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Supporting Information

Copper-catalyzed asymmetric alkynylation of pyrazole-4,5-diones with chloramphenicol base-derived hydroxyl oxazoline ligands

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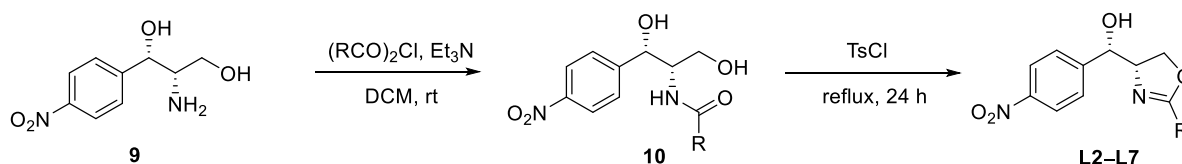
1. General Information

All commercially available reagents were used without further purification. Chromatography was conducted by using 300–400 mesh silica gel. ^1H and ^{13}C spectra of known compounds were in accordance with those described in the literatures. ^1H (400 MHz or 600 MHz), ^{13}C (100 MHz or 150 MHz) NMR and ^{19}F (376 MHz) were recorded on a Bruker Avance 400 spectrometer in CDCl_3 or DMSO using tetramethylsilane (TMS) as internal standards. Coupling constants (J) are given in Hz and are uncorrected and multiplicities for coupled signals were denoted as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad, apt. = apparent and dd = double doublet etc. High-resolution mass spectra (HRMS) were recorded on a Bruker TOF Premier, by the ESI method. Melting points (m.p.) were recorded on an SRS-optic melting point apparatus. Optical rotation was obtained from Rudolph Research Analytical Autopol VI automatic polarimeter. Chiral HPLC was performed using Daicel Chiralcel analytical column. Unless otherwise noted, all products are isolated yields.

2. Experimental Procedures

2.1 Preparation of chloramphenicol base (ANP)-derived ligands (L1–L7)

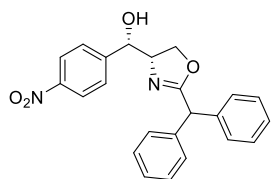
ANP-derived amino alcohol ligand **L1** was prepared by the reported literature.¹ The product matched the known ^1H NMR spectra. Typical procedure for the preparation of ANP-derived hydroxyl oxazolines ligands **L2–L7**.²



To a solution of (1*S*,2*S*)-2-amino-1-(*p*-nitrophenyl) propane 1, 3-diol **9** (4.24 g, 20 mmol) in 40 mL CH_2Cl_2 was added triethylamine (10.1 g, 0.1 mol). Then the mixture was cooled to 0°C , alkyl or aryl anhydride (20 mmol) was added dropwise. The reaction was allowed to warm to room temperature until the consumption of starting material was observed by TLC. The reaction was quenched by water (200 mL), and organic materials were extracted with dichloromethane (30 mL x 3). The combined extracts were washed with brine, and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel ($\text{DCM}/\text{CH}_3\text{OH}=100:1$) to afford **10**.

TsCl was added to a solution of **10** in CH_2Cl_2 , the resulting mixture was brought to reflux for 24 h. The reaction was quenched by water (150 mL), and organic materials were extracted with dichloromethane (30 mL x 3). The combined extracts were washed with brine, and dried over anhydrous Na_2SO_4 . The solvent was removed under reduced pressure and the residue was purified by flash chromatography on silica gel followed by recrystallization from EtOAc/Hexane to afford **L2–L7**. The compounds (**L2–L5**) matched the known ^1H NMR spectra.

(*S*)-((*S*)-2-benzhydryl-4,5-dihydrooxazol-4-yl) (4-nitrophenyl) methanol (**L6**)

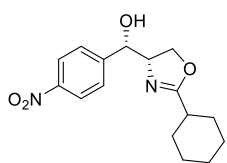


Prepared by the general procedure from anhydride diphenylacetic acid, and **L6** was isolated as a white solid, ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 8.14 – 8.09 (m, 2H), 7.59 – 7.57 (m, 2H), 7.28 – 7.14 (m, 10H), 5.93 (d, $J = 4.4$ Hz, 1H), 5.02 (s, 1H), 4.95 – 4.93 (m, 1H), 4.51 (td, $J = 8.4, 3.9$ Hz, 1H), 4.25 – 4.23 (m, 2H). ^{13}C NMR (100 MHz, $\text{DMSO}-d_6$) δ 167.7, 150.4, 147.0, 140.4, 140.2, 129.0, 128.9, 128.7, 128.6, 128.5, 127.2, 127.1, 123.0, 72.2, 71.2, 68.7, 50.4. HRMS (ESI) m/z calcd for $\text{C}_{23}\text{H}_{21}\text{N}_2\text{O}_4$ [$\text{M} + \text{H}$] $^+$: 389.1496,

found: 389.1492.

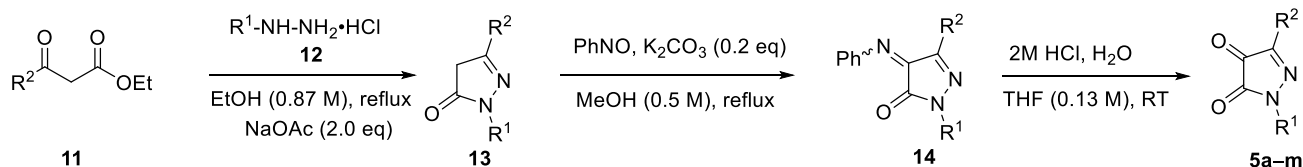
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(S)-((S)-2-cyclohexyl-4,5-dihydrooxazol-4-yl) (4-nitrophenyl) methanol (L7)



Prepared by the general procedure from cyclohexanecarbonyl, and **L7** was isolated as a white solid, $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$) δ 8.18 – 8.15 (m, 2H), 7.61 – 7.59 (m, 2H), 5.75 (d, $J = 4.8$ Hz, 1H), 4.86 – 4.83 (m, 1H), 4.42 – 4.36 (m, 1H), 4.13 – 4.05 (m, 2H), 2.11 – 2.05 (m, 1H), 1.70 – 1.47 (m, 5H), 1.26 – 1.10 (m, 5H). $^{13}\text{C NMR}$ (100 MHz, $\text{DMSO-}d_6$) δ 170.8, 150.5, 146.9, 128.6, 122.9, 72.4, 71.1, 68.0, 36.8, 29.8, 29.7, 25.9, 25.3. **HRMS (ESI)** m/z calcd for $\text{C}_{16}\text{H}_{21}\text{N}_2\text{O}_4$ [$\text{M} + \text{H}$] $^+$: 305.1496, found: 305.1491.

2.2 General synthesis of pyrazole-4,5-dione (5a-m)³



To a solution of **11** (20 mmol, 1.0 equiv.) in ethanol (30 mL, 0.87 M) was added **12** (40 mmol, 2.0 equiv.) and sodium acetate (3.29 g, 40 mmol, 2.0 equiv.). A reflux condenser was then fitted to the reaction flask, and the reaction mixture was refluxed overnight with stirring and under an atmosphere of nitrogen. After cooling to room temperature, the mixture was diluted with water, transferred to a separatory funnel, and extracted with CH_2Cl_2 . The combined organic layers were washed with brine, dried over Na_2SO_4 , then vacuo and the residue were chromatographed giving compound pyrazolon derivative **13**.

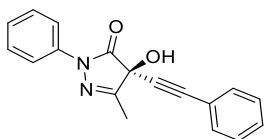
Add PhNO (1.0 equiv.) to a solution of pyrazolon derivative **13** (1.0 equiv.) in MeOH (0.6 M) and the K_2CO_3 (0.2 equiv.) was added at once, the mixture was refluxed for 3 hours. The solvent was removed under reduced pressure and the crude product was directly purified by flash column chromatography (silica, *n*-pentane / diethyl ether) to afford the desired product **14**.

To a solution of pyrazolon-derived phenyl-ketimine **14** in THF (0.13 M), 2 M HCl was added and stirring at room temperature in 10 minutes–5.5 hours. The reaction mixture was neutralized with a saturated solution of H_2O and extracted with CH_2Cl_2 . The organic layer was dried over Na_2SO_4 , evaporated in vacuo and the compound **5** was purified by flash chromatography. The products matched the known $^1\text{H NMR}$ spectra.

2.3 General procedure for the asymmetric alkylation of pyrazole-4,5-dione

To a mixture of CuI (3.8 mg, 0.02 mmol), **L5** (6.1 mg, 0.022 mmol), 4Å MS (50 mg), 2-methyltetrahydrofuran (0.25 mL) was added under an atmosphere of nitrogen and the mixture was stirred at room temperature for 2 hours. Then phenylacetylene (**6a-t**) (14 μL , 0.12 mmol) was added to the mixture. After stirred for 30 minutes at the same temperature, pyrazole-4,5-dione (**5a-m**) (18.8 mg, 0.1 mmol) and 2-methyltetrahydrofuran (0.25 mL) were added in one portion. The mixture was stirred at -10 °C until the starting material was completely consumed (TLC monitoring). After completion, the crude product was concentrated under reduced pressure to dryness, purification by column chromatography on silica gel (PE/EA=10:1) afforded the alkylation products (**7a-t** and **8a-m**).

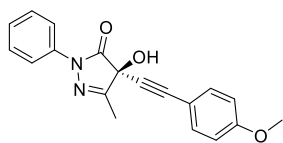
(S)-4-hydroxy-5-methyl-2-phenyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (7a)



White solid, 27.6 mg, 95% yield. mp = 130.2–132.7 °C. $[\alpha]_{\text{D}}^{25} = -380.4$ ($c = 0.27$ in CH_2Cl_2). 98% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_{\text{R}} = 12.0$ min (minor), 15.0 min (major). {Lit.⁴ $[\alpha]_{\text{D}}^{25} = -380.4$ ($c = 0.27$, CH_2Cl_2) for (S)-enantiomer}. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.82 – 7.80 (m, 2H), 7.37 – 7.31 (m, 4H), 7.29 – 7.24 (m, 1H), 7.21 – 7.17 (m, 2H), 7.16 – 7.11 (m, 1H), 4.20 (s, 1H), 2.26 (s, 3H). $^{13}\text{C NMR}$ (100 MHz, Chloroform-*d*) δ 168.8, 158.0, 136.4, 131.1, 128.4, 127.9, 127.3, 124.6, 119.8, 118.0, 87.8, 80.7, 72.1, 12.0. **HRMS (ESI)** m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 312.0875, found: 312.0874.

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(S)-4-hydroxy-4-((4-methoxyphenyl) ethynyl)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7b)



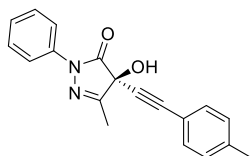
White solid, 28.8 mg, 90% yield. mp = 204.3–206.8 °C. $[\alpha]_D^{25} = -325.6$ ($c = 0.12$ in CH_2Cl_2). 93% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 21.9$ min (minor), 19.0 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.90 – 7.87 (m, 2H), 7.43 – 7.26 (m, 4H), 7.23 – 7.20 (m, 1H), 6.83 – 6.75 (m, 2H), 4.36 (s, 1H), 3.80 (s, 3H), 2.34 (s, 3H). **$^{13}\text{C NMR}$**

(100 MHz, Chloroform-*d*) δ 168.7, 159.5, 157.7, 136.5, 132.8, 127.9, 124.5, 117.9, 113.0, 111.7, 88.1, 79.5, 72.0, 54.3, 12.0.

HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{NaO}_3$ [$\text{M} + \text{Na}$] $^+$: 343.1053, found: 343.1057.

(S)-4-hydroxy-5-methyl-2-phenyl-4-(*p*-tolylethynyl)-2,4-dihydro-3H-pyrazol-3-one (7c)

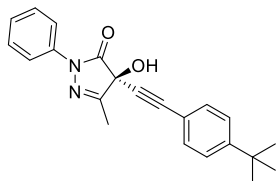


White solid, 28.3 mg, 93% yield. mp = 138.2–140.5 °C. $[\alpha]_D^{25} = -278.5$ ($c = 0.27$ in CH_2Cl_2). 90% ee. **HPLC**

(CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 14.9$ min (minor), 13.5 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.90 – 7.88 (m, 2H), 7.43 – 7.39 (m, 2H), 7.33 (d, $J = 7.8$ Hz, 2H), 7.23 – 7.19 (m, 1H), 7.08 (d, $J = 7.8$ Hz, 2H), 4.29 (s, 1H), 2.34 (s, 6H). **$^{13}\text{C NMR}$**

(100 MHz, Chloroform-*d*) δ 168.5, 157.5, 138.9, 136.5, 131.1, 128.1, 127.9, 124.5, 117.9, 116.6, 88.2, 80.0, 71.9, 20.6, 12.0. **HRMS (ESI)** m/z calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 327.1104, found: 327.1102.

(S)-4-((4-(*tert*-butyl)phenyl) ethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7d)

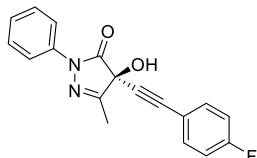


White solid, 31.1 mg, 90% yield. mp = 124.6–126.4 °C. $[\alpha]_D^{25} = -288.9$ ($c = 0.24$ in CH_2Cl_2). 93% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 15.6$ min (minor), 10.7 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.90 – 7.88 (m, 2H), 7.43 – 7.37 (m, 4H), 7.30 – 7.28 (m, 2H), 7.23 – 7.19 (m, 1H), 4.56 (s, 1H), 2.34 (s, 3H), 1.29 (s, 9H). **$^{13}\text{C NMR}$**

(100 MHz, Chloroform-*d*) δ 168.7, 157.8, 151.9, 136.4, 130.9, 127.9, 124.5, 124.3, 117.9, 116.7, 88.2, 80.1, 72.0, 33.8, 30.1, 12.0. **HRMS (ESI)** m/z calcd for $\text{C}_{22}\text{H}_{22}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 369.1573, found: 369.1572.

(S)-4-((4-fluorophenyl)ethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7e)

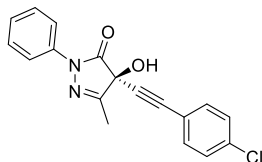


White solid, 28.3 mg, 92% yield. mp = 140.2–142.3 °C. $[\alpha]_D^{25} = -282.9$ ($c = 0.23$ in CH_2Cl_2). 97% ee. **HPLC**

(CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 13.8$ min (minor), 16.2 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.82 – 7.79 (m, 2H), 7.39 – 7.31 (m, 3H), 7.18 – 7.12 (m, 2H), 6.94 – 6.89 (m, 2H), 4.25 – 4.23 (m, 1H), 2.26 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.5, 162.2 (d, $J = 251.7$ Hz), 157.4, 136.4, 133.3 (d, $J = 8.7$ Hz), 127.9, 124.6, 117.9,

115.9 (d, $J = 3.6$ Hz), 114.8 (d, $J = 22.3$ Hz), 86.8, 80.5, 71.9, 12.0. **$^{19}\text{F NMR}$** (376 MHz, Chloroform-*d*) δ -108.4. **HRMS (ESI)** m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{NaO}_2\text{F}$ [$\text{M} + \text{Na}$] $^+$: 331.0853, found: 331.0854.

(S)-4-((4-chlorophenyl) ethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7f)

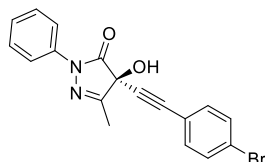


White solid, 28.2 mg, 87% yield. mp = 154.2–156.3 °C. $[\alpha]_D^{25} = -295.2$ ($c = 0.18$ in CH_2Cl_2). 92% ee. **HPLC**

(CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 16.3$ min (minor), 17.7 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.89 – 7.86 (m, 2H), 7.44 – 7.36 (m, 3H), 7.30 – 7.27 (m, 3H), 7.24 – 7.20 (m, 1H), 4.09 (s, 1H), 2.33 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.3, 157.2, 136.4, 134.9, 132.4, 127.9, 127.8, 124.6, 118.2, 117.9, 86.7, 81.6, 71.8, 12.1. **HRMS**

(ESI) m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{NaO}_2\text{Cl}$ [$\text{M} + \text{Na}$] $^+$: 347.0558, found: 347.0551.

(S)-4-((4-bromophenyl) ethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7g)



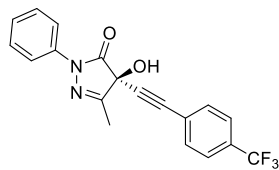
White solid, 31.3 mg, 86% yield. mp = 151.2–153.7 °C. $[\alpha]_D^{25} = -229.0$ ($c = 0.24$ in CH_2Cl_2). 95% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 8.4$ min (minor), 10.1 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.89 – 7.86 (m, 2H), 7.46 – 7.39 (m, 4H), 7.33 – 7.29 (m, 2H), 7.24 – 7.20 (m, 1H), 3.88 (s, 1H), 2.33 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.2, 157.1, 136.4, 132.5, 130.7, 127.9, 124.6, 123.2, 118.6, 117.9, 86.7, 81.8, 71.8,

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12.1. **HRMS (ESI)** m/z calcd for $C_{19}H_{16}N_2NaO_2$ [$M + Na$] $^+$: 389.9975, found: 389.9980.

(S)-4-hydroxy-5-methyl-2-phenyl-4-((4-(trifluoromethyl)phenyl)ethynyl)-2,4-dihydro-3H-pyrazol-3-one (7h)

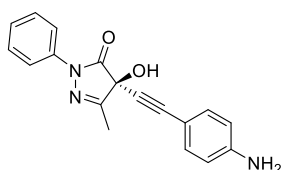


White solid, 32.2 mg, 90% yield. mp = 153.2–155.3 °C. $[\alpha]_D^{25} = -252.4$ ($c = 0.30$ in CH_2Cl_2). 89% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 15.5$ min (minor), 17.1 min (major). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.90 – 7.87 (m, 2H), 7.54 – 7.53(m, 4H), 7.43 – 7.39 (m, 2H), 7.24 (d, $J = 7.4$ Hz, 1H), 4.75 (s, 1H), 2.35 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 168.5, 157.4, 136.3, 131.4, 130.2 (d, $J = 32.9$ Hz), 128.0, 124.8, 124.3 (q, $J = 3.8$ Hz),

123.5, 122.6 (d, $J = 272.5$ Hz), 117.9, 86.3, 82.9, 71.9, 12.1. **^{19}F NMR** (376 MHz, Chloroform-*d*) δ -63.1. **HRMS (ESI)** m/z calcd for $C_{19}H_{13}N_2NaO_2F_3$ [$M + Na$] $^+$: 381.0821, found: 381.0810.

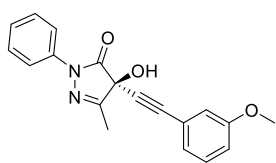
(S)-4-((4-aminophenyl) ethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7i)



Brown oil, 25.6 mg, 84% yield. $[\alpha]_D^{25} = -87.7$ ($c = 0.16$ in CH_2Cl_2). 88% ee. **HPLC** (CHIRALCEL OD-H), *n*-hexane/2-propanol = 70/30, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 31.8$ min (minor), 14.5 min (major). **1H NMR** (400 MHz, DMSO-*d*₆) δ 7.81 – 7.78 (m, 2H), 7.49 – 7.46 (m, 1H), 7.45 – 7.42 (m, 1H), 7.25 – 7.20 (m, 1H), 7.16 – 7.11 (m, 2H), 6.53 – 6.49 (m, 2H), 5.67 (s, 2H), 2.21 (s, 3H). **^{13}C NMR** (150 MHz, DMSO-*d*₆) δ 169.4, 159.9, 150.2, 137.3, 133.1, 129.0, 125.0, 118.1, 113.4, 105.7, 89.1, 79.8, 72.3,

12.5. **HRMS (ESI)** m/z calcd for $C_{18}H_{15}N_3NaO_2$ [$M + Na$] $^+$: 328.1056, found: 328.1059.

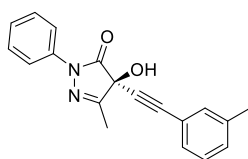
(S)-4-hydroxy-4-((3-methoxyphenyl) ethynyl)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7j)



White solid, 27.2 mg, 85% yield. mp = 107.7–109.3 °C. $[\alpha]_D^{25} = -294.1$ ($c = 0.3$ in CH_2Cl_2). 91% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 15.4$ min (minor), 20.3 min (major). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.90 – 7.88 (m, 2H), 7.43 – 7.39 (m, 2H), 7.24 – 7.17 (m, 2H), 7.05 – 7.03 (m, 1H), 6.97 – 6.96 (m, 1H), 6.92 – 6.89 (m, 1H), 4.07 (s, 1H), 3.77 (s, 3H), 2.34 (s, 3H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 168.4, 158.2, 157.4, 136.4, 128.4, 127.9, 124.6,

123.7, 120.7, 117.9, 115.7, 115.4, 87.8, 80.4, 71.9, 54.3, 12.0. **HRMS (ESI)** m/z calcd for $C_{19}H_{16}N_2NaO_3$ [$M + Na$] $^+$: 343.1053, found: 343.1049.

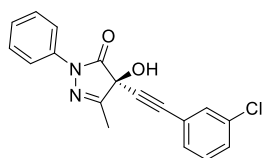
(S)-4-hydroxy-5-methyl-2-phenyl-4-(*m*-tolylethynyl)-2,4-dihydro-3H-pyrazol-3-one (7k)



White solid, 28.6 mg, 94% yield. mp = 138.2–140.5 °C. $[\alpha]_D^{25} = -297.2$ ($c = 0.20$ in CH_2Cl_2). 96% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 9.9$ min (minor), 12.9 min (major). **1H NMR** (400 MHz, Chloroform-*d*) δ 7.81 – 7.79 (m, 2H), 7.34 – 7.30 (m, 2H), 7.17 – 7.10 (m, 3H), 7.07 – 7.05 (m, 2H), 4.54 (s, 1H), 2.25 – 2.19 (m, 6H). **^{13}C NMR** (100 MHz, Chloroform-*d*) δ 168.7, 157.7, 137.1, 136.5, 131.7, 129.4, 128.3, 127.9, 127.2, 124.5, 119.6, 118.0, 88.1, 80.4, 72.0,

20.1, 12.0. **HRMS (ESI)** m/z calcd for $C_{19}H_{16}N_2NaO_2$ [$M + Na$] $^+$: 327.1104, found: 327.1095.

(S)-4-((3-chlorophenyl) ethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7l)

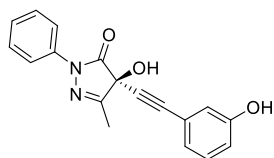


White solid, 29.2 mg, 90% yield. mp = 154.2–157.3 °C. $[\alpha]_D^{25} = -254.2$ ($c = 0.16$ in CH_2Cl_2). 95% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 9.4$ min (minor), 13.1 min (major). **1H NMR** (400 MHz, DMSO-*d*₆) δ 7.82 – 7.77 (m, 3H), 7.63 – 7.62(m, 1H), 7.55 – 7.42(m, 4H), 7.26 – 7.22 (m, 1H), 2.25 (s, 3H). **^{13}C NMR** (100 MHz, DMSO-*d*₆) δ 169.4, 160.0, 137.8, 133.9, 131.8, 131.2, 131.1, 130.5, 129.6, 125.8, 122.8, 118.7, 85.9, 84.6, 72.7, 13.2. **HRMS (ESI)**

m/z calcd for $C_{18}H_{13}N_2NaO_2Cl$ [$M + Na$] $^+$: 347.0558, found: 347.0568.

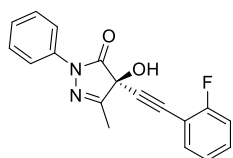
4-hydroxy-4-((3-hydroxyphenyl) ethynyl)-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7m)

SUPPORTING INFORMATION



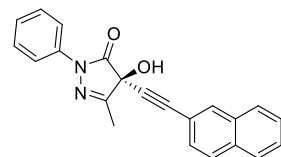
Brown oil, 24.1 mg, 79% yield. $[\alpha]_{\text{D}}^{25} = -60.3$ ($c = 0.16$ in CH_2Cl_2). 81% ee. **HPLC** (CHIRALCEL AD-H), n -hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_{\text{R}} = 15.9$ min (minor), 17.6 min (major). **$^1\text{H NMR}$** (400 MHz, $\text{DMSO-}d_6$) δ 9.77 (s, 1H), 7.82 – 7.78 (m, 2H), 7.72 – 7.69 (m, 1H), 7.48 – 7.44 (m, 2H), 7.25 – 7.18 (m, 2H), 6.95 – 6.92 (m, 1H), 6.86 – 6.84 (m, 2H), 2.23 (s, 3H). **$^{13}\text{C NMR}$** (150 MHz, $\text{DMSO-}d_6$) δ 169.1, 159.6, 157.3, 137.2, 129.9, 129.0, 125.2, 122.5, 121.0, 118.2, 118.1, 117.2, 87.1, 82.1, 72.2, 12.5. **HRMS (ESI)** m/z calcd for $\text{C}_{18}\text{H}_{14}\text{N}_2\text{NaO}_3$ $[\text{M} + \text{Na}]^+$: 329.0897, found: 329.0897.

(S)-4-((2-fluorophenyl)ethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7n)



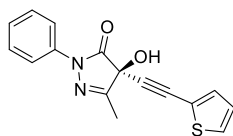
White solid, 28.6 mg, 93% yield. mp = 140.2–143.3 °C. $[\alpha]_{\text{D}}^{25} = -302.1$ ($c = 0.16$ in CH_2Cl_2). 90% ee. **HPLC** (CHIRALCEL AD-H), n -hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_{\text{R}} = 12.3$ min (minor), 17.0 min (major). **$^1\text{H NMR}$** (400 MHz, $\text{DMSO-}d_6$) δ 7.81 – 7.79 (m, 2H), 7.61 – 7.59 (m, 1H), 7.54 – 7.45 (m, 3H), 7.36 – 7.33 (m, 1H), 7.27 – 7.23 (m, 2H), 2.25 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, $\text{DMSO-}d_6$) δ 169.4, 162.8 (d, $J = 250.8$ Hz), 159.9, 137.8, 134.4, 132.7 (d, $J = 8.2$ Hz), 129.6, 125.8, 125.4 (d, $J = 3.6$ Hz), 118.8, 116.3 (d, $J = 20.3$ Hz), 109.2 (d, $J = 15.1$ Hz), 88.4 (d, $J = 3.4$ Hz), 80.9, 72.8, 13.1. **$^{19}\text{F NMR}$** (376 MHz, Chloroform- d) δ -108.7. **HRMS (ESI)** m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{NaO}_2\text{F}$ $[\text{M} + \text{Na}]^+$: 331.0853, found: 331.0844.

(S)-4-hydroxy-5-methyl-4-(naphthalen-2-ylethynyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7o)



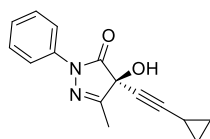
White solid, 32.6 mg, 96% yield. mp = 134.2–136.5 °C. $[\alpha]_{\text{D}}^{25} = -312.4$ ($c = 0.22$ in CH_2Cl_2). 94% ee. **HPLC** (CHIRALCEL AD-H), n -hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_{\text{R}} = 16.8$ min (minor), 19.8 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform- d) δ 7.99 (s, 1H), 7.93 – 7.90 (m, 2H), 7.80 – 7.77 (m, 1H), 7.74 – 7.72 (m, 2H), 7.51 – 7.39 (m, 5H), 7.23 (d, $J = 7.4$ Hz, 1H), 4.33 (s, 1H), 2.38 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform- d) δ 168.6, 157.5, 136.4, 132.3, 131.8, 131.6, 127.9, 127.1, 126.9, 126.8, 126.3, 125.7, 124.6, 117.9, 117.0, 88.3, 80.9, 72.0, 12.1. **HRMS (ESI)** m/z calcd for $\text{C}_{22}\text{H}_{16}\text{N}_2\text{NaO}_2$ $[\text{M} + \text{Na}]^+$: 363.1104, found: 363.1101.

(S)-4-hydroxy-5-methyl-2-phenyl-4-(thiophen-3-ylethynyl)-2,4-dihydro-3H-pyrazol-3-one (7p)



White solid, 27.5 mg, 93% yield. mp = 153.2–155.3 °C. $[\alpha]_{\text{D}}^{25} = -252.4$ ($c = 0.30$ in CH_2Cl_2). 97% ee. **HPLC** (CHIRALCEL AD-H), n -hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_{\text{R}} = 12.4$ min (minor), 16.3 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform- d) δ 7.89 – 7.86 (m, 2H), 7.43 – 7.38 (m, 2H), 7.32 – 7.30 (m, 1H), 7.28 – 7.27 (m, 1H), 7.23 – 7.19 (m, 1H), 6.97 – 6.95 (m, 1H), 4.48 (s, 1H), 2.34 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform- d) δ 168.4, 157.4, 136.3, 133.2, 128.0, 127.9, 126.1, 124.6, 119.5, 118.0, 84.4, 81.4, 72.1, 12.1. **HRMS (ESI)** m/z calcd for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{NaO}_2\text{S}$ $[\text{M} + \text{Na}]^+$: 319.0502, found: 319.0496.

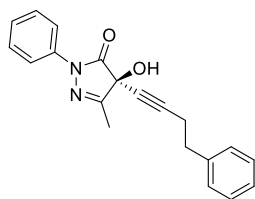
(S)-4-(cyclopropylethynyl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7q)



White solid, 18.3 mg, 72% yield. mp = 126.3–128.2 °C. $[\alpha]_{\text{D}}^{25} = -224.6$ ($c = 0.21$ in CH_2Cl_2). 79% ee. **HPLC** (CHIRALCEL AD-H), n -hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_{\text{R}} = 8.8$ min (minor), 11.7 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform- d) δ 7.88 – 7.85 (m, 2H), 7.42 – 7.38 (m, 2H), 7.22 – 7.18 (m, 1H), 4.17 (s, 1H), 2.24 (s, 3H), 1.29 – 1.25 (m, 1H), 0.84 – 0.73 (m, 4H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform- d) δ 170.3, 159.3, 138.0, 129.3, 125.9, 119.3, 94.4, 73.0, 68.9, 13.3, 9.2, 9.1, 1.5. **HRMS (ESI)** m/z calcd for $\text{C}_{15}\text{H}_{14}\text{N}_2\text{NaO}_2$ $[\text{M} + \text{Na}]^+$: 277.0947, found: 277.0933.

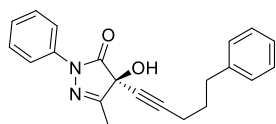
(S)-4-hydroxy-5-methyl-2-phenyl-4-(4-phenylbut-1-yn-1-yl)-2,4-dihydro-3H-pyrazol-3-one (7r)

SUPPORTING INFORMATION



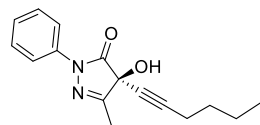
Yellow oil, 21.3 mg, 67% yield. $[\alpha]_D^{25} = -101.7$ ($c = 0.06$ in CH_2Cl_2). 90% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 12.2$ min (minor), 16.4 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.80 – 7.77 (m, 2H), 7.35 – 7.30 (m, 2H), 7.21 – 7.17 (m, 2H), 7.15 – 7.07 (m, 4H), 4.01 (s, 1H), 2.73 (t, $J = 7.4$ Hz, 2H), 2.46 (t, $J = 7.4$ Hz, 2H), 2.09 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.8, 157.8, 138.8, 136.5, 128.3, 127.9, 127.4, 125.5, 124.5, 117.9, 88.8, 73.3, 71.5, 33.2, 20.0, 11.8. **HRMS (ESI)** m/z calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 341.1260, found: 341.1253.

(S)-4-hydroxy-5-methyl-2-phenyl-4-(5-phenylpent-1-yn-1-yl)-2,4-dihydro-3H-pyrazol-3-one (7s)



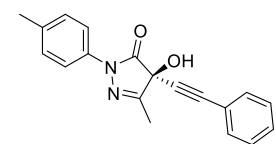
Yellow oil, 21.6 mg, 65% yield. $[\alpha]_D^{25} = -3.87$ ($c = 0.31$ in CH_2Cl_2). 83% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 9.1$ min (minor), 10.4 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.80 – 7.78 (m, 2H), 7.33 – 7.29 (m, 2H), 7.20 – 7.16 (m, 2H), 7.14 – 7.10 (m, 2H), 7.07 – 7.05 (m, 2H), 4.18 (s, 1H), 2.60 (t, $J = 7.3$ Hz, 2H), 2.19 (s, 3H), 2.15 (t, $J = 7.3$ Hz, 2H), 1.79 – 1.72 (m, 2H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.9, 157.9, 140.0, 136.5, 127.9, 127.5, 127.4, 125.0, 124.5, 117.9, 89.4, 73.0, 71.6, 33.7, 28.5, 17.2, 11.9. **HRMS (ESI)** m/z calcd for $\text{C}_{21}\text{H}_{20}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 355.1417, found: 355.1407.

(S)-4-(hex-1-yn-1-yl)-4-hydroxy-5-methyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (7t)



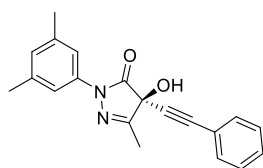
Yellow oil, 19.4 mg, 72% yield. $[\alpha]_D^{25} = -177.7$ ($c = 0.10$ in CH_2Cl_2). 89% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 7.6$ min (minor), 9.7 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.89 – 7.86 (m, 2H), 7.42 – 7.38 (m, 2H), 7.22 – 7.18 (m, 1H), 4.48 (s, 1H), 2.26 (s, 3H), 2.23 (t, $J = 7.1$ Hz, 2H), 1.52 – 1.45 (m, 2H), 1.40 – 1.32 (m, 2H), 0.87 (t, $J = 7.1$ Hz, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 169.1, 158.1, 136.5, 127.9, 124.4, 117.9, 89.9, 72.3, 71.6, 29.0, 20.9, 17.5, 12.5, 11.8. **HRMS (ESI)** m/z calcd for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 293.1260, found: 293.1250.

(S)-4-hydroxy-5-methyl-4-(phenylethynyl)-2-(p-tolyl)-2,4-dihydro-3H-pyrazol-3-one (8a)



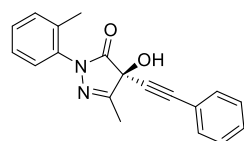
White solid, 27.4 mg, 90% yield. mp = 132.5–134.7 °C. $[\alpha]_D^{25} = -242.1$ ($c = 0.31$ in CH_2Cl_2). 98% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 13.3$ min (minor), 24.5 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.90 – 7.87 (m, 2H), 7.43 – 7.36 (m, 2H), 7.28 – 7.25 (m, 2H), 7.21 – 7.14 (m, 3H), 4.31 (s, 1H), 2.34 – 2.29 (m, 6H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.5, 157.6, 134.3, 134.0, 131.2, 128.4, 128.4, 119.8, 118.1, 118.0, 87.7, 80.8, 71.9, 20.0, 12.0. **HRMS (ESI)** m/z calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 327.1108, found: 327.1105.

(S)-2-(3,5-dimethylphenyl)-4-hydroxy-5-methyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8b)



White solid, 27.0 mg, 85% yield. mp = 83.5–84.2 °C. $[\alpha]_D^{25} = -297.0$ ($c = 0.23$ in CH_2Cl_2). 92% ee. **HPLC** (CHIRALCEL OD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 7.1$ min (minor), 12.7 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.42 (s, 2H), 7.36 – 7.34 (m, 2H), 7.28 – 7.24 (m, 1H), 7.21 – 7.17 (m, 2H), 6.78 (s, 1H), 4.27 (s, 1H), 2.29 – 2.26 (m, 9H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.5, 157.4, 137.7, 136.2, 131.2, 128.5, 127.3, 126.4, 119.8, 115.8, 87.7, 80.8, 71.9, 20.4, 12.0. **HRMS (ESI)** m/z calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 341.1260, found: 341.1257.

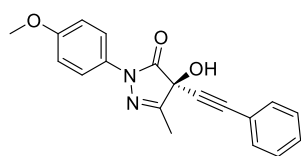
(S)-4-hydroxy-5-methyl-4-(phenylethynyl)-2-(o-tolyl)-2,4-dihydro-3H-pyrazol-3-one (8c)



White solid, 27.1 mg, 89% yield. mp = 98.4–100.5 °C. $[\alpha]_D^{25} = -227.8$ ($c = 0.27$ in CH_2Cl_2). 90% ee. **HPLC** (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 9.5$ min (minor), 11.1 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.70 – 7.67 (m, 2H), 7.46 – 7.43 (m, 2H), 7.35 – 7.33 (m, 1H), 7.31 – 7.29 (m, 3H), 7.04 – 7.02 (m, 1H), 4.49 (s, 1H), 2.39 (s, 3H), 2.34 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.7, 157.6, 137.9, 136.3, 131.2, 128.5, 127.7, 127.3, 125.4, 119.8, 118.6, 115.2, 87.9, 80.7, 71.9, 20.5, 12.0. **HRMS (ESI)** m/z calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{NaO}_2$ [$\text{M} + \text{Na}$] $^+$: 327.1104, found: 327.1095.

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(S)-4-hydroxy-2-(4-methoxyphenyl)-5-methyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8d)

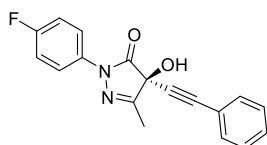


White solid, 28.8 mg, 90% yield. mp = 156.8–158.5 °C. $[\alpha]_D^{25} = -51.49$ ($c = 0.16$ in CH_2Cl_2). 76% ee.

HPLC (CHIRALCEL OD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 19.5$ min (minor), 10.5 min (major). **$^1\text{H NMR}$** (600 MHz, Chloroform-*d*) δ 7.78 – 7.76 (m, 2H), 7.46 – 7.44 (m, 2H), 7.37 – 7.27 (m, 3H), 6.94 – 6.92 (m, 2H), 4.73 (s, 1H), 3.83 (s, 3H), 2.34 (s, 3H). **$^{13}\text{C NMR}$** (150 MHz, Chloroform-*d*) δ 169.4, 158.6, 157.3, 132.2, 130.7, 129.5, 128.3, 120.9, 114.1, 88.8,

81.8, 72.8, 55.5, 13.0. **HRMS (ESI)** m/z calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{NaO}_3$ $[\text{M} + \text{Na}]^+$: 343.1053, found: 343.1052.

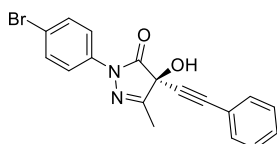
(S)-2-(4-fluorophenyl)-4-hydroxy-5-methyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8e)



White solid, 28.3 mg, 92% yield. mp = 126.5–128.8 °C. $[\alpha]_D^{25} = -268.3$ ($c = 0.22$ in CH_2Cl_2). 88% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 9.3$ min (minor), 10.6 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.75 – 7.67 (m, 2H), 7.47 – 7.44 (m, 2H), 7.38 – 7.28 (m, 4H), 6.93 – 6.88 (m, 1H), 4.25 (s, 1H), 2.34 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.5, 161.8 (d, $J = 245.1$ Hz), 157.7, 137.8 (d, $J = 10.8$ Hz), 131.2, 129.2 (d, $J = 9.1$ Hz), 128.7, 127.4, 119.6, 113.0 (d, $J = 3.1$ Hz), 111.2 (d, $J = 21.2$ Hz), 105.2 (d, $J = 27.2$ Hz), 88.2, 80.3, 71.9, 12.0. **$^{19}\text{F NMR}$** (376 MHz, Chloroform-*d*) δ -111.1. **HRMS (ESI)** m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_2\text{NaO}_2\text{F}$ $[\text{M} + \text{Na}]^+$: 331.0853, found: 331.0859.

(S)-2-(4-bromophenyl)-4-hydroxy-5-methyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8f)

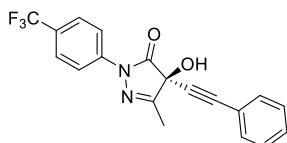


White solid, 24.4 mg, 91% yield. mp = 115.3–117.5 °C. $[\alpha]_D^{25} = -220.6$ ($c = 0.25$ in CH_2Cl_2). 89% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 11.7$ min (minor), 18.3 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.73 – 7.70 (m, 2H), 7.43 – 7.40 (m, 2H), 7.37 – 7.34 (m, 2H), 7.30 – 7.26 (m, 1H), 7.23 – 7.18 (m, 2H), 4.70 (s, 1H), 2.26 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.7, 158.0, 135.5, 131.2, 130.9, 128.6, 127.4, 119.6, 119.3, 117.5,

88.1, 80.4, 71.9, 12.0. **HRMS (ESI)** m/z calcd for $\text{C}_{18}\text{H}_{12}\text{N}_2\text{NaO}_2\text{Br}$ $[\text{M} + \text{Na}]^+$: 389.9985, found: 389.9980.

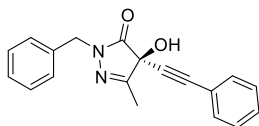
(S)-4-hydroxy-5-methyl-4-(phenylethynyl)-2-(4-(trifluoromethyl)phenyl)-2,4-dihydro-3H-pyrazol-3-one (8g)



White solid, 32.2 mg, 90% yield. mp = 172.5–173.5 °C. $[\alpha]_D^{25} = -232.5$ ($c = 0.27$ in CH_2Cl_2). 79% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 11.0$ min (minor), 16.5 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 8.06 (d, $J = 8.5$ Hz, 2H), 7.65 (d, $J = 8.5$ Hz, 2H), 7.46 – 7.44 (m, 2H), 7.39 – 7.28 (m, 3H), 4.37 (s, 1H), 2.36 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ 168.9, 158.1, 139.2, 131.2, 128.8, 127.4, 126.1 (d, $J = 32.9$ Hz), 125.1 (q, $J = 3.8$ Hz), 123.0 (d, $J = 271.7$ Hz), 119.5, 117.4, 88.4, 80.2, 71.9, 12.1. **$^{19}\text{F NMR}$** (376 MHz, Chloroform-*d*) δ -62.2. **HRMS (ESI)** m/z calcd for $\text{C}_{19}\text{H}_{13}\text{N}_2\text{NaO}_2\text{F}_3$ $[\text{M} + \text{Na}]^+$: 381.0821, found: 381.0812.

(S)-2-(4-benzylphenyl)-4-hydroxy-5-methyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8h)

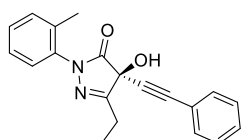


White solid, 24.3 mg, 80% yield. mp = 95.3–96.3 °C. $[\alpha]_D^{25} = -157.9$ ($c = 0.11$ in CH_2Cl_2). 78% ee. **HPLC**

(CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 16.9$ min (minor), 20.3 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.45 – 7.43 (m, 2H), 7.36 – 7.34 (m, 1H), 7.33 – 7.28 (m, 7H), 4.82 (s, 2H), 4.42 (s, 1H), 2.21 (s, 3H). **$^{13}\text{C NMR}$** (100 MHz, Chloroform-*d*) δ

170.4, 157.4, 134.7, 131.2, 128.4, 127.7, 127.3, 127.0, 126.8, 119.9, 87.5, 80.7, 70.8, 47.2, 11.9. **HRMS (ESI)** m/z calcd for $\text{C}_{19}\text{H}_{16}\text{N}_2\text{NaO}_2$ $[\text{M} + \text{Na}]^+$: 327.1104, found: 327.1088.

(S)-5-ethyl-4-hydroxy-4-(phenylethynyl)-2-(o-tolyl)-2,4-dihydro-3H-pyrazol-3-one (8i)



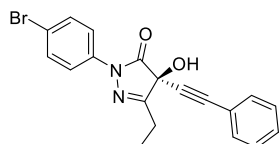
White solid, 27.3 mg, 88% yield. mp = 85.2–87.2 °C. $[\alpha]_D^{25} = -251.6$ ($c = 0.15$ in CH_2Cl_2). 86% ee. **HPLC**

(CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, $t_R = 8.6$ min (minor), 10.5 min (major). **$^1\text{H NMR}$** (400 MHz, Chloroform-*d*) δ 7.64 – 7.61 (m, 2H), 7.38 – 7.36 (m, 2H), 7.29 – 7.18 (m, 4H), 6.95 (d, $J = 7.6$ Hz, 1H), 3.96 (s, 1H), 2.67 (q, $J = 7.4$ Hz, 2H), 2.32 (s, 3H), 1.32 (t, J

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= 7.4 Hz, 3H). **¹³C NMR** (100 MHz, Chloroform-*d*) δ 168.6, 161.0, 137.9, 136.5, 131.1, 128.5, 127.7, 127.3, 125.4, 119.8, 118.5, 115.2, 87.7, 81.1, 71.9, 20.6, 20.1, 8.7. **HRMS (ESI)** *m/z* calcd for C₂₀H₁₈N₂NaO₂ [M + Na]⁺: 341.1260, found: 341.1257.

(S)-2-(4-bromophenyl)-5-ethyl-4-hydroxy-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8j)

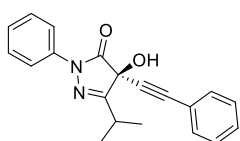


White solid, 34.8 mg, 91% yield. mp = 169.8–171.3 °C. [α]_D²⁵ = -236.1 (*c* = 0.23 in CH₂Cl₂). 98% ee.

HPLC (CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, *t_R* = 12.9 min (minor), 23.1 min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.82 (d, *J* = 8.5 Hz, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.44 – 7.42 (m, 2H), 7.38 – 7.34 (m, 1H), 7.31 – 7.26 (m, 2H), 4.43 (s, 1H), 2.75 (q, *J* = 7.4 Hz, 2H), 1.39 (t, *J* = 7.4 Hz, 3H). **¹³C NMR** (150 MHz, Chloroform-*d*) δ 169.7, 162.7,

136.6, 132.1, 131.9, 129.6, 128.4, 120.7, 120.3, 118.4, 89.0, 81.8, 72.9, 21.1, 9.6. **HRMS (ESI)** *m/z* calcd for C₁₉H₁₅N₂NaO₂Br [M + Na]⁺: 405.0209, found: 405.0211.

(S)-4-hydroxy-5-isopropyl-2-phenyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8k)

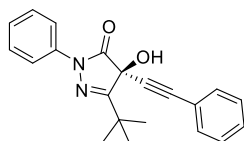


White solid, 28.6 mg, 90% yield. mp = 130.9–133.2 °C. [α]_D²⁵ = -186.7 (*c* = 0.21 in CH₂Cl₂). 93% ee. **HPLC**

(CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, *t_R* = 10.3 min (minor), 15.3 min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.83 – 7.81 (m, 2H), 7.37 – 7.29 (m, 4H), 7.27

– 7.22 (m, 1H), 7.20 – 7.16 (m, 2H), 7.13 – 7.09 (m, 1H), 4.65 (d, *J* = 20.4 Hz, 1H), 3.02 – 3.00 (m, 1H), 1.39 – 1.31 (m, 6H). **¹³C NMR** (100 MHz, Chloroform-*d*) δ 168.7, 164.0, 136.6, 131.1, 128.4, 127.9, 127.3, 124.5, 120.0, 117.9, 87.9, 81.4, 72.1, 28.0, 19.7, 19.1. **HRMS (ESI)** *m/z* calcd for C₂₀H₁₈N₂NaO₂ [M + Na]⁺: 341.1260, found: 341.1254.

(S)-5-(tert-butyl)-4-hydroxy-2-phenyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8l)

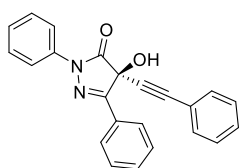


White solid, 27.2 mg, 82% yield. mp = 135.2–138.7 °C. [α]_D²⁵ = -104.1 (*c* = 0.17 in CH₂Cl₂). 75% ee. **HPLC**

(CHIRALCEL AD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, *t_R* = 10.2 min (minor), 17.2 min (major). **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.84 – 7.82 (m, 2H), 7.35 – 7.29 (m, 4H),

7.25 – 7.09 (m, 4H), 4.38 (s, 1H), 1.42 (s, 9H). **¹³C NMR** (100 MHz, Chloroform-*d*) δ 169.0, 165.5, 136.6, 131.0, 128.3, 127.8, 127.3, 124.4, 120.1, 117.9, 88.1, 82.0, 72.3, 35.4, 27.9. **HRMS (ESI)** *m/z* calcd for C₂₁H₂₀N₂NaO₂ [M + Na]⁺: 355.1417, found: 355.1412.

