Supporting Information

Exploration of cytotoxic potential and tubulin polymerization inhibition activity of *cis*-stilbene-1,2,3-triazole congeners

Darshana Bora[a], Khan Mehtab Samir[a], Anamika Sharma[b], Shrilekha Chilvery[b], Sapana Bansod[b], Stephy Elza John[a], Mursalim Ali Khan[a], Chandraiah Godugu[b,*], Nagula Shankaraiah[a,*]

[a]*Department of Medicinal Chemistry,* [b]*Department of Pharmacology and Toxicology, National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad - 500 037, India*

*Corresponding author; E-mail.: shankar@niperhyd.ac.in; shankarnbs@gmail.com (Nagula Shankaraiah); chandra.niperhyd@gov.in (Chandraiah Godugu)

Contents

1. Experimental section

1.1. Chemistry

1.1.1. General

All reagents and solvents were obtained from commercial suppliers and were used without further purification. Analytical thin-layer chromatography (TLC) was performed on MERCK precoated silica gel 60-F254 (0.5 mm) aluminium plates. Visualization of the spots on TLC plates was achieved by UV light. ^{1}H and ^{13}C NMR spectra were recorded on Bruker 500 and 125 MHz, respectively by making a solution of samples in the DMSO using tetramethylsilane (TMS) as the internal standard. Chemical shifts for ^{1}H and ^{13}C are reported in parts per million (ppm) downfield from tetramethylsilane. Spin multiplicities are described as s (singlet), brs (broad singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Coupling constant (*J*) values are reported in hertz (Hz). HRMS were determined with Agilent QTOF mass spectrometer 6540 series instrument. Wherever required, column chromatography was performed using silica gel (60-120). The reactions wherever anhydrous conditions required are carried out under nitrogen positive pressure using freshly distilled solvents. All evaporation of solvents was carried out under reduced pressure using rotary evaporator below 45 ^{o}C. Melting points were determined with an electrothermal digital melting point apparatus IA9100 and are uncorrected. The names of all the compounds given in the experimental section were taken from Chem Bio Draw Ultra, Version 12.0.

The benzyl and phenacyl azides were synthesized from previously reported procedures.[1]

1.1.2. General procedure for the synthesis of compounds 4a,b:

In an oven-dry RBF equipped with a magnetic stir bar and added **3a** or **3b** (2 g) under nitrogen conditions in DMF as a solvent. Added KOH (1.5 equiv.) to the above reaction mixture at 0 ^{o}C and stir for 15 min. Then propargyl bromide (1.1 equiv.) was added and stirred the reaction mixture at room temperature for 1 h. After completion of the reaction mixture, added ice to the reaction mixture and extracted with ethyl acetate and water. The organic layer dried over sodium sulfate and concentrated under reduced pressure. The crude mixture was purified using column chromatography with 20% ethyl acetate in hexane solvent system to deliver the final compounds **4a** and **b**.

Prop-2-yn-1-yl (E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (4a): (2 g) 90% yield; Yellow solid; MP: 267-269 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.72 (s, 1H), 7.02 (d, J = 8.2 Hz,

1H), 6.84-6.88 (m, 2H), 6.80 (d, *J* = 1.8 Hz, 1H), 6.73 (dd, *J* = 1.8, 6.2 Hz, 1H), 6.59 (d, *J* = 1.1 Hz, 1H), 4.79-4.81 (m, 2H), 3.78 (s, 3H), 3.73 (s, 3H), 3.69 (s, 3H), 3.39 (s, 3H), 3.31 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.8, 150.5, 149.5, 149.0, 148.3, 140.8, 129.3, 128.5, 127.0, 125.5, 122.4, 113.7, 113.4, 112.6, 111.7,.79.2, 78.0, 56.1, 56.0, 55.9, 55.1, 52.6 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{22}H_{23}O_6^+$ 383.1489, found 383.1476.

Prop-2-yn-1-yl (E)-2-(benzo[d][1,3]dioxol-5-yl)-3-(3,4-dimethoxyphenyl)acrylate (4b): (1.9 g) 85% yield; Yellow solid; MP: 283-285 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6): δ 7.72 (s, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.87-6.90 (m, 1H), 6.83-6.86 (m, 1H), 6.78 (d, *J* = 1.5Hz, 1H), 6.67 (dd, *J* = 1.6, 6.2 Hz, 1H), 6.64 (d, *J* = 1.7 Hz, 1H), 6.06 (s, 2H), 4.78-4.82 (m, 2H), 3.73 (s, 3H), 3.45 (s, 3H), 3.31 (s, 1H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 166.6, 150.5, 148.4, 148.1, 147.3, 141.2, 129.7, 129.0, 126.9, 125.4, 123.5, 113.5, 111.7, 110.4, 109.2, 101.6, 79.1, 78.1, 55.9, 55.2, 52.7 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{21}H_{19}O_6^+$ 367.1176, found 367.1168.

1.1.3. General procedure for the synthesis of compounds 9a-j and 10a-j

To a mixture of (*E*)-prop-2-yn-1-yl-2,3-diphenylacrylate derivatives **4a**,**b** (1 equiv.) and substituted benzyl azide (**6a-j**) or phenacyl azide (**8a-f**, 1 equiv.) in *tert*-butanol:water (1:1), copper sulphate (10 mol%) and sodium ascorbate (20 mol%) was added and stirred at room temperature till complete consumption of the starting materials as determined by TLC. The reaction mixture was then extracted using ethyl acetate (3x25 mL) and water. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under vacuum, then the residue obtained was chromatographed on silica gel (elution with hexane and ethyl acetate mixture in 30:70) to provide the desired hybrids **9a-j** and **10a-j** in moderate to good yields.

***(1-Benzyl-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9a)*:** (118.6 mg) 88% yield; white solid; mp: 137-139 ^{o}C; FT-IR (cm^{-1}): 3074, 2941, 2839, 1703, 1619, 1513; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.20 (s, 1H), 7.68 (s, 1H), 7.40-7.31 (m, 5H), 6.97 (d, *J* = 8.2 Hz, 1H), 6.86-6.80 (m, 2H), 6.77 (d, *J* = 1.9 Hz, 1H), 6.69 (dd, *J* = 1.9, 6.2 Hz, 1H), 6.57 (d, *J* = 1.8 Hz, 1H), 5.61 (s, 2H), 5.25 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.63 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 150.4, 149.5, 148.9, 148.3, 142.9, 140.4, 136.4, 129.7, 129.2, 128.6, 128.6, 128.4, 127.2, 125.3, 125.2, 122.4, 113.9, 113.4, 112.6, 111.7, 58.2, 56.0, 56.0, 55.9, 55.1, 53.3 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{30}N_3O_6^+$ 516.2129, found 516.2141.

***(1-(4-Methylbenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9b)*:** (113.6 mg) 82% yield; white solid; mp: 112-114 ºC; FT-IR (cm^{-1}): 3087, 3008, 2940, 2836, 1700, 1512; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.15 (s, 1H), 7.68 (s, 1H), 7.23-7.17 (m, 4H), 6.97 (d, J = 8.2 Hz, 1H) 6.87-6.80 (m, 2H), 6.77 (d, J = 1.8 Hz, 1H), 6.69 (dd, J = 1.8, 6.3 Hz, 1H), 6.57 (d, J = 1.6 Hz, 1H), 5.54 (s, 2H), 5.24 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H), 2.29 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 150.4, 149.5, 148.9, 148.3, 142.8, 140.4, 138.0, 133.4, 129.7, 128.6, 128.5, 127.2, 125.3, 125.0, 122.4, 113.9, 113.4, 112.6, 111.7, 58.2, 56.0, 56.0, 55.9, 55.1, 53.1, 21.1 ppm; HRMS (ESI) *m/z*: $[M+H]^+$calcd. for $C_{30}H_{32}N_3O_6^+$ 530.2286, found 530.2300.

***(1-(4-Bromobenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9c)*:** (116.4 mg) 75% yield; white solid; mp: 115-117 ºC; FT-IR (cm^{-1}): 3087, 2936, 2840, 1702, 1512, 1246; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.21 (s, 1H), 7.68 (s, 1H), 7.59 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H), 6.98 (d, J = 8.2 Hz, 1H), 6.87-6.81 (m, 2H), 6.77 (bs, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.57 (s,1H), 5.60 (s, 2H), 5.25 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 150.4, 149.5, 149.0, 148.4, 142.9, 140.4, 135.8, 132.1, 130.6, 129.7, 125.4, 125.3, 122.4, 121.9, 114.0, 113.4, 112.6, 11.7, 58.2, 56.0, 55.9, 55.1, 52.5 ppm; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{29}H_{28}BrN_3NaO_6^+$ 616.1054, found 616.1071.

***(1-(4-Fluorobenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9d)*:** (115.8 mg) 83% yield; white solid; mp: 122-126 ºC; FT-IR (cm^{-1}): 3002, 2939, 1701, 1513, 1245, 1021; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.19 (s, 1H), 7.68 (s, 1H), 7.40 (t, J = 5.9 Hz, 2H), 7.21 (t, J = 8.7 Hz, 2H), 6.97 (d, J = 8.1 Hz, 1H), 6.88-6.81 (m, 2H), 6.77 (s, 1H), 6.69 (d, J = 8.0 Hz, 1H), 6.57 (s, 1H), 5.60 (s, 2H), 5.25 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 161.4, 150.4, 149.5, 148.9, 148.3, 142.9, 140.4, 132.6, 132.6, 130.8, 130.7, 129.7, 128.6, 127.1, 125.4, 125.2, 122.4, 116.1, 115.9, 113.9, 113.4, 112.6, 111.7, 58.2, 56.0, 56.0, 55.9, 55.1, 52.4 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{29}FN_3O_6^+$ 534.2035, found 534.2048.

***(1-(4-Nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9e)*:** (114.3 mg) 78% yield; white solid; mp: 119-123 ºC; FT-IR (cm^{-1}): 2938, 2839, 1703, 1513, 1233, 1137; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.28 (s, 1H), 8.24 (d, J = 8.6 Hz, 2H), 7.69 (s, 1H), 7.54 (d, J = 8.6 Hz, 2H), 6.98 (d, J = 8.2 Hz, 1H), 6.87-6.81 (m, 2H), 6.78 (d, J

= 1.4 Hz, 1H), 6.70 (dd, *J* = 1.5, 1.6 Hz, 1H), 6.57 (bs, 1H), 5.80 (s, 2H), 5.28 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 150.4, 149.4, 148.9, 148.3, 147.7, 143.8, 143.0, 140.4, 129.6, 129.5, 128.6, 127.1, 125.7, 125.4, 124.4, 122.4, 113.8, 113.3, 112.5, 111.7, 58.1, 56.0, 56.0, 55.9, 55.1, 52.3 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{29}N_4O_8^+$ 561.1980, found 561.1969.

***(1-(3-Chlorobenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9f)*:** (114.9 mg) 80% yield; white solid; mp: 116-118 ºC; FT-IR (cm^{-1}): 3008, 2937, 2838, 1702, 1513, 1246; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.26 (s, 1H), 7.68 (s, 1H), 7.43-7.40 (m, 3H), 7.30-7.26 (m, 1H), 6.97 (d, *J* = 8.3 Hz, 1H), 6.86-6.84 (m, 2H), 6.77 (d, *J* = 1.9 Hz, 1H), 6.69 (dd, *J* = 1.9, 6.2 Hz,1H), 6.57 (d, *J* = 1.8 Hz, 1H), 5.63 (s, 2H), 5.26 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.63 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 150.4, 149.5, 148.9, 148.3, 143.0, 140.4, 138.8, 133.7, 131.1, 129.7, 128.6, 128.6, 128.3, 127.1, 125.4, 125.3, 122.4, 113.9, 113.4, 112.6, 111.7, 58.2, 56.0, 56.0, 55.9, 55.1, 52.5 ppm, HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{29}ClN_3O_6^+$ 550.1739, found 550.1752.

***(1-(2-Fluorobenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9g)*:** (111.6 mg) 80% yield; white solid; mp: 116-119 ºC; FT-IR (cm^{-1}): 3072, 3000, 2958, 2839, 1703, 1513; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.18 (s, 1H), 7.68 (s, 1H), 7.48-7.40 (m, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.30-7.20 (m, 2H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.88-6.80 (m, 2H), 6.77 (s, 1H), 6.70 (d, *J* = 7.2 Hz, 1H), 6.57 (s, 1H), 5.68 (s, 2H), 5.26 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 161.5, 159.6, 150.4, 149.4, 148.9, 148.3, 142.8, 140.4, 131.3, 131.2, 129.7, 128.6, 127.1, 125.4, 125.3, 125.3, 123.2, 123.1, 122.4, 116.1, 116.0, 113.8, 113.3, 112.6, 111.7, 58.1, 56.0, 55.9, 55.1, 47.4, 47.3 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{29}FN_3O_6^+$ 534.2035, found 534.2051.

***(1-(2-Nitrobenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (9h)*:** (109.9 mg) 75% yield; white solid; mp: 138-146 ºC; FT-IR (cm^{-1}): 3078, 2942, 1699, 1513, 1215, 1018; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.22 (s, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.69 (s, 1H), 7.65 (t, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.88-6.81 (m, 2H), 6.78 (d, *J* = 1.4 Hz, 1H), 6.70 (dd, *J* = 1.4, 6.7 Hz, 1H), 6.58 (bs, 1H), 5.98 (s, 2H), 5.29 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 150.4, 149.5, 148.9, 148.3, 148.0,

142.9, 140.4, 134.8, 131.2, 130.5, 130.1, 129.7, 128.6, 127.1, 126.0, 125.5, 125.4, 122.4, 113.9, 113.4, 112.6, 111.7, 58.1, 56.0, 56.0, 55.9, 55.1, 50.4 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{29}N_4O_8^+$ 561.1980, found 561.1996.

***(1-(2,5-Dimethylbenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)-acrylate (9i)*:** (102.3 mg) 72% yield; white solid; mp: 120-125 °C; FT-IR (cm^{-1}): 3087, 2991, 2918, 2839, 1705, 1512; ^{1}H NMR (500 MHz, DMSO-d_6):δ 8.16 (s, 1H), 7.67 (s, 1H), 6.98-6.95 (m, 2H), 6.92 (s, 2H), 6.86-6.83 (m, 1H), 6.83-6.80 (m, 1H), 6.77 (d, *J* = 1.6 Hz, 1H), 6.69 (dd, *J* = 1.6, 6.5 Hz, 1H), 6.56 (d, *J* = 1.4 Hz,1H), 5.50 (s, 2H), 5.25 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.63 (s, 3H), 3.38 (s, 3H), 2.24 (s, 6H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 150.4, 149.5, 148.9, 148.3, 142.8, 142.8, 140.4, 138.3, 136.2, 130.0, 129.7, 128.6, 127.1, 126.1, 125.3, 125.2, 122.4, 113.9, 113.4, 112.6, 111.7, 58.2, 56.0, 56.0, 55.9, 55.1, 53.2, 21.2 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{34}N_3O_6^+$ 544.2442, found 544.2460.

***(1-(2,5-Difluorobenzyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl) acrylate (9j)*:** (102.4 mg) 71% yield; white solid; mp: 108-112 °C; FT-IR (cm^{-1}): 3079, 3009, 2950, 2840, 1703, 1512; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.22 (s, 1H),7.68 (s, 1H), 7.36-7.21 (m, 3H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.87-6.80 (m, 2H), 6.77 (d, *J* = 1.8 Hz, 1H), 6.69 (dd, *J* = 1.9, 6.2 Hz, 1H), 6.57 (d, *J* = 1.7 Hz, 1H), 5.67 (s, 2H), 5.26 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.64 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 167.3, 157.5, 155.8, 150.4, 149.5, 148.9, 148.3, 142.9, 140.4, 129.7, 128.6, 127.1, 125.5, 125.3, 125.0, 124.9, 122.4, 117.9, 117.8, 117.7, 117.7, 117.5, 117.5, 113.9, 113.4, 112.6, 111.7, 58.1, 56.0, 55.9, 55.1, 47.1 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{28}F_2N_3O_6^+$ 552.1941, found 552.1956.

***(1-(2-Oxo-2-phenylethyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)-acrylate (10a)*:** (93.8 mg) 66% yield; pale yellow solid; mp: 150-154 °C; FT-IR (cm^{-1}): 3129, 3074, 2941, 2839, 1694, 1381; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.14 (s, 1H), 8.09 (dd, *J* = 0.8, 7.1 Hz, 2H), 7.77-7.73 (m, 1H), 7.71 (s, 1H), 7.62 (t, *J* = 7.9 Hz, 2H), 7.00 (d, *J* = 8.2 Hz, 1H), 6.88-6.82 (m, 2H), 6.80 (d, *J* = 1.9 Hz, 1H), 6.72 (dd, *J* = 1.8, 6.2 Hz, 1H), 6.58 (d, *J* = 1.6 Hz, 1H), 6.21 (s, 2H), 5.33 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.39 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 192.5, 167.3, 150.4, 149.5, 149.0, 148.4, 142.5, 140.4, 134.7, 134.6, 129.8, 129.4, 128.7, 128.6, 127.2, 126.9, 125.3, 122.5,

113.9, 113.4, 112.7, 111.7, 58.2, 56.3, 56.1, 56.0, 55.9, 55.1 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{30}N_3O_7^+$ 544.2078, found 544.2093.

***(1-(2-Oxo-2-(p-tolyl)ethyl)-1H-1,2,3-triazol-4-yl)methyl-(E)-2,3-bis(3,4-dimethoxyphenyl)-acrylate (10b)*:** (90.4 mg) 62% yield; pale yellow solid; mp: 92-102 °C; FT-IR (cm^{-1}): 2938, 2836, 1599, 1512, 1216, 1135; ^1H NMR (500 MHz, DMSO-d_6): δ 8.13 (s, 1H), 7.98 (d, J = 8.1 Hz, 2H), 7.71 (s, 1H), 7.42 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 8.2 Hz, 1H), 6.89-6.81 (m, 3H), 6.72 (dd, J = 1.6, 6.5 Hz, 1H), 6.58 (bs, 1H), 6.16 (s, 2H), 5.32 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.39 (s, 3H), 2.42 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 192.0, 167.3, 150.4, 149.5, 148.9, 148.3, 145.3, 142.4, 140.4, 132.1, 129.9, 129.8, 128.7, 128.6, 127.2, 126.9, 125.3, 122.4, 113.9, 113.4, 112.6, 111.7, 58.2, 56.2, 56.1, 56.0, 55.9, 55.1, 21.7 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{32}N_3O_7^+$ 558.2235, found 558.2252.

***1-(2-(4-Methoxyphenyl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (10c)*:** (104.9 mg) 70% yield; white solid; mp: 78-82 °C; FT-IR (cm^{-1}): 3147, 2937, 2837, 1598, 1217, 1135, 1021, 805, 600; ^1H NMR (500 MHz, DMSO-d_6): δ 8.12 (s, 1H), 8.05 (d, J = 8.7 Hz, 2H), 7.71 (s, 1H), 7.13 (d, J = 8.7 Hz, 2H), 7.00 (d, J = 8.1 Hz, 1H), 6.88-6.82 (m, 2H), 6.80 (s, 1H), 6.75-6.71 (m, 1H), 6.59 (s, 1H), 6.13 (s, 2H), 5.32 (s, 2H), 3.89 (s, 3H), 3.78 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.39 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 190.7, 167.3, 164.4, 150.4, 149.5, 148.9, 148.3, 142.5, 140.4, 131.0, 129.8, 128.6, 127.4, 127.2, 126.9, 125.3, 122.4, 113.9, 113.4, 112.6, 111.7, 58.2, 56.1, 56.0, 56.0, 55.9, 55.1 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{31}H_{32}N_3O_8^+$ 574.2184, found 574.2177.

***(1-(2-(4-Chlorophenyl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl (E)-2,3-bis(3,4-dimethoxy-phenyl)acrylate (10d)*:** (104.2 mg) 69% yield; pale yellow solid; mp: 81-85 °C; FT-IR (cm^{-1}): 2936, 2836, 1699, 1511, 1217, 1135; ^1H NMR (500 MHz, DMSO-d_6): δ 8.13 (s, 1H),8.09 (d, J = 8.5 Hz, 2H), 7.72-7.70 (m, 2H), 7.69-7.68 (m, 1H), 6.99 (d, J = 8.2 Hz, 1H), 6.87-6.82 (m, 2H), 6.80 (d, J = 1.8 Hz, 1H), 6.72 (dd, J = 1.8, 6.2 Hz, 1H), 6.58 (d, J = 1.4 Hz, 1H), 6.19 (s, 2H), 5.32 (s, 2H), 3.78 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.39 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 191.7, 167.3, 150.4, 149.5, 148.9, 148.3, 142.5, 140.4, 139.6, 133.3, 130.5, 129.7, 129.5, 128.6, 127.2, 126.9, 125.4, 122.4, 113.9, 113.4,

112.6, 111.7, 58.2, 56.3, 56.0, 56.0, 55.9, 55.1 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{29}ClN_3O_7^+$ 578.1689, found 578.1693.

***(1-(2-(4-Bromophenyl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl-(E)-2,3-bis(3,4-dimethoxy-phenyl)acrylate (10e)*:** (110.5 mg) 68% yield; pale yellow solid; mp: 120-125 °C; FT-IR (cm^{-1}): 2939, 2836, 1701, 1513, 1219, 1137; ^1H NMR (500 MHz, DMSO-d_6): δ 8.13 (s, 1H), 8.01 (d, *J* = 8.3 Hz, 2H), 7.84 (d, *J* = 8.1 Hz, 2H), 7.71 (s, 1H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.89-6.78 (m, 3H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.58 (s, 1H), 6.19 (s, 2H), 5.32 (s, 2H), 3.78 (s, 3H), 3.72 (s, 3H), 3.67 (s, 3H), 3.39 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 191.9, 167.3, 150.4, 149.5, 148.9, 148.3, 142.5, 140.4, 133.6, 132.5, 130.6, 129.7, 128.8, 128.6, 127.1, 126.9, 125.4, 122.4, 113.9, 113.3, 112.6, 111.7, 58.2, 56.3, 56.0, 56.0, 55.9, 55.1 ppm; HRMS (ESI) *m/z* :$[M+H]^+$ calcd. for $C_{30}H_{29}BrN_3O_7^+$ 622.1183, found 622.1200.

***(1-(2-(3,4-Dichlorophenyl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl-(E)-2,3-bis(3,4-dimethoxyphenyl)acrylate (10f)*:** (102.3 mg) 64% yield; pale yellow solid; mp: 156-160 °C; FT-IR (cm^{-1}): 3100, 2959, 2839, 1700, 1512, 1247; ^1H NMR (500 MHz, DMSO-d_6): δ 8.30 (d, *J* = 2.0 Hz, 1H), 8.12 (s, 1H), 8.01 (dd, *J* = 2.0, 6.3 Hz, 1H), 7.91 (d, *J* = 8.3 Hz, 1H), 7.71 (s, 1H), 6.99 (d, *J* = 8.2 Hz, 1H), 6.87-6.82 (m, 2H), 6.79 (d, *J* = 1.9 Hz, 1H), 6.71 (dd, *J* = 1.9, 6.2 Hz, 1H), 6.58 (d, *J* = 1.7 Hz, 1H), 6.21 (s, 2H), 5.32 (s, 2H), 3.77 (s, 3H), 3.72 (s, 3H), 3.66 (s, 3H), 3.38 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 191.1, 167.3, 150.4, 149.5, 148.9, 148.3, 142.6, 140.4, 137.4, 134.8, 132.5, 131.8, 130.6, 129.7, 128.6, 127.1, 126.8, 125.4, 122.4, 113.8, 113.3, 112.6, 111.7, 58.2, 56.4, 56.0, 55.9, 55.1 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{28}Cl_2N_3O_7^+$ 612.1299, found 612.1314.

