Electronic Supplementary Material (ESI) for Chem Commun.

Supporting Information

Employing a $PhI(OAc)_2$-mediated domino reaction to assemble nitrogen-containing heterocyclic derivatives and assessing their anti-inflammatory activity

Xinyue Li,‡[a] Yuhua Fang,‡[a] Yuanyuan Zhao,[a] Shenshen Luo,[a] Yuhui Xue,[a] Tingting Yong,[a] and Bin Wang*[a,b]

a. College of Chinese Medicine, the First Affiliated Hospital, and Key Laboratory of Xin'an Medicine of the Ministry of Education, Anhui University of Chinese Medicine, Hefei, 230038, P. R. China;

b. Institute of Pharmaceutical Chemistry, Anhui Academy of Chinese Medicine, Hefei, 230038, P. R. China;

Fax: (+86) 551-65169371;

E-mail: bw5654@ahtcm.edu.cn;

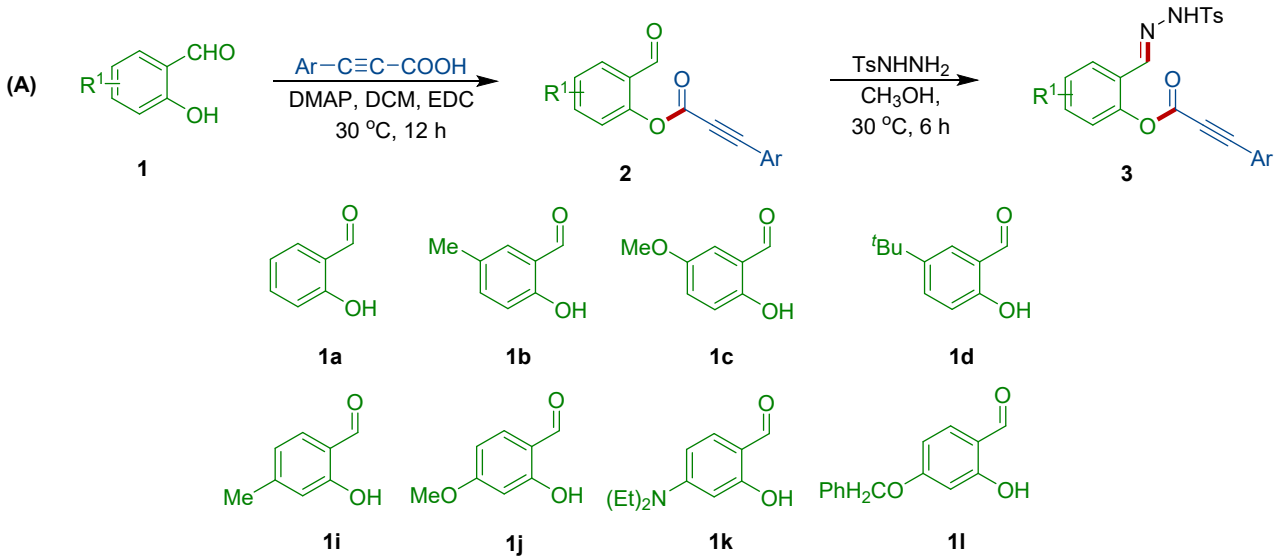
‡ These authors contributed equally.

Contents

1. General remarks

All solvents used were of analytical grade. Unless otherwise specified, all commercially available reagents were used without further purification. Fluorescence spectra in solution were obtained using a Hitachi F-4500 instrument. A JASCO FP-6300 Spectrofluorometer was used to measure fluorescence spectra in the solid state. Absorption spectra in solution were recorded on a PGENERAL TU-1901 UV-VIS Spectrophotometer, while a JASCO V-550 UV/vis Spectrophotometer was used for solid-state absorption measurements. 1H and 13C NMR spectra were recorded on Bruker AC-300 FT (400 MHz and 100 MHz), Agilent VNMRS-600 (600 MHz and 151 MHz), and Bruker-500 MHz (500 MHz and 126 MHz) spectrometers, with tetramethylsilane as the internal reference. Chemical shifts (δ) and coupling constants (J) are reported in ppm and Hz, respectively. High-resolution mass spectra (HRMS) of the products were obtained using a Xevo G2-XS QTOF/MS detector. Melting points were determined on an SGW® X-4B instrument. GC-MS data were measured using a Bruker GC-MS 456-Scion. Column chromatography was generally performed on silica gel (200-300 mesh), and reactions were monitored by thin-layer chromatography (TLC) using silica gel GF254 plates, with UV light used to visualize the progress of the reactions.

2. The Synthesis of starting materials



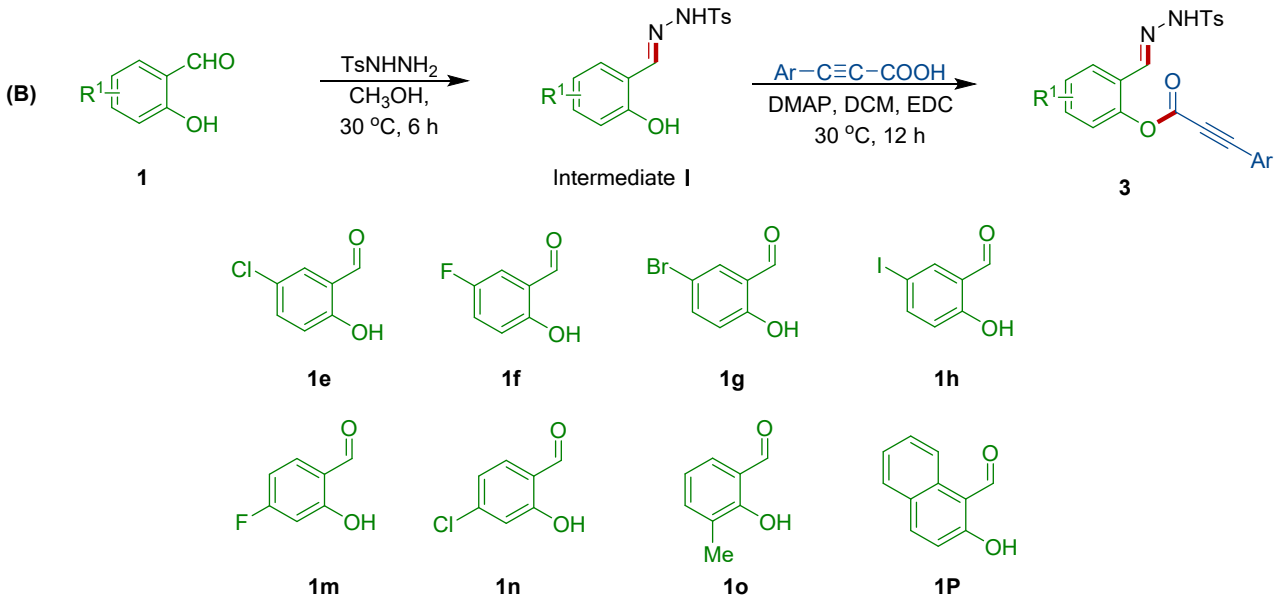
Method A: Synthesis of substrate **3a-3d, 3i-3l** [1-3]

Salicylaldehyde 1**a** (10 mmol, 1066 µL), 3-phenylpropionic acid (10 mmol, 1461 mg), DMAP (0.5 mmol, 61 mg), and 10 mL of anhydrous CH_2Cl_2 were transferred into a Schlenk tube. The reaction mixture was then placed in an ice bath on a magnetic stirrer. Afterward, a solution consisting of 10 mL CH_2Cl_2 containing EDC (5 mmol, 885 mg) was added drop by drop. The resulting solution was allowed to react at 30 °C for a duration of 12 hours, during which it transformed into a clarified solution. Upon completing the reaction period, the mixture was extracted using CH_2Cl_2 and an unsaturated sodium chloride solution. The organic phase was dried over anhydrous Na_2SO_4, and concentrated. The crude product was purified by flash column chromatography using a mixture of petroleum ether and CH_2Cl_2 in a 2:1 ratio to give 283.6 mg (11%) of product **2a** as a white solid. Notably, various other substituted salicylaldehydes (**1b, 1c, 1d, 1i, 1j, 1k,** and **1l**) were subjected to the same methodology to generate analogous products.

Next, in a flask, a *p*-toluenesulfonizide (1.2 mmol, 223.5 mg) solution containing 5 mL of methanol was heated to 60 °C, followed by gradual cooling to reach room temperature. Subsequently, a CH_2Cl_2 solution containing substrate **2a** (1 mmol, 250 mg) was added drop by drop to the above-mentioned solution. The reaction mixture was stirred at 30 °C for 6 hours. Water was added to the mixture, which was extracted with CH_2Cl_2. The organic phase was washed with water, dried over anhydrous Na_2SO_4, and concentrated. The obtained crude product was purified by flash column chromatography using CH_2Cl_2 and ethyl acetate in a 100:1 ratio to give 345.7 mg (83%) of product **3a** as a white solid.

This synthesis methodology was further applied to synthesizing other substrates ((**3b**, **3c**, **3d**, **3i**, **3j**, **3k**, and **3l**)) with analogous reactions ensuing.

Method B: Synthesis of substrate **3e-3h，3m-3p** [4-6]

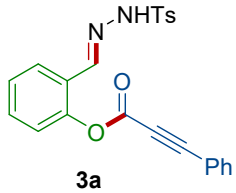


In a flask, a *p*-toluenesulfonizide (1.2 mmol, 223.5 mg) solution containing 5 mL of methanol was heated to 60 °C, followed by gradual cooling to reach room temperature. Subsequently, a CH_2Cl_2 solution containing substrate Salicylaldehyde 1**a** (10 mmol, 1066 μL) was meticulously added drop by drop to the above-mentioned solution. The reaction mixture was stirred at 30 °C for 6 hours. Water was added to the mixture, which was extracted with CH_2Cl_2. The organic phase was washed with water, dried over anhydrous Na_2SO_4, and concentrated. The obtained crude product was purified by flash column chromatography using CH_2Cl_2 and ethyl acetate in a 100:1 ratio to give 345.7 mg (83%) of intermediate **Ie** as a white solid.

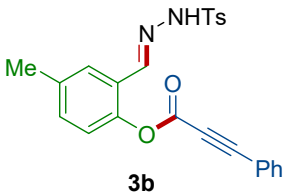
Next, intermediate **Ie** (10 mmol)**,** 3-phenylpropionic acid (10 mmol, 1461.4 mg), DMAP (0.5 mmol, 61 mg), and 10 mL of anhydrous CH_2Cl_2 were transferred into a Schlenk tube. The reaction mixture was then placed in an ice bath on a magnetic stirrer. Afterward, a solution consisting of 10 mL CH_2Cl_2 containing EDC (5 mmol, 885 mg) was added drop by drop. The resulting solution was allowed to react at 30 °C for a duration of 12 hours, during which it transformed into a clarified solution. Upon completing the reaction period, the mixture was extracted using CH_2Cl_2 and an unsaturated sodium chloride solution. The organic phase was dried over anhydrous Na_2SO_4, and concentrated. The obtained crude product was purified by flash column chromatography using a mixture of petroleum ether and CH_2Cl_2 in a 2:1 ratio to give 284 mg (83%) of product **3e** as a white solid.

Notably, many other substituted salicylaldehydes (**1b-n**) were subjected to the same methodology to generate analogous products. This methodology was further applied to synthesizing other substrates (**3b-n**) with analogous reactions.

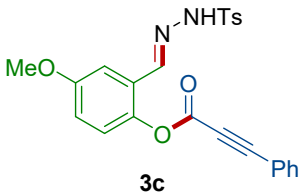
3. Substrate characterization



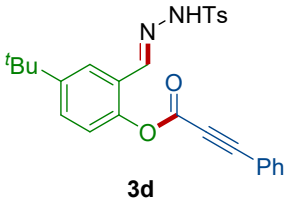
3a



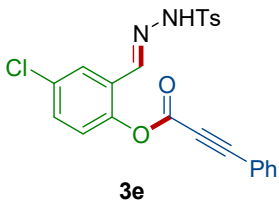
3b



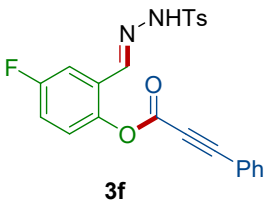
3c



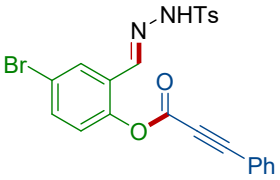
3d



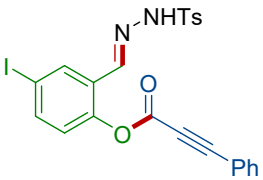
3e



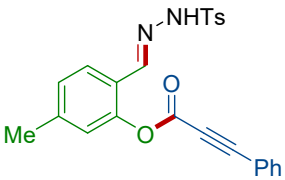
3f



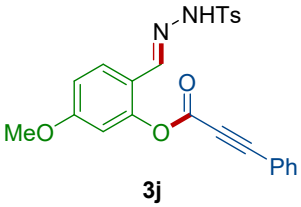
3g



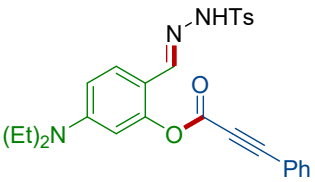
3h



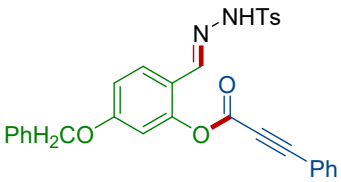
3i



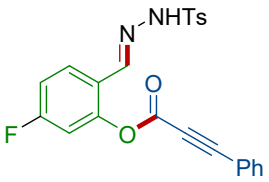
3j



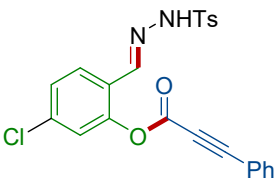
3k



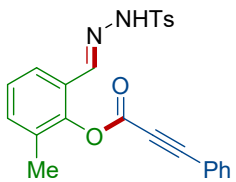
3l



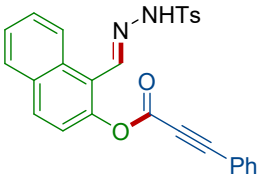
3m



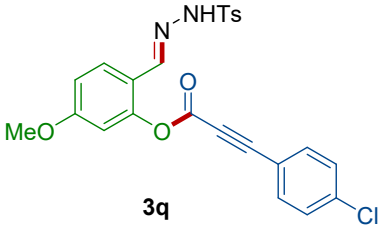
3n



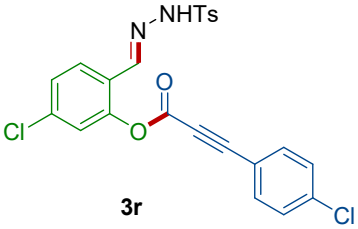
3o



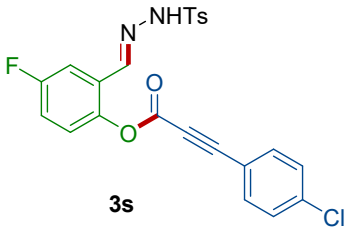
3p



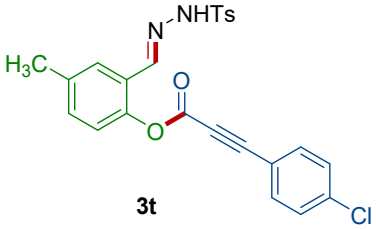
3q



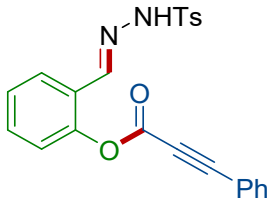
3r



3s



3t



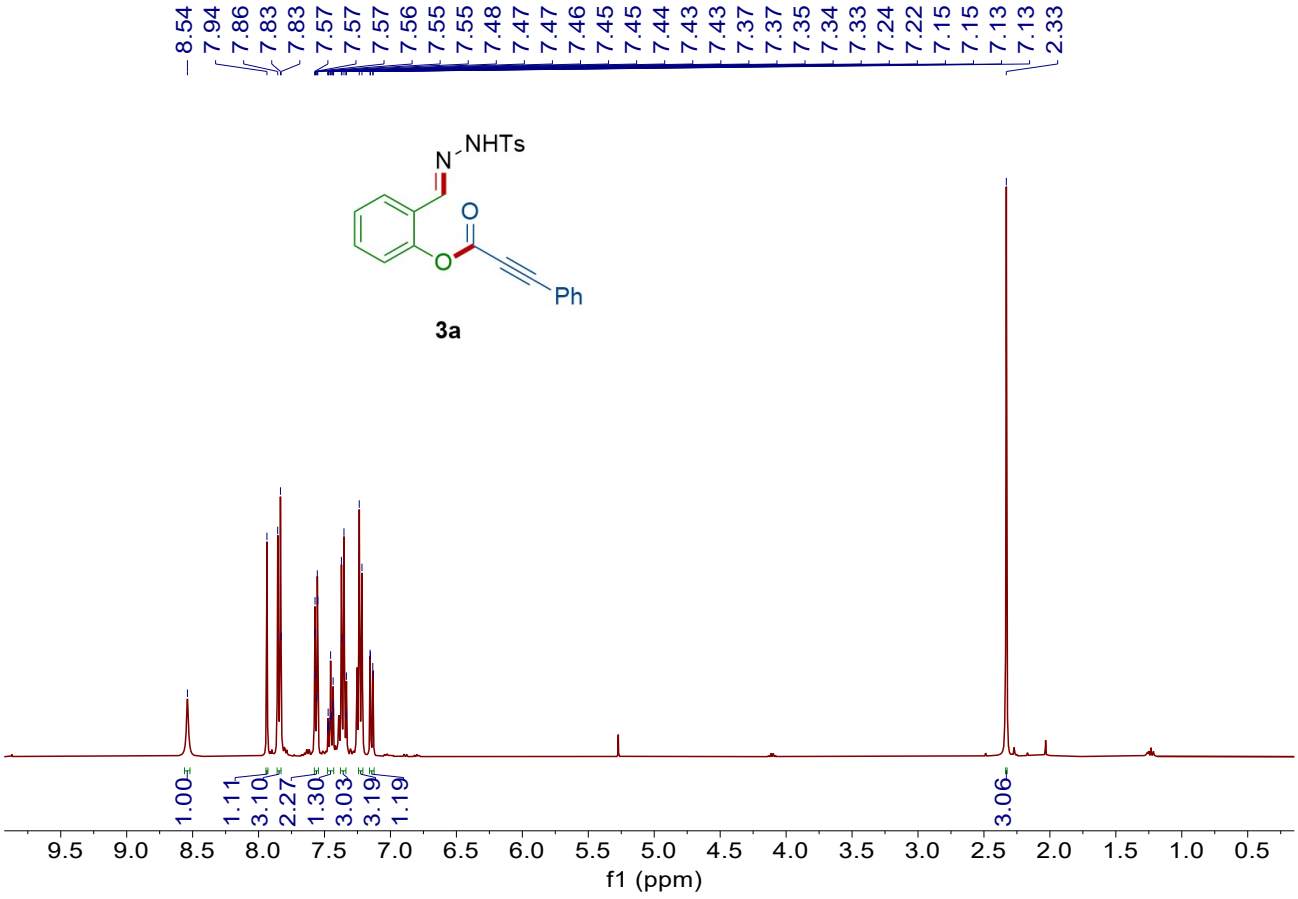
(E)-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3a)**.

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 92% yield;

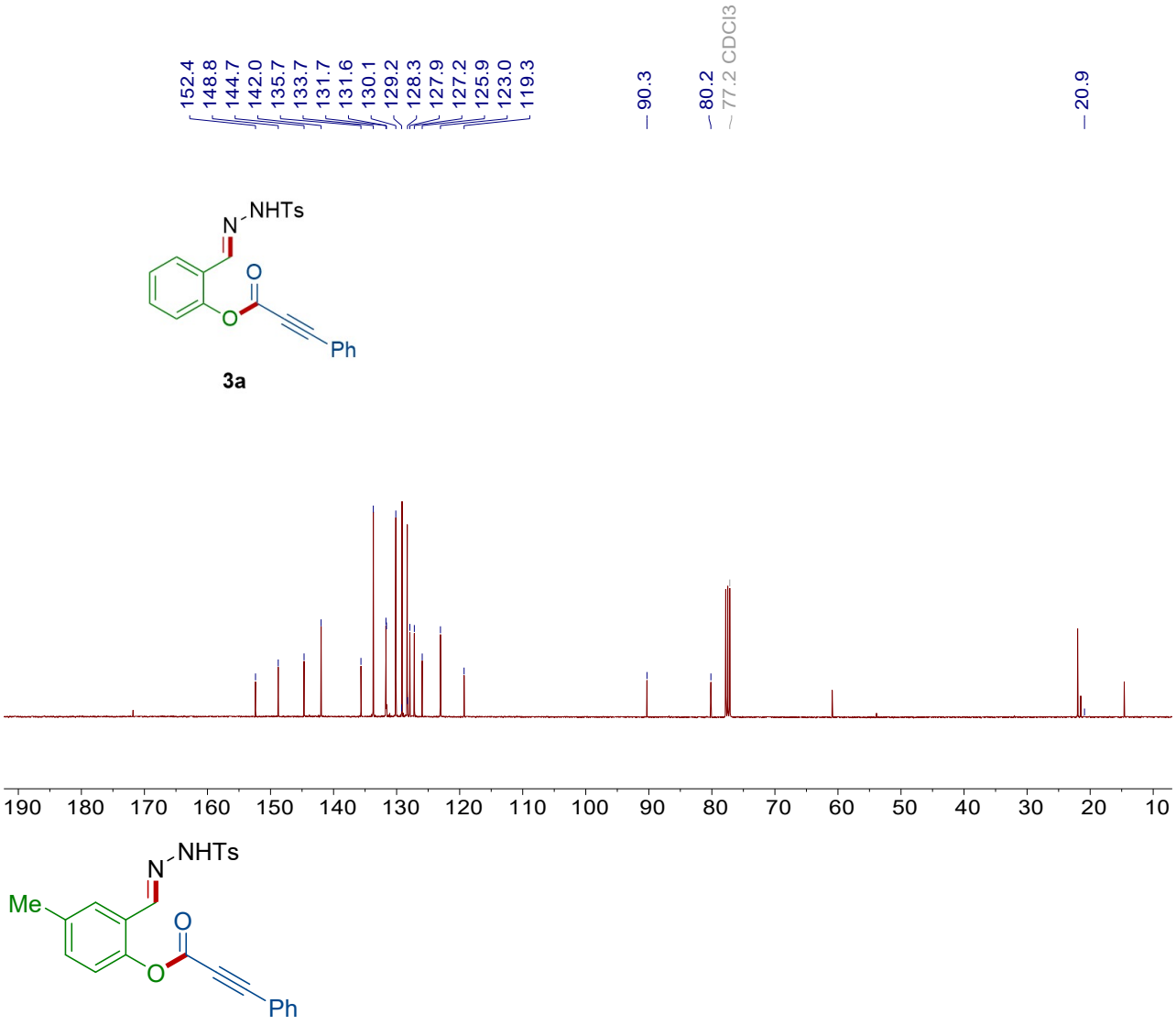
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 (s, 1H), 7.98 (s, 1H), 7.93 – 7.86 (m, 3H), 7.67 – 7.60 (m, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 3H), 7.30 (t, *J* = 7.4 Hz, 3H), 7.20 (d, *J* = 8.2 Hz, 1H), 2.40 (s, 3H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.4, 148.8, 144.7, 142.0, 135.7, 133.7, 131.7, 131.6, 130.1, 127.9, 127.2, 125.9, 123.1, 119.3, 90.3, 80.2.

^{1}H NMR spectrum of **3a** ($CDCl_3$, 400 MHz)



^{13}C NMR spectrum of **3a** ($CDCl_3$, 101 MHz)



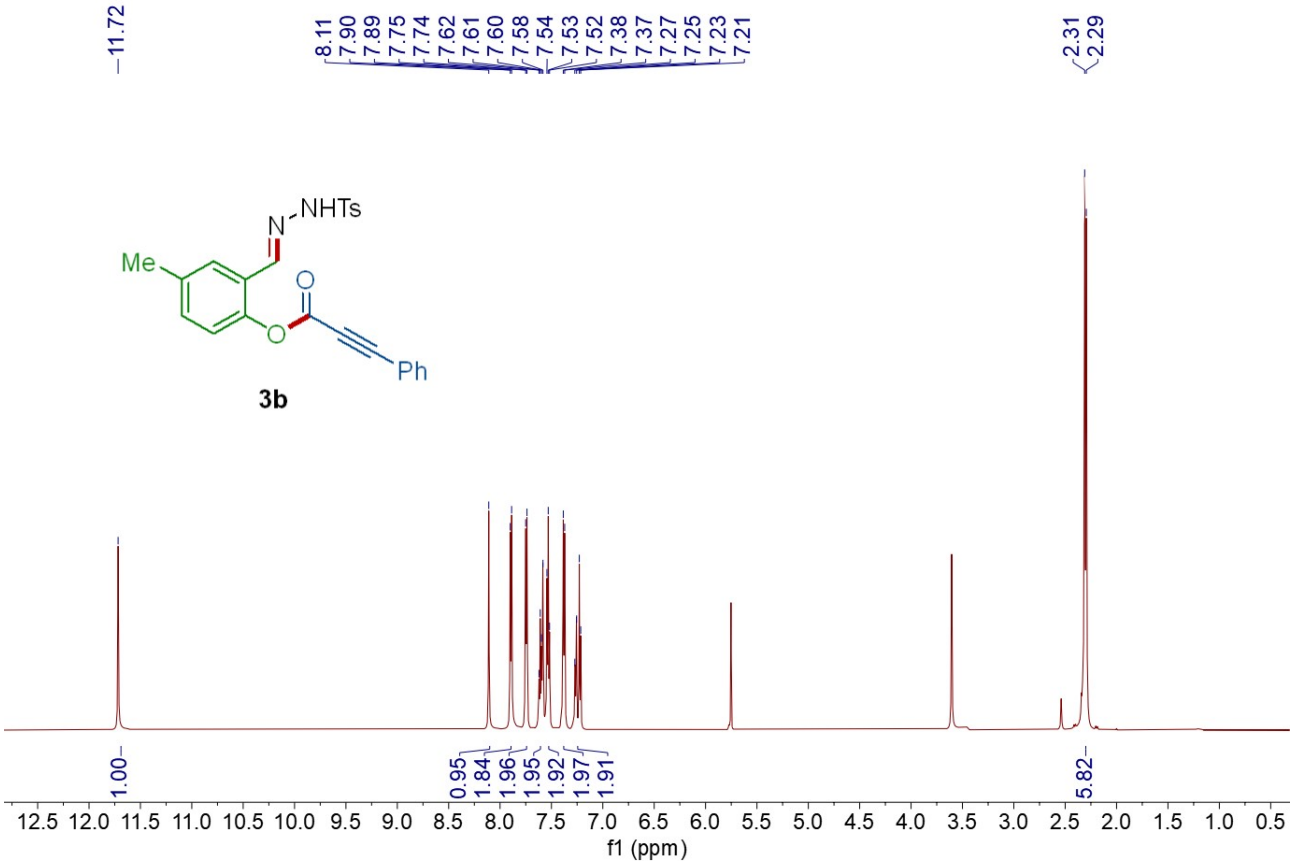
(E)-4-methyl-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3b)**.

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 80% yield;

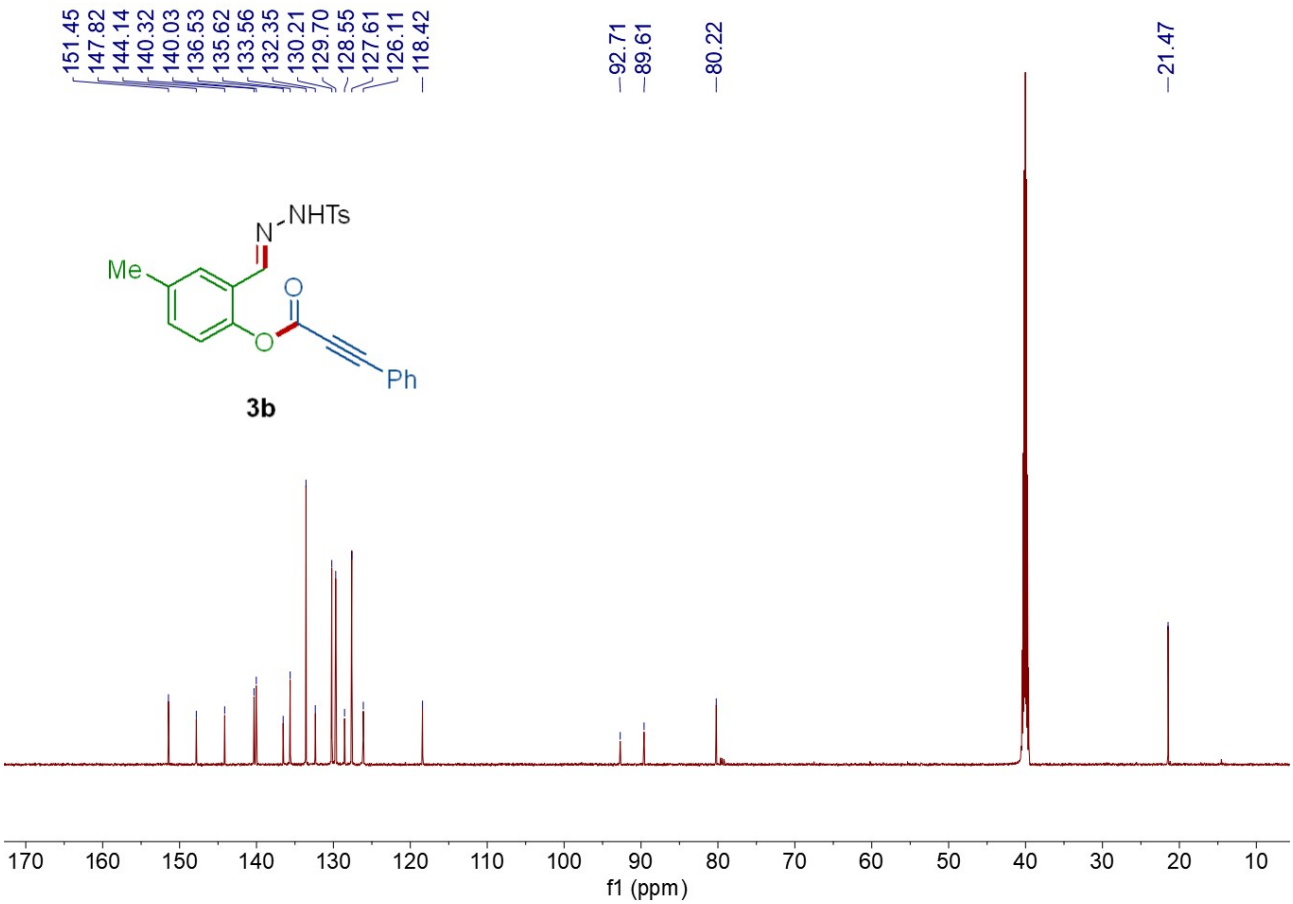
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.72 (s, 1H), 8.11 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.74 (d, *J* = 7.7 Hz, 2H), 7.60 (dd, *J* = 15.4, 7.9 Hz, 2H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.30 – 7.19 (m, 2H), 2.30 (d, *J* = 9.5 Hz, 6H);

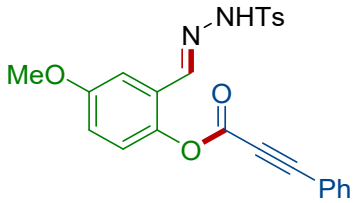
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.5, 147.8, 144.1, 140.3, 140.0, 136.5, 135.6, 133.6, 132.4, 130.2, 129.7, 128.6, 127.6, 126.1, 118.4, 92.7, 89.6, 80.2, 21.5.

^{1}H NMR spectrum of **3b** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3b** (DMSO-d_6, 151 MHz)





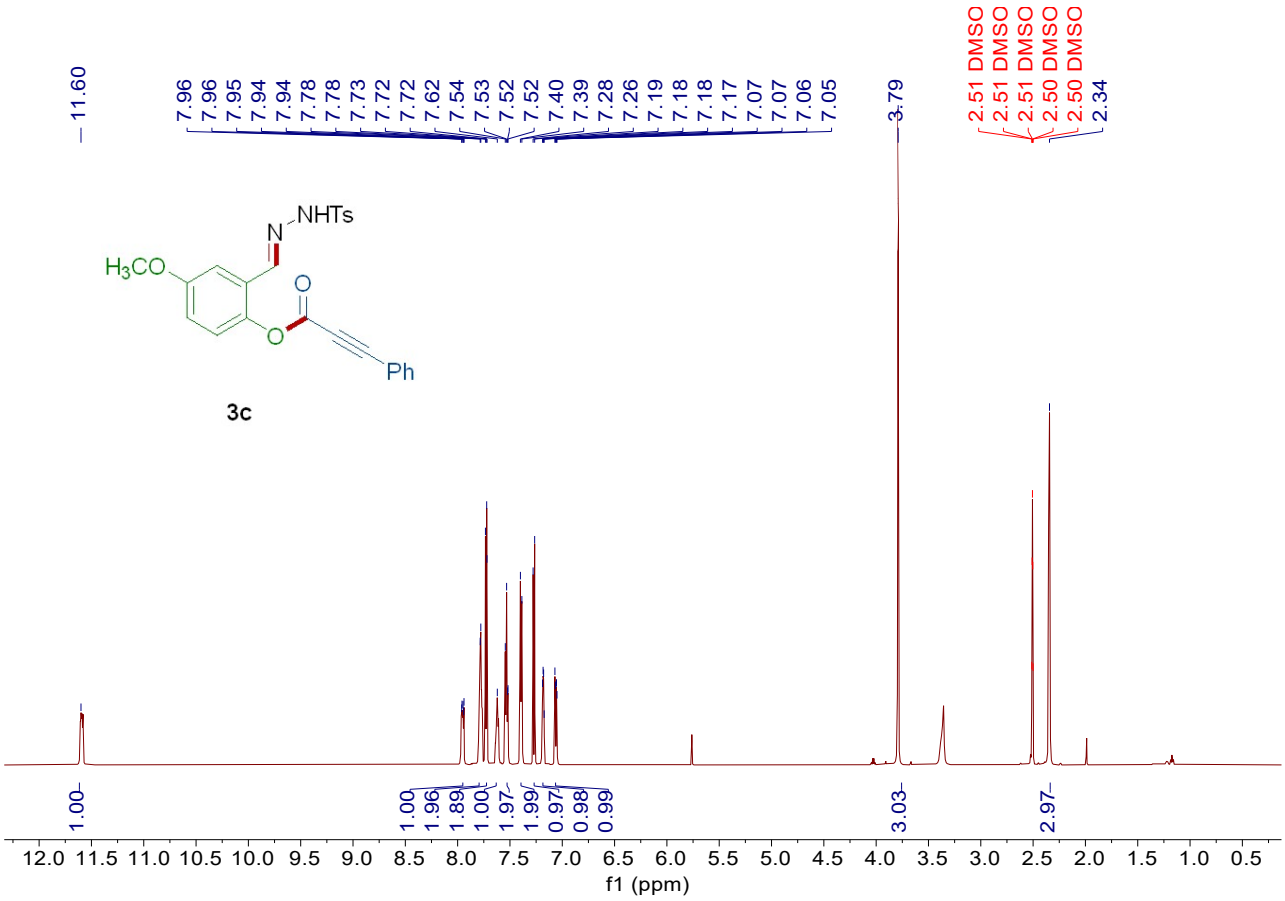
(E)-4-methoxy-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3c).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 85% yield;

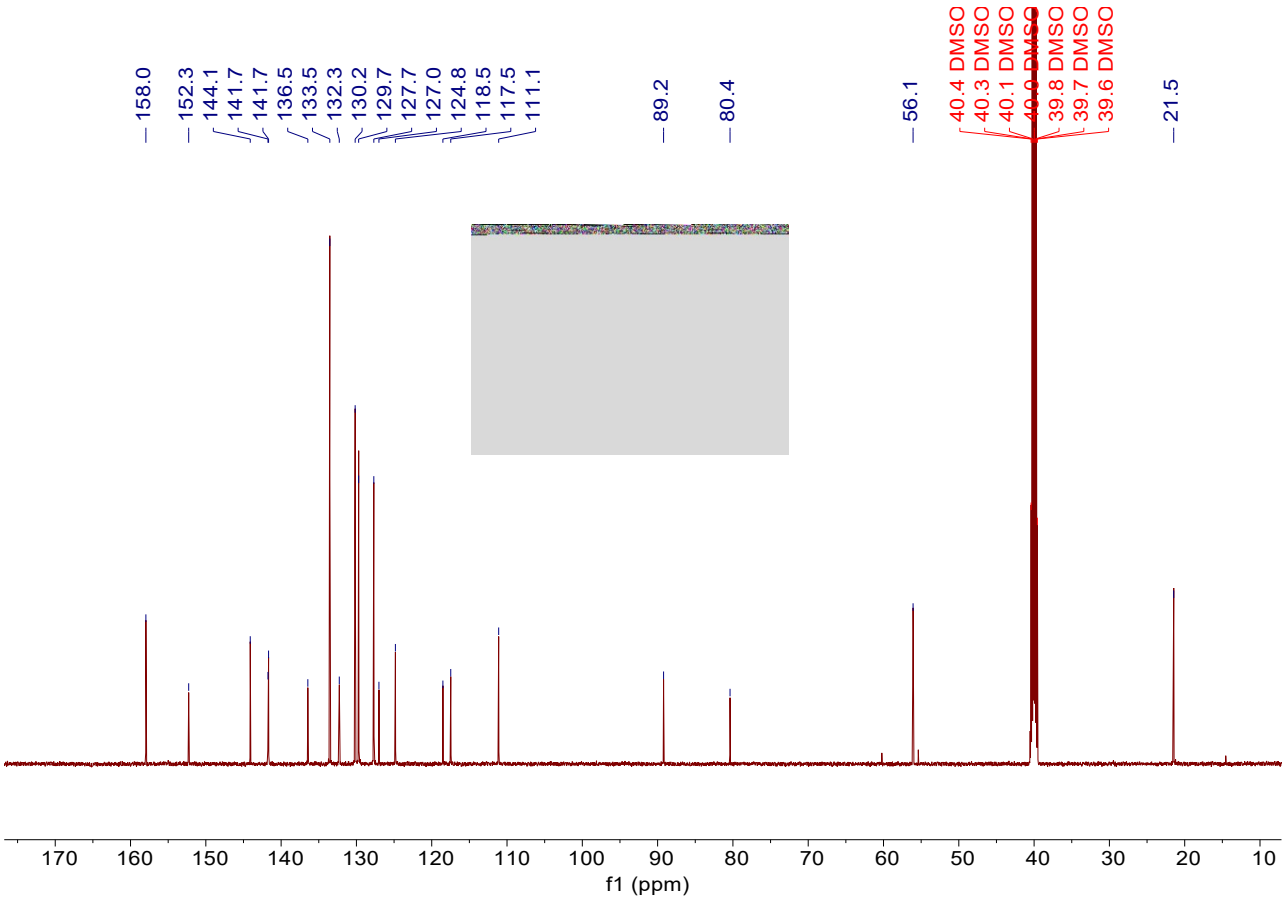
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.60 (s, 1H), 7.99 – 7.91 (m, 1H), 7.78 (s, 2H), 7.73 (d, *J* = 8.8 Hz, 2H), 7.62 (s, 1H), 7.53 (t, *J* = 6.6 Hz, 2H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.27 (d, *J* = 8.9 Hz, 1H), 7.18 (d, *J* = 3.0 Hz, 1H), 7.06 (dd, *J* = 9.0, 2.8 Hz, 1H), 3.79 (s, 3H), 2.34 (s, 3H);

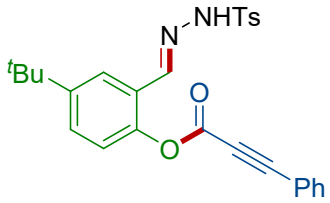
^{13}C NMR (151 MHz, DMSO-d_6) δ 158.0, 152.3, 144.1, 141.8, 141.7, 136.5, 133.5, 132.3, 130.2, 129.7, 127.7, 127.0, 124.8, 118.5, 117.5, 111.1, 89.2, 80.4, 56.1, 21.5.

^{1}H NMR spectrum of **3c** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3c** (DMSO-d_6, 151 MHz)





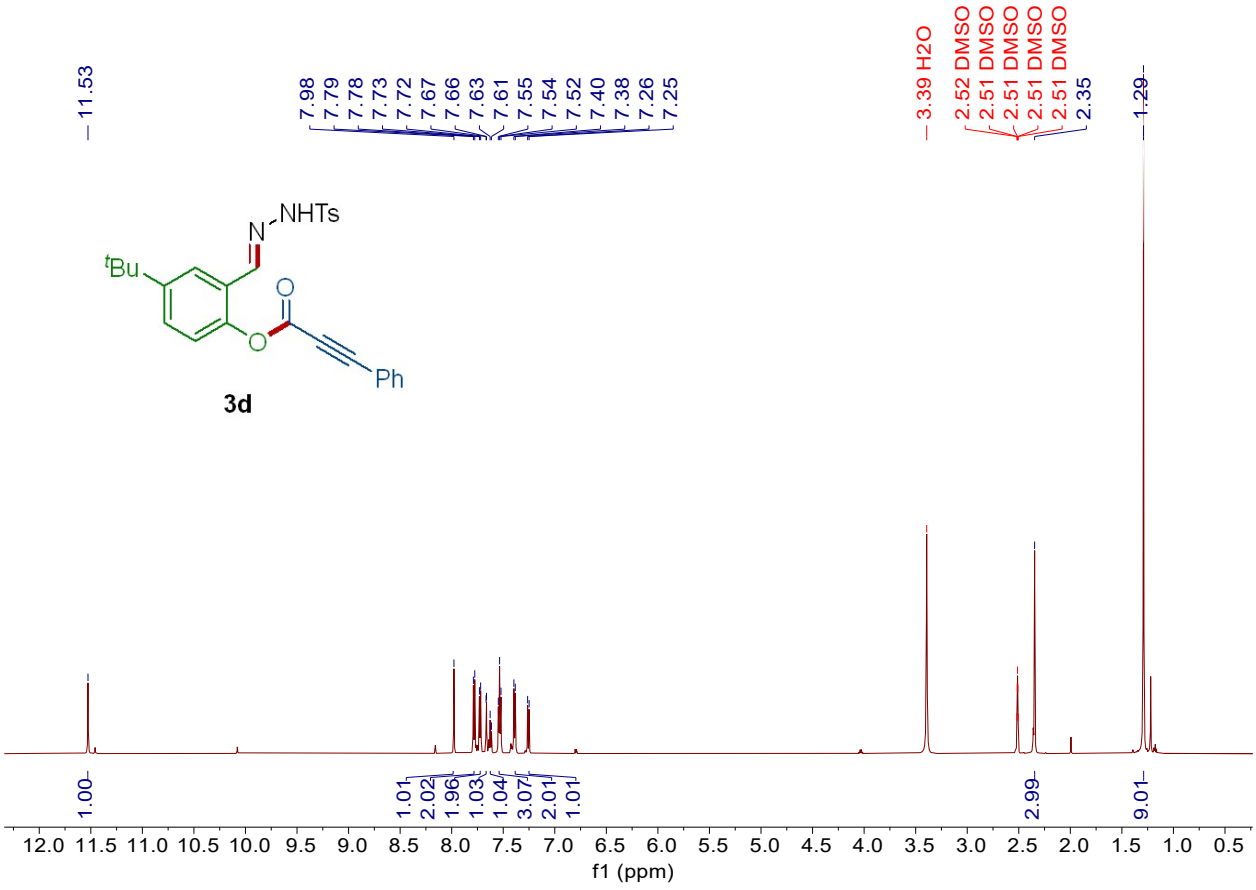
(E)-4-(tert-butyl)-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3d).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 87% yield;

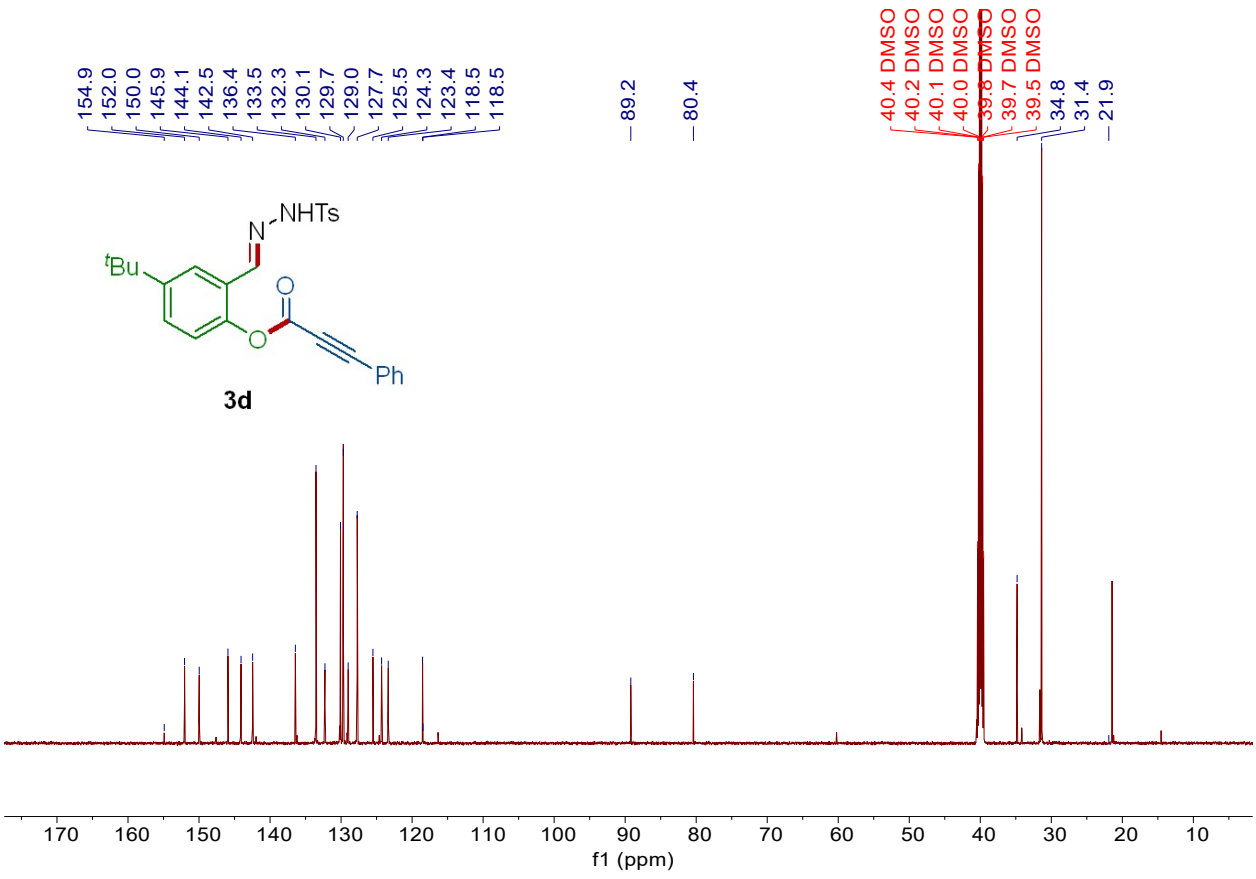
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.53 (s, 1H), 7.98 (s, 1H), 7.78 (d, *J* = 6.2 Hz, 2H), 7.72 (d, *J* = 8.7 Hz, 2H), 7.66 (d, *J* = 2.5 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 3H), 7.39 (d, *J* = 8.1 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 1H), 2.35 (s, 3H), 1.29 (s, 9H);

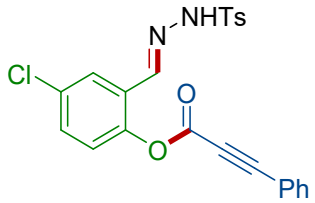
^{13}C NMR (151 MHz, DMSO-d_6) δ 152.0, 150.0, 145.9, 144.1, 142.5, 136.4, 133.5, 132.3, 130.2, 130.1, 129.7, 129.0, 127.7, 125.5, 124.3, 123.4, 118.5, 89.2, 80.4, 34.8, 31.4, 21.5.

