Supplementary Information

Catalyst-Free Synthesis of Isoxazolidine from Nitrosoarene and Haloalkyne *via* 1,2-Halo-Migration/[2+3] Cycloaddition Cascade

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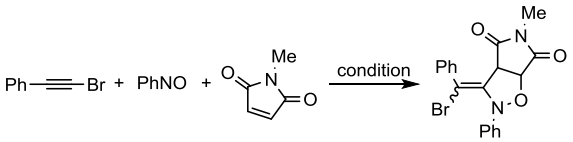
1. Optimization of reaction conditions

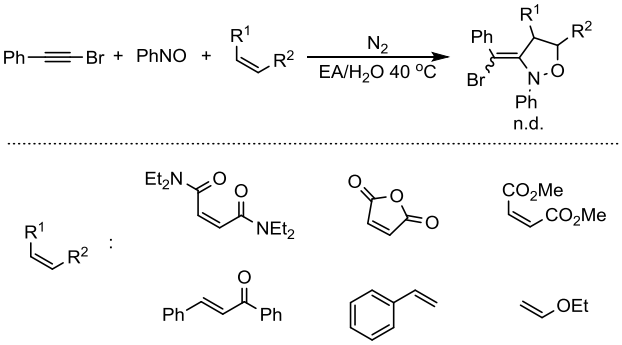


1a 2a 3a 4a

entry	catalyst	solvent	Temp. (^{o}C)	**4a** yield (%)[b]	**Z:E**
1	-	$CHCl_3$	40	40	69:31
2	TMSOTf (10%)	$CHCl_3$	40	trace	-
3	AcOH (50%)	$CHCl_3$	40	trace	-
4	-	H_2O	40	trace	-
5	-	$CHCl_3/H_2O$[c]	40	71	70:30
6	-	THF/H_2O[c]	40	78	75:25
7	-	DCE/H_2O[c]	40	79	71:29
8	-	$Acetone/H_2O$[c]	40	50	70:30
9	-	$MeCN/H_2O$[c]	40	60	68:32
10	**-**	**EA/H_2O**[c]	**40**	**89**[d]	**69:31**
11	-	EA/H_2O[c]	60	50	69:31
12	-	EA/H_2O[c]	rt	53	71:29
13[e]	-	EA/H_2O[c]	40	72	70:30
14	-	EA	40	52	75:25

[a]Unless otherwise noted, the reaction was performed with **1a** (0.4 mmol), **2a** (0.6 mmol) and **3a** (0.2 mmol) for 11 h, under N_2 atmosphere. [b]The yield was determined by ^{1}H NMR using CH_3NO_2 as an internal standard. [c]Organic solvent : H_2O = 3:1. [d]isolated yield. [e] under air atmosphere.

2. Attempts of other alkenes as trapping agents



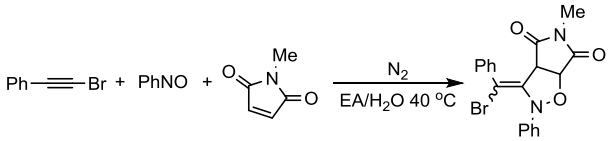
3. Experimental procedures and spectroscopic data

3.1 General information

All reactions were carried out under an inert atmosphere of dry N_2 in Schlenk tube, solvents were

purified by standard method. ^{1}H, ^{13}C, ^{19}F NMR spectra were recorded on either a Bruker AVANCE 400 (400 MHz for ^{1}H; 101 MHz for ^{13}C; 376 MHz for ^{19}F) or Bruker AVANCE 500 (500 MHz for ^{1}H; 126 MHz for ^{13}C). ^{1}H NMR and ^{13}C NMR chemical shifts were determined relative to internal standard TMS at δ 0.0 and ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as external standard. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Infrared (IR) spectra are recorded on a Nicolet 210 spectrophotometer and were recorded in potassium bromide (KBr) pellet. Mass spectra (MS) were obtained using ESI mass spectrometer. Melting points were determined using a hot stage apparatus. All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature.

3.2 Typical procedure for the synthesis of 4

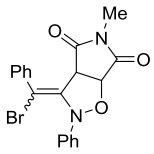


1a **2a** **3a** **4a**

In a Schlenk tube with a magnetic bar under nitrogen atmosphere, EA (1 ml), H_2O (0.3 ml), the substrates of bromoalkyne **1a** (72 mg, 0.4 mmol), nitrosobenzene **2a** (64 mg, 0.6 mmol) and maleimide **3a** (22 mg, 0.2 mmol) were added. The mixture was stirred at 40 ^{o}C for 11 h until the substrate **3a** was completely consumed. After adding Na_2SO_4 to remove water, the mixture was washed by EA for three times. The combined organic solvent was evaporated by rotary evaporator, and the residue was purified by flash column chromatography on silica gel using EtOAc/petroleum ether as eluent to afford the product **4a** (71 mg, 0.18 mmol).

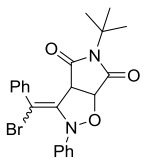
The procedures of other substrates **1**, nitrosobenzenes **2** and maleimide **3**, were similar with that mentioned above.

3-(bromo(phenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione (4a)



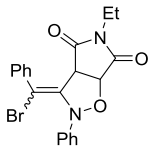
89% yield (71 mg, Z:E = 69:31), single Z-isomer (64 mg) could be obtained after silica gel isomerization at 40 ^{o}C, yellow solid (Z-isomer), m. p. (Z-isomer) 119-120 ^{o}C, R_f (Z-isomer) = 0.45 (EtOAc/petroleum ether = 1/3), R_f (E-isomer) = 0.45 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.00 – 7.85 (m, 2H), 7 .41 – 7.36 (m, 3H), 7.26 – 7.14 (m, 2H), 7.07 (d, J = 8.0 Hz, 2H), 6.95 (t, J = 7.3 Hz, 1H), 4.84 (d, J = 7.1 Hz, 1H), 4.13 (d, J = 7.1 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.6, 172.1, 145.7, 136.6, 136.4, 130.0, 129.4, 129.1, 128.5, 124.4, 121.1, 115.7, 77.6, 50.46, 24.9; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.66 (d, J = 7.7 Hz, 2H), 7.49 - 6.99 (7H), 6.92 (t, J = 7.3 Hz, 1H), 4.98 (d, J = 7.2 Hz, 1H), 4.77 (d, J = 7.2 Hz, 1H), 2.41 (s, 3H); IR (KBr, cm^{-1}) for Z-isomer: 3777, 3709, 3664, 3639, 3601, 3176, 1810, 1725, 1668, 1585, 585, 479, 405; HRMS (ESI) Calcd for $C_{19}H_{16}BrN_2O_3$ $(M+H)^+$ 399.0339, found 399.0336.

3-(bromo(phenyl)methylene)-5-(tert-butyl)-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4b)



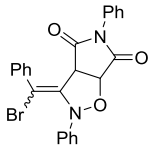
76% yield (67 mg, Z:E = 72:28), yellow solid (Z+E mixture), m. p. (Z+E mixture) 121-125 ^{o}C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.98 (d, J = 6.7 Hz, 2H), 7.48 – 6.89 (8H), 4.73 (d, J = 7.4 Hz, 1H), 4.06 (d, J = 7.4 Hz, 1H), 1.09 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 173.5, 172.7, 146.0, 136.8, 136.7, 129.9, 129.5, 129.2, 128.5, 124.1, 120.9, 115.7, 77.3, 59.5, 50.3, 27.3; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.71 (d, J = 7.4 Hz, 2H), 7.48 – 6.89 (8H), 4.82 (d, J = 7.7 Hz, 1H), 4.63 (d, J = 7.7 Hz, 1H), 1.11 (s, 9H); IR (Z+E mixture, KBr, cm^{-1}) 3671, 3063, 2978, 1780, 1712, 1595, 1538, 1487, 1446, 1336, 1263, 1169, 756, 694; HRMS (ESI) Calcd for $C_{22}H_{22}BrN_2O_3$ $(M+H)^+$ 441.0808, found 441.0804.

3-(bromo(phenyl)methylene)-5-ethyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione (4c)



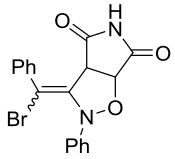
78% yield (64 mg, Z:E = 72:28), yellow solid (Z+E mixture), m. p. (Z+E mixture) 85-88 ^{o}C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.10 – 7.94 (m, 2H), 7.53 – 6.80 (8H), 4.89 (d, J = 7.2 Hz, 1H), 4.17 (d, J = 7.2 Hz, 1H), 3.10 (q, J = 7.2 Hz, 2H), 0.40 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.3, 171.8, 145.8, 136.6, 136.2, 130.0, 129.4, 129.2, 128.5, 124.3, 121.3, 115.5, 77.7, 50.5, 34.4, 11.1; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.70 (d, J = 7.3 Hz, 2H), 7.53 – 6.80 (8H), 4.97 (d, J = 7.4 Hz, 1H), 4.75 (d, J = 7.4 Hz, 1H), 3.10 (q, J = 7.2 Hz, 2H), 0.40 (t, J = 7.2 Hz, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3477, 3361, 3063, 2983, 2943, 2882, 1784, 1714, 1591, 1488, 1449, 1393, 1347, 1229, 749, 697; HRMS (ESI) Calcd for $C_{20}H_{18}BrN_2O_3$ $(M+H)^+$ 413.0495, found 413.0486.

3-(bromo(phenyl)methylene)-2,5-diphenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione (4d)



85% yield (78 mg, Z:E = 74:26), yellow solid (Z+E mixture), m. p. (Z+E mixture) 147-149 ^{o}C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.99 (d, J = 6.9 Hz, 2H), 7.49 – 6.91 (11H), 6.32 (d, J = 7.4 Hz, 2H), 5.02 (d, J = 7.3 Hz, 1H), 4.32 (d, J = 7.3 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 171.8, 171.3, 146.0, 136.5, 136.3, 130.8, 130.1, 129.6, 129.5, 129.11, 129,07, 128.6, 126.1, 124.5, 121.6, 115.8, 77.8, 50.6; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.70 (d, J = 7.6 Hz, 2H), 7.52 – 6.93 (11H), 6.37 (d, J = 7.2 Hz, 2H), 5.10 (d, J = 7.5 Hz, 1H), 4.90 (d, J = 7.5 Hz, 1H); IR (Z+E mixture, KBr, cm^{-1}) 3646, 3315, 3062, 2983, 1785, 1723, 1589, 1491, 1450, 1380, 1250, 1198, 898, 852, 748, 695; HRMS (ESI) Calcd for $C_{24}H_{18}BrN_2O_3$ $(M+H)^+$ 461.0495, found 461.0488.

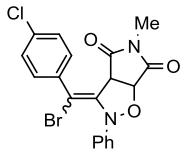
3-(bromo(phenyl)methylene)-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione (4e)



59% yield (45 mg, Z:E = 76:24), yellow liquid (Z+E mixture), R_f (Z+E mixture) = 0.3 (EtOAc/petroleum ether = 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.37 (br, 1H), 8.00 – 7.93 (m, 2H), 7.49 – 6.96 (6H), 6.68 (s, 1H), 4.93 (d, J = 7.0 Hz, 1H), 4.28 (d, J = 6.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.9, 172.1, 145.5, 136.6, 135. 8, 135.1, 130.0, 129.4, 129.2, 128.6, 124.5, 116.1, 78.7, 51.8; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.96 (br, 1H), 7.69(m, 2H), 7.49 – 6.96 (6H), 6.68 (s, 1H), 5.02 (d, J = 7.1 Hz, 1H), 4.83 (d, J = 7.0 Hz, 1H); IR (Z+E mixture, KBr, cm^{-1}) 3645, 333, 3061, 2985,

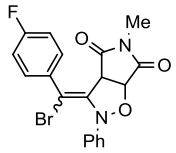
1780, 1720, 1580, 1451, 1250, 1198, 896, 851; HRMS (ESI) Calcd for $C_{18}H_{14}BrN_2O_3$ $(M+H)^+$ 385.0182, found 385.0185.

3-(bromo(4-chlorophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4f)



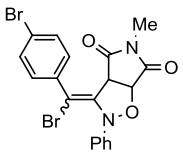
85% yield (73 mg, Z:E = 78:22), yellow solid (Z+E mixture), m. p. (Z+E mixture) 135-139 ^oC, R_f (Z+E mixture) = 0.5 (EtOAc/petroleum ether = 1/3); ^1H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.01 (d, J = 7.2 Hz, 2H), 7.55 – 6.89 (7H), 4.93 (d, J = 7.0 Hz, 1H), 4.22 (d, J = 7.1 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.6, 172.1, 145.7, 136.6, 136.4, 130.0, 129.4, 129.1, 128.5, 124.4, 121.2, 115.7, 77.6, 50.4, 24.9; ^1H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.67 (d, J = 7.5 Hz, 2H), 7.55 – 6.89 (7H), 5.00 (d, J = 7.0 Hz, 1H), 4.79 (d, J = 7.1 Hz, 1H), 2.43 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3743, 3646, 3071, 2984, 1786, 1712, 1589, 1486, 1440, 1384, 1289, 1124, 892, 835, 670; HRMS (ESI) Calcd for $C_{19}H_{15}BrClN_2O_3$ $(M+H)^+$ 432.9949, found 432.9950.

3-(bromo(4-fluorophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4g)



68% yield (56 mg, Z:E = 76:24), Z-isomer (major, 43 mg) and E-isomer (minor, 13 mg) could be obtained simply by column chromatography on silica gel, light yellow solid (Z-isomer), m. p. (Z-isomer) 88-89 ^oC, R_f (Z-isomer) = 0.4 (EtOAc/petroleum ether = 1/3), light yellow solid (E-isomer, unstable), R_f (E-isomer, unstable) = 0.3 (EtOAc/petroleum ether = 1/3); ^1H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.10 – 7.95 (m, 2H), 7.31-7.26 (m, 2H), 7.18 – 7.13 (m, 4H), 7.04 (t, J = 7.2 Hz, 1H), 4.95 (d, J = 7.0 Hz, 1H), 4.19 (d, J = 7.0 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.5, 172.1, 163.5 (d, J = 251.0 Hz), 145.6, 136.6, 132.7 (d, J = 3.5 Hz), 131.6 (d, J = 8.5 Hz), 129.1, 124.5, 120.0, 115.6 (d, J = 21.8 Hz), 115.6, 77.6, 50.4, 24.9; ^{19}F NMR (376 MHz, $CDCl_3$) for Z-isomer: δ -110.1; ^1H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.72 – 7.64 (m, 2H), 7.31 – 6.94 (7H), 5.01 (d, J = 7.2 Hz, 1H), 4.78 (d, J = 7.2 Hz, 1H), 2.43 (s, 3H); IR (KBr, cm^{-1}) for Z-isomer: 3669, 3073, 2980, 1710, 1597, 1507, 1442, 1381, 1237, 1157, 838, 755, 613; HRMS (ESI) Calcd for $C_{19}H_{13}BrFN_2O_3$ $(M-H)^-$ 415.0099, found 415.0096.

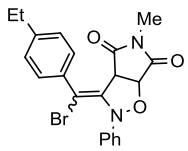
3-(bromo(4-bromophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4h)



84% yield (79 mg, Z:E = 83:17), Z-isomer (major, 66 mg) and E-isomer (minor, 13 mg) could be obtained simply by column chromatography on silica gel, yellow solid (Z-isomer), m. p. (Z-isomer) 144-145 ^oC, R_f (Z-isomer) = 0.4 (EtOAc/petroleum ether = 1/3); yellow solid (E-isomer), m. p. (E-isomer) 126-127 ^oC, R_f (E-isomer) = 0.3 (EtOAc/petroleum ether = 1/3); ^1H NMR (500 MHz, $CDCl_3$) for Z-isomer: δ 7.91 (d, J = 8.6 Hz, 2H), 7.61 (d, J = 8.6 Hz, 2H), 7.29 (t, J = 8.0 Hz, 2H), 7.16 – 7.08 (m, 2H), 7.04 (t, J = 7.1 Hz, 1H), 4.94 (d, J = 7.0 Hz, 1H), 4.18 (d, J = 7.1 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) for Z-isomer: δ 172.4, 172.0, 145.5, 136.8, 135.5, 131.8, 131.0, 129.2, 124.6, 124.5, 119.7, 115.6, 77.6, 50.5, 25.0; ^1H NMR (500 MHz, $CDCl_3$) for E-isomer: δ 7.61 – 7.52 (m, 2H), 7.45 – 7.36 (m, 2H), 7.17 – 7.14 (m, 2H), 6.99 – 6.88 (m, 3H), 5.01 (d, J = 7.2 Hz, 1H), 4.77 (d, J = 7.2 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) for E-isomer: δ 172.7, 171.2, 145.8, 136.6, 135.0, 131.5, 130.7, 129.0, 124.6, 123.7, 118.2, 115.8, 76.8, 53.9, 24.9; IR (KBr, cm^{-1}) for

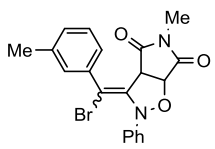
Z-isomer: 3707, 3668, 3147, 1796, 1725, 1586, 1429, 1372, 1277, 829, 781, 538, 465; IR (KBr, cm^{-1}) for E-isomer: 3743, 3066, 1703, 1580, 1483, 1281, 1122, 1008, 945, 755; HRMS (ESI) Calcd for $C_{19}H_{13}Br2N_2O_3$ $(M-H)^-$ 474.9298, found 474.9293.

3-(bromo(4-ethylphenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4i)



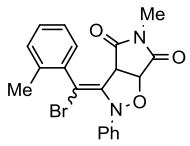
98% yield (84 mg, Z:E = 33:67), yellow solid (Z+E mixture), m. p. (Z+E mixture) 102-105 °C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.59 (d, J = 8.1 Hz, 2H), 7.30 – 6.90 (7H), 4.98 (d, J = 7.2 Hz, 1H), 4.79 (d, J = 7.2 Hz, 1H), 2.58 (q, J = 7.5 Hz, 2H), 2.42 (s, 3H), 1.18 (t, J = 7.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for E-isomer: δ 172.9, 171.5, 146.4, 145.8, 135.5, 133.5, 129.1, 128.9, 127.7, 124.3, 120.3, 115.9, 76.8, 53.9, 28.5, 24.7, 15.0; ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.92 (d, J = 7.9 Hz, 2H), 7.30 – 6.90 (7H), 4.91 (d, J = 7.2 Hz, 1H), 4.22 (d, J = 7.0 Hz, 1H), 2.71 (q, J = 7.7 Hz, 2H), 2.42 (s, 3H), 1.28 (t, J = 7.6 Hz, 3H). IR (Z+E mixture, KBr, cm^{-1}) 3670, 2966, 2901, 1789, 1717, 1594, 1487, 1431, 1378, 1283, 1122, 760; HRMS (ESI) Calcd for $C_{21}H_{19}BrN_2NaO_3$ $(M+Na)^+$ 449.0471, found 449.0472.

3-(bromo(m-tolyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione (4j)



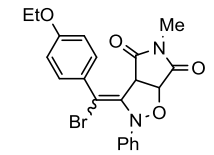
93% yield (77 mg, Z:E = 85:15), yellow solid (Z+E mixture), m. p. (Z+E mixture) 123-126 °C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.81 (s, 1H), 7.77 (d, J = 7.7 Hz, 1H), 7.38 – 6.88 (7H), 4.88 (d, J = 7.1 Hz, 1H), 4.19 (d, J = 7.0 Hz, 1H), 2.43 (s, 3H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.6, 172.0, 145.9, 138.3, 136.6, 136.2, 130.7, 130.0, 129.1, 128.4, 126.5, 124.3, 121.3, 115.7, 77.6, 50.5, 24.8, 21.3; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.44 (d, J = 8.2 Hz, 2H), 7.38 – 6.88 (7H), 4.95 (d, J = 7.2 Hz, 1H), 4.75 (d, J = 7.2 Hz, 1H), 2.40 (s, 3H), 2.26 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3709, 3061, 2986, 1788, 1714, 1593, 1486, 1432, 1377, 1283, 761, 650, 586; HRMS (ESI) Calcd for $C_{20}H_{17}BrN_2NaO_3$ $(M+Na)^+$ 435.0315, found 435.0311.

3-(bromo(o-tolyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione (4k)



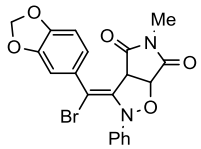
77% yield (64 mg, Z:E = 48:52), yellow solid (Z+E mixture), m. p. (Z+E mixture) 159-162 °C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (Z+E mixture, 400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.36 (s, 4H), 7.32 – 7.27 (m, 6H), 7.21 (d, J = 7.6 Hz, 4H), 7.11 – 7.00 (m, 3H), 4.97 (d, J = 6.7 Hz, 1H), 4.93 (d, J = 7.0 Hz, 1H), 4.20 (d, J = 7.0 Hz, 1H), 3.88 (d, J = 6.8 Hz, 1H), 2.61 (s, 3H), 2.42 (s, 3H), 2.37 (s, 6H); ^{13}C NMR (Z+E mixture, 101 MHz, $CDCl_3$) δ 172.8, 172.7, 171.3, 170.8, 145.7, 145.6, 139.3, 137.6, 136.7, 135.4, 135.4, 132.4, 131.1, 130.5, 130.1, 130.0, 129.1, 129.1, 127.6, 126.4, 125.9, 124.7, 124.6, 118.6, 117.4, 116.4, 116.1, 77.8, 77.6, 51.0, 50.7, 24.81, 24.75, 20.3, 19.6; IR (Z+E mixture, KBr, cm^{-1}) 3669, 3145, 1822, 1716, 1592, 1518, 1484, 1427, 1375, 750, 718; HRMS (ESI) Calcd for $C_{20}H_{18}BrN_2O_3$ $(M+H)^+$ 413.0495, found 413.0488.

3-(bromo(4-ethoxyphenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4l)



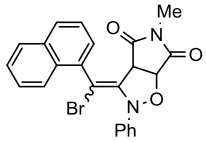
58% yield (NMR detected, Z:E = 78:22), single Z-isomer (45 mg) could be obtained after column chromatography on silica gel, yellow solid (Z-isomer), m. p. (Z-isomer) 100-101 ^{o}C, R_f (Z-isomer) = 0.3 (EtOAc/petroleum ether = 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.97 (d, J = 8.3 Hz, 2H), 7.30 – 7.27 (m, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.02 (t, J = 7.3 Hz, 1H), 6.96 (d, J = 8.4 Hz, 2H), 4.92 (d, J = 7.1 Hz, 1H), 4.22 (d, J = 7.0 Hz, 1H), 4.09 (q, J = 6.9 Hz, 2H), 2.41 (s, 3H), 1.45 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.7, 172.3, 160.3, 145.9, 135.3, 131.0, 129.1, 128.7, 124.3, 121.9, 115.5, 114.3, 77.7, 63.7, 50.3, 24.9, 14.8; IR (KBr, cm^{-1}) for Z-isomer: 3610, 2981, 2961, 1713, 1598, 1510, 1438, 1384, 1257, 1174, 825, 760, 695; HRMS (ESI) Calcd for $C_{21}H_{18}BrN_2O_4$ $(M-H)^-$ 441.0455, found 441.0448.

3-(benzo[d][1,3]dioxol-5-ylbromomethylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]--isoxazole-4,6(5H)-dione (4m)



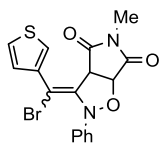
50% yield (NMR detected, Z:E = 80:20), single Z-isomer (40 mg) could be obtained after column chromatography on silica gel, yellow solid (Z-isomer), m. p. (Z-isomer) 110-111 ^{o}C, R_f (Z-isomer) = 0.3 (EtOAc/petroleum ether = 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.63 (d, J = 8.1 Hz, 1H), 7.46 (s, 1H), 7.30 (d, J = 7.6 Hz, 2H), 7.13 (d, J = 7.9 Hz, 2H), 7.03 (t, J = 7.3 Hz, 1H), 6.89 (d, J = 8.1 Hz, 1H), 6.04 (s, 2H), 4.94 (d, J = 7.1 Hz, 1H), 4.25 (d, J = 7.0 Hz, 1H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.6, 172.2, 149.1, 147.7, 145.8, 135.8, 130.3, 129.1, 124.4, 124.0, 121.3, 115.6, 109.9, 108.1, 101.7, 77.6, 50.4, 24.9; IR (KBr, cm^{-1}) for Z-isomer: 3673, 3129, 1824, 1710, 1504, 1481, 1349, 1259, 1035, 804, 750, 540; HRMS (ESI) Calcd for $C_{20}H_{16}BrN_2O_5$ $(M+H)^+$ 443.0237, found 443.0230.

3-(bromo(naphthalen-1-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4n)



52% yield (47 mg, Z:E = 82:18), yellow solid (Z+E mixture), m. p. (Z+E mixture) 120-125 ^{o}C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (500 MHz, $CDCl_3$) for Z-isomer: δ 8.09 (d, J = 8.3 Hz, 1H), 8.03 (dd, J = 7.1, 1.2 Hz, 1H), 7.98 – 7.04 (10H), 4.86 (d, J = 7.1 Hz, 1H), 3.78 (d, J = 7.1 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) for Z-isomer: δ 172.7, 171.3, 145.7, 138.8, 133.7, 132.7, 130.8, 130.5, 129.2, 128.8, 127.3, 126.6, 125.3, 124.7, 124.6, 117.0, 116.9, 116.2, 77.6, 50.7, 24.8; ^{1}H NMR (500 MHz, $CDCl_3$) for E-isomer: δ 8.12 (d, J = 8.5 Hz, 1H), 7.98 – 7.04 (11H), 4.97 (d, J = 7.2 Hz, 1H), 4.28 (d, J = 7.2 Hz, 1H), 2.32 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3620, 3489, 3309, 3059, 2987, 1788, 1716, 1591, 1491, 1435, 1379, 1284,789, 765; HRMS (ESI) Calcd for $C_{23}H_{18}BrN_2O_3$ $(M+H)^+$ 449.0495, found 449.0495.

