Supporting Information

Rapid, Scalable Assembly of Stereochemically Rich, Mono- and Bicyclic Acyl Sultams

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General Experimental Methods

All air and moisture sensitive reactions were carried out in flame- or oven-dried glassware under argon atmosphere using standard gas tight syringes, cannula, and septa. Stirring was achieved with oven-dried, magnetic stir bars. CH_2Cl_2 was purified by passage through the Solv-Tek purification system employing activated Al_2O_3 (Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520). Et_3N was purified by passage over basic alumina and stored over KOH. Flash column chromatography was performed with SiO_2 from Mallinckrodt Chemicals (V120-25, Silica gel, 60 A, 40–63 μm). Thin layer chromatography was performed on silica gel 60F254 plates (EMD-5715-7, Merck). Deuterated solvents were purchased from Cambridge Isotope laboratories. ^{1}H, ^{13}C NMR spectra were recorded on a Bruker DRX-400 spectrometer operating at 400 MHz as well as a Bruker DRX-500 spectrometer operating at 500 MHz, 126 MHz respectively. The reference for $CDCl_3$ was set up at 7.28 ppm and acetone at 2.05 ppm. High-resolution mass spectrometry (HRMS) and FAB spectra were obtained in one of two manners: (i) on a VG Instrument ZAB double-focusing mass spectrometer and (ii) on a LCT Premier Spectrometer (Micromass UK Limited) operating on ESI (MeOH). Gas chromatography (GC) was performed using an Agilent Technologies 6890N. GC/mass spectrometry was performed using a Quattro micro GC (Micromass UK Limited).

General Procedure A: preparation of vinyl sulfonamide. To a round bottom flask containing a solution of amine (1.0 equiv.) in dry CH_2Cl_2 (0.5 M), was added Et_3N (2.0 equiv.). The reaction mixture was cooled to 0 ºC, stirred for 20 min, after which 2-chloroethane sulfonyl chloride (1.0 equiv.) was added to the reaction mixture in a drop-wise fashion. The reaction was warmed to rt and left to stir overnight. The reaction was quenched with 10% aq. HCl, the organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x). The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure to afford the desired vinyl sulfonamide.

General Procedure B: one-pot, sequential (Michael and amide coupling). To a round-bottomed flask attached with a condenser/pressure tube containing a solution of sulfonamide (172 mmol, 1.0 equiv.) in MeOH (0.5 M) and water (0.5 M), was added Et_3N (516 mmol, 3.0 equiv.) followed by amino acid (172 mmol, 1.0 equiv.). The reaction mixture was stirred at 60 ºC for 12 h, after which the solvents were evaporated to dryness. To the crude mixture, DMF (0.05 M) was added, followed by EDC (344 mmol, 2.0 equiv.), HOBt (34.4 mmol, 0.2 equiv.) and Et_3N (344 mmol, 2.0 equiv.). The reaction was stirred at rt for 12 h, followed by evaporation of DMF upon completion of reaction. Water was added to the crude mixture, which was extracted with EtOAc (2x). The organic layer was separated and the combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography (100% EtOAc).

General Procedure C: one-pot, sequential 3-component (sulfonylation, Michael and amide coupling). To a round bottom flask/pressure tube containing a solution of amine (3.8 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.5 M), was added Et_3N (7.6 mmol, 2.0 equiv.). The reaction mixture was cooled to 0 ºC, stirred for 20 min followed by the drop-wise addition of 2-chloroethane sulfonyl chloride (3.8 mmol, 1.0 equiv.). The reaction was warmed to rt and left to stir overnight. CH_2Cl_2 was removed *in vacuo* upon completion of the reaction. MeOH (0.5 M), water (0.5 M), Et_3N (11.4 mmol, 3.0 equiv.) and amino acid (3.8 mmol, 1.0 equiv.) were added to the reaction mixture, which was stirred at 60 ºC for 12 h, after which the solvents were evaporated to dryness. DMF (0.05 M) (for cyclic amino acids), EDC (7.6 mmol, 2.0 equiv.), HOBt (0.76 mmol, 0.2 equiv.) and Et_3N (7.6 mmol, 2.0 equiv.) were added to the crude mixture. The reaction was stirred at rt for 12 h, followed by evaporation of DMF. Water was added to the crude mixture, which was extracted with EtOAc (2x). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography (100% EtOAc). For acyclic amino acids, $CHCl_3$ was utilized as the solvent, followed by addition of EDC (7.6 mmol, 2.0 equiv.), HOBt (0.76 mmol, 0.2 equiv.) and Et_3N (7.6 mmol, 2.0 equiv.). The reaction was stirred at 50 ºC for 12 h after which time; water (equal volume of $CHCl_3$ used) was added to the crude mixture and extraction of aqueous layer with EtOAc (2x). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography (100% EtOAc).

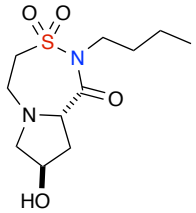
General Procedure D: one-pot, sequential 4-component (sulfonylation, Michael addition, amide coupling and carbamate formation. To a pressure tube containing a solution of amine (0.38 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.5 M), was added Et_3N (0.76 mmol, 2.0 equiv.). The reaction mixture was cooled to 0 ºC, stirred for 20 min, after which 2-chloroethane sulfonyl chloride (0.38 mmol, 1.0 equiv.) was added drop-wise. The reaction mixture was warmed to rt and left to stir overnight. CH_2Cl_2 was removed *in vacuo* upon the completion of reaction, followed by addition of MeOH (0.5 M), water (0.5 M), Et_3N (1.14 mmol, 3.0 equiv.) and amino acid (0.38 mmol, 1.0 equiv.). The reaction was stirred at 60 ºC for 12 h. Upon the removal of solvents, $CHCl_3$ (0.05 M) was added to the crude mixture followed by EDC (0.46 mmol, 1.2 equiv.), HOBt (0.076 mmol, 0.2 equiv.) and Et_3N (0.76 mmol, 2.0 equiv.) for the amide coupling reaction. The reaction was stirred at 50 ºC for 12 h, followed by evaporation of solvent. Carbamoylation commenced with addition of CH_2Cl_2 (0.5 M), isocyanate (0.76 mmol, 2 equiv.), DMAP (0.19 mmol, 0.5 equiv.) and Et_3N (0.76 mmol, 2 equiv.). The reaction was stirred overnight at 50 ºC after which time, water was added to the crude mixture, followed by extraction with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc (2x). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography (1:1 EtOAc:Hexane).

General Procedure E: one-pot, sequential 4-component (sulfonylation, Michael addition, amide coupling and click reaction). To a pressure tube containing a solution of amine (0.38 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.5 M), was added Et_3N (0.79 mmol, 2.0 equiv.). The reaction mixture was cooled to 0 ºC, stirred for 20 min, after which 2-chloroethane sulfonyl chloride (0.38 mmol, 1.0 equiv.) was added drop-wise. The reaction was warmed to rt and left to stir overnight. After completion of the reaction, CH_2Cl_2 was removed under reduced pressure. MeOH (0.5 M), water (0.5 M), Et_3N (1.14 mmol, 3.0 equiv.) and amino acid (0.38 mmol, 1.0 equiv.) were next added to the mixture for the Michael reaction. The mixture was stirred at 60 ºC in a sealed tube for 12 h, after which the solvents were again evaporated to dryness. $CHCl_3$ (0.05 M) was added to the crude mixture followed by EDC (0.46 mmol, 1.2 equiv.), HOBt (0.076 mmol, 0.2 equiv.) and Et_3N (0.76 mmol, 2.0 equiv.) for the amide formation reaction. The reaction was stirred at 50 ºC for 12 h, followed by evaporation of solvent. Next, step-wise addition of CH_2Cl_2, alkyl azide and *t*-butanol was performed, followed by sequential addition of aqueous solutions of $CuSO_4$ (0.19 mmol, 0.5 equiv.) and L-Na-Ascorbate (0.23 mmol, 0.6 equiv.). The reaction was stirred overnight at rt, after which time, water was added to the crude mixture, followed by extraction with EtOAc. The organic layer was separated, and the aqueous layer extracted with EtOAc (2x). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography (100% EtOAc).

General Procedure F: one-pot, sequential 4-component (sulfonylation, Michael, amide coupling and esterification). A solution of amine (0.38 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.5 M), along with Et_3N (0.76 mmol, 2.0 equiv.) was added to a pressure tube. The reaction mixture was cooled to 0 ºC, stirred for 20 min, after which 2-chloroethane sulfonyl chloride (0.38 mmol, 1.0 equiv.) was added to the reaction mixture in a drop-wise manner. The reaction was warmed to rt and left to stir overnight. CH_2Cl_2 was removed *in vacuo* upon the completion of reaction, followed by addition of MeOH (0.5 M), water (0.5 M), Et_3N (1.14 mmol, 3.0 equiv.) and amino acid (0.38 mmol, 1 equiv.) for the Michael reaction. The reaction mixture was stirred at 60 ºC in a sealed tube for 12 h, after which solvents were evaporated to dryness. $CHCl_3$ (0.05 M) was added to the crude mixture followed by EDC (0.46 mmol, 1.2 equiv.), HOBt (0.076 mmol, 0.2 equiv.) and Et_3N (0.76 mmol, 2.0 equiv.) for the amide coupling reaction. The reaction was stirred for 12 h at 50 ºC. After completion of the reaction, additional EDC (0.46 mmol, 1.2 equiv.), HOBt (0.57 mmol, 1.5 equiv.), Et_3N (0.76 mmol, 2.0 equiv.) and carboxylic acid were added to the mixture for the esterification step. The reaction was again stirred overnight at 50 ºC. Upon completion of the reaction, water was added to the crude mixture, which was extracted with EtOAc. The organic layer was separated and the aqueous layer was extracted with EtOAc (2x). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography (1:1 EtOAc:Hexane).

General Procedure G: one-pot, sequential 5-component (sulfonylation, Michael addition, amide coupling, esterification and click reaction). To a pressure tube containing a solution of amine (0.38 mmol, 1.0 equiv.) in dry CH_2Cl_2 (0.5 M), was added Et_3N (0.76 mmol, 2.0 equiv.). The reaction mixture was cooled to 0 ºC, stirred for 20 min, after which 2-chloroethane sulfonyl chloride (0.38 mmol, 1.0 equiv.) was added in a drop-wise manner. The reaction was warmed to rt and left to stir overnight. After completion of the reaction, CH_2Cl_2 was removed *in vacuo,* followed by addition of MeOH (0.5 M), water (0.5 M), Et_3N (1.14 mmol, 3.0 equiv.) and amino acid for the Michael reaction. The reaction mixture was stirred at 60 ºC for 12 h in the sealed tube. The solvents were evaporated to dryness. Amide coupling reaction commenced with addition of $CHCl_3$ (0.05 M), followed by EDC (0.46 mmol, 1.2 equiv.), HOBt (0.076 mmol, 0.2 equiv.) and Et_3N (0.76 mmol, 2.0 equiv.). The reaction was stirred at 50 ºC for 12 h. Upon completion of the reaction, EDC (0.76 mmol, 1.2 equiv.), HOBt (0.57 mmol, 1.5 equiv.) and Et_3N (0.76 mmol, 2.0 equiv.) were added to the crude mixture, followed by the carboxylic acid for the esterification step. The reaction was heated at 50 ºC for 12 h and solvent was removed under reduced pressure. Next, step-wise addition of CH_2Cl_2, alkyl azide and *t*-BuOH was performed, followed by sequential addition of aqueous solutions of $CuSO_4$ (0.19 mmol, 0.5 equiv.) and L-Na-ascorbate (0.23 mmol, 0.6 equiv.). The reaction was stirred overnight at rt, after which time, water was added to the crude mixture, followed by extraction with EtOAc. The organic layer was separated, and the aqueous layer extracted with EtOAc (2x). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford the crude product, which was purified by flash chromatography (2:1 EtOAc:Hexane).

(8*R*,9a*S*)-8-hydroxy-2-butylhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10a)



According to the reaction protocol described in general procedure **B**, compound **10a** (67%, 2.04 g) was isolated after chromatography as a light orange solid.

M. P. 112–113 ºC;

R_f = 0.56 (100% EtOAc);

FTIR (neat) 3637, 3102, 2991, 2901, 1712, 1453, 1349, 1193 cm^{-1};

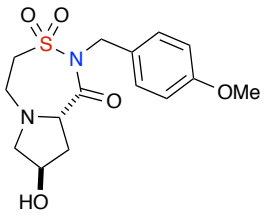
$[\alpha]_D^{20}$ = +23.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 4.44–4.36 [m, 2H, $NCH_2C\underline{H}(OH)CH_2C\underline{H}(C{=}O)$], 3.90–3.74 [m, 2H, $(C{=}O)NC\underline{H}_2CH_2CH_2CH_3$], 3.50–3.35 [m, 4H, $O_2SC\underline{H}_2C\underline{H}_aH_bNC\underline{H}_aH_bCH(OH)$], 3.27 (dt, *J* = 12.2, 3.2 Hz, 1H, $O_2SCH_2CH_a\underline{H}_bN$), 2.75 [dddd, *J* = 12.8, 5.9, 5.9 1.0 Hz, 1H, $NCH_2CH(OH)C\underline{H}_aH_bCH(C{=}O)$], 2.67 [ddd, *J* = 9.9, 5.2, 1.2 Hz, 1H, $NCH_aH_bCH(OH)CH_2CH(C{=}O)$], 1.96 [dddd, *J* = 13.2, 8.9, 5.6, 1.2 Hz, 1H, $NCH_2CH(OH)CH_a\underline{H}_bCH(C{=}O)$], 1.68–1.56 (m, 3H, OH, n-butyl), 1.41–1.30 (m, 2H, n-butyl), 0.94 (td, *J* = 7.4, 1.8 Hz, 3H, n-butyl);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.0, 62.9, 61.5, 58.7, 55.9, 50.4, 46.8, 32.4, 31.5, 19.6, 13.5;

HRMS calculated for $C_{11}H_{20}N_2O_4SH$ $(M+H)^+$ 277.1222; found 277.1222 (TOF MS ES^+).

(8*R*,9a*S*)-8-hydroxy-2-(4-methoxybenzyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10b)



According to the reaction protocol described in general procedure **B**, compound **10b** (72%, 1.02 g) was isolated after chromatography as a dark orange solid.

M. P. 125–127 ºC;

R_f = 0.38 (100% EtOAc);

FTIR (thin film) 3365, 3299, 3155, 2956, 1708, 1444, 1355, 1155, 1213, 835 cm^{-1};

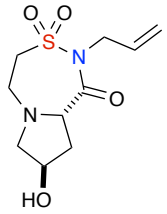
$[\alpha]_D^{20}$ = +26.6° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.37–7.33 (m, 2H), 6.87–6.83 (m, 2H), 5.09 (d, *J* = 15.0 Hz, 1H, $NC\underline{H}_aH_bPh$), 4.85 (d, *J* = 14.9 Hz, 1H, $NCH_a\underline{H}_bPh$), 4.42 [dd, *J* = 8.8, 5.8 Hz, 1H, $NCH_2CH(OH)CH_2C\underline{H}(C{=}O)$], 4.39 [dddd, *J* = 5.4, 5.4, 5.3, 5.3 Hz, 1H, $NCH_2C\underline{H}(OH)CH_2CH(C{=}O)$], 3.80 (s, 3H, Ar-$OC\underline{H}_3$), 3.45–3.33 (m, 3H, $O_2SC\underline{H}_2C\underline{H}_aH_bN$), 3.23–3.10 [m, 2H, $O_2SCH_2CH_a\underline{H}_bNC\underline{H}_aH_bCH(OH)$], 2.75 [dddd, *J* = 12.5, 5.8, 5.8, 1.0 Hz, 1H, $NCH_2CH(OH)C\underline{H}_aH_bCH(C{=}O)$], 2.64 [ddd, *J* = 9.8, 5.3, 1.1 Hz, 1H, $O_2SCH_2CH_aH_bNCH_a\underline{H}_bCH(OH)$], 1.95 [dddd, *J* = 14.4, 8.7, 5.7, 1.1 Hz, 1H, $NCH_2CH(OH)CH_a\underline{H}_bCH(C{=}O)$], 1.89 (s, 1H, OH);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.5, 159.1, 130.1 (2), 128.7, 113.8 (2), 77.3, 70.17, 64.1, 56.5, 55.3, 52.4, 48.1, 36.6;

HRMS calculated for $C_{15}H_{20}N_2O_5SNa$ $(M+Na)^+$ 363.0991; found 363.1004 (TOF MS ES^+).

(8*R*,9a*S*)-2-allyl-8-hydroxyhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10c, 27a)



According to the reaction protocol described in general procedure **B**, compound **10c** (86%, 12.1 g) was isolated after chromatography as a light brown solid.

According to the reaction protocol described in general procedure **C**, compound **27a** (39%, 0.15 g) was isolated after chromatography as a white solid.

M. P. 113–116 ºC;

R_f = 0.42 (100% EtOAc);

$[\alpha]_D^{20}$ = +25.8° (*c* = 0.36, MeOH);

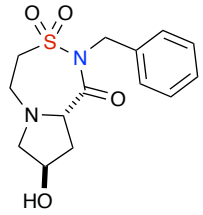
FTIR (thin film) 3373, 3331, 2928, 1705, 1647, 1447, 1344, 1150, 1082, 989, 915 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 5.88 (dddd, *J* = 17.2, 10.3, 6.2, 5.3 Hz, 1H, $CH_2C\underline{H}{=}CH_2$), 5.35 (dddd, *J* = 17.1, 1.4, 1.4, 1.4 Hz, 1H, $CH_2CH{=}CH_{cis}\underline{H}_{trans}$), 5.24 (dddd, *J* = 10.3, 1.2, 1.2, 1.2 Hz, 1H, $CH_2CH{=}C\underline{H}_{cis}H_{trans}$), 4.51–4.36 [m, 4H, $NCH_2C\underline{H}(OH)CH_2C\underline{H}(C{=}O)NC\underline{H}_2$], 3.52–3.33 [m, 4H, $O_2SC\underline{H}_2C\underline{H}_aH_bNC\underline{H}_aH_bCH(OH)$], 3.29 (dt, *J* = 12.7, 3.5 Hz, 1H, $O_2SCH_2CH_a\underline{H}_bN$), 2.76 [dddd, *J* = 12.8, 5.8, 5.8, 1.0 Hz, 1H, $NCH_2CH(OH)C\underline{H}_aH_bCH(C{=}O)$], 2.68 [ddd, *J* = 9.9, 5.3, 1.2 Hz, 1H, $NCH_a\underline{H}_bCH(OH)CH_2CH(C{=}O)$], 1.96 [dddd, *J* = 14.2, 8.8, 5.7, 1.2 Hz, 1H, $NCH_2CH(OH)CH_a\underline{H}_bCH(C{=}O)$], 1.57 (s, 1H, OH);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.3, 132.2, 118.5, 70.4, 64.3, 64.3, 56.7, 52.7, 47.8, 36.7;

HRMS calculated for $C_{10}H_{16}N_2O_4SH$ $(M + H)^+$ 261.0909; found 261.0894 (TOF MS ES^+).

(8*R*,9a*S*)-2-benzyl-8-hydroxyhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10d, 27b)



According to the reaction protocol described in general procedure **B**, compound **10d** (76%, 5.05 g) was isolated after chromatography as a light brown solid.

According to the reaction protocol described in general procedure **C**, compound **27b** (69%, 0.51 g) was isolated after chromatography as a light brown solid.

M. P. 109–110 ºC;

R_f = 0.52 (100% EtOAc);

FTIR (neat) 3639, 3109, 2953, 2901, 1701, 1454, 1360, 1142, 1102, 712 cm^{-1};

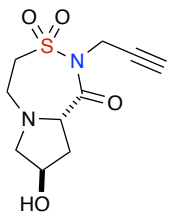
$[\alpha]_D^{20}$ = +25.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.42–7.37 (m, 2H), 7.36–7.32 (m, 2H), 7.31–7.28 (m, 1H), 5.13 (d, *J* = 15.1 Hz, 1H, NC$\underline{H}_a$H$_b$Ph), 4.90 (d, *J* = 15.1 Hz, 1H, NCH$_a\underline{H}_b$Ph), 4.46 [dd, *J* = 10.6, 6.0 Hz, 1H, NCH$_2$CH(OH)CH$_2$C$\underline{H}$(C=O)], 4.42 [dddd, *J* = 5.2, 5.2, 5.2, 5.2 Hz, 1H, NCH$_2$C$\underline{H}$(OH)CH$_2$CH(C=O)], 3.49–3.42 (m, 1H, O$_2$SC$\underline{H}_a$H$_b$CH$_2$N), 3.41–3.35 (m, 2H, O$_2$SCH$_a\underline{H}_b$C$\underline{H}_a$H$_b$N), 3.26–3.17 (m, 2H, O$_2$SCH$_2$CH$_a\underline{H}_b$NC$\underline{H}_a$H$_b$), 2.76 [dddd, *J* = 13.5, 5.9, 5.9, 1.0 Hz, 1H NCH$_2$CH(OH)C$\underline{H}_a$H$_b$CH(C=O)], 2.65 [ddd, *J* = 9.9, 5.2, 1.2 Hz, 1H, O$_2$SCH$_2$CH$_2$NCH$_a\underline{H}_b$)], 2.07 (bs, 1H, OH), 1.95 [dddd, *J* = 13.3, 8.5, 5.6, 1.0 Hz, 1H, NCH$_2$CH(OH)CH$_a\underline{H}_b$CH(C=O)];

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.6, 136.3, 128.6, 128.1(2), 127.7(2), 63.9, 61.6, 58.9, 55.4, 50.3, 49.0, 32.3;

HRMS calculated for $C_{14}H_{18}N_2O_4SH$ $(M+H)^+$ 311.1066; found 311.1061 (TOF MS ES^+).

(8*R*,9a*S*)-8-hydroxy-2-(prop-2-yn-1-yl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10e)



According to the reaction protocol described in general procedure **B**, compound **10e** (64%, 28.1 g) was isolated after chromatography as a light brown solid.

M. P. 94–95 ºC;

R_f = 0.38 (100% EtOAc);

FTIR (thin film) 3566, 3172, 2979, 2077, 1681, 1357, 1155, 1070 cm^{-1};

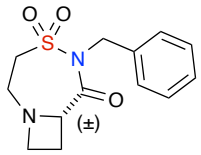
$[\alpha]_D^{20}$ = +22.7° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 4.73 (dd, *J* = 17.5, 2.4 Hz, 1H, $NC\underline{H}_aH_bCCH$), 4.51 (dd, *J* = 17.5, 2.4 Hz, 1H, $NCH_a\underline{H}_bCCH$), 4.47–4.40 [m, 2H, $NCH_2C\underline{H}(OH)CH_2C\underline{H}(C{=}O)$], 3.55–3.44 (m, 3H, $O_2SC\underline{H}_2C\underline{H}_aH_bN$), 3.42 [ddd, *J* = 9.9, 4.7, 1.0 Hz, 1H, $NC\underline{H}_aH_bCH(OH)CH_2$], 3.30 (dd, *J* = 9.1, 3.4 Hz, 1H, $O_2SCH_2CH_a\underline{H}_bN$), 2.76 [dddd, *J* = 13.0, 6.0, 5.9, 1.0 Hz, 1H, $NCH_2CH(OH)C\underline{H}_aH_b$], 2.69 [ddd, *J* = 9.9, 5.2, 1.1 Hz, 1H, $NCH_a\underline{H}_bCH(OH)CH_2$], 2.30 (dd, *J* = 2.4, 2.3 Hz, 1H, $NCH_2CC\underline{H}$), 1.98 [dddd, *J* = 13.3, 8.6, 5.6, 1.1 Hz, 1H, $NCH_2CH(OH)CH_a\underline{H}_b$], 1.61 (s, 1H, OH);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.2, 77.8, 71.9, 70.2, 64.1, 63.7, 56.6, 52.3, 36.5, 34.4;

HRMS calculated for $C_{10}H_{14}N_2O_4SNa$ $(M+Na)^+$ 281.0572; found 281.0580 (TOF MS ES^+).

5-benzyl-4-thia-1,5-diazabicyclo[5.2.0]nonan-6-one 4,4-dioxide (11, 27c)



According to the reaction protocol described in general procedure **B**, compound **11** (75%, 0.21 g) was isolated after chromatography as a yellow solid.

According to the reaction protocol described in general procedure **C**, compound **27c** (85%, 0.102 g) was isolated after chromatography as a white solid.

M. P. 82–84 ºC;

R_f = 0.53 (1:1 Hexane:EtOAc);

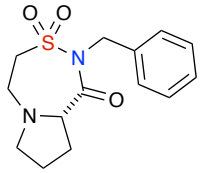
FTIR (thin film) 2974, 2839, 1712, 1693, 1496, 1371, 1149, 1037, 727 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.44–7.39 (m, 2H), 7.38–7.33 (m, 2H), 7.32–7.27 (m, 1H), 5.17 (d, *J* = 15.2 Hz, 1H, $NC\underline{H}_aH_bPh$), 4.87 (d, *J* = 15.3 Hz, 1H, $NCH_a\underline{H}_bPh$), 4.56 (dd, *J* = 8.2, 8.2 Hz, 1H, $C{=}OC\underline{H}CH_2$), 3.38–3.29 (m, 2H, $O_2SC\underline{H}_aH_bCH_2NC\underline{H}_aH_bCH_2$), 3.22–3.09 (m, 3H, $O_2SCH_a\underline{H}_bC\underline{H}_aH_bNCH_a\underline{H}_bCH_2$), 3.05–3.00 (m, 1H, $O_2SCH_2CH_a\underline{H}_bNCH_2$), 2.61 [dddd, *J* = 10.4, 10.4, 8.5, 8.5 Hz, 1H, $NCH_2C\underline{H}_aH_bCH(C{=}O)$], 2.13 [dddd, *J* = 10.4, 7.6, 7.6, 2.0 Hz, 1H, $NCH_2CH_a\underline{H}_bCH(C{=}O)$];

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.9, 136.5, 128.5 (2), 128.1 (2), 127.6, 65.8, 55.4, 51.4, 50.5, 48.0, 20.5;

HRMS calculated for $C_{13}H_{16}N_2O_3SH$ $(M+H)^+$ 281.0960, found 281.0968 (TOF MS ES^+).

(*S*)-2-benzylhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (12, 27d)



According to the reaction protocol described in general procedure **B**, compound **12** (82%, 0.097 g) was isolated after chromatography as a white solid.

According to the reaction protocol described in general procedure **C**, compound **27d** (85%, 0.098 g) was isolated after chromatography as a white solid.

M. P. 89–91 ºC;

R_f = 0.52 (1:1 Hexane:EtOAc);

FTIR (thin film) 2927, 1701, 1454, 1365, 1218, 1151, 732 cm^{-1};

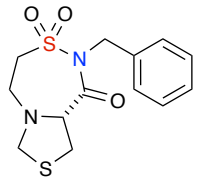
$[\alpha]_D^{20}$ = +29.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.43–7.39 (m, 2H), 7.36–7.31 (m, 2H), 7.30–7.26 (m, 1H), 5.14 (d, *J* = 15.2 Hz, 1H, NCH_aH_bPh), 4.93 (d, *J* = 15.1 Hz, 1H, NCH_aH_bPh), 4.16 (dd, *J* = 9.8, 2.5 Hz, 1H, $C{=}OCHCH_2$), 3.39–3.34 (m, 1H, $O_2SCH_aH_bCH_2$), 3.28–3.19 (m, 3H, $O_2SCH_aH_bCH_2N$), 3.17–3.12 [m, 1H, $NCH_aH_bCH_2CH_2CH(C{=}O)$], 2.70–2.63 [m, 1H, $NCH_aH_bCH_2CH_2CH(C{=}O)$], 2.63–2.54 [m, 1H, $NCH_2CH_2CH_aH_bCH(C{=}O)$], 1.95–1.85 [m, 1H, $NCH_2CH_2CH_aH_bCH(C{=}O)$], 1.82–1.74 [m, 2H $NCH_2CH_2CH_2CH(C{=}O)$];

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.9, 136.5, 128.5 (2), 128.3 (2), 127.6, 64.3, 57.8, 56.2, 50.7, 48.6, 27.2, 24.7;

HRMS calculated for $C_{14}H_{18}N_2O_3SH$ $(M+H)^+$ 295.1116, found 295.1116 (TOF MS ES^+).

(*R*)-2-benzylhexahydro-1*H*-thiazolo[4,3-*d*][1,2,5]thiadiazepin-1-one 3,3-dioxide (13, 27e)



According to the reaction protocol described in general procedure **B**, compound **13** (70%, 0.098 g) was isolated after chromatography as a brown solid.

According to the reaction protocol described in general procedure **C**, compound **27e** (76%, 0.21 g) was isolated after chromatography as a brown solid.

M. P. 98–99 ºC;

R_f = 0.51 (1:1 Hexane:EtOAc);

FTIR (thin film) 2927, 1701, 1496, 1456, 1373, 1151, 1022, 730 cm^{-1};

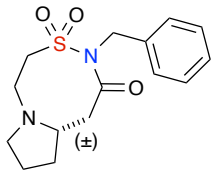
$[\alpha]_D^{20}$ = -21.7° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.43–7.39 (m, 2H), 7.37–7.32 (m, 2H), 7.32–7.27 (m, 1H), 5.17 (d, *J* = 15.1 Hz, 1H, $NC\underline{H}_aH_bPh$), 4.92 (d, *J* = 15.1 Hz, 1H, $NCH_a\underline{H}_bPh$), 4.44 (dd, *J* = 7.3, 5.4 Hz, 1H, $C{=}OC\underline{H}CH_2$), 4.21 (d, *J* = 9.1 Hz, 1H, $NC\underline{H}_aH_bS$), 3.89 (d, *J* = 9.1 Hz, 1H, $NCH_a\underline{H}_bS$), 3.69 (dd, *J* = 12.1, 5.4 Hz, 1H, $NCH_2SC\underline{H}_aH_bCH$), 3.61–3.54 (m, 1H, $O_2SC\underline{H}_aH_bCH_2N$), 3.43–3.38 (m, 1H, $O_2SCH_2C\underline{H}_aH_bN$), 3.34–3.23 (m, 2H, $O_2SCH_a\underline{H}_bCH_a\underline{H}_bN$), 3.16 (dd, *J* = 12.1, 7.3 Hz, 1H, $NCH_2SCH_a\underline{H}_bCH$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 167.0, 136.4, 128.6 (2), 128.4 (2), 127.8, 67.3, 60.9, 55.8, 51.7, 48.7, 34.1;

HRMS calculated for $C_{13}H_{16}N_2O_3S_2H$ $(M+H)^+$ 313.0681, found 313.0685 (TOF MS ES$^+$).

3-benzylhexahydro-1*H*-pyrrolo[2,1-*e*][1,2,6]thiadiazocin-2(3*H*)-one 4,4-dioxide (14)



According to the reaction protocol described in general procedure **B**, compound **14** (65%, 0.096 g) was isolated after chromatography as a light yellow solid.

