Organocatalytic Asymmetric [3 + 3] Annulation Reaction Between 5-Aminopyrazoles and Enynones: Synthesis of Pyrazolo[3,4-b]pyridines

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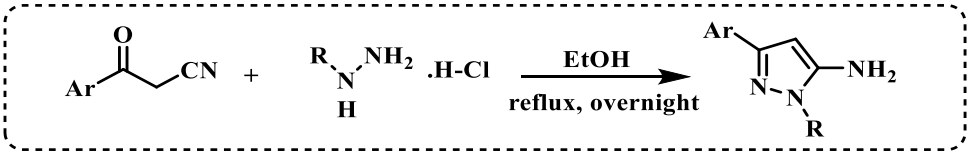
1.General Information:

All dry solvents were dried using activated 4Å molecular sieves and stored under argon. For thin layer chromatography (TLC), silica gel plates with fluorescence indicator 254 nm were used and compounds were visualized by irradiation with UV light and/or by I2. Celite® 512 medium was used for filtrations. Flash column chromatography was performed using 100-200 or 230-400 mesh silica gel. Petroleum ether and ethyl acetate for flash chromatography were acquired from commercial sources and were used without purification. NMR spectra were acquired on a Bruker 400 MHz, 500 MHz and 600 MHz spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CDCl_3$, 7.26 ppm for ^1H NMR and 77.23 ppm for ^{13}C NMR respectively. ^{13}C spectra were acquired on a broad band decoupled mode. For 1H-NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, ddd = doublet of doublet of doublets, t = triplet, q = quartet, dt = doublet of triplets, m = multiplet), coupling constants (Hz) and integration. Using ESI mode HRMS spectra were recorded. Enantiomeric ratios were determined by HPLC analysis performed on Chiral Columns using a Phenomenex Lux Cellulose-1 Chiral LC Columns.

2.Preparation of Starting materials and Catalysts:

General Procedure for Amino Pyrazole Synthesis:

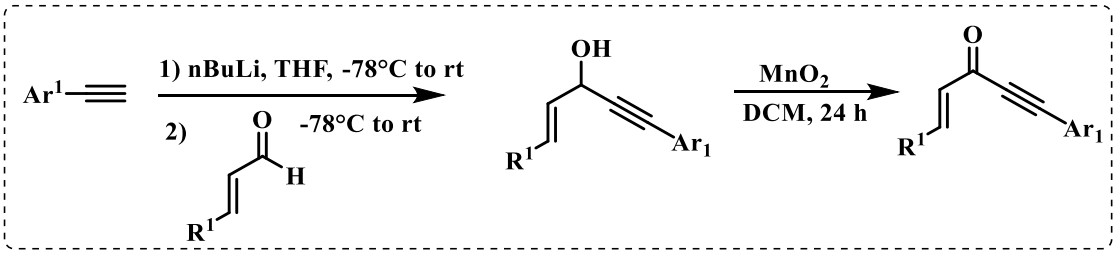
Amino pyrazoles were prepared according to previously reported procedures.[1]



A solution of requisite aryl formyl acetonitrile (1 mmol, 1 equiv) and Hydrazine monohydrochloride (2 mmol, 2 equiv) in EtOH (0.3 M relative to aryl formyl acetonitrile) was heated to reflux overnight. After cooling to room temperature, volatile materials were condensed in vacuo. The residue was dissolved in CH_2Cl_2 and saturated $NaHCO_3$ (aq). The layers were separated, and the aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were washed with brine and dried with anhydrous Na_2SO_4. The salts were removed via gravity filtration, and volatile materials were condensed in vacuo. The crude mixture was purified by flash column chromatography on silica gel.

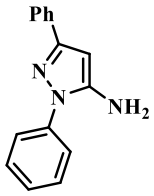
General Procedure for Enynones Synthesis:

Enynones were prepared according to previously reported procedures.[2]



To a stirred solution of alkyne (1 eq) in THF (150 mL) at -78 ºC, was added nBuLi (1.6 M in hex., 1.1 eq) dropwise and stirred for 10 minutes. The solution was warmed to room temperature for 20 minutes before returning to -78 ºC. A solution of aldehyde (1 eq) in THF (5 mL) was added and the reaction warmed to room temperature and stirred for 4 hours. Saturated NH_4Cl (100 mL) was added and subsequently extracted with EtOAc (3 x 100 mL), wished with brine (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to afford a crude residue. To a stirred solution of the crude residue in DCM (150 mL) was added manganese dioxide (25 eq) and stirred for 24 hours. The mixture was filtered through celite then concentrated in vacuo. Purification was achieved by flash chromatography to afford enynone.[2]

Scope of Amino-Pyrazole



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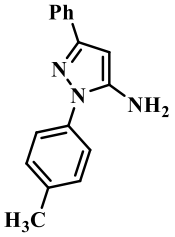

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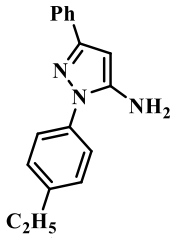

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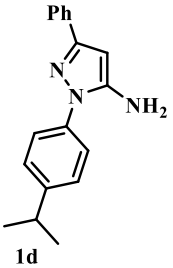

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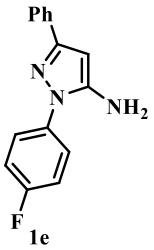

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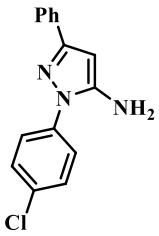

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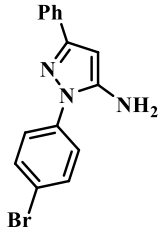

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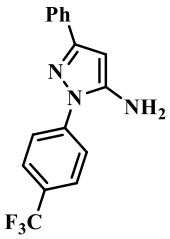

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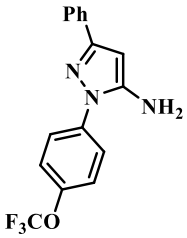

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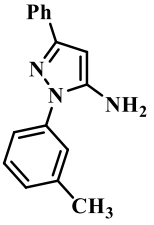

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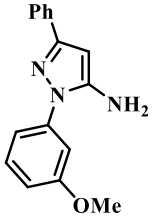

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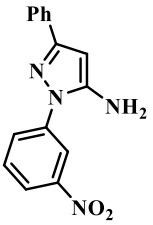

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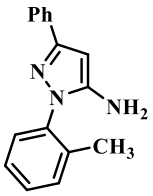

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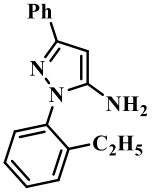

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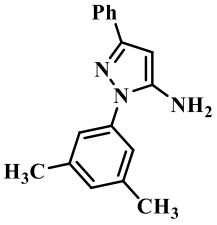

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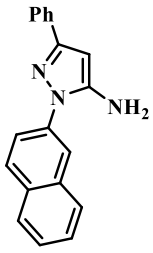

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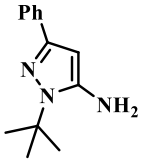

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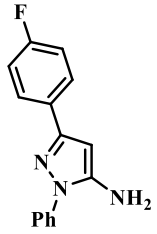

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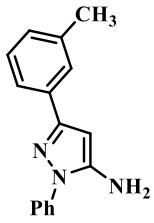

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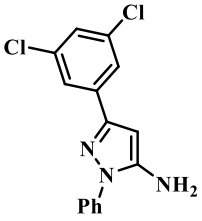

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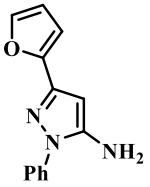

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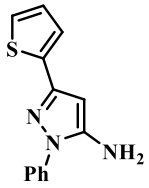

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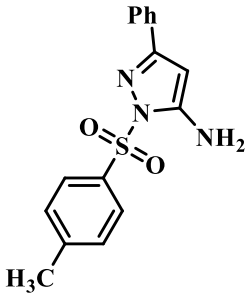
Unsuccessful pyrazole amine



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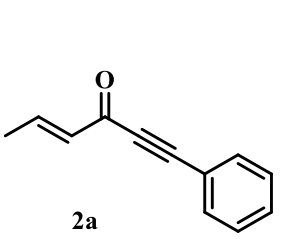
**The desired intermediate formed, but further cyclization did not happen.

Scope of Enynones



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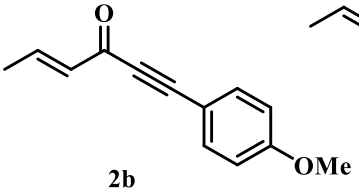

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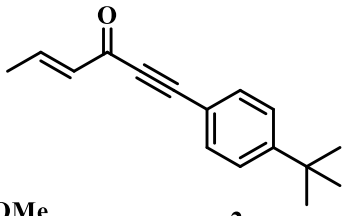

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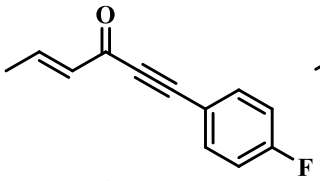

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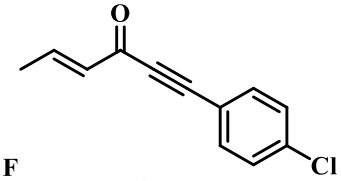

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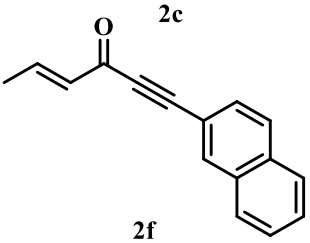

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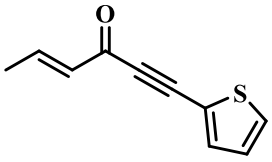

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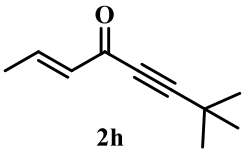

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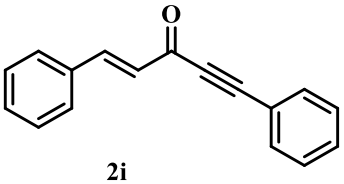

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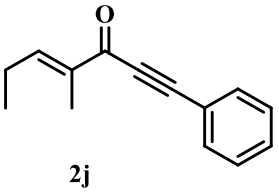
Unsuccessful Enynones



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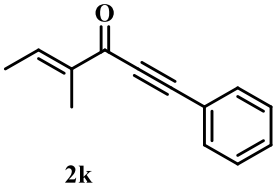

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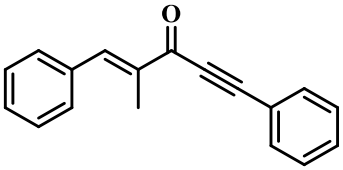

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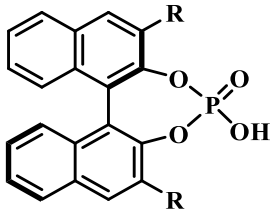
**The desired intermediate formed, but further cyclization did not happen.

General Procedure for Synthesis of catalyst:

The catalyst (**I - VIII**) was prepared according to reported procedures.[3,4]



I, R = phenyl
II, R = 2-naphthyl
III, R = 9-anthracenyl
IV, R = $SiPh_3$

V, R = 3,5-$(CF_3)_2C_6H_3$
VI, R = 2,4,6-$(^iPr)_3C_6H_2$
VII, R = 2,4,6-$(C_6H_{11})_3C_6H_2$
VIII, R = 2,3,4,5,6-Me_5C_6

REFERENCES:

1.X. Gao, C. Li, L. Chen and X. Li, *Org. Lett.*, 2023, **25**, 7628–7632.

2.B. Dong, Z. Li, W. Li, J. Deng, J. Yan, Y. Guo, K.-K. Wang, S. Qian, Z. Wang and X.-L. He, *Adv. Synth. Catal.*, DOI:10.1002/adsc.202401072.

3.F. Romanov-Michailidis, L. Guénée and A. Alexakis, *Angewandte Chemie International Edition*, 2013, **52**, 9266–9270.

4.S. Saha and C. Schneider, *Chemistry – A European Journal*, 2015, **21**, 2348–2352.

3. Optimization Study:

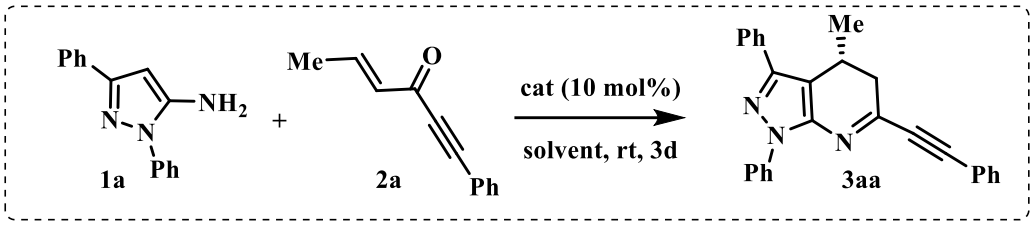
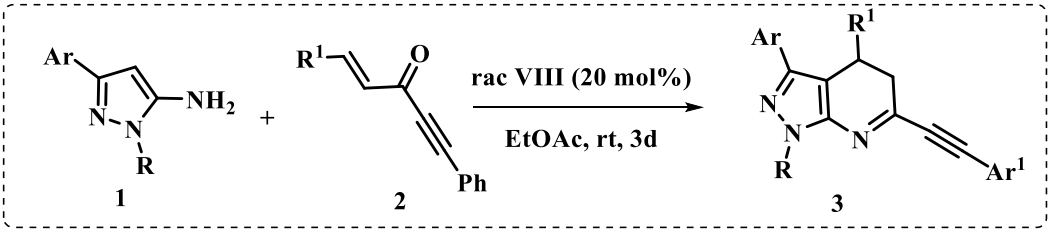


Table 1. Catalyst screening and optimization of reaction conditions:

Entry[a]	Catalyst	Solvent	Yield(3a)[b]	Ee(3a)[c]
1	**I**	toluene	45	32
2	**II**	toluene	55	35
3	**III**	toluene	60	59
4	**IV**	toluene	44	20
5	**V**	toluene	50	15
6	**VI**	toluene	42	49
7	**VII**	toluene	44	53
8	**VIII**	toluene	57	65
9	**VIII**	mesitylene	30	51
10	**VIII**	$PhCF_3$	42	53
11	**VIII**	CH_2Cl_2	40	71
12	**VIII**	$CHCl_3$	42	73
13	**VIII**	cyclohexane	25	53
14	**VIII**	EtOAc	57	85
15	**VIII**	MeOAc	67	57
16[d]	**VIII**	EtOAc	64	89
17[d,e]	**VIII**	EtOAc	65	93
18[d,e,f]	**VIII**	EtOAc	65	95

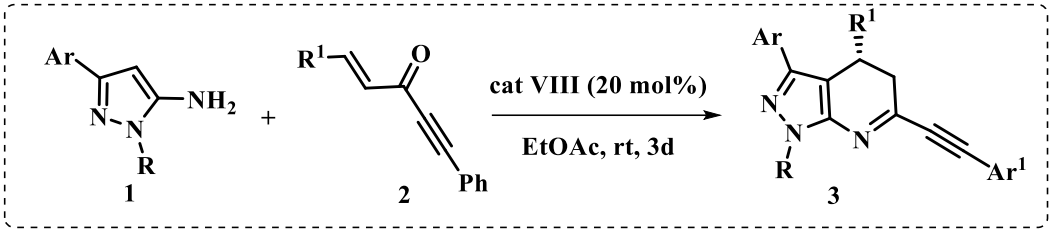
[a] Unless specified, 0.1 mmol of **1a** and 0.1 mmol of **2a** were stirred in 1 mL solvent with 10 mol% chiral catalyst at room temperature for 3 days. [b]Isolated yield after silica gel column chromatography. [c]Determined by HPLC using stationary phase chiral column. [d]With 20 mol% catalyst. [e] Reaction was run with 1.5 equiv of **1a**. [f]Reaction was run in 1.5 mL EtOAc.

4. General Procedure for the Synthesis of racemic pyrazolo pyridine derivatives (*rac*-3):



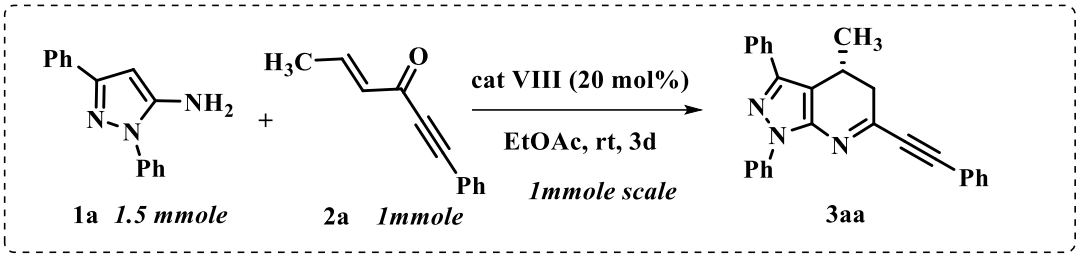
To a stirred solution of pyrazol-amine 1 (0.15 mmol) and enynones 2 (0.1 mmol) in dry EtOAc (1.5 mL) at room temperature, were added racemic catalyst VIII 20 mol%, and the reaction was allowed to run at the same temperature for 3 days. After full consumption of starting materials, the solvents were removed under reduced pressure and purified by flash column chromatography (petroleum ether : ethyl acetate = 99:1) to give racemic pyazolo pyridine (3a-i). All the volatiles were evaporated and the racemic product (*rac*-3) samples for HPLC analysis were obtained by preparative TLC (Merck silica gel 60 F254 pre-coated plates of 0.25 mm thickness) using 15-20% DCM in petroleum ether.

5. General Procedure for the Synthesis of chiral pyrazolo pyridine derivatives(*chi*-3):



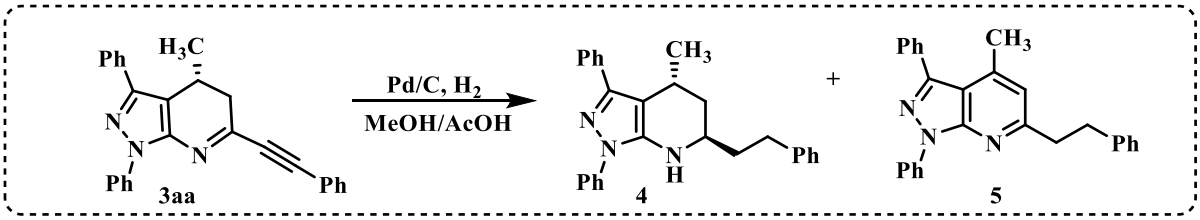
To a stirred solution of pyrazol-amine 1 (0.15 mmol) and enynones 2 (0.1 mmol) in dry EtOAc (1.5 mL) at room temperature, were added catalyst VIII 20 mol%, and the reaction was allowed to run at the same temperature for 3 days. After full consumption of starting materials, the solvents were removed under reduced pressure and purified by flash column chromatography (petroleum ether : ethyl acetate = 99:1) to give pyazolo pyridine (3a-i).

6. Procedure for the scale-up experiment:



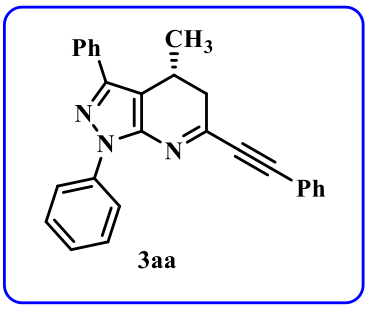
In a 25 ml rb, equipped with a magnetic stirring bar, was charged with 2a (170.21mg, 1 mmol, 1.0 equiv), 1a (235.11mg, 1.5 mmol, 1.5 equiv), and cat. VIII (128.0mg, 0.2 mmol, 0.2 equiv) followed by addition of 15 mL dry EtOAc and stirred at rt until TLC revealed complete consumption of 2a (3days). The crude residue was directly purified by silica gel flash column chromatography (petroleum ether : ethyl acetate = 99:1) to obtain 3aa (251.0 mg, 65% yield, 95% ee).

7. Synthetic transformation of 3aa:



To a solution of 3aa (38.7 mg, 0.10 mmol, 1.0 equiv) in MeOH (5.0 mL) was added Pd/C (10 wt%) (20.0 mg) and AcOH (1.0 mL). This flask was in a vacuum and back-filled with H_2 (1 atm). After being stirred at room temperature overnight, the reaction solution was filtered, and the filtered-cake was washed with MeOH (5.0 mL). The filtrate was evaporated under vacuo, and purified by silica gel column chromatography using hexane:ethyl acetate (20/1) as the eluent to give the product as brown semi solid in 37% yield (14.54 mg) and in white solid 40% yield (15..72 mg).

8. Charecterization data of pyazolo pyridine derivatives:



3aa

(*R*)-4-methyl-1,3-diphenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (26.0 mg, isolated yield: 67%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 140-143 °C.

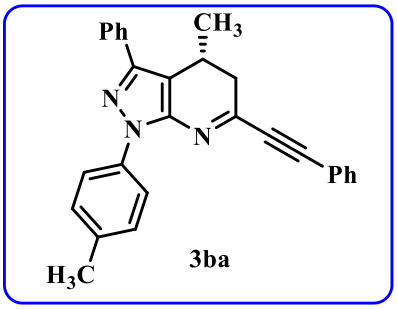
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.92 (m, 2H), 7.89 – 7.83 (m, 2H), 7.62 – 7.57 (m, 2H), 7.51 – 7.42 (m, 4H), 7.42 – 7.34 (m, 4H), 7.34 – 7.27 (m, 1H), 3.42 (ddt, *J* = 11.5, 7.0, 3.5 Hz, 1H), 2.91 (dd, *J* = 17.0, 8.4 Hz, 1H), 2.74 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 146.5, 145.7, 139.0, 133.7, 132.5, 129.9, 128.9, 128.7, 128.6, 127.9, 126.7, 126.7, 123.1, 121.5, 108.6, 95.1, 90.0, 38.9, 24.3, 19.9.

ESI HRMS: calcd. for $C_{27}H_{23}N_3$ $[M+H]^+$ 388.1809, found 388.1804.

Optical rotation: $[\alpha]_D^{20}$ = -60.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 8.2 min, t_{minor} = 14.0 min).



3ba

(*R*)-4-methyl-3-phenyl-6-(phenylethynyl)-1-(p-tolyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (27.2 mg, isolated yield: 68%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 133-135 °C.

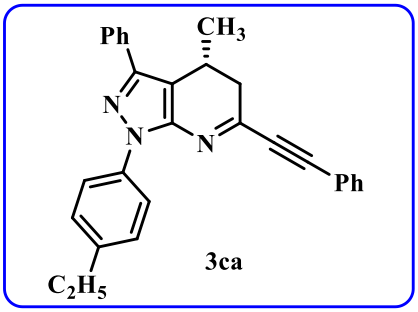
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.59 (d, *J* = 7.1 Hz, 2H), 7.39 (ddd, *J* = 18.5, 12.8, 7.0 Hz, 6H), 7.27 (d, *J* = 8.1 Hz, 2H), 3.42 (p, *J* = 7.8 Hz, 1H), 2.90 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.78 – 2.67 (m, 1H), 2.39 (s, 3H), 1.22 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.2, 146.2, 145.6, 136.6, 136.6, 133.7, 132.4, 129.8, 129.5, 128.6, 128.5, 127.8, 126.7, 123.0, 121.5, 108.3, 94.9, 90.1, 38.9, 24.4, 21.1, 20.0.

ESI HRMS: calcd. for $C_{28}H_{24}N_3$ $[M+H]^+$ 402.1965, found 402.1947.

Optical rotation: $[\alpha]_D^{20}$ = -37.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 93%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 8.0 min, t_{minor} = 15.6 min).



3ca

(*R*)-1-(4-ethylphenyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Brown solid (23.6 mg, isolated yield: 57%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 135-137 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 2H), 7.81 (d, *J* = 8.1 Hz, 2H), 7.62 – 7.56 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.41 – 7.26 (m, 6H), 3.41 (qd, *J* = 7.1, 3.6 Hz, 1H), 2.90 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.77 – 2.65 (m, 3H), 1.26 (t, *J* = 7.6 Hz, 3H), 1.22 (d, *J* = 7.0 Hz, 3H).

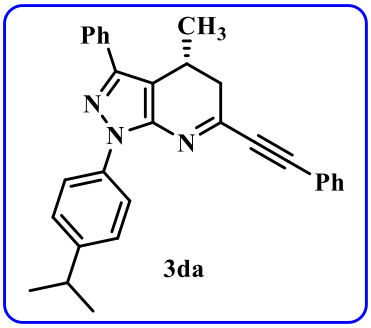
^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3, 146.2, 145.6, 143.0, 136.7, 133.8, 132.5, 129.8, 128.6, 128.5, 128.4, 127.8, 126.7, 123.2, 121.5, 108.3, 95.0, 90.1, 38.9, 28.6, 24.4, 20.0, 15.7.

ESI HRMS: calcd. for $C_{29}H_{26}N_3$ $[M+H]^+$ 416.2122, found 416.2120.

Optical rotation: $[\alpha]_D^{20}$ = -33.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 91%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 7.7 min, t_{minor} = 15.8 min).

(*R*)-4-methyl-3-phenyl-6-(phenylethynyl)-1-(p-tolyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine



3da

Brown solid (21.4 mg, isolated yield: 50%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 125-127 °C.

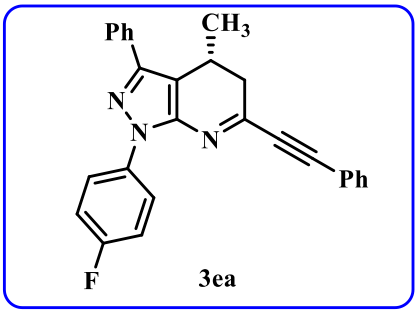
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz, 2H), 7.80 (d, *J* = 8.1 Hz, 2H), 7.63 – 7.57 (m, 2H), 7.44 (t, *J* = 7.5 Hz, 2H), 7.41 – 7.27 (m, 6H), 3.44 (td, *J* = 8.5, 4.2 Hz, 1H), 2.99 – 2.93 (m, 1H), 2.93 – 2.86 (m, 1H), 2.74 (dd, *J* = 17.0, 2.4 Hz, 1H), 1.29 – 1.26 (m, 6H), 1.23 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3, 147.6, 146.2, 145.6, 136.7, 133.8, 132.5, 129.8, 128.6, 128.6, 128.5, 127.8, 126.9, 126.7, 123.2, 121.5, 108.3, 95.0, 90.1, 38.9, 33.9, 24.4, 24.1, 24.0, 20.0.

ESI HRMS: calcd. for $C_{30}H_{28}N_3$ $[M+H]^+$ 430.2278, found 430.2271.

Optical rotation: $[\alpha]_D^{20}$ = -62.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 91%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 7.3 min, t_{minor} = 17.0 min).



3ea

(*R*)-1-(4-fluorophenyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (28.0 mg, isolated yield: 69%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 140-143 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.90 (m, 2H), 7.87 – 7.82 (m, 2H), 7.62 – 7.58 (m, 2H), 7.47 – 7.35 (m, 6H), 7.16 (t, *J* = 8.7 Hz, 2H), 3.47 – 3.37 (m, 1H), 2.91 (dd, *J* = 17.1, 8.4 Hz, 1H), 2.75 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H).

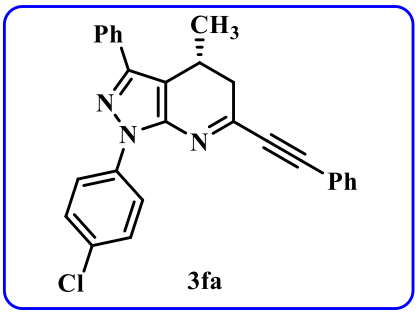
^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 160.2, 152.8, 146.5, 145.6, 135.2, 135.2, 133.5, 132.5, 130.0, 128.7, 128.6, 128.0, 126.7, 124.7, 124.6, 121.4, 115.9, 115.6, 108.5, 95.4, 89.9, 38.9, 24.3, 20.0.

^{19}F NMR (377 MHz, $CDCl_3$) δ -115.7.
The coupling constant between C-F are as follow.
^{1}J = (162.60 – 160.15) * 101 = 247.45 Hz, ^{2}J = (115.86 – 115.63) * 100 = 23.23 Hz, ^{3}J = (124.73 – 124.65) * 100 = 8.08 Hz, ^{4}J = (135.21 – 135.18) * 100 = 3.03 Hz.

ESI HRMS: calcd. for $C_{27}H_{21}FN_3$ $[M+H]^+$ 406.1715, found 406.1690.

Optical rotation: $[\alpha]_D^{20}$ = -23.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 91%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 8.0 min, t_{minor} = 17.0 min).



(*R*)-1-(4-chlorophenyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (27.4 mg, isolated yield: 65%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 155-157 °C.

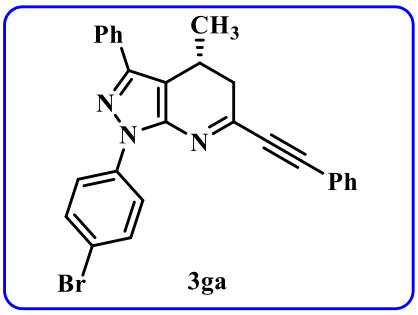
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.97 – 7.93 (m, 2H), 7.87 – 7.83 (m, 2H), 7.63 – 7.59 (m, 2H), 7.43 (ddd, *J* = 14.3, 10.1, 5.9 Hz, 6H), 7.39 – 7.35 (m, 2H), 3.47 – 3.37 (m, 1H), 2.90 (dd, *J* = 17.0, 8.4 Hz, 1H), 2.75 (dd, *J* = 17.1, 2.4 Hz, 1H), 1.21 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.8, 146.7, 145.8, 137.6, 133.4, 132.5, 132.2, 130.0, 129.0, 128.7, 128.6, 128.1, 126.7, 123.9, 121.3, 108.8, 95.5, 89.9, 38.8, 24.3, 19.9.

ESI HRMS: calcd. for $C_{27}H_{21}ClN_3$ $[M+H]^+$ 422.1419, found 422.1390.

Optical rotation: $[\alpha]_D^{20}$ = -22.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 91%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 8.0 min, t_{minor} = 17.9 min).



(*R*)-1-(4-bromophenyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (25.6 mg, isolated yield: 55%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 135-137 °C.

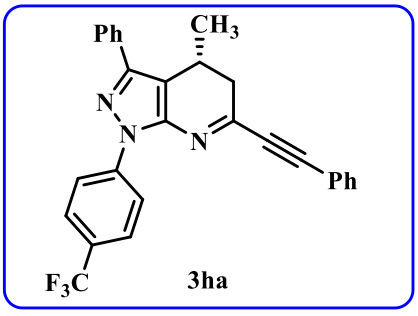
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.88 (m, 2H), 7.87 – 7.83 (m, 2H), 7.60 (td, *J* = 7.5, 1.8 Hz, 4H), 7.48 – 7.34 (m, 6H), 3.48 – 3.37 (m, 1H), 2.91 (dd, *J* = 17.1, 8.4 Hz, 1H), 2.75 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 152.8, 146.8, 145.8, 138.1, 133.4, 132.5, 132.0, 130.0, 128.7, 128.6, 128.1, 126.7, 124.2, 121.4, 120.1, 108.8, 95.5, 89.9, 38.8, 24.3, 19.9.

ESI HRMS: calcd. for $C_{27}H_{21}BrN_3$ $[M+H]^+$ 466.0914, found 466.0894.

Optical rotation: $[\alpha]_D^{20}$ = +12.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 87%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 8.1 min, t_{minor} = 18.0 min).



(*R*)-4-methyl-3-phenyl-6-(phenylethynyl)-1-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (23.6 mg, isolated yield: 52%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 141-143 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.3 Hz, 2H), 7.89 – 7.83 (m, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.65 – 7.56 (m, 2H), 7.49 – 7.35 (m, 6H), 3.46 – 3.37 (m, 1H), 2.91 (dd, *J* = 17.1, 8.4 Hz, 1H), 2.76 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H).

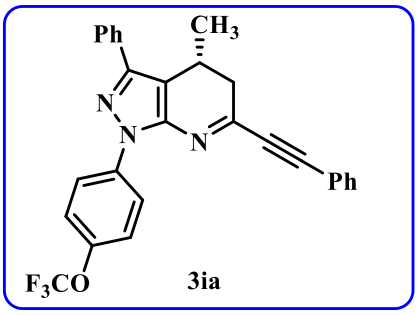
^{13}C NMR (101 MHz, $CDCl_3$) δ 153.1, 147.3, 146.2, 141.8, 133.3, 132.5, 130.0, 128.7, 128.6, 128.2, 126.8, 126.2, 126.1, 126.1, 126.1, 125.5, 122.8, 122.4, 121.3, 109.2, 95.7, 89.9, 38.8, 24.2, 19.8.

^{19}F NMR (377 MHz, $CDCl_3$) δ -62.2.
The coupling constant between C-F are as follow.
^{1}J = 124.18 (q, 272.7 Hz), ^{2}J = 128.15 (q, 32 Hz), ^{3}J = 126.11 (q, 4.04 Hz).

ESI HRMS: calcd. for $C_{28}H_{21}F_3N_3$ $[M+H]^+$ 456.1683, found 456.1662.

Optical rotation: $[\alpha]_D^{20}$ = -32.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 77%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 7.1 min, t_{minor} = 16.9 min).



3ia

(*R*)-4-methyl-3-phenyl-6-(phenylethynyl)-1-(4-(trifluoromethoxy)phenyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (22.1 mg, isolated yield: 47%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 146-148 °C.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 – 8.00 (m, 2H), 7.85 (d, J = 7.6 Hz, 2H), 7.64 – 7.59 (m, 2H), 7.45 (q, J = 6.3 Hz, 3H), 7.38 (dd, J = 12.5, 5.2 Hz, 3H), 7.33 (d, J = 8.6 Hz, 2H), 3.47 – 3.39 (m, 1H), 2.92 (dd, J = 17.1, 8.4 Hz, 1H), 2.76 (dd, J = 17.0, 2.4 Hz, 1H), 1.23 (d, J = 7.0 Hz, 3H).

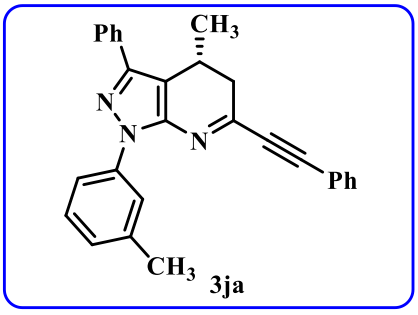
^{13}C NMR (126 MHz, $CDCl_3$) δ 152.9, 147.5, 146.9, 145.8, 137.6, 133.4, 132.5, 130.0, 128.7, 128.6, 128.1, 126.7, 124.0, 121.6, 121.3, 108.8, 95.6, 89.8, 38.9, 24.3, 19.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -57.9
The coupling constant between C-F are as follow.
^{1}J = 120.68 (q, 255 Hz), ^{2}J = 147.60 (q, 1.25 Hz).

ESI HRMS: calcd. for $C_{28}H_{21}F_3N_3O$ $[M+H]^+$ 472.1632, found 472.1595.

Optical rotation: $[\alpha]_D^{20}$ = +40.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 89%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 6.5 min, t_{minor} = 15.3 min).



3ja

(*R*)-4-methyl-3-phenyl-6-(phenylethynyl)-1-(m-tolyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (18.1 mg, isolated yield: 45%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 131-133 °C.

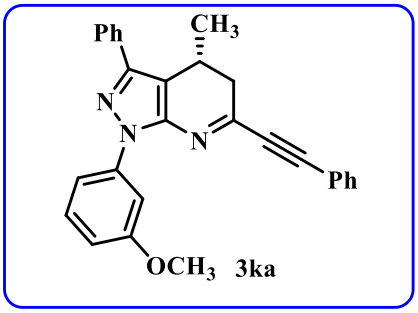
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.77 (m, 2H), 7.64 (d, *J* = 7.8 Hz, 2H), 7.56 – 7.50 (m, 2H), 7.40 – 7.26 (m, 7H), 7.06 (d, *J* = 7.6 Hz, 1H), 3.35 (dtt, *J* = 13.9, 7.0, 3.6 Hz, 1H), 2.89 – 2.81 (m, 1H), 2.68 (dd, *J* = 17.0, 2.5 Hz, 1H), 2.37 (s, 3H), 1.15 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.4, 146.3, 145.7, 138.9, 138.8, 133.7, 132.5, 129.8, 128.7, 128.7, 128.5, 127.9, 127.7, 126.7, 123.7, 121.5, 120.5, 108.4, 95.1, 90.0, 38.9, 24.3, 21.6, 19.9.

ESI HRMS: calcd. for $C_{28}H_{24}N_3$ $[M+H]^+$ 402.1965, found 402.1932.

Optical rotation: $[\alpha]_D^{20}$ = -52.3 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 7.5 min, t_{minor} = 13.2 min).



3ka

(*R*)-1-(3-methoxyphenyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Orange solid (23.7 mg, isolated yield: 57%); R_f = 0.65 in 0.5:9.5 ethyl acetate/hexane; M.P. 132-135 °C.

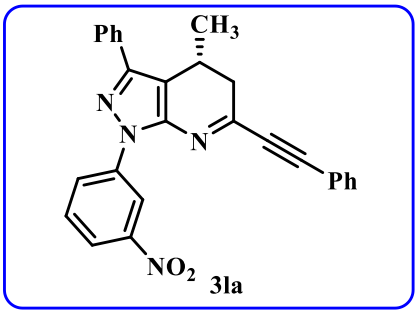
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.84 (m, 2H), 7.63 – 7.52 (m, 4H), 7.47 – 7.32 (m, 7H), 6.89 – 6.84 (m, 1H), 3.87 (s, 3H), 3.46 – 3.36 (m, 1H), 2.90 (dd, *J* = 17.0, 8.4 Hz, 1H), 2.74 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.22 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.1, 152.4, 146.4, 145.8, 140.1, 133.6, 132.5, 129.8, 129.6, 128.6, 128.5, 127.9, 126.7, 121.5, 115.5, 112.8, 108.6, 95.1, 90.0, 55.5, 38.8, 24.3, 19.9.

ESI HRMS: calcd. for $C_{28}H_{24}N_3O$ $[M+H]^+$ 418.1914, found 418.1875.

Optical rotation: $[\alpha]_D^{20}$ = -55.3 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 81%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 10.2 min, t_{minor} = 17.9 min).



3la

(*R*)-4-methyl-1-(3-nitrophenyl)-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (18.6 mg, isolated yield: 43%); R_f = 0.60 in 0.5:9.5 ethyl acetate/hexane; M.P. 152-155 °C.

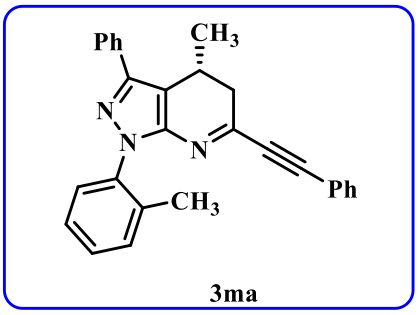
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (t, *J* = 2.2 Hz, 1H), 8.50 – 8.44 (m, 1H), 8.14 (ddd, *J* = 8.2, 2.3, 1.0 Hz, 1H), 7.89 – 7.86 (m, 2H), 7.62 (dd, *J* = 8.2, 2.1 Hz, 3H), 7.47 (td, *J* = 7.3, 1.3 Hz, 2H), 7.43 – 7.36 (m, 4H), 3.44 (tt, *J* = 9.5, 5.8 Hz, 1H), 2.94 (dd, *J* = 17.2, 8.5 Hz, 1H), 2.79 (dd, *J* = 17.2, 2.5 Hz, 1H), 1.23 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.5, 148.7, 147.6, 146.2, 140.2, 133.0, 132.6, 130.1, 129.7, 128.8, 128.6, 128.4, 127.8, 126.8, 121.2, 120.8, 117.3, 109.4, 96.1, 89.8, 38.8, 24.2, 19.8.

ESI HRMS: calcd. for $C_{27}H_{21}N_4O_2$ $[M+H]^+$ 433.1660, found 433.1675.

Optical rotation: $[\alpha]_D^{20}$ = +87.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 87%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 13.9 min, t_{minor} = 27.5 min).



3ma

(*R*)-4-methyl-3-phenyl-6-(phenylethynyl)-1-(o-tolyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (26.1 mg, isolated yield: 65%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 133-135 °C.

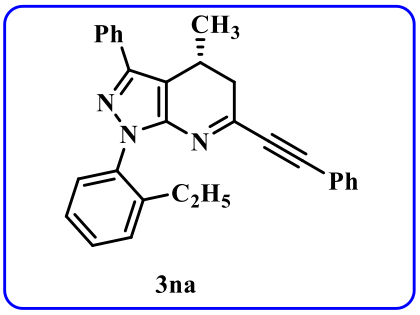
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.82 (m, 2H), 7.57 – 7.52 (m, 2H), 7.43 (t, *J* = 7.8 Hz, 3H), 7.38 – 7.29 (m, 7H), 3.46 (pt, *J* = 7.1, 3.1 Hz, 1H), 2.92 (dd, *J* = 17.1, 8.5 Hz, 1H), 2.74 (dd, *J* = 17.1, 2.5 Hz, 1H), 2.24 (s, 3H), 1.25 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 146.7, 146.3, 137.5, 135.6, 133.8, 132.4, 131.1, 129.8, 128.8, 128.6, 128.5, 128.0, 127.8, 126.6, 126.4, 121.5, 106.9, 95.1, 89.9, 39.3, 24.5, 20.3, 18.2.

ESI HRMS: calcd. for $C_{28}H_{24}N_3$ $[M+H]^+$ 402.1965, found 402.1961.

Optical rotation: $[\alpha]_D^{20}$ = -82.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 7.6 min, t_{minor} = 15.6 min).



3na

(*R*)-1-(2-ethylphenyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (24.1mg, isolated yield: 58%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 131-133 °C.

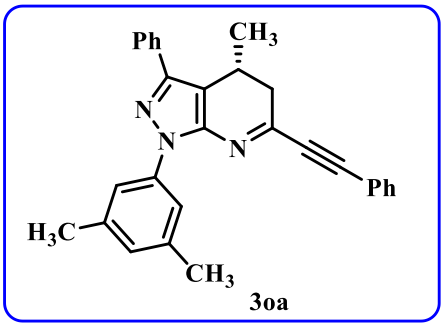
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.57 – 7.51 (m, 2H), 7.49 – 7.38 (m, 5H), 7.40 – 7.28 (m, 7H), 3.51 – 3.41 (m, 1H), 2.92 (dd, *J* = 17.2, 8.4 Hz, 1H), 2.74 (dd, *J* = 17.2, 2.4 Hz, 1H), 2.57 (q, *J* = 7.5 Hz, 2H), 1.26 (d, *J* = 7.0 Hz, 3H), 1.14 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.5, 146.8, 146.1, 141.4, 137.0, 133.9, 132.4, 129.8, 129.3, 129.1, 128.6, 128.5, 128.3, 127.7, 126.6, 126.3, 121.5, 106.8, 95.1, 89.9, 39.3, 24.6, 24.5, 20.3, 14.5.

ESI HRMS: calcd. for $C_{29}H_{26}N_3$ $[M+H]^+$ 416.2122, found 416.2137.

Optical rotation: $[\alpha]_D^{20}$ = -88.6 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 91%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 6.8 min, t_{minor} = 11.7 min).



3oa

(*R*)-1-(3,5-dimethylphenyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Orange solid (25.0mg, isolated yield: 60%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 142-145 °C.

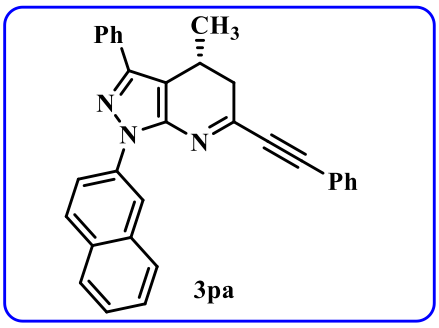
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.84 (m, 2H), 7.61 (t, *J* = 1.6 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.49 (d, *J* = 1.6 Hz, 2H), 7.48 – 7.41 (m, 3H), 7.41 – 7.33 (m, 4H), 6.98 – 6.94 (m, 1H), 3.47 – 3.37 (m, 1H), 2.91 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.74 (dd, *J* = 17.0, 2.6 Hz, 1H), 2.39 (s, 6H), 1.22 (d, *J* = 7.0 Hz, 4H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.3, 146.2, 145.7, 138.7, 138.6, 133.7, 132.4, 129.8, 128.8, 128.6, 128.5, 127.8, 126.8, 121.5, 121.2, 108.3, 95.0, 90.1, 38.9, 24.3, 21.5, 19.9.

ESI HRMS: calcd. for $C_{29}H_{26}N_3$ $[M+H]^+$ 416.2122, found 416.2102.

Optical rotation: $[\alpha]_D^{20}$ = +40.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 89%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 7.4 min, t_{minor} = 13.5 min).



(*R*)-4-methyl-1-(naphthalen-2-yl)-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (19.7 mg, isolated yield: 45%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 181-183 °C.

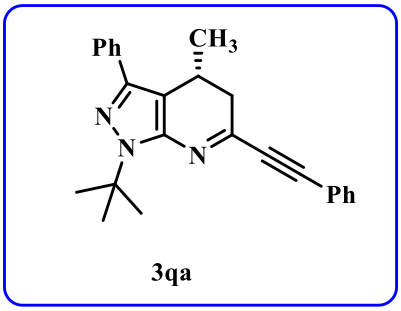
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (d, *J* = 2.2 Hz, 1H), 8.17 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.93 – 7.89 (m, 2H), 7.87 – 7.85 (m, 1H), 7.63 – 7.60 (m, 2H), 7.51 – 7.49 (m, 1H), 7.48 – 7.45 (m, 2H), 7.39 (dtd, *J* = 11.7, 7.1, 5.2 Hz, 4H), 3.46 (pd, *J* = 7.1, 2.4 Hz, 1H), 2.95 (dd, *J* = 16.9, 8.4 Hz, 1H), 2.78 (dd, *J* = 17.0, 2.4 Hz, 1H), 1.25 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.6, 146.7, 146.0, 136.6, 133.6, 133.5, 132.5, 132.1, 129.9, 128.8, 128.7, 128.6, 128.4, 128.0, 127.7, 126.8, 126.4, 125.9, 121.9, 121.5, 120.8, 108.7, 95.2, 90.1, 38.9, 24.4, 19.9.

ESI HRMS: calcd. for $C_{31}H_{24}N_3$ $[M+H]^+$ 438.1965, found 438.1930.

Optical rotation: $[\alpha]_D^{20}$ = +50.3 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 89%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 11.2 min, t_{minor} = 21.4 min).



(*R*)-1-(tert-butyl)-4-methyl-3-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (22.8mg, isolated yield: 62%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 152-155 °C.

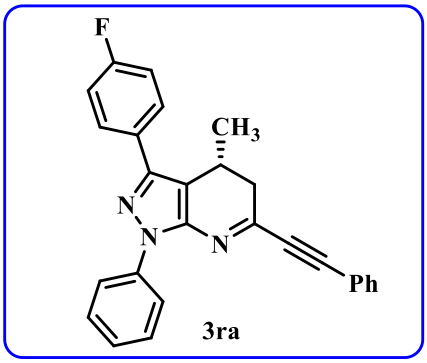
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 – 7.75 (m, 2H), 7.61 – 7.57 (m, 2H), 7.41 – 7.36 (m, 5H), 7.29 (s, 1H), 3.34 – 3.25 (m, 1H), 2.78 (dd, *J* = 16.9, 8.3 Hz, 1H), 2.63 (dd, *J* = 17.0, 2.5 Hz, 1H), 1.77 (s, 9H), 1.16 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 149.1, 145.7, 142.6, 134.6, 132.3, 129.6, 128.5, 128.5, 127.1, 126.4, 121.8, 107.9, 93.3, 90.4, 60.4, 38.7, 30.0, 24.2, 20.1.

ESI HRMS: calcd. for $C_{25}H_{26}N_3$ $[M+H]^+$ 368.2122, found 368.2119.

Optical rotation: $[\alpha]_D^{20}$ = -45.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 93%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 99.5/0.5, flow rate 0.3 mL/min, λ = 254 nm (t_{major} = 16.9 min, t_{minor} = 23.0 min).



(*R*)-3-(4-fluorophenyl)-4-methyl-1-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (21.5 mg, isolated yield: 53%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 143-145 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 – 7.83 (m, 2H), 7.79 – 7.73 (m, 2H), 7.57 – 7.50 (m, 2H), 7.43 – 7.38 (m, 2H), 7.36 – 7.28 (m, 3H), 7.28 – 7.22 (m, 1H), 7.10 – 7.03 (m, 2H), 3.35 – 3.27 (m, 1H), 2.85 (dd, *J* = 17.1, 8.4 Hz, 1H), 2.68 (dd, *J* = 17.0, 2.5 Hz, 1H), 1.14 (d, *J* = 7.0 Hz, 3H).

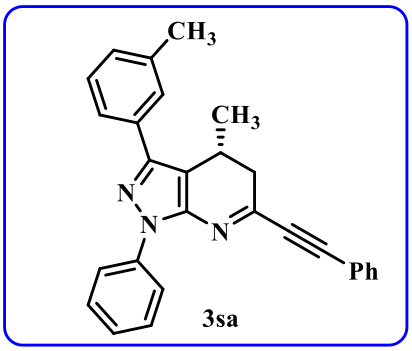
^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8, 161.4, 152.6, 145.7, 145.6, 138.9, 132.5, 129.9, 129.8, 129.8, 129.0, 128.6, 128.4, 128.4, 126.8, 123.0, 121.4, 115.7, 115.5, 108.2, 95.3, 89.9, 38.8, 24.3, 19.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -114.0.
The coupling constant between C-F are as follow.
^{1}J = (163.83 – 161.37) * 101 = 248.46 Hz, ^{2}J = (115.75 – 115.51) * 101 = 24.24 Hz, ^{3}J = (128.44 – 128.36) * 101 = 8.08 Hz, ^{4}J = (129.85 – 129.82) * 100 = 3.03 Hz.

ESI HRMS: calcd. for $C_{27}H_{21}FN_3$ $[M+H]^+$ 406.1715, found 406.1675.

Optical rotation: $[\alpha]_D^{20}$ = +15.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 93%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 7.9 min, t_{minor} = 10.8 min).



3sa

(*R*)-4-methyl-1-phenyl-6-(phenylethynyl)-3-(m-tolyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (27.7 mg, isolated yield: 69%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 132-135 °C.

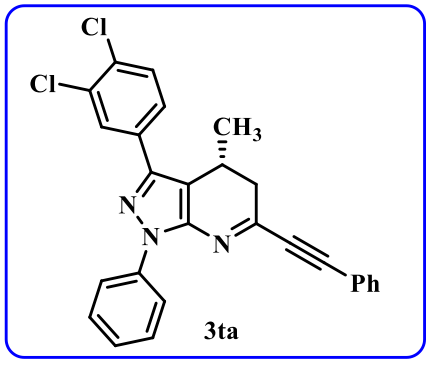
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.92 (m, 2H), 7.73 (s, 1H), 7.64 – 7.57 (m, 3H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.37 (q, *J* = 7.0 Hz, 3H), 7.34 – 7.27 (m, 2H), 7.17 (d, *J* = 7.6 Hz, 1H), 3.41 (pd, *J* = 7.0, 2.5 Hz, 1H), 2.90 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.73 (dd, *J* = 17.0, 2.5 Hz, 1H), 2.42 (s, 3H), 1.21 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.4, 146.6, 145.7, 139.0, 138.3, 133.5, 132.5, 129.9, 129.0, 128.7, 128.6, 128.5, 127.4, 126.7, 123.8, 123.1, 121.5, 108.6, 95.1, 90.1, 38.9, 24.4, 21.6, 20.0.

ESI HRMS: calcd. for $C_{28}H_{24}N_3$ $[M+H]^+$ 402.1965, found 402.1935.

Optical rotation: $[\alpha]_D^{20}$ = -62.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 7.5 min, t_{minor} = 13.7 min).



3ta

(*R*)-3-(3,4-dichlorophenyl)-4-methyl-1-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (31.5 mg, isolated yield: 69%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 140-143 °C.

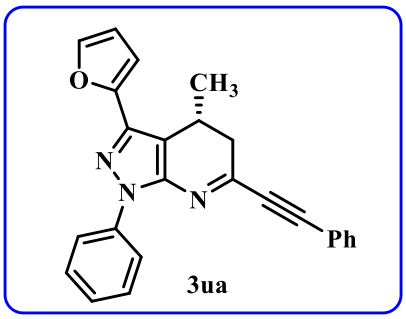
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, *J* = 2.1 Hz, 1H), 7.94 – 7.90 (m, 2H), 7.68 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.60 (dt, *J* = 6.7, 1.6 Hz, 2H), 7.51 – 7.45 (m, 3H), 7.42 – 7.35 (m, 3H), 7.35 – 7.31 (m, 1H), 3.37 (ddt, *J* = 11.8, 7.1, 3.5 Hz, 1H), 2.91 (dd, *J* = 17.1, 8.4 Hz, 1H), 2.76 (dd, *J* = 17.1, 2.3 Hz, 1H), 1.20 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 152.8, 145.9, 144.1, 138.8, 133.8, 132.9, 132.5, 131.7, 130.6, 130.0, 129.0, 128.6, 128.3, 127.1, 125.7, 123.1, 121.3, 108.6, 95.6, 89.9, 38.7, 24.3, 19.9.

ESI HRMS: calcd. for $C_{27}H_{20}Cl_2N_3$ $[M+H]^+$ 456.1029, found 456.0995.

Optical rotation: $[\alpha]_D^{20}$ = +92.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 93%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 8.1 min, t_{minor} = 11.3 min).



(*R*)-3-(furan-2-yl)-4-methyl-1-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (22.6 mg, isolated yield: 60%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 144-146 °C.

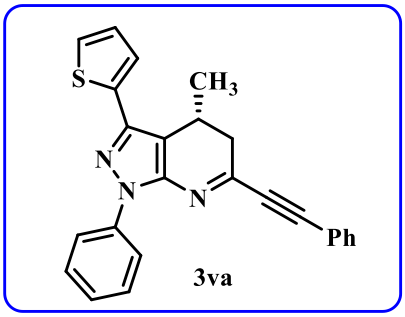
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.87 (m, 2H), 7.62 – 7.57 (m, 2H), 7.53 – 7.45 (m, 3H), 7.42 – 7.36 (m, 3H), 7.31 (td, *J* = 7.3, 1.2 Hz, 1H), 6.77 (d, *J* = 3.4 Hz, 1H), 6.52 (dd, *J* = 3.4, 1.8 Hz, 1H), 3.48 – 3.39 (m, 1H), 2.92 (dd, *J* = 17.2, 8.8 Hz, 1H), 2.77 (dd, *J* = 17.2, 1.9 Hz, 1H), 1.23 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 153.0, 148.7, 145.4, 142.2, 139.4, 138.7, 132.5, 129.9, 128.9, 128.5, 126.9, 123.2, 121.4, 111.3, 108.0, 106.8, 95.2, 90.0, 38.7, 23.9, 20.1.

ESI HRMS: calcd. for $C_{25}H_{20}N_3O$ $[M+H]^+$ 378.1601, found 378.1590.

Optical rotation: $[\alpha]_D^{20}$ = -20.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 97%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 7.6 min, t_{minor} = 14.3 min).



(*R*)-4-methyl-1-phenyl-6-(phenylethynyl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Brown solid (23.6mg, isolated yield: 60%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 142-144 °C.

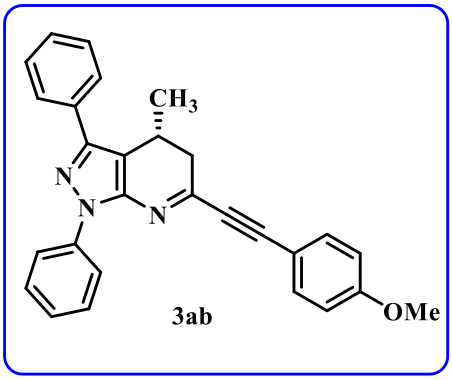
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.60 (dd, *J* = 6.3, 1.8 Hz, 2H), 7.49 – 7.44 (m, 2H), 7.39 (tt, *J* = 5.8, 1.4 Hz, 4H), 7.30 (tt, *J* = 7.0, 1.4 Hz, 2H), 7.11 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.42 – 3.33 (m, 1H), 2.92 (dd, *J* = 17.1, 8.6 Hz, 1H), 2.78 (dd, *J* = 17.2, 1.8 Hz, 1H), 1.23 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.7, 145.6, 142.0, 138.7, 136.1, 132.5, 129.9, 128.9, 128.6, 127.5, 126.8, 124.9, 124.2, 123.1, 121.4, 107.8, 95.3, 90.0, 38.7, 24.0, 19.6.

ESI HRMS: calcd. for $C_{25}H_{20}N_3S$ $[M+H]^+$ 394.1373 , found 394.1370.

Optical rotation: $[\alpha]_D^{20}$ = +30.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 99%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 8.7 min, t_{minor} = 15.8 min).



(*R*)-6-((4-methoxyphenyl)ethynyl)-4-methyl-1,3-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (27.1 mg, isolated yield: 65%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 165-167 °C.

