Supporting Information

Synthesis of New Spiro Pyrrole/Pyrrolizine/Thiazole Derivatives via (3+2) Cycloaddition Reaction

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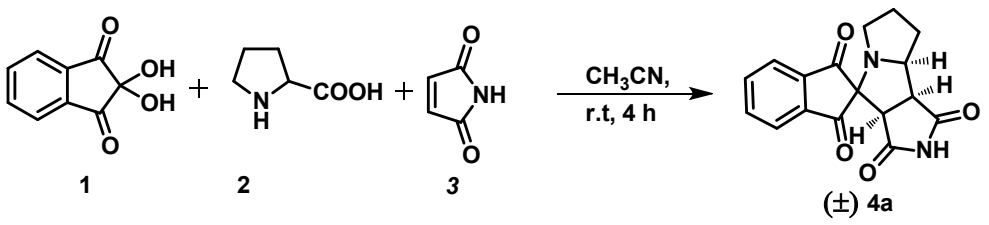
Table of Content

General remarks and materials:

Commercially available Ninhydrin, L-amino acids, maleimide, isothiocynates, phenacyl bromide and all solvents were purchased from Sigma Aldrich and Alpha Aesar Company and used without further purification as received. Reactions were monitored by TLC by exposure to iodine vapours and a solution of *p*-anisaldehyde. Thin layer chromatography (TLC) was performed using precoated glass silica gel plates and visualized by UV fluorescence of 254 nm short wavelength ultraviolet light. All products were purified by column chromatography using Merck 60-120 mesh silica gel. All ^{1}H and ^{13}C NMR spectra were recorded in deuterated chloroform ($CDCl_3$) or $CDCl_3$+DMSO-d_6 (deuterated dimethyl sulfoxide) (6:4) on Avance 300 or Avance 400 or Avance 500 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual $CHCl_3$ (1H: δ 7.26 ppm, ^{13}C: δ 77.00 ppm) as an internal reference. Coupling constants (*j*) are reported in Hertz (Hz). Peak multiplicity is indicated as follows: s-singlet, d-doublet, t-triplet, q-quartet, m-multiplet and dd-doublet of doublet. Coupling constants (*j*) were expressed in Hertz (Hz). Mass spectra were recorded by using 70 eV spectrometer. Melting points were measured on a BUCHI melting point machine. IR spectra were recorded on Thermo Nicolet FT/IR-5700 spectrometer. High resolution mass spectrums (HRMS) were recorded using Applied Bio-Sciences HRMS spectrometer at national center for mass spectroscopy-IICT.

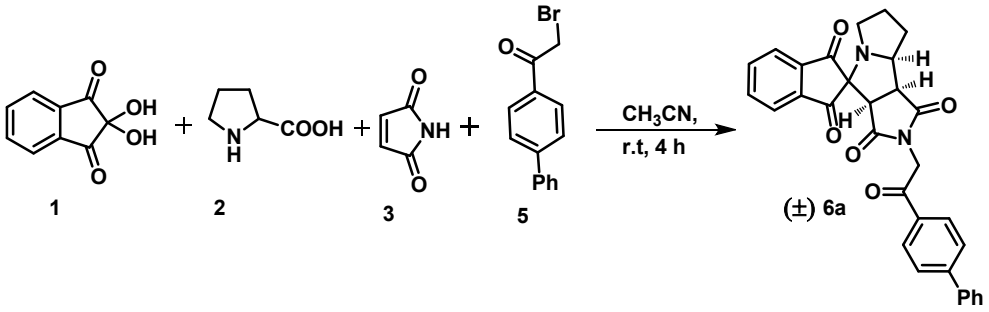
Representative Procedure for Three-Component Pyrrolizine Synthesis:

To a solution of ninhydrin **1** (1 mmol) in acetonitrile, proline **2** (1.2 mmol) and the maleimide **3** (1 mmol) were added at room temperature. The reaction was stirred for 4 hrs and the conversion was monitored by TLC. The solvent was removed in vacuo. The crude product was purified by column chromatography using petroleum hexane–ethyl acetate (8:2) mixture as an eluent to get pure compound **4a**.



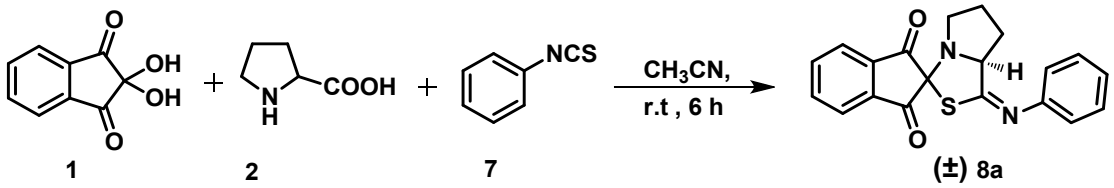
Representative Procedure for Four-Component Pyrrolizine Synthesis:.

To a solution of ninhydrin **1** (1 mmol) in acetonitrile, proline **2** (1.2 mmol) and the maleimide **3** (1 mmol) were added at room temperature and the reaction was stirred for 3 hrs then phenacyl bromide **5** (1 mmol) was added further reaction was stirred for 1 hr and the conversion was monitored by TLC. The solvent was removed in vacuo. The crude product was purified by column chromatography using petroleum hexane–ethyl acetate (8:2) mixture as an eluent to get pure compound **6a**.



Representative Procedure for Synthesis of Thiazole derivatives:

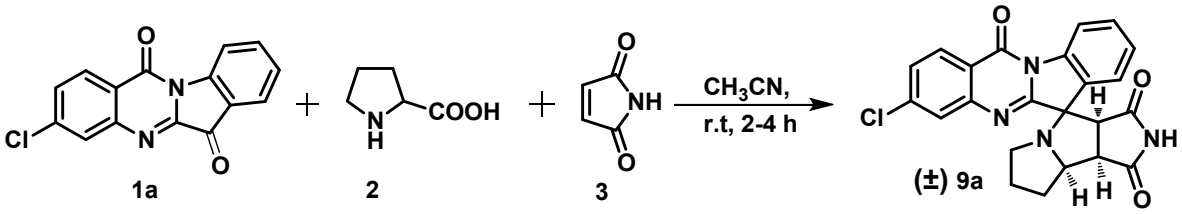
To a solution of ninhydrin **1** (1 mmol) in acetonitrile, proline **2** (1.2 mmol) and the phenyl isothiocynate **7** (1 mmol) were added at room temperature. The reaction was stirred for 6 hrs and the conversion was monitored by TLC. The solvent was removed in vacuo. The crude product was purified by column chromatography using petroleum hexane–ethyl acetate (8 : 2) mixture as an eluent to get pure compound **8a**.



Representative Procedure for Synthesis Tryptanthrins derivatives:

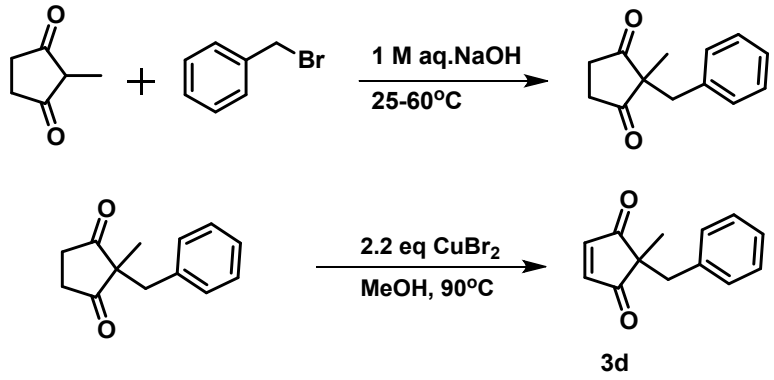
Tryptanthrins were synthesized by using literature known procedure[18]. To a solution of isatoic anhydride (1 mmol) in toluene, isatin (1.2 mmol) and Et_3N (5 mmol) were added then reaction mixture was refluxed for 18 h the conversion was monitored by TLC. Then reaction mixture was quenched with H_2O and then extracted with EtOAc (2×20). The organic layers were dried with sodium sulfate, filtered, and concentrated purified via column chromatography (eluted with EtOAc/ hexanes) to give desired product yellow solid.

To a solution of 3-chloroindolo[2,1-b]quinazoline-6,12-dione **1**a (1 mmol) in acetonitrile, proline **2** (1.2 mmol) and the maleimide **3** (1 mmol) were added at room temperature. The reaction was stirred for 2-4 hrs and the conversion was monitored by TLC. The solvent was removed in vacuo. The crude product was purified by column chromatography using petroleum hexane–ethyl acetate (8:2) mixture as an eluent to get pure compound **9a**.



Procedure for synthesis of 2-benzyl-2-methylcyclopent-4-ene-1,3-dione 3{*4*}:

For two steps synthesis of 2-benzyl-2-methylcyclopent-4-ene-1,3-dione **3d**, procedure was adapted from literature[19].



Crystal structure data for compound 3'-benzyl-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4e):

X-ray data for the compound **4e** (Figure S1) was collected at room temperature on a Bruker D8 QUEST instrument with an IμS Mo microsource (λ = 0.7107 A) and a PHOTON-100 detector. The raw data frames of KA181 were reduced and corrected for absorption effects using the Bruker Apex 3 software suite programs [1]. The structure was solved using intrinsic phasing method [2] and further refined with the SHELXL [2] program and expanded using Fourier techniques. Anisotropic displacement parameters were included for all non-hydrogen atoms. . The N-bound H atom was located in difference Fourier maps, and their positions and isotropic displacement parameters were refined. All C bound H atoms of were positioned geometrically and treated as riding on their parent C atoms [C-H = 0.93-0.97 Å, and $U_{iso}(H) = 1.5U_{eq}(C)$ for methyl H or $1.2U_{eq}(C)$ for other H atoms].

Crystal Data for 4e: $C_{21}H_{16}N_2O_4$ (*M* =360.37 g/mol): monoclinic, space group $P2_1/n$ (no. 14), *a* = 9.965(8) Å, *b* = 8.009(6) Å, *c* = 21.306(16) Å, *β* = 90.73(2)°, *V* = 1700(2) Å^3, *Z* = 4, *T* = 294.15 K, μ(Mo Kα) = 0.099 mm^{-1}, *Dcalc* = 1.4077 g/cm^3, 21266 reflections measured (4.5° ≤ 2Θ ≤ 66.76°), 5937 unique (R_{int} = 0.0482, R_{sigma} = 0.0480) which were used in all calculations. The final R_1 was 0.0533 (I>2σ(I)) and wR_2 was 0.1498 (all data). **CCDC 1850526** contains supplementary Crystallographic data for the structure. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44(0) 1223 336 033; email: deposit@ccdc.cam.ac.uk].

1. SMART & SAINT. Software Reference manuals. Versions 6.28a & 5.625, Bruker Analytical X-ray Systems Inc., Madison, Wisconsin, U.S.A., 2001.
2. Sheldrick, G. M. (2015). Acta Cryst. C71, 3–8.

Figure caption: The molecular structure of KA532, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level.

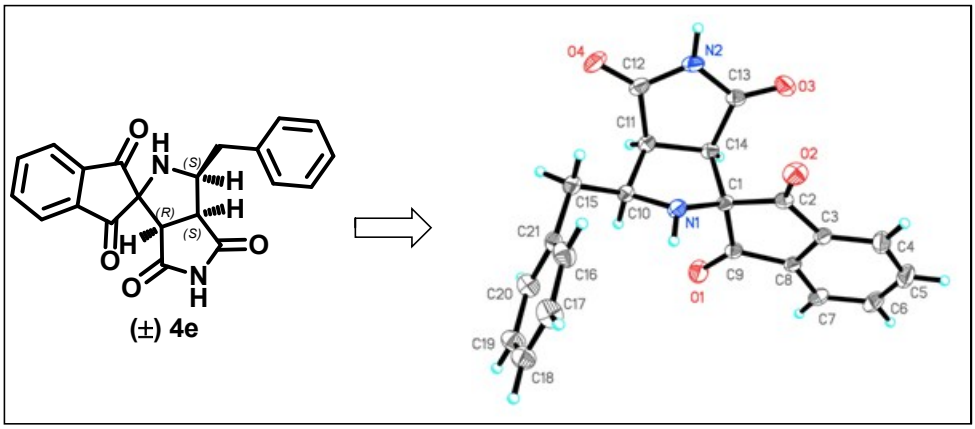
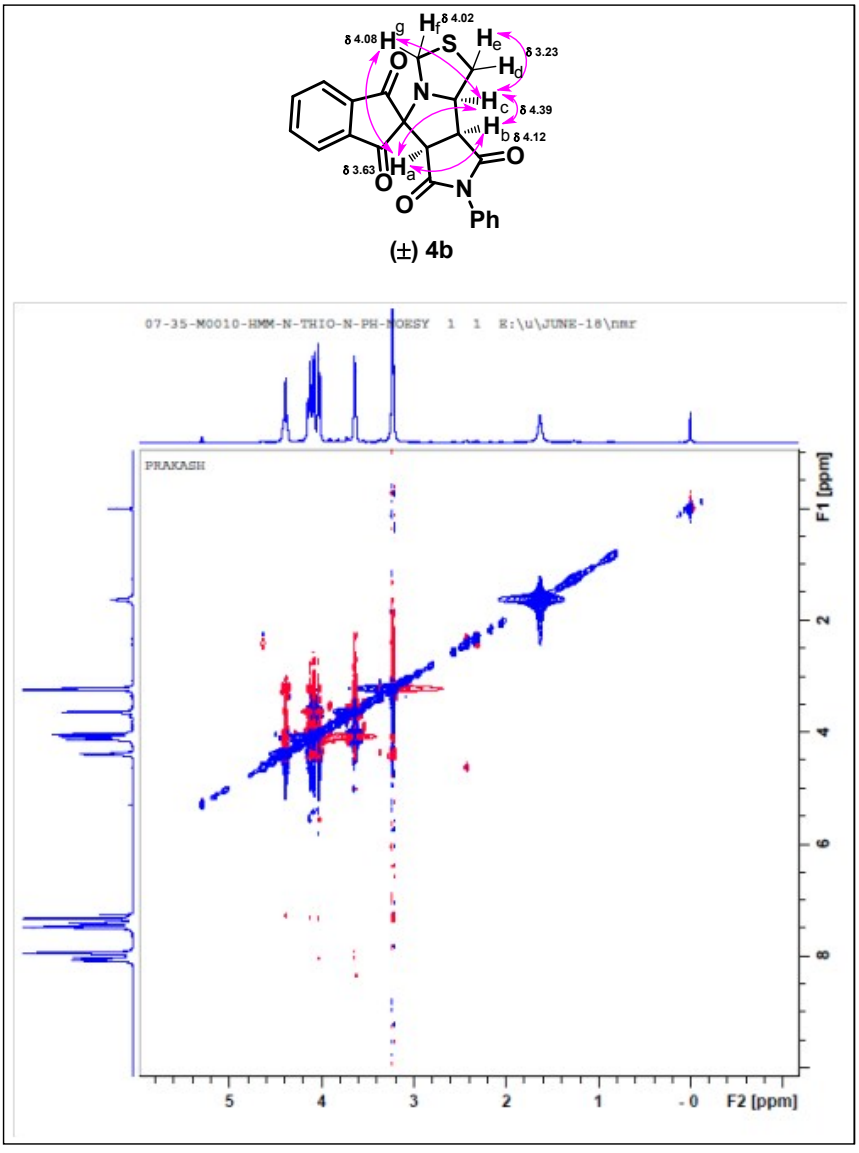


Figure S1. ORTEP Diagram of compound **4e**

NOESY studies of compound (4b):

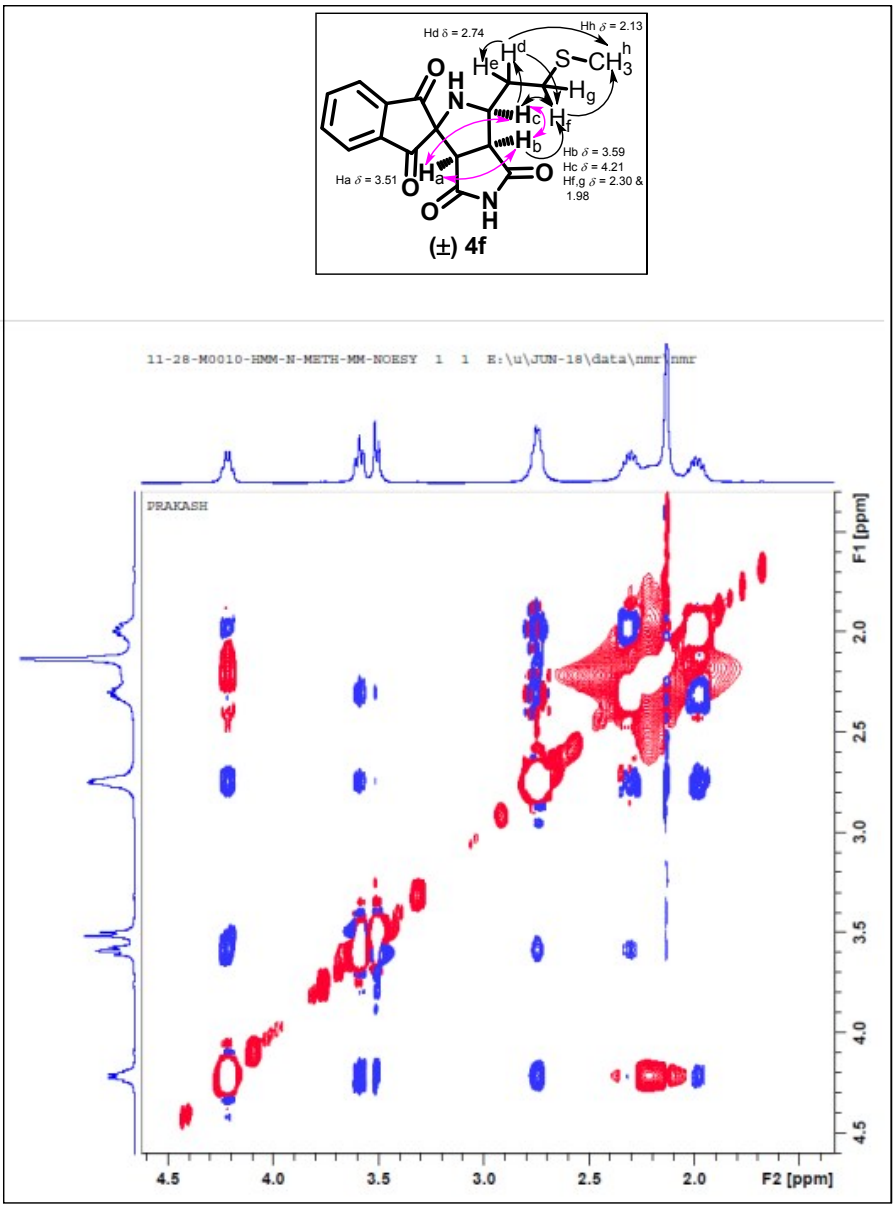
Further, the relative stereochemistry of structure **4b** was confirmed by NOESY studies. From the study**,** it is evident there exist strong NOE cross-peaks intensities for protons Ha-Hb at δ 3.63/4.12, Ha-Hc at δ 3.63/4.39 and Hb-Hc at δ 4.12/4.39 which supports Ha, Hb and Hc protons are in a cis relationship. Further, no NOESY correlation between Hc and Hd protons has been identified, whereas there exist correlation between protons Hc and He at δ = 4.39 and 3.23 respectively (Figure S2)



FigureS2: NOE correlation and 500 MHz NOESY Spectrum of compound **4b** in $CDCl_3$.

NOESY studies of compound (4f):

The stereochemistry of the cycloadducts **(4f)** was deduced on the basis of the NOESY spectrum, experiment demonstrates that strong NOE intensities cross-peaks Ha-Hc δ 3.51/4.21, Ha-Hb δ 3.51/3.59 and Hb-Hc δ 3.59/4.21 revealing that these protons are in a cis relationship. Further, from NOESY experiment it indicated that there is also special interaction due to closely related protons Hc-Hd, Hc-Hf, Hf-Hh protons (Figure S3).



FigureS3. NOE correlation and 400 MHz NOESY Spectrum of compound **4f** in $CDCl_3$.

Spectroscopic Data of Compounds Obtained in this Study:

6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine] 1,1',3,3'(2'H,3a'H,8b'H)-tetraone (4a): White solid; Mp 163-165°C; IR (KBr): ν_{max} 2969, 1711, 1603, 1340, 1273, 1191, 1090, 755, 631 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 – 7.99 (m, 2H), 7.93 – 7.88 (m, 2H), 4.29 (td, *J* = 7.4, 2.7 Hz, 1H), 4.07 (d, *J* = 9.9 Hz, 1H), 3.75 – 3.62 (m, 1H), 3.50 – 3.40 (m, 1H), 2.86 – 2.80 (m, 1H), 2.68 (dt, *J* = 12.7, 4.9 Hz, 1H), 2.28 – 2.23 (m, 1H), 2.03 – 1.97 (m, 1H), 1.85 – 1.77 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 204.6, 203.2, 182.4, 181.2, 146.5, 144.6, 141.5, 141.4, 128.7, 128.1, 77.4, 72.5, 60.6, 53.2, 51.4, 31.0, 29.9. MS (ESI) m/z = 311 $[M+H]^+$; HRMS (ESI) Calcd. $C_{17}H_{15}O_4N_2$ $[M+H]^+$: 311.10400, found: 311.10263.

1',8b'-dihydrospiro[indene-2,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-1,3,6',8'(3'H,5a'H,7'H,8a'H)-tetraone (4b): White solid; Mp 187-189°C; IR (KBr): ν_{max} 3226, 2937, 1716, 1596, 1346, 1265, 1196, 1076, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.03 (m, 2H), 7.98 – 7.95 (m, 2H), 4.30 (dd, *J* = 10.5, 6.2 Hz, 1H), 4.01 (t, *J* = 9.6 Hz, 1H), 3.89 (d, *J* = 9.8 Hz, 1H), 3.69 (dd, *J* = 9.3, 3.0 Hz, 1H), 3.59 (d, *J* = 9.2 Hz, 1H), 3.19 (d, *J* = 3.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 204.0, 181.0, 180.7, 144.9, 142.0, 141.8, 128.87, 128.2, 77.5, 76.3, 75.5, 60.1, 57.9, 55.2, 52.1, 38.5. MS (ESI) m/z = 329 $[M+H]^+$; HRMS (ESI) Calcd. $C_{16}H_{13}O_4N_2S$ $[M+H]^+$: 329.05901, found: 329.05905.

3'-isobutyl-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4c): Brown solid; Mp 180-182°C; IR (KBr): ν_{max} 2083, 1785, 1702, 1652, 1423, 1342, 1024,964, 898, 742, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.07 – 8.01 (m, 2H), 7.95 – 7.91 (m, 2H), 4.12-3.89 (m, 1H), 3.56 – 3.47 (m, 2H), 1.90 – 1.82 (m, 2H), 1.58 – 1.51 (m, 1H), 0.98 (d, *J* = 5.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 197.3, 175.3, 174.9, 141.4, 139.8, 136.9, 136.7, 124.3, 124.2, 72.1, 61.1, 54.7, 52.1, 39.4, 26.3, 23.2, 22.0. MS (ESI) m/z = 327 $[M+H]^+$; HRMS (ESI) Calcd. $C_{18}H_{18}O_4N_2$ $[M+H]^+$: 327.13553, found: 327.13593.

3'-isopropyl-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4d): Yellow solid; Mp 236-238°C; IR (KBr): ν_{max} 2087, 1786, 1702, 1653, 1536, 1426, 1320, 1105, 1046, 986, 856, 742, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.06 – 8.03 (m, 2H), 7.95 – 7.90 (m, 2H), 3.71 – 3.62 (m, 2H), 3.50 (d, *J* = 7.3 Hz, 1H), 2.13 –

2.05 (m, 1H), 1.25 (d, *J* = 6.4 Hz, 3H), 1.05 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 200.3, 197.7, 176.6, 176.1, 141.2, 139.3, 136.6, 136.1, 124.0, 123.3, 71.3, 69.3, 54.3, 50.4, 29.3, 21.3, 21.2. MS (ESI) m/z = 313 $[M+H]^+$; HRMS (ESI) Calcd. $C_{17}H_{17}O_4N_2$ $[M+H]^+$: 313.11887, found: 313.11828.

3'-benzyl-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4e): Pale yellow solid; Mp 210-212°C; IR (KBr): ν_{max} 2956, 1758, 1642, 1523, 1489, 1203, 1047, 964, 845, 756, 635 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 – 8.02 (m, 1H), 7.98 (dt, *J* = 5.2, 3.4 Hz, 1H), 7.93 – 7.89 (m, 2H), 7.35 (d, *J* = 7.2 Hz, 2H), 7.29 (dd, *J* = 10.4, 4.8 Hz, 2H), 7.20 (t, *J* = 7.3 Hz, 1H), 4.42 – 4.39 (m, 1H), 3.61 (t, *J* = 7.7 Hz, 1H), 3.50 (d, *J* = 7.9 Hz, 1H), 3.46 (dd, *J* = 14.4, 4.9 Hz, 1H), 2.88 (dd, *J* = 14.4, 9.5 Hz, 1H), 2.37 (bs, NH). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 205.5, 202.2, 181.7, 180.8, 146.2, 144.3, 144.1, 141.2, 133.7, 133.1, 131.0, 128.6, 128.3, 76.1, 67.1, 58.9, 55.3, 41.8. MS (ESI) m/z = 361 $[M+H]^+$; HRMS (ESI) Calcd. $C_{21}H_{16}O_4N_2$ $[M+H]^+$: 361.12029, found: 361.11828.

3'-(2-(methylthio)ethyl)-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4f): White solid; Mp 170-172°C; IR (KBr): ν_{max} 2961, 1714, 1595, 1498, 1458, 1384, 1265, 1191, 1110, 748, 696 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.08 – 8.00 (m, 2H), 7.96 – 7.91 (m, 2H), 4.22 (dd, *J* = 14.0, 7.3 Hz, 1H), 3.59 (t, *J* = 7.7 Hz, 1H), 3.51 (d, *J* = 7.8 Hz, 1H), 2.78 – 2.71 (m, 2H), 2.30 (dt, *J* = 14.3, 7.0 Hz, 1H), 2.13 (s, 3H), 2.03 – 1.95 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 197.4, 175.4, 175.0, 141.4, 139.7, 137.0, 136.8, 124.4, 124.3, 71.8, 61.6, 54.6, 51.5, 31.9, 30.2, 15.5. MS (ESI) m/z = 344 $[M+H]^+$; HRMS (ESI) Calcd. $C_{17}H_{16}O_4N_2S$ $[M+H]^+$: 345.09194, found: 345.09035.

7-benzyl-7-methyl-2,3-dihydro-1H-spiro[cyclopenta[a]pyrrolizine-5,2'-indene]-1',3',6,8(5aH,7H,8aH,8bH)-tetraone (4g): Yellow solid; Mp 148-150°C; IR (KBr): ν_{max} 2975, 1758, 1702, 1526, 1278, 1042, 975, 875, 752, 687 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.99 (m, 1H), 7.95 – 7.91 (m, 1H), 7.88 – 7.83 (m, 2H), 7.31 – 7.25 (m, 3H), 7.01 (dd, *J* = 6.3, 2.7 Hz, 2H), 4.04 (dd, *J* = 9.4, 4.1 Hz, 1H), 3.47 (d, *J* = 12.4 Hz, 1H), 2.89 (s, 2H), 2.67 – 2.48 (m, 3H), 2.22 – 2.12 (m, 1H), 1.85 – 1.64 (m, 3H), 1.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 217.3, 216.7, 196.9, 195.4, 142.0, 141.3, 136.4, 136.1, 135.0, 131.2, 129.5, 128.7, 127.7, 124.5, 124.0, 78.2, 69.2, 64.1, 61.1, 56.6, 48.9, 45.7, 30.5, 24.7, 18.5. MS (ESI) m/z = 414 $[M+H]^+$; HRMS (ESI) Calcd. $C_{26}H_{23}O_4N$ $[M+H]^+$: 414.17024, found: 414.16998.

7-benzyl-7-methyl-1,8b-dihydrospiro[cyclopenta[3,4]pyrrolo[1,2-c]thiazole-5,2'-indene]-1',3',6,8(3H,5aH,7H,8aH)-tetraone (4h): Yellow solid; Mp 138-140°C; IR (KBr): ν_{max} 2978, 1758, 1642, 1542, 1478, 1248, 1023, 964, 875, 757, 645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.97 (m, 2H), 7.95 – 7.90 (m, 2H), 7.25 (dd, *J* = 6.0, 3.5 Hz, 3H), 6.95 (dd, *J* = 6.6, 2.9 Hz, 2H), 4.20 – 4.16 (m, 1H), 3.89 (d, *J* = 9.5 Hz, 1H), 3.63 (d, *J* = 9.5 Hz, 1H), 3.20 – 3.17 (m, 1H), 3.14 (d, *J* = 11.3 Hz, 1H), 2.98 – 2.88 (m, 3H), 2.58 (dd, *J* = 11.4, 3.1 Hz, 1H), 1.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.2, 215.5, 198.2, 141.3, 140.7, 136.9, 136.7, 134.9, 129.3, 128.9, 127.7, 124.1, 124.0, 77.9, 73.0, 61.4, 58.3, 56.5, 52.2, 45.2, 37.3, 18.7. MS (ESI) m/z = 432 $[M+H]^+$; HRMS (ESI) Calcd. $C_{25}H_{21}O_4NS$ $[M+H]^+$: 432.12676, found: 432.12641.

2'-phenyl-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (4i): White solid; Mp 166-168°C; IR (KBr): ν_{max} 2961, 1710, 1594, 1498, 1457, 1384, 1264, 1190, 1109, 748, 696 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.00 (m, 2H), 7.94 – 7.88 (m, 2H), 7.50 (t, *J* = 7.6 Hz, 2H), 7.43 – 7.37 (m, 3H), 4.35 (dd, *J* = 15.1, 7.3 Hz, 1H), 3.86 (d, *J* = 8.7 Hz, 1H), 3.75 (t, *J* = 8.5 Hz, 1H), 2.81 – 2.71 (m, 2H), 2.41 – 2.34 (m, 1H), 2.09 – 1.96 (m, 2H), 1.91 – 1.83 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.4, 198.5, 175.3, 174.7, 141.9, 140.3, 136.8, 136.6, 131.8, 129.2, 128.8, 126.5, 124.2, 123.7, 73.5, 68.5, 54.1, 47.8, 47.4, 26.0, 24.9. MS (ESI) m/z = 387 $[M+H]^+$; HRMS (ESI) Calcd. $C_{23}H_{19}O_4N_2$ $[M+H]^+$: 387.13607, found: 387.13393.

7'-phenyl-1',8b'-dihydrospiro[indene-2,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-1,3,6',8'(3'H,5a'H,7'H,8a'H)-tetraone (4j): Yellow solid; Mp 196-198°C; IR (KBr): ν_{max} 3021, 2944, 1712, 1594, 1498, 1387, 1260, 1198, 1041, 899, 751, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.02 (m, 2H), 7.97 – 7.92 (m, 2H), 7.51 (t, *J* = 1.4 Hz, 2H), 7.42 (dt, *J* = 4.6, 1.8 Hz, 1H), 7.33 (d, *J* = 2.1 Hz, 2H), 4.39 (q, *J* = 8.4 Hz, 1H), 4.12 (ddd, *J* = 17.7, 11.4, 7.3 Hz, 2H), 4.02 (d, *J* = 5.0 Hz, 1H), 3.63 (d, *J* = 9.5 Hz, 1H), 3.23 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 199.7, 198.7, 174.1, 173.9, 142.1, 140.6, 137.2, 137.1, 131.4, 129.3, 129.1, 126.7, 124.3, 123.9, 73.3, 71.2, 53.6, 51.1, 46.5, 34.4. MS (ESI) m/z = 405 $[M+H]^+$; HRMS (ESI) Calcd. $C_{22}H_{17}O_4N_2S$ $[M+H]^+$: 405.09020, found: 405.09035.

