Supporting Information

A versatile entry to unnatural, disulfide-linked amino acids and peptides through the disulfuration of azlactones

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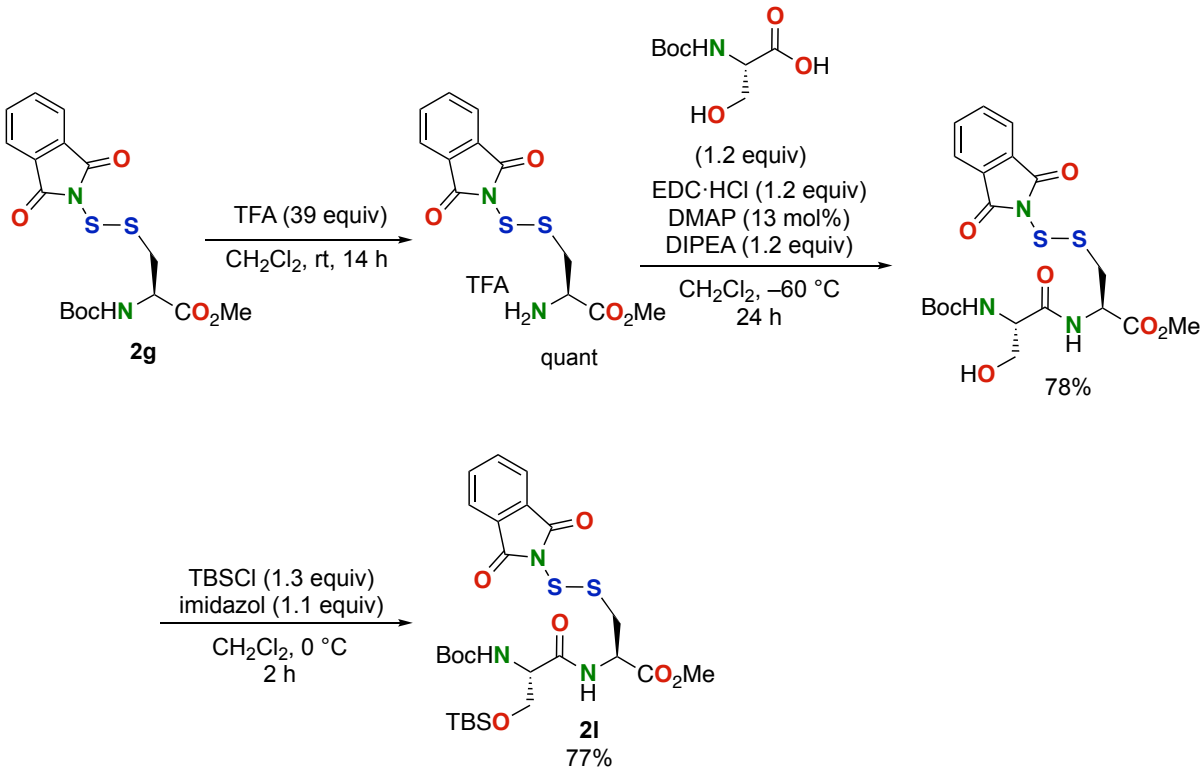
General Remarks

All reactions were performed with dry glassware under atmosphere of nitrogen unless otherwise noted. The ^{1}H NMR spectra were obtained with a Varian Mercury 400 NMR spectrometer at 400 MHz, a JEOL ECZ-500R at 500 MHz, or a JEOL JNM-ECA-600 at 600 MHz. The ^{13}C NMR spectra were obtained with a Varian Mercury 400 NMR spectrometer at 101 MHz, a JEOL ECZ-500R at 125 MHz, or a JEOL JNM-ECA-600 at 150 MHz, respectively. All NMR measurements were carried out at 25 ºC unless otherwise noted. Chemical shifts are reported in parts per million (ppm) downfield from $(CH_3)_4Si$ (δ 0.00 for ^{1}H NMR in $CDCl_3$) or the solvent peak (δ 3.31 for ^{1}H NMR in CD3OD, δ 77.16 for ^{13}C NMR in $CDCl_3$, or δ 49.00 for ^{13}C NMR in CD_3OD). The abbreviations s, d, t, q, m, and br signify singlet, doublet, triplet, quartet, multiplet, and broad, respectively. High-resolution mass spectra (HRMS) were recorded on a JEOL JMS-700 spectrometer equipped with a double focusing mass analyzer or a JMS-T100GC spectrometer equipped with a TOF mass analyzer. Column chromatography was performed with silica gel (Kanto Chemical, 60 (spherical, neutral), 37563-84).

4-Methyl-2-phenyloxazol-5(4*H*)-one (**1a**),[S1] 4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (**1b**),[S2] 4-benzyl-2-phenyloxazol-5(4*H*)-one (**1e**),[S1] 4-((1*H*-indol-3-yl)methyl)-2-phenyloxazol-5(4*H*)-one (**1f**),[S3] 4-isopropyl-2-phenyloxazol-5(4*H*)-one (**1g**),[S4] 4-ethyl-2-phenyloxazol-5(4*H*)-one (**1h**),[S5] 4-allyl-2-phenyloxazol-5(4*H*)-one (**1i**),[S1] 2-(4-chlorophenyl)-4-methyloxazol-5(4*H*)-one (**1j**),[S1] 2-(allyldisulfanyl)isoindoline-1,3-dione (**2a**),[S6] 2-((2-methylallyl)disulfanyl)isoindoline-1,3-dione (**2b**),[S6] 2-((2-bromoallyl)disulfanyl)isoindoline-1,3-dione (**2c**),[S6] 2-(dodecyldisulfanyl)isoindoline-1,3-dione (**2d**),[S7] 2-(*tert*-butyldisulfanyl)isoindoline-1,3-dione (**2e**),[S7] 2-((4-methoxybenzyl)disulfanyl)isoindoline-1,3-dione (**2f**),[S7] methyl *N*-(*tert*-butoxycarbonyl)-*S*-((1,3-dioxoisoindolin-2-yl)thio)-L-cysteinate

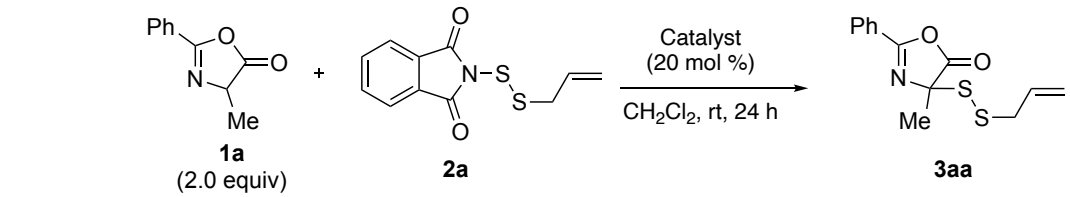
(**2g**),[S8] 2-(phenyldisulfanyl)isoindoline-1,3-dione (**2h**),[S7] 2-(*p*-tolyldisulfanyl)isoindoline-1,3-dione (**2i**),[S9] 2-((4-methoxyphenyl)disulfanyl)isoindoline-1,3-dione (**2j**),[S9] *N*-(morpholine-4-dithio)phthalimide (**2k**),[S6] 2-((2-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)allyl)disulfanyl)isoindoline-1,3-dione (**2m**),[S6] *N,N'*-thiobis(phthalimide) (**7**),[S9] *N,N'*-dithiobis(phthalimide) (**11**),[S6] 2-(2-mercaptophenyl)acetic acid,[S10,S11] 2-(((1,3-dioxoisoindolin-2-yl)disulfanyl)methyl)allyl (*S*)-2-(4-isobutylphenyl)propanoate (**21**),[S6] and H-Gly-Gly-OMe·HCl (**23**)[S12] were prepared according to the reported methods. All other chemical reagents used were commercial grade and used as received.

Preparation of peptide-based *N*-dithiophthalimide 2l



Scheme S1. Preparation of peptide-based *N*-dithiophthalimide **2l**

Preliminary investigation of the enantioselective reaction



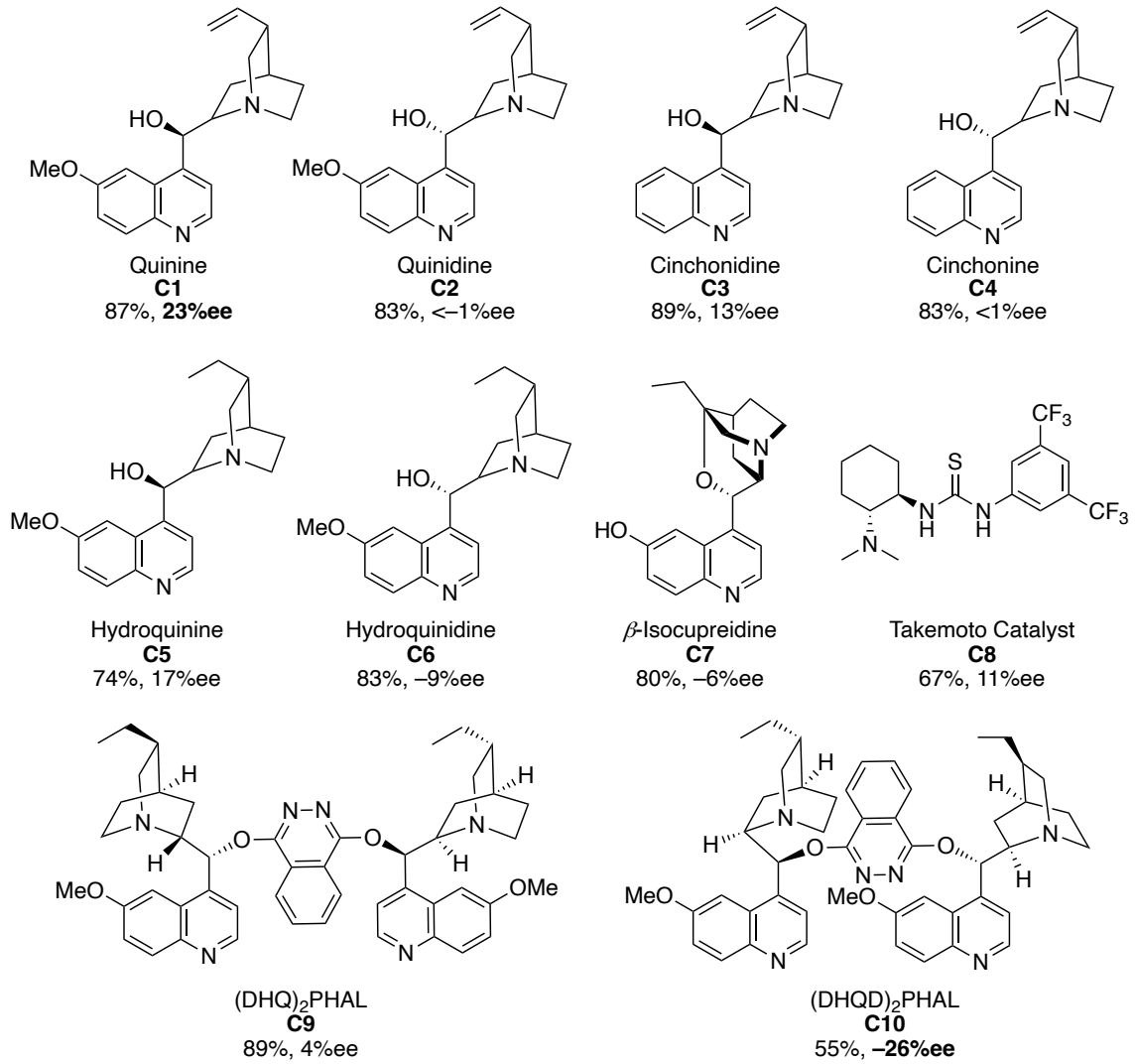
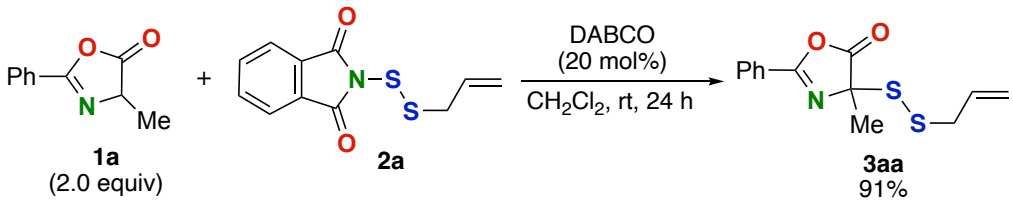


Figure S1. Enantioselective reaction

Experimental Procedures

*A typical procedure for the disulfuration of azlactones **1** with N-(organodithio)phthalimides **2***

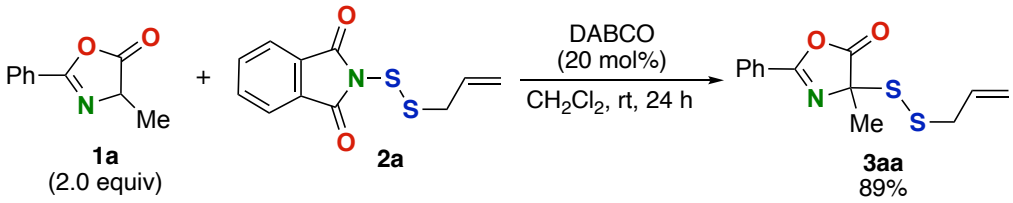


To a mixture of 4-methyl-2-phenyloxazol-5(4*H*)-one (**1a**) (35.8 mg, 0.204 mmol, 2.03 equiv) and 2-(allyldisulfanyl)isoindoline-1,3-dione (**2a**) (25.3 mg, 0.101 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (1.0 mL) was added DABCO (2.3 mg, 21 μmol, 20 mol%) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 9 g, hexane/EtOAc = 20/1 to 8/1) to give 4-(allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (25.5 mg, 91.3 μmol, 90.7%) as a colorless oil.

According to the procedure for preparing 4-(allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**), 4-(allyldisulfanyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (**3ba**) (31.1 mg, 91.4%), *N*-(4-(4-(allyldisulfanyl)-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)butyl)benzamide (**3ca**) (47.2 mg, quant), 4-(allyldisulfanyl)-4-isobutyl-2-phenyloxazol-5(4*H*)-one (**3da**) (32.6 mg, quant, 1.0 equiv of DABCO was used), 4-(allyldisulfanyl)-4-benzyl-2-phenyloxazol-5(4*H*)-one (**3ea**) (32.8 mg, 91.7%), 4-((1*H*-indol-3-yl)methyl)-4-(allyldisulfanyl)-2-phenyloxazol-5(4*H*)-one (**3fa**) (35.0 mg, 88.1%), 4-(allyldisulfanyl)-4-isopropyl-2-phenyloxazol-5(4*H*)-one (**3ga**) (32.2 mg, quant), 4-(allyldisulfanyl)-4-ethyl-2-phenyloxazol-5(4*H*)-one (**3ha**) (27.8 mg, 93.8%), 4-allyl-4-(allyldisulfanyl)-2-phenyloxazol-5(4*H*)-one (**3ia**) (26.9 mg, 87.1%), 4-(allyldisulfanyl)-2-(4-chlorophenyl)-4-methyloxazol-5(4*H*)-one (**3ja**) (78.4 mg, 81.8%), *tert*-butyl ((4-(allyldisulfanyl)-4-benzyl-5-oxo-4,5-dihydrooxazol-2-yl)methyl)carbamate (**3ka**) (34.0 mg, 83.3%, 6.0 equiv of *tert*-butyl ((4-benzyl-5-oxo-4,5-dihydrooxazol-2-yl)methyl)carbamate (**1k**) was used with DIPEA (20 mol%) at –78 °C), 4-methyl-4-((2-methylallyl)disulfanyl)-2-phenyloxazol-5(4*H*)-one (**3ab**) (23.3 mg, 78.9%), 4-((2-bromoallyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3ac**) (30.1 mg, 83.8%), 4-(dodecyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3ad**) (34.2 mg, 83.8%), 4-(*tert*-butyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3ae**) (21.3 mg, 71.7%), 4-((4-methoxybenzyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3af**) (36.8 mg, quant), methyl *N*-(*tert*-butoxycarbonyl)-*S*-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)thio)-L-cysteinate (**3ag**) (41.1 mg, 88.3%, 1:1 dr), 4-methyl-2-phenyl-4-(phenyldisulfanyl)oxazol-5(4*H*)-one (**3ah**) (95.8%, ^{1}H NMR yield based on 1,1,2,2,-tetrachloroethane, azlactone (4.0 equiv) and DABCO (40 mol%) at 0 °C), 4-methyl-2-phenyl-4-(*p*-tolyldisulfanyl)oxazol-5(4*H*)-one (**3ai**) (97.0%, ^{1}H NMR yield based on 1,1,2,2,-tetrachloroethane, azlactone (4.0 equiv) and DABCO (40 mol%) at 0 °C), 4-((4-methoxyphenyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aj**) (80.1%, ^{1}H NMR yield based on 1,1,2,2,-tetrachloroethane, azlactone (4.0 equiv) and DABCO (40 mol%) at 0 °C), 4-methyl-4-(morpholinodisulfanyl)-2-phenyloxazol-5(4*H*)-one (**3ak**) (28.6 mg, 87.7%, K_2CO_3 (1.0 equiv)), methyl *N*-(*N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyldimethylsilyl)-L-seryl)-*S*-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)thio)-L-cysteinate (**3al**) (41.5 mg, 87.0%, 1.1:1 dr), 4-methyl-4-((2-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)allyl)disulfanyl)-2-phenyloxazol-5(4*H*)-one (**3am**) (44.4 mg,

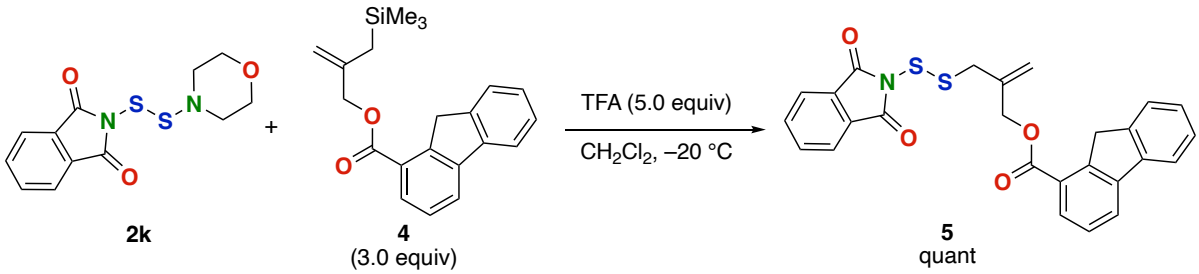
82.8%, 1:1 dr), 2-(((4-benzyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)methyl)allyl 9*H*-fluorene-1-carboxylate (**6**) (27.0 mg, 93.0%), (2*S*,3*S*,4*R*,5*S*,6*R*)-2-(acetoxymethyl)-6-((4-isopropyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (**10**) (25.6 mg, 42.8%, 1:1 dr), 4-(((3-(9,10-ethanoanthracen-9(10*H*)-yl)propyl)(methyl)amino)disulfanyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (**14**) (46.7 mg, 80.7%), and 2-(((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)methyl)allyl (2*S*)-2-(4-isobutylphenyl)propanoate (**22**) (40.8 mg, 81.2%, 1:1 dr) were prepared from the corresponding azlactones **1** and *N*-(organodithio)phthalimides **2**.

*A typical procedure for the disulfuration reaction using 1 mmol of N-(allyldithio)phthalimide (**2a**)*



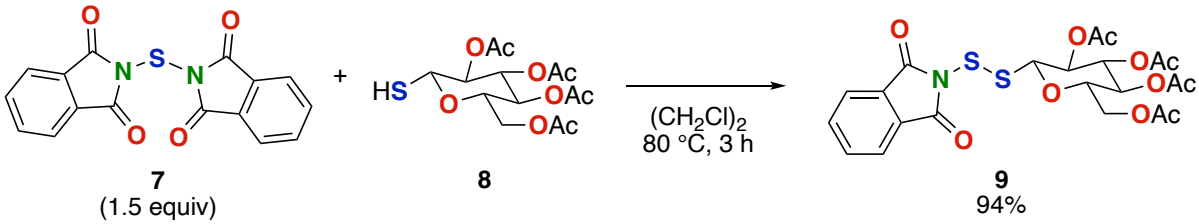
To a mixture of 4-methyl-2-phenyloxazol-5(4*H*)-one (**1a**) (351 mg, 2.00 mmol, 2.00 equiv) and 2-(allyldisulfanyl)isoindoline-1,3-dione (**2a**) (252 mg, 1.00 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (10.0 mL) was added DABCO (22.8 mg, 0.203 mmol, 20.3 mol%) at room temperature. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 30 g, hexane/EtOAc = 20/1 to 8/1) to give 4-(allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (250 mg, 0.895 mmol, 89.2%) as a colorless oil.

*Synthesis of 2-(((1,3-dioxoisoindolin-2-yl)disulfanyl)methyl)allyl 9H-fluorene-1-carboxylate (**5**) from N-(morpholine-4-dithio)phthalimide (**2k**)*



N-(Morpholine-4-dithio)phthalimide (**2k**) (44.7 mg, 0.151 mmol, 1.00 equiv) and 2-((trimethylsilyl)methyl)allyl 9*H*-fluorene-1-carboxylate (**4**) (151 mg, 0.449 mmol, 2.98 equiv) were dissolved in CH_2Cl_2 (1.0 mL) at room temperature. After stirring for 10 min at –20 °C, to the mixture was added TFA (58.0 μL, 0.757 mmol, 5.02 equiv) at the same temperature. After stirring for 1 h at the same temperature, to the mixture was added aqueous saturated solution of sodium bicarbonate (7 mL). The mixture was extracted with EtOAc (7 mL × 3), washed with brine (7 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 6 g, hexane/EtOAc = 12/1 to 2/1) to give 2-(((1,3-dioxoisoindolin-2-yl)disulfanyl)methyl)allyl 9*H*-fluorene-1-carboxylate (**5**) (71.7 mg, 0.151 mmol, quant) as a colorless solid.

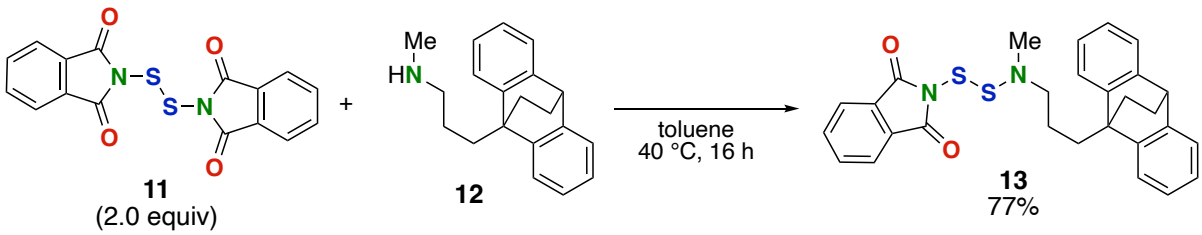
*Synthesis of (2S,3S,4R,5S,6R)-2-(acetoxymethyl)-6-((1,3-dioxoisoindolin-2-yl)disulfanyl)tetrahydro-2H-pyran-3,4,5-triyl triacetate (**9**) from N,N'-thiobis(phthalimide) (**7**) and 1-thio-β-D-glucose tetraacetate (**8**)*



7 (1.5 equiv) **8** **9** 94%

To a mixture of *N,N'*-thiobis(phthalimide) (**7**) (486 mg, 1.50 mmol, 1.50 equiv) suspended in 1,2-dichloroethane (0.5 mL) was slowly added 1-thio-β-D-glucose tetraacetate (**8**) (365 mg, 1.00 mmol, 1.00 equiv) dissolved in 1,2-dichloroethane (5 mL) at room temperature. After stirring for 3 h at 80 °C, the mixture was concentrated under reduced pressure. The residue was dilute with EtOAc (10 mL). After filtration, the filtrate was washed with 10% aqueous solution of potassium carbonate (10 mL × 6) and brine (10 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, 7 g, hexane/EtOAc = 4/1 to 1/1) to give (2*S*,3*S*,4*R*,5*S*,6*R*)-2-(acetoxymethyl)-6-((1,3-dioxoisoindolin-2-yl)disulfanyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (**9**) (508 mg, 0.938 mmol, 93.6%) as a colorless solid.

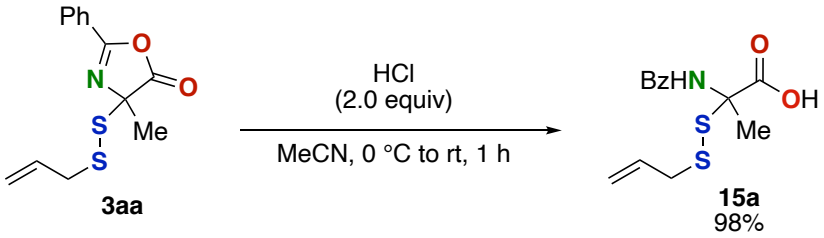
*Synthesis of 2-(((3-(9,10-ethanoanthracen-9(10H)-yl)propyl)(methyl)amino)disulfanyl)isoindoline-1,3-dione (**13**) from N,N'-dithiobis(phthalimide) (**11**)*



11 (2.0 equiv) **12** **13** 77%

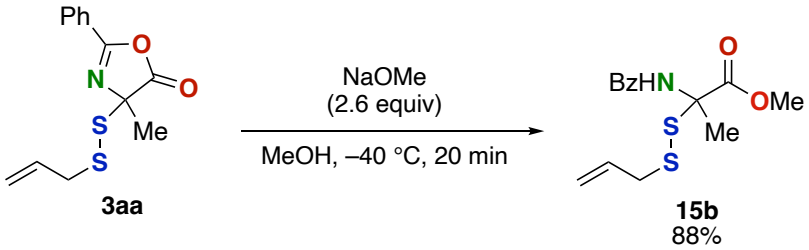
To a mixture of *N,N'*-dithiobis(phthalimide) (**11**) (71.6 mg, 0.201 mmol, 1.99 equiv) suspended in toluene (3.0 mL) was slowly added 9-(γ-methylaminopropyl)-9,10-dihydro-9,10-ethanoanthracene (maprotiline) (**12**) (28.0 mg, 0.101 mmol, 1.00 equiv) dissolved in toluene (1.0 mL) at 40 °C. After stirring for 16 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 20 g, hexane/EtOAc = 6/1 to 4/1) to give 2-(((3-(9,10-ethanoanthracen-9(10*H*)-yl)propyl)(methyl)amino)disulfanyl)isoindoline-1,3-dione (**13**) (38.0 mg, 78.1 μmol, 77.4%) as a colorless solid.

Transformation to carboxylic acid via the acid-mediated ring-opening



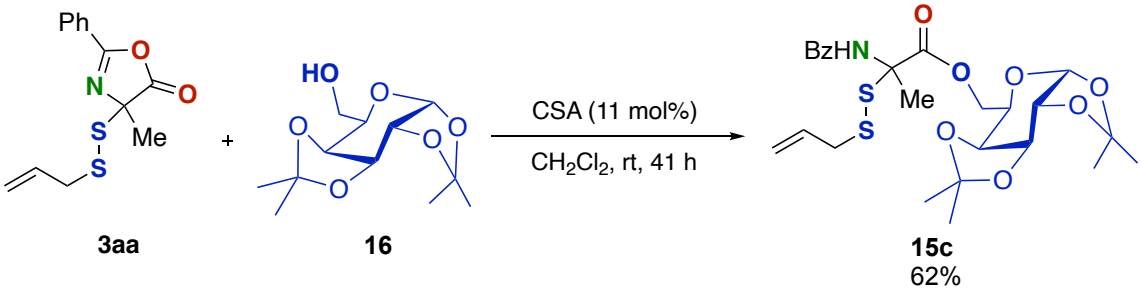
To a mixture of 4-(allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (422 mg, 1.51 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (1.0 mL) was slowly added 12 M HCl aq. (250 µL, 3.00 mmol, 1.99 equiv) at 0 °C. After stirring for 1 h at room temperature, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 2 g, hexane/EtOAc = 1/1) to give 2-(allyldisulfanyl)-2-benzamidopropanoic acid (**15a**) (441 mg, 1.48 mmol, 98.2%) as a colorless oil.

Transformation to methyl ester via the ring-opening by NaOMe



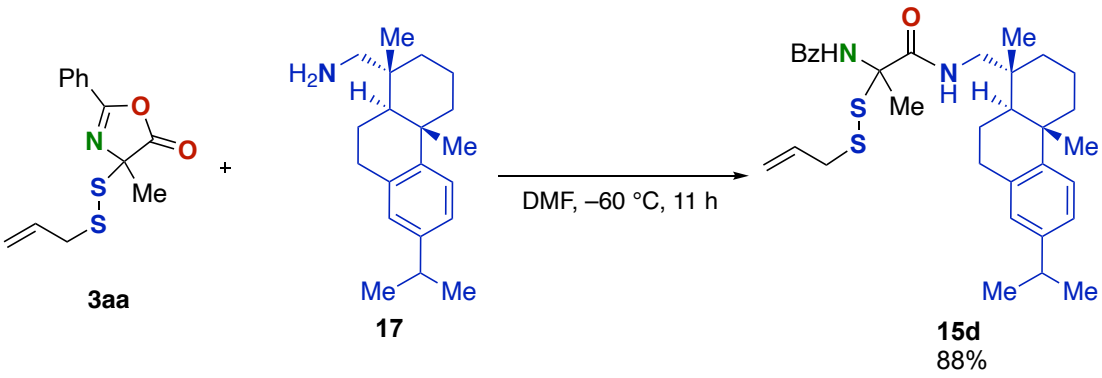
To a mixture of 4-(allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (28.3 mg, 0.101 mmol, 1.00 equiv) dissolved in MeOH (0.5 mL) was slowly added sodium methoxide (14.1 mg, 0.261 mmol, 2.58 equiv) in MeOH (0.75 mL) at –40 °C. After stirring for 20 min at same temperature, to the mixture was added aqueous saturated solution of ammonium chloride (7 mL). The mixture was extracted with EtOAc (7 mL × 3), washed with brine (7 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 5 g, hexane/EtOAc = 20/1 to 8/1) to give methyl 2-(allyldisulfanyl)-2-benzamidopropanoate (**15b**) (27.6 mg, 88.6 µmol, 87.5%) as a colorless oil.

Transformation to ester via the acid-catalyzed ring-opening by the sugar



((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-Tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)methanol (**16**) (52.3 mg, 0.201 mmol) was dissolved in dry CH_2Cl_2 (1.0 mL) at room temperature and stirred for 10 minutes to prepare stock solution. (4-(Allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (14.3 mg, 51.2 µmol, 1.00 equiv) and (-)-10-camphorsulfonic acid (1.3 mg, 5.6 µmol, 11 mol%) were dissolved in 0.25 mL of the stock solution. After stirring for 41 hours at room temperature, to the mixture was added aqueous saturated solution of sodium bicarbonate (5 mL). The mixture was washed with aqueous saturated solution of sodium bicarbonate (5 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 2 g, hexane/EtOAc = 10/1 to 1/1) to give ((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)methyl 2-(allyldisulfanyl)-2-benzamidopropanoate (**15c**) (17.0 mg, 31.5 µmol, 61.5%, 1:1 dr) as a colorless oil.

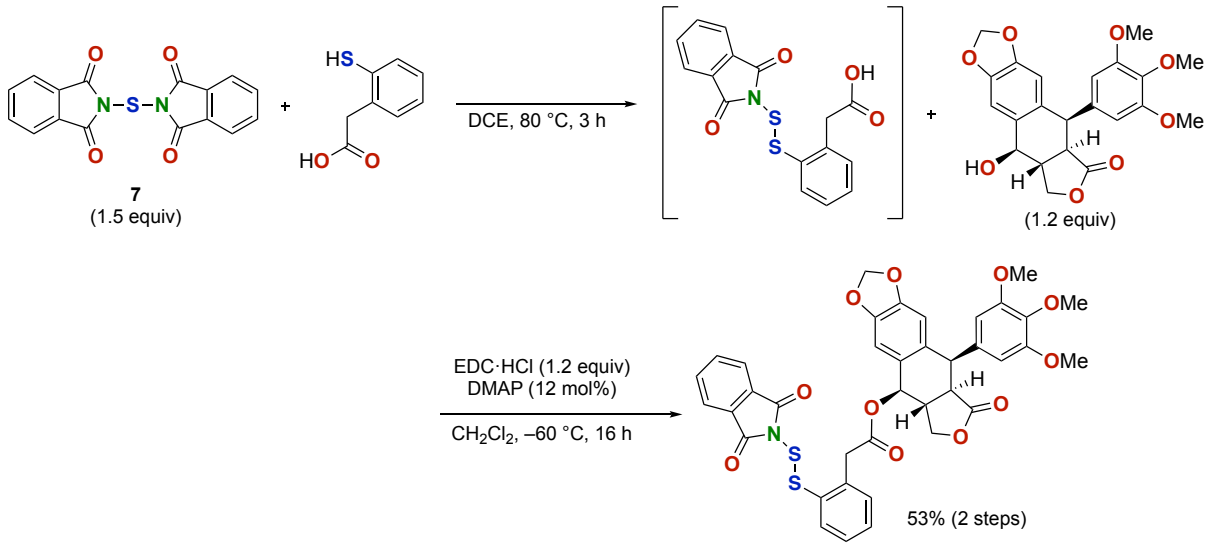
Transformation to amide via the ring-opening by the amine



4-(Allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (14.2 mg, 50.8 µmol, 1.00 equiv) was dissolved in DMF (0.5 mL) at –60 °C. After stirring for 20 min at –60 °C, to the mixture was added ((1*R*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methanamine (**17**) (14.6 mg, 51.1 µmol, 1.01 equiv) at the same temperature. After stirring for 11 h at the same temperature, to the mixture was added aqueous saturated solution of ammonium chloride (5 mL). The mixture was extracted with EtOAc (5 mL × 3), washed with brine (5 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 2 g, hexane/EtOAc = 30:1 to 1/1) to give *N*-(2-(allyldisulfanyl)-1-((((1*R*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-1-oxopropan-2-yl)benzamide (**15d**) (25.2 mg, 44.6 µmol, 87.8%, 1:1 dr) as a colorless oil.

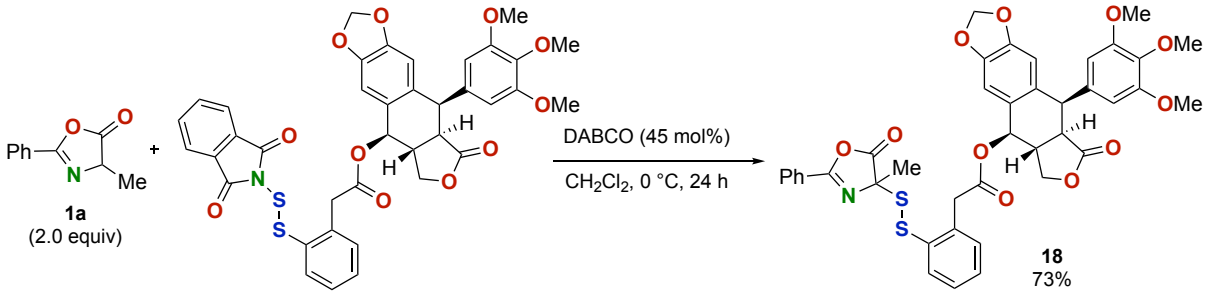
According to the procedure for preparing *N*-(2-(allyldisulfanyl)-1-((((1*R*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-1-oxopropan-2-yl)benzamide (**15d**), *N*-(2-(allyldisulfaneyl)-1-(butylamino)-4-(methylthio)-1-oxobutan-2-yl)benzamide (**15e**) (39.3 mg, 93.9%) was prepared from 4-(allyldisulfanyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (**3ba**) and butylamine.

Synthesis of (5R,5aR,8aR,9R)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetate from N,N'-thiobis(phthalimide) (7)



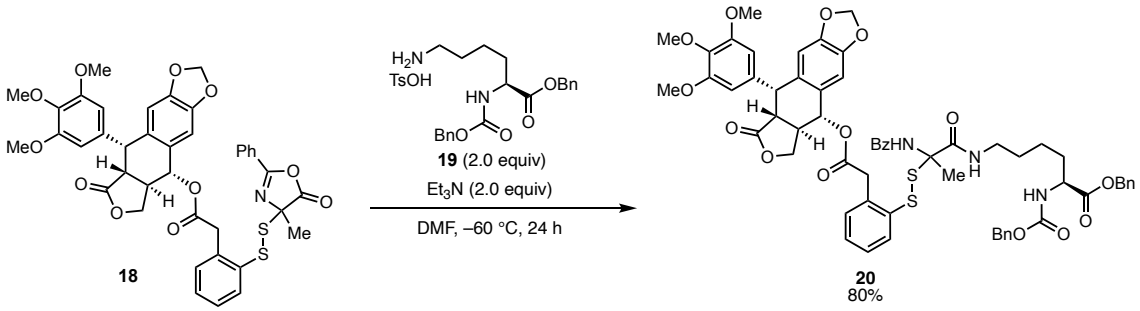
To a mixture of *N,N'*-thiobis(phthalimide) (**7**) (488 mg, 1.50 mmol, 1.49 equiv) suspended in 1,2-dichloroethane (5 mL) was slowly added 2-(2-mercaptophenyl)acetic acid (171 mg, 1.02 mmol, 1.00 equiv) at room temperature. After stirring for 3 h at 80 °C, the mixture was filtered, and the filtrate was concentrated under reduced pressure to obtain the crude 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetic acid. To a mixture of the crude 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetic acid and (5*R*,5a*R*,8a*R*,9*R*)-9-hydroxy-5-(3,4,5-trimethoxyphenyl)-5,8,8a,9-tetrahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-6(5a*H*)-one (506 mg, 1.22 mmol, 1.20 equiv) dissolved in CH_2Cl_2 (5 mL) were added EDC·HCl (230 mg, 1.20 mmol, 1.18 equiv) and DMAP (15.3 mg, 0.125 mmol, 12.3 mol%) at –60 °C. After stirring for 16 h at the same temperature, to the mixture was added aqueous saturated solution of sodium bicarbonate (15 mL). The mixture was extracted with EtOAc (15 mL × 3), washed with brine (15 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 15 g, hexane/EtOAc = 5/1 to 1/1) to give (5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetate (398 mg, 0.537 mmol, 52.8%) as a yellow solid.

*Synthesis of (5R,5aR,8aR,9R)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl 2-(2-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)phenyl)acetate (**18**) from (5R,5aR,8aR,9R)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-d][1,3]dioxol-5-yl 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetate*



To a mixture of 4-methyl-2-phenyloxazol-5(4*H*)-one (**1a**) (34.3 mg, 0.196 mmol, 1.96 equiv) and (5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetate (74.2 mg, 0.100 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (1.0 mL) was added DABCO (5.0 mg, 45 µmol, 45 mol%) at 0 °C. After stirring for 24 h at the same temperature, to the mixture was added aqueous saturated solution of ammonium chloride (7 mL). The mixture was extracted with EtOAc (5 mL × 3), washed with brine (7 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 2 g, hexane/EtOAc = 5/1 to 1/1) to give (5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)phenyl)acetate (**18**) (56.2 mg, 73.0 µmol, 73.0%, 1.7:1 dr) as a colorless solid.