^{1}H NMR spectrum of **3d** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3d** (DMSO-d_6, 151 MHz)





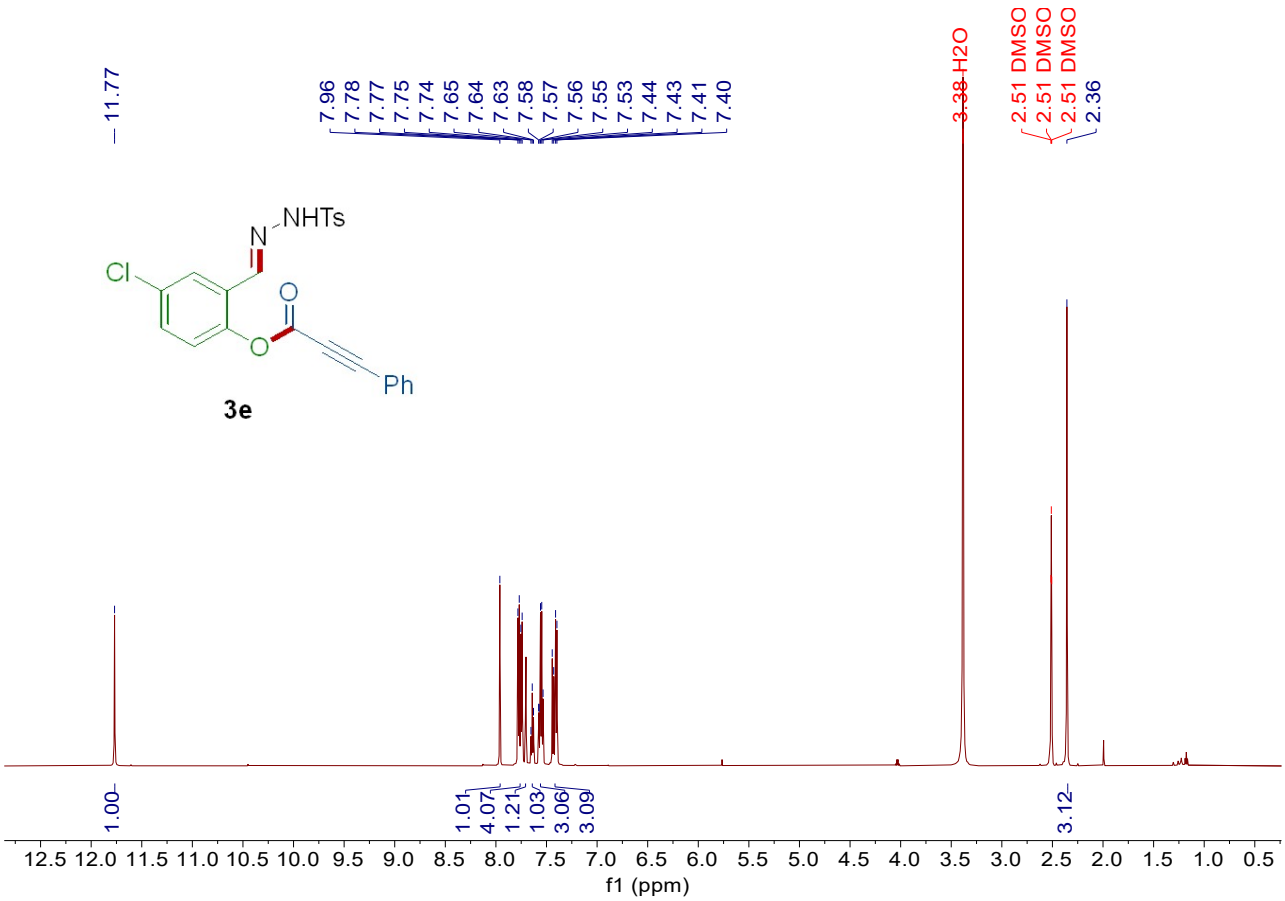
(E)-4-chloro-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3e).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 40% yield;

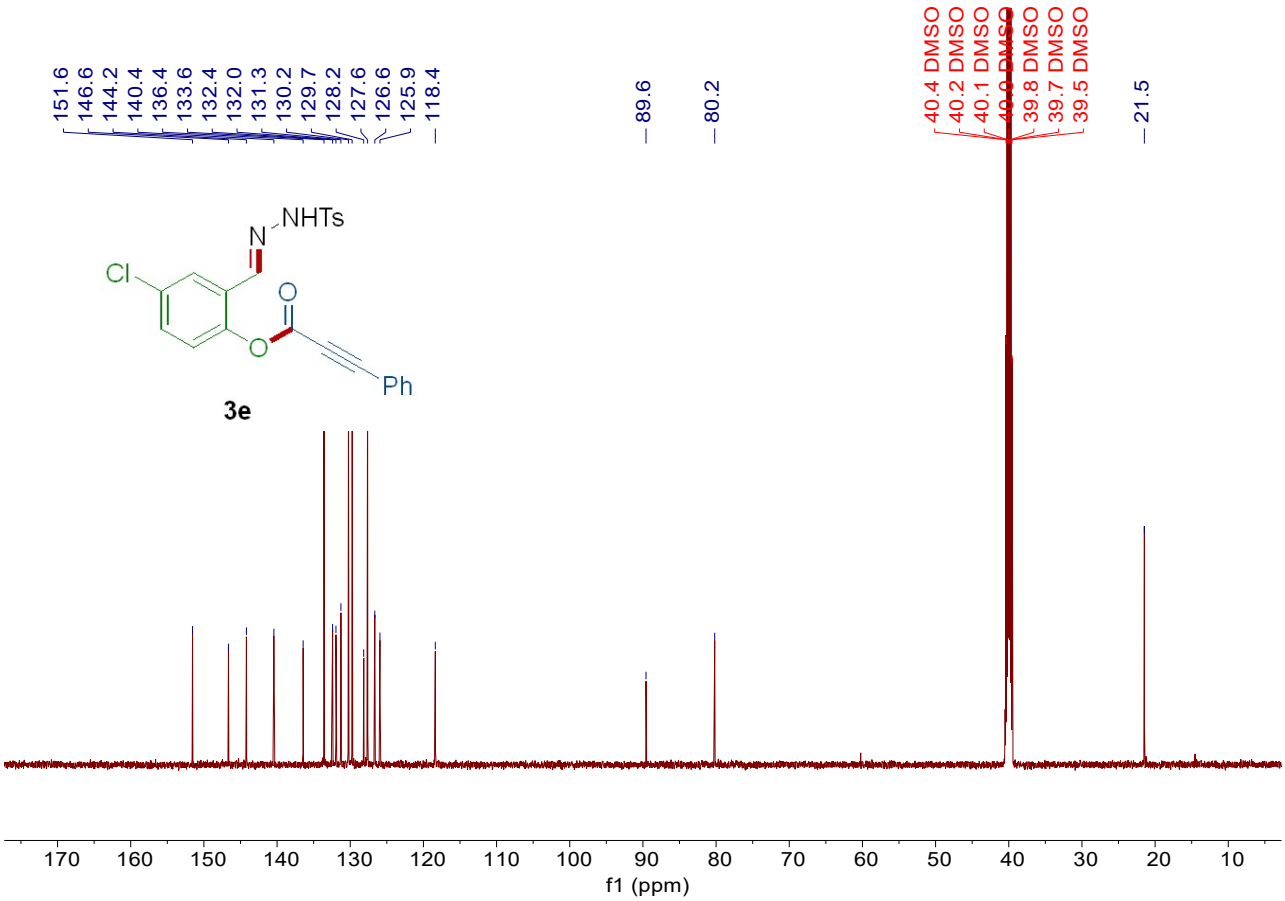
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.77 (s, 1H), 7.96 (s, 1H), 7.76 (dd, *J* = 17.4, 7.8 Hz, 4H), 7.70 (d, *J* = 2.6 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.59 – 7.52 (m, 3H), 7.42 (dd, *J* = 19.5, 8.4 Hz, 3H), 2.36 (s, 3H).

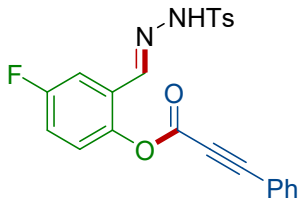
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.6, 146.6, 144.2, 140.4, 136.4, 133.6, 132.4, 132.0, 131.3, 130.2, 129.7, 128.2, 127.6, 126.6, 125.9, 118.4, 89.6, 80.2, 21.5.

^{1}H NMR spectrum of **3e** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3e** (DMSO-d_6, 151 MHz)





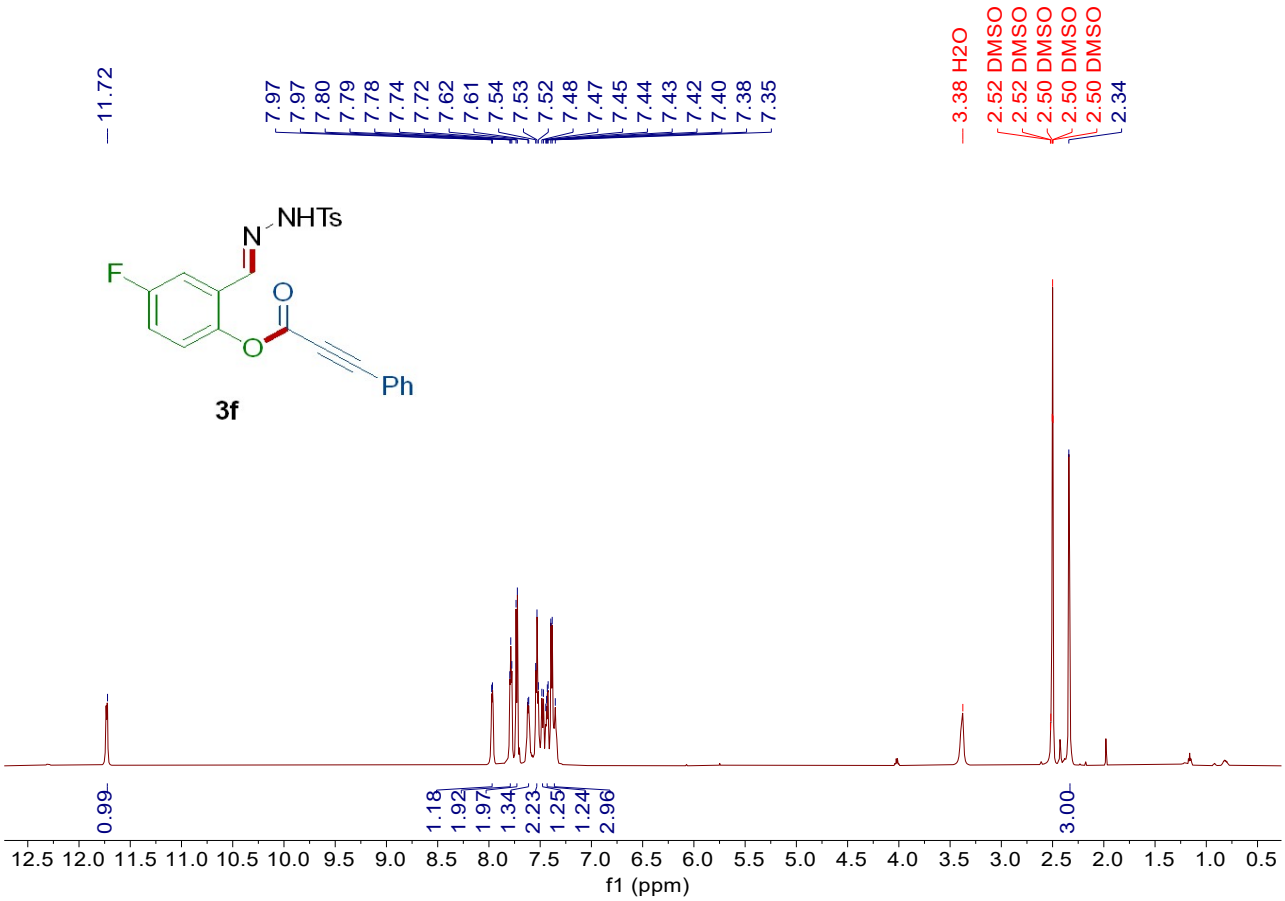
(E)-4-fluoro-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3f).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a faint yellow solid: 35% yield;

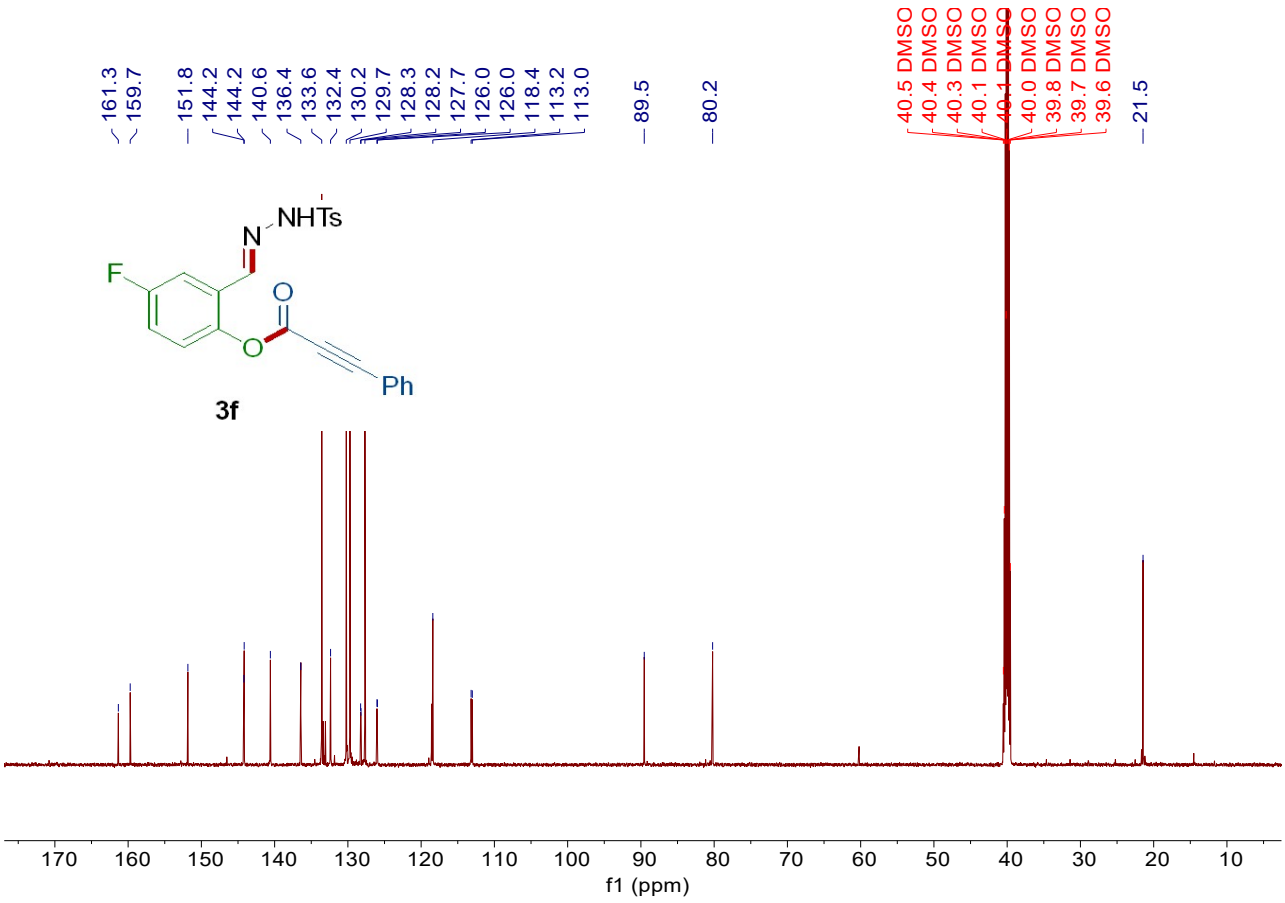
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.72 (s, 1H), 7.97 (d, *J* = 4.7 Hz, 1H), 7.82 – 7.76 (m, 2H), 7.73 (d, *J* = 7.7 Hz, 2H), 7.62 (d, *J* = 7.0 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.48 (d, *J* = 9.3 Hz, 1H), 7.43 (dd, *J* = 9.0, 4.7 Hz, 1H), 7.41 – 7.31 (m, 3H), 2.34 (s, 3H).

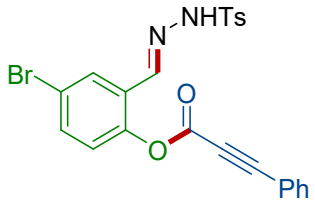
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.8, 144.2, 144.2, 140.6, 136.4, 133.6, 132.4, 130.2, 129.7, 127.7, 118.6, 118.4, 113.2, 113.0, 89.5, 80.2, 21.5.

^{1}H NMR spectrum of **3f** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3f** (DMSO-d_6, 151 MHz)





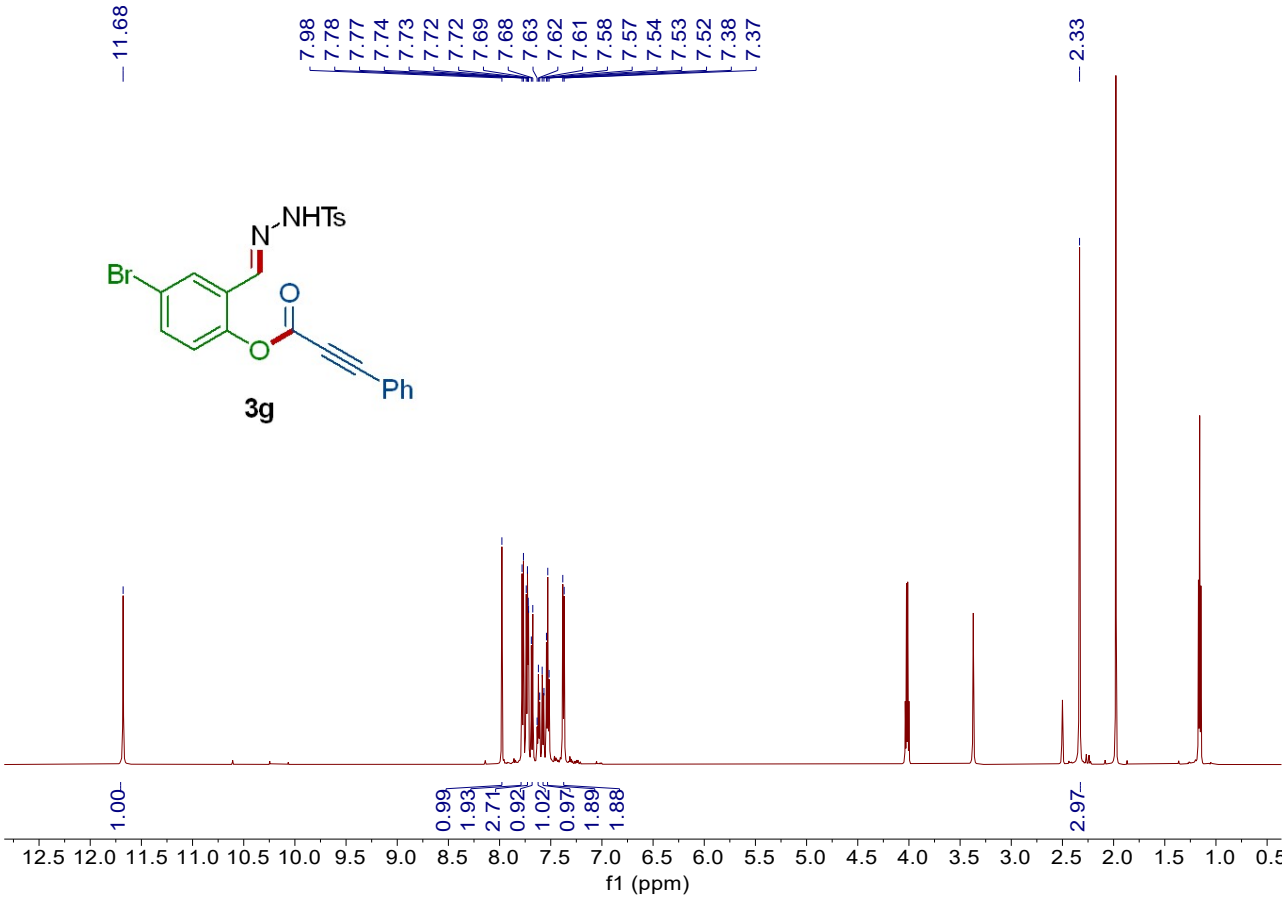
(E)-4-bromo-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3g).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 40% yield;

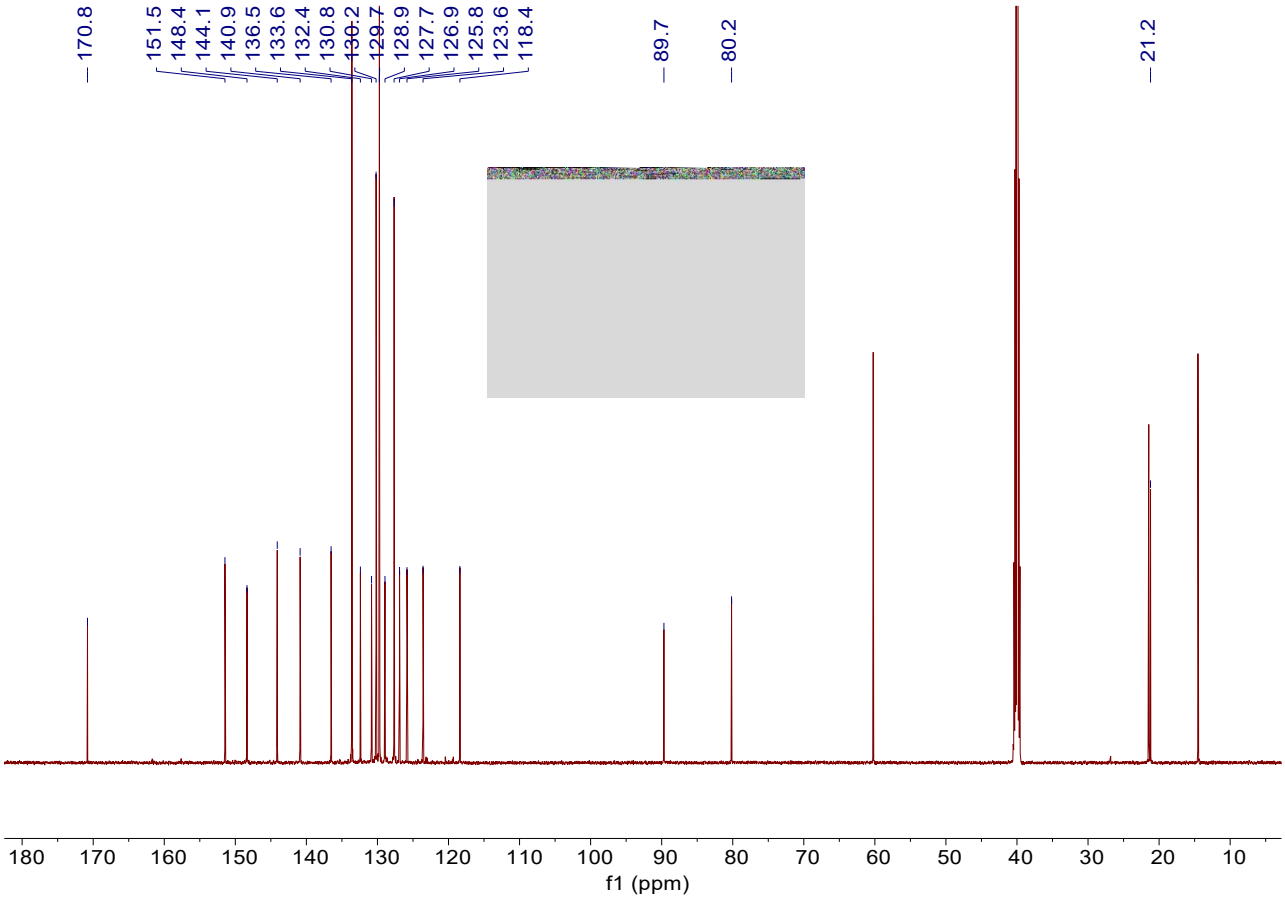
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.68 (s, 1H), 7.98 (s, 1H), 7.77 (d, *J* = 8.1 Hz, 2H), 7.75 – 7.70 (m, 3H), 7.68 (d, *J* = 8.5 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 10.4 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 2.33 (s, 3H).

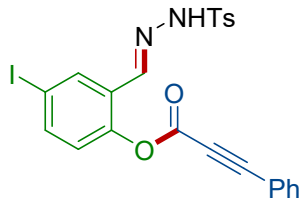
^{13}C NMR (151 MHz, DMSO-d_6) δ 170.8, 151.5, 148.4, 144.1, 140.9, 136.5, 133.6, 132.4, 130.8, 130.2, 129.7, 128.9, 127.7, 126.9, 125.8, 123.6, 118.4, 89.7, 80.2, 21.2.

^{1}H NMR spectrum of **3g** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3g** (DMSO-d_6, 151 MHz)





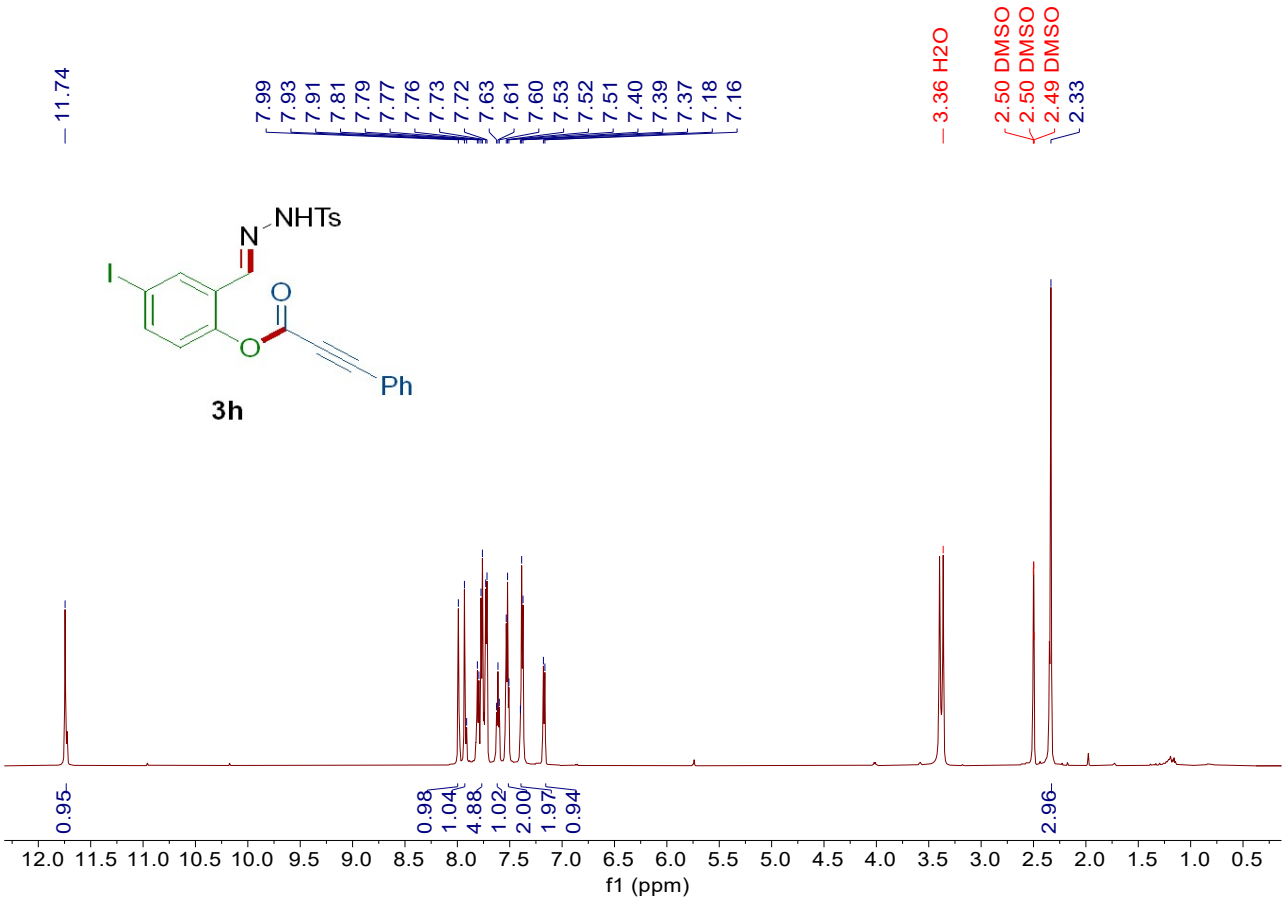
(E)-4-iodo-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3h).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 37% yield;

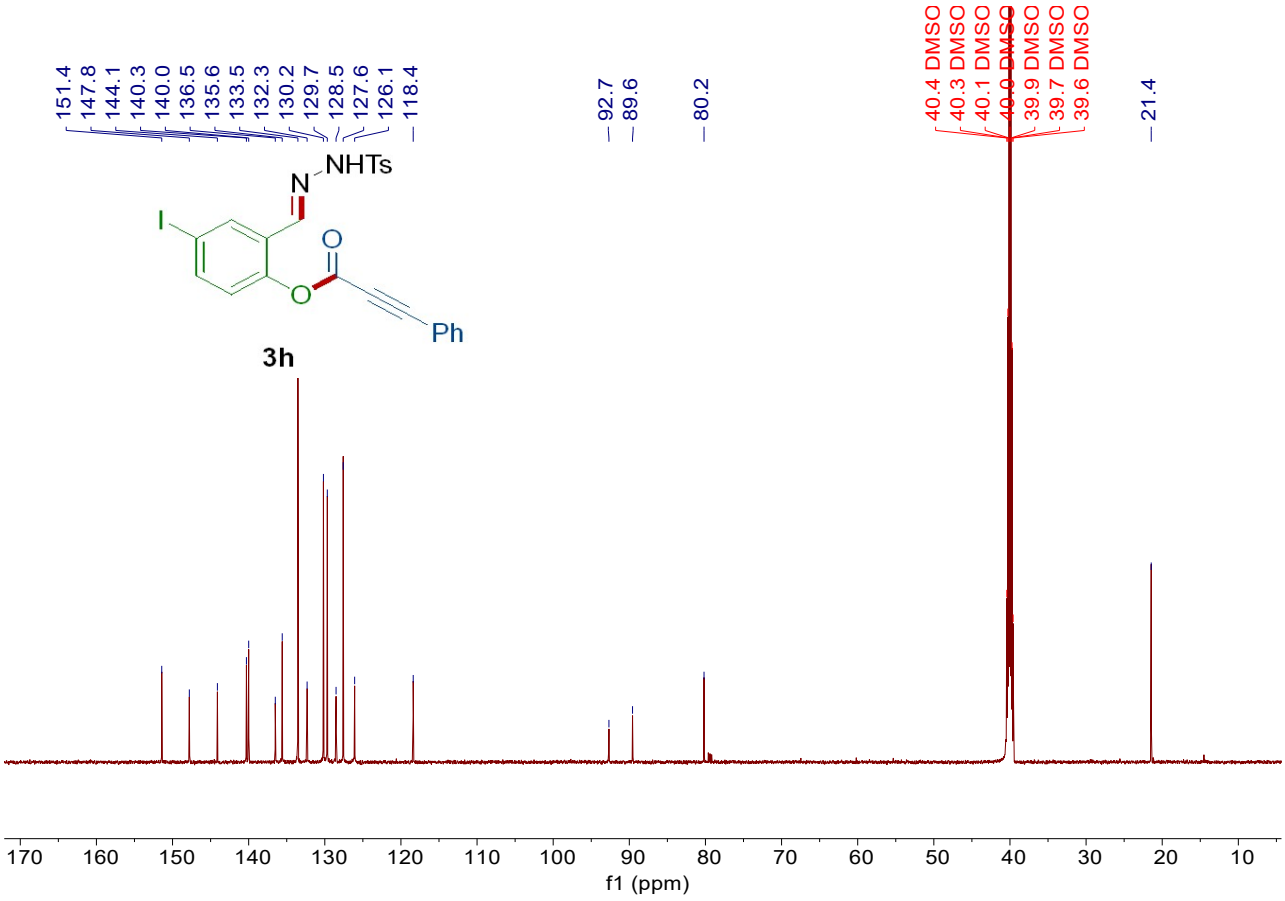
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.74 (s, 1H), 7.99 (s, 1H), 7.93 (s, 1H), 7.85 – 7.68 (m, 5H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 8.5 Hz, 1H), 2.33 (s, 3H).

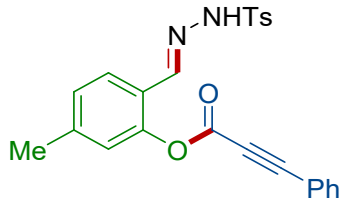
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.4, 147.8, 144.1, 140.3, 140.0, 136.5, 135.6, 133.5, 132.3, 130.2, 129.7, 128.5, 127.6, 126.1, 118.4, 92.7, 89.6, 80.2, 21.4.

^{1}H NMR spectrum of **3h** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3h** (DMSO-d_6, 151 MHz)





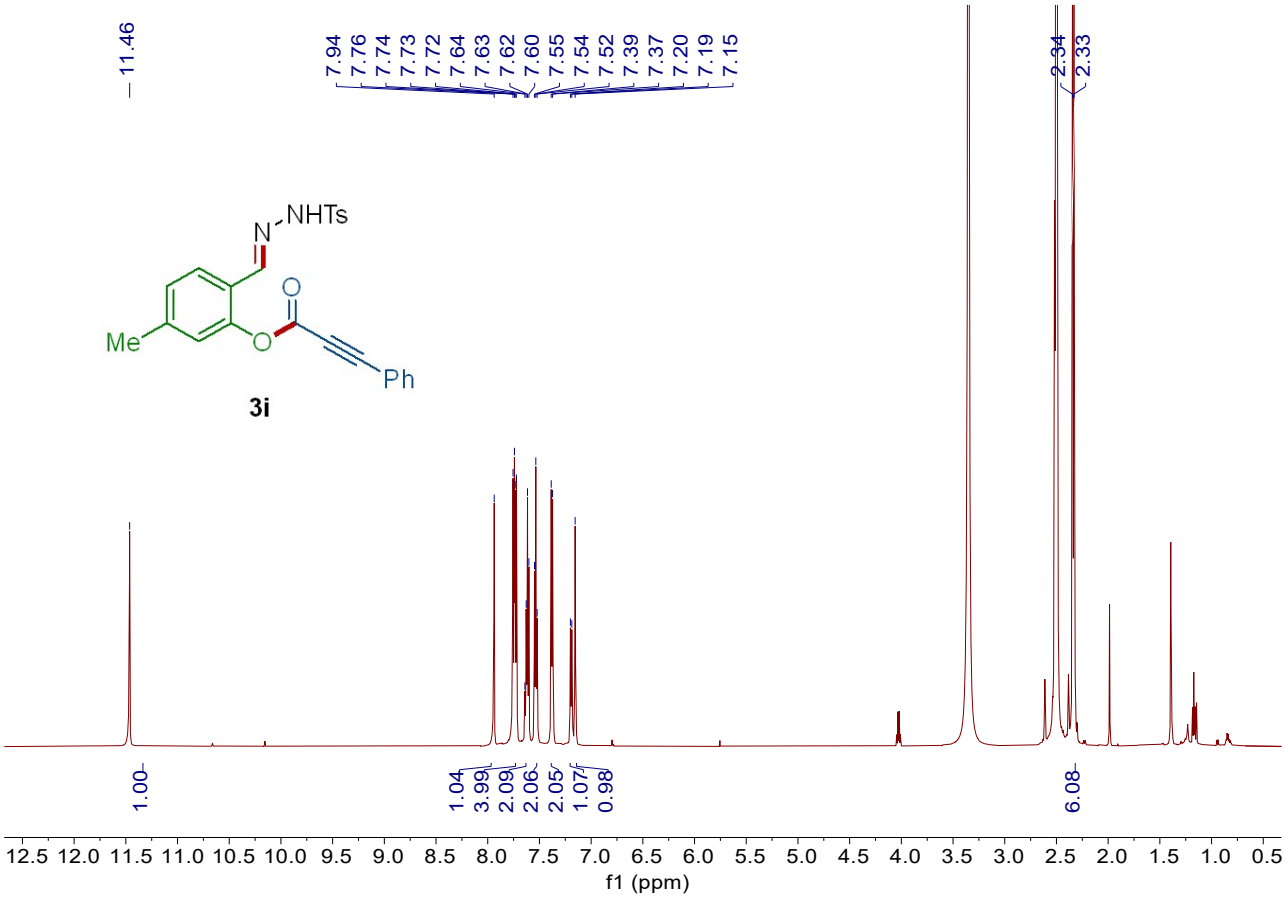
(E)-5-methyl-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3i).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 79% yield;

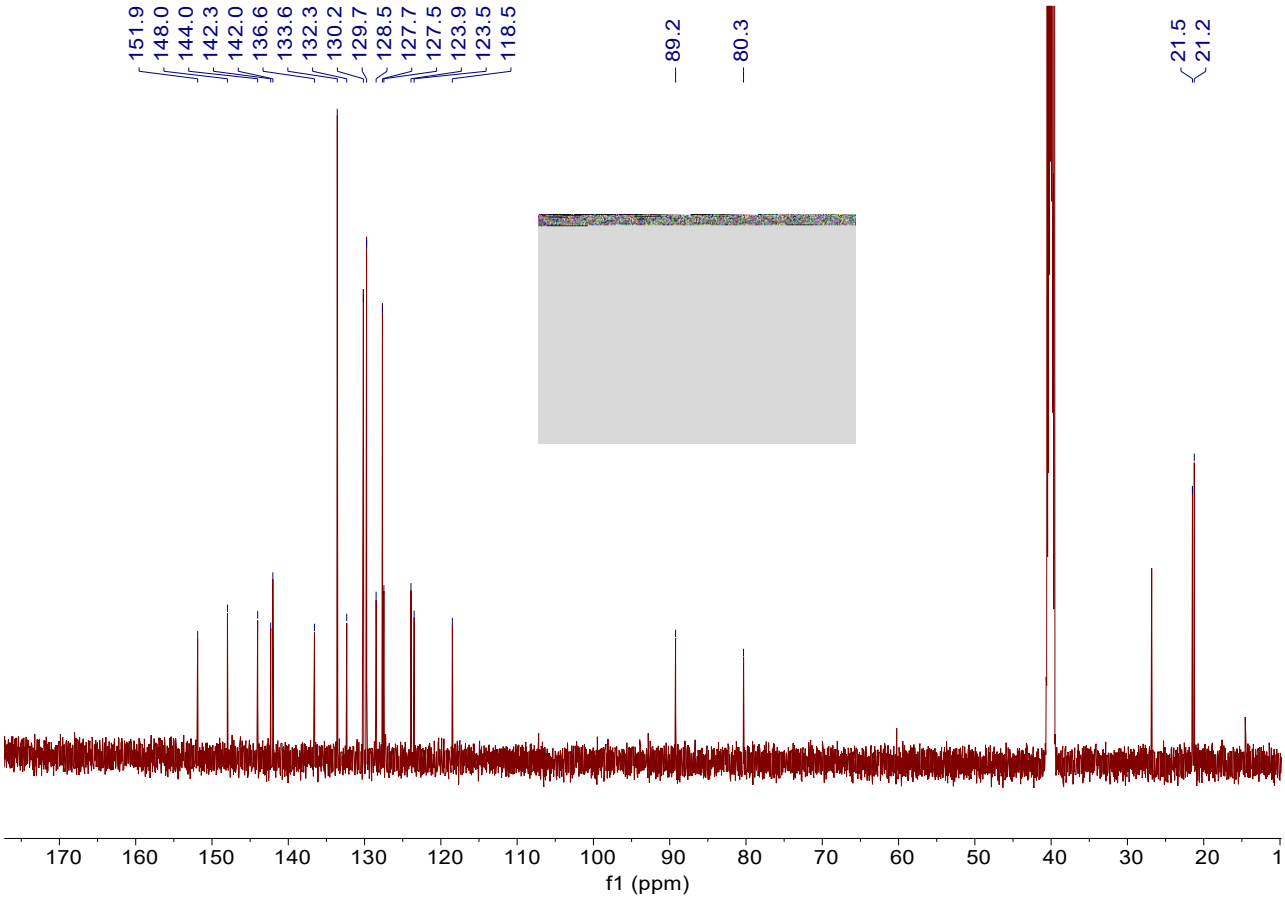
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.46 (s, 1H), 7.94 (s, 1H), 7.74 (dd, *J* = 12.0, 7.6 Hz, 4H), 7.62 (q, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 1H), 7.15 (s, 1H), 2.34 (d, *J* = 8.8 Hz, 6H).

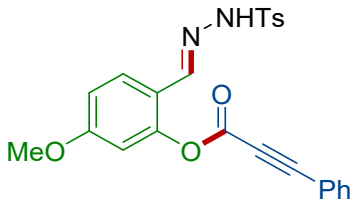
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.9, 148.0, 144.0, 142.3, 142.0, 136.6, 133.6, 132.3, 130.2, 129.7, 128.5, 127.7, 127.5, 123.9, 123.5, 118.5, 89.2, 80.3, 21.5, 21.2.

