Electronic Supplementary Information

Total Synthesis of Thioamycolamide A via a Biomimetic Route

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28 pages

Table of contents

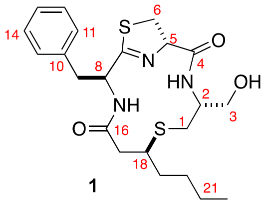
General remarks

^{1}H and ^{13}C NMR spectra were recorded on Bruker AVANCE DMX 600 NMR (600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR), JEOL ECA500 (500 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR), or JEOL ECZ600 (600 MHz for ^{1}H NMR and 150 MHz for ^{13}C NMR) spectrometer. Chemical shifts are denoted in δ (ppm) relative to residual solvent peaks as internal standard ($CDCl_3$, ^{1}H δ 7.25, ^{13}C δ 77.2, CD_3OD, ^{1}H δ 3.31, ^{13}C δ 49.0, DMSO-d_6, ^{1}H δ 2.50, ^{13}C δ 39.5). ESI-MS and LC-MS experiments were recorded on a Shimadzu LCMS-IT-TOF. Optical rotations were recorded on JASCO P-2200 polarimeter. CD spectra were measured on JASCO J-715 circular dichroism spectrometer with a 1 mm path length cell. High performance liquid chromatography (HPLC) experiments were performed with SHIMADZU HPLC system equipped with LC-20AD intelligent pump. All reactions sensitive to air and/or moisture were conducted under nitrogen atmosphere using dry, freshly distilled solvents, unless otherwise noted. All reagents were used as supplied unless otherwise stated. Analytical thin-layer chromatography (TLC) was performed using E. Merck Silica gel 60 F_{254} pre-coated plates. Silica gel column chromatography was performed using 40-50 μm Silica Gel 60N (Kanto Chemical Co., Inc.).

NMR data of natural **1** and synthetic **1** in DMSO-d_6

Table S1. ^{1}H NMR data (600 MHz) and ^{13}C NMR data (150 MHz) of natural **1** and synthetic **1** in DMSO-d_6.

pos	natural **1**		pos	synthetic **1**	
	δ_C, type	δ_H (J in Hz)		δ_C, type	δ_H (J in Hz)
1	34.9, CH_2	2.79, dd (13.0, 8.8) 3.10, dd (13.0, 4.3)	1	34.9, CH_2	2.79, dd (13.1, 8.8) 3.10, dd (13.0, 4.3)
2	50.6, CH	3.39, m	2	50.6, CH	3.39, m
3	61.9, CH_2	3.21, m 3.51, m	3	61.9, CH_2	3.22, m 3.51, d (10.1)
4	170.2, C		4	170.3, C	
5	77.7, CH	5.08, t (6.7)	5	77.7, CH	5.08, m
6	36.8, CH_2	3.56, d (6.7)	6	36.8, CH_2	3.56, m
7	177.7, C		7	177.7, C	
8	54.3, CH	4.54, m	8	54.3, CH	4.54, m
9	37.6, CH_2	2.96, dd (13.9, 9.9)	9	37.6, CH_2	2.95, dd (13.9, 10.0)
		3.03, dd (13.9, 5.0)			3.03, dd (13.9, 5.0)
10	137.4, C		10	137.4, C	
11/15	129.1, CH	7.32, t (7.9)	11/15	129.1, CH	7.32, t (7.8)
12/14	128.3, CH	7.29, t (7.6)	12/14	128.3, CH	7.30, t (7.6)
13	126.6, CH	7.22, t (7.1)	13	126.7, CH	7.22, m
16	171.6, C		16	171.6, C	
17	42.5, CH_2	2.39, d(8.3)	17	42.5, CH_2	2.39, m
18	45.7, CH	2.90, m	18	45.8, CH	2.90, m
19	36.8, CH_2	1.42, m	19	36.9, CH_2	1.42, m
		1.54, m			1.55, m
20	28.8, CH_2	1.35, m	20	28.8, CH_2	1.35, m
		1.45, m			1.45, m
21	21.8, CH_2	1.28, m	21	21.9, CH_2	1.28, m
22	14.0, CH_3	0.87, t (7.3)	22	14.0, CH_3	0.87, t (7.3)
2-NH		6.77, d (5.7)	2-NH		6.77, d (5.7)
3-OH		4.82, s	3-OH		4.82, s
8-NH		8.85, d (6.7)	8-NH		8.84, d (6.8)



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Cytotoxicity assay of natural **1** and synthetic **1** against HT1080 and HeLa S3 cells

Cytotoxicity of compounds against HT1080 and HeLa S3 cell lines was evaluated by a WST-8 colorimetric assay (Cell Counting Kit-8, Dojindo). Cells were cultured in 96-well plates (3000 cells/well) for 24 h followed by exposure to natural **1** and synthetic **1** for 72 h, and then the viability was assessed by WST-8. The absorbance was measured at 450 nm using an iMark microplate reader (BIO-RAD). Adriamycin was evaluated as a positive control. IC_{50} values are shown as the mean ± SD (n = 4).

Table S2. Cytotoxic activities (IC_{50}) of natural **1** and synthetic **1**.

Sample	Cytotoxic activity (μM)	
	HT 1080	Hela S3
natural **1**	9.60 ± 1.03	15.47 ± 3.54
synthetic **1**	11.61 ± 1.44	14.74 ± 5.16
Adriamycin	0.30 ± 0.05	0.37 ± 0.06

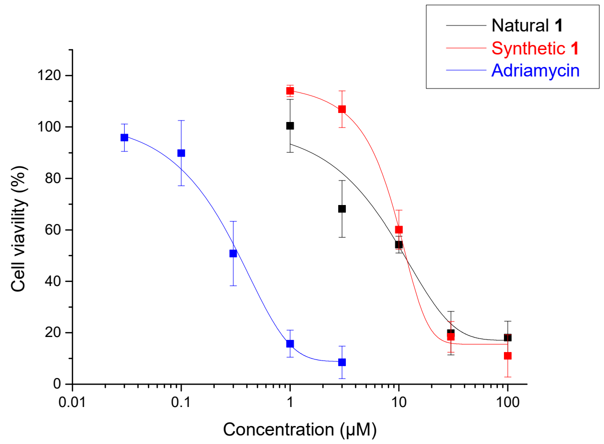


Fig. S1 Cytotoxicity assay against HT1080 cell.

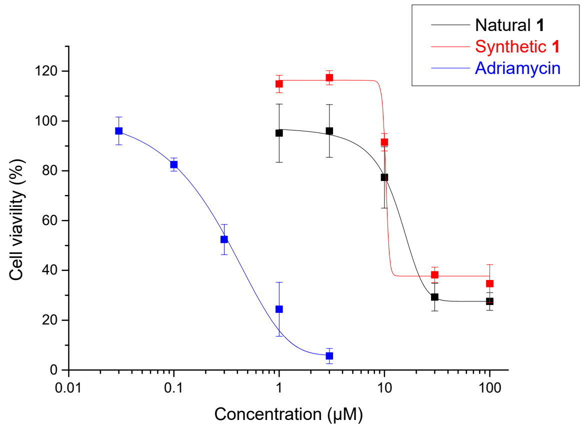
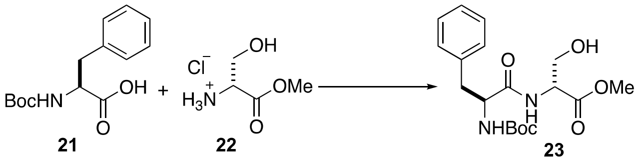
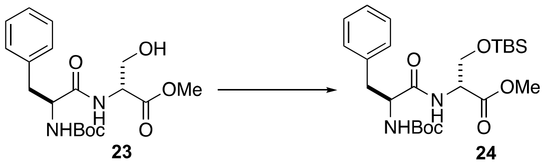


Fig. S2 Cytotoxicity assay against HeLa-S3 cell.

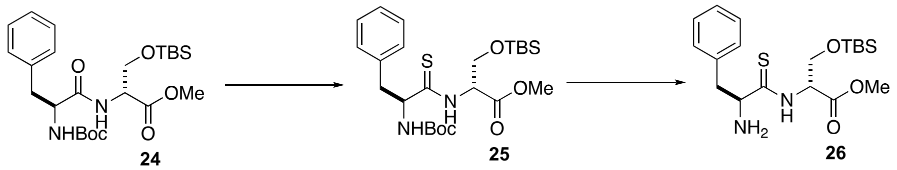
Synthetic procedures and compound characterizations



To a solution of Boc-L-Phe-OH (**21**) (1.00 g, 3.77 mmol) and H-D-Ser-OMe·HCl (**22**) (645 mg, 4.15 mmol) in DMF (15 mL) were added *N*-methylmorpholine (0.47 mL, 4.17 mmol), Oxyma (589 mg, 4.14 mmol), and EDCI·HCl (795 mg, 4.15 mmol) at 0 °C. After being stirred at room temperature overnight, saturated aqueous NH_4Cl (20 mL) was added to the reaction mixture. The resulting solution was extracted with EtOAc (40 mL × 2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane = 1:1) to afford dipeptide **23** (1.31 g, 95%) as a white foam: $[\alpha]^{20}_{D} = -6.5$ (*c* 0.14, MeOH); ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.3 Hz, 2H), 7.25 (m, 3H), 6.72 (d, *J* = 7.3 Hz, 1H), 5.12 (d, *J* = 6.5 Hz, 1H), 4.57 (m, 1H), 4.38 (d, *J* = 6.3 Hz, 1H), 3.78 (m, 1H), 3.74 (s, 3H), 3.06 (d, *J* = 7.2 Hz, 2H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3, 170.7, 155.8, 136.7, 129.4, 128.9, 127.3, 80.8, 62.7, 56.3, 54.8, 52.9, 38.8, 28.4; HRMS (ESI) calcd for $C_{18}H_{26}N_2O_6Na^+$ $[M+H]^+$ 389.1683, found 389.1703.

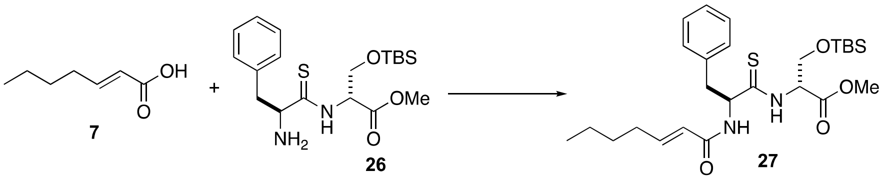


To a solution of **23** (760 mg, 2.07 mmol) in DMF (15 mL) were added TBSCl (469 mg, 3.11 mmol) and imidazole (424 mg, 6.23 mmol) at 0 °C. After being stirred at room temperature for 30 min, saturated aqueous NH_4Cl (20 mL) was added to the reaction mixture. The mixture was extracted with EtOAc (20 mL × 2). The combined organic layer was washed with brine (40 mL × 2), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane = 1:4) to afford **24** (991 mg, 99%) as a white foam: $[\alpha]^{20}_{D} = -17.1$ (*c* 0.63, MeOH); ^1H NMR (500 MHz, $CDCl_3$) δ 7.21 (m, 2H), 7.14 (m, 3H), 6.82 (d, *J* = 7.4 Hz, 1H), 5.23 (d, *J* = 7.7 Hz, 1H), 4.56 (d, *J* = 7.7 Hz, 1H), 4.44 (d, *J* = 7.2 Hz, 1H), 3.93 (d, *J* = 9.7 Hz, 1H), 3.63 (s, 3H), 3.57 (d, *J* = 7.7 Hz, 1H), 3.10 (dd, *J* = 13.8, 6.5 Hz, 1H), 2.96 (dd, *J* = 13.4, 7.2 Hz, 1H), 1.32 (s, 9H), 0.78 (s, 9H), –0.06 (s, 3H), –0.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 170.5, 155.3, 136.8, 129.2, 128.4, 126.7, 79.8, 63.2, 55.5, 54.0, 52.2, 38.3, 28.1, 25.6, 18.0, –5.6, –5.9; HRMS (ESI) calcd for $C_{24}H_{40}N_2O_6SiNa^+$ $[M+H]^+$ 503.2548, found 503.2541.

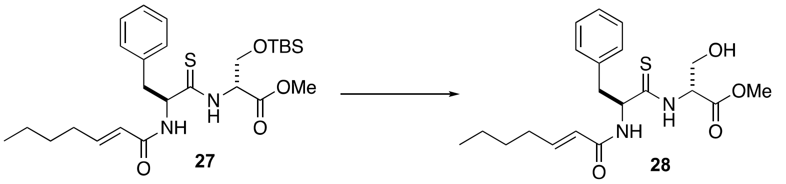


To a solution of **24** (984 mg, 2.05 mmol) in THF (15 mL) was added Lawesson's reagent (498 mg, 1.23 mmol) at room temperature. After being stirred at 70 °C for 1 h in a sealed tube, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane = 1:10) to afford practically pure **25** (1.02 g, Figures S11, S12, and S43), which was used in the next reaction without further purification.

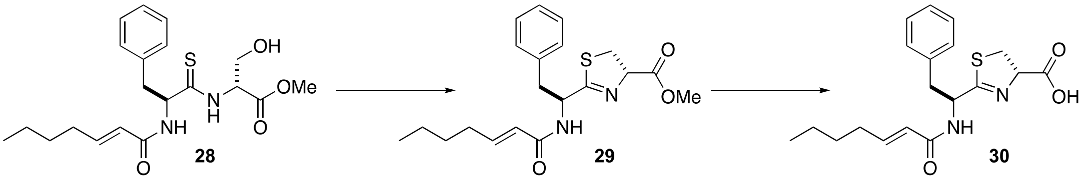
To a solution of the above **25** (1.02 g, ca 2.05 mmol) in CH_2Cl_2 (20 mL) was added 2,6-lutidine (1.40 mL, 12.1 mmol) at room temperature, followed by dropwise addition of TMSOTf (1.46 mL, 8.08 mmol). The mixture was stirred at room temperature for 8 h, then quenched by addition of MeOH (5 mL). The reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2 /MeOH/Et_3N = 200:1:0.5) to afford **26** as a light yellow oil (763 mg, 94% for 2 steps from **24**): $[\alpha]^{20}_{D} = -16.1$ (*c* 0.33, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (m, 2H), 7.22 (m, 3H), 5.25 (s, 1H), 4.11 (dd, *J* = 10.3, 2.6 Hz, 1H), 4.06 (dd, *J* = 10.1, 3.7 Hz, 1H), 3.97 (dd, *J* = 10.3, 3.1 Hz, 1H), 3.75 (s, 3H), 3.60 (dd, *J* = 13.8, 3.7 Hz, 1H), 2.60 (dd, *J* = 13.8, 10.1 Hz, 1H), 0.83 (s, 9H), 0.00 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.6, 169.7, 138.1, 129.2, 128.7, 126.9, 63.7, 62.3, 58.9, 52.4, 43.6, 25.6, 18.0, –5.6, –5.7; HRMS (ESI) calcd for $C_{19}H_{33}N_2O_3SSi^+$ $[M + H]^+$ 397.1976, found 397.1990.



To a solution of **26** (148 mg, 0.370 mmol) and 2-heptenoic acid (**7**) (52.5 mg, 0.410 mmol) in DMF (3 mL) were added Oxyma (58.3 mg, 0.410 mmol) and EDCI·HCl (78.6 mg, 0.410 mmol) at 0 °C. After being stirred at room temperature overnight, saturated aqueous NH_4Cl (10 mL) was added to the reaction mixture. The mixture was extracted with EtOAc (10 mL × 2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane = 1:5) to afford **27** (171 mg, 90%) as a colorless oil: $[\alpha]^{20}_{D} = -29.5$ (*c* 0.12, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 7.7 Hz, 1H), 7.23 (m, 2H), 7.18 (m, 3H), 6.80 (dt, *J* = 15.1, 6.9 Hz, 1H), 6.64 (d, *J* = 7.9 Hz, 1H), 5.77 (d, *J* = 15.3 Hz, 1H), 5.03 (m, 2H), 3.90 (dd, *J* = 10.2, 2.6 Hz, 1H), 3.67 (s, 3H), 3.43 (dd, *J* = 10.2, 3.4 Hz, 1H), 3.25 (dd, *J* = 13.4, 6.2 Hz, 1H), 3.08 (dd, *J* = 13.4, 8.1 Hz, 1H), 2.14 (td, *J* = 8.1, 1.2 Hz, 2H), 1.39 (m, 2H), 1.29 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H), 0.79 (s, 9H), -0.05 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.0, 169.3, 165.3, 145.8, 136.7, 129.3, 128.6, 127.0, 123.2, 62.2, 60.7, 59.4, 52.5, 42.1, 31.8, 30.3, 25.6, 22.3, 18.1, 13.9, -5.5, -5.8; HRMS (ESI) calcd for $C_{26}H_{43}N_2O_4SSi^+$ $[M + H]^+$ 507.2707, found 507.2724.

