Supporting Information for Publication

Synthesis of 1,2,3-triazole-fused N-heterocycles from N-alkynyl hydroxyisoindolinones and sodium azide via Huisgen reaction

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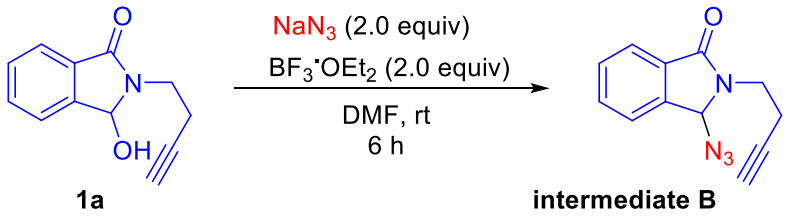
Synthesis of Intermediate B:



1a **intermediate B**

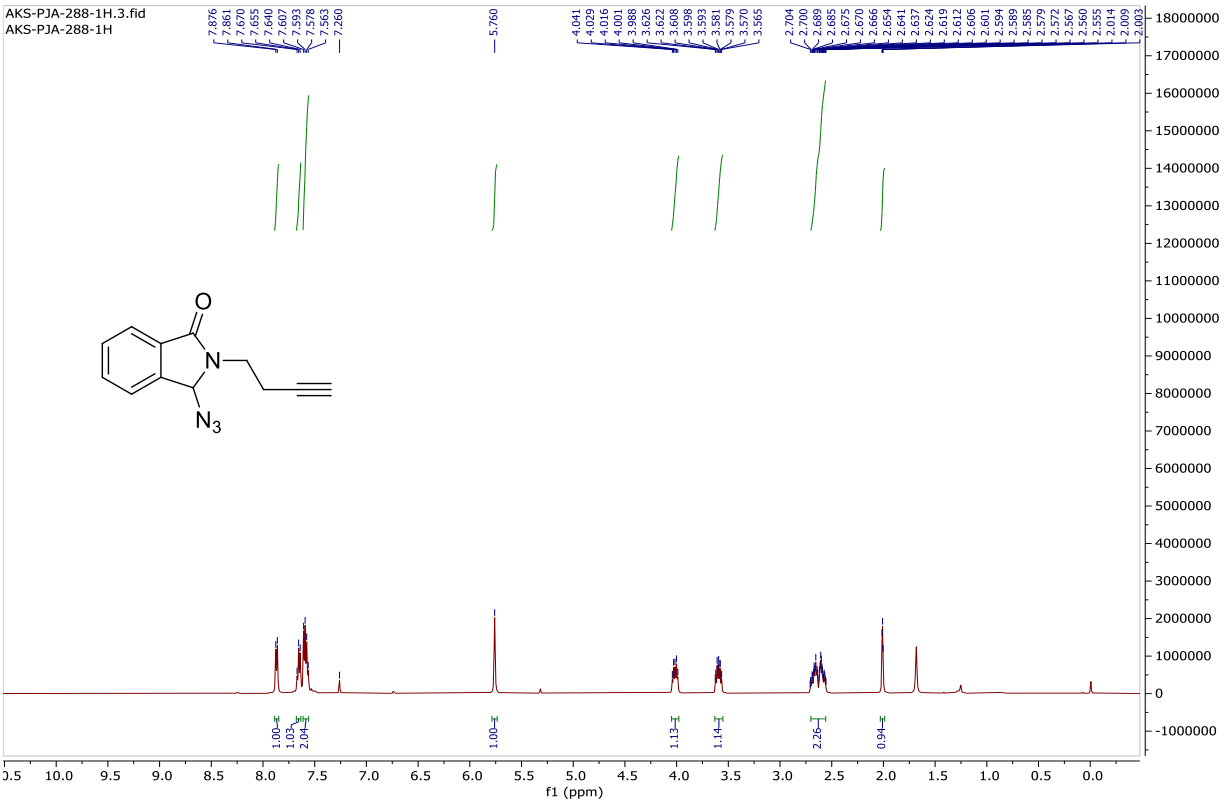
Experimental Procedure for the Synthesis of Intermediate B

To a stirred solution of 2-(but-3-yn-1-yl)-3-hydroxyisoindolinone (0.25 mmol, 1 equiv) and sodium azide (0.5 mmol, 2 equiv) in DMF (2 ml) was added $BF_3{\cdot}OEt_2$ (0.5 mmol, 2 equiv) dropwise at 0 °C under nitrogen atmosphere. The reaction mixture was then allowed to stir at room temperature and the reaction time was monitored by TLC. After completion of the reaction, the reaction mixture was diluted with ethyl acetate, sodium bicarbonate and saturated brine solution. The organic phase was extracted with ice water (3 × 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel to give the corresponding intermediate **B** in 71% yield which was confirmed by ^1H, ^{13}C and HRMS analysis.

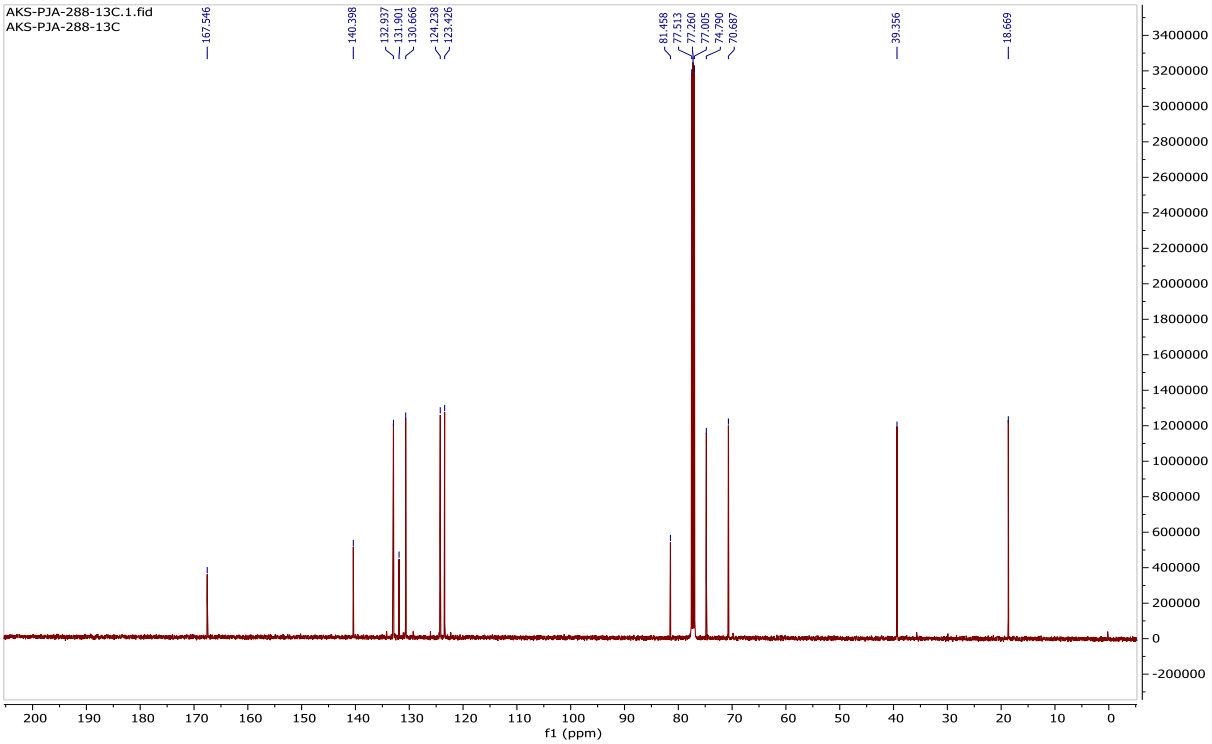
3-Azido-2-(but-3-yn-1-yl)isoindolin-1-one (B):

Yellow gummy; R_f (Hexane/EtOAc, 3:1) 0.50. Yield 40 mg, 71%; ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.5 Hz, 1 H), 7.66 (t, *J* = 7.5 Hz, 1 H), 7.61–7.56 (m, 2 H), 5.76 (s, 1 H), 4.04–3.99 (m, 1 H), 3.63–3.57 (m, 1 H), 2.71–2.56 (m, 2 H), 2.01 (t, *J* = 2.5 Hz, 1 H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 167.5, 140.4, 132.9, 131.9, 130.7, 124.2, 123.4, 81.5, 74.8, 70.7, 39.4, 18.7; IR (KBr, neat) 3299, 2923, 2101, 1705, 1404, 1209, 1134, 1026, 744, 642 cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{11}N_4O$ $(M + H)^+$ 227.0927, found 227.0936.

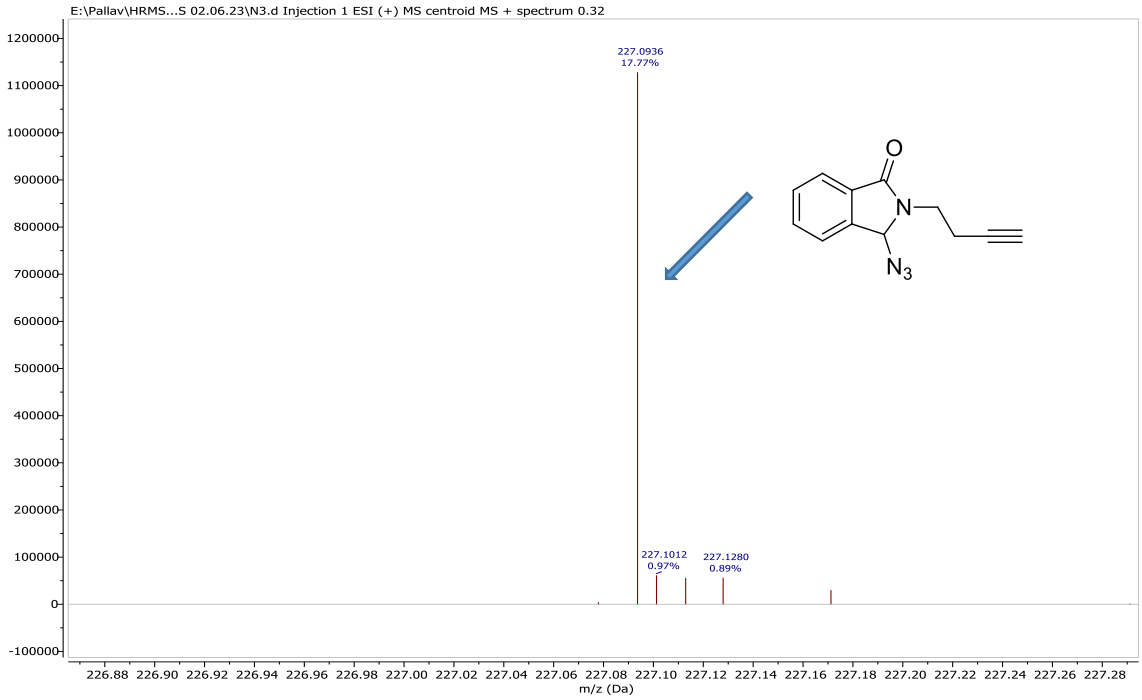
^{1}H spectrum of intermediate **B** (500 MHz, $CDCl_3$)



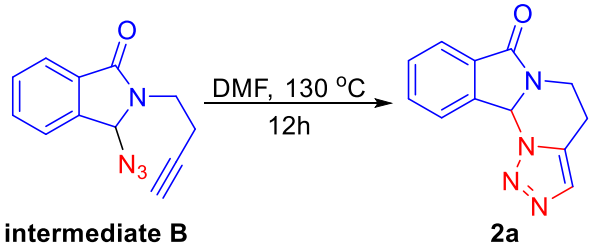
^{13}C {^{1}H} spectrum of intermediate **B** (125 MHz, $CDCl_3$)



HRMS spectrum of intermediate **B**



Control Reaction for the Synthesis of 2a:

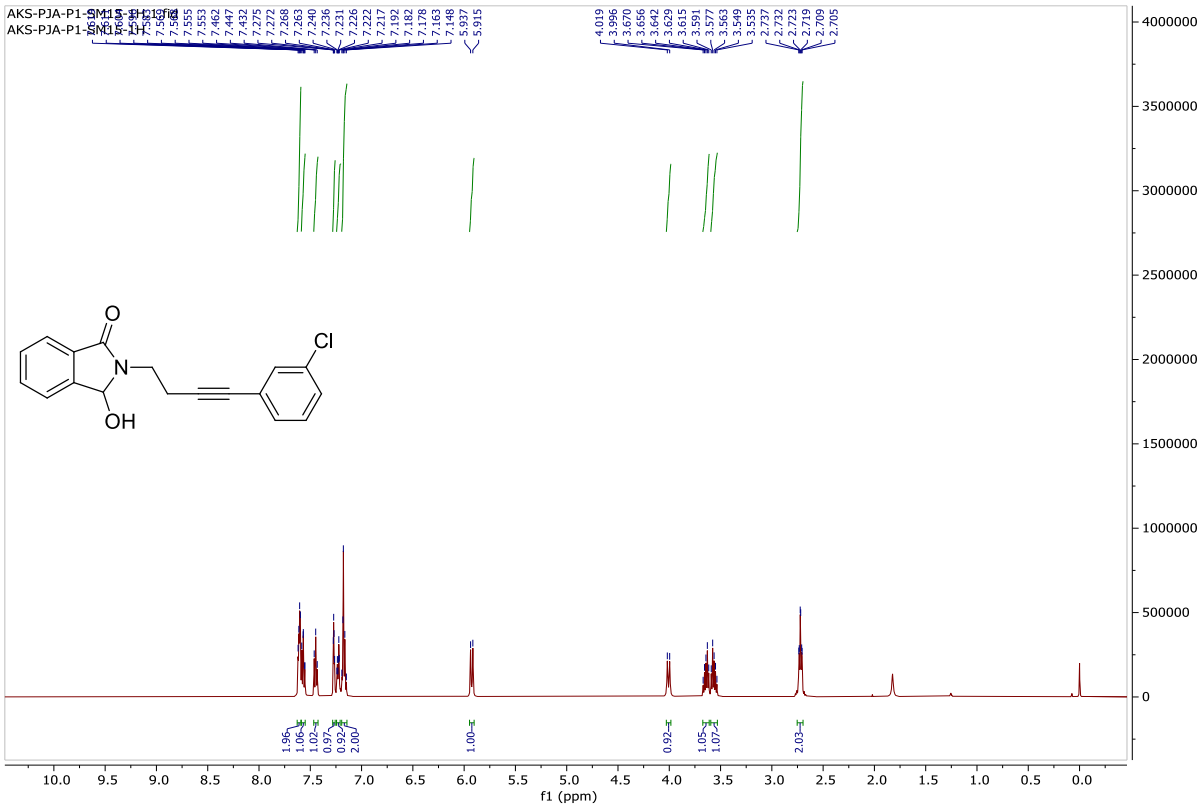


intermediate B **2a**

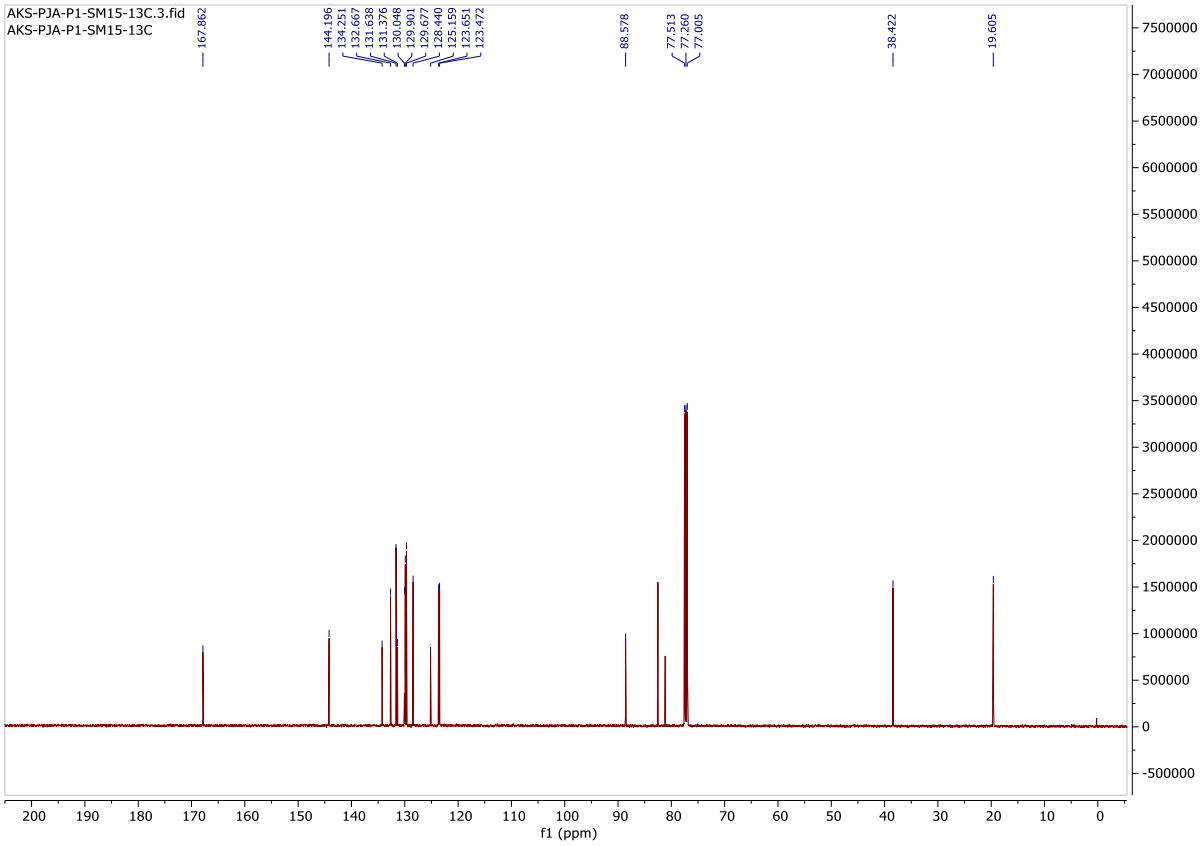
Experimental Procedure for the Synthesis of 2a from Intermediate B.

The compound **B** (0.18 mmol, 1.0 equiv) was dissolved in DMF (2.0 ml) and the reaction mixture was allowed to stir at 130 °C under nitrogen atmosphere. The progress of the reaction was monitored by TLC and after completion of the reaction, the reaction mixture was allowed to room temperature and diluted with ethyl acetate. The organic phase was extracted with ice water (3 × 10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in rotary evaporator. The crude was subjected to column chromatography over silica gel to give the corresponding product **2a** in 80% yield.

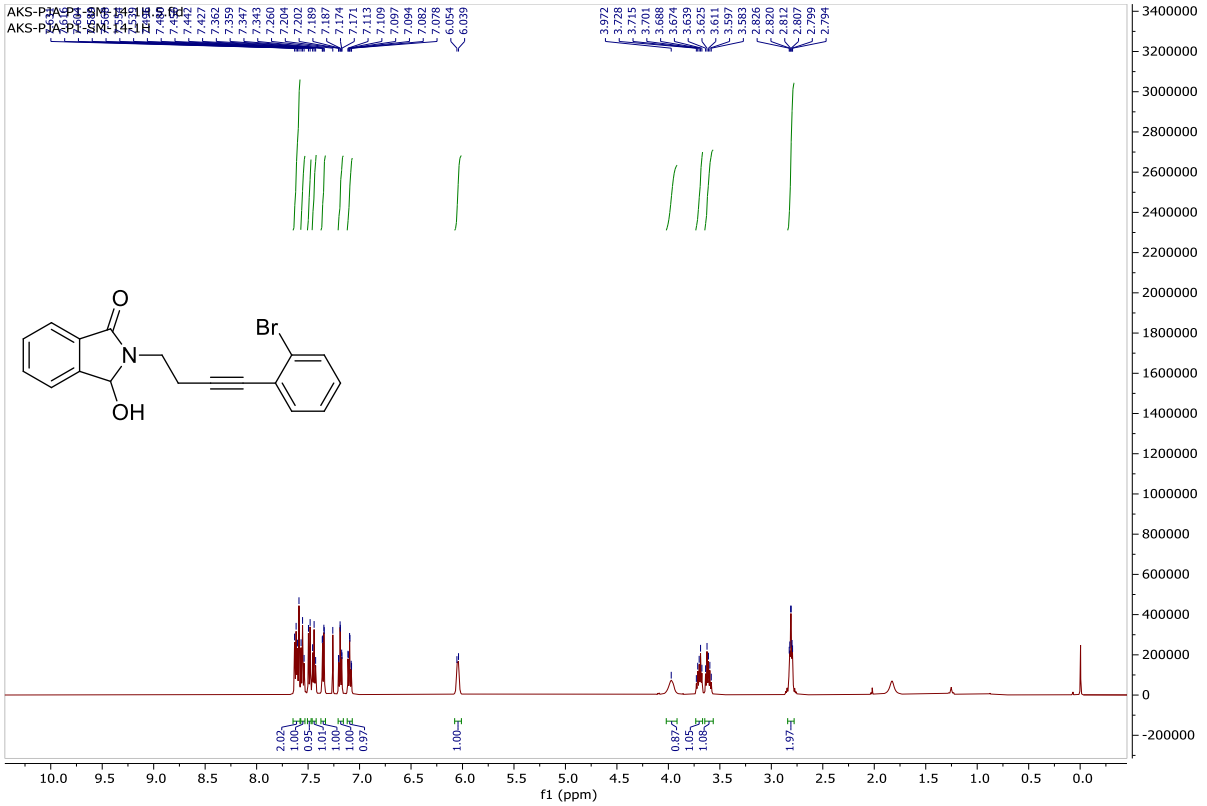
^{1}H spectrum of compound **1c** (500 MHz, $CDCl_3$)



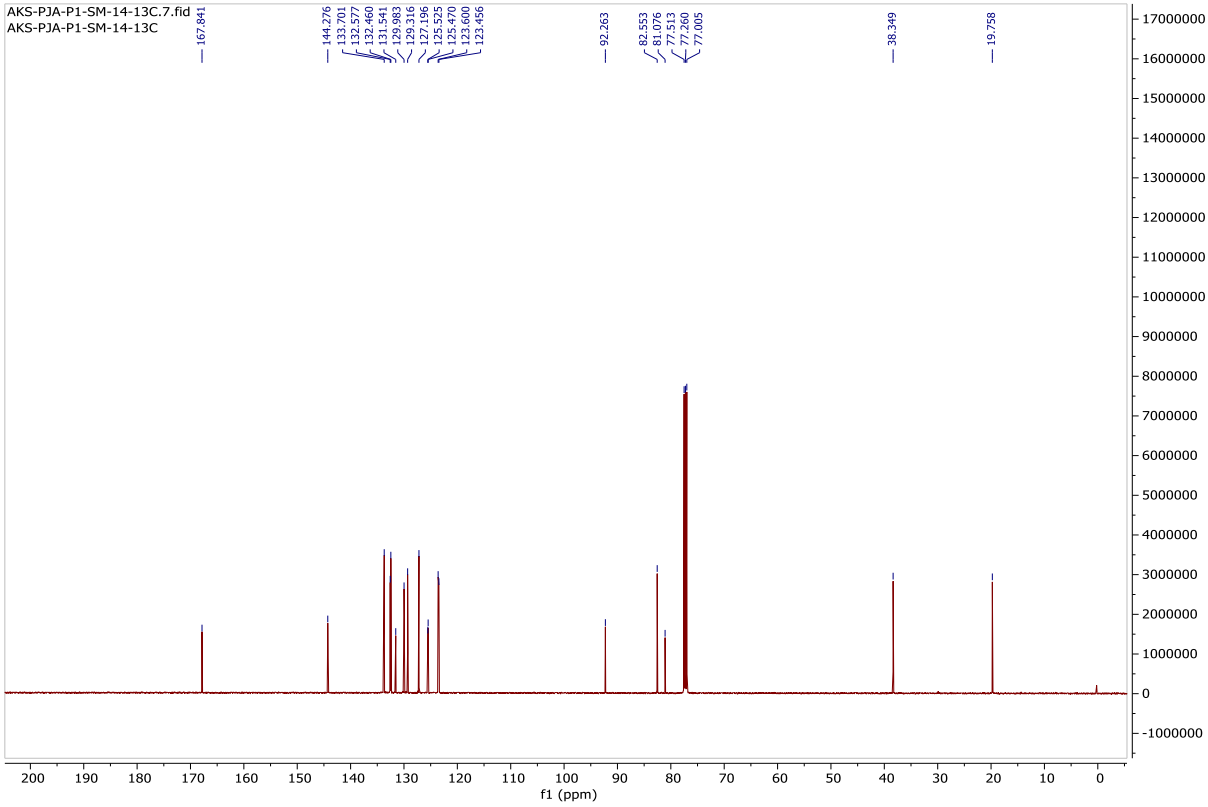
$^{13}C\{^{1}H\}$ spectrum of compound **1c** (125 MHz, $CDCl_3$)



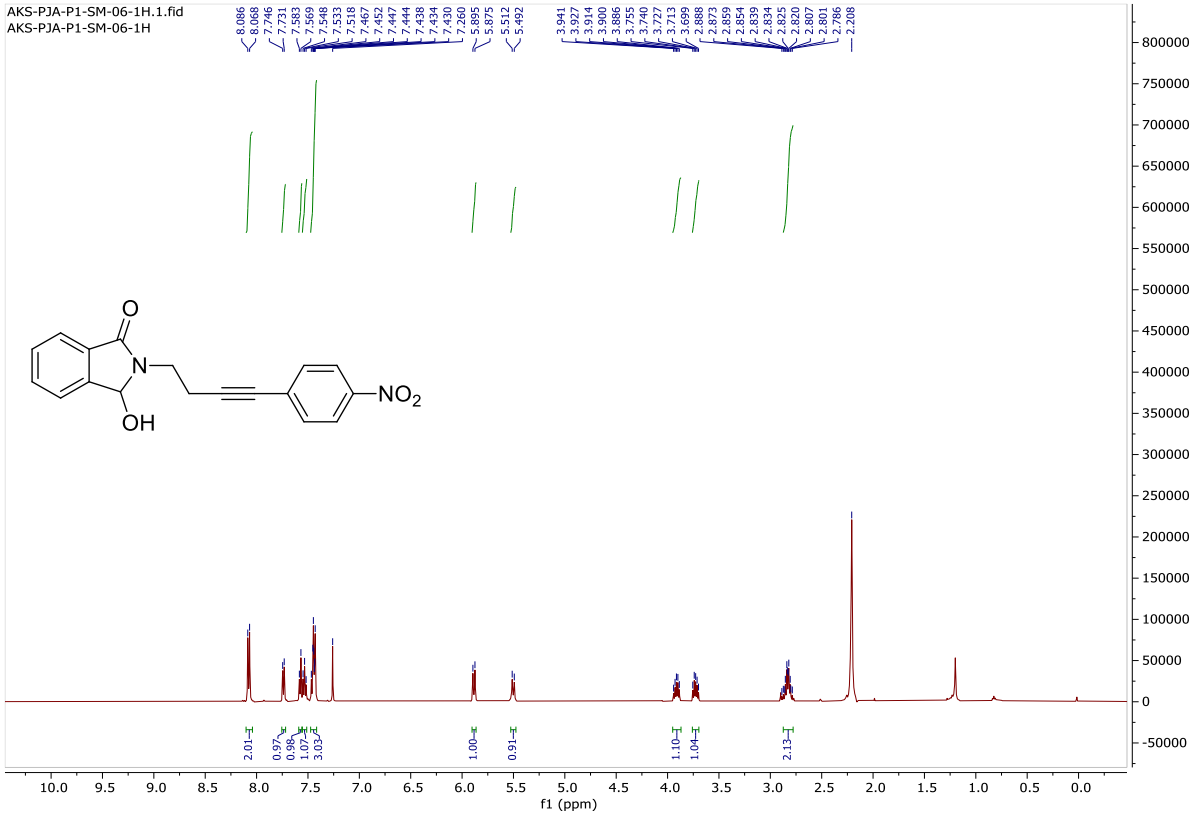
^{1}H spectrum of compound **1e** (500 MHz, $CDCl_3$)



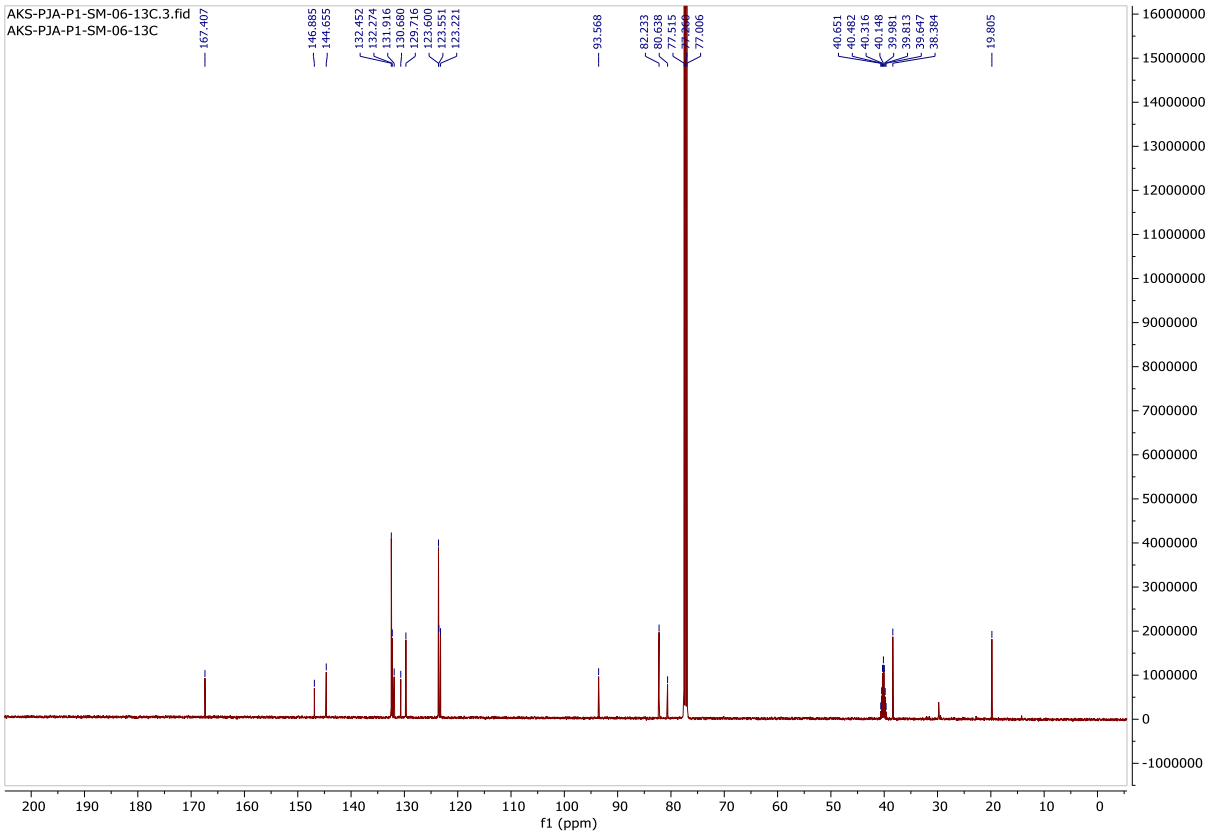
$^{13}C\{^{1}H\}$ spectrum of compound **1e** (125 MHz, $CDCl_3$)



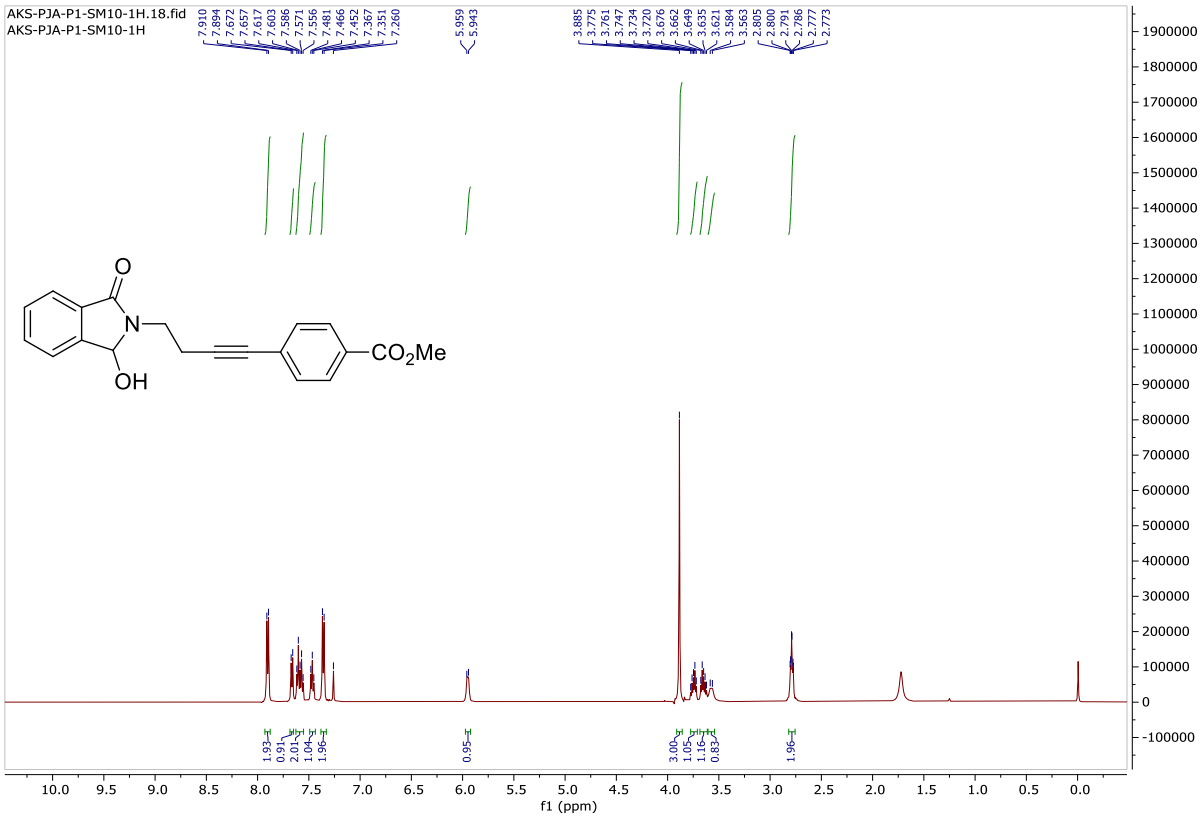
^{1}H spectrum of compound **1h** (500 MHz, $CDCl_3$/DMSO–d_6)



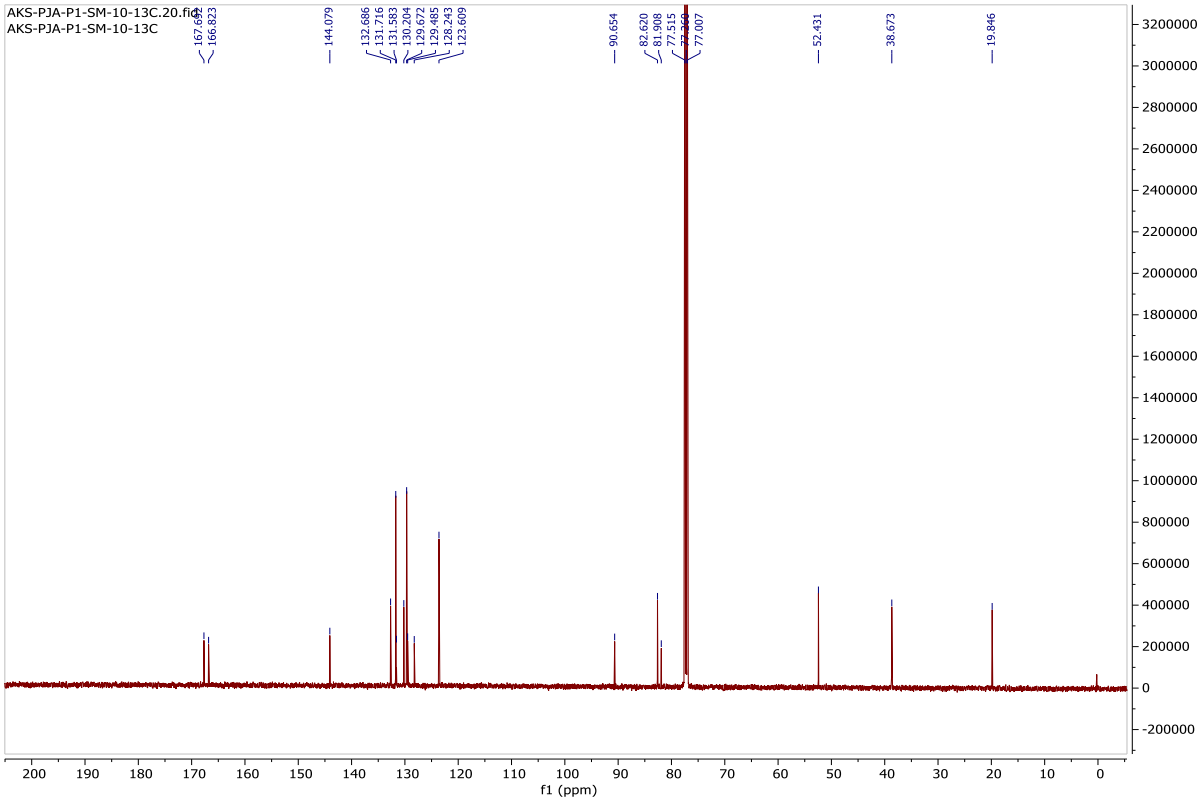
^{13}C{^{1}H} spectrum of compound **1h** (500 MHz, $CDCl_3$/DMSO–d_6)



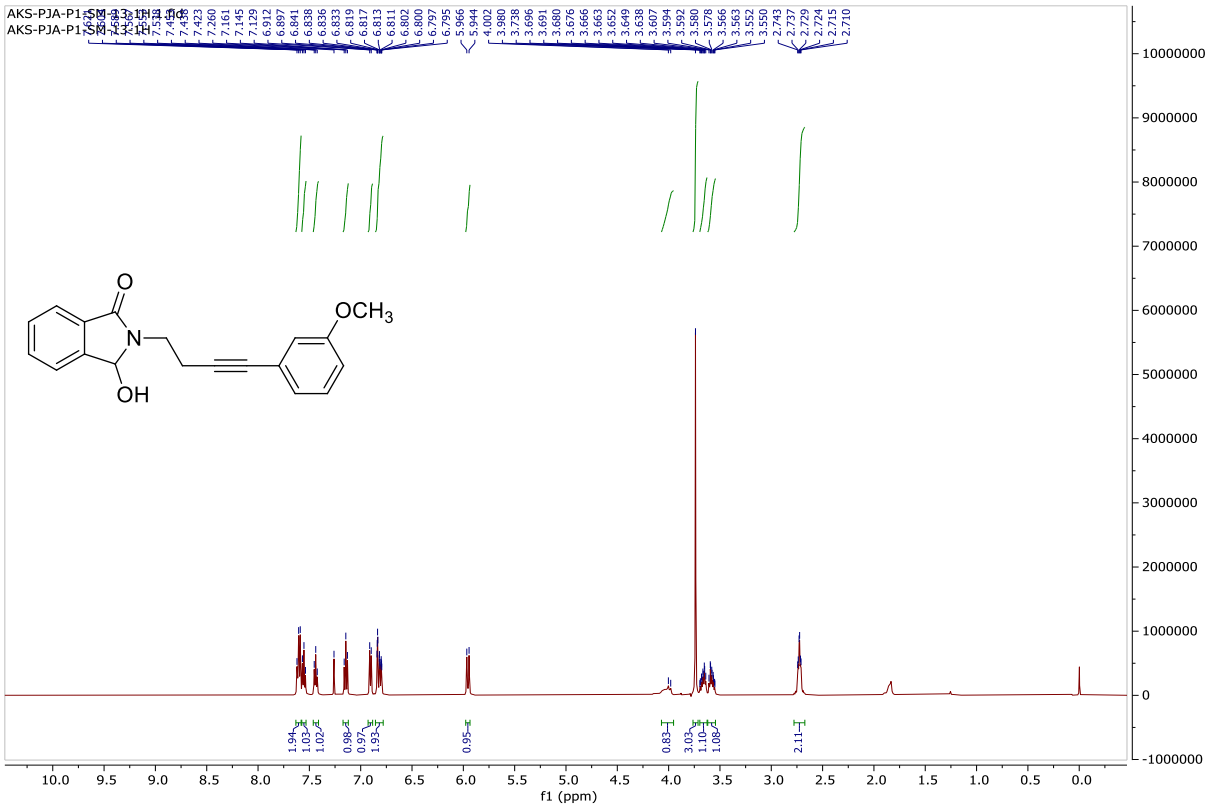
^{1}H spectrum of compound **1i** (500 MHz, $CDCl_3$)



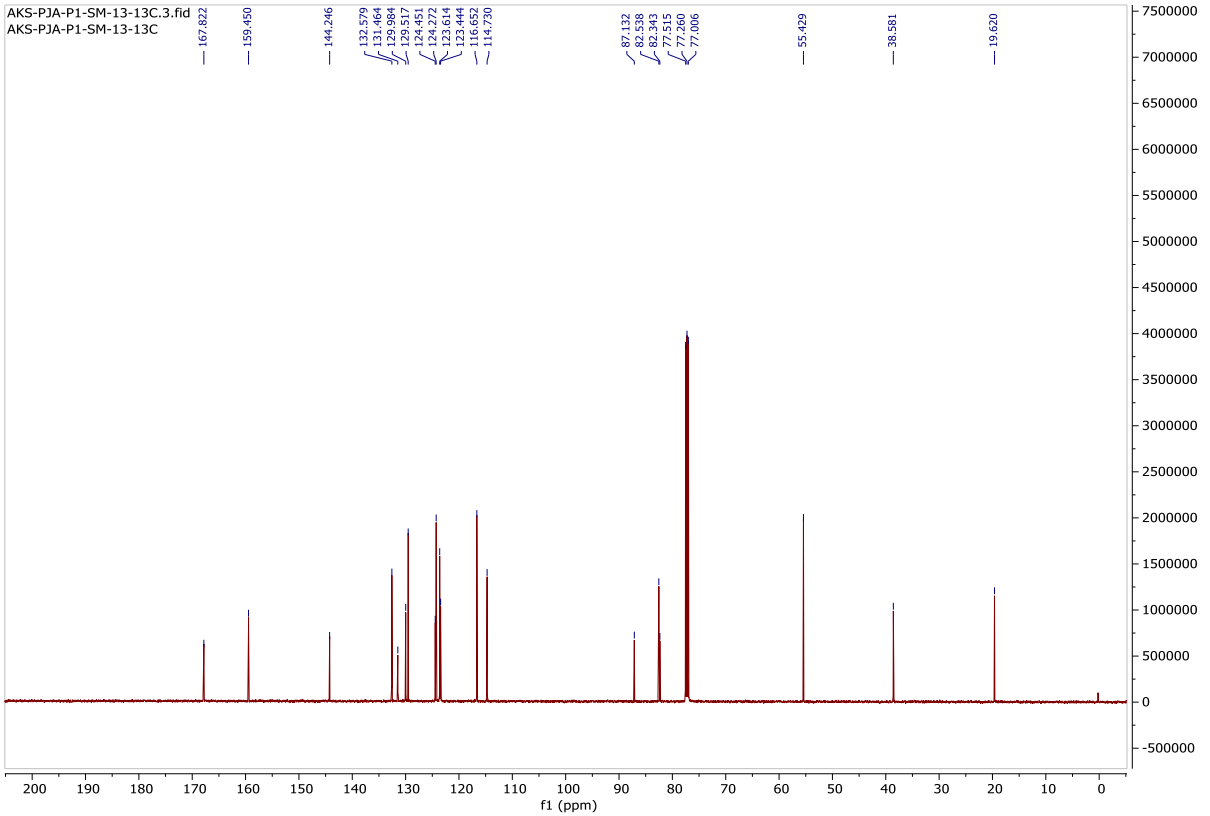
^{13}C{^{1}H} spectrum of compound **1i** (125 MHz, $CDCl_3$)



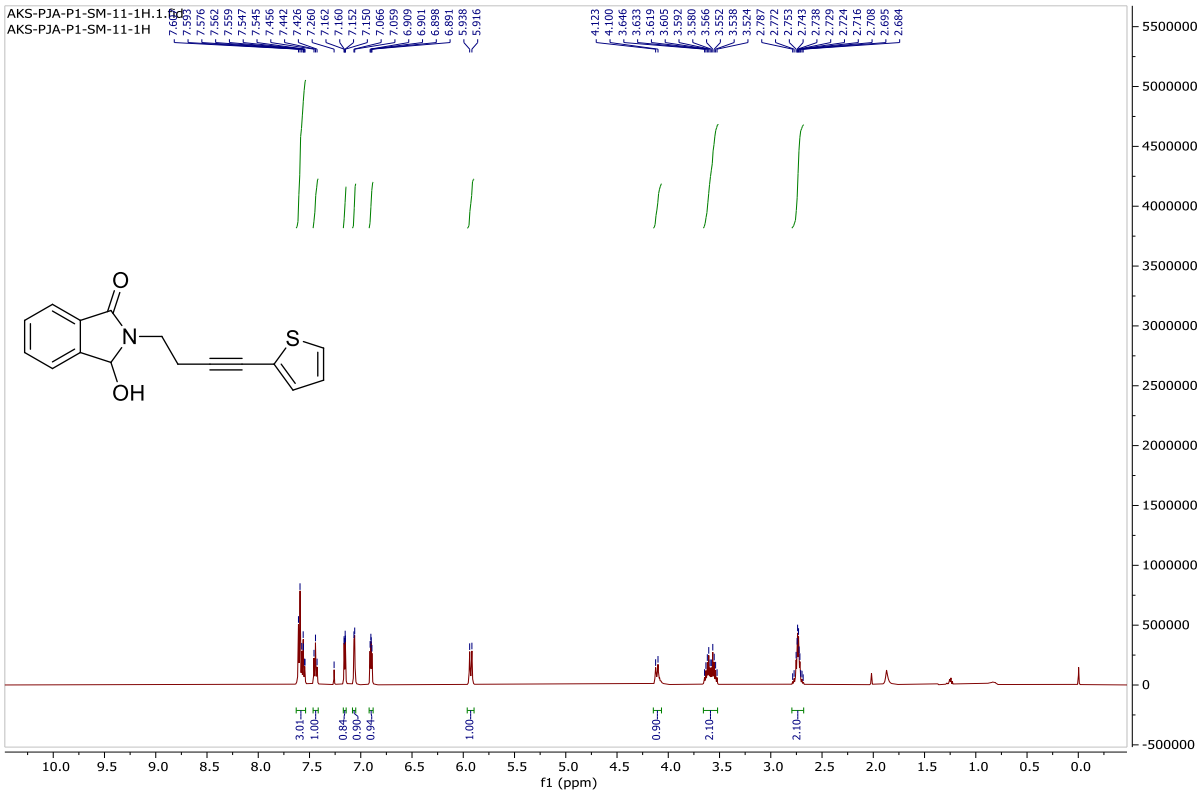
^{1}H spectrum of compound **1l** (500 MHz, $CDCl_3$)



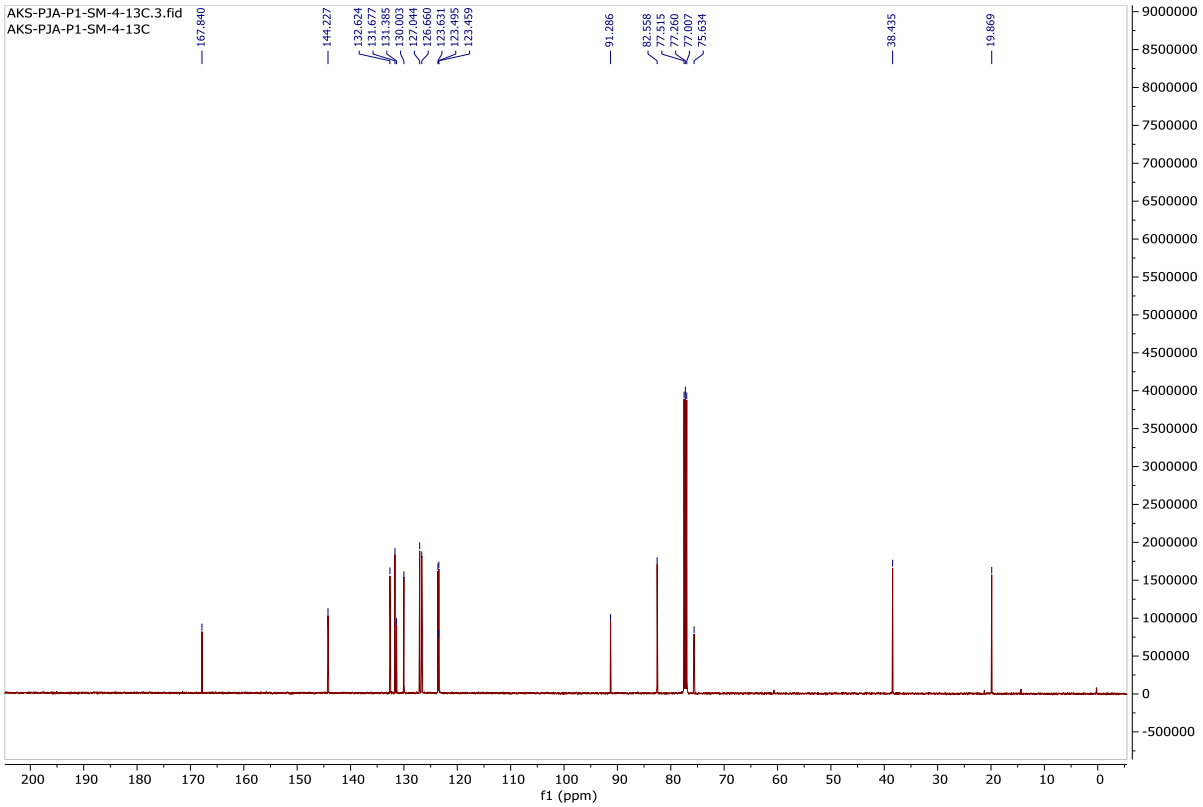
^{13}C{^{1}H} spectrum of compound **1l** (125 MHz, $CDCl_3$)



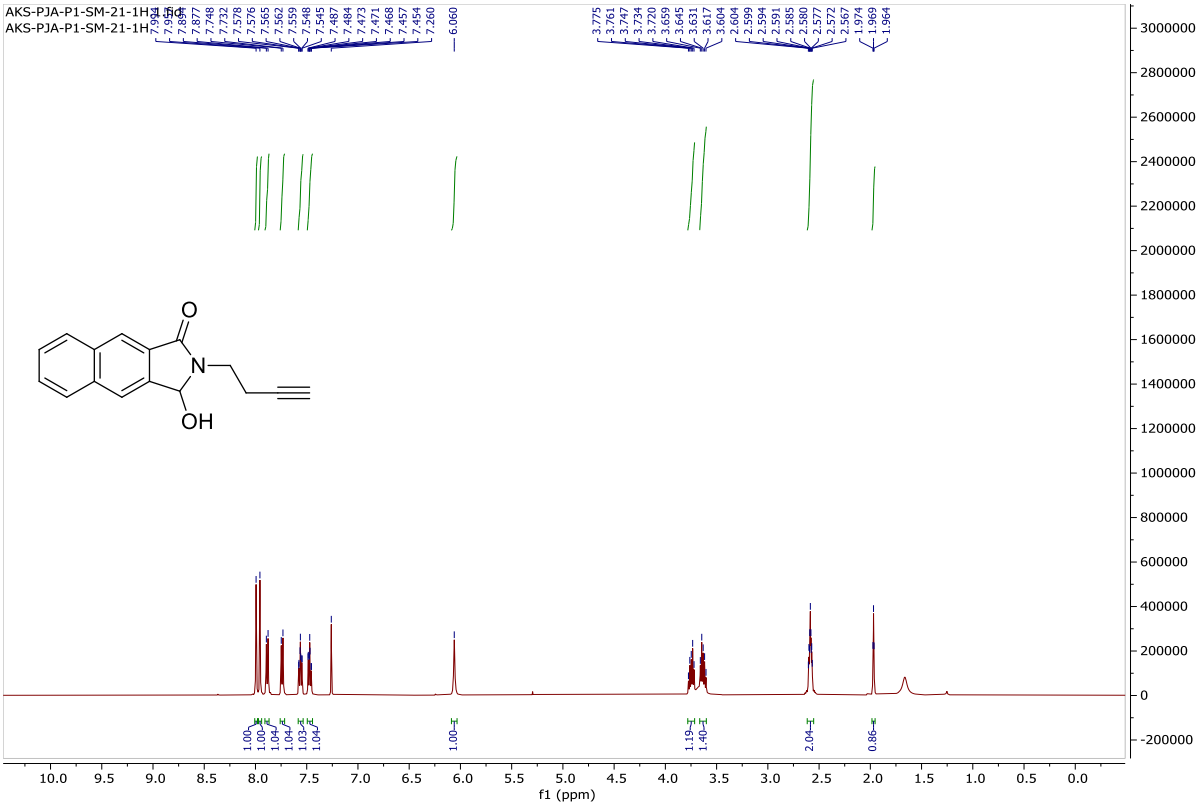
^{1}H spectrum of compound **1o** (500 MHz, $CDCl_3$)



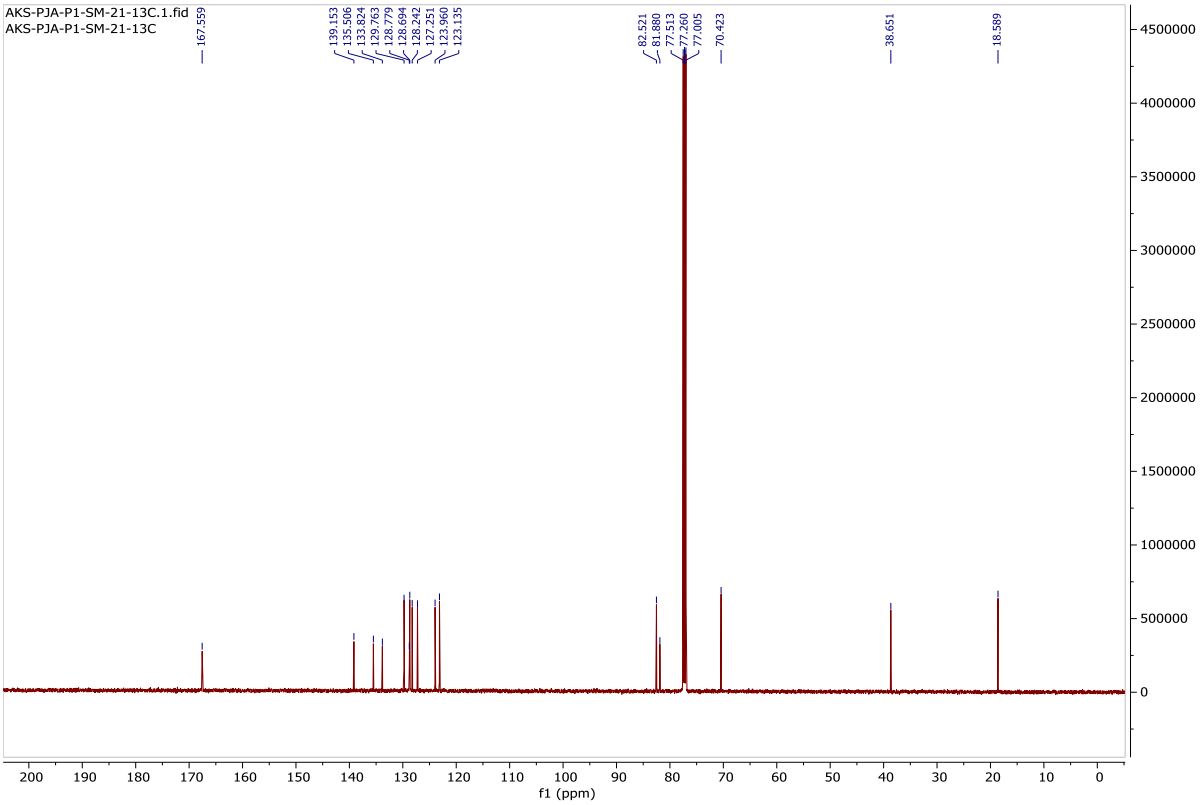
^{13}C{^{1}H} spectrum of compound **1o** (125 MHz, $CDCl_3$)



