Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information for:

“Isolable Small-Molecule Cysteine Sulfenic Acid”

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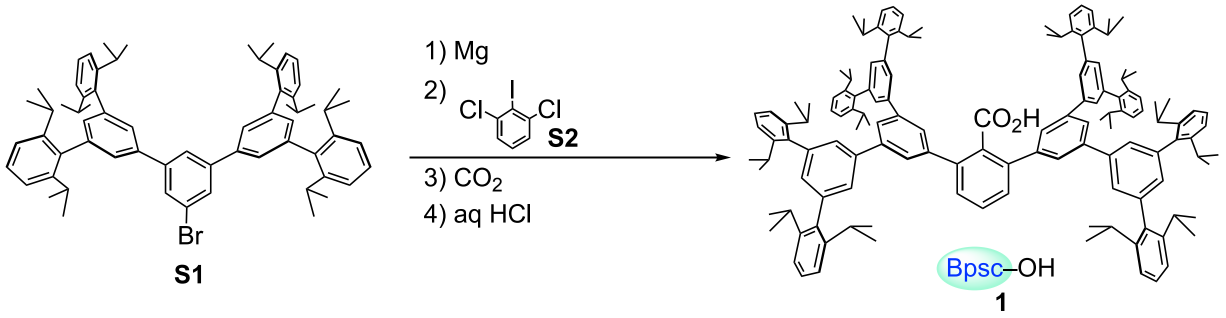
Contents

1. Experimental Section

General experimental methods: Unless otherwise stated, all operations were performed by using high-vacuum and standard Schlenk techniques under an argon atmosphere or in an MBraun UNIlab glove box under an argon atmosphere. THF (anhydrous) was purchased from Kanto Chemical and passed through a Kayama Oxygen solvent purification system prior to use. Dichloromethane, chloroform, $CDCl_3$, and C_6D_6 were purchased from commercial sources and distilled over CaH_2. Compounds **S1**[i] and **S2**[ii] were prepared according to the literature procedure. Other chemicals were purchased from commercial sources and used as received. Silica gel column chromatography was performed using Kanto silica gel N60 or Merck silica gel 60. Preparative thin layer chromatography (PTLC) was performed using Merck silica gel 60 PF_{254}. Preparative gel permeation liquid chromatography (GPLC) was performed by LC-918 and LC-9210 NEXT with JAI gel 1H and 2H columns (Japan Analytical Industry) with chloroform as solvent. ^1H NMR spectra were recorded on a JEOL ECX-500, a JEOL ECX-400, a JEOL ECS-400, or a JEOL LAMBDA-400, and the chemical shifts of ^1H are referenced to the residual proton signal of $CDCl_3$ (δ 7.25) or C_6D_6 (δ 7.20). No-D NMR spectra were recorded on a JEOL ECX-500 or a JEOL ECS-400. ^{13}C NMR spectra were recorded on a JEOL ECX-500 or a JEOL ECX-400, and the chemical shifts of ^{13}C are referenced to the signal of $CDCl_3$ (δ 77.0) or C_6D_6 (δ 128.0). All spectra were assigned with the aid of DEPT, COSY, HMQC, and HMBC NMR experiments. IR spectra were recorded on a JASCO FT/IR-4100 by utilizing a KBr disk unless otherwise noted. Mass spectra were measured on a JEOL JMS-T100GCv "AccuTOF GCv" using a field desorption probe. Melting points were measured with a Yanaco MP-S3 and are uncorrected.

Synthesis of Bpsc–OH (1).

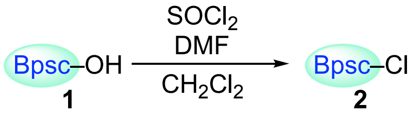


Scheme S1

To a Grignard reagent prepared by the reaction of **S1** (10.0 g, 10.5 mmol) and magnesium turnings (344 mg, 14.7 mmol) in THF (35 mmol) was added a solution of 1,3-dichloro-2-iodobenzene (**S2**) (945 mg, 3.47 mmol) in THF (15 mL) at 85 ˚C. After the reaction mixture was stirred at 85 ˚C overnight, it was cooled to ambient temperature and the system was filled with CO_2 by means of a balloon. The reaction mixture under CO_2 atmosphere was heated at 90 ˚C for 3.5 h and then treated with 1 M aq. HCl at 0 ˚C. After extraction with ether, the combined organic layer was dried over $MgSO_4$ and evaporated in vacuo. To the crude mixture was added EtOH, and the mixture was heated at 85 ˚C for 2 h. After cooling to ambient temperature, precipitates were collected by filtration. It was purified by silica gel column chromatography (hexane/$CHCl_3$ = 2:1) to afford Bpsc–OH (**1**) (3.16 g, 1.68 mmol, 49%) as colorless crystals.

1: colorless crystals; mp 236.5-238.5 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.03 (48H, d, J = 6.5 Hz), 1.10 (48H, d, J = 6.5 Hz), 2.74 (16H, septet, J = 6.5 Hz), 6.99 (4H, t, J = 1.5 Hz), 7.17 (16H, d, J = 7.5 Hz), 7.31 (8H, t, J = 7.5 Hz), 7.43 (8H, d, J = 1.5 Hz), 7.45-7.54 (3H, m), 7.71 (4H, d, J = 1.5 Hz), 7.84 (2H, t, J = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 24.35 (q), 24.51 (q), 30.60 (d), 122.71 (d), 125.84 (d), 126.30 (d), 126.62 (d), 128.16 (d), 129.62 (d), 130.02 (d), 130.41 (d), 131.87 (s), 139.20 (s), 140.23 (s), 140.43 (s), 141.27 (s), 141.54 (s), 141.89 (s), 170.01 (s); IR(KBr) ν_{max}/cm^{-1} 1732 (C=O), 3625 (O–H). Elemental Analysis: Found: C, 89.58; H, 8.36. Calc. for $C_{139}H_{158}O_2$: C, 89.72; H, 8.56%.

Synthesis of Bpsc–Cl (2).

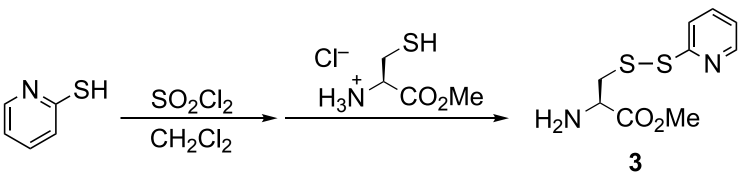


Scheme S2

To a solution of **1** (1.60 g, 0.855 mmol) in CH_2Cl_2 (8.6 mL) was added DMF (427 μL) and thionyl chloride (302 μL, 4.27 mmol) at ambient temperature. After stirring for 2.5 h at ambient temperature, the reaction mixture was evaporated in vacuo. The resulting solid was washed with hexane/EtOH (v/v = 1/10) and collected by filtration to give Bpsc–Cl (**2**) (1.51 g, 0.804 mmol, 94%) as colorless crystals.

2: colorless crystals; mp 248.9-250.5 ºC (dec). ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.02 (48H, d, J = 7.0 Hz), 1.09 (48H, d, J = 7.0 Hz), 2.73 (16H, septet, J = 7.0 Hz), 6.99 (4H, t, J = 1.0 Hz), 7.16 (16H, d, J = 7.5 Hz), 7.31 (8H, t, J = 7.5 Hz), 7.45 (8H, d, J = 1.5 Hz), 7.50-7.59 (3H, m), 7.68 (4H, d, J = 1.5 Hz), 7.90 (1H, t, J = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 24.22 (q), 24.38 (q), 30.48 (d), 122.59 (d), 126.09 (d), 126.47 (d), 127.04 (d), 128.02 (d), 129.67 (d), 130.46 (d), 130.85 (d), 137.39 (s), 139.03 (s), 139.97 (s), 140.20 (s), 141.22 (s), 141.97 (s), 146.79 (s), 153.87 (s); IR(KBr) ν_{max}/cm^{-1} 1792 (C=O). Elemental Analysis: Found: C, 89.09; H, 8.17. Calc. for $C_{139}H_{157}ClO$: C, 88.84; H, 8.42%.

Synthesis of *S*-(pyridine-2-sulfanyl)cysteine (3).



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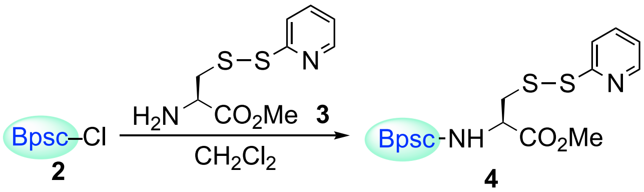
Scheme S3

To a solution of pyridine-2-thiol (148 mg, 1.26 mmol) in CH_2Cl_2 (2.1 mL) was added a solution of sulfuryl chloride (0.24 mL, 3.0 mmol) in CH_2Cl_2 (1.0 mL) at 0 ˚C. The reaction mixture was stirred at ambient temperature for 2 h and then evaporated in vacuo. After addition of a 2 mL of CH_2Cl_2 followed by evaporation to dryness was repeated two times, acetic acid (2.0 mL) was added to the resulting residue to give a yellow suspension. To this suspension was added *L*-cysteine methyl ester hydrochloride (215 mg, 1.25 mmol) in acetic acid (2.3 mL) at ambient temperature. After stirring for 2 h, the reaction mixture was neutralized (pH 7) with sat. aq. $NaHCO_3$. After extraction with $CHCl_3$, the combined organic layer was dried over $MgSO_4$ and evaporated in vacuo to give *S*-(pyridine-2-sulfanyl)cysteine (**3**) (272 mg, 1.11 mmol, 88%) as yellow oil, which was readily used in the next step without further purification.

3: yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 2.96 (1H, dd, *J* = 8.4 Hz, 13.9 Hz), 3.23 (1H, dd, *J* = 4.4 Hz, 13.9 Hz), 3.71 (3H, s), 3.81 (1H, dd, *J* = 4.4 Hz, 8.4 Hz), 7.09-7.14 (1H, m), 7.59-7.66 (2H, m), 8.46-8.50 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 44.19, 52.33, 53.54, 120.21, 120.98, 136.97, 149.82, 159.24, 173.95.

Synthesis of 4.



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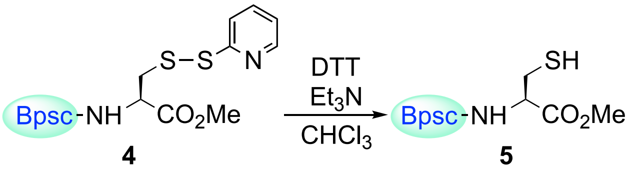
Scheme S4

To a solution of **2** (926 mg, 0.492 mmol) and **3** (272 mg, 1.11 mmol) in CH_2Cl_2 (12 mL) was added Et_3N (0.21 mL, 1.5 mmol) at 0 ˚C. The reaction mixture was stirred at 0 ˚ C for 30 min and then at ambient temperature overnight. After the resulting mixture was washed with aq. NH_4Cl and brine, the organic layer was dried over $MgSO_4$ and evaporated in vacuo. Purification by silica gel column chromatography ($CHCl_3$/hexane = 5:6) afforded **4** (967 mg, 0.463 mmol, 94%) as colorless crystals.

4: colorless crystals; mp 204.2-206.3 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.01 (24H, d, *J* = 6.8 Hz), 1.02 (24H, d, *J* = 6.8 Hz), 1.07 (24H, d, *J* = 6.8 Hz), 1.08 (24H, d, *J* = 6.8 Hz), 2.08-2.18 (1H, m), 2.66-2.81 (16H, m), 2.96 (3H, s), 3.20-3.28 (1H, m), 4.44-4.51 (1H, m), 6.57 (1H, d, *J* = 8.1 Hz), 6.22-6.67 (1H, m), 6.91-7.00 (5H, m), 7.14-7.19 (16H, m), 7.31 (8H, t, *J* = 7.4 Hz), 7.37-7.43 (11H, m), 7.45-7.50 (1H, m, A of AB_2), 7.57 (4H, d, *J* = 1.6 Hz), 7.77 (2H, t, *J* = 1.6 Hz), 9.83 (1H, d, *J* = 7.6 Hz). HRMS (FD-TOF) *m/z* 2085.2494 $[M]^+$ (calc. for $C_{148}H_{168}N_2O_3S_2$, 2085.2496).

Synthesis of the cradled Cys–SH 5.

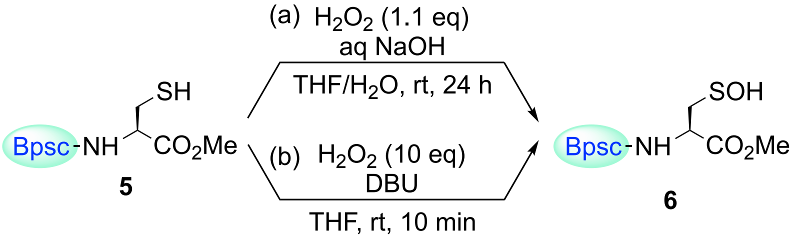


Scheme S5

To a solution of **4** (418 mg, 0.20 mmol) in $CHCl_3$ (4 mL) were added D,L-dithiothreitol (DTT, 154 mg, 1.0 mmol) and Et_3N (140 μL, 1.0 mmol) at ambient temperature. The reaction mixture was stirred at ambient temperature for 1.5 h and then treated with aq. NH_4Cl. The organic layer was washed successively with aq. NH_4Cl and brine and then dried over $MgSO_4$. After evaporation in vacuo, the crude mixture was purified by silica gel column chromatography ($CHCl_3$/hexane = 1:1) to afford **5** (361 mg, 0.18 mmol, 91%) as colorless crystals.

5: colorless crystals; mp 233.5-235.0 °C. ^1H NMR (500 MHz, $CDCl_3$) δ_H 0.38 (1H, t, *J* = 6.8 Hz), 1.02 (24H, d, *J* = 6.8 Hz), 1.03 (24H, d, *J* = 6.8 Hz), 1.09 (24H, d, *J* = 6.8 Hz), 1.11 (24H, d, *J* = 6.8 Hz), 2.25-2.30 (1H, m), 2.41-2.46 (1H, m), 2.67-2.79 (16H, m), 3.03 (3H, s), 4.51-4.54 (1H, m), 6.42 (1H, d, *J* = 7.5 Hz), 6.98 (4H, t, *J* = 1.5 Hz), 7.14-7.19 (16H, m), 7.31 (8H, t, *J* = 7.6 Hz), 7.41 (8H, d, *J* = 1.5 Hz), 7.44-7.51 (3H, AB_2), 7.67 (4H, d, *J* = 1.5 Hz), 7.78 (2H, t, *J* = 1.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ_C 24.32 (q), 24.49 (q), 26.30 (t), 30.56 (d), 52.41 (q), 53.39 (d), 122.66 (d), 126.21 (d), 126.70 (d), 127.11 (d), 128.08 (d), 129.44 (d), 129.91 (d), 130.46 (d), 135.12 (s), 139.17 (s), 140.14 (s), 140.53 (s), 141.20 (s), 141.73 (s), 141.97 (s), 146.89 (s), 168.11 (s), 169.74 (s). Elemental Analysis: Found: C, 86.59; H, 8.40; N, 0.57; S, 1.89. Calc. for $C_{143}H_{165}NO_3S$: C, 86.84; H, 8.41; N, 0.71; S, 1.62%.