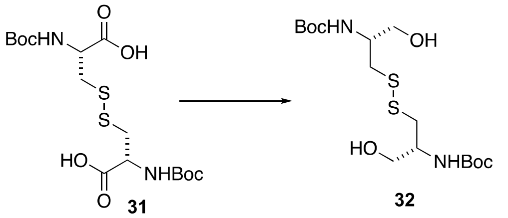


To a solution of **27** (169 mg, 0.33 mmol) in THF (3 mL) were added AcOH (22.6 µL, 0.4 mmol) and TBAF (1 M in THF, 0.4 mL, 0.4 mmol) at 0 °C. After being stirred at room temperature for 3 h, the reaction mixture was diluted with EtOAc (10 mL), and then washed with saturated aqueous NH_4Cl (10 mL) and brine (10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane = 1:2) to afford **28** (122 mg, 93%) as a white foam: $[\alpha]^{20}_{D} = -0.9$ (*c* 0.30, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.95 (d, *J* = 7.3 Hz, 1H), 7.20 (m, 5H), 6.80 (d, *J* = 8.3 Hz, 1H), 6.73 (dt, *J* = 15.3, 6.9 Hz, 1H), 5.77 (dt, *J* = 15.3, 1.3 Hz, 1H), 5.18 (dt, *J* = 8.4, 6.7 Hz, 1H), 5.00 (m, 1H), 3.82 (dd, *J* = 11.8, 3.2 Hz, 1H), 3.66 (s, 3H), 3.56 (dd, *J* = 11.9, 3.1 Hz, 1H), 3.21 (dd, *J* = 13.1, 6.4 Hz, 1H), 3.06 (dd, *J* = 13.1, 8.6 Hz, 1H), 2.12 (m, 2H), 1.37 (m, 2H), 1.28 (m, 2H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 169.7, 165.8, 146.4, 136.6, 129.6, 128.5, 127.0, 123.0, 61.5, 60.4, 60.1, 52.8, 42.5, 31.8, 30.2, 22.3, 13.9; HRMS (ESI) calcd for $C_{20}H_{28}N_2O_4SNa^+$ $[M + Na]^+$ 415.1662, found 415.1661.



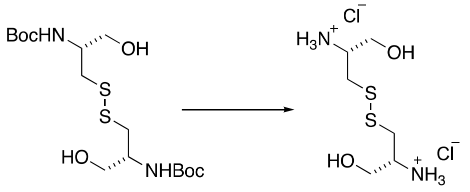
To a solution of **28** (115 mg, 0.29 mmol) in CH_2Cl_2 (3 mL) was added DAST (100 µL, 0.80 mmol) at –78 °C. After being stirred at –78 °C for 1 h, the reaction mixture was poured to ice-water (10 mL) and extracted with EtOAc (10 mL × 2). The combined organic layer was washed with brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford practically pure **29** (107 mg, Figures S19, S20, and S47) as a white powder, which was used in the next reaction without further purification to avoid the epimerization.

To a solution of the above **29** (27.5 mg, ca 73 µmol) in 1,2-dichloroethane (1 mL) was added trimethyltin hydroxide (40 mg, 0.22 mmol) at room temperature. The reaction mixture was heated at 80 °C for 1 h, and then concentrated under reduced pressure. The residue was dissolved in EtOAc (10 mL), washed with 0.01 M $KHSO_4$ aqueous solution (5 mL × 5) and brine (10 mL), dried over $MgSO_4$, filtered and concentrated to afford practically pure **30** (26.4 mg, Figures S21, S22, and S30) as a white foam, which was used in the next reaction without further purification to avoid the epimerization.



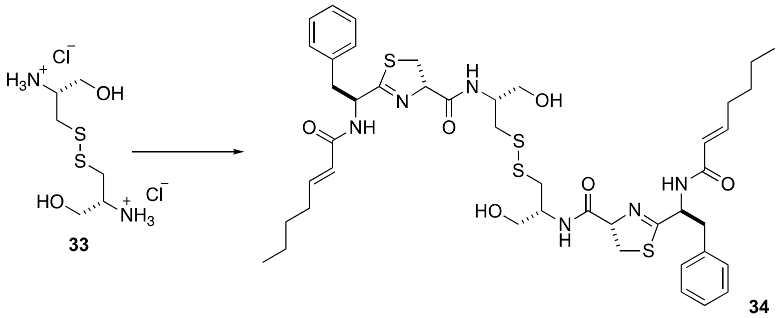
31 **32**

To a solution of **31** (2.98 g, 6.8 mmol) in THF (40 mL) were added *N*-methylmorpholine (1.64 mL, 14.9 mmol) and isobutyl chloroformate (1.95 mL, 14.8 mmol) at –10 °C. After being stirred for 15 min, $NaBH_4$ (1022 mg, 27.0 mmol) was added to the solution. After being stirred for 15 min at –10 °C, saturated aqueous NH_4Cl (40 mL) was added to the reaction mixture. The mixture was extracted with EtOAc (50 mL × 2). The combined organic layer was washed with brine (80 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc/hexane = 2:1) to afford **32** (2.27 g, 81%) as a white powder: $[\alpha]^{20}_{D} = 85.1$ (*c* 0.77, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 6.55 (d, $J = 8.3$ Hz, 1H), 3.85 (m, 1H), 3.62 (dd, $J = 11.1, 4.9$ Hz, 1H), 3.57 (dd, $J = 11.1, 5.5$ Hz, 1H), 2.97 (dd, $J = 13.7, 5.7$ Hz, 1H), 2.82 (dd, $J = 13.7, 7.8$ Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, CD_3OD) δ 158.0, 80.2, 63.9, 53.4, 41.5, 28.8; HRMS (ESI) calcd for $C_{16}H_{32}N_2O_6S_2Na^+$ $[M + Na]^+$ 435.1594, found 435.1587.



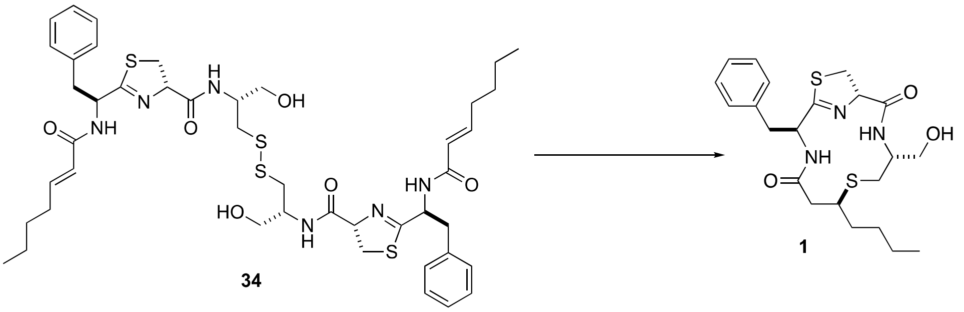
32 **33**

To **32** (283 mg, 0.69 mmol) was added 2 M HCl in ethanol (3 mL) at room temperature. After being stirred for 1 h, the reaction mixture was concentrated to afford **33** (196 mg, 100%) as a white foam, which was used in the next reaction without further purification: $[\alpha]^{20}_{D} = -100$ (*c* 0.29, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 3.88 (dd, $J = 11.8, 3.7$ Hz, 1H), 3.76 (dd, $J = 11.8, 5.4$ Hz, 1H), 3.60 (m, 1H), 3.12 (dd, $J = 14.4, 6.6$ Hz, 1H), 3.05 (dd, $J = 14.4, 7.1$ Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 61.2, 53.3, 37.0; HRMS (ESI) calcd for $C_6H_{17}N_2O_2S_2^+$ $[M + H]^+$ 213.0726, found 213.0730.



33 **34**

To a solution of **33** (8.6 mg, 30.2 μmol) and **30** (24 mg, 67 μmol) in DMF (0.5 mL) were added *i*-Pr_2NEt (12 μL, 67 μmol), Oxyma (9.5 mg, 67 μmol), and EDCI·HCl (13 mg, 67 μmol) at 0 °C. After being stirred at 0 °C for 2 h and at room temperature for 2 h, saturated aqueous NH_4Cl (5 mL) was added to the reaction mixture. The resulting solution was extracted with EtOAc (5 mL × 2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography ($CHCl_3$/MeOH = 50:1) to afford **34** (25.6 mg, 94%) as a white foam: $[\alpha]^{20}_{D} = -86.3$ (c 0.50, MeOH); ^1H NMR (500 MHz, CD_3OD) δ 7.26 (m, 4H), 7.20 (m, 1H), 6.75 (dt, J = 15.3, 7.0 Hz, 1H), 5.91 (dt, J = 15.4, 1.4 Hz, 1H), 5.09 (t, J = 8.9 Hz, 1H), 4.95 (dd, J = 9.3, 5.6 Hz, 1H), 4.22 (m, 1H), 3.68 (dd, J = 11.4, 4.8 Hz, 2H), 3.59 (m, 2H), 3.52 (dd, J = 11.2, 8.2 Hz, 1H), 3.31 (m, 1H), 3.06 (dt, J = 13.9, 7.7 Hz, 1H), 2.92 (dd, J = 13.8, 8.1 Hz, 1H), 2.18 (m, 2H), 1.43 (m, 2H), 1.34 (m, 2H), 0.92 (t, J = 7.3 Hz, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ 178.6, 173.1, 168.7, 147.0, 138.5, 130.3, 129.5, 127.8, 124.0, 80.0, 63.4, 55.2, 52.3, 40.6, 39.7, 36.6, 32.8, 23.3, 14.2; HRMS (ESI) calcd for $C_{44}H_{61}N_6O_6S_4^+$ $[M + H]^+$ 897.3530, found 897.3527.



34

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To a solution of **34** (23.0 mg, 25.6 μmol) in MeOH/aqueous buffer (pH 9, $Na_2CO_3/NaHCO_3$) (10 mL/10 mL) was added TCEP·HCl (22 mg, 76.8 μmol) at room temperature. The reaction mixture was stirred for 30 min and then diluted with pH 9 $Na_2CO_3/NaHCO_3$ buffer (20 mL). The reaction mixture was allowed to room temperature for an additional 2 days. The mixture was extracted with EtOAc (50 mL × 2). The combined organic layer was washed with brine (80 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by reversed-phase HPLC [column: PEGASIL ODS SP100 20 × 250 mm; eluent: MeOH/H_2O = 70/30, 8.0 mL/min; detection: UV 210 nm] to afford **1** (15.4 mg, t_R 31.0 min, 67%) as a white foam: $[\alpha]^{20}_{D} = -70.4$ (c 0.39, MeOH); ^1H NMR (600 MHz, DMSO-d_6) δ 8.84 (d, J = 6.8 Hz, 1H), 7.31 (m, 4H), 7.22 (t, J = 7.1 Hz, 1H), 6.77 (d, J = 5.7 Hz, 1H), 5.08 (dd, J = 7.1, 6.2 Hz, 1H), 4.82 (s, 1H), 4.54 (td, J = 9.3, 5.6 Hz, 1H), 3.56 (d, J = 6.8 Hz, 2H), 3.51 (d, J = 10.1 Hz, 1H), 3.39 (m, 1H), 3.21 (t, J = 7.1 Hz, 1H), 3.10 (dd, J = 13.0, 4.3 Hz, 1H), 3.03 (dd, J = 13.9, 5.1 Hz, 1H), 2.95 (dd, J = 13.9, 9.9 Hz, 1H), 2.90 (m, 1H), 2.79 (dd, J = 13.1, 8.8 Hz, 1H), 2.39 (m, 2H), 1.55 (m, 1H), 1.41 (m, 3H), 1.27 (m, 2H), 0.87 (t, J = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, DMSO-d_6) δ 177.7, 171.6, 170.3, 137.4, 129.1, 128.3, 126.7, 77.7, 61.9, 54.3, 50.6, 45.8, 42.5, 37.6, 36.9, 36.8, 34.9, 28.8, 14.0; HRMS (ESI) calcd for $C_{22}H_{32}N_3O_3S_2^+$ $[M + H]^+$ 450.1880, found 450.1892.

Table S3. Optimization of the cyclization condition.

entry	solvent	yield[b]
1	0.1 M PBS buffer, pH 8/MeOH[a] (= 4:1)	5%
2	MeOH, 5% TEA	<1%
3	0.1 M $NaHCO_3$ solution, pH 8.3/MeOH (= 4:1)	45%
4	0.1 M $Na_2CO_3/NaHCO_3$ buffer, pH 9/MeOH (= 4:1)	71% (67%)[c]
5	0.1 M $Na_2CO_3/NaHCO_3$ buffer, pH 10/MeOH (= 4:1)	48%

(a) MeOH was added to dissolve **34**. (b) Estimated by HPLC. (c) Isolated yield.

Spectral Data

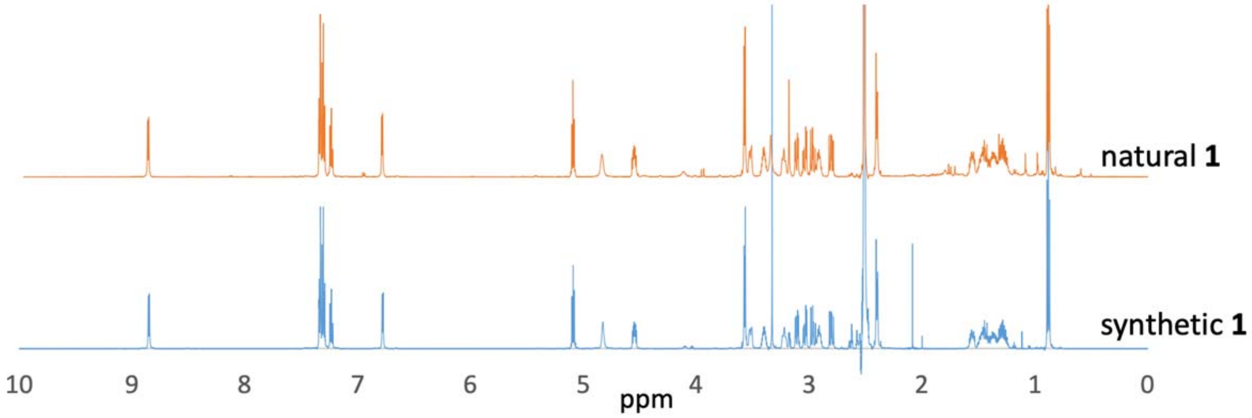

Fig. S3 Comparison of the ^{1}H NMR spectra of natural **1** and synthetic **1**. 600 MHz in DMSO-d_6