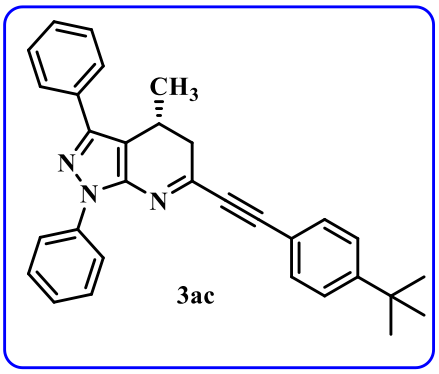
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.92 (m, 2H), 7.90 – 7.84 (m, 2H), 7.56 – 7.51 (m, 2H), 7.45 (dt, *J* = 11.2, 7.6 Hz, 4H), 7.38 – 7.27 (m, 2H), 6.89 (d, *J* = 8.8 Hz, 2H), 3.82 (s, 3H), 3.46 – 3.36 (m, 1H), 2.89 (dd, *J* = 16.9, 8.3 Hz, 1H), 2.73 (dd, *J* = 17.0, 2.5 Hz, 1H), 1.21 (d, *J* = 6.9 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0, 152.7, 146.4, 145.9, 139.1, 134.3, 133.7, 128.9, 128.7, 127.9, 126.7, 126.7, 123.1, 114.3, 113.4, 108.4, 96.0, 89.5, 55.4, 38.9, 24.4, 19.9.

ESI HRMS: calcd. for $C_{28}H_{24}N_3O$ $[M+H]^+$ 418.1914, found 418.1897.

Optical rotation: $[\alpha]_D^{20}$ = -15.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 91%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 10.4 min, t_{minor} = 18.7 min).



(*R*)-6-((4-(tert-butyl)phenyl)ethynyl)-4-methyl-1,3-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (24.4mg, isolated yield: 53%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 173-175 °C.

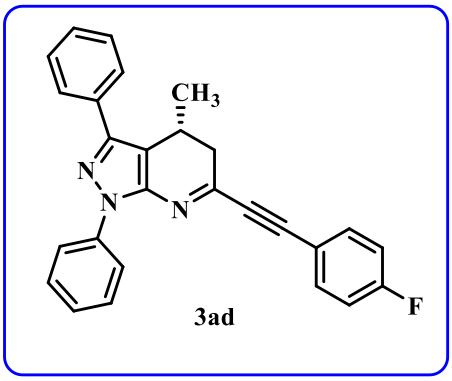
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.84 (m, 2H), 7.81 – 7.78 (m, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.42 – 7.37 (m, 3H), 7.34 (t, *J* = 7.4 Hz, 3H), 7.30 – 7.20 (m, 2H), 3.36 (td, *J* = 7.9, 2.3 Hz, 1H), 2.84 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.68 (dd, *J* = 17.0, 2.5 Hz, 1H), 1.26 (s, 9H), 1.16 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 153.5, 152.7, 146.4, 145.8, 139.0, 133.7, 132.3, 128.9, 128.6, 127.9, 126.7, 125.6, 123.1, 118.4, 108.5, 95.7, 89.7, 38.9, 35.0, 31.1, 24.3, 19.9.

ESI HRMS: calcd. for $C_{31}H_{30}N_3$ $[M+H]^+$ 444.2435, found 444.2415.

Optical rotation: $[\alpha]_D^{20}$ = -30.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 5.3 min, t_{minor} = 7.6 min).



(*R*)-6-((4-fluorophenyl)ethynyl)-4-methyl-1,3-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (27.2 mg, isolated yield: 67%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 156-159 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.92 (m, 2H), 7.88 – 7.85 (m, 2H), 7.62 – 7.57 (m, 2H), 7.46 (dt, *J* = 11.4, 7.7 Hz, 4H), 7.38 – 7.28 (m, 2H), 7.08 (t, *J* = 8.6 Hz, 2H), 3.43 (ddd, *J* = 8.5, 7.0, 2.4 Hz, 1H), 2.91 (dd, *J* = 17.0, 8.4 Hz, 1H), 2.74 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.22 (d, *J* = 6.9 Hz, 3H).

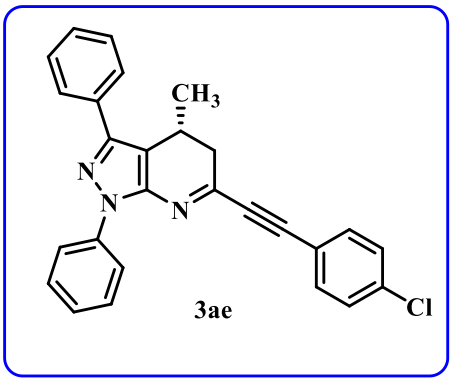
^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 162.2, 152.3, 146.5, 145.7, 139.0, 134.6, 134.5, 133.6, 128.9, 128.7, 127.9, 126.8, 126.7, 123.1, 117.6, 117.6, 116.1, 115.9, 108.5, 93.9, 89.8, 38.8, 24.3, 19.9.

^{19}F NMR (377 MHz, $CDCl_3$) δ -107.9.
The coupling constant between C-F are as follow.
^1J = (164.70– 162.19) * 101 = 253.51 Hz, ^2J = (116.13 – 115.91) * 101 = 22.22 Hz, ^3J = (134.63 – 134.54) * 101 = 9.09 Hz, ^4J = (117.62 – 117.58) * 100 = 4.04 Hz.

ESI HRMS: calcd. for $C_{27}H_{21}FN_3$ $[M+H]^+$ 406.1715, found 406.1699.

Optical rotation: $[\alpha]_D^{20}$ = -50.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 93%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 6.5 min, t_{minor} = 10.3 min).



3ae

(*R*)-6-((4-chlorophenyl)ethynyl)-4-methyl-1,3-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (27.4 mg, isolated yield: 65%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 188-190 °C.

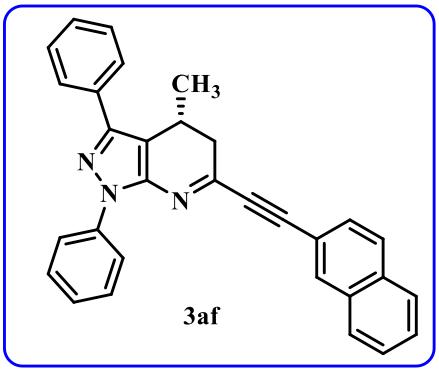
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 2H), 7.88 – 7.84 (m, 2H), 7.51 (dd, *J* = 8.3, 6.3 Hz, 3H), 7.47 – 7.42 (m, 3H), 7.38 – 7.29 (m, 4H), 3.47 – 3.38 (m, 1H), 2.90 (dd, *J* = 17.1, 8.4 Hz, 1H), 2.72 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.21 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.1, 146.5, 145.6, 139.0, 136.1, 133.7, 133.6, 129.0, 129.0, 128.7, 128.0, 126.8, 126.7, 123.1, 119.9, 108.6, 93.7, 90.8, 38.8, 24.3, 19.9.

ESI HRMS: calcd. for $C_{27}H_{21}ClN_3$ $[M+H]^+$ 422.1419, found 422.1394.

Optical rotation: $[\alpha]_D^{20}$ = -7.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 91%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 6.5 min, t_{minor} = 10.7 min).



3af

(*R*)-4-methyl-6-(naphthalen-2-ylethynyl)-1,3-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (25.0mg, isolated yield: 55%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 184-187 °C.

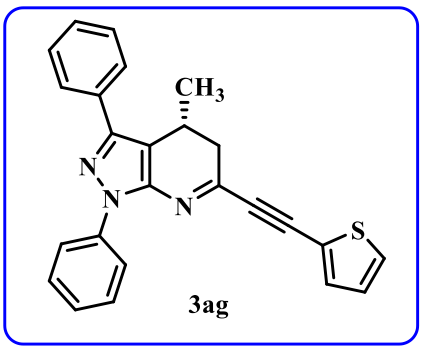
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 1.6 Hz, 1H), 7.91 – 7.87 (m, 2H), 7.81 – 7.76 (m, 2H), 7.74 – 7.71 (m, 3H), 7.51 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.44 – 7.41 (m, 2H), 7.39 (s, 1H), 7.36 (t, *J* = 7.2 Hz, 2H), 7.28 – 7.19 (m, 2H), 3.33 (dtd, *J* = 14.0, 7.1, 2.5 Hz, 1H), 2.84 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.69 (dd, *J* = 17.0, 2.5 Hz, 1H), 1.14 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.4, 146.5, 145.8, 139.1, 134.0, 133.7, 133.5, 133.3, 132.9, 129.0, 128.7, 128.4, 128.3, 128.1, 127.9, 127.9, 127.6, 126.9, 126.7, 123.1, 118.7, 108.6, 95.6, 90.4, 38.9, 24.4, 20.0.

ESI HRMS: calcd. for $C_{31}H_{24}N_3$ $[M+H]^+$ 438.1965, found 438.1945.

Optical rotation: $[\alpha]_D^{20}$ = -17.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 99%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 12.8 min, t_{minor} = 24.8 min).



3ag

(*R*)-4-methyl-1,3-diphenyl-6-(thiophen-2-ylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (23.6 mg, isolated yield: 60%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 163-165 °C.

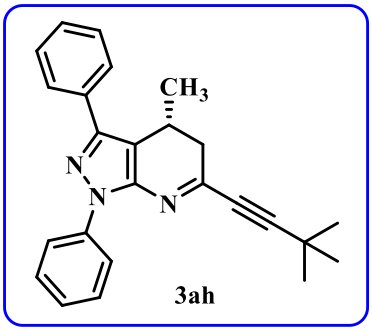
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 – 7.83 (m, 2H), 7.79 – 7.76 (m, 2H), 7.41 – 7.32 (m, 6H), 7.29 – 7.19 (m, 2H), 6.95 (dd, *J* = 5.2, 3.7 Hz, 1H), 3.38 – 3.28 (m, 1H), 2.80 (dd, *J* = 17.0, 8.3 Hz, 1H), 2.63 (dd, *J* = 17.0, 2.5 Hz, 1H), 1.12 (d, *J* = 7.0 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0, 146.5, 145.8, 139.0, 134.8, 133.7, 133.6, 130.1, 129.0, 128.7, 127.9, 127.6, 126.7, 123.1, 121.4, 108.5, 94.1, 88.8, 38.6, 24.3, 19.9.

ESI HRMS: calcd. for $C_{25}H_{20}N_3S$ $[M+H]^+$ 394.1373 , found 394.1359.

Optical rotation: $[\alpha]_D^{20}$ = -20.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 274 nm (t_{major} = 9.3 min, t_{minor} = 17.5 min).



(*R*)-6-(3,3-dimethylbut-1-yn-1-yl)-4-methyl-1,3-diphenyl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (16.5 mg, isolated yield: 45%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 166-170 °C.

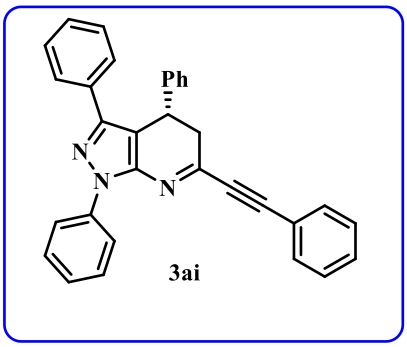
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 – 7.90 (m, 2H), 7.86 – 7.83 (m, 2H), 7.44 (dt, *J* = 11.2, 7.8 Hz, 4H), 7.36 – 7.32 (m, 1H), 7.31 – 7.26 (m, 1H), 3.35 (ddt, *J* = 12.8, 7.0, 3.5 Hz, 1H), 2.78 (dd, *J* = 17.0, 8.4 Hz, 1H), 2.59 (dd, *J* = 17.0, 2.5 Hz, 1H), 1.33 (s, 9H), 1.18 (d, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 153.4, 146.3, 145.7, 139.1, 133.8, 128.9, 128.6, 127.8, 126.7, 126.6, 123.0, 108.3, 105.6, 80.6, 39.3, 30.5, 28.3, 24.3, 20.0.

ESI HRMS: calcd. for $C_{25}H_{26}N_3$ $[M+H]^+$ 368.2122, found 368.2119.

Optical rotation: $[\alpha]_D^{20}$ = -25.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 4.1 min, t_{minor} = 5.2 min).



(*S*)-1,3,4-triphenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.

Yellow solid (19.2mg, isolated yield: 55%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 163-165 °C.

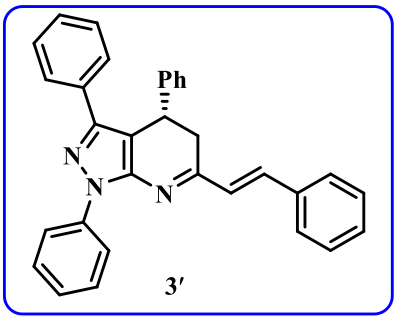
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 2H), 7.62 – 7.58 (m, 2H), 7.51 (td, *J* = 6.8, 1.7 Hz, 4H), 7.38 – 7.32 (m, 4H), 7.32 – 7.26 (m, 5H), 7.24 – 7.21 (m, 1H), 7.19 – 7.16 (m, 2H), 4.44 (dd, *J* = 9.3, 2.5 Hz, 1H), 3.17 (dd, *J* = 17.0, 9.3 Hz, 1H), 3.06 (dd, *J* = 17.0, 2.4 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.0, 146.5, 145.8, 139.0, 134.8, 133.7, 133.6, 130.1, 129.0, 128.7, 127.9, 127.6, 126.7, 123.1, 121.4, 108.5, 94.1, 88.8, 38.6, 24.3, 19.9.

ESI HRMS: calcd. for $C_{25}H_{26}N_3$ $[M+H]^+$ 350.1965, found 350.1960.

Optical rotation: $[\alpha]_D^{20}$ = -5.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 89%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 8.6 min, t_{minor} = 14.4 min).



***(S,E)*-1,3,4-triphenyl-6-styryl-4,5-dihydro-1H-pyrazolo[3,4-b]pyridine.**

Yellow solid (21.6mg, isolated yield: 48%); R_f = 0.70 in 0.5:9.5 ethyl acetate/hexane; M.P. 168-170 °C.

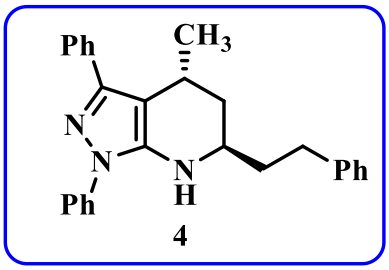
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.06 (m, 2H), 7.64 – 7.60 (m, 2H), 7.55 – 7.46 (m, 4H), 7.37 – 7.29 (m, 5H), 7.29 – 7.22 (m, 4H), 7.20 – 7.12 (m, 4H), 7.06 (d, *J* = 16.5 Hz, 1H), 4.49 (dd, *J* = 9.1, 2.3 Hz, 1H), 3.26 (dd, *J* = 16.5, 2.3 Hz, 1H), 2.99 (dd, *J* = 16.5, 9.1 Hz, 1H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 165.9, 148.0, 147.3, 143.3, 142.6, 139.3, 138.3, 135.6, 133.2, 130.3, 129.4, 128.9, 128.9, 128.8, 128.4, 127.7, 127.6, 127.0, 126.9, 126.6, 122.8, 105.7, 34.9, 34.1.

ESI HRMS: calcd. for $C_{25}H_{26}N_3$ $[M+H]^+$ 452.2122, found 452.2113.

Optical rotation: $[\alpha]_D^{20}$ = 0.0 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 3%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 90/10, flow rate 1.0 mL/min, λ = 220 nm (t_{major} = 7.5 min, t_{minor} = 10.0 min).



(*R*)-3-(furan-2-yl)-4-methyl-1-phenyl-6-(phenylethynyl)-4,5-dihydro-1H-pyrazolo[3,4-b]pyridin.

Yellow solid (14.5mg, isolated yield: 37%); R_f = 0.50 in 1:9 ethyl acetate/hexane; M.P. 144-147 °C.

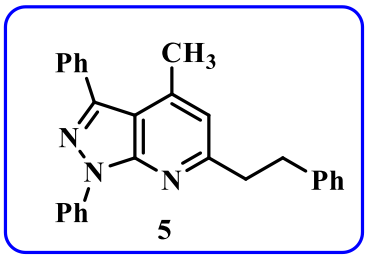
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.65 (m, 2H), 7.62 – 7.59 (m, 2H), 7.47 – 7.43 (m, 2H), 7.41 (dd, *J* = 4.1, 1.4 Hz, 1H), 7.40 – 7.36 (m, 2H), 7.34 – 7.31 (m, 1H), 7.30 – 7.29 (m, 1H), 7.28 – 7.27 (m, 1H), 7.19 (dd, *J* = 7.7, 2.3 Hz, 3H), 3.62 (s, 1H), 3.38 – 3.28 (m, 1H), 3.20 (dp, *J* = 10.3, 6.4 Hz, 1H), 2.83 – 2.70 (m, 2H), 2.12 (dd, *J* = 12.5, 7.1 Hz, 1H), 1.92 (dtd, *J* = 8.6, 6.5, 4.0 Hz, 2H), 1.38 (dd, *J* = 21.7, 13.3 Hz, 1H), 1.07 (d, *J* = 6.5 Hz, 3H).5

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 144.9, 141.4, 139.0, 135.0, 129.4, 128.6, 128.3, 128.2, 128.0, 127.5, 126.4, 126.2, 122.5, 104.0, 53.6, 40.3, 37.5, 32.3, 26.8, 20.6.

ESI HRMS: calcd. for $C_{25}H_{26}N_3$ $[M+H]^+$ 394.2278, found 394.2277.

Optical rotation: $[\alpha]_D^{20}$ = -17.5 (c 0.04, $CHCl_3$)

HPLC Analysis: ee = 95%, Chiral Phenomenex Lux Cellulose-1 (Chiral LC Columns), n-Hexane/i-PrOH = 95/5, flow rate 1.0 mL/min, λ = 254 nm (t_{major} = 22.3 min, t_{minor} = 58.6 min).



4-methyl-6-phenethyl-1,3-diphenyl-1H-pyrazolo[3,4-b]pyridine.

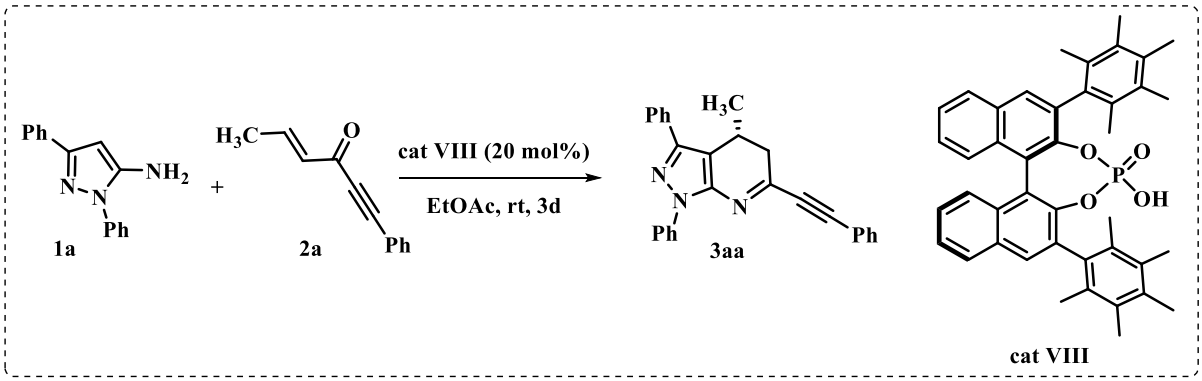
White solid (15.5mg, isolated yield: 40%); R_f = 0.50 in 1:9 ethyl acetate/hexane; M.P. 153-155 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.41 – 8.33 (m, 2H), 7.67 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.53 – 7.45 (m, 5H), 7.34 – 7.26 (m, 5H), 7.22 – 7.18 (m, 1H), 6.85 – 6.81 (m, 1H), 3.26 – 3.18 (m, 4H), 2.39 (d, *J* = 0.9 Hz, 3H)

^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 144.9, 141.4, 139.0, 135.0, 129.4, 128.6, 128.3, 128.2, 128.0, 127.5, 126.4, 126.2, 122.5, 104.0, 53.6, 40.3, 37.5, 32.3, 26.8, 20.6.

ESI HRMS: calcd. for $C_{25}H_{24}N_3$ $[M+H]^+$ 390.1965, found 390.1966.

9. Reaction study:



In an oven-dried screw cap vial equipped with a magnetic stir bar was charged with 1a(0.15 mmol, 1.5 equiv.), V catalyst (0.02 mmol, 20 mol%). Then, 1.5ml EtOAc was added in the mixture. After that, enynone 2a (0.1mmol, 1 equiv.) was added to the mixture and stirred at room temperature with 300 rpm. [The study done with various time interval and yield was measured using ^{1}H-NMR by dibromoethane as internal standard].

Note: Before measuring reaction yield, the reaction was quenched with NEt_3.

Entry	Time (hrs)	Yield of 3aa	ee of 3aa
1	0	-	-
2	6	37	70
3	12	40	75
4	18	43	80
5	24	45	85
6	30	47	87
7	36	51	91
8	42	55	93
9	48	58	95
10	54	60	95
11	60	63	95
12	66	65	95
13	72	65	95

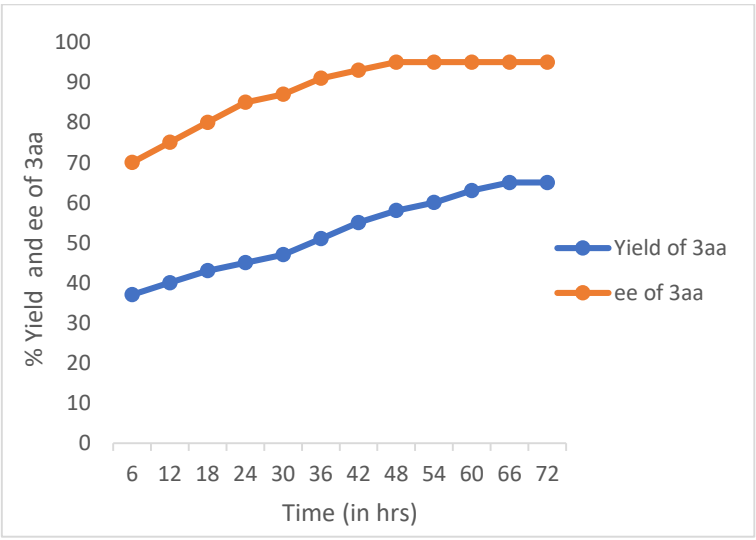


Fig. S1: Overall reaction profile of the reaction

Non-Linear effects experiment :

Completely dissolving the optically pure R- and S- phosphoric acid with ratios from 9.5/.5, 9/1, 8.5/1.5, 8/2, 7.5/2.5, 7/3, 6.5/3.5, 6/4, 5.5/4.5 in EtOAc. Upon removal of the solvent, optically active chiral phosphoric acid with 90% ee, 80% ee, 70% ee, 60% ee, 50% ee, 40% ee, 30% ee, 20% ee and 10% ee was obtained. Under optimal conditions, the reaction was carried out using the chiral phosphoric acid with different optical purities as the catalyst. The experiment revealed that the initial ee values in the product showed a deterministic linear relationship with the ee values in the catalyst at room temperature which suggests a single catalyst molecule is involved in the enantio-determining step.

Entry	ee of ligand(%)	ee of 3a(%)
1	10	5
2	20	13
3	30	20
4	40	45
5	50	57
6	60	69
7	70	75
8	80	81
9	90	88
10	100	95

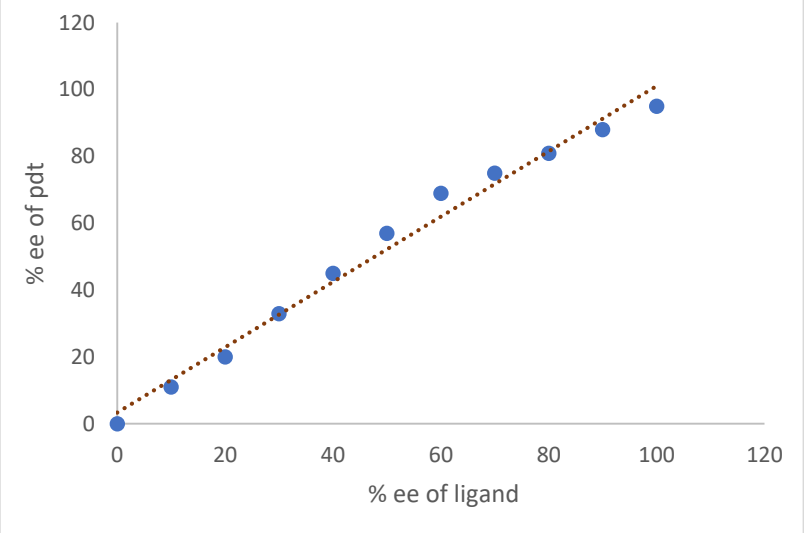


Fig. S2: Examination of non linear effect at room temperature

10. Single crystal X-ray diffraction analysis:

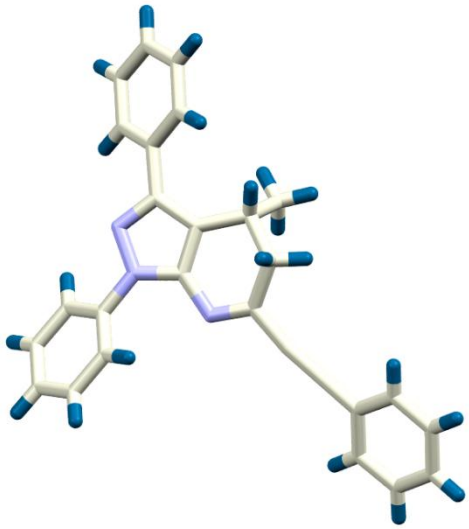
Single crystal X-ray diffraction analysis of 3aa:

Method for crystal growth: In a round bottom flask, compound 3aa dissolved in minimum amount of hexane/DCM (1:1) and it kept in dark place at room temperature for slow evaporation to get crystal of 3aa. The needle shaped crystal was then subjected to X-ray diffraction.

CCDC No.	2527132
Identification code	dds_pyr_yn_chyral_0m_a
Empirical formula	$C_{27}H_{21}N_3$
Formula weight	387.47
Temperature/K	297.00
Crystal system	monoclinic
Space group	$P2_1$
a/Å	10.9402(7)
b/Å	8.5319(5)
c/Å	11.4283(7)
α/°	90
β/°	97.701(2)
γ/°	90
Volume/Å^3	1057.10(11)
Z	2
ρ_{calc}g/cm^3	1.217
μ/mm^{-1}	0.071
F(000)	408.0
Crystal size/mm^3	0.3 × 0.25 × 0.2
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	3.756 to 50.05
Index ranges	$-13 \le h \le 12$, $-10 \le k \le 10$, $-13 \le l \le 13$
Reflections collected	25911
Independent reflections	3726 [R_{int} = 0.0506, R_{sigma} = 0.0388]
Data/restraints/parameters	3726/1/272
Goodness-of-fit on F^2	1.112
Final R indexes [I>=2σ (I)]	R_1 = 0.0440, wR_2 = 0.0862

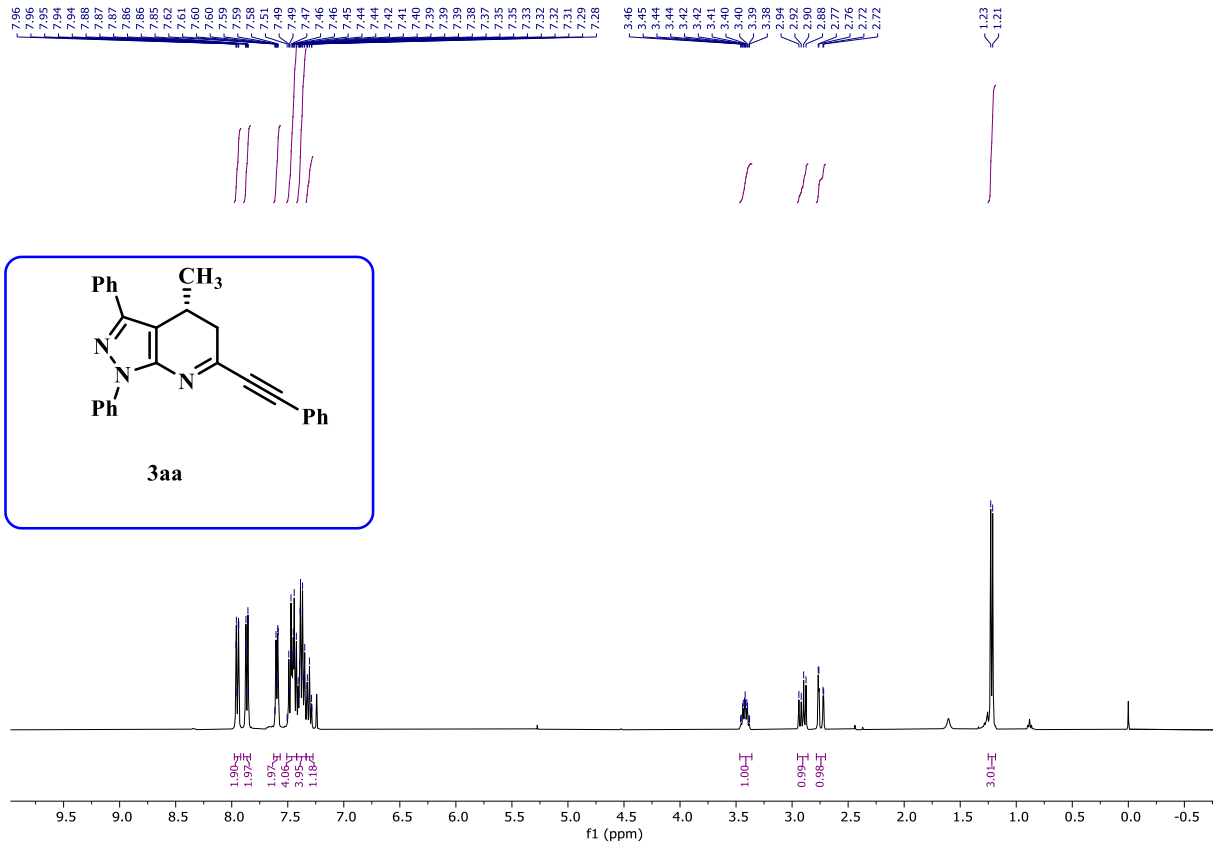
Final R indexes [all data] $R_1 = 0.0737$, $wR_2 = 0.1010$

Largest diff. peak/hole / e Å^{-3} 0.11/-0.17

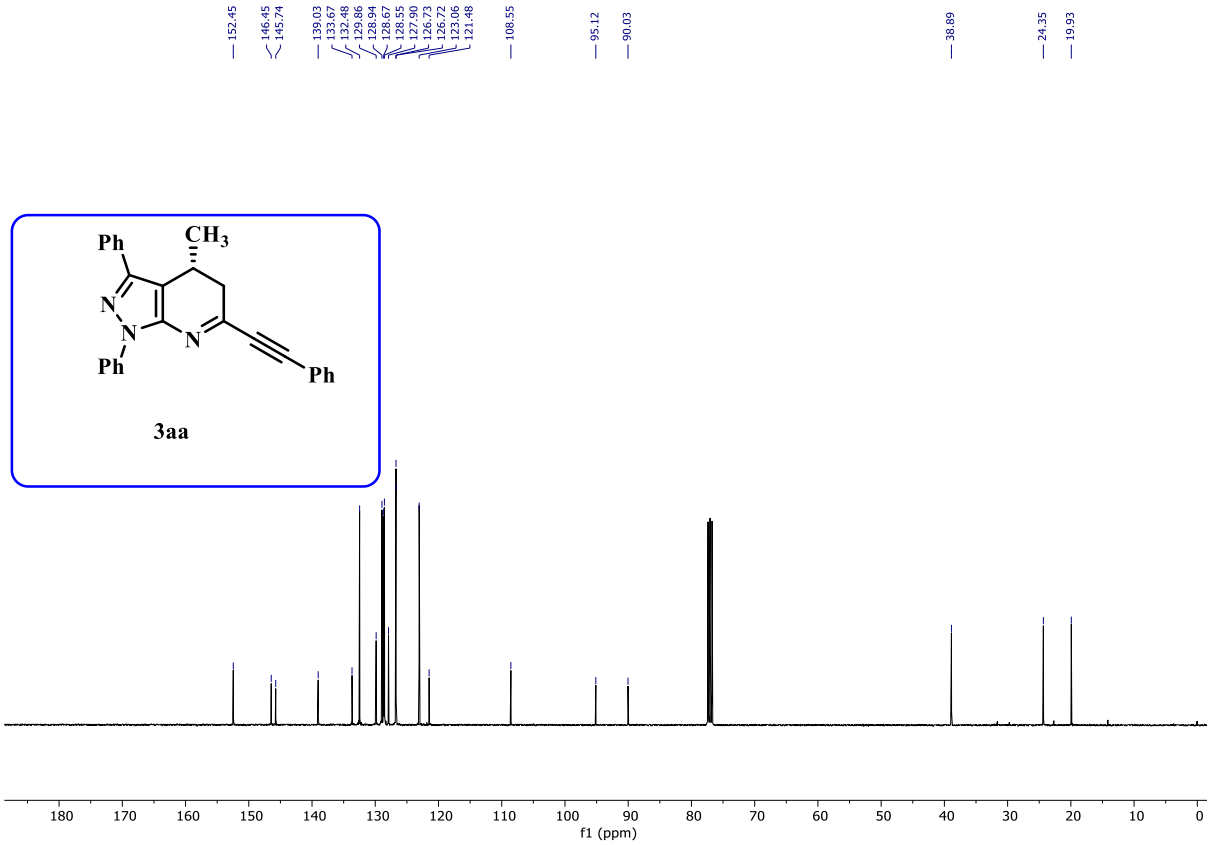


ORTEP representation of the X-ray structure of **3aa** (thermal ellipsoids at 30% probability)

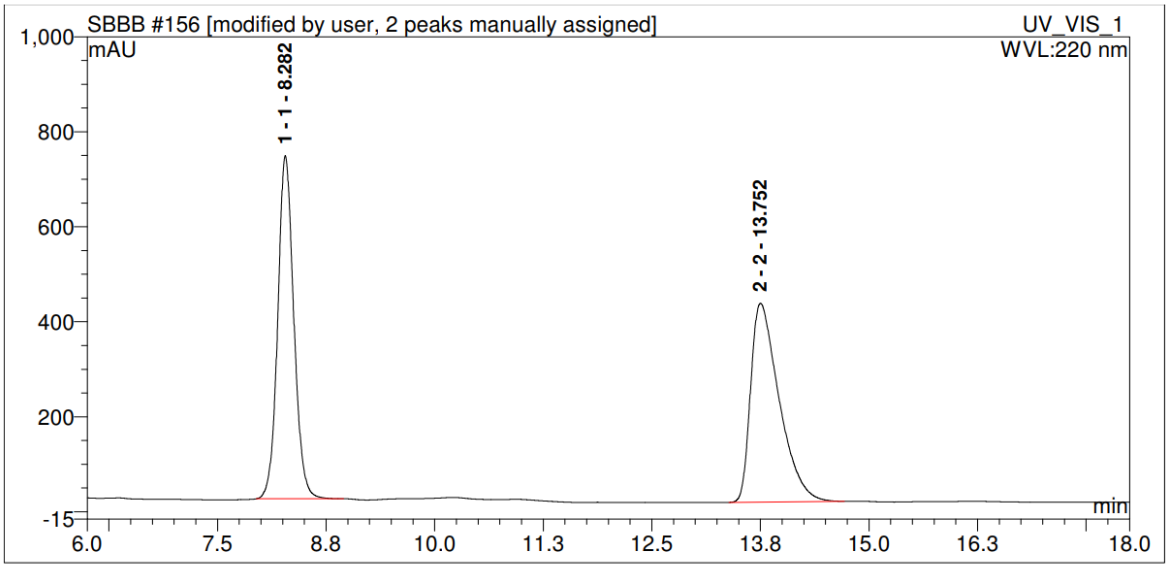
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

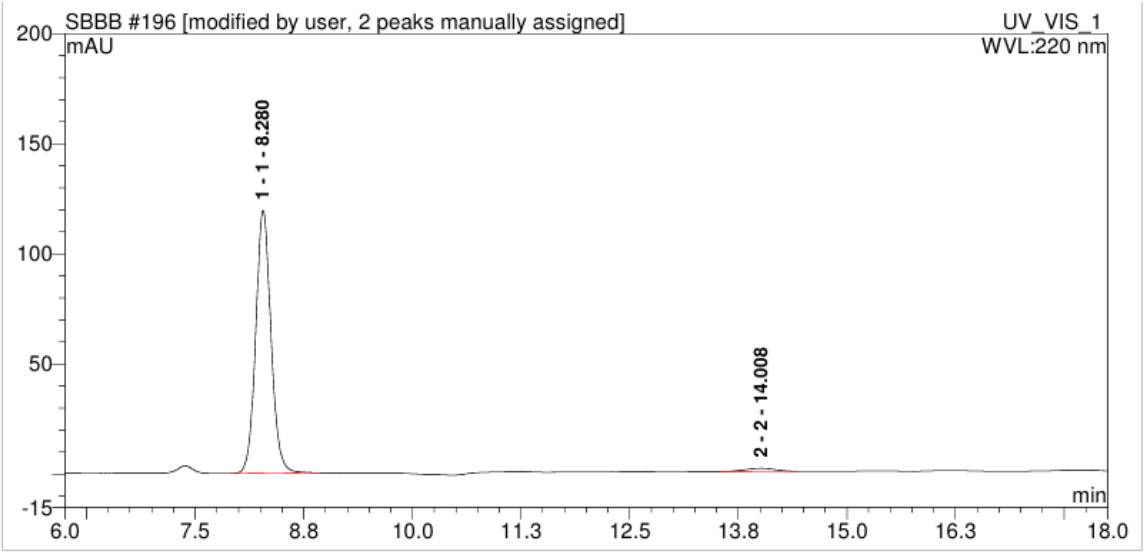


HPLC Spectra of *rac*-3aa



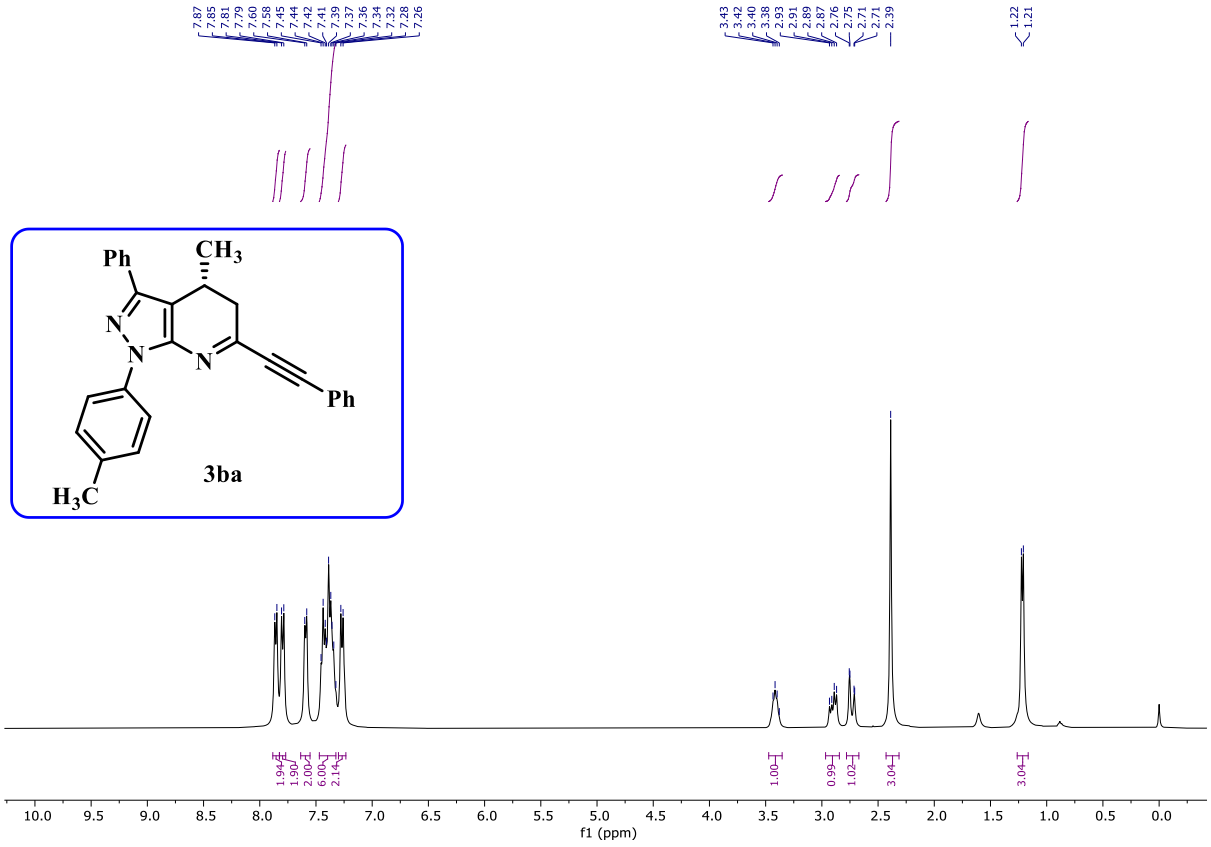
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.281666667	155.0683	49.38380155	722.3134	n.a.
2	2	13.75166667	158.9381	50.61619845	418.6095	n.a.

HPLC Spectra of *chi*-3aa

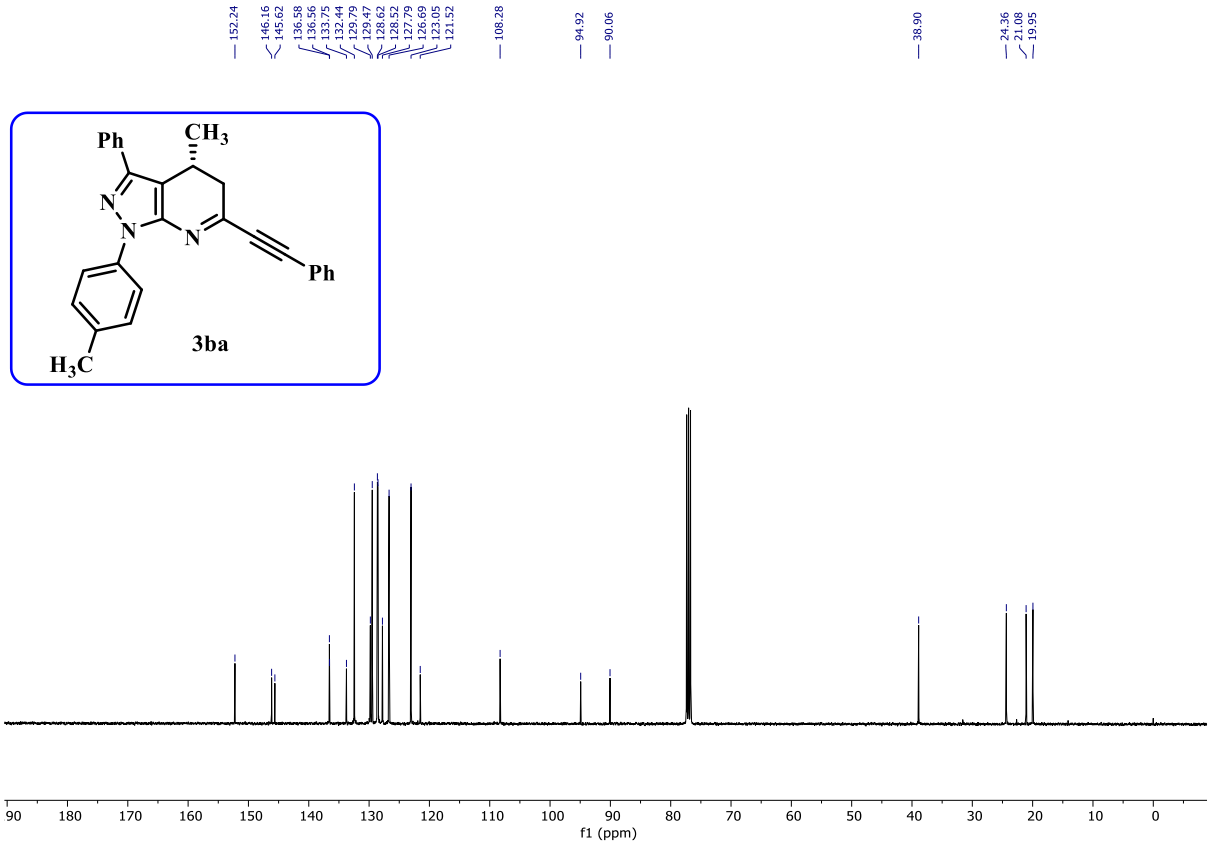


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.28	24.34776	97.90661322	119.3042	n.a.
2	2	14.00833333	0.520591	2.093386779	1.38927	n.a.

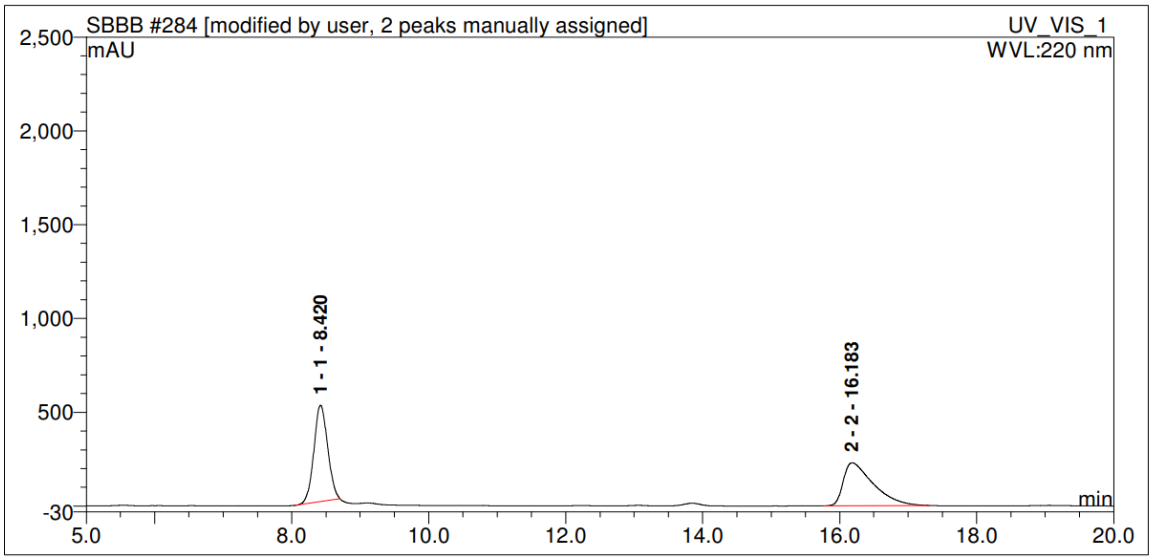
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

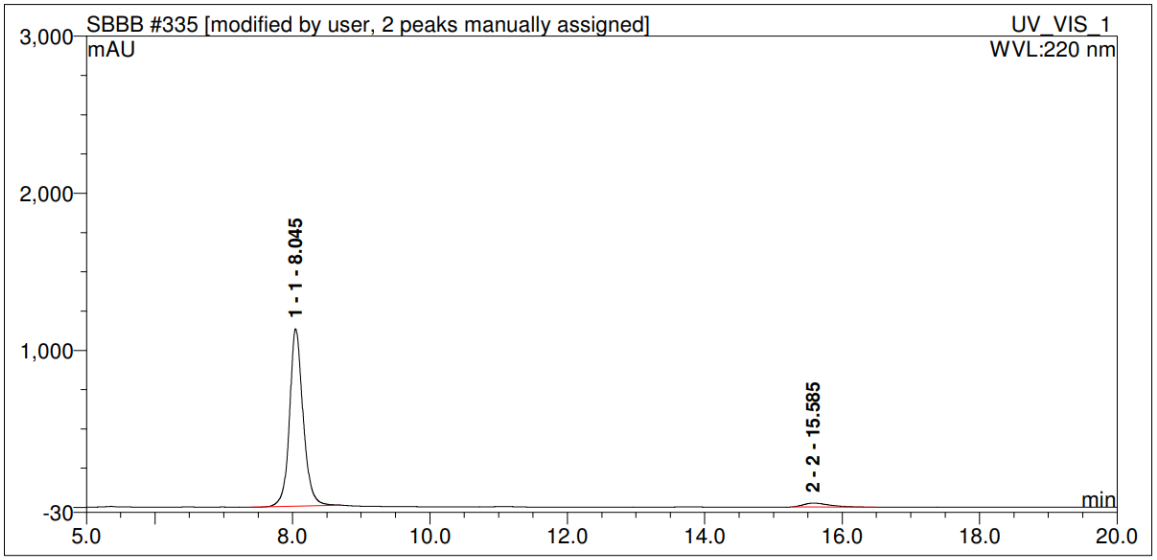


HPLC Spectra of *rac*-3ba



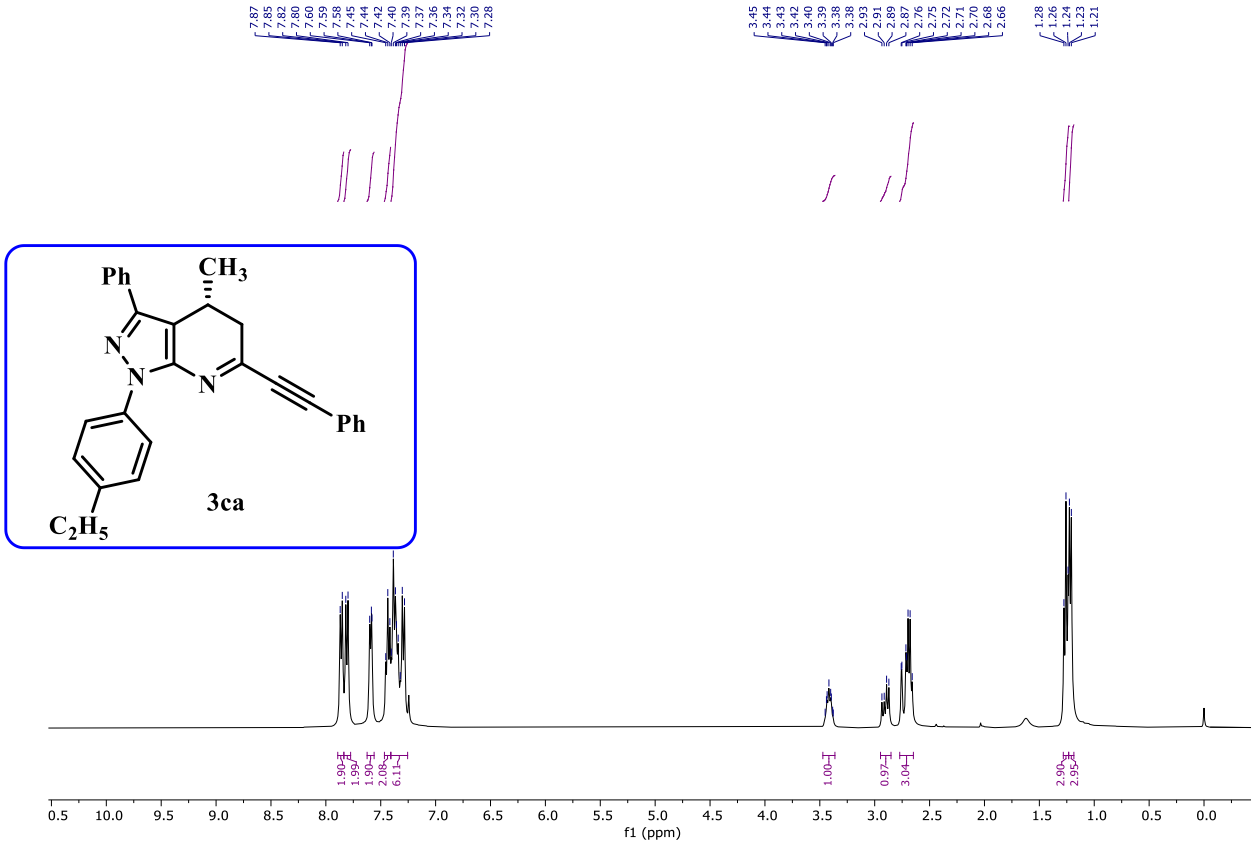
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.42	119.7228	50.81484278	513.4631	n.a.
2	2	16.18333333	115.8832	49.18515722	229.0772	n.a.

HPLC Spectra of *chi*-3ba

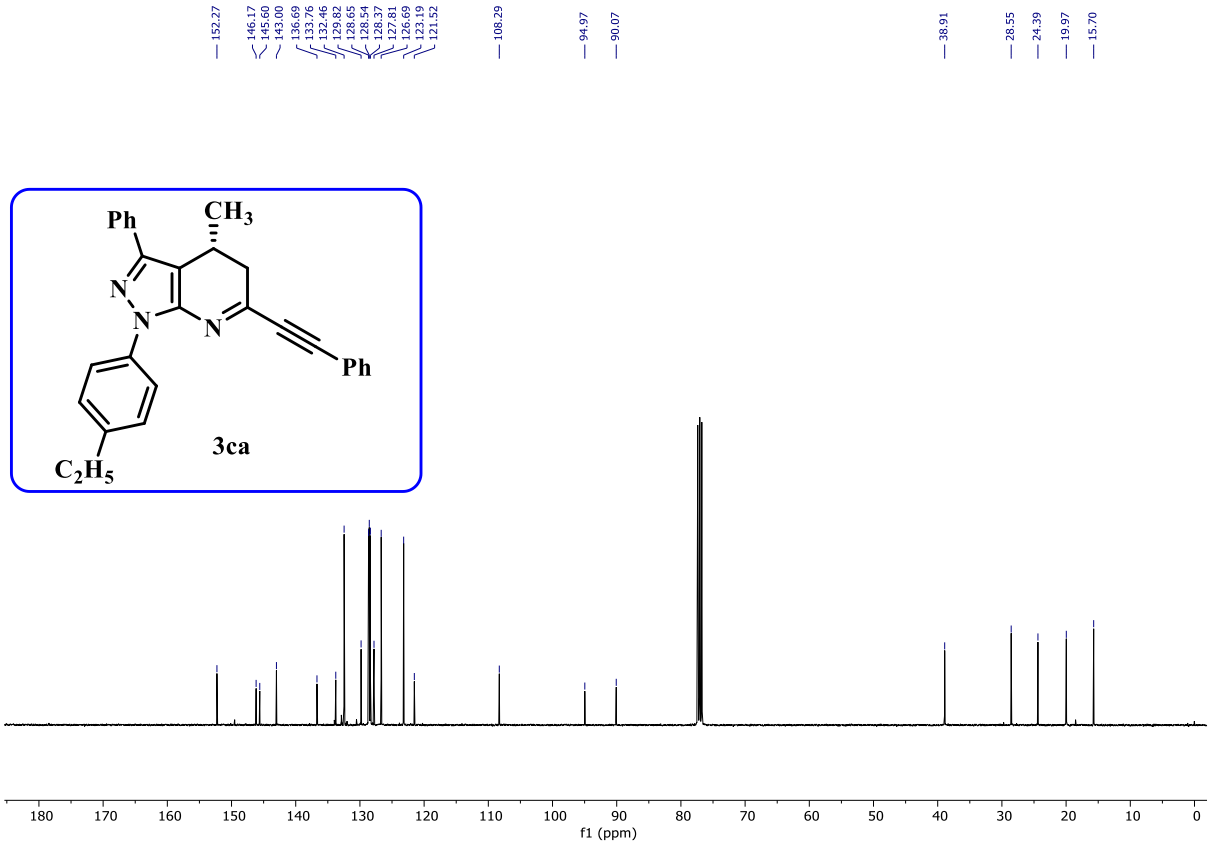


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.045	258.8647	96.01609752	1129.51	n.a.
2	2	15.585	10.74082	3.983902481	24.50435	n.a.