Synthesis of the cradled Cys–SOH 6.



Scheme S6

(a) Reaction using NaOH as base

To a solution of **5** (32.1 mg, 16.2 μmol) in THF (2 mL) was added 0.1 M aq. NaOH (180 μL, 18 μmol) at ambient temperature. The reaction mixture was degassed through freeze-pump-thaw cycles, and the flask was then flushed with argon. To this solution was added 30% H_2O_2 (2.1 μL, 18 μmol) at ambient temperature. The reaction mixture was stirred for 24 h at ambient temperature and treated with aq. NH_4Cl. After extraction with ether, the combined organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo, and the crude mixture was purified by silica gel column chromatography ($CHCl_3$/hexane = 1:2) to afford **6** (8.7 mg, 4.4 μmol, 27%) as colorless crystals.

(b) Reaction using DBU as base

To a solution of **5** (27.6 mg, 13.9 μmol) in THF (2 mL) was added DBU (42 μL, 0.28 mmol) at ambient temperature. The reaction mixture was degassed through freeze-pump-thaw cycles, and the flask was then flushed with argon. To this solution was added 30% aq. H_2O_2 (17 μL, 0.14 mmol) at ambient temperature. The reaction mixture was stirred for 10 min at ambient temperature and then treated with aq. NH_4Cl. After extraction with ether, the combined organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo, and the crude mixture was purified by silica gel column chromatography ($CHCl_3$/hexane = 2:3 to AcOEt/hexane = 2:1) to afford **6** (10.0 mg, 5.0 μmol, 36%) as colorless crystals.

6: Colorless crystals; mp 214-217 °C (dec.). ^{1}H NMR (500 MHz, C_6D_6) δ_H 1.14 (24H, d, *J* = 6.9 Hz), 1.15 (24H, d, *J* = 6.9 Hz), 1.19 (48H, d, *J* = 6.9 Hz), 1.56 (1H, dd, *J* = 11.2, 14.2 Hz), 2.77 (3H, s), 2.99-3.09 (16H, m), 3.21 (1H, dd, *J* = 3.8, 14.2 Hz), 4.22-4.27 (1H, m), 5.36 (1H, s, -SO*H*), 5.77 (1H, d, *J* = 8.0 Hz), 7.03-7.10 (3H, AB_2 pattern), 7.13 (4H, t, *J* = 1.5 Hz), 7.25 (16H, d, *J* = 7.7 Hz), 7.39 (8H, t, *J* = 7.7 Hz), 7.68 (8H, d, *J* = 1.5 Hz), 7.91 (4H, d, *J* = 1.4 Hz), 8.06 (2H, t, *J* = 1.4 Hz); ^{13}C NMR (125 MHz, C_6D_6) δ_C 24.3 (q), 24.4 (q), 24.5 (q), 24.6 (q), 30.9 (d), 44.4 (t), 50.2 (d), 51.8 (q), 122.9 (d), 126.1 (d), 127.2 (d), 128.3 (d), 128.5 (d), 129.6 (d), 129.8 (d), 130.9 (d), 135.3 (s), 139.5 (s), 140.9 (s), 141.5 (s), 141.6 (s), 141.9 (s), 142.4 (s), 147.0 (s), 147.0 (s), 169.8 (s), 171.0 (s); IR (CCl_4, 10.4 mM) ν_{max}/cm^{-1} 3100–3400 (br, O-H). Elemental Analysis: Found: C, 86.52; H, 8.31; N, 0.74; S, 1.48. Calc. for $C_{143}H_{165}NO_4S$: C, 86.14; H, 8.34; N, 0.70; S, 1.61%.

X-ray crystallographic analysis of Cys–SOH 6.

Single crystals of **6**•4C_5H_{12}•2$C_4H_{10}O_2$ were grown in their pentane-dimethoxyethane solution. A colorless crystal of **6**•4.5C_5H_{12} was mounted on a loop. All measurements were made on a Rigaku/Saturn CCD with VariMax Mo with graphite monochromated Mo-Kα radiation (λ = 0.71075

Å) at –153 ˚C. Crystallographic and experimental data are listed in Table S1. The structures were solved by the direct method (SIR97) and refined by full-matrix least squares on F^2 (SHELXL-2018/3). The non-hydrogen atoms were refined anisotropically, except for the minor components of the disordered isopropyl groups. The hydrogen atoms bonded to carbon atoms were idealized by using the riding models. The hydrogen atoms bonded to N1 and O1 were treated as HFIX 43 and HFIX 147 command, respectively. The solvent molecules in the voids were highly disordered and were impossible to refine using conventional discrete-atom models. Therefore, the residual electron density was treated as diffuse contributions using the SQUEEZE procedure as implemented in PLATON. A total solvent-accessible void volume of 5040 Å^3 with a total electron count of 1093 (consistent with four molecules of pentane and two molecules of dimethoxyethane per formula) was found in the unit cell.

Table S1. Crystal data and structure refinement for **6**•$4C_5H_{12}$•$2C_4H_{10}O_2$.

Empirical fomula	$C_{143}H_{165}NO_4S$••$4C_5H_{12}$•$2C_4H_{10}O_2$	
Fomula weight	2462.63	
Temperature	123(2) K	
wavelength	0.71075 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 13.461(2) Å	α = 90°
	b = 27.545(4) Å	β = 90°
	c = 42.227(6) Å	γ = 90°
Volume	15658(4) Å^3	
Z	4	
D_{calc}	0.846 g/cm^3	
Absorption coefficient	0.075 mm^{-1}	
F_{000}	4312	
Crystal size	0.30 x 0.24 x 0.07 mm^3	
Theta range for data collection	3.03 to 25.00°.	
Index ranges	$-16<=h<=11, -32<=k<=12, -49<=l<=36$	
Reflections collected	29055	
Independent reflections	23475 [R_{int} = 0.0620]	
Max. and min. transmission	0.9951 and 0.9794	

data / restraints / parameters	23475 / 0 / 1396
Goodness-of-fit on F^2	0.995
Final *R* induces ($I>4\sigma(I)$)	$R1 = 0.0765$, $wR2 = 0.1450$
R induces (all data)	$R1 = 0.1403$, $wR2 = 0.1705$
Largest diff. peak and hole	0.24 and –0.27 e.Å^{-3}

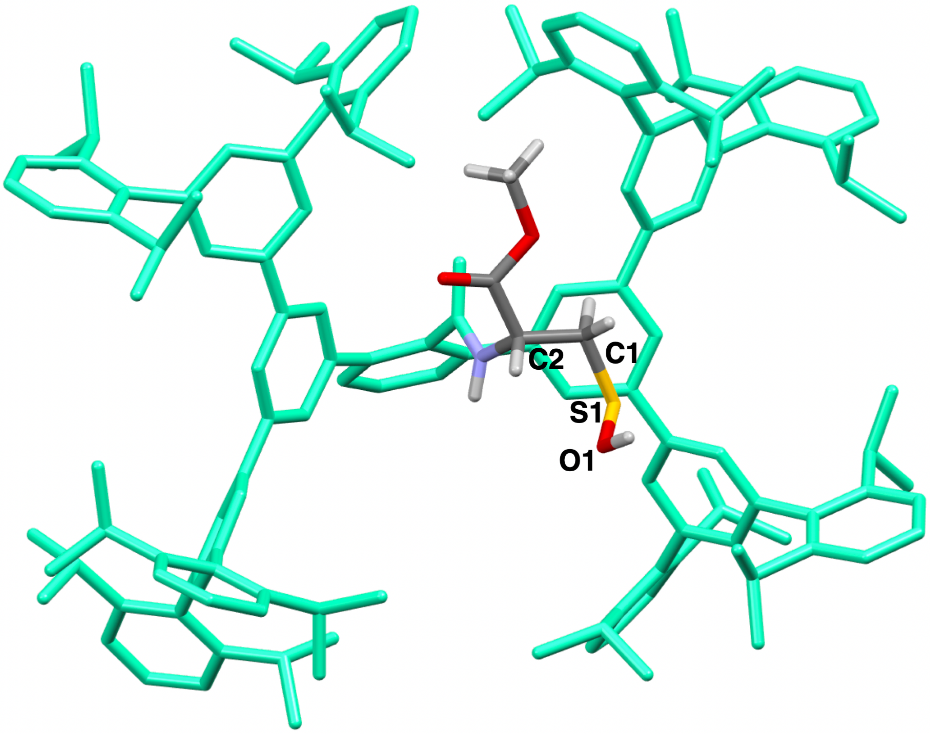


Figure. S1 Crystal structure of Cys–SOH 6 (hydrogen atoms of the Bpsc group are omitted for clarity).

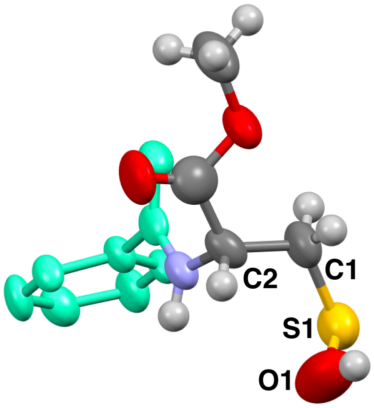
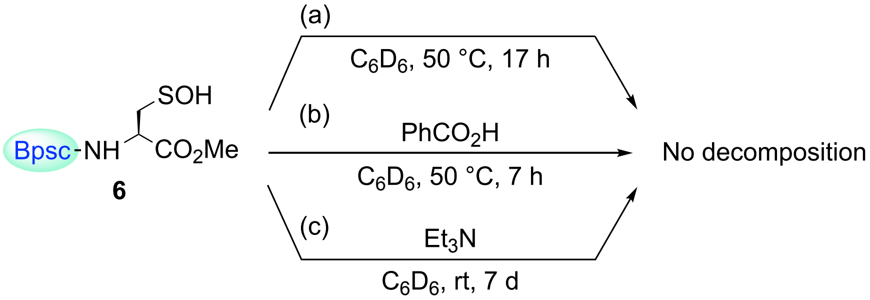


Figure. S2 Thermal ellipsoid representation of the cysteine unit of 6 (50% probability).

Thermal stability of Cys–SOH 6 in solution.



Scheme S7

(a) Without additives (50 ˚C in C_6D_6)

A solution of **6** (15.3 mg, 7.7 µmol) in C_6D_6 (0.6 mL) was placed in a 5 mm o/d NMR tube with a J-young valve, and the tube was carefully sealed. The solution was heated at 50 ˚C for 17 h by means of an oil bath. No decomposition of 6 was observed in ^{1}H NMR spectroscopy.

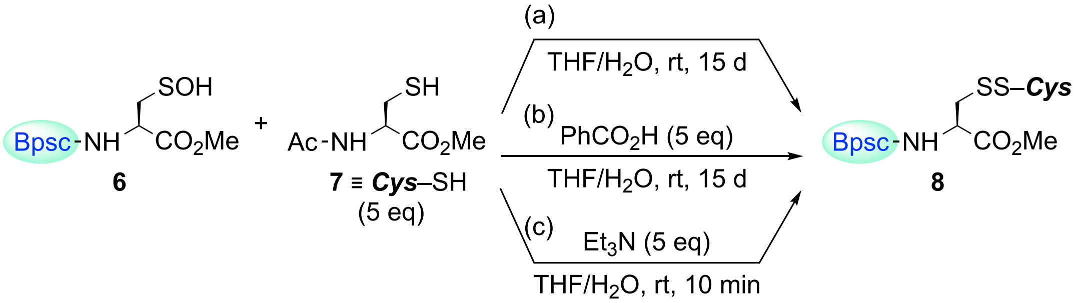
(b) In the presence of benzoic acid (50 ˚C in C_6D_6)

A solution of **6** (7.6 mg, 3.8 µmol) and benzoic acid (2.3 mg, 19 µmol) in C_6D_6 (0.6 mL) was placed in a 5 mm o/d NMR tube with a J-young valve, and the tube was carefully sealed. The solution was heated at 50 ˚C for 7 h by means of an oil bath. No decomposition of **6** was observed in ^{1}H NMR spectroscopy.

(c) In the presence of triethylamine (ambient temperature in C_6D_6)

A solution of **6** (6.4 mg, 3.2 µmol) and Et_3N (2.2 µL, 16 µmol) in C_6D_6 (0.6 mL) was placed in a 5 mm o/d NMR tube with a J-young valve, and the tube was carefully sealed. The solution was left at ambient temperature for 7 d. No decomposition of **6** was observed in ^{1}H NMR spectroscopy.

Reaction of Cys–SOH 11 with *N*-acetylcysteine methyl ester (7).



Scheme S8

General procedure: To a solution of **6** (32.4 mg, 16.2 µmol) in THF (1.2 mL) were added *N*-acetylcysteine methyl ester (**7**) (14.3 mg, 81 µmol) and 1,3,5-trimethoxybenene (3 mg, internal standard) in a glove box at ambient temperature. This solution was divided equally among three, and each was placed to a 5 mm o/d NMR tube with a J-young valve. The resulting three samples were used for the following NMR experiments. The yield of disulfide **8** was estimated by no-D NMR spectroscopy based on internal standard.

(a) Without additives

To a solution in a J-young NMR tube were added THF (150 μL) and H_2O (50 μL), and the tube was carefully sealed. The sample was left at ambient temperature, and the reaction was monitored by no-D NMR spectroscopy. After 15 days, **8** was formed in 54% yield.

(b) In the presence of benzoic acid

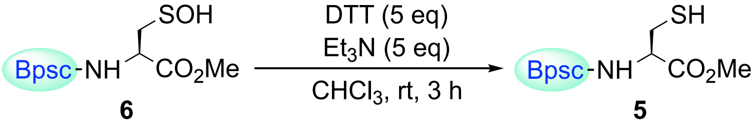
To a solution in a J-young NMR tube were added benzoic acid (3.3 mg, 27 μmol), THF (150 μL) and H_2O (50 μL), and the tube was carefully sealed. The sample was left at ambient temperature, and the reaction was monitored by no-D NMR spectroscopy. After 15 days, **8** was formed in 55% yield.

(c) In the presence of triethylamine

To a solution in a J-young NMR tube were added Et_3N (3.8 mg, 27 μmol), THF (150 μL) and H_2O (50 μL), and the tube was carefully sealed. The sample was left at ambient temperature. After 10 min, **8** was formed quantitatively.

8: Colorless crystals; mp 200.0-201.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ_H 1.03 (24H, d, J = 7.0 Hz), 1.03 (24H, d, J = 7.0 Hz), 1.10 (24H, d, J = 6.8 Hz), 1.11 (24H, d, J = 6.8 Hz), 1.84 (3H, s), 2.13 (1H, dd, J = 6.1 Hz, 14.0 Hz), 2.64 (1H, dd, J = 4.6 Hz, 14.0 Hz), 2.68-2.80 (16H, m), 2.81 (1H, dd, J = 3.1 Hz, 14.1 Hz), 3.02 (1H, dd, J = 5.1 Hz, 14.1 Hz), 3.05 (3H, s), 3.52 (3H, s), 4.47-4.51 (1H, m), 4.58-4.63 (1H, m), 6.31 (1H, d, J = 7.7 Hz), 6.42 (1H, d, J = 8.2 Hz), 6.98 (4H, t, J = 1.5 Hz), 7.17 (16H, d, J = 7.7 Hz), 7.31 (8H, t, J = 7.7 Hz), 7.41 (8H, d, J = 1.5 Hz), 7.41-7.51 (3H, m), 7.66 (4H, d, J = 1.7 Hz), 7.78 (2H, d, J = 1.7 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 22.8 (q), 24.3 (q), 24.4 (q), 30.5 (d), 39.4 (t), 42.0 (t), 50.2 (d), 51.4 (d), 52.4 (q), 52.5 (q), 122.6 (d), 125.9 (d), 126.6 (d), 127.1 (d), 128.0 (d), 129.4 (d), 129.9 (d), 130.4 (d), 134.7 (s), 139.1 (s), 140.2 (s), 140.5 (s), 141.2 (s), 141.6 (s), 141.7 (s), 146.8 (s), 167.9 (s), 169.8 (s), 170.2 (s), 170.52 (s). Elemental Analysis: Found: C, 83.15; H, 8.45; N, 1.19; S, 2.69. Calc. for $C_{149}H_{174}N_2O_6S_2$: C, 83.12; H, 8.15; N, 1.30; S, 2.98%.