^{1}H NMR spectrum of **3i** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3i** ($CDCl_3$, 151 MHz)





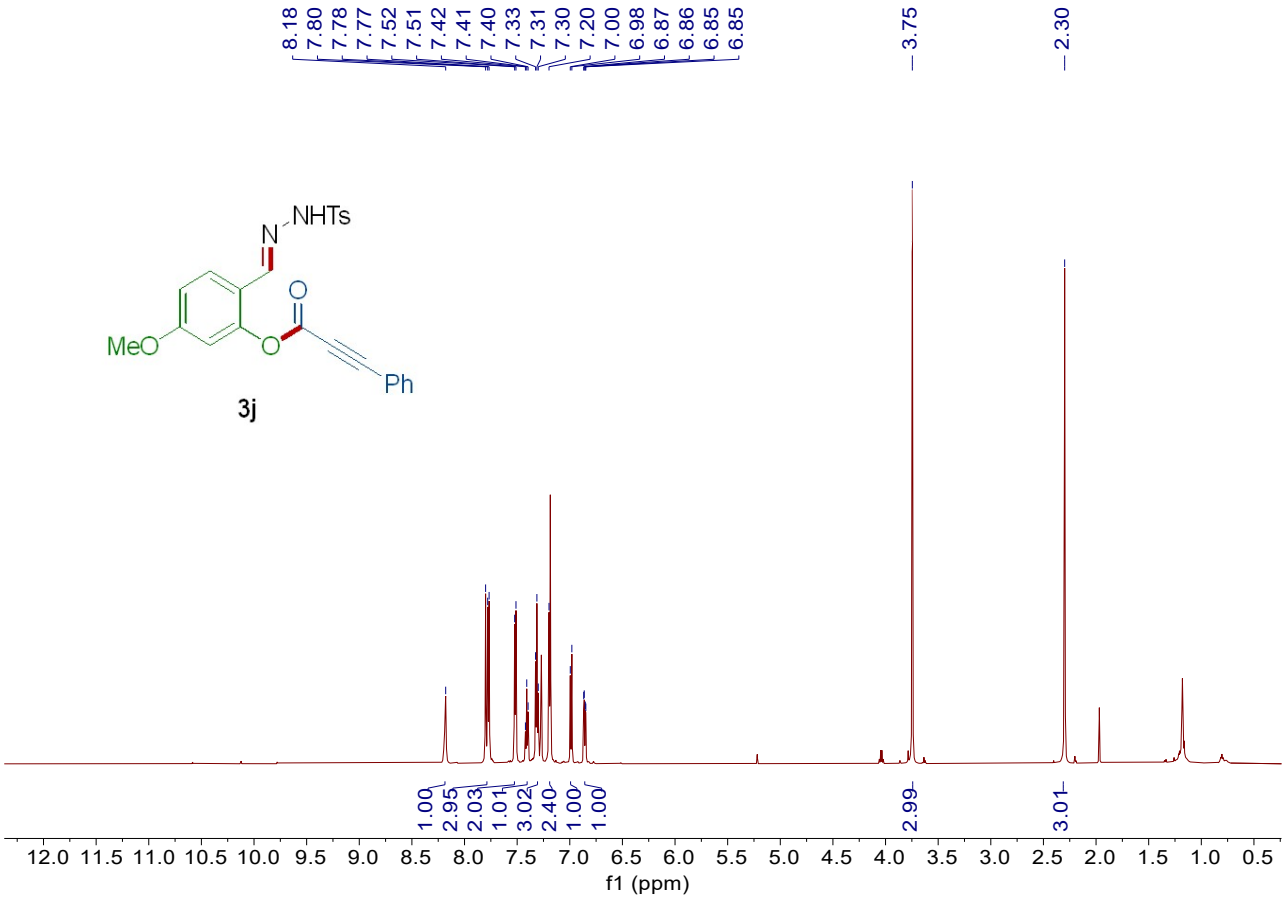
(E)-5-methoxy-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3j).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 80% yield;

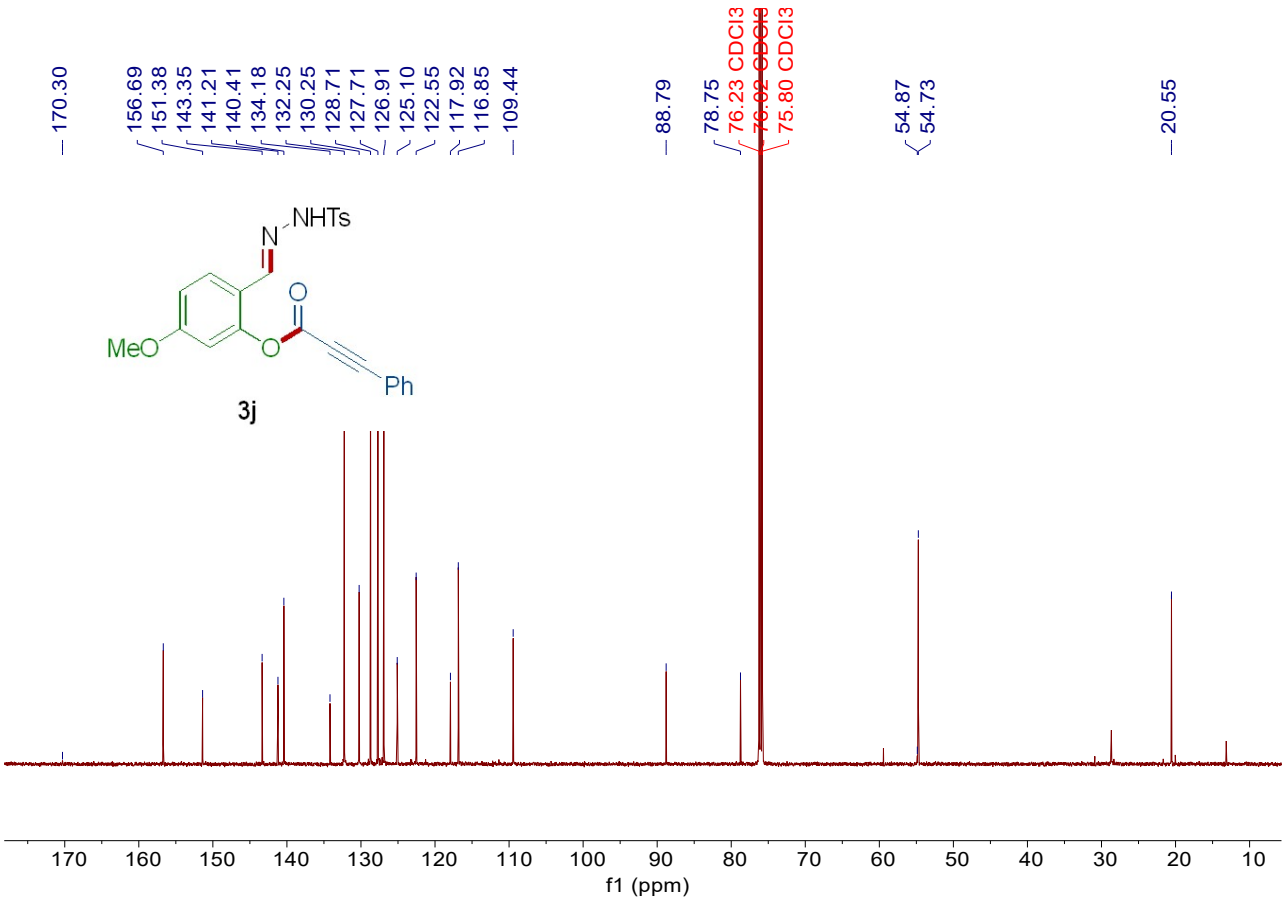
^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.18 (s, 1H), 7.83 – 7.75 (m, 3H), 7.52 (d, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 1H), 7.31 (t, *J* = 7.7 Hz, 3H), 7.19 (d, *J* = 7.5 Hz, 2H), 6.99 (d, *J* = 8.9 Hz, 1H), 6.86 (dd, *J* = 8.9, 3.1 Hz, 1H), 3.75 (s, 3H), 2.30 (s, 3H).

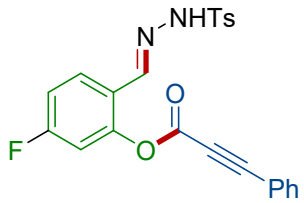
^{13}C NMR (151 MHz, Chloroform-*d*) δ 157.7, 152.4, 144.3, 142.2, 141.4, 135.2, 133.2, 131.2, 129.7, 128.7, 127.9, 126.1, 123.5, 118.9, 117.8, 110.4, 89.8, 79.7, 55.7, 21.5.

^{1}H NMR spectrum of **3j** ($CDCl_3$, 600 MHz)



^{13}C NMR spectrum of **3j** ($CDCl_3$, 151 MHz)





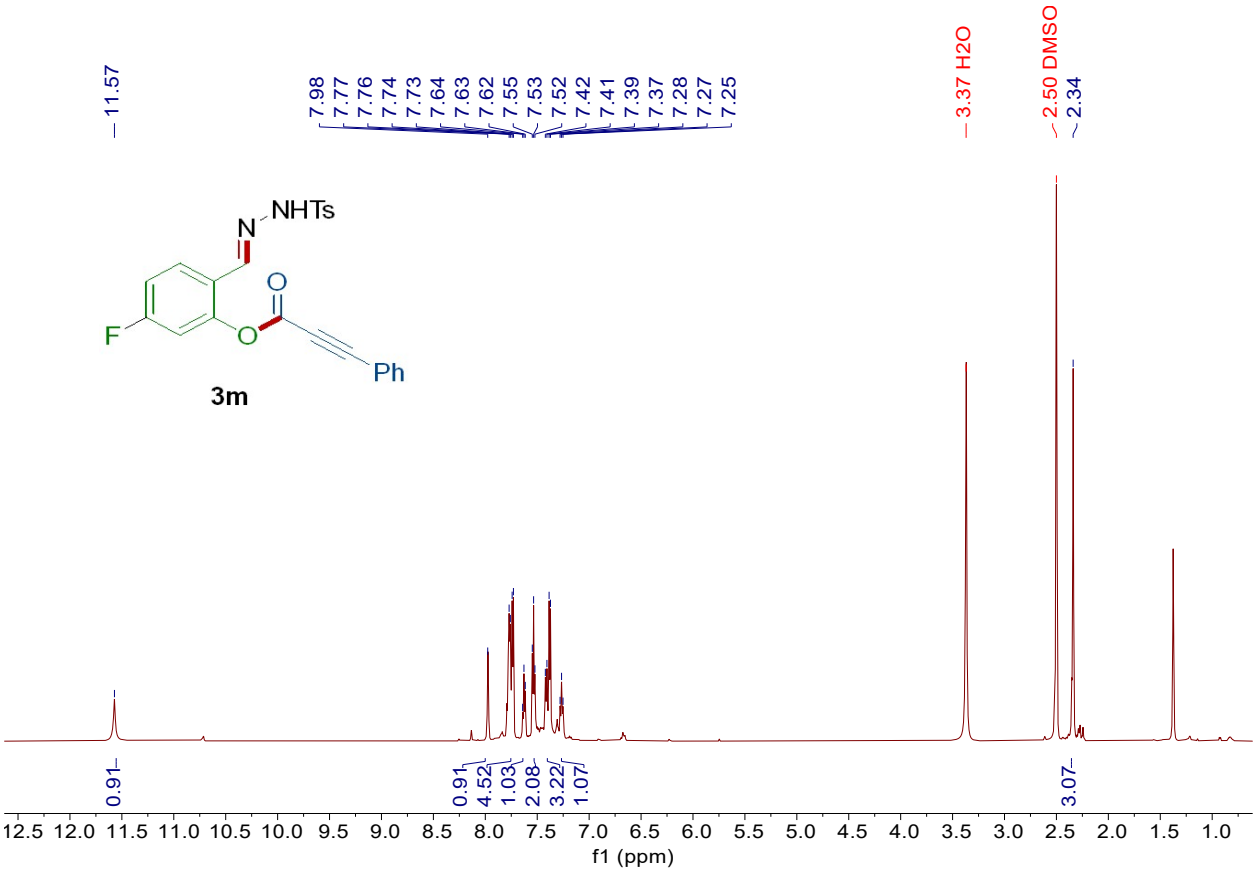
(E)-4-fluoro-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3m).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a faint yellow solid: 35% yield;

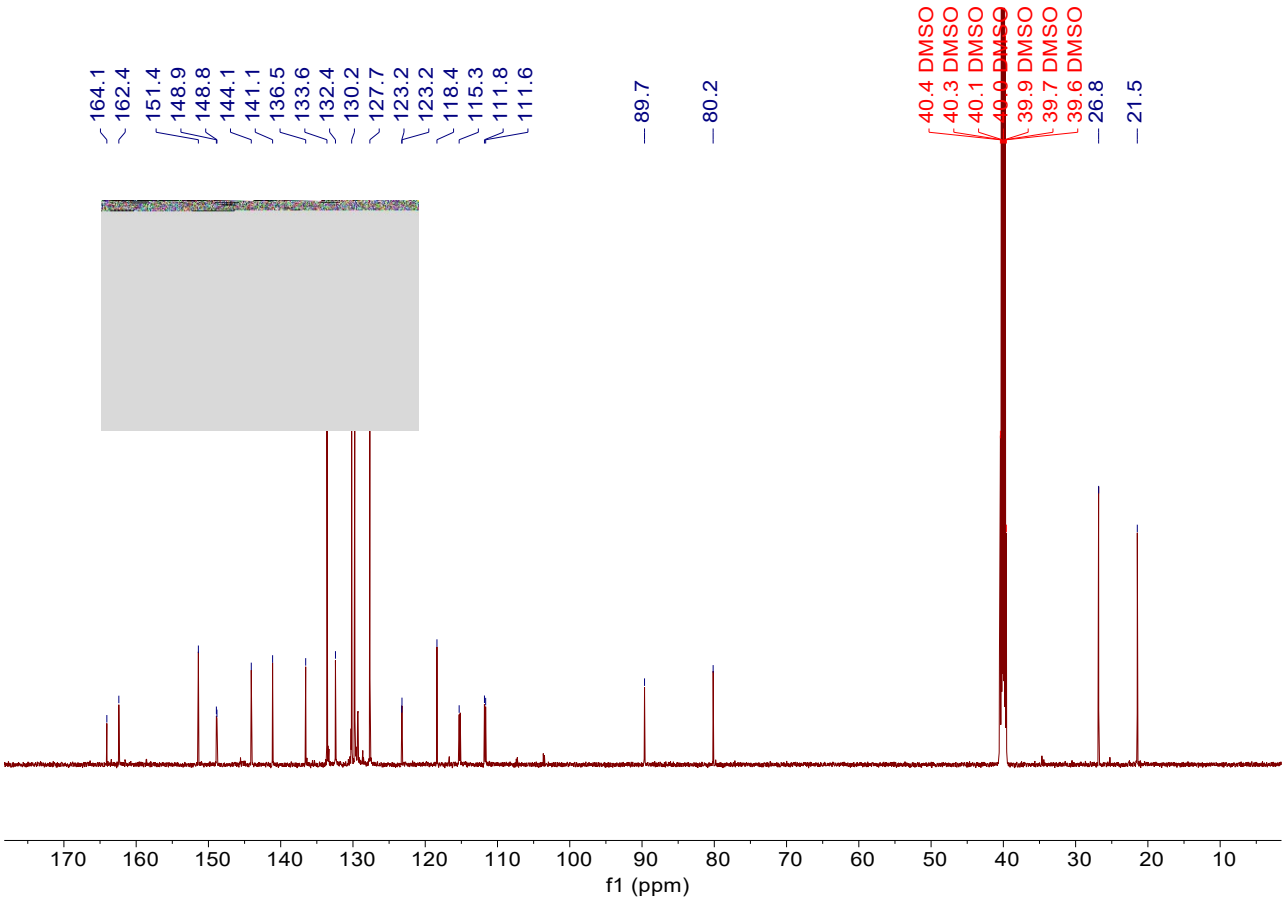
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.72 (s, 1H), 7.97 (d, *J* = 4.7 Hz, 1H), 7.82 – 7.76 (m, 2H), 7.73 (d, *J* = 7.7 Hz, 2H), 7.62 (d, *J* = 7.0 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.48 (d, *J* = 9.3 Hz, 1H), 7.43 (dd, *J* = 9.0, 4.7 Hz, 1H), 7.41 – 7.31 (m, 3H), 2.34 (s, 3H).

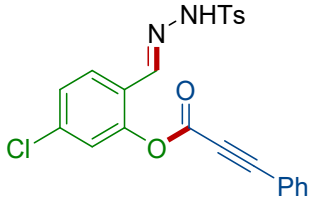
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.8, 144.2, 144.2, 140.6, 136.4, 133.6, 132.4, 130.2, 129.7, 127.7, 118.6, 118.4, 113.2, 113.0, 89.5, 80.2, 21.5.

^{1}H NMR spectrum of **3m** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3m** (DMSO-d_6, 151 MHz)





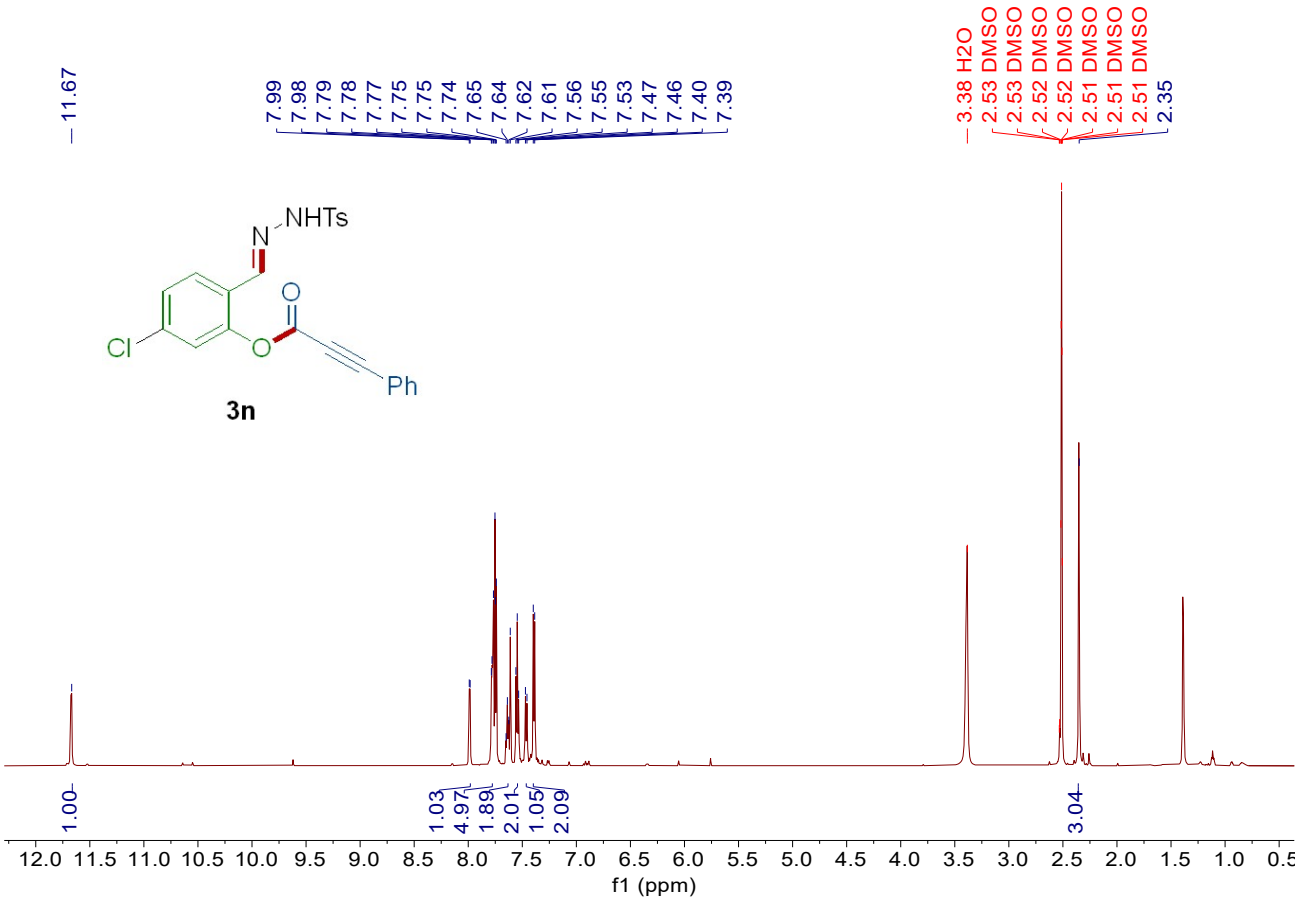
(E)-5-chloro-2-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3n).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 37% yield;

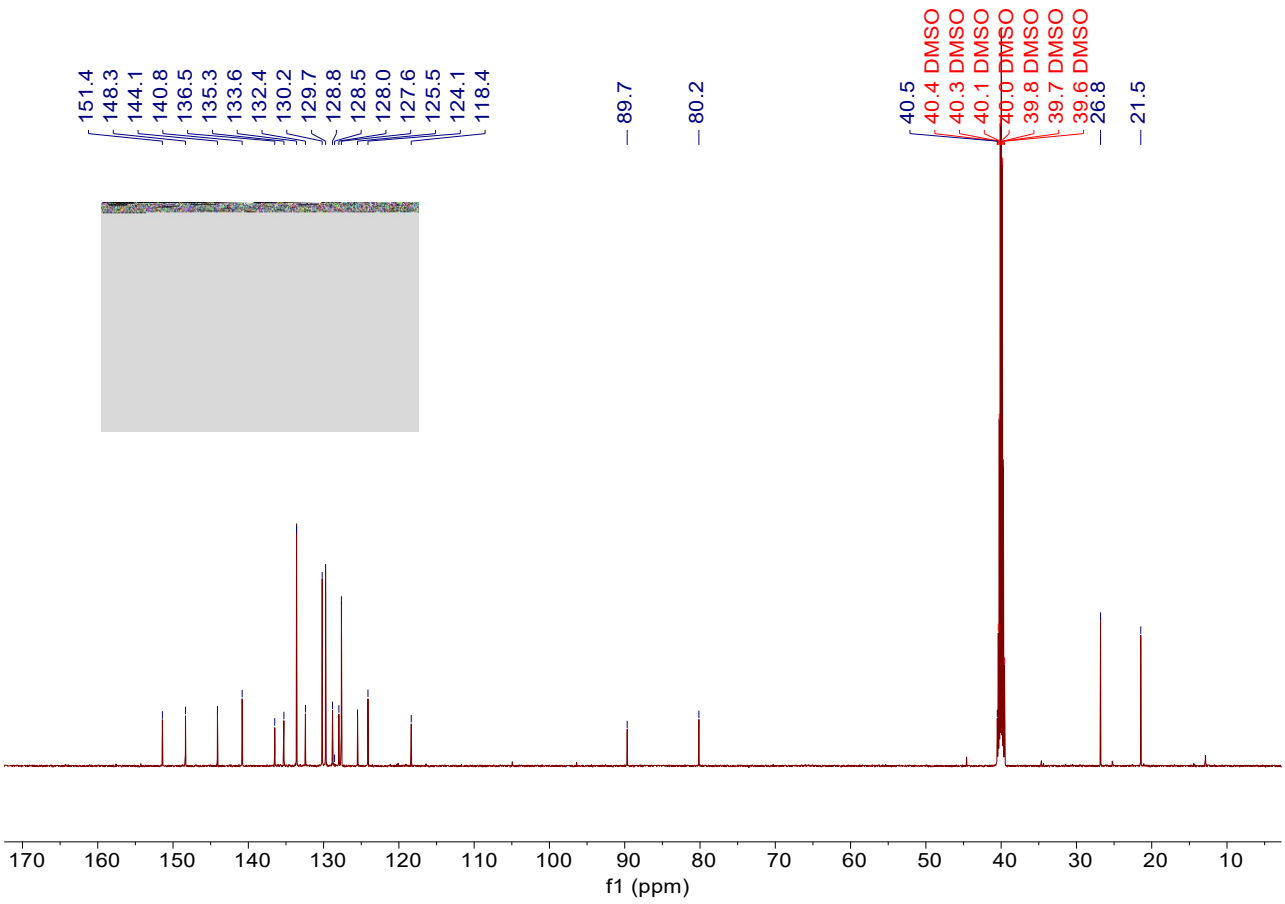
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.67 (s, 1H), 7.99 (d, J = 4.9 Hz, 1H), 7.85 – 7.70 (m, 5H), 7.62 (d, J = 16.0 Hz, 2H), 7.55 (t, J = 7.6 Hz, 2H), 7.46 (d, J = 8.4 Hz, 1H), 7.39 (d, J = 7.9 Hz, 2H), 2.35 (s, 3H).

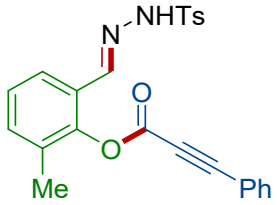
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.4, 148.4, 144.1, 140.8, 136.5, 135.3, 133.6, 132.4, 130.2, 129.7, 128.8, 128.0, 127.6, 125.5, 124.1, 118.4, 89.7, 80.2, 26.8, 21.5.

^{1}H NMR spectrum of **3n** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3n** (DMSO-d_6, 151 MHz)





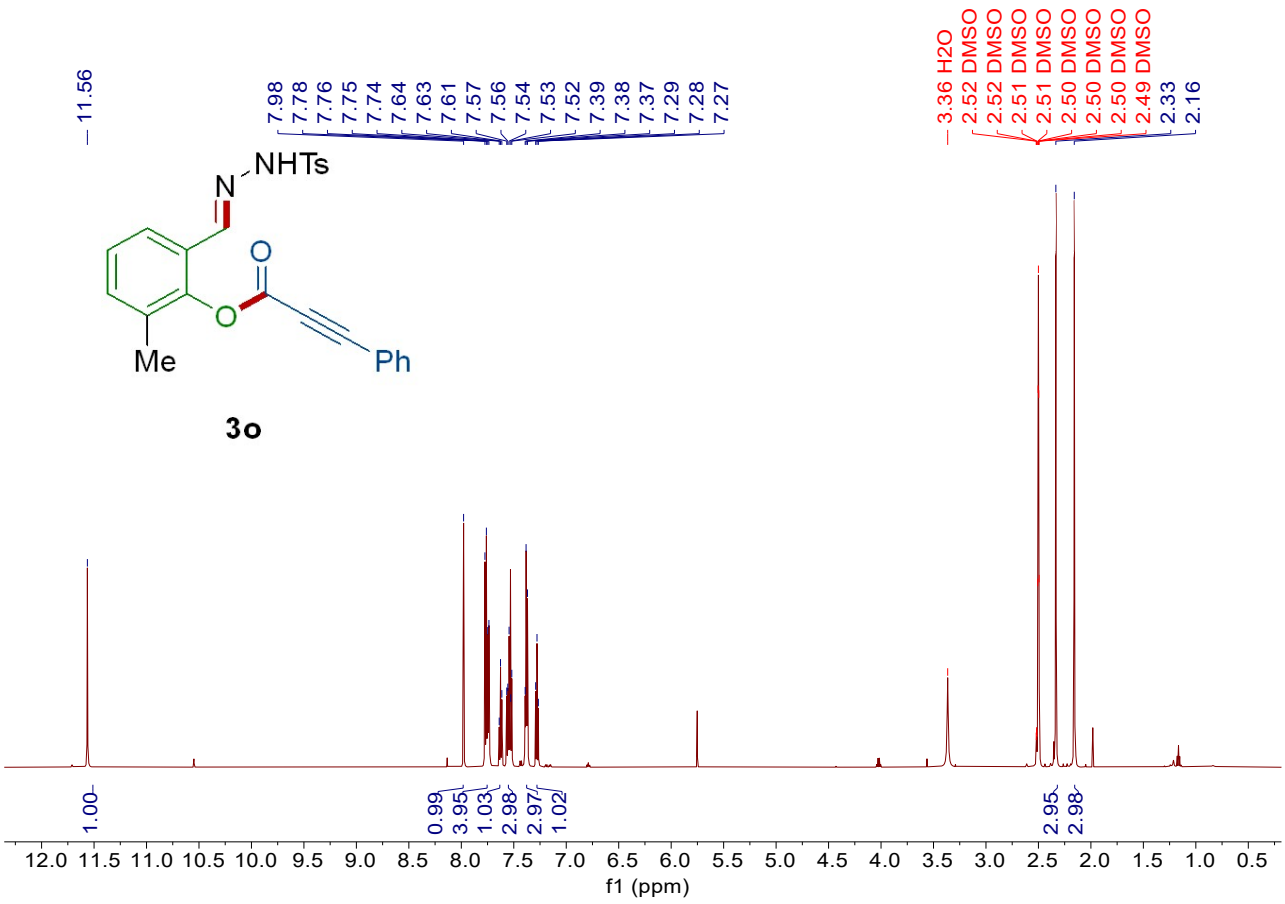
(E)-2-methyl-6-((2-tosylhydrazono)methyl)phenyl 3-phenylpropiolate **(3o).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 72% yield;

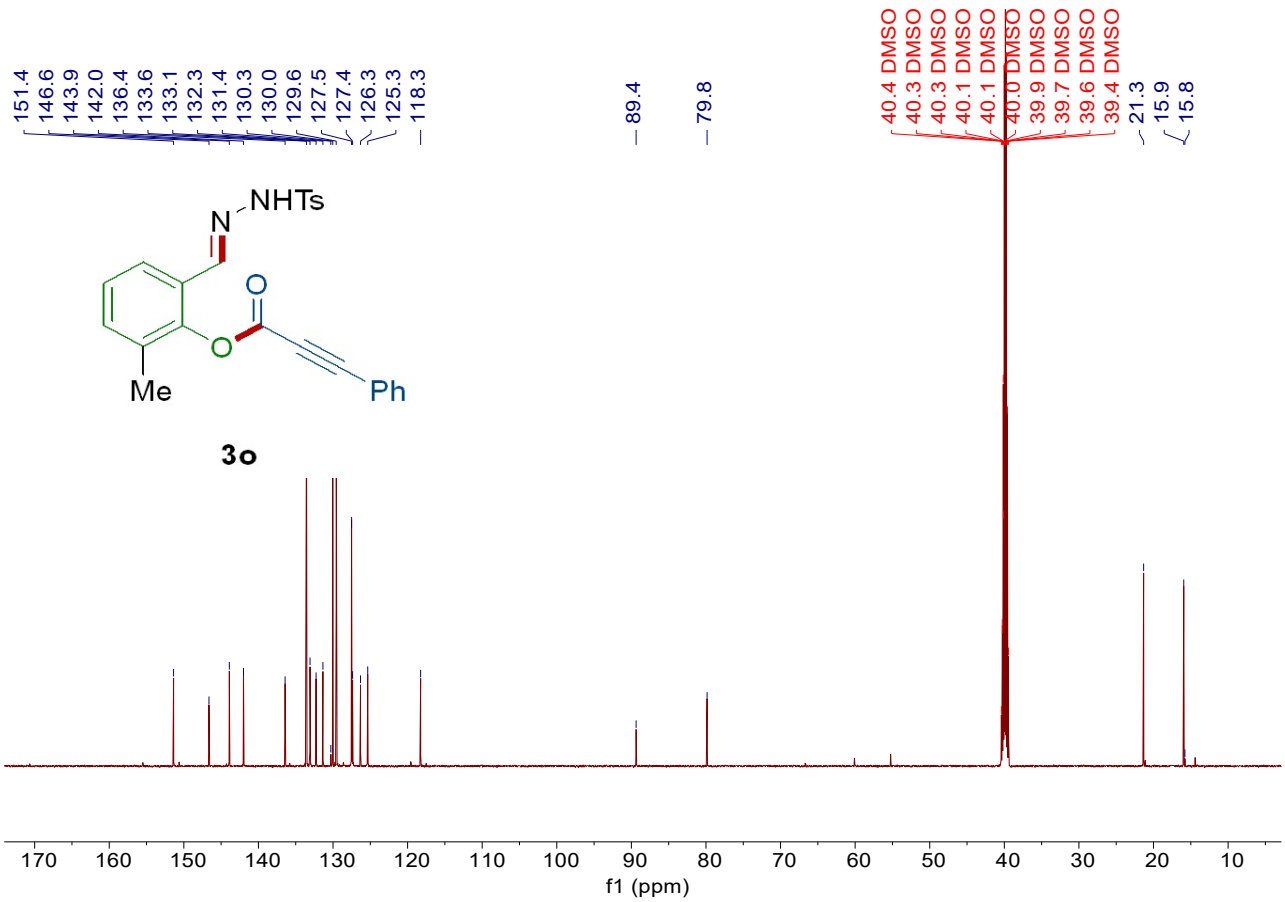
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.56 (s, 1H), 7.98 (s, 1H), 7.76 (dd, *J* = 14.7, 8.2 Hz, 4H), 7.67 – 7.59 (m, 1H), 7.54 (dt, *J* = 15.6, 7.8 Hz, 3H), 7.38 (d, *J* = 8.0 Hz, 3H), 7.28 (t, *J* = 7.7 Hz, 1H), 2.33 (s, 3H), 2.16 (s, 3H).

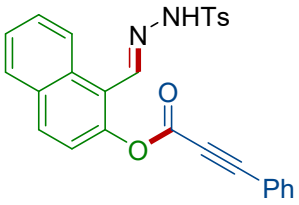
^{13}C NMR (151 MHz, DMSO-d_6) δ 151.4, 146.6, 143.9, 142.0, 136.4, 133.6, 133.1, 132.3, 131.4, 130.0, 129.6, 127.5, 127.4, 126.3, 125.4, 118.3, 79.9, 21.3, 15.9.

^{1}H NMR spectrum of **3o** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3o** (DMSO-d_6, 151 MHz)





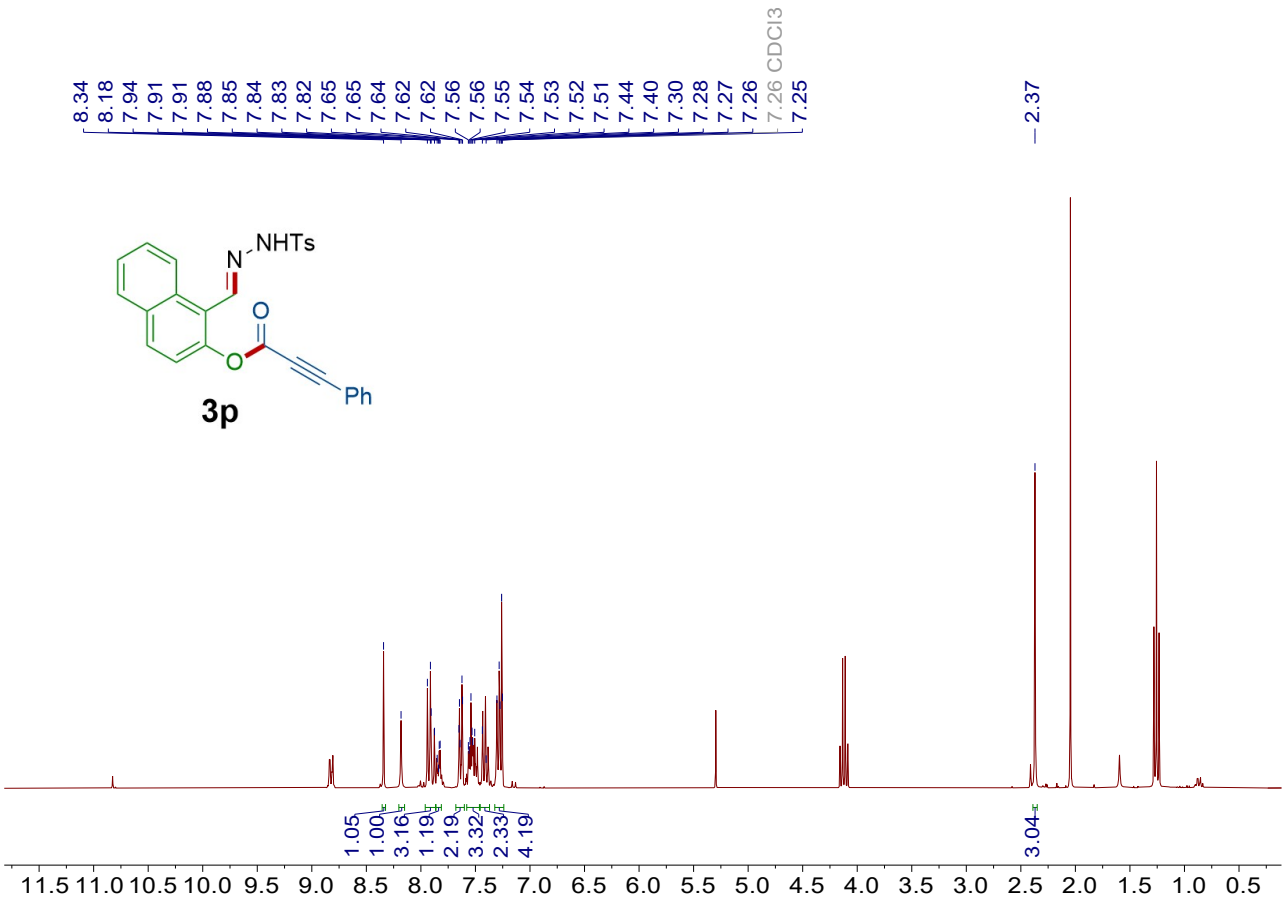
(E)-3-((2-tosylhydrazono)methyl)naphthalen-2-yl 3-phenylpropiolate **(3p)**.

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 72% yield;

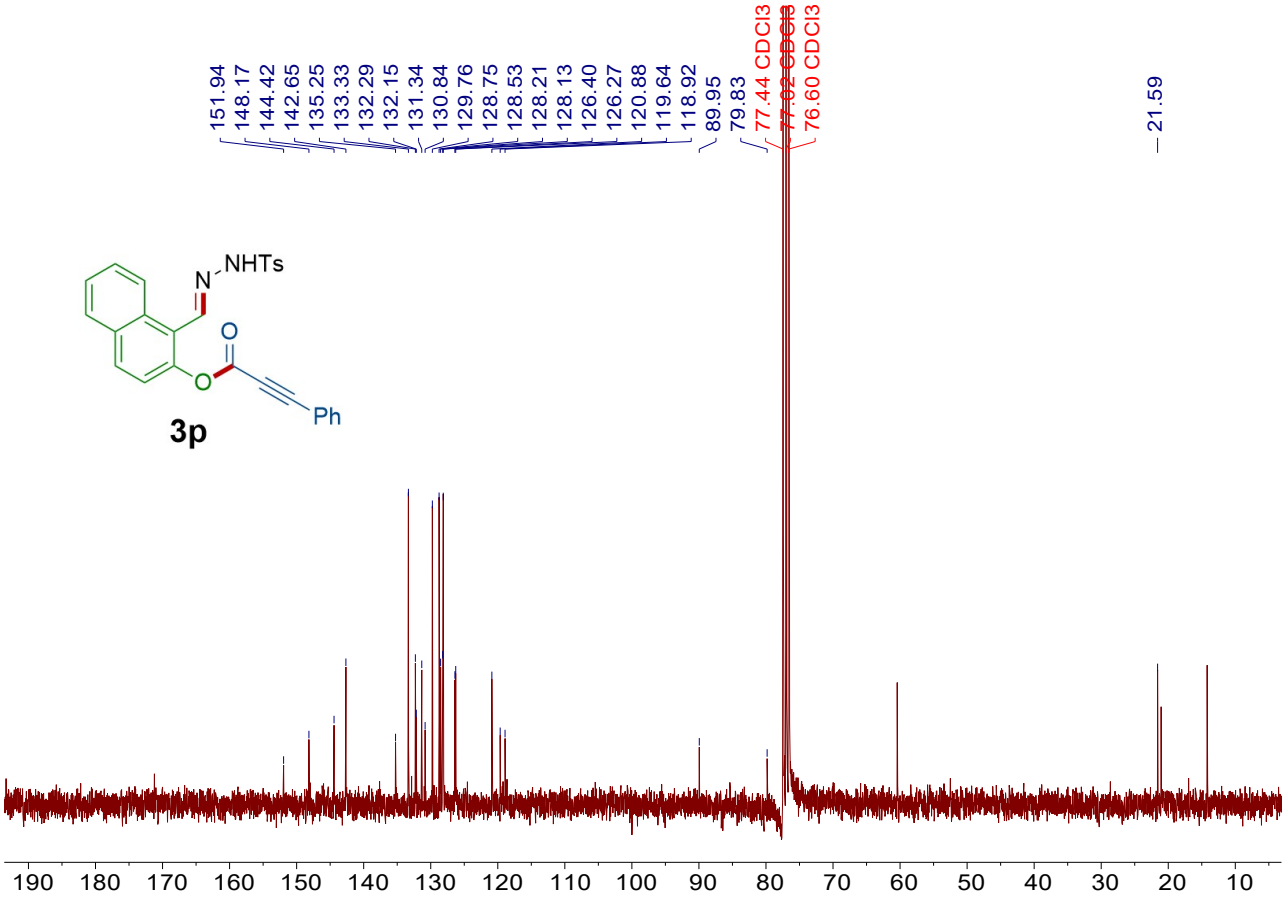
^{1}H NMR (300 MHz, Chloroform-*d*) δ 8.34 (s, 1H), 8.18 (s, 1H), 7.91 (dd, *J* = 10.4, 8.5 Hz, 3H), 7.84 (dd, *J* = 6.6, 3.0 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.58 – 7.46 (m, 3H), 7.46 – 7.37 (m, 2H), 7.32 – 7.24 (m, 4H), 2.37 (s, 3H).

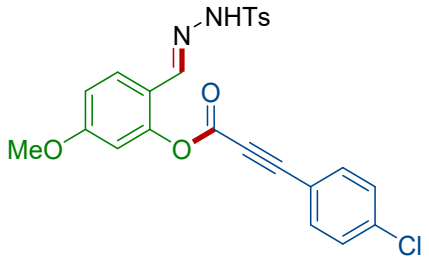
^{13}C NMR (75 MHz, Chloroform-*d*) δ 151.9, 148.2, 144.4, 142.7, 135.3, 133.3, 132.3, 132.2, 131.3, 130.8, 129.8, 128.8, 128.5, 128.2, 128.1, 126.4, 126.3, 120.9, 119.6, 118.9, 89.9, 79.8, 21.6.

^{1}H NMR spectrum of **3p** (CDCl3, 300 MHz)



^{13}C NMR spectrum of **3p** ($CDCl_3$, 75 MHz)





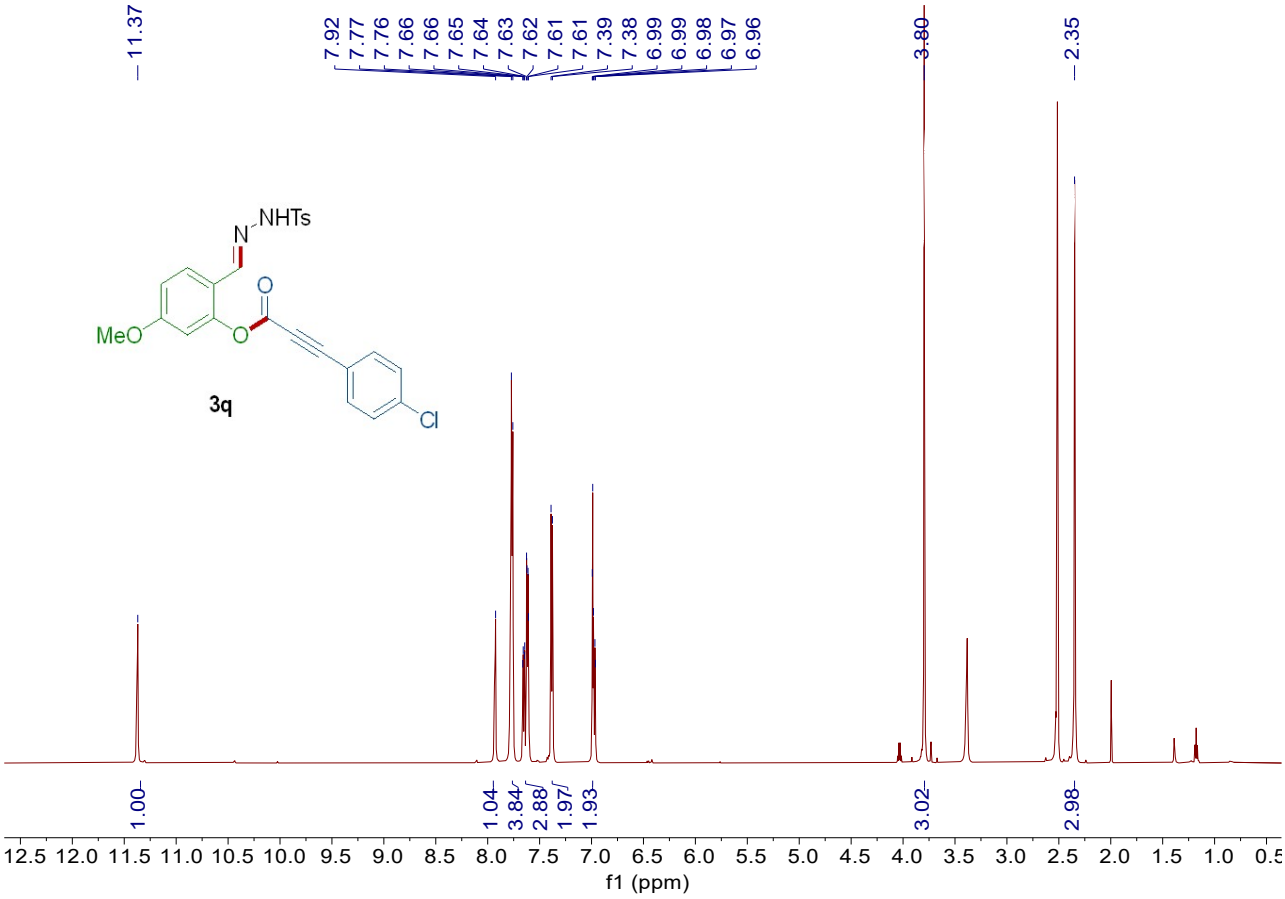
(E)-5-methoxy-2-((2-tosylhydrazono)methyl)phenyl 3-(4-chlorophenyl)propiolate **(3q).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 87% yield;

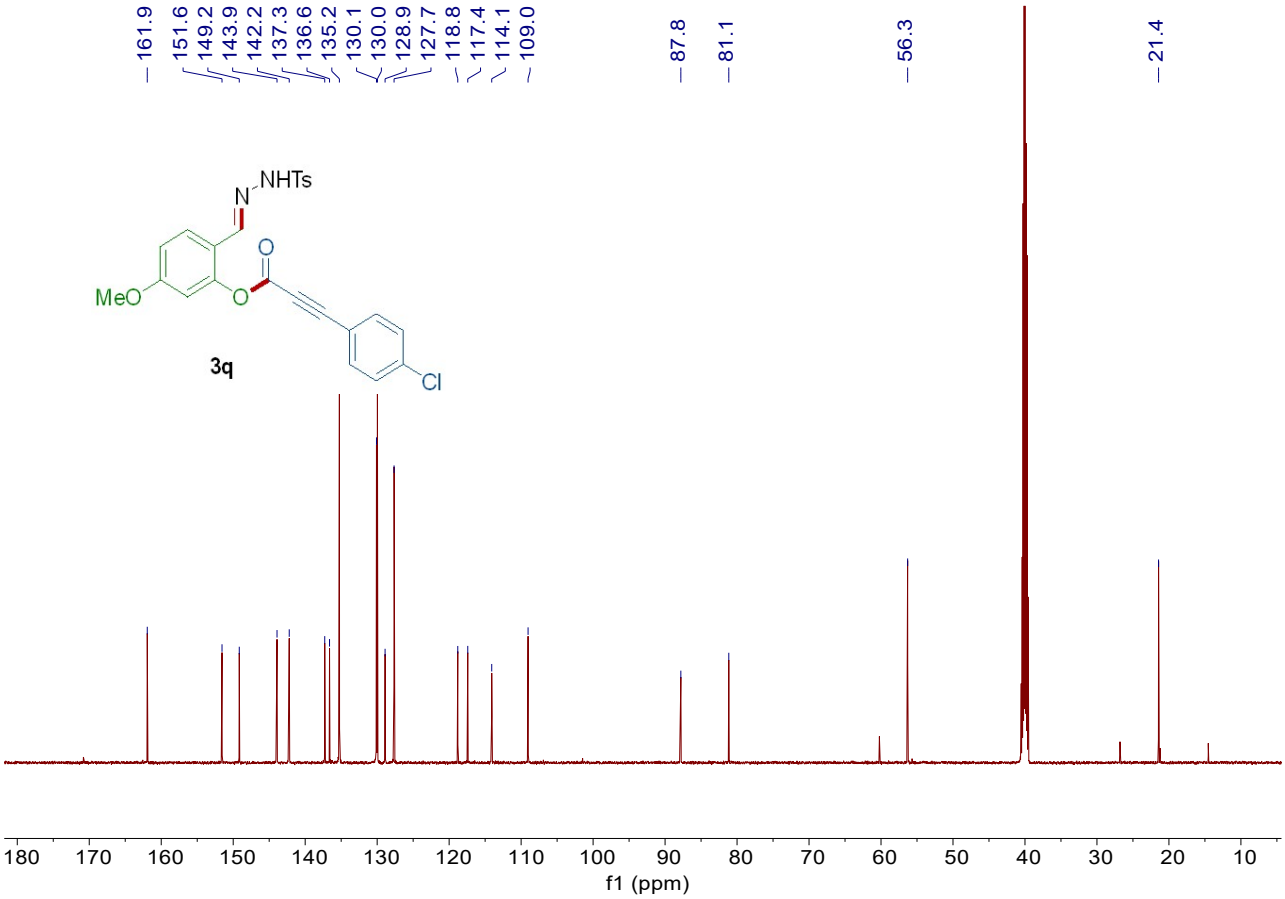
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.37 (s, 1H), 7.92 (s, 1H), 7.76 (d, *J* = 8.4 Hz, 4H), 7.63 (ddd, *J* = 21.4, 8.6, 2.3 Hz, 3H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.09 – 6.89 (m, 2H), 3.80 (s, 3H), 2.35 (s, 3H).

