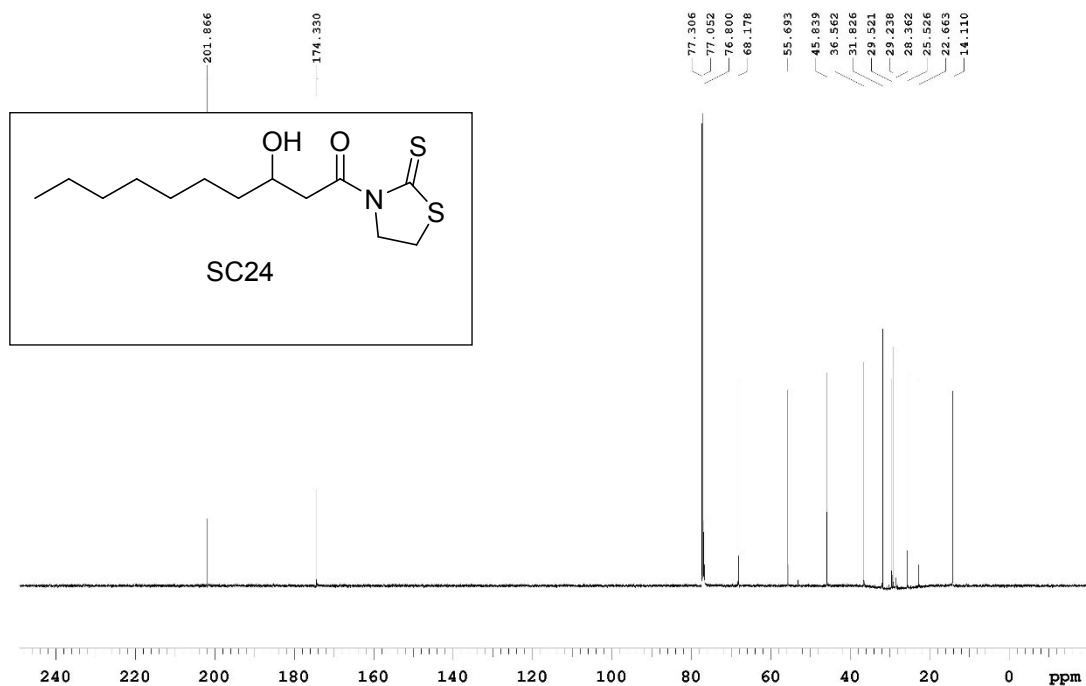
Randy, RS-2-18
125.691 MHz C13[1H] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, cold dual probe



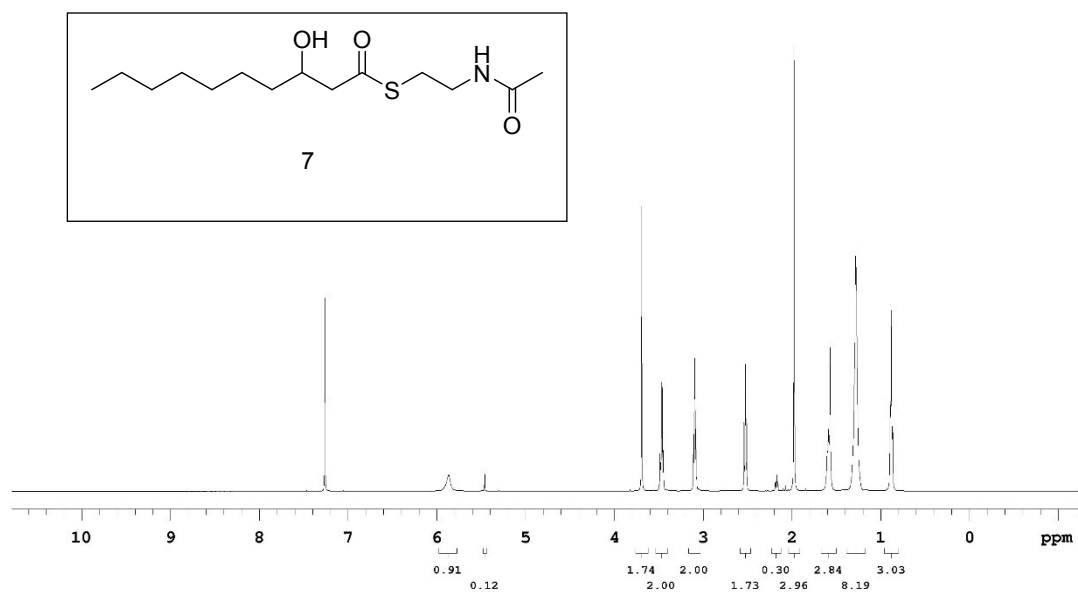
Randy, RS-2-57
499.797 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



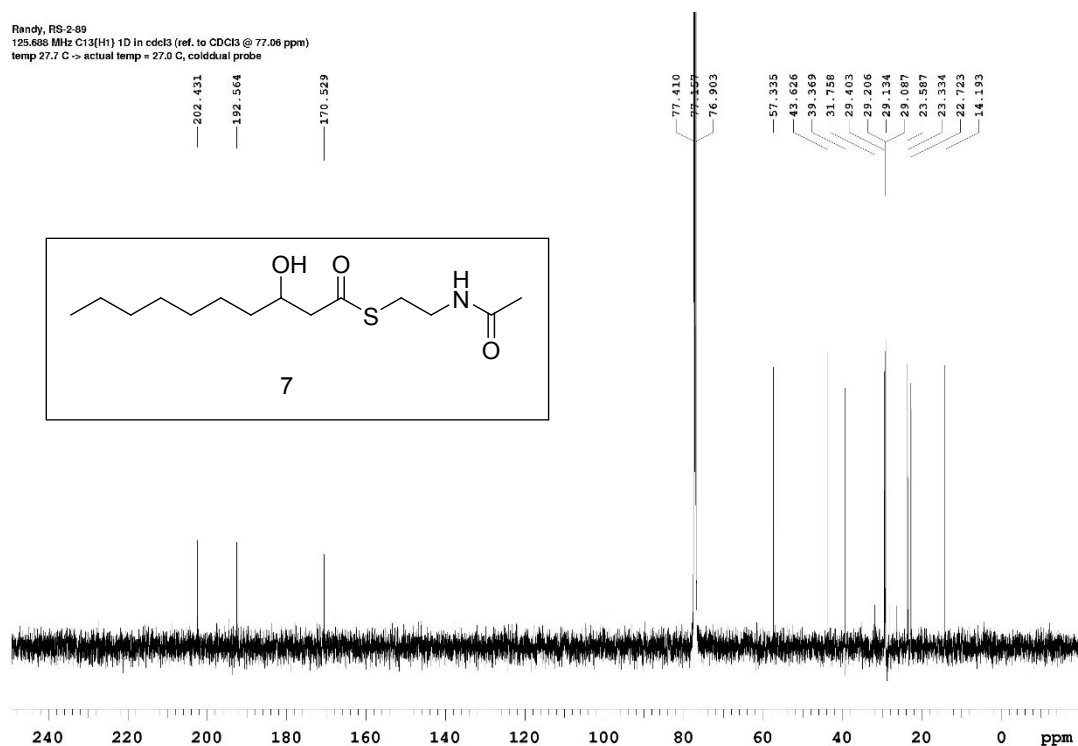
Randy, RS-2-57
125.686 MHz ¹³C[¹H] 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



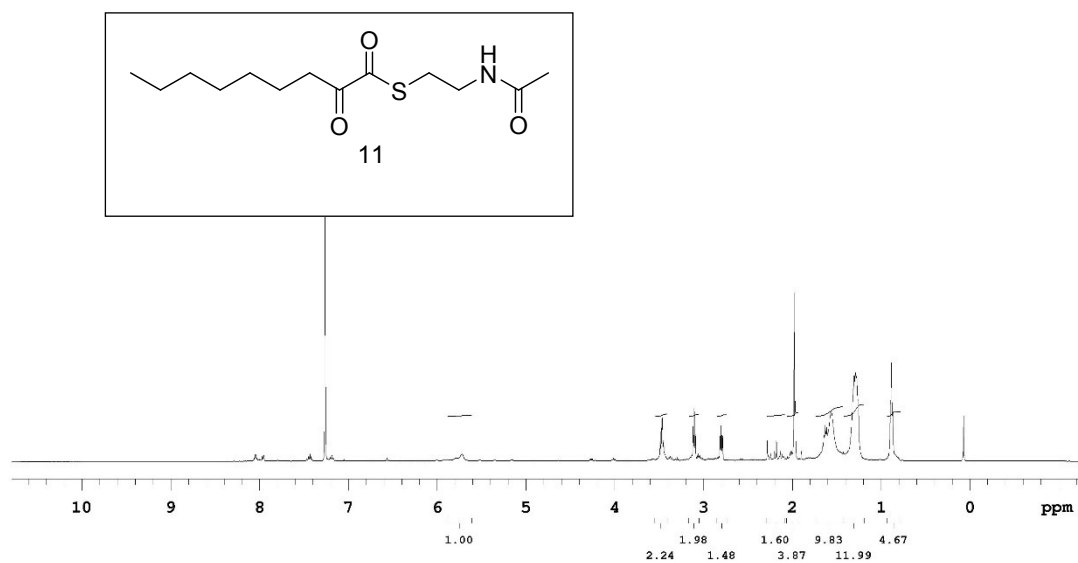
Randy, RS-2-89
499.797 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldlual probe



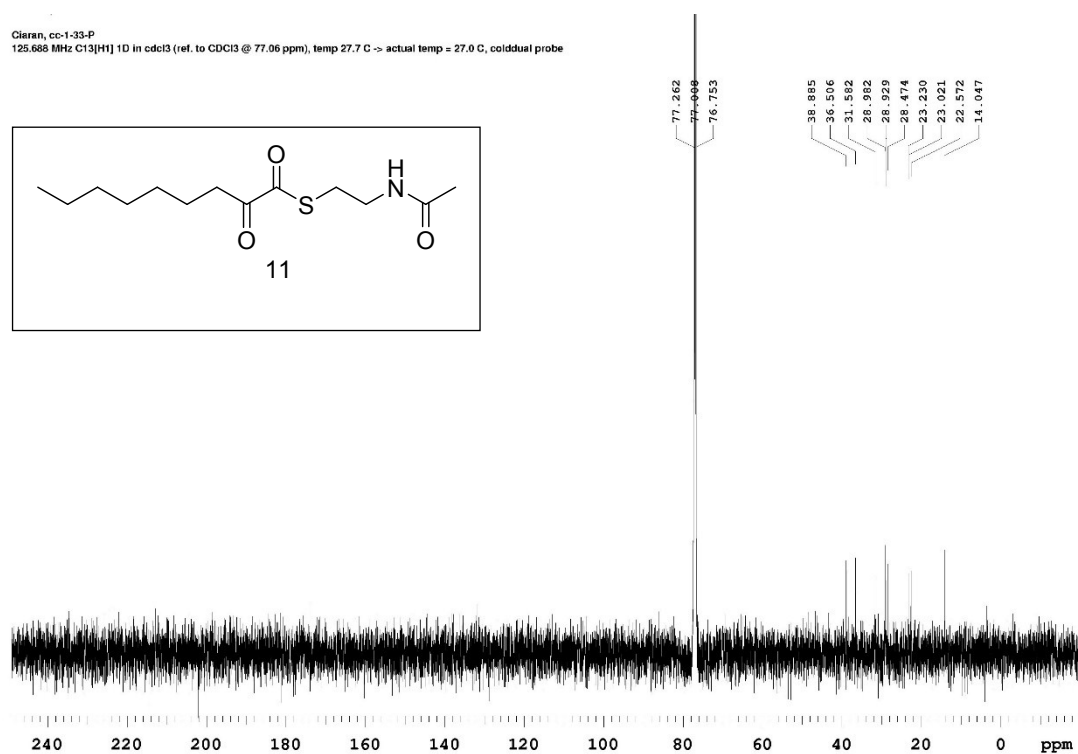
Randy, RS-2-89
125.688 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldlual probe



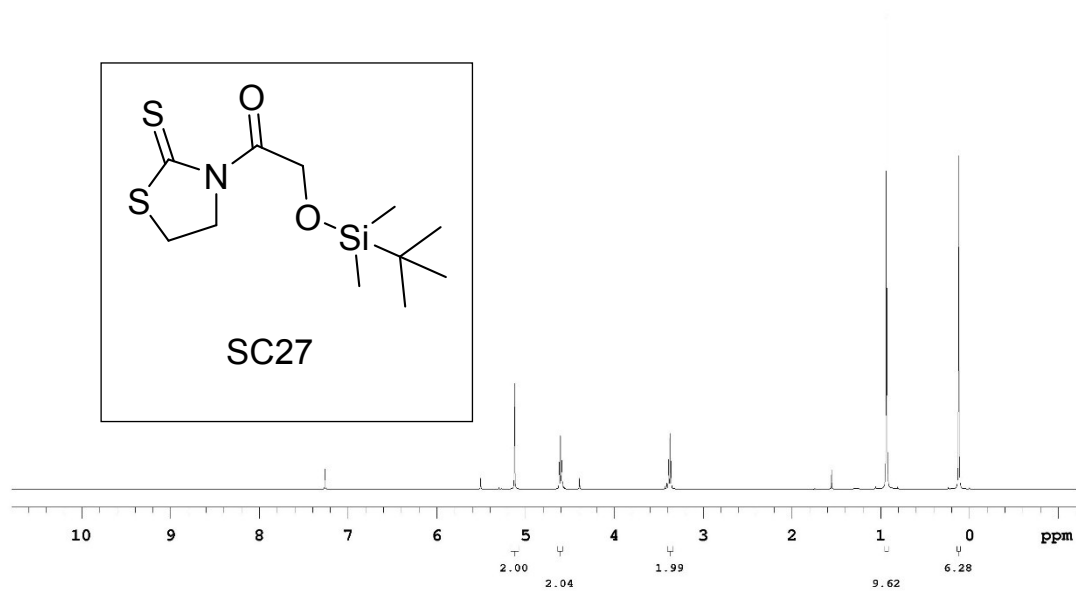
Ciaran, cc-1-33-P
499.797 MHz ¹H PRESAT in cdCl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldual probe