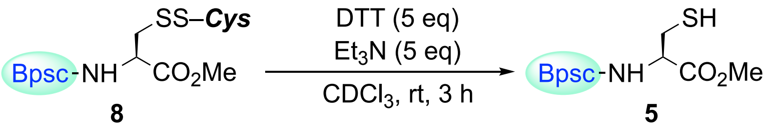
Reduction of Cys–SOH 6 with DTT.



Scheme S9

To a solution of **6** (30.9 mg, 15.5 μmol) in $CHCl_3$ (2 mL) were added DTT (12.2 mg, 77.4 μmol) and Et_3N (11 μL, 77 μmol) at ambient temperature. The reaction mixture was stirred for 3 h at ambient temperature and then treated with saturated aq. NH_4Cl. After extraction with $CHCl_3$, the combined organic layer was washed with brine and dried over $MgSO_4$. The crude mixture was purified by PTLC (SiO_2/$CHCl_3$/hexane = 1:2) to afford **5** (26.2 mg, 13.2 μmol, 85%).

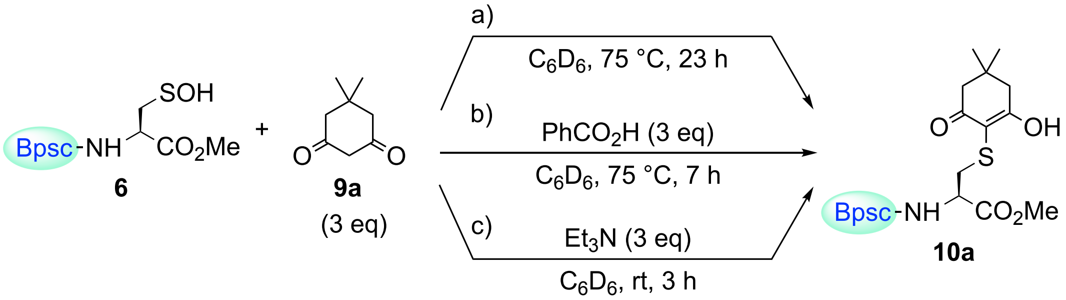
Reduction of disulfide 8 with DTT.



Scheme S10

To a solution of **8** (21.0 mg, 9.8 μmol) in $CDCl_3$ (0.6 mL) in a 5 mm o/d NMR tube were added DTT (7.6 mg, 48 μmol) and Et_3N (6.7 μL, 48 μmol) at ambient temperature. The reaction at ambient temperature was monitored by ^1H NMR spectroscopy. It was found that **8** was totally consumed after 3 h and **5** was formed quantitatively. After evaporation of the solvent, the crude mixture was purified by PTLC (SiO_2/$CHCl_3$/hexane = 1:2) to afford **5** (19.2 mg, 9.7 μmol, 99%).

Reaction of Cys–SOH 11 with dimedone (9a).



Scheme S11

General procedure: To a solution of **6** in C_6D_6 (0.6 mL) in a 5 mm o/d NMR tube with a J-young valve were added dimedone (**9a**) and additives at ambient temperature, and the tube was carefully sealed. The reactions were conducted under the indicated conditions and monitored by ^1H NMR spectroscopy (at ambient temperature). When **6** was consumed totally, the reaction mixture was treated with saturated aq. $NaHCO_3$. After extraction with CH_2Cl_2, the combined organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated in vacuo, and the crude mixture was purified by PTLC (SiO_2/ $CHCl_3$/hexane = 2:1) to afford **10a** as colorless crystals.

(a) Without additives

Reagents: **6** (22.1 mg, 11.1 μmol), **9a** (4.6 mg, 33 μmol)

Conditions: 75 °C, 23 h

Result: **10a** (17.9 mg, 8.4 μmol, 76%)

(b) In the presence of benzoic acid

Reagents: **6** (21.3 mg, 10.7 μmol), **9a** (4.5 mg, 32 μmol), benzoic acid (3.9 mg, 32 μmol)

Conditions: 75 °C, 7 h

Result: **10a** (19.7 mg, 9.3 μmol, 87%)

(c) In the presence of triethylamine

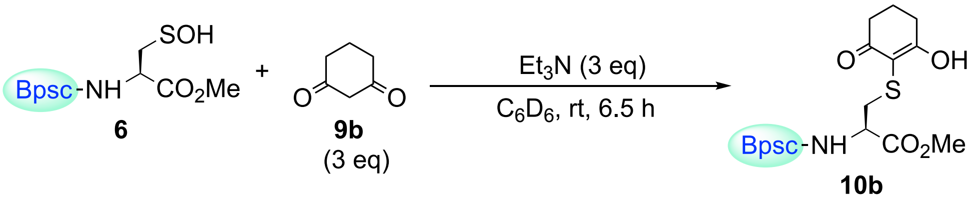
Reagents: **6** (20.4 mg, 10.2 μmol), **9a** (4.3 mg, 30 μmol), Et_3N (7 μL, 30 μmol)

Conditions: ambient temperature, 3 h

Result: **10a** (20.5 mg, 9.7 μmol, 95%)

10a: Colorless crystals; mp 218.0-220.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 0.85 (3H, s), 0.87 (3H, s), 1.02 (24H, d, *J* = 7.0 Hz), 1.03 (24H, d, *J* = 7.0 Hz), 1.08 (24H, d, *J* = 7.0 Hz), 1.09 (24H, d, *J* = 7.0 Hz), 1.81 (1H, dd, *J* = 8.5 Hz, 14 Hz), 1.87 (2H, ABq, *J* = 18 Hz), 2.04 (2H, ABq, *J* = 18 Hz), 2.51 (1H, dd, *J* = 2.0 Hz, 14 Hz), 2.69-2.80 (16H, m), 2.98 (3H, s), 4.04-4.12 (1H, m), 6.59 (1H, d, *J* = 8.0 Hz), 6.97 (4H, t, *J* = 1.0 Hz), 7.16 (16H, d, *J* = 8.0 Hz), 7.31 (8H, t, *J* = 8.0 Hz), 7.41 (8H, d, *J* = 1.0 Hz), 7.40-7.50 (3H, m), 7.67 (4H, d, *J* = 1.5 Hz), 7.79 (2H, t, *J* = 1.5 Hz), 9.62 (1H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 24.2 (q), 24.3 (q), 24.4 (q), 27.8 (q), 28.4 (q), 30.5 (d), 31.2 (s), 39.2 (t), 42.7 (t). 51.2 (t), 52.4 (d), 53.1 (q), 104.6 (s), 122.6 (d), 126.2 (d), 126.7 (d), 127.7 (d), 128.0 (d), 129.2 (d), 130.0 (d), 130.3 (d), 134.6 (s), 139.2 (s), 140.3 (s), 140.7 (s), 141.1 (s), 141.3 (s), 141.7 (s), 146.8 (s), 146.9 (s), 168.8 (s), 169.9 (s), 179.8 (s), 195.0 (s); LRMS (FD-TOF) *m/z* 2115 ([M]$^+$). Elemental Analysis: Found: C, 85.65; H, 8.61; N, 0.57; S, 1.22. Calc. for $C_{151}H_{175}NO_5S_2$: C, 85.71; H, 8.34; N, 0.66; S, 1.52%.

Reaction of a cradled Cys–SOH 6 with cyclohexane-1,3-dione (9b).

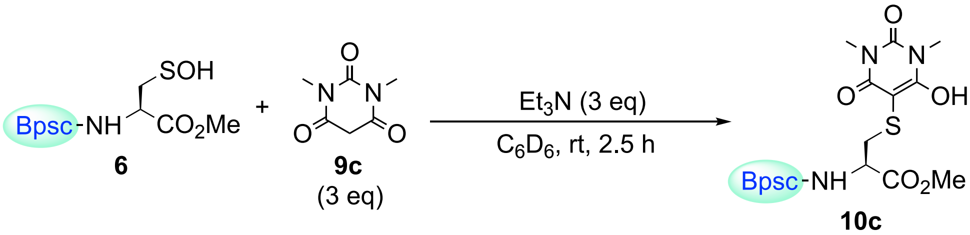


Scheme S12

To a solution of **6** (7.70 mg, 3.86 μmol) in C_6D_6 (0.5 mL) in a 5 mm o/d NMR tube with a J-young valve were added cyclohexane-1,3-dione (**9b**) (1.3 mg, 12 μmol) and Et_3N (1.6 μL, 12 μmol) at ambient temperature, and the tube was carefully sealed. The mixture was kept at ambient temperature for 6.5 h. The crude products were purified by GPC ($CHCl_3$) to afford **10b** (7.9 mg, 3.4 μmol, 98%) as colorless crystals.

10b: Colorless crystals; mp 212.0-214.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.03 (48H, d, J = 6.8 Hz), 1.09 (24H, d, J = 6.8 Hz), 1.10 (24H, d, J = 6.8 Hz), 1.56-1.69 (2H, m), 1.92-2.10 (4H, m), 2.15-2.20 (1H, m), 2.51 (1H, dd, J = 14.0, 2.3 Hz), 2.72-2.79 (16H, m), 2.97 (3H, s), 4.08 (1H, td, J = 8.0, 2.3 Hz), 6.83 (1H, d, J = 7.9 Hz), 6.98 (4H, br), 7.17 (16H, d, J = 7.4 Hz), 7.32 (8H, t, J = 7.9 Hz), 7.41 (8H, br), 7.43-7.45 (2H, m, B of AB_2), 7.48-7.51 (1H, m, A of AB_2), 7.68 (4H, d, J = 1.1 Hz), 7.79 (2H, br), 9.24 (1H, br s); ^{13}C NMR (125 MHz, $CDCl_3$) δ_C 19.6 (t), 24.10 (q), 24.12 (q), 24.3 (q), 28.9 (t), 30.3 (d), 37.0 (t), 38.0 (t), 52.1 (q), 52.6 (d), 105.5 (s), 122.4 (d), 126.0 (d), 126.6 (d), 127.3 (d), 127.8 (d), 129.1 (d), 129.8 (d), 130.1 (d), 134.6 (s), 139.0 (s), 140.2 (s), 140.6 (s), 140.9 (s), 141.3 (s), 141.5 (s), 146.7 (s), 146.7 (s), 168.9 (s), 169.7 (s), 181.0 (s), 195.1 (s); HRMS (FD-TOF) *m/z* 2086.2879 [M^+] (calc. for $C_{149}H_{171}N_3O_6S$, 2086.2878).

Reaction of a cradled Cys–SOH 6 with 1,3-dimethylbarbituric acid (9c).

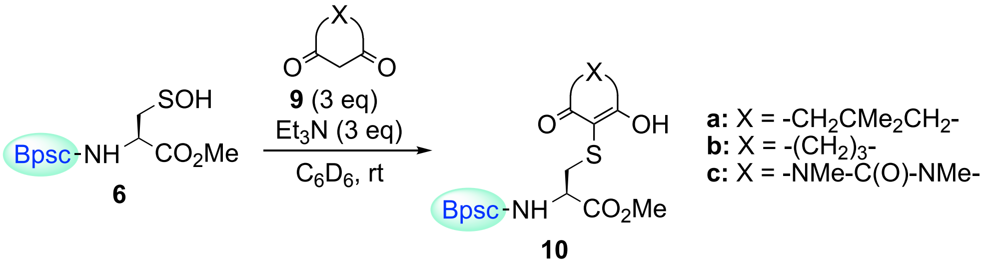


Scheme S13

To a solution of **6** (8.58 mg, 4.30 μmol) in C_6D_6 (0.5 mL) in a 5 mm o/d NMR tube with a J-young valve were added 1,3-dimethylbarbituric acid (**9c**) (2.0 mg, 13 μmol) and Et_3N (1.8 μL, 13 μmol) at ambient temperature, and the tube was carefully sealed. The mixture was kept at ambient temperature for 2.5 h. The crude products were purified by GPC ($CHCl_3$) to afford **10c** (9.2 mg, 3.4 μmol, 80%) as colorless crystals.

10c: Colorless crystals; mp 209.5-211.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ_H 1.03-1.06 (48H, m), 1.07-1.11 (48H, m), 1.88 (1H, t, J = 12.8 Hz), 2.70-2.79 (16H, m), 2.82-2.83 (4H, m), 2.92 (3H, s), 3.23 (3H, s), 4.06-4.10 (1H, m), 6.58 (1H, d, J = 8.5 Hz), 6.99 (4H, br), 7.17 (16H, d, J = 7.9 Hz), 7.33 (8H, t, J = 7.9 Hz), 7.41 (8H, d, J = 1.2 Hz), 7.45-7.47 (2H, m, B of AB_2), 7.51-7.54 (1H, m, A of AB_2), 7.63 (4H, d, J = 1.7 Hz), 7.82 (2H, br), 10.8 (1H, br s); ^{13}C NMR (126 MHz, $CDCl_3$) δ_C 23.99 (q), 24.01(q), 24.3 (q), 28.3 (q), 29.6 (q), 30.3 (d), 39.6 (t), 52.2 (q), 53.0 (d), 80.9 (s), 122.5 (d), 126.0 (d), 126.4 (d), 126.8 (d), 127.9 (d), 129.5 (d), 129.9 (d), 130.3 (d), 133.8 (d), 138.9 (s), 140.3 (s), 140.5 (s), 140.96 (s), 141.03 (s), 141.7 (s), 146.6 (s), 150.6 (s), 162.4 (s), 162.8 (s), 169.3 (s), 170.6 (s); HRMS (FD-TOF) *m/z* 2130.2879 $[M]^+$ (calc. for $C_{149}H_{171}N_3O_6S$, 2130.2888).