(S)-4-hydroxy-2,5-diphenyl-4-(phenylethynyl)-2,4-dihydro-3H-pyrazol-3-one (8m)



White solid, 31.7 mg, 90% yield. mp = 204.3–207.8 °C. [α]_D²⁵ = -51.1 (*c* = 0.16 in CH₂Cl₂). 80% ee. **HPLC**

(CHIRALCEL OD-H), *n*-hexane/2-propanol = 90/10, flow rate 0.8 mL/min, detection at 254 nm, *t_R* = 8.5 min (minor), 10.6 min (major). **¹H NMR** (400 MHz, DMSO-*d*₆) δ 8.19 – 8.16 (m, 2H), 7.96 – 7.94 (m, 2H), 7.59 –

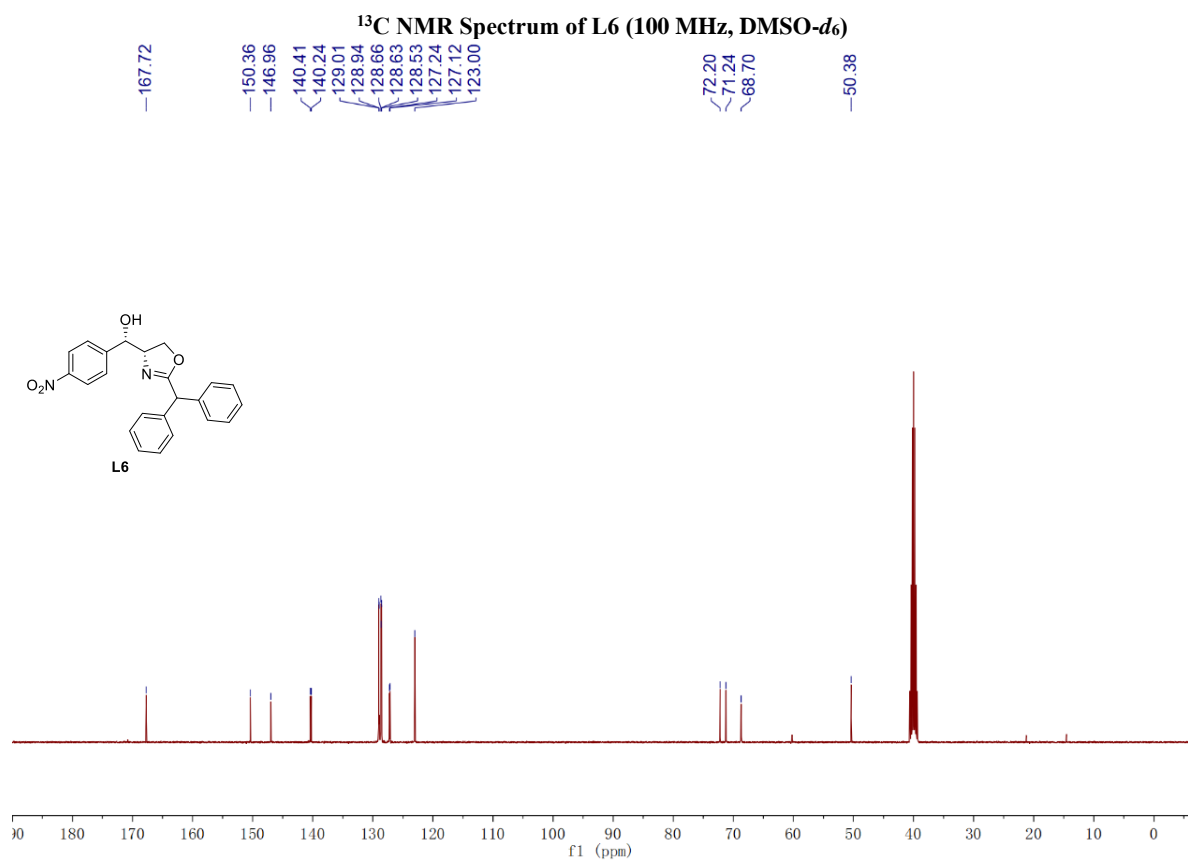
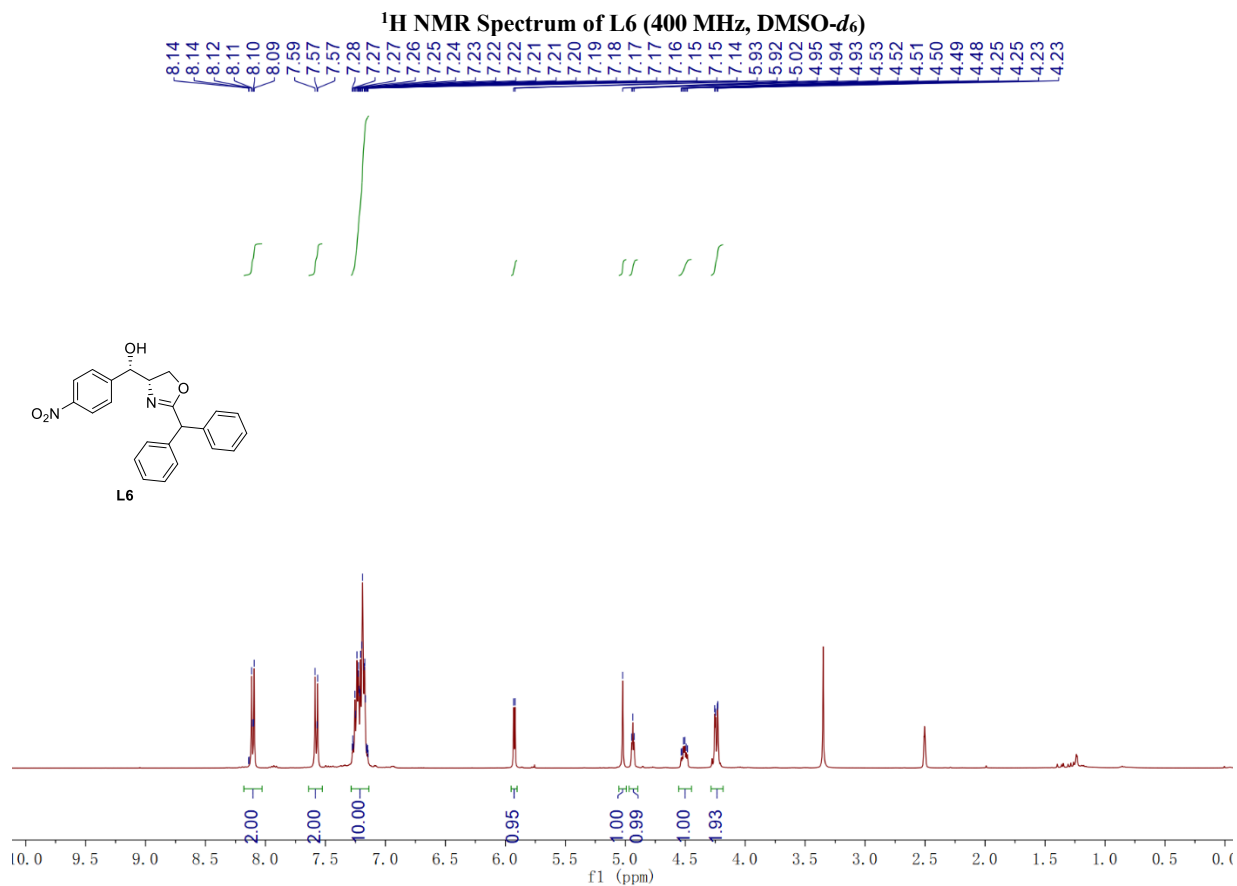
7.51 (m, 5H), 7.45 – 7.37 (m, 5H), 7.33 – 7.31 (m, 1H). **¹³C NMR** (100 MHz, DMSO-*d*₆) δ 169.9, 156.5, 137.8, 132.2, 131.7, 130.3, 129.7, 129.5, 129.4, 128.8, 127.4, 126.2, 120.7, 119.1, 88.4, 84.3, 72.0. **HRMS (ESI)** *m/z* calcd for C₂₃H₁₆N₂NaO₂ [M + Na]⁺: 375.1104, found: 375.1091.

3. Reference

- (1) Jiang, B. Chen, Z. Xiong, W., *Chem. Commun.*, **2002**, 1524–1525.
- (2) Chen, L. Huang, G. Liu, M. Huang, Z. Chen, F.-E. *Adv. Syn. Catal.*, **2018**, 360, 3497–3501.
- (3) Wang, R. H. Li, Y. L. He, H. J. Xiao, Y. C.; Chen, F. E. *Chem. Eur. J.*, **2021**, 27, 4302–4306.
- (4) Lu, J. Luo, L. S. Sha, F. Li, Q. Wu, X. Y. *Chem. Commun.*, **2019**, 55, 11603–11606.

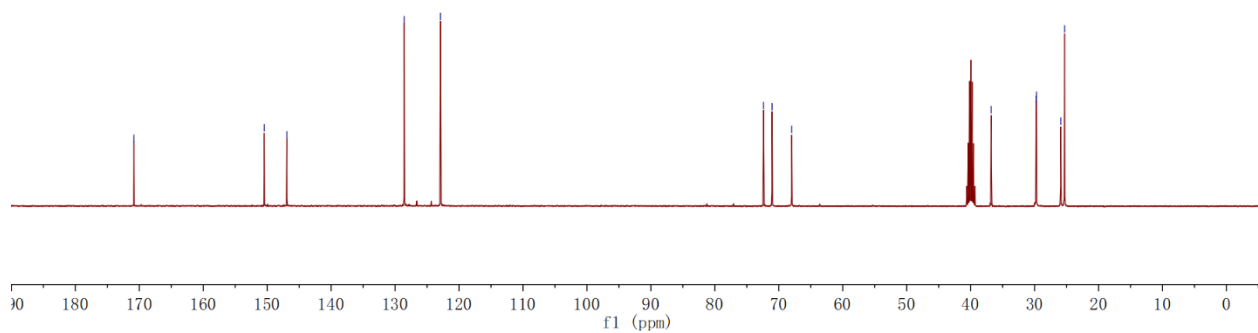
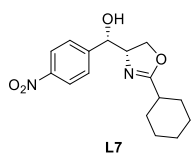
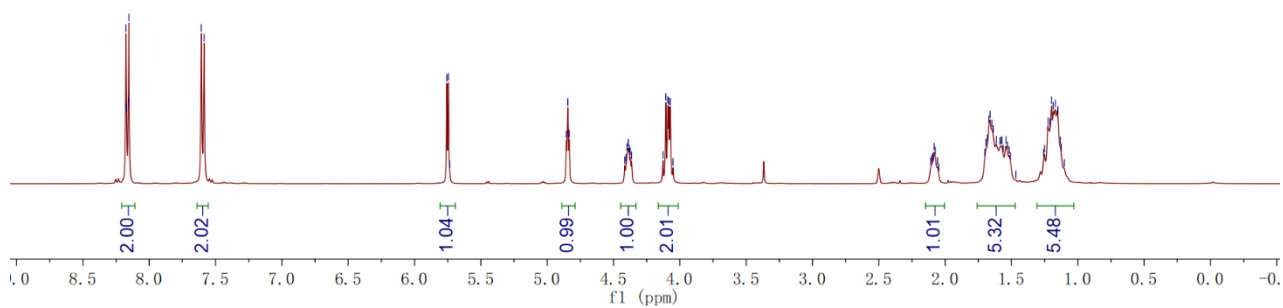
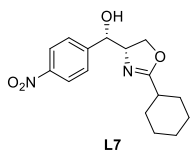
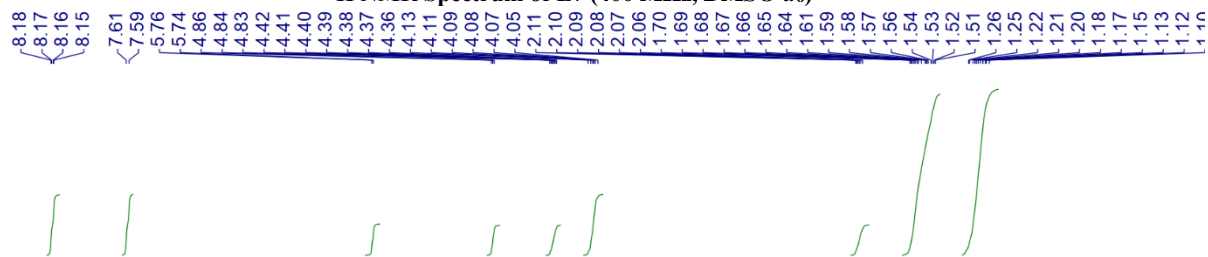
SUPPORTING INFORMATION

4. Spectral Data



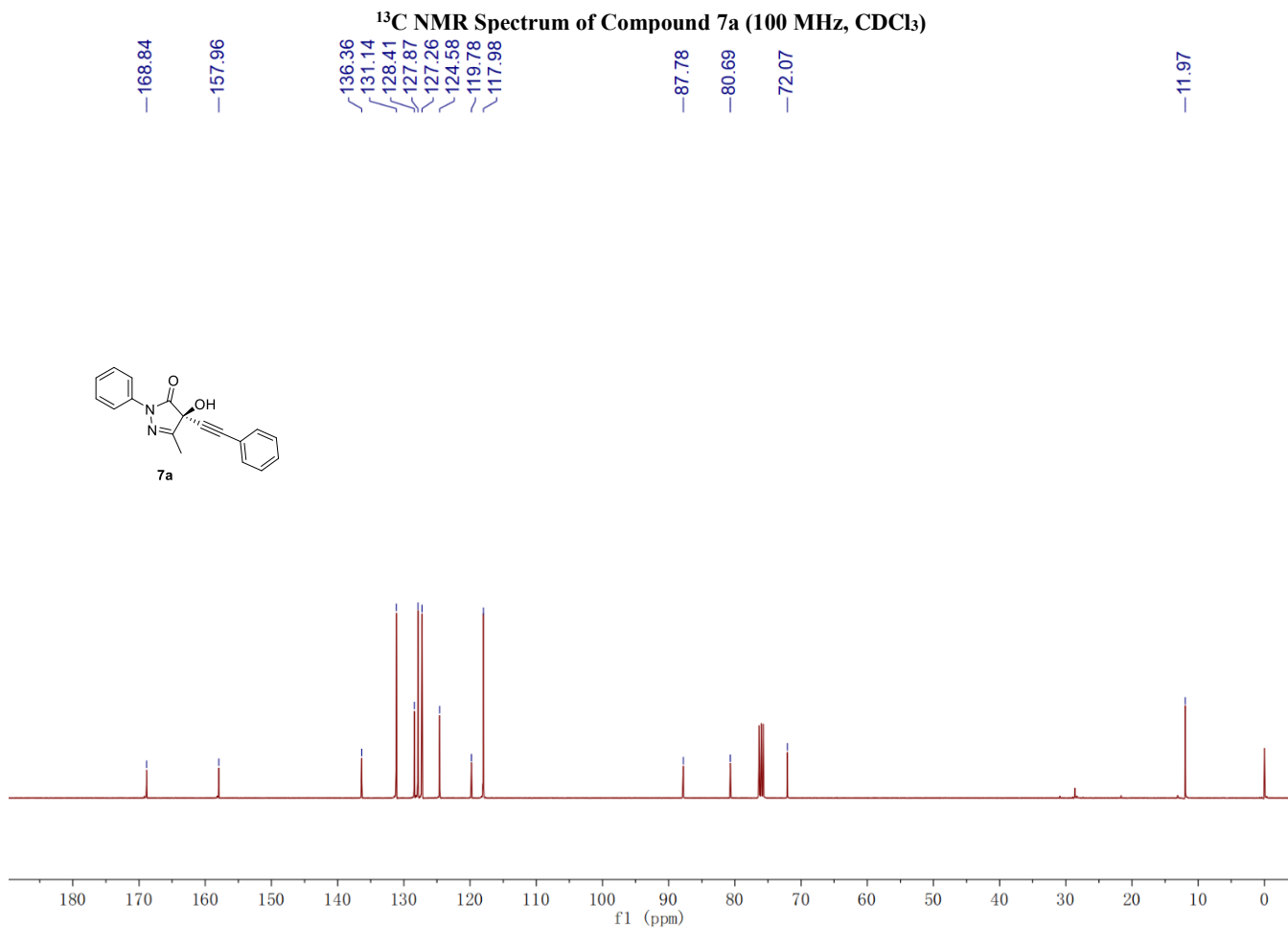
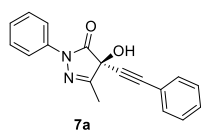
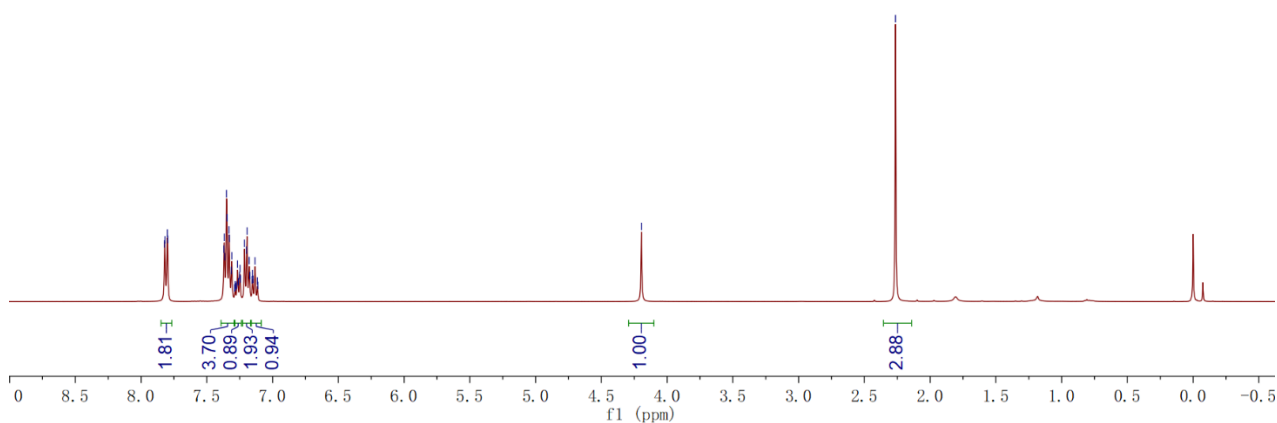
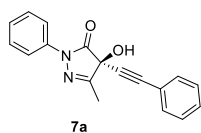
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¹H NMR Spectrum of L7 (400 MHz, DMSO-*d*₆)



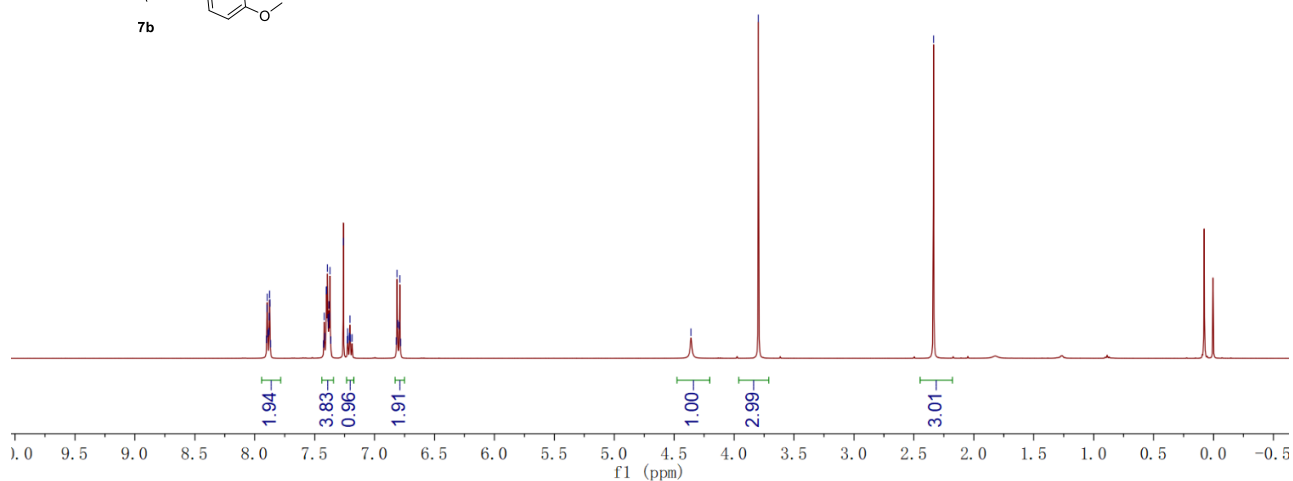
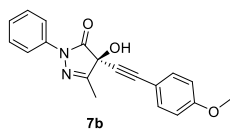
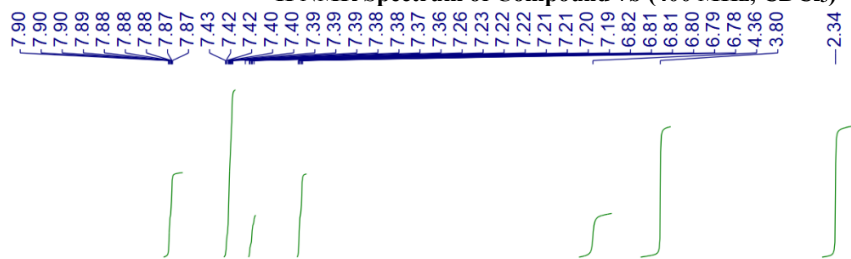
SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7a (400 MHz, CDCl₃)

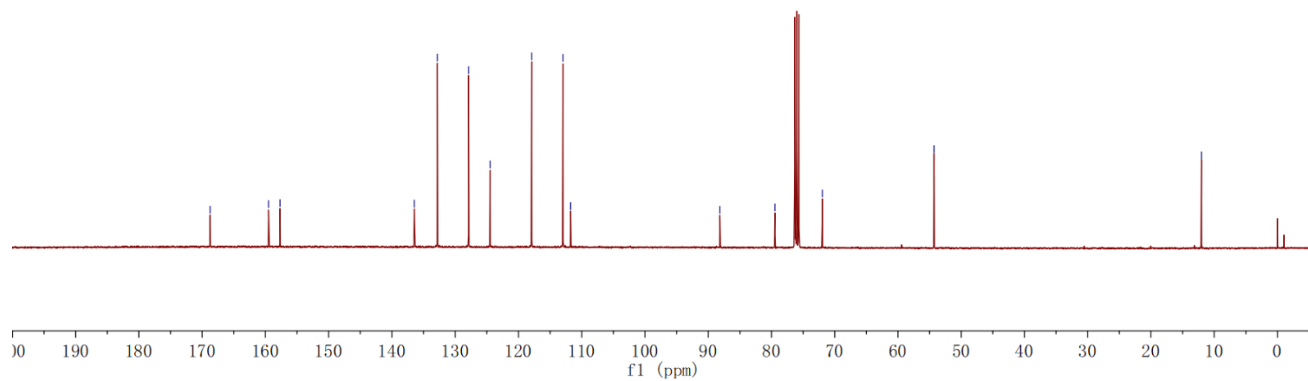
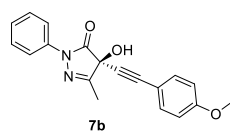


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7b (400 MHz, CDCl₃)

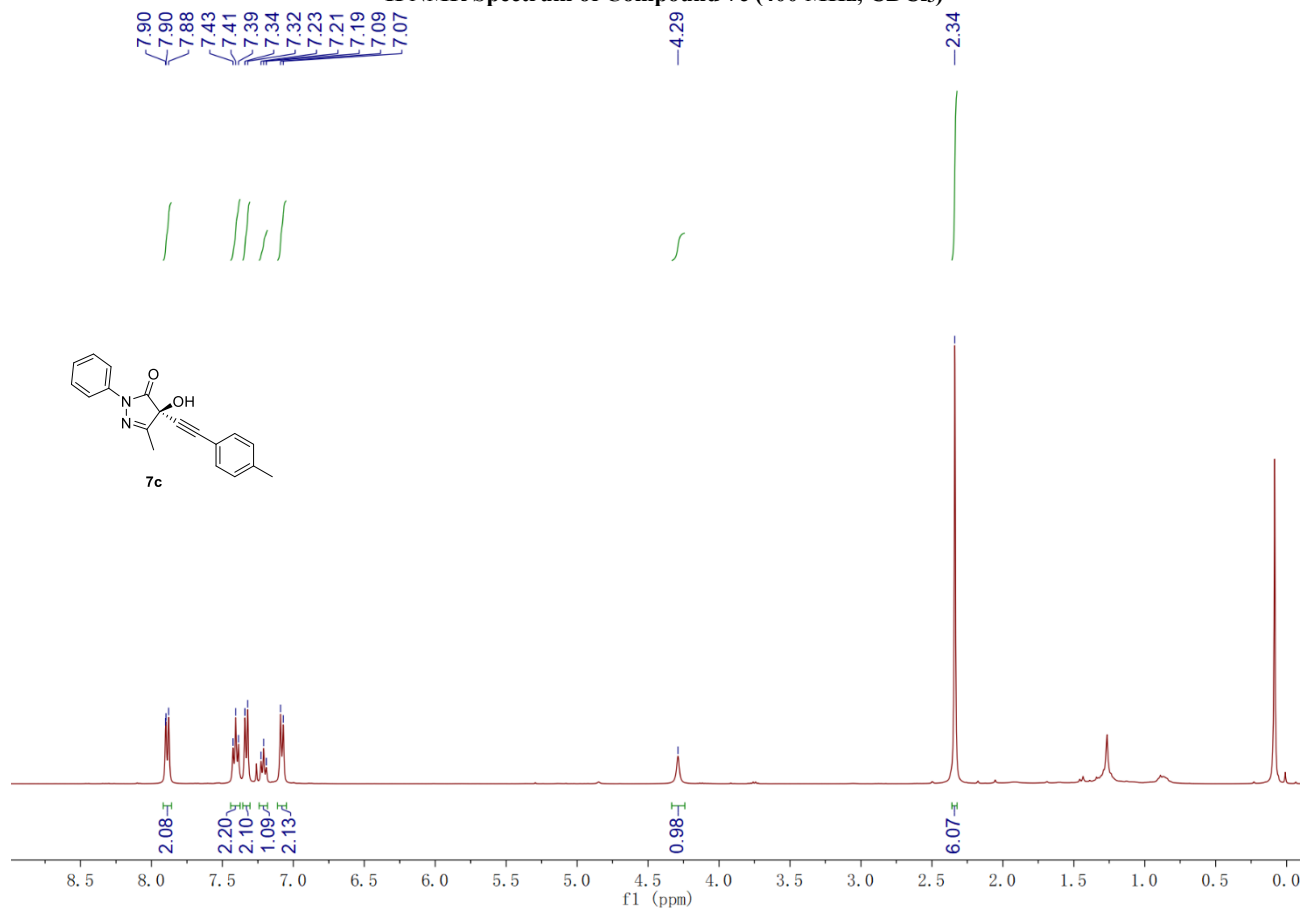


¹³C NMR Spectrum of Compound 7b (100 MHz, CDCl₃)

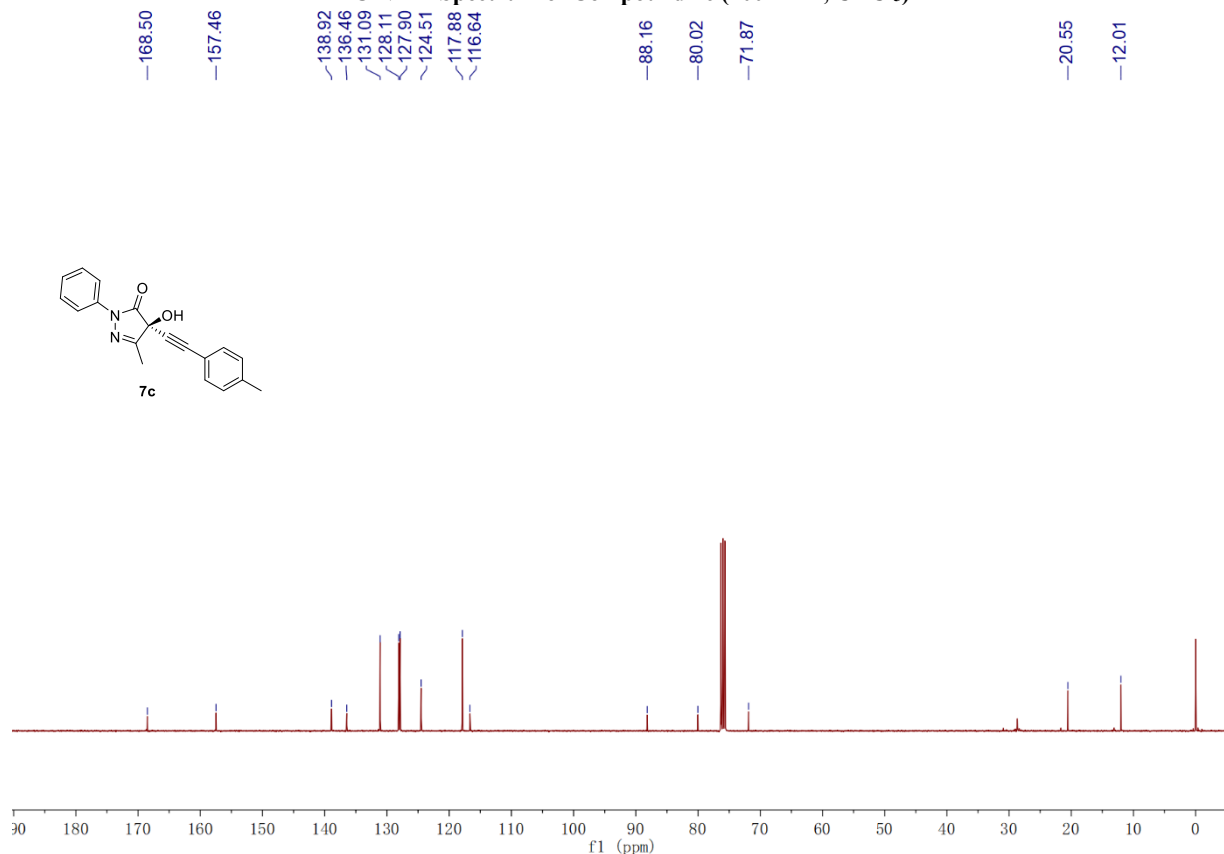


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7c (400 MHz, CDCl₃)

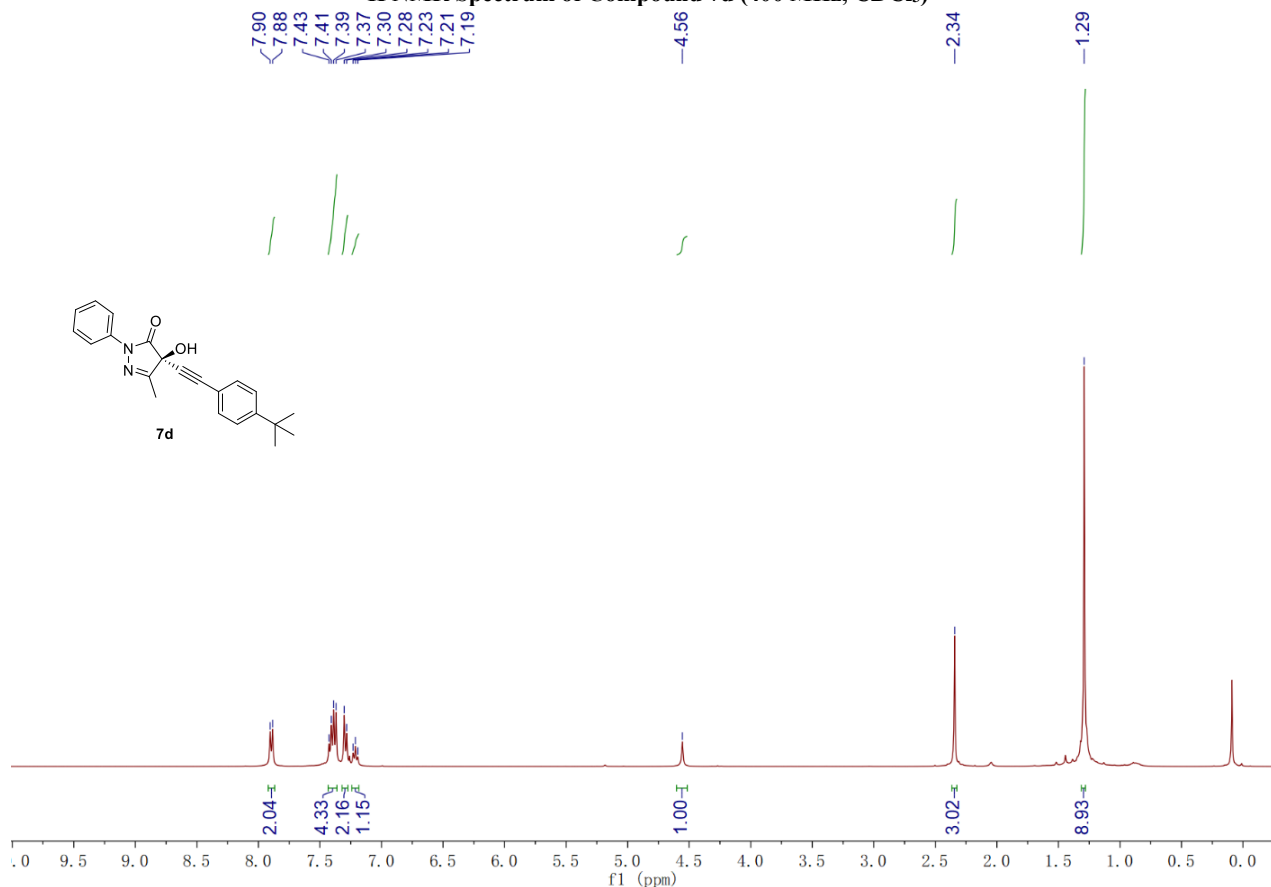


¹³C NMR Spectrum of Compound 7c (100 MHz, CDCl₃)

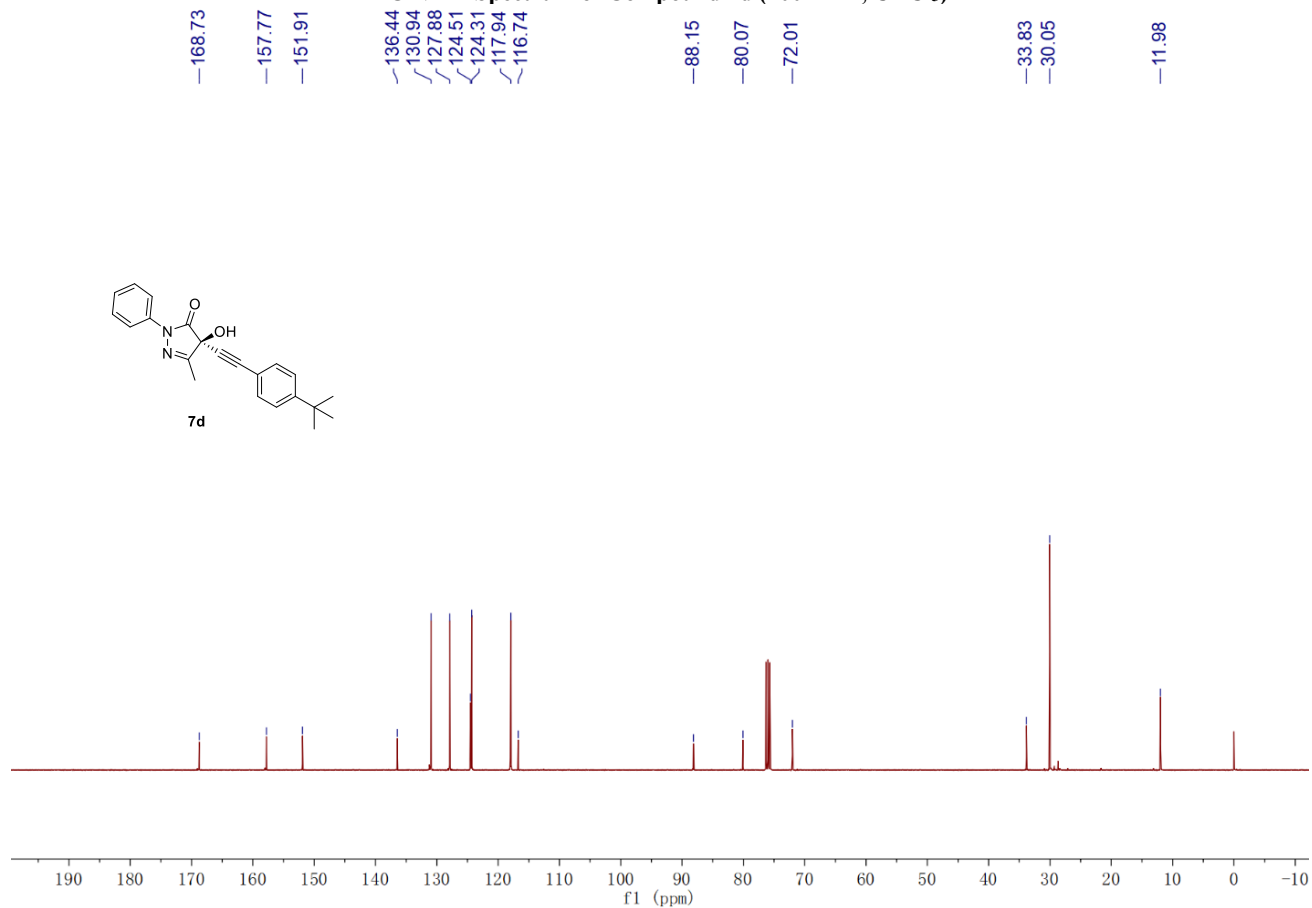


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7d (400 MHz, CDCl₃)

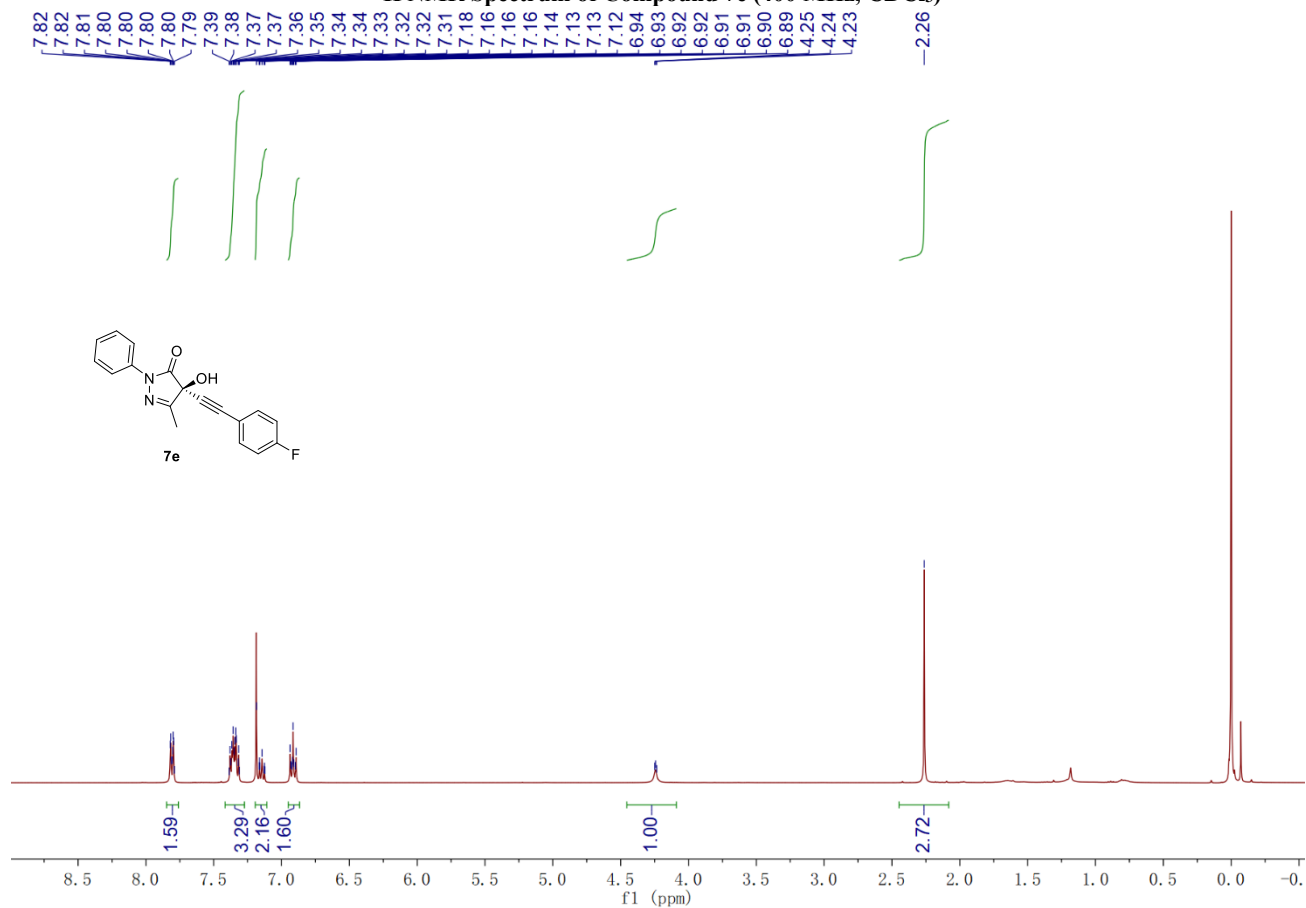


¹³C NMR Spectrum of Compound 7d (100 MHz, CDCl₃)

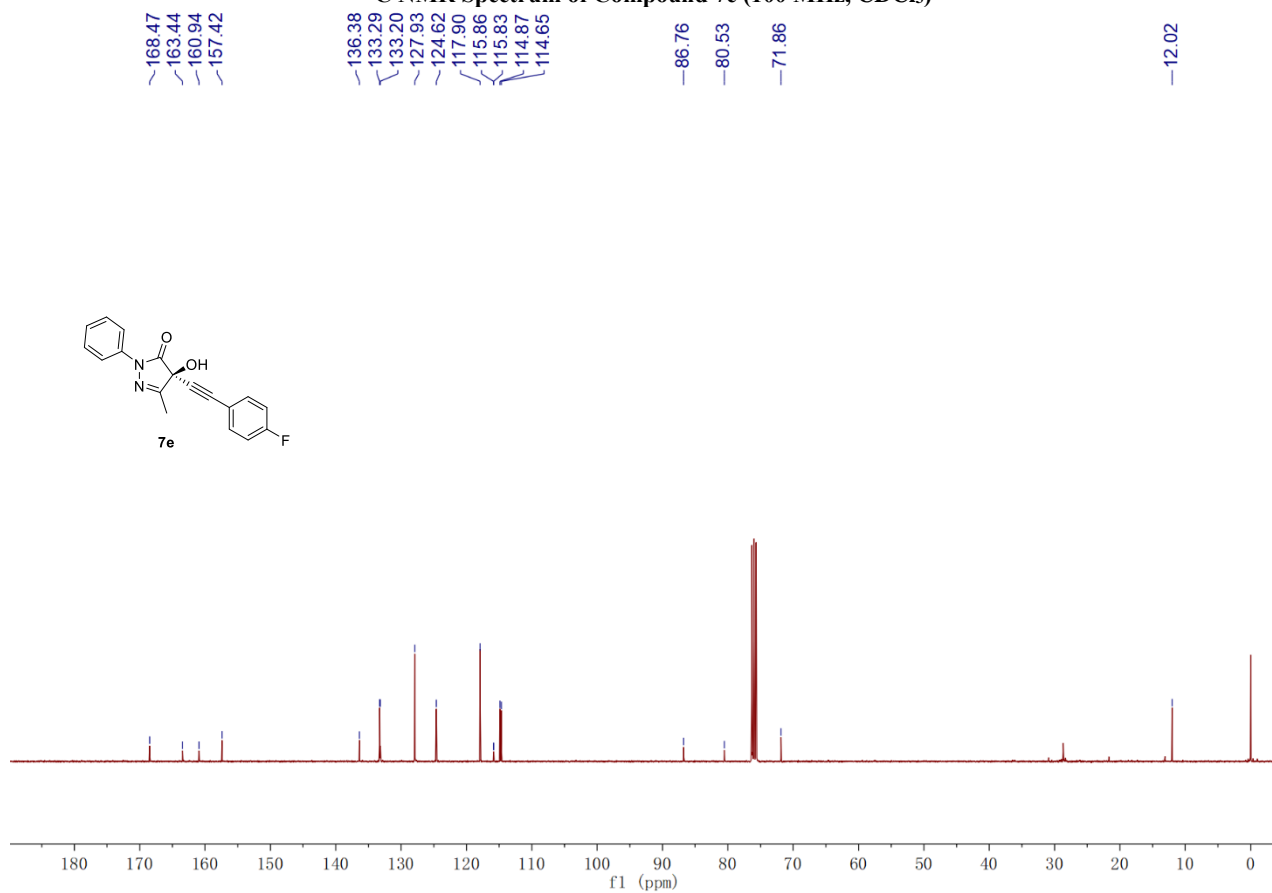


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7e (400 MHz, CDCl₃)



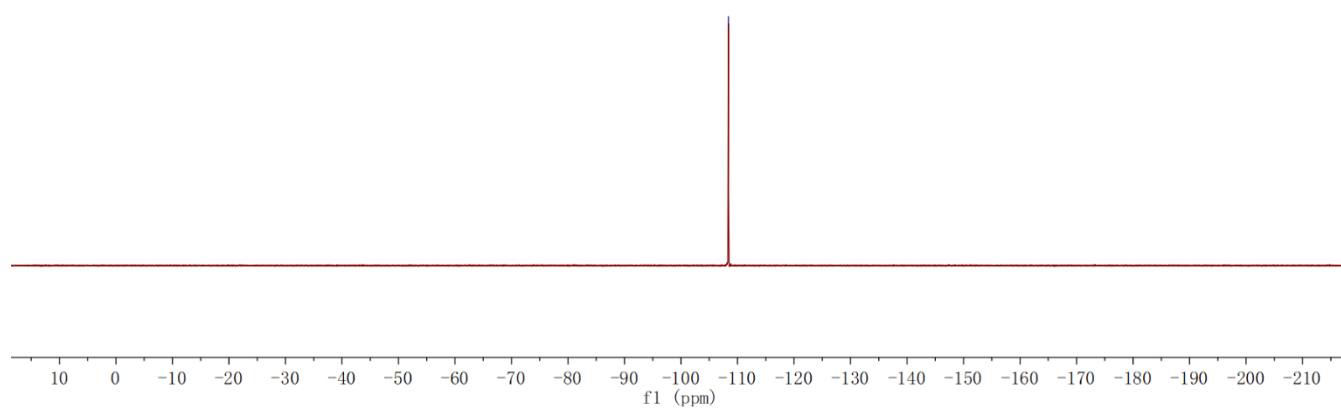
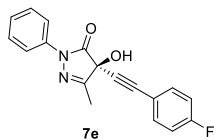
¹³C NMR Spectrum of Compound 7e (100 MHz, CDCl₃)