M. P. 87–90 ºC;

R_f = 0.70 (1:1 Hexane:EtOAc);

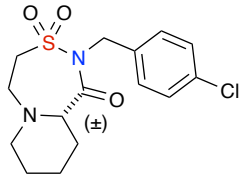
FTIR (thin film) 3286, 2931, 1703, 1645, 1494, 1454, 1398, 1284, 1137, 730 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.48–7.43 (m, 2H), 7.34–7.25 (m, 3H), 5.51 (d, *J* = 14.9 Hz, 1H, $NC\underline{H}_aH_bPh$), 4.75 (d, *J* = 14.8 Hz, 1H, $NCH_a\underline{H}_bPh$), 4.08 (dd, *J* = 12.4, 8.6 Hz, 1H, $O_2SC\underline{H}_aH_bCH_2N$), 3.30–3.20 (m, 1H, $O_2SCH_a\underline{H}_bCH_2N$), 3.07–2.93 (m, 4H, $O_2SCH_2C\underline{H}_2NC\underline{H}$, $NC\underline{H}_aH_bCH_2$), 2.81–2.68 [m, 1H, $NCHC\underline{H}_aH_b(C{=}O)$], 2.54 [d, *J* = 13.0 Hz, 1H, $NCHCH_a\underline{H}_b(C{=}O)$], 2.47 (dd, *J* = 16.8, 8.2 Hz, 1H, $NCH_a\underline{H}_bCH_2$), 2.10–1.91 [m, 2H, $NCH_2C\underline{H}_aH_bC\underline{H}_aH_bCH(C{=}O)$], 1.85–1.71 [m, 2H, $NCH_2CH_a\underline{H}_bCH_a\underline{H}_bCH(C{=}O)$];

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.7, 136.4, 129.2 (2), 128.2 (2), 127.7, 64.2, 56.8, 56.2, 48.5, 47.7, 37.5, 29.8, 22.6;

HRMS calculated for $C_{15}H_{20}N_2O_3SH$ $(M+H)^+$ 309.1273, found 309.1282 (TOF MS ES$^+$).

2-(4-chlorobenzyl)octahydro-1*H*-pyrido[2,1-*d*][1,2,5]thiadiazepin-1-one 3,3-dioxide (15, 27f)



According to the reaction protocol described in general procedure **B**, compound **15** (75%, 0.105 g) was isolated after chromatography as a brown solid.

According to the reaction protocol described in general procedure **C**, compound **27f** (82%, 0.11 g) was isolated after chromatography as a brown solid.

M. P. 88–91 ºC;

R_f = 0.45 (1:1 Hexane:EtOAc);

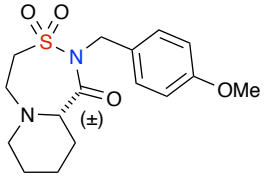
FTIR (thin film) 2975, 2923, 2833, 1704, 1444, 1355, 1153, 825 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.43–7.38 (m, 2H), 7.32–7.28 (m, 2H), 5.06 (d, *J* = 15.0 Hz, 1H, NC$\underline{H}_a$H$_b$Ph), 4.88 (d, *J* = 15.0 Hz, 1H, NCH$_a\underline{H}_b$Ph), 4.28 (dd, *J* = 3.8, 3.4 Hz, 1H, C=OC$\underline{H}$CH$_2$), 3.79 (m, 1H, O$_2$SC$\underline{H}_a$H$_b$CH$_2$N), 3.40–3.32 (m, 1H, O$_2$SCH$_2$C$\underline{H}_a$H$_b$N), 3.28–3.19 (m, 2H, O$_2$SCH$_a\underline{H}_b$CH$_a\underline{H}_b$N), 2.52–2.42 (m, 2H, NC$\underline{H}_2$CH$_2$), 2.10–2.03 (m, 1H, NCH$_2$CH$_2$CH$_2$C$\underline{H}_a$H$_b$CH), 1.80–1.67 (m, 1H, NCH$_2$CH$_2$C$\underline{H}_a$H$_b$CH$_2$CH), 1.63 (m, 1H, NCH$_2$C$\underline{H}_a$H$_b$CH$_2$CH$_2$CH), 1.60–1.49 (m, 3H, NCH$_2$CH$_a\underline{H}_b$CH$_a\underline{H}_b$CH$_a\underline{H}_b$CH);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 173.0, 135.7, 133.7, 130.2 (2), 128.7 (2), 60.7, 53.0, 52.1, 47.7, 47.6, 27.4, 25.8, 19.9;

HRMS calculated for $C_{15}H_{19}ClN_2O_3SH$ $(M+H)^+$ 343.0883, found 343.0883 (TOF MS ES^+).

2-(4-methoxybenzyl)octahydro-1*H*-pyrido[2,1-*d*][1,2,5]thiadiazepin-1-one 3,3-dioxide (16)



According to the reaction protocol described in general procedure **B**, compound **16** (71%, 0.105 g) was isolated after chromatography as a dark yellow solid.

M. P. 91–93 ºC;

R_f = 0.37 (1:1 Hexane:EtOAc);

FTIR (thin film) 2979, 2927, 1704, 1444, 1357, 1155, 842 cm^{-1};

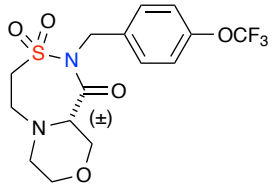
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.44–7.40 (m, 2H), 6.87–6.84 (m, 2H), 5.13 (d, *J* = 14.7 Hz, 1H, NC$\underline{H}_a$H$_b$Ph), 4.85 (d, *J* = 14.7 Hz, 1H, NCH$_a\underline{H}_b$Ph), 4.28 (dd, *J* = 4.7, 2.7 Hz, 1H, C=OC$\underline{H}$CH$_2$), 3.81 (s, 3H, Ar-OC$\underline{H}_3$), 3.79–3.71 (m, 1H, O$_2$SC$\underline{H}_a$H$_b$CH$_2$N), 3.35–3.28 (m, 1H, O$_2$SCH$_2$C$\underline{H}_a$H$_b$N), 3.25–3.17 (m, 2H, O$_2$SCH$_a\underline{H}_b$CH$_a\underline{H}_b$N), 2.45–2.39 (m, 2H, NC$\underline{H}_2$CH$_2$), 2.13–2.05 (m, 1H, NCH$_2$CH$_2$CH$_2$C$\underline{H}_a$H$_b$CH), 1.81–1.70

(m, 1H, $NCH_2CH_2C\underline{H}_aH_bCH_2CH$), 1.62 (m, 1H, $NCH_2C\underline{H}_aH_bCH_2CH_2CH$), 1.65–1.47 (m, 3H, $NCH_2CH_a\underline{H}_bCH_a\underline{H}_bCH_a\underline{H}_bCH$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 173.0, 159.2, 130.5 (2), 129.4, 113.6 (2), 60.6, 55.2, 53.0, 52.1, 47.6, 27.4, 29.7, 25.8, 19.8;

HRMS calculated for $C_{16}H_{22}N_2O_4SH$ $(M+H)^+$ 339.1379, found 339.1388 (TOF MS ES^+).

2-(4-(trifluoromethoxy)benzyl)hexahydro-[1,4]oxazino[3,4-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (17)



According to the reaction protocol described in general procedure **B**, compound **17** (47%, 0.18 g) was isolated after chromatography as a yellow solid.

M. P. 102–107 ºC;

R_f = 0.53 (100% EtOAc);

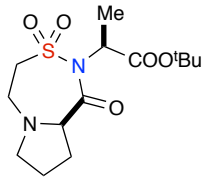
FTIR (thin film) 3121, 2962, 2916, 1682, 1508, 1435, 1346, 1219, 1151, 1043, 851 cm^{-1};

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.55 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 7.8 Hz, 2H), 5.12 (d, *J* = 14.9 Hz, 1H, $NC\underline{H}_aH_bPh$), 4.95 (d, *J* = 14.9 Hz, 1H, $NCH_a\underline{H}_bPh$), 4.34 (d, *J* = 10.9 Hz, 1H, $NCH_2CH_2OC\underline{H}_aH_bCH$), 4.11 [m, 1H, $OCH_2C\underline{H}(C{=}O)$], 3.94–3.84 (m, 1H, $O_2SC\underline{H}_aH_bCH_2N$), 3.76 (ddd, *J* = 10.9, 3.3, 1.6 Hz, 1H, $NCH_2C\underline{H}_aH_bOCH_2CH$), 3.69–3.60 (m, 2H, $NCH_2CH_aH_bOCH_a\underline{H}_bCH$), 3.47–3.39 (m, 1H, $O_2SCH_2C\underline{H}_aH_bN$), 3.31 (dd, *J* = 14.3, 14.2 Hz, 2H, $O_2SCH_a\underline{H}_bCH_a\underline{H}_bN$), 2.77 (dd, *J* = 11.2, 11.1 Hz, 1H, $NC\underline{H}_aH_bCH_2O$), 2.38 (d, *J* = 11.9 Hz, 1H, $NCH_a\underline{H}_bCH_2O$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.2, 148.9, 135.6, 130.6 (2), 121.0 (2), 120.4 (d, J_{C-F} = 257.4 Hz), 67.5, 66.9, 61.3, 52.7, 51.7, 47.8, 47.2;

HRMS calculated for $C_{15}H_{17}F_3N_2O_5SH$ $(M + H)^+$ 395.0898; found 395.0913 (TOF MS ES^+).

(*S*)-*tert*-butyl 2-((*S*)-3,3-dioxido-1-oxohexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-2(1*H*)-yl)propanoate (18)



According to the reaction protocol described in general procedure **B**, compound **18** (77%, 0.49 g) was isolated after chromatography as a light brown solid.

M. P. 84–86 ºC;

R_f = 0.55 (1:1 Hexane:EtOAc);

FTIR (thin film) 2943, 2829, 1731, 1703, 1697, 1444, 1357, 1182 cm^{-1};

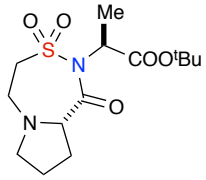
$[\alpha]_D^{20}$ = -29.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 4.90 [q, *J* = 6.9 Hz, 1H, NC<u>H</u>(CH_3)$CO_2{}^t$Bu], 4.14 (dd, *J* = 9.8, 2.5 Hz, 1H, C=OC<u>H</u>CH_2), 3.70 (ddd, *J* = 14.0, 10.2, 6.0 Hz, 1H, $O_2SC\underline{H}_aH_bCH_2$), 3.40 (dt, *J* = 14.0, 2.8 Hz, 1H, $O_2SCH_a\underline{H}_bCH_2$), 3.35–3.22 (m, 2H, $O_2SCH_2C\underline{H}_2N$), 3.16–3.11 (m, 1H, $NC\underline{H}_aH_bCH_2CH_2CH$), 2.66–2.56 (m, 2H, $NCH_a\underline{H}_bCH_2CH_a\underline{H}_bCH$), 1.93–1.83 (m, 1H, $NCH_2CH_2C\underline{H}_aH_bCH$), 1.83–1.70 (m, 2H, $NCH_2C\underline{H}_2CH_2CH$), 1.57 [d, *J* = 6.9 Hz, 3H, NCH(C<u>H</u>$_3$)$CO_2{}^t$Bu], 1.45 [s, 9H, $CO_2C(C\underline{H}_3)_3$];

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.6, 168.6, 82.0, 63.6, 57.7, 56.1, 55.4, 50.5, 27.8, 27.2, 24.8, 16.3 (3);

HRMS calculated for $C_{14}H_{24}N_2O_5SNa$ $(M+Na)^+$ 355.1304, found 355.1309 (TOF MS ES^+).

(*S*)-*tert*-butyl 2-((*R*)-3,3-dioxido-1-oxohexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-2(1*H*)-yl)propanoate (19)



According to the reaction protocol described in general procedure **B**, compound **19** (80%, 0.51 g) was isolated after chromatography as a dark brown solid.

M. P. 84–85 ºC;

R_f = 0.51 (1:1 Hexane:EtOAc);

FTIR (thin film) 2943, 2871, 1737, 1703, 1697, 1444, 1384, 1325, 1126 cm^{-1};

$[\alpha]_D^{20}$ = +15.7° (*c* = 2.0, $CHCl_3$);

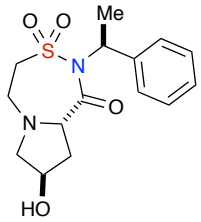
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 4.91 [q, *J* = 6.9 Hz, 1H, NC<u>H</u>(CH_3)$CO_2{}^t$Bu], 4.46–4.37 (m, 2H, C=OC<u>H</u>CH_2, $O_2SC\underline{H}_aH_bCH_2N$), 3.69 (ddd, *J* = 13.4, 12.1, 4.3 Hz, 1H, $O_2SCH_a\underline{H}_bCH_2N$), 3.51–3.36 (m, 3H, $O_2SCH_2C\underline{H}_2N\underline{H}_aH_b$), 3.33–3.26 (m, 1H, $O_2SCH_2CH_2NH_a\underline{H}_b$), 2.74 (ddd, *J* = 12.9, 5.8, 5.8 Hz, 1H, $NCH_2CH_2CH_a\underline{H}_bCH$), 2.67 (dd, *J* = 9.6, 5.6 Hz, 1H, $NCH_2CH_2C\underline{H}_aH_bCH$), 1.94 (ddd, *J* = 13.2, 8.5, 5.6 Hz, 1H,

$NCH_2C\underline{H}_aH_bCH_2CH$), 1.64–1.60 (m, 1H, $NCH_2CH_a\underline{H}_bCH_2CH$), 1.58 [d, J = 7.0 Hz, 3H, $NCH(C\underline{H}_3)CO_2{}^tBu$], 1.46 [s, 9H, $CO_2C(C\underline{H}_3)_3$];

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.3, 169.3, 82.1, 64.3, 57.8, 56.6, 55.0, 50.8, 27.9, 27.3, 24.5, 16.7 (3);

HRMS calculated for $C_{14}H_{24}N_2O_5SNa$ $(M+Na)^+$ 355.1304, found 355.1304 (TOF MS ES$^+$).

(8*R*,9a*S*)-8-hydroxy-2-((*S*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (22)



According to the reaction protocol described in general procedure **B**, compound **22** (85%, 0.50 g) was isolated after chromatography as a dark yellow solid.

M. P. 104–106 ºC;

R_f = 0.52 (100% EtOAc);

FTIR (thin film) 3523, 3392, 2835, 1701, 1496, 1375, 1276, 1147, 734 cm^{-1};

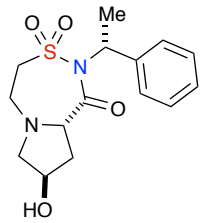
$[\alpha]_D^{20}$ = +23.7° (c = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.44–7.39 (m, 2H), 7.37–7.32 (m, 2H), 7.28–7.24 (m, 1H), 5.89 (q, J = 7.1 Hz, 1H, $NC\underline{H}CH_3Ph$), 4.41 (dd, J = 8.7, 6.0 Hz, 1H, $C{=}OC\underline{H}CH_2$), 4.29 [dddd, J = 5.4, 5.4, 5.3, 5.3 Hz, 1H, $CH_2C\underline{H}(OH)CH_2$], 3.54–3.41 (m, 3H, $O_2SC\underline{H}_2C\underline{H}_aH_bN$), 3.35 [dd, J = 9.9, 4.6 Hz, 1H, $NC\underline{H}_aH_bCH(OH)CH_2CH(C{=}O)$], 3.31–3.25 (m, 1H, $O_2SCH_2CH_a\underline{H}_bN$), 2.68–2.60 [m, 2H, $NCH_a\underline{H}_bCH(OH)C\underline{H}_aH_bCH(C{=}O)$], 1.97–1.92 [m, 1H, $(OH)CHCH_a\underline{H}_bCH(C{=}O)$], 1.91 (d, J = 7.1 Hz, 3H, $NCHC\underline{H}_3Ph$), 1.61 (bs, 1H, OH);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.0, 138.8, 126.7 (2), 125.6, 125.1 (2), 68.6, 63.7, 62.6, 55.5, 55.0, 50.9, 35.2, 16.5;

HRMS calculated for $C_{15}H_{20}N_2O_4SNa$ $(M+Na)^+$ 347.1041, found 347.1042 (TOF MS ES$^+$).

(8*R*,9a*S*)-8-hydroxy-2-((*R*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (23)



According to the reaction protocol described in general procedure **B**, compound **23** (73%, 0.48 g) was isolated after chromatography as a brown solid.

M. P. 106–109 ºC;

R_f = 0.47 (100% EtOAc);

FTIR (thin film) 3651, 3276, 2979, 1713, 1435, 1383, 1221, 1151, 742 cm^{-1};

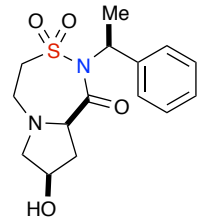
$[\alpha]_D^{20}$ = +21.6° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.35–7.31 (m, 2H), 7.30–7.24 (m, 2H), 7.21–7.16 (m, 1H), 5.88 (q, *J* = 7.1 Hz, 1H, NC<u>H</u>CH_3Ph), 4.36–4.28 [m, 2H, CH_2C<u>H</u>(OH)CH_2C<u>H</u>CH_2(C=O)], 3.35–3.27 (m, 2H, O_2SC<u>H_2</u>CH_2N), 3.19 (dt, *J* = 13.5, 3.4 Hz, 1H, O_2SCH_2C<u>H_a</u>H_bN), 3.13 (dt, *J* = 13.2, 3.4 Hz, 1H, $O_2SCH_2CH_a$<u>H_b</u>N), 3.03 [ddd, *J* = 13.8, 12.4, 4.0 Hz, 1H, NCH_a<u>H_b</u>CH(OH)CH_2CH(C=O)], 2.62 [ddd, *J* = 12.9, 7.0, 6.0 Hz, 1H, NC<u>H_a</u>H_bCH(OH)CH_2CH(C=O)], 2.57 [ddd, *J* = 9.8, 5.2, 0.8 Hz, 1H, NCH_2CH(OH)CH_a<u>H_b</u>CH(C=O)], 1.84 [dddd, *J* = 14.2, 8.6, 5.5, 1.1 Hz, 1H, NCH_2CH(OH)C<u>H_a</u>H_bCH(C=O)], 1.77 (d, *J* = 7.1 Hz, 3H, NCHC<u>H_3</u>Ph), 1.60 (bs, 1H, OH);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.6, 139.8, 128.2 (2), 127.2, 127.1 (2), 70.2, 65.0, 64.2, 57.0, 56.0, 52.4, 36.8, 17.4;

HRMS calculated for $C_{15}H_{20}N_2O_4SH$ $(M+H)^+$ 325.1222, found 325.1221 (TOF MS ES^+).

(8*R*,9a*R*)-8-hydroxy-2-((*S*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (24)



According to the reaction protocol described in general procedure **B**, compound **24** (75%, 0.51 g) was isolated after chromatography as a dark yellow solid.

M. P. 106–107 ºC;

R_f = 0.58 (100% EtOAc);

FTIR (thin film) 3539, 3280, 2975, 1755, 1631 1452, 1321, 1276, 1151, 734 cm^{-1};

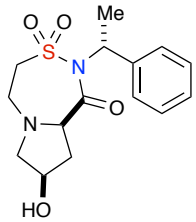
$[\alpha]_D^{20}$ = -19.7° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.42–7.35 (m, 4H), 7.34–7.29 (m, 1H), 5.22–5.10 (m, 1H, NC<u>H</u>CH_3Ph), 4.82 (bs, 1H, OH), 4.63 [dddd, *J* = 6.9, 6.9, 6.8, 6.8 Hz, 1H, $CH_2C\underline{H}(OH)CH_2$], 3.47–3.45 (m, 1H, C=OC<u>H</u>CH_2), 3.07 [dd, *J* = 12.4, 1.4 Hz, 1H, NC<u>H</u>$_a$H$_b$CH(OH)CH_2], 3.01–2.82 (m, 3H, $O_2SC\underline{H_2}C\underline{H}_aH_bN$), 2.70 (ddd, *J* = 12.3, 7.3, 5.4 Hz, 1H, $O_2SCH_2CH_a\underline{H}_bN$), 2.16 [d, *J* = 11.3 Hz, 1H, NCH$_a$<u>H</u>$_b$CH(OH)CH_2], 2.05 [ddd, *J* = 12.4, 4.6, 1.6 Hz, 1H, $NCH_2CH(OH)CH_a\underline{H}_b$], 1.78 [dd, *J* = 10.7, 1.8 Hz, 1H, $NCH_2CH(OH)C\underline{H}_aH_b$], 1.55 (d, *J* = 7.3 Hz, 3H, NCHC<u>H</u>$_3$Ph);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.4, 142.7, 129.0 (2), 128.0, 126.3 (2), 79.5, 62.5, 55.6, 53.9, 52.4, 48.7, 39.1, 24.2;

HRMS calculated for $C_{15}H_{20}N_2O_4SNa$ $(M+Na)^+$ 347.1041, found 347.1037 (TOF MS ES$^+$).

(8*R*,9a*R*)-8-hydroxy-2-((*R*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (25)



According to the reaction protocol described in general procedure **B**, compound **25** (70%, 0.49 g) was isolated after chromatography as a dark yellow solid.

M. P. 108–110 ºC;

R_f = 0.53 (100% EtOAc);

FTIR (thin film) 3523, 3110, 2941, 2835, 1701, 1448, 1375, 1209, 1151, 734 cm^{-1};

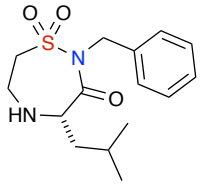
$[\alpha]_D^{20}$ = -15.7° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.39–7.35 (m, 4H), 7.33–7.26 (m, 1H), 5.61 (d, *J* = 7.34, 1H, NC<u>H</u>CH_3Ph), 4.81 (bs, 1H, OH), 4.61 [dddd, *J* = 7.0, 7.0, 6.9, 6.9 Hz, 1H, $CH_2C\underline{H}(OH)CH_2$], 3.46–3.43 (m, 1H, C=OC<u>H</u>CH_2), 3.11 [dd, *J* = 10.7, 1.4 Hz, 1H, NC<u>H</u>$_a$H$_b$CH(OH)CH_2], 3.01–2.91 (m, 2H, $O_2SC\underline{H_2}CH_2N$), 2.81–2.74 (m, 1H, $O_2SCH_2C\underline{H}_aH_bN$), 2.64–2.56 (m, 1H, $O_2SCH_2CH_a\underline{H}_bN$), 2.02–1.97 [m, 1H, NCH$_a$<u>H</u>$_b$CH(OH)$CH_2$], 1.89–1.85 [m, 1H, $NCH_2CH(OH)CH_a\underline{H}_b$], 1.76 [dd, *J* = 10.8, 1.8 Hz, 1H, $NCH_2CH(OH)C\underline{H}_aH_b$], 1.53 (d, *J* = 6.9 Hz, 3H, NCHC<u>H</u>$_3$Ph);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.7, 143.0, 129.1 (2), 127.8, 126.4 (2), 79.5, 62.4, 55.3, 53.8, 52.1, 48.3, 39.1, 24.1;

HRMS calculated for $C_{15}H_{20}N_2O_4SNa$ $(M+Na)^+$ 347.1041, found 347.1044 (TOF MS ES$^+$).

(*S*)-2-benzyl-4-isobutyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26a, 27g)



According to the reaction protocol described in general procedure **B**, compound **26a** (63%, 5.05 g) was isolated after chromatography as a light yellow solid.

According to the reaction protocol described in general procedure **C**, compound **27g** (61%, 0.49 g) was isolated after chromatography as a light yellow solid.

M. P. 74–76 ºC;

R_f = 0.56 (100% EtOAc);

FTIR (thin film) 3357, 3087, 2952, 1697, 1585, 1467, 1365, 1209, 1147 cm^{-1};

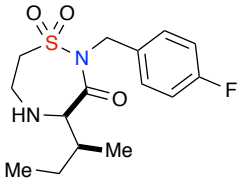
$[\alpha]_D^{20}$ = +25.0° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.43–7.39 (m, 2H), 7.36–7.31 (m, 2H), 7.31–7.25 (m, 1H), 5.18 (d, *J* = 15.0 Hz, 1H, $NCH_a\underline{H}_bPh$), 4.89 (d, *J* = 14.9 Hz, 1H, $NC\underline{H}_aH_bPh$), 4.18 (dd, *J* = 8.6, 4.7 Hz, 1H, $HNC\underline{H}CH_2$), 3.55–3.45 (m, 1H, $O_2SC\underline{H}_aH_bCH_2$), 3.36 (ddd, *J* = 14.7, 4.1, 2.8 Hz, 1H, $O_2SCH_a\underline{H}_bCH_2$), 3.28 (dt, *J* = 14.3, 2.7 Hz, 1H, $CH_2CH_a\underline{H}_bNH$), 2.94 (ddd, *J* = 14.2, 12.1, 4.1 Hz, 1H, $CH_2C\underline{H}_aH_bNH$), 1.78–1.69 (m, 2H, $CHC\underline{H}_2CH$), 1.41 (p, *J* = 9.2 Hz, 1H, $CH_3C\underline{H}CH_3$), 0.95 (d, *J* = 6.1 Hz, 3H, $C\underline{H}_3CHCH_3$,), 0.93 (d, *J* = 6.0 Hz, 3H, $CH_3CHC\underline{H}_3$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 173.2, 147.2, 136.5, 128.4 (2), 127.6 (2), 58.3, 56.8, 48.2, 45.3, 40.7, 24.5, 23.0, 22.1;

HRMS calculated for $C_{15}H_{22}N_2O_3SNa$ $(M+Na)^+$ 333.1429; found 333.1429 (TOF MS ES^+).

(4*S*)-4-(*sec*-butyl)-2-(4-fluorobenzyl)-1,2,5-thiadiazepan-3-one 1,1-dioxide (26b, 27h)



According to the reaction protocol described in general procedure **B**, compound **26b** (65%, 0.21 g) was isolated after chromatography as a light yellow solid.

According to the reaction protocol described in general procedure **C**, compound **27h** (65%, 0.21 g) was isolated after chromatography as a light yellow solid.

M. P. 79–81 ºC;

R_f = 0.45 (100% EtOAc);

FTIR (thin film) 3363, 2960, 2929, 2873, 1697, 1467, 1365, 1147, 812 cm^{-1};

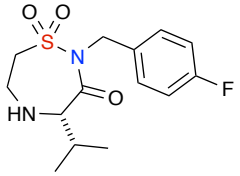
$[\alpha]_D^{20}$ = +32.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.45–7.39 (m, 2H), 7.06–6.99 (m, 2H), 5.12 (d, *J* = 14.9 Hz, 1H, NCH_aH_bPh), 4.87 (d, *J* = 14.9 Hz, 1H, NCH_aH_bPh), 3.93 [d, *J* = 6.8 Hz, 1H, HNCH(C=O)], 3.52–3.42 (m, 2H, $O_2SCH_2CH_2NH$), 3.29 (dt, *J* = 14.2, 2.7 Hz, 1H, $O_2SCH_2CH_aH_bNH$), 2.89 (ddd, *J* = 14.2, 10.7, 5.7 Hz, 1H, $O_2SCH_2CH_aH_bNH$), 1.92 (ddqd, *J* = 9.4, 7.4, 6.6, 3.1 Hz, 1H, $CH_3CH_2CHCH_3$), 1.66 (dqd, *J* = 13.4, 7.6, 3.2 Hz, 1H, $CH_3CH_aH_bCHCH_3$), 1.16 (ddq, *J* = 13.0, 9.1, 7.3 Hz, 1H, $CH_3CH_aH_bCHCH_3$), 0.98 (d, *J* = 6.6 Hz, 3H, $CH_3CH_2CHCH_3$), 0.93 (t, *J* = 7.4 Hz, 3H, $CH_3CH_2CHCH_3$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 172.7, 162.3 ($^1J_{C–F}$ = 246.5 Hz), 132.6 ($^4J_{C–F}$ = 3.25 Hz), 130.7 ($^3J_{C–F}$ = 8.12 Hz, 2), 115.5 ($^2J_{C–F}$ = 21.42 Hz, 2), 64.6, 56.9, 47.5, 45.5, 35.9, 24.5, 16.4, 11.3;

HRMS calculated for $C_{15}H_{21}FN_2O_3SNa$ $(M+Na)^+$ 351.1155; found 351.1154 (TOF MS ES^+).

(*S*)-2-(4-fluorobenzyl)-4-isopropyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26c)



According to the reaction protocol described in general procedure **B**, compound **26c** (67%, 0.21 g) was isolated after chromatography as a light brown solid.

M. P. 85–87 ºC;

R_f = 0.39 (100% EtOAc);

FTIR (thin film) 3357, 2954, 2929, 1697, 1693, 1540, 1457, 1365, 1209, 1141, 842 cm^{-1};

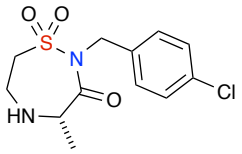
$[\alpha]_D^{20}$ = +31.4° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.45–7.40 (m, 2H), 7.05–7.00 (m, 2H), 5.13 (d, *J* = 14.9 Hz, 1H, NCH_aH_bPh), 4.88 (d, *J* = 15.0 Hz, 1H, NCH_aH_bPh), 3.85 [d, *J* = 6.5 Hz, 1H, HNCH(C=O)], 3.50–3.46 (m, 2H, $O_2SCH_2CH_2NH$), 3.31 (ddd, *J* = 14.2, 2.6, 2.6 Hz, 1H, $O_2SCH_2CH_aH_bNH$), 2.90 (ddd, *J* = 14.3, 9.0, 7.4 Hz, 1H, $O_2SCH_2CH_aH_bNH$), 2.23–2.13 (dqq, *J* = 6.5, 6.5, 6.5 Hz, 1H, CH_3CHCH_3), 1.00 (d, *J* = 6.7 Hz, 6H, CH_3CHCH_3);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 172.8, 163.3 ($^1J_{C–F}$ = 242.5 Hz), 132.5 ($^4J_{C–F}$ = 3.28 Hz), 130.5 ($^3J_{C–F}$ = 8.11 Hz, 2), 115.5 (^2J = 21.42 Hz, 2), 65.6, 57.0, 47.5, 45.6, 29.3, 20.3, 17.7;

HRMS (ESI) m/z calculated for $C_{14}H_{19}FN_2O_3SNa$ $(M+Na)^+$ 337.0998, found 337.0998 (TOF MS ES^+).

(*S*)-2-(4-chlorobenzyl)-4-methyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26d)



According to the reaction protocol described in general procedure **B**, compound **26d** (65%, 0.102 g) was isolated after chromatography as a light yellow solid.

M. P. 98–100 ºC;

R_f = 0.53 (100% EtOAc);

FTIR (thin film) 3357, 2954, 2867, 1697, 1496, 1456, 1336, 1209, 1147, 862 cm^{-1};

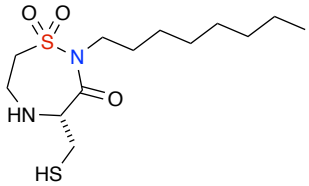
$[\alpha]_D^{20}$ = +22.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.38–7.32 (m, 2H), 7.31–7.24 (m, 2H), 5.09 (d, *J* = 15.0 Hz, 1H, NC$\underline{H}_a$$H_b$Ph), 4.84 (d, *J* = 15.0 Hz, 1H, NC$H_a\underline{H}_b$Ph), 4.21 [q, *J* = 6.8, Hz, 1H, HNC$\underline{H}$(C=O)], 3.55 (ddd, *J* = 15.2, 12.0, 3.2 Hz, 1H, O_2SC$\underline{H}_a$$H_b$$CH_2$NH), 3.40–3.27 (m, 2H, O_2SC$H_a\underline{H}_b$C$\underline{H}_a$$H_b$N), 3.04–2.93 (m, 1H, O_2SCH_2C$H_a\underline{H}_b$N), 1.30 (d, *J* = 6.7 Hz, 3H, NHCHC$\underline{H}_3$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 175.9, 136.1, 134.0, 129.4 (2), 128.9 (2), 56.3, 52.2, 46.5, 42.4, 19.0;

HRMS (ESI) m/z calculated for $C_{12}H_{15}ClN_2O_3SH$ $(M+H)^+$ 303.0570, found 303.0566 (TOF MS ES^+).