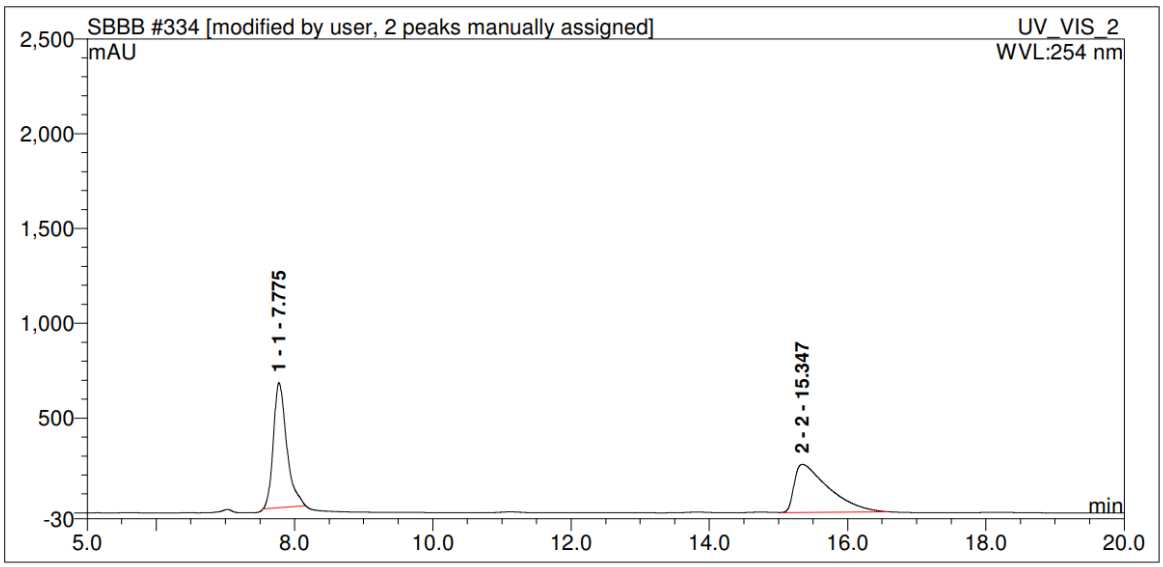
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

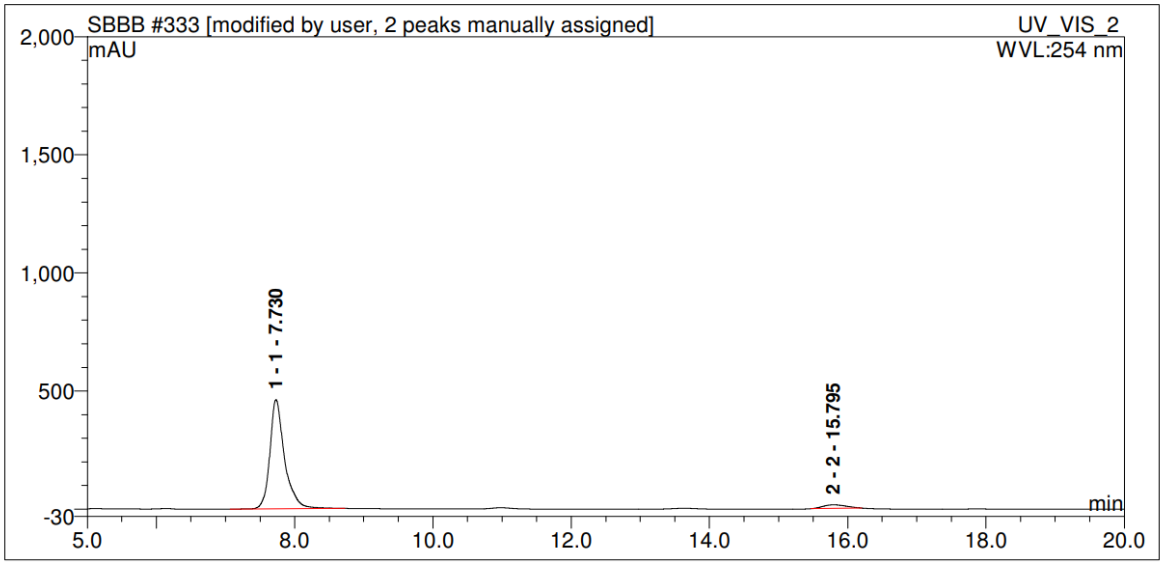


HPLC Spectra of *rac*-3ca



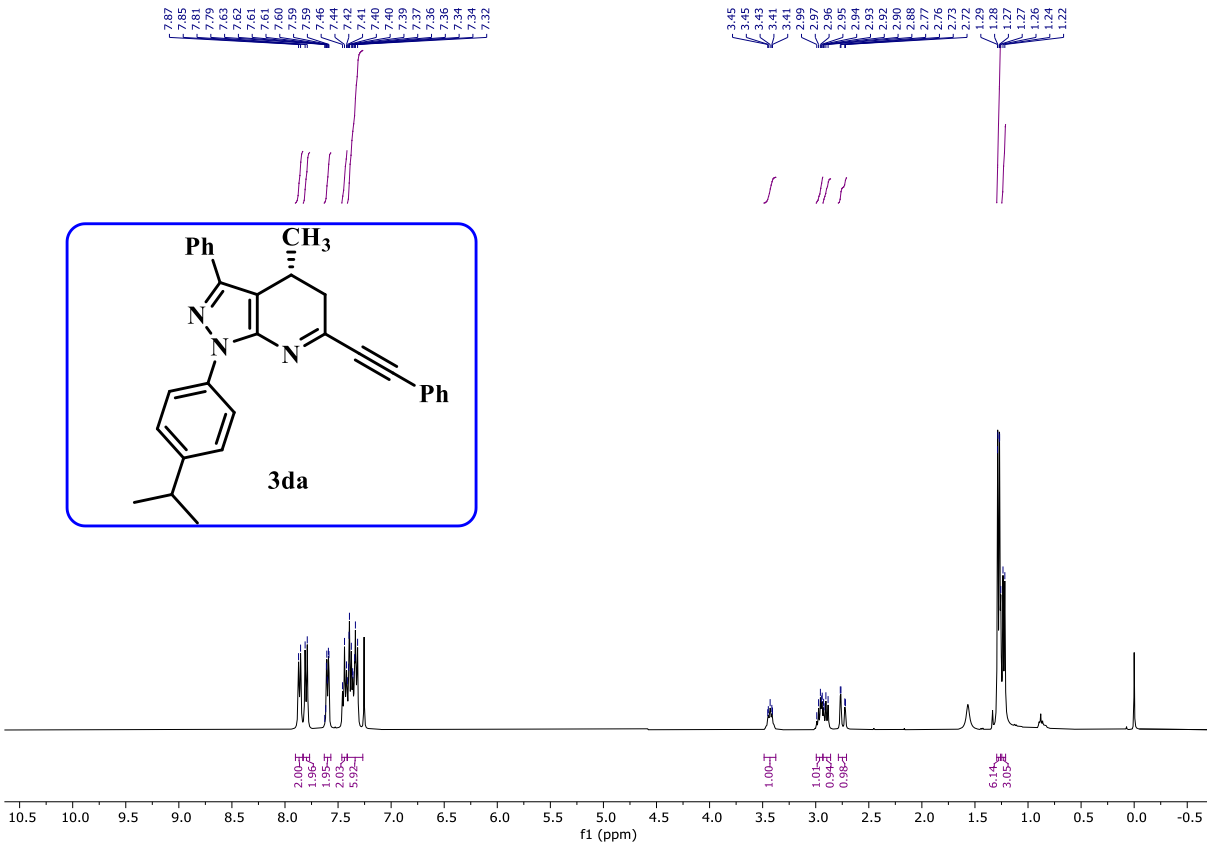
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.775	147.7027	50.515673	659.3833	n.a.
2	2	15.34666667	144.6871	49.484327	253.6808	n.a.

HPLC Spectra of *chi*-3ca

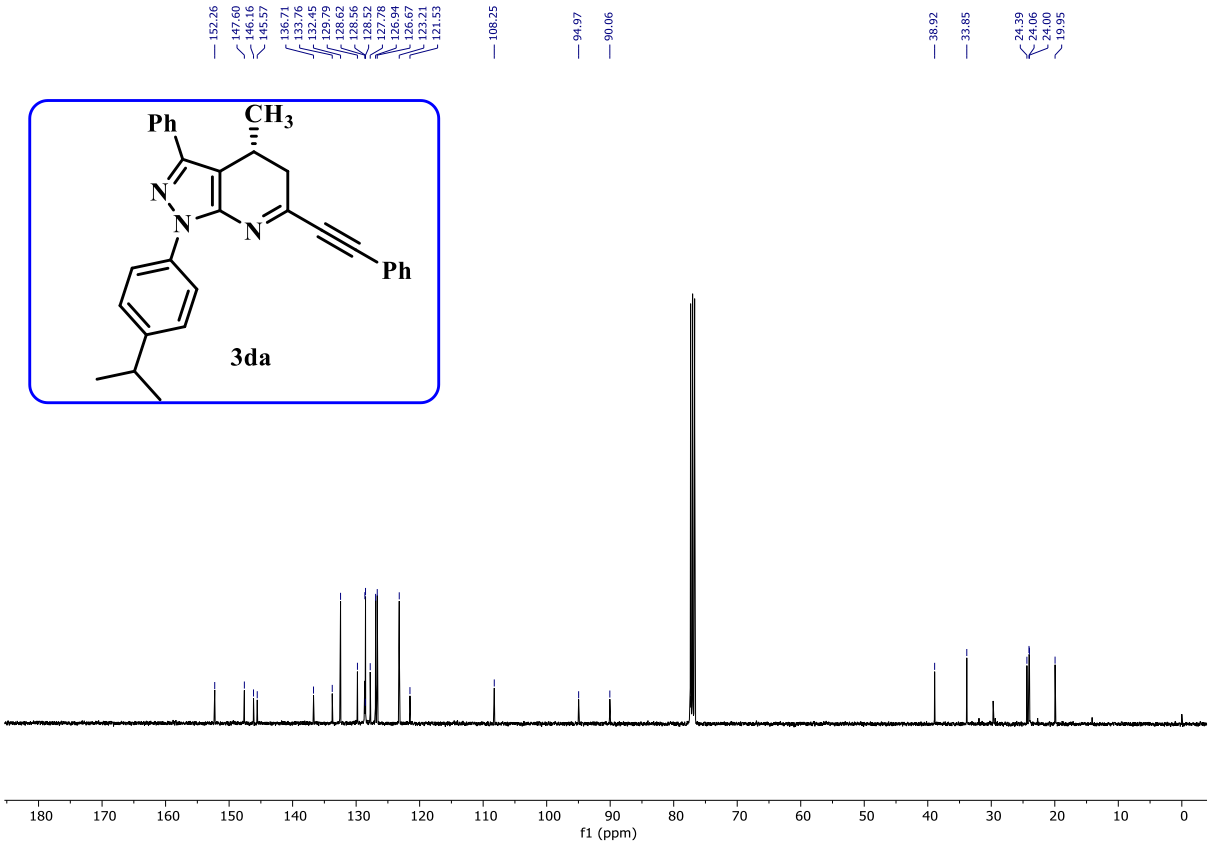


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.73	114.3147	95.04213297	461.6938	n.a.
2	2	15.795	5.963221	4.957867035	15.25081	n.a.

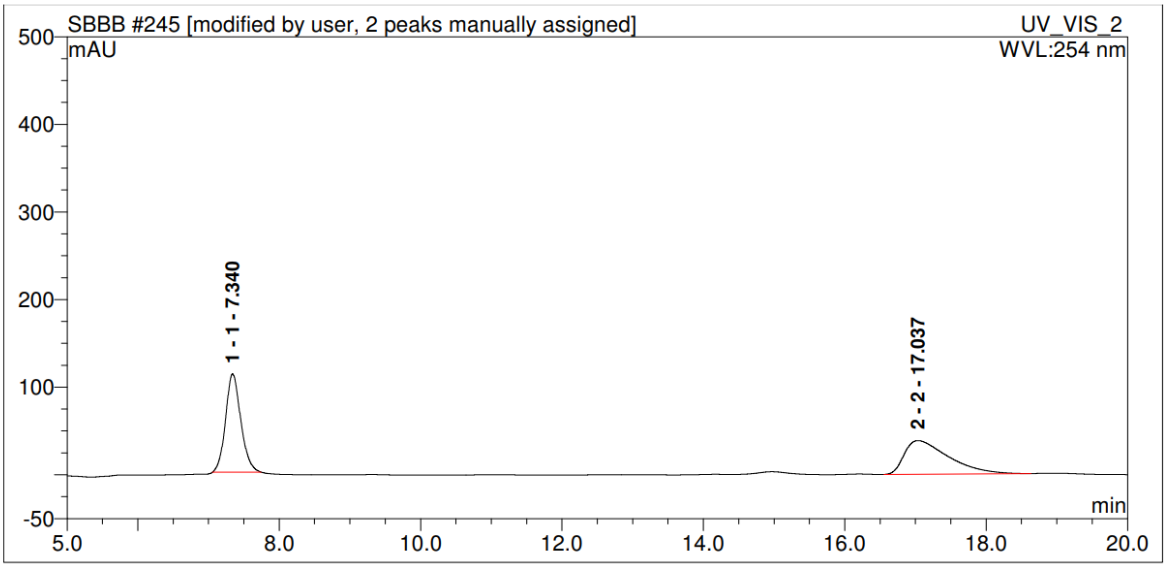
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

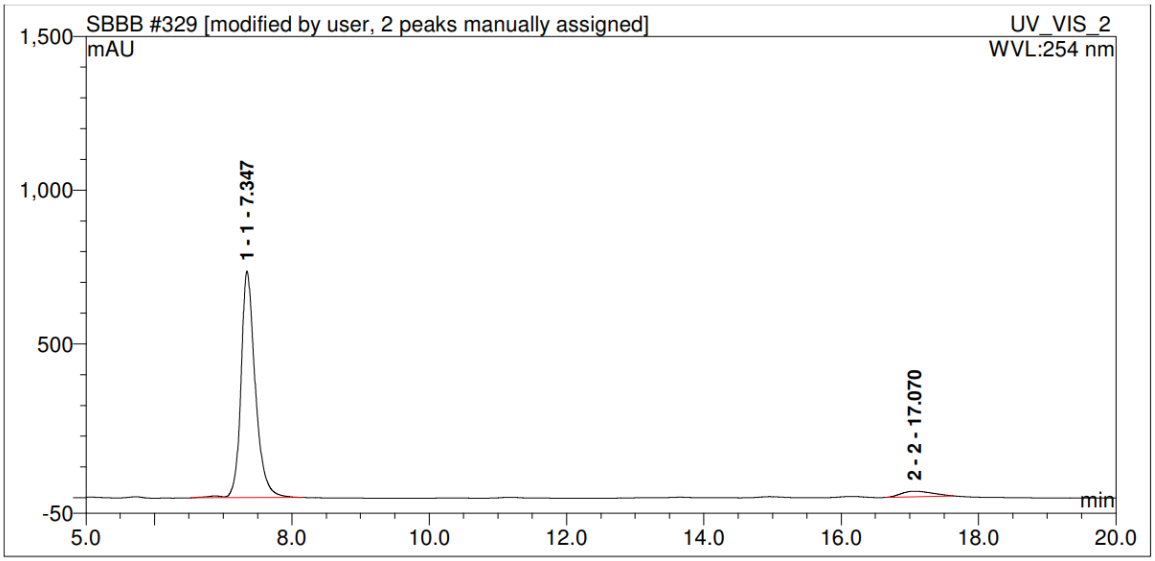


HPLC Spectra of *rac*-3da



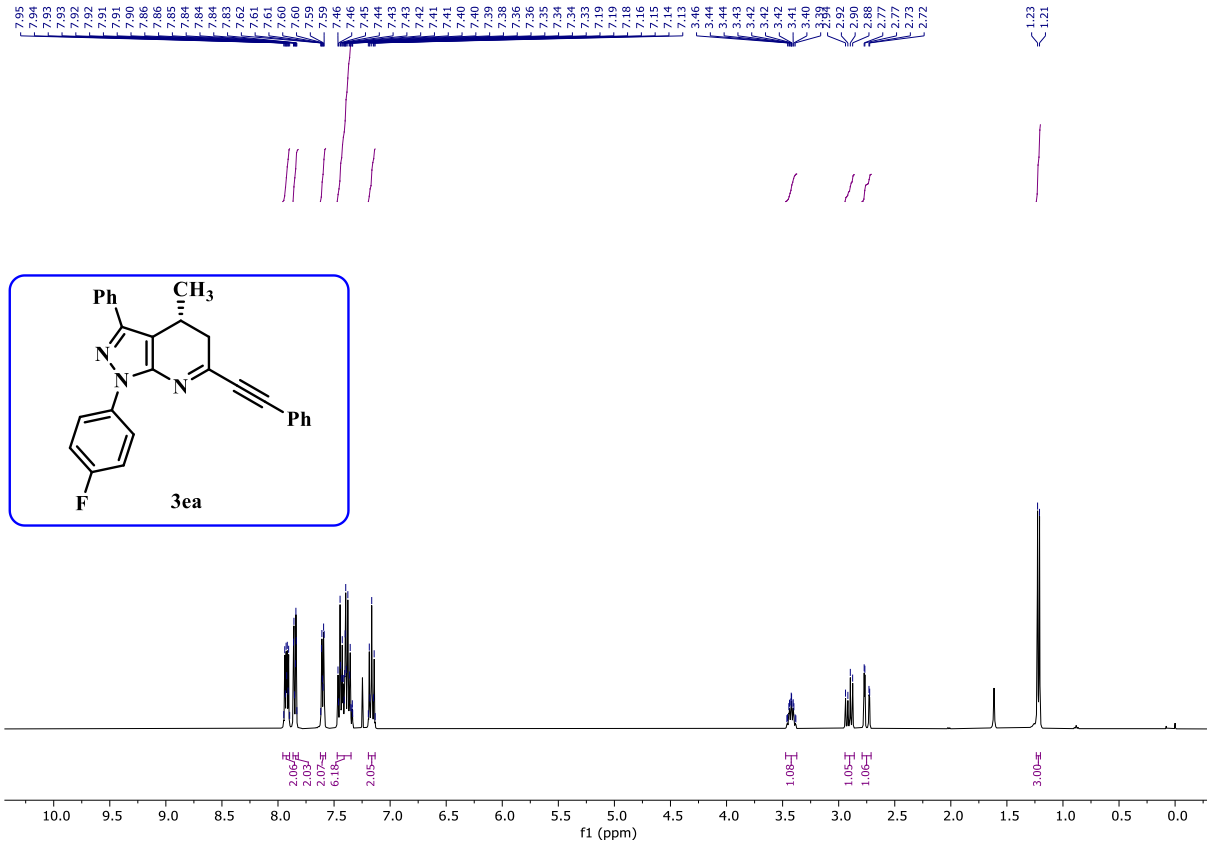
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.34	28.01244	50.27135062	112.1376	n.a.
2	2	17.03666667	27.71003	49.72864938	38.3671	n.a.

HPLC Spectra of *chi*-3da

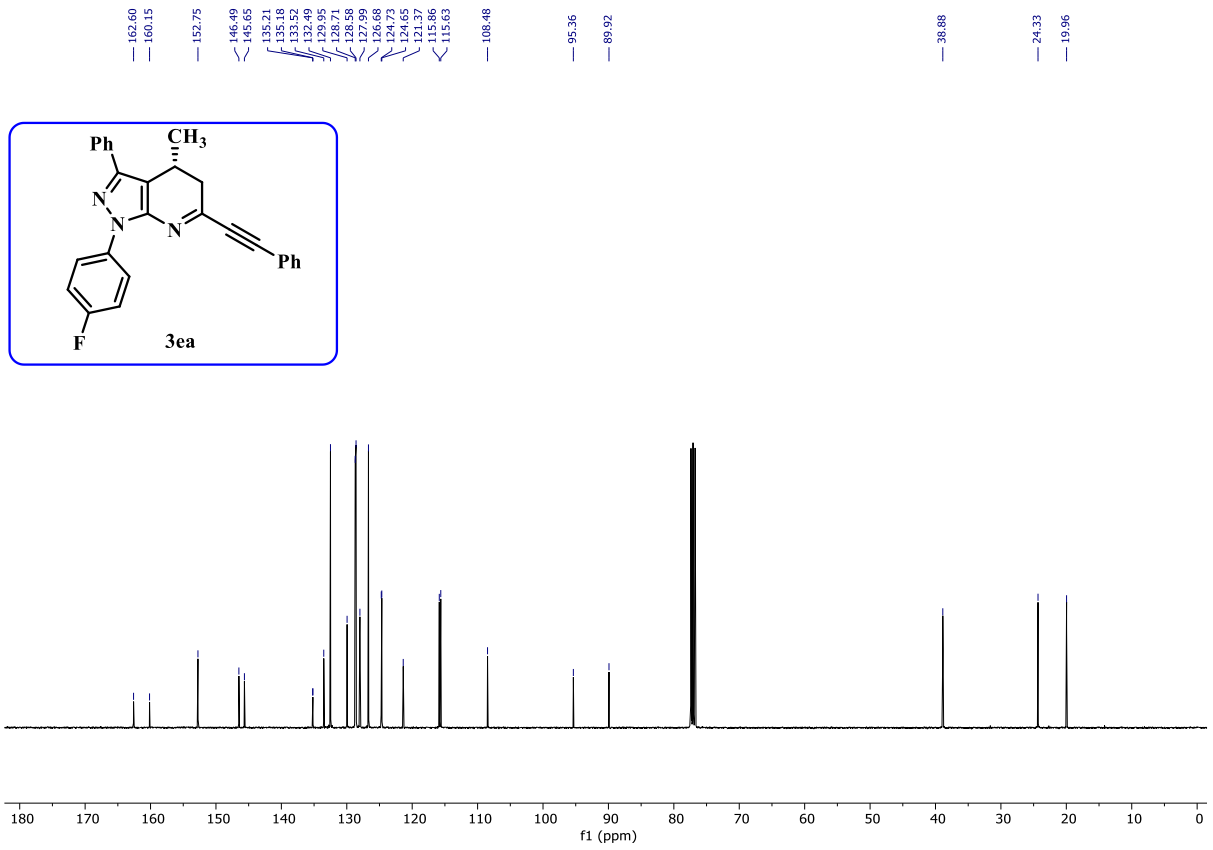


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.346666667	177.8517	95.02512447	736.0352	n.a.
2	2	17.07	9.311115	4.974875526	17.92928	n.a.

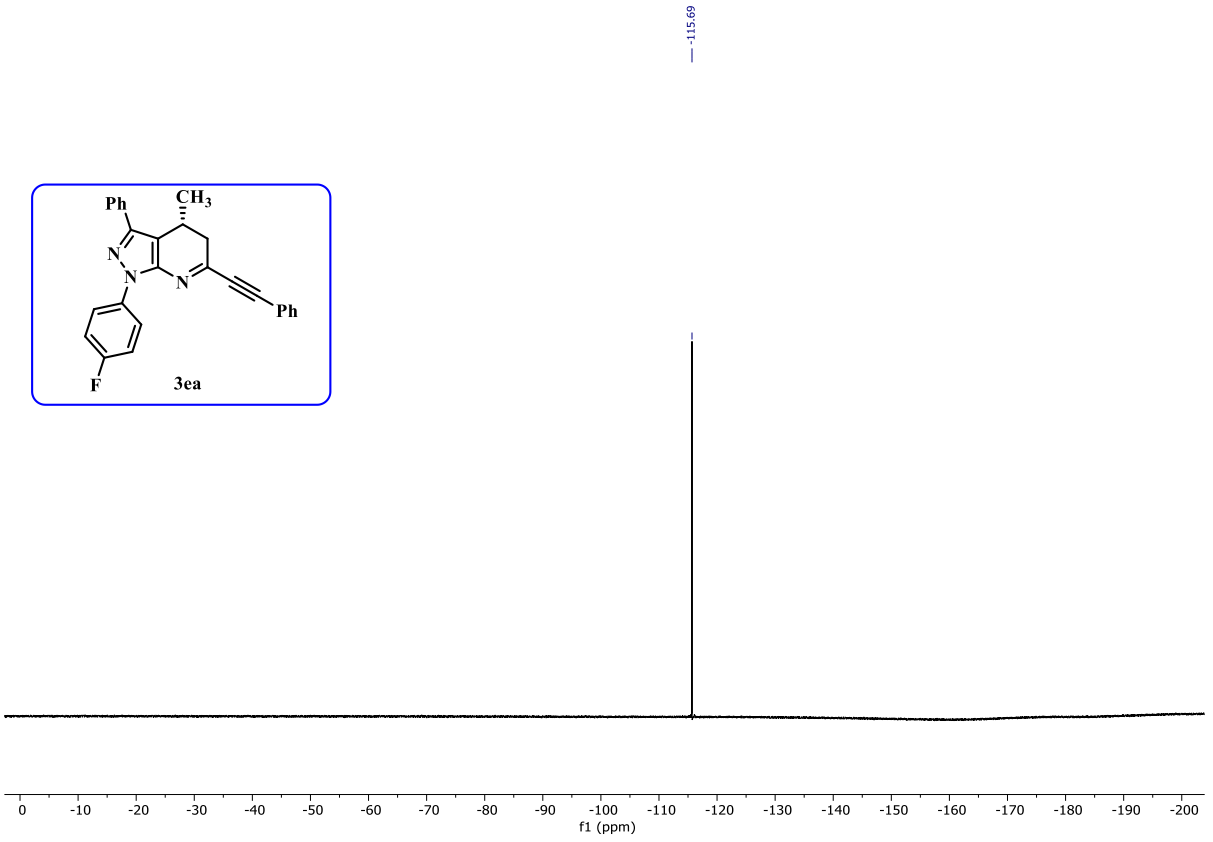
^{1}H NMR (400 MHz, $CDCl_3$)



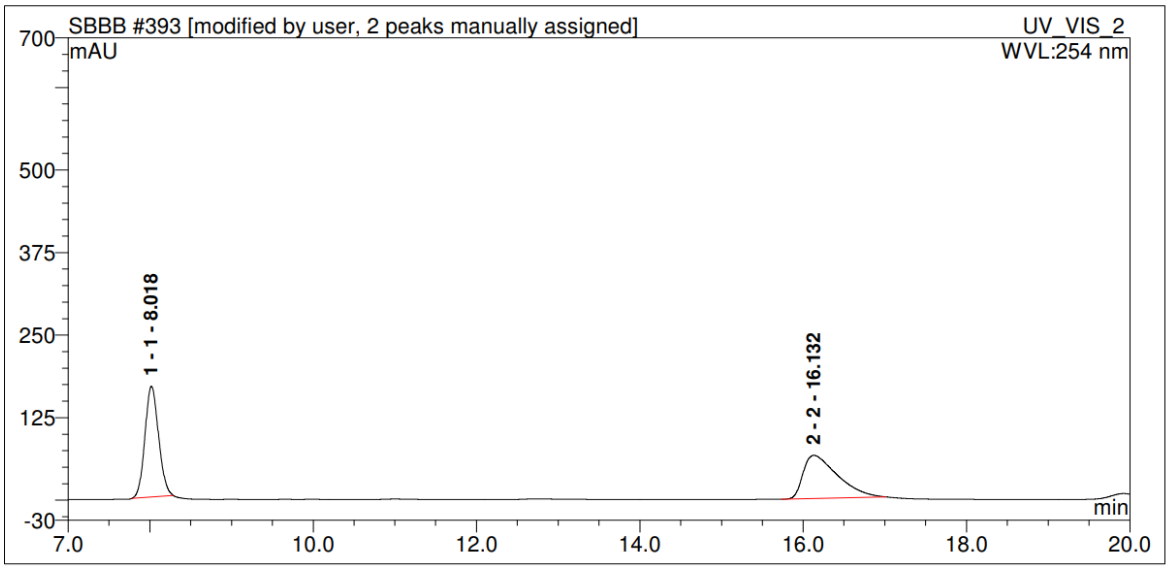
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

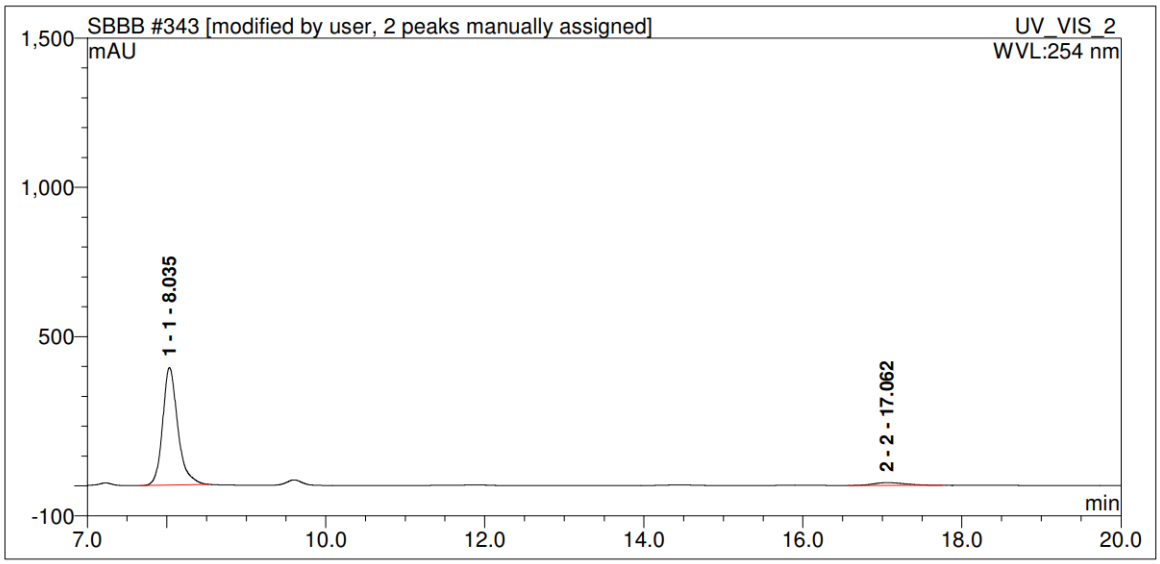


HPLC Spectra of *rac*-3ea



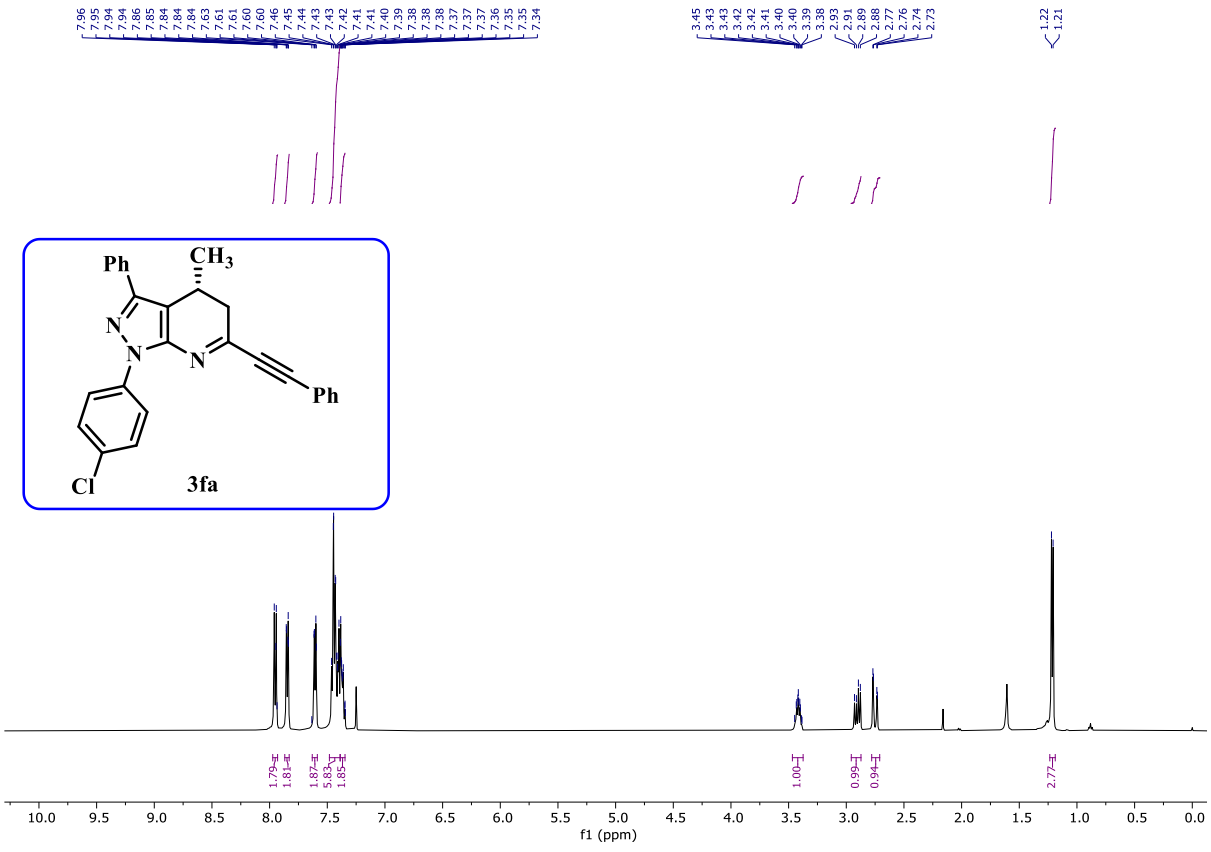
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.018333333	32.52465	50.59066482	167.5756	n.a.
2	2	16.13166667	31.76518	49.40933518	65.38138	n.a.

HPLC Spectra of *rac*-3ea

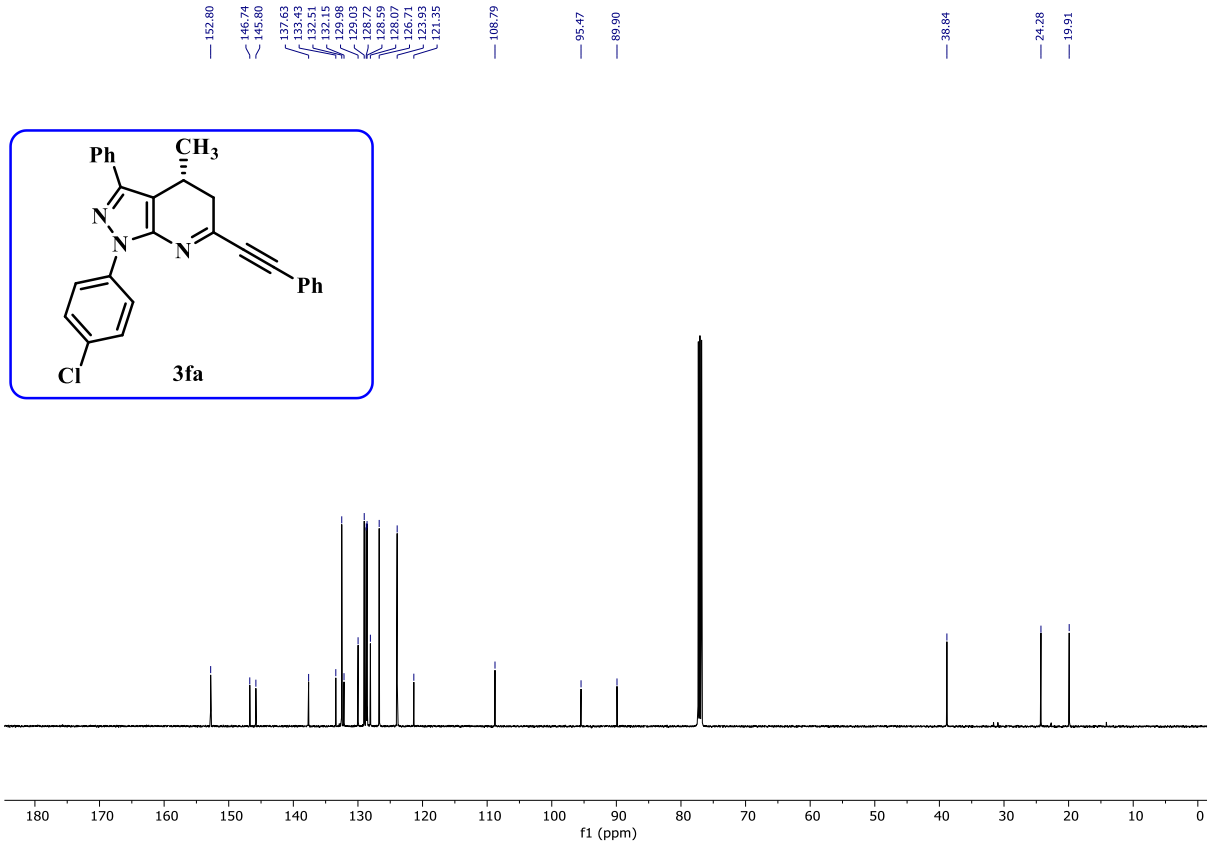


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.035	87.01328	95.16858393	393.2946	n.a.
2	2	17.06166667	4.417396	4.831416069	9.30754	n.a.

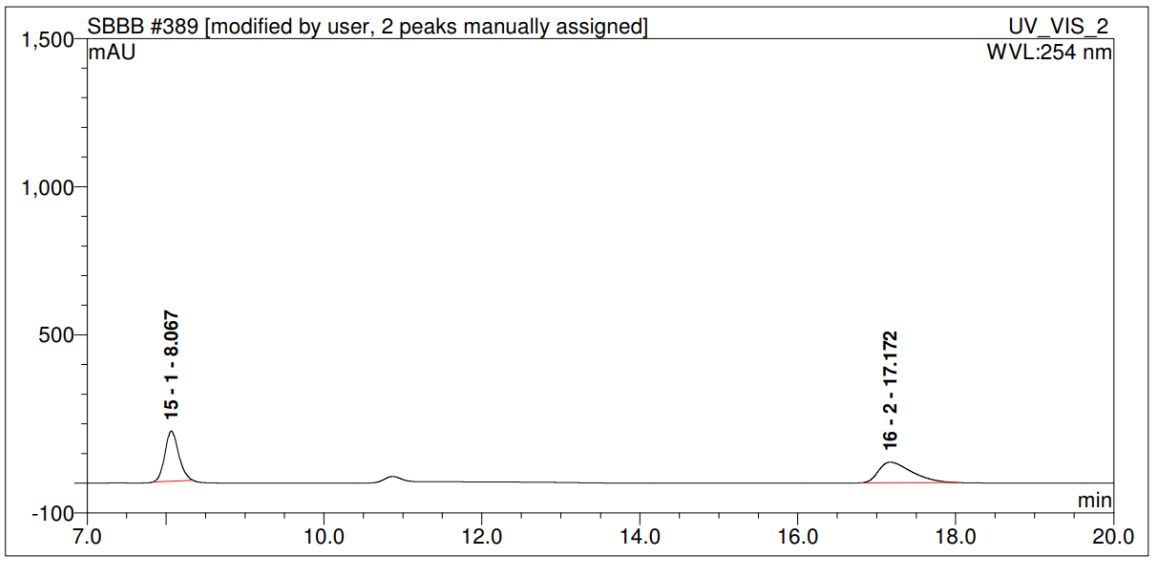
^{1}H NMR (500 MHz, $CDCl_3$)



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

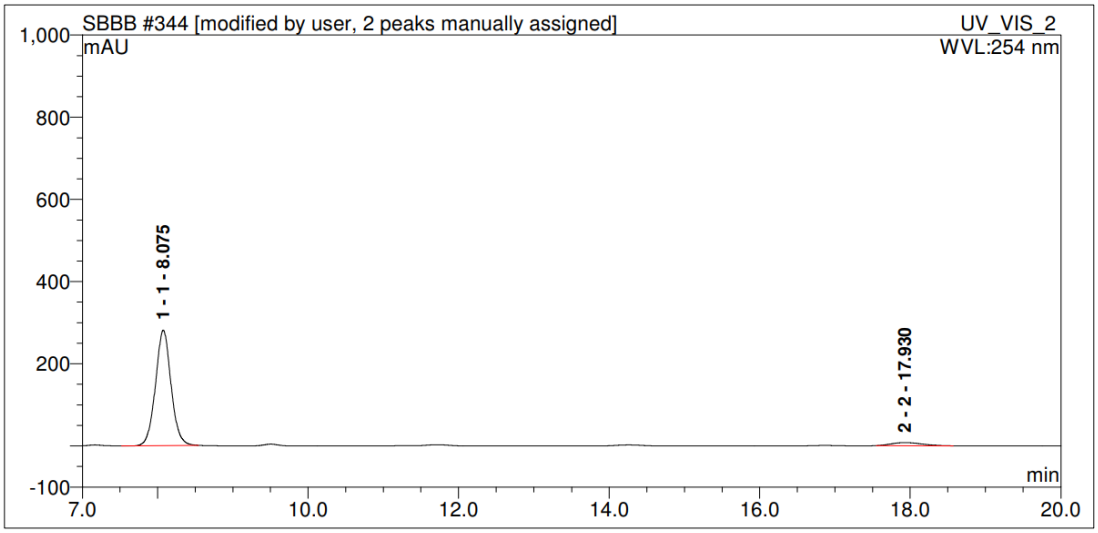


HPLC Spectra of *rac*-3fa



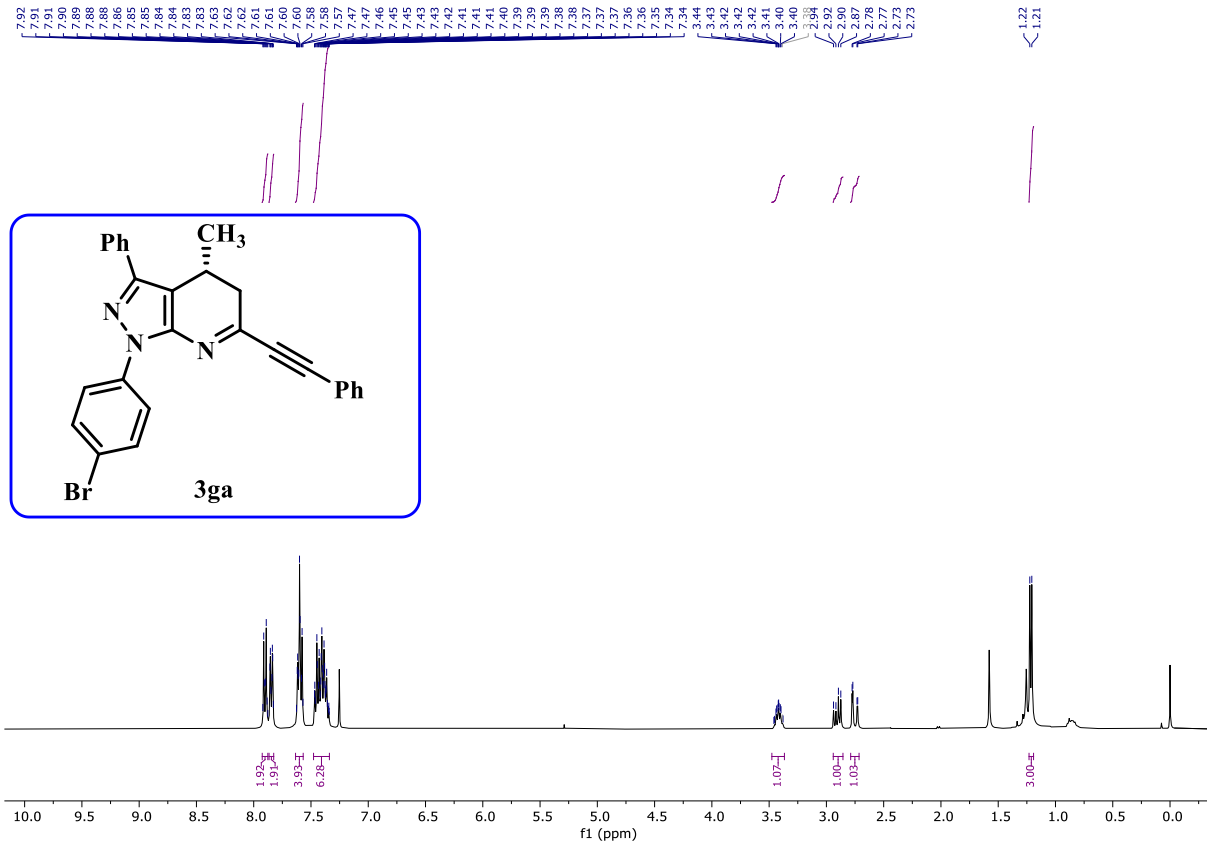
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
15	1	8.066666667	34.11701	50.17410781	168.8715	n.a.
16	2	17.17166667	33.88024	49.82589219	69.58131	n.a.

HPLC Spectra of *chi*-3fa

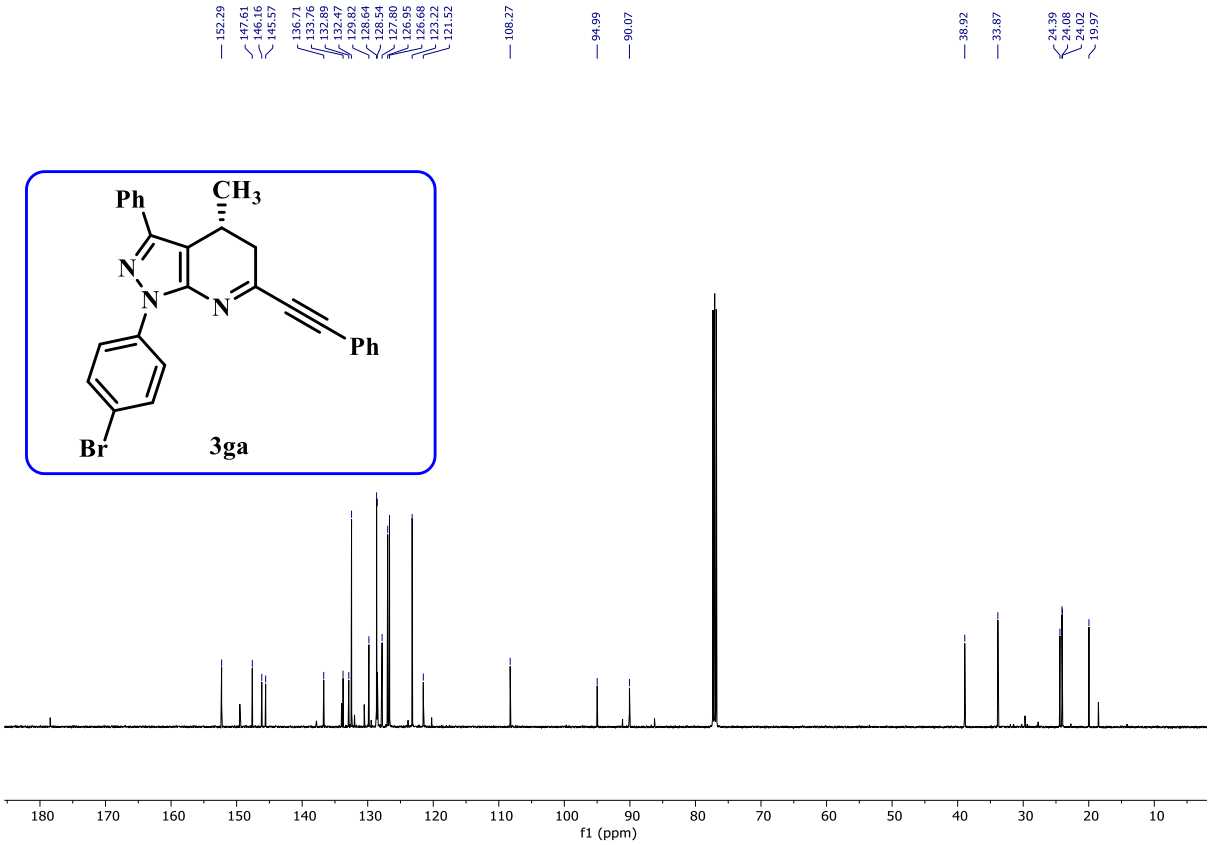


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.075	67.41895	95.01315406	281.3444	n.a.
2	2	17.93	3.538541	4.98684594	7.58936	n.a.

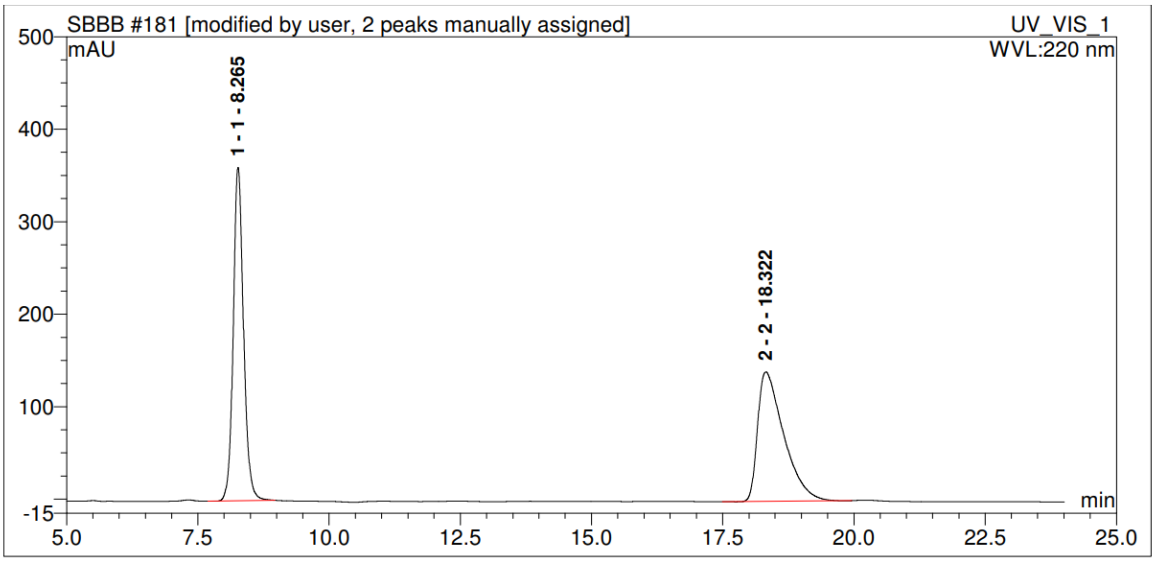
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (151 MHz, $CDCl_3$)

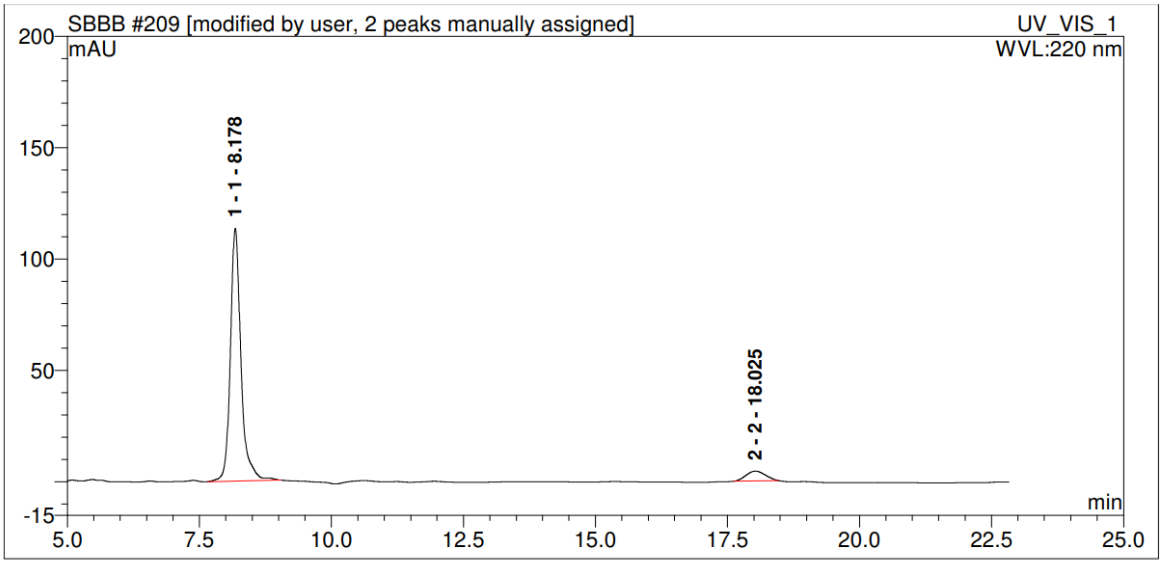


HPLC Spectra of *rac*-3ga



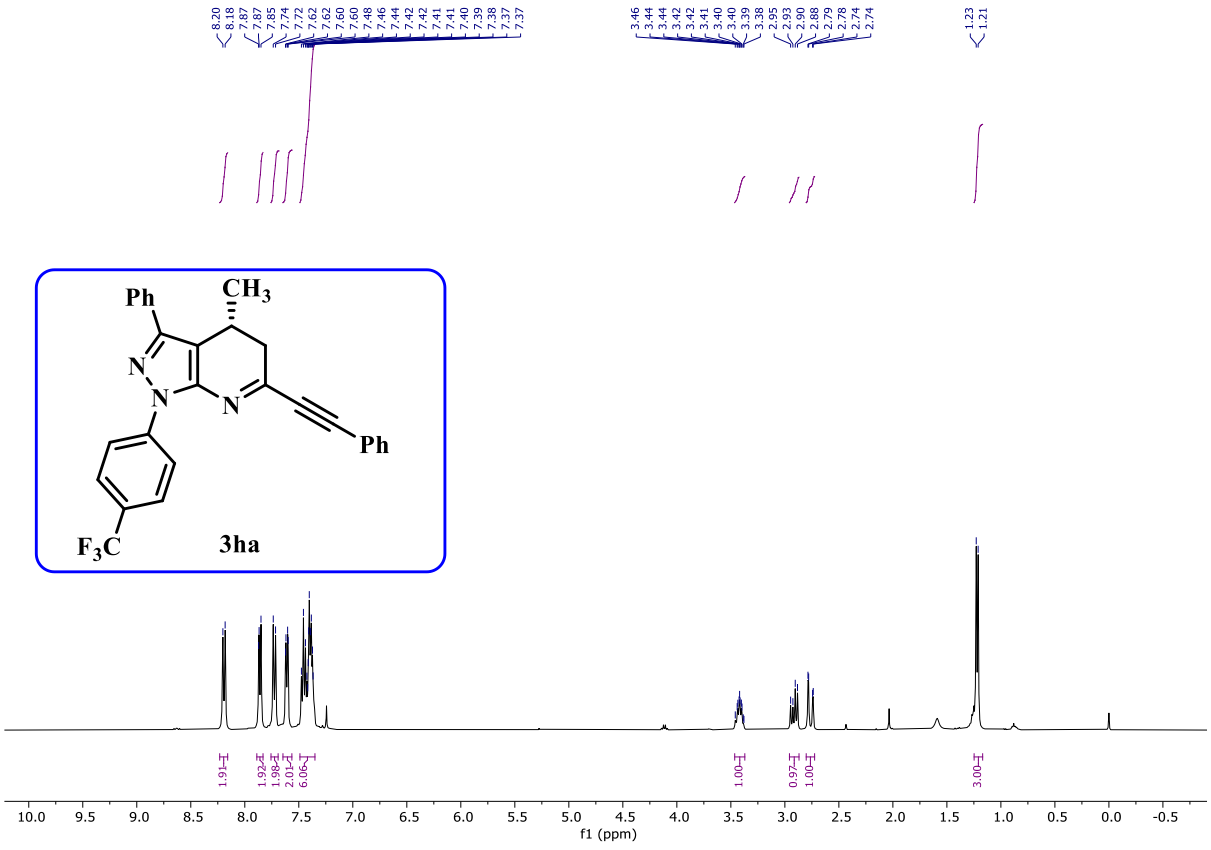
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.265	81.96833	50.38539014	360.3995	n.a.
2	2	18.32166667	80.71441	49.61460986	140.0702	n.a.

HPLC Spectra of *chi*-3ga

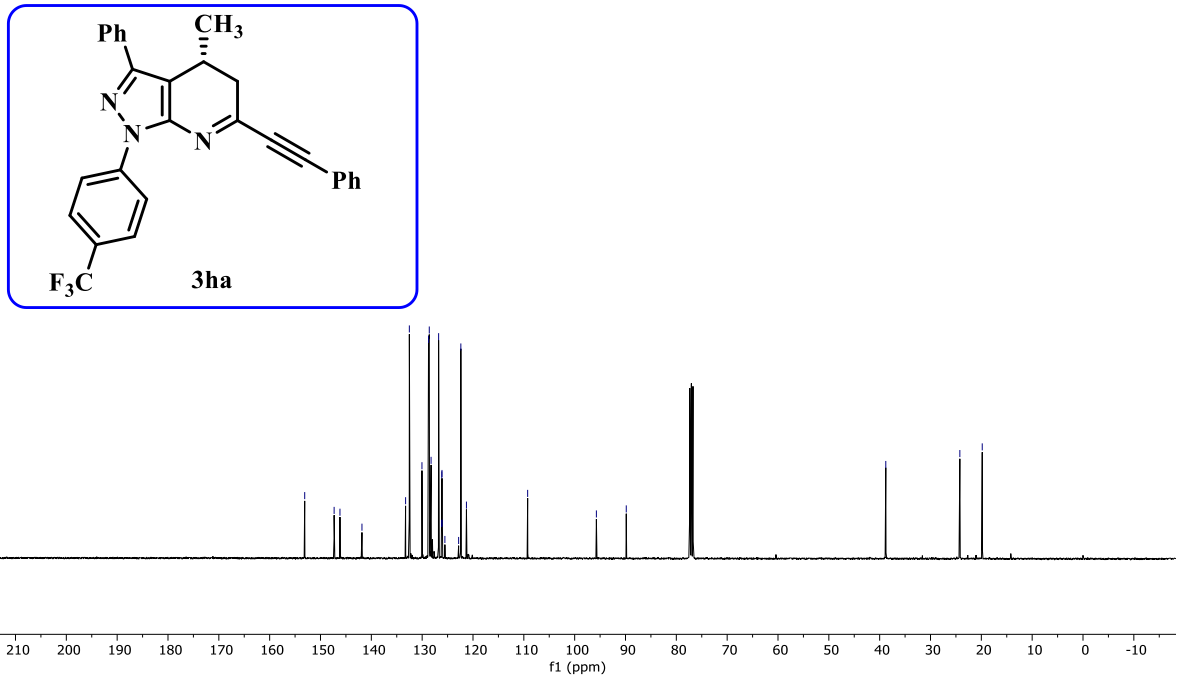


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.178333333	26.48595	93.41170626	113.3929	n.a.
2	2	18.025	1.868045	6.58829374	4.39991	n.a.