SUPPORTING INFORMATION

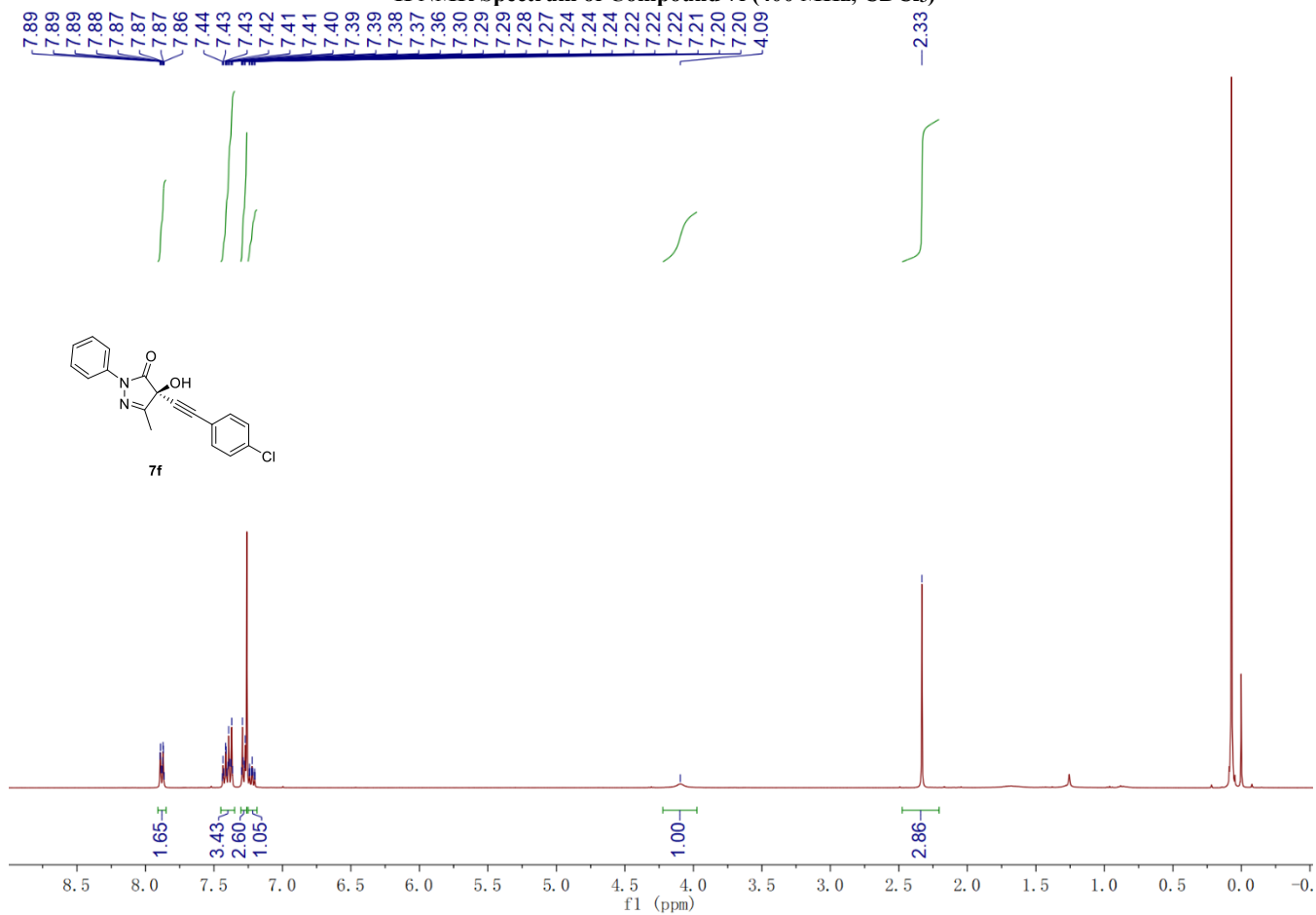
^{19}F NMR Spectrum of Compound 7e (376 MHz, CDCl_3)

---108.39

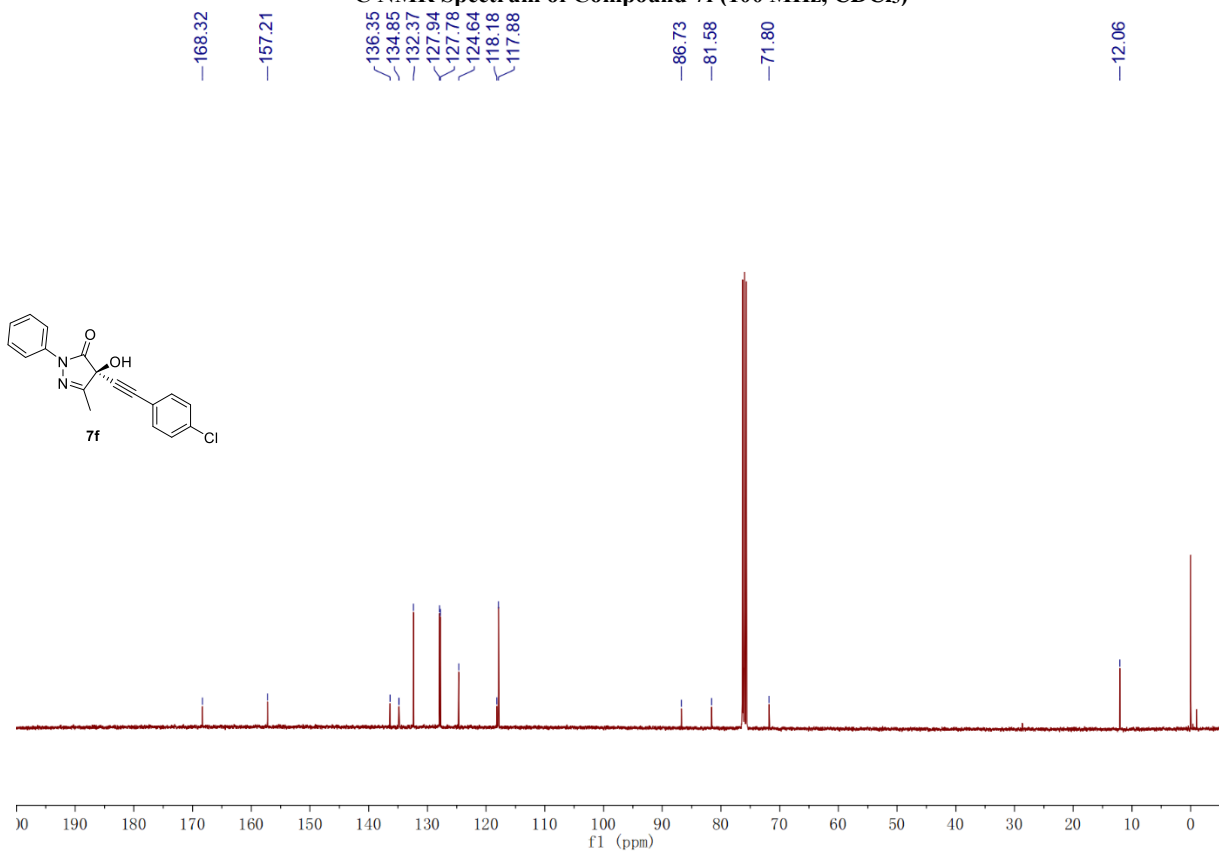


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7f (400 MHz, CDCl₃)

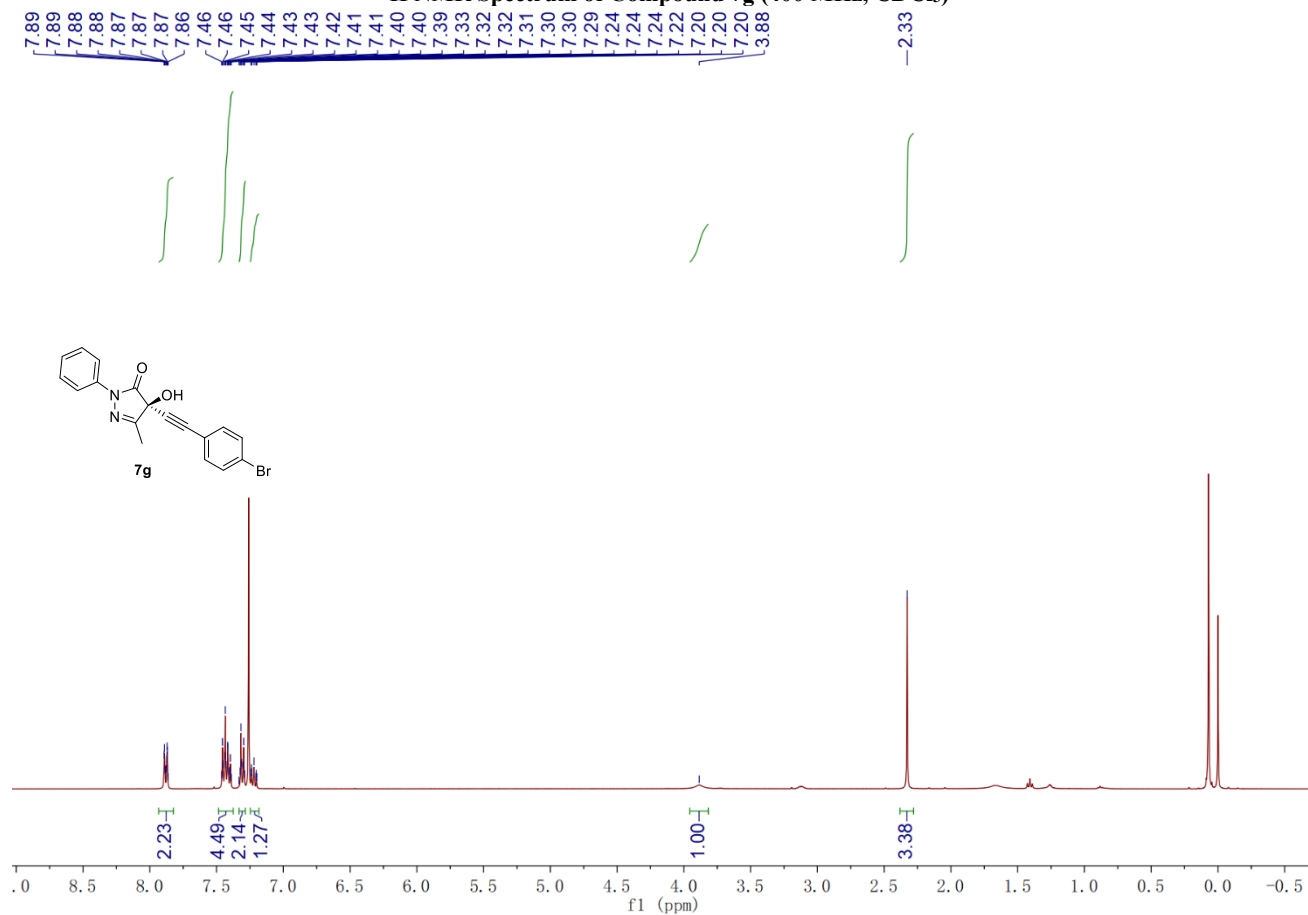


¹³C NMR Spectrum of Compound 7f (100 MHz, CDCl₃)

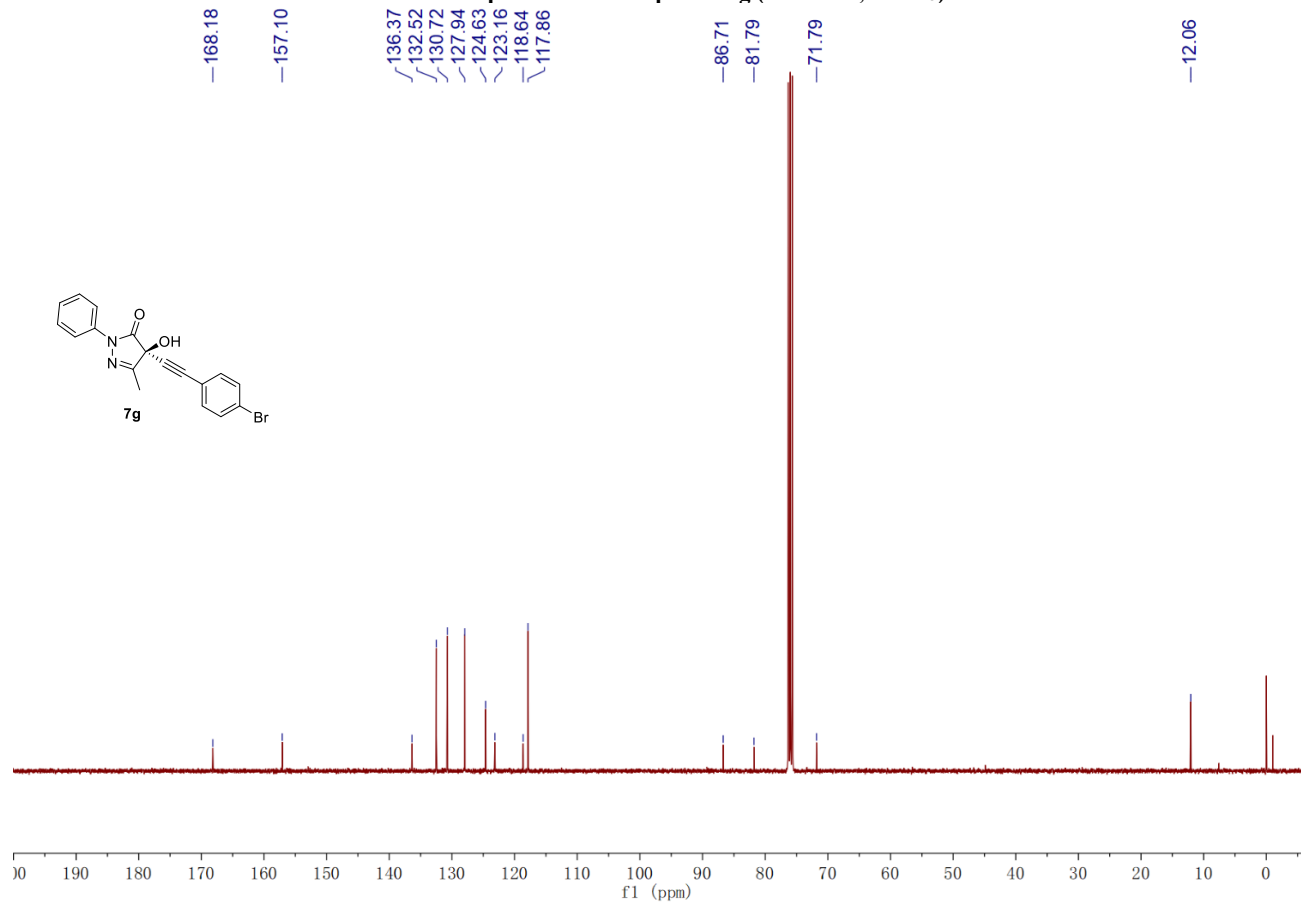


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7g (400 MHz, CDCl₃)

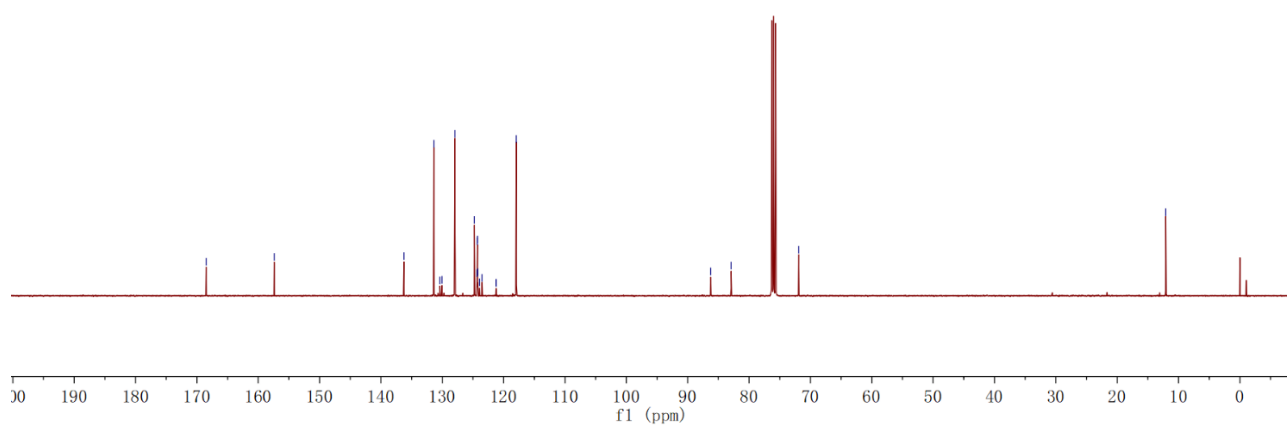
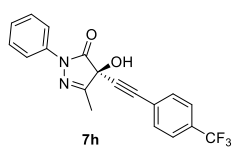
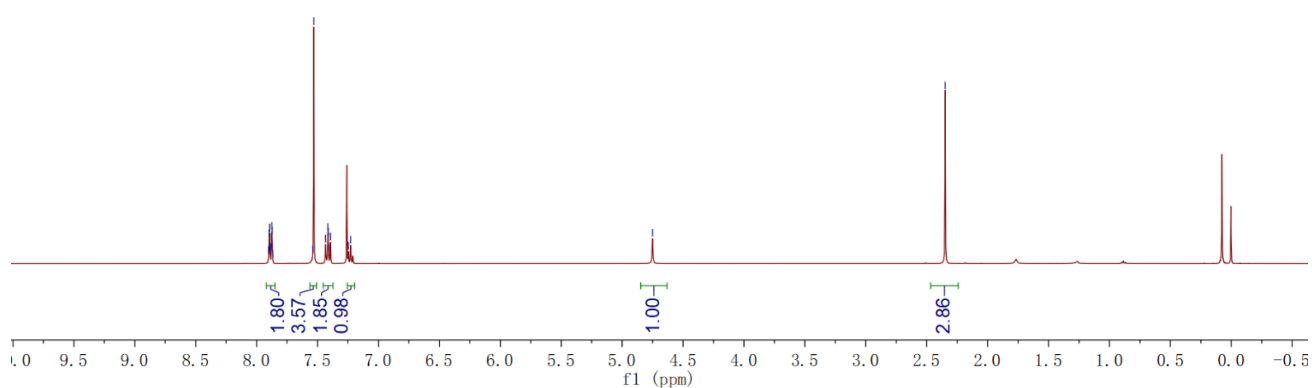
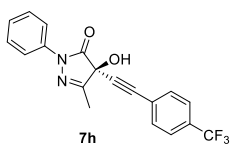
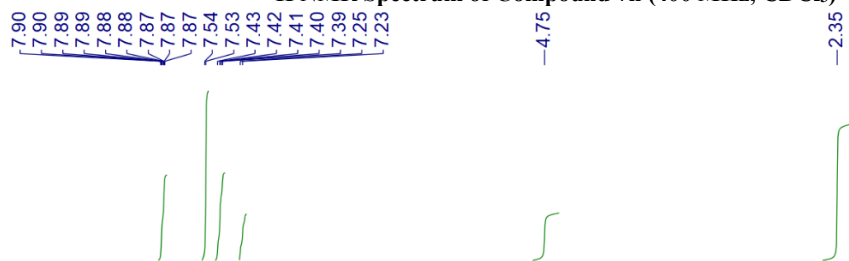


¹³C NMR Spectrum of Compound 7g (100 MHz, CDCl₃)



SUPPORTING INFORMATION

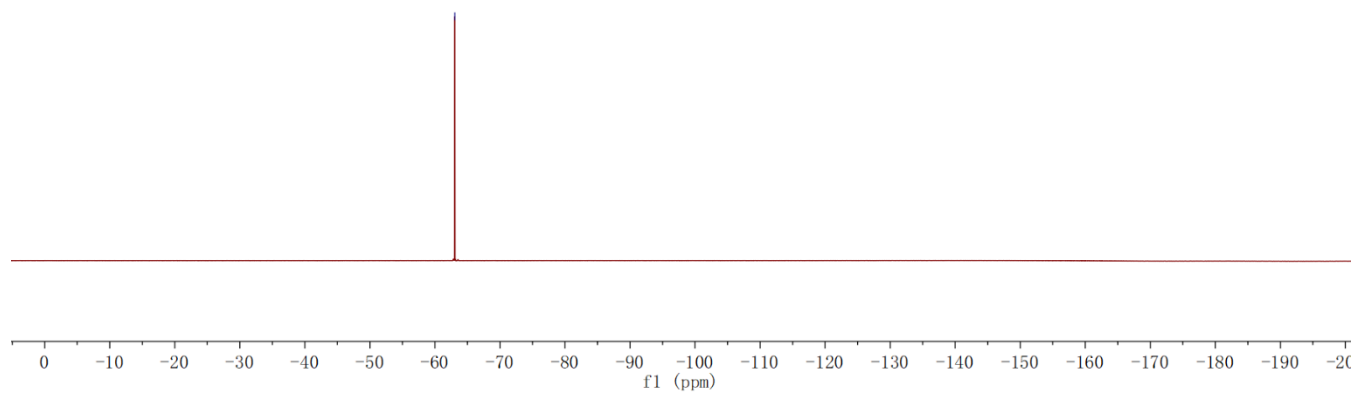
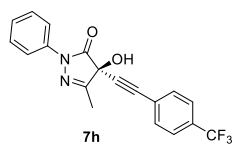
¹H NMR Spectrum of Compound 7h (400 MHz, CDCl₃)



SUPPORTING INFORMATION

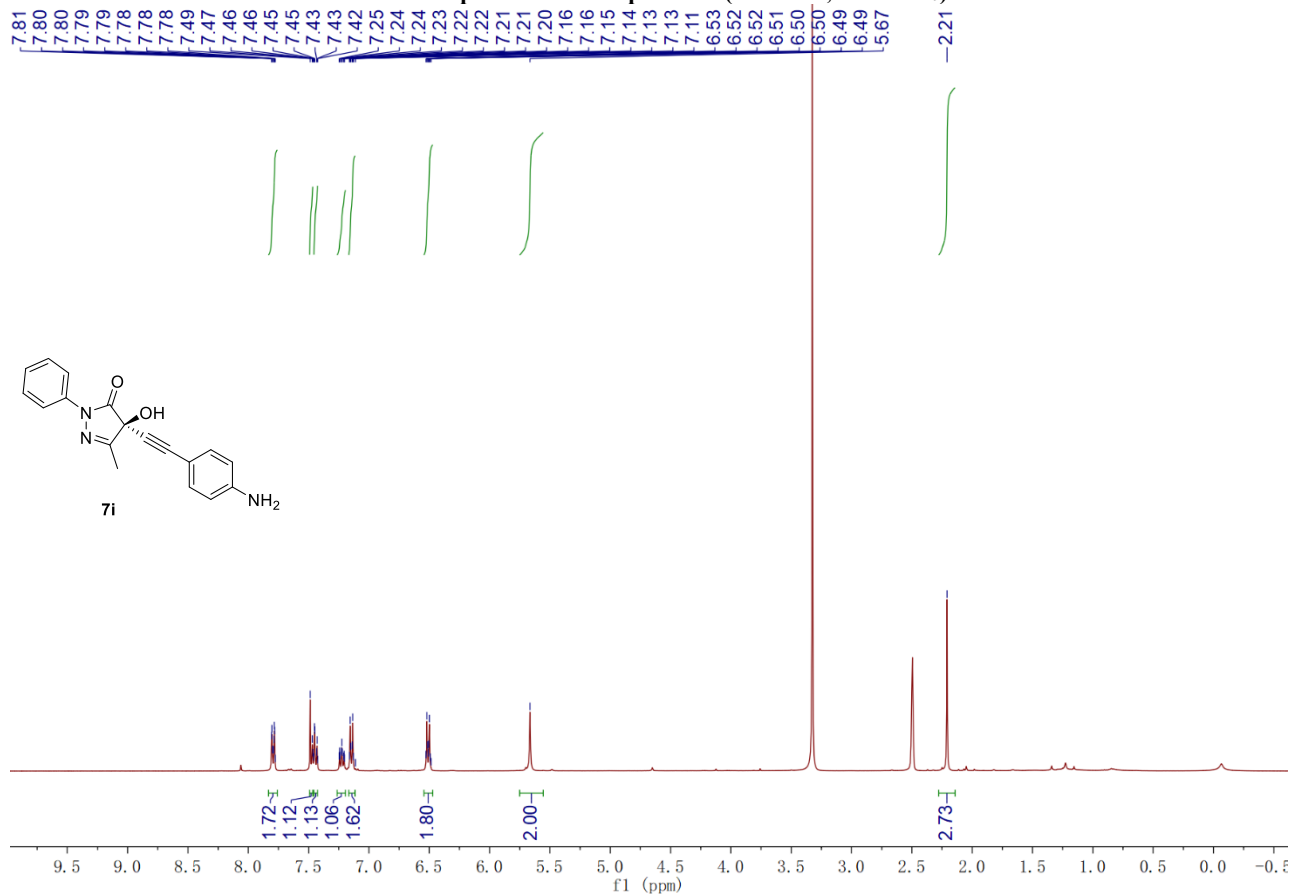
¹⁹F NMR Spectrum of Compound 7h (376 MHz, CDCl₃)

---63.06

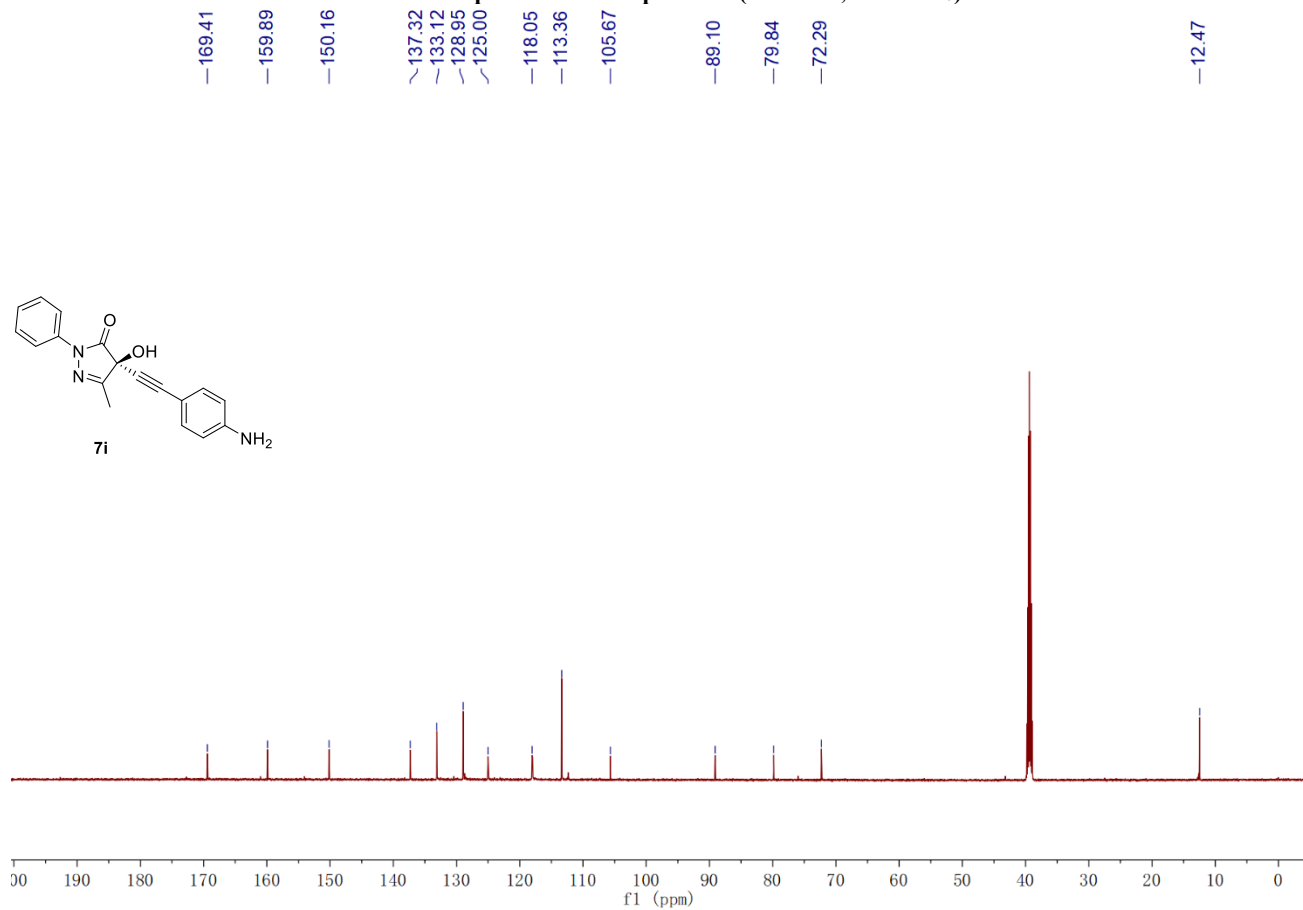


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7i (400 MHz, DMSO-d₆)

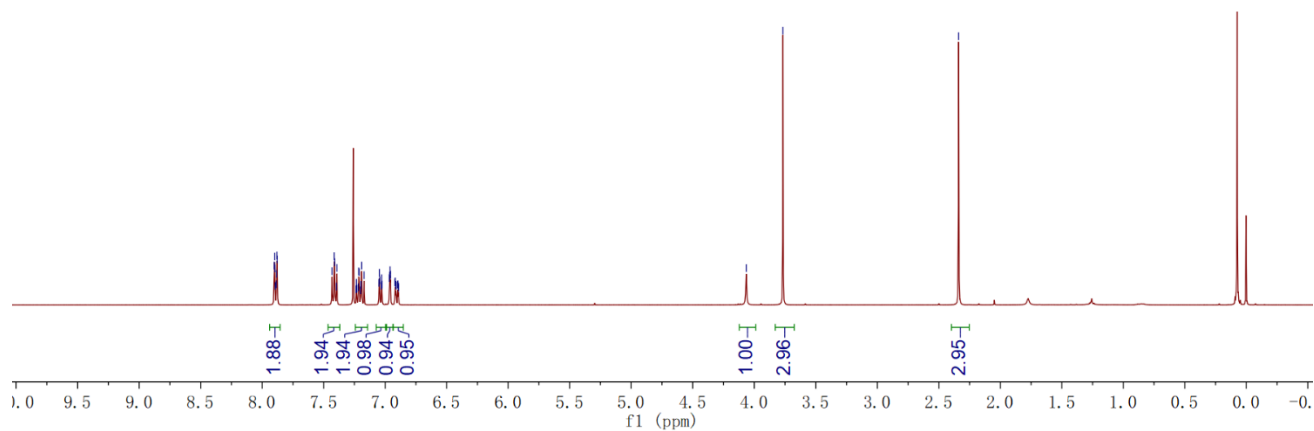
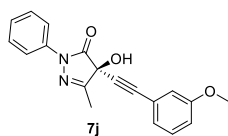


¹³C NMR Spectrum of Compound 7i (150 MHz, DMSO-d₆)

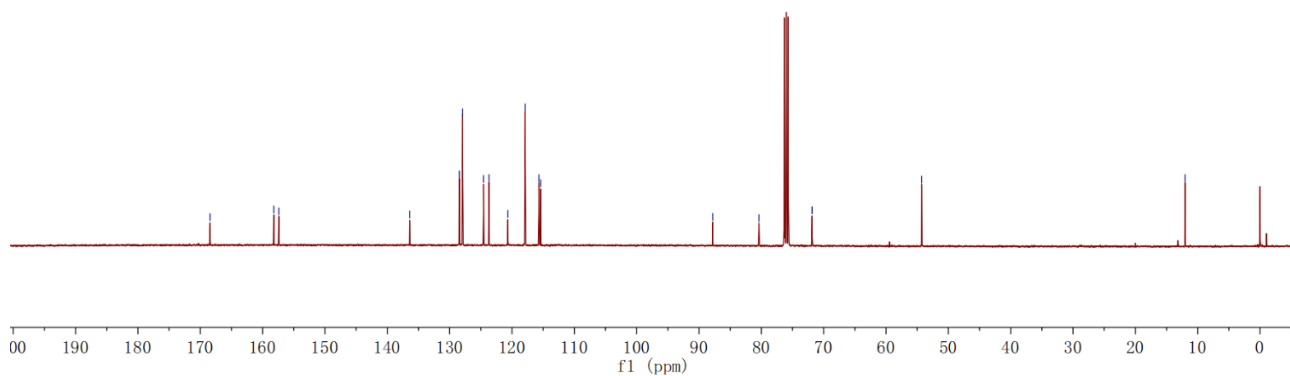
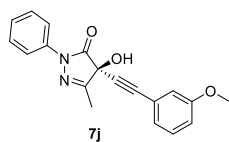


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7j (400 MHz, CDCl₃)



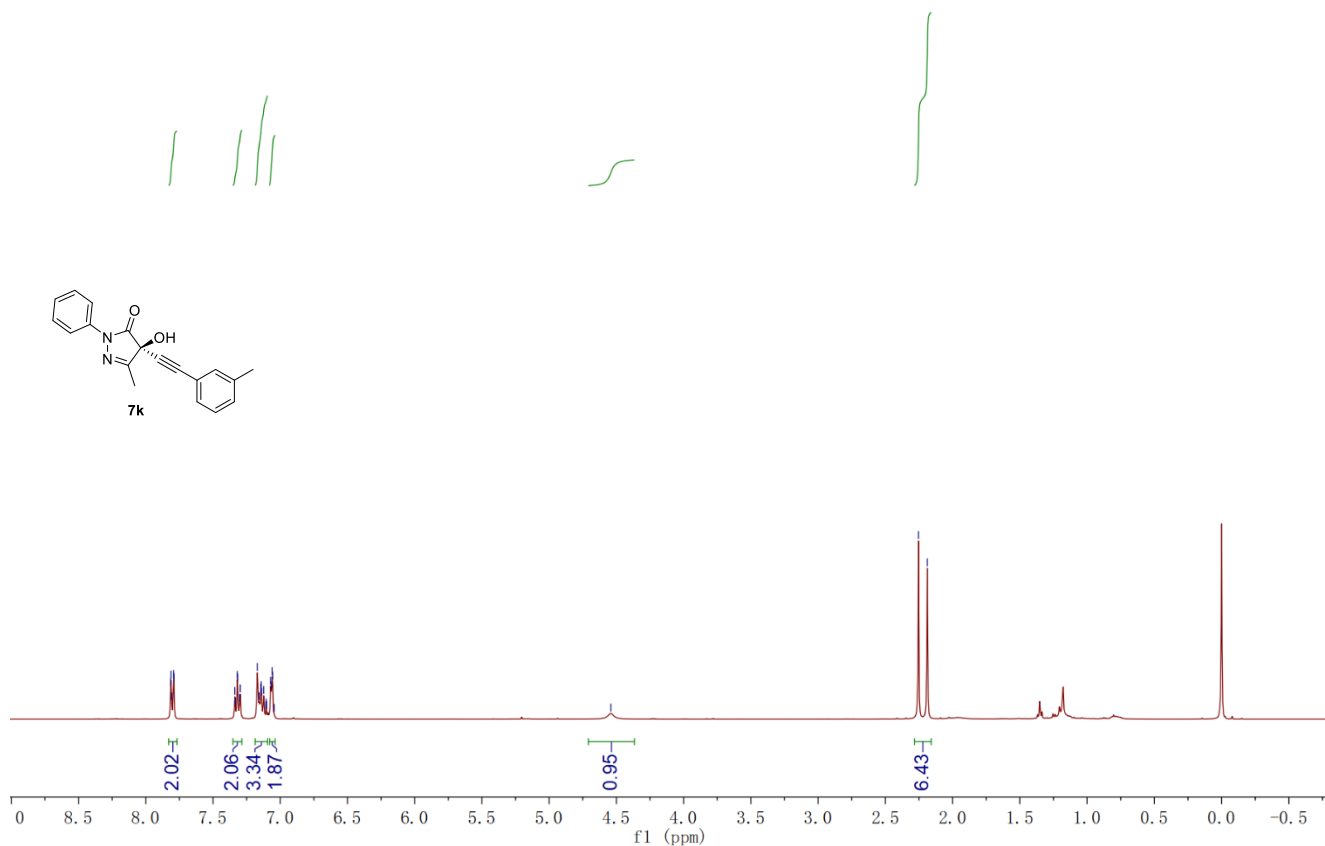
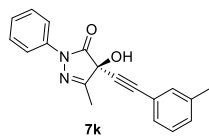
¹³C NMR Spectrum of Compound 7j (100 MHz, CDCl₃)



SUPPORTING INFORMATION

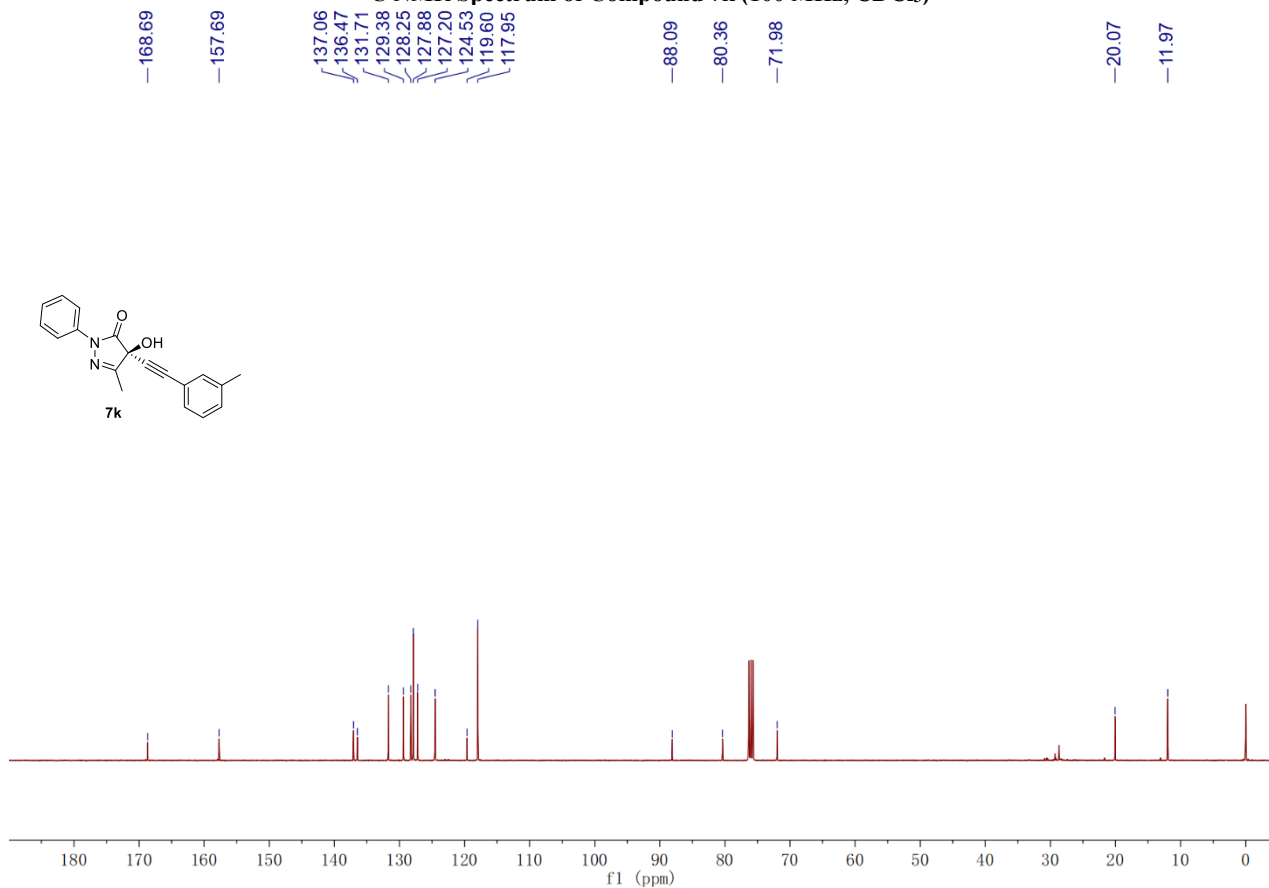
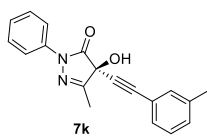
¹H NMR Spectrum of Compound 7k (400 MHz, CDCl₃)

7.81, 7.81, 7.81, 7.79, 7.79, 7.34, 7.33, 7.32, 7.32, 7.30, 7.30, 7.17, 7.16, 7.14, 7.14, 7.14, 7.12, 7.11, 7.10, 7.10, 7.07, 7.07, 7.06, 7.05, 4.54, 2.25, 2.19



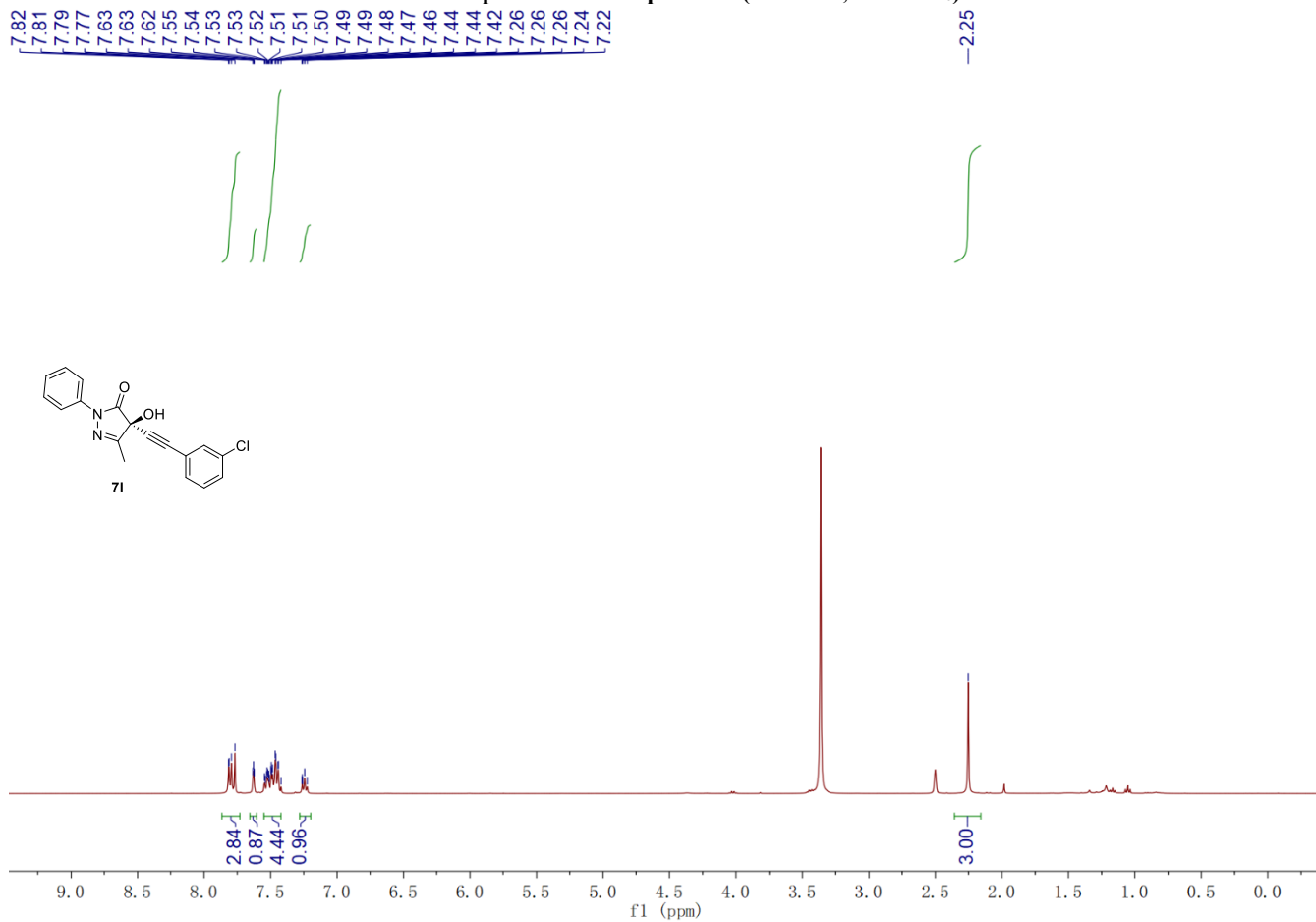
¹³C NMR Spectrum of Compound 7k (100 MHz, CDCl₃)

168.69, 157.69, 137.06, 136.47, 131.71, 129.38, 128.25, 127.88, 127.20, 124.53, 119.60, 117.95, 88.09, 80.36, 71.98, 20.07, 11.97

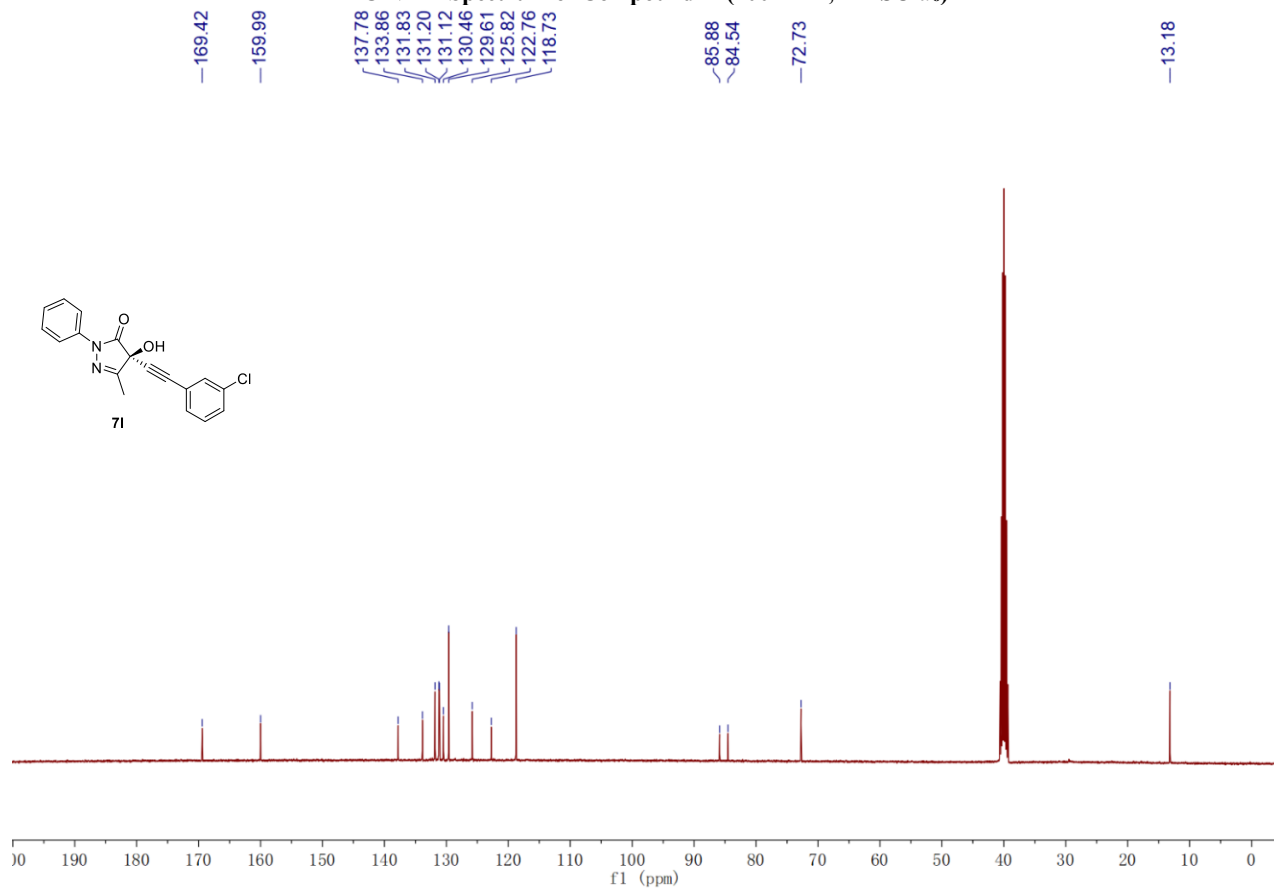


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 71 (400 MHz, DMSO-d₆)