(*R*)-4-(mercaptomethyl)-2-octyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26e)



According to the reaction protocol described in general procedure **B**, compound **26e** (33%, 0.051 g) was isolated after chromatography as a light yellow solid.

M. P. 124–126 ºC;

R_f = 0.41 (100% EtOAc);

FTIR (thin film) 2954, 2931, 1693, 1456, 1355, 1209, 1151 cm^{-1};

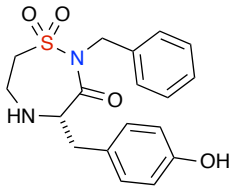
$[\alpha]_D^{20}$ = +20.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 4.18–4.05 [m, 1H, HNC$\underline{H}$(C=O)], 3.87–3.72 (m, 2H, O_2SC$\underline{H}_2$$CH_2$N), 3.46–3.34 (m, 2H, NC$\underline{H}_2$$CH_2$), 3.32–3.20 (m, 2H, O_2SCH_2C$\underline{H}_2$N), 3.16–3.10 (m, 1H, NHCHC$\underline{H}_a$$H_b$SH), 2.68–2.61 (m, 1H, NHCHC$H_a\underline{H}_b$SH), 2.62–2.55 (m, 1H, among n-octyl), 1.93–1.83 (m, 1H, among n-octyl), 1.81–1.71 (m, 2H, among n-octyl), 1.69–1.58 (m, 2H, among n-octyl), 1.36–1.25 (m, 6H, among n-octyl) 0.92 (t, *J* = 6.8 Hz, 3H, among n-octyl);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.5, 64.3, 58.1, 55.7, 51.0, 46.4, 31.3, 29.4, 27.0, 26.1, 24.7, 22.8, 14.0;

HRMS calculated for $C_{13}H_{26}N_2O_3S_2Na$ $(M+Na)^+$ 345.1283, found 345.1284 (TOF MS ES^+).

(*S*)-2-benzyl-4-(4-hydroxybenzyl)-1,2,5-thiadiazepan-3-one 1,1-dioxide (26f)



According to the reaction protocol described in general procedure **B**, compound **26f** (41%, 0.11 g) was isolated after chromatography as a white solid.

M. P. 106–109 ºC;

R_f = 0.31 (100% EtOAc);

FTIR (thin film) 3601, 3200, 2946, 2933, 2870, 1693, 1612, 1454, 1305, 1149, 831, 703 cm^{-1};

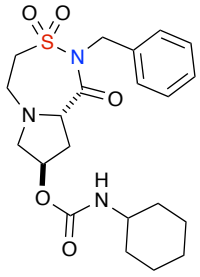
$[\alpha]_D^{20}$ = -28.2° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, Acetone) δ ppm 8.16 (s, 1H, Ar-OH), 7.39–7.34 (m, 2H), 7.34–7.29 (m, 2H), 7.28–7.23 (m, 1H), 7.12 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.5 Hz, 2H), 5.01 (d, *J* = 15.5 Hz, 1H, NCH_aH_bPh), 4.92 (d, *J* = 15.3 Hz, 1H, NCH_aH_bPh), 4.33 [dd, *J* = 8.6, 5.6 Hz, 1H, $HNCH(C{=}O)$], 3.51–3.38 (m, 2H, $O_2SCH_2CH_2NH$), 3.32–3.22 (m, 2H, $O_2SCH_2CH_2NH$), 3.12 (dd, *J* = 14.3, 5.6 Hz, 1H, $HNCHCH_aH_bPhOH$), 2.64 (dd, *J* = 14.3, 8.6 Hz, 1H, $HNCHCH_aH_bPhOH$);

^{13}C NMR (126 MHz, Acetone) δ ppm 173.9, 156.9, 138.6, 131.3 (2), 130.2, 129.2 (2), 128.8 (2), 128.2, 116.0 (2), 63.0, 57.1, 49.1, 46.6, 38.0;

HRMS calculated for $C_{18}H_{20}N_2O_4SH$ $(M+H)^+$ 361.1222, found 361.1200 (TOF MS ES^+).

(8*R*,9a*S*)-2-benzyl-3,3-dioxido-1-oxooctahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-8-yl cyclohexylcarbamate (28)



According to the reaction protocol described in general procedure **D**, compound **28** (37%, 0.102 g) was isolated after chromatography as a white solid.

M. P. 125–126 ºC;

R_f = 0.32 (1:1 Hexane:EtOAc);

FTIR (thin film) 3328, 2927, 1693, 1625, 1573, 1446, 1347, 1244, 1153, 1026, 742 cm^{-1};

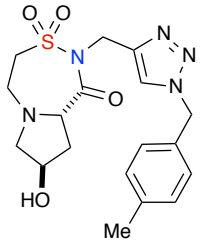
$[\alpha]_D^{20}$ = +17.5° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.40 (d, *J* = 7.2 Hz, 2H), 7.34 (dd, *J* = 8.1, 6.8 Hz, 2H), 7.30–7.26 (m, 1H), 5.16 (d, *J* = 15.1 Hz, 1H, NC$\underline{H}_a$$H_b$Ph), 5.11–5.05 (m, 1H, $NCH_2C\underline{H}CH_2CH$), 4.91 (d, *J* = 15.1 Hz, 1H, $NCH_a\underline{H}_b$Ph), 4.66 (bs, 1H, NH), 4.38 [t, *J* = 7.8 Hz, 1H, $NCH_2CHCH_2C\underline{H}$(C=O)], 3.55 (dd, *J* = 11.4, 4.4 Hz, 1H, NC$\underline{H}_a$$H_b$$CHCH_2$), 3.51–3.31 (m, 3H, $O_2SC\underline{H}_a$$H_b$$C\underline{H}_a$$H_b$$NCH_2CHOCONHC\underline{H}$), 3.28–3.15 (m, 2H, $O_2SCH_a\underline{H}_bCH_a\underline{H}_bN$), 2.78–2.68 (m, 2H, $NCH_a\underline{H}_bCHC\underline{H}_a$$H_b$CH), 2.14–2.06 (m, 1H, $NCH_2CHCH_a\underline{H}_bCH$), 1.98–1.89 (m, 2H, among Cy), 1.76–1.67 (m, 2H, among Cy), 1.65–1.57 (m, 1H, among Cy), 1.42–1.29 (m, 2H, among Cy), 1.23–1.02 (m, 3H, among Cy);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.0, 154.8, 136.5, 128.6 (2), 128.3 (2), 127.7, 73.2, 64.4, 62.5, 56.5, 52.9, 49.9, 48.5, 34.4, 33.4 (2), 25.4 (2), 24.8;

HRMS calculated for $C_{21}H_{29}N_3O_5SH$ $(M+H)^+$ 436.1906, found 436.1910 (TOF MS ES$^+$).

(8*R*,9a*S*)-8-hydroxy-2-((1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl)methyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (29)



According to the reaction protocol described in general procedure **E**, compound **29** (45%, 0.097 g) was isolated after chromatography as a white solid.

M. P. 125–126 ºC;

R_f = 0.27 (100% EtOAc);

FTIR (neat) 3685, 3380, 3353, 2972, 1708, 1444, 1355, 1218, 1151, 881 cm^{-1};

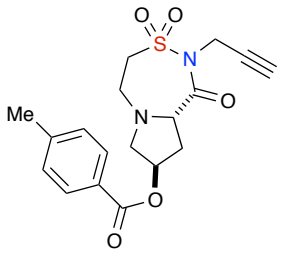
$[\alpha]_D^{20}$ = +17.5° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.45 (s, 1H, c-N=NN$\underline{H}$C=C), 7.21–7.13 (m, 4H), 5.49 (d, *J* = 14.8 Hz, 1H, NCH_2-triazole-C$\underline{H}_a$$H_b$-Ar), 5.44 (d, *J* = 14.7 Hz, 1H, NCH_2-triazole-$CH_a\underline{H}_b$-Ar), 5.12 (d, *J* = 15.6 Hz, 1H, NC$\underline{H}_a$$H_b$-triazole-$CH_2$-Ar), 5.06 (d, *J* = 15.5 Hz, 1H, $NCH_a\underline{H}_b$-triazole-CH_2-Ar), 4.50–4.42 [m, 1H, $NCH_2CH(OH)CH_2C\underline{H}$(C=O)], 4.34 [dddd, *J* = 5.2, 5.2, 5.1, 4.7 Hz, 1H, $NCH_2C\underline{H}(OH)CH_2$], 3.77–3.67 (m, 1H, $O_2SC\underline{H}_a$$H_b$$CH_2N$), 3.52–3.23 [m, 5H, $O_2SCH_a\underline{H}_bC\underline{H}_2NC\underline{H}_a$$H_b$$CH(O\underline{H})CH_2$], 2.78–2.62 [m, 2H, $NCH_a\underline{H}_bCH(OH)C\underline{H}_a$$H_b$], 2.36 (s, 3H, Ar-$CH_3$), 1.99–1.92 [m, 1H, $NCH_2CH(OH)CH_a\underline{H}_b$];

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 171.0, 143.6, 138.6, 131.5, 129.8 (2), 128.0 (2), 122.6, 70.0, 64.0, 63.6, 55.7, 53.7, 52.0, 40.1, 36.4, 21.1;

HRMS calculated for $C_{18}H_{23}N_5O_4SH$ $(M+H)^+$ 406.1549, found 406.1558 (TOF MS ES$^+$).

(8*R*,9a*S*)-3,3-dioxido-1-oxo-2-(prop-2-yn-1-yl)octahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-8-yl 4-methylbenzoate (30)



According to the reaction protocol described in general procedure **F**, compound **30** (42%, 0.096 g) was isolated after chromatography as a white solid.

M. P. 117–119 ºC;

R_f = 0.62 (1:1 Hexane:EtOAc);

FTIR (thin film) 3365, 2975, 2929, 2254, 1735, 1708, 1444, 1355, 1220, 1153, 887 cm^{-1};

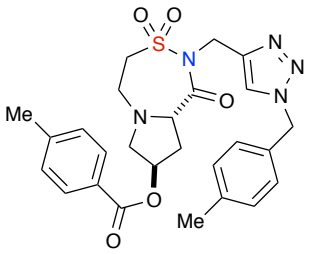
$[\alpha]_D^{20}$ = +18.4° (*c* = 2.0, $CHCl_3$);

^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.93 (d, *J* = 8.2 Hz, 2H), 7.27 (d, *J* = 7.8 Hz, 2H), 5.42 [dd, *J* = 4.1, 4.0 Hz, 1H, $NCH_2C\underline{H}(OCOAr)CH_2CH$], 4.76 (dd, *J* = 17.5, 2.5 Hz, 1H, $NC\underline{H}_aH_bCCH$), 4.53 (dd, *J* = 17.6, 2.5 Hz, 1H, $NCH_a\underline{H}_bCCH$), 4.49 [t, *J* = 8.0 Hz, 1H, $NCH_2CHCH_2C\underline{H}(C{=}O)$], 3.72 (dd, *J* = 11.3, 4.5 Hz, 1H, $O_2SC\underline{H}_aH_bCH_2N$), 3.60–3.44 (m, 3H, $O_2SCH_a\underline{H}_bC\underline{H}_aH_bNC\underline{H}_aH_b$), 3.37–3.29 (m, 1H, $O_2SCH_2CH_a\underline{H}_bN$), 2.95–2.87 (m, 2H, $NCH_a\underline{H}_bCHC\underline{H}_aH_bCH$), 2.44 (s, 3H, Ar-$C\underline{H}_3$), 2.32 (t, *J* = 2.5 Hz, 1H, $NCH_2CC\underline{H}$), 2.31–2.28 (m, 1H, $NCH_2CHCH_a\underline{H}_bCH$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.0, 165.6, 144.1, 129.6 (2), 129.2 (2), 127.0, 77.8, 73.4, 72.1, 64.2, 62.3, 56.6, 52.9, 34.4, 34.1, 21.7;

HRMS calculated for $C_{18}H_{20}N_2O_5SH$ $(M+H)^+$ 377.1171, found 377.1171 (TOF MS ES^+).

(8*R*,9a*S*)-2-((1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl)methyl)-3,3-dioxido-1-oxooctahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-8-yl 4-methylbenzoate (31)



According to the reaction protocol described in general procedure **G**, compound **31** (35%, 0.091 g) was isolated after chromatography as a yellow solid.

M. P. 127–129 ºC;

R_f = 0.65 (100% EtOAc);

FTIR (thin film) 3392, 2931, 2854, 1701, 1693, 1496, 1352, 1220, 1151, 1058, 891 cm^{-1};

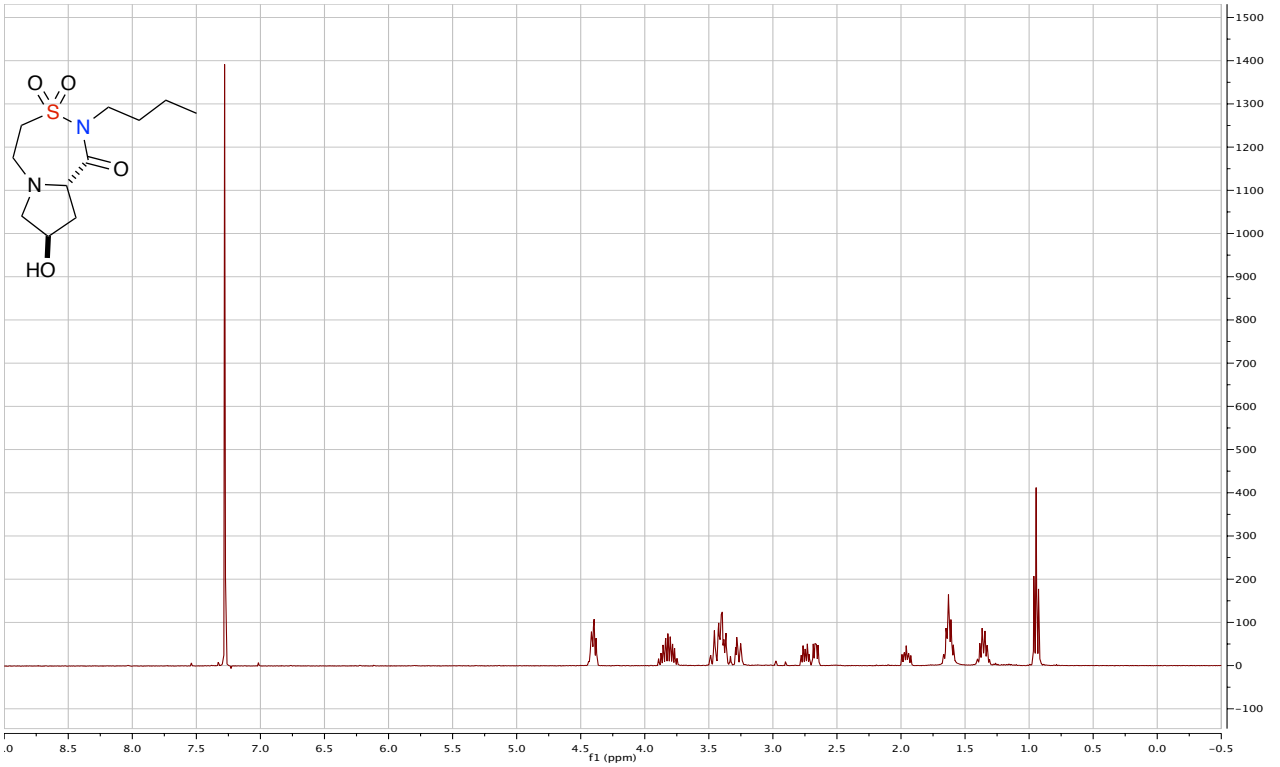
$[\alpha]_D^{20}$ = +18.8° (*c* = 2.0, $CHCl_3$);

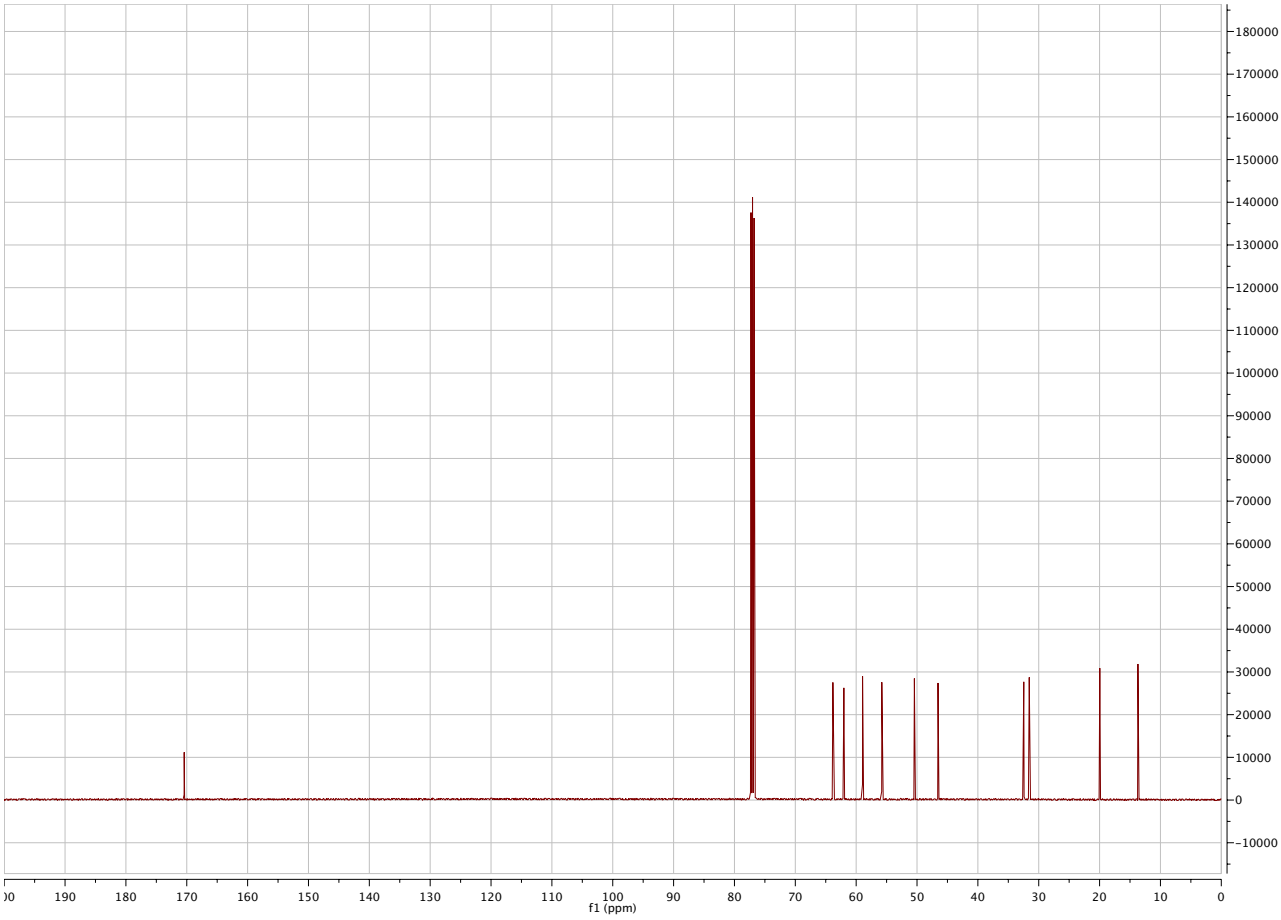
^{1}H NMR (500 MHz, $CDCl_3$) δ ppm 7.92 (d, *J* = 8.2 Hz, 2H), 7.45 (s, 1H, c-N=NNHC=C), 7.31–7.24 (m, 2H), 7.22–7.14 (m, 4H), 5.51 (d, *J* = 14.6 Hz, 1H, NCH_2-triazole-CH_aH_b-Ar), 5.44 (d, *J* = 14.6 Hz, 1H, NCH_2-triazole-CH_aH_b-Ar), 5.34 [dddd, *J* = 4.5, 4.4, 4.4 and 4.3 Hz, 1H, $NCH_2CH(OCOAr)CH_2$], 5.13 (d, *J* = 15.3 Hz, 1H, NCH_aH_b-triazole-CH_2-Ar), 5.11 (d, *J* = 15.3 Hz, 1H, NCH_aH_b-triazole-CH_2-Ar), 4.49 [t, *J* = 7.8 Hz, 1H, $NCH_2CHCH_2CH(C{=}O)$], 3.81–3.71 (m, 1H, $O_2SCH_aH_bCH_2N$), 3.60 (dd, *J* = 11.2, 4.5 Hz, 1H, NCH_aH_bCHCH_2), 3.52–3.37 (m, 2H, $O_2SCH_aH_bCH_aH_bN$), 3.26 (dt, *J* = 12.8, 3.7 Hz, 1H, $O_2SCH_2CH_aH_bN$), 2.88–2.78 (m, 2H, $NCH_aH_bCHCH_aH_b$), 2.43 (s, 3H, Ar-CH_3), 2.37 (s, 3H, Ar-CH_3), 2.24 (dddd, *J* = 13.9, 8.2, 4.2, 1.5 Hz, 1H, $NCH_2CHCH_aH_b$);

^{13}C NMR (126 MHz, $CDCl_3$) δ ppm 170.4, 166.0, 144.1, 143.4, 139.0, 131.5, 129.8 (2), 129.6 (2), 129.2 (2), 128.1 (2), 127.0, 122.7, 73.3, 64.2, 62.1, 55.9, 54.0, 52.8, 40.3, 34.0, 21.8, 21.2;

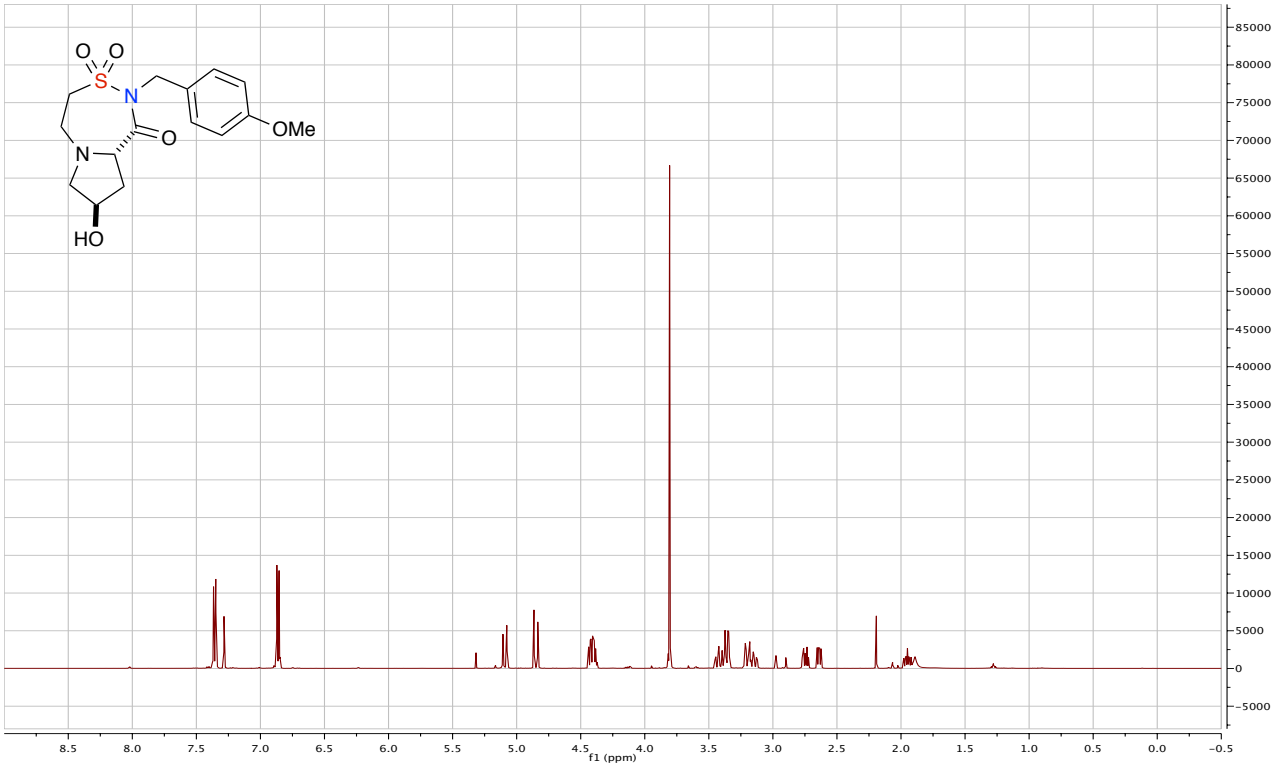
HRMS calculated for $C_{26}H_{29}N_5O_5SH$ $(M+H)^+$ 524.1968, found 524.1968 (TOF MS ES^+).

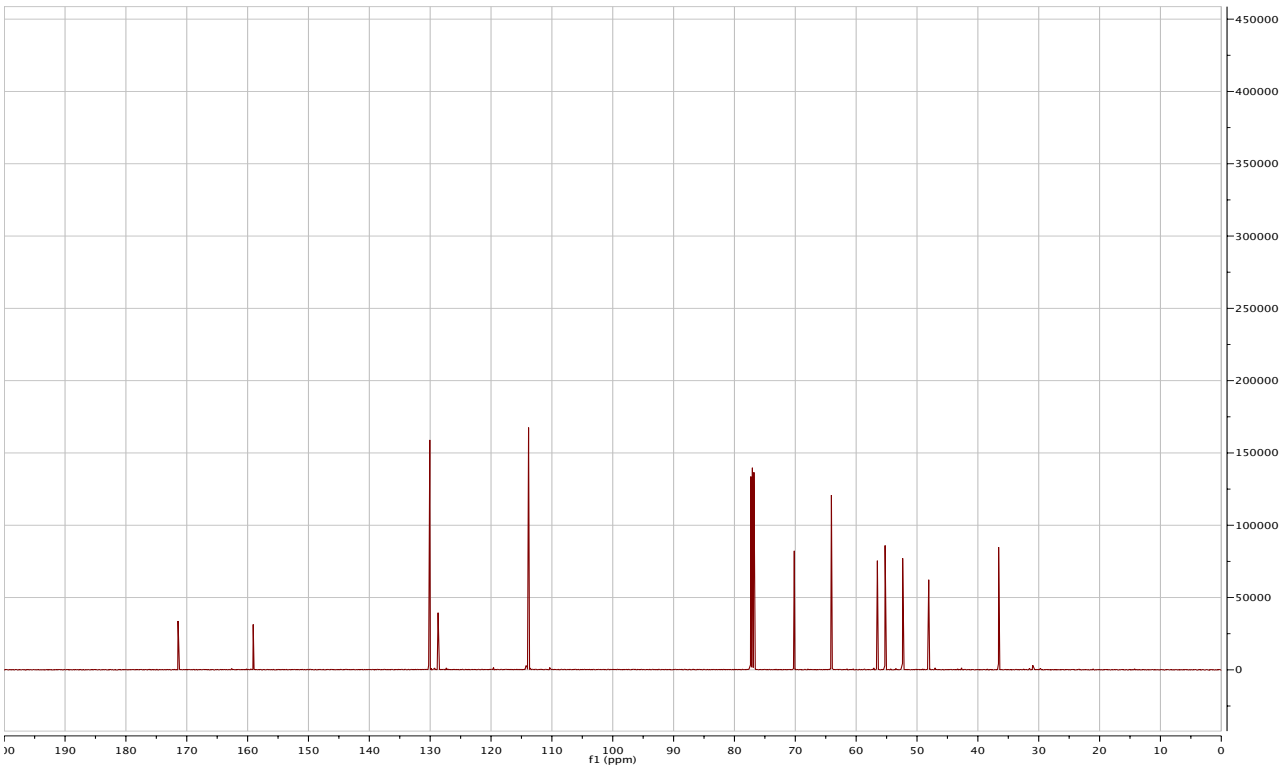
(8*R*,9a*S*)-8-hydroxy-2-butylhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10a)



