Supplementary Information

Synthesis of pyranopyrazoles with a chiral quaternary carbon stereocenter *via* copper-catalyzed enantioselective [3+3] cycloaddition

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CONTENT

1. General Information

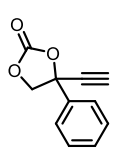
Reagents and Solvents: PE refers to petroleum ether b.p. 60 − 90 °C and EA refers to ethyl acetate. All starting materials were commercially available and were used without further purification unless otherwise stated.

Chromatography: Flash column chromatography was carried out using commercially available 200-300 mesh under pressure unless otherwise indicated. Gradient flash chromatography was conducted eluting with PE/EA, they are listed as volume ratios.

Data collection: ^{1}H, ^{13}C and ^{19}F NMR spectra were collected on BRUKER AV-300 (300 MHz) or BRUKER AV-400 (400 MHz) spectrometer using $CDCl_3$ or DMSO-d_6 as solvent. Chemical shifts of ^{1}H NMR were recorded in parts per million (ppm, δ) relative to tetramethylsilane (δ = 0.00 ppm) with the solvent resonance as an internal standard ($CDCl_3$: δ = 7.26 ppm). Data are reported as follows: chemical shift in ppm (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, brs = broad singlet, m = multiplet), coupling constant (Hz), and integration. Chemical shifts of ^{13}C NMR were reported in ppm with the solvent as the internal standard ($CDCl_3$: δ = 77.16 ppm). High Resolution Mass measurement was performed on Agilent Q-TOF 6520 mass spectrometer with electron spray ionization (ESI) as the ion source. Melting point (m.p.) was measured on a microscopic melting point apparatus. Optical rotations were measured on an automatic polarimeter with $[\alpha]_D^{20}$ values reported in degrees; concentration (*c*) is in g/100 mL. The enantiomeric excess (ee) was determined by HPLC analysis on Agilent 1260 Infinity II Prime using Daicel CHIRALPAK® column OD-3, AD-H, IA-H. X-ray diffraction analyses were carried out on a microcrystalline powder using a Rigaku Oxford Diffraction XtaLAB Synergy-S diffractometer using Cu radiation (λ = 1.54178 Å)

2. Preparation of Substrates 1 and Substrates 2

Table S1. Substrates 1 and Substrates 2



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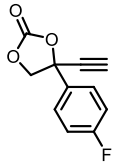

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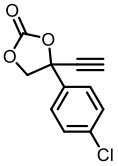

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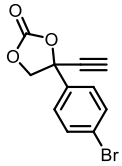

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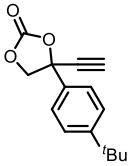

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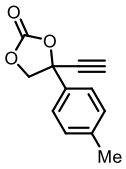

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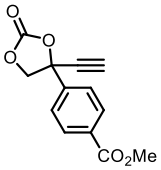

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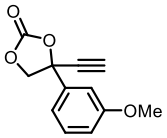

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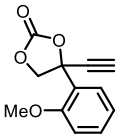

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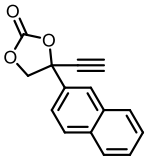

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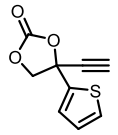

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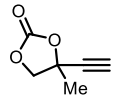

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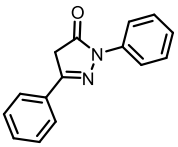

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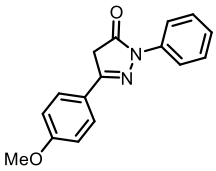

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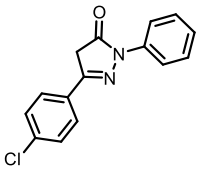

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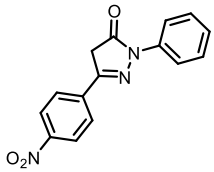

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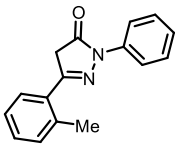

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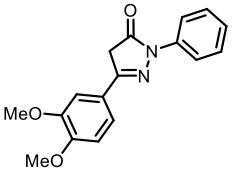

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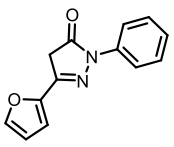

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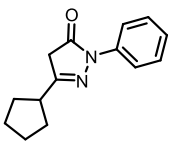

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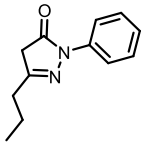

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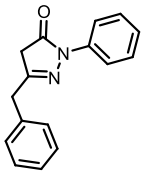

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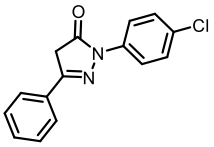

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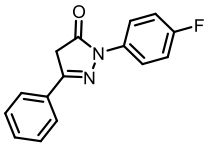

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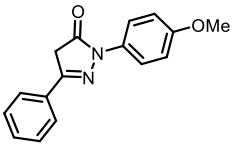

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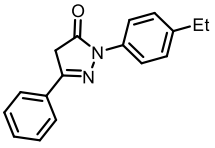

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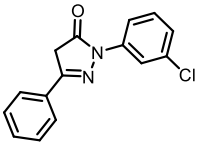

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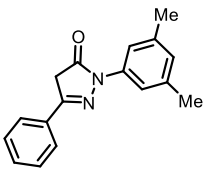

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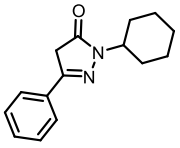
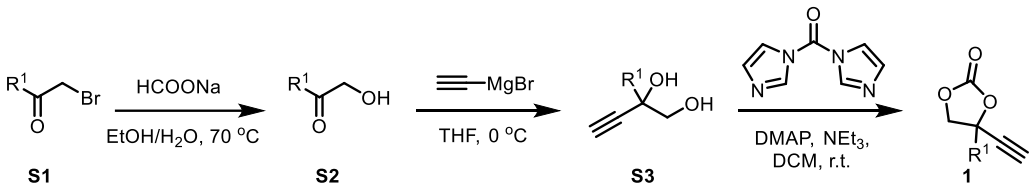


2q

2.1 Experimental Procedures and Characterization Data of 1:

Substrates **1,** were synthesized according to reported procedures[1,2], characterization of unreported **1e** was listed below:



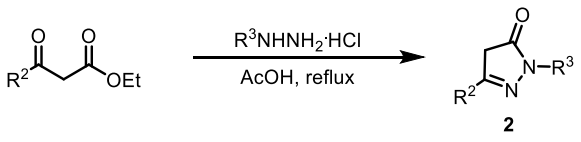
HCOONa (14.3 g, 210.0 mmol, 7.0 equiv), EtOH (80.0 mL), H_2O (40.0 mL) was added to a dry flask followed by **S1** (30.0 mmol, 1.0 equiv). The reaction mixture was stirred at 70 ℃ for 12 h. After concentrated under vacuum, the residue was added EA (100.0 mL), H_2O (50.0 mL), the aqueous layer was extracted with EA (50.0 mLx3). The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 and then concentrated under reduced pressure to afford the crude product **S2**.

A dry flask was charged with the crude product **S2** dissloved in THF (50.0 mL) under argon atmosphere, and cooled to 0 °C. Ethynylmagnesium bromide (180 mL, 90.0 mmol, 0.5 M in THF) was added dropwise and the resulting mixture was stirred for 12 h at room temperature. The reaction was quenched with sat. aq. NH_4Cl solution and subsequently diluted with H_2O (100 mL). The aqueous phase was extracted with EA (50.0 mLx3). Then the combined organic layers were washed by brine, dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford the crude product **S3.**

To the compound **S3** was added DCM (40.0 mL), Et_3N (4.1 mL, 30.0 mmol, 1.0 equiv), DMAP (366.5 mg, 3.0 mmol, 0.1 equiv) and 1,1'-carbonyldiimidazole (4.9 g, 30.0 mmol, 1.0 equiv). The mixture was stirred for 12 h at room temperature. After concentrated under vacuum, the residue was purified by silica gel column chromatography to give products **1a-1l.**

2.2 General Procedure for Preparation of 2

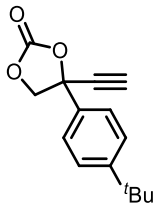
Substrates **2** were synthesized according to reported procedures[3], characterization of unreported **2d**, **2e, 2f, 2g, 2h, 2i, 2j, 2l, 2n, 2o and 2p** were listed below:



To a solution of β-ketoester (15.0 mmol, 1.0 equiv) in acetic acid (10.0 mL) at room temperature was added corresponding hydrazine hydrochloride (15.0 mmol, 1.0 equiv). The mixture was continued to reflux until TLC indicated the completion of the reaction (8-24 h). The solvent was removed and the residue was recrystallized from ethanol or purified by column chromatography on silica gel to give the desired products **2.**

2.3 Characterization of the Substrates

4-(4-(tert-butyl)phenyl)-4-ethynyl-1,3-dioxolan-2-one (1e)



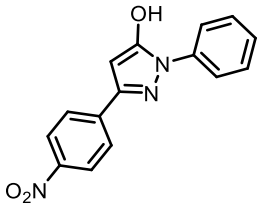
Purification by flash column chromatography (PE/EA = 8/1) to provide **1e** (2.1 g, 30% yield); white solid, **m.p.** 85 – 87 °C, R_f = 0.4 (PE/EA = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 – 7.44 (m, 4H), 4.76 (d, *J* = 8.5 Hz, 1H), 4.50 (d, *J* = 8.5 Hz, 1H), 2.99 (s, 1H), 1.32 (s, 9H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 153.2, 133.5, 126.1, 125.1, 79.9, 79.2, 78.7, 77.2, 34.8, 31.2 ppm.

HRMS (ESI) *m*/*z* Calcd for $[C_{15}H_{16}O_3 + H]^+$ 245.1172, found 245.1173.

3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-5-ol (2d)



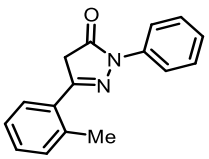
Purification by flash column chromatography (DCM/EA = 100/1) to provide **2d** (3.5 g, 83% yield), light yellow solid, **m.p.** 180 – 181 °C, R_f = 0.3 (PE/EA = 4/1).

^{1}H NMR (300 MHz, DMSO-d_6) δ 12.13 (s, 1H), 8.30 – 8.26 (m, 2H), 8.14 – 8.10 (m, 2H), 7.89 – 7.85 (m, 2H), 7.56 – 7.50 (m, 2H), 7.37 – 7.32 (m, 1H), 6.24 (s, 1H) ppm.

^{13}C NMR (75 MHz, DMSO-d_6) δ 154.7, 148.0, 147.0, 140.3, 139.0, 129.4, 126.7, 126.3, 124.4, 122.0, 86.6 ppm.

HRMS (ESI) *m*/*z* Calcd for $[C_{15}H_{11}N_3O_3 + H]^+$ 282.0873, found 282.0873.