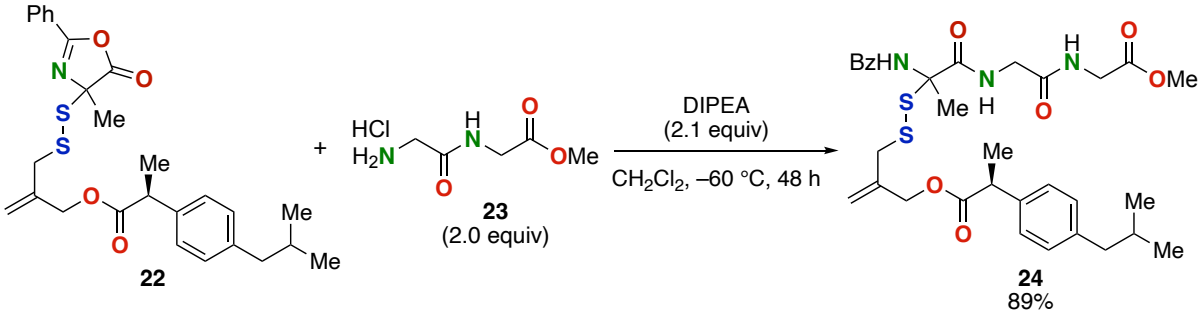
*Transformation to SMDC (**20**) via the ring-opening by benzyl ((benzyloxy)carbonyl)-L-lysinate p-toluenesulfonate (**19**)*



To a mixture of (5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)phenyl)acetate (**18**) (38.5 mg, 50.0 µmol, 1.00 equiv) dissolved in DMF (1.0 mL) was added benzyl ((benzyloxy)carbonyl)-*L*-lysinate *p*-toluenesulfonate (**19**) (54.5 mg, 0.10 mmol, 2.0 equiv) at –60 °C. After stirring for 15 minutes, Et_3N (13.8 µL, 0.10 mmol, 2.0 equiv) was added at –60 °C. After stirring for 24 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 3 g, hexane/EtOAc = 5/1 to 1/1) to give benzyl N^6-(2-benzamido-

2-((2-(2-oxo-2-(((5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl)oxy)ethyl)phenyl)disulfanyl)propanoyl)-N^2-((benzyloxy)carbonyl)-*L*-lysinate (**20**) (45.6 mg, 40.0 μmol, 80%, 1.3:1 dr) as a yellow oil.

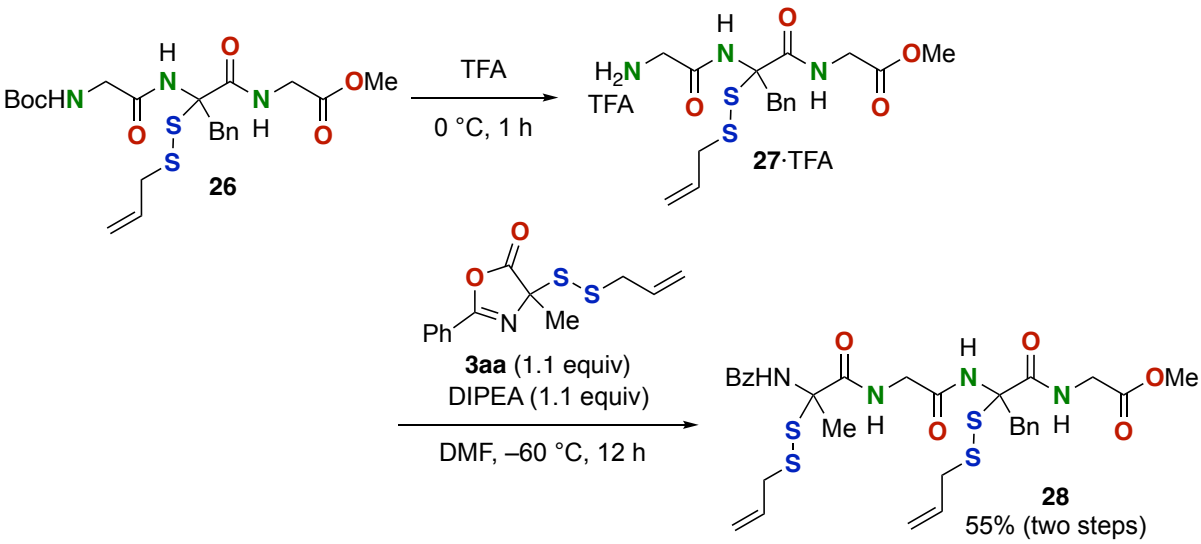
A typical procedure for the synthesis of SS-linked peptides via ring opening by amino acid or peptide



To a mixture of 2-(((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)methyl)allyl (2*S*)-2-(4-isobutylphenyl)propanoate (**22**) (50.2 mg, 0.101 mmol, 1.00 equiv) and glycylglycine methyl ester hydrochloride (**23**) (36.5 mg, 0.200 mmol, 1.98 equiv) suspended in CH_2Cl_2 (1.0 mL) was added DIPEA (37.5 μL, 0.215 mmol, 2.13 equiv) at –60 °C. After stirring for 48 h at the same temperature, the mixture was concentrated under reduced pressure. The residue was diluted with EtOAc (7 mL). The mixture was washed with aqueous saturated solution of ammonium chloride (7 mL), extracted with EtOAc (7 mL × 3) and brine (7 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under the reduced pressure, and the residue was purified by column chromatography (silica gel, 7 g, $CHCl_3$/MeOH = 100/1 to 40/1) to give 10-benzamido-10-methyl-14-methylene-3,6,9-trioxo-2-oxa-11,12-dithia-5,8-diazapentadecan-15-yl (2*S*)-2-(4-isobutylphenyl)propanoate (**24**) (57.5 mg, 89.3 μmol, 88.5%, 1:1 dr) as a colorless oil.

According to the procedure for preparing 10-benzamido-10-methyl-14-methylene-3,6,9-trioxo-2-oxa-11,12-dithia-5,8-diazapentadecan-15-yl (2*S*)-2-(4-isobutylphenyl)propanoate (**24**), methyl (2-(allyldisulfanyl)-2-(2-((*tert*-butoxycarbonyl)amino)acetamido)-3-phenylpropanoyl)glycinate (**26**) (25.9 mg, 82.4%) was prepared from the corresponding *SS*-linked azlactones.

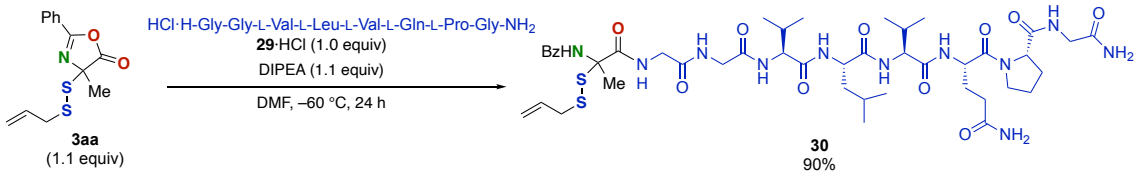
Further peptide elongation



Methyl (2-(allyldisulfanyl)-2-(2-((*tert*-butoxycarbonyl)amino)acetamido)-3-phenylpropanoyl)glycinate (**26**) (220 mg, 0.442 mmol, 1.00 equiv) was dissolved in TFA (0.52 mL) at 0 °C. After stirring for 1 hour at the same temperature, the mixture was concentrated under reduced pressure to give TFA salt of methyl (2-(allyldisulfanyl)-2-(2-aminoacetamido)-3-phenylpropanoyl)glycinate (**27**·TFA) (218 mg) as an orange oil. The crude **27**·TFA was used in the next transformation without further purification.

To a mixture of TFA salt of methyl (2-(allyldisulfanyl)-2-(2-aminoacetamido)-3-phenylpropanoyl)glycinate (**27**·TFA) (23.3 mg, 45.6 µmol, 1.00 equiv) dissolved in DMF (0.46 mL) was added DIPEA (8.50 µL, 48.8 µmol, 1.07 equiv) at –60 °C. After stirring for 15 min at the same temperature, to the mixture was added 4-(allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (14.3 mg, 51.2 µmol, 1.12 equiv) at the same temperature. After stirring for 12 h at the same temperature, to the mixture was added aqueous saturated solution of ammonium chloride (5 mL). The mixture was extracted with EtOAc (5 mL × 2), washed with brine (5 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 2 g, $CHCl_3$/MeOH = 70/1 to 20/1) to give methyl (2-(allyldisulfanyl)-2-(2-(2-(allyldisulfanyl)-2-benzamidopropanamido)acetamido)-3-phenylpropanoyl)glycinate (**28**) (17.6 mg, 26.0 µmol, 55.0%, 1.1 dr (two step yield)) as a colorless oil.

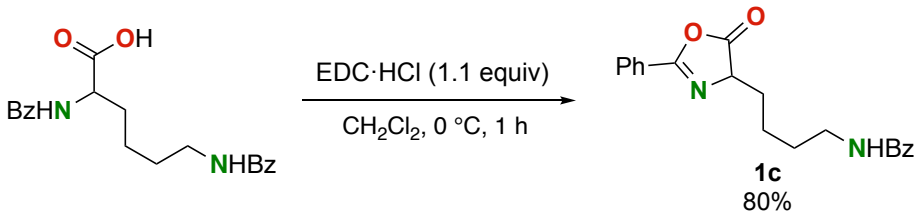
Synthesis of SS-linked oligopeptides via ring-opening by oligopeptides



4-(Allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) (6.2 mg, 0.022 mmol) was dissolved in dry DMF (100 µL) at –60 °C and stirred for 10 minutes to prepare stock solution. To a solution of H-Gly-Gly-L-Val-L-Leu-L-Val-L-Gln-L-Pro-Gly-NH_2·HCl (**29**·HCl) (3.8 mg, 5.0 µmmol, 1.0 equiv) and DIPEA (0.95 µL, 5.5 µmmol, 1.1 equiv) dissolved in dry DMF (25.0 µL) was added 25.0 µL of the stock solution at –60 °C. After stirring for 24 hours at the same temperature, the mixture was concentrated under reduced pressure. The residue was

purified by column chromatography (silica gel, 2 g, $CHCl_3$/MeOH = 100/1 to 1/1) to give (2*S*)-1-((2-(allyldisulfanyl)-2-benzamidopropanoyl)glycylglycyl-L-valyl-L-leucyl-L-valyl-L-glutaminyl)-*N*-(2-amino-2-oxoethyl)pyrrolidine-2-carboxamide (**30**) (4.5 mg, 4.5 μmol, 90%, 1.1:1 dr) as a colorless solid.

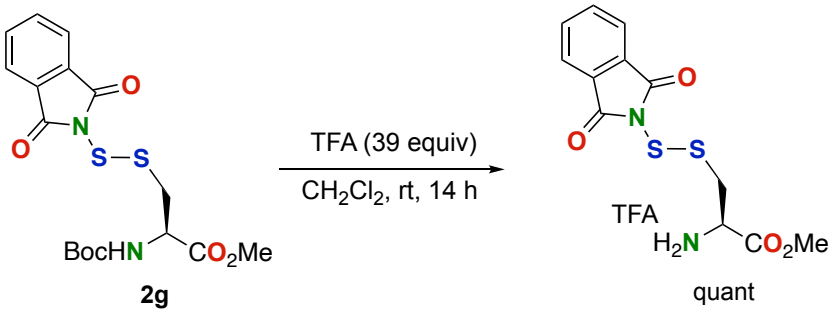
*A typical procedure for the synthesis of azlactones **1***



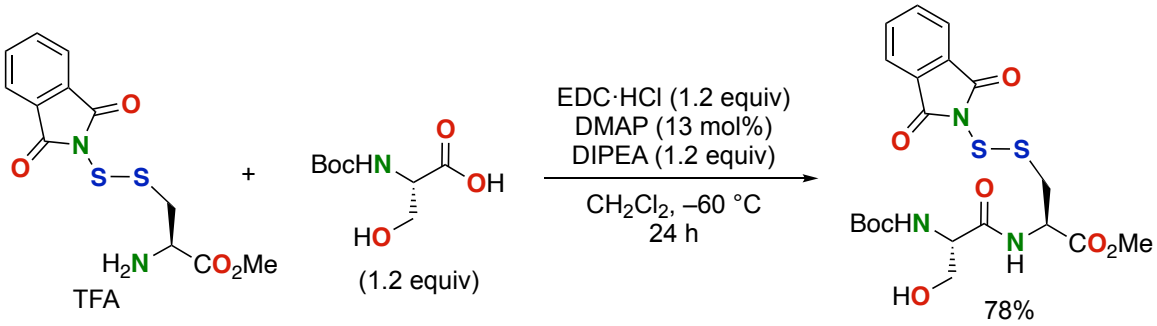
To a mixture of Bz-Lys(Bz)-OH (355 mg, 1.00 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (10 mL) was added EDC·HCl (212 mg, 1.11 mmol, 1.10 equiv) at 0 °C. After stirring for 1 h at the same temperature, to the mixture was added CH_2Cl_2 (10 mL), washed with aqueous saturated solution of $NaHCO_3$ (10 mL × 2), H_2O (10 mL), brine (10 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure to give *N*-(4-(5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)butyl)benzamide (**1c**) (270 mg, 0.803 mmol, 80.1%) as a colorless solid.

According to the procedure for preparing *N*-(4-(5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)butyl)benzamide (**1c**), *tert*-butyl ((4-benzyl-5-oxo-4,5-dihydrooxazol-2-yl)methyl)carbamate (**1k**) (914 mg, 3.00 mmol, quant) was prepared from the corresponding peptide.

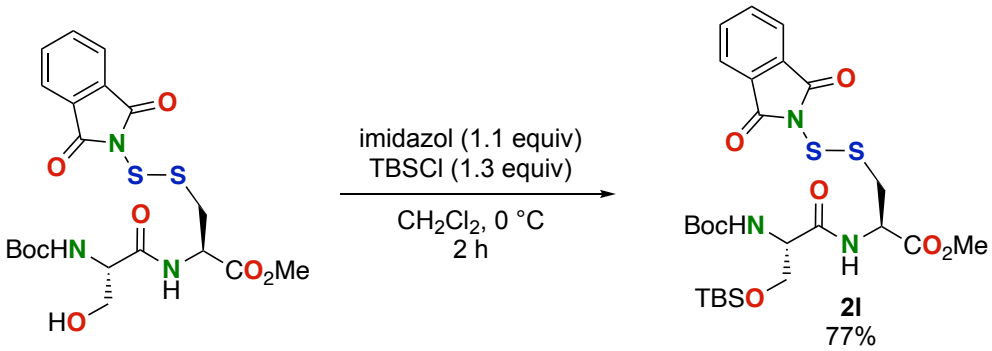
*Synthesis of peptide-based N-dithiophthalimide **2l***



To a mixture of methyl *N*-(*tert*-butoxycarbonyl)-*S*-((1,3-dioxoisoindolin-2-yl)thio)-L-cysteinate (**2g**) (207 mg, 0.502 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (8 mL) was added TFA (1.5 mL, 19.6 mmol, 39.1 equiv) at 0 °C. After stirring for 14 h at room temperature, the mixture was concentrated under reduced pressure to give TFA salt of methyl *S*-((1,3-dioxoisoindolin-2-yl)thio)-L-cysteinate (237 mg, 0.555 mmol, quant) as a brown oil.

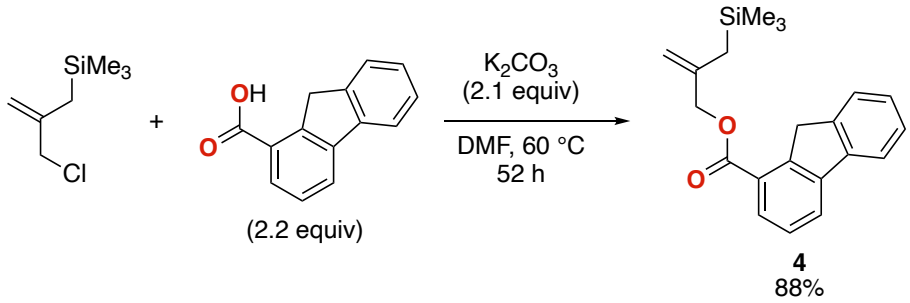


To a mixture of TFA salt of methyl *S*-((1,3-dioxoisoindolin-2-yl)thio)-L-cysteinate (429 mg, 1.00 mmol, 1.00 equiv) and Boc-L-Ser-OH (250 mg, 1.22 mmol, 1.21 equiv) suspended in CH_2Cl_2 (5 mL) were added DMAP (15.9 mg, 0.130 mmol, 12.9 mol%), EDC·HCl (232 mg, 1.21 mmol, 1.20 equiv), and DIPEA (0.21 mL, 1.2 mmol, 1.2 equiv) at –60 °C. After stirring for 24 h at the same temperature, the mixture was diluted with EtOAc (15 mL), washed with H_2O (10 mL), extracted with EtOAc (15 mL × 2), washed with brine (30 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under the reduced pressure, and the residue was purified by column chromatography (silica gel, 5 g, hexane/EtOAc = 4/1 then $CHCl_3$/MeOH = 40/1) to give methyl *N*-((*tert*-butoxycarbonyl)-L-seryl)-*S*-((1,3-dioxoisoindolin-2-yl)thio)-L-cysteinate (390 mg, 0.782 mmol, 77.7%) as a colorless solid.



To a mixture of methyl *N*-((*tert*-butoxycarbonyl)-L-seryl)-*S*-((1,3-dioxoisoindolin-2-yl)thio)-L-cysteinate (322 mg, 0.645 mmol, 1.00 equiv) dissolved in CH_2Cl_2 (2.9 mL) were added imidazole (48.7 mg, 0.715 mmol, 1.11 equiv) and TBSCl (127 mg, 0.840 mmol, 1.30 equiv) at 0 °C. After stirring for 2 h at the same temperature, the mixture was added H_2O (10 mL), extracted with EtOAc (10 mL × 3), washed with brine (15 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under the reduced pressure, and the residue was purified by column chromatography (silica gel, 6 g, hexane/EtOAc = 1/4 then $CHCl_3$/MeOH = 40/1) to give methyl *N*-(*N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyldimethylsilyl)-L-seryl)-*S*-((1,3-dioxoisoindolin-2-yl)thio)-L-cysteinate (**2l**) (303 mg, 0.494 mmol, 76.6%) as a colorless solid.

*Synthesis of 2-((trimethylsilyl)methyl)allyl 9H-fluorene-1-carboxylate (**4**) from (2-(chloromethyl)allyl)trimethylsilane and 9H-fluorene-1-carboxylic acid*

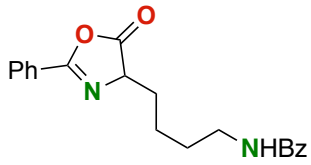


To a mixture of 9*H*-fluorene-1-carboxylic acid (367 mg, 1.75 mmol, 2.18 equiv) and potassium carbonate (237 mg, 1.71 mmol, 2.14 equiv) suspended in DMF (5.6 mL) was added (2-(chloromethyl)allyl)trimethylsilane (145 μL, 0.801 mmol, 1.00 equiv) at room temperature. After stirring for 52 h at 60 °C, to the mixture was added H_2O (10 mL). The mixture was extracted with EtOAc (10 mL × 3), the combined organic extract was washed with H_2O (15 mL × 3) and brine (15 mL), and dried ($MgSO_4$). After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, 9 g, hexane/EtOAc = 80/1 to 20/1) to give 2-((trimethylsilyl)methyl)allyl 9*H*-fluorene-1-carboxylate (**4**) (238 mg, 0.707 mmol, 88.3%) as a colorless oil.

Characterization Data of New Compounds

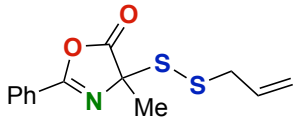
tert-Butyl ((4-benzyl-5-oxo-4,5-dihydrooxazol-2-yl)methyl)carbamate (**1k**)[S13], (2*S*,3*S*,4*R*,5*S*,6*R*)-2-(acetoxymethyl)-6-((1,3-dioxoisoindolin-2-yl)disulfanyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (**9**)[S9], and 2-(((3-(9,10-ethanoanthracen-9(10*H*)-yl)propyl)(methyl)amino)disulfanyl)isoindoline-1,3-dione (**13**)[S8] were identical in spectra data with those reported in the literature.

***N*-(4-(5-Oxo-2-phenyl-4,5-dihydrooxazol-4-yl)butyl)benzamide (1c)**



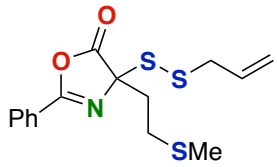
Colorless solid; TLC R_f 0.32 ($CHCl_3$/MeOH = 30/1); m.p. 113-115 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01-7.97 (m, 2H), 7.76-7.74 (m, 2H), 7.61-7.56 (m, 1H), 7.51-7.46 (m, 3H), 7.44-7.38 (m, 2H), 6.26 (br s, 1H), 4.42 (dd, *J* = 7.4, 5.6 Hz, 1H), 3.54-3.46 (m, 2H), 2.14-2.04 (m, 1H), 1.96-1.82 (m, 1H), 1.76-1.68 (m, 2H), 1.65-1.57 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 178.3, 167.6, 161.8, 134.7, 132.8, 131.4, 128.8, 128.5, 127.9, 126.8, 125.8, 65.2, 39.6, 31.1, 29.1, 22.8; **HRMS** (FAB$^+$) Calcd for $C_{20}H_{21}N_2O_3^+$ $[M+H]^+$ 337.1547, found 337.1549.v

4-(Allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (3aa)



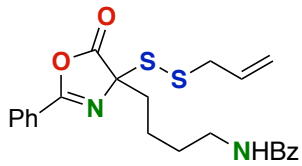
Colorless oil; TLC R_f 0.40 (hexane/EtOAc = 4/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09-8.06 (m, 2H), 7.65-7.61 (m, 1H), 7.53 (app. t, *J* = 7.9 Hz, 2H), 5.72-5.61 (m, 1H), 5.11-5.05 (m, 2H), 3.32 (d, *J* = 7.6 Hz, 2H), 1.85 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 177.0, 161.6, 133.3, 132.0, 129.0, 128.3, 125.3, 119.7, 76.7, 42.8, 21.0; **HRMS** (FAB$^+$) Calcd for $C_{13}H_{14}NO_2S_2^+$ $[M+H]^+$ 280.0460, found 280.0471.

4-(Allyldisulfanyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (3ba)



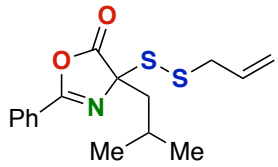
Colorless oil; TLC R_f 0.32 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10-8.05 (m, 2H), 7.66-7.60 (m, 1H), 7.56-7.50 (m, 2H), 5.71-5.60 (m, 1H), 5.12-5.03 (m, 2H), 3.33-3.27 (m, 2H), 2.67-2.40 (m, 4H), 2.06 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.8, 162.5, 133.5, 132.0, 129.1, 128.4, 125.4, 119.9, 79.5, 42.9, 33.5, 29.7, 15.1; **HRMS** (FAB$^+$) Calcd for $C_{15}H_{18}NO_2S_3^+$ $[M+H]^+$ 340.0494, found 340.0501.

_N_-(4-(4-(Allyldisulfanyl)-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)butyl)benzamide (3ca)



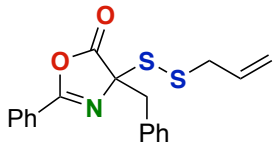
Colorless oil; TLC R_f 0.20 (hexane/EtOAc = 2/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09-8.01 (m, 2H), 7.75-7.68 (m, 2H), 7.66-7.59 (m, 1H), 7.52 (app. t, J = 7.8 Hz, 2H), 7.48-7.43 (m, 1H), 7.39 (app. t, J = 7.8 Hz, 2H), 6.36 (t, J = 5.7 Hz, 1H), 5.70-5.57 (m, 1H), 5.11-5.01 (m, 2H), 3.41 (dd, J = 13.1, 6.8 Hz, 2H), 3.29 (d, J = 7.4 Hz, 2H), 2.19 (t, J = 8.7 Hz, 2H), 1.72-1.61 (m, 2H), 1.61-1.34 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.7, 167.7, 162.0, 134.7, 133.5, 132.0, 131.5, 129.1, 128.6, 128.4, 126.9, 125.2, 119.8, 80.6, 43.0, 39.6, 34.1, 29.3, 22.5; **HRMS** (FAB^+) Calcd for $C_{23}H_{25}N_2O_3S_2^+$ $[M+H]^+$ 441.1301, found 441.1320.

4-(Allyldisulfanyl)-4-isobutyl-2-phenyloxazol-5(4*H*)-one (3da)



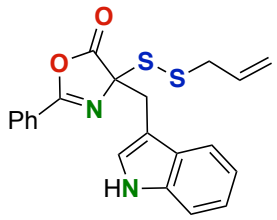
Colorless oil; TLC R_f 0.37 (hexane/EtOAc = 10/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11-8.07 (m, 2H), 7.66-7.60 (m, 1H), 7.56-7.51 (m, 2H), 5.70-5.59 (m, 1H), 5.10-5.02 (m, 2H), 3.28 (d, J = 7.6 Hz, 2H), 2.18-2.06 (m, 2H), 1.84 (sep, J = 6.7 Hz, 1H), 0.95 (d, J = 6.7 Hz, 3H), 0.89 (d, J = 6.7 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 177.3, 161.5, 133.4, 132.2, 129.1, 128.4, 125.6, 119.7, 80.5, 43.1, 42.9, 26.4, 23.7, 22.9; **HRMS** (FAB^+) Calcd for $C_{16}H_{20}NO_2S_2^+$ $[M+H]^+$ 321.0930, found 321.0939.

4-(Allyldisulfanyl)-4-benzyl-2-phenyloxazol-5(4*H*)-one (3ea)



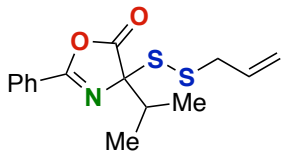
Colorless oil; TLC R_f 0.43 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99-7.94 (m, 2H), 7.61-7.55 (m, 1H), 7.50-7.44 (m, 2H), 7.27-7.15 (m, 5H), 5.73-5.61 (m, 1H), 5.13-5.04 (m, 2H), 3.45 (s, 2H), 3.33 (ddd, J = 8.0, 1.0, 1.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.1, 161.8, 133.6, 133.3, 132.1, 130.3, 129.0, 128.5, 128.3, 127.7, 125.2, 119.9, 81.4, 42.9, 40.6; **HRMS** (FAB^+) Calcd for $C_{19}H_{18}NO_2S_2^+$ $[M+H]^+$ 356.0773, found 356.0778.

4-((1*H*-Indol-3-yl)methyl)-4-(allyldisulfanyl)-2-phenyloxazol-5(4*H*)-one (3fa)



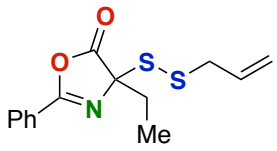
Yellow solid; TLC R_f 0.23 (hexane/EtOAc = 3/1); m.p. 103-104 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (s, 1H), 7.94-7.89 (m, 2H), 7.79-7.74 (m, 1H), 7.56-7.51 (m, 1H), 7.45-7.39 (m, 2H), 7.27-7.23 (m, 1H), 7.14-7.06 (m, 3H), 5.75-5.63 (m, 1H), 5.13-5.05 (m, 2H), 3.66 (d, J = 14.4 Hz, 1H), 3.61 (d, J = 14.4 Hz, 1H), 3.40-3.29 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.6, 161.9, 135.8, 133.2, 132.2, 128.9, 128.3, 127.4, 125.3, 124.2, 122.3, 119.82, 119.78, 119.7, 111.0, 108.3, 81.8, 42.9, 30.9; **HRMS** (FAB^+) Calcd for $C_{21}H_{19}N_2O_2S_2^+$ $[M+H]^+$ 395.0882, found 395.0888.

4-(Allyldisulfanyl)-4-isopropyl-2-phenyloxazol-5(4*H*)-one (3ga)



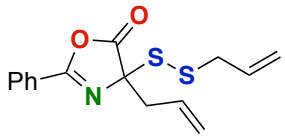
Colorless oil; TLC R_f 0.33 (hexane/EtOAc = 16/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13-8.05 (m, 2H), 7.65-7.59 (m, 1H), 7.56-7.50 (m, 2H), 5.72-5.60 (m, 1H), 5.11-5.03 (m, 2H), 3.33-3.23 (m, 2H), 2.48 (sep, J = 6.8 Hz, 1H), 1.23 (d, J = 6.8 Hz, 3H), 1.04 (d, J = 6.8 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.8, 161.8, 133.3, 132.2, 129.1, 128.4, 125.4, 119.7, 85.3, 42.8, 33.7, 18.2, 17.7; **HRMS** (FAB^+) Calcd for $C_{15}H_{18}NO_2S_2^+$ $[M+H]^+$ 308.0773, found 308.0771.

4-(Allyldisulfanyl)-4-ethyl-2-phenyloxazol-5(4*H*)-one (3ha)



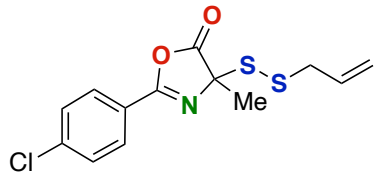
Colorless oil; TLC R_f 0.42 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.0 Hz, 2H), 7.66-7.60 (m, 1H), 7.57-7.50 (m, 2H), 5.72-5.60 (m, 1H), 5.11-5.03 (m, 2H), 3.35-3.25 (m, 2H), 2.27-2.13 (m, 2H), 1.01 (t, J = 7.4 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.7, 162.0, 133.4, 132.1, 129.1, 128.4, 125.3, 119.8, 81.6, 43.0, 28.2, 9.4; **HRMS** (FAB^+) Calcd for $C_{14}H_{16}NO_2S_2^+$ $[M+H]^+$ 294.0617, found 294.0617.

4-Allyl-4-(allyldisulfanyl)-2-phenyloxazol-5(4*H*)-one (3ia)



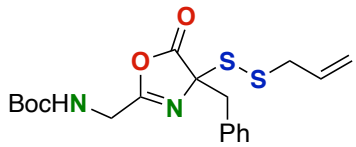
Colorless oil; TLC R_f 0.48 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11-8.04 (m, 2H), 7.66-7.59 (m, 1H), 7.57-7.49 (m, 2H), 5.77-5.61 (m, 2H), 5.25 (d, J = 17.2 Hz, 1H), 5.17 (d, J = 10.1 Hz, 1H), 5.11-5.02 (m, 2H), 3.37-3.28 (m, 2H), 2.97-2.84 (m, 2H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.2, 162.0, 133.5, 132.2, 129.9, 129.1, 128.5, 125.4, 121.4, 119.8, 80.5, 43.0, 39.0; **HRMS** (FAB$^+$) Calcd for $C_{15}H_{16}NO_2S_2^+$ $[M+H]^+$ 306.0617, found 306.0610.

4-(Allyldisulfanyl)-2-(4-chlorophenyl)-4-methyloxazol-5(4*H*)-one (3ja)



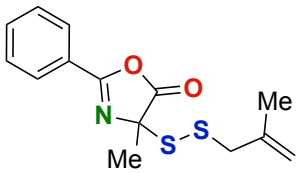
Colorless oil; TLC R_f 0.47 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 8.6 Hz, 2H), 5.72-5.61 (m, 1H), 5.14-5.06 (m, 2H), 3.30 (d, J = 7.4 Hz, 2H), 1.84 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.9, 160.9, 140.0, 132.1, 129.7, 129.6, 123.9, 119.9, 76.8, 42.9, 21.1; **HRMS** (FAB$^+$) Calcd for $C_{13}H_{13}{}^{35}ClNO_2S_2^+$ $[M+H]^+$ 314.0071, found 314.0081.

***tert*-Butyl ((4-(allyldisulfanyl)-4-benzyl-5-oxo-4,5-dihydrooxazol-2-yl)methyl)carbamate (3ka)**



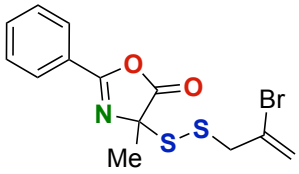
Colorless oil; TLC R_f 0.40 (hexane/EtOAc = 3/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29-7.22 (m, 3H), 7.22-7.15 (m, 2H), 5.84-5.71 (m, 1H), 5.25-5.16 (m, 2H), 4.96 (br s, 1H), 4.19 (dd, J = 18.3, 5.6 Hz, 1H), 4.00 (dd, J = 18.3, 5.6 Hz, 1H), 3.42-3.28 (m, 4H), 1.46 (s, 9H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 175.3, 163.4, 155.2, 133.1, 132.1, 130.1, 129.3, 128.9, 128.5, 127.8, 119.8, 80.4, 79.8, 42.5, 40.3, 38.1, 28.2; **HRMS** (FAB$^+$) Calcd for $C_{19}H_{25}N_2O_4S_2^+$ $[M+H]^+$ 409.1250, found 409.1256.

4-Methyl-4-((2-methylallyl)disulfanyl)-2-phenyloxazol-5(4*H*)-one (3ab)



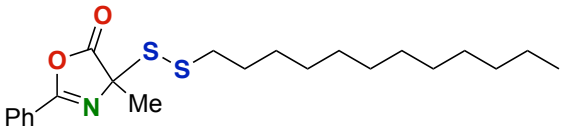
Colorless oil; TLC R_f 0.48 (hexane/EtOAc = 4/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09-8.05 (m, 2H), 7.65-7.59 (m, 1H), 7.56-7.49 (m, 2H), 4.86-4.83 (m, 1H), 4.81-4.79 (m, 1H), 3.28 (d, J = 0.8 Hz, 2H), 1.84 (s, 3H), 1.67-1.65 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 177.2, 161.6, 139.5, 133.5, 129.1, 128.4, 125.3, 116.3, 76.9, 47.5, 21.1, 20.9; **HRMS** (FAB^+) Calcd for $C_{14}H_{16}NO_2S_2^+$ $[M+H]^+$ 294.0617, found 294.0620.

4-((2-Bromoallyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (3ac)



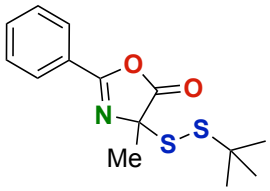
Colorless oil ; TLC R_f 0.40 (hexane/EtOAc = 4/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08-8.03 (m, 2H), 7.66-7.60 (m, 1H), 7.56-7.50 (m, 2H), 5.75-7.72 (m, 1H), 5.52 (d, J = 1.9 Hz, 1H), 3.59-3.55 (m, 2H), 1.85 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 177.1, 161.9, 133.6, 129.2, 128.4, 126.9, 125.2, 121.6, 76.9, 49.7, 21.2; **HRMS** (FAB^+) Calcd for $C_{13}H_{13}{}^{79}BrNO_2S_2^+$ $[M+H]^+$ 357.9566, found 357.9567.

4-(Dodecyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (3ad)



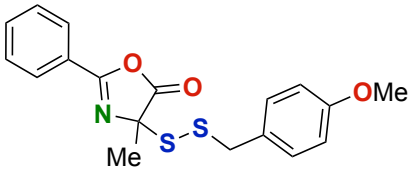
Colorless oi; TLC R_f 0.40 (hexane/EtOAc = 30/1); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.07-8.05 (m, 2H), 7.63-7.60 (m, 1H), 7.54-7.50 (m, 2H), 2.73-2.62 (m, 2H), 1.84 (s, 3H), 1.54-1.45 (m, 2H), 1.33-1.15 (m, 18H), 0.90-0.86 (t, J = 4.8 Hz, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 177.1, 161.4, 133.2, 128.9, 128.2, 125.3, 76.8, 40.2, 31.9, 29.60, 29.59, 29.5, 29.4, 29.3, 29.1, 29.0, 28.3, 22.7, 21.0, 14.1; **HRMS** (FAB^+) Calcd for $C_{22}H_{34}NO_2S_2^+$ $[M+H]^+$ 408.2025, found 408.2021.

4-(*tert*-Butyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (3ae)



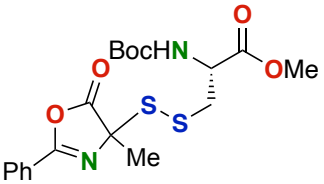
Colorless solid; TLC R_f 0.53 (hexane/EtOAc = 4/1); m.p. 92-94 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06-8.01 (m, 2H), 7.64-7.58 (m, 1H), 7.54-7.48 (m, 2H), 1.83 (s, 3H), 1.22 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 177.1, 161.4, 133.3, 129.0, 128.4, 125.4, 76.0, 48.5, 30.5, 21.9; **HRMS** (FAB^+) Calcd for $C_{14}H_{18}NO_2S_2^+$ $[M+H]^+$ 296.0773, found 296.0770.

4-((4-Methoxybenzyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (3af)



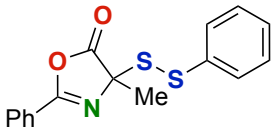
Colorless oil; TLC R_f 0.37 (hexane/EtOAc = 4/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.15-8.09 (m, 2H), 7.69-7.62 (m, 1H), 7.59-7.52 (m, 2H), 7.00-6.94 (m, 2H), 6.76-6.70 (m, 2H), 3.87 (s, 2H), 3.75 (s, 3H), 1.87 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 177.3, 161.7, 159.2, 133.5, 130.7, 129.2, 128.4, 127.8, 125.3, 114.1, 77.2, 55.3, 44.2, 21.1; **HRMS** (FAB^+) Calcd for $C_{18}H_{18}NO_3S_2^+$ $[M+H]^+$ 360.0723, found 360.0732.

Methyl *N*-(*tert*-butoxycarbonyl)-*S*-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)thio)-L-cysteinate (3ag)



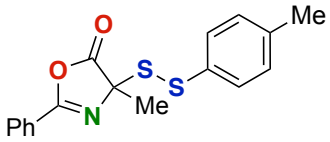
Isolated as a 1:1 mixture of diastereomers; Colorless oil; TLC R_f 0.66 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08-8.04 (m, 2H+2H), 7.66-7.61 (m, 1H+1H), 7.56-7.51 (m, 2H+2H), 5.42-5.24 (m, 1H+1H), 4.58-4.48 (m, 1H+1H), 3.73 (s, 3H), 3.71 (s, 3H), 3.24-3.00 (m, 2H+2H), 1.83 (s, 3H+3H), 1.43 (s, 9H), 1.41 (s, 9H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.63, 176.57, 170.75, 170.71, 161.8, 161.7, 154.9, 154.8, 133.41, 133.40, 129.0, 128.9, 128.23, 128.22, 124.99, 124.97, 80.2, 76.7, 76.6, 52.73, 52.72, 52.52, 52.50, 42.3, 42.0, 28.19, 28.16, 21.0, 20.9; **HRMS** (FAB^+) Calcd for $C_{19}H_{25}N_2O_6S_2^+$ $[M+H]^+$ 441.1149, found 441.1151.

4-Methyl-2-phenyl-4-(phenyldisulfanyl)oxazol-5(4*H*)-one (3ah)



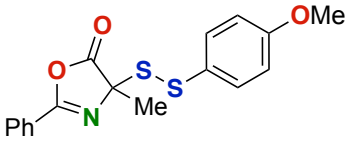
Colorless oil; TLC R_f 0.50 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (d, J = 7.4 Hz, 2H), 7.56 (app. t, J = 7.4 Hz, 1H), 7.46-7.36 (m, 4H), 7.24-7.16 (m, 3H), 1.87 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.2, 161.8, 135.6, 133.2, 128.8, 128.7, 128.33, 128.26, 127.5, 125.0, 77.1, 21.0; **HRMS** (FAB^+) Calcd for $C_{16}H_{14}NO_2S_2^+$ $[M+H]^+$ 360.0460, found 360.0458.