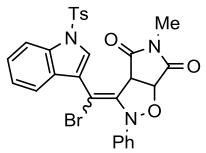
3-(bromo(thiophen-3-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4o)



93% yield (75 mg, Z:E = 78:22), yellow solid (Z+E mixture), m. p. (Z+E mixture) 160-163 ^{o}C R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400

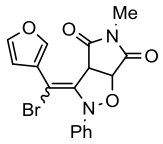
MHz, $CDCl_3$) for Z-isomer: δ 8.60 (d, J = 2.8 Hz, 1H), 7.60 (d, J = 5.1 Hz, 1H), 7.41 – 6.97 (6H), 4.95 (d, J = 7.1 Hz, 1H), 4.39 (d, J = 7.1 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.6, 145.9, 136.9, 135.3, 129.1, 128.8, 126.9, 126.1, 124.4, 116.0, 115.5, 77.8, 50.5, 24.9; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.65 (d, J = 2.8 Hz, 1H), 7.50 (d, J = 5.2 Hz, 1H), 7.41 – 6.97 (6H), 4.95 (d, J = 7.1 Hz, 1H), 4.82 (d, J = 7.2 Hz, 1H), 2.42 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3670, 3483, 3225, 2987, 1789, 1730, 1592, 1487, 1432, 1281, 1084, 842, 627; HRMS (ESI) Calcd for $C_{17}H1_3BrN_2NaO_3S$ $(M+Na)^+$ 426.9722, found 426.9730.

3-(bromo(1-tosyl-1H-indol-3-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]--isoxazole-4,6(5H)-dione (4p)



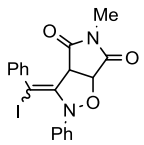
60% yield (NMR detected, Z:E = 78:22), single Z-isomer (66 mg) could be obtained after column chromatography on silica gel, yellow solid (Z-isomer), m. p. (Z-isomer) 158-159 ^{o}C, R_f (Z-isomer) = 0.4 (DCM/petroleum ether/EtOAc = 10/10/1); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.94 (s, 1H), 8.04 (d, J = 8.4 Hz, 1H), 7.96 – 7.88 (m, 3H), 7.40 (t, J = 7.8 Hz, 1H), 7.36 – 7.26 (m, 5H), 7.19 – 7.12 (m, 2H), 7.06 (t, J = 7.4 Hz, 1H), 4.95 (d, J = 7.1 Hz, 1H), 4.18 (d, J = 7.0 Hz, 1H), 2.48 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.7, 172.3, 145.7, 145.6, 137.3, 134.9, 134.9, 130.1, 129.2, 128.5, 127.8, 127.3, 125.5, 124.6, 123.6, 121.6, 117.1, 115.8, 113.6, 111.7, 77.8, 51.0, 25.1, 21.7; IR (KBr, cm^{-1}) for Z-isomer: 3671, 3124, 3062, 2977, 1919, 1790, 1594, 1542, 1448, 1371, 1174, 917, 749, 572, 491; HRMS (ESI) Calcd for $C_{28}H_{23}BrN_3O_5S$ $(M+H)^+$ 592.0536, found 592.0540.

3-(bromo(furan-3-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione (4q)



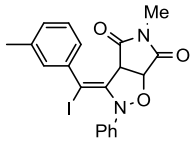
56% yield (44 mg, Z:E = 77:23), yellow solid (Z+E mixture), m. p. (Z+E mixture) 108-109 ^{o}C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.62 (s, 1H), 7.52 (s, 1H), 7.36 – 6.97 (5H), 6.92 (s, 1H), 5.01 (d, J = 7.1 Hz, 1H), 4.42 (d, J = 7.1 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.7, 172.4, 145.8, 143.6, 142.9, 134.7, 129.1, 124.5, 123.0, 115.6, 112.1, 111.4, 78.1, 50.3, 24.9; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.65 (s, 1H), 7.36 – 6.97 (6H), 6.70 (s, 1H), 4.96 (d, J = 7.2 Hz, 1H), 4.78 (d, J = 7.2 Hz, 1H), 2.43 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3669, 3146, 2926, 1713, 1594, 1495, 1437, 1383, 1277, 1081, 1024, 749, 698, 600; HRMS (ESI) Calcd for $C_{17}H_{14}BrN_2O_4$ $(M+H)^+$ 389.0131, found 389.0133.

3-(iodo(phenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione (4s)



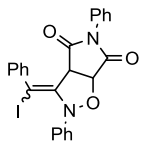
69% yield (61 mg, Z:E = 94:6), white solid (Z+E mixture), m. p. (Z+E mixture) 140-141 ^{o}C, R_f (Z+E mixture) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.89 (d, J = 7.5 Hz, 2H), 7.46 – 7.36 (m, 3H), 7.29 (t, J = 7.5 Hz, 2H), 7.17 (d, J = 7.9 Hz, 2H), 7.03 (t, J = 7.4 Hz, 1H), 4.95 (d, J = 7.0 Hz, 1H), 4.18 (d, J = 7.1 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.7, 171.8, 145.4, 140.7, 139.7, 129.6, 129.4, 129.1, 128.5, 124.5, 116.0, 98.9, 78.1, 49.4, 24.8; IR (Z+E mixture, KBr, cm^{-1}) 3674, 3060, 1789, 1715, 1592, 1487, 1432, 1378, 1284, 1199, 844, 696, 562; HRMS (ESI) Calcd for $C_{19}H_{14}IN_2O_3$ $(M-H)^-$ 445.0055, found 445.0052

3-(iodo(m-tolyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione (4t)



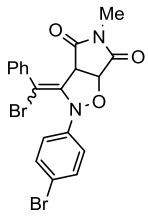
40% yield (NMR detected, Z:E = 92:8), single Z-isomer (34 mg) could be obtained after column chromatography on silica gel, white solid (Z-isomer), m. p. (Z-isomer) 115-116 ^{o}C, R_f (Z-isomer) = 0.4 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.73 (s, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.34 – 7.27 (m, 3H), 7.21 – 7.15 (m, 3H), 7.03 (t, J = 7.3 Hz, 1H), 4.93 (d, J = 7.1 Hz, 1H), 4.18 (d, J = 7.1 Hz, 1H), 2.43 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.7, 171.9, 145.5, 140.5, 139.6, 138.3, 130.4, 130.0, 129.1, 128.3, 126.5, 124.5, 116.0, 99.3, 78.1, 49.4, 24.8, 21.4; IR (KBr, cm^{-1}) for Z-isomer: 3743, 3663, 3058, 2971, 1786, 1713, 1590, 1485, 1436, 1377, 1124, 753, 697; HRMS (ESI) Calcd for $C_{20}H_{18}IN_2O_3$ $(M+H)^+$ 461.0357, found 461.0359.

3-(iodo(phenyl)methylene)-2,5-diphenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione (4u)



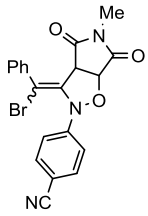
50% yield (51 mg, Z:E = 92:8), light yellow solid (Z+E mixture), m. p. (Z+E mixture) 130-131 ^{o}C; R_f (Z+E mixture) = 0.3 (EtOAc/petroleum ether = 1/3) ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.90 (d, J = 7.5 Hz, 2H), 7.45 – 7.39 (m, 3H), 7.35 (t, J = 7.4 Hz, 2H), 7.29 – 7.26 (m, 5H), 7.14 (t, J = 7.3 Hz, 1H), 6.34 (d, J = 7.3 Hz, 2H), 5.12 (d, J = 7.1 Hz, 1H), 4.36 (d, J = 7.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 171.8, 171.0, 145.6, 140.6, 139.7, 130.7, 129.7, 129.6, 129.5, 129.2, 129.0, 128.5, 126.1, 124.6, 116.1, 99.4, 78.2, 49.5; IR (Z+E mixture, KBr, cm^{-1}) 3062, 2923, 2849, 1691, 1595, 1470, 1451, 1329, 1278, 1235, 1022, 912, 757, 696; HRMS (ESI) Calcd for $C_{24}H_{17}IN_2NaO_3$ $(M+Na)^+$ 531.0176, found 531.0186.

3-(bromo(phenyl)methylene)-2-(4-bromophenyl)-5-methyltetrahydro-4H-pyrrolo[3,4-d]--isoxazole-4,6(5H)-dione (4w)



63% yield (60 mg, Z:E = 69:31), yellow solid (Z+E mixture), m. p. (Z+E mixture) 135-139 ^{o}C, R_f (Z+E mixture) = 0.3 (EtOAc/petroleum ether = 1/3); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 7.99 (dd, J = 7.3, 2.1 Hz, 2H), 7.53 – 7.18 (5H), 7.07 – 6.97 (m, 2H), 4.93 (d, J = 7.1 Hz, 1H), 4.23 (d, J = 7.1 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 172.4, 171.9, 144.9, 136.3, 135.9, 132.1, 130.2, 129.4, 128.6, 121.6, 117.4, 117.2, 77.7, 50.4, 25.1; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.64 (d, J = 6.8 Hz, 2H), 7.53 – 7.18 (5H), 6.92 – 6.78 (m, 2H), 5.02 (d, J = 7.3 Hz, 1H), 4.78 (d, J = 7.3 Hz, 1H), 2.51 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3745, 3620, 3488, 3063, 2980, 1787, 1714, 1480, 1435, 1379, 1286, 1123, 823, 701; HRMS (ESI) Calcd for $C_{19}H_{15}Br_2N_2O_3$ $(M+H)^+$ 476.9444, found 476.9438.

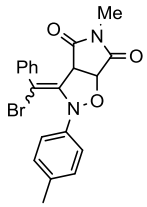
4-(3-(bromo(phenyl)methylene)-5-methyl-4,6-dioxohexahydro-2H-pyrrolo[3,4-d]isoxazol-2-yl)benzo nitrile (4x)



63% yield (53 mg, Z:E = 67:33), light yellow solid (Z+E mixture), m. p. (Z+E mixture) 120-124 ^{o}C, R_f (Z+E mixture) = 0.3 (EtOAc/petroleum ether = 1/3.5); ^{1}H NMR (400 MHz, $CDCl_3$) for Z-isomer: δ 8.06 – 7.91 (m, 2H), 7.70 – 6.89 (7H), 4.97 (d, J = 7.0 Hz, 1H), 4.25 (d, J = 7.1 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) for Z-isomer: δ 171.9, 171.6, 149.2, 135.9, 134.8, 133.3, 130.5, 129.3, 128.7, 123.0, 115.5, 107.2, 53.2, 50.1, 25.2; ^{1}H NMR (400 MHz, $CDCl_3$) for E-isomer: δ 7.65 (d, J = 7.6

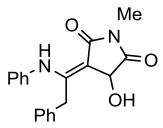
Hz, 2H), 7.60 – 6.60 (7H), 5.09 (J = 7.2 Hz, 1H), 4.78 (d, J = 7.2 Hz, 1H), 2.51 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3483, 3370, 3062, 2986, 2236, 1789, 1715, 1601, 1495, 1432, 1379, 1286, 841, 734; HRMS (ESI) Calcd for $C_{20}H_{15}BrN_3O_3$ $(M+H)^+$ 424.0291, found 424.0293.

3-(bromo(phenyl)methylene)-5-methyl-2-(p-tolyl)tetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione (4y)



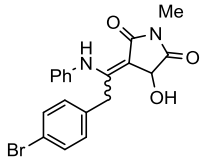
84% yield (NMR detected, Z:E = 74:26), single Z-isomer (67 mg) could be obtained after column chromatography on silica gel, yellow solid (Z-isomer), m. p. (Z-isomer) 150-151 ^oC, R_f (Z-isomer) = 0.4 (EtOAc/petroleum ether = 1/3); ^1H NMR (500 MHz, $CDCl_3$) for Z-isomer: δ 7.98 (d, J = 6.8 Hz, 2H), 7.54 – 7.37 (m, 3H), 7.09 (d, J = 8.3 Hz, 2H), 7.04 (d, J = 8.3 Hz, 2H), 4.92 (d, J = 7.1 Hz, 1H), 4.23 (d, J = 7.1 Hz, 1H), 2.45 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) for Z-isomer: δ 171.6, 171.0, 142.3, 135.7, 135.5, 133.1, 128.9, 128.6, 128.4, 127.5, 119.4, 115.0, 76.6, 49.6, 23.9, 19.6; IR (KBr, cm^{-1}) for Z-isomer: 3743, 3644, 3293, 2979, 1783, 1711, 1503, 1435, 1379, 1279, 1119, 744, 692; HRMS (ESI) Calcd for $C_{20}H_{18}BrN_2O_3$ $(M+H)^+$ 413.0495, found 413.0490.

(Z)-3-hydroxy-1-methyl-4-(2-phenyl-1-(phenylamino)ethylidene)pyrrolidine-2,5-dione (5a)



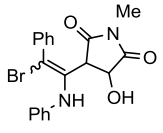
75% yield (48 mg), yellow solid, m. p. 65-66 ^oC, R_f = 0.3 (EtOAc/petroleum ether = 1/1); ^1H NMR (400 MHz, $CDCl_3$) δ 10.47 (s, 1H), 7.29 (d, J = 7.0 Hz, 1H), 7.21 (m,5H), 7.06 (d, J = 7.0 Hz, 2H), 7.01 (d, J = 7.7 Hz, 2H), 4.68 (s, 1H), 4.02 (d, J = 15.6 Hz, 1H), 3.88 (d, J = 15.5 Hz, 1H), 3.21 (br, 1H), 3.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.8, 171.5, 159.4, 137.7, 135.9, 129.2, 128.7, 128.2, 126.8, 126.5, 125.9, 94.4, 68.0, 34.1, 23.9; IR (KBr, cm^{-1}) 3744, 3646, 3271, 3059, 2940, 1745, 1701, 1588, 1493, 1442, 1269, 1184, 1102, 1022, 746; HRMS (ESI) Calcd for $C_{19}H_{18}N_2NaO_3$ $(M+Na)^+$ 345.1210, found 345.1208.

3-(2-(4-bromophenyl)-1-(phenylamino)ethylidene)-4-hydroxy-1-methylpyrrolidine-2,5-dione (5h)



50% yield (40 mg, Z:E = 89:11), light yellow solid (Z+E mixture), m. p. (Z+E mixture) 124-125 ^oC, R_f (Z+E mixture) = 0.3 (EtOAc/petroleum ether = 1/1); ^1H NMR (500 MHz, $CDCl_3$) for Z-isomer: δ 10.40 (s, 1H), 7.35 – 7.26 (m, 4H), 7.22 (d, J = 7.3 Hz, 1H), 6.98 (d, J = 6.0 Hz, 2H), 6.91 (d, J = 6.4 Hz, 2H), 4.73 (s, 1H), 3.95 (d, J = 15.5 Hz, 1H), 3.81 (d, J = 15.6 Hz, 1H), 3.60 (br, 1H), 3.02 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) for Z-isomer: δ 176.9, 171.4, 158.7, 137.6, 134.9, 131.6, 130.0, 129.3, 126.7, 126.0, 120.7, 94.5, 68. 0, 33.7, 23.9; IR (Z+E mixture, KBr, cm^{-1}) 3745, 3620, 3276, 3055, 2926, 1702, 1668, 1592, 1489, 1442, 1382, 1266, 1020, 798, 745; HRMS (ESI) Calcd for $C_{19}H_{17}BrN_2NaO_3$ $(M+Na)^+$ 423.0315, found 423.0319.

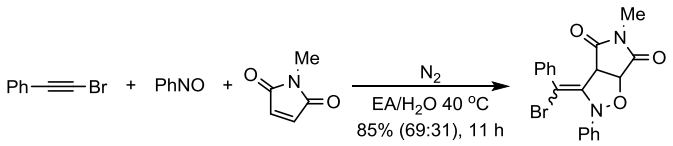
3-(2-bromo-2-phenyl-1-(phenylamino)vinyl)-4-hydroxy-1-methylpyrrolidine-2,5-dione (6)



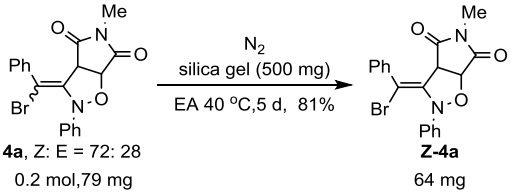
50% yield (40 mg, Z:E = 71:29), yellow solid (Z+E mixture), m. p. (Z+E mixture) 156-160 ^oC, R_f (Z+E mixture) = 0.3 (EtOAc/petroleum ether = 1/1); ^1H NMR (500 MHz, $CDCl_3$) for Z-isomer: δ 7.85 (dd, J = 6.7, 2.9 Hz, 2H), 7.38 – 6.95 (8H), 4.85 (s, 1H), 4.44 (d, J = 6.2 Hz, 1H), 3.89 (d, J = 6.1 Hz, 1H), 3.42 (br, 1H), 2.31 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) for Z-isomer: δ 169.5, 146.1, 137.6, 137.5, 129.6, 129.5, 128.9, 128.3, 124.4, 118.2, 117.5, 87.3, 83.2, 51.3, 27.4; ^1H NMR (500 MHz, $CDCl_3$) for E-isomer: δ 8.07 – 7.95 (m, 2H), 7.42 – 6.91 (8H), 4.85 (m, 1H), 4.75 (dd, J = 6.6, 4.7 Hz, 1H), 4.03 (d, J = 6.7 Hz, 1H), 3.42 (s, 1H),

2.45 (s, 3H); IR (Z+E mixture, KBr, cm^{-1}) 3071, 2955, 1750, 1711, 1598, 1500, 1425, 1277, 1234, 802, 688; HRMS (ESI) Calcd for $C_{19}H_{18}BrN_2O_3$ $(M+H)^+$ 401.0495, found 401.0497.

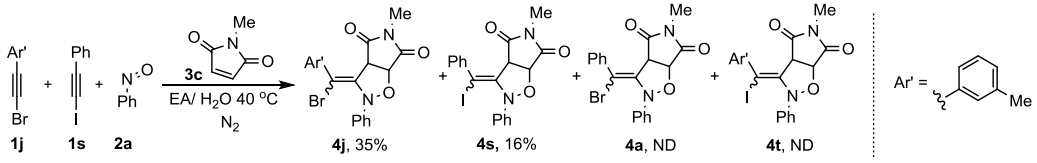
3.3 Gram-Scale Reaction of 4a

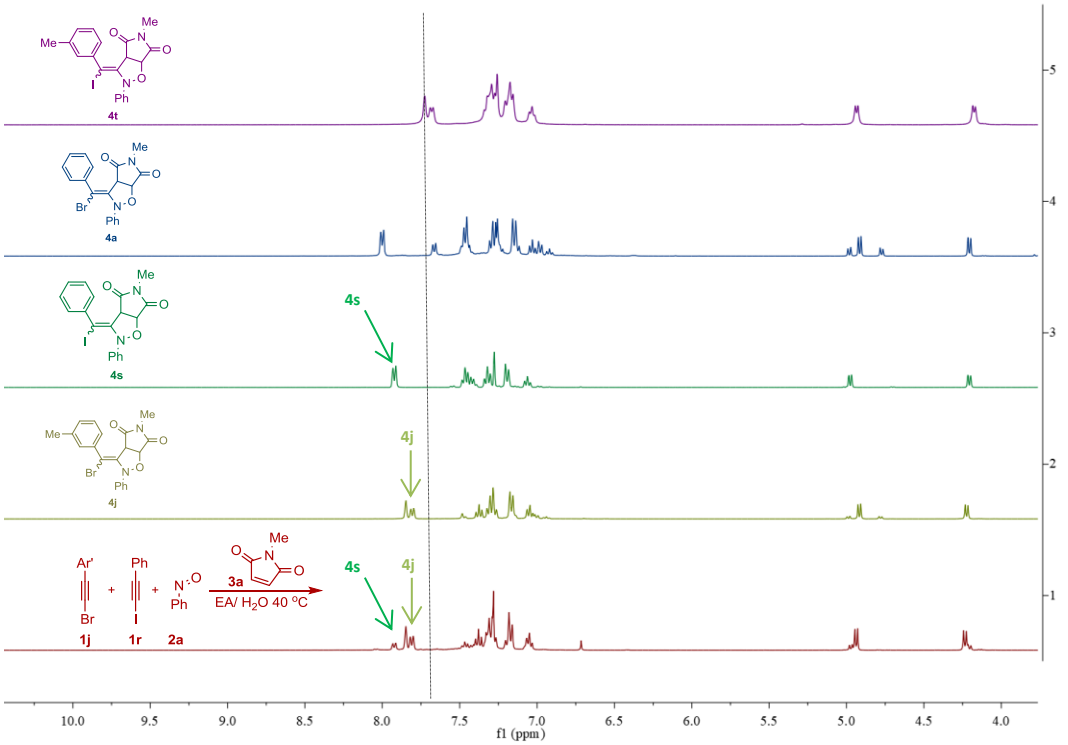


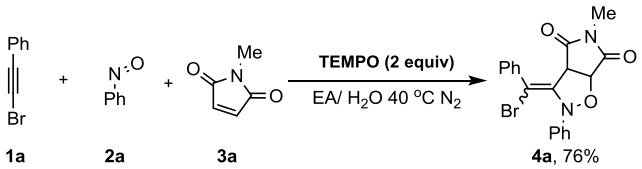
3.4 Isomerization reaction of 4a to Z-4a



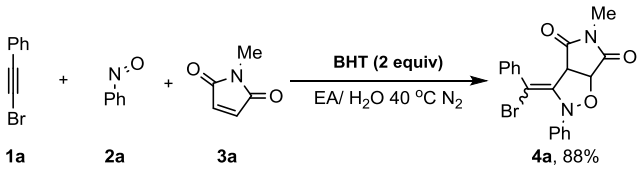
3.5 Control Reactions





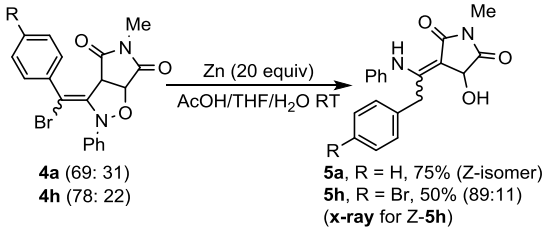


In a Schlenk tube with a magnetic bar under nitrogen atmosphere, EA (1 ml), H_2O (0.3 ml), the substrates of bromoalkyne **1a** (72 mg, 0.4 mmol), nitrosobenzene **2a** (64 mg, 0.6 mmol), maleimide **3a** (22 mg, 0.2 mmol) and TEMPO (62 mg, 0.4 mmol) were added. The mixture was stirred at 40 ^oC for 11 h. After remove of the water by Na_2SO_4, extracted by EA for three times, the organic solvent was evaporated by rotary evaporator to afford the crude product **4a** (76%, NMR yield).



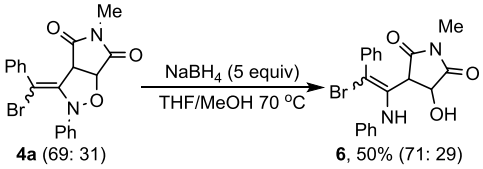
In a Schlenk tube with a magnetic bar under nitrogen atmosphere, EA (1 ml), H_2O (0.3 ml), the substrates of bromoalkyne **1a** (72 mg, 0.4 mmol), nitrosobenzene **2a** (64 mg, 0.6 mmol), maleimide **3a** (22 mg, 0.2 mmol) and BHT (88 mg, 0.4 mmol) were added. The mixture was stirred at 40 ^oC for 11 h. After remove of the water by Na_2SO_4, extracted by EA for three times, the organic solvent was evaporated by rotary evaporator to afford the crude product **4a** (88%, NMR yield).

3.6 Experimental procedures for the synthesis of compounds 5 and 6



In a Schlenk tube with a magnetic bar under nitrogen atmosphere, AcOH (0.5 ml), THF (1.5 ml), H_2O (1.0 ml), **4a** (80 mg, 0.2 mmol) and Zn powder (260 mg, 4 mmol) were added. The mixture was stirred at room temperature until **4a** was completely consumed. After neutralization by adding saturated $NaHCO_3$ aqueous solution, extracted by EA for 3 times, the organic solvent was evaporated by rotary evaporator, and the residue was purified by flash column chromatography on silica gel using EtOAc/petroleum ether as eluent to afford the product **5a** (48 mg, 0.15 mmol).

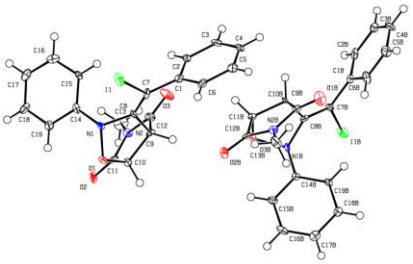
The procedures of substrate **4h**, were similar with that mentioned above.

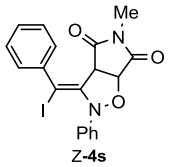


In a Schlenk tube with a magnetic bar under nitrogen atmosphere, THF (4.0 ml), **4a** (80 mg, 0.2 mmol) and $NaBH_4$ (38 mg, 1.0 mmol) were added. The mixture was stirred at 70 ^oC for 15 min, fowllowed by adding MeOH (0.4 mL) and kept stirred until the starting material was consumed. After rapid filtration of silica gel, the solvent was evaporated by rotary evaporator, and the residue was purified by flash column chromatography on silica gel using EtOAc/petroleum ether as eluent to afford the product **6** (40 mg, 0.1 mmol).