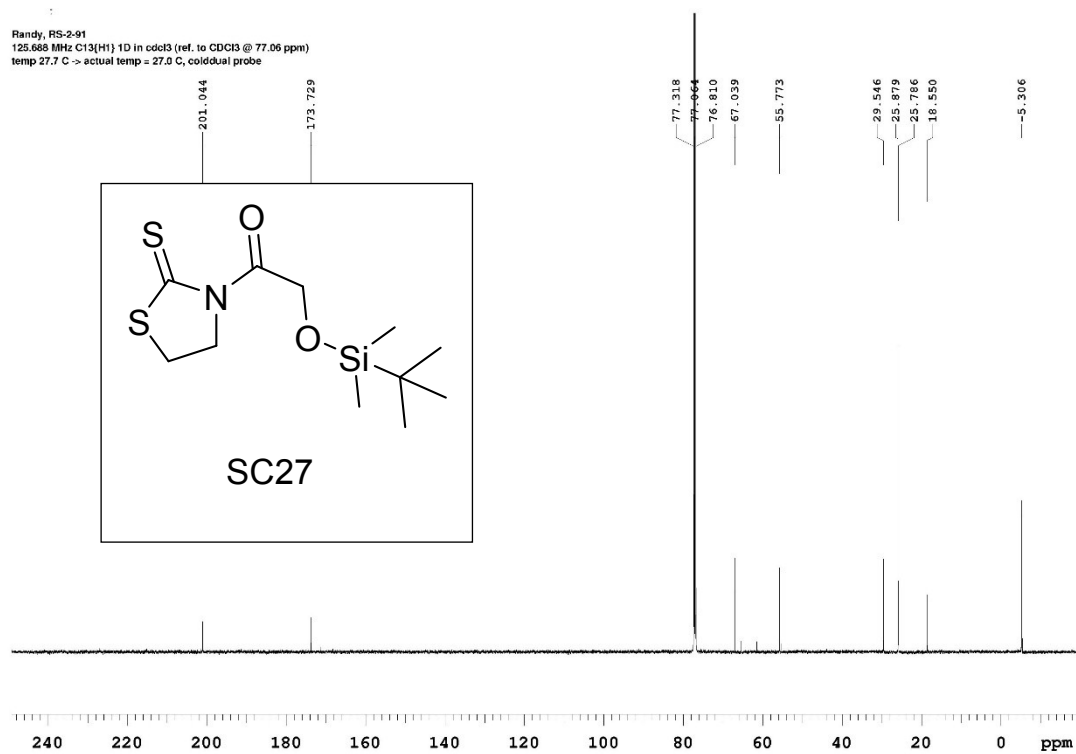
Ciaran, cc-1-33-P
125.688 MHz ¹³C[¹H] 1D in cdCl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldual probe



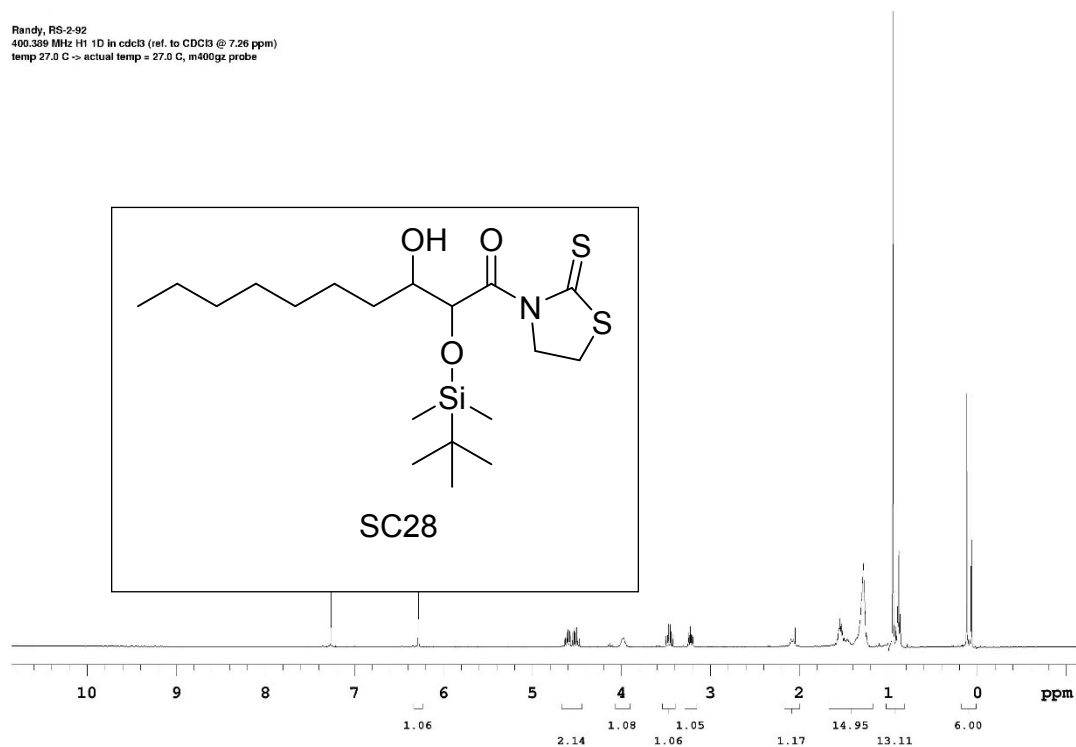
Randy, RS-2-91
 499.797 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
 temp 27.7 C -> actual temp = 27.0 C, coldlual probe



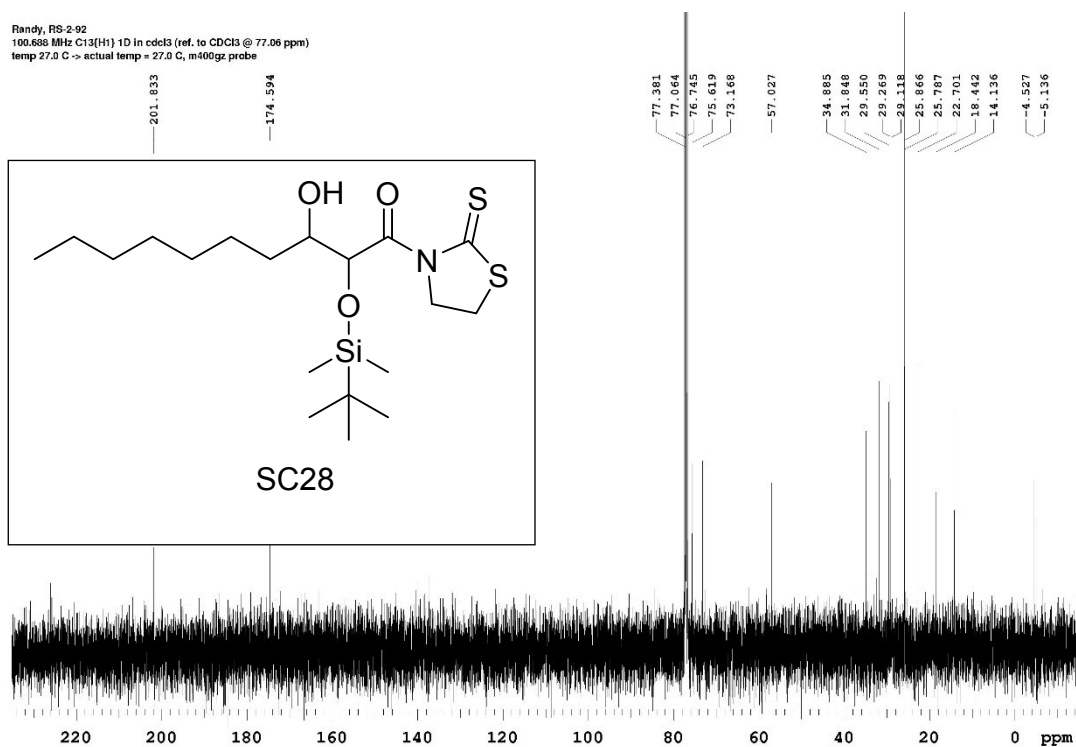
Randy, RS-2-91
 125.688 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
 temp 27.7 C -> actual temp = 27.0 C, coldlual probe



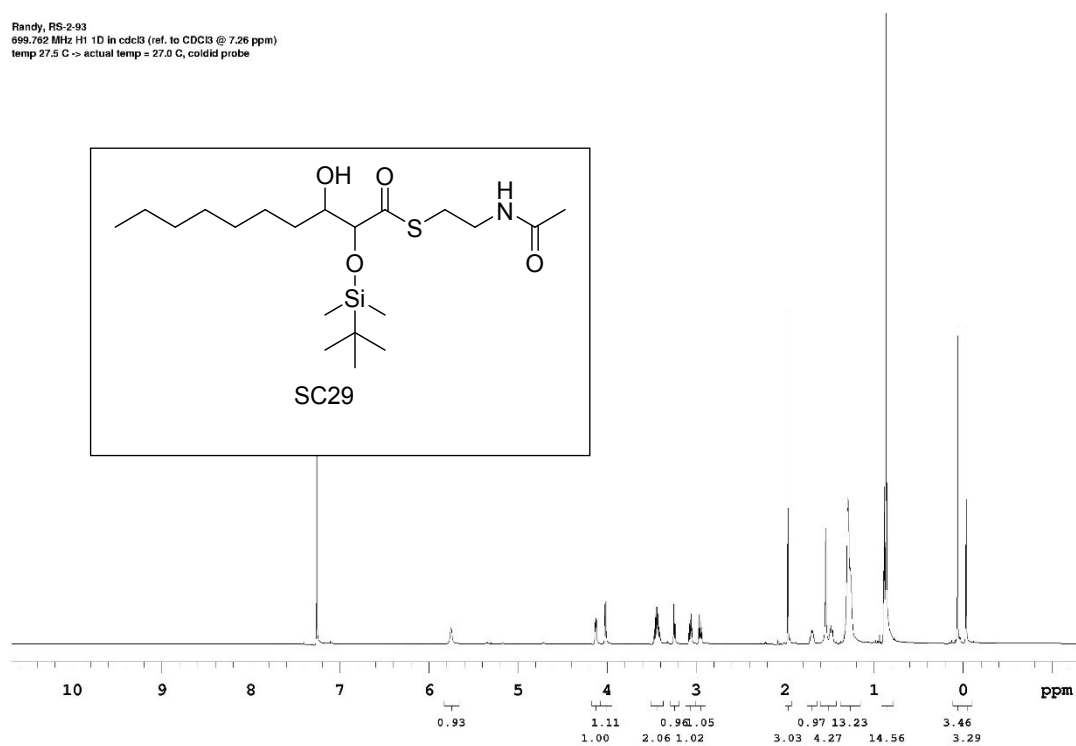
Randy, RS-2-92
400.309 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
temp 27.0 C -> actual temp = 27.0 C, m400gz probe



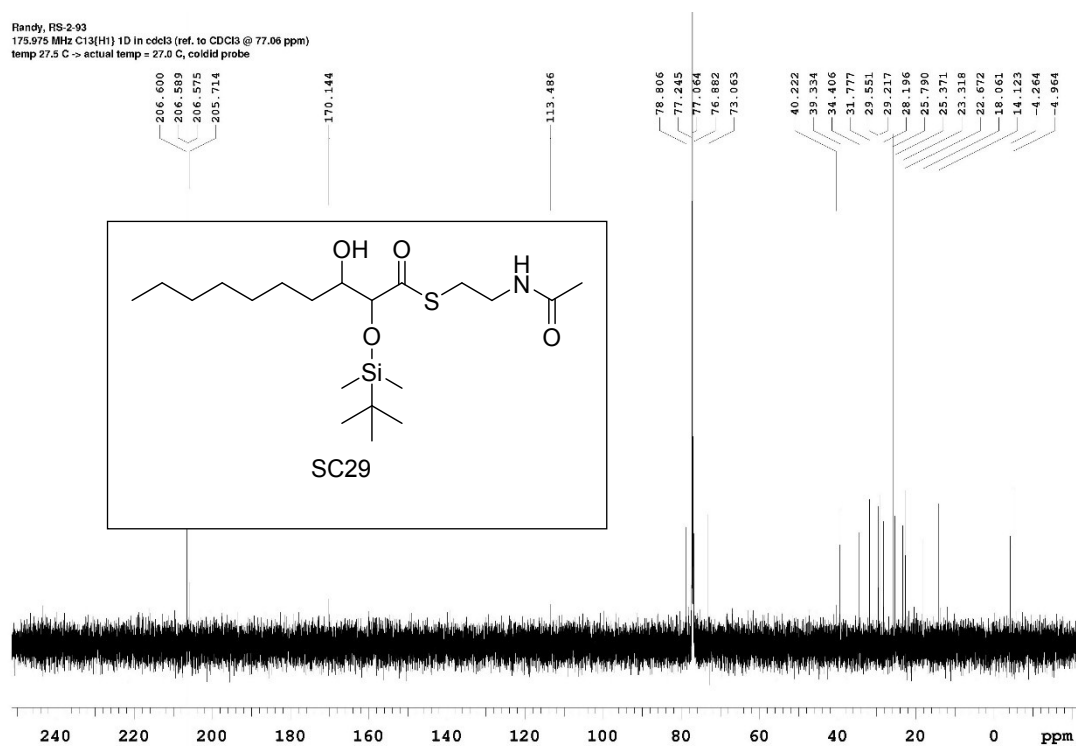
Randy, RS-2-92
100.688 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
temp 27.0 C -> actual temp = 27.0 C, m400gz probe