4-Methyl-2-phenyl-4-(*p*-tolyldisulfanyl)oxazol-5(4*H*)-one (3ai)



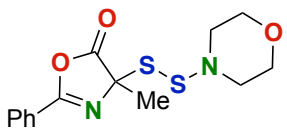
Colorless oil; TLC R_f 0.50 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.85 (d, J = 7.8 Hz, 2H), 7.58 (app. t, J = 7.2 Hz, 1H), 7.48-7.41 (m, 2H), 7.32-7.24 (m, 2H), 6.99 (d, J = 7.8 Hz, 2H), 2.78 (s, 3H), 1.84 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.2, 161.8, 137.9, 133.2, 132.1, 129.6, 129.2, 128.7, 128.3, 125.0, 76.9, 21.1, 21.0; **HRMS** (FAB^+) Calcd for $C_{17}H_{16}NO_2S_2^+$ $[M+H]^+$ 330.0617, found 330.0638.

4-((4-Methoxyphenyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (3aj)



Colorless oil; TLC R_f 0.30 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, J = 7.8 Hz, 2H), 7.60 (app. t, J = 7.4 Hz, 1H), 7.47 (app. t, J = 7.7 Hz, 2H), 7.34-7.30 (m, 2H), 6.70 (d, J = 8.8 Hz, 2H), 3.75 (s, 3H), 1.83 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.3, 161.6, 159.9, 133.2, 132.2, 128.8, 128.3, 126.3, 125.2, 114.5, 76.8, 55.3, 21.0; **HRMS** (FAB^+) Calcd for $C_{17}H_{16}NO_3S_2^+$ $[M+H]^+$ 346.0566, found 330.0563.

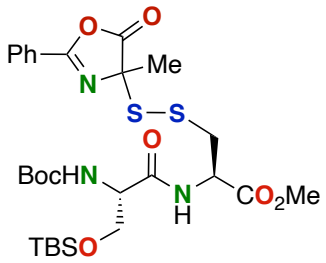
4-Methyl-4-(morpholinodisulfanyl)-2-phenyloxazol-5(4*H*)-one (3ak)



Colorless solid; TLC R_f 0.28 (hexane/EtOAc = 5/1); m.p. 77-80 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (dd, J = 8.4, 1.3 Hz, 2H), 7.65-7.59 (m, 1H), 7.55-7.49 (m, 2H), 3.62-3.51 (m,

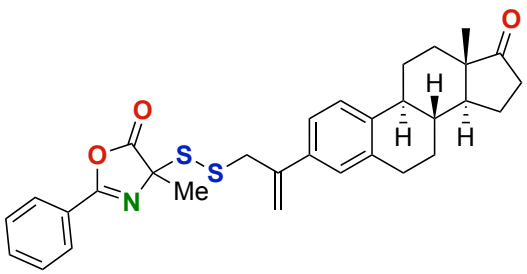
4H), 2.88-2.83 (m, 2H), 2.77-2.68 (m, 2H), 1.87 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 177.2, 161.5, 133.5, 129.1, 128.3, 125.4, 75.3, 67.0, 55.7, 22.6; **HRMS** (FAB^+) Calcd for $C_{14}H_{17}N_2O_3S_2^+$ $[M+H]^+$ 360.0675, found 360.0669.

Methyl *N*-(*N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyldimethylsilyl)-L-seryl)-*S*-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)thio)-L-cysteinate (3al)



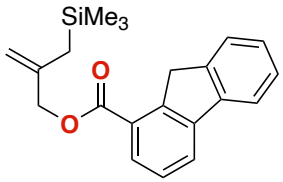
Isolated as a 1.1:1 mixture of diastereomers; Colorless oil; R_f 0.25 (hexane/EtOAc = 3/1); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.07-8.03 (m, 2H+2H), 7.63 (app. t, J = 7.5 Hz, 1H+1H), 7.53 (app. t, J = 7.9 Hz, 2H+2H), 5.33 (br s, 1H+1H), 4.84-4.76 (m, 1H+1H), 4.15 (br s, 1H), 4.11 (br s, 1H), 4.01-3.96 (m, 1H+1H), 3.76-3.73 (m, 3H+1H+1H), 3.70 (s, 3H), 3.67-3.61 (m, 1H+1H), 3.23-3.04 (m, 2H+2H), 1.83 (s, 3H+3H), 1.46 (s, 9H+9H), 0.87 (s, 9H+9H), 0.07-0.06 (m, 6H+6H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.8, 176.7, 170.64, 170.58, 170.15, 170.06, 162.0, 161.9, 155.6, 133.64, 133.59, 129.2, 129.1, 128.5, 128.4, 125.20, 125.17, 80.3, 76.90, 76.88, 63.2, 55.6, 52.8, 51.9, 51.8, 42.2, 41.6, 28.4, 26.00, 25.96, 21.2, 21.1, 18.3, –5.30, –5.32, –5.4; **HRMS** (FAB^+) Calcd for $C_{28}H_{44}N_3O_8S_2Si^+$ $[M+H]^+$ 642.2334, found. 642.2332.

4-Methyl-4-((2-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)allyl)disulfanyl)-2-phenyloxazol-5(4*H*)-one (3am)



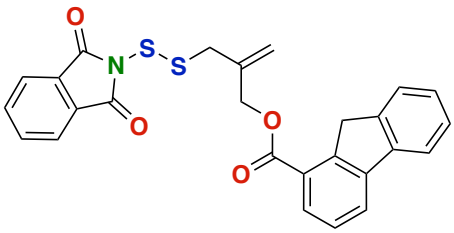
Isolated as a 1:1 mixture of diastereomers; Yellow oil; R_f 0.33 (hexane/EtOAc = 3/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.10-8.05 (m, 2H+2H), 7.66-7.62 (m, 1H+1H), 7.55-7.52 (m, 2H+2H), 7.18-7.07 (m, 3H+3H), 5.43-5.40 (m, 1H+1H), 5.10-5.08 (m, 1H+1H), 3.78-3.75 (m, 2H+2H), 2.90-2.84 (m, 2H+2H), 2.54-2.47 (m, 1H+1H), 2.43-2.38 (m, 1H+1H), 2.33-2.20 (m, 1H+1H), 2.20-1.95 (m, 4H+4H), 1.86 (s, 3H+3H), 1.65-1.43 (m, 6H+6H), 0.90 (s, 3H+3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 221.0, 177.3, 161.7, 141.6, 139.8, 136.6, 135.9, 133.5, 129.1, 128.4, 126.8, 125.6, 125.4, 123.6, 117.0, 76.9, 50.6, 48.1, 44.7, 44.473, 44.465, 38.1, 36.0, 31.7, 29.5, 26.6, 25.7, 21.7, 21.2, 14.0; **HRMS** (FAB^+) Calcd for $C_{31}H_{34}NO_3S_2^+$ $[M+H]^+$ 532.1975, found 532.1977.

2-((Trimethylsilyl)methyl)allyl 9*H*-fluorene-1-carboxylate (4)



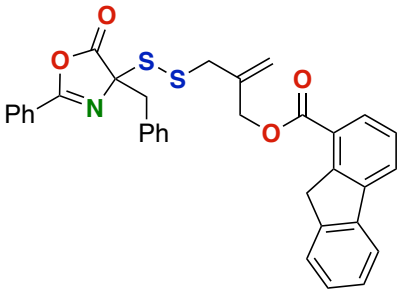
Colorless oil; TLC R_f 0.38 (hexane/EtOAc = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.7 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.49 (app. t, *J* = 7.7 Hz, 1H), 7.40 (app. t, *J* = 7.2 Hz, 1H), 7.35 (app. t, *J* = 7.4 Hz, 1H), 5.05-5.02 (m, 1H), 4.81 (s, 1H), 4.76 (s, 2H), 4.29 (s, 2H), 1.67 (s, 2H), 0.09 (s, 9H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 166.5, 145.6, 143.9, 143.2, 141.9, 140.5, 128.6, 127.5, 127.2, 127.1, 126.9, 125.1, 124.2, 120.0, 109.8, 68.2, 38.9, 23.8, –1.3; **HRMS** (EI^+) Calcd for $C_{21}H_{24}O_2Si^+$ $[M]^+$ 336.1540, found 336.1546.

2-(((1,3-Dioxoisoindolin-2-yl)disulfanyl)methyl)allyl 9*H*-fluorene-1-carboxylate (5)



Colorless solid; TLC R_f 0.49 (hexane/EtOAc = 3/1); m.p. 132-135 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ 8.01 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.97 (d, *J* = 7.6 Hz, 1H), 7.90-7.86 (m, 2H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.75-7.71 (m, 2H), 7.60 (d, *J* = 7.3 Hz, 1H), 7.47 (app. t, *J* = 7.6 Hz, 1H), 7.40 (app. t, *J* = 7.4, Hz, 1H), 7.35 (app. dt, *J* = 7.4, 1.2 Hz, 1H), 5.61 (s, 1H), 5.47 (d, *J* = 1.1 Hz, 1H), 4.94 (s, 2H), 4.23 (s, 2H), 3.90 (s, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.8, 166.3, 145.6, 143.7, 143.1, 140.4, 138.3, 134.8, 132.2, 128.6, 127.5, 127.2, 126.8, 126.6, 125.1, 124.3, 124.1, 120.0, 119.5, 65.7, 44.0, 38.8; **HRMS** (EI^+) Calcd for $C_{26}H_{19}NO_4S_2^+$ $[M]^+$ 473.0750, found 473.0751.

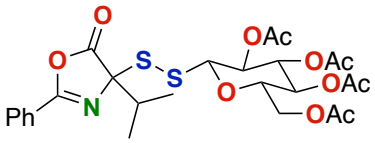
2-(((4-Benzyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)methyl)allyl 9*H*-fluorene-1-carboxylate (6)



Colorless oil; TLC R_f 0.30 (hexane/EtOAc = 8/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00-7.96 (m, 2H), 7.95-7.90 (m, 2H), 7.81 (d, *J* = 7.2 Hz, 1H), 7.60 (d, *J* = 6.8 Hz, 1H), 7.57-7.52 (m,

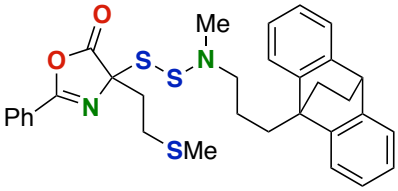
1H), 7.50-7.33 (m, 5H), 7.25-7.14 (m, 5H), 5.34 (s, 1H), 5.19 (s, 1H), 4.83 (s, 2H), 4.24 (s, 2H), 3.50 (s, 2H), 3.45 (s, 2H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 175.9, 166.1, 161.8, 145.5, 143.6, 143.1, 140.3, 138.0, 133.4, 133.3, 130.2, 129.6, 128.9, 128.7, 128.5, 128.4, 128.2, 127.9, 127.6, 127.4, 127.1, 126.7, 126.5, 125.01, 124.99, 124.2, 119.9, 81.3, 65.4, 42.5, 40.6, 38.7; **HRMS** (FAB$^+$) Calcd for $C_{34}H_{28}NO_4S_2^+$ $[M+H]^+$ 578.1454, found 578.1463.

(2*S*,3*S*,4*R*,5*S*,6*R*)-2-(Acetoxymethyl)-6-((4-isopropyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (10)



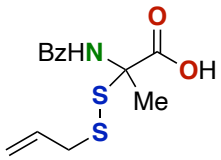
Isolated as a 1:1 mixture of diastereomers; Colorless oil; TLC R_f 0.15 (hexane/EtOAc = 3/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09-8.04 (m, 2H+2H), 7.66-7.58 (m, 1H+1H), 7.56-7.48 (m, 2H+2H), 5.22-5.00 (m, 2H+3H), 4.85 (dd, *J* = 10.4, 9.0 Hz, 1H), 4.56 (d, *J* = 10.4 Hz, 1H), 4.41 (d, *J* = 9.5 Hz, 1H), 4.26-4.24 (m, 1H+1H), 4.20-4.15 (m, 1H), 3.95-3.87 (m, 1H), 3.74-3.69 (m, 1H), 3.61-3.57 (m, 1H), 2.49-2.40 (m, 1H+1H), 2.09 (s, 3H), 2.07 (s, 3H), 2.01 (s, 3H+3H+3H), 2.00 (s, 3H), 1.95 (s, 3H), 1.94 (s, 3H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.21 (d, *J* = 6.8 Hz, 3H), 1.051 (d, *J* = 6.8 Hz, 3H), 1.047 (d, *J* = 6.8 Hz, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.4, 176.1, 170.88, 170.87, 170.4, 170.1, 169.5, 169.4, 169.2, 162.5, 162.4, 133.6, 133.5, 129.1, 129.0, 128.55, 128.49, 125.5, 125.3, 84.4, 76.7, 76.3, 73.9, 70.0, 68.05, 67.97, 62.1, 61.8, 34.7, 34.6, 20.92, 20.89, 20.73, 20.69, 20.65, 20.6, 20.3, 18.0, 17.9, 17.67, 17.65; **HRMS** (FAB$^+$) Calcd for $C_{26}H_{32}NO_{11}S_2^+$ $[M+H]^+$ 598.1411, found. 598.1400.

4-(((3-(9,10-Ethanoanthracen-9(10*H*)-yl)propyl)(methyl)amino)disulfanyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (14)



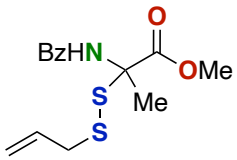
Pale yellow oil; TLC R_f 0.51 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.2 Hz, 2H), 7.56 (app. t, *J* = 7.4 Hz, 1H), 7.47 (app. t, *J* = 7.8 Hz, 2H), 7.27-7.20 (m, 2H), 7.14-7.02 (m, 6H), 4.25-4.20 (m, 1H), 3.02-2.90 (m, 2H), 2.70 (s, 3H), 2.67-2.50 (m, 4H), 2.26 (t, *J* = 8.3 Hz, 2H), 2.07 (s, 3H), 1.90-1.80 (m, 2H), 1.80-1.73 (m, 2H), 1.47-1.38 (m, 2H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 176.9, 162.3, 145.21, 145.17, 144.90, 144.87, 133.3, 129.0, 128.3, 125.4, 125.22, 125.21, 125.19, 123.31, 121.27, 121.18, 121.16, 77.7, 60.7, 46.4, 44.6, 44.5, 35.0, 29.5, 28.1, 27.6, 23.2, 15.0; **HRMS** (FAB$^+$) Calcd for $C_{32}H_{35}N_2O_2S_3^+$ $[M+H]^+$ 575.1855, found. 575.1868.

2-(Allyldisulfanyl)-2-benzamidopropanoic acid (15a)



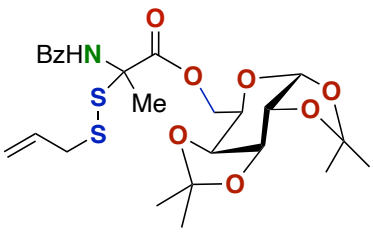
Colorless oil; TLC R_f 0.63 ($CHCl_3$/MeOH = 5/1); **^{1}H NMR** (400 MHz, CD_3OD) δ 7.90-7.85 (m, 2H), 7.60-7.54 (m, 1H), 7.52-7.45 (m, 2H), 5.80-5.69 (m, 1H), 5.06 (s, 1H), 5.02-5.01 (m, 1H), 3.30-3.19 (m, 2H), 1.95 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, CD_3OD) δ 173.8, 168.5, 134.8, 133.9, 133.1, 129.6, 128.3, 119.2, 68.7, 42.7, 24.5; **HRMS** (FAB^+) Calcd for $C_{13}H_{16}NO_3S_2^+$ $[M+H]^+$ 298.0566, found 298.0578.

Methyl 2-(allyldisulfanyl)-2-benzamidopropanoate (15b)



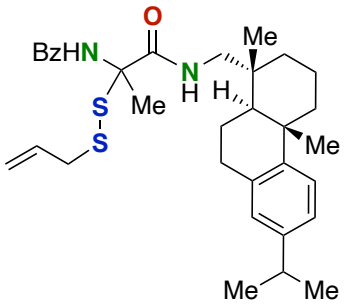
Colorless oil; TLC R_f 0.30 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87-7.84 (m, 2H), 7.60-7.56 (m, 1H), 7.56-7.51 (m, 1H), 7.51-7.44 (m, 2H), 5.78-5.67 (m, 1H), 5.12-5.03 (m, 2H), 3.87 (s, 3H), 3.24 (d, J = 7.4 Hz, 2H), 2.09 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 171.7, 166.1, 134.2, 132.4, 132.0, 128.7, 127.1, 119.3, 66.4, 53.5, 42.0, 22.1; **HRMS** (FAB^+) Calcd for $C_{14}H_{18}NO_3S_2^+$ $[M+H]^+$ 312.0723, found 312.0722.

((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-Tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)methyl 2-(allyldisulfanyl)-2-benzamidopropanoate (15c)



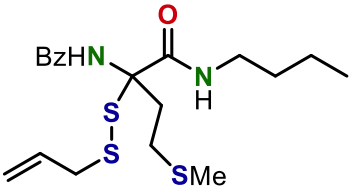
Isolated as a 1:1 mixture of diastereomers, Colorless oil; TLC R_f 0.18 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89-7.82 (m, 2H+2H), 7.64-7.58 (m, 1H+1H), 7.58-7.51 (m, 1H+1H), 7.50-7.42 (m, 2H+2H), 5.79-5.65 (m, 1H+1H), 5.60-5.50 (m, 1H+1H), 5.11-5.02 (m, 2H+2H), 4.66-4.59 (m, 1H+1H), 4.48-4.31 (m, 2H+2H), 4.31-4.23 (m, 1H+1H), 4.16-4.04 (m, 1H+1H), 3.82-3.70 (m, 1H+1H), 3.25 (t, J = 6.7 Hz, 2H+2H), 2.12 (s, 3H+3H), 1.51-1.42 (m, 6H+6H), 1.33 (s, 6H+6H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 170.99, 170.96, 166.0, 165.9, 132.54, 132.46, 132.00, 131.98, 128.70, 128.69, 127.08, 127.07, 119.24, 119.19, 109.72, 109.70, 108.85, 108.84, 96.3, 96.2, 70.9, 70.81, 70.75, 70.66, 70.64, 70.56, 70.48, 70.43, 66.7, 66.5, 66.0, 65.6, 65.3, 65.1, 42.2, 42.1, 26.0, 25.9, 24.94, 24.91, 24.40, 24.39, 24.28, 22.0; **HRMS** (FAB^+) Calcd for $C_{25}H_{34}NO_8S_2^+$ $[M+H]^+$ 540.1720, found 540.1727.

***N*-(2-(Allyldisulfanyl)-1-((((1*R*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-1-oxopropan-2-yl)benzamide (15d)**



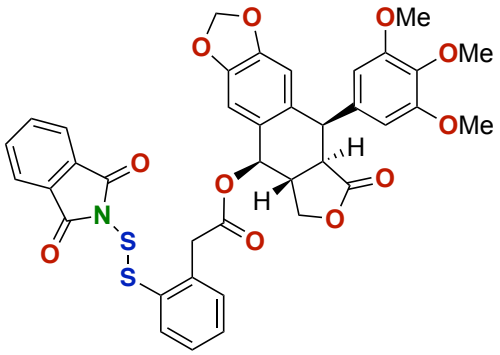
Isolated as a 1:1 mixture of diastereomers, Colorless oil; TLC R_f 0.23 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.24 (s, 1H+1H), 7.85-7.81 (m, 2H+2H), 7.54-7.43 (m, 3H+3H), 7.16 (d, J = 8.1 Hz, 1H+1H), 7.04-6.96 (m, 1H+1H), 6.90-6.84 (m, 1H+1H), 6.51-6.42 (m, 1H+1H), 5.72-5.56 (m, 1H+1H), 5.10-4.96 (m, 2H+2H), 3.39-3.08 (m, 3H+3H), 2.98-2.76 (m, 3H+3H), 2.30 (d, J = 12.9 Hz, 1H+1H), 2.06 (s, 3H), 2.04 (s, 3H), 1.88-1.36 (m, 9H+9H), 1.28-1.20 (m, 9H+9H), 1.00 (s, 3H), 0.97 (s, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 171.7, 171.6, 165.52, 165.51, 146.9, 146.8, 145.61, 145.57, 134.6, 134.50, 134.45, 134.4, 132.39, 132.38, 131.87, 131.86, 128.7, 127.0, 126.85, 126.77, 124.2, 124.1, 123.9, 123.8, 119.3, 119.1, 69.1, 68.9, 51.3, 51.1, 46.4, 45.6, 41.7, 41.6, 38.30, 38.27, 37.67, 37.65, 37.54, 37.46, 36.30, 36.25, 33.39, 30.35, 30.2, 25.3, 23.95, 23.93, 23.8, 23.7, 19.12, 18.55, 18.51, 18.42, 18.40; **HRMS** (FAB^+) Calcd for $C_{33}H_{45}N_2O_2S_2^+$ $[M+H]^+$ 565.2917, found 565.2921.

***N*-(2-(Allyldisulfanyl)-1-(butylamino)-4-(methylthio)-1-oxobutan-2-yl)benzamide (15e)**



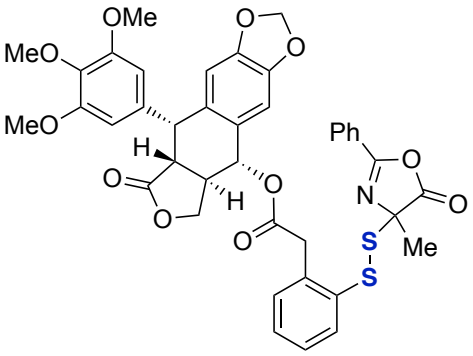
Colorless oil; TLC R_f 0.22 (hexane/EtOAc = 5/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.91-7.87 (m, 2H), 7.58-7.51 (m, 1H), 7.50-7.44 (m, 2H), 6.44 (br s, 1H), 5.75-5.64 (m, 1H), 5.10-5.00 (m, 2H), 3.55-3.47 (m, 1H), 3.43-3.30 (m, 2H), 3.23 (d, J = 7.1 Hz, 2H), 2.51-2.43 (m, 1H), 2.33-2.24 (m, 1H), 2.11-2.01 (m, 1H), 2.06 (s, 3H), 1.61-1.53 (m, 2H), 1.44-1.36 (m, 2H), 0.97 (t, J = 7.3 Hz, 3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) Peak splitting due to rotamers was observed. δ 171.1, 170.2, 165.4, 165.1, 134.4, 133.1, 132.6, 132.2, 132.0, 128.9, 128.8, 127.2, 127.1, 119.4, 118.2, 72.1, 68.3, 41.9, 40.5, 40.4, 36.6, 35.2, 33.4, 31.5, 29.0, 28.6, 20.2, 15.7, 13.8; **HRMS** (FAB^+) Calcd for $C_{19}H_{29}N_2O_2S_3^+$ $[M+H]^+$ 413.1386, found 413.1391.

(5*R*,5a*R*,8a*R*,9*R*)-8-Oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetate



Colorless oil; TLC R_f 0.29 (hexane/EtOAc = 1/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.91-7.88 (m, 2H), 7.80-7.77 (m, 2H), 7.42 (app. dt, *J* = 7.5, 1.6 Hz, 1H), 7.42 (app. dt, *J* = 7.5, 1.6 Hz, 1H), 7.30-7.25 (m, 1H), 6.67 (s, 1H), 6.51 (s, 1H), 6.34 (s, 2H), 5.979 (d, *J* = 7.2 Hz, 1H), 5.976 (d, *J* = 7.2 Hz, 1H), 5.73 (d, *J* = 8.4 Hz, 1H), 4.56 (d, *J* = 3.9 Hz, 1H), 4.24 (dd, *J* = 9.2, 6.4 Hz, 1H), 3.98-3.93 (m, 1H), 3.90 (d, *J* = 14.9 Hz, 1H), 3.81 (s, 3H), 3.78-3.75 (m, 1H), 3.74 (s, 6H), 2.87-2.71 (m, 2H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 173.5, 171.2, 166.7, 152.5, 148.1, 147.5, 137.0, 135.5, 134.8, 134.7, 133.9, 132.7, 132.2, 132.0, 130.8, 129.4, 128.9, 127.9, 124.1, 109.5, 108.0, 106.9, 101.5, 74.3, 71.1, 60.6, 56.1, 45.3, 43.6, 39.5, 38.6; **HRMS** (FAB^+) Calcd for $C_{38}H_{31}NO_{11}S_2^+$ $[M]^+$ 741.1339, found 741.1365.

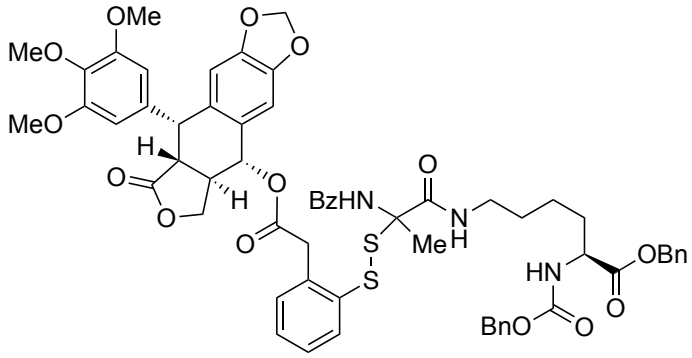
(5*R*,5a*R*,8a*R*,9*R*)-8-Oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)phenyl)acetate (18)



Isolated as a 1.7:1 mixture of diastereomers; Colorless oil; TLC R_f 0.45 (hexane/EtOAc = 1/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80-7.68 (m, 2H+2H), 7.63-7.51 (m, 1H+1H), 7.49-7.38 (m, 2H+2H), 7.32-7.7.18 (m, 3H+3H), 7.12-7.02 (m, 1H+1H), 6.77-6.68 (m, 1H, minor), 6.61 (s, 1H, minor), 6.54-6.48 (m, 2H, major), 6.38 (s, 2H, minor), 6.33 (s, 2H, major), 6.10-5.95 (m, 2H+2H), 5.90-5.72 (m, 1H+1H), 4.60-4.54 (m, 1H+1H), 4.41-3.92 (m, 3H+3H), 3.83-3.70 (m, 9H+9H), 3.56-3.48 (m, 1H, major), 2.95-2.69 (m, 3H+2H), 1.89-1.80 (m, 3H+3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) The peaks are intricately split probably due to the generation of conformers. δ 176.9, 175.91, 175.89, 173.67, 173.64, 171.3, 171.2, 162.0, 161.9, 152.8, 148.3, 147.72, 139.8, 139.7, 138.63, 138.56, 137.3, 135.6, 135.5, 134.94, 134.86, 133.59, 133.58, 132.39, 132.35, 131.2, 131.1, 130.7, 128.9, 128.67, 128.65, 128.51, 128.48, 128.37, 128.36,

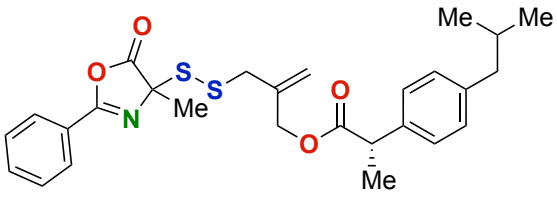
128.1, 127.9, 125.0, 109.8, 109.7, 108.2, 107.01, 107.00, 101.72, 101.71, 76.4, 76.3, 74.5, 74.4, 71.4, 71.3, 60.9, 56.30, 56.29, 45.6, 45.5, 43.83, 43.81, 40.2, 40.1, 39.49, 39.48, 38.74, 38.73, 38.6, 22.4, 22.3, 21.37; **HRMS** (FAB$^+$) Calcd for $C_{40}H_{35}NO_{11}S_2^+$ [M]$^+$ 769.1646, found 769.1657.

Benzyl N^6-(2-benzamido-2-((2-(2-oxo-2-(((5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl)oxy)ethyl)phenyl)disulfanyl)propanoyl)-N^2-((benzyloxy)carbonyl)-*L*-lysinate (20)



Isolated as a 1.3:1 mixture of diastereomers; Yellow oil; R_f 0.28 (hexane/EtOAc = 1/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83-7.78 (m, 2H+2H), 7.56-7.38 (m, 3H+3H), 7.38-7.25 (m, 13H+13H), 7.24-7.18 (m, 1H+1H), 6.69-6.65 (m, 1H+1H), 6.54-6.50 (m, 1H+1H), 6.38-6.33 (m, 2H+2H), 5.99-5.93 (m, 2H+2H), 5.86-5.83 (m, 1H+1H), 5.15-5.07 (m, 3H+3H), 4.60-4.55 (m, 1H+1H), 4.39 (br s, 1H+1H), 4.34-4.28 (m, 1H+1H), 4.15-4.10 (m, 1H+1H), 4.00-3.85 (m, 2H+2H), 3.80 (s, 4H+4H), 3.76-3.73 (m, 3H+3H), 3.71 (s, 6H+6H), 3.23 (br s, 1H+1H), 2.92-2.75 (m, 3H+3H), 1.70-1.25 (m, 8H+8H), 0.90-0.85 (m, 1H+1H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) The peaks are intricately split probably due to the generation of conformers. δ 173.69, 173.67, 172.4, 171.6, 171.5, 169.4, 165.3, 156.2, 152.8, 148.34, 148.33, 147.74, 147.72, 137.3, 136.4, 136.0, 135.2, 134.92, 134.90, 134.8, 133.5, 132.5, 132.4, 132.2, 131.1, 131.0, 130.2, 129.8, 129.2, 128.9, 128.85, 128.77, 128.76, 128.735, 128.725, 128.71, 128.68, 128.67, 128.64, 128.56, 128.44, 128.40, 128.33, 128.30, 128.23, 128.18, 128.1, 127.7, 127.5, 127.0, 109.8, 108.2, 107.10, 107.07, 101.7, 74.53, 74.51, 73.38, 73.36, 71.5, 67.3, 67.13, 67.09, 60.9, 56.31, 56.28, 53.9, 45.61, 45.57, 43.84, 40.0, 39.7, 38.7, 32.0, 31.0, 29.82, 29.77, 22.8, 22.5, 14.3, 14.2; **HRMS** (ESI$^+$) Calcd for $C_{61}H_{61}N_3O_{15}S_2Na^+$ [M+Na]$^+$ 1162.3436, found 1162.3423.

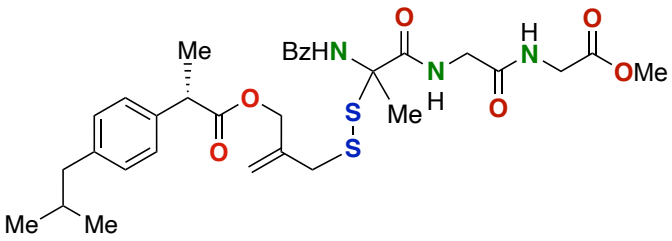
2-(((4-Methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)methyl)allyl (2*S*)-2-(4-isobutylphenyl)propanoate (22)



Isolated as a 1:1 mixture of diastereomers; Colorless oil; TLC R_f 0.33 (hexane/EtOAc = 6/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08-8.00 (m, 2H+2H), 7.66-7.59 (m, 1H+1H), 7.55-7.49 (m, 2H+2H), 7.18-7.14 (m, 2H+2H), 7.08-7.03 (m, 2H+2H), 5.06-5.02 (m, 1H+1H), 5.02-4.97 (m,

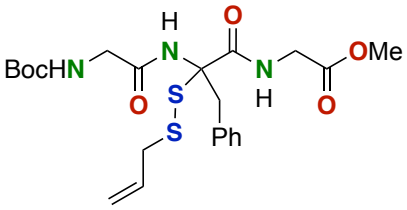
1H+1H), 4.55-4.43 (m, 2H+2H), 3.682 (q, J = 7.2 Hz, 1H), 3.678 (q, J = 7.2 Hz, 1H), 3.24-3.15 (m, 2H+2H), 2.42 (d, J = 7.2 Hz, 2H), 2.41 (d, J = 7.2 Hz, 2H), 1.87-1.74 (m, 4H+4H), 1.474 (d, J = 7.2 Hz, 3H), 1.471 (d, J = 7.2 Hz, 3H), 0.871 (d, J = 6.6 Hz, 3H+3H), 0.865 (d, J = 6.6 Hz, 3H+3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 177.2, 177.1 174.2, 161.72, 161.71, 140.7, 137.84, 137.83, 137.6, 133.5, 129.4 , 128.4, 127.3, 125.2, 118.6, 118.5, 76.8, 76.7, 64.92, 64.90, 45.2, 45.1, 42.19, 42.17, 30.3, 22.5, 21.2, 18.37, 18.36; **HRMS** (FAB$^+$) Calcd for $C_{27}H_{32}NO_4S_2^+$ $[M+H]^+$ 498.1767, found 498.1773.

10-Benzamido-10-methyl-14-methylene-3,6,9-trioxo-2-oxa-11,12-dithia-5,8-diazapentadecan-15-yl (2*S*)-2-(4-isobutylphenyl)propanoate (24)



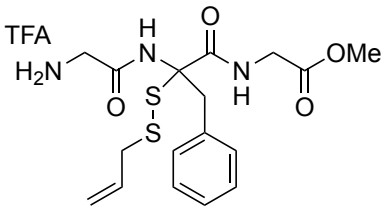
Isolated as a 1:1 mixture of diastereomers; Colorless oil; TLC R_f 0.27 ($CHCl_3$/MeOH = 30/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88-7.78 (m, 3H+3H), 7.56-7.49 (m, 1H+1H), 7.48-7.40 (m, 2H+2H), 7.19-7.13 (m, 2H+2H), 7.10-7.03 (m, 2H+2H), 5.01-4.94 (m, 2H+2H), 4.60-4.46 (m, 2H+2H), 4.13-3.93 (m, 4H+4H), 3.75-3.63 (m, 4H+4H), 3.16 (s, 2H+2H), 2.43 (d, J = 7.1 Hz, 2H+2H), 1.98 (s, 3H+3H), 1.89-1.75 (m, 1H+1H), 1.47 (d, J = 7.1 Hz, 3H+3H), 0.87 (d, J = 6.6 Hz, 6H+6H); **^{13}C{^{1}H} NMR** (150 MHz, CD_3OD) δ 175.8, 173.7, 172.1, 171.7, 169.8, 141.8, 140.40, 140.36, 139.22, 139.17, 134.7, 133.5, 130.4, 129.7, 129.0, 128.3, 117.6, 79.4, 71.4, 65.8, 52.7, 46.2, 46.0, 44.0, 42.9, 41.7, 31.4, 26.4, 22.7, 18.6; **HRMS** (FAB$^+$) Calcd for $C_{32}H_{42}N_3O_7S_2^+$ $[M+H]^+$ 644.2459, found 644.2460.

Methyl (2-(allyldisulfanyl)-2-(2-((*tert*-butoxycarbonyl)amino)acetamido)-3-phenylpropanoyl)glycinate (26)



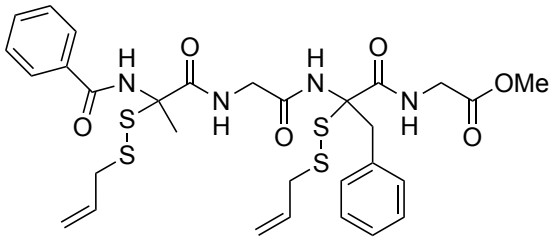
Colorless oil; TLC R_f 0.46 ($CHCl_3$/MeOH = 40/1); **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.50 (br s, 1H), 7.27-7.21 (m, 3H), 7.13-7.08 (m, 2H), 7.14 (br s, 1H), 5.83-6.75 (m, 1H), 5.20-5.15 (m, 2H), 5.09 (br s, 1H), 4.15-4.03 (m, 3H), 3.81 (s, 3H), 3.76 (d, J = 5.6 Hz, 2H), 3.38-3.30 (m, 3H), 1.43 (s, 9H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 169.85, 169.76, 168.5, 156.0, 134.5, 132.7, 130.0, 128.6, 127.6, 119.6, 80.5, 72.4, 52.7, 45.1, 42.1, 42.0, 40.5, 28.4; **HRMS** (FAB$^+$) Calcd for $C_{22}H_{32}N_3O_6S_2^+$ $[M+H]^+$ 498.1727, found. 498.1734.

TFA salt of methyl (2-(allyldisulfanyl)-2-(2-aminoacetamido)-3-phenylpropanoyl)glycinate (27·TFA)



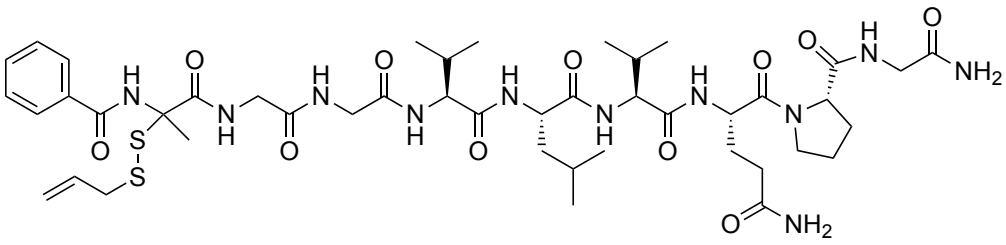
Isolated as the TFA salt with slight impurities. Orange oil; **^{1}H NMR** (400 MHz, CD_3OD) δ 7.27-7.17 (m, 5H), 5.91-5.77 (m, 1H), 5.22-5.10 (m, 2H), 4.08-3.67 (m, 7H), 3.52-3.32 (m, 4H); **^{13}C{^{1}H} NMR** (150 MHz, CD_3OD) δ 171.45, 171.43, 166.4, 135.7, 134.3, 131.4, 129.2, 124.1, 119.3, 73.8, 49.9, 43.0, 42.5, 42.2, 41.0; **HRMS** (FAB^+) Calcd for $C_{17}H_{24}N_3O_4S_2^+$ $[M+H]^+$ 398.1203, found 398.1210.

Methyl (2-(allyldisulfanyl)-2-(2-(2-(allyldisulfanyl)-2-benzamidopropanamido)acetamido)-3-phenylpropanoyl)glycinate (28)



Isolated as a 1:1 mixture of diastereomers; Orange oil; TLC R_f 0.45 ($CHCl_3$/MeOH = 20/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.89-7.83 (m, 2H+2H), 7.57-7.51 (m, 1H+1H), 7.50-7.43 (m, 3H+3H), 7.26-7.20 (m, 2H+2H), 7.13-6.95 (m, 2H+2H), 6.27 (br s, 1H), 5.84-5.65 (m, 2H+2H), 5.55 (br s, 1H), 5.20-5.02 (m, 4H+4H), 4.13-4.00 (m, 2H+2H), 3.97-3.85 (m, 2H), 3.82-3.79 (m, 3H+3H), 3.78-3.70 (m, 2H), 3.37-3.21 (m, 6H+6H), 2.13-2.07 (m, 3H+3H); **^{13}C{^{1}H} NMR** (150 MHz, $CDCl_3$) δ 171.8, 171.7, 171.6, 169.58, 169.56, 169.55, 169.5, 166.80, 166.75, 165.8, 165.7, 165.6, 134.3, 134.2, 132.63, 132.60, 132.49, 132.45, 132.00, 131.96, 129.83, 129.75, 129.73, 128.7, 128.50, 128.46, 127.59, 127.55, 127.3, 127.1, 127.0, 123.6, 119.4, 119.33, 119.30, 119.2, 72.6, 72.5, 68.5, 68.40, 68.39, 52.62, 52.61, 52.59, 52.58, 44.3, 44.2, 43.1, 42.03, 41.95, 41.90, 41.87, 41.84, 41.75, 41.0, 40.54, 40.48, 23.41, 23.36, 23.34; **HRMS** (FAB^+) Calcd for $C_{30}H_{37}N_4O_6S_4^+$ $[M+H]^+$ 677.1590, found 677.1590.