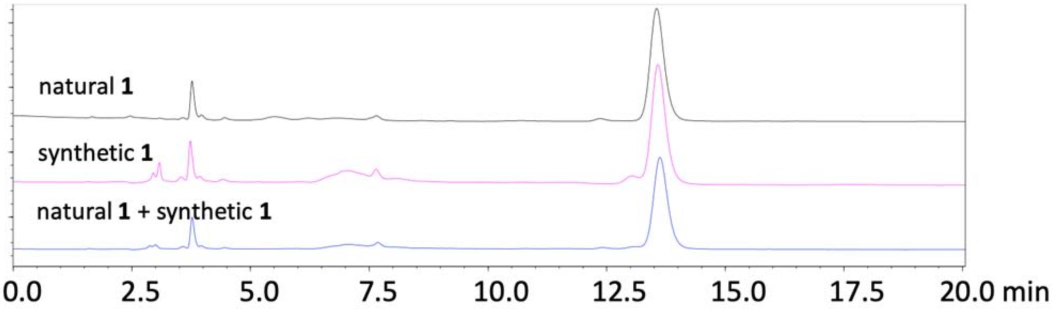

Fig. S4 HPLC charts of natural **1** and synthetic **1**. (column: PEGASIL ODS SP100 4.6 × 250 mm; eluent: MeOH/H_2O = 70/30, 1.0 mL/min; detection: UV 210 nm)

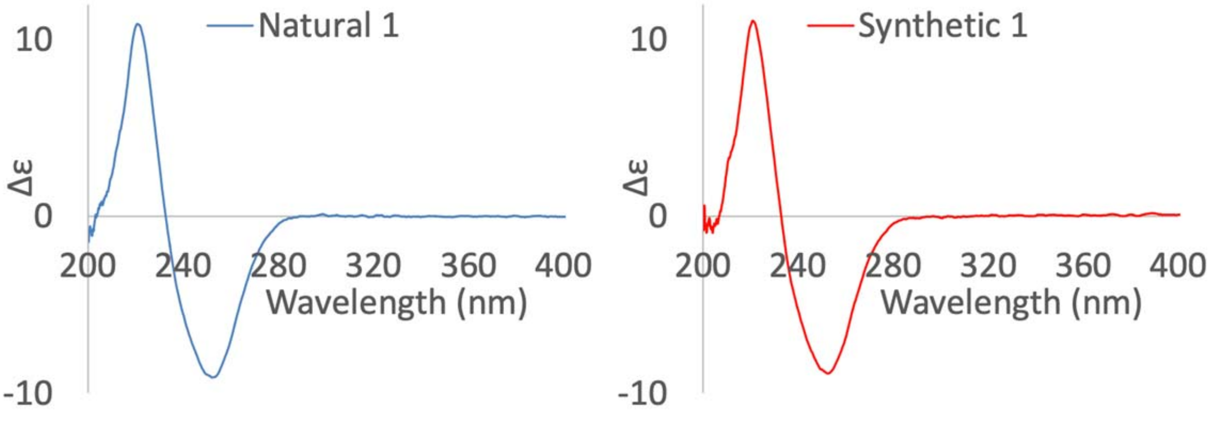

Fig. S5 Comparison of the CD spectra of natural **1** and synthetic **1** in MeOH.

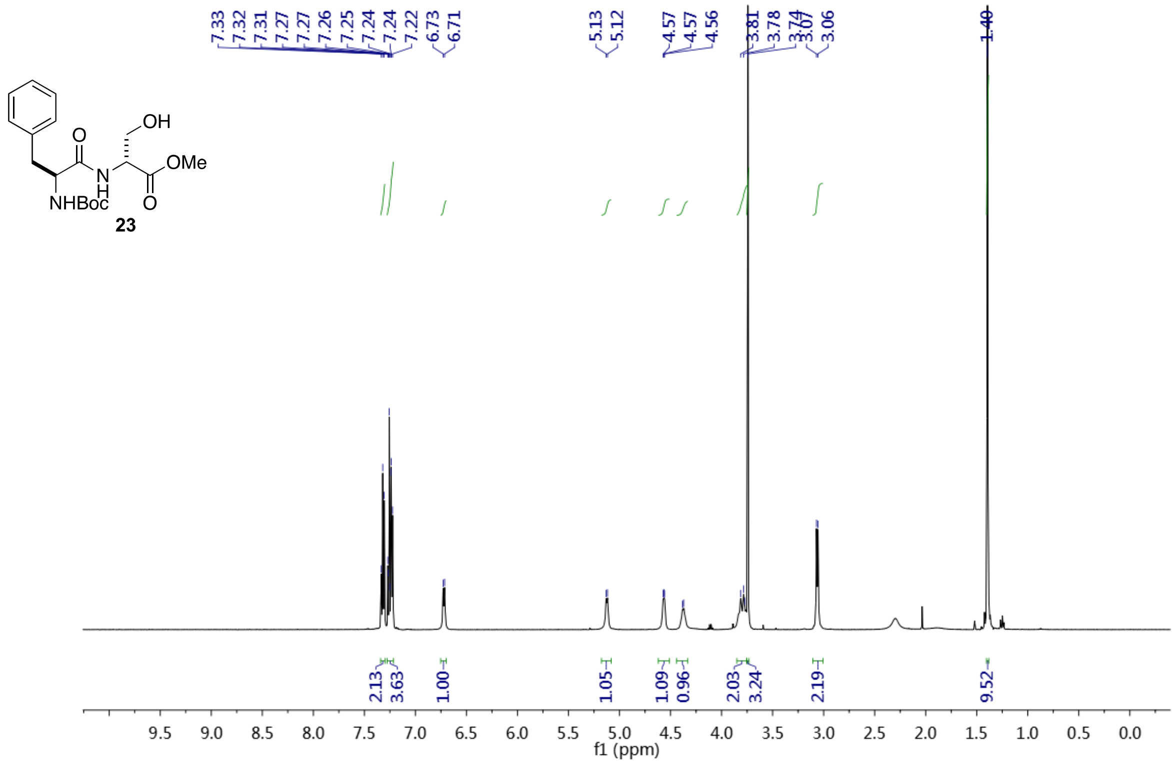

Fig. S6 ^{1}H NMR spectrum (500 MHz) of **23** in $CDCl_3$.

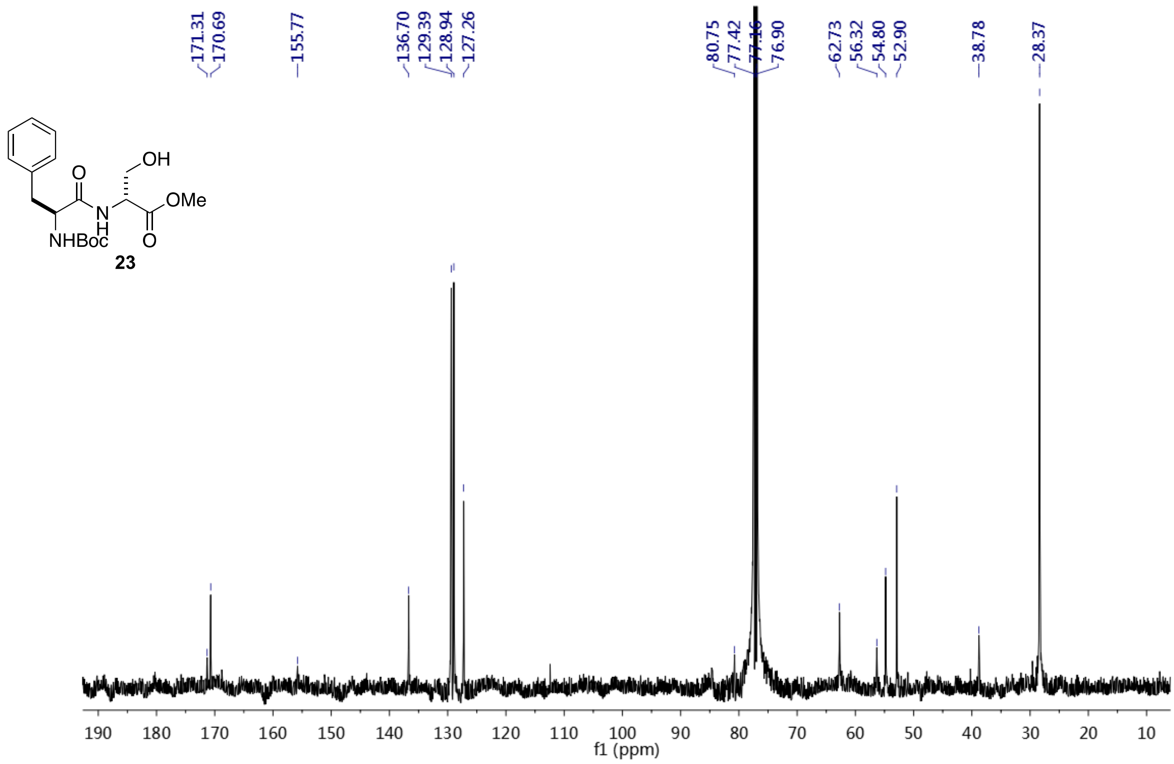

Fig. S7 ^{13}C NMR spectrum (125 MHz) of **23** in $CDCl_3$.

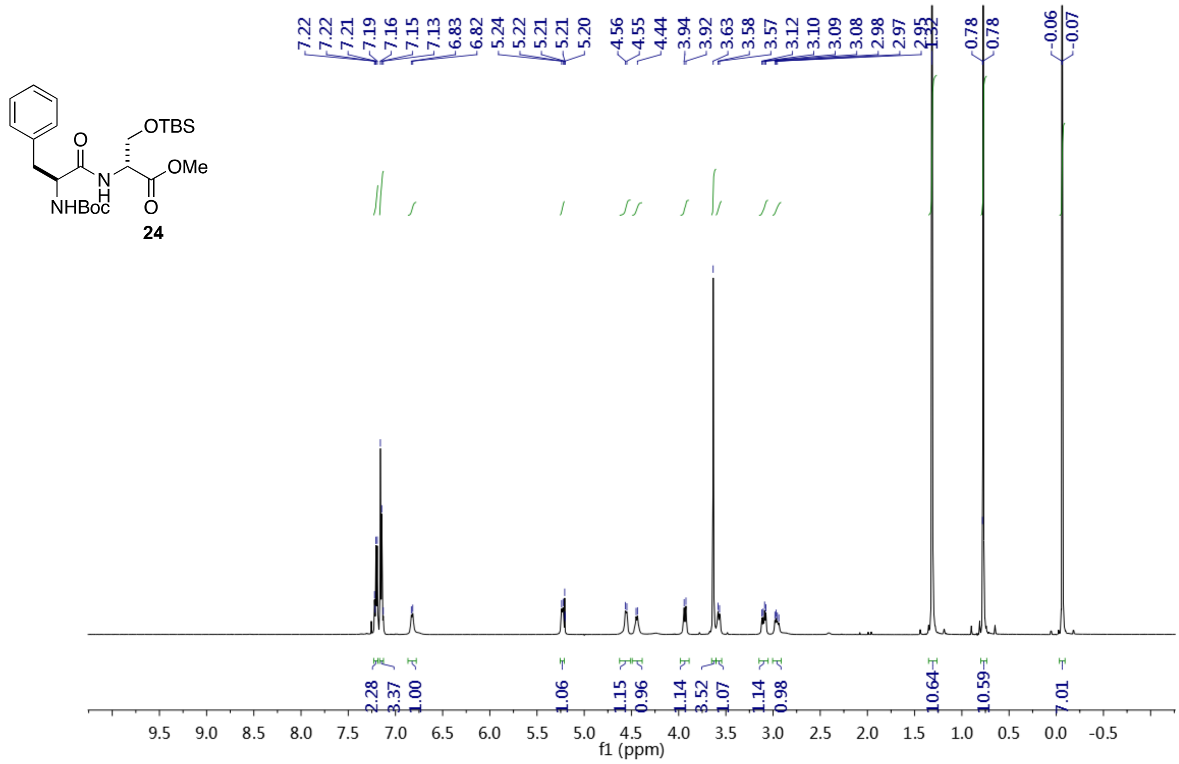

Fig. S8 ^{1}H NMR spectrum (500 MHz) of **24** in $CDCl_3$.

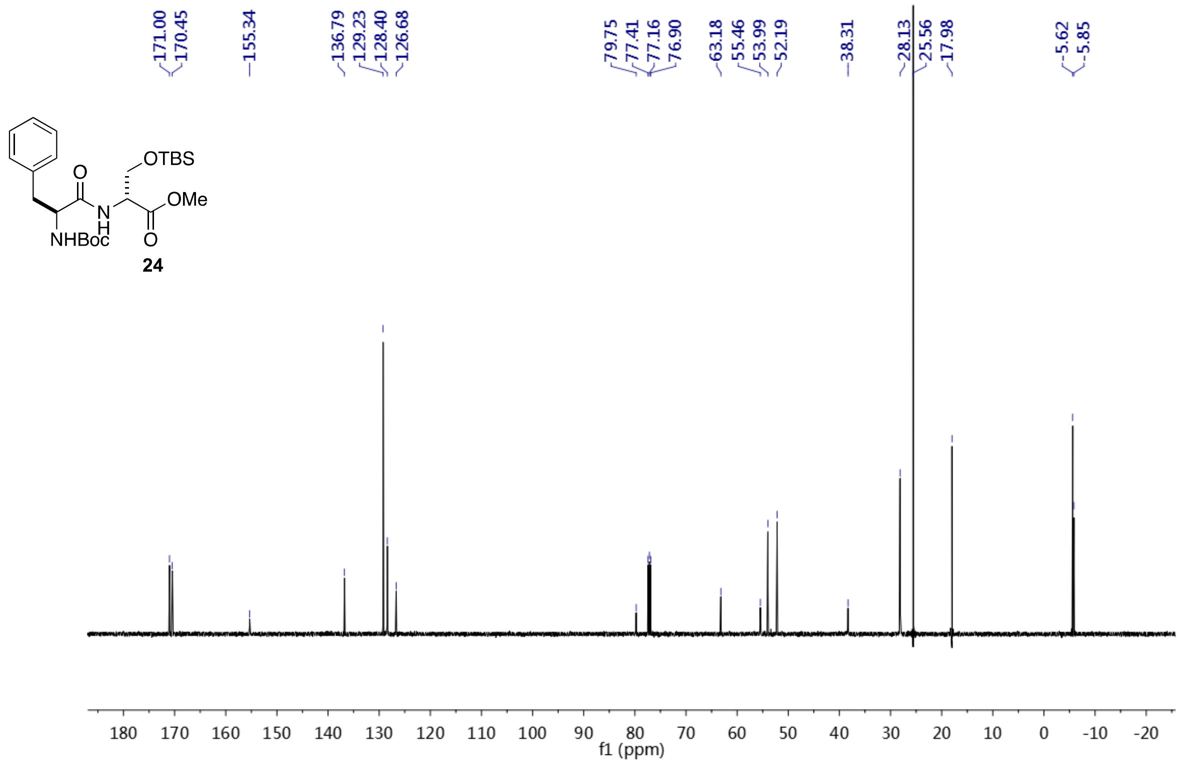

Fig. S9 ^{13}C NMR spectrum (125 MHz) of **24** in $CDCl_3$.