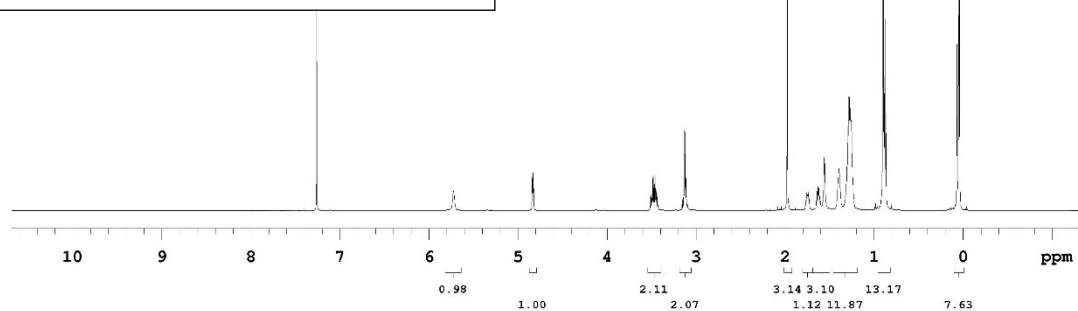
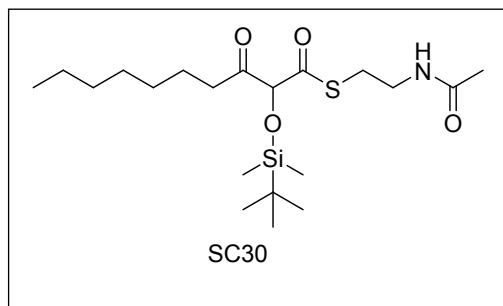
Randy, RS-2-93
 699.762 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
 temp 27.5 C -> actual temp = 27.0 C, coldid probe



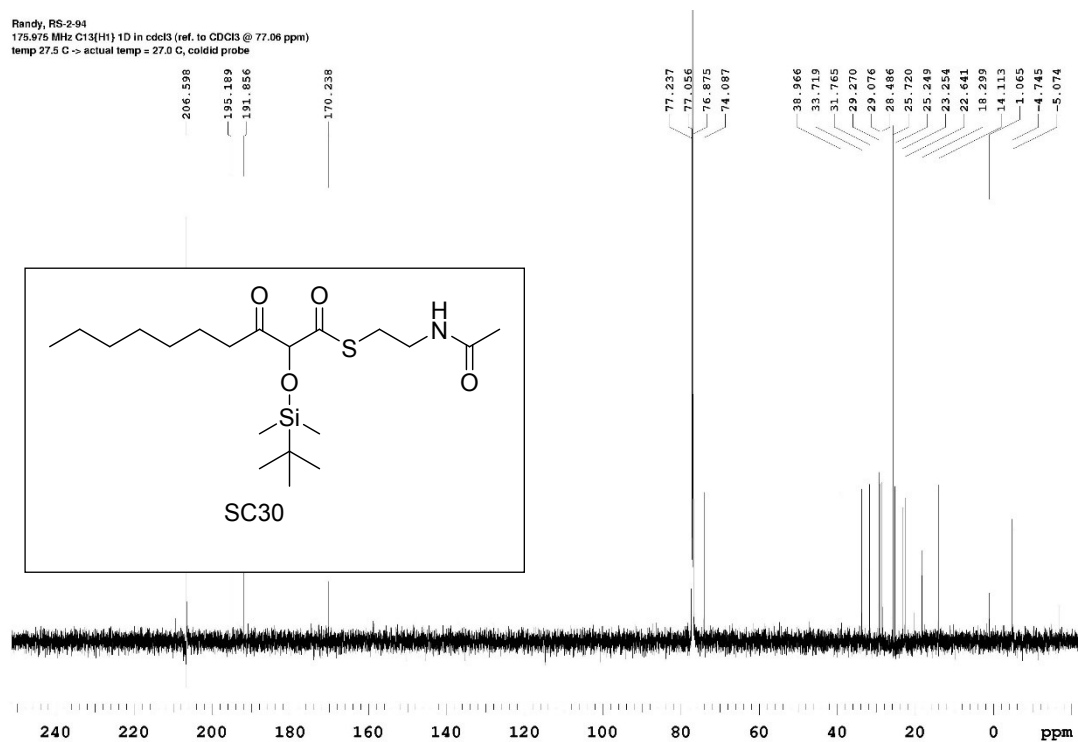
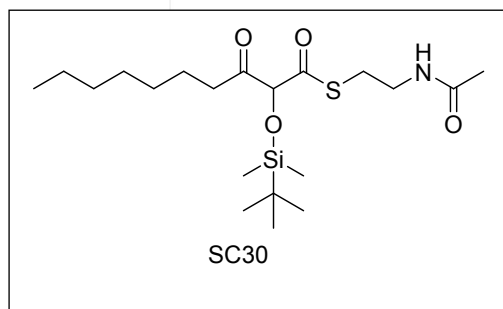
Randy, RS-2-93
 175.975 MHz ¹³C 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
 temp 27.5 C -> actual temp = 27.0 C, coldid probe



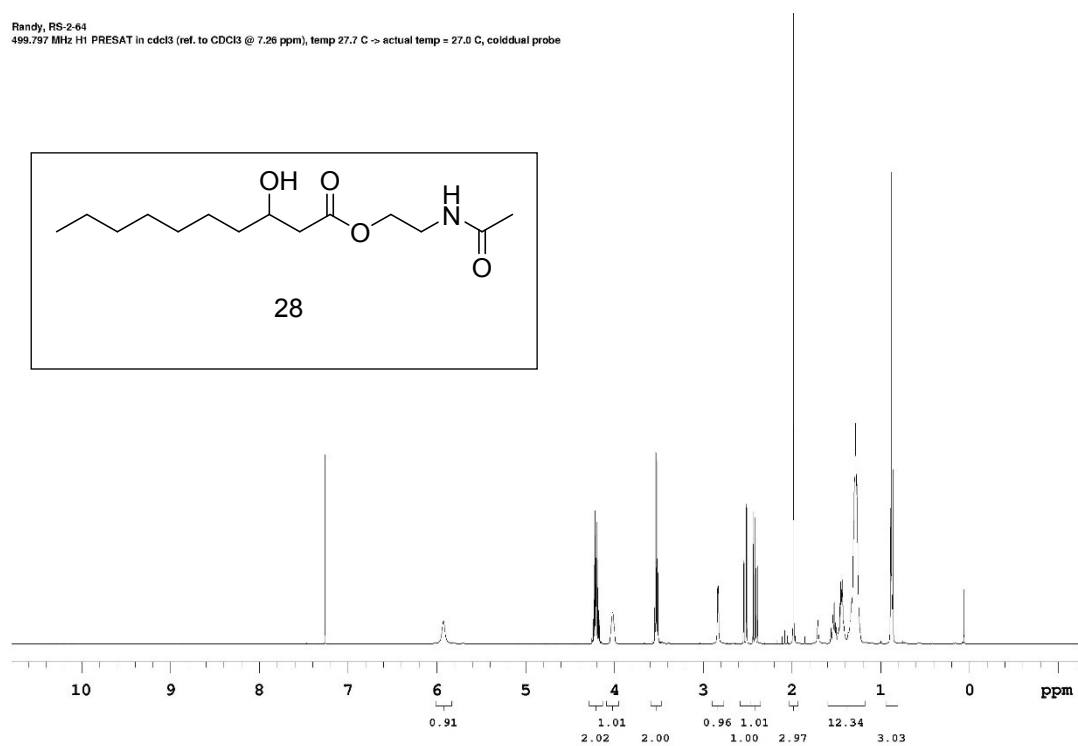
Randy, RS-2-94
 699.762 MHz ¹H 1D in cdCl₃ (ref. to CDCl₃ @ 7.26 ppm)
 temp 27.5 C -> actual temp = 27.0 C, coldid probe



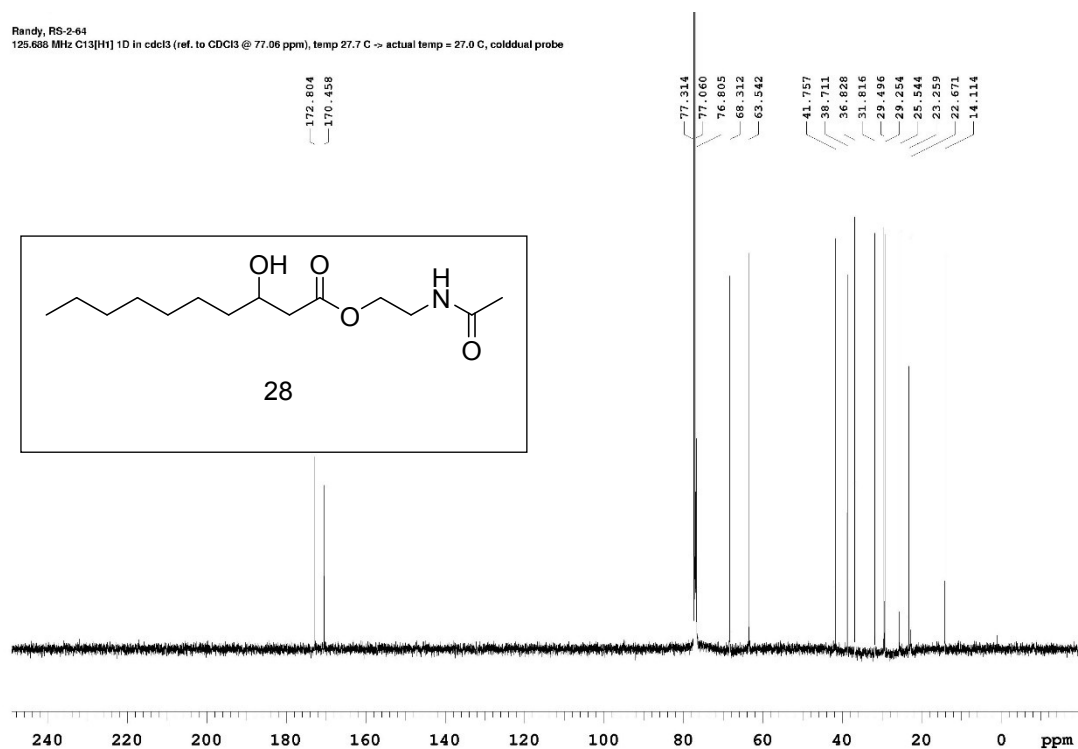
Randy, RS-2-94
 175.975 MHz ¹³C{¹H} 1D in cdCl₃ (ref. to CDCl₃ @ 77.06 ppm)
 temp 27.5 C -> actual temp = 27.0 C, coldid probe



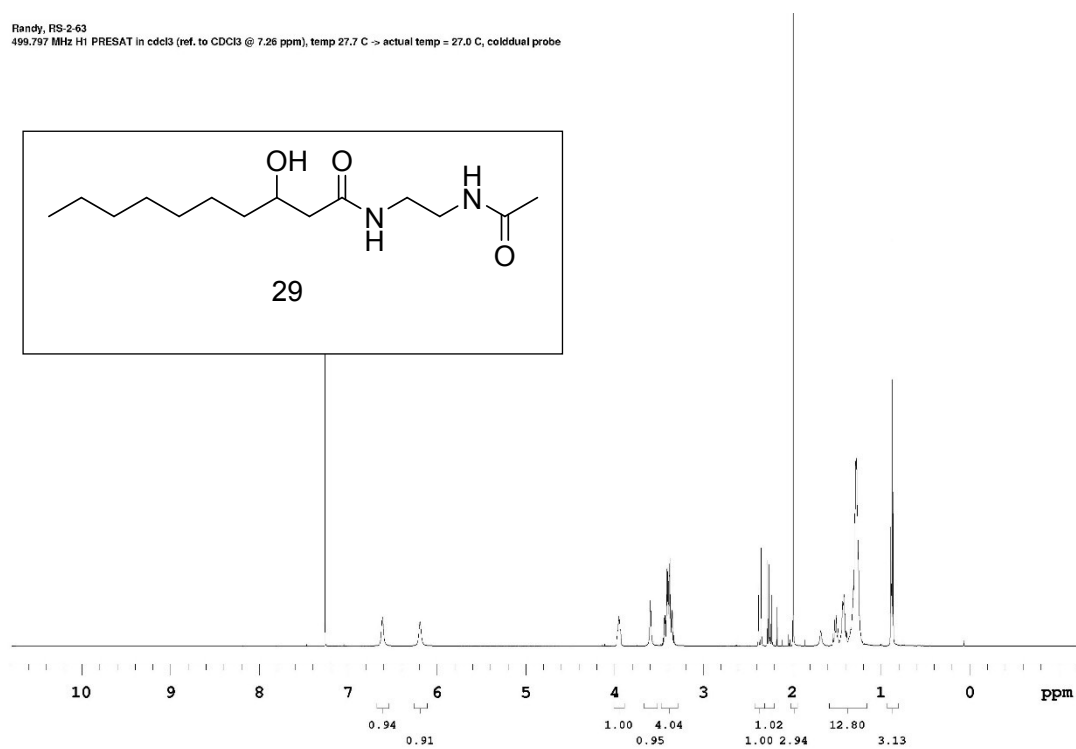
Randy, RS-2-64
499.797 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