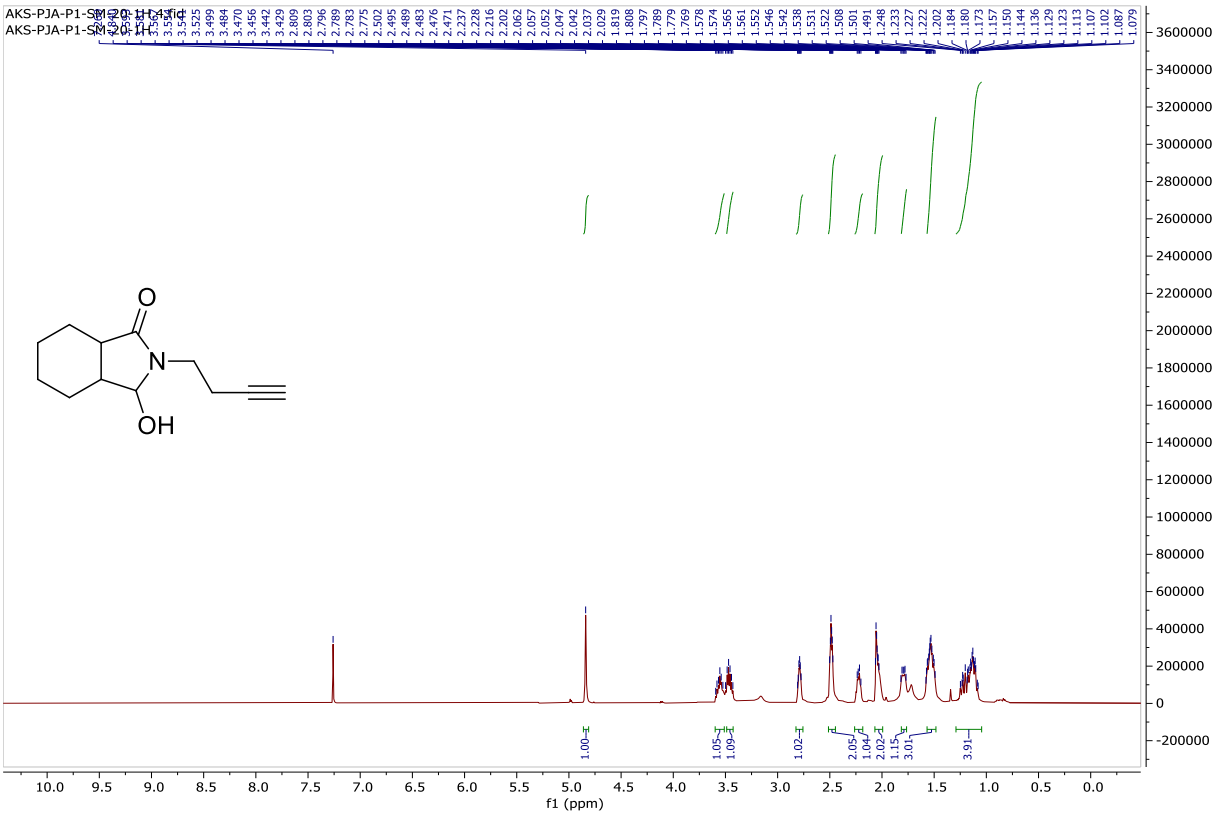
^{1}H spectrum of compound **1p** (500MHz, $CDCl_3$)



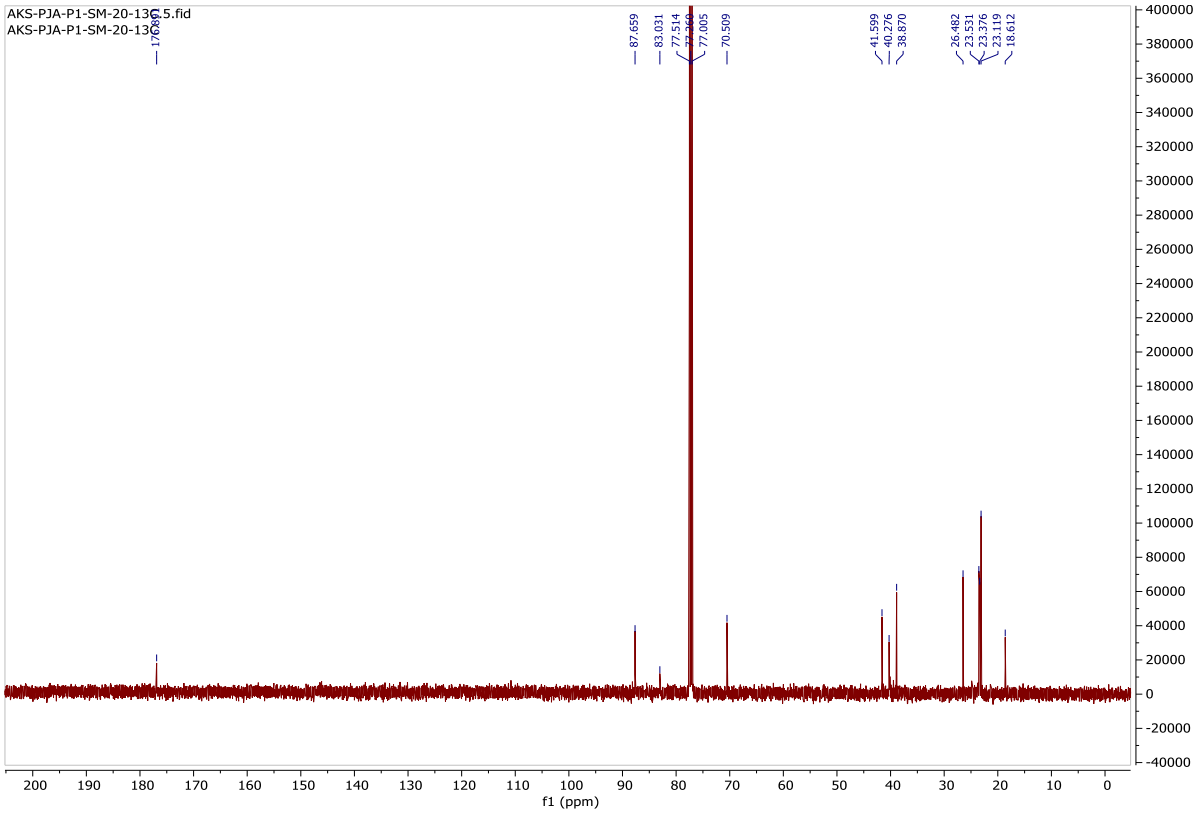
^{13}C{^{1}H} spectrum of compound **1p** (125 MHz, $CDCl_3$)



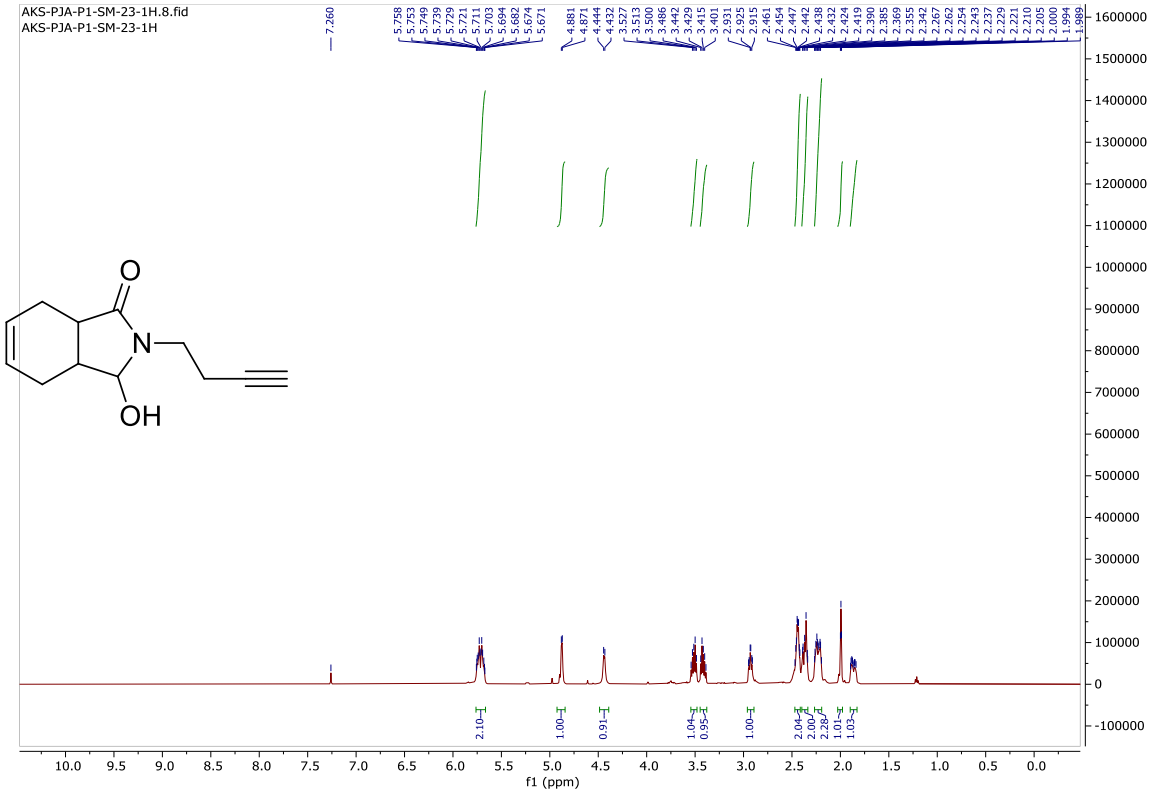
^{1}H spectrum of compound **1q** (500 MHz, $CDCl_3$)



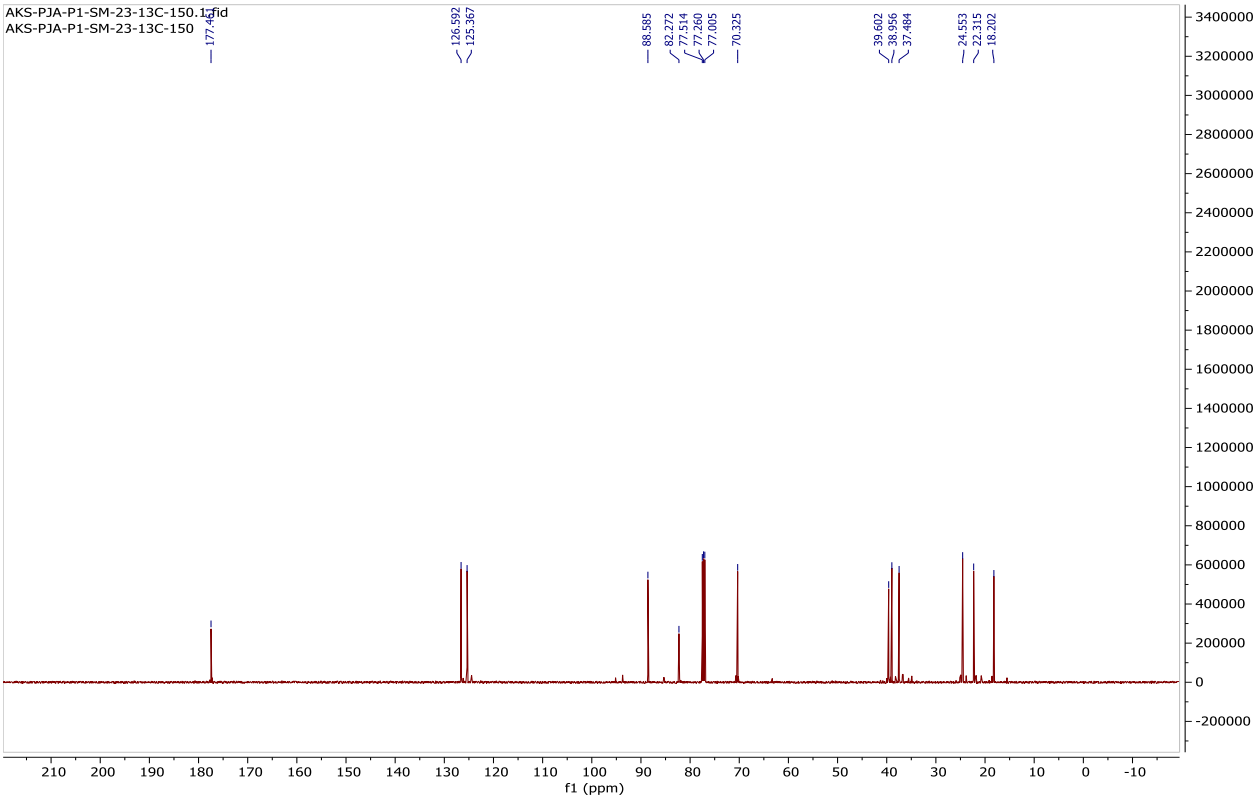
^{13}C{^{1}H} spectrum of compound **1q** (125 MHz, $CDCl_3$)



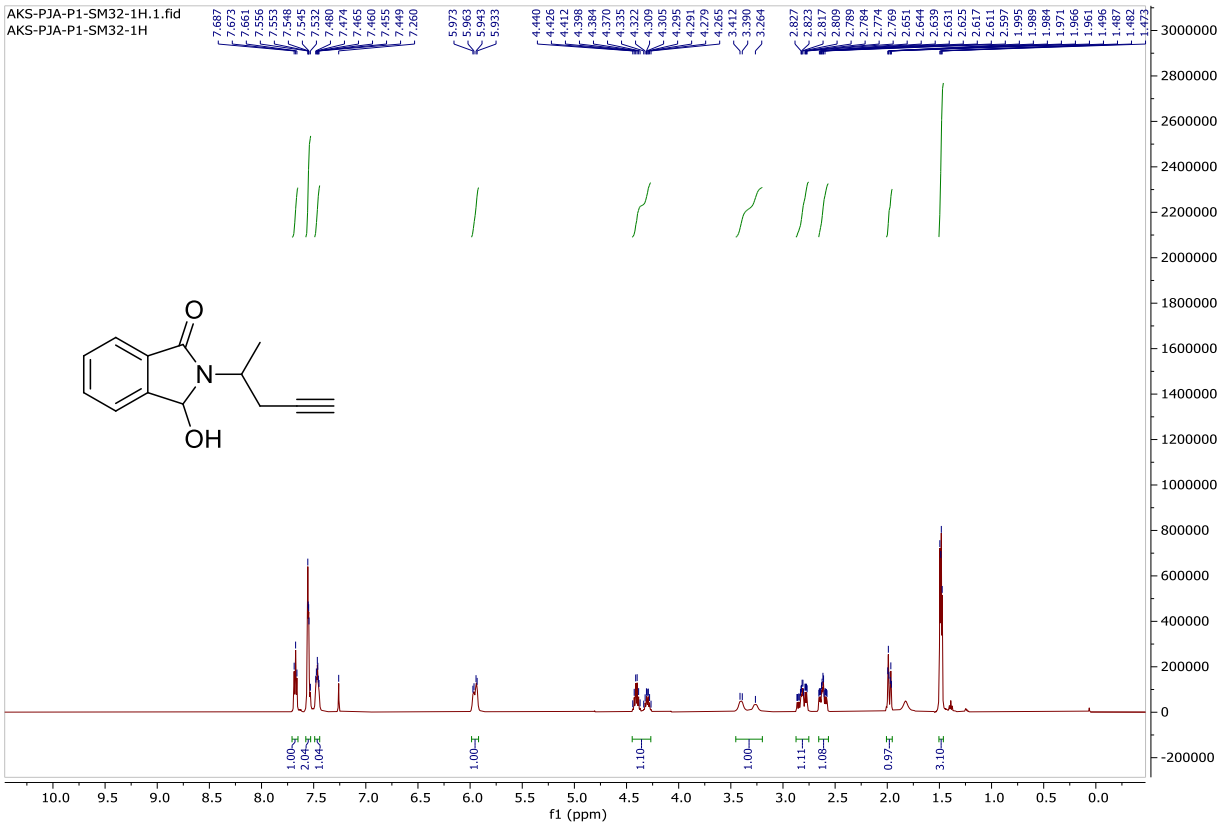
^{1}H spectrum of compound **1r** (500 MHz, $CDCl_3$)



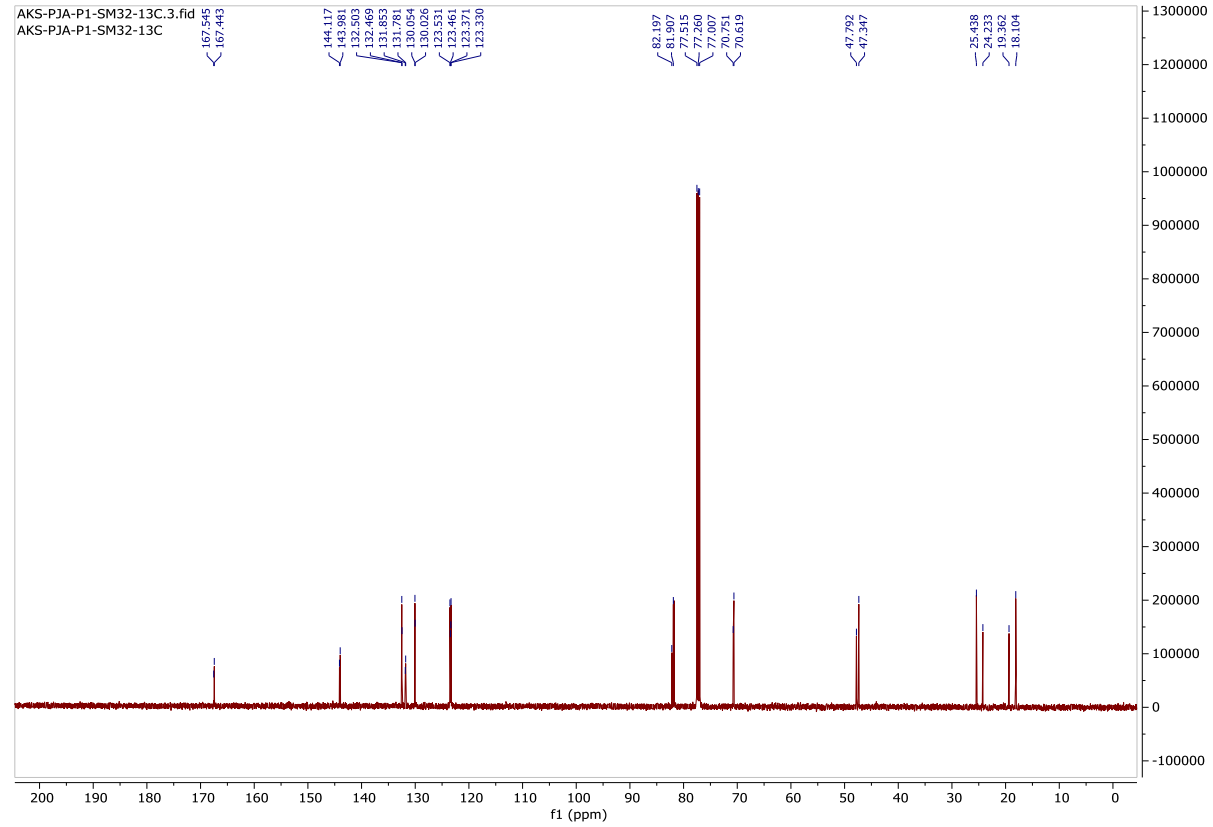
^{13}C{^{1}H} spectrum of compound **1r** (125 MHz, $CDCl_3$)



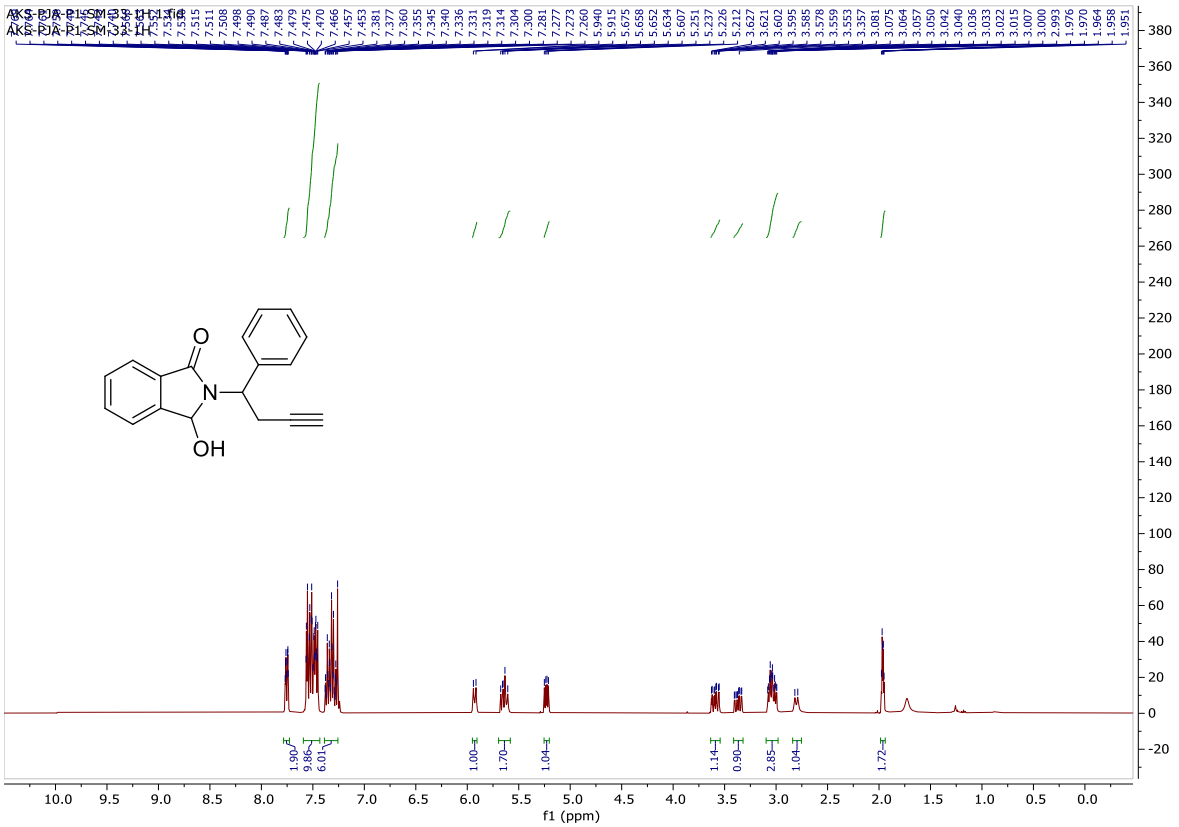
^{1}H spectrum of compound **1s** (500 MHz, $CDCl_3$)



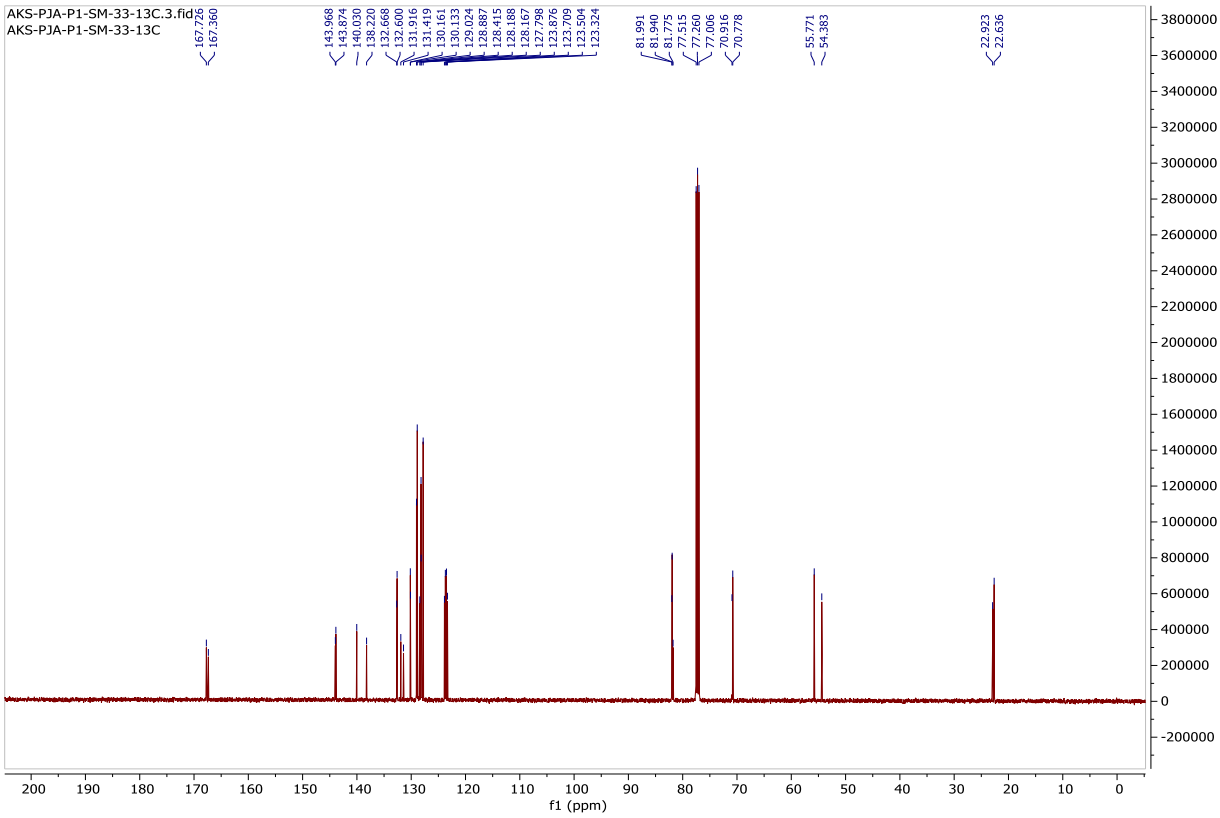
^{13}C{^{1}H} spectrum of compound **1s** (125 MHz, $CDCl_3$)



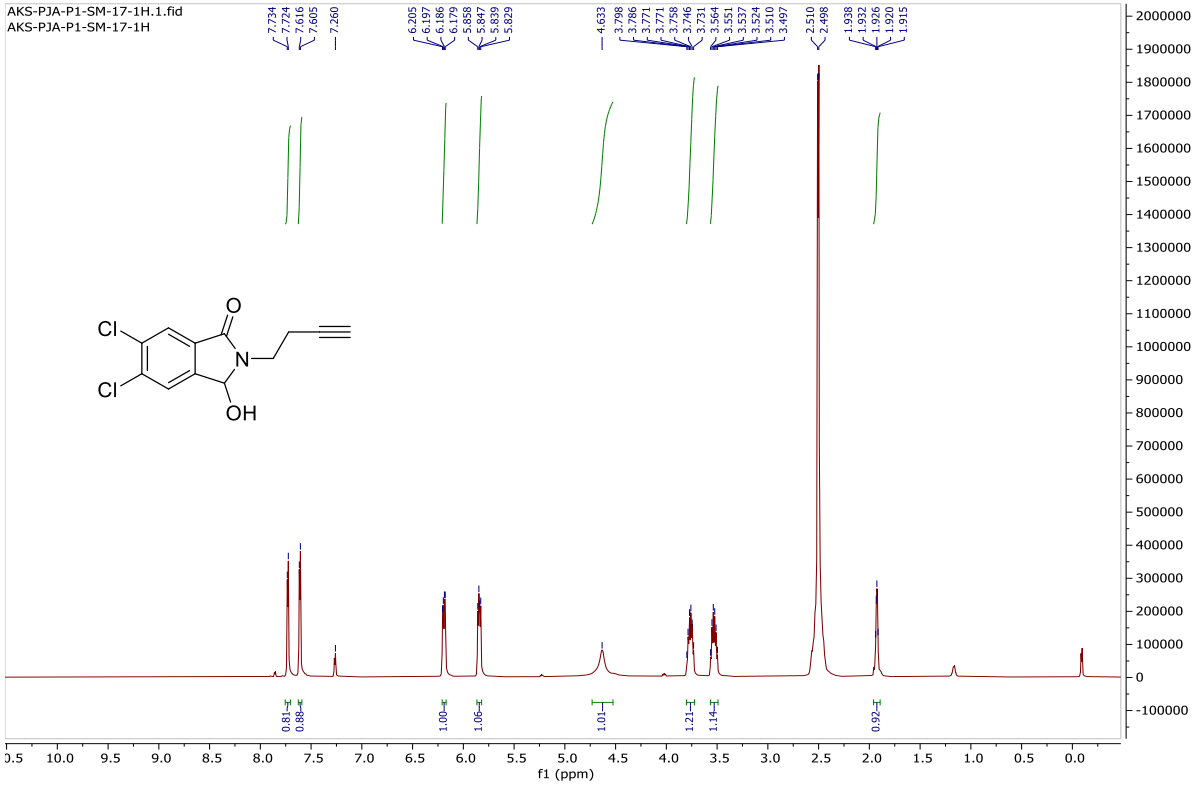
^{1}H spectrum of compound **1t** (500 MHz, $CDCl_3$)



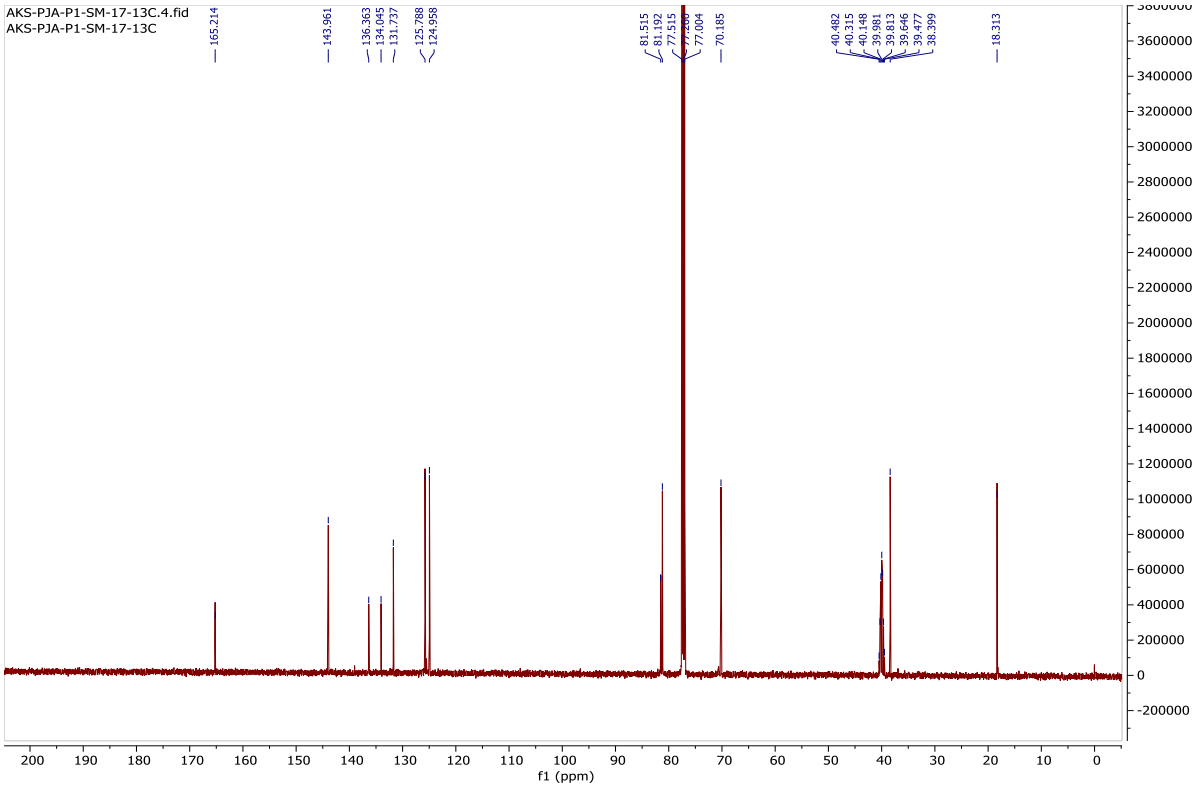
$^{13}C\{^{1}H\}$ spectrum of compound **1t** (125 MHz, $CDCl_3$)



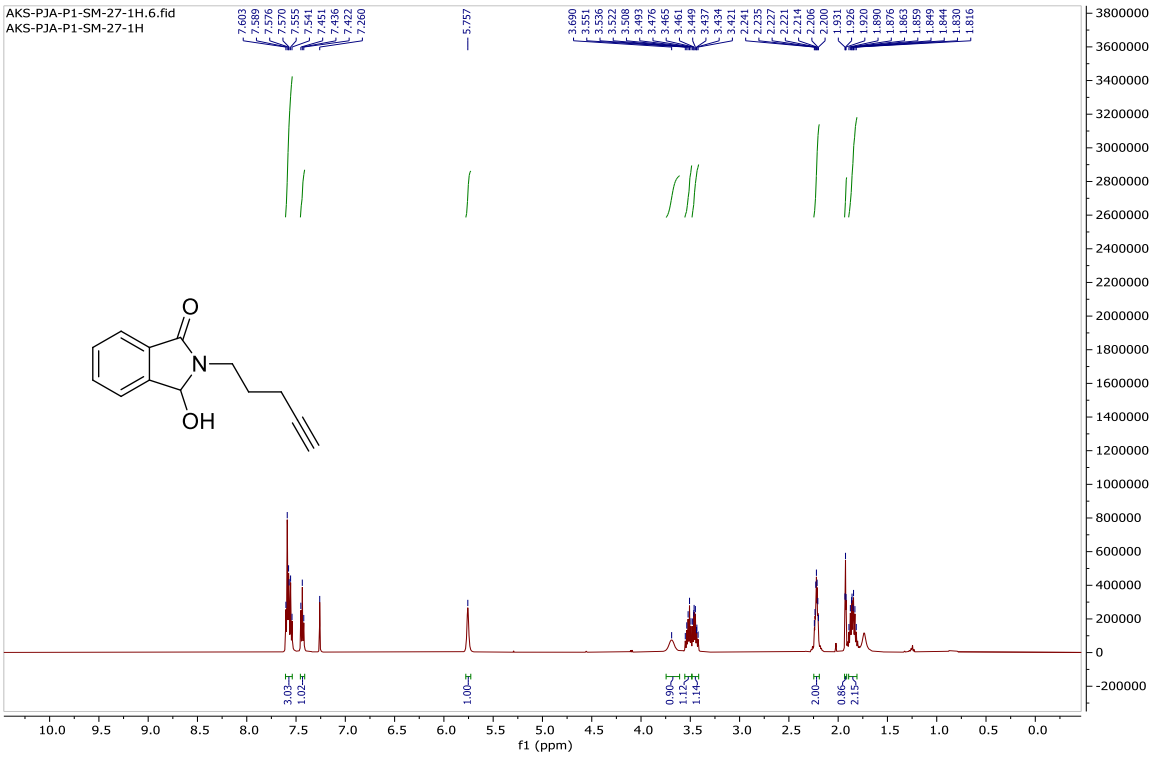
^{1}H spectrum of compound **1u** (500 MHz, $CDCl_3$/DMSO–d_6)



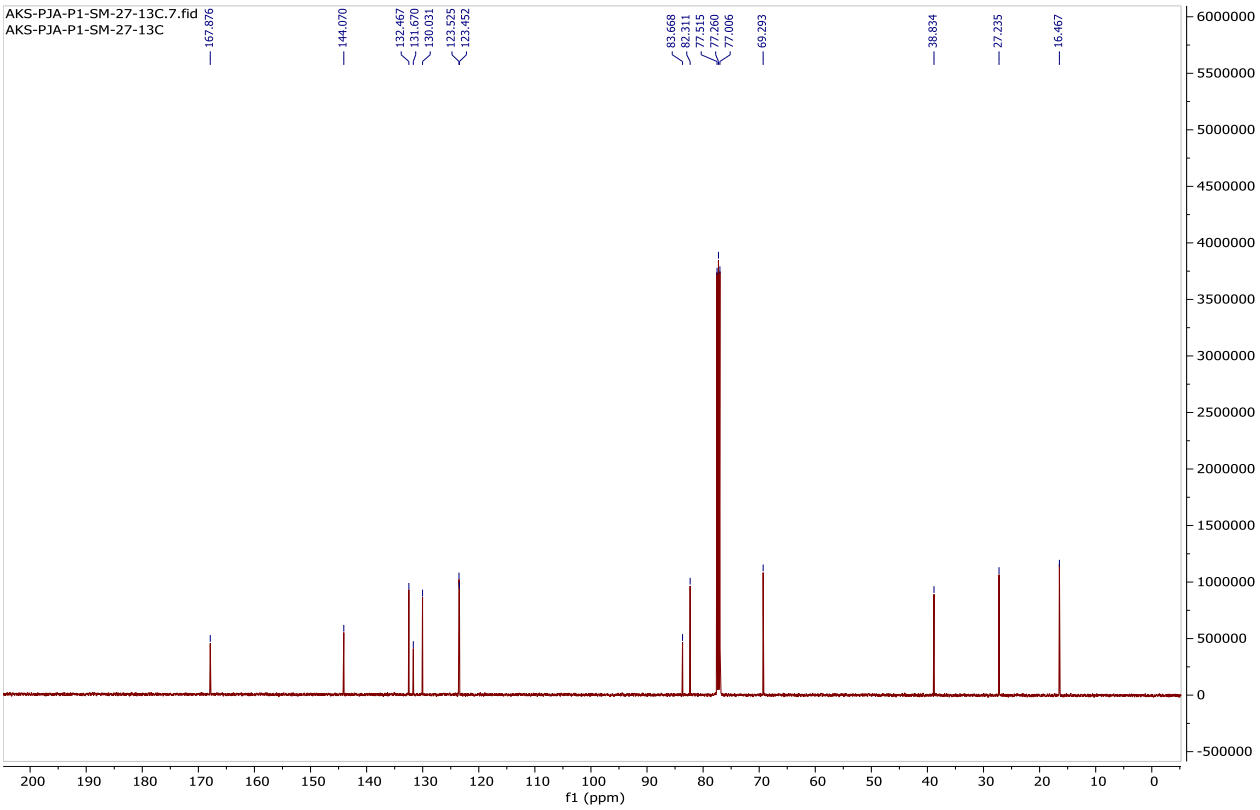
^{13}C{^{1}H} spectrum of compound **1u** (125 MHz, $CDCl_3$/DMSO–d_6)



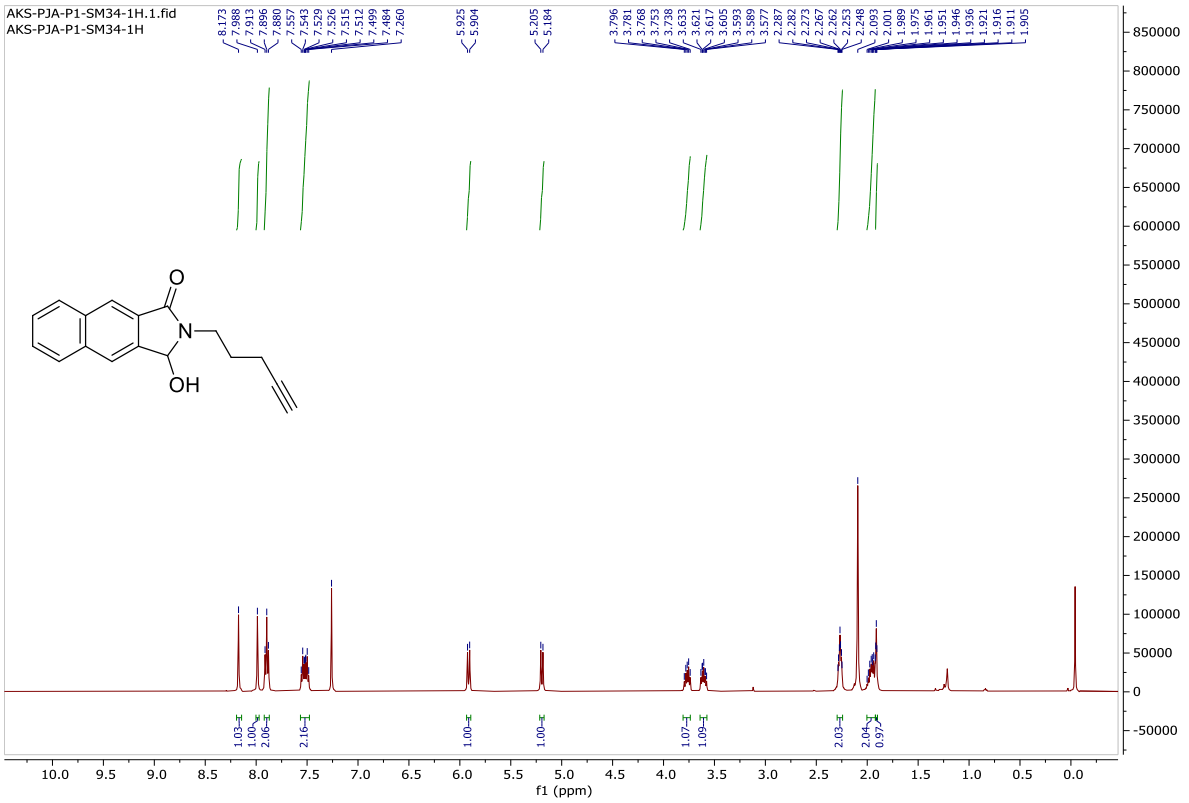
^{1}H spectrum of compound **1v** (500 MHz, $CDCl_3$)



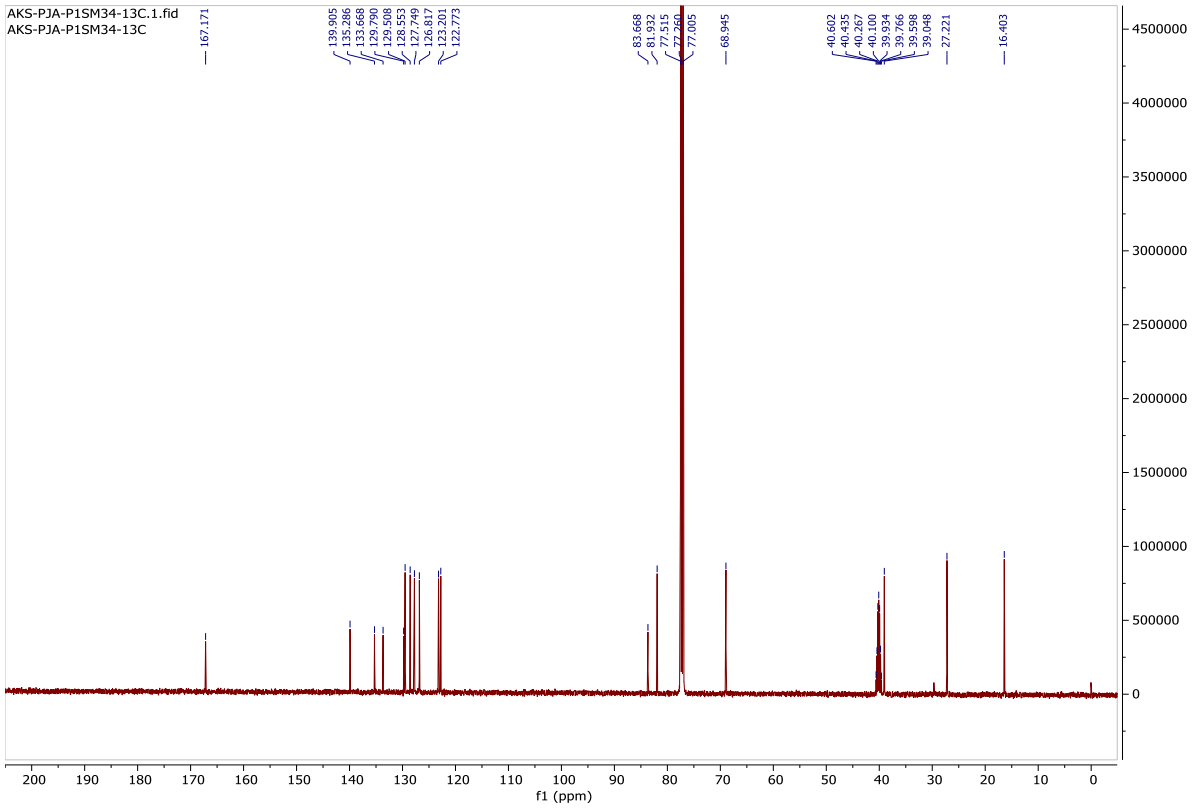
^{13}C{^{1}H} spectrum of compound **1v** (125 MHz, $CDCl_3$)



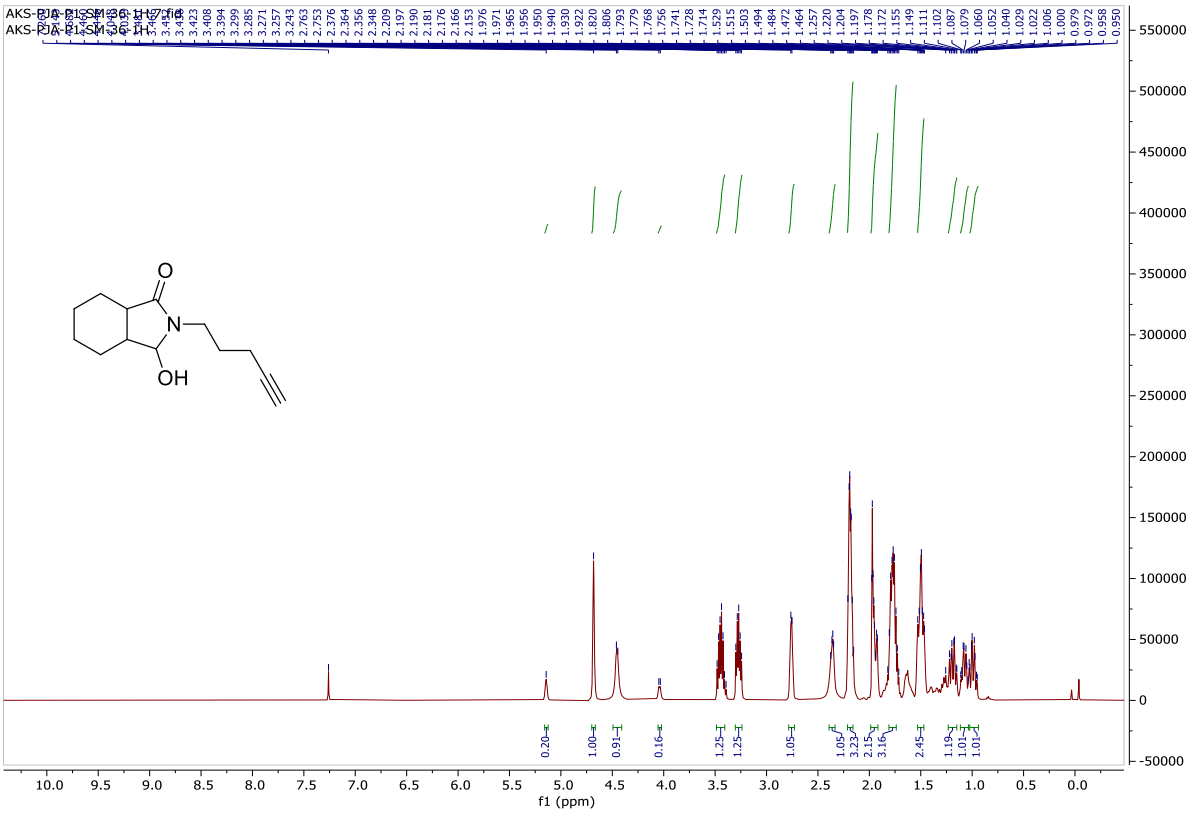
^{1}H spectrum of compound **1w** (500 MHz, $CDCl_3$/DMSO–d_6)



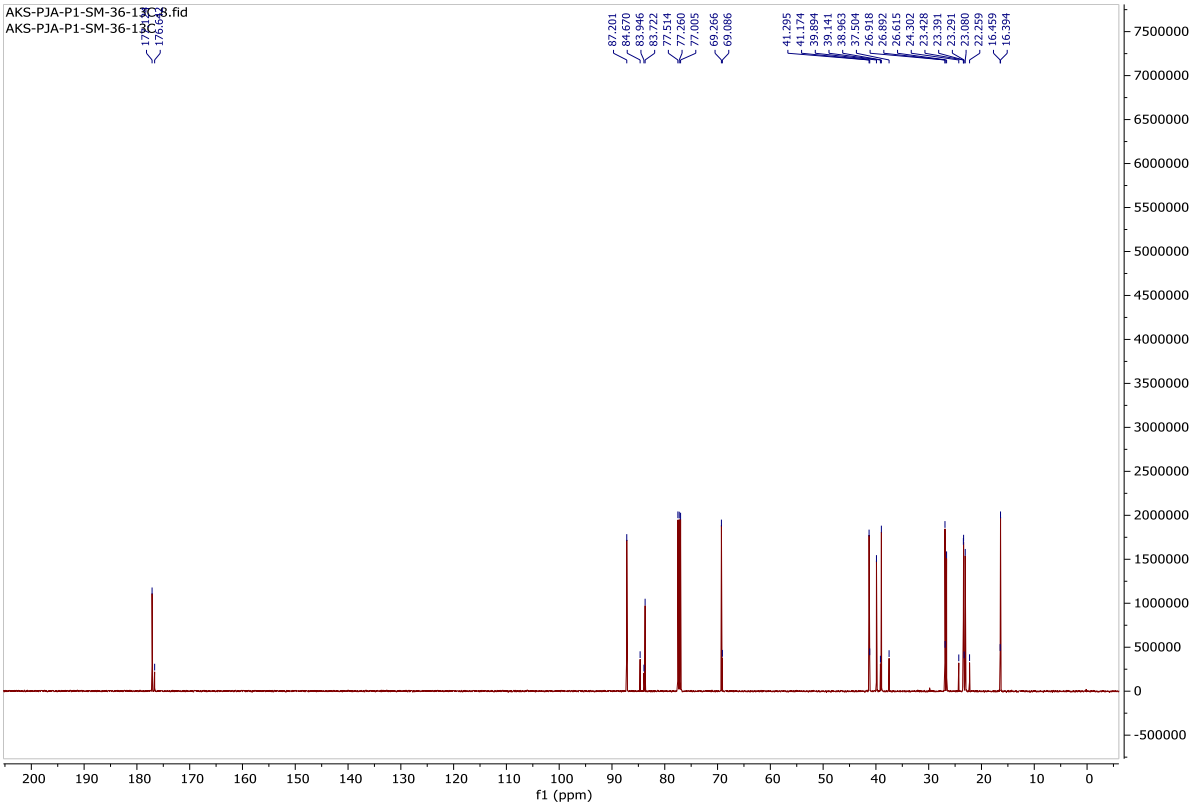
^{13}C{^{1}H} spectrum of compound **1w** (500 MHz, $CDCl_3$/DMSO–d_6)



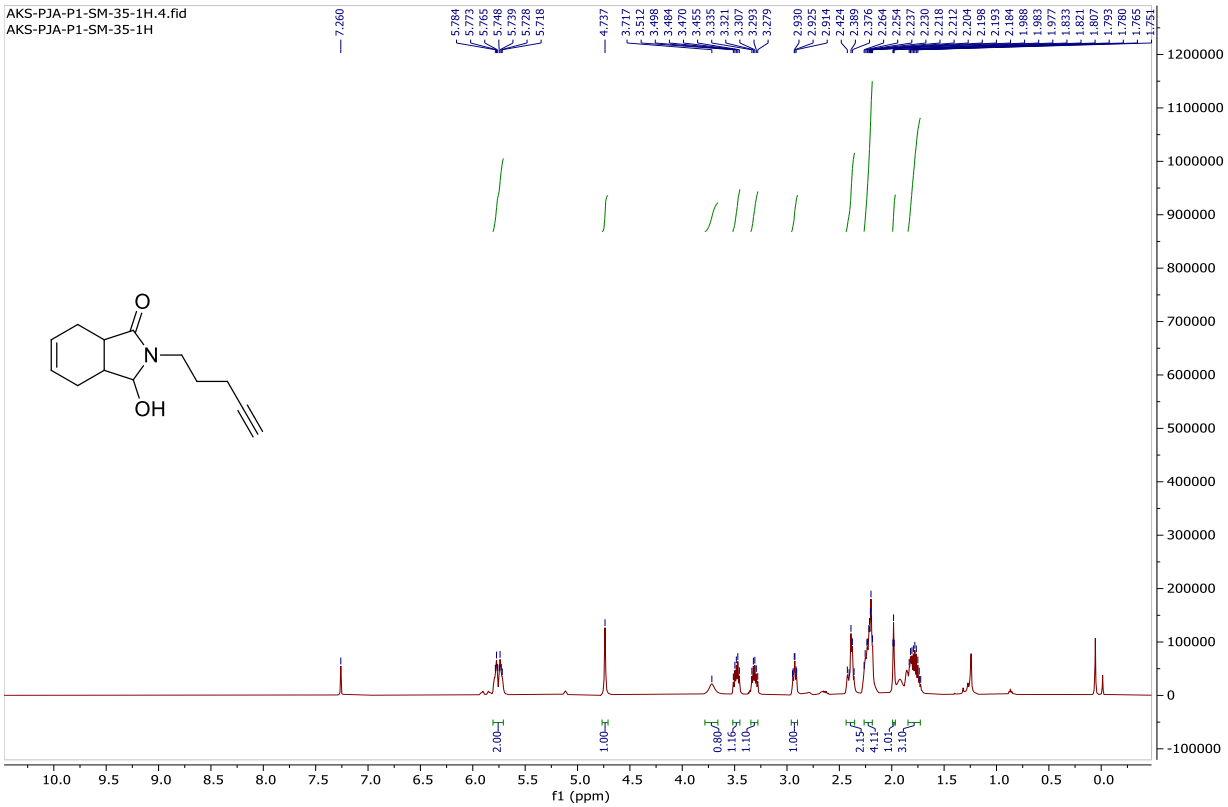
^{1}H spectrum of compound **1x** (500 MHz, $CDCl_3$)