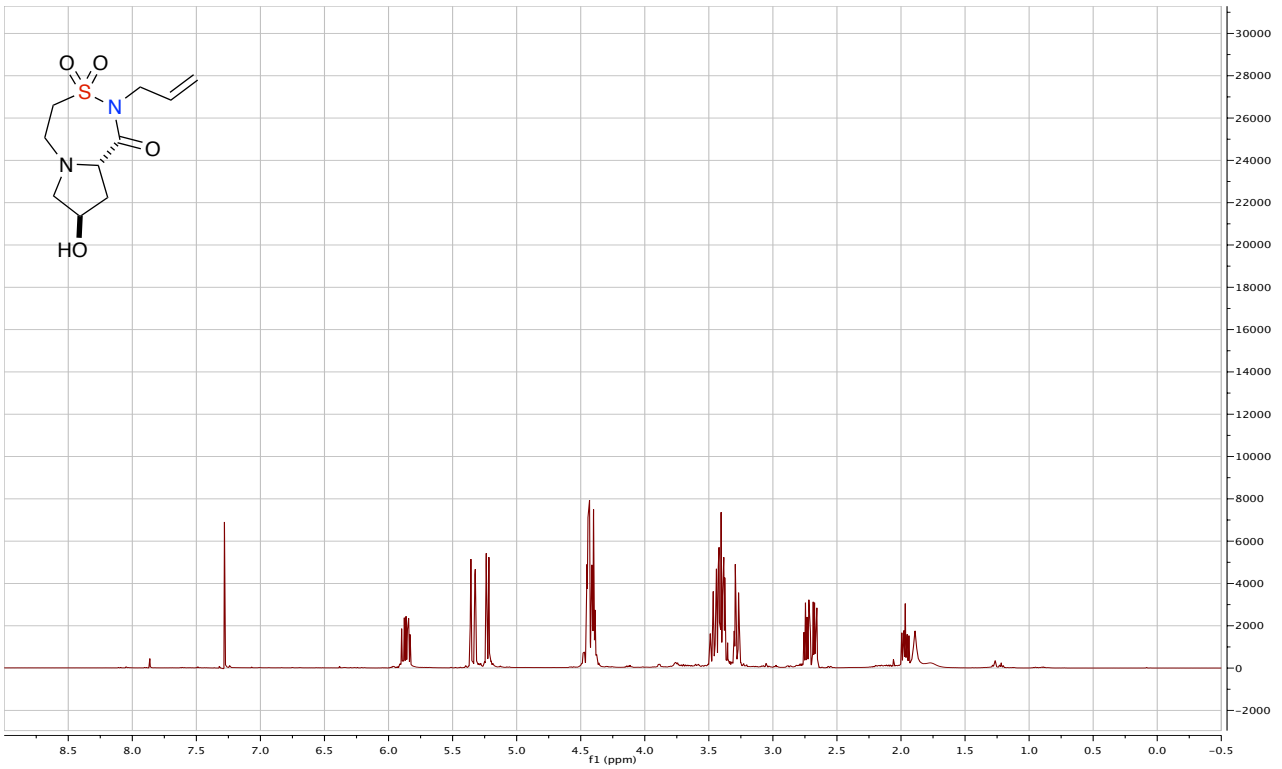


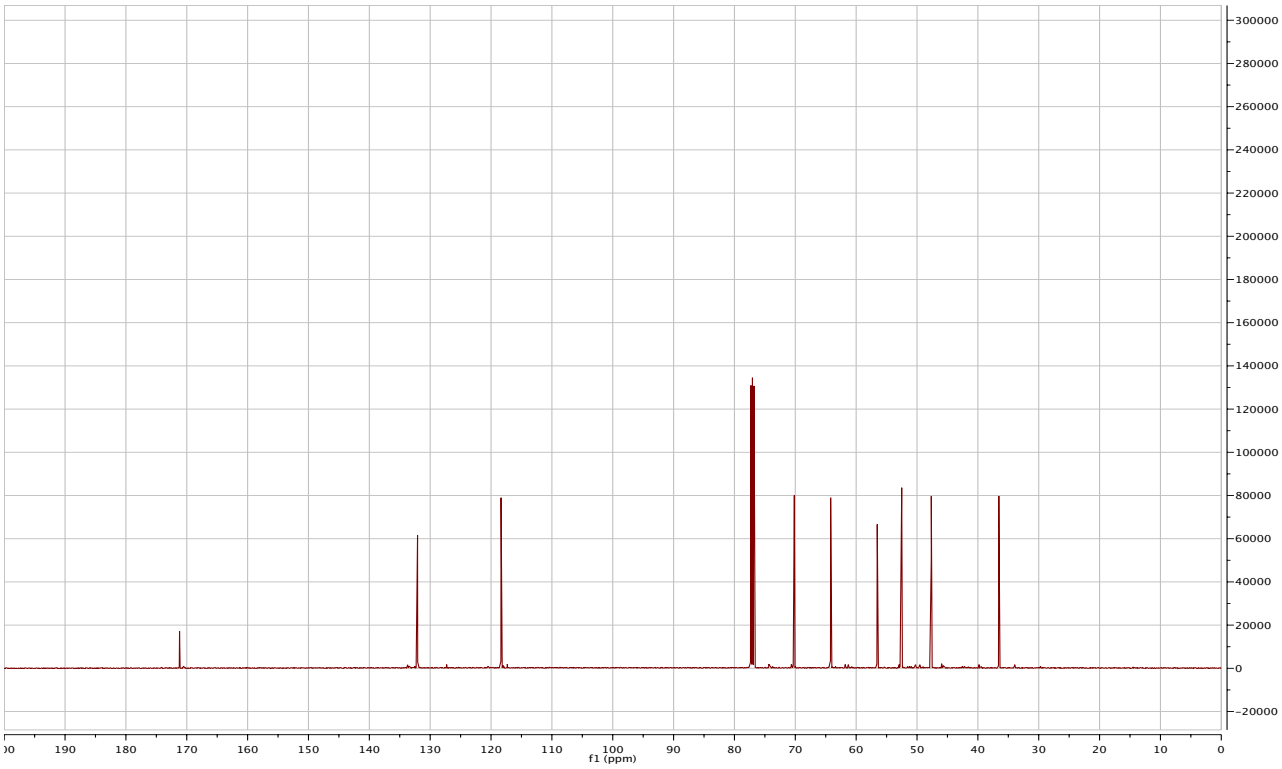
(8*R*,9a*S*)-8-hydroxy-2-(4-methoxybenzyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10b)



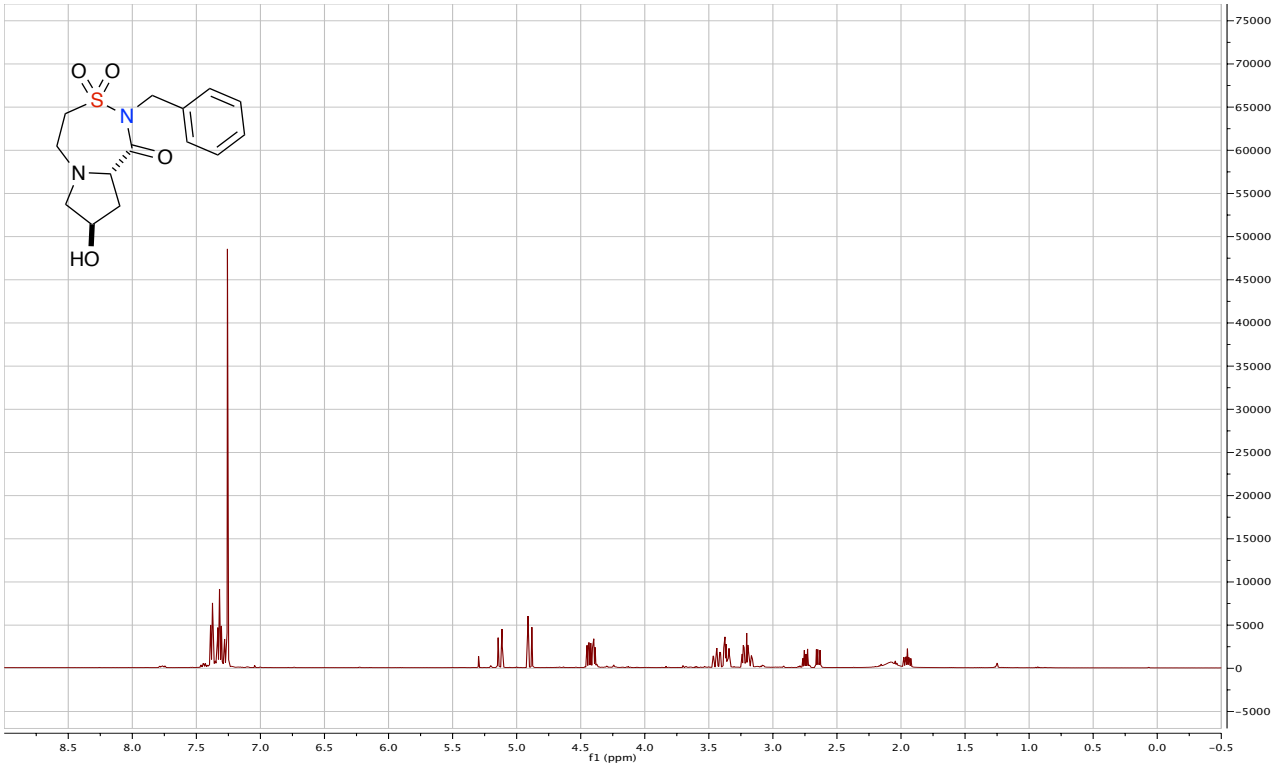


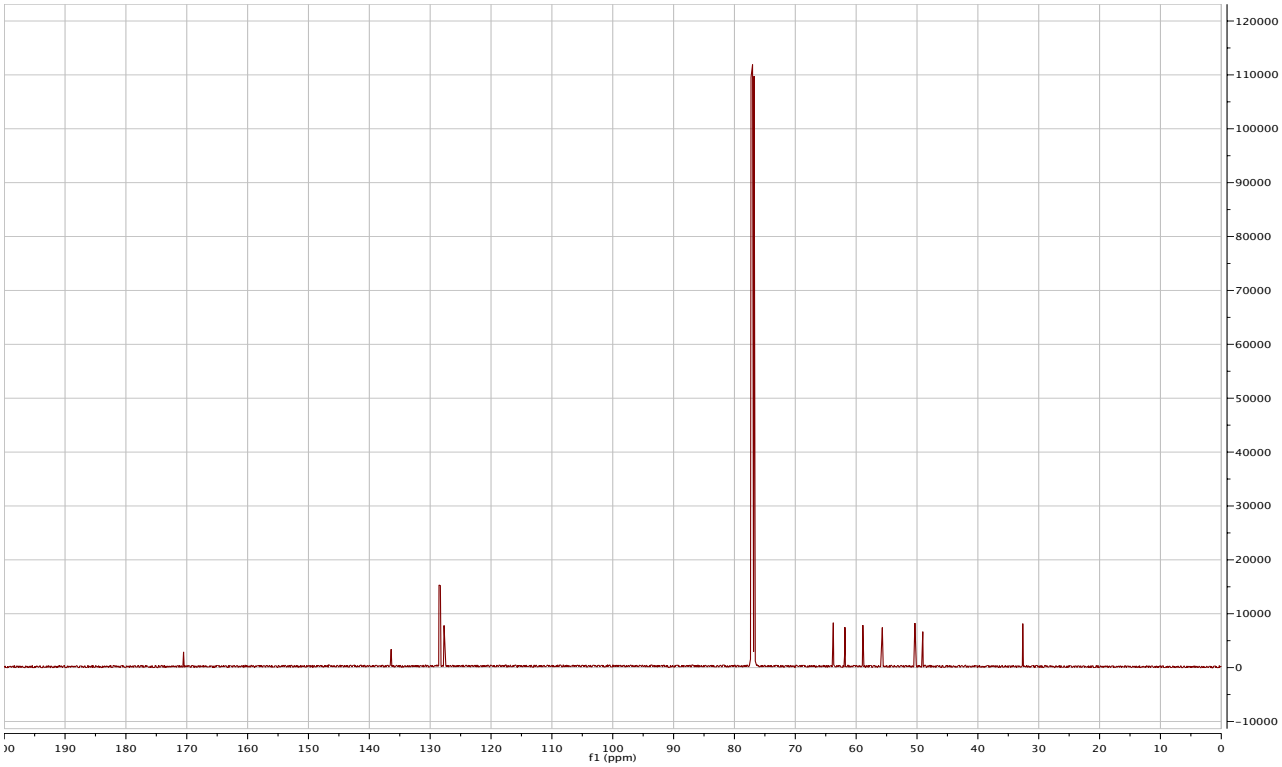
(8*R*,9a*S*)-2-allyl-8-hydroxyhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10c, 27a)



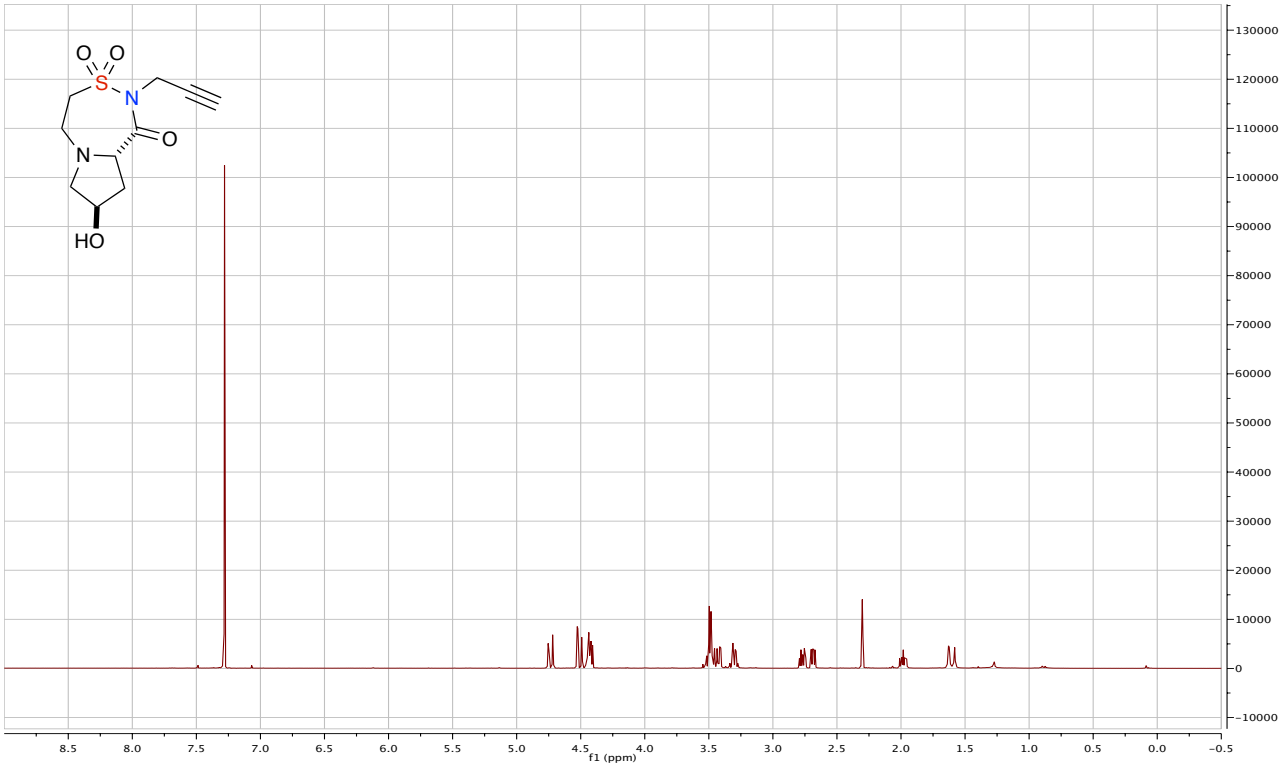


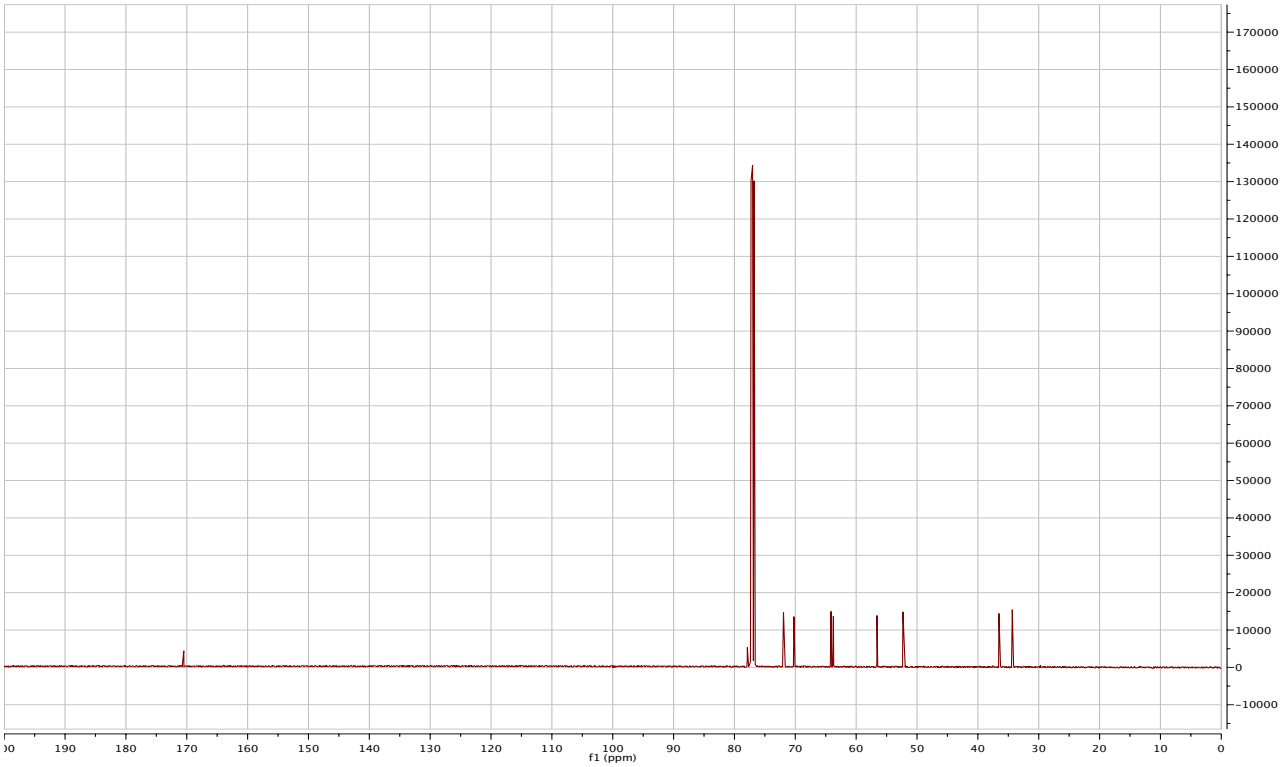
(8*R*,9a*S*)-2-benzyl-8-hydroxyhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10d, 27b)



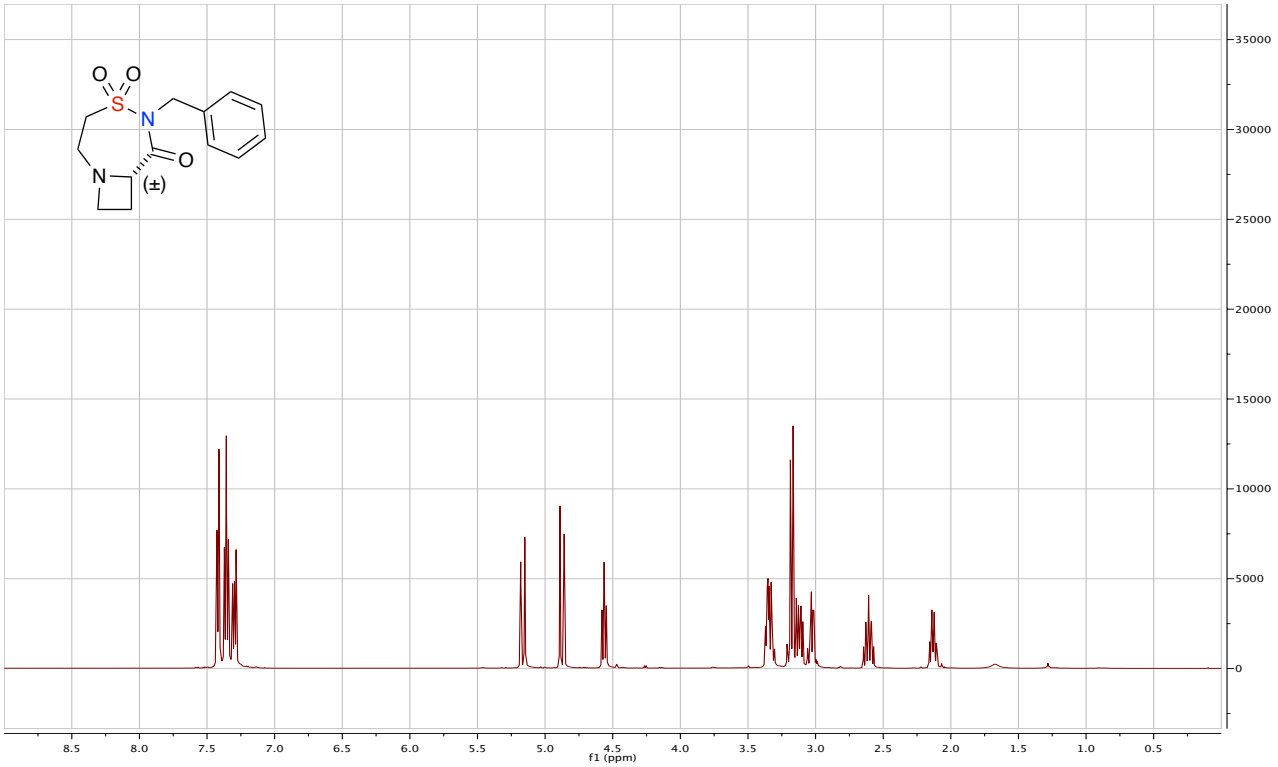


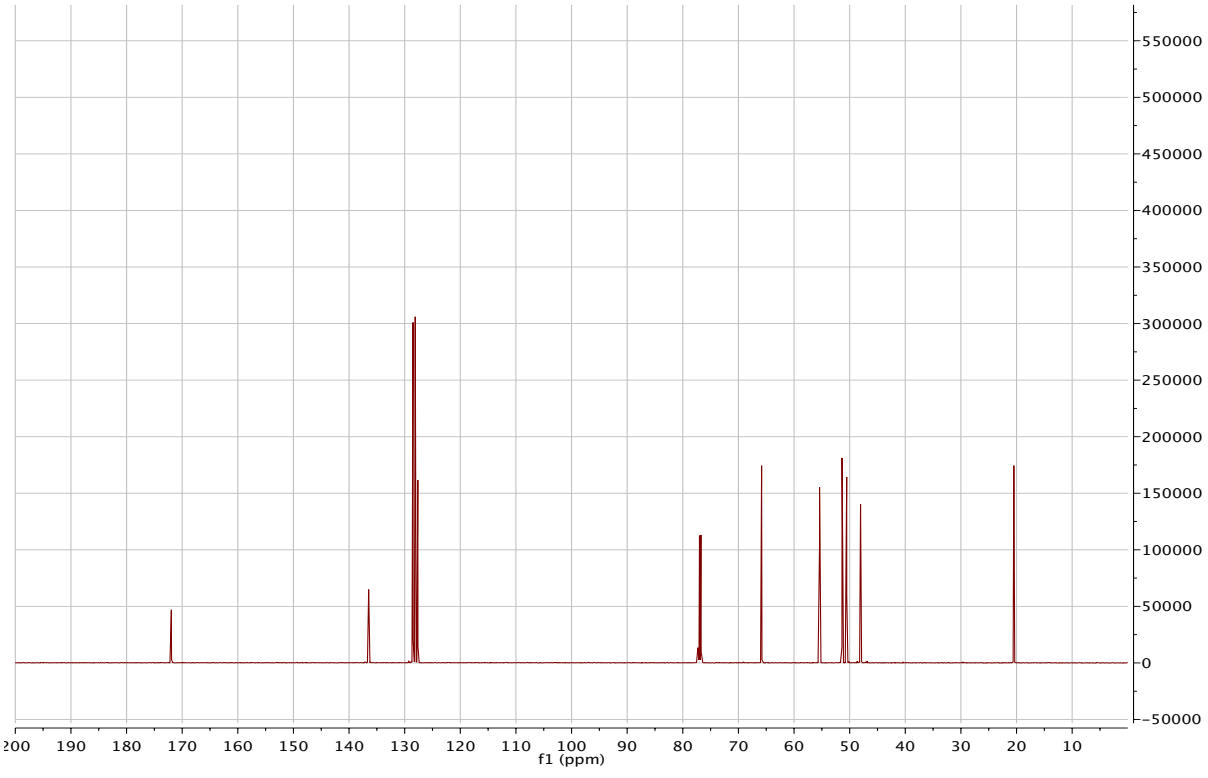
(8*R*,9a*S*)-8-hydroxy-2-(prop-2-yn-1-yl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (10e)



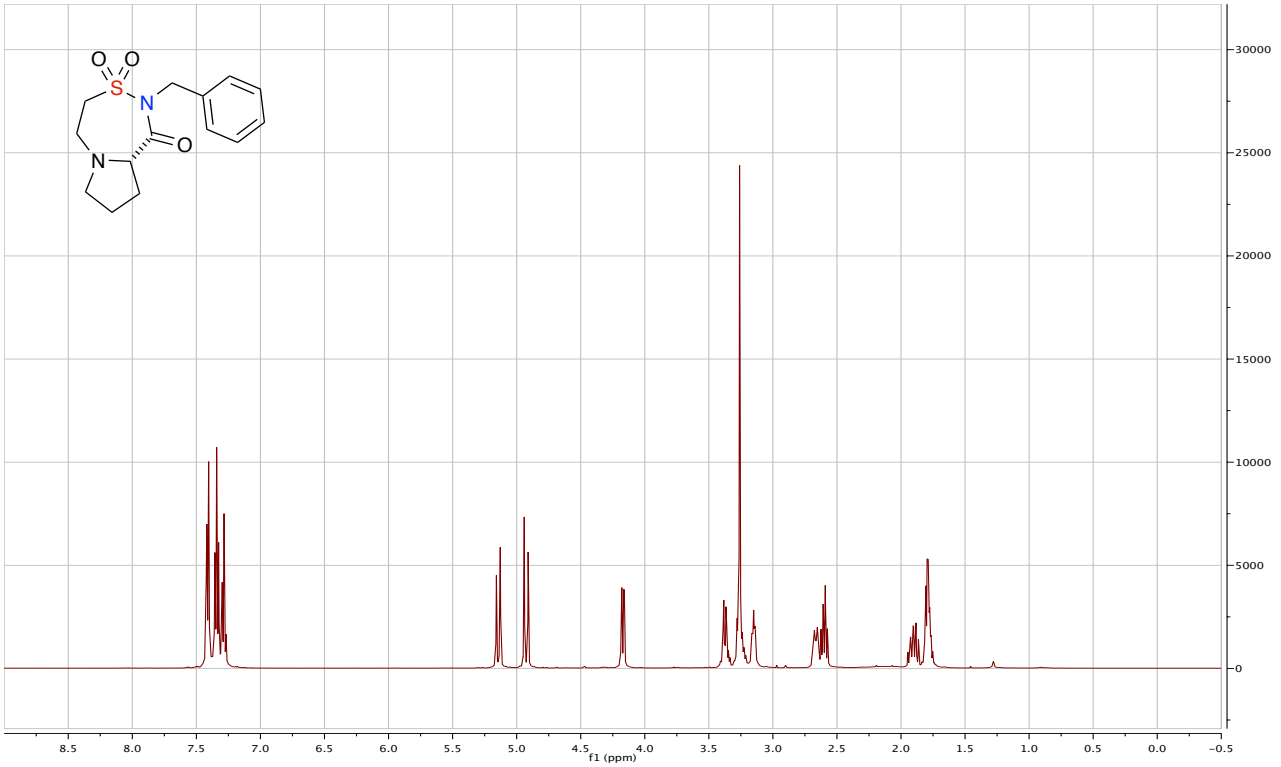


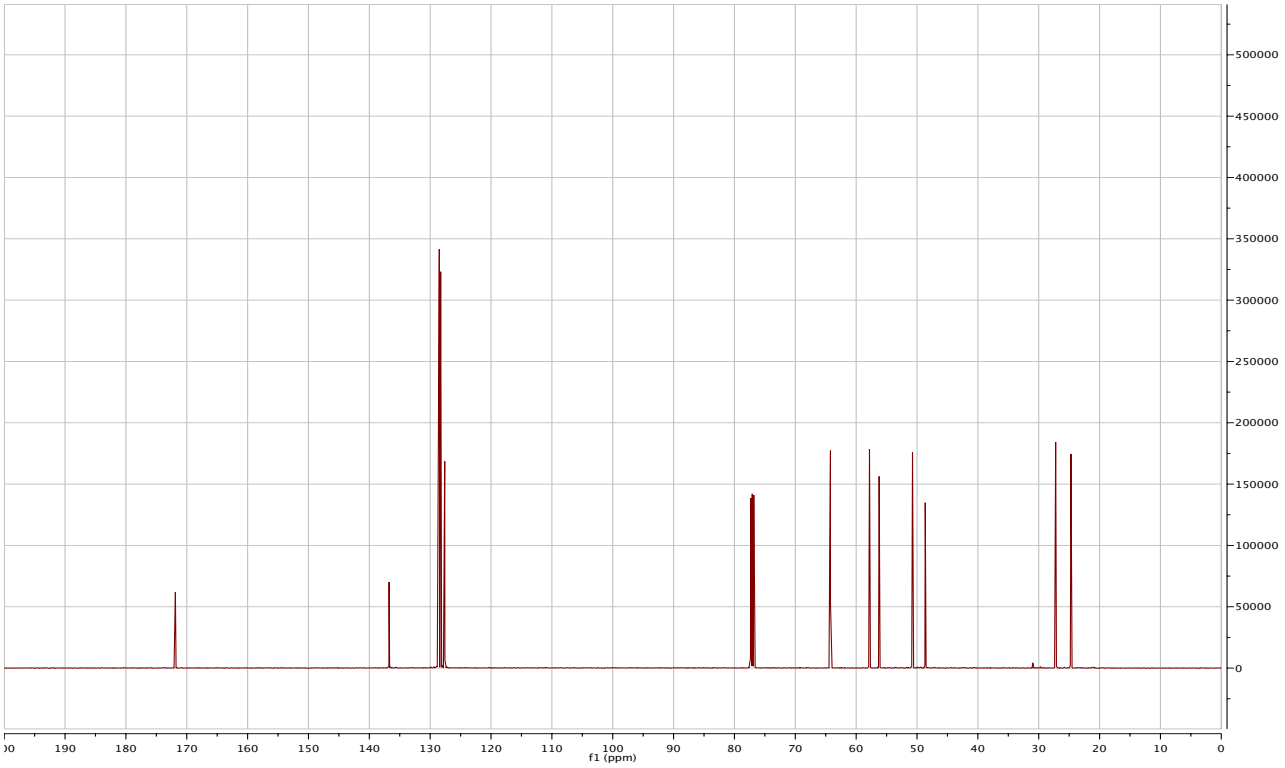
5-benzyl-4-thia-1,5-diazabicyclo[5.2.0]nonan-6-one 4,4-dioxide (11, 27c)