(2*S*)-1-((2-(Allyldisulfanyl)-2-benzamidopropanoyl)glycylglycyl-L-valyl-L-leucyl-L-valyl-L-glutaminyl)-*N*-(2-amino-2-oxoethyl)pyrrolidine-2-carboxamide (30)



Isolated as a 1:1 mixture of diastereomers; Colorless solid; m.p. 155-158 °C; TLC R_f 0.45 ($CHCl_3$/MeOH = 5/1); **^{1}H NMR** (400 MHz, CD_3OD) δ 8.02-7.96 (m, 2H+2H), 7.63-7.57 (m, 1H+1H), 7.54-7.47 (m, 2H+2H), 5.83-5.69 (m, 1H+1H), 5.09-4.98 (m, 2H+2H), 4.61-4.56 (m, 1H+1H), 4.40-4.30 (m, 2H+2H), 4.12-4.08 (m, 1H+1H), 4.01-3.91 (m, 3H+3H), 3.77-3.69 (m, 4H+4H), 3.29-3.19 (m, 4H+4H), 2.39-2.03 (m, 8H+8H), 1.95-1.92 (m, 5H+5H), 1.75-1.58 (m, 3H+3H), 1.05-0.83 (m, 18H+18H); **^{13}C{^{1}H} NMR** (150 MHz, CD_3OD) δ 177.83, 177.80, 175.1, 175.0, 174.67, 174.61, 174.4, 174.3, 174.1, 173.9, 172.82, 172.77, 172.50, 172.47, 172.2, 172.1, 170.2, 170.1, 163.3, 163.1, 134.61, 134.58, 134.21, 134.16, 133.62, 133.56, 129.7, 129.13, 129.11, 119.3, 119.1, 79.5, 71.8, 71.5, 71.4, 62.4, 62.3, 61.8, 61.6, 55.8, 53.5, 53.3, 52.0, 51.9, 44.7, 43.9, 43.8, 43.7, 43.53, 43.25, 43.21, 41.12, 41.07, 31.9, 31.8, 31.3, 31.2, 30.5, 30.4, 28.2, 28.1, 26.9, 26.3, 26.13, 26.12, 25.8, 23.6, 23.5, 21.6, 21.4, 19.75, 19.73, 19.68, 19.1, 19.0, 18.7, 17.3, 13.1; **HRMS** (FAB^+) Calcd for $C_{45}H_{70}N_{11}O_{11}S_2^+$ $[M+H]^+$ 1004.4692, found 1004.4711.

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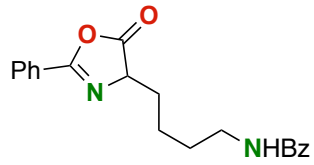
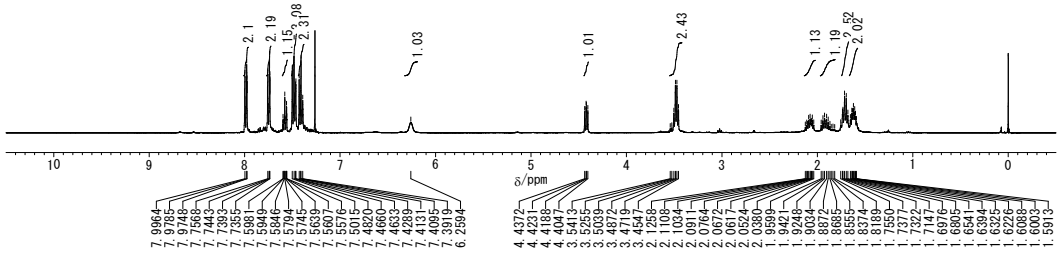
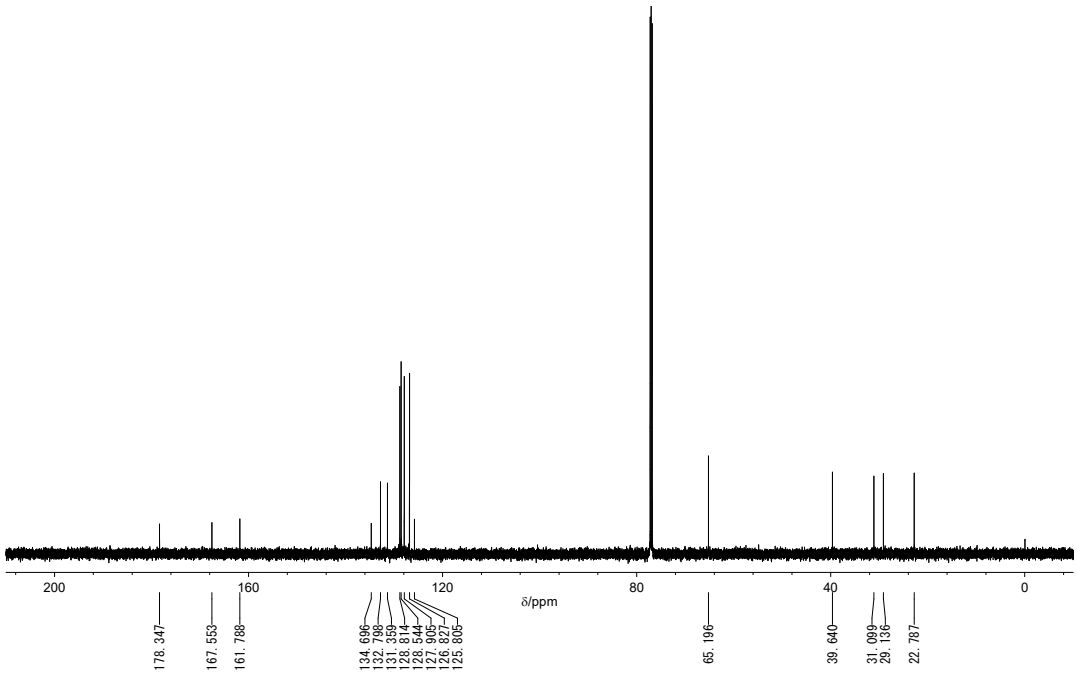
S13 D. Uraguchi, Y. Asai, T. Ooi, *Angew. Chem. Int. Ed.* **2009**, *48*, 733-737.

^{1}H and ^{13}C NMR Spectra of Compounds

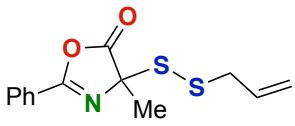
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *N*-(4-(5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)butyl)benzamide (**1c**) ($CDCl_3$)

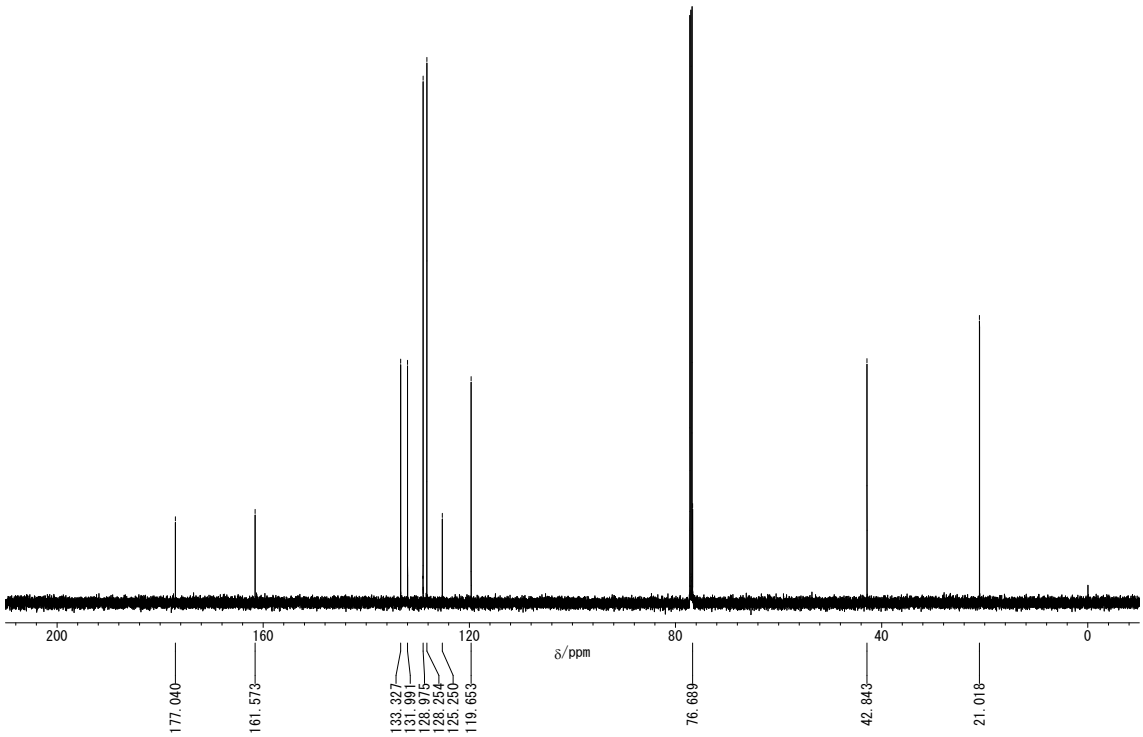




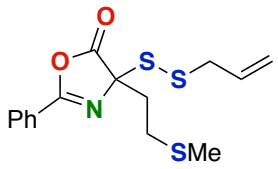


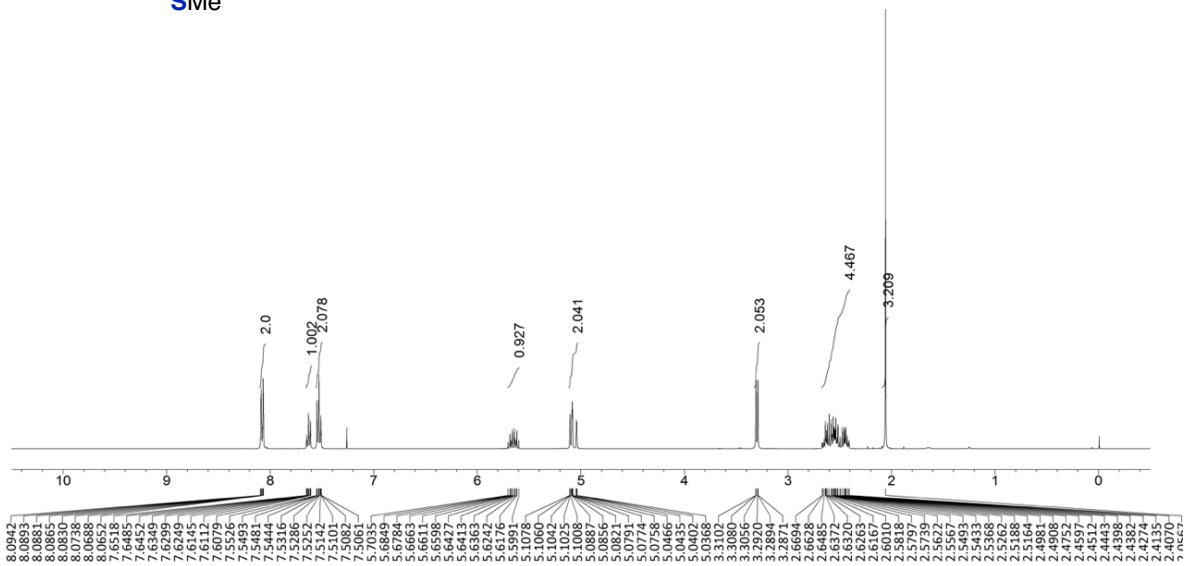
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 4-(allyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aa**) ($CDCl_3$)

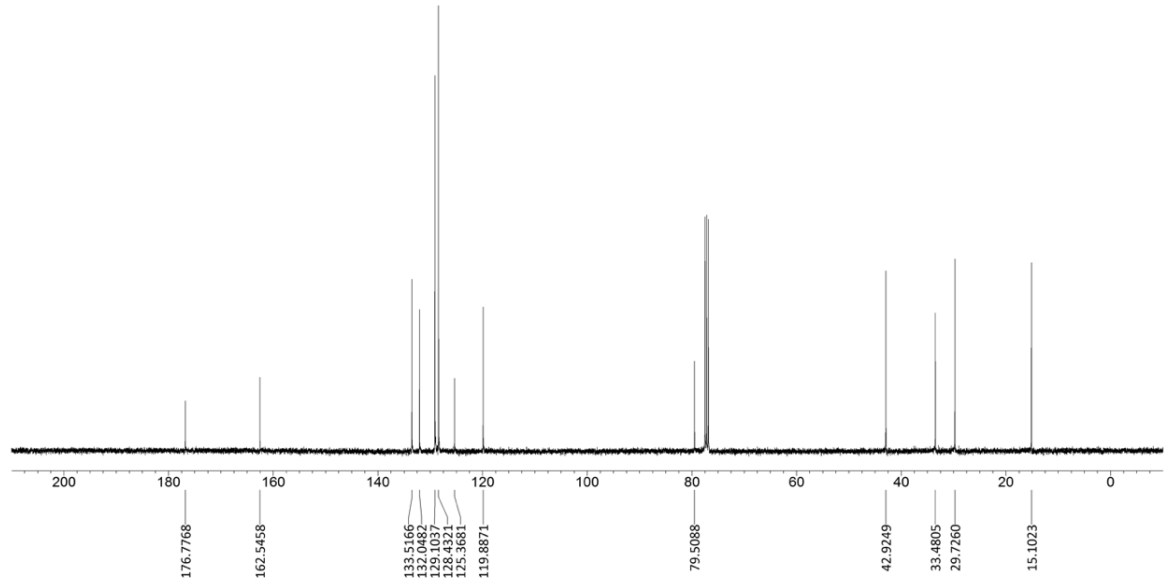




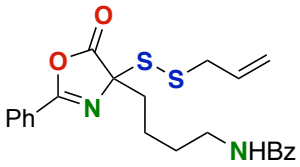
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(allyldisulfanyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (**3ba**) ($CDCl_3$)

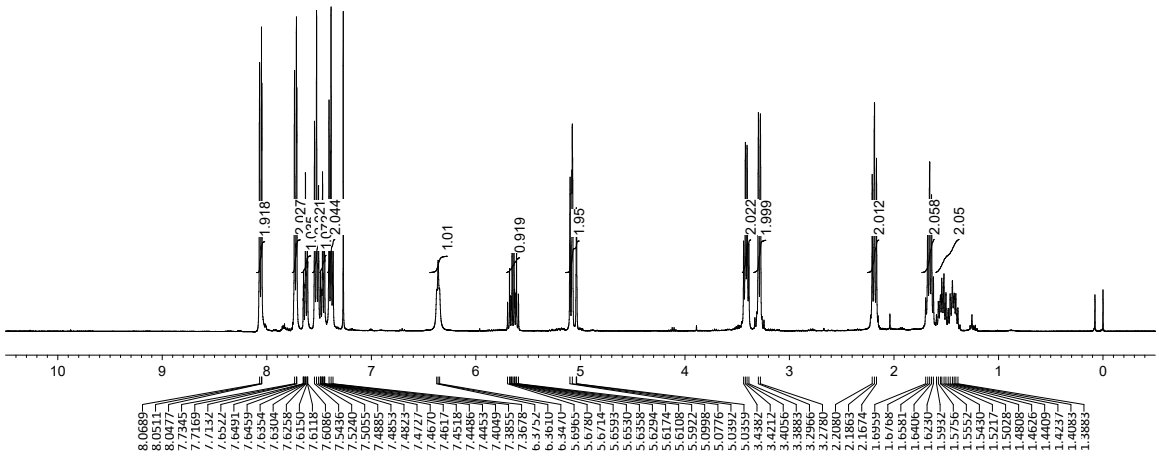


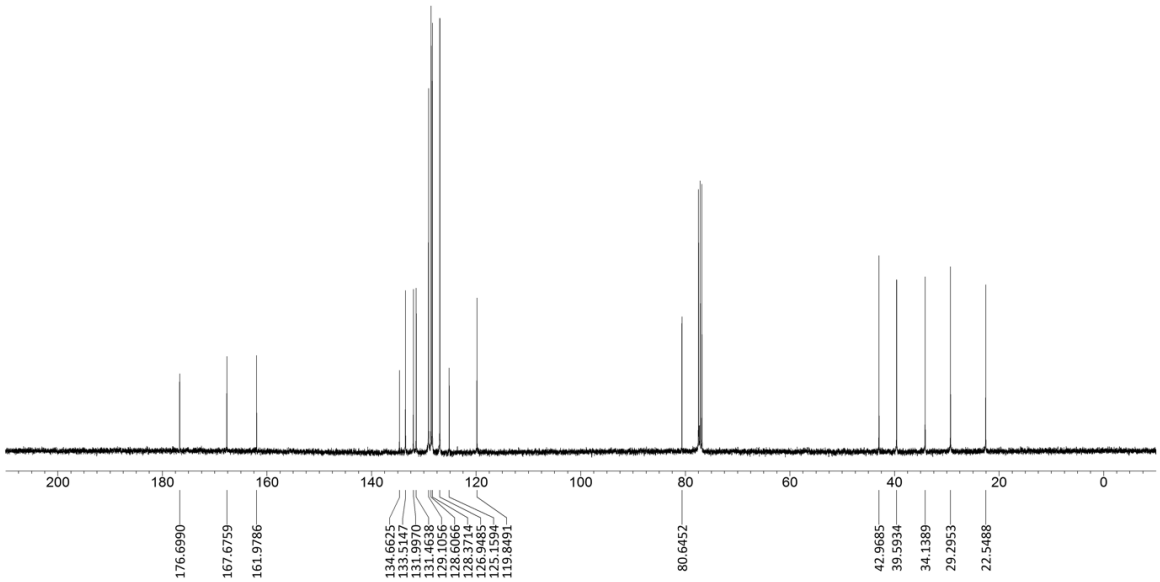




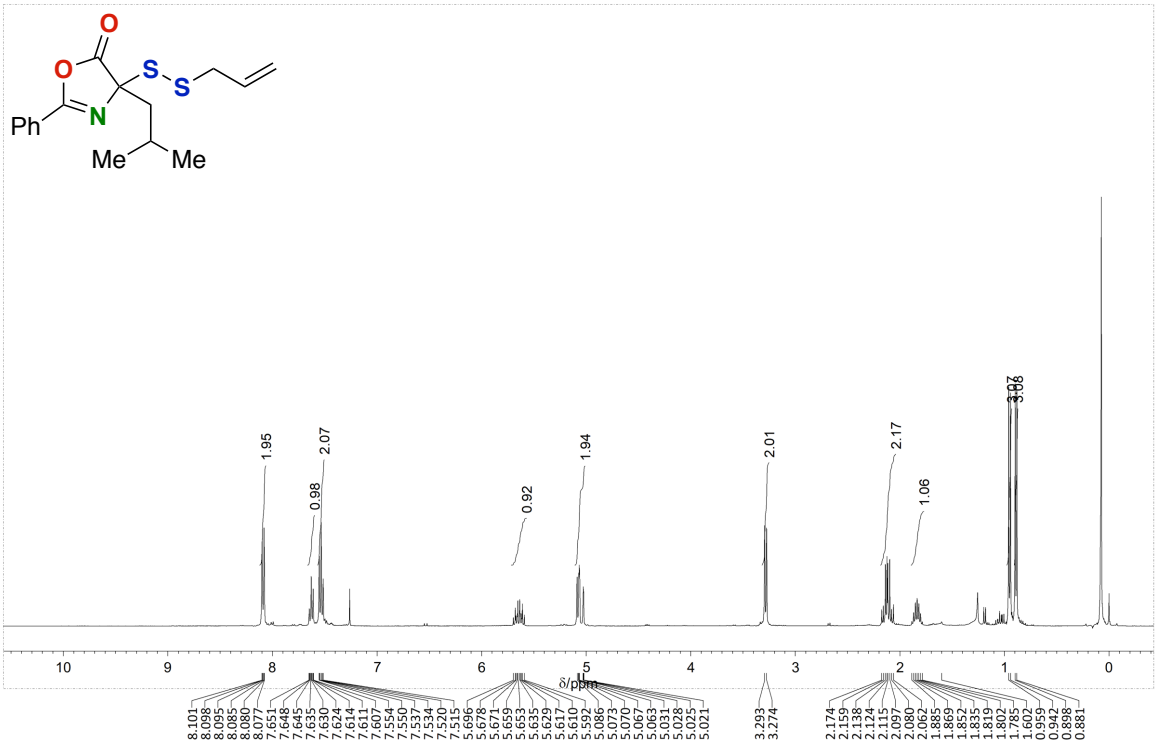
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of *N*-(4-(4-(allyldisulfanyl)-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)butyl)benzamide (**3ca**) ($CDCl_3$)

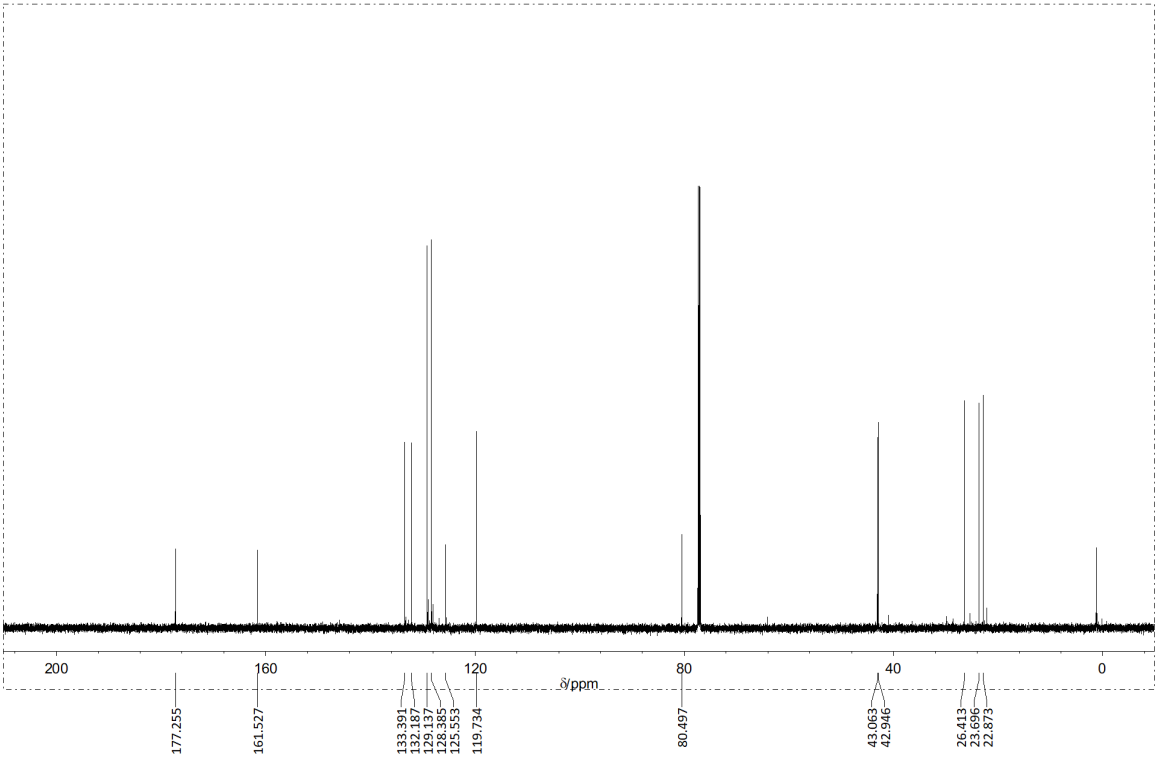




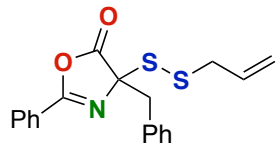


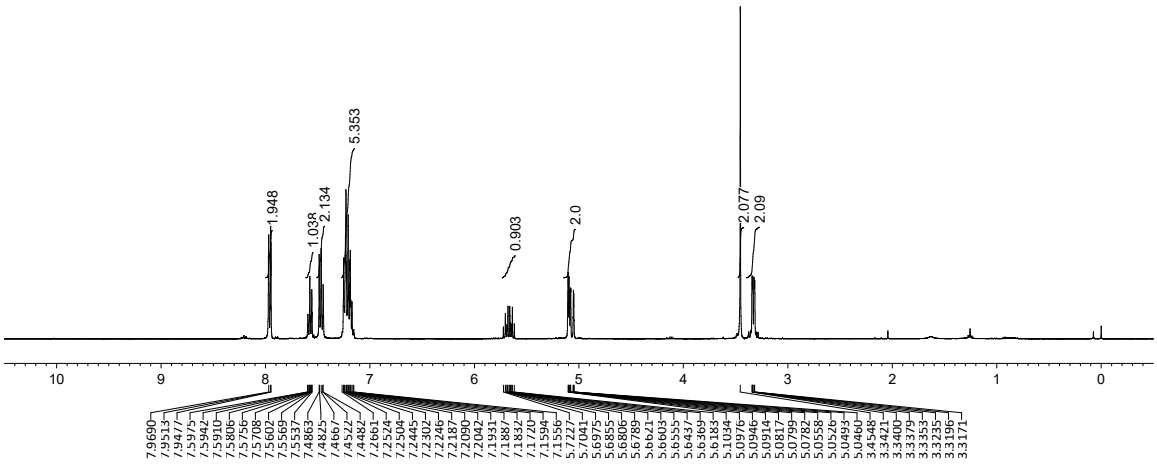
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(allyldisulfanyl)-4-isobutyl-2-phenyloxazol-5(4*H*)-one (**3da**) ($CDCl_3$)

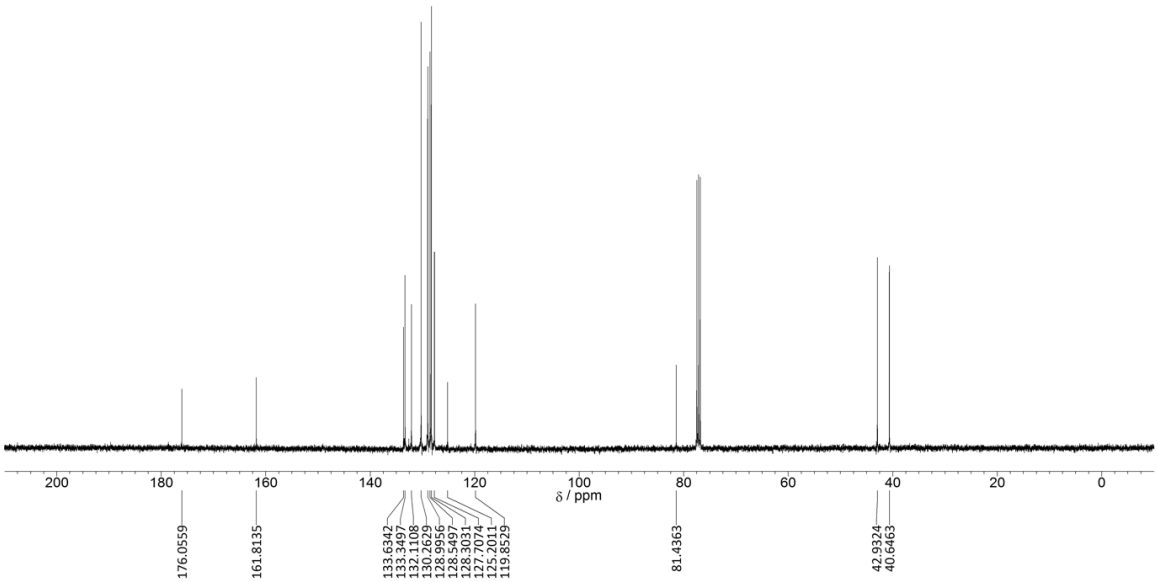




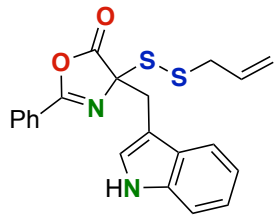
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(allyldisulfanyl)-4-benzyl-2-phenyloxazol-5(4*H*)-one (**3ea**) ($CDCl_3$)

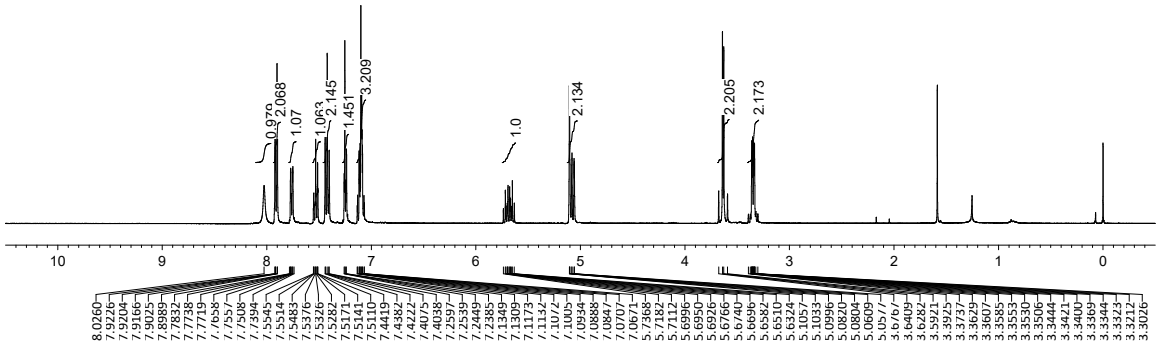


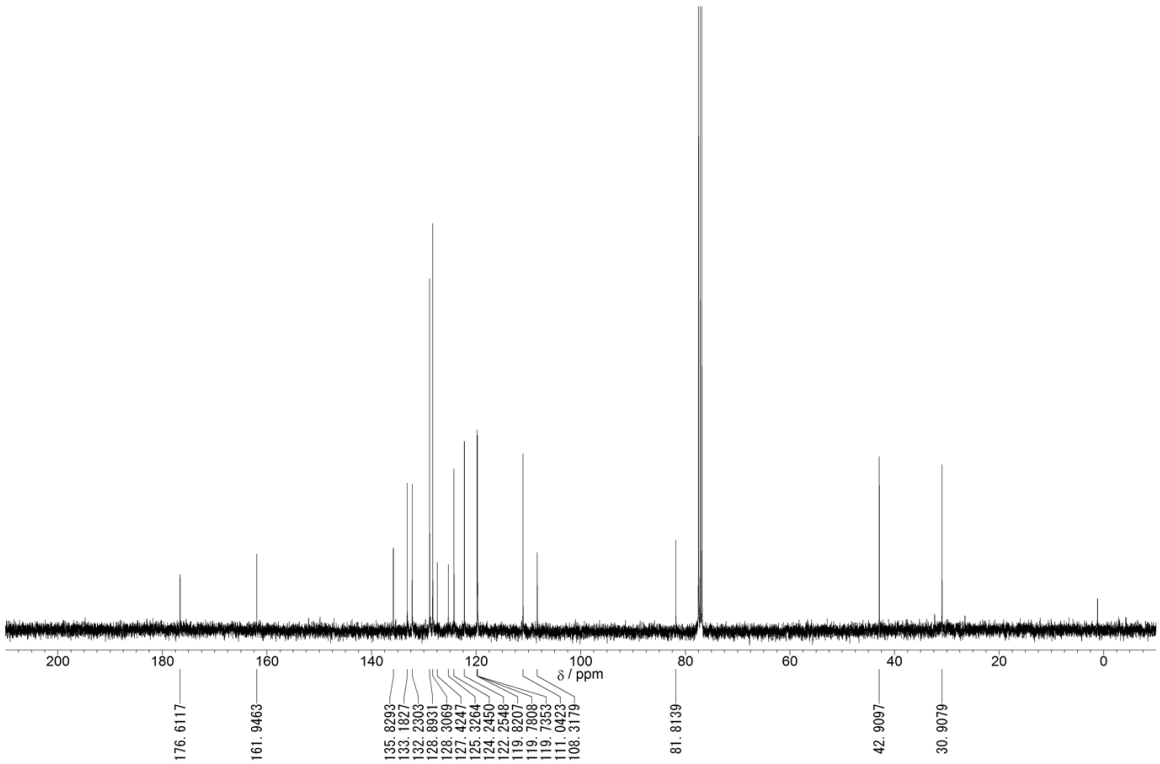




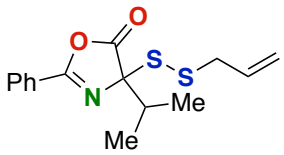
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-((1*H*-indol-3-yl)methyl)-4-(allyldisulfanyl)-2-phenyloxazol-5(4*H*)-one (**3fa**) ($CDCl_3$)

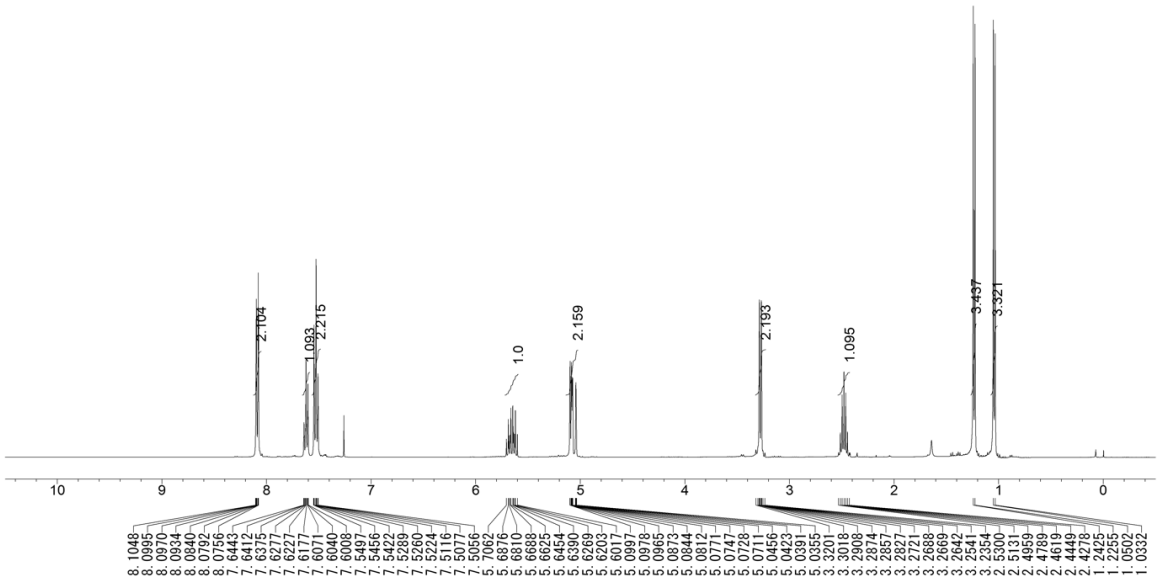


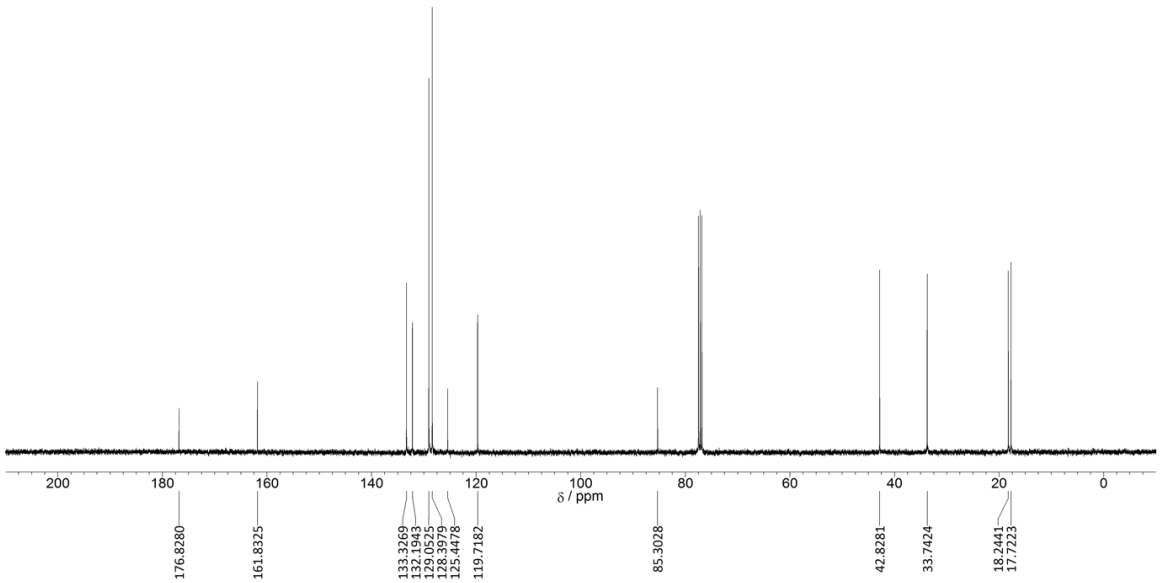




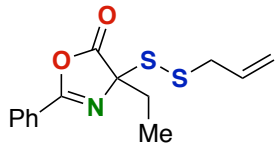
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(allyldisulfanyl)-4-isopropyl-2-phenyloxazol-5(4*H*)-one (**3ga**) ($CDCl_3$)