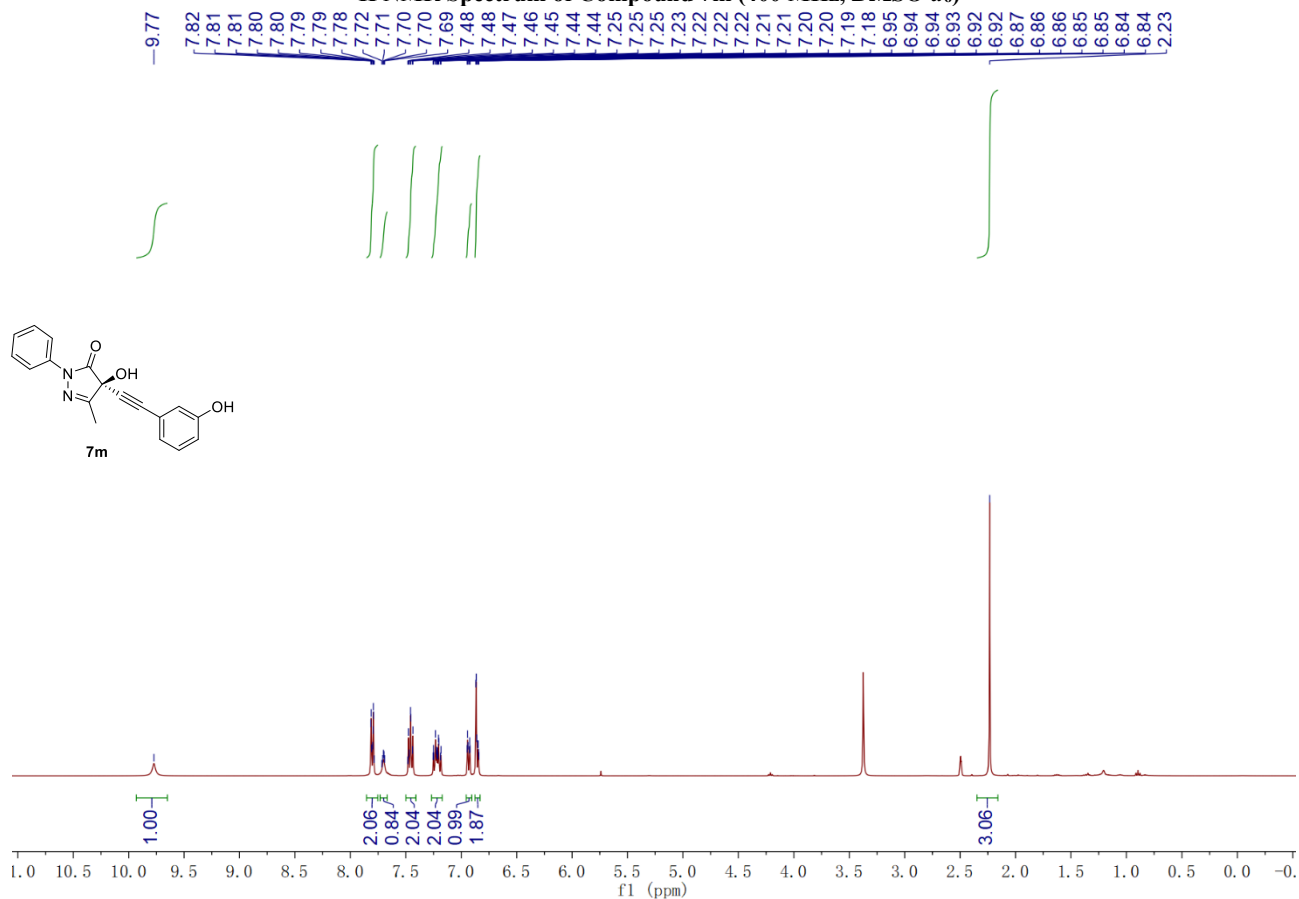


¹³C NMR Spectrum of Compound 71 (100 MHz, DMSO-d₆)

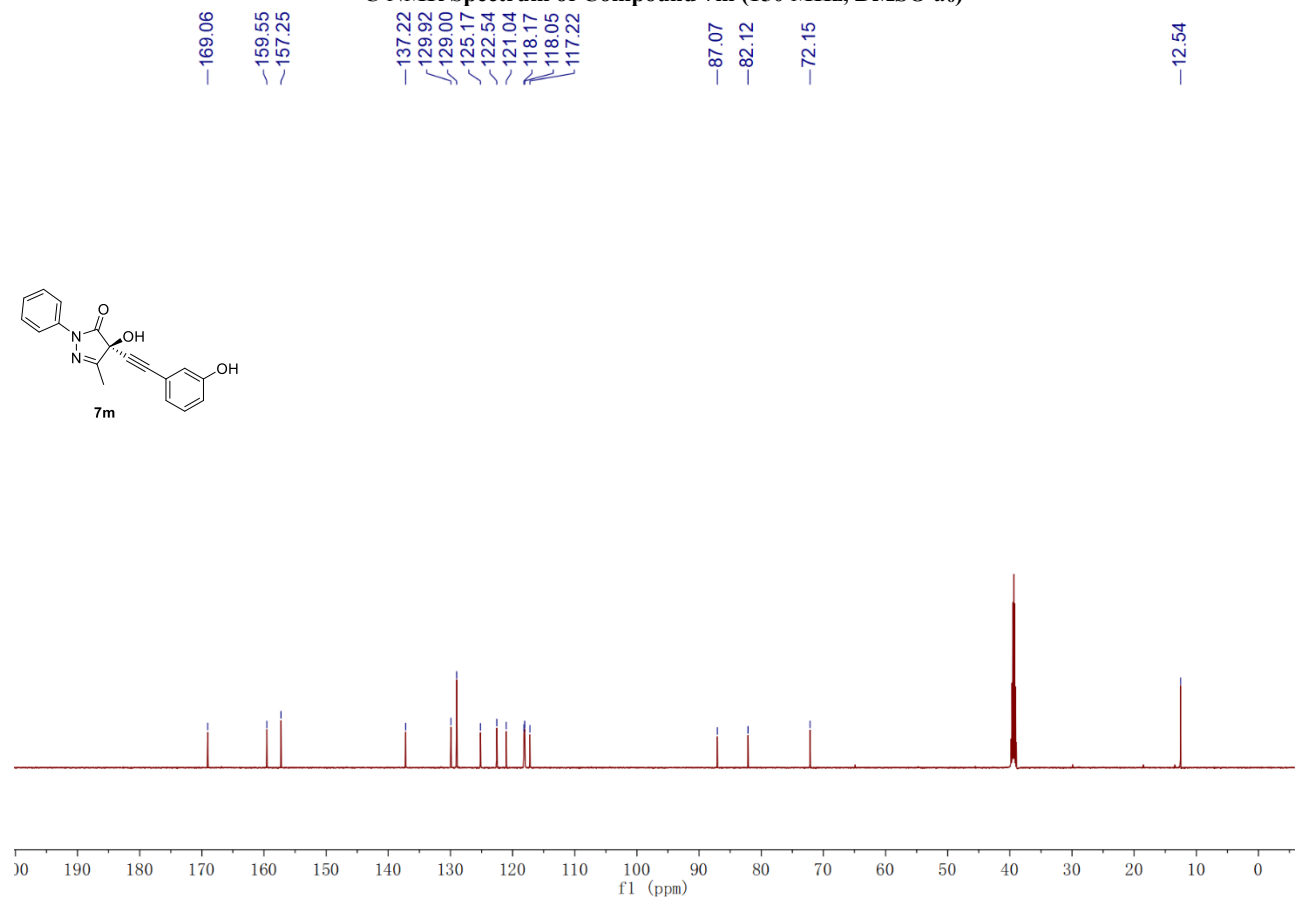


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7m (400 MHz, DMSO-*d*₆)

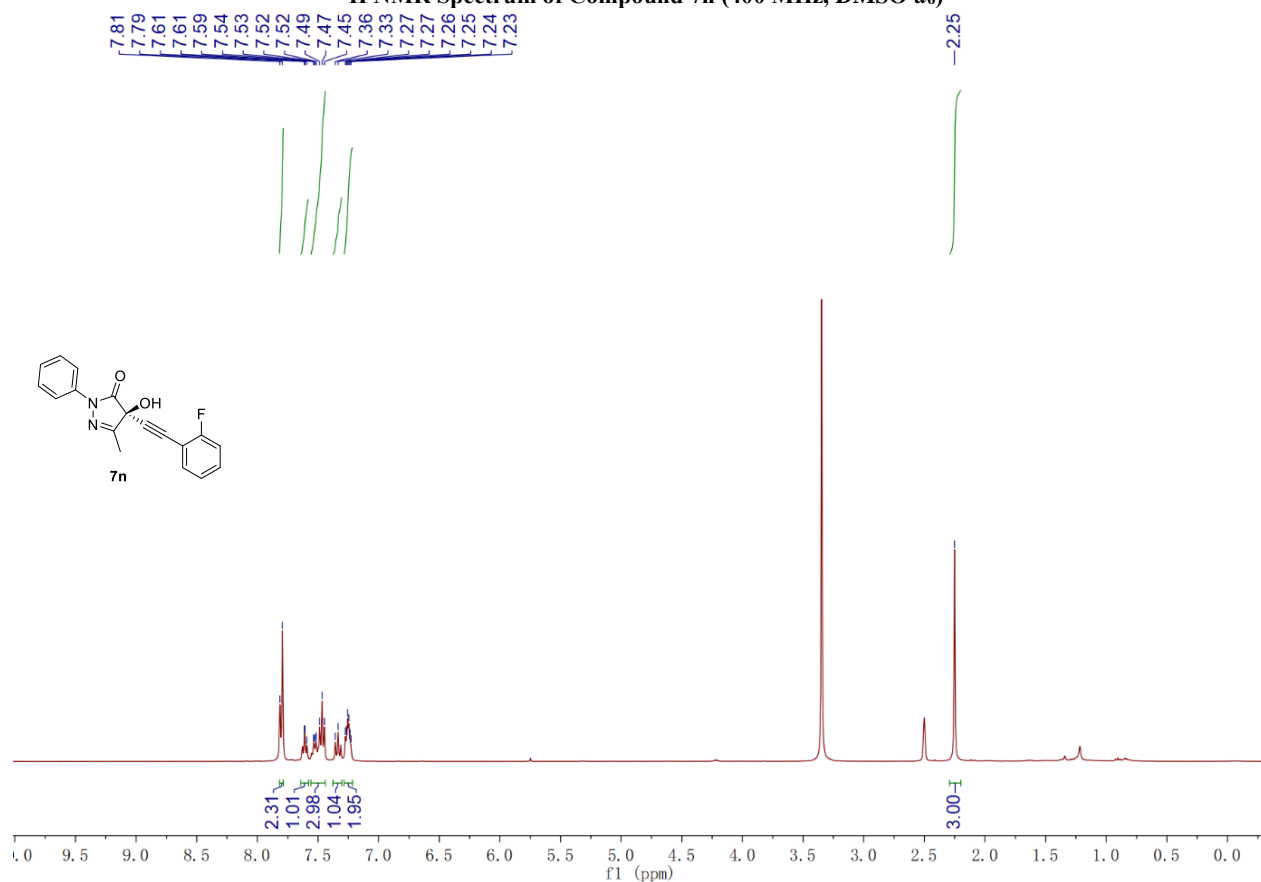


¹³C NMR Spectrum of Compound 7m (150 MHz, DMSO-*d*₆)

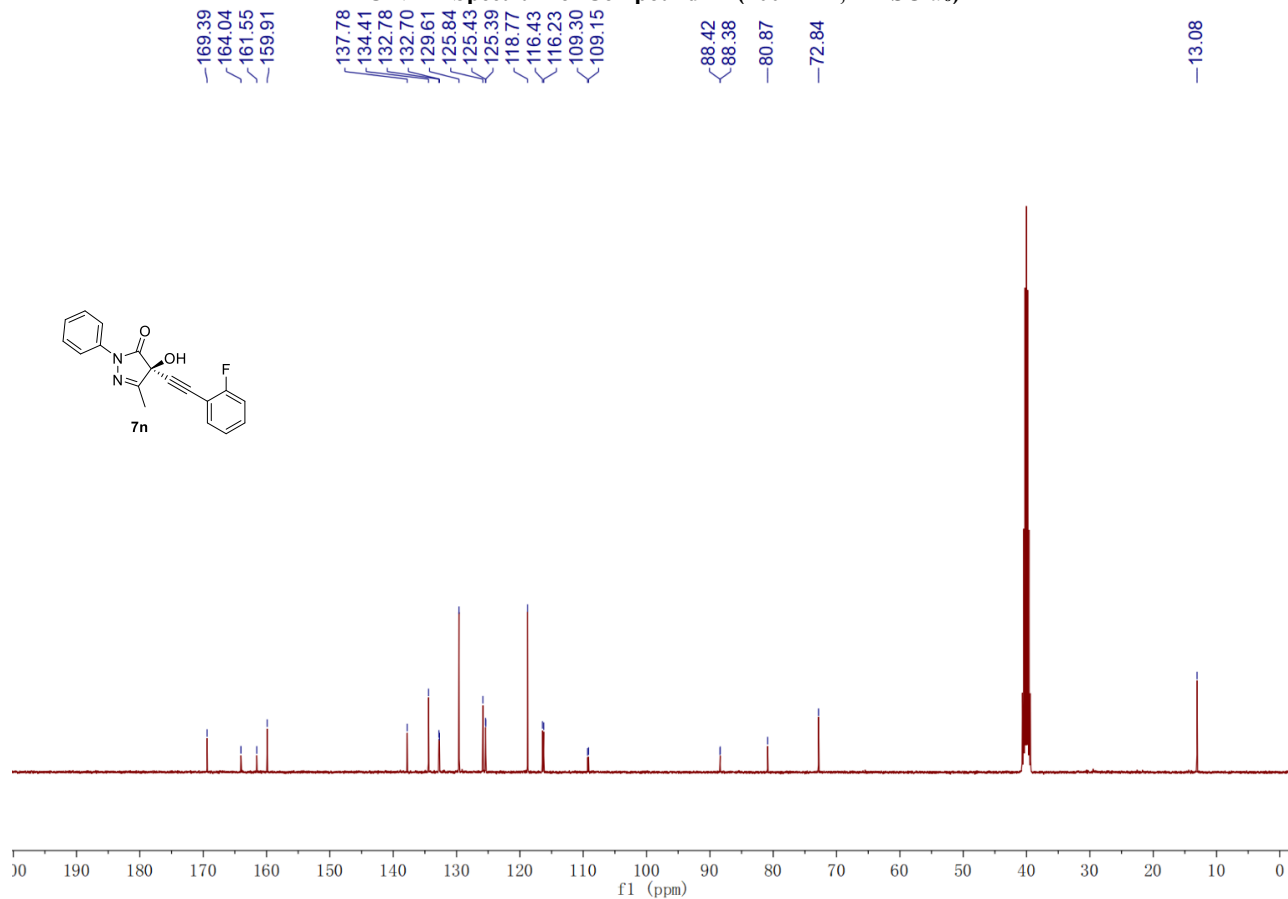


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7n (400 MHz, DMSO-*d*₆)



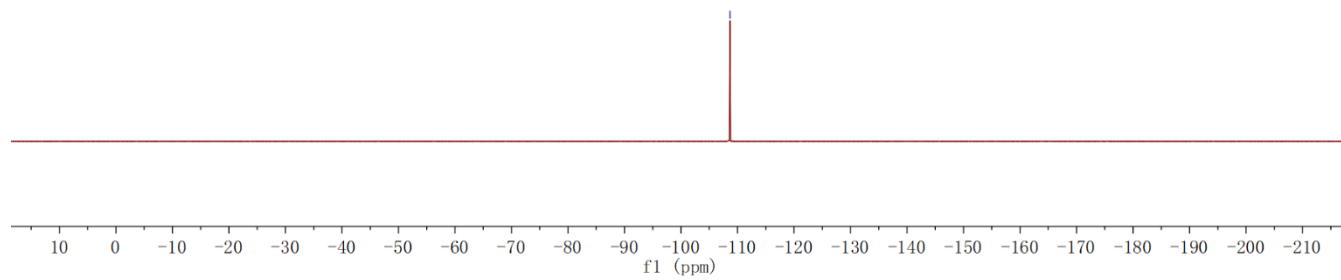
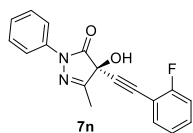
¹³C NMR Spectrum of Compound 7n (100 MHz, DMSO-*d*₆)



SUPPORTING INFORMATION

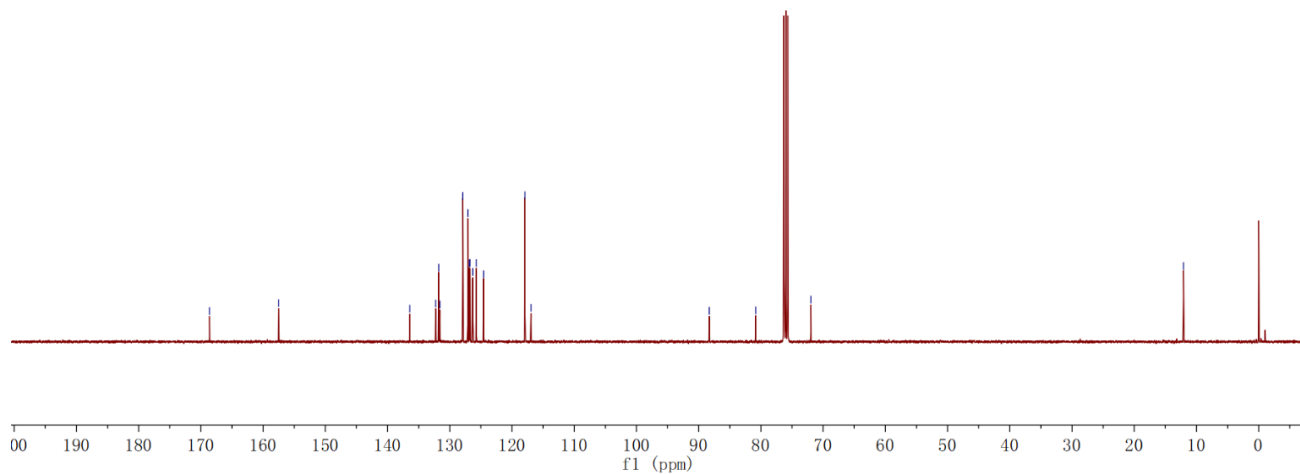
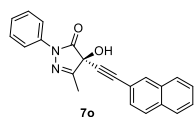
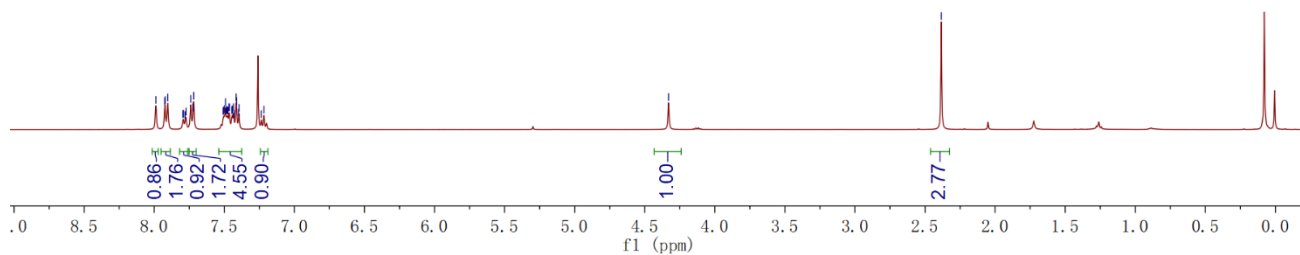
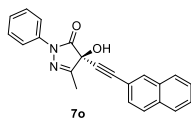
¹⁹F NMR Spectrum of Compound 7n (376 MHz, CDCl₃)

--108.67



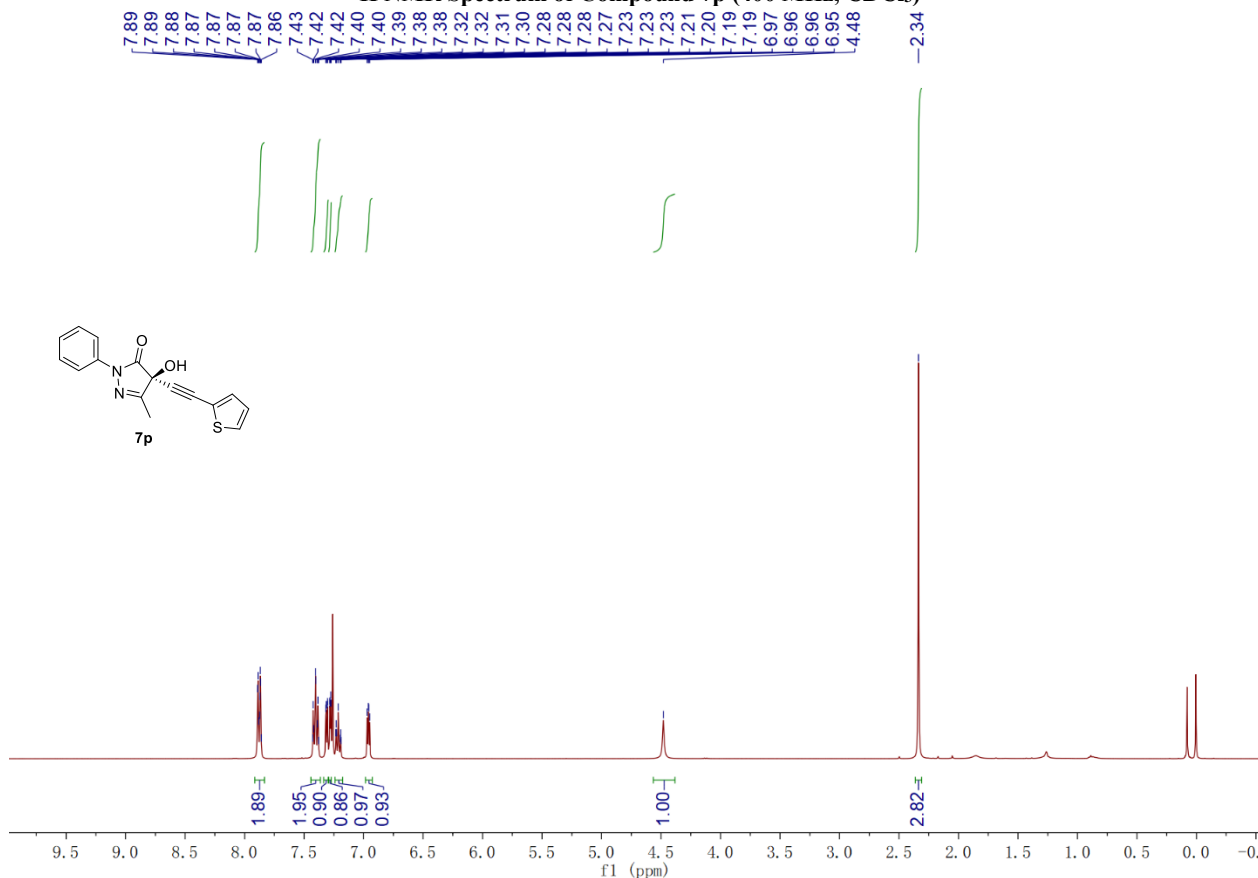
SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7o (400 MHz, CDCl₃)

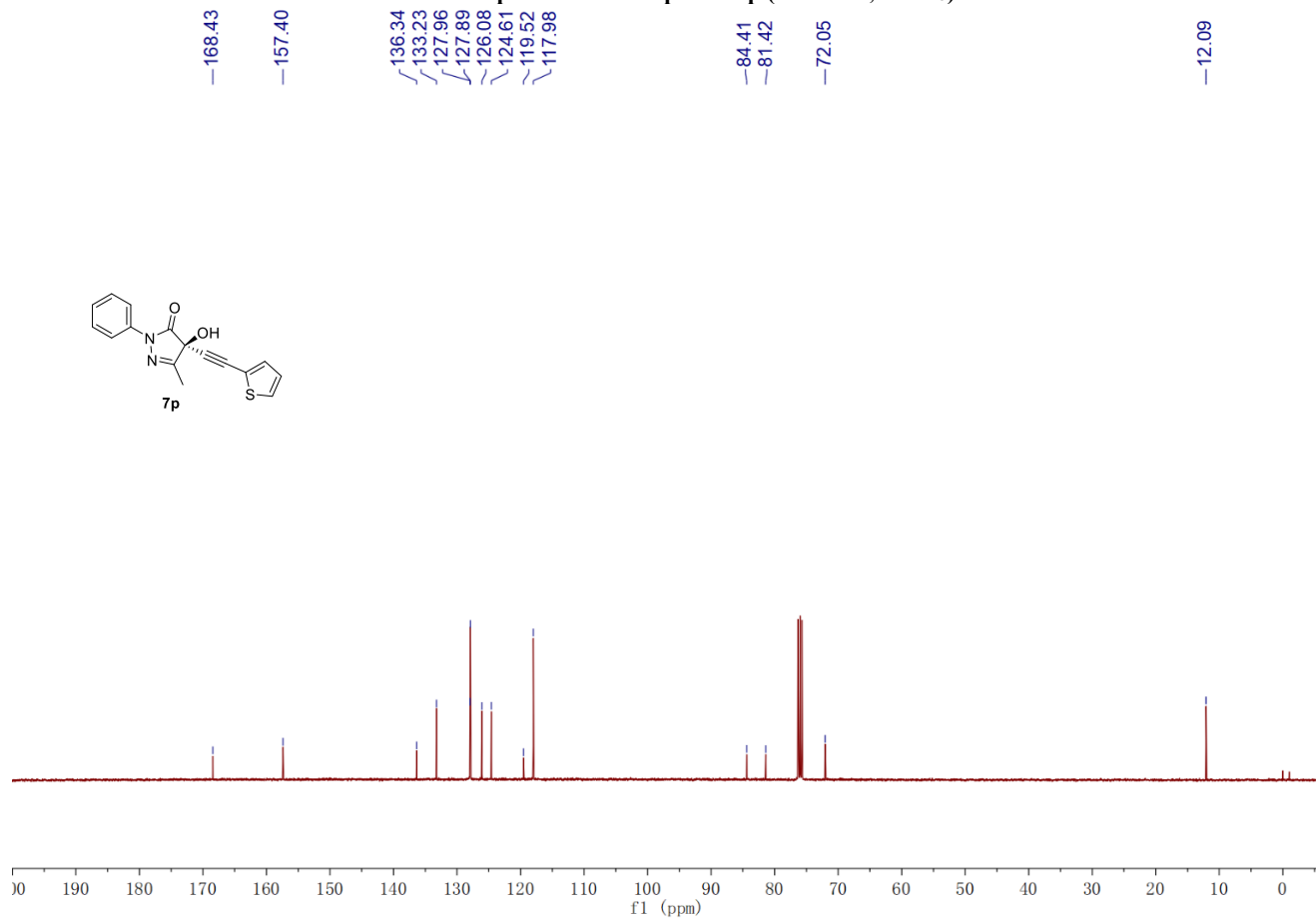


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7p (400 MHz, CDCl₃)

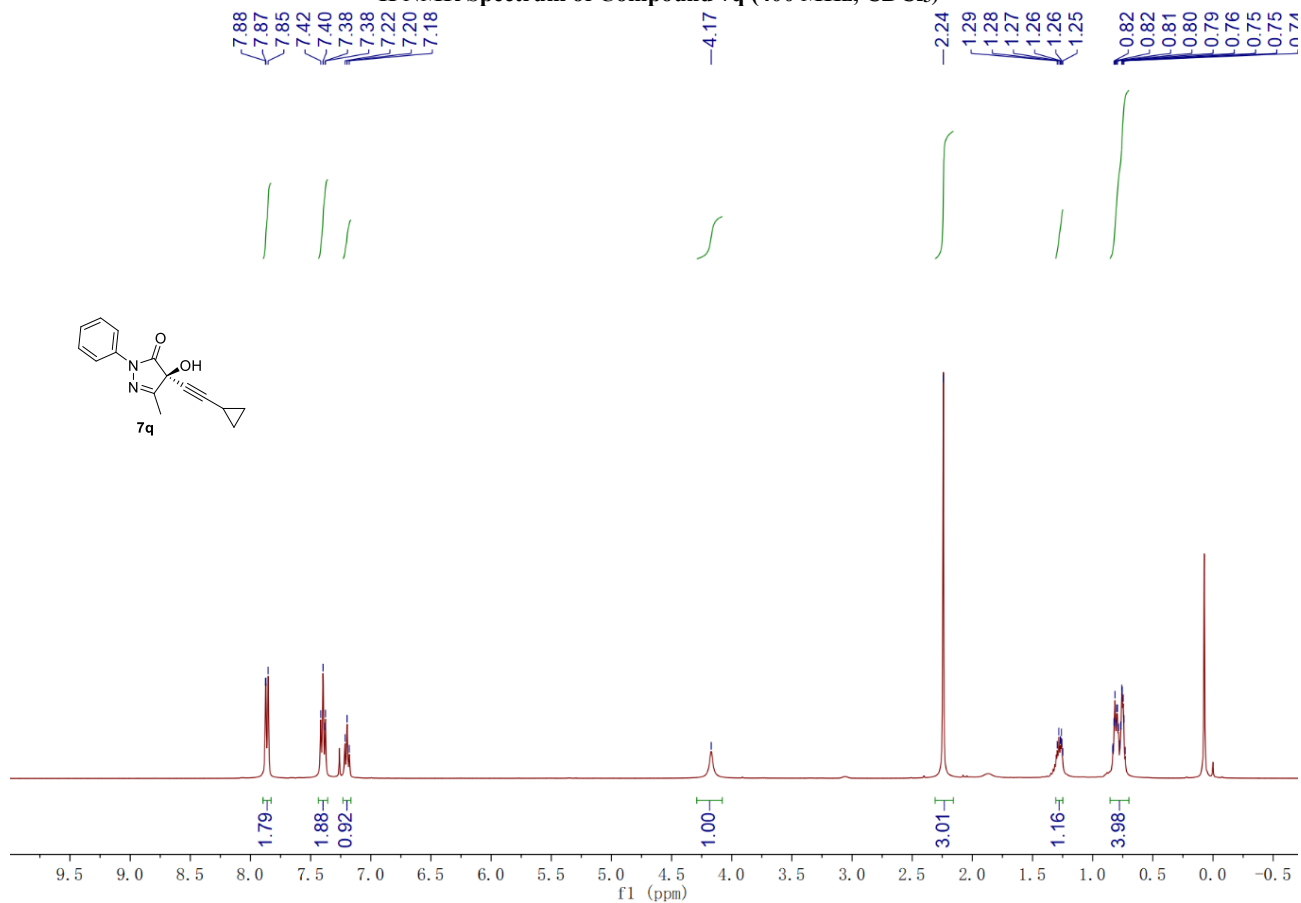


¹³C NMR Spectrum of Compound 7p (100 MHz, CDCl₃)

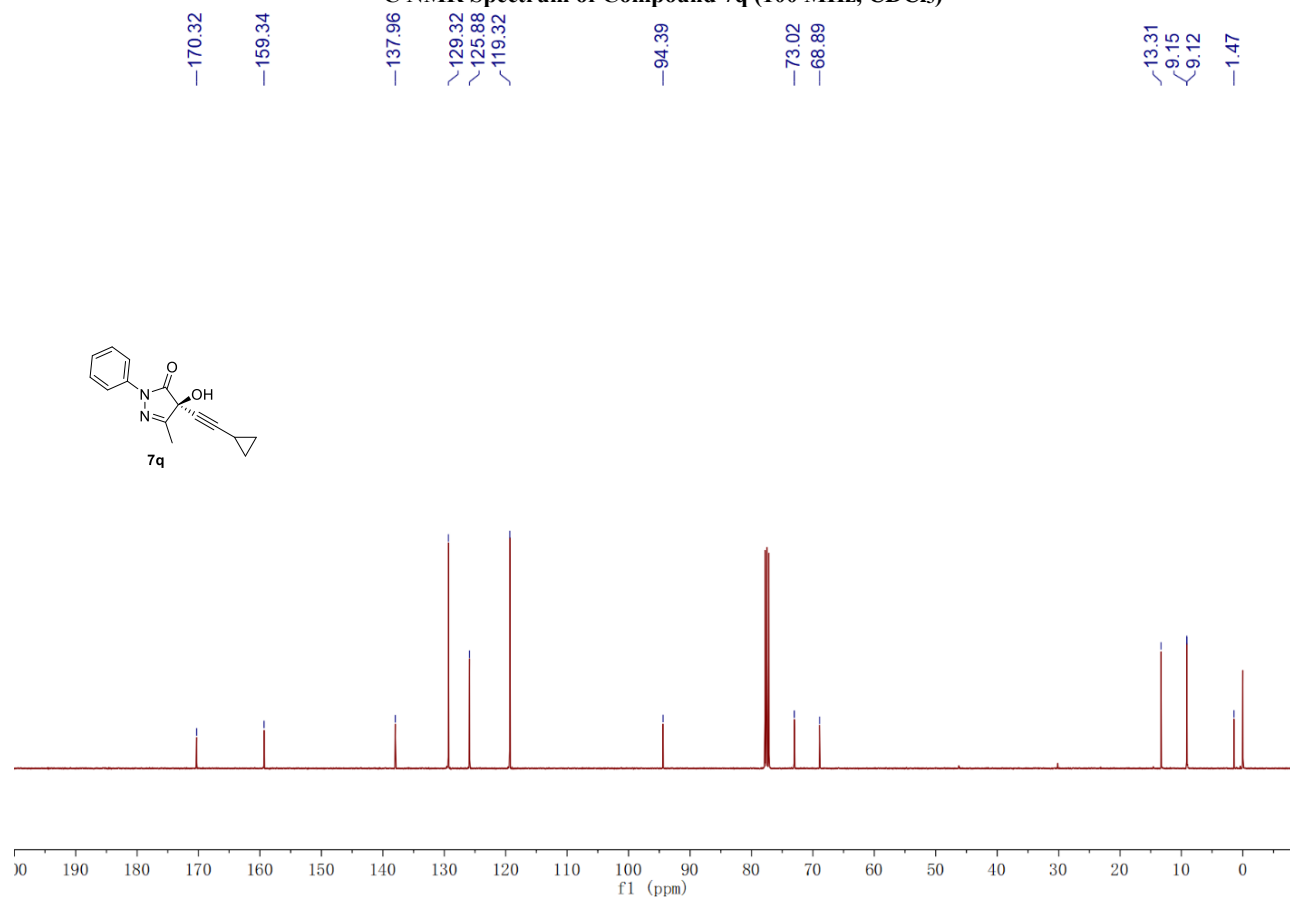


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7q (400 MHz, CDCl₃)

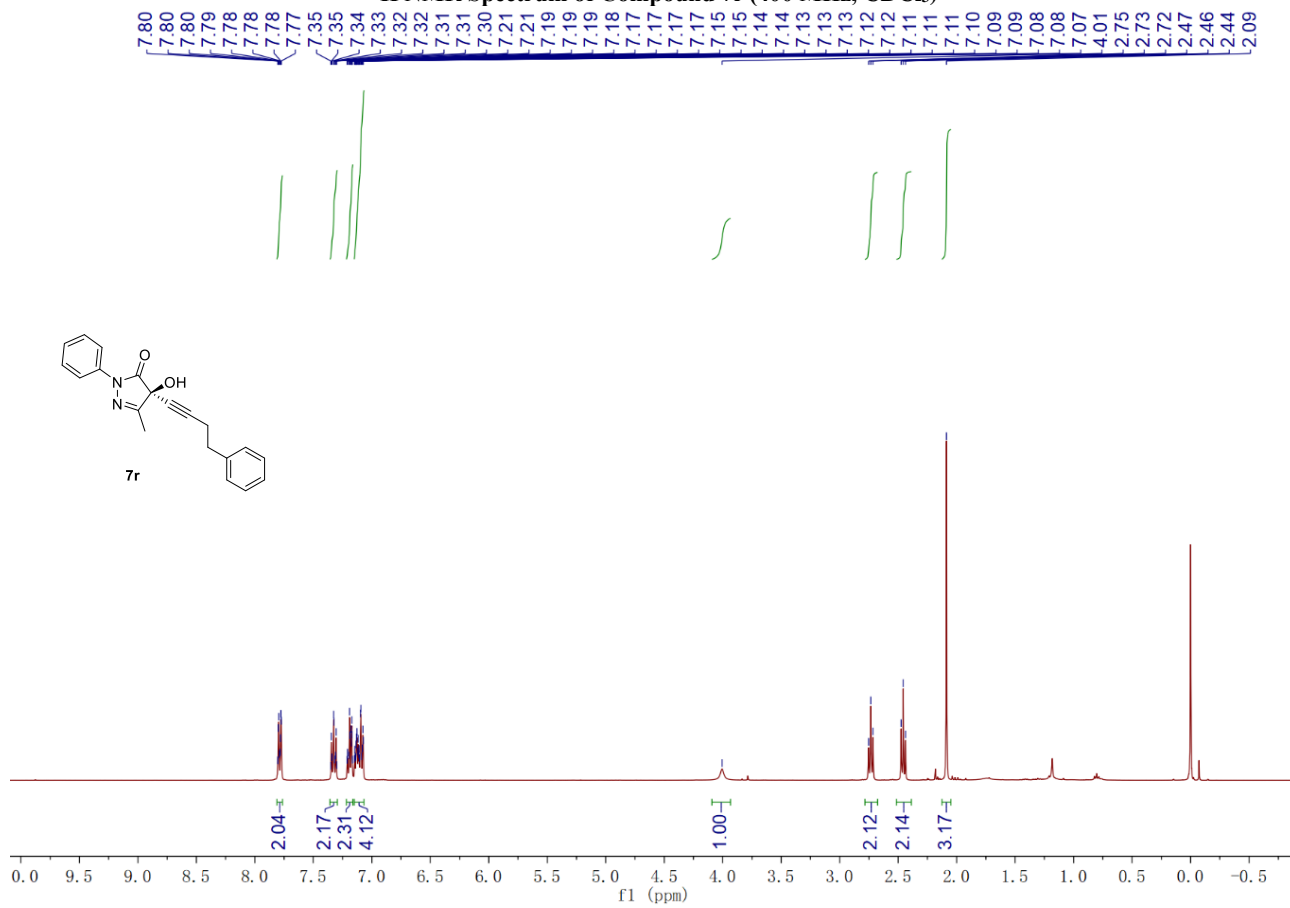


¹³C NMR Spectrum of Compound 7q (100 MHz, CDCl₃)

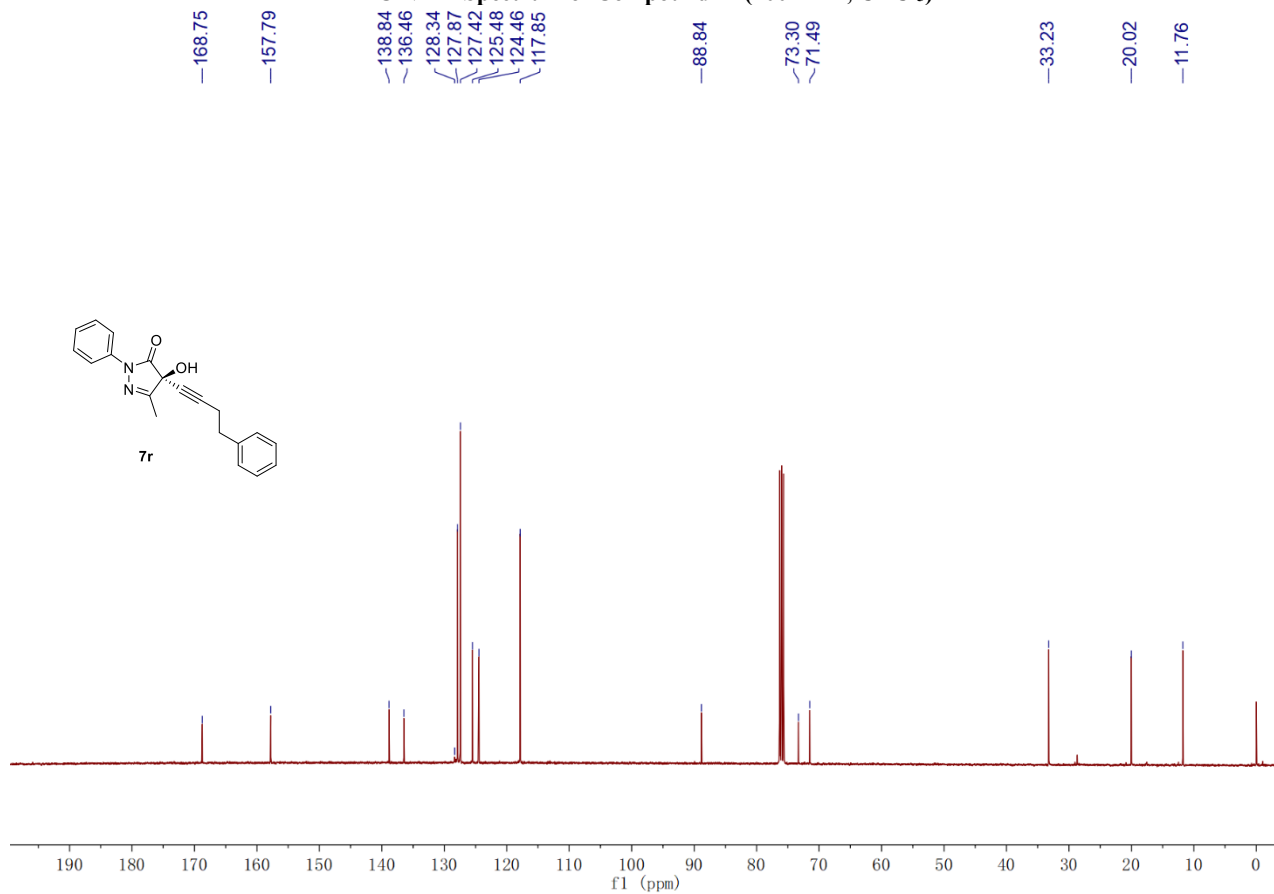


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7r (400 MHz, CDCl₃)

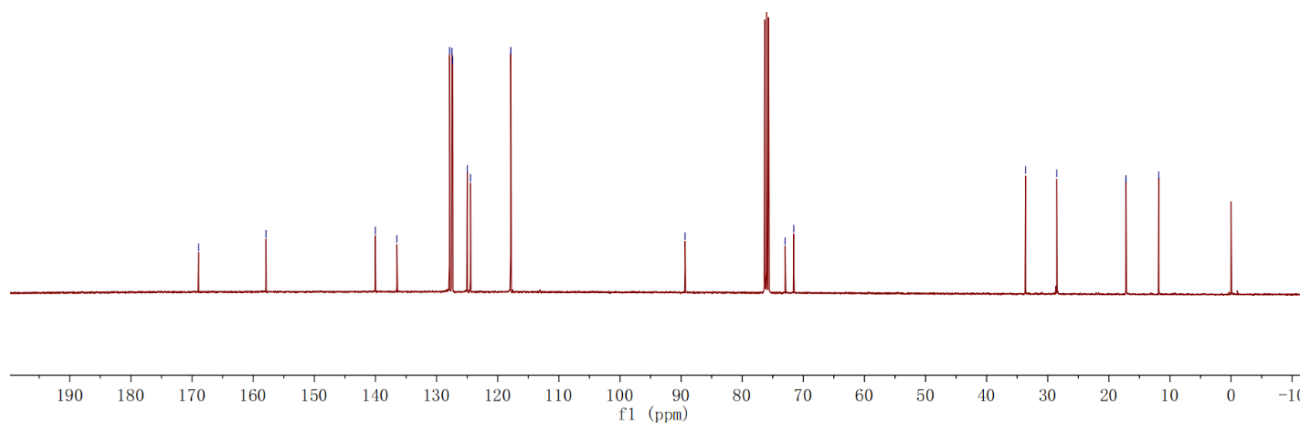
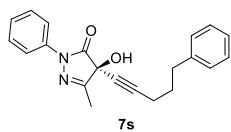
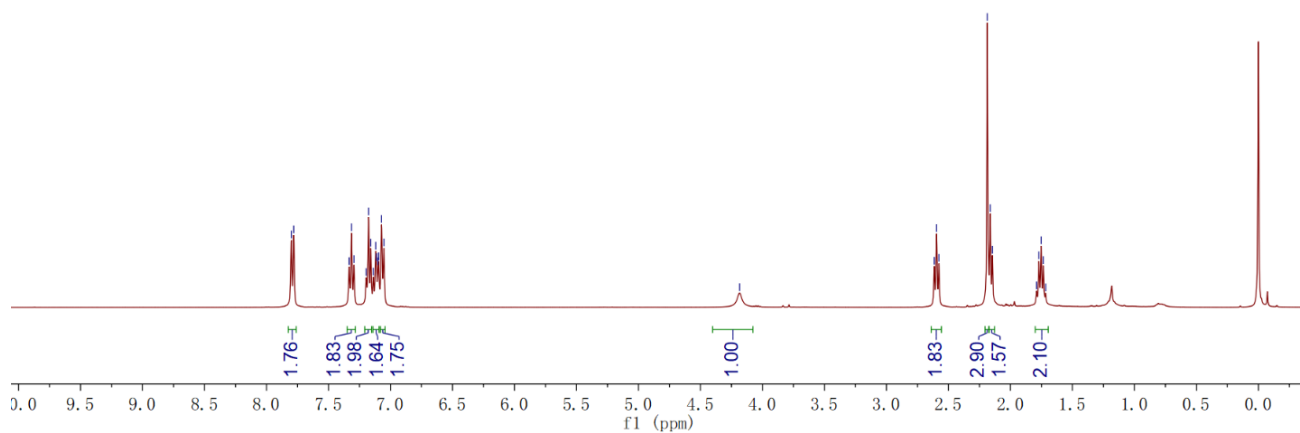
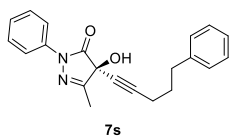
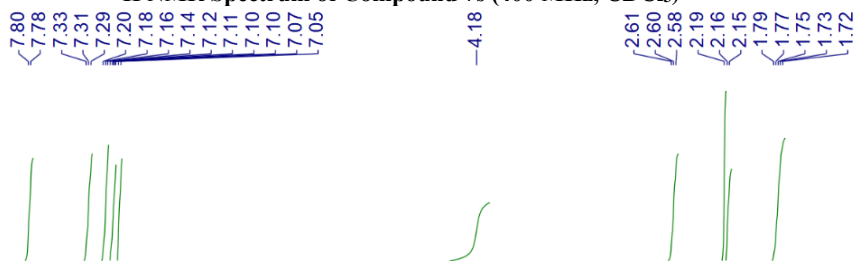


¹³C NMR Spectrum of Compound 7r (100 MHz, CDCl₃)