6-isopropyl-6,6a-dihydrospiro[furo[3,4-c]pyrrole-4,2'-indene]-1,1',3,3'(3aH,5H)-tetraone (4k): White solid; Mp 212-214°C; IR (KBr): ν_{max} 3264, 3087, 29666, 1716, 1597, 1467, 1341, 1260, 1192, 1063, 924, 753 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ 8.07 – 7.94 (m, 4H),

3.93 (dd, *J* = 8.1, 6.9 Hz, 1H), 3.76 (m, 2H), 2.11 – 1.97 (m, 1H), 1.21 (d, *J* = 6.4 Hz, 3H), 1.03 (d, *J* = 6.5 Hz, 3H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 199.7, 196.6, 169.7, 140.6, 139.3, 136.4, 136.1, 123.5, 123.2, 70.5, 68.2, 51.8, 49.7, 29.0, 20.7, 20.3. MS (ESI) m/z = 314 $[M+H]^+$

3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indeno[1,2-b]quinoxaline-11,4'-pyrrolo[3,4-a]pyrrolizine]-1',3'(2'H)-dione (4l): Yellow solid; Mp 252-254°C; IR (KBr): ν_{max} 3071, 2965, 1772, 1714, 1581, 1466, 1339, 1190, 1109, 762 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ 11.27 (s, 1H), 8.17 – 8.06 (m, 3H), 7.80 – 7.69 (m, 2H), 7.61 – 7.48 (m, 3H), 4.61 (dd, *J* = 13.5, 7.3 Hz, 1H), 3.80 (d, *J* = 7.7 Hz, 1H), 3.68 (t, *J* = 7.5 Hz, 1H), 2.59-2.48 (m, 1H), 2.39-2.12 (m, 1H), 2.06 – 1.90 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 182.9, 181.9, 167.9, 157.4, 149.1, 147.0, 145.9, 142.1, 135.8, 134.6, 134.5, 134.4, 133.8, 133.7, 132.1, 126.5, 73.4, 70.7, 63.7, 51.2, 46.8, 31.1, 27.9. MS (ESI) m/z = 383 $[M+H]^+$; HRMS (ESI) Calcd. $C_{23}H_{19}O_2N_4$ $[M+H]^+$: 383.15038, found: 383.15025.

1',7',8a',8b'-tetrahydrospiro[indeno[1,2-b]quinoxaline-11,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-6',8'(3'H,5a'H)-dione (4m): Yellow solid; Mp 241-243°C; IR (KBr): ν_{max} 3024, 2952, 1775, 1720, 1579, 1535, 1341, 1208, 1076, 899, 745, 670 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ 11.54 (s, 1H), 8.19 – 8.08 (m, 3H), 7.82 – 7.74 (m, 2H), 7.62 – 7.50 (m, 3H), 4.93 (dd, *J* = 8.7, 4.1 Hz, 1H), 3.88 (d, *J* = 7.9 Hz, 1H), 3.77 (t, *J* = 7.7 Hz, 1H), 3.16 d, *J* = 5.0 Hz, 1H), 2.97 – 2.92 (m, 1H), 2.62 – 2.56 (m, 2H). ^{13}C NMR (75 MHz, DMSO-d_6) δ 176.6, 175.7, 161.5, 152.0, 142.8, 142.0, 140.5, 136.8, 130.9, 129.8, 129.6, 129.2, 128.8, 128.6, 126.6, 121.4, 67.8, 67.2, 58.8, 44.3, 43.1, 28.0. MS (ESI) m/z = 401 $[M+H]^+$

3-methyl-3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indeno[1,2-b]quinoxaline-11,4'-pyrrolo[3,4-a]pyrrolizine]-1',3'(2'H)-dione (4n): White solid; Mp 266-268°C; IR (KBr): ν_{max} 3207, 3082, 1775, 1719, 1580, 1337, 1207, 1105, 829, 756, 667 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 – 8.15 (m, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 17.9 Hz, 1H), 7.59 – 7.45 (m, 4H), 4.65 (dd, *J* = 14.5, 7.3 Hz, 1H), 3.88 (d, *J* = 7.7 Hz, 1H), 3.75 (t, *J* = 3.7 Hz, 1H), 2.60 (s, 3H), 2.40 (dd, *J* = 8.9, 5.4 Hz, 1H), 2.03 – 1.94 (m, 3H), 1.30 – 1.22 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 176.3, 170.7, 161.9, 152.6, 143.7, 140.4, 137.7, 131.1, 130.1, 128.2, 126.9, 122.1, 68.8, 66.0, 58.9, 46.5, 42.0, 31.6, 26.4, 23.2, 22.6, 21.8, 14.1. MS (ESI) m/z = 397 $[M+H]^+$; HRMS (ESI) Calcd. $C_{24}H_{20}O_2N_4$ $[M+H]^+$: 397.16716, found: 397.16590.

3-methyl-1',7',8a',8b'-tetrahydrospiro[indeno[1,2-b]quinoxaline-11,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-6',8'(3'H,5a'H)-dione (4o): Yellow solid; Mp 230-232°C; IR (KBr): ν_{max} 2956, 1786, 1703, 1648, 1523, 1456, 1123, 1078, 975, 826, 687 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ 11.53 (s, 1H), 8.12 (dd, *J* = 6.5, 3.3 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.90 (s, 1H), 7.62 – 7.49 (m, 4H), 4.91 (dd, *J* = 5.0, 6.6 Hz, 1H), 3.86 (d, *J* = 7.9 Hz, 1H), 3.77 (t, *J* = 5.7 Hz, 1H), 3.14 (dd, *J* = 11.2, 6.1 Hz, 2H), 2.94 (d, *J* = 5.3 Hz, 1H), 2.62 (s, 3H), 2.60 – 2.58 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.8, 181.1, 165.7, 157.2, 148.1, 147.3, 145.42, 144.1, 142.0, 137.0, 136.1, 135.9, 135.0, 131.8, 126.6, 72.9, 72.8, 64.0, 49.8, 48.4, 33.3, 26.4. MS (ESI) m/z = 415 $[M+H]^+$; HRMS (ESI) Calcd. $C_{23}H_{18}O_2N_4S$ $[M+H]^+$: 415.12382, found: 415.12232.

3-nitro-3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indeno[1,2-b]quinoxaline-11,4'-pyrrolo[3,4-a]pyrrolizine]-1',3'(2'H)-dione (4p): Yellow solid; Mp 243-245°C; IR (KBr): ν_{max} 3021, 2973, 1772, 1716, 1587, 1503, 1343, 1214, 1075, 744, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.87 (d, *J* = 2.3 Hz, 1H), 8.49 (dd, *J* = 9.1, 2.4 Hz, 1H), 8.27 (d, *J* = 6.7 Hz, 1H), 8.22 (d, *J* = 9.1 Hz, 1H), 7.79 (d, *J* = 7.0 Hz, 1H), 7.68 (dt, *J* = 12.7, 6.3 Hz, 2H), 4.90 (dd, *J* = 8.5, 5.6 Hz, 1H), 4.28 (d, *J* = 9.9 Hz, 1H), 3.66 – 3.61 (m, 1H), 2.98 – 2.91 (m, 1H), 2.70 (t, *J* = 7.1 Hz, 1H), 2.41 (dd, *J* = 12.2, 10.2 Hz, 1H), 2.11-2.09 (m, 1H), 1.87 – 1.83 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.1, 176.3, 164.2, 155.7, 146.5, 146.2, 145.3, 139.2, 136.9, 132.9, 130.3, 126.3, 125.4, 123.2, 122.9, 72.5, 66.3, 55.4, 55.1, 49.1, 30.1, 25.3. MS (ESI) m/z = 428 $[M+H]^+$; HRMS (ESI) Calcd. $C_{23}H_{18}O_4N_5$ $[M+H]^+$: 428.13374, found: 428.13533.

7-benzyl-7-methyl-2,3,8a,8b-tetrahydro-1H-spiro[cyclopenta[a]pyrrolizine-5,11'-indeno[1,2-b]quinoxaline]-6,8(5aH,7H)-dione (4q): Brown solid; Mp 207-209°C; IR (KBr): ν_{max} 2971, 2937, 1757, 1716, 1581, 1059, 1369, 1337, 1231, 1082, 1040, 760, 702 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 6.3 Hz, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.87 (d, *J* = 8.2 Hz, 1H), 7.68 (dd, *J* = 8.3, 7.0 Hz, 1H), 7.65 – 7.56 (m, 4H), 7.29 (dd, *J* = 6.6, 3.6 Hz, 3H), 7.05 – 7.01 (m, 2H), 4.71 – 4.64 (m, 1H), 3.68 (d, *J* = 12.3 Hz, 1H), 2.86 – 2.82 (m, 3H), 2.74 (dd, *J* = 11.2, 8.8 Hz, 1H), 2.66 (t, *J* = 7.7 Hz, 1H), 2.39 – 2.29 (m, 1H), 1.96 – 1.86 (m, 2H), 1.78 – 1.67 (m, 1H), 1.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 217.2, 216.2, 162.2, 152.9, 144.7, 142.4, 140.7, 138.2, 135.5, 131.4, 130.2, 129.7, 129.6, 129.2, 129.1, 129.1, 128.6, 127.6, 125.9,

122.9, 67.6, 64.3, 61.7, 59.2, 50.5, 46.1, 31.0, 25.4, 24.9, 18.3. MS (ESI) m/z = 486 $[M+H]^+$; HRMS (ESI) Calcd. $C_{32}H_{28}O_2N_3$ $[M+H]^+$: 486.21503, found: 486.21760.

2'-(2-(biphenyl-4-yl)-2-oxoethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (6a): White solid; Mp 168-170°C; IR (KBr): ν_{max} 2935, 1700, 1603, 1415, 1340, 1279, 1236, 1181, 994, 916, 844, 761, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.99 (m, 3H), 7.92 – 7.86 (m, 2H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.62 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.3 Hz, 3H), 7.42 (d, *J* = 7.2 Hz, 1H), 5.02 (d, *J* = 17.3 Hz, 1H), 4.89 (d, *J* = 17.3 Hz, 1H), 4.29 (td, *J* = 7.1, 2.9 Hz, 1H), 4.21 (d, *J* = 9.8 Hz, 1H), 3.55 (dd, *J* = 9.8, 6.7 Hz, 1H), 2.92 (dd, *J* = 16.8, 9.9 Hz, 1H), 2.69 (t, *J* = 8.3 Hz, 1H), 2.27 (dd, *J* = 17.4, 9.2 Hz, 1H), 2.11 – 1.98 (m, 2H), 1.88 – 1.75 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.8, 196.1, 189.8, 176.5, 174.9, 146.7, 141.5, 141.2, 139.6, 136.6, 136.2, 133.1, 129.0, 128.7, 128.4, 127.4, 127.3, 124.4, 124.0, 74.4, 68.4, 53.8, 50.7, 48.6, 44.9, 29.9, 29.4, 24.8. MS (ESI) m/z = 505 $[M+H]^+$; HRMS (ESI) Calcd. $C_{31}H_{25}O_5N_2$ $[M+H]^+$: 505.17510, found: 505.17580.

2'-(2-(4-chlorophenyl)-2-oxoethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (6b): White solid; Mp 152-154°C; IR (KBr): ν_{max} 2956, 1719, 1524, 1436, 1421, 1341, 1226, 1180, 914, 823, 721 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.99 (m, 2H), 7.93 – 7.89 (m, 4H), 7.50 – 7.46 (m, 2H), 4.91 (dd, *J* = 17.3, 3.1 Hz, 2H), 4.33 (dd, *J* = 15.0, 7.1 Hz, 1H), 3.82 (d, *J* = 8.6 Hz, 1H), 3.75 (t, *J* = 8.4 Hz, 1H), 2.97 – 2.91 (m, 1H), 2.70 (td, *J* = 8.4, 4.8 Hz, 1H), 2.30 – 2.25 (m, 1H), 2.06 – 2.00 (m, 2H), 1.89 – 1.83 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 197.4, 189.0, 175.7, 174.7, 141.9, 140.6, 136.7, 136.5, 135.1, 132.7, 129.5, 129.2, 124.2, 123.7, 72.6, 67.8, 54.0, 50.8, 48.1, 47.1, 44.9, 25.9, 24.7. MS (ESI) m/z = 463 $[M+H]^+$; HRMS (ESI) Calcd. $C_{25}H_{20}O_5N_2Cl$ $[M+H]^+$: 463.10672, found: 463.10553.

2'-(2-(4-bromophenyl)-2-oxoethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (6c): White solid; Mp 148-150°C; IR (KBr): ν_{max} 2985, 1789, 1721, 1656, 1475, 1325, 1178, 1085, 996, 789, 645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.00 (m, 2H), 7.90 (dd, *J* = 3.9, 2.1 Hz, 2H), 7.84 – 7.81 (m, 2H), 7.64 (dd, *J* = 8.5, 5.3 Hz, 2H), 4.92 (dd, *J* = 15.6, 12.5 Hz, 2H), 4.37 – 4.28 (m, 1H), 3.82 (d, *J* = 8.7 Hz, 1H), 3.76 (t, *J* = 8.4 Hz, 1H), 2.98 – 2.90 (m, 1H), 2.70 (td, *J* = 9.5, 3.6 Hz, 1H), 2.31 – 2.23 (m, 2H), 2.06 – 1.99 (m, 1H), 1.90 – 1.83 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ

199.0, 197.3, 189.3, 175.6, 174.8, 170.4, 141.9, 140.0, 136.7, 136.5, 135.1, 133.1, 132.4, 132.2, 131.7, 131.5, 129.6, 129.3, 124.2, 123.7, 72.6, 67.9, 54.0, 48.1, 47.2, 44.9, 25.9, 24.7. MS (ESI) m/z = 507 $[M+H]^+$; HRMS (ESI) Calcd. $C_{25}H_{19}O_5N_2Br$ $[M+H]^+$: 507.05766, found: 507.05501.

3-chloro-6',7',8',8a'-tetrahydro-1'H,12H-spiro[indolo[2,1-b]quinazoline-6,4'-pyrrolo[3,4-a]pyrrolizine]-1',3',12(2'H,3a'H,8b'H)-trione (9a): Yellow solid; Mp 251-253°C; IR (KBr): ν_{max} 3086, 2958, 1773, 1716, 1675, 1606, 1477, 1328, 1194, 833, 769 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$+DMSO-d_6) δ 8.52 (d, *J* = 8.6 Hz, 1H), 8.36 (d, *J* = 7.2 Hz, 1H), 7.80 (dd, *J* = 13.3, 10.1, Hz, 2H), 7.58 (d, *J* = 1.3 Hz, 1H), 7.46 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.28 (d, *J* = 2.0 Hz, 1H), 4.59 (q, *J* = 7.1 Hz, 1H), 3.94 (d, *J* = 7.7 Hz, 1H), 3.60 (t, *J* = 7.5 Hz, 1H), 2.62 – 2.57 (m, 1H), 2.43 (t, *J* = 6.9 Hz, 1H), 2.19 – 2.06 (m, 2H), 2.05 – 1.93 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 182.3, 180.9, 164.1, 163.7, 151.4, 143.2, 139.4, 136.0, 135.0, 134.5, 132.9, 132.3, 131.4, 131.3, 126.2, 122.4, 72.9, 69.5, 65.5, 50.3, 46.4, 31.2, 27.7. MS (ESI) m/z = 433 $[M+H]^+$; HRMS (ESI) Calcd. $C_{23}H_{17}O_3N_4$ $[M+H]^+$: 433.10819, found: 433.10619.

3-fluoro-6',7',8',8a'-tetrahydro-1'H,12H-spiro[indolo[2,1-b]quinazoline-6,4'-pyrrolo[3,4-a]pyrrolizine]-1',3',12(2'H,3a'H,8b'H)-trione (9b): Brown solid; Mp 257-259°C; IR (KBr): ν_{max} 3199, 2989, 1789, 1721, 1657, 1606, 1478, 1389, 1256, 1085, 833, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.55 – 8.50 (m, 1H), 8.32 (d, *J* = 8.0 Hz, 1H), 7.88 – 7.79 (m, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 2.5 Hz, 1H), 7.01 (d, *J* = 3.5 Hz, 1H), 4.58 (q, *J* = 7.3 Hz, 1H), 3.96 (d, *J* = 7.6 Hz, 1H), 3.59 (td, *J* = 7.5, 2.2 Hz, 1H), 2.57 (d, *J* = 1.8 Hz, 2H), 2.43 – 2.37 (m, 1H), 2.15 – 2.05 (m, 1H), 1.93 (dd, *J* = 19.9, 3.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6) δ 182.1, 180.3, 166.8, 164.1, 163.8, 151.3, 140.5, 139.3, 132.8, 132.2, 131.3, 126.3, 122.6, 122.5, 121.6, 121.5, 118.8, 118.5, 73.0, 69.5, 65.6, 50.4, 46.4, 31.2, 27.8. MS (ESI) m/z = 417 $[M+H]^+$; HRMS (ESI) Calcd. $C_{23}H_{18}O_3N_4F$ $[M+H]^+$: 417.13439, found: 417.13575.

7-benzyl-3'-fluoro-7-methyl-2,3,8a,8b-tetrahydro-1H,12'H-spiro[cyclopenta[a]pyrrolizine-5,6'-indolo[2,1-b]quinazoline]-6,8,12'(5aH,7H)-trione (9c): Brown solid; Mp 220-222°C; IR (KBr): ν_{max} 2906, 1784, 1723, 1568, 1324, 1275, 1178, 1040, 986, 976, 888, 756, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (dd, *J* = 8.9, 4.8 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.70 (t, *J* = 1.2 Hz, 1H), 7.52 – 7.45 (m, 2H), 7.33 – 7.30 (m, 3H), 7.22 (dd, *J* = 8.8, 2.6 Hz, 1H), 7.16 (dd, *J* =

8.0, 2.5 Hz, 1H), 7.05 – 7.01 (m, 2H), 4.69 (dd, *J* = 9.4, 5.9 Hz, 1H), 3.54 (d, *J* = 12.4 Hz, 1H), 2.88 (s, 2H), 2.78 (dd, *J* = 12.4, 5.9 Hz, 1H), 2.67 – 2.58 (m, 2H), 2.38 – 2.34 (m, 1H), 1.93 – 1.78 (m, 3H), 1.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 216.1, 215.9, 162.0, 159.7, 159.1, 146.3, 136.6, 135.0, 134.5, 130.6, 129.7, 128.7, 127.8, 127.4, 126.9, 121.8, 118.8, 118.8, 117.5, 117.2, 113.1, 112.8, 76.1, 66.9, 64.7, 60.8, 60.5, 50.0, 46.0, 31.0, 25.4, 18.0. MS (ESI) m/z = 520 $[M+H]^+$; HRMS (ESI) Calcd. $C_{32}H_{27}O_3N_3F$ $[M+H]^+$: 520.20145, found: 520.20310.

1'-(phenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8a): Yellow solid; Mp 131-133°C; IR (KBr): ν_{max} 2985, 1747, 1712, 1593, 1462, 1311, 1275, 1214, 1044, 743, 666 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.09 (m, 1H), 8.06 (ddd, *J* = 5.6, 2.7, 1.7 Hz, 1H), 7.92 – 7.89 (m, 2H), 7.47 (tdd, *J* = 8.4, 7.0, 1.5 Hz, 4H), 7.39 (dt, *J* = 4.1, 1.8 Hz, 1H), 6.04 (dd, *J* = 6.3, 4.1 Hz, 1H), 3.53 (td, *J* = 9.7, 6.1 Hz, 1H), 3.02 (dd, *J* = 6.6, 3.4 Hz, 1H), 2.17 – 2.01 (m, 2H), 1.97 – 1.83 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.5, 193.9, 193.1, 143.5, 142.3, 137.3, 136.3, 131.7, 129.6, 128.4, 127.3, 126.0, 124.4, 124.3, 119.9, 90.1, 49.3, 30.0, 24.6. MS (ESI) m/z = 349 $[M+H]^+$

1'-(3-chlorophenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8b): Yellow solid; Mp 121-123°C; IR (KBr): ν_{max} 3020, 1747, 1714, 1591, 1448, 1243, 1215, 1045, 752, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.12 (m, 1H), 8.07 (dd, *J* = 4.0, 2.5 Hz, 1H), 7.94 – 7.90 (m, 2H), 7.49 (t, *J* = 1.9 Hz, 1H), 7.45 – 7.41 (m, 1H), 7.38 – 7.35 (m, 2H), 6.04 (dd, *J* = 6.4, 3.7 Hz, 1H), 3.53 (td, *J* = 9.7, 6.3 Hz, 1H), 3.05 – 2.99 (m, 1H), 2.21 – 2.13 (m, 1H), 2.07 – 2.03 (m, 1H), 1.93 – 1.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.2, 194.5, 193.2, 143.5, 142.2, 138.4, 136.4, 135.1, 131.7, 130.5, 128.5, 127.5, 126.1, 124.4, 124.1, 119.9, 90.0, 49.2, 29.9, 24.5. MS (ESI) m/z = 383 $[M+H]^+$

1'-(4-chlorophenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8c): Yellow solid; Mp 124-126°C; IR (KBr): ν_{max} 3024, 1749, 1725, 1652, 1489, 1285, 1089, 756, 669 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.05 (m, 2H), 7.93 – 7.90 (m, 2H), 7.48 – 7.39 (m, 4H), 6.02 (dd, *J* = 6.4, 3.8 Hz, 1H), 3.51 (td, *J* = 9.6, 6.3 Hz, 1H), 3.04 – 2.98 (m, 1H), 2.19 – 2.13 (m, 1H), 2.06 – 2.05 (m, 1H), 1.93 – 1.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.3, 194.4, 193.3, 183.7, 143.5, 142.3, 136.4, 134.1, 131.7, 129.8, 129.8, 127.2, 126.9, 124.4, 124.3, 119.9, 89.9, 49.2, 30.0, 24.5. MS (ESI) m/z = 383 $[M+H]^+$

1'-(4-fluorophenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8d): Yellow solid; Mp 118-120°C; IR (KBr): ν_{max} 3020, 1749, 1712, 1509, 1407, 1276, 1214, 1046, 747, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.05 (m, 2H), 7.94 – 7.89 (m, 2H), 7.43 (dd, *J* = 4.4, 2.4 Hz, 2H), 7.21 (t, *J* = 2.7 Hz, 2H), 5.98 (dd, *J* = 6.2, 4.0 Hz, 1H), 3.52 (td, *J* = 9.7, 6.3 Hz, 1H), 3.05 – 3.00 (m, 1H), 2.17 – 2.03 (m, 2H), 1.94 – 1.83 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.4, 194.5, 193.3, 143.5, 142.3, 136.4, 133.2, 131.7, 128.0, 127.9, 127.4, 124.4, 124.3, 120.0, 116.8, 116.6, 90.1, 49.2, 30.0, 24.5. MS (ESI) m/z = 367 $[M+H]^+$

1'-(4-methoxyphenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8e): Yellow solid; Mp 125-127°C; IR (KBr): ν_{max} 3020, 2985, 1714, 1705, 1511, 1479, 1345, 1214, 1046, 931, 742, 667 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.13 – 8.05 (m, 2H), 7.94 – 7.88 (m, 2H), 7.35 (s, *J* = 2.1 Hz, 1H), 7.01 (d, *J* = 2.1 Hz, 1H), 5.94 (dd, *J* = 6.2, 4.2 Hz, 1H), 3.83 (s, 3H), 3.51 (dt, *J* = 9.6, 4.8 Hz, 1H), 3.03 – 2.98 (m, 1H), 2.15 – 2.02 (m, 2H), 1.99 – 1.83 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6, 193.9, 193.5, 159.3, 143.5, 142.3, 136.3, 136.3, 129.8, 127.3, 124.4, 124.3, 114.9, 114.8, 90.2, 84.9, 55.5, 55.4, 49.2, 30.0, 24.6. MS (ESI) m/z = 379 $[M+H]^+$

1'-(4-(trifluoromethyl)phenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8f): Pale yellow solid; Mp 132-134°C; IR (KBr): ν_{max} 3156, 2989, 1789, 1721, 1653, 1528, 1384, 1287, 1089, 986, 758, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.13 (d, *J* = 5.5 Hz, 1H), 8.07 (d, *J* = 5.3 Hz, 1H), 7.93 (t, *J* = 9.0 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 2H),6.14 (dd, 6.4,3.5 Hz), 3.53 (dt, *J* = 16.0, 8.1 Hz, 1H), 3.05 – 3.00 (m, 1H), 2.30 – 2.18 (m, 1H), 2.07 – 2.03 (m, 1H), 1.90 – 1.85 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.1, 194.7, 193.1, 183.7, 150.2, 143.6, 142.2, 136.4, 131.7, 126.6, 125.9, 124.5, 124.4, 120.0, 89.9, 58.5, 49.3, 32.8, 30.0, 24.5, 19.0. MS (ESI) m/z = 417 $[M+H]^+$

1'-(3-acetylphenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8g): Yellow solid; Mp 123-125°C; IR (KBr): ν_{max} 2933, 1759, 1711, 1591, 1449, 1354, 1270, 1222, 1149, 755, 678 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 – 8.12 (m, 1H), 8.09 – 8.05 (m, 2H), 7.97 – 7.90 (m, 3H), 7.72 – 7.70 (m, 1H), 7.60 (t, *J* = 7.9 Hz, 1H), 6.12 (dd, *J* = 6.6, 3.8 Hz, 1H), 3.58 – 3.50 (m, 1H), 3.06 – 2.99 (m, 1H), 2.63 (s, 3H), 2.20 – 2.13 (m, 1H), 2.09 – 2.00 (m, 1H), 1.94 – 1.84 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.9,

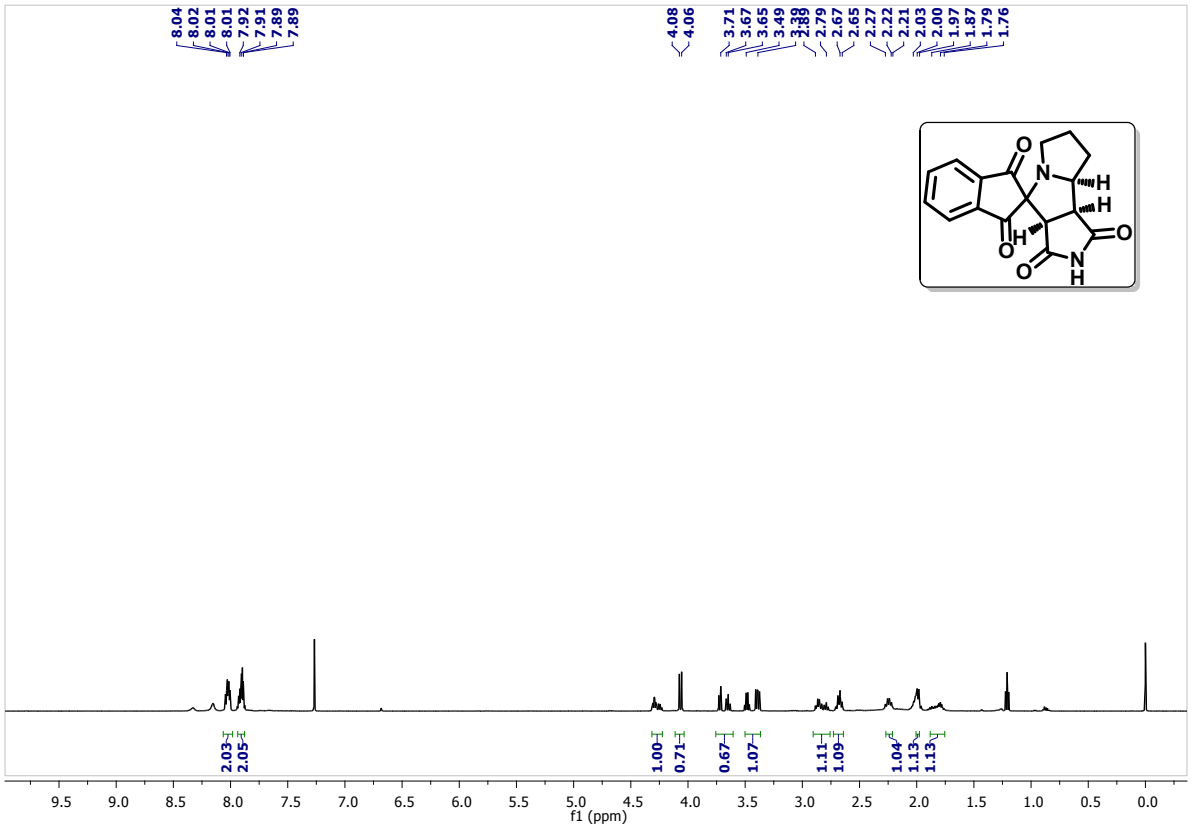
196.2, 194.5, 193.2, 143.5, 142.3, 138.3, 136.4, 131.7, 130.3, 129.8, 128.0, 126.9, 125.5, 124.5, 124.4, 119.9, 89.9, 49.3, 30.0, 26.7, 24.6. MS (ESI) m/z = 391 $[M+H]^+$

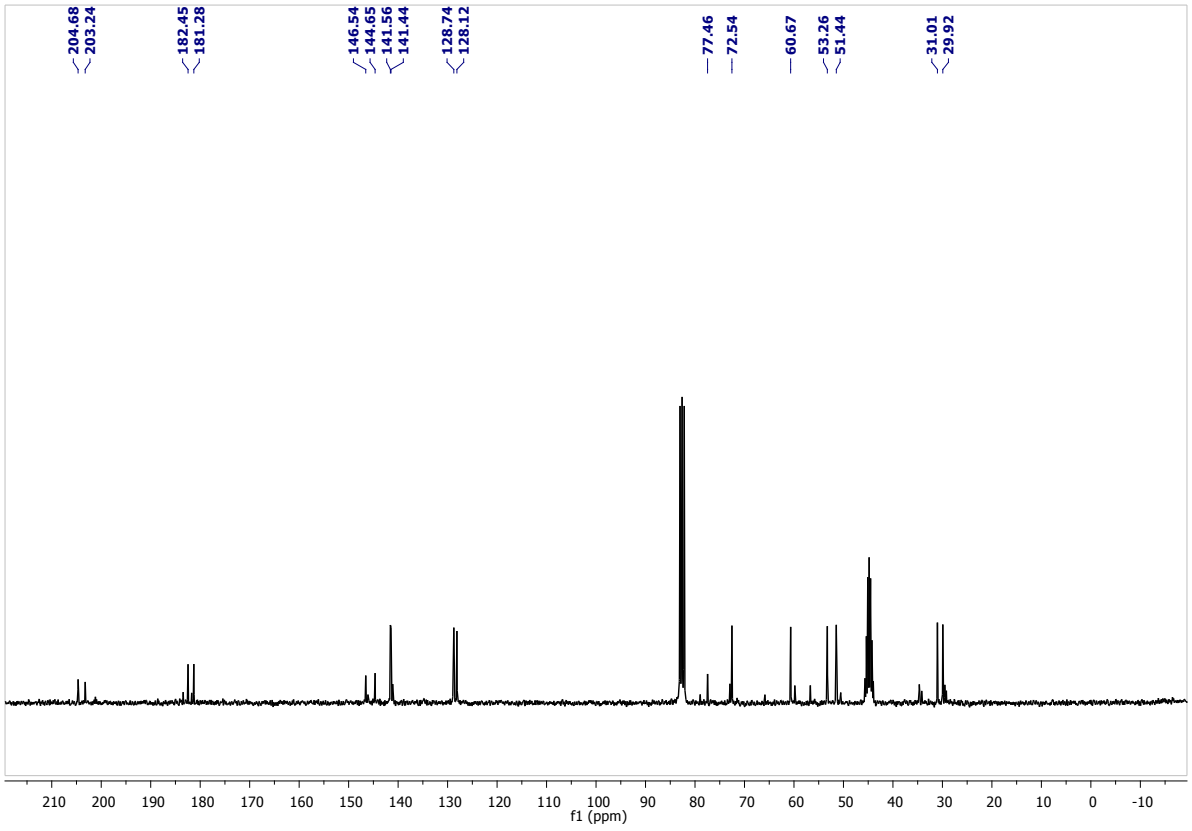
1'-(benzylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8h): Yellow solid; Mp 162-164°C; IR (KBr): ν_{max} 2089, 1756, 1702, 1589, 1458, 1398, 1320, 1258, 1089, 986, 728, 669 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.05 (m, 2H), 7.94 – 7.90 (m, 2H), 7.40 – 7.32 (m, 5H), 5.41 (d, *J* = 14.9 Hz, 1H), 5.32 (d, *J* = 11.6 Hz, 1H), 4.60 (d, *J* = 14.9 Hz, 1H), 3.30 (dd, *J* = 12.6, 6.5 Hz, 1H), 2.07 – 2.02 (m, 2H), 1.90 – 1.81 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.02, 194.0, 192.8, 143.1, 142.4, 136.4, 136.3, 134.0, 128.9, 128.2, 127.9, 124.4, 124.2, 87.4, 85.0, 84.9, 83.8, 48.9, 48.5, 30.1, 25.1. MS (ESI) m/z = 363 $[M+H]^+$