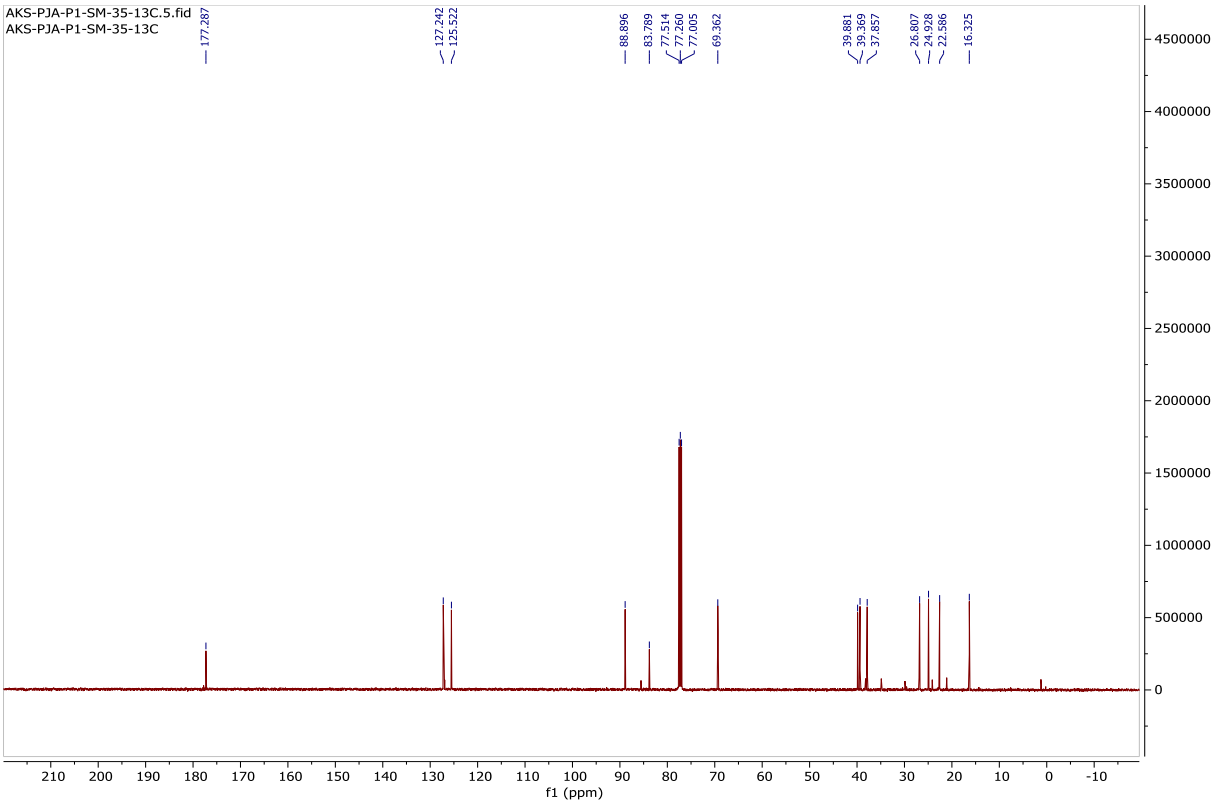
^{13}C{^{1}H} spectrum of compound **1x** (500 MHz, $CDCl_3$)



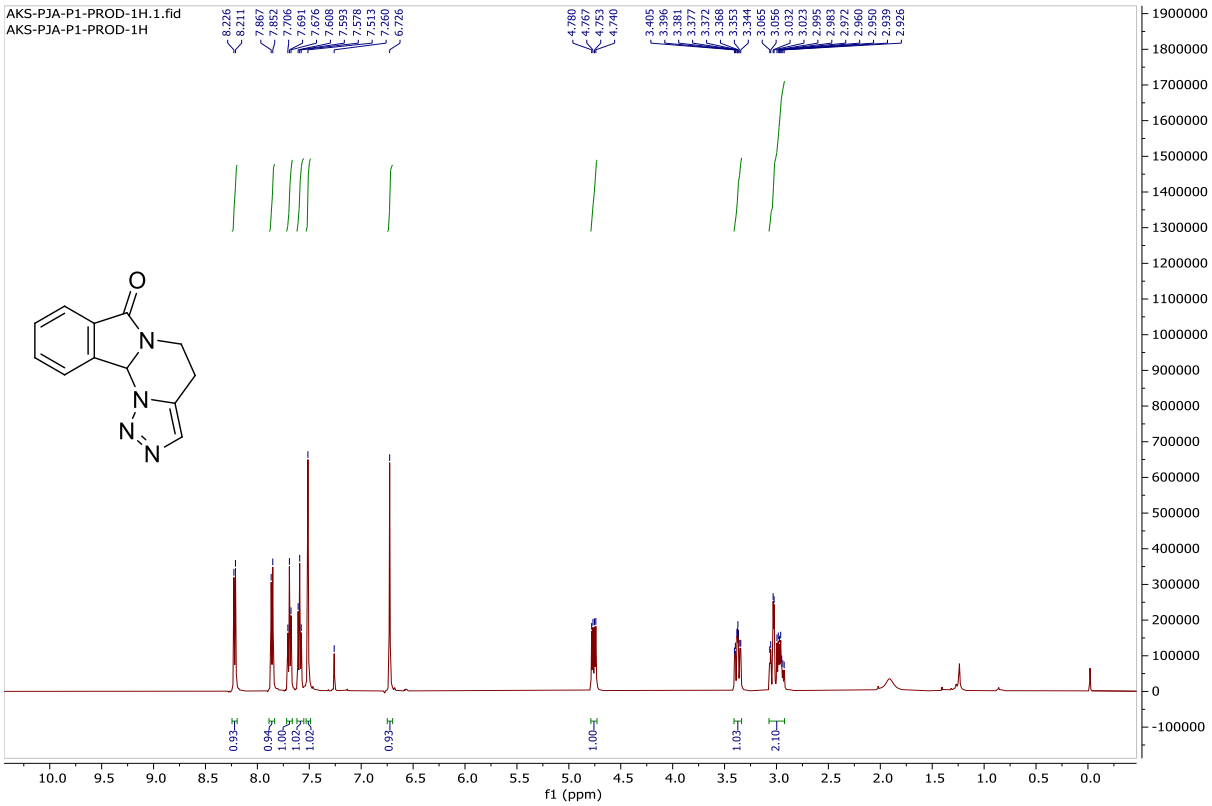
^{1}H spectrum of compound **1y** (500 MHz, $CDCl_3$)



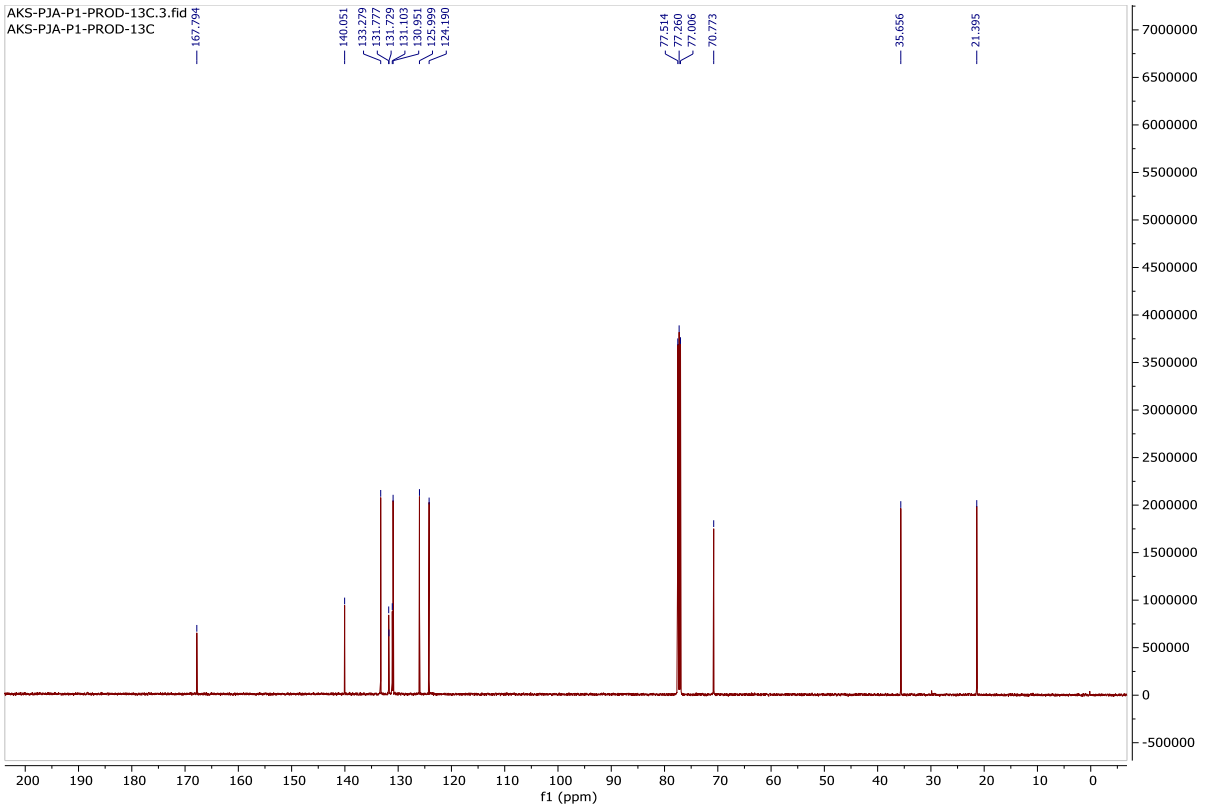
^{13}C{^{1}H} spectrum of compound **1y** (500 MHz, $CDCl_3$)



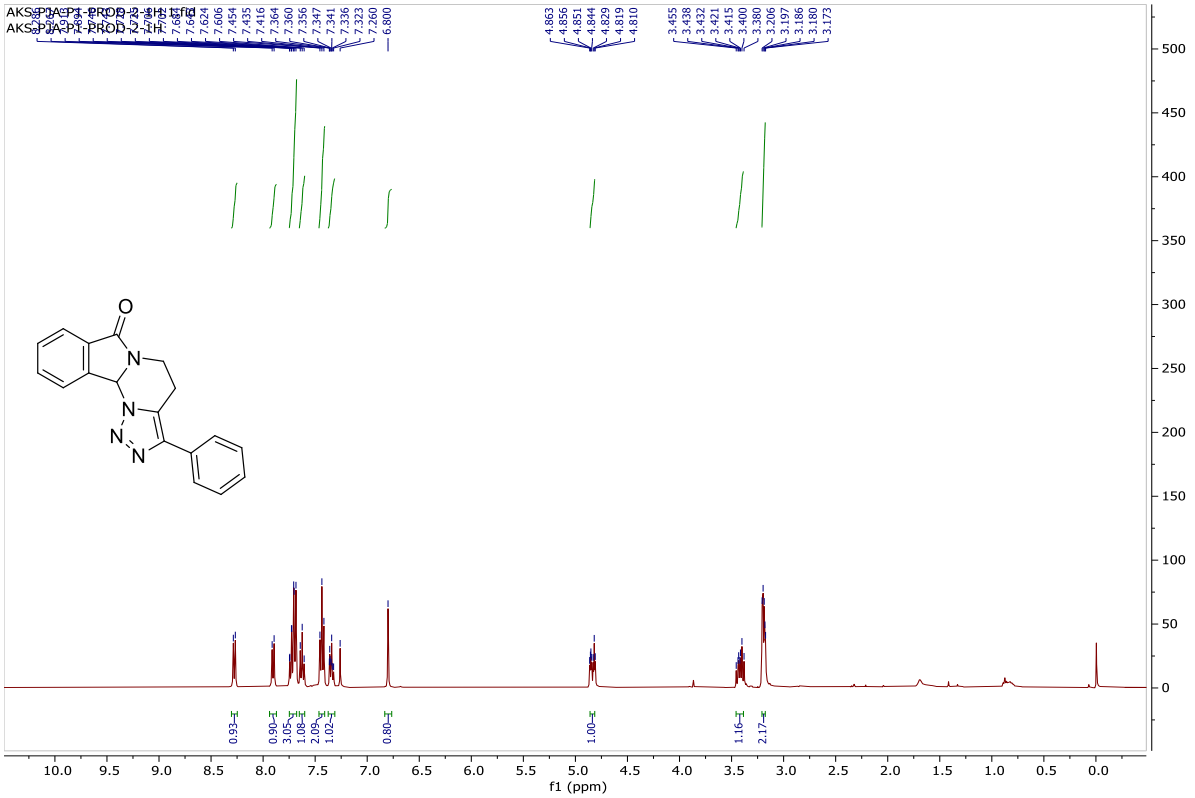
^{1}H spectrum of compound **2a** (500 MHz, $CDCl_3$)



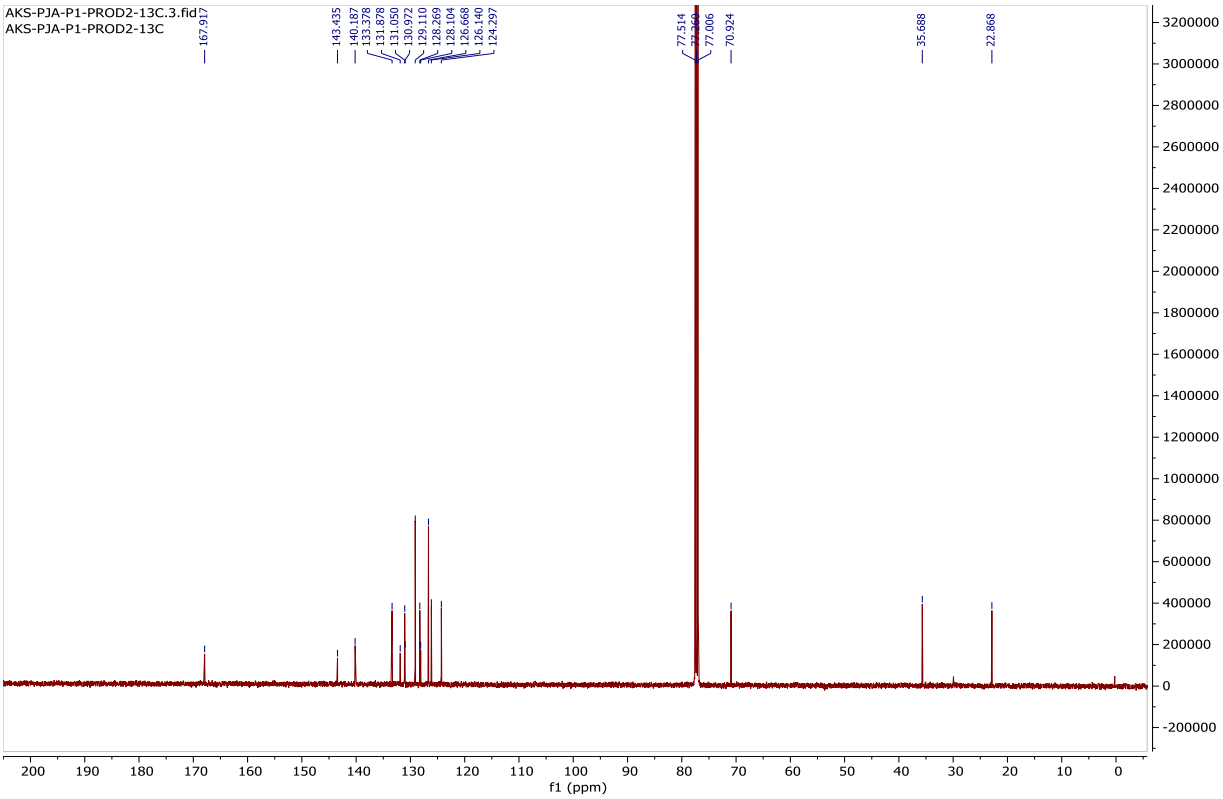
^{13}C {^{1}H} spectrum of compound **2a** (125 MHz, $CDCl_3$)



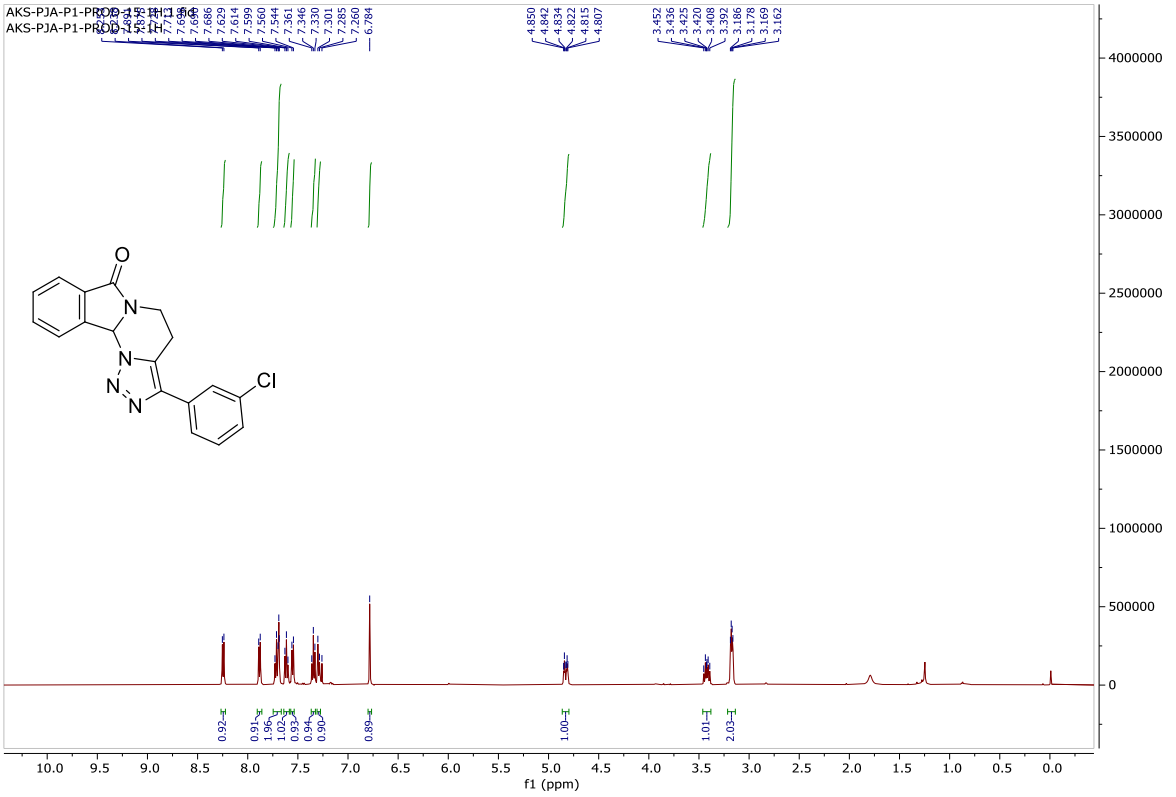
^{1}H spectrum of compound **2b** (400 MHz, $CDCl_3$)



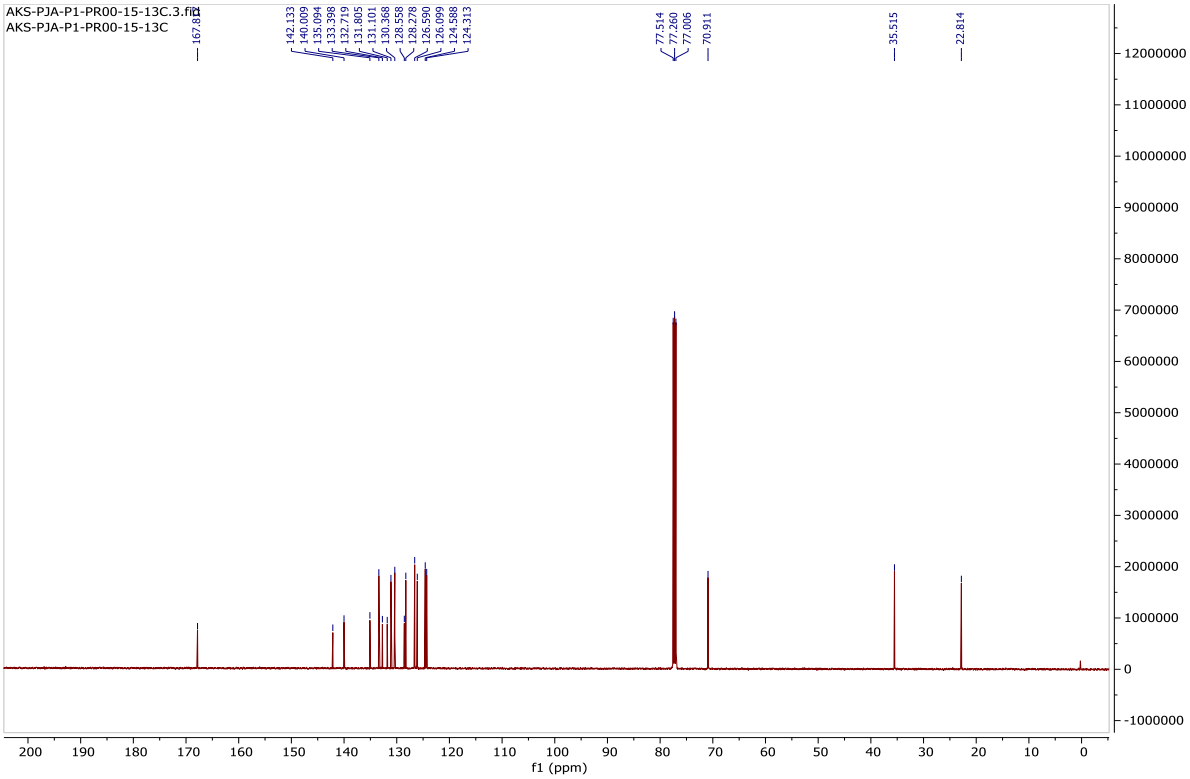
^{13}C {^{1}H} spectrum of compound **2b** (125 MHz, $CDCl_3$)



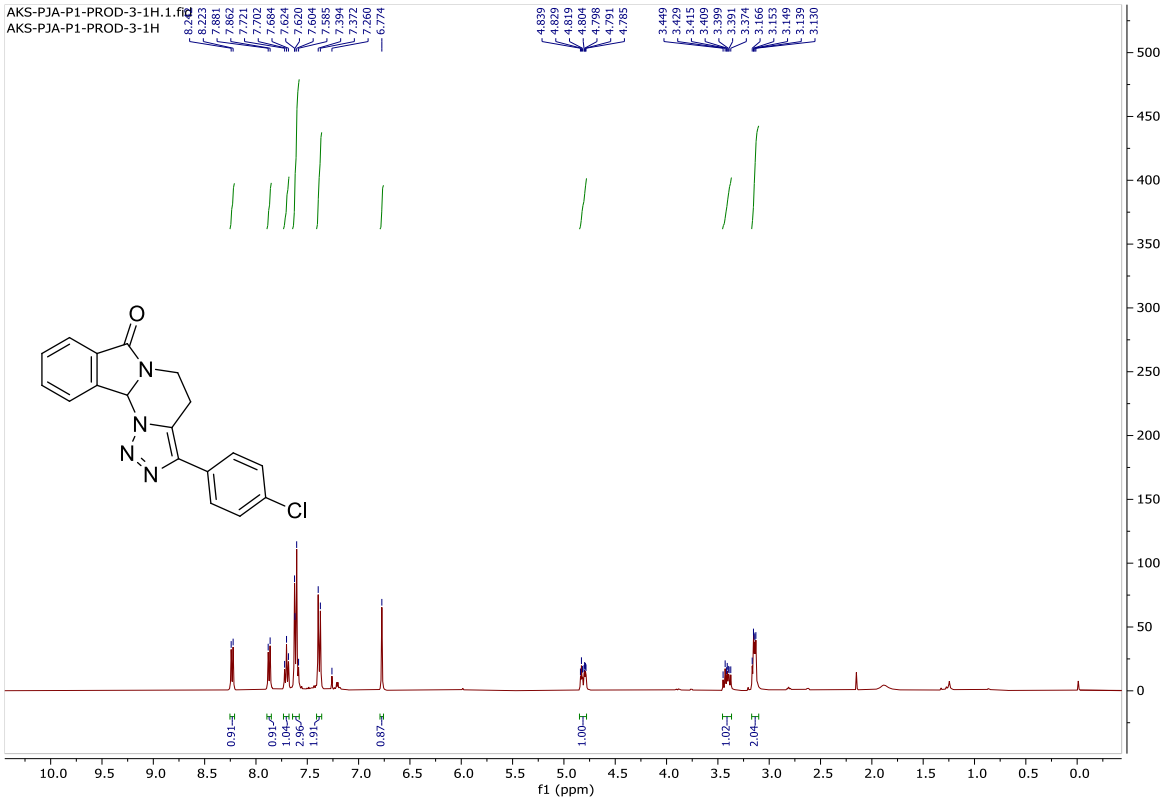
^{1}H spectrum of compound **2c** (500MHz, $CDCl_3$)



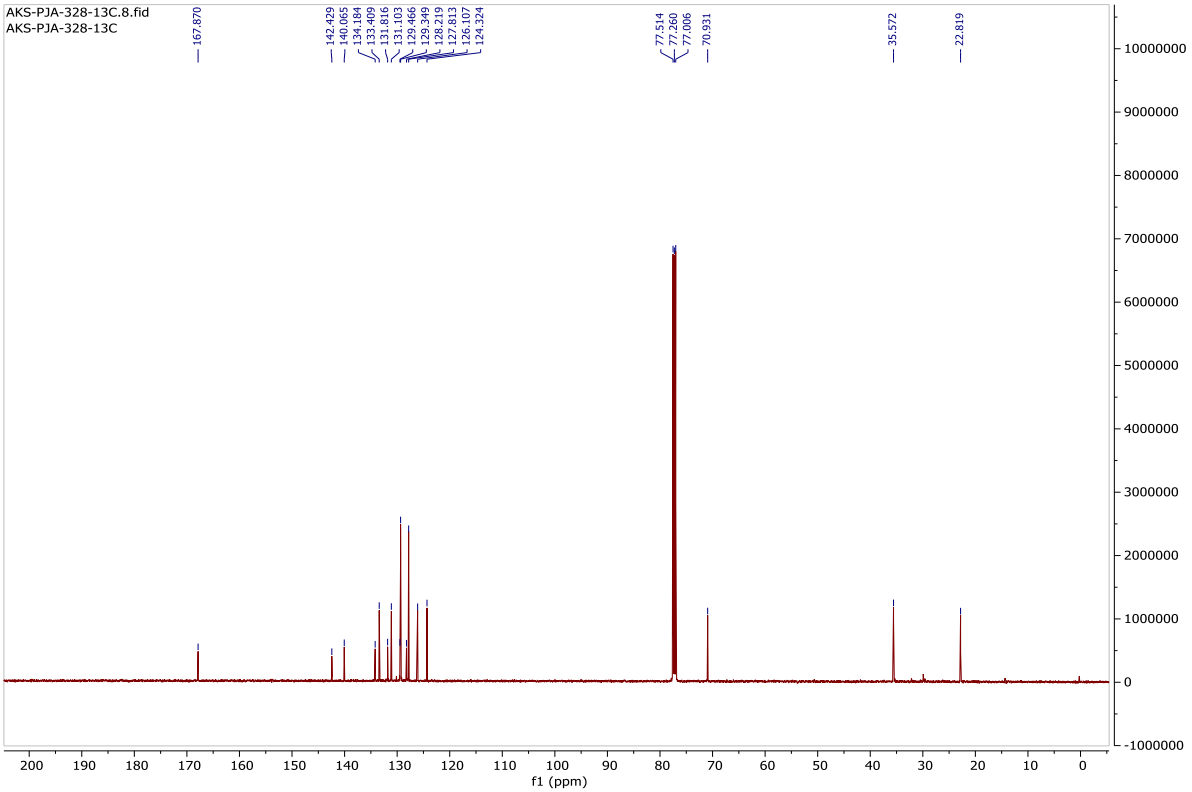
^{13}C {^{1}H} spectrum of compound **2c** (125MHz, $CDCl_3$)



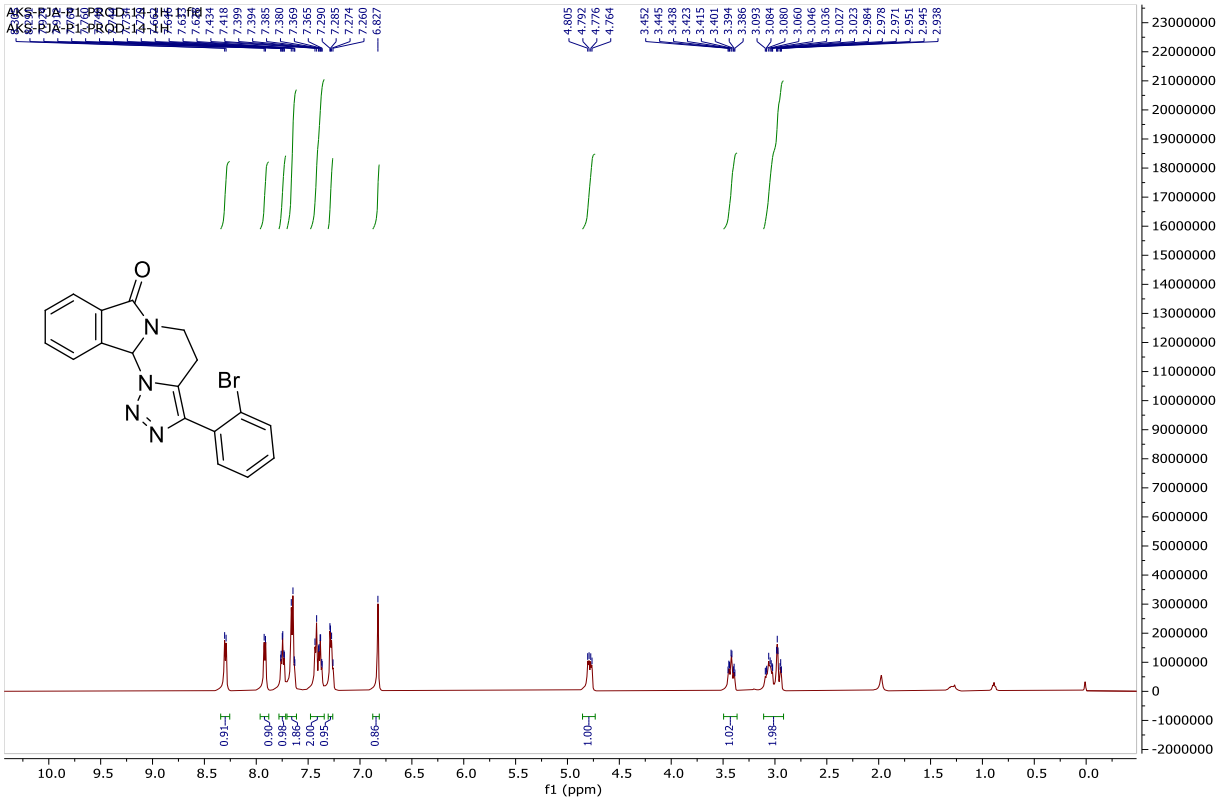
^{1}H spectrum of compound **2d** (400 MHz, $CDCl_3$)



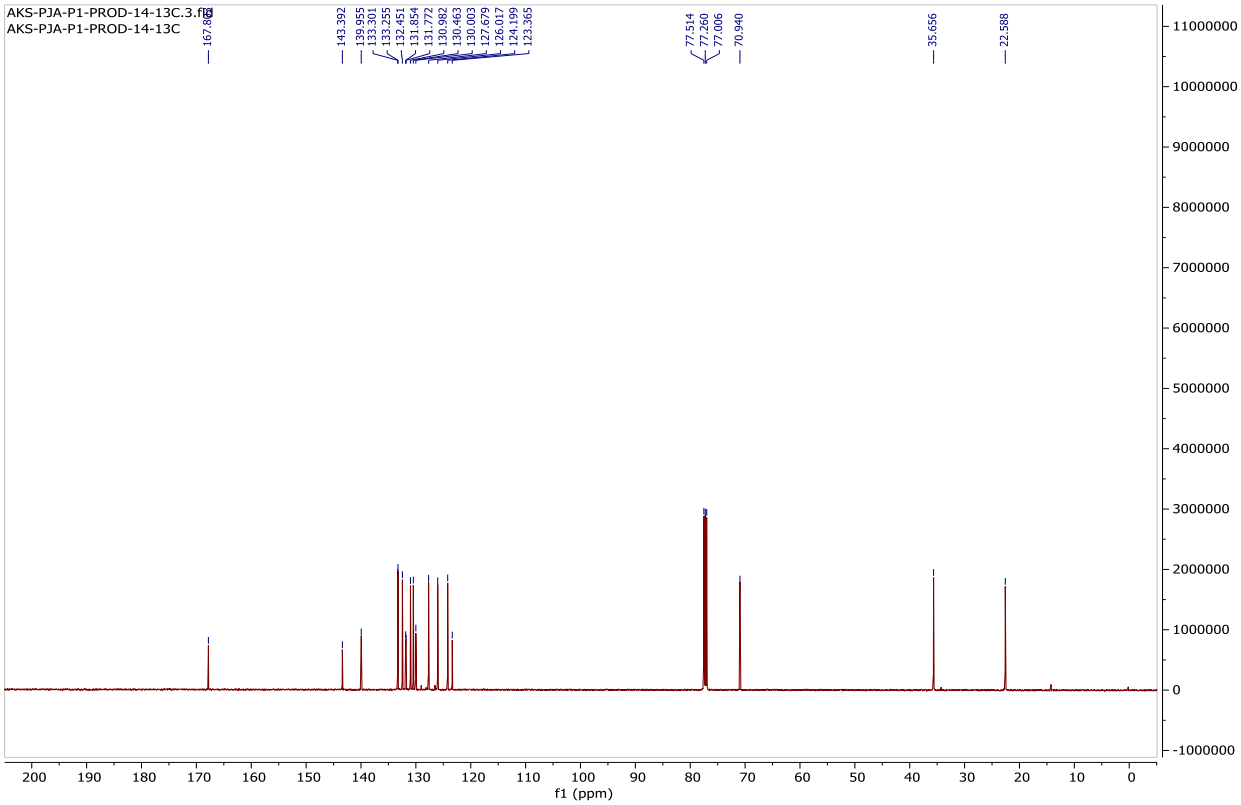
^{13}C {^{1}H} spectrum of compound **2d** (125 MHz, $CDCl_3$)



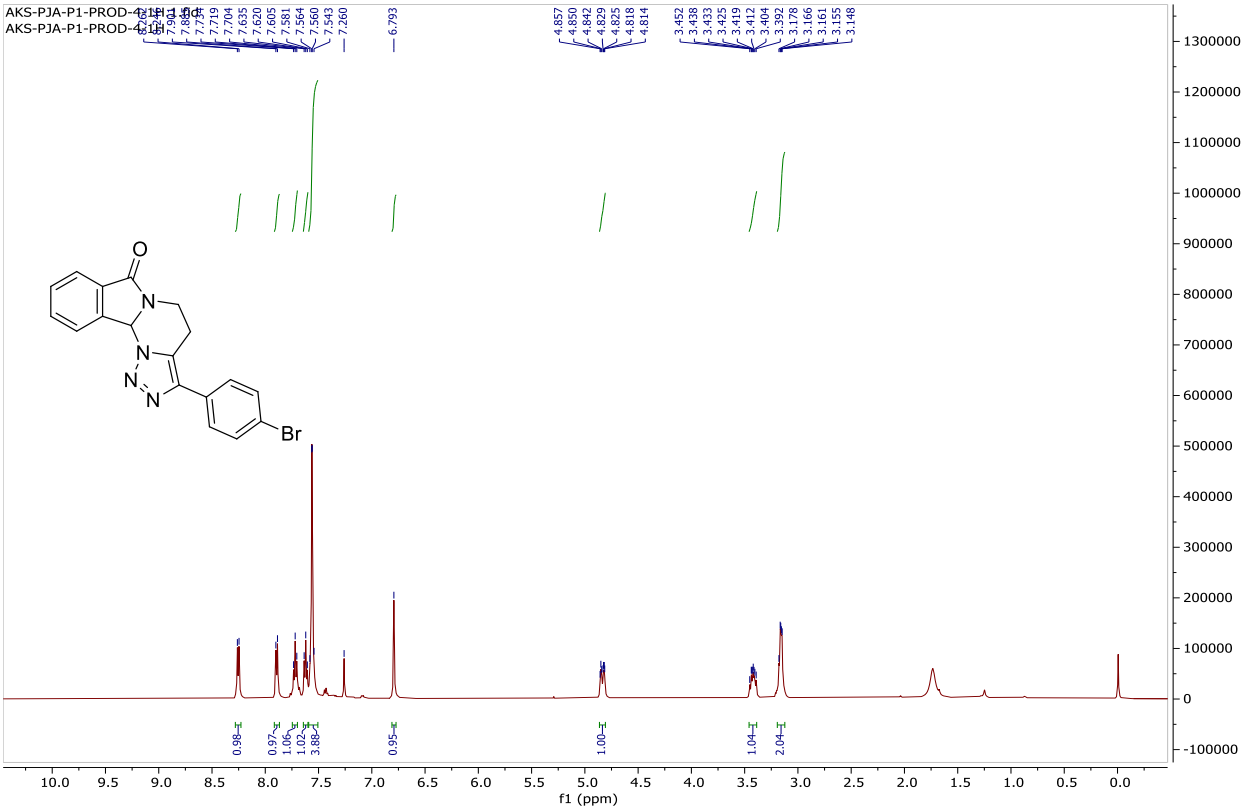
^{1}H spectrum of compound **2e** (500MHz, $CDCl_3$)



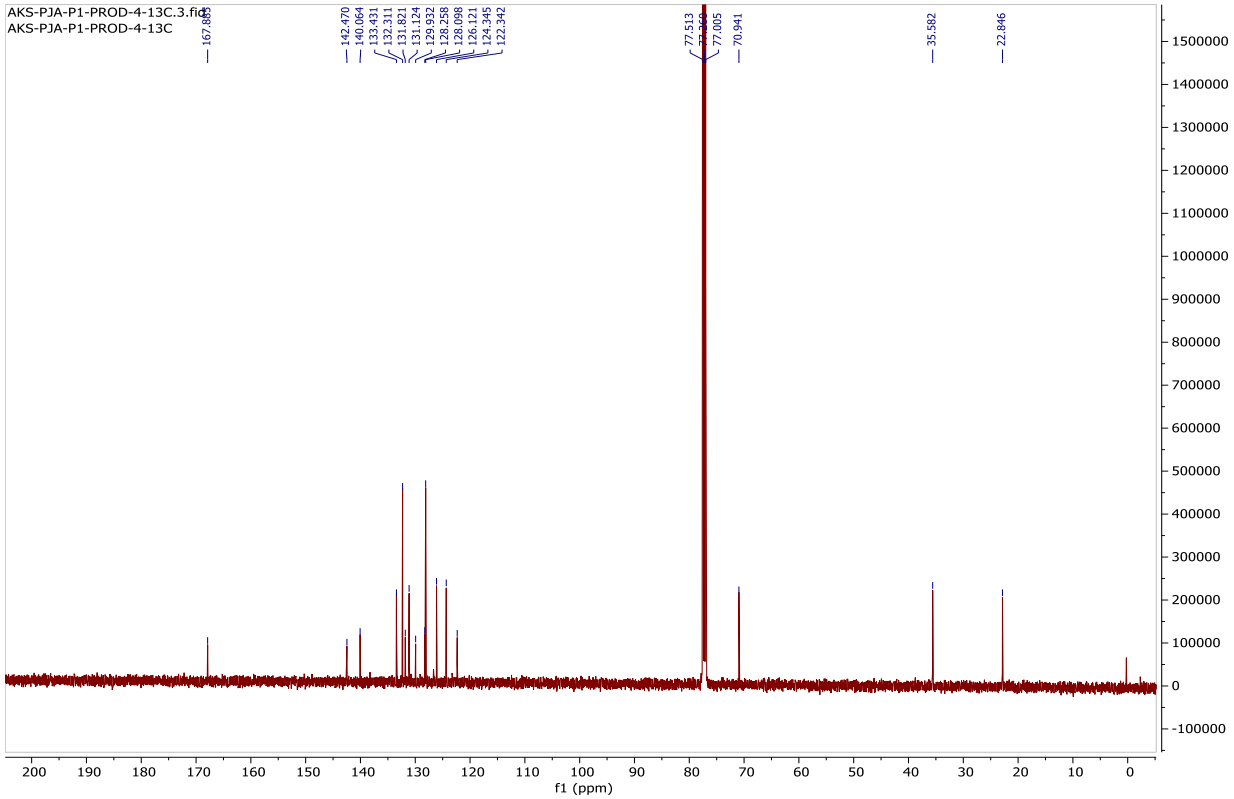
^{13}C {^{1}H} spectrum of compound **2e** (125MHz, $CDCl_3$)



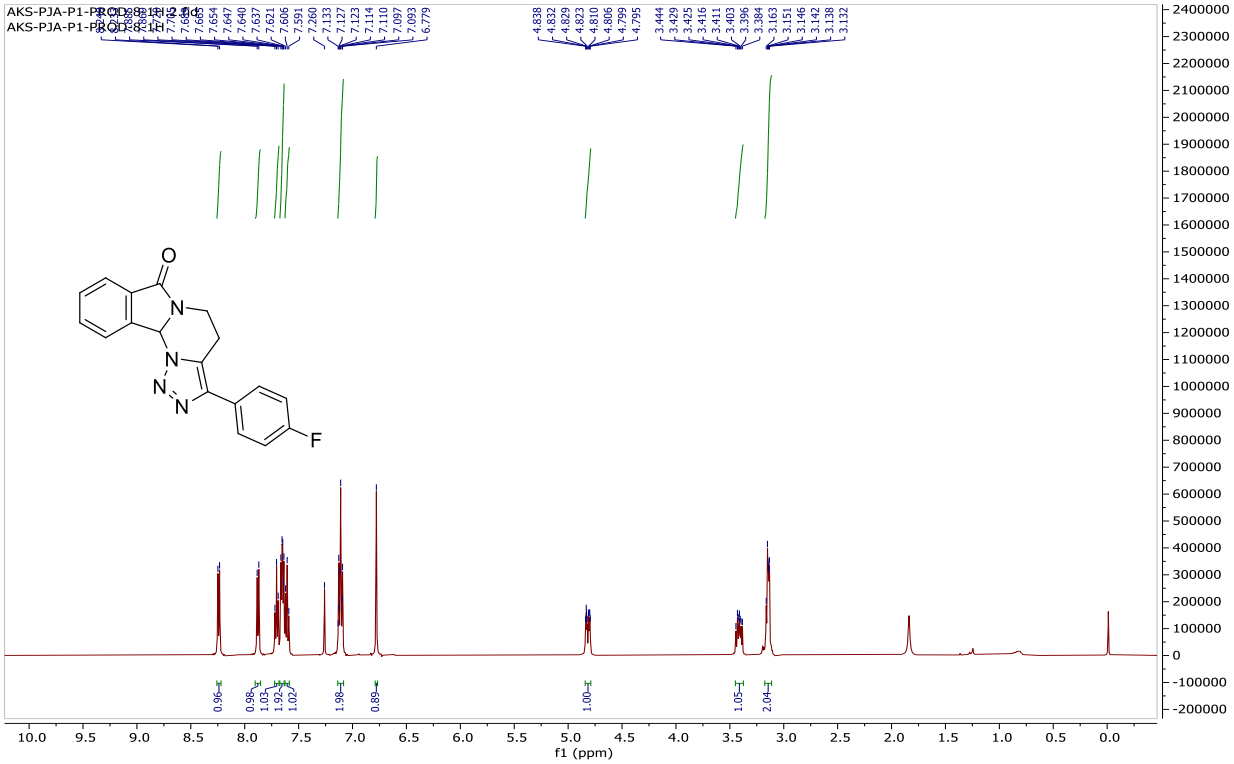
^{1}H spectrum of compound **2f** (500 MHz, $CDCl_3$)



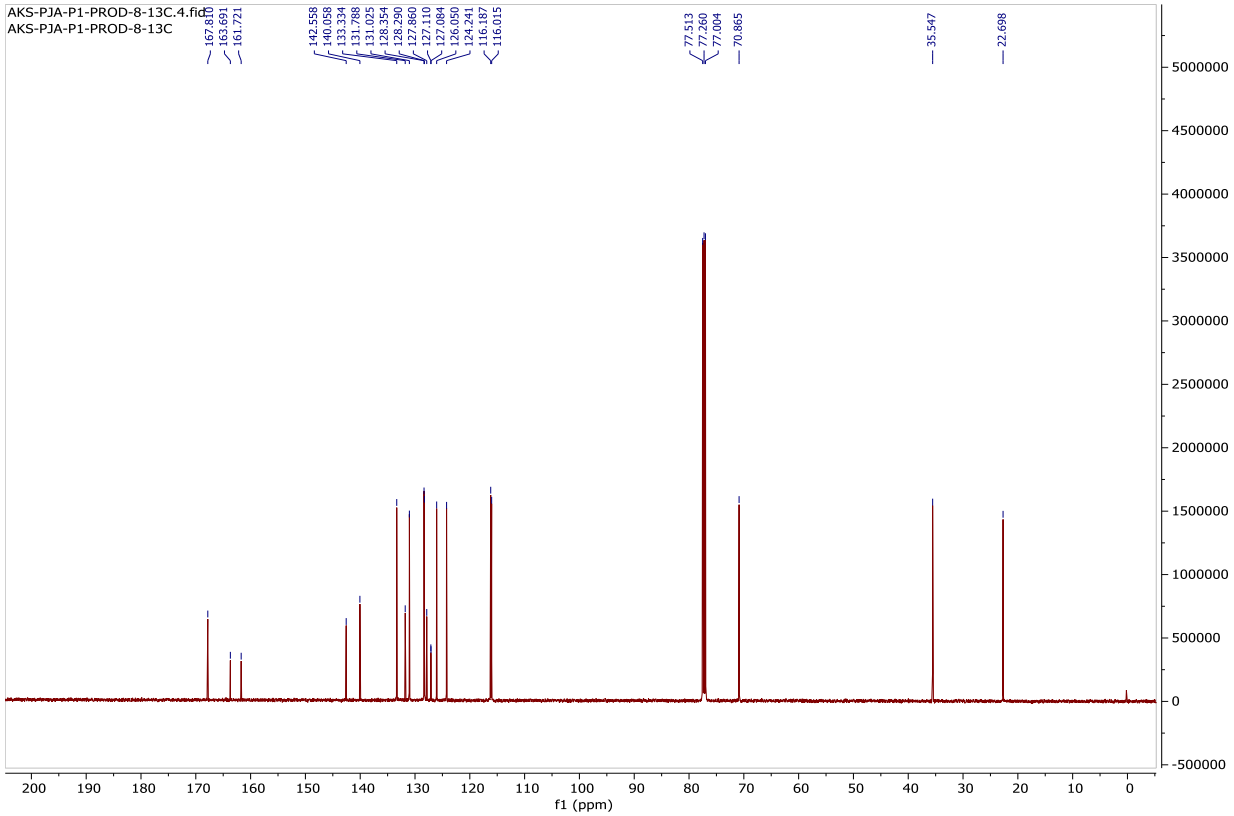
^{13}C {^{1}H} spectrum of compound **2f** (125 MHz, $CDCl_3$)



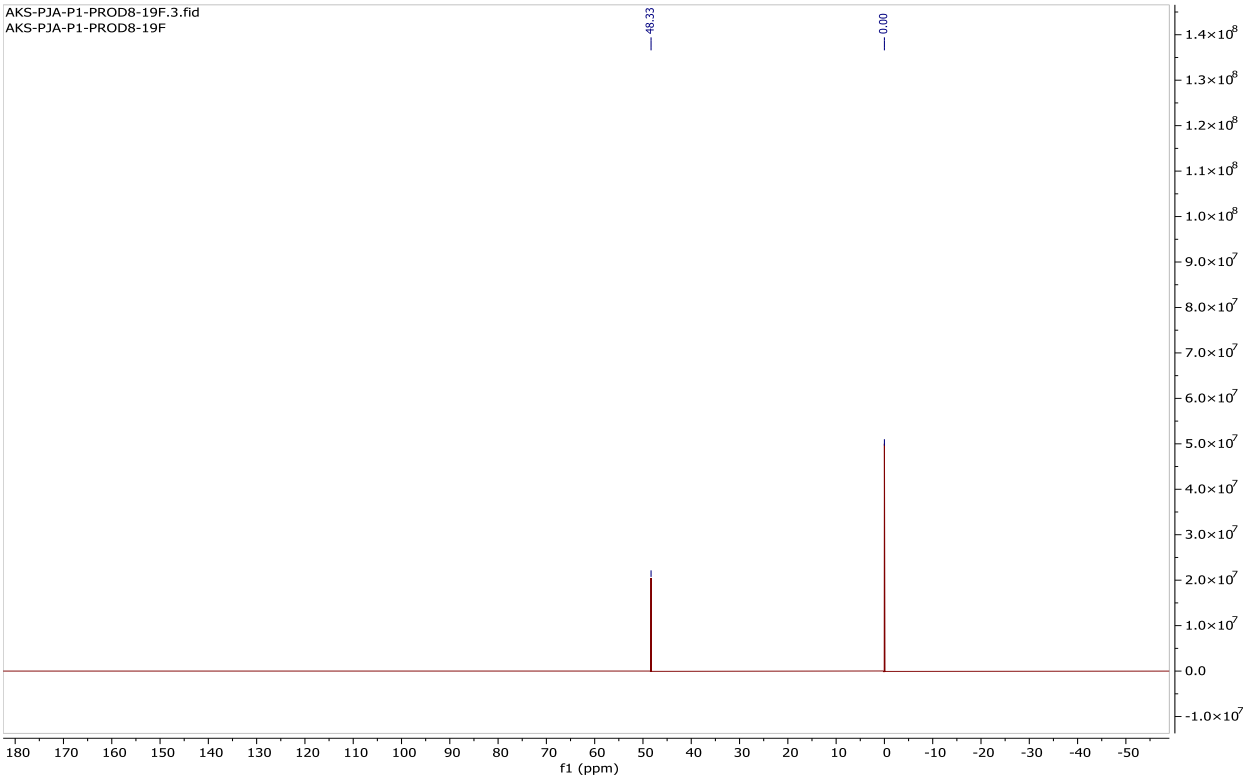
^{1}H spectrum of compound **2g** (500MHz, $CDCl_3$)



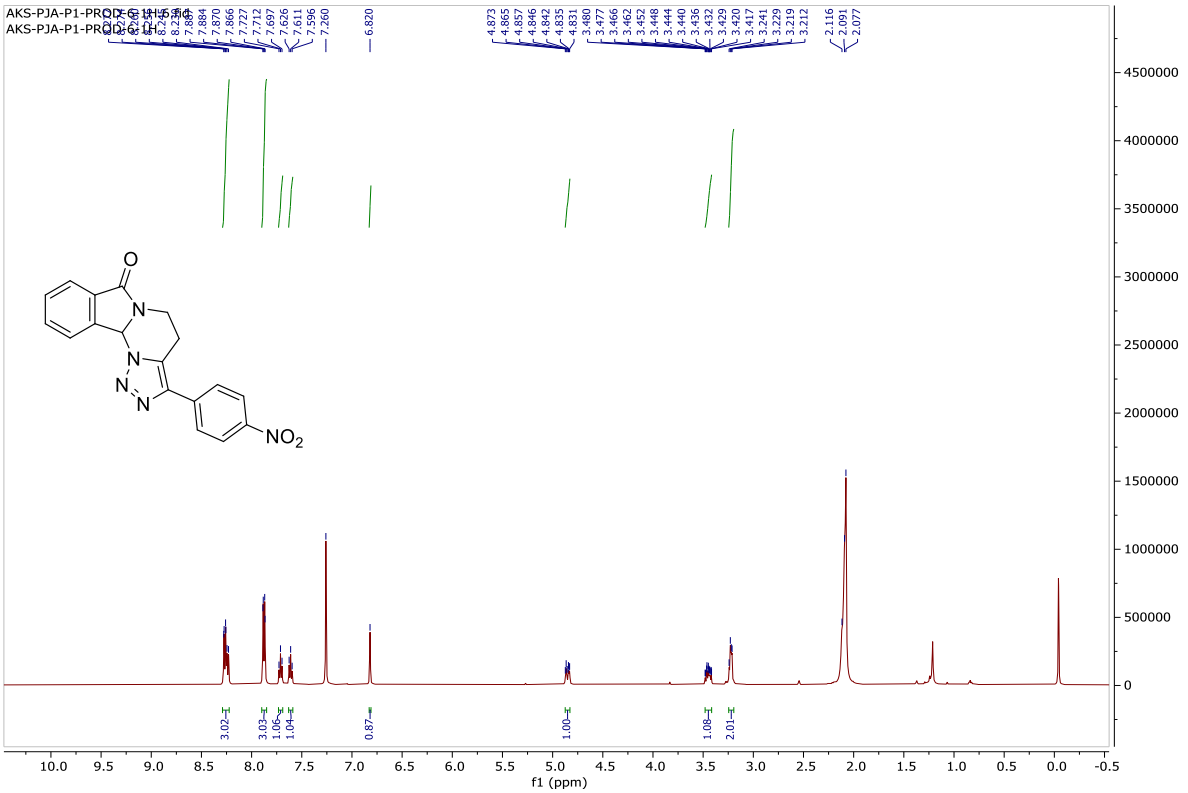
^{13}C {^{1}H} spectrum of compound **2g** (125 MHz, $CDCl_3$)