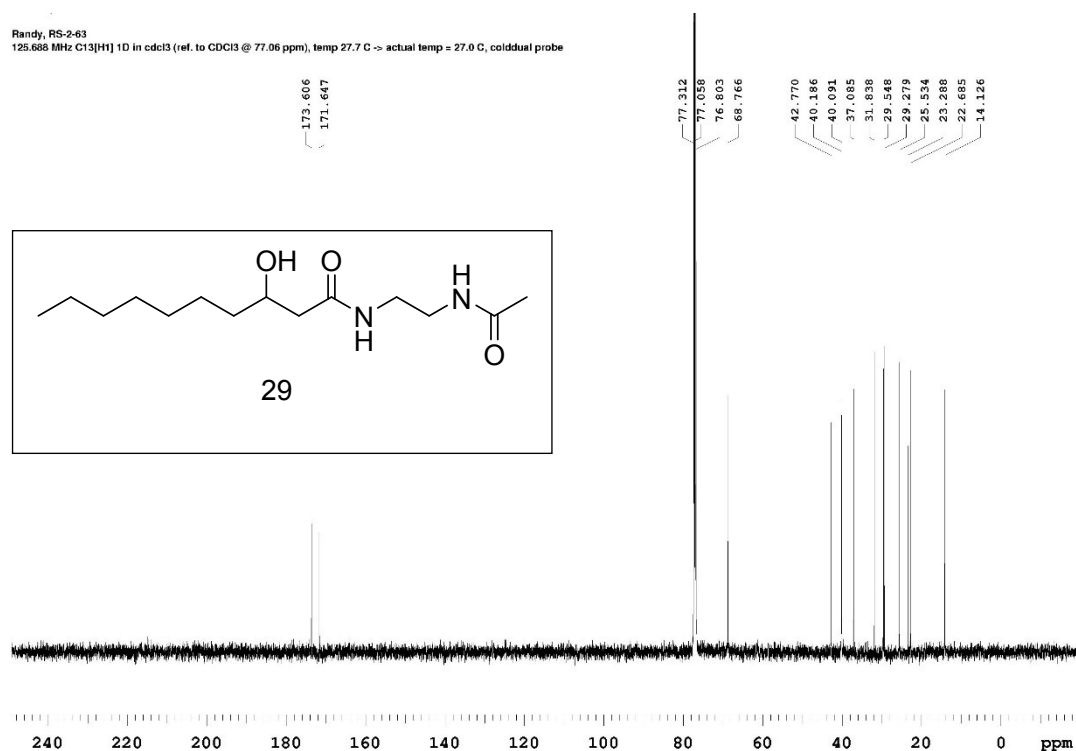
Randy, RS-2-64
125.688 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



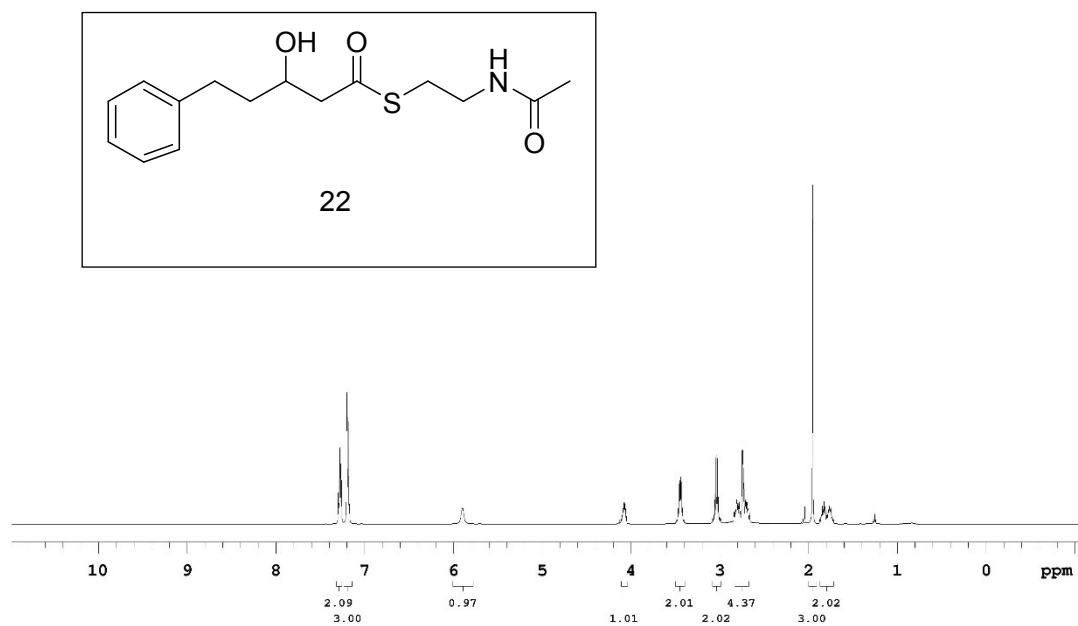
Randy, RS-2-63
499.797 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



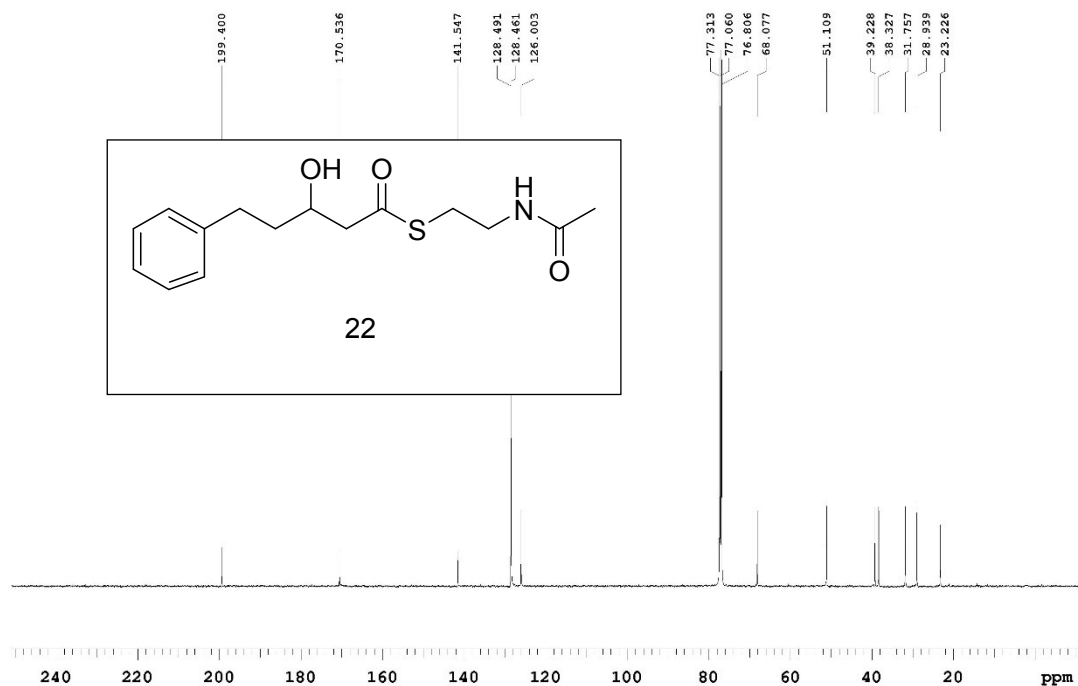
Randy, RS-2-63
125.688 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



Randy, RS-2-29
499.806 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C → actual temp = 27.0 C, coldlual probe



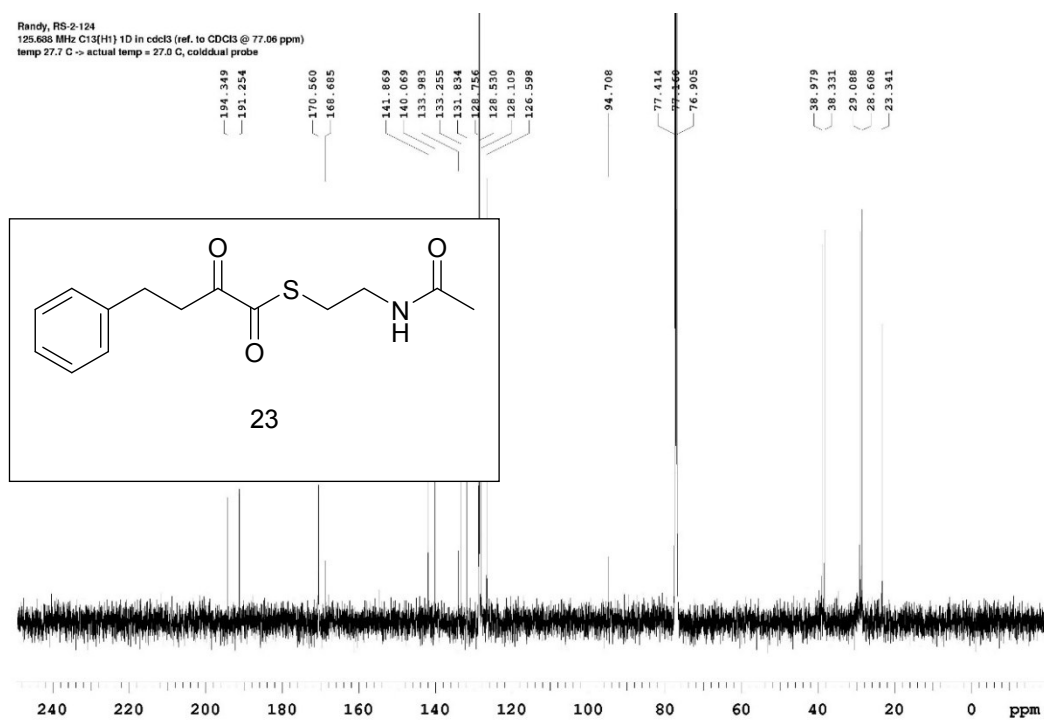
Randy, RS-2-29
125.691 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C → actual temp = 27.0 C, coldlual probe



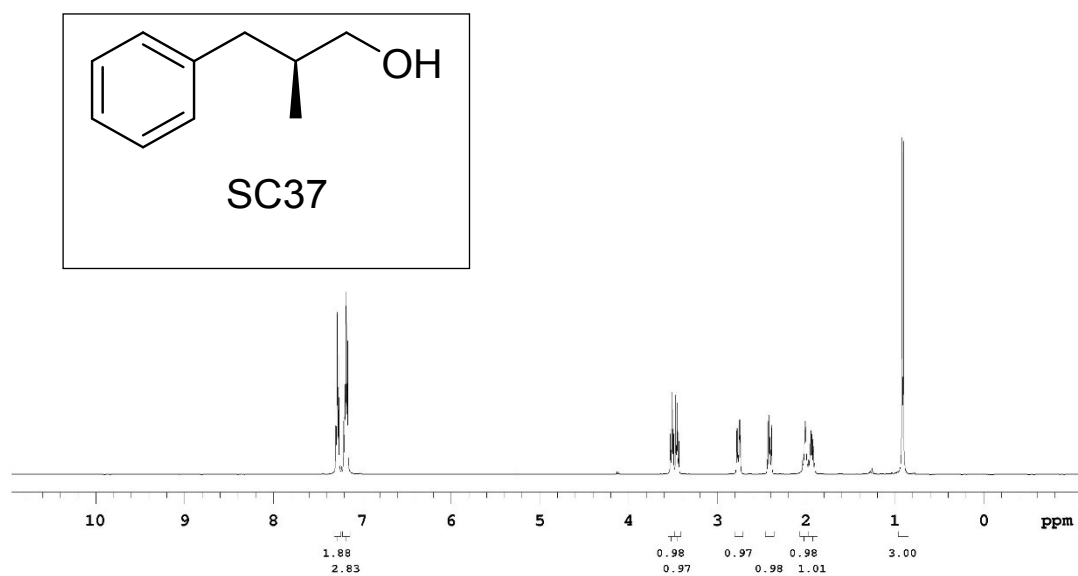
Randy, RS-2-124
496.767 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldlual probe



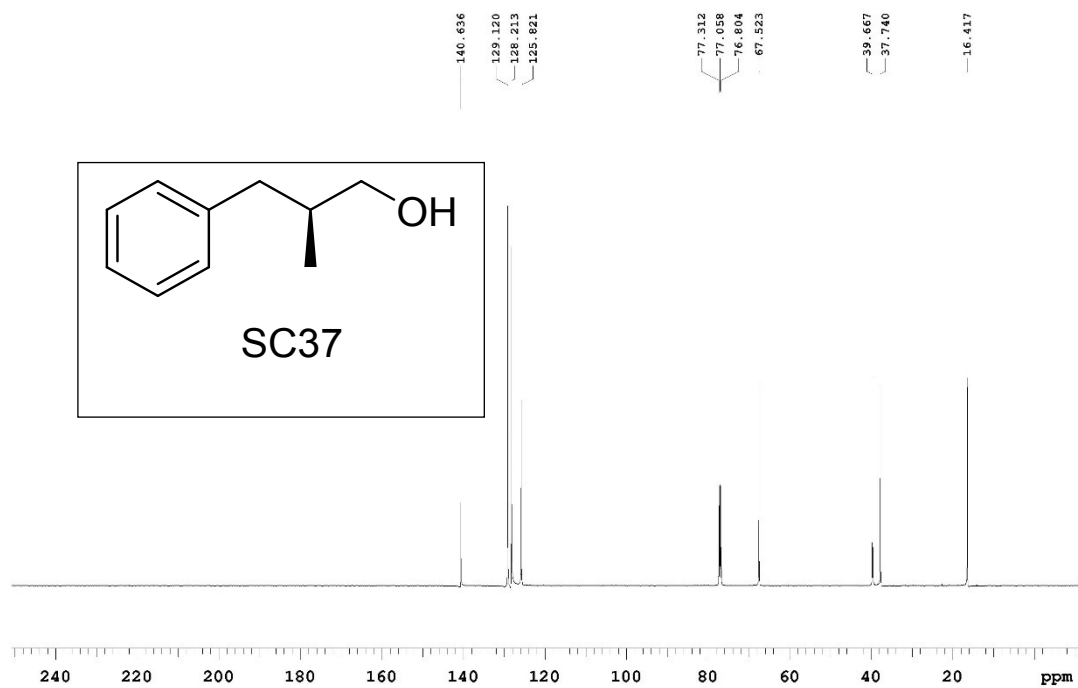
Randy, RS-2-124
125.688 MHz ¹³C 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
temp 27.7 C -> actual temp = 27.0 C, coldlual probe