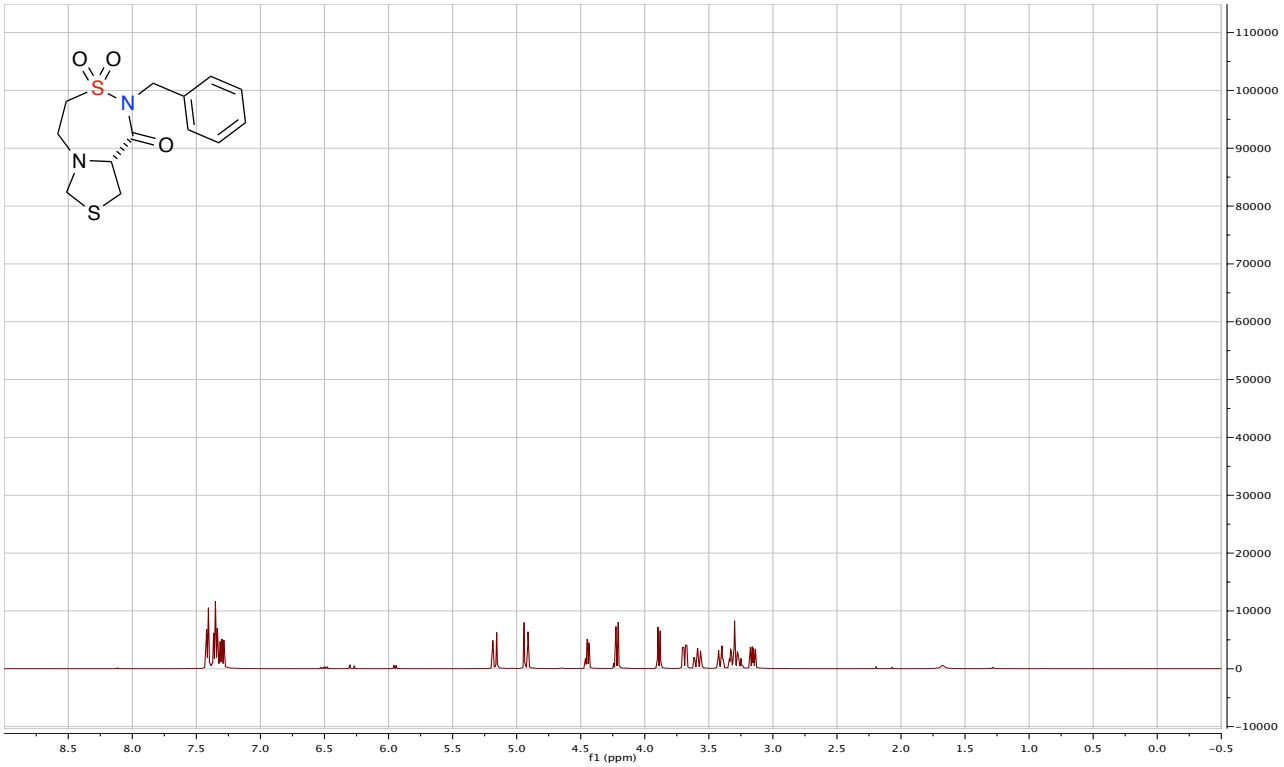


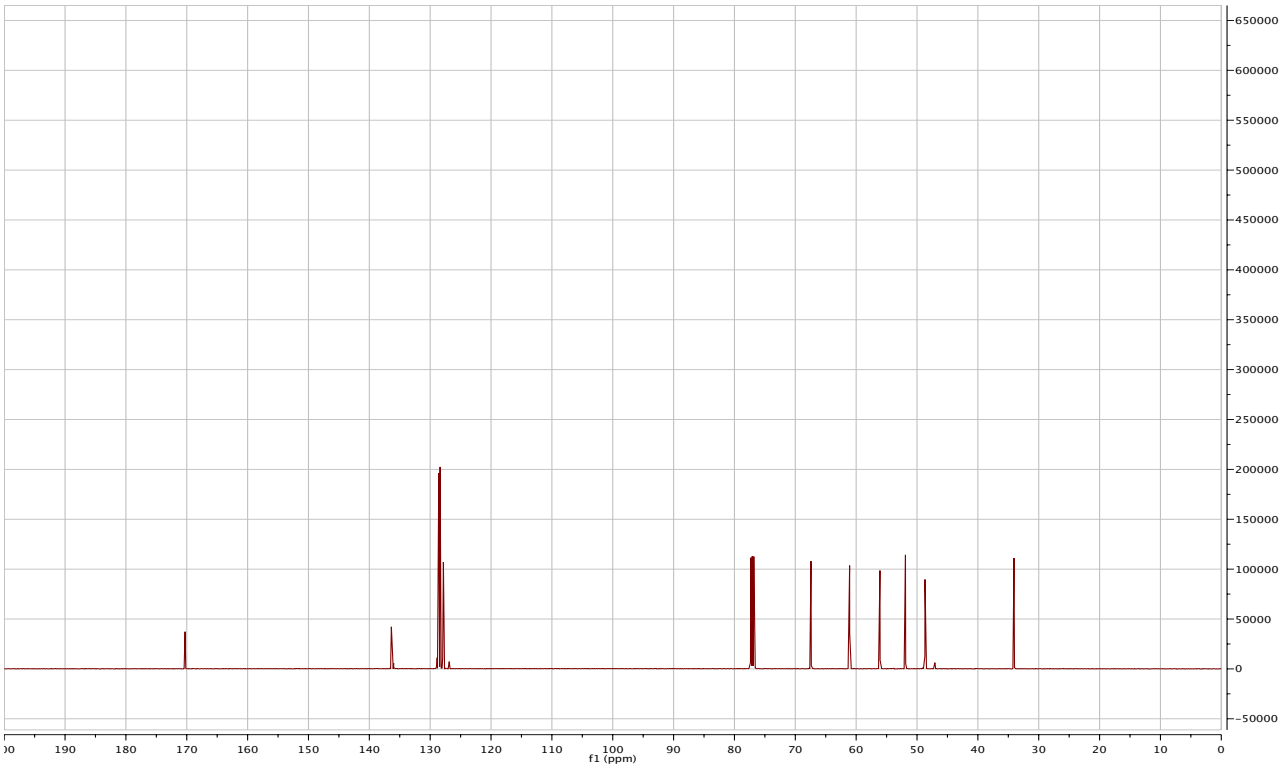
(*S*)-2-benzylhexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (12, 27d)



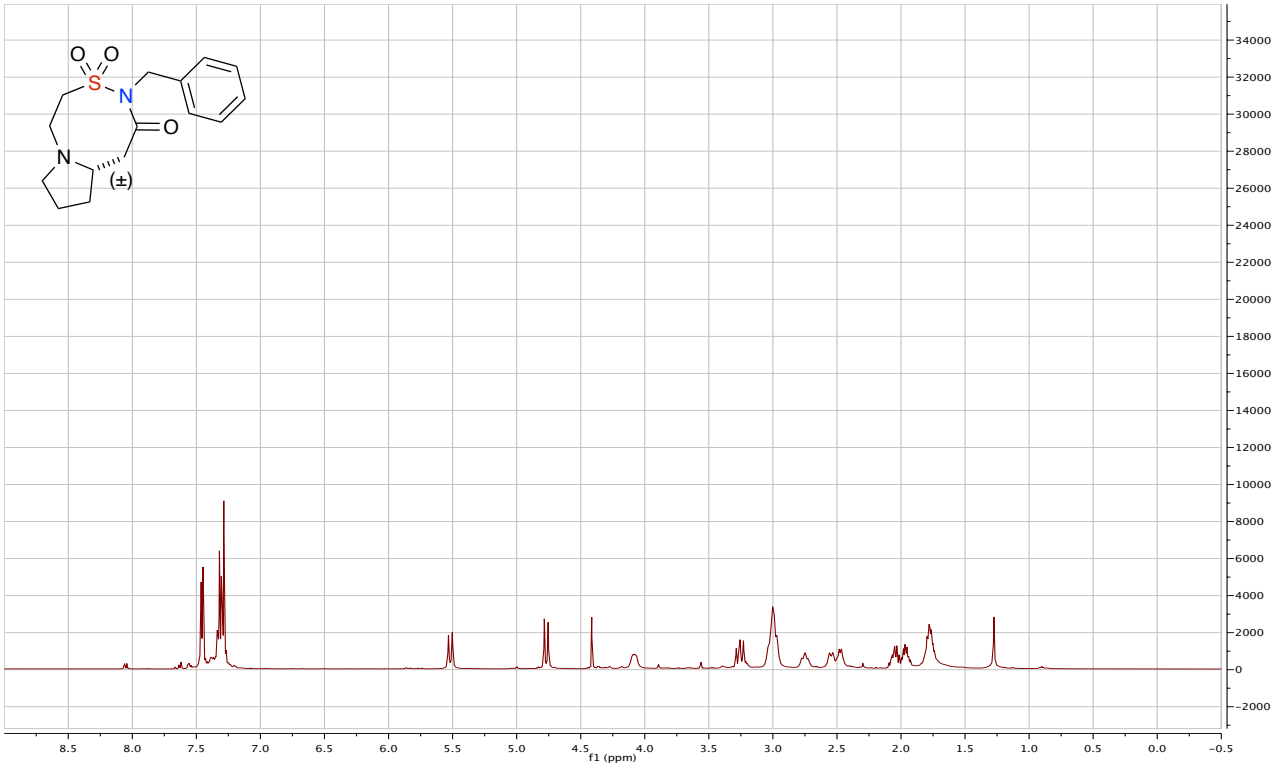


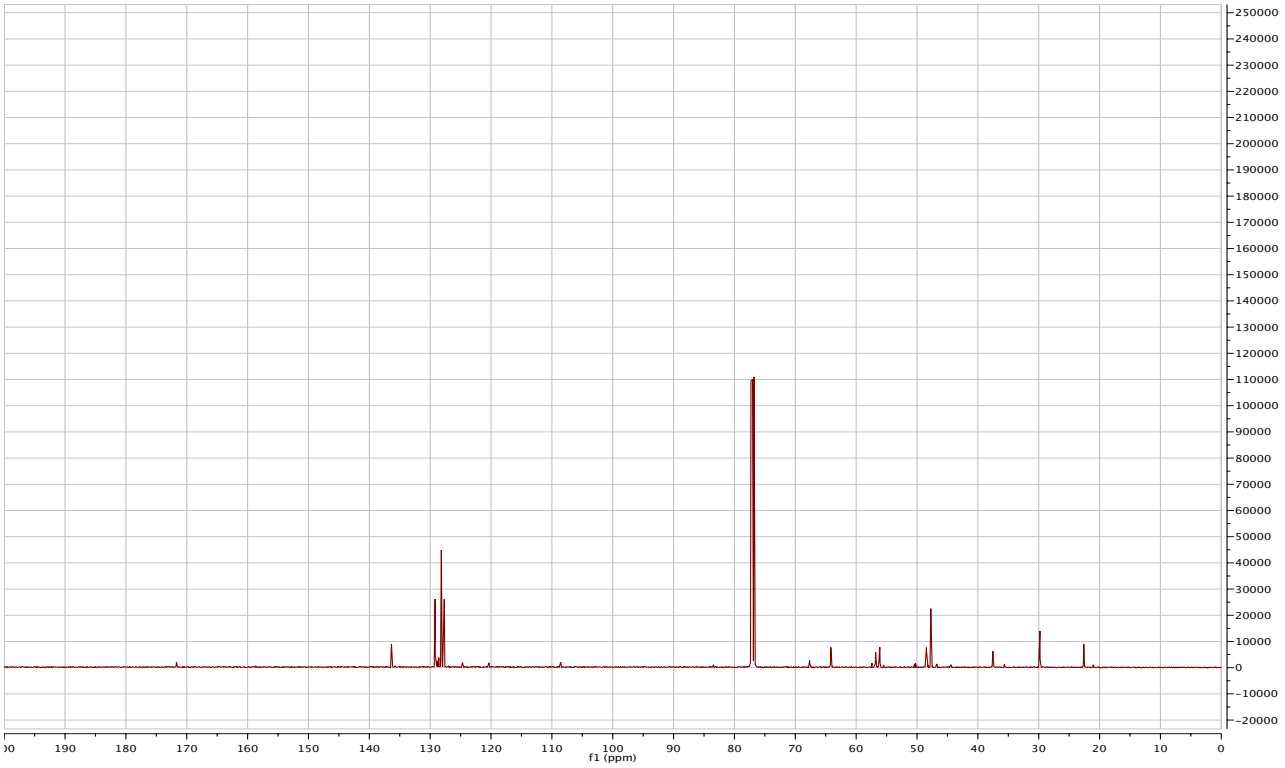
(*R*)-2-benzylhexahydro-1*H*-thiazolo[4,3-*d*][1,2,5]thiadiazepin-1-one 3,3-dioxide (13, 27e)



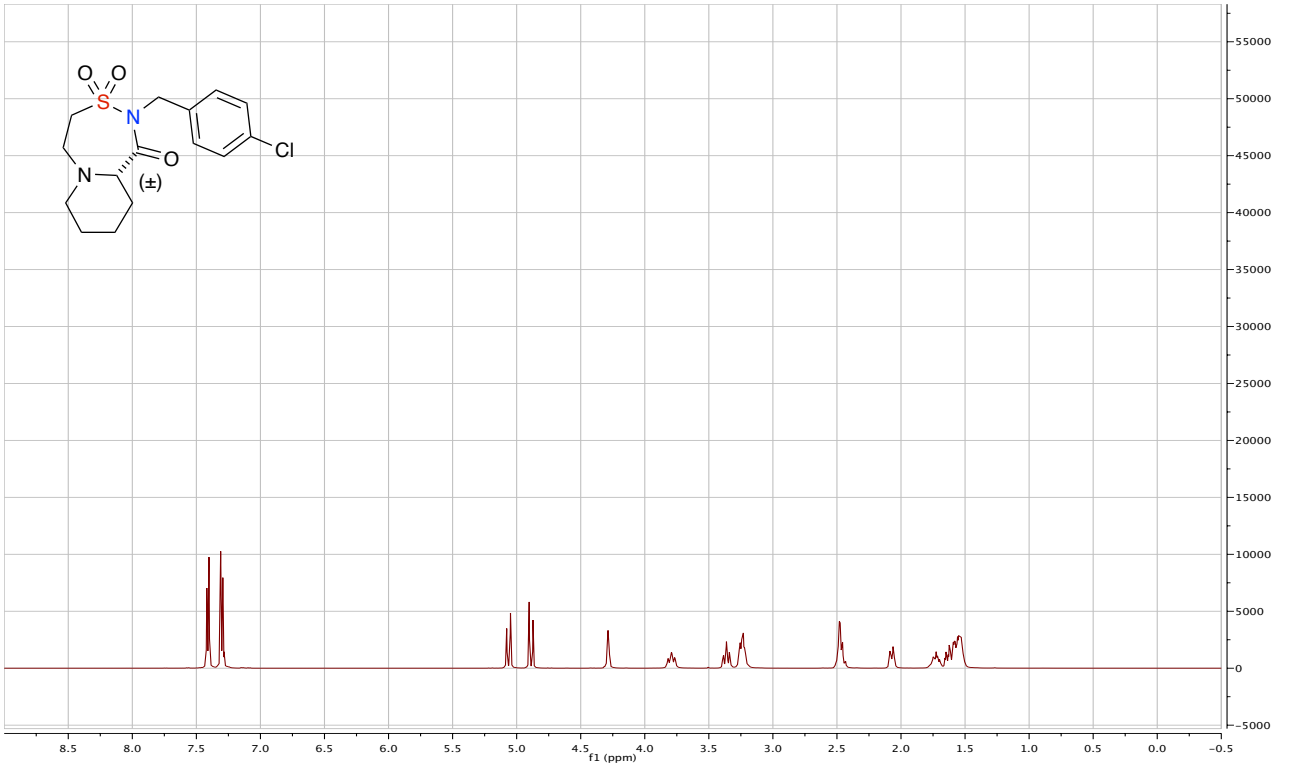


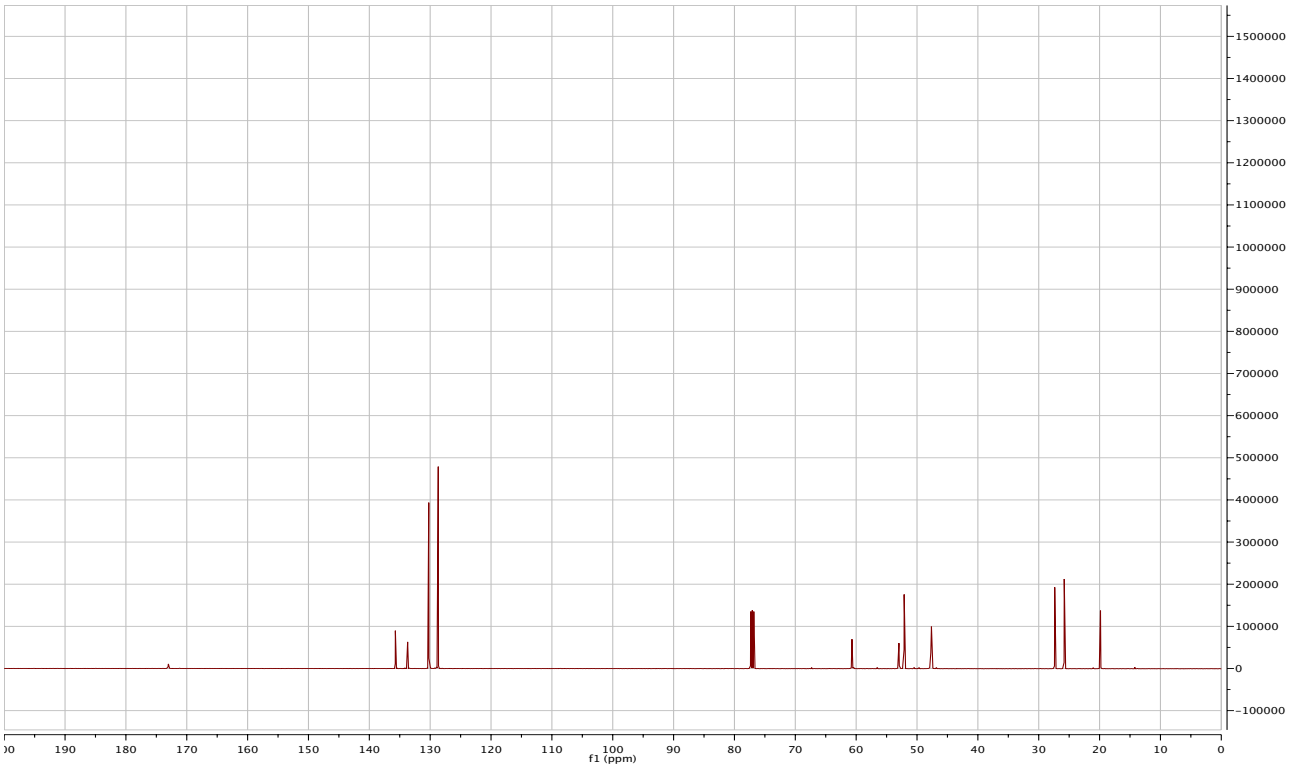
3-benzylhexahydro-1*H*-pyrrolo[2,1-*e*][1,2,6]thiadiazocin-2(3*H*)-one 4,4-dioxide (14)



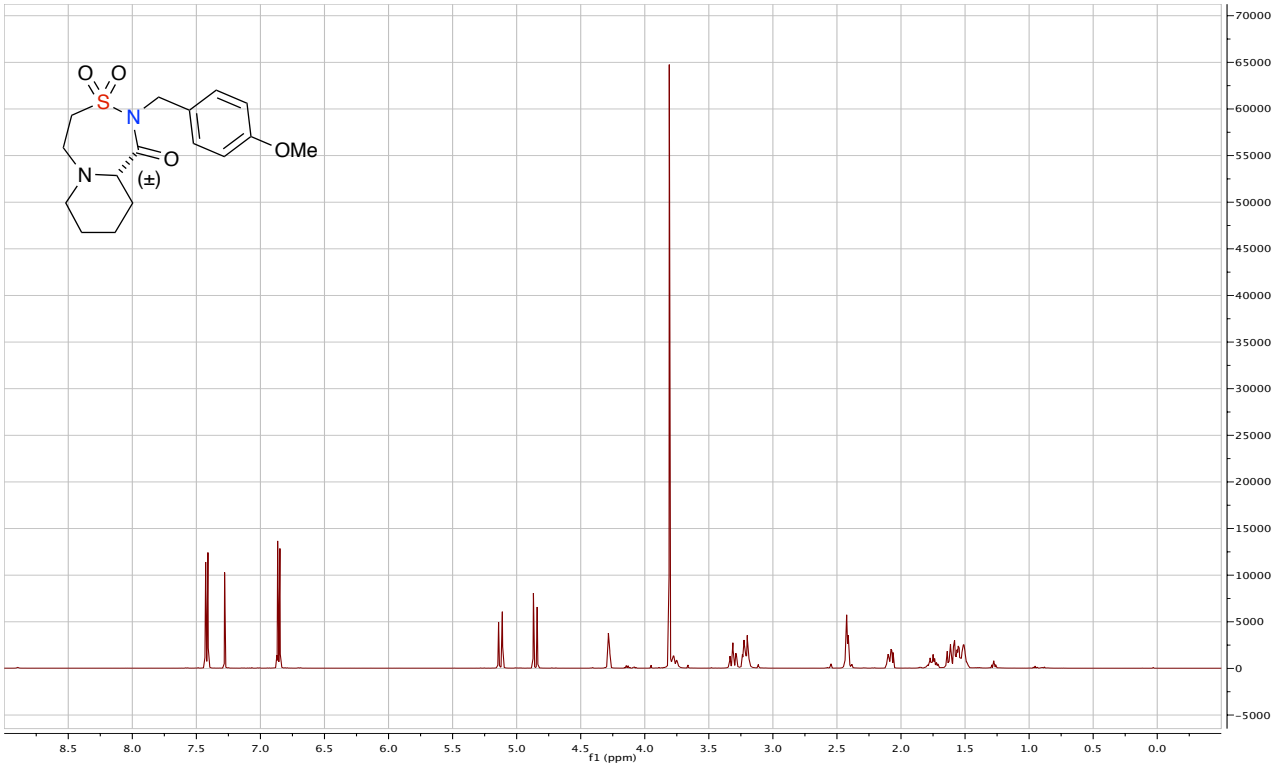


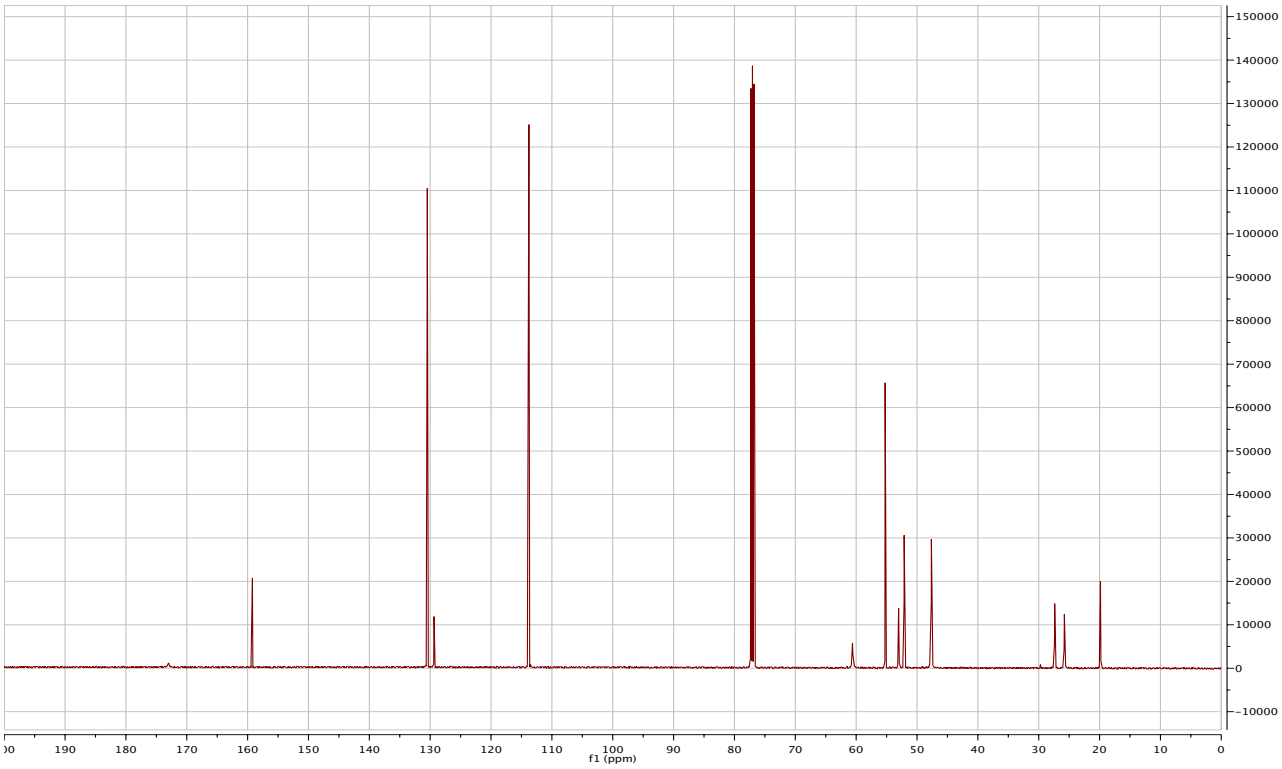
2-(4-chlorobenzyl)octahydro-1*H*-pyrido[2,1-*d*][1,2,5]thiadiazepin-1-one 3,3-dioxide (15, 27f)



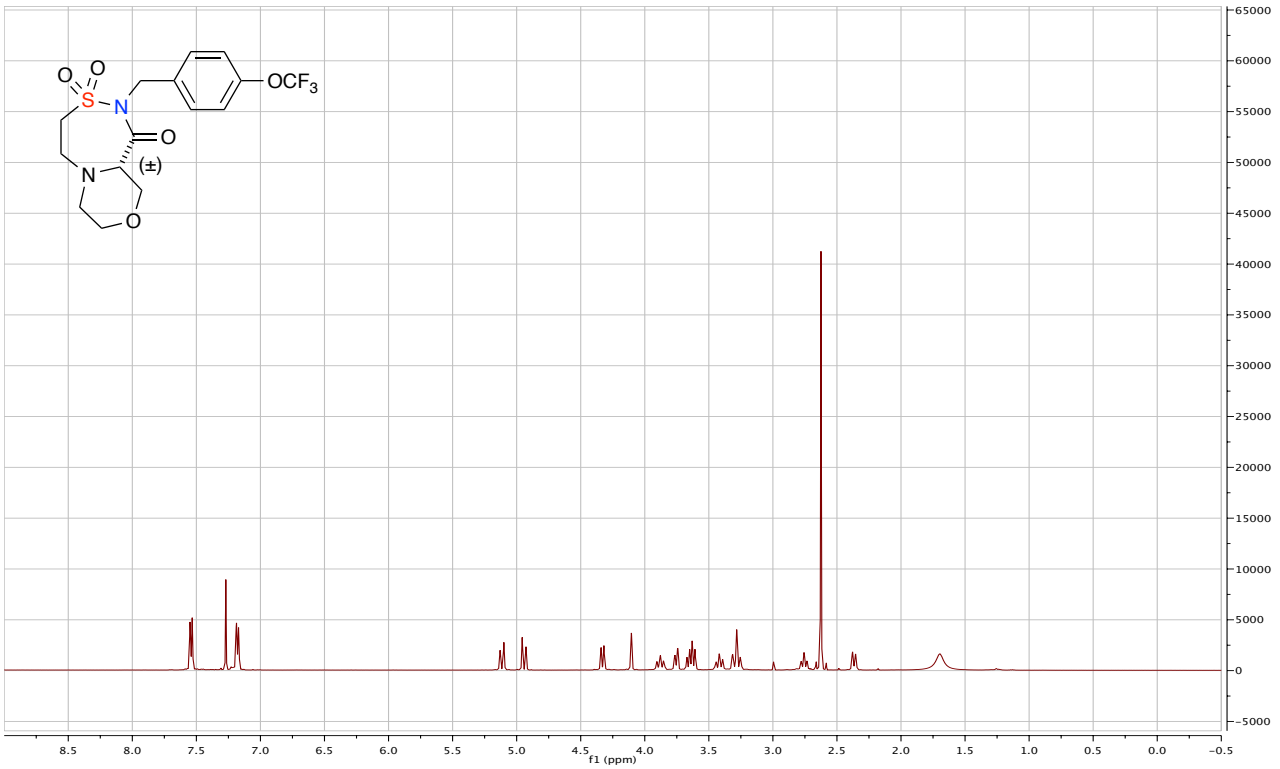


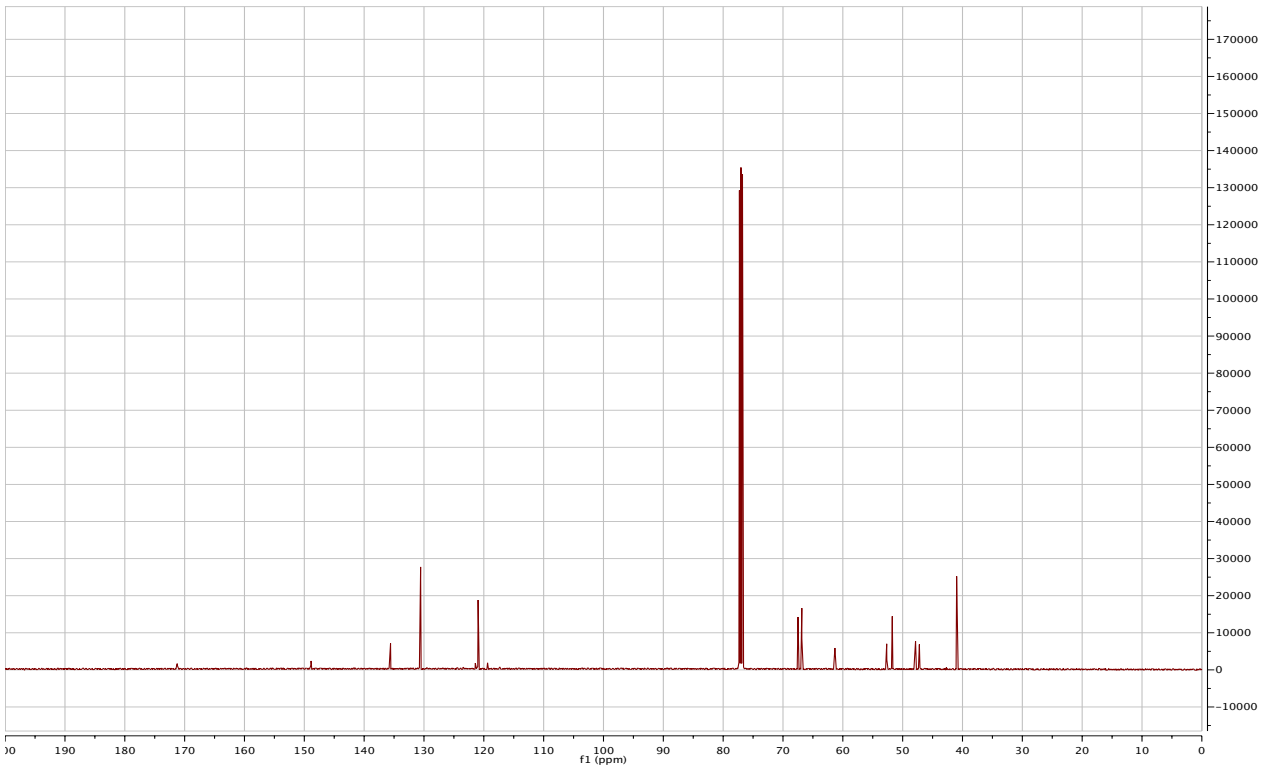
2-(4-methoxybenzyl)octahydro-1*H*-pyrido[2,1-*d*][1,2,5]thiadiazepin-1-one 3,3-dioxide (16)