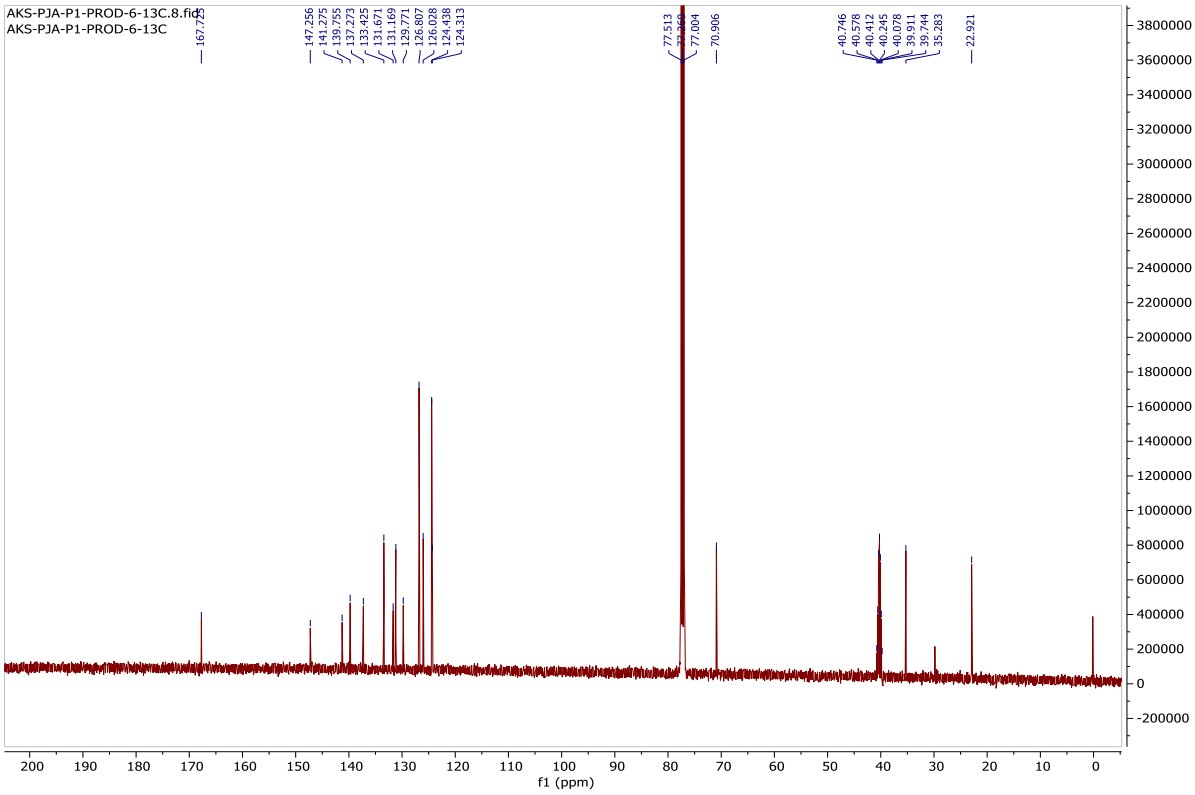
^{19}F spectrum of compound **2g** (470 MHz, $C_6F_6/CDCl_3$)



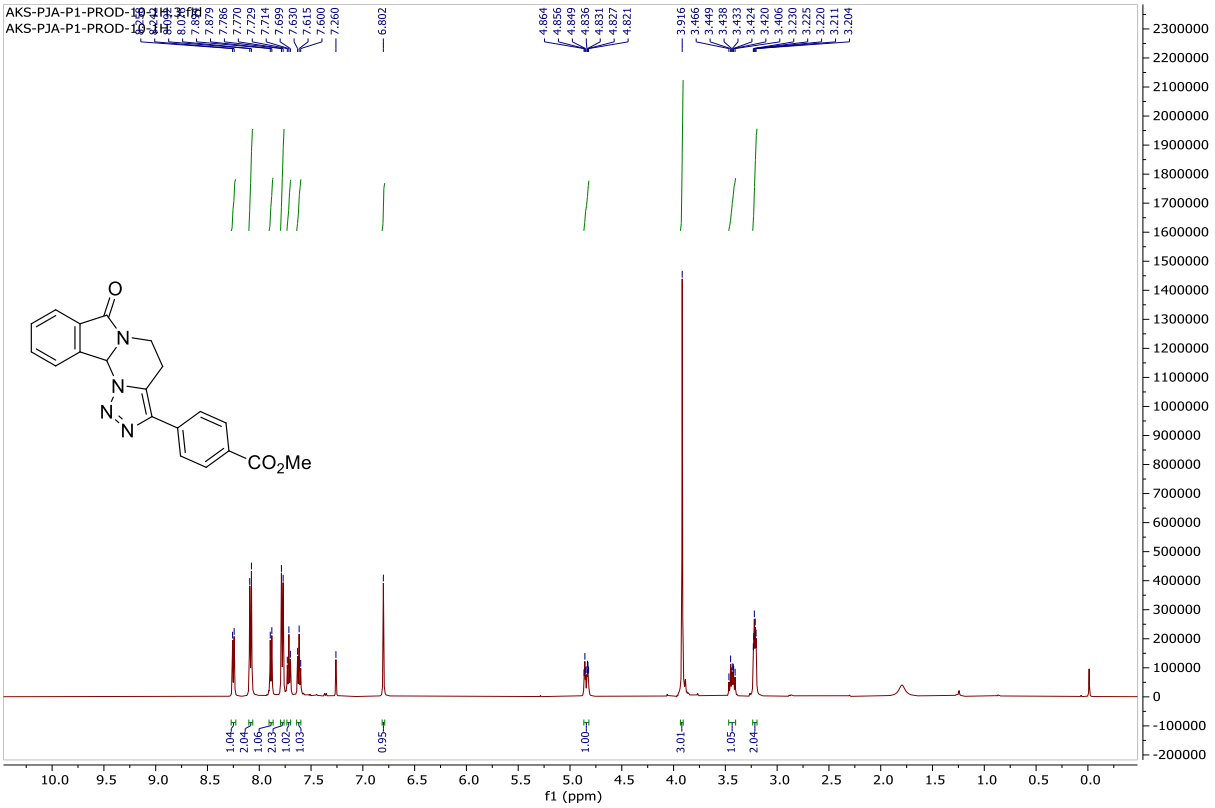
^{1}H spectrum of compound **2h** (500 MHz, $CDCl_3$/DMSO–d_6)



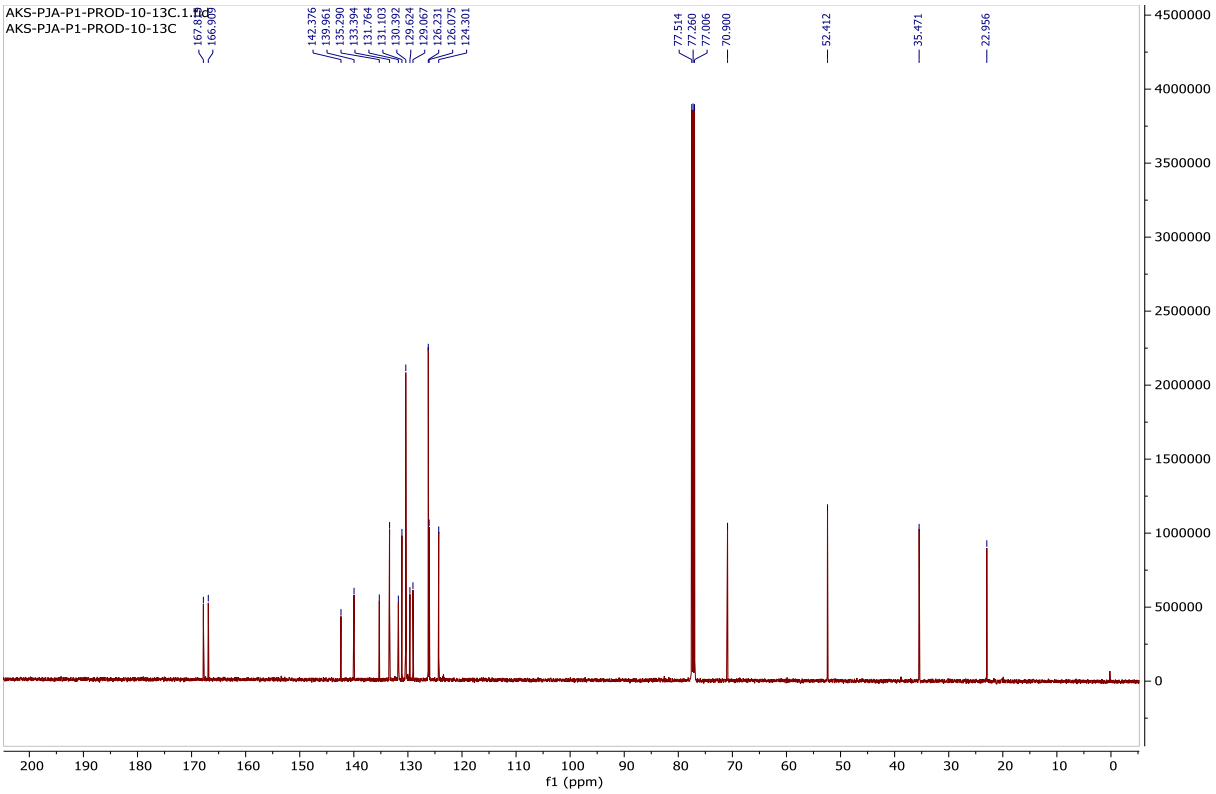
^{13}C {^{1}H} spectrum of compound **2h** (125 MHz, $CDCl_3$/DMSO–d_6)



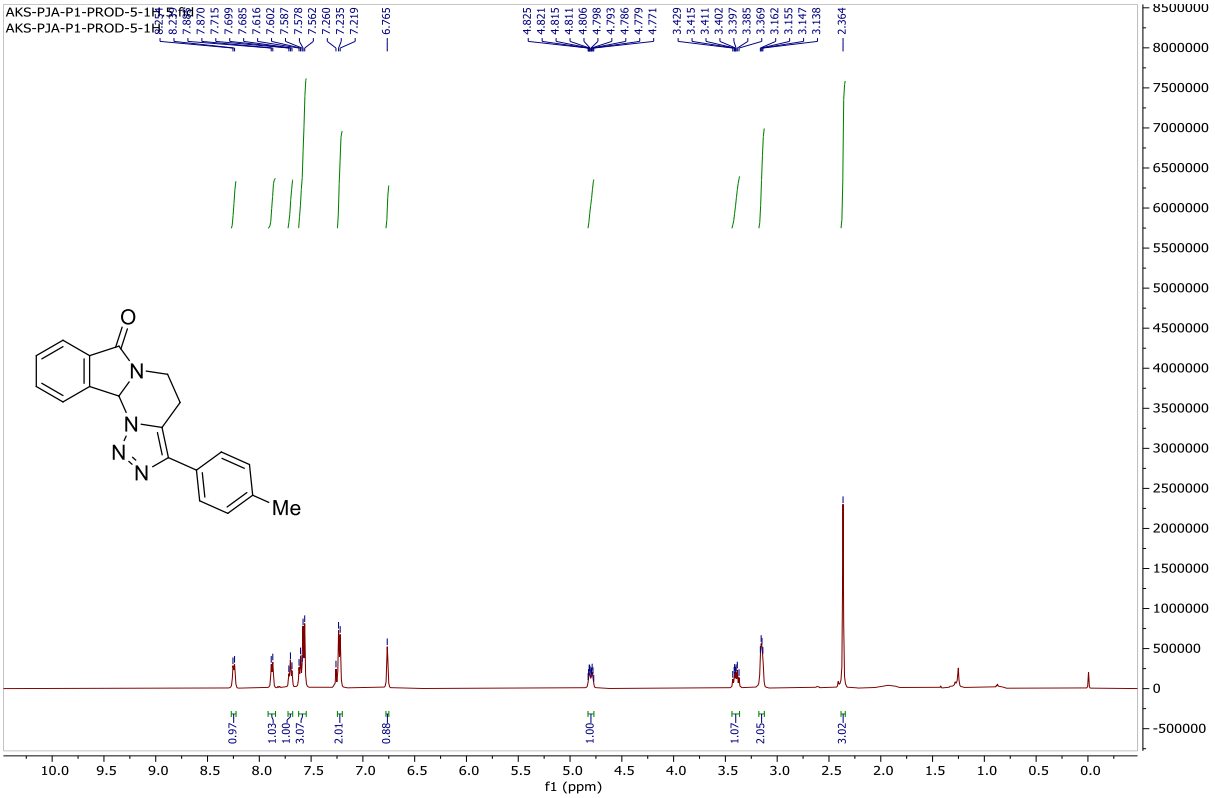
^{1}H spectrum of compound **2i** (500 MHz, $CDCl_3$)



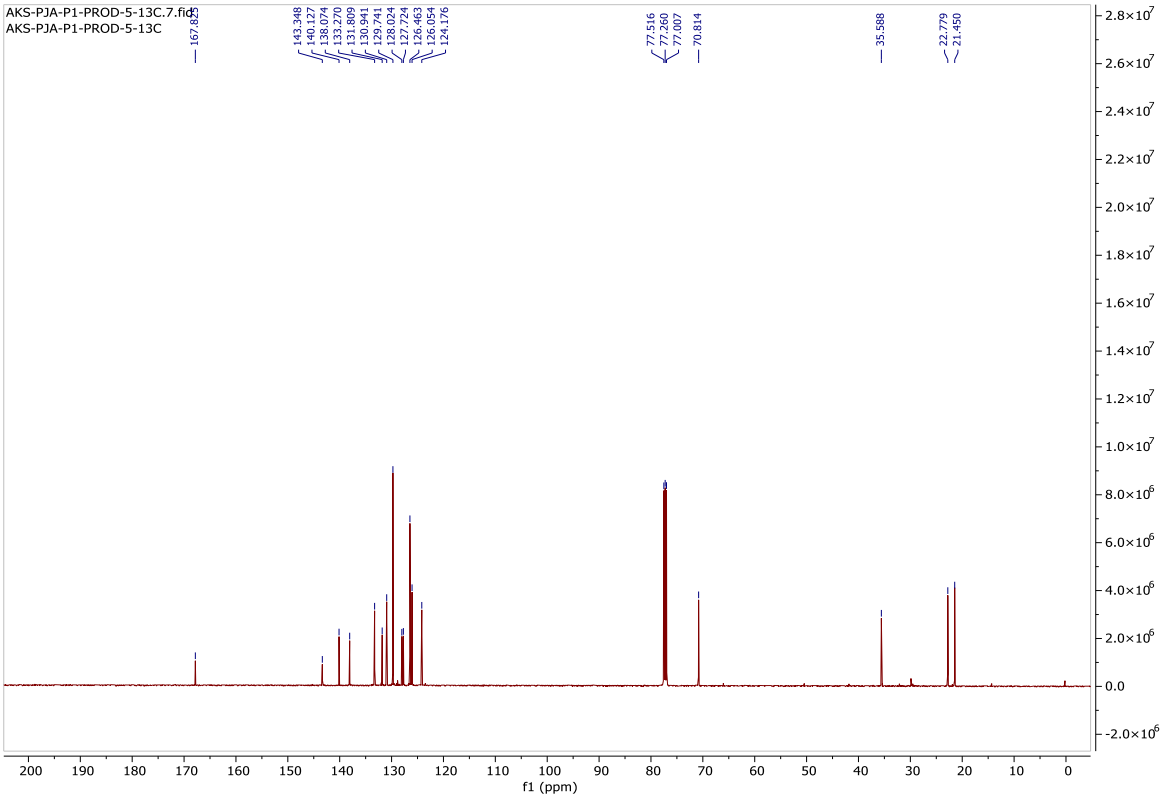
^{13}C {^{1}H} spectrum of compound **2i** (125 MHz, $CDCl_3$)



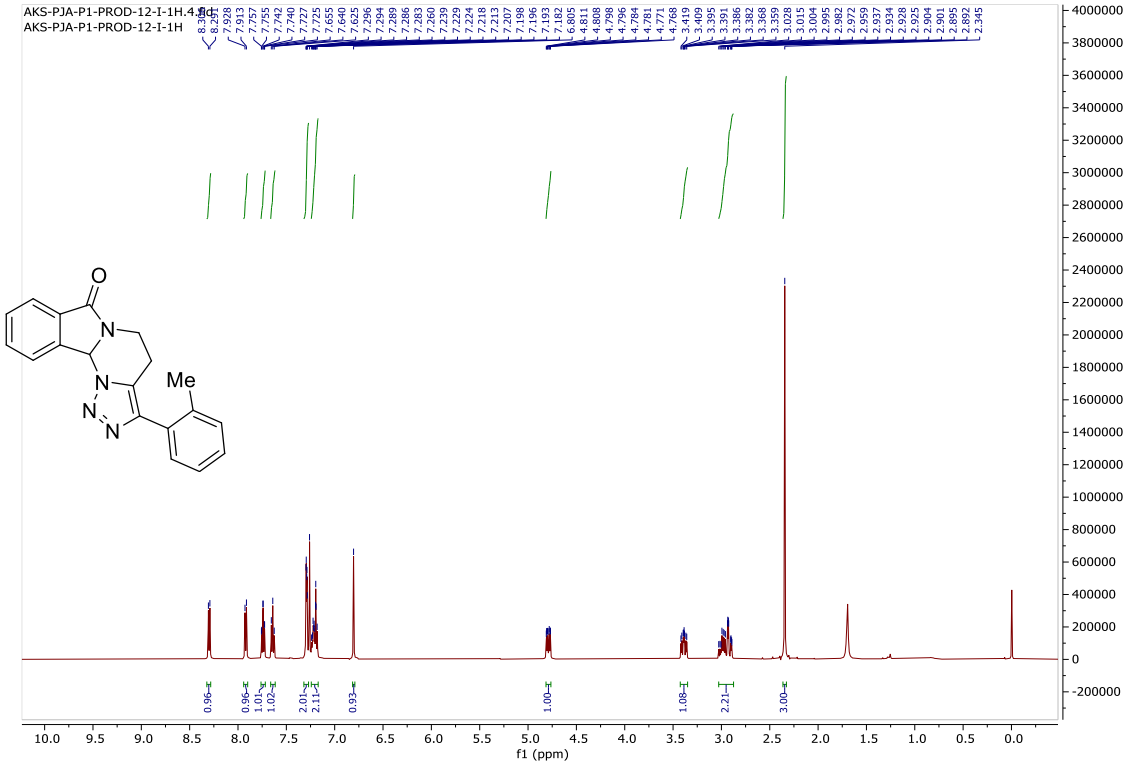
^{1}H spectrum of compound **2j** (500 MHz, $CDCl_3$)



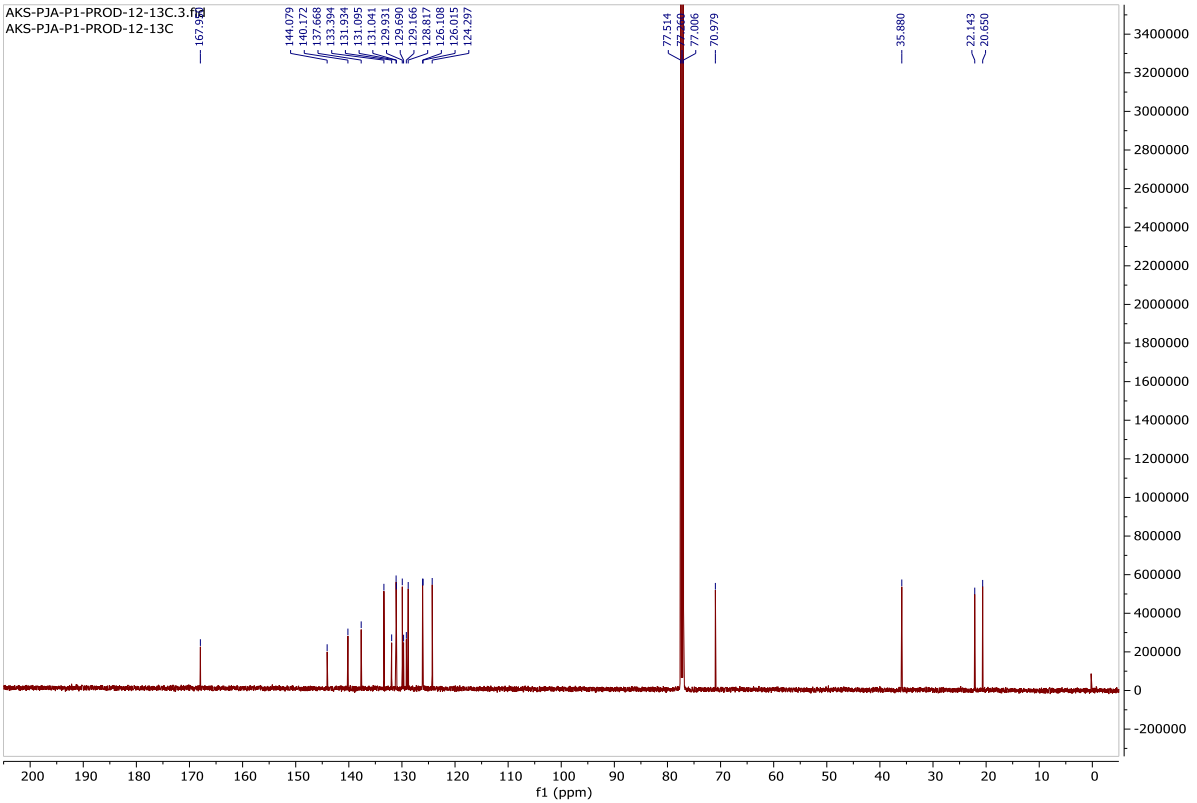
^{13}C {^{1}H} spectrum of compound **2j** (125 MHz, $CDCl_3$)



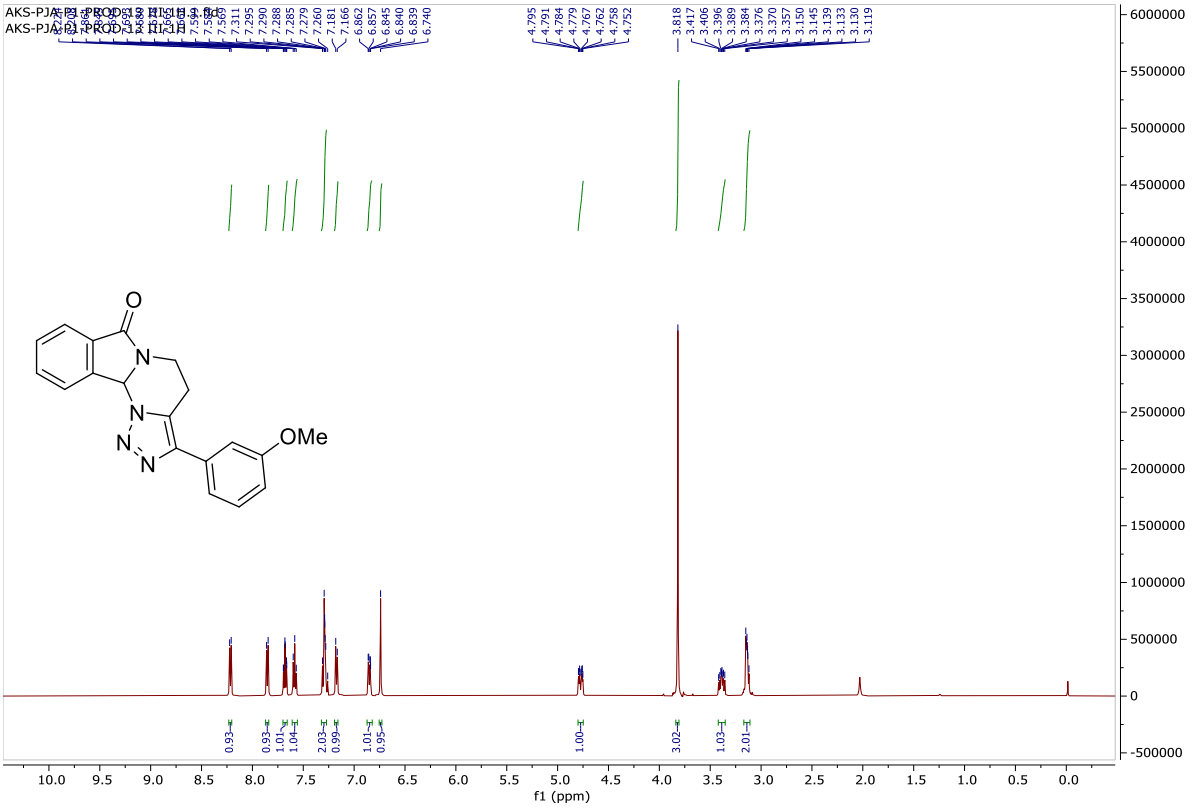
^{1}H spectrum of compound **2k** (500 MHz, $CDCl_3$)



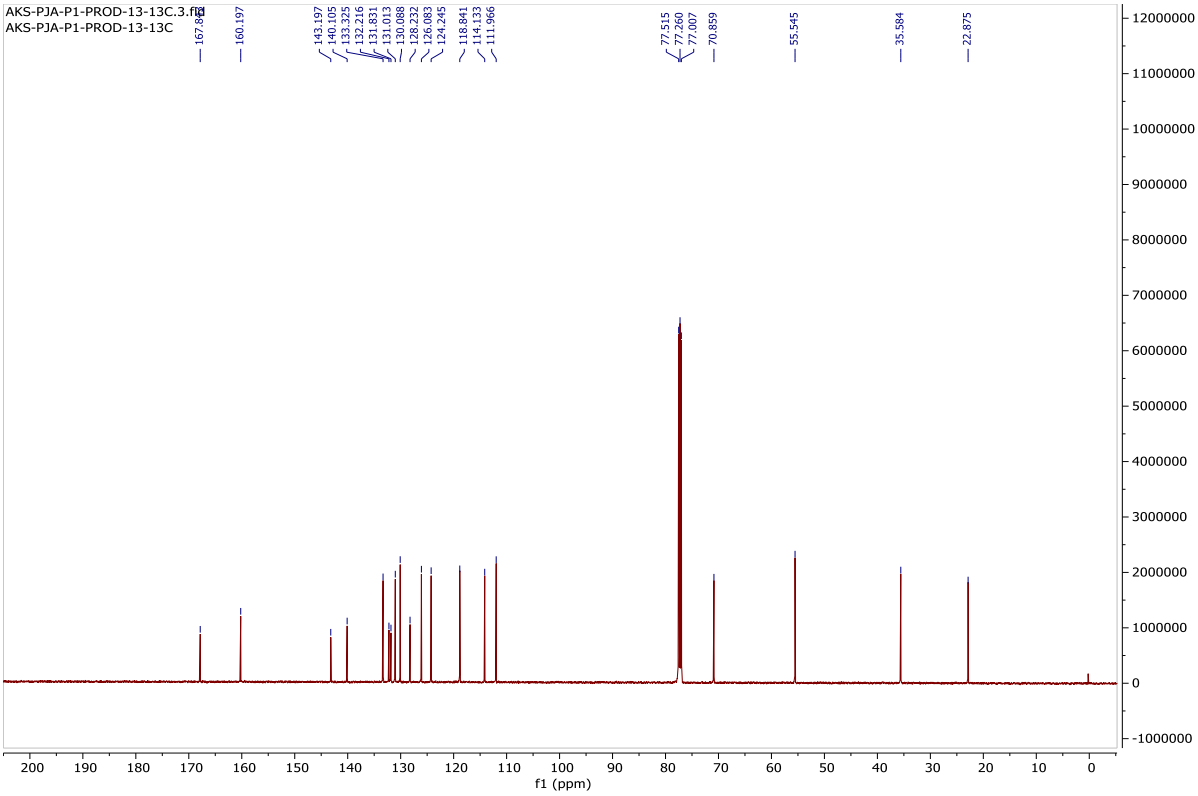
^{13}C {^{1}H} spectrum of compound **2k** (125 MHz, $CDCl_3$)



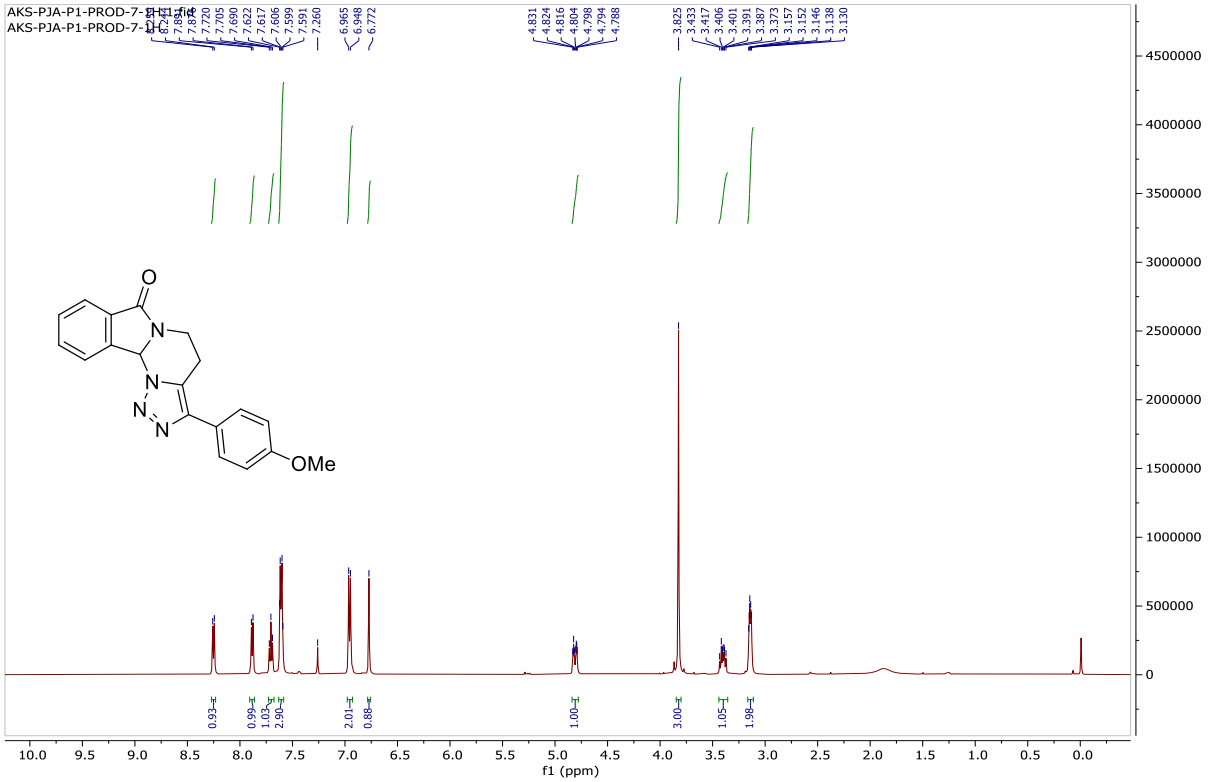
^{1}H spectrum of compound **2l** (500 MHz, $CDCl_3$)



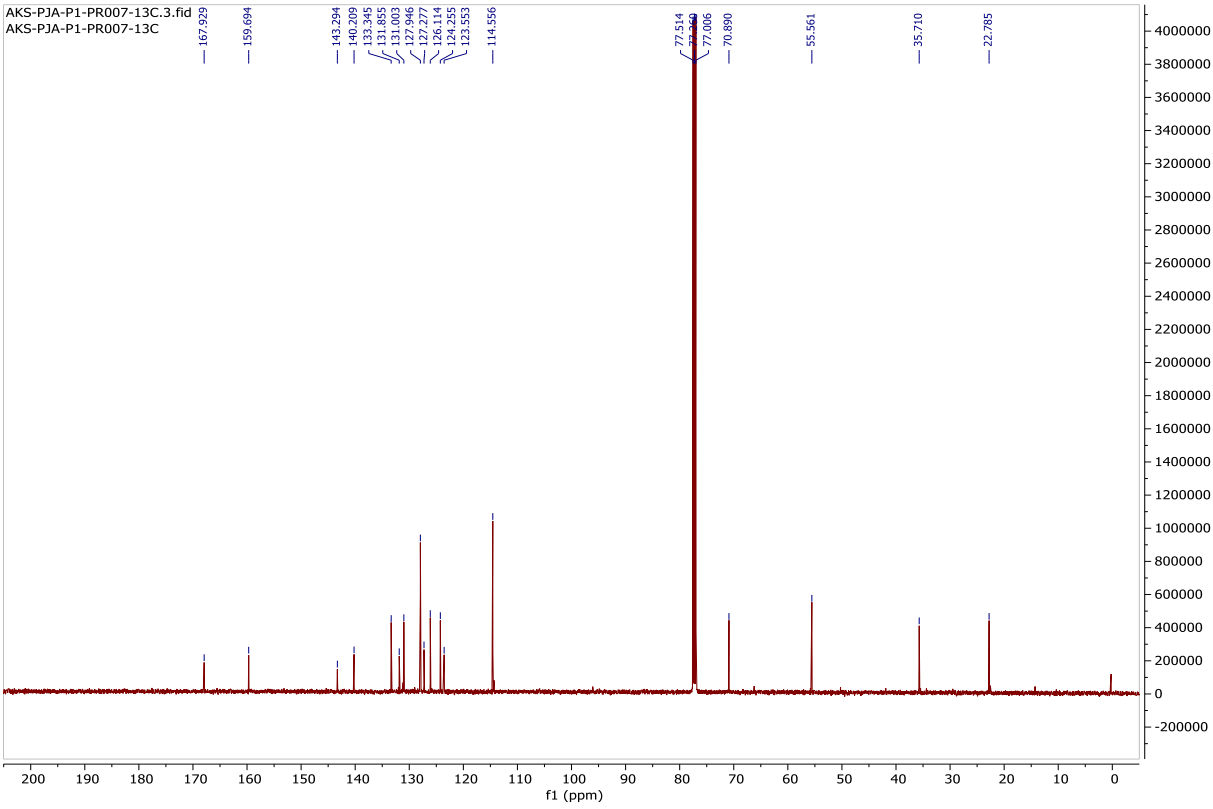
^{13}C {^{1}H} spectrum of compound **2l** (125 MHz, $CDCl_3$)



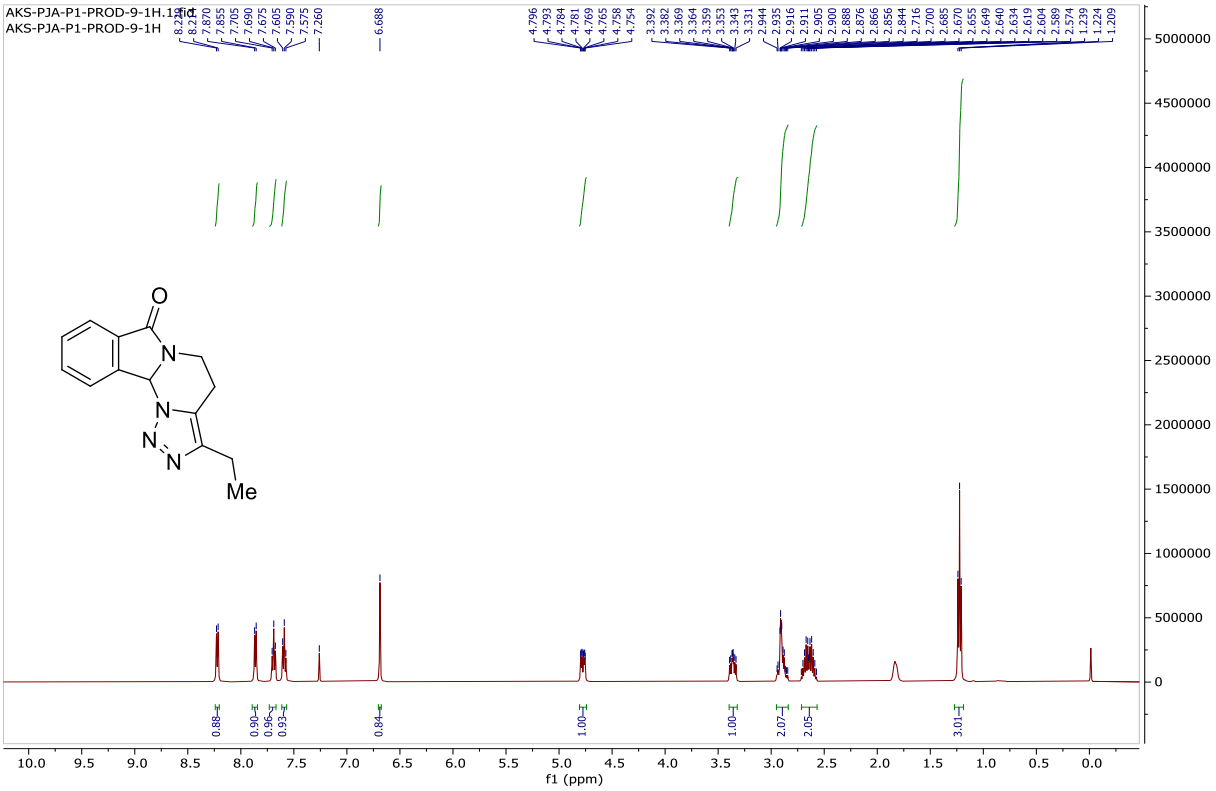
^{1}H spectrum of compound **2m** (500 MHz, $CDCl_3$)



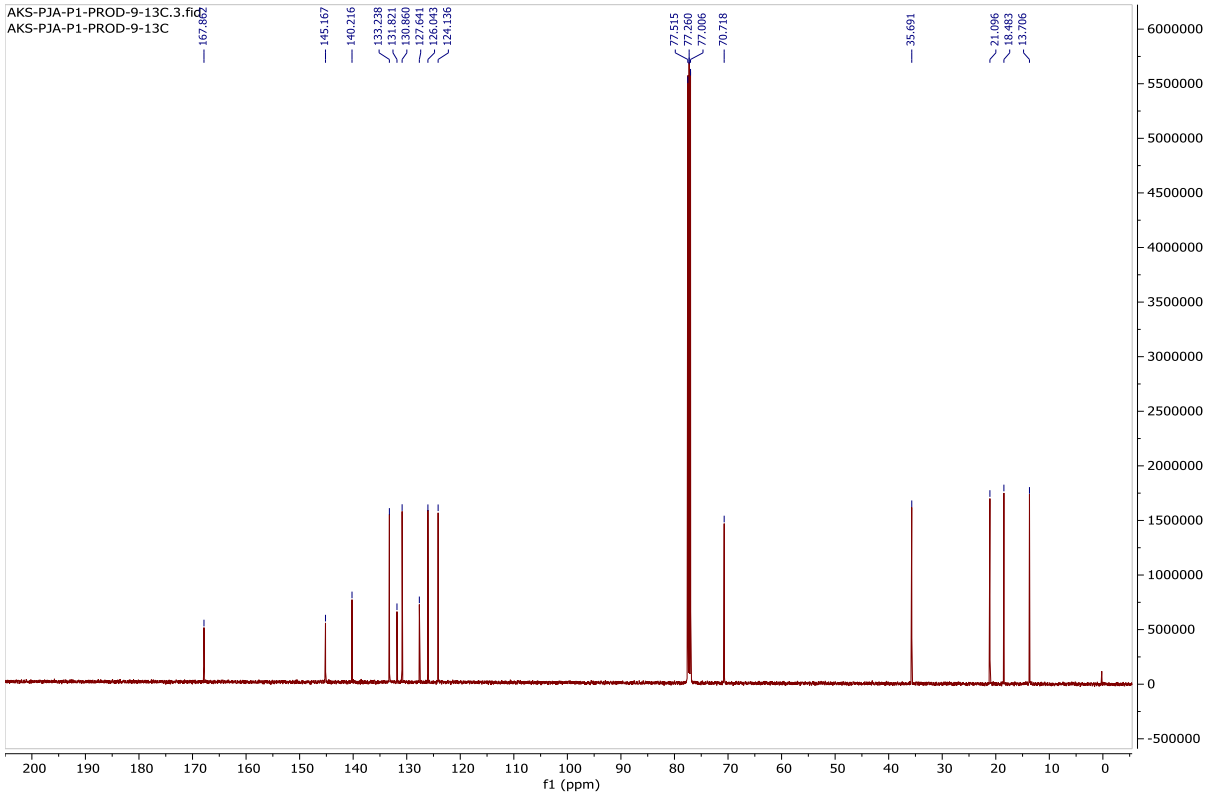
^{13}C {^{1}H} spectrum of compound **2m** (125 MHz, $CDCl_3$)



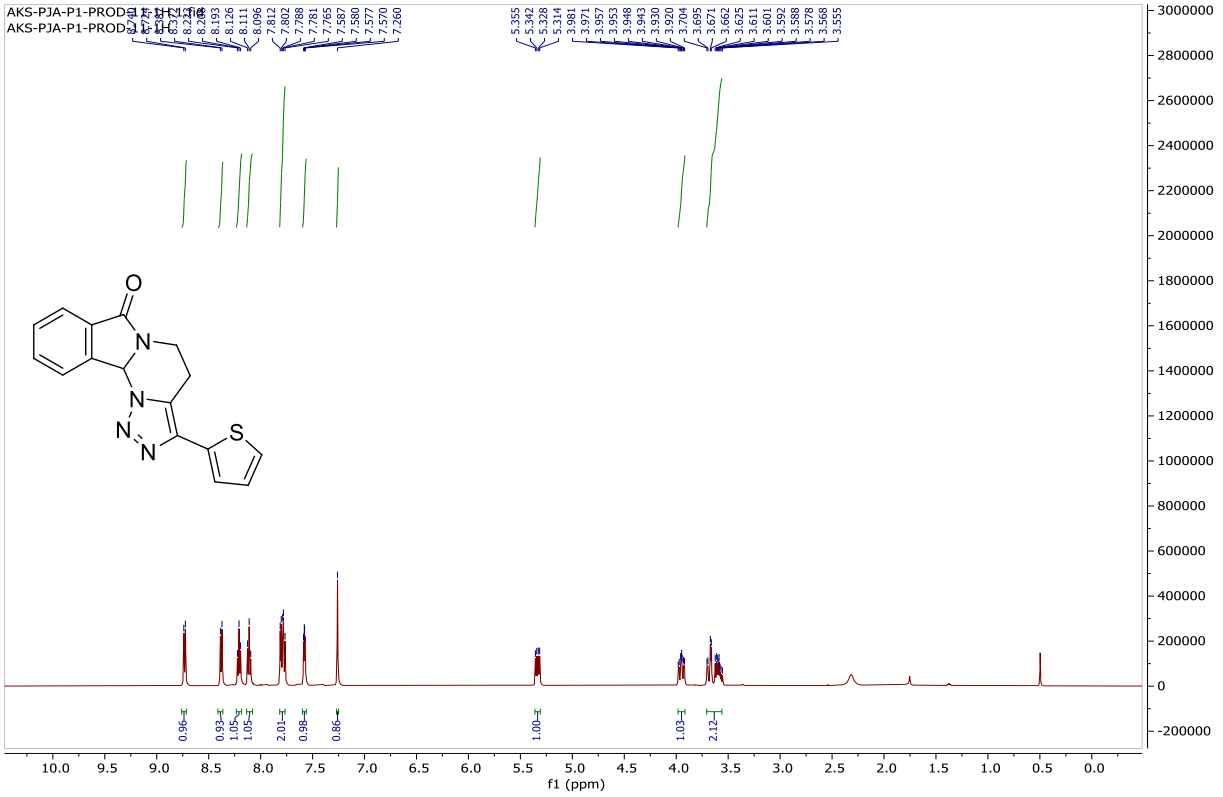
^{1}H spectrum of compound **2n** (500 MHz, $CDCl_3$)



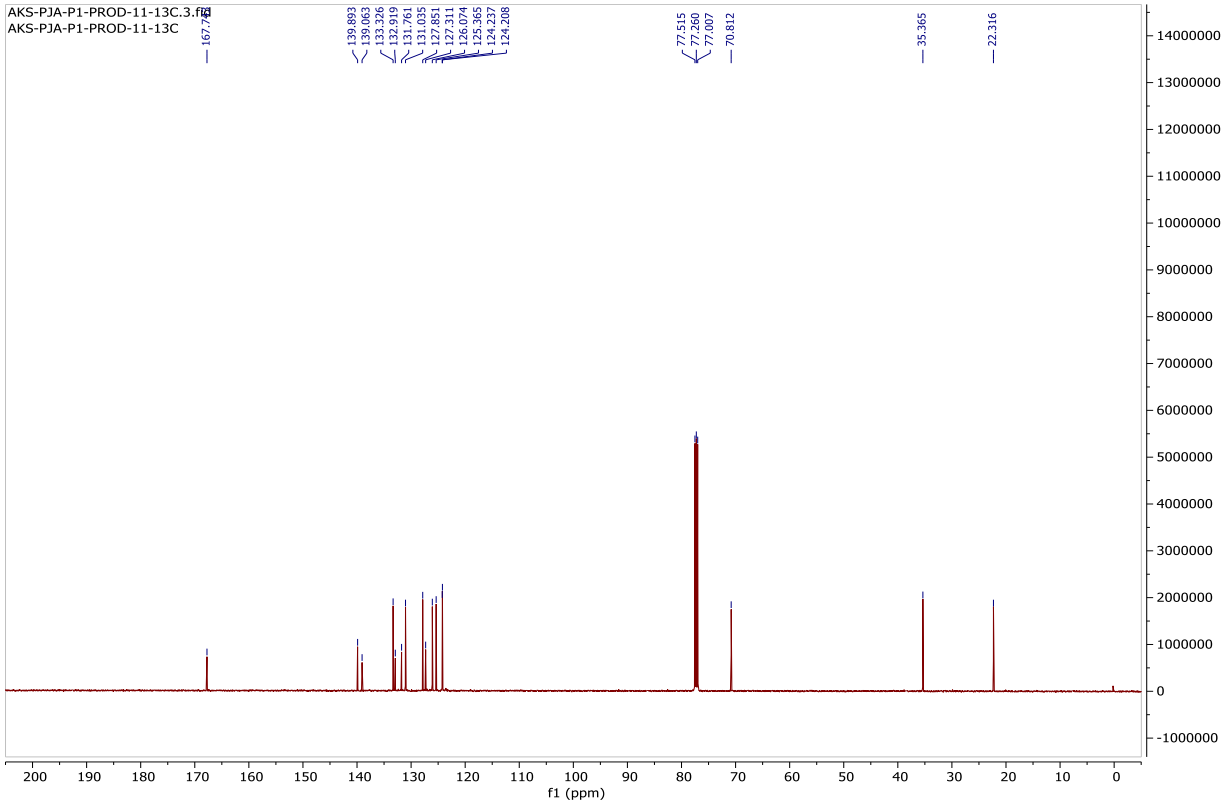
^{13}C {^{1}H} spectrum of compound **2n** (125MHz, $CDCl_3$)



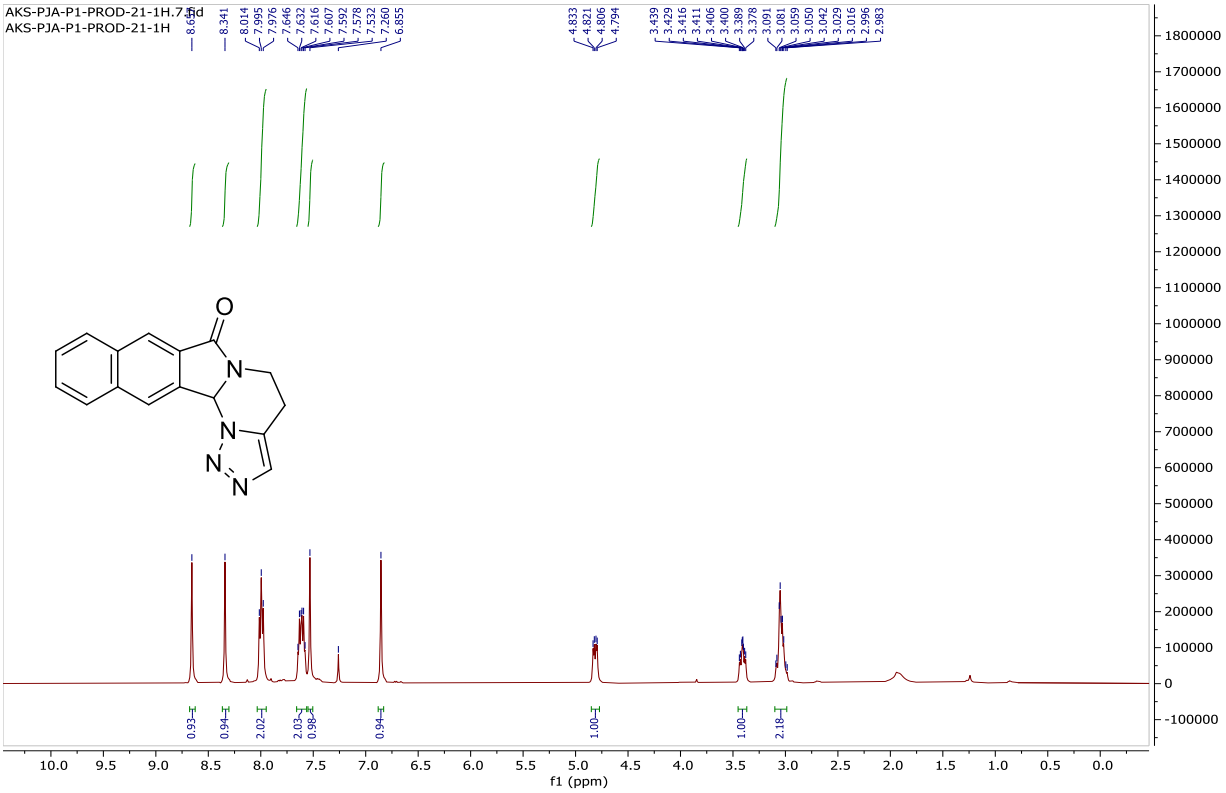
^{1}H spectrum of compound **2o** (500 MHz, $CDCl_3$)



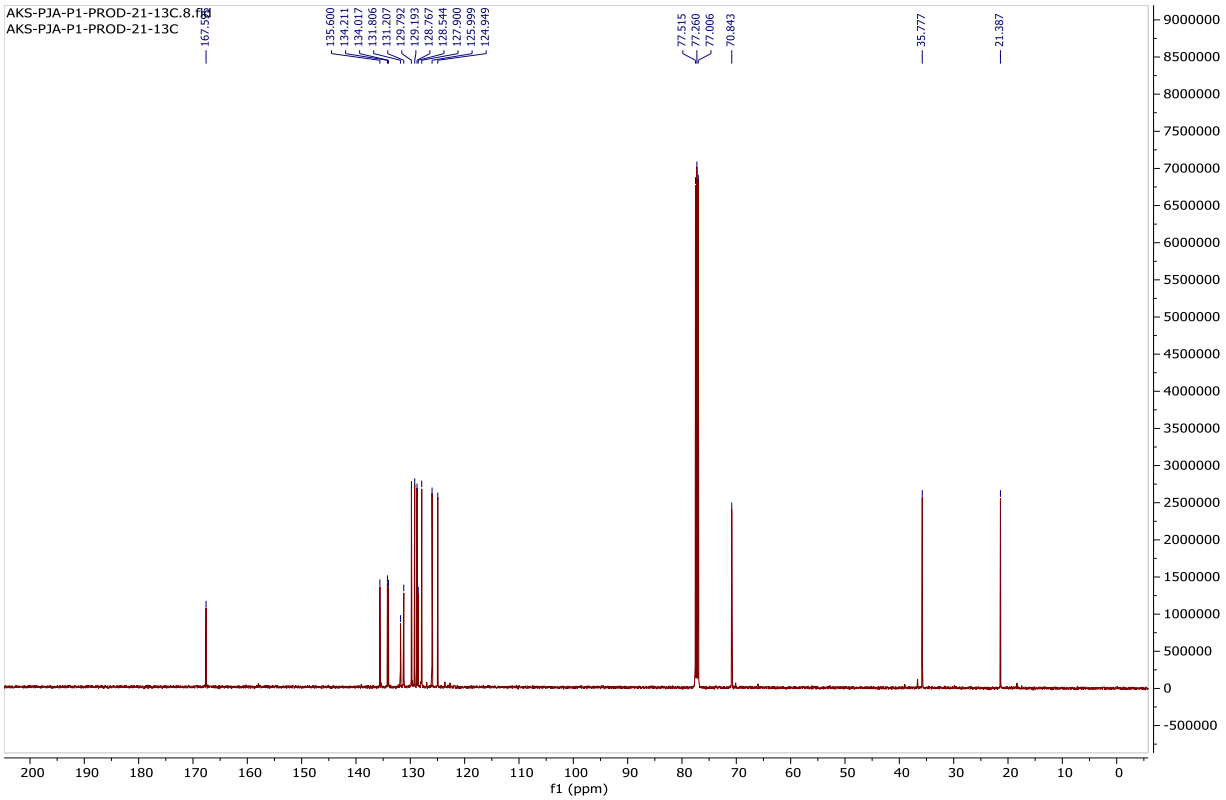
^{13}C {^{1}H} spectrum of compound **2o** (125 MHz, $CDCl_3$)



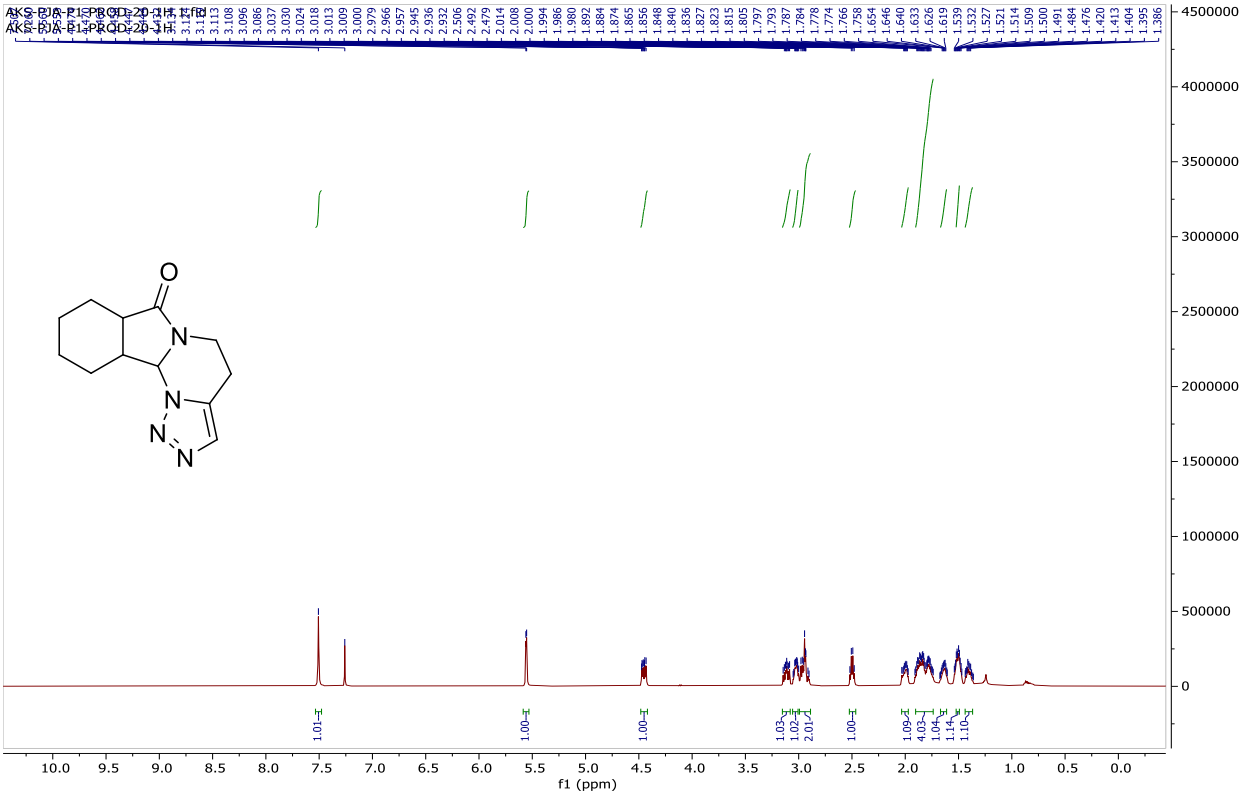
^{1}H spectrum of compound **2p** (500MHz, $CDCl_3$)