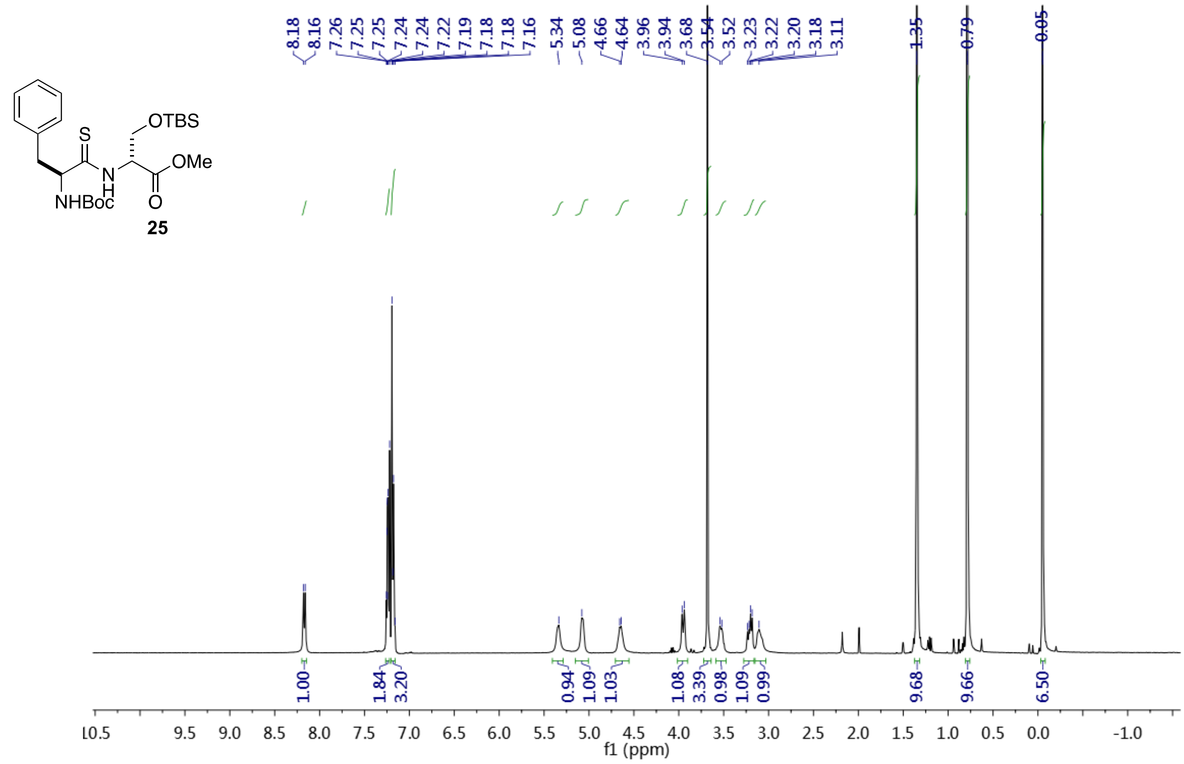

Fig. S10 ^{1}H NMR spectrum (500 MHz) of **25** in $CDCl_3$.

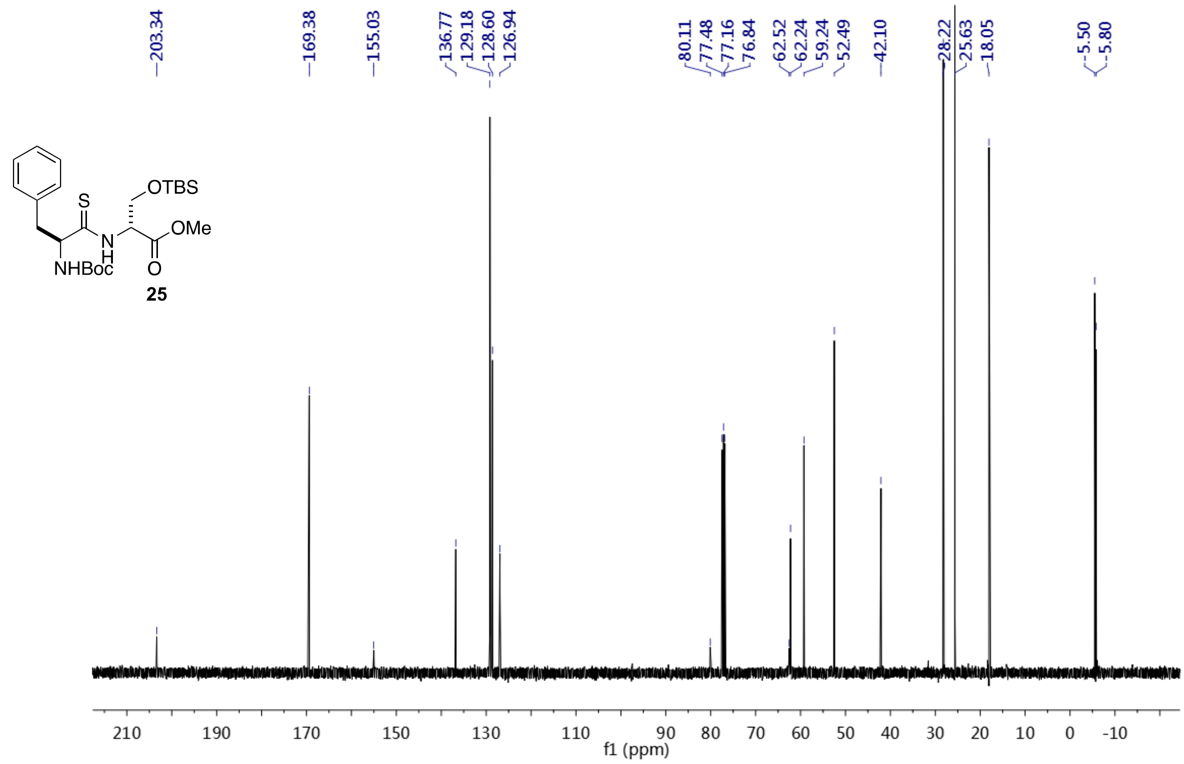

Fig. S11 ^{13}C NMR spectrum (125 MHz) of **25** in $CDCl_3$.

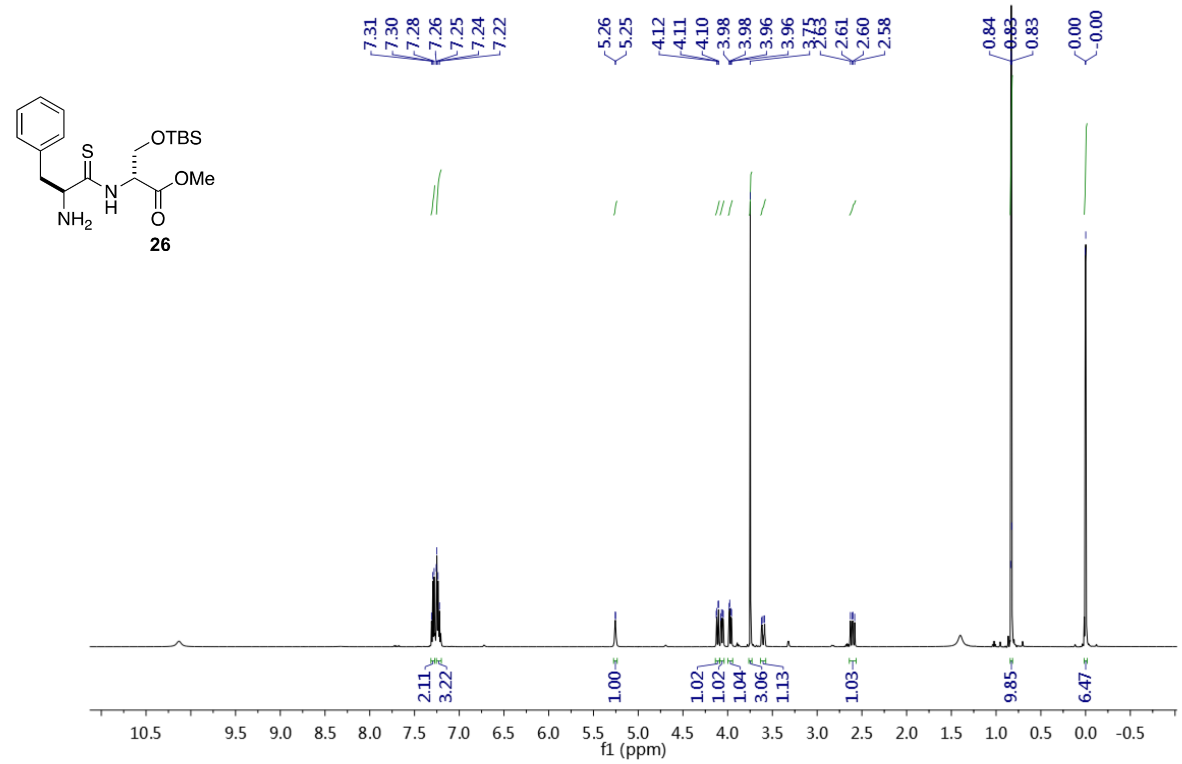

Fig. S12 ^{1}H NMR spectrum (500 MHz) of **26** in $CDCl_3$.

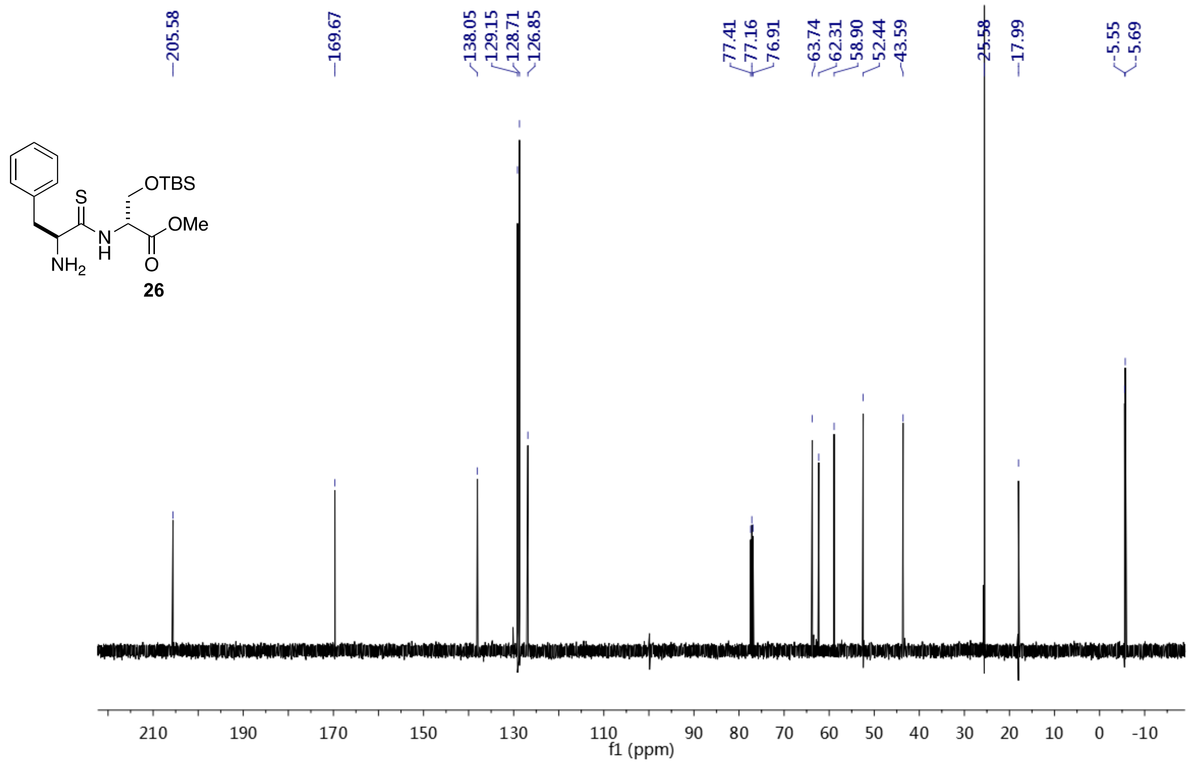

Fig. S13 ^{13}C NMR spectrum (125 MHz) of **26** in $CDCl_3$.

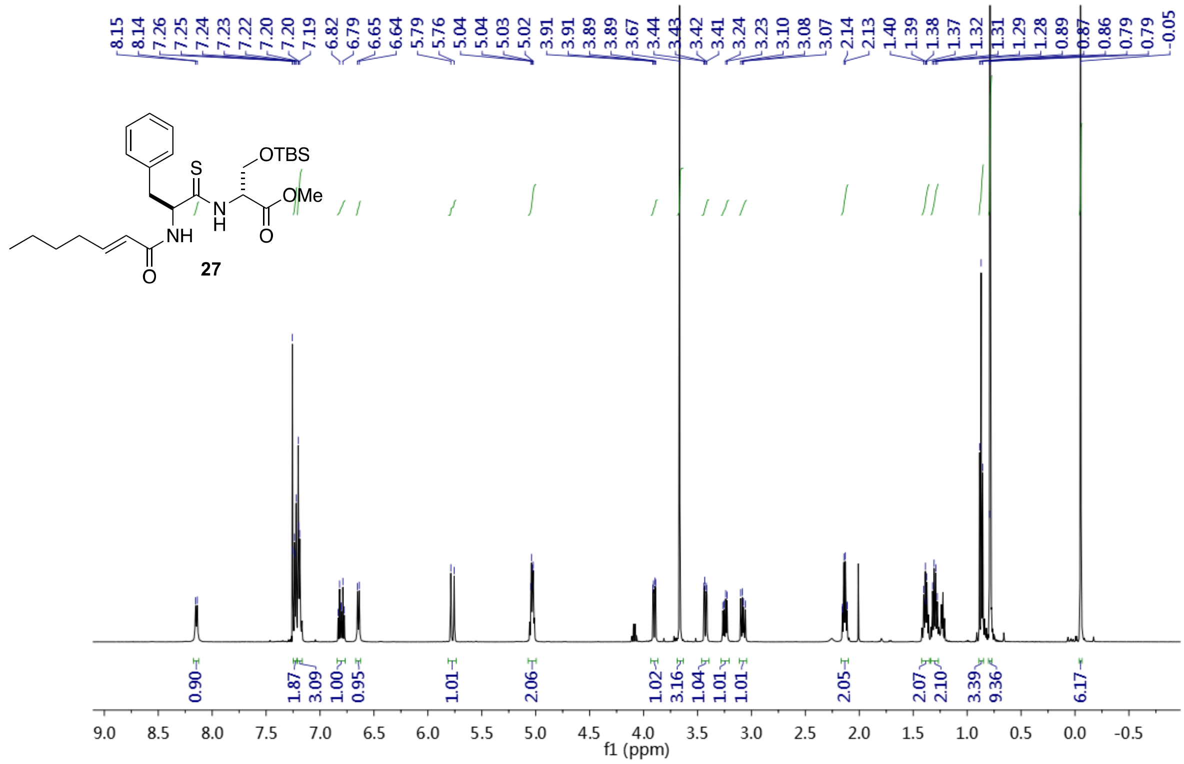

Fig. S14 ^{1}H NMR spectrum (500 MHz) of **27** in CDCl$_3$.

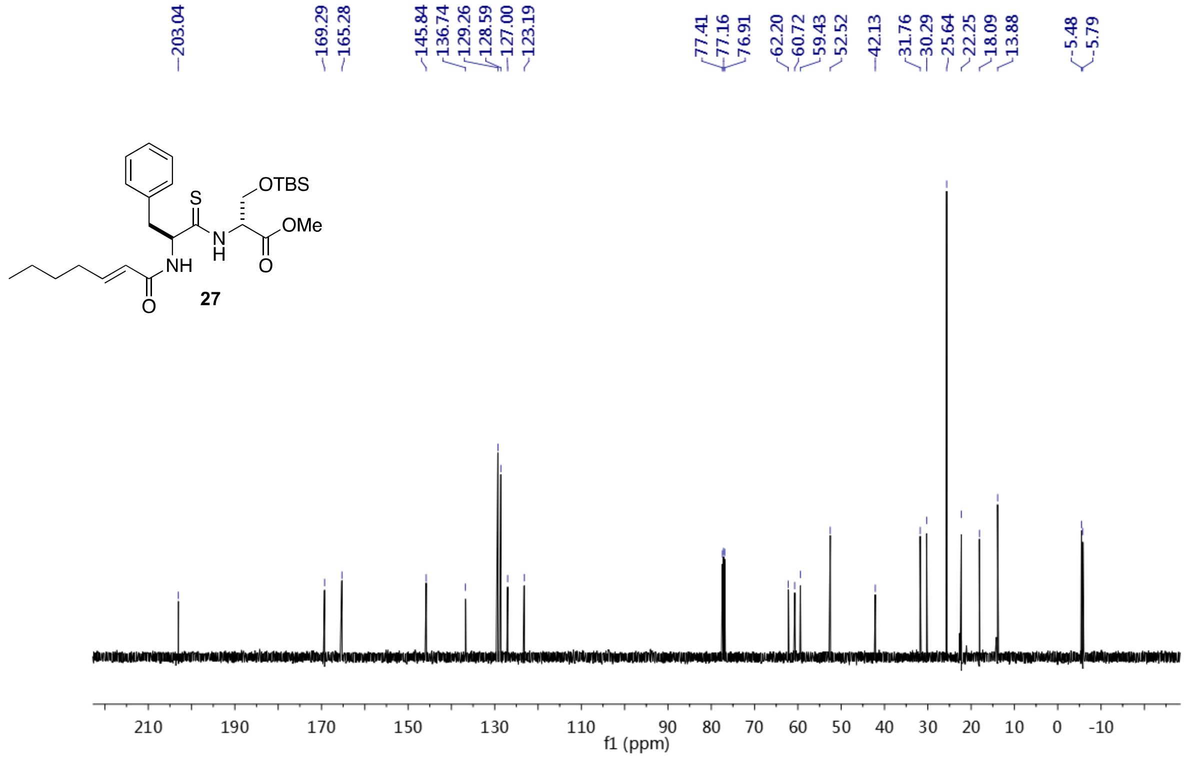

Fig. S15 ^{13}C NMR spectrum (125 MHz) of **27** in CDCl$_3$.