4. X-Ray diffraction analysis

4.1 Crystal data and structure refinement for Z-4s

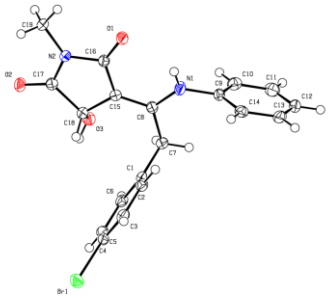


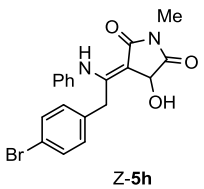


CCDC	2023473
Identification code	yst-I
Empirical formula	$C_{19}H_{15}IN_2O_3$

Formula weight	446.23
Temperature/K	100.00(10)
Crystal system	orthorhombic
Space group	$Pca2_1$
a/Å	20.0555(10)
b/Å	7.4291(5)
c/Å	23.0509(12)
α/°	90
β/°	90
γ/°	90
Volume/$Å^3$	3434.5(3)
Z	8
$\rho_{calc}g/cm^3$	1.726
μ/mm^{-1}	1.885
F(000)	1760.0
Crystal size/mm^3	0.12 × 0.1 × 0.09
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.43 to 49.988
Index ranges	$-23 \leq h \leq 22$, $-7 \leq k \leq 8$, $-27 \leq l \leq 26$
Reflections collected	9747
Independent reflections	5136 [R_{int} = 0.0322, R_{sigma} = 0.0502]
Data/restraints/parameters	5136/19/453
Goodness-of-fit on F^2	1.026
Final R indexes [I>=2σ (I)]	R_1 = 0.0330, wR_2 = 0.0638
Final R indexes [all data]	R_1 = 0.0404, wR_2 = 0.0678
Largest diff. peak/hole / e $Å^{-3}$	0.77/-0.71
Flack parameter	0.26(3)

4.2 Crystal data and structure refinement for Z-5h





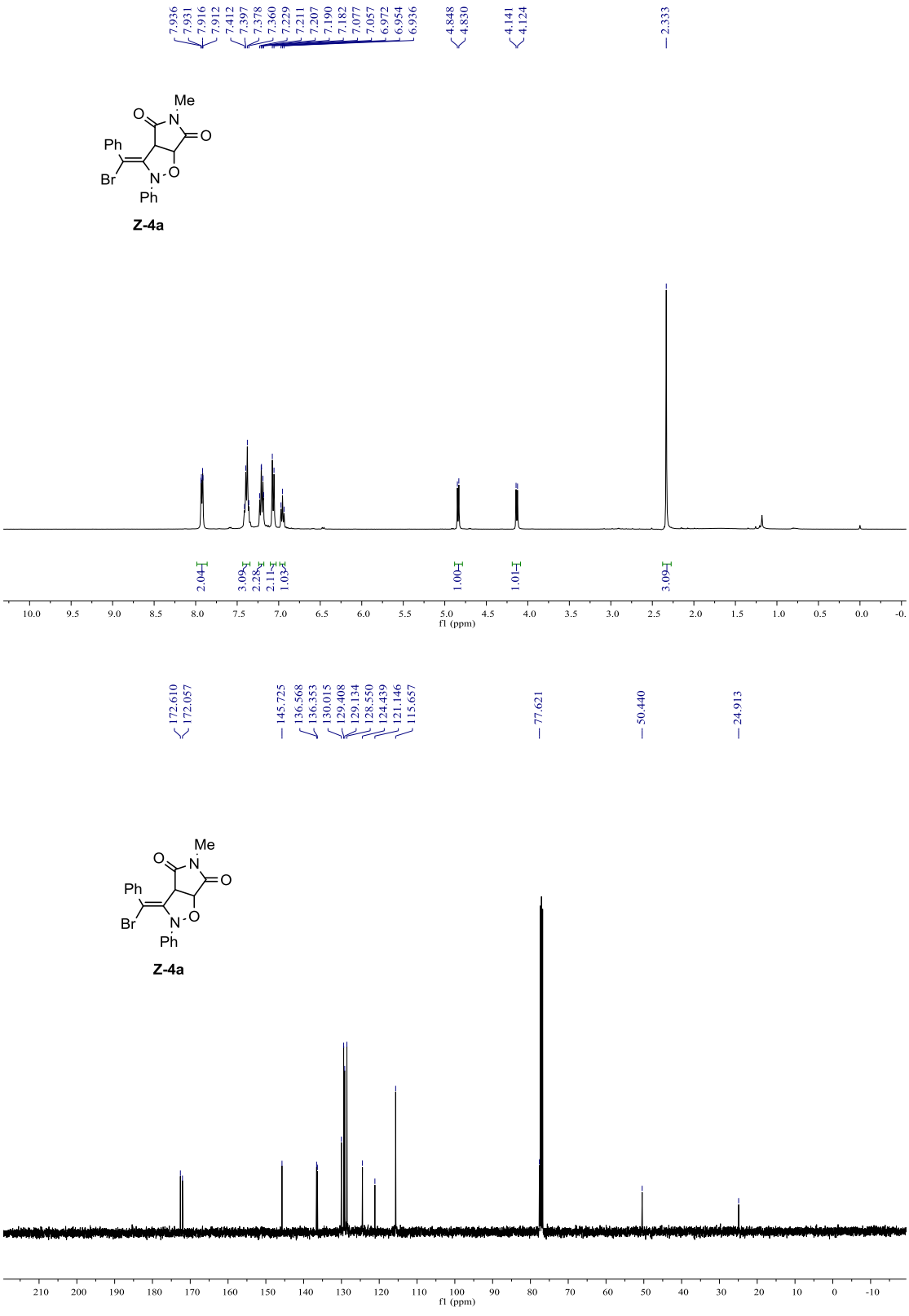
Z-**5h**

CCDC	2023472
Identification code	9st229
Empirical formula	$C_{19}H_{17}BrN_2O_3$

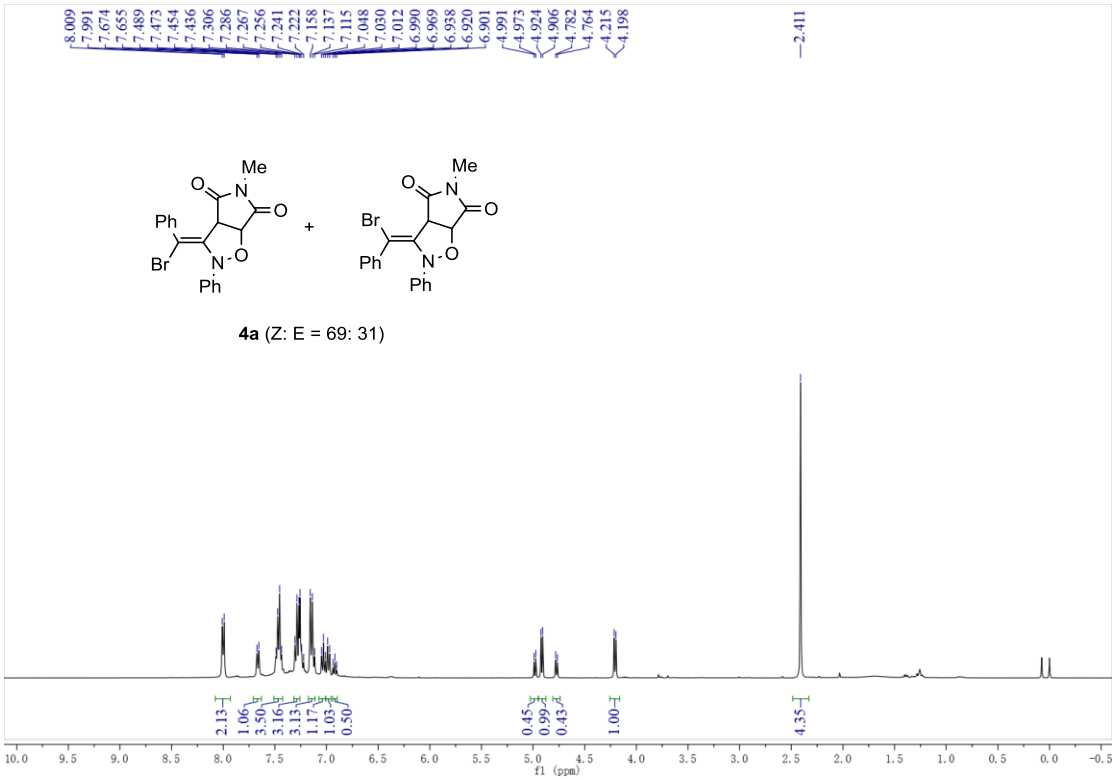
Formula weight	401.25
Temperature/K	100.00(10)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	12.4819(3)
b/Å	5.4926(2)
c/Å	25.2518(7)
α/°	90
β/°	101.834(3)
γ/°	90
Volume/Å^3	1694.42(9)
Z	4
ρ_{calc}g/cm^3	1.573
μ/mm^{-1}	3.488
F(000)	816.0
Crystal size/mm^3	0.12 × 0.11 × 0.1
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.154 to 147.156
Index ranges	$-15 \leq h \leq 14$, $-3 \leq k \leq 6$, $-31 \leq l \leq 25$
Reflections collected	5983
Independent reflections	3295 [R_{int} = 0.0302, R_{sigma} = 0.0406]
Data/restraints/parameters	3295/0/228
Goodness-of-fit on F^2	1.047
Final R indexes [I>=2σ (I)]	R_1 = 0.0308, wR_2 = 0.0772
Final R indexes [all data]	R_1 = 0.0374, wR_2 = 0.0817
Largest diff. peak/hole / e Å^{-3}	0.36/-0.37

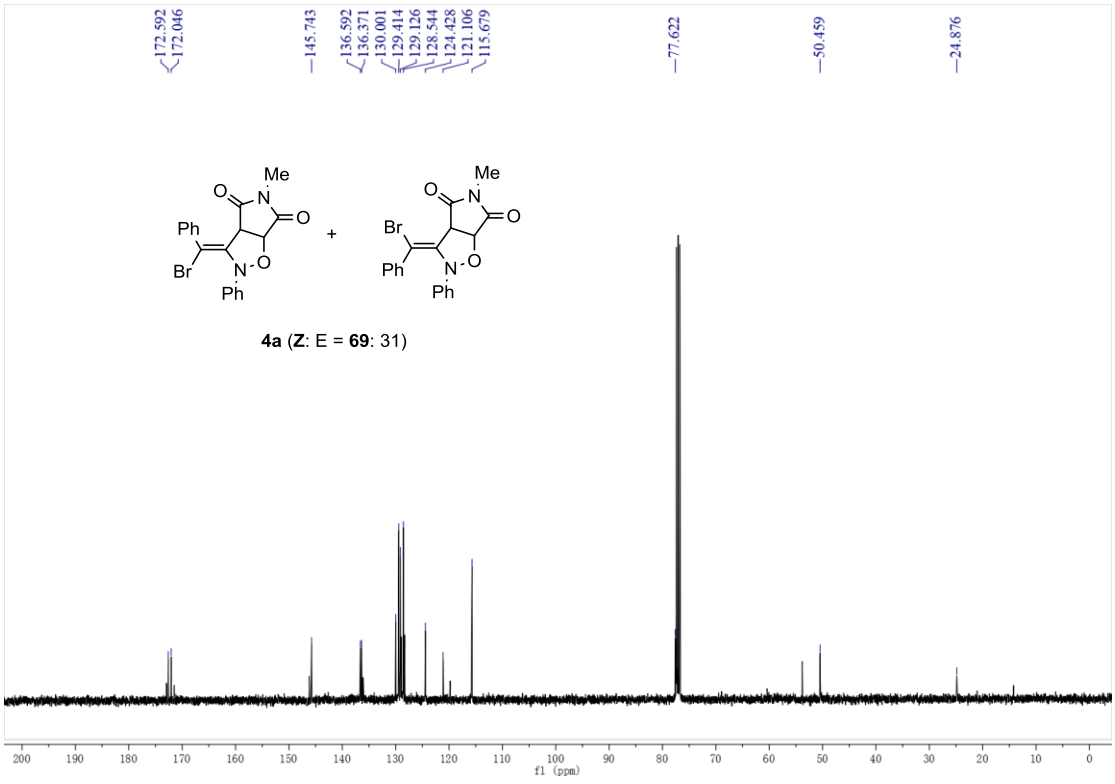
5. Copies of NMR spectrum

***(Z)-3-(bromo(phenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione* (Z-4a)**

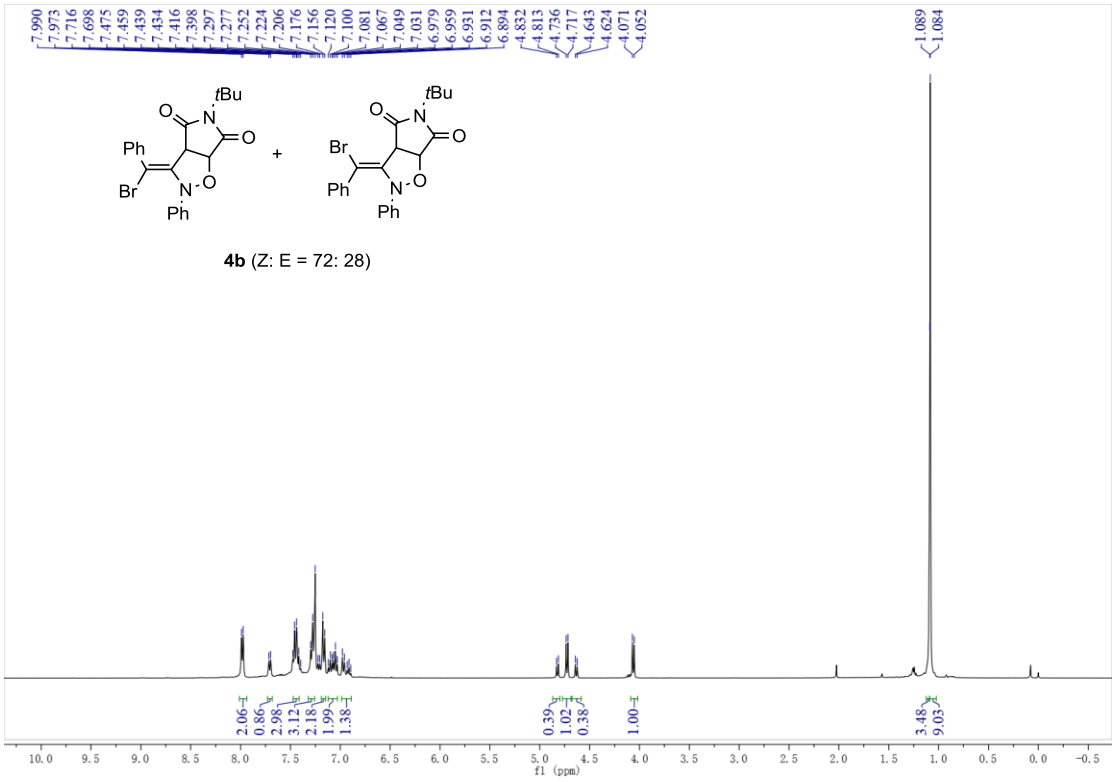


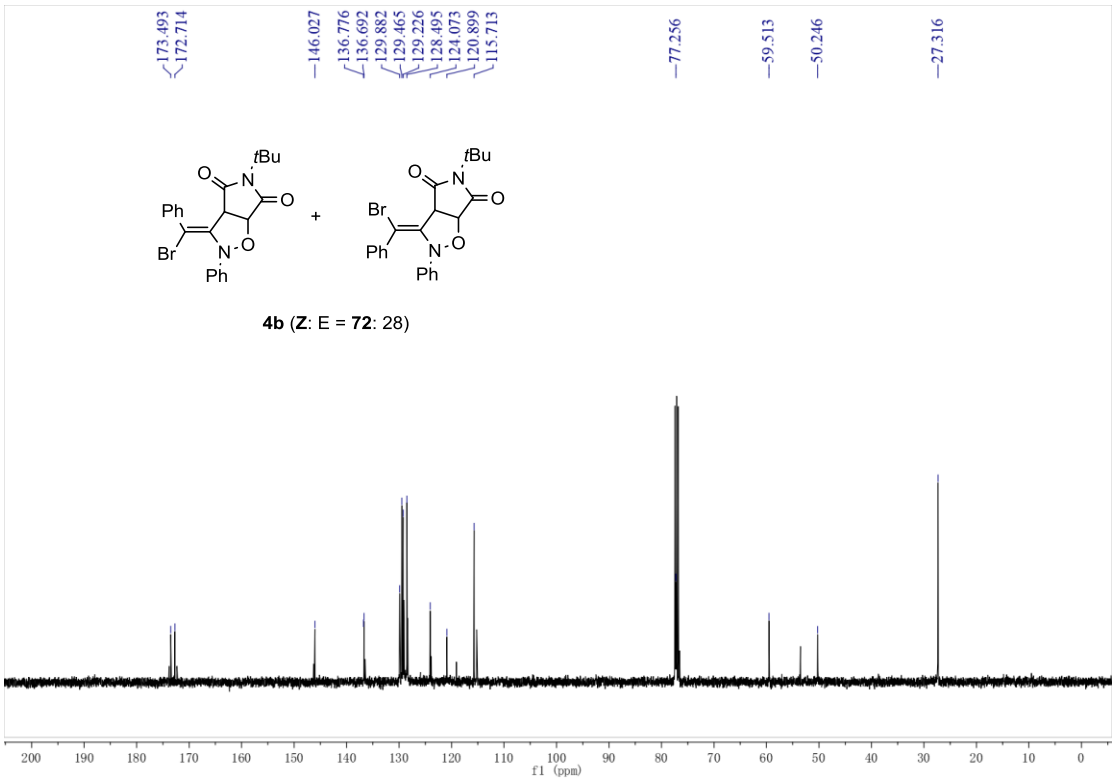
***3-(bromo(phenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione* (4a)**



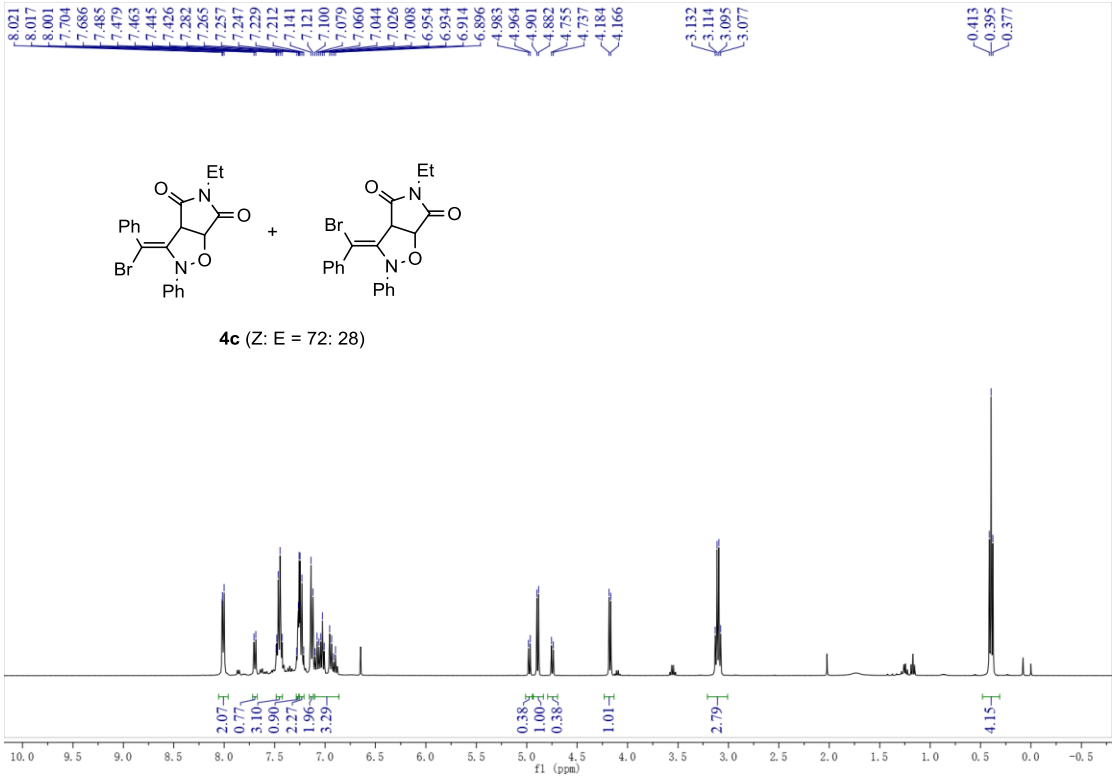


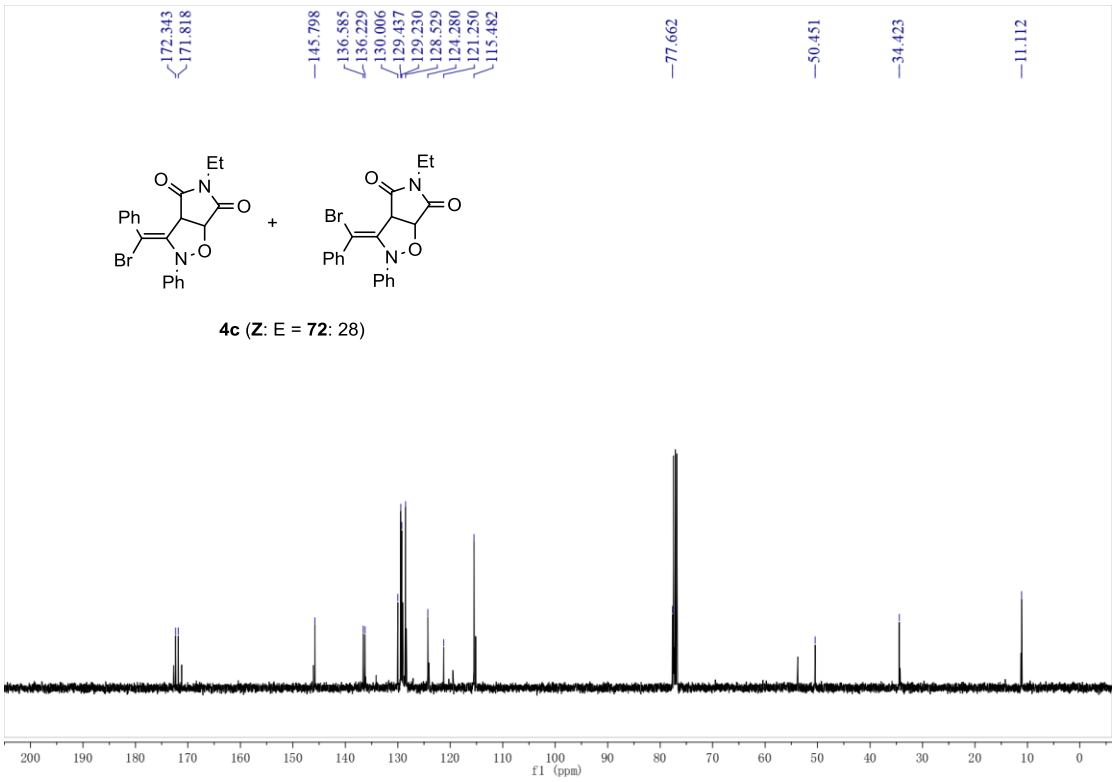
3-(bromo(phenyl)methylene)-5-(tert-butyl)-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione **(4b)**



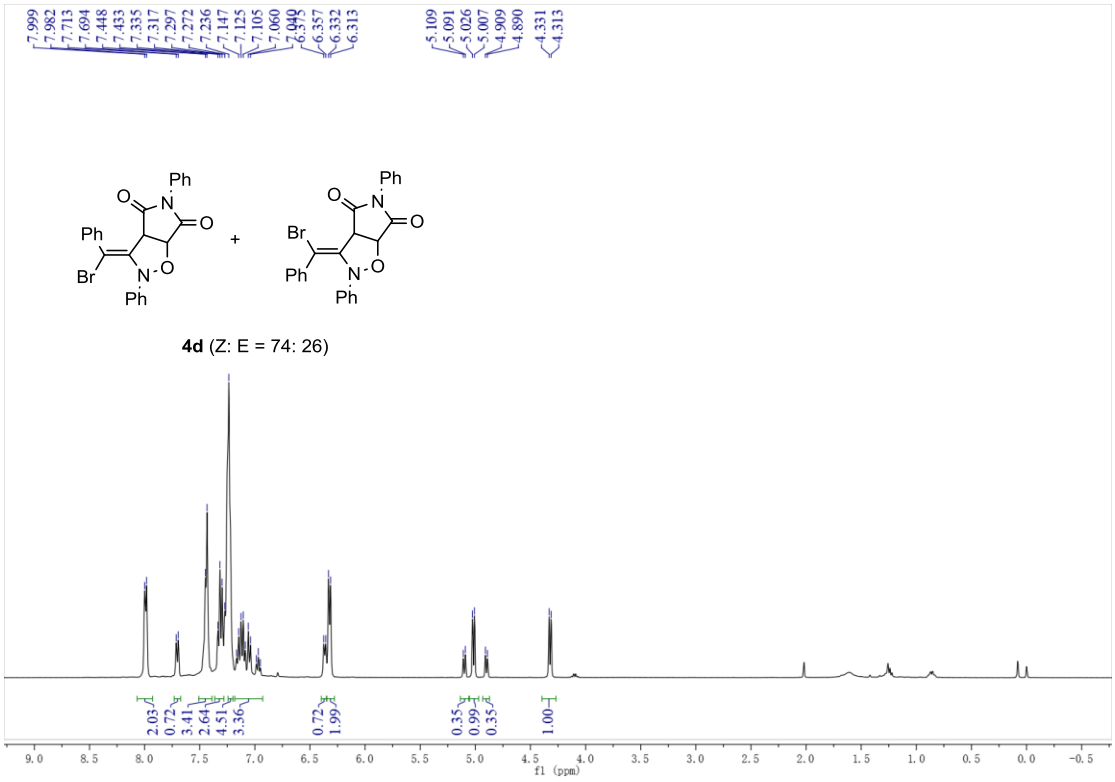


***3-(bromo(phenyl)methylene)-5-ethyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione* (4c)**

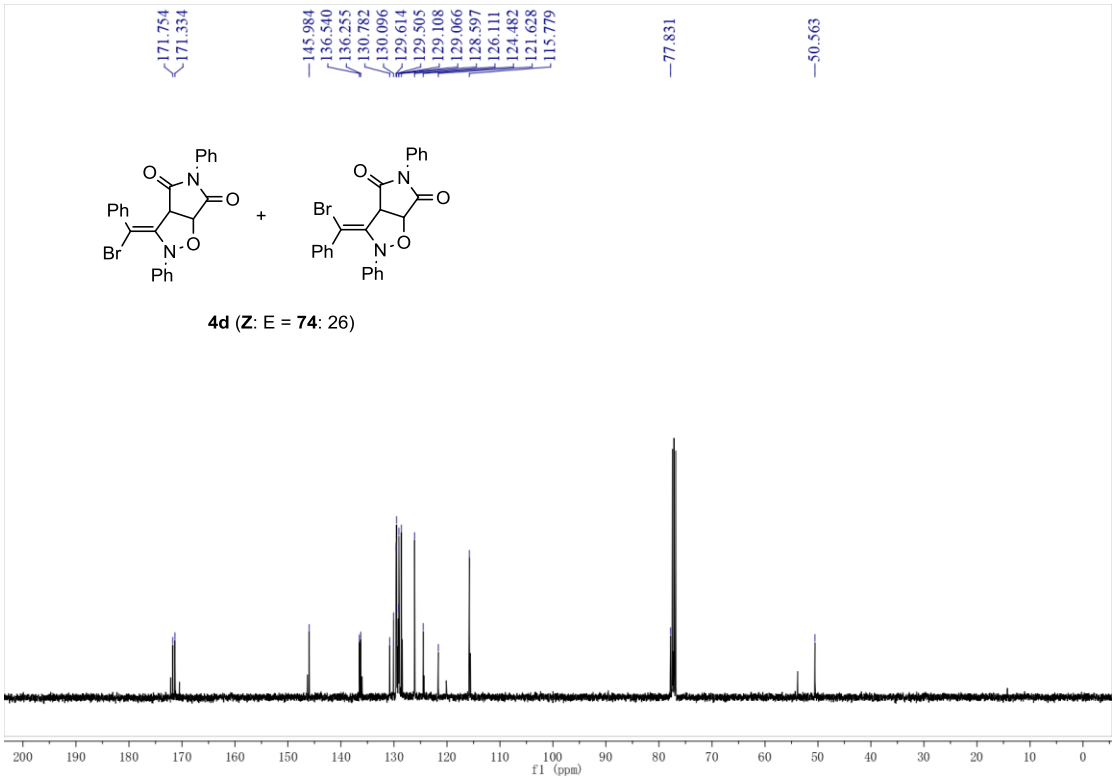




3-(bromo(phenyl)methylene)-2,5-diphenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione **(4d)**