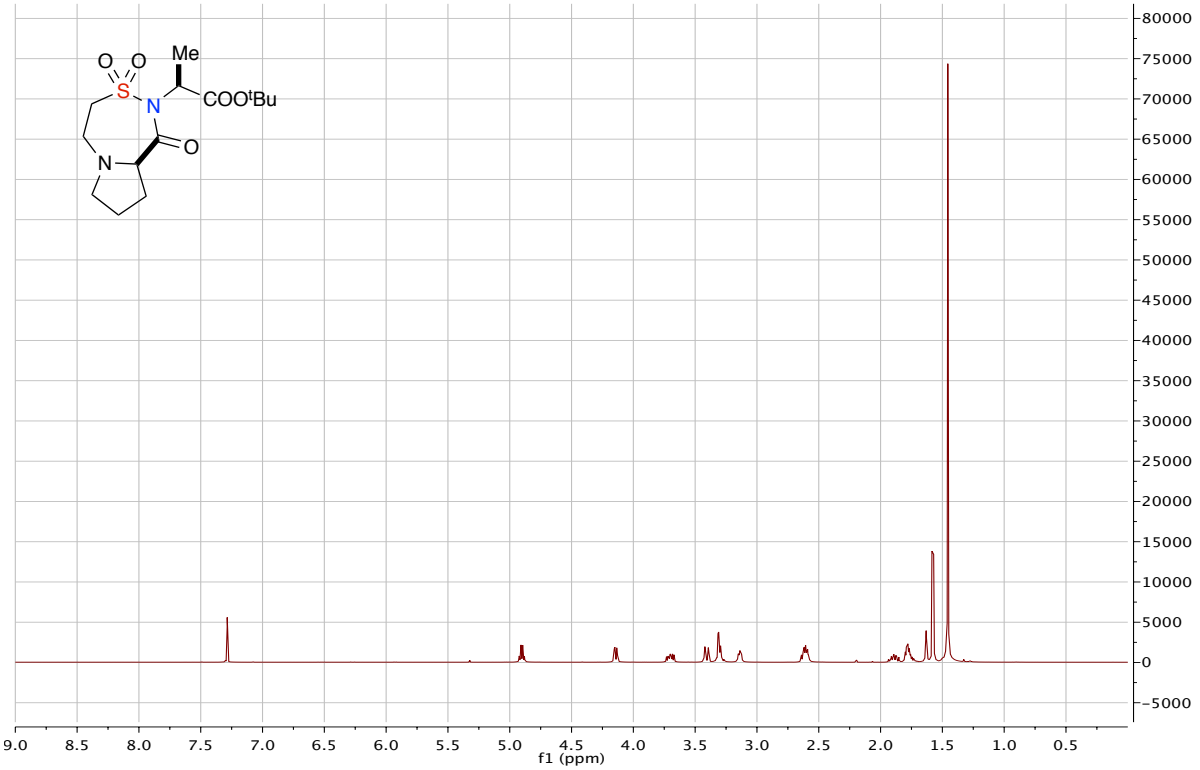


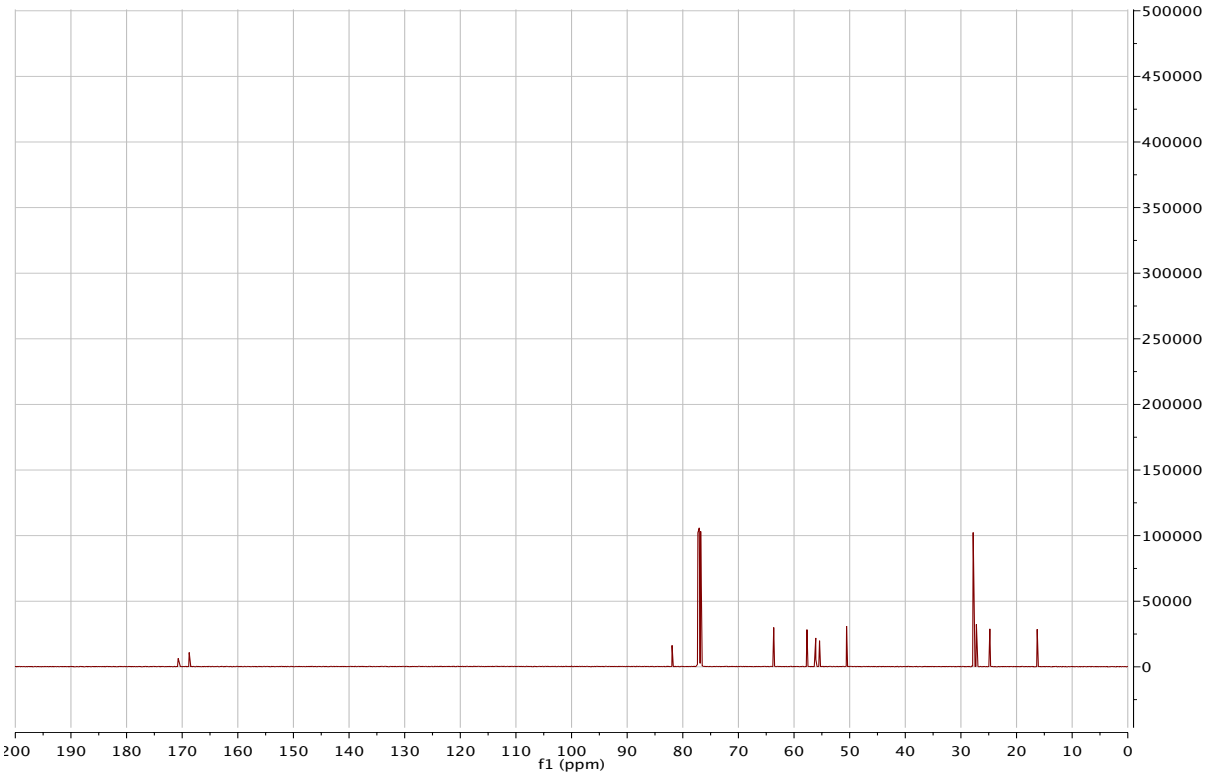
2-(4-(trifluoromethoxy)benzyl)hexahydro-[1,4]oxazino[3,4-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (17)



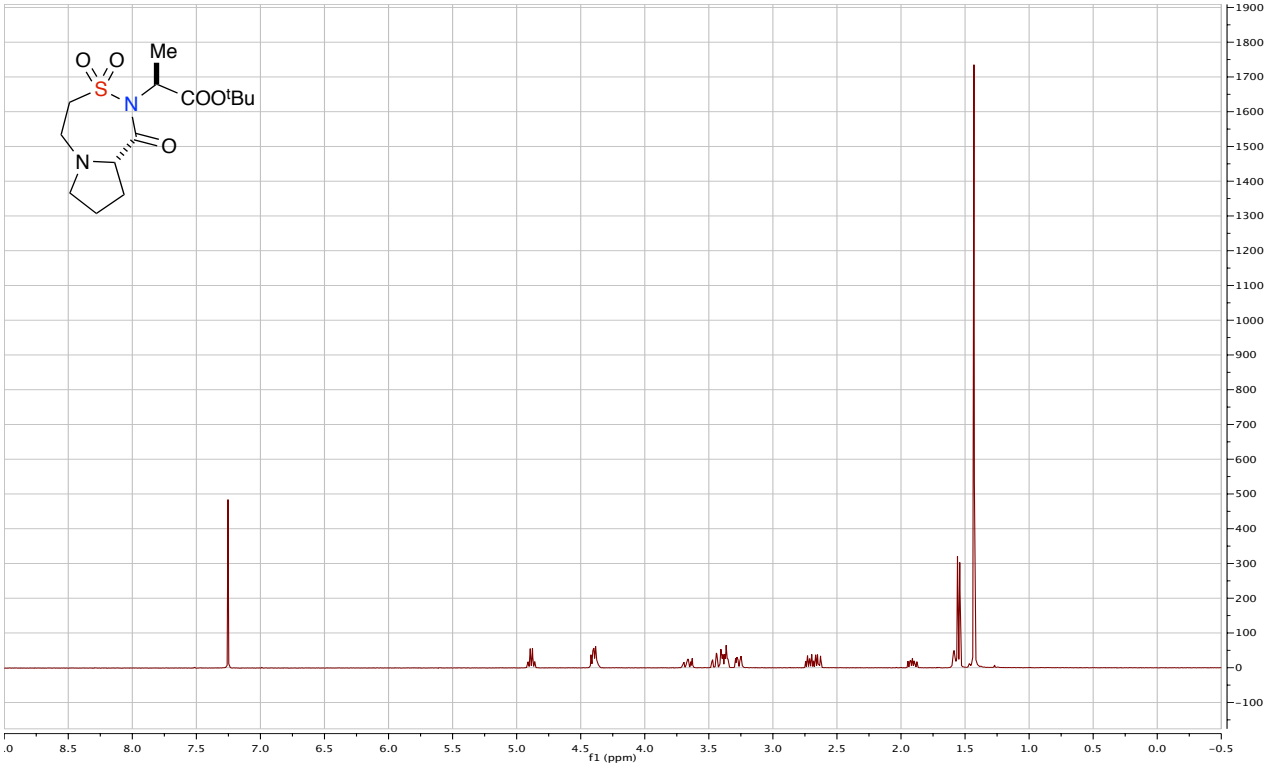


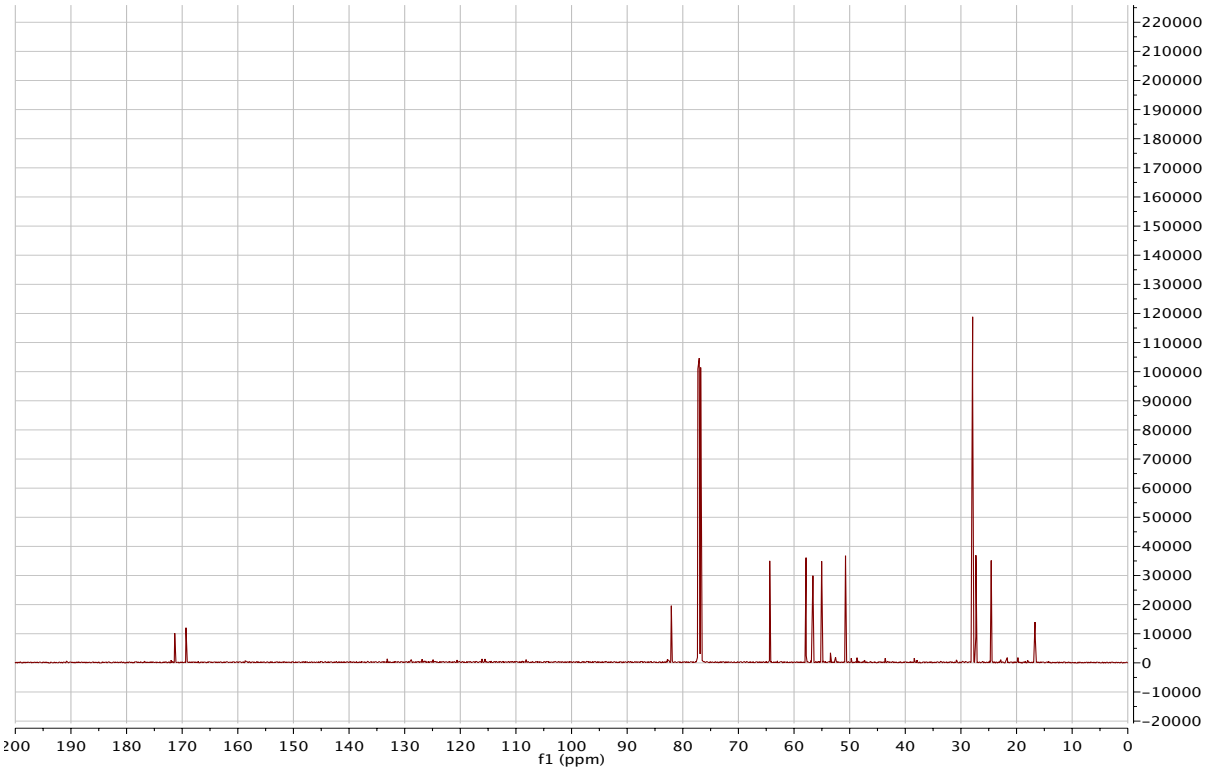
(*S*)-*tert*-butyl 2-((*S*)-3,3-dioxido-1-oxohexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-2(1*H*)-yl)propanoate (18)



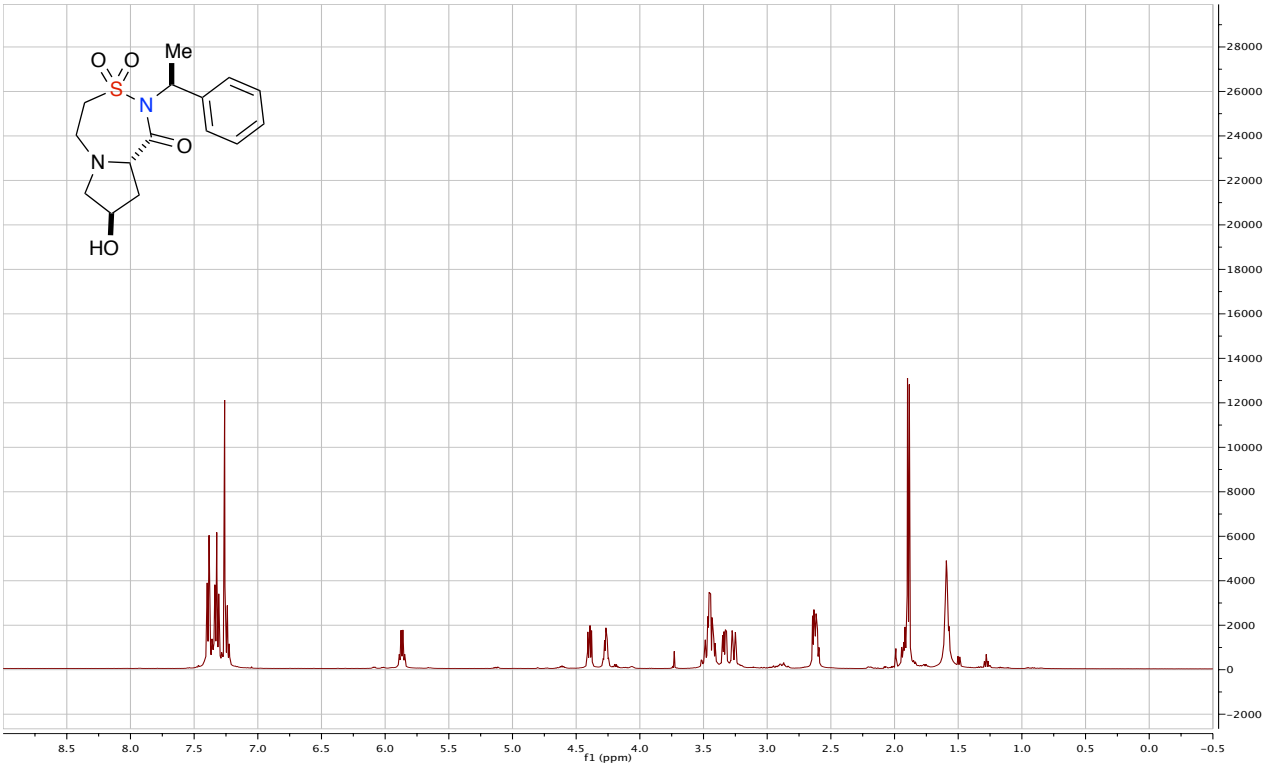


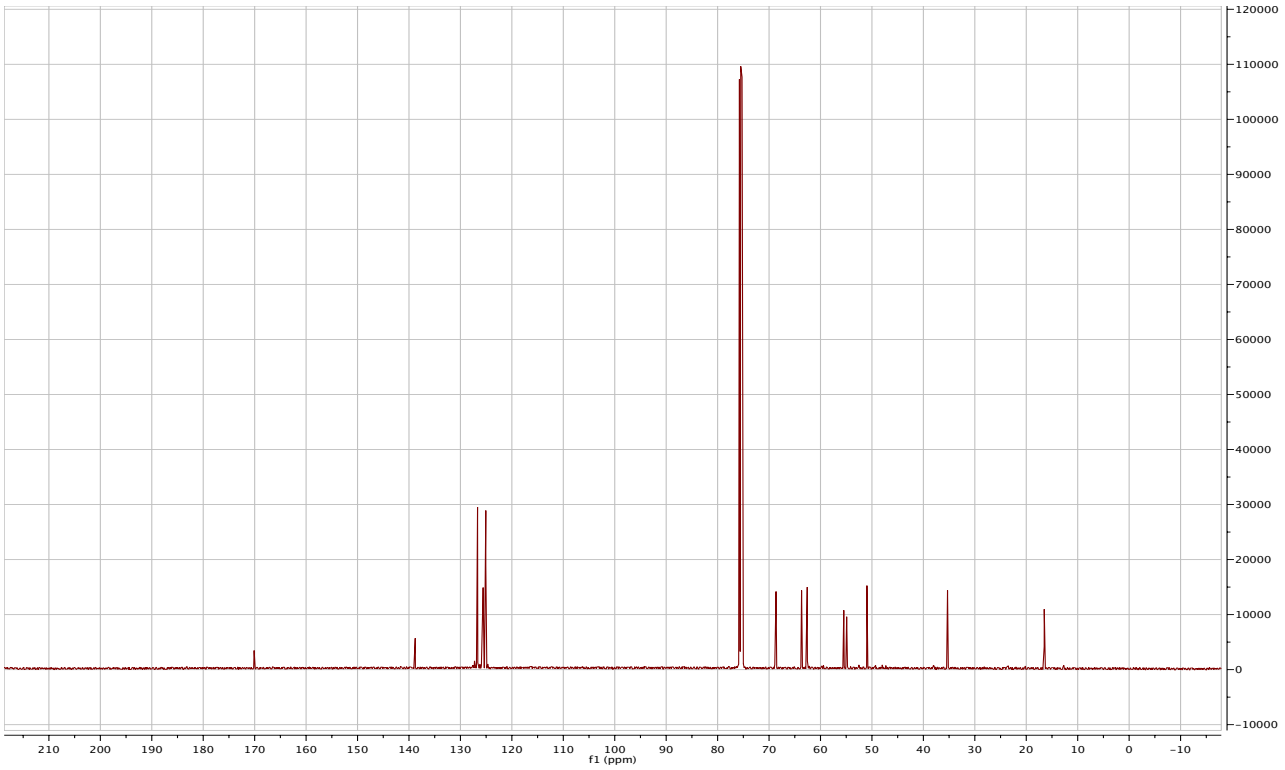
(*S*)-*tert*-butyl 2-((*R*)-3,3-dioxido-1-oxohexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-2(1*H*)-yl)propanoate (19)



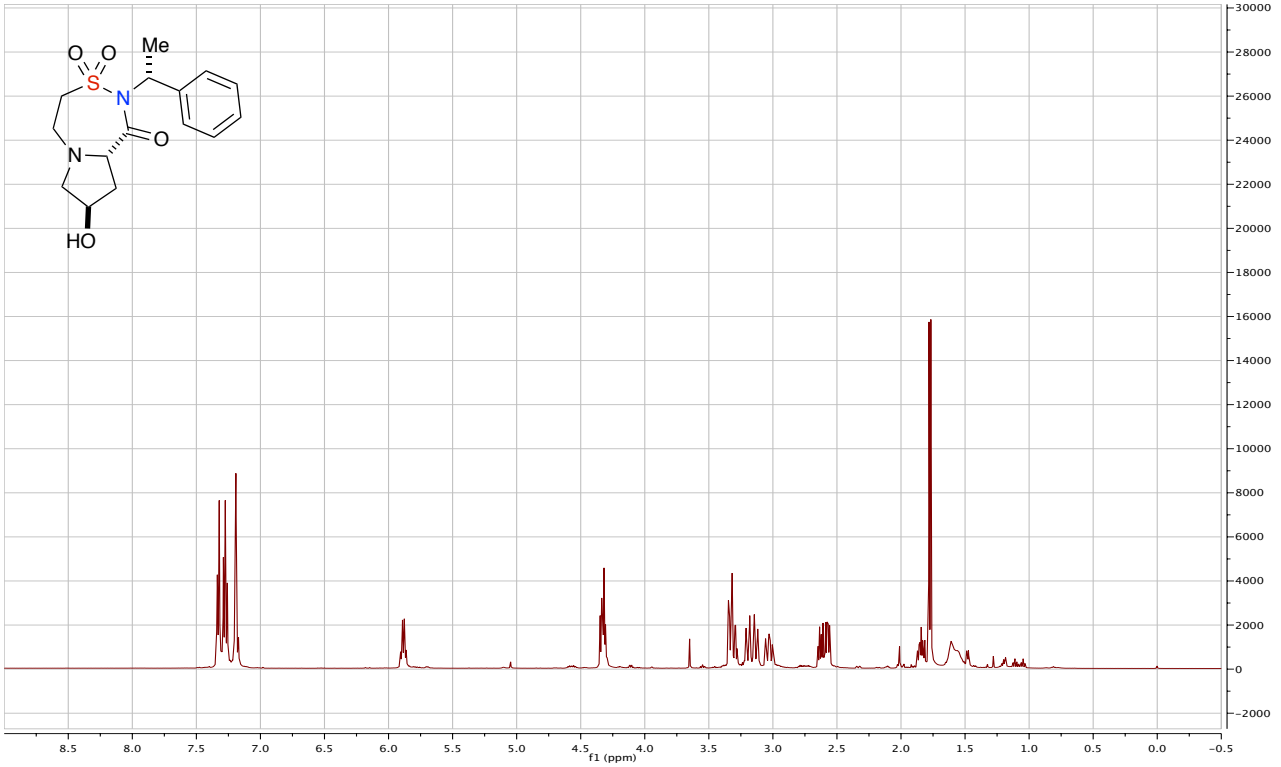


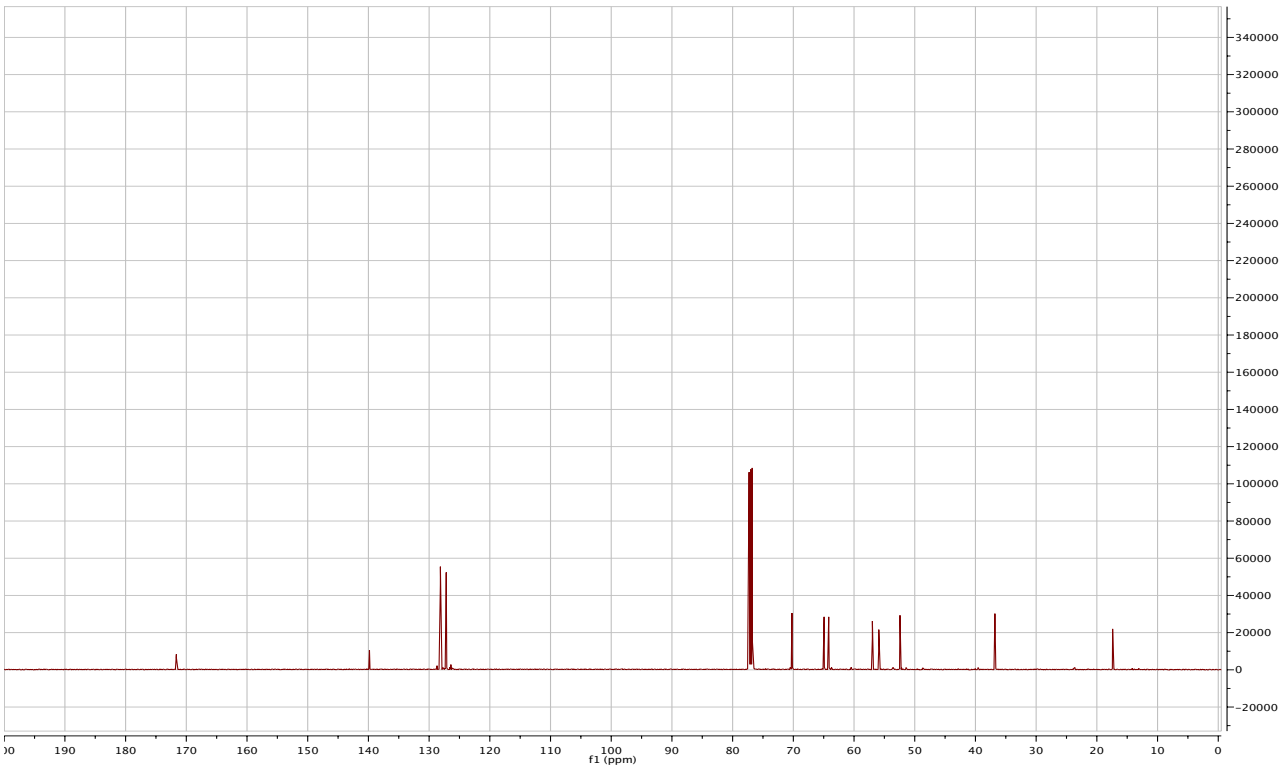
8*R*,9a*S*)-8-hydroxy-2-((*S*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (22)



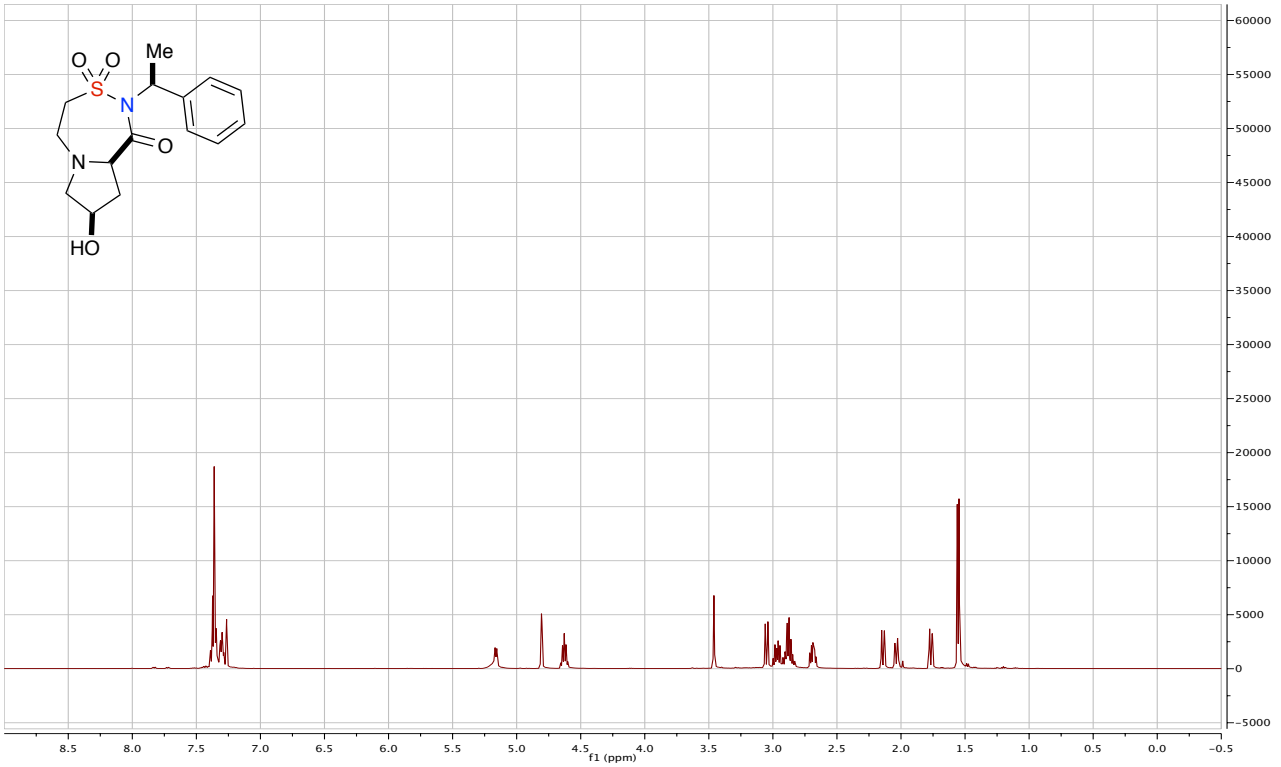


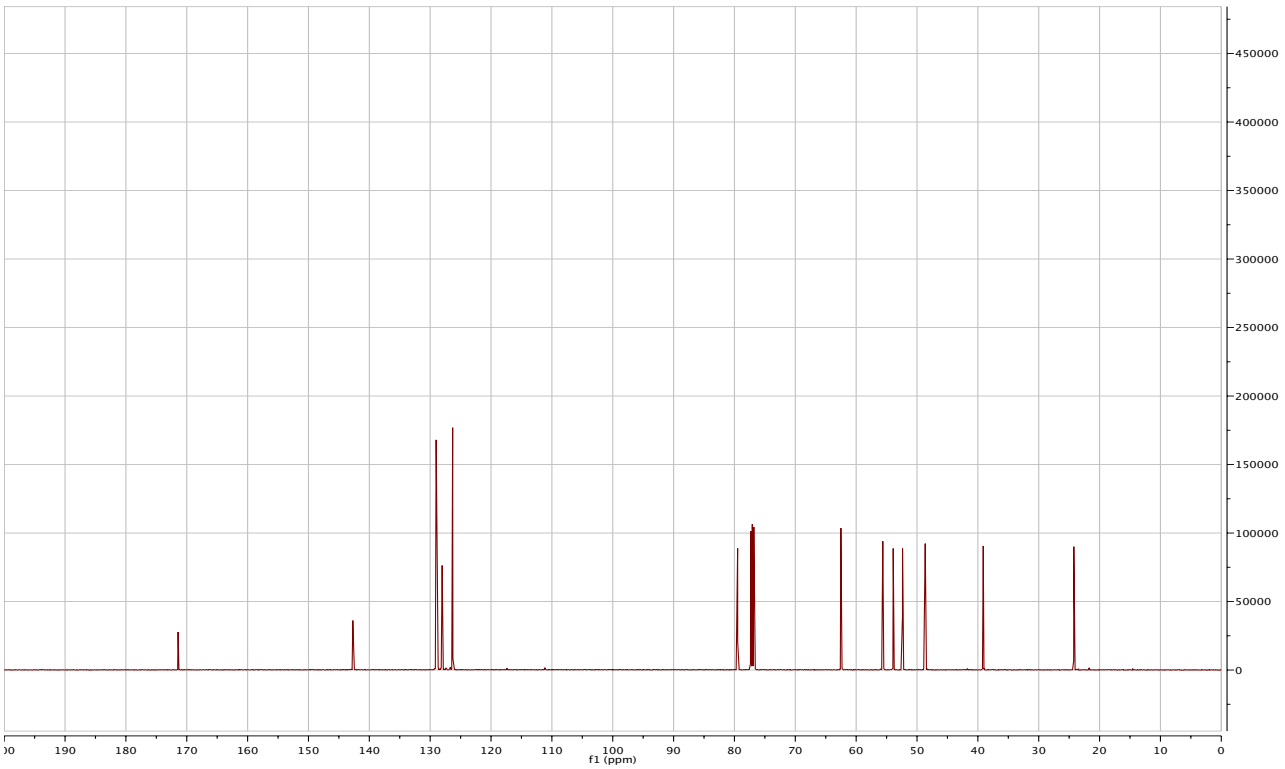
(8*R*,9a*S*)-8-hydroxy-2-((*R*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (23)