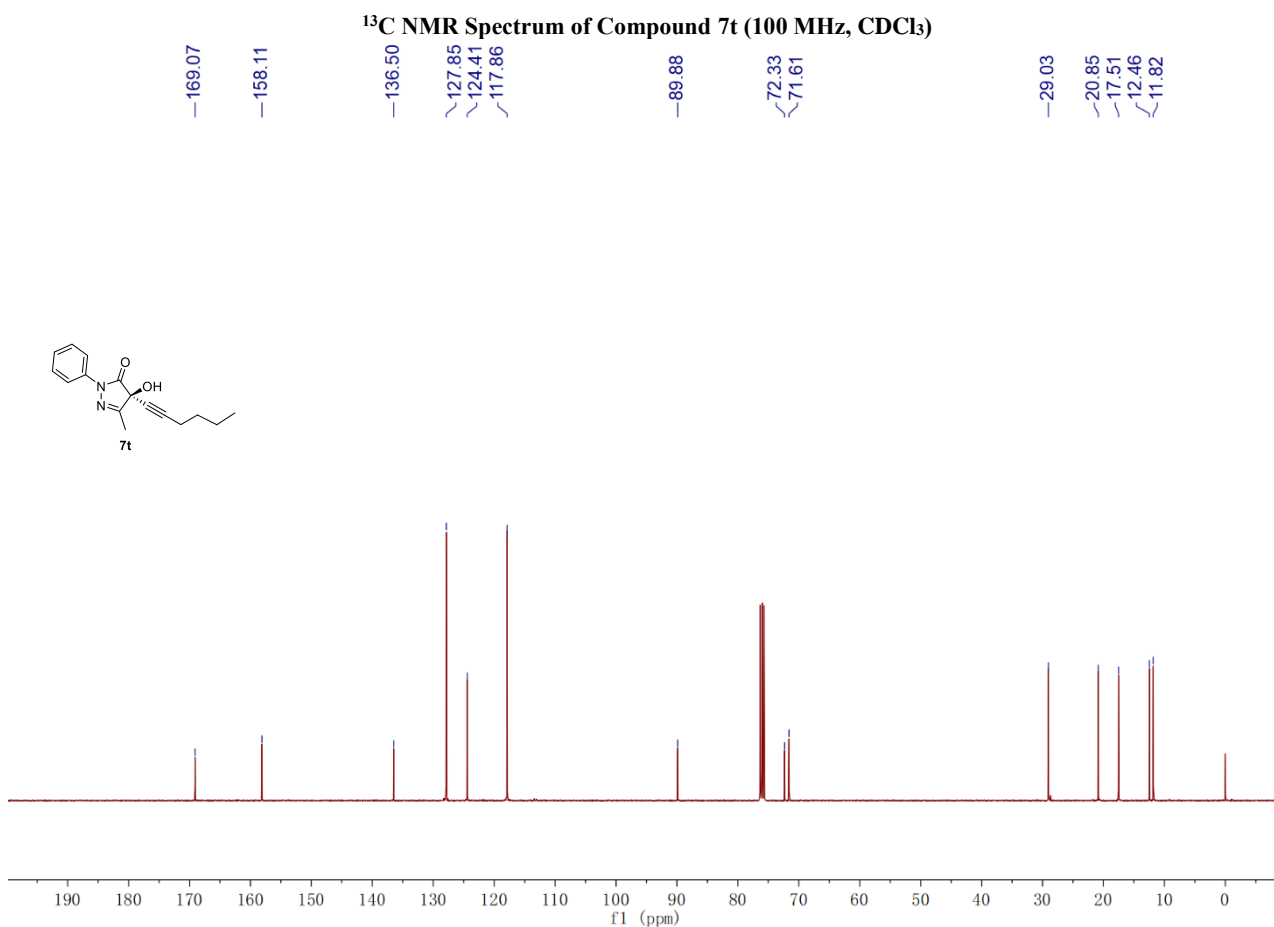
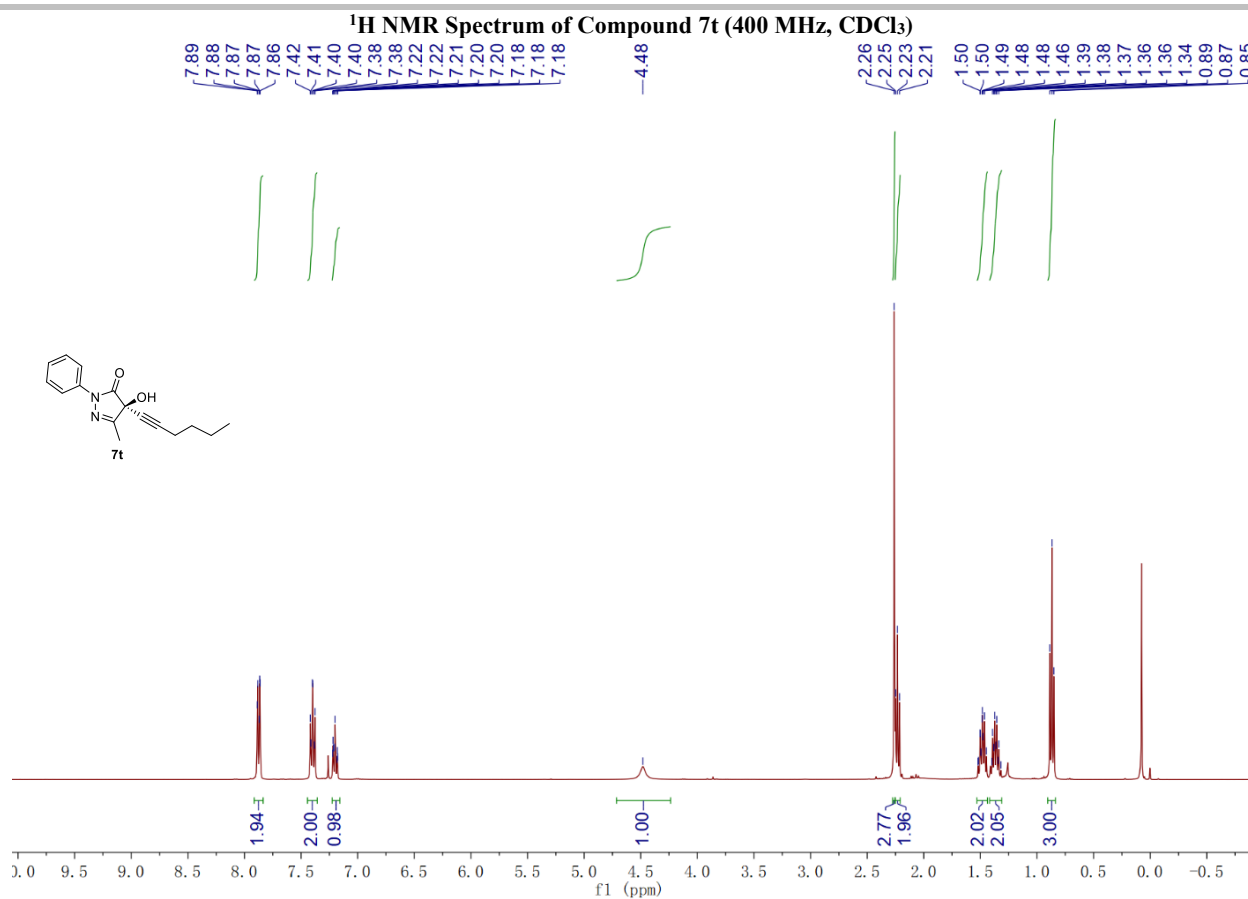


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 7s (400 MHz, CDCl₃)

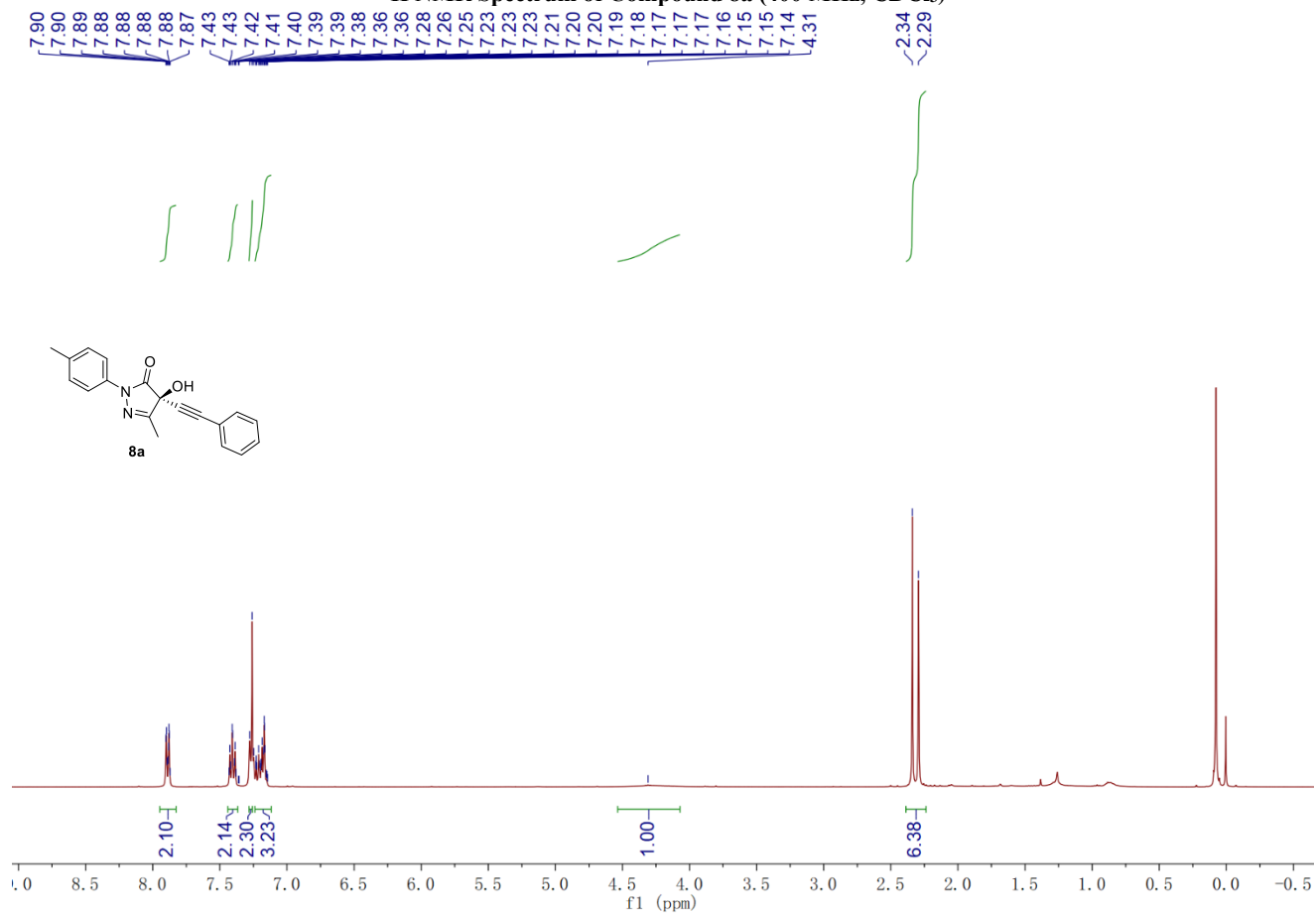


SUPPORTING INFORMATION

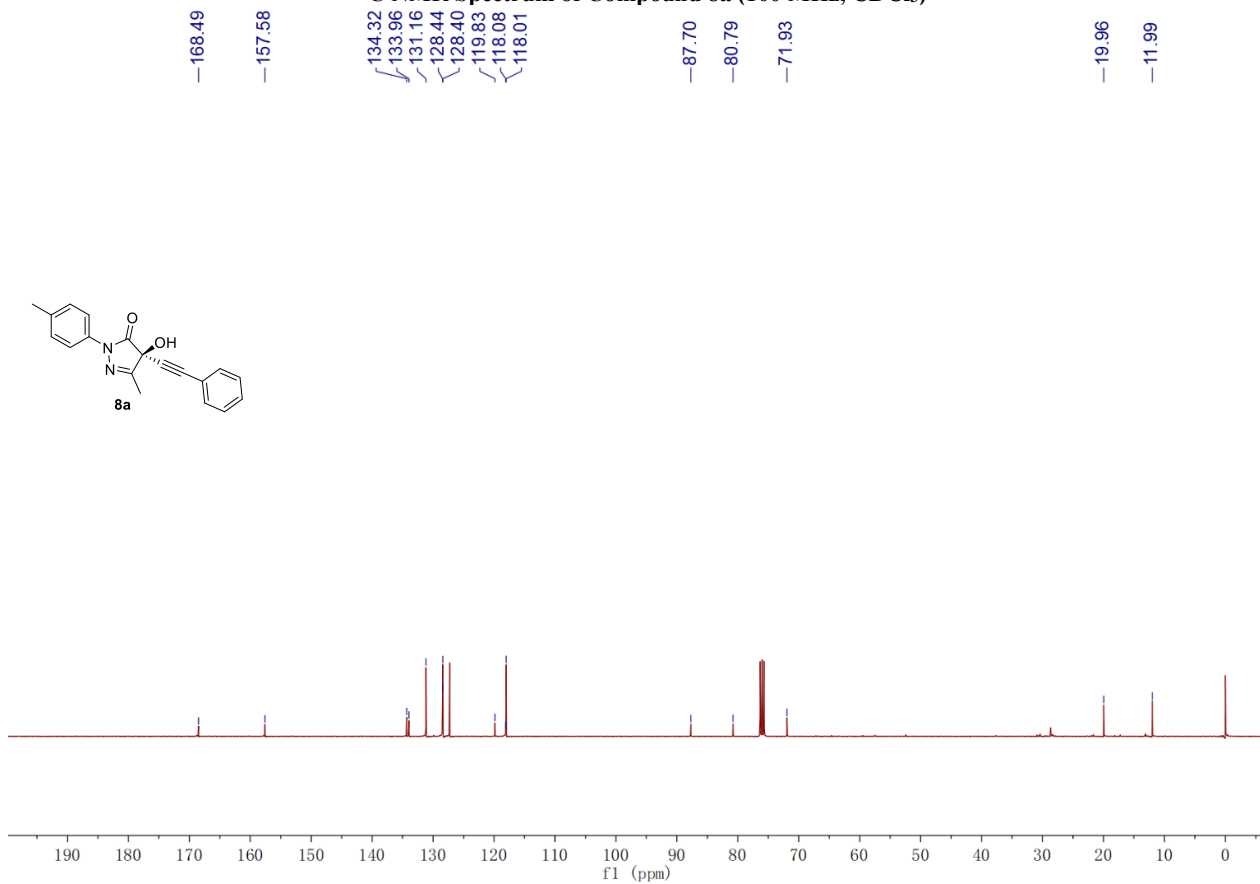


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8a (400 MHz, CDCl₃)

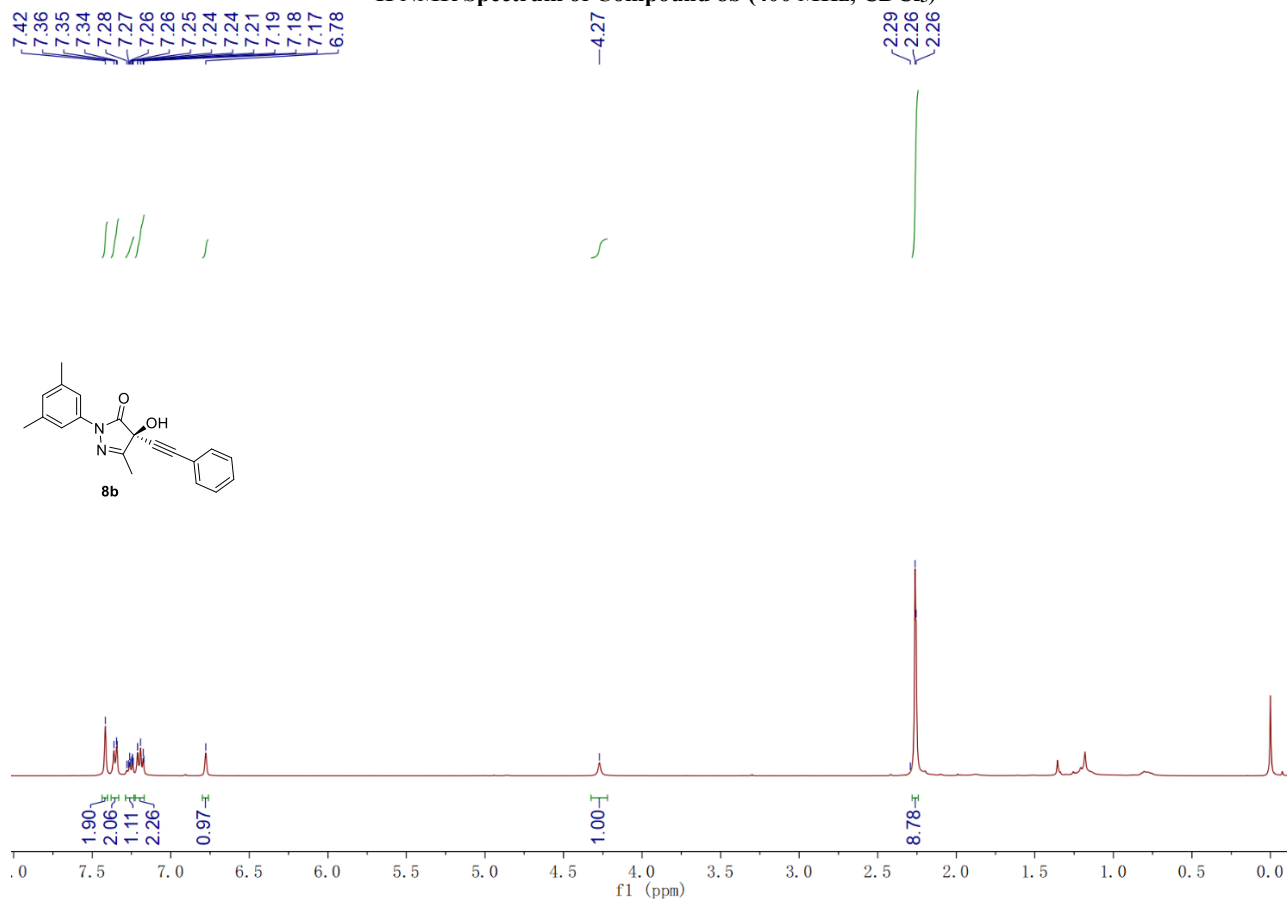


¹³C NMR Spectrum of Compound 8a (100 MHz, CDCl₃)

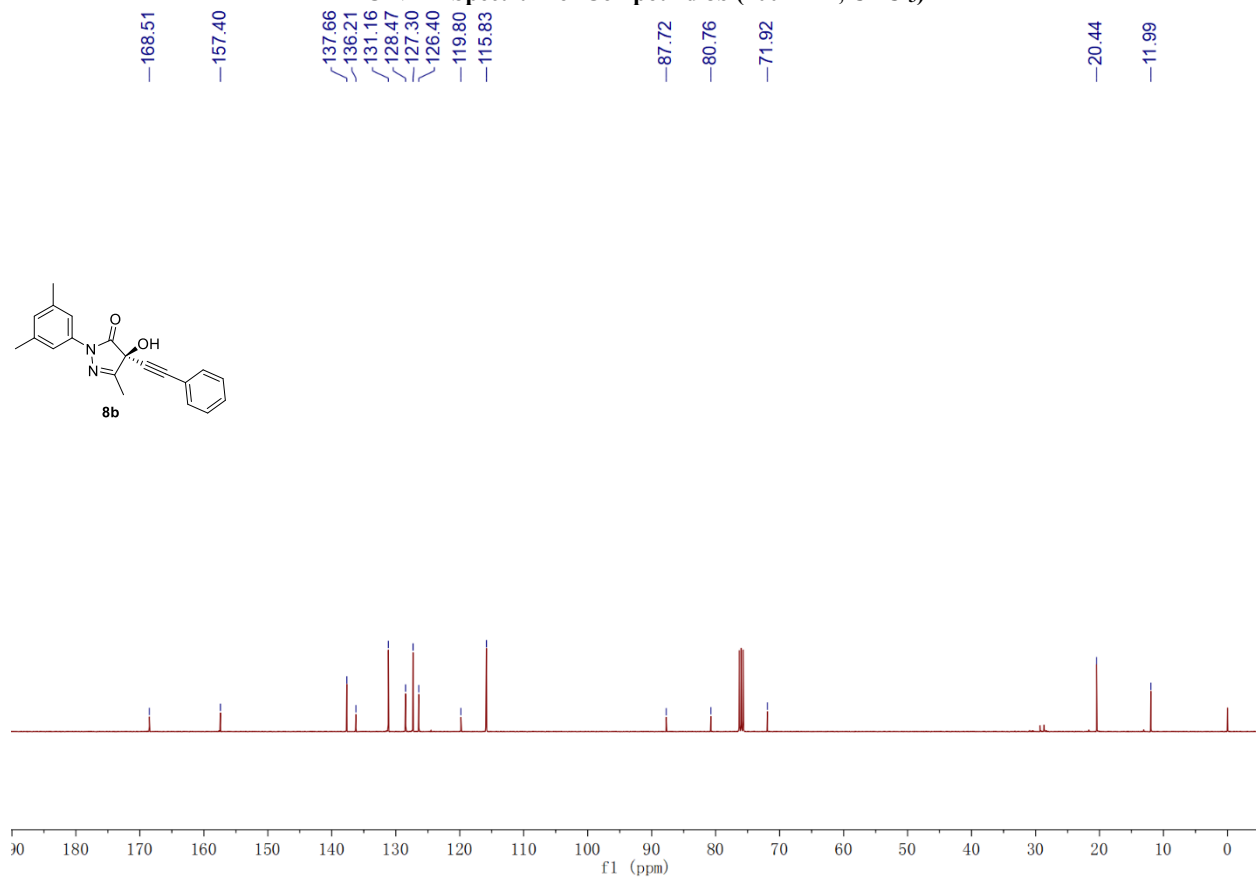


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8b (400 MHz, CDCl₃)

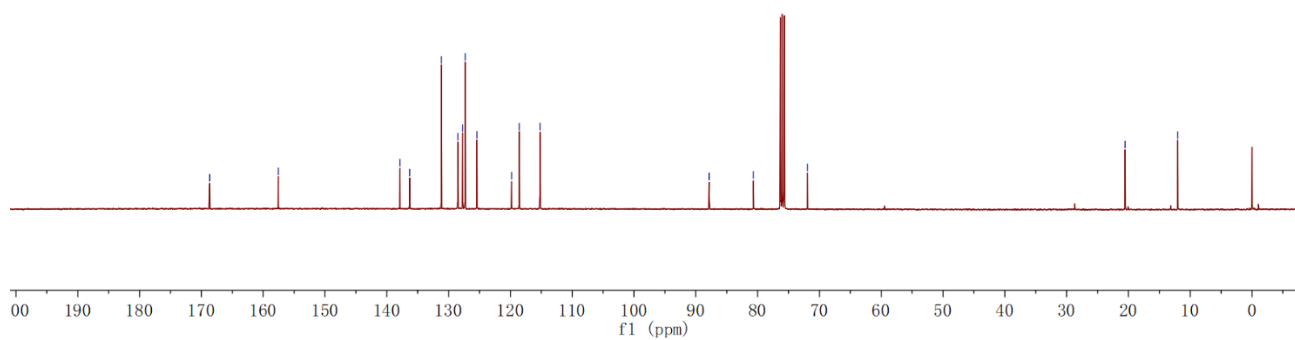
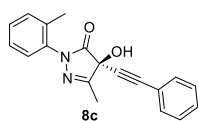
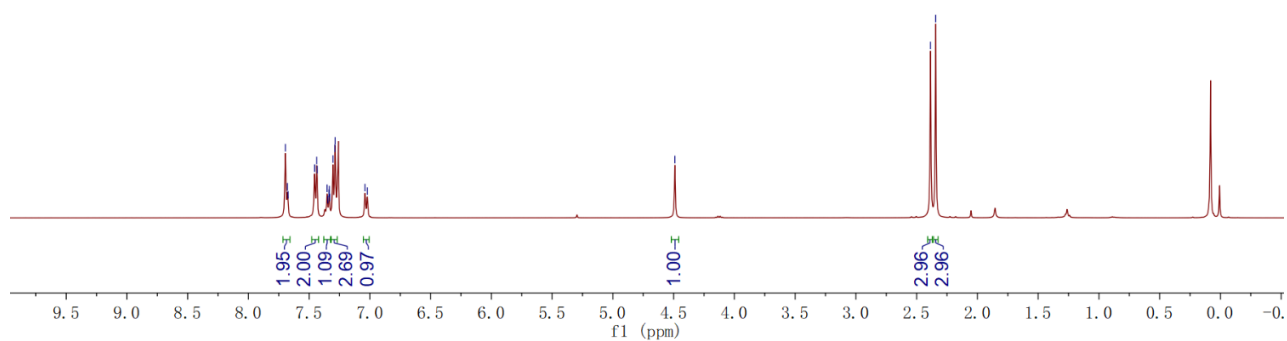
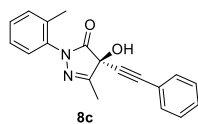


¹³C NMR Spectrum of Compound 8b (100 MHz, CDCl₃)



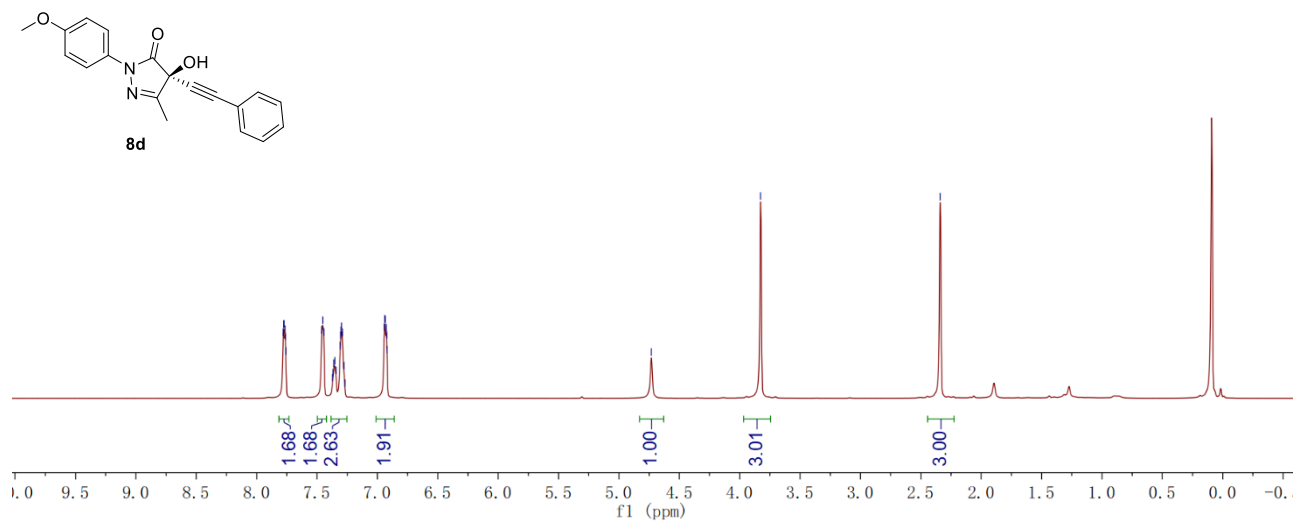
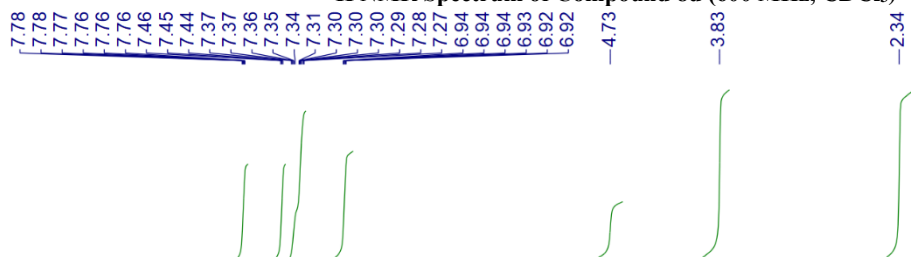
SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8c (400 MHz, CDCl₃)

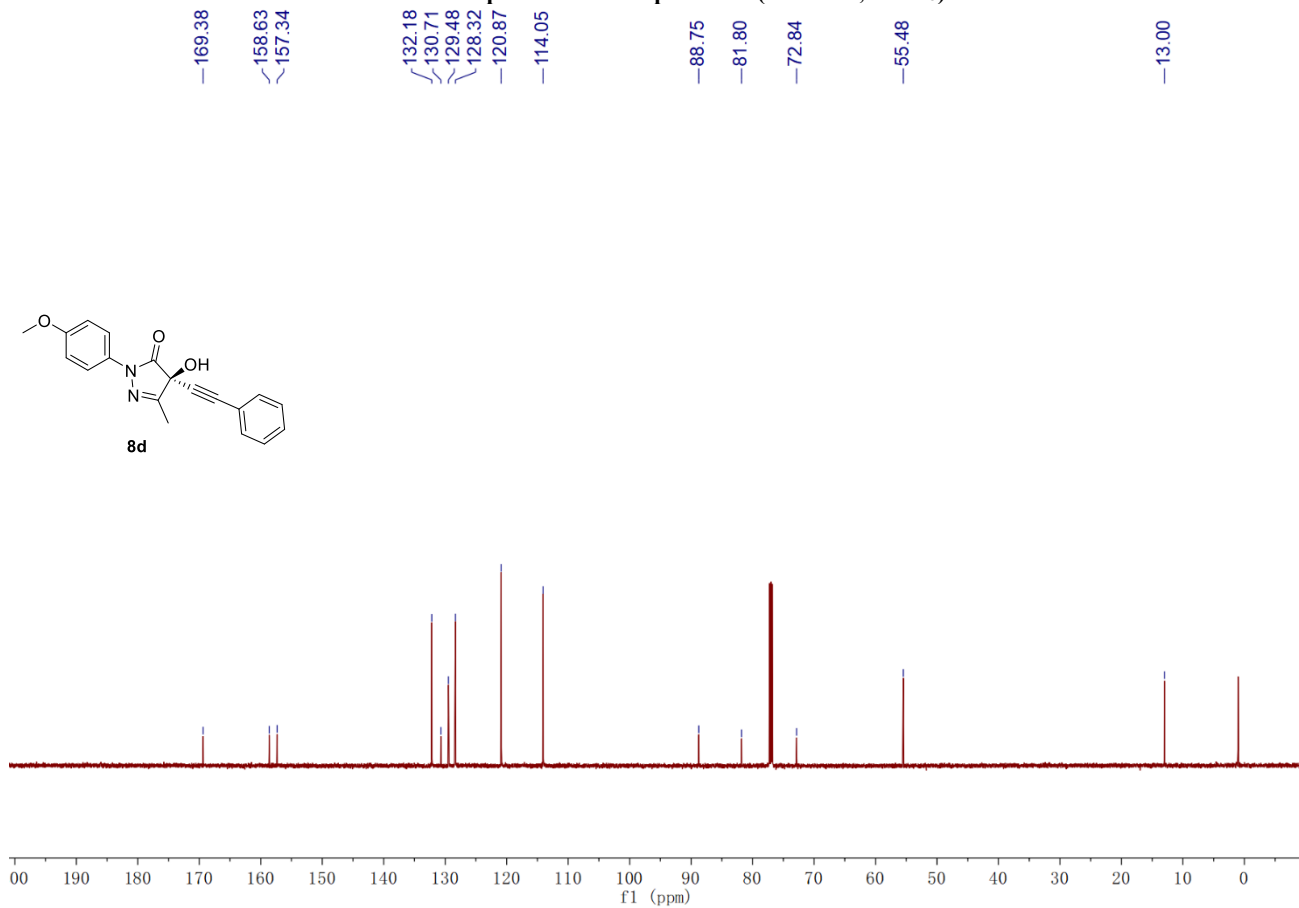


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8d (600 MHz, CDCl₃)

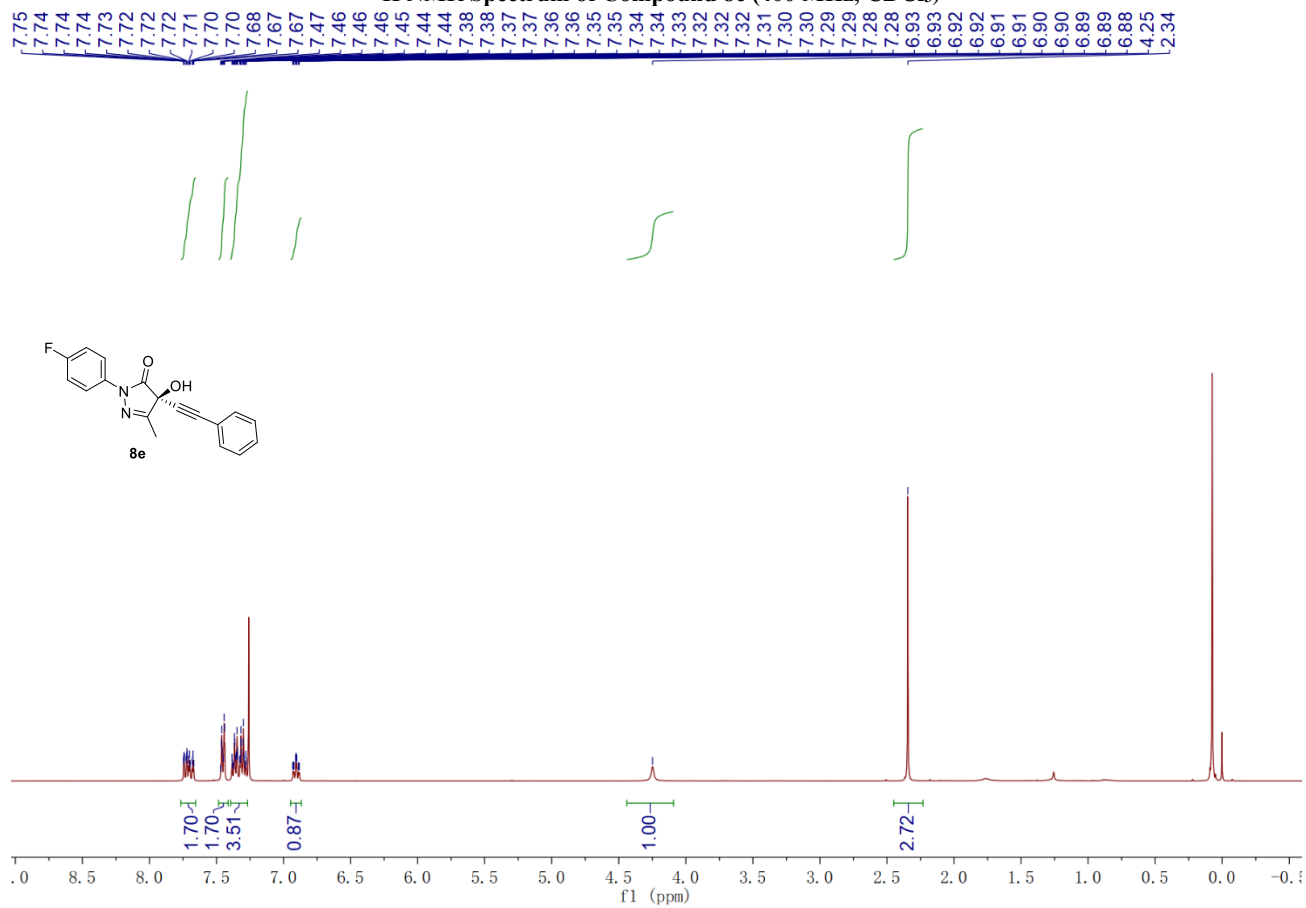


¹³C NMR Spectrum of Compound 8d (150 MHz, CDCl₃)

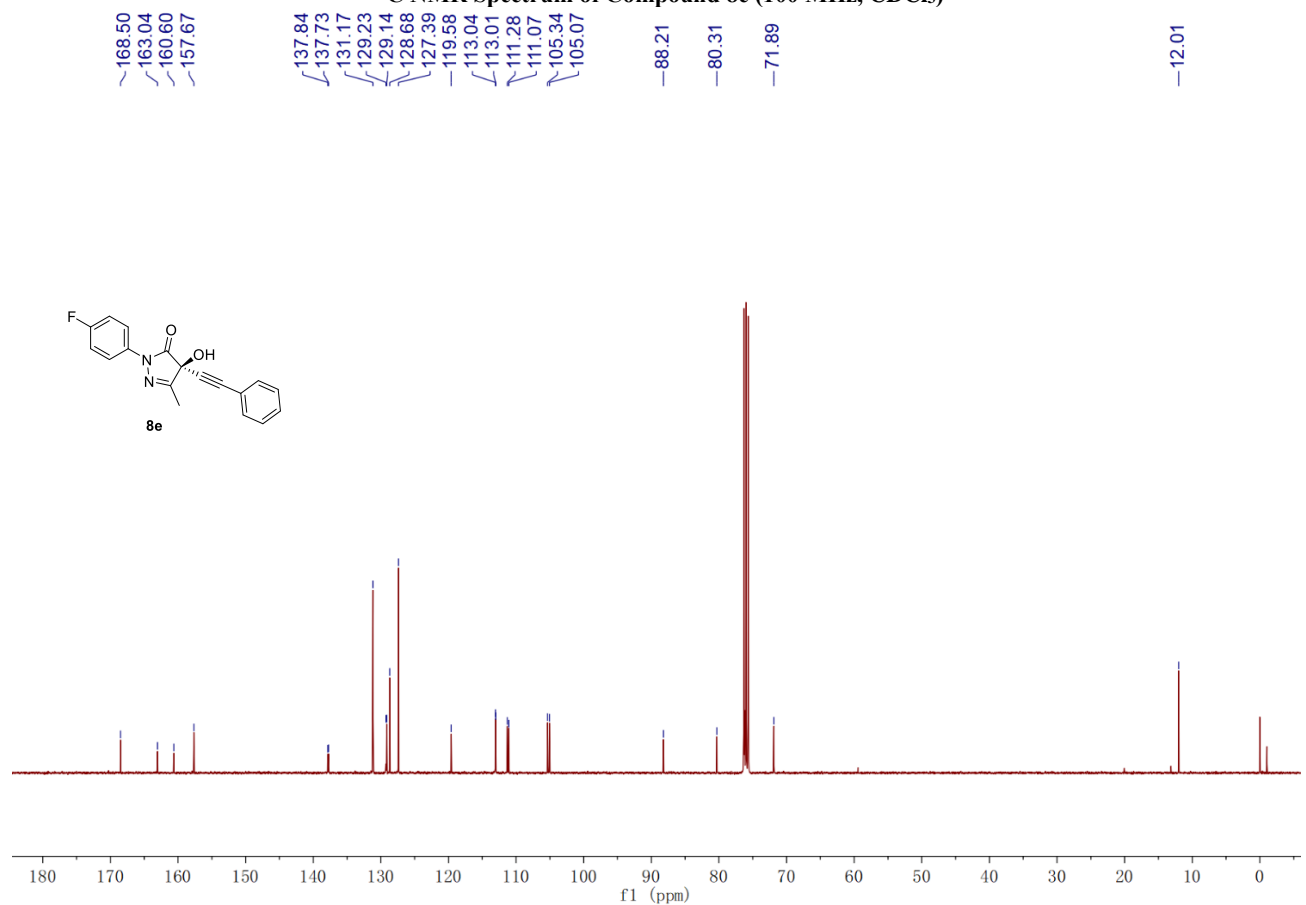


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8e (400 MHz, CDCl₃)



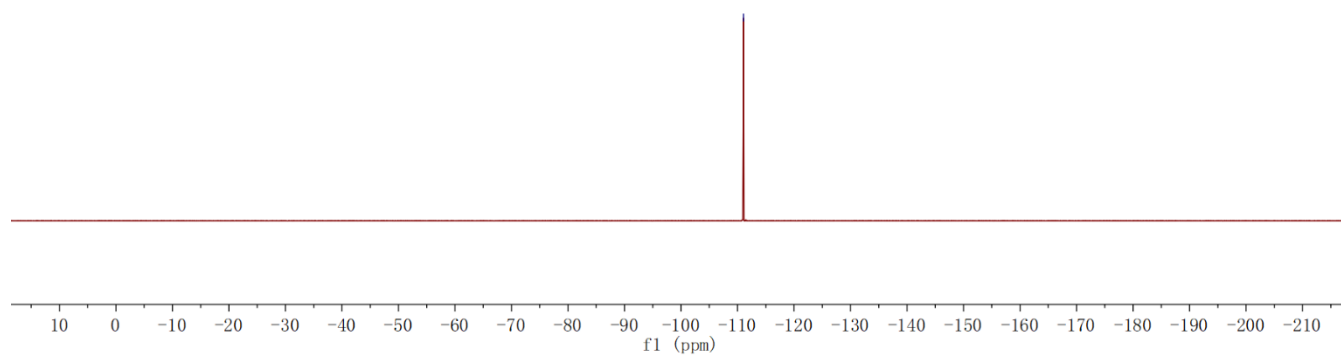
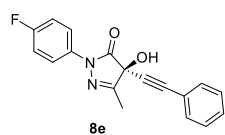
¹³C NMR Spectrum of Compound 8e (100 MHz, CDCl₃)



SUPPORTING INFORMATION

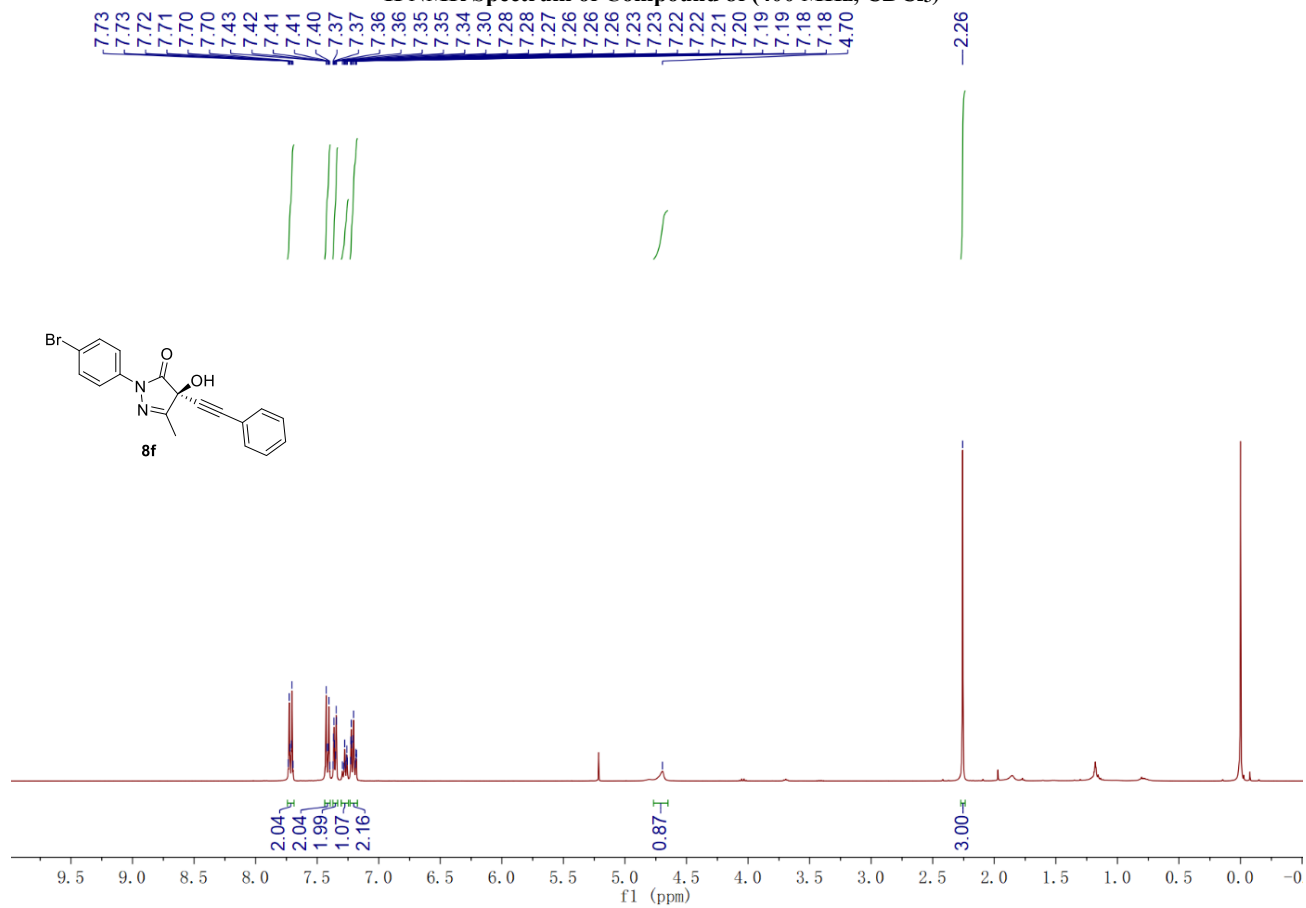
¹⁹F NMR Spectrum of Compound **8e** (376 MHz, CDCl₃)

---111.06

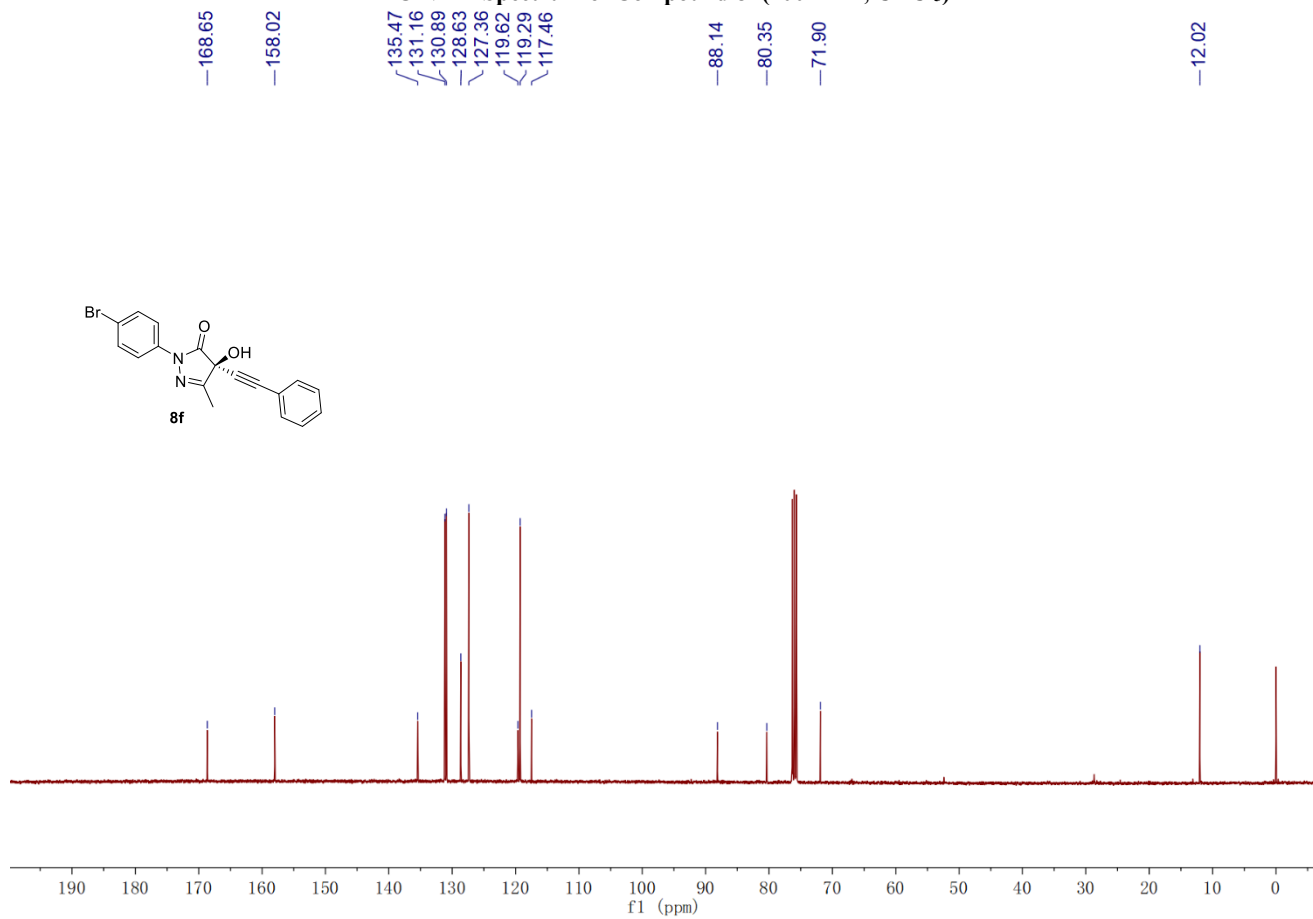


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8f (400 MHz, CDCl₃)

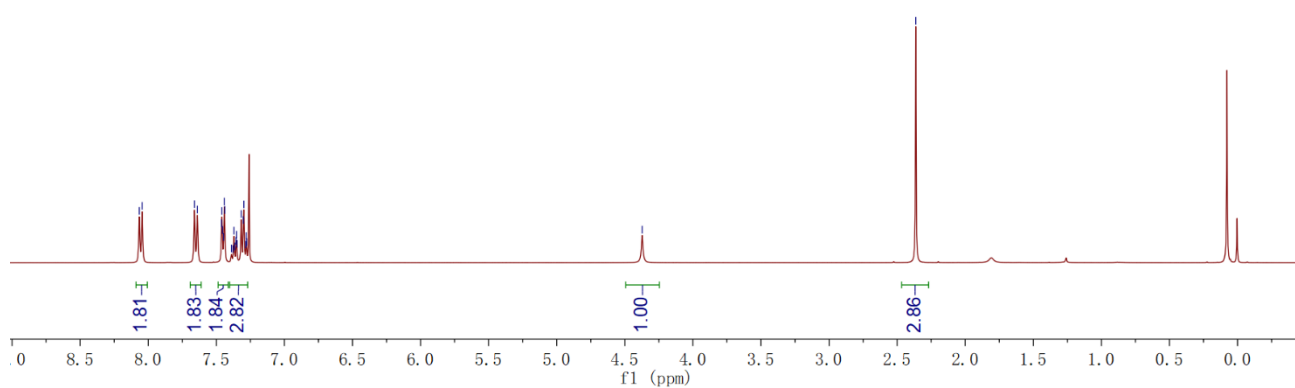
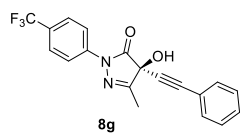
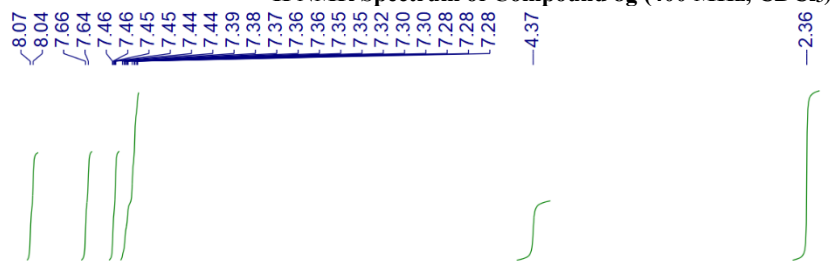