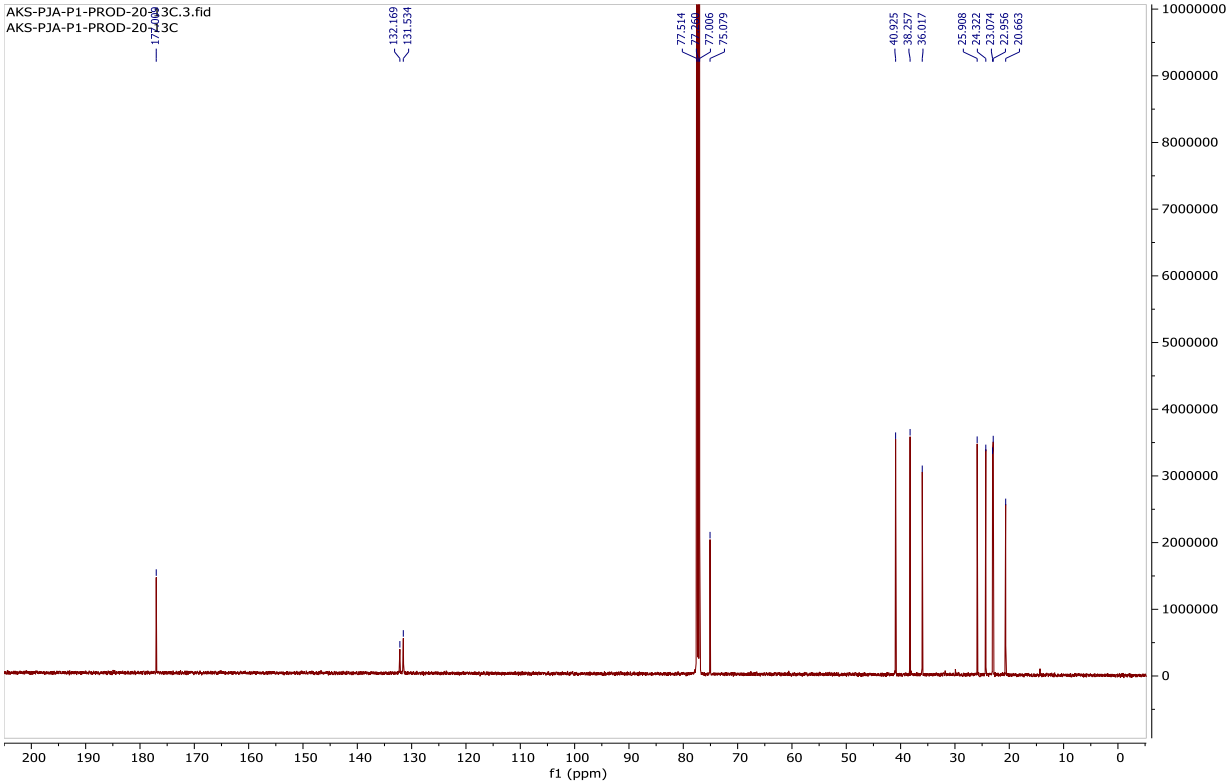
^{13}C {^{1}H} spectrum of compound **2p** (125 MHz, $CDCl_3$)



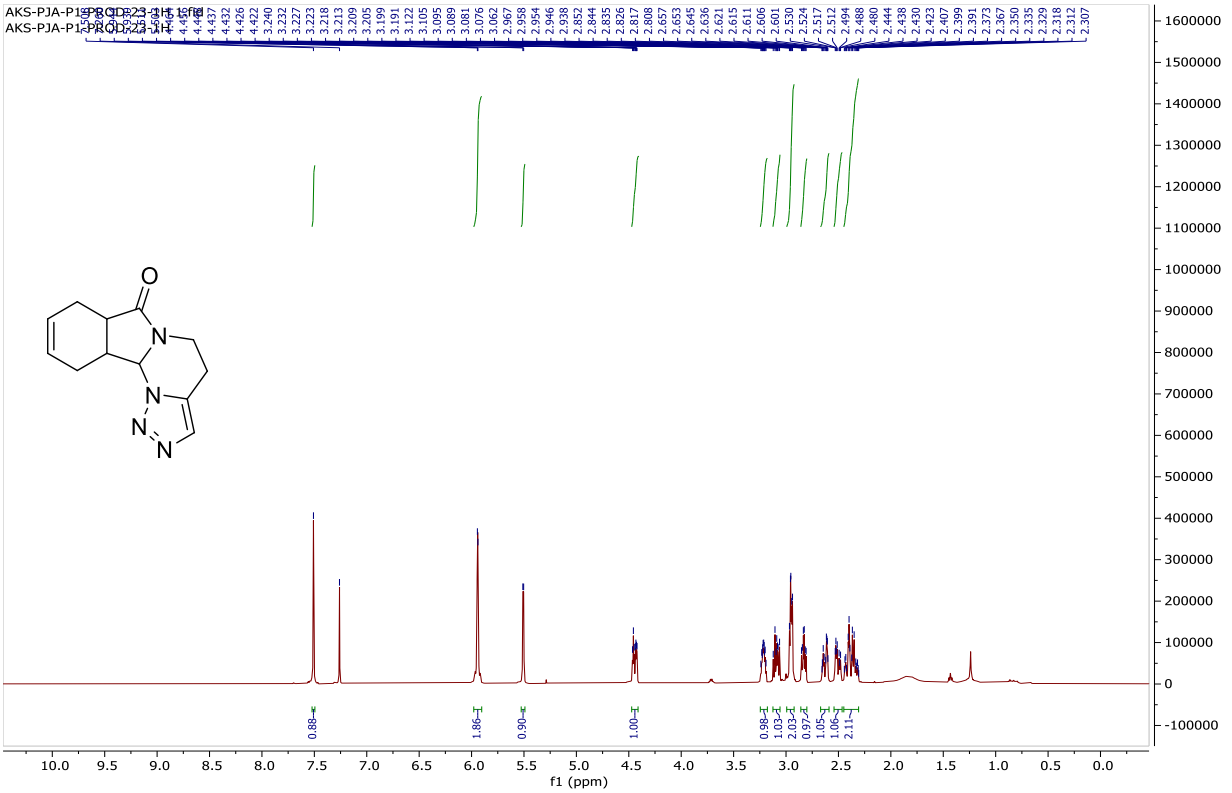
^{1}H spectrum of compound **2q** (500 MHz, $CDCl_3$)



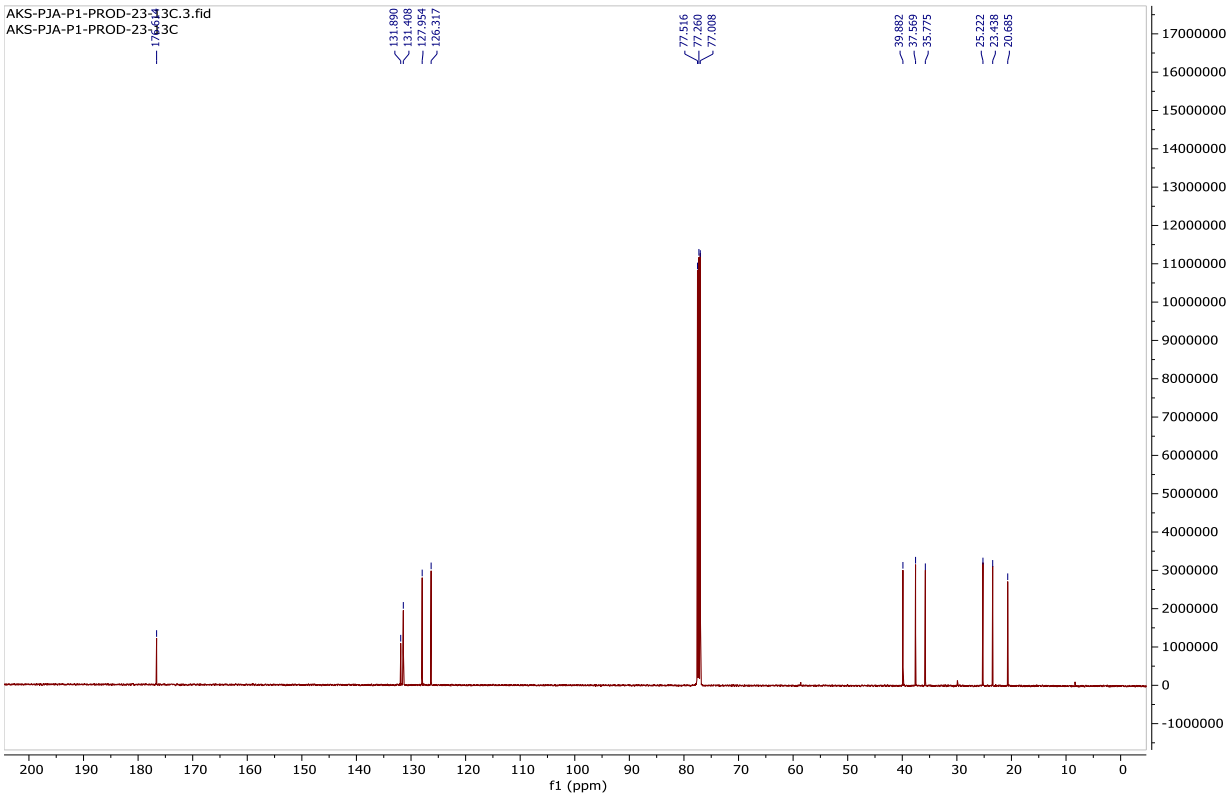
^{13}C {^{1}H} spectrum of compound **2q** (125 MHz, $CDCl_3$)



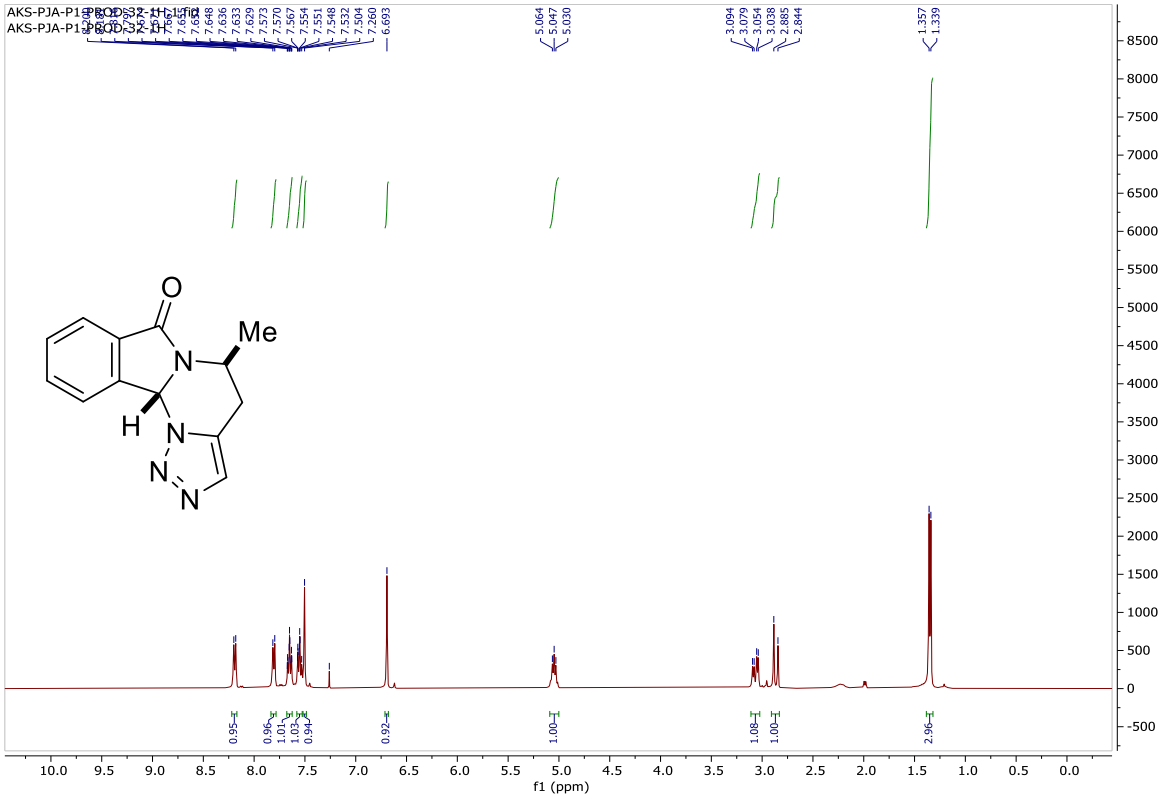
^{1}H spectrum of compound **2r** (500 MHz, $CDCl_3$)



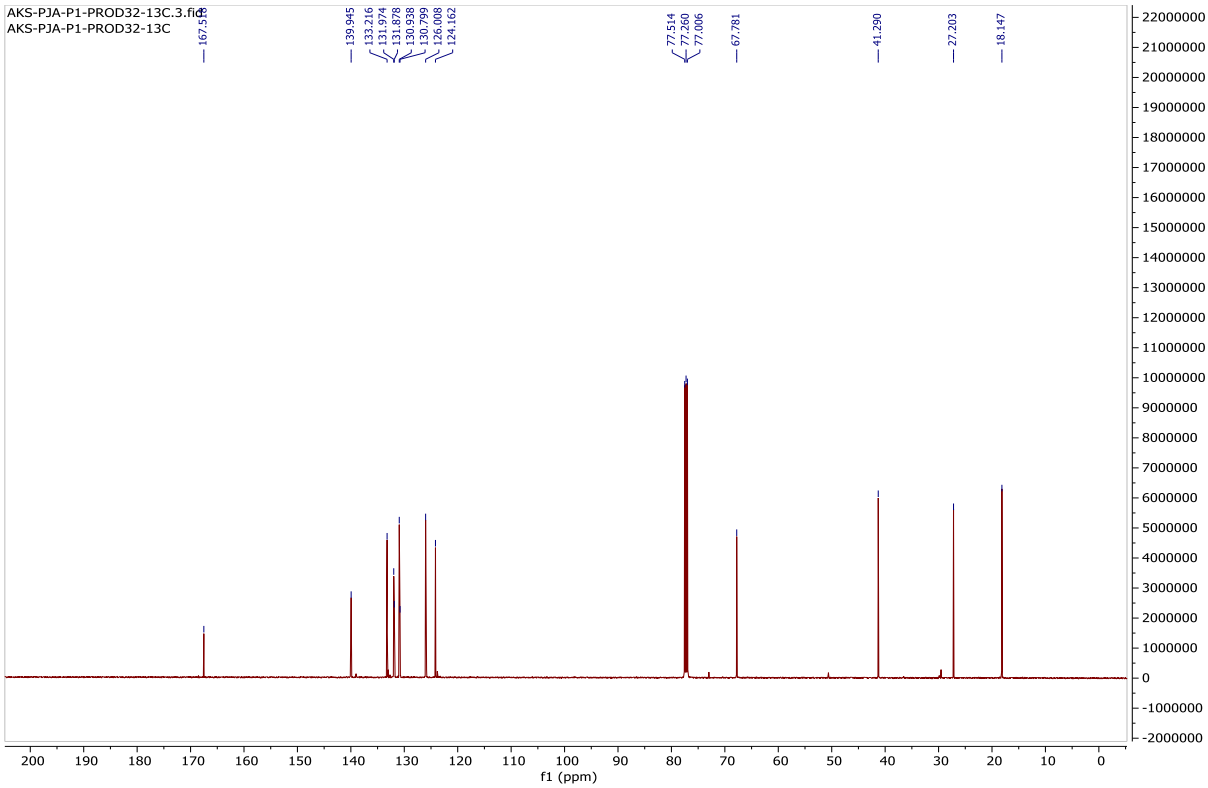
^{13}C {^{1}H} spectrum of compound **2r** (125MHz, $CDCl_3$)



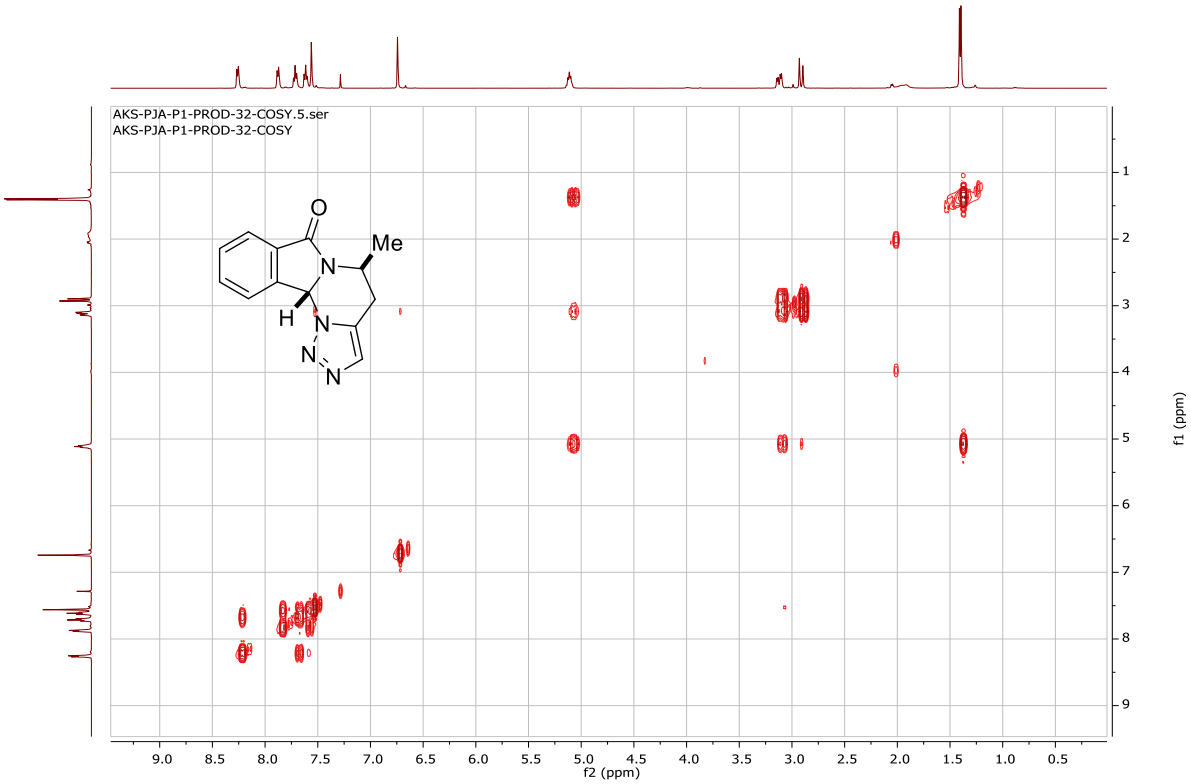
^{1}H spectrum of compound **2s** (400 MHz, $CDCl_3$)



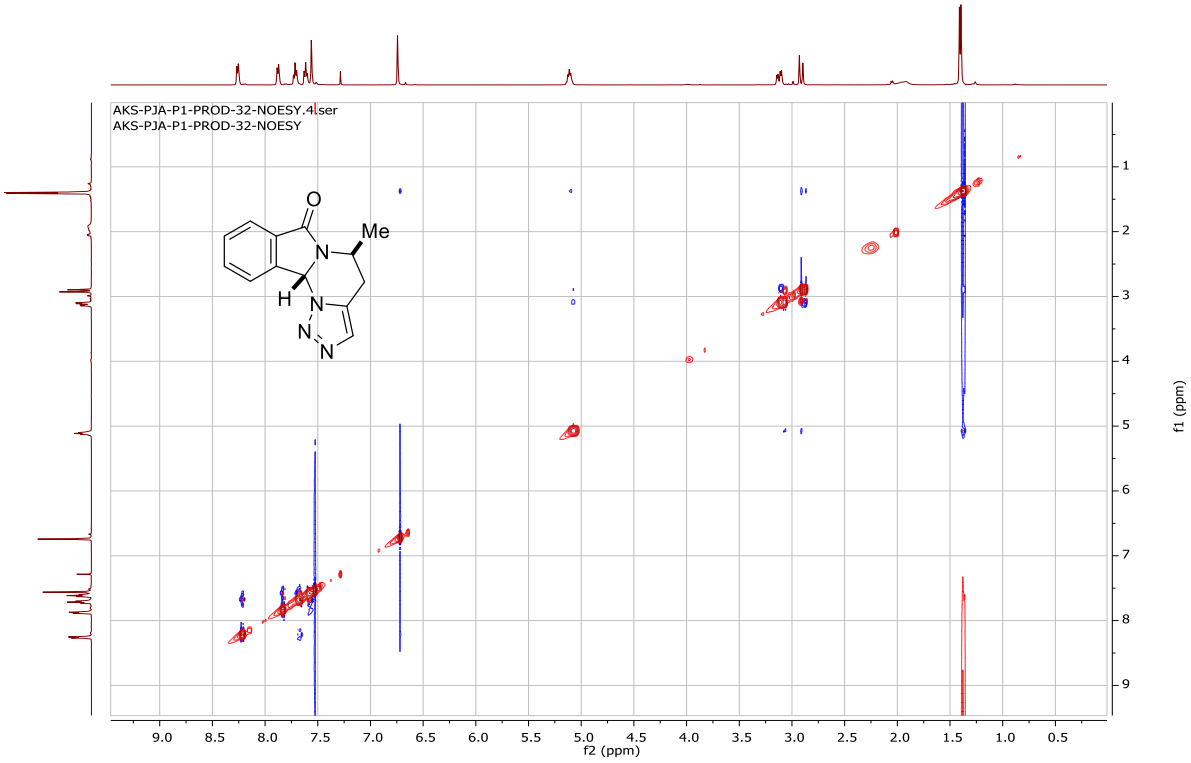
^{13}C {^{1}H} spectrum of compound **2s** (125 MHz, $CDCl_3$)



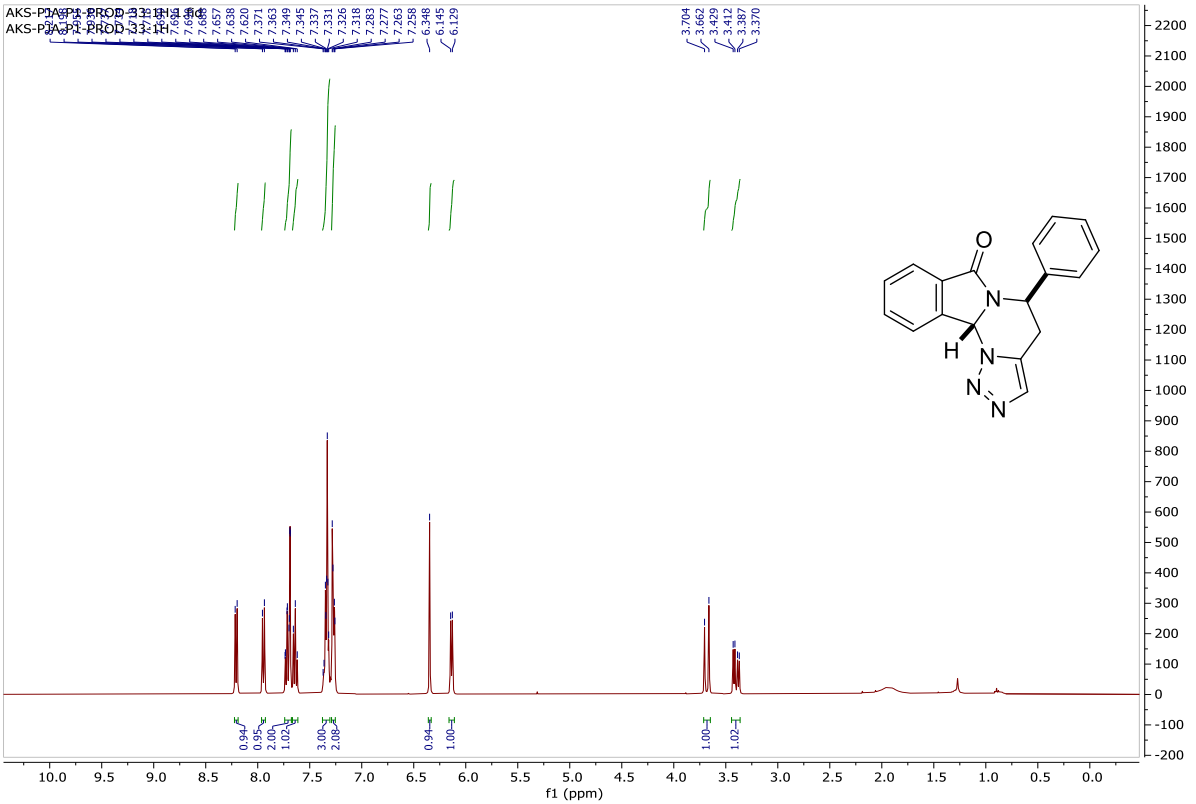
COSY spectrum of compound **2s** (400 MHz, $CDCl_3$)



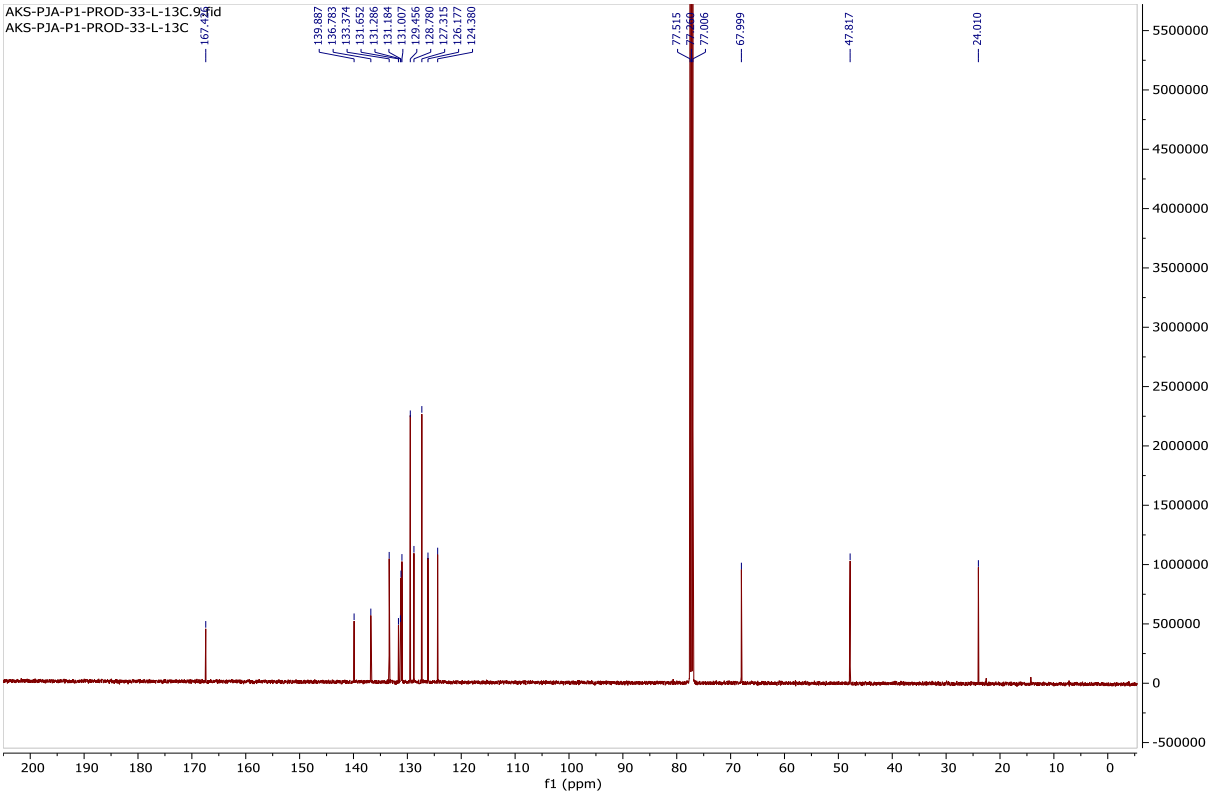
NOESY spectrum of compound **2s** (400 MHz, $CDCl_3$)



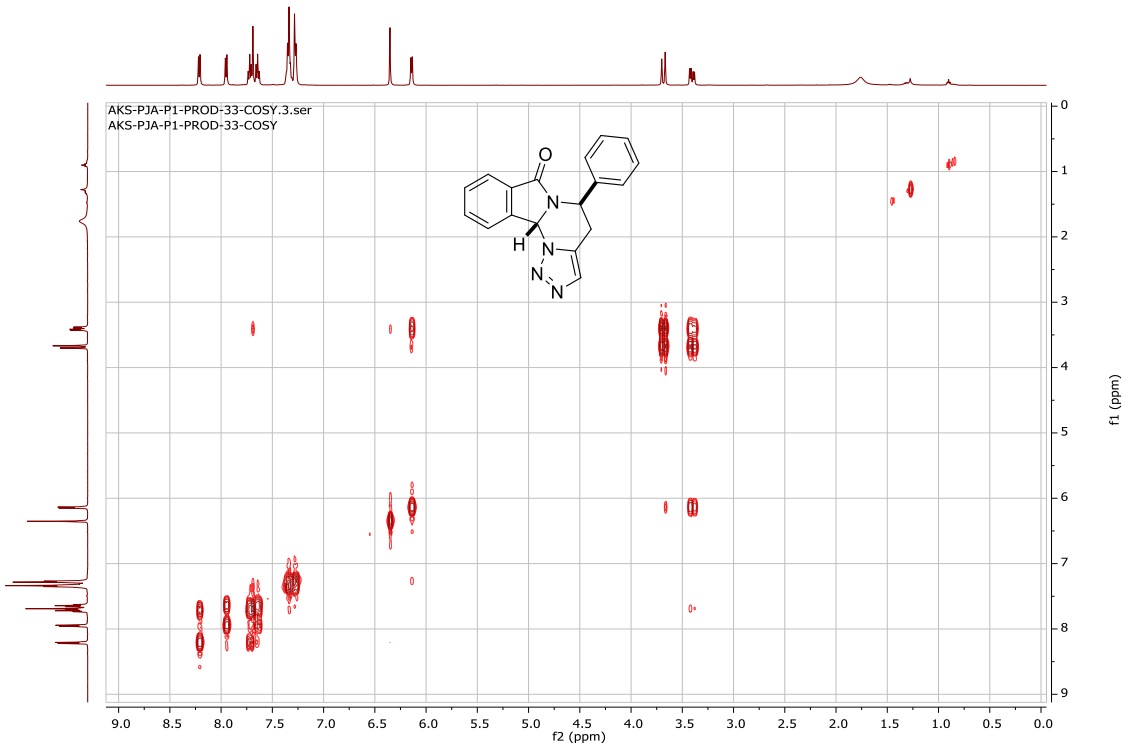
^{1}H spectrum of compound **2t** (400 MHz, $CDCl_3$)



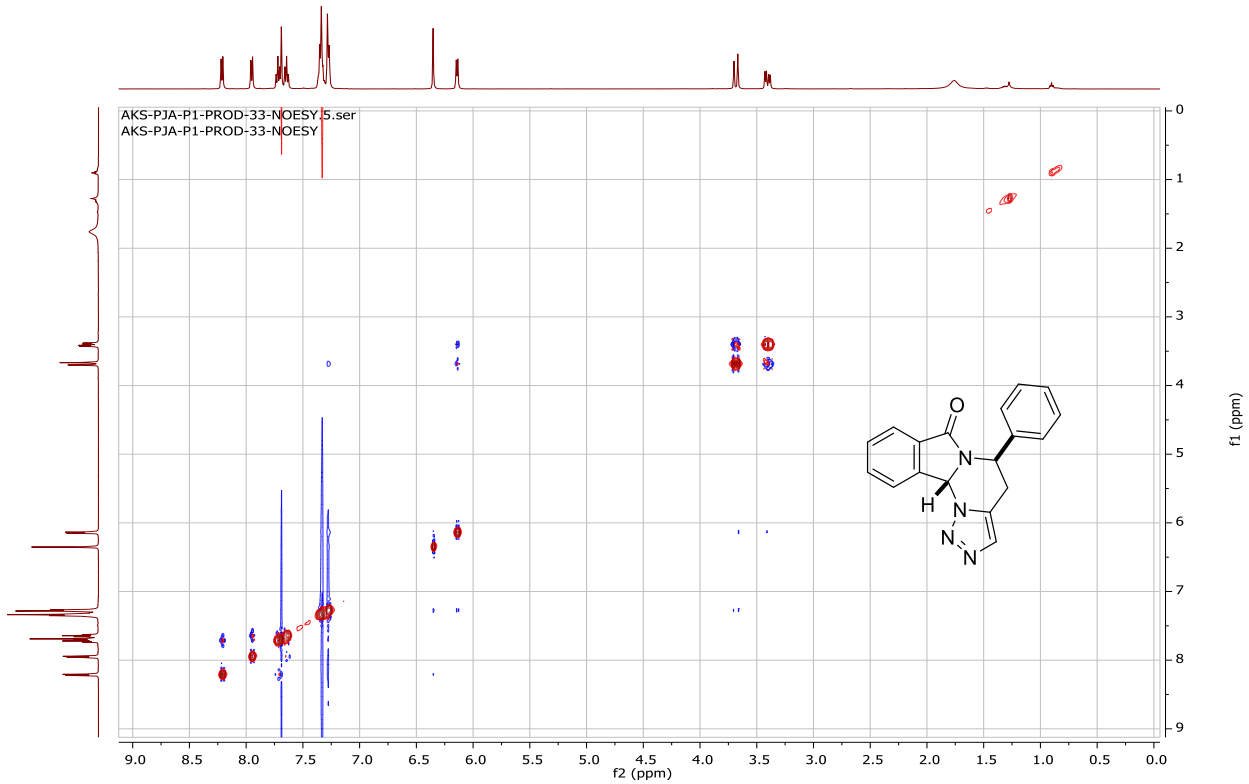
^{13}C {^{1}H} spectrum of compound **2t** (125 MHz, $CDCl_3$)



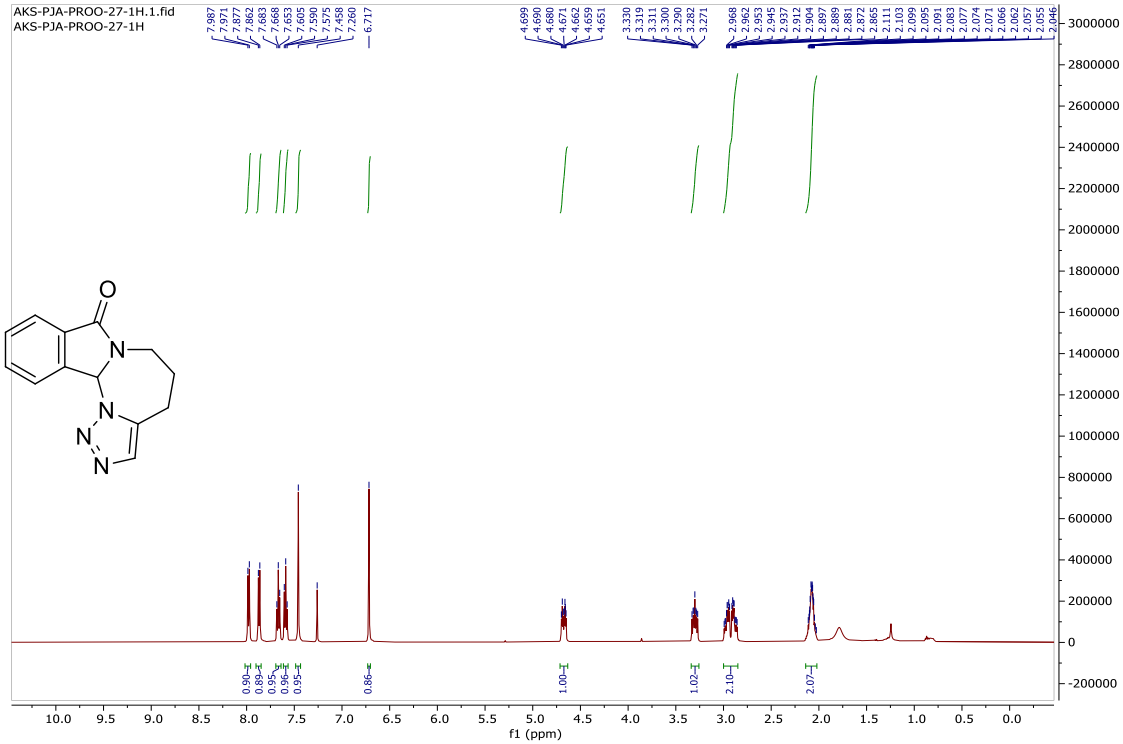
COSY spectrum of compound **2t** (400 MHz, $CDCl_3$)



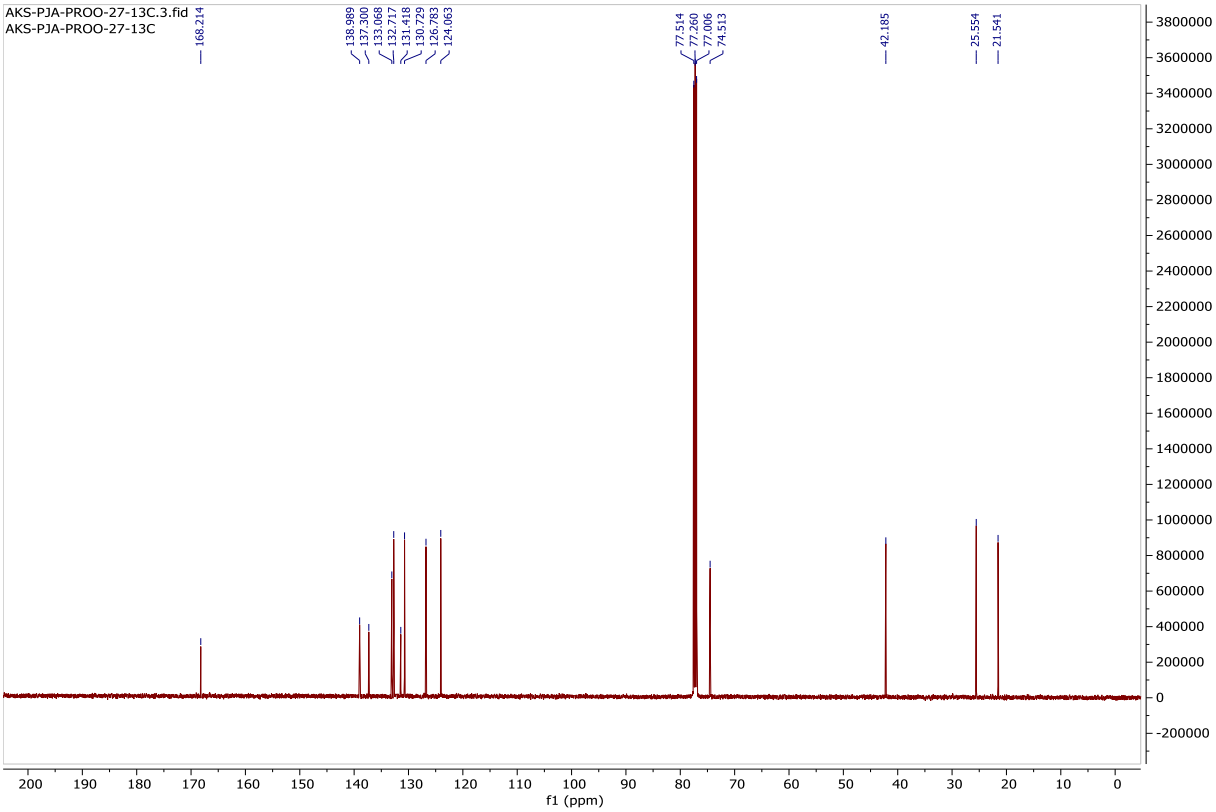
NOESY spectrum of compound **2t** (400 MHz, $CDCl_3$)



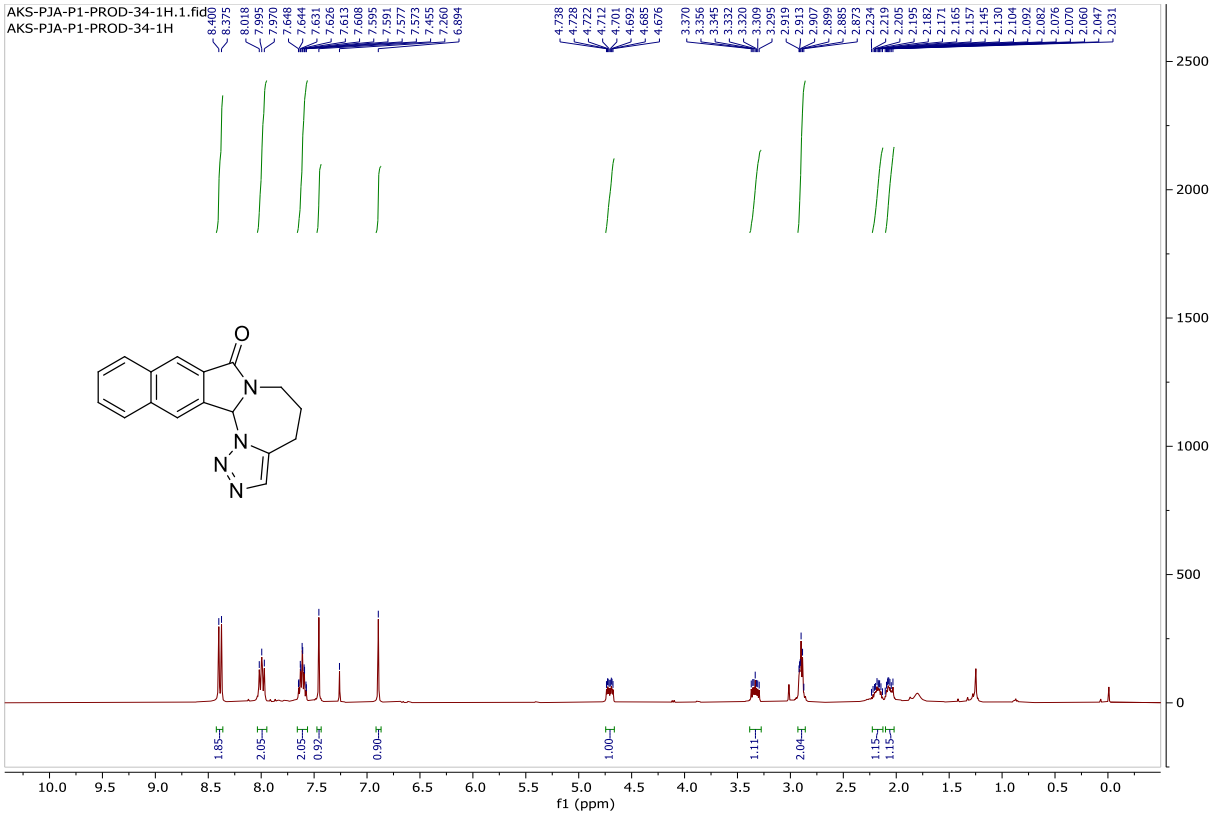
^{1}H spectrum of compound **2v** (500 MHz, $CDCl_3$)



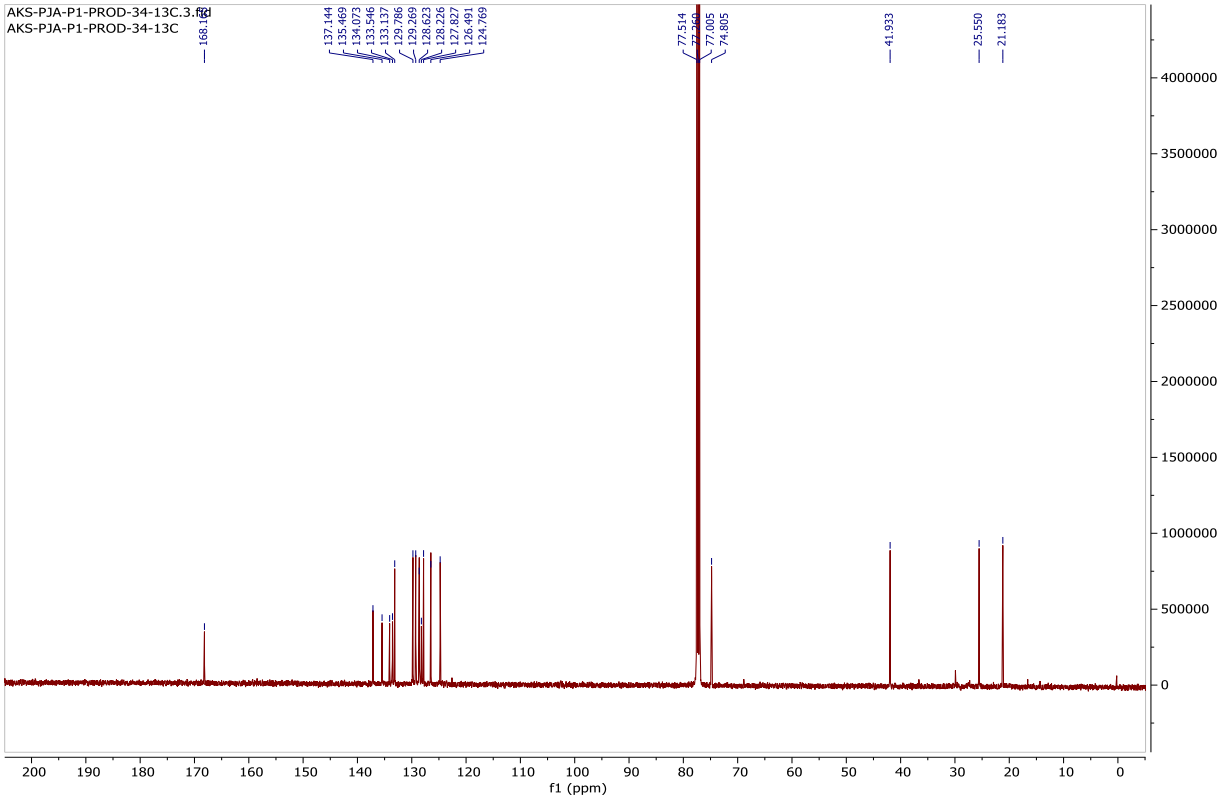
^{13}C {^{1}H} spectrum of compound **2v** (125 MHz, $CDCl_3$)



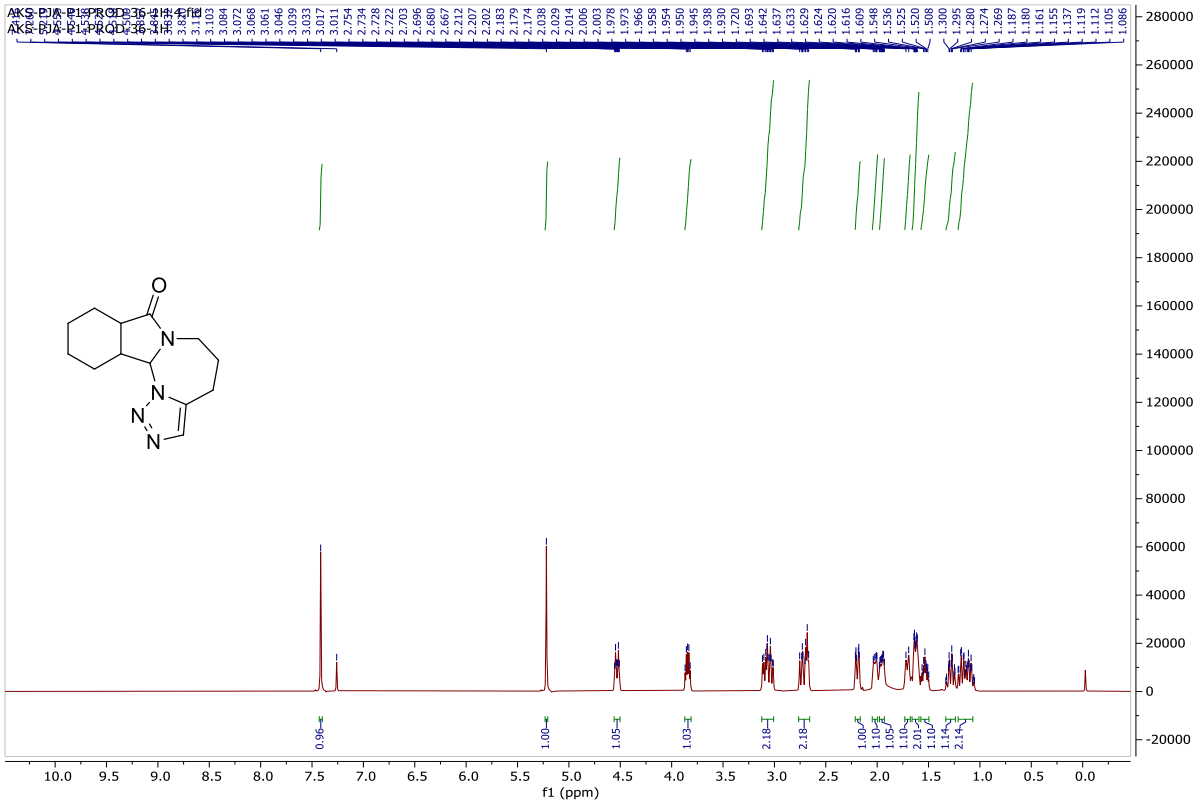
^{1}H spectrum of compound **2w** (400 MHz, $CDCl_3$)



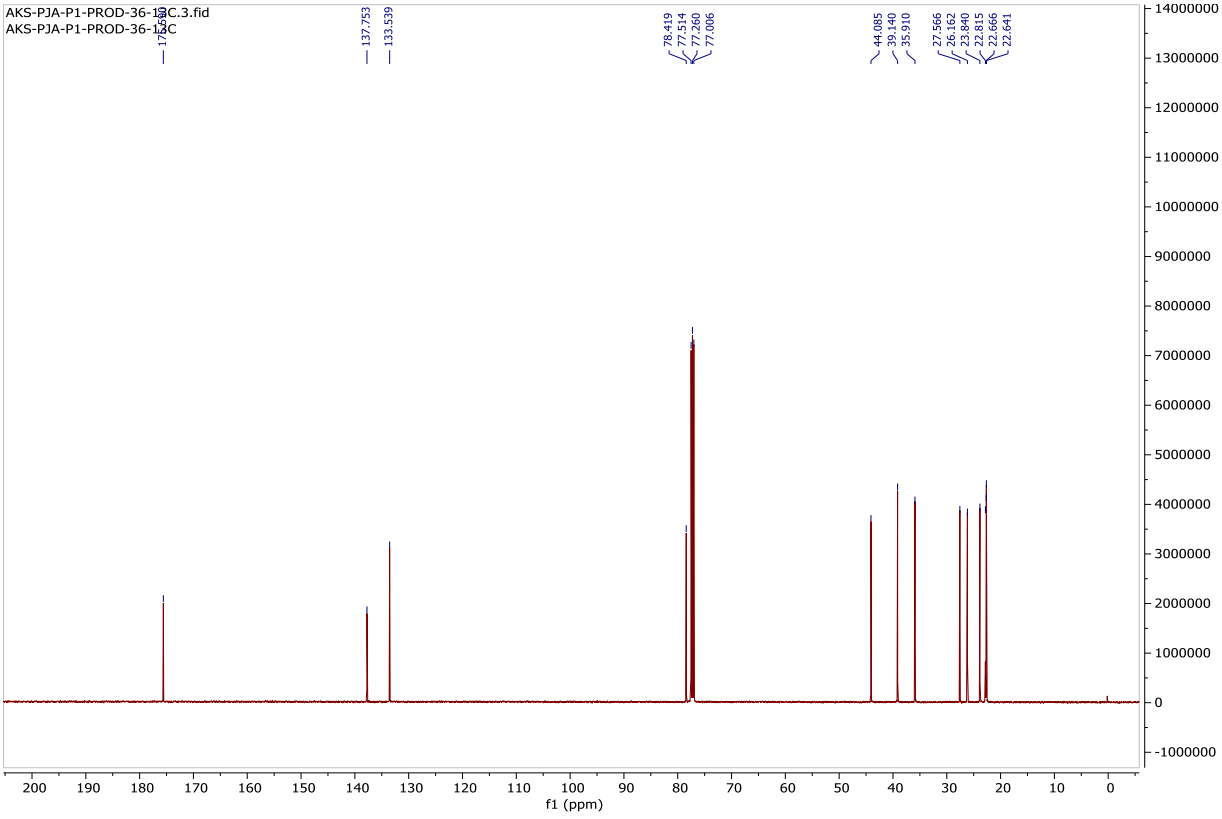
^{13}C {^{1}H} spectrum of compound **2w** (125 MHz, $CDCl_3$)



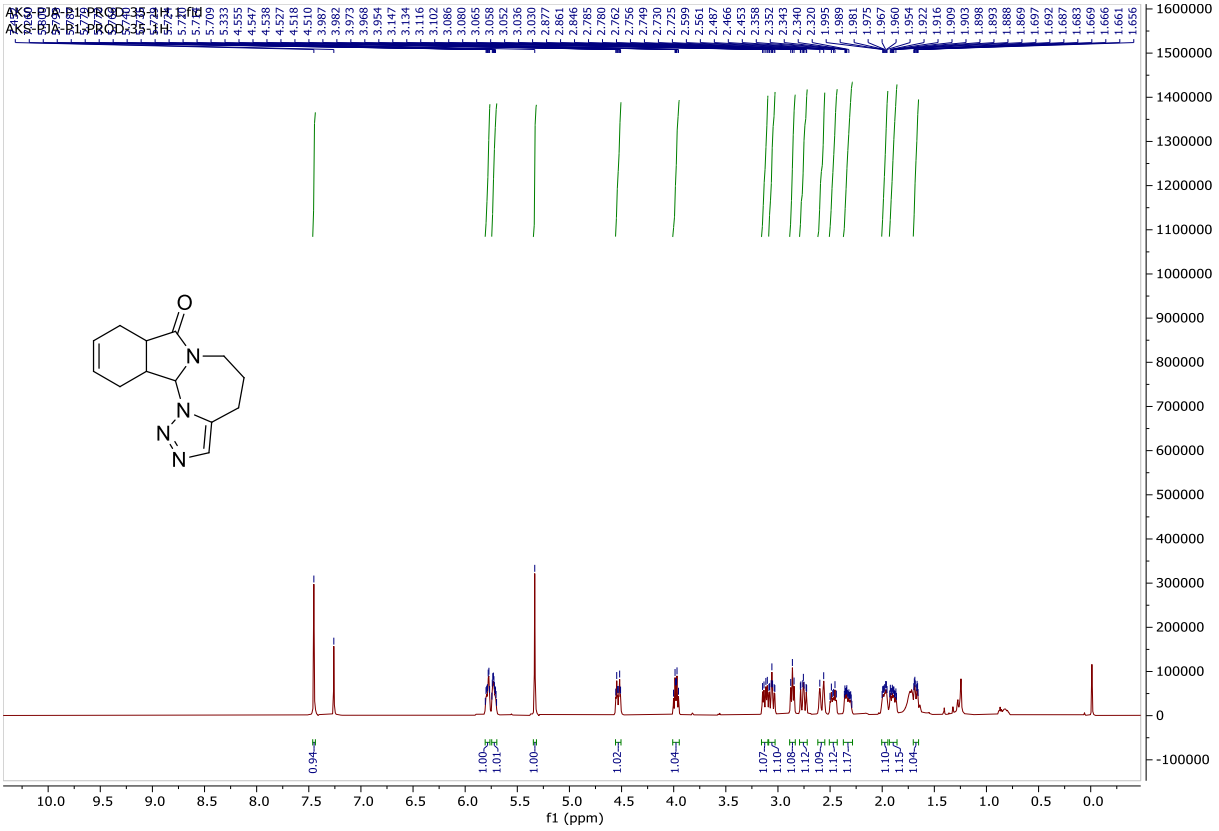
^{1}H spectrum of compound **2x** (500 MHz, $CDCl_3$)