***(E)-(1-(2-Oxo-2-phenylethyl)-1H-1,2,3-triazol-4-yl)methyl-2-(benzo[d]-[1,3]dioxol-5-yl)-3-(3,4-dimethoxyphenyl)acrylate (10g)*:** (93.5 mg) 65% yield; pale yellow solid; mp: 100-103 °C; FT-IR (cm^{-1}): 3359, 2939, 1412, 1321, 1114, 1067; ^1H NMR (500 MHz, DMSO-d_6): δ 8.13 (s, 1H), 8.08 (d, *J* = 7.8 Hz, 2H), 7.74 (t, *J* = 7.5 Hz, 1H), 7.71 (s, 1H), 7.62 (d, *J* = 7.2 Hz, 2H), 6.96 (d, *J* = 8.1 Hz, 1H), 6.88-6.81 (m, 2H), 6.77 (s, 1H), 6.67 (dd, *J* = 1.5, 6.3 Hz 1H), 6.63 (s, 1H), 6.21 (s, 2H), 6.05 (s, 2H), 5.32 (s, 2H), 3.73 (s, 3H), 3.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 192.6, 167.2, 150.4, 148.4, 148.0, 147.3, 142.5, 140.8, 134.7, 134.5, 129.9, 129.4, 128.6, 127.0, 125.3, 123.6, 113.4, 111.7, 110.5, 109.2, 101.6, 58.3, 56.3, 55.9, 55.2 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{26}N_3O_7^+$ 528.1765, found 528.1769.

***(E)-(1-(2-(4-Methoxyphenyl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl-2-(benzo[d][1,3]dioxol-5-yl)-3-(3,4-dimethoxyphenyl)acrylate (10h)*:** (103.4 mg) 68% yield; white solid; mp: 120-123 ^{o}C; FT-IR (cm^{-1}): 3083, 2924, 2851, 1689, 1601, 1231; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.12 (s, 1H), 8.05 (dt, J = 1.9, 8.8 Hz, 2H), 7.71 (s, 1H), 7.13 (dt, J = 1.7, 8.9 Hz, 2H), 6.96 (d, J = 7.9 Hz, 1H), 6.88-6.81 (m, 2H), 6.77 (d, J = 1.6 Hz, 1H), 6.67 (dd, J = 1.6, 6.3 Hz, 1H), 6.63 (d, J = 1.8 Hz, 1H), 6.13 (s, 2H), 6.05 (s, 2H), 5.31 (s, 2H), 3.88 (s, 3H), 3.73 (s, 3H), 3.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 190.7, 167.2, 164.4, 150.5, 148.4, 148.0, 147.2, 142.4, 140.7, 131.0, 129.9, 127.4, 127.0, 126.9, 125.3, 123.6, 114.7, 113.5, 111.8, 110.5, 109.2, 101.5, 58.3, 56.1, 55.9, 55.2 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{30}H_{28}N_3O_8^+$ 558.1871, found 558.1797.

***(E)-(1-(2-(4-Chlorophenyl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl-2-(benzo[d][1,3-dioxol-5-yl)-3-(3,4-dimethoxyphenyl)acrylate (10i)*:** (91.9 mg) 60% yield; pale yellow solid; mp: 78-82 ^{o}C; FT-IR (cm^{-1}): 2970, 1699, 1514, 1402, 1218, 1142; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.12 (s, 1H), 8.08 (d, J = 8.5 Hz, 2H), 7.72-7.70 (m, 2H), 7.70-7.78 (m, 1H), 6.96 (d, J = 7.9 Hz, 1H), 6.89-6.86 (m, 1H), 6.85-6.89 (m, 1H), 6.80-6.75 (m, 1H), 6.67 (dd, J = 1.4, 6.5 Hz, 1H), 6.64-6.61 (m, 1H), 6.19 (s, 2H), 6.05 (s, 2H), 5.32 (s, 2H), 3.73 (s, 3H), 3.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 191.7, 167.1, 150.5, 148.4, 148.0, 147.2, 142.5, 140.7, 139.6, 133.3, 130.5, 129.9, 129.5, 127.0, 126.8, 125.3, 123.6, 113.5, 111.8, 110.5, 109.2, 101.5, 58.3, 56.3, 55.9, 55.2 ppm; HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $C_{29}H_{25}ClN_3O_7^+$ 562.1376, found 562.1381.

***(E)-(1-(2-(3,4-Dichlorophenyl)-2-oxoethyl)-1H-1,2,3-triazol-4-yl)methyl-2-(benzo[d][1,3]-dioxol-5-yl)-3-(3,4-dimethoxyphenyl)acrylate (10j)*:** (105.6 mg) 65% yield; pale yellow solid; mp: 107-110 ^{o}C; FT-IR (cm^{-1}): 2955, 2844, 1704, 1514, 1421, 1216; ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.30 (d, J = 1.5Hz, 1H), 8.11 (s, 1H), 8.01 (dd, J = 1.3, 1.0 Hz, 1H), 7.90 (d, J = 8.3 Hz, 1H), 7.71 (s, 1H), 6.96 (d, J = 7.9 Hz, 1H), 6.89-6.85 (m, 1H), 6.85-6.81 (m, 1H), 6.77 (s, 1H), 6.66 (d, J = 7.9 Hz, 1H), 6.62 (s, 1H), 6.21 (s, 2H), 6.05 (s, 2H), 5.32 (s, 2H), 3.73 (s, 3H), 3.45 (s, 3H) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ 191.7, 167.1, 150.5, 148.4, 148.0, 147.2, 142.5, 140.8, 139.6, 133.3, 129.9, 129.5, 129.5, 127.0, 126.9, 125.3, 123.6, 113.5, 111.8, 110.5, 109.2, 101.5, 58.3, 56.3, 55.9, 55.2 ppm; HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $C_{29}H_{23}Cl_2N_3NaO_7^+$ 618.0805, found 618.0805.

1.2 Pharmacology

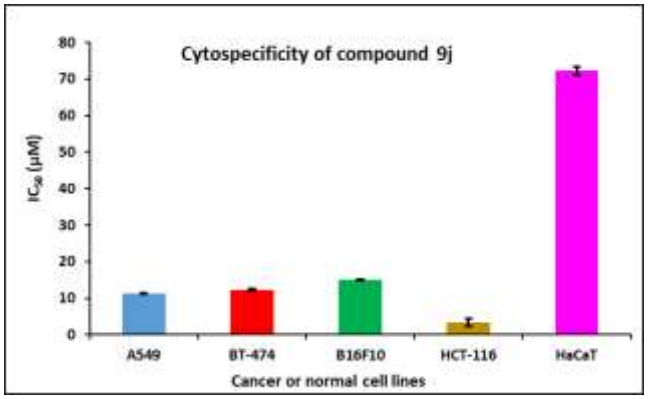


Figure S1. Cytospecificity of compound **9j** towards cancer cell lines.

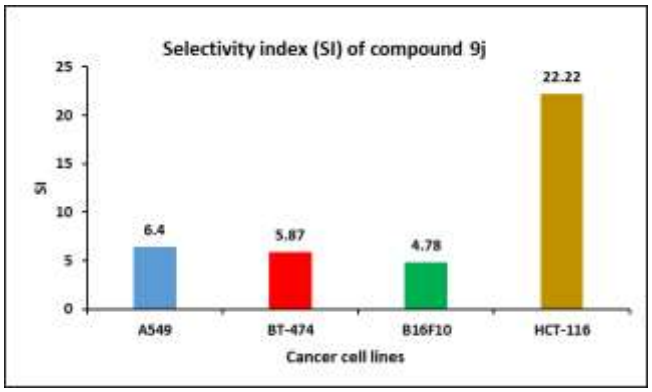


Figure S2. Selectivity Index (SI) of potent molecule **9j**.

1.2.1 Cell culture

The lung carcinoma (A-459), mouse skin melanoma (B16F10), breast carcinoma (BT474), colorectal carcinoma (HCT-116) and normal epidermal keratinocytes (HaCaT) cells were maintained in 1% antibiotic-antimycotic stabilized suitable media solution enriched with 10% fetal bovine serum (FBS). The cells were incubated at 37 ^{o}C with 5% CO_2 and 98% relative humidity. The sub-culturing was done after the cells obtained 80-90% confluency utilizing a 0.25% trypsin/1 mM EDTA solution for further passage. The 10 mM stock solution of compounds and standard was prepared by dissolving in DMSO. Required concentrations were further obtained by suitable dilutions with respective media.

1.2.2 MTT assay

MTT assay is a colourimetric, sensitive and reliable indicator of cell viability that involves the reduction of MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) into insoluble formazan by mitochondrial succinate dehydrogenase enzyme. Metabolically active cells can reduce the MTT and the level of absorbance determined the viability of cells. The

experiment started with, cells seeding in 96-well plates (1×10^3-4×10^3 cells per well in 100 µl of complete medium) and incubated for overnight to grow and attach to walls. Then the media was replaced with fresh complete media (media with 10% FBS) containing different concentrations of compounds and kept in an incubator again for 24 h. After the completion of the incubation period, the media was aspirated and 100 µl of media (with 0.5 mg/mL MTT) was added and incubated at 37 °C for 4 h. Then the supernatant media was removed from the wells and 200 µL of DMSO was added to dissolve the formed formazan crystals. The absorbance was recorded at 570 nM wavelength using a spectrophotometric multimode plate reader (Spectra Max, M4 Molecular Devices, USA).

1.2.3. Phase-contrast microscopy

The HCT-116 cells were plated (1×10^6 cells/mL in RPMI media with 10% FBS) in 24 well culture plates and allowed to adhere for 24 h incubation at 37 °C in 5% CO_2 atmosphere. Later, media was replaced with fresh complete media (media with 10 % FBS) with different concentrations of compound **9j** (1.62, 3.25 and 6.50 µM) and colchicine (0.55 µM). After 24 h of incubation, cell viability and morphological changes were observed by capturing images using a phase-contrast microscope (Nikon, Inc. Japan) at 20X magnification. [2]

1.2.4. DAPI nucleic acid staining

Here cells were seeded at the density of 1×10^6 cells/well in 24 well plates and allowed to culture for 24 h. and then incubated with gradient concentrations (1.62, 3.25 and 6.50 µM) of compound **9j** and colchicine (0.55 µM) for 24 h. After incubation, cells were washed with PBS and fixed with 4% paraformaldehyde for 30 min, later paraformaldehyde was removed from wells and cells were permeabilized with 0.1% Triton X for 15 min, followed by staining with 1 µM DAPI for 15 min. After 15 min staining solution was removed from the wells and 1-2 times washed with PBS to measure the fluorescent intensity. A fluorescence microscope was used to observe cells and captured images with wavelengths of excitation at 350 nm and emission at 460 nm using a DAPI filter at 20X magnifications [3,4].

1.2.5. Acridine orange (AO)/Ethidium bromide staining

HCT-116 cells were plated at a concentration of 1×10^6 cells/mL in 24 well plates. Then treated with various concentrations of compound **9j** (1.62, 3.25 and 6.50 µM) and colchicine (0.55 µM) and incubated for 24 h. After that media was removed from each well and acridine orange and ethidium bromide in equal volume (10 µg/ml) was added to each well

with 1 mL PBS. Immediately the cells were visualized under a fluorescence microscope (Nikon, Inc. Japan) with excitation (488 nm) and emission (550 nm) at 20X magnification. [5,6]

1.2.6. Annexin V/Propidium iodide assay

Briefly, 1×10^6 cells/well were seeded in a 6 well plate and synchronized in incomplete media for 2 h and then treated with different concentrations of compound **9j** and colchicine for 24 h. Then the media of each well was collected in different 15 ml centrifuge tubes and cells were trypsinized. The trypsinized cells were mixed with the respective media containing centrifuge tubes and centrifuge for 5 min. Then the supernatant was removed from each tube and the cells pellet was dissolved in a binding buffer containing 10 µL PI (50 µg/mL) and 10 µL annexin V-FITC stain for 15 min. Further, flow cytometric analysis was performed using a flow cytometer (BD FACSVerseTM, USA).[7,8]

1.2.7 Cell cycle analysis

HCT-116 cells were cultured in RPMI medium in 6 well plates for 24 h. Prior to the treatment with molecule **9j** at various concentrations (1.62, 3.25 and 6.50 µM) and colchicine (0.55 µM) in a complete medium for 24 h, cells were synchronized in an incomplete medium (without FBS) for 2 h. Further cells of each well were trypsinized and centrifuged in different 15 ml centrifuge tubes and then fixed cells with 70% ethanol at 4 °C for overnight. Fixed cells were further centrifuged and the cells pellet was washed with cell cycle buffer before being stained with propidium iodide (50 µg/mL) with RNase A for 20 min at 37 °C in dark. The arrest in the phase of the cell cycle of HCT-116 cells treated with different concentrations of 9j and colchicine was analyzed by flow cytometer BD FACSVerseTM (BD Biosciences, USA).[9]

1.2.8 Tubulin polymerization assay

To examine the effect of compound **9j** on tubulin inhibition, a fluorescence-based *in vitro* tubulin polymerization assay was executed based on the manufacturer's protocol (Cytoskeleton, Inc. BK011).[10] Colchicine was used as a standard in the assay at 0.55 µM final concentration and 1.62, 3.25 and 6.50 µM concentrations of compound 9j were used for the assay. The 50% tubulin polymerization inhibitory concentration of 9j was calculated based on the result of the assay.[11,12]

1.3. Molecular docking

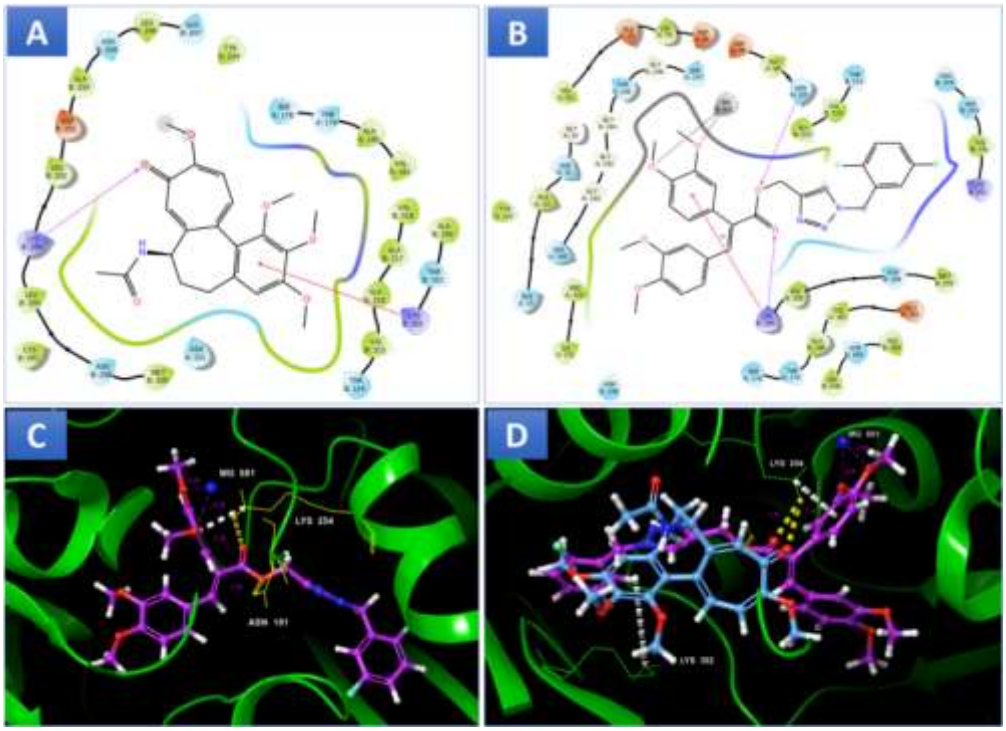


Figure S3. A) 2D interaction of **9j**, B) 2D interaction of colchicine with tubulin protein (PDB ID: 3E22). The pink arrow indicates hydrogen bonding, red line denotes pi-cation interaction and the grey line indicates interaction with the metal ion. C) 3D interaction indicating the interaction of compound **9j** with the amino acid of tubulin protein. The yellow colour line show hydrogen interaction, green line indicates pi-cation interaction and red line denotes metal interaction. **D**) Overlay of compound **9j** and colchicine at active site of tubulin protein.

2. Spectra

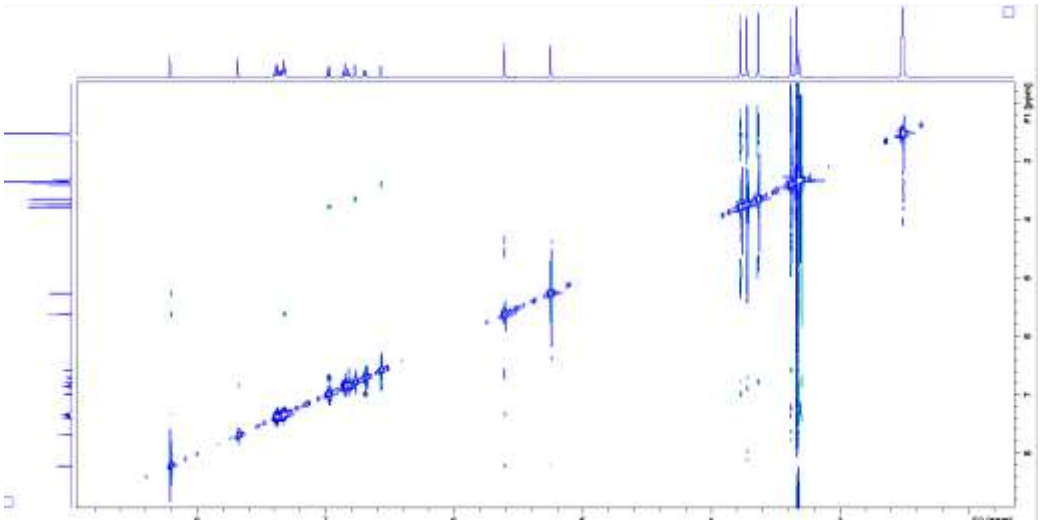


Figure S4. Full NOESY spectra of compound **9a**.

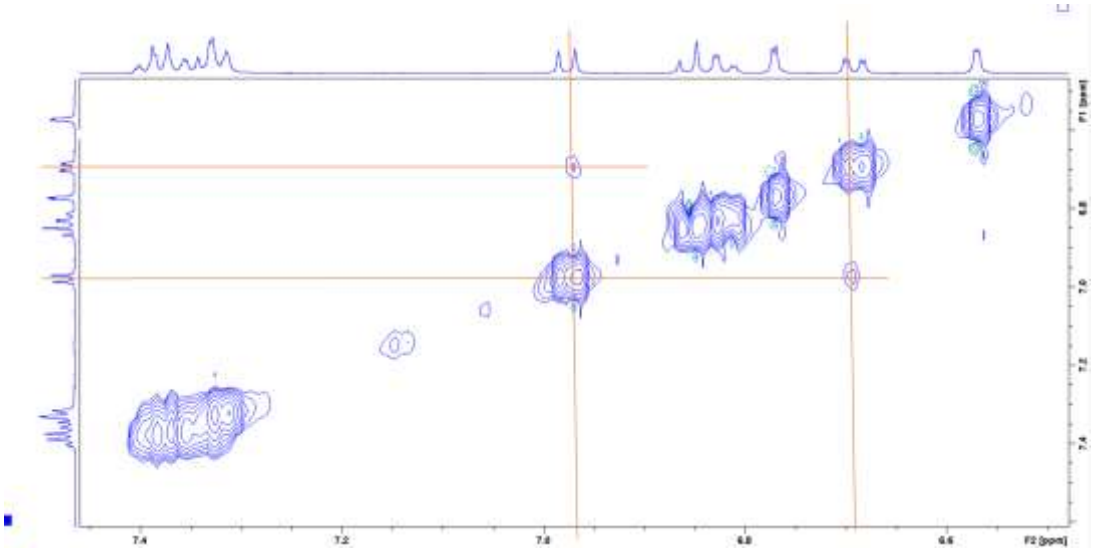


Figure S5. Expended NOESY spectra of compound **9a**.

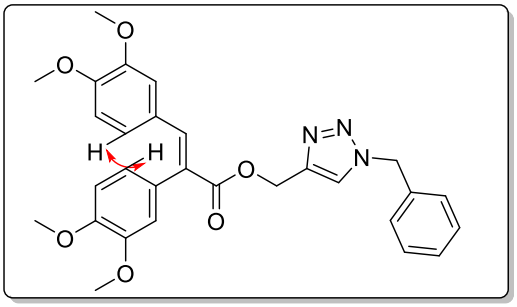
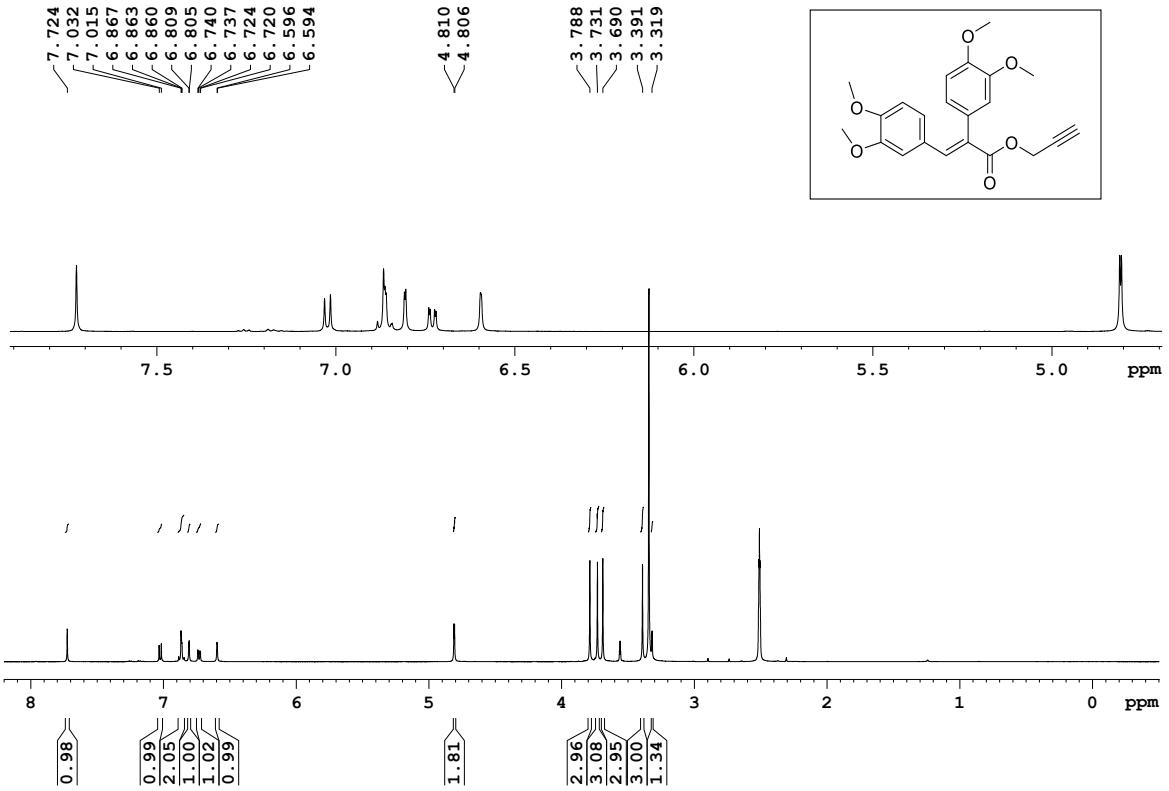
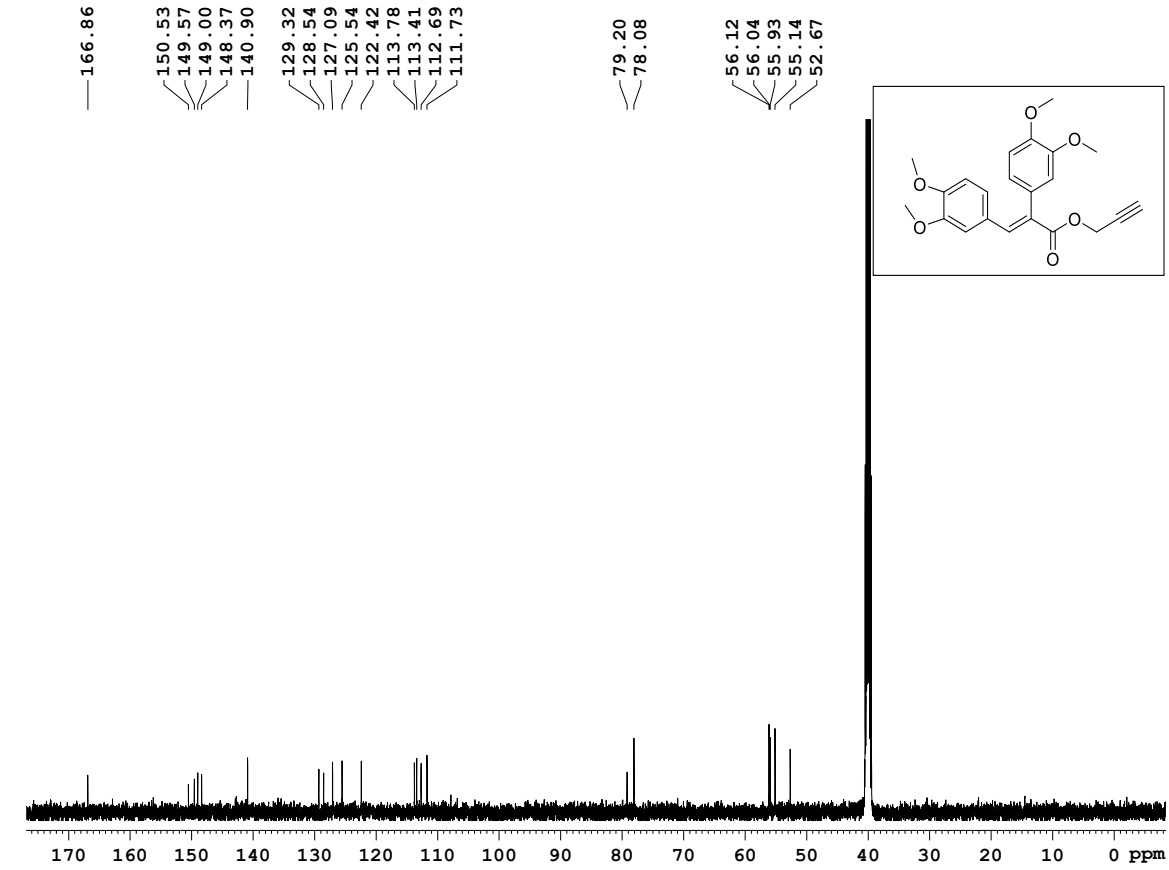


Figure S6. Determination of configuration for representative compound **9a** by NOE analysis.