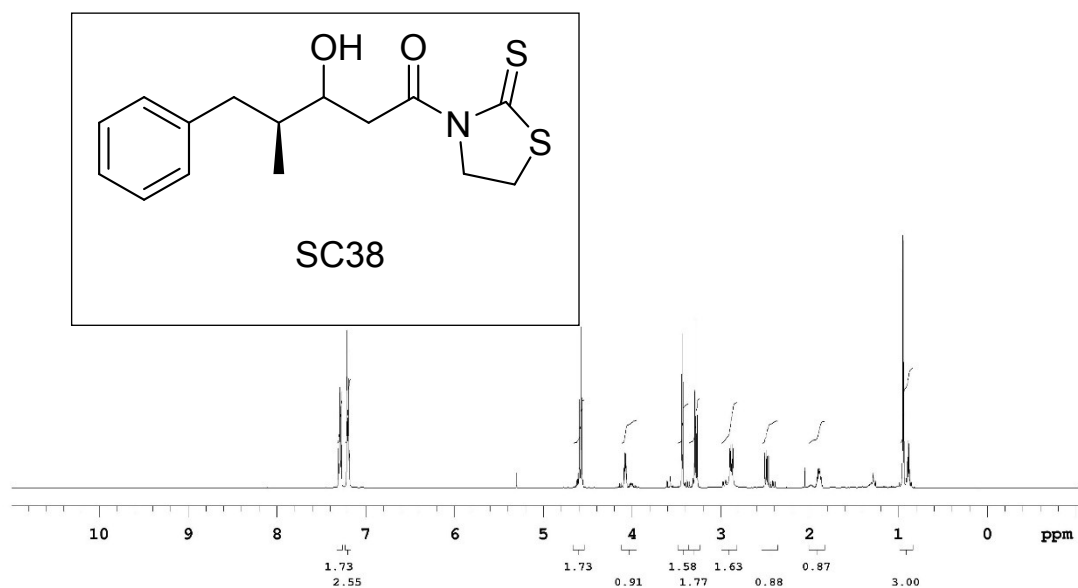
Randy, RS-2-33
499.806 MHz ¹H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



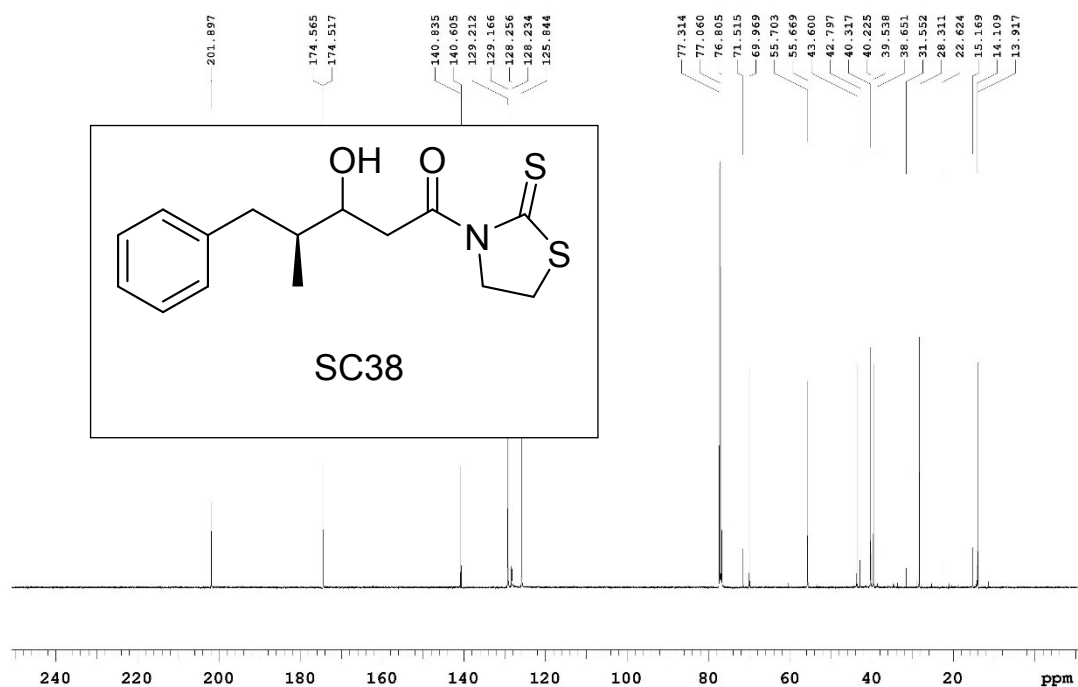
Randy, RS-2-33
125.691 MHz ¹³C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



Randy, RS-2-41
499.806 MHz ¹H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



Randy, RS-2-41
125.691 MHz ¹³C[¹H] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe





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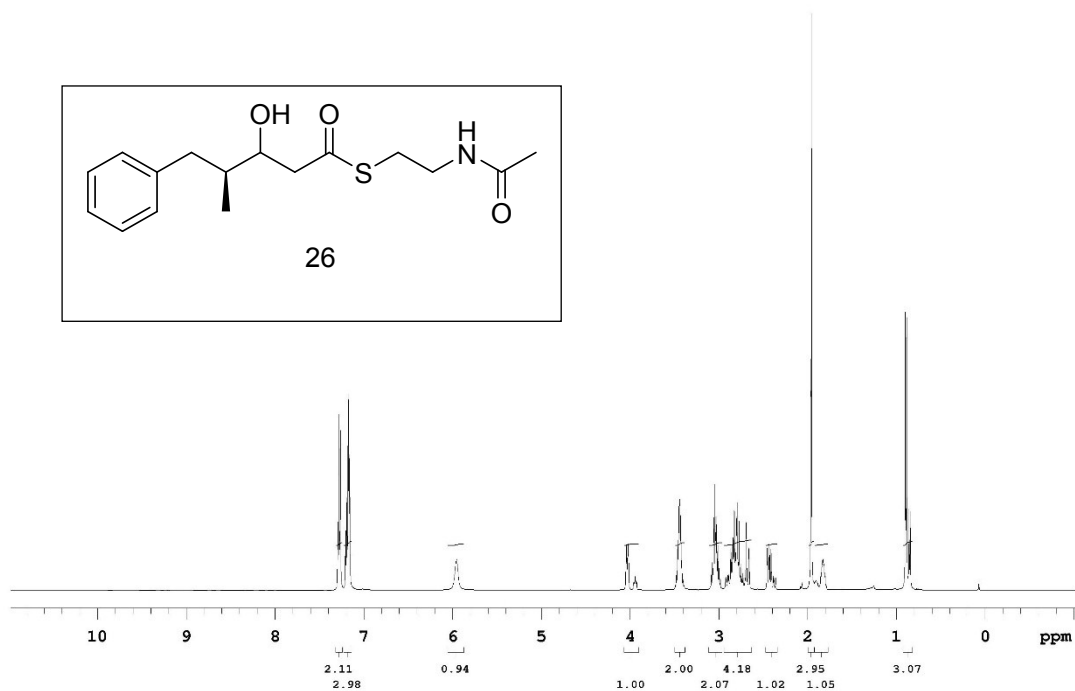
Recorded on: u500, Jan 20 2016
Pulse Sequence: PRESAT

Sweep Width(Hz): 6009.62
Digital Res.(Hz/pt): 0.16

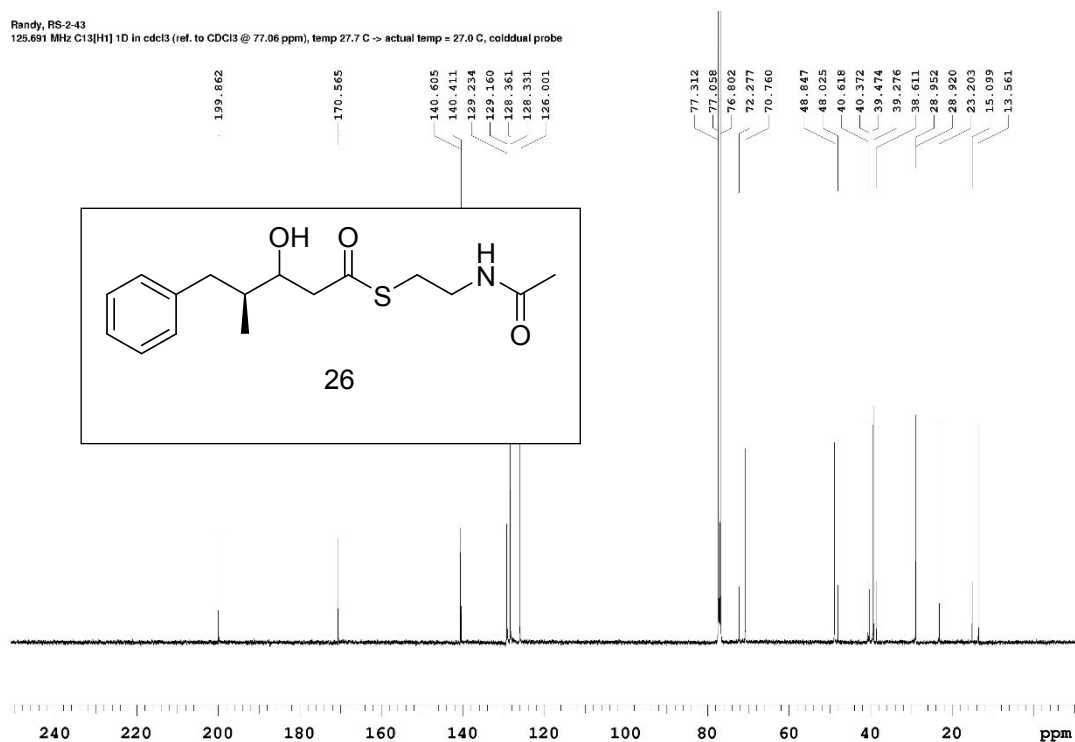
Acquisition Time(s): 5
Hz per mm(Hz/mm): 25.04

Relaxation Delay(s): 0.1
Completed Scans: 16

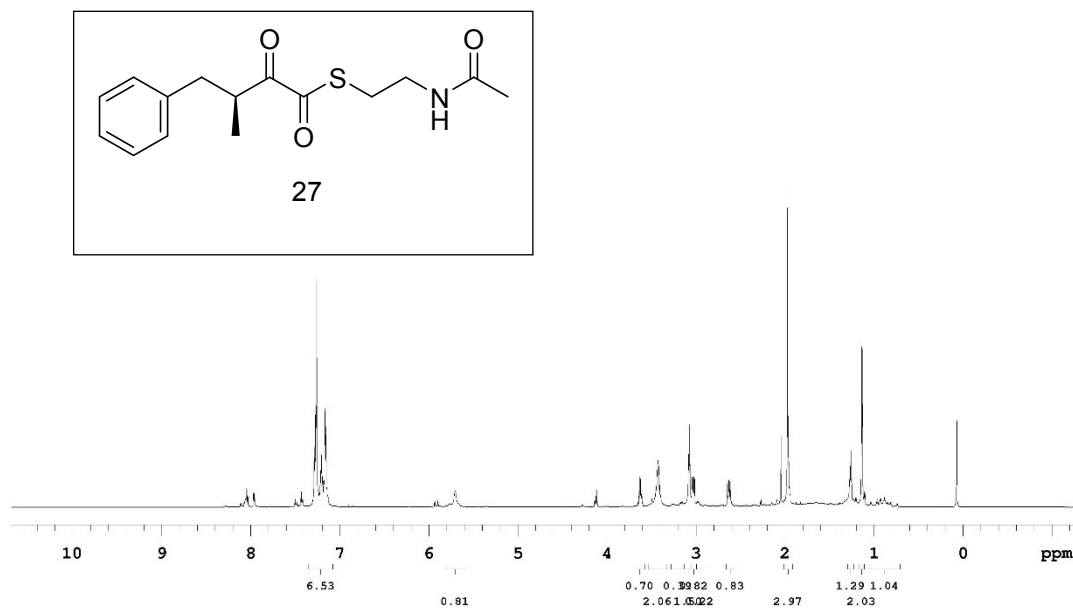
Randy, RS-2-43
499.806 MHz ¹H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, cold dual probe