1'-(isopropylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8i): Yellow solid; Mp 158-160°C; IR (KBr): ν_{max} 2956, 1756, 1658, 1524, 1421, 1158, 963, 896, 785, 701, 668 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 – 8.02 (m, 2H), 7.90 (dt, *J* = 10.4, 3.5 Hz, 2H), 5.38 (dd, *J* = 7.6, 5.5 Hz, 1H), 4.90 (dd, *J* = 13.8, 6.9 Hz, 1H), 3.09 – 3.04 (m, 1H), 2.98 – 2.92 (m, 1H), 1.40 (d, *J* = 6.9 Hz, 3H), 1.35 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.0, 190.7, 142.9, 142.5, 136.4, 136.1, 124.2, 124.0, 85.7, 48.96, 47.1, 33.5, 26.1, 20.5, 19.2. MS (ESI) m/z = 315 $[M+H]^+$

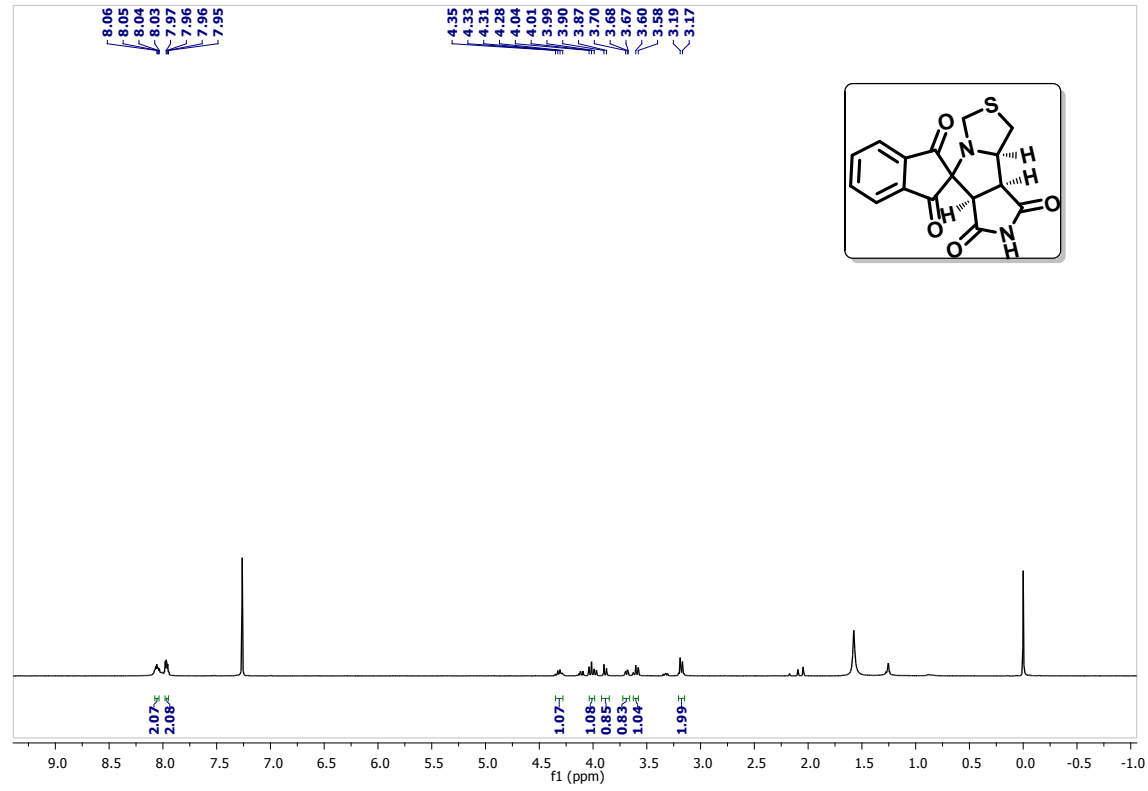
^1H and ^{13}C NMR spectral copies of compounds:

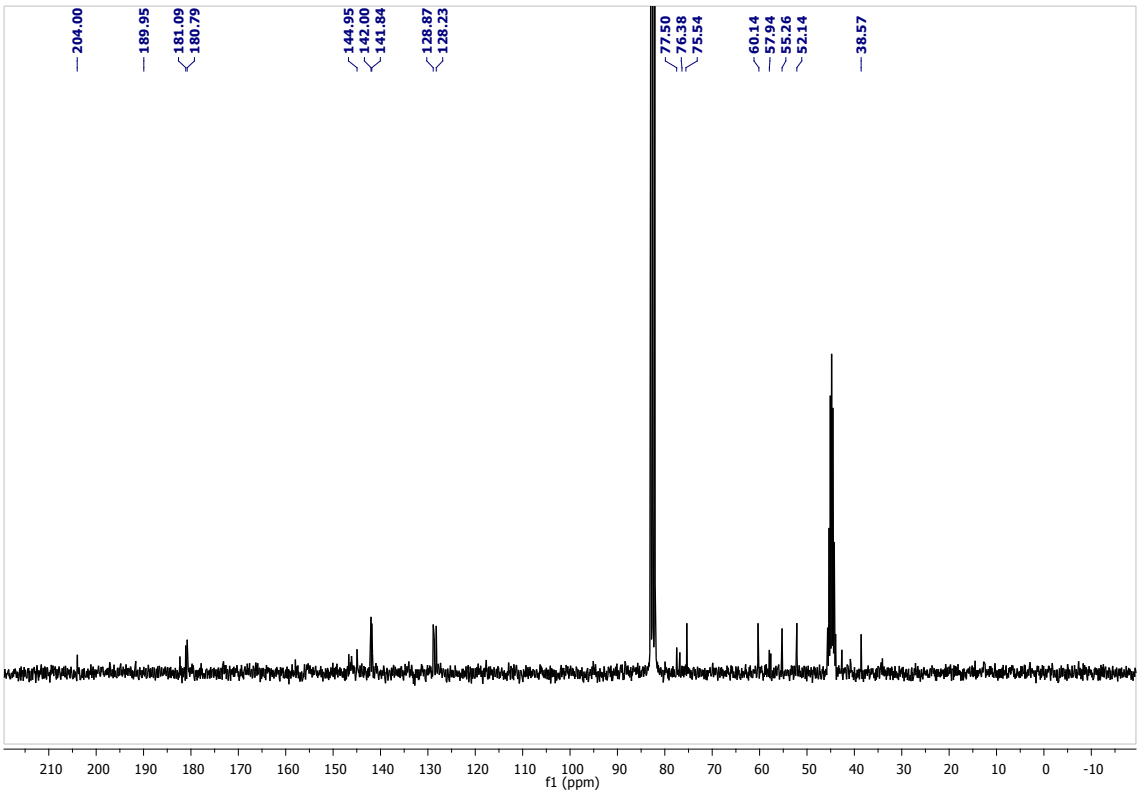
6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine] 1,1',3,3'(2'H,3a'H,8b'H)-tetraone (4a):



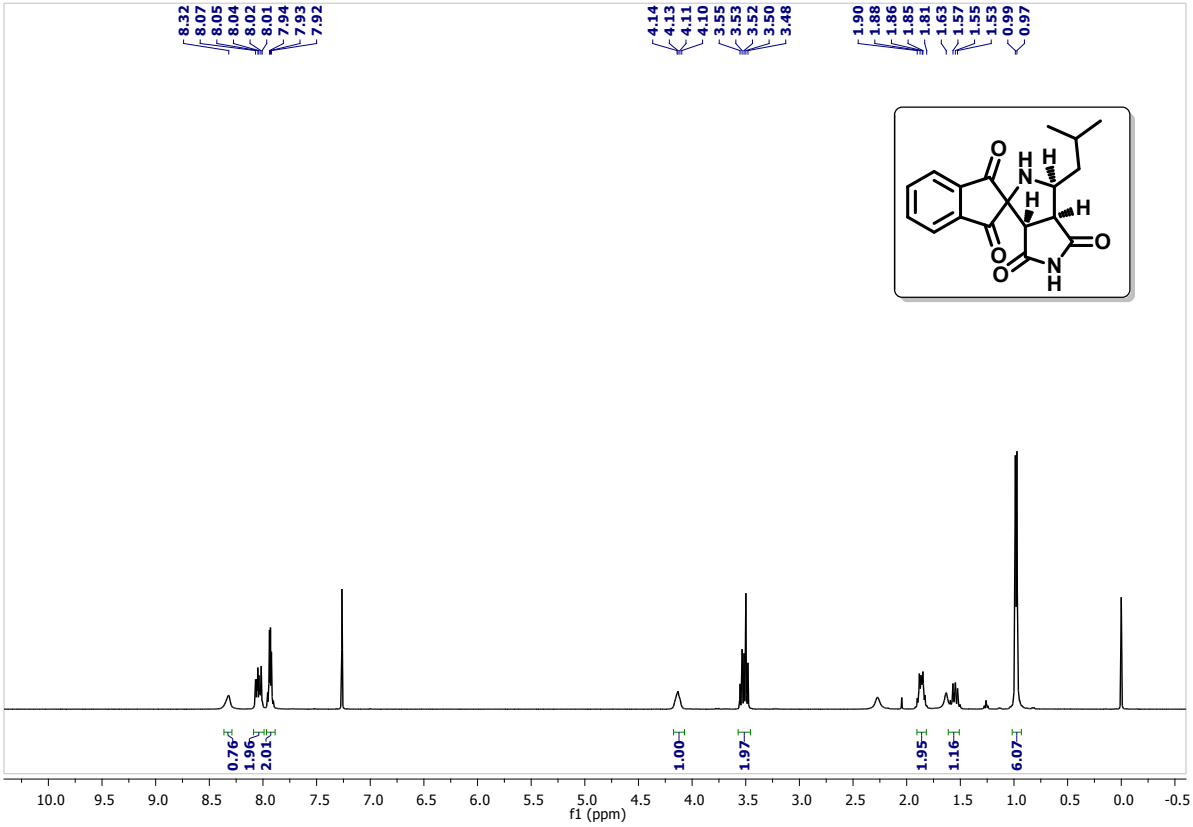


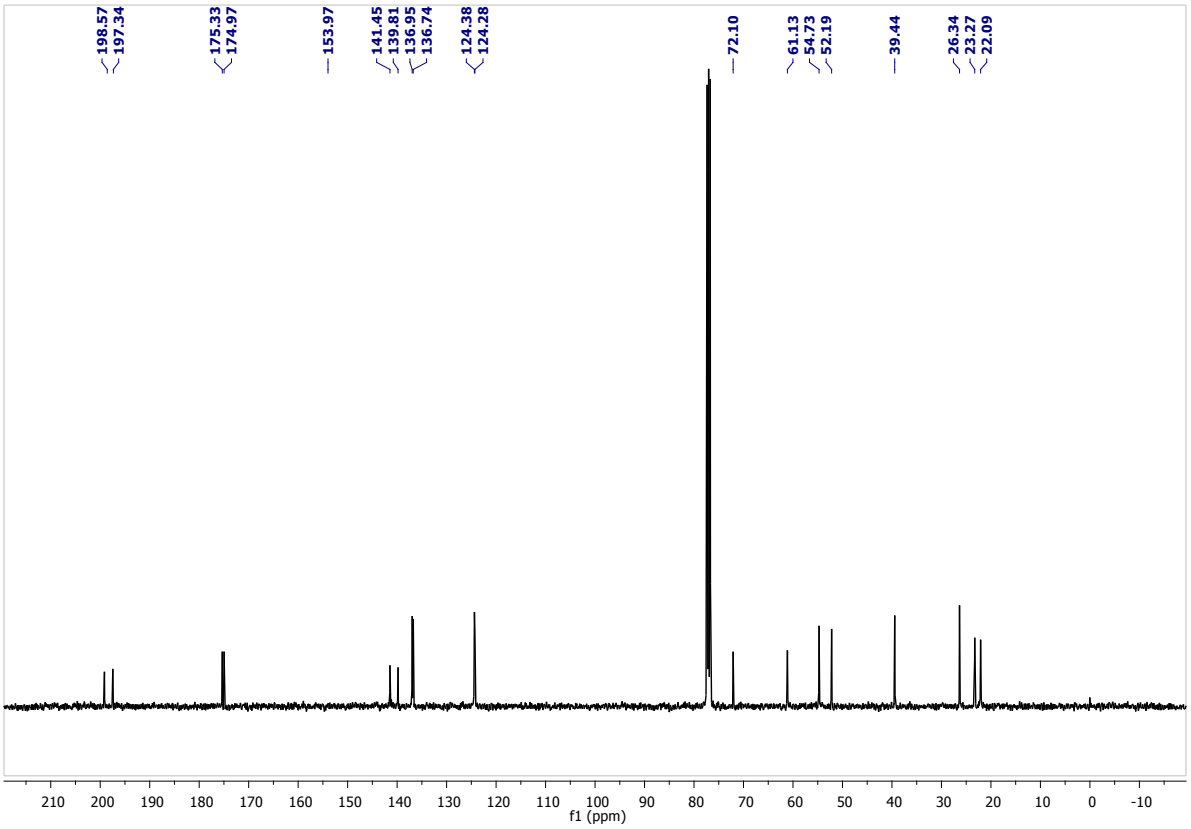
1',8b'-dihydrospiro[indene-2,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-1,3,6',8'(3'H,5a'H,7'H,8a'H)-tetraone (4b):



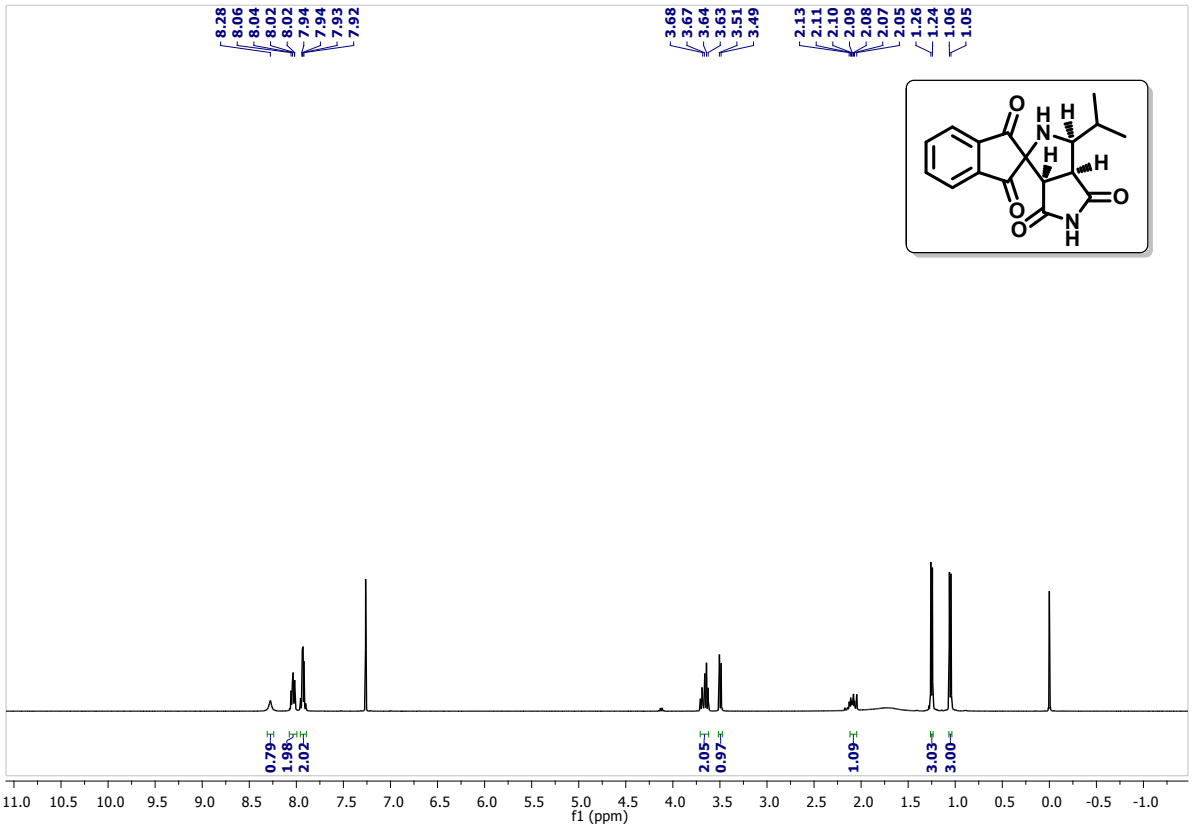


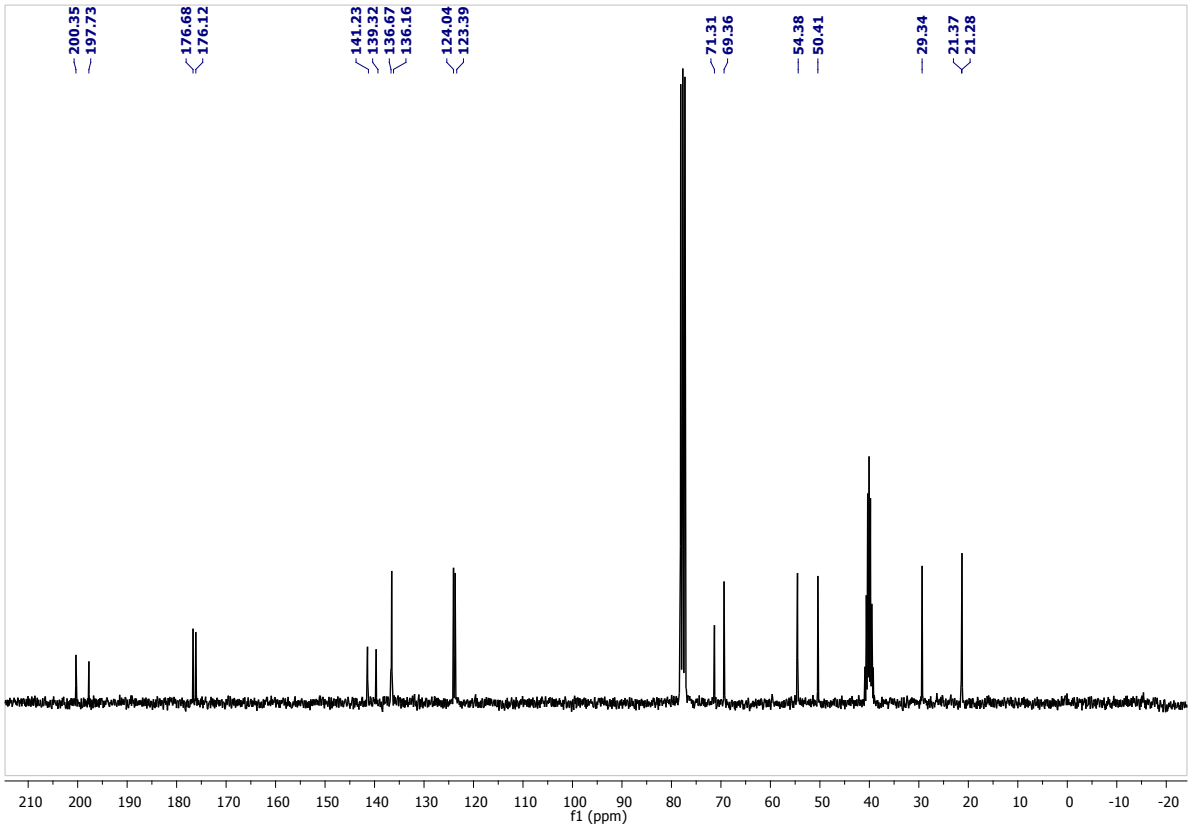
3'-isobutyl-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4c):



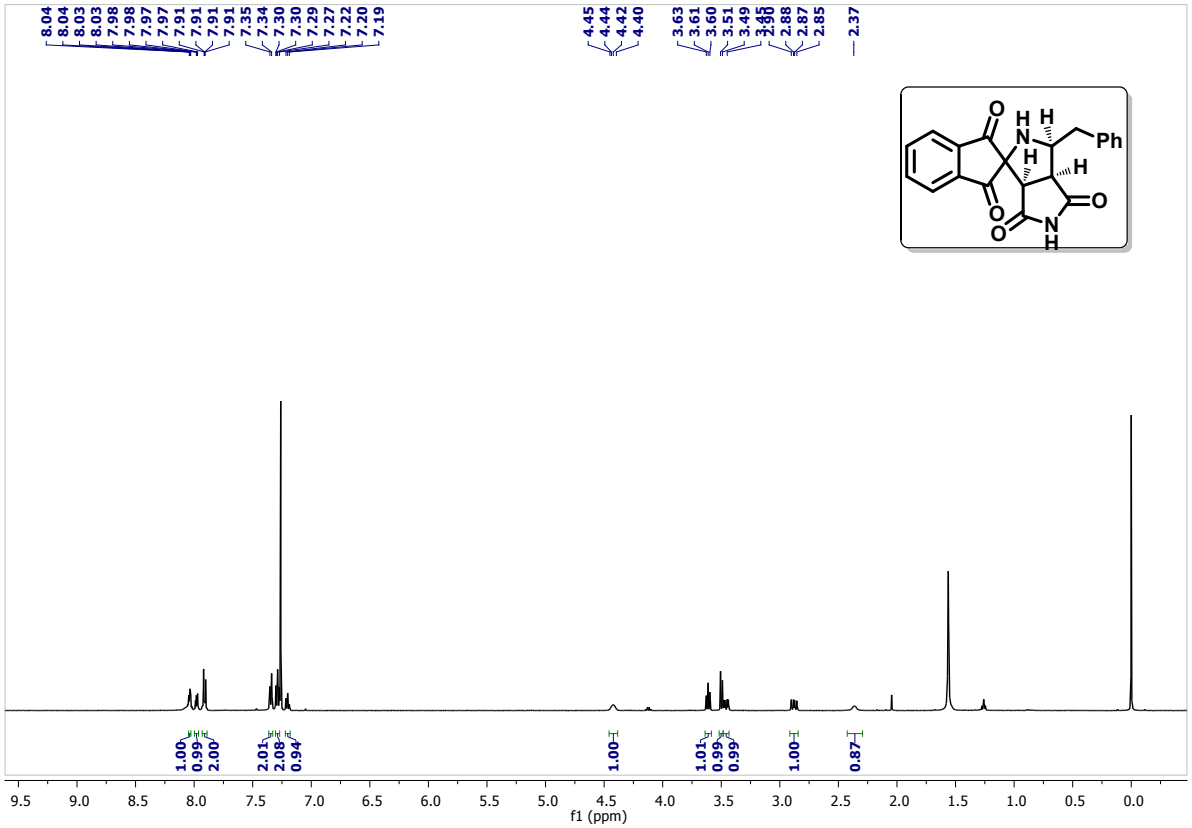


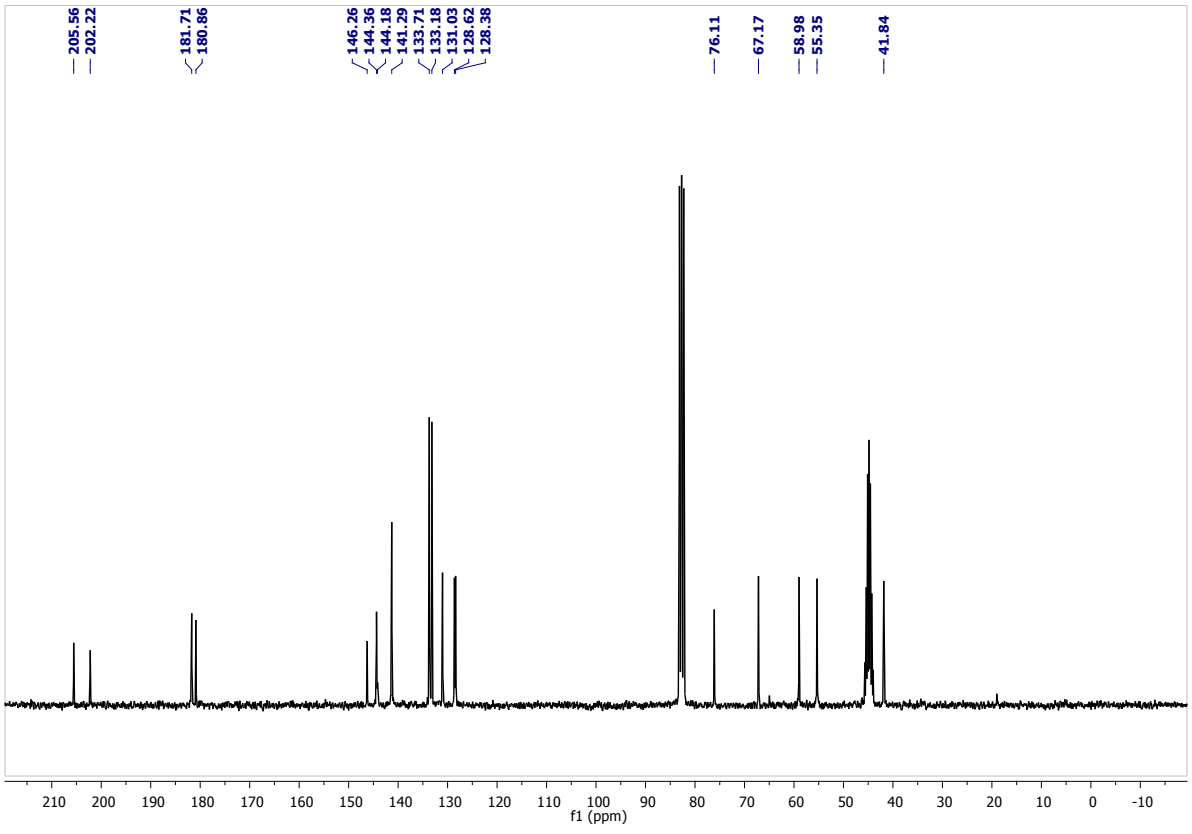
3'-isopropyl-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4d):



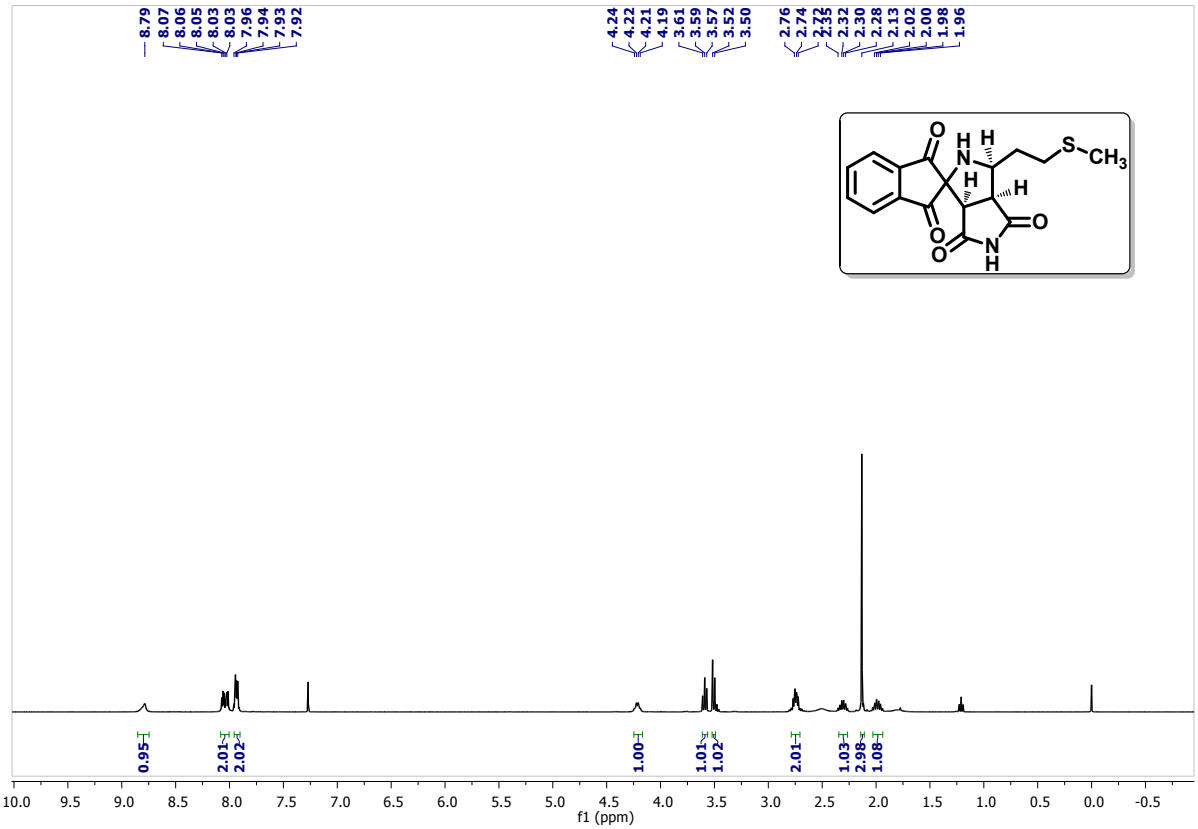


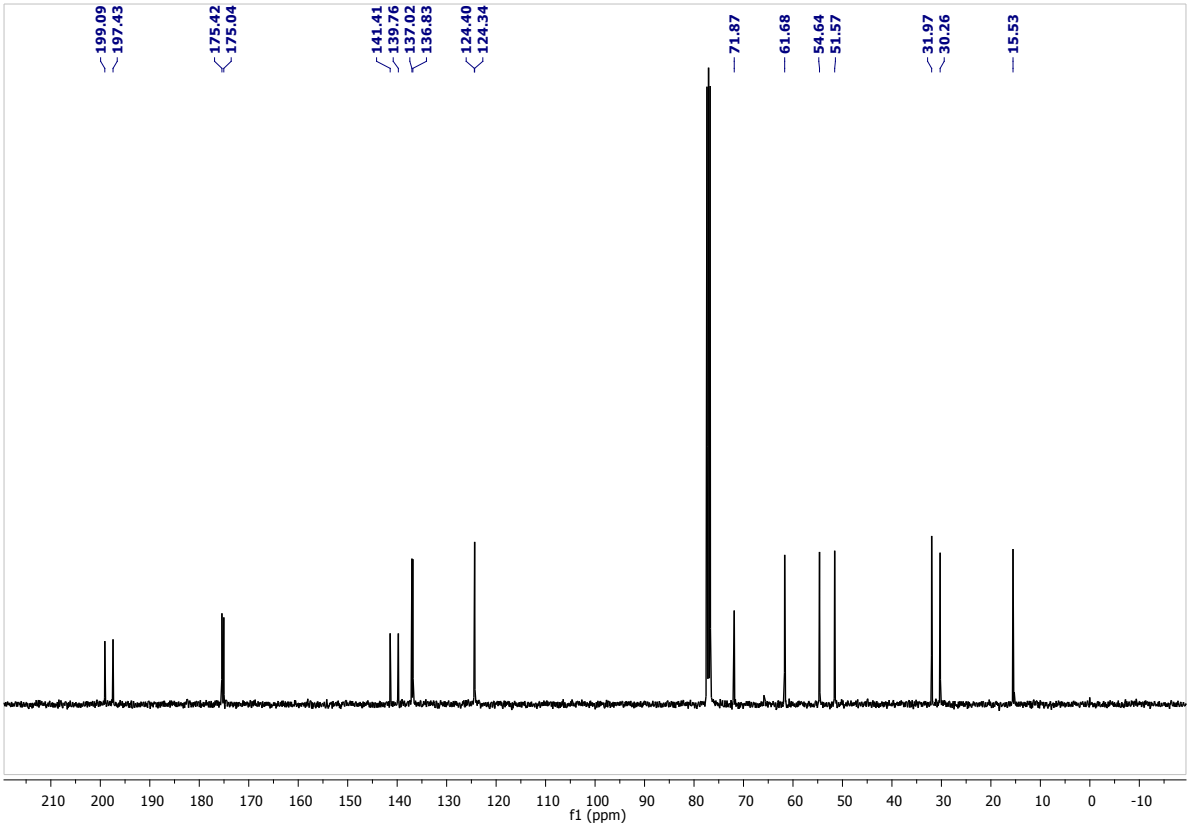
3'-benzyl-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4e):