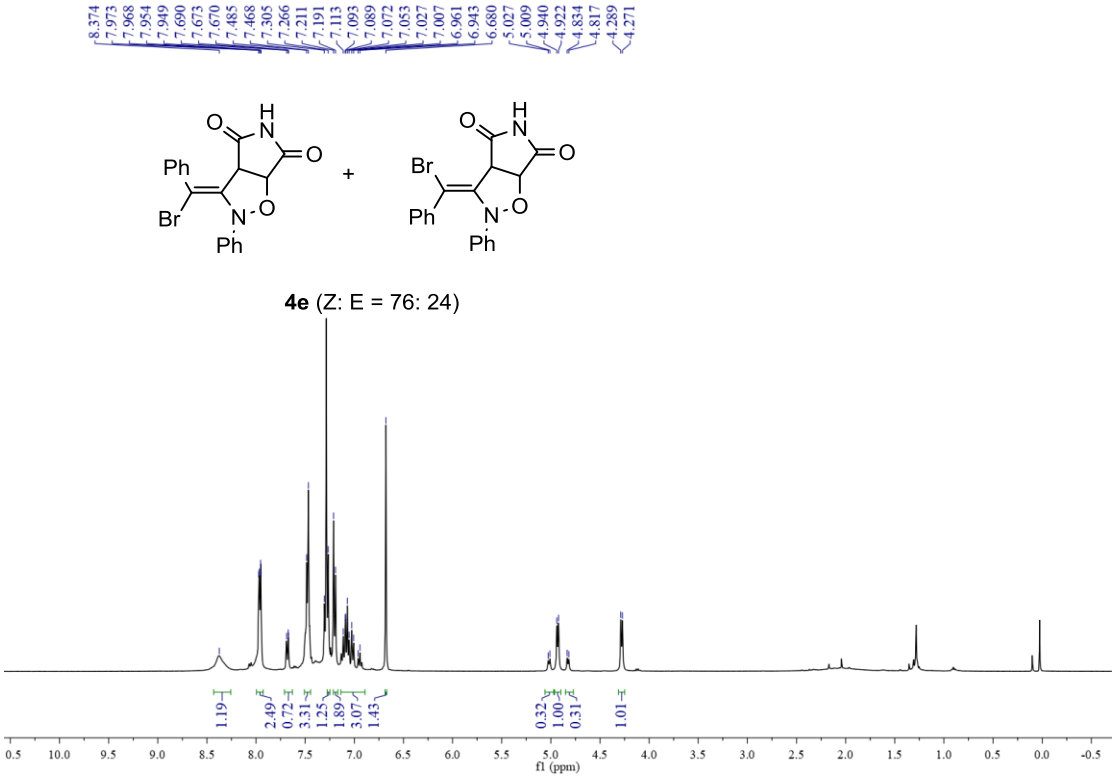


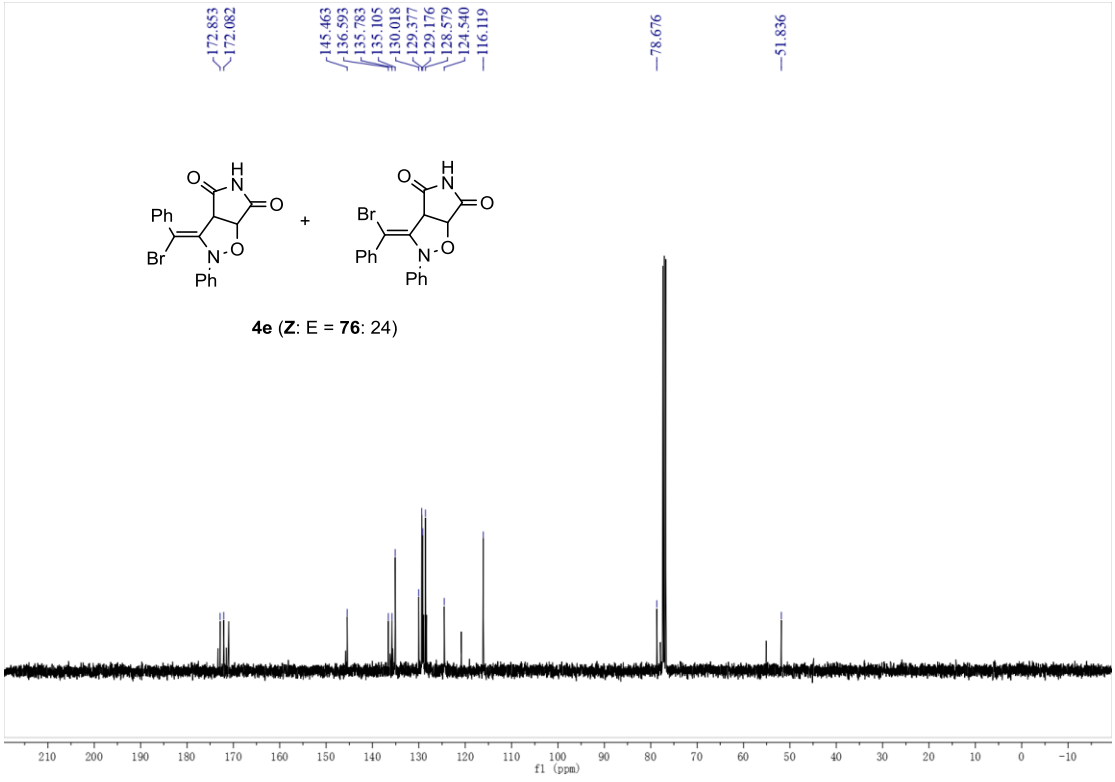
4d (Z: E = 74: 26)



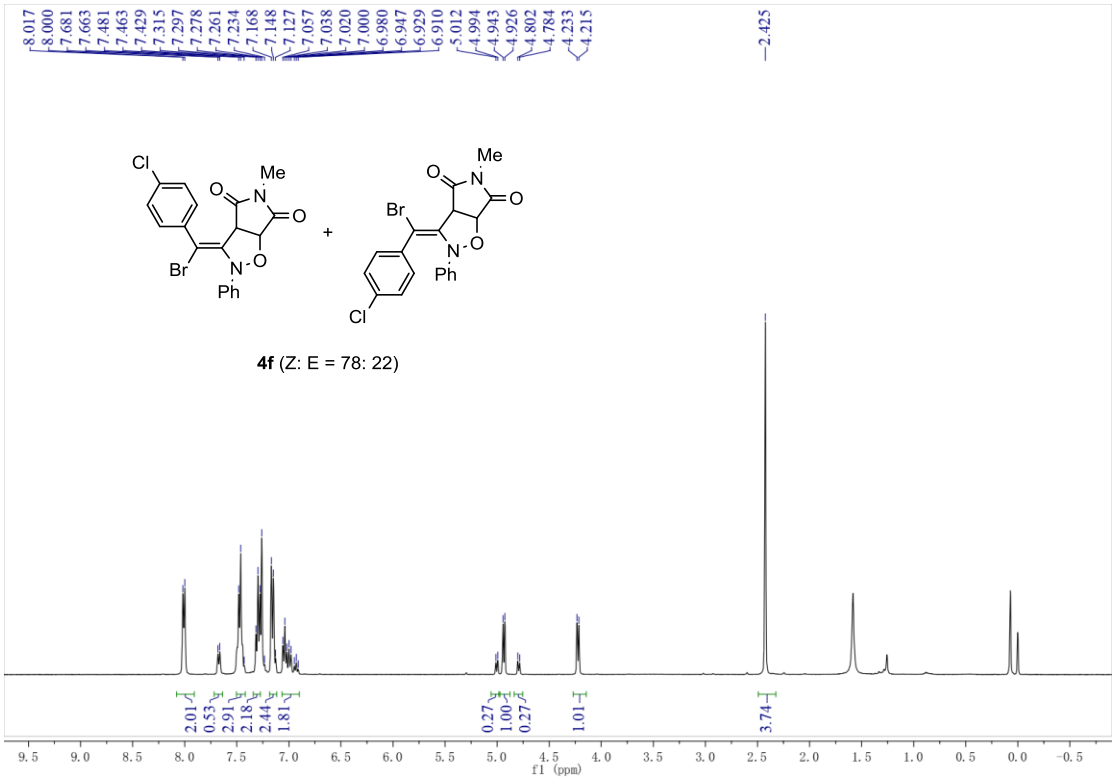
4d (**Z**: E = **74**: 26)

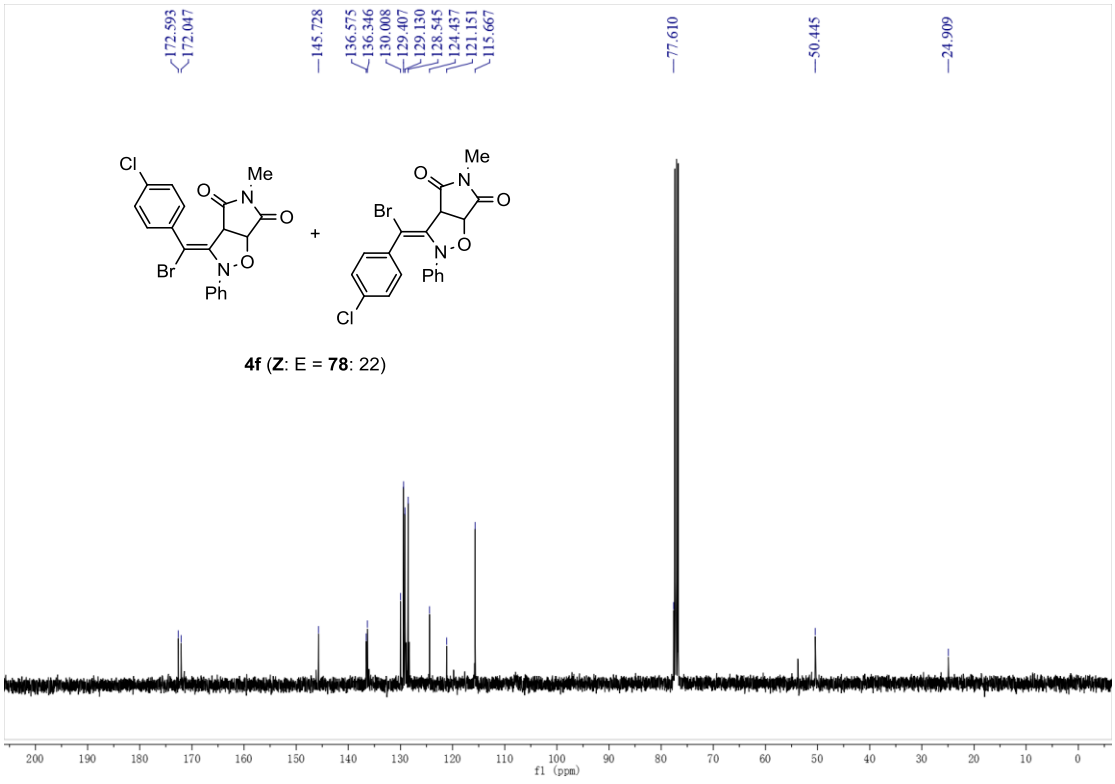
(Z)-3-(bromo(phenyl)methylene)-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione **(4e)**



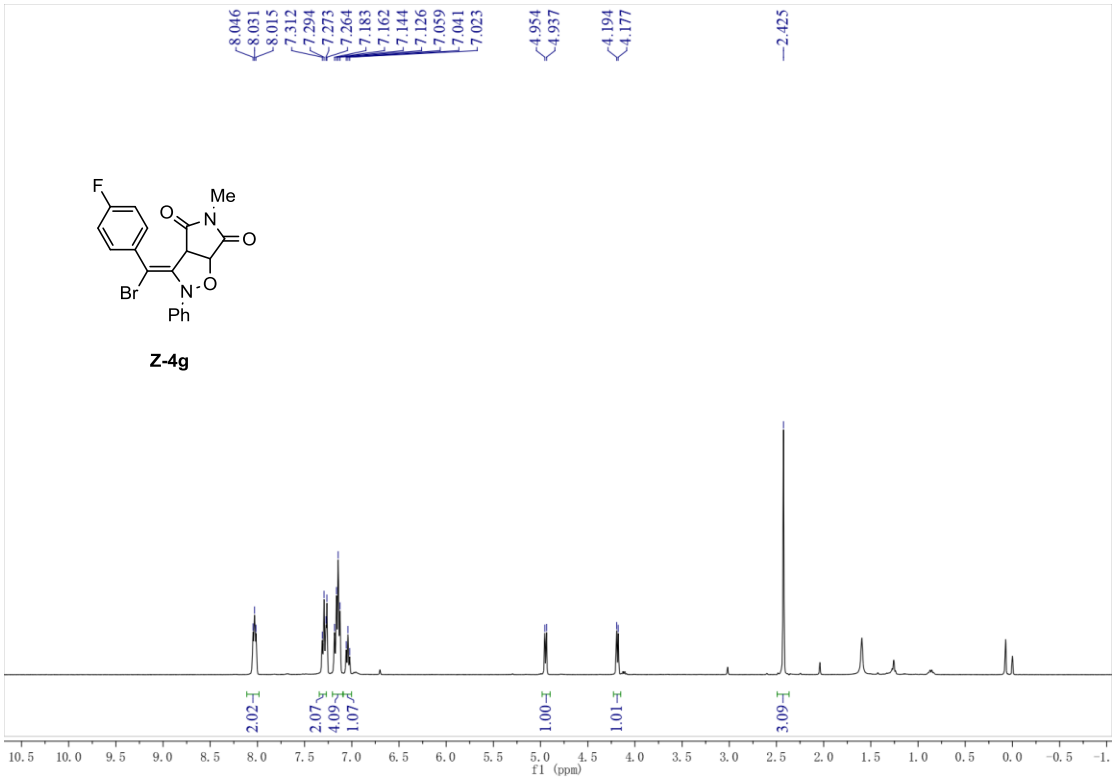


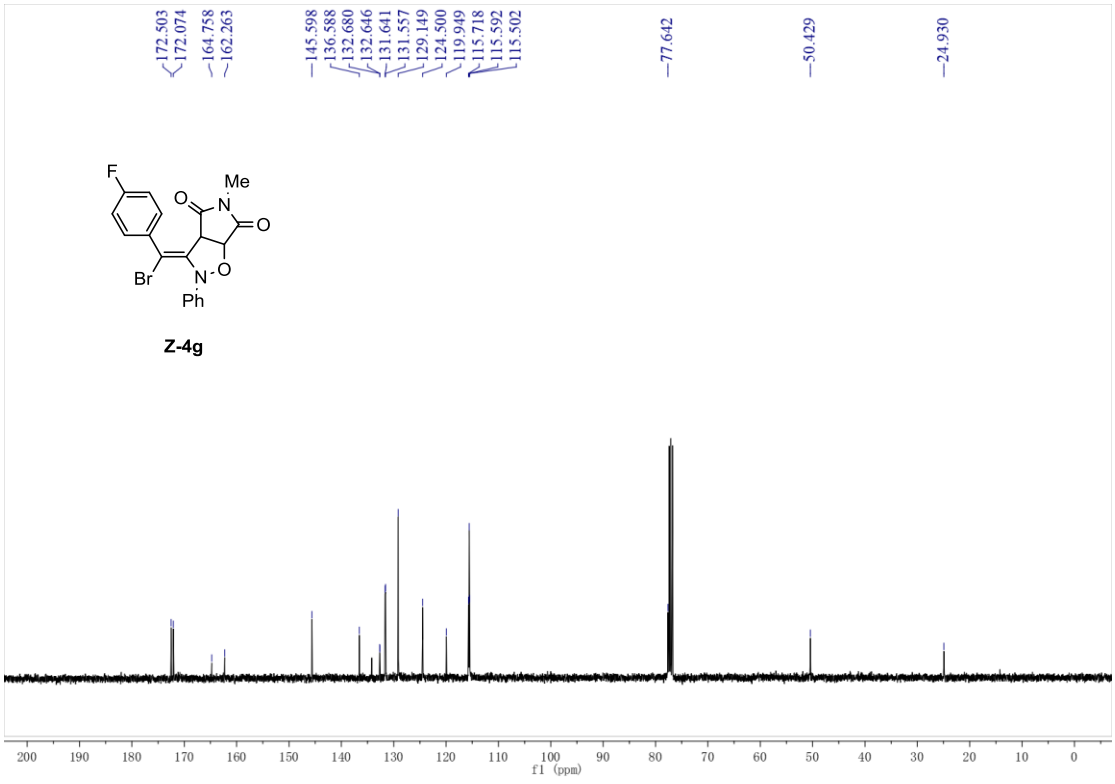
***3-(bromo(4-chlorophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (4f)**

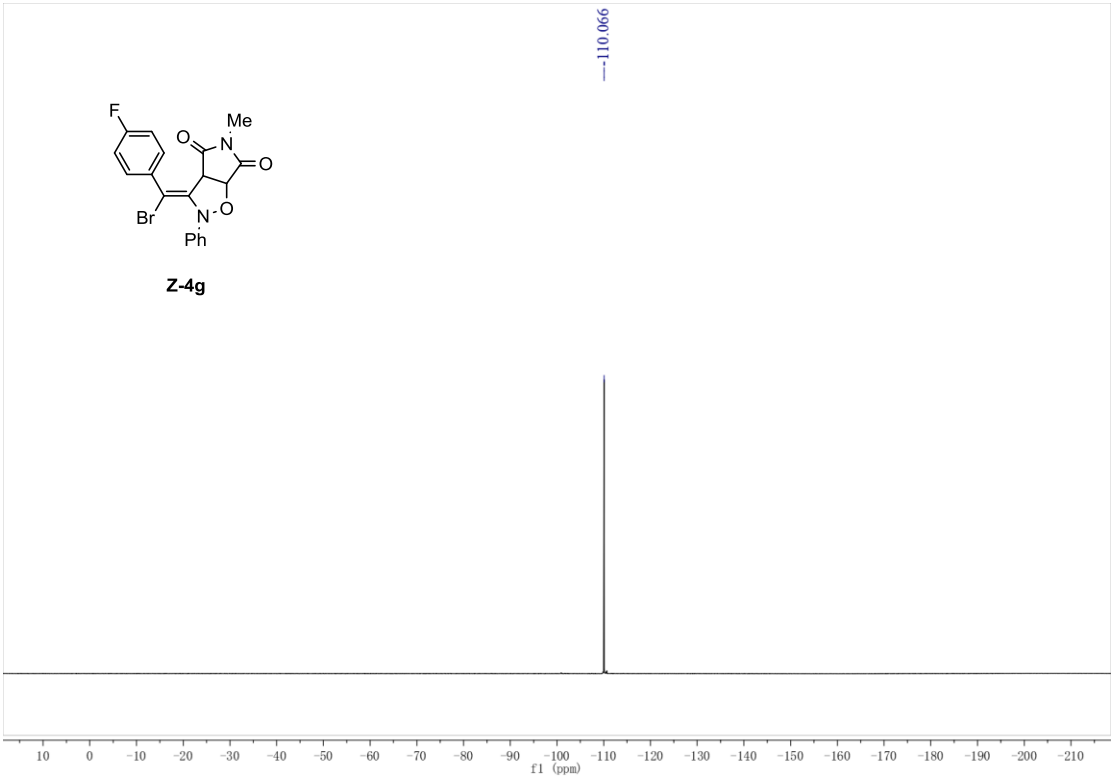




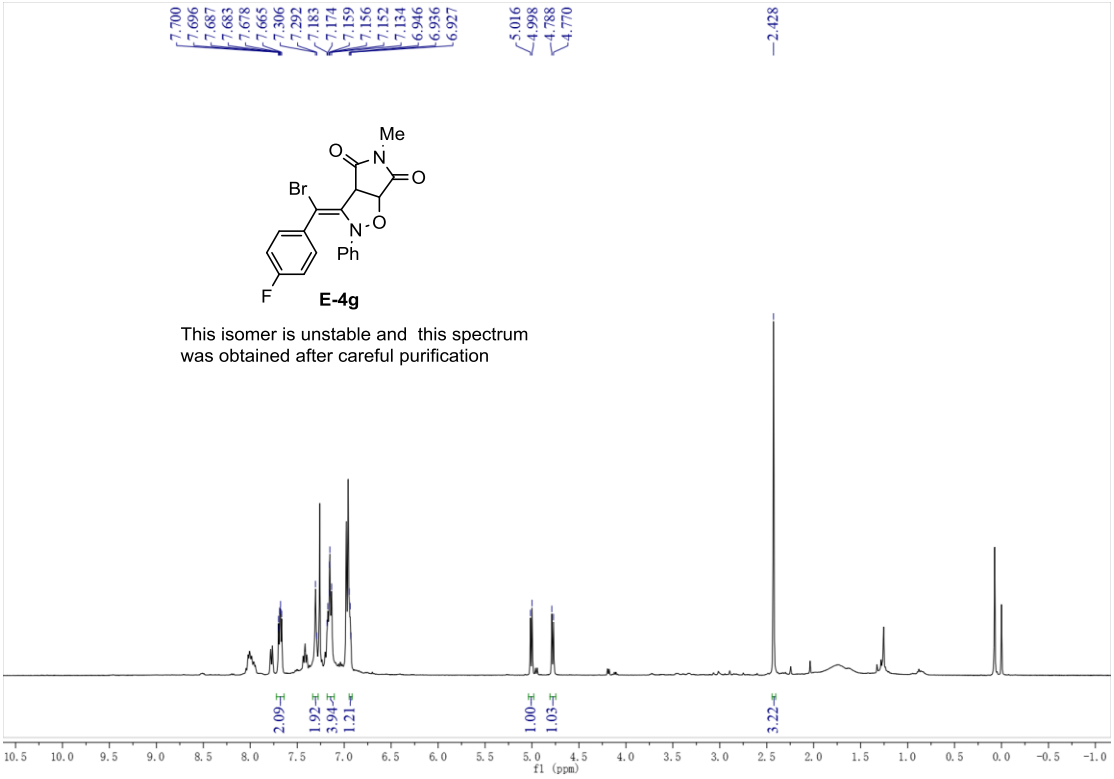
***(Z)-3-(bromo(4-fluorophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (Z-4g)**