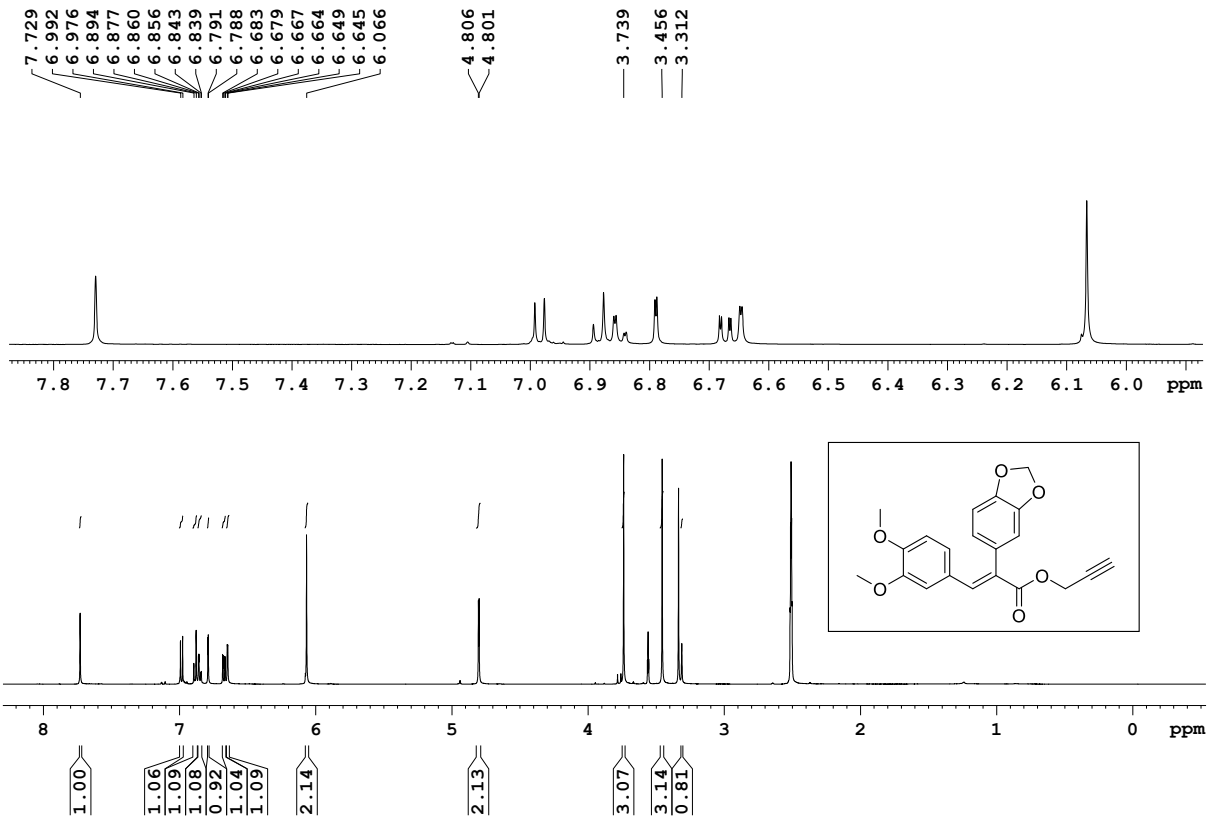
The interaction between the proton of aryl rings (6.97 and 6.79 ppm) of stilbene moiety for compound **9a** in NOESY NMR conforms to the *E*-configuration of stilbene rings.



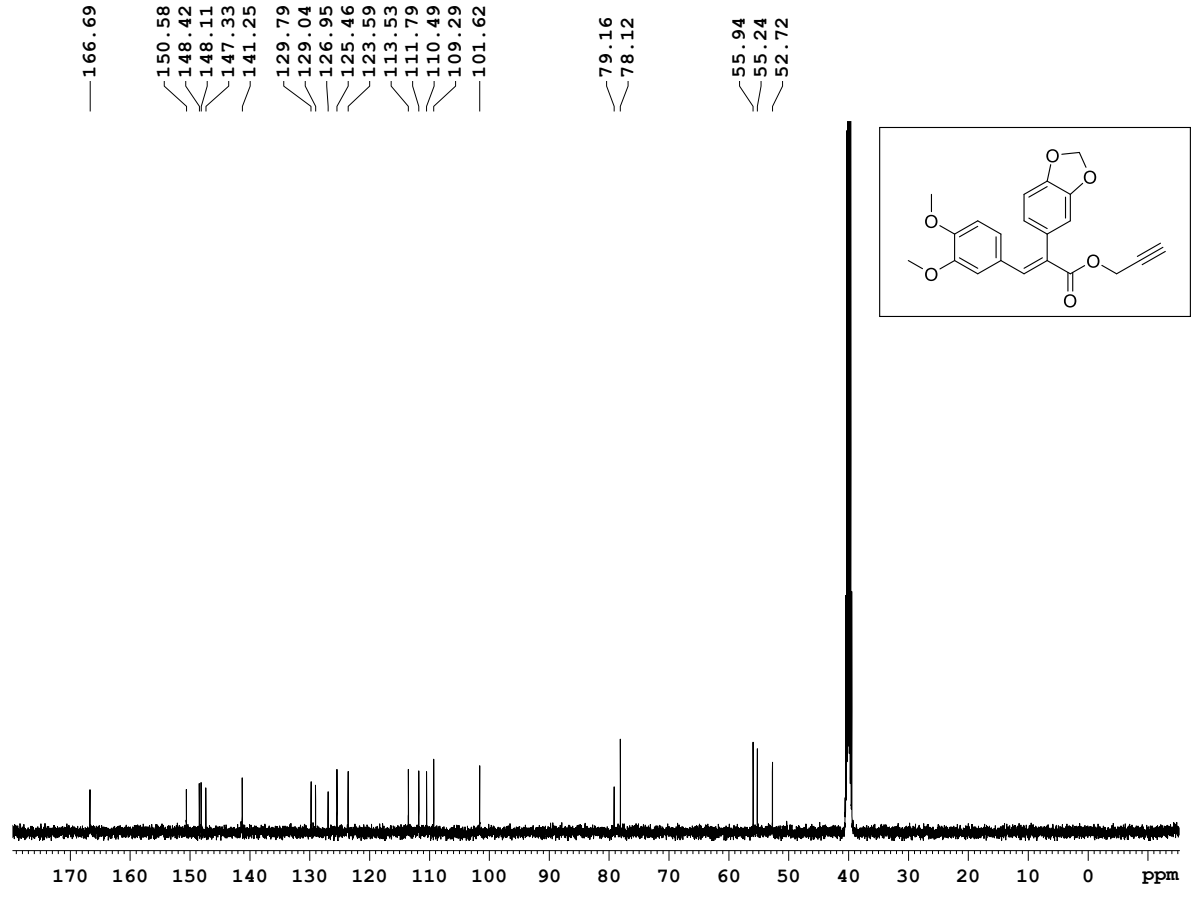
Compound **4a**: ^{1}H NMR (500 MHz, DMSO-d_6)



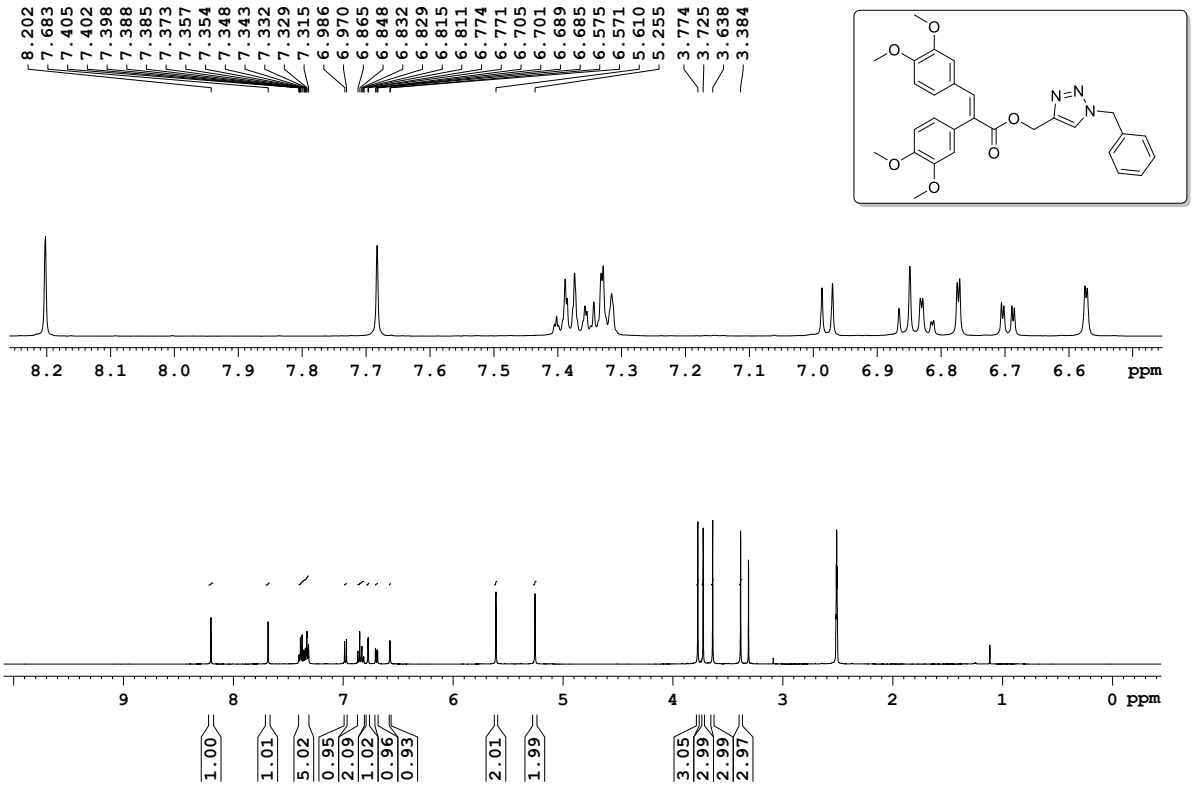
Compound **4a**: ^{13}C NMR (125 MHz, DMSO-d_6)



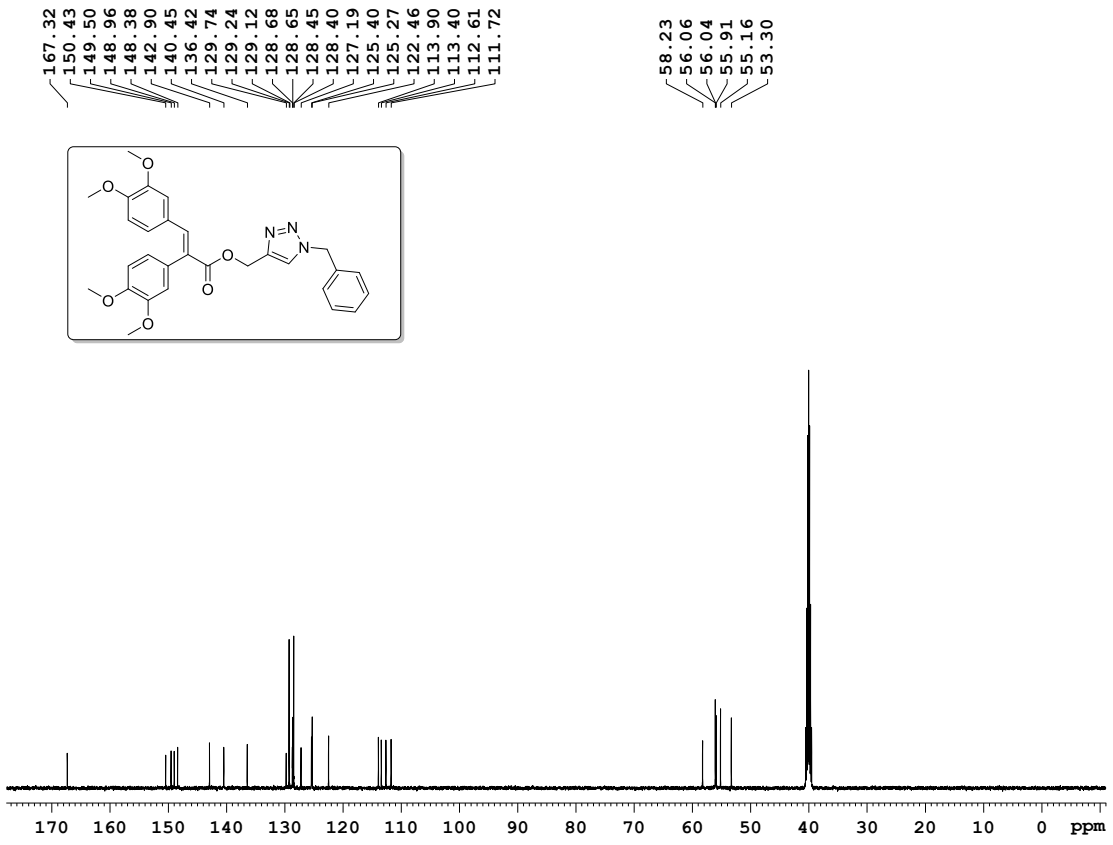
Compound **4b**: ^{1}H NMR (500 MHz, DMSO-d_6)



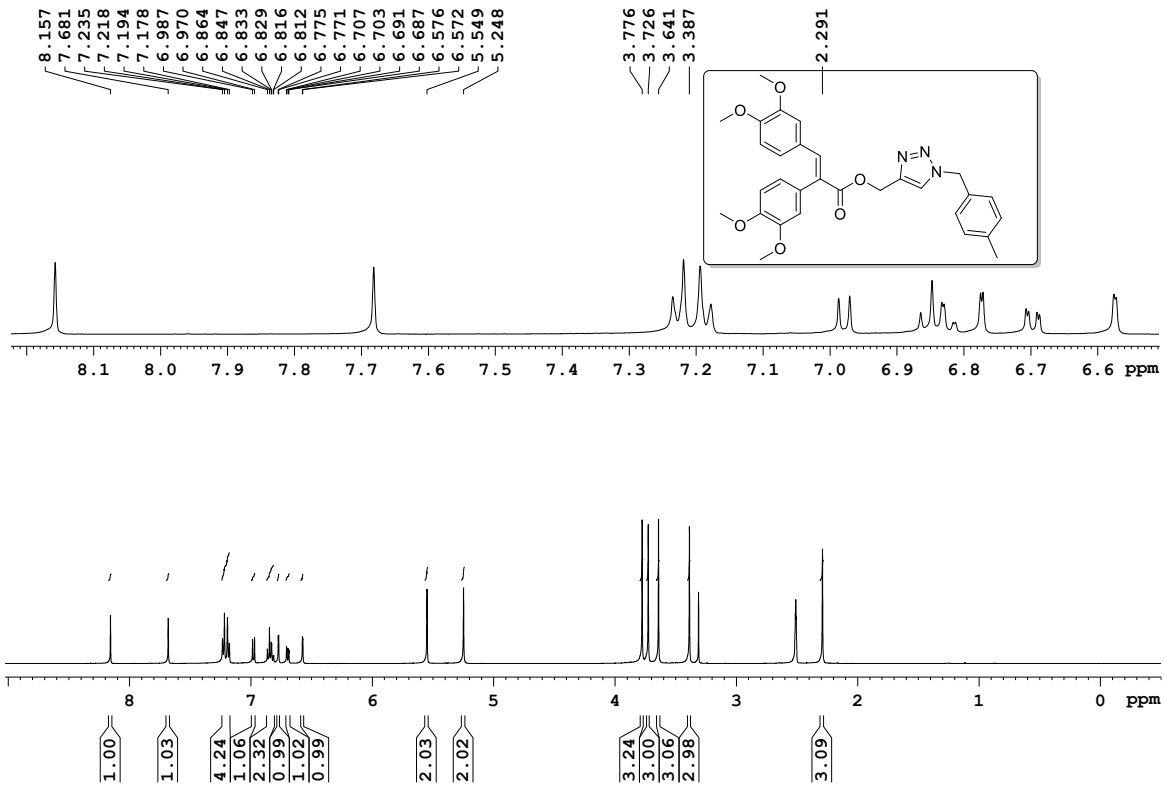
Compound **4b**: ^{13}C NMR (125 MHz, DMSO-d_6)



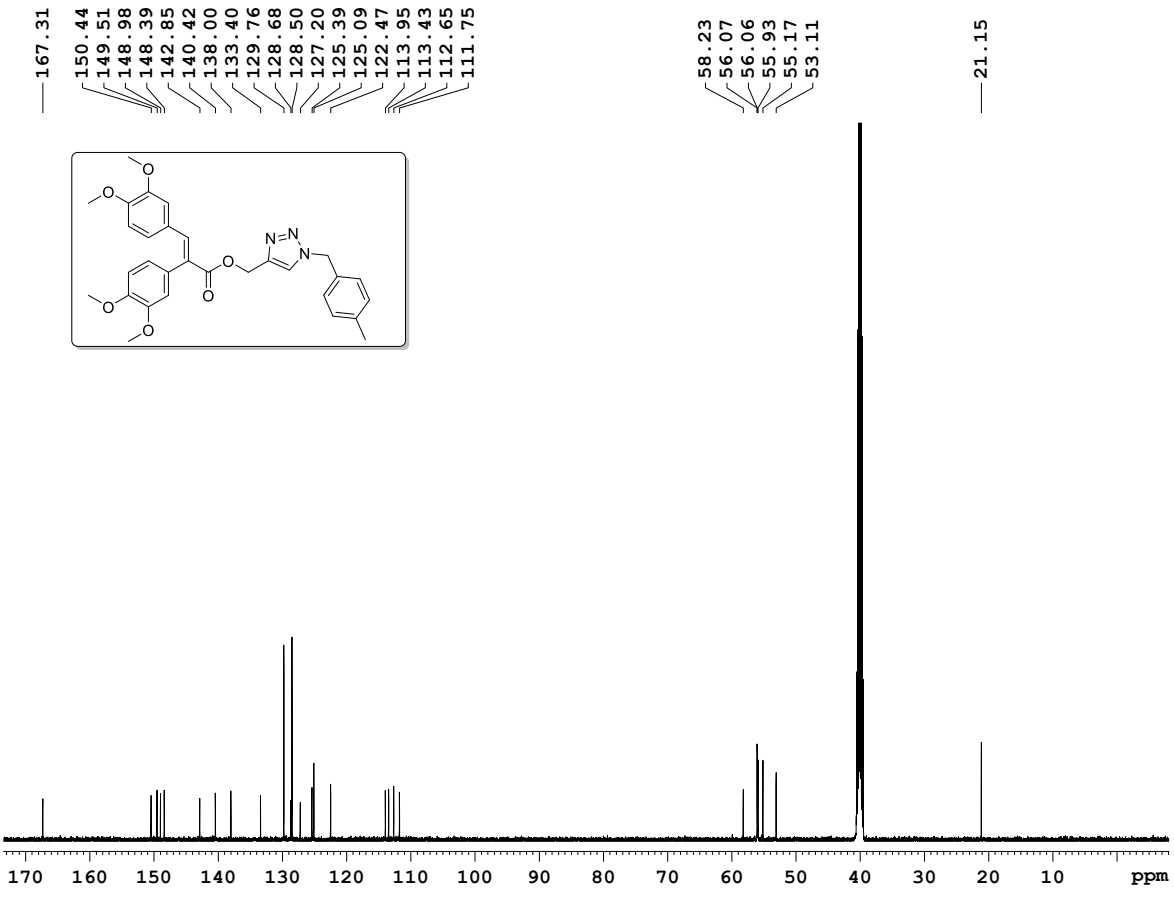
Compound **9a**: ^{1}H NMR (500 MHz, DMSO-d_6)