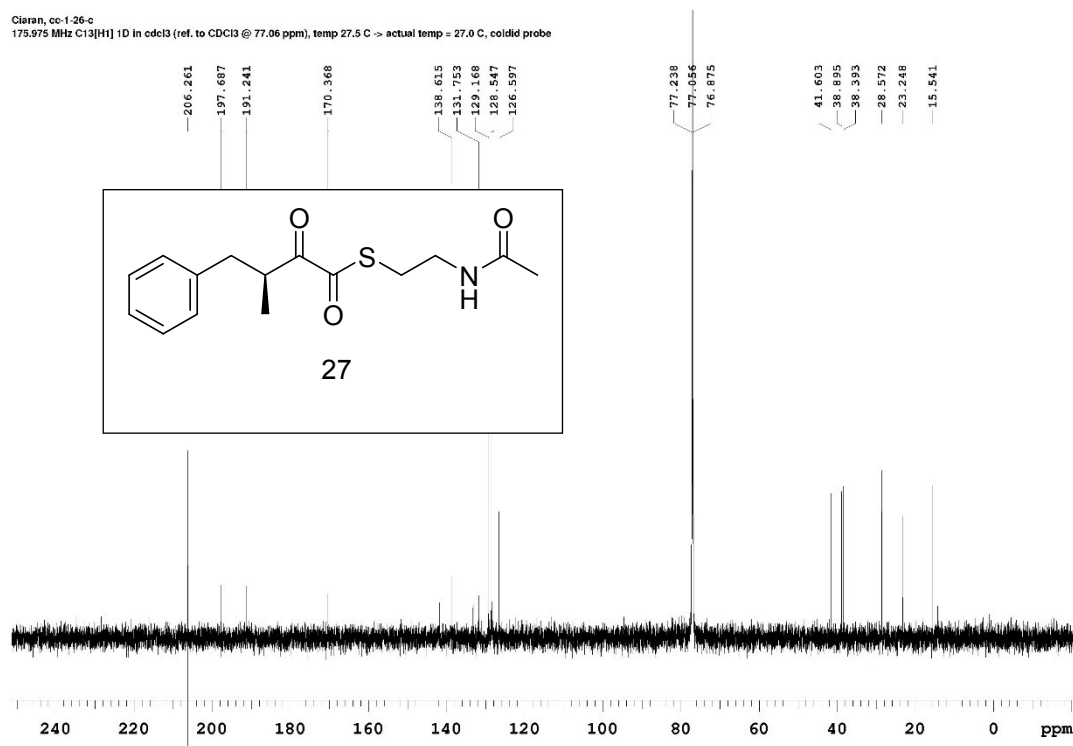
Randy, RS-2-43
125.691 MHz ¹³C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, cold dual probe



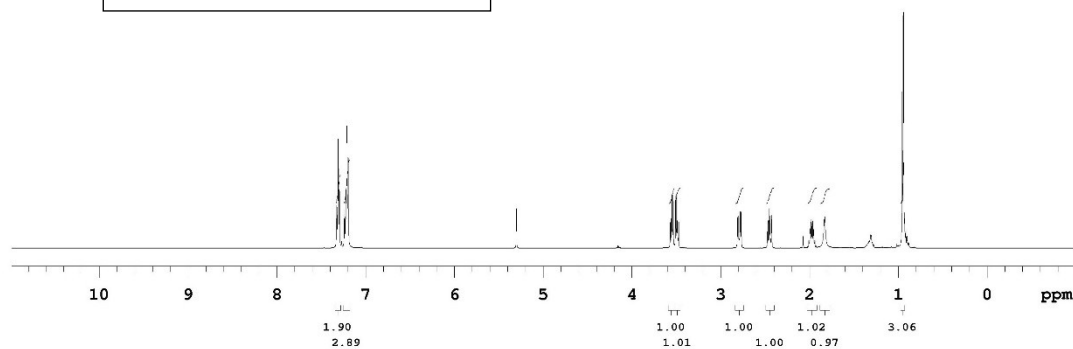
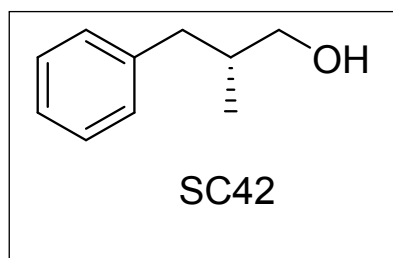
Ciaran, cc-1-26-c
 999.762 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.5 C -> actual temp = 27.0 C, coldid probe



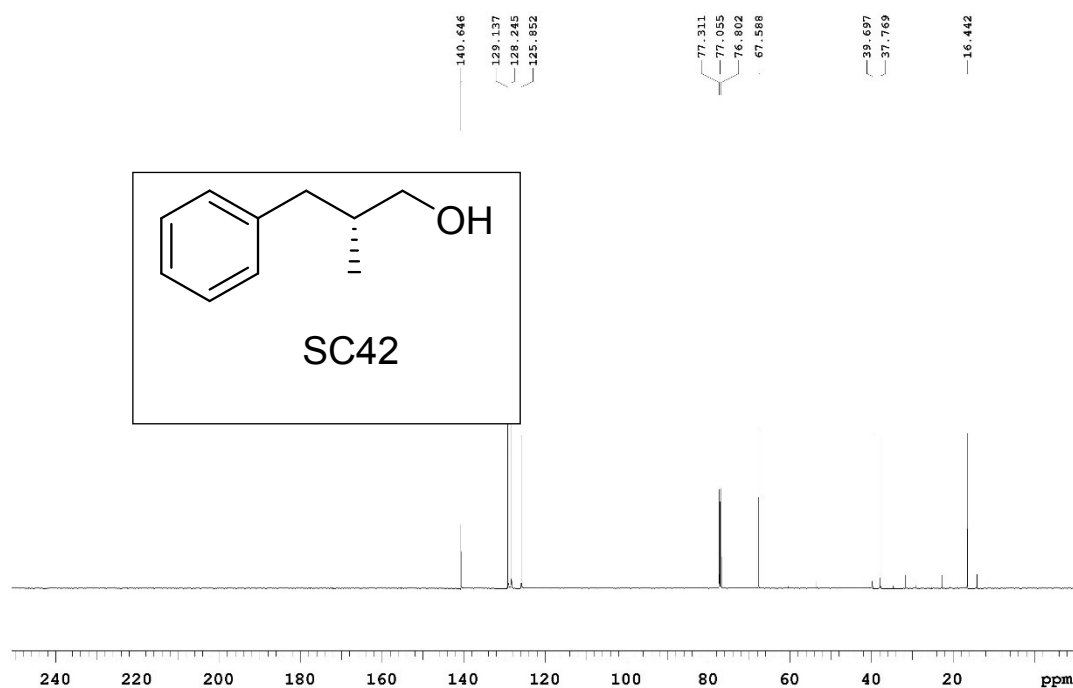
Ciaran, cc-1-26-c
 175.975 MHz ¹³C NMR in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.5 C -> actual temp = 27.0 C, coldid probe



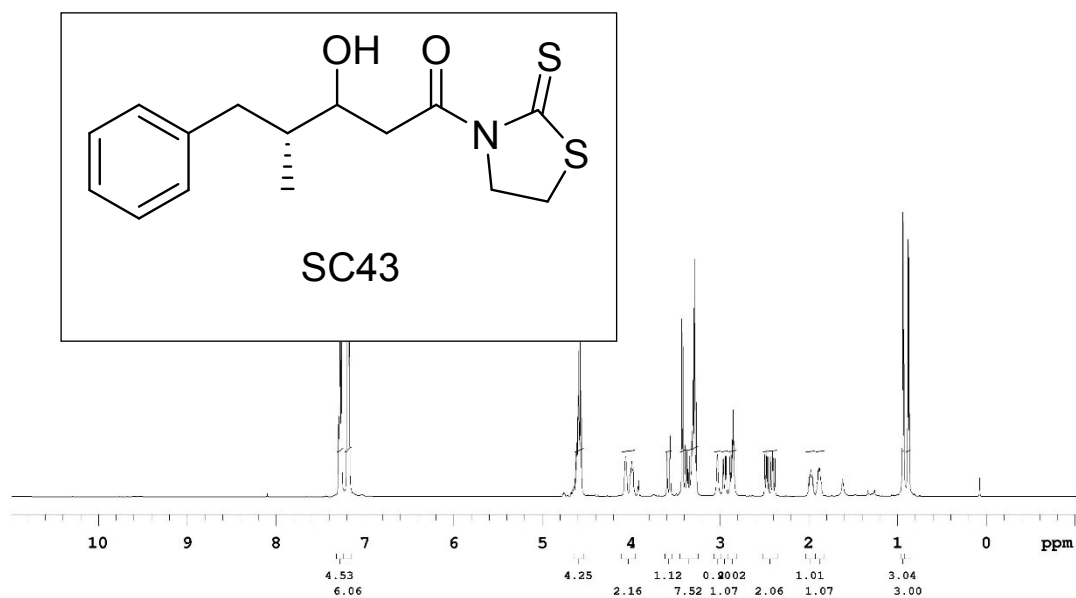
Randy, RS-2-37
499.806 MHz ¹H1 PRESAT in cdcl3 (ref. to CDCl3 @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



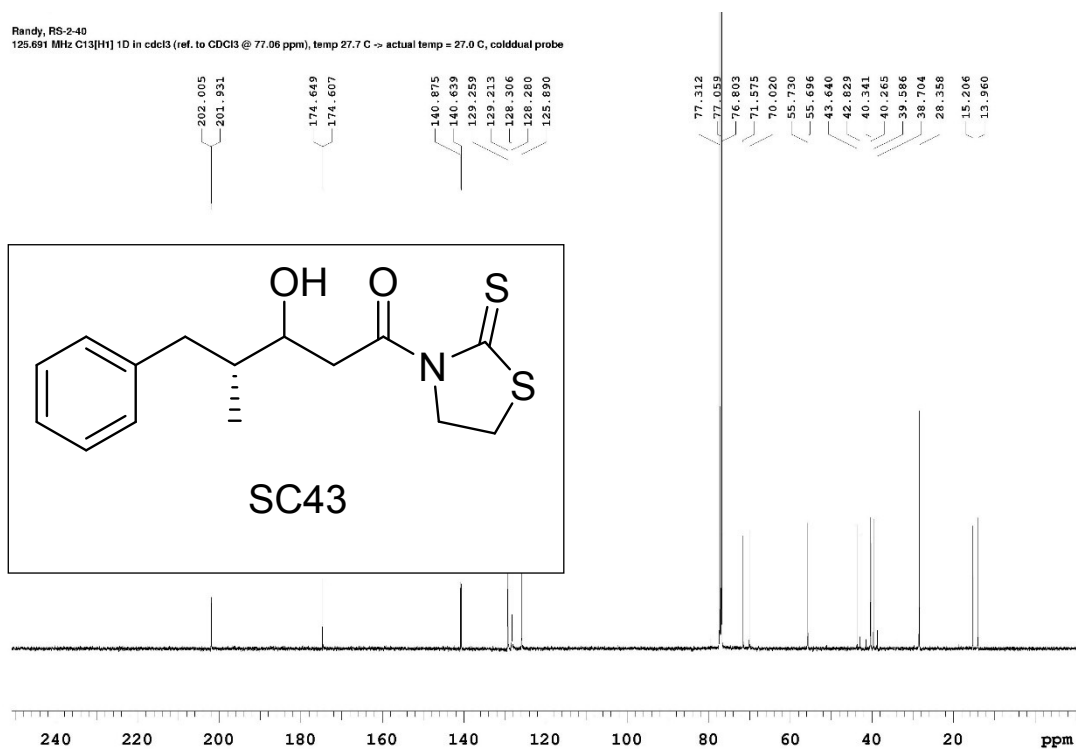
Randy, RS-2-37
125.691 MHz ¹³C13[H1] 1D in cdcl3 (ref. to CDCl3 @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



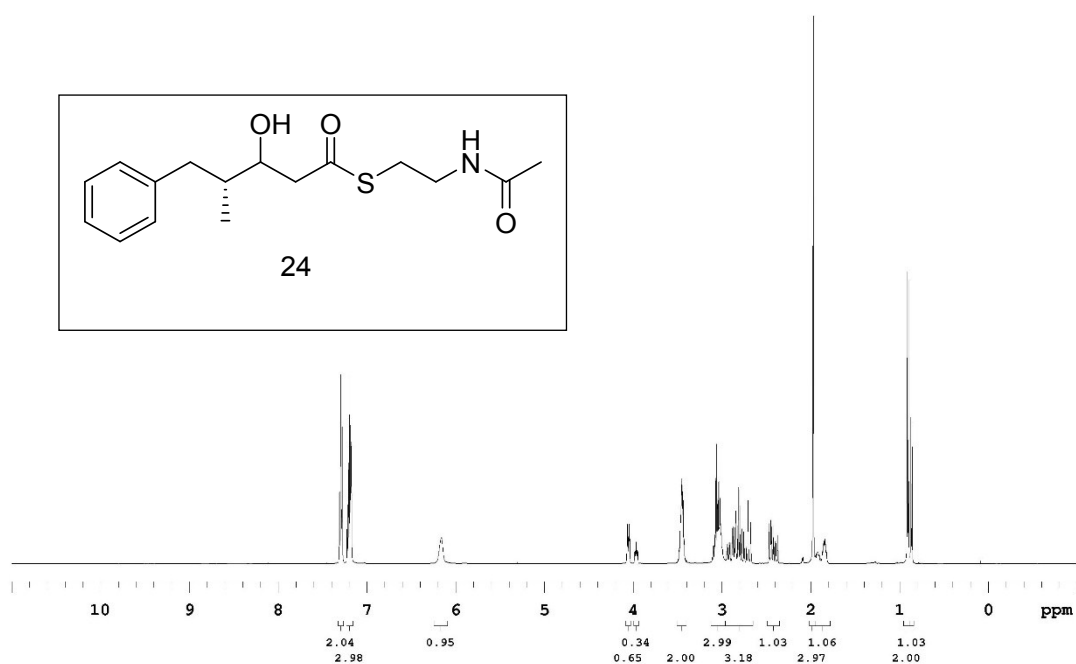
Randy, RS-2-40
499.806 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