Kinetic measurements of the reactions of Cys–SOH 6 with 1,3-dicarbonyl compounds



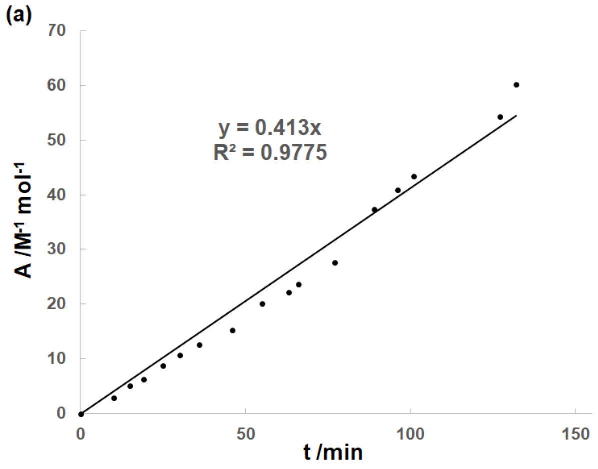
Scheme S14

General procedure: To a solution of **6** in C_6D_6 (0.5 mL) in a 5 mm o/d NMR tube with a J-young valve were added a 1,3-dicarbonyl compound (3 eq) and Et_3N (3 eq) at ambient temperature, and the tube was carefully sealed. The mixture was kept at ambient temperature and ^1H NMR spectrum was recorded about every 5 minutes. Concentrations of **6**, products and a diketone were monitored by ^1H NMR spectroscopy using bis(trimethylsilyl)methane as an internal standard. The second-order rate constants were evaluated using a least-squares computer program (Excel program) from the plot $((1/([\text{diketones}]_0–[\mathbf{6}]_0)\ln([\text{diketones}][\mathbf{6}]_0/[\mathbf{6}][\text{diketones}]_0)$ / M^{-1} vs. t /min).

$A = (1/([\text{diketones}]_0–[\mathbf{6}]_0)\ln([\text{diketones}][\mathbf{6}]_0/[\mathbf{6}][\text{diketones}]_0)$.

(i) Reaction of Cys–SOH 6 with dimedone (9a) to produce 10a.

Reagents: **6** (10.8 mg, 5.42 μmol), dimedone (**9a**) (2.3 mg, 16 μmol) and Et_3N (2.3 μL, 16 μmol).



(b)

t/min	conv. (%)	[11]	[15a]	A/M^{-1}
0	0	10.840	0.000	0.000
10	9	9.864	2.956	2.956
15	15	9.214	5.150	5.150
19	18	8.889	6.324	6.324
25	24	8.238	8.847	8.847
30	28	7.805	10.675	10.675
36	32	7.371	12.636	12.636
46	37	6.829	15.301	15.301
55	45	5.962	20.161	20.161
63	48	5.637	22.211	22.211
66	50	5.420	23.659	23.659
77	55	4.878	27.604	27.604
89	65	3.794	37.319	37.319
96	68	3.469	40.877	40.877
101	70	3.252	43.467	43.467
127	77	2.493	54.350	54.350
132	80	2.168	60.201	60.201

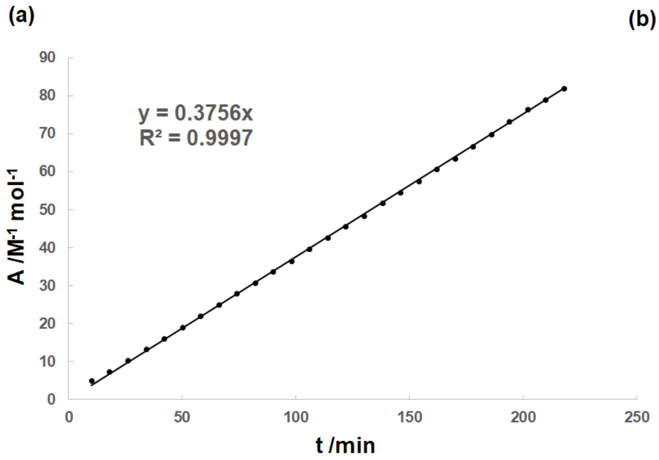
(c)

$k = 0.41$ min^{-1} mol^{-1}

Figure. S3 (a) Second-order plot (A / M^{-1} vs. t / min), (b) table of time dependence of conversion, [6], [9a] and A, (c) reaction rate.

(ii) Reaction of Cys–SOH 6 with cyclohexane-1,3-dione (9b) to produce 10b.

Reagents: **6** (7.70 mg, 3.86 μmol), cyclohexane-1,3-dione (**9b**) (1.3 mg, 12 μmol), and Et_3N (1.6 μL, 12 μmol).



(b)

t/min	conv. (%)	[**11**]	[**15b**]	A/M^{-1}
10	11	6.855	0.865	5.046
18	16	6.485	1.235	7.461
26	21	6.078	1.642	10.335
34	26	5.696	2.024	13.261
42	31	5.357	2.363	16.079
50	35	5.028	2.692	19.032
58	39	4.716	3.004	22.062
66	43	4.439	3.281	24.962
74	46	4.175	3.545	27.946
82	49	3.934	3.786	30.871
90	52	3.709	4.011	33.791
98	54	3.513	4.207	36.519
106	57	3.303	4.417	39.653
114	60	3.112	4.608	42.719
122	62	2.942	4.778	45.614
130	64	2.788	4.932	48.437
138	66	2.614	5.106	51.826
146	68	2.479	5.241	54.635
154	70	2.348	5.372	57.544
162	71	2.211	5.509	60.788
170	73	2.105	5.615	63.454
178	74	1.986	5.734	66.633
186	76	1.872	5.848	69.868
194	77	1.764	5.956	73.161
202	78	1.665	6.055	76.355
210	79	1.589	6.131	78.993
218	80	1.506	6.214	81.995

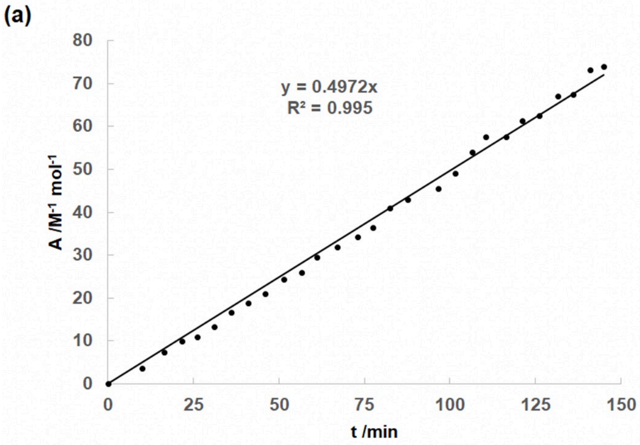
(c)

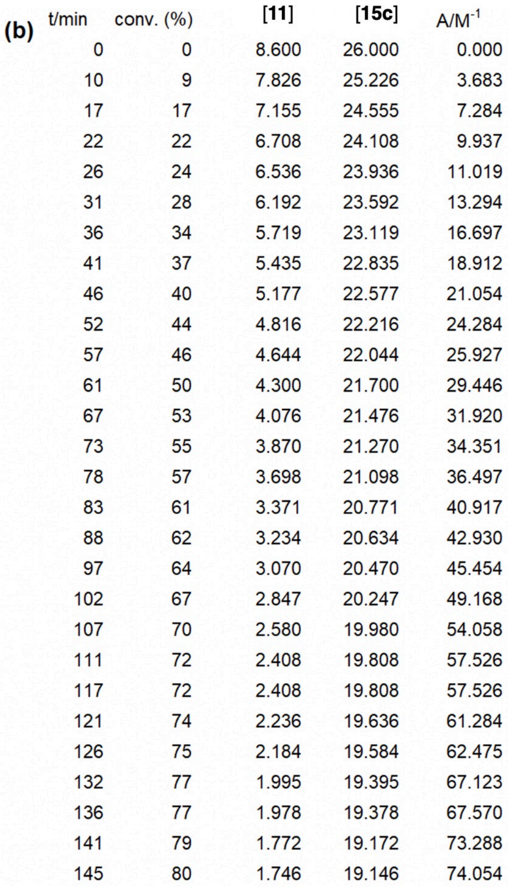
$k = 0.38\ \mathrm{min^{-1}\ mol^{-1}}$

Figure. S4 (a) Second-order plot (A / M^{-1} vs. t / min), (b) table of time dependence of conversion, [6], [9b] and A, (c) reaction rate.

(iii) Reaction of Cys–SOH 6 with 1,3-dimethylbarbituric acid (9c) to produce 10c.

Reagents: **6** (8.58 mg, 4.30 μmol), 1,3-dimethylbarbituric acid (**9c**) (2.0 mg, 13 μmol), and Et_3N (1.8 μL, 13 μmol).




(b)

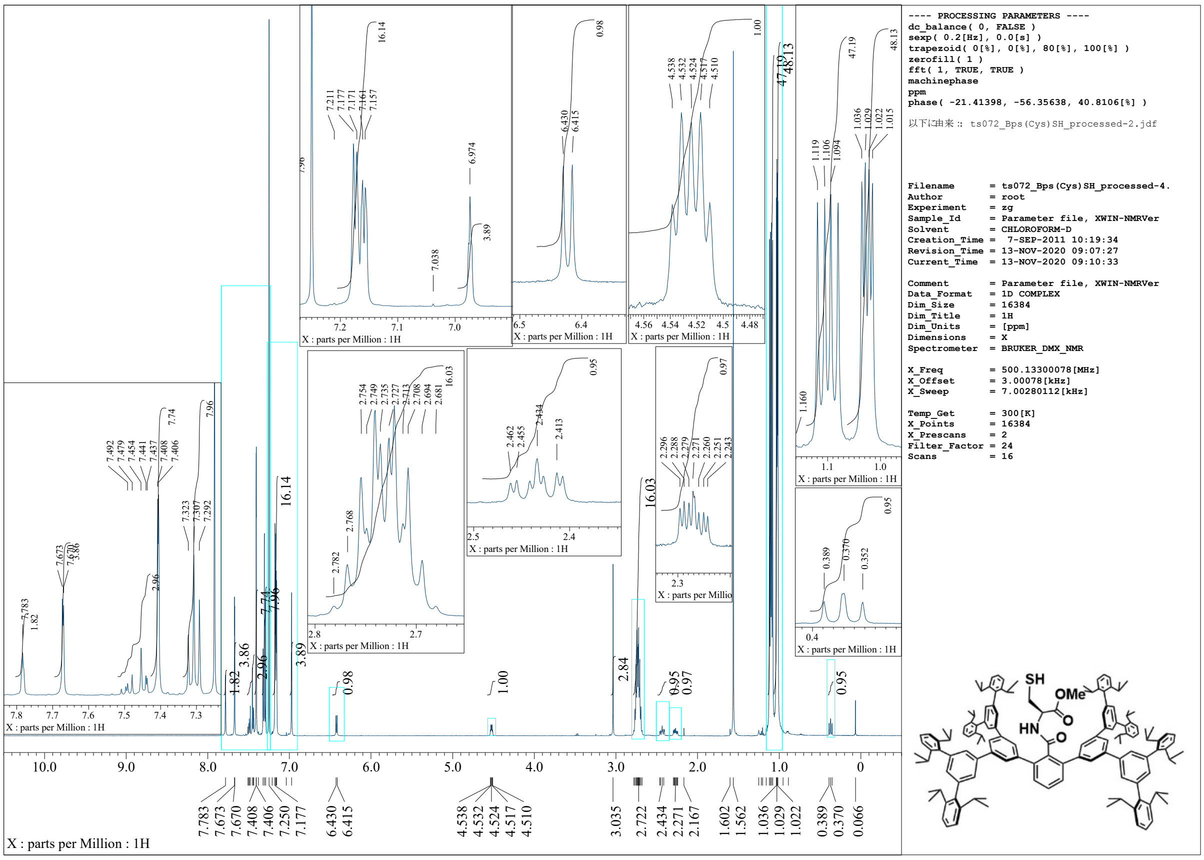
t/min	conv. (%)	[11]	[15c]	A/M^{-1}
0	0	8.600	26.000	0.000
10	9	7.826	25.226	3.683
17	17	7.155	24.555	7.284
22	22	6.708	24.108	9.937
26	24	6.536	23.936	11.019
31	28	6.192	23.592	13.294
36	34	5.719	23.119	16.697
41	37	5.435	22.835	18.912
46	40	5.177	22.577	21.054
52	44	4.816	22.216	24.284
57	46	4.644	22.044	25.927
61	50	4.300	21.700	29.446
67	53	4.076	21.476	31.920
73	55	3.870	21.270	34.351
78	57	3.698	21.098	36.497
83	61	3.371	20.771	40.917
88	62	3.234	20.634	42.930
97	64	3.070	20.470	45.454
102	67	2.847	20.247	49.168
107	70	2.580	19.980	54.058
111	72	2.408	19.808	57.526
117	72	2.408	19.808	57.526
121	74	2.236	19.636	61.284
126	75	2.184	19.584	62.475
132	77	1.995	19.395	67.123
136	77	1.978	19.378	67.570
141	79	1.772	19.172	73.288
145	80	1.746	19.146	74.054

(c)

***k* = 0.50 min^{-1} mol^{-1}**

Figure. S5 (a) Second-order plot (A / M^{-1} vs. t / min) (b) table of time dependence of conversion, [6], [9c] and A, (c) reaction rate.

2. NMR spectra



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Experiment      = zg
Sample_Id       = Parameter file, XWIN-NMRVer
Solvent         = CHLOROFORM-D
Creation_Time   =  7-SEP-2011 10:19:34
Revision_Time   = 13-NOV-2020 09:07:27
Current_Time    = 13-NOV-2020 09:10:33

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X_Freq          = 500.13300078[MHz]
X_Offset        = 3.00078[kHz]
X_Sweep         = 7.00280112[kHz]

Temp_Get        = 300[K]
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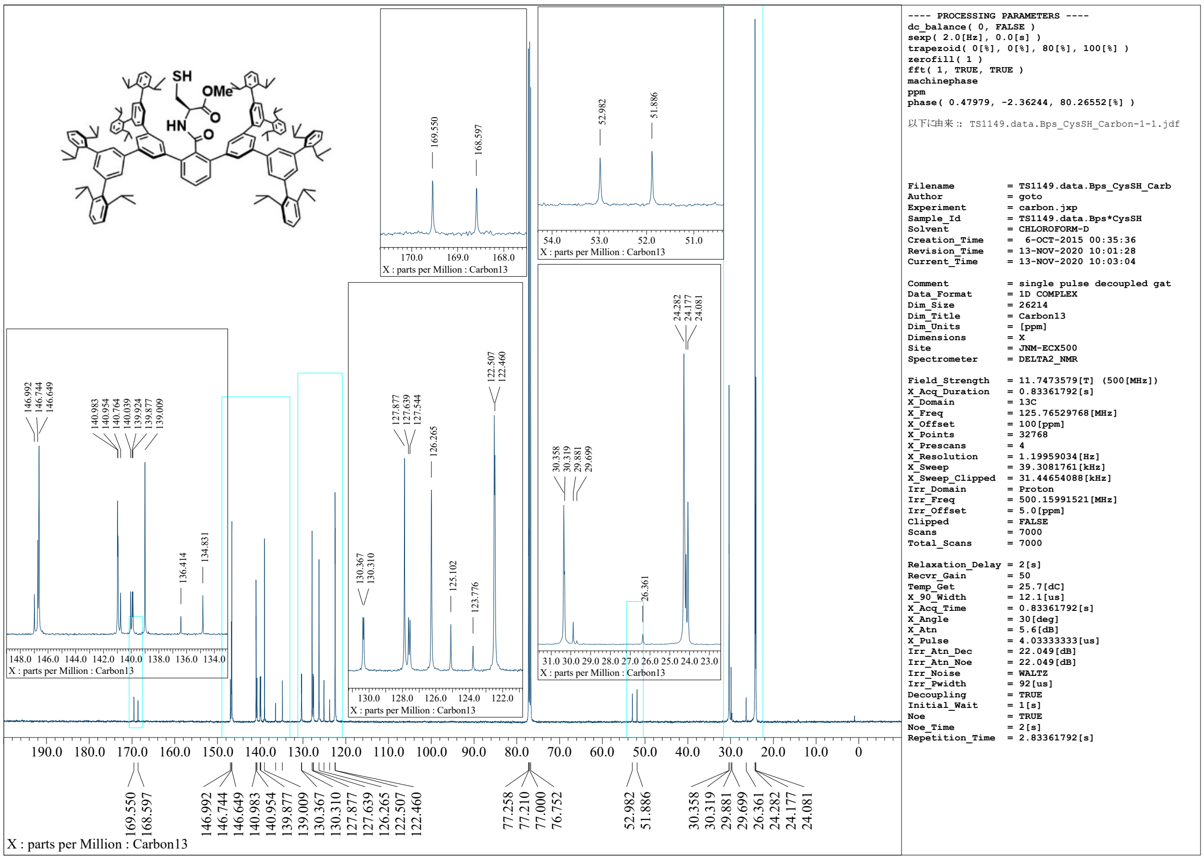
Figure S6. ^{1}H NMR (500 MHz, CDCl$_3$) spectrum of **5**.