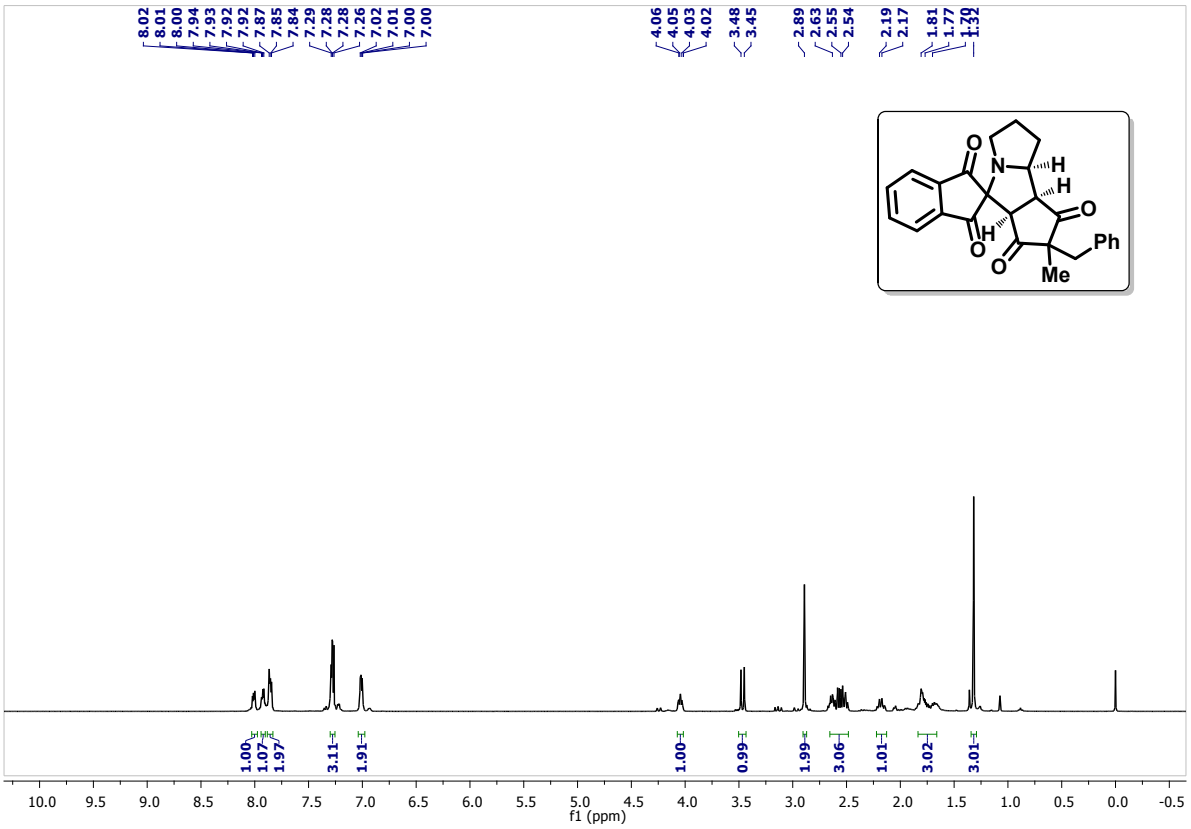


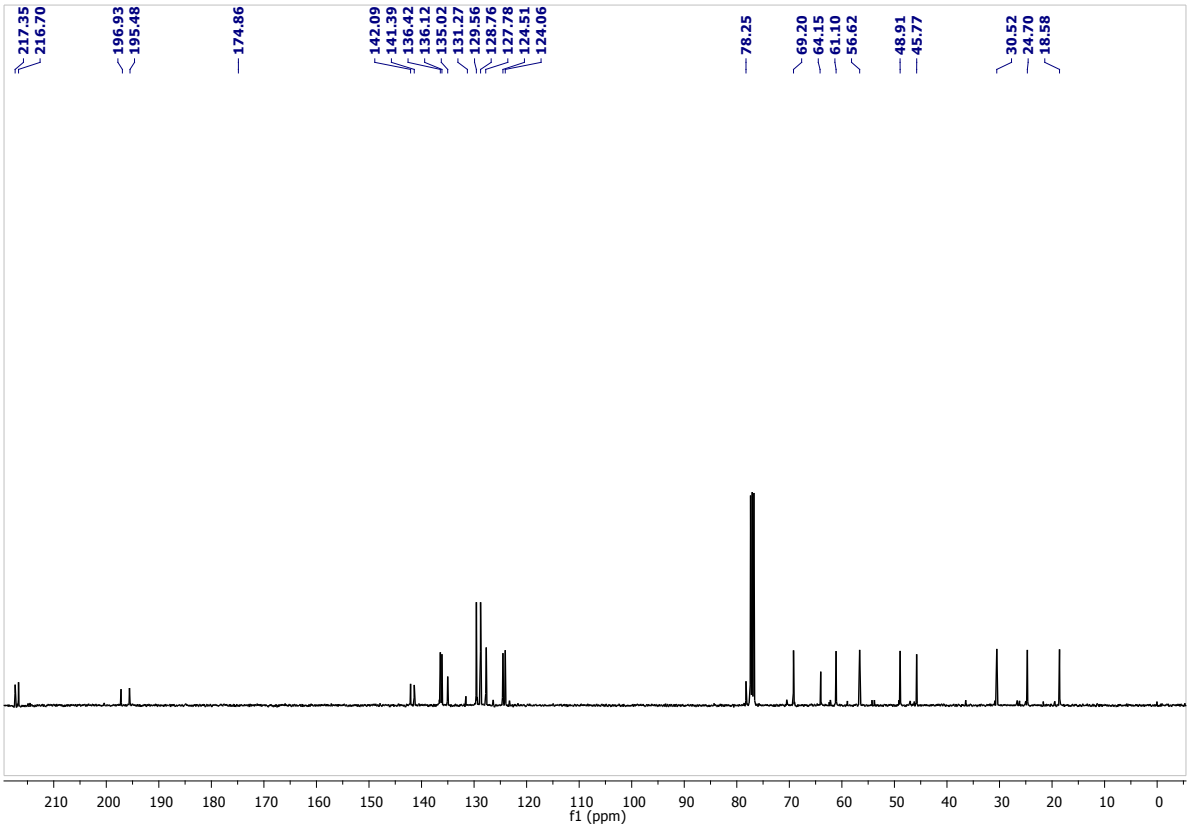
3'-(2-(methylthio)ethyl)-3',3a'-dihydro-2'H-spiro[indene-2,1'-pyrrolo[3,4-c]pyrrole]-1,3,4',6'(5'H,6a'H)-tetraone (4f):



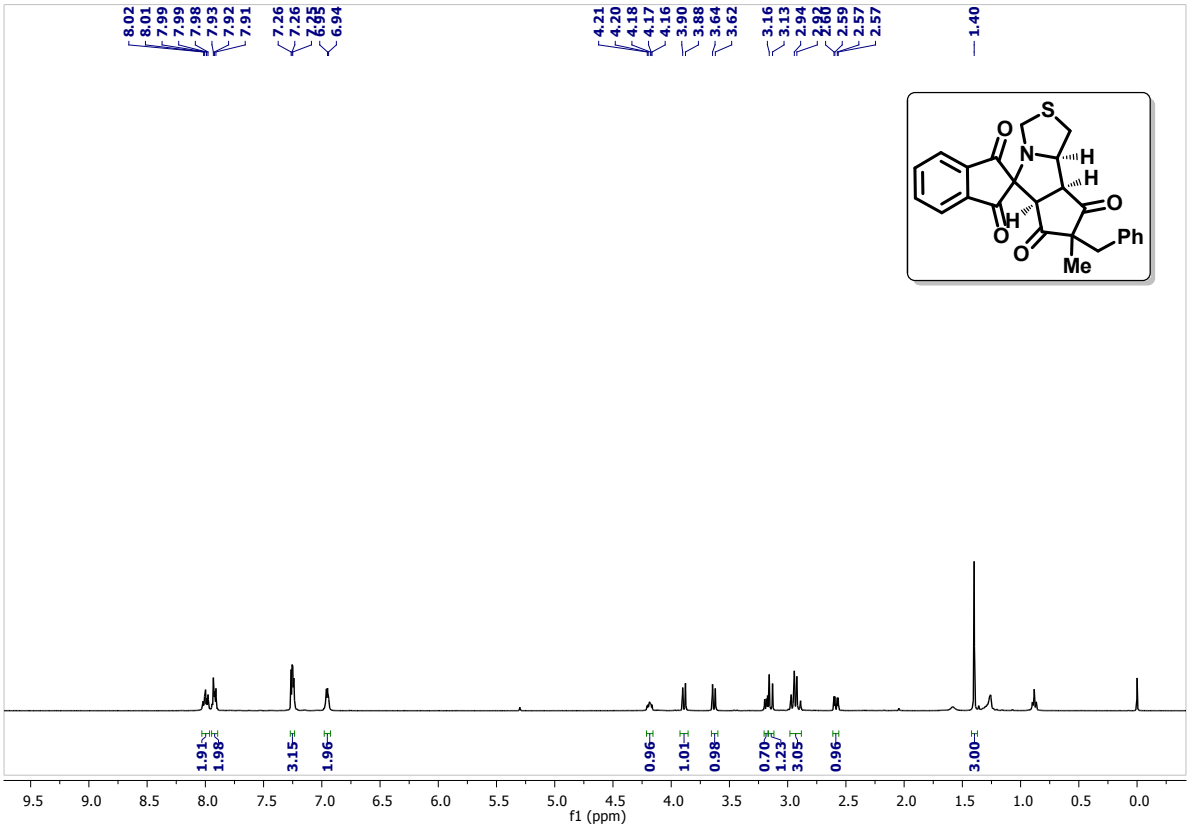


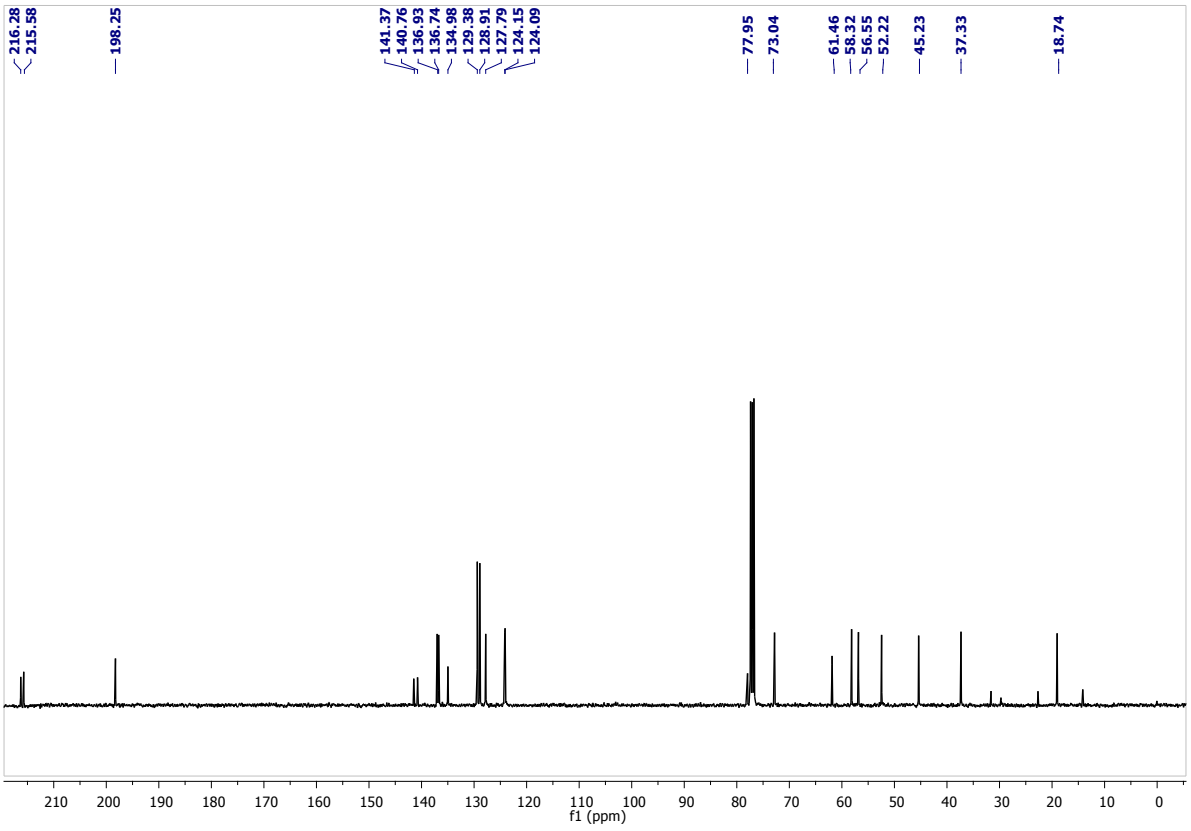
7-benzyl-7-methyl-2,3-dihydro-1H-spiro[cyclopenta[a]pyrrolizine-5,2'-indene]-1',3',6,8(5aH,7H,8aH,8bH)-tetraone (4g):



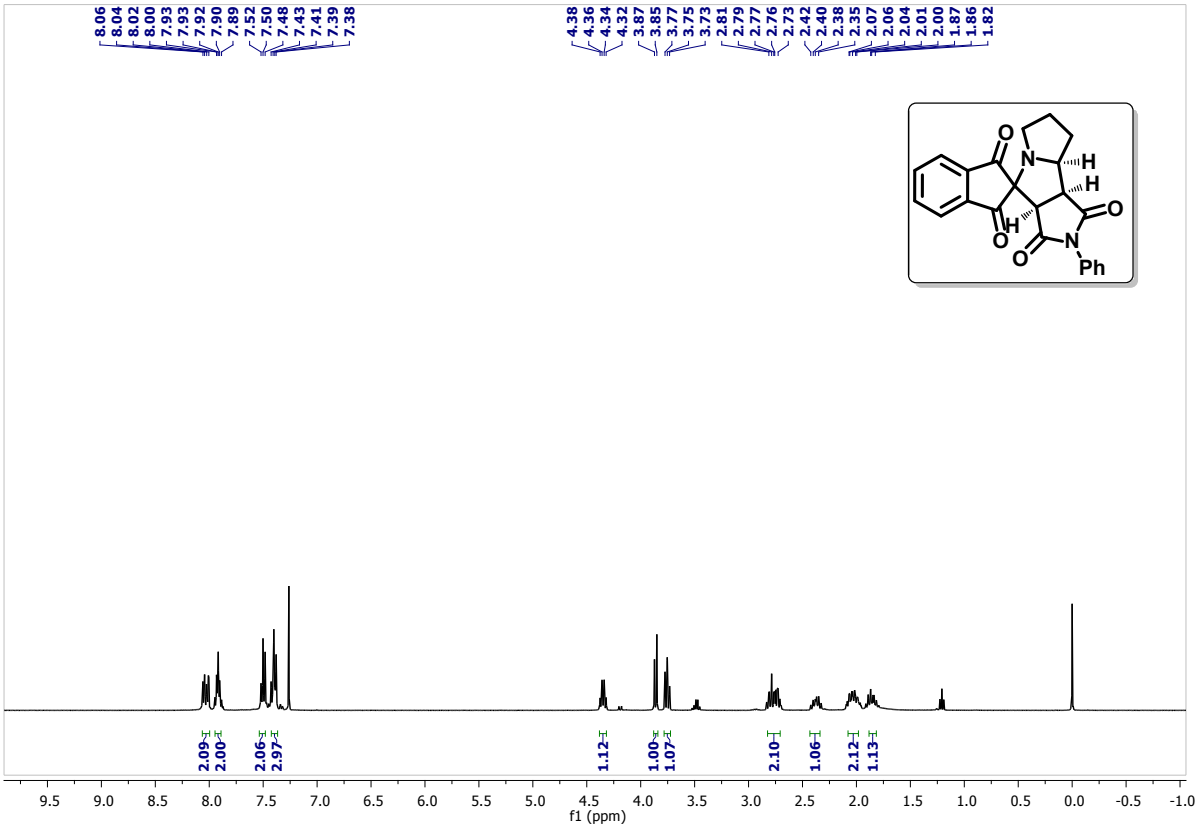


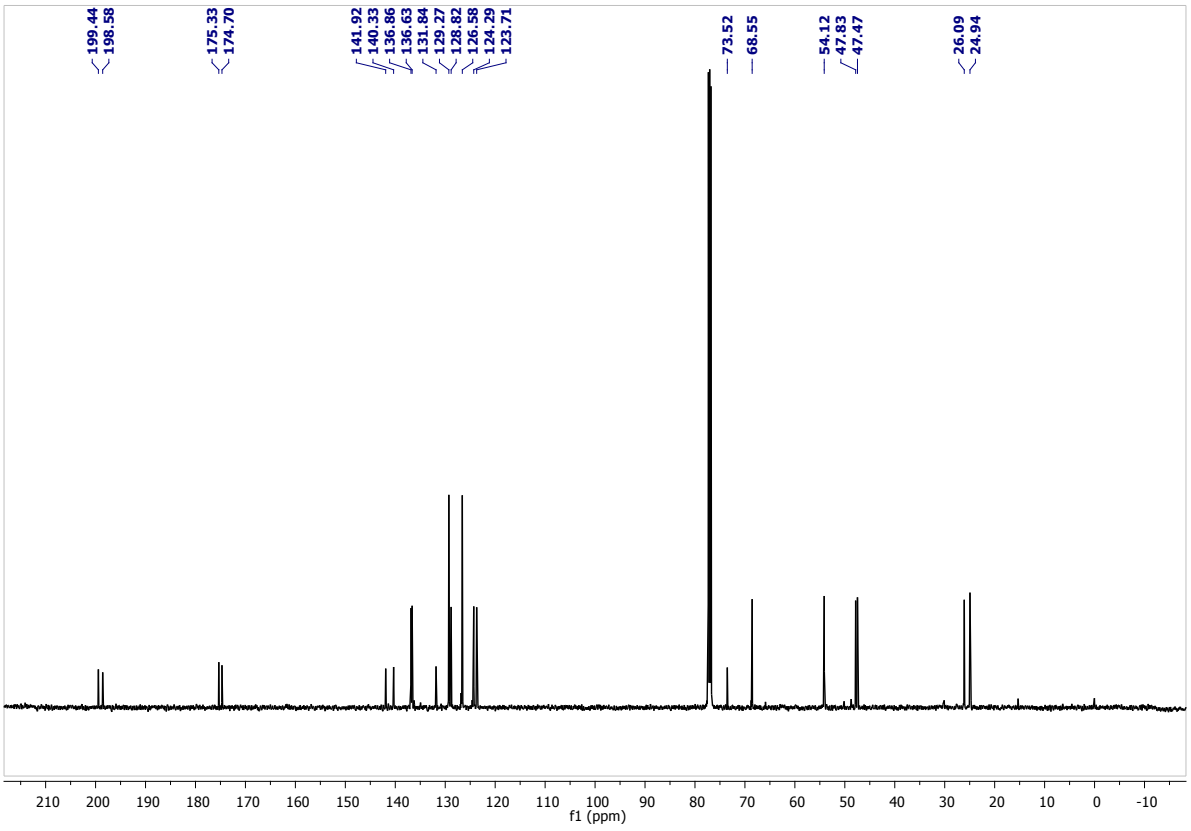
7-benzyl-7-methyl-1,8b-dihydrospiro[cyclopenta[3,4]pyrrolo[1,2-c]thiazole-5,2'-indene]-1',3',6,8(3H,5aH,7H,8aH)-tetraone (4h):



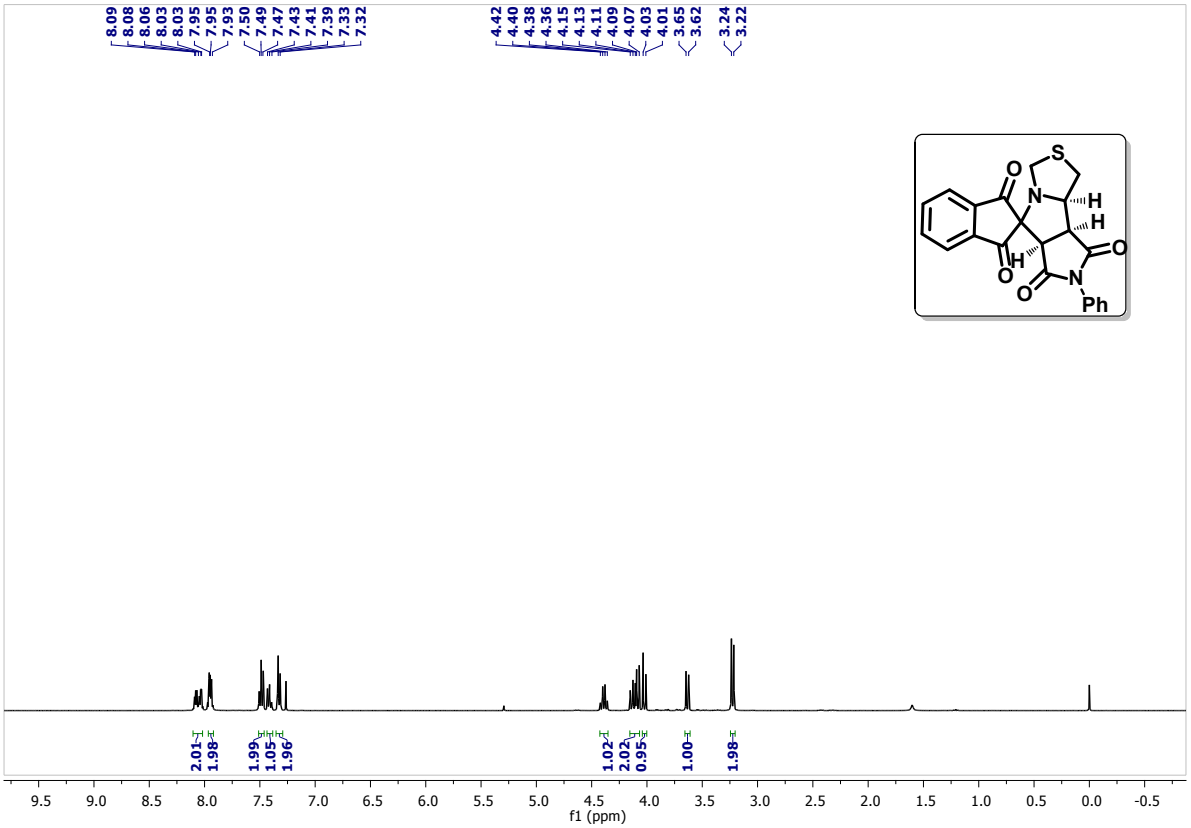


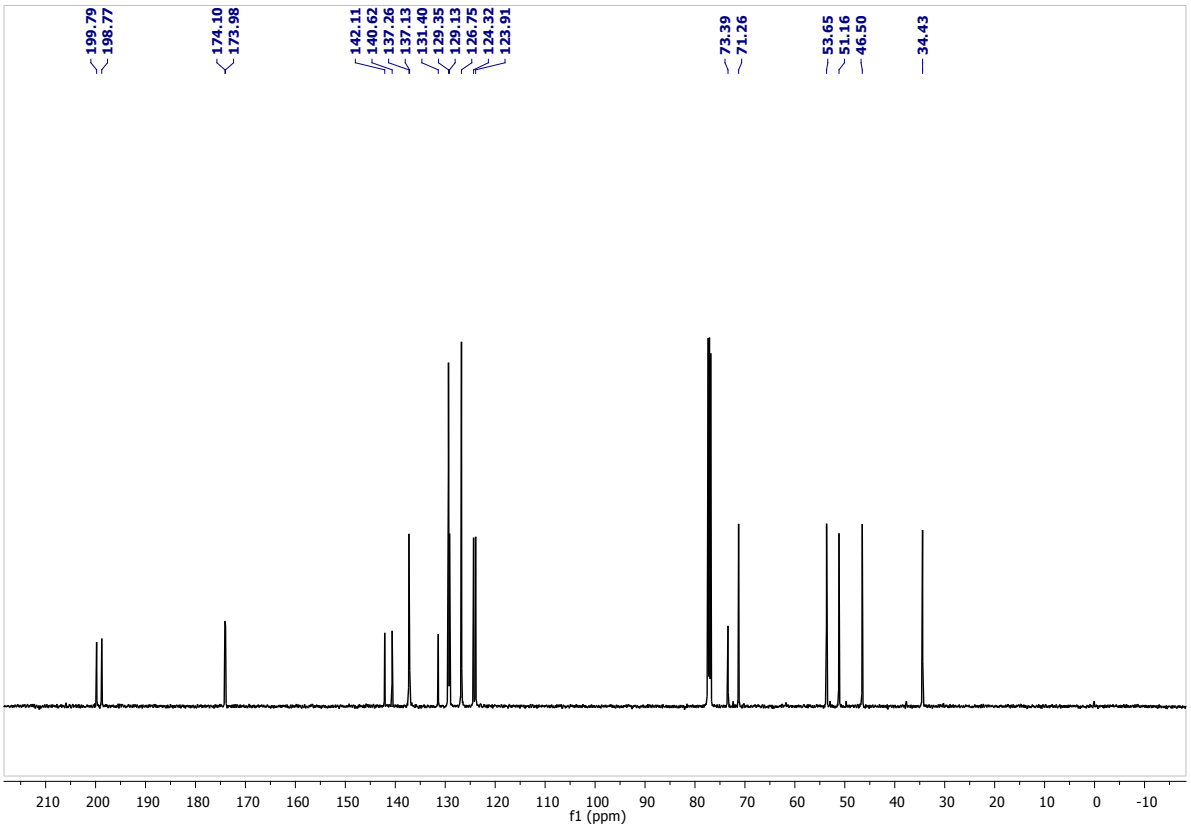
2'-phenyl-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (4i):



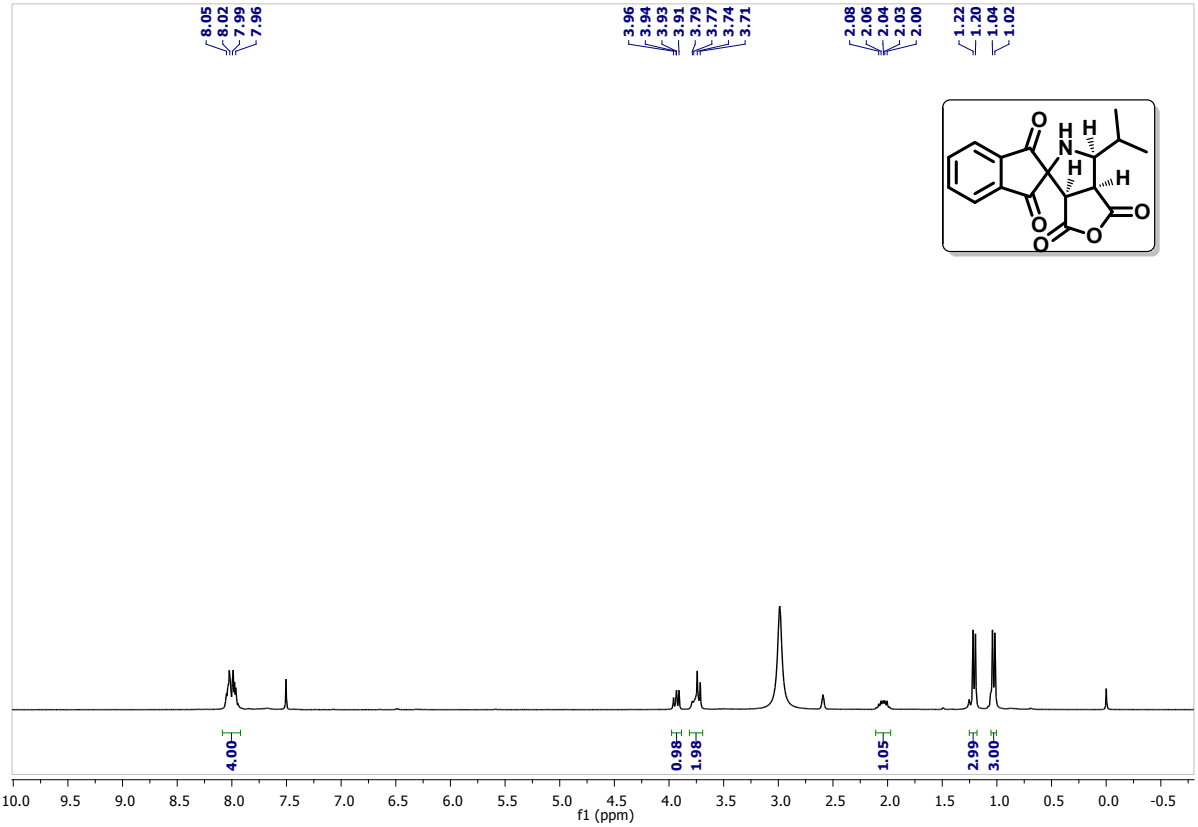


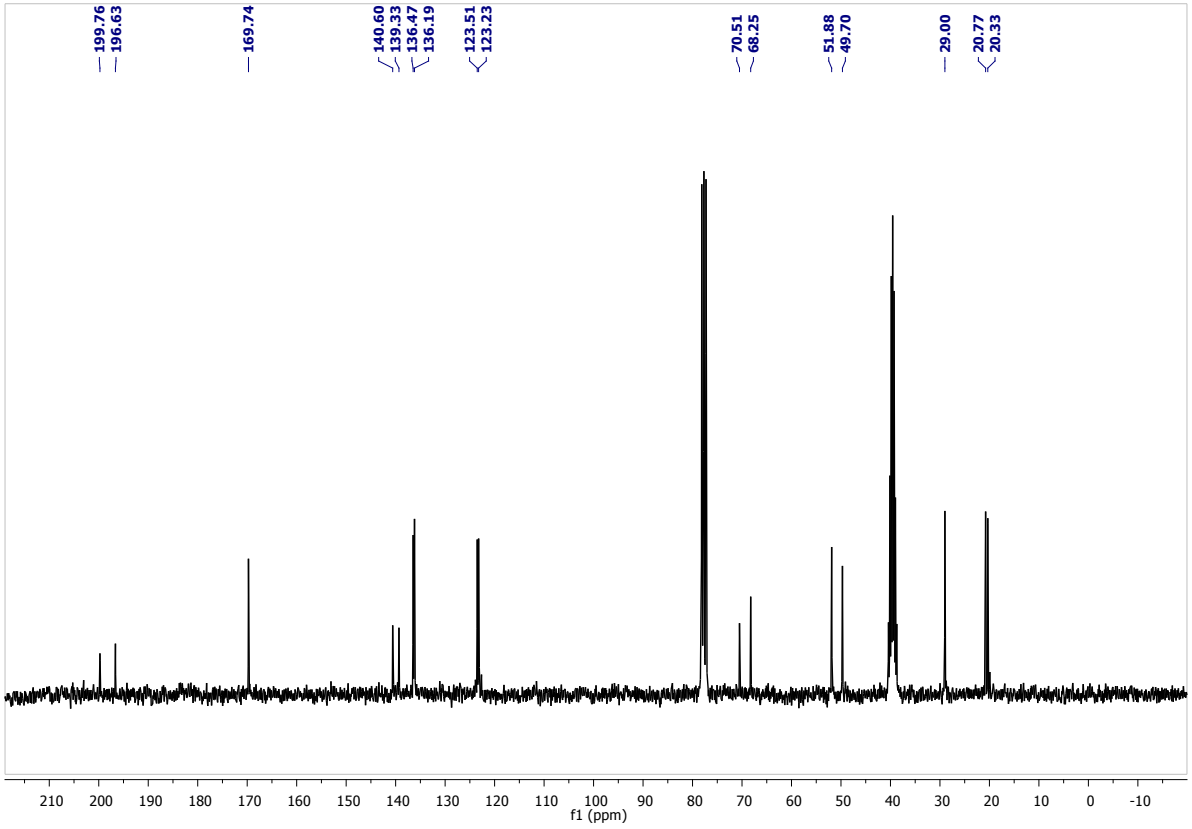
7'-phenyl-1',8b'-dihydrospiro[indene-2,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-1,3,6',8'(3'H,5a'H,7'H,8a'H)-tetraone (4j):