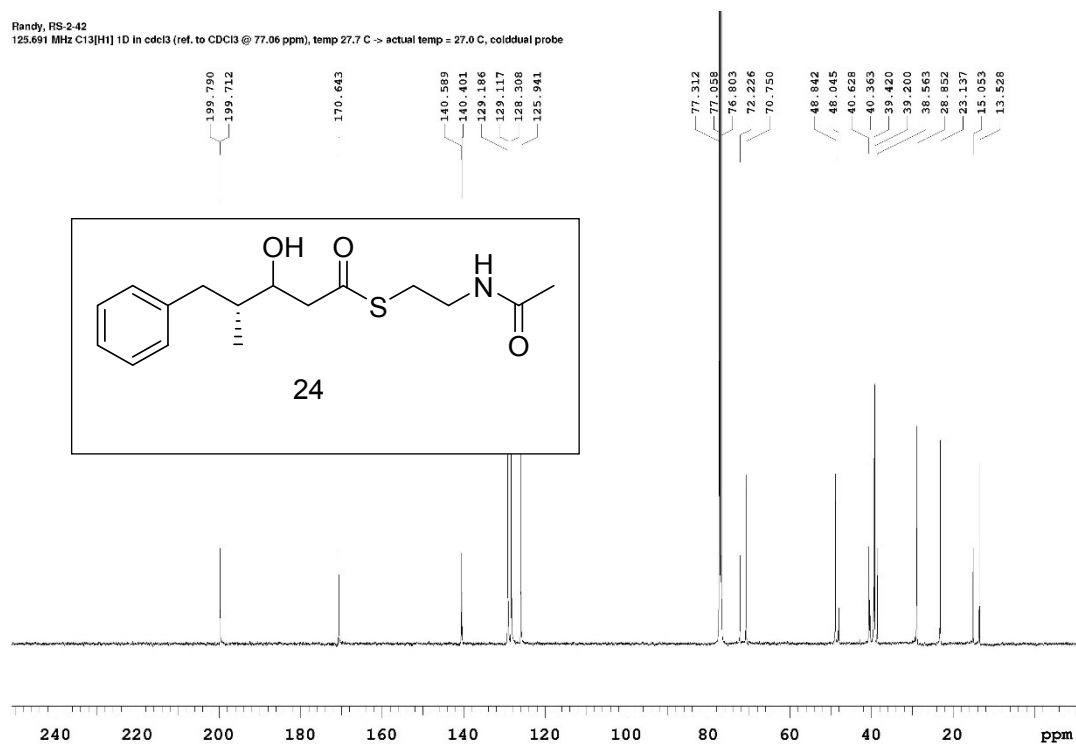
Randy, RS-2-40
125.691 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



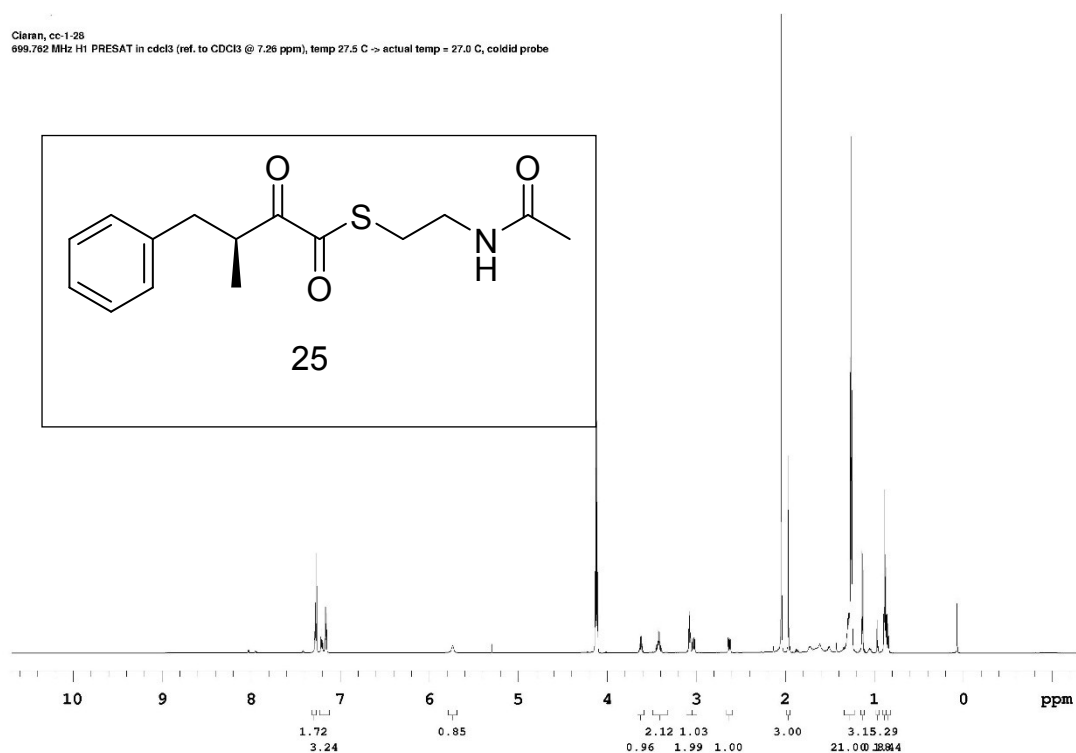
Randy, RS-2-42
499.806 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



Randy, RS-2-42
125.691 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



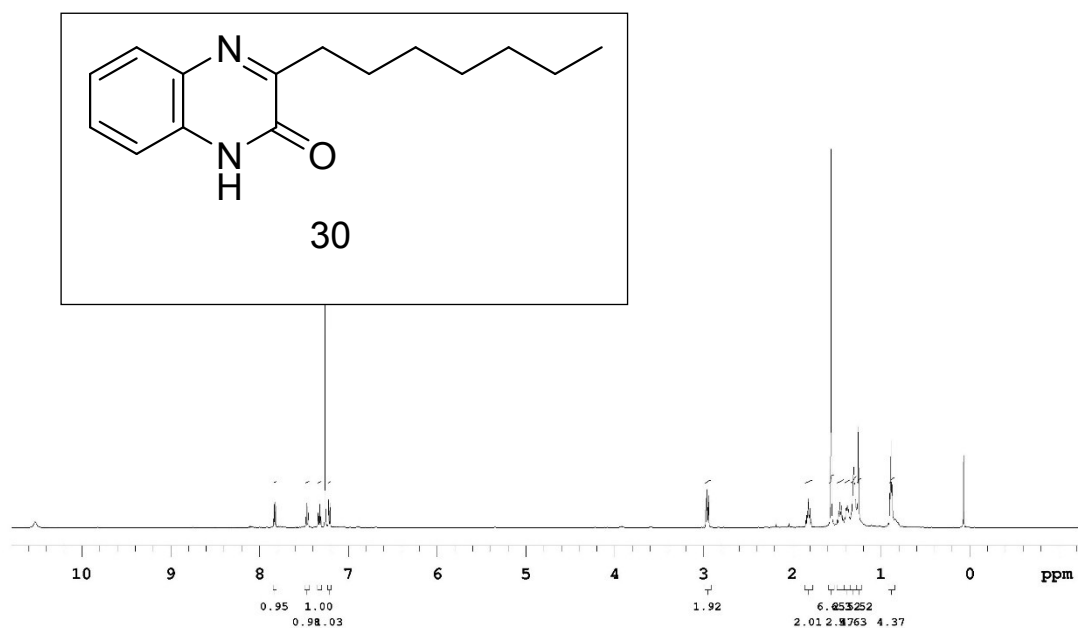
Ciaran, cc-1-28
 999.782 MHz ¹H PRESAT in cdCl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.5 C -> actual temp = 27.0 C, coldid probe



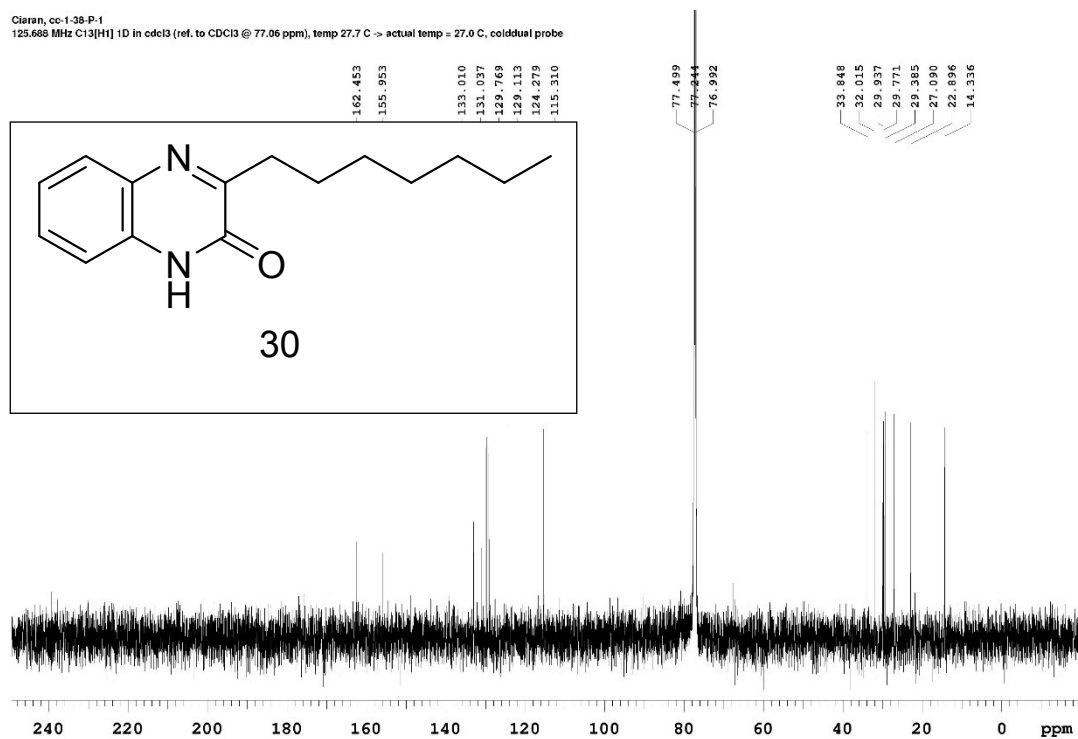
Ciaran, cc-1-28
 175.975 MHz ¹³C[¹H] 1D in cdCl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.5 C -> actual temp = 27.0 C, coldid probe



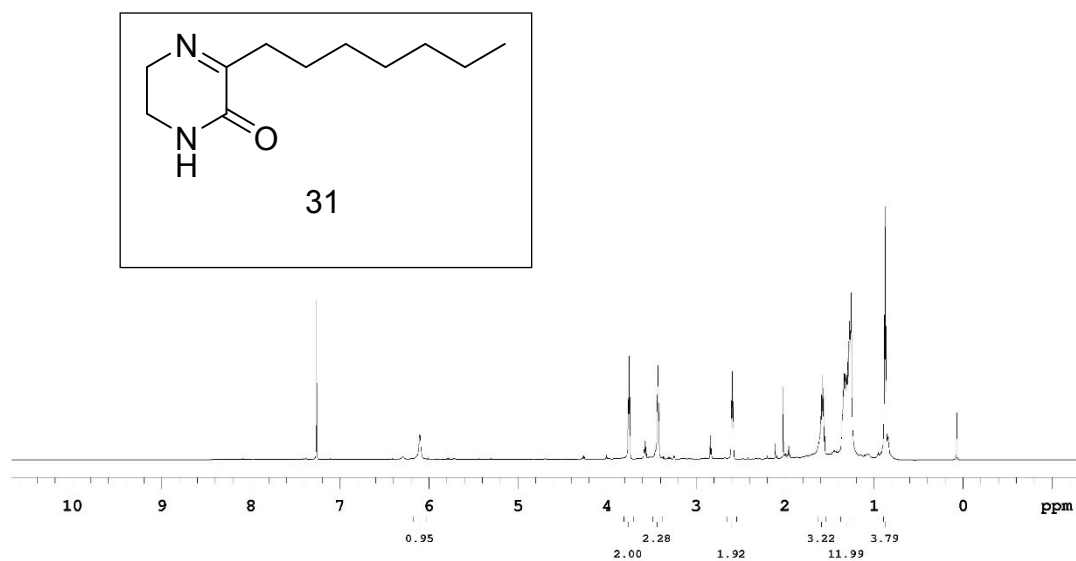
Ciaran, cc-1-38-P-1
499.797 MHz ¹H PRESAT in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