2-phenyl-5-(o-tolyl)-2,4-dihydro-3H-pyrazol-3-one (2e)



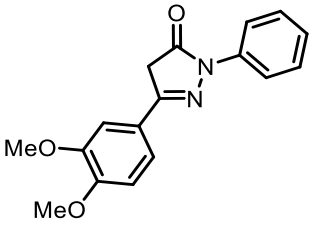
Purification by flash column chromatography (PE/EA = 5/1) to provide **2e** (3.4 g, 90% yield), white solid, **m.p.** 94 – 95 °C, R_f = 0.3 (PE/EA = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 – 7.95 (m, 2H), 7.46 – 7.37 (m, 3H), 7.34 – 7.25 (m, 3H), 7.24 – 7.18 (m, 1H), 3.87 (s, 2H), 2.71 (s, 3H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.0, 155.9, 138.3, 137.9, 132.2, 130.0, 129.4, 128.9, 128.9, 126.2, 125.2, 118.7, 41.6, 23.4 ppm.

HRMS (ESI) *m*/*z* Calcd for $[C_{16}H_{14}N_2O + H]^+$ 251.1179, found 251.1180.

5-(3,4-dimethoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2f)



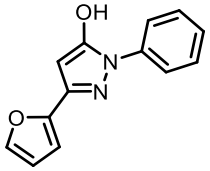
Purification by flash column chromatography (PE/EA = 5/1) to provide **2f** (2.5 g, 56% yield), light yellow solid, **m.p.** 126 – 128 °C, R_f = 0.3 (PE/EA = 4/1).

^{1}H NMR (300 MHz, $CDCl_3$) 7.98 – 7.94 (m, 2H), 7.46 – 7.40 (m, 3H), 7.26 – 7.19 (m, 1H), 7.14 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 3.97 (s, 3H), 3.93 (s, 3H), 3.82 (s, 2H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 154.5, 151.4, 149.4, 138.1, 128.9, 125.2, 123.8, 120.1, 119.1, 110.7, 107.6, 56.1, 56.0, 39.7 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{17}H_{16}N_2O_3 + H]^+$ 297.1234, found 297.1239.

3-(furan-2-yl)-1-phenyl-1H-pyrazol-5-ol (2g)



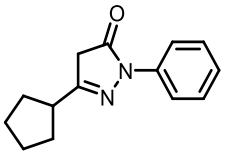
Purification by flash column chromatography (DCM/EA = 100/1) to provide **2g** (3.1 g, 91% yield), white solid, **m.p.** 175 – 177 °C, R_f = 0.3 (PE/EA = 5/1).

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.94 (s, 1H), 7.83 – 7.80 (m, 2H), 7.72 (d, *J* = 2.0 Hz, 1H), 7.51 – 7.45 (m, 2H), 7.31 – 7.27 (m, 1H), 6.79 (d, *J* = 3.3 Hz, 1H), 6.57 (dd, *J* = 3.4, 1.8 Hz, 1H), 5.88 (s, 1H) ppm.

^{13}C NMR (101 MHz, DMSO-d_6) δ 153.9, 149.1, 143.0, 142.9, 139.1, 129.4, 126.3, 121.7, 112.0, 106.7, 85.4 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{13}H_{10}N_2O_2 + H]^+$ 227.0815, found 227.0816.

5-cyclopentyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2h)



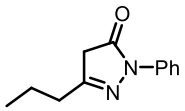
Purification by flash column chromatography (PE/EA = 5/1) to provide **2h** (2.7 g, 78% yield), white solid, **m.p.** 119 – 121 °C, R_f = 0.3 (PE/EA = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.86 (m, 2H), 7.41 – 7.35 (m, 2H), 7.19 – 7.14 (m, 1H), 3.41 (s, 2H), 2.97 – 2.87 (m, 1H), 2.03 – 1.90 (m, 2H), 1.76 – 1.67 (m, 6H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 162.9, 138.2, 128.8, 124.9, 118.9, 41.5, 40.5, 30.7, 25.4 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{14}H_{16}N_2O + H]^+$ 229.1335, found 229.1337.

2-phenyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one (2i)



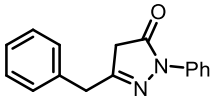
Purification by flash column chromatography (PE/EA = 5/1) to provide **2i** (2.3 g, 77% yield), white solid, **m.p.** 108 – 110 °C, R_f = 0.3 (PE/EA = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.48 – 7.29 (m, 2H), 7.25 – 7.09 (m, 1H), 3.40 (s, 2H), 2.46 (t, *J* = 7.4 Hz, 2H), 1.67 (q, *J* = 7.8 Hz, 2H), 1.02 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.7, 160.1, 138.2, 129.0, 125.1, 119.0, 41.9, 33.3, 20.1, 13.9 ppm.

HRMS (ESI) *m*/*z* Calcd for $[C_{12}H_{14}N_2O + H]^+$ 203.1179, found 203.1183.

5-benzyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2j)



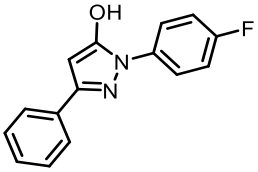
Purification by flash column chromatography (PE/EA = 5/1) to provide **2j** (2.6 g, 70% yield), white solid, **m.p.** 128 – 130 °C, R_f = 0.3 (PE/EA = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 (d, *J* = 7.5 Hz, 2H), 7.44 – 7.34 (m, 3H), 7.34 – 7.26 (m, 3H), 7.26 – 7.23 (m, 1H), 7.19 (t, *J* = 7.4 Hz, 1H), 3.82 (s, 2H), 3.32 (s, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.5, 158.6, 138.1, 135.6, 129.1, 128.9, 128.8, 127.4, 125.1, 118.9, 41.1, 38.0 ppm.

HRMS (ESI) *m*/*z* Calcd for $[C_{16}H_{14}N_2O + H]^+$ 251.1179, found 251.1180.

1-(4-fluorophenyl)-3-phenyl-1H-pyrazol-5-ol (2l)



Purification by flash column chromatography (DCM/EA = 100/1) to provide **2l** (3.3 g, 86% yield), white solid, **m.p.** 153 – 155 °C, R_f = 0.3 (PE/EA = 5/1).

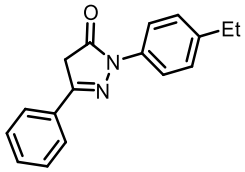
^{1}H NMR (300 MHz, DMSO-d_6) δ 11.95 (s, 1H), 7.93 – 7.85 (m, 4H), 7.47 – 7.42 (m, 2H), 7.39 – 7.31 (m, 3H), 6.08 (s, 1H) ppm.

^{13}C NMR (75 MHz, DMSO-d_6) δ 160.3 (d, $^1J_{C\text{-}F}$ = 242.8 Hz), 154.2, 150.2, 135.8, 133.9 (d, $^4J_{C\text{-}F}$ = 2.8 Hz), 129.0, 128.3, 125.6, 123.6 (d, $^3J_{C\text{-}F}$ = 8.3 Hz), 116.1 (d, $^2J_{C\text{-}F}$ = 22.5 Hz), 85.5 ppm.

^{19}F NMR (282 MHz, DMSO-d_6) δ -116.76 ppm.

HRMS (ESI) m/z Calcd for $[C_{15}H_{11}FN_2O + H]^+$ 255.0928, found 255.0933.

2-(4-ethylphenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (2n)



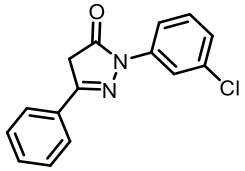
Purification by flash column chromatography (PE/EA = 5/1) to provide **2n** (3.0 g, 76% yield), white solid, **m.p.** 98 – 100 °C, R_f = 0.3 (PE/EA = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 – 7.81 (m, 2H), 7.73 – 7.67 (m, 2H), 4(m, 3H), 7.24 – 7.20 (m, 2H), 3.70 (s, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 154.5, 141.4, 135.9, 131.0, 130.6, 128.9, 128.30, 126.0, 119.2, 39.5, 28.4, 15.7 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{17}H_{16}N_2O + H]^+$ 265.1335, found 265.1336.

2-(4-nitrophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (2o)



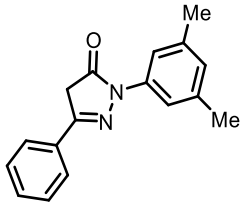
Purification by flash column chromatography (DCM/EA = 100/1) to provide **2o** (2.27 g, 56% yield), white solid, **m.p.** 110 – 112 °C, R_f = 0.4 (PE/EA = 5/1).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (t, *J* = 2.1 Hz, 1H), 7.89 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.71– 7.63 (m, 2H), 7.45 – 7.36 (m, 3H), 7.27 (t, *J* = 8.1 Hz, 1H), 7.13– 7.09 (m, 1H), 3.68 (s, 2H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 155.0, 139.2, 134.6, 131.0, 130.5, 130.0, 129.0, 126.1, 125.0, 118.6, 116.5, 39.6 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{15}H_{11}ClN_2O + H]^+$ 271.0633, found 271.0638.

2-(3,5-dimethylphenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (2p)



Purification by flash column chromatography (PE/EA = 5/1) to provide **2p** (2.3 g, 58% yield), light brown solid, **m.p.** 116 – 118 °C, R_f = 0.3 (PE/EA = 5/1).

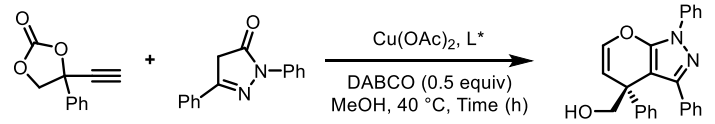
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 – 7.72 (m, 2H), 7.57 (s, 2H), 7.45 – 7.40 (m, 3H), 6.84 (s, 1H), 3.75 (s, 2H), 2.35 (s, 6H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 154.5, 138.6, 138.0, 131.0, 130.7, 128.9, 127.2, 126.0, 117.0, 39.6, 21.6 ppm.

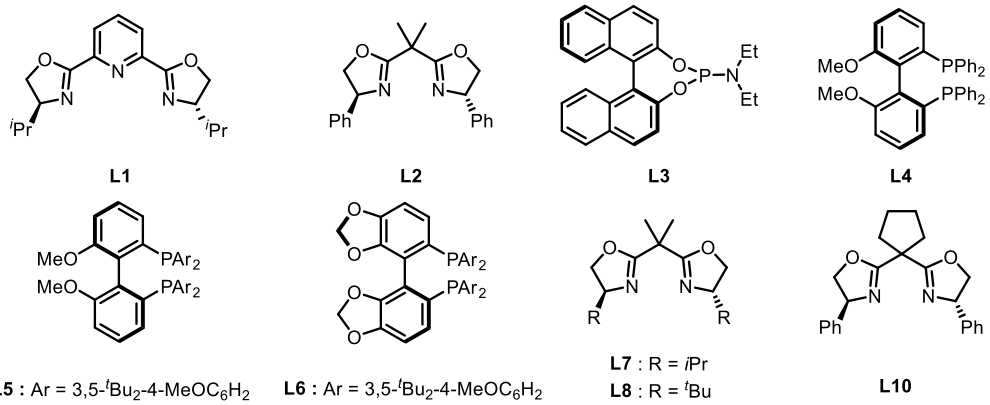
HRMS (ESI) *m/z* Calcd for $[C_{17}H_{16}N_2O + H]^+$ 265.1335, found 265.1336.