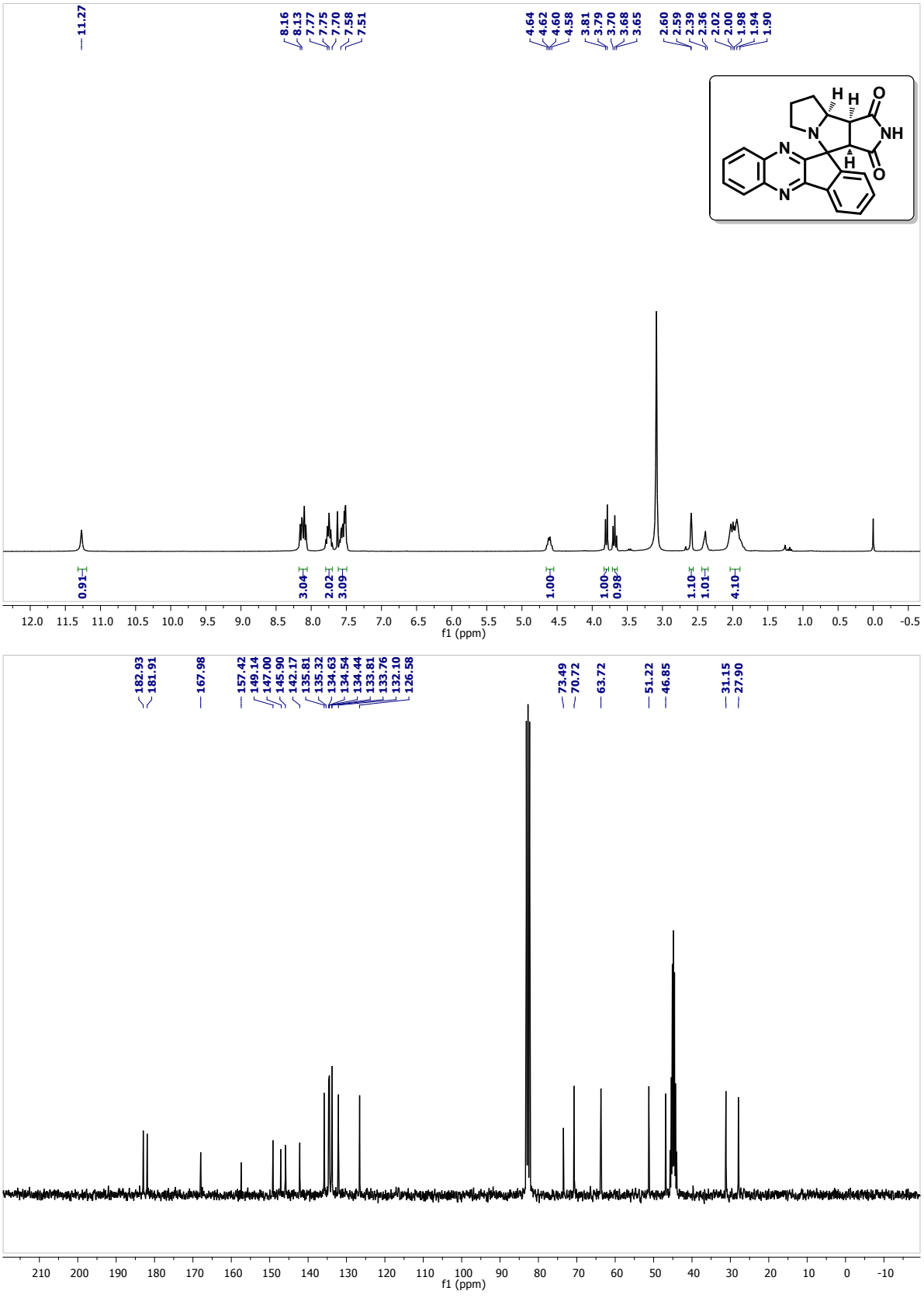


6-isopropyl-6,6a-dihydrospiro[furo[3,4-c]pyrrole-4,2'-indene]-1,1',3,3'(3aH,5H)-tetraone (4k):

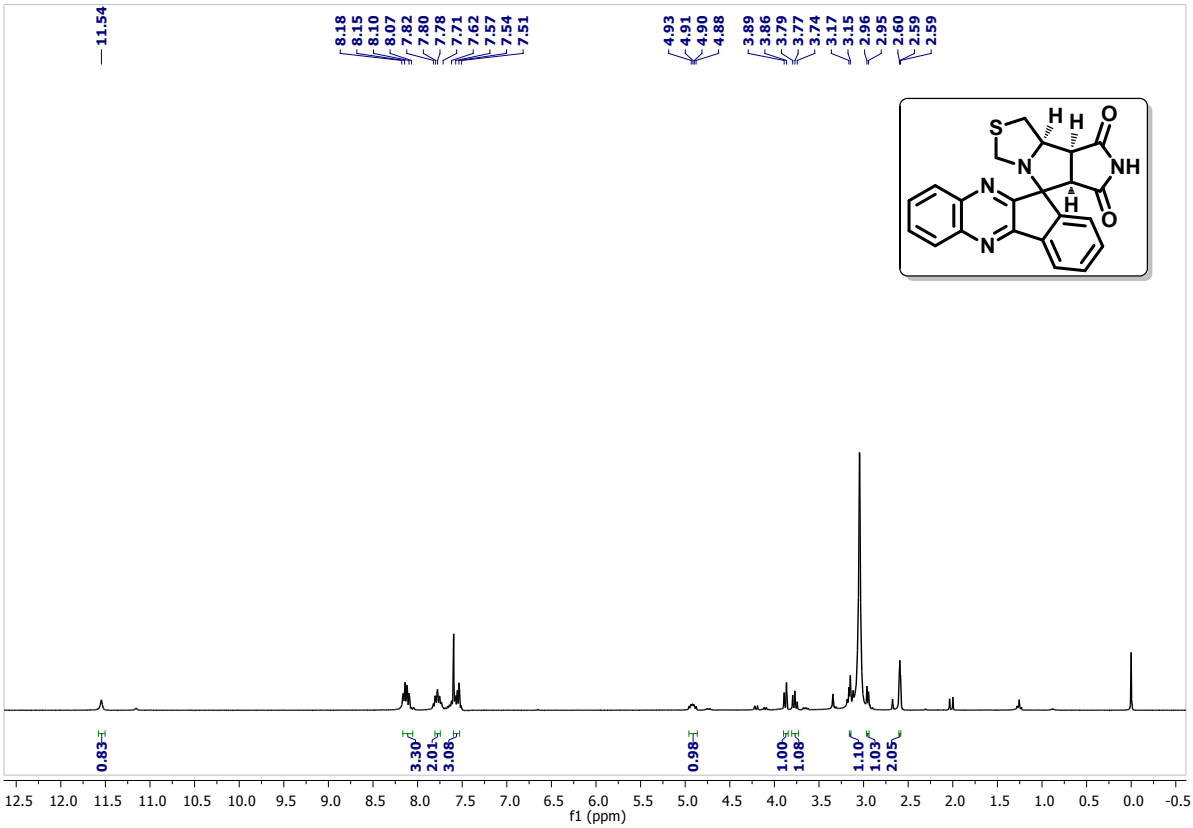


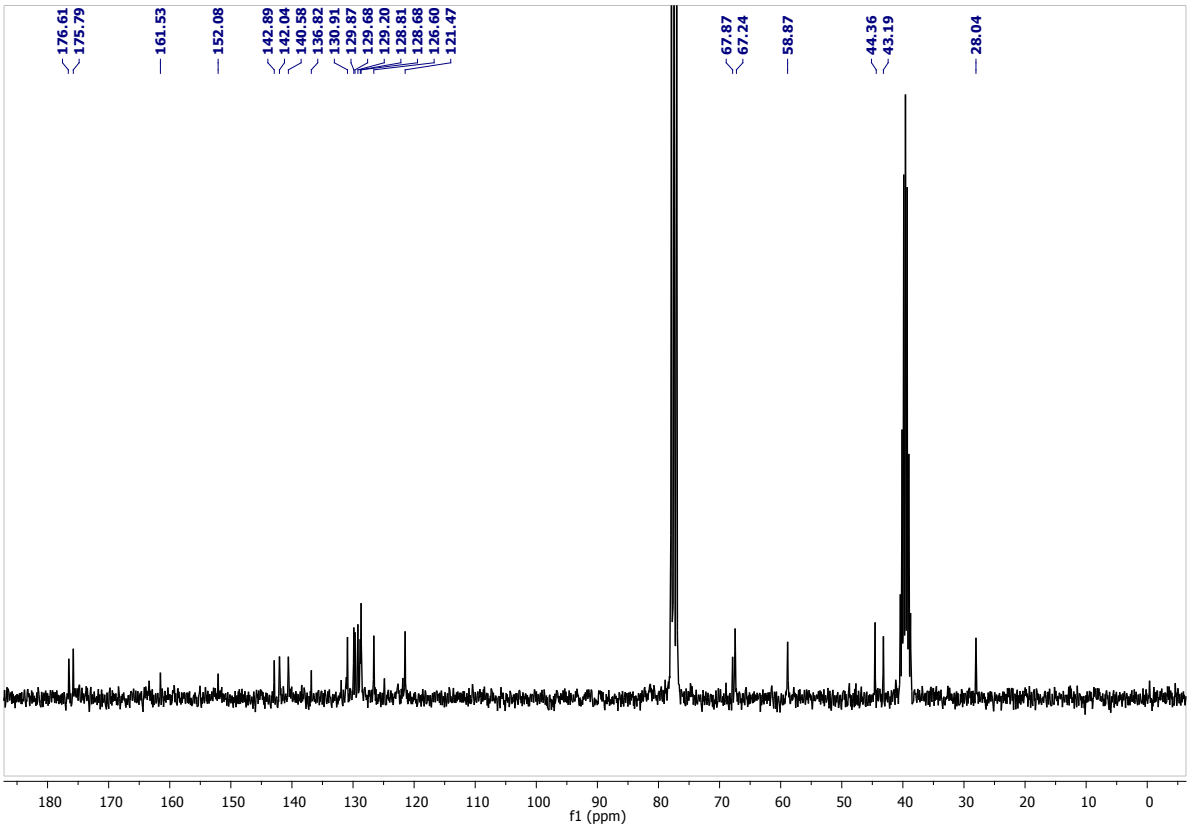


3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indeno[1,2-b]quinoxaline-11,4'-pyrrolo[3,4-a]pyrrolizine]-1',3'(2'H)-dione (4l):

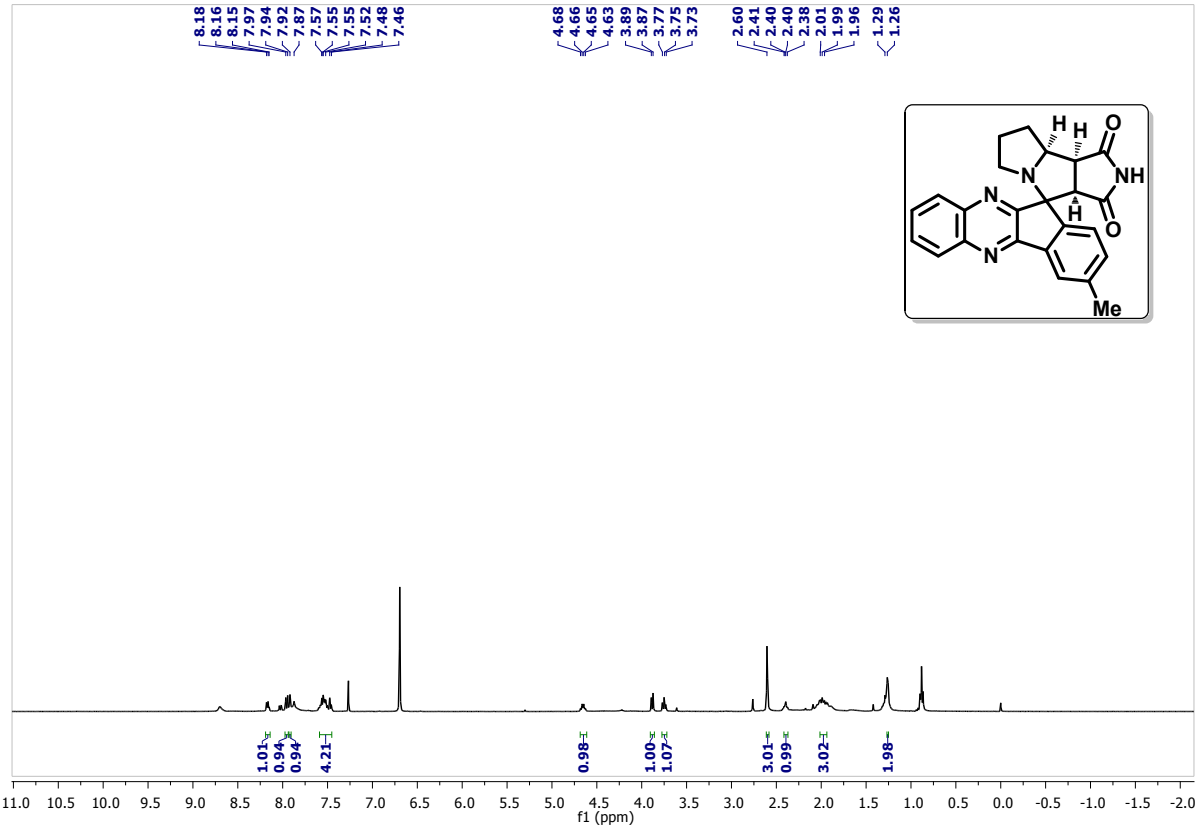


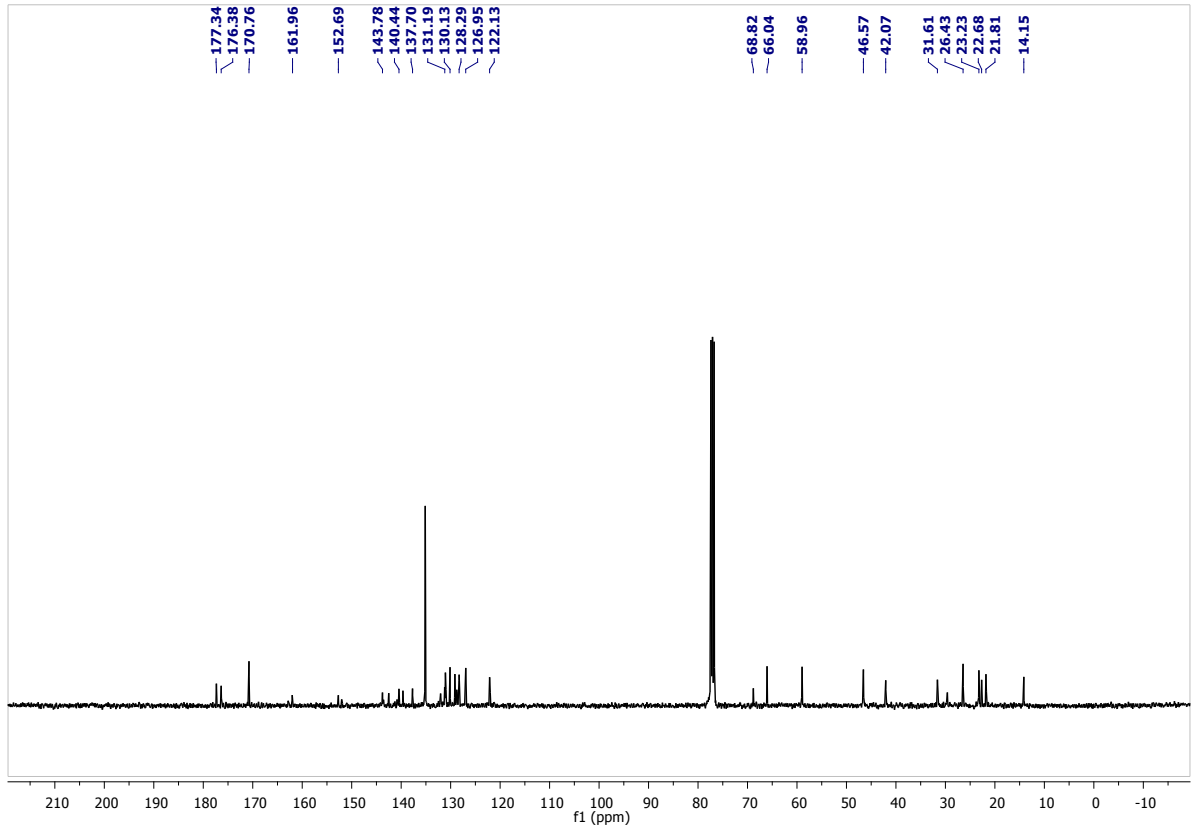
1',7',8a',8b'-tetrahydrospiro[indeno[1,2-b]quinoxaline-11,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-6',8'(3'H,5a'H)-dione (4m):



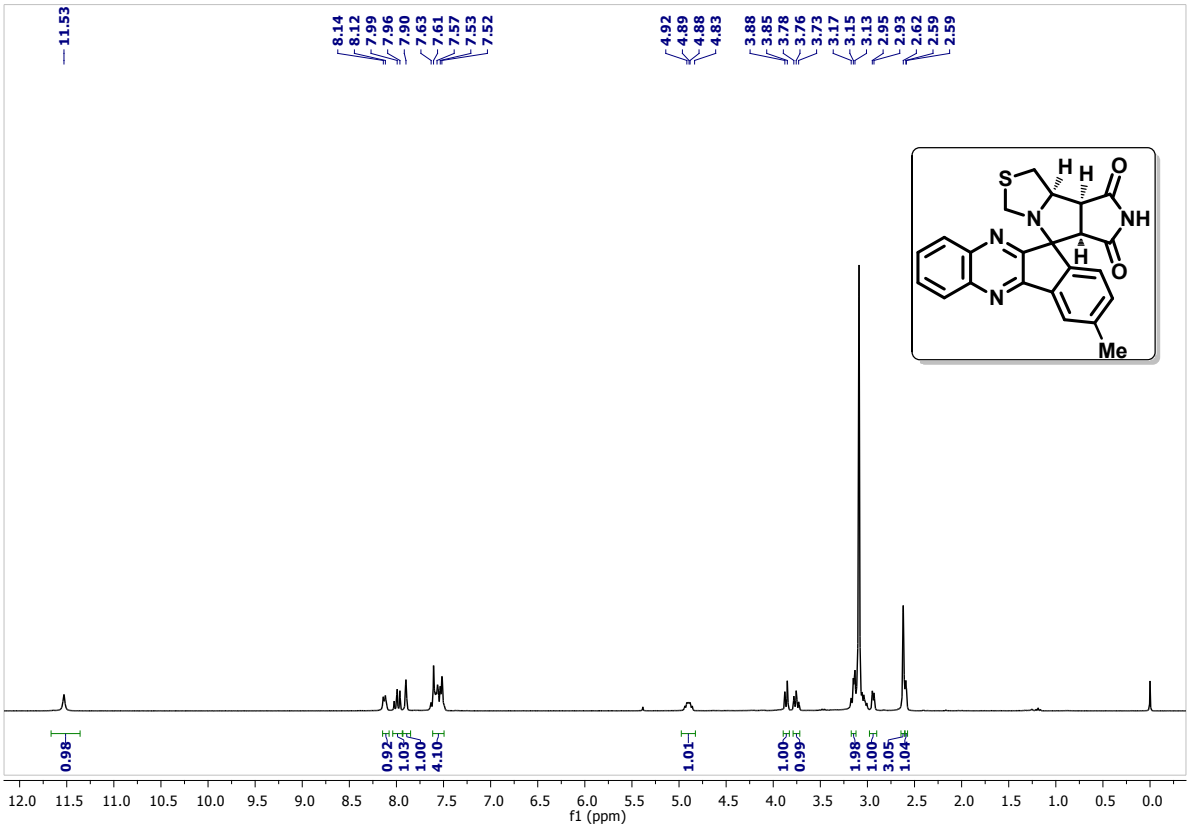


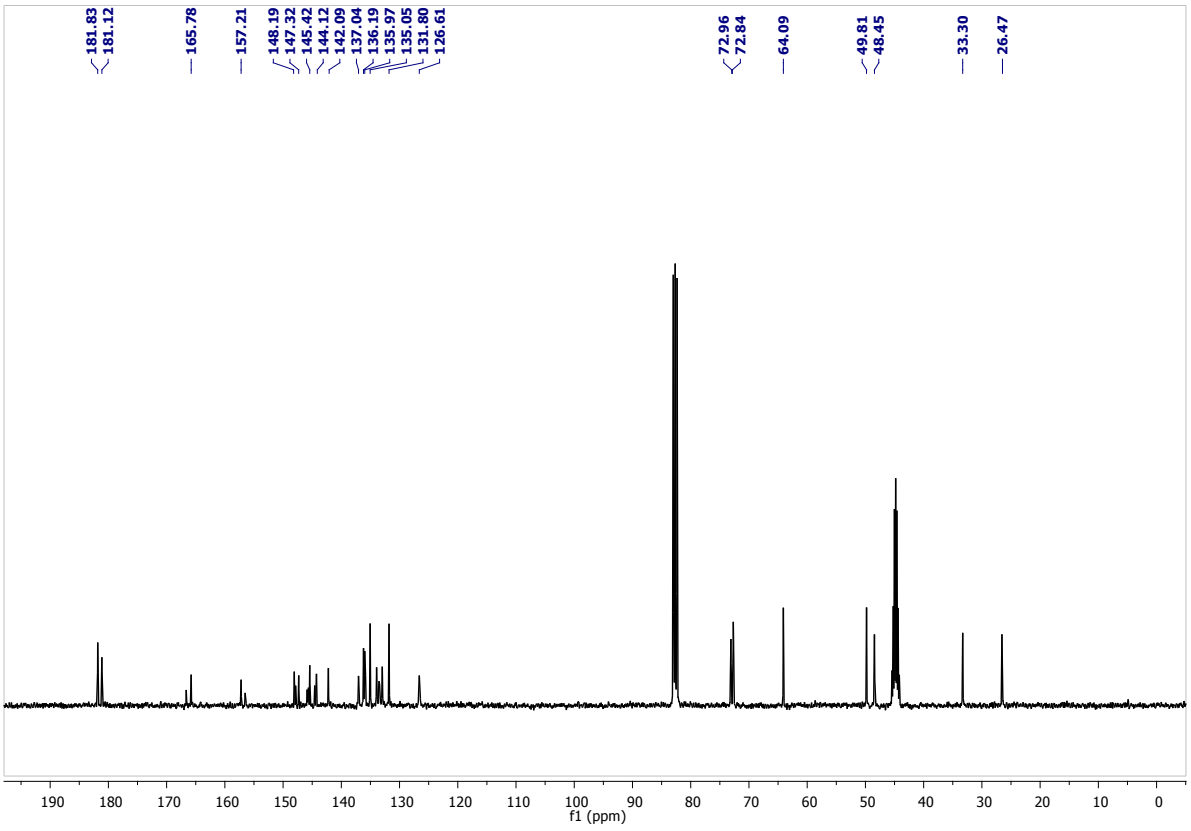
3-methyl-3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indeno[1,2-b]quinoxaline-11,4'-pyrrolo[3,4-a]pyrrolizine]-1',3'(2'H)-dione (4n):



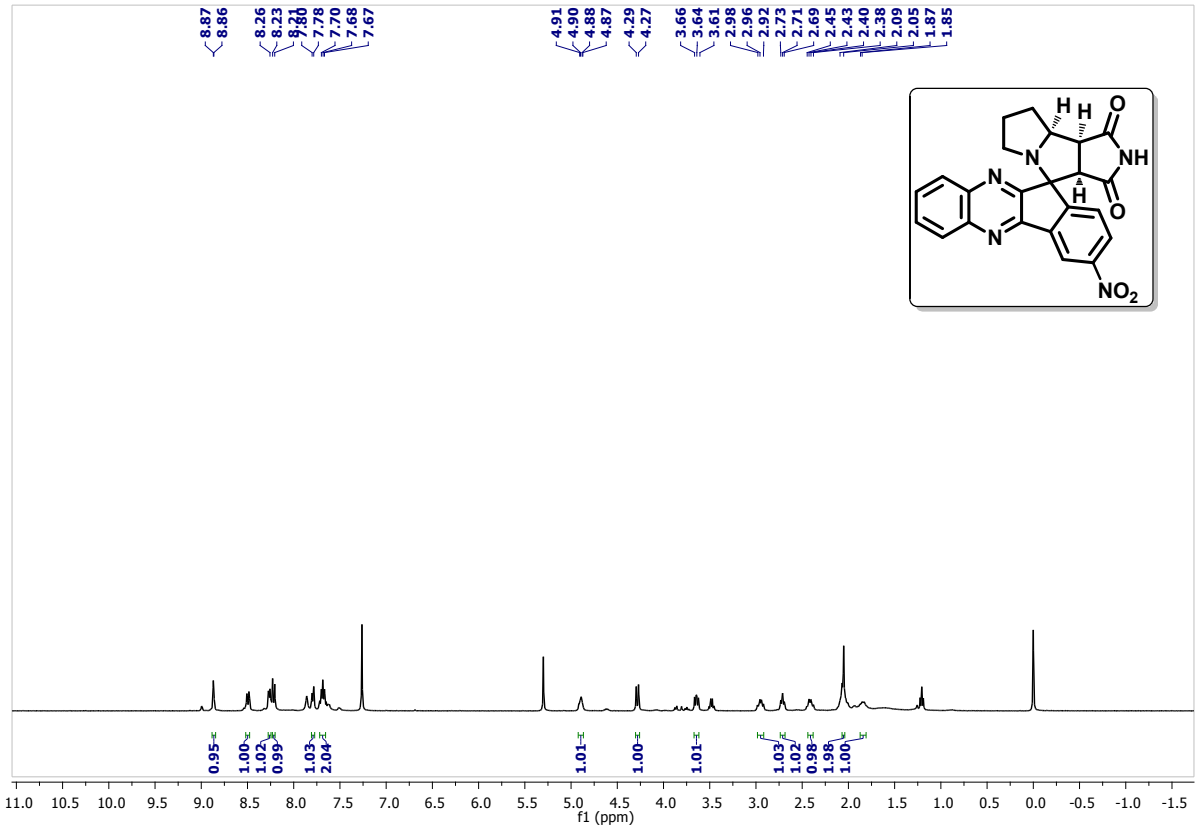


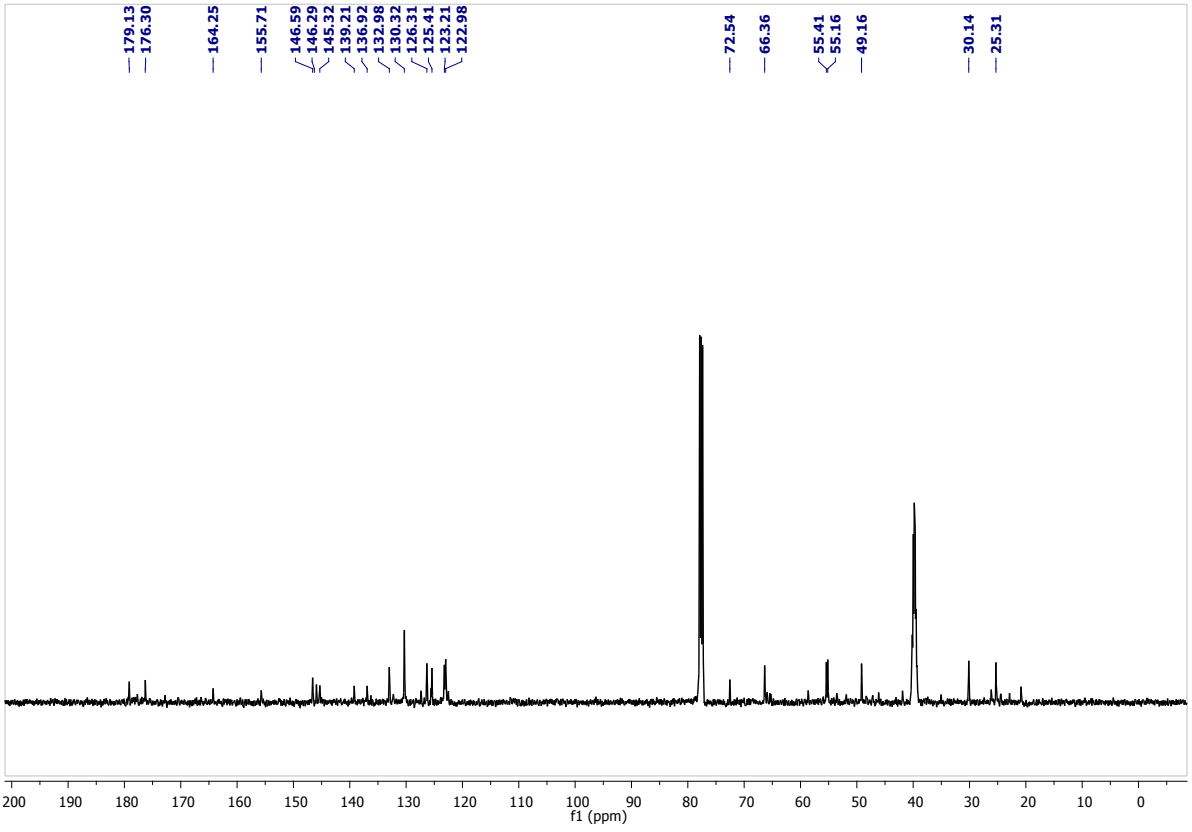
3-methyl-1',7',8a',8b'-tetrahydrospiro[indeno[1,2-b]quinoxaline-11,5'-pyrrolo[3',4':3,4]pyrrolo[1,2-c]thiazole]-6',8'(3'H,5a'H)-dione (4o):