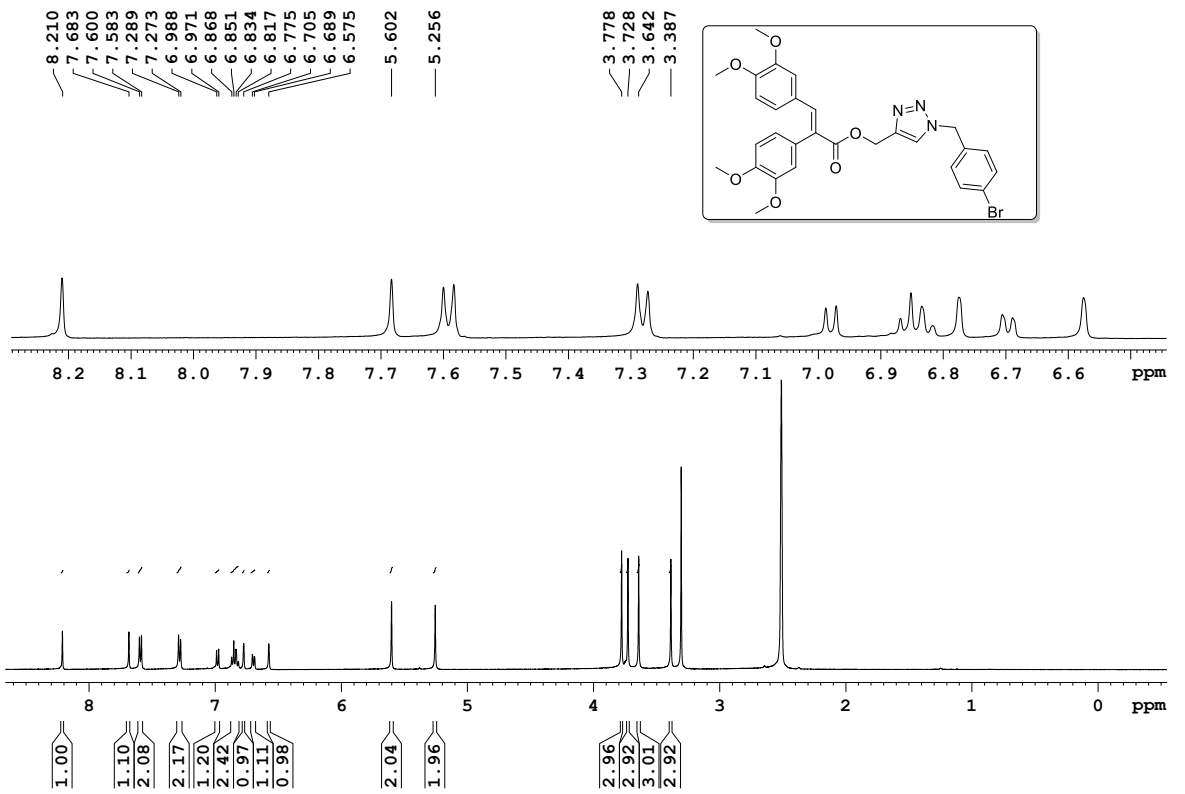
Compound **9a**: ^{13}C NMR (125 MHz, DMSO-d_6)



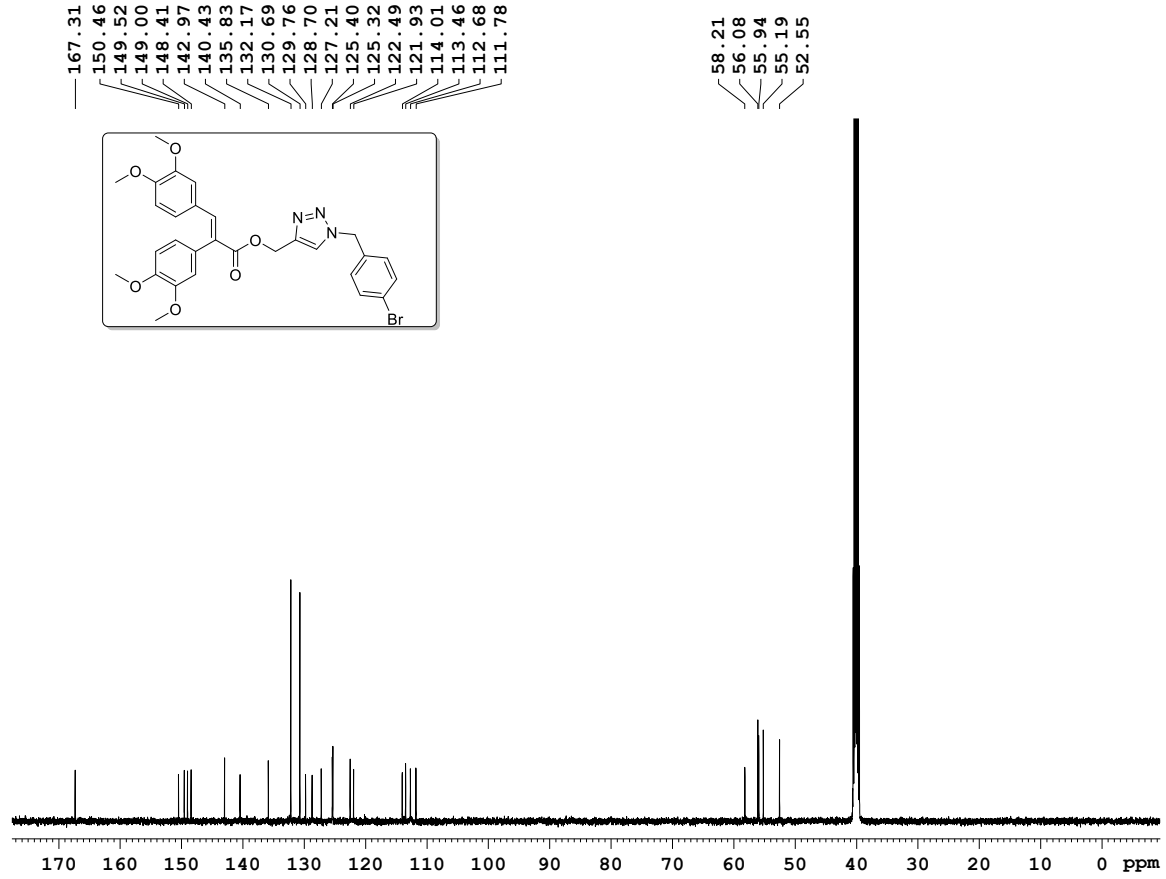
Compound **9b**: ^{1}H NMR (500 MHz, DMSO-d_6)



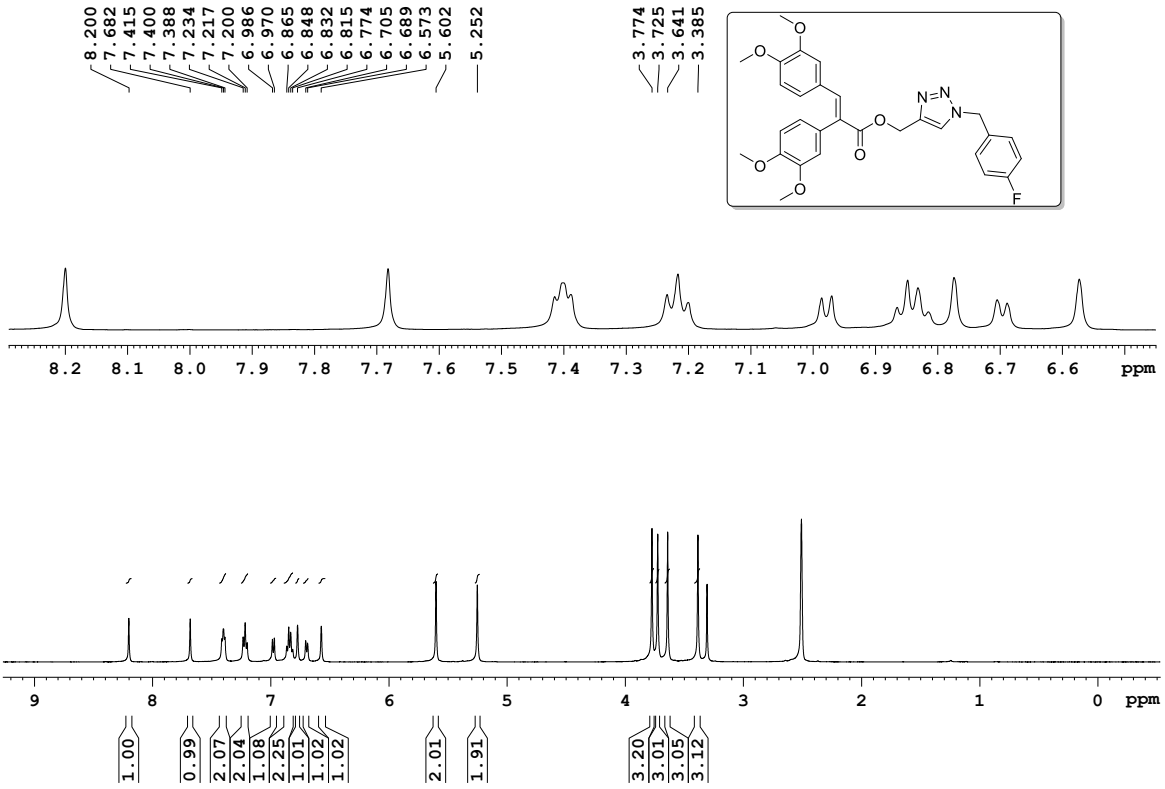
Compound **9b**: ^{13}C NMR (125 MHz, DMSO-d_6)



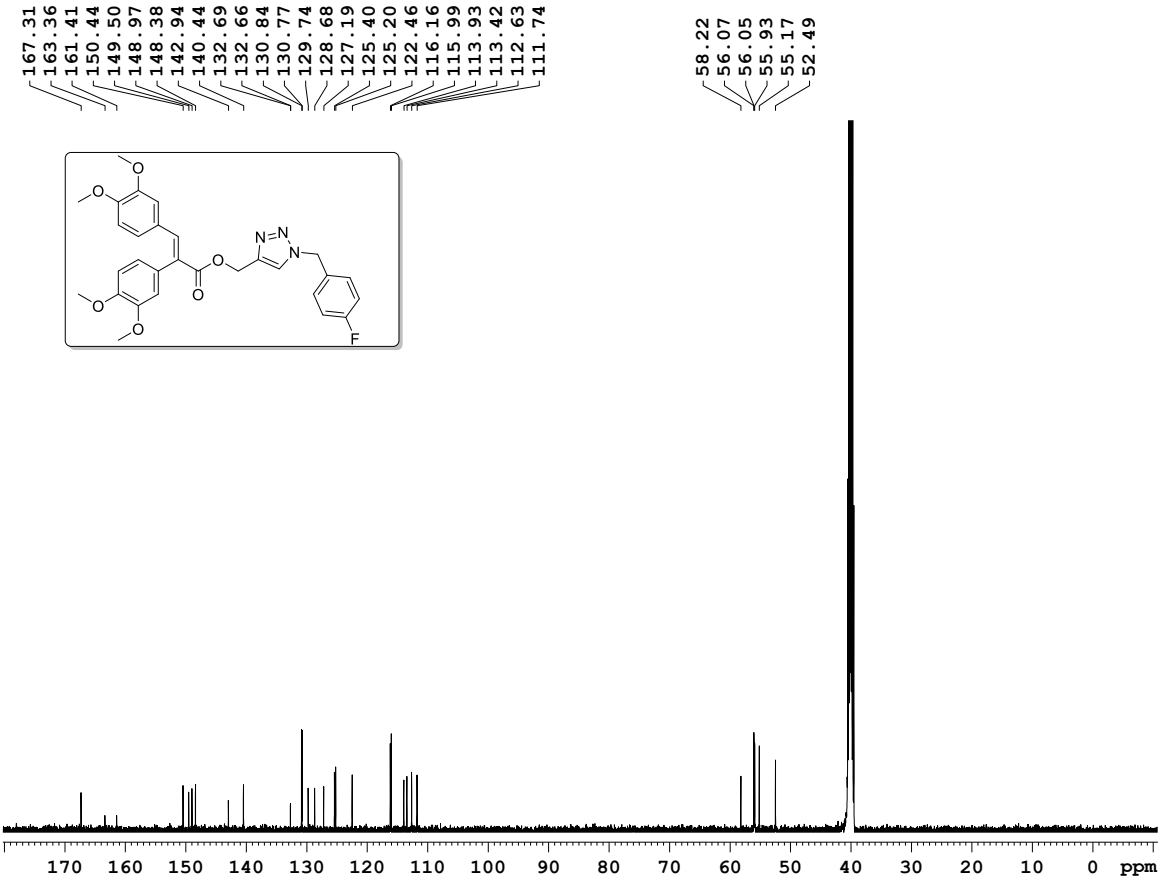
Compound **9c**: ^{1}H NMR (500 MHz, DMSO-d_6)



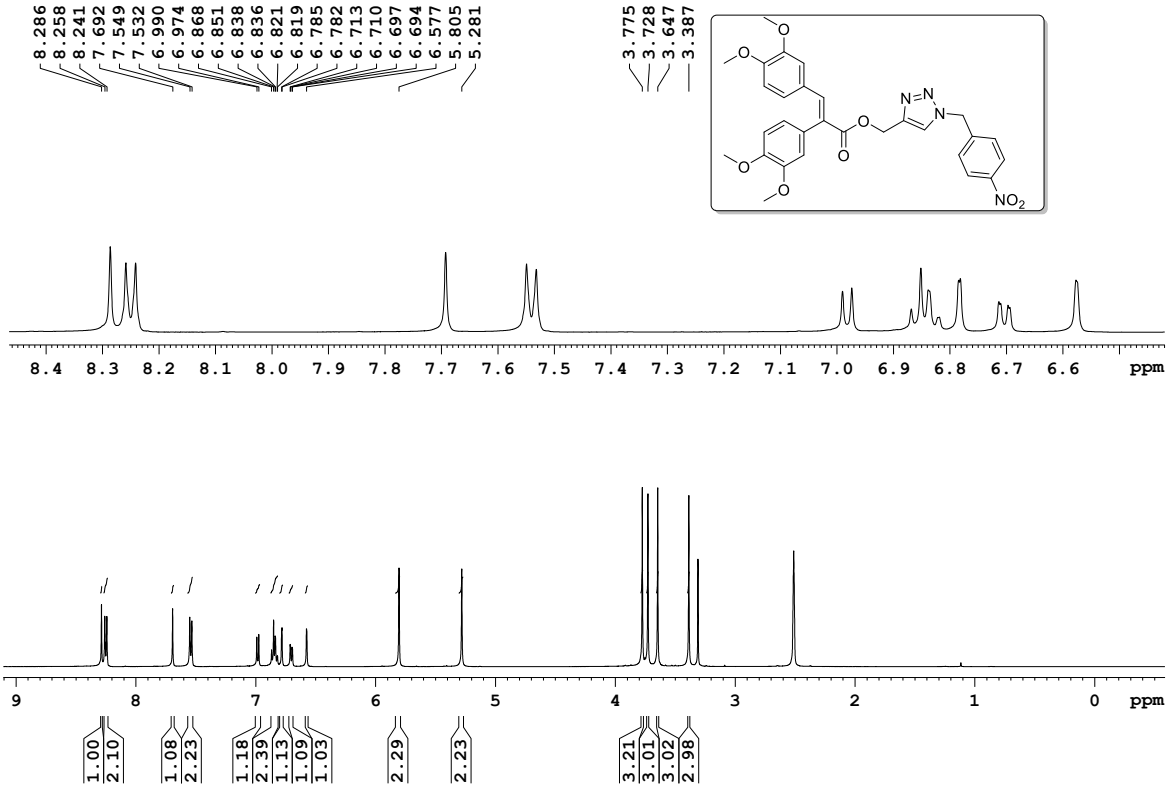
Compound **9c**: ^{13}C NMR (125 MHz, DMSO-d_6)



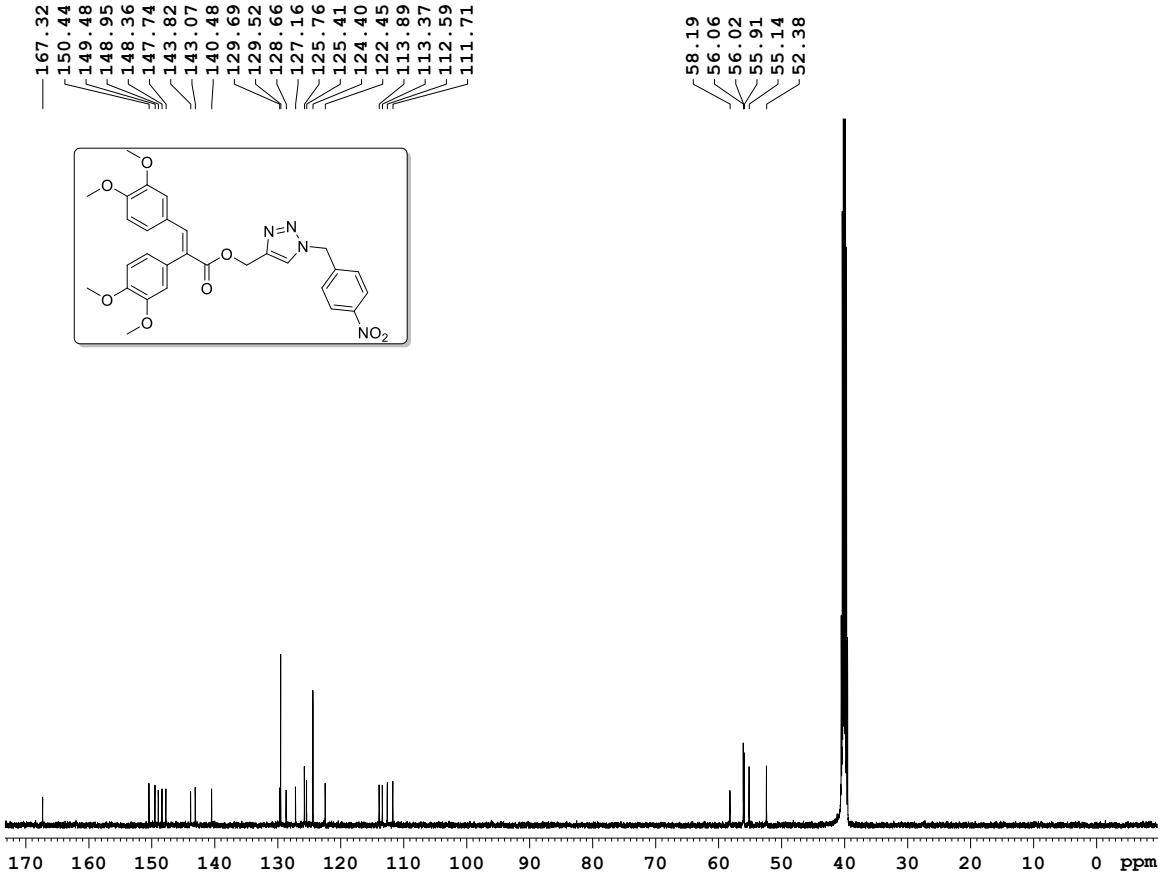
Compound **9d**: ^{1}H NMR (500 MHz, DMSO-d_6)



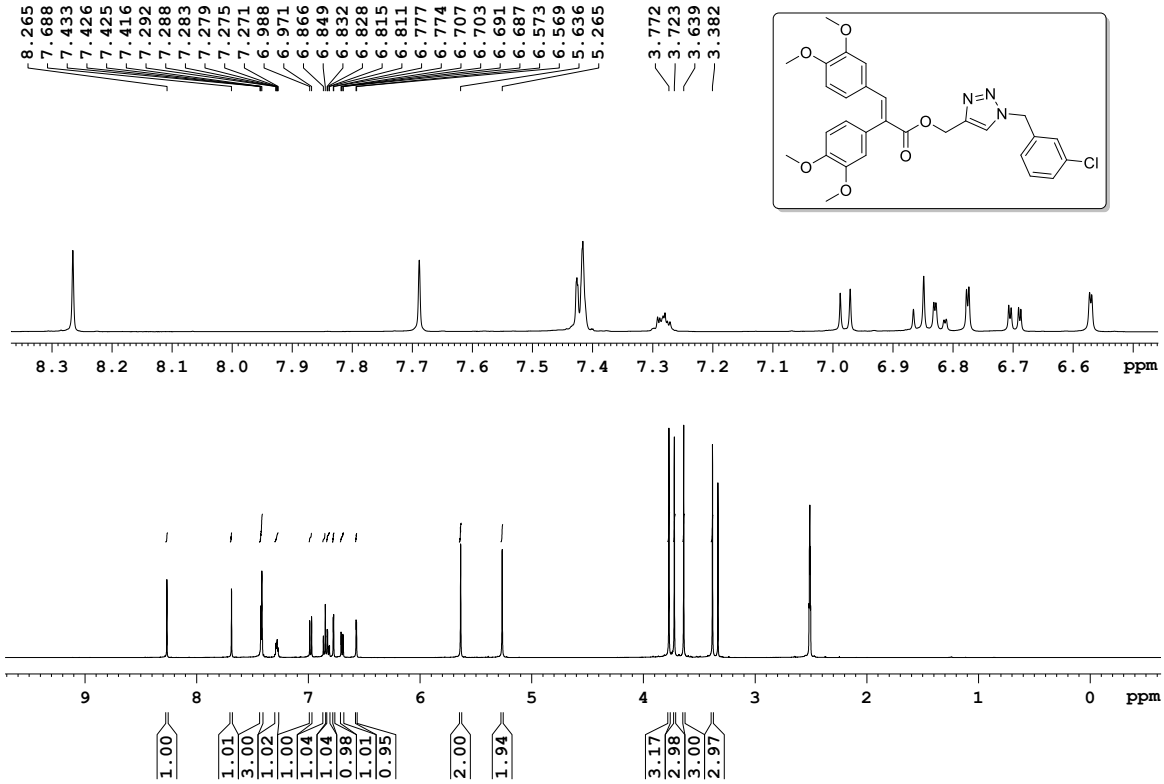
Compound **9d**: ^{13}C NMR (125 MHz, DMSO-d_6)



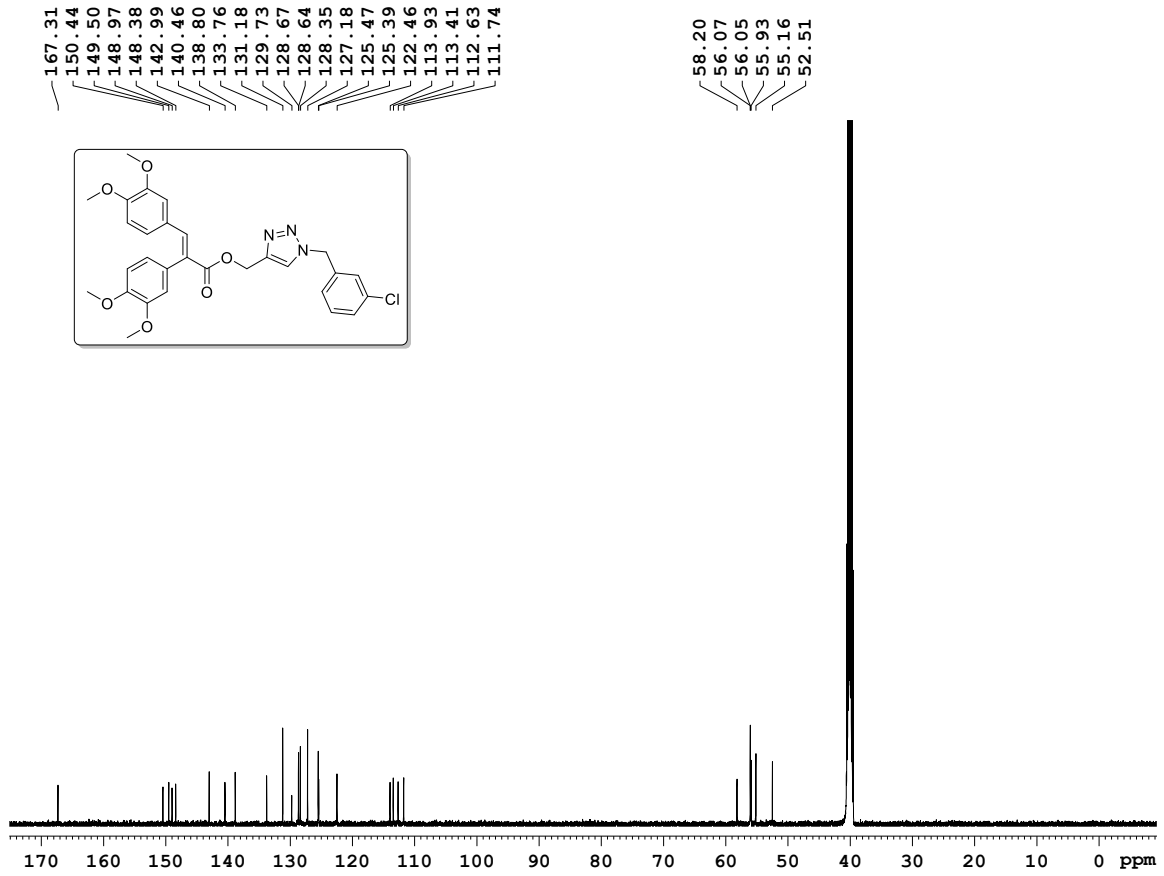
Compound **9e**: ^{1}H NMR (500 MHz, DMSO-d_6)