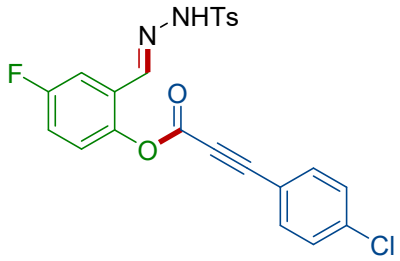
^{13}C NMR (151 MHz, DMSO-d_6) δ 161.9, 151.6, 149.2, 143.9, 142.2, 137.3, 136.6, 135.3, 130.1, 130.0, 128.9, 127.7, 118.8, 117.4, 114.1, 109.0, 87.8, 81.2, 56.3, 21.4.

^{1}H NMR spectrum of **3q** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3q** (DMSO-d_6, 151 MHz)





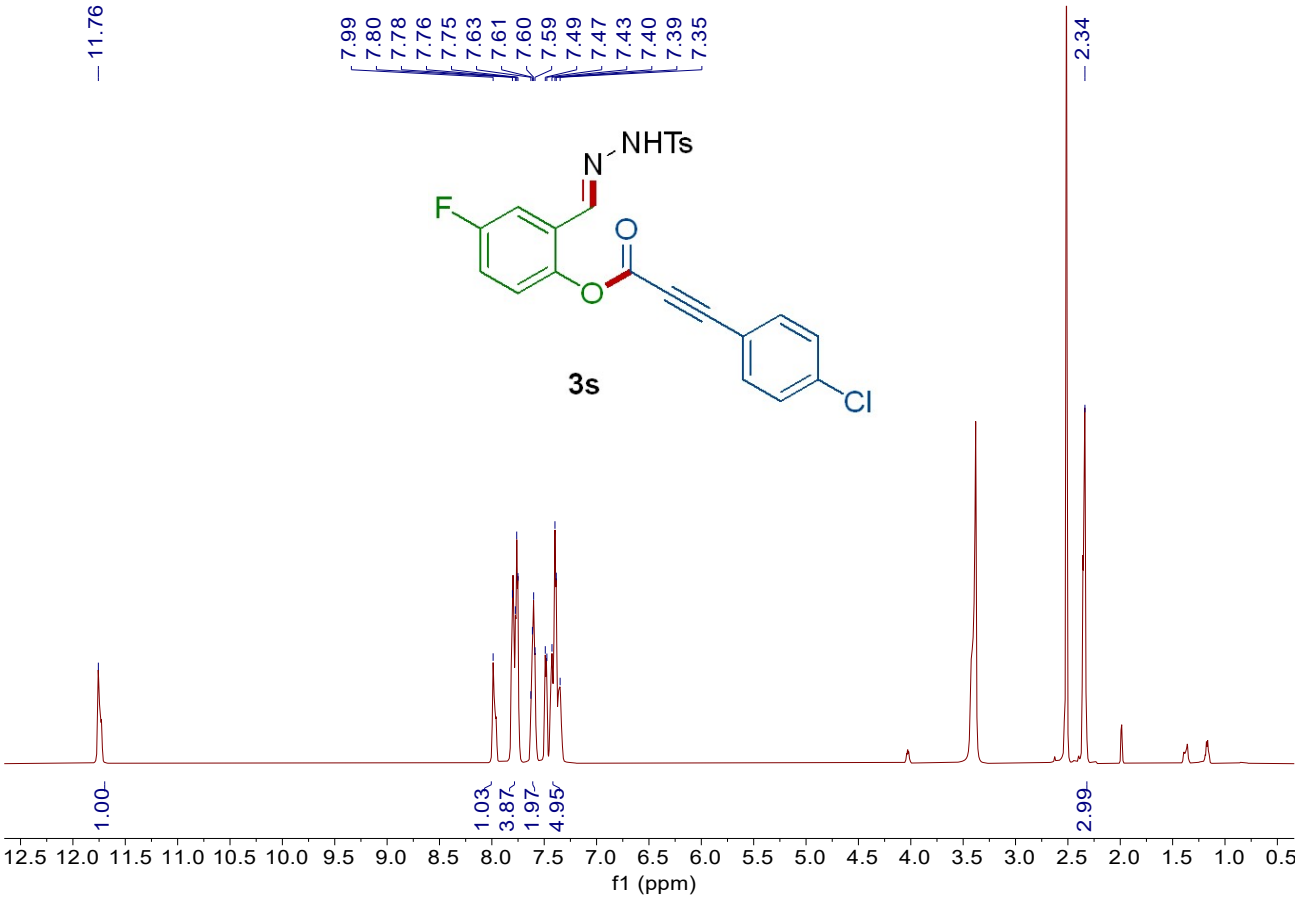
(E)-4-fluoro-2-((2-tosylhydrazono)methyl)phenyl 3-(4-chlorophenyl)propiolate **(3s).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a faint yellow solid: 45% yield;

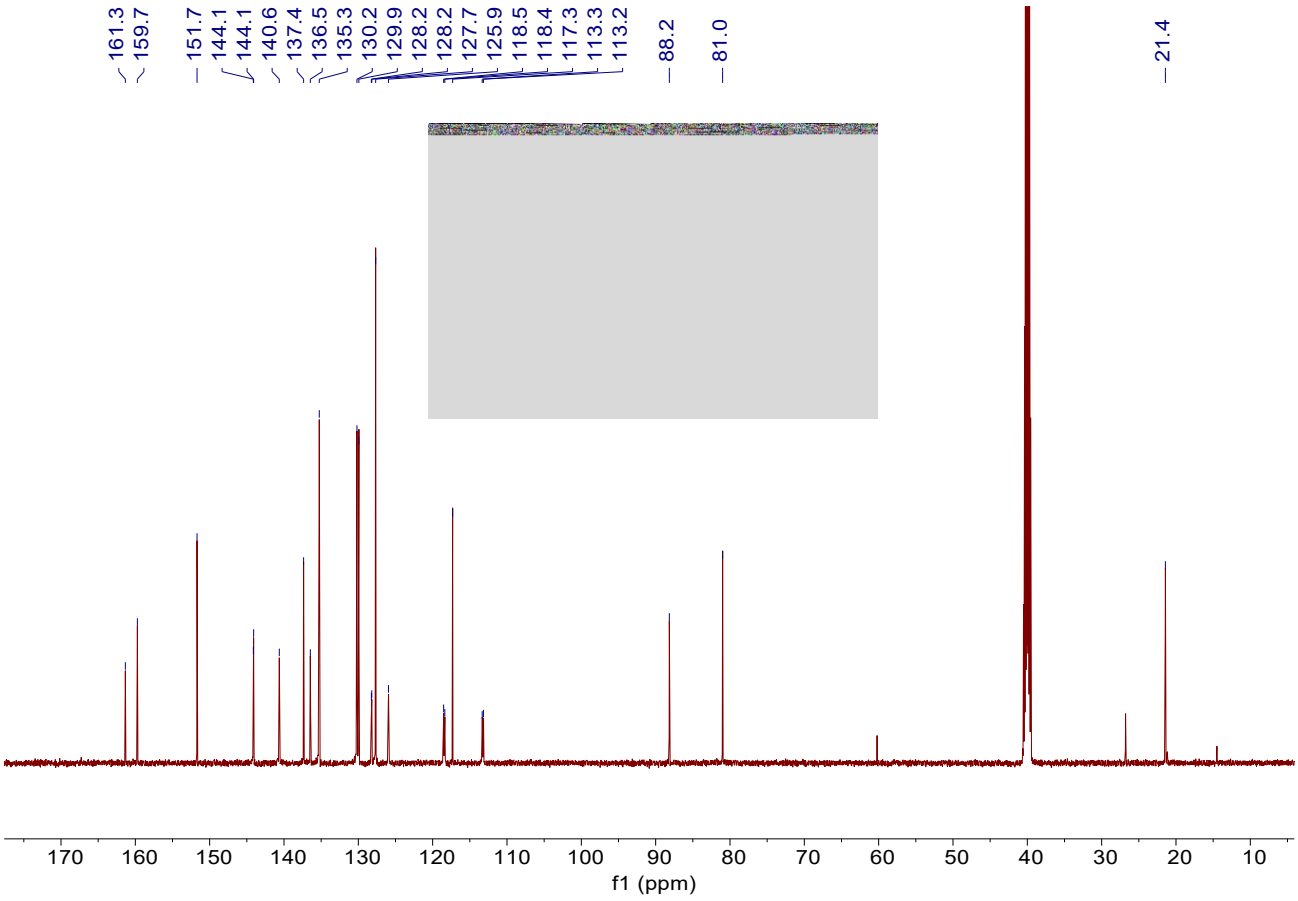
^{1}H NMR (600 MHz, DMSO-d_6) δ 11.76 (s, 1H), 7.99 (s, 1H), 7.86 – 7.70 (m, 4H), 7.61 (q, *J* = 8.4, 7.9 Hz, 2H), 7.54 – 7.29 (m, 5H), 2.34 (s, 3H.

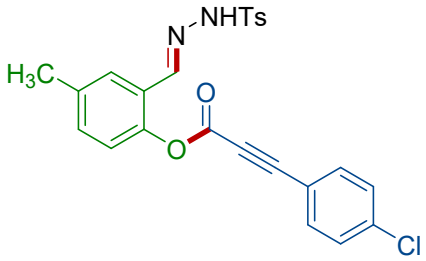
^{13}C NMR (151 MHz, DMSO-d_6) δ 161.3, 159.7, 151.7, 144.1, 144.1, 140.6, 137.4, 136.5, 135.3, 130.2, 129.9, 128.2, 128.2, 127.7, 125.9, 118.5, 118.4, 117.3, 113.3, 113.2, 88.2, 90.0, 21.4.

^{1}H NMR spectrum of **3s** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3s** (DMSO-d_6, 151 MHz)





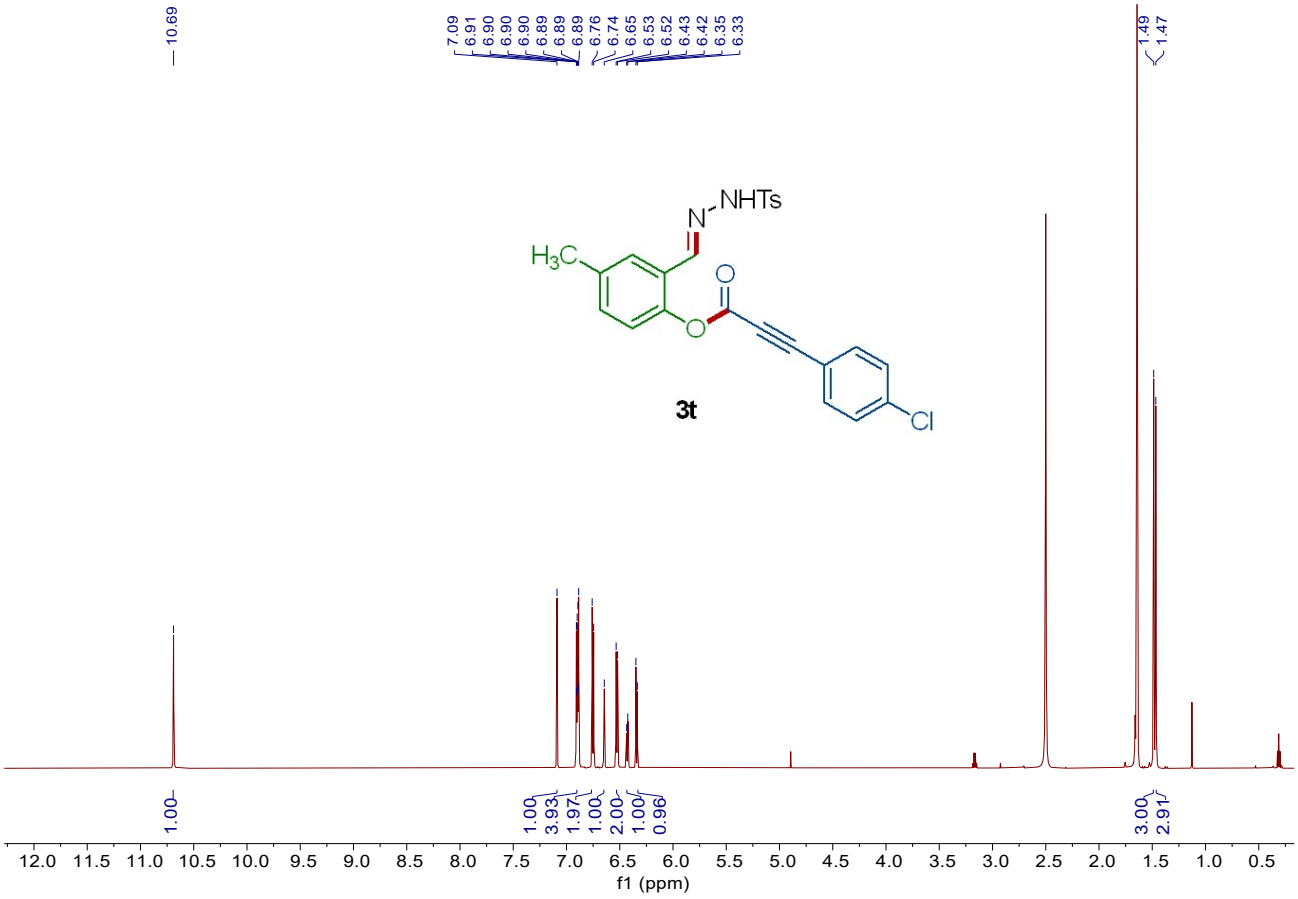
(E)-5-methoxy-2-((2-tosylhydrazono)methyl)phenyl 3-(4-chlorophenyl)propiolate **(3t).**

This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 85% yield;

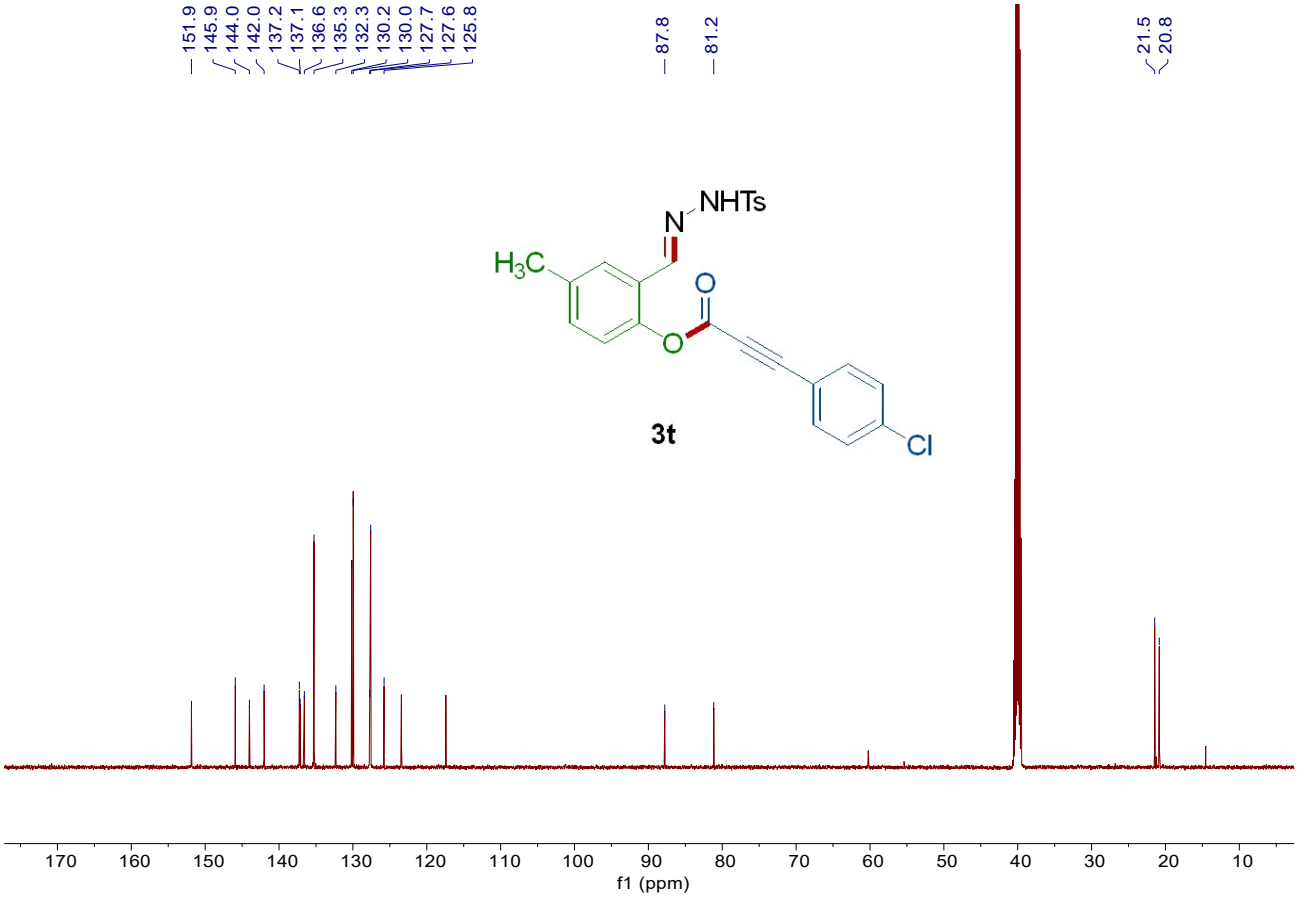
^{1}H NMR (600 MHz, DMSO-d_6) δ 10.69 (s, 1H), 7.09 (s, 1H), 6.96 – 6.84 (m, 4H), 6.75 (d, J = 8.5 Hz, 2H), 6.65 (s, 1H), 6.53 (d, J = 8.1 Hz, 2H), 6.43 (d, J = 6.2 Hz, 1H), 6.34 (d, J = 8.2 Hz, 1H), 1.49 (s, 3H), 1.47 (s, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 151.9, 145.9, 144.0, 142.0, 137.1, 136.6, 132.3, 130.2, 130.0, 127.7, 127.6, 125.8, 87.8, 81.2, 21.5, 20.8.

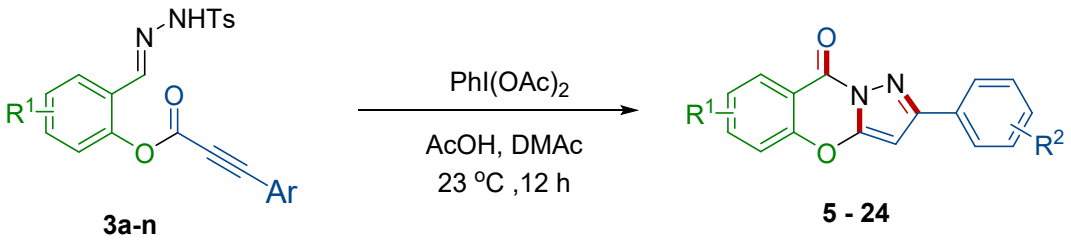
^{1}H NMR spectrum of **3t** (DMSO-d_6, 600 MHz)



^{13}C NMR spectrum of **3t** (DMSO-d_6, 151 MHz)


151.9
145.9
144.0
142.0
137.2
137.1
136.6
135.3
132.3
130.2
130.0
127.7
127.6
125.8
87.8
81.2
21.5
20.8
NHTs
N
H3C
O
O
Cl
3t
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

4. General Procedure



3a-n **5 - 24**

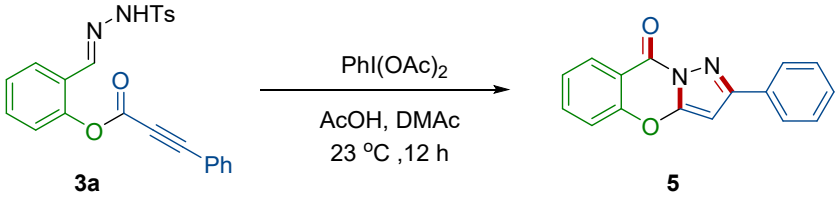
In a Schlenk tube, Substrate **3a** (0.5 mmol, 209.2 mg), the oxidant iodophenyldiacetic acid (1.0 mmol, 322 mg), and AcOH (10 mmol, 572 µL) were meticulously weighed. This assembly was stirred at room temperature in the presence of 4 mL of DMAc, and the reaction proceeded at 23 °C for a span of 12 hours. After the reaction, an equal volume of H_2O was added, filtered, and the residue was recrystallized to obtain the target product; alternatively, elution was also performed using a petroleum ether: ethyl acetate mixture in a 3:1 ratio. This comprehensive process led to isolating a pure product (white crystal) weighing 106.5 mg, yielding an impressive 81%. This method was similarly applied to synthesizing other target compounds (**4b-n**), resulting in comparable outcomes.

It is worth noting that the experimental details for the purification of compounds **24** and **27** using the recrystallisation method are outlined as follows:
Weighing 50 mg of compound **24** into a 25 mL round-bottom flask, 5 mL of dichloromethane (AR grade) was added, and the mixture was heated with stirring to 39 °C. After the complete dissolution of the sample, 2.5 mL of petroleum ether (AR grade) was slowly added, and the mixture was cooled to 23 °C, leading to the precipitation of a solid. After filtration, the filter cake was transferred to a 10 mL round-bottom flask, and after rotary evaporation at 40 °C for 15 minutes, it was weighed, yielding 36 mg of yellow solid compound **24**.

Similarly, 50 mg of compound **27** was weighed into a 25 mL round-bottom flask, and 4 mL of ethyl acetate (AR grade) was added. The mixture was heated by stirring at 76 °C until the sample was completely dissolved, followed by the slow addition of 2 mL of petroleum ether (AR grade) and cooling at room temperature (23 °C), leading to solid precipitation. After filtration, the filter cake was transferred to a 10 mL round-bottom flask, and after rotary evaporation at 50 °C for 15 minutes, it was weighed, yielding 32 mg of yellow solid compound **27**.

5. Optimization of the reaction conditions

Table S1 Preliminary Optimization of Reaction Conditions Using Substrate **3a**[a]



3a **5**

Entry	Solvent	Oxidant	Additives	T/°C	Time	Yield[%][b]
1	DMF	$PhI(OAc)_2$	None	75	4 h	22
2	DMAc	$PhI(OAc)_2$	None	75	4 h	40
3	DMSO	$PhI(OAc)_2$	None	75	4 h	n.d.
4	NMP	$PhI(OAc)_2$	None	75	4 h	n.d.
5	DMAc	$PhI(OAc)_2$	AcOH	75	4 h	61
6	DMAc	$PhI(OAc)_2$	TFA	75	4 h	45
7	DMAc	$PhI(OAc)_2$	HBF_4	75	4 h	26
8	DMAc	$PhI(OAc)_2$	$(CH_2COOH)_2$	75	4 h	trace
9	DMAc	$PhI(OAc)_2$	HCl	75	4 h	n.d.
10	DMAc	$PhI(OAc)_2$	DMAP	75	4 h	n.d.
11	DMAc	$PhI(OAc)_2$	CH_3COONa	75	4 h	n.d.
12	DMAc	$PhI(OAc)_2$	Et_3N	75	4 h	11
13	DMAc	$PhI(OAc)_2$	K_3PO_4	75	4 h	n.d.
14	DMAc	$PhI(OAc)_2$	Na_2CO_3	75	4 h	42
15	DMAc	$NaIO_4$	AcOH	75	4 h	44
16	DMAc	$PhI(OTFA)_2$	AcOH	75	4 h	23
17	DMAc	I_2	AcOH	75	4 h	n.d.
18	DMAc	$PhI(OAc)_2$	AcOH	23	4 h	25
19	DMAc	$PhI(OAc)_2$	AcOH	45	4 h	48
20	DMAc	$PhI(OAc)_2$	AcOH	65	4 h	52
21	DMAc	$PhI(OAc)_2$	AcOH	85	4 h	73
22	DMAc	$PhI(OAc)_2$	AcOH	95	4 h	51
23	DMAc	$PhI(OAc)_2$	AcOH	85	2 h	24
24	DMAc	$PhI(OAc)_2$	AcOH	85	6 h	69
25	DMAc	$PhI(OAc)_2$	AcOH	23	8 h	45
26	DMAc	$PhI(OAc)_2$	AcOH	23	12 h	60
27	DMAc	$PhI(OAc)_2$	AcOH	23	18 h	59
28[c]	DMAc	$PhI(OAc)_2$	AcOH	23	12 h	71
29[d]	DMAc	$PhI(OAc)_2$	AcOH	23	12 h	**81**
30[e]	DMAc	$PhI(OAc)_2$	AcOH	23	12 h	64

[a] Reaction conditions: **3** (0.25 mmol), $PhI(OAc)_2$ (0.5 mmol), AcOH (1.0 mmol), DMAc (2.0 mL), 23 °C, 12 h,

[b] Yield of isolated product. DMAc = *N,N*-Dimethylacetamide, TFA = Trifluoroacetic acid.

[c] AcOH (2.5 mmol). [d] AcOH (5.0 mmol). [e] AcOH (7.5 mmol)

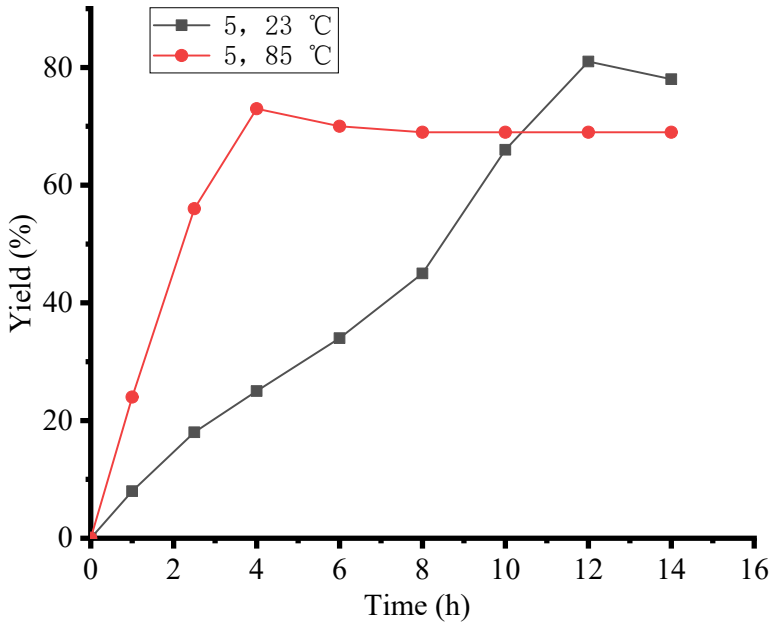
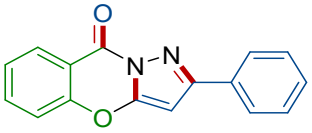
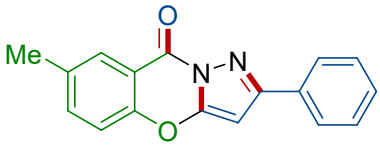


Fig. S1 Yield vs. time trend chart of product **5** at two different temperatures (23 and 85 °C)

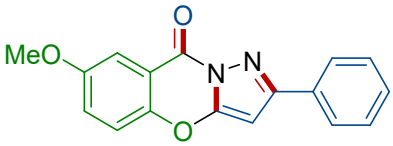
6. Product Characterization



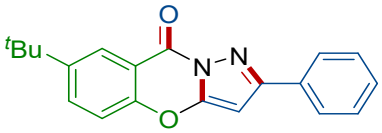
2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(5).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 81% yield; m.p. = 200–202 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, *J* = 8.1, 1.7 Hz, 1H), 8.09 – 7.90 (m, 2H), 7.78 (ddd, *J* = 8.8, 7.2, 1.7 Hz, 1H), 7.45 (qd, *J* = 6.3, 3.4 Hz, 5H), 6.43 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.2, 153.9, 153.8, 152.2, 136.0, 131.6, 129.9, 128.8, 128.8, 126.8, 125.2, 117.0, 114.2, 86.7. HR-MS（ESI）calcd for $C_{16}H_{11}N_2O_2^+$ [M+H]$^+$: 263.0821, found 263.0819.



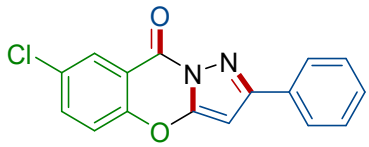
7-methyl-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(6).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a pale yellowish white solid: 87% yield; m.p. = 206–207 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 1.1 Hz, 1H), 8.02 – 7.93 (m, 6H), 7.55 (dd, *J* = 8.5, 2.3 Hz, 3H), 7.48 – 7.37 (m, 9H), 7.31 (d, *J* = 8.5 Hz, 3H), 6.39 (s, 3H), 2.46 (s, 8H).. ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.0, 153.8, 152.2, 151.9, 136.9, 135.2, 131.6, 129.8, 128.7, 128.1, 126.7, 116.6, 113.7, 86.4, 20.7. HR-MS（ESI）calcd for $C_{17}H_{13}N_2O_2^+$ [M+H]$^+$: 277.0977, found 277.0983.



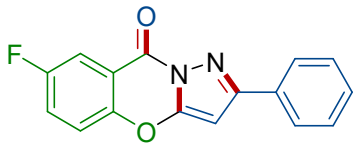
7-methoxy-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(7).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a pale yellowish white solid: 79% yield; m.p. = 215–216 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 6.6 Hz, 2H), 7.72 (s, 1H), 7.44 (q, *J* = 7.3, 6.8 Hz, 3H), 7.34 (d, *J* = 6.9 Hz, 2H), 6.39 (s, 1H), 3.91 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.8, 156.2, 153.9, 152.2, 148.4, 131.6, 129.9, 128.8, 126.9, 125.4, 118.3, 114.4, 108.5, 86.3, 56.3. HR-MS（ESI）calcd for $C_{17}H_{13}N_2O_3^+$ [M+H]$^+$: 293.0926, found 293.0815.



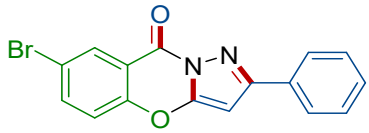
7-(tert-butyl) -2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(8).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 63.9% yield; m.p. = 136-137 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.36 (t, *J* = 2.9 Hz, 1H), 8.01 (ddd, *J* = 8.3, 4.3, 1.8 Hz, 2H), 7.82 (dt, *J* = 8.5, 2.8 Hz, 1H), 7.44 (tdd, *J* = 14.2, 5.5, 2.4 Hz, 3H), 7.40 – 7.36 (m, 1H), 6.41 (dd, *J* = 4.8, 2.0 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.1, 154.1, 152.3, 151.9, 148.7, 133.8, 131.7, 129.9, 128.8, 126.9, 124.8, 116.6, 113.6, 86.5, 35.0, 31.4. HR-MS（ESI）calcd for $C_{20}H_{18}N_2NaO_2^+$ [M+Na]$^+$: 342.1344, found 342.1342.



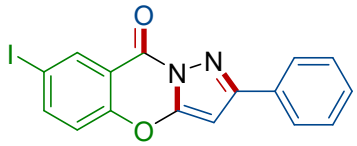
7-chloro-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(9).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 71.2% yield; m.p. = 195-197 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.41 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 7.4 Hz, 2H), 7.79 (t, *J* = 7.8 Hz, 1H), 7.49 – 7.44 (m, 4H), 6.44 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 152.7, 152.3, 151.9, 136.1, 131.4, 130.9, 130.2, 128.9, 128.1, 126.9, 118.7, 115.4, 87.1. HR-MS（ESI）calcd for $C_{16}H_{10}ClN_2O_2^+$ $[M+H]^+$: 297.0431, found 297.0439.



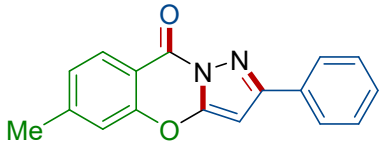
7-fluoro-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(10).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 77.2% yield; m.p. = 225-226 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.06 (d, *J* = 9.4 Hz, 1H), 8.00 (d, *J* = 6.5 Hz, 2H), 7.50 – 7.42 (m, 5H), 6.45 (s, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 157.9, 156.6, 152.9, 152.1, 131.4, 130.1, 128.9, 126.9, 124.1, 123.8, 119.1, 119.0, 114.3, 114.0, 86.9. HR-MS（ESI）calcd for $C_{16}H_{10}FN_2O_2^+$ $[M+H]^+$: 281.0721 , found 281.0712.



7-bromo-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(11).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 67% yield; m.p. = 246-247 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 7.4 Hz, 2H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 4H), 6.44 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3 (s), 165.7 (s), 155.1 (d, *J* = 11.7 Hz), 152.8 (s), 152.1 (s), 135.9 (s), 131.3 (d, *J* = 11.0 Hz), 129.8 (s), 129.1 (s), 128.0 (s), 114.0 (s), 113.8 (s), 110.9 (s), 104.5 (s), 104.2 (s), 86.9 (s). HR-MS（ESI）calcd for $C_{16}H_{10}BrN_2O_2^+$ $[M+H]^+$:388.9787, found 388.9796.

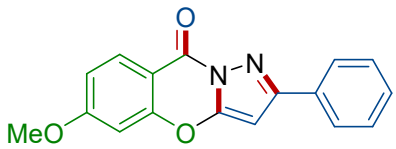


7-iodo-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(12).** This title compound was prepared according to the general working procedure to give the product as a white solid with yield of 61.5%.; m.p. = 278-280 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (d, *J* = 2.0 Hz, 1H), 8.04 (dd, *J* = 8.8, 2.1 Hz, 1H), 8.02 – 7.97 (m, 2H), 7.46 (d, *J* = 7.0 Hz, 3H), 7.23 (d, *J* = 8.8 Hz, 1H), 6.46 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.6, 153.5, 152.5, 151.9, 144.6, 137.3, 131.4, 130.2, 128.9, 126.9, 119.1, 116.1, 87.9, 87.2. HR-MS（ESI）calcd for $C_{16}H_{10}IN_2O_2^+$ $[M+H]^+$:388.9787, found 388.9796.

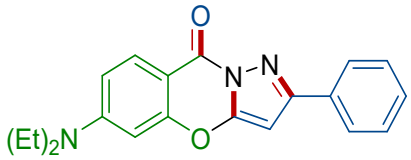


6-methyl-2-phenyl-9H-benzo[e]pyrazolo[5,1-*b*][1,3]oxazin-9-one **(13).** This title compound was prepared

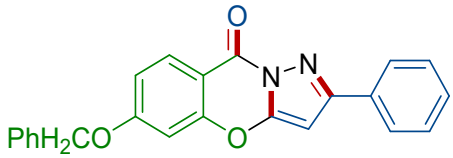
according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 67.2% yield; m.p. = 186-187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.99 (d, *J* = 6.6 Hz, 2H), 7.44 (q, *J* = 7.9, 7.1 Hz, 3H), 7.22 (s, 2H), 6.40 (s, 1H), 2.51 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 153.9, 153.8, 152.2, 147.9, 131.7, 129.9, 128.8, 128.5, 126.8, 126.6, 116.9, 111.7, 86.6, 22.2. HR-MS（ESI）calcd for $C_{17}H_{13}N_2O_2^+$ [M+H]$^+$: 277.0977, found 277.0983.



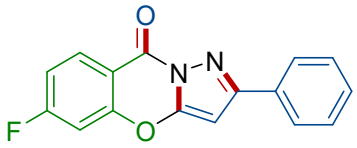
6-methoxy-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(14).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 61.5% yield; m.p. = 208-209 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.9 Hz, 1H), 7.98 (d, *J* = 7.1 Hz, 2H), 7.43 (dt, *J* = 14.3, 6.9 Hz, 3H), 6.97 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.84 (d, *J* = 2.2 Hz, 1H), 6.39 (s, 1H), 3.93 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.8, 155.7, 155.5, 153.5, 152.2, 131.6, 130.0, 129.7, 128.7, 126.7, 113.4, 107.2, 100.3, 86.5, 56.1. HR-MS（ESI）calcd for $C_{17}H_{13}N_2O_3^+$ [M+H]$^+$:293.0926, found 293.0815.



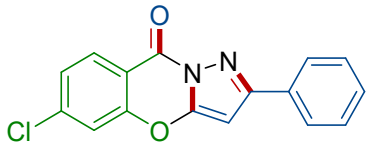
6-(diethylamino)-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(15).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 58.5% yield; m.p. = 179-180 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 9.86 (s, 1H), 7.72 (d, *J* = 8.9 Hz, 1H), 7.67 – 7.62 (m, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 2H), 6.59 (d, *J* = 8.9 Hz, 1H), 6.36 (d, *J* = 1.8 Hz, 1H), 3.42 (q, *J* = 7.1 Hz, 4H), 1.21 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (151 MHz, cdcl$_3$) δ 186.3, 153.2, 153.1, 152.2, 133.4, 133.2, 131.2, 128.8, 119.3, 116.2, 109.2, 104.4, 89.1, 80.2, 45.1, 12.5. HR-MS（ESI）calcd for $C_{16}H_{11}N_2O_2^+$ [M+H]$^+$: 331.1556, found 331.1554.



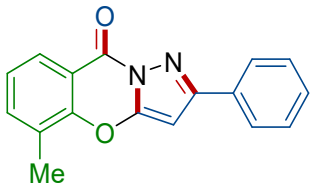
6-phenoxy-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(16).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 52.3% yield; m.p. =154-155 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (s, 1H), 7.99 (s, 2H), 7.42 (qd, *J* = 12.6, 11.6, 5.1 Hz, 8H), 7.03 (s, 1H), 6.91 (s, 1H), 6.38 (s, 1H), 5.18 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 155.7, 155.7, 153.6, 152.3, 135.4, 131.7, 130.2, 129.8, 128.9, 128.8, 128.7, 127.7, 126.8, 114.1, 107.5, 101.4, 86.6, 70.9. HR-MS（ESI）calcd for $C_{23}H_{17}N_2O_3^+$ [M+H]$^+$: 392.1137, found 392.1235.



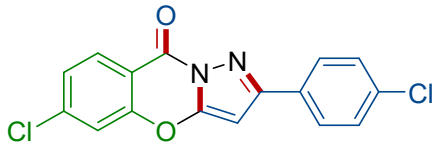
6-fluoro-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(17).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 72.4% yield; m.p. =274-278 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 8.8, 6.0 Hz, 1H), 7.98 (d, *J* = 7.3 Hz, 2H), 7.44 (d, *J* = 7.2 Hz, 3H), 7.23 – 7.10 (m, 2H), 6.44 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 165.8, 156.2, 155.2, 155.1, 152.9, 152.1, 131.4, 131.4, 131.3, 130.1, 128.9, 126.8, 113.9, 113.7, 111.1, 111.0, 104.5, 104.3, 87.1. HR-MS（ESI）calcd for $C_{16}H_{10}FN_2O_2^+$ [M+H]$^+$: 281.0721, found 281.0712.



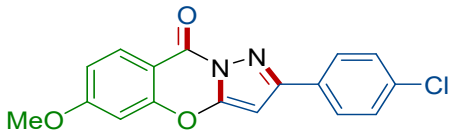
6-chloro-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(18).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 69.5% yield; m.p. =248-249 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (d, *J* = 8.5 Hz, 1H), 7.97 (dd, *J* = 7.6, 1.9 Hz, 2H), 7.49 – 7.39 (m, 5H), 6.44 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.4, 154.0, 153.0, 151.9, 142.2, 131.4, 130.1, 129.9, 128.9, 126.8, 126.1, 117.3, 112.9, 87.2. HR-MS（ESI）calcd for $C_{16}H_{10}ClN_2O_2^+$ [M+H]$^+$: 297.0439, found 297.0431.



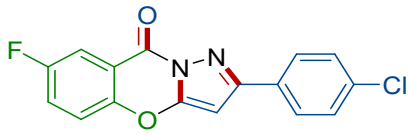
5-methyl-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(19).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 79% yield; m.p. =196-197 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.22 (s, 1H), 8.03 – 7.96 (m, 2H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.47 – 7.40 (m, 3H), 7.32 (t, *J* = 7.6 Hz, 1H), 6.45 (s, 1H), 2.52 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 156.1, 154.0, 152.3, 152.2, 137.1, 131.7, 129.9, 128.8, 126.8, 126.6, 126.4, 124.7, 114.0, 86.7, 15.6. HR-MS（ESI）calcd for $C_{17}H_{13}N_2O_2^+$ [M+H]$^+$: 277.0977, found 277.0983.



7-chloro-2-(4-chlorophenyl)-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(20).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 74.5% yield; m.p. =282-283 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 2.5 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.74 (dd, *J* = 8.9, 2.6 Hz, 1H), 7.44 (dd, *J* = 8.7, 1.8 Hz, 3H), 6.44 (s, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.6, 152.2, 136.2, 131.0, 129.8, 129.1, 128.0, 118.6, 115.2, 86.9. HR-MS（ESI）calcd for $C_{16}H_9Cl_2N_2O_2^+$ [M+H]$^+$: 331.0036, found 331.0041.

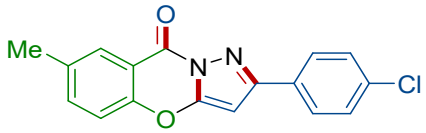


6-methoxy-2-(4-chlorophenyl)-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(21).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 86.2% yield; m.p. =208-209 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.26 (dd, *J* = 8.8, 3.5 Hz, 1H), 7.94 – 7.87 (m, 2H), 7.41 (dd, *J* = 8.4, 3.5 Hz, 2H), 6.99 – 6.94 (m, 1H), 6.86 – 6.81 (m, 1H), 6.35 (d, *J* = 3.5 Hz, 1H), 3.94 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 155.8, 154.5, 153.5, 152.4, 135.8, 130.3, 130.2, 129.1, 128.0, 113.7, 107.2, 100.4, 86.5, 56.2. HR-MS（ESI）calcd for $C_{17}H_{11}ClN_2O_3^+$ [M+H]$^+$: 327.0536, found 327.0535.

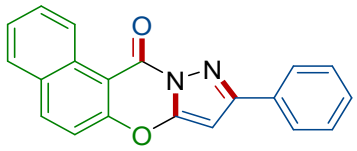


6-fluoro-2-(4-chlorophenyl)-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(22).** This title compound was prepared

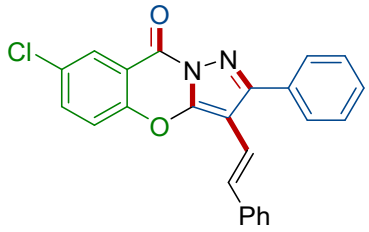
according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 80.2% yield; m.p. =254-255 °C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.43 (dd, *J* = 8.8, 6.1 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.24 – 7.13 (m, 2H), 6.43 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 165.7, 155.1, 155.0, 152.8, 152.1, 135.9, 131.3, 131.2, 129.8, 129.1, 128.0, 114.0, 113.8, 110.9, 104.5, 104.2, 86.9. HR-MS（ESI）calcd for $C_{16}H_8ClFN_2NaO_2^+$ [M+Na]$^+$: 338.0234, found 338.0224.



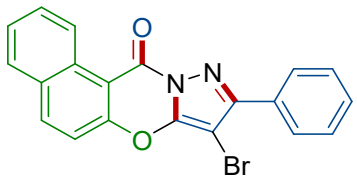
7-methyl-2-(4-chlorophenyl)-2-phenyl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(23).** This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a white solid: 60.2% yield; m.p. =220-221 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.95 (d, *J* = 8.3 Hz, 2H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 1H), 6.40 (s, 1H), 2.49 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9, 153.8, 152.3, 152.0, 137.2, 135.8, 135.4, 130.1, 129.0, 128.2, 128.0, 116.8, 113.7, 86.4, 20.9. HR-MS（ESI）calcd for $C_{16}H_{11}N_2O_2^+$ [M+H]$^+$: 311.0587, found 311.0577.