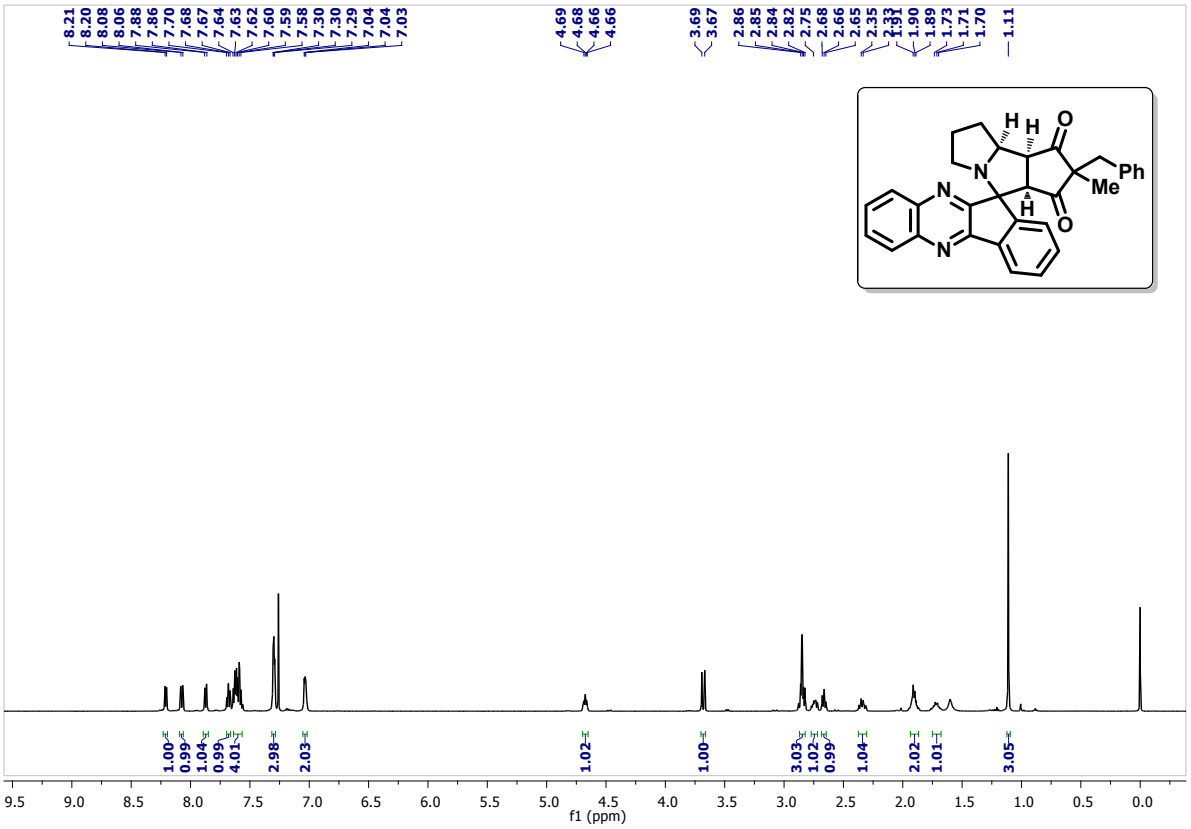


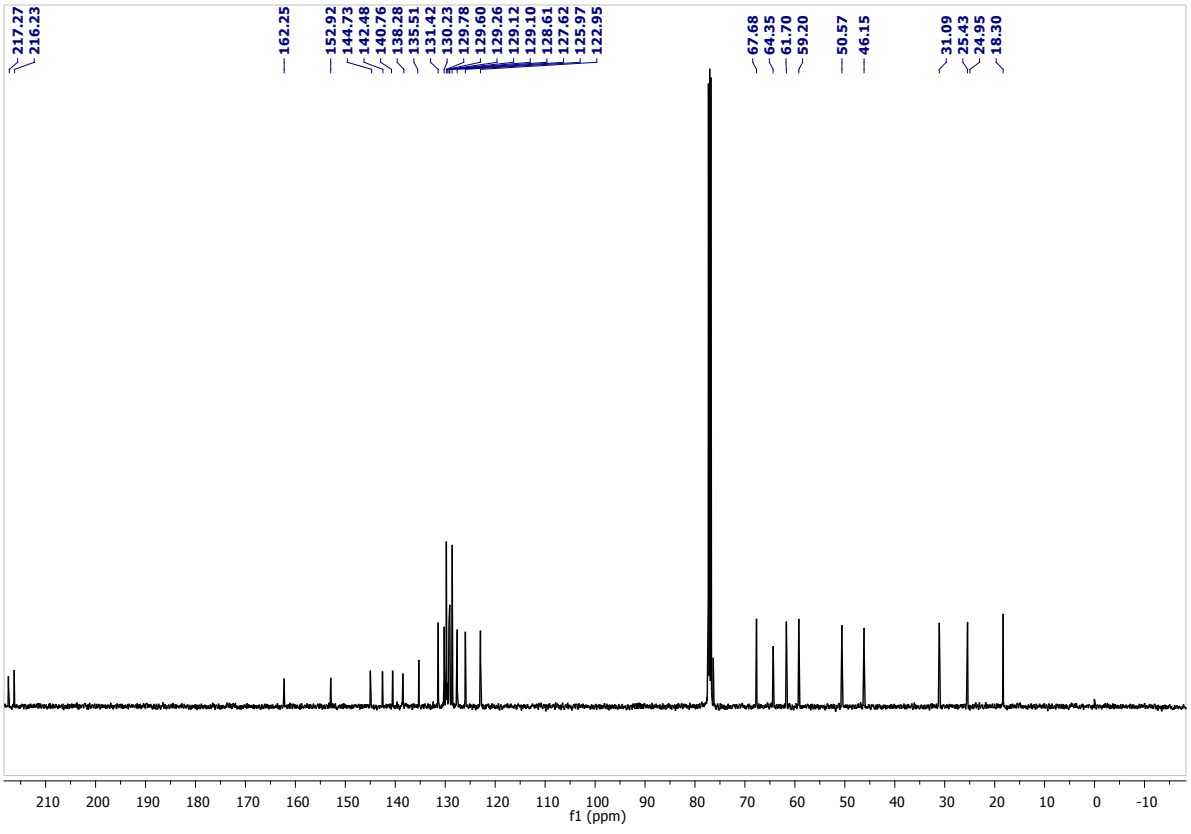
3-nitro-3a',6',7',8',8a',8b'-hexahydro-1'H-spiro[indeno[1,2-b]quinoxaline-11,4'-pyrrolo[3,4-a]pyrrolizine]-1',3'(2'H)-dione (4p):



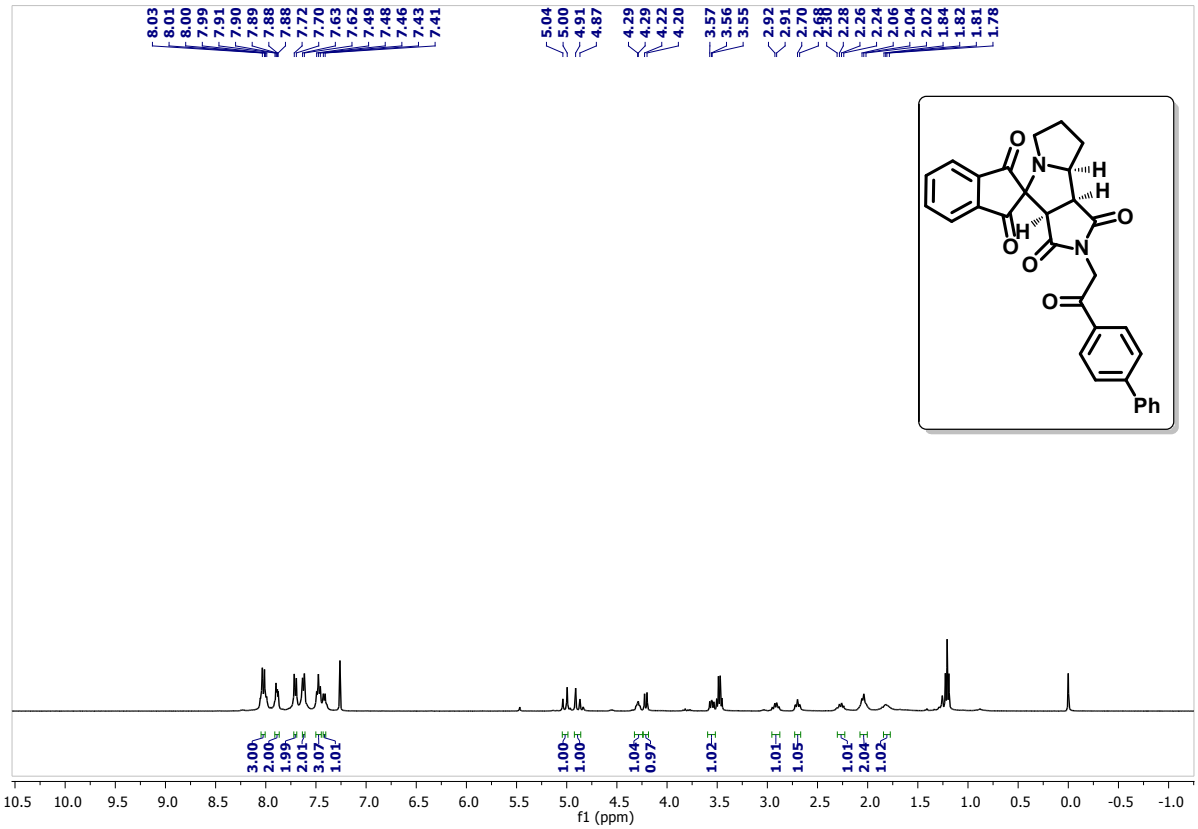


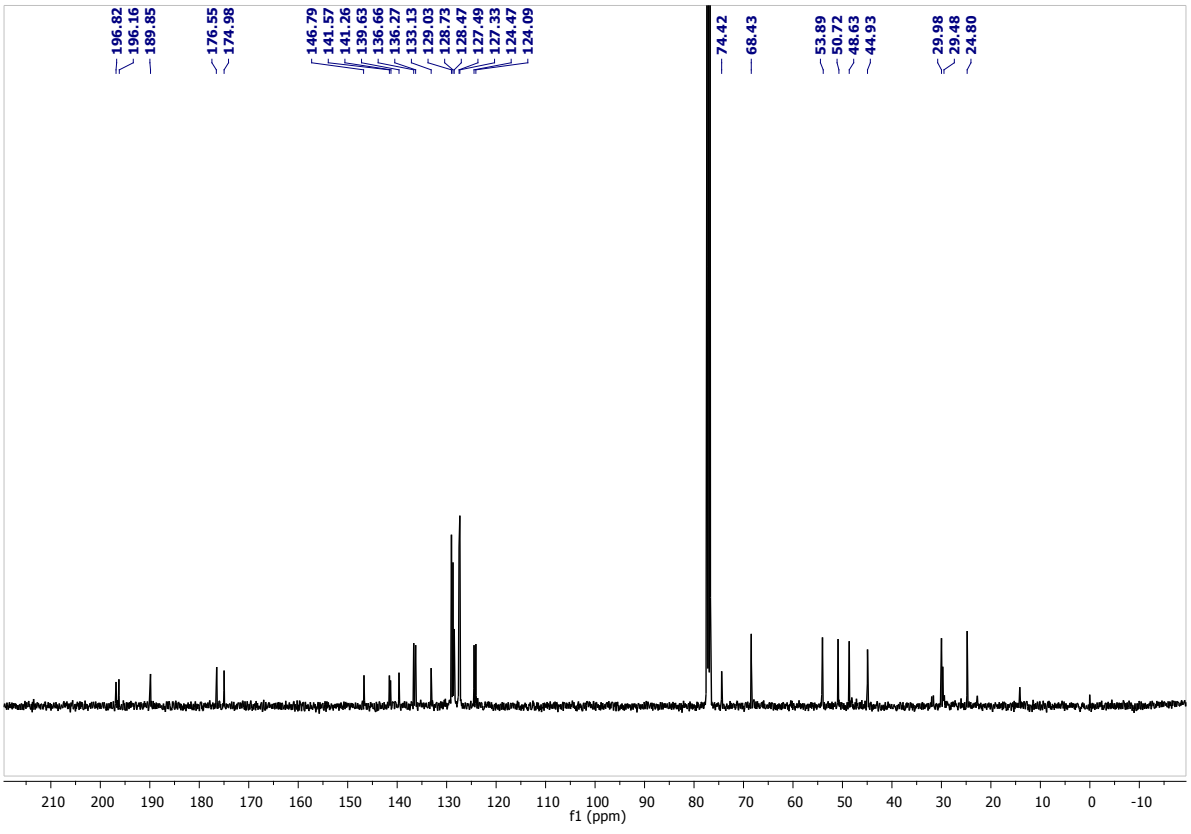
7-benzyl-7-methyl-2,3,8a,8b-tetrahydro-1H-spiro[cyclopenta[a]pyrrolizine-5,11'-indeno[1,2-b]quinoxaline]-6,8(5aH,7H)-dione (4q):



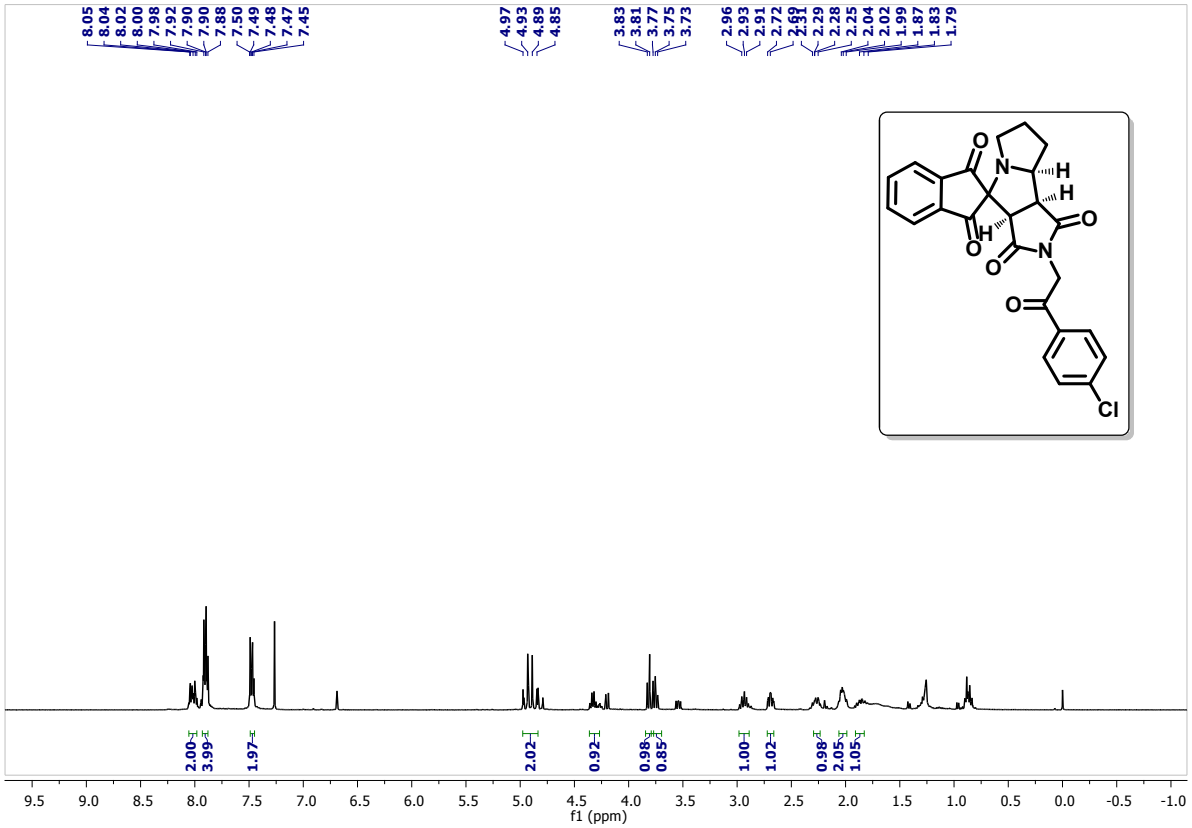


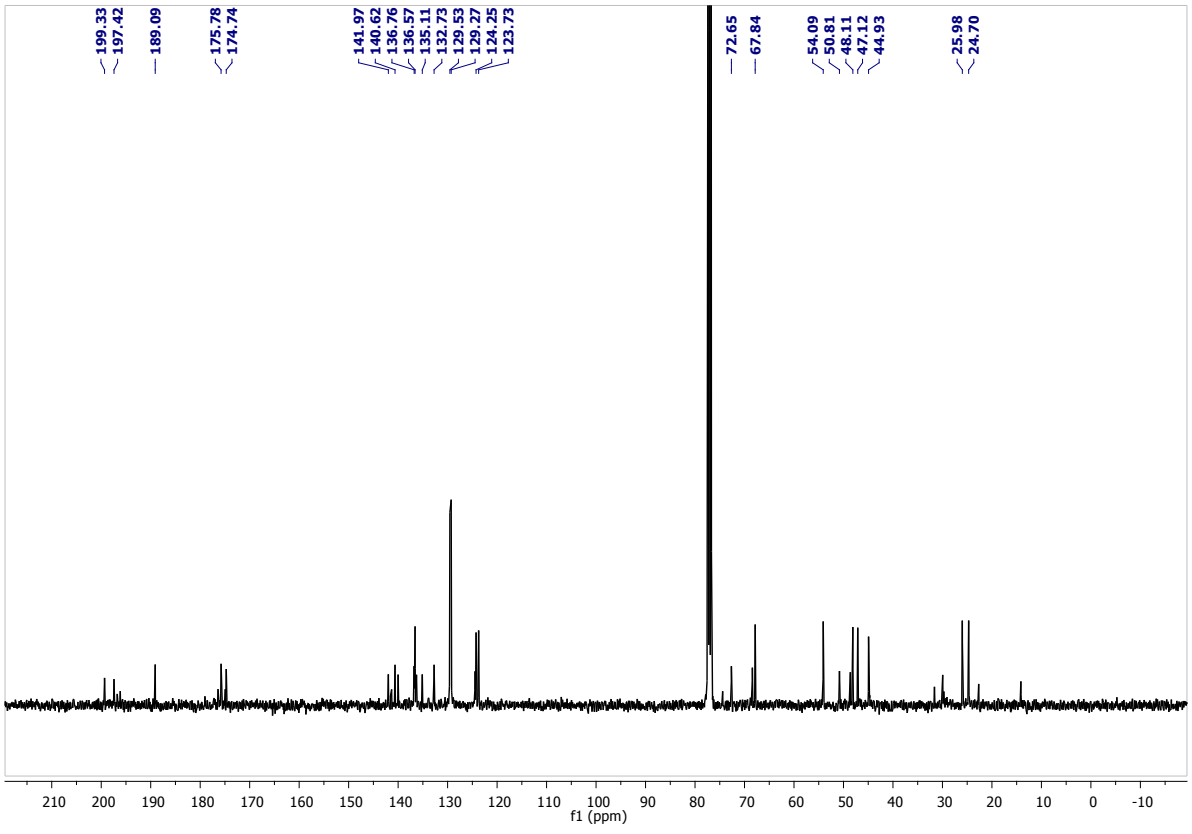
2'-(2-(biphenyl-4-yl)-2-oxoethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (6a):



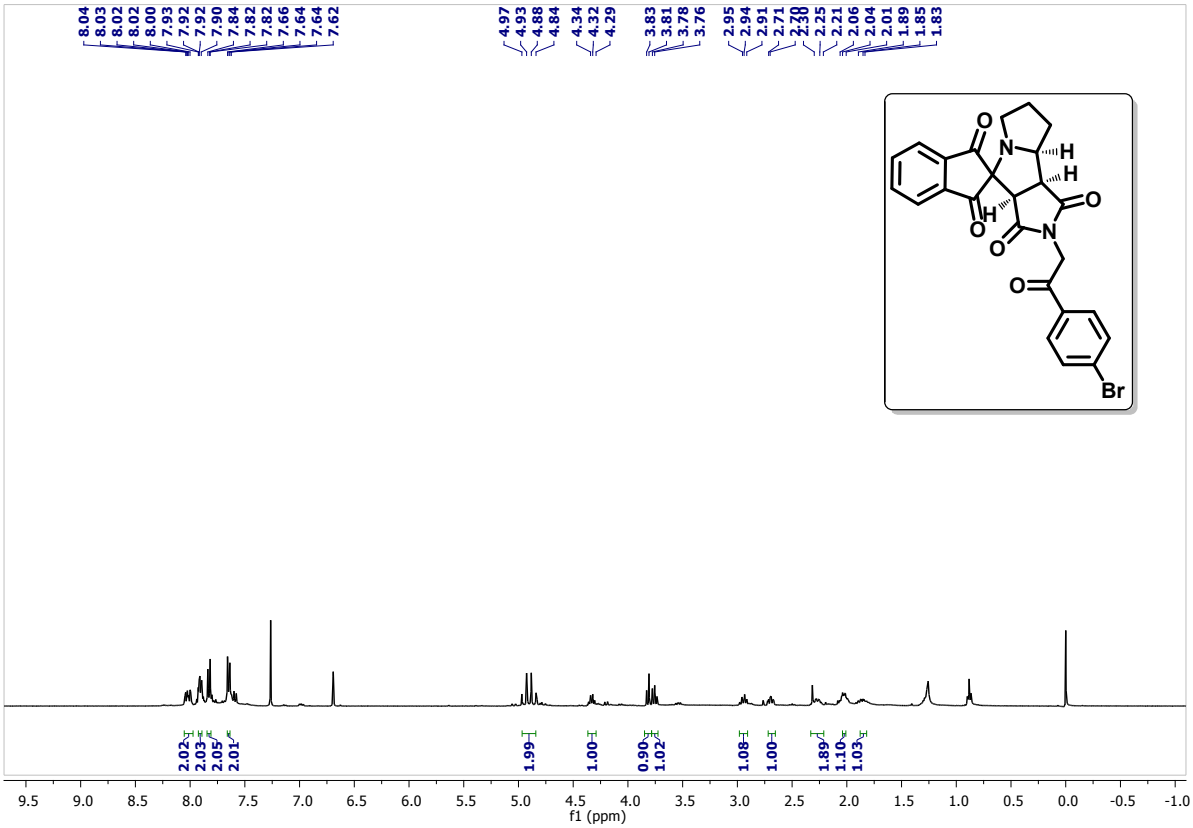


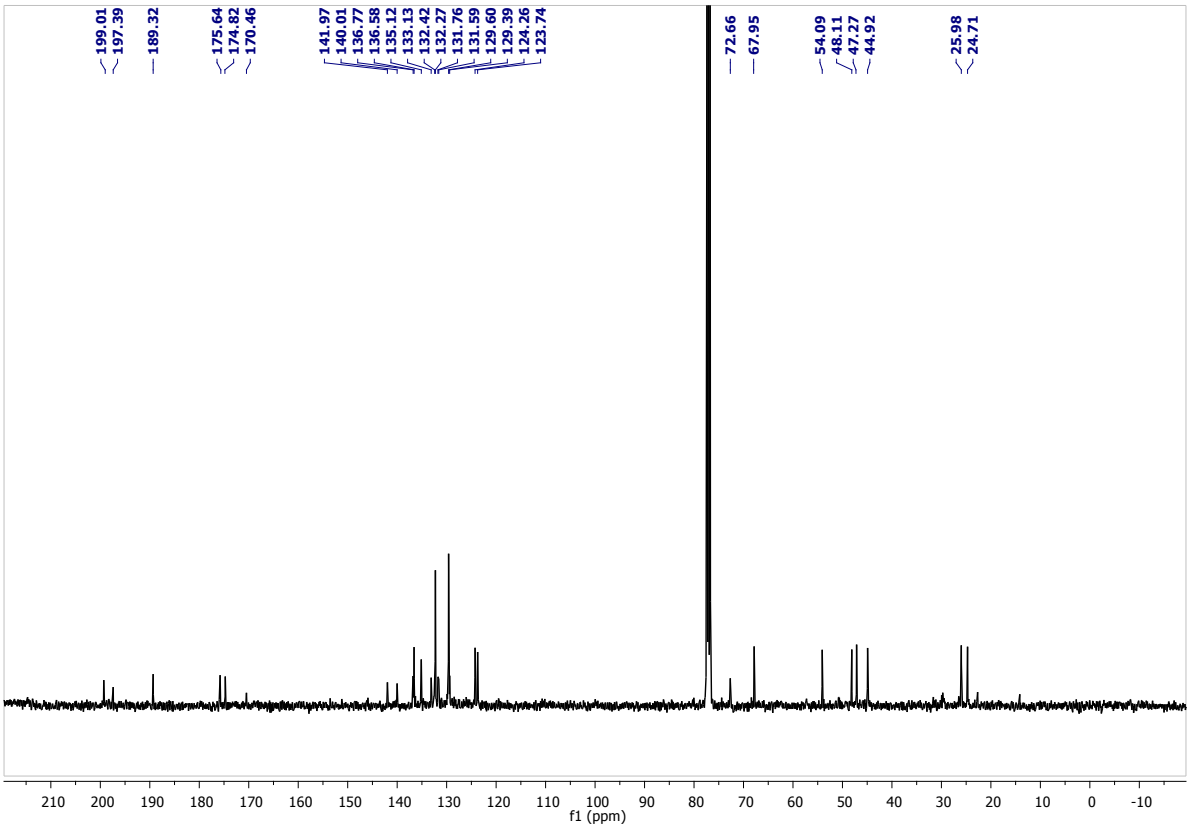
2'-(2-(4-chlorophenyl)-2-oxoethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (6b):



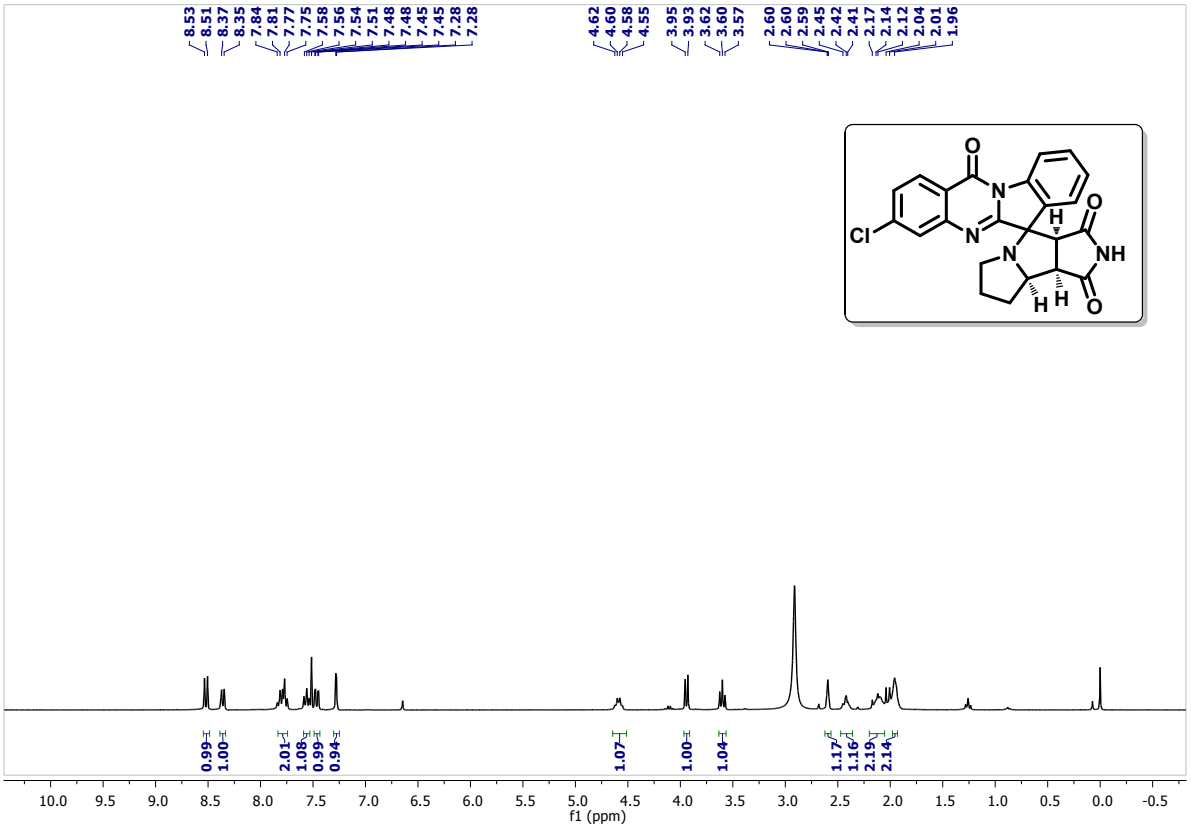


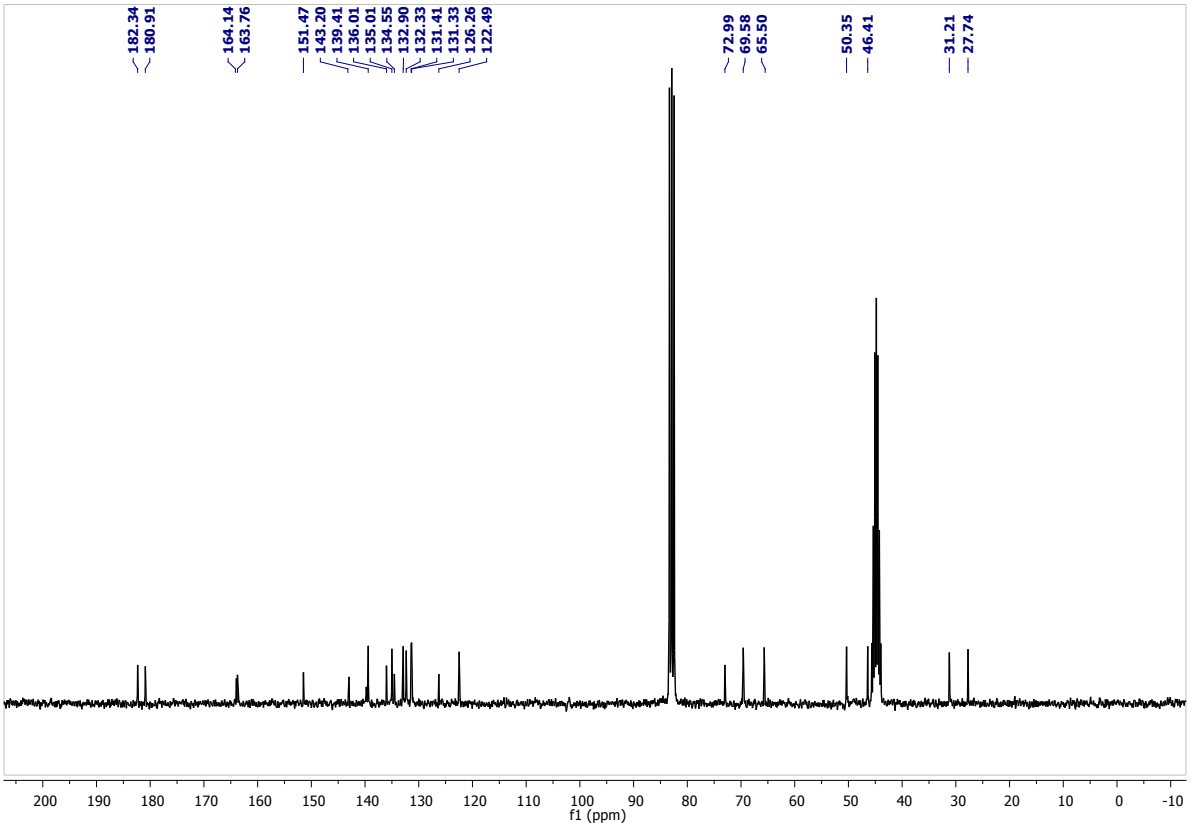
2'-(2-(4-bromophenyl)-2-oxoethyl)-6',7',8',8a'-tetrahydro-1'H-spiro[indene-2,4'-pyrrolo[3,4-a]pyrrolizine]-1,1',3,3'(2'H,3a'H,8b'H)-tetraone (6c):