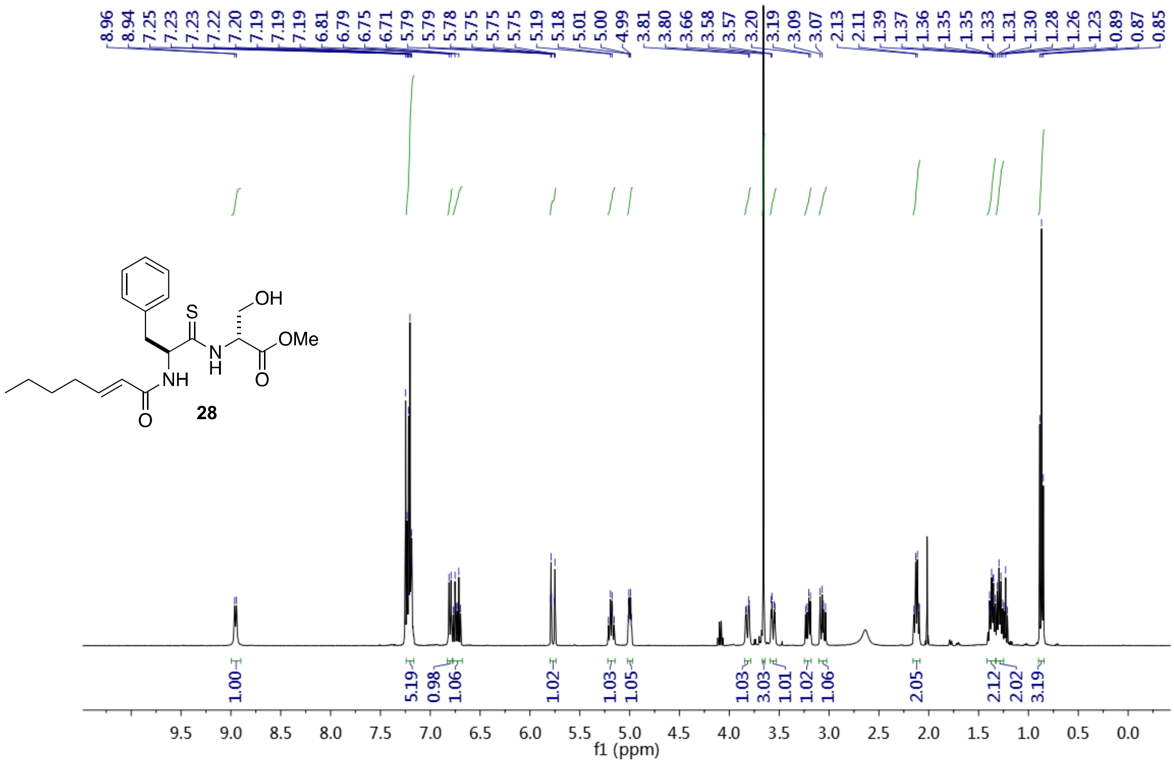

Fig. S16 ^{1}H NMR spectrum (500 MHz) of **28** in $CDCl_3$.

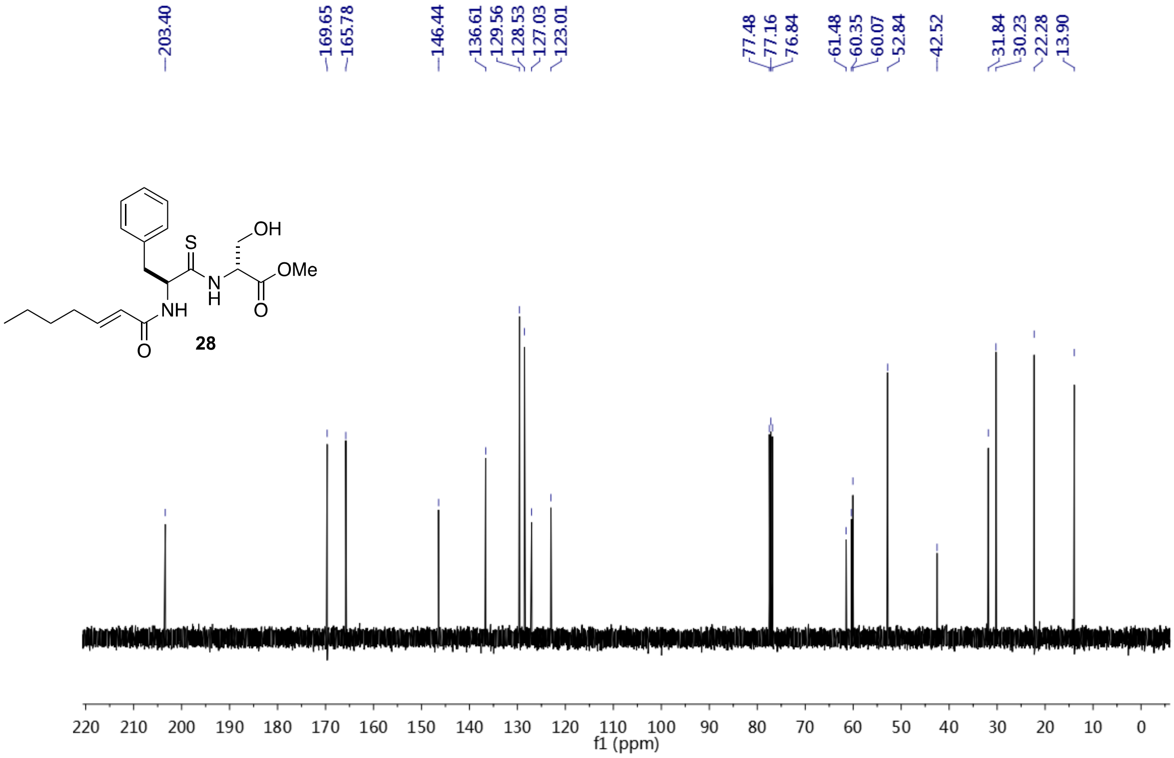

Fig. S17 ^{13}C NMR spectrum (125 MHz) of **28** in $CDCl_3$.

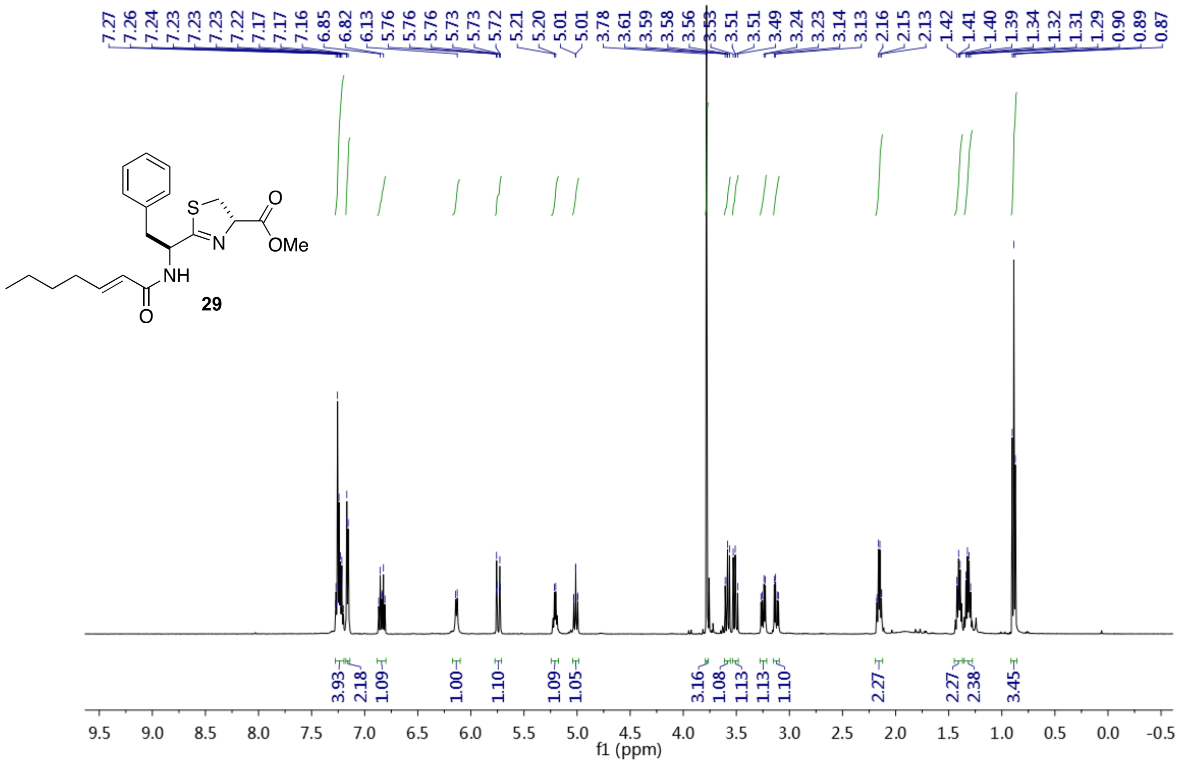

Fig. S18 ^{1}H NMR spectrum (500 MHz) of **29** in $CDCl_3$.

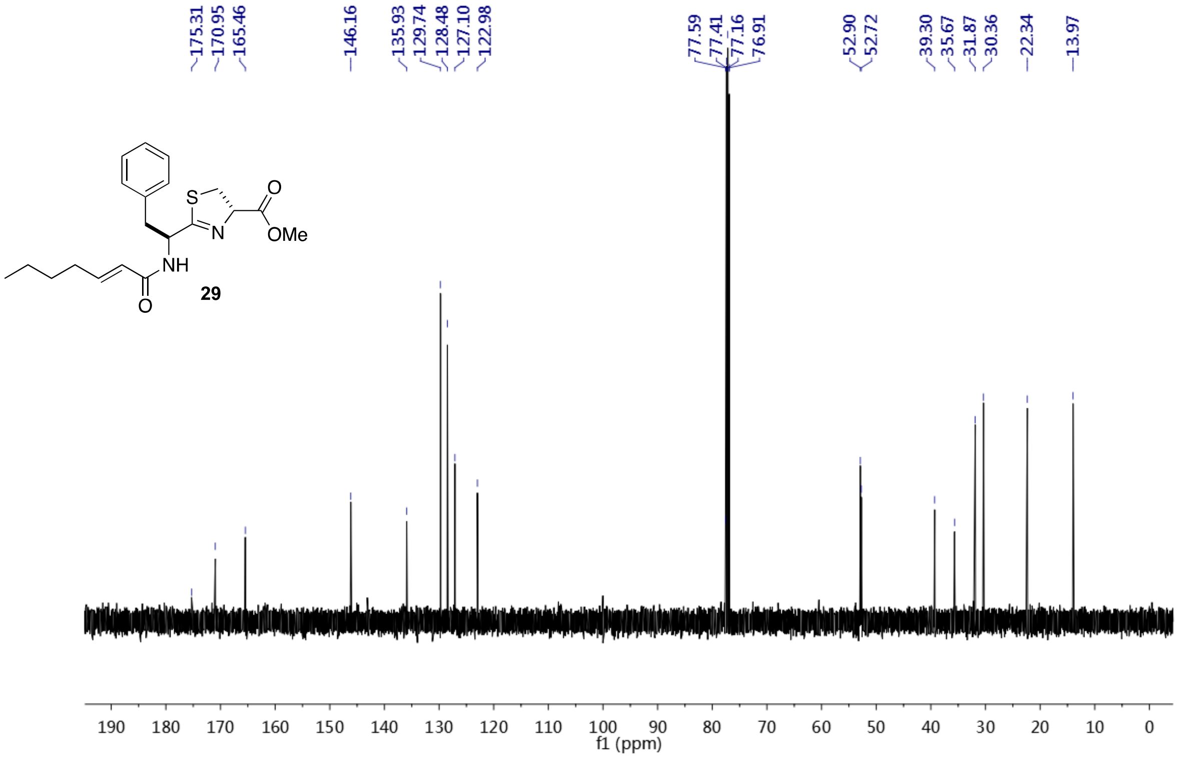

Fig. S19 ^{13}C NMR spectrum (125 MHz) of **29** in $CDCl_3$.

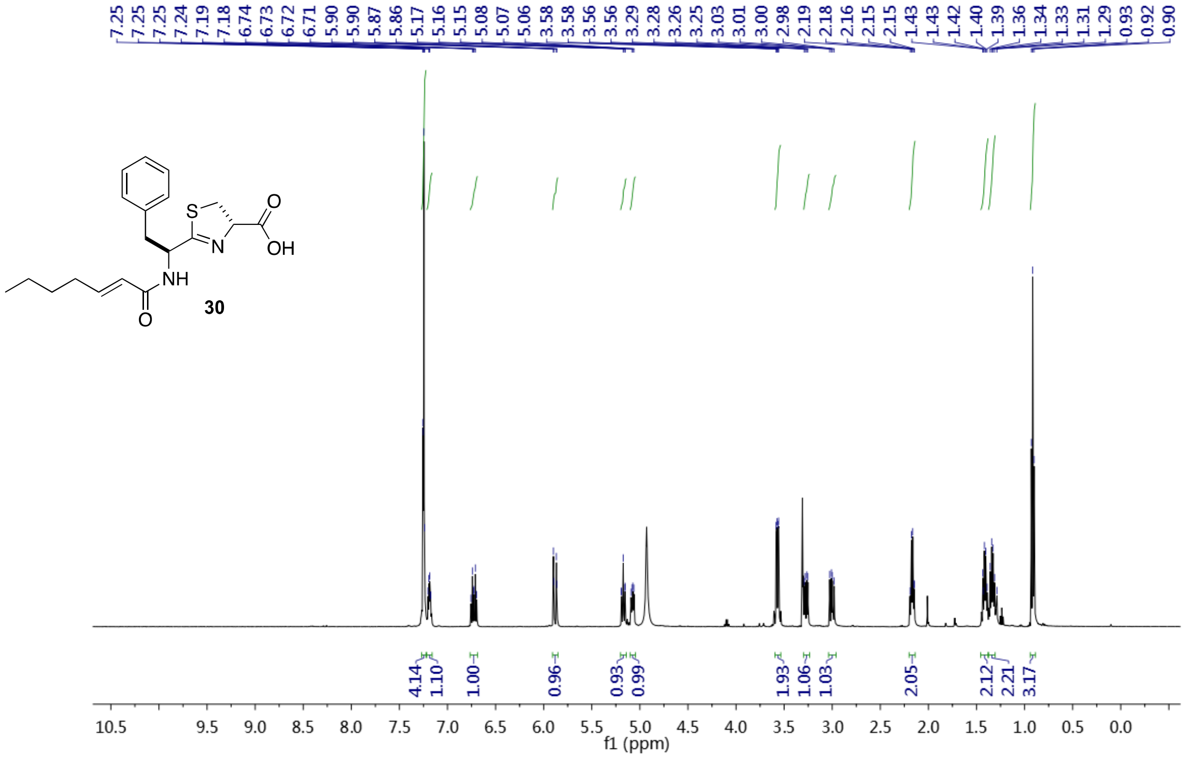

Fig. S20 ^{1}H NMR spectrum (500 MHz) of **30** in CD_3OD.