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Revision_Time      = 13-NOV-2020 10:01:28
Current_Time       = 13-NOV-2020 10:03:04

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Dim_Size           = 26214
Dim_Title          = Carbon13
Dim_Units          = [ppm]
Dimensions         = X
Site               = JNM-ECX500
Spectrometer       = DELTA2_NMR

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Irr_Freq           = 500.15991521[MHz]
Irr_Offset         = 5.0[ppm]
Clipped            = FALSE
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Total_Scans        = 7000

Relaxation_Delay   = 2[s]
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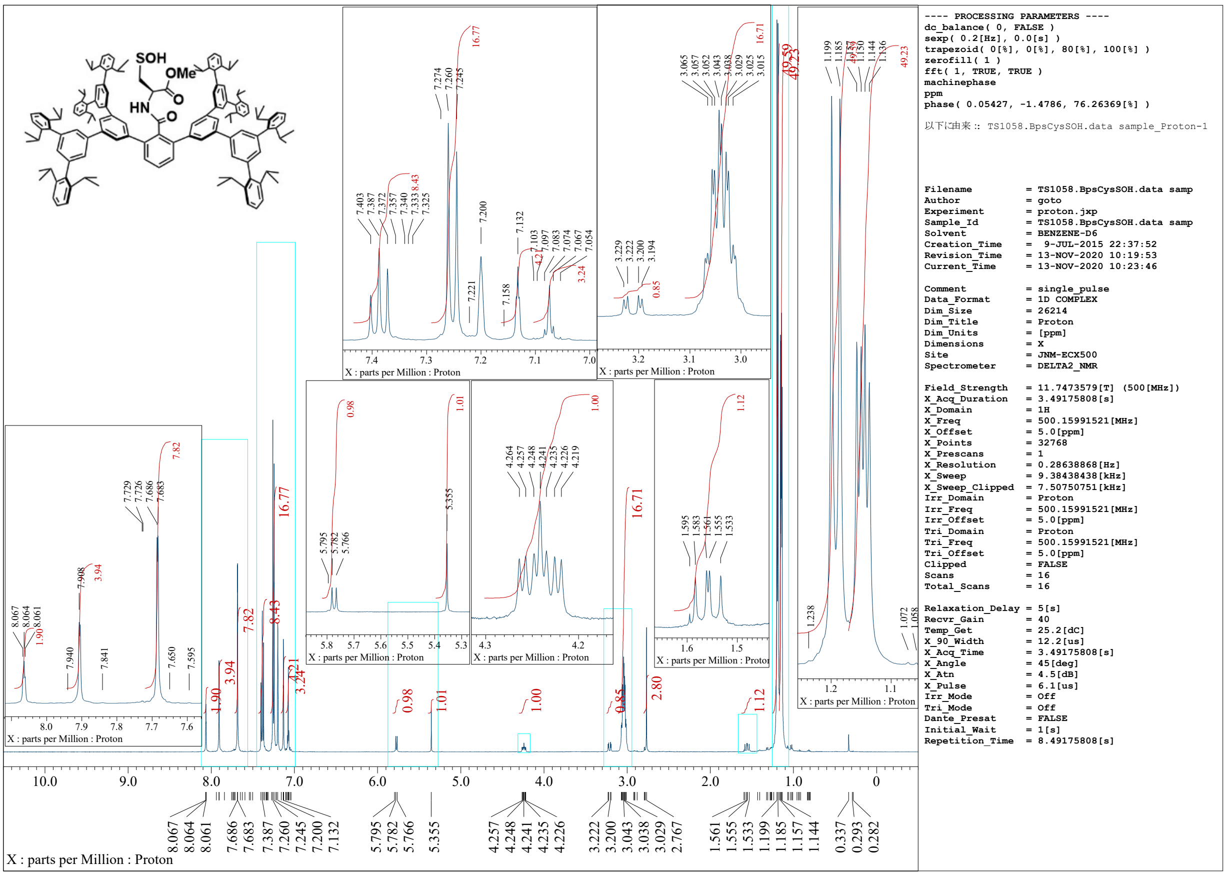
X_Acq_Time         = 0.83361792[s]
X_Angle            = 30[deg]
X_Atn              = 5.6[dB]
X_Pulse            = 4.03333333[us]
Irr_Atn_Dec        = 22.049[dB]
Irr_Atn_Noe        = 22.049[dB]
Irr_Noise          = WALTZ
Irr_Pwidth         = 92[us]
Decoupling         = TRUE
Initial_Wait       = 1[s]
Noe                = TRUE
Noe_Time           = 2[s]
Repetition_Time    = 2.83361792[s]
```

Figure S7. ^{13}C NMR (125 MHz, CDCl$_3$) spectrum of **5**.



```
---- PROCESSING PARAMETERS ----
dc_balance( 0, FALSE )
sexp( 0.2[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( 0.05427, -1.4786, 76.26369[%] )

以下に由来 :: TS1058.BpsCysSOH.data sample_Proton-1



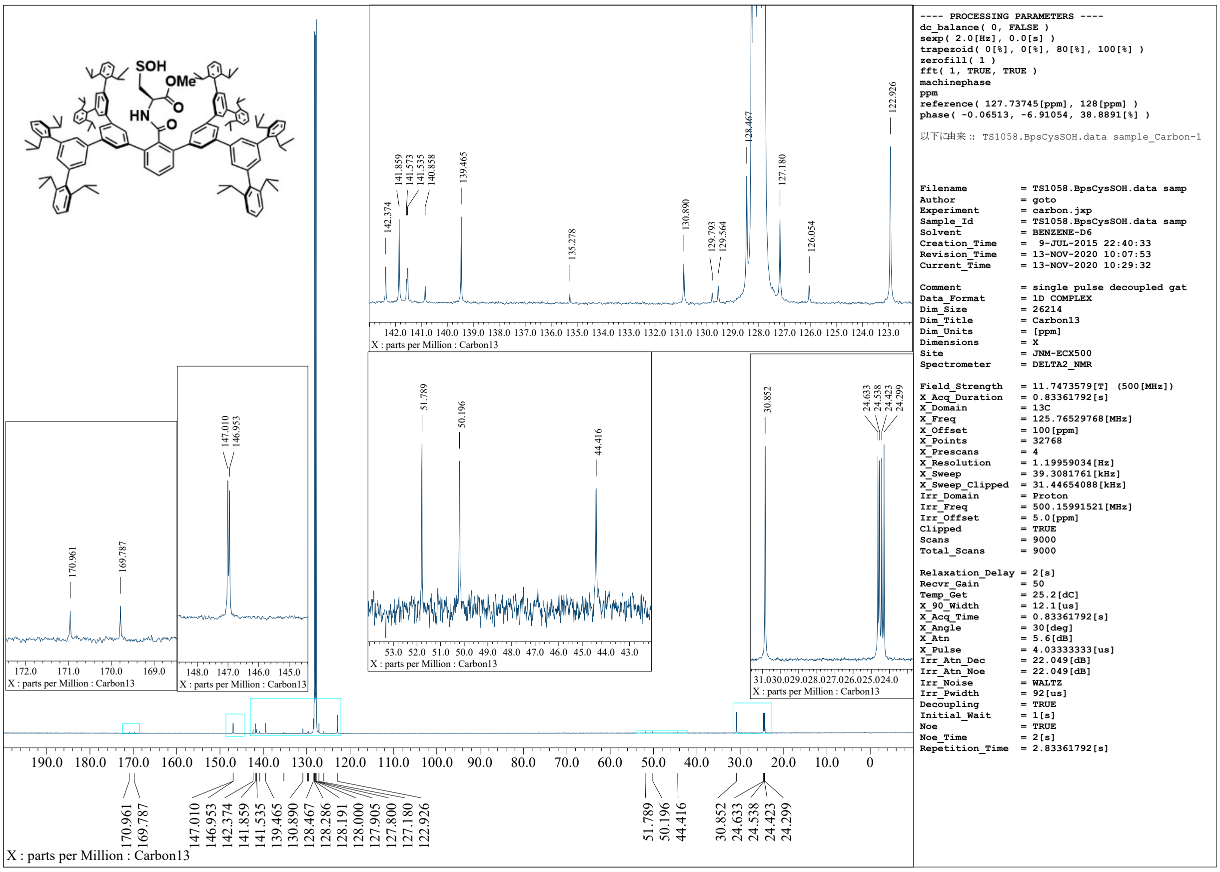
Filename          = TS1058.BpsCysSOH.data samp
Author            = goto
Experiment        = proton.jxp
Sample_Id         = TS1058.BpsCysSOH.data samp
Solvent           = BENZENE-D6
Creation_Time     =  9-JUL-2015 22:37:52
Revision_Time     = 13-NOV-2020 10:19:53
Current_Time      = 13-NOV-2020 10:23:46

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = Proton
Dim_Units         = [ppm]
Dimensions        = X
Site              = JNM-ECX500
Spectrometer      = DELTA2_NMR

Field_Strength    = 11.7473579[T] (500[MHz])
X_Acq_Duration    = 3.49175808[s]
X_Domain          = 1H
X_Freq            = 500.15991521[MHz]
X_Offset          = 5.0[ppm]
X_Points          = 32768
X_Prescans        = 1
X_Resolution      = 0.28638868[Hz]
X_Sweep           = 9.38438438[kHz]
X_Sweep_Clipped   = 7.50750751[kHz]
Irr_Domain        = Proton
Irr_Freq          = 500.15991521[MHz]
Irr_Offset        = 5.0[ppm]
Tri_Domain        = Proton
Tri_Freq          = 500.15991521[MHz]
Tri_Offset        = 5.0[ppm]
Clipped           = FALSE
Scans             = 16
Total_Scans       = 16

Relaxation_Delay = 5[s]
Recvr_Gain        = 40
Temp_Get          = 25.2[dC]
X_90_Width        = 12.2[us]
X_Acq_Time        = 3.49175808[s]
X_Angle           = 45[deg]
X_Atn             = 4.5[dB]
X_Pulse           = 6.1[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 8.49175808[s]
```

Figure S8. ^{1}H NMR (500 MHz, C_6D_6) spectrum of **6**.



```
---- PROCESSING PARAMETERS ----
dc_balance( 0, FALSE )
sexp( 2.0[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
reference( 127.73745[ppm], 128[ppm] )
phase( -0.06513, -6.91054, 38.8891[%] )

以下に由来 :: TS1058.BpsCysSOH.data sample_Carbon-1



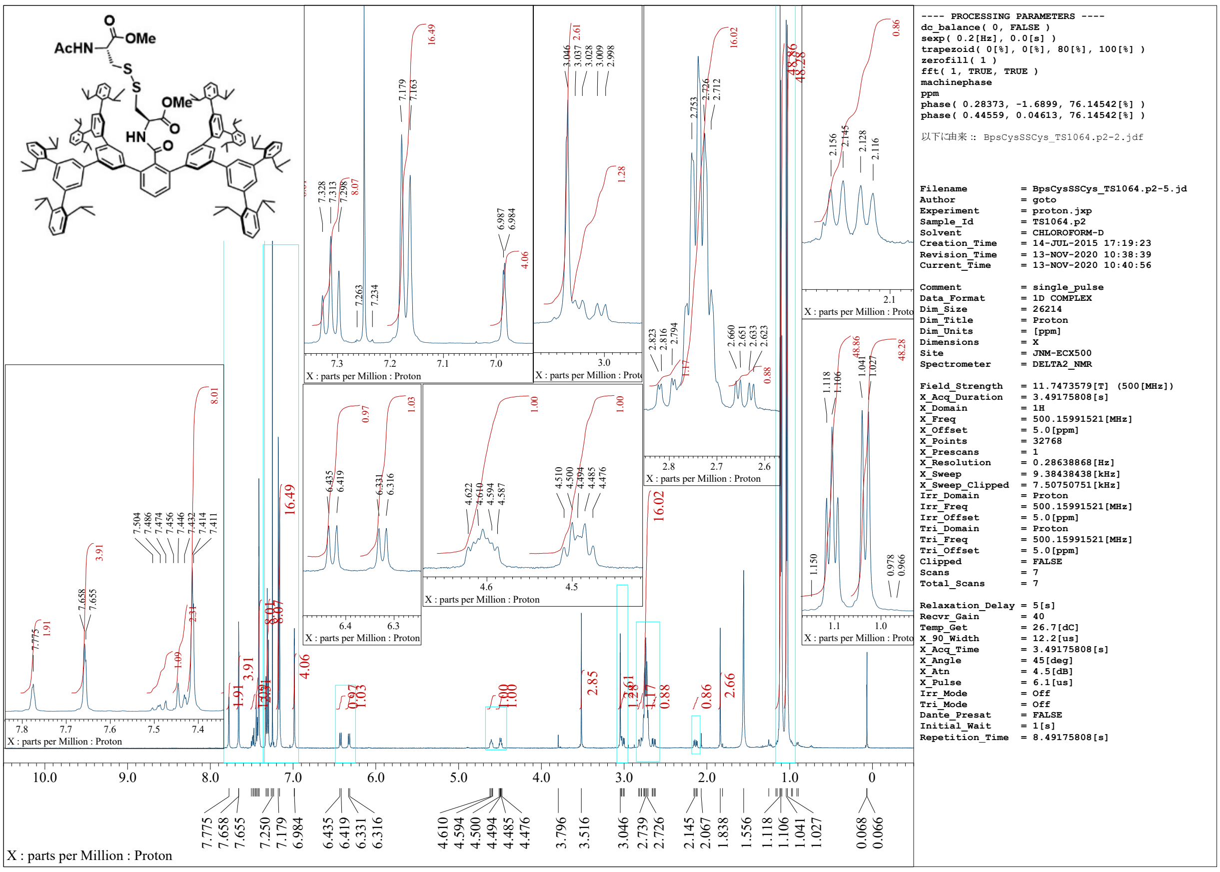
Filename          = TS1058.BpsCysSOH.data samp
Author            = goto
Experiment        = carbon.jxp
Sample_Id         = TS1058.BpsCysSOH.data samp
Solvent           = BENZENE-D6
Creation_Time     =  9-JUL-2015 22:40:33
Revision_Time     = 13-NOV-2020 10:07:53
Current_Time      = 13-NOV-2020 10:29:32

Comment           = single pulse decoupled gat
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = Carbon13
Dim_Units         = [ppm]
Dimensions        = X
Site              = JNM-ECX500
Spectrometer      = DELTA2_NMR

Field_Strength    = 11.7473579[T] (500[MHz])
X_Acq_Duration    = 0.83361792[s]
X_Domain          = 13C
X_Freq            = 125.76529768[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 1.19959034[Hz]
X_Sweep           = 39.3081761[kHz]
X_Sweep_Clipped   = 31.44654088[kHz]
Irr_Domain        = Proton
Irr_Freq          = 500.15991521[MHz]
Irr_Offset        = 5.0[ppm]
Clipped           = TRUE
Scans             = 9000
Total_Scans       = 9000

Relaxation_Delay = 2[s]
Recvr_Gain        = 50
Temp_Get          = 25.2[dC]
X_90_Width        = 12.1[us]
X_Acq_Time        = 0.83361792[s]
X_Angle           = 30[deg]
X_Atn             = 5.6[dB]
X_Pulse           = 4.03333333[us]
Irr_Atn_Dec       = 22.049[dB]
Irr_Atn_Noe       = 22.049[dB]
Irr_Noise         = WALTZ
Irr_Pwidth        = 92[us]
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 2.83361792[s]
```

Figure S9. ^{13}C NMR (125 MHz, C_6D_6) spectrum of **6**.