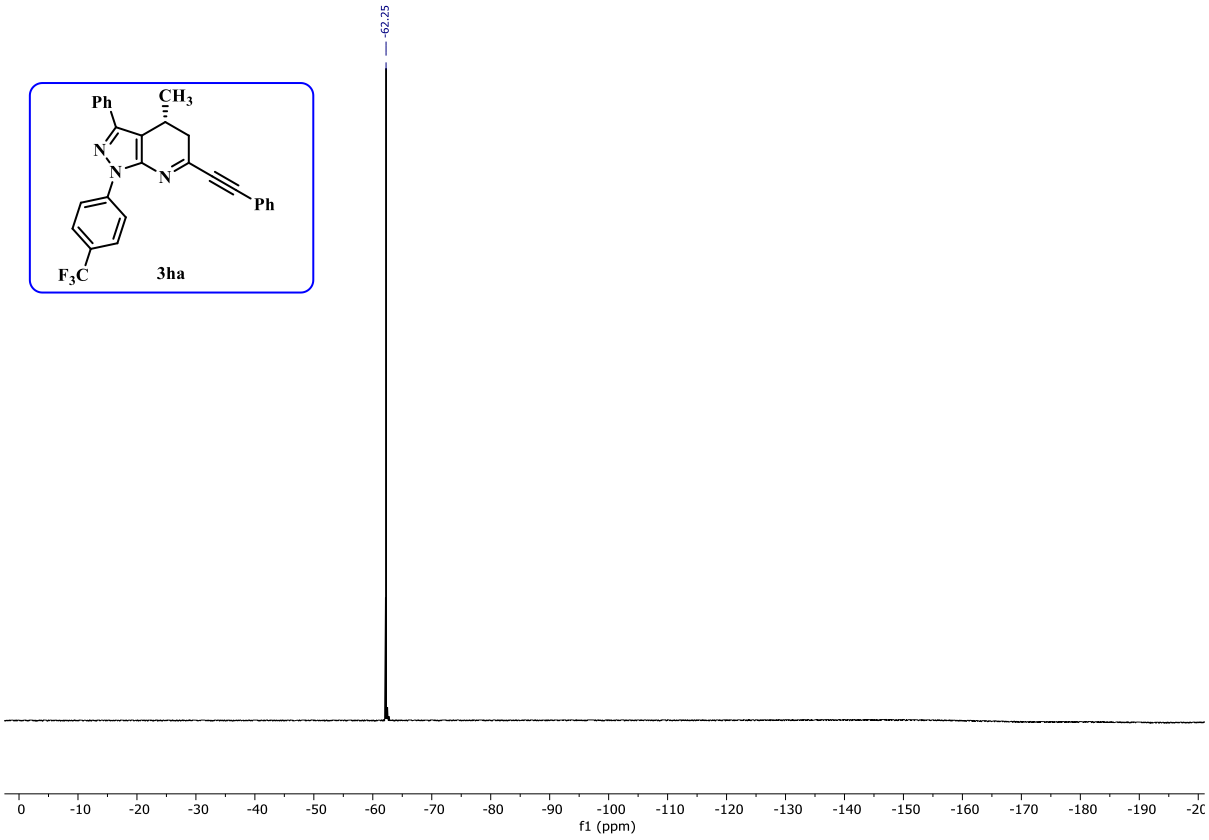
^{1}H NMR (400 MHz, $CDCl_3$)



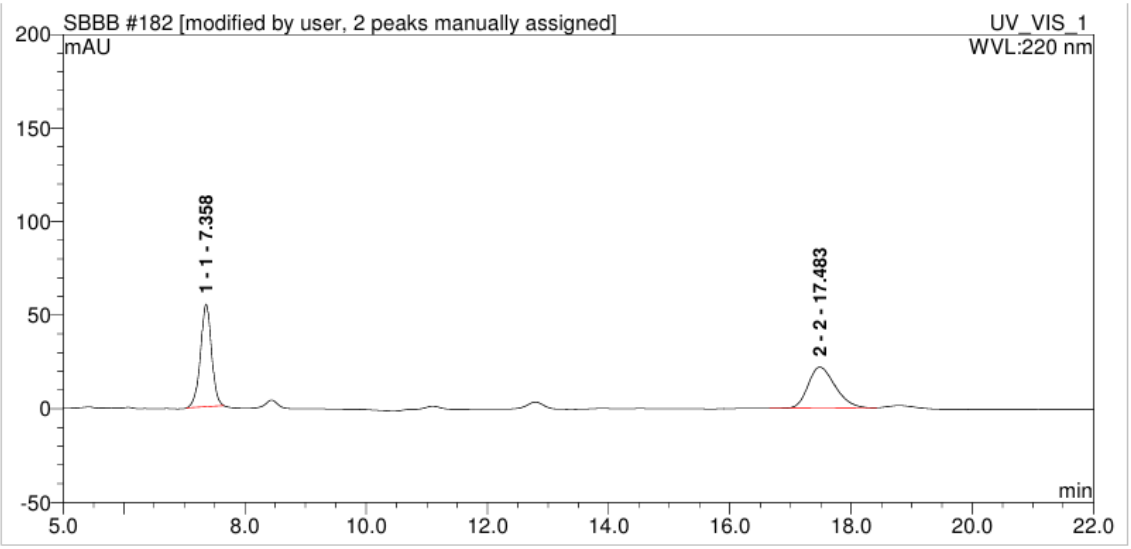
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

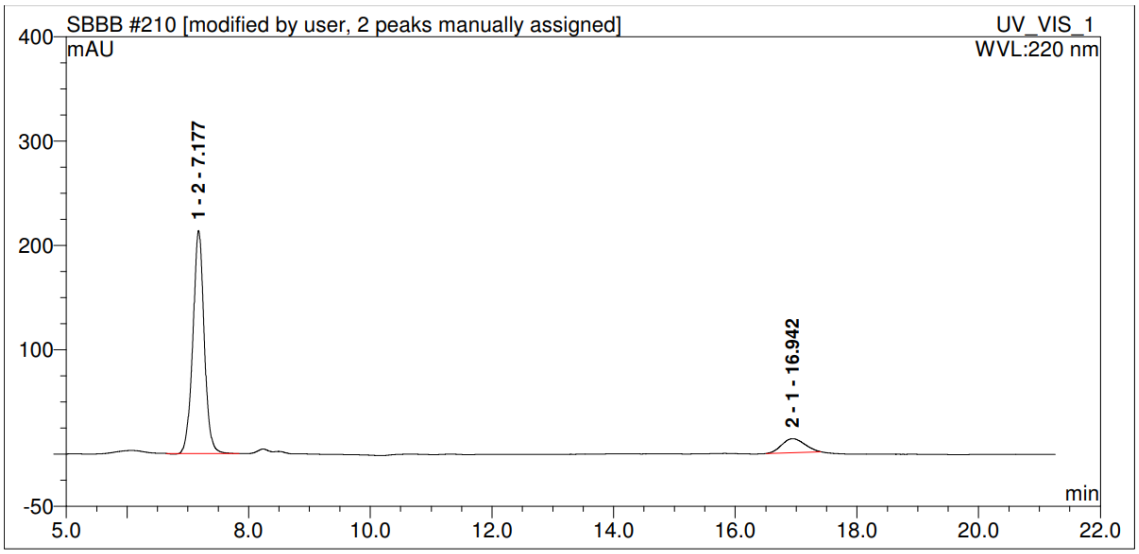


HPLC Spectra of *rac*-3ha



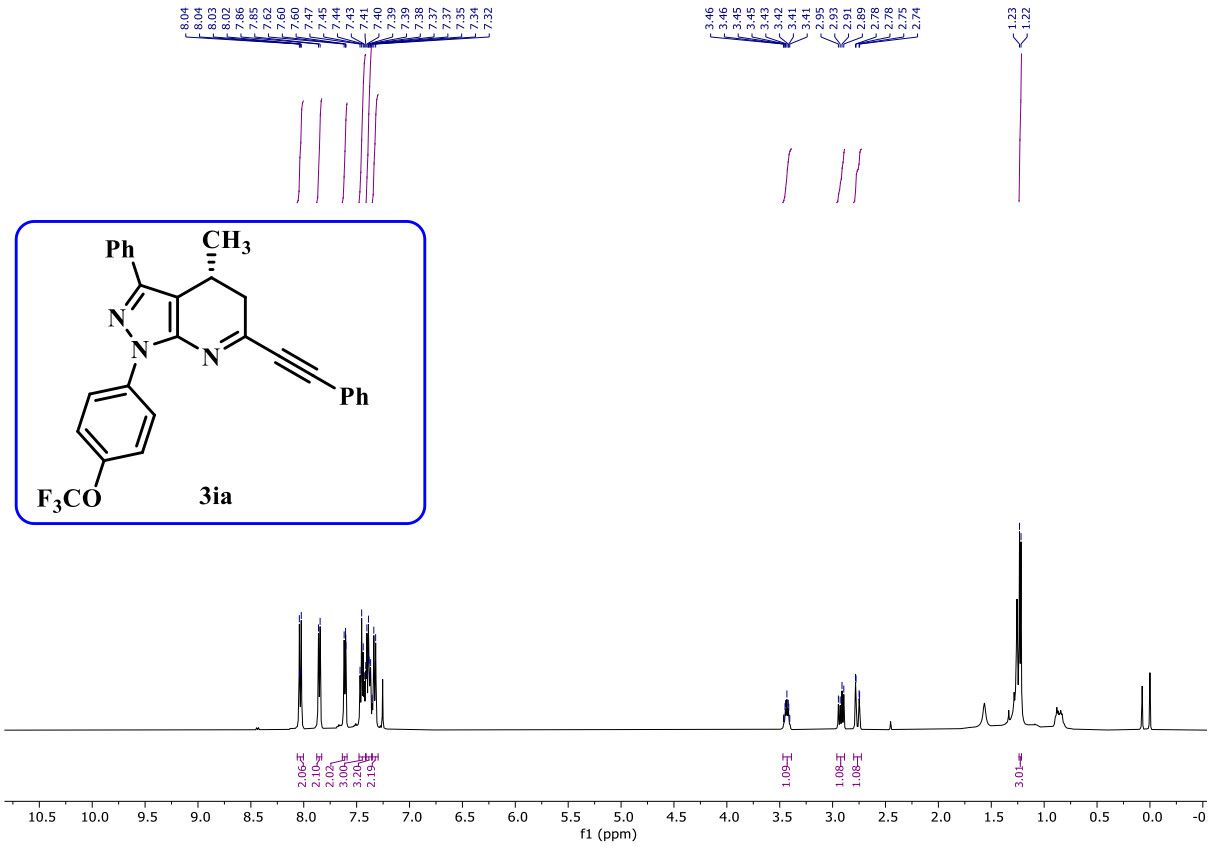
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.358333333	11.60523	50.64971911	54.72833	n.a.
2	2	17.48333333	11.30749	49.35028089	21.87914	n.a.

HPLC Spectra of *chi*-3ha

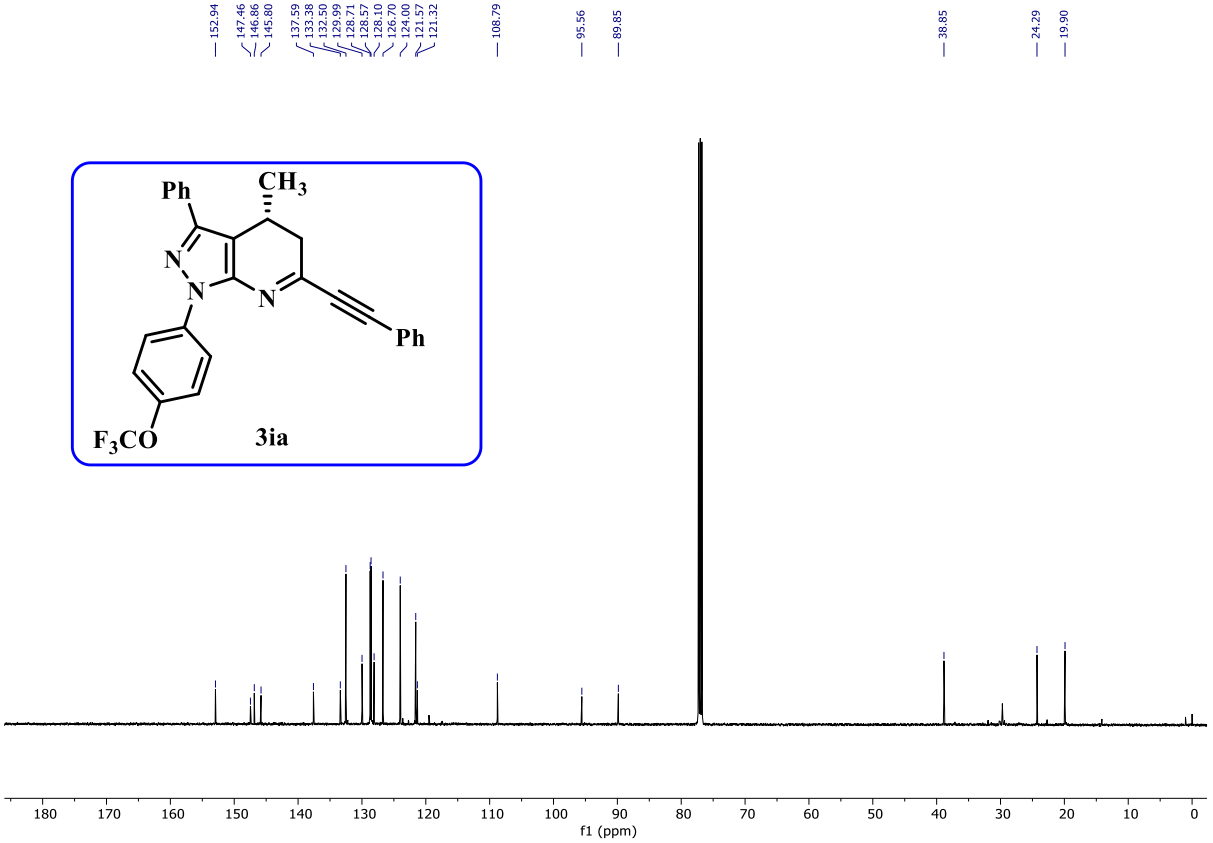


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	2	7.176666667	46.16238	88.81535488	213.7131	n.a.
2	1	16.94166667	5.813295	11.18464512	13.37947	n.a.

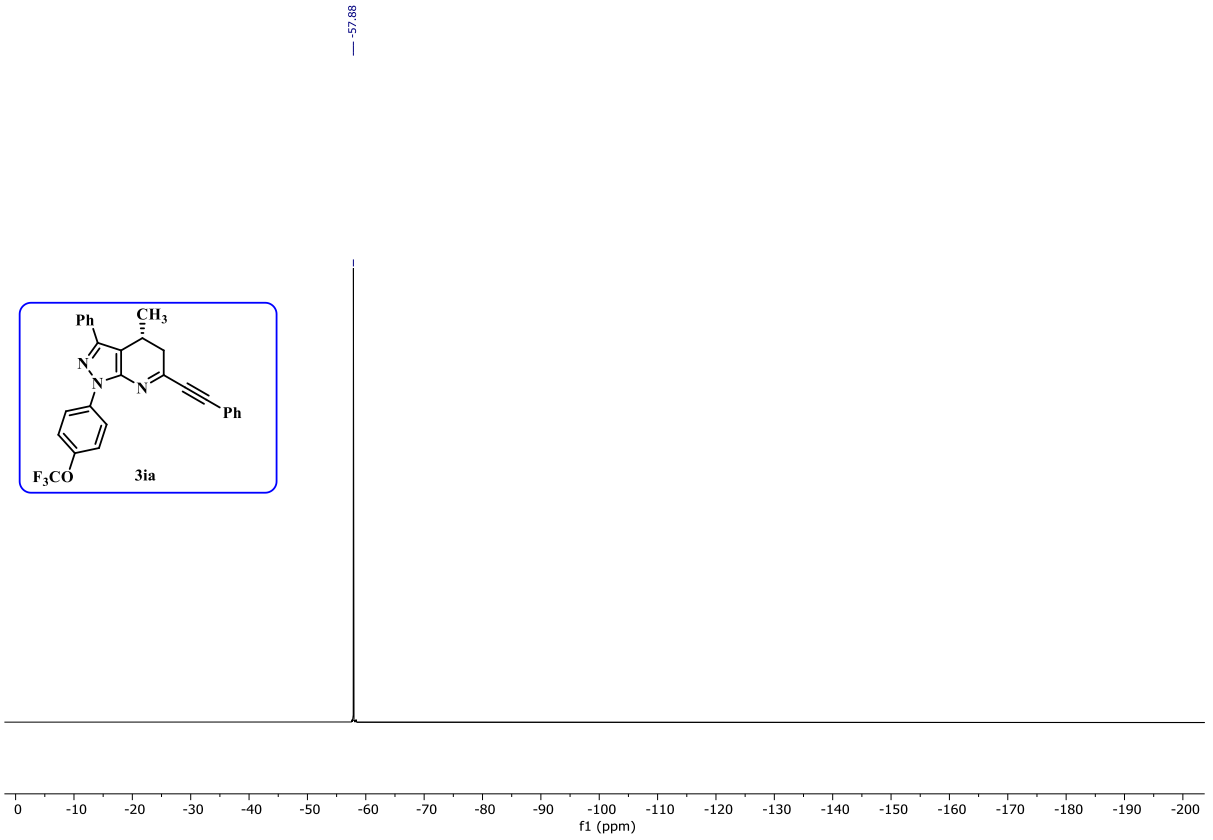
^{1}H NMR (500 MHz, $CDCl_3$)



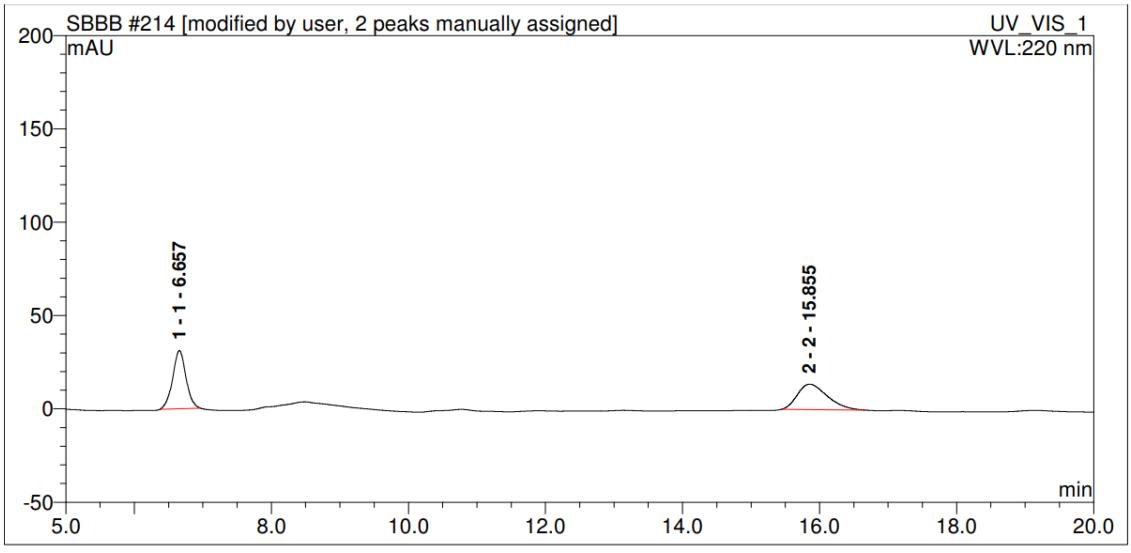
^{13}C NMR (126 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

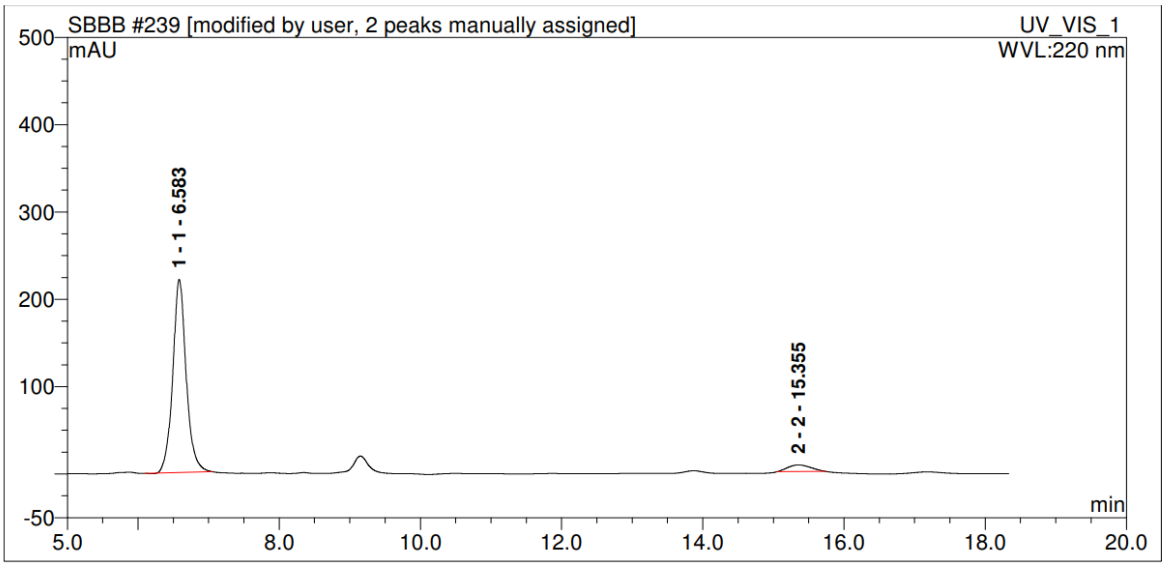


HPLC Spectra of *rac*-3ia



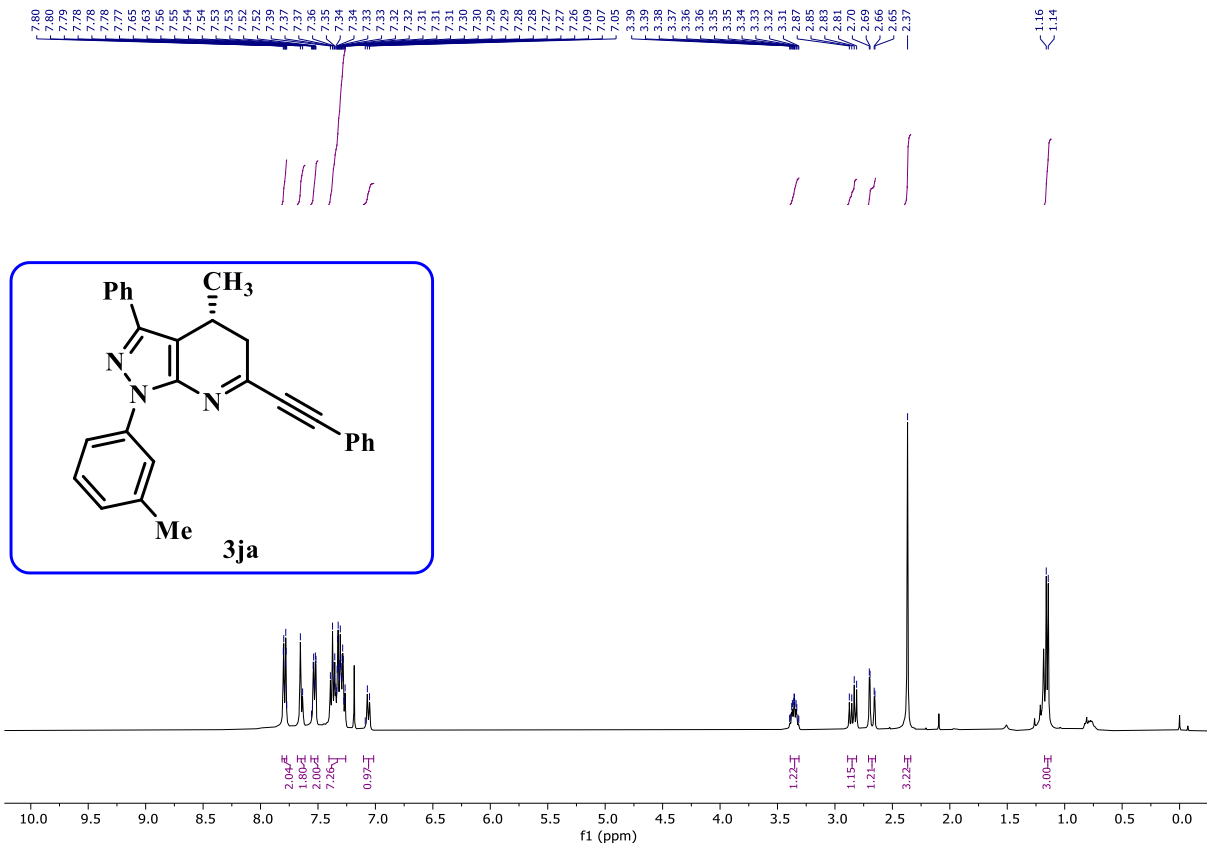
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.656666667	7.068418	50.36697728	31.31264	n.a.
2	2	15.855	6.965416	49.63302272	13.67386	n.a.

HPLC Spectra of *chi*-3ia

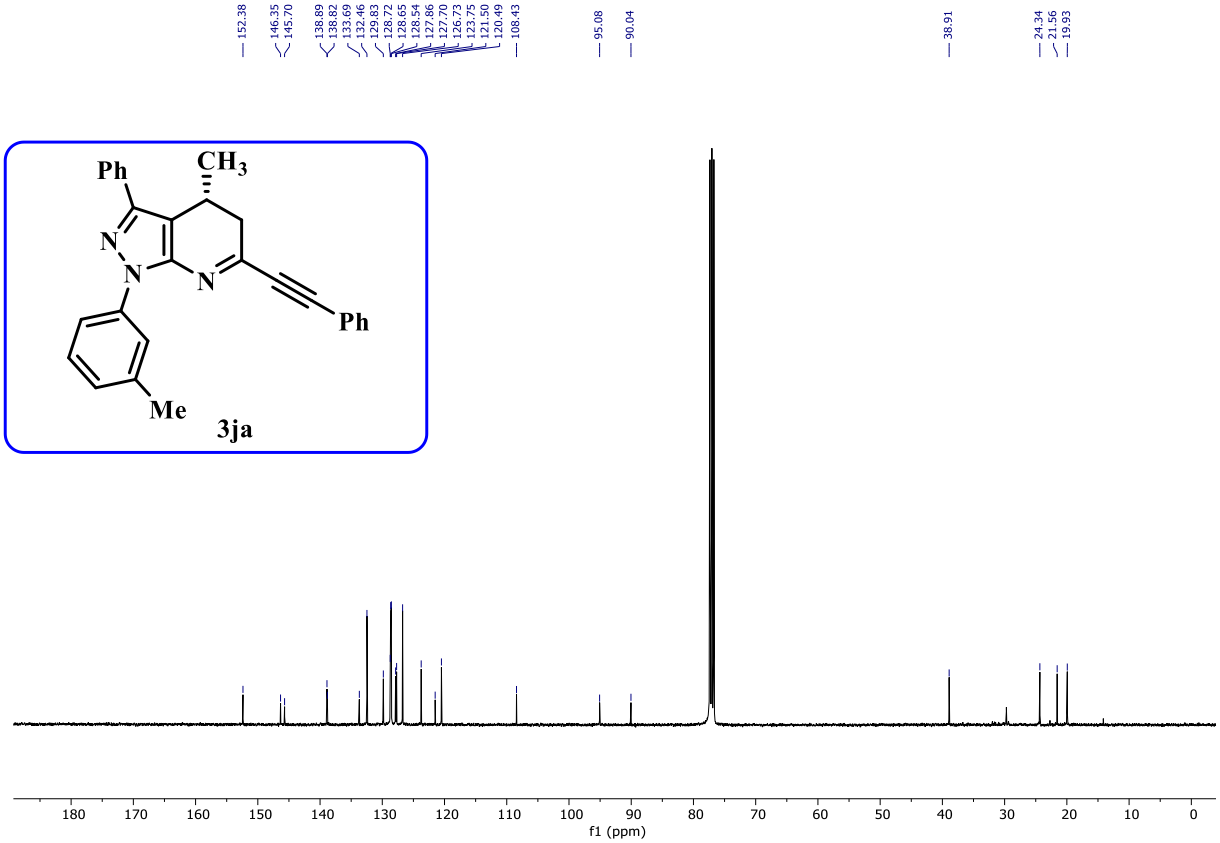


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.583333333	48.81916	94.42429231	221.2538	n.a.
2	2	15.355	2.882747	5.575707694	7.60216	n.a.

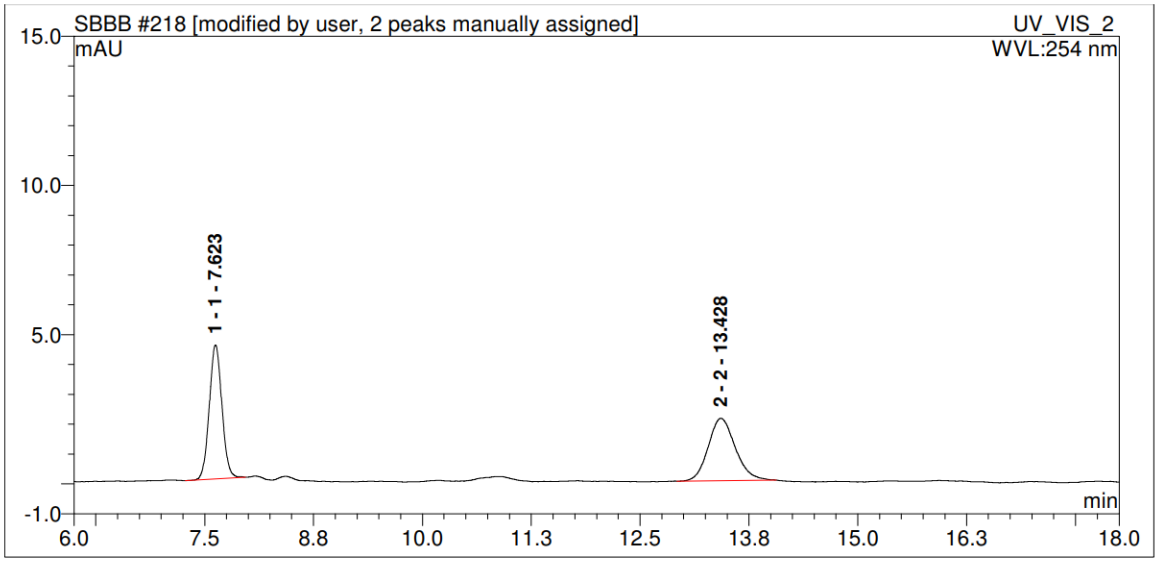
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

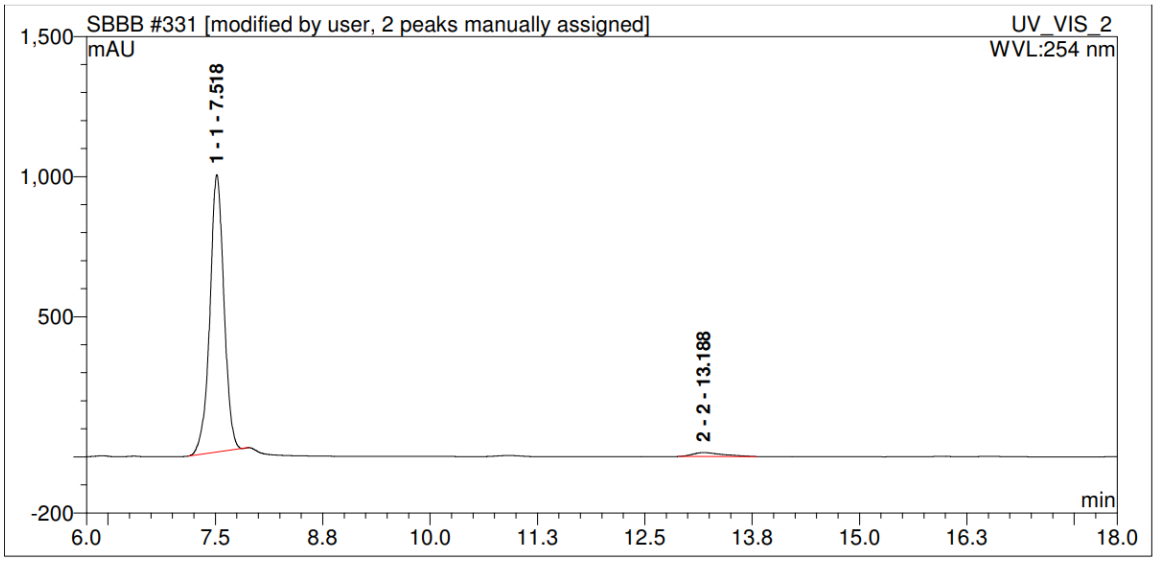


HPLC Spectra of *rac*-3ja



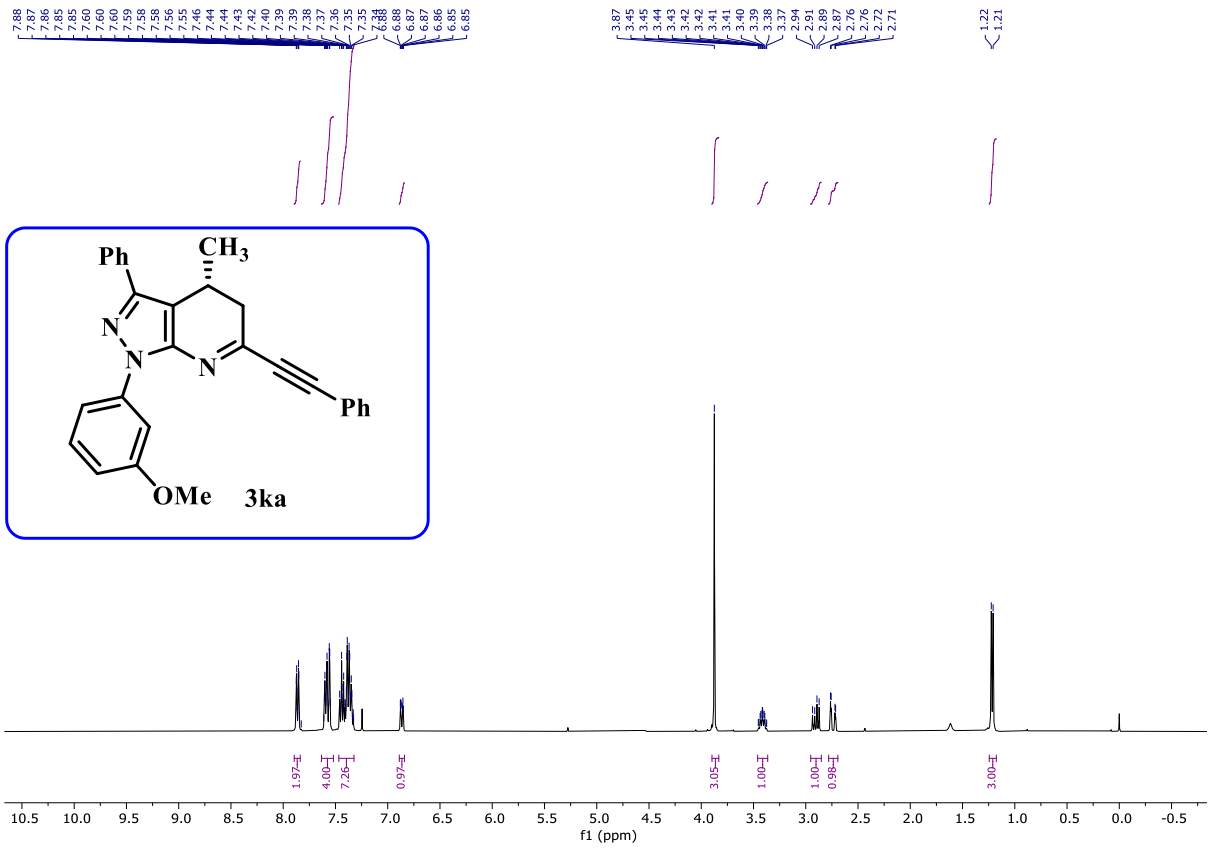
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.623333333	0.755363	50.01148111	4.48158	n.a.
2	2	13.42833333	0.755016	49.98851889	2.09297	n.a.

HPLC Spectra of *chi*-3ja

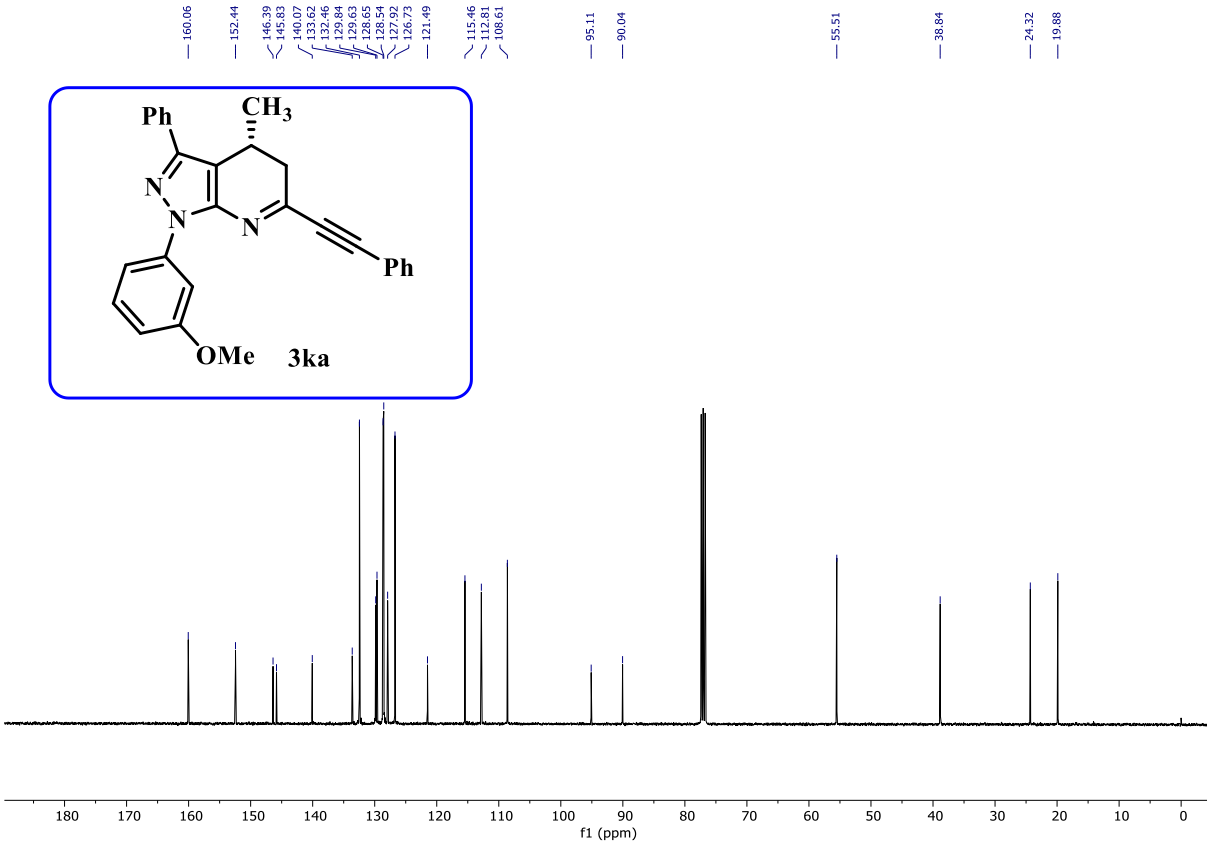


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.518333333	188.7809	97.08886731	990.0971	n.a.
2	2	13.18833333	5.660447	2.911132693	13.87066	n.a.

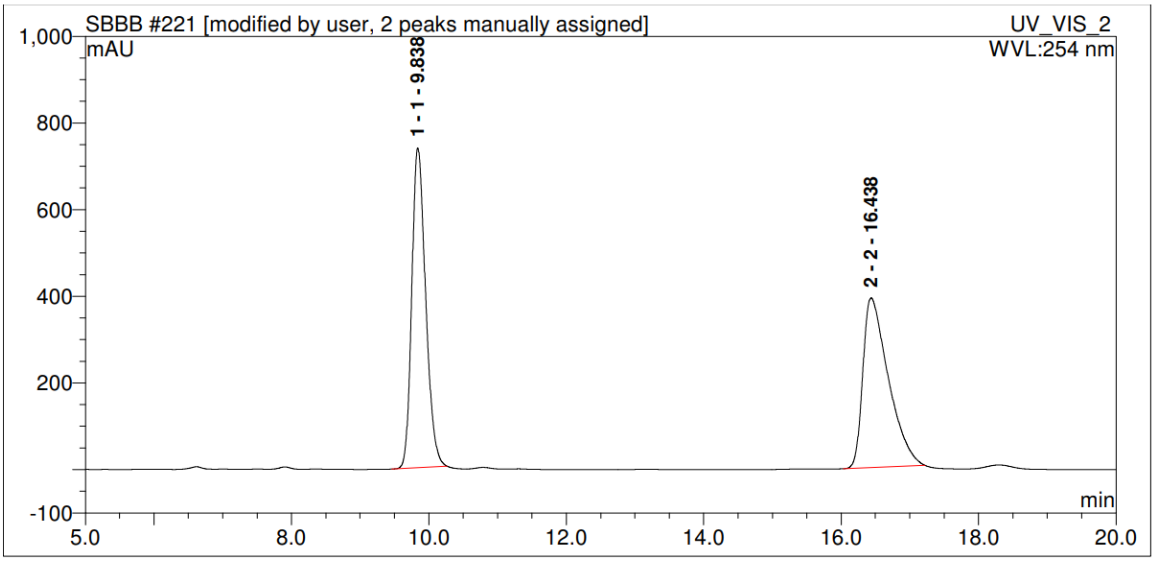
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

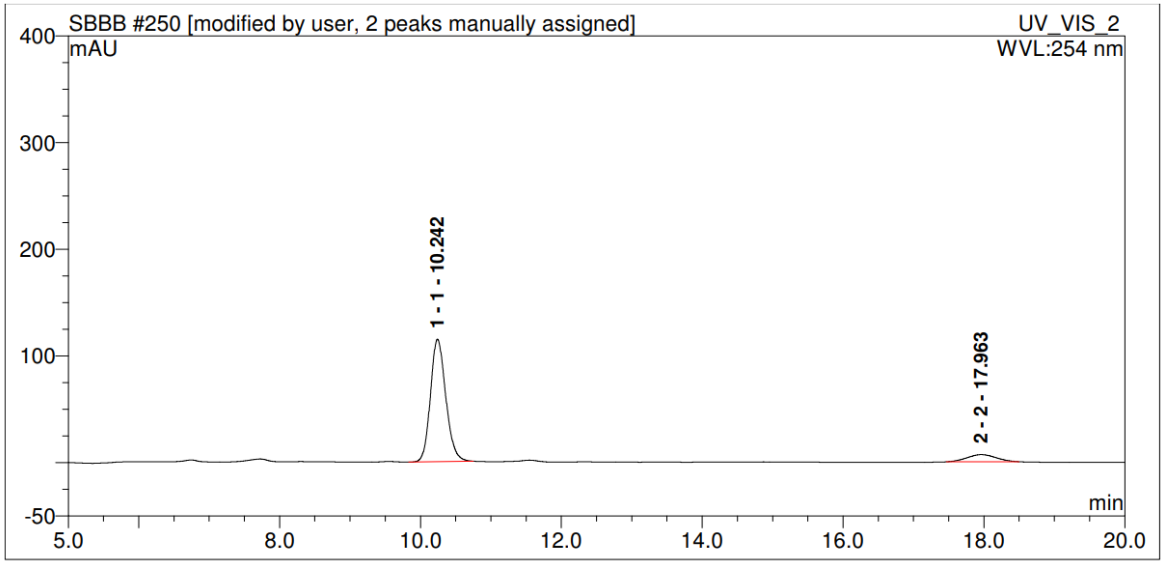


HPLC Spectra of *rac*-3ka



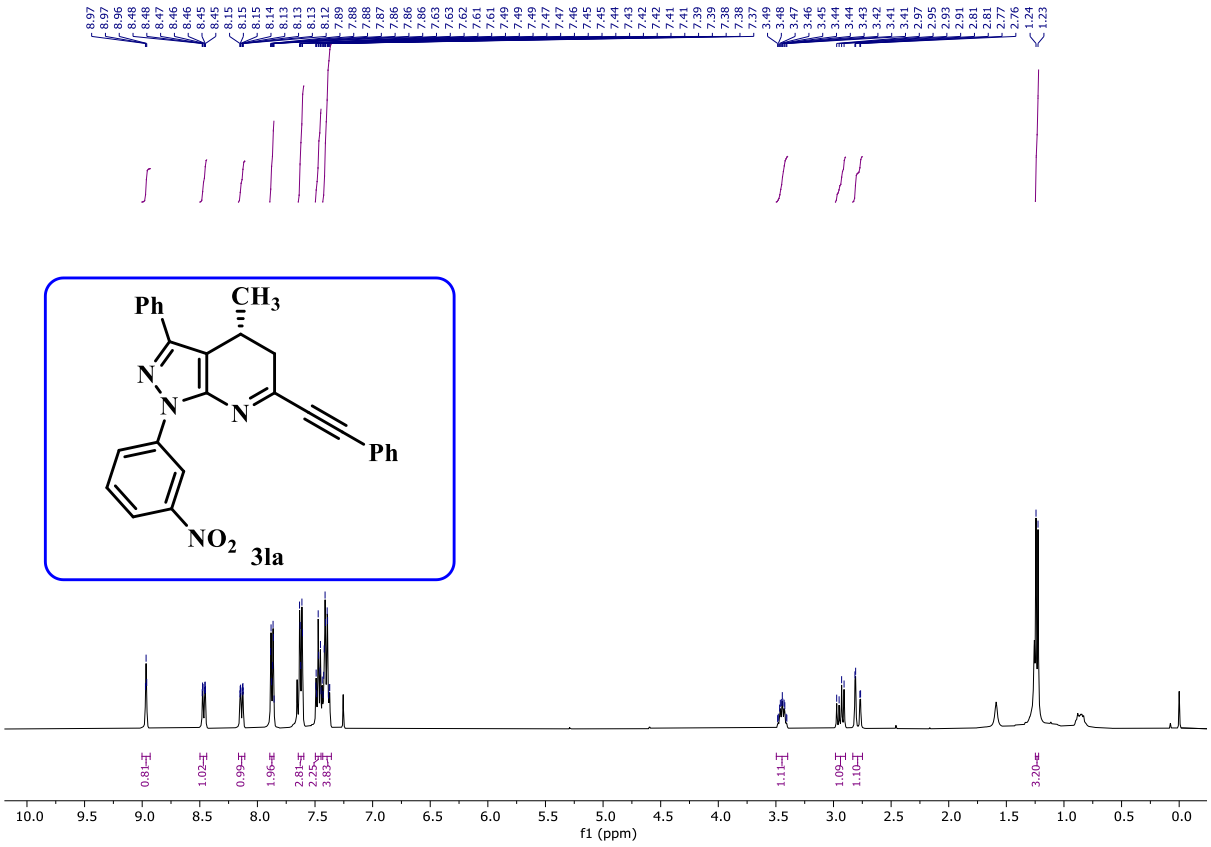
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	9.838333333	172.6159	50.6671476	738.1081	n.a.
2	2	16.43833333	168.0702	49.3328524	391.6546	n.a.

HPLC Spectra of *chi*-3ka

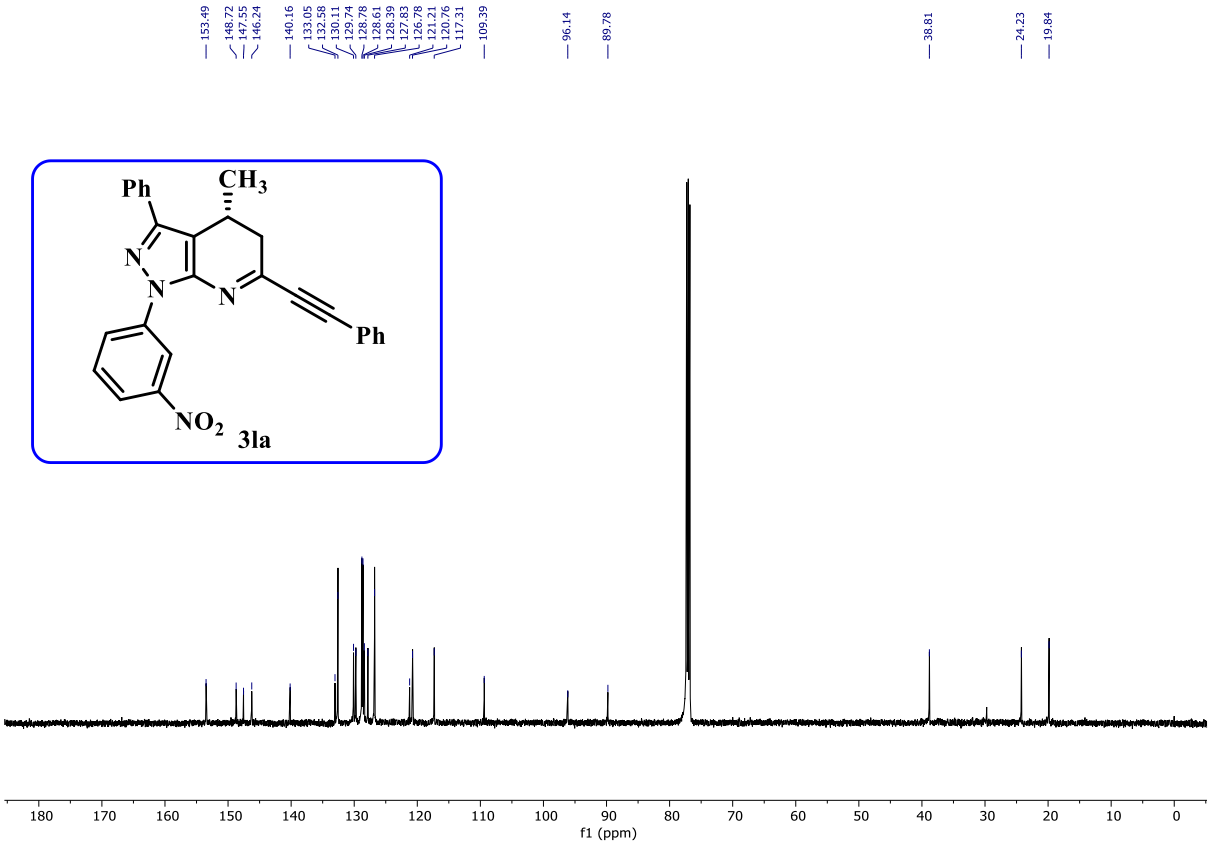


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	10.24166667	29.0041	90.09977097	114.8781	n.a.
2	2	17.96333333	3.186992	9.900229026	6.69269	n.a.

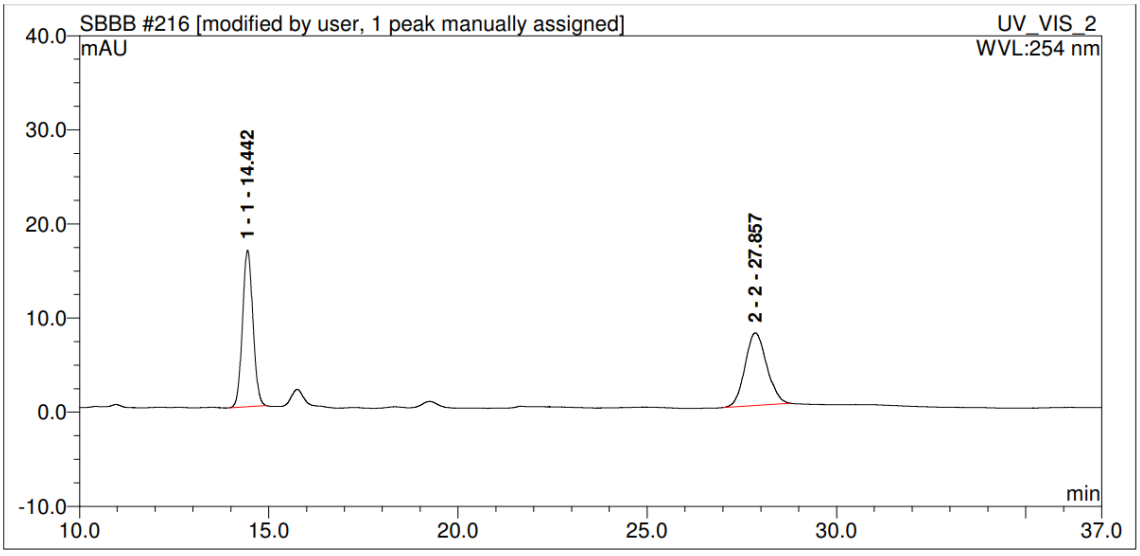
^{1}H NMR (400 MHz, $CDCl_3$)



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

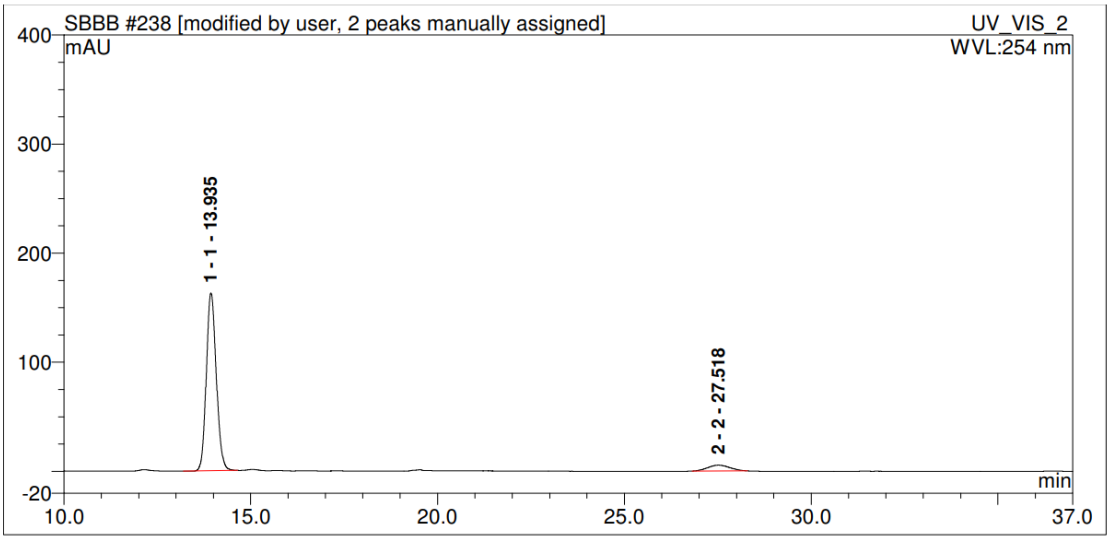


HPLC Spectra of *rac*-3la



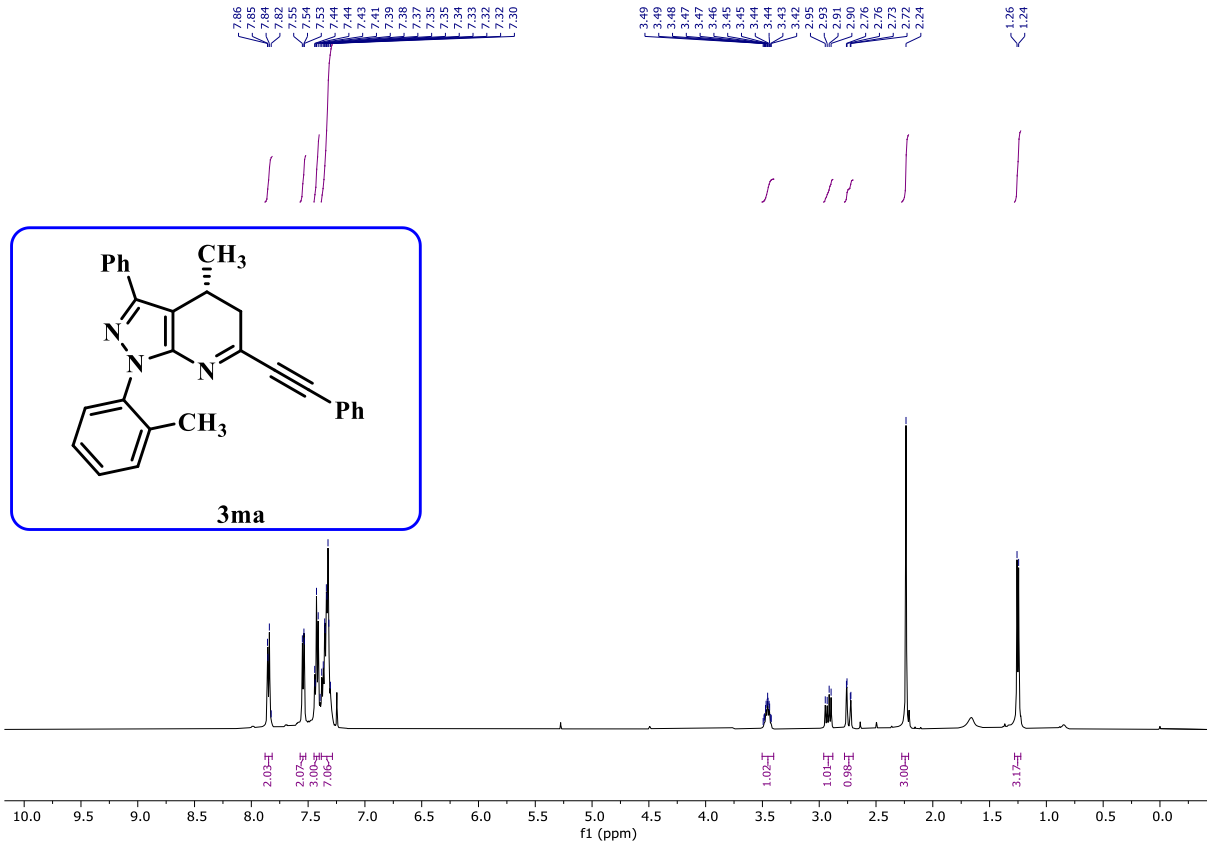
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	14.44166667	5.326216	50.96887529	16.62751	n.a.
2	2	27.85666667	5.123723	49.03112471	7.71619	n.a.