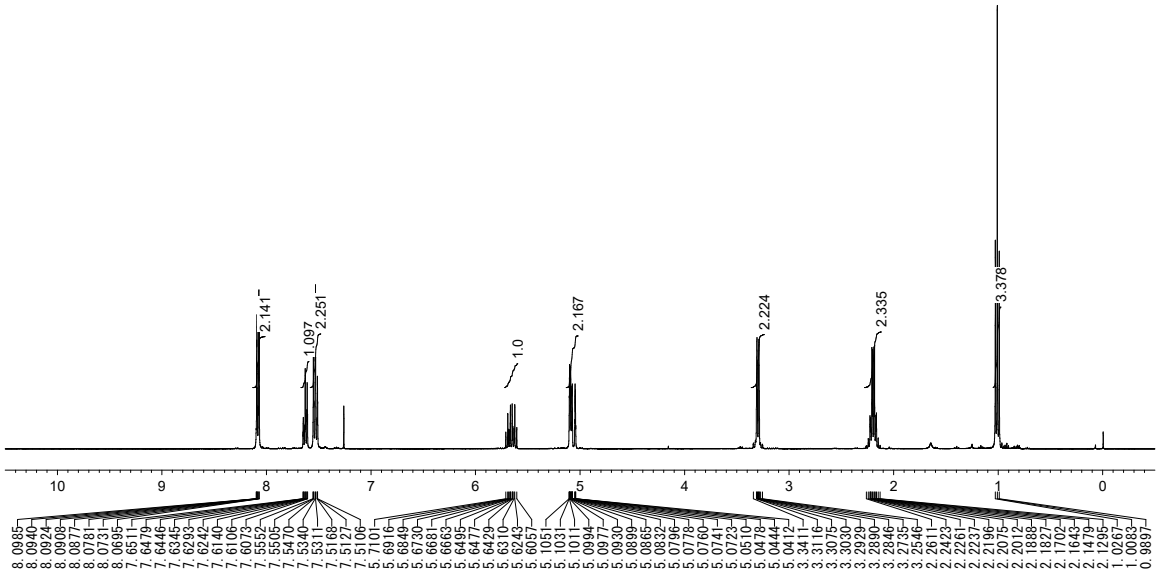


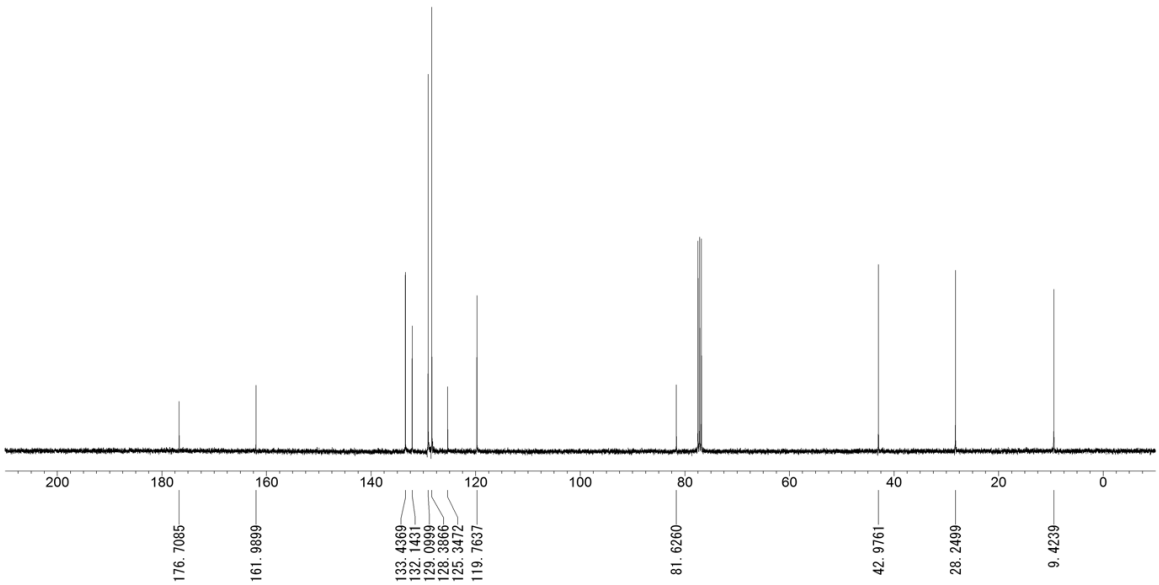




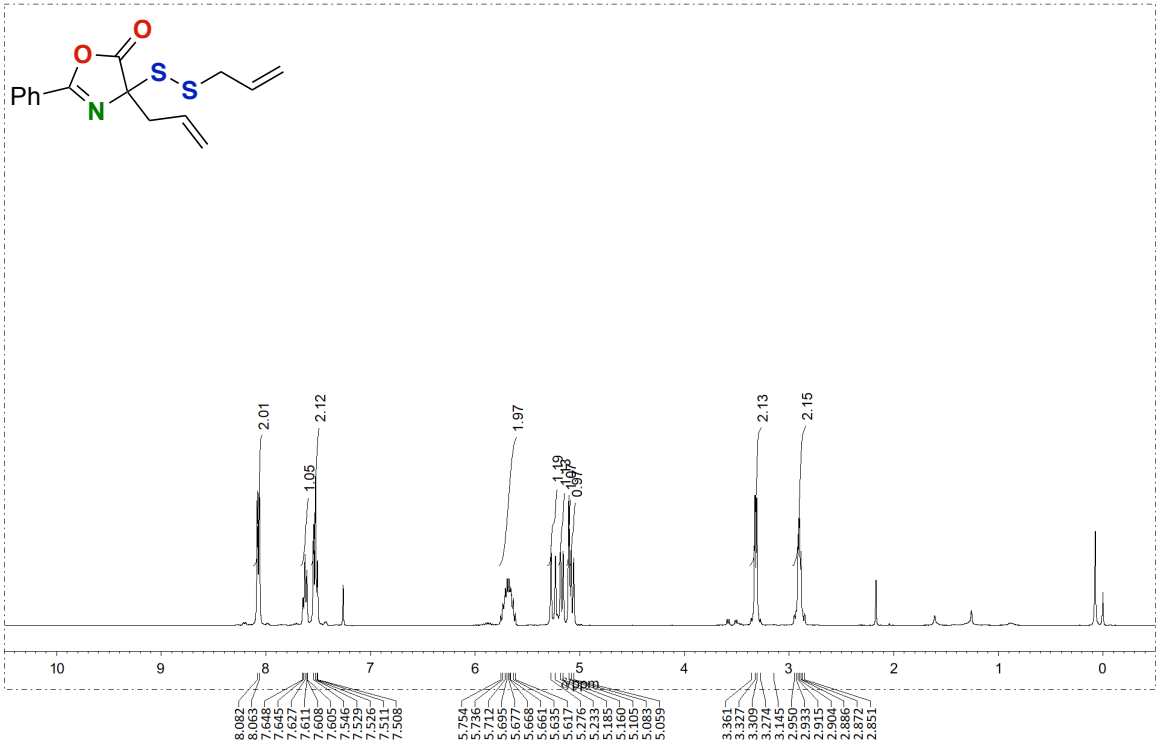
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(allyldisulfanyl)-4-ethyl-2-phenyloxazol-5(4*H*)-one (**3ha**) ($CDCl_3$)

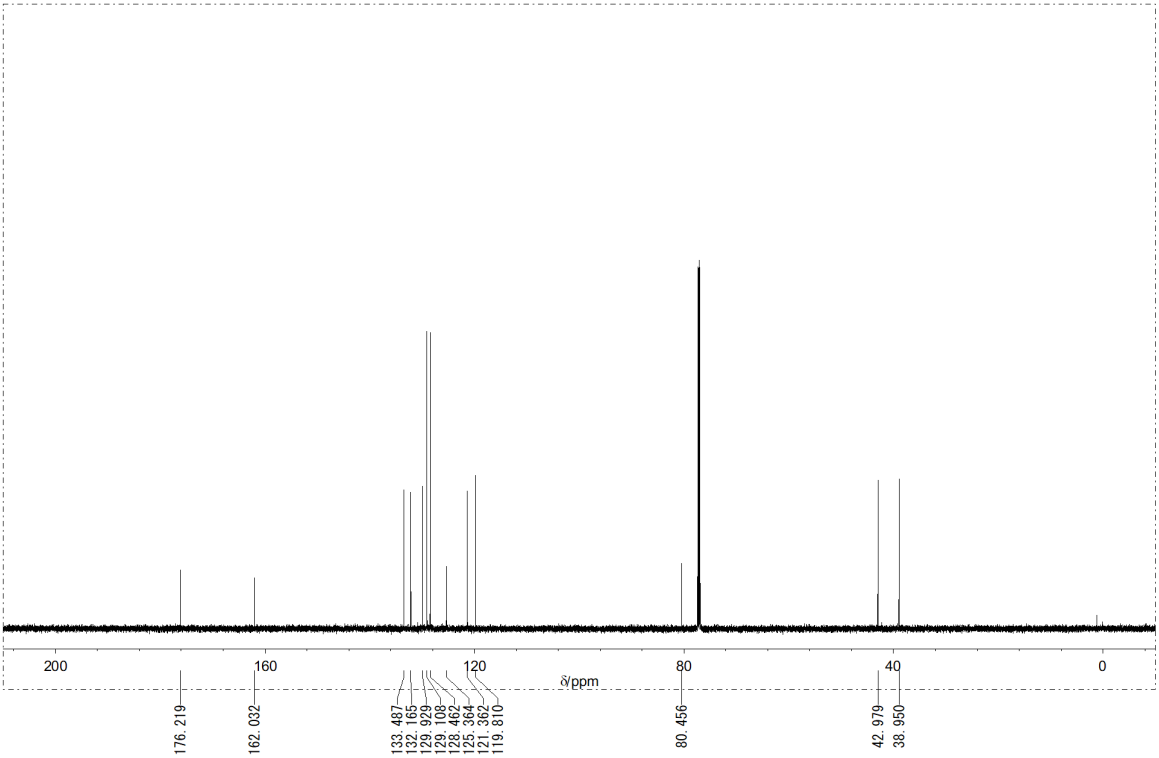




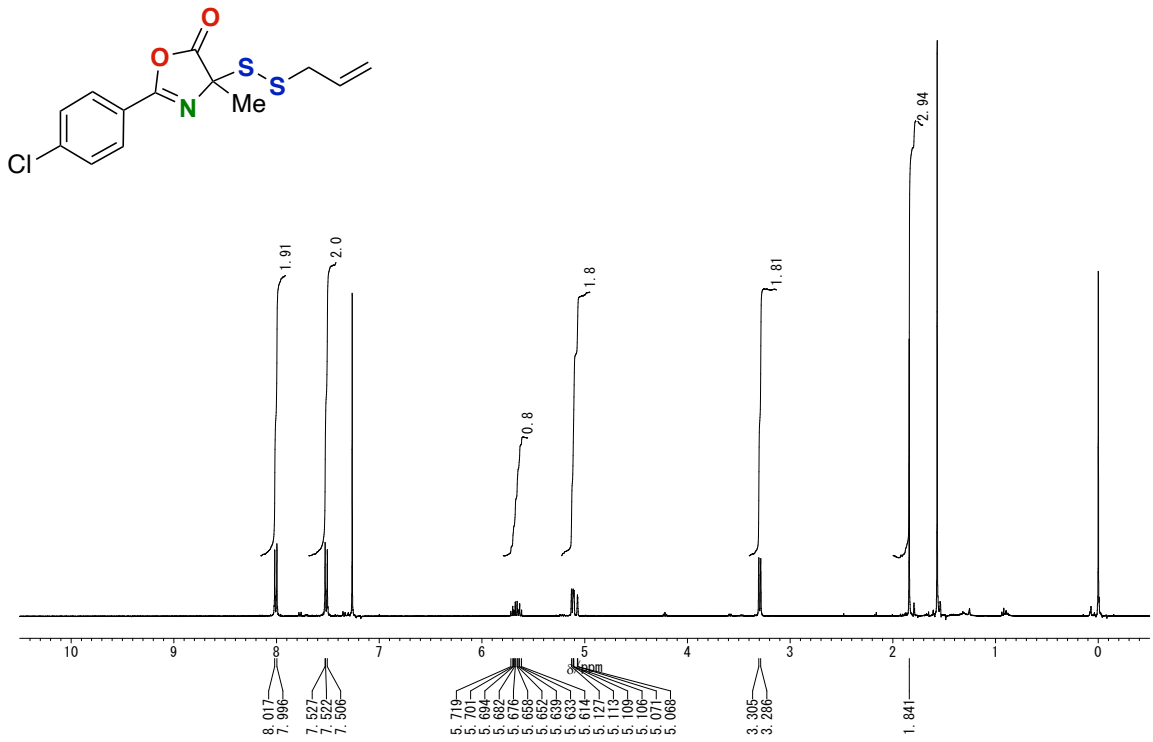


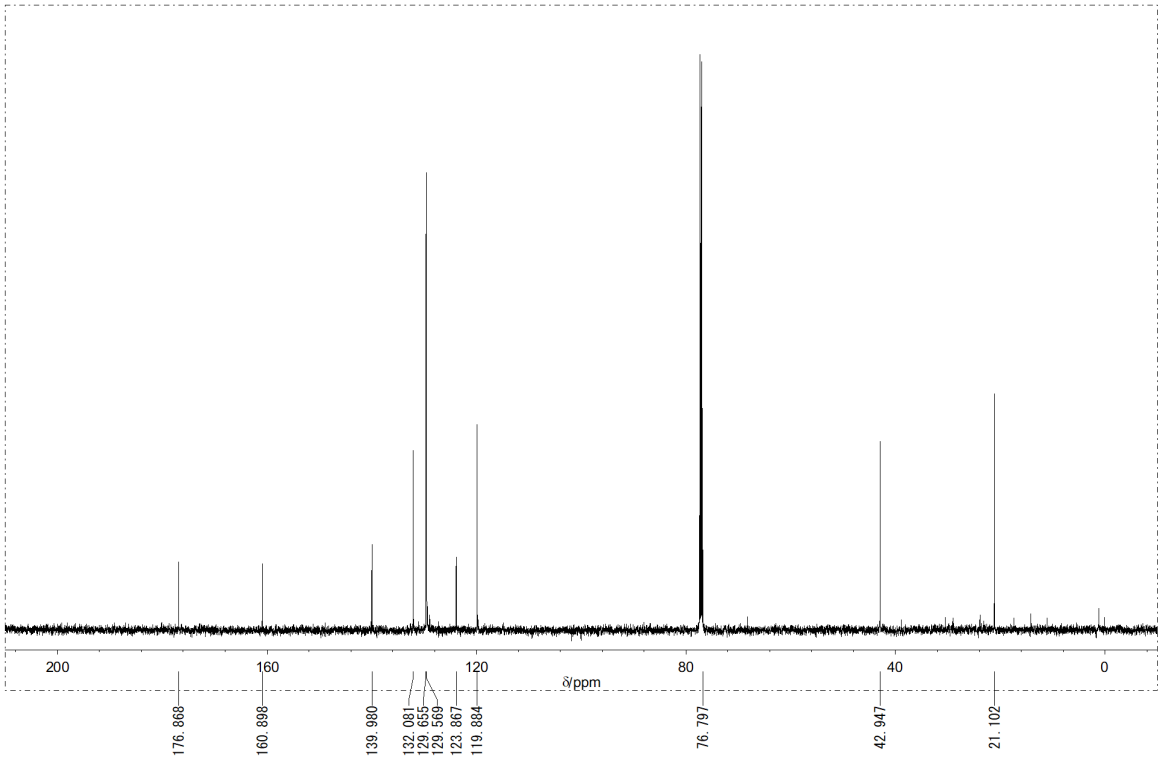
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 4-allyl-4-(allyldisulfanyl)-2-phenyloxazol-5(4*H*)-one (**3ia**) ($CDCl_3$)



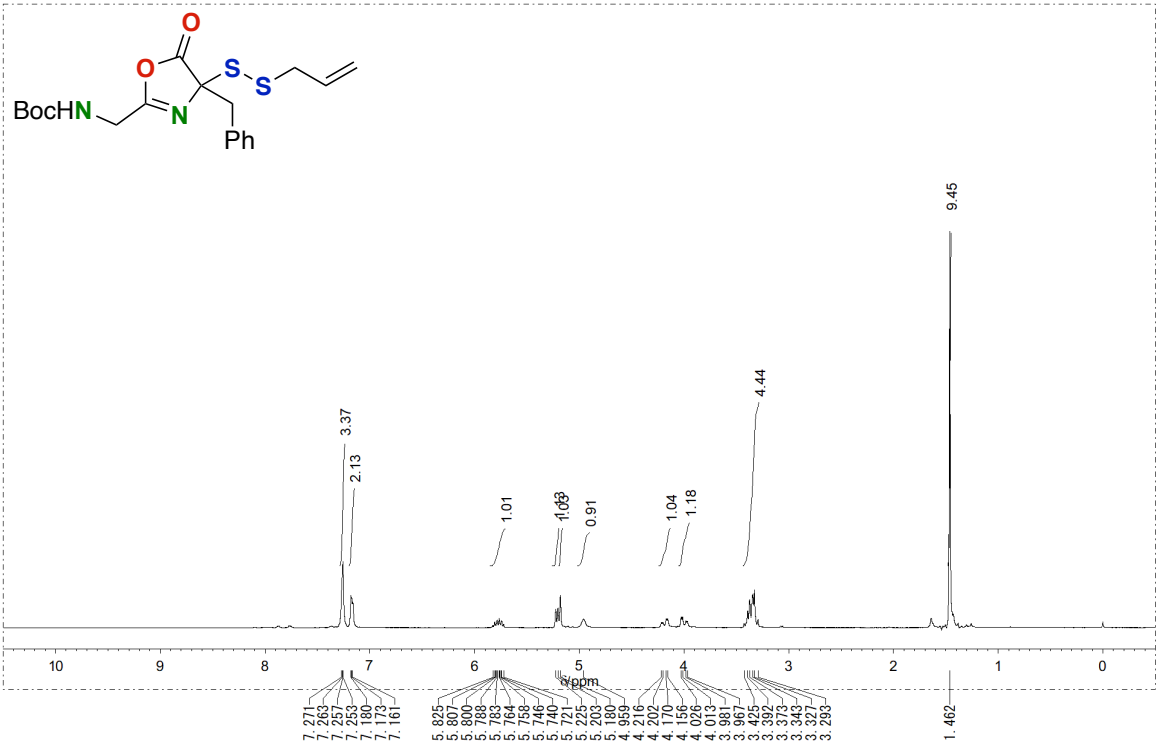


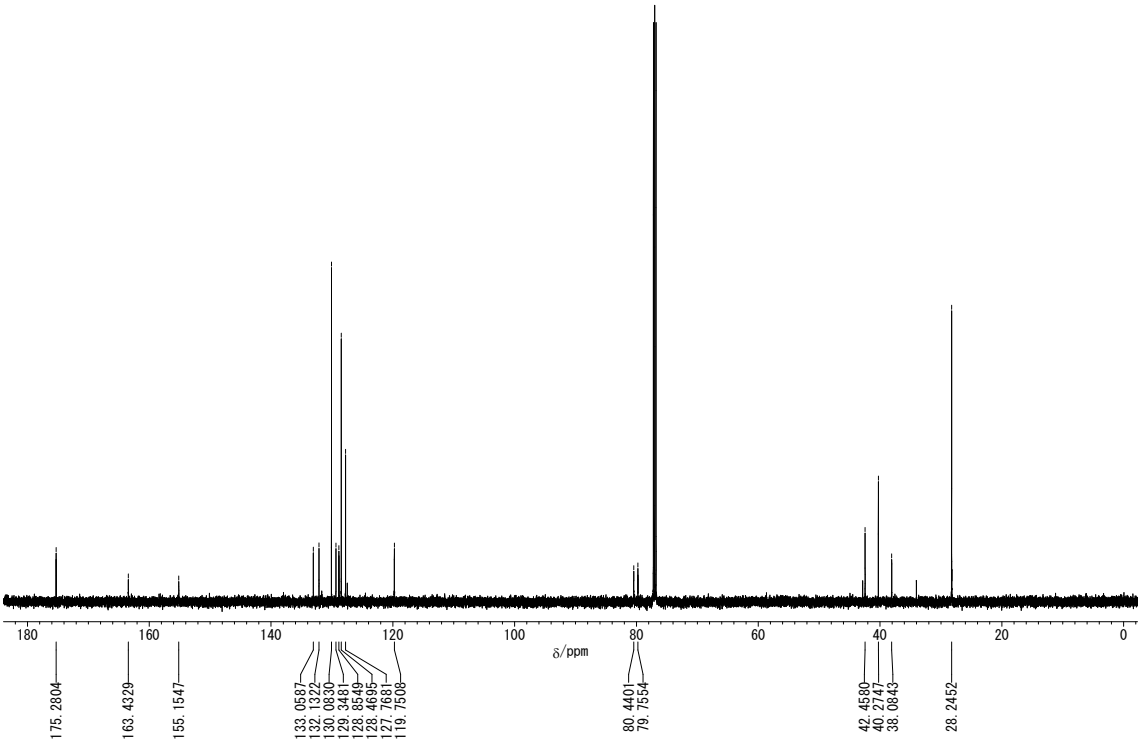
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 4-(allyldisulfanyl)-2-(4-chlorophenyl)-4-methyloxazol-5(4*H*)-one (**3ja**) ($CDCl_3$)



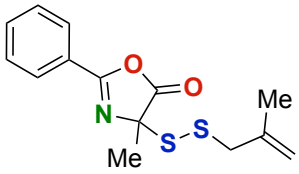


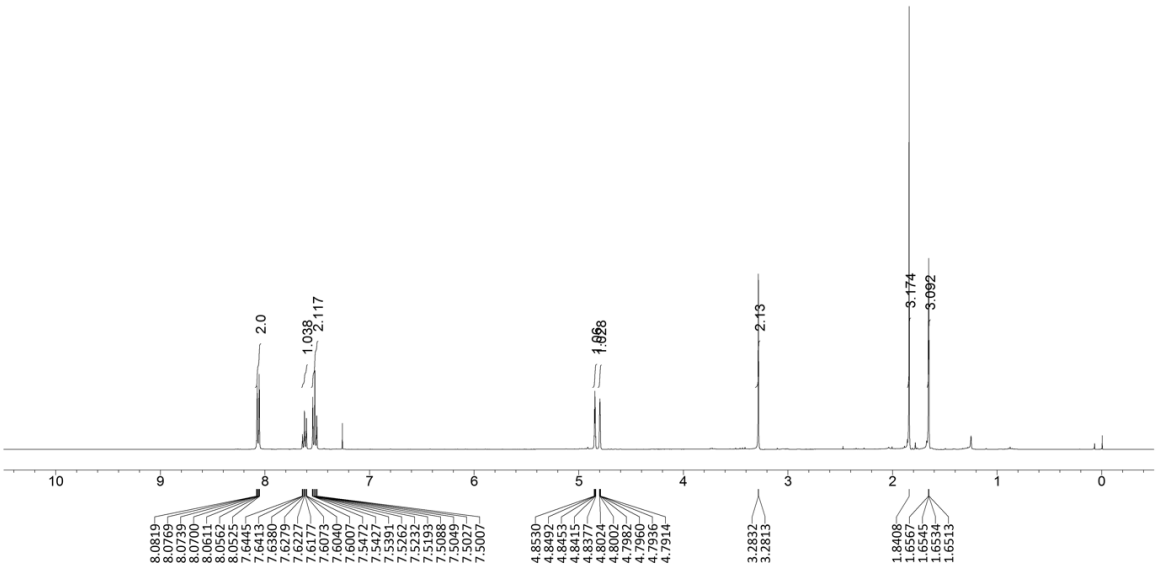
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of *tert*-butyl ((4-(allyldisulfanyl)-4-benzyl-5-oxo-4,5-dihydrooxazol-2-yl)methyl)carbamate (**3ka**) ($CDCl_3$)

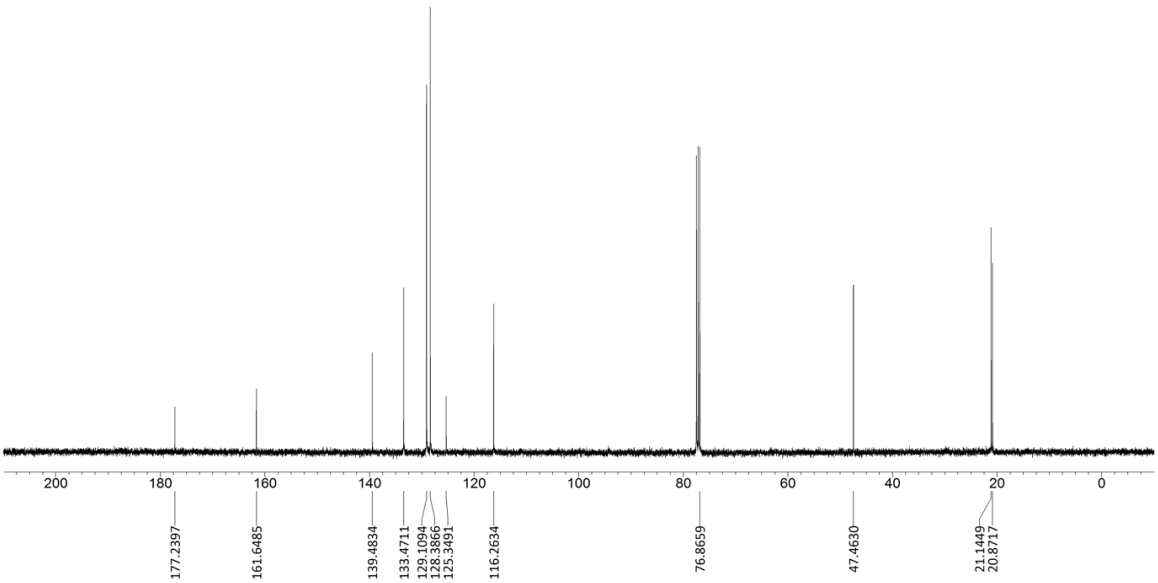




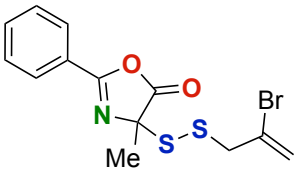
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-methyl-4-((2-methylallyl)disulfanyl)-2-phenyloxazol-5(4*H*)-one (**3ab**) ($CDCl_3$)

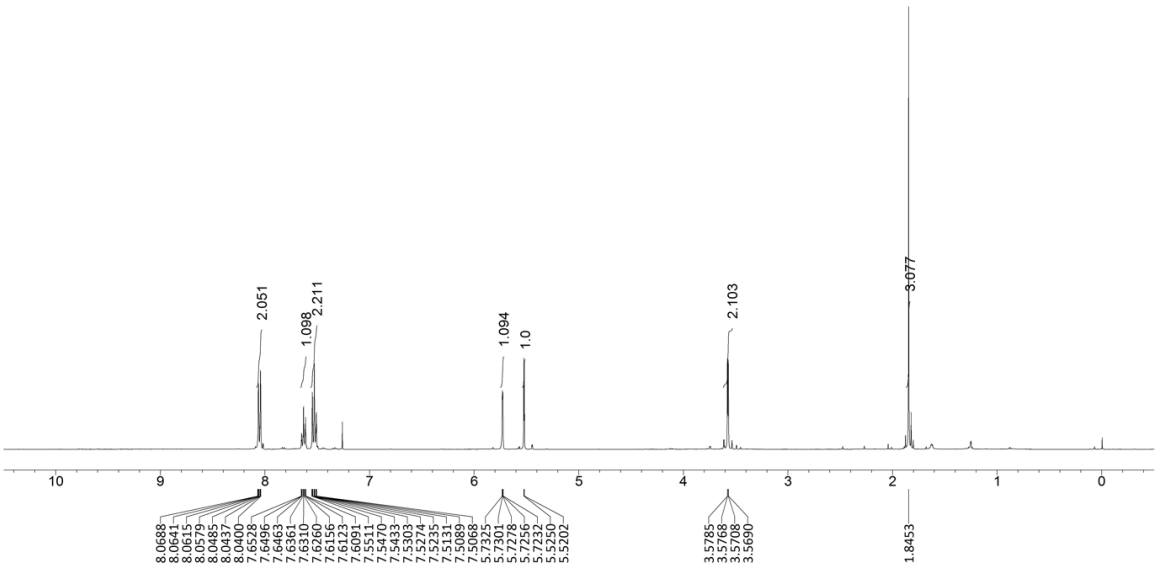


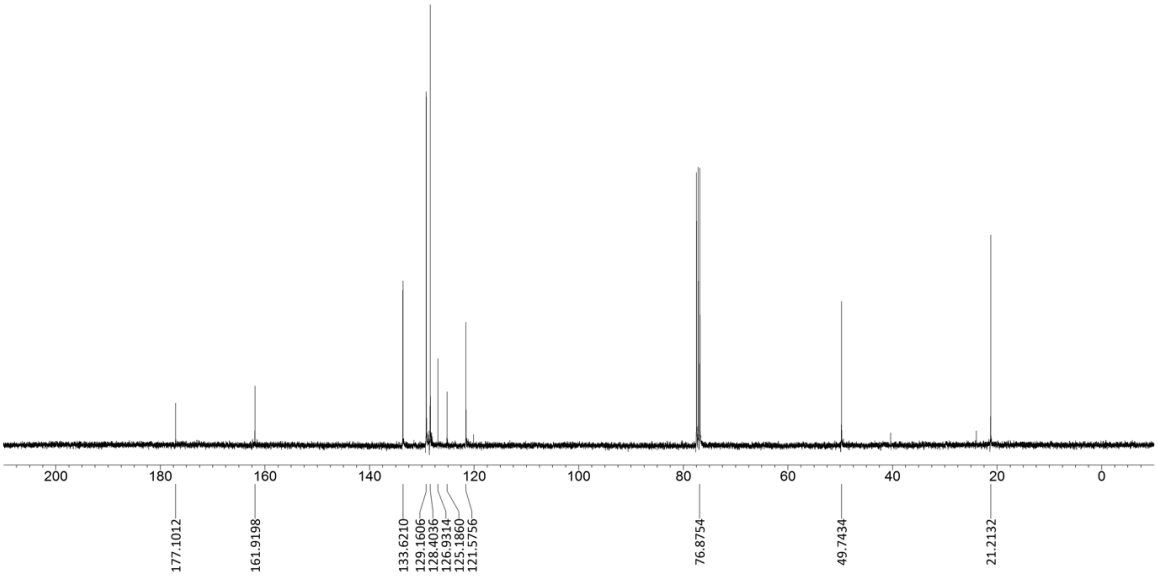




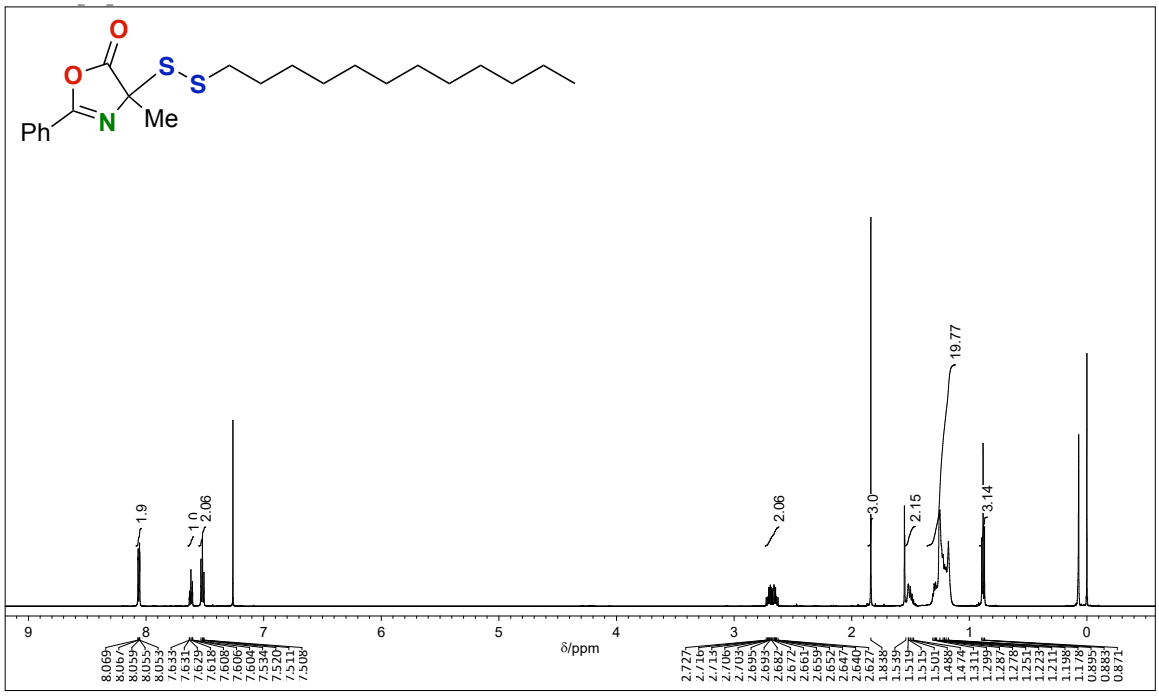
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-((2-bromoallyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3ac**) ($CDCl_3$)

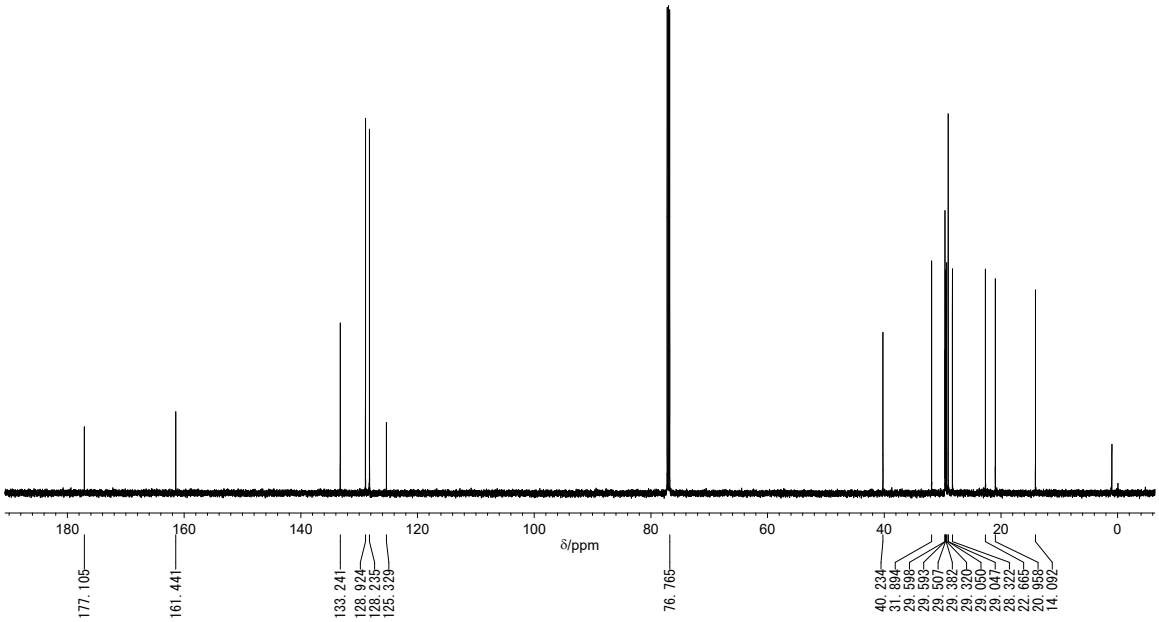




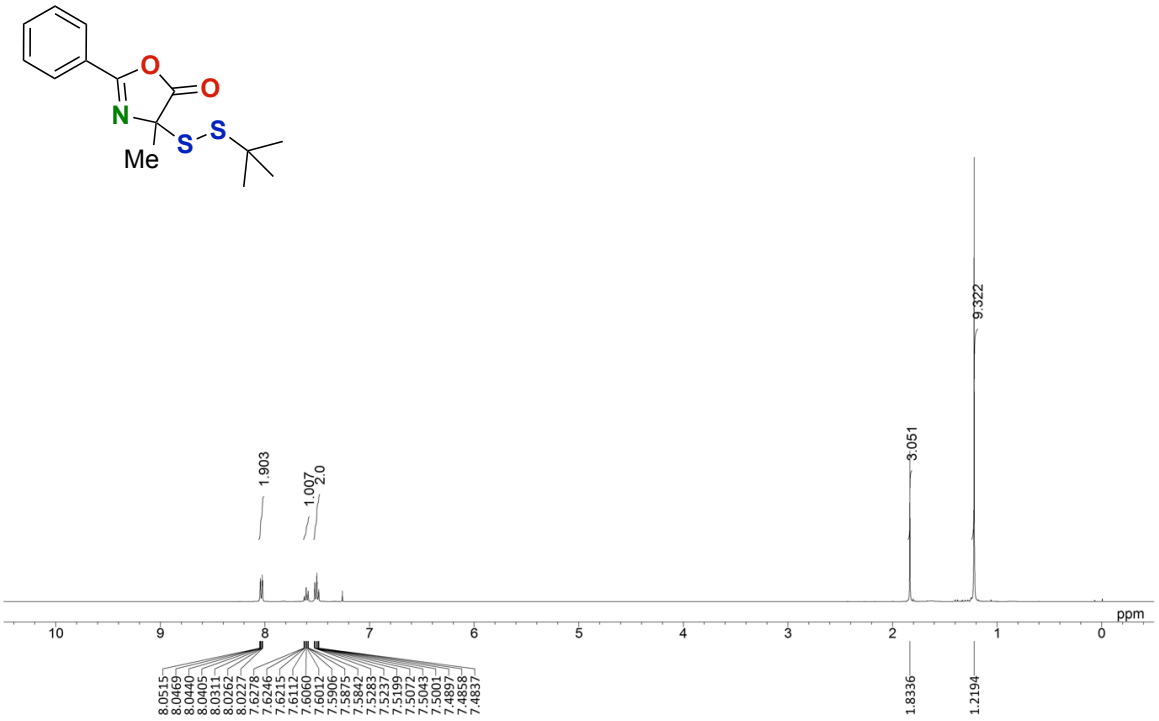


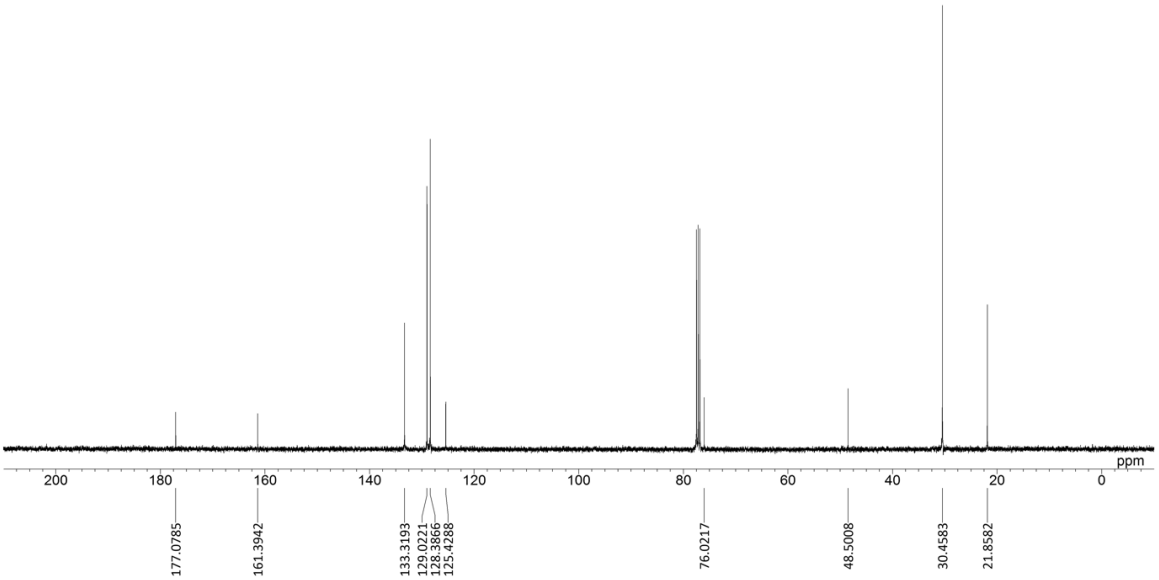
^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra of 4-(dodecyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3ad**) ($CDCl_3$)



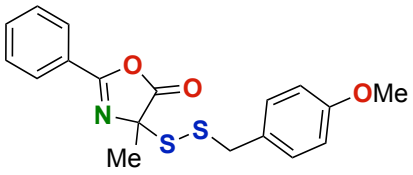


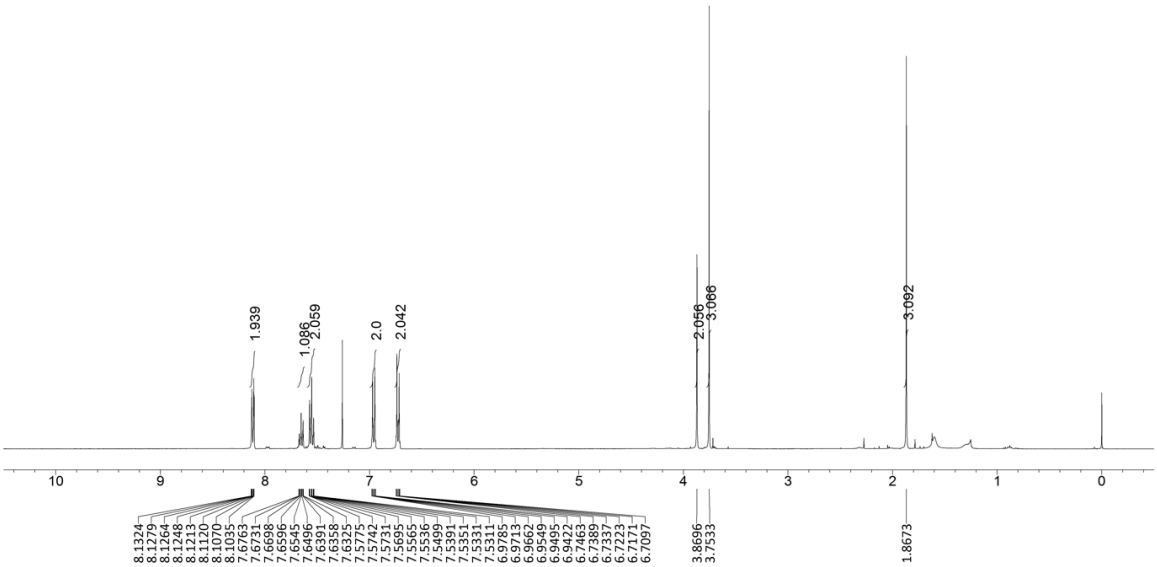
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-(*tert*-butyldisulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3ae**) ($CDCl_3$)