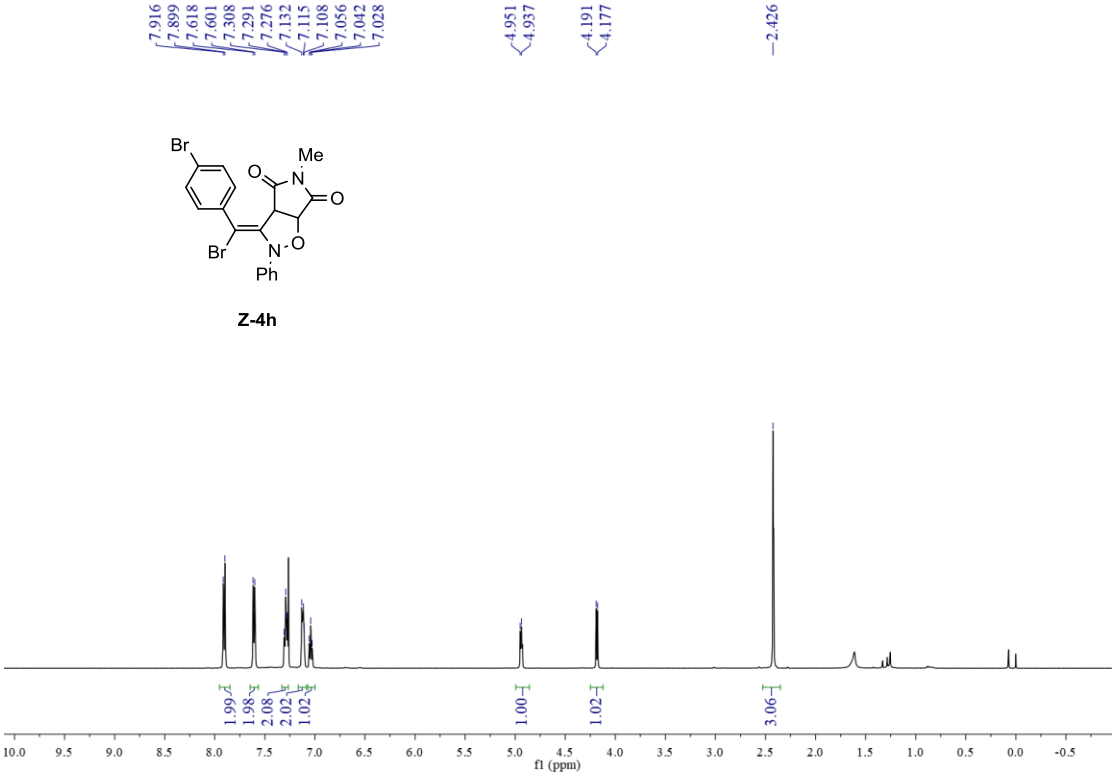




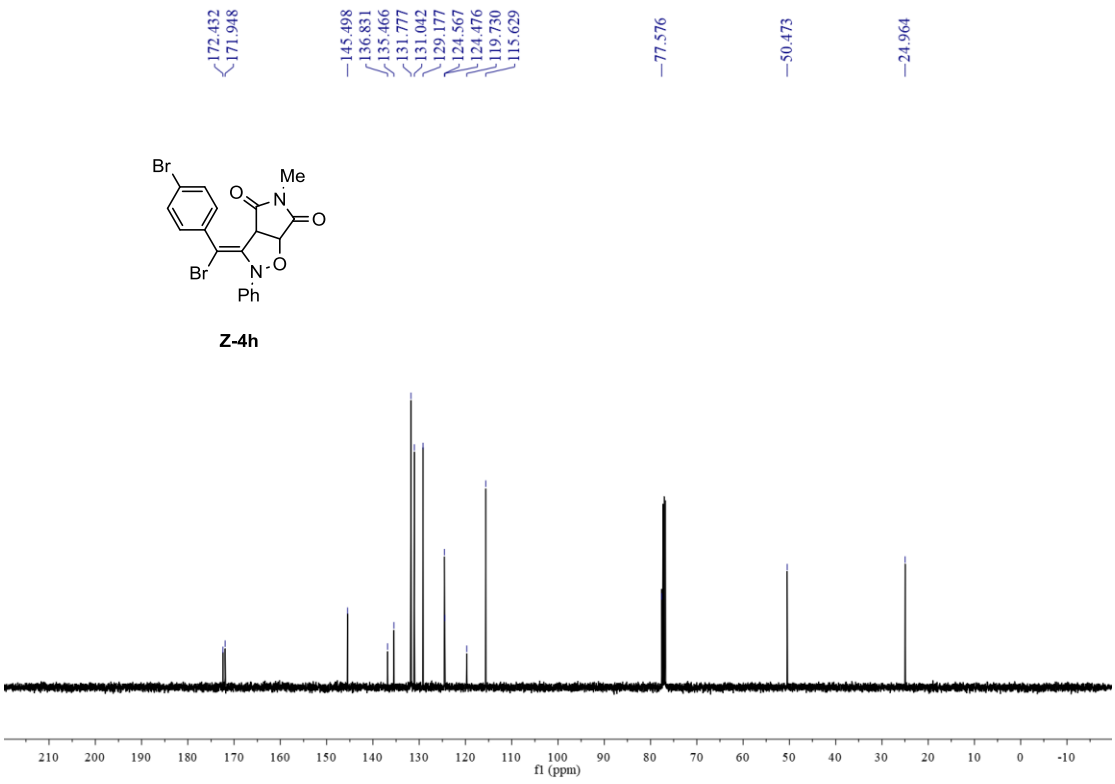
(E)-3-(bromo(4-fluorophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione **(E-4g)**



***(Z)-3-(bromo(4-bromophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (Z-4h)**

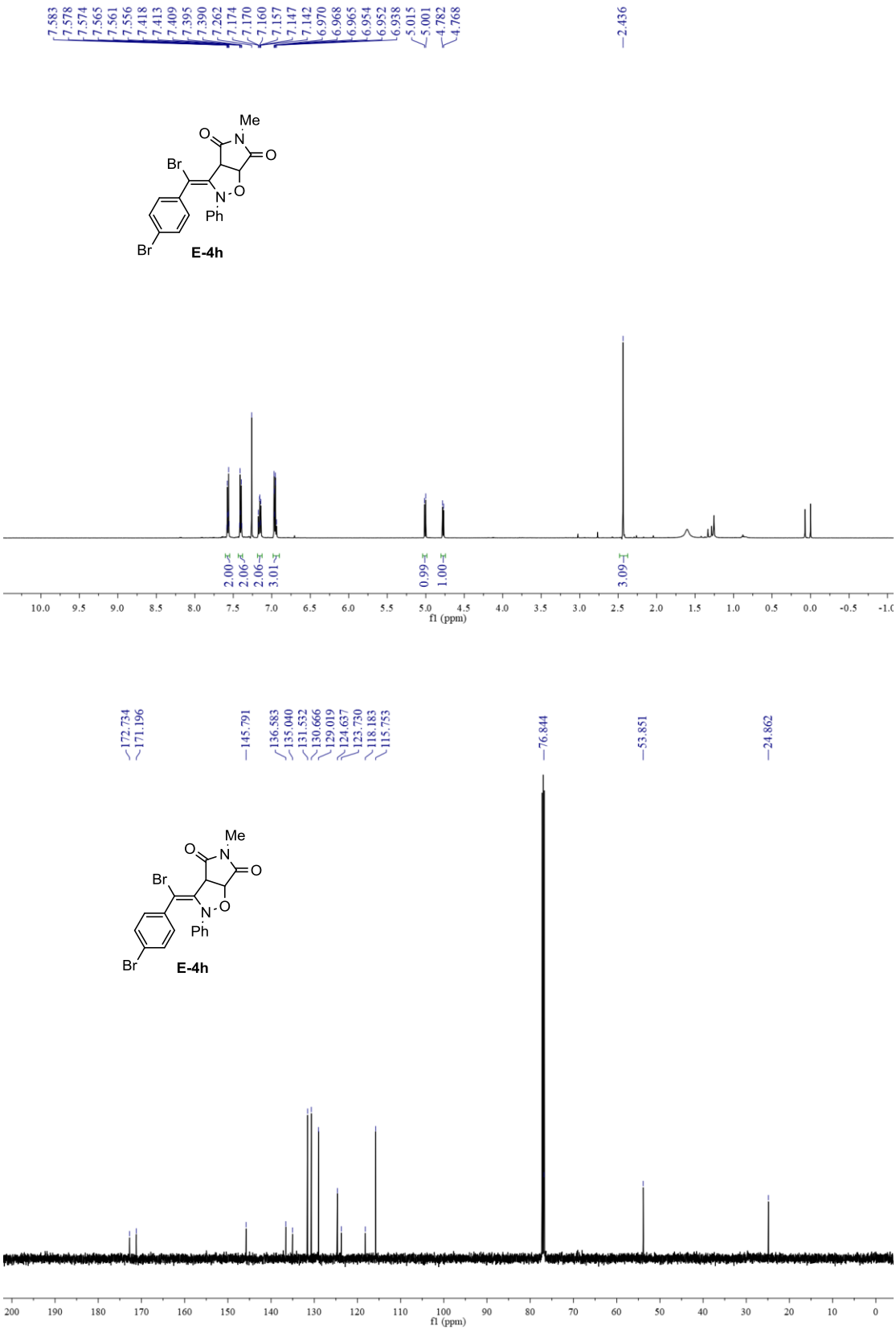


Z-4h

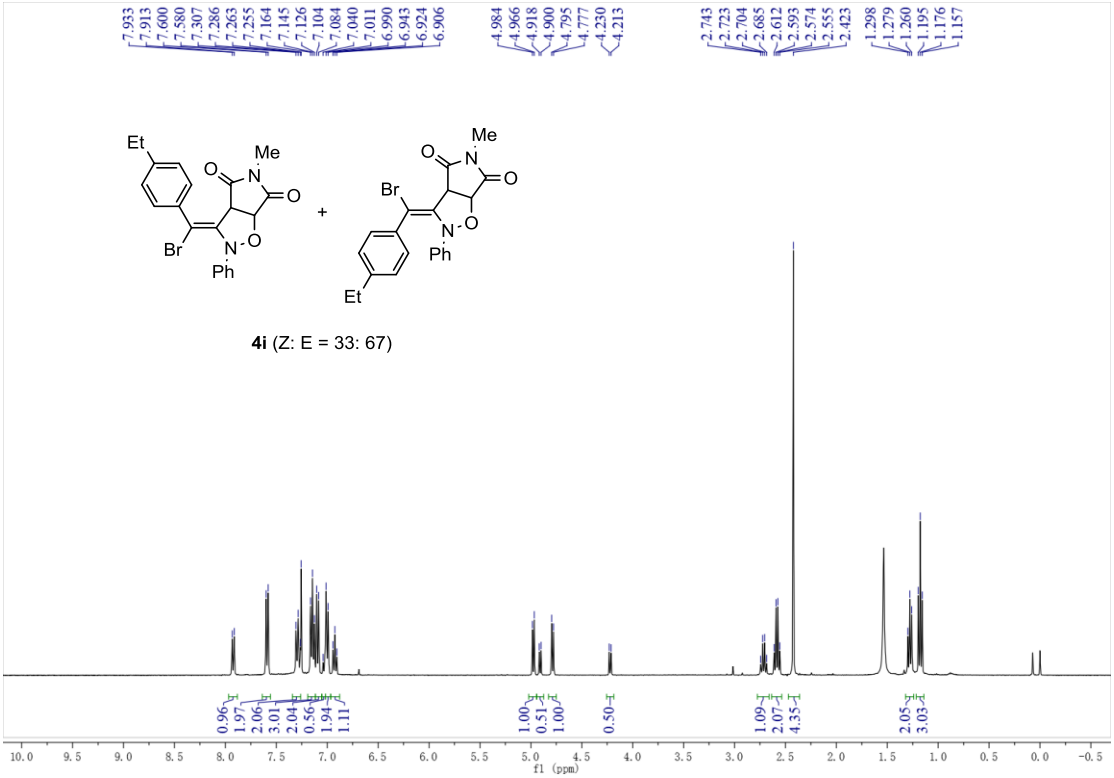


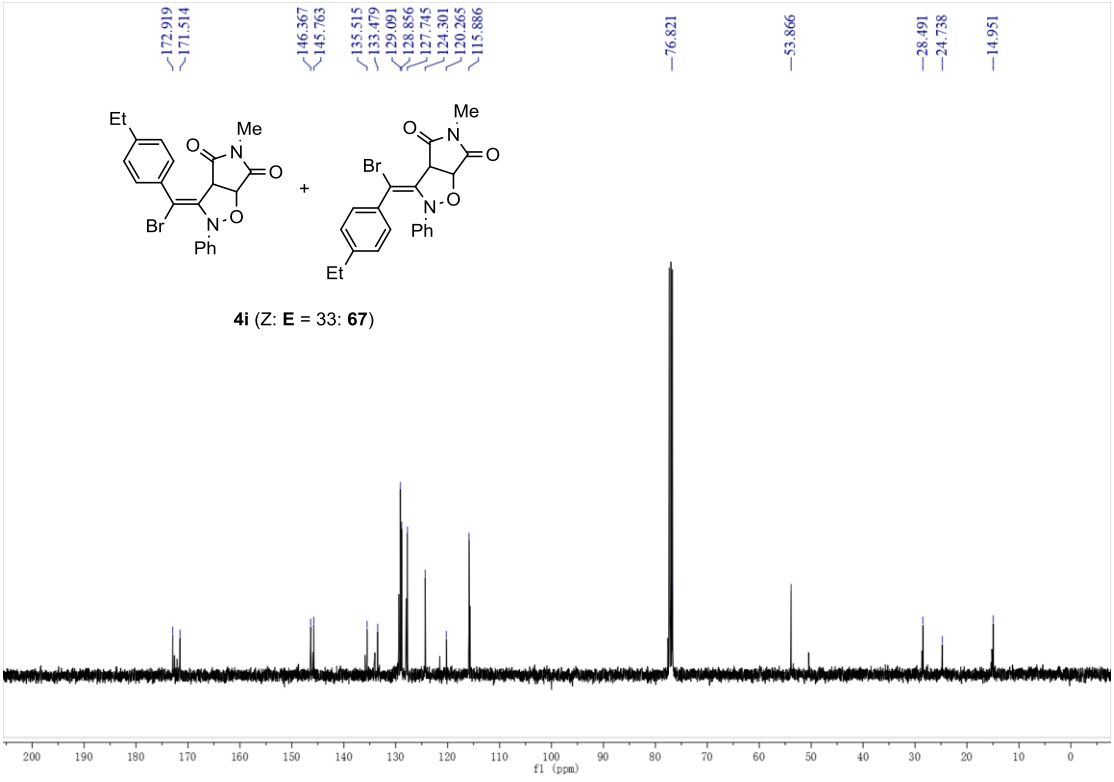
Z-4h

***(E)-3-(bromo(4-bromophenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (E-4h)**

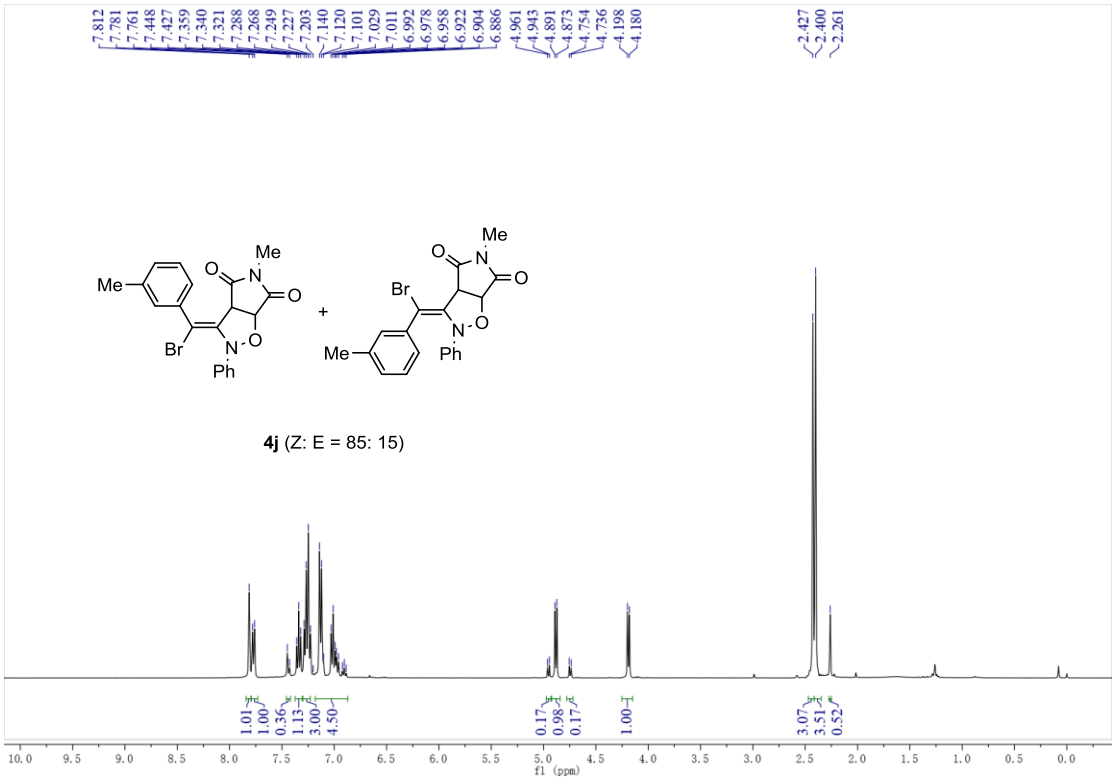


***3-(bromo(4-ethylphenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (4i)**

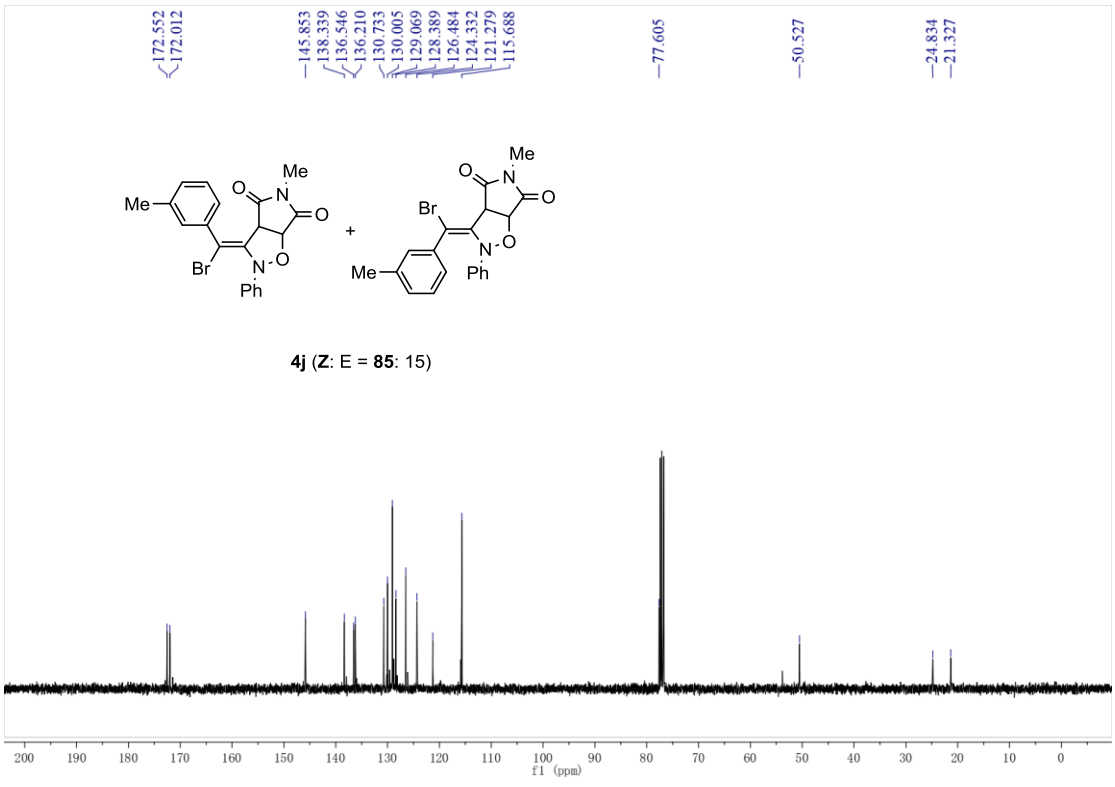




***3-(bromo(m-tolyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione* (4j)**

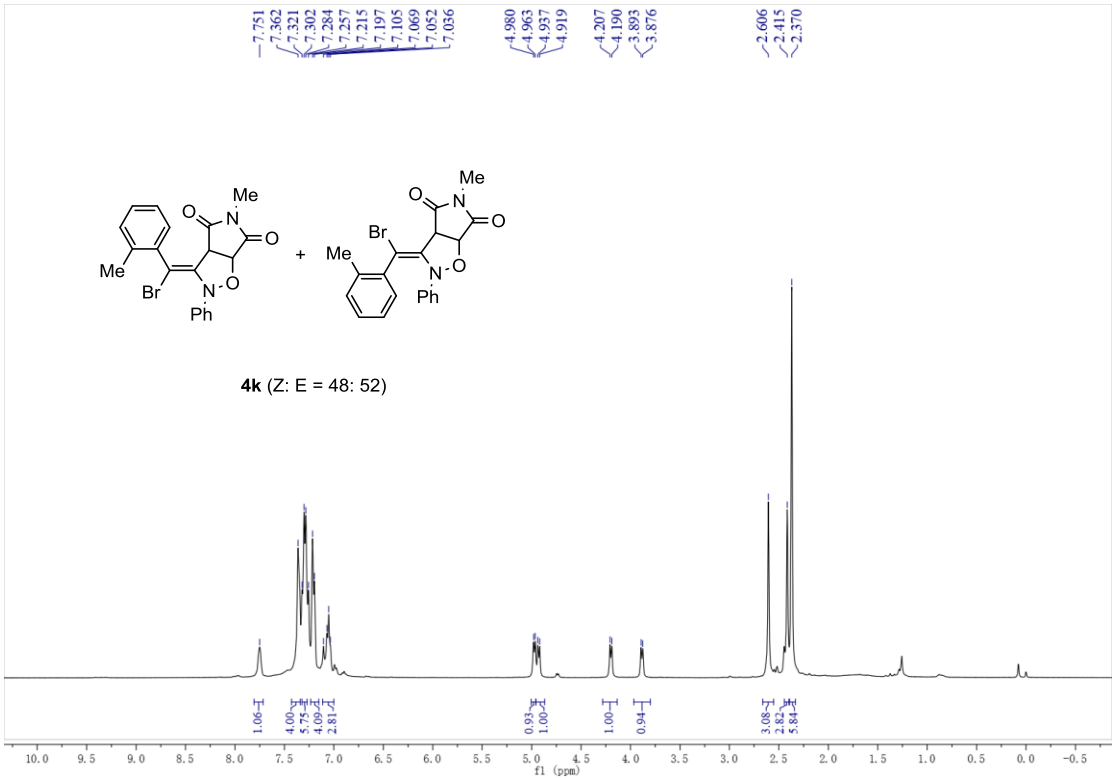


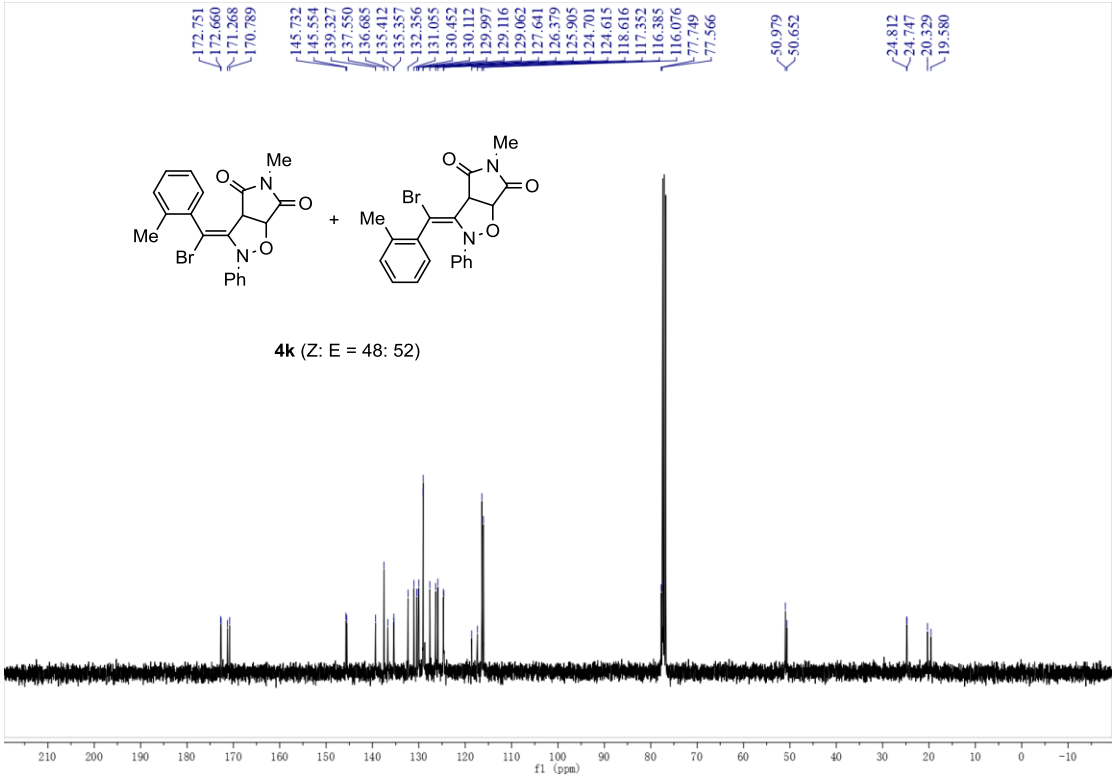
4j (Z: E = 85: 15)



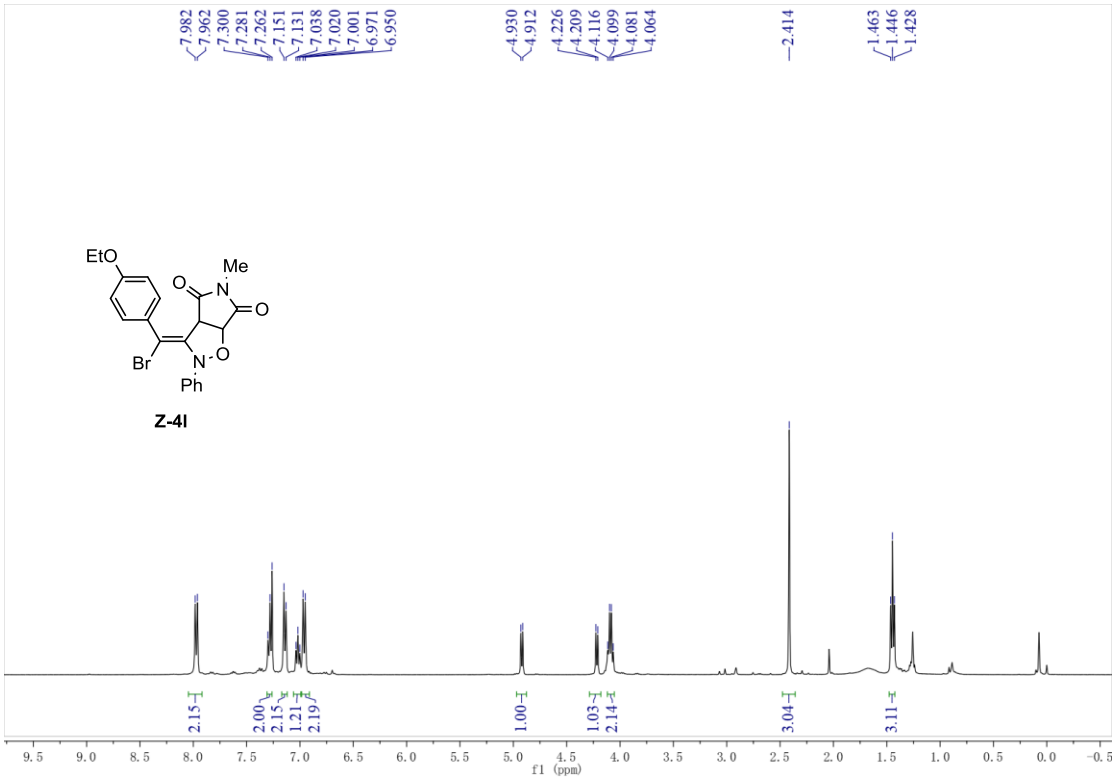
4j (**Z**: E = **85**: 15)