HPLC Spectra of *chi*-3la

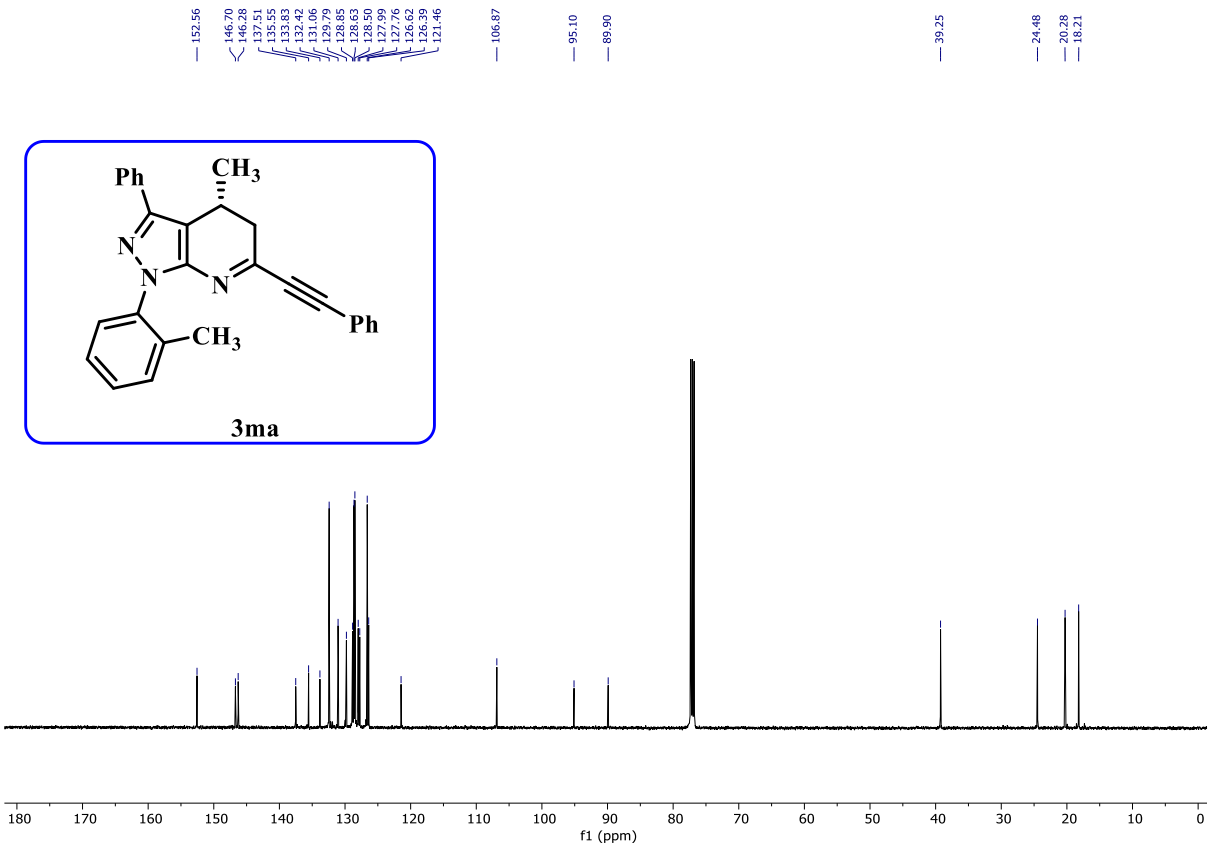


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	13.935	50.30634	93.1978818	162.8618	n.a.
2	2	27.51833333	3.671647	6.802118203	5.34572	n.a.

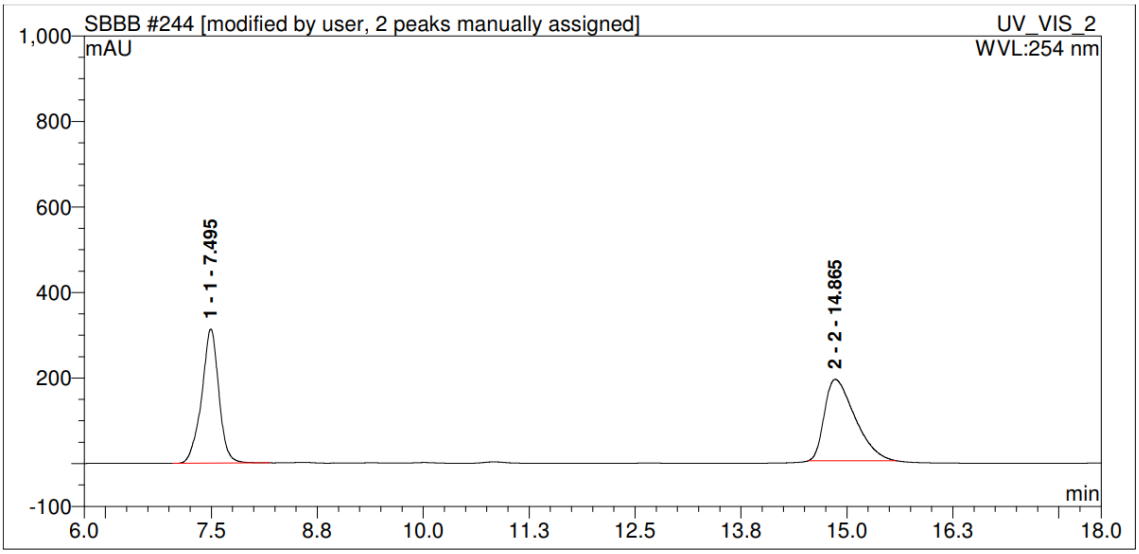
^{1}H NMR (500 MHz, $CDCl_3$)



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

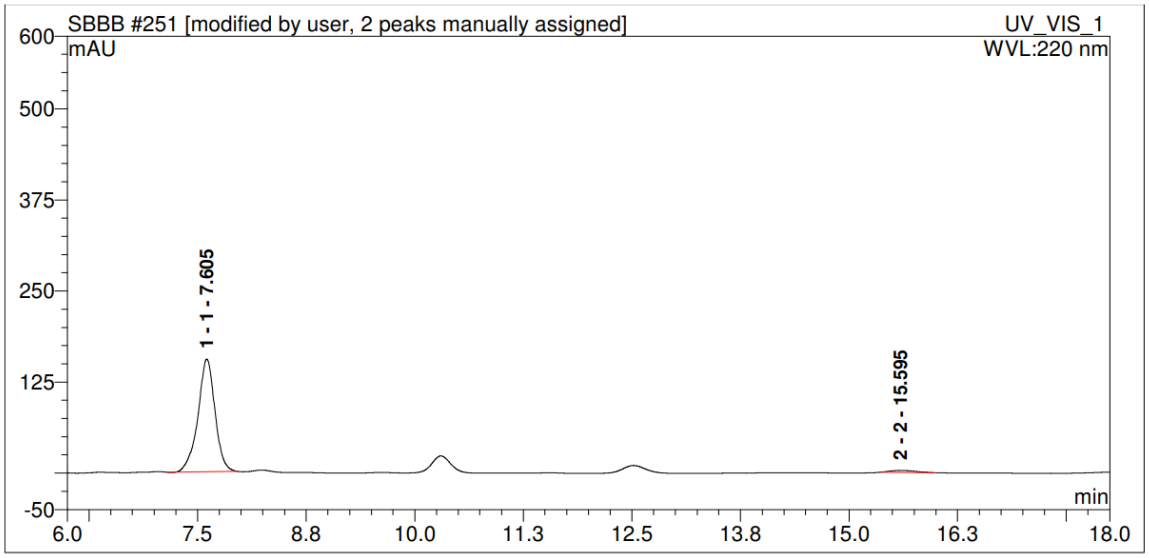


HPLC Spectra of *rac*-3ma



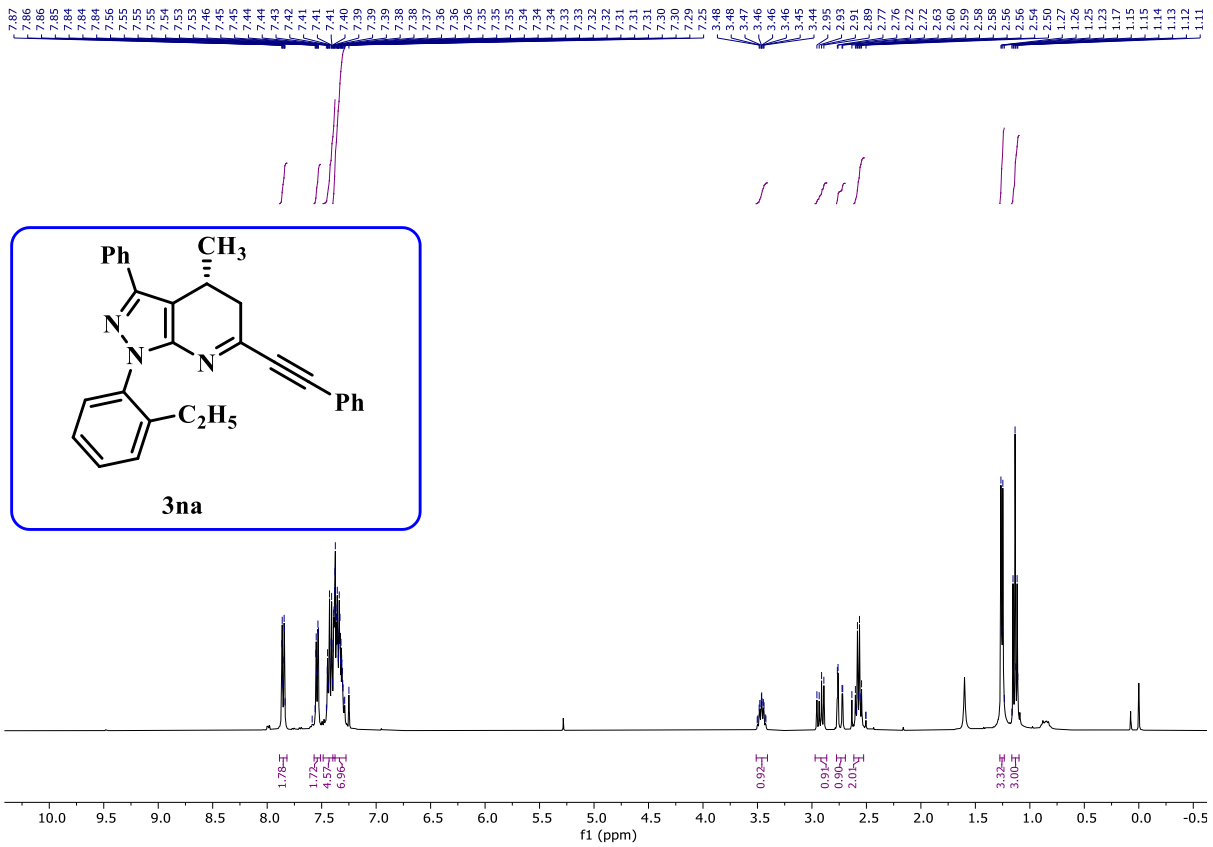
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.495	73.79999	48.14742368	313.4215	n.a.
2	2	14.865	79.47922	51.85257632	190.36	n.a.

HPLC Spectra of *chi*-3ma

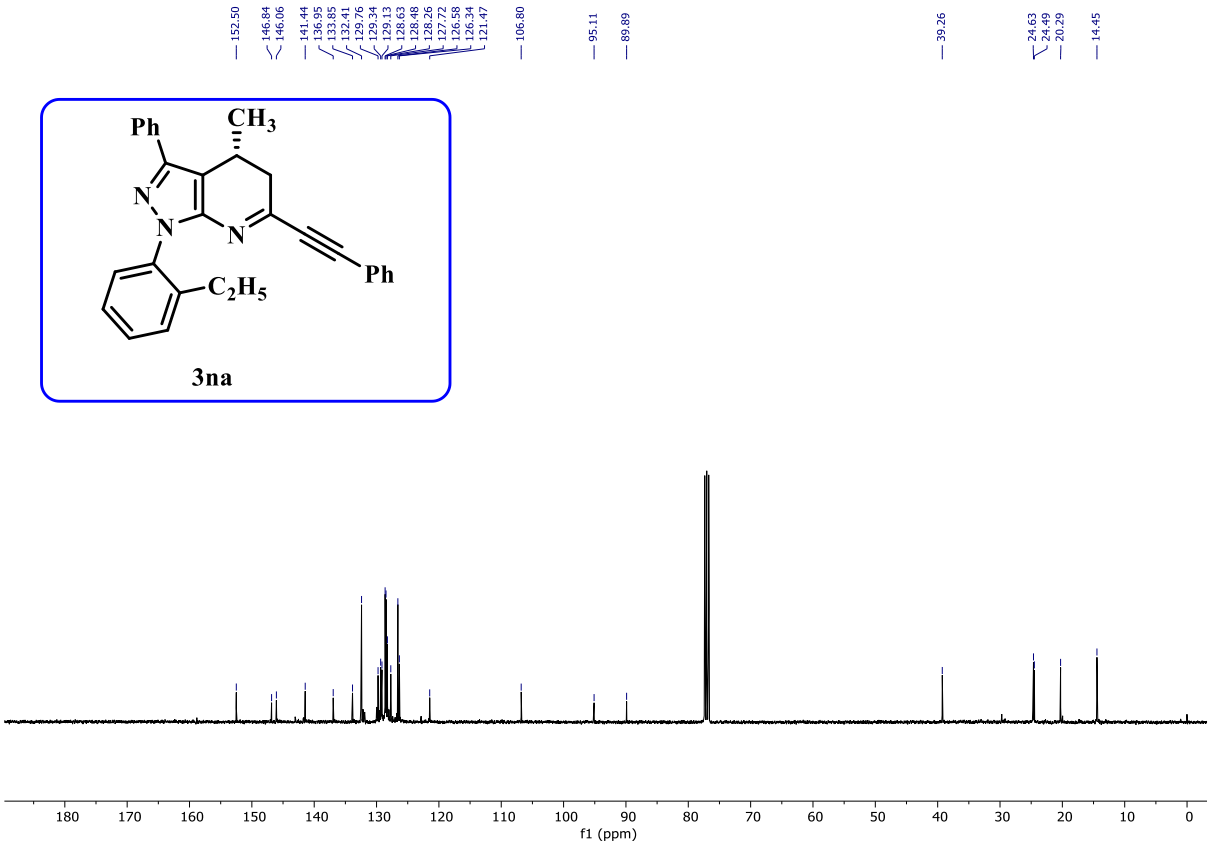


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.605	35.23898	97.49626802	154.6847	n.a.
2	2	15.595	0.904947	2.503731983	2.7207	n.a.

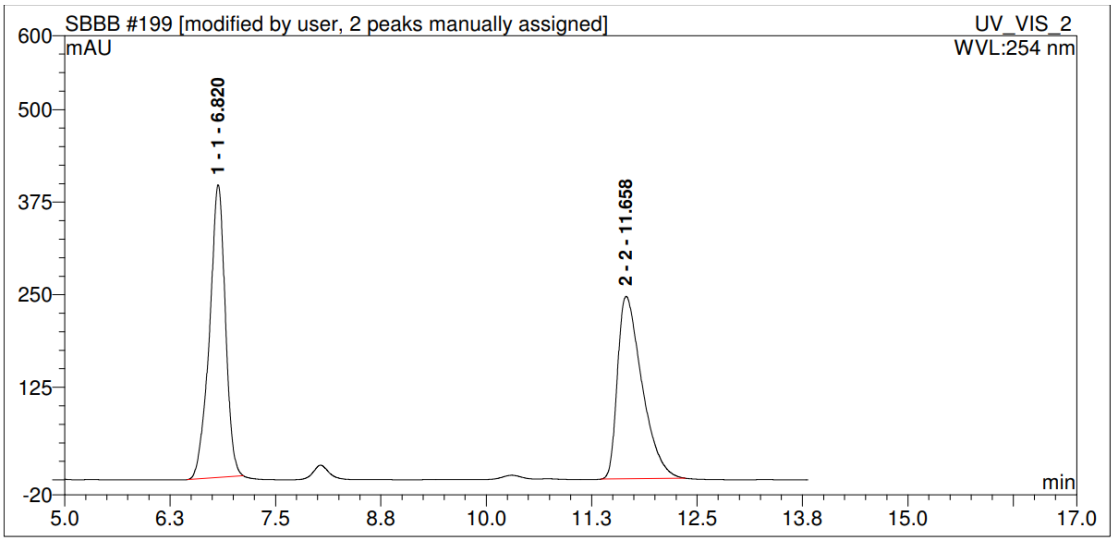
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

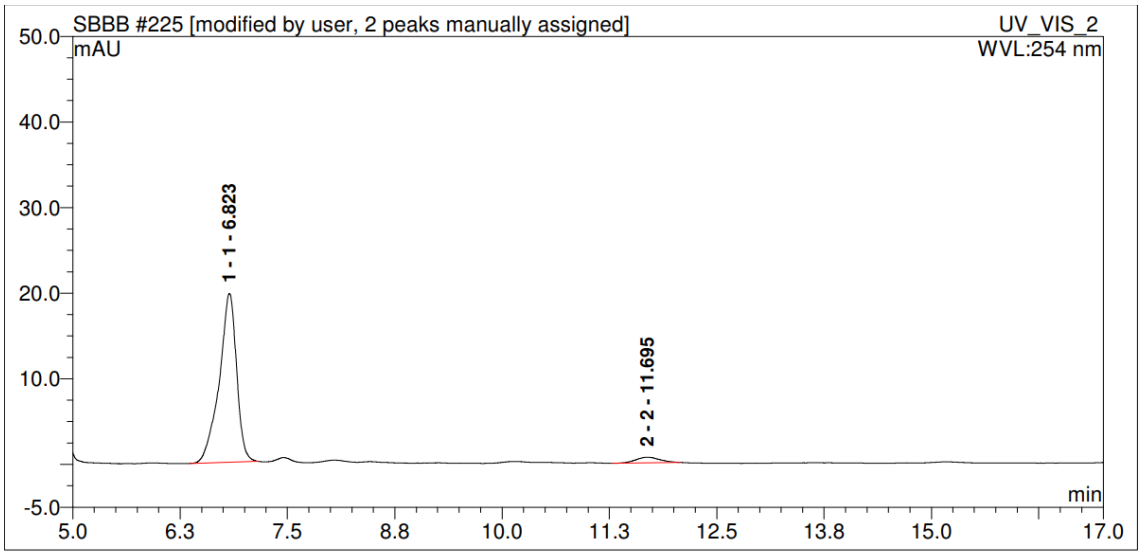


HPLC Spectra of *rac*-3na



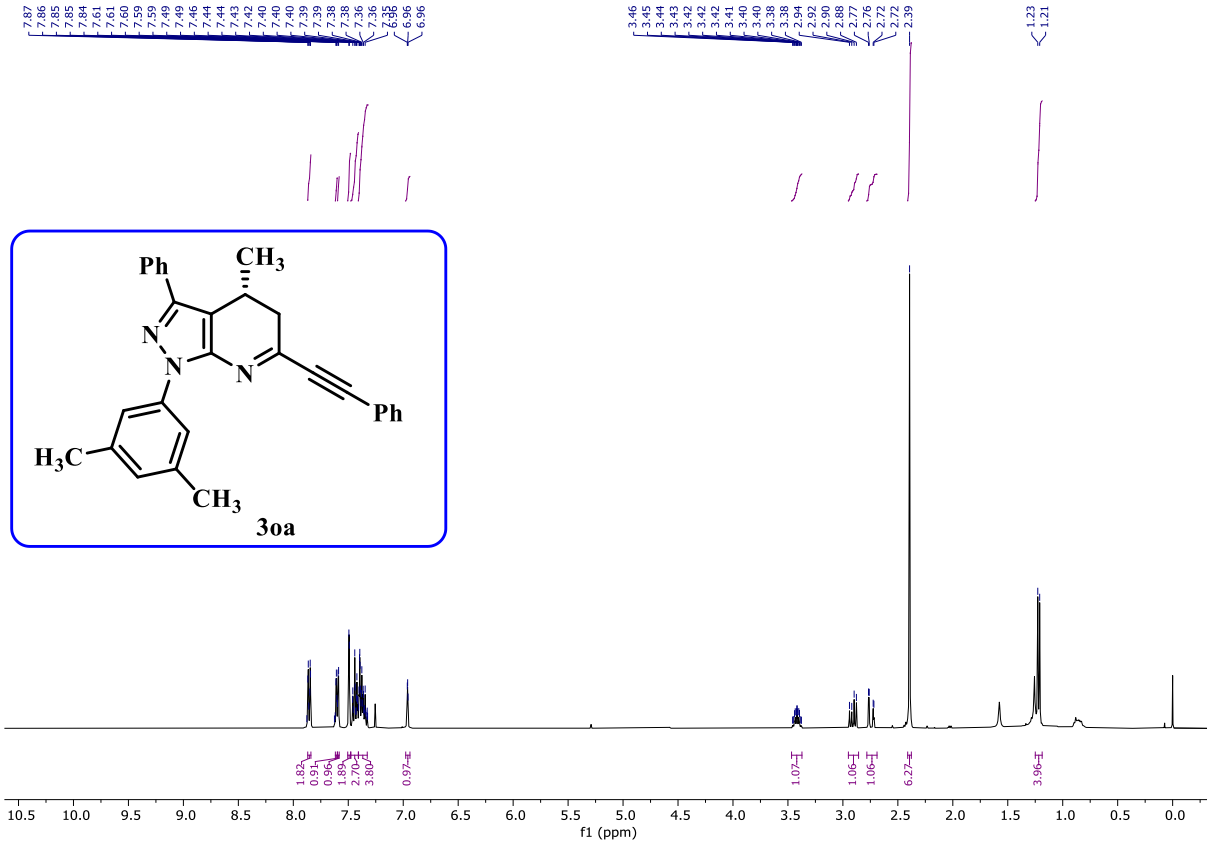
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.82	86.24093	50.9321988	395.0592	n.a.
2	2	11.65833333	83.08404	49.0678012	246.6065	n.a.

HPLC Spectra of *chi*-3na

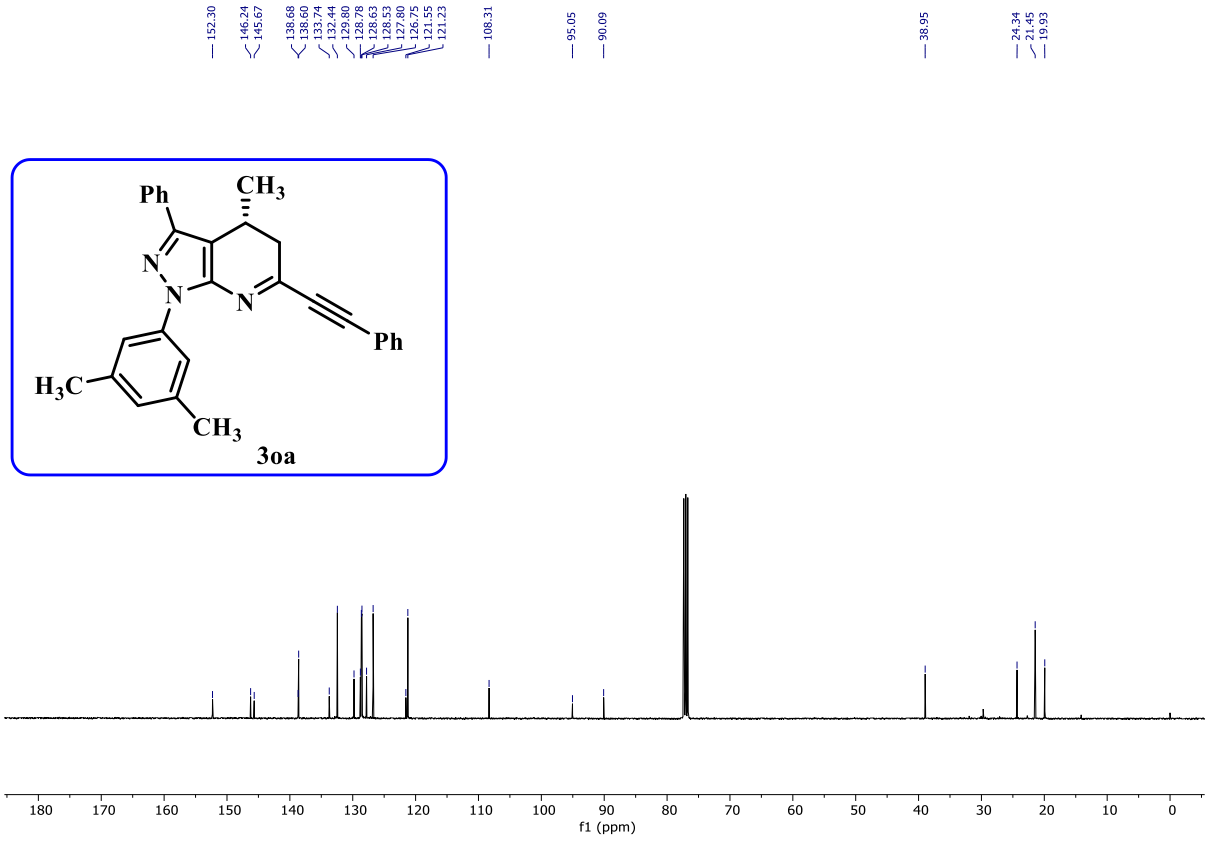


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.823333333	4.620517	95.62005046	19.69891	n.a.
2	2	11.695	0.211646	4.37994954	0.65473	n.a.

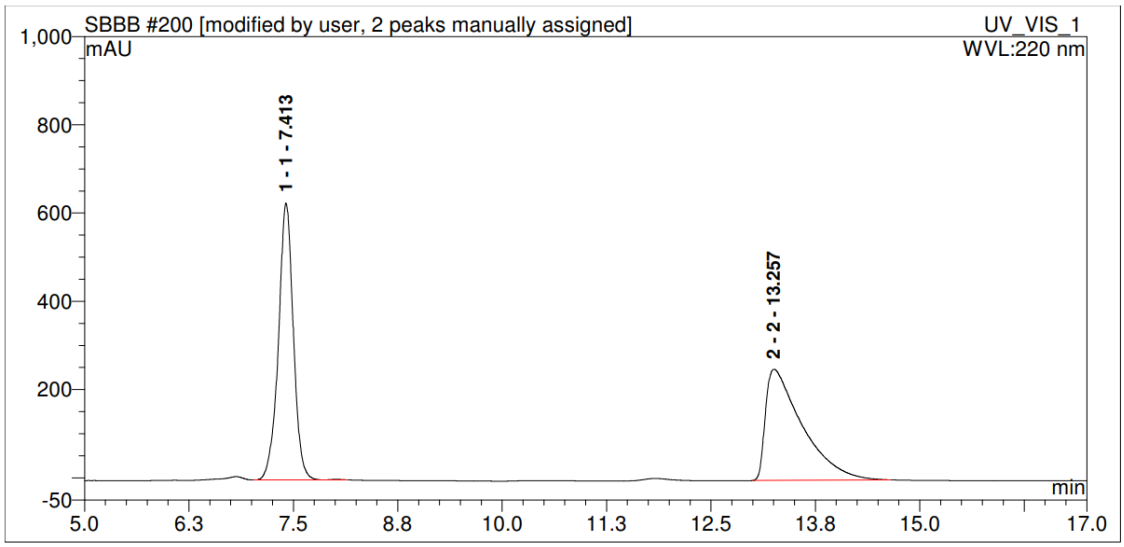
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

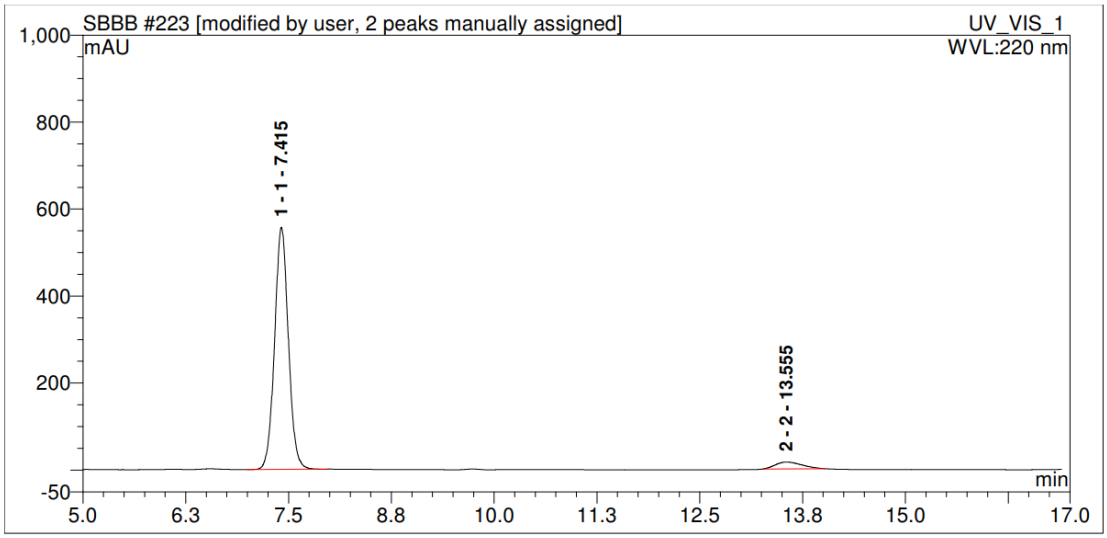


HPLC Spectra of *rac*-3oa



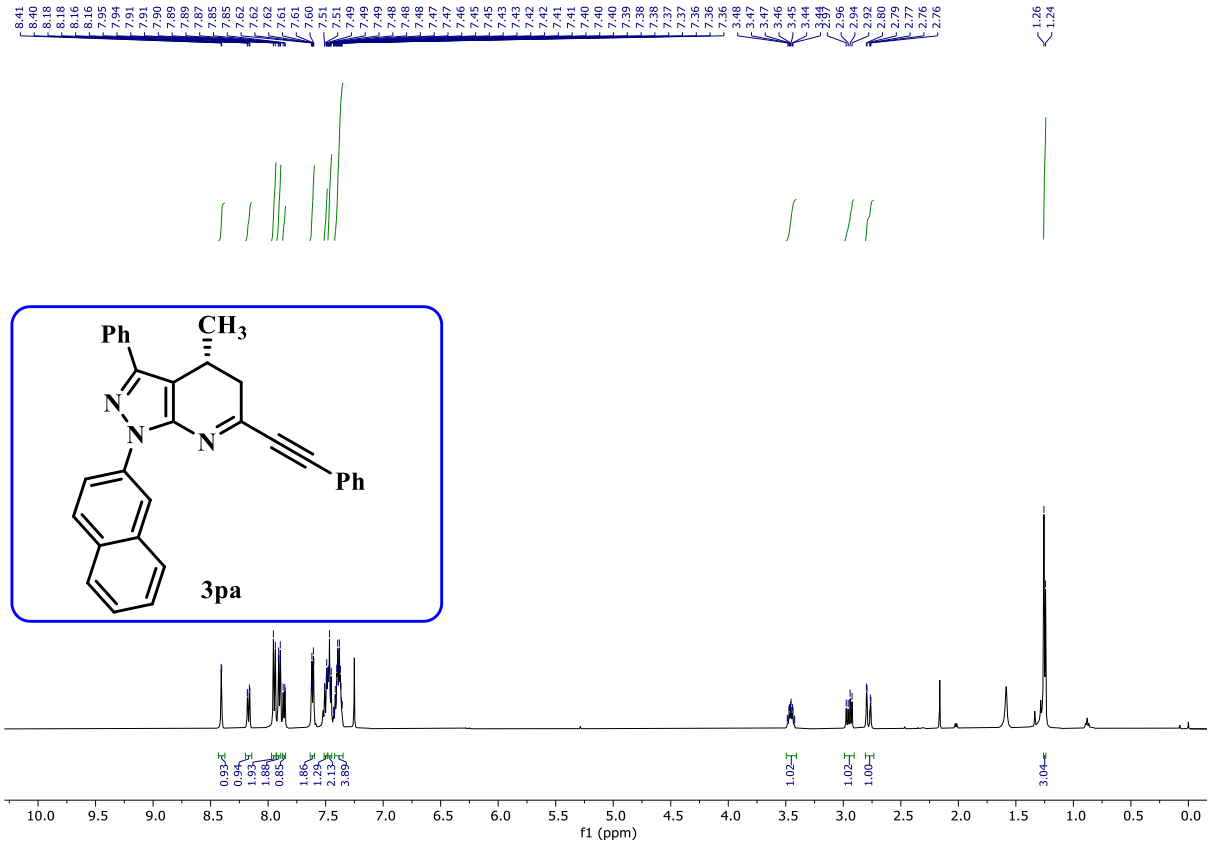
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.413333333	130.1141	50.37799049	627.3457	n.a.
2	2	13.25666667	128.1616	49.62200951	251.9068	n.a.

HPLC Spectra of *chi*-3oa

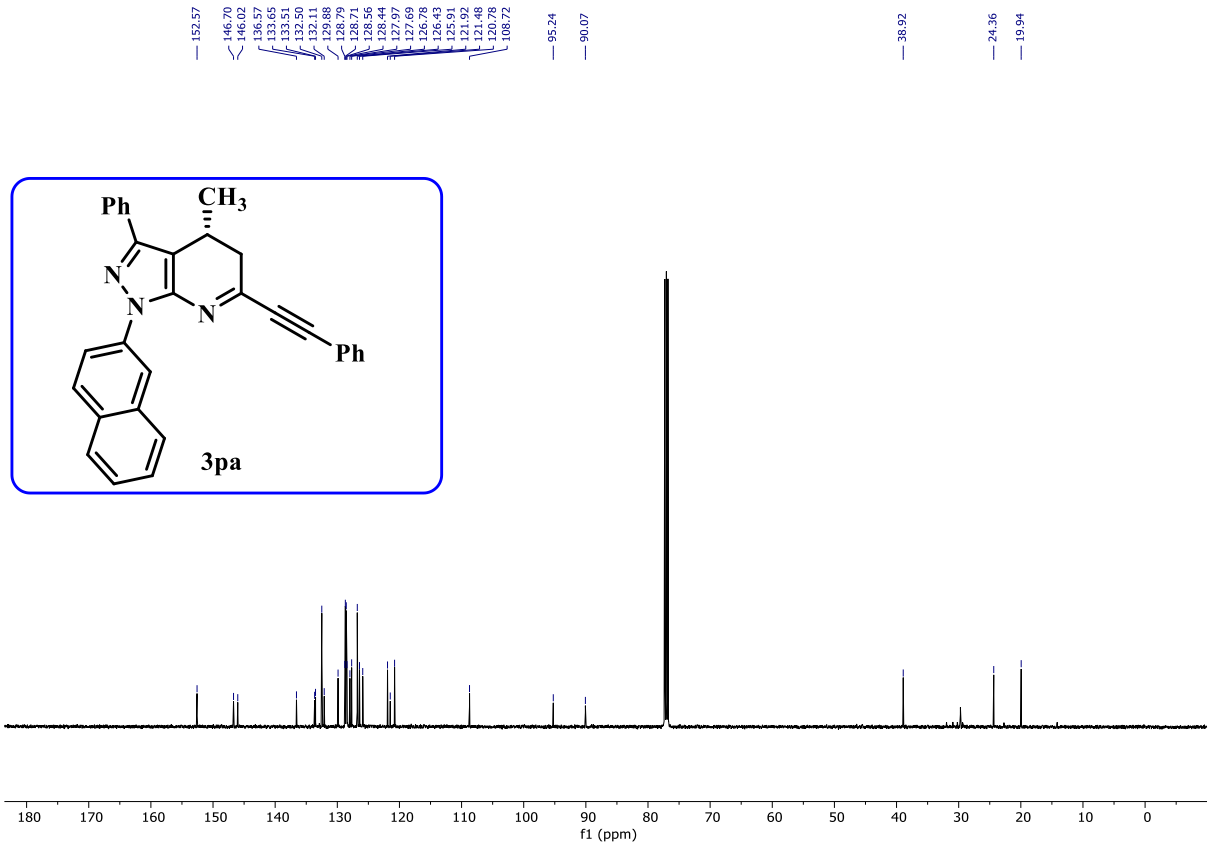


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.415	108.2097	94.87747756	556.5802	n.a.
2	2	13.555	5.842342	5.122522441	15.67718	n.a.

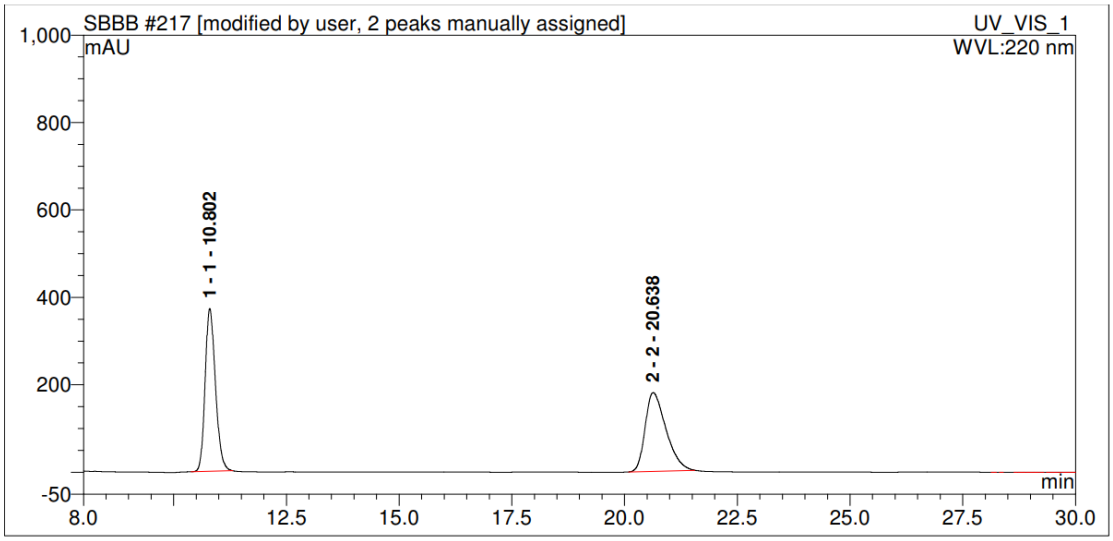
^{1}H NMR (500 MHz, $CDCl_3$)



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

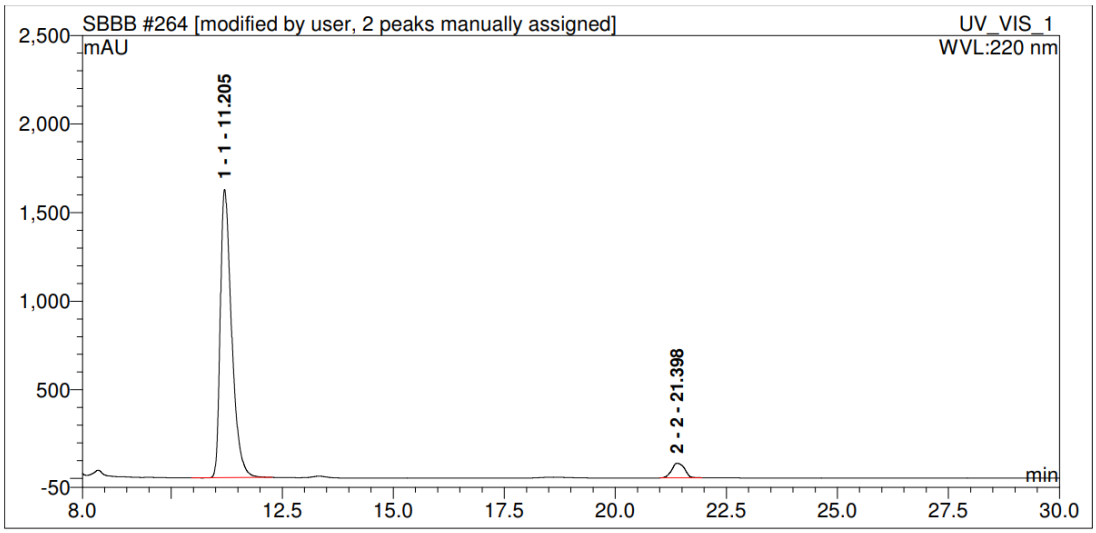


HPLC Spectra of *rac*-3pa



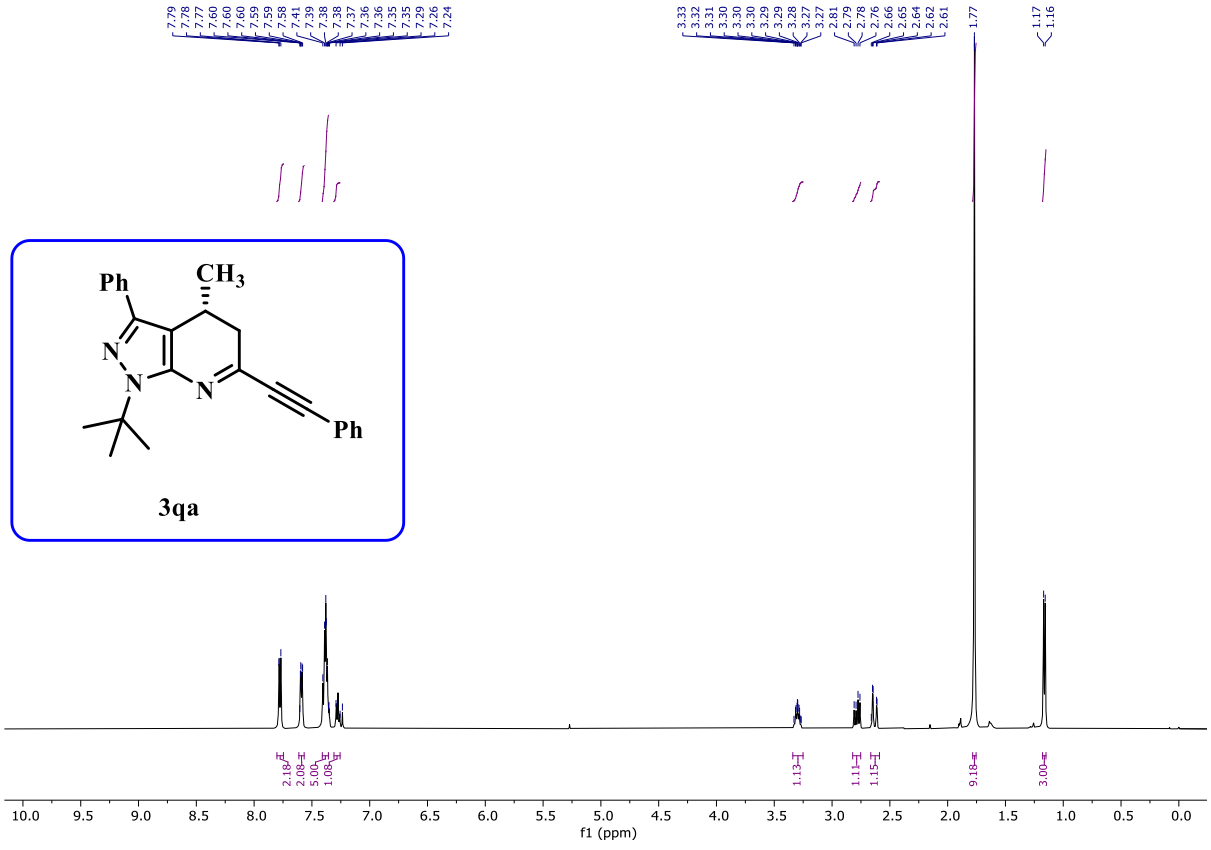
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	10.80166667	99.03669	50.64241326	372.7054	n.a.
2	2	20.63833333	96.52407	49.35758674	180.1181	n.a.

HPLC Spectra of *chi*-3pa

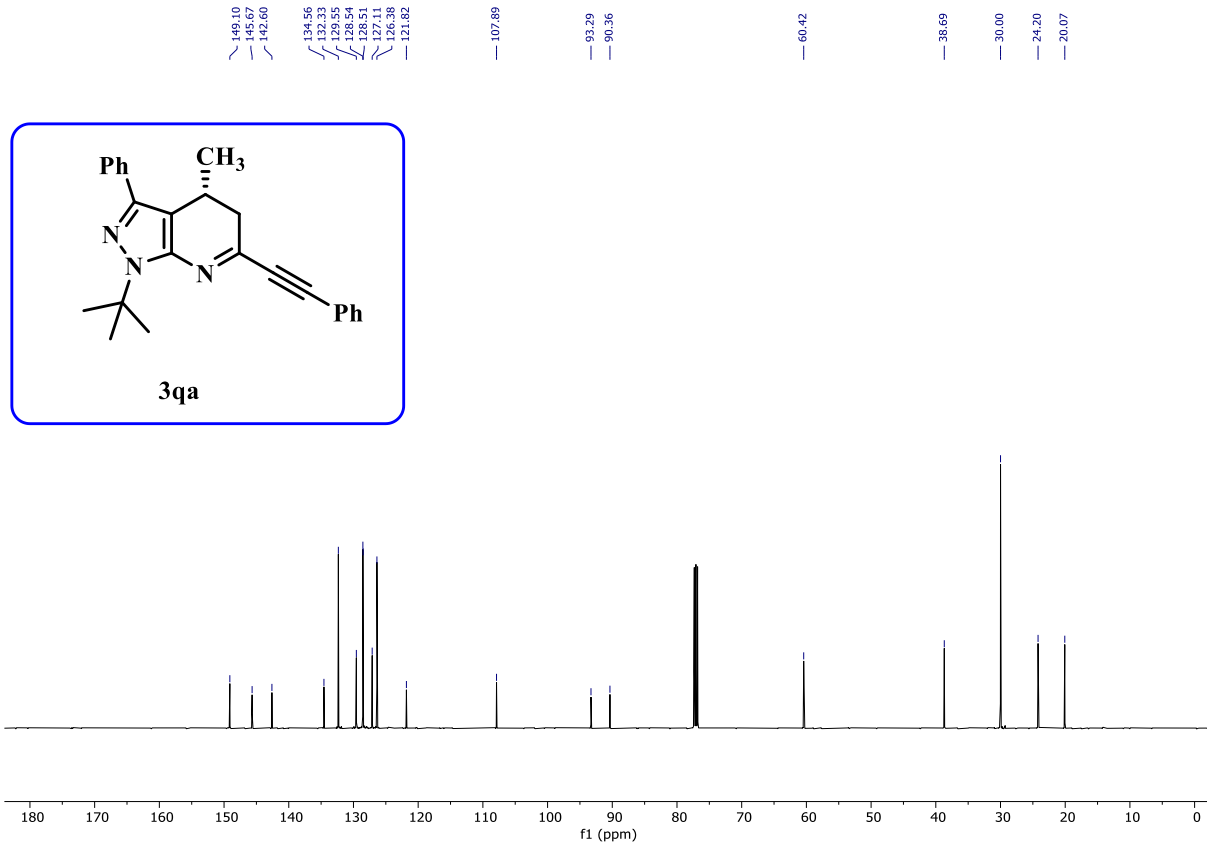


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	11.205	482.0124	94.59655803	1627.135	n.a.
2	2	21.39833333	27.53299	5.40344197	81.67526	n.a.

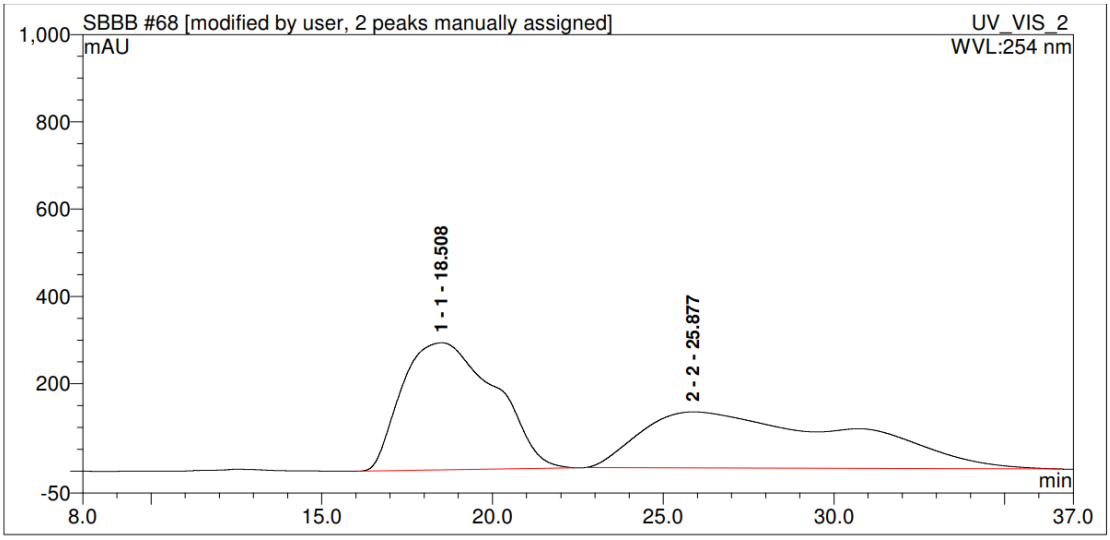
^{1}H NMR (500 MHz, $CDCl_3$)



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

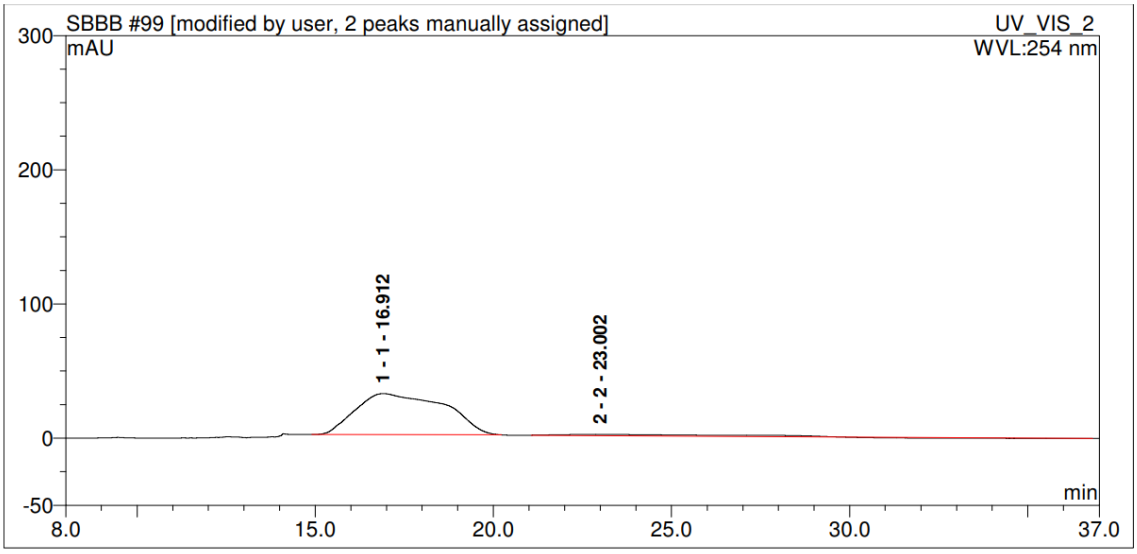


HPLC Spectra of *rac*-3qa



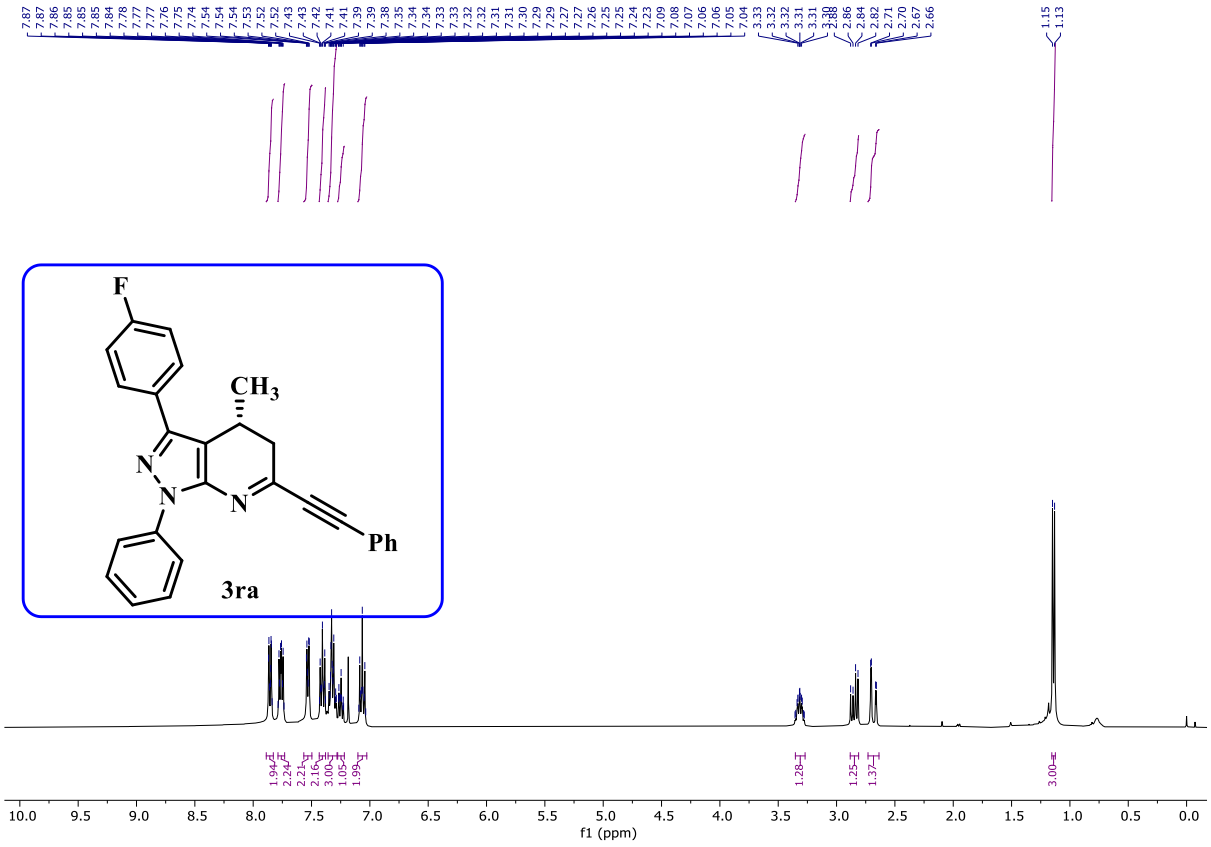
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	18.50833333	923.1979	50.03396614	291.1494	n.a.
2	2	25.87666667	921.9444	49.96603386	128.2073	n.a.

HPLC Spectra of *chi*-3qa

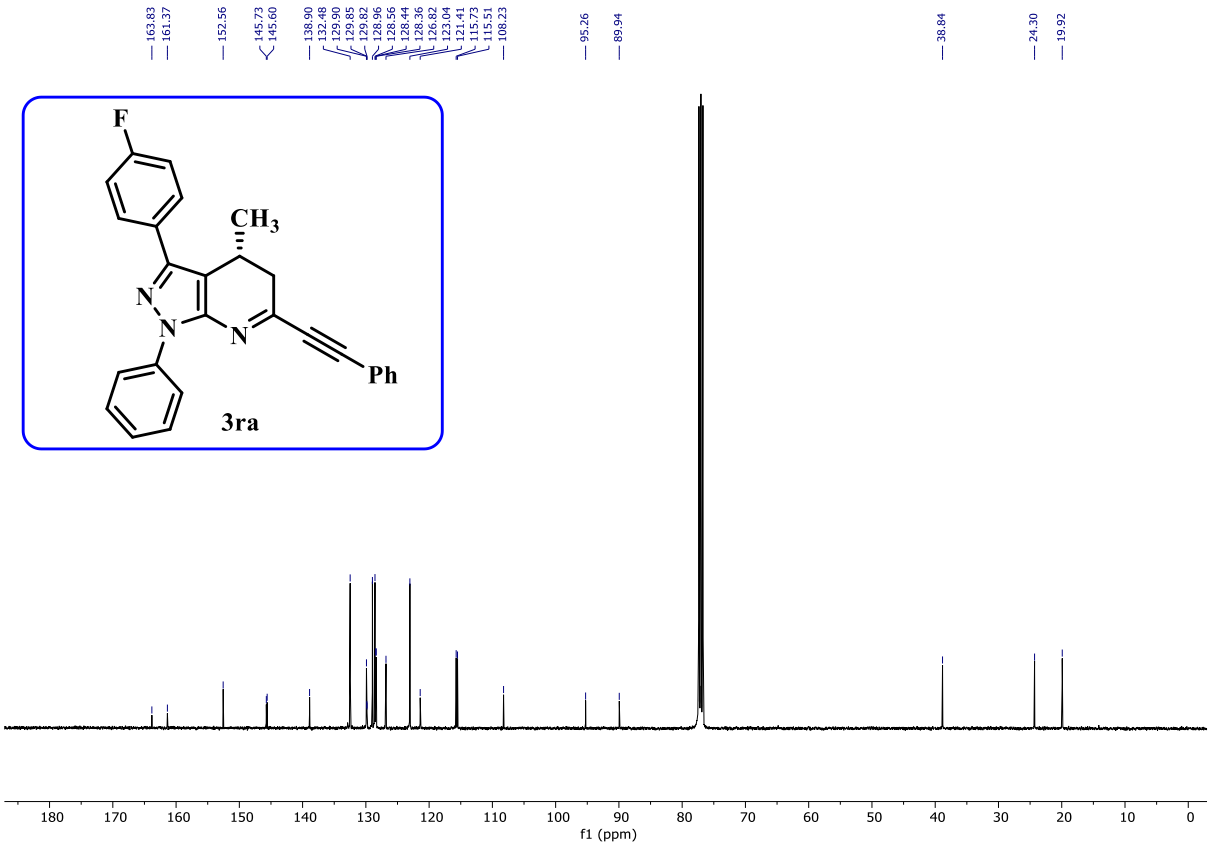


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	16.91166667	88.99842	96.20344722	30.66646	n.a.
2	2	23.00166667	3.512215	3.796552781	0.87608	n.a.