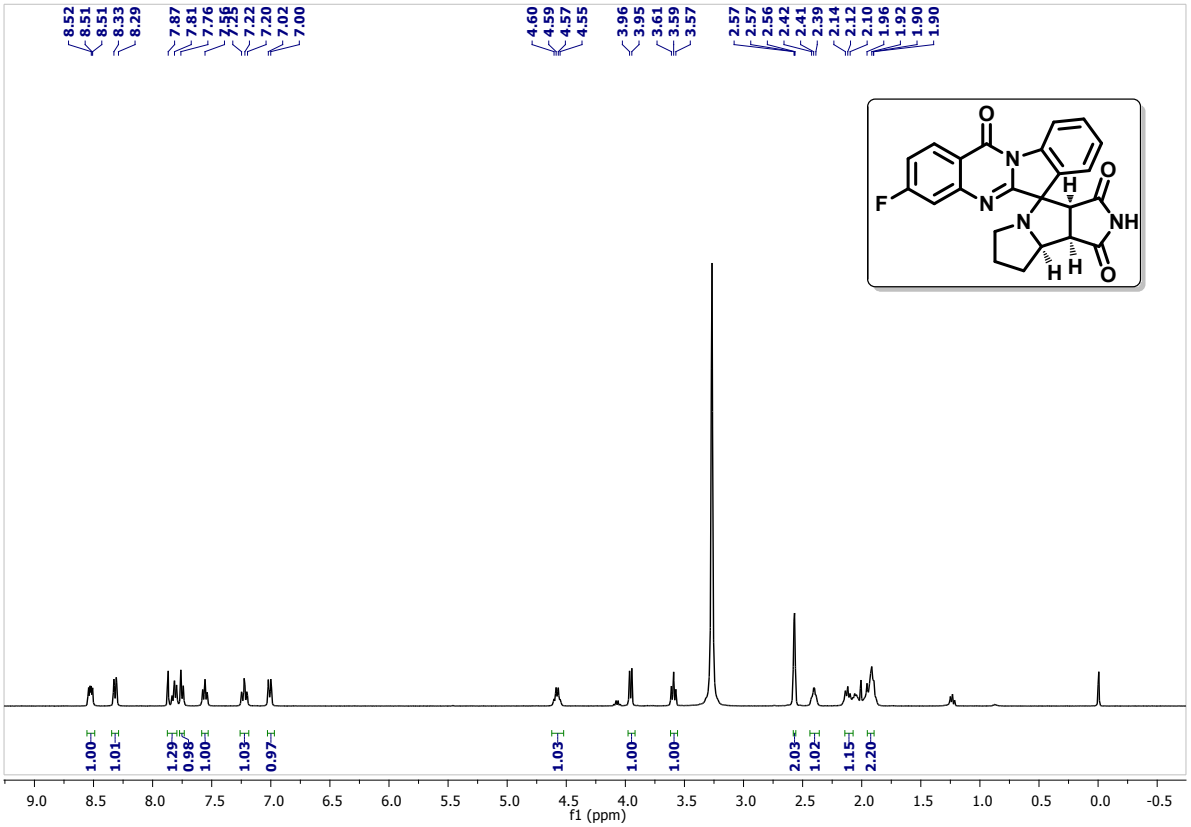


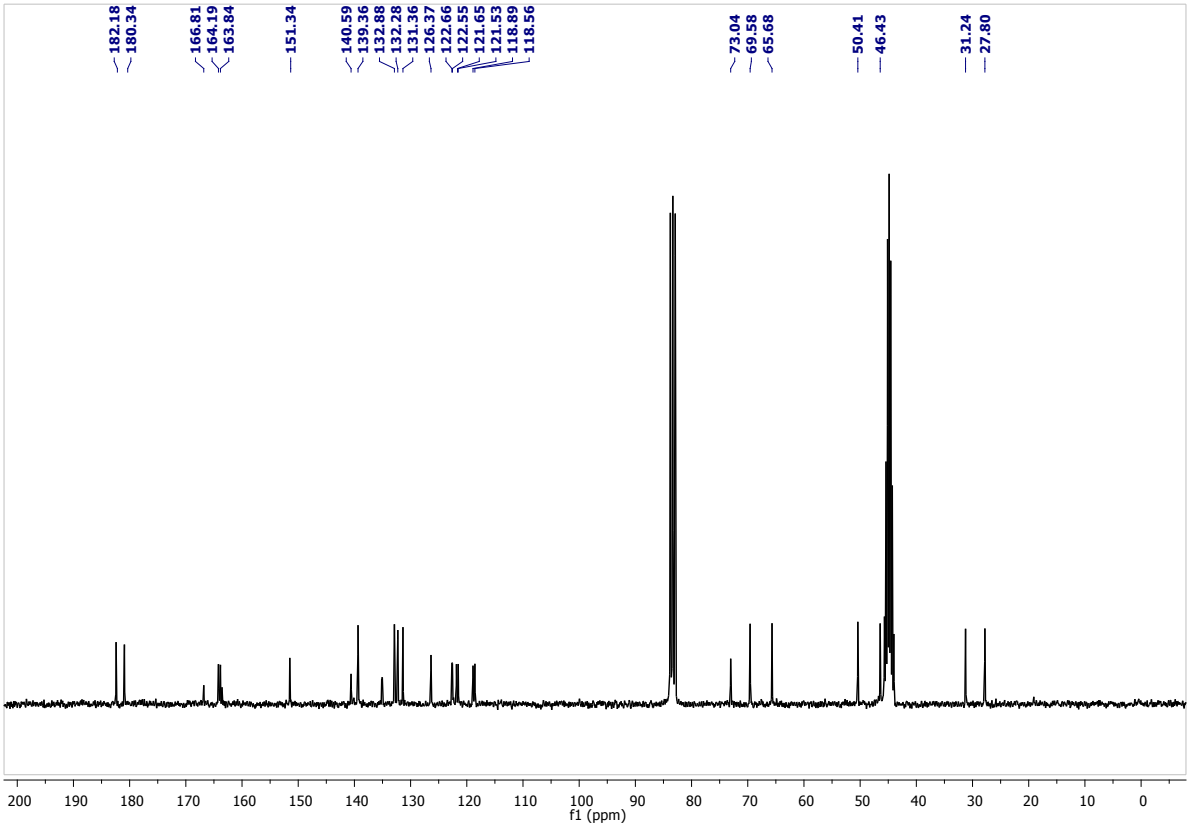
3-chloro-6',7',8',8a'-tetrahydro-1'H,12H-spiro[indolo[2,1-b]quinazoline-6,4'-pyrrolo[3,4-a]pyrrolizine]-1',3',12(2'H,3a'H,8b'H)-trione (9a):



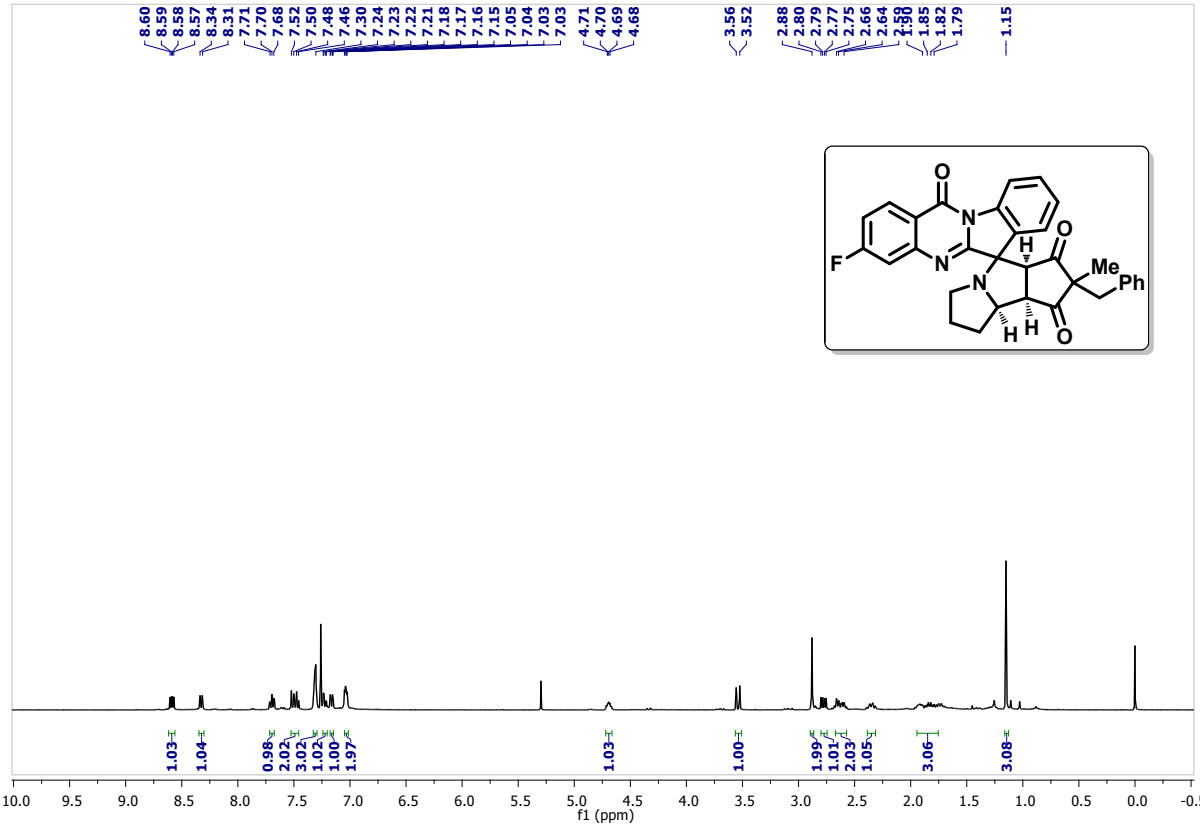


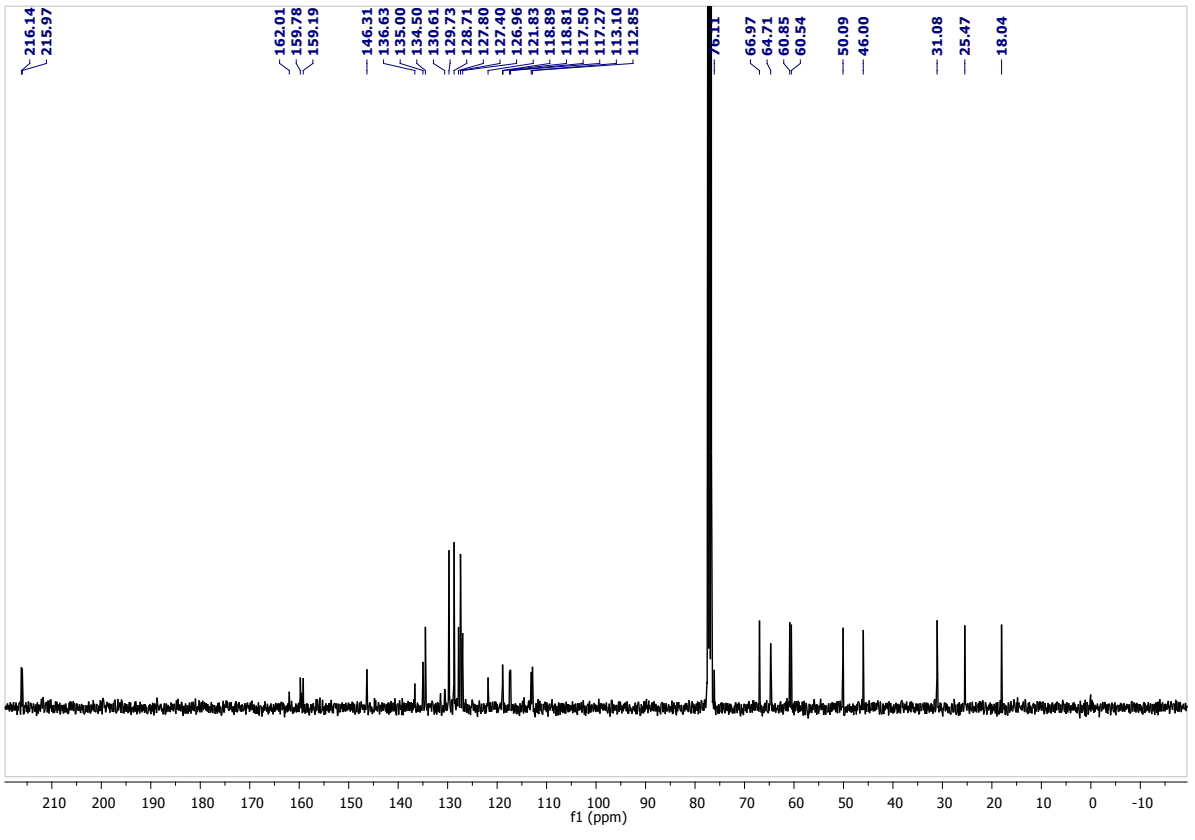
3-fluoro-6',7',8',8a'-tetrahydro-1'H,12H-spiro[indolo[2,1-b]quinazoline-6,4'-pyrrolo[3,4-a]pyrrolizine]-1',3',12(2'H,3a'H,8b'H)-trione (9b):



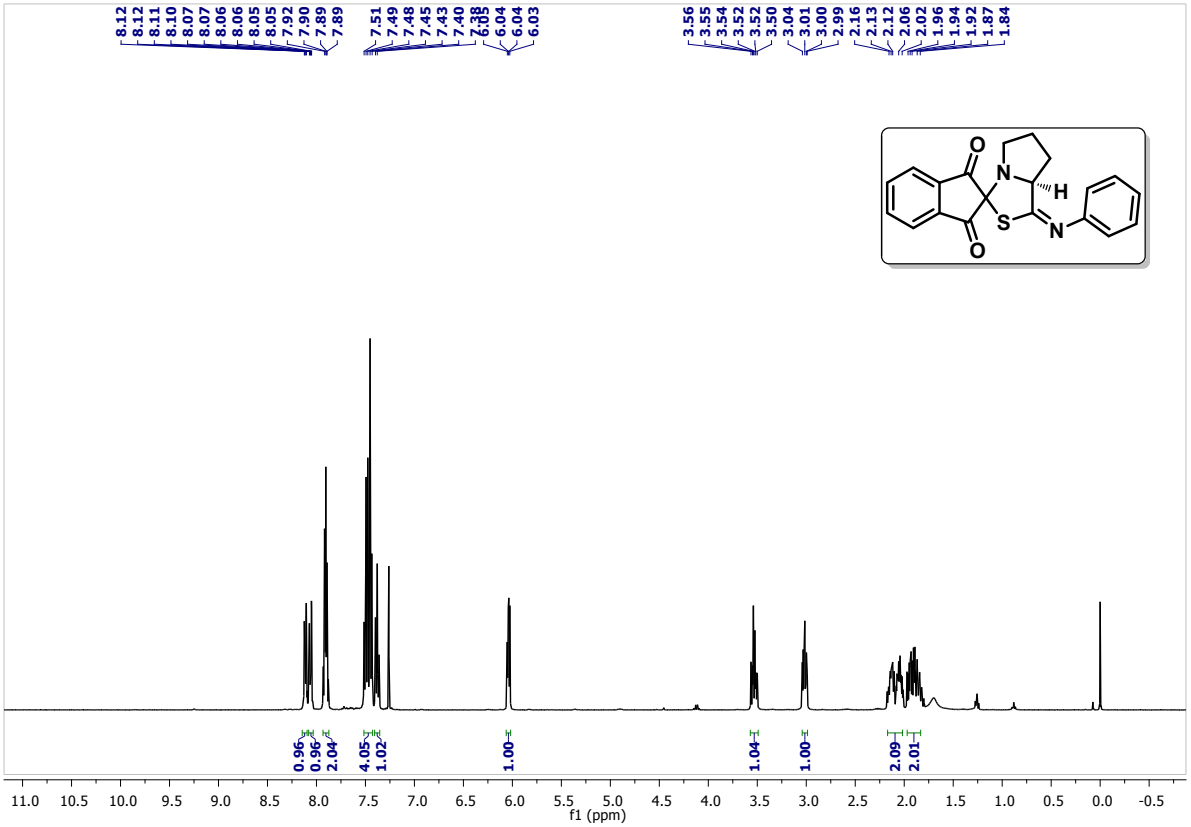


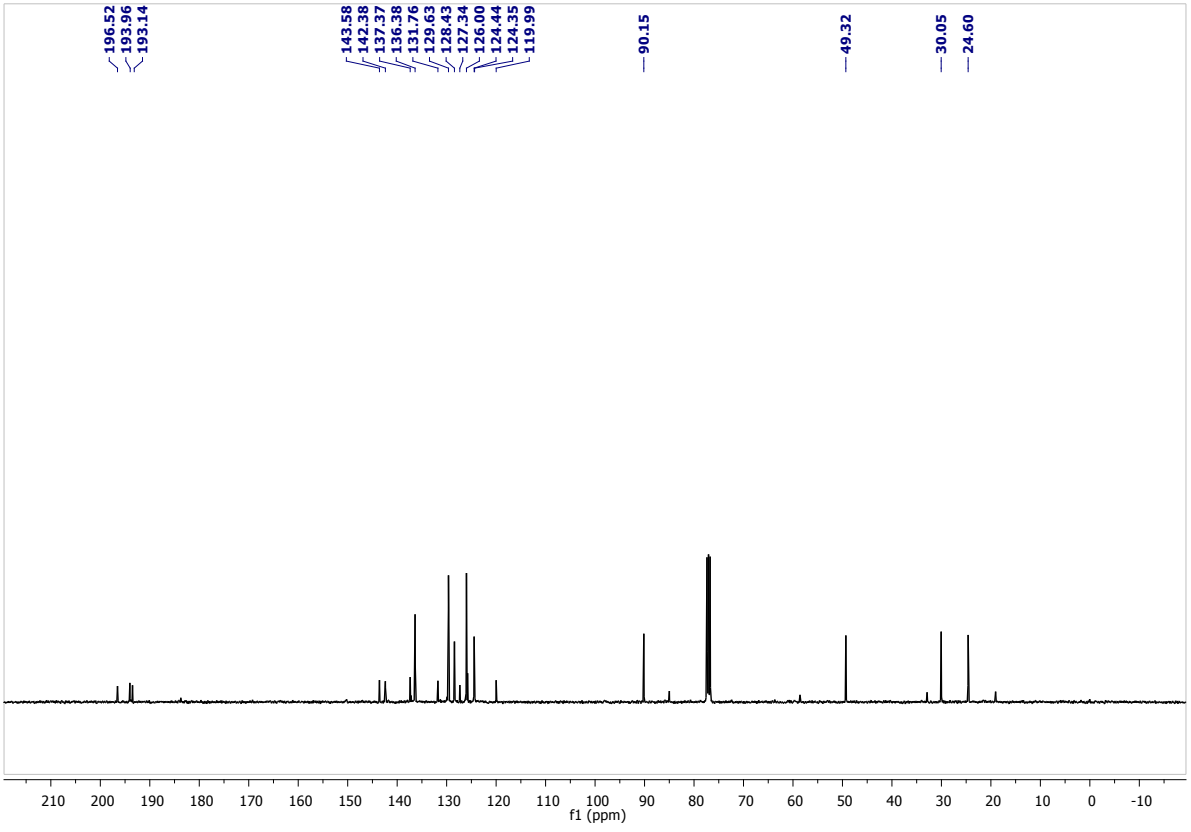
7-benzyl-3'-fluoro-7-methyl-2,3,8a,8b-tetrahydro-1H,12'H spiro[cyclopenta[a]pyrrolizine-5,6'-indolo[2,1-b]quinazoline]-6,8,12'(5aH,7H)-trione (9c):



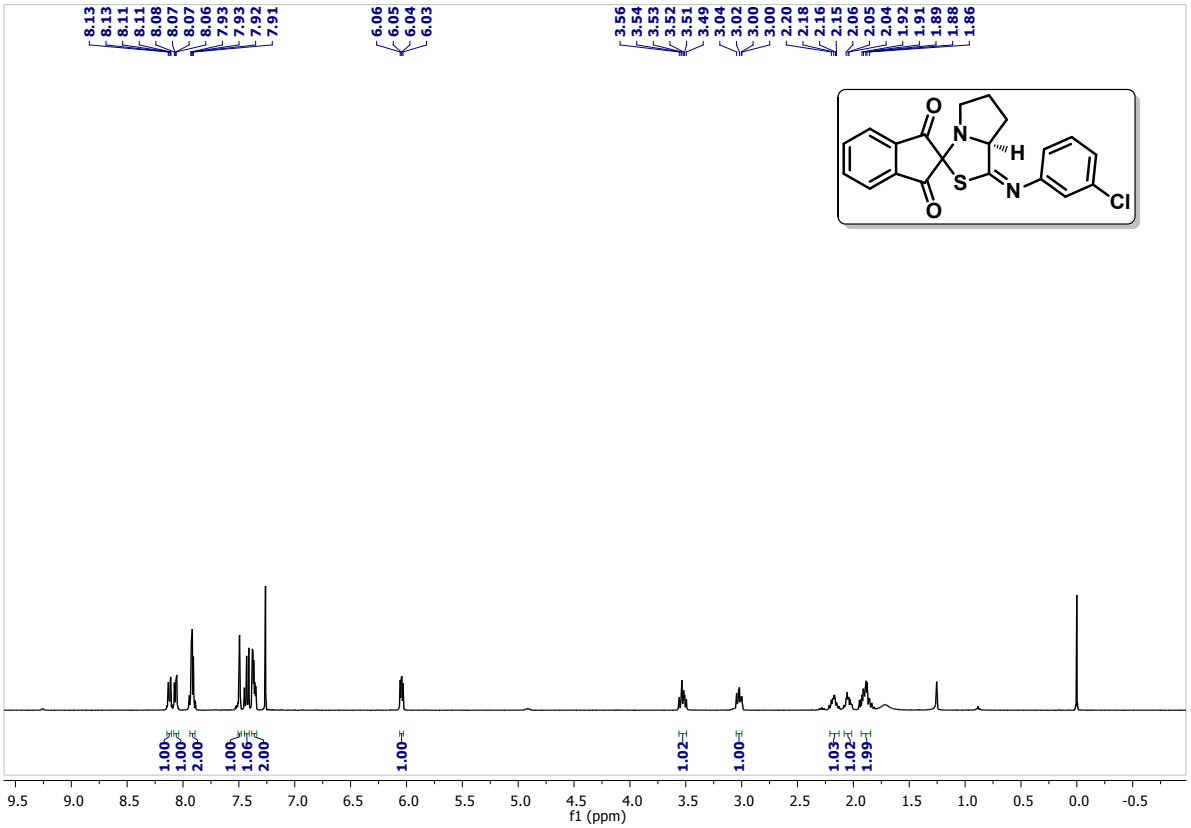


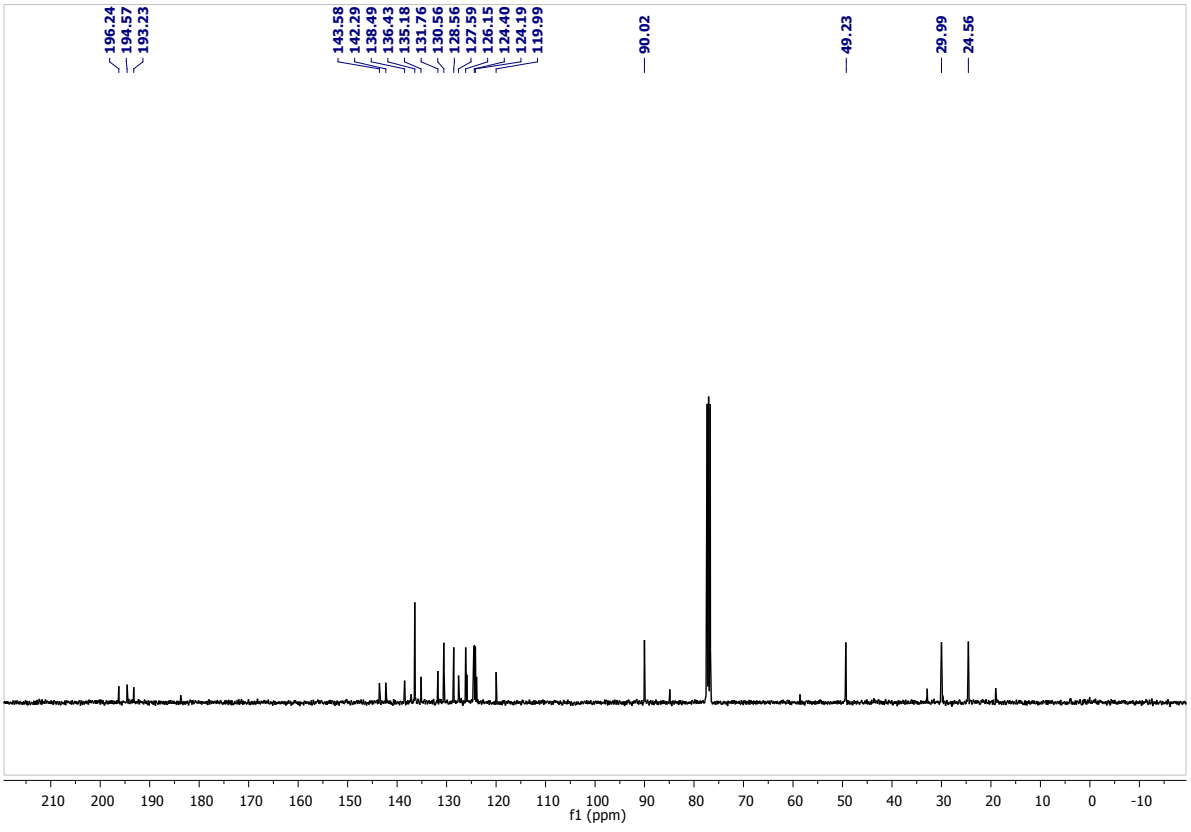
1'-(phenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8a):



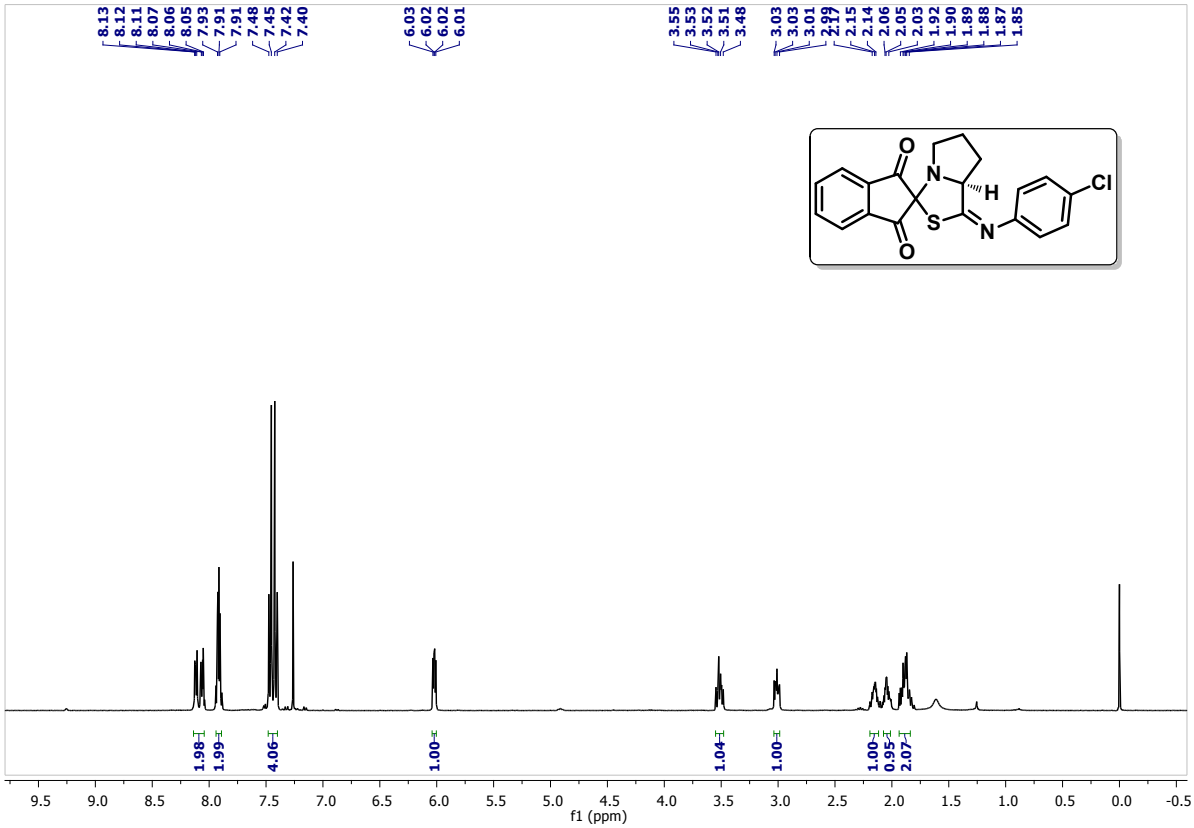


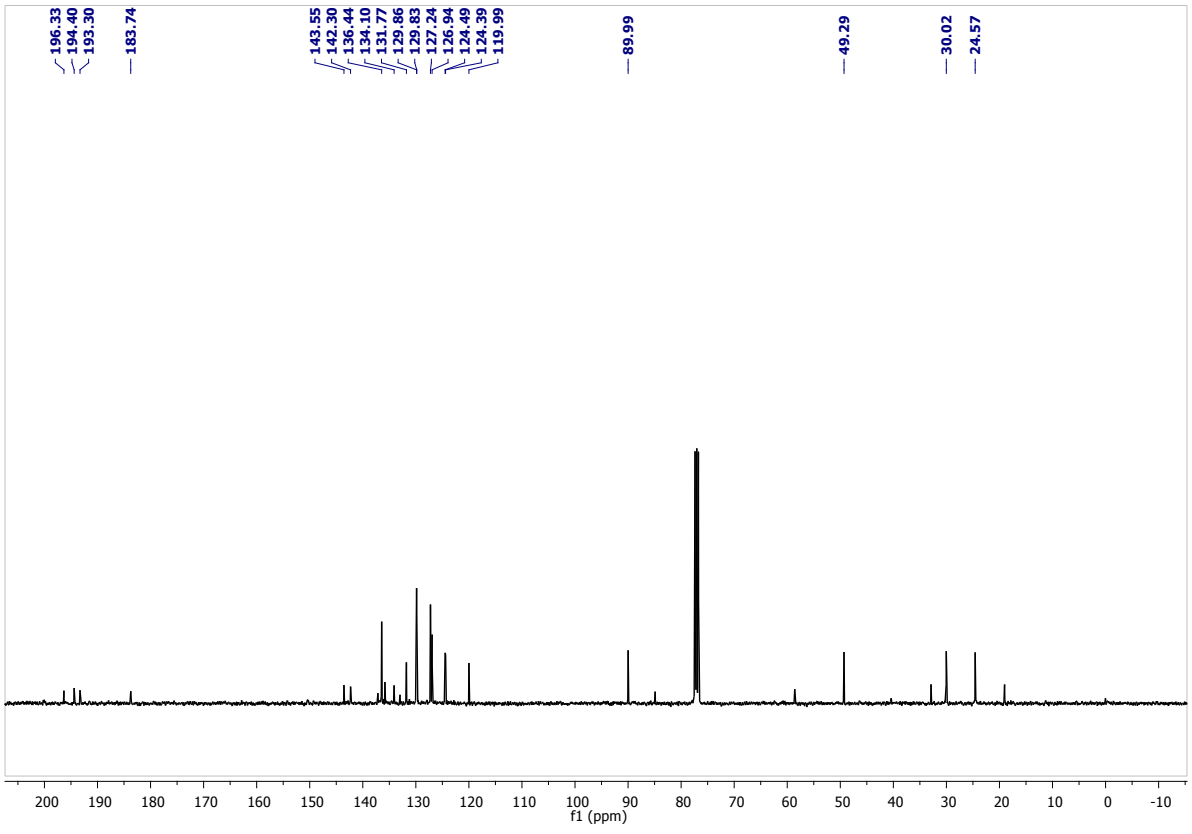
1'-(3-chlorophenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8b):