```
---- PROCESSING PARAMETERS ----
dc_balance( 0, FALSE )
sexp( 0.2[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( 0.28373, -1.6899, 76.14542[%] )
phase( 0.44559, 0.04613, 76.14542[%] )

以下に由来 :: BpsCysSSCys_TS1064.p2-2.jdf



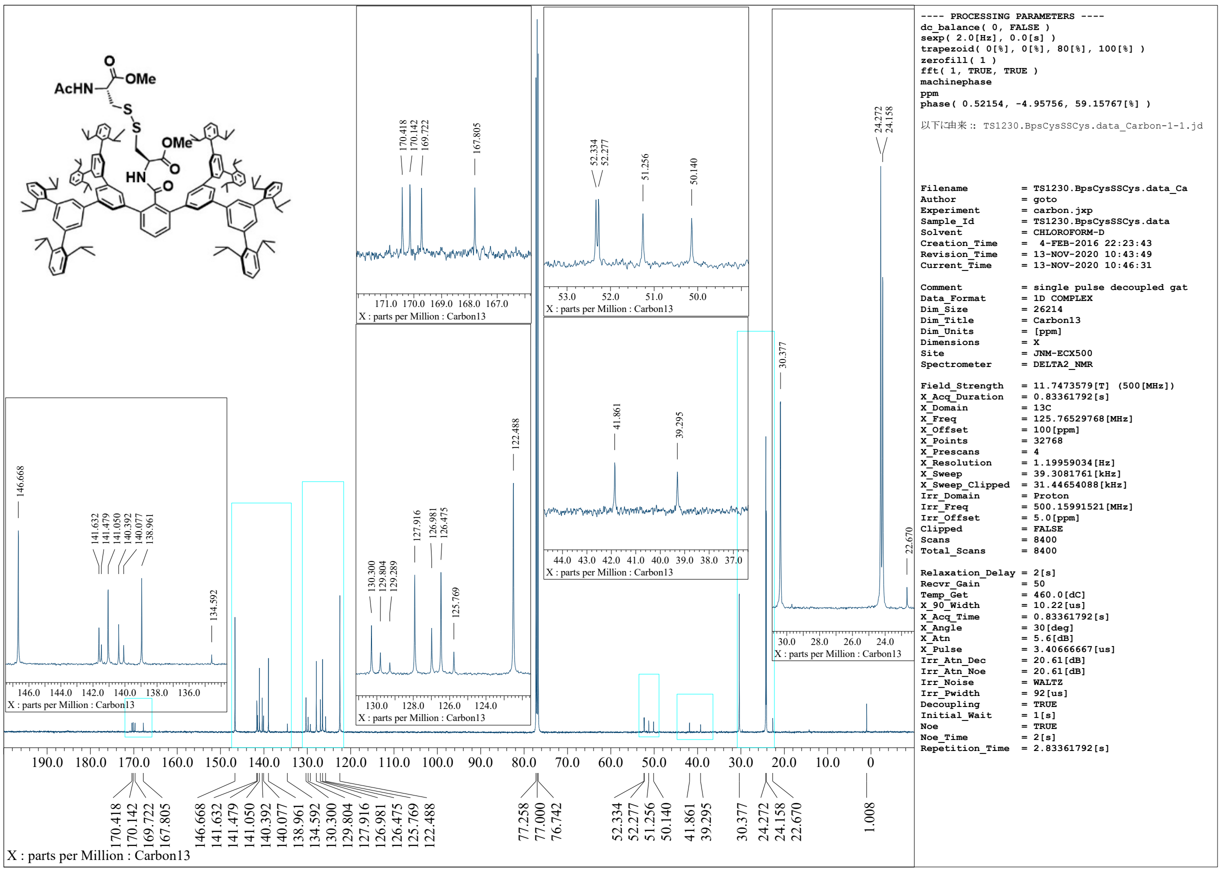
Filename          = BpsCysSSCys_TS1064.p2-5.jd
Author            = goto
Experiment        = proton.jxp
Sample_Id         = TS1064.p2
Solvent           = CHLOROFORM-D
Creation_Time     = 14-JUL-2015 17:19:23
Revision_Time     = 13-NOV-2020 10:38:39
Current_Time      = 13-NOV-2020 10:40:56

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = Proton
Dim_Units         = [ppm]
Dimensions        = X
Site              = JNM-ECX500
Spectrometer      = DELTA2_NMR

Field_Strength    = 11.7473579[T] (500[MHz])
X_Acq_Duration    = 3.49175808[s]
X_Domain          = 1H
X_Freq            = 500.15991521[MHz]
X_Offset          = 5.0[ppm]
X_Points          = 32768
X_Prescans        = 1
X_Resolution      = 0.28638868[Hz]
X_Sweep           = 9.38438438[kHz]
X_Sweep_Clipped   = 7.50750751[kHz]
Irr_Domain        = Proton
Irr_Freq          = 500.15991521[MHz]
Irr_Offset        = 5.0[ppm]
Tri_Domain        = Proton
Tri_Freq          = 500.15991521[MHz]
Tri_Offset        = 5.0[ppm]
Clipped           = FALSE
Scans             = 7
Total_Scans       = 7

Relaxation_Delay  = 5[s]
Recvr_Gain        = 40
Temp_Get          = 26.7[dC]
X_90_Width        = 12.2[us]
X_Acq_Time        = 3.49175808[s]
X_Angle           = 45[deg]
X_Atn             = 4.5[dB]
X_Pulse           = 6.1[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 8.49175808[s]
```

Figure S10. ^{1}H NMR (500 MHz, CDCl$_3$) spectrum of **8**.



```
---- PROCESSING PARAMETERS ----
dc_balance( 0, FALSE )
sexp( 2.0[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( 0.52154, -4.95756, 59.15767[%] )

以下に由来 :: TS1230.BpsCysSSCys.data_Carbon-1-1.jd



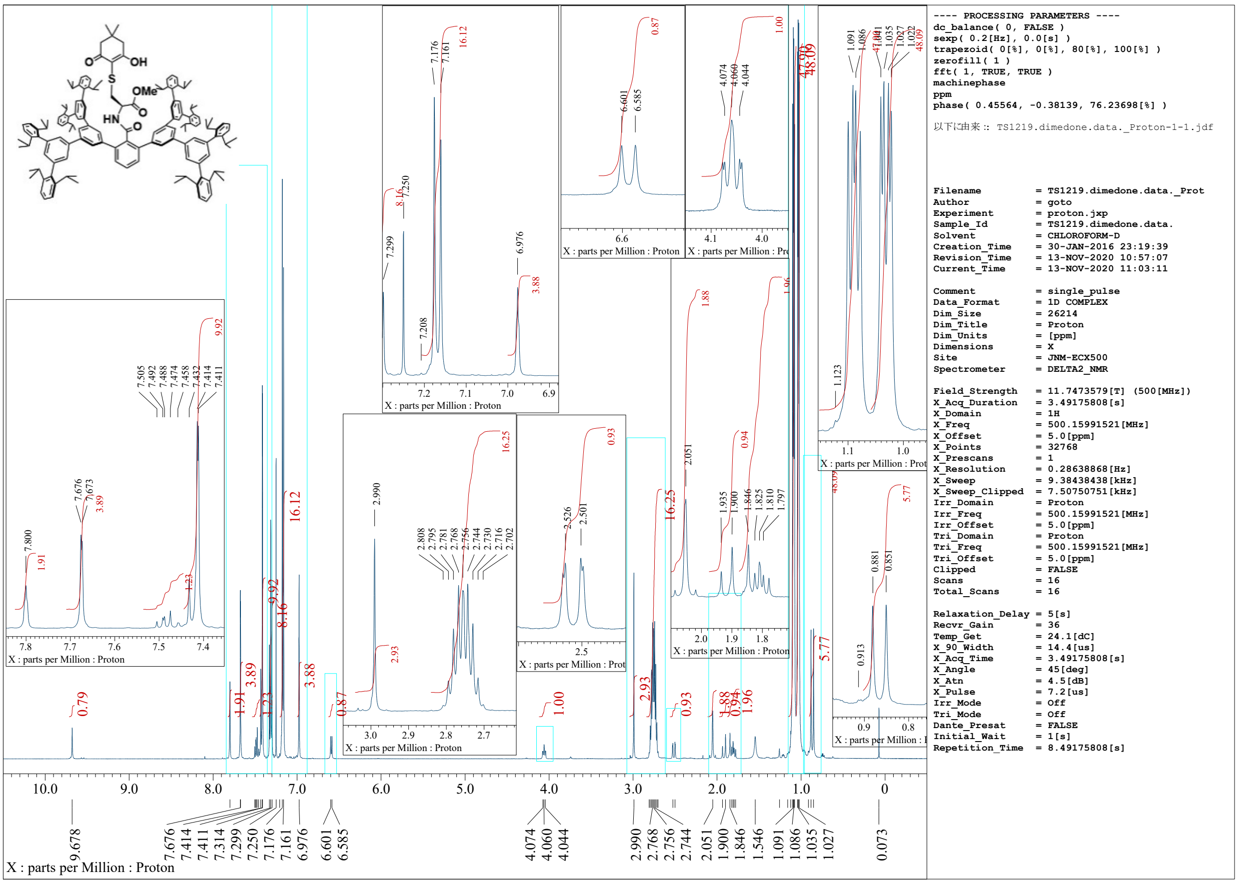
Filename          = TS1230.BpsCysSSCys.data_Ca
Author            = goto
Experiment        = carbon.jxp
Sample_Id         = TS1230.BpsCysSSCys.data
Solvent           = CHLOROFORM-D
Creation_Time     =  4-FEB-2016 22:23:43
Revision_Time     = 13-NOV-2020 10:43:49
Current_Time      = 13-NOV-2020 10:46:31

Comment           = single pulse decoupled gat
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = Carbon13
Dim_Units         = [ppm]
Dimensions        = X
Site              = JNM-ECX500
Spectrometer      = DELTA2_NMR

Field_Strength    = 11.7473579[T] (500[MHz])
X_Acq_Duration    = 0.83361792[s]
X_Domain          = 13C
X_Freq            = 125.76529768[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 1.19959034[Hz]
X_Sweep           = 39.3081761[kHz]
X_Sweep_Clipped   = 31.44654088[kHz]
Irr_Domain        = Proton
Irr_Freq          = 500.15991521[MHz]
Irr_Offset        = 5.0[ppm]
Clipped           = FALSE
Scans             = 8400
Total_Scans       = 8400

Relaxation_Delay  = 2[s]
Recvr_Gain        = 50
Temp_Get          = 460.0[dC]
X_90_Width        = 10.22[us]
X_Acq_Time        = 0.83361792[s]
X_Angle           = 30[deg]
X_Atn             = 5.6[dB]
X_Pulse           = 3.40666667[us]
Irr_Atn_Dec       = 20.61[dB]
Irr_Atn_Noe       = 20.61[dB]
Irr_Noise         = WALTZ
Irr_Pwidth        = 92[us]
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 2.83361792[s]
```

Figure S11. ^{13}C NMR (125 MHz, CDCl$_3$) spectrum of **8**.



```
---- PROCESSING PARAMETERS ----
dc_balance( 0, FALSE )
sexp( 0.2[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( 0.45564, -0.38139, 76.23698[%] )

以下に由来 :: TS1219.dimedone.data._Proton-1-1.jdf

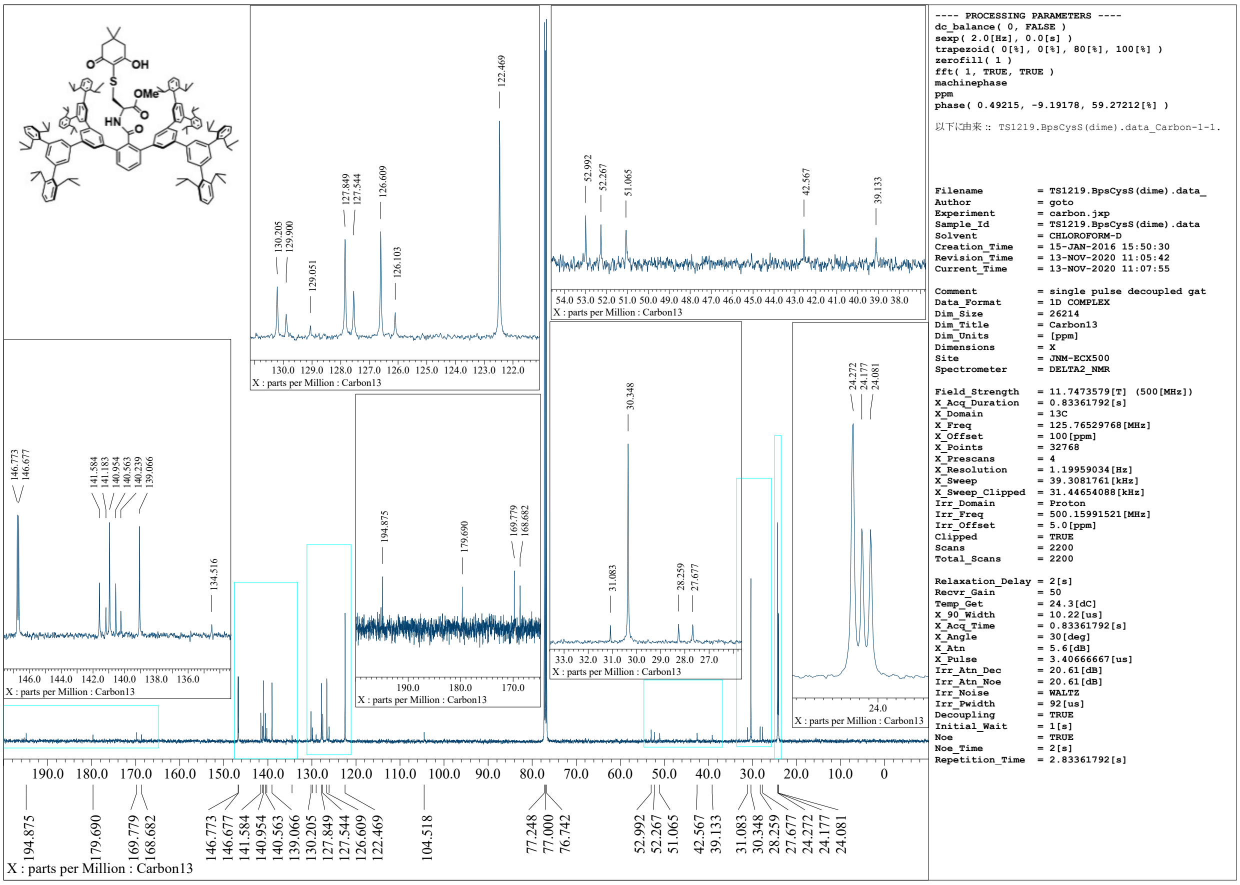
Filename          = TS1219.dimedone.data._Prot
Author            = goto
Experiment        = proton.jxp
Sample_Id         = TS1219.dimedone.data.
Solvent           = CHLOROFORM-D
Creation_Time     = 30-JAN-2016 23:19:39
Revision_Time     = 13-NOV-2020 10:57:07
Current_Time      = 13-NOV-2020 11:03:11