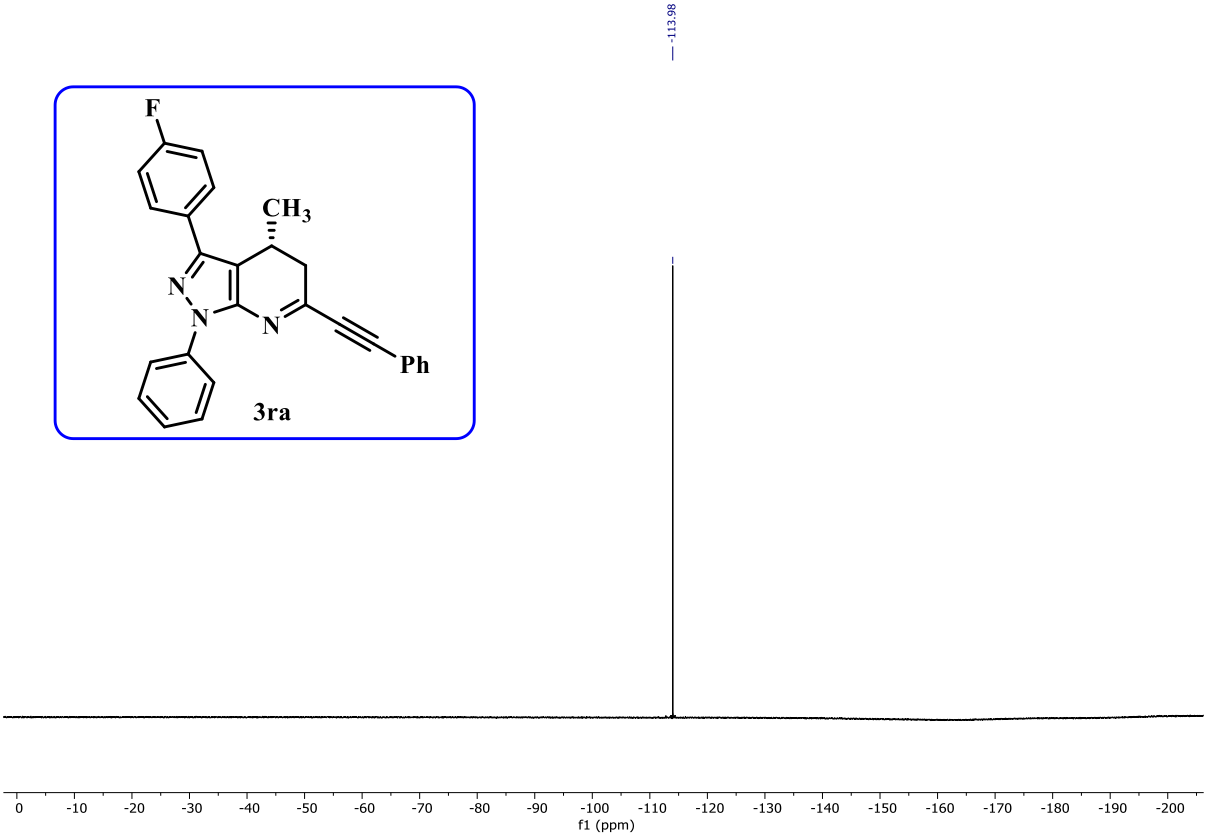
^{1}H NMR (400 MHz, $CDCl_3$)



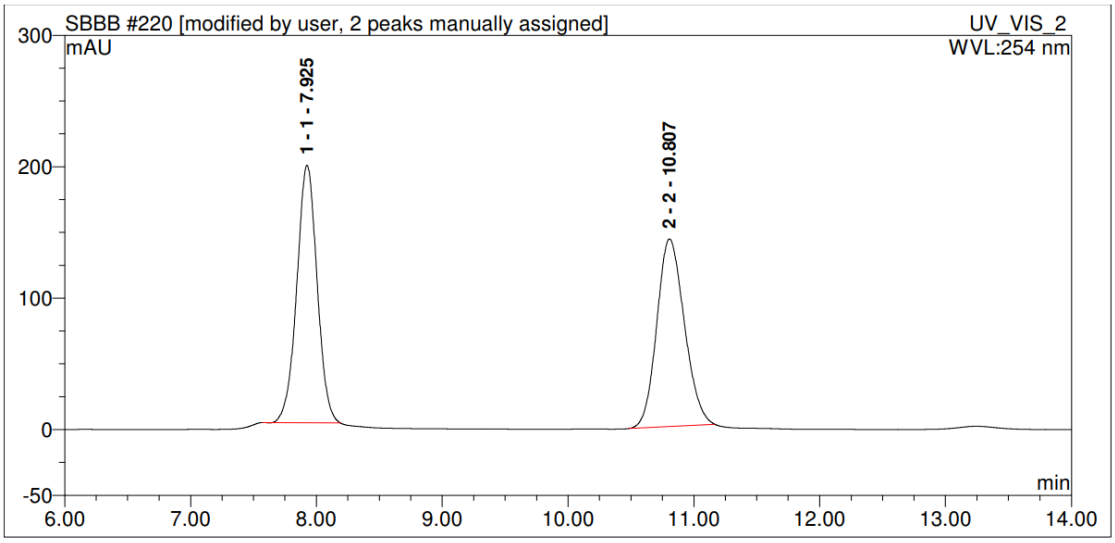
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

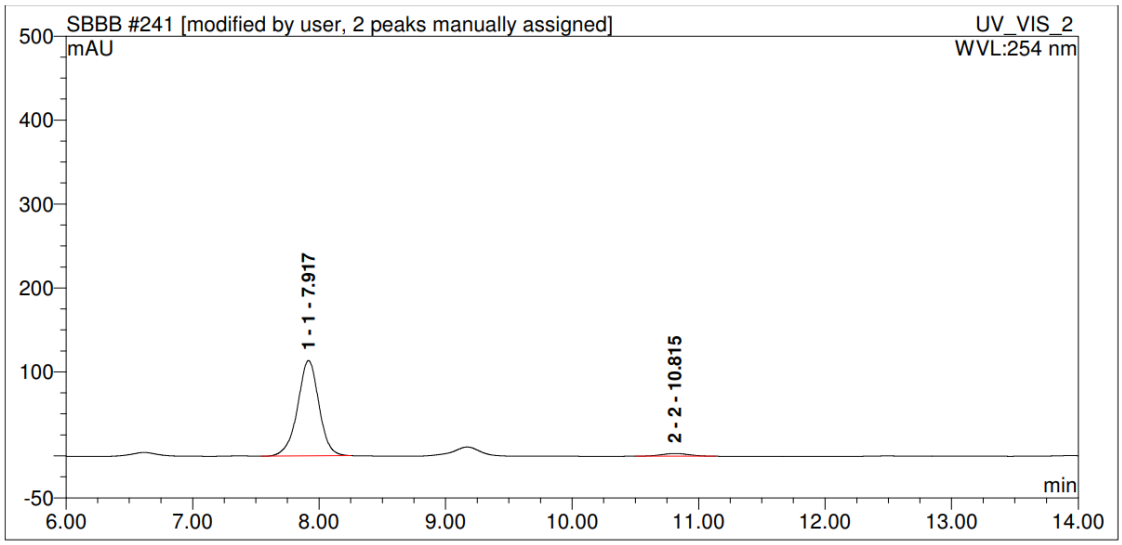


HPLC Spectra of *rac*-3ra



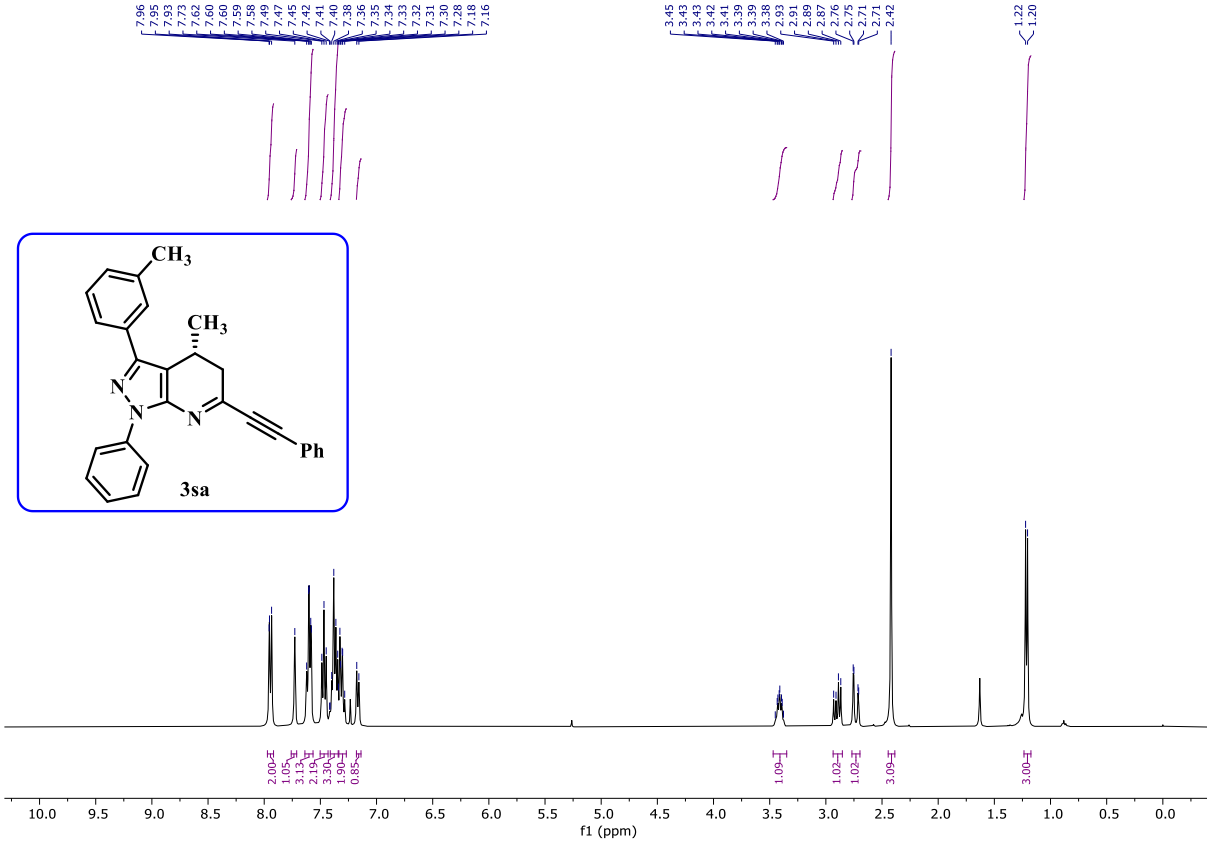
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.925	36.72254	50.34984475	196.1081	n.a.
2	2	10.80666667	36.21222	49.65015525	142.7504	n.a.

HPLC Spectra of *chi*-3ra

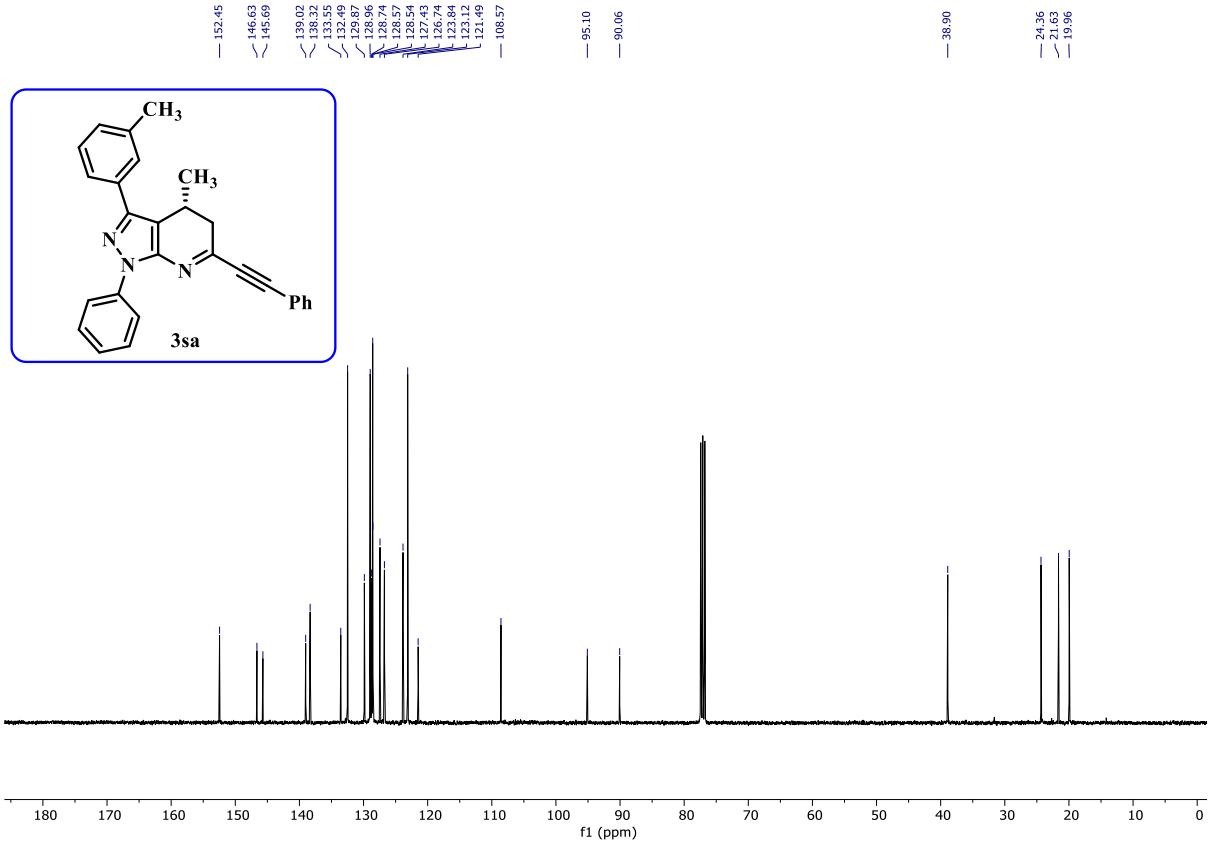


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.916666667	22.28797	96.45898965	113.7876	n.a.
2	2	10.815	0.818192	3.541010353	3.21176	n.a.

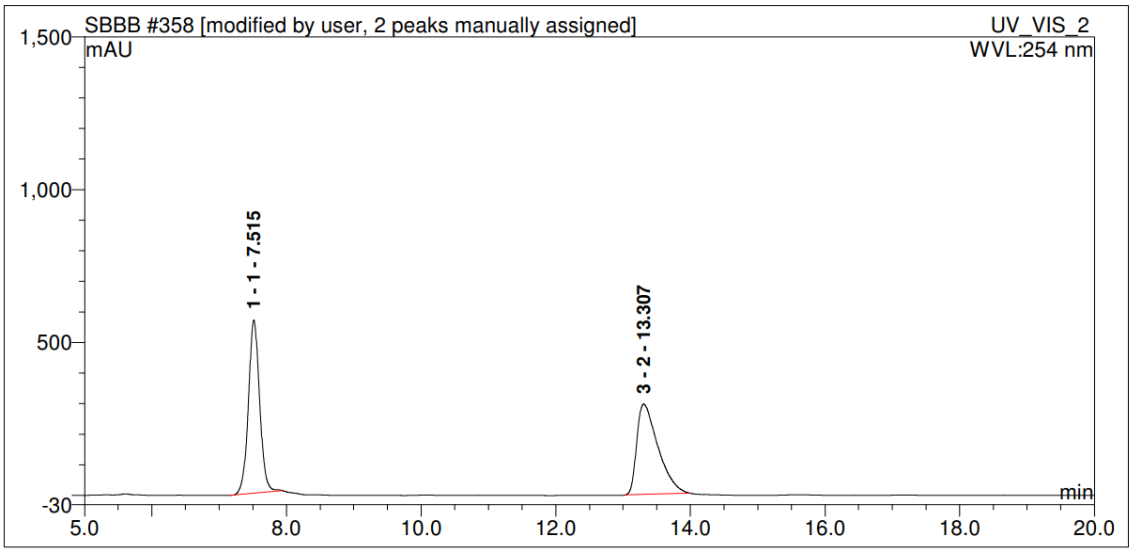
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

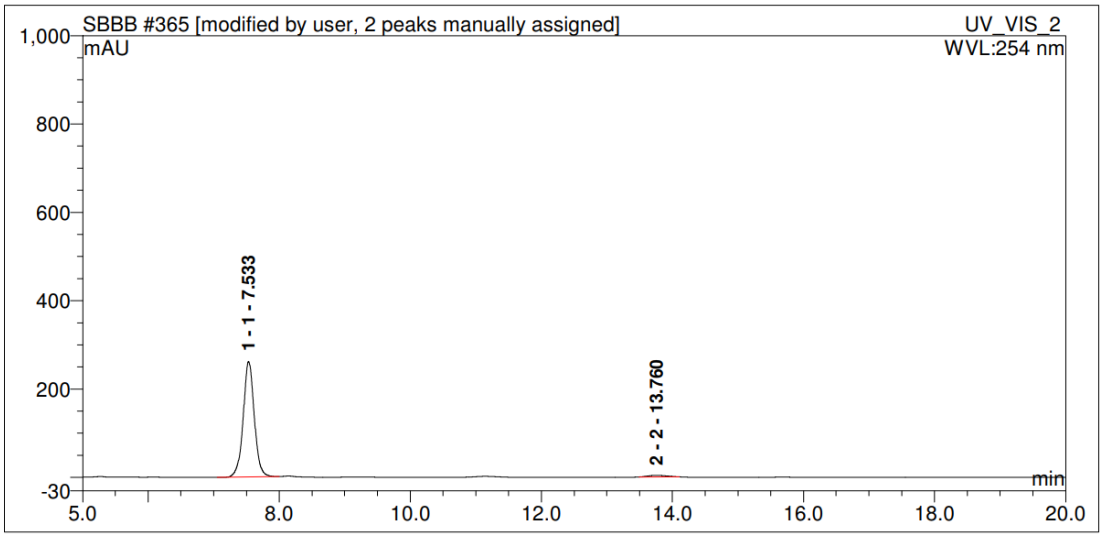


HPLC Spectra of *rac*-3sa



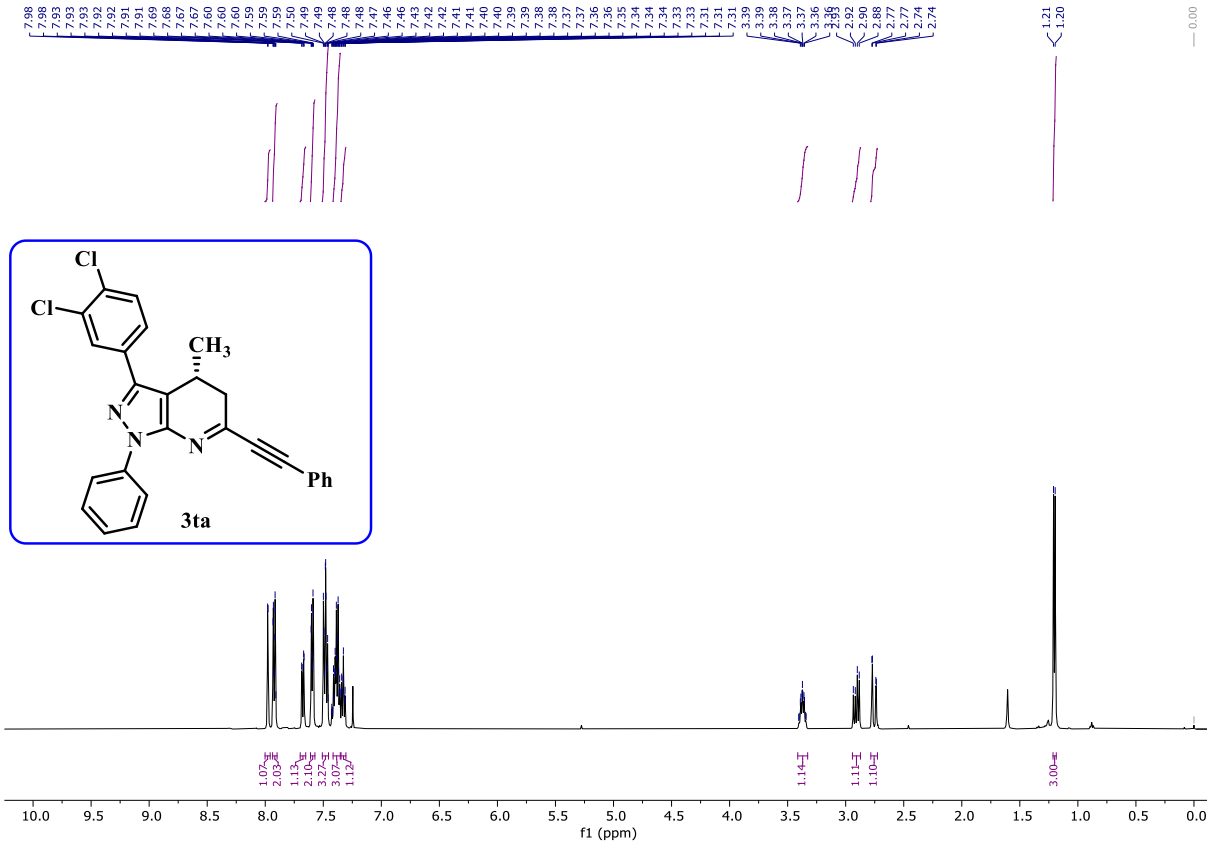
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.515	109.6872	50.45793635	566.8723	n.a.
3	2	13.30666667	107.6962	49.54206365	295.5105	n.a.

HPLC Spectra of *chi*-3sa

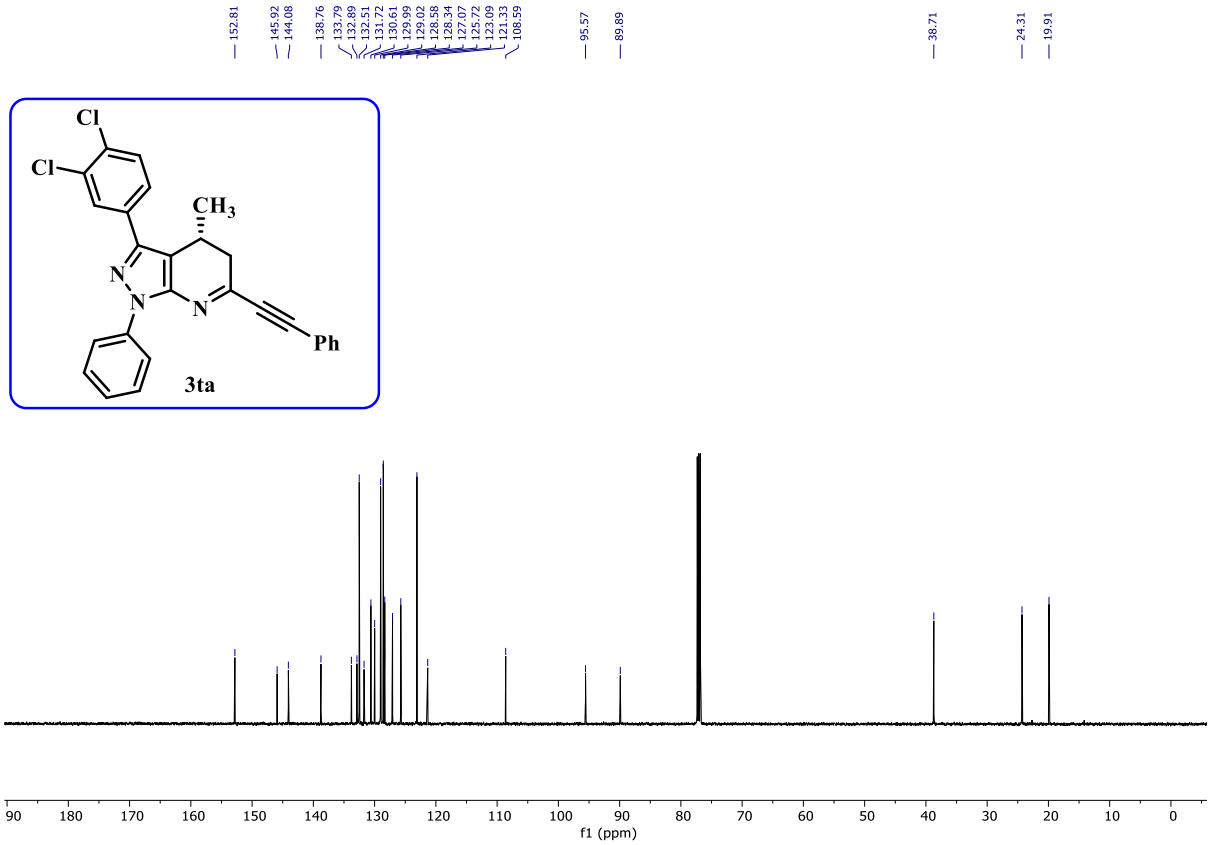


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.533333333	51.33841	97.67820487	261.5254	n.a.
2	2	13.76	1.220306	2.321795128	3.56382	n.a.

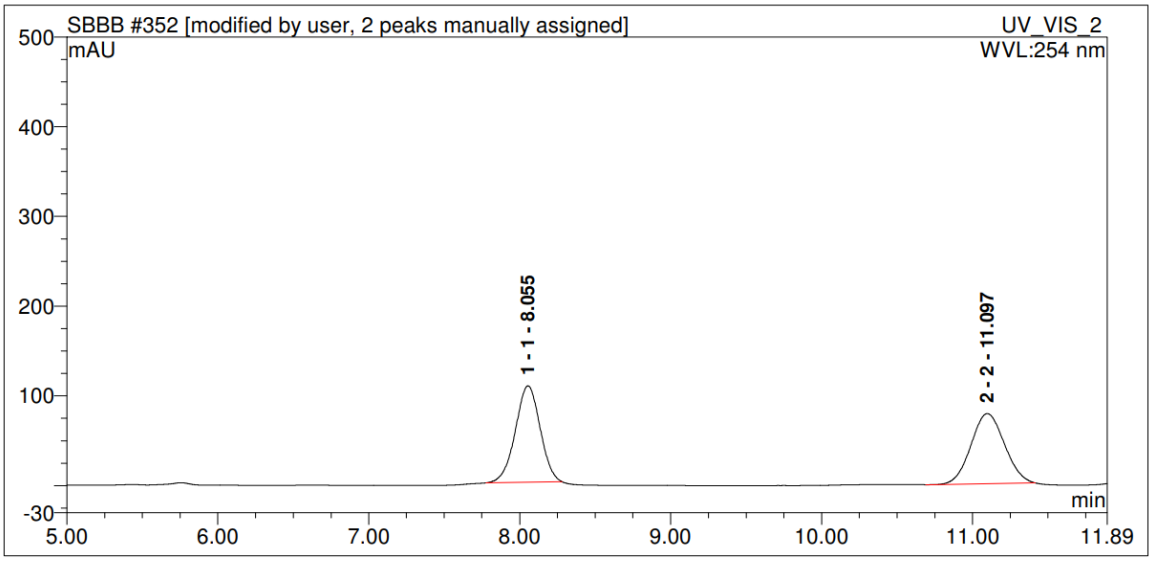
^{1}H NMR (500 MHz, $CDCl_3$)



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

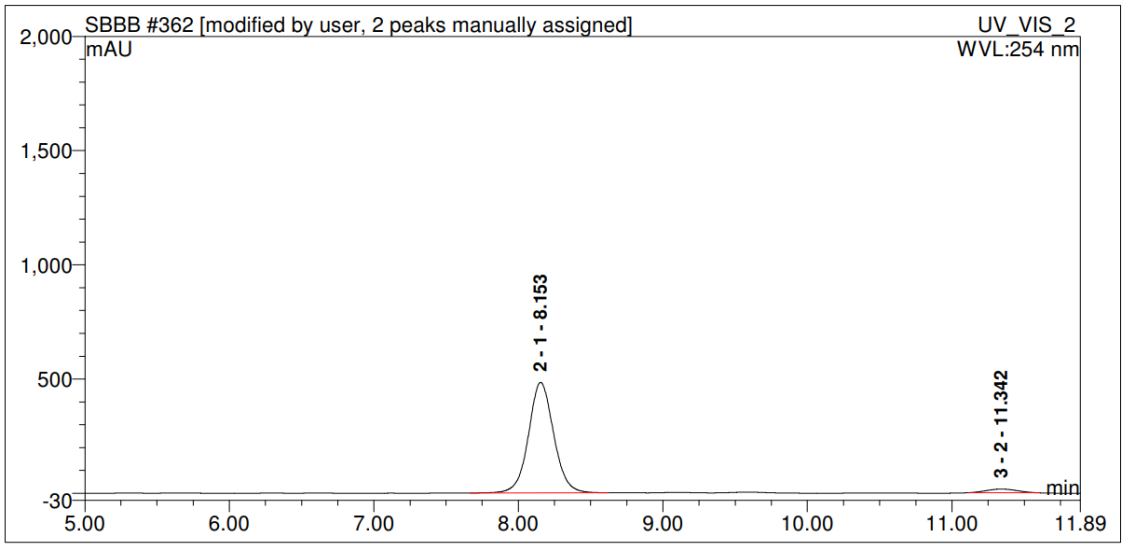


HPLC Spectra of *rac*-3ta



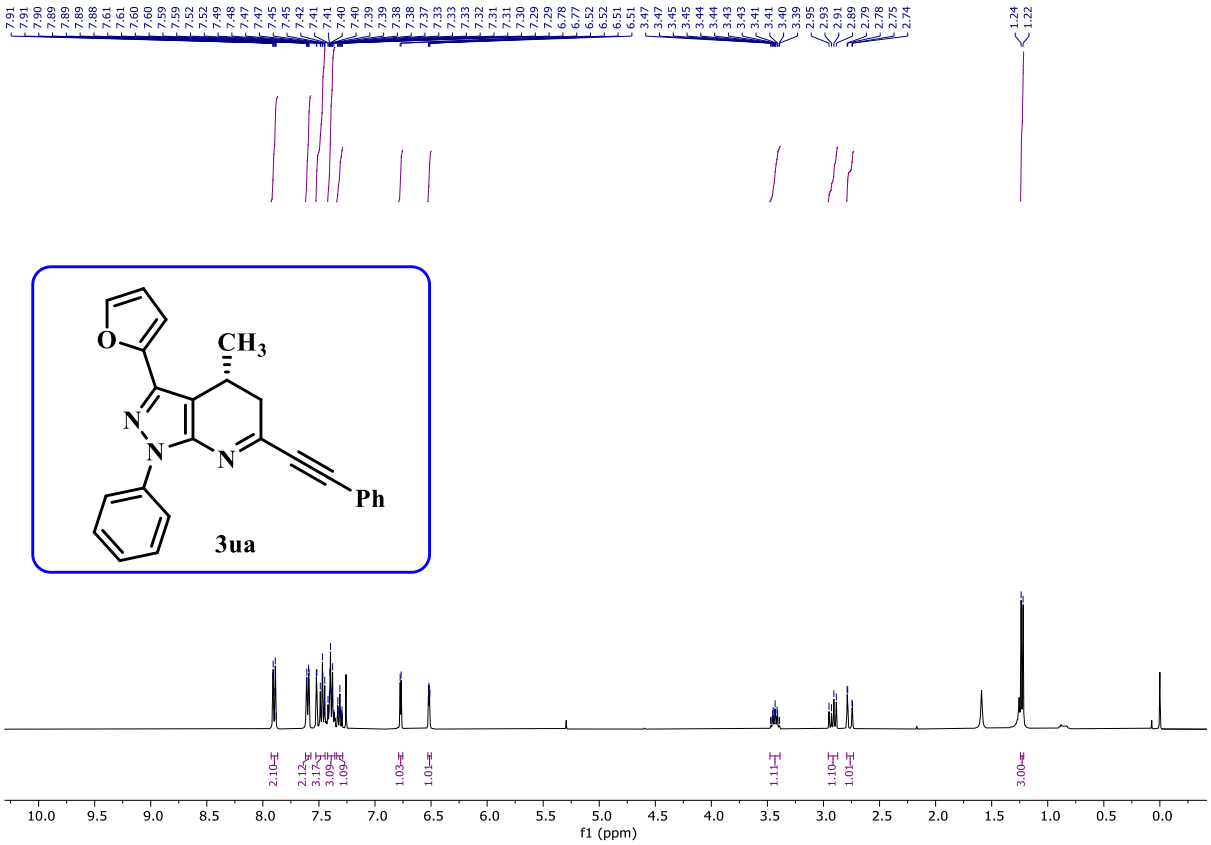
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.055	20.43732	50.42605448	107.4227	n.a.
2	2	11.09666667	20.09197	49.57394552	78.13037	n.a.

HPLC Spectra of *chi*-3ta

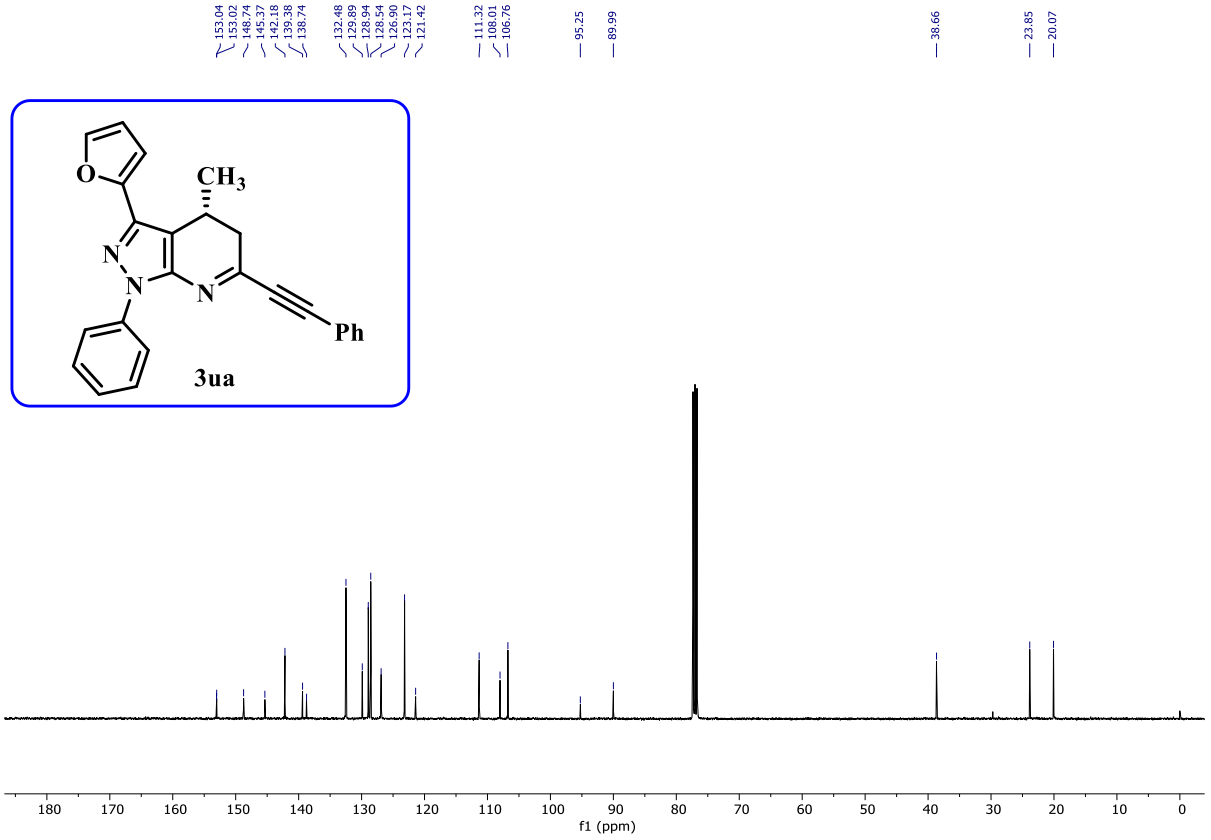


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
2	1	8.153333333	97.81376	96.09353794	483.4702	n.a.
3	2	11.34166667	3.976389	3.906457021	16.21877	n.a.

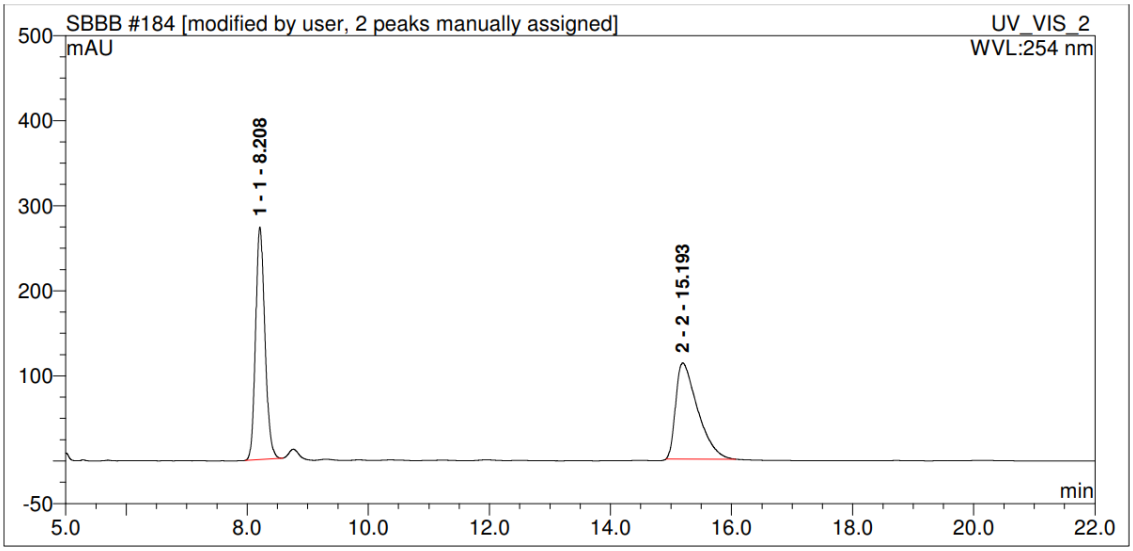
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

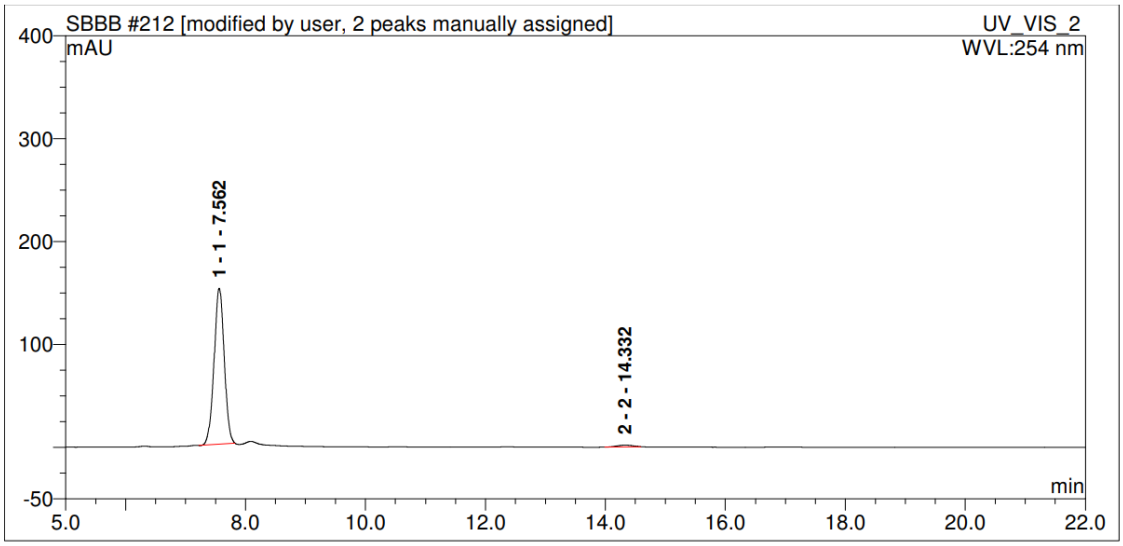


HPLC Spectra of *rac*-3ua



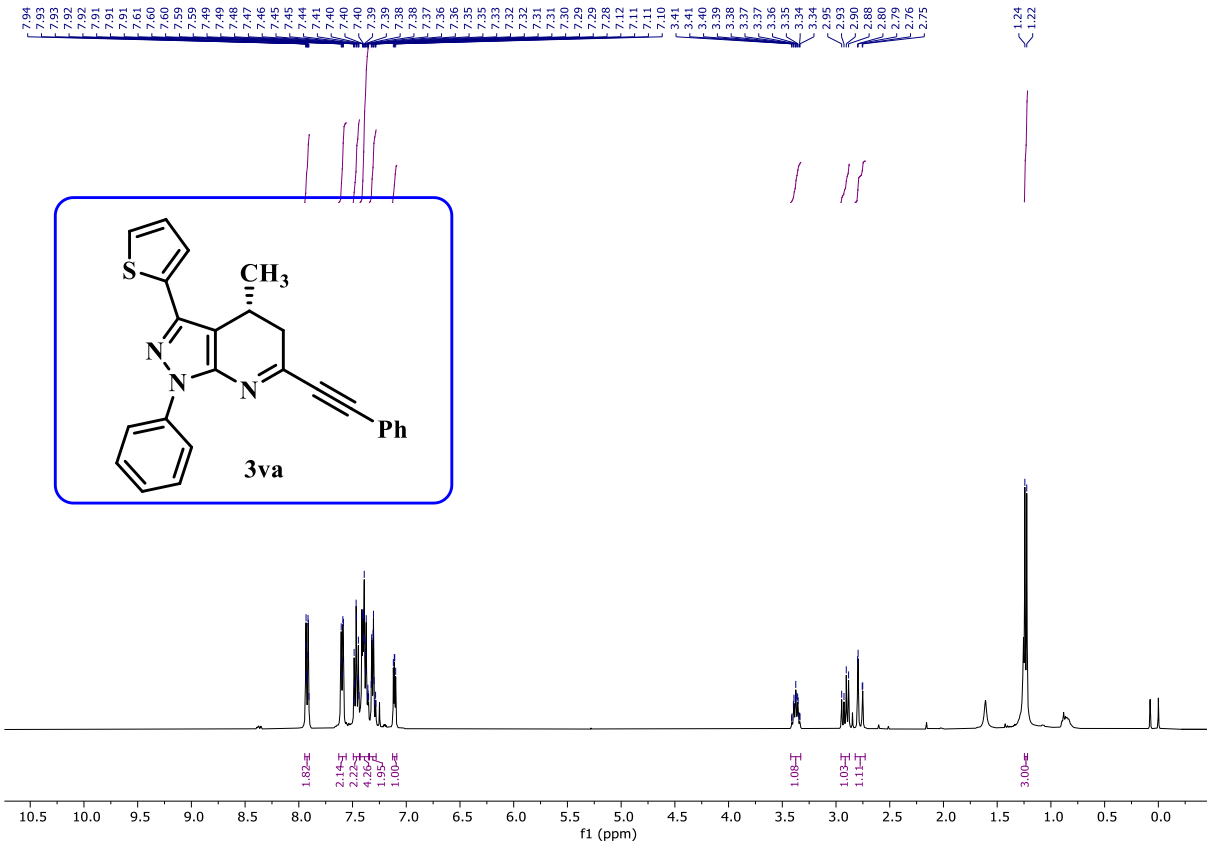
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.208333333	48.80437	50.82218925	273.1509	n.a.
2	2	15.19333333	47.22528	49.17781075	112.8454	n.a.

HPLC Spectra of *chi*-3ua

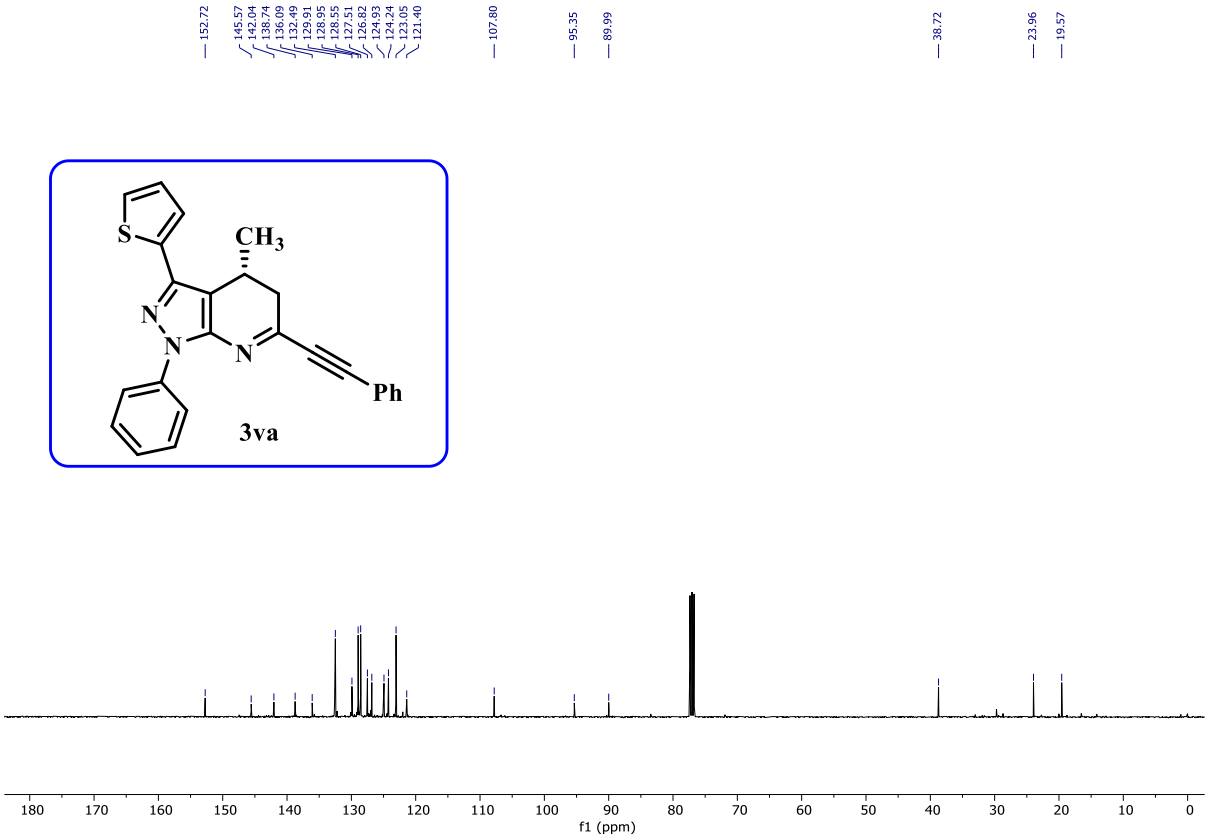


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.561666667	29.82879	98.31233084	151.6218	n.a.
2	2	14.33166667	0.512053	1.687669163	1.6754	n.a.

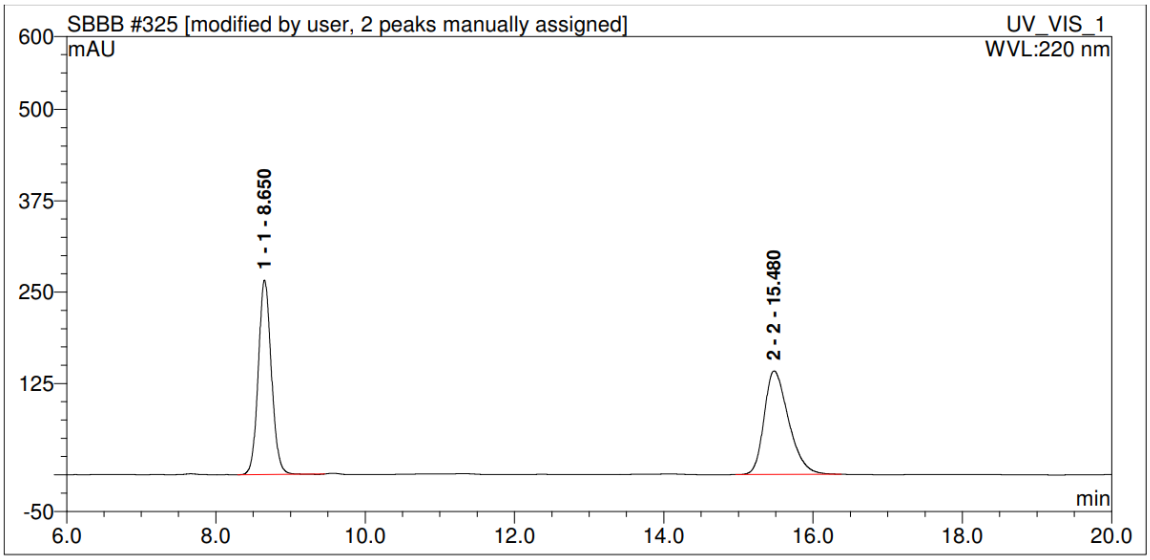
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

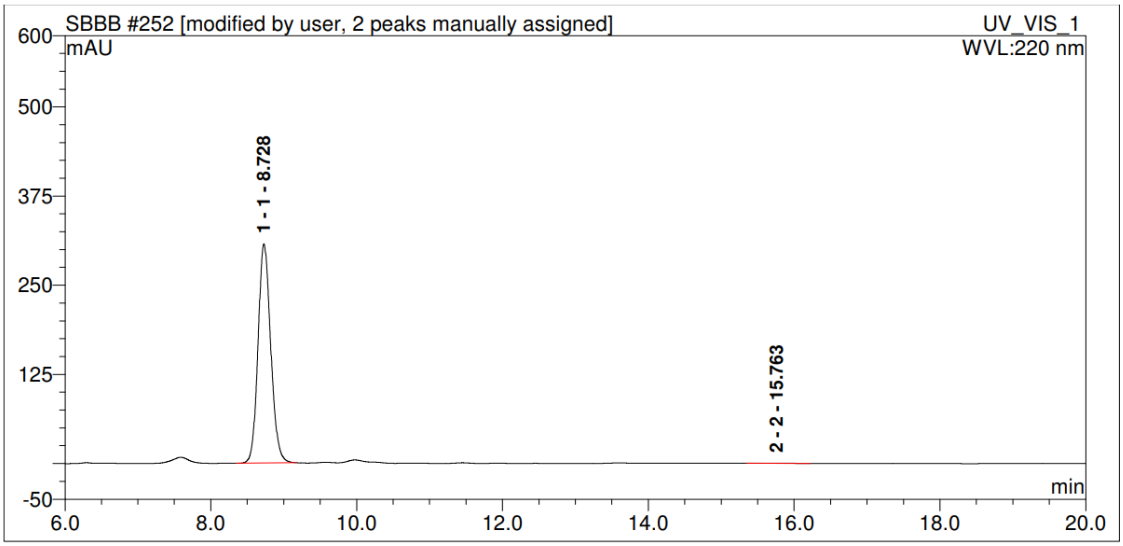


HPLC Spectra of *rac*-3va



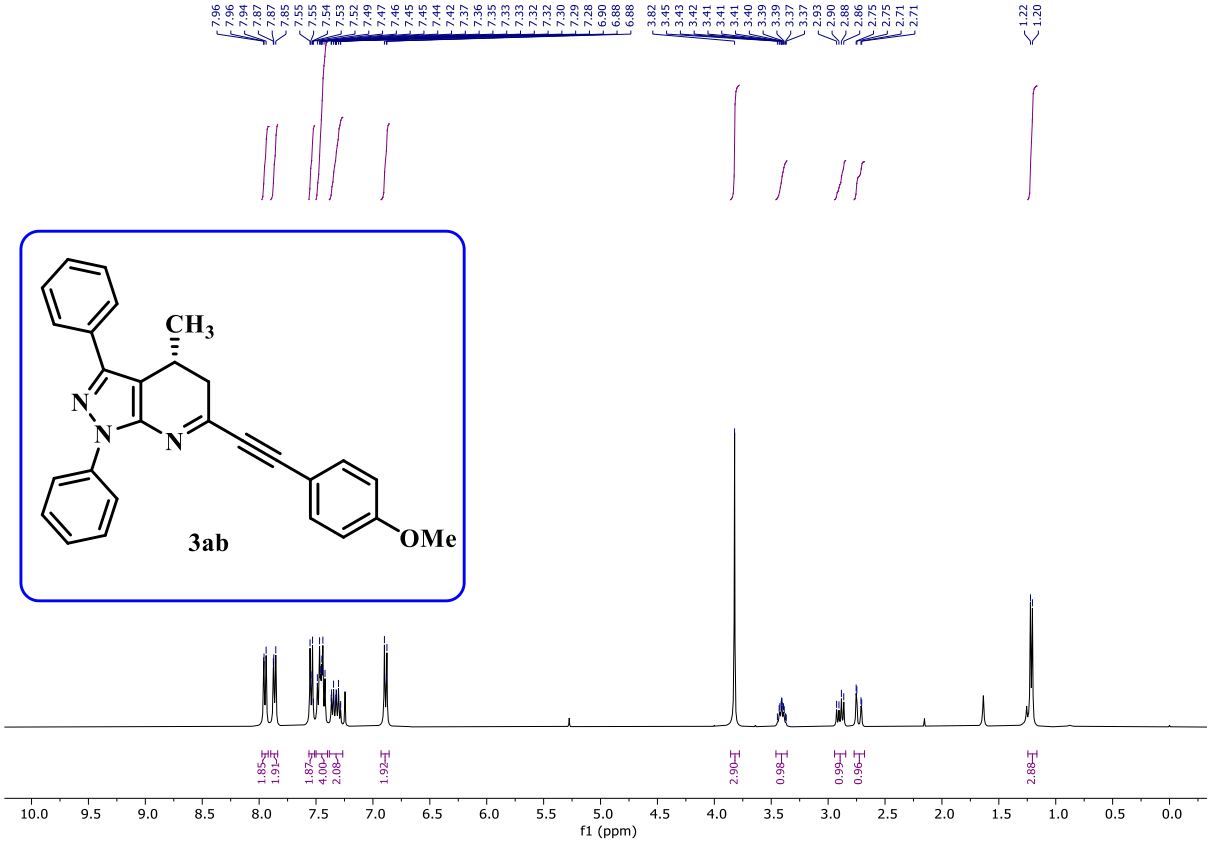
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.65	54.09253	50.11330022	266.1491	n.a.
2	2	15.48	53.84794	49.88669978	141.7828	n.a.

HPLC Spectra of *chi*-3va

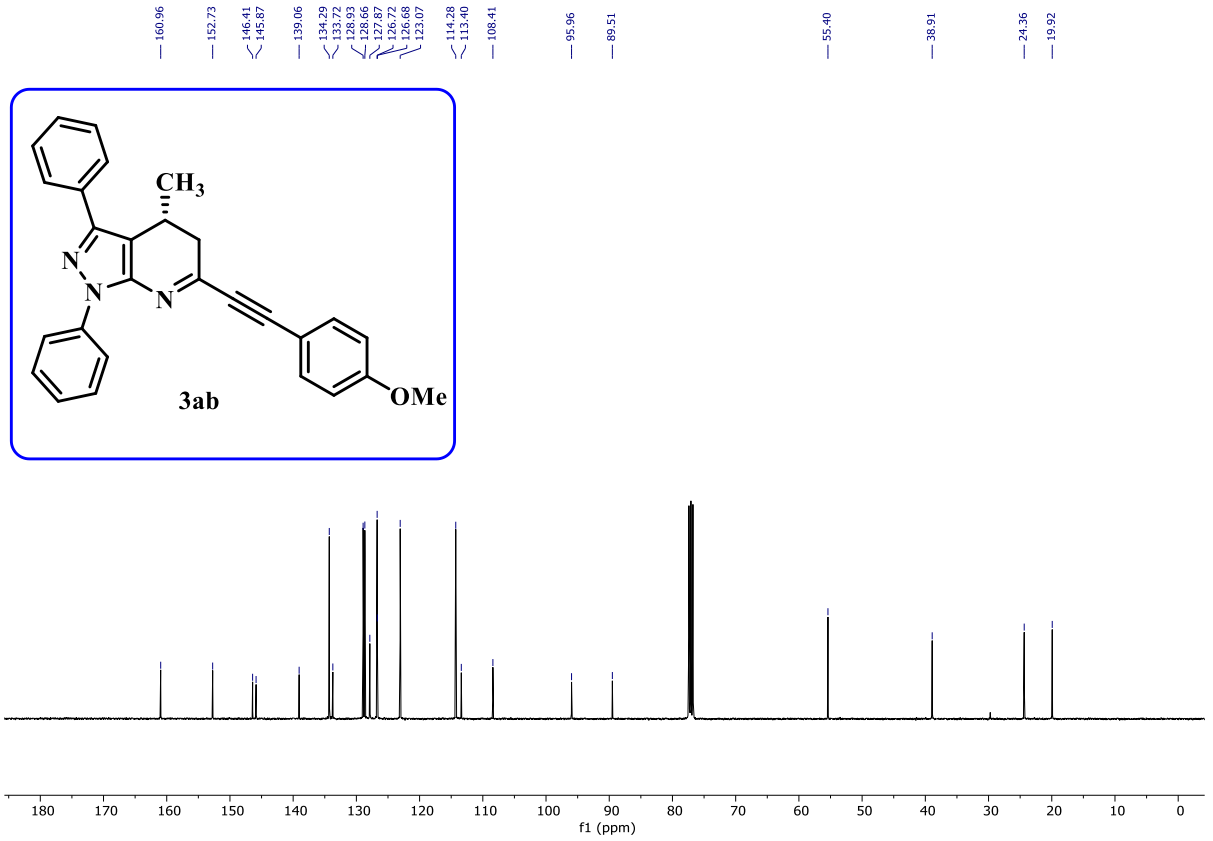


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.728333333	61.97929	99.82249369	307.3067	n.a.
2	2	15.76333333	0.110213	0.1775063059	0.34713	n.a.