3. Reaction Optimization

Table S2. Screening of ligands[a]



1a 2a 3aa

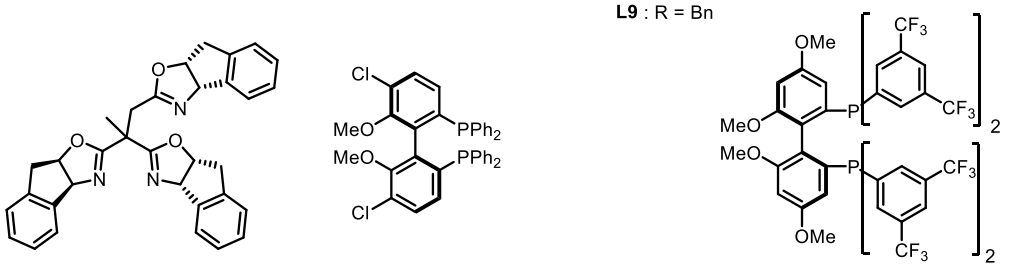


L1 L2 L3 L4

L5 : Ar = 3,5-^{t}Bu$_2$-4-MeOC$_6$H$_2$ L6 : Ar = 3,5-^{t}Bu$_2$-4-MeOC$_6$H$_2$

L7 : R = *i*Pr
L8 : R = ^{t}Bu
L9 : R = Bn

L10

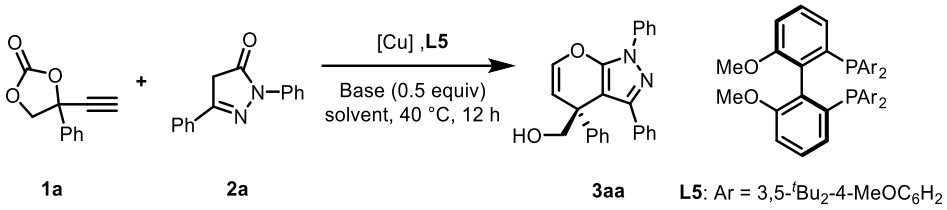


L11 L12 L13

entry[a]	L	*T* (°C)	Time (h)	yield/%[b]	er/%[c]
1	**L1**	40	12	54	53.5:46.5
2	**L2**	40	12	60	76.5:23.5
3	**L3**	40	12	20	50:50
4	**L4**	40	12	32	50:50
5	**L5**	40	12	84	96.5:3.5
6	**L6**	40	12	71	91.5:8.5
7	**L7**	40	12	43	58:42
8	**L8**	40	12	55	67.5:32.5
9	**L9**	40	12	58	56:44
10	**L10**	40	12	17	68:32
11	**L11**	40	12	37	63.5:36.5
11	**L12**	40	12	35	54:46
12	**L13**	40	12	30	53.5:46.5
13	**L5**	40	24	88	92.5:7.5

[a]Reaction conditions: **1a** (0.15 mmol, 3.0 equiv), **2a** (0.05 mmol, 1.0 equiv), $Cu(OAc)_2$ (5.0 mol%), ligand (7.5 mol%), MeOH (0.5 mL), DABCO (0.5 equiv), 40 °C, Time (h), under argon. [b]Isolated yields. [c]The *er* value was determined by HPLC.

Table S3. Screening of catalyst, solvent and base

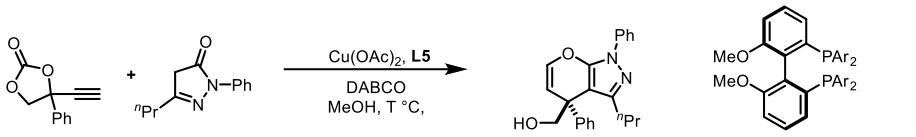


1a **2a** **3aa** **L5**: Ar = 3,5-^{t}Bu$_2$-4-MeOC$_6$H$_2$

entry[a]	[Cu]	L	Base	solvent	yield/%[b]	er/%[c]
1	$Cu(OAc)_2$	**L5**	DIPEA	MeOH	65	92:8
2	$Cu(OAc)_2$	**L5**	Et_3N	MeOH	20	90.5:9.5
3	$Cu(OAc)_2$	**L5**	Cy_2NMe	MeOH	80	89.5:10.5
4	$Cu(OAc)_2$	**L5**	DMAP	MeOH	80	50:50
5	$Cu(OAc)_2$	**L5**	DABCO	MeOH	84	96.5:3.5
6	$Cu(OAc)_2$	**L5**	Cs_2CO_3	MeOH	73	87:13
7	$Cu(OAc)_2$	**L5**	KOAc	MeOH	40	92:8
8	$Cu(CH_3CN)_4PF_6$	**L5**	DABCO	MeOH	96	89.5:10.5
9	$Cu(CH_3CN)_4BF_4$	**L5**	DABCO	MeOH	70	92.5:7.5
10	$Cu(OTf)_{1/2}\cdot C_6H_6$	**L5**	DABCO	MeOH	85	90:10
11	$Cu(OTf)_2$	**L5**	DABCO	MeOH	65	94:6
12	$Cu(OAc)_2$	**L5**	DABCO	EtOH	80	83.5:16.5
13	$Cu(OAc)_2$	**L5**	DABCO	*i*PrOH	61	80:20
14	$Cu(OAc)_2$	**L5**	DABCO	Toluene	<20	50:50
15	$Cu(OAc)_2$	**L5**	DABCO	DMF	20	78.5:21.5
16	$Cu(OAc)_2$	**L5**	DABCO	THF	40	64:36
17	$Cu(OAc)_2$	**L5**	DABCO	DCM	trace	50:50
18[d]	$Cu(OAc)_2$	**L5**	DABCO	MeOH	88	80:20
19[e]	$Cu(OAc)_2$	**L5**	DABCO	MeOH	--	--
20[f]	$Cu(OAc)_2$	**L5**	DABCO	MeOH	75	96:4
21[g]	$Cu(OAc)_2$	**L5**	DABCO	MeOH	47	96.5:3.5

[a]Unless otherwise stated, the reactions were performed with **1a** (0.15 mmol, 3.0 equiv), **2a** (0.05 mmol, 1.0 equiv), [Cu] (5.0 mol%), **L5** (7.5 mol%), solvent (0.5 mL), Base (0.025 mmol, 0.5 equiv), 40 °C, 12 h, under argon. [b]Isolated yields. [c]The *er* value was determined by HPLC. [d]At 60 °C. [e]At 25 °C. [f]With 1.5 equivalent of **2a,** 1.0 equivalent of **1a**. [g]With 1.5 equivalent of **1a,** 1.0 equivalent of **2a**.

Table S4. Screening of reaction conditions

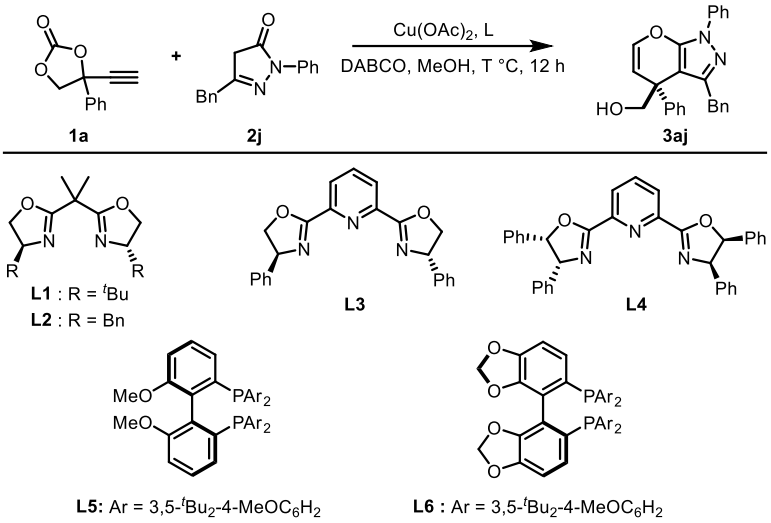


1a **2i** **3ai** **L5** : Ar = 3,5-^{t}Bu$_2$-4-MeOC$_6$H$_2$

entry[a]	DABCO (equiv)	*T* (°C)	Time (h)	yield/%[b]	er/%[c]
1	0.5	40	12	--	--
2[d]	0.5	40	12	--	--
3[d]	0.5	40	24	7	79.5:20.5
4	0.5	50	12	10	79:21
5[d]	0.5	50	12	22	80:20
6[d]	0.5	50	24	39	78:22

[a]Reaction conditions: **1a** (0.15 mmol, 3.0 equiv), **2i** (0.05 mmol, 1.0 equiv), $Cu(OAc)_2$ (5.0 mol%), ligand (7.5 mol%), MeOH (0.5 mL), DABCO (0.5 equiv), T °C, Time (h), under argon. [b]Isolated yields. [c]The *er* value was determined by HPLC. [d] $Cu(OAc)_2$ (10.0 mol%), **L5** (15.0 mol%).

Table S5. Screening of reaction conditions

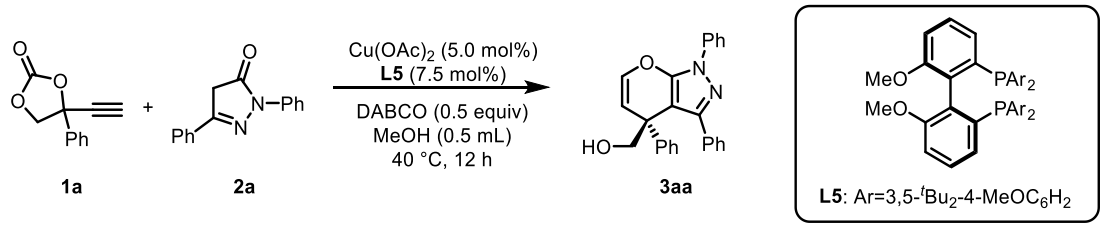


entry[a]	L	DABCO (equiv)	*T* (°C)	Time (h)	yield/%[b]	er/%[c]
1	**L1**	0.5	40	12	8	56.5:43.5
2	**L2**	0.5	40	12	21	60.5:39.5
3	**L3**	0.5	40	12	10	55.5:44.5
4	**L4**	0.5	40	12	9	55.5:44.5
5	**L6**	0.5	40	12	6	50:50
6	**L5**	0.5	40	12	12	66.5:33.5
7	**L5**	1.0	40	12	17	67.5:32.5
8	**L5**	1.5	40	12	16	67.5:32.5
9	**L5**	2.0	40	12	7	67.5:32.5
10[d]	**L5**	1.5	50	12	45	69.5:30.5
11[d]	**L5**	1.5	50	24	53	64.5:35.5

[a]Reaction conditions: **1a** (0.15 mmol, 3.0 equiv), **2j** (0.05 mmol, 1.0 equiv), $Cu(OAc)_2$ (5.0 mol%), ligand (7.5 mol%), MeOH (0.5 mL), DABCO, T °C, 12 h, under argon. [b]Isolated yields. [c]The *er* value was determined by HPLC. [d] $Cu(OAc)_2$ (10.0 mol%), **L5** (15.0 mol%).