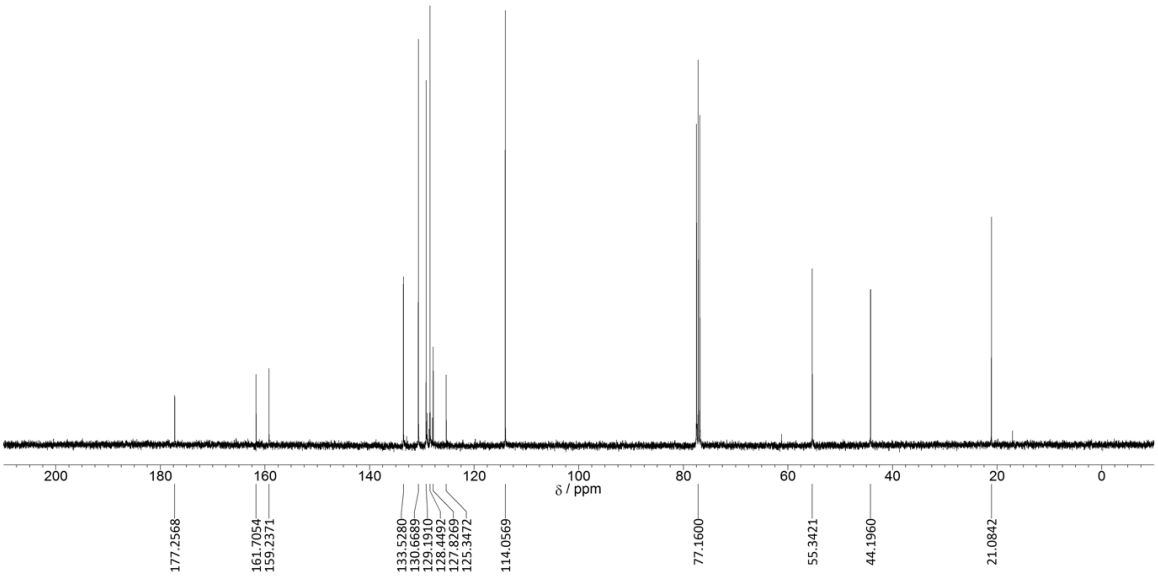




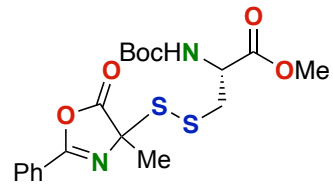
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-((4-methoxybenzyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3af**) ($CDCl_3$)

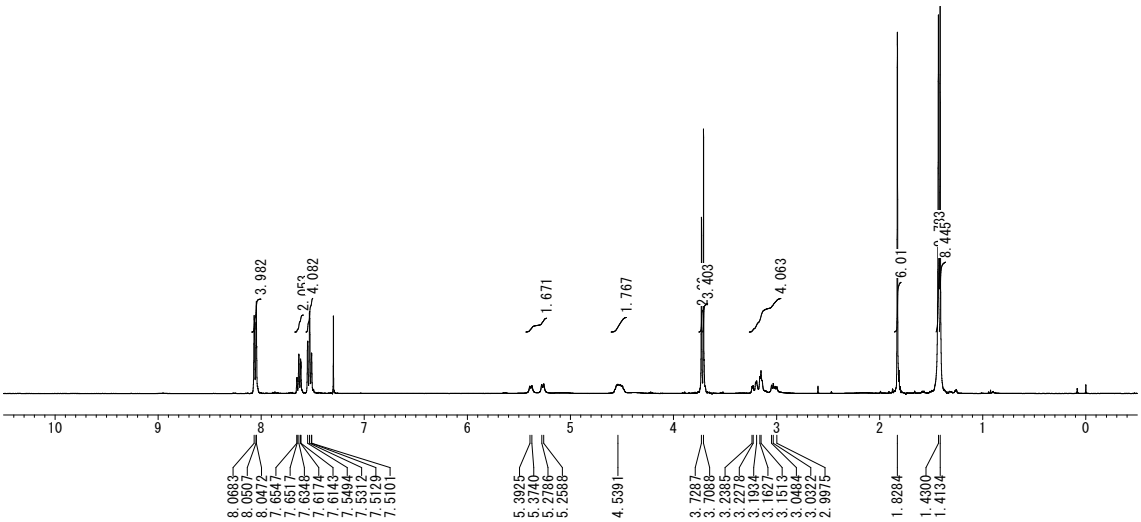


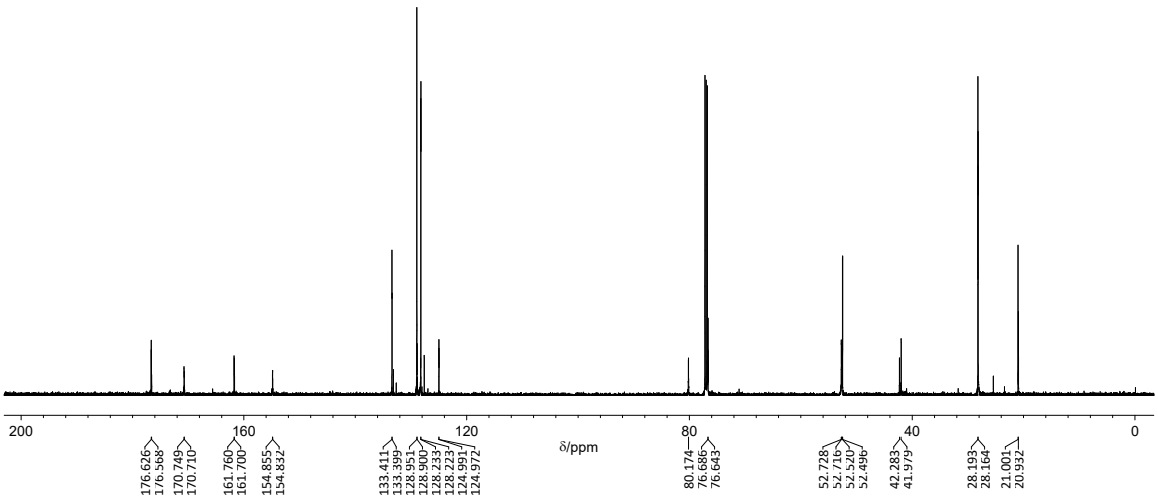




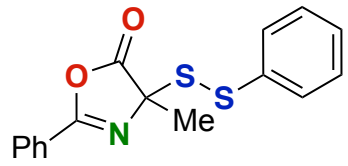
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of methyl *N*-(*tert*-butoxycarbonyl)-*S*-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)thio)-L-cysteinate (**3ag**) ($CDCl_3$)

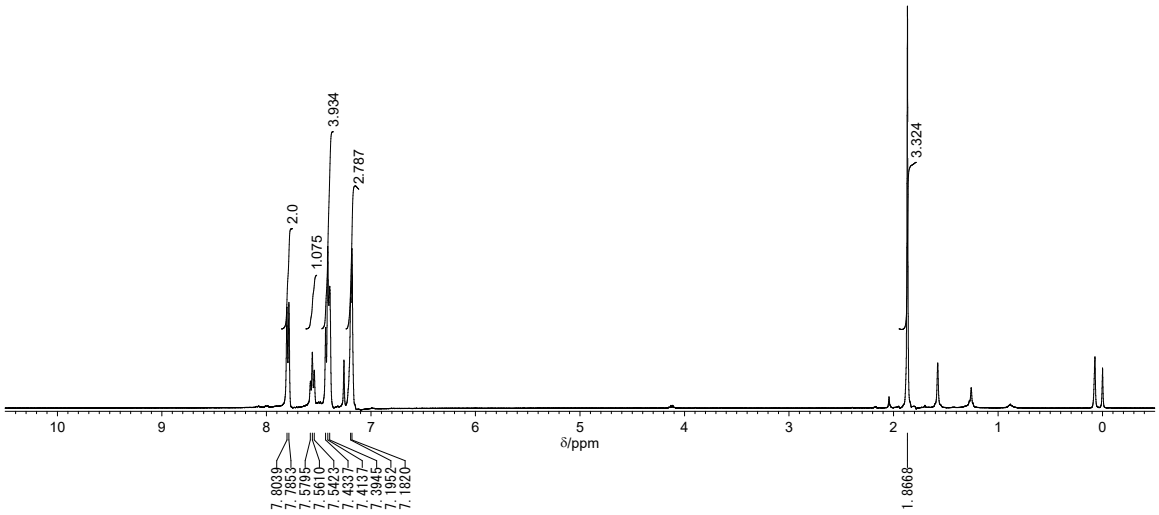


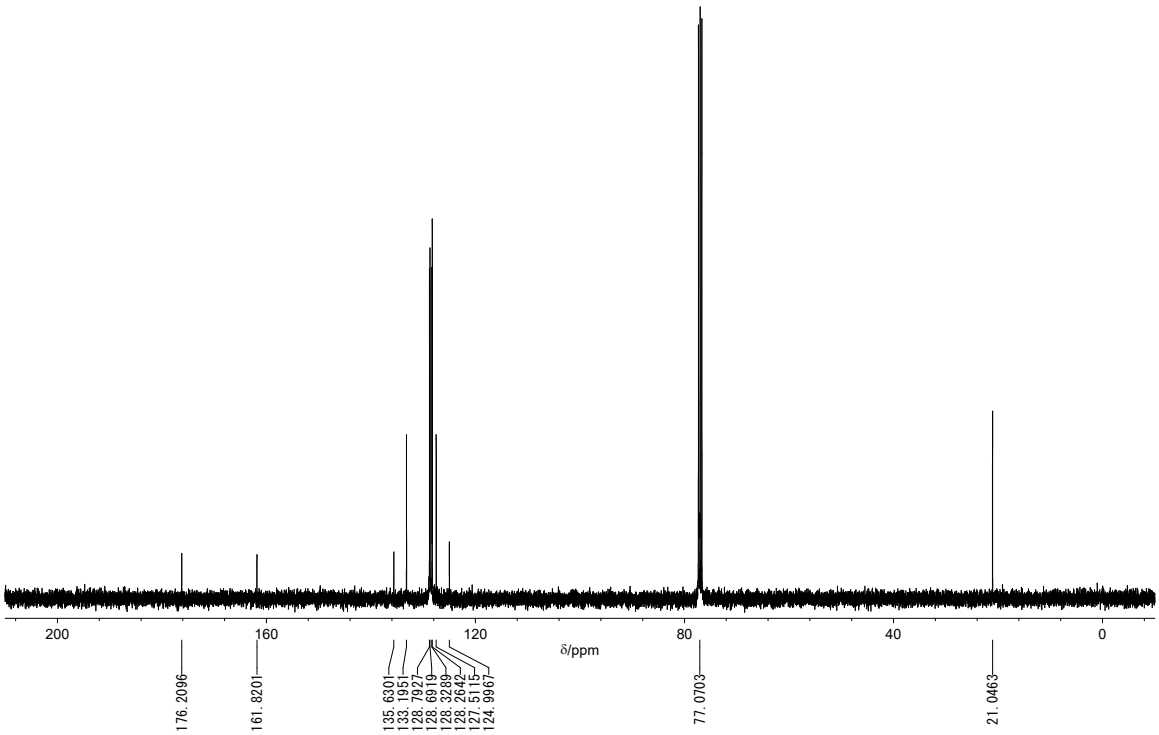




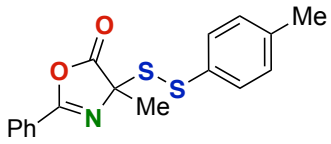
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-methyl-2-phenyl-4-(phenyldisulfanyl)oxazol-5(4*H*)-one (**3ah**) ($CDCl_3$)

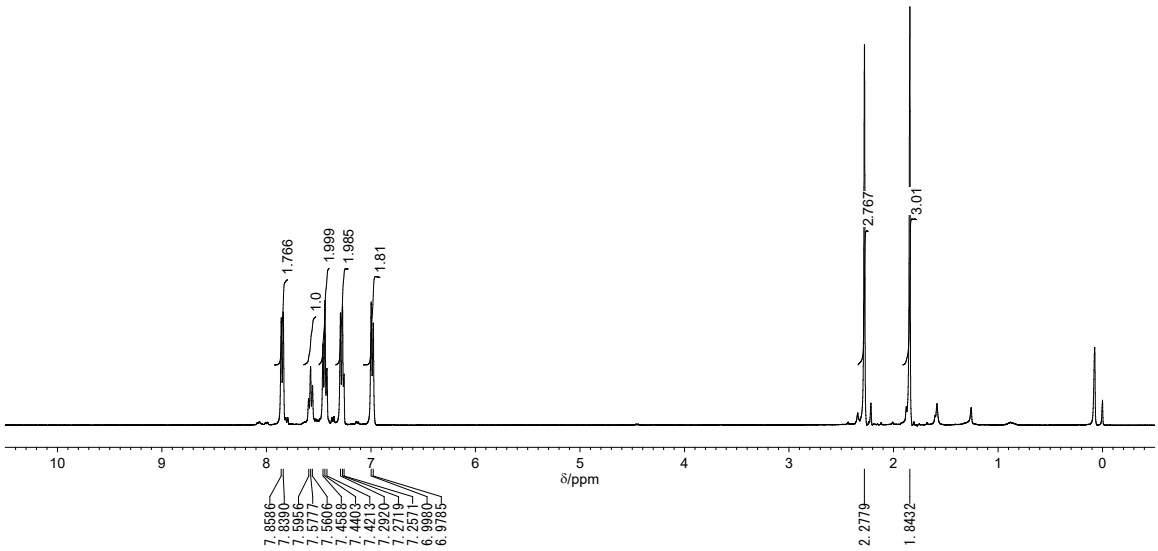


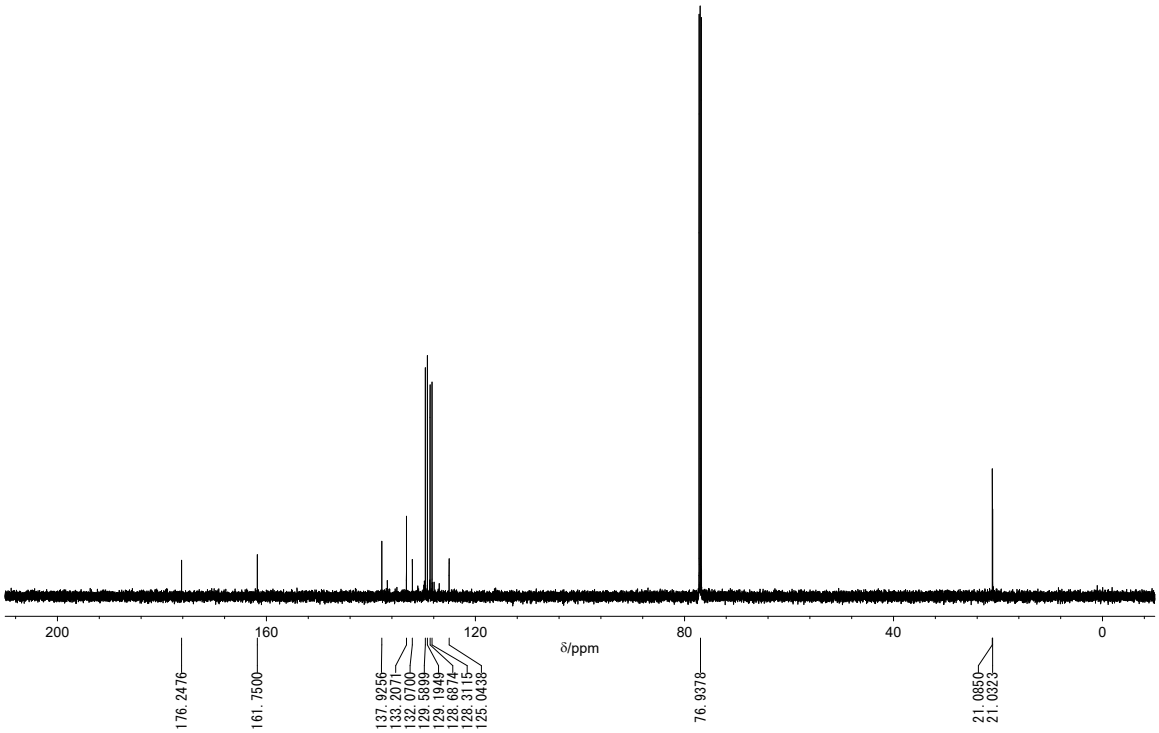




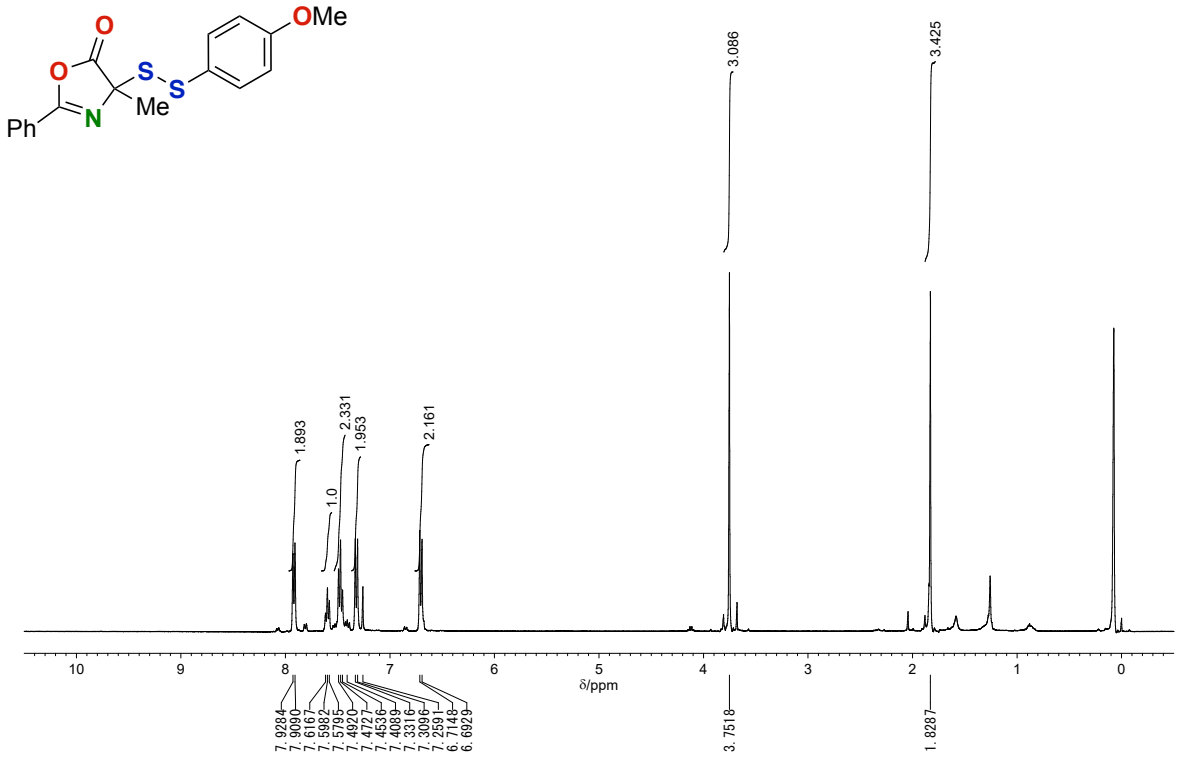
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 4-methyl-2-phenyl-4-(*p*-tolyldisulfanyl)oxazol-5(4*H*)-one (**3ai**) ($CDCl_3$)

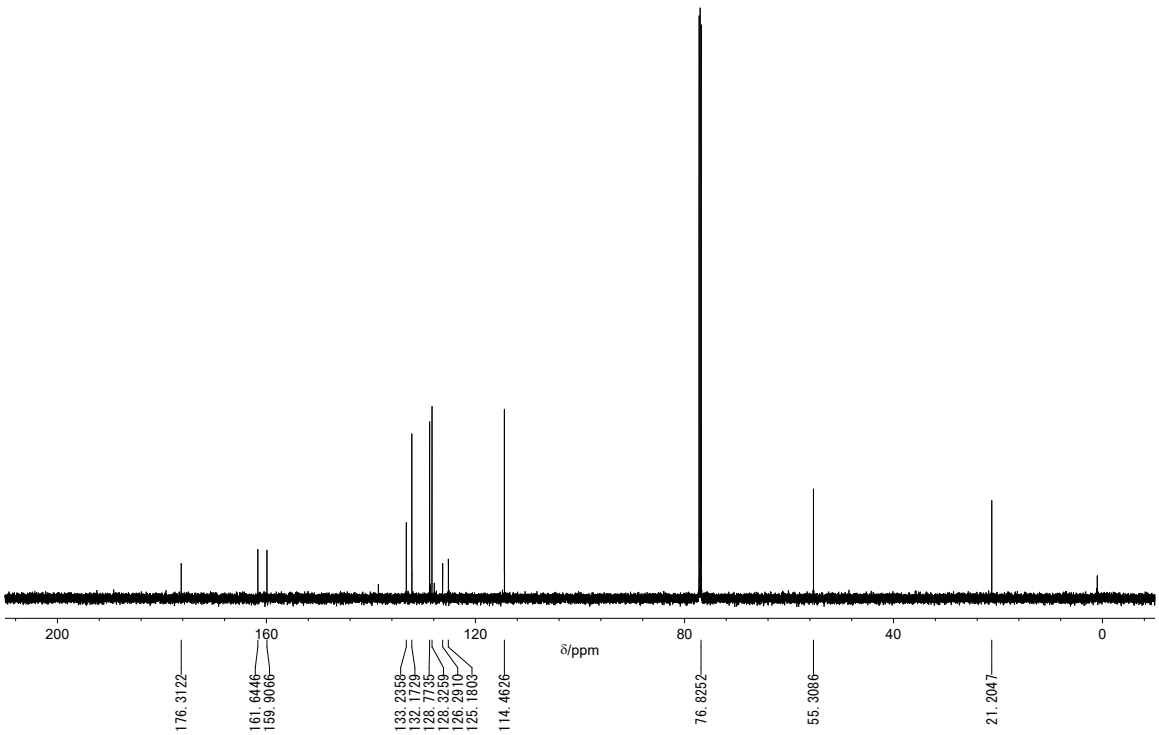




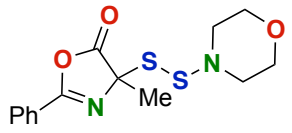


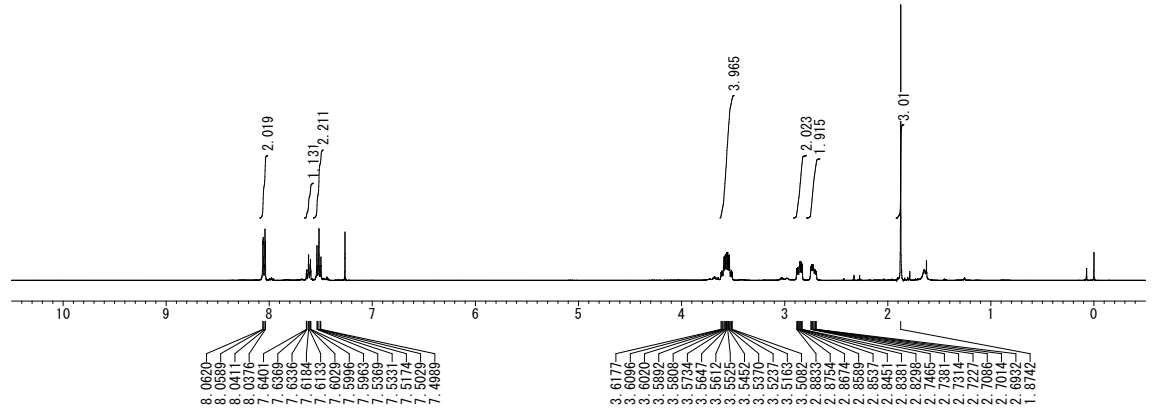
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 4-((4-methoxyphenyl)disulfanyl)-4-methyl-2-phenyloxazol-5(4*H*)-one (**3aj**) ($CDCl_3$)

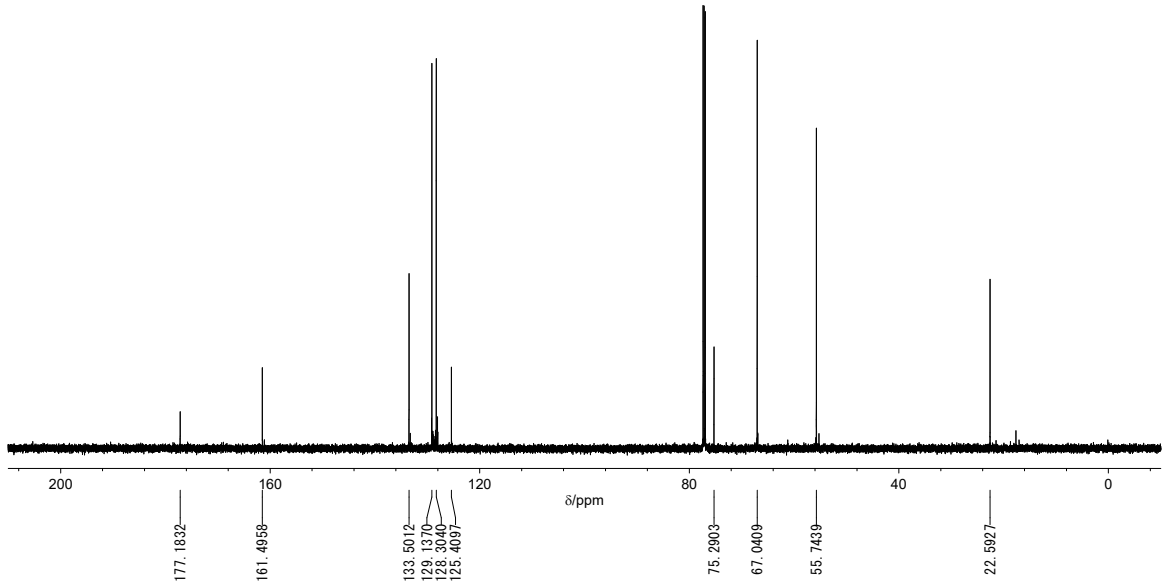




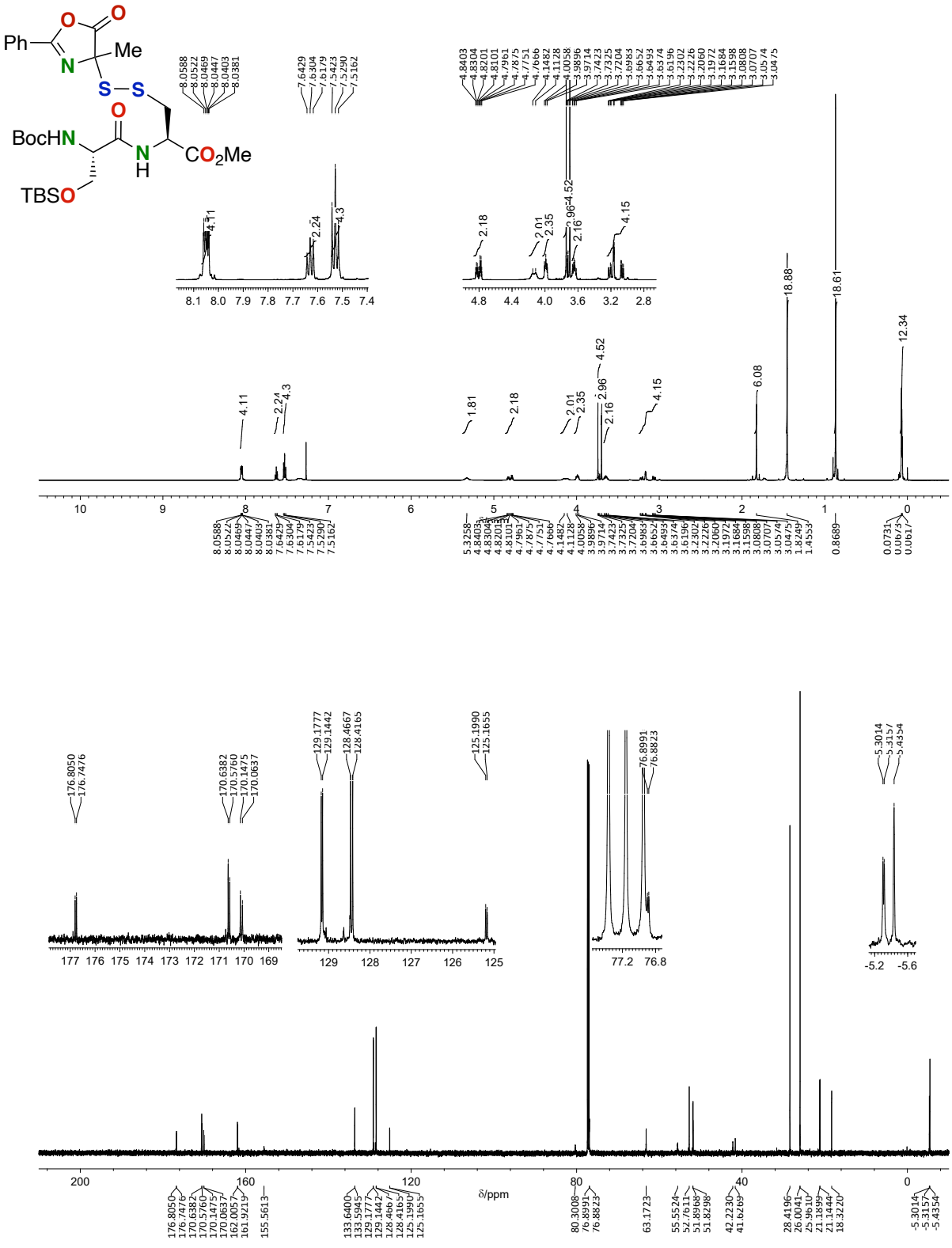
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 4-methyl-4-(morpholinodisulfanyl)-2-phenyloxazol-5(4*H*)-one (**3ak**) ($CDCl_3$)



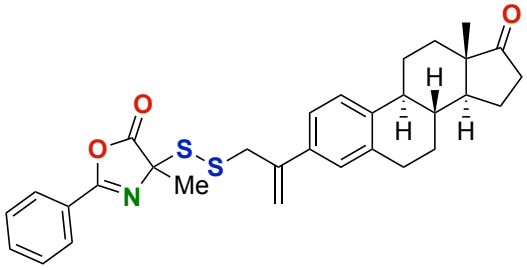


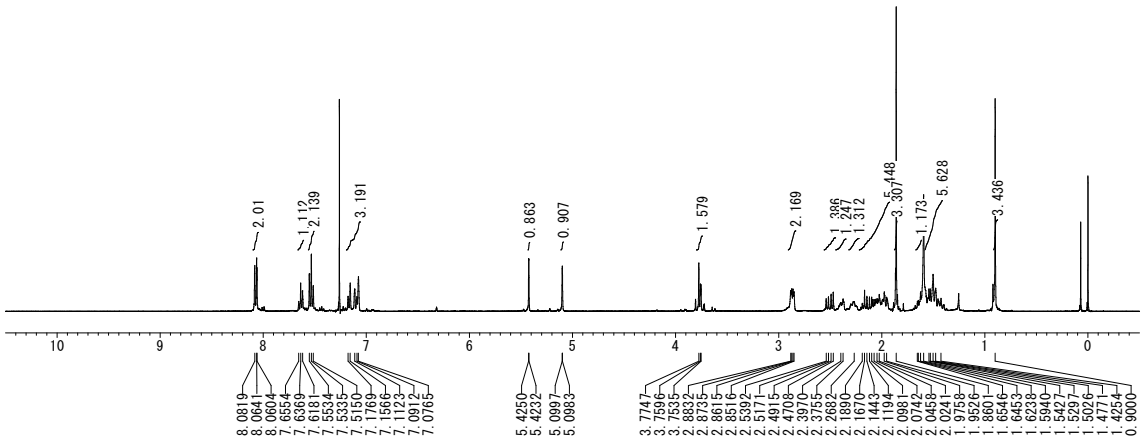


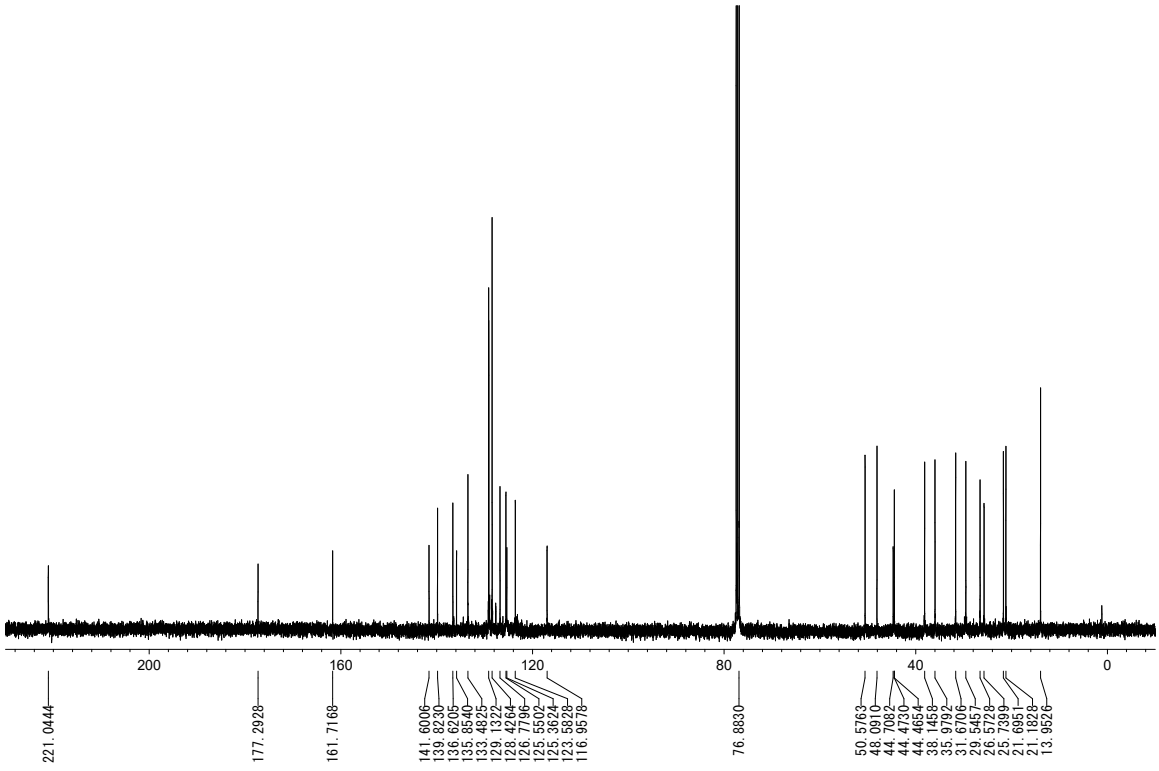
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of methyl *N*-(*N*-(*tert*-butoxycarbonyl)-*O*-(*tert*-butyldimethylsilyl)-L-seryl)-*S*-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)thio)-L-cysteinate (**3al**) ($CDCl_3$)



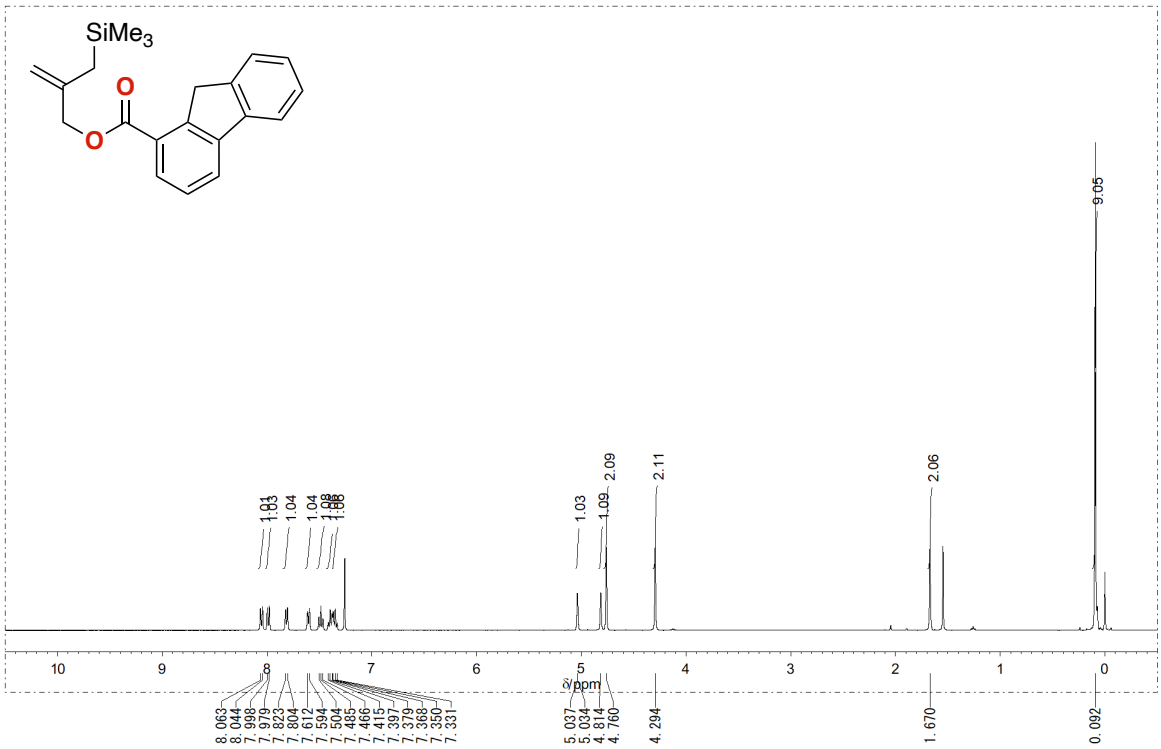
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 4-methyl-4-((2-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)allyl)disulfanyl)-2-phenyloxazol-5(4*H*)-one (**3am**) ($CDCl_3$)