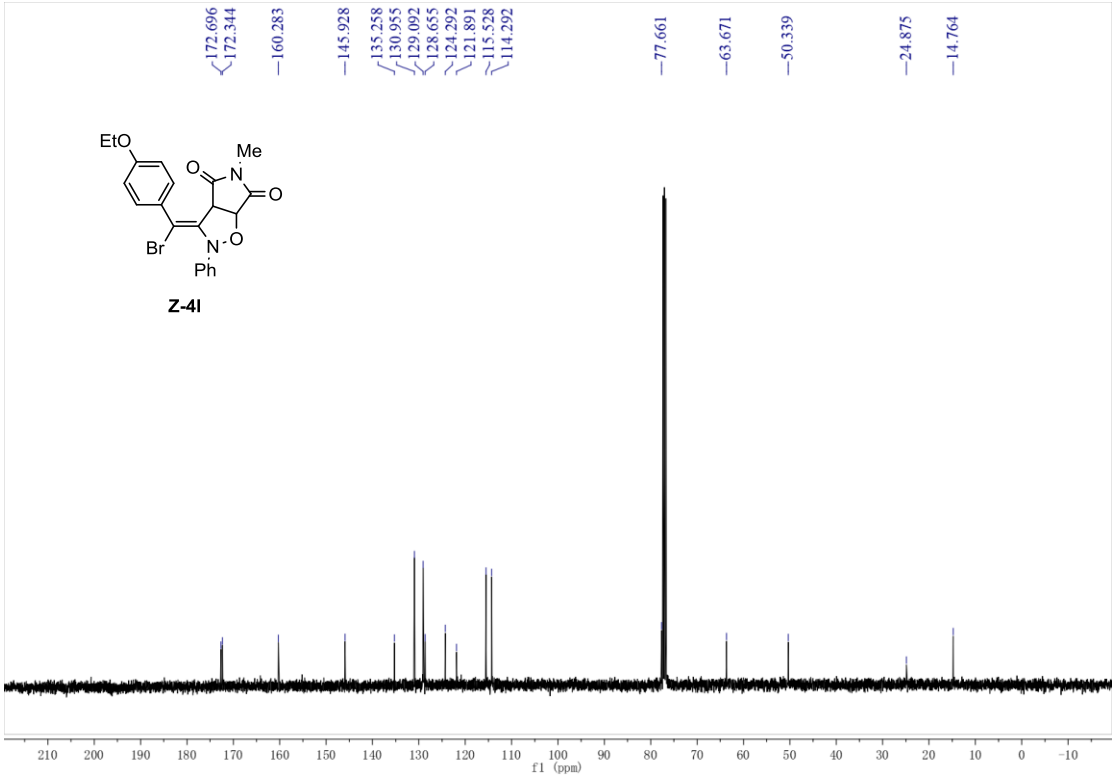
***3-(bromo(o-tolyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione* (4k)**



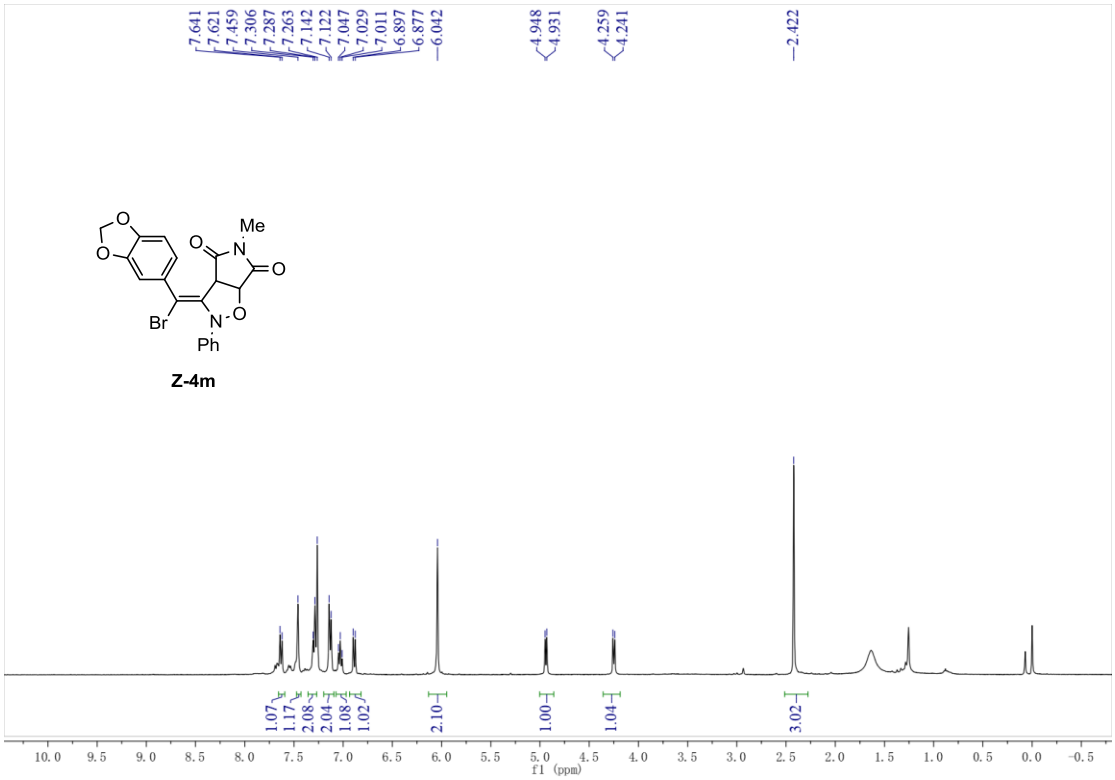


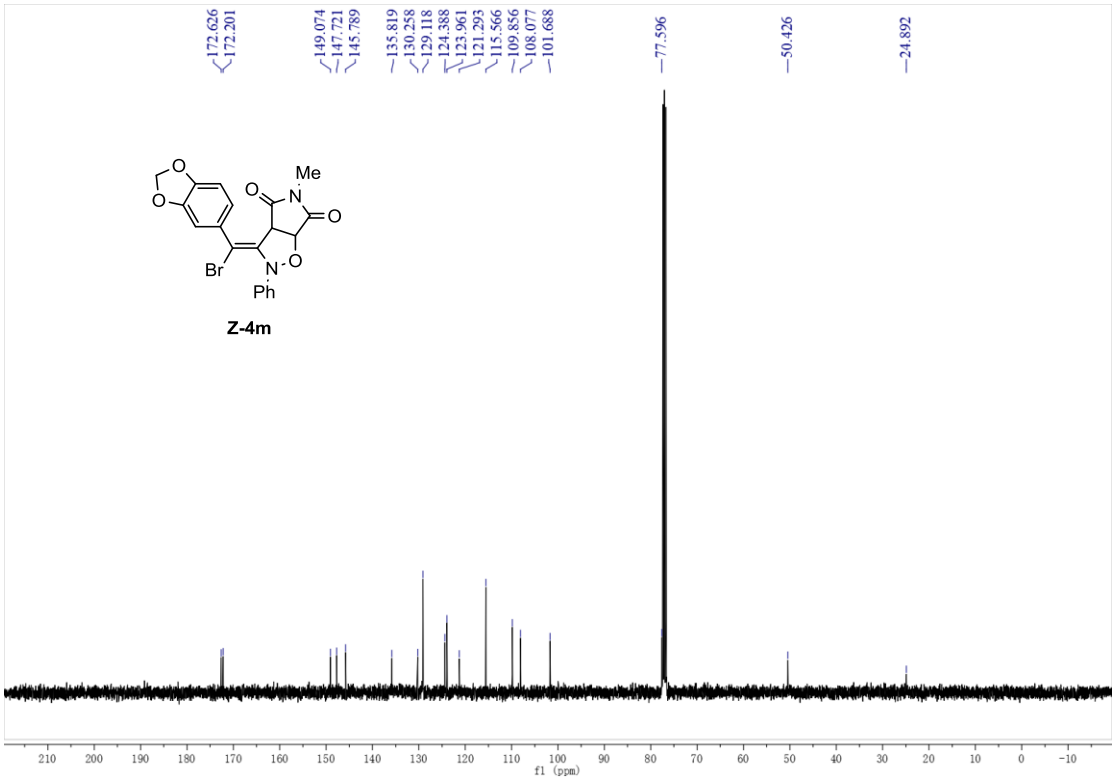
***(Z)-3-(bromo(4-ethoxyphenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (Z-4l)**



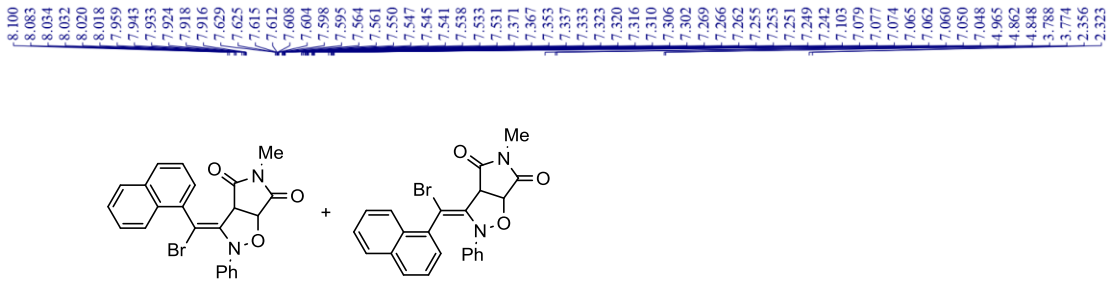


***(Z)-3-(benzo[d][1,3]dioxol-5-ylbromomethylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]--isoxazole-4,6(5H)-dione* (Z-4m)**

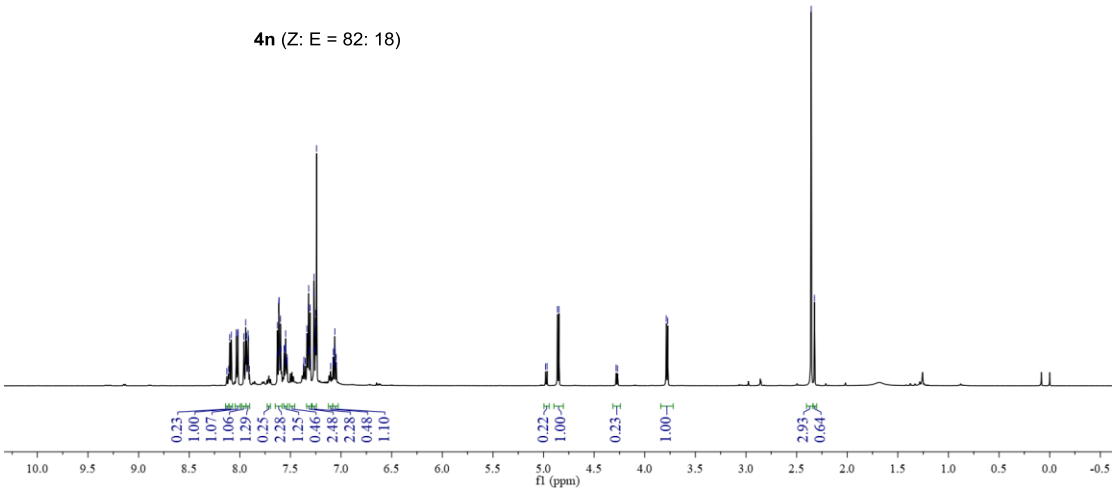


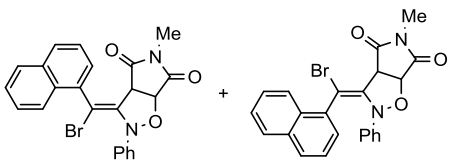


***3-(bromo(naphthalen-1-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (4n)**

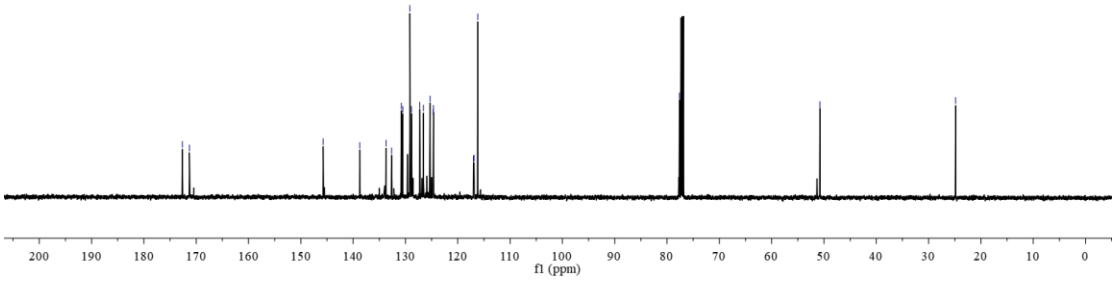


4n (Z: E = 82: 18)

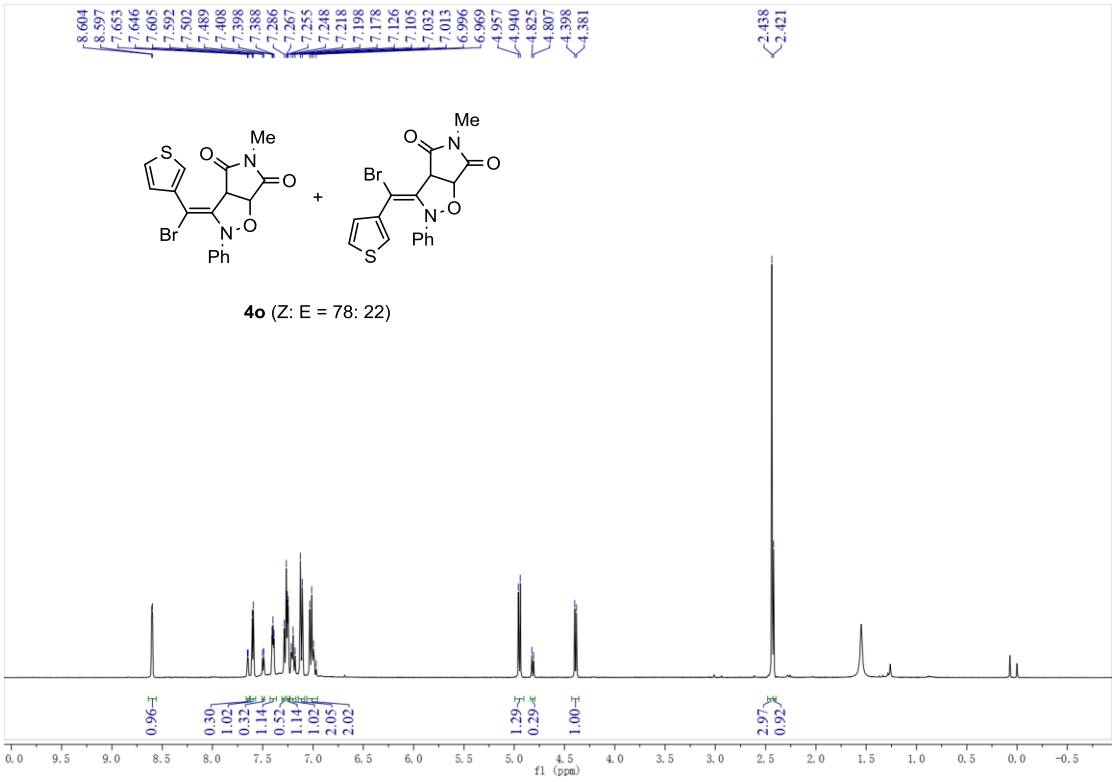


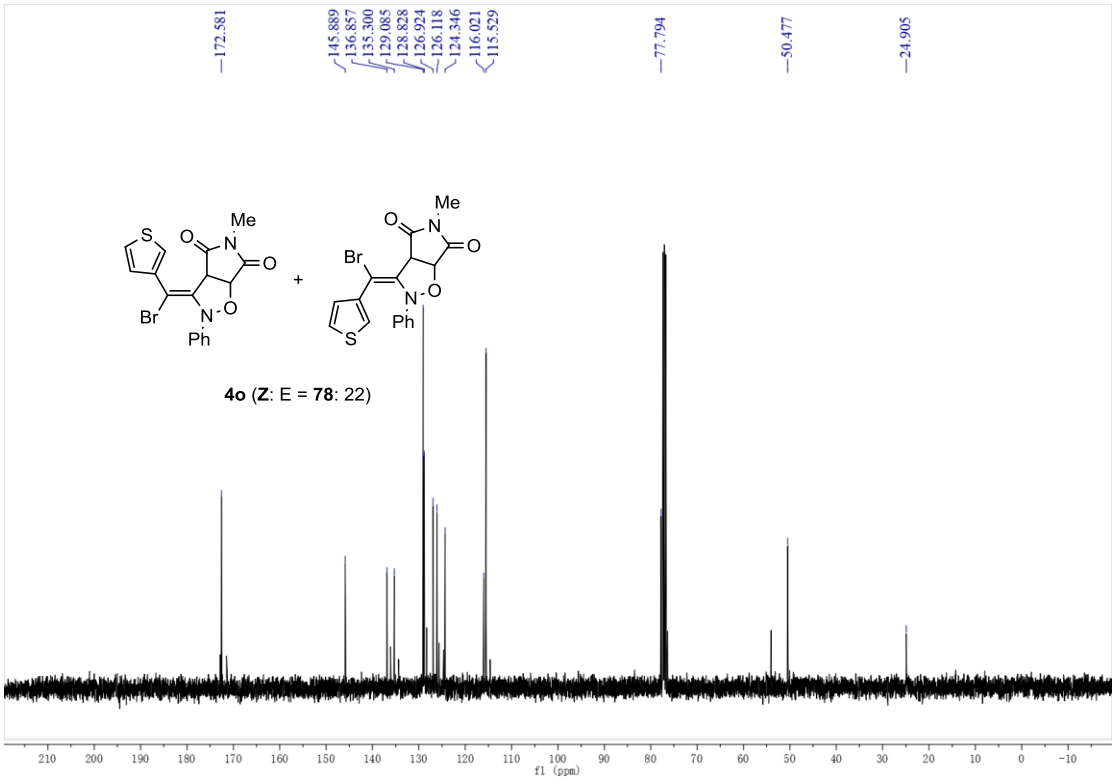


4n (**Z**: E = **82**: 18)

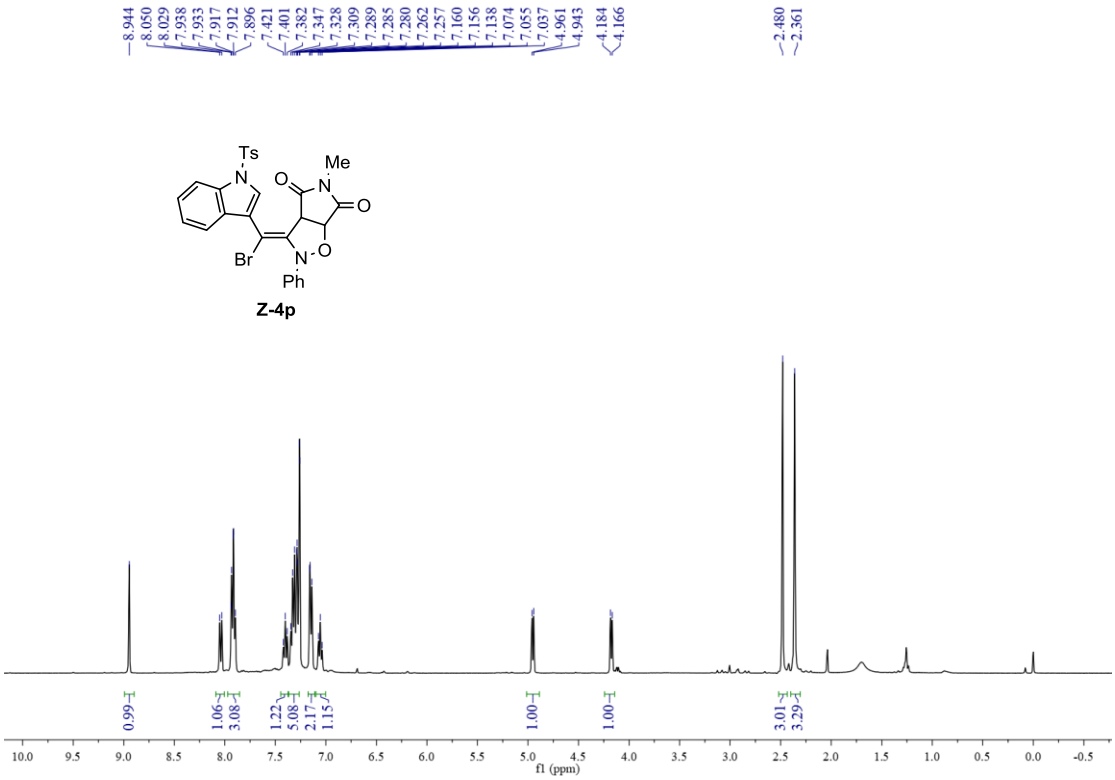


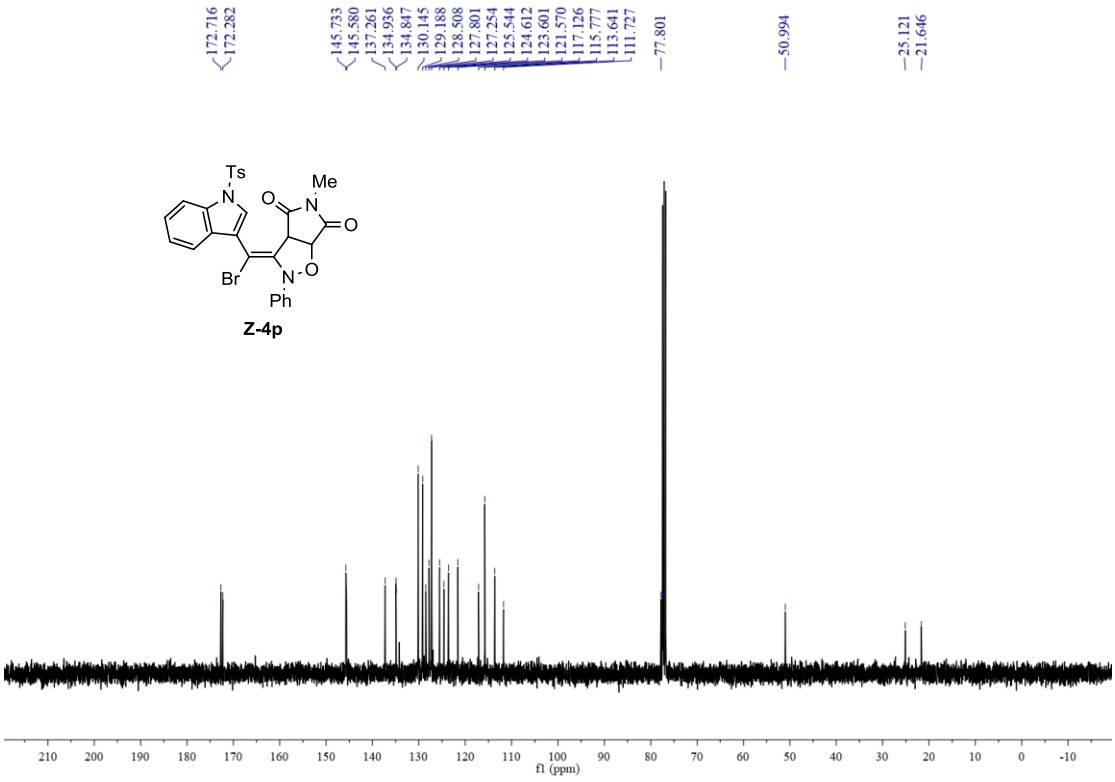
***3-(bromo(thiophen-3-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (4o)**



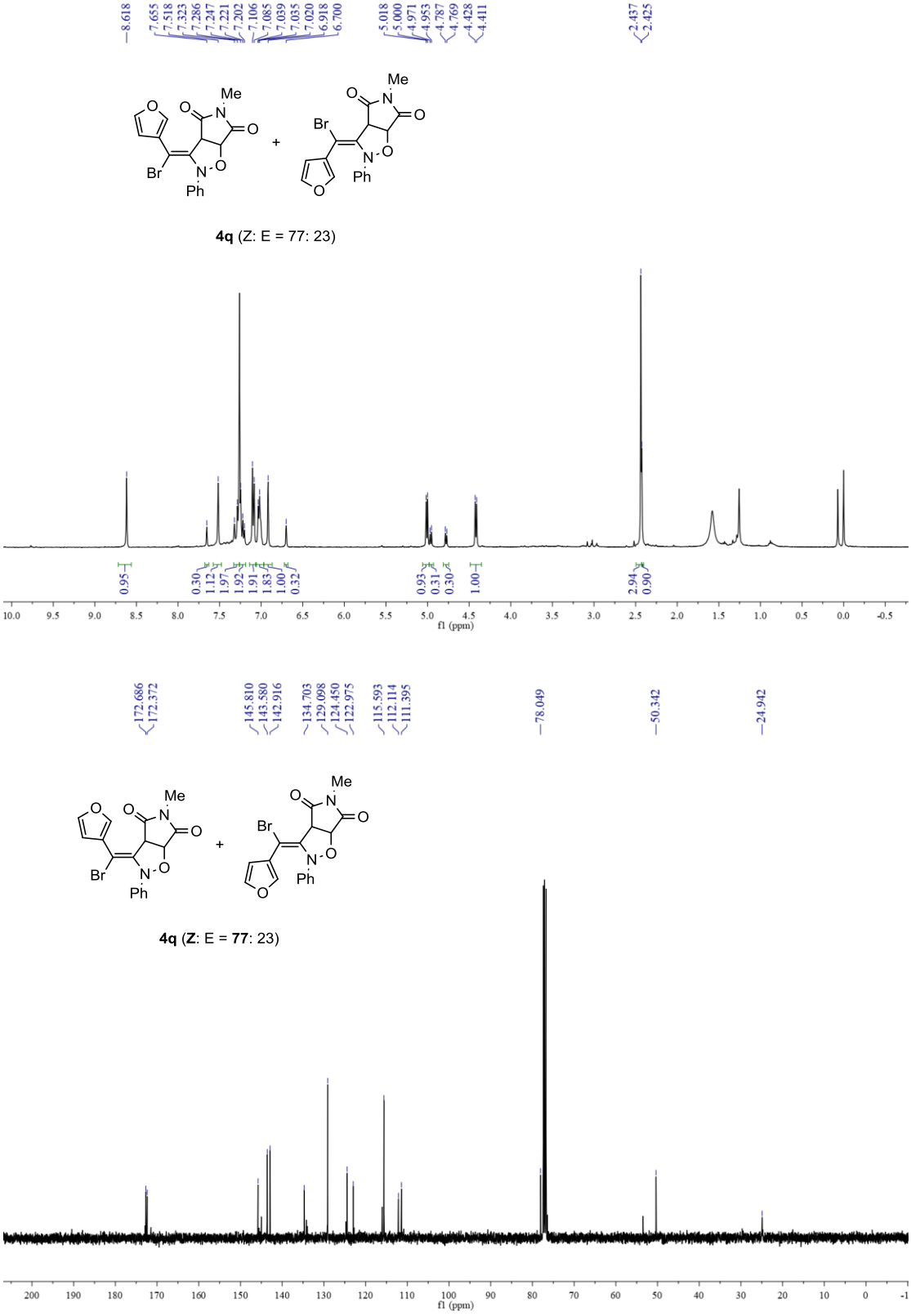


***(Z)-3-(bromo(1-tosyl-1H-indol-3-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]--isoxazole-4,6(5H)-dione* (Z-4p)**