4. General Procedure for Copper-Catalyzed Asymmetric Synthesis of Pyranopyrazoles

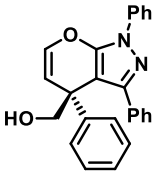
4.1 General Procedure



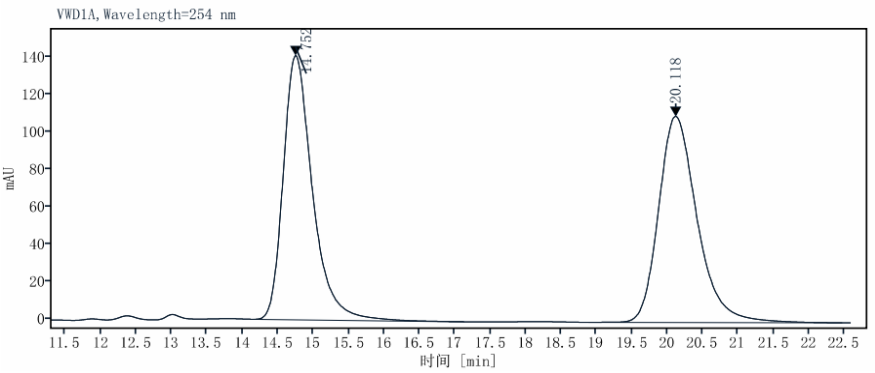
To an oven-dried 10-mL schlenk tube equipped with a tefloncoated magnetic stir bar was added $Cu(OAc)_2$ (0.5 mg, 0.0025 mmol, 5.0 mol%), **L5** (4.4 mg, 0.00375 mmol, 7.5 mol%), **2a** (11.8 mg, 0.05 mmol, 1.0 equiv) and DABCO (2.8 mg, 0.025 mmol, 0.5 equiv). Then the schlenk tube was evacuated and filled with argon for three times. After that, **1a** (28.2 mg, 0.15 mmol, 3.0 equiv, if **1** is solid, it was added to the tube before evacuation) and MeOH (0.5 mL) were added under argon atmosphere via a syringe. The reaction mixture was stirred at 40 °C for 12 h. After completion of the reaction, the reaction mixture was concentrated in vacuum and the crude product was purified by flash chromatography on silica gel (PE/EA, 20:1 to 7:1) to afford the desired product **3aa** (16.0 mg) in 84% yield.

4.2 Characterization of the Products

(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3aa)



Purification by flash column chromatography (PE/EA = 7:1) generated **3aa** (16.0 mg, 84% yield); 96.5:3.5 er; white solid; **m.p.** 168 – 170 ºC; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -40 (c = 0.08, MeOH); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.89 – 7.85 (m, 2H), 7.49 – 7.43 (m, 2H), 7.34 – 7.20 (m, 7H), 7.18 – 7.07 (m, 4H), 6.73 (d, *J* = 6.0 Hz, 1H), 4.97 (d, *J* = 6.1 Hz, 1H), 4.04 – 3.94 (m, 2H), 1.61 (t, *J* = 5.9 Hz, 1H) ppm.
^{13}C NMR (75 MHz, $CDCl_3$) 148.9, 147.9, 145.9, 138.6, 138.1, 133.6, 129.2, 128.7, 128.6, 128.2, 128.1, 127.2, 127.0, 126.6, 121.1, 110.6, 98.1, 66.8, 45.7 ppm.
HRMS (ESI) *m/z* Calcd for $[C_{25}H_{20}N_2O_2 + H]^+$ 381.1598, found 381.1601.
HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 15.5 min (major), t_{R2} = 21.2 min (minor).



RetTime[min]	Type	Width[min]	Area[mAD*s]	Height[mAU]	Area%
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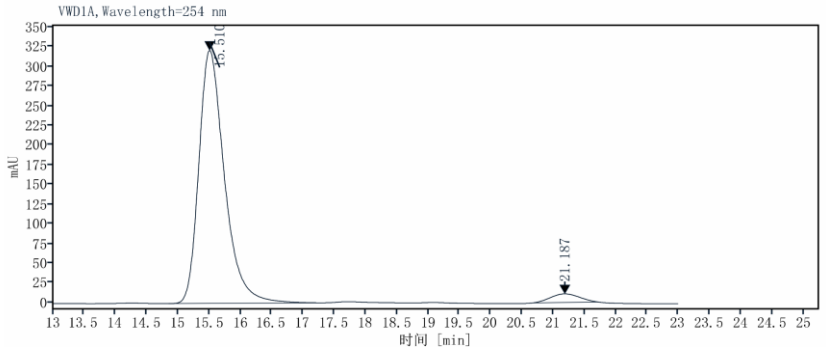
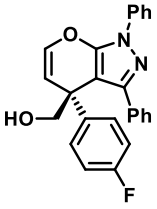
20.118	BB	3.5767	4172.2593	110.3030	50.6309



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
15.510	BB	2.4417	9165.2120	321.2851	96.3108
21.187	MM m	0.5155	351.0786	10.9071	3.6892

(R)-(4-(4-fluorophenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ba)



Purification by flash column chromatography (PE/EA = 7:1) generated **3ba** (14.5 mg, 73% yield); 93.5:6.5 er; white solid; **m.p.** 178 – 180 °C; R_f = 0.4 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -19 (c = 0.10, MeOH).

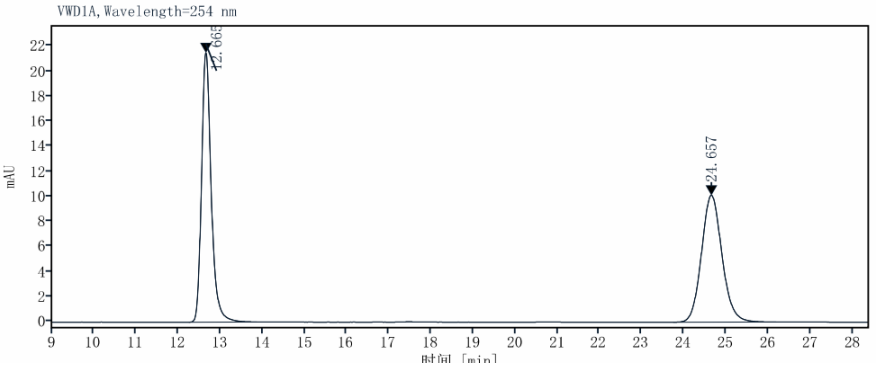
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.85 (m, 2H), 7.51 – 7.44 (m, 2H), 7.34 – 7.16 (m, 6H), 7.11 – 6.98 (m, 4H), 6.76 (d, *J* = 6.0 Hz, 1H), 4.96 (d, *J* = 6.0 Hz, 1H), 4.02 – 3.94 (m, 2H), 1.55 (s, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.5 (d, $^1J_{C\text{-}F}$ = 245.0 Hz), 148.8, 147.7, 141.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 138.7, 138.1, 133.5, 129.2, 128.9 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 128.6, 128.3, 128.1, 126.6, 121.1, 115.4 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 110.3, 98.2, 67.0, 45.2 ppm.

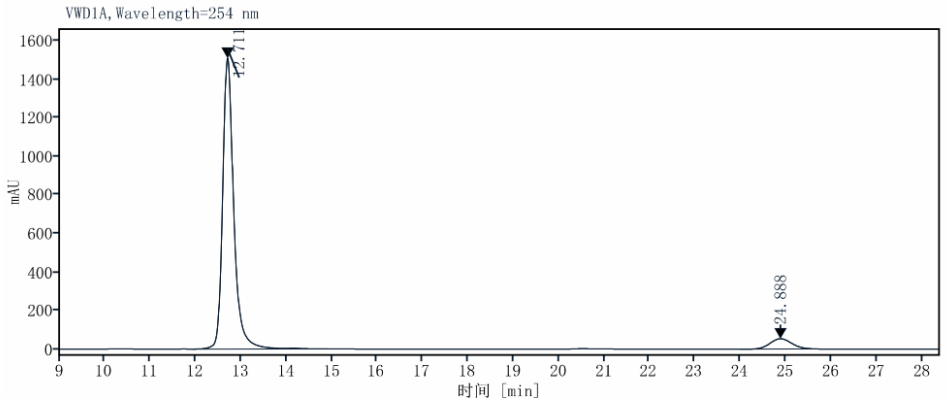
^{19}F NMR (282 MHz, $CDCl_3$) δ -115.46 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{19}FN_2O_2 + H]^+$ 399.1503, found 399.1507.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254 nm, t_{R1} = 12.7 min (major), t_{R2} = 24.9 min (minor).

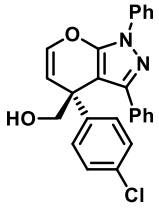


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
12.665	BB	1.6050	342.3488	21.5177	49.9927
24.657	BB	2.4317	342.4485	10.1431	50.0073

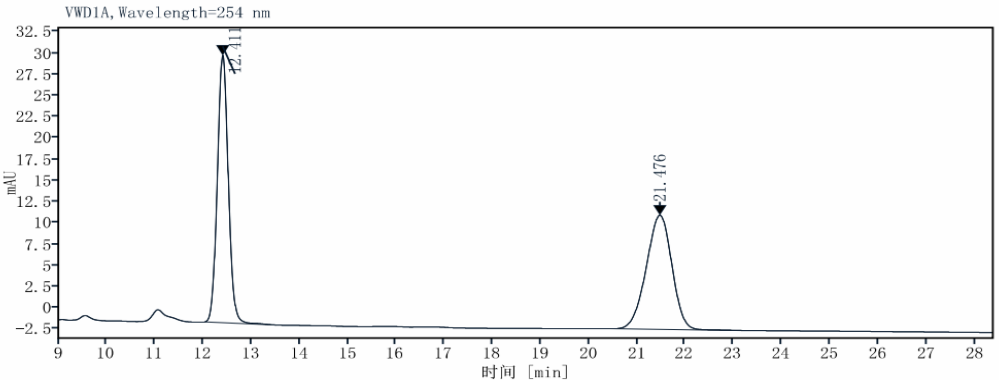


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
12.711	BB m	0.2580	25852.0827	1508.2840	93.5309
24.888	MM m	0.5165	1788.0610	53.6964	6.4691