¹³C NMR Spectrum of Compound 8f (100 MHz, CDCl₃)

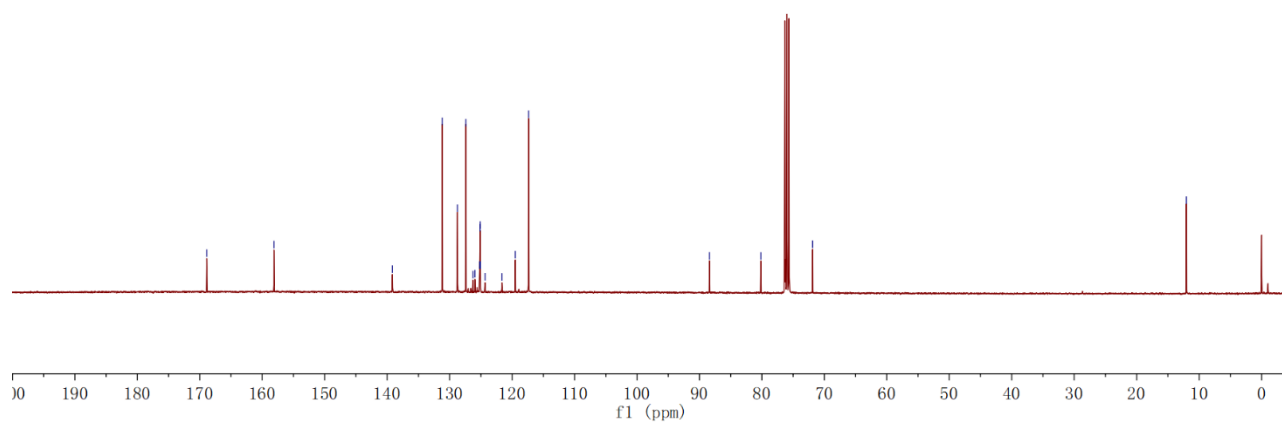
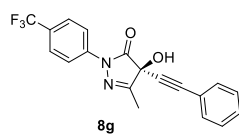
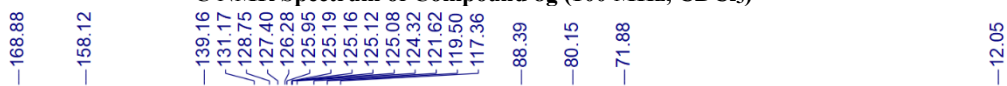


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8g (400 MHz, CDCl₃)



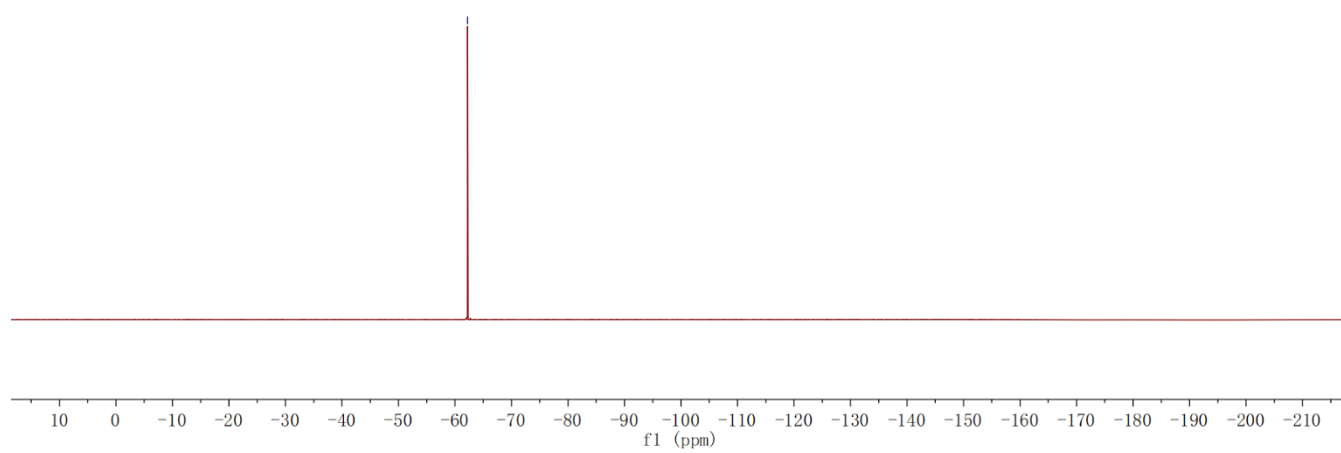
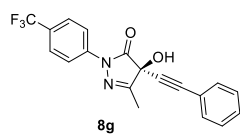
¹³C NMR Spectrum of Compound 8g (100 MHz, CDCl₃)



SUPPORTING INFORMATION

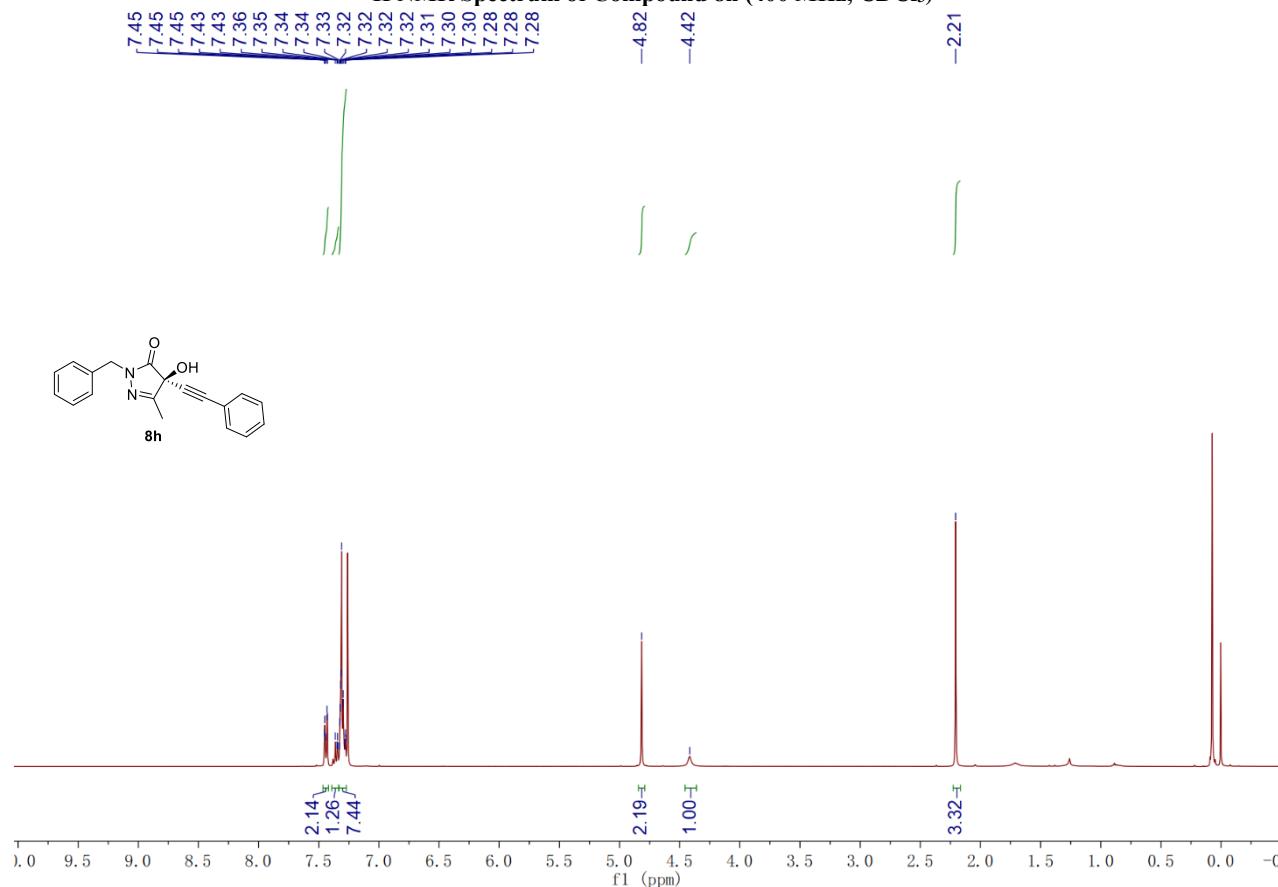
^{19}F NMR Spectrum of Compound 8g (376 MHz, CDCl_3)

62.23

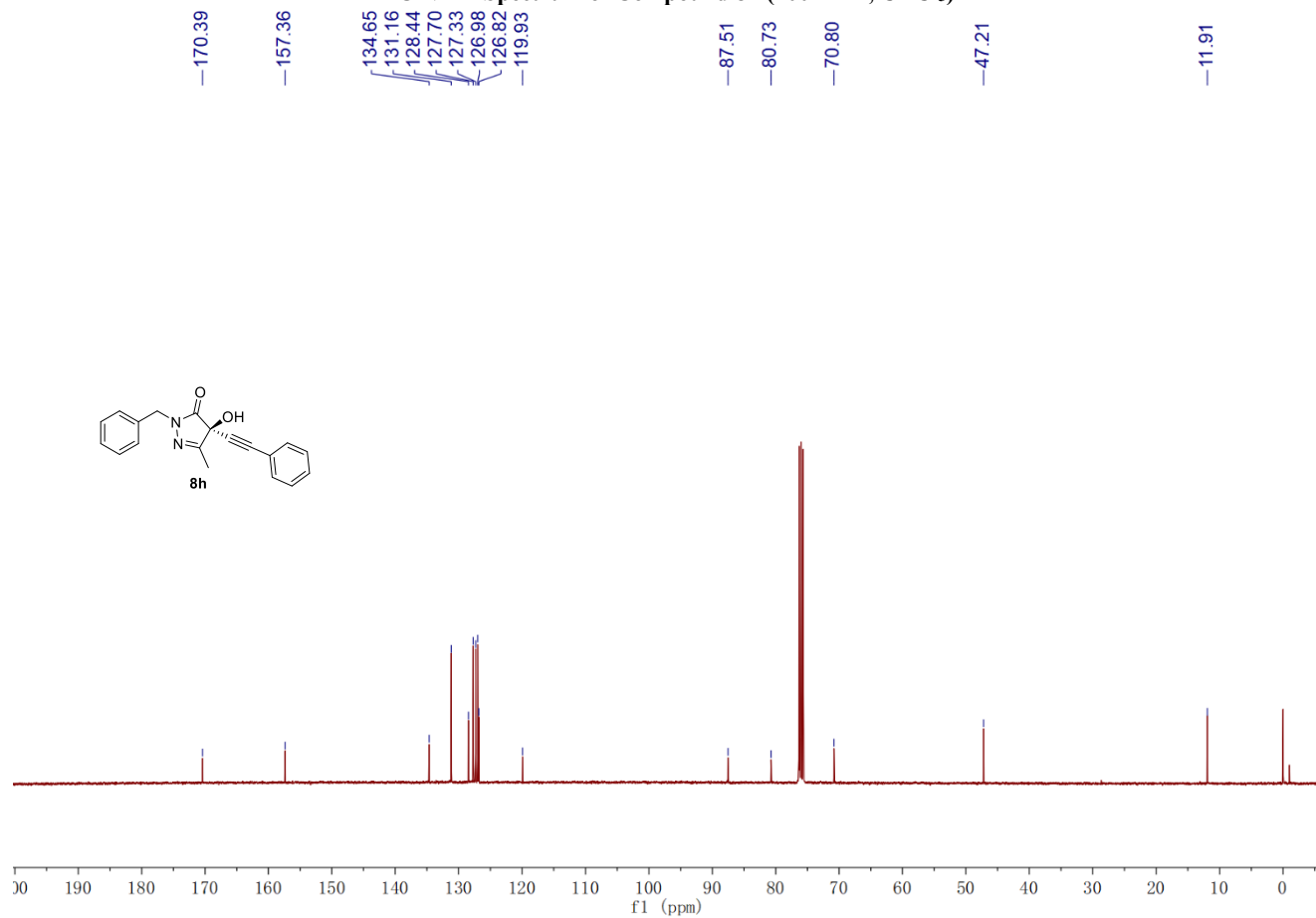


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8h (400 MHz, CDCl₃)

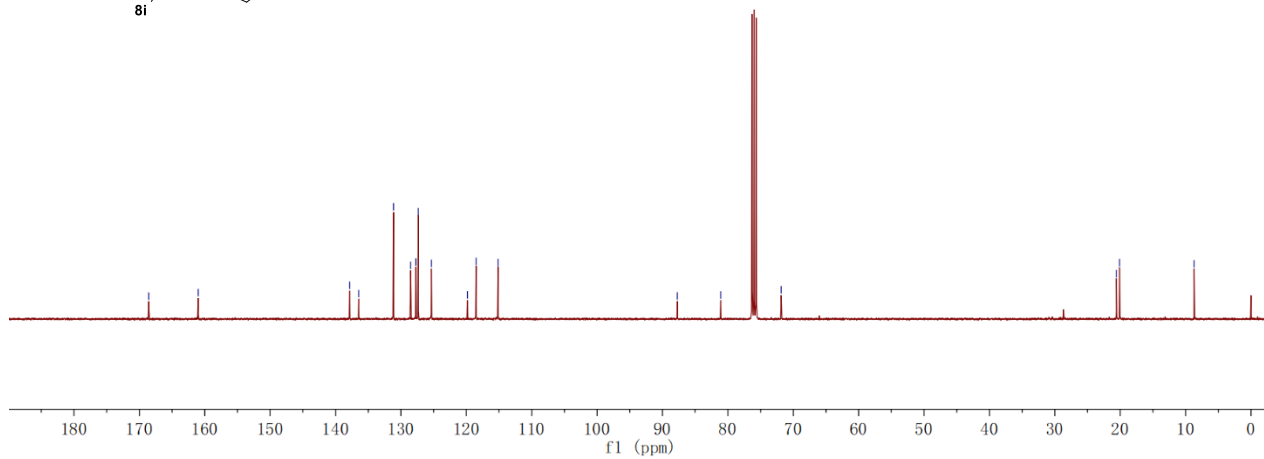
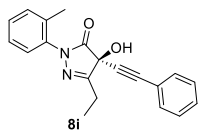
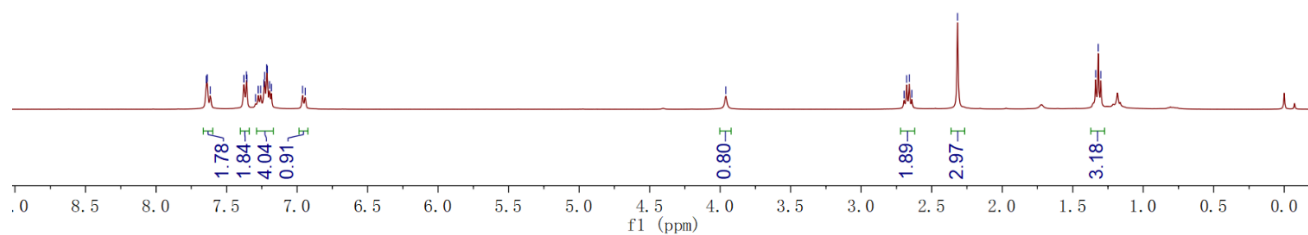
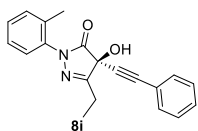
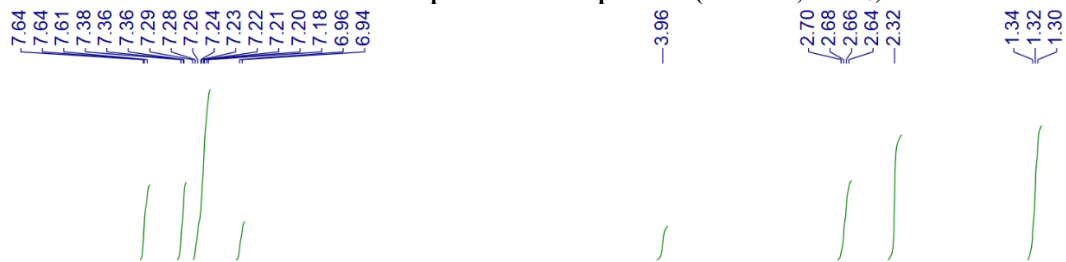


¹³C NMR Spectrum of Compound 8h (100 MHz, CDCl₃)



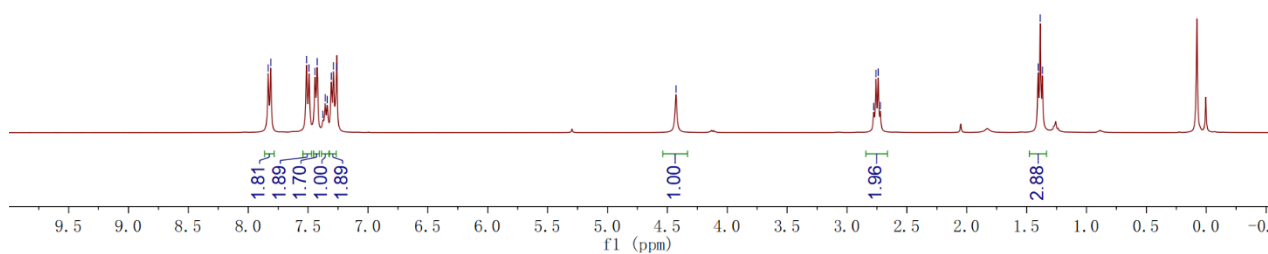
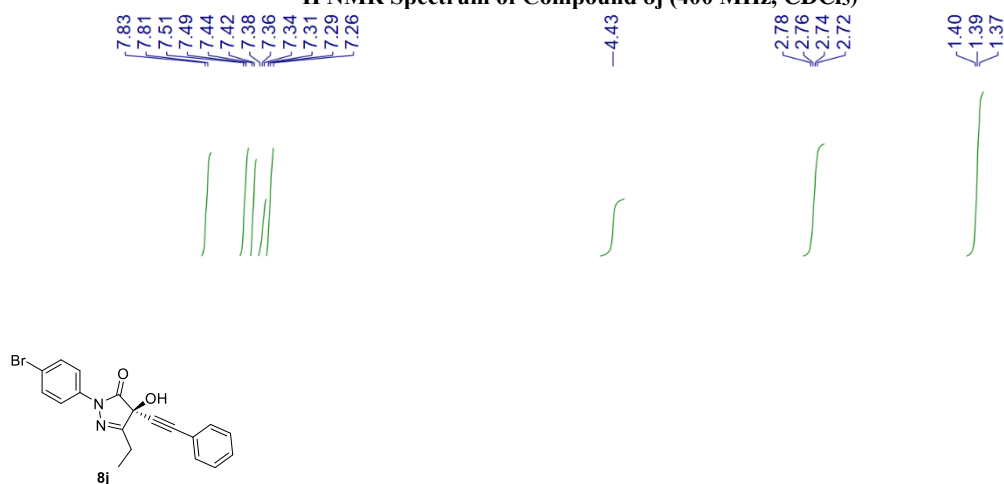
SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8i (400 MHz, CDCl₃)

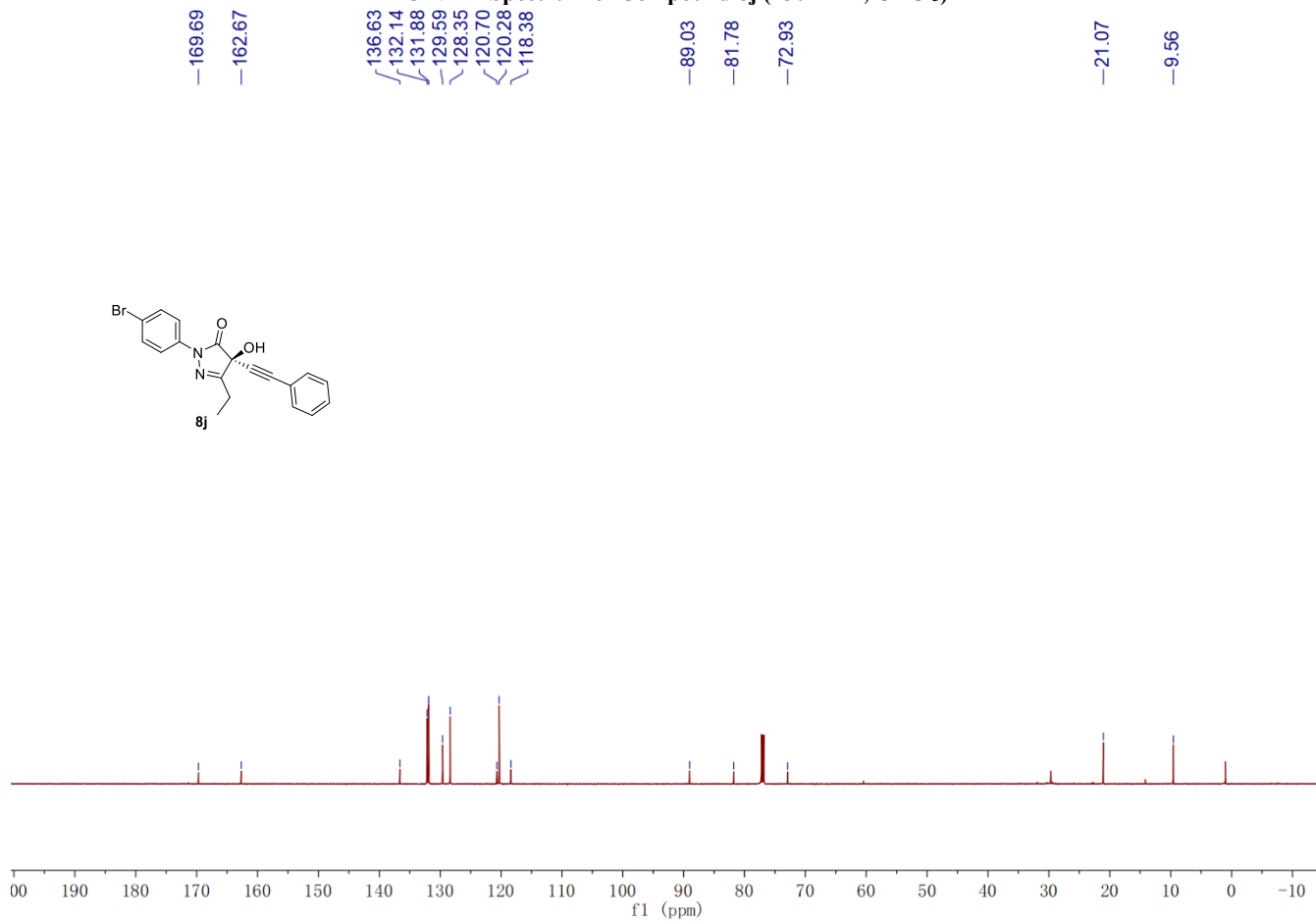


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8j (400 MHz, CDCl₃)

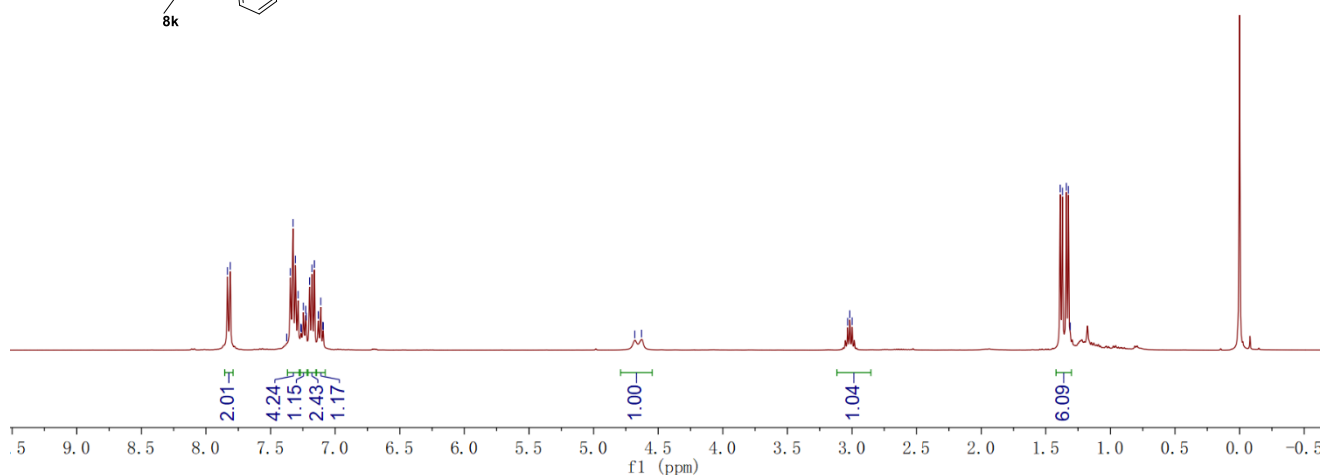
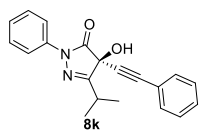
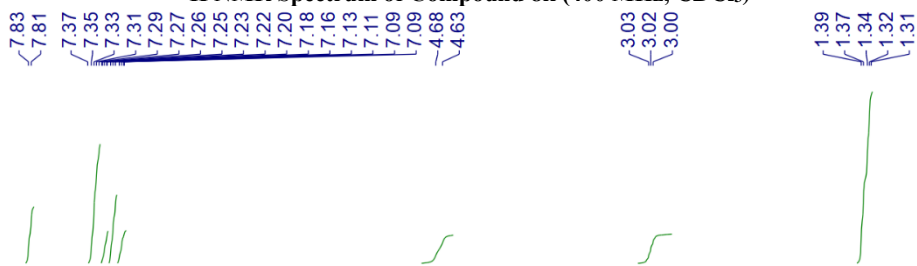


¹³C NMR Spectrum of Compound 8j (150 MHz, CDCl₃)

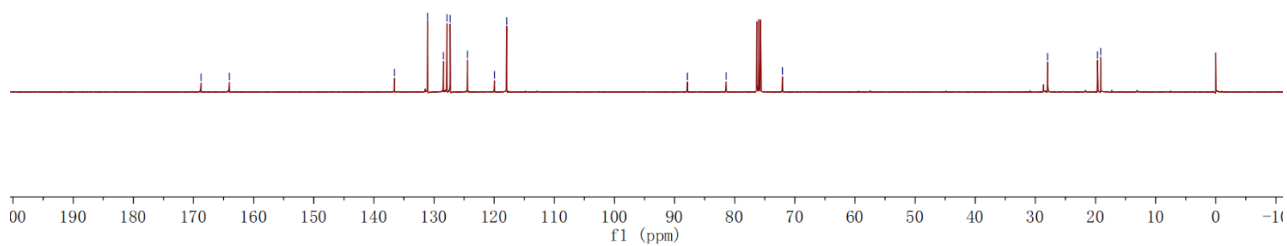
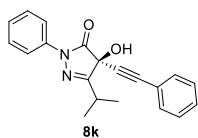
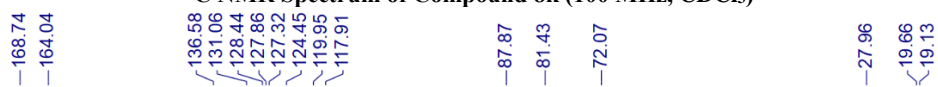


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8k (400 MHz, CDCl₃)

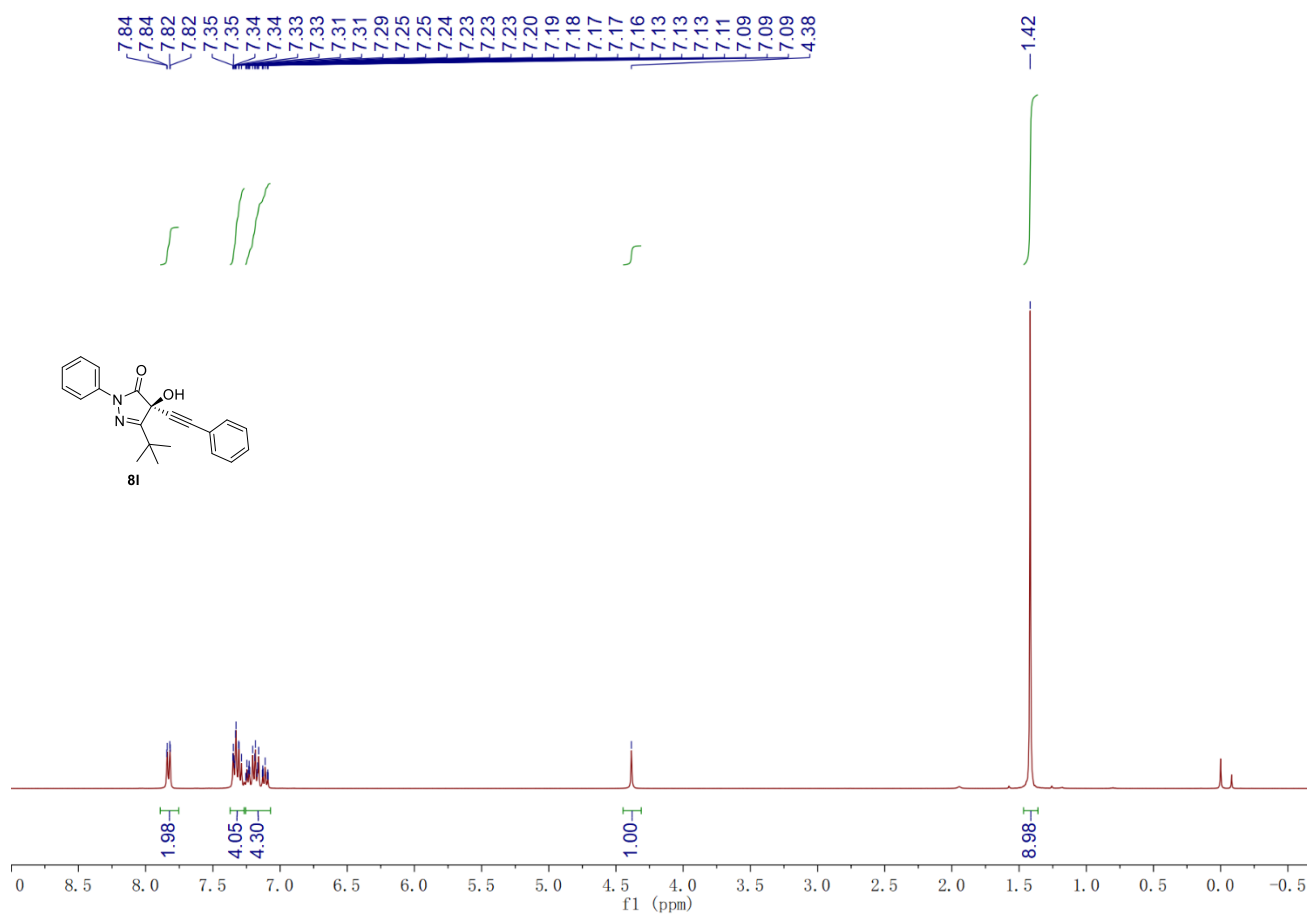


¹³C NMR Spectrum of Compound 8k (100 MHz, CDCl₃)

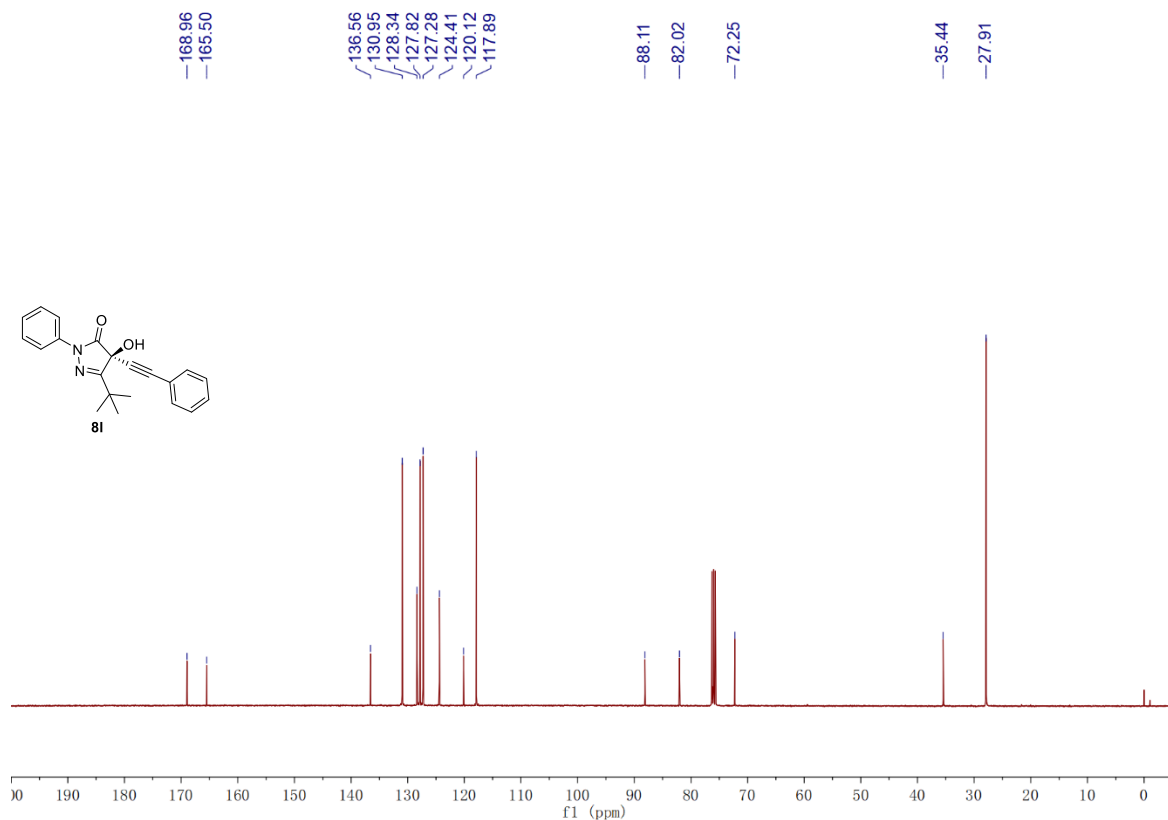


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8I (400 MHz, CDCl₃)

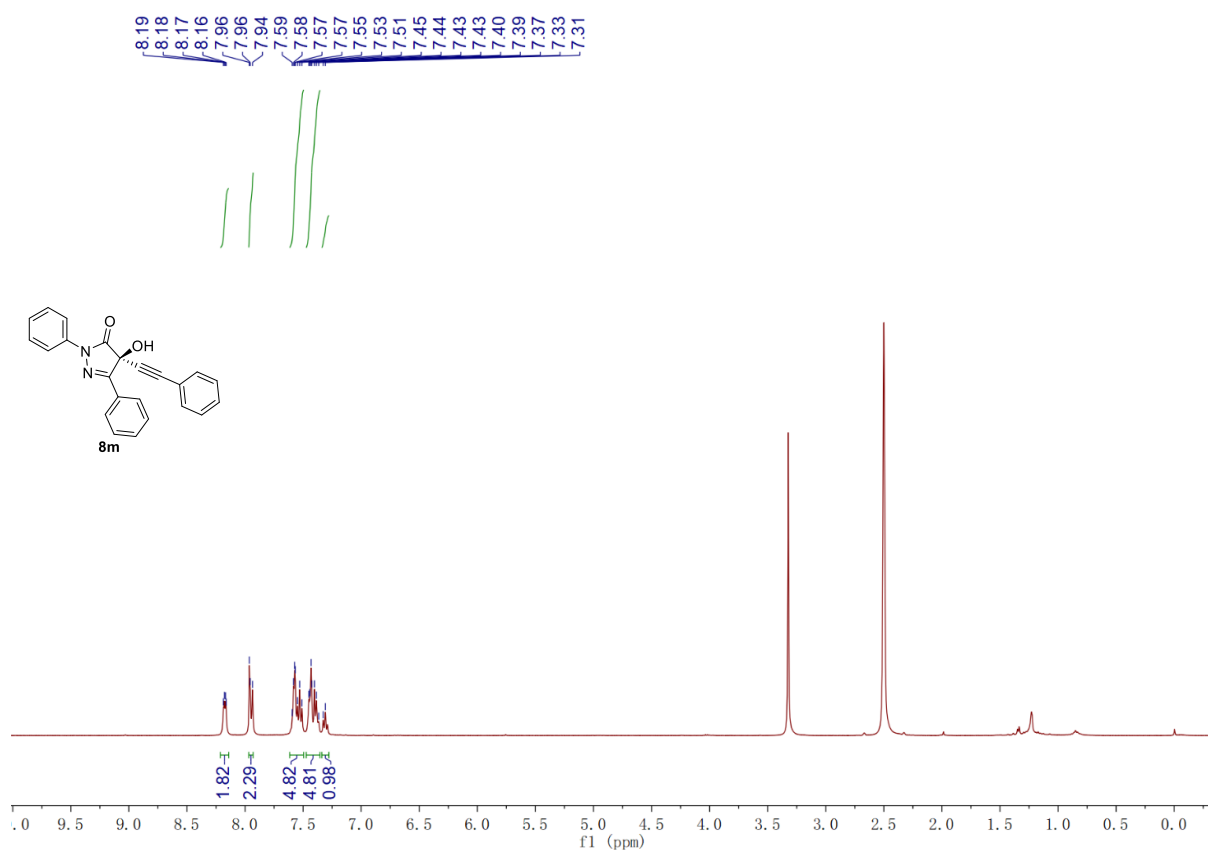


¹³C NMR Spectrum of Compound 8I (100 MHz, CDCl₃)

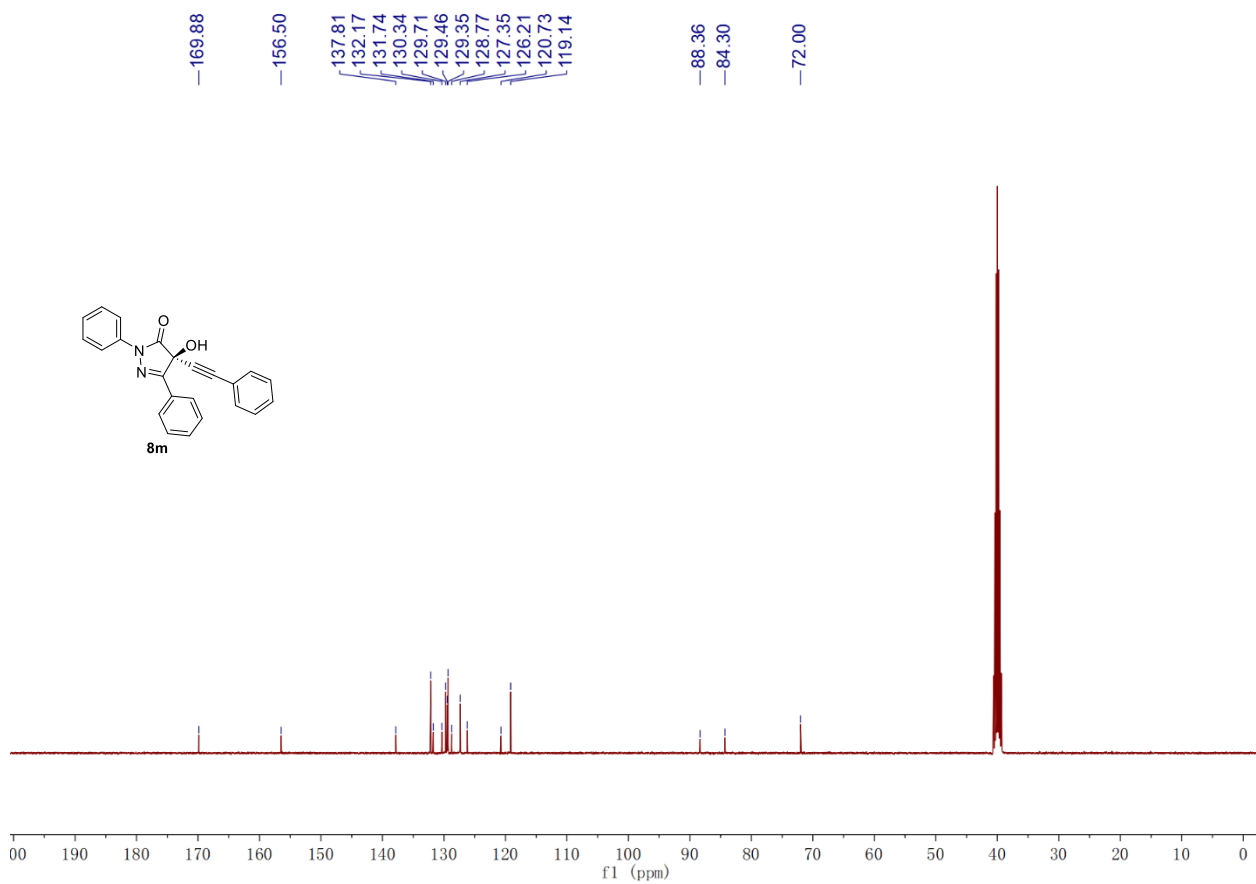


SUPPORTING INFORMATION

¹H NMR Spectrum of Compound 8m (400 MHz, DMSO-*d*₆)

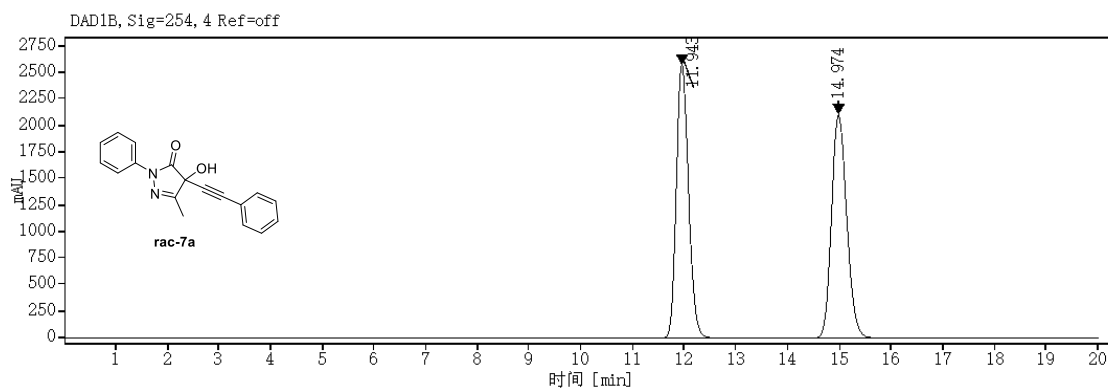


¹³C NMR Spectrum of Compound 8m (100 MHz, DMSO-*d*₆)

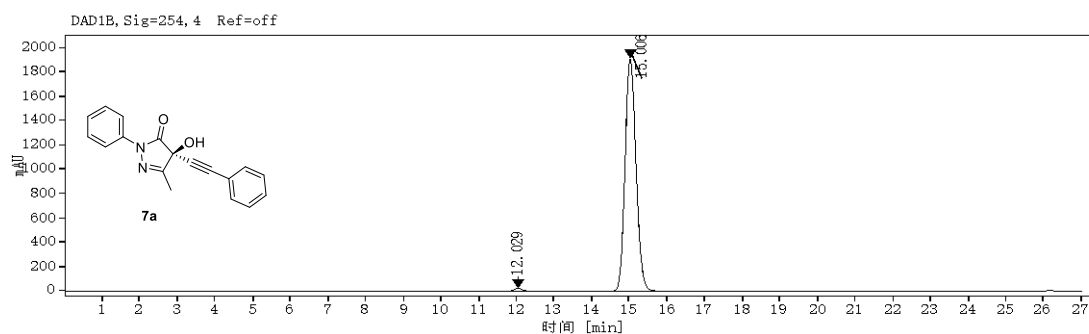


SUPPORTING INFORMATION

5.HPLC Spectra

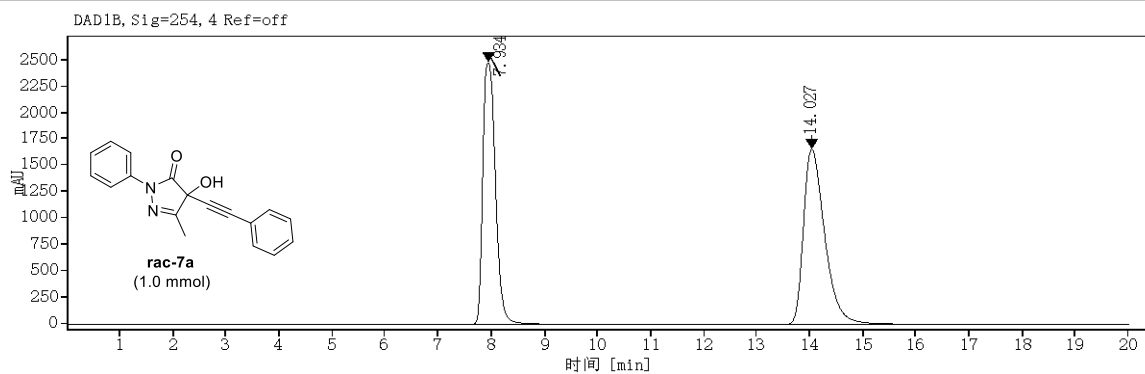


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14.974	BB	1.74	43016.37	2101.85	50.36

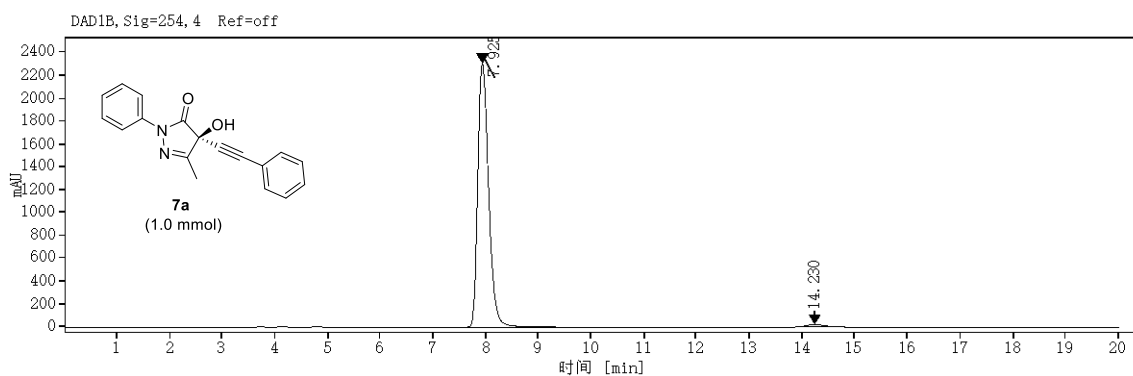


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15.006	MM m	0.31	38531.72	1913.11	99.13