2-phenyl-11H-naphtho[2,3-e]pyrazolo[5,1-b][1,3]oxazin-11-one **(24)**. This title compound was prepared according to the general working procedure and purified by recrystallisation to give the product as a yellow solid: 57% yield; m.p.=289-290 °C; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 9.85 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 9.1 Hz, 1H), 8.04 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.91 (d, *J* = 8.1 Hz, 1H), 7.86 – 7.76 (m, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.54 – 7.40 (m, 4H), 6.53 (s, 1H), 5.29 (s, CH_2Cl_2). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 155.5, 155.3, 154.2, 150.9, 137.8, 131.7, 131.1, 130.6, 130.2, 129.7, 128.7, 128.7, 126.7, 126.6, 126.5, 116.3, 106.4, 86.0. HR-MS（ESI）calcd for $C_{20}H_{12}N_2NaO_2^+$ [M+Na]$^+$ 335.0976, found 335.0791.



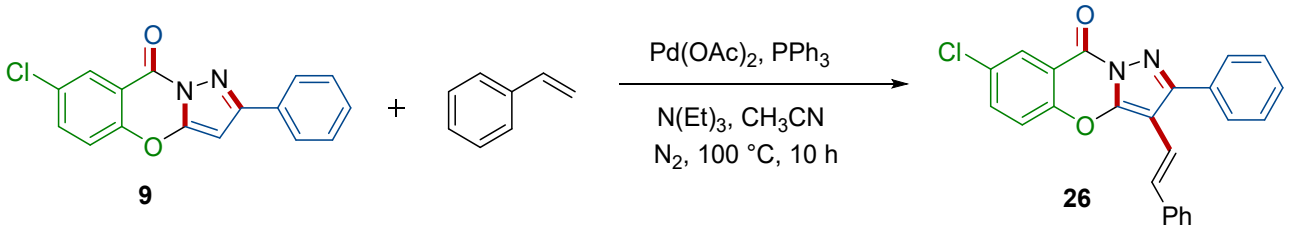
(E)-7-chloro-2-phenyl-3-styryl-9H-benzo[e]pyrazolo[5,1-b][1,3]oxazin-9-one **(26)**. This title compound was prepared according to the general working procedure and purified by column chromatography to give the product as a yellow solid: 76.6% yield; m.p. =296-297 °C; ^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.42 (s, 1H), 8.10 (d, *J* = 8.1 Hz, 1H), 7.83 (t, *J* = 8.0 Hz, 3H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 6.6 Hz, 3H), 7.31 (t, *J* = 5.7 Hz, 4H), 6.95 (s, 1H).^{13}C NMR (151 MHz, $CDCl_3$) δ 163.64, 163.45, 145.17, 141.80, 135.7, 135.7, 135.2, 133.9, 130.7, 129.9, 129.9, 129.8, 129.7, 128.9, 128.6, 128.3, 125.7, 125.3, 121.2. HR-MS（ESI）calcd for $C_{24}H_{16}ClN_2O_2^+$ [M+H]$^+$: 399.0900, found 399.0904.



3-bromo-2-phenyl-11H-naphtho[2,3-e]pyrazolo[5,1-b][1,3]oxazin-11-one **(27).** This title compound was prepared according to the general working procedure and purified by recrystallisation to give the product as a yellow solid: 82% yield; m.p. =287-288 ^{o}C; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.82 (d, *J* = 8.7 Hz, 1H), 8.26 (d, *J* = 9.0 Hz, 1H), 8.20 – 8.15 (m, 2H), 7.96 (d, *J* = 6.5 Hz, 1H), 7.86 (ddd, *J* = 8.6, 7.0, 1.4 Hz, 1H), 7.69 – 7.60 (m, 2H), 7.58 – 7.51 (m, 3H), 4.12 (q, O*CH$_2$-Ethyl acetate*), 2.04 (s, *CH$_3$*CO-*Ethyl acetate*), 1.64 (s, H_2O), 1.26 (t, *CH$_3$*CH$_2$-*Ethyl acetate*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.4, 153.5, 152.7, 148.2, 138.3, 131.0, 130.8, 130.7, 130.5, 129.9, 128.8, 128.5, 128.4, 126.9, 126.4, 116.4, 106.5. HR-MS（ESI）calcd for $C_{20}H_{11}BrN_2O_2^+$ $[M+H]^+$: 391.0082, found 391.0077.

7. Synthetic Application

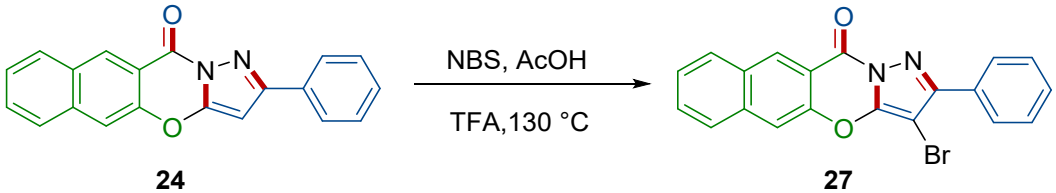
7.1 Transformation of product 9



9 26

In a nitrogen atmosphere, 4-aminomethylbenzoic acid (**9**, 0.2 mmol, 59.3 mg), palladium acetate (0.01 mmol), triphenylphosphine (0.02 mmol), styrene (0.4 mmol), triethylamine (0.2 mmol), and acetonitrile (0.5 mL) were subjected to a reaction at 100 °C for a duration of 10 hours. After the reaction, the mixture was gradually cooled to room temperature, followed by consecutive extractions using ethyl acetate for three cycles. The organic layers were then consolidated, treated with anhydrous sodium sulfate (Na_2SO_4) to eliminate moisture, and subsequently subjected to vacuum drying. The resultant product was further refined through purification using a mixture of petroleum ether and ethyl acetate in a 1:2 ratio as the eluent. This process yielded a white solid weighing 45.6 mg, yielding 76.6%.

7.2 Transformation of product 24



24 27

A solution of the **24** (0.2 mmol, 62.4 mg) and the 1.1 equiv of NBS in HOAc (1 mL) was heated at gentle reflux (open con denser) with the reaction progress followed by TLC. After the reaction, the mixture was gradually cooled to room temperature, followed by consecutive extractions using ethyl acetate for three cycles. The organic layers were then consolidated, treated with anhydrous sodium sulfate (Na_2SO_4) to eliminate moisture, and subsequently subjected to vacuum drying. The resultant product was further refined through purification using a mixture of petroleum ether and ethyl acetate in a 1:2 ratio as the eluent. This process yielded a yellow solid weighing 53 mg, yielding 82 %.

7.3 Fluorescence analysis of product 7

Taking product **7** as the representative, its ultraviolet absorption spectrum and fluorescence absorption spectrum were tested, as shown in Figure S2.

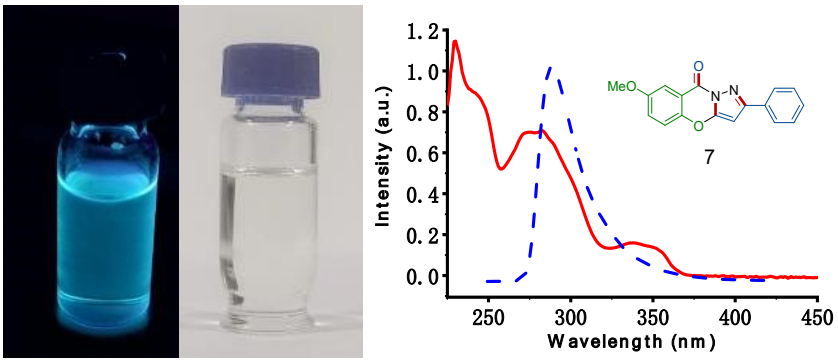


Fig. S2 The UV (displayed in red) and fluorescence (represented by blue) spectra of product **7**

7.4 MH7A assay

Cell seeding:

MH7A cells in the logarithmic growth phase were chosen. A single-cell suspension of 8000 cells/mL was prepared after cell counting, with 100 μL inoculated per well in a 96-well plate.

Preparation of test sample solutions:

Suitable samples were weighed and dissolved in DMEM medium under aseptic conditions to prepare concentrations of 12.5, 25, 50, 100, and 200 μg/mL for each sample solution.

The anti-inflammatory effects of products 6,8 and 20-22 on MH7A cells were determined by CCK-8 method:

Detailed cell preparation:

1. MH7A cells in the logarithmic growth phase were selected.
2. The original cell culture medium in the cell culture bottle was aspirated.
3. 2 mL of PBS was added and washed 1-2 times, then the PBS was aspirated.
4. 1 mL of trypsin was added, and the bottom of the cell bottle was tapped. Under the microscope, it was observed that the cells became round and detached from the bottom of the bottle.
5. 2 mL of cell culture medium was added to terminate digestion. The cell suspension was gently pipetted up and down.
6. The cell suspension was transferred to a centrifuge tube and centrifuged at 1200 rpm for 5 minutes.
7. The supernatant was aspirated, and 1 mL of cell culture medium was added. The cells were gently resuspended by pipetting.
8. In a 1.5 mL EP tube, 100 μL of the cell suspension and 900 μL of cell culture medium were added (diluted 10 times), and gently mixed.
9. Cell counting was performed under a microscope using a cell counting plate, and the cell concentration was adjusted to 8000 cells/well.
10. The cells were inoculated into a 96-well plate and incubated in a 5% CO_2, 100% humidity, 37 °C incubator.
11. After the cell adhesion growth in each well reached 70-80%, the cells were stimulated with TNF-α (10 ng/mL) for 12 hours.
12. The cells were then treated with different concentrations (12.5, 25, 50, 100, 200 μg/mL) for 24 hours.
13. 10 μL of CCK-8 solution was added to each well, and the plates were incubated for 1 hour.
14. The absorbance (OD) value of each well at 450 nm was measured using an enzyme-labeled instrument, and the mean value was calculated to determine the cell survival rate.

Data processing and mapping:

The experimental data were reported as mean ± standard deviation (SD), and analysis of variance (ANOVA) was selected as the statistical method. Statistical analysis was performed using GraphPad Prism 6 software, with a significance level set at $p < 0.05$ to determine significant differences.

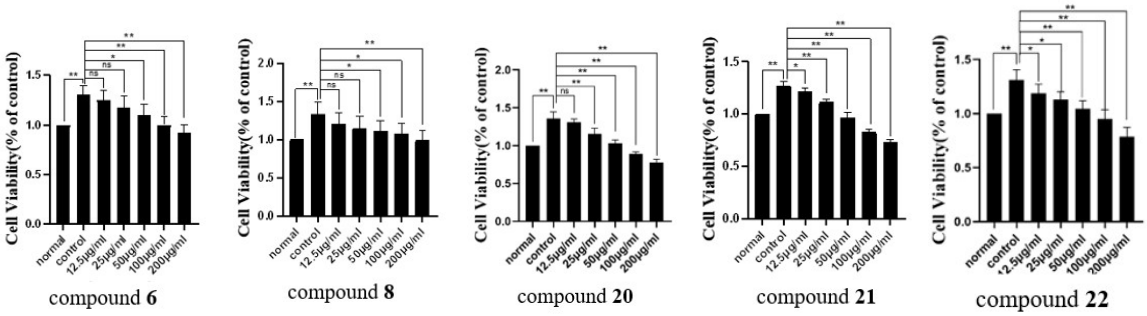


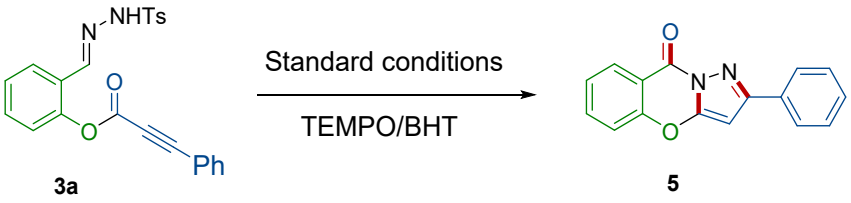
Fig. S3 The effects of products **6**, **8**, **20**, **21**, and **22** on the proliferation of MH7A cells (*p < 0.05, **p < 0.01).

Table S2 he IC_{50} values for products **6**, **8**, **20**, **21** and **22**

Products	**6**	**8**	**20**	**21**	**22**
IC_{50} (μg/mL)	88.5	115.9	120.9	64.3	49.5

8. Mechanistic Studies

8.1 Radical experiments

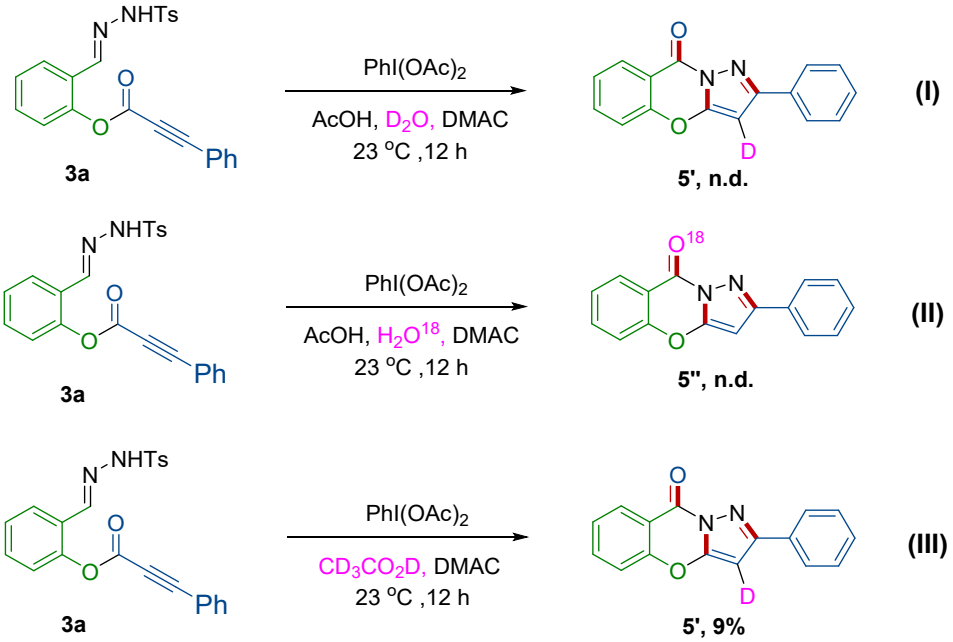


3a **5**

TEMPO (1.0 equiv.): 25 %
BHT (1.0 equiv.): 15 %

Following the prescribed procedure, the standard conditions introduced TEMPO (1.0 equiv) and BHT (1.0 equiv) into the reaction system. Upon completion of the reaction, the resultant product **5** was isolated, yielding 25% and 15% in the TEMPO and BHT systems, respectively.

8.2 Isotope experiments



(I) In a Schlenk tube, Substrate **3a** (0.5 mmol, 209.2 mg), the oxidant iodophenyldiacetic acid (1.0 mmol, 322 mg), HOAc (10 mmol, 572 µL), and D_2O (1.0 mmol, 18 µL) were meticulously weighed. This assembly was stirred at room temperature in the presence of 4 mL of DMAc, and the reaction proceeded at 23 °C for 12 hours. Following the completion of the reaction, an extraction process was carried out utilizing ethyl acetate and an unsaturated sodium chloride solution. The resultant mixture underwent column chromatography, followed by the careful drying of the sample. Elution was then performed using a petroleum ether: ethyl acetate mixture in a 3:1 ratio. This comprehensive process led to isolating a pure product (white crystal) weighing 106.5 mg, yielding an impressive 81 %.

(II) In a Schlenk tube, Substrate **3a** (0.5 mmol, 209.2 mg), the oxidant iodophenyldiacetic acid (1.0 mmol, 322 mg), HOAc (10 mmol, 572 µL), and H_2O^{18} (1.0 mmol, 20 µL) were meticulously weighed. This assembly was stirred at room temperature in the presence of 4 mL of DMAc, and the reaction proceeded at 23 °C for 12 hours. Following the completion of the reaction, an extraction process was carried out utilizing ethyl acetate and an unsaturated sodium chloride solution. The resultant mixture underwent column chromatography, followed by the careful drying of the sample. Elution was then performed using a petroleum ether: ethyl acetate mixture in a 3:1 ratio. This comprehensive process led to the isolation of a pure product (white crystal) weighing 105 mg, yielding an impressive 80 %.

(III) In a Schlenk tube, Substrate **3a** (0.5 mmol, 209.2 mg), the oxidant iodophenyldiacetic acid (1.0 mmol, 322 mg), and CD_3CO_2D (10 mmol, 572 µL) were meticulously weighed. This assembly was stirred at room temperature in the presence of 5 mL of DMAc, and the reaction proceeded at 23 °C for a span of 12 hours. Following the completion of the reaction, an extraction process was carried out utilizing ethyl acetate and an unsaturated sodium chloride solution. The resultant mixture underwent column chromatography, followed by the careful drying of the sample. Elution was then performed using a petroleum ether: ethyl acetate mixture in a 3:1 ratio. This comprehensive process led to isolating a pure product (white crystal) weighing 102.7 mg, yielding an impressive 78%.

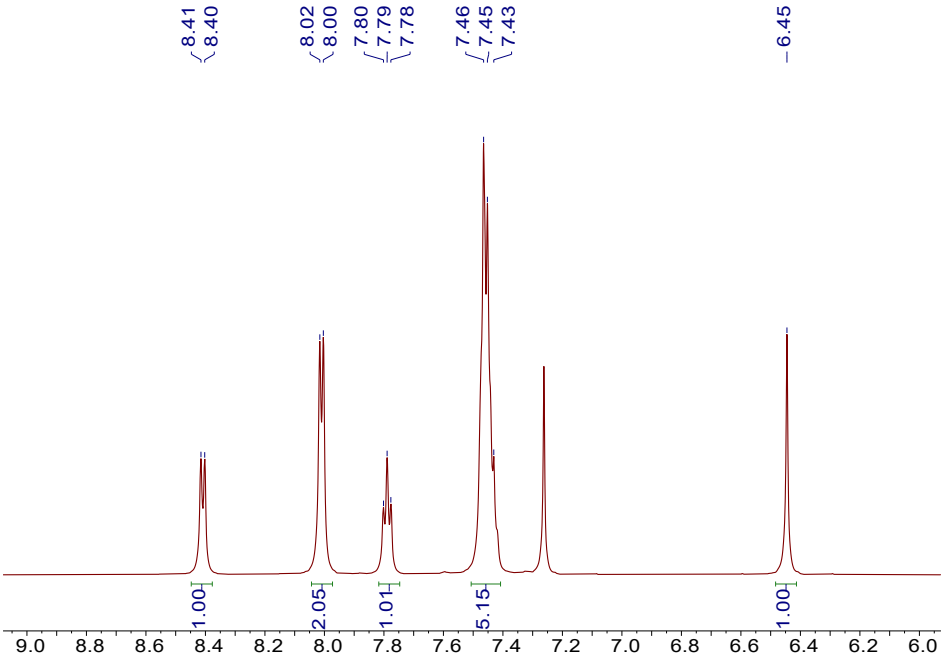


Fig. S4 The comparison of ^{1}H NMR spectra after labeling with D_2O by experiment **I**

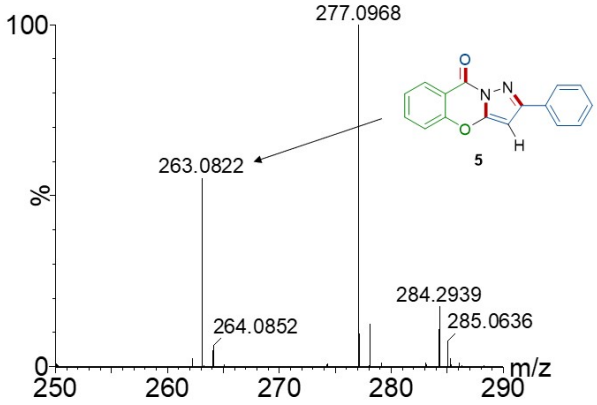


Fig.S5 High-resolution mass spectrum of product **5** after experiment **II** labeled with H_2O^{18}

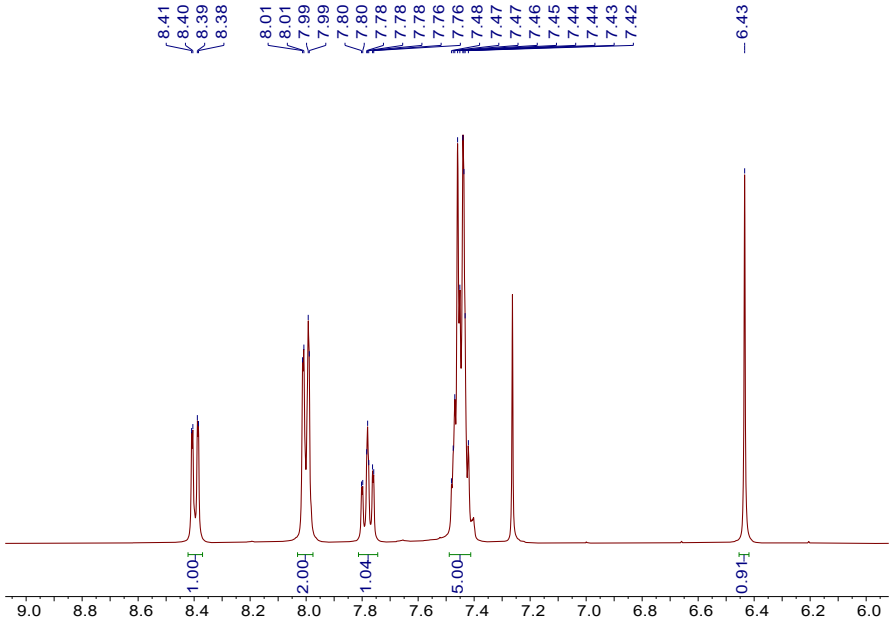
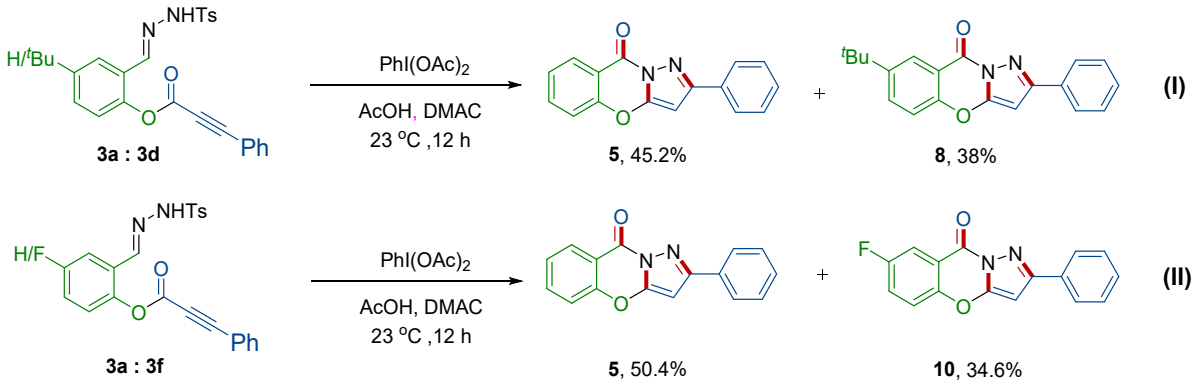


Fig.S6 ^{1}H NMR spectra of product **5** after experiment **III** labeled with CD_3CO_2D

8.3 Kinetic studies

8.3.1 Intermolecular Competition Experiments



A mixture of aldehyde **3a** and **3e** (the molar ratio being 1:1) (0.5 mmol), iodophenyldiacetic acid (1.0 mmol, 322 mg), and HOAc (10 mmol, 572 µL) were meticulously weighed. This assembly was stirred at room temperature in the presence of 4 mL of DMAc, and the reaction proceeded at 23 °C for 12 hours. Following the completion of the reaction, an extraction process was carried out utilizing ethyl acetate and an unsaturated sodium chloride solution. The resultant mixture underwent column chromatography, followed by the careful drying of the sample. Purification by column chromatography on silica gel (*n*-hexane/Dichloromethane: 1/1→1/4) yielded the corresponding products **5** (29.7 mg, 45.2%) and **4** (26.6 mg, 38%).

A mixture of aldehyde **3a** and **3f** (the molar ratio being 1:1) (0.5 mmol), iodophenyldiacetic acid (1.0 mmol, 322mg), and HOAc (10 mmol, 572 µL) were meticulously weighed. This assembly was stirred at room temperature in the presence of 4 mL of DMAc, and the reaction proceeded at 23 °C for 12 hours. Following the completion of the reaction, an extraction process was carried out utilizing ethyl acetate and an unsaturated sodium chloride solution. The resultant mixture underwent column chromatography, followed by the careful drying of the sample. Purification by column chromatography on silica gel (*n*-hexane/Dichloromethane: 1/1→1/4) yielded the corresponding products **5** (5 mg, %) and **4** (27.5mg, 34.6%).

8.3.2 Hammett Correlation Analysis

A series of reactions were performed with electronically differentiated substrate **3** under standard reaction conditions. Purification by column chromatography on silica gel afforded the desired products **4**. The Hammett correlation is listed in **Table S3**, and the corresponding result of the Hammett plot is shown in **Figure S7**.

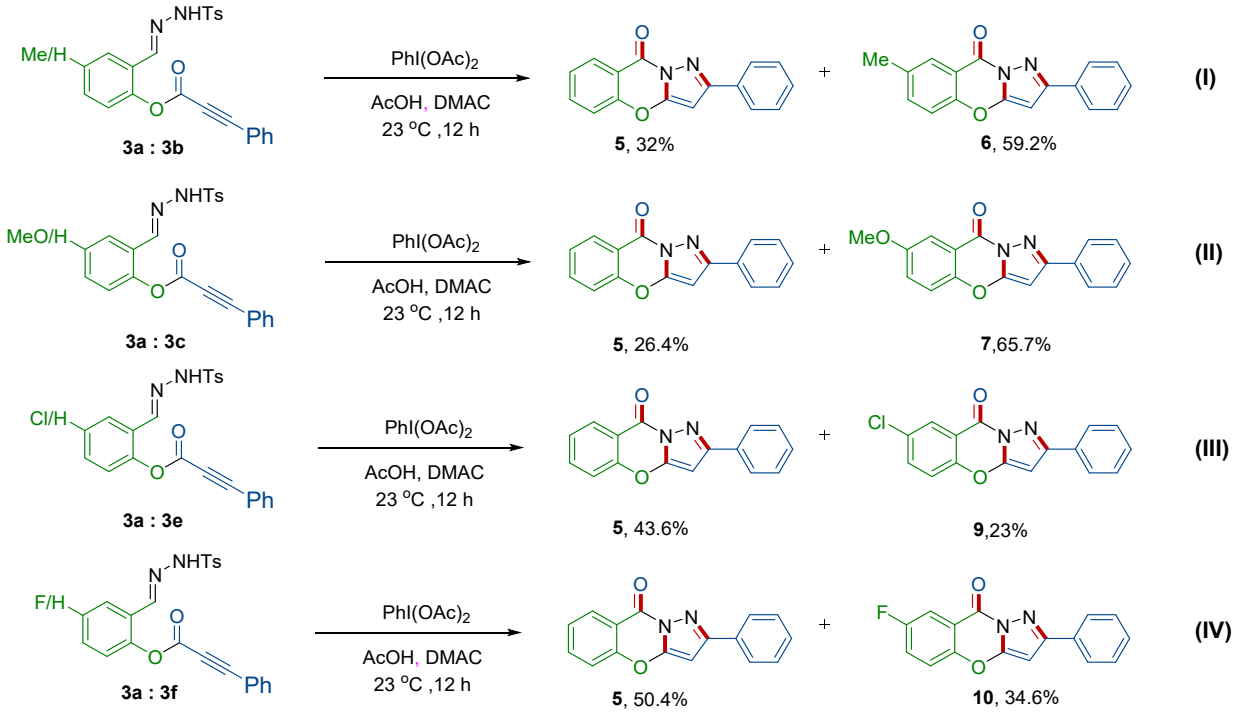


Table S3 The outcomes of the Hammett correlation analysis

R_{para}	k/k_0	$\log(k/k_0)$	σ_{para}
F	0.6863	-0.1634	0.062
Cl	0.5275	-0.2778	0.227
Me	1.8500	0.2672	-0.170
OCH_3	2.4896	0.3961	-0.268

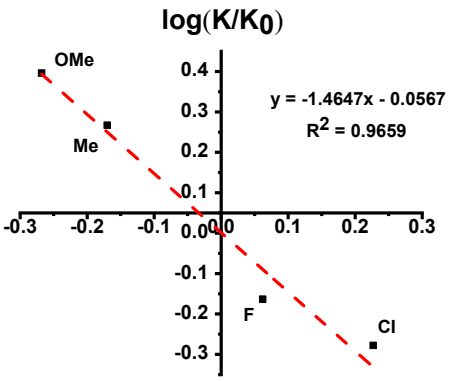


Fig. S7 Correlation of $\log(k/k_0)$ Values with σ Constants for Substrate **3** with different substituents

The Hammett equation was established in this experiment. The negative ρ (ρ = -1.46, σ_{para} = R^2 = 0.96) obtained from the Hammett correlation indicated that the positive charge was formed in the product determination step, and it was concluded that the electrophilic mechanism occurred in the C-H bond splitting step.

8.4 Possible mechanism

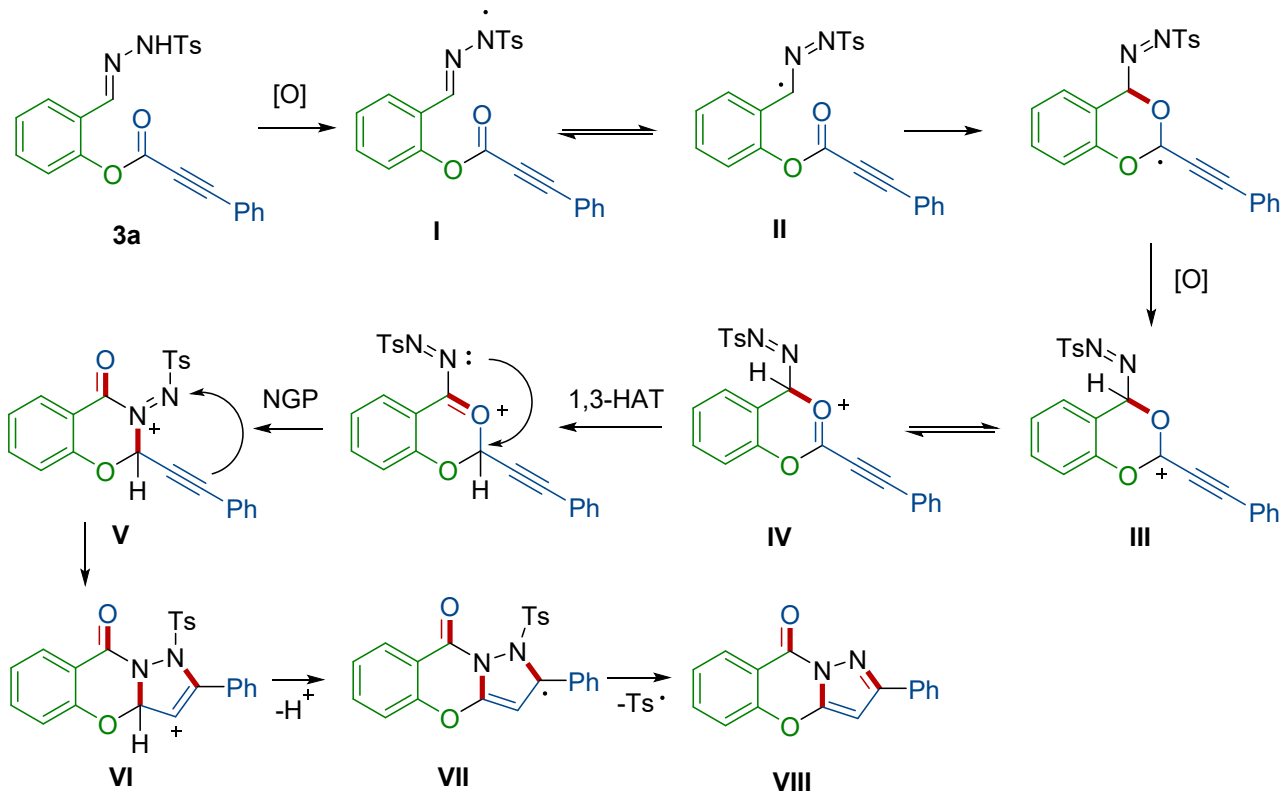


Fig. S8 Potential Reaction Mechanisms Explained

9. X-ray Crystal data

Crystallographic data for compound **6** (CCDC-2292549) has been deposited with the Cambridge Crystallographic Data Centre, Copies of the data can be obtained, free of charge, on application to CCDC (Email:deposit@ccdc.cam.ac.uk).

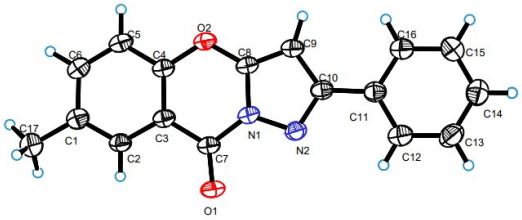


Fig. S9 Crystal Structure Analysis of Product **6** by X-ray Diffraction

Bond precision:	C-C = 0.0035 A	Wavelength=1.54184	
Cell:	a=5.65731(16)	b=5.65731(16)	c=20.6396(6)
	alpha=90	beta=93.064(2)	gamma=90
Temperature:	293 K		
	Calculated		Reported
Volume	655.79(3)		655.79(3)
Space group	P 21/n		P 1 21 1
Hall group	-P 2yb		-P 2yb
Moiety formula	C_{17} H_{12} N_2 O_2		C_{17} H_{12} N_2 O_2
Sum formula	C_{17} H_{12} N_2 O_2		C_{17} H_{12} N_2 O_2
Mr	276.29		276.29
Dx, g cm^{-3}	1.399		1.399
Z	2		2
Mu (mm^{-1})	0.759		0.759
F000	288.0		288.0
F000’	288.88		
h, k, lmax	7, 6, 25		6, 6, 25
Nref	2586[1432]		1870
Tmin, Tmax	0.827, 0.853		0.723, 1.000
Tmin’	0.875		
Correction method= # Reported T Limits: Tmin=0.723 Tmax=1.000			
AbsCorr = MULTI-SCAN			
Data completeness= 1.31/0.72		Theta(max)= 72.824	
R(reflections)= 0.0351(1822)		wR2(reflections)= 0.0949(1870)	
S = 1.058	Npar = 192		

10. Reference

[1] C. E. Song, D. U. Jung, S. Y. Choung, E. J. Roh., S. G. Lee. *Angew. Chem.Int. Edit.*, 2004, 43(45): 6183-6185.

[2] A. H. Bansode, S. R. Shaikh, R. G. Gonnade, N. T. Patil. *Chem. Commun.*, 2017, 53(65): 9081-9084.

[3] F. Li, J. Nie, L. Sun, Y. Zheng, J. A. Ma. *Angew. Chem.Int. Edit.*, 2013, 52(24):6255-8.

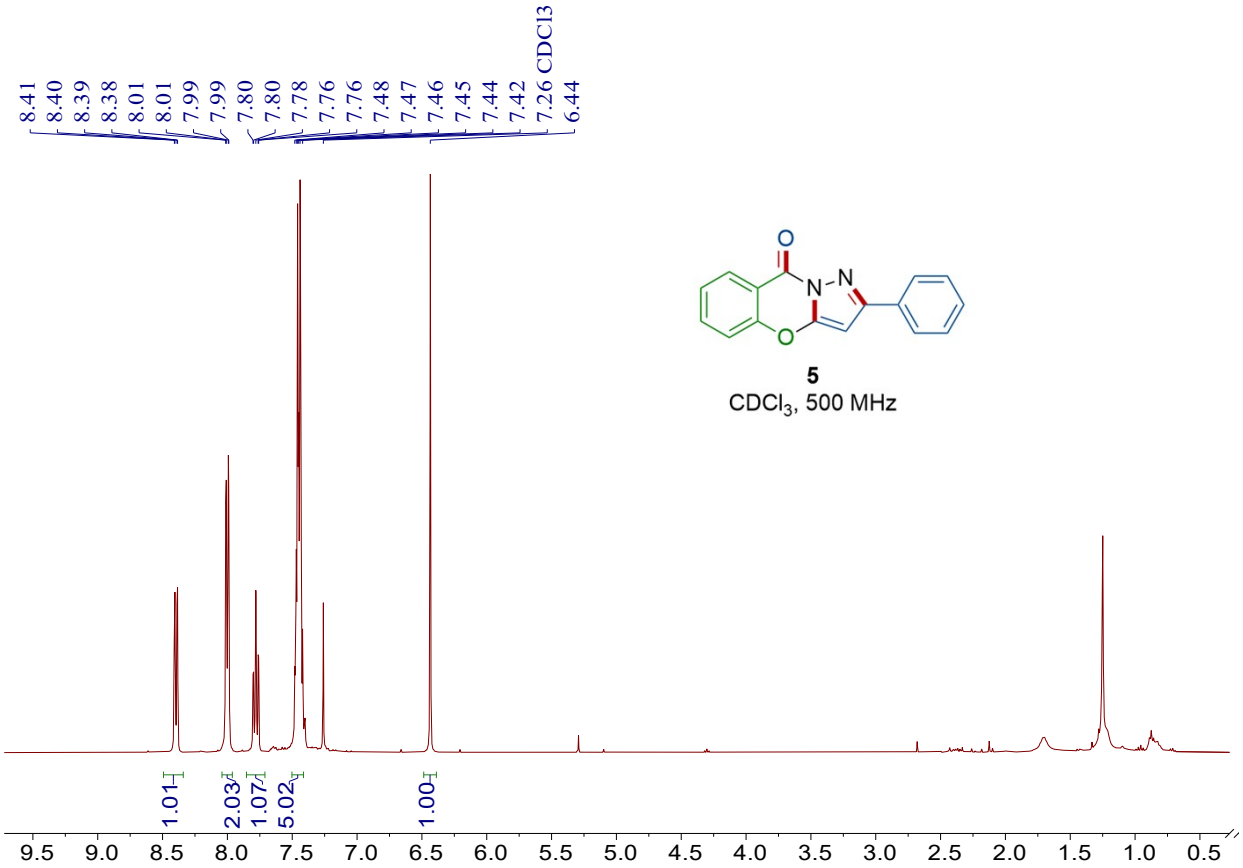
[4] B. S. Zhang, Y. T. He, Y. F. Qiu, J. Y. Hu, Y. C. Yang, Y. M. Liang. *Chem. Eur. J.*, 2015, 21(4): 1468-1473.

[5] L. Zhou, F. Ye, Y. Zhang, J. Wang. *J. Am. Chem. Soc.*, 2010, 132(39): 13590-13591.

[6] S. Manna S, K. R. Prabhu. *Org. Lett.*, 2023, 25(5): 810-815.

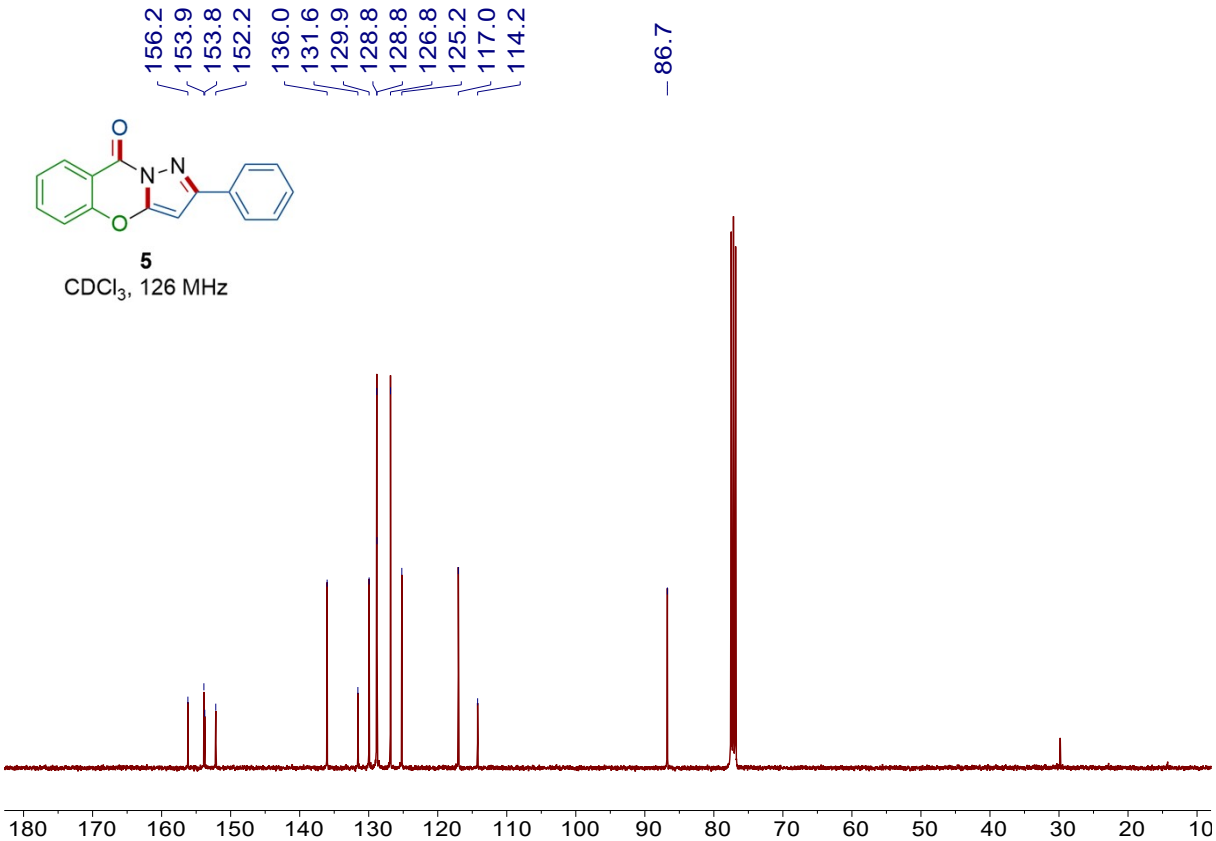
11. The ^{1}H NMR and ^{13}C NMR Spectra of products

^{1}H NMR spectrum of **5** ($CDCl_3$, 500 MHz)



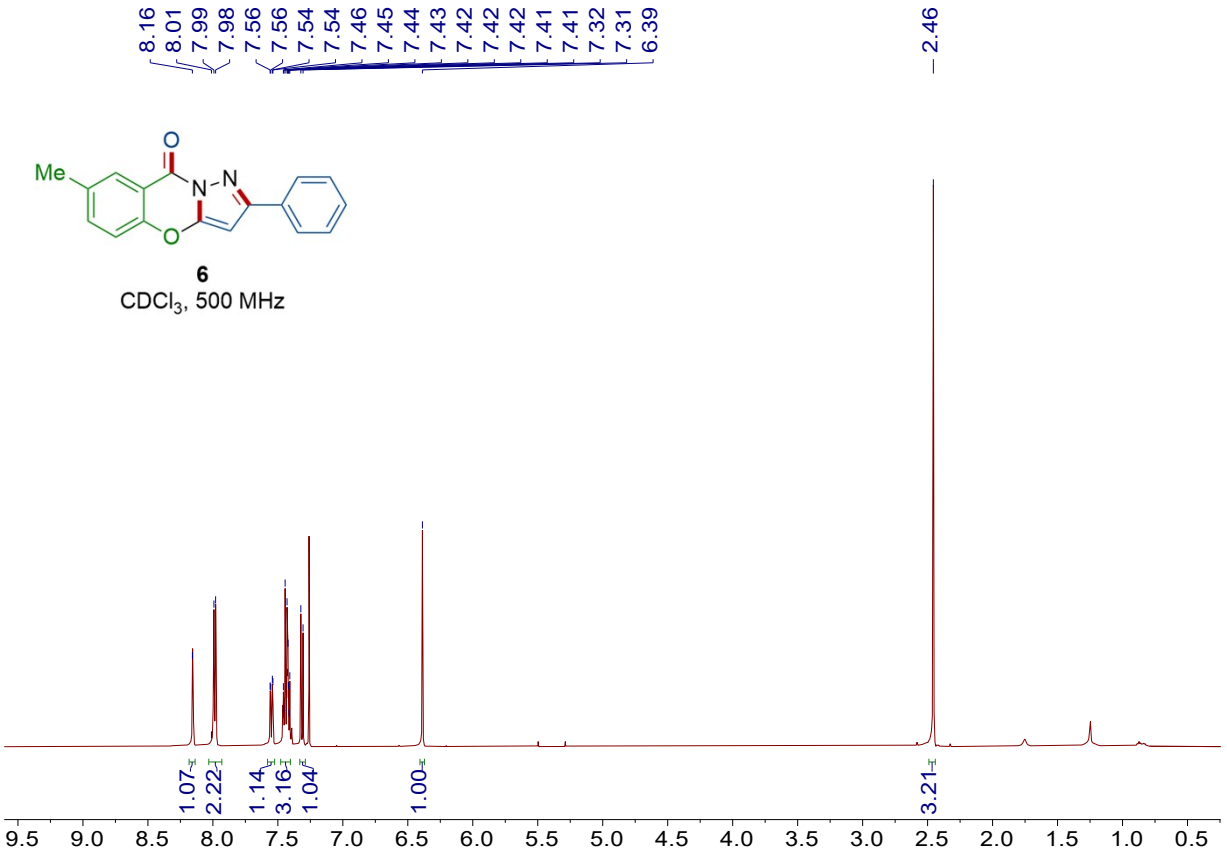
5
$CDCl_3$, 500 MHz

^{13}C NMR spectrum of **5** ($CDCl_3$, 126 MHz)