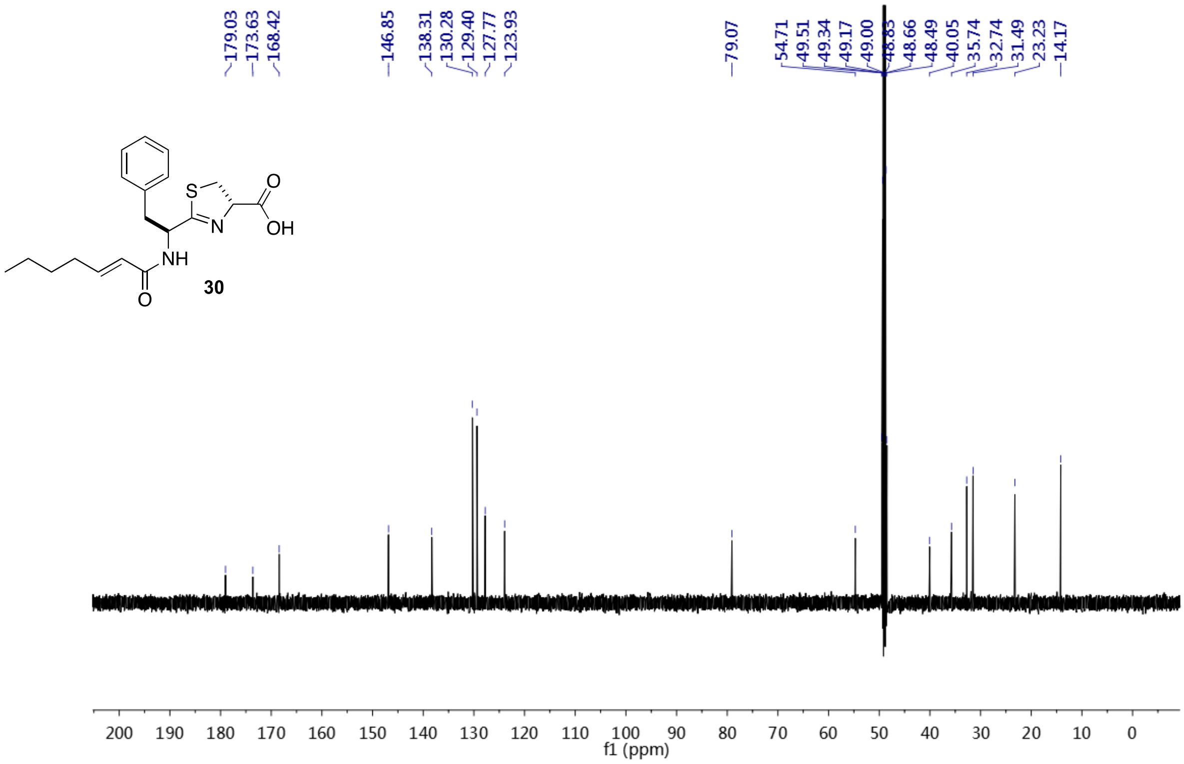

Fig. S21 ^{13}C NMR spectrum (125 MHz) of **30** in CD_3OD.

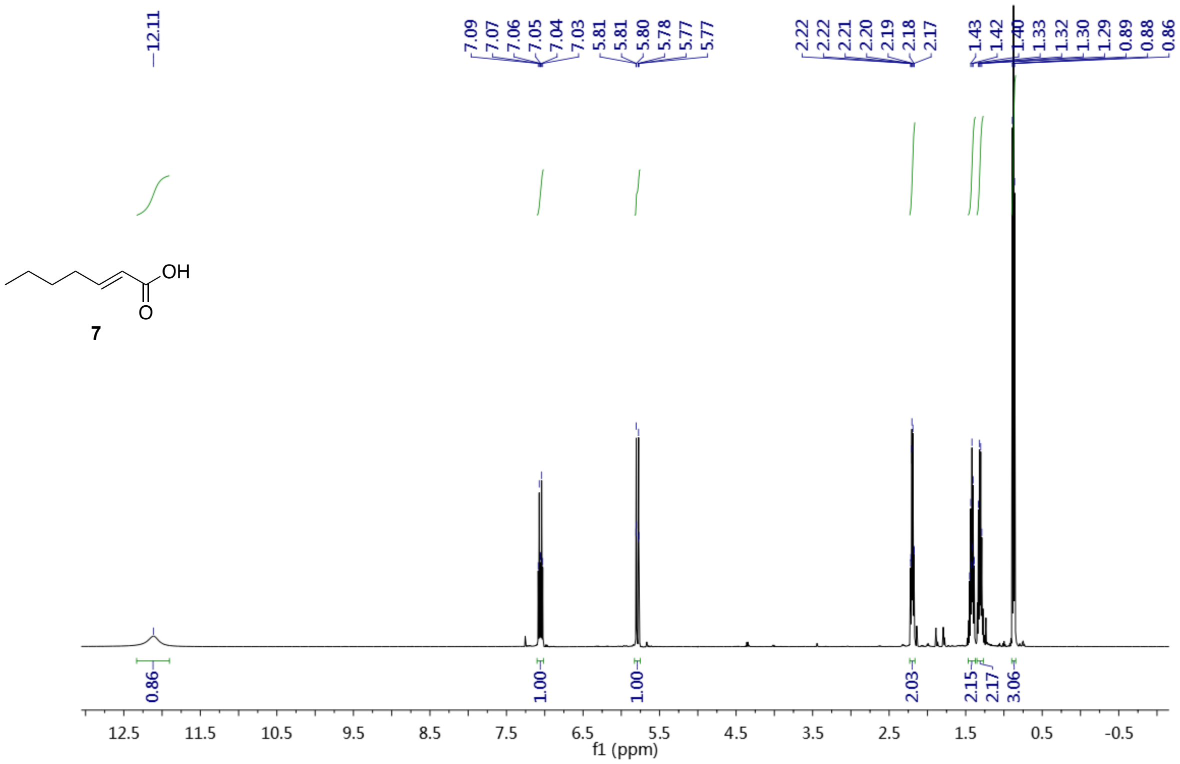

Fig. S22 ^{1}H NMR spectrum (500 MHz) of **7** in $CDCl_3$.

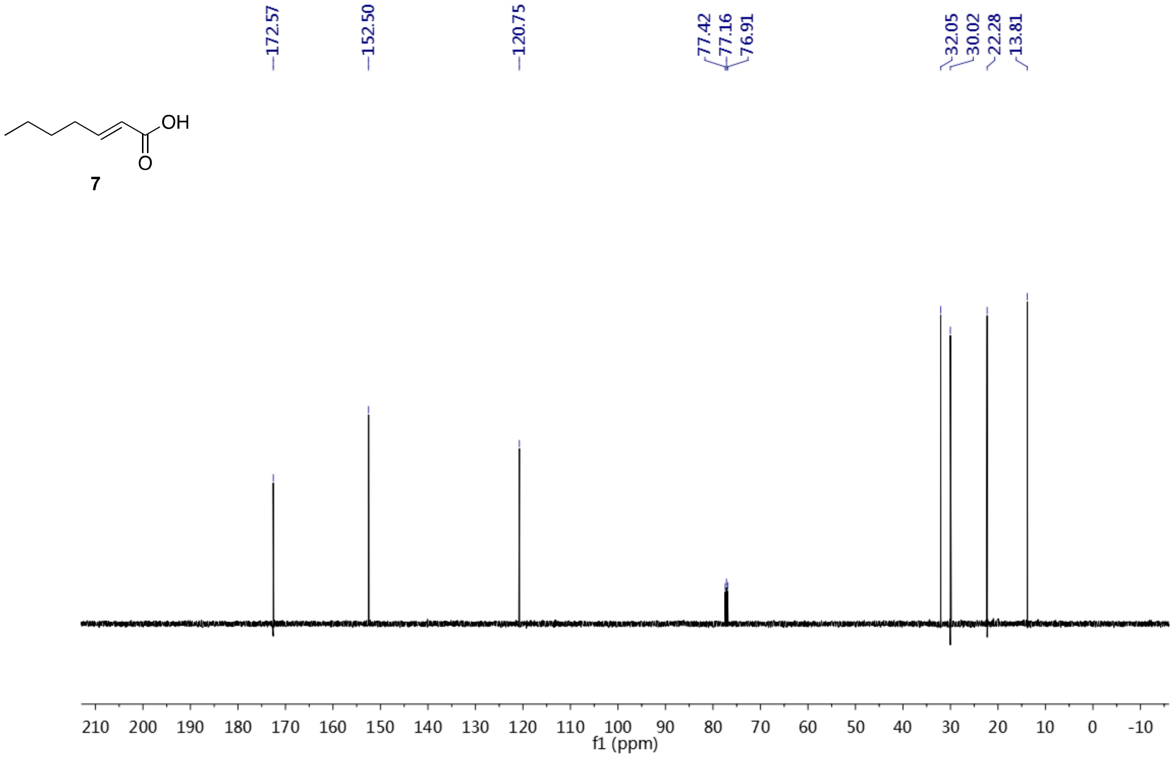

Fig. S23 ^{13}C NMR spectrum (125 MHz) of **7** in $CDCl_3$.

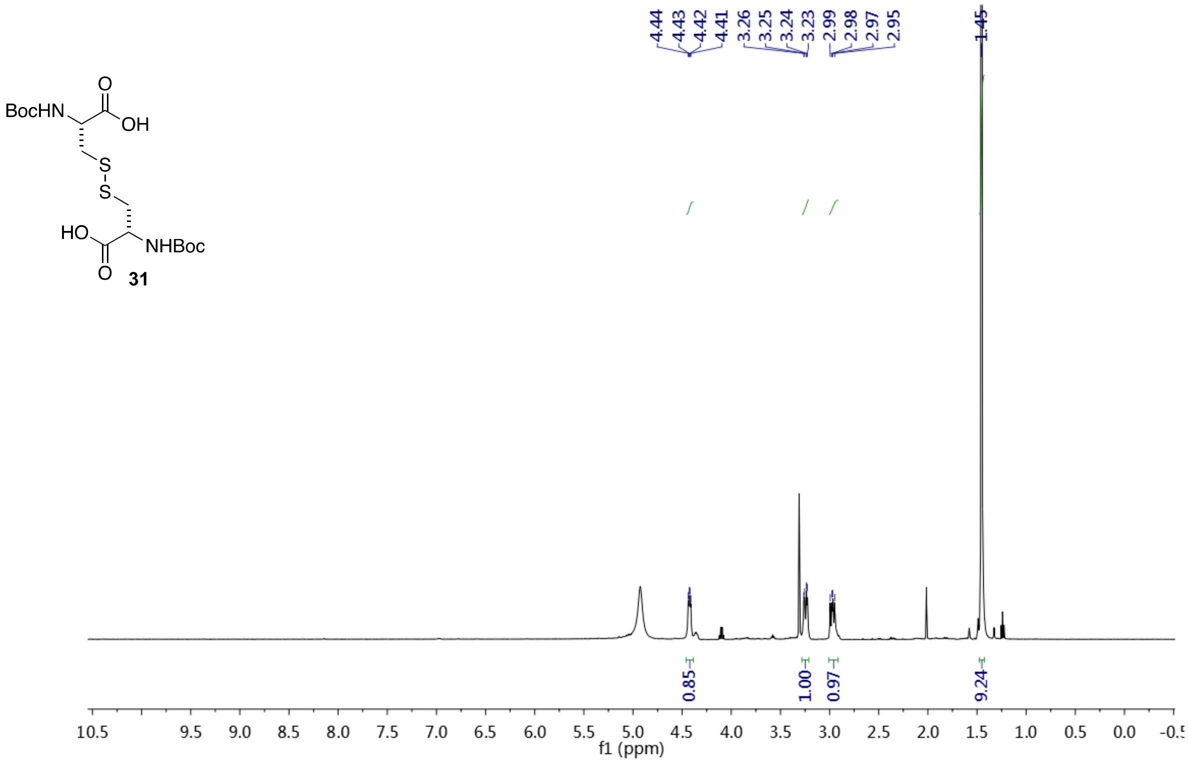

Fig. S24 ^{1}H NMR spectrum (500 MHz) of **31** in CD_3OD.

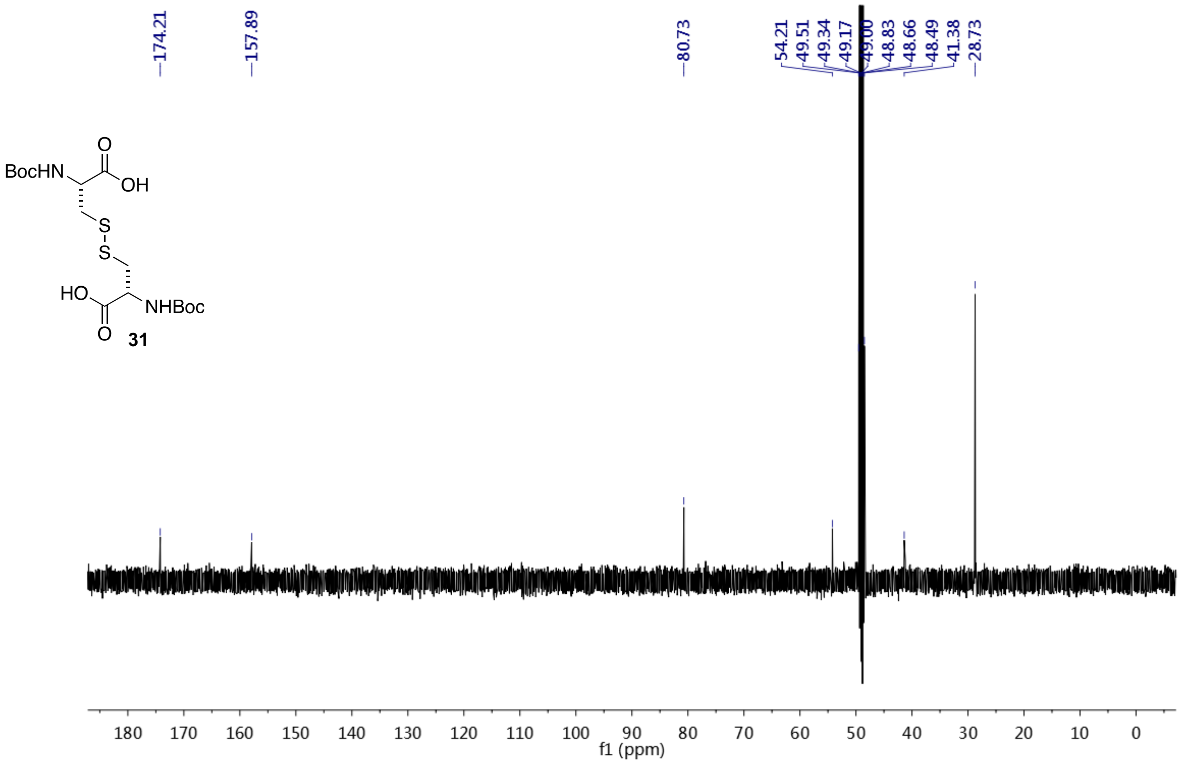

Fig. S25 ^{13}C NMR spectrum (125 MHz) of **31** in CD_3OD.