SUPPORTING INFORMATION

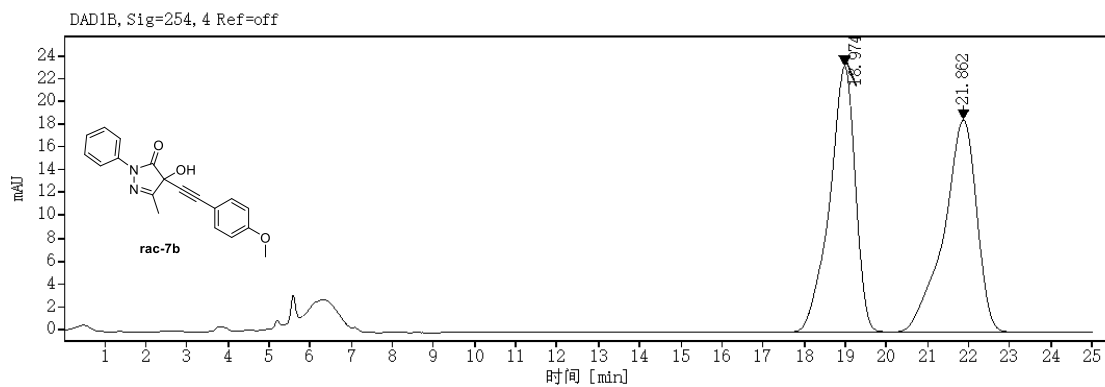


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
7.934	VV	1.88	41002.92	2477.82	47.07
14.027	VM m	0.43	46111.21	1656.34	52.93

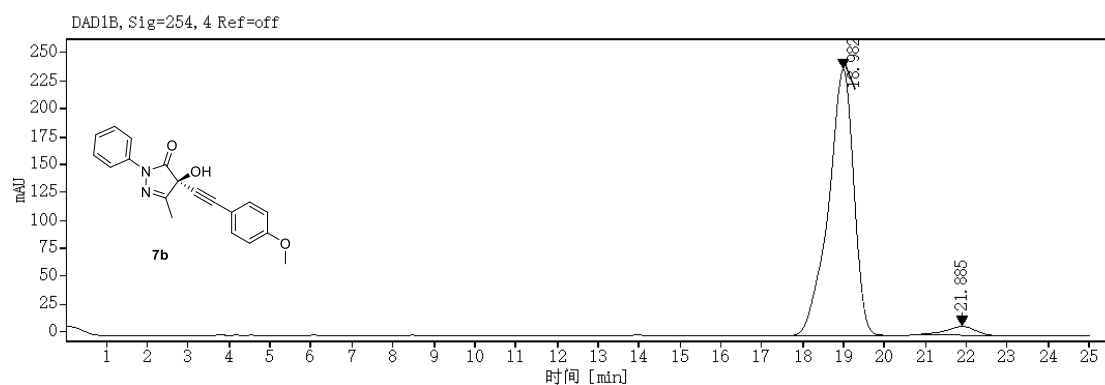


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
7.925	BB	2.22	32991.02	2306.71	98.45
14.230	MM m	0.39	518.14	20.92	1.55

SUPPORTING INFORMATION

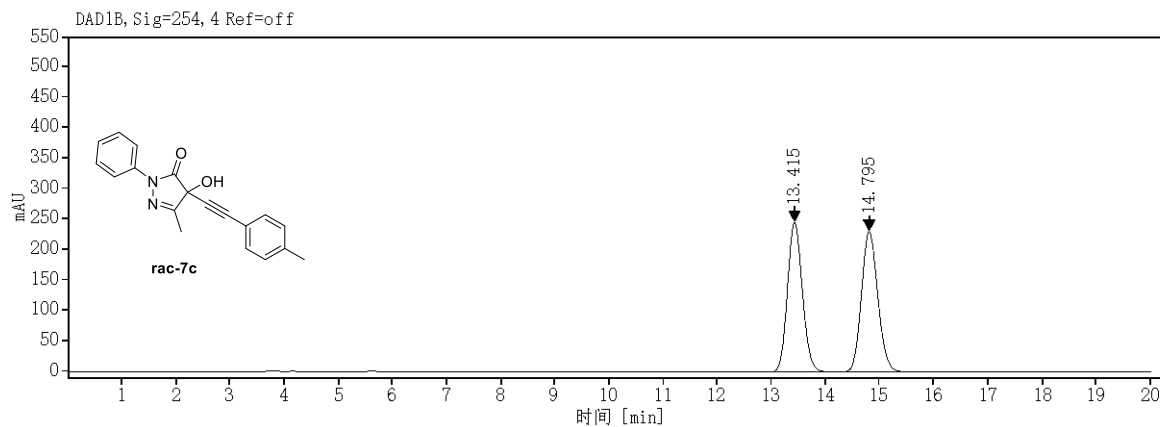


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
18.974	BB	2.44	1008.88	23.21	49.45
21.862	BB	3.06	1031.14	18.55	50.55

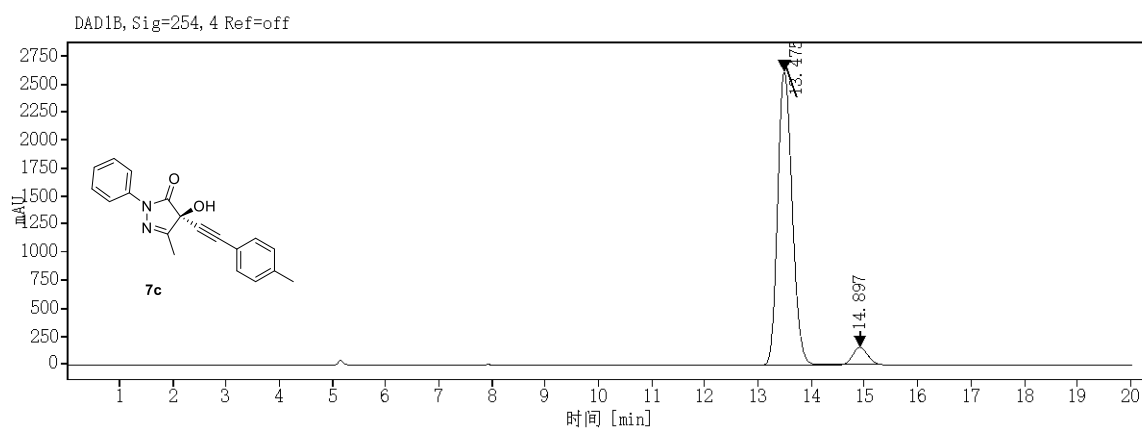


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
18.982	MM m	0.64	10232.81	238.00	96.36
21.885	MB m	0.74	386.09	7.64	3.64

SUPPORTING INFORMATION

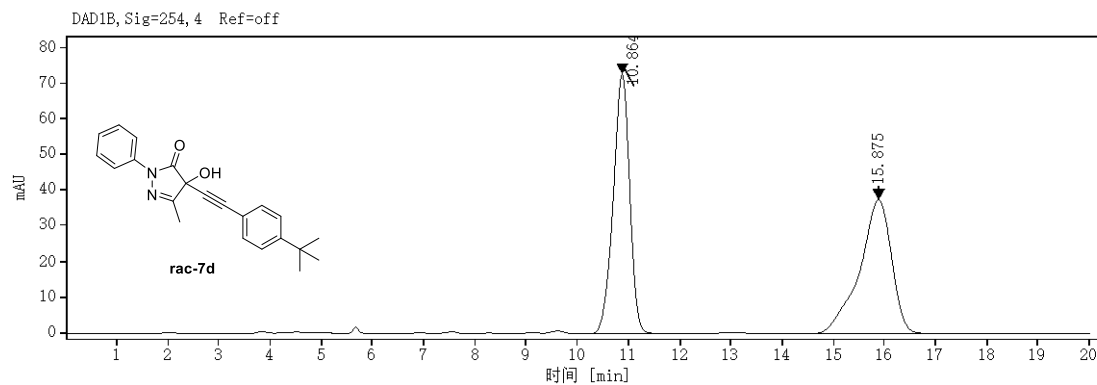


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.415	BB	1.38	4719.95	246.10	49.26
14.795	BB	1.98	4862.32	230.86	50.74

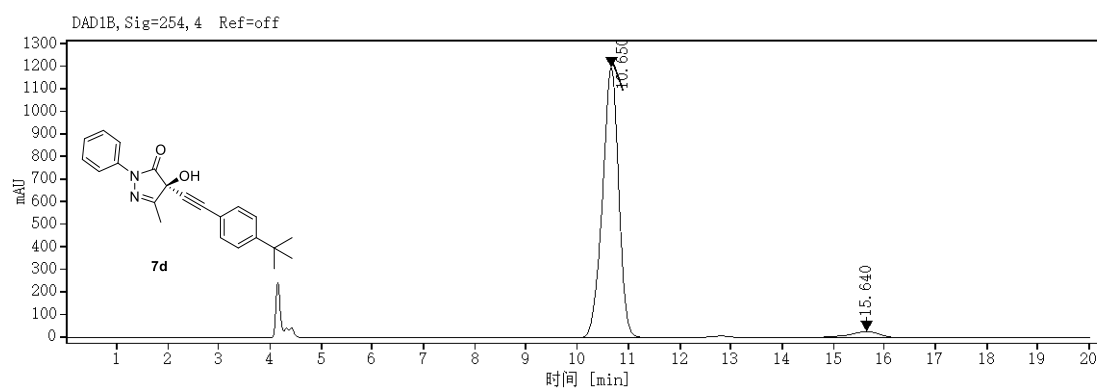


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.475	MM m	0.29	49310.90	2608.40	94.77
14.897	MM m	0.29	2720.80	150.86	5.23

SUPPORTING INFORMATION

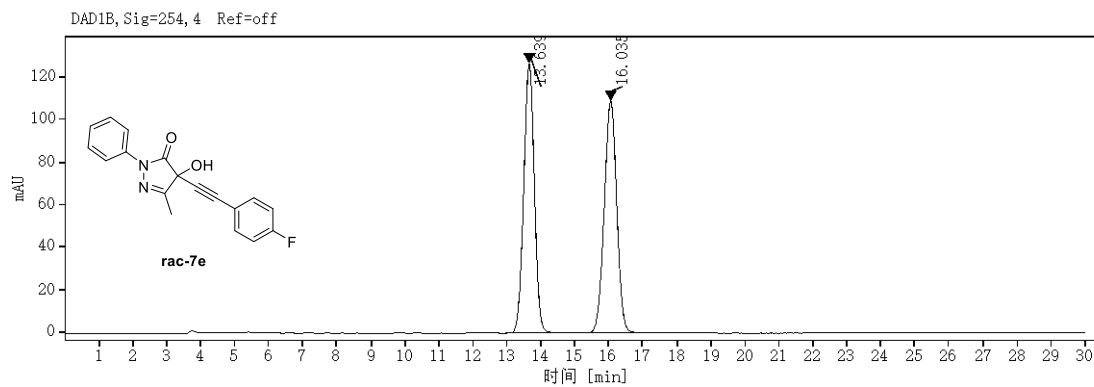


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.864	BB	1.89	1625.58	72.80	49.81
15.875	BB	3.21	1637.78	37.53	50.19

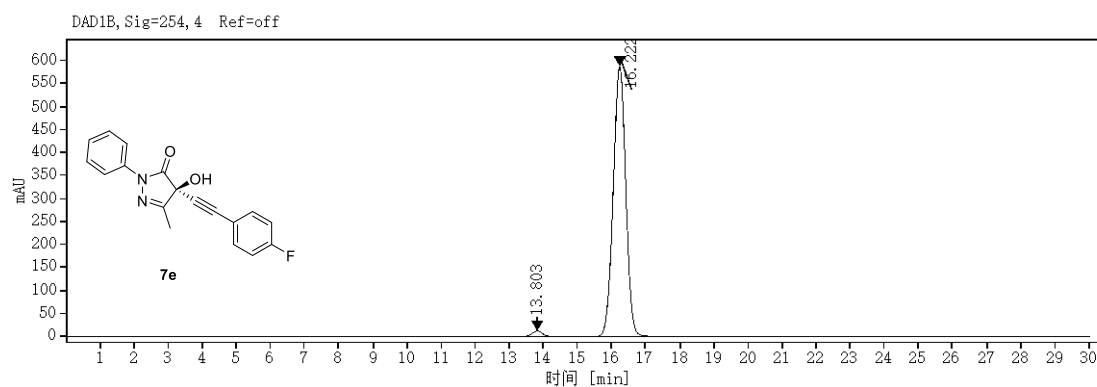


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.650	MM m	0.34	26479.81	1200.28	96.28
15.640	MM m	0.59	1022.27	26.13	3.72

SUPPORTING INFORMATION

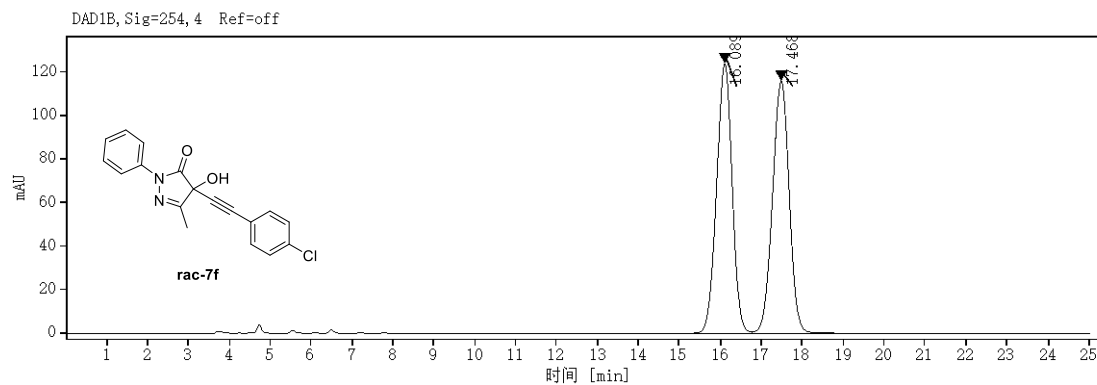


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.639	BB	2.22	2750.40	126.57	49.65
16.035	BB	2.74	2789.26	108.97	50.35

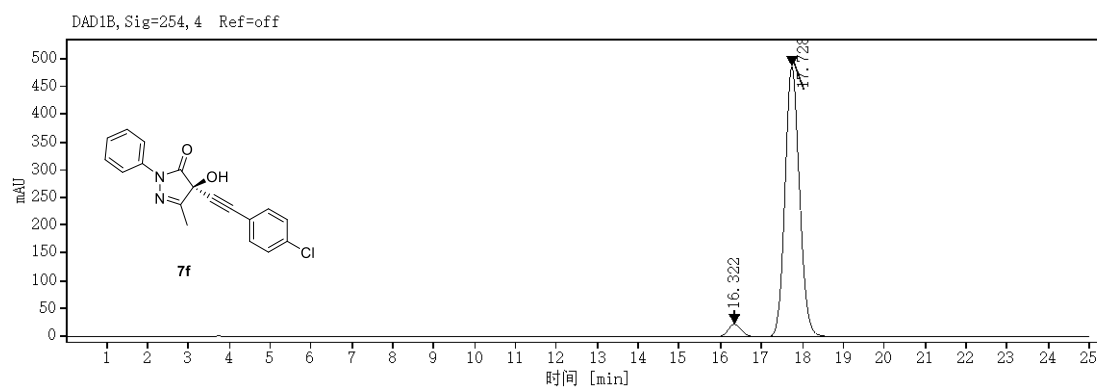


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.803	BB	1.32	267.65	12.26	1.75
16.222	BB	3.28	15032.14	588.26	98.25

SUPPORTING INFORMATION

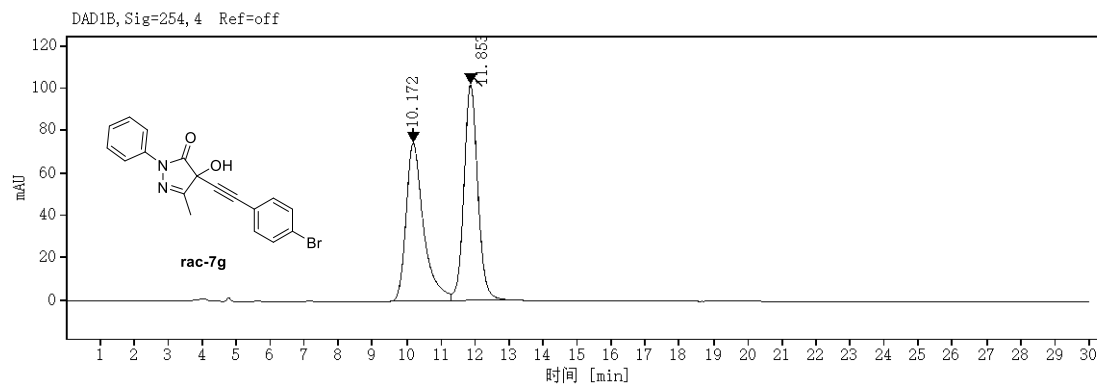


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.089	BV	1.66	3286.72	124.33	50.00
17.468	VB	2.21	3286.59	116.22	50.00

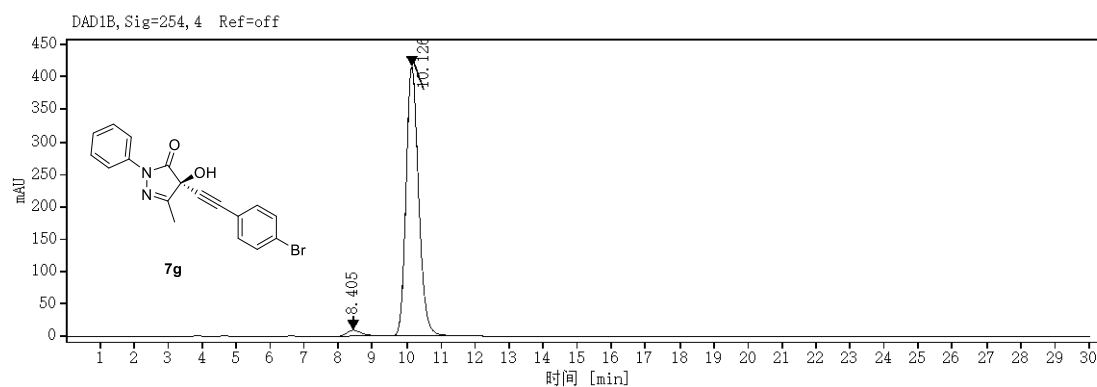


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.322	MM m	0.34	495.45	22.37	3.95
17.728	BB	2.14	12037.73	487.72	96.05

SUPPORTING INFORMATION

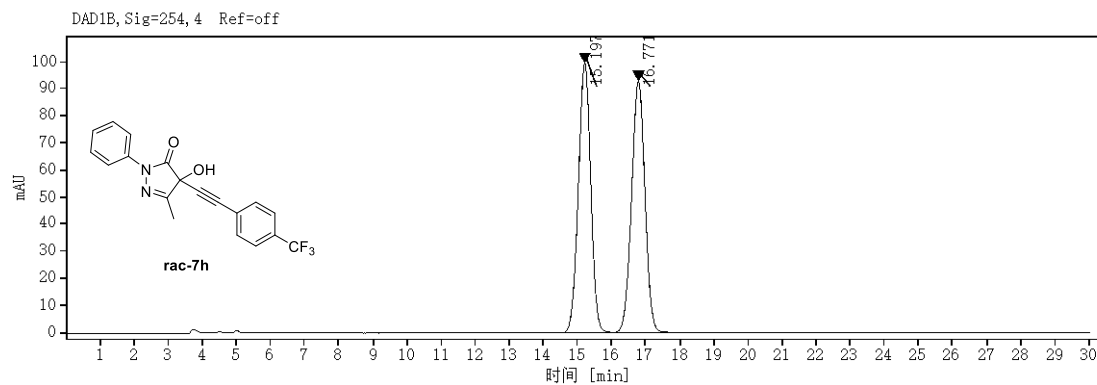


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.172	BM m	0.53	2658.71	74.70	48.13
11.853	MM m	0.43	2865.06	101.96	51.87

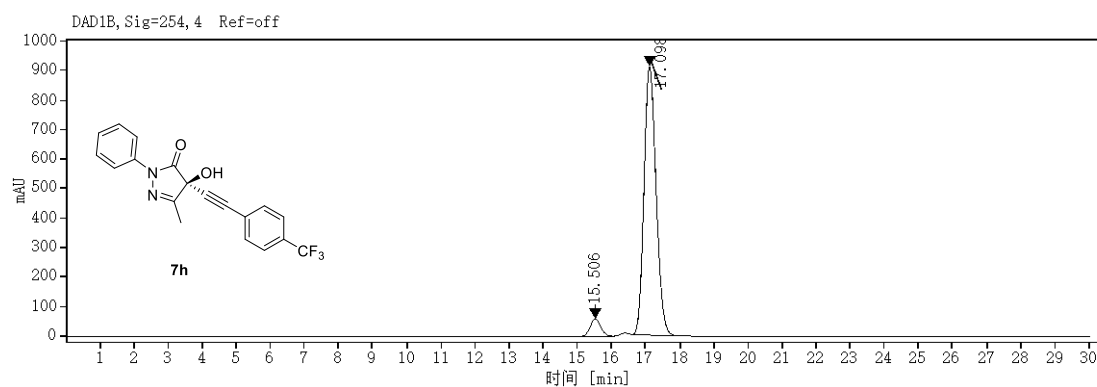


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.405	BM m	0.43	255.10	8.92	2.34
10.126	BB	1.88	10656.74	417.17	97.66

SUPPORTING INFORMATION

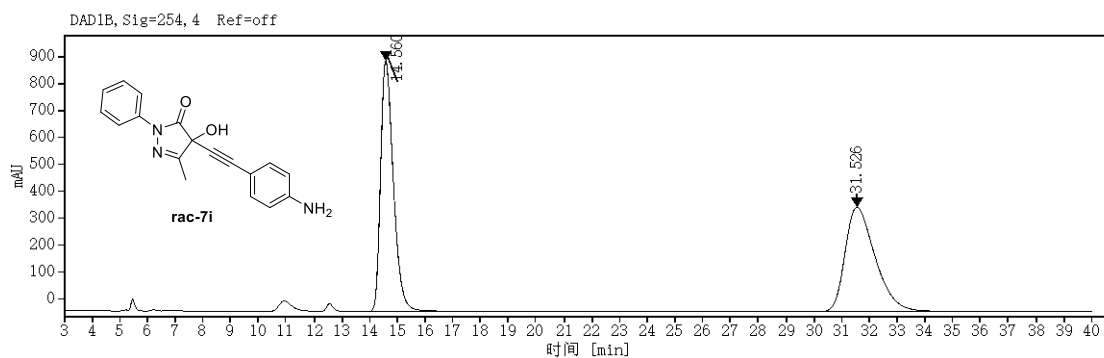


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.197	BB	1.62	2511.24	99.31	49.84
16.771	BB	2.36	2527.34	92.60	50.16

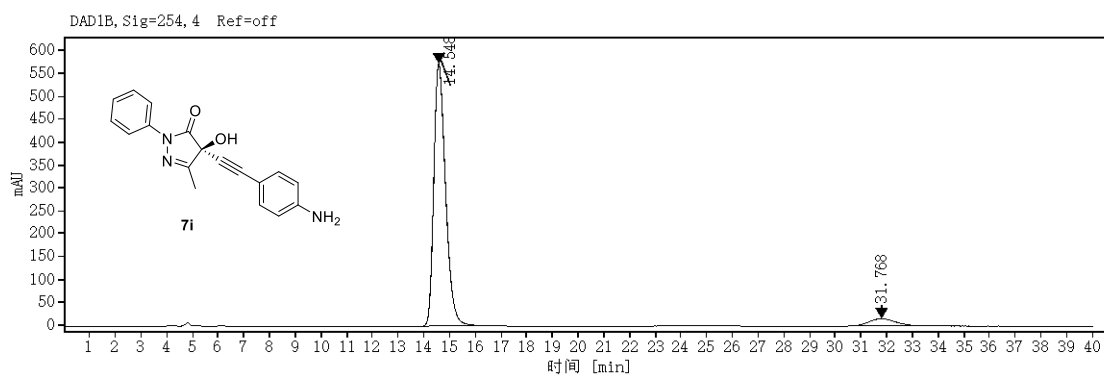


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.506	MM m	0.33	1249.64	58.44	5.30
17.098	MM m	0.38	22328.24	911.21	94.70

SUPPORTING INFORMATION

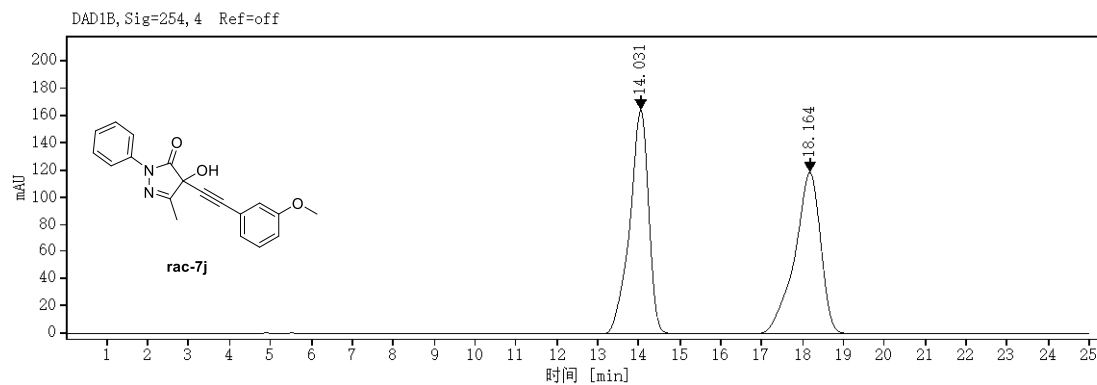


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.560	BM m	0.49	29735.62	933.51	50.46
31.526	BB	4.67	29193.64	388.35	49.54

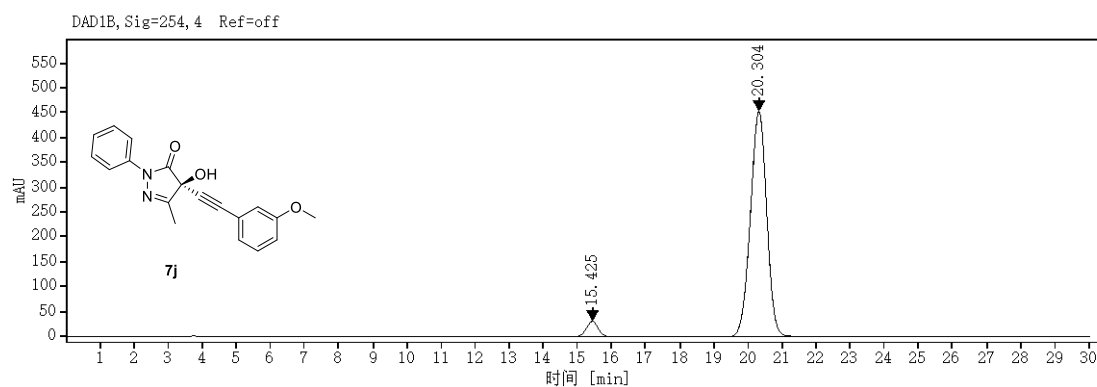


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.548	BM m	0.49	18086.15	571.83	94.23
31.768	MM m	0.85	1108.25	15.50	5.77

SUPPORTING INFORMATION

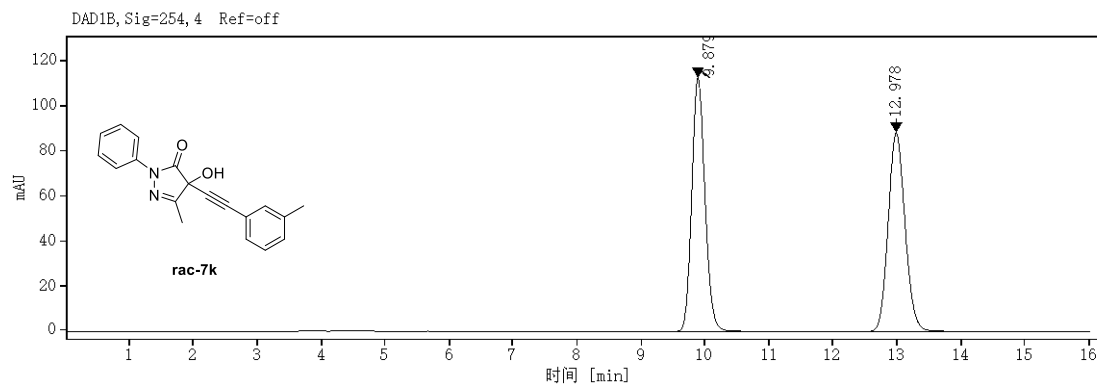


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
14.031	BM m	0.48	5251.31	164.30	50.13
18.164	BB	3.13	5223.68	118.57	49.87

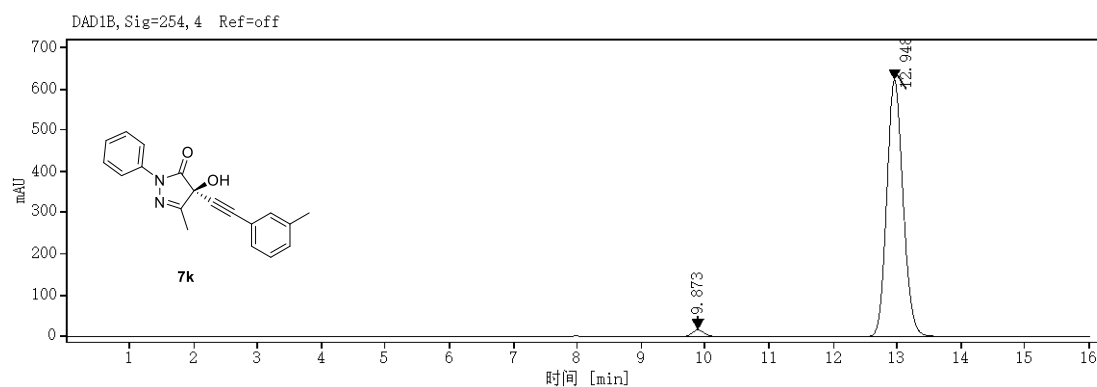


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.425	BM m	0.37	735.38	30.85	4.64
20.304	BB	3.94	15115.10	453.62	95.36

SUPPORTING INFORMATION

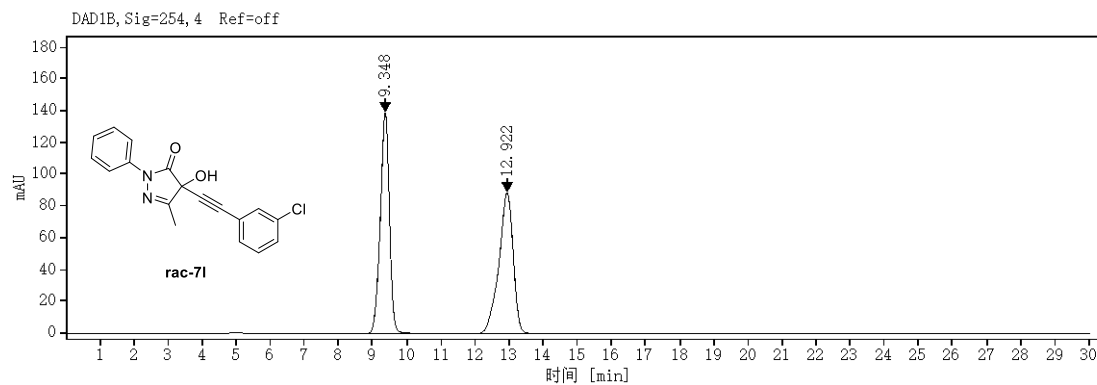


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.879	BB	1.61	1614.95	112.65	49.96
12.978	BB	1.53	1617.45	88.29	50.04

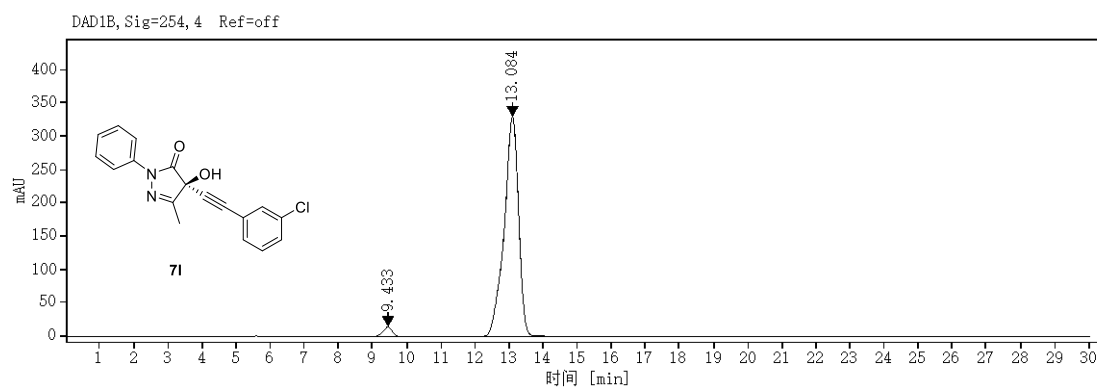


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.873	MM m	0.20	207.87	16.00	1.84
12.948	BM m	0.28	11067.05	623.36	98.16

SUPPORTING INFORMATION

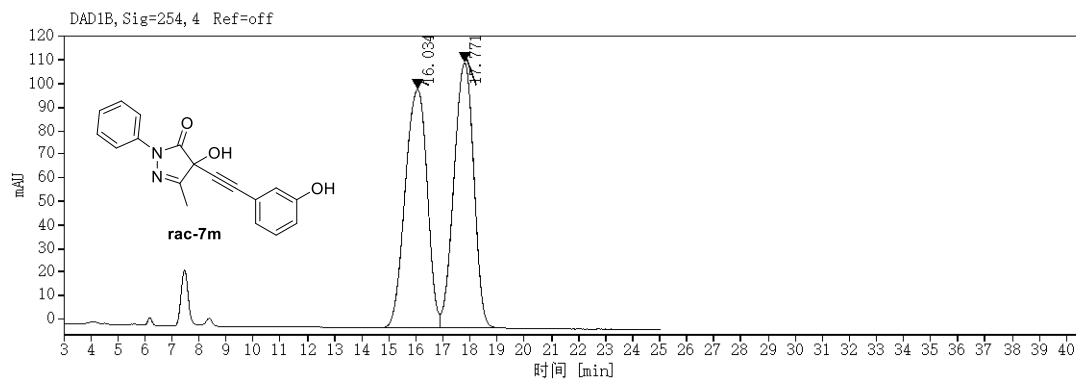


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.348	BB	1.96	2595.42	139.32	50.10
12.922	BB	2.06	2584.91	88.77	49.90

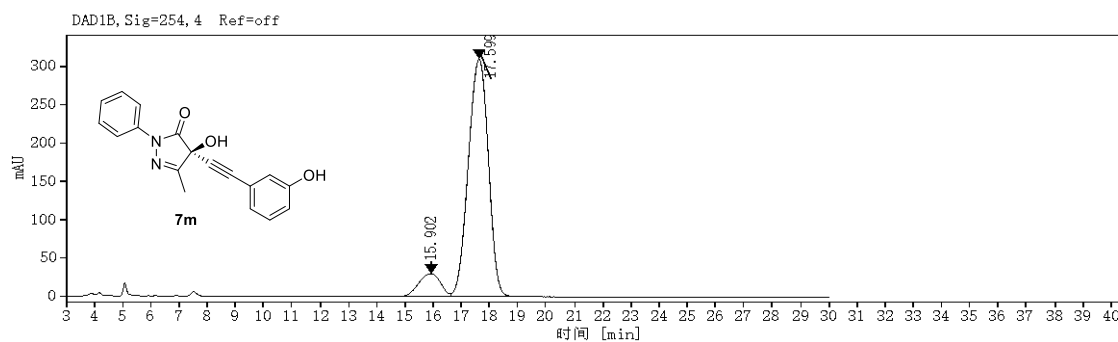


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.433	MM m	0.27	257.60	14.36	2.59
13.084	BB	2.81	9688.96	329.48	97.41

SUPPORTING INFORMATION

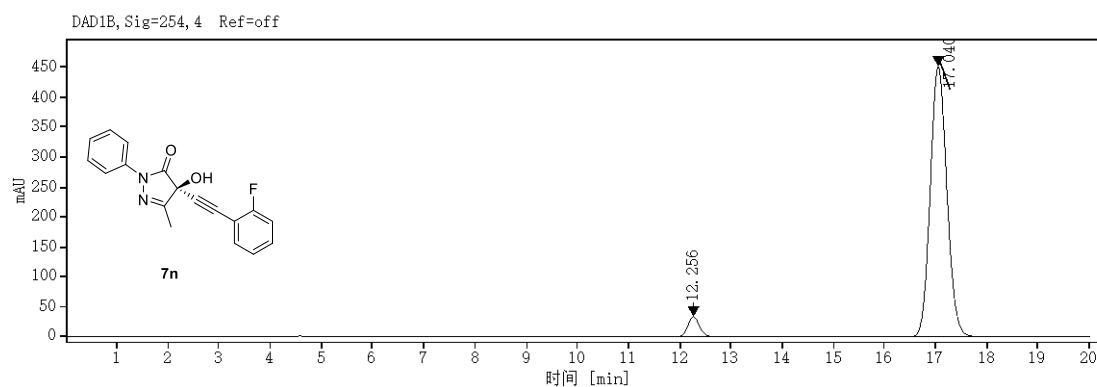
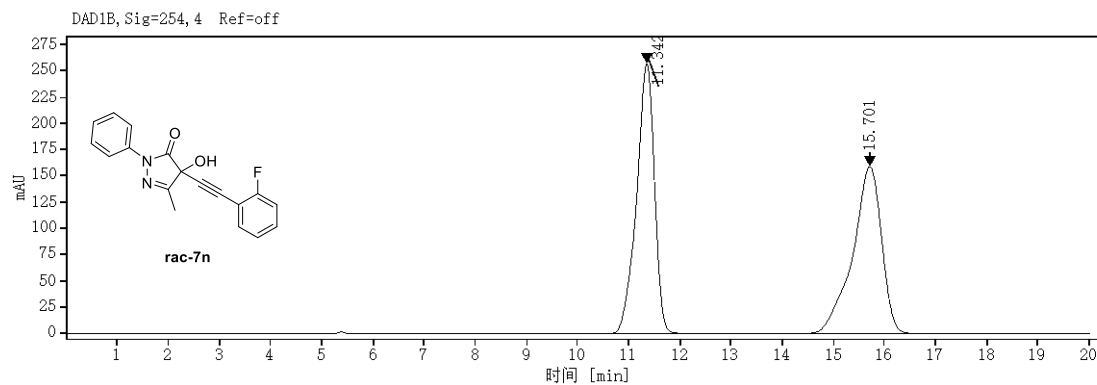


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.034	BV	2.13	5722.08	101.32	49.91
17.771	VV	2.07	5743.11	112.82	50.09

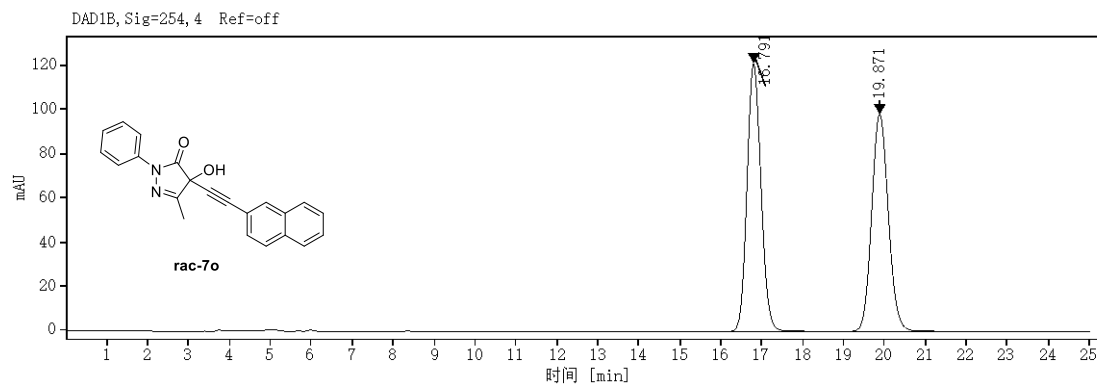


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
15.902	BV	1.84	1609.79	29.65	9.48
17.599	VV	2.64	15371.07	311.72	90.52

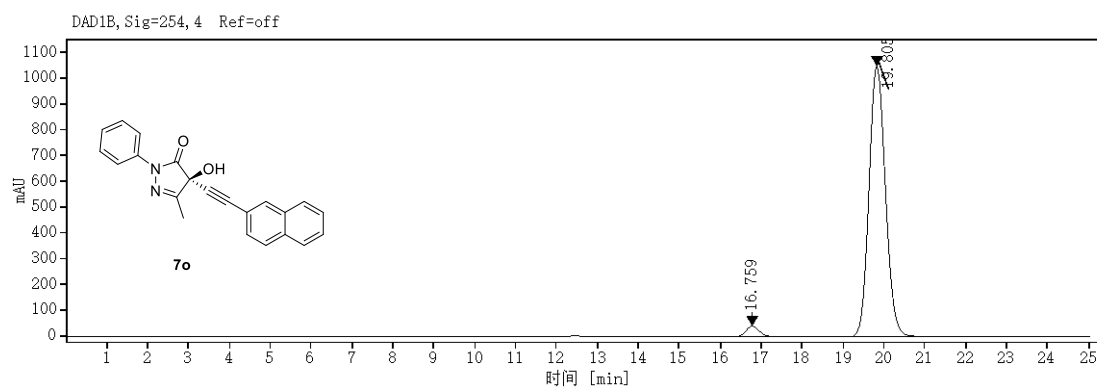
SUPPORTING INFORMATION



SUPPORTING INFORMATION

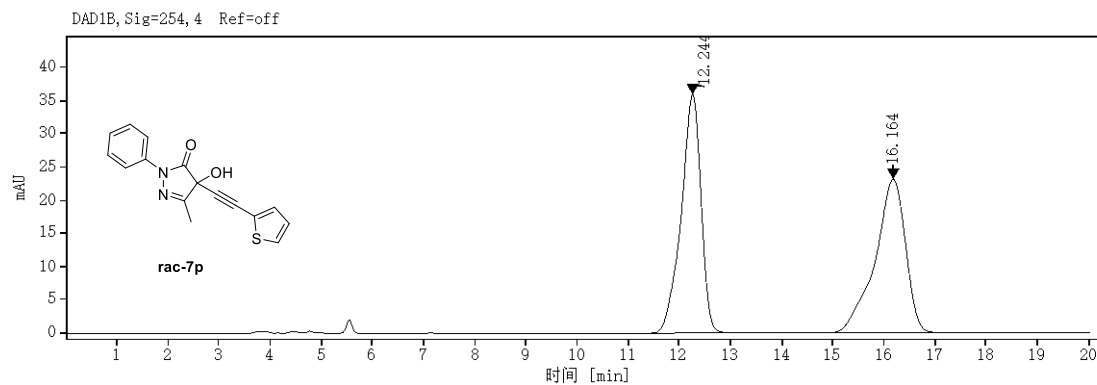


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.791	BB	2.19	2871.91	121.39	50.89
19.871	BB	2.45	2771.54	98.18	49.11

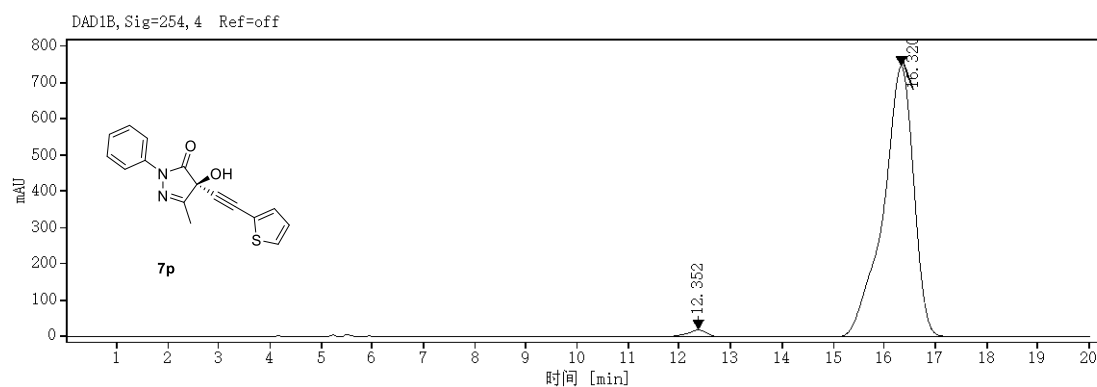


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.759	MM m	0.35	881.98	39.74	2.95
19.805	BM m	0.43	29036.63	1044.82	97.05

SUPPORTING INFORMATION

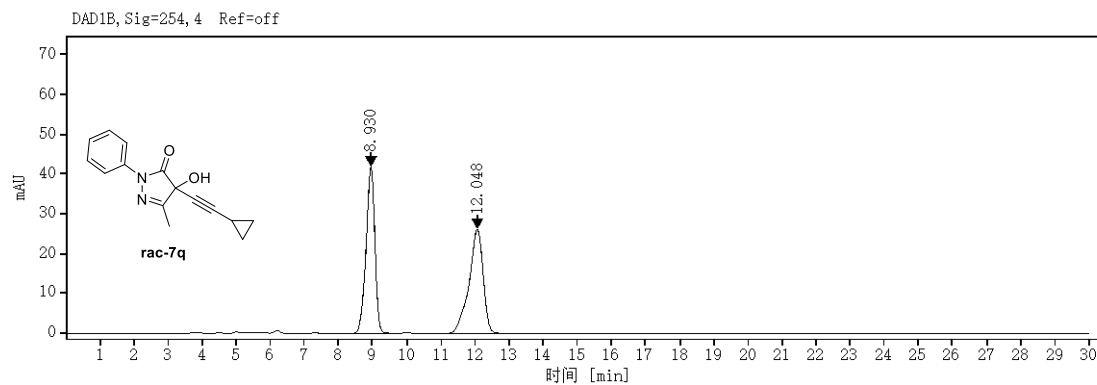


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.244	BB	1.90	966.31	35.87	50.14
16.164	BB	2.71	960.74	23.11	49.86

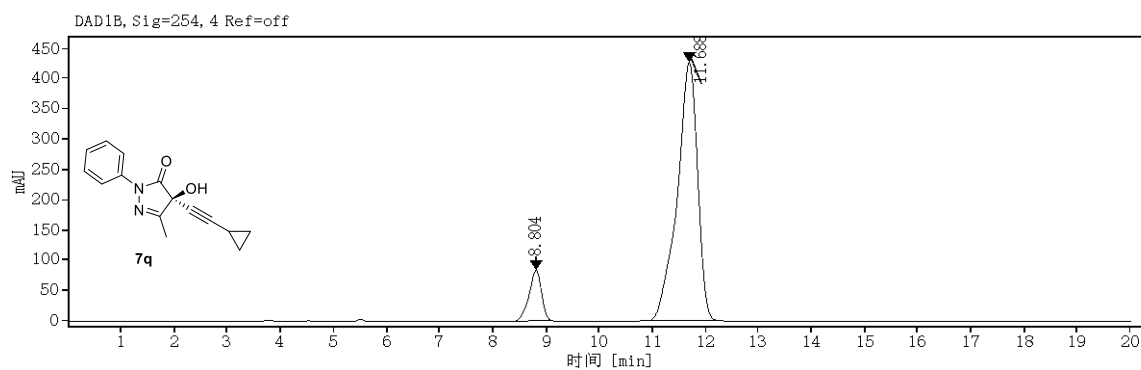


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.352	MM m	0.39	466.40	18.31	1.49
16.320	BM m	0.62	30882.92	745.98	98.51

SUPPORTING INFORMATION

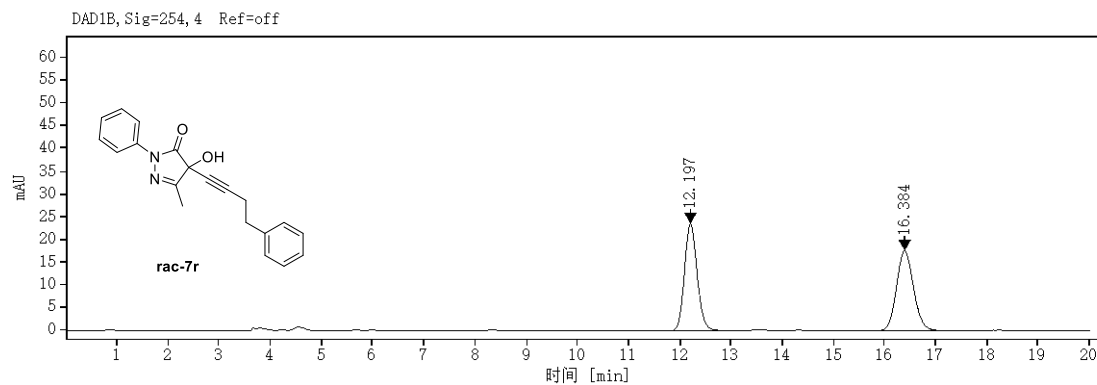


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.930	BB	1.33	753.06	41.89	50.00
12.048	BB	1.88	753.01	26.19	50.00