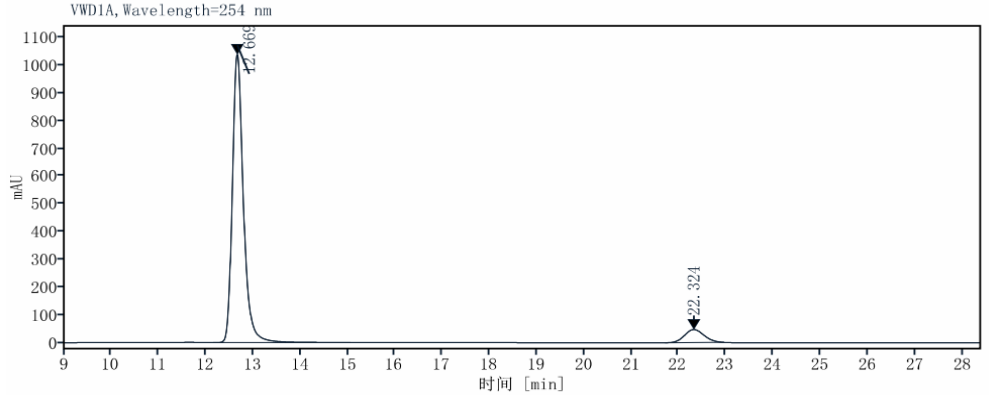
(R)-(4-(4-chlorophenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ca)



Purification by flash column chromatography (PE/EA = 7:1) generated **3ca** (14.7 mg, 71% yield); 92.6:7.4 er; whitesolid; **m.p.** 200 – 202 °C; R_f = 0.5 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -30 (c = 0.12, MeOH).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.86 (m, 2H), 7.50 – 7.45 (m, 2H), 7.34 – 7.24 (m, 4H), 7.23 – 7.17 (m, 4H), 7.12 – 7.09 (m, 2H), 6.77 (d, *J* = 6.1 Hz, 1H), 4.97 (d, *J* = 6.1 Hz, 1H), 3.98 (d, *J* = 4.8 Hz, 2H), 1.51 (t, *J* = 6.4 Hz, 1H) ppm.
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 147.7, 144.4, 138.8, 138.0, 133.4, 132.8, 129.2, 128.8, 128.7, 128.6, 128.4, 128.2, 126.7, 121.1, 110.1, 97.9, 66.9, 45.3 ppm.
HRMS (ESI) *m/z* Calcd for $[C_{25}H_{19}ClN_2O_2 + H]^+$ 415.1208, found 415.1215;
HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 12.7 min (major), t_{R2} = 22.3 min (minor).

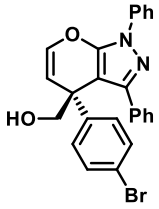


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
12.411	MB m	0.2448	499.2687	31.5237	50.0570
21.476	BB	2.6967	498.1320	13.4622	49.9430



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
12.669	BB	2.8900	16841.4311	1036.8323	92.6281
22.324	MM m	0.4441	1340.3446	46.9442	7.3719

(R)-(4-(4-bromophenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3da)



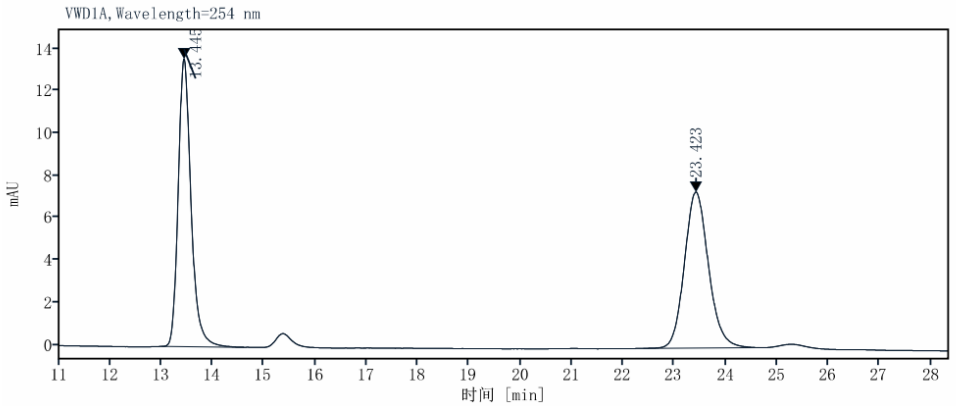
Purification by flash column chromatography (PE/EA = 7:1) generated **3da** (17.4 mg, 76% yield); 96:4 er; white solid; **m.p.** 200 – 202 °C; R_f = 0.5 (PE/EA = 4/1); $[\alpha]_D^{20}$ = - 32 (c = 0.11, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.85 (m, 2H), 7.50 – 7.42 (m, 4H), 7.34 – 7.25 (m, 2H), 7.23 – 7.10 (m, 6H), 6.77 (d, *J* = 6.1 Hz, 1H), 4.97 (d, *J* = 6.0 Hz, 1H), 4.03 – 3.95 (m, 2H), 1.53 (s, 1H) ppm.

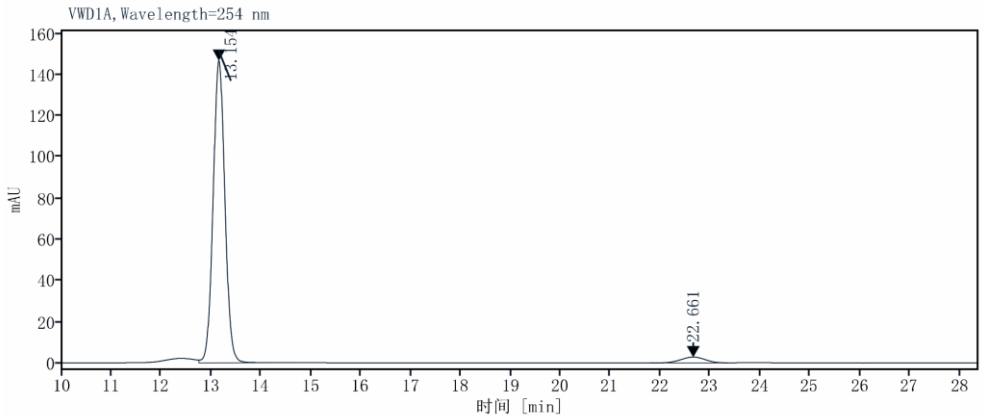
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 147.7, 144.9, 138.9, 138.0, 133.4, 131.7, 129.2, 129.0, 128.6, 128.4, 128.2, 126.7, 121.1, 121.0, 110.0, 97.8, 66.8, 45.4 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{19}BrN_2O_2 + H]^+$ 459.0703, found 459.0703.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 13.1 min (major), t_{R2} = 22.7 min (minor).

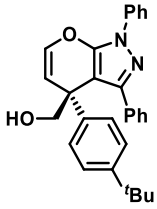


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
13.445	BB	1.6000	236.3607	13.6068	49.5151
23.423	BB	2.2567	240.9896	7.3788	50.4849



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
13.154	VB	1.9005	2413.6432	146.7455	96.1762
22.661	BB	1.5583	95.9635	2.8475	3.8238

(R)-(4-(4-(tert-butyl)phenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ea)



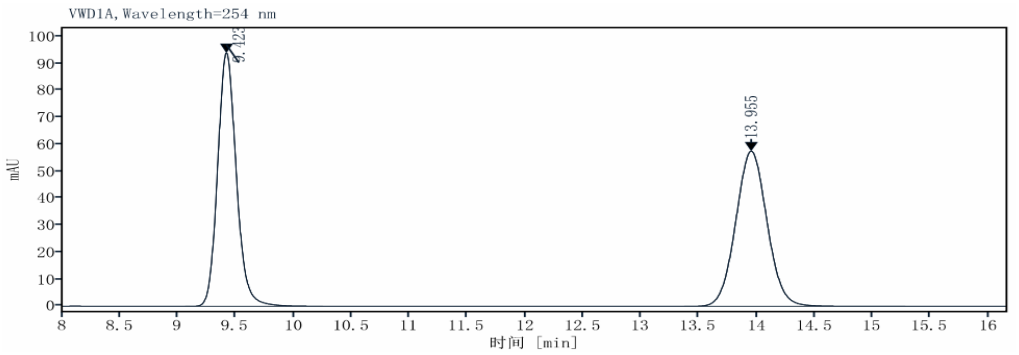
Purification by flash column chromatography (PE/EA = 7:1) generated **3ea** (17.9 mg, 82% yield); 93.5:6.5 er; white solid; **m.p.** 170 – 172 °C; R_f = 0.5 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -126 (c = 0.09, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.7 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.36 – 7.27 (m, 3H), 7.25 – 7.05 (m, 7H), 6.77 (d, *J* = 6.2 Hz, 1H), 5.01 (d, *J* = 6.2 Hz, 1H), 4.00 (s, 2H), 1.46 (s, 1H), 1.32 (s, 9H) ppm.

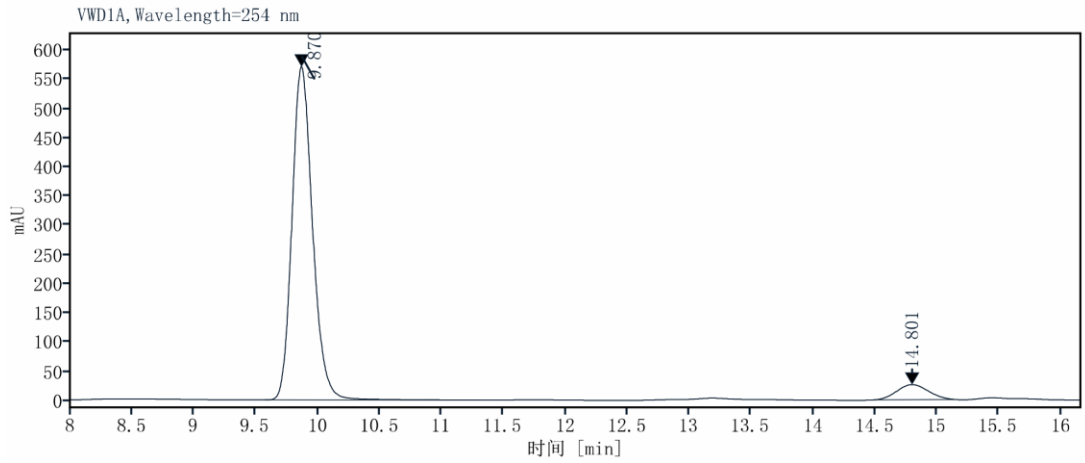
^{13}C NMR (75 MHz, $CDCl_3$) δ 150.0, 149.0, 147.8, 142.9, 138.7, 138.2, 133.7, 129.2, 128.7, 128.2, 128.0, 126.9, 126.6, 125.6, 121.2, 110.6, 98.4, 67.0, 45.4, 34.5, 31.4 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{29}H_{28}N_2O_2+H]^+$ 437.2224, found 437.2233.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 9.9 min (major), t_{R2} = 14.8 min (minor).