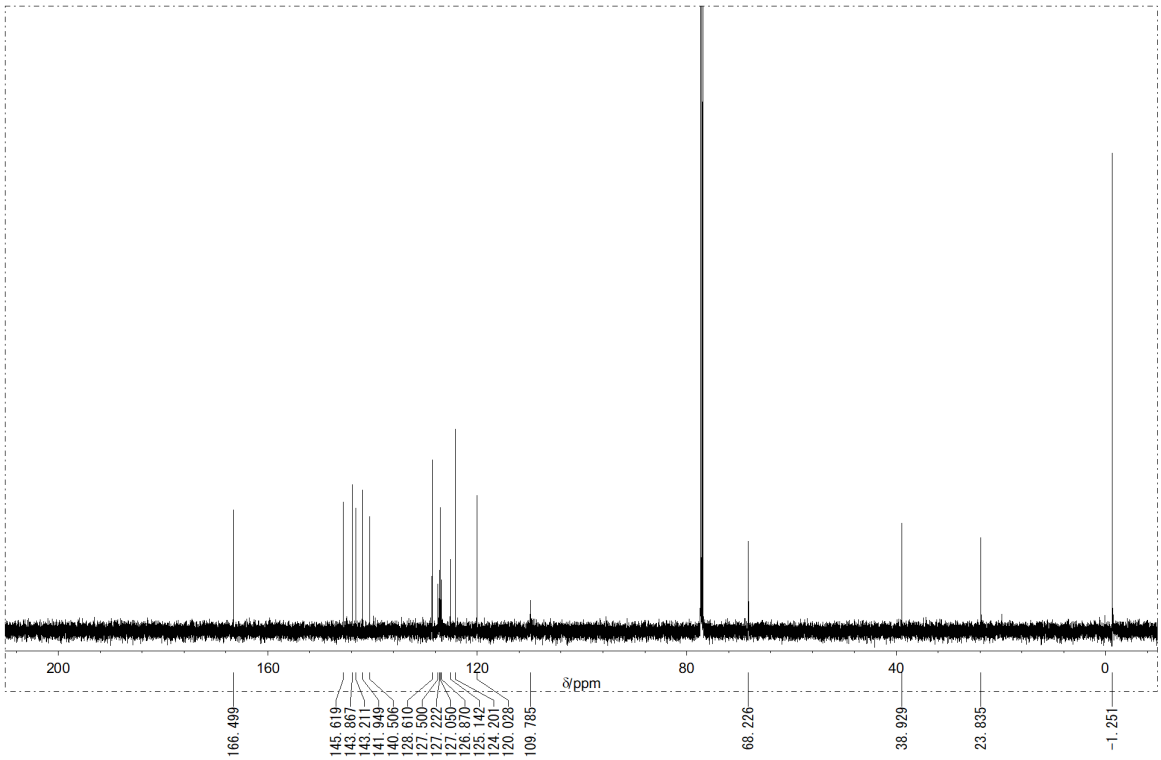




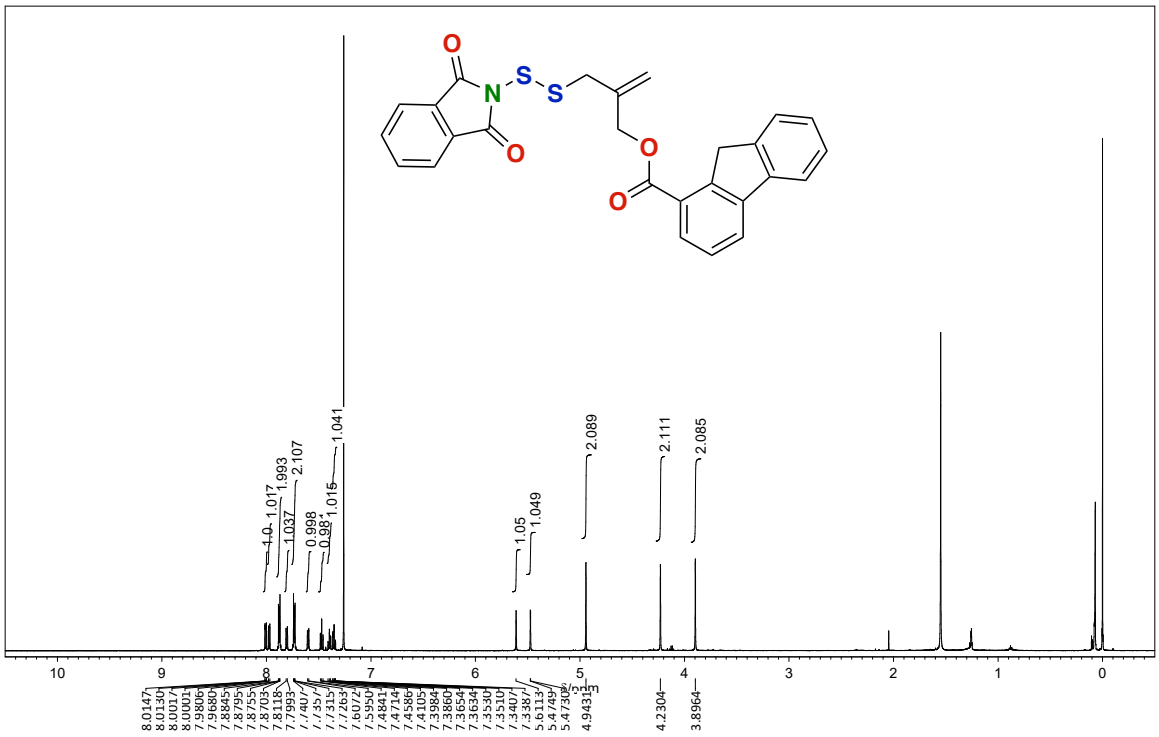


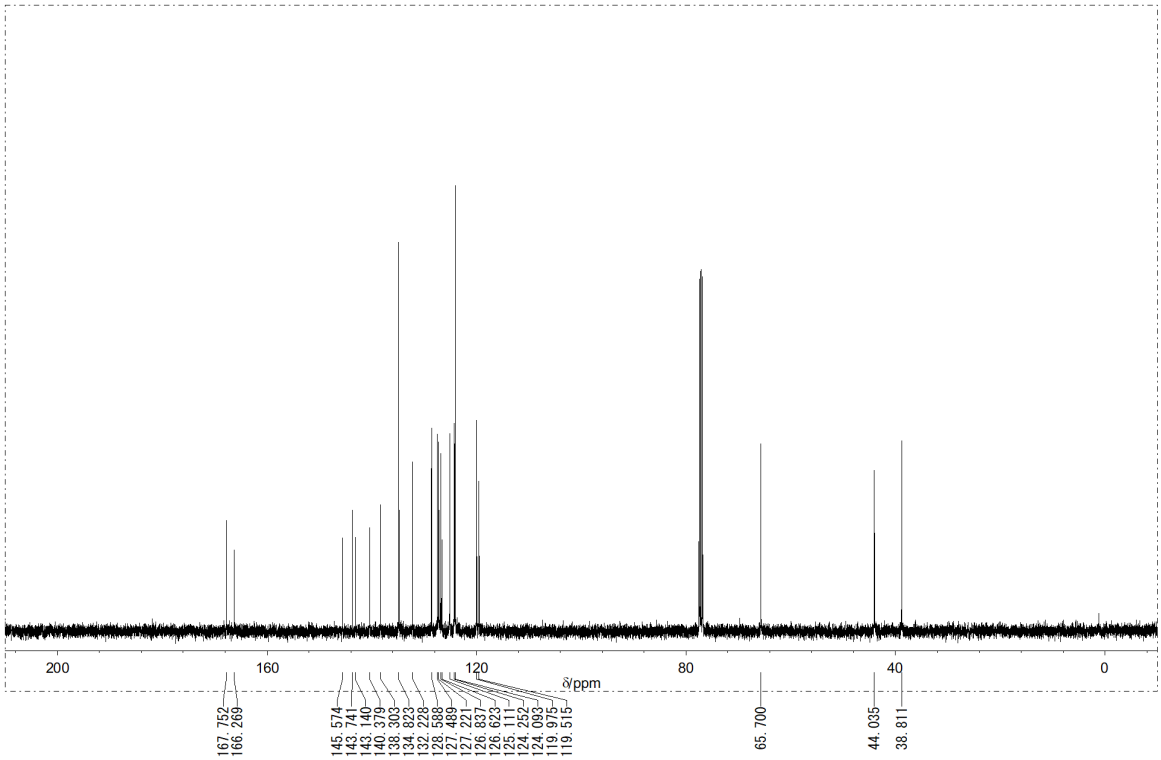
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 2-((trimethylsilyl)methyl)allyl 9*H*-fluorene-1-carboxylate (**4**) ($CDCl_3$)



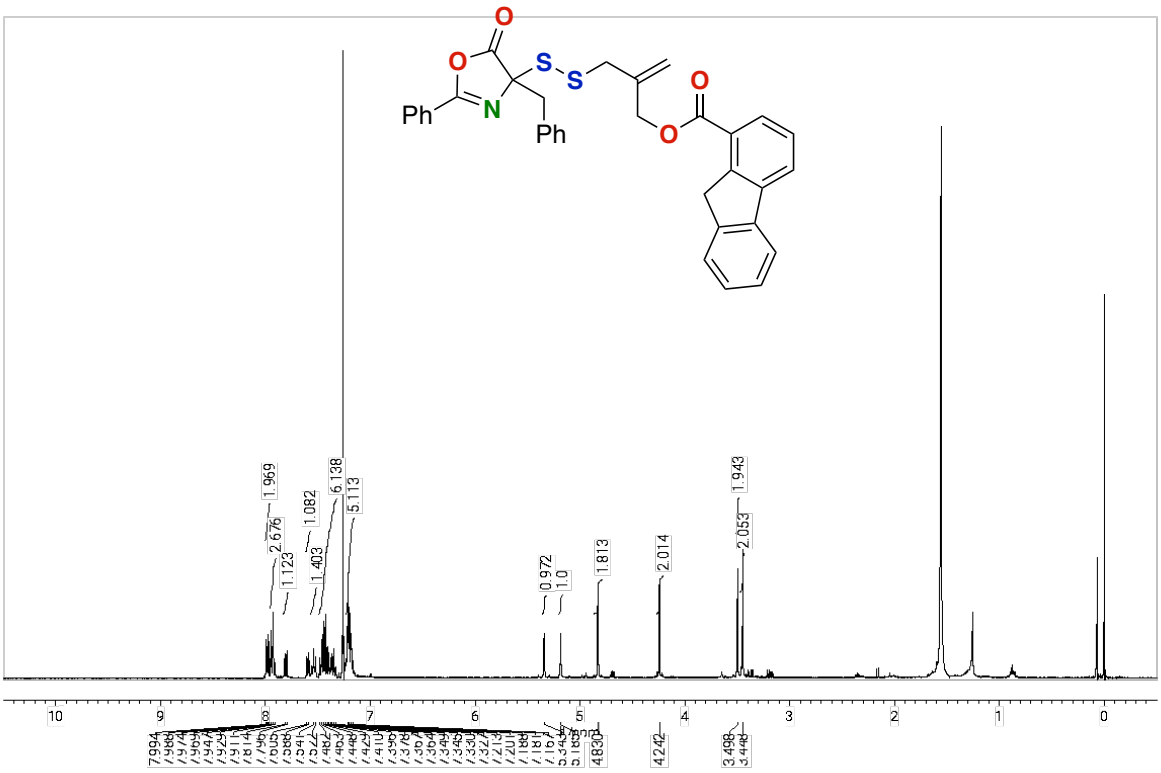


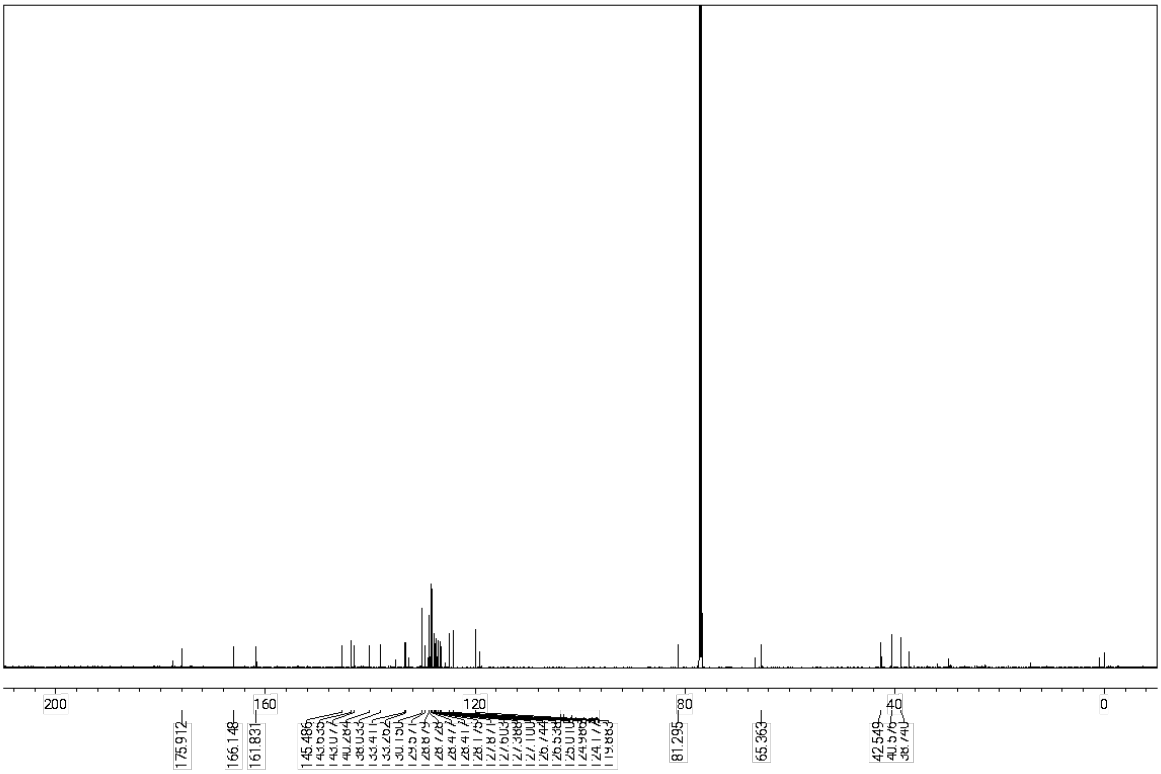
^{1}H NMR (600 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(((1,3-dioxoisoindolin-2-yl)disulfanyl)methyl)allyl 9*H*-fluorene-1-carboxylate (**5**) ($CDCl_3$)



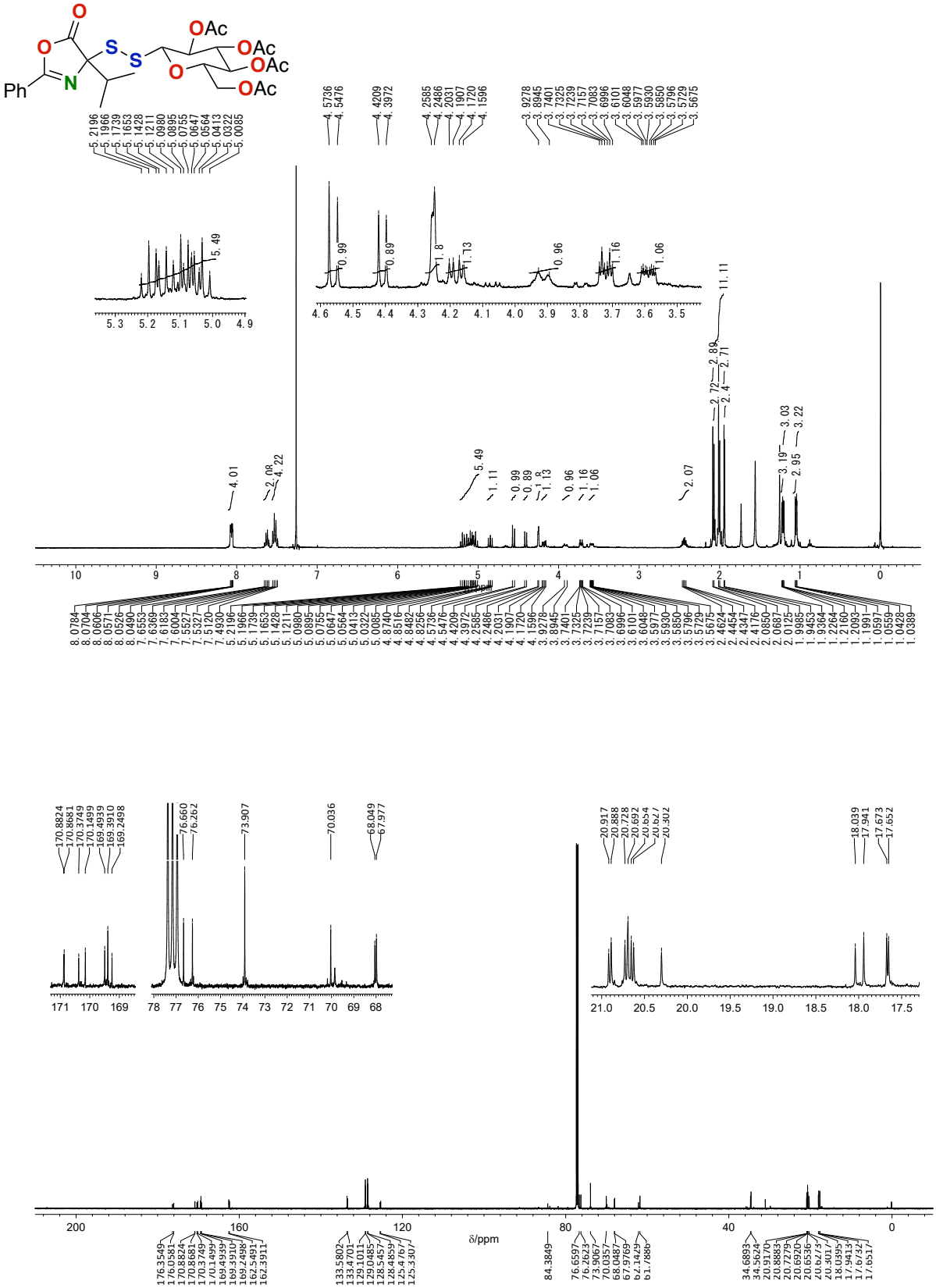


^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 2-(((4-benzyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)methyl)allyl 9*H*-fluorene-1-carboxylate (**6**) ($CDCl_3$)

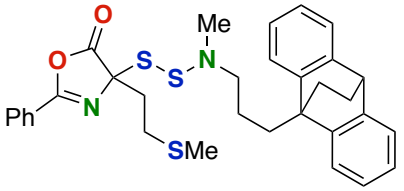


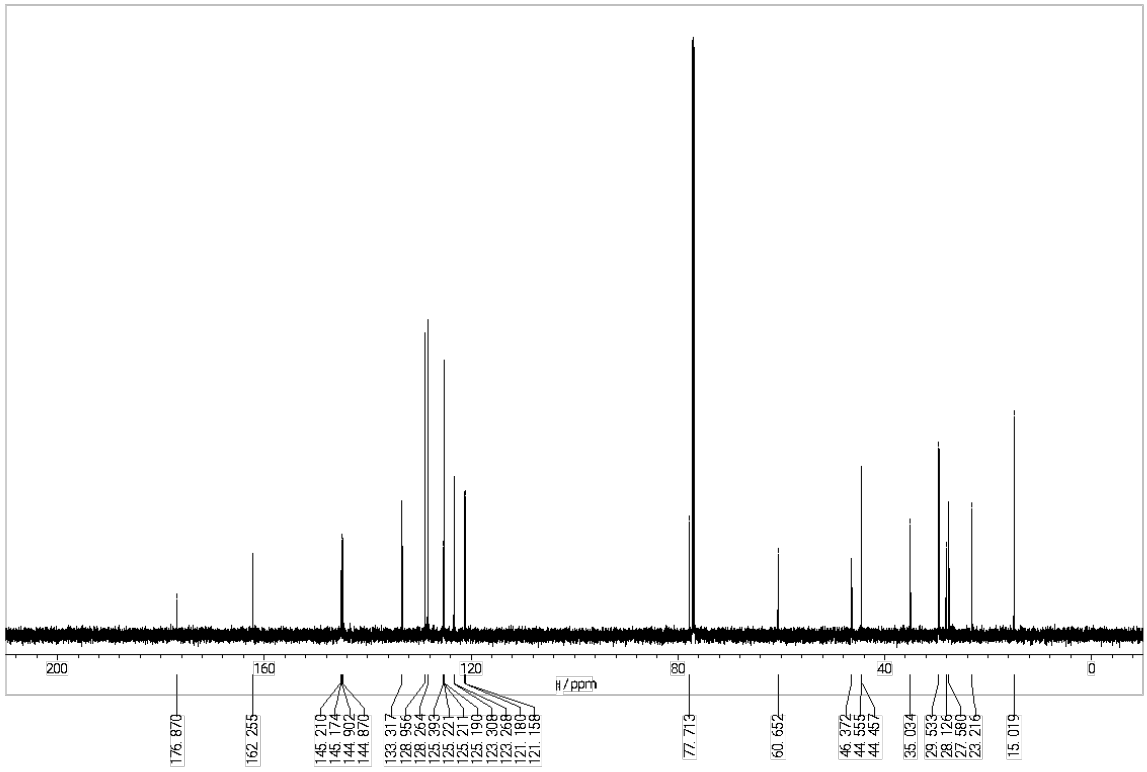


^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of (2*S*,3*S*,4*R*,5*S*,6*R*)-2-(acetoxymethyl)-6-((4-isopropyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)tetrahydro-2*H*-pyran-3,4,5-triyl triacetate (**10**) ($CDCl_3$)

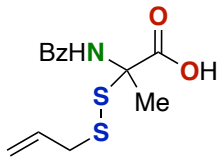


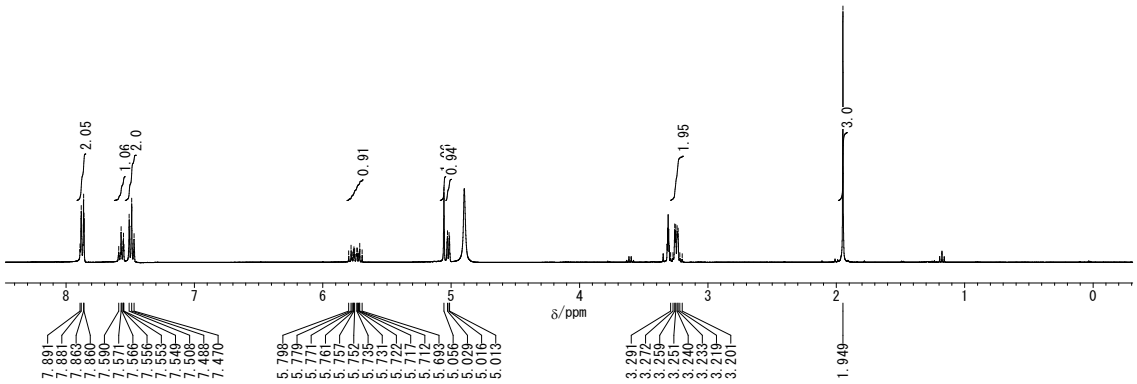
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 4-(((3-(9,10-ethanoanthracen-9(10*H*)-yl)propyl)(methyl)amino)disulfanyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (**14**) ($CDCl_3$)

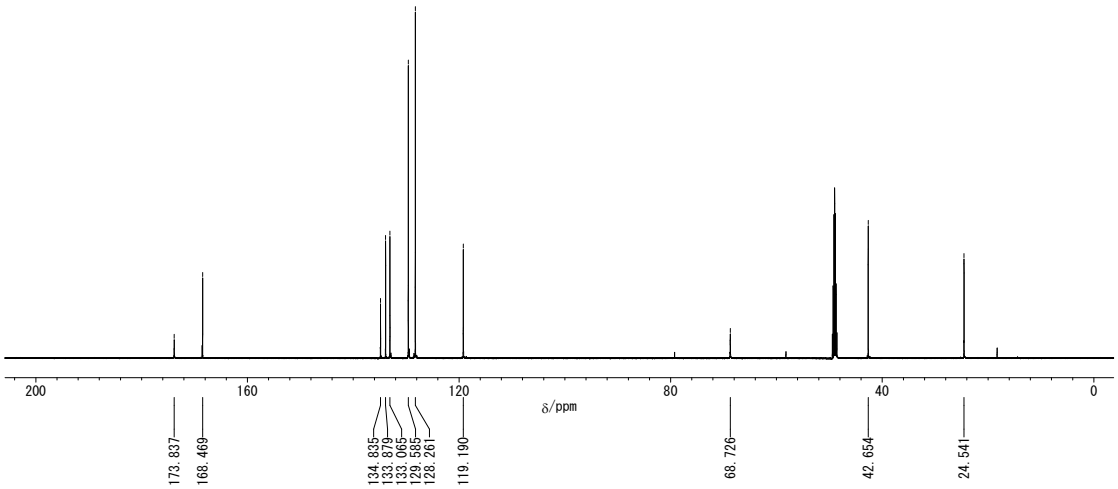




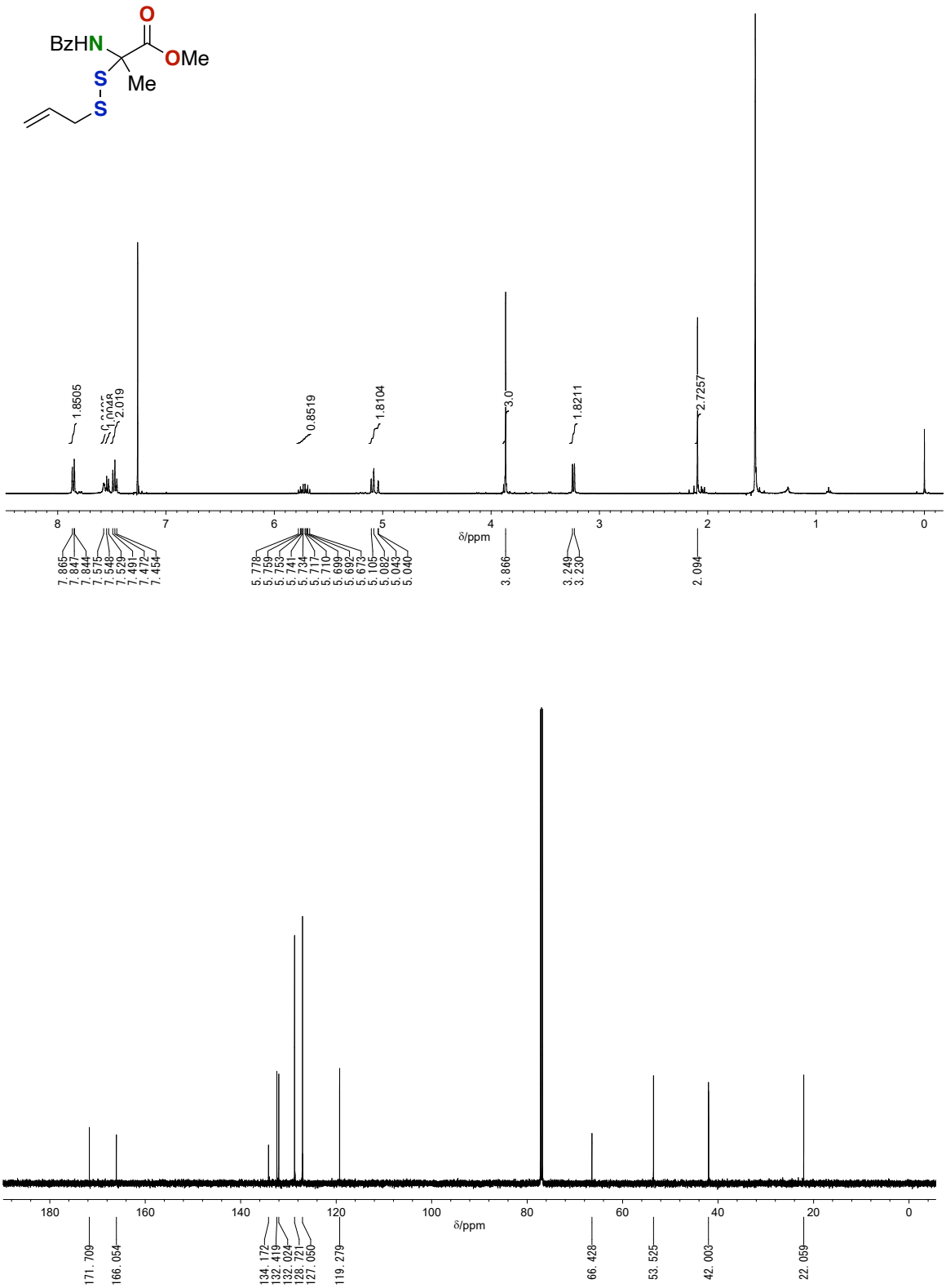
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of 2-(allyldisulfanyl)-2-benzamidopropanoic acid (**15a**) (CD_3OD)



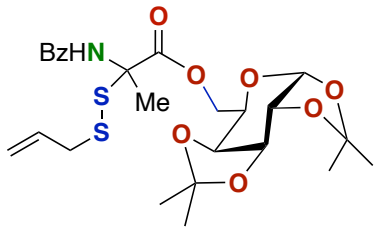


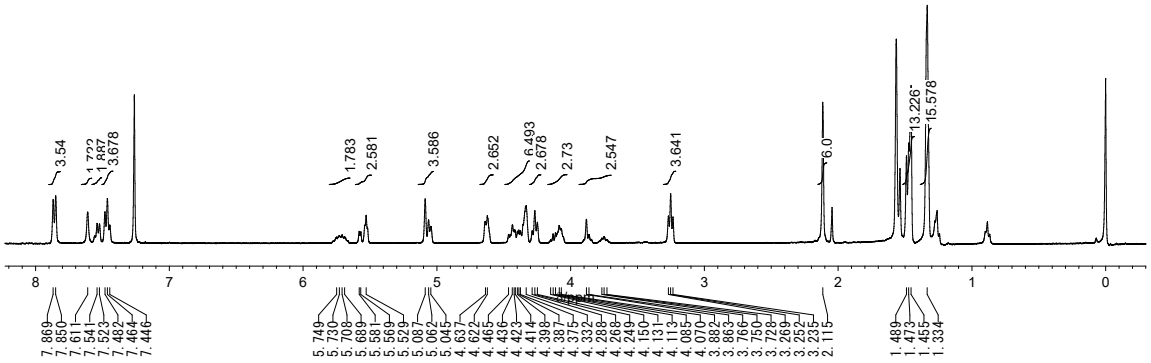


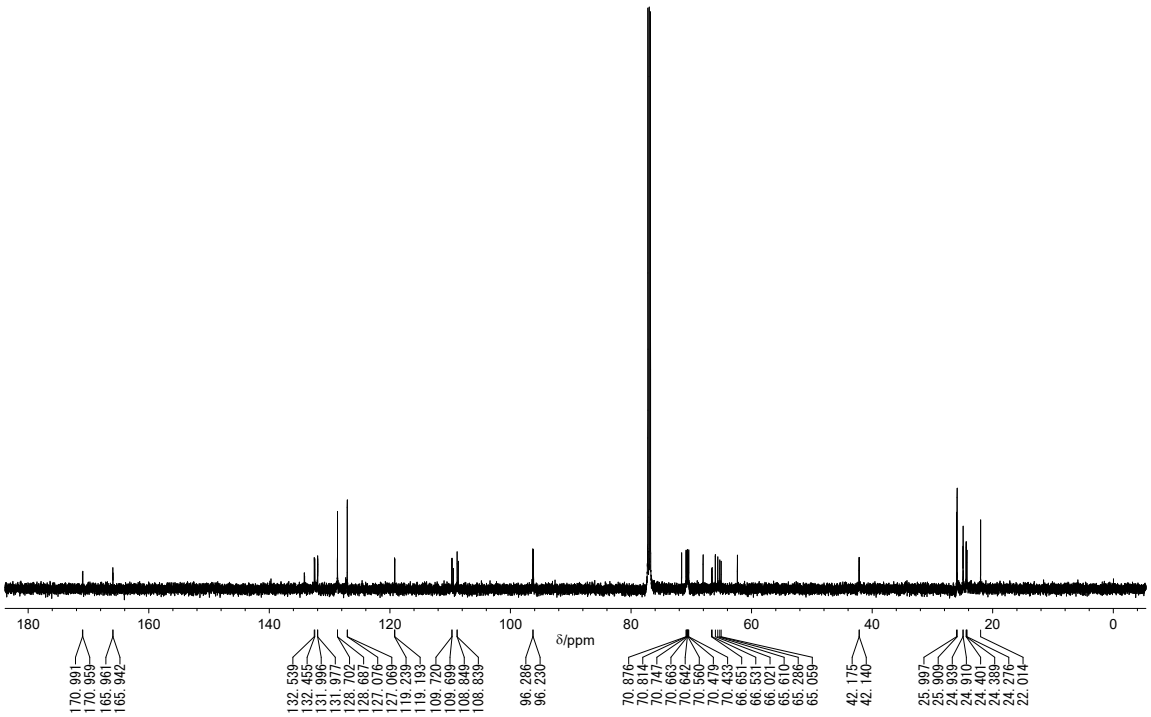
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of methyl 2-(allyldisulfanyl)-2-benzamidopropanoate (**15b**) ($CDCl_3$)



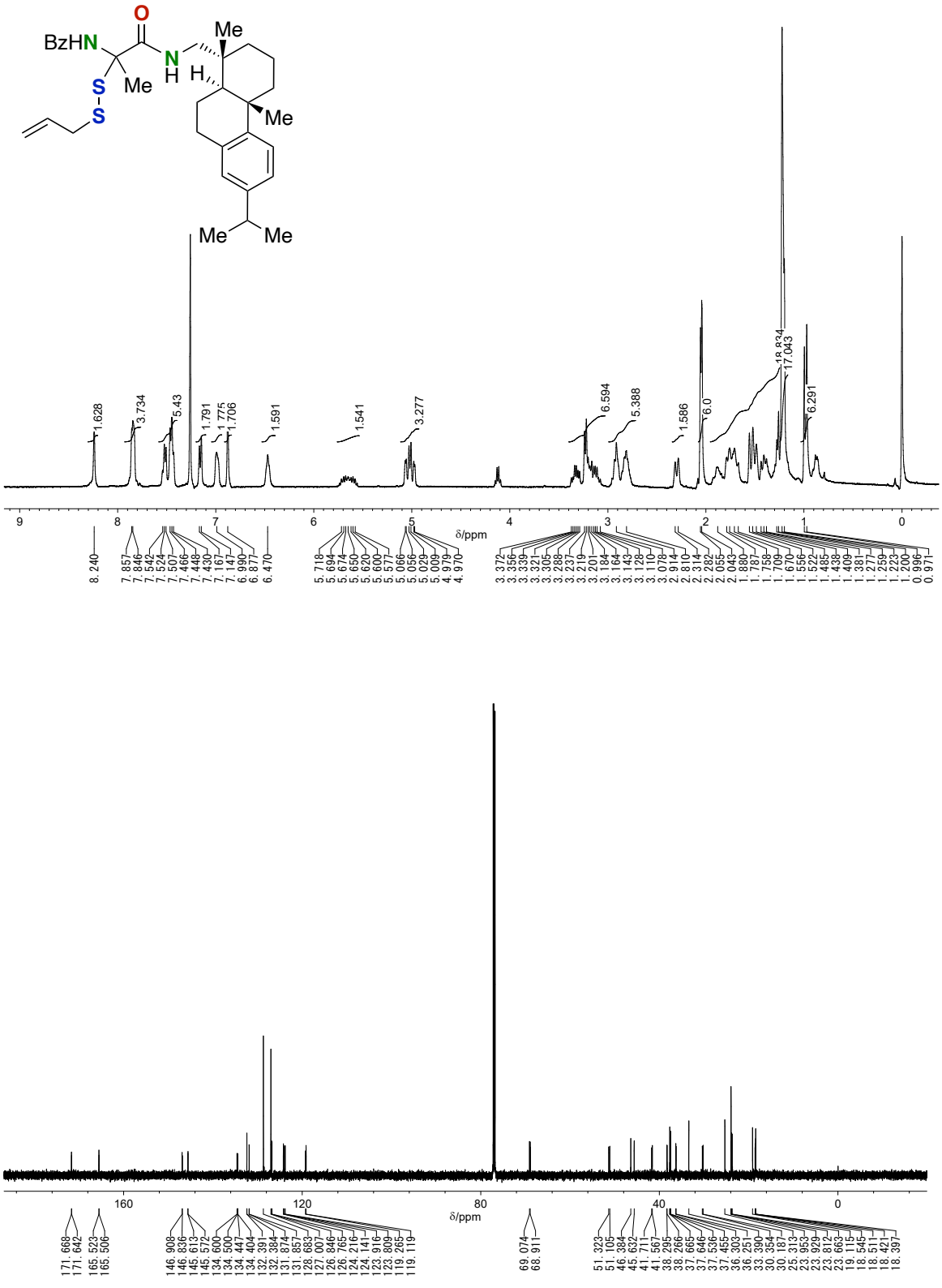
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of ((3a*R*,5*R*,5a*S*,8a*S*,8b*R*)-2,2,7,7-tetramethyltetrahydro-5*H*-bis([1,3]dioxolo)[4,5-*b*:4',5'-*d*]pyran-5-yl)methyl 2-(allyldisulfanyl)-2-benzamidopropanoate (**15c**) ($CDCl_3$)



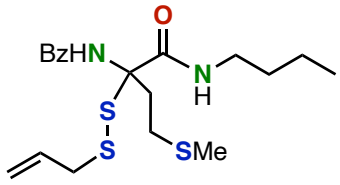


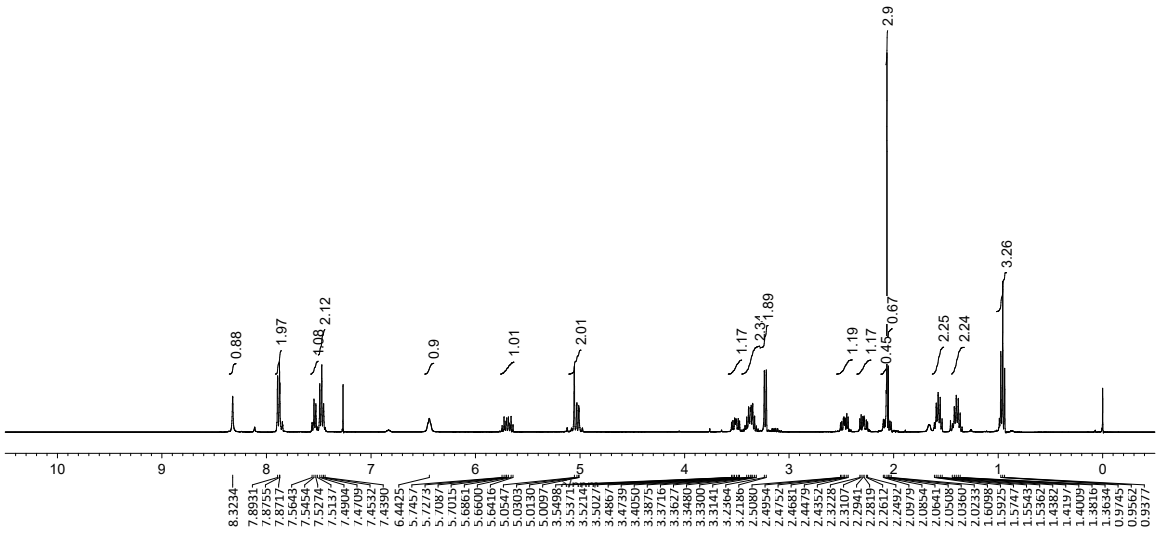


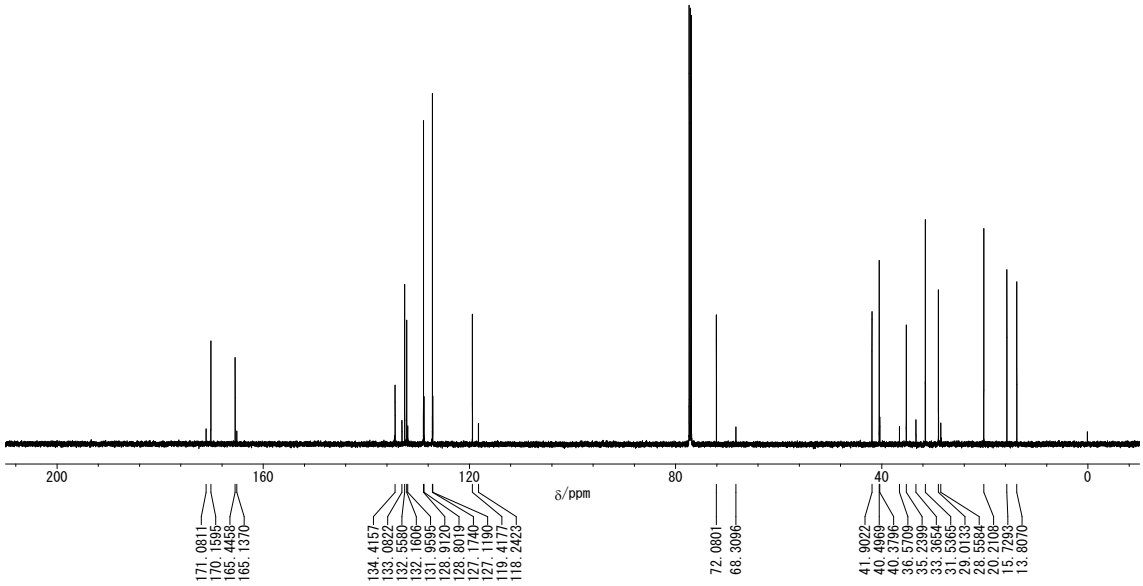
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of *N*-(2-(allyldisulfanyl)-1-((((1*R*,4a*S*,10a*R*)-7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,9,10,10a-octahydrophenanthren-1-yl)methyl)amino)-1-oxopropan-2-yl)benzamide (**15d**) ($CDCl_3$)