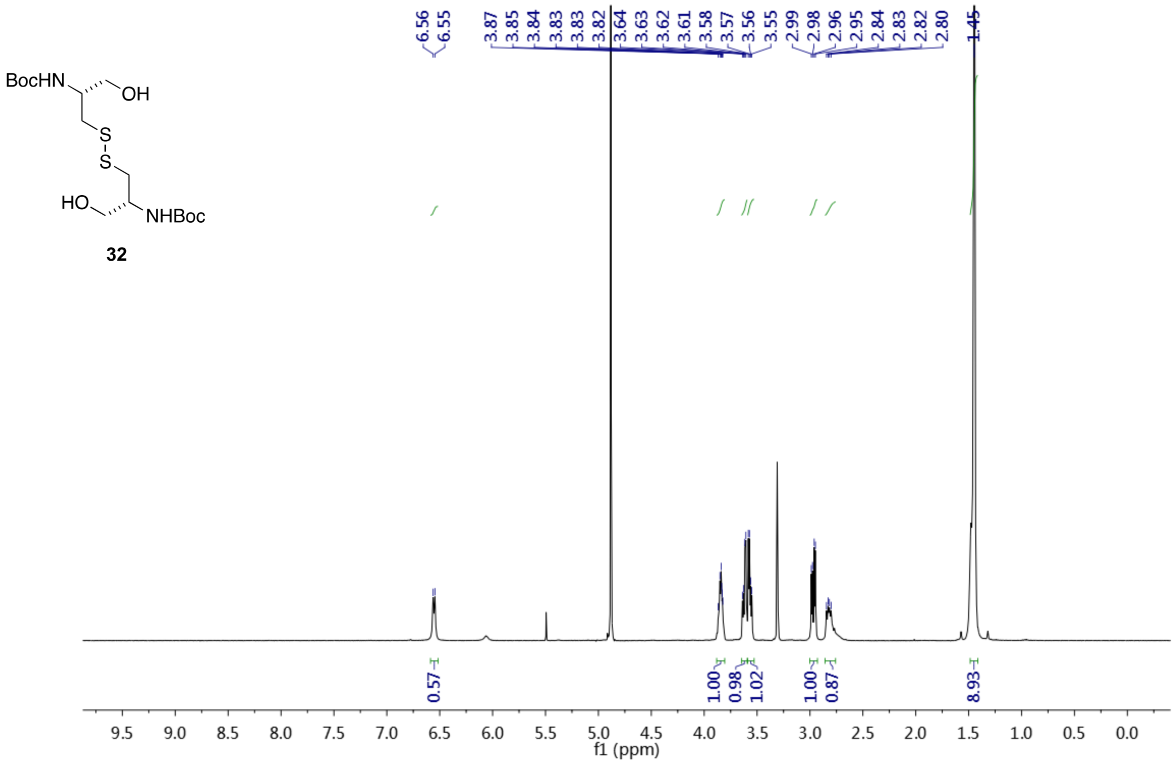

Fig. S26 ^{1}H NMR spectrum (500 MHz) of **32** in CD_3OD.

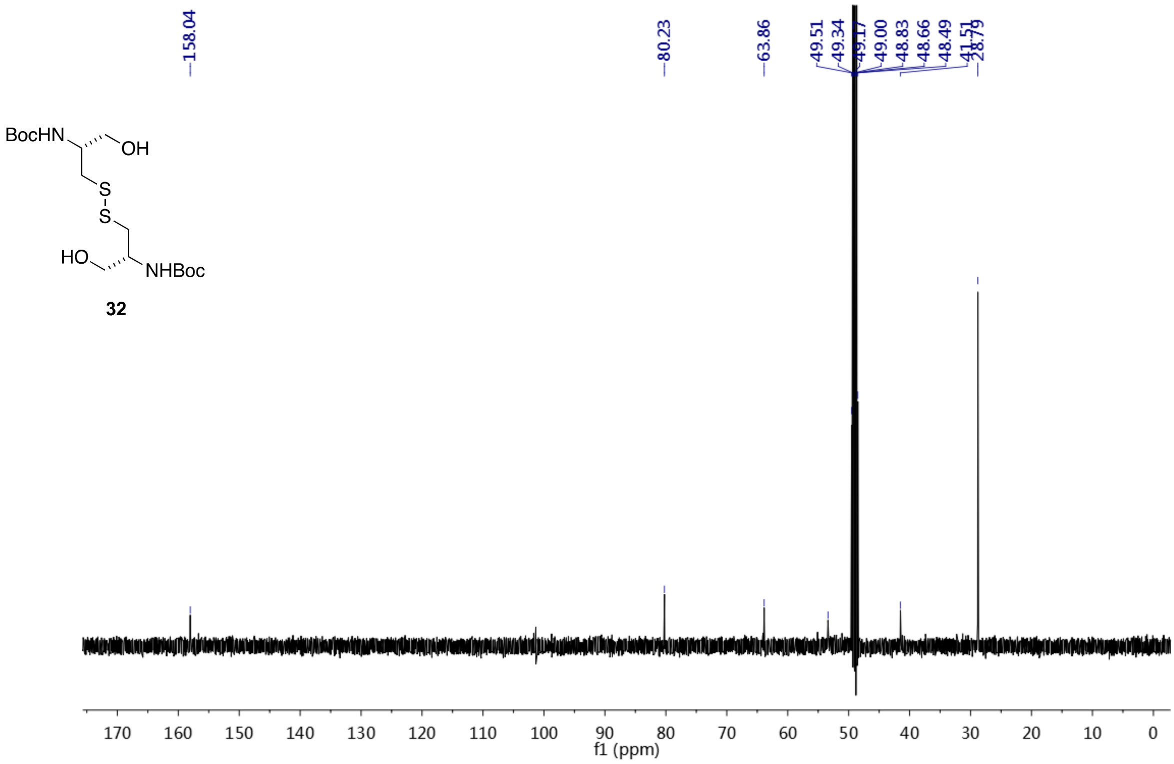

Fig. S27 ^{13}C NMR spectrum (125 MHz) of **32** in CD_3OD.

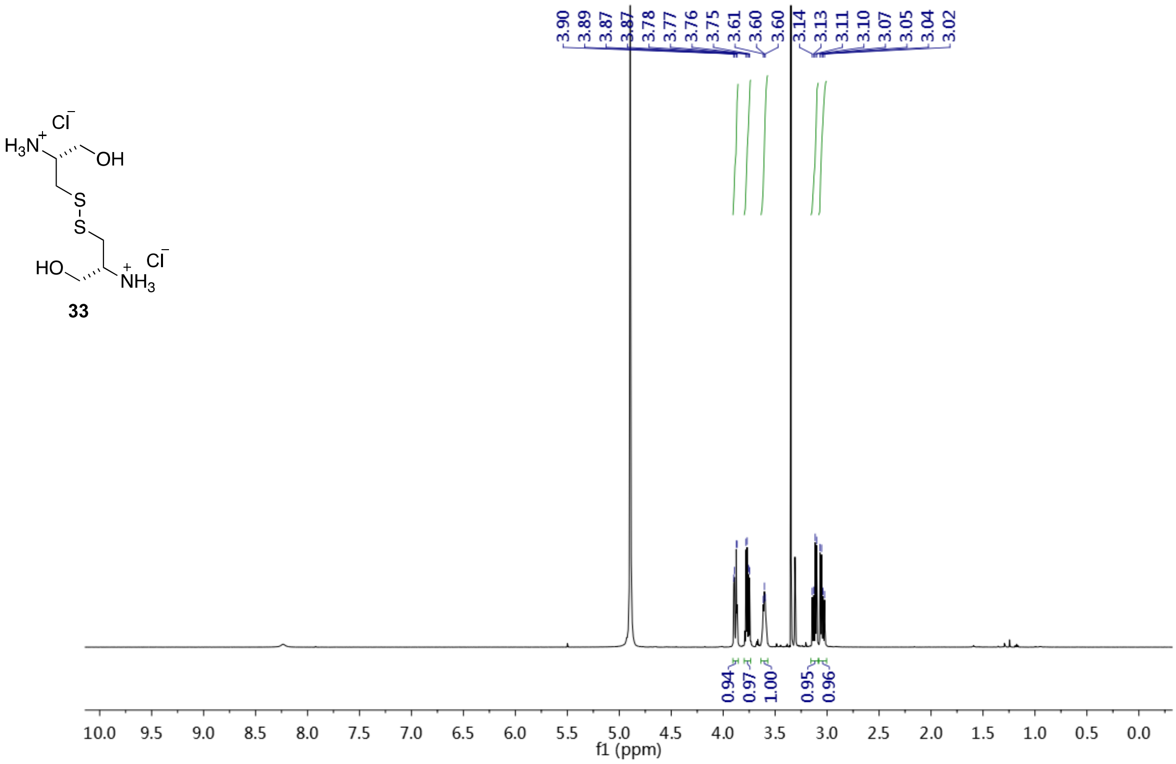

Fig. S28 ^{1}H NMR spectrum (500 MHz) of **33** in CD_3OD.

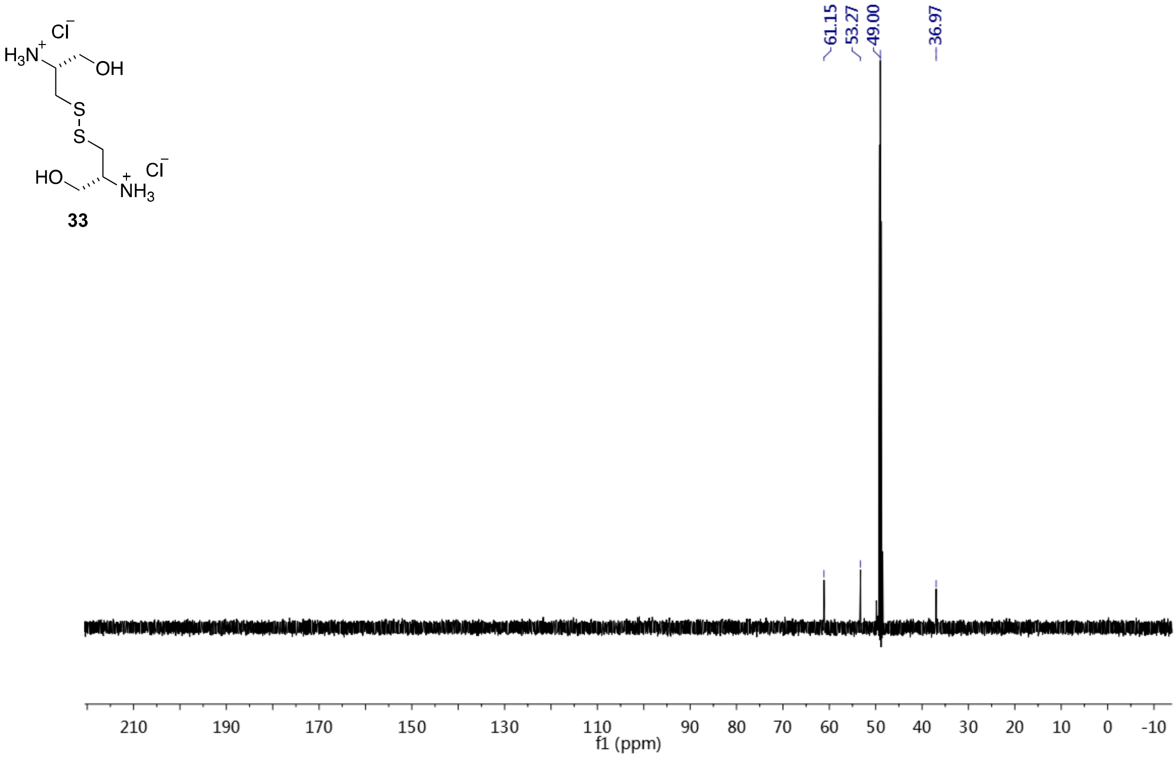

Fig. S29 ^{13}C NMR spectrum (125 MHz) of **33** in CD_3OD.

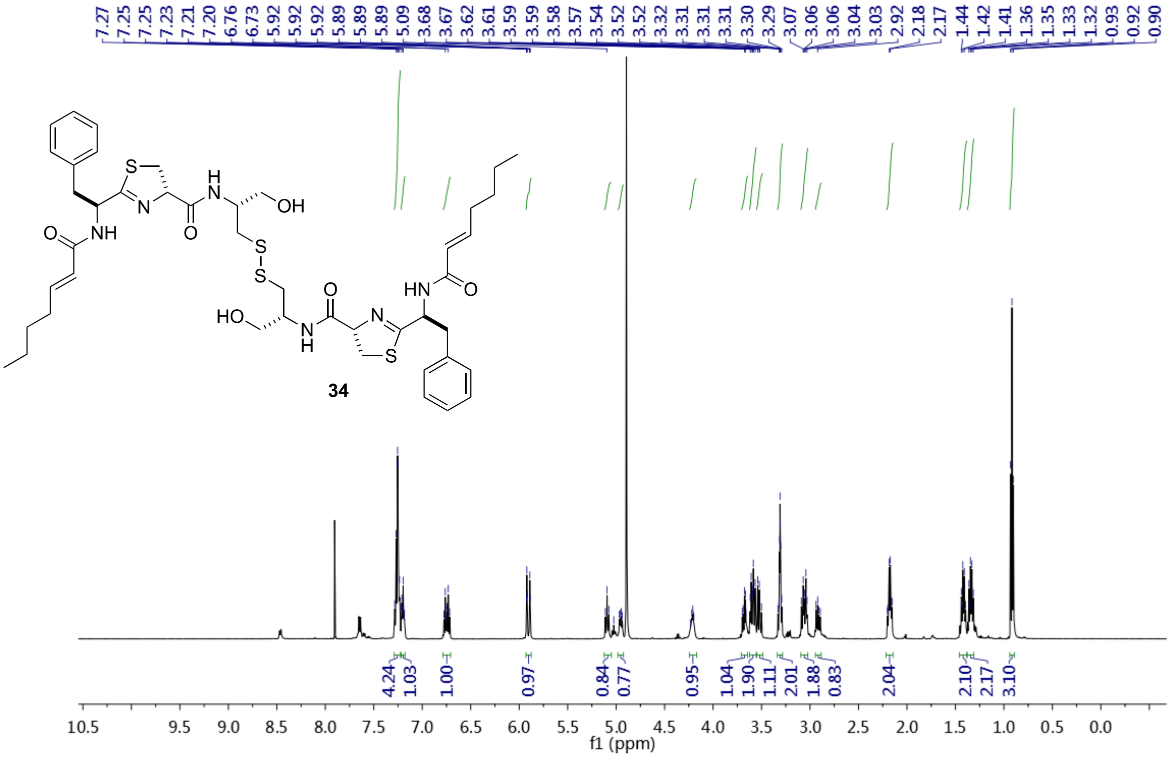

Fig. S30 ^{1}H NMR spectrum (500 MHz) of **34** in CD_3OD.

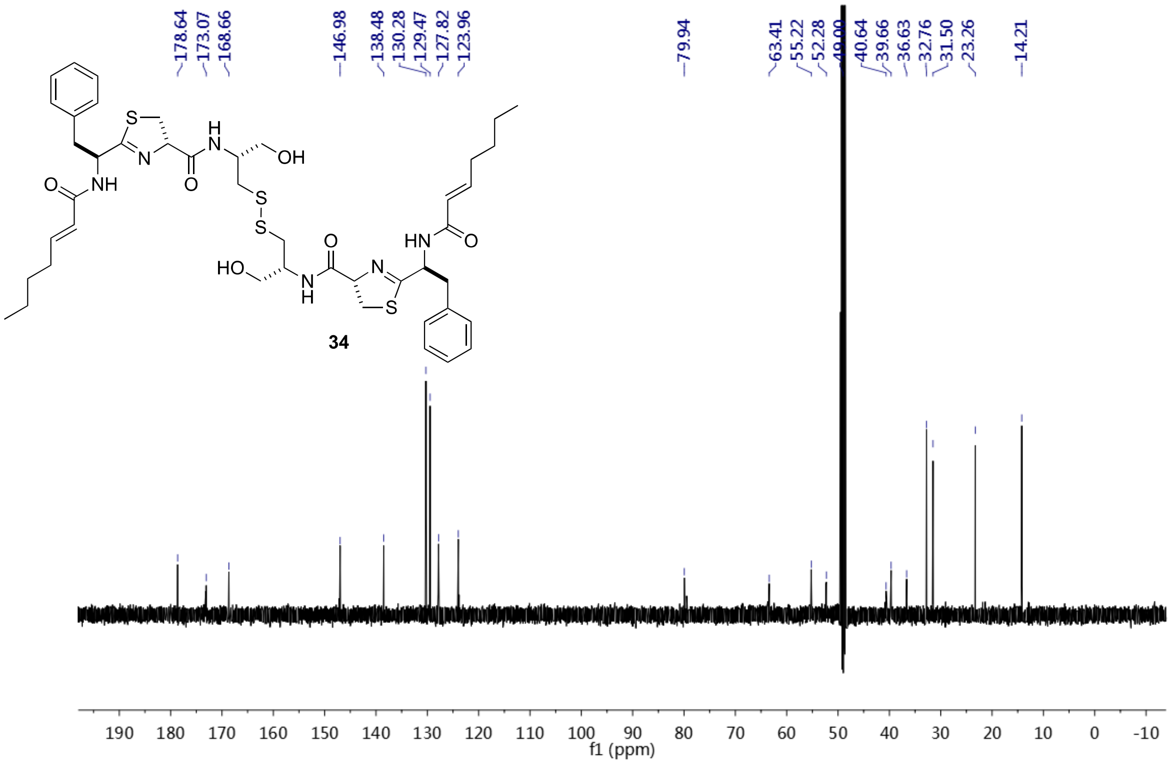

Fig. S31 ^{13}C NMR spectrum (125 MHz) of **34** in CD_3OD.