Comment           = single_pulse
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = Proton
Dim_Units         = [ppm]
Dimensions        = X
Site              = JNM-ECX500
Spectrometer      = DELTA2_NMR

Field_Strength    = 11.7473579[T] (500[MHz])
X_Acq_Duration    = 3.49175808[s]
X_Domain          = 1H
X_Freq            = 500.15991521[MHz]
X_Offset          = 5.0[ppm]
X_Points          = 32768
X_Prescans        = 1
X_Resolution      = 0.28638868[Hz]
X_Sweep           = 9.38438438[kHz]
X_Sweep_Clipped   = 7.50750751[kHz]
Irr_Domain        = Proton
Irr_Freq          = 500.15991521[MHz]
Irr_Offset        = 5.0[ppm]
Tri_Domain        = Proton
Tri_Freq          = 500.15991521[MHz]
Tri_Offset        = 5.0[ppm]
Clipped           = FALSE
Scans             = 16
Total_Scans       = 16

Relaxation_Delay  = 5[s]
Recvr_Gain        = 36
Temp_Get          = 24.1[dC]
X_90_Width        = 14.4[us]
X_Acq_Time        = 3.49175808[s]
X_Angle           = 45[deg]
X_Atn             = 4.5[dB]
X_Pulse           = 7.2[us]
Irr_Mode          = Off
Tri_Mode          = Off
Dante_Presat      = FALSE
Initial_Wait      = 1[s]
Repetition_Time   = 8.49175808[s]
```

Figure S12. ^1H NMR (500 MHz, $CDCl_3$) spectrum of **10a**.



```
---- PROCESSING PARAMETERS ----
dc_balance( 0, FALSE )
sexp( 2.0[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( 0.49215, -9.19178, 59.27212[%] )

以下に由来 :: TS1219.BpsCysS(dime).data_Carbon-1-1.

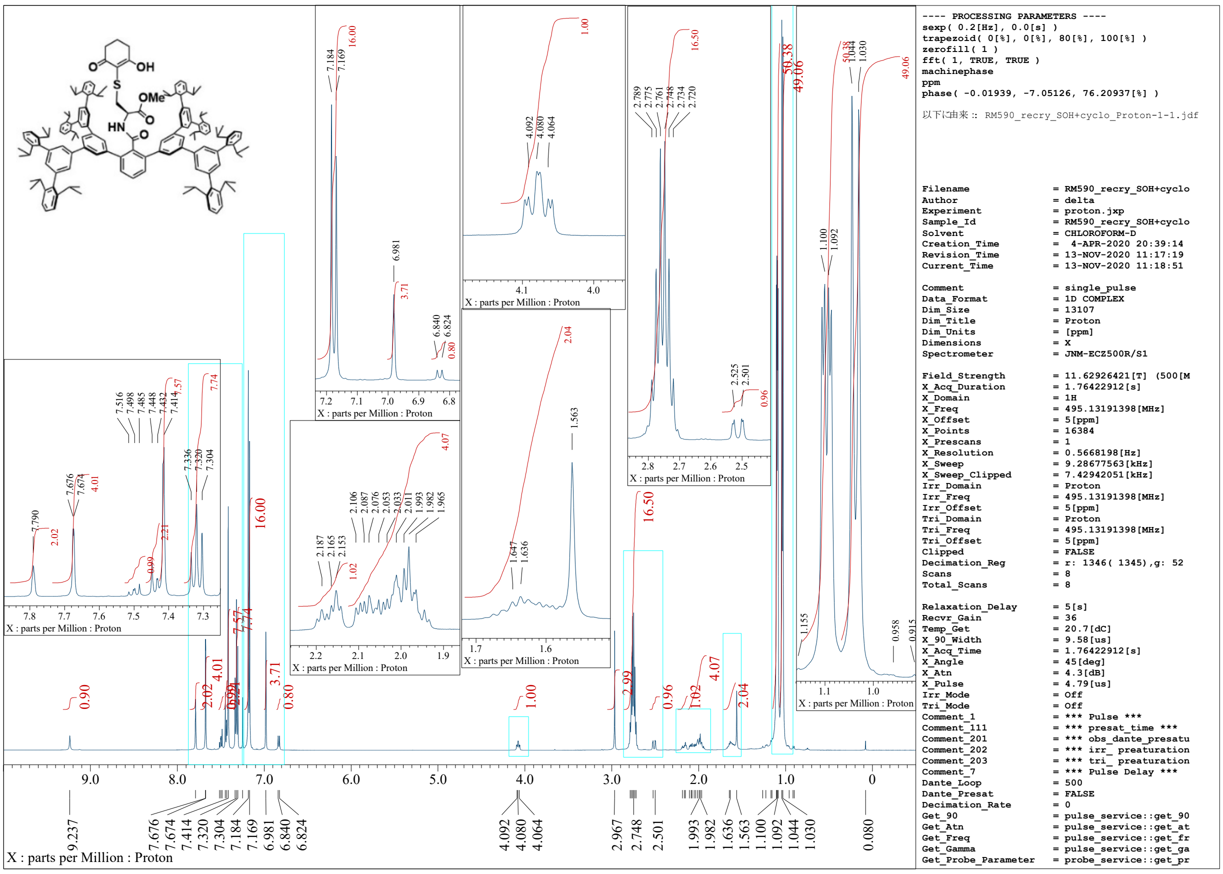
Filename          = TS1219.BpsCysS(dime).data_
Author            = goto
Experiment        = carbon.jxp
Sample_Id         = TS1219.BpsCysS(dime).data
Solvent           = CHLOROFORM-D
Creation_Time     = 15-JAN-2016 15:50:30
Revision_Time     = 13-NOV-2020 11:05:42
Current_Time      = 13-NOV-2020 11:07:55

Comment           = single pulse decoupled gat
Data_Format       = 1D COMPLEX
Dim_Size          = 26214
Dim_Title         = Carbon13
Dim_Units         = [ppm]
Dimensions        = X
Site              = JNM-ECX500
Spectrometer      = DELTA2_NMR

Field_Strength    = 11.7473579[T] (500[MHz])
X_Acq_Duration    = 0.83361792[s]
X_Domain          = 13C
X_Freq            = 125.76529768[MHz]
X_Offset          = 100[ppm]
X_Points          = 32768
X_Prescans        = 4
X_Resolution      = 1.19959034[Hz]
X_Sweep           = 39.3081761[kHz]
X_Sweep_Clipped   = 31.44654088[kHz]
Irr_Domain        = Proton
Irr_Freq          = 500.15991521[MHz]
Irr_Offset        = 5.0[ppm]
Clipped           = TRUE
Scans             = 2200
Total_Scans       = 2200

Relaxation_Delay  = 2[s]
Recvr_Gain        = 50
Temp_Get          = 24.3[dC]
X_90_Width        = 10.22[us]
X_Acq_Time        = 0.83361792[s]
X_Angle           = 30[deg]
X_Atn             = 5.6[dB]
X_Pulse           = 3.40666667[us]
Irr_Atn_Dec       = 20.61[dB]
Irr_Atn_Noe       = 20.61[dB]
Irr_Noise         = WALTZ
Irr_Pwidth        = 92[us]
Decoupling        = TRUE
Initial_Wait      = 1[s]
Noe               = TRUE
Noe_Time          = 2[s]
Repetition_Time   = 2.83361792[s]
```

Figure S13. ^{13}C NMR (125 MHz, $CDCl_3$) spectrum of **10a**.



```
---- PROCESSING PARAMETERS ----
sexp( 0.2[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( -0.01939, -7.05126, 76.20937[%] )

以下に由来 :: RM590_recry_SOH+cyclo_Proton-1-1.jdf

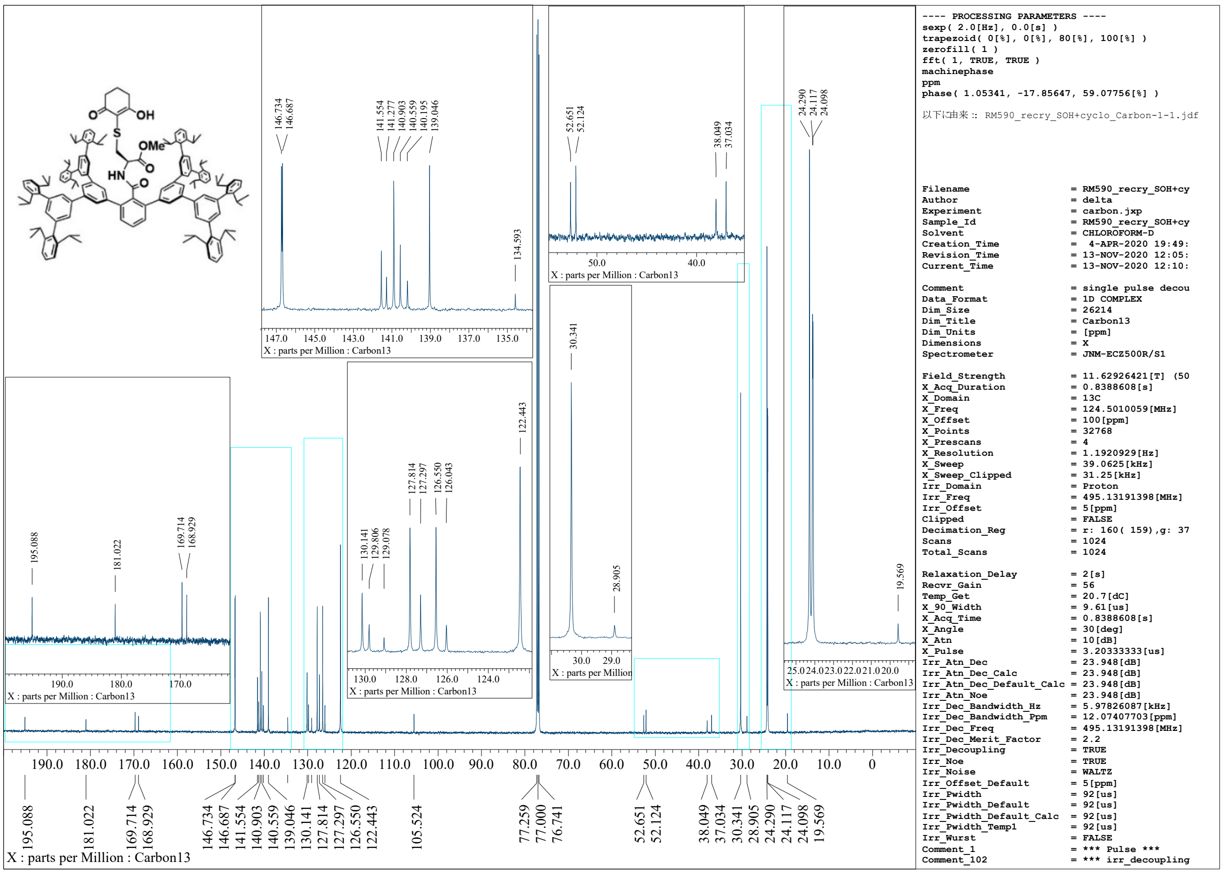
Filename                = RM590_recry_SOH+cyclo
Author                  = delta
Experiment              = proton.jxp
Sample_Id               = RM590_recry_SOH+cyclo
Solvent                 = CHLOROFORM-D
Creation_Time           =  4-APR-2020 20:39:14
Revision_Time           = 13-NOV-2020 11:17:19
Current_Time            = 13-NOV-2020 11:18:51

Comment                 = single_pulse
Data_Format             = 1D COMPLEX
Dim_Size                = 13107
Dim_Title               = Proton
Dim_Units               = [ppm]
Dimensions              = X
Spectrometer            = JNM-ECZ500R/S1

Field_Strength          = 11.62926421[T] (500[M
X_Acq_Duration          = 1.76422912[s]
X_Domain                = 1H
X_Freq                  = 495.13191398[MHz]
X_Offset                = 5[ppm]
X_Points                = 16384
X_Prescans              = 1
X_Resolution            = 0.5668198[Hz]
X_Sweep                 = 9.28677563[kHz]
X_Sweep_Clipped         = 7.42942051[kHz]
Irr_Domain              = Proton
Irr_Freq                = 495.13191398[MHz]
Irr_Offset              = 5[ppm]
Tri_Domain              = Proton
Tri_Freq                = 495.13191398[MHz]
Tri_Offset              = 5[ppm]
Clipped                 = FALSE
Decimation_Reg          = r: 1346( 1345),g: 52
Scans                   = 8
Total_Scans             = 8

Relaxation_Delay        = 5[s]
Recvr_Gain              = 36
Temp_Get                = 20.7[dC]
X_90_Width              = 9.58[us]
X_Acq_Time              = 1.76422912[s]
X_Angle                 = 45[deg]
X_Atn                   = 4.3[dB]
X_Pulse                 = 4.79[us]
Irr_Mode                = Off
Tri_Mode                = Off
Comment_1               = *** Pulse ***
Comment_111             = *** presat_time ***
Comment_201             = *** obs_dante_presatu
Comment_202             = *** irr_ preaturation
Comment_203             = *** tri_ preaturation
Comment_7               = *** Pulse Delay ***
Dante_Loop              = 500
Dante_Presat            = FALSE
Decimation_Rate         = 0
Get_90                  = pulse_service::get_90
Get_Atn                 = pulse_service::get_at
Get_Freq                = pulse_service::get_fr
Get_Gamma               = pulse_service::get_ga
Get_Probe_Parameter     = probe_service::get_pr
```

Figure S14. ^{1}H NMR (500 MHz, CDCl$_3$) spectrum of **10b**.