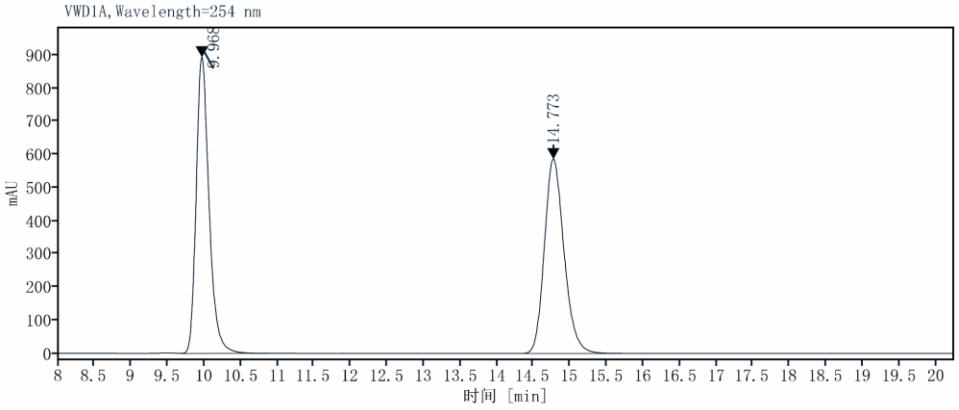


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
9.423	BB	1.1850	1056.8520	93.9186	49.4155
13.955	BB	1.9067	1081.8533	57.4899	50.5845

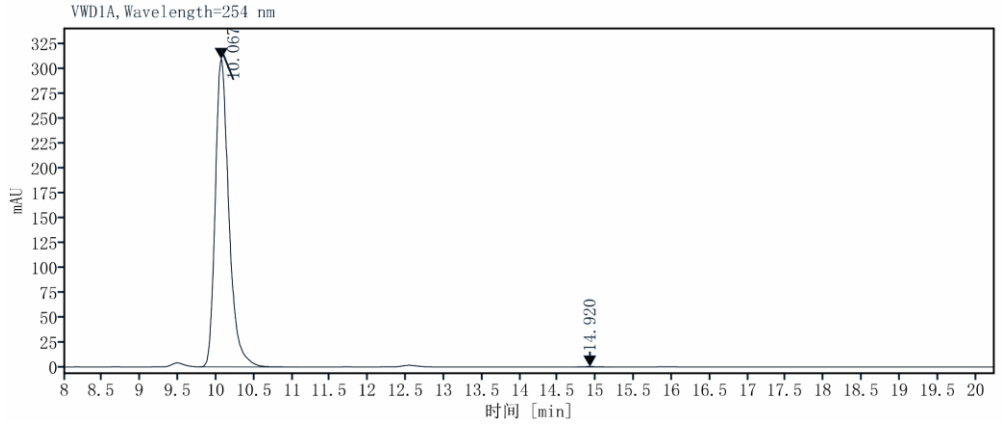


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
9.870	BB	1.7433	6602.6736	571.3523	93.5170
14.801	MM m	0.2784	457.7264	25.8668	6.4830

After recrystallization

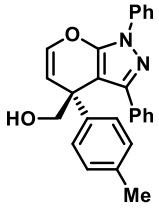


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
9.968	VB	1.1931	10949.4576	894.4878	49.9376
14.773	BB	2.2217	10976.8018	587.0876	50.0624



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
10.067	VB	1.2818	3885.4032	310.5558	99.8275
14.920	MM m	0.2435	6.7128	0.4291	0.1725

(R)-(1,3-diphenyl-4-(p-tolyl)-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3fa)



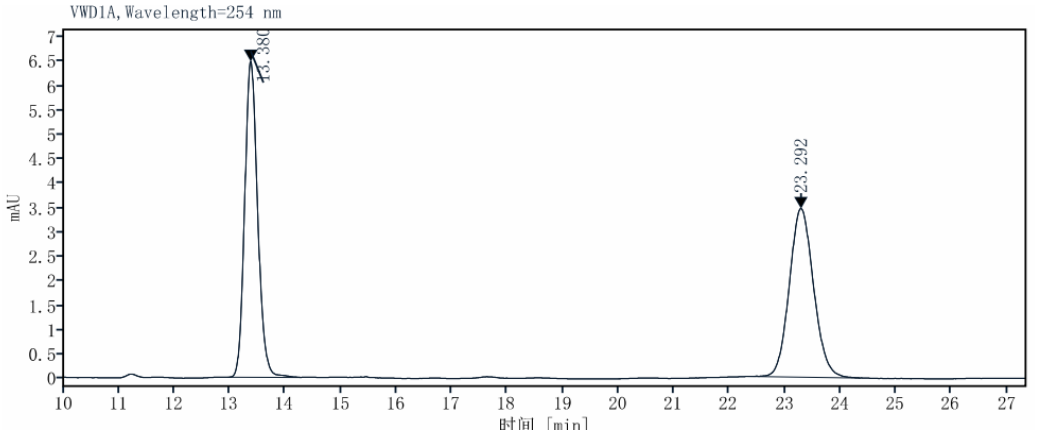
Purification by flash column chromatography (PE/EA = 7:1) generated **3fa** (15.8 mg, 80% yield); 93.5:6.5 er; white solid; **m.p.** 178 – 180 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -31 (c = 0.19, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.52 – 7.40 (m, 2H), 7.33 – 7.26 (m, 1H), 7.25 – 7.13 (m, 9H), 6.75 (d, *J* = 6.0 Hz, 1H), 4.98 (d, *J* = 6.1 Hz, 1H), 4.04 – 3.96 (m, 2H), 2.35 (s, 3H), 1.49 (s, 1H) ppm.

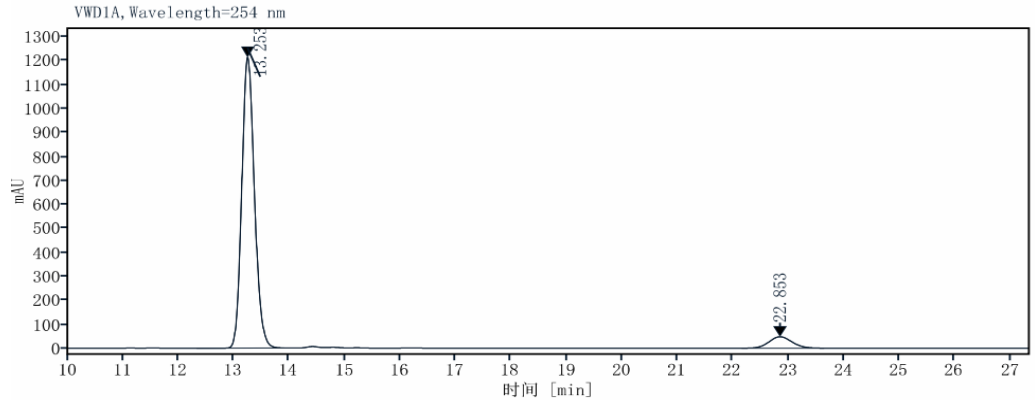
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.8, 147.9, 143.0, 138.5, 138.2, 136.7, 133.6, 129.4, 129.1, 128.6, 128.2, 128.1, 127.0, 126.5, 121.1, 110.9, 98.0, 66.8, 45.5, 21.1 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{26}H_{22}N_2O_2+H]^+$ 395.1754, found 395.1753.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 13.3 min (major), t_{R2} = 22.9 min (minor).

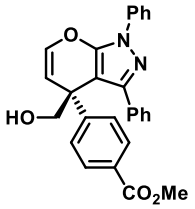


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
13.380	BB	1.3100	105.5845	6.4815	50.0562
23.292	MB m	0.4703	105.3474	3.4592	49.9438

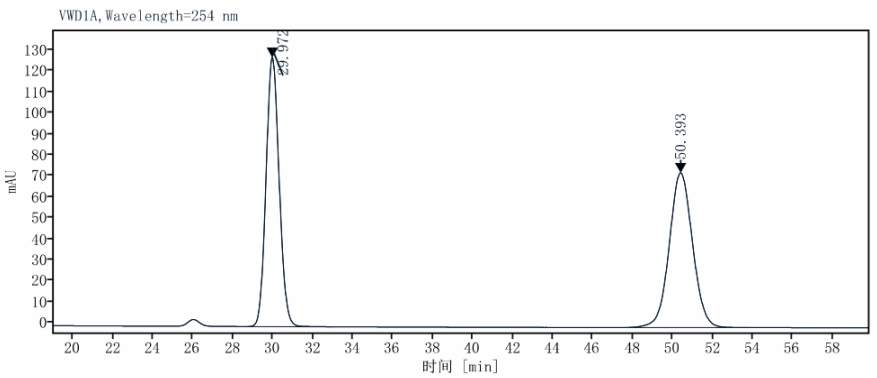


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
13.253	BM m	0.2452	19279.9372	1214.2337	93.3534
22.853	MM m	0.4473	1372.6903	47.6134	6.6466

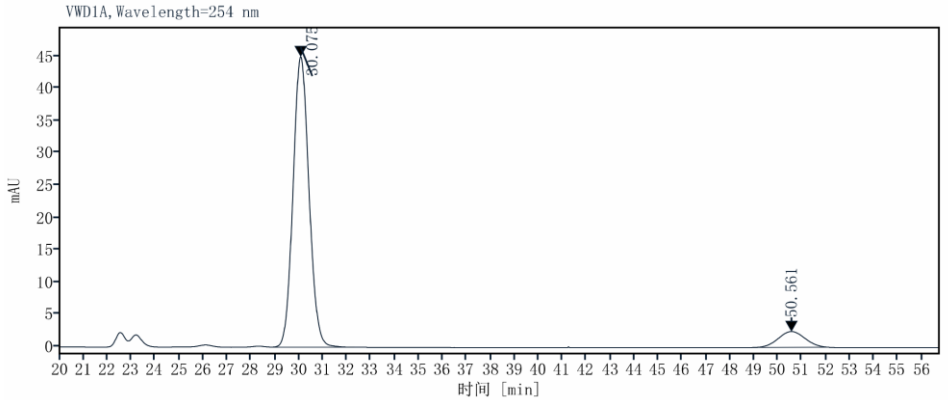
methyl (R)-4-(4-(hydroxymethyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)benzoate (3ga)



Purification by flash column chromatography (PE/EA = 5:1) generated **3ga** (13.8 mg, 63% yield); 91.5:8.5 er; white solid; **m.p.** 158 – 160 ºC; R_f = 0.3 (PE/EA = 2/1); $[\alpha]_D^{20}$ = -12 (c = 0.18, MeOH).
^{1}H NMR (300 MHz, DMSO-*d6*) δ 7.90 – 7.81 (m, 4H), 7.55 – 7.43 (m, 4H), 7.36 – 7.32 (m, 1H), 7.27 – 7.14 (m, 3H), 7.10 – 7.06 (m, 2H), 6.95 (d, *J* = 6.0 Hz, 1H), 5.11 (d, *J* = 6.0 Hz, 1H), 5.02 (t, *J* = 5.2 Hz, 1H), 4.02 (dd, *J* = 10.6, 5.4 Hz, 1H), 3.81 – 3.74 (m, 4H) ppm.
^{13}C NMR (75 MHz, DMSO-*d6*) δ 166.5, 152.2, 148.7, 147.5, 138.5, 138.2, 134.2, 129.9, 129.7, 128.6, 128.4, 128.3, 128.1, 127.1, 121.1, 110.9, 99.7, 66.3, 52.6, 45.7 ppm.
HRMS (ESI) *m/z* Calcd for $[C_{27}H_{22}N_2O_4 + H]^+$ 439.1652, found 439.1658.
HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 30.1 min (major), t_{R2} = 50.6 min (minor).