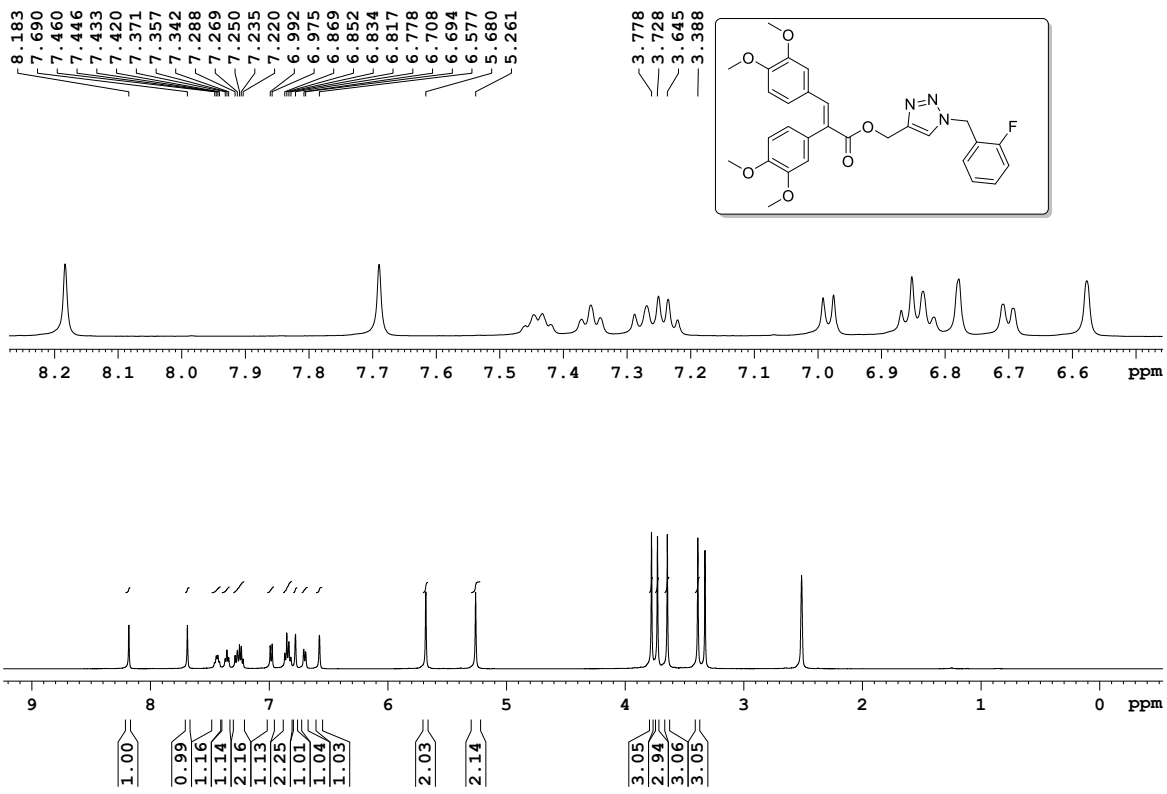
Compound **9e**: ^{13}C NMR (125 MHz, DMSO-d_6)



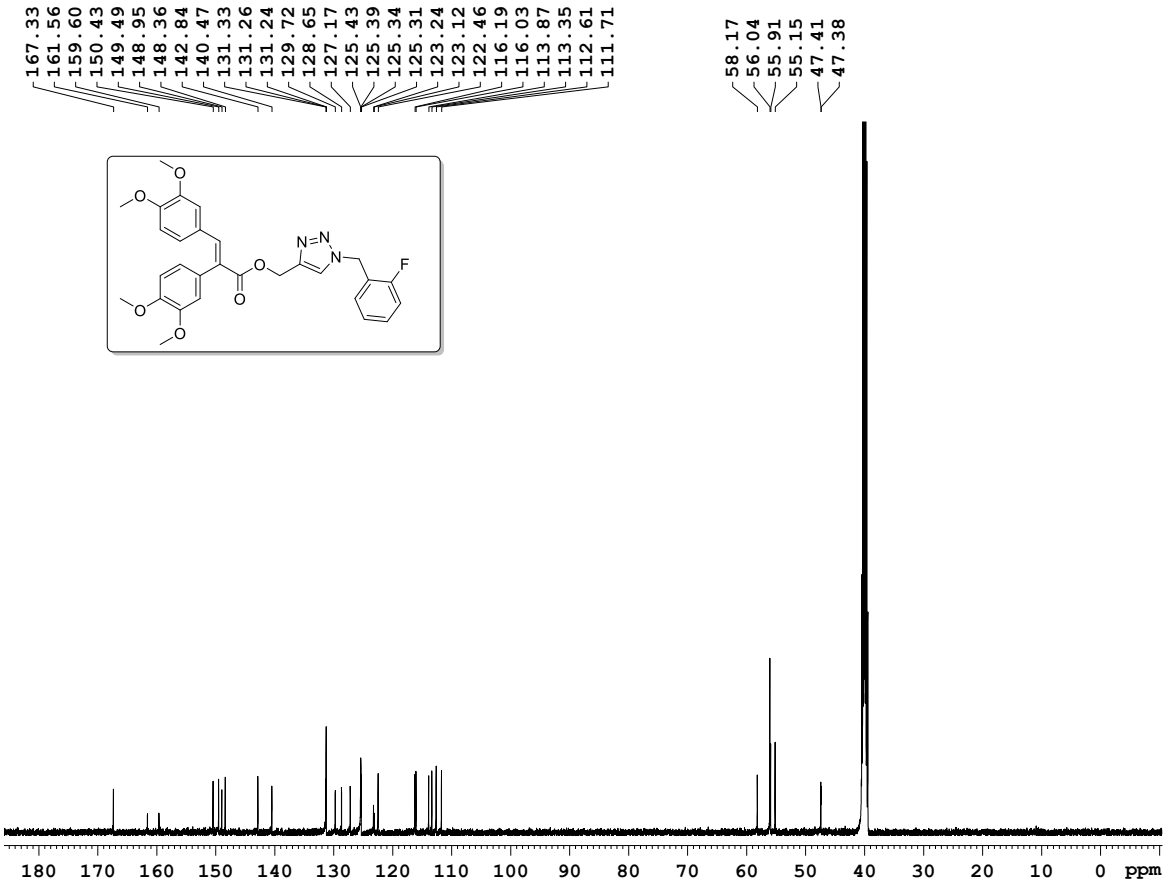
Compound **9f**: ^{1}H NMR (500 MHz, DMSO-d_6)



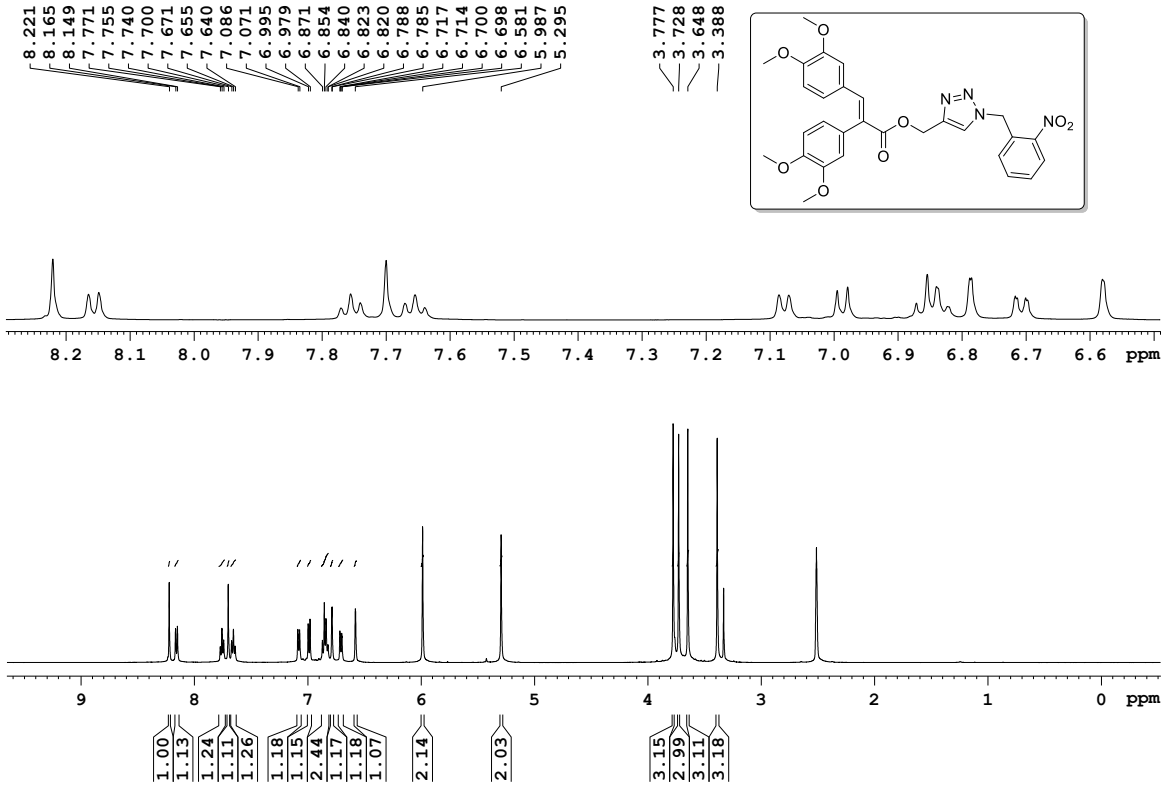
Compound **9f**: ^{13}C NMR (125 MHz, DMSO-d_6)



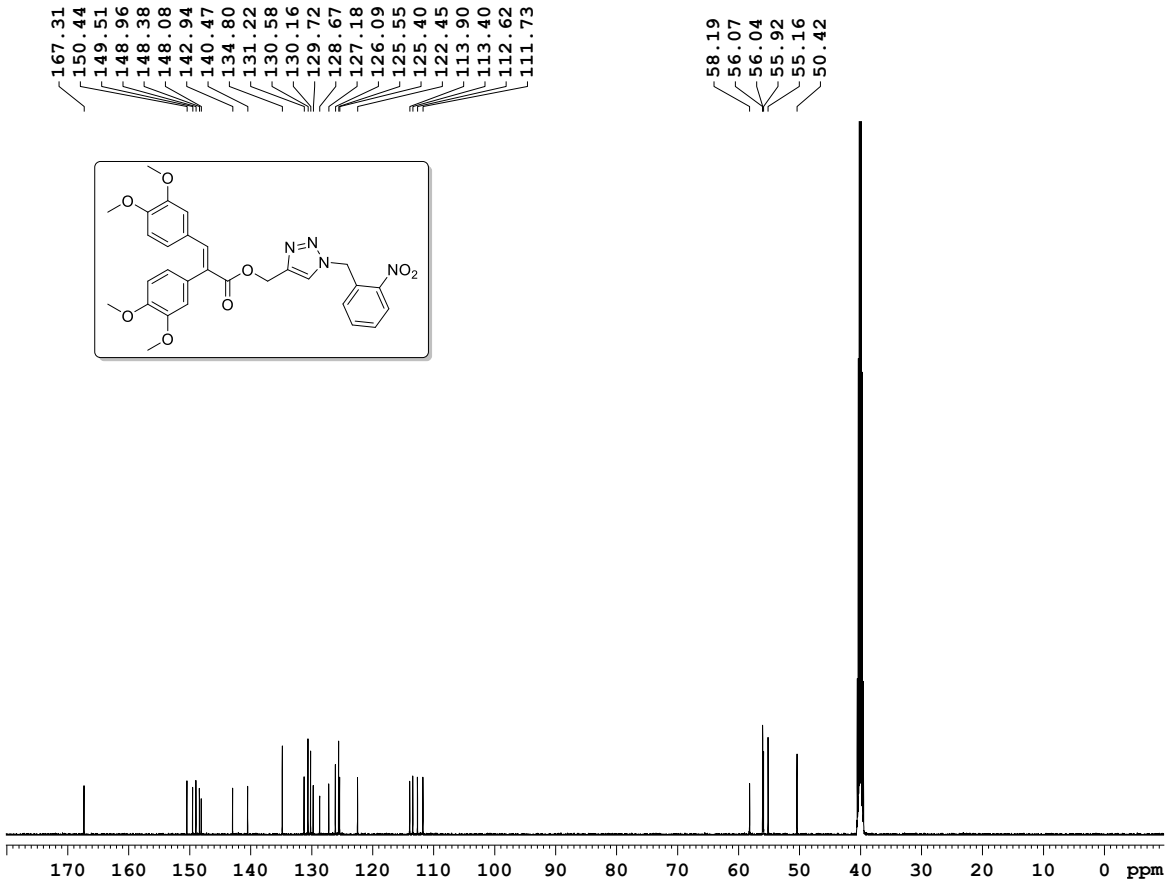
Compound **9g**: ^{1}H NMR (500 MHz, DMSO-d_6)



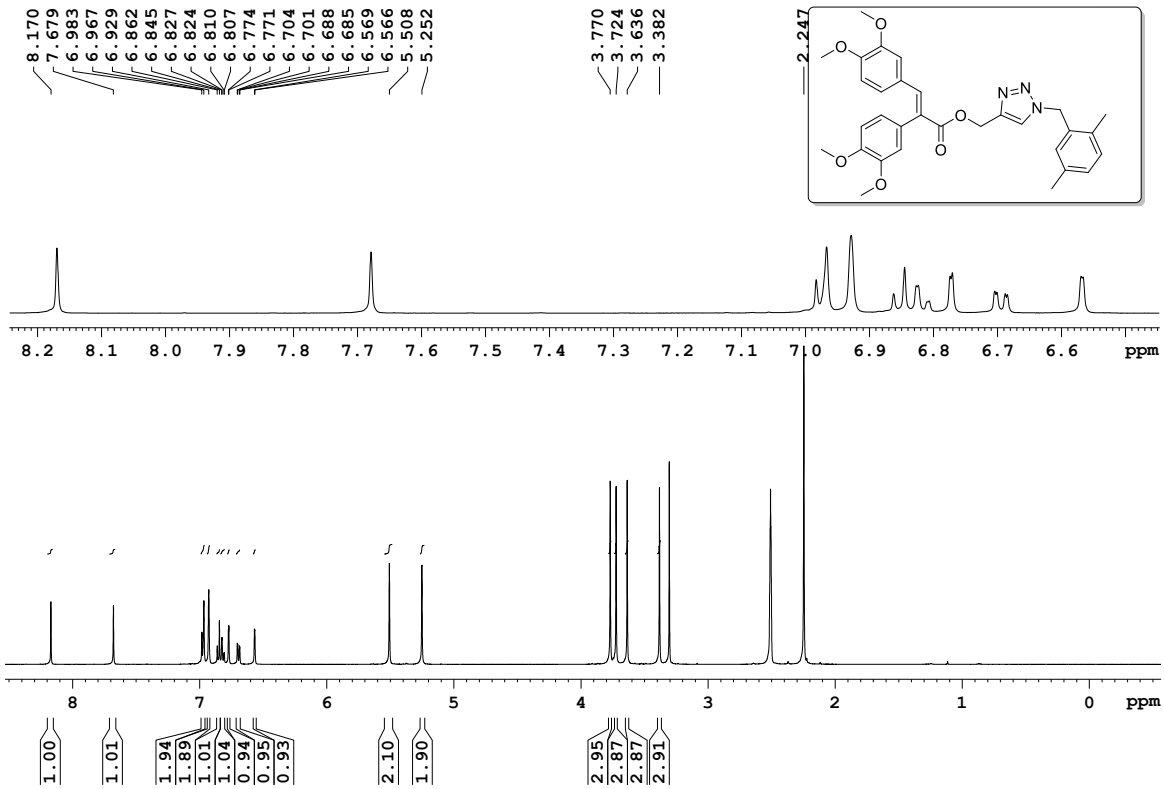
Compound **9g**: ^{13}C NMR (125 MHz, DMSO-d_6)



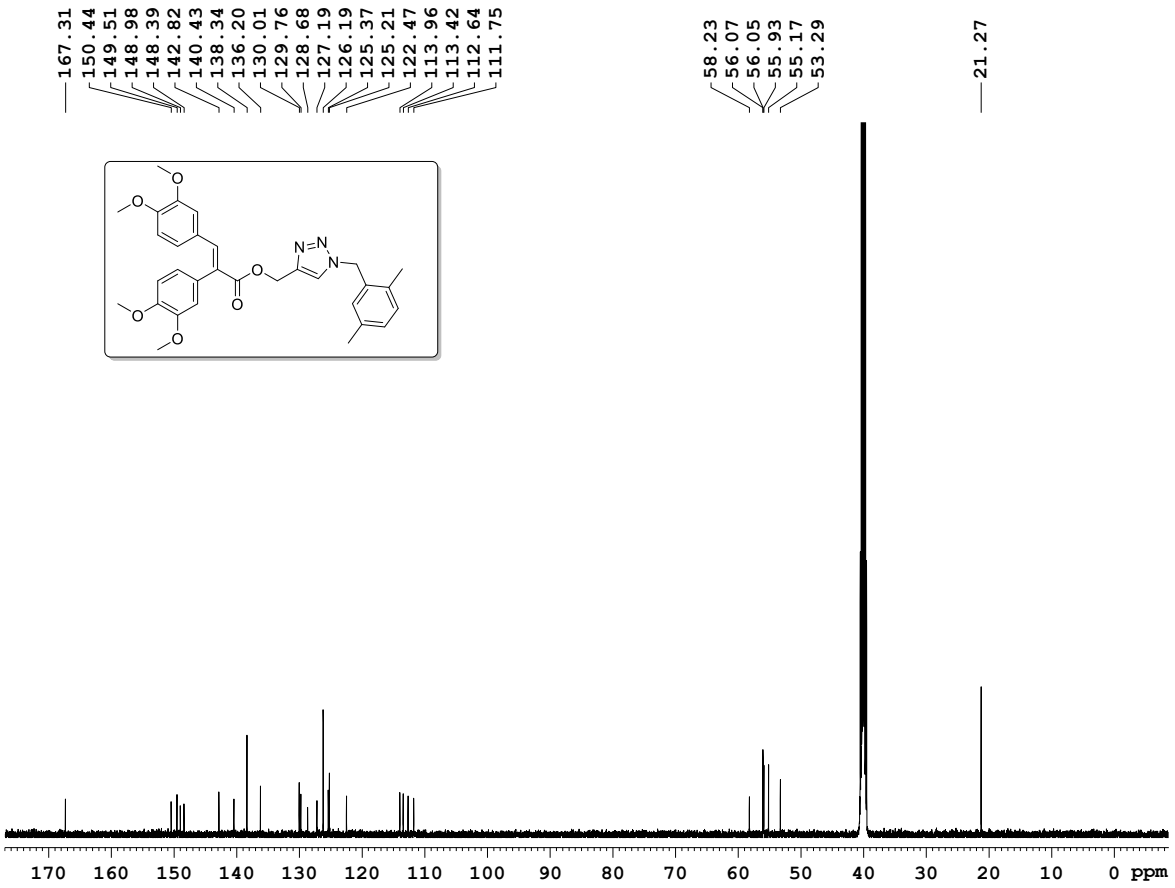
Compound **9h**: ^{1}H NMR (500 MHz, DMSO-d_6)



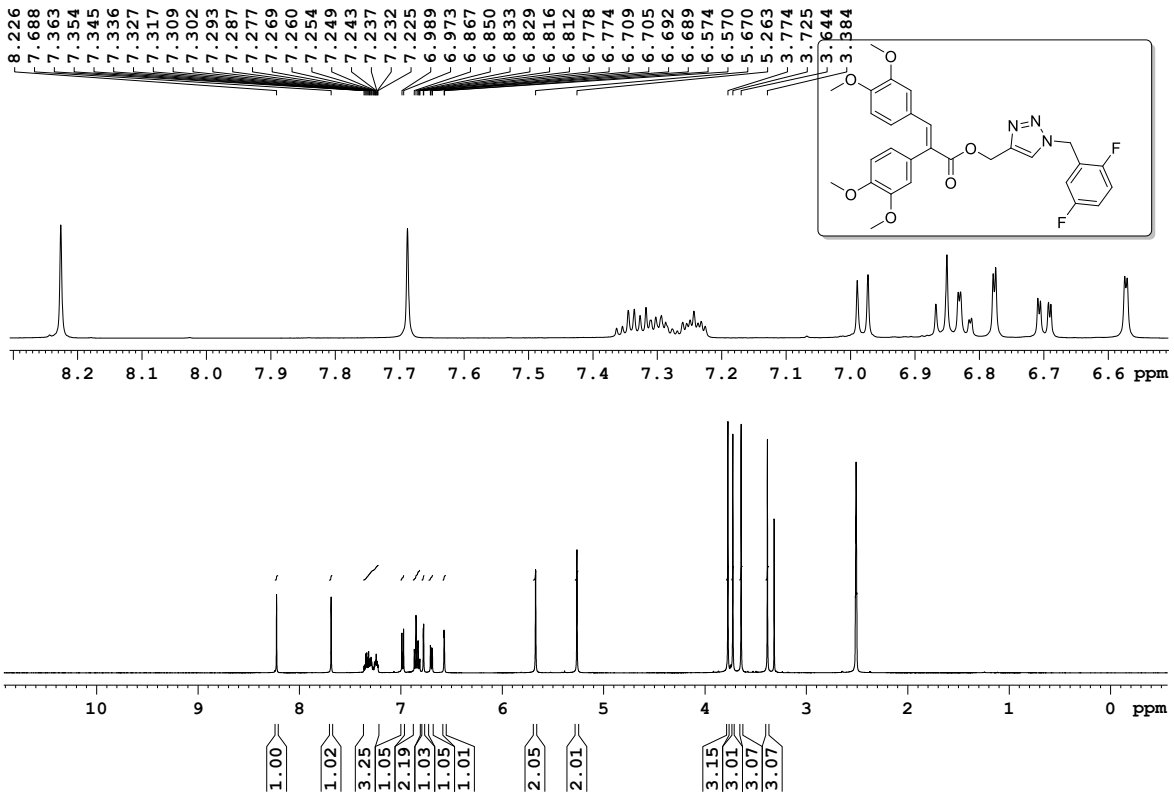
Compound **9h**: ^{13}C NMR (125 MHz, DMSO-d_6)