```
---- PROCESSING PARAMETERS ----
sexp( 2.0[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( 1.05341, -17.85647, 59.07756[%] )

以下に由来 :: RM590_recry_SOH+cyclo_Carbon-1-1.jdf

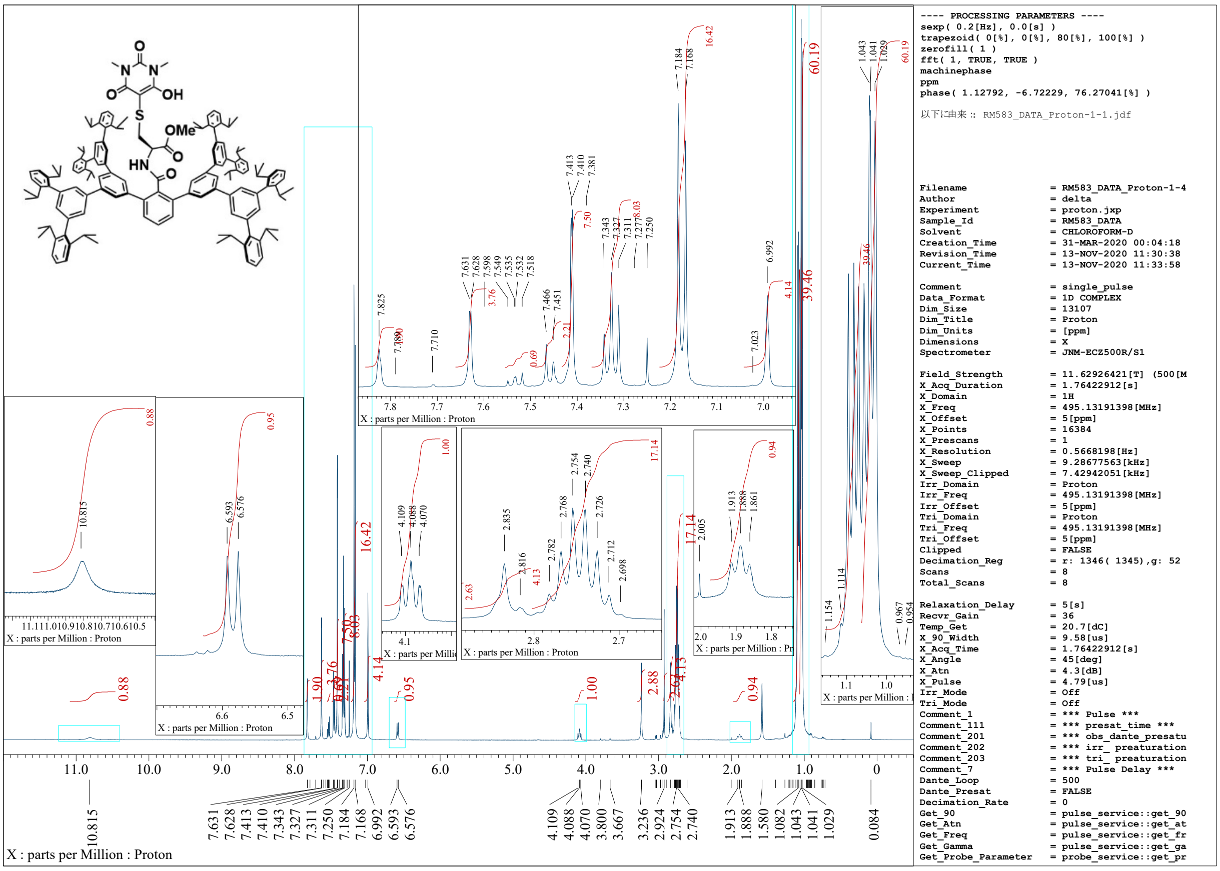
Filename                    = RM590_recry_SOH+cy
Author                      = delta
Experiment                  = carbon.jxp
Sample_Id                   = RM590_recry_SOH+cy
Solvent                     = CHLOROFORM-D
Creation_Time               =  4-APR-2020 19:49:
Revision_Time               = 13-NOV-2020 12:05:
Current_Time                = 13-NOV-2020 12:10:

Comment                     = single pulse decou
Data_Format                 = 1D COMPLEX
Dim_Size                    = 26214
Dim_Title                   = Carbon13
Dim_Units                   = [ppm]
Dimensions                  = X
Spectrometer                = JNM-ECZ500R/S1

Field_Strength              = 11.62926421[T] (50
X_Acq_Duration              = 0.8388608[s]
X_Domain                    = 13C
X_Freq                      = 124.5010059[MHz]
X_Offset                    = 100[ppm]
X_Points                    = 32768
X_Prescans                  = 4
X_Resolution                = 1.1920929[Hz]
X_Sweep                     = 39.0625[kHz]
X_Sweep_Clipped             = 31.25[kHz]
Irr_Domain                  = Proton
Irr_Freq                    = 495.13191398[MHz]
Irr_Offset                  = 5[ppm]
Clipped                     = FALSE
Decimation_Reg              = r: 160( 159),g: 37
Scans                       = 1024
Total_Scans                 = 1024

Relaxation_Delay            = 2[s]
Recvr_Gain                  = 56
Temp_Get                    = 20.7[dC]
X_90_Width                  = 9.61[us]
X_Acq_Time                  = 0.8388608[s]
X_Angle                     = 30[deg]
X_Atn                       = 10[dB]
X_Pulse                     = 3.20333333[us]
Irr_Atn_Dec                 = 23.948[dB]
Irr_Atn_Dec_Calc            = 23.948[dB]
Irr_Atn_Dec_Default_Calc    = 23.948[dB]
Irr_Atn_Noe                 = 23.948[dB]
Irr_Dec_Bandwidth_Hz        = 5.97826087[kHz]
Irr_Dec_Bandwidth_Ppm       = 12.07407703[ppm]
Irr_Dec_Freq                = 495.13191398[MHz]
Irr_Dec_Merit_Factor        = 2.2
Irr_Decoupling              = TRUE
Irr_Noe                     = TRUE
Irr_Noise                   = WALTZ
Irr_Offset_Default          = 5[ppm]
Irr_Pwidth                  = 92[us]
Irr_Pwidth_Default          = 92[us]
Irr_Pwidth_Default_Calc     = 92[us]
Irr_Pwidth_Temp1            = 92[us]
Irr_Wurst                   = FALSE
Comment_1                   = *** Pulse ***
Comment_102                 = *** irr_decoupling
```

Figure S15. ^{13}C NMR (125 MHz, CDCl$_3$) spectrum of **10b**.



```
---- PROCESSING PARAMETERS ----
sexp( 0.2[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( 1.12792, -6.72229, 76.27041[%] )

以下に由来 :: RM583_DATA_Proton-1-1.jdf



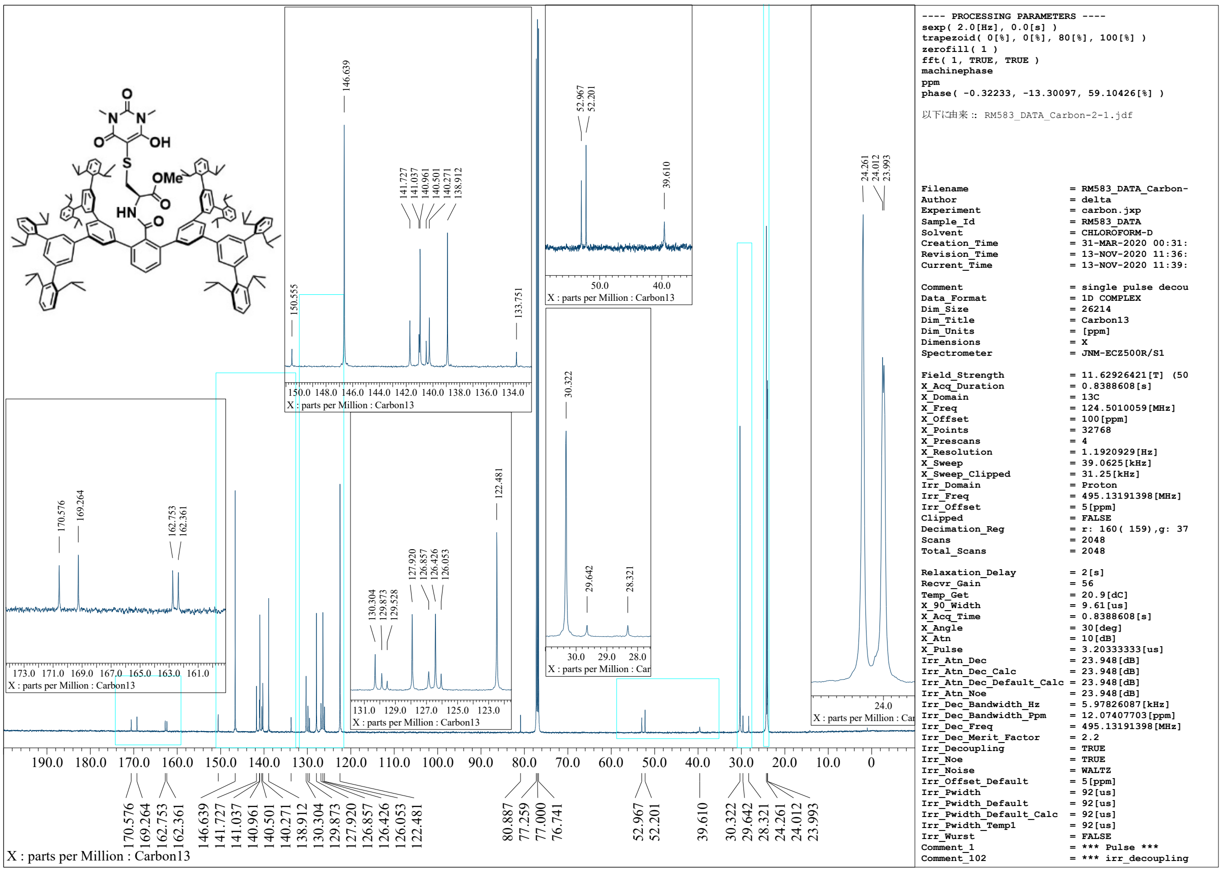
Filename              = RM583_DATA_Proton-1-4
Author                = delta
Experiment            = proton.jxp
Sample_Id             = RM583_DATA
Solvent               = CHLOROFORM-D
Creation_Time         = 31-MAR-2020 00:04:18
Revision_Time         = 13-NOV-2020 11:30:38
Current_Time          = 13-NOV-2020 11:33:58

Comment               = single_pulse
Data_Format           = 1D COMPLEX
Dim_Size              = 13107
Dim_Title             = Proton
Dim_Units             = [ppm]
Dimensions            = X
Spectrometer          = JNM-ECZ500R/S1

Field_Strength        = 11.62926421[T] (500[M
X_Acq_Duration        = 1.76422912[s]
X_Domain              = 1H
X_Freq                = 495.13191398[MHz]
X_Offset              = 5[ppm]
X_Points              = 16384
X_Prescans            = 1
X_Resolution          = 0.5668198[Hz]
X_Sweep               = 9.28677563[kHz]
X_Sweep_Clipped       = 7.42942051[kHz]
Irr_Domain            = Proton
Irr_Freq              = 495.13191398[MHz]
Irr_Offset            = 5[ppm]
Tri_Domain            = Proton
Tri_Freq              = 495.13191398[MHz]
Tri_Offset            = 5[ppm]
Clipped               = FALSE
Decimation_Reg        = r: 1346( 1345),g: 52
Scans                 = 8
Total_Scans           = 8

Relaxation_Delay      = 5[s]
Recvr_Gain            = 36
Temp_Get              = 20.7[dC]
X_90_Width            = 9.58[us]
X_Acq_Time            = 1.76422912[s]
X_Angle               = 45[deg]
X_Atn                 = 4.3[dB]
X_Pulse               = 4.79[us]
Irr_Mode              = Off
Tri_Mode              = Off
Comment_1             = *** Pulse ***
Comment_111           = *** presat_time ***
Comment_201           = *** obs_dante_presatu
Comment_202           = *** irr_ preaturation
Comment_203           = *** tri_ preaturation
Comment_7             = *** Pulse Delay ***
Dante_Loop            = 500
Dante_Presat          = FALSE
Decimation_Rate       = 0
Get_90                = pulse_service::get_90
Get_Atn               = pulse_service::get_at
Get_Freq              = pulse_service::get_fr
Get_Gamma             = pulse_service::get_ga
Get_Probe_Parameter   = probe_service::get_pr
```

Figure S16. ^{1}H NMR (500 MHz, CDCl$_3$) spectrum of **10c**.



```
---- PROCESSING PARAMETERS ----
sexp( 2.0[Hz], 0.0[s] )
trapezoid( 0[%], 0[%], 80[%], 100[%] )
zerofill( 1 )
fft( 1, TRUE, TRUE )
machinephase
ppm
phase( -0.32233, -13.30097, 59.10426[%] )

以下に由来 :: RM583_DATA_Carbon-2-1.jdf



Filename                  = RM583_DATA_Carbon-
Author                    = delta
Experiment                = carbon.jxp
Sample_Id                 = RM583_DATA
Solvent                   = CHLOROFORM-D
Creation_Time             = 31-MAR-2020 00:31:
Revision_Time             = 13-NOV-2020 11:36:
Current_Time              = 13-NOV-2020 11:39:

Comment                   = single pulse decou
Data_Format               = 1D COMPLEX
Dim_Size                  = 26214
Dim_Title                 = Carbon13
Dim_Units                 = [ppm]
Dimensions                = X
Spectrometer              = JNM-ECZ500R/S1

Field_Strength            = 11.62926421[T] (50
X_Acq_Duration            = 0.8388608[s]
X_Domain                  = 13C
X_Freq                    = 124.5010059[MHz]
X_Offset                  = 100[ppm]
X_Points                  = 32768
X_Prescans                = 4
X_Resolution              = 1.1920929[Hz]
X_Sweep                   = 39.0625[kHz]
X_Sweep_Clipped           = 31.25[kHz]
Irr_Domain                = Proton
Irr_Freq                  = 495.13191398[MHz]
Irr_Offset                = 5[ppm]
Clipped                   = FALSE
Decimation_Reg            = r: 160( 159),g: 37
Scans                     = 2048
Total_Scans               = 2048

Relaxation_Delay          = 2[s]
Recvr_Gain                = 56
Temp_Get                  = 20.9[dC]
X_90_Width                = 9.61[us]
X_Acq_Time                = 0.8388608[s]
X_Angle                   = 30[deg]
X_Atn                     = 10[dB]
X_Pulse                   = 3.20333333[us]
Irr_Atn_Dec               = 23.948[dB]
Irr_Atn_Dec_Calc          = 23.948[dB]
Irr_Atn_Dec_Default_Calc  = 23.948[dB]
Irr_Atn_Noe               = 23.948[dB]
Irr_Dec_Bandwidth_Hz      = 5.97826087[kHz]
Irr_Dec_Bandwidth_Ppm     = 12.07407703[ppm]
Irr_Dec_Freq              = 495.13191398[MHz]
Irr_Dec_Merit_Factor      = 2.2
Irr_Decoupling            = TRUE
Irr_Noe                   = TRUE
Irr_Noise                 = WALTZ
Irr_Offset_Default        = 5[ppm]
Irr_Pwidth                = 92[us]
Irr_Pwidth_Default        = 92[us]
Irr_Pwidth_Default_Calc   = 92[us]
Irr_Pwidth_Temp1          = 92[us]
Irr_Wurst                 = FALSE
Comment_1                 = *** Pulse ***
Comment_102               = *** irr_decoupling
```

Figure S17. ^{13}C NMR (125 MHz, CDCl$_3$) spectrum of **10c**.

3. References

i) S. Sase, R. Kimura, R. Masuda and K. Goto, *New J. Chem.*, 2019, **43**, 6830-6833.

ii) J. D. Kehlbeck, E. J. Dimise, S. M. Sparks, S. Ferrara, J. M. Tanski and C. M. Anderson, *Synthesis*, 2007, 1979-1983.