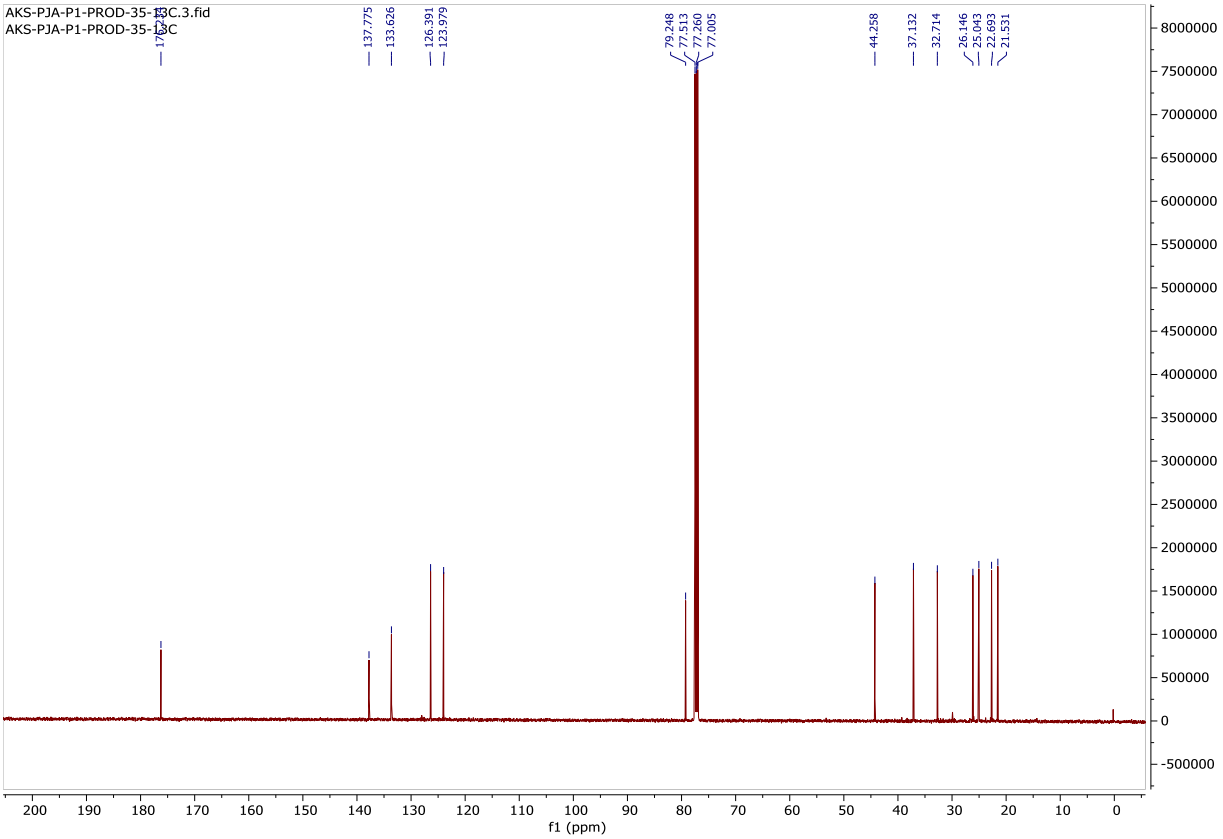
^{13}C {^{1}H} spectrum of compound **2x** (125 MHz, $CDCl_3$)



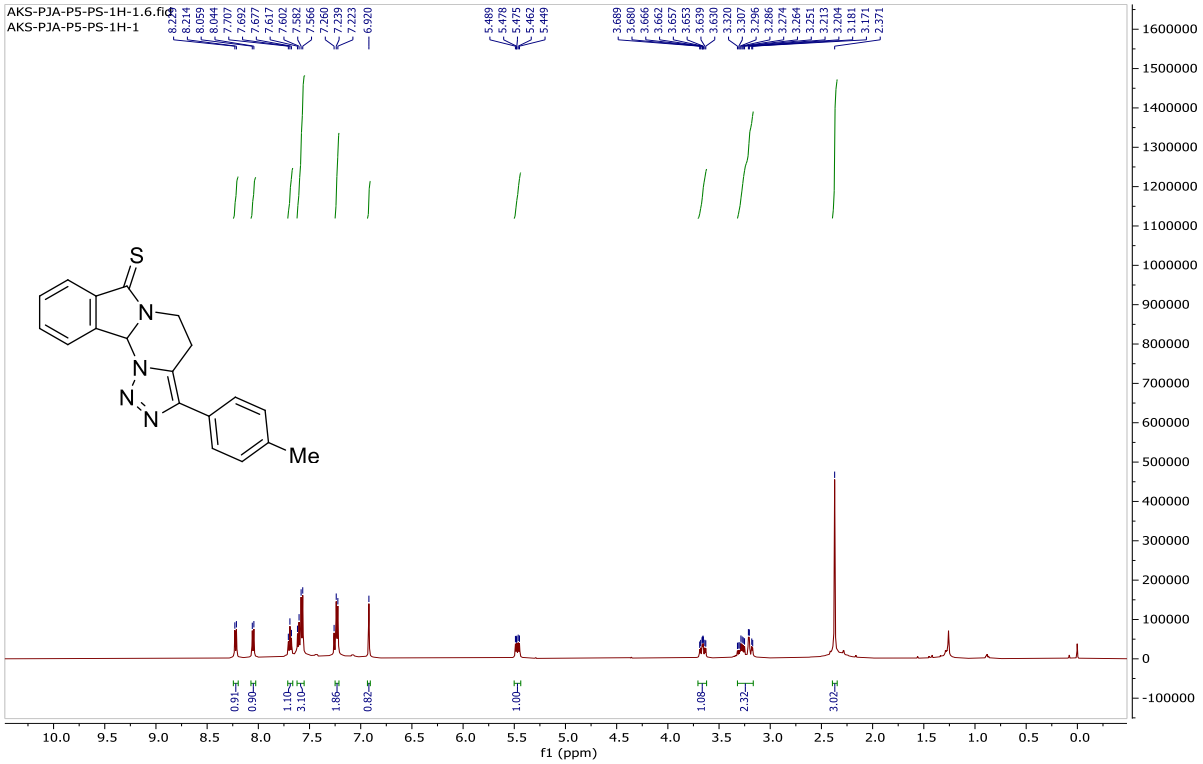
^{1}H spectrum of compound **2y** (500 MHz, $CDCl_3$)



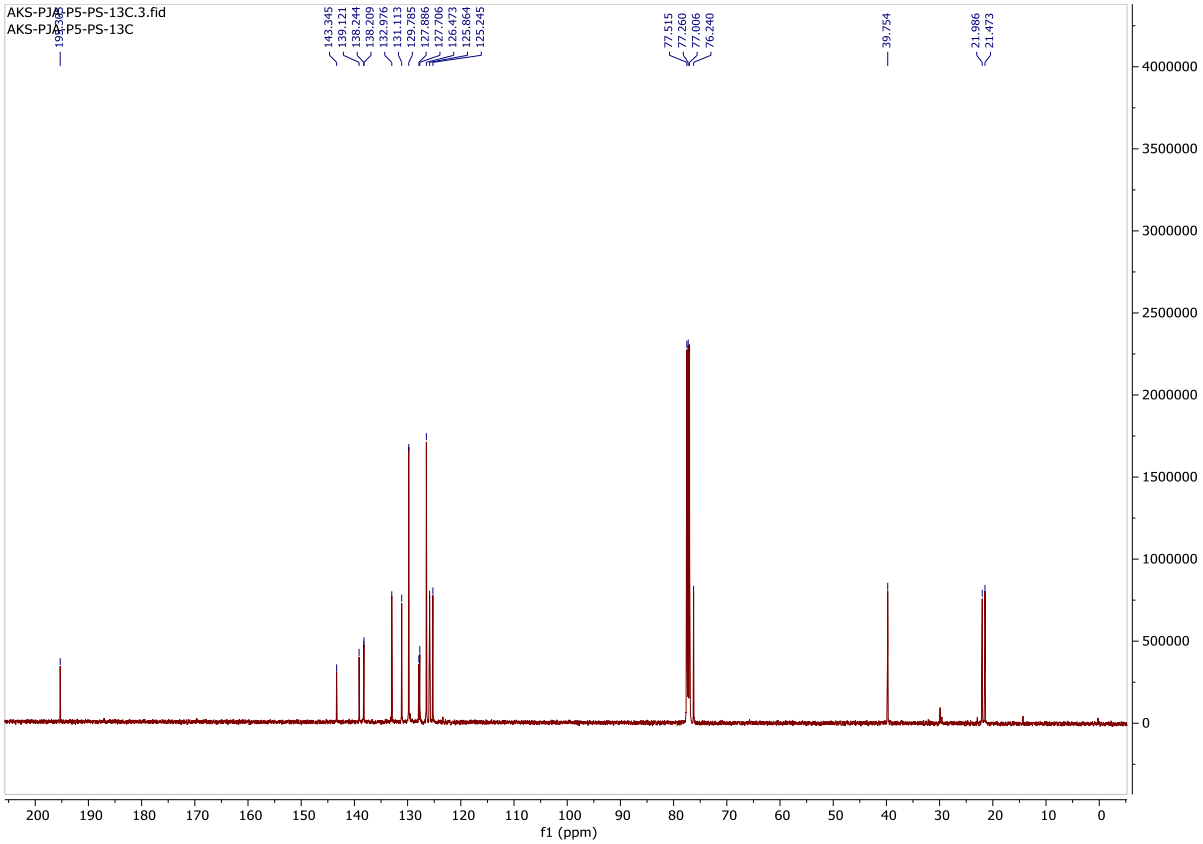
^{13}C {^{1}H} spectrum of compound **2y** (125 MHz, $CDCl_3$)



^{1}H spectrum of compound **3j** (500 MHz, $CDCl_3$)



^{13}C {^{1}H} spectrum of compound **3j** (125 MHz, $CDCl_3$)



Single crystal X-ray diffraction:

1. Single crystal of compound **2a** (m.p. 188-190 ^{o}C) was obtained by slow evaporation of hexane and ethyl acetate solution (9:1). The Bruker SMART APEX-II CCD diffractometer was used to collect the intensity data. The instrument is equipped with a fine focus 1.75 kW sealed tube Mo Kα radiation (λ = 0.71073 Å) at 298(2) K, with increasing ω (width of 0.3° per frame) at a scan speed of 3 s/frame. The data acquisition was done with the SMART software. The SAINT and XPREP software were implemented for data integration and reduction.[1] Multiscan empirical absorption corrections were employed to the data using the program SADABS.[2] Structure was solved by direct methods using SHELXS- 2016 and refined with full-matrix least-squares on F2 using SHELXL- 2016/6.[3] Structural illustrations have been drawn with ORTEP-3 for Windows.[4] The detailed data collection and structure refinement are summarized in Table S49, CCDC 2269135 **2a** contained supplementary crystallographic data for this note.

Reference:

1) SMART; SAINT; XPREP; Siemens Analytical X-ray Instruments Inc.: Madison, WI, 1995.

2) Sheldrick, G. M. SADABS: Software for Empirical Absorption Correction University of Gottingen, Institut fur Anorganiche Chemieder Universitat: Gottingen, Germany, 1999.

3) Sheldrick, G. M. SHELXS-2014, Program for the crystal structure solution; University of Göttingen: Göttingen, Germany, 2014.

4) Farrugia, L. J. XRDIFF: simulation of X-ray diffraction patterns, *J. Appl. Crystallogr*. **1997**, *30*, 565.

Table S49: The crystal parameters of compound 2a

	CCDC 2269135
Formula	$C_{12}H_{12}N_4O_2$
Formula weight	244.26
T/K	298(2)
Crystal system	monoclinic
Space group	P 21
a/Å	10.0470(8)
b/Å	4.9832(4)
c/Å	11.8477(10)
α/°	90
β/°	104.242(2)
γ/°	90
V/Å^3	574.98(8)
Z	2
Abs. Coeff./mm^{-1}	0.100
Abs. Correction	multi-scan
GOF on F^2	0.715
Final *R* indices [$I > 2\sigma(I)$]	*R1* = 0.0357 *wR2* = 0.1020
R indices [all data]	*R1* = 0.0405 *wR2* = 0.1103

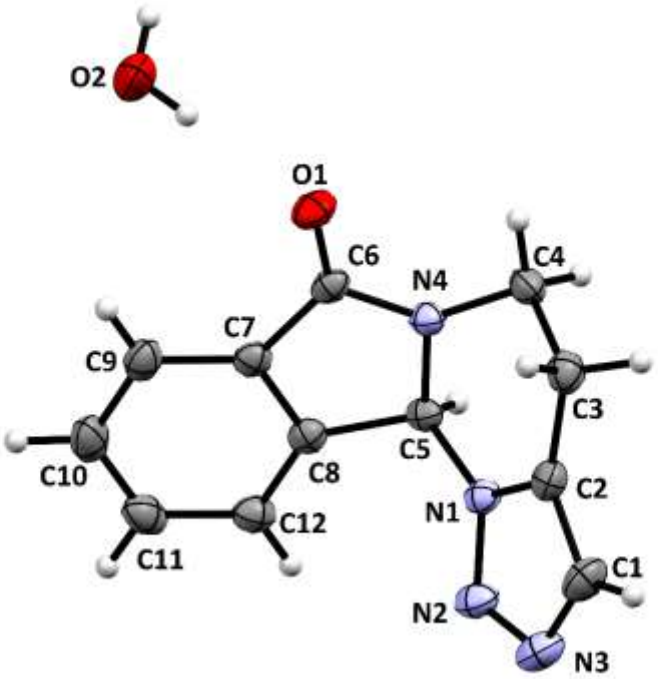
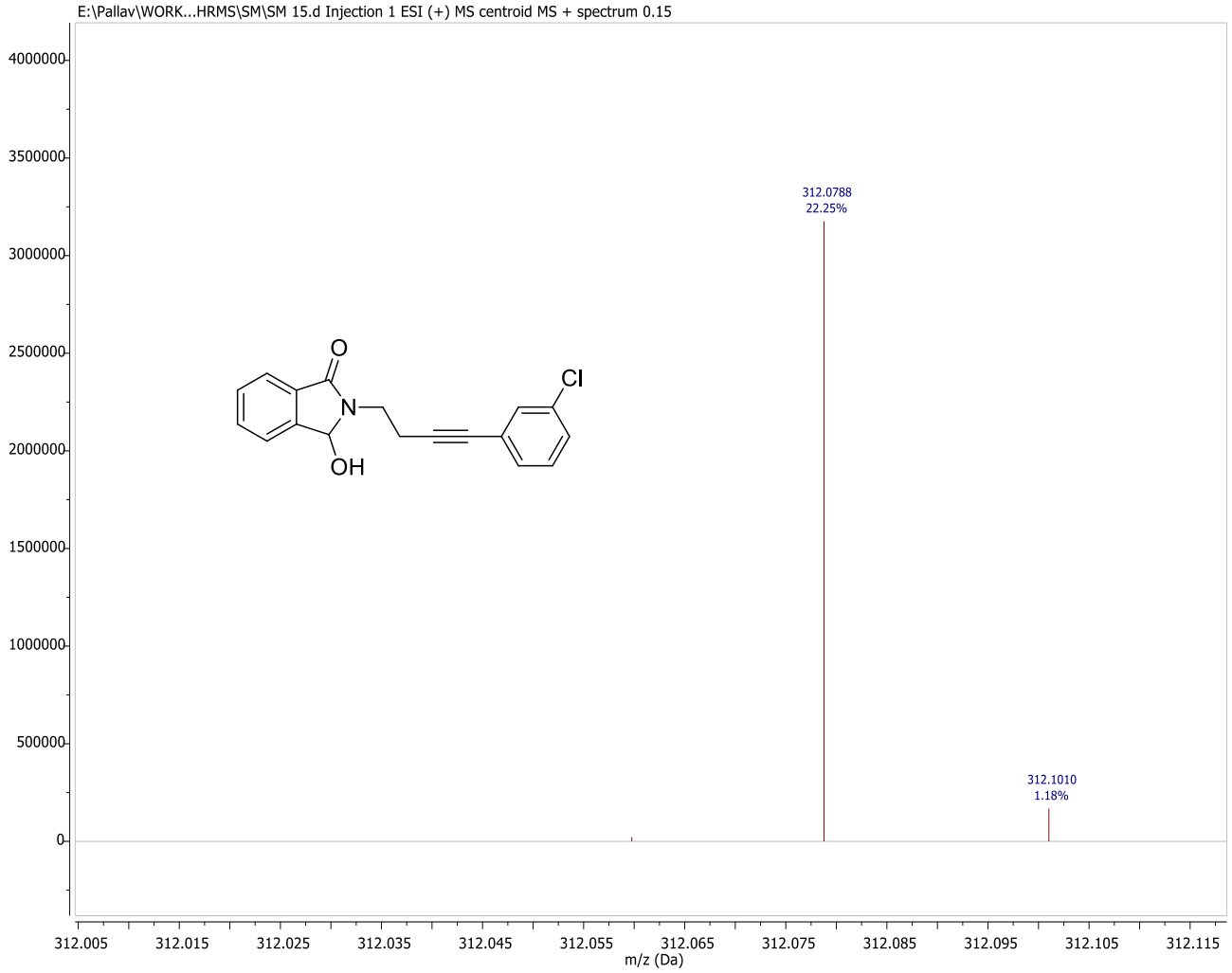
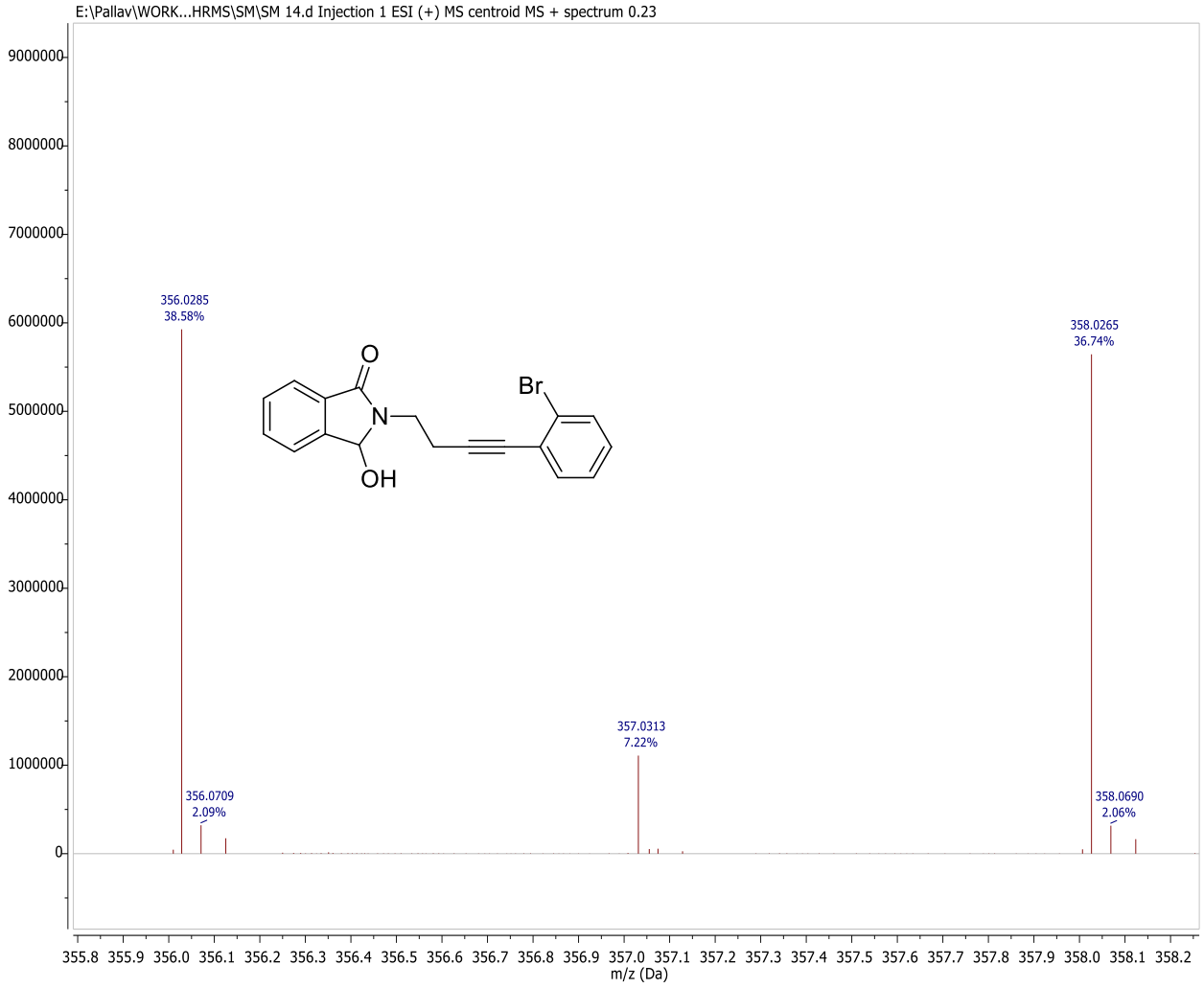


Figure S50: ORTEP diagram of compound 2a using thermal ellipsoids of 30% probability