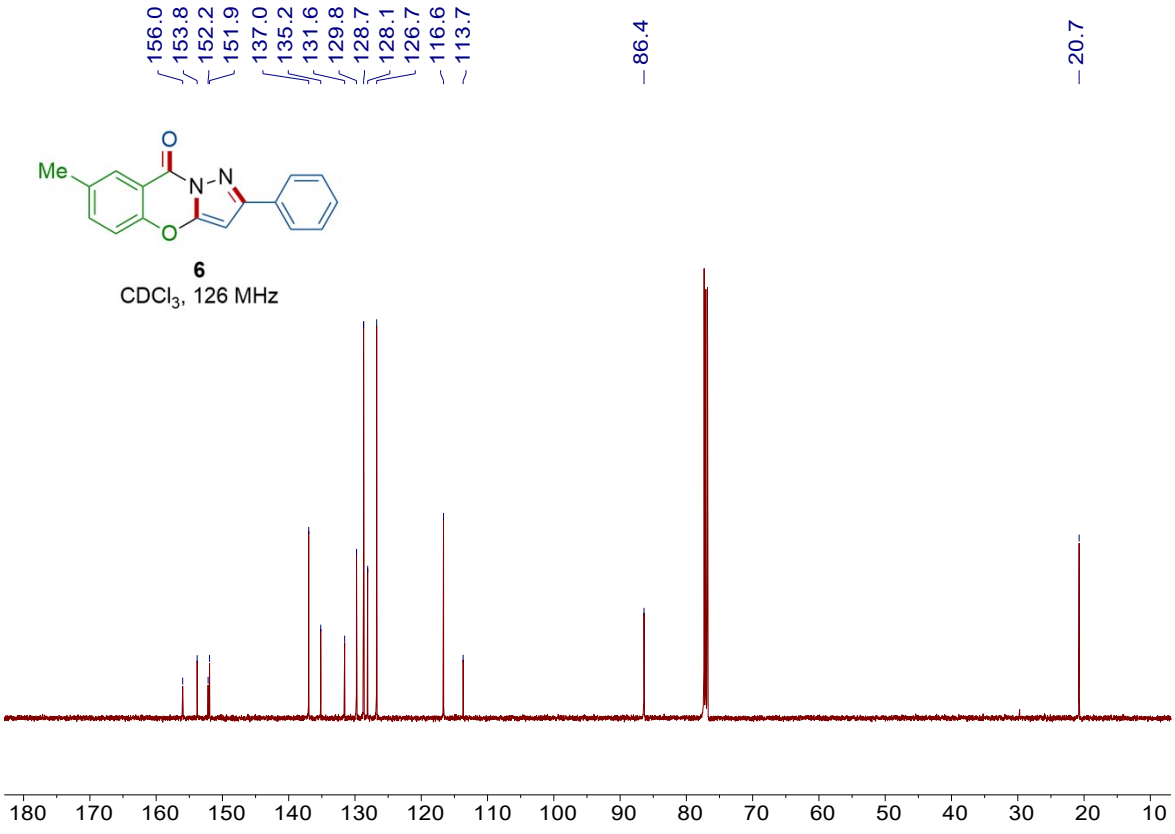


5
$CDCl_3$, 126 MHz

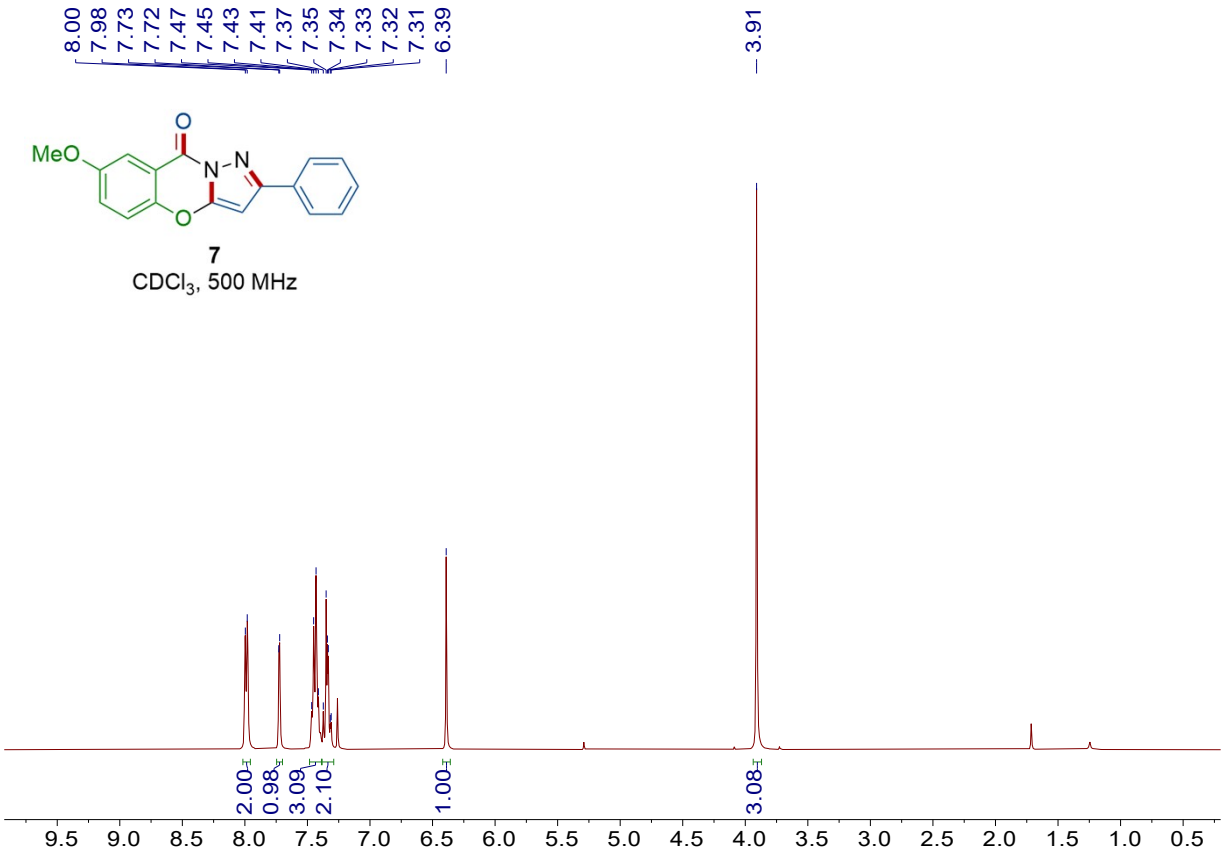
^{1}H NMR spectrum of **6** ($CDCl_3$, 500 MHz)



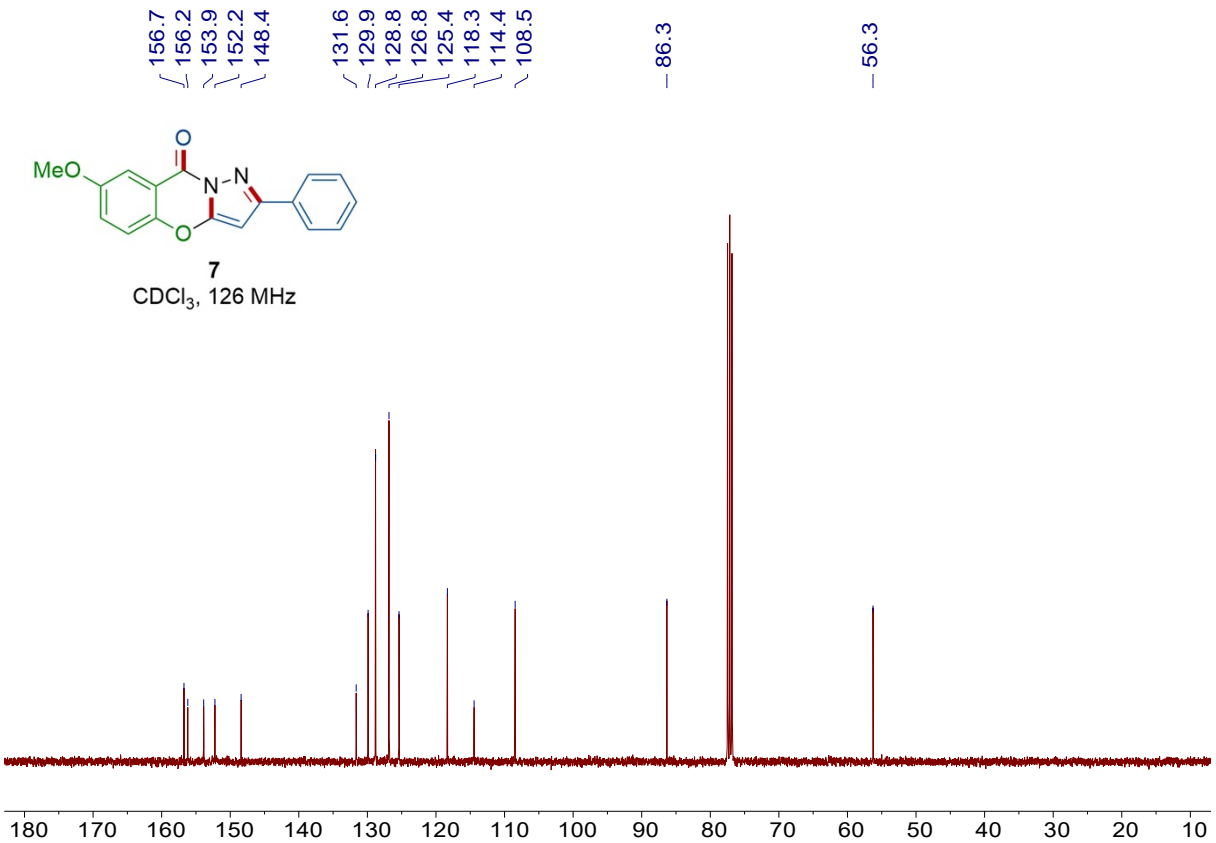
^{13}C NMR spectrum of **6** ($CDCl_3$, 126 MHz)



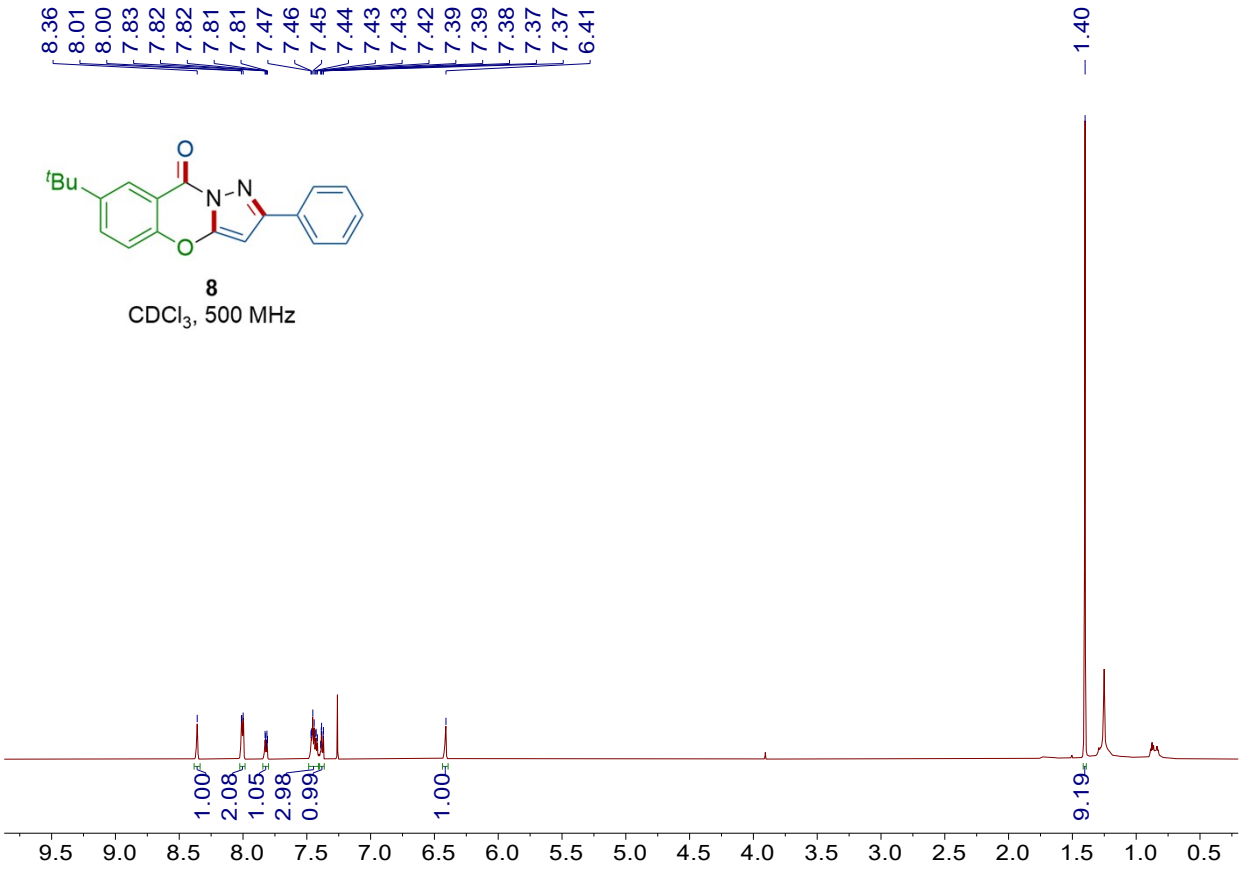
^{1}H NMR spectrum of **7** ($CDCl_3$, 500 MHz)



^{13}C NMR spectrum of **7** ($CDCl_3$, 126 MHz)

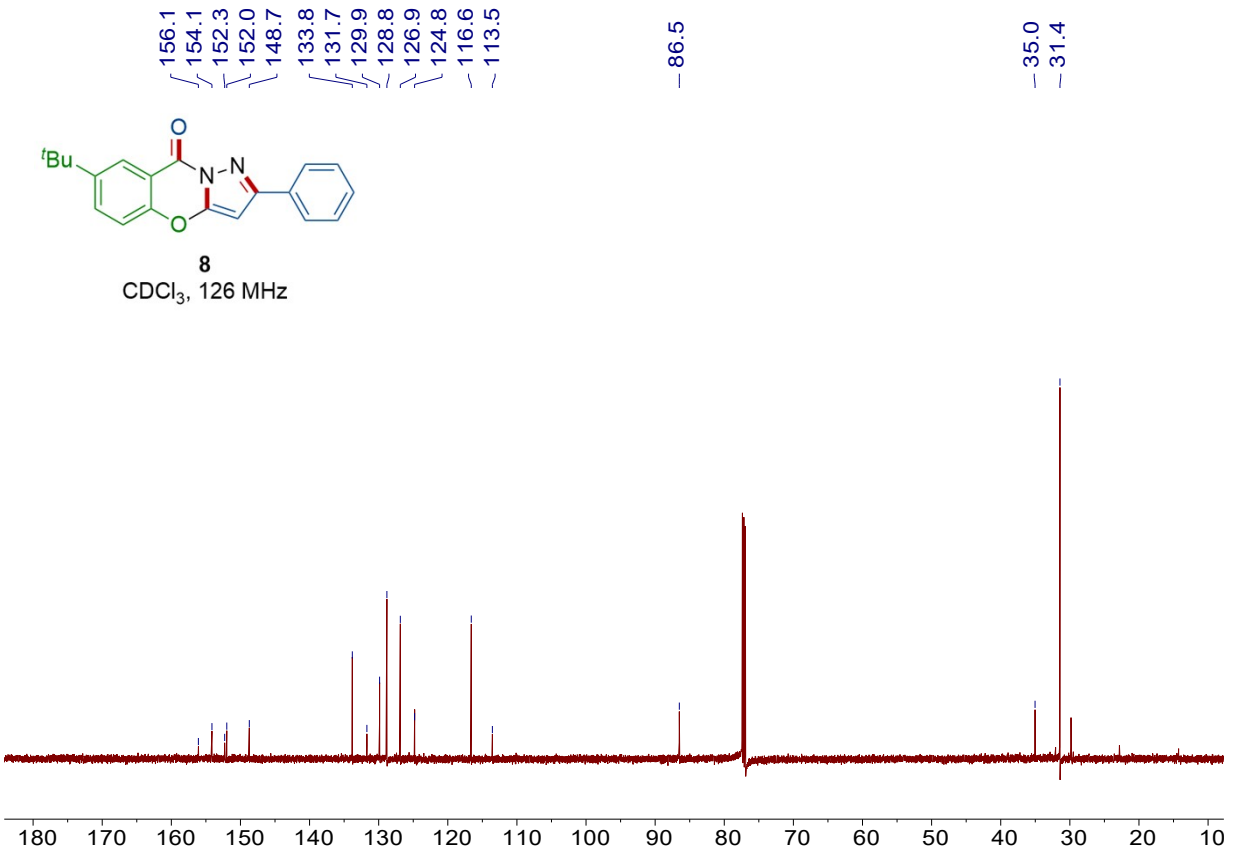


^{1}H NMR spectrum of **8** ($CDCl_3$, 500 MHz)



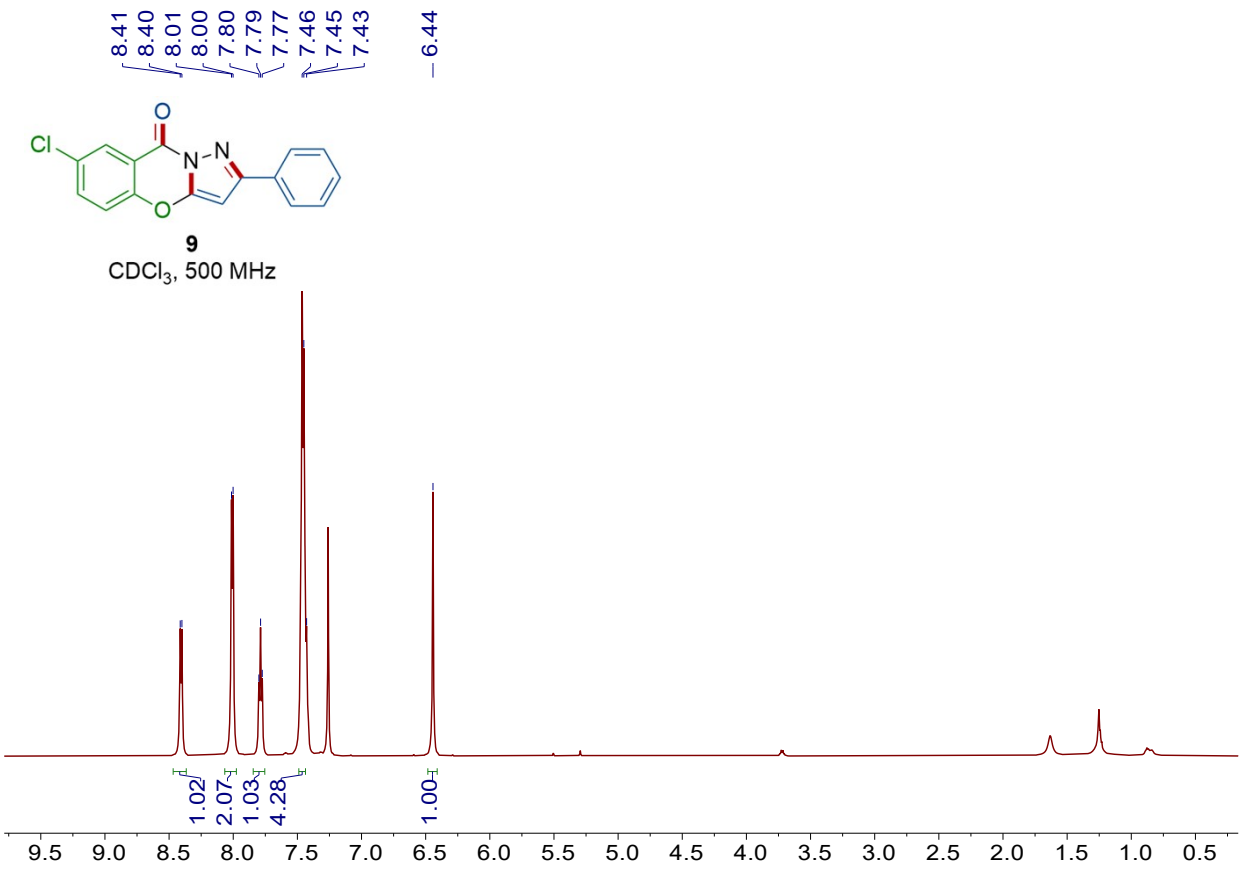
8
$CDCl_3$, 500 MHz

^{13}C NMR spectrum of **8** ($CDCl_3$, 126 MHz)

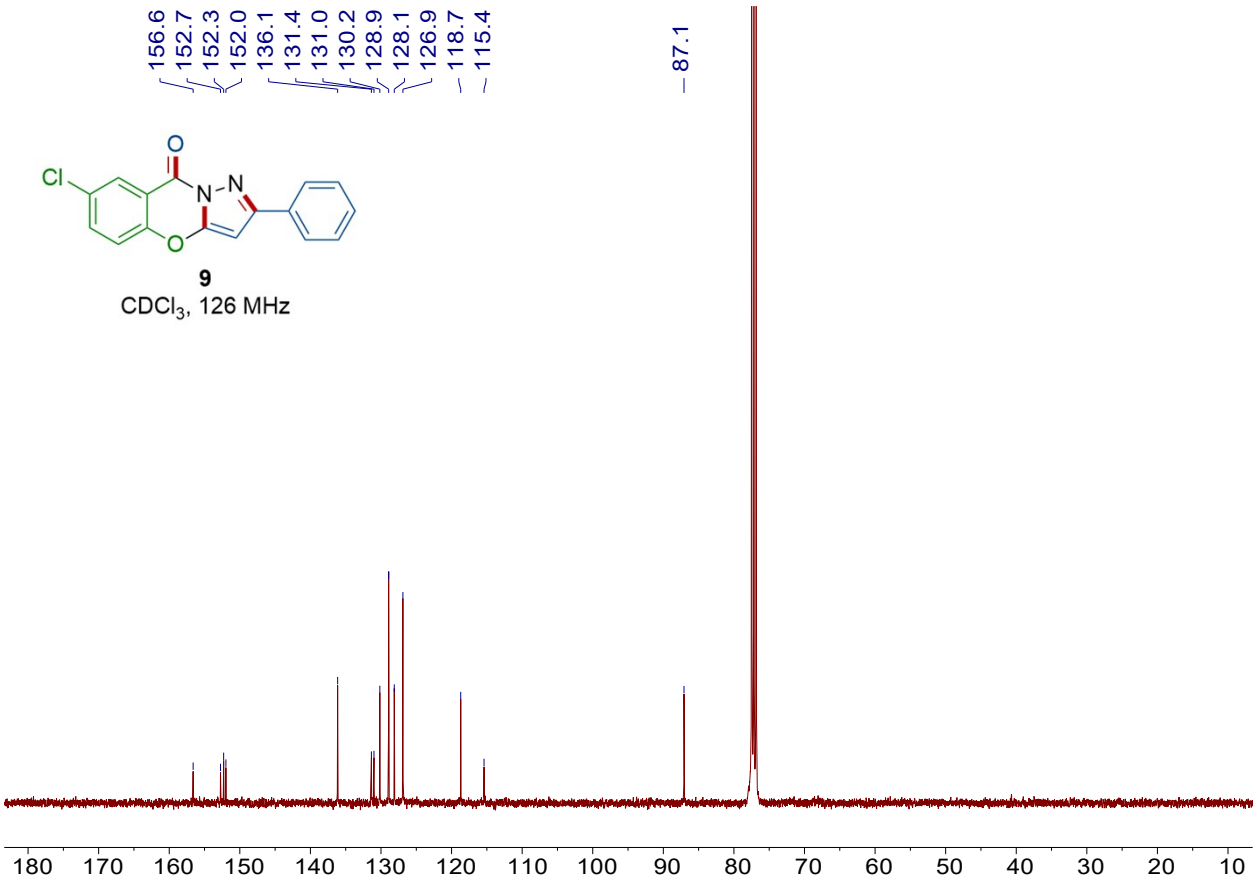


8
$CDCl_3$, 126 MHz

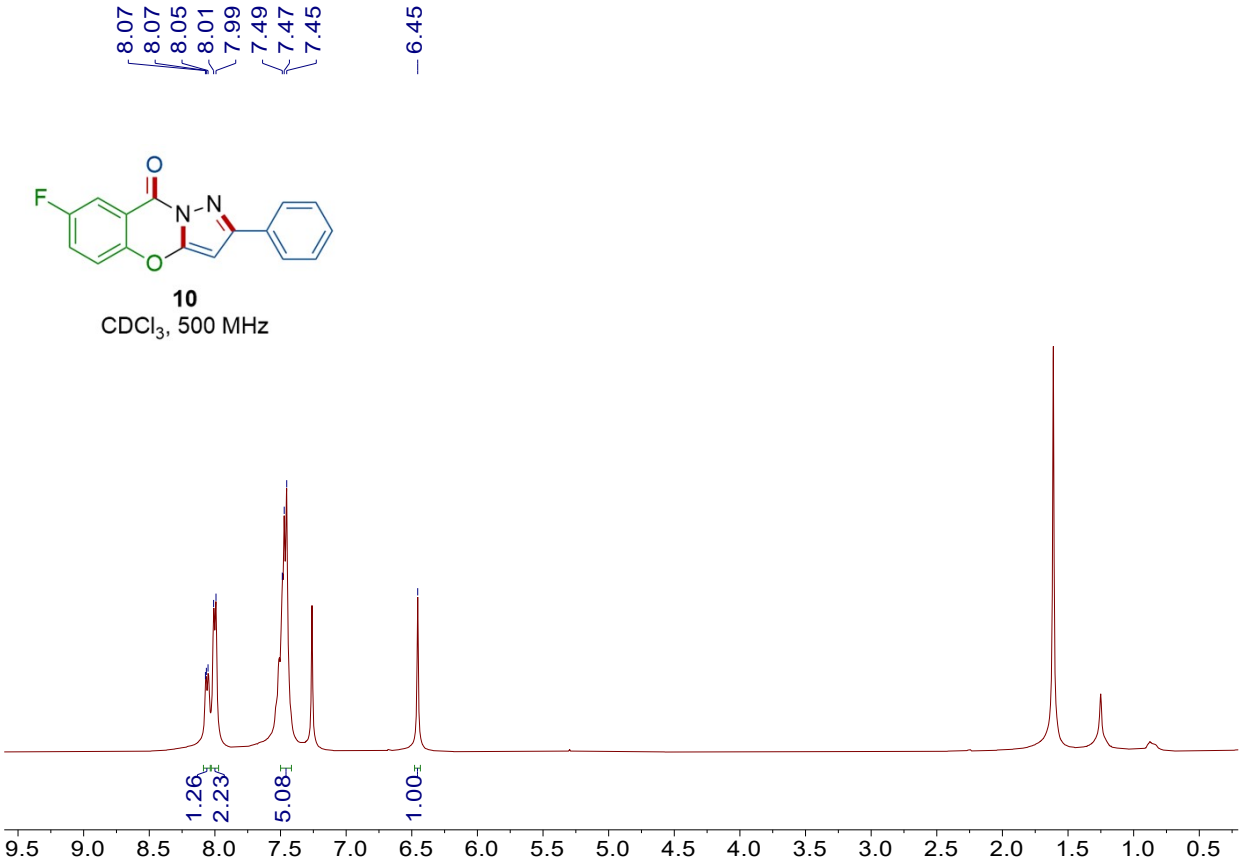
^{1}H NMR spectrum of **9** ($CDCl_3$, 500 MHz)



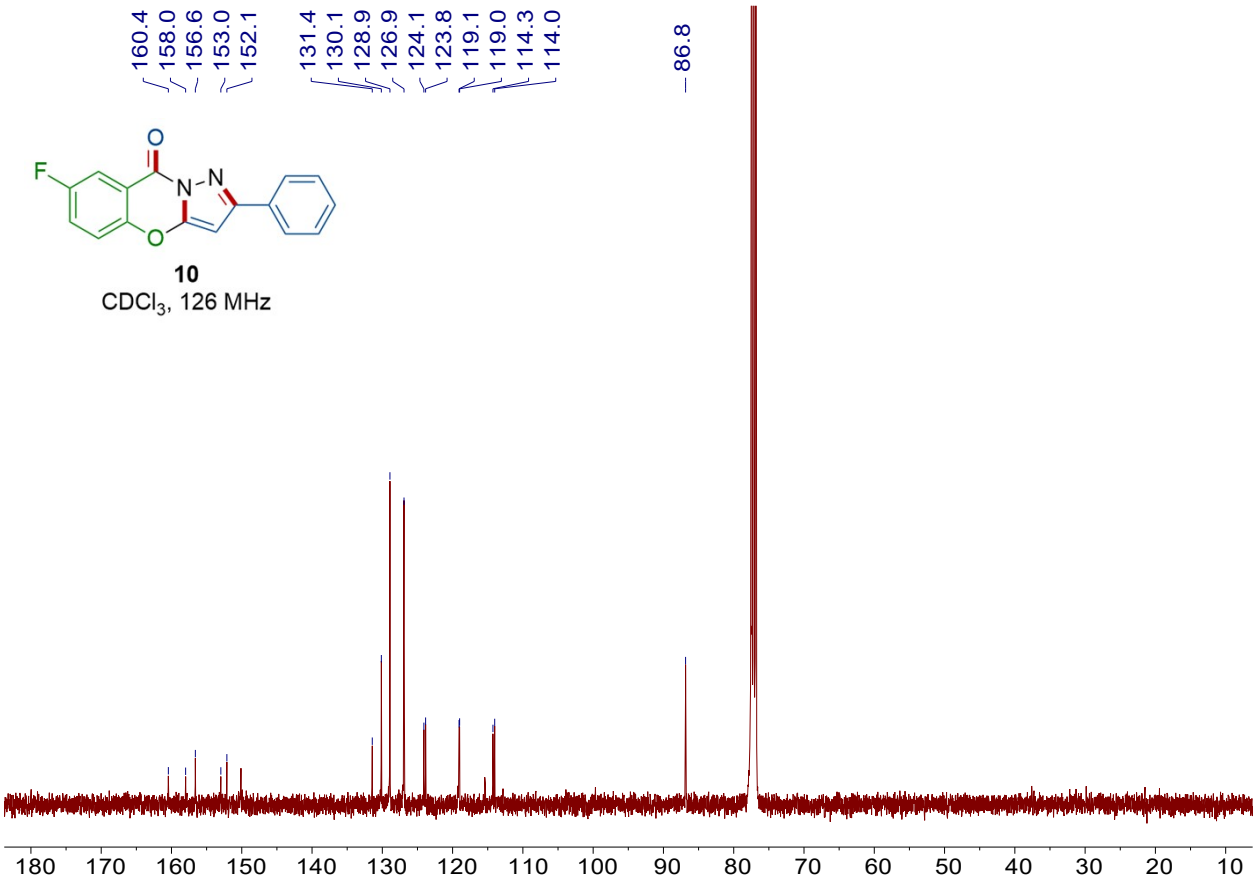
^{13}C NMR spectrum of **9** ($CDCl_3$, 126 MHz)



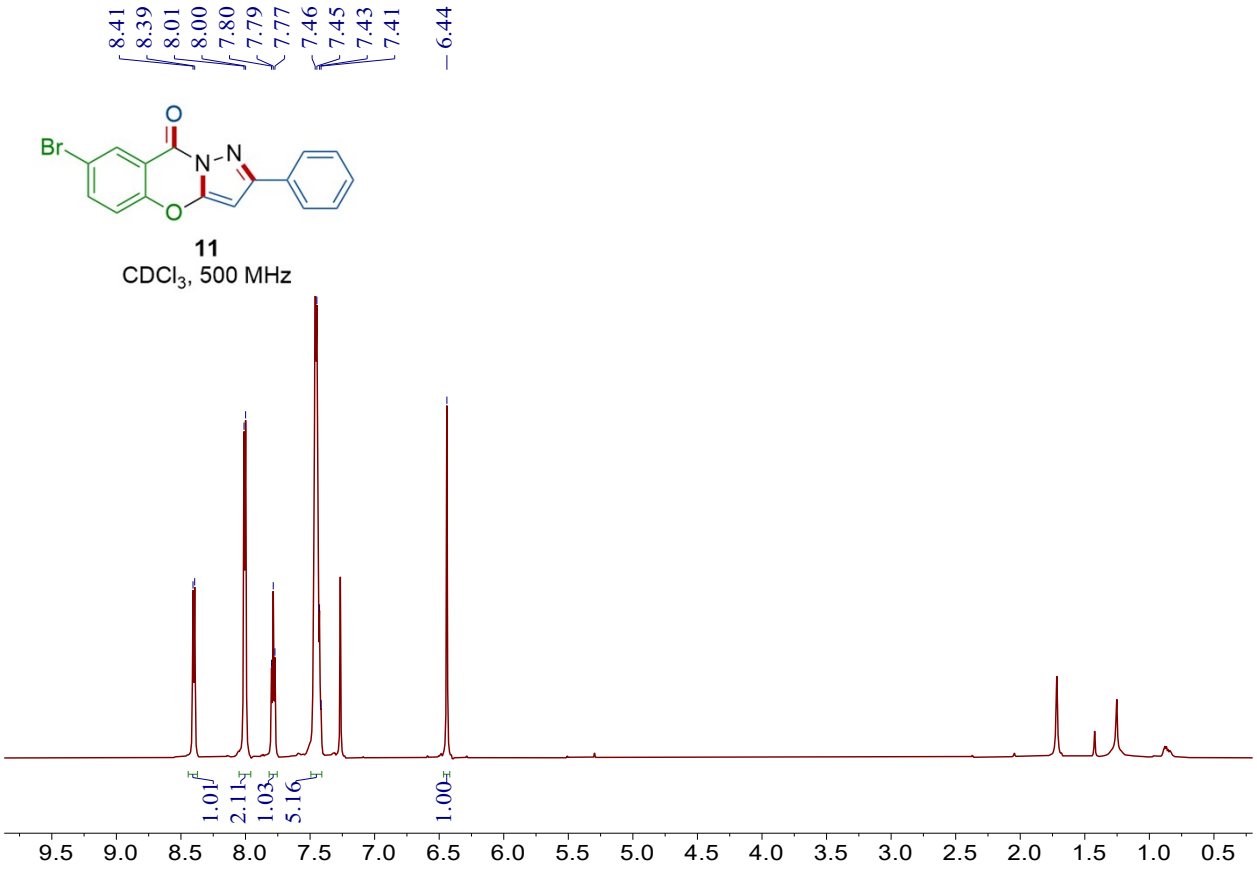
^{1}H NMR spectrum of **10** ($CDCl_3$, 500 MHz)



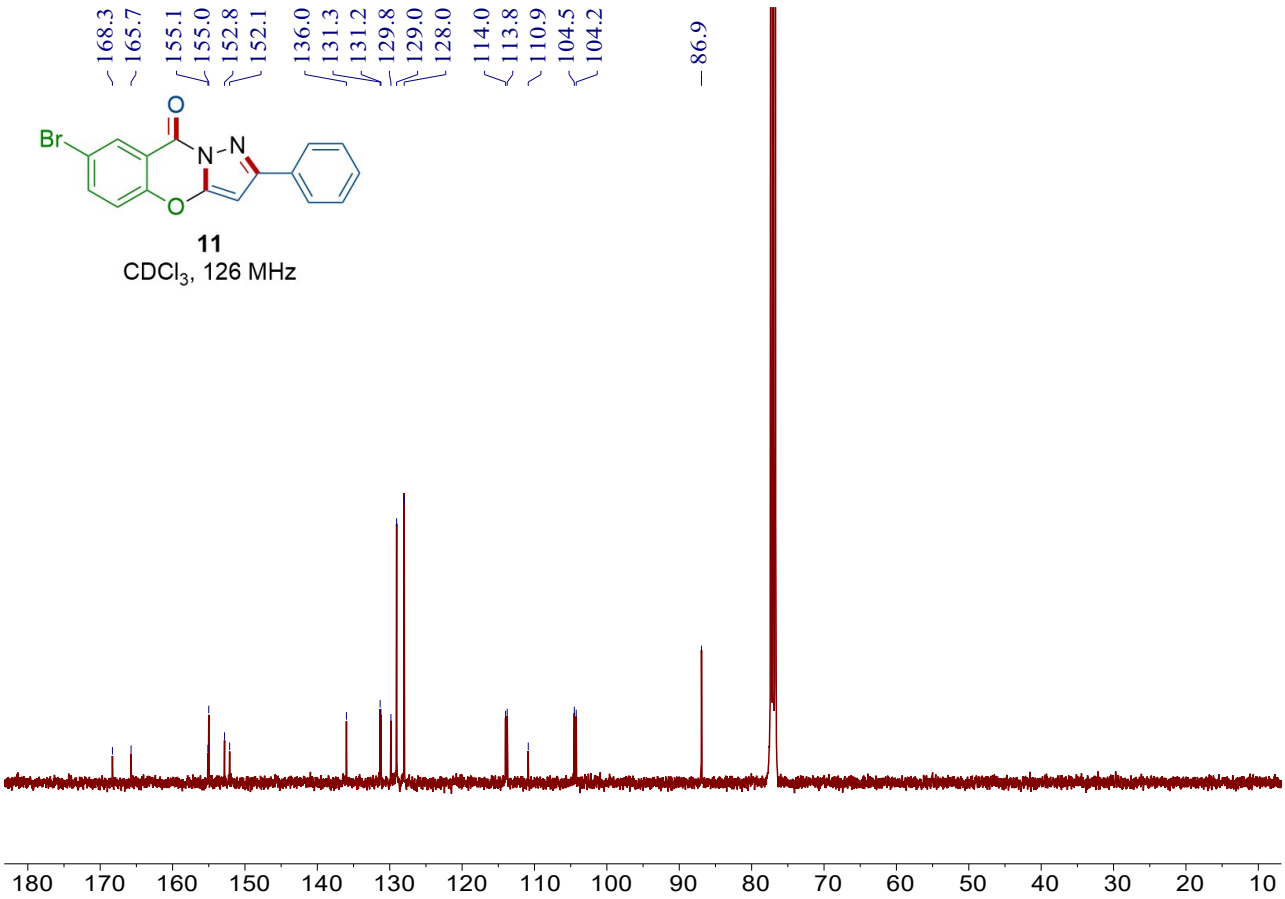
^{13}C NMR spectrum of **10** ($CDCl_3$, 126 MHz)



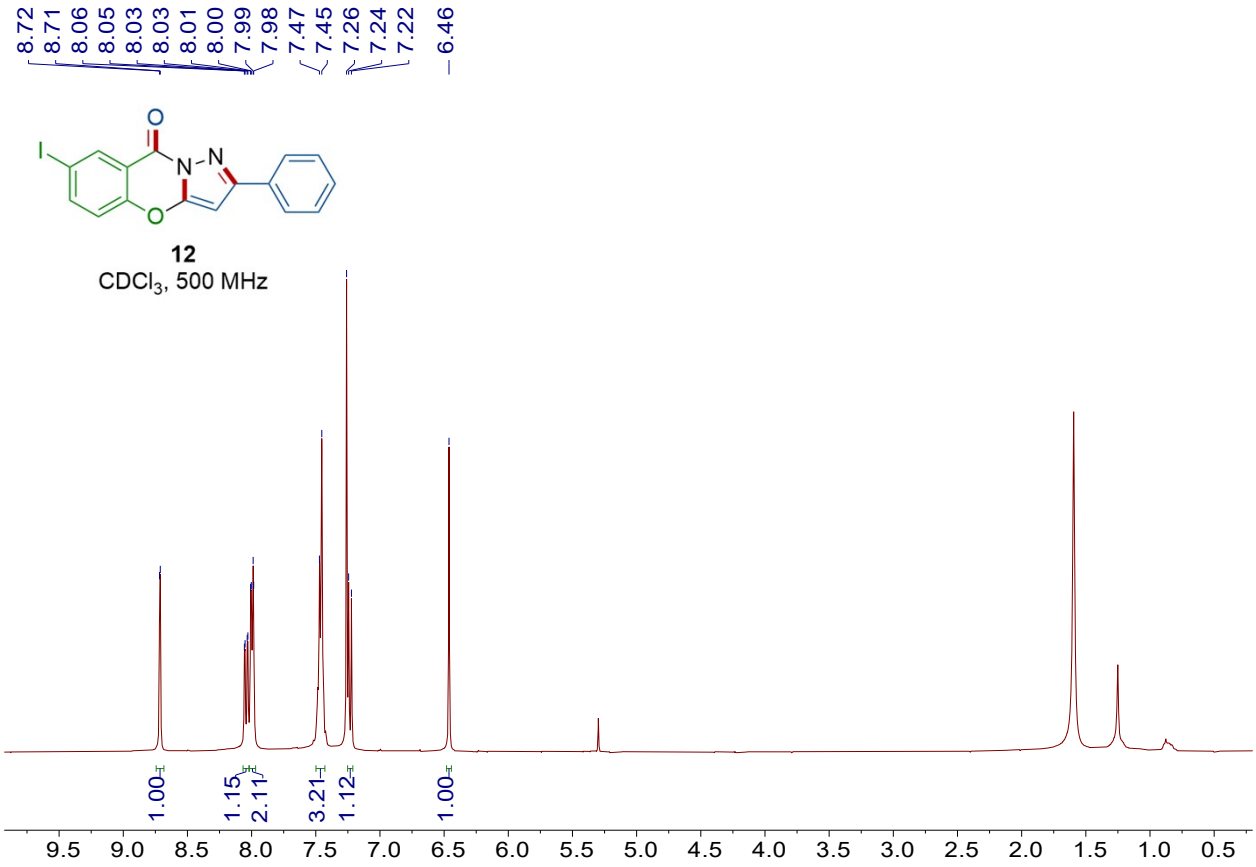
^{1}H NMR spectrum of **11** ($CDCl_3$, 500 MHz)



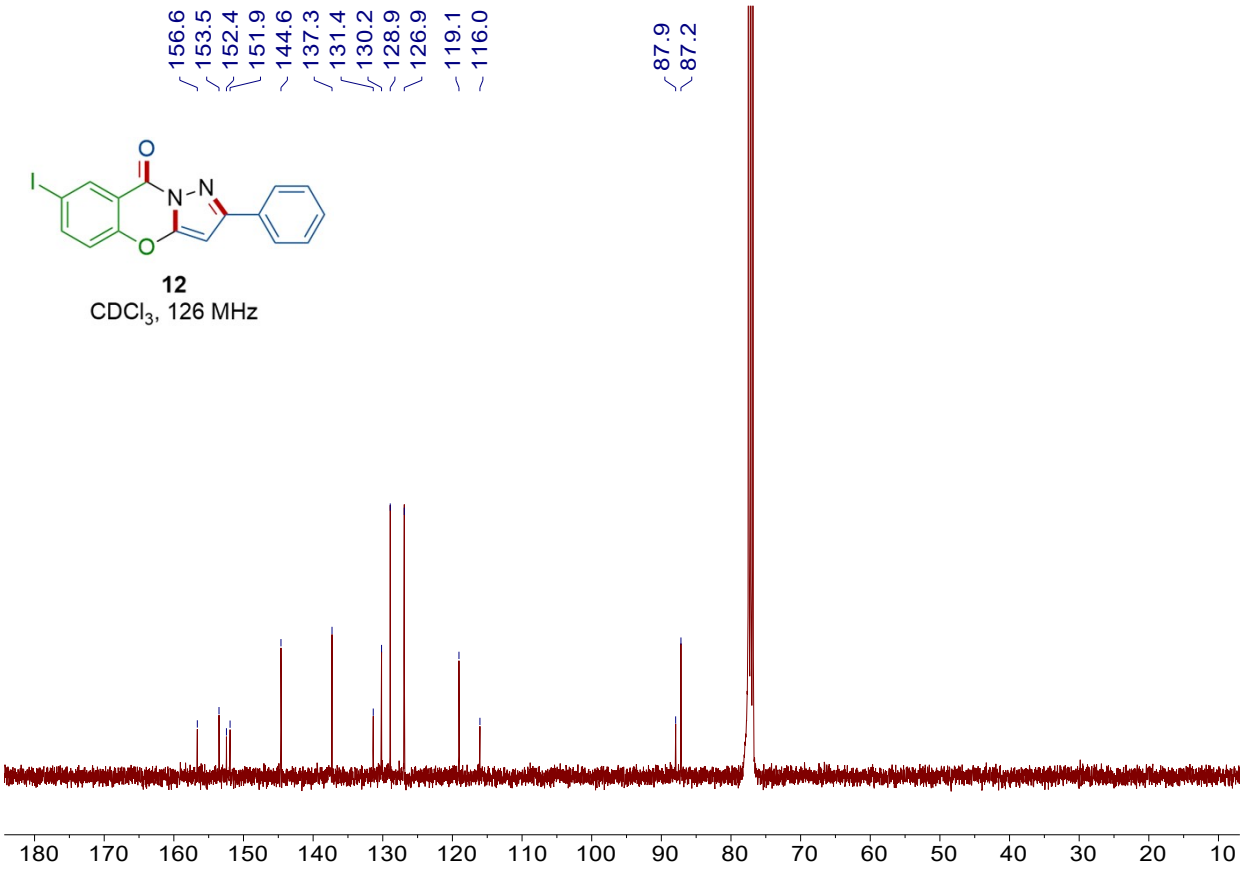
^{13}C NMR spectrum of **11** ($CDCl_3$, 126 MHz)