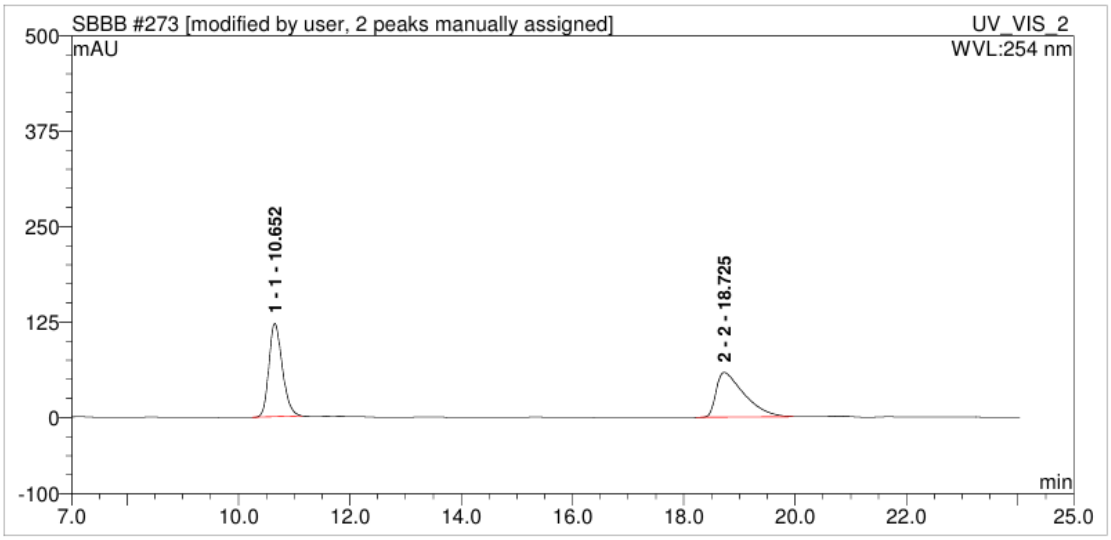
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

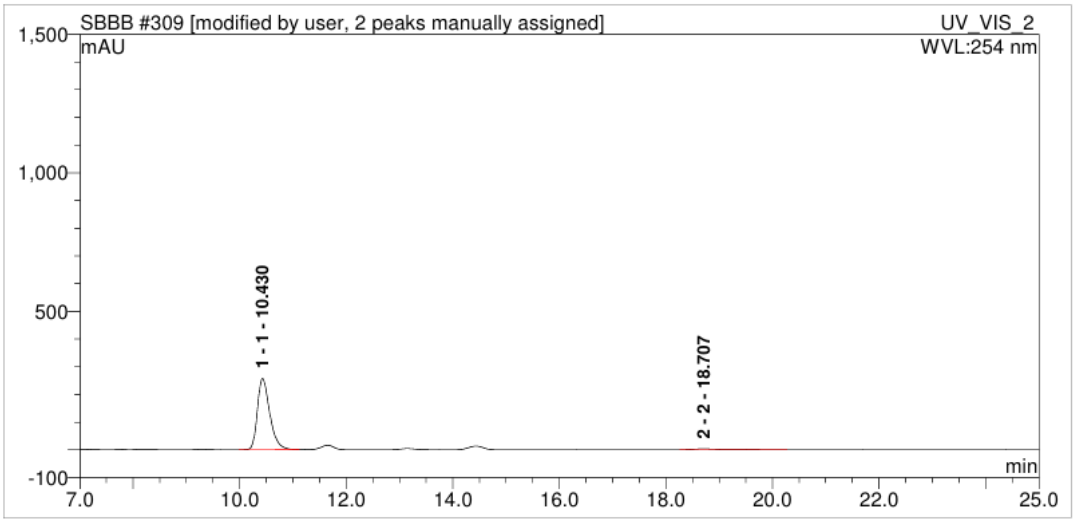


HPLC Spectra of *rac*-3ab



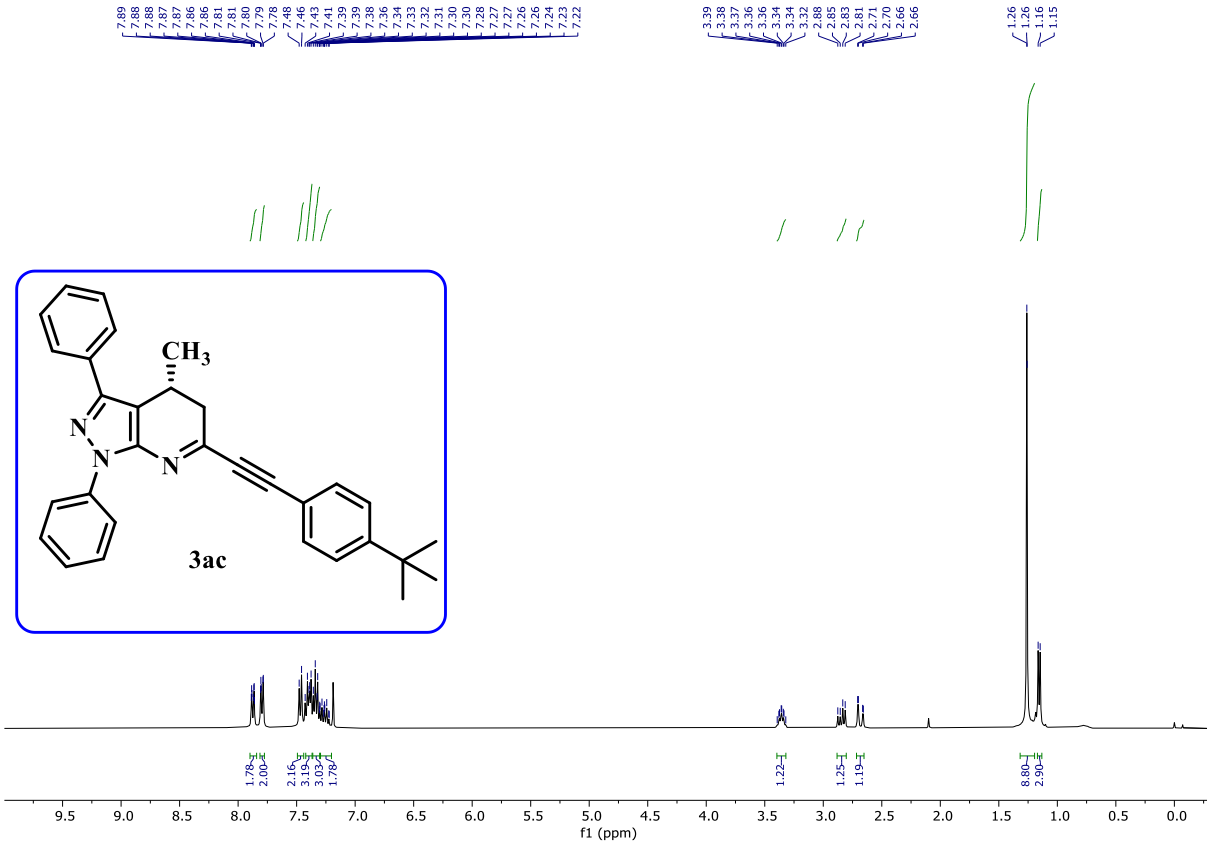
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	10.65166667	34.0754	50.07627664	122.0438	n.a.
2	2	18.725	33.9716	49.92372336	58.53928	n.a.

HPLC Spectra of *chi*-3ab

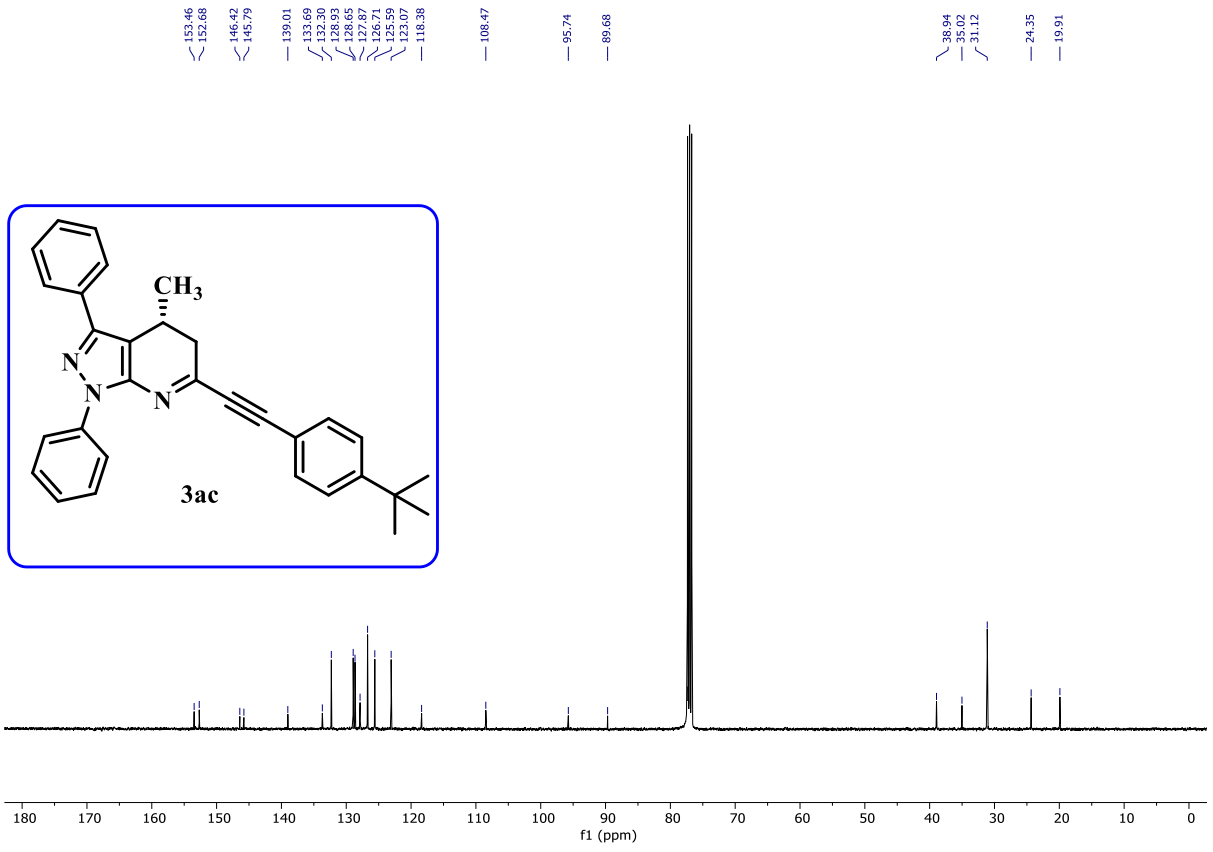


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	10.43	69.12506	95.49504758	257.1115	n.a.
2	2	18.70666667	3.260956	4.50495242	4.01239	n.a.

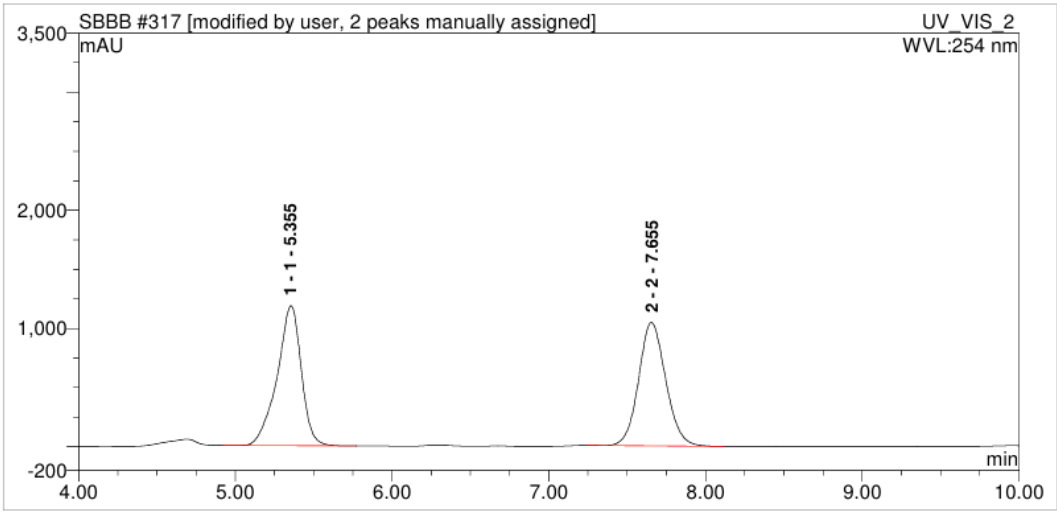
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

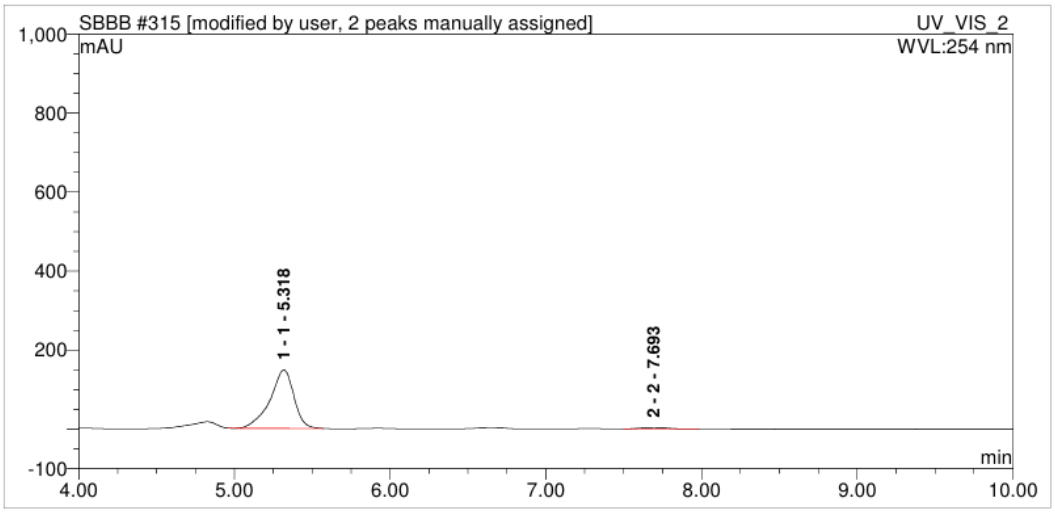


HPLC Spectra of *rac*-3ac



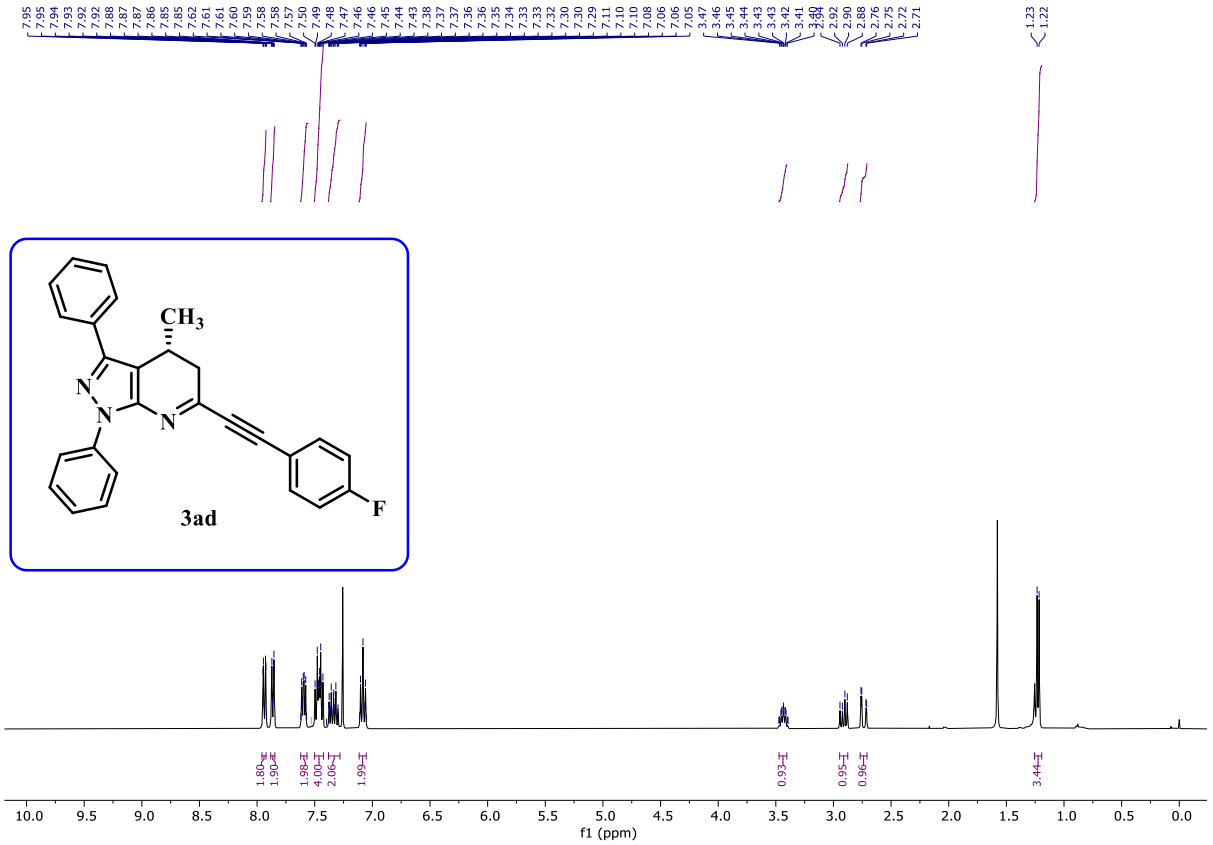
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	5.355	212.0765	50.39397377	1186.044	n.a.
2	2	7.655	208.7605	49.60602623	1043.349	n.a.

HPLC Spectra of *chi*-3ac

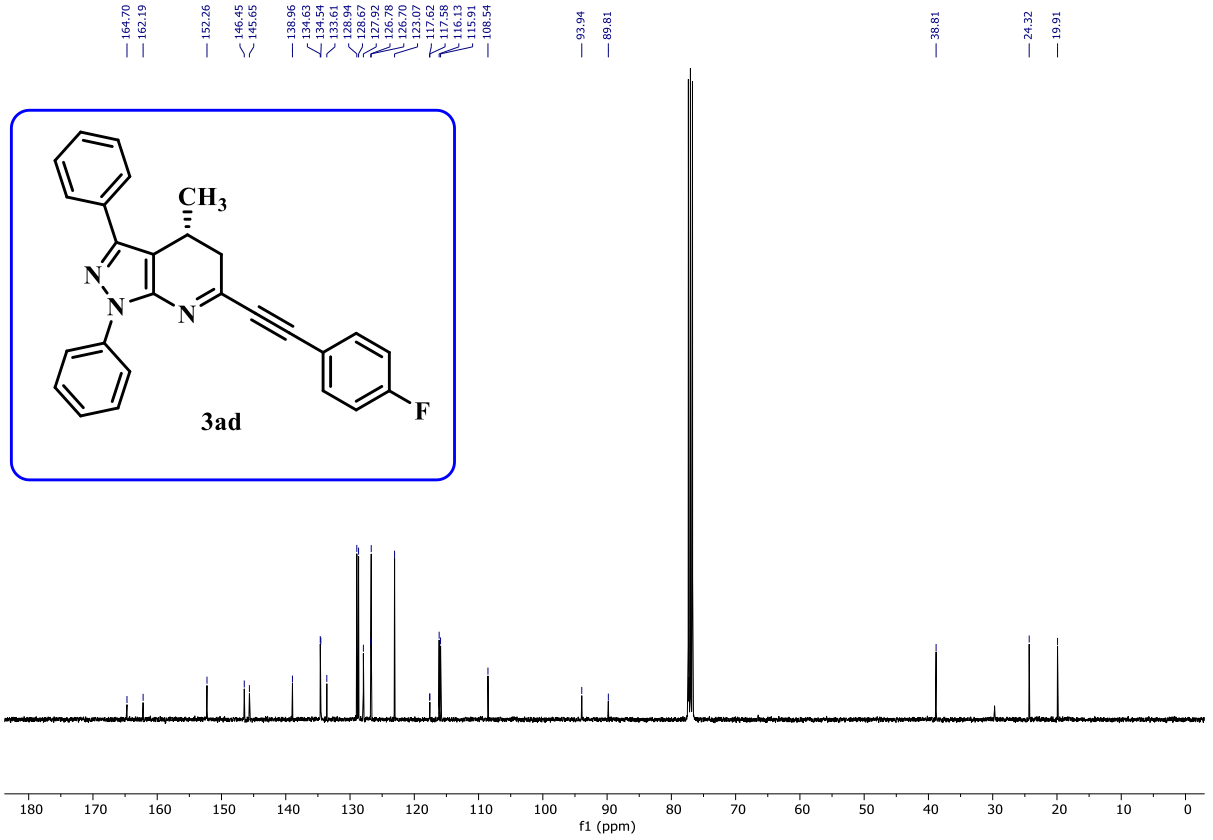


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	5.318333333	26.2219	97.79575056	147.8379	n.a.
2	2	7.693333333	0.591024	2.204249443	3.15228	n.a.

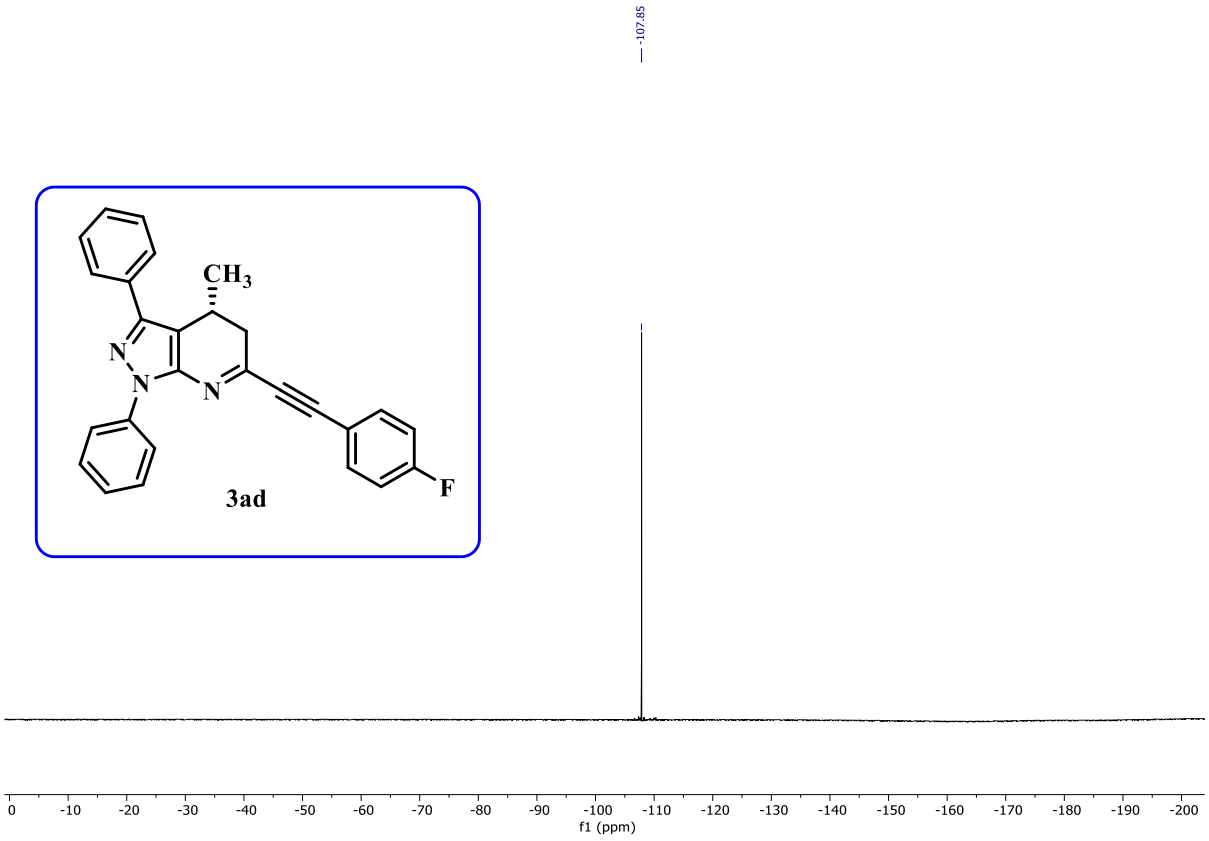
^{1}H NMR (400 MHz, $CDCl_3$)



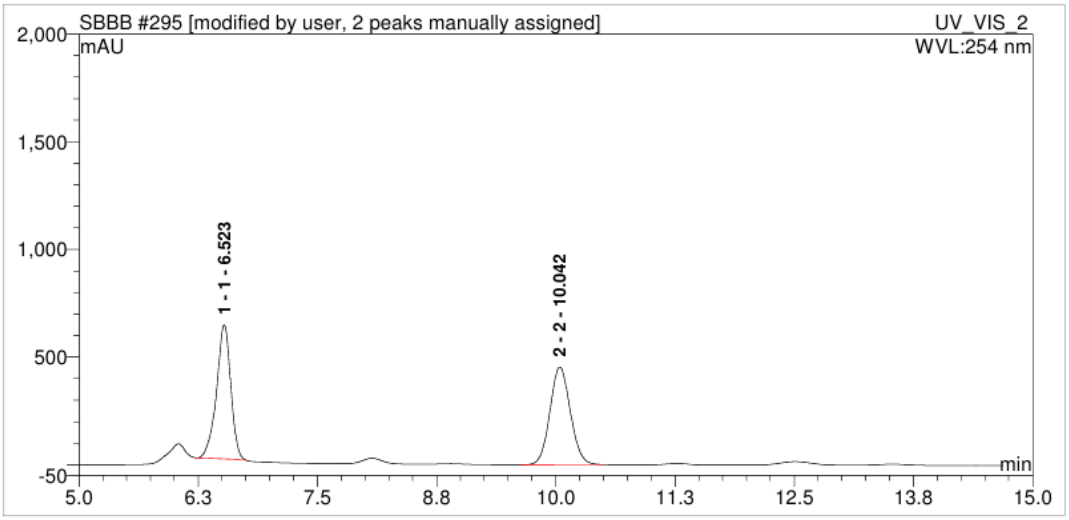
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)

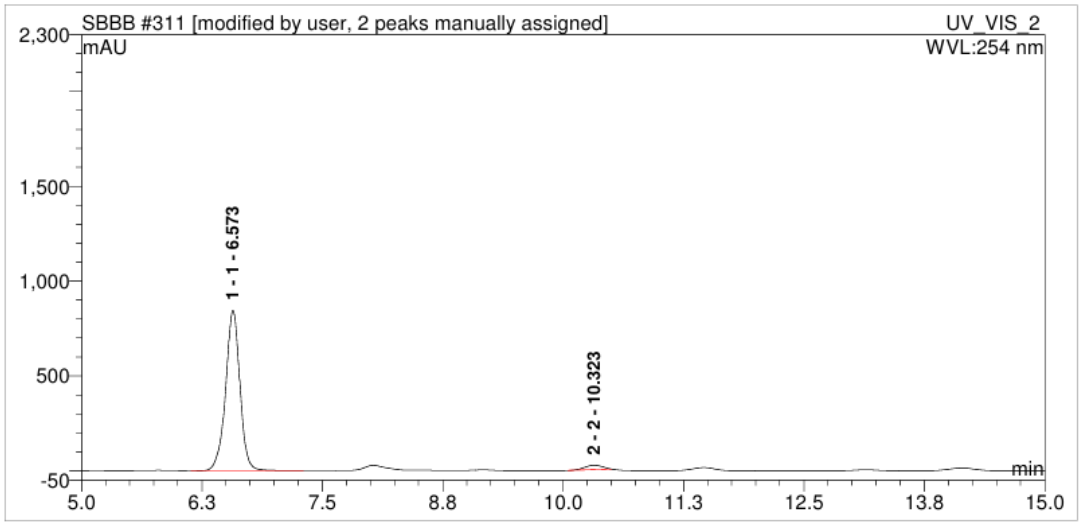


HPLC Spectra of *rac*-3ad



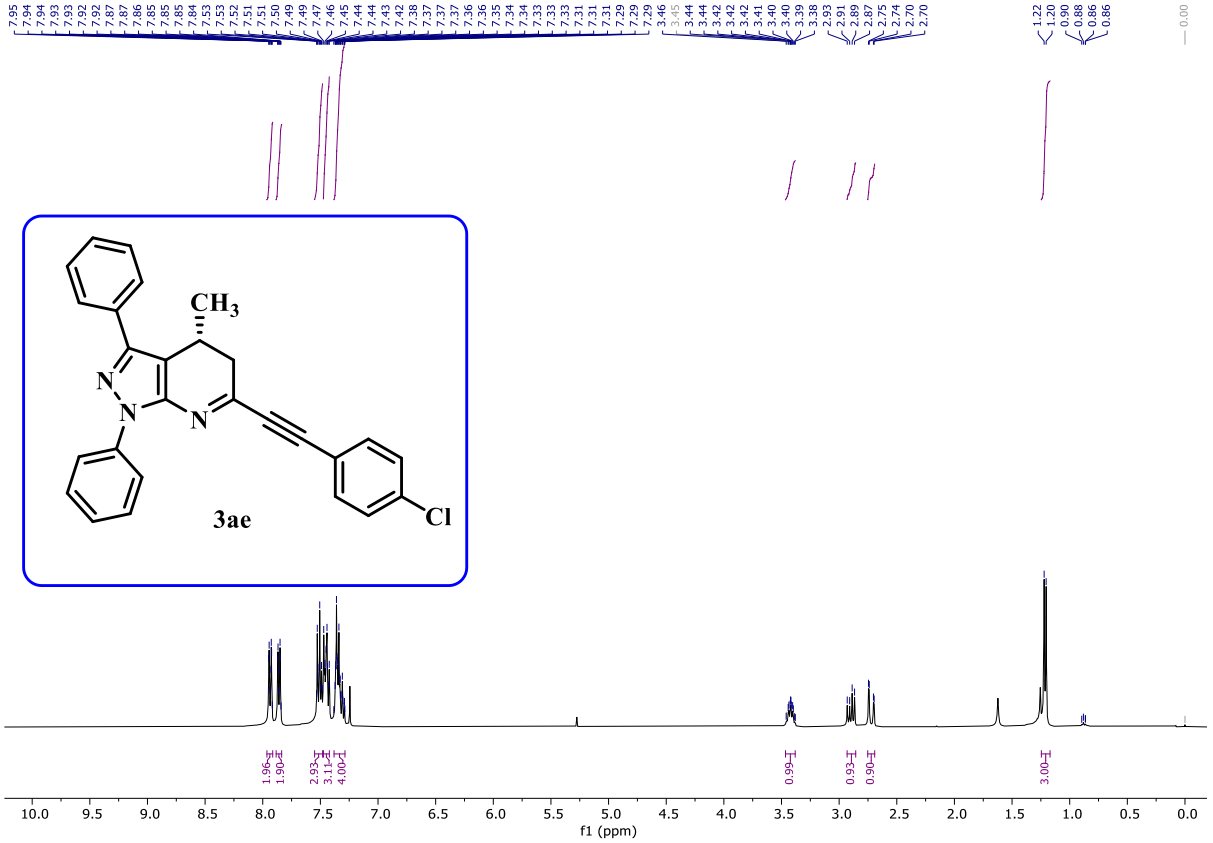
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.523333333	108.0288	49.03556335	622.6325	n.a.
2	2	10.04166667	112.2782	50.96443665	453.2101	n.a.

HPLC Spectra of *chi*-3ad

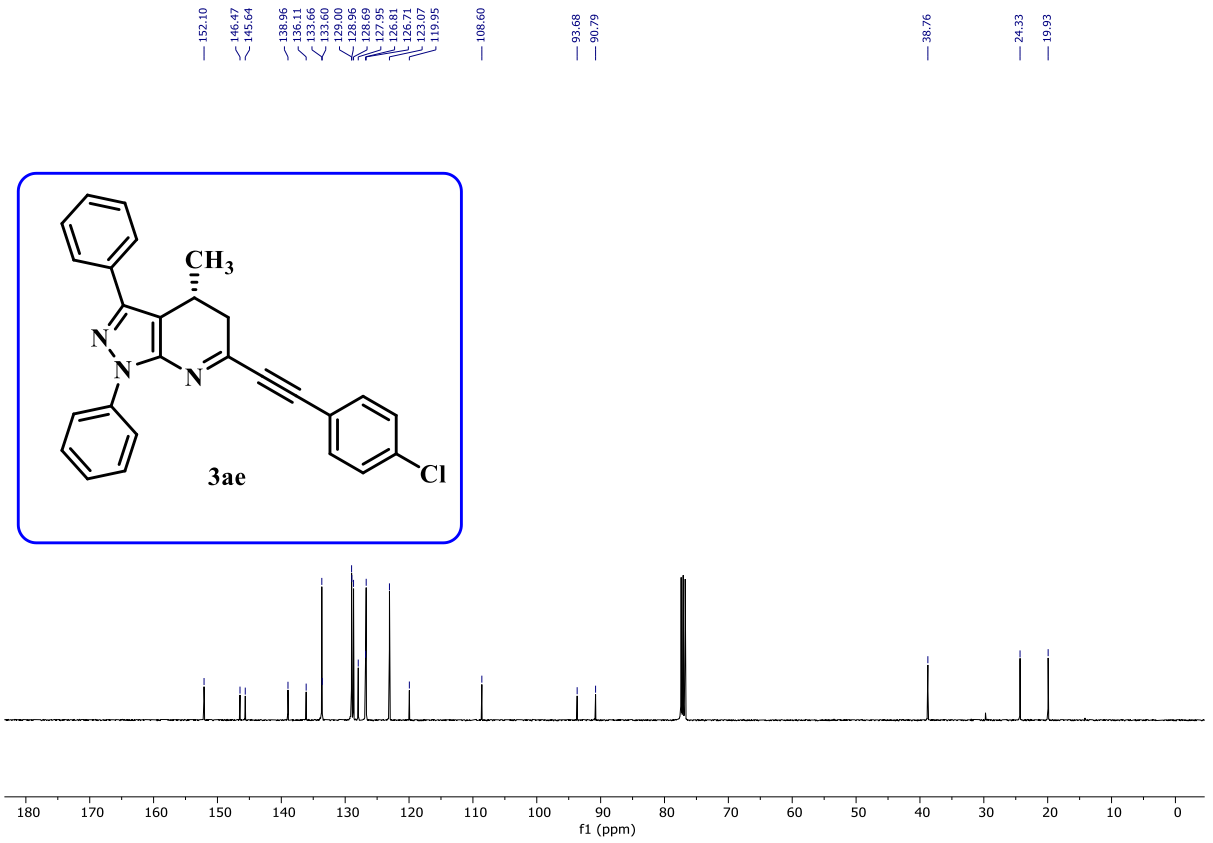


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.573333333	145.4385	96.67075511	844.1064	n.a.
2	2	10.32333333	5.008757	3.329244889	23.28428	n.a.

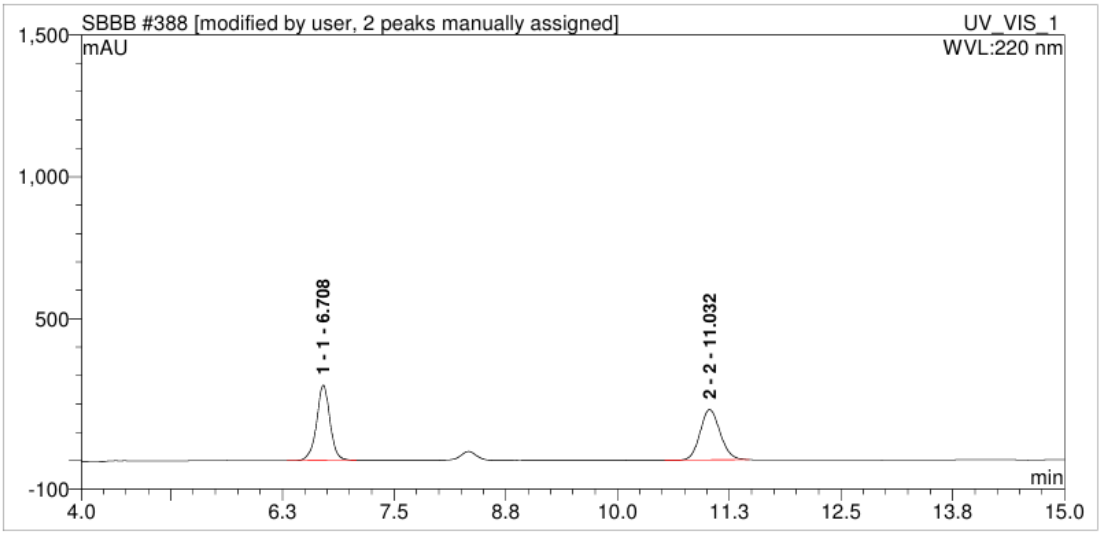
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

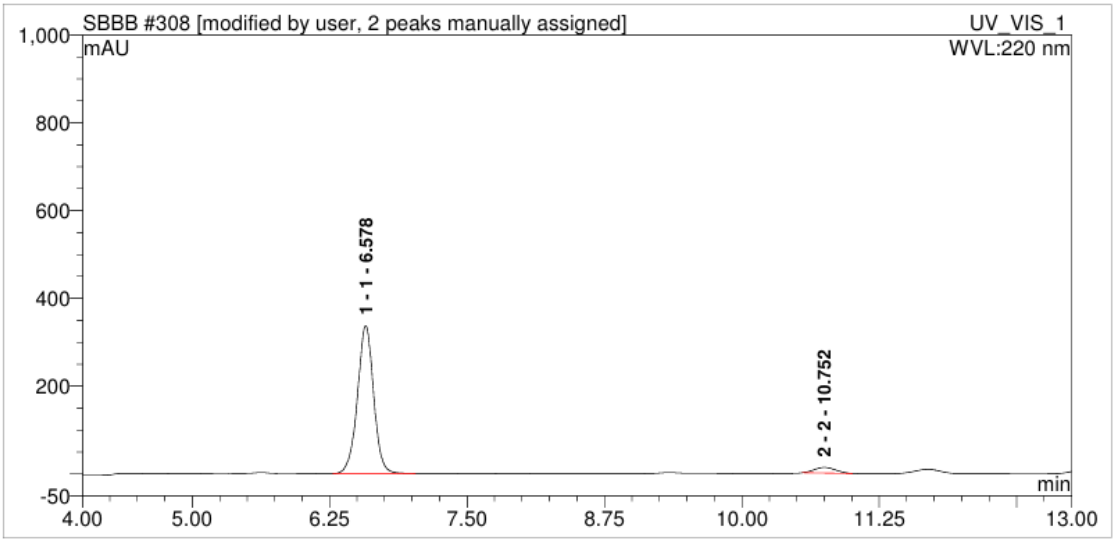


HPLC Spectra of *rac*-3ae



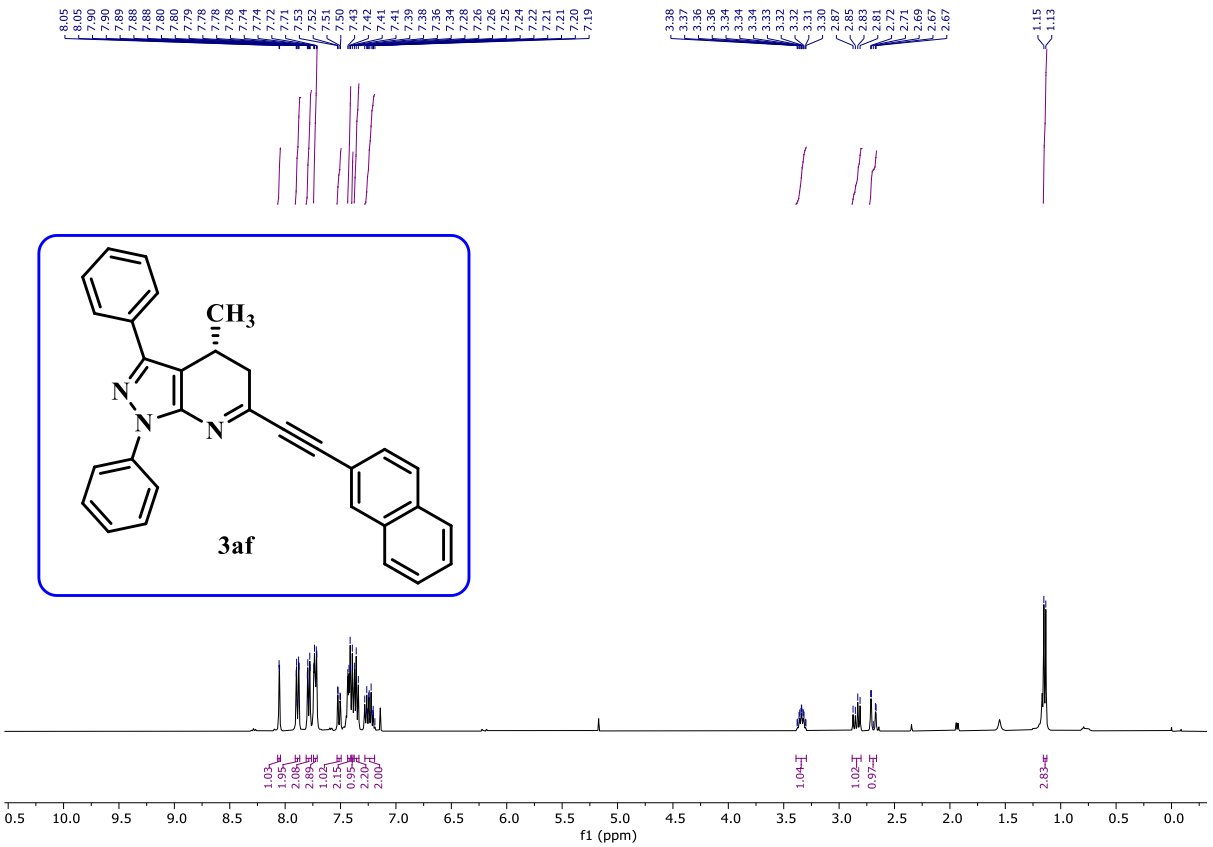
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.708333333	46.29894	50.15633749	265.2409	n.a.
2	2	11.03166667	46.01032	49.84366251	177.2285	n.a.

HPLC Spectra of *chi*-3ae

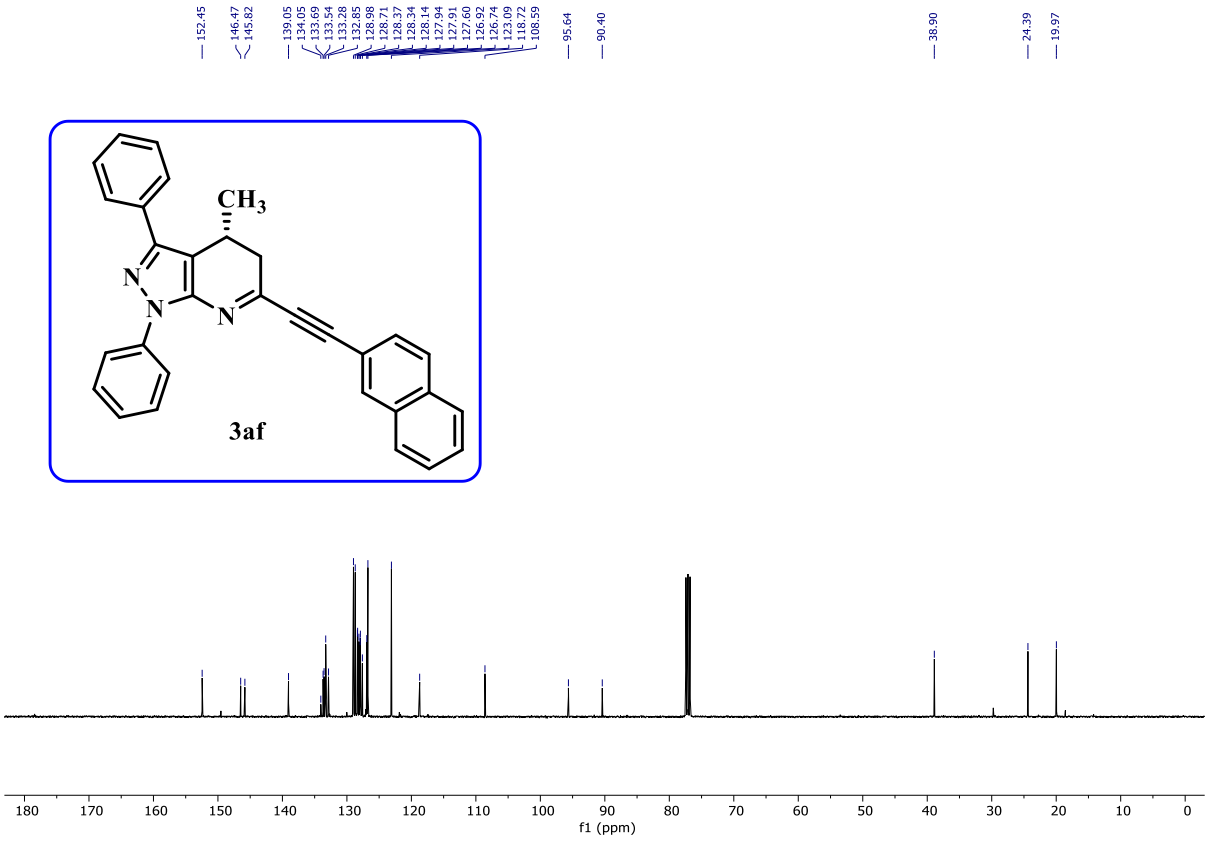


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	6.578333333	57.60876	95.30843357	337.1054	n.a.
2	2	10.75166667	2.835797	4.691566433	12.79814	n.a.

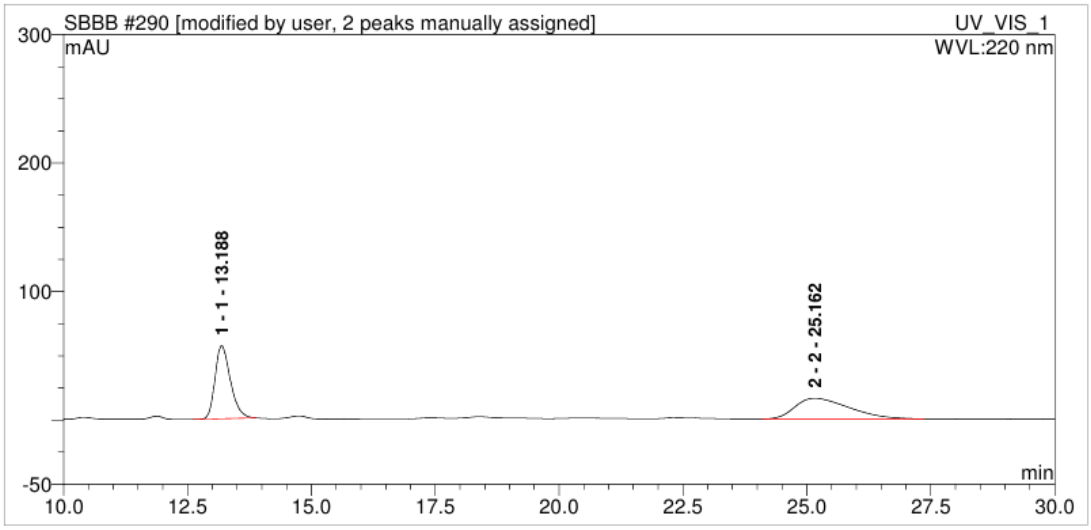
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

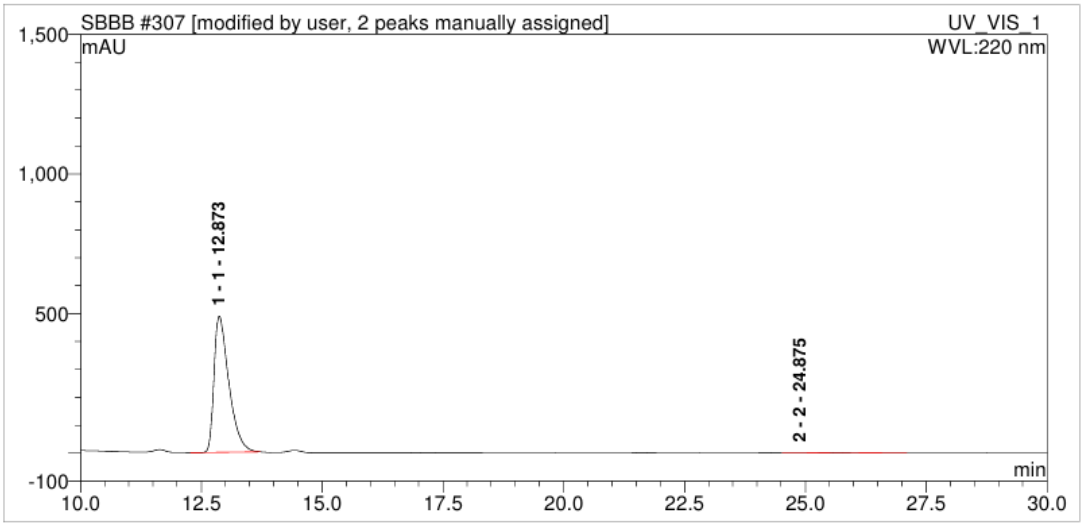


HPLC Spectra of *rac*-3af



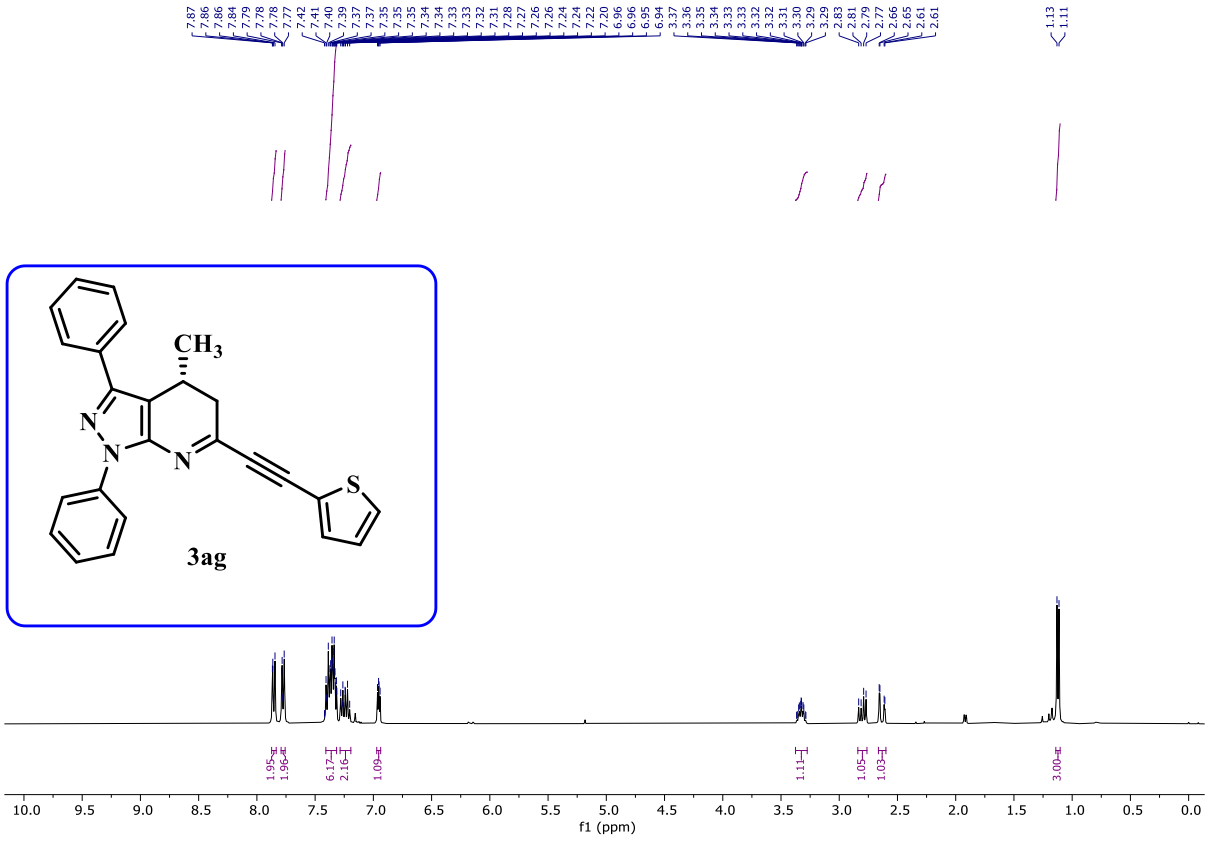
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	13.18833333	20.52865	50.34296562	56.88801	n.a.
2	2	25.16166667	20.24894	49.65703438	16.05286	n.a.

HPLC Spectra of *chi*-3af

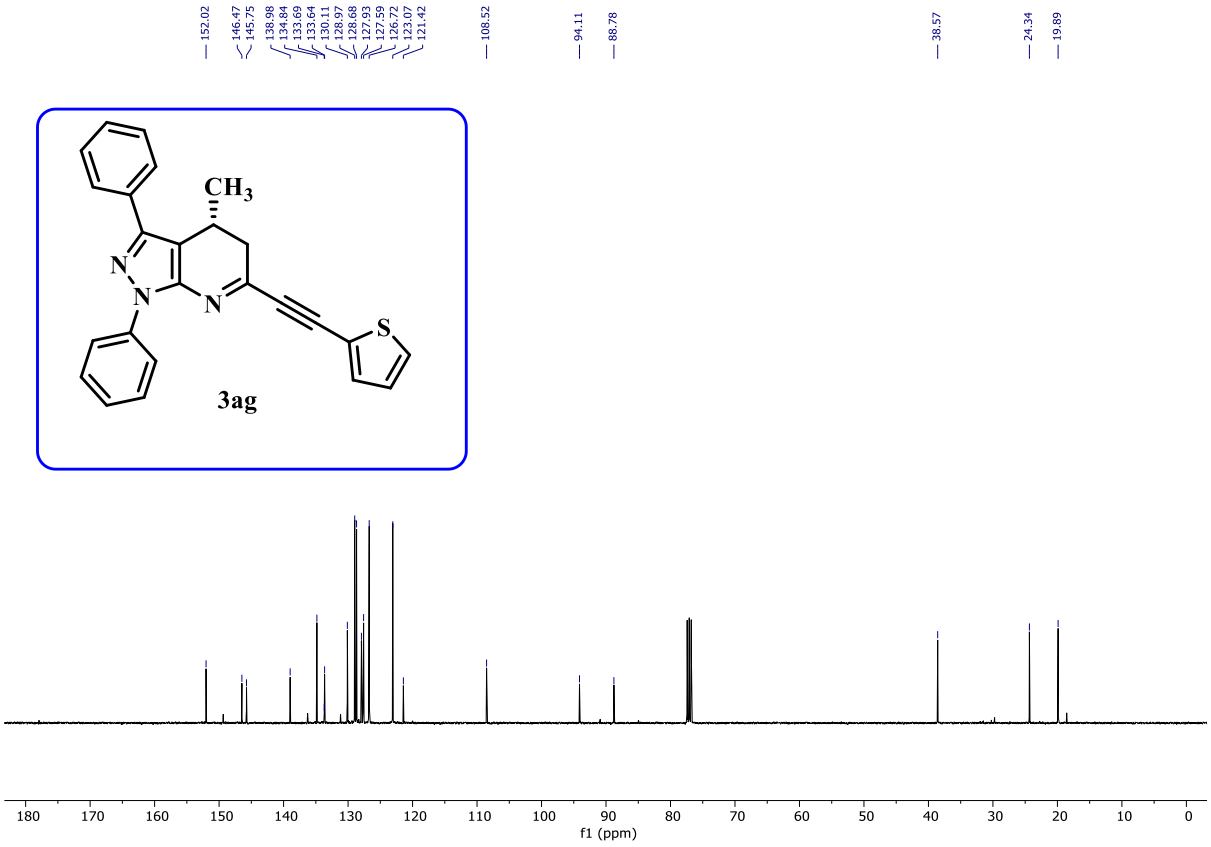


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	12.87333333	173.5329	99.98549309	488.1626	n.a.
2	2	24.875	0.025178	0.01450691437	1.0031	n.a.