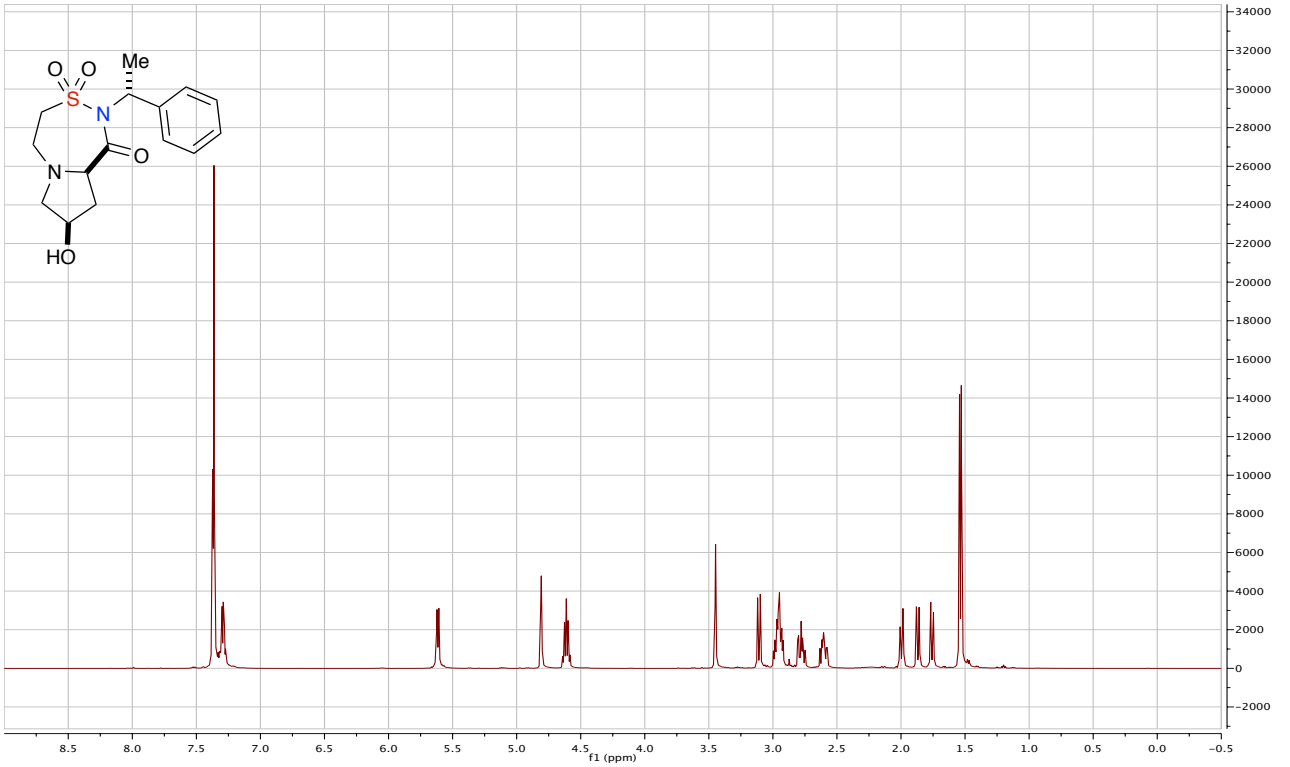


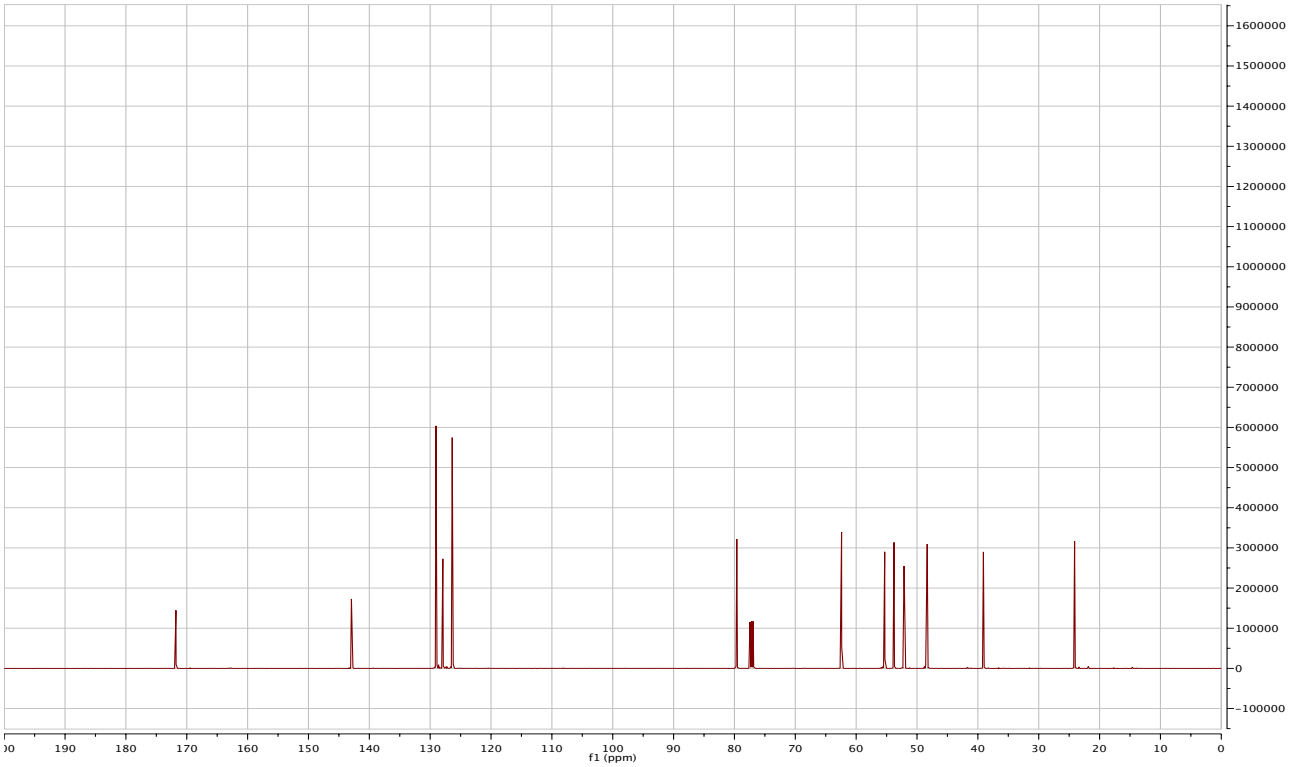
(8*R*,9a*R*)-8-hydroxy-2-((*S*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (24)



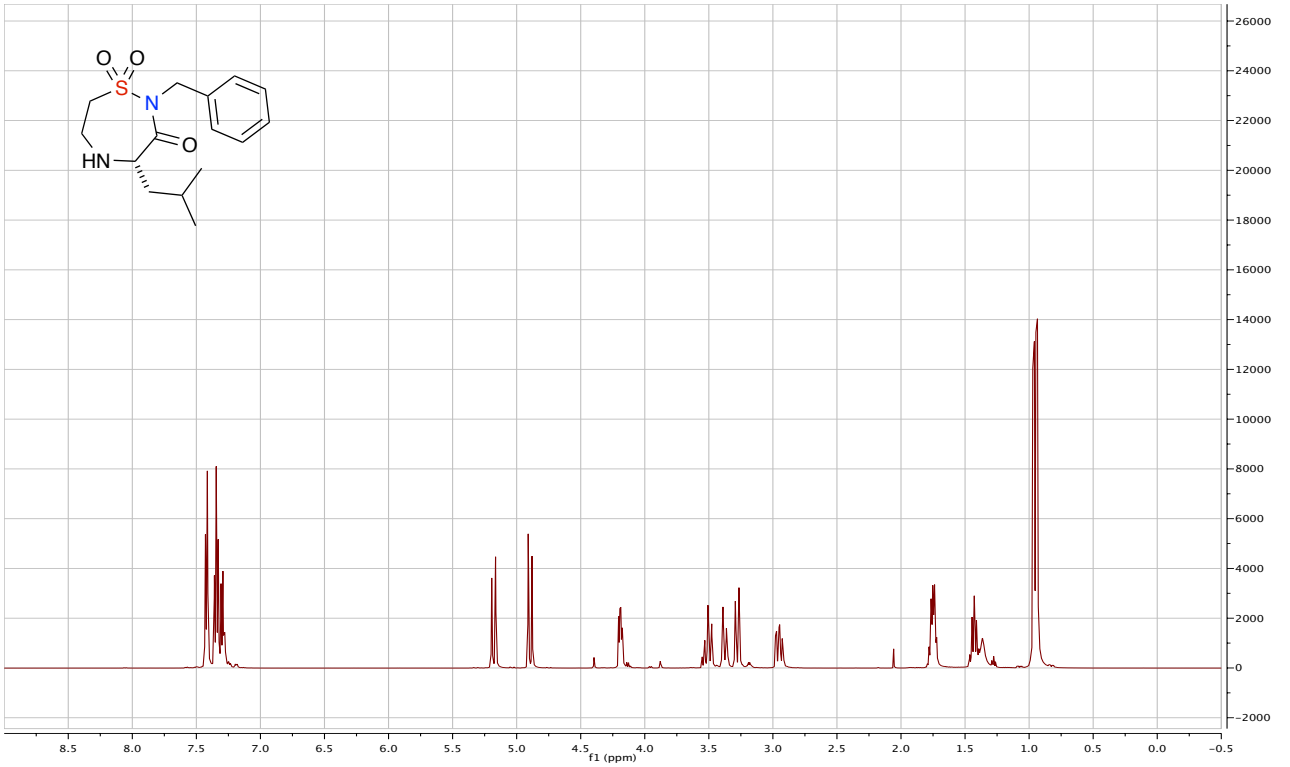


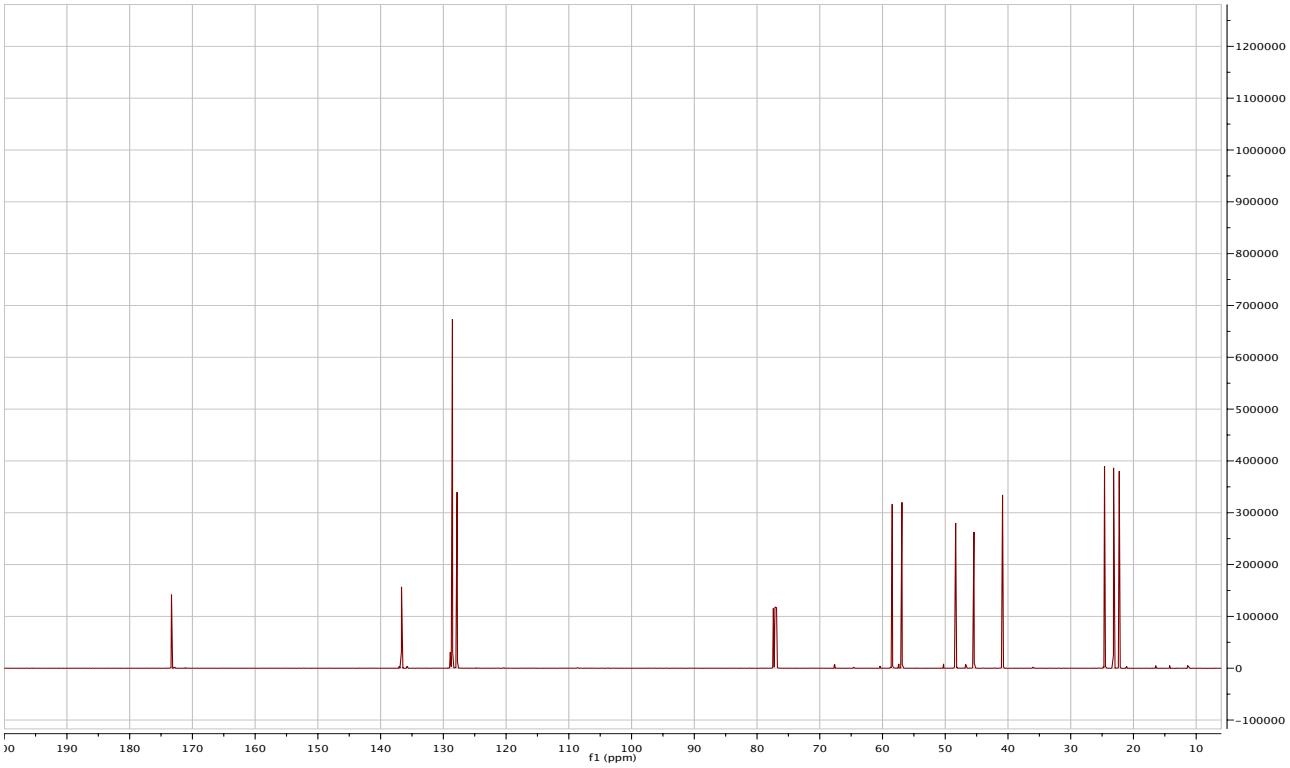
(8*R*,9a*R*)-8-hydroxy-2-((*R*)-1-phenylethyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (25)



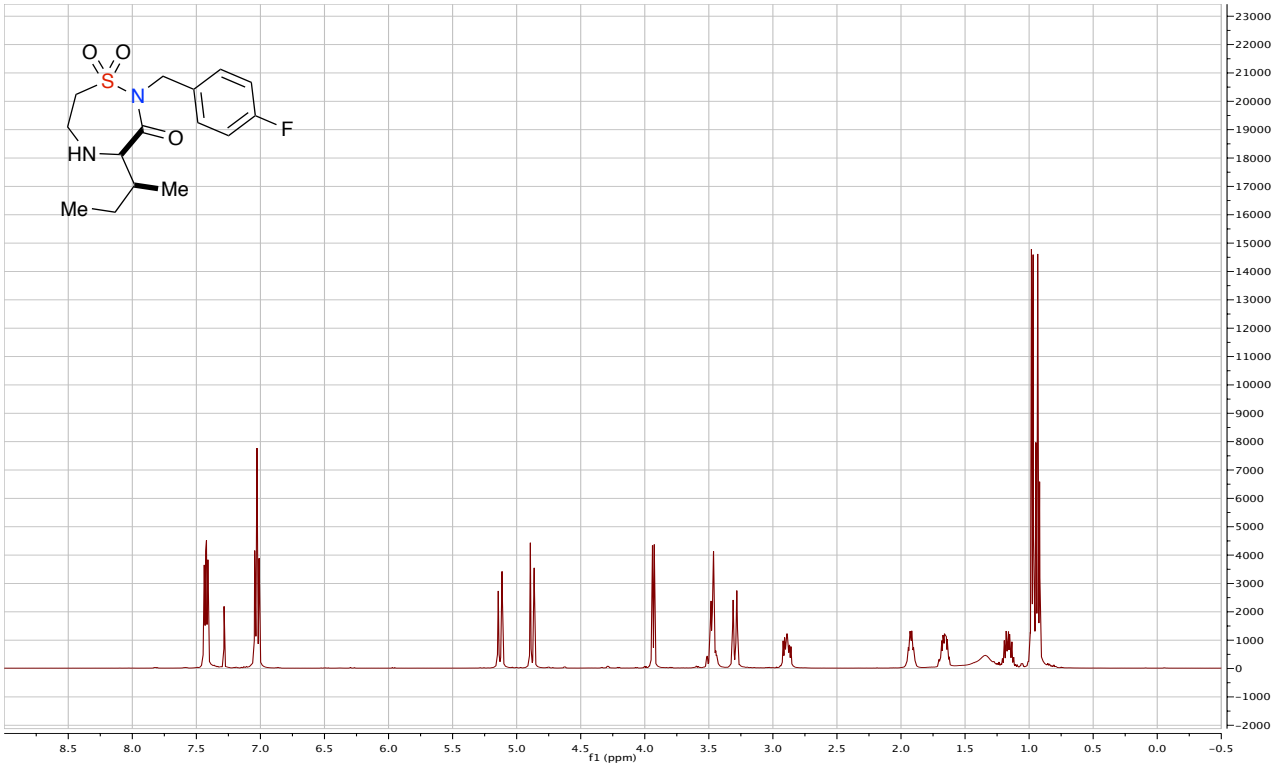


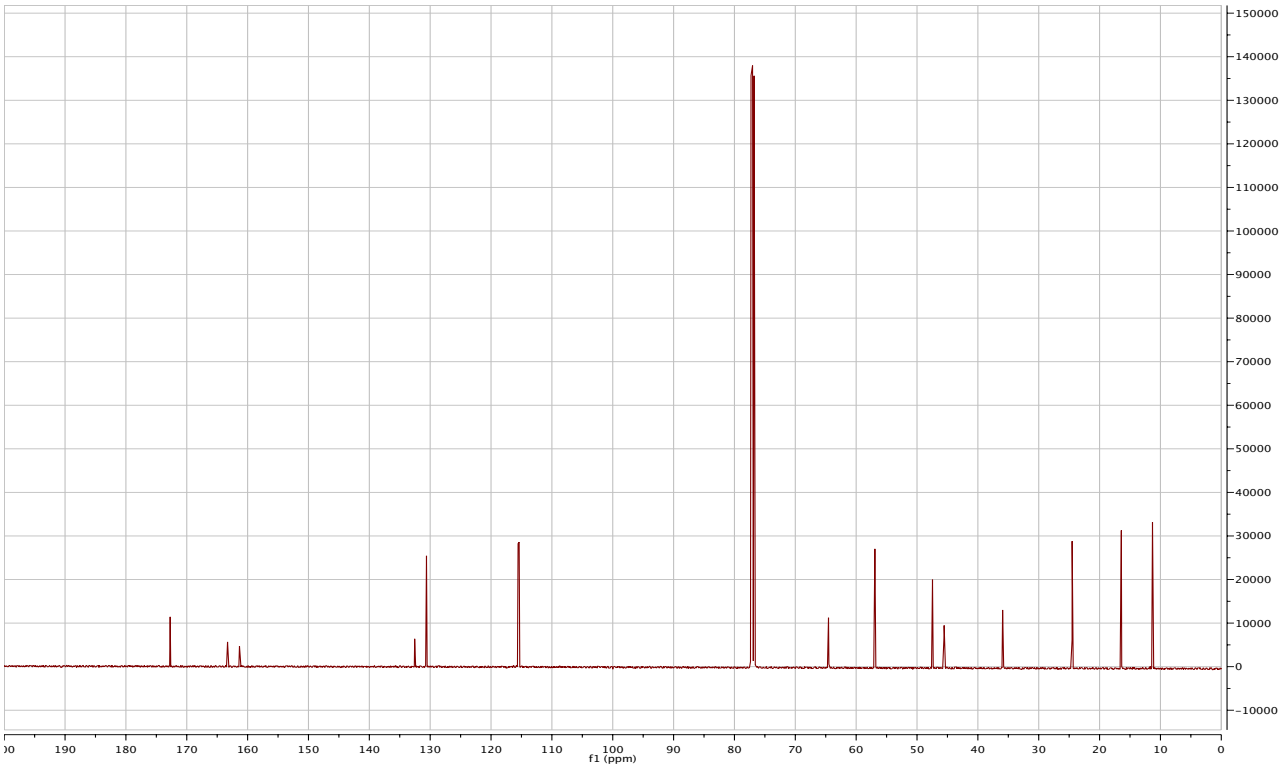
(*S*)-2-benzyl-4-isobutyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26a, 27g)



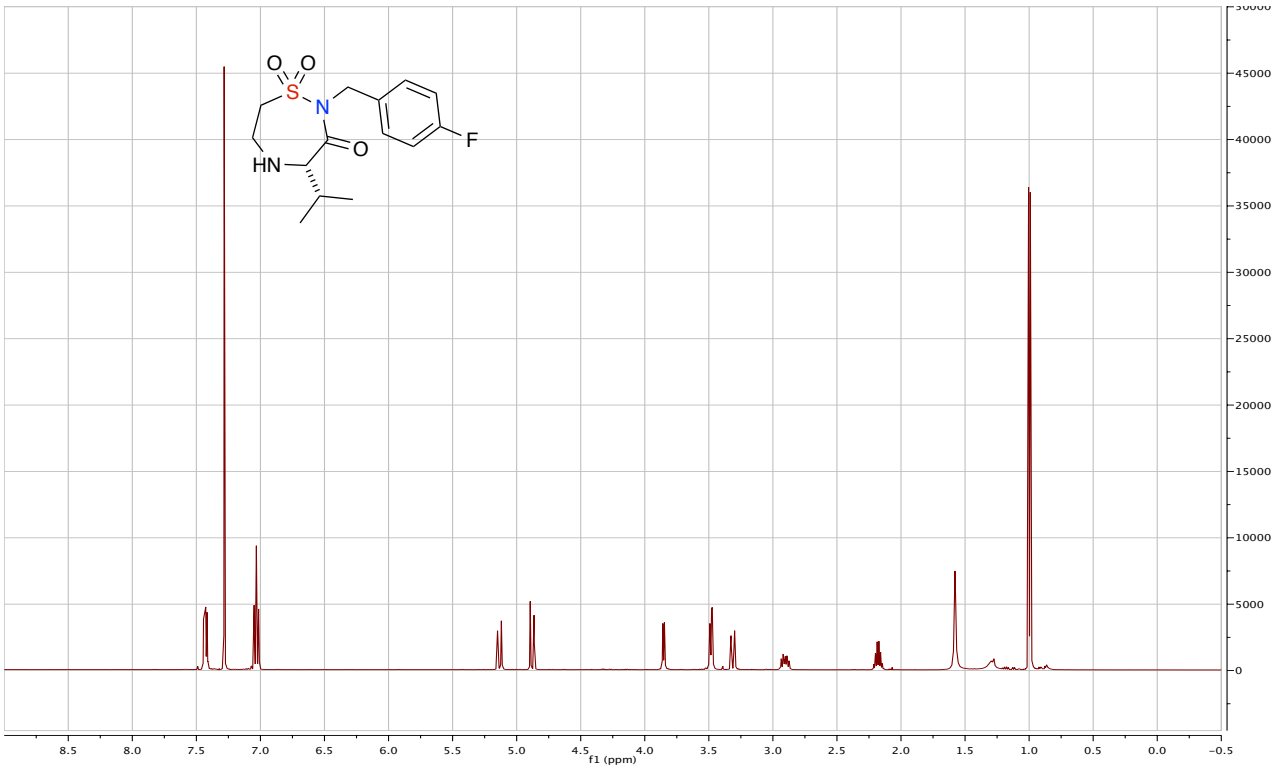


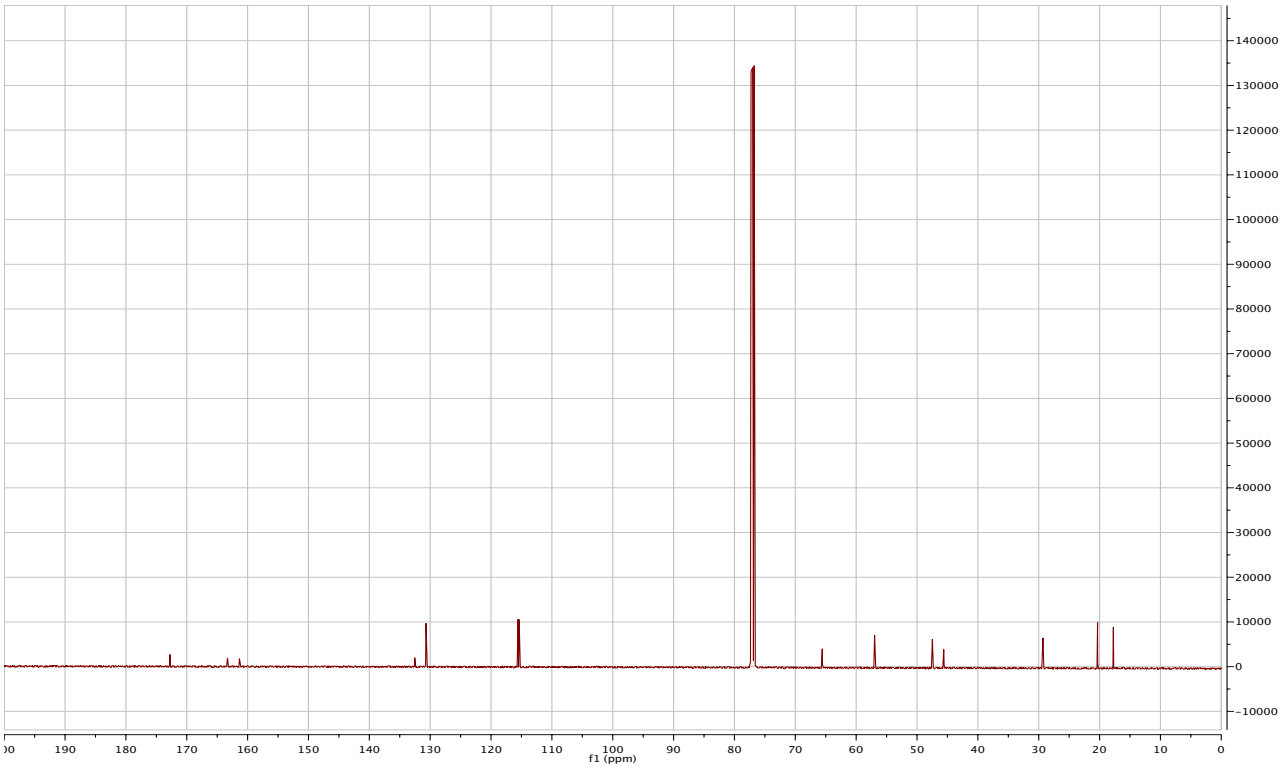
(4*S*)-4-(*sec*-butyl)-2-(4-fluorobenzyl)-1,2,5-thiadiazepan-3-one 1,1-dioxide (26b, 27h)



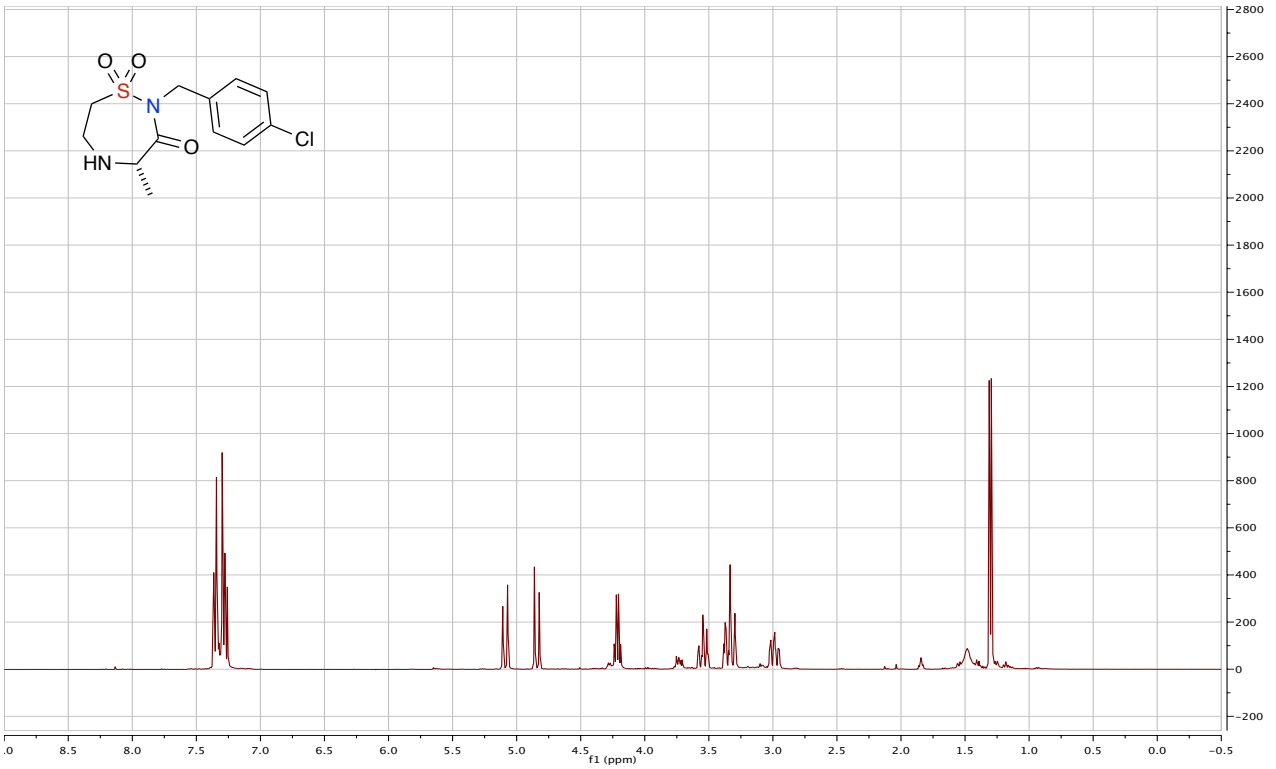


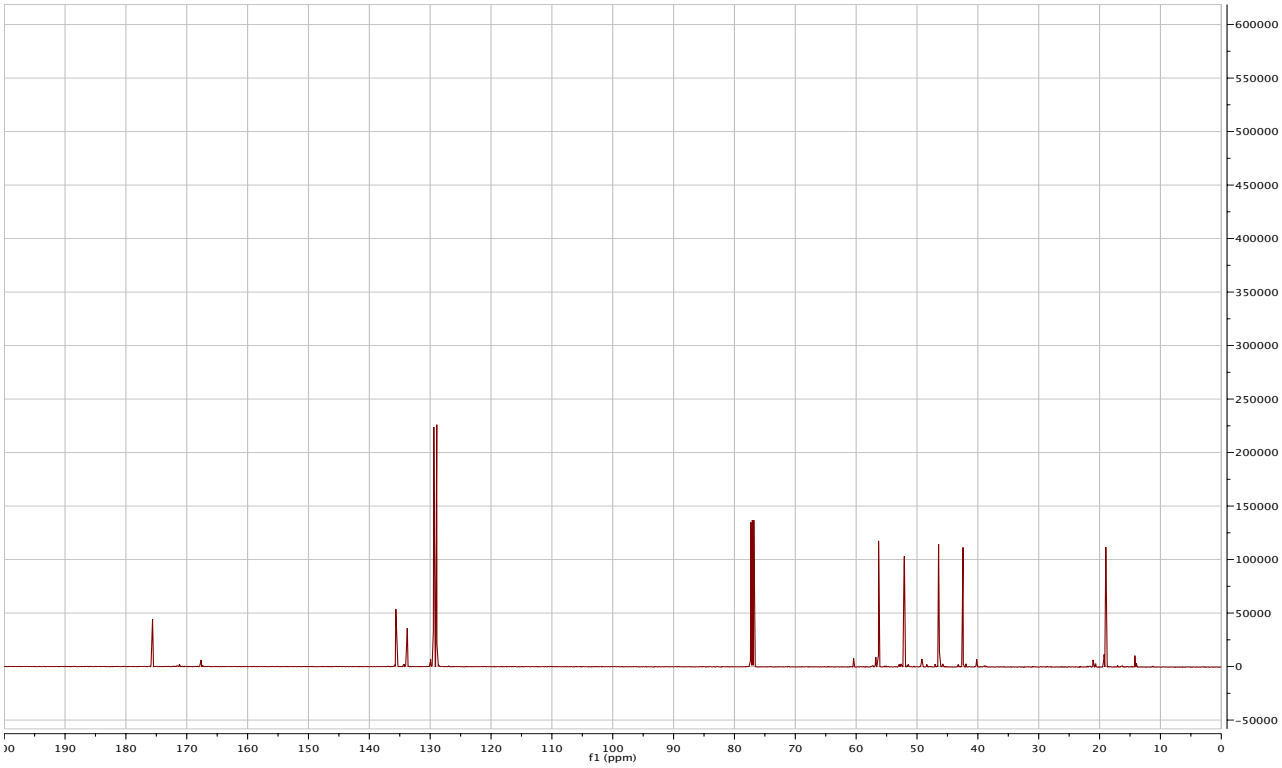
(*S*)-2-(4-fluorobenzyl)-4-isopropyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26c)