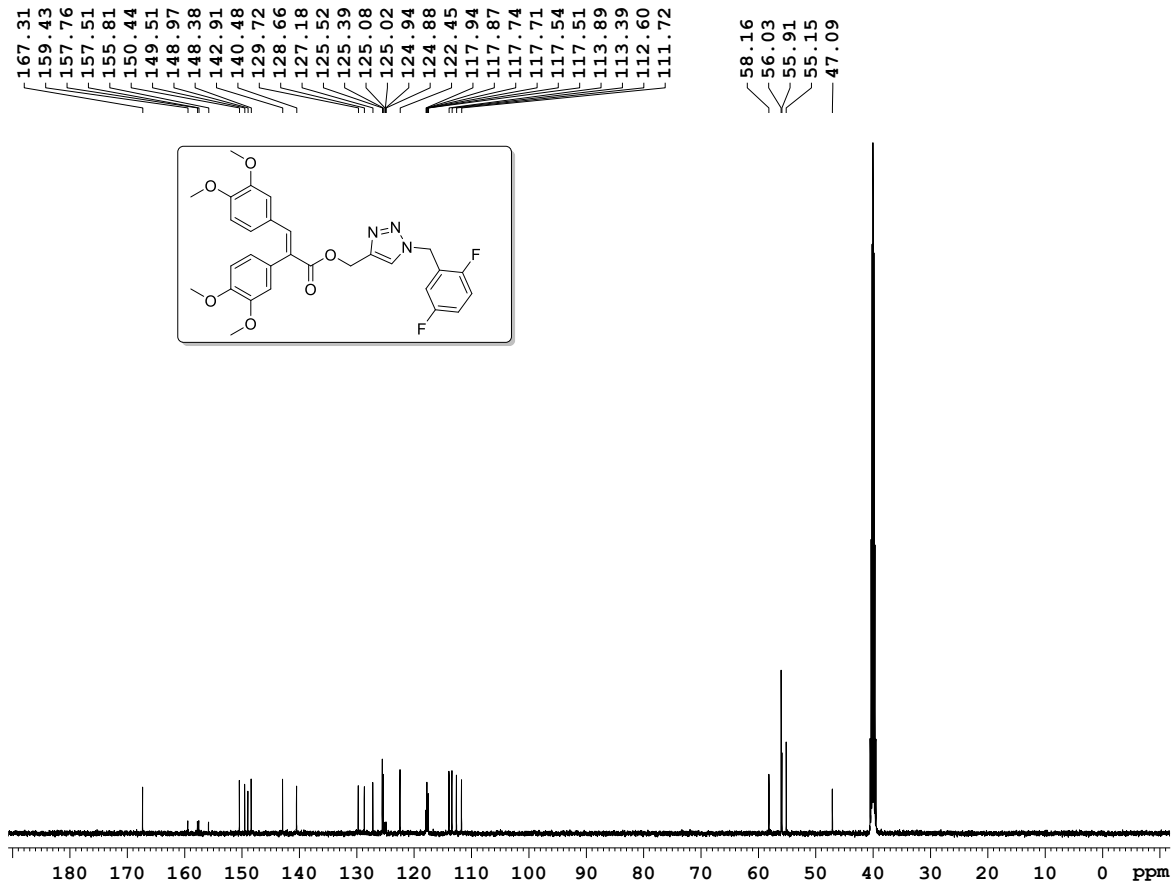
Compound **9i**: ^{1}H NMR (500 MHz, DMSO-d_6)



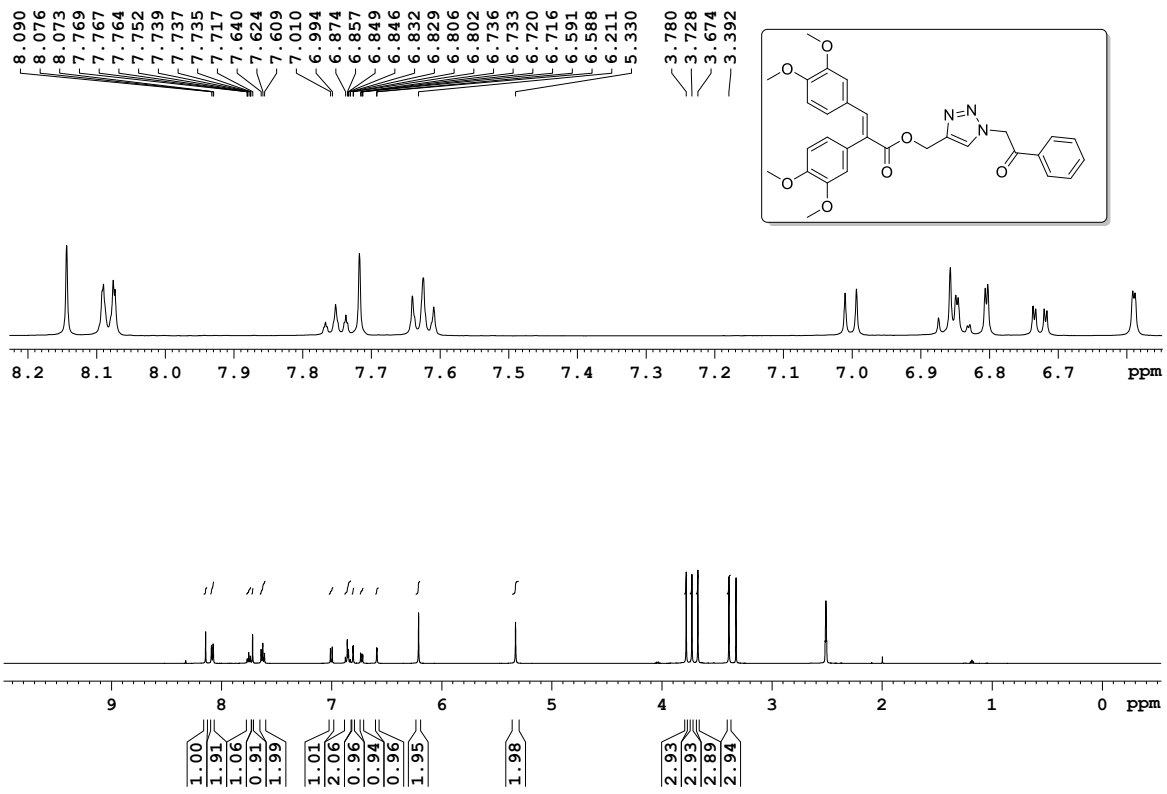
Compound **9i**: ^{13}C NMR (125 MHz, DMSO-d_6)



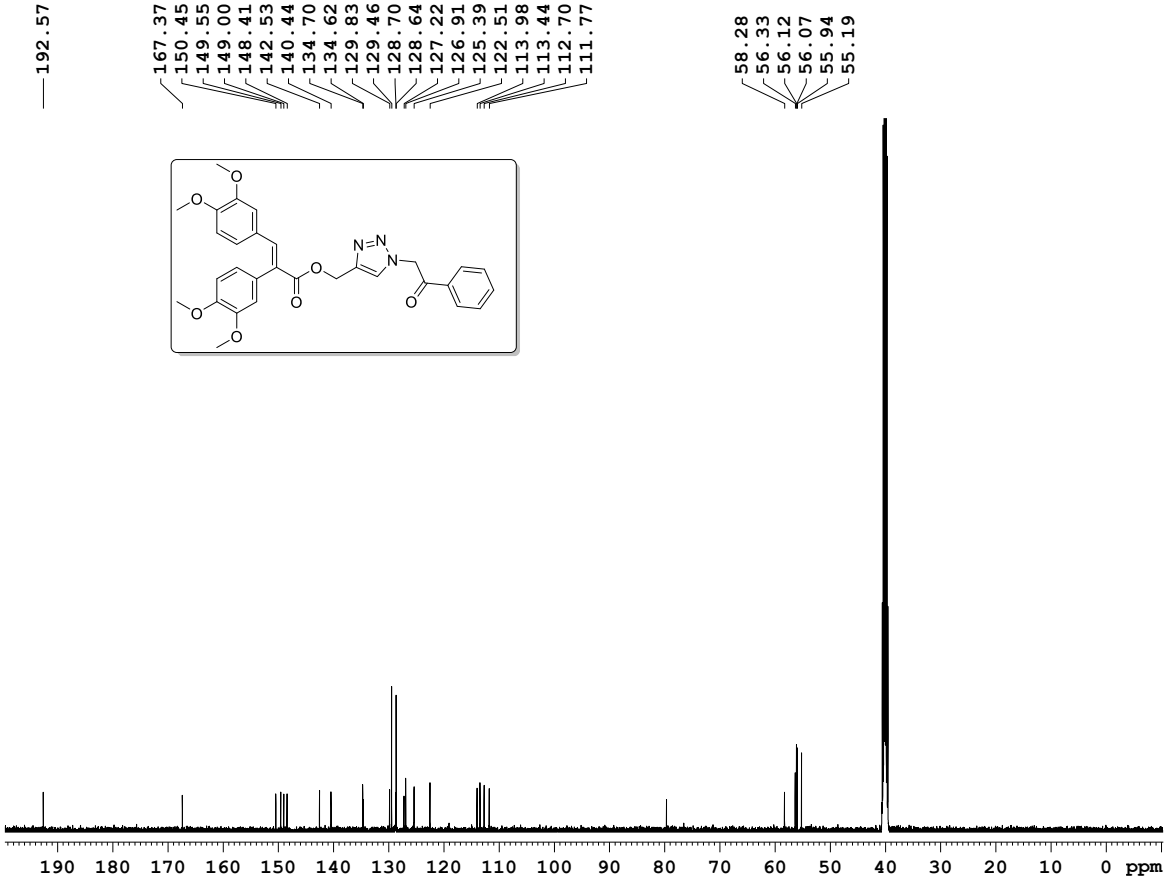
Compound **9j**: ^{1}H NMR (500 MHz, DMSO-d_6)



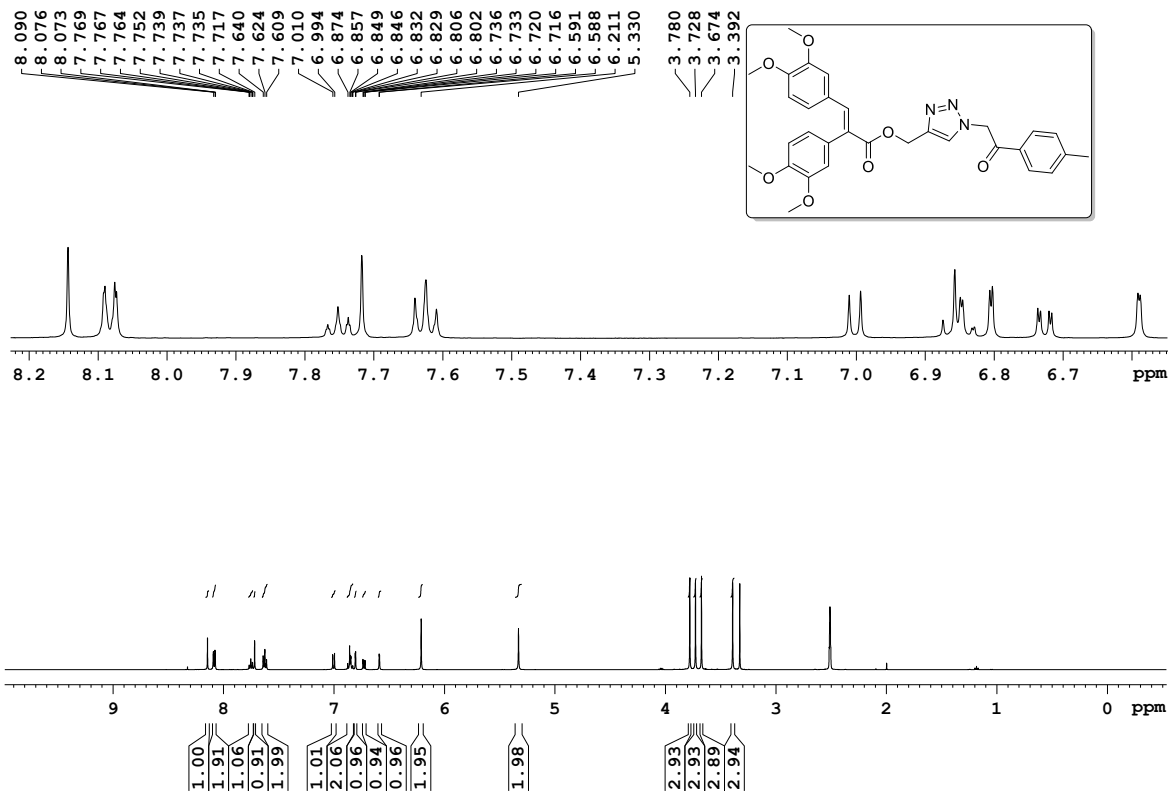
Compound **9j**: ^{13}C NMR (125 MHz, DMSO-d_6)



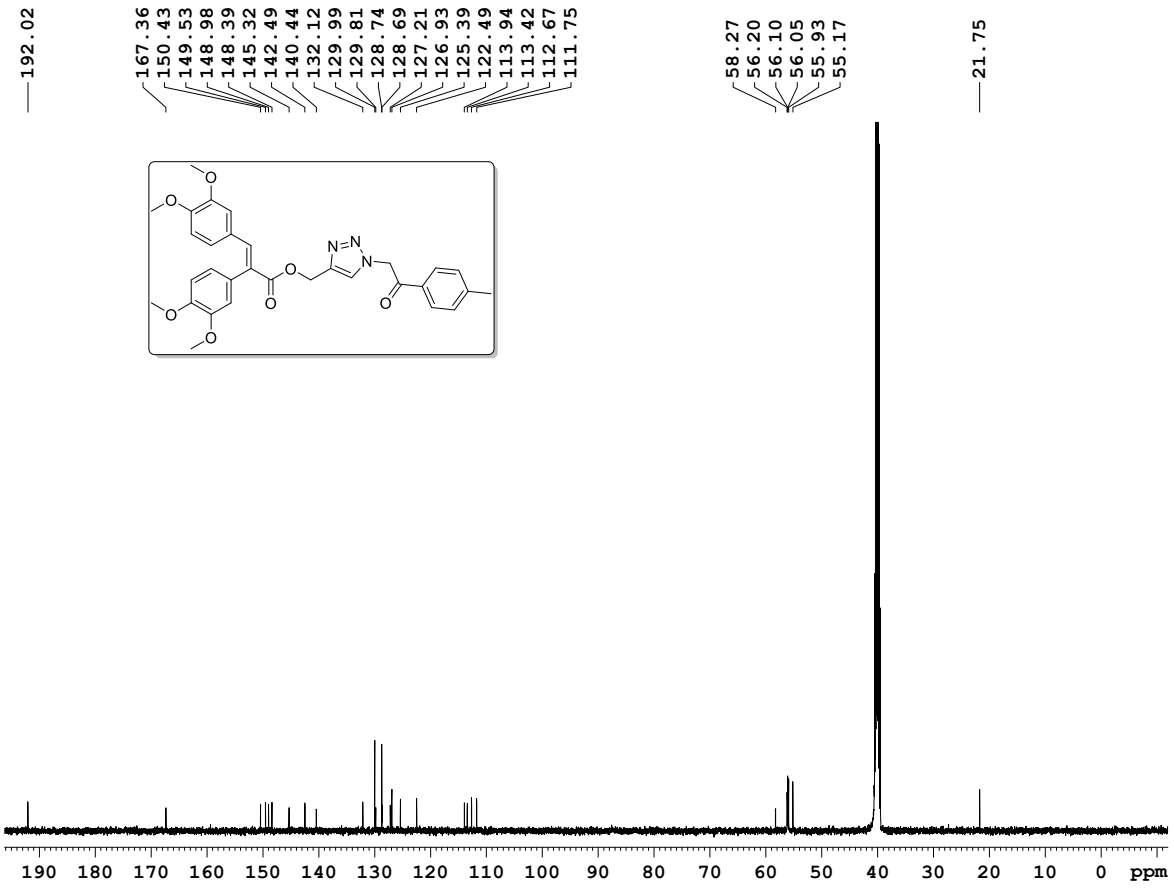
Compound **10a**: ^{1}H NMR (500 MHz, DMSO-d_6)



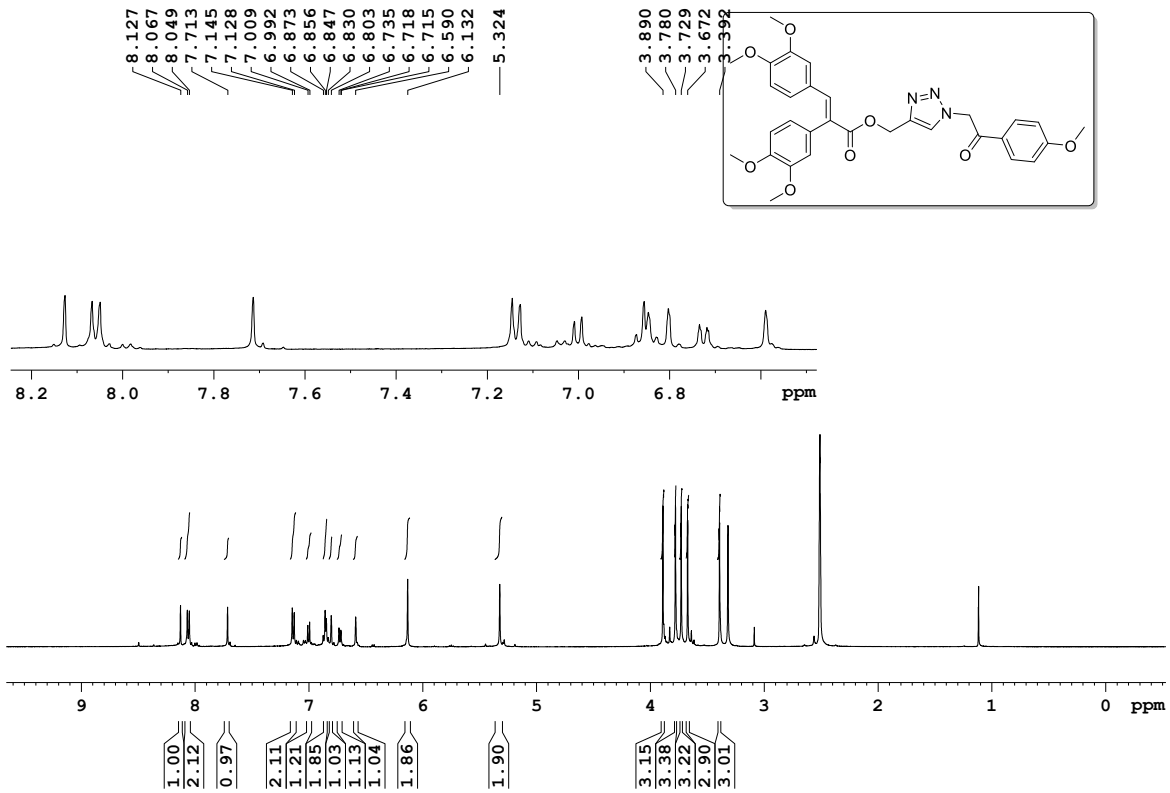
Compound **10a**: ^{13}C NMR (125 MHz, DMSO-d_6)



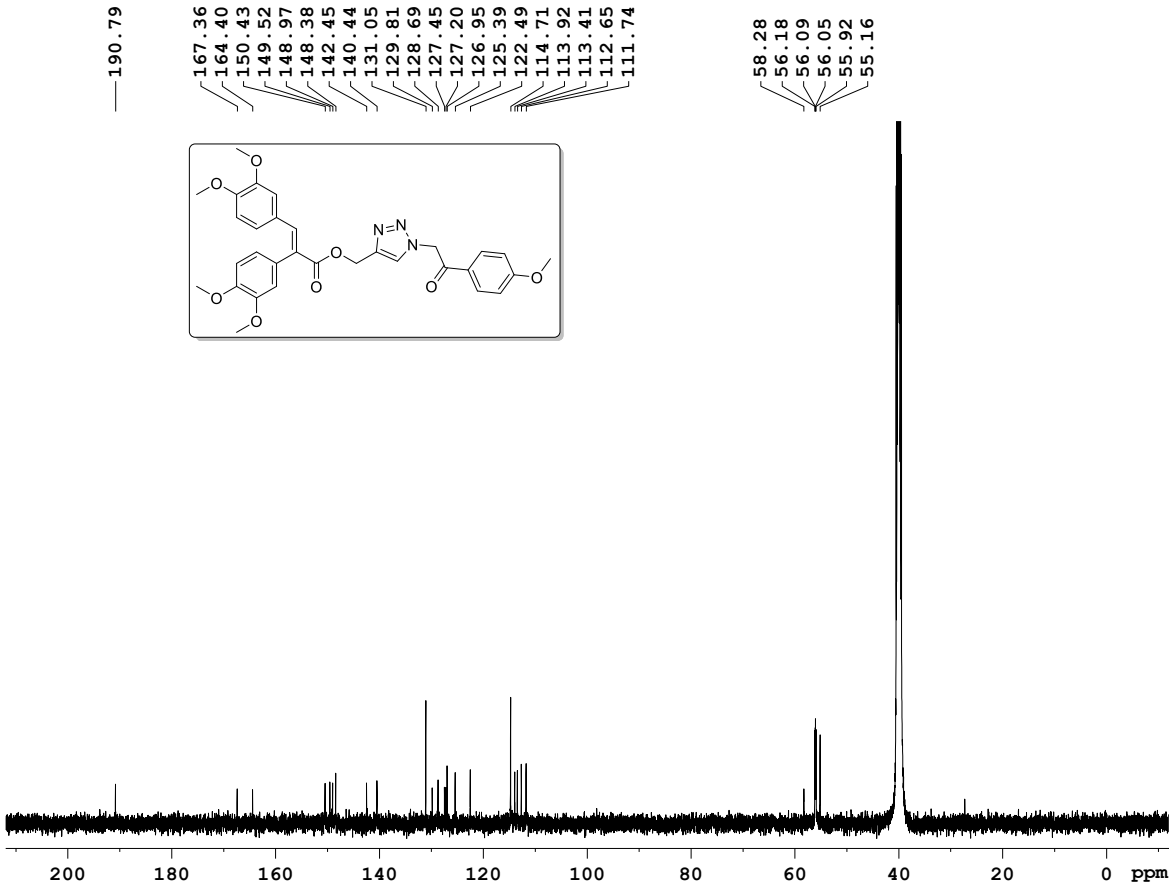
Compound **10b**: ^{1}H NMR (500 MHz, DMSO-d_6)