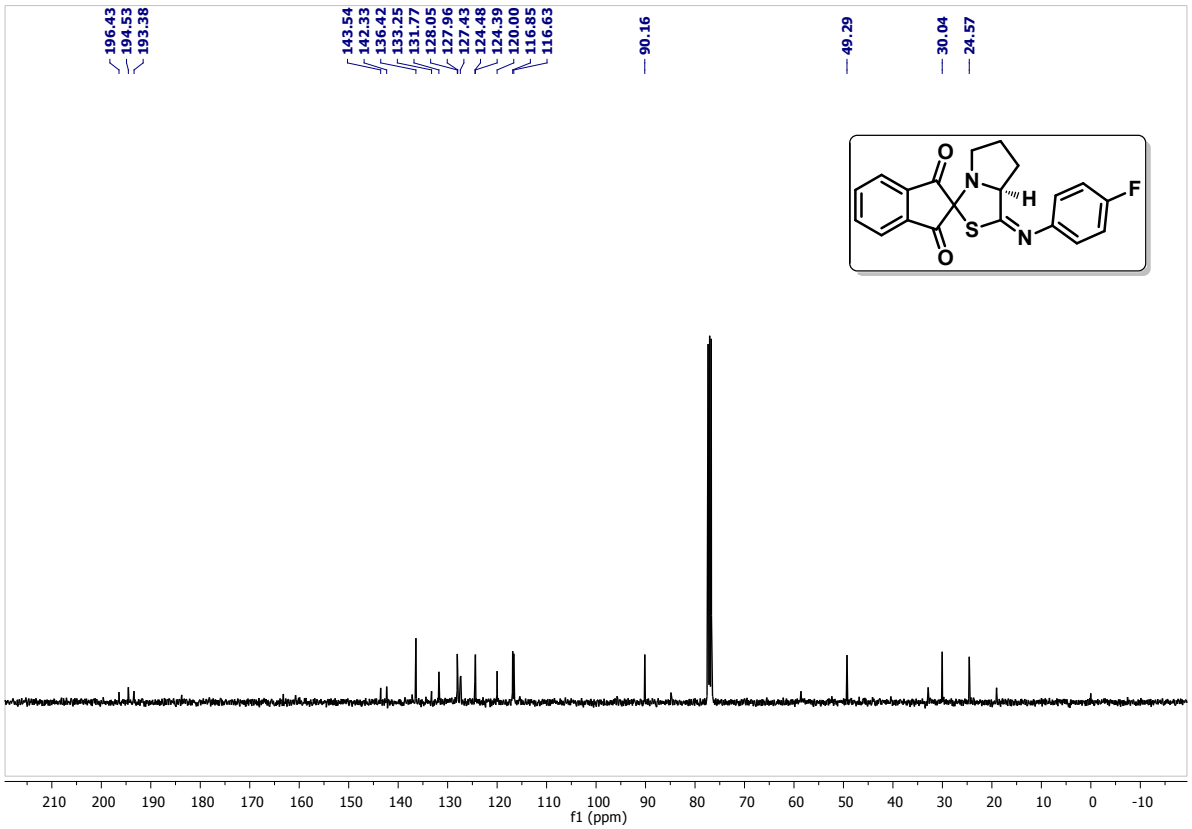


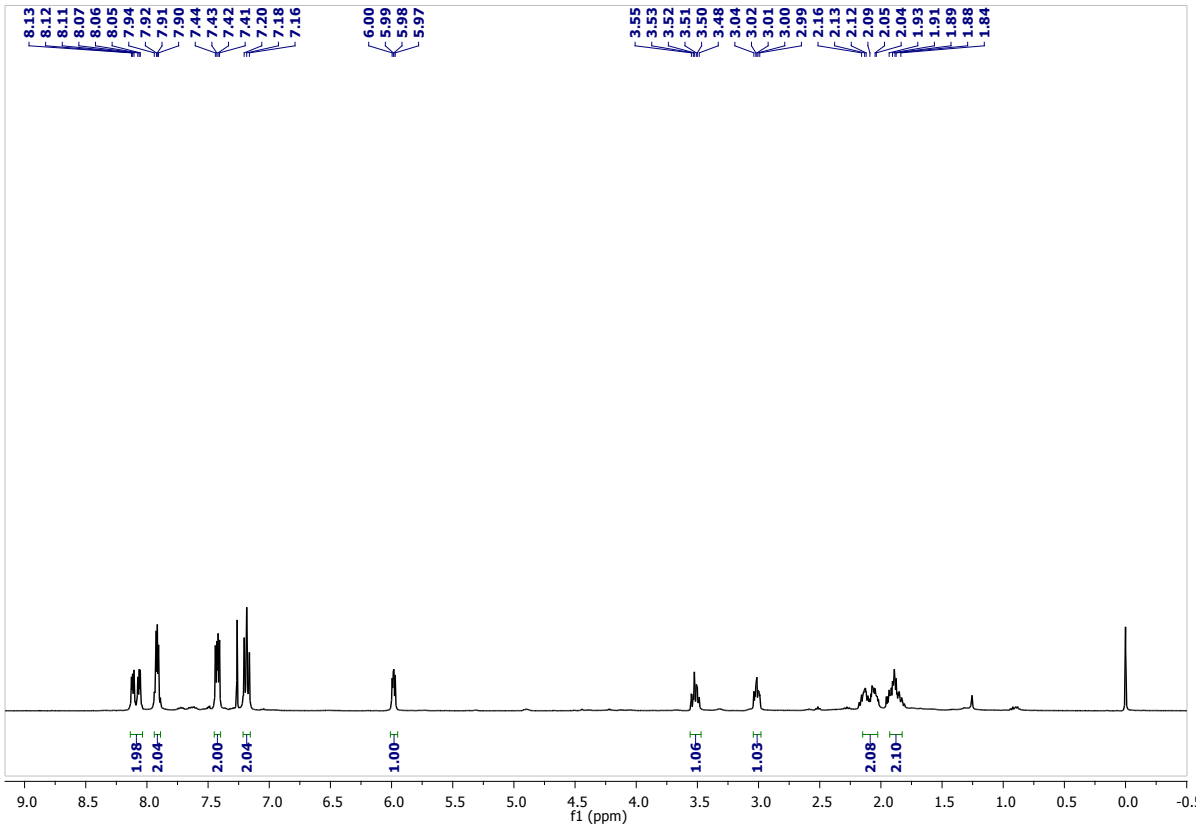
1'-(4-chlorophenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8c):



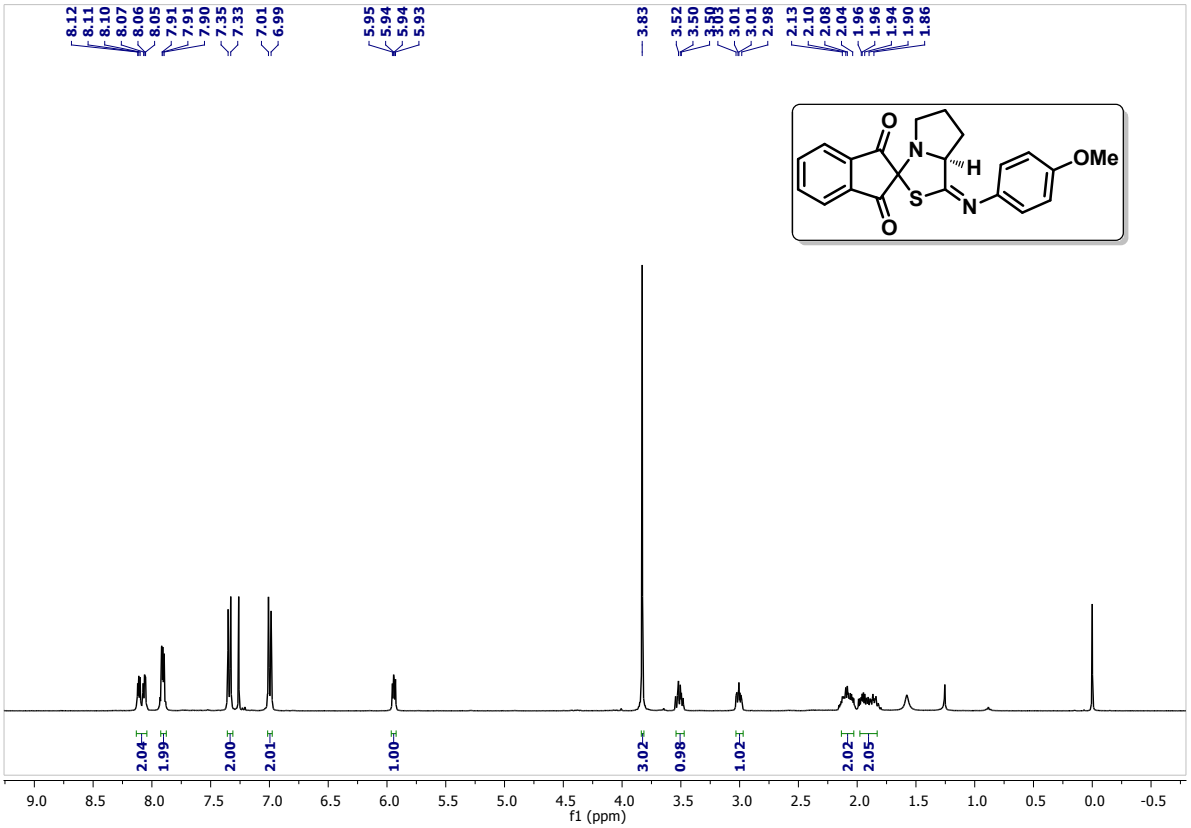


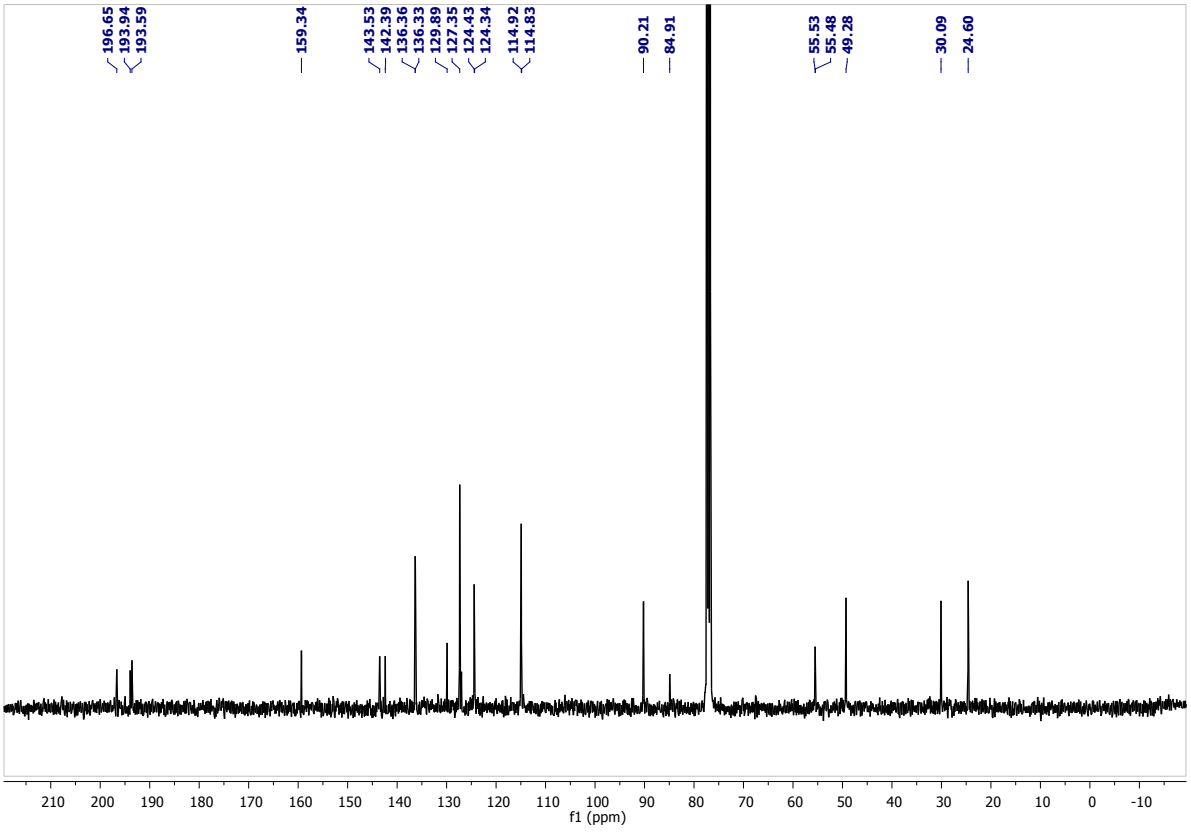
1'-(4-fluorophenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8d):



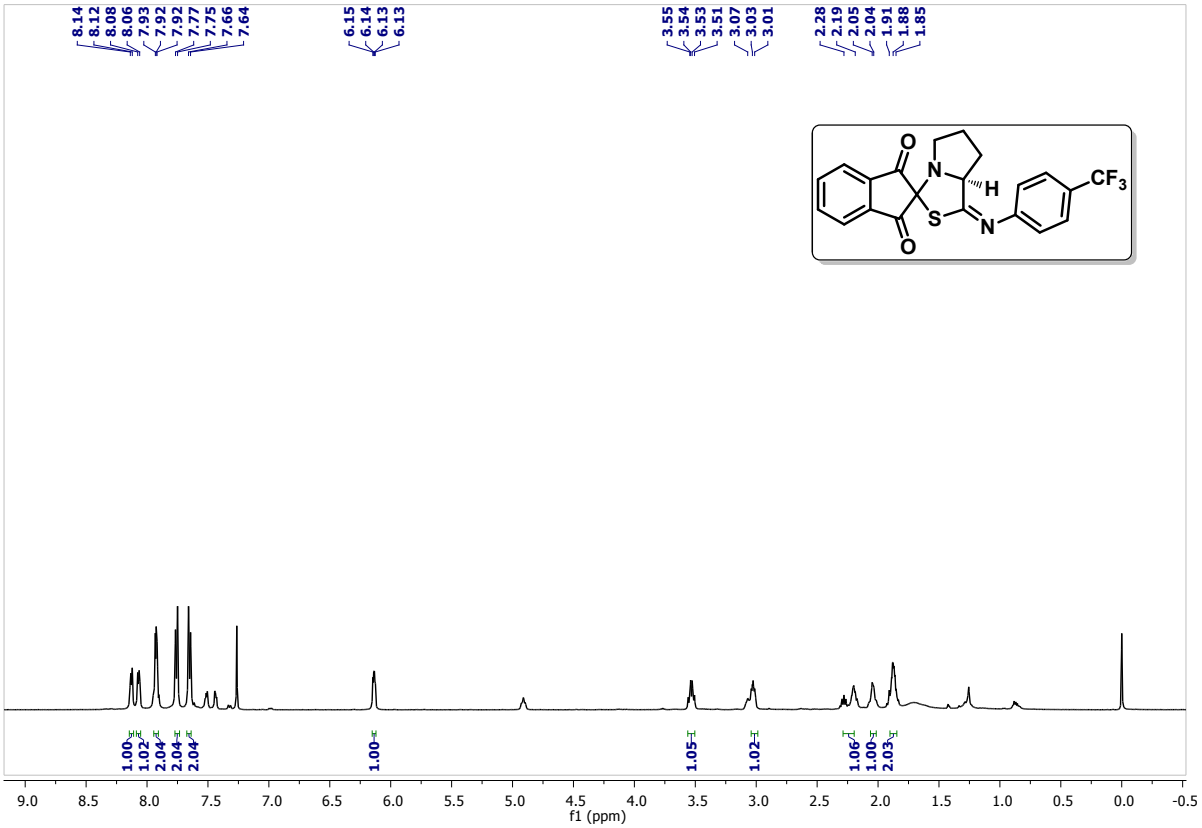


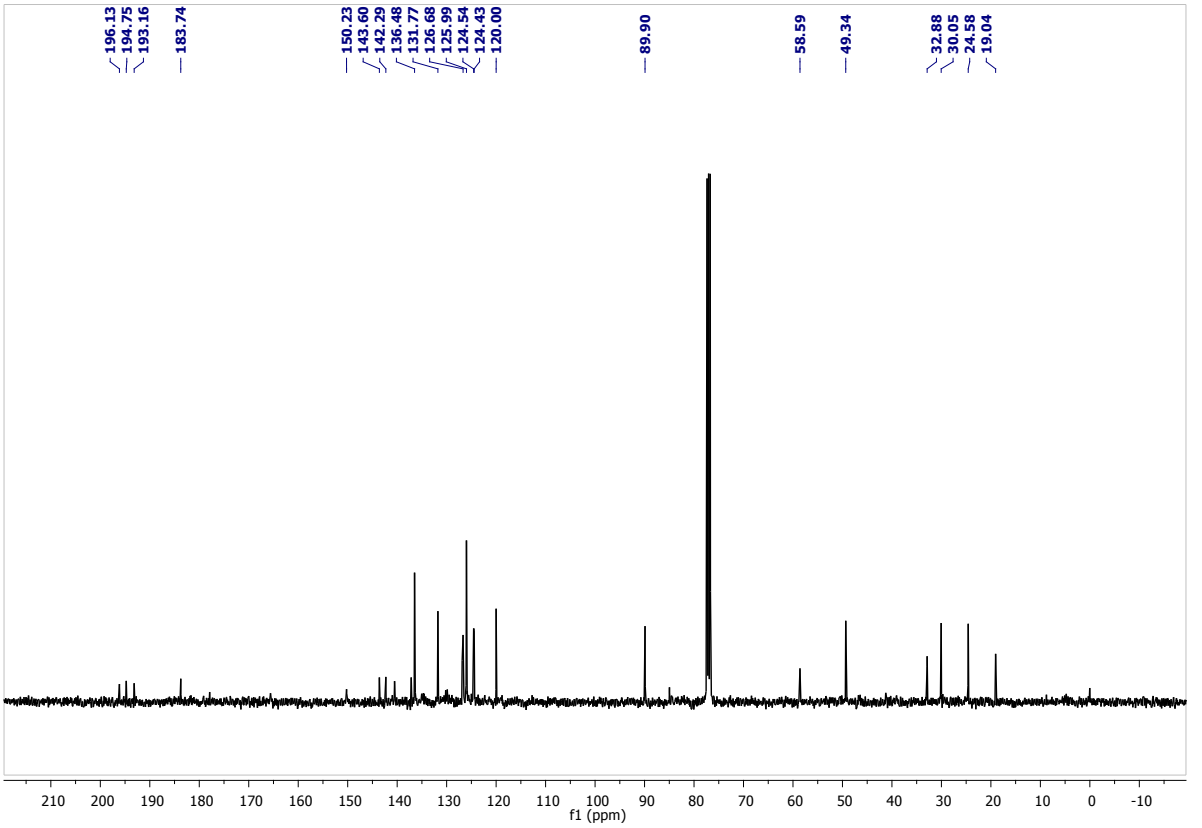
1'-(4-methoxyphenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8e):



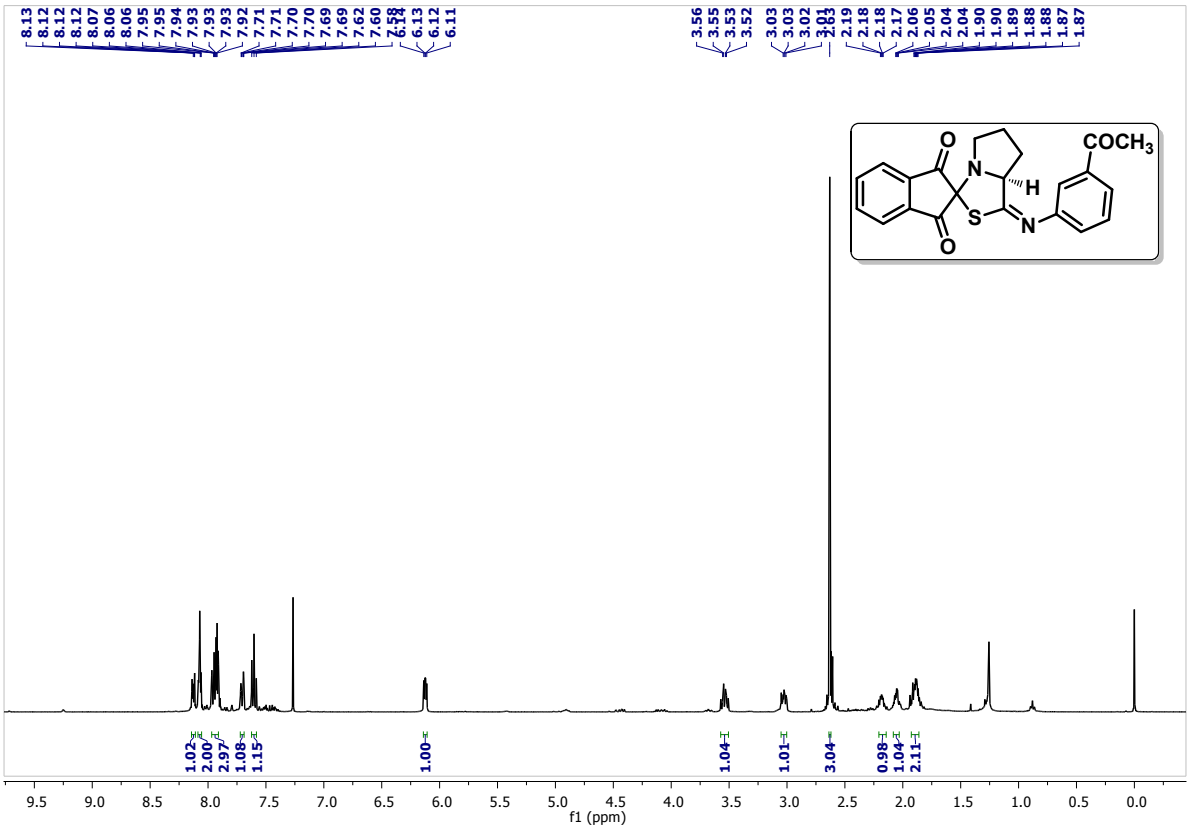


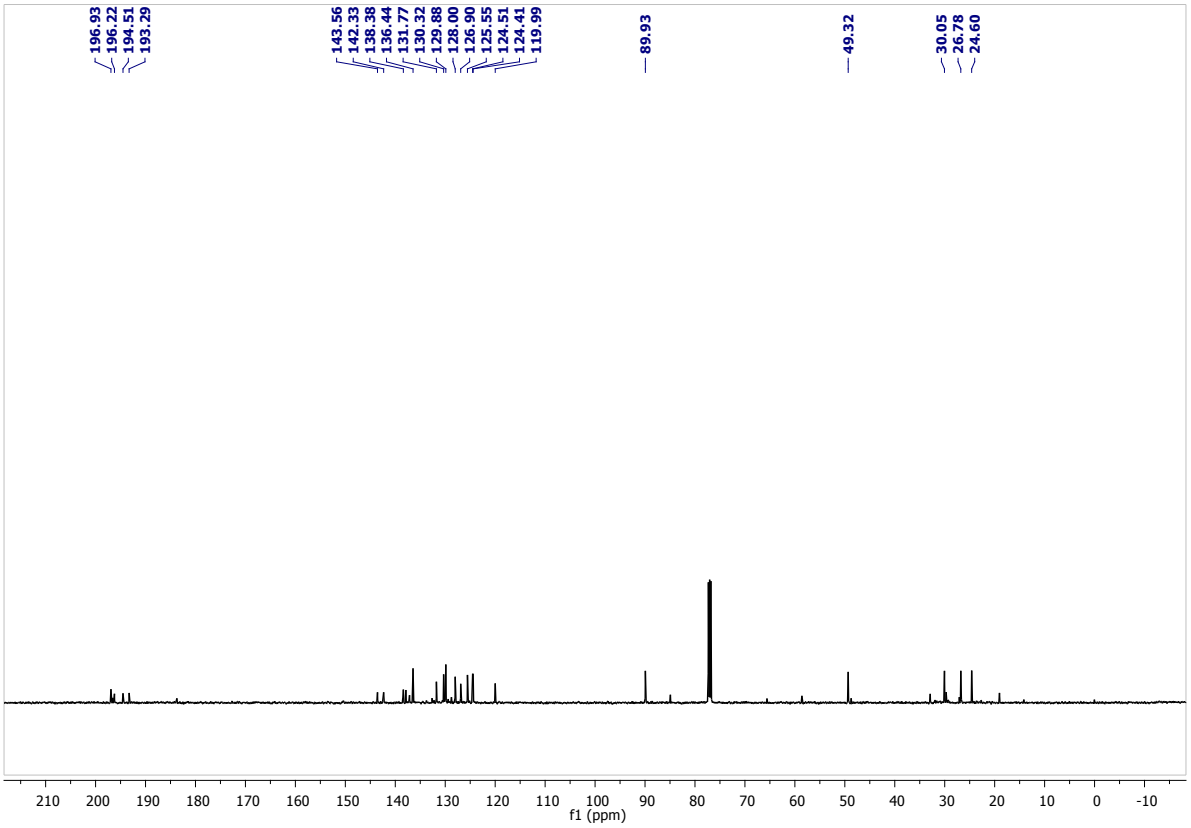
1'-(4-(trifluoromethyl)phenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8f):



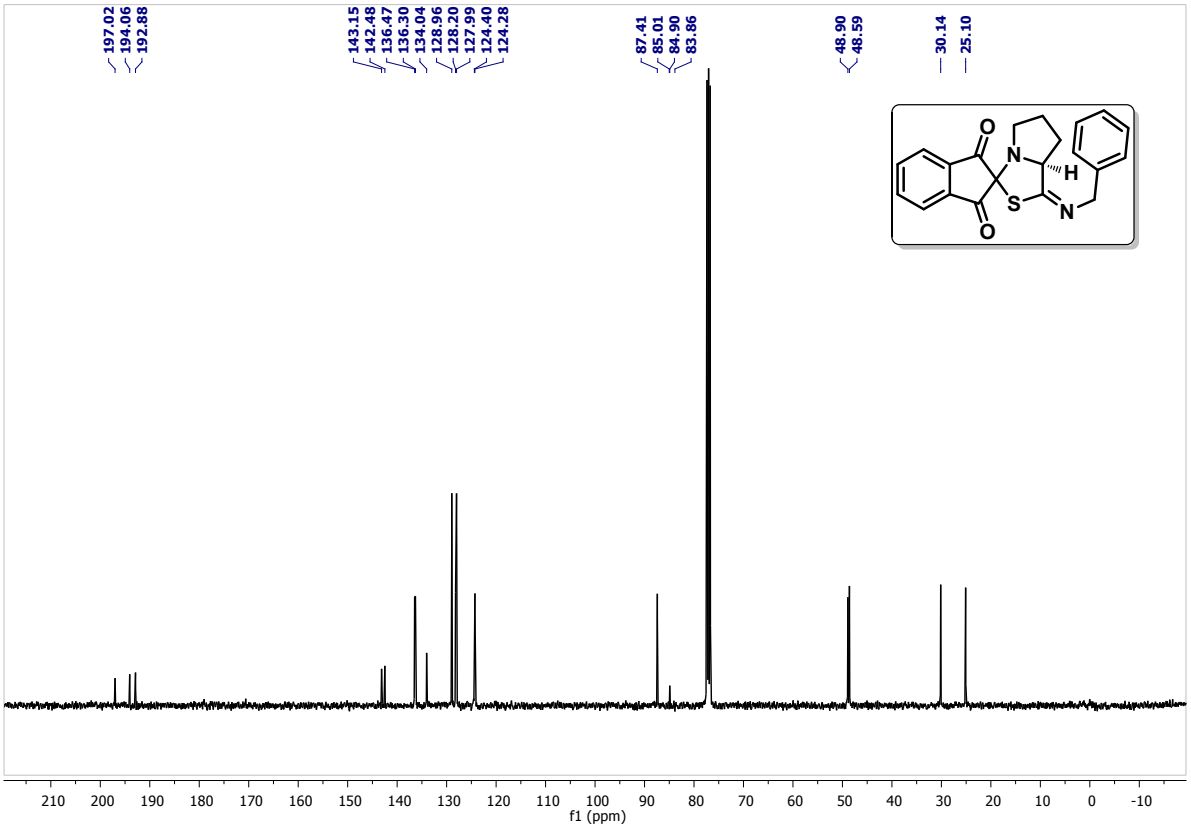


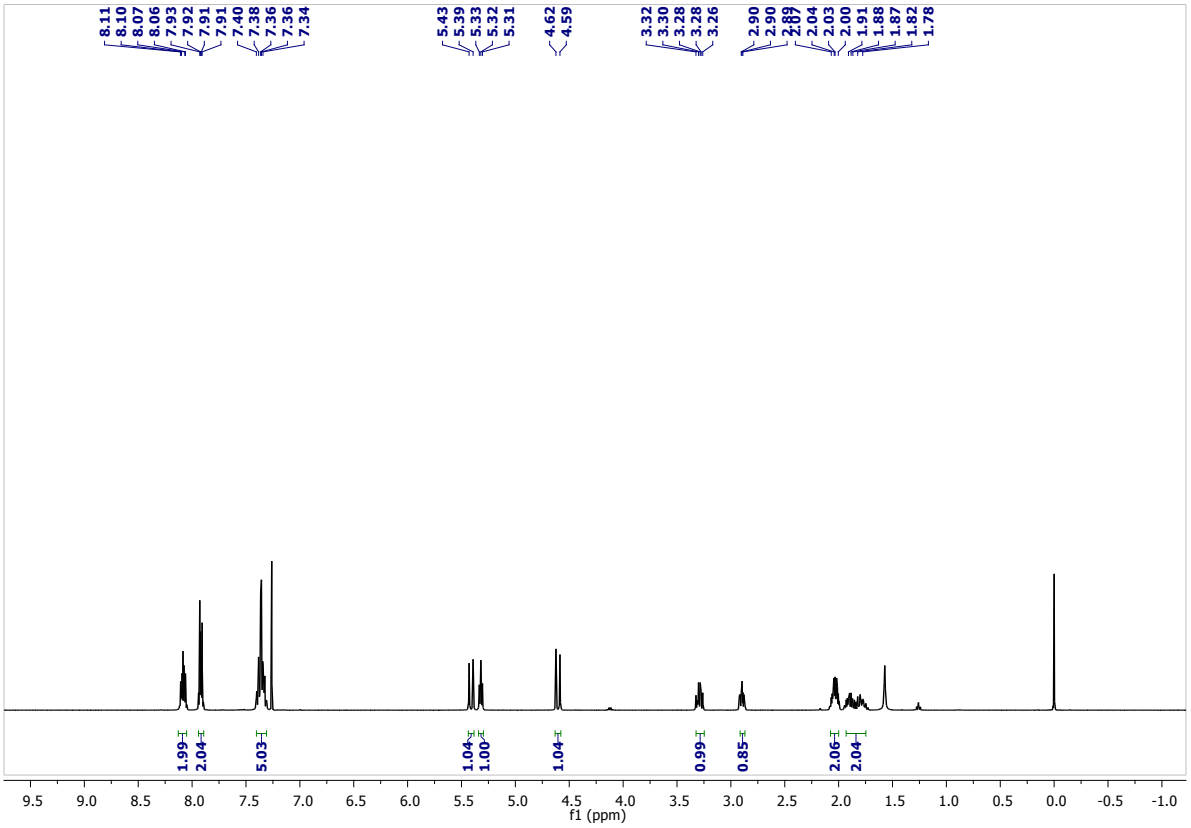
1'-(3-acetylphenylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8g):





1'-(benzylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8h):





1'-(isopropylimino)-5',6',7',7a'-tetrahydro-1'H-spiro[indene-2,3'-pyrrolo[1,2-c]thiazole]-1,3-dione (8i):