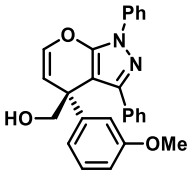


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
29.972	BB	4.2933	5864.7889	128.3078	49.5311
50.393	BB	6.2333	5975.8192	73.7777	50.4689



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
30.075	BB	3.4567	2077.2602	44.9618	91.5409
50.561	MM m	0.9684	191.9552	2.4625	8.4591

(R)-(4-(3-methoxyphenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ha)



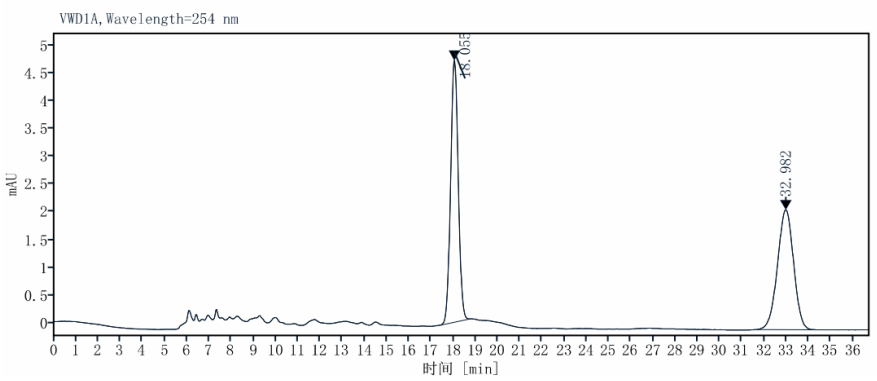
Purification by flash column chromatography (PE/EA = 7:1) generated **3ha** (16.0 mg, 78% yield); 94.5:5.5 er; white solid; **m.p.** 158 – 160 °C; R_f = 0.3 (PE/EA = 3/1); $[\alpha]_D^{20}$ = -9 (c = 0.20, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 – 7.85 (m, 2H), 7.50 – 7.44 (m, 2H), 7.33 – 7.14 (m, 7H), 6.87 – 6.78 (m, 3H), 6.76 (d, *J* = 6.1 Hz, 1H), 5.00 (d, *J* = 6.1 Hz, 1H), 4.00 (s, 2H), 3.75 (s, 3H), 1.50 (s, 1H) ppm.

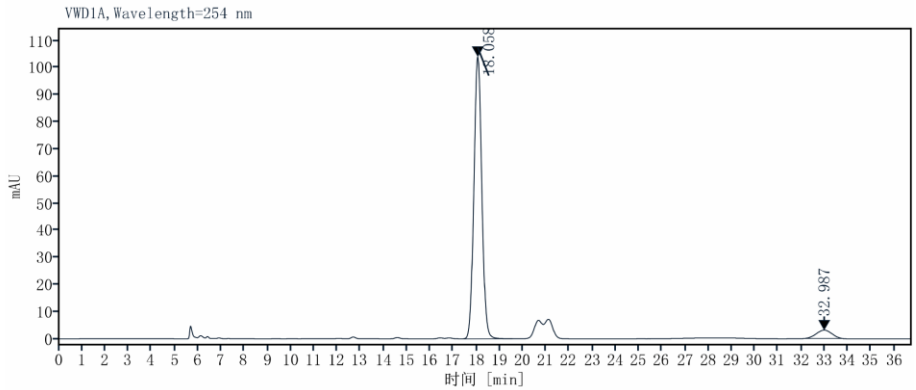
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.9, 148.9, 147.9, 147.5, 138.7, 138.2, 133.6, 129.7, 129.2, 128.7, 128.3, 128.1, 126.6, 121.2, 119.4, 113.8, 111.9, 110.5, 98.0, 66.8, 55.3, 45.8 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{26}H_{22}N_2O_3 + H]^+$ 411.1703, found 411.1707.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 18.1 min (major), t_{R2} = 33.0 min (minor).

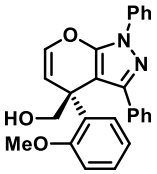


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
18.055	BB	1.3050	112.6098	4.7276	50.8457
32.982	BB	2.5767	108.8639	2.1619	49.1543



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
18.058	BB	2.1661	2467.7480	104.1300	94.5634
32.987	MM m	0.6988	141.8744	3.0720	5.4366

(R)-(4-(2-methoxyphenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ia)



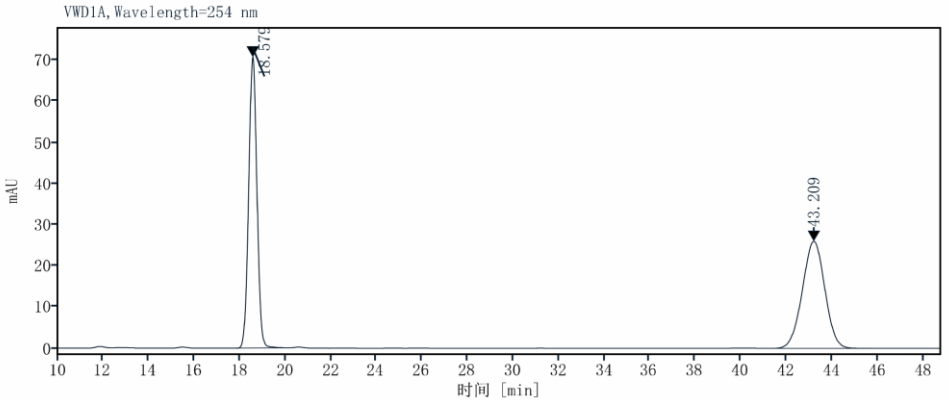
Purification by flash column chromatography (PE/EA = 5:1) generated **3ia** (10.6 mg, 52% yield); 95:5 er; white solid; **m.p.** 162 – 164 °C; R_f = 0.4 (PE/EA = 2/1); $[\alpha]_D^{20}$ = - 8 (c = 0.15, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.50 – 7.43 (m, 2H), 7.32 – 7.16 (m, 8H), 6.95 – 6.90 (m, 2H), 6.68 (d, *J* = 6.1 Hz, 1H), 5.38 (d, *J* = 6.1 Hz, 1H), 4.34 (d, *J* = 10.9 Hz, 1H), 3.89 (d, *J* = 10.9 Hz, 1H), 3.74 (s, 3H), 1.69 (s, 1H) ppm.

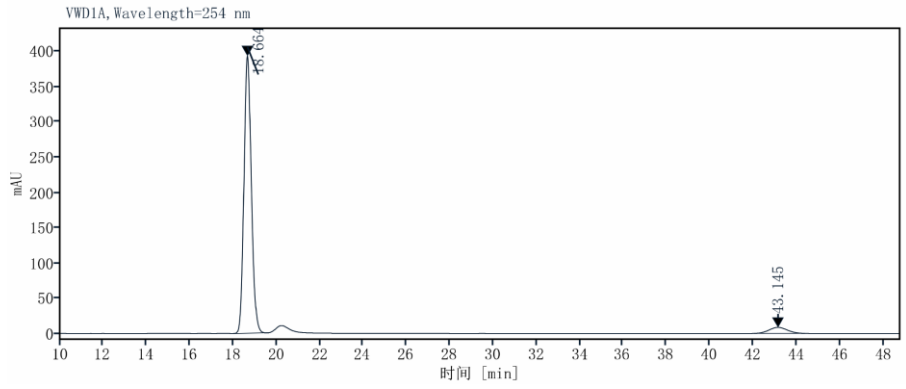
^{13}C NMR (75 MHz, $CDCl_3$) δ 157.2, 148.8, 148.1, 138.8, 138.2, 133.8, 132.4, 129.5, 129.2, 128.7, 128.2, 128.1, 126.5, 121.2, 121.0, 112.3, 108.7, 97.8, 66.2, 55.5, 45.9 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{26}H_{22}N_2O_3 + H]^+$ 411.1703, found 411.1706.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ=254nm, t_{R1} = 18.7 min (major), t_{R2} = 43.1 min (minor).

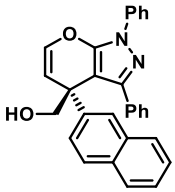


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
18.579	BB	2.3183	1785.2562	70.7864	49.9818
43.209	BB	4.3933	1786.5537	26.0505	50.0182

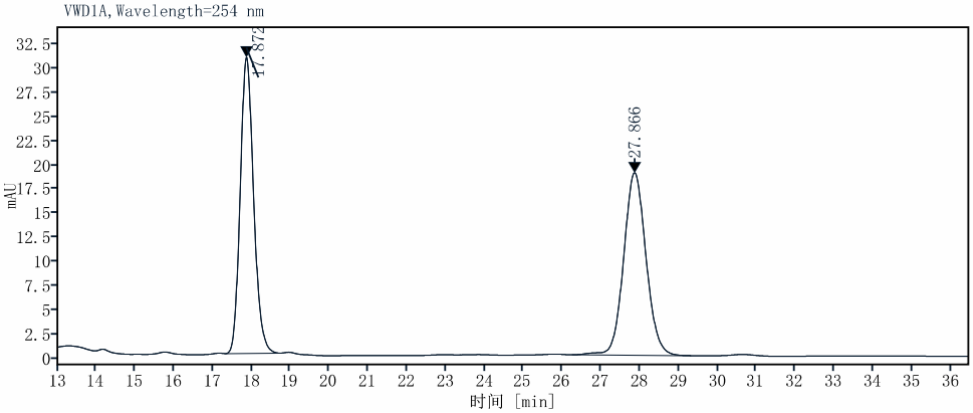


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
18.664	BM m	0.3647	9289.6270	393.1760	94.8778
43.145	MM m	0.8974	501.5263	8.5491	5.1222

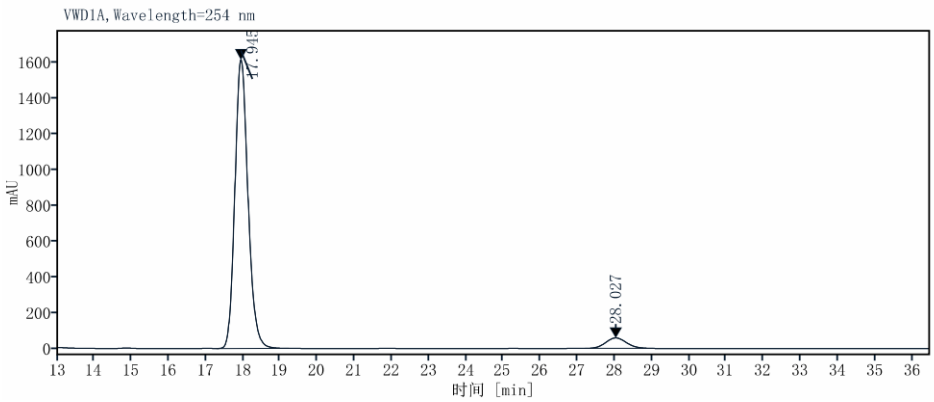
(R)-(4-(naphthalen-2-yl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ja)



Purification by flash column chromatography (PE/EA = 7:1) generated **3ja** (18.1 mg, 84% yield); 94.5:5.5 er; white solid; **m.p.** 176 – 178 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -24 (c = 0.20, MeOH).
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 – 7.81 (m, 2H), 7.74 – 7.71 (m, 2H), 7.68 – 7.65 (m, 1H), 7.53 (d, *J* = 1.9 Hz, 1H), 7.42 – 7.35 (m, 5H), 7.25 – 7.19 (m, 1H), 7.14 – 7.07 (m, 1H), 7.03 – 6.95 (m, 4H), 6.69 (d, *J* = 6.0 Hz, 1H), 4.95 (d, *J* = 6.0 Hz, 1H), 4.09 – 4.00 (m, 2H), 1.57 (s, 1H) ppm.
^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 147.9, 143.0, 138.9, 138.2, 133.5, 133.2, 132.3, 129.2, 128.65, 128.60, 128.3, 128.1, 127.6, 126.6, 126.4, 126.2, 126.1, 124.9, 121.1, 110.5, 98.1, 66.9, 45.9 ppm.
HRMS (ESI) *m/z* Calcd for $[C_{29}H_{22}N_2O_2 + H]^+$ 431.1754, found 431.1755.
HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ=254nm, t_{R1} = 17.9 min (major), t_{R2} = 28.0 min (minor).