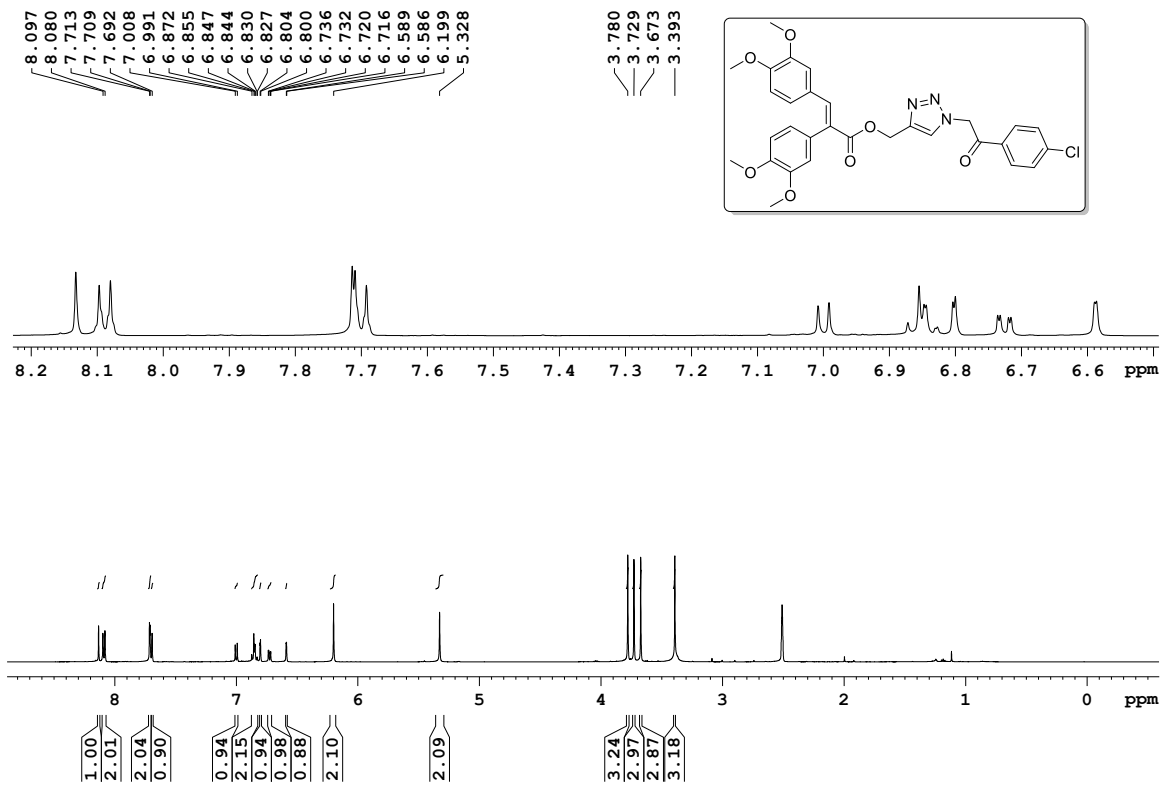
Compound **10b**: ^{13}C NMR (125 MHz, DMSO-d_6)



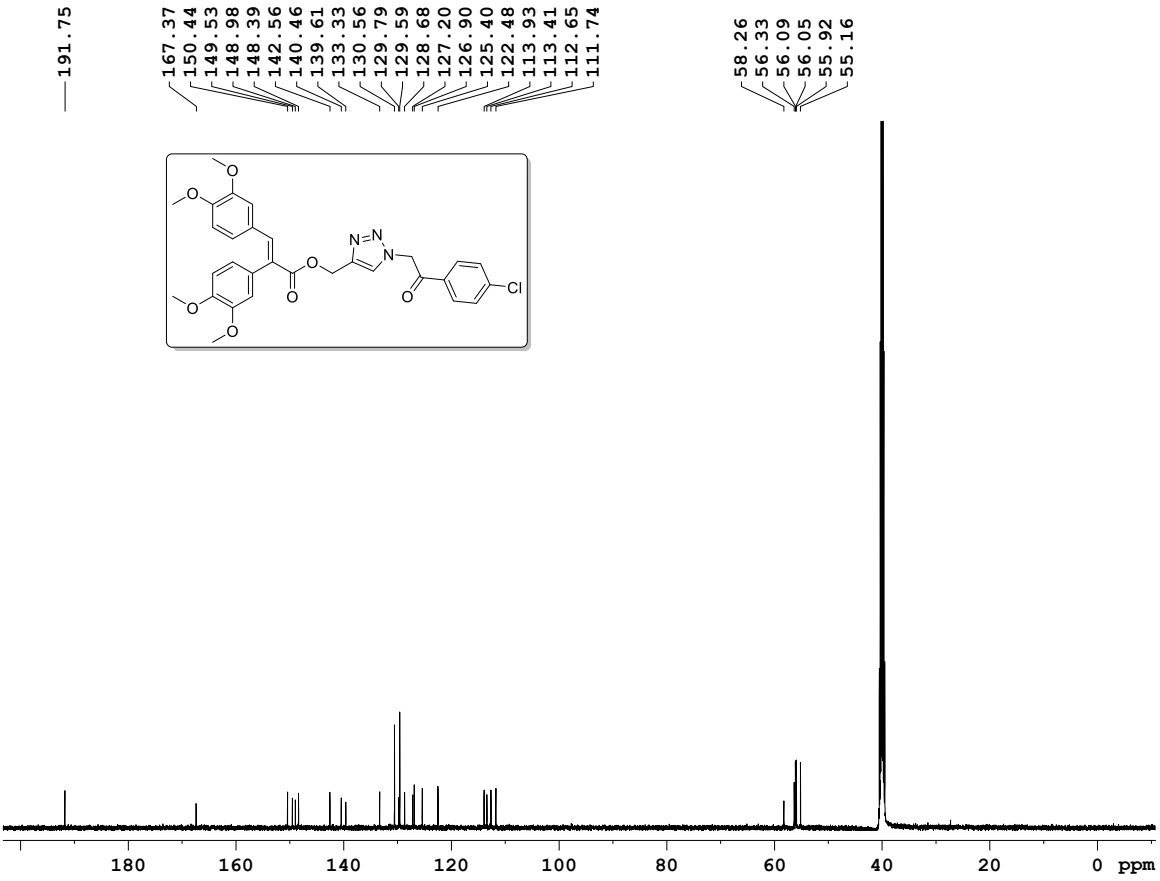
Compound **10c**: ^{1}H NMR (500 MHz, DMSO-d_6)



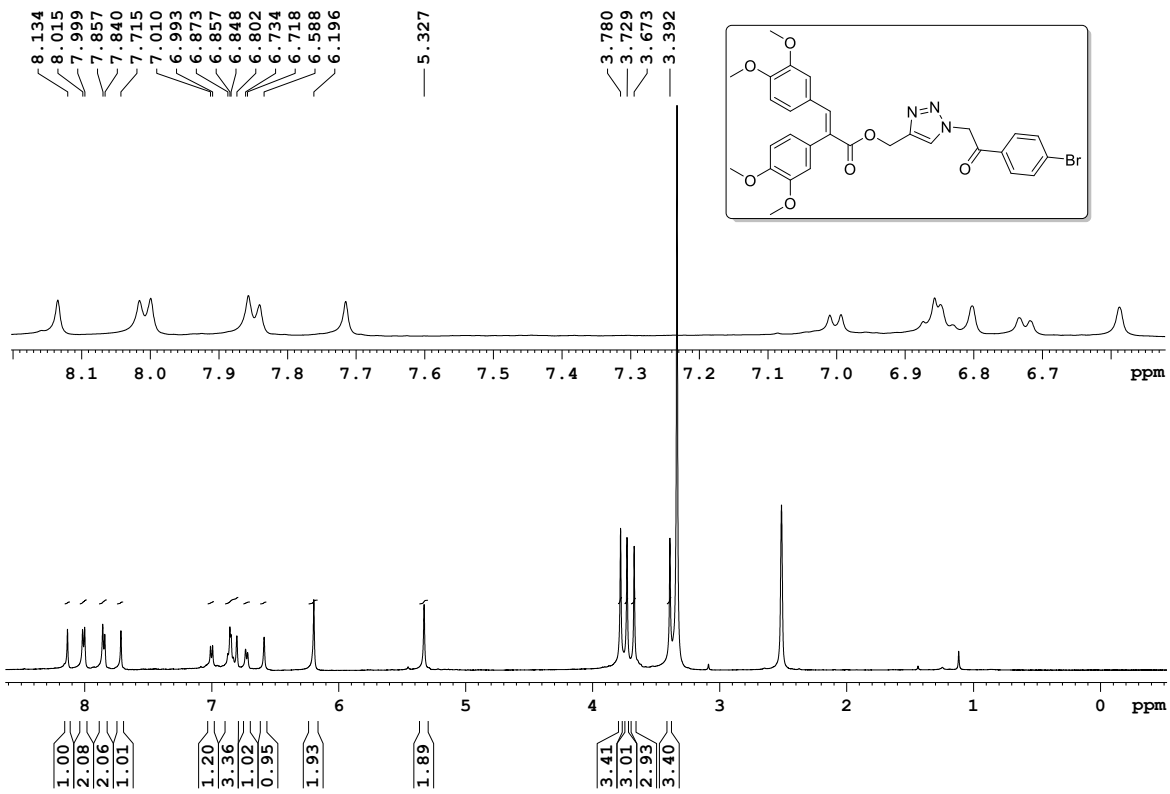
Compound **10c**: ^{13}C NMR (125 MHz, DMSO-d_6)



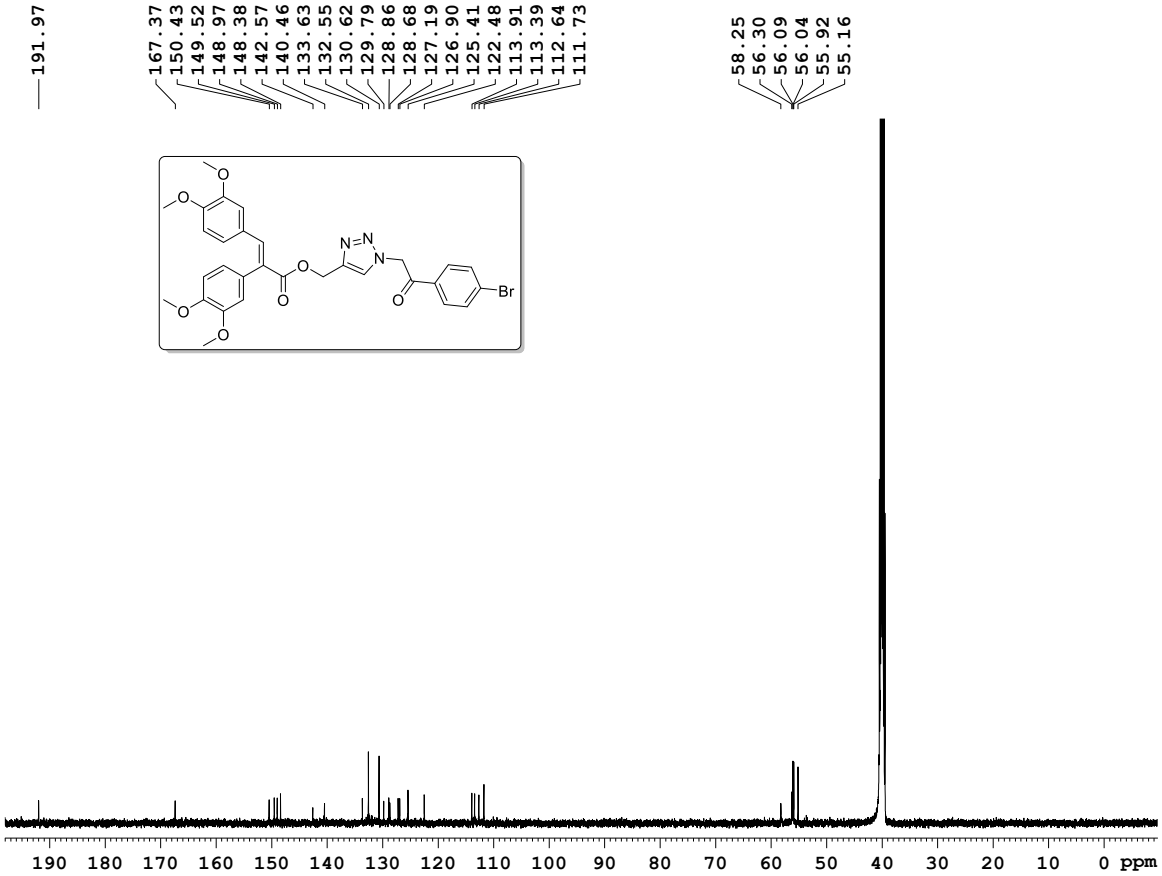
Compound **10d**: ^{1}H NMR (500 MHz, DMSO-d_6)



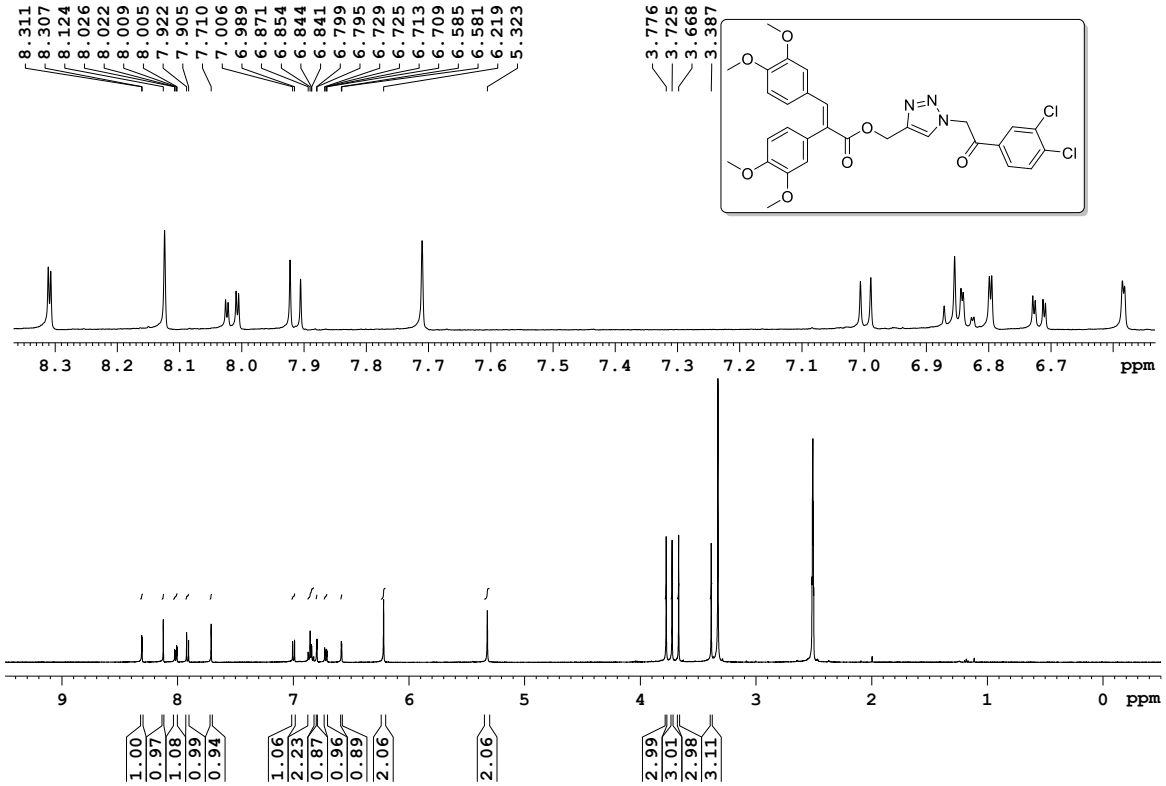
Compound **10d**: ^{13}C NMR (125 MHz, DMSO-d_6)



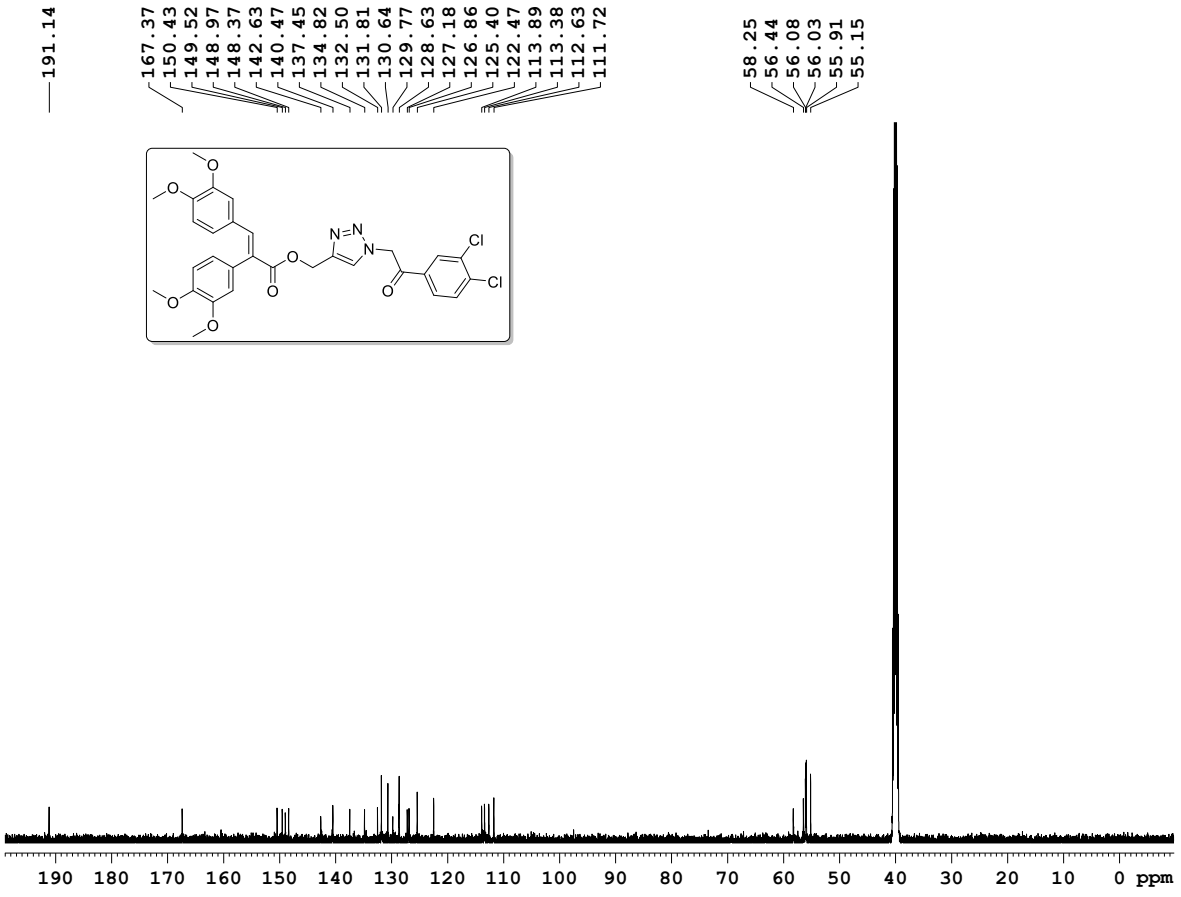
Compound **10e**: ^{1}H NMR (500 MHz, DMSO-d_6)



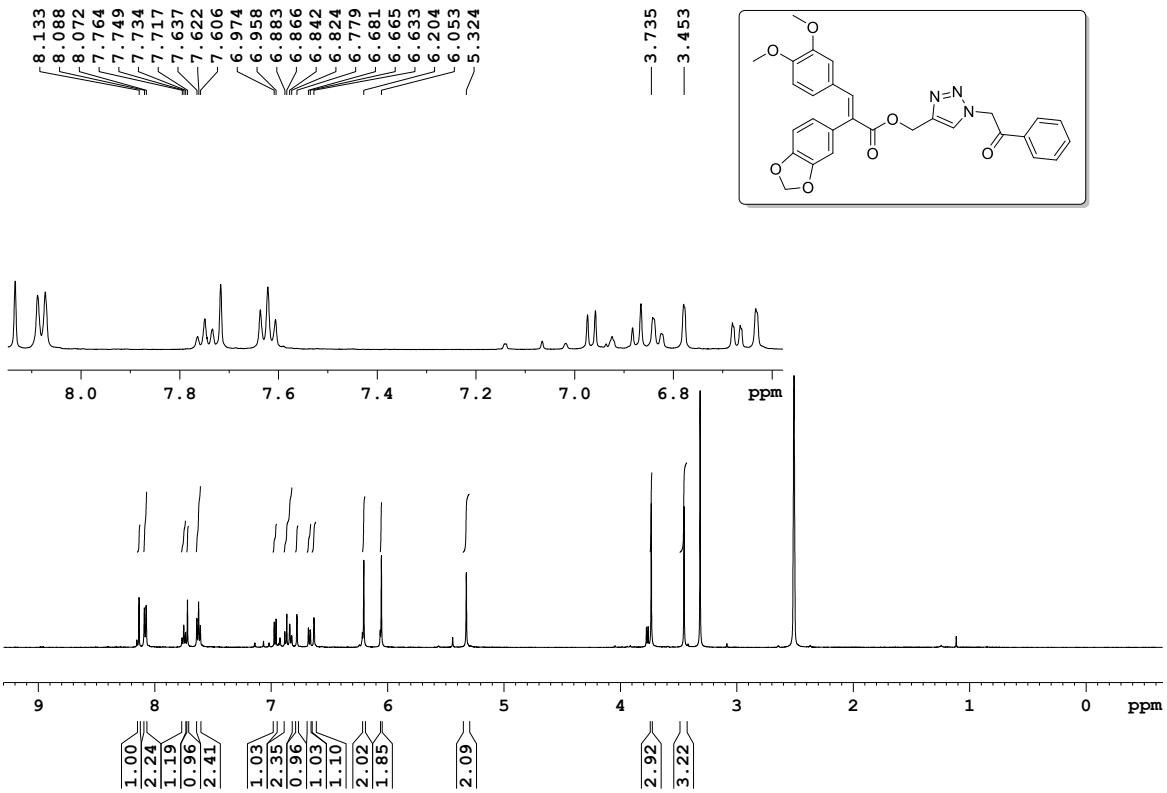
Compound **10e**: ^{13}C NMR (125 MHz, DMSO-d_6)



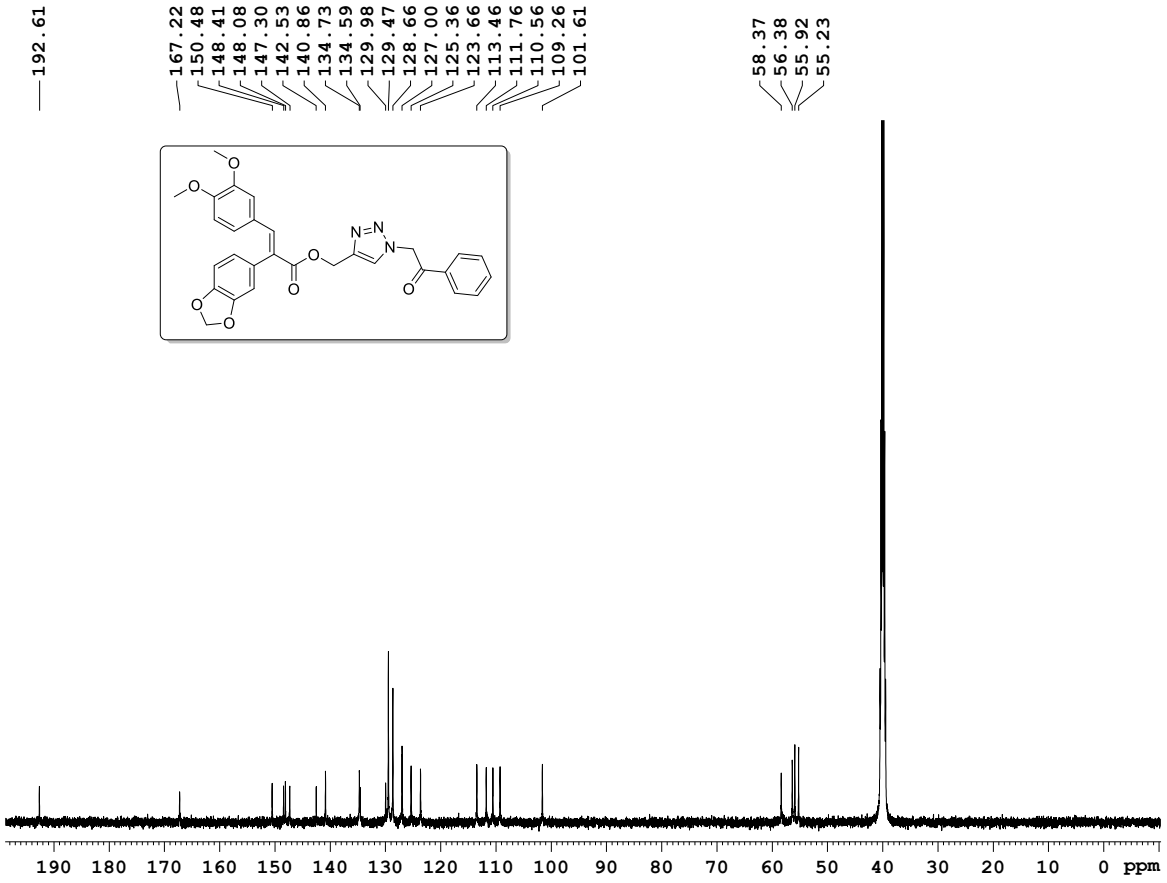
Compound **10f**: ^{1}H NMR (500 MHz, DMSO-d_6)