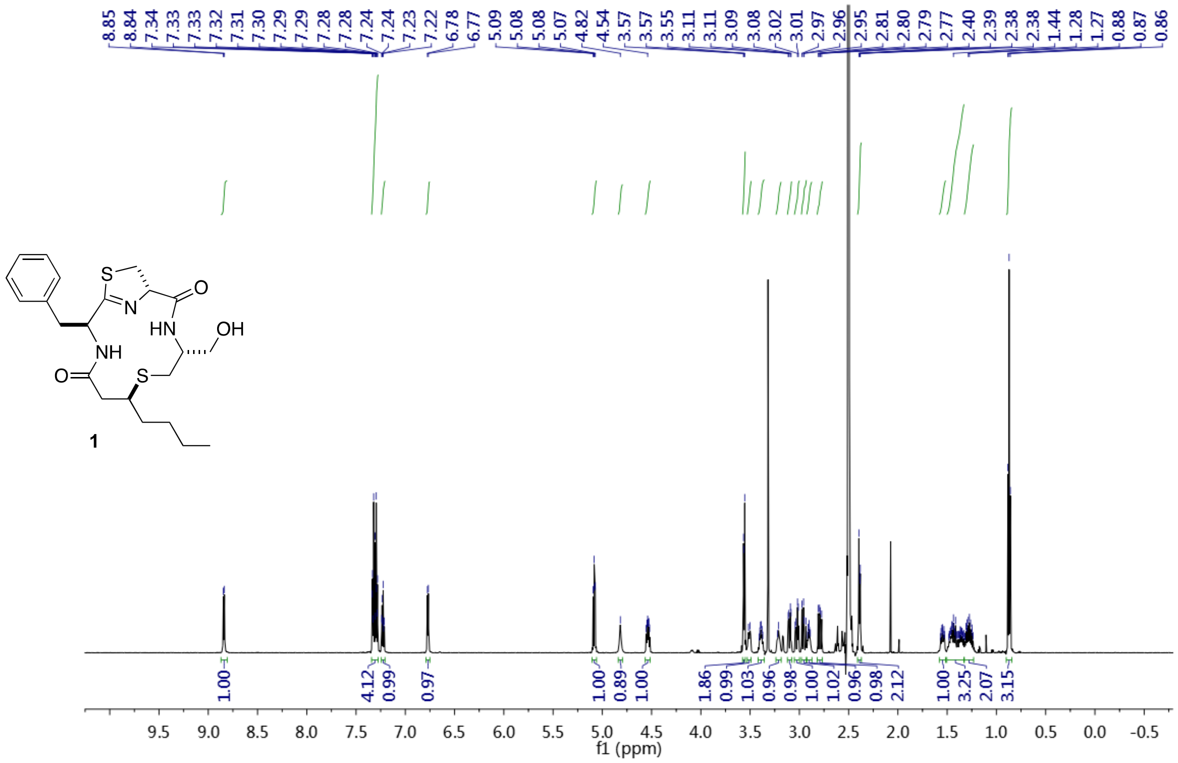

Fig. S32 ^{1}H NMR spectrum (600 MHz) of synthetic **1** in DMSO-d_6.

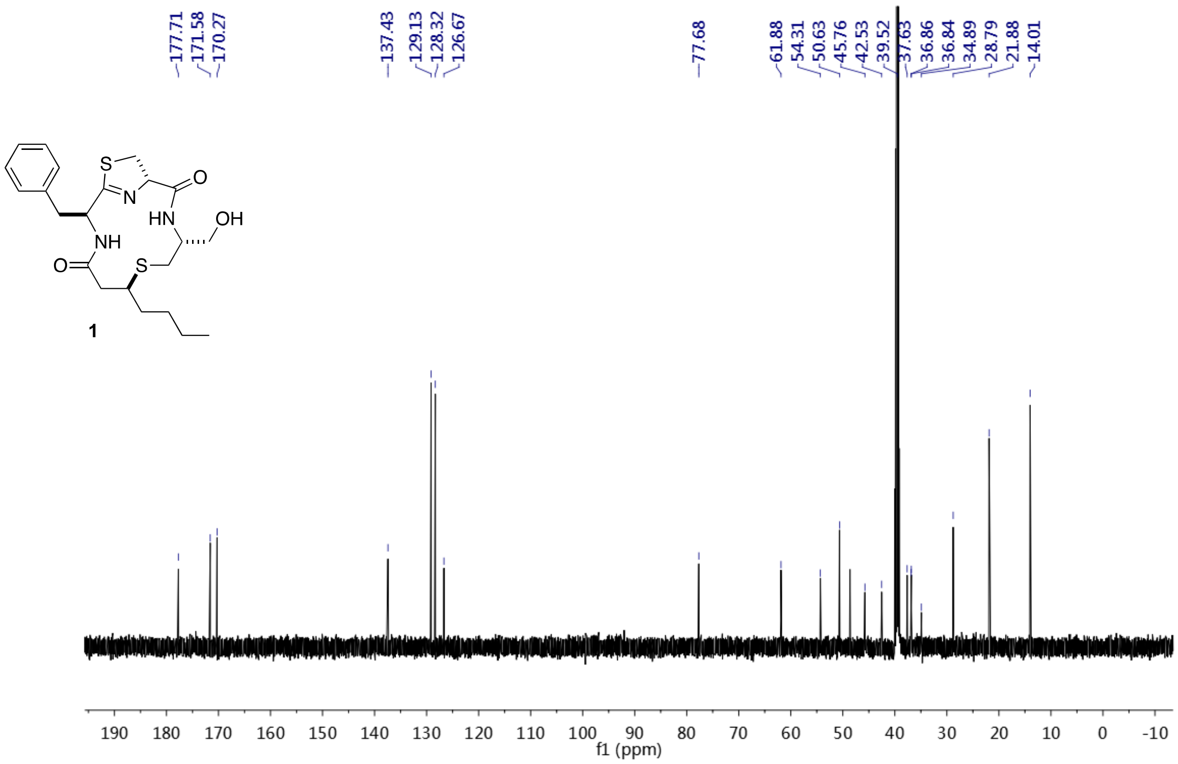

Fig. S33 ^{13}C NMR spectrum (150 MHz) of synthetic **1** in DMSO-d_6.

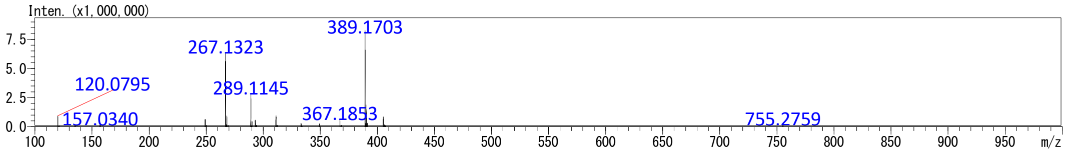

Fig. S34 HRMS for compound **23**.

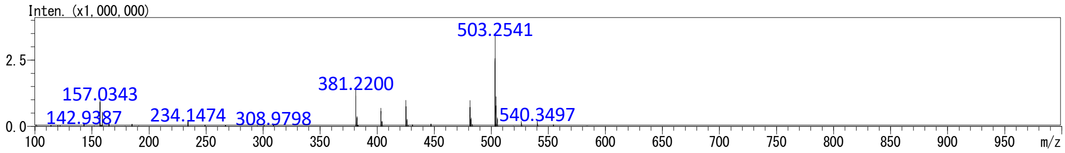

Fig. S35 HRMS for compound **24**.

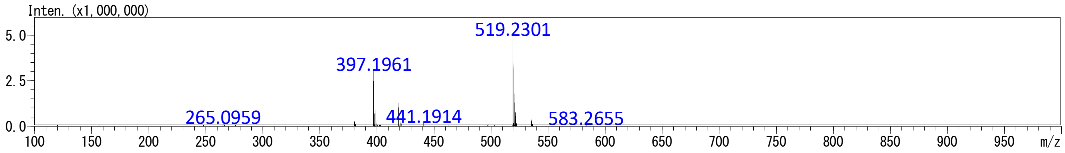

Fig. S36 HRMS for compound **25**.

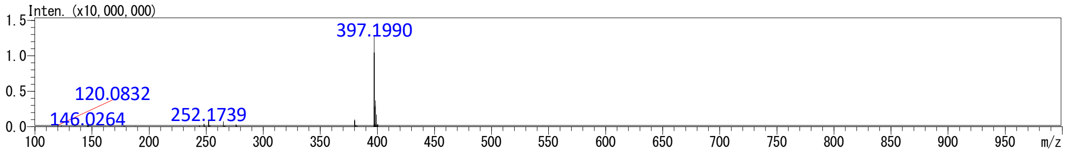

Fig. S37 HRMS for compound **26**.

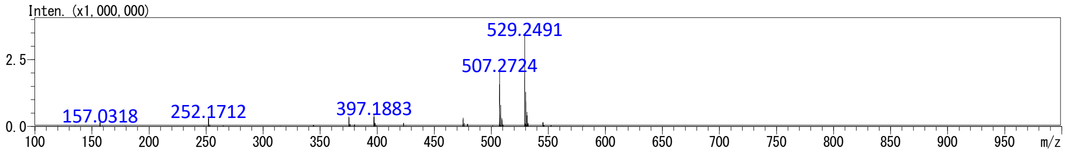

Fig. S38 HRMS for compound **27**.

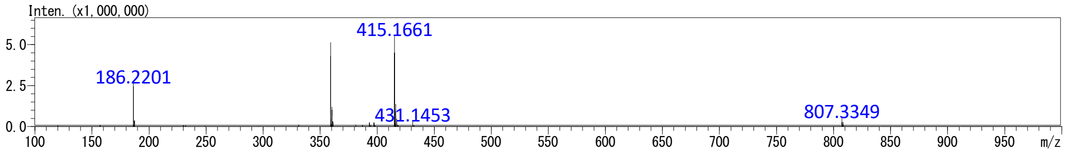

Fig. S39 HRMS for compound **28**.

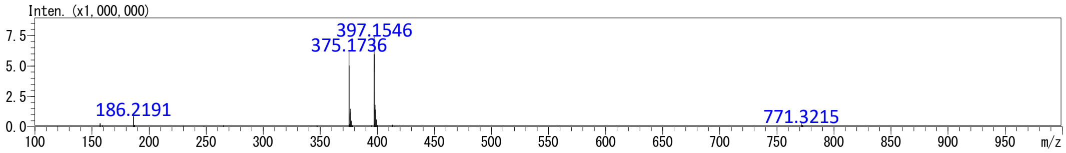

Fig. S40 HRMS for compound **29**.

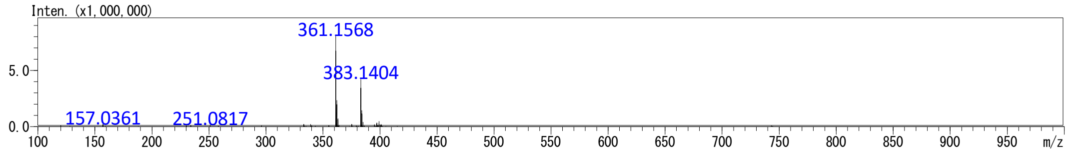

Fig. S41 HRMS for compound **30**.

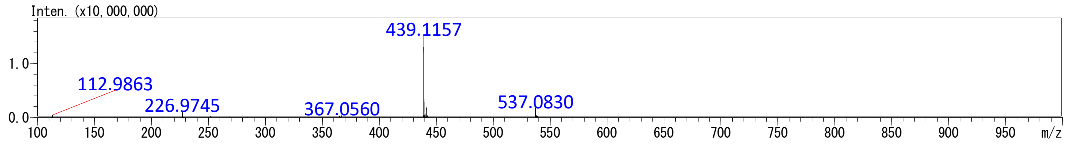

Fig. S42 HRMS for compound **31**.

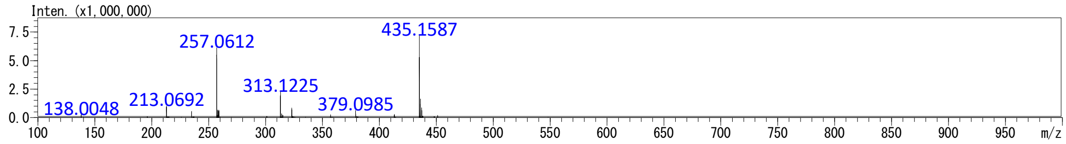

Fig. S43 HRMS for compound **32**.

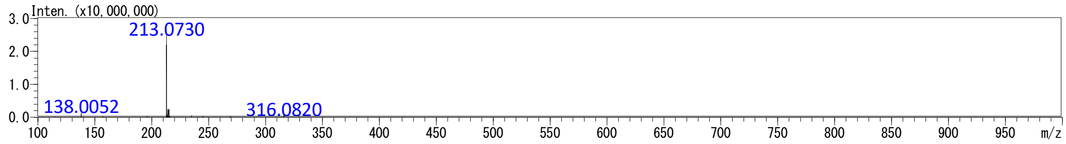

Fig. S44 HRMS for compound **33**.

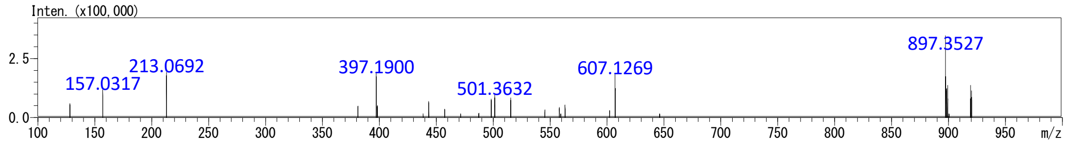

Fig. S45 HRMS for compound **34**.

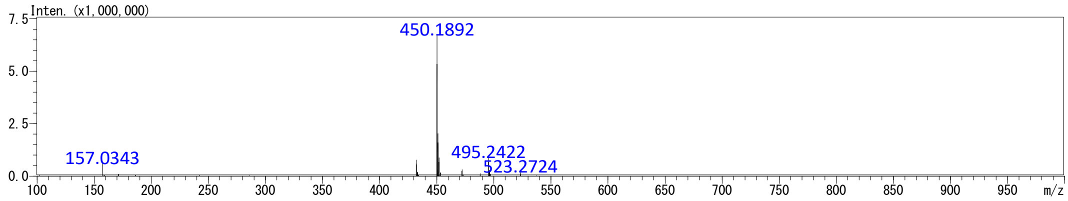

Fig. S46 HRMS for synthetic **1**.

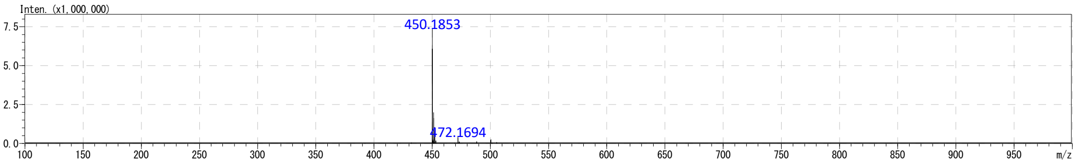

Fig. S47 HRMS for natural **1**.