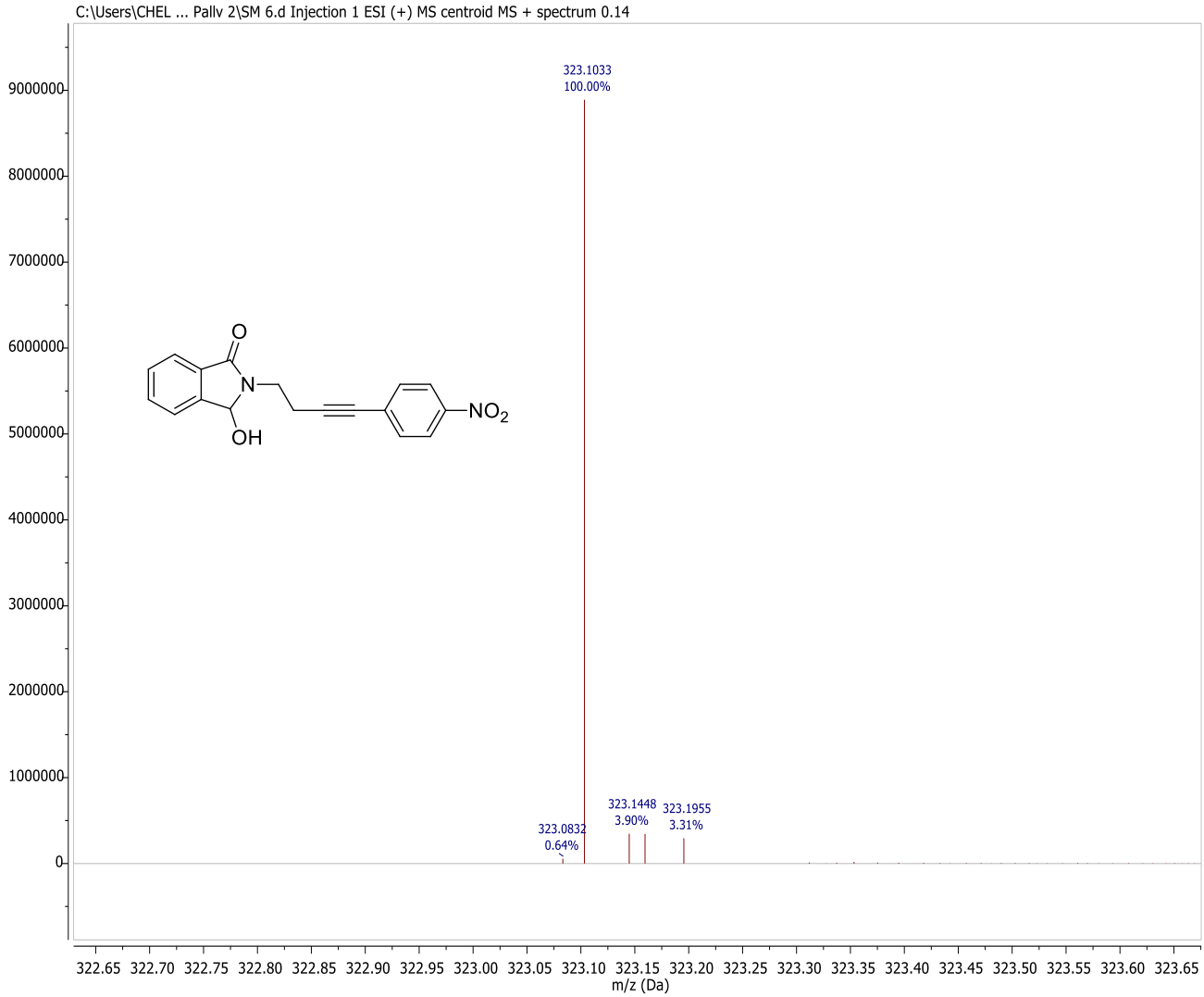
HRMS spectrum of **1c**



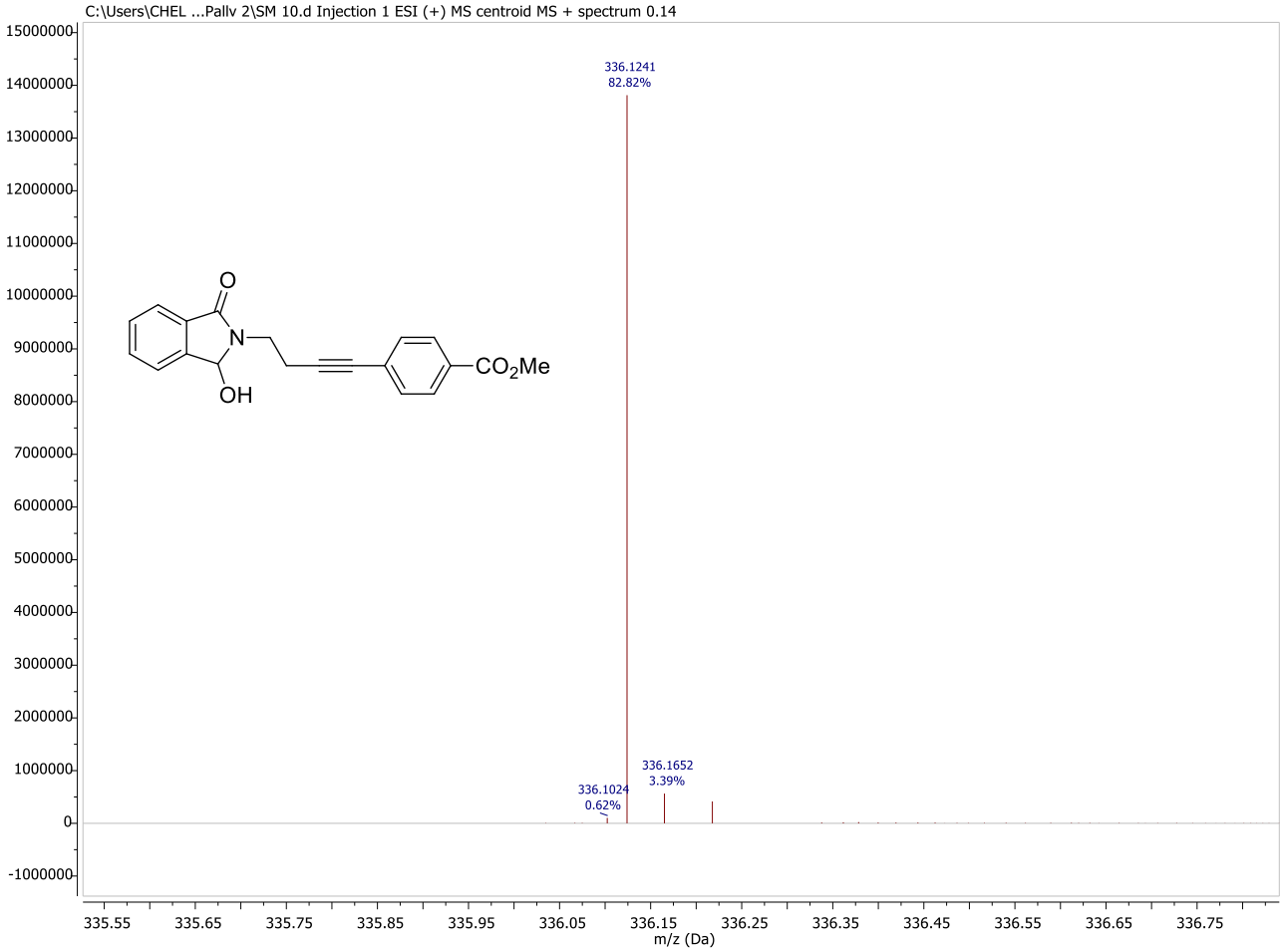
HRMS spectrum of **1e**



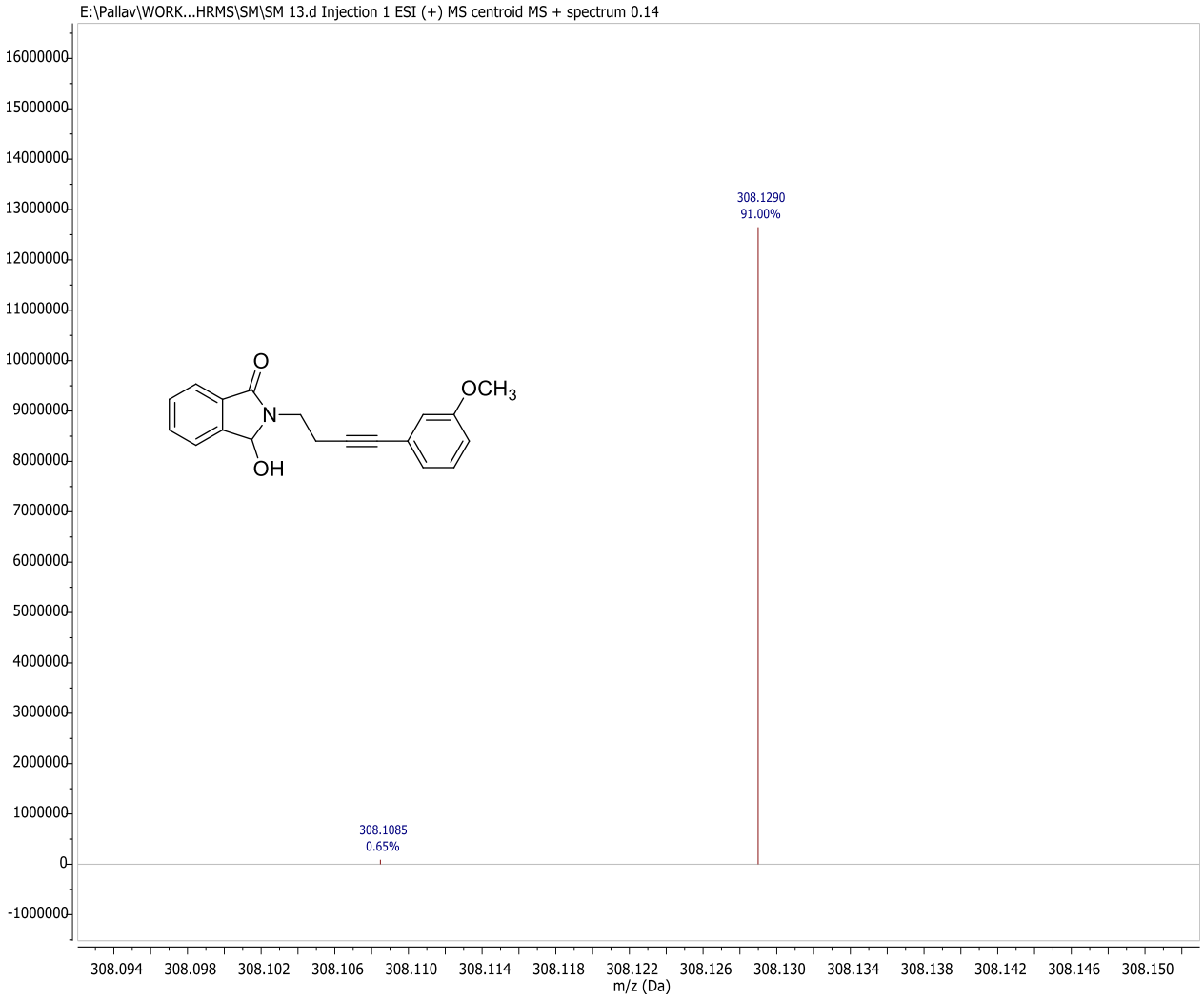
HRMS spectrum of **1h**



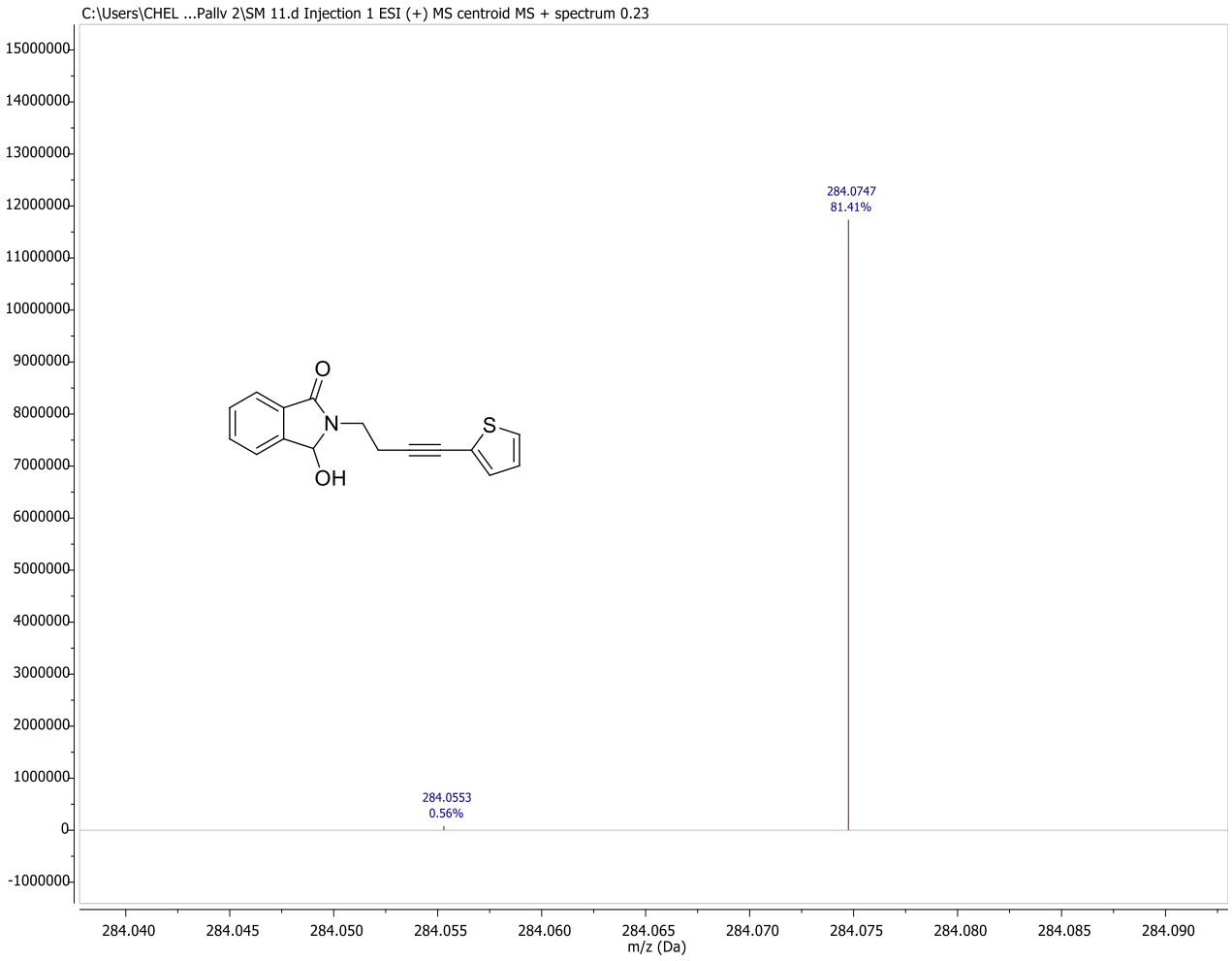
HRMS spectrum of **1i**



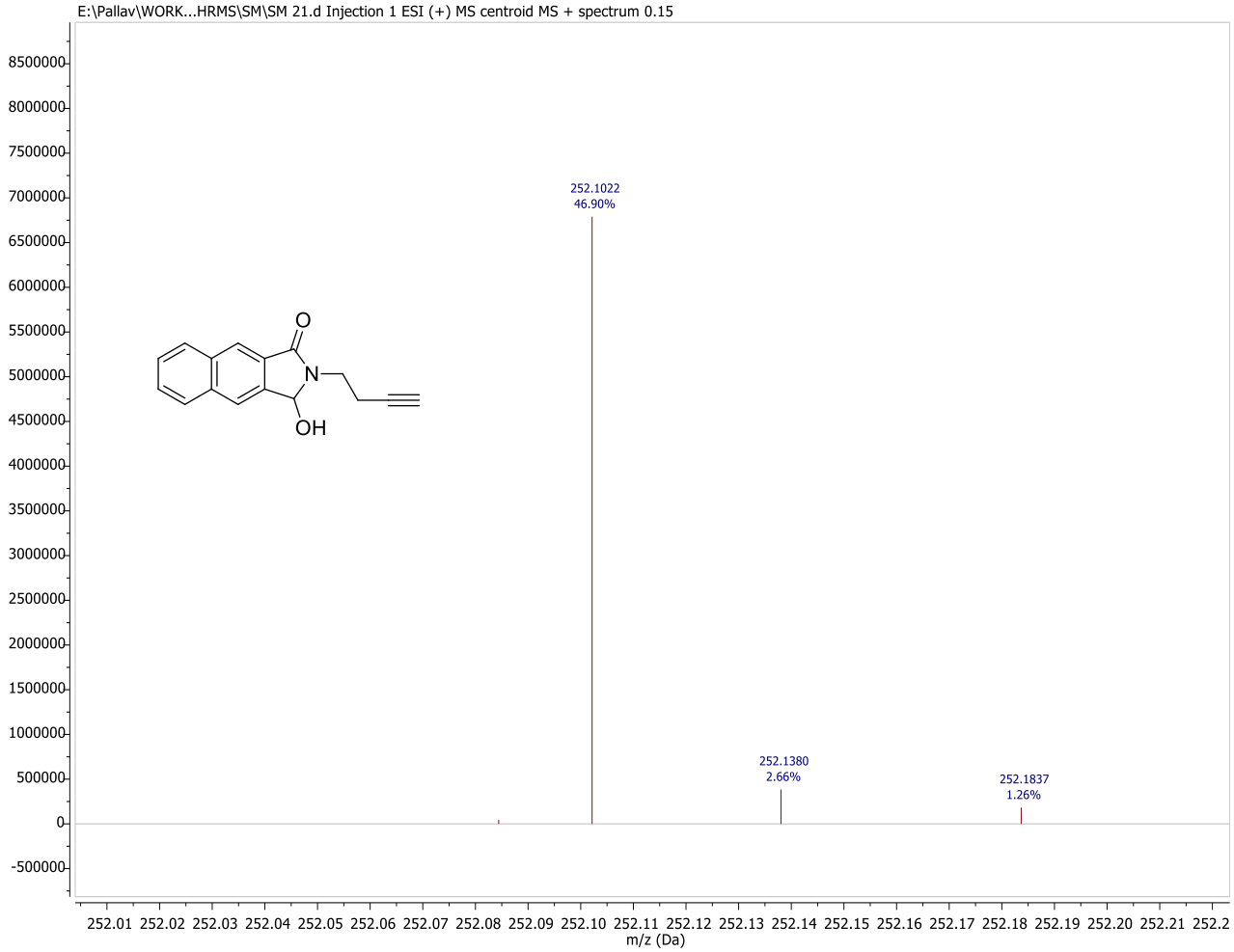
HRMS spectrum of **1l**



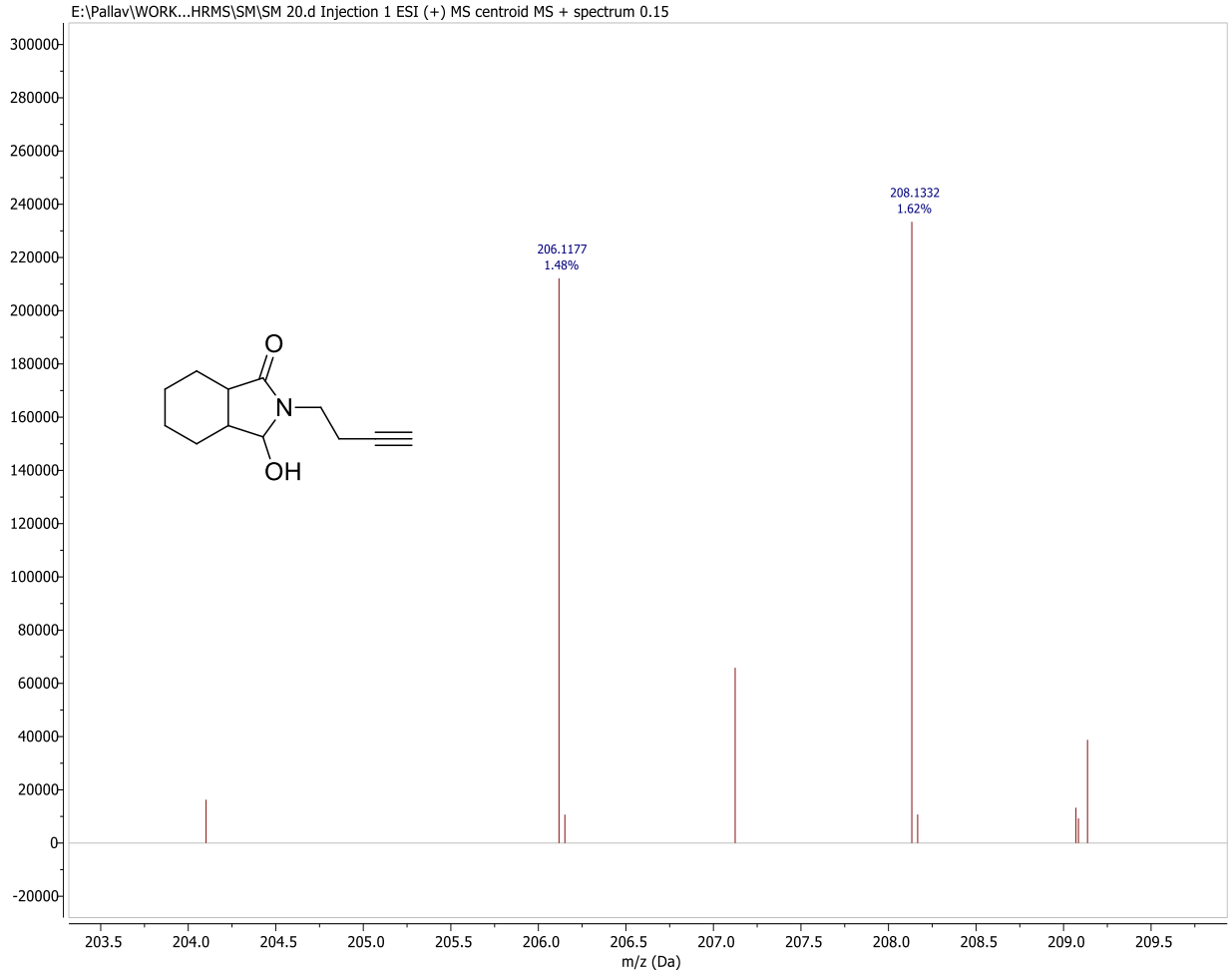
HRMS spectrum of **1o**



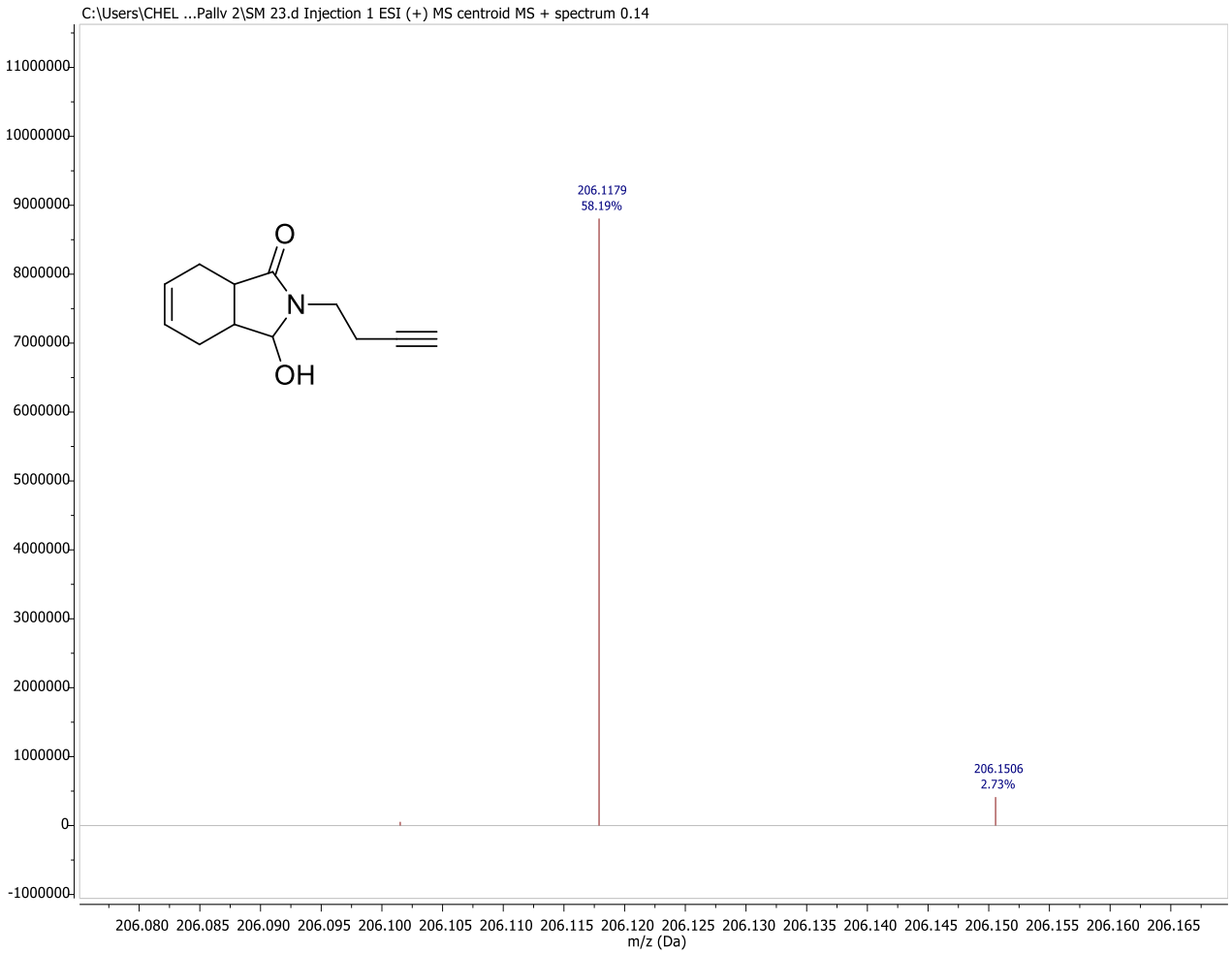
HRMS spectrum of **1p**



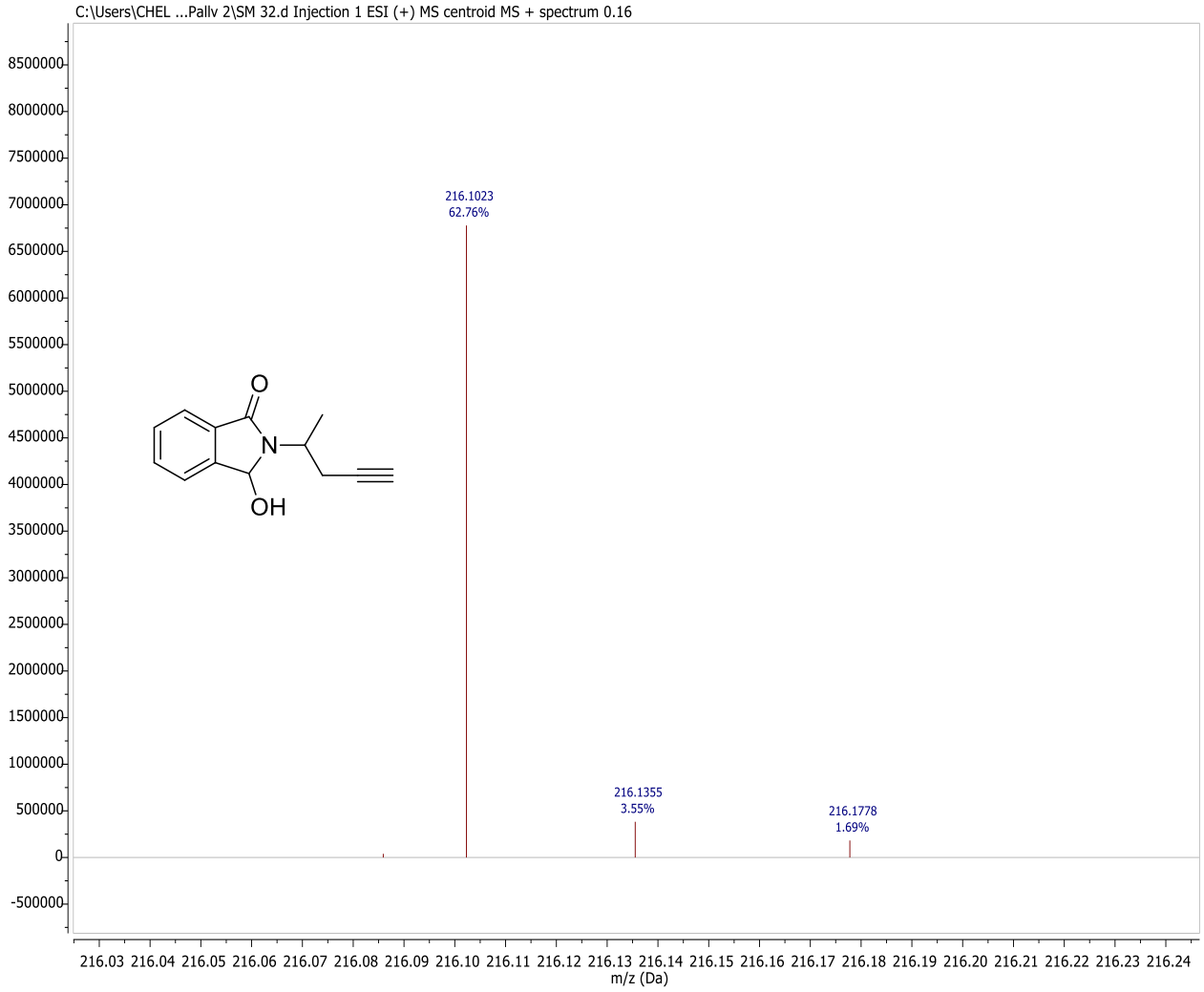
HRMS spectrum of **1q**



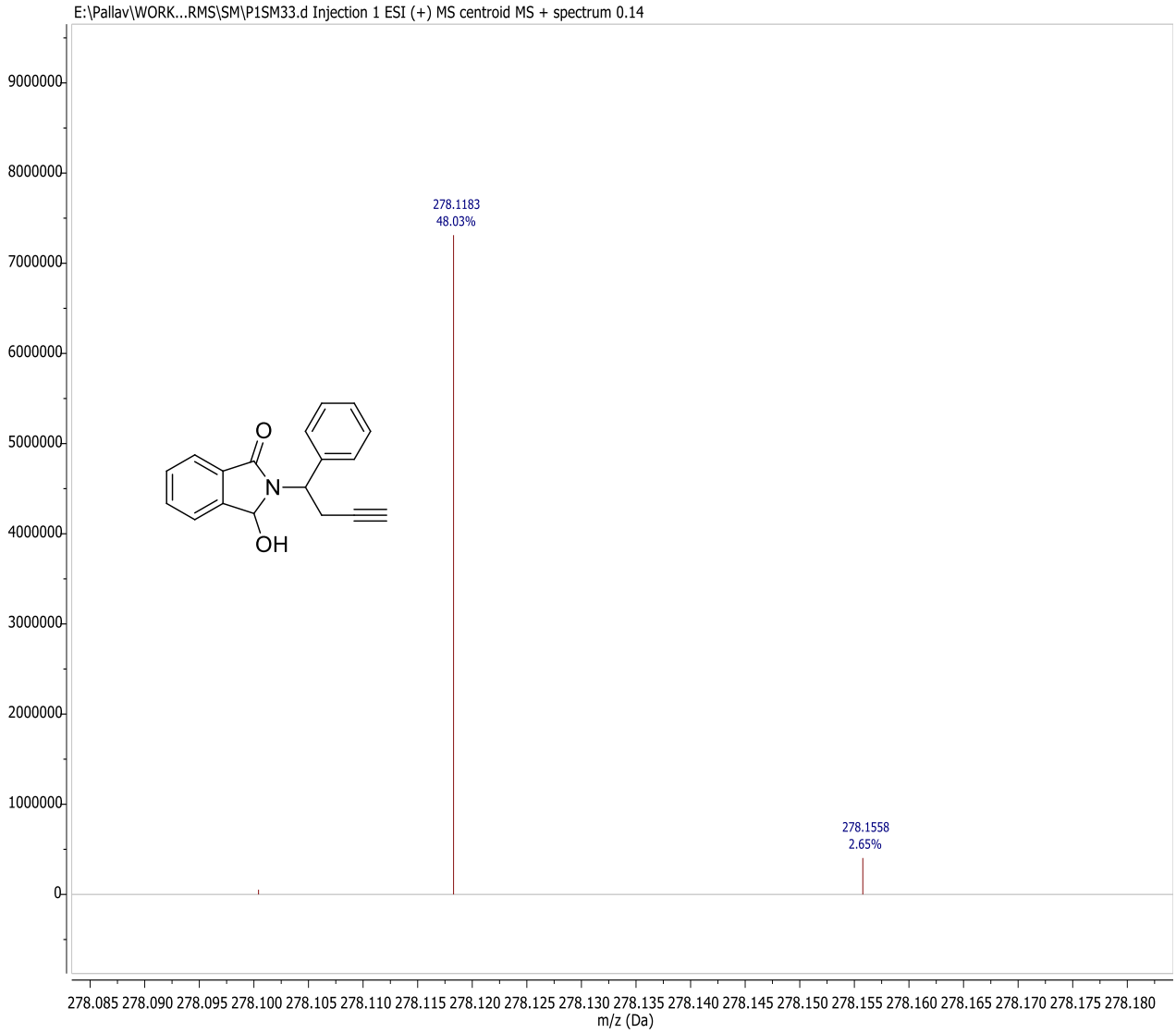
HRMS spectrum of **1r**



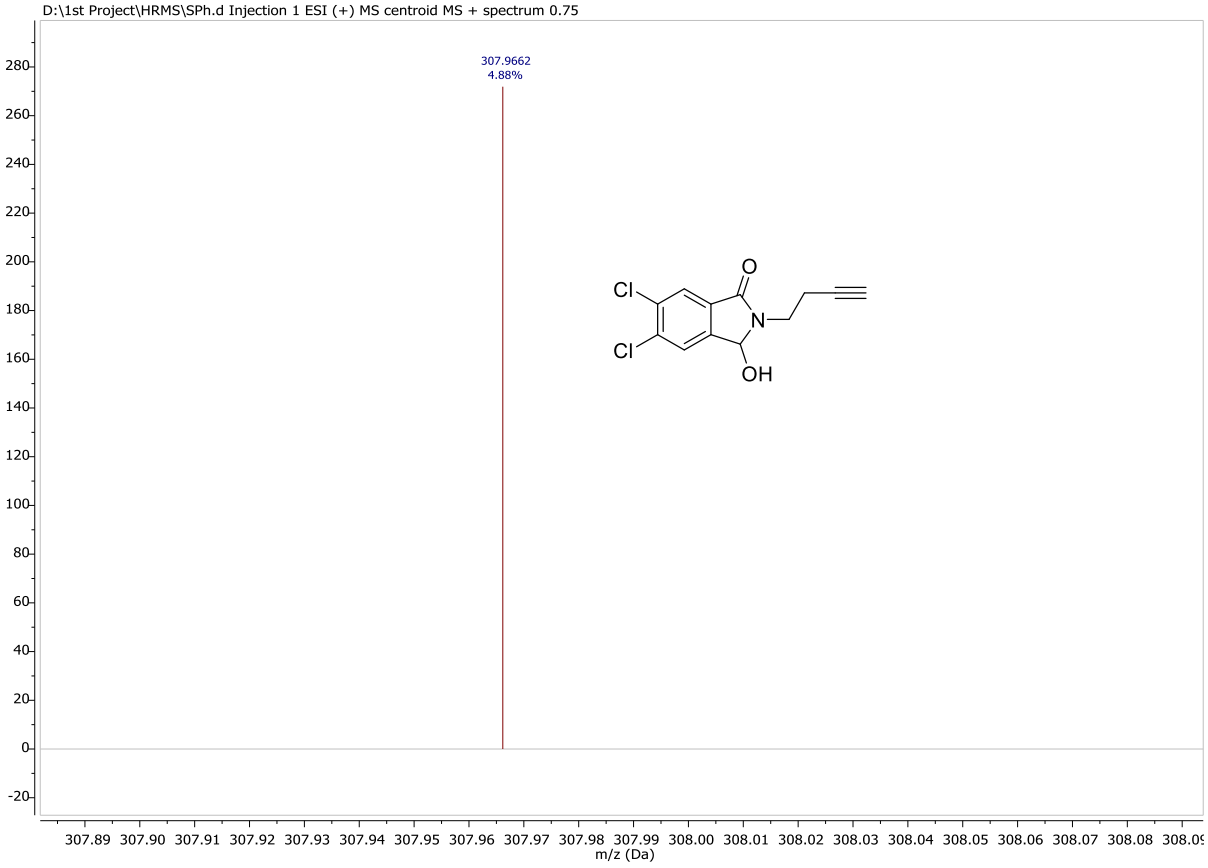
HRMS spectrum of **1s**



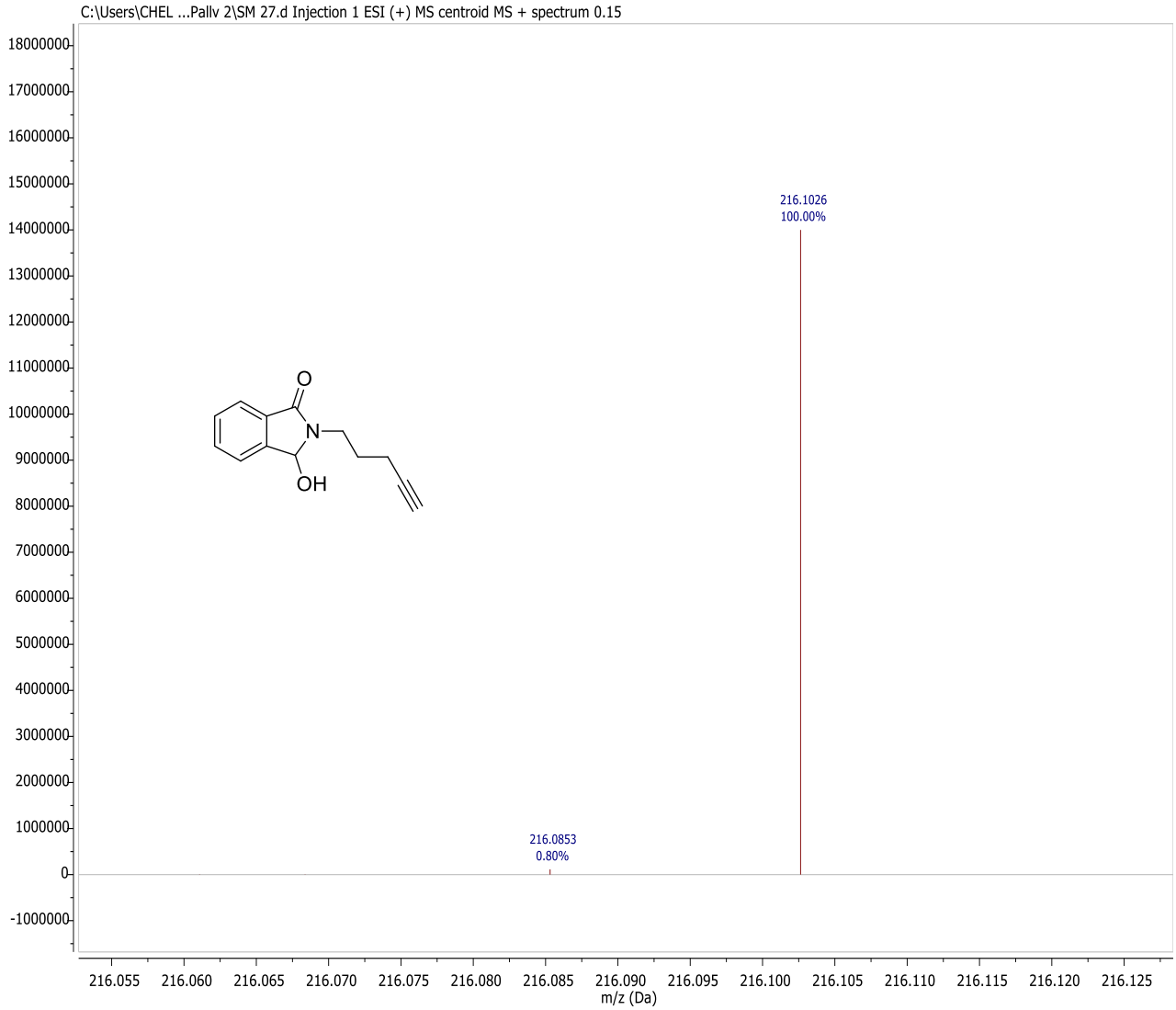
HRMS spectrum of **1t**



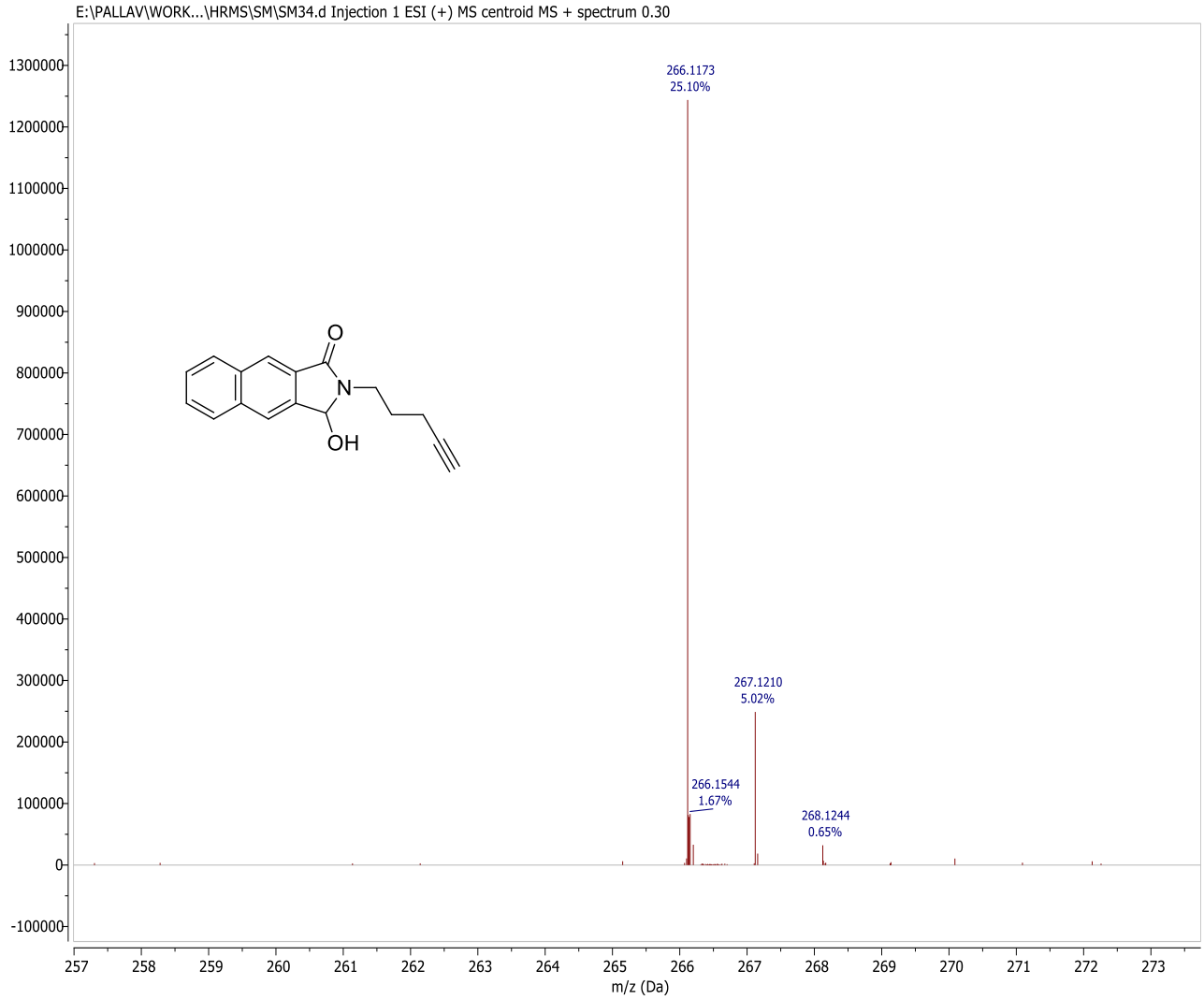
HRMS spectrum of **1u**



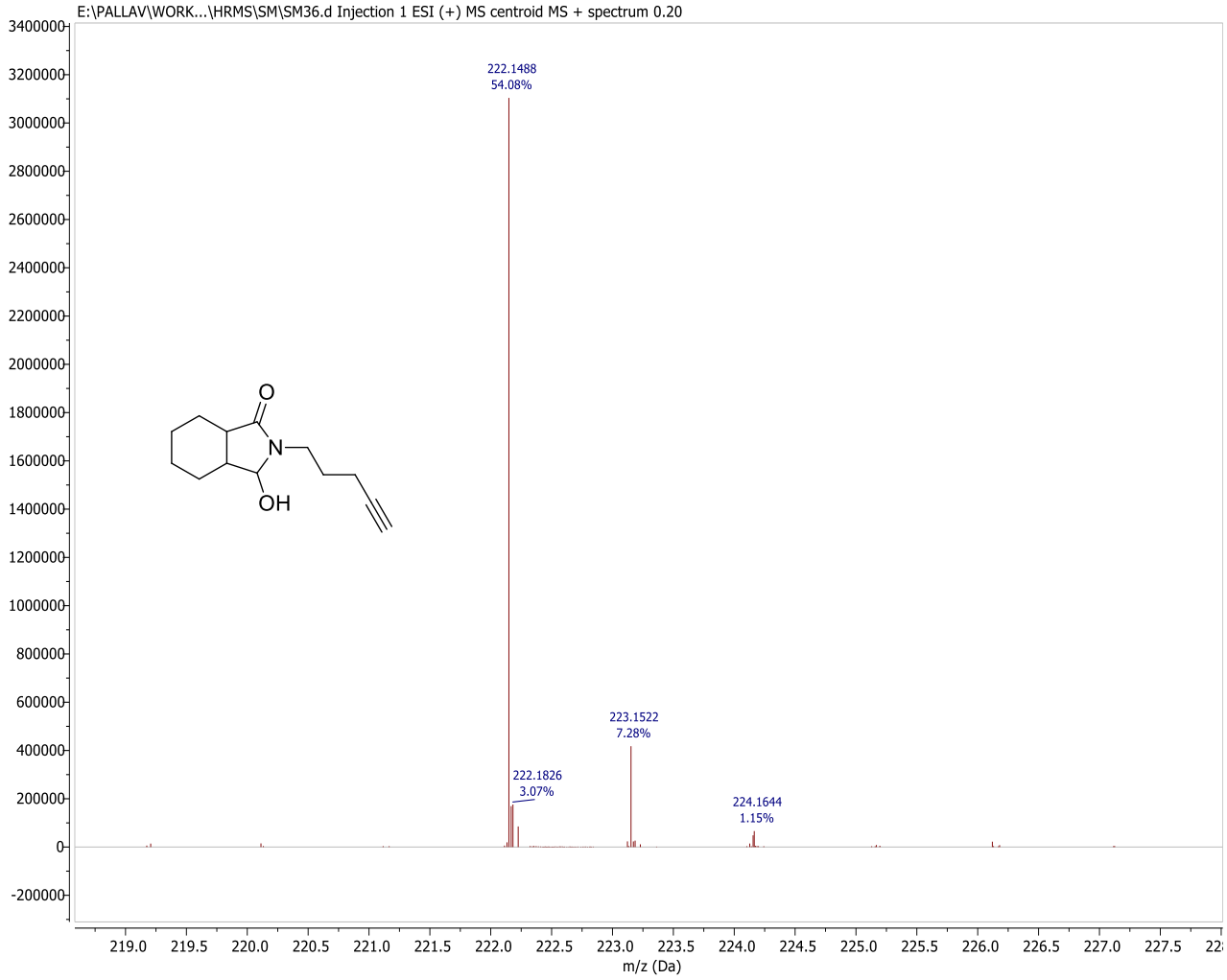
HRMS spectrum of **1v**



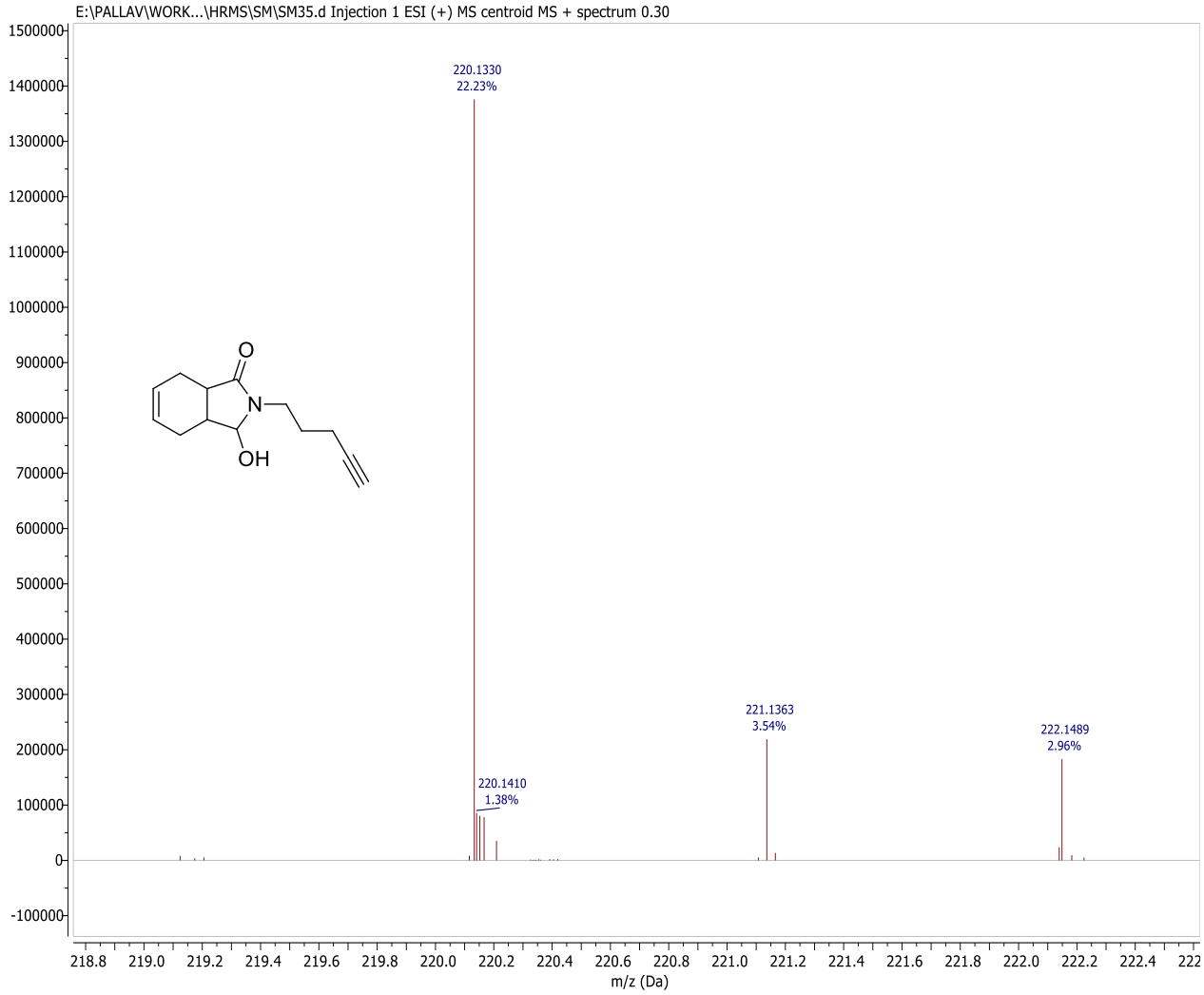
HRMS spectrum of **1w**



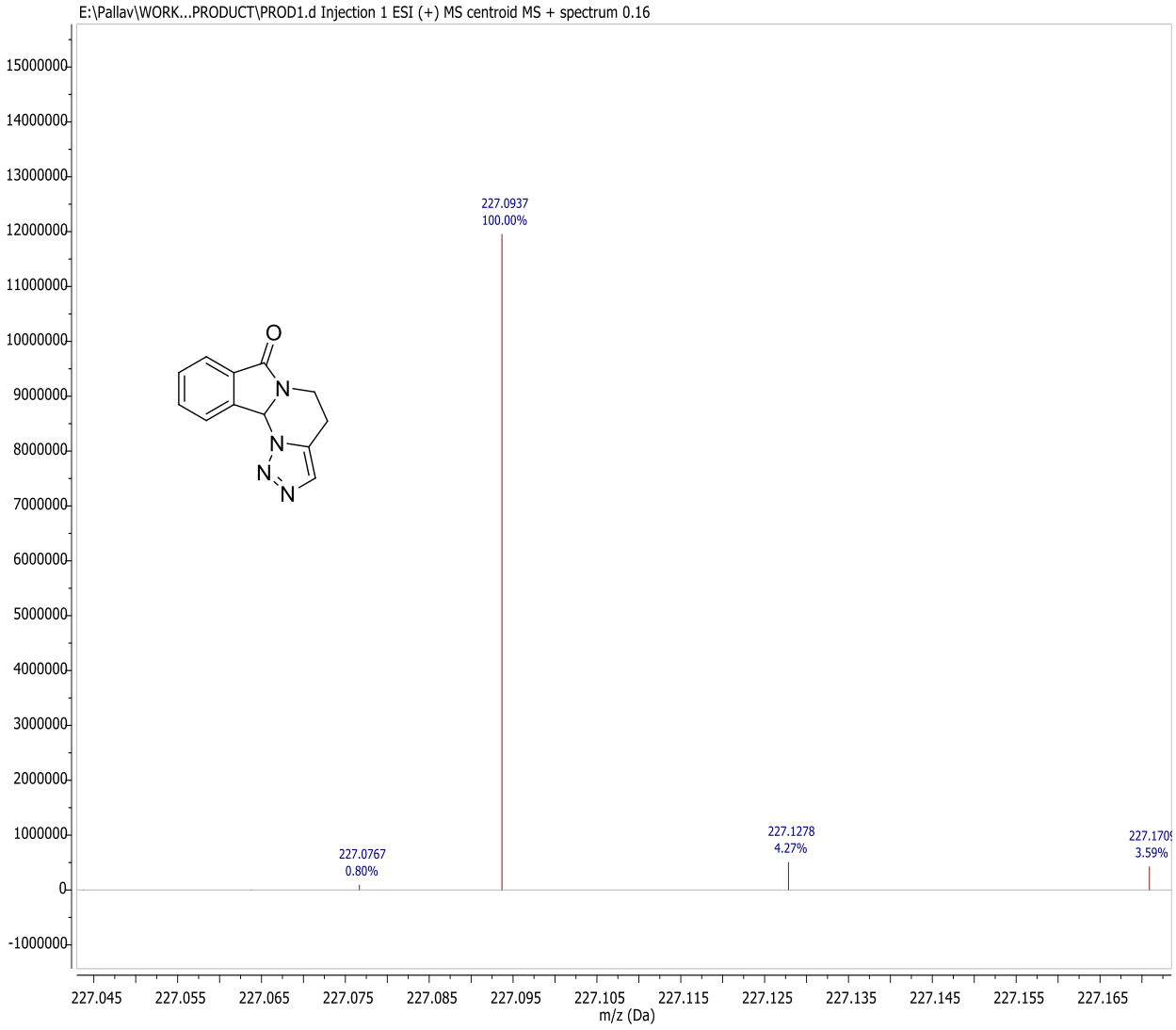
HRMS spectrum of **1x**



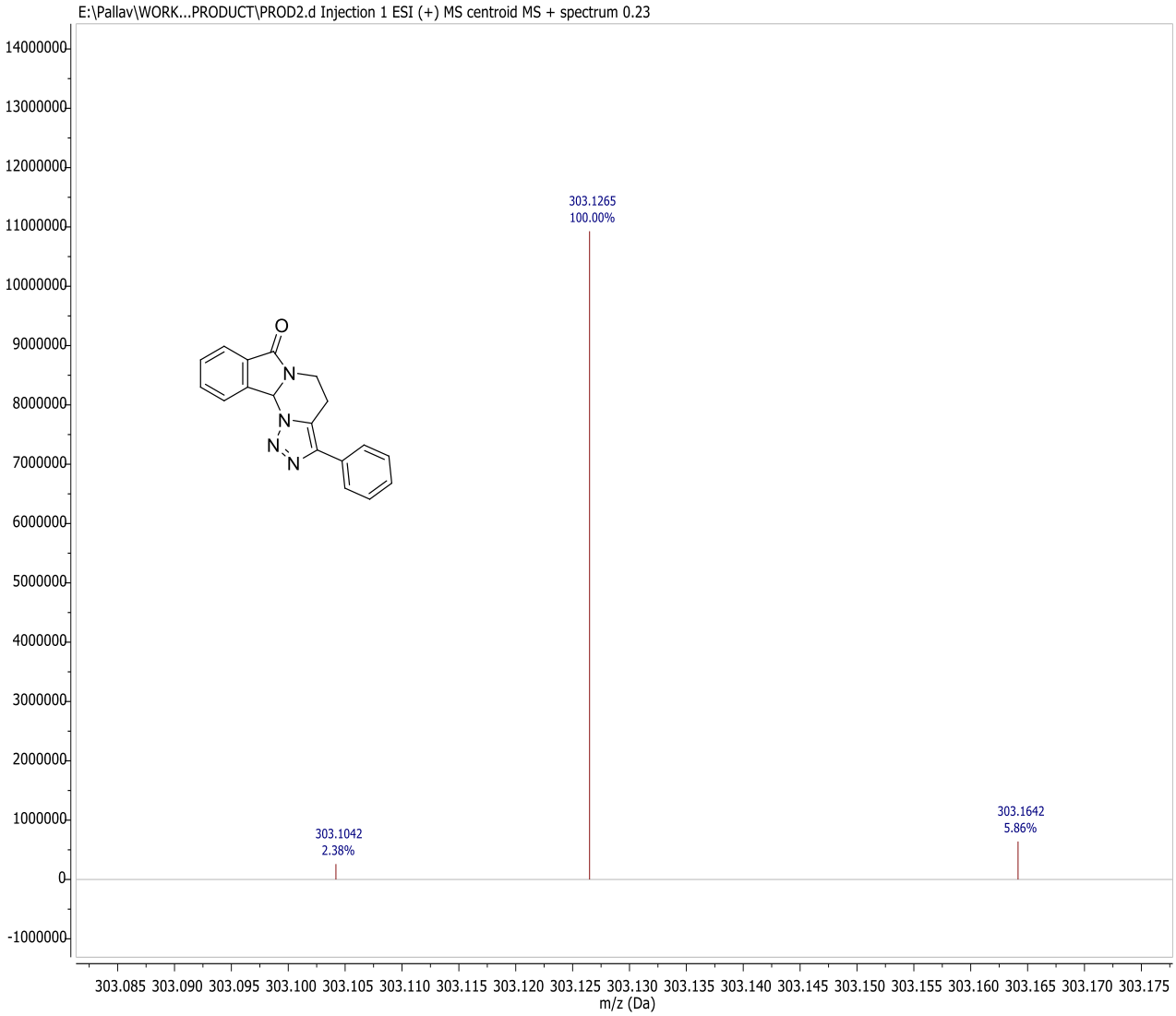
HRMS spectrum of **1y**



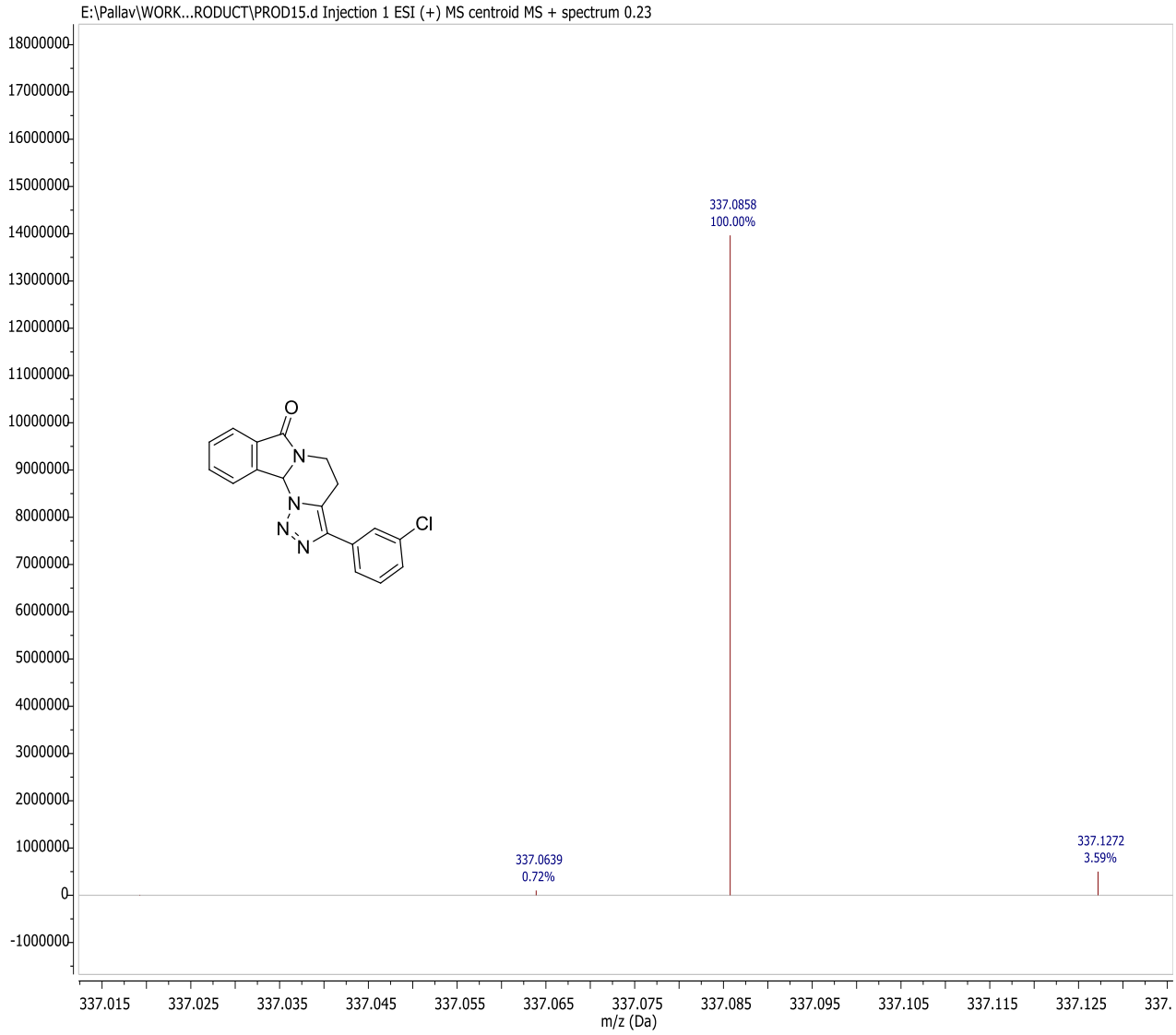
HRMS spectrum of **2a**



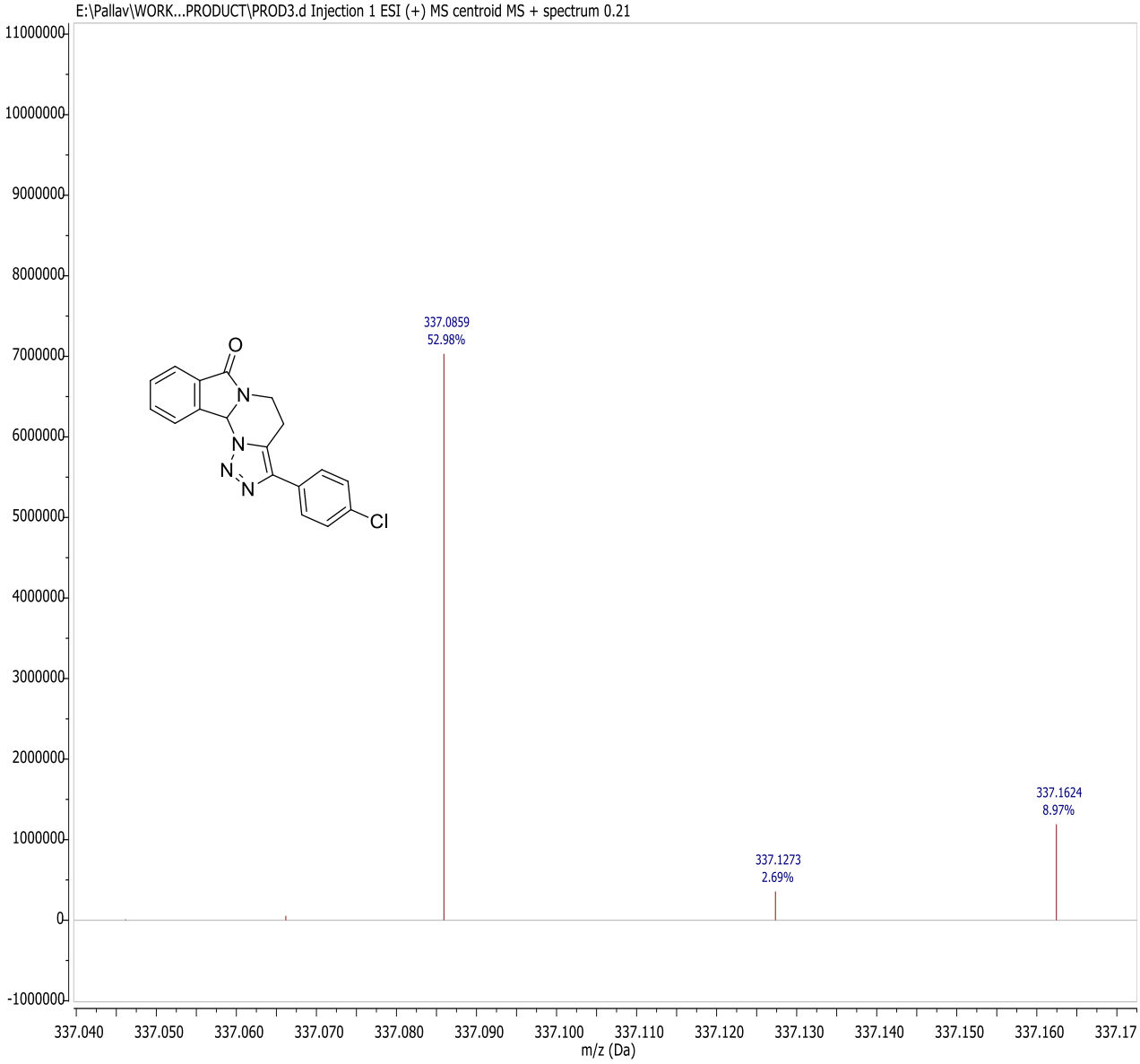
HRMS spectrum of **2b**



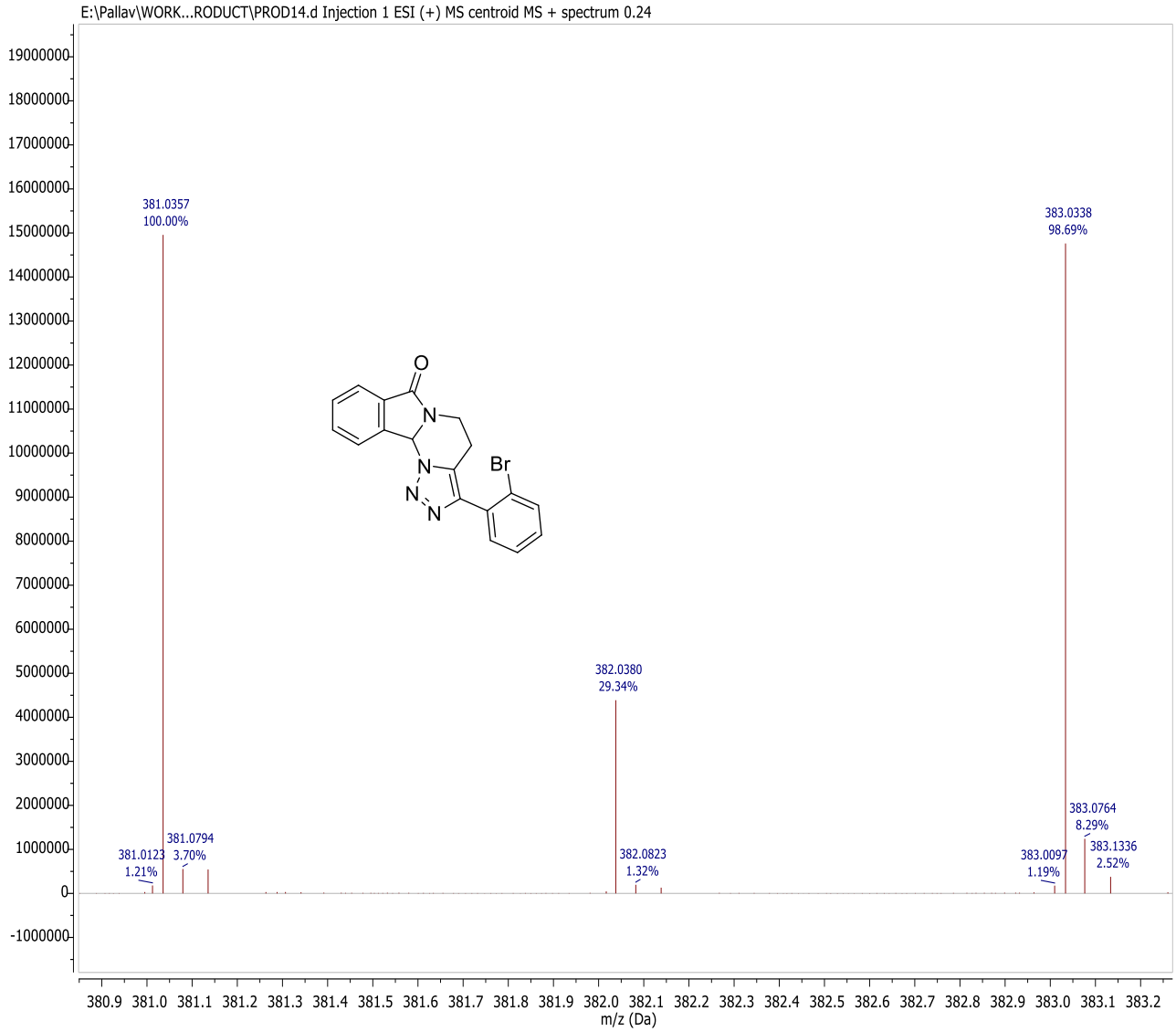
HRMS spectrum of **2c**



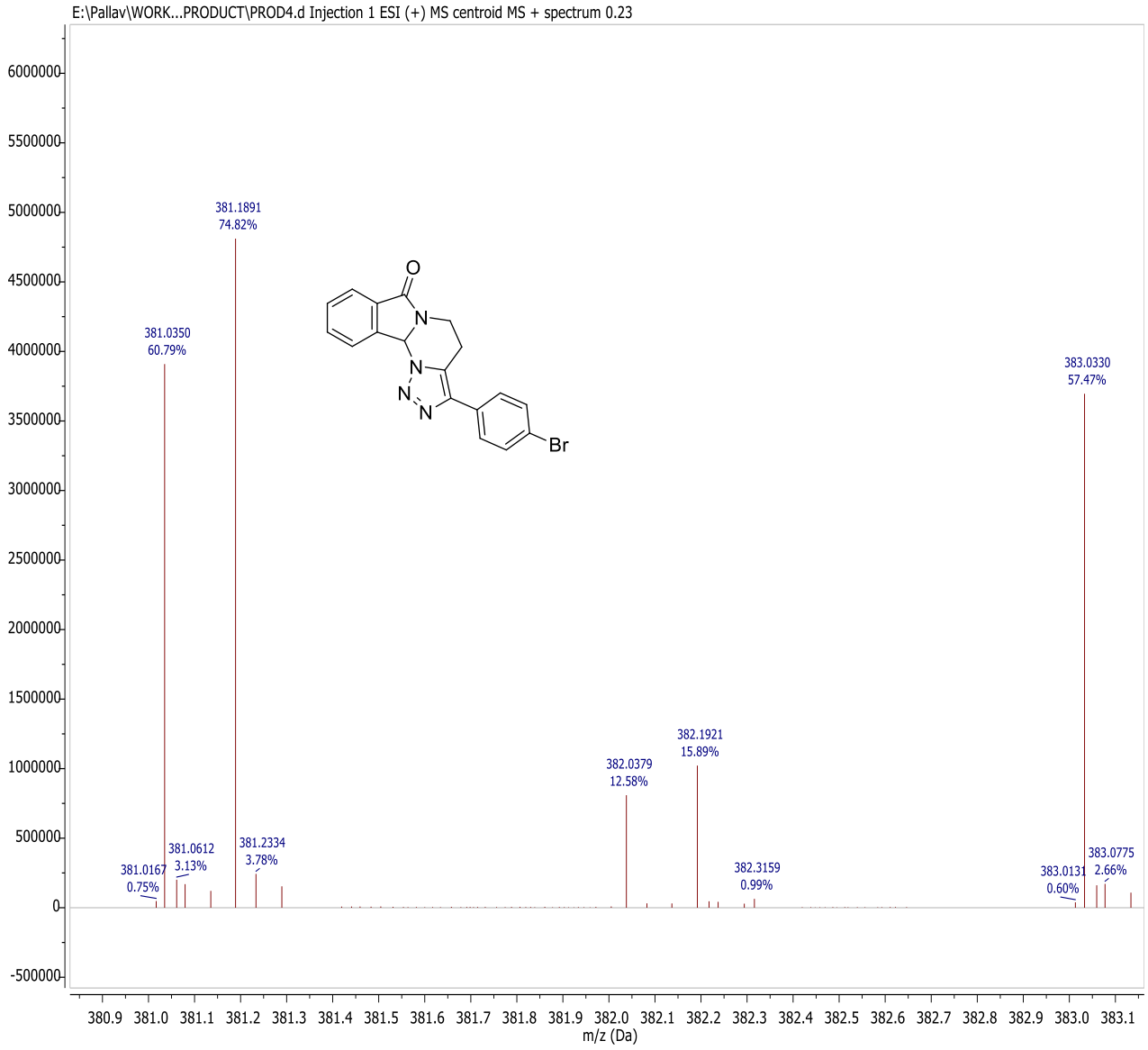