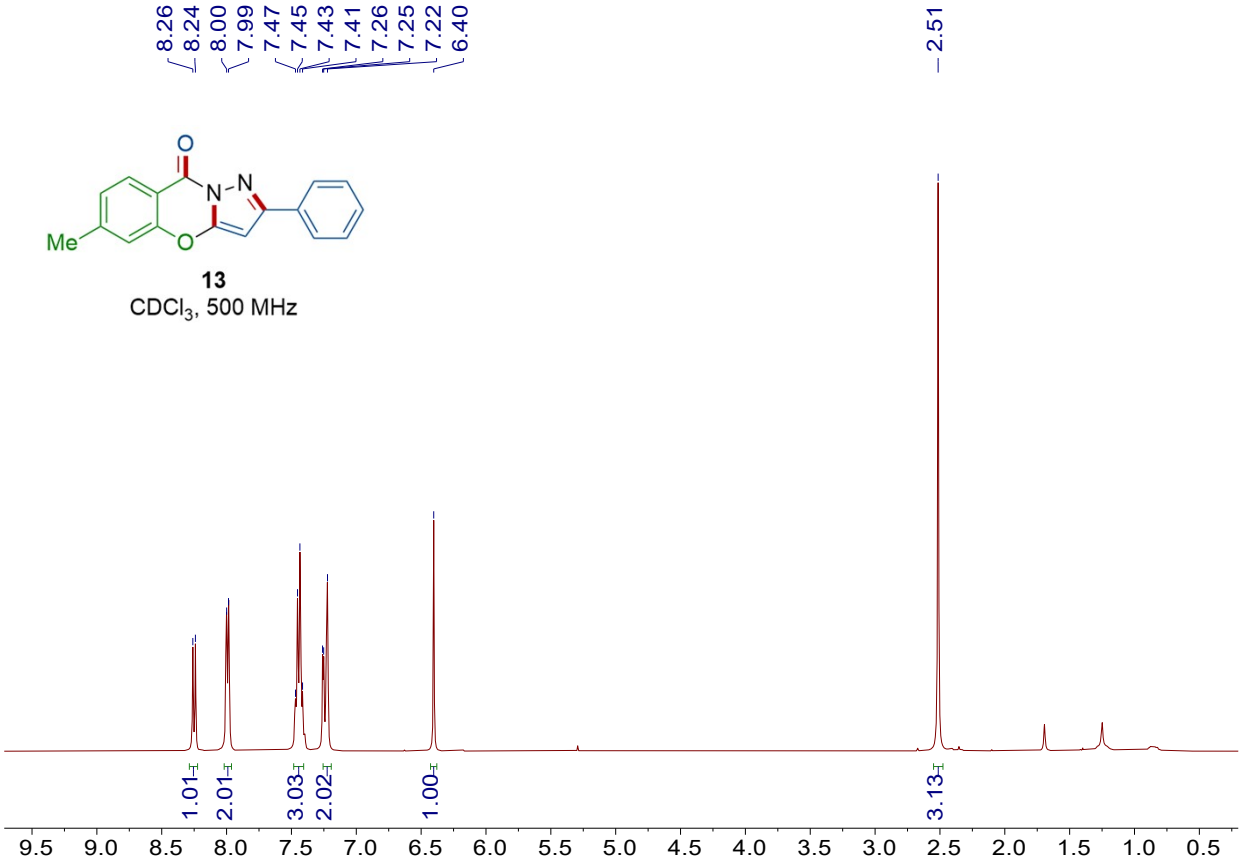
^{1}H NMR spectrum of **12** ($CDCl_3$, 500 MHz)



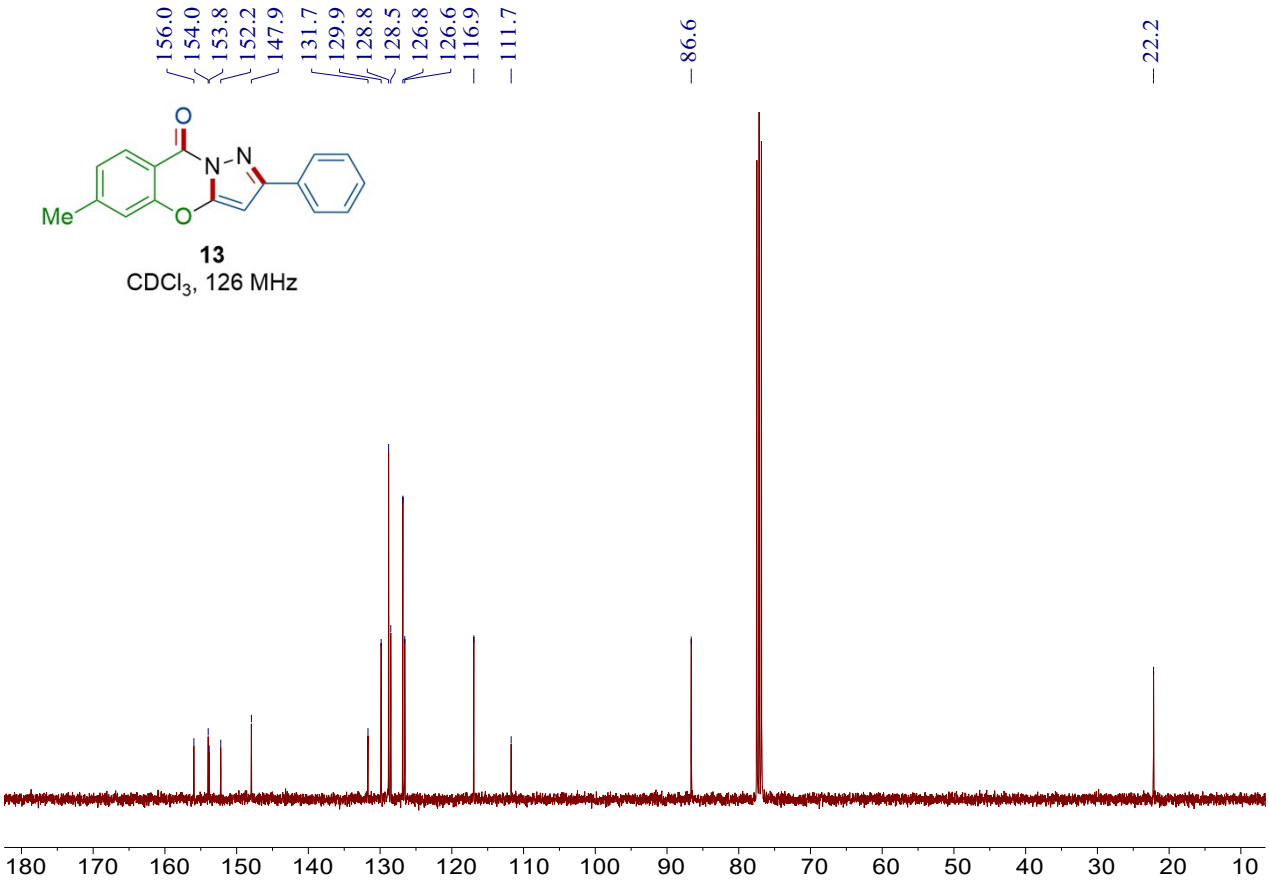
^{13}C NMR spectrum of **12** ($CDCl_3$, 126 MHz)



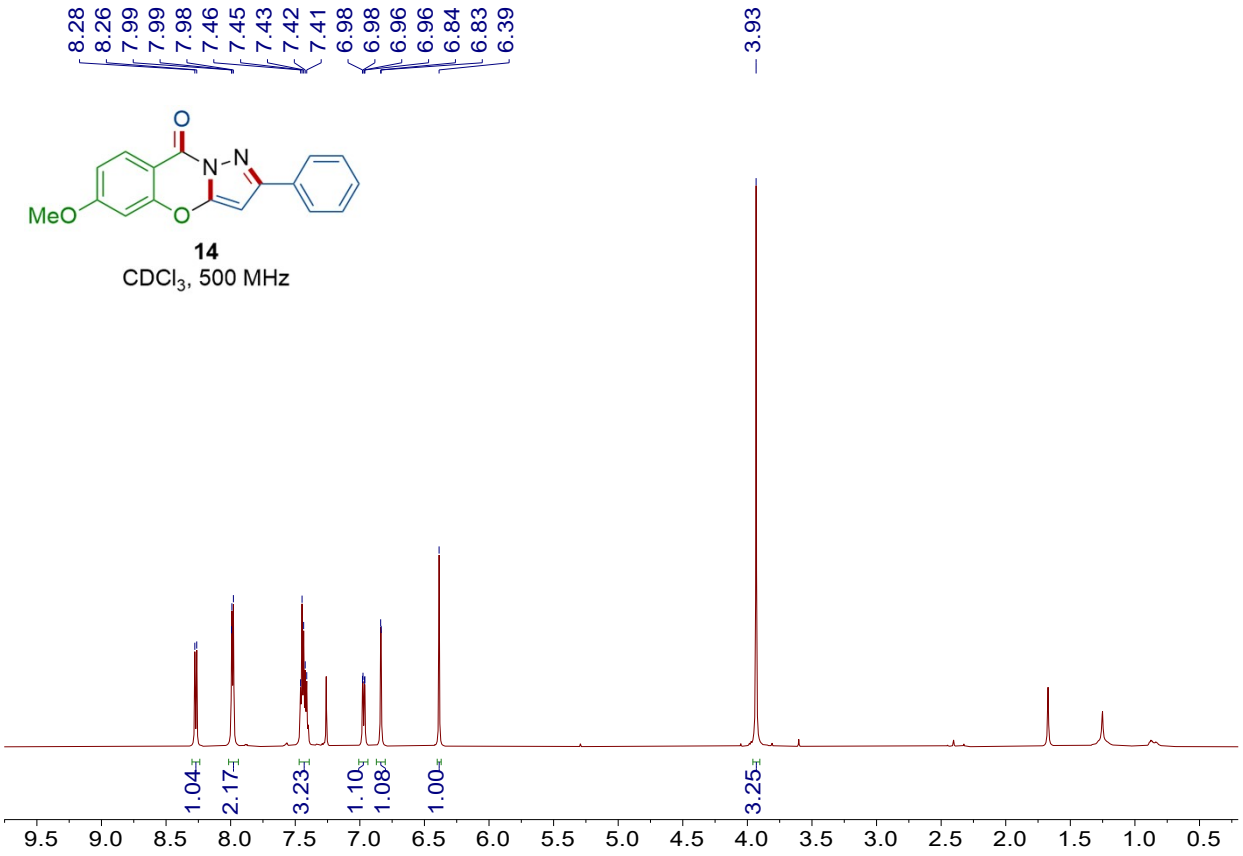
^{1}H NMR spectrum of **13** ($CDCl_3$, 500 MHz)



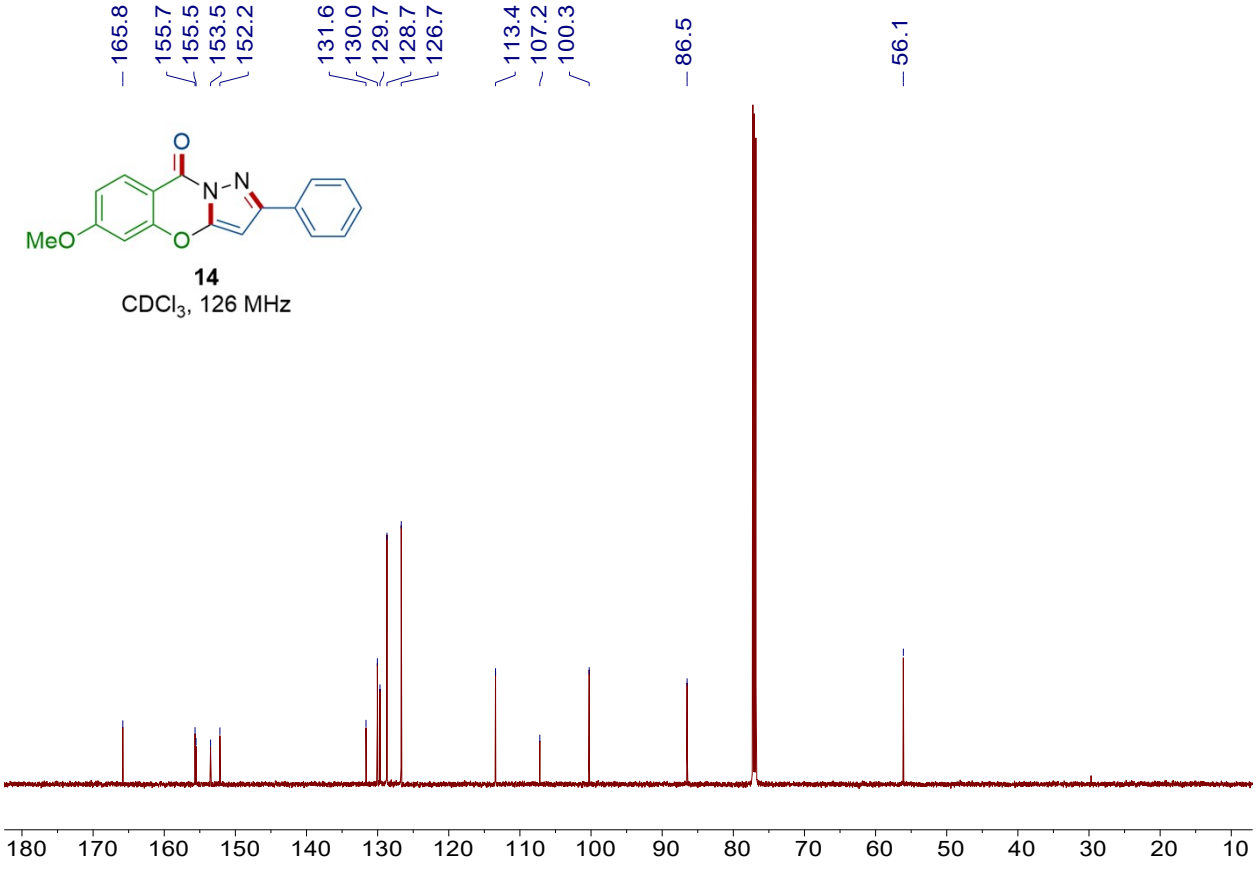
^{13}C NMR spectrum of **13** ($CDCl_3$, 126 MHz)



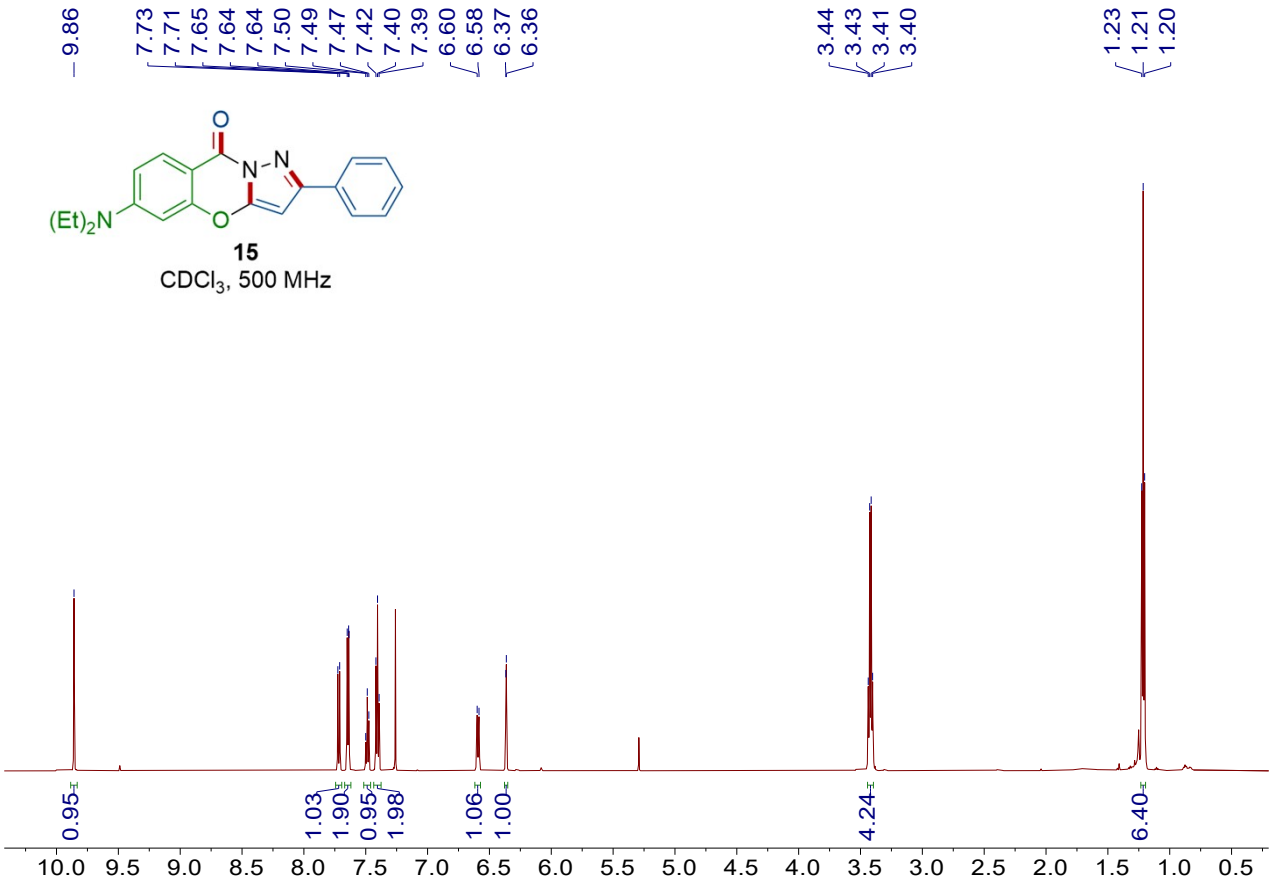
^{1}H NMR spectrum of **14** ($CDCl_3$, 500 MHz)



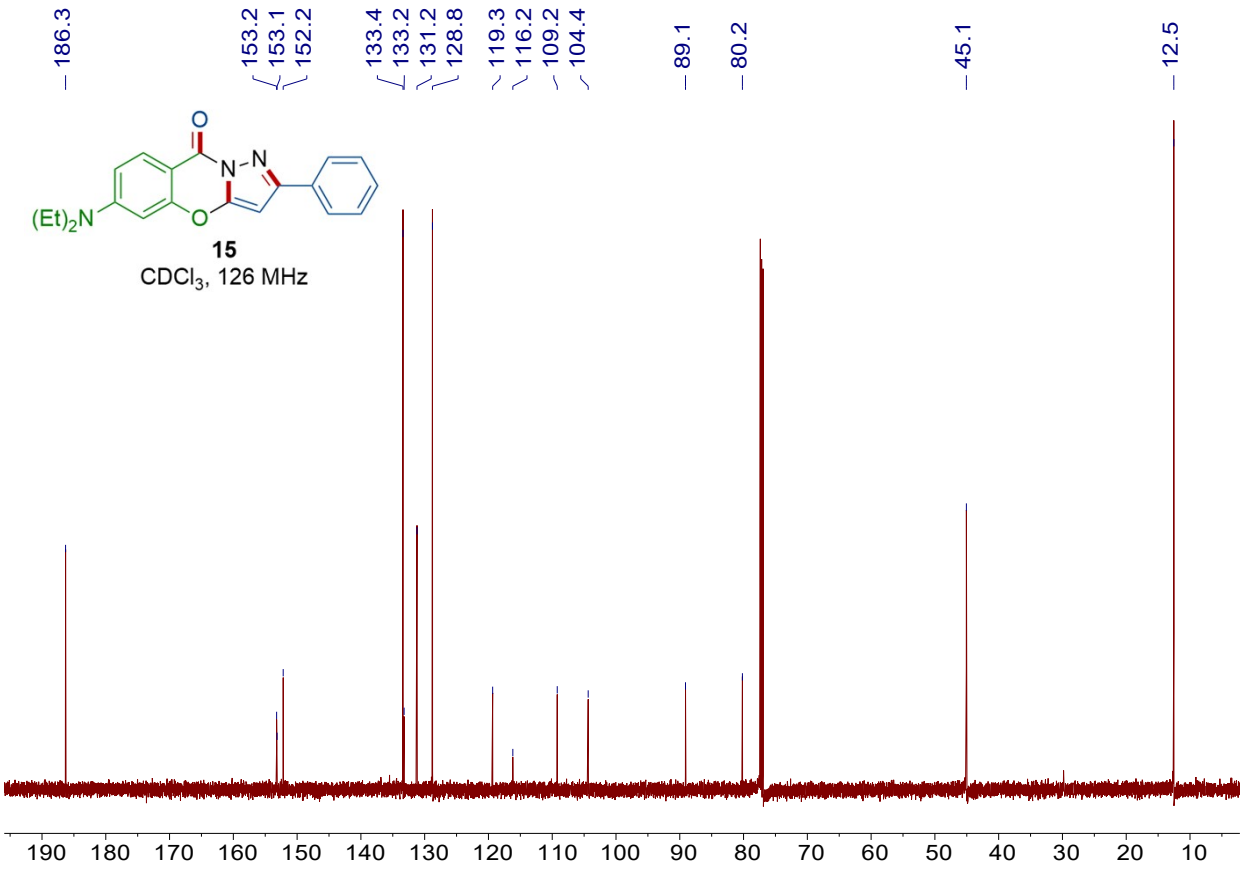
^{13}C NMR spectrum of **14** ($CDCl_3$, 126 MHz)



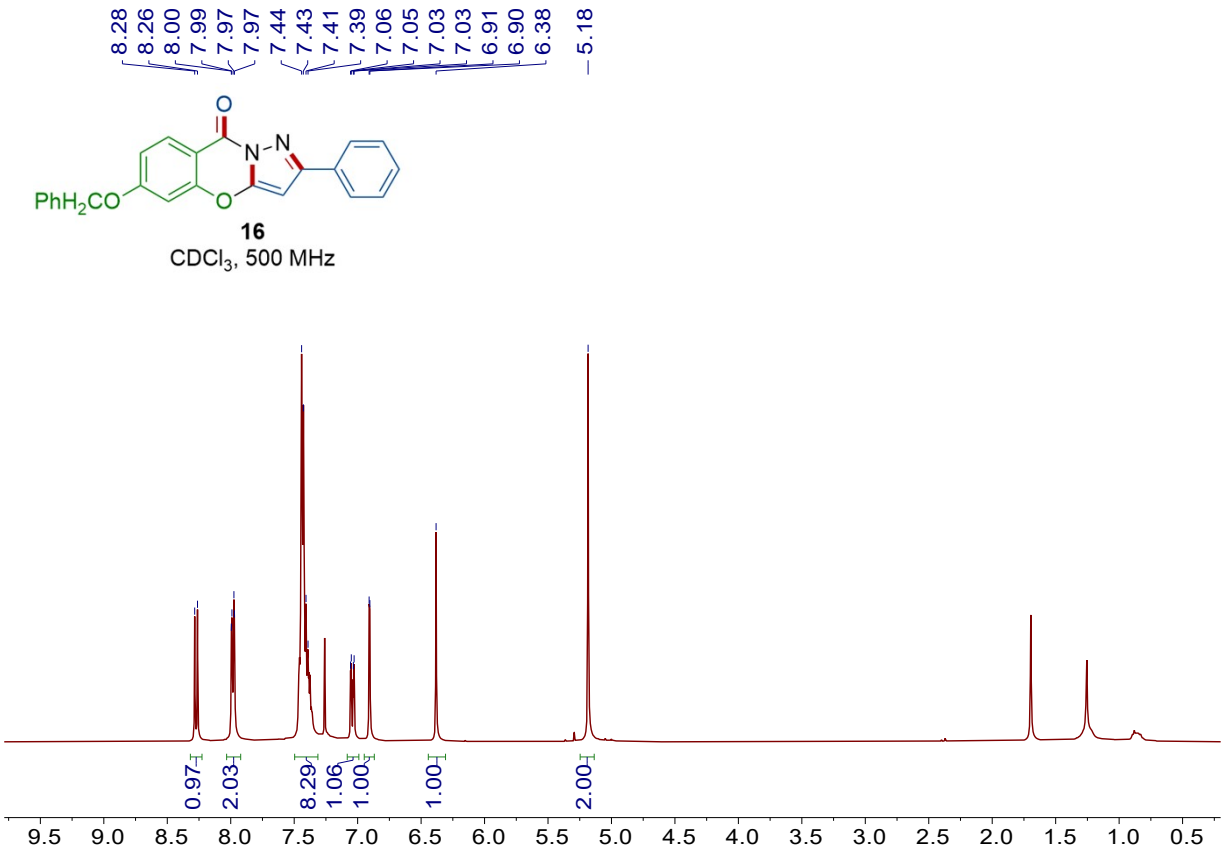
^{1}H NMR spectrum of **15** ($CDCl_3$, 500 MHz)



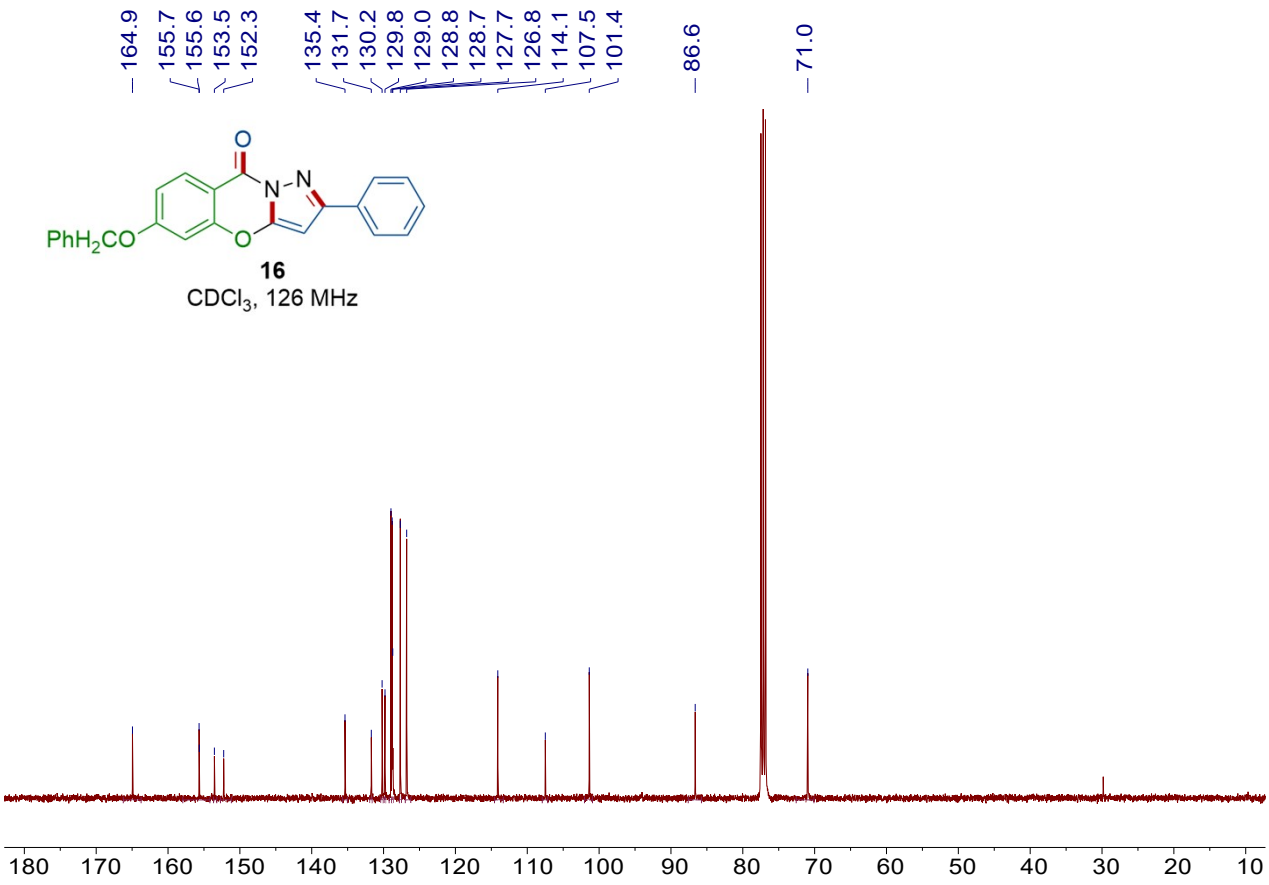
^{13}C NMR spectrum of **15** ($CDCl_3$, 126 MHz)



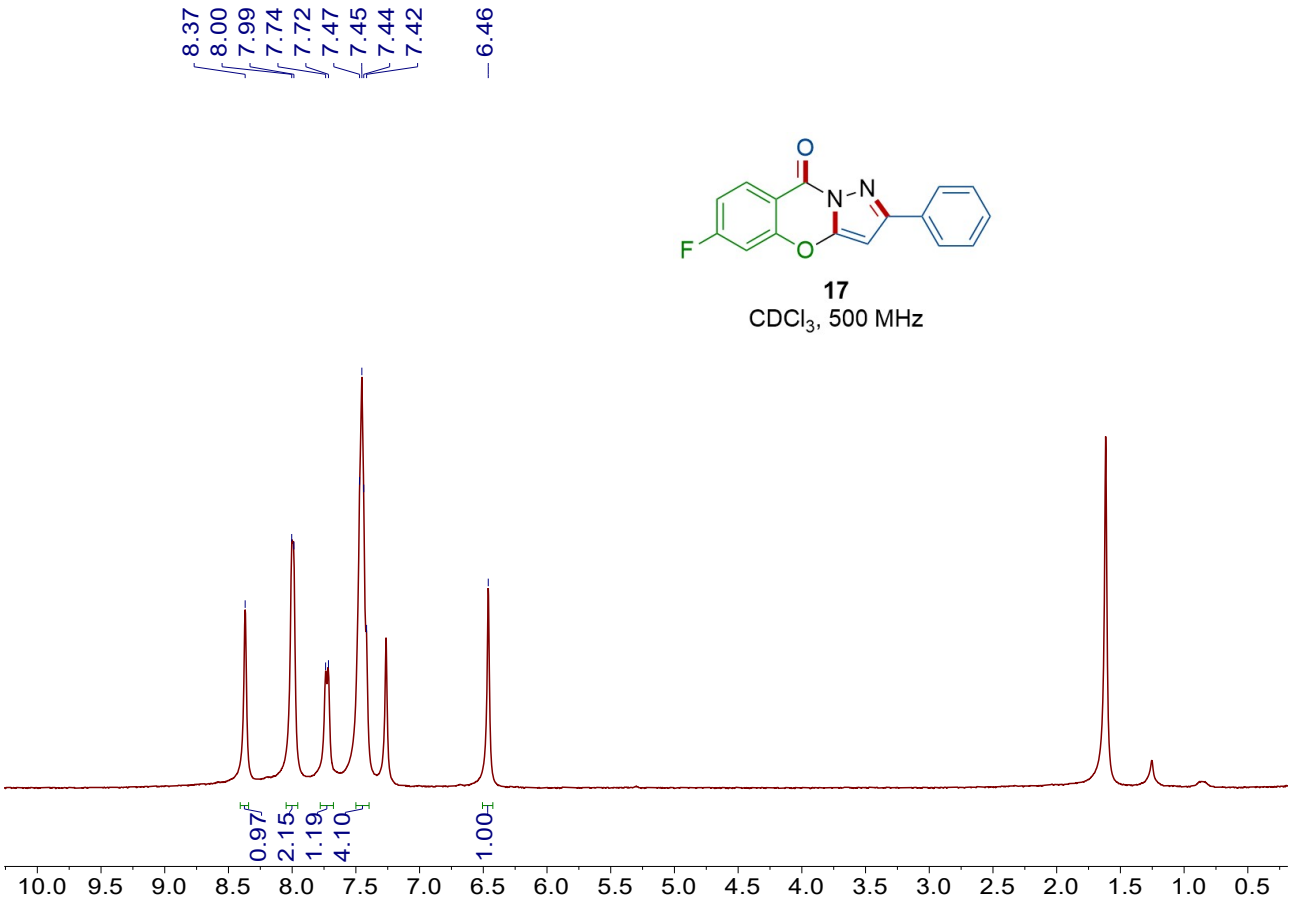
^{1}H NMR spectrum of **16** ($CDCl_3$, 500 MHz)



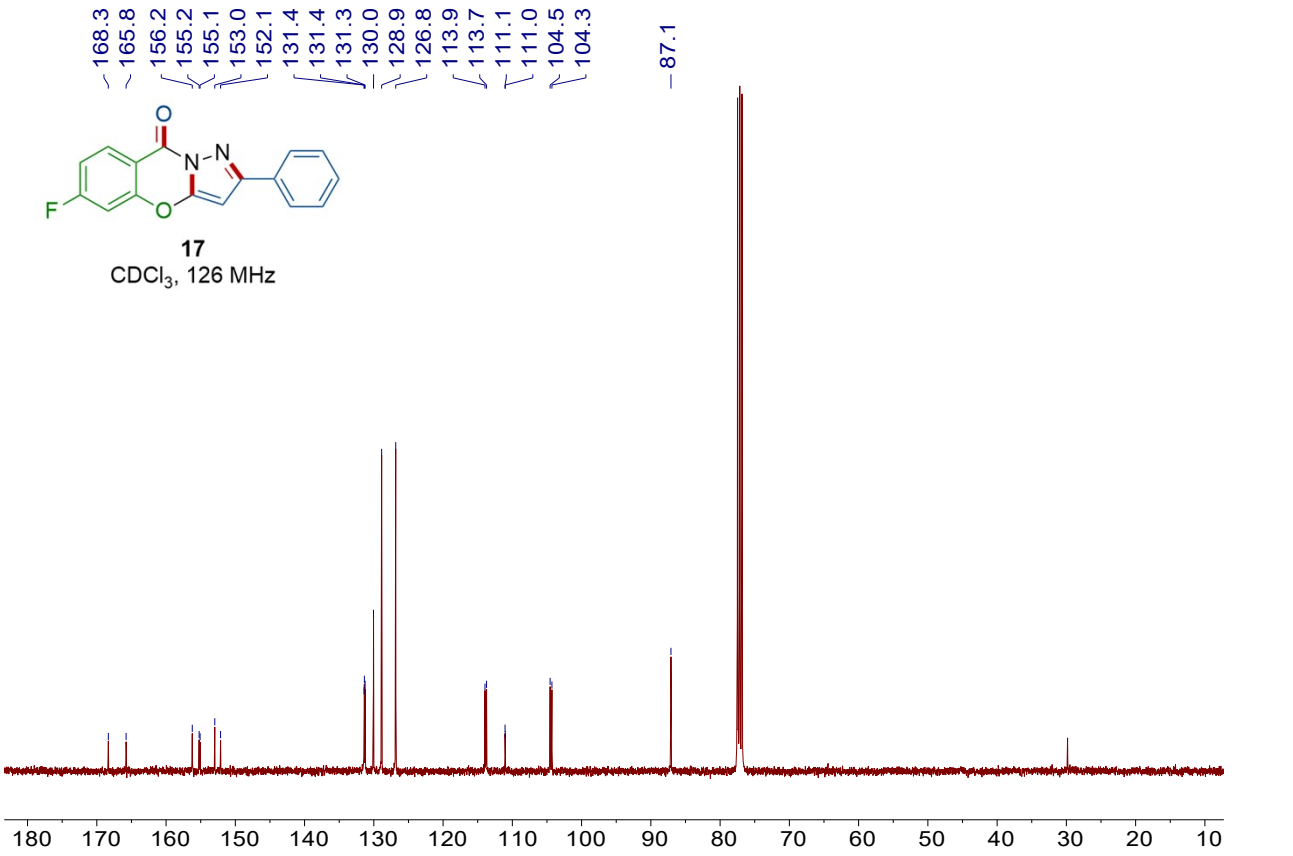
^{13}C NMR spectrum of **16** ($CDCl_3$, 126 MHz)



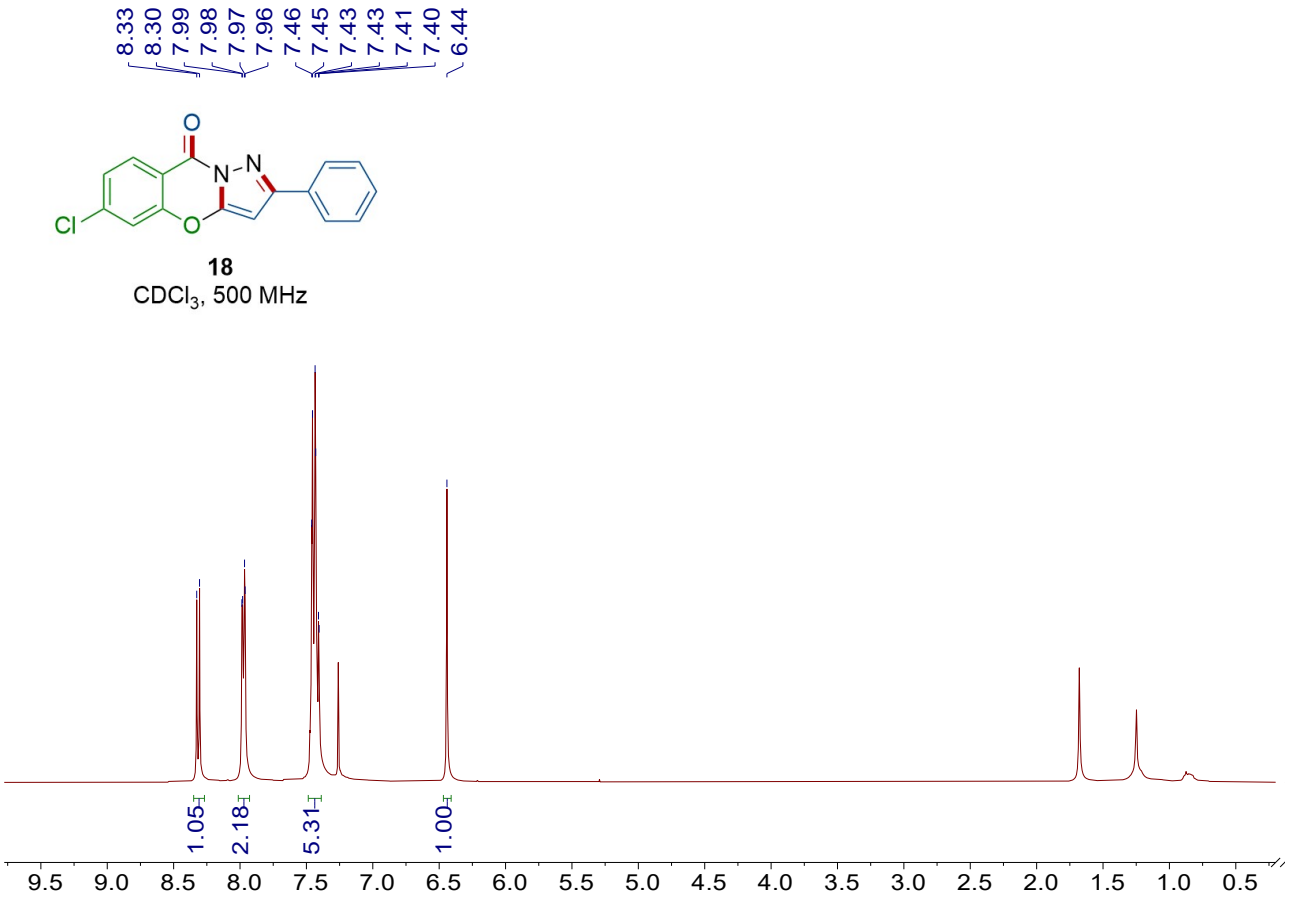
^{1}H NMR spectrum of **17** ($CDCl_3$, 500 MHz)



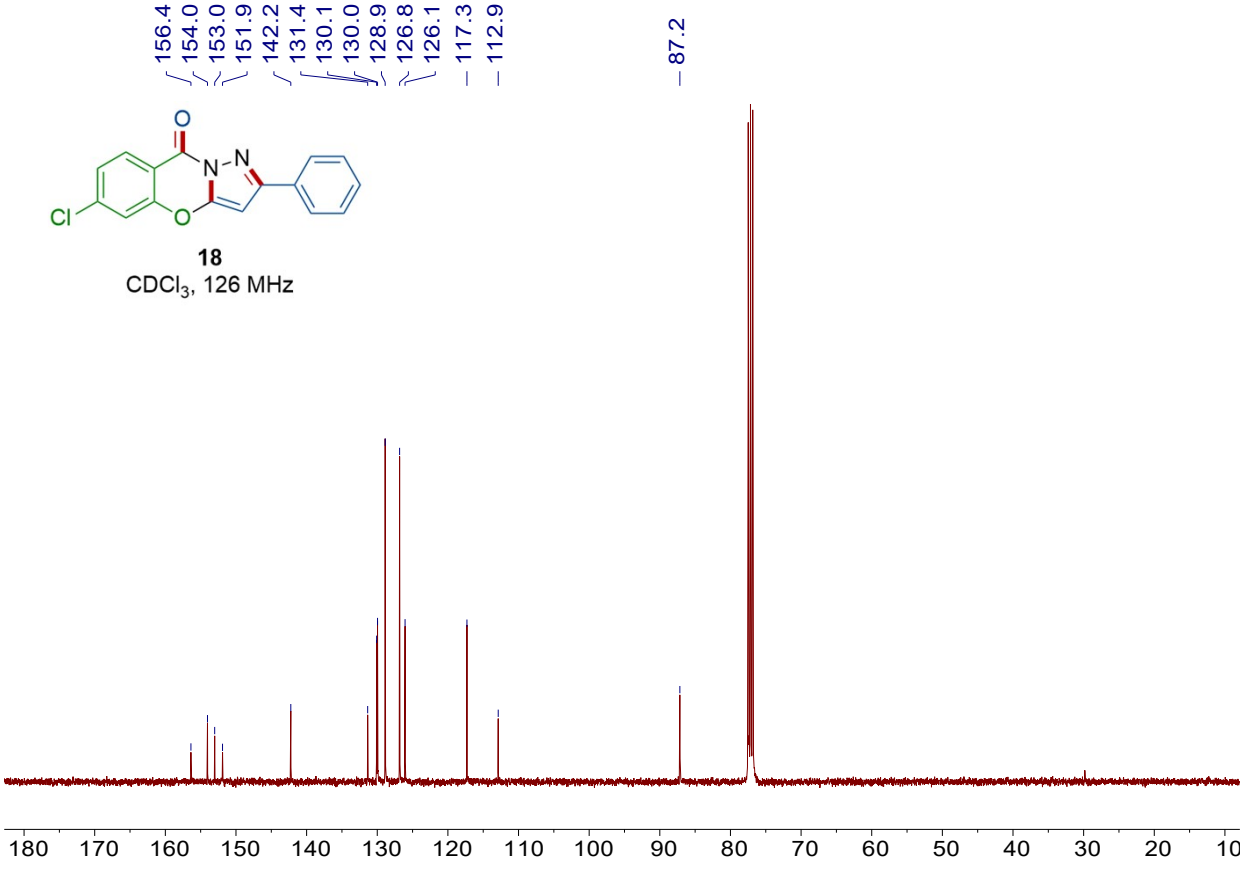
^{13}C NMR spectrum of **17** ($CDCl_3$, 126 MHz)



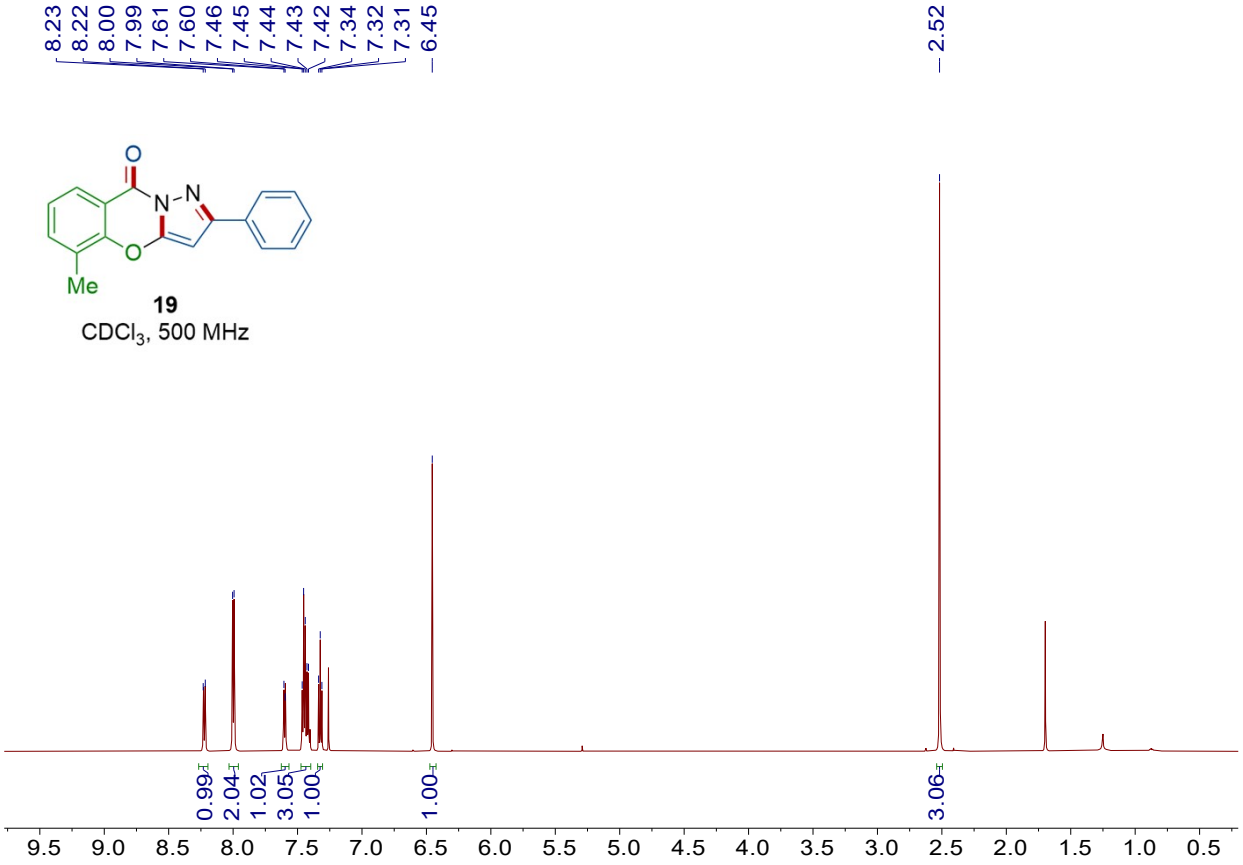
^{1}H NMR spectrum of **18** ($CDCl_3$, 500 MHz)