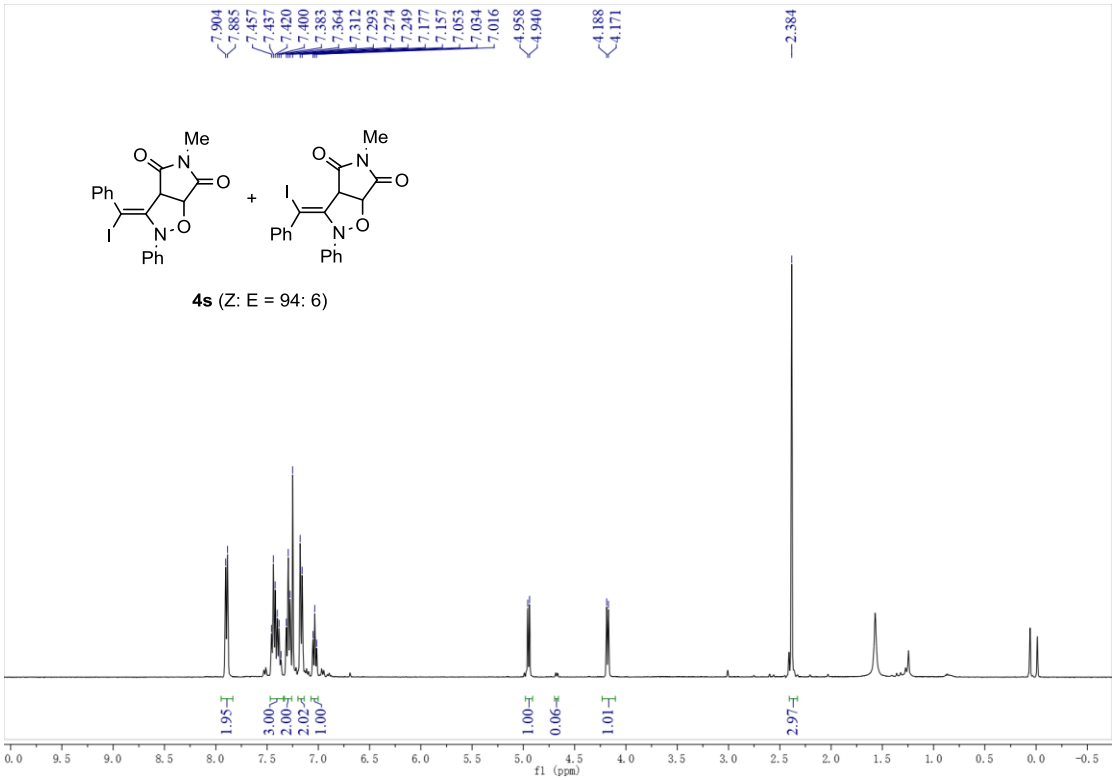


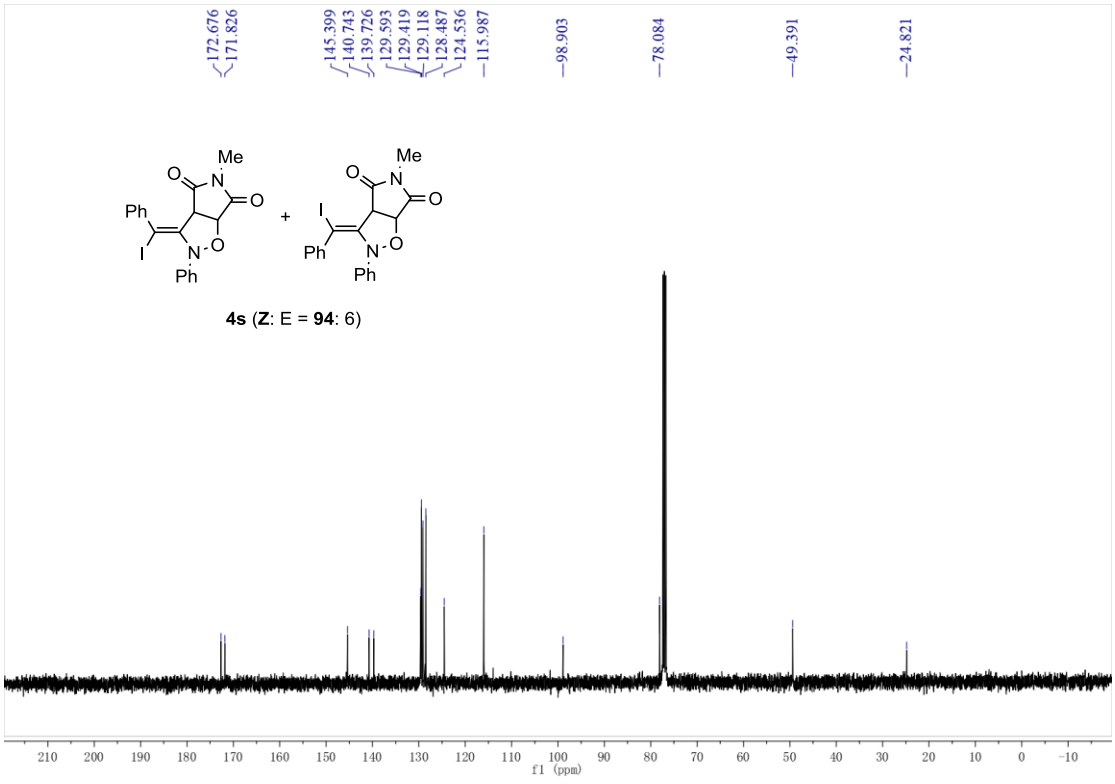
***3-(bromo(furan-3-yl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione* (4q)**



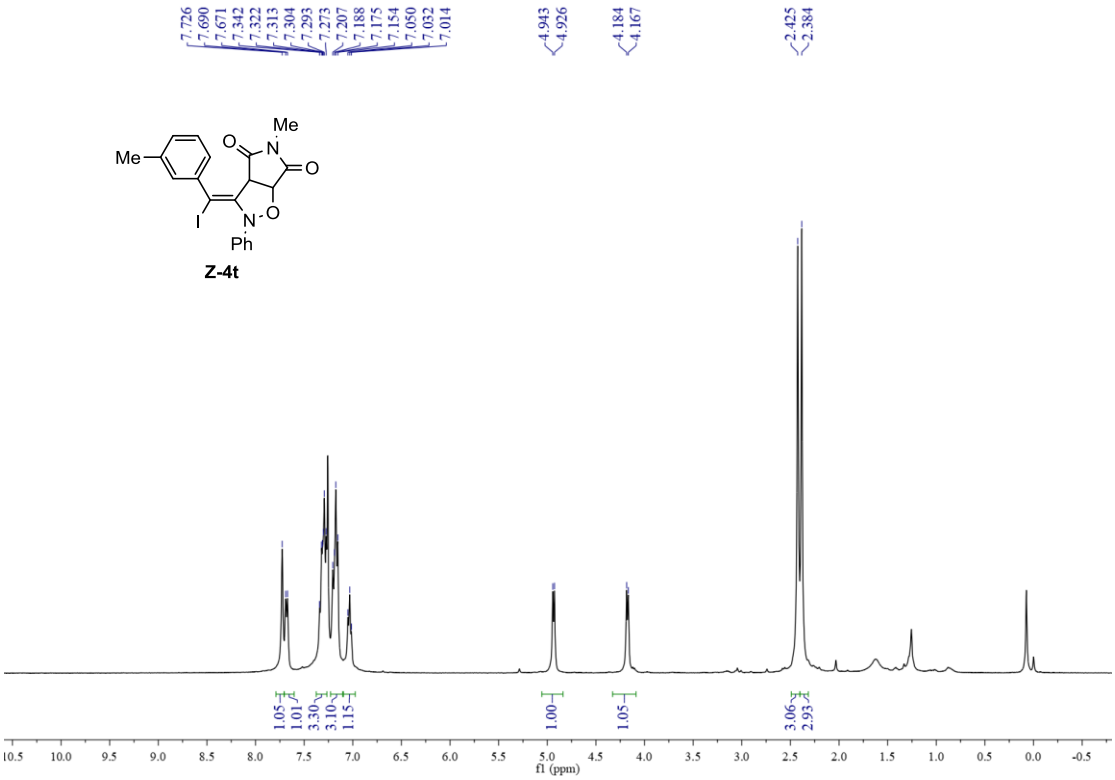
3-(iodo(phenyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione

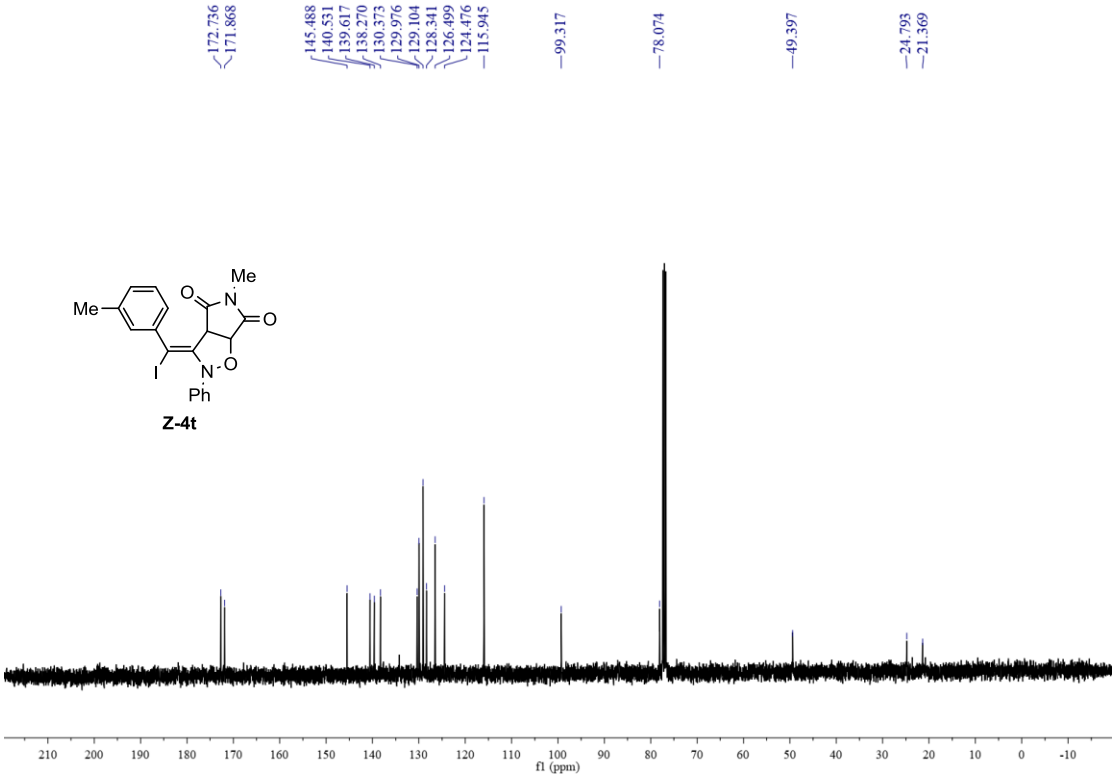
(4s)



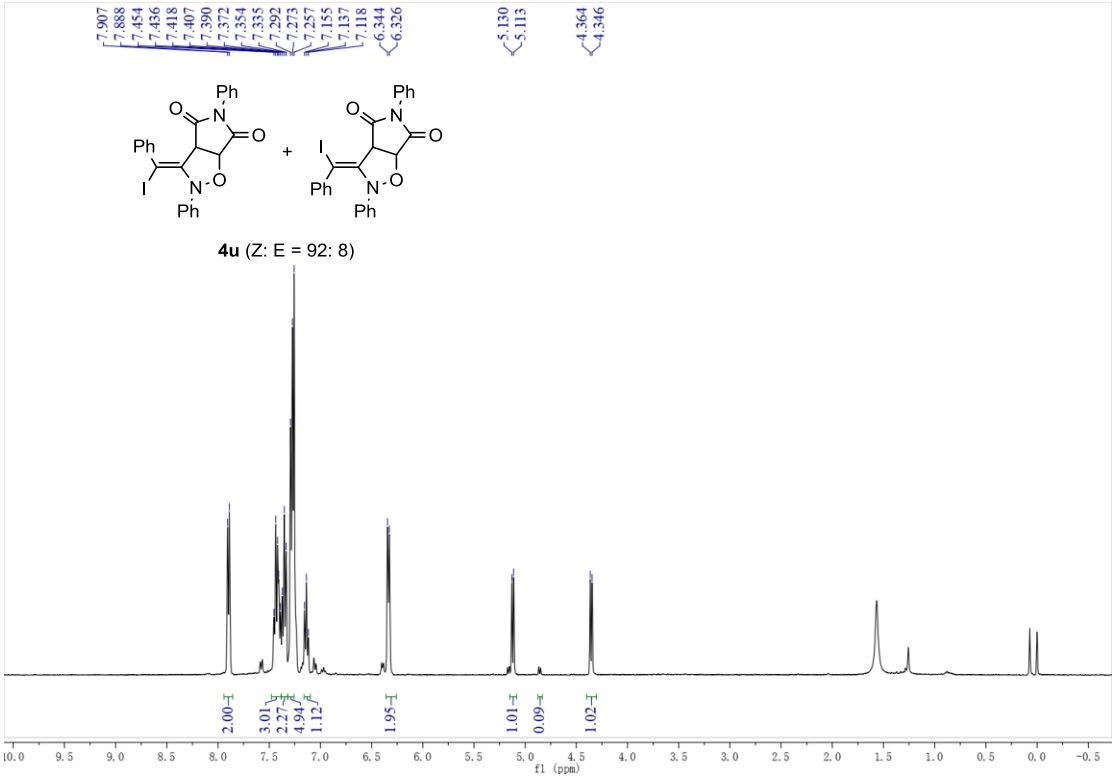


***(Z)-3-(iodo(m-tolyl)methylene)-5-methyl-2-phenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)--dione* (Z-4t)**

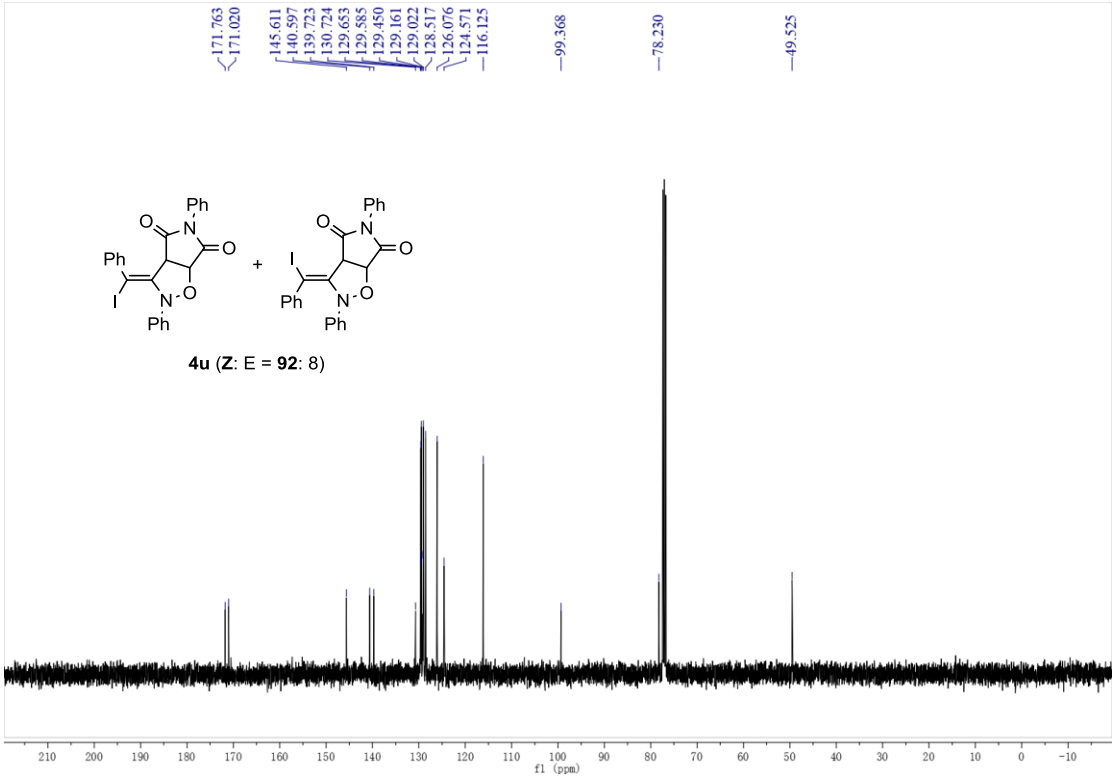




3-(iodo(phenyl)methylene)-2,5-diphenyltetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione **(4u)**

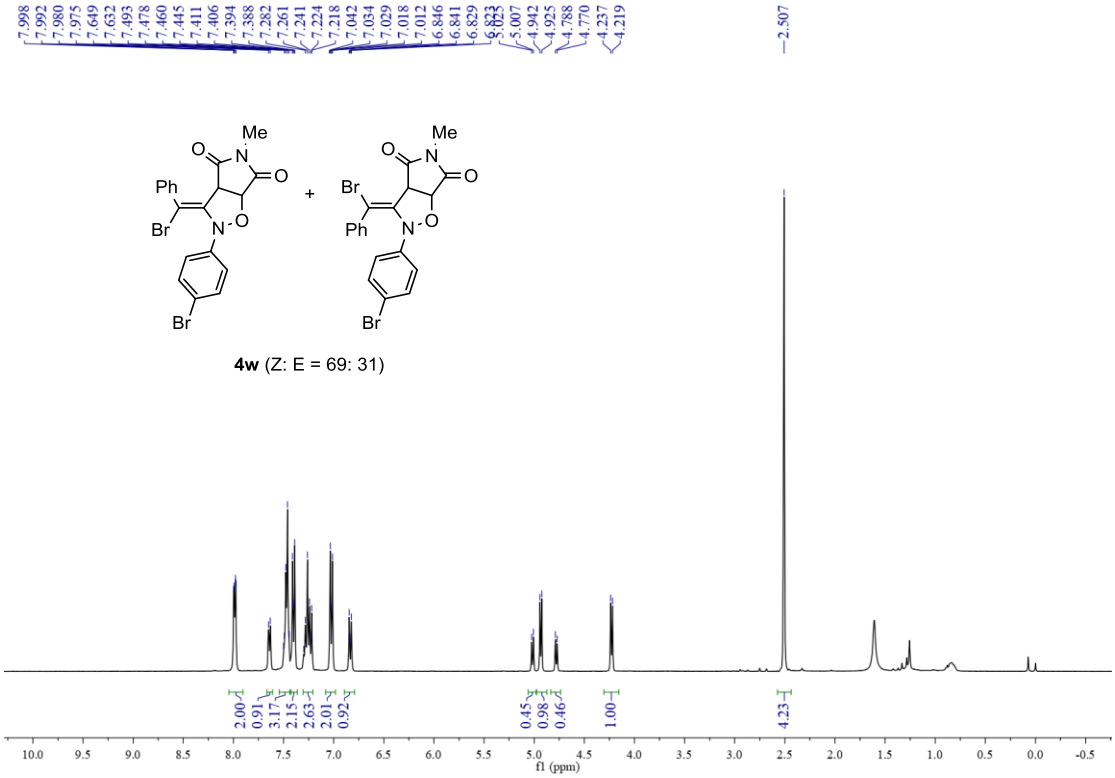


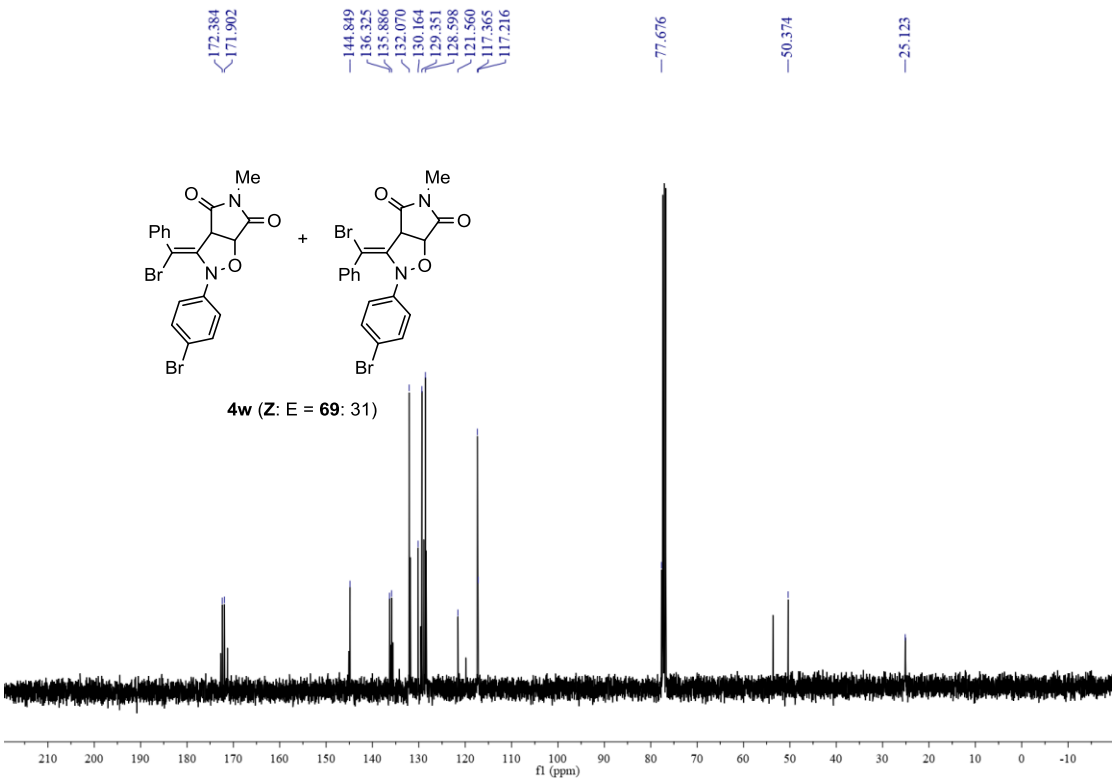
4u (Z: E = 92: 8)



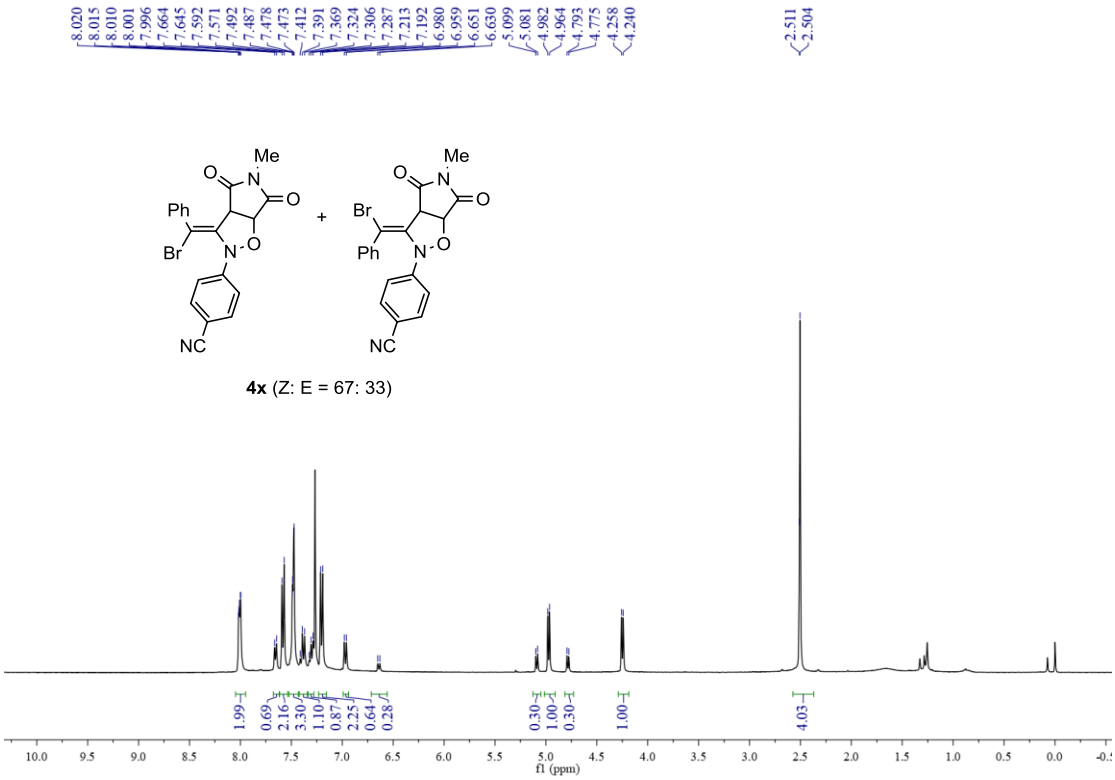
4u (**Z**: E = **92**: 8)