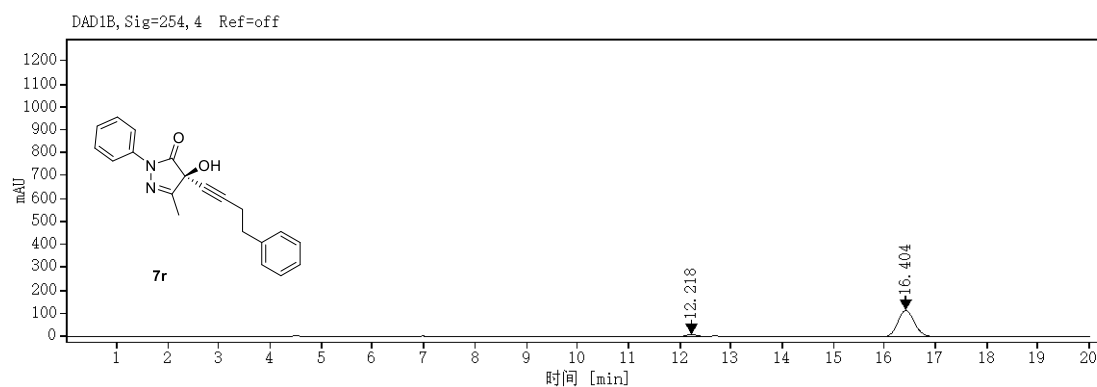


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.804	MM m	0.25	1348.96	83.14	10.57
11.688	MM m	0.40	11409.81	426.56	89.43

SUPPORTING INFORMATION

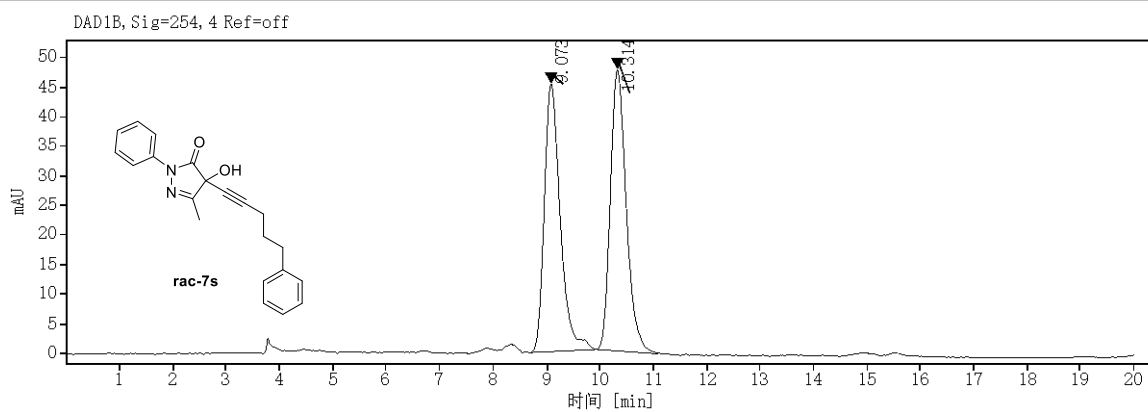


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.197	BB	1.24	405.10	23.59	49.94
16.384	BB	1.42	406.04	17.61	50.06

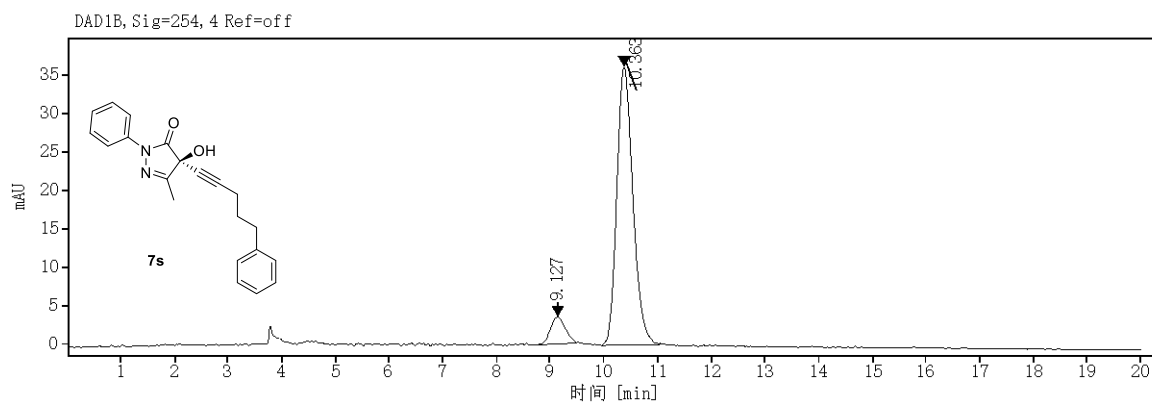


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.218	MM m	0.23	133.63	9.02	4.86
16.404	BB	1.98	2613.63	115.71	95.14

SUPPORTING INFORMATION

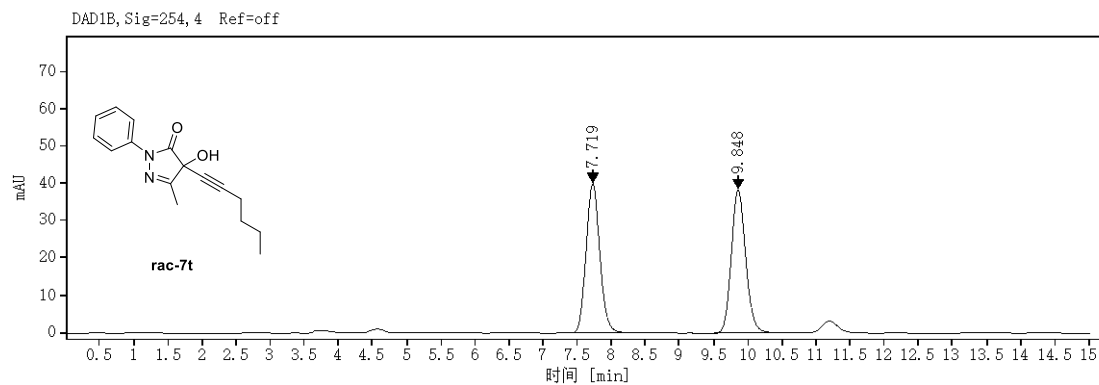


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.073	BM m	0.31	938.50	45.31	48.85
10.314	BV	1.14	982.63	47.64	51.15

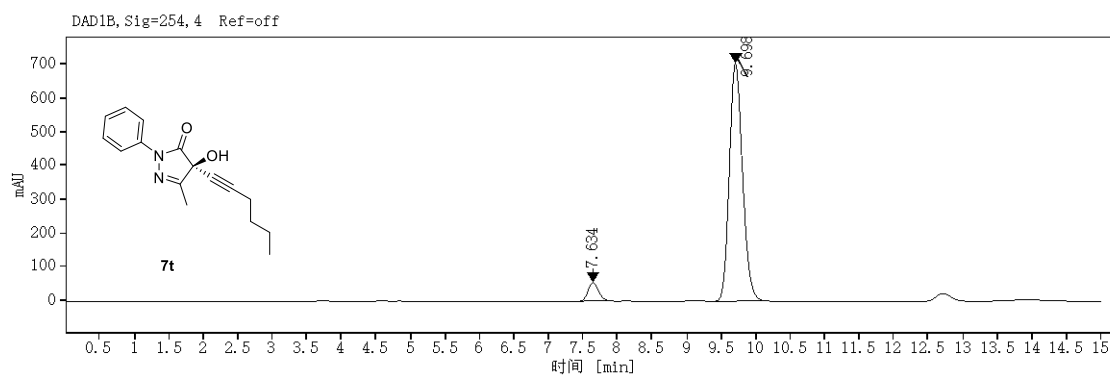


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.127	BM m	0.24	68.08	3.53	8.26
10.363	BM m	0.32	756.16	36.30	91.74

SUPPORTING INFORMATION

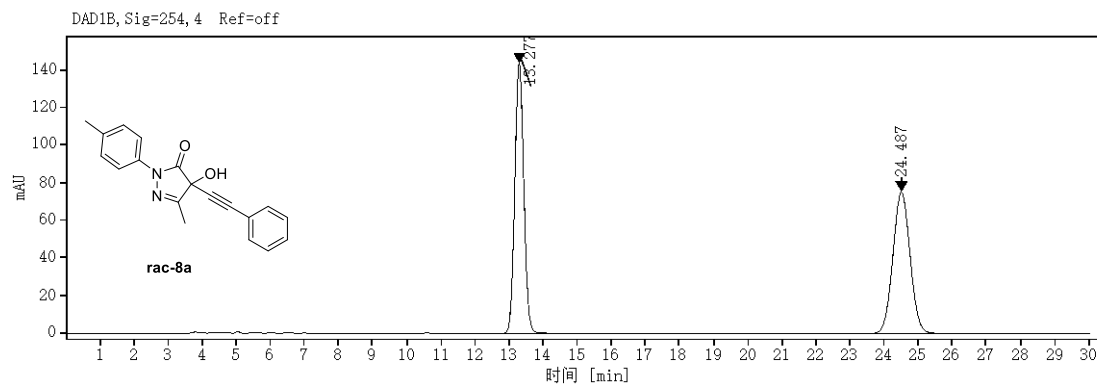


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
7.719	BB	1.39	564.50	40.13	50.12
9.848	BB	1.05	561.90	38.50	49.88

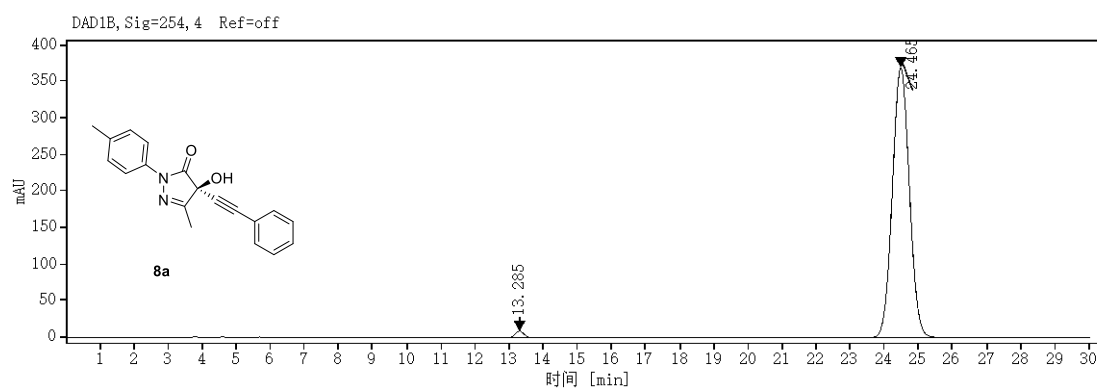


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
7.634	MM m	0.16	559.39	53.92	5.65
9.698	VM m	0.21	9342.64	702.50	94.35

SUPPORTING INFORMATION

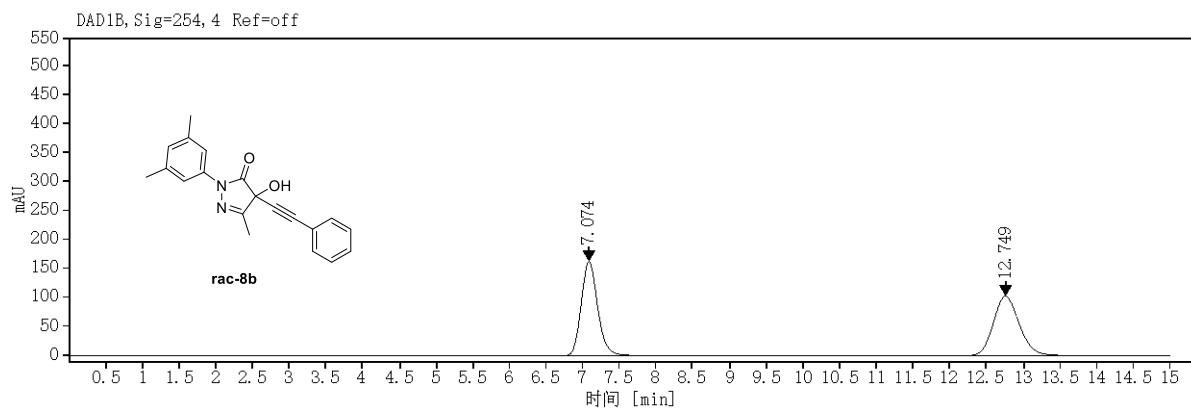


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.277	BB	1.76	2629.36	143.63	49.99
24.487	BB	2.39	2630.89	75.19	50.01

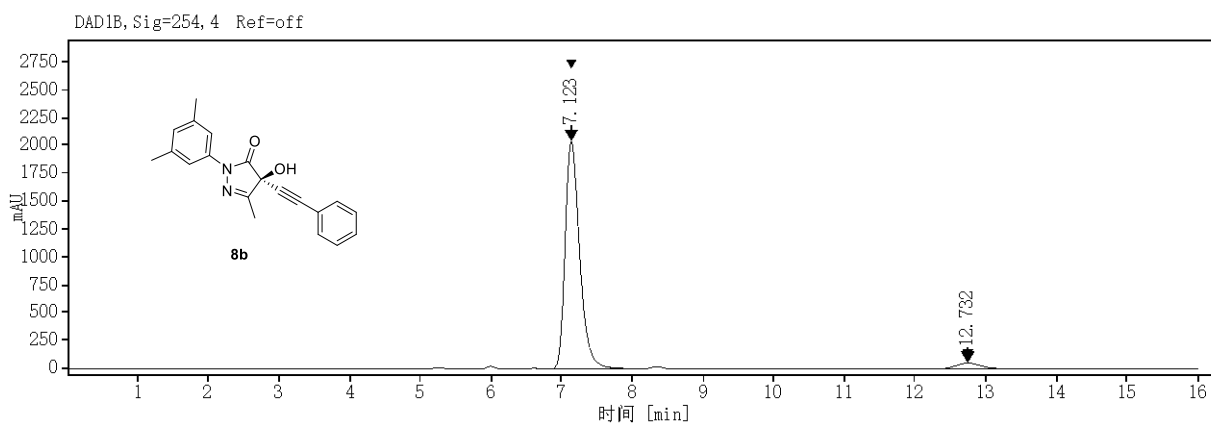


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
13.285	MM m	0.27	152.36	8.93	1.18
24.465	MM m	0.54	12795.48	369.72	98.82

SUPPORTING INFORMATION

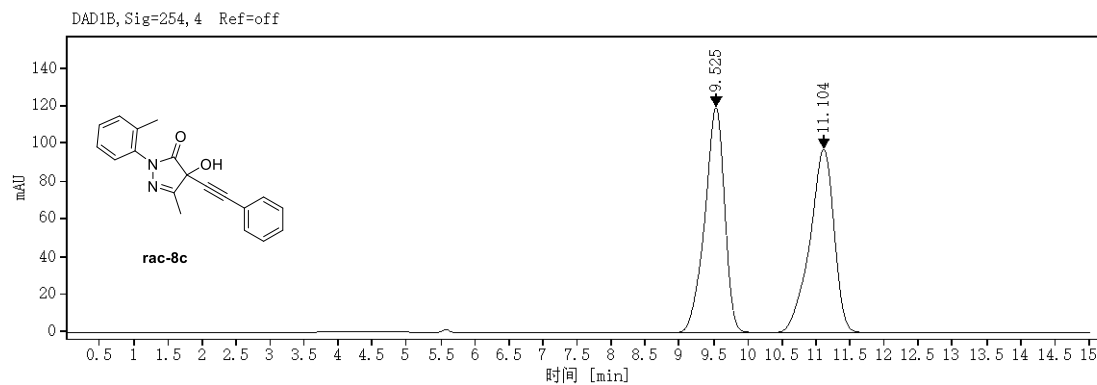


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
7.074	VV	1.42	2565.48	163.31	49.93
12.749	BBA	3.11	2572.27	103.36	50.07

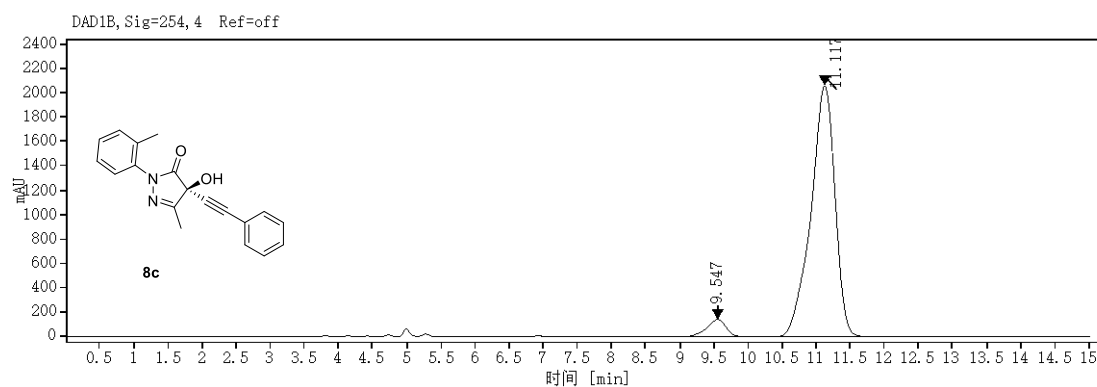


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
7.123	BM m	0.22	28979.82	2041.62	96.09
12.732	MM m	0.37	1180.02	50.66	3.91

SUPPORTING INFORMATION

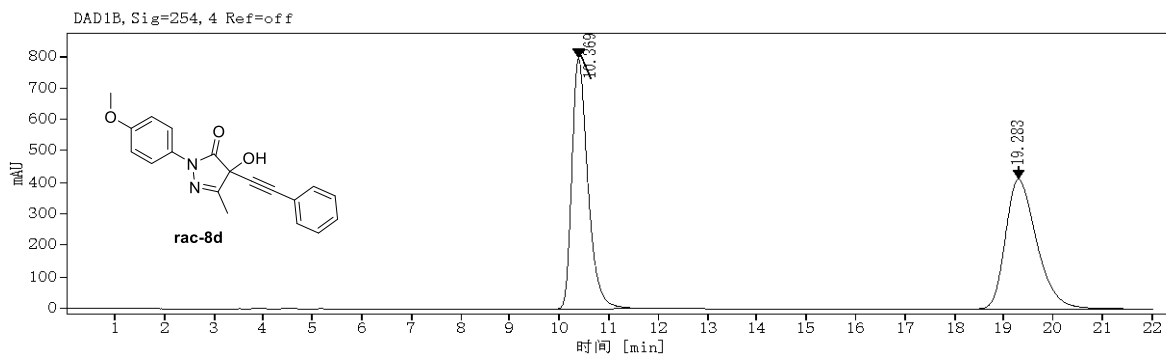


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.525	BM m	0.31	2407.91	119.37	50.07
11.104	BM m	0.37	2401.14	97.29	49.93

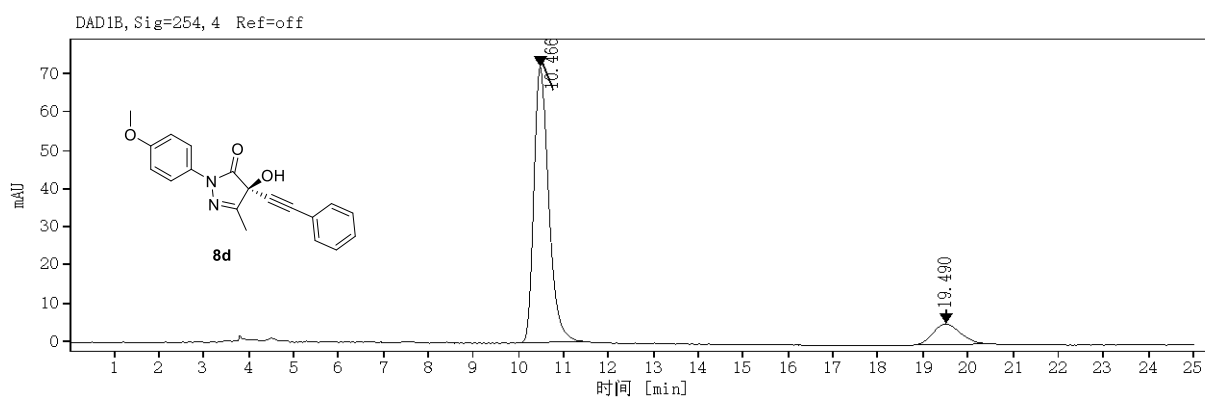


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.547	MM m	0.29	2712.02	140.51	5.10
11.117	MM m	0.37	50442.47	2063.28	94.90

SUPPORTING INFORMATION

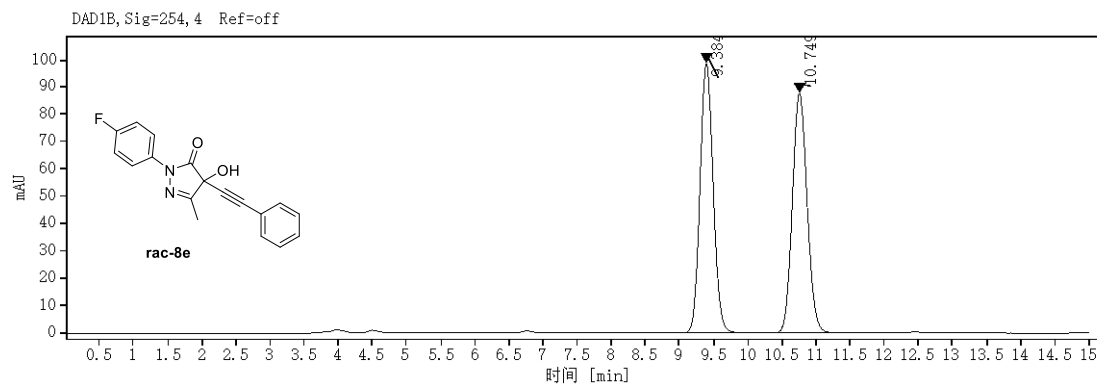


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.369	BV	1.95	18010.10	797.18	49.76
19.283	BBA	3.81	18183.29	412.83	50.24

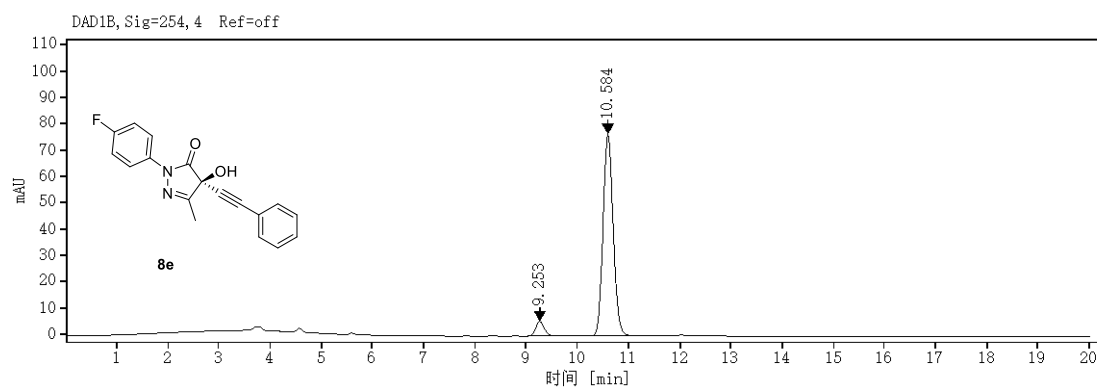


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.466	BM m	0.35	1646.60	72.06	87.85
19.490	MM m	0.52	227.67	5.34	12.15

SUPPORTING INFORMATION

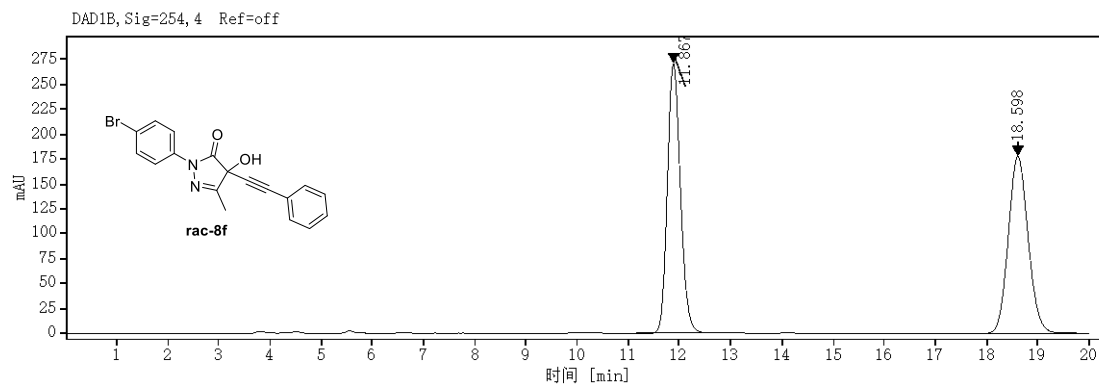


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.384	BB	1.36	1327.37	98.91	50.09
10.749	BB	1.33	1322.66	87.99	49.91

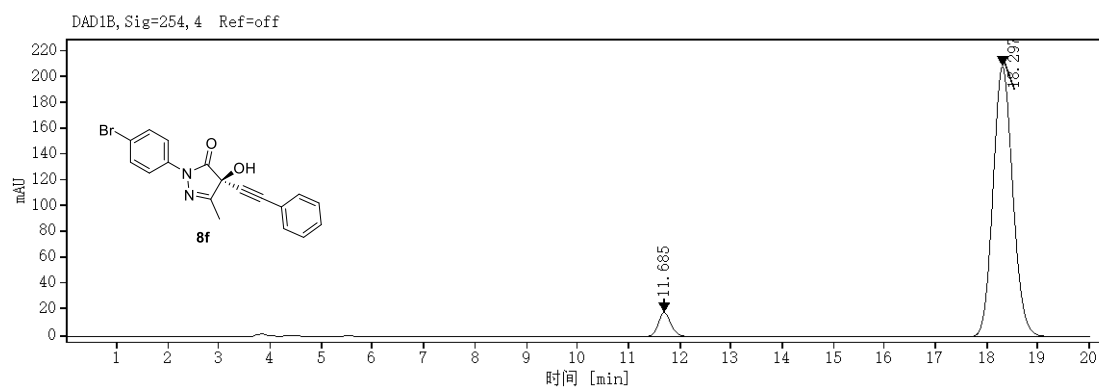


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
9.253	MM m	0.18	64.67	5.51	5.79
10.584	BM m	0.21	1052.15	76.57	94.21

SUPPORTING INFORMATION

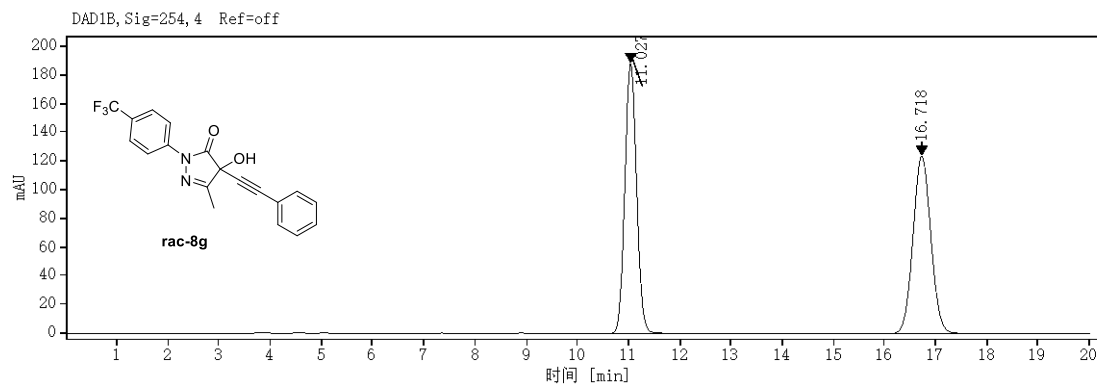


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
11.867	BB	1.68	4793.81	271.22	50.03
18.598	BB	1.99	4788.37	178.10	49.97

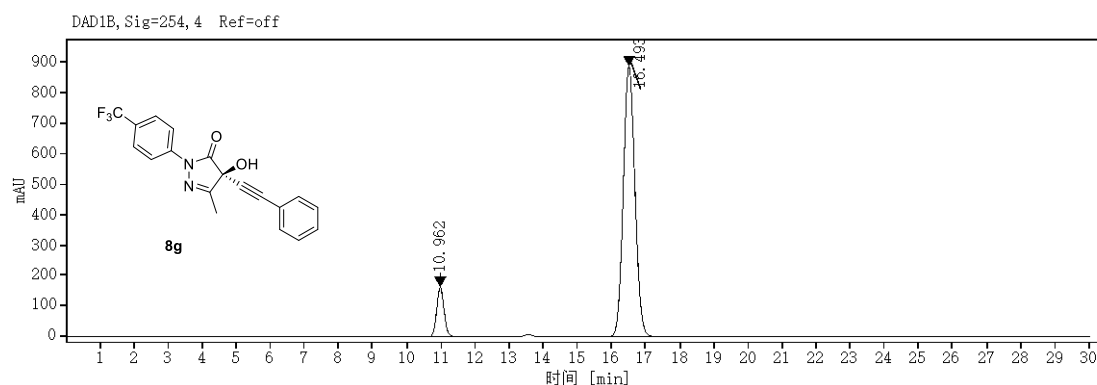


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
11.685	BB	1.20	323.06	18.47	5.45
18.297	BB	2.06	5605.18	209.13	94.55

SUPPORTING INFORMATION

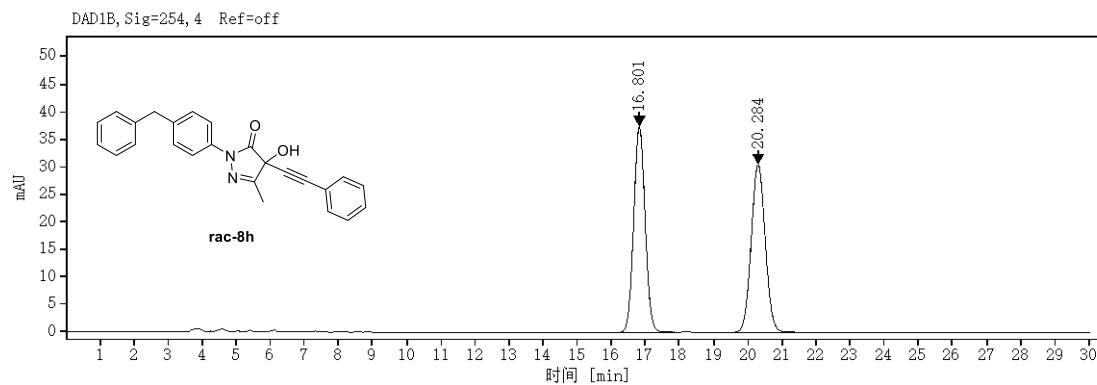


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
11.027	BM m	0.25	2984.97	188.33	49.92
16.718	BM m	0.38	2994.40	123.65	50.08

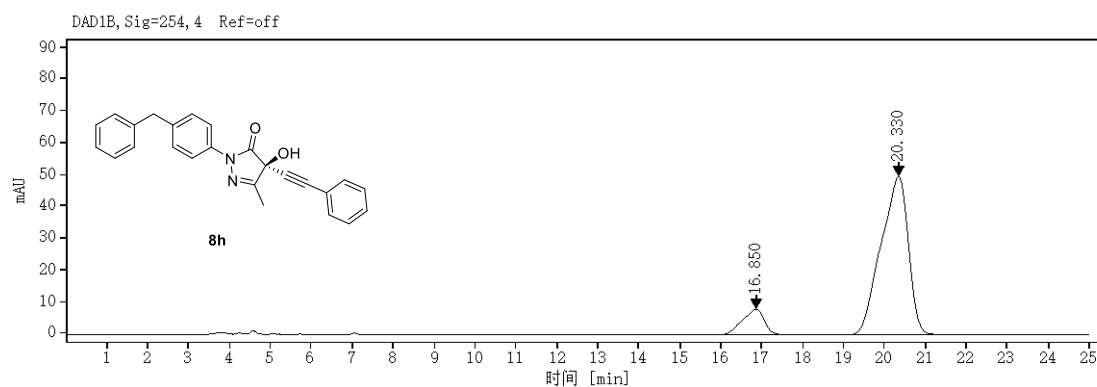


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.962	MM m	0.23	2453.57	163.24	10.45
16.493	MM m	0.37	21021.56	889.82	89.55

SUPPORTING INFORMATION

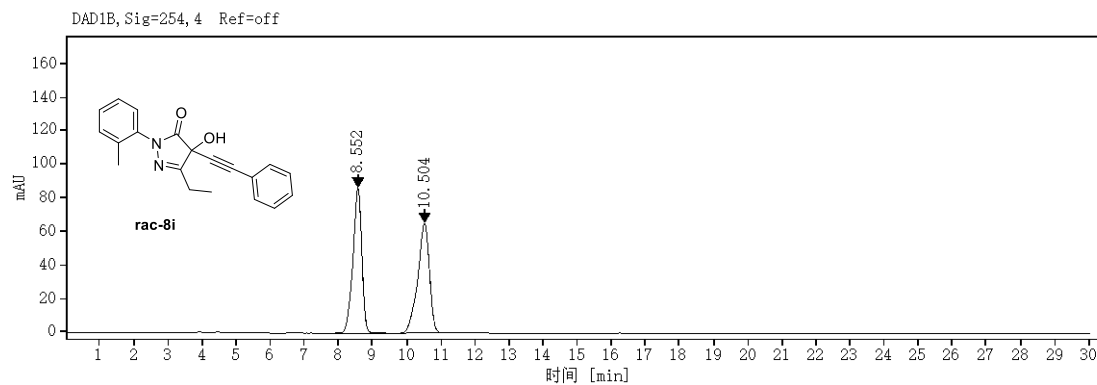


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.801	BB	1.72	872.74	37.45	49.94
20.284	BB	2.20	874.80	30.55	50.06

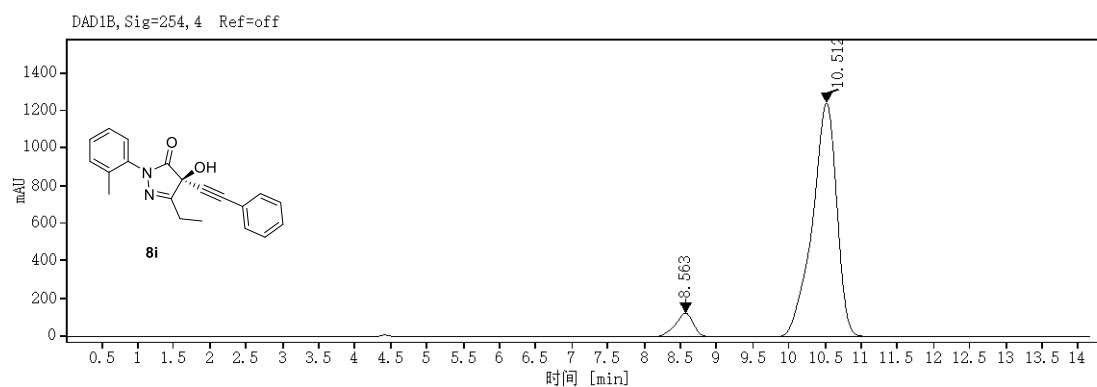


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
16.850	MM m	0.53	289.68	7.93	11.18
20.330	MM m	0.66	2302.04	49.65	88.82

SUPPORTING INFORMATION

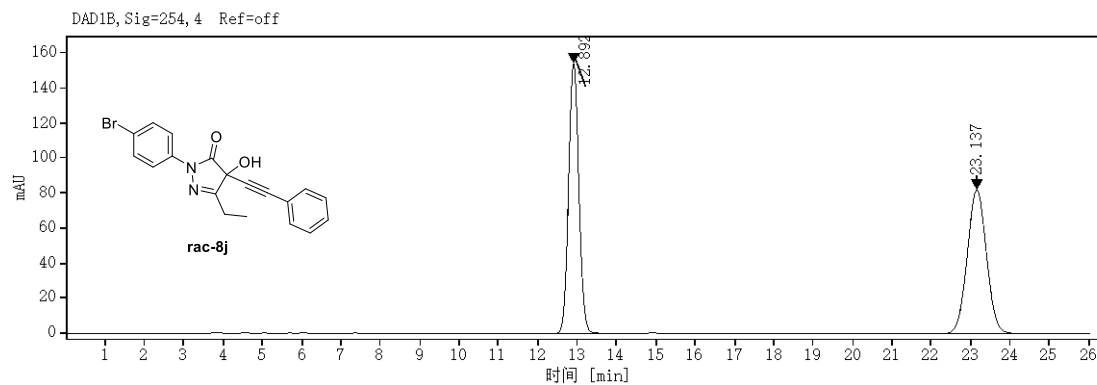


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.552	BB	1.76	1566.96	86.27	50.16
10.504	BB	1.41	1556.76	65.21	49.84

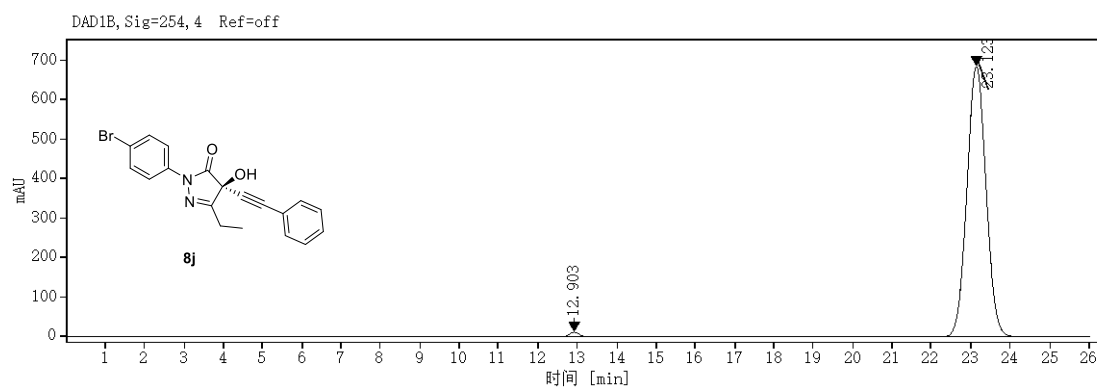


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.563	MM m	0.26	2180.29	124.71	6.97
10.512	BM m	0.35	29104.44	1241.82	93.03

SUPPORTING INFORMATION

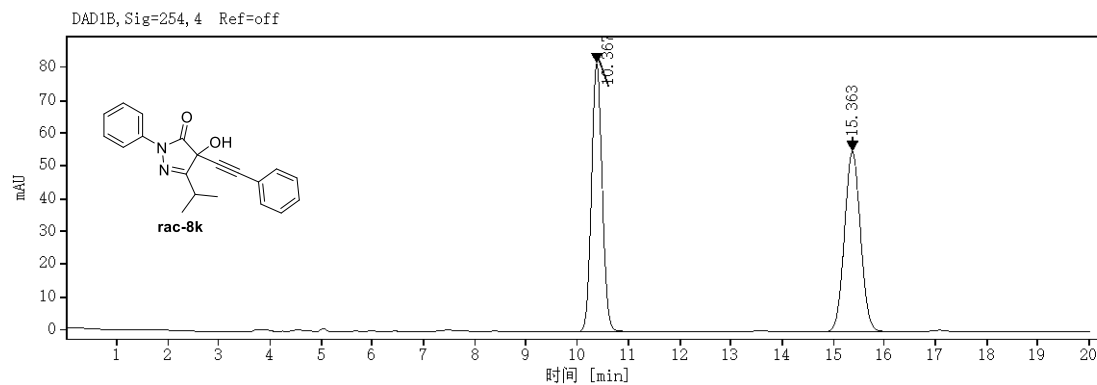


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.892	BM m	0.28	2780.52	154.03	50.06
23.137	BM m	0.53	2774.33	81.92	49.94

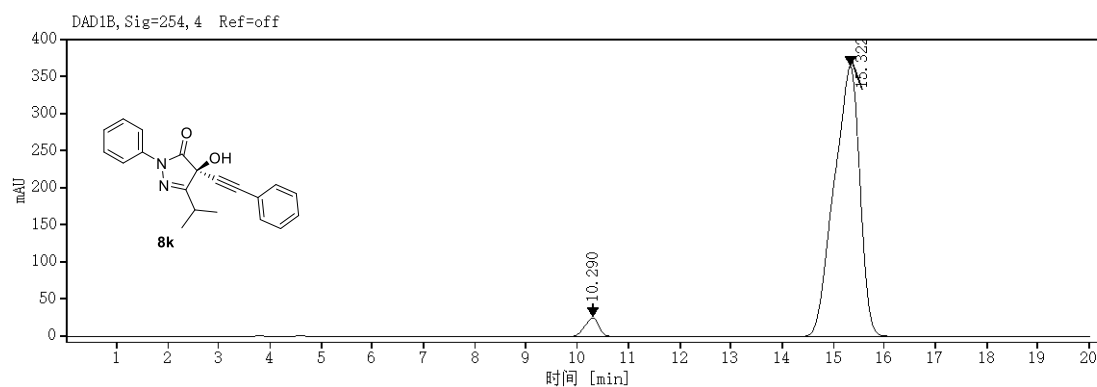


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
12.903	BM m	0.27	205.63	11.74	0.88
23.123	BB	3.71	23205.11	686.14	99.12

SUPPORTING INFORMATION

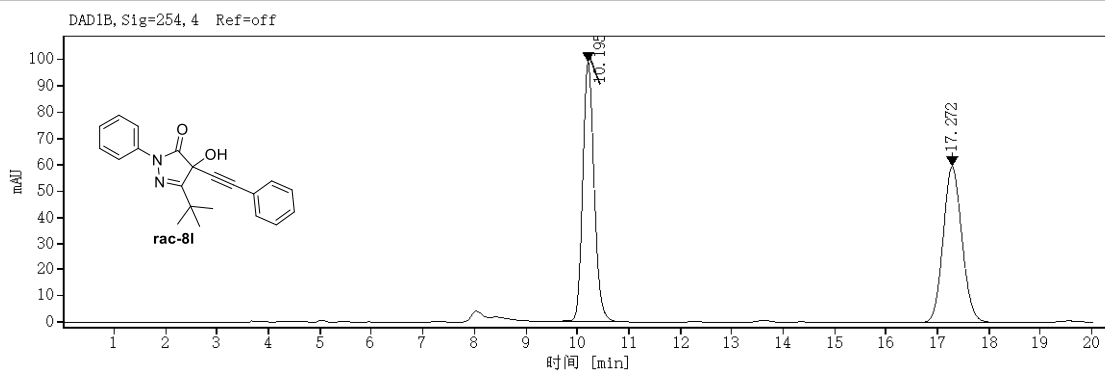


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.367	BB	0.95	1177.66	81.73	49.70
15.363	BB	1.59	1191.77	54.90	50.30

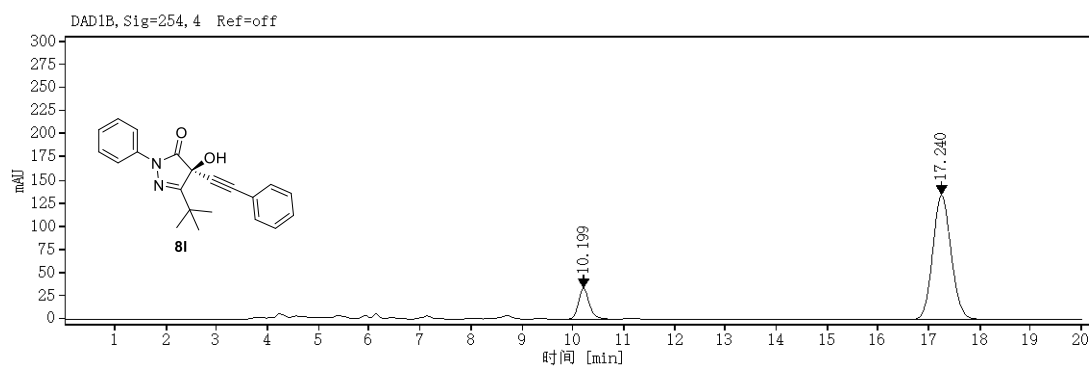


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.290	BM m	0.30	484.57	25.25	3.68
15.322	BM m	0.50	12684.00	363.75	96.32

SUPPORTING INFORMATION

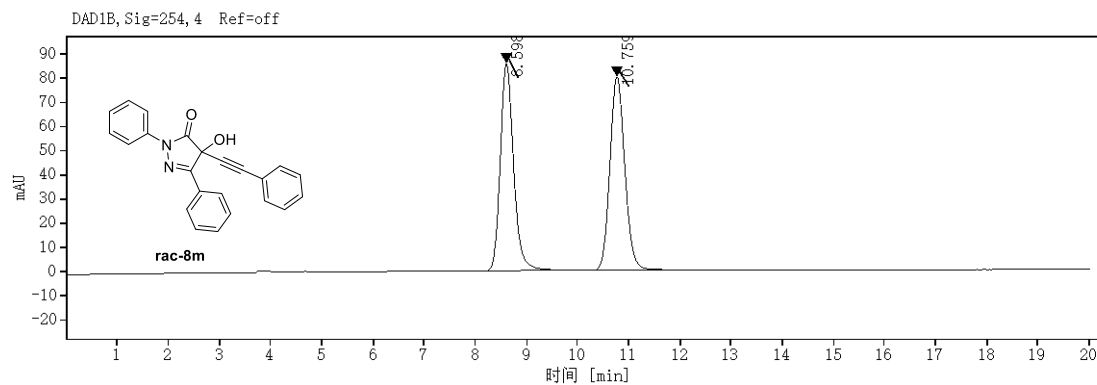


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.195	MM m	0.24	1519.46	98.98	50.27
17.272	MM m	0.39	1503.26	59.46	49.73

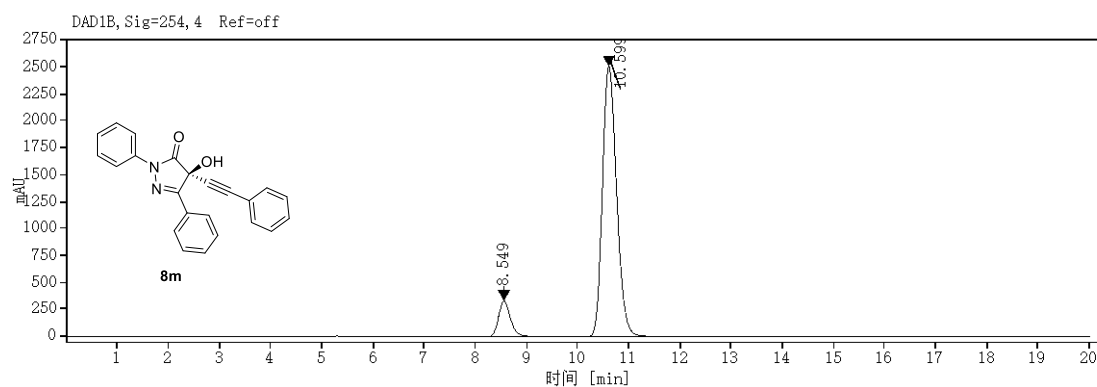


RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
10.199	BM m	0.22	483.00	32.97	12.60
17.240	BM m	0.39	3350.14	134.24	87.40

SUPPORTING INFORMATION



RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.598	BM m	0.27	1542.94	85.42	48.92
10.759	BM m	0.31	1611.16	79.67	51.08



RetTime [min]	Type	Width [min]	Area [mAU * s]	Height [mAU]	Area%
8.549	MM m	0.25	5300.02	331.93	9.94
10.599	BM m	0.30	48042.88	2507.21	90.06