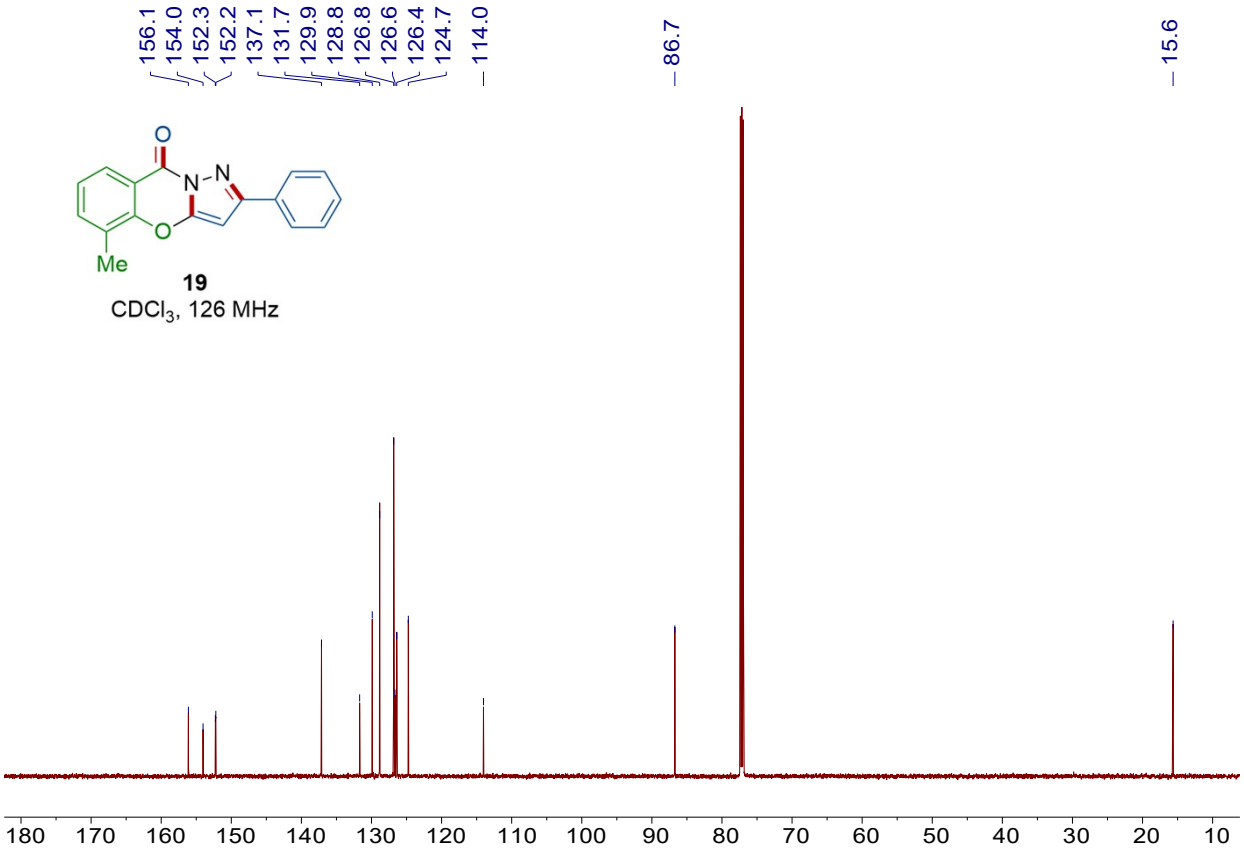
^{13}C NMR spectrum of **18** ($CDCl_3$, 126 MHz)



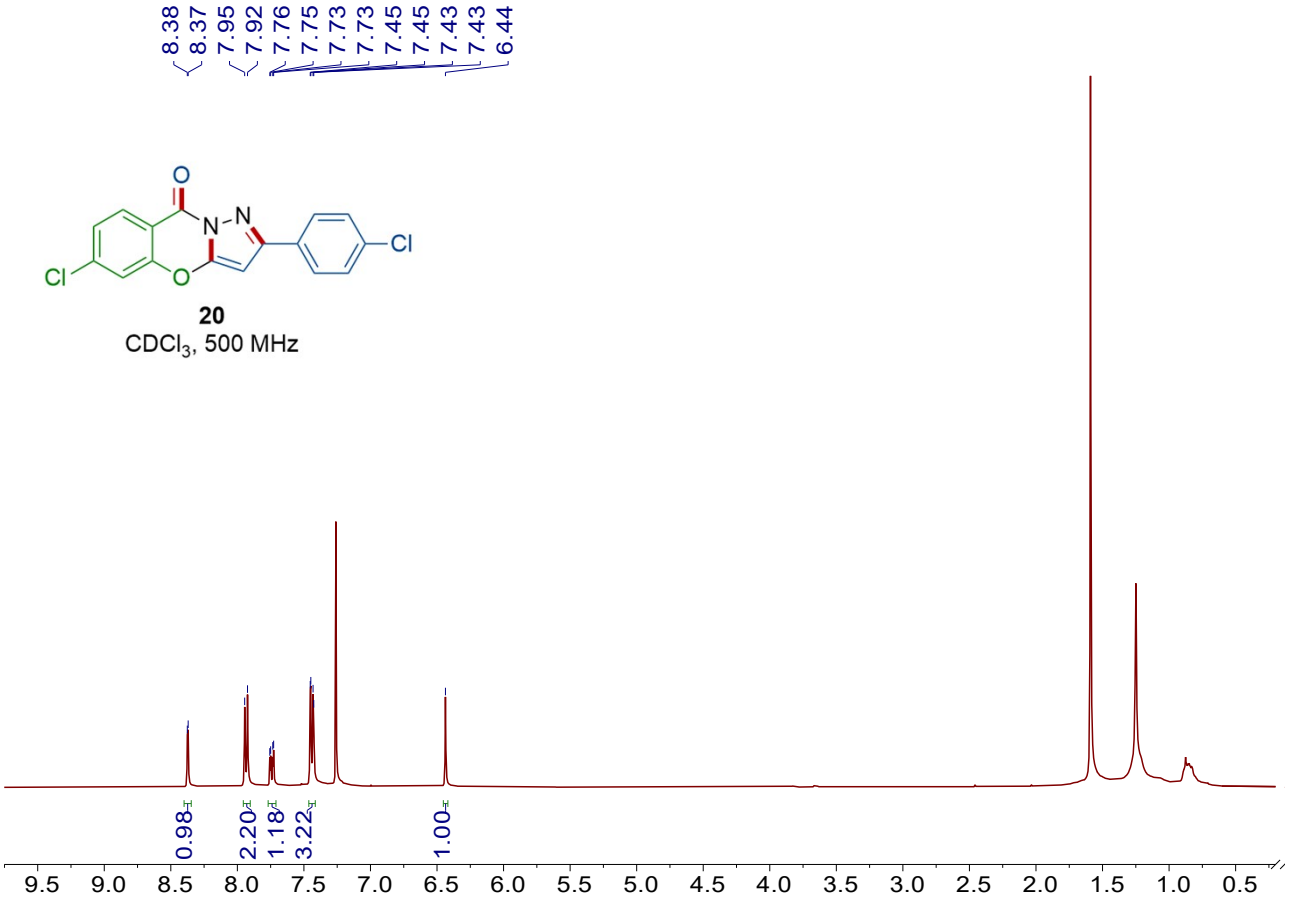
^{1}H NMR spectrum of **19** ($CDCl_3$, 500 MHz)



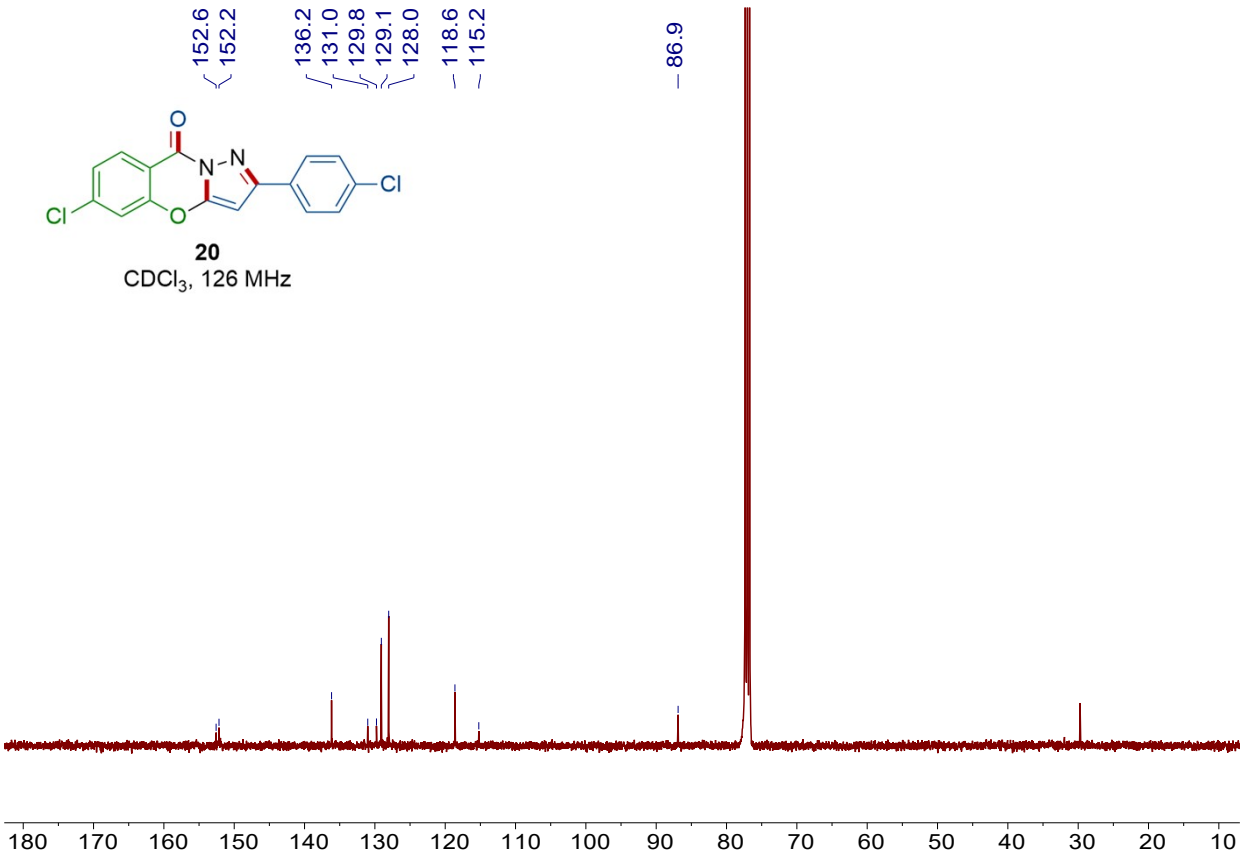
^{13}C NMR spectrum of **19** ($CDCl_3$, 126 MHz)



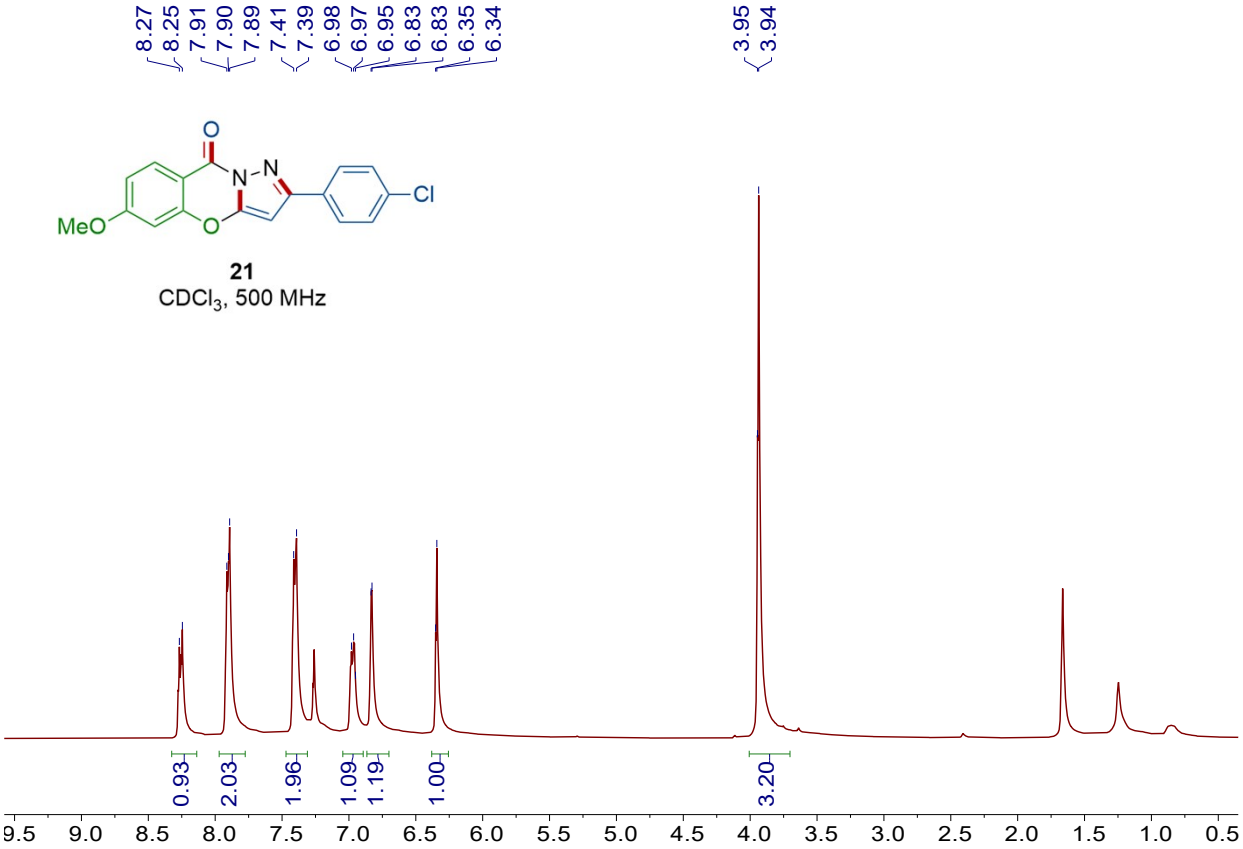
^{1}H NMR spectrum of **20** ($CDCl_3$, 500 MHz)



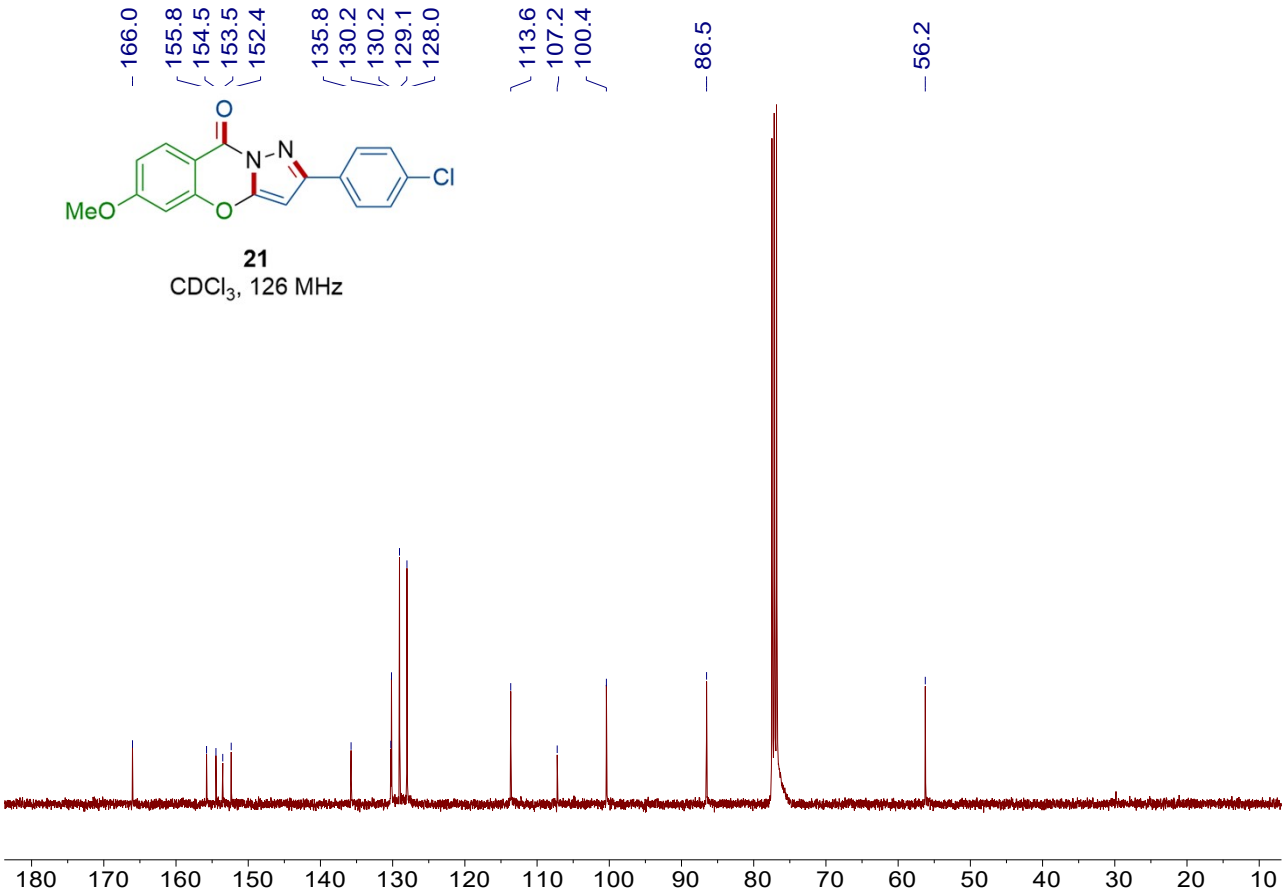
^{13}C NMR spectrum of **20** ($CDCl_3$, 126 MHz)



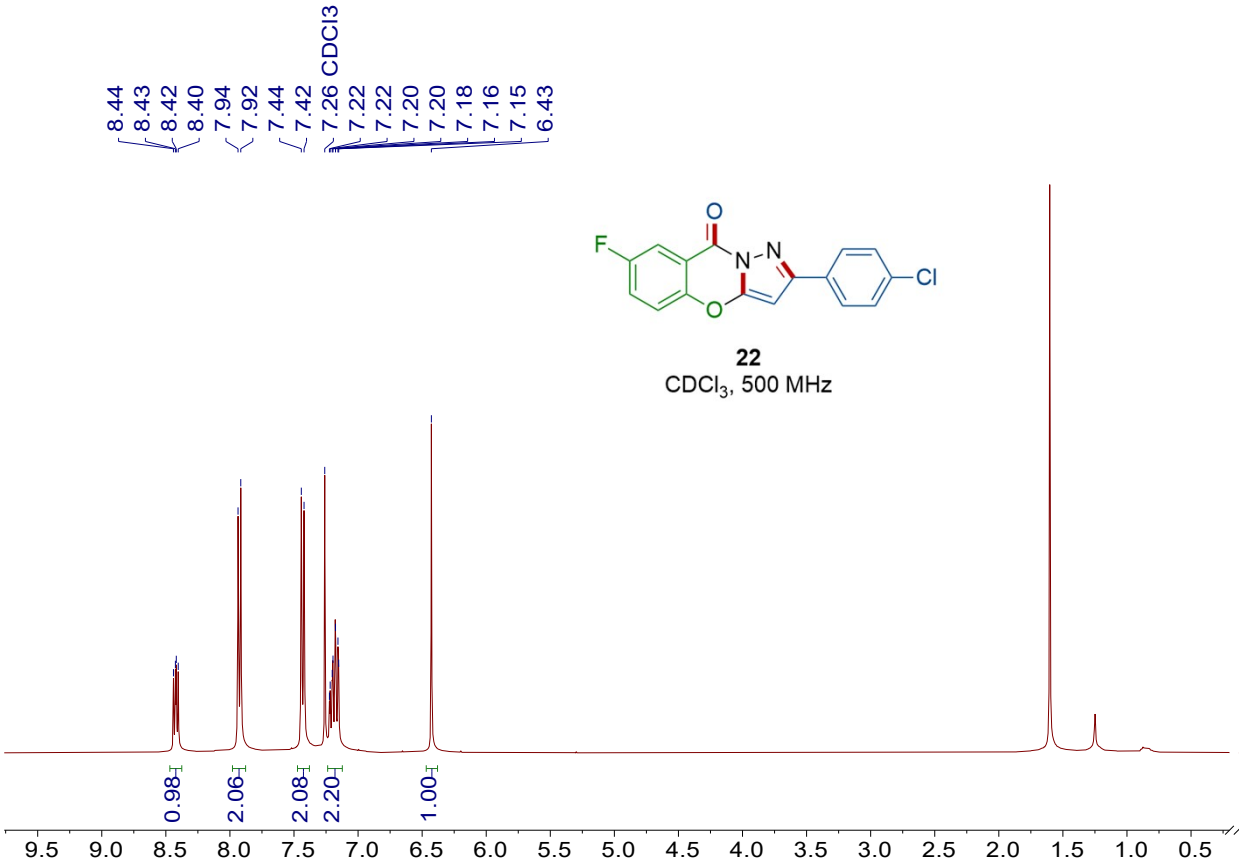
^{1}H NMR spectrum of **21** ($CDCl_3$, 500 MHz)



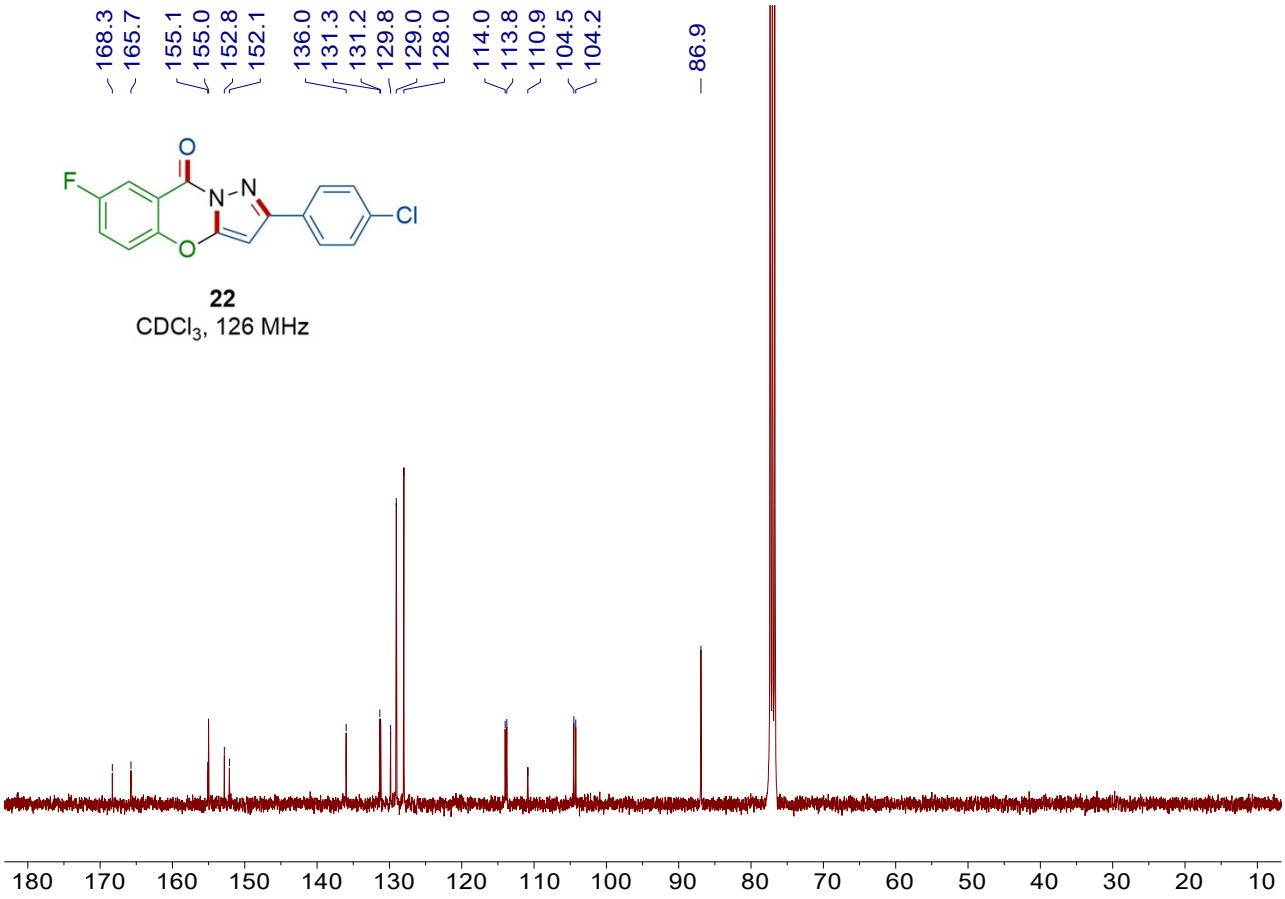
^{13}C NMR spectrum of **21** ($CDCl_3$, 126 MHz)



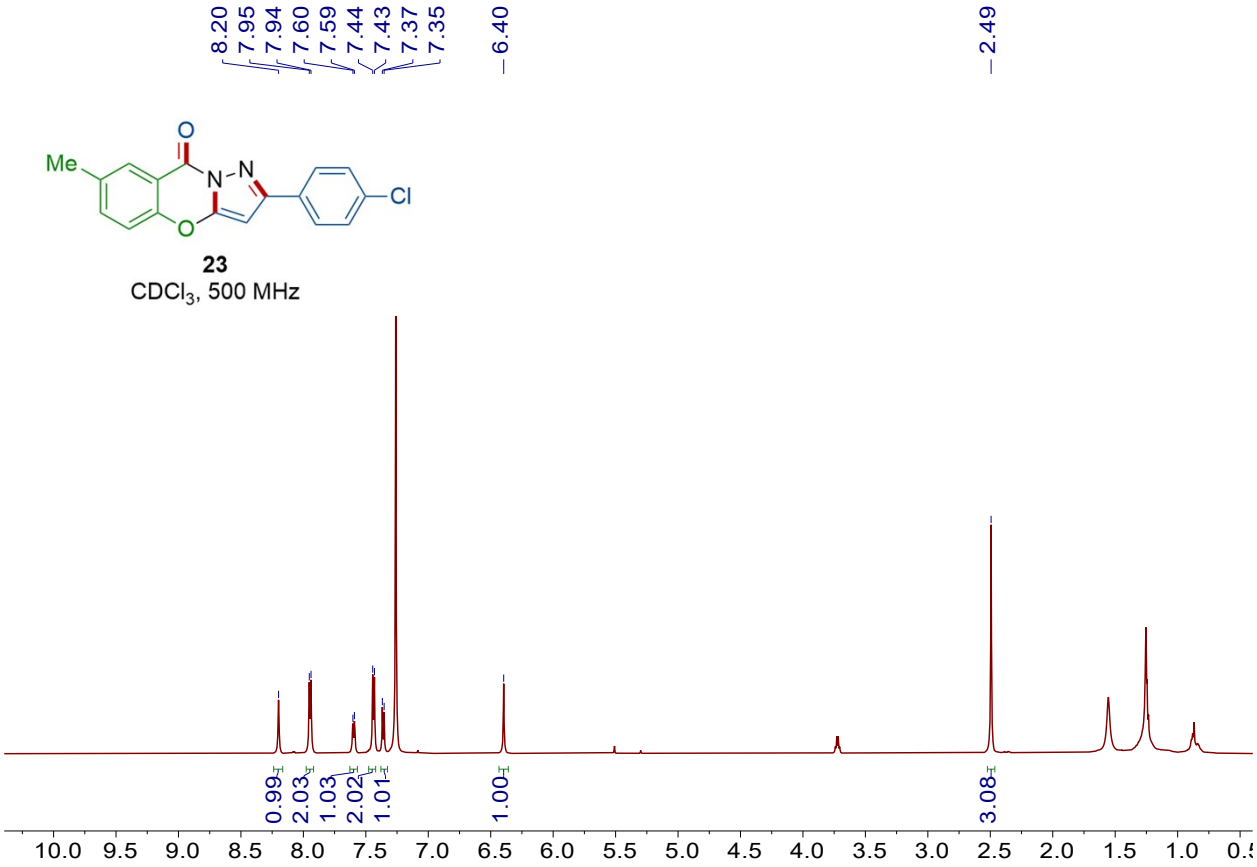
^{1}H NMR spectrum of **22** ($CDCl_3$, 500 MHz)



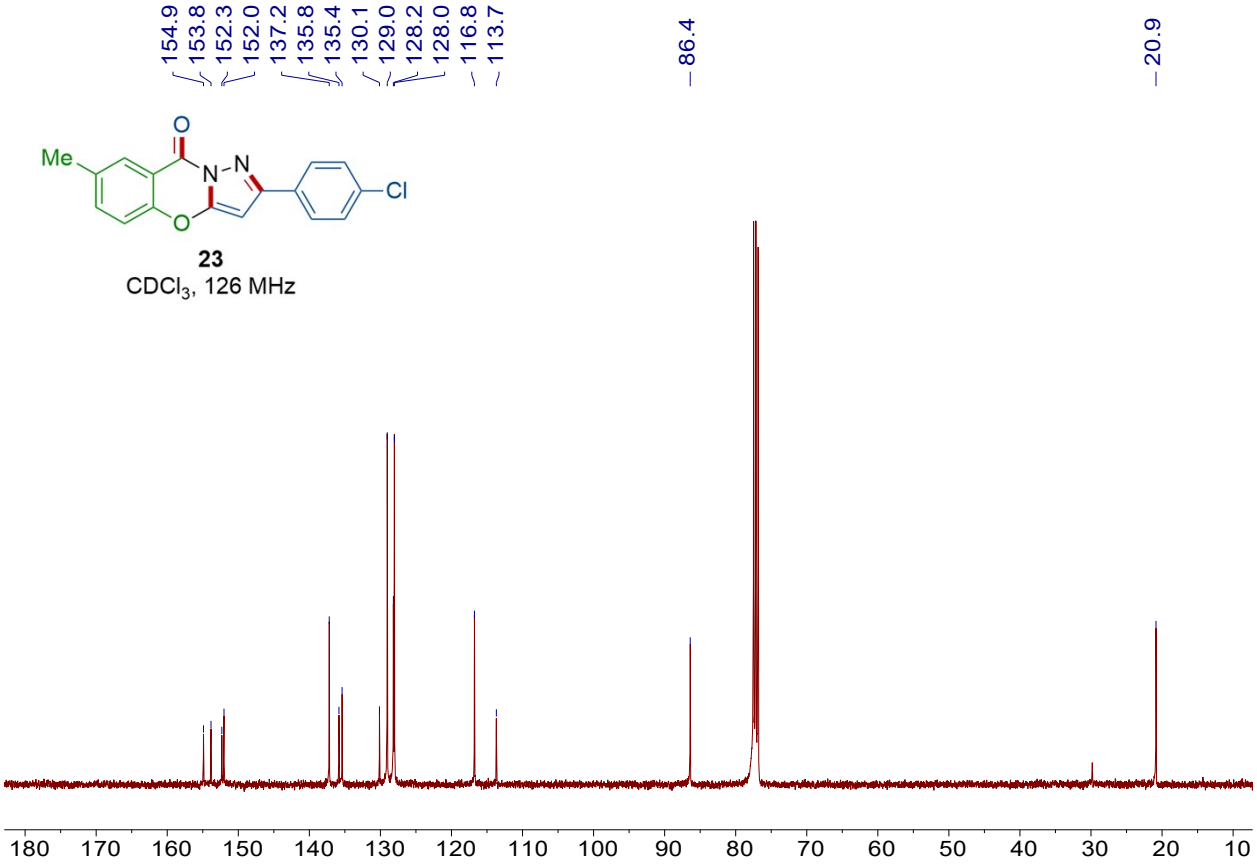
^{13}C NMR spectrum of **22** ($CDCl_3$, 126 MHz)



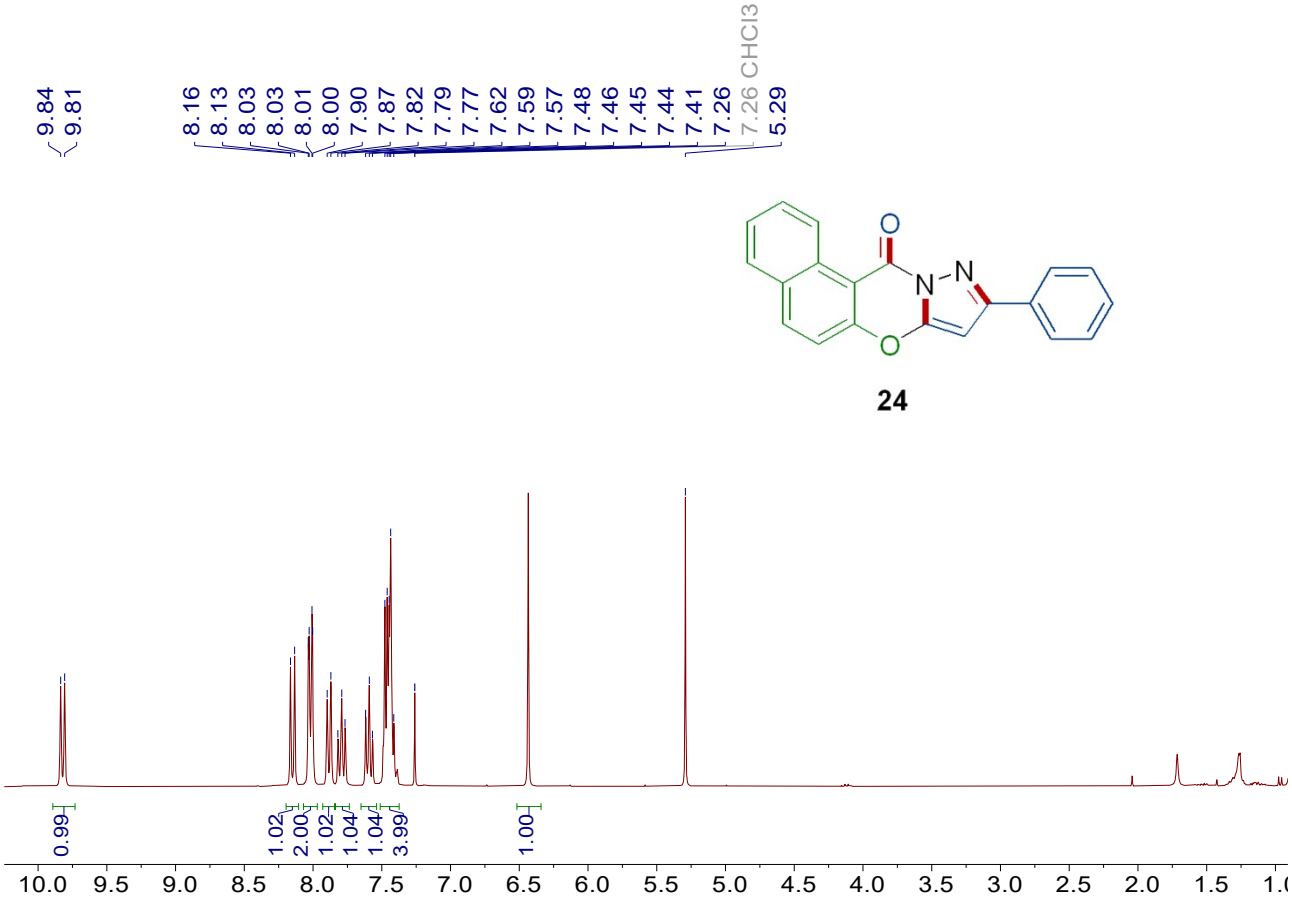
^{1}H NMR spectrum of **23** ($CDCl_3$, 500 MHz)



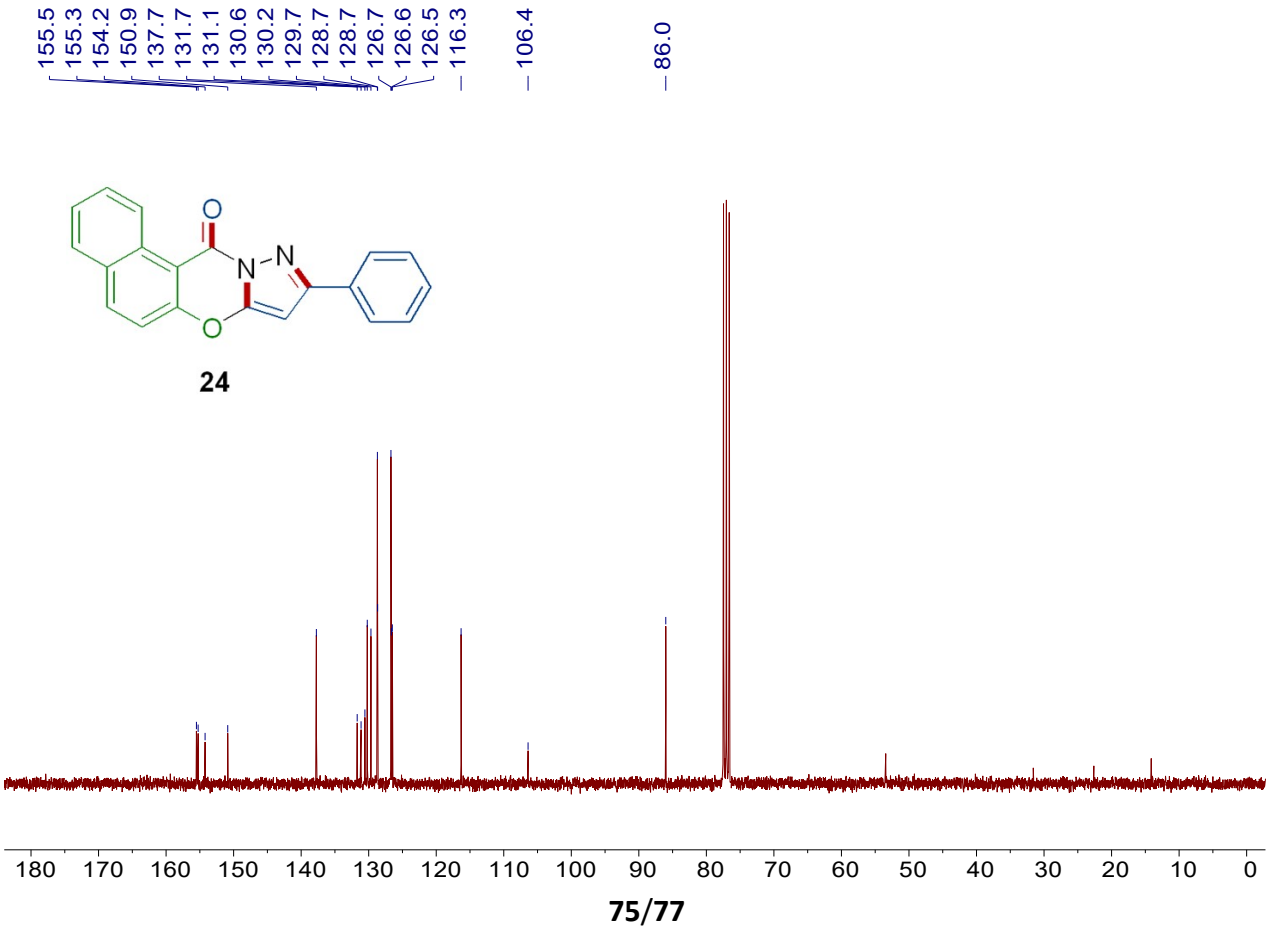
^{13}C NMR spectrum of **23** ($CDCl_3$, 126 MHz)



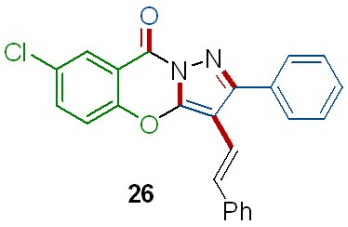
^{1}H NMR spectrum of **24** ($CDCl_3$, 400 MHz)

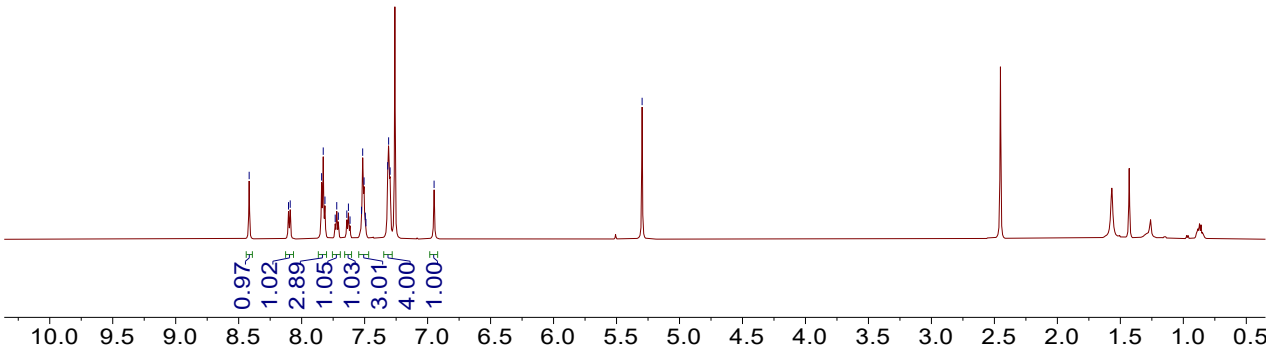


^{13}C NMR spectrum of **24** ($CDCl_3$, 126 MHz)

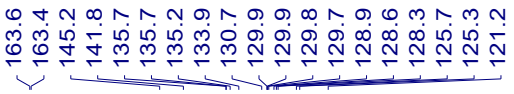


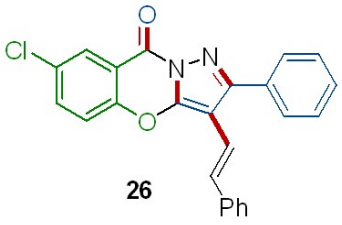
^{1}H NMR spectrum of **26** ($CDCl_3$, 500 MHz)



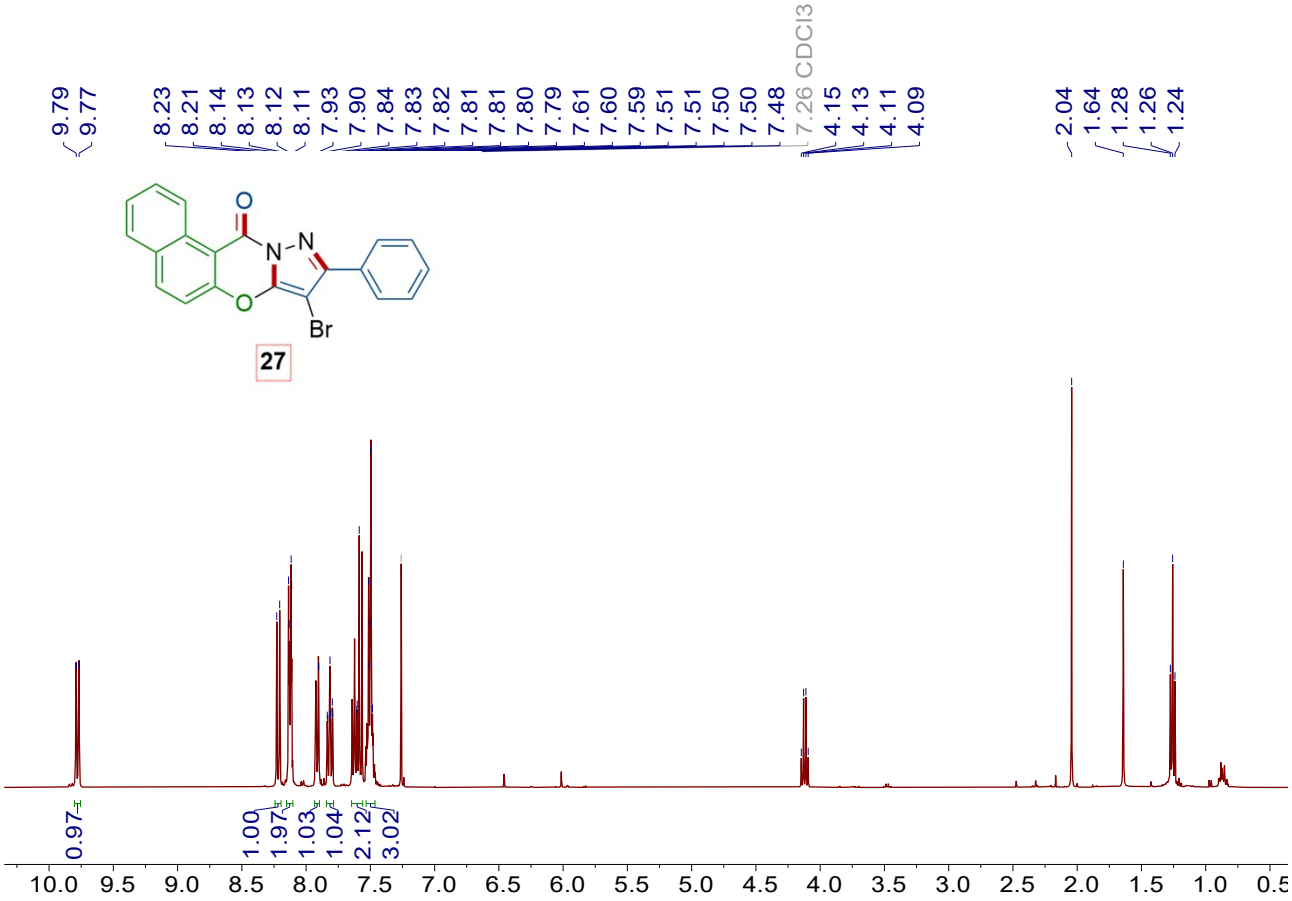


^{13}C NMR spectrum of **26** ($CDCl_3$, 126 MHz)





^{1}H NMR spectrum of **27** ($CDCl_3$, 500 MHz)



^{13}C NMR spectrum of **27** ($CDCl_3$, 126 MHz)