HRMS spectrum of **2d**



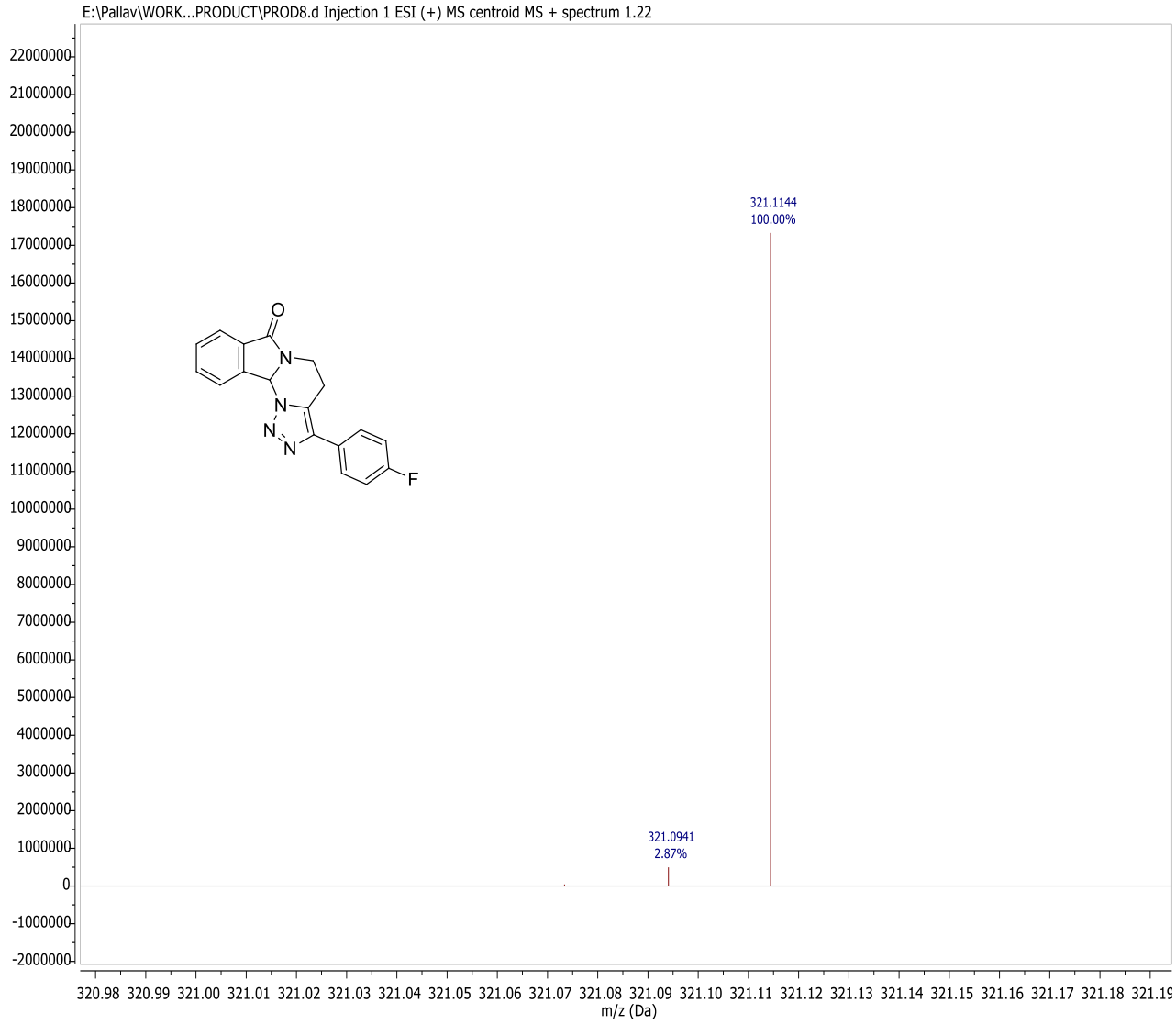
HRMS spectrum of **2e**



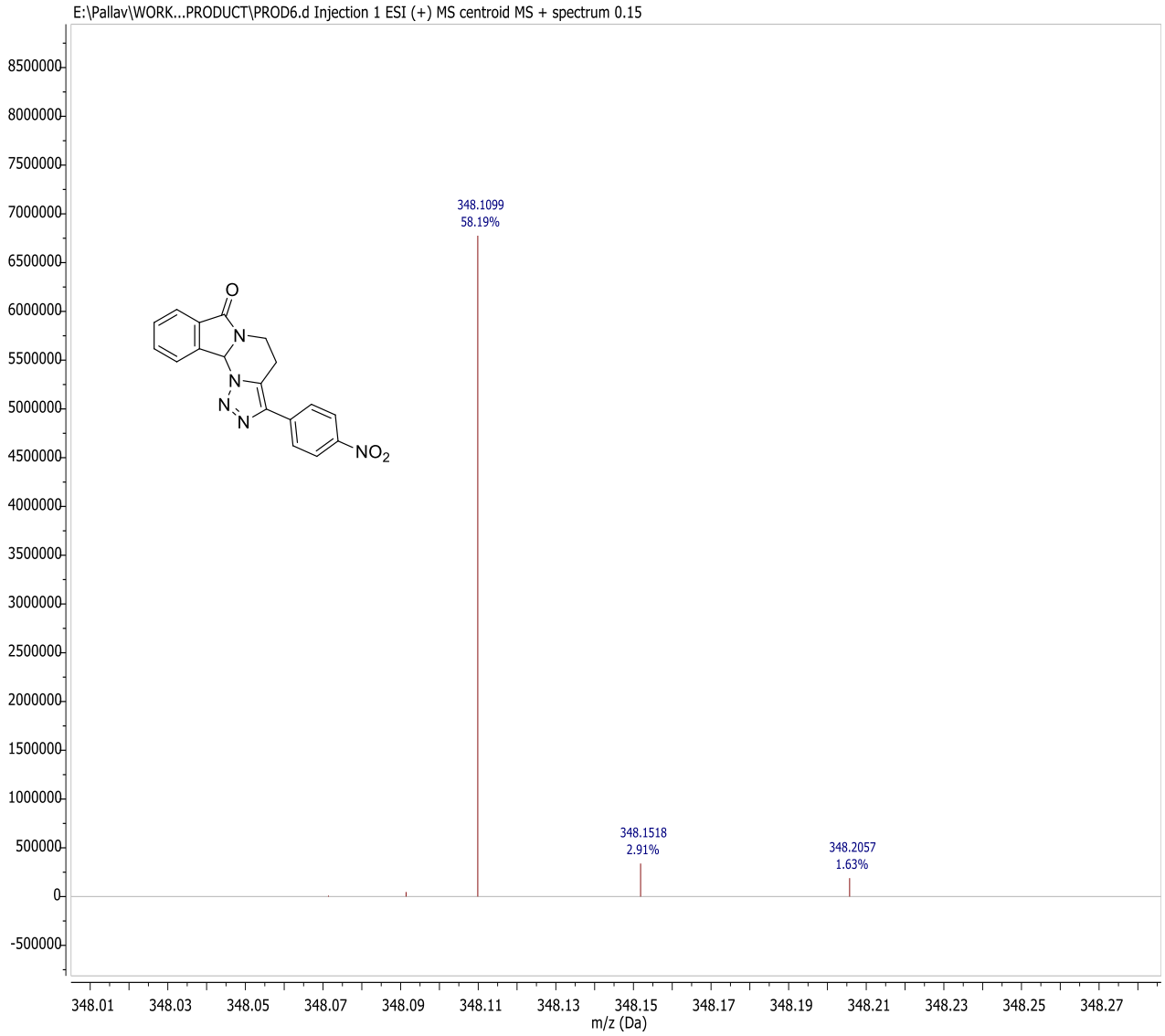
HRMS spectrum of **2f**



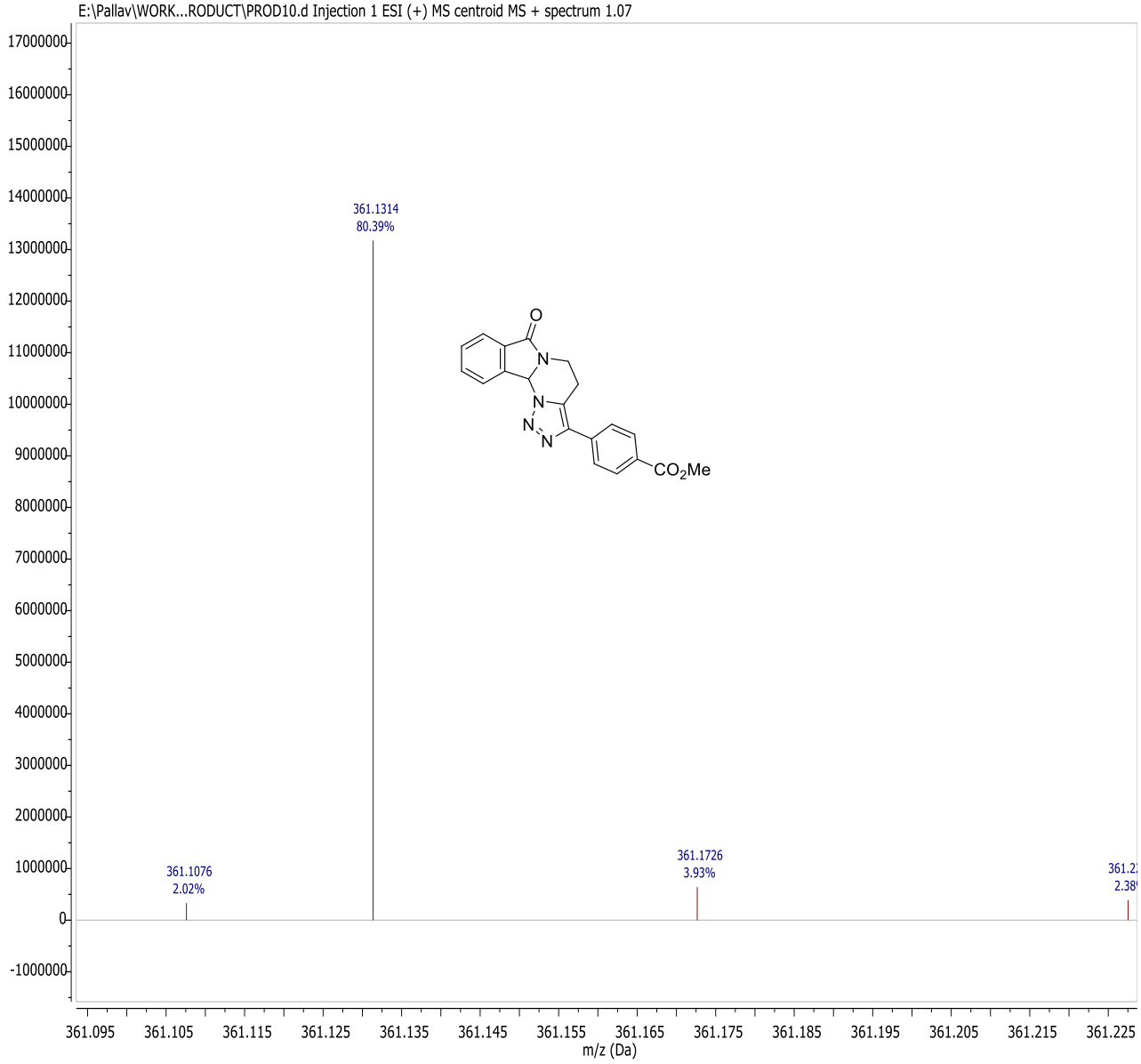
HRMS spectrum of **2g**



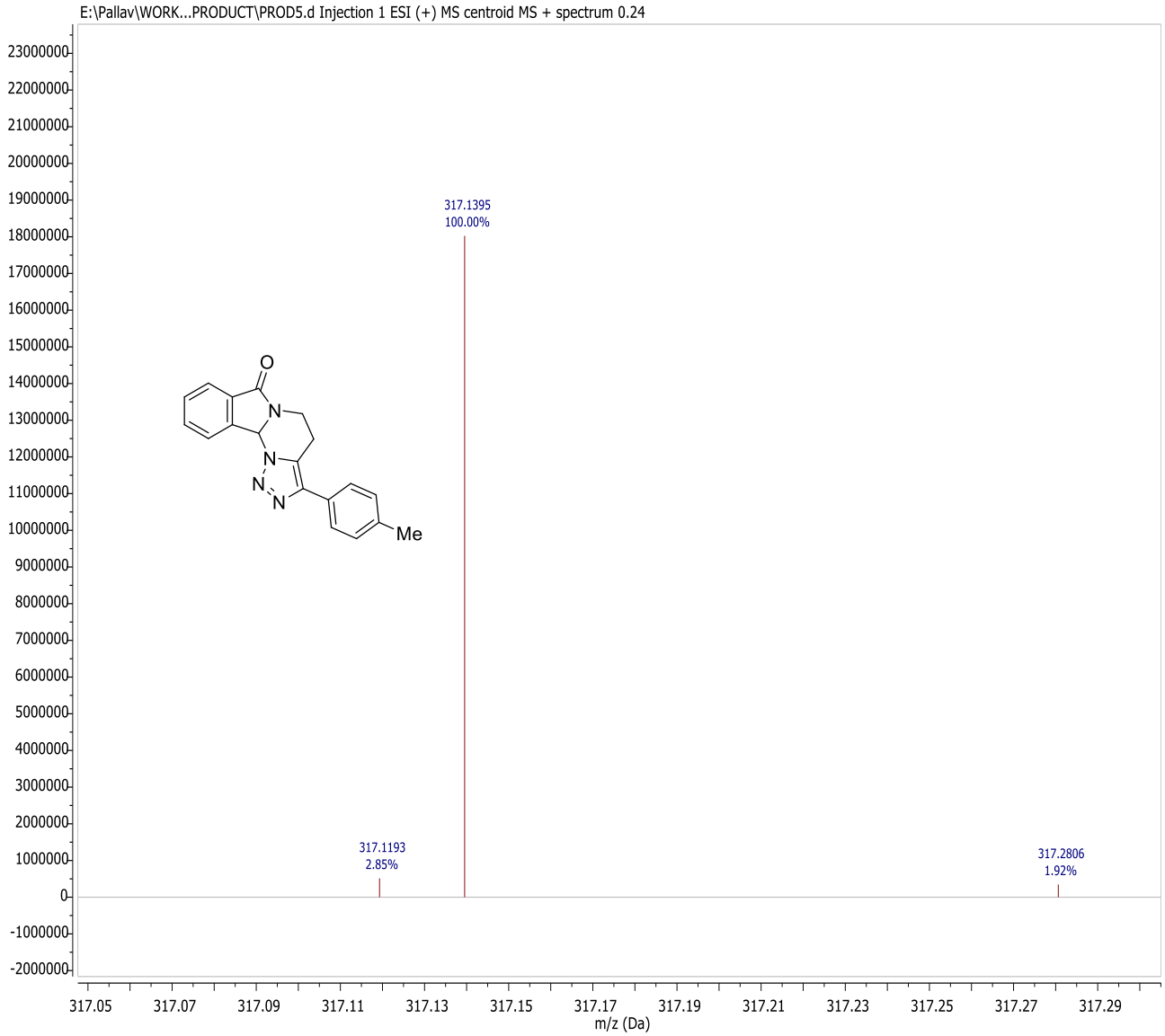
HRMS spectrum of **2h**



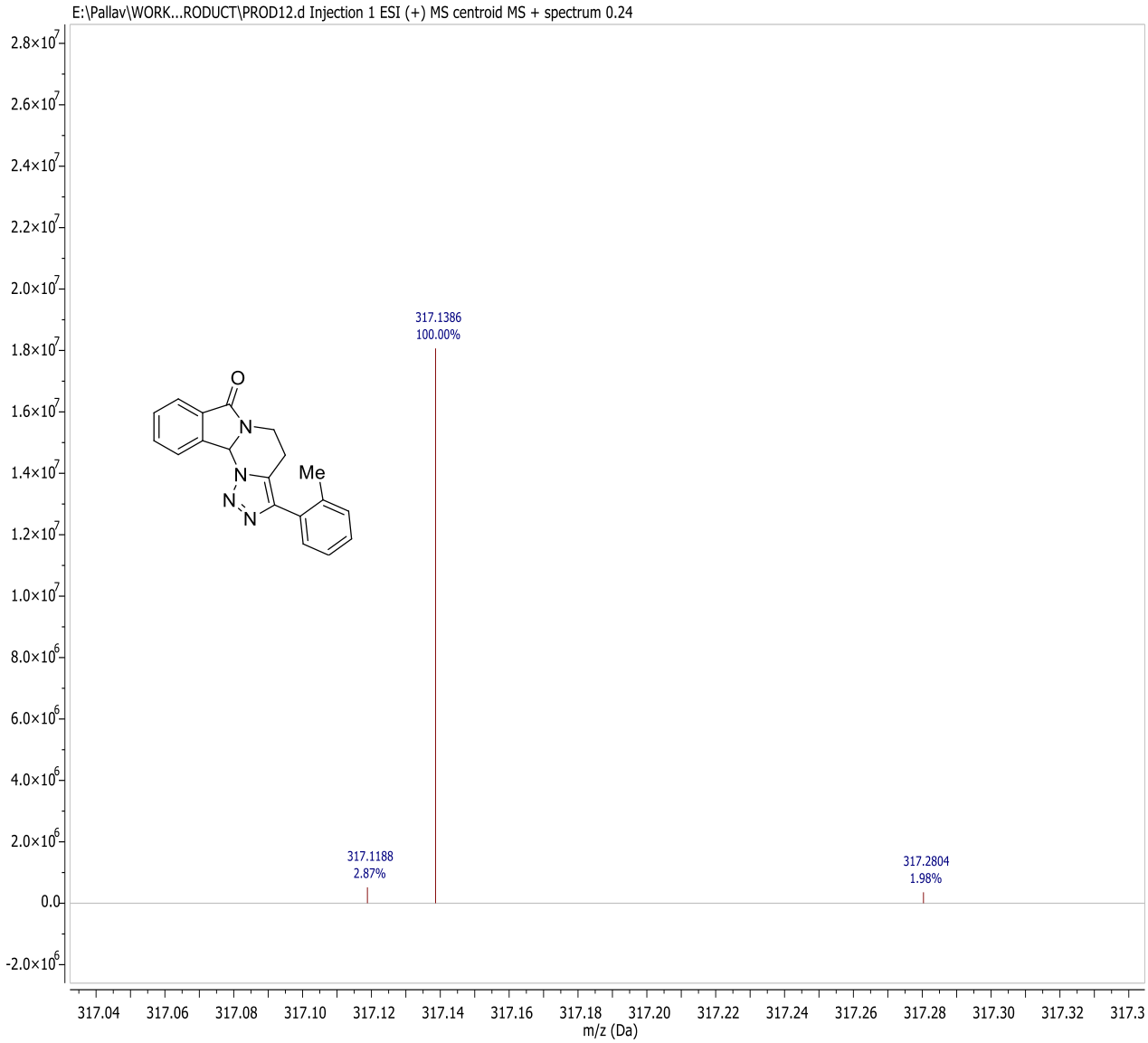
HRMS spectrum of **2i**



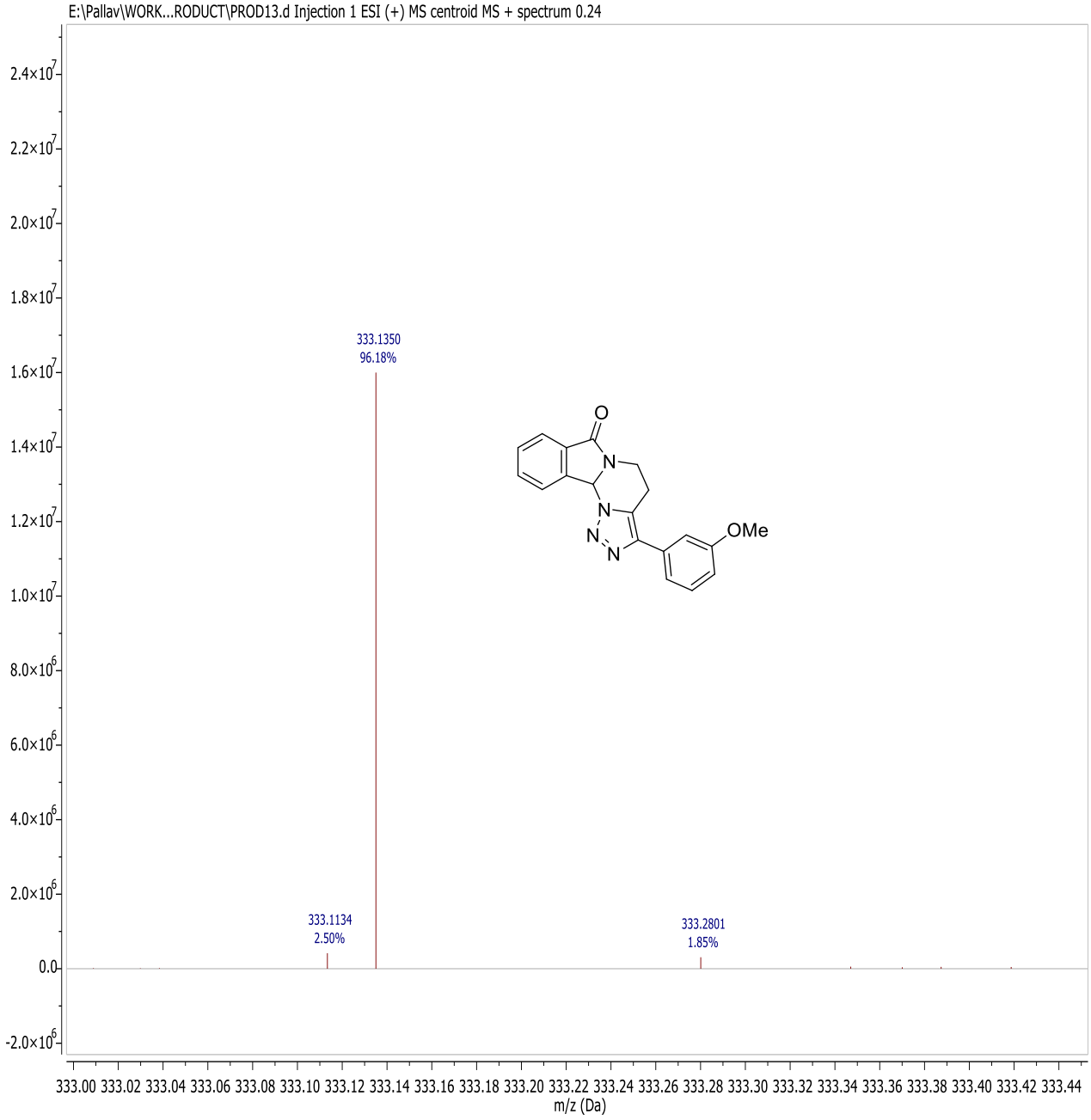
HRMS spectrum of **2j**



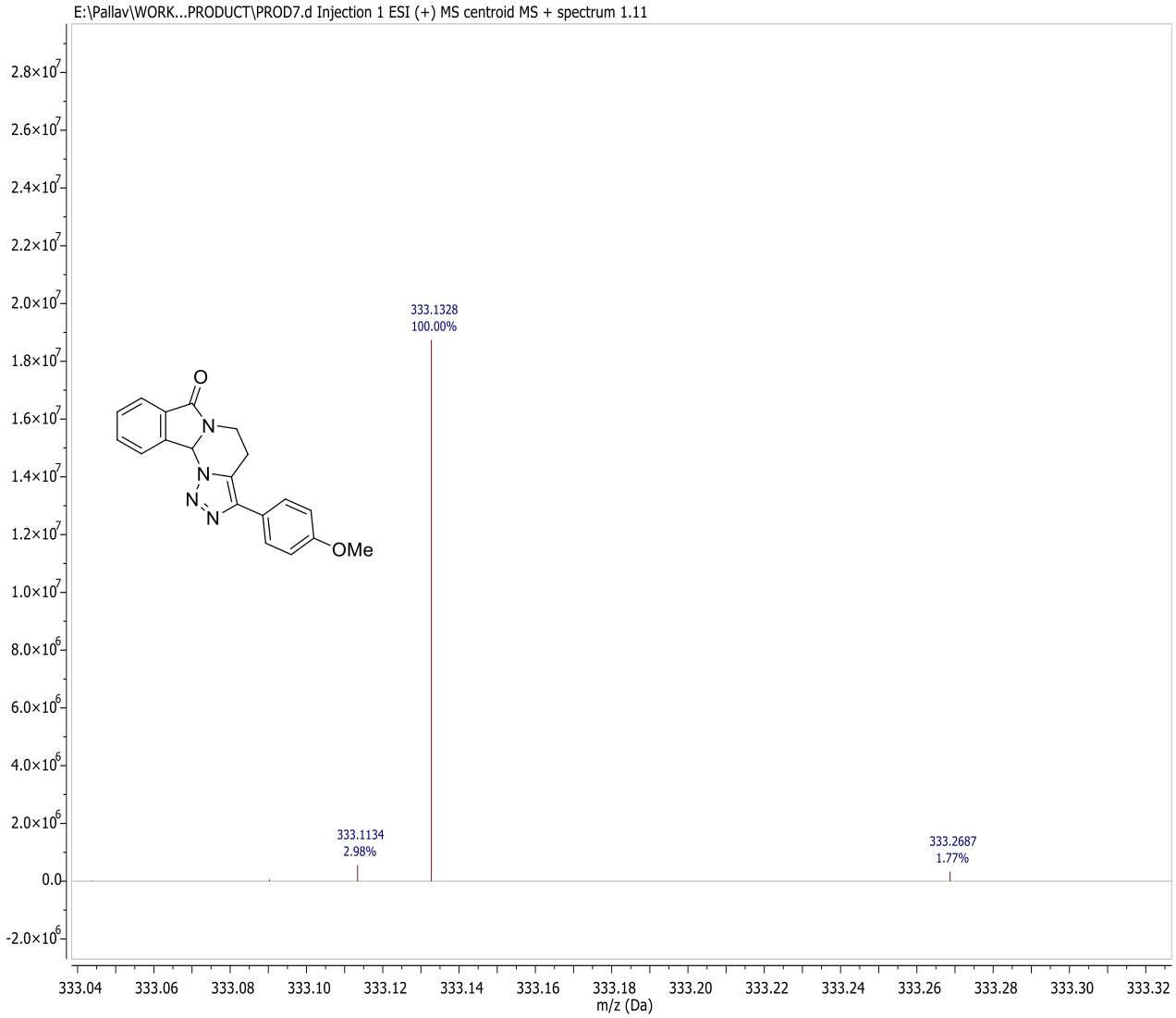
HRMS spectrum of **2k**



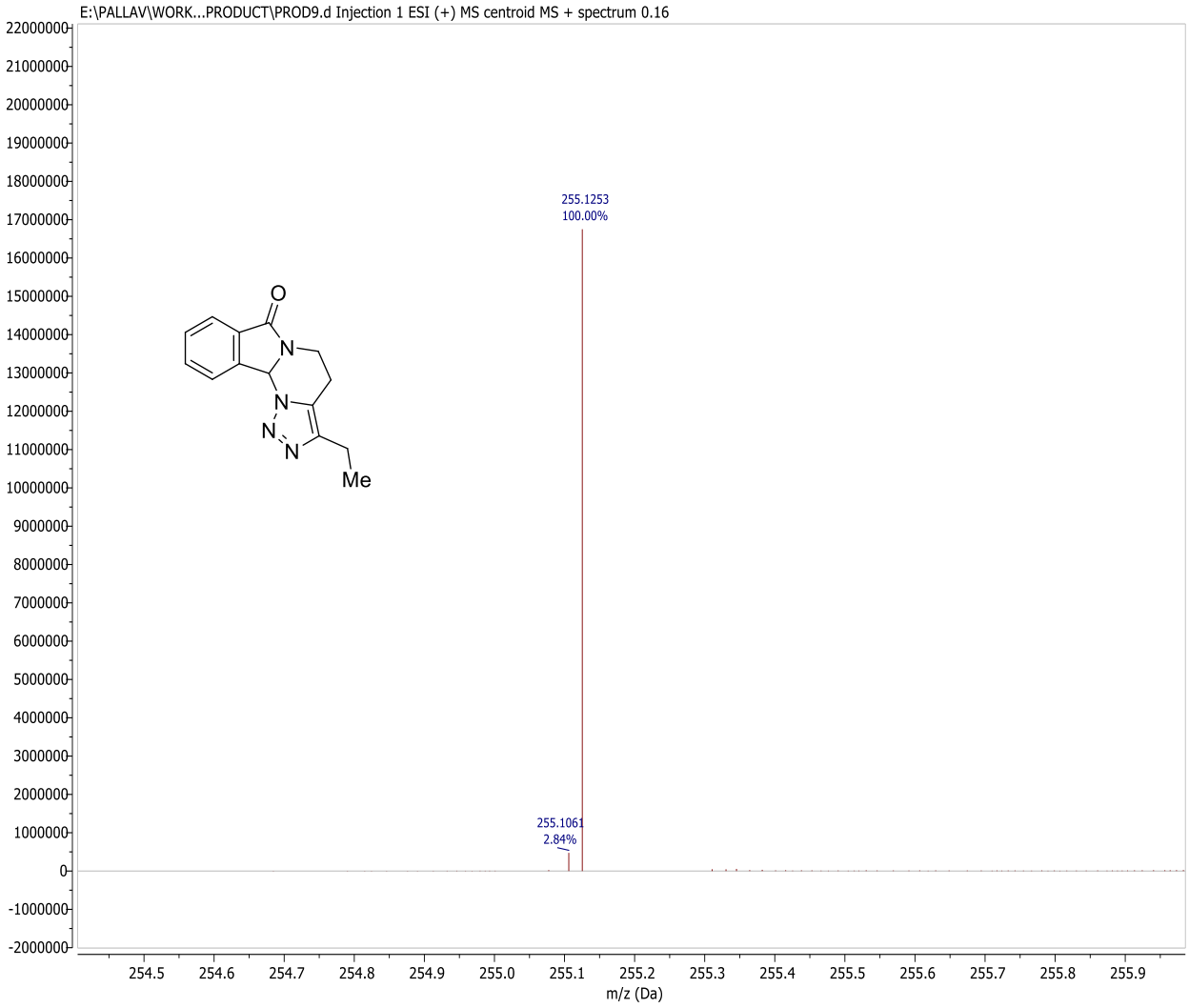
HRMS spectrum of **2l**



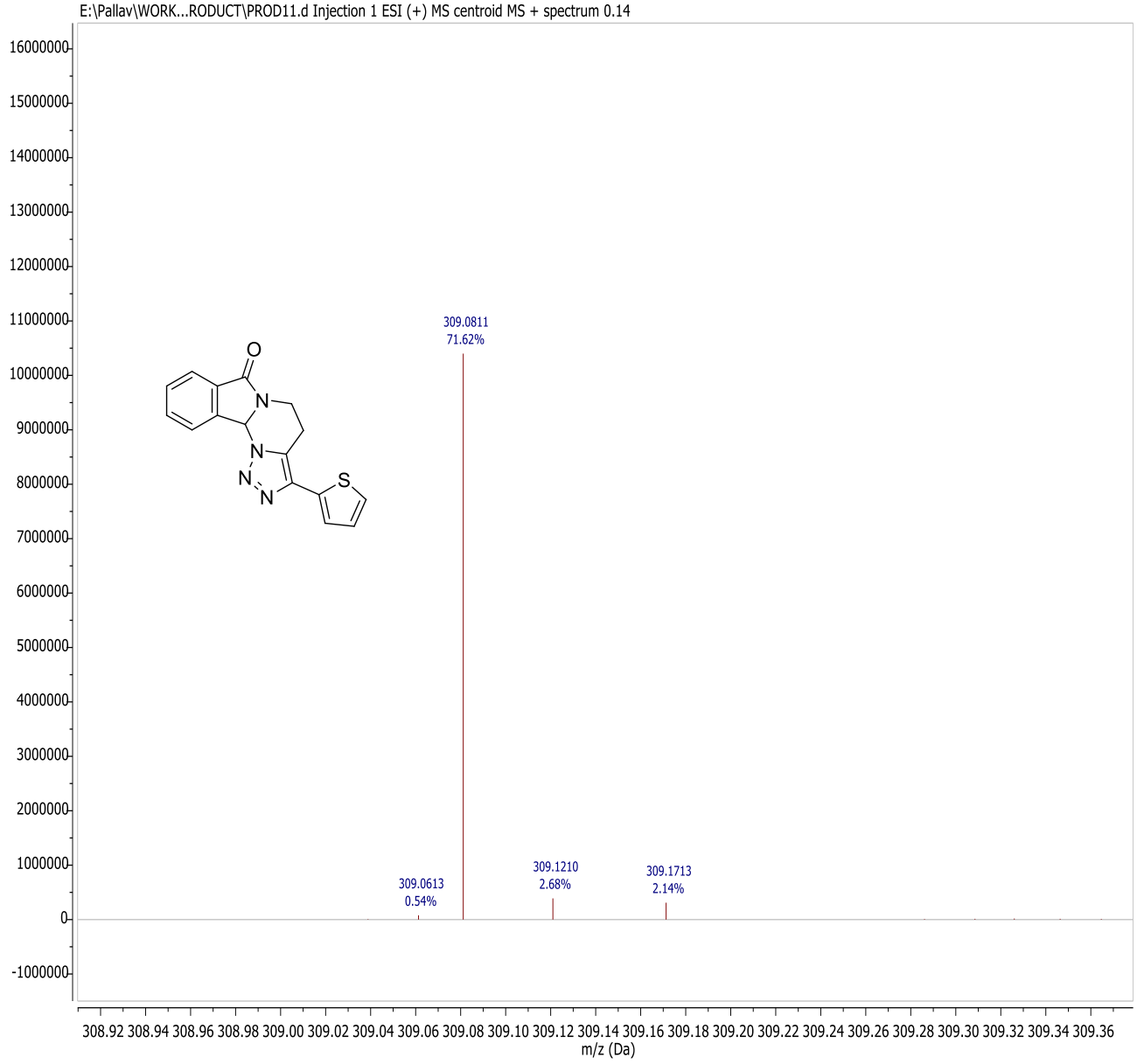
HRMS spectrum of **2m**



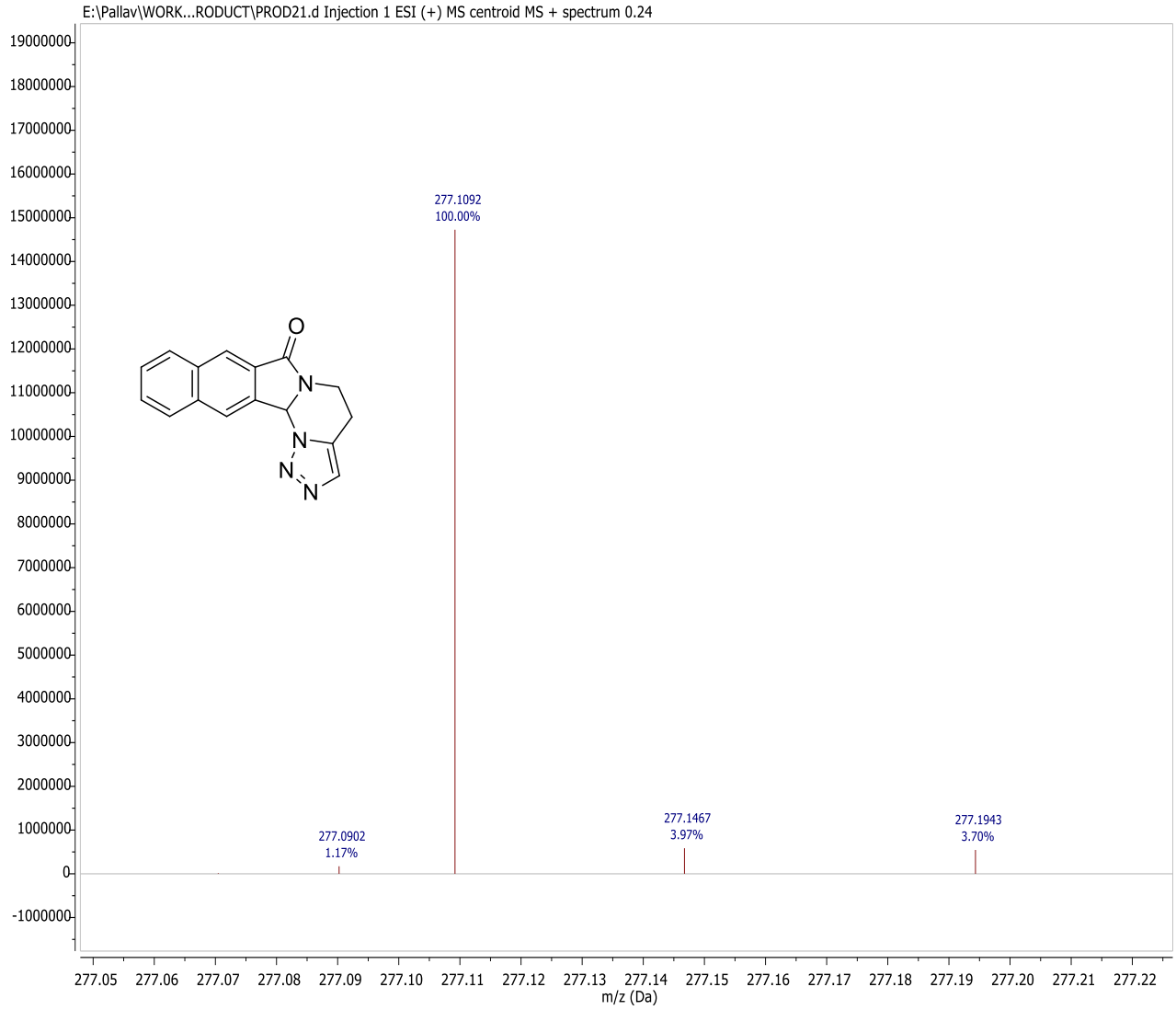
HRMS spectrum of **2n**



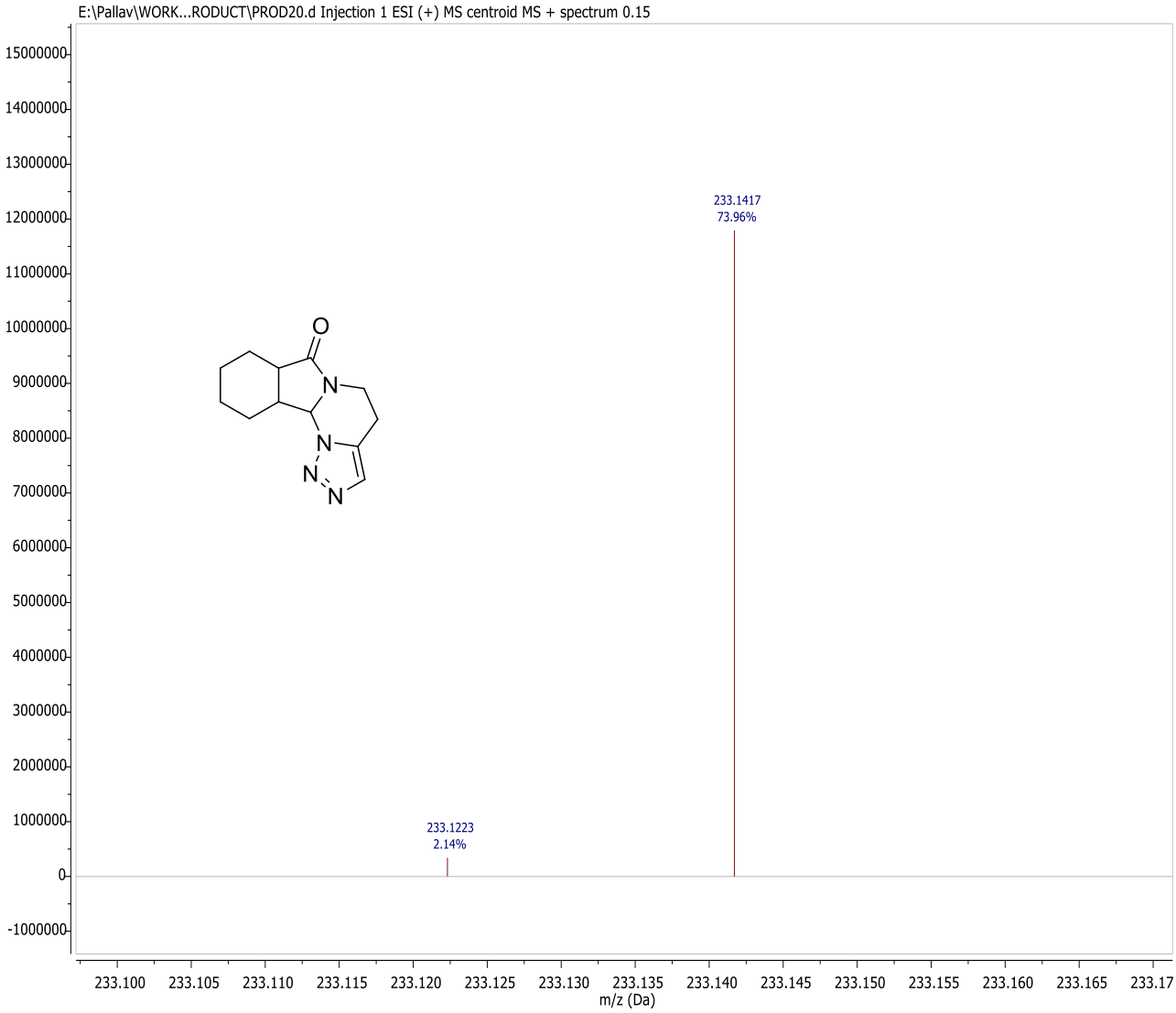
HRMS spectrum of **2o**



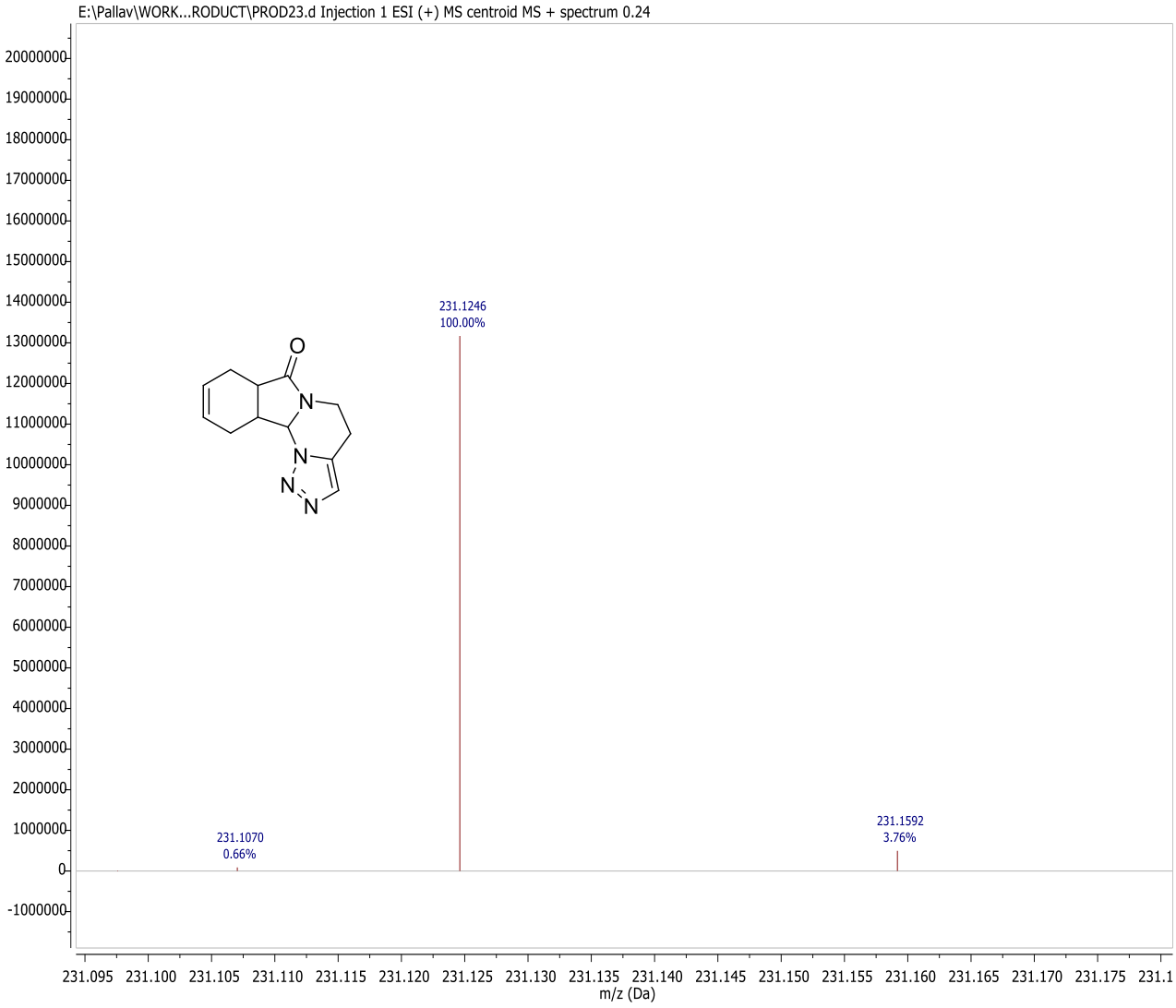
HRMS spectrum of **2p**



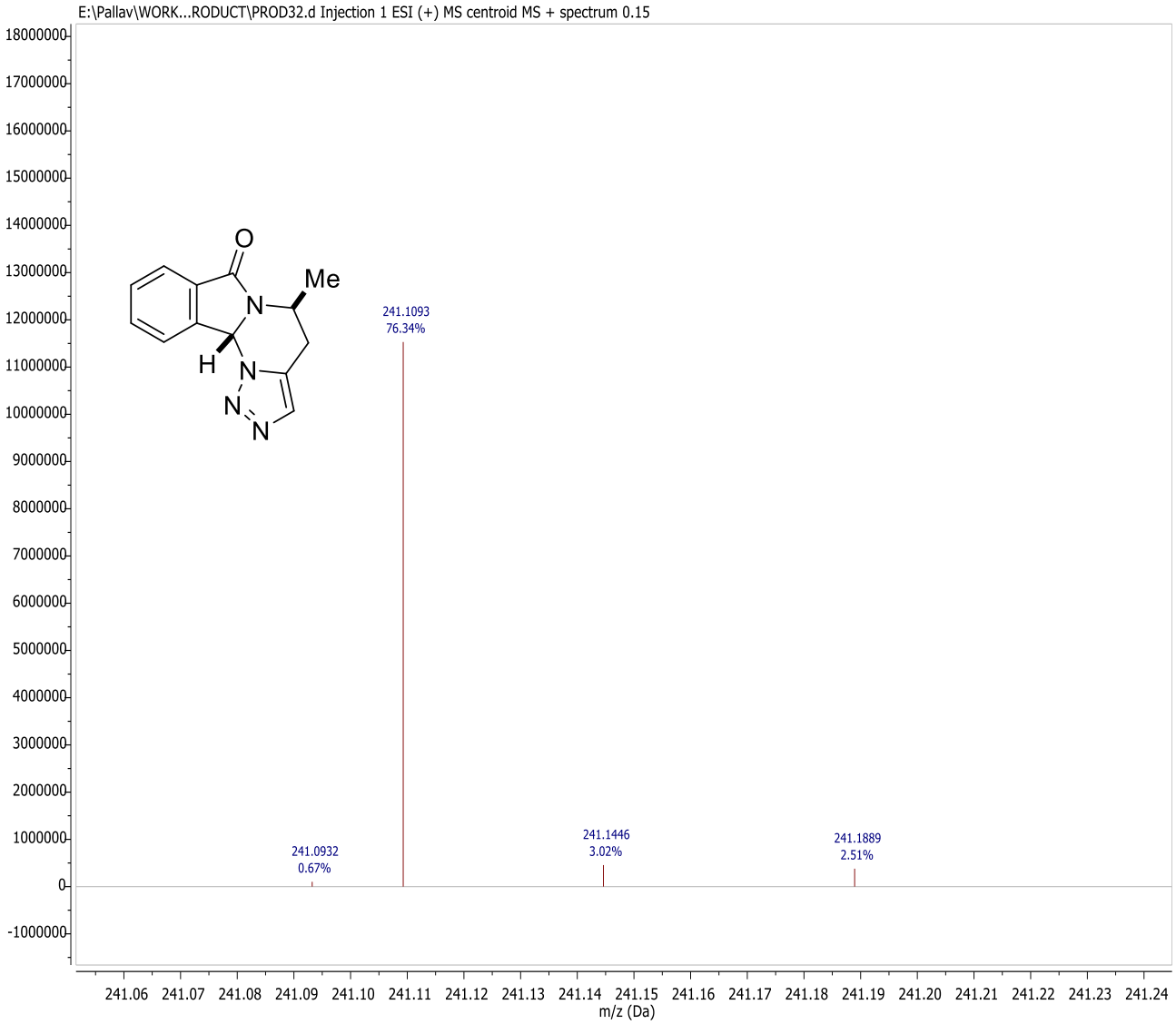
HRMS spectrum of **2q**



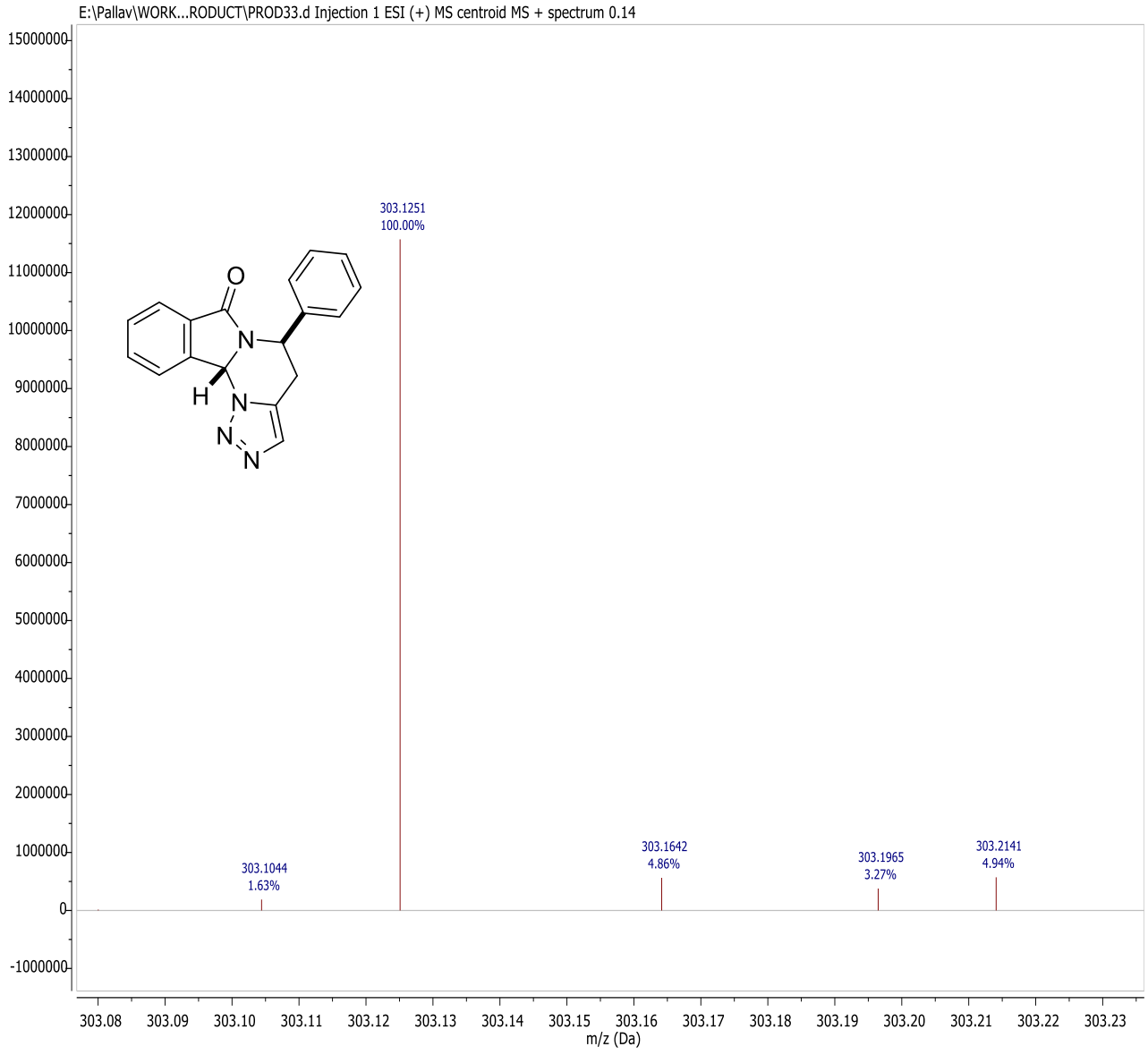
HRMS spectrum of **2r**



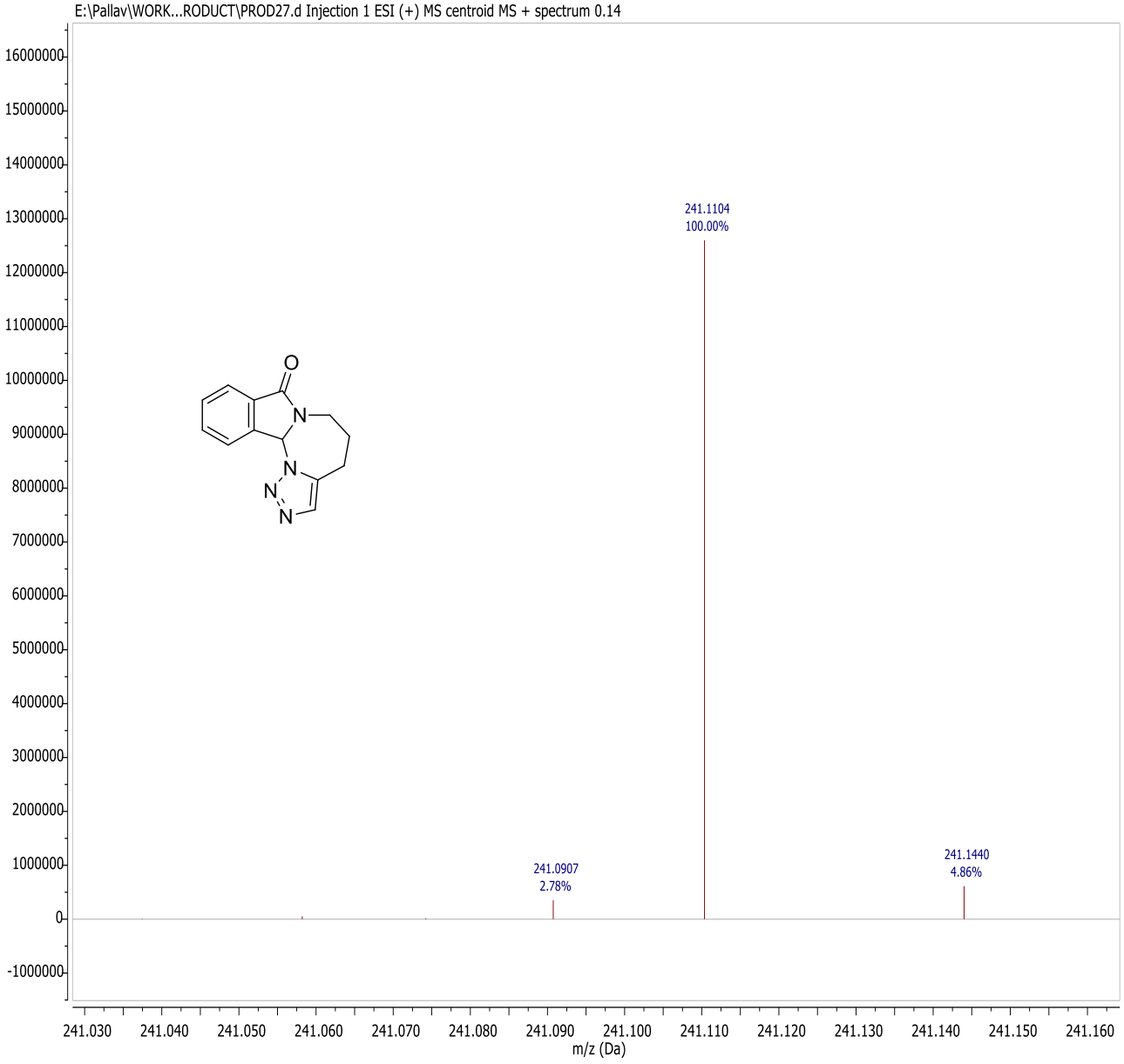
HRMS spectrum of **2s**



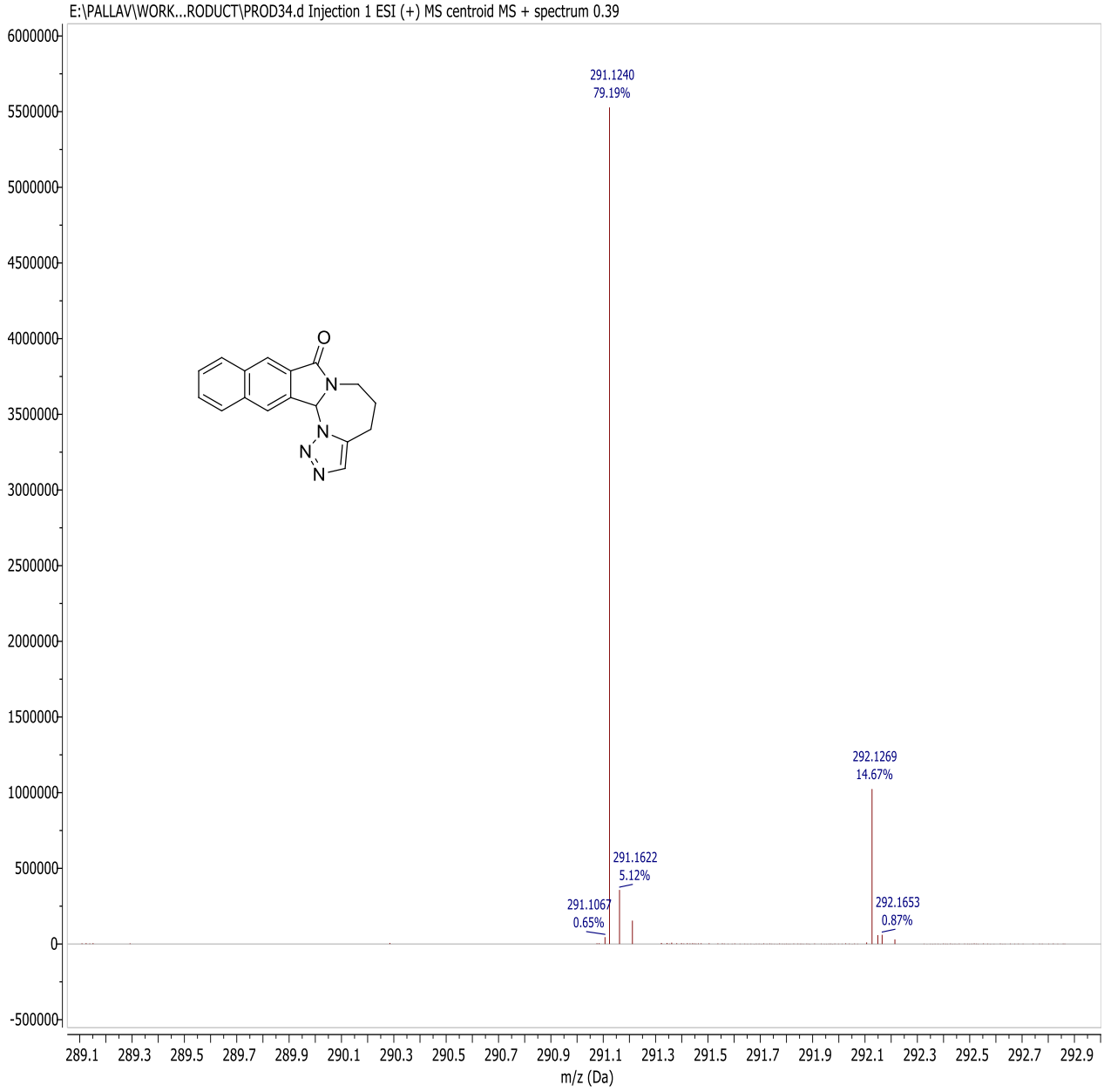
HRMS spectrum of **2t**



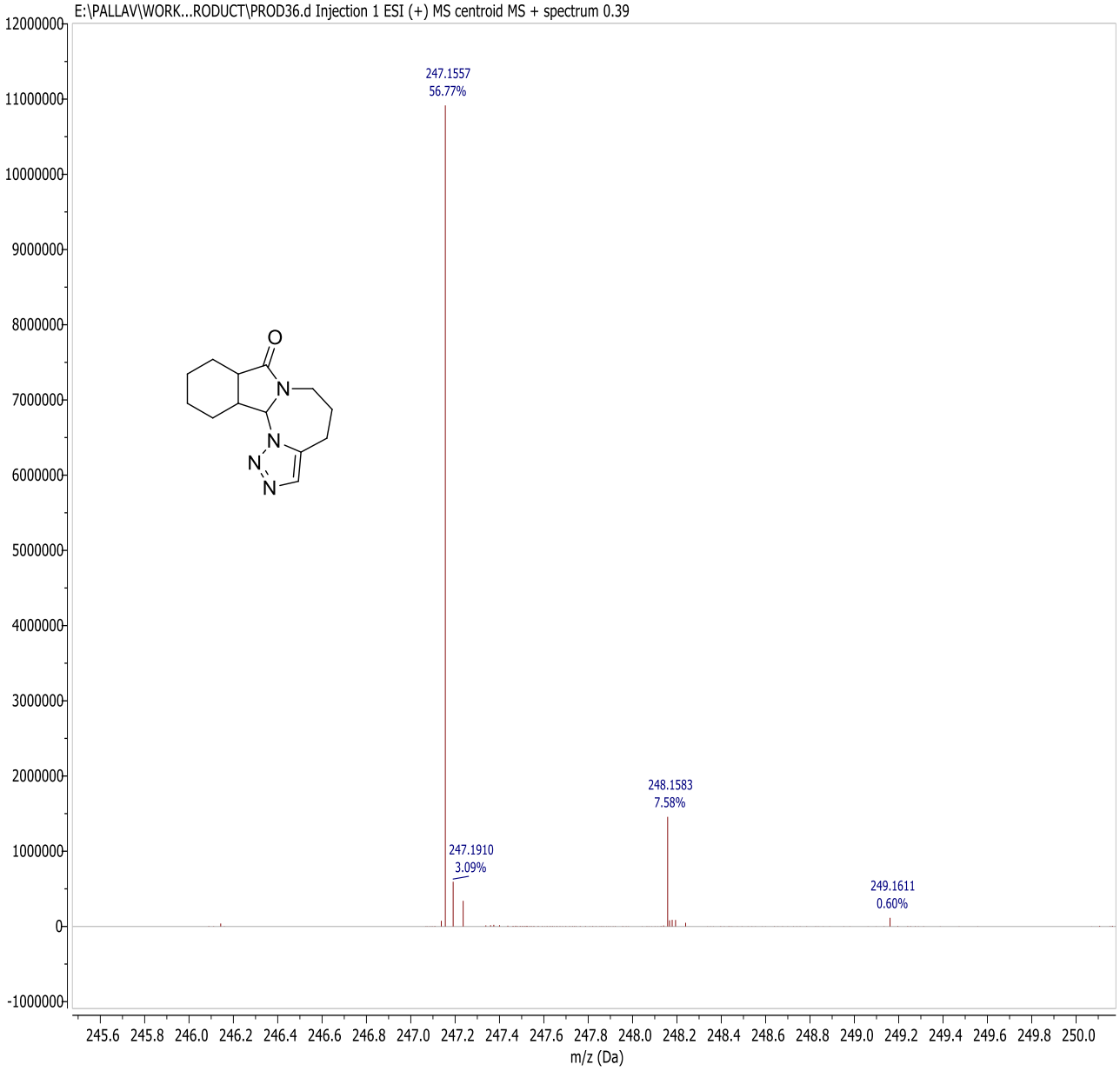
HRMS spectrum of **2v**



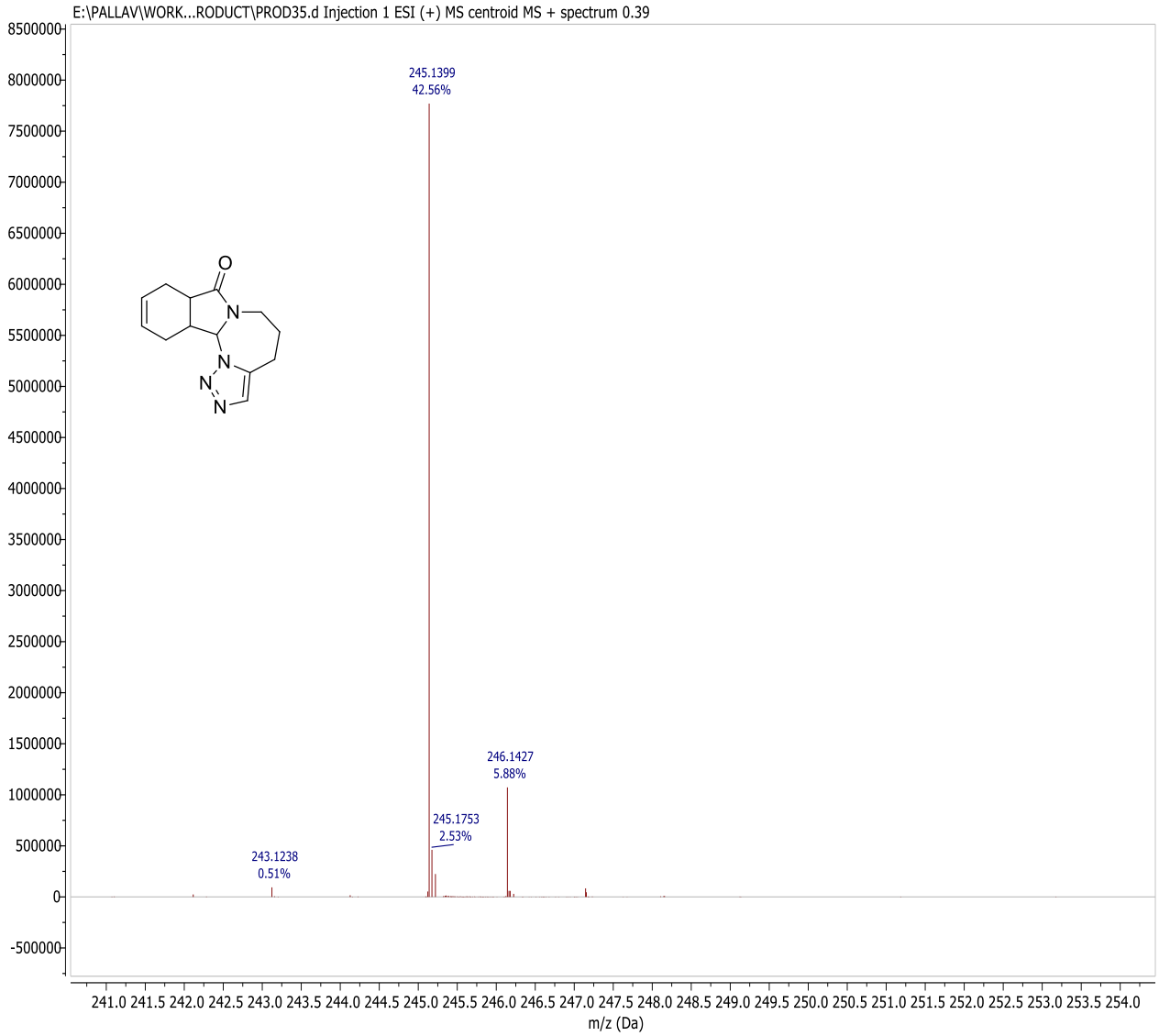
HRMS spectrum of **2w**



HRMS spectrum of **2x**



HRMS spectrum of **2y**



HRMS spectrum of **3j**