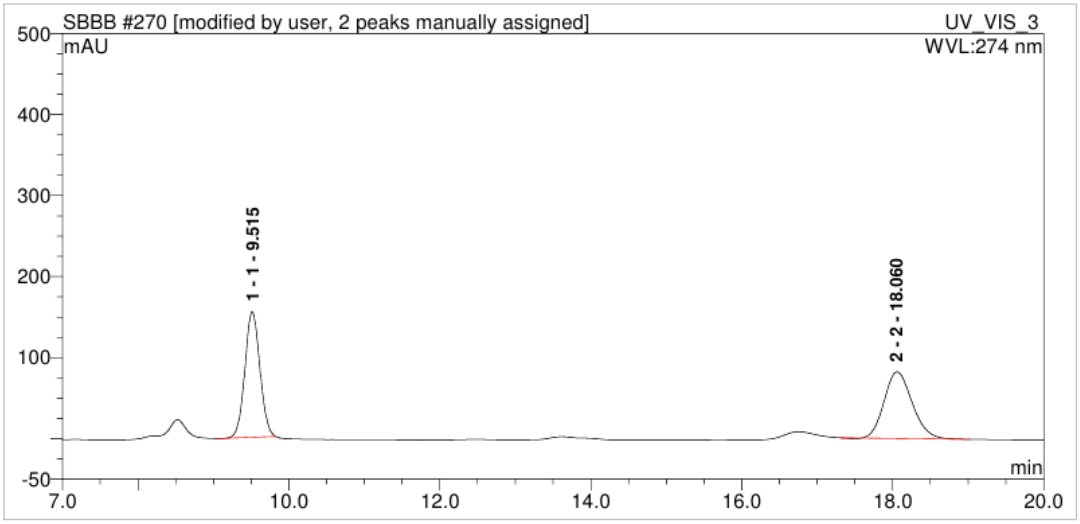
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

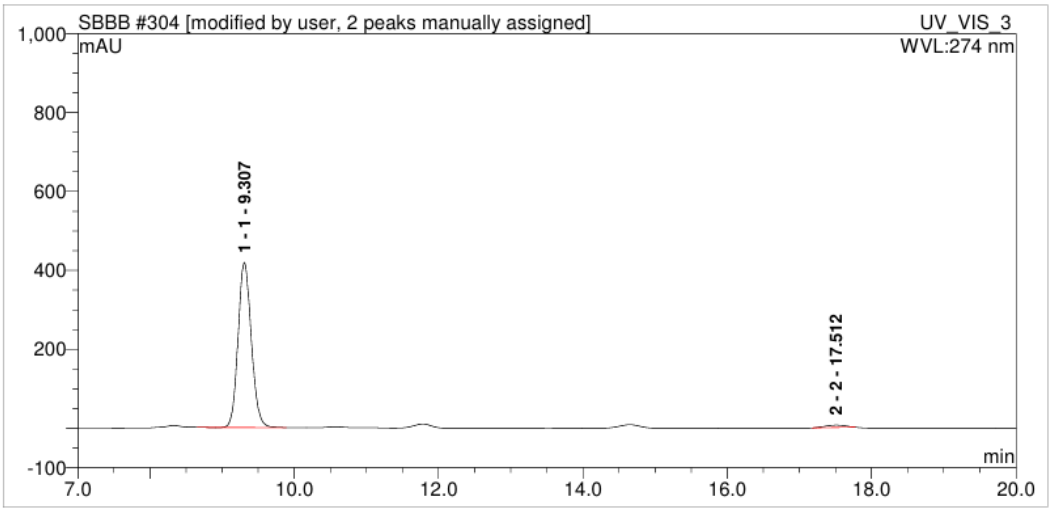


HPLC Spectra of *rac*-3ag



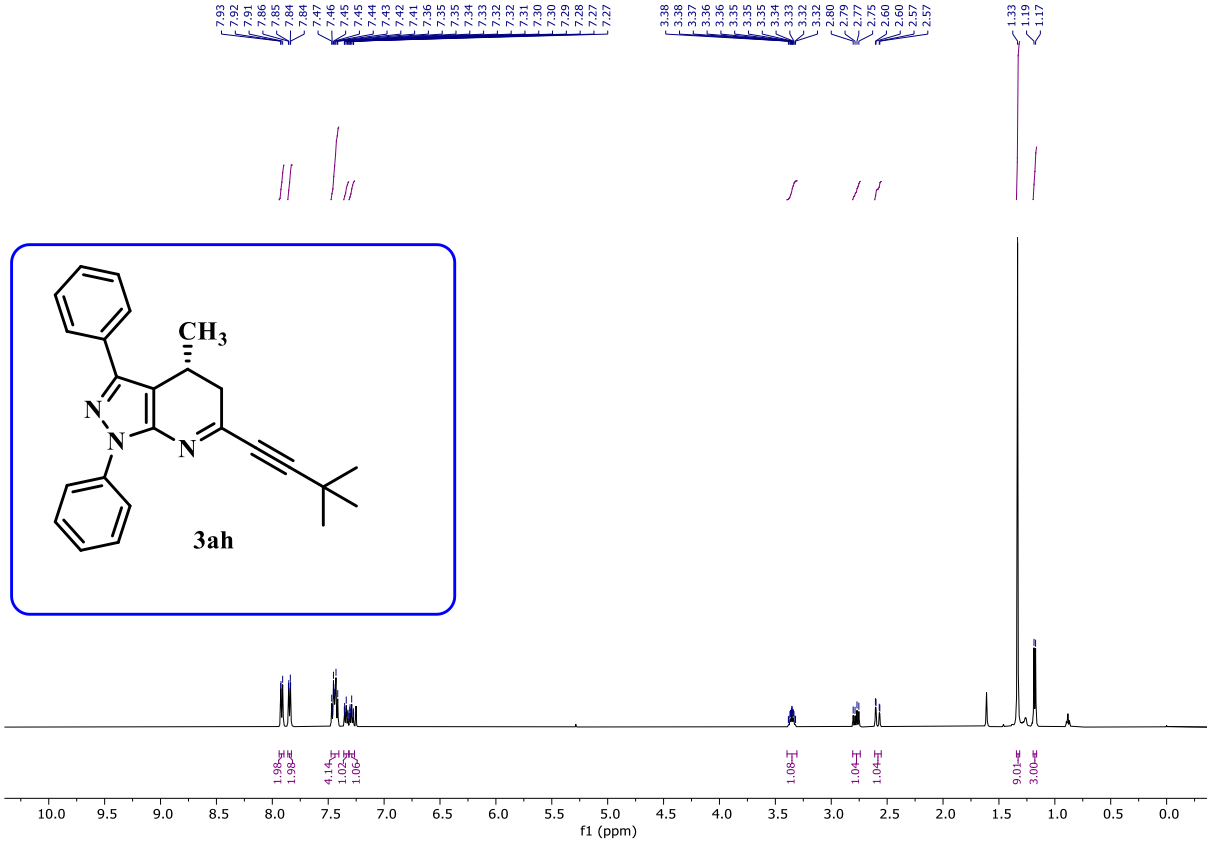
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	9.515	35.765	50.31284023	155.3328	n.a.
2	2	18.06	35.32023	49.68715977	82.2659	n.a.

HPLC Spectra of *chi*-3ag

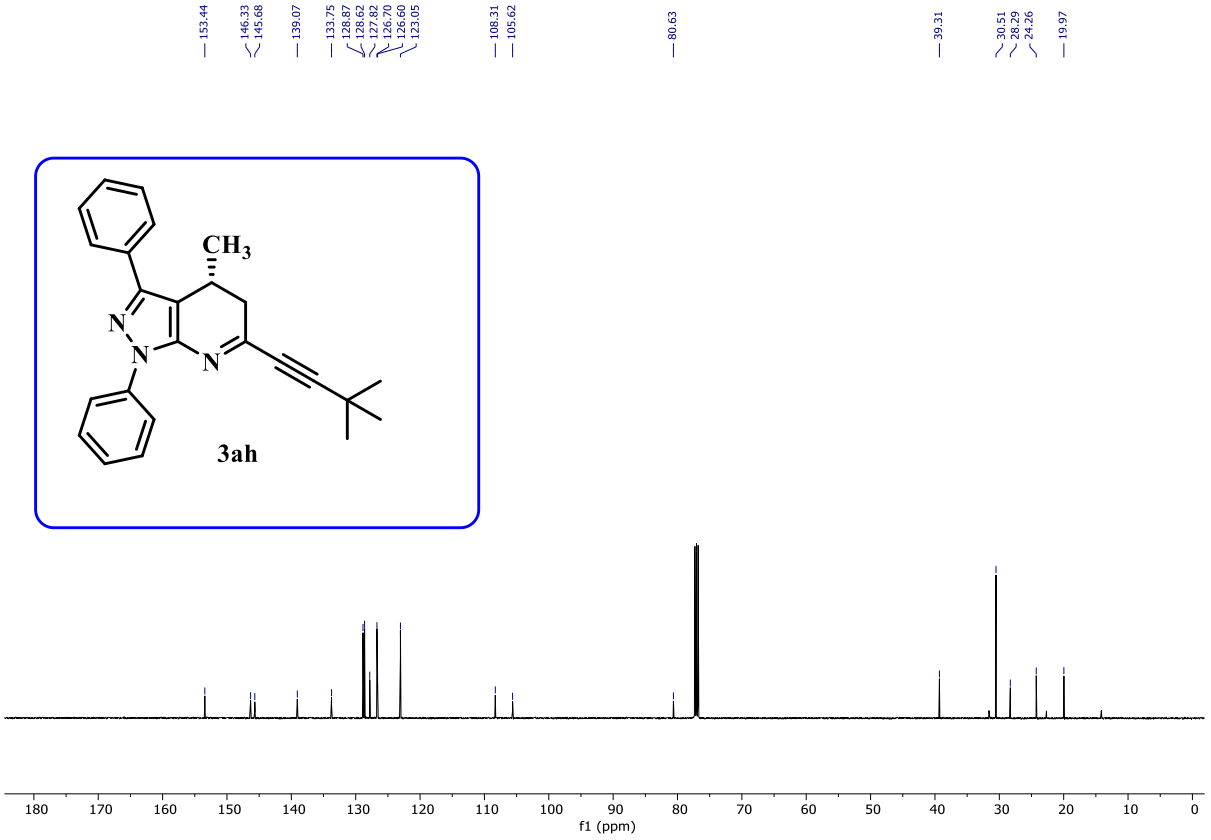


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	9.306666667	88.87701	97.79829764	417.9446	n.a.
2	2	17.51166667	2.00086	2.201702358	6.12748	n.a.

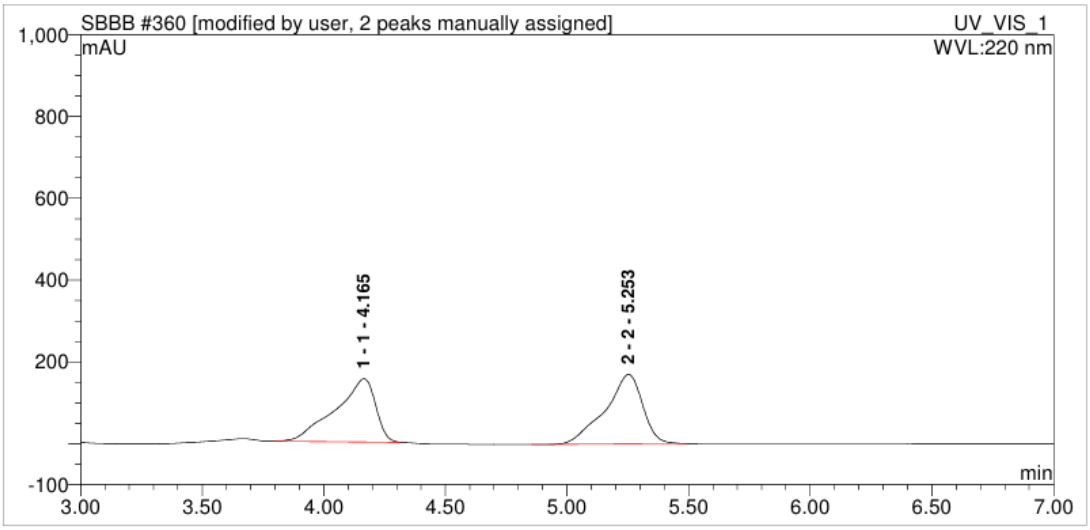
^{1}H NMR (500 MHz, $CDCl_3$)



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

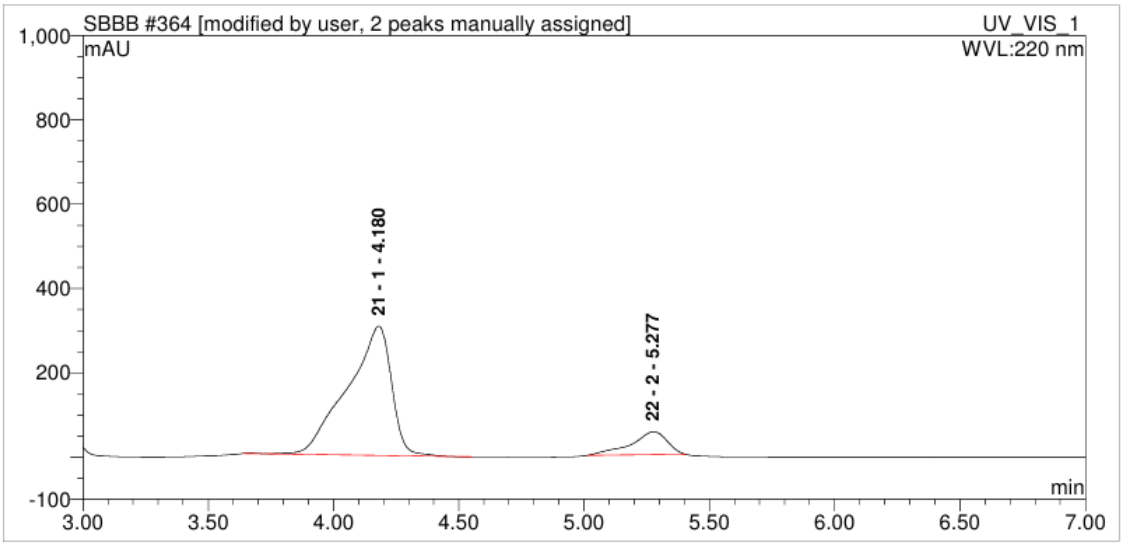


HPLC Spectra of *rac*-3ah



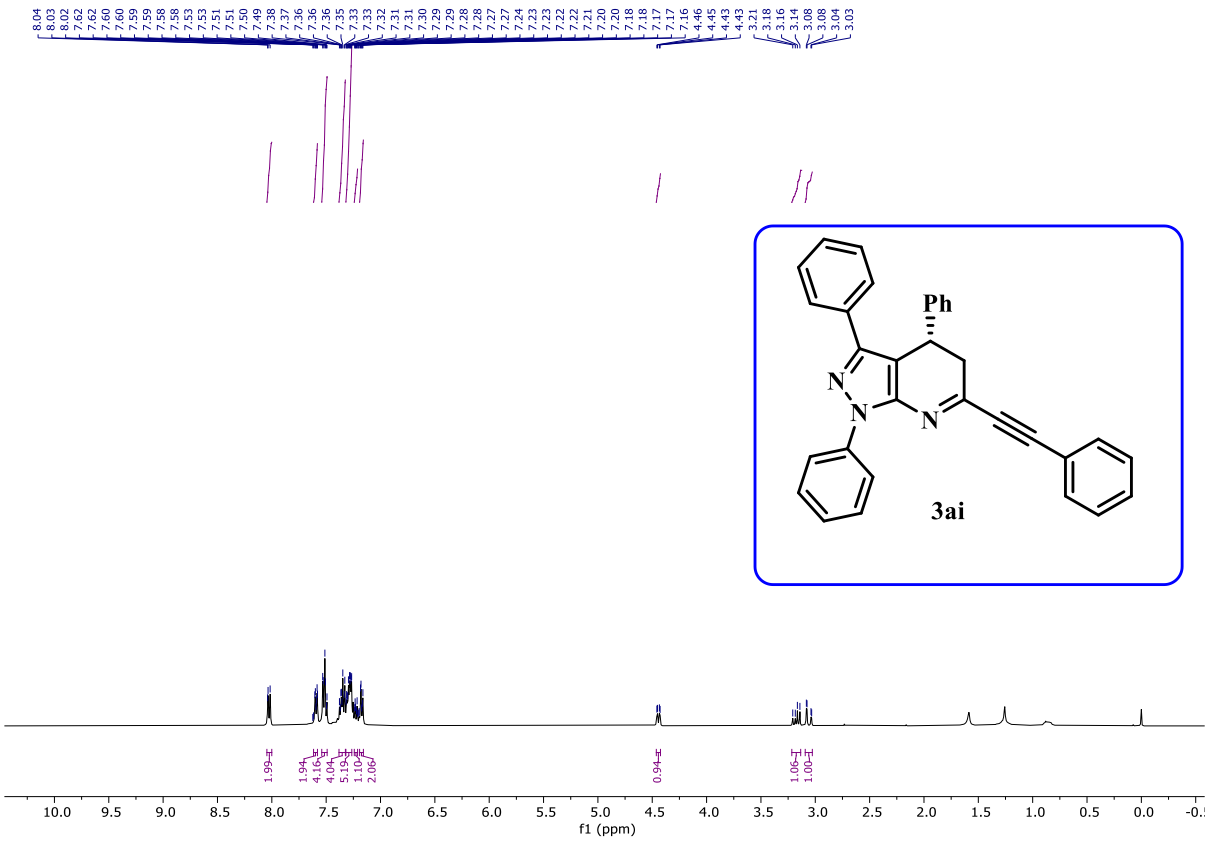
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	4.165	29.65074	49.24976262	154.6905	n.a.
2	2	5.253333333	30.5541	50.75023738	170.1549	n.a.

HPLC Spectra of *chi*-3ah

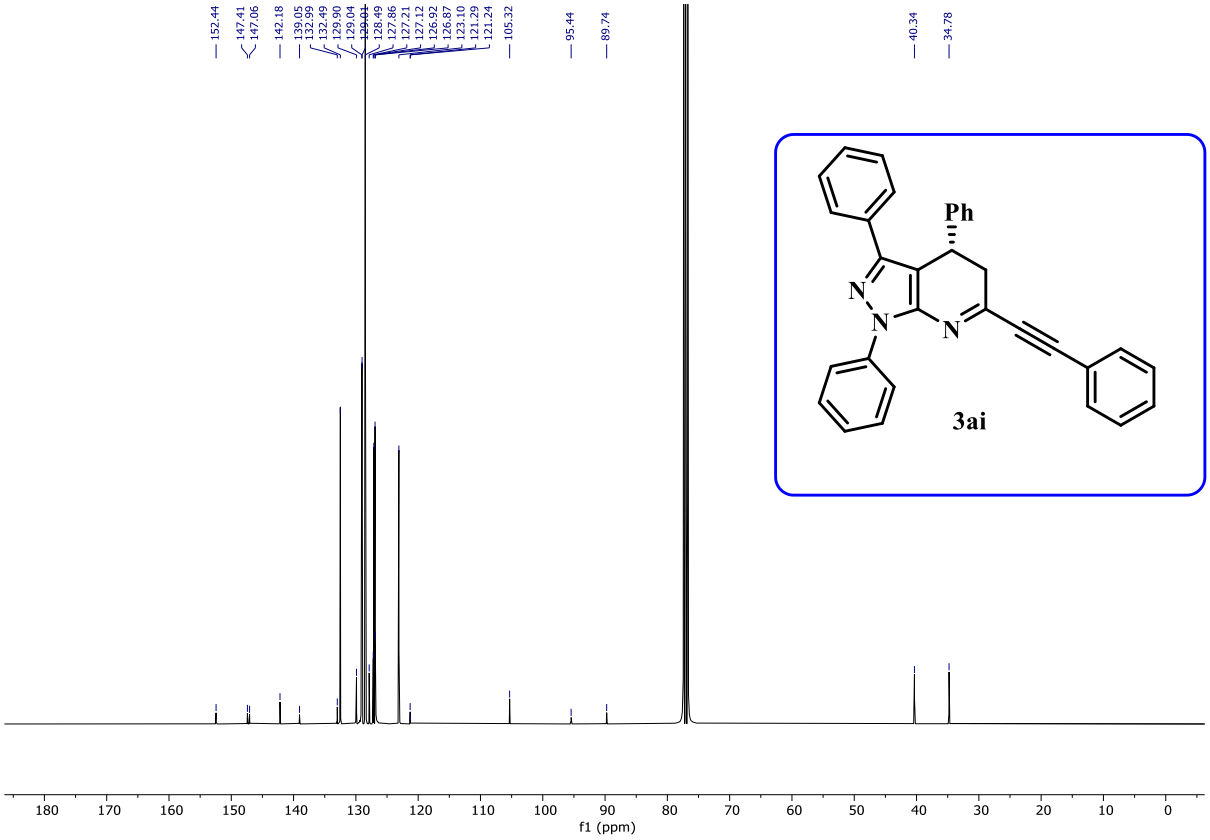


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	Peak 1	0.05166666667	0.001489	0.002074342475	0.02431	n.a.
21	1	4.18	62.6773	87.31449231	306.8813	n.a.
22	2	5.276666667	9.104598	12.68343335	54.43033	n.a.

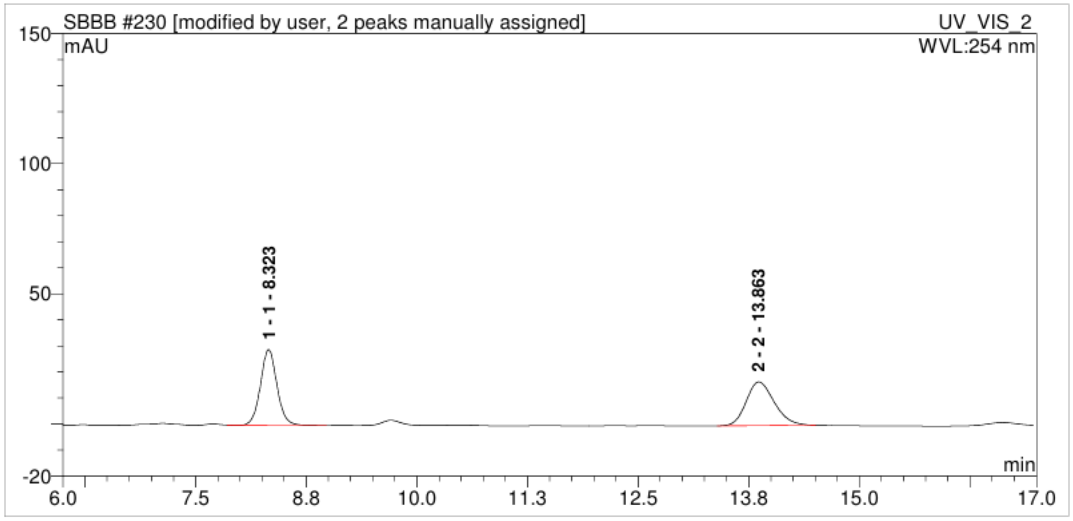
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)

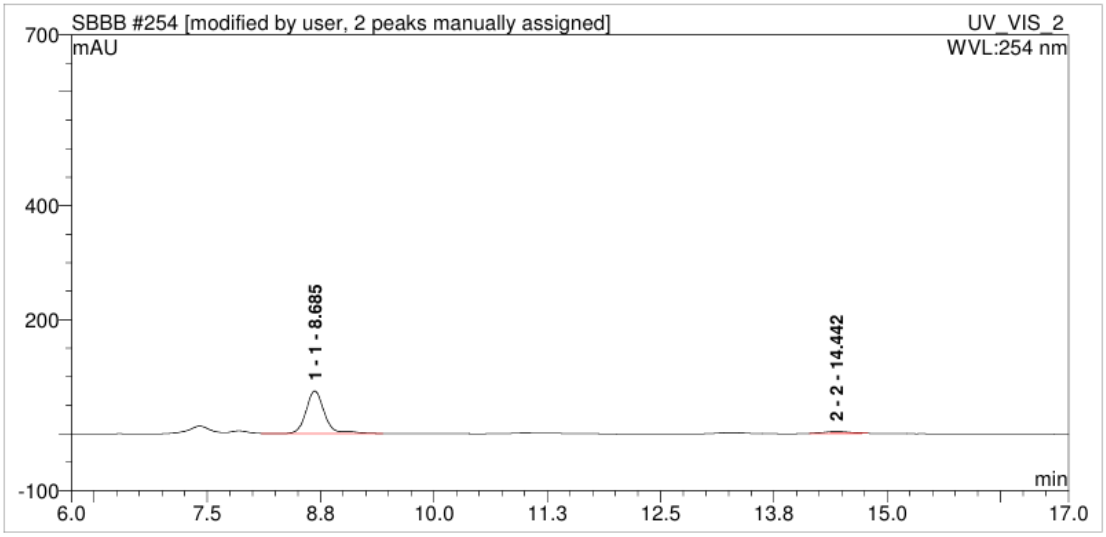


HPLC Spectra of *rac*-3ai



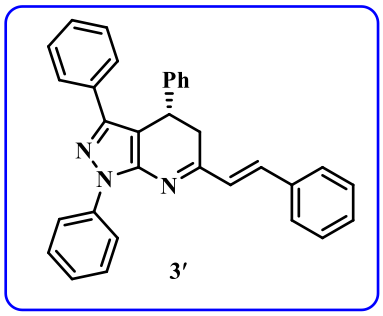
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.323333333	6.142488	49.85480728	28.95388	n.a.
2	2	13.86333333	6.178266	50.14519272	16.79822	n.a.

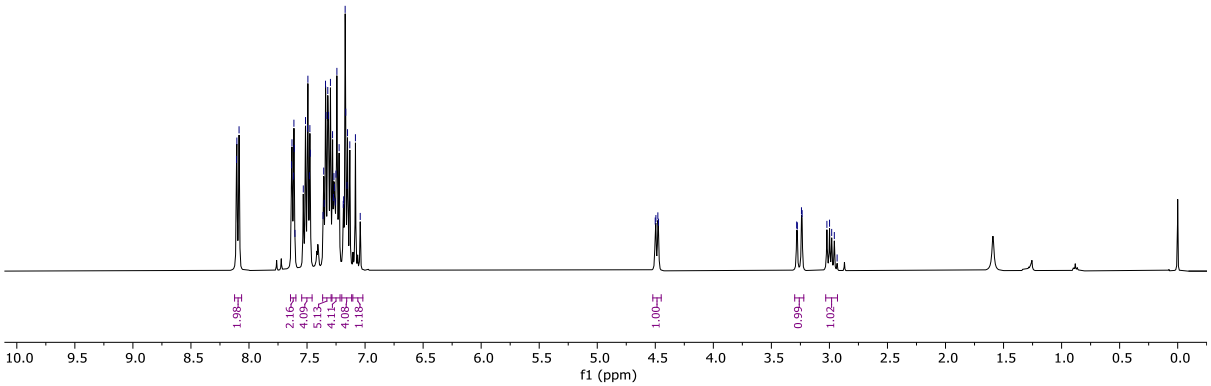
HPLC Spectra of *chi*-3ai



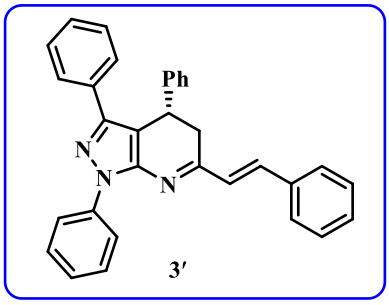
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	8.685	17.34364	94.21978376	74.58025	n.a.
2	2	14.44166667	1.064001	5.780216237	3.16703	n.a.

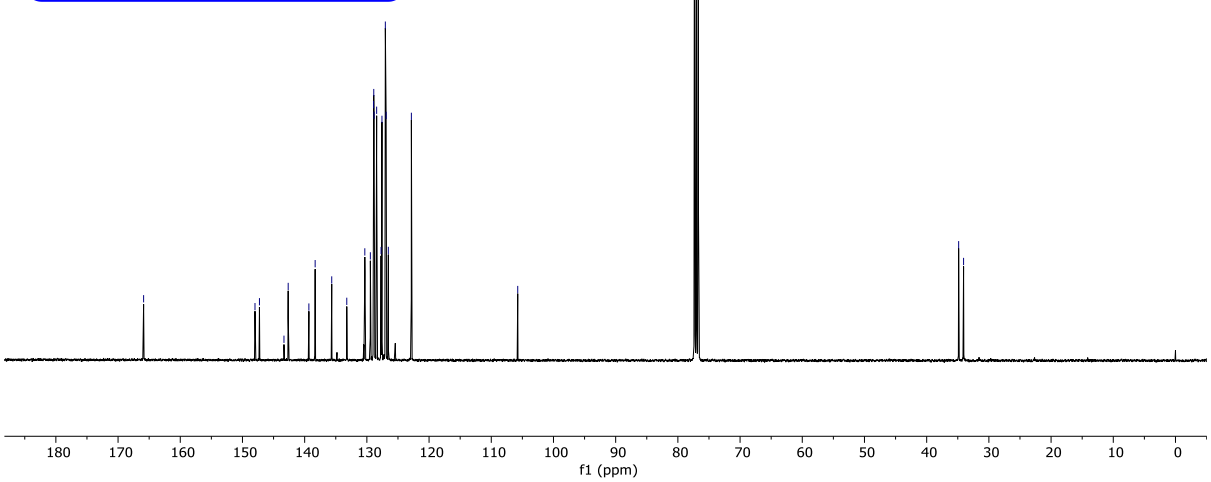
^{1}H NMR (400 MHz, $CDCl_3$)



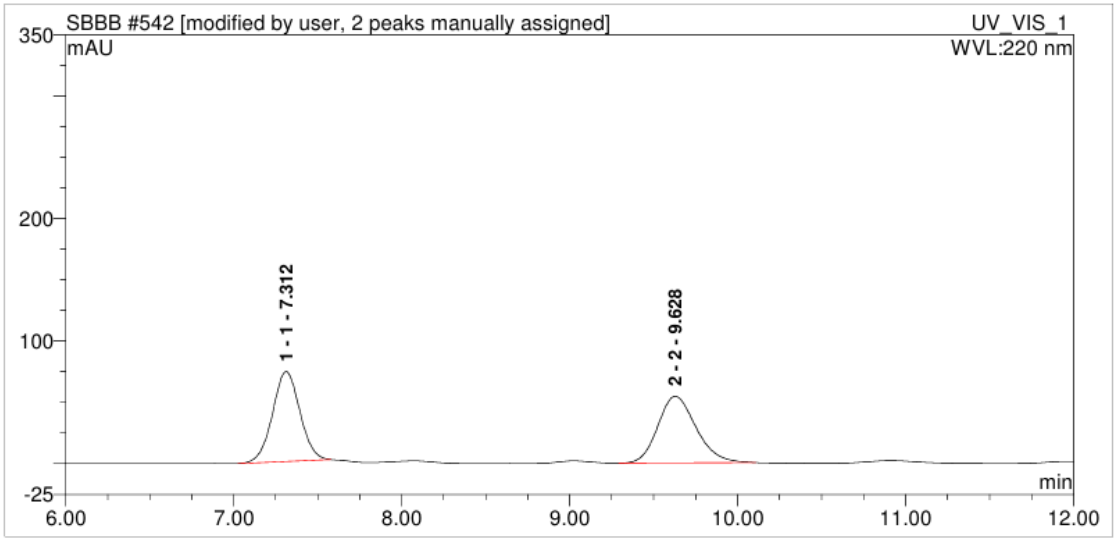


^{13}C NMR (101 MHz, $CDCl_3$)



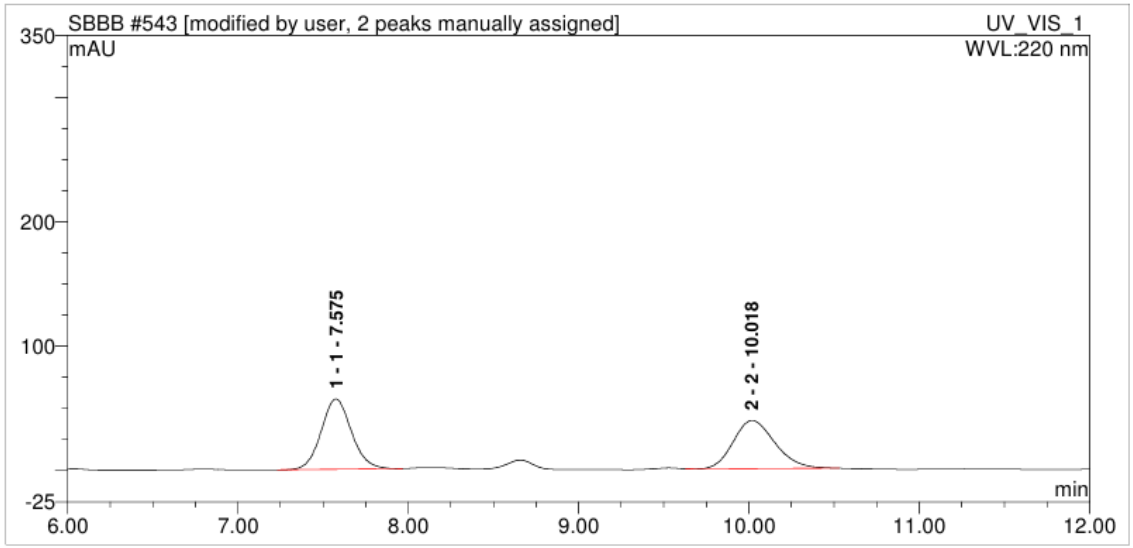


HPLC Spectra of *rac*-3'



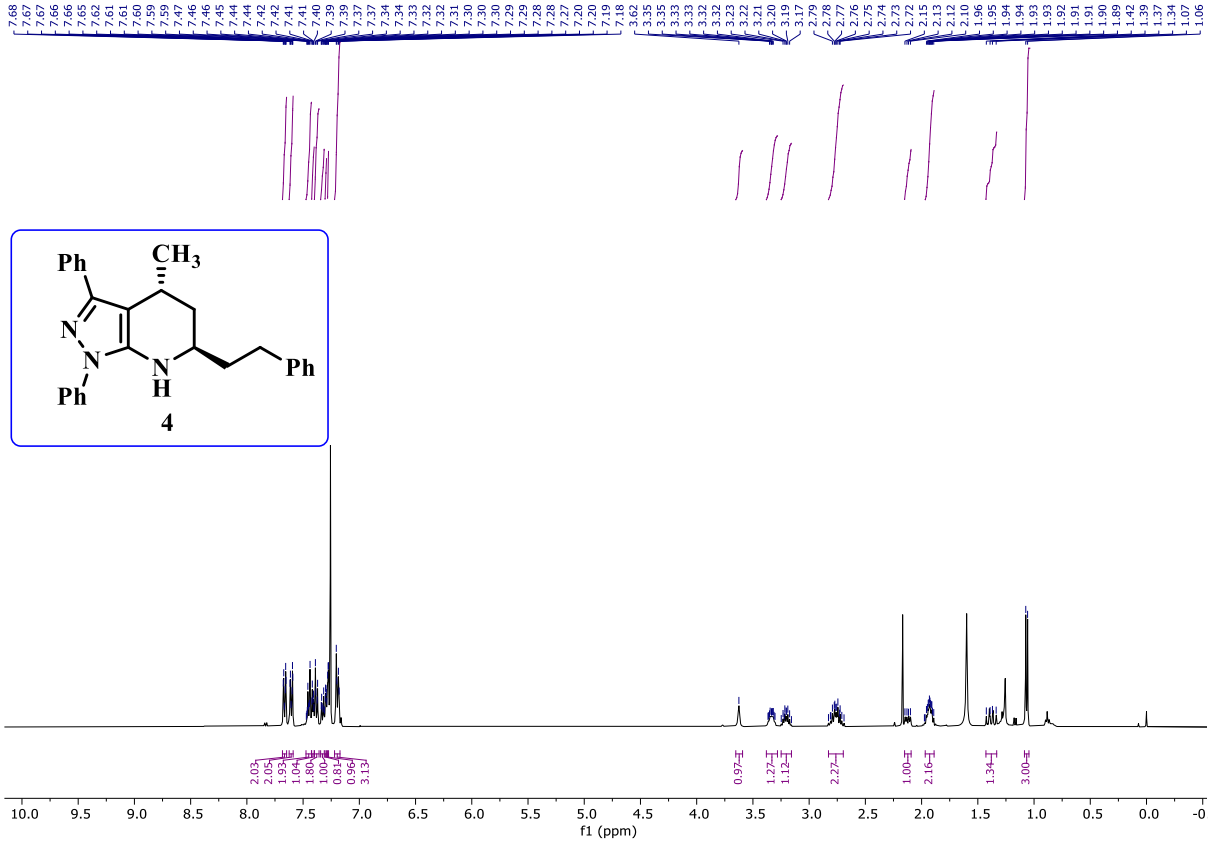
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.311666667	13.84283	49.1299216	73.26139	n.a.
2	2	9.628333333	14.33314	50.8700784	54.29273	n.a.

HPLC Spectra of *chi*-3'

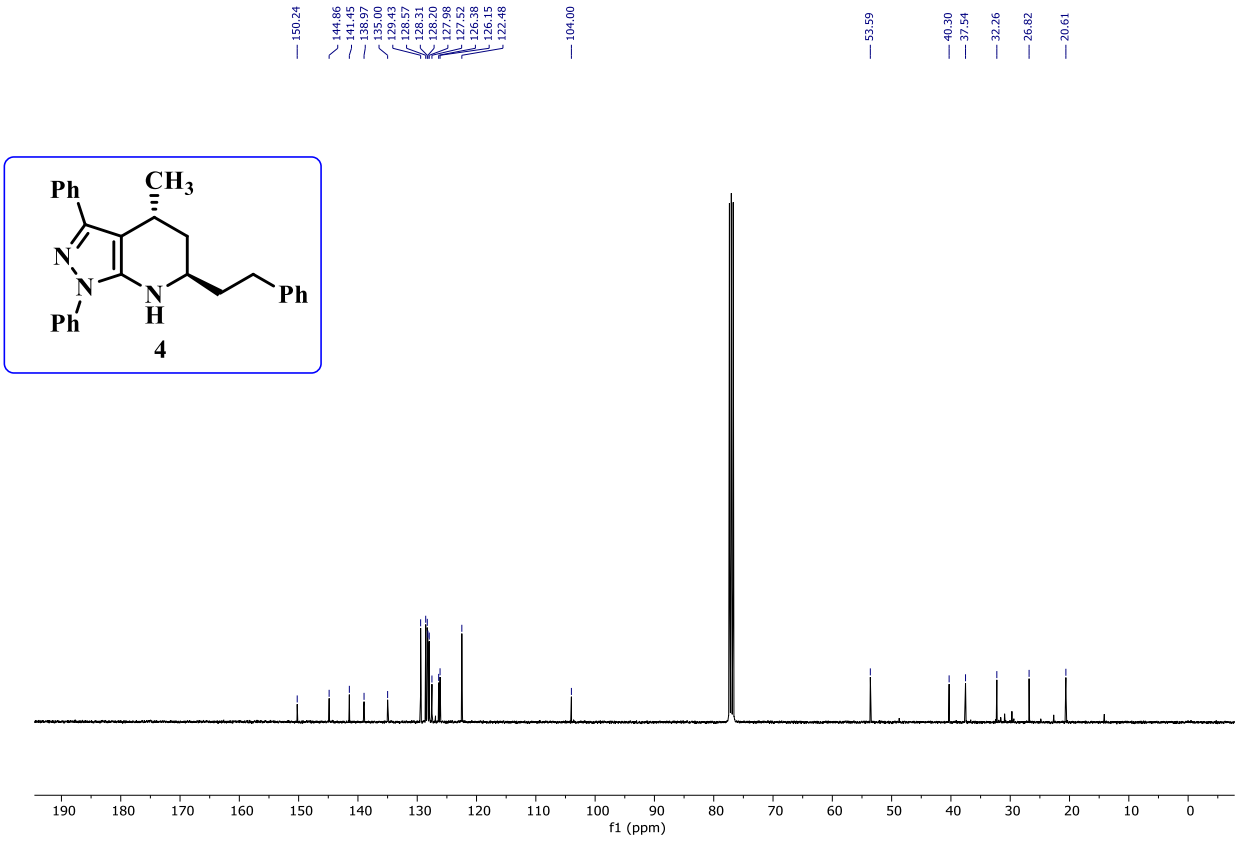


No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	7.575	11.60491	51.53043964	56.40401	n.a.
2	2	10.01833333	10.91559	48.46956036	38.68338	n.a.

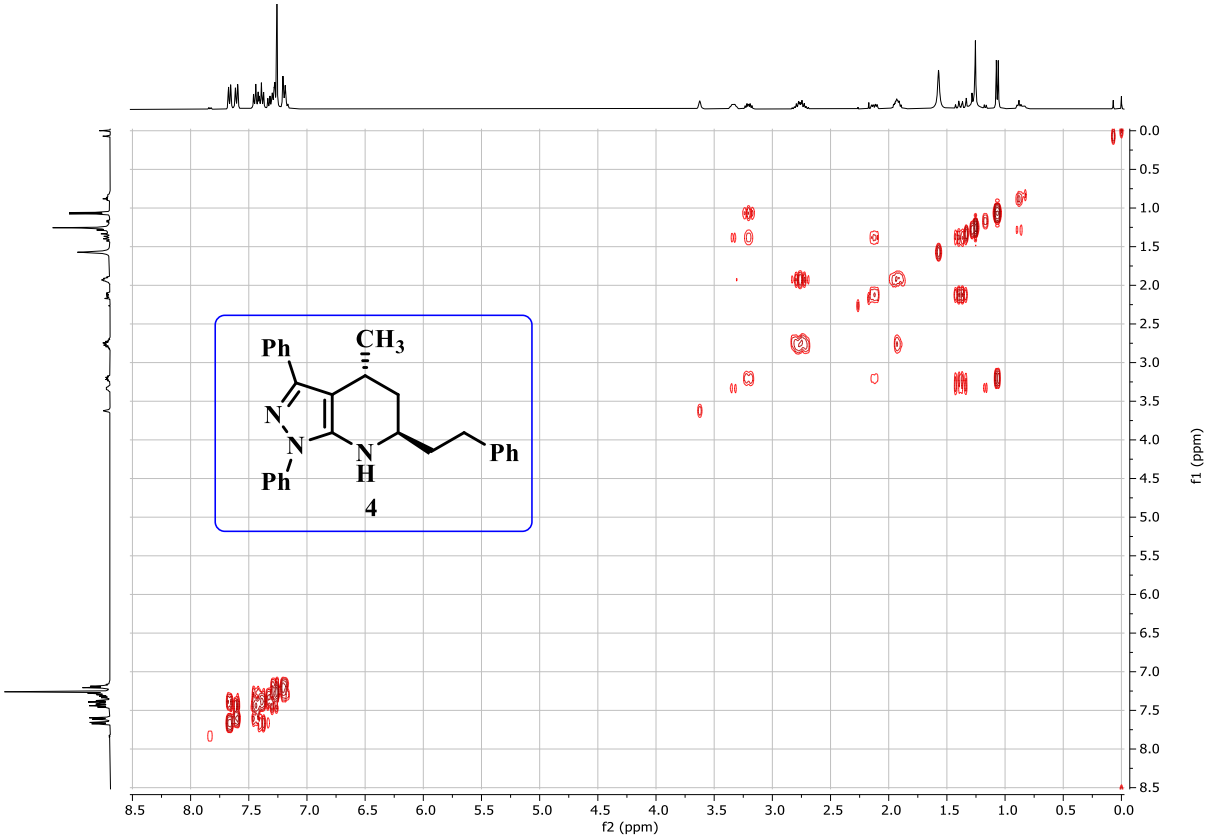
^{1}H NMR (400 MHz, $CDCl_3$)



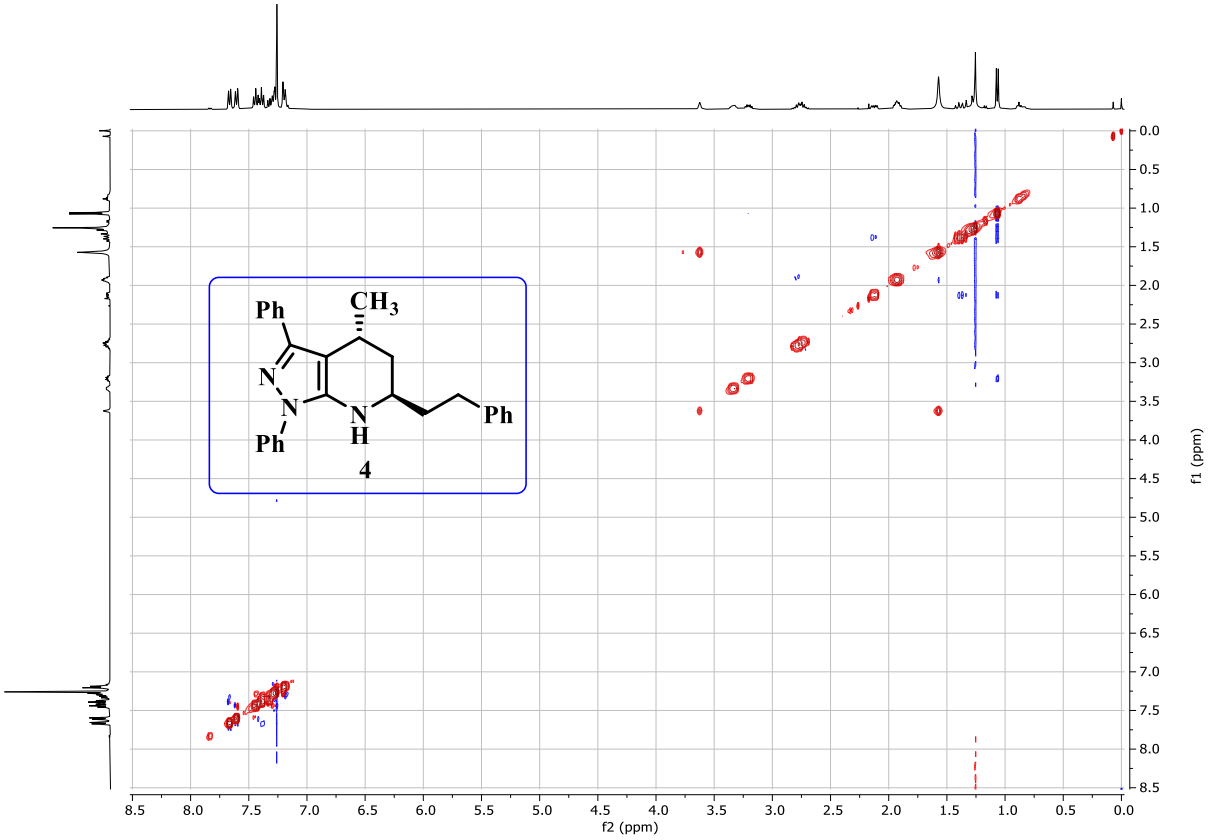
^{13}C NMR (101 MHz, $CDCl_3$)



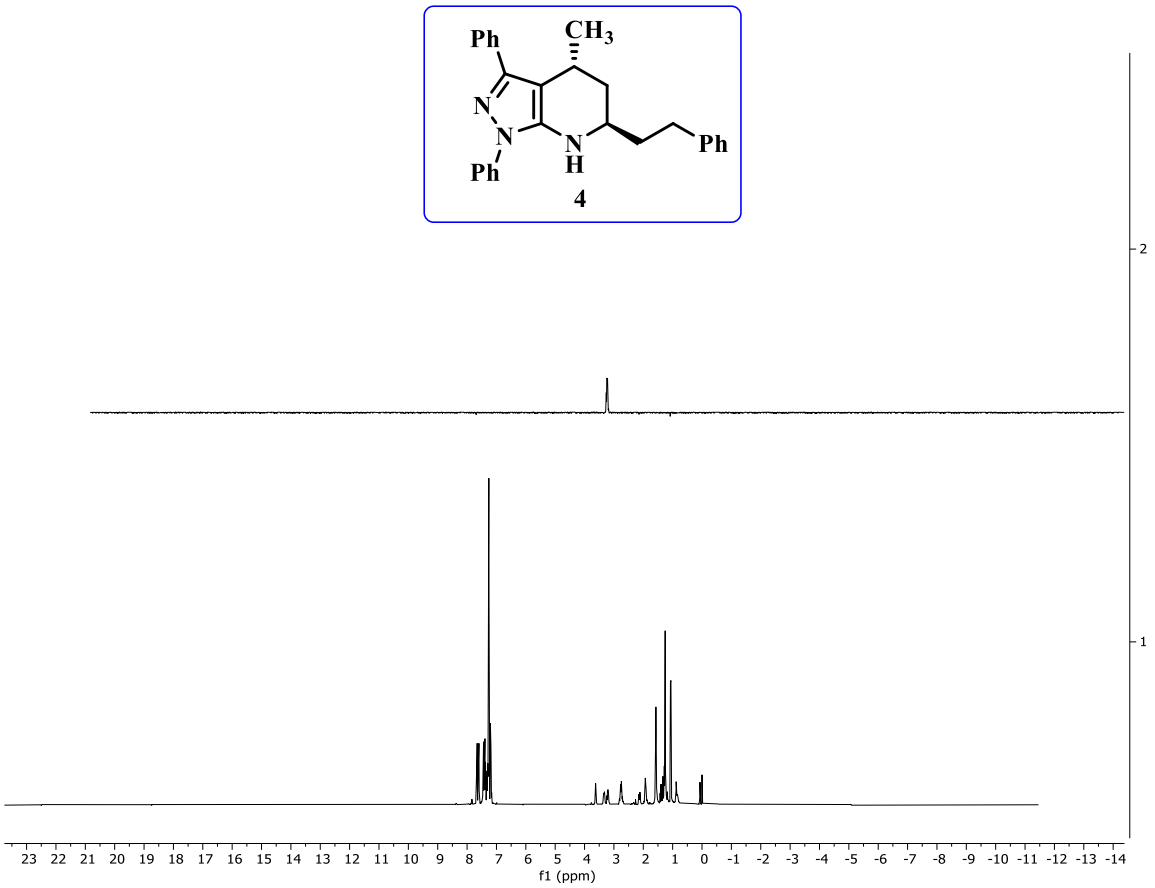
COSY (400 MHz, $CDCl_3$)



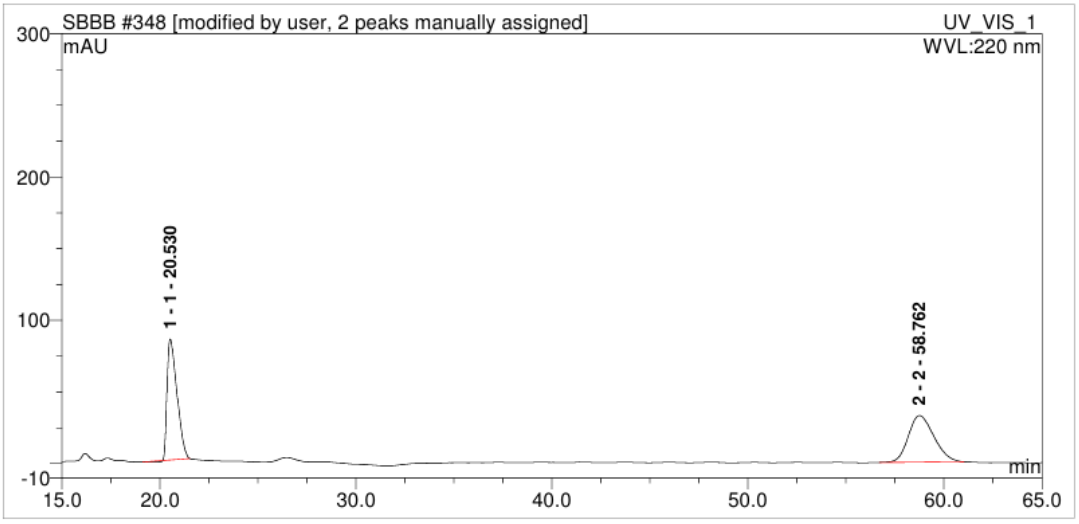
NOSEY (400 MHz, $CDCl_3$)



1D NOE (400 MHz, $CDCl_3$)

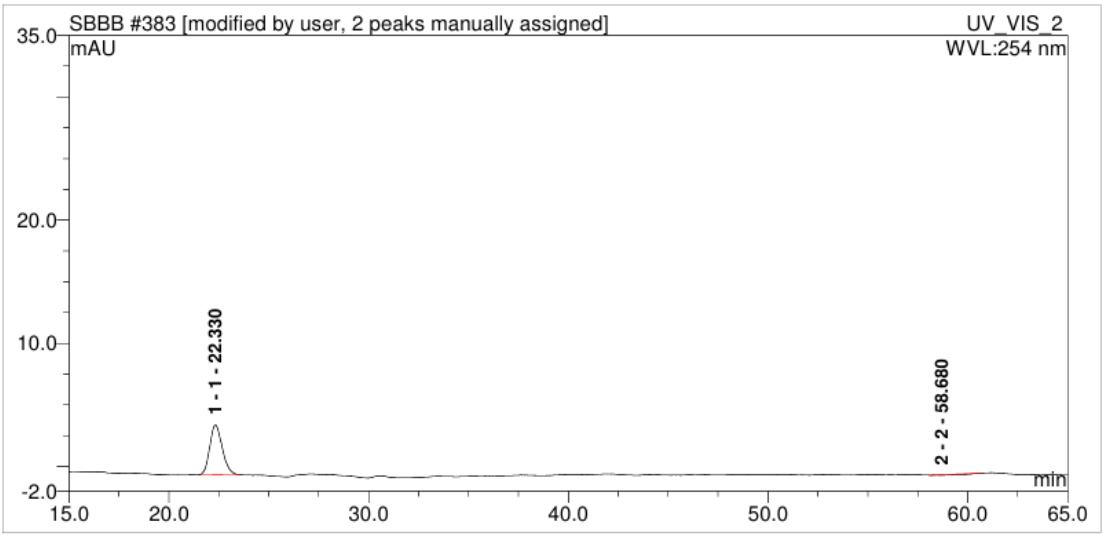


HPLC Spectra of *rac*-4



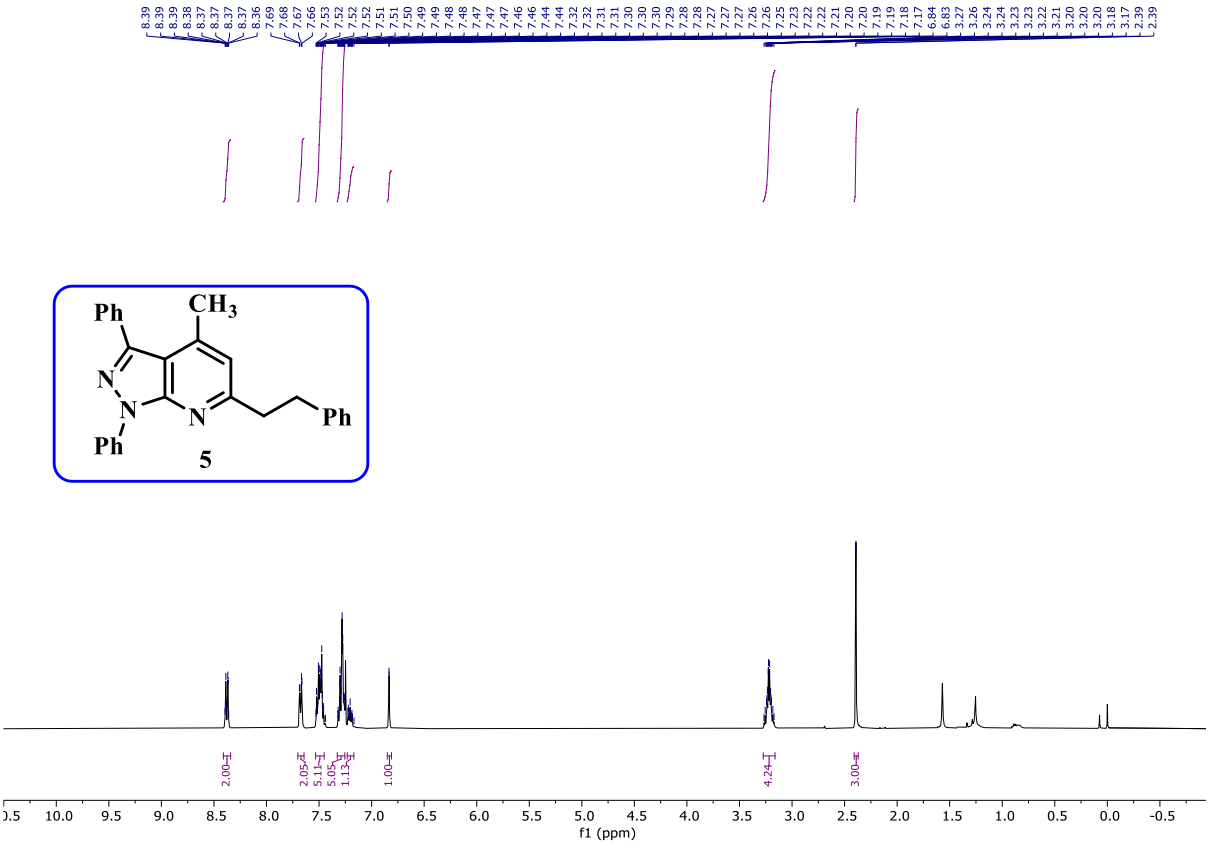
No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	20.53	48.87725	49.91393627	84.33812	n.a.
2	2	58.76166667	49.04581	50.08606373	32.48036	n.a.

HPLC Spectra of *chi*-4



No.	Peak Name	Ret.Time (detected) min	Area mAU*min	Rel.Area(ident.) %	Height mAU	Amount
1	1	22.33	2.90525	97.25389522	4.00527	n.a.
2	2	58.68	0.082034	2.746104777	0.04476	n.a.

^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)