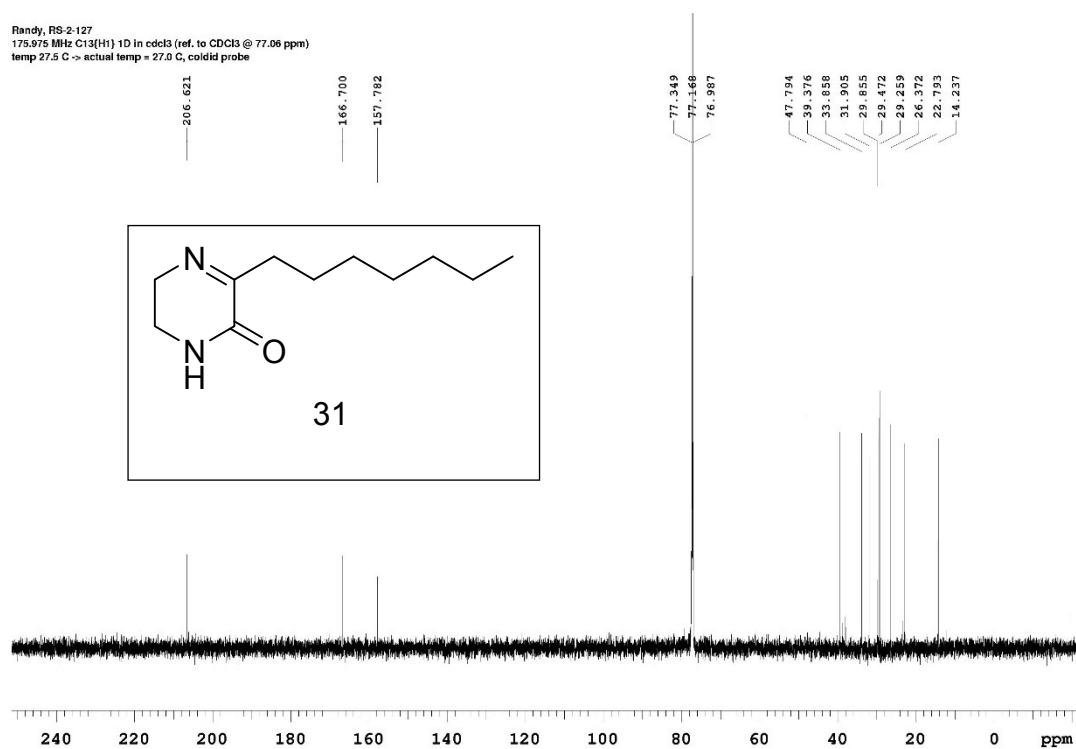
Ciaran, cc-1-38-P-1
125.688 MHz ¹³C[¹H] 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm), temp 27.7 C -> actual temp = 27.0 C, coldlual probe



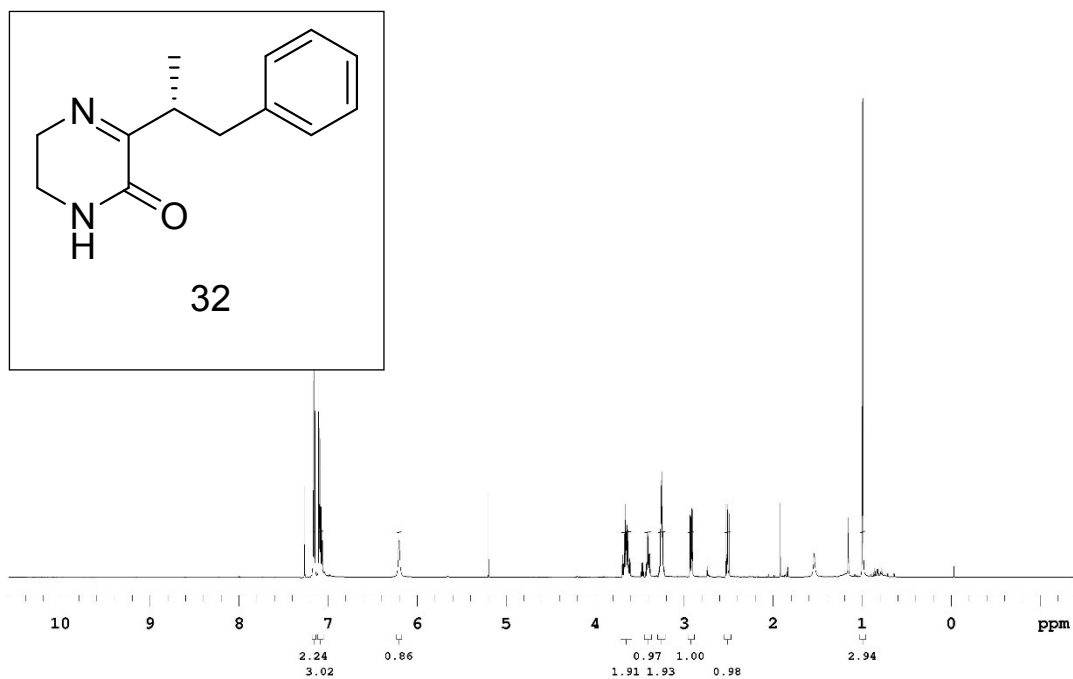
Randy, RS-2-127
 699.762 MHz ¹H 1D in cdcl₃ (ref. to CDCl₃ @ 7.26 ppm)
 temp 27.5 C -> actual temp = 27.0 C, coldid probe



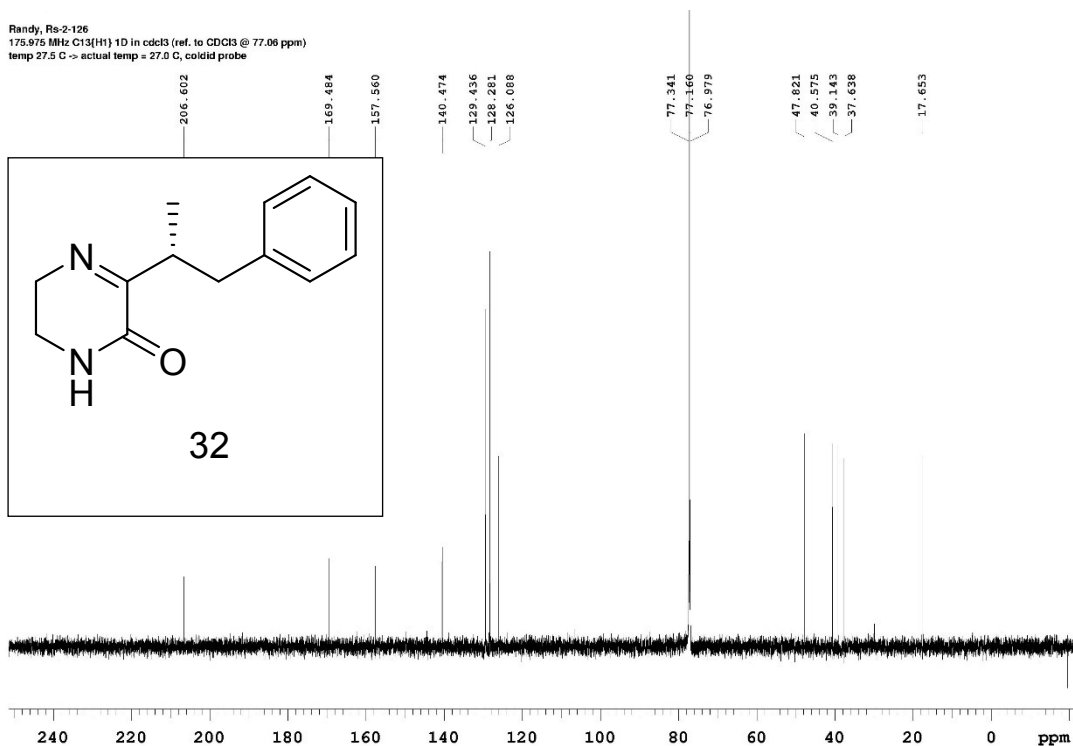
Randy, RS-2-127
 175.975 MHz ¹³C{¹H} 1D in cdcl₃ (ref. to CDCl₃ @ 77.06 ppm)
 temp 27.5 C -> actual temp = 27.0 C, coldid probe



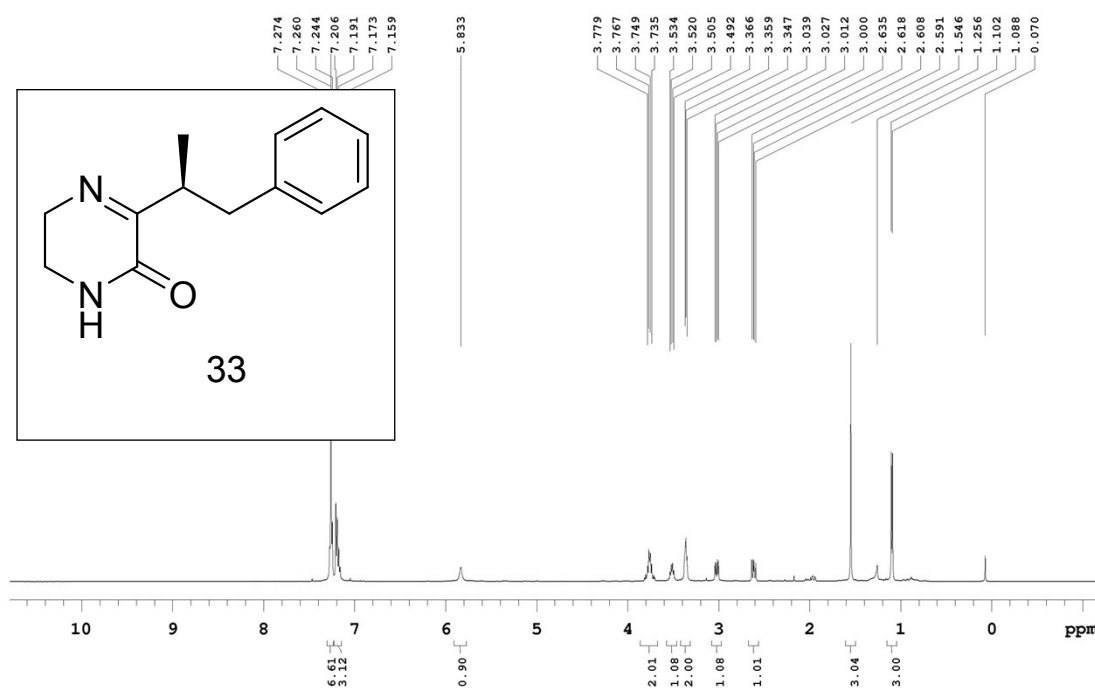
Randy, Re-2-126
 699.762 MHz ¹H 1D in cdCl₃ (ref. to CDCl₃ @ 7.26 ppm)
 temp 27.5 C => actual temp = 27.0 C, coldid probe



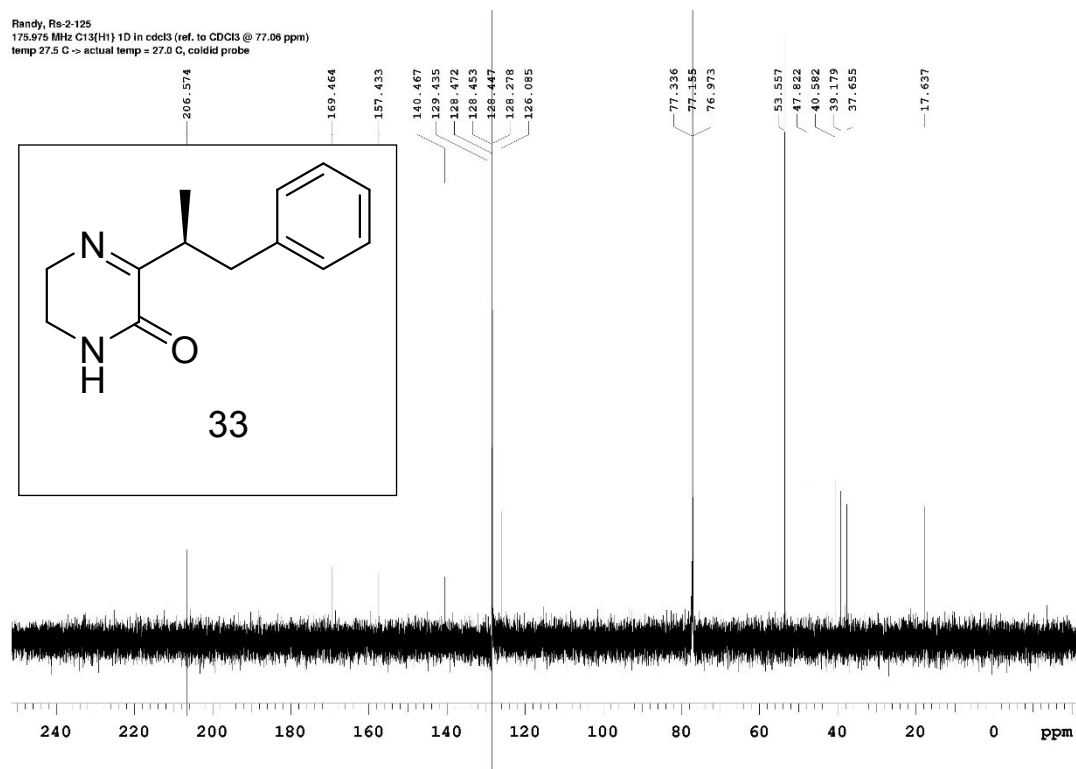
Randy, Re-2-126
 175.975 MHz ¹³C{¹H} 1D in cdCl₃ (ref. to CDCl₃ @ 77.06 ppm)
 temp 27.5 C => actual temp = 27.0 C, coldid probe



Randy, RS-2-125
 499.797 MHz ¹H 1D in cdCl₃ (ref. to CDCl₃ @ 7.26 ppm)
 temp 27.7 C -> actual temp = 27.0 C, coldidual probe



Randy, RS-2-125
 175.975 MHz ¹³C 1D in cdCl₃ (ref. to CDCl₃ @ 77.06 ppm)
 temp 27.5 C -> actual temp = 27.0 C, coldidual probe



Supplemental References

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