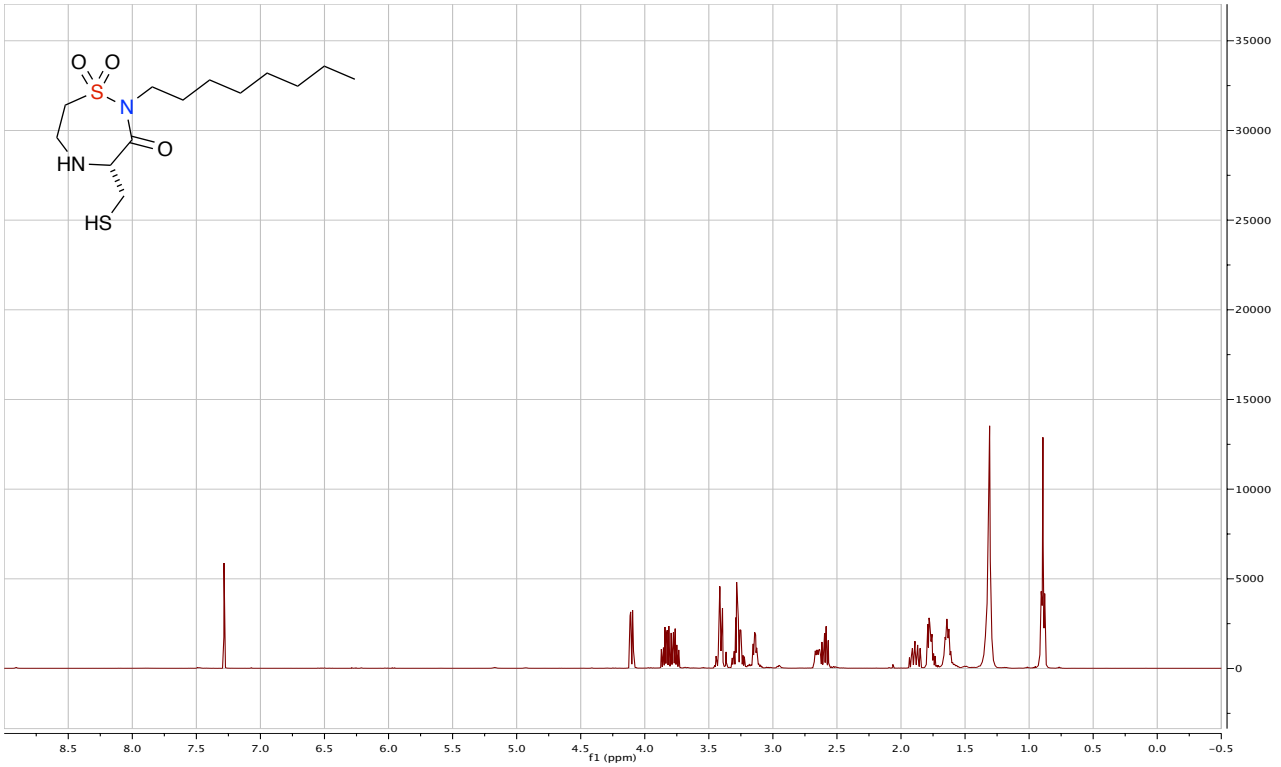


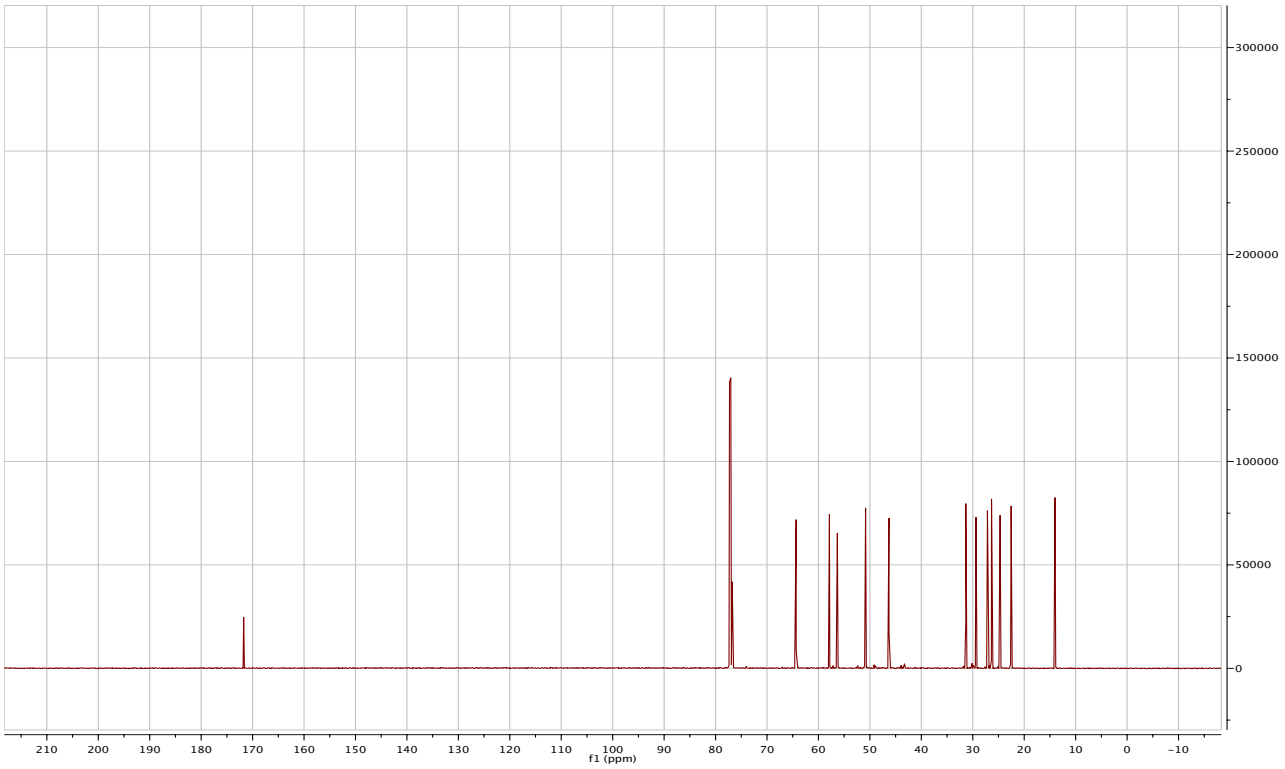
(*S*)-2-(4-chlorobenzyl)-4-methyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26d)



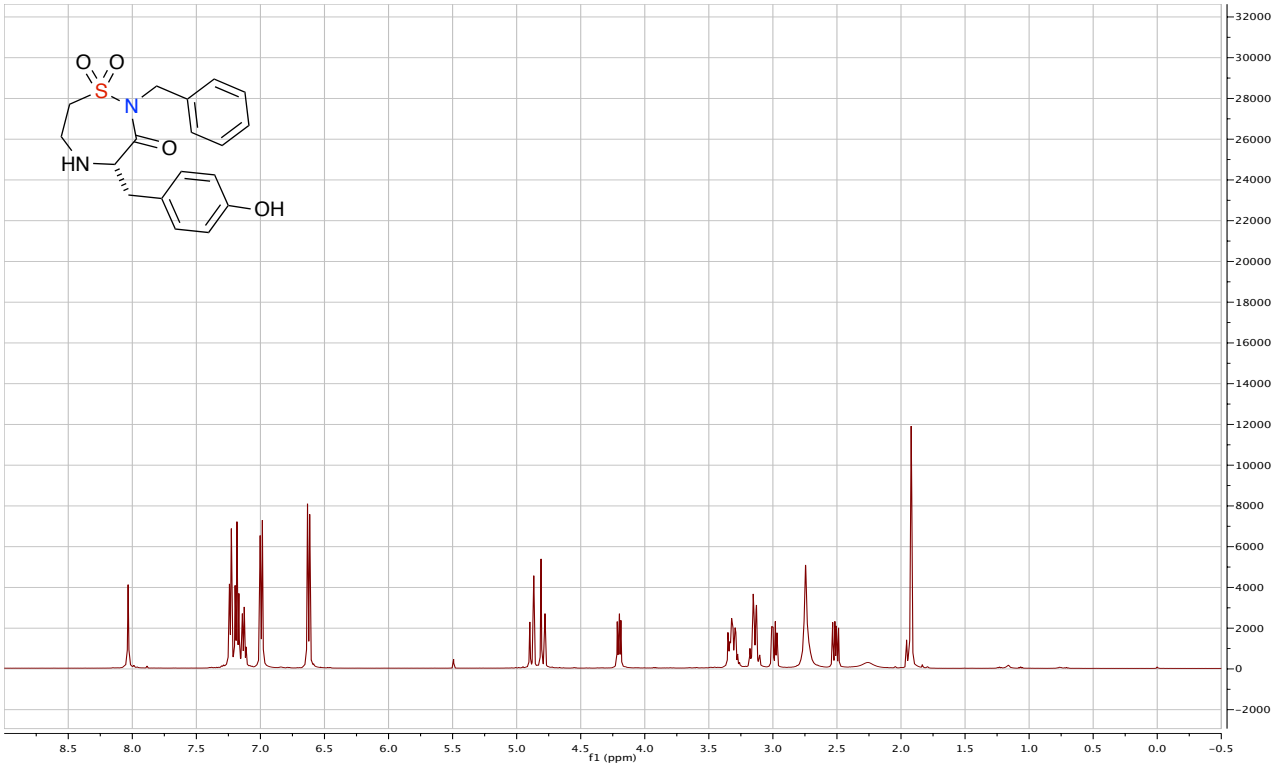


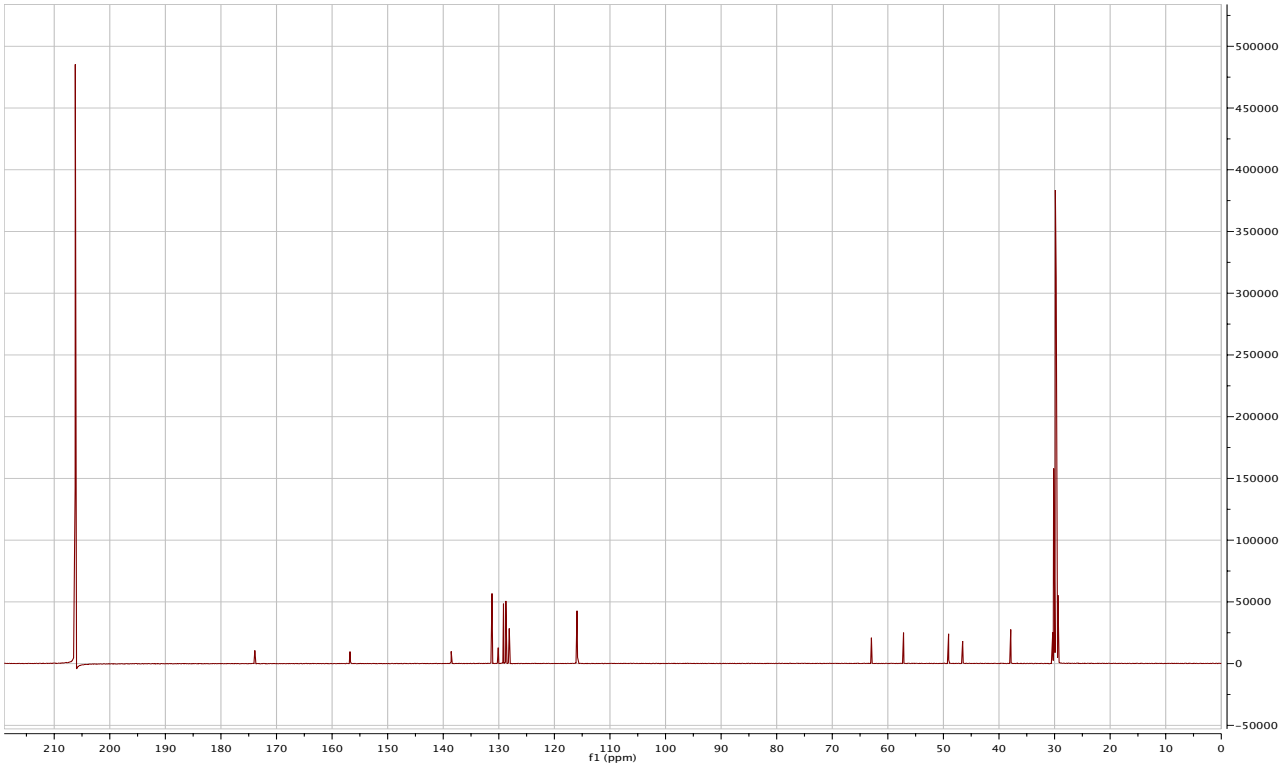
(*R*)-4-(mercaptomethyl)-2-octyl-1,2,5-thiadiazepan-3-one 1,1-dioxide (26e)



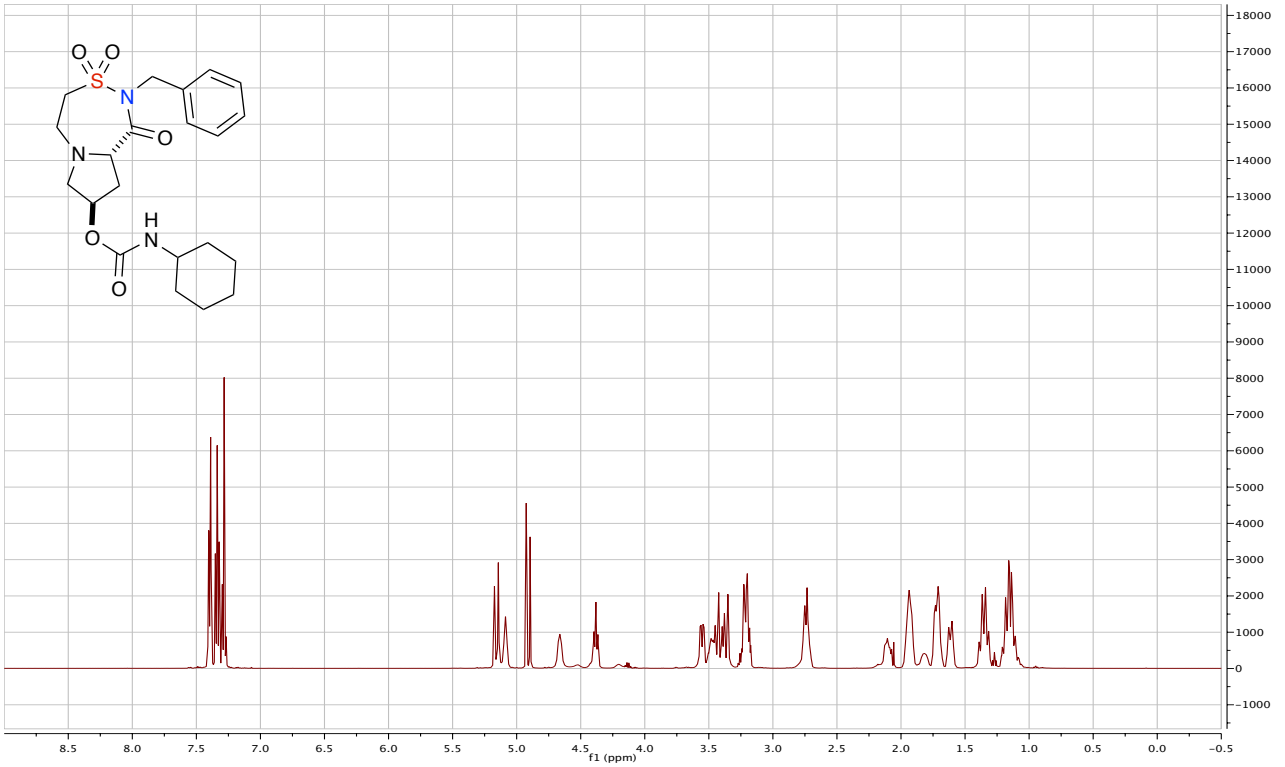


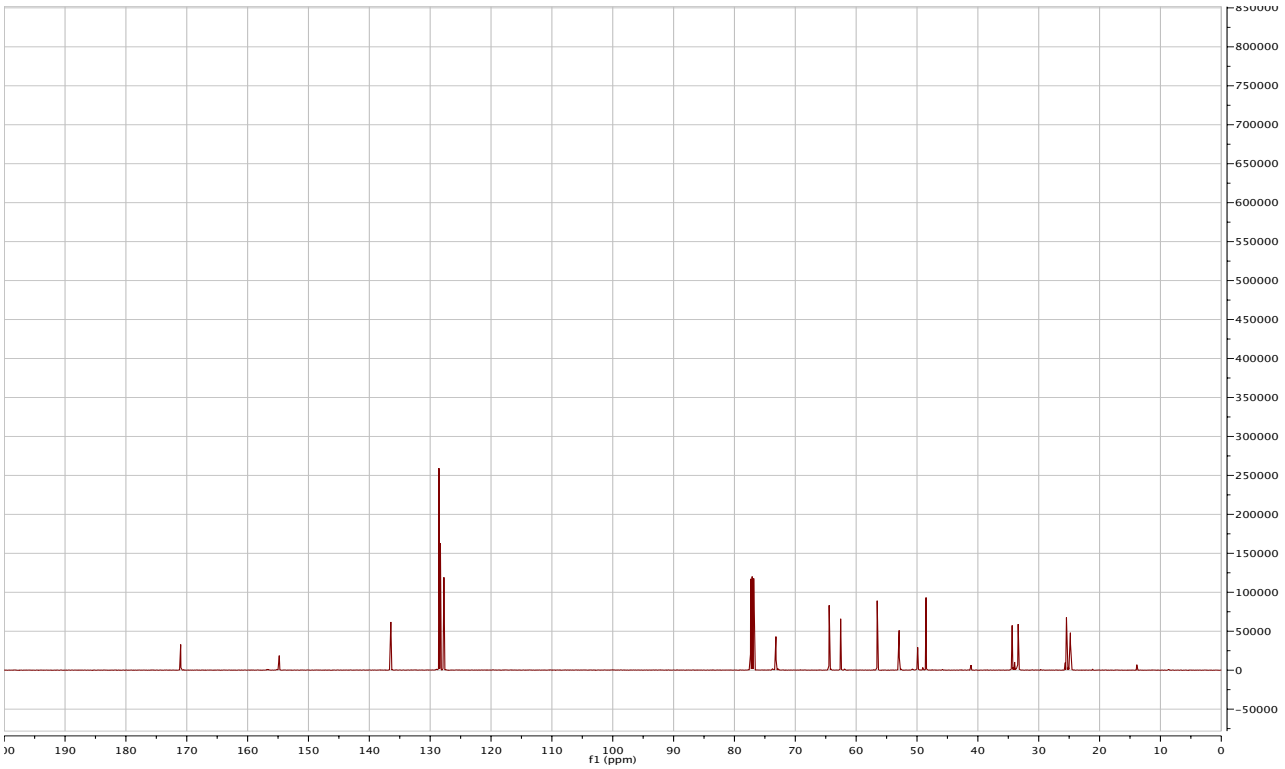
(*S*)-2-benzyl-4-(4-hydroxybenzyl)-1,2,5-thiadiazepan-3-one 1,1-dioxide (26f)



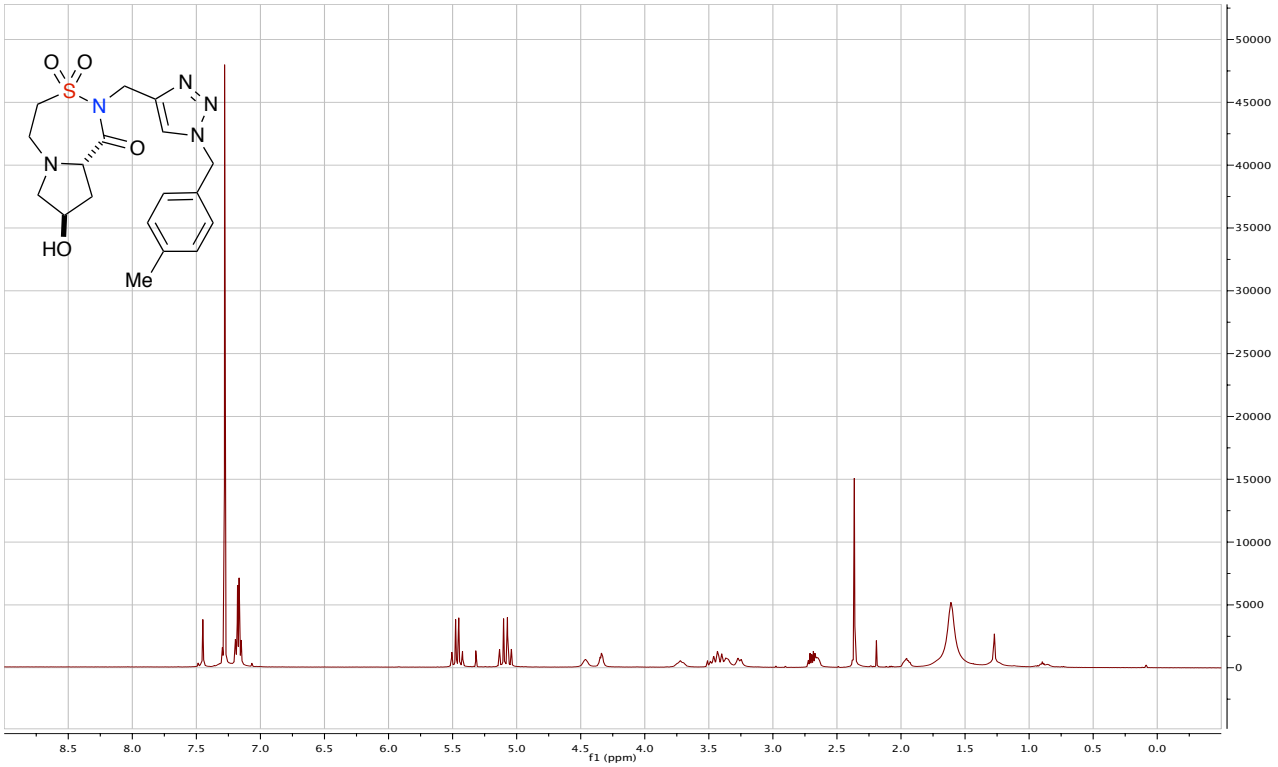


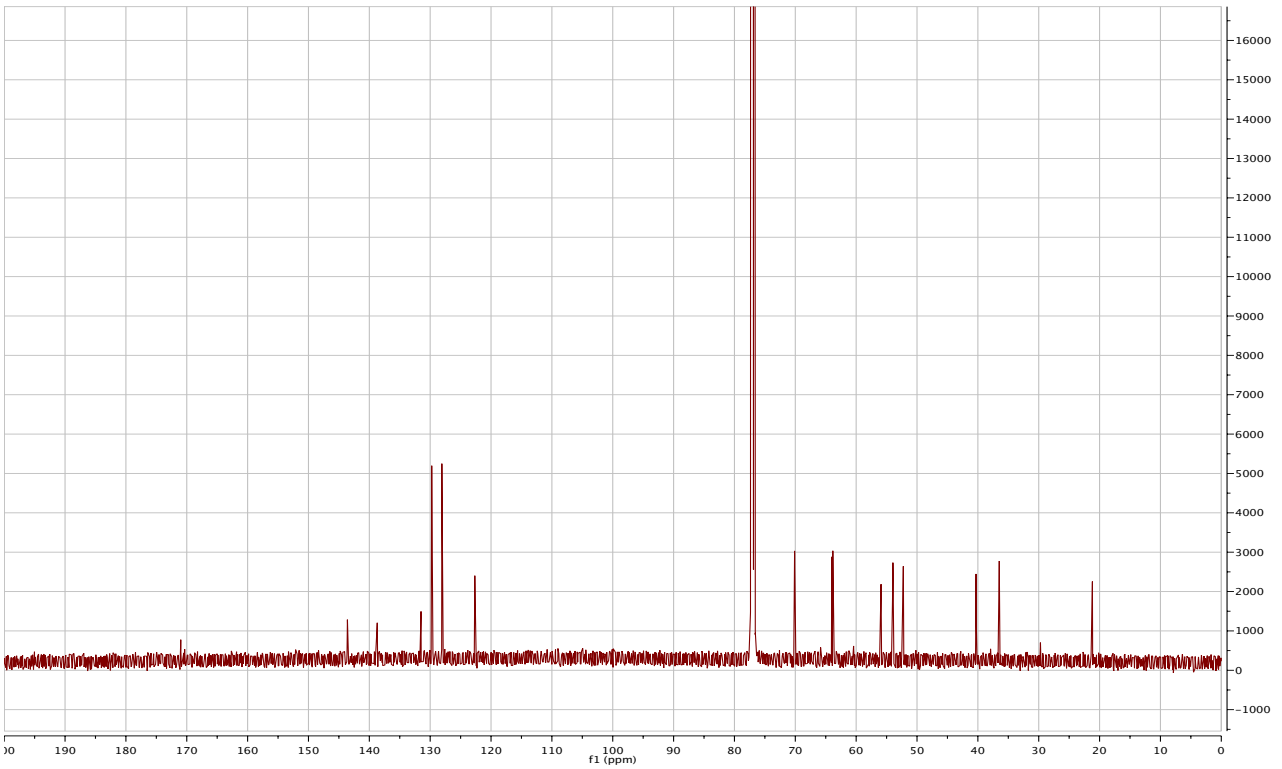
(8*R*,9a*S*)-3,3-dioxido-1-oxo-2-(prop-2-yn-1-yl)octahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-8-yl phenylcarbamate (28)



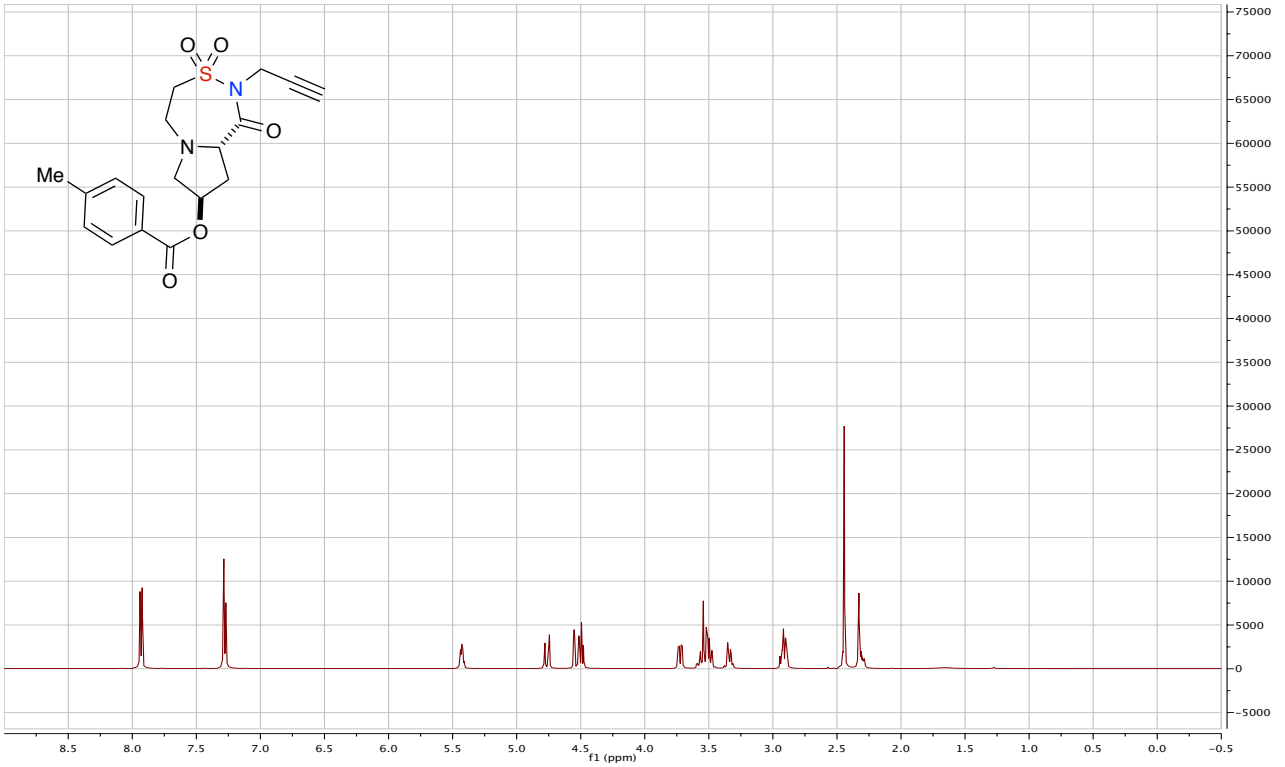


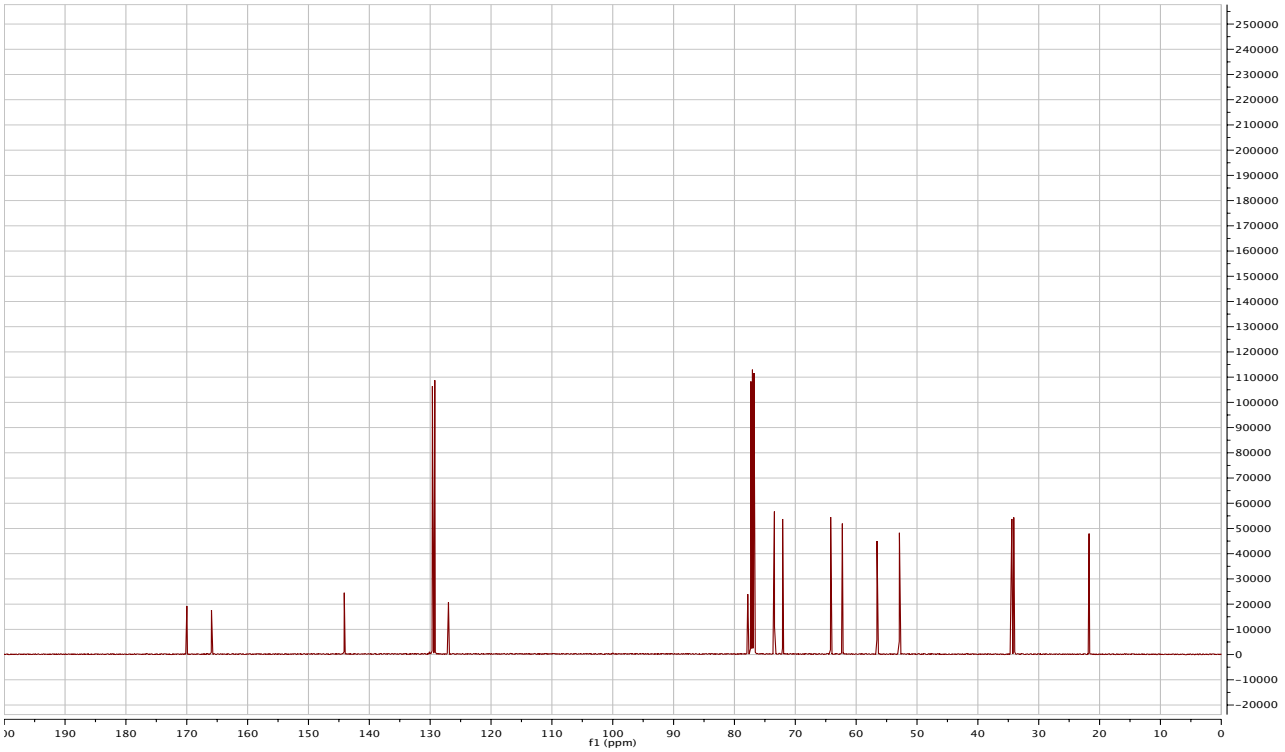
(8*R*,9a*S*)-8-hydroxy-2-((1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl)methyl)hexahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-1(2*H*)-one 3,3-dioxide (29)





(8*R*,9a*S*)-3,3-dioxido-1-oxo-2-(prop-2-yn-1-yl)octahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-8-yl 4-methylbenzoate (30)





(8*R*,9a*S*)-2-((1-(4-methylbenzyl)-1*H*-1,2,3-triazol-4-yl)methyl)-3,3-dioxido-1-oxooctahydropyrrolo[2,1-*d*][1,2,5]thiadiazepin-8-yl 4-methylbenzoate (31)