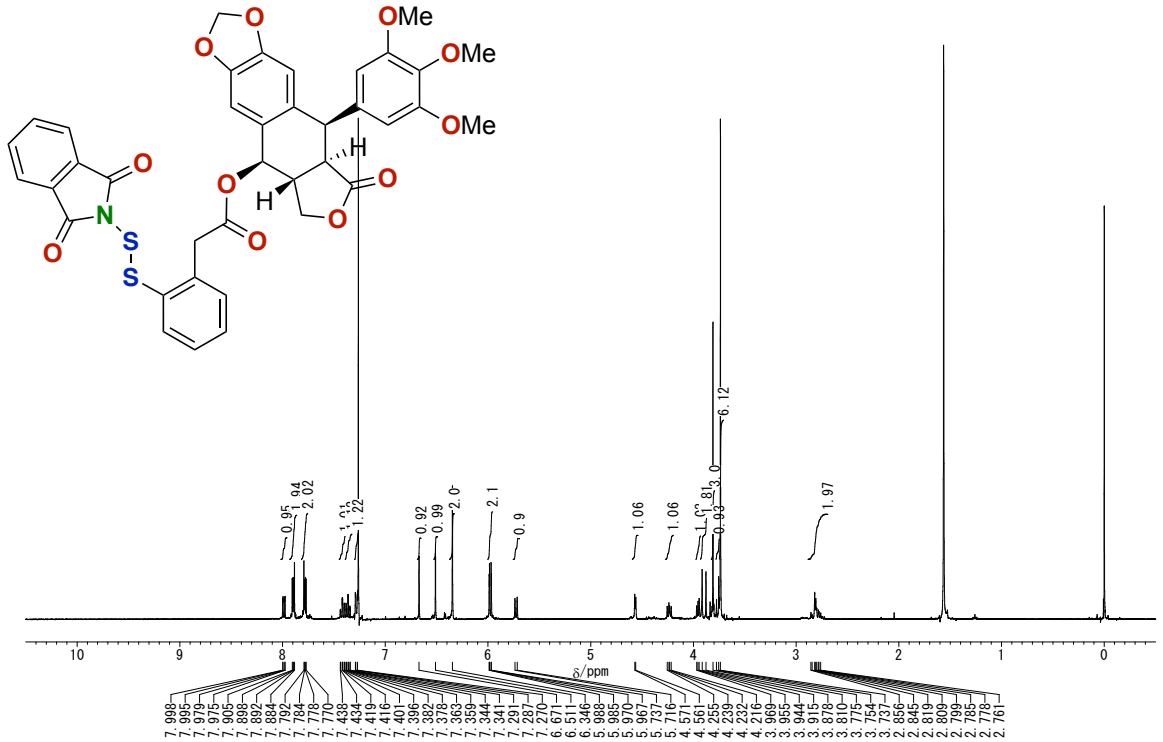
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of *N*-(2-(allyldisulfanyl)-1-(butylamino)-4-(methylthio)-1-oxobutan-2-yl)benzamide (**15e**) ($CDCl_3$)

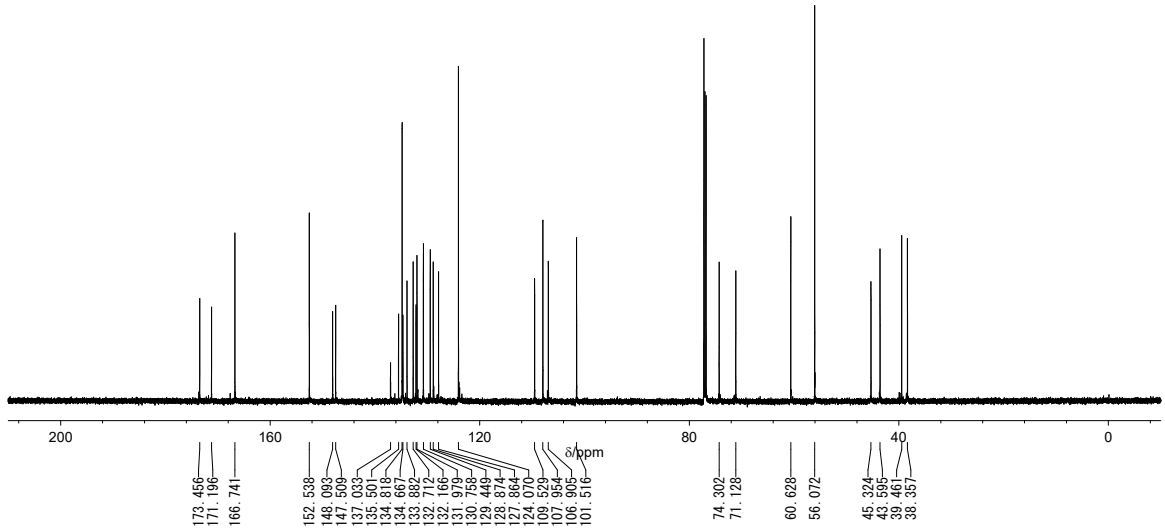




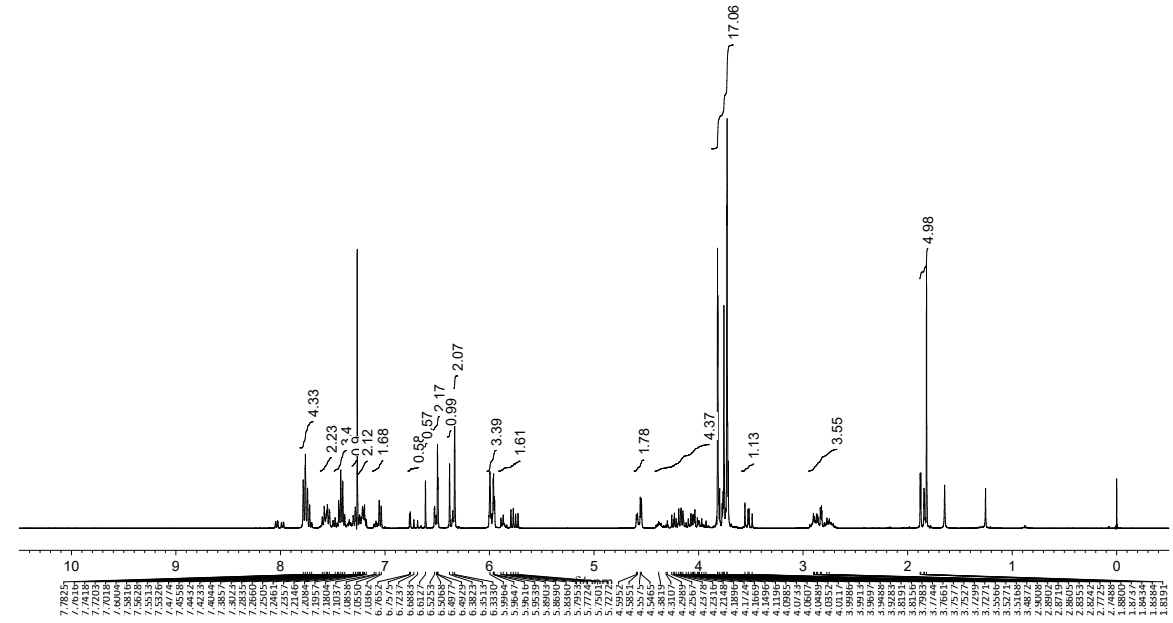


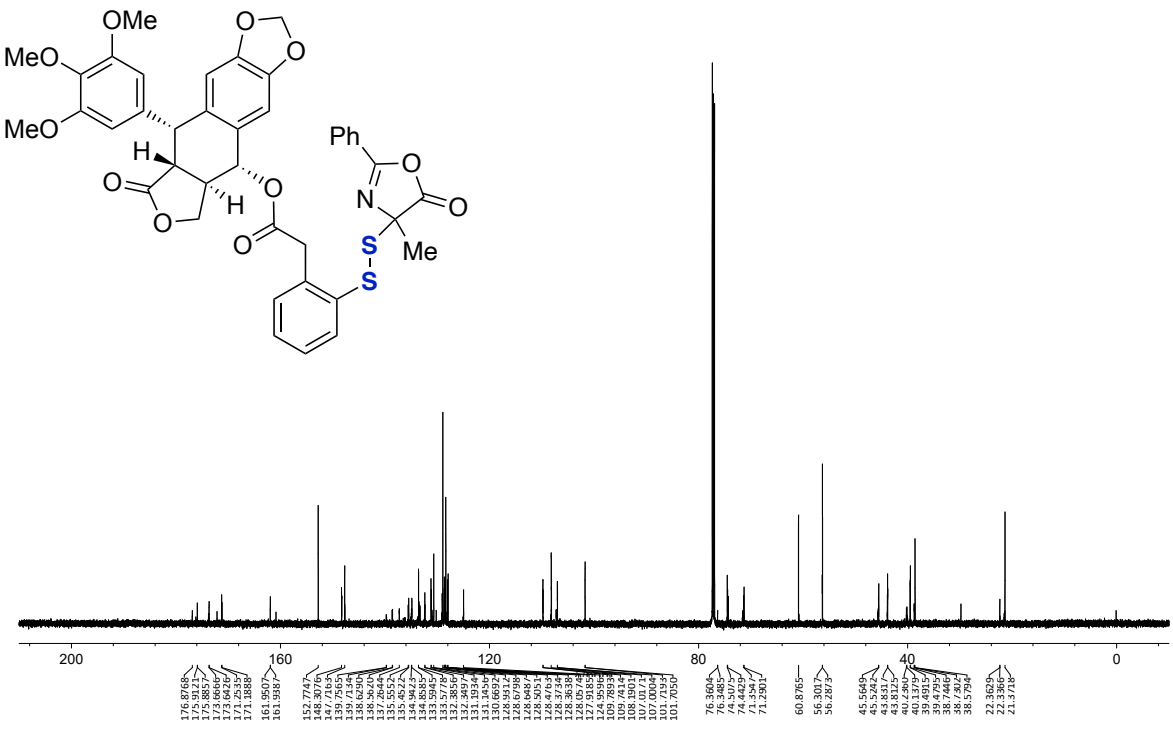
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of (5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((1,3-dioxoisoindolin-2-yl)disulfanyl)phenyl)acetate ($CDCl_3$)



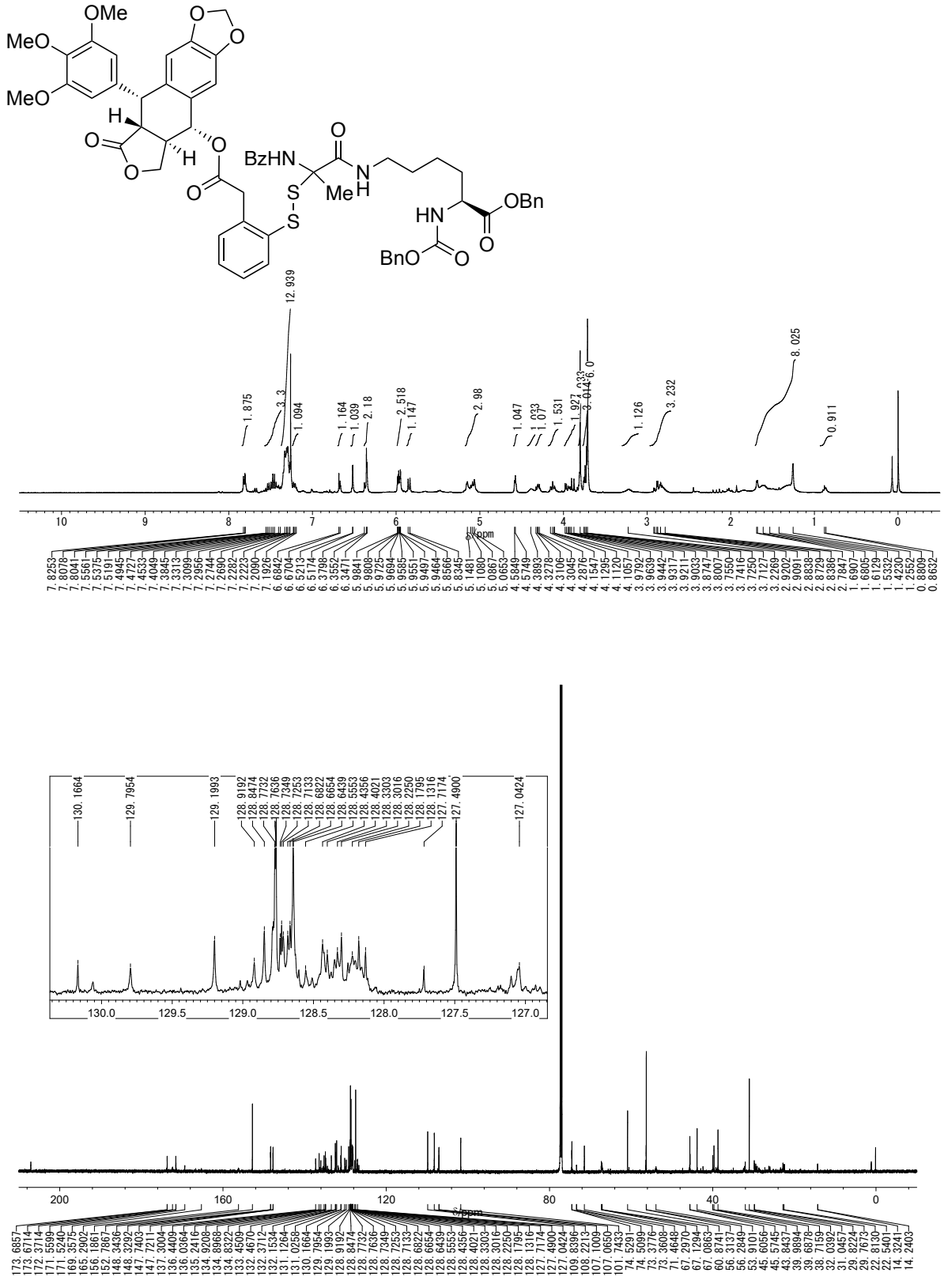


^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of (5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl 2-(2-((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)phenyl)acetate (**18**) ($CDCl_3$)

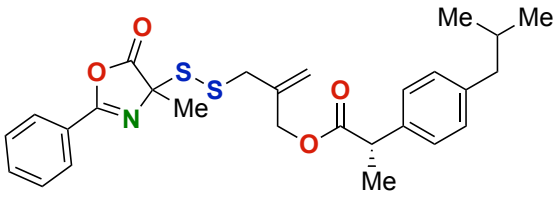


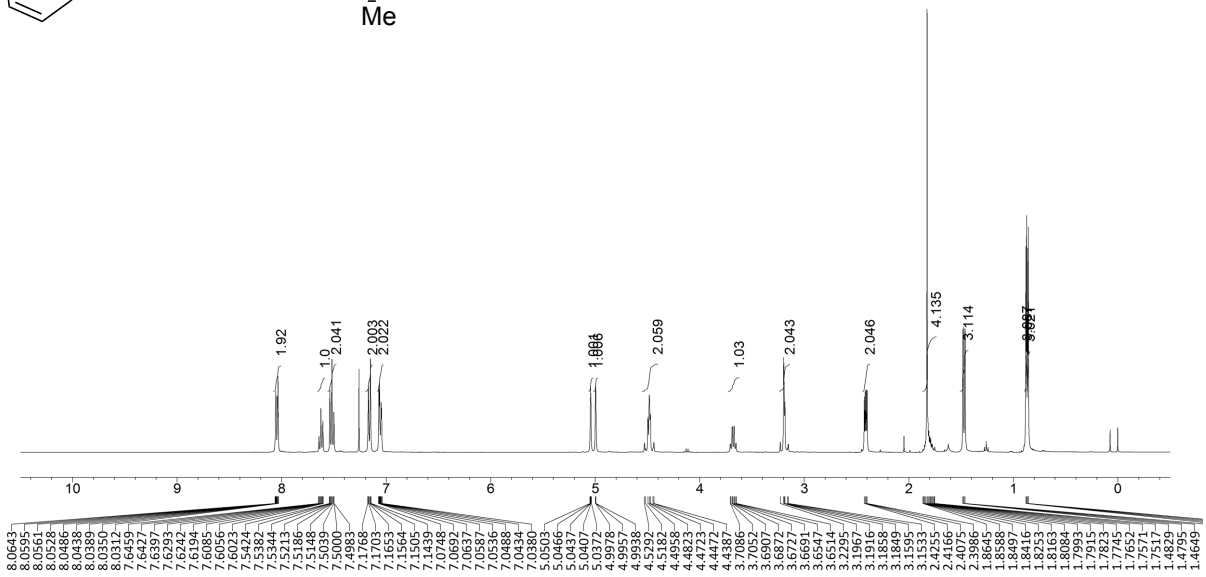


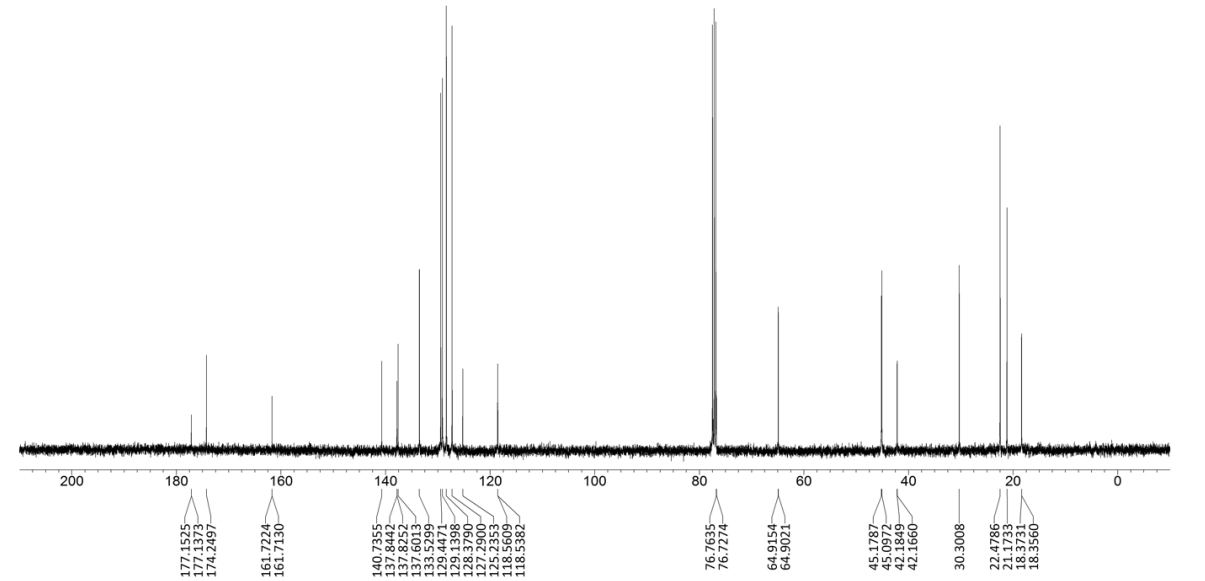
^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of benzyl N^{6}-(2-benzamido-2-((2-(2-oxo-2-(((5*R*,5a*R*,8a*R*,9*R*)-8-oxo-9-(3,4,5-trimethoxyphenyl)-5,5a,6,8,8a,9-hexahydrofuro[3',4':6,7]naphtho[2,3-*d*][1,3]dioxol-5-yl)oxy)ethyl)phenyl)disulfanyl)propanoyl)-N^{2}-((benzyloxy)carbonyl)-*L*-lysinate (**20**) ($CDCl_3$)



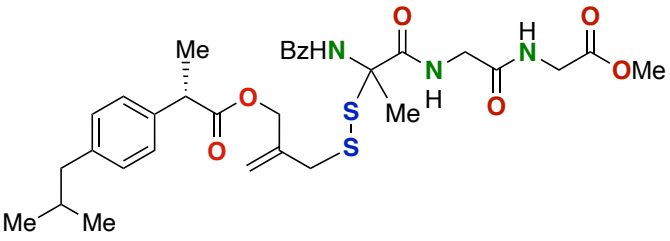
^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra of 2-(((4-methyl-5-oxo-2-phenyl-4,5-dihydrooxazol-4-yl)disulfanyl)methyl)allyl (2*S*)-2-(4-isobutylphenyl)propanoate (**22**) ($CDCl_3$)

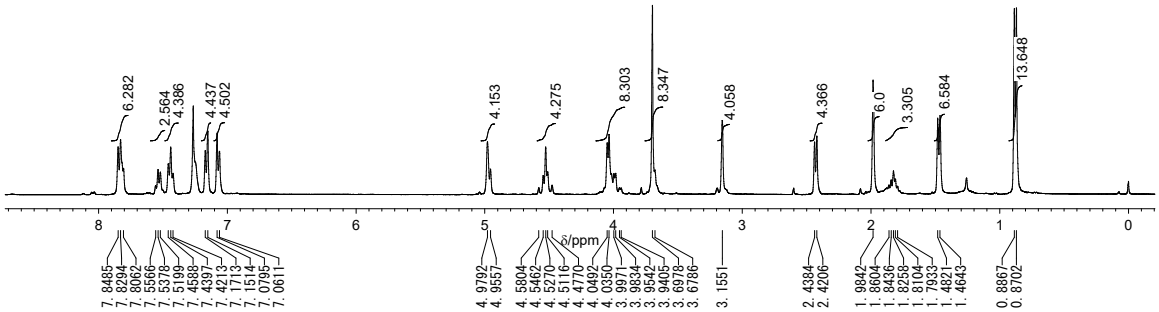


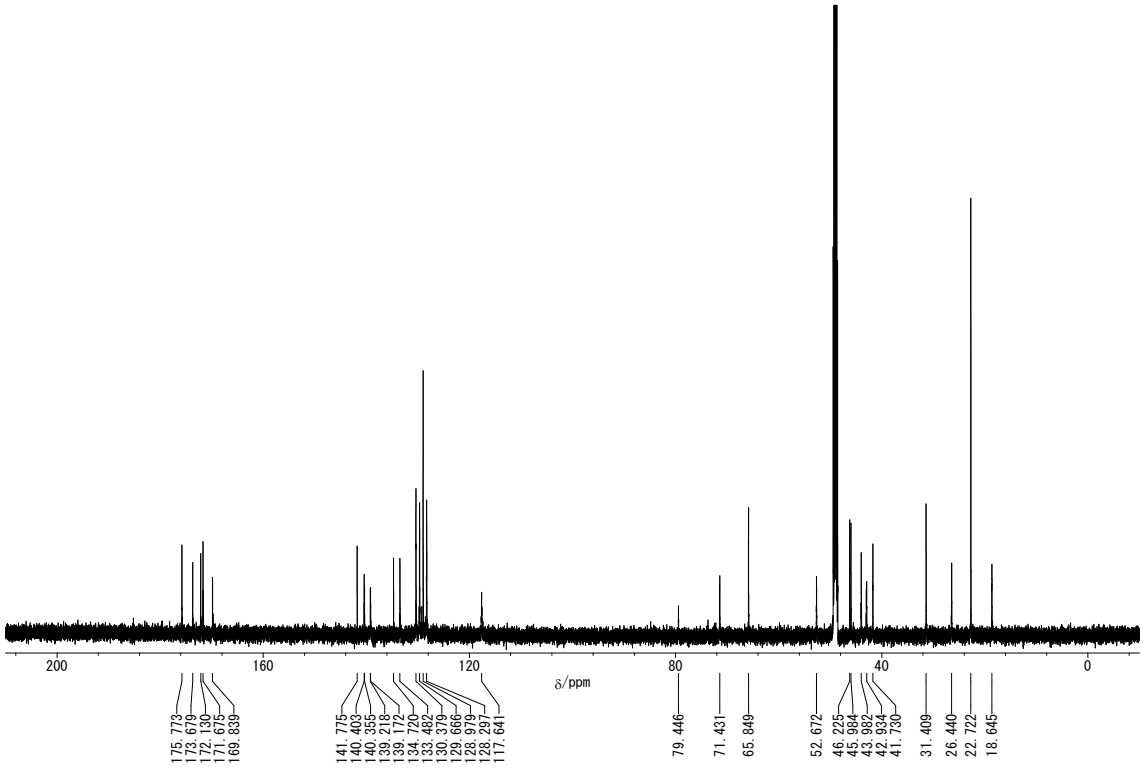




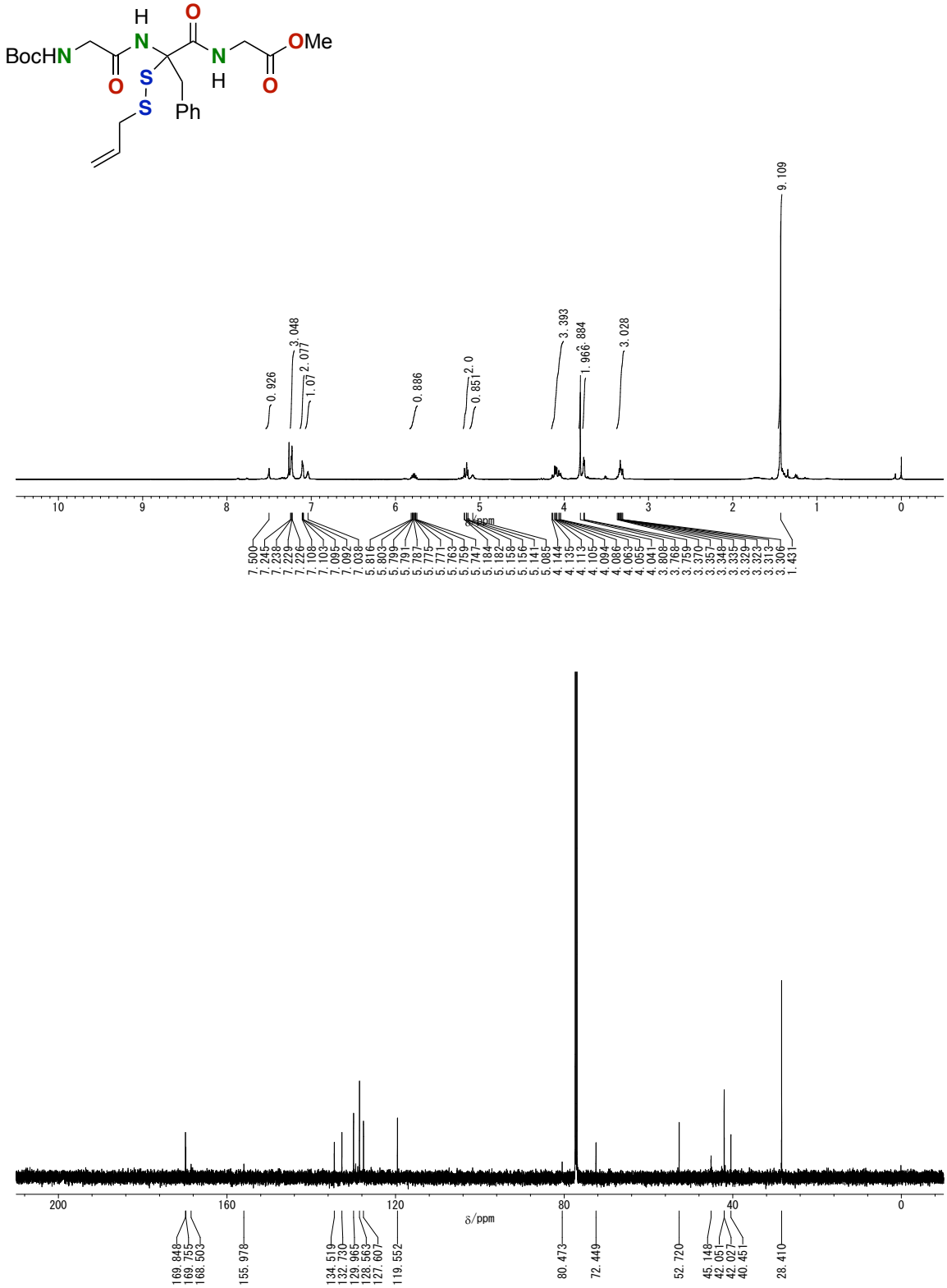
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, CD_3OD) spectra of 10-benzamido-10-methyl-14-methylene-3,6,9-trioxo-2-oxa-11,12-dithia-5,8-diazapentadecan-15-yl (2*S*)-2-(4-isobutylphenyl)propanoate (**24**)



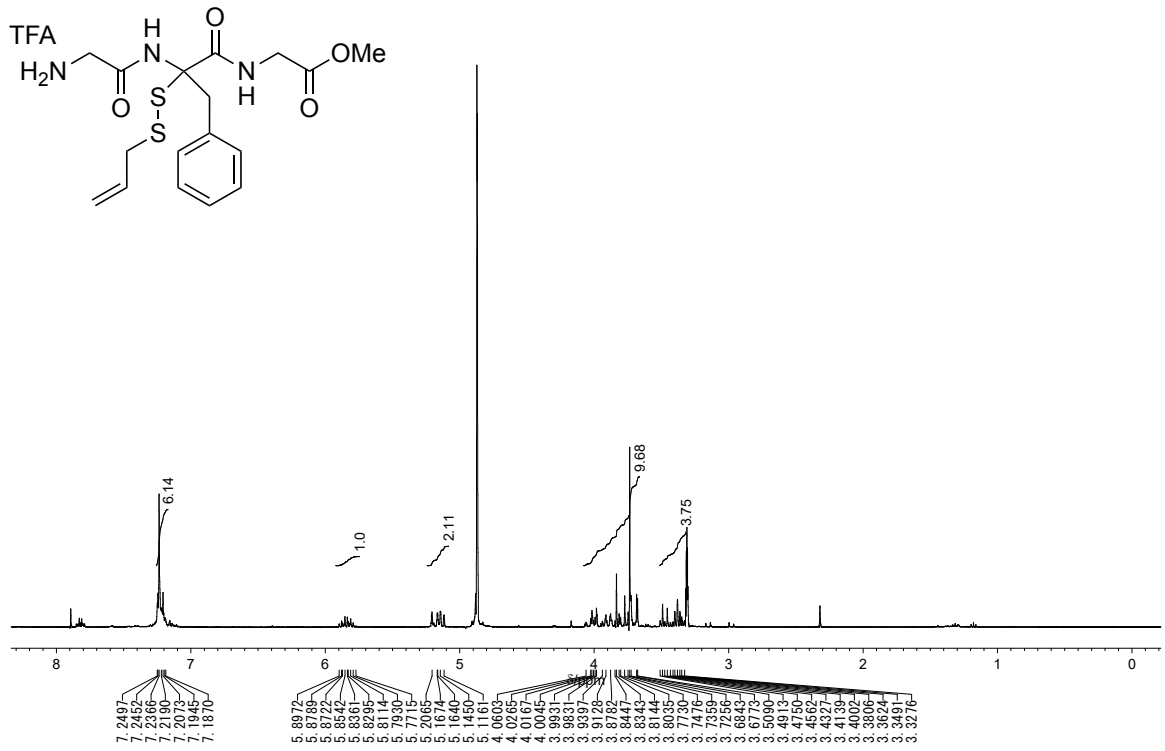


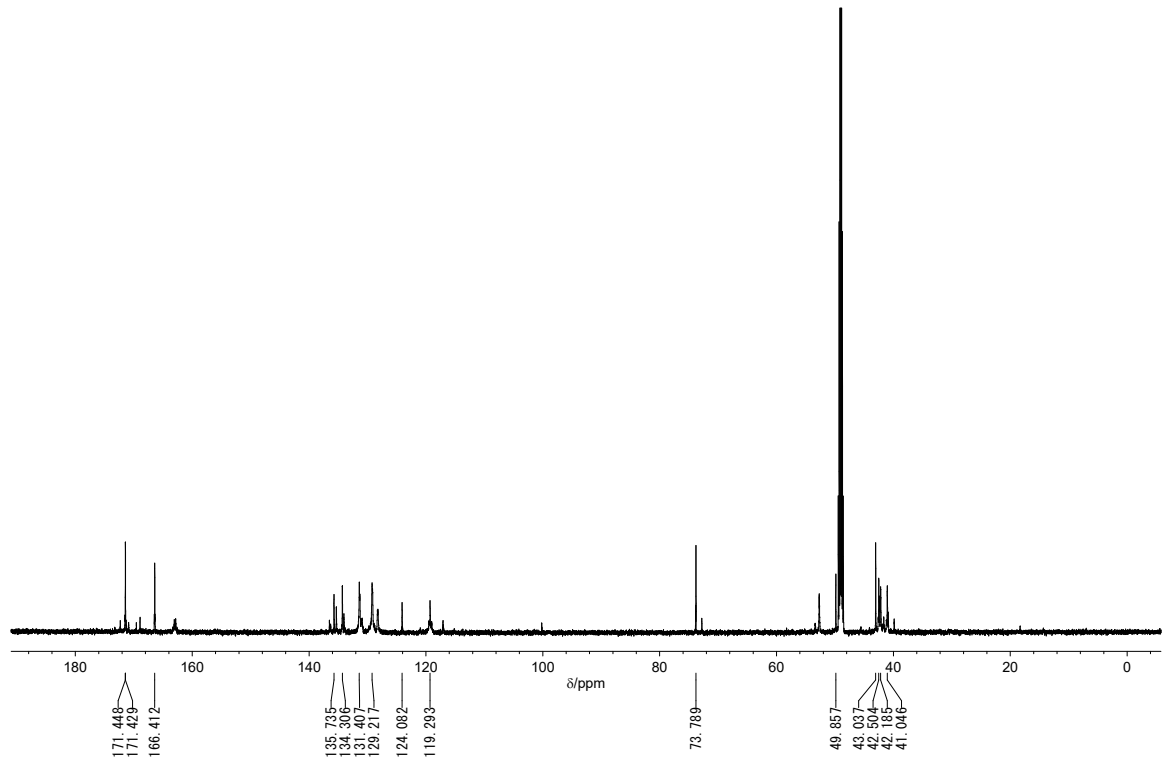


^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) spectra of methyl (2-(allyldisulfanyl)-2-(2-((*tert*-butoxycarbonyl)amino)acetamido)-3-phenylpropanoyl)glycinate (**26**) ($CDCl_3$)

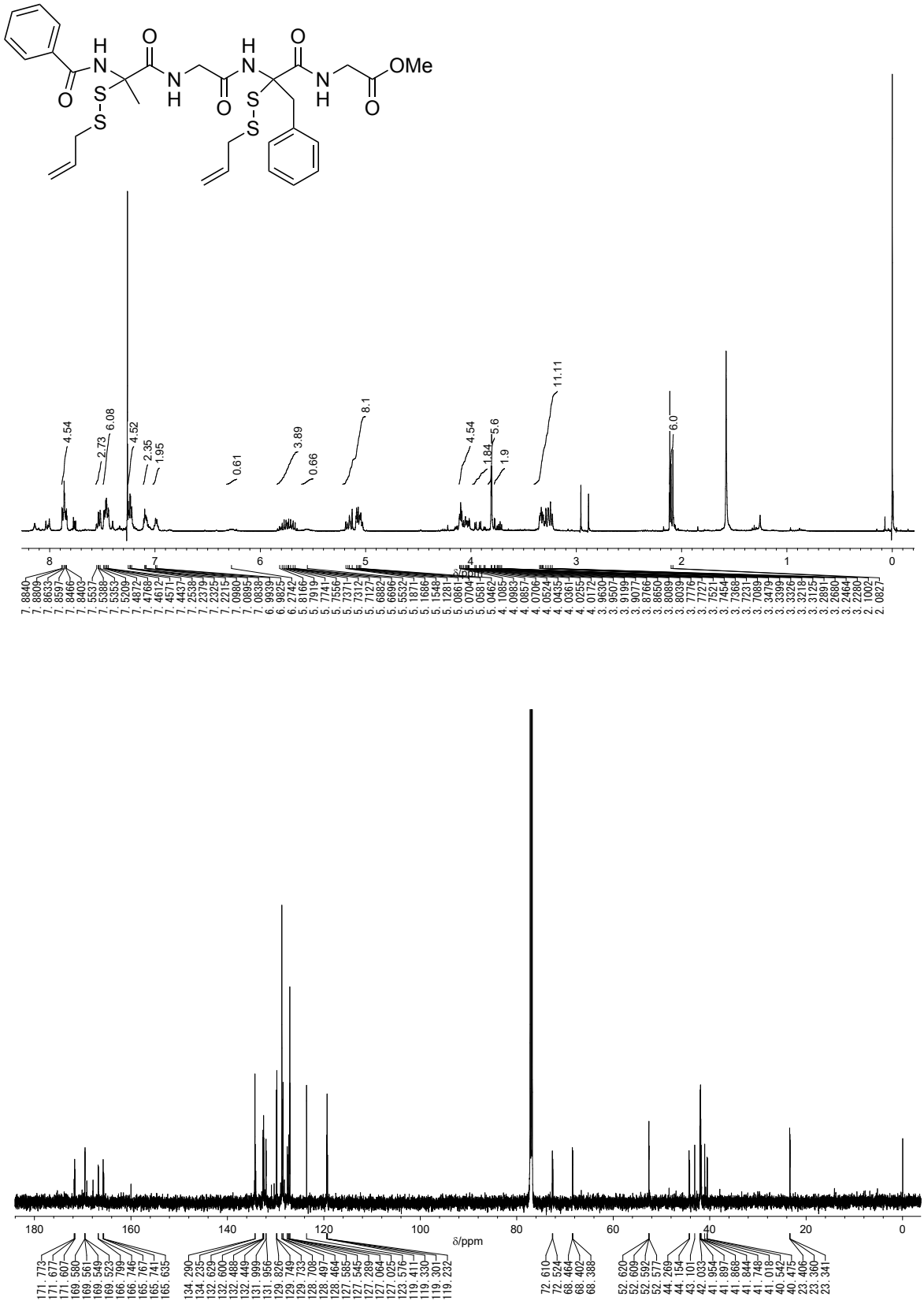


^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of TFA salt of methyl (2-(allyldisulfanyl)-2-(2-aminoacetamido)-3-phenylpropanoyl)glycinate (**27**·TFA) (CD_3OD, Isolated as the TFA salt with slight impurities.)





^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of methyl (2-(allyldisulfanyl)-2-(2-(2-(allyldisulfanyl)-2-benzamidopropanamido)acetamido)-3-phenylpropanoyl)glycinate (**28**) ($CDCl_3$)



^{1}H NMR (400 MHz) and ^{13}C NMR (150 MHz) spectra of (2*S*)-1-((2-(allyldisulfanyl)-2-benzamidopropanoyl)glycylglycyl-L-valyl-L-leucyl-L-valyl-L-glutaminyl)-*N*-(2-amino-2-oxoethyl)pyrrolidine-2-carboxamide (**30**) (CD_3OD)