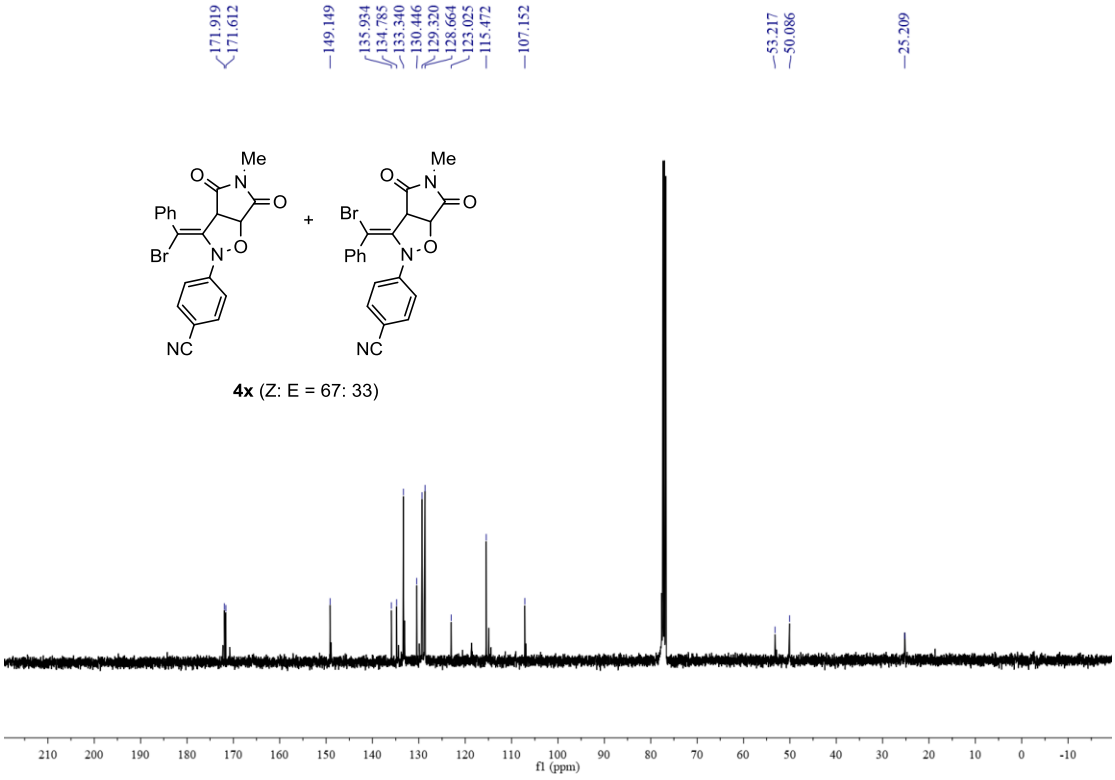
***3-(bromo(phenyl)methylene)-2-(4-bromophenyl)-5-methyltetrahydro-4H-pyrrolo[3,4-d]isoxazole--4,6(5H)-dione* (4w)**



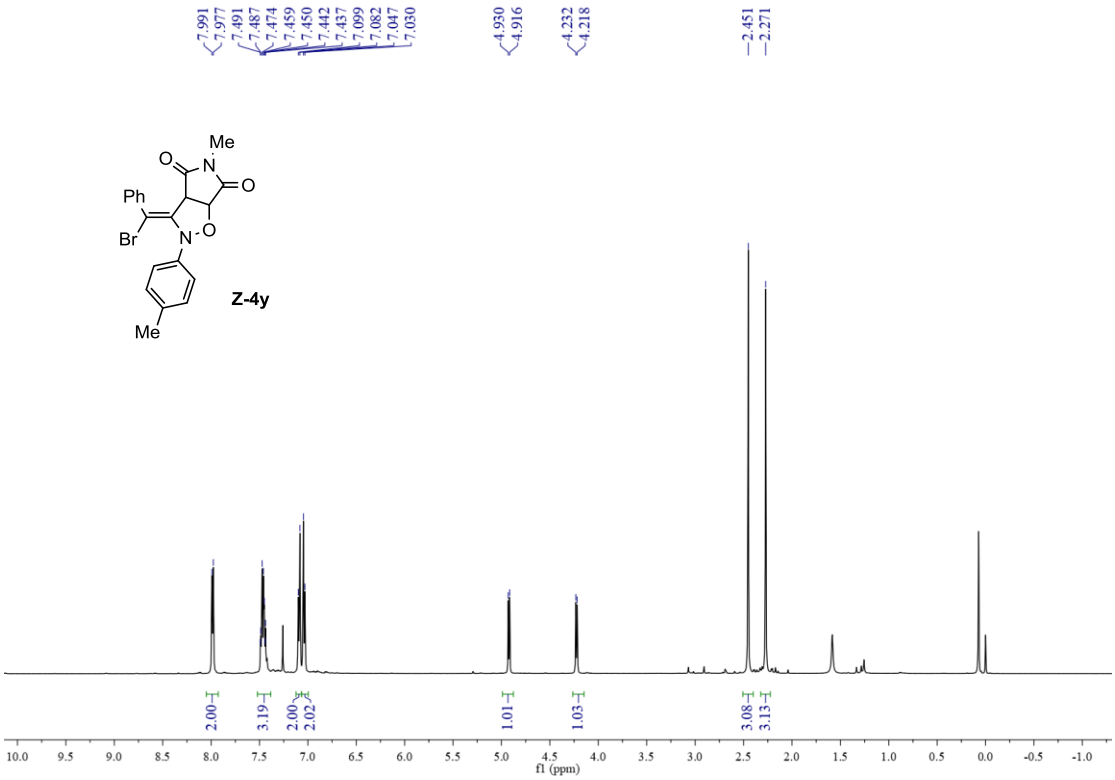


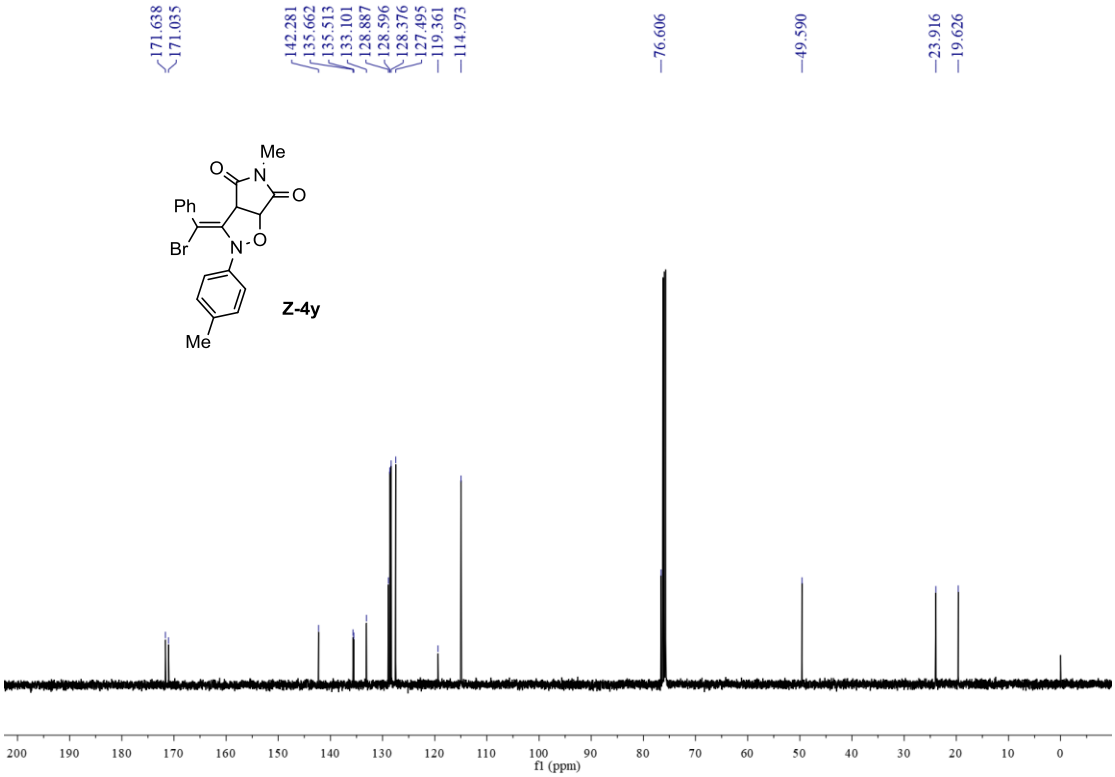
4-(3-(bromo(phenyl)methylene)-5-methyl-4,6-dioxohexahydro-2H-pyrrolo[3,4-d]isoxazol-2-yl)benzo nitrile (4x)



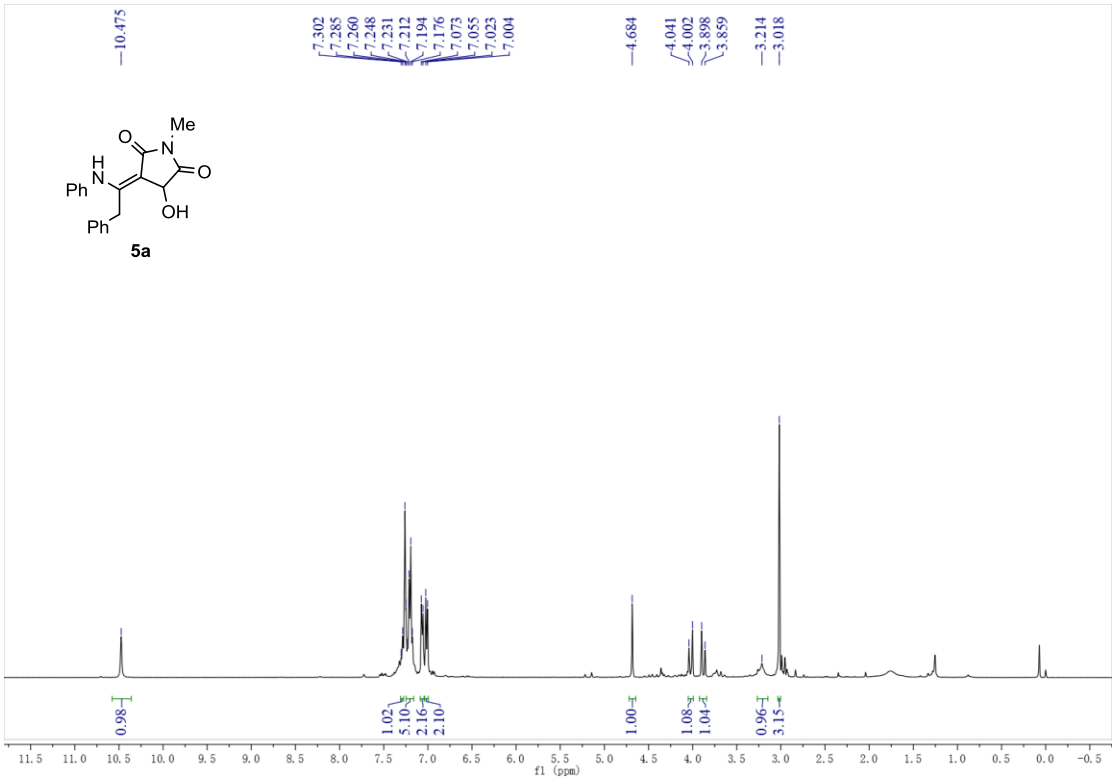


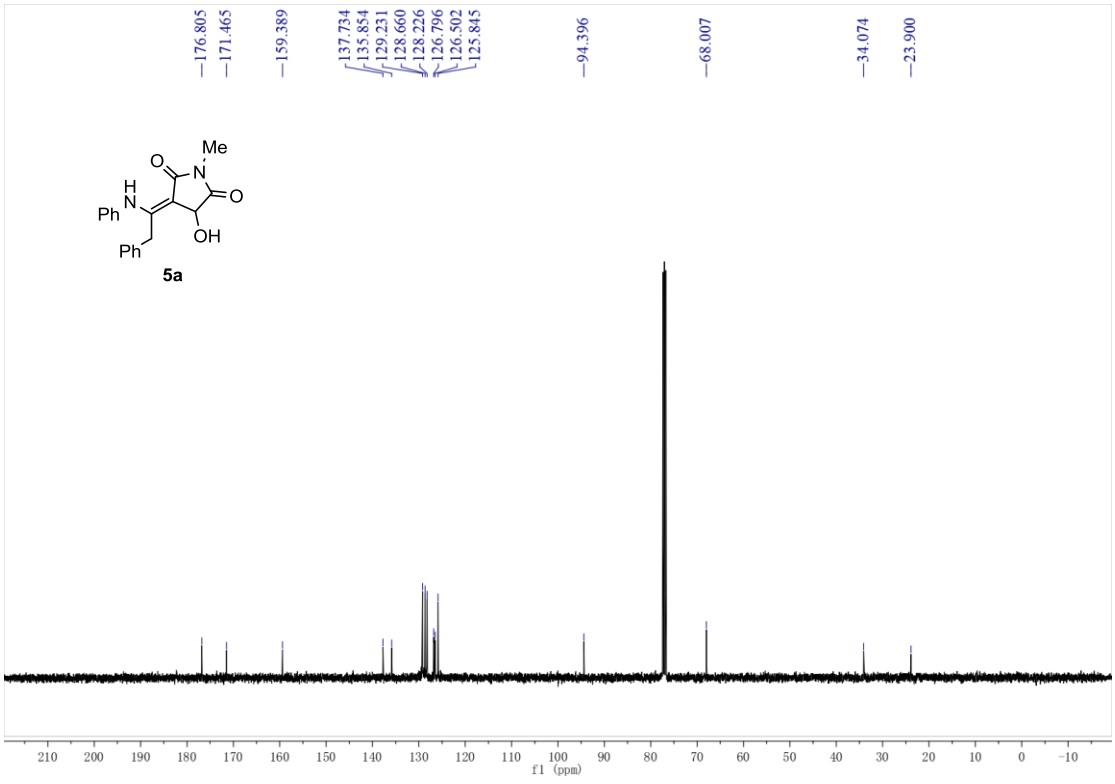
***(Z)-3-(bromo(phenyl)methylene)-5-methyl-2-(p-tolyl)tetrahydro-4H-pyrrolo[3,4-d]isoxazole-4,6(5H)-dione* (Z-4y)**



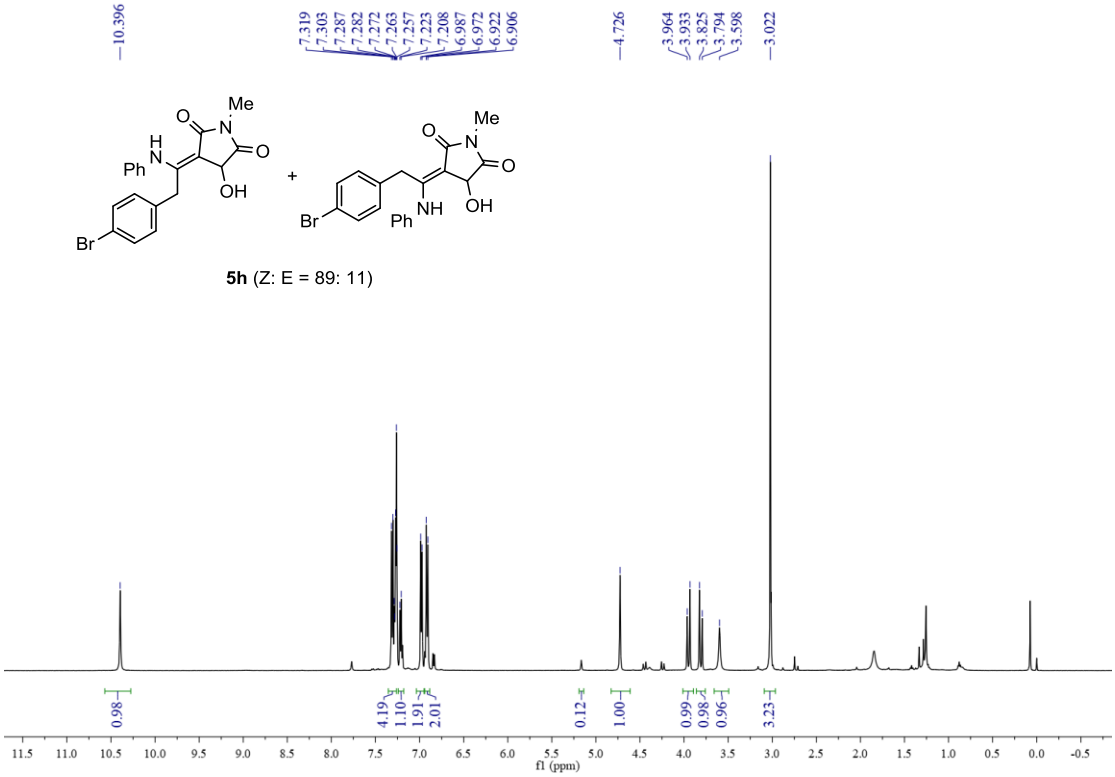


(Z)-3-hydroxy-1-methyl-4-(2-phenyl-1-(phenylamino)ethylidene)pyrrolidine-2,5-dione **(5a)**

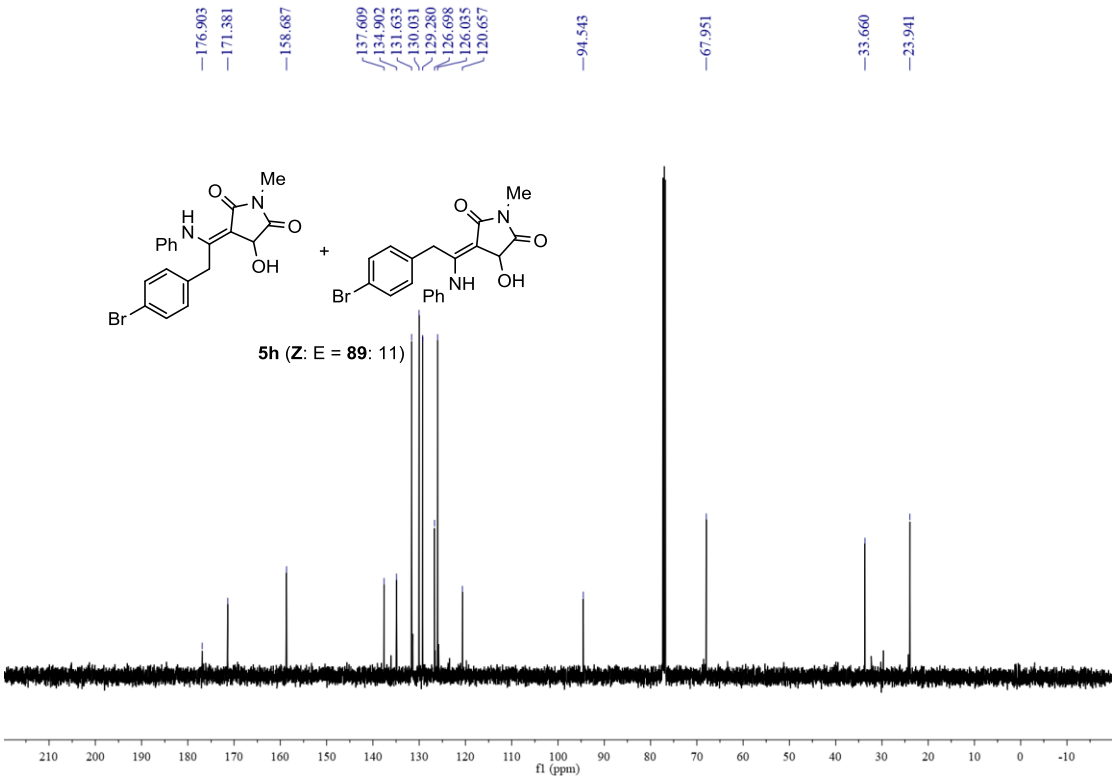




3-(2-(4-bromophenyl)-1-(phenylamino)ethylidene)-4-hydroxy-1-methylpyrrolidine-2,5-dione **(5h)**

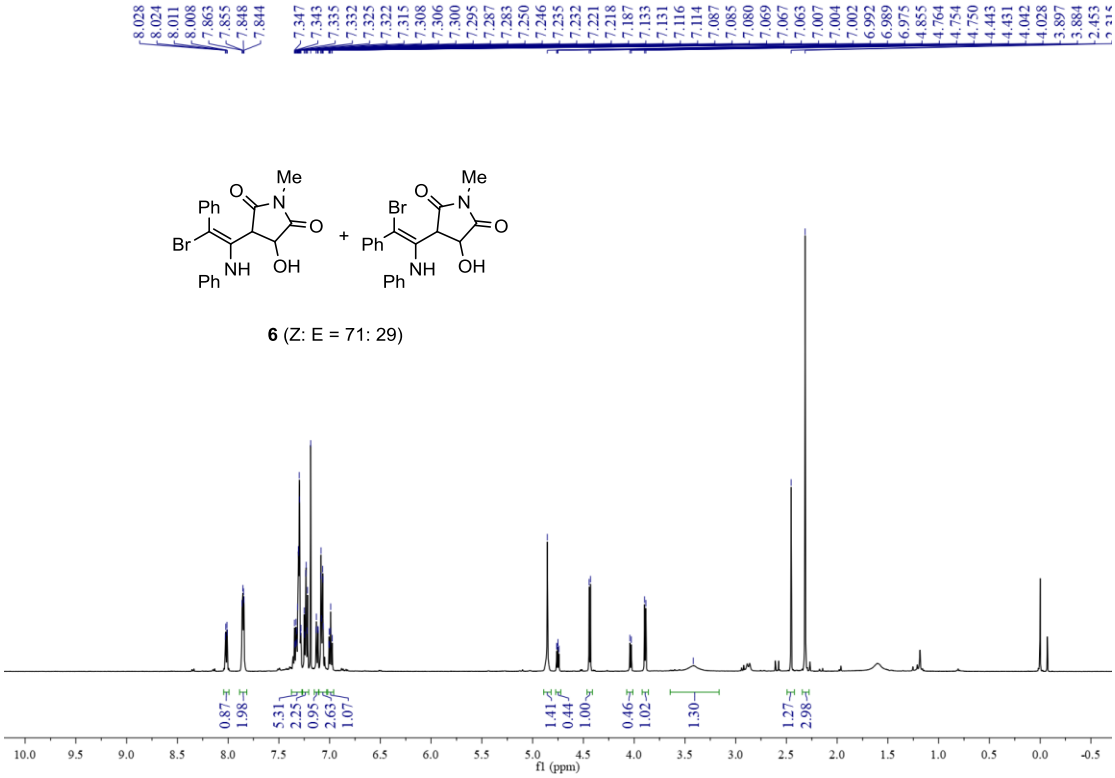


5h (Z: E = 89: 11)

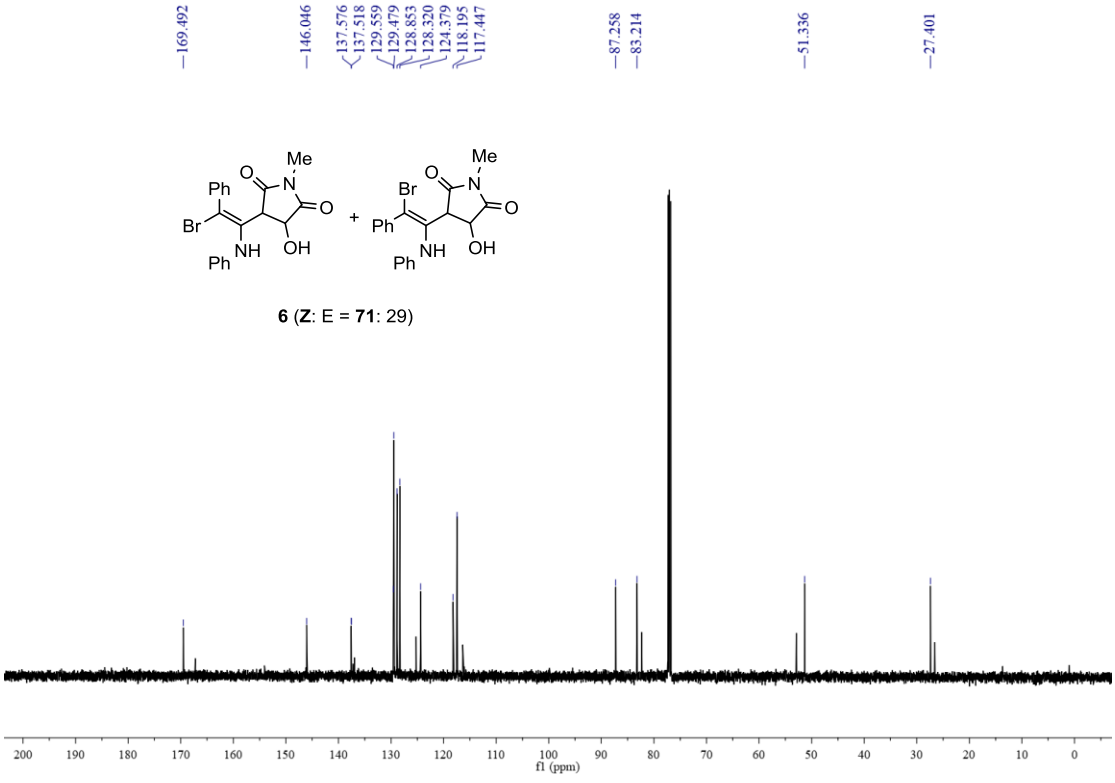


5h (**Z**: E = **89**: 11)

3-(2-bromo-2-phenyl-1-(phenylamino)vinyl)-4-hydroxy-1-methylpyrrolidine-2,5-dione **(6)**



6 (Z: E = 71: 29)



6 (**Z**: E = **71**: 29)