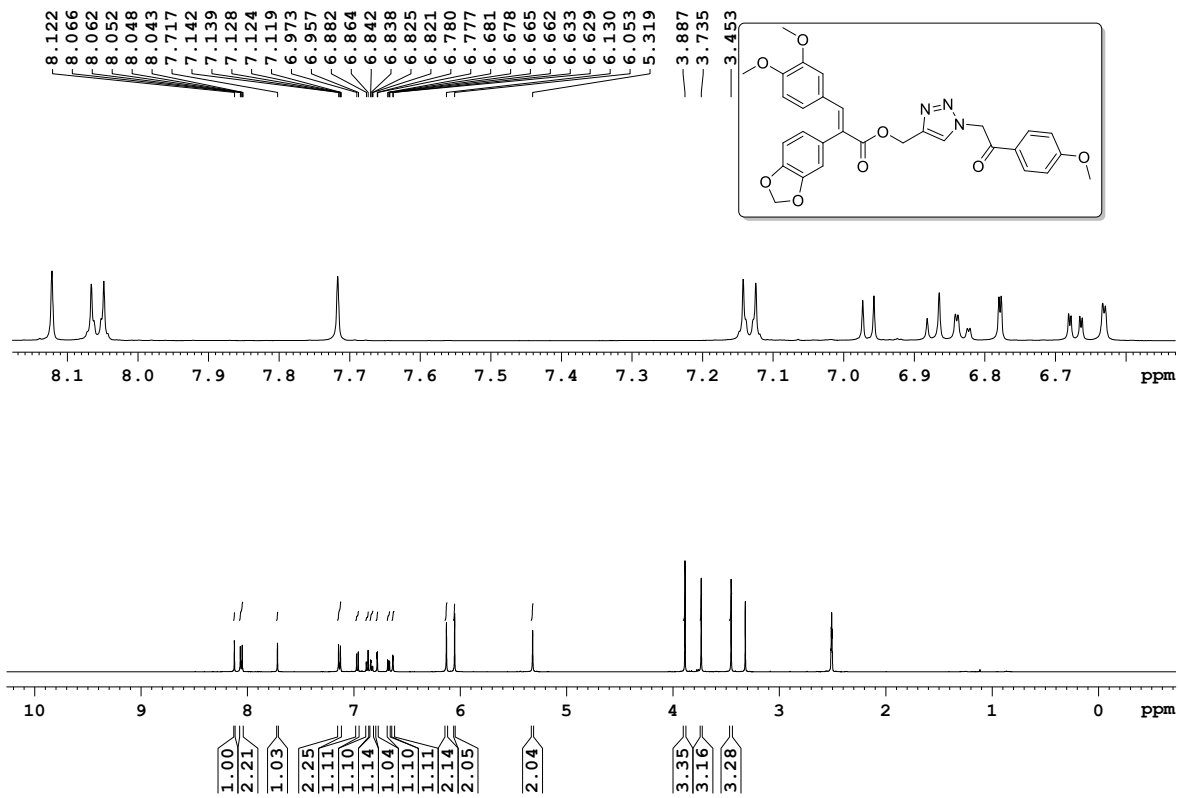
Compound **10f**: ^{13}C NMR (125 MHz, DMSO-d_6)



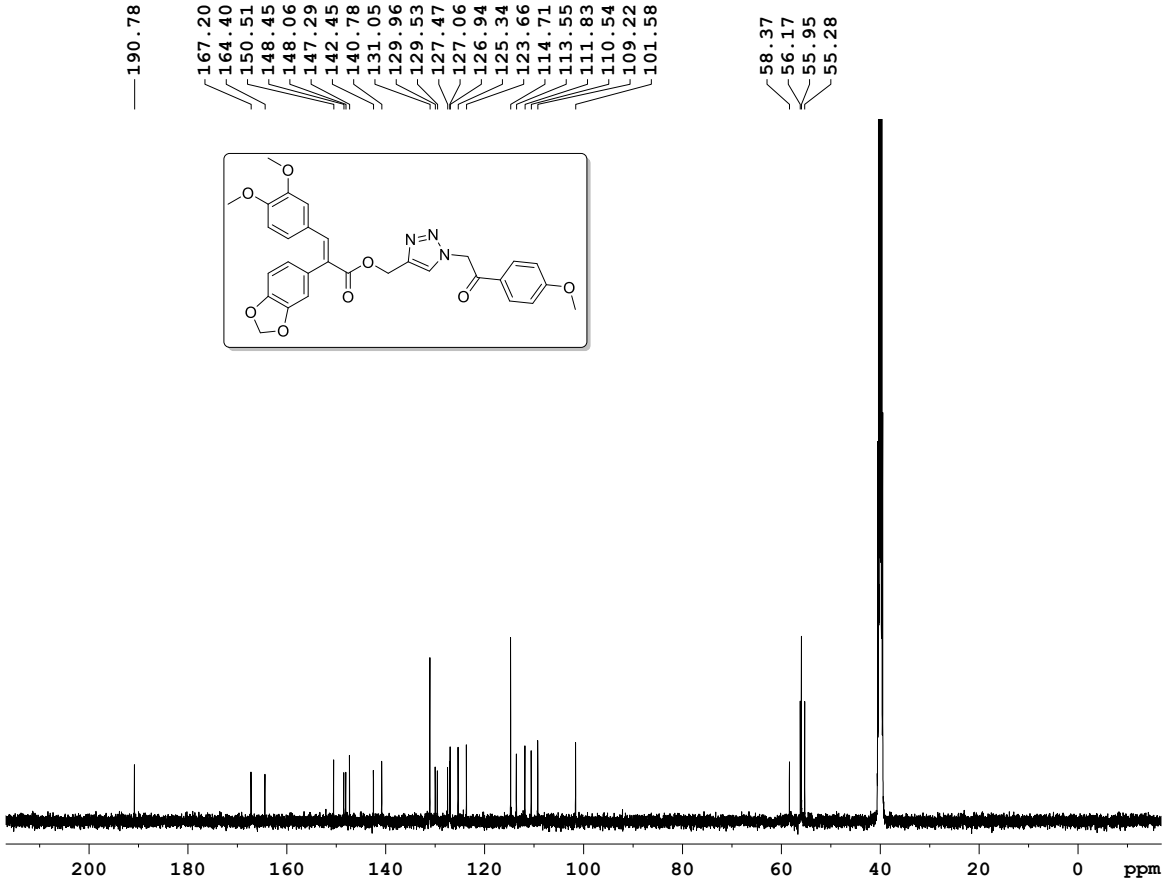
Compound **10g**: ^{1}H NMR (500 MHz, DMSO-d_6)



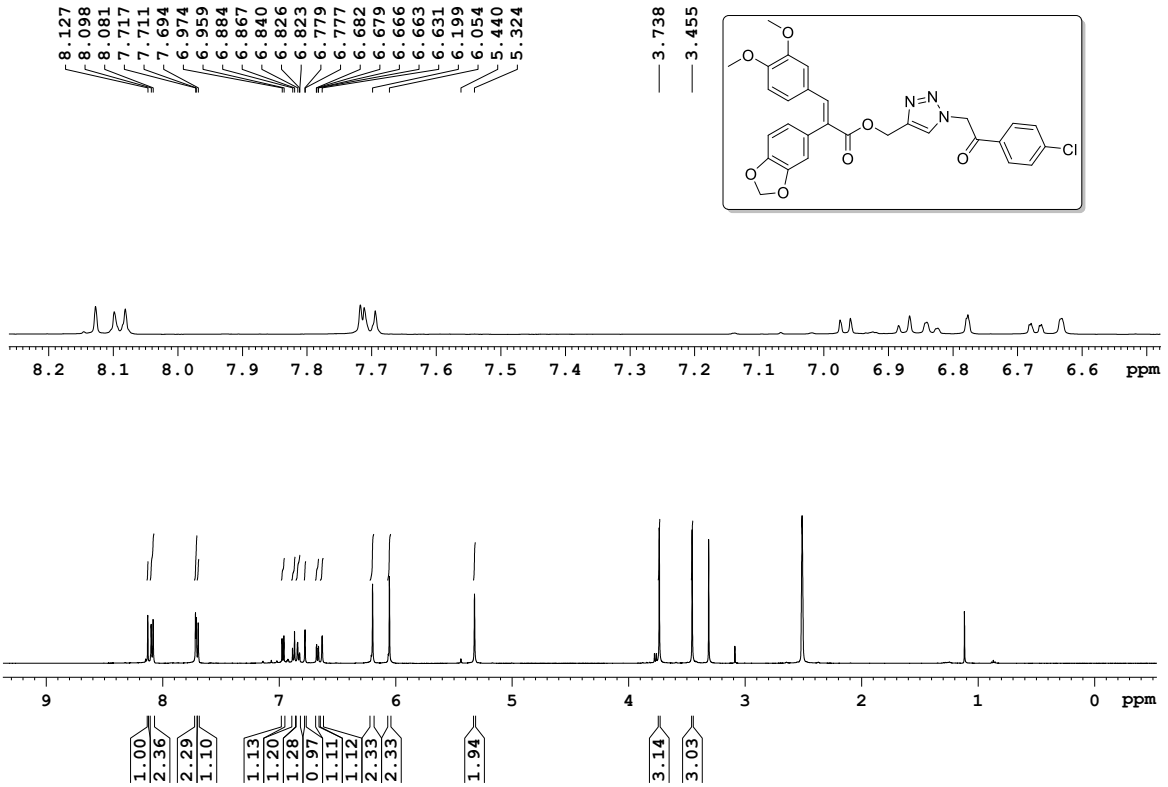
Compound **10g**: ^{13}C NMR (125 MHz, DMSO-d_6)



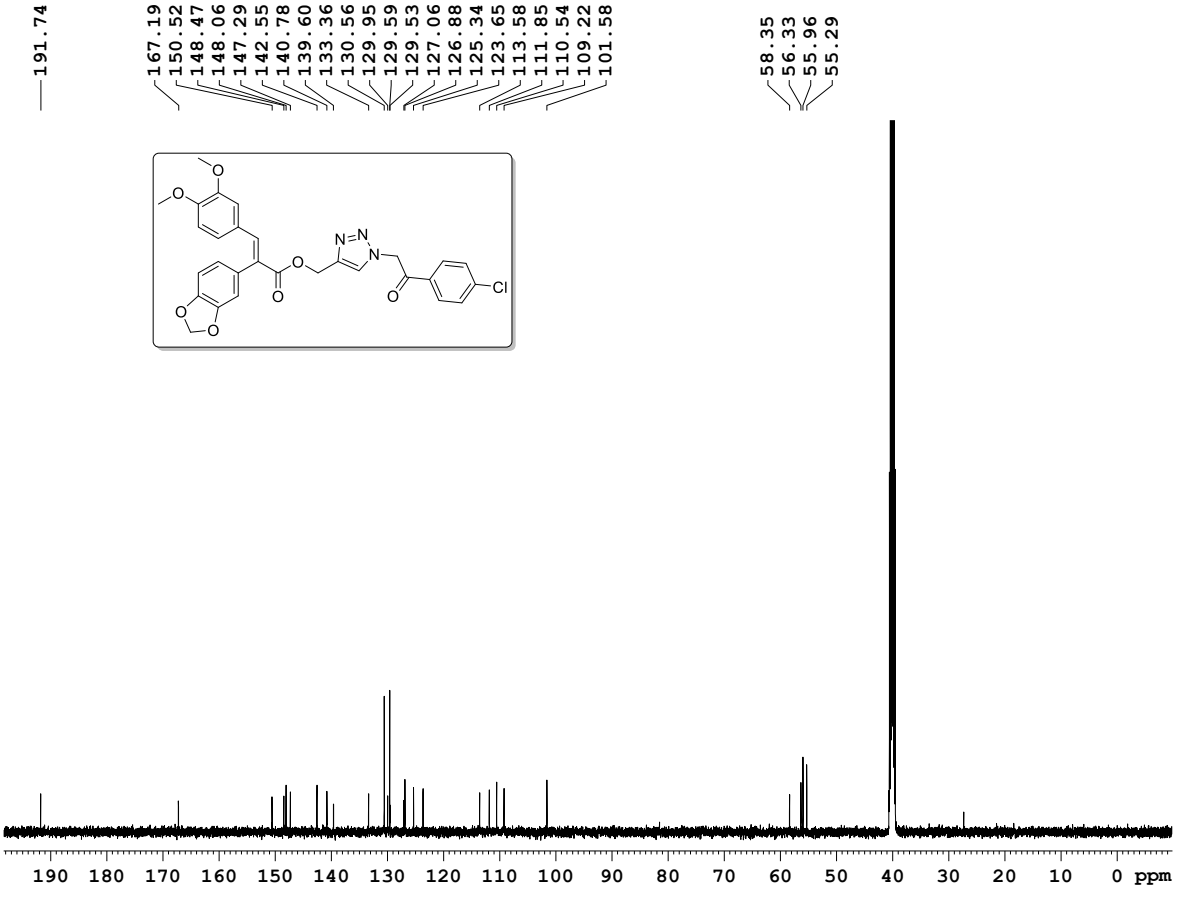
Compound **10h**: ^{1}H NMR (500 MHz, DMSO-d_6)



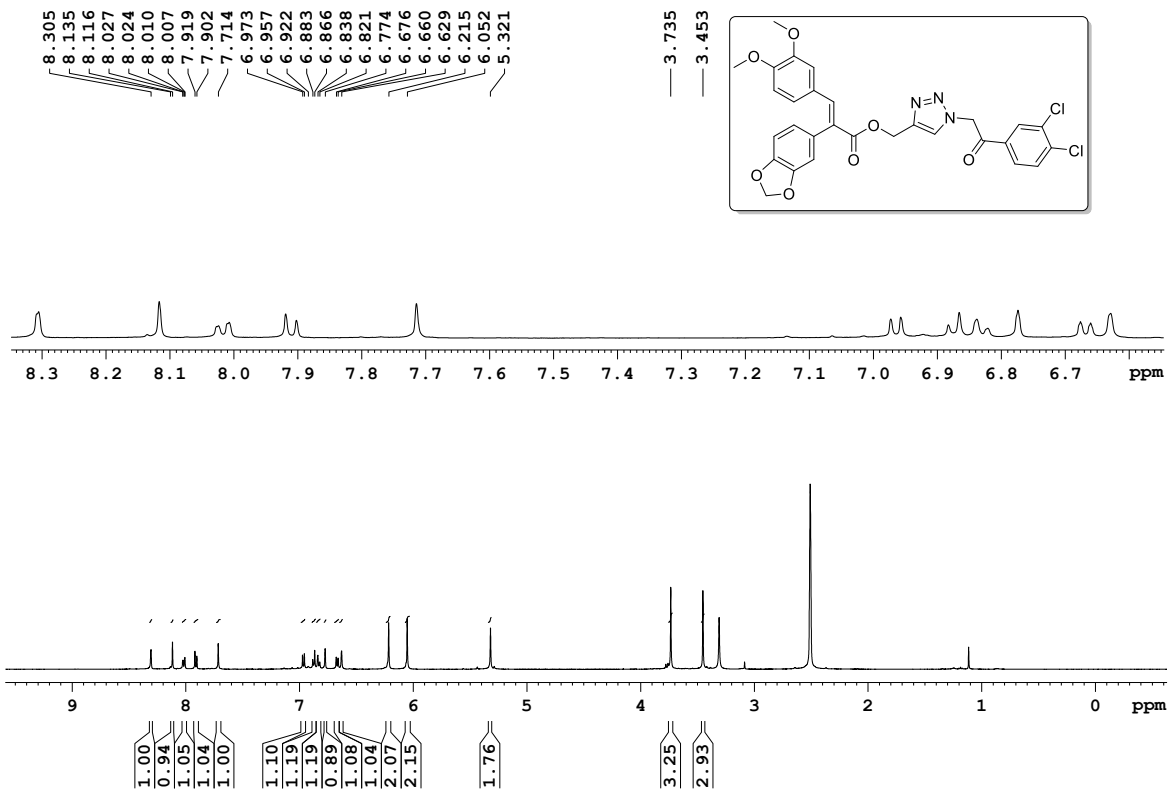
Compound **10h**: ^{13}C NMR (125 MHz, DMSO-d_6)



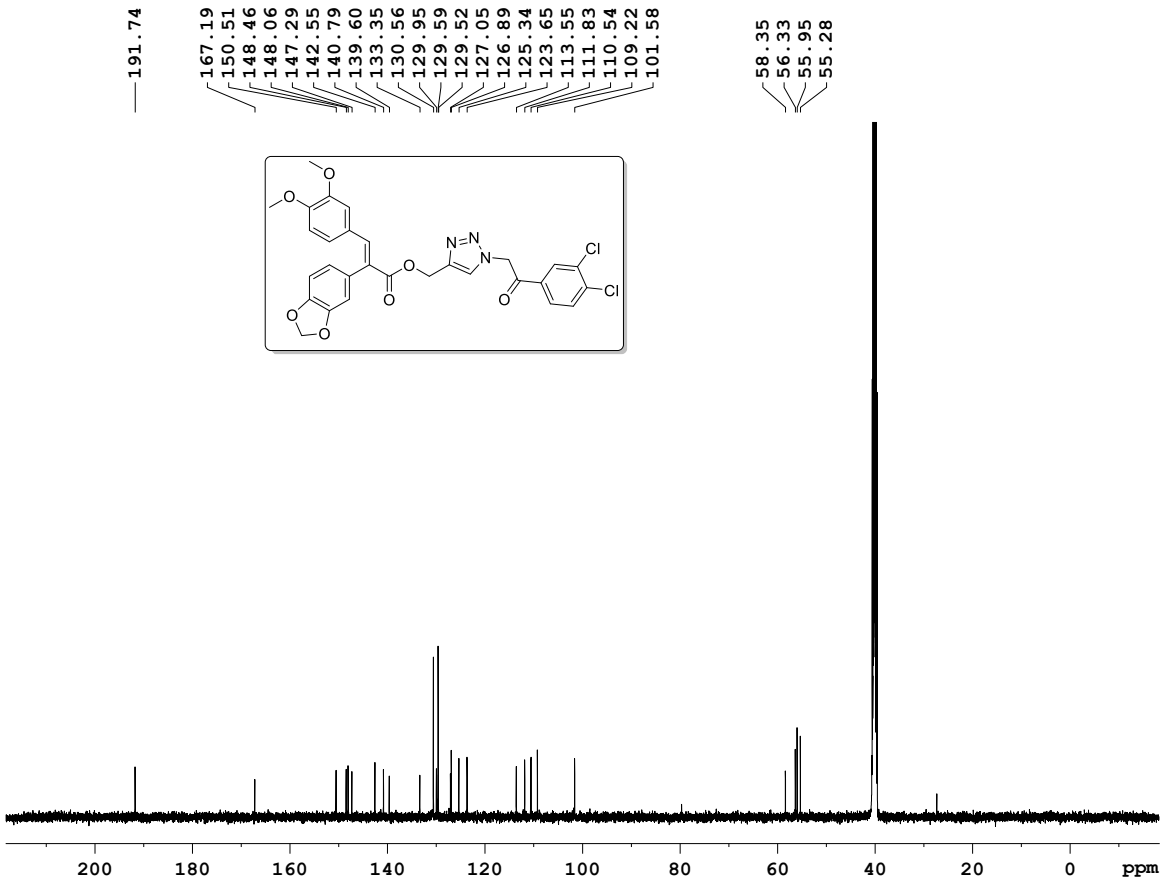
Compound **10i**: ^{1}H NMR (500 MHz, DMSO-d_6)



Compound **10i**: ^{13}C NMR (125 MHz, DMSO-d_6)



Compound **10j**: ^{1}H NMR (500 MHz, DMSO-d_6)



Compound **10j**: ^{13}C NMR (125 MHz, DMSO-d_6)

3. References

1 a) R. A. Maurya, P. R. Adiyala, D. Chandrasekhar, C. N. Reddy, J. S. Kapure, A. Kamal, *ACS Comb. Sci*., 2014, **16**, 466−477. b) B. Prasad, M. Phanindrudu, D. K. Tiwari, J. Org. Chem., 2019, 84, 12334-12343. c) Y. Ju, D. Kumar, R. S. Varma, *J. Org. Chem*., 2006, **71**, 6697-6700.

2 M. Kadagathur, S. Patra, G. Decabattula, J. George, R. Phanindranath, A. S. Shaikh, D. K. Sigalapalli, C. Godugu, N. Nagesh, N. D. Tangellamudi, N. Shankaraiah, *Eur. J. Med. Chem*., 2022, **5**, 114465.

3 K. Munyenyembe, C. Timmons, A. K. M. Weiner, L. A. Katz, Y. Yan, *Eur. J. Protistol*. 2021, **81**, 125840.

4 S. Hamada, S. Fujita, *Histochemistry*, 1983,**79**, 219-226.

5 D. K. Sigalapalli, G. Kiranmai, R. Tokala, C. Tripura, R. Ambatwar, S. N. Nunewar, M. Kadagathur, N. S. Hankaraiah, N. Nagesh, B. N. Babu, N. D. Tangellamusi, *New J. Chem*., 2021, **45**, 18908-18923.

6 S. Kasibhatla, G. P. Amarante-Mendes, D. Finucane, T. Brunner, E. D. Bossy-Wetzel, *CSH Protoc*., 2006, **3**, pdb.prot4493.

7 A. M. Rieger, N. L. Nelson, J. D. Konowalchuk, D. R. Barreda, *J. Vis. Exp*., 2011, **20**, 2597.

8 TACS™ Annexin V-FITC Apoptosis Detection Annexin V Kit (rndsystems.com)

9 S. P. Khathi, B. Chandrasekaran, S. Karunanidhi, C. L. Tham, F. Kozielski, N. Sayyad, R. Karpoormath, *Bioorg. Med. Chem. Lett*., 2018, **28**, 2930-2938.

10 bk011p.pdf (cytoskeleton.com)

11 M. Hasanpourghadi, C. Karthikeyan, A. K. Pandurangan, C. Y. Looi, P. Trivedi, K. Kobayashi, K. Tanaka, W. F. Wong, M. R. Mustafa MR, *J. Ecp. Clin. Cancer Res*., 2016, **35**, 38.

12 M. Chen, X. Lei, C. Shi, M. Huang, X. Li, B. Wu, Z. Li, W. Han, B. Du, J. Hu, Q. Nie, W. Mai, N. Ma, N. Xu, X. Zhang, C. Fan, A. Hong, M. Xia, L. Luo, A. Ma, H. Li, Q. Yu, H. Chen, D. Zhang, W. Ye, *J. Clin. Invest*., 2017, **127**, 3689-3701.