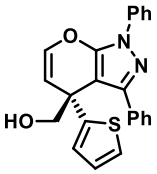


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
17.872	BB	1.4033	735.1699	30.6124	49.3183
27.866	BB	3.0567	755.4938	18.8499	50.6817



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
17.945	VB	1.9428	39730.4694	1616.2474	94.5649
28.027	BM m	0.6069	2283.4829	58.5627	5.4351

(R)-(1,3-diphenyl-4-(thiophen-2-yl)-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ka)



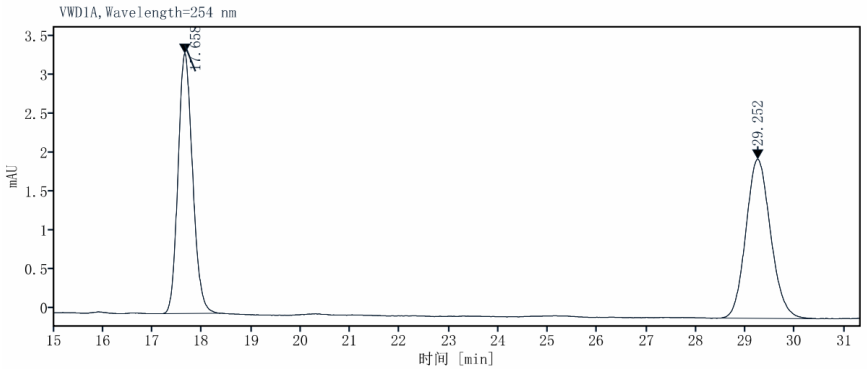
Purification by flash column chromatography (PE/EA = 7:1) generated **3ka** (16.0 mg, 83% yield); 94:6 er; white solid; **m.p.** 181 – 183 °C; R_f = 0.3 (PE/EA = 4/1) $[\alpha]_D^{20}$ = -29 (c = 0.10, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.85 (m, 2H), 7.50 – 7.45 (m, 2H), 7.34 – 7.23 (m, 7H), 6.95 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.78 (dd, *J* = 3.6, 1.2 Hz, 1H), 6.75 (d, *J* = 6.1 Hz, 1H), 5.09 (d, *J* = 6.0 Hz, 1H), 4.02 (dd, *J* = 10.7, 5.6 Hz, 1H), 3.93 (dd, *J* = 10.8, 7.0 Hz, 1H), 1.57 (t, *J* = 6.5 Hz, 1H) ppm.

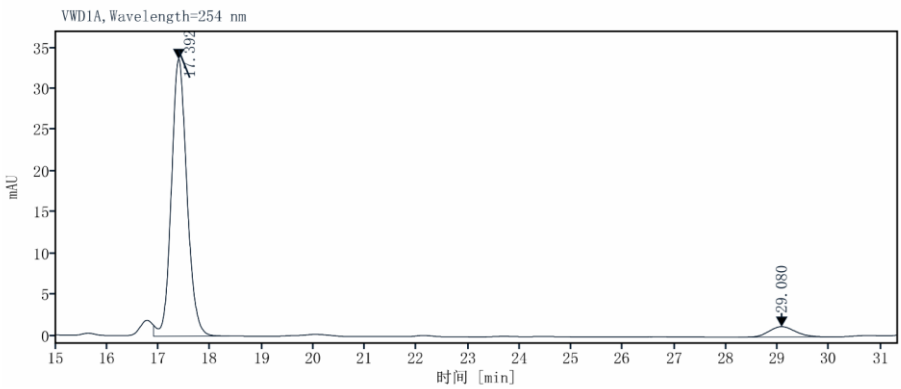
^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 148.8, 147.4, 138.6, 138.0, 133.6, 129.1, 128.6, 128.3, 128.2, 126.8, 126.6, 125.2, 123.4, 121.2, 110.3, 98.2, 67.6, 43.7 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{23}H_{18}N_2O_2S + H]^+$ 387.1162, found 387.1166.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 17.4 min (major), t_{R2} = 29.1 min (minor).

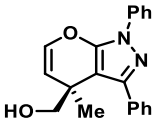


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
17.658	BB	1.1633	68.3405	3.3406	49.0382
29.252	BB	1.9867	71.0213	2.0441	50.9618



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
17.392	MB m	0.3223	708.4939	33.6975	94.1717
29.080	MM m	0.4987	43.8487	1.2578	5.8283

(R)-(4-methyl-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3la)



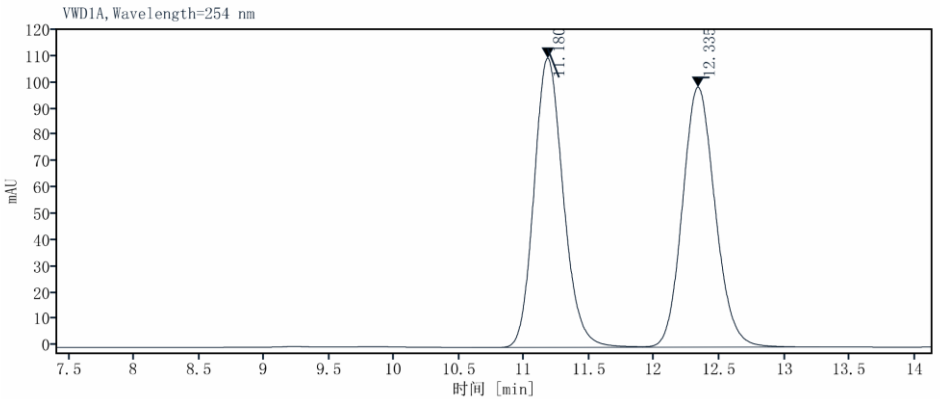
Purification by flash column chromatography (PE/EA = 7:1) generated **3la** (6.2 mg, 39% yield); 77:23 er; white solid; **m.p.** 113 – 115 ºC; R_f = 0.3 (PE/EA = 5/1); $[\alpha]_D^{20}$ = -0.66 (c = 0.46, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 2H), 7.55 – 7.51 (m, 2H), 7.46 – 7.38 (m, 5H), 7.30 – 7.27 (m, 1H), 6.69 (d, *J* = 6.1 Hz, 1H), 4.78 (d, *J* = 6.1 Hz, 1H), 3.57 (d, *J* = 10.8 Hz, 1H), 3.30 (d, *J* = 10.9 Hz, 1H), 1.64 (s, 1H), 1.20 (s, 3H) ppm.

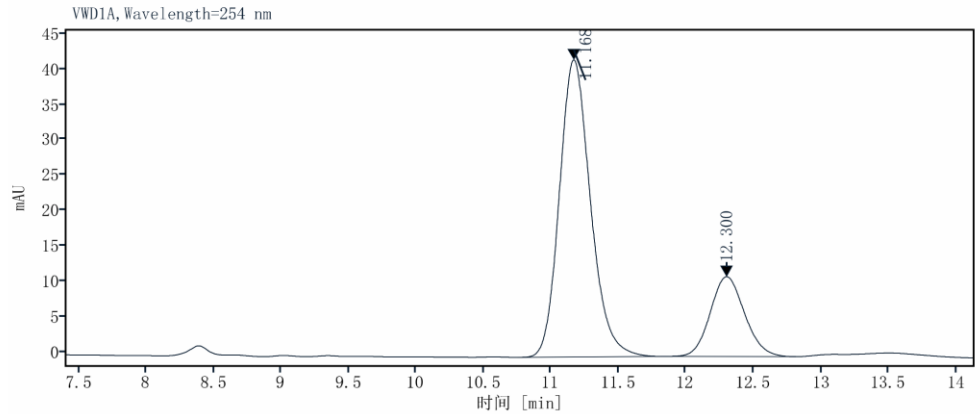
^{13}C NMR (75 MHz, $CDCl_3$) δ149.8, 147.1, 139.5, 138.1, 134.6, 129.4, 129.1, 128.5, 128.3, 126.5, 121.2, 110.9, 99.8, 70.5, 38.2, 26.6 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{20}H_{18}N_2O_2 + H]^+$ 319.1441 found 319.1445.

HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 11.2 min (major), t_{R2} = 12.3 min (minor).

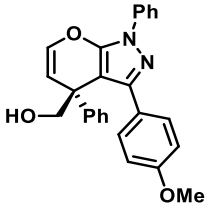


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
11.180	BV	1.3117	1727.6409	110.1721	49.9266
12.335	VB	1.3583	1732.7215	99.0716	50.0734

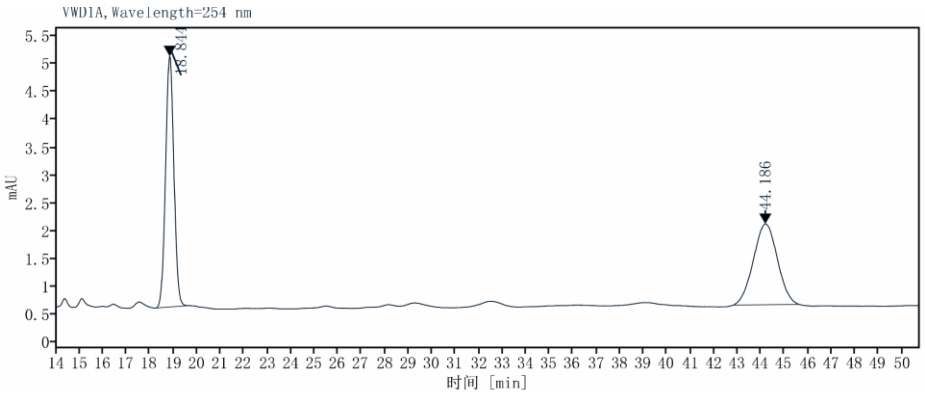


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
11.168	BB	1.0706	671.7863	41.8965	77.1435
12.300	BB	0.9867	199.0402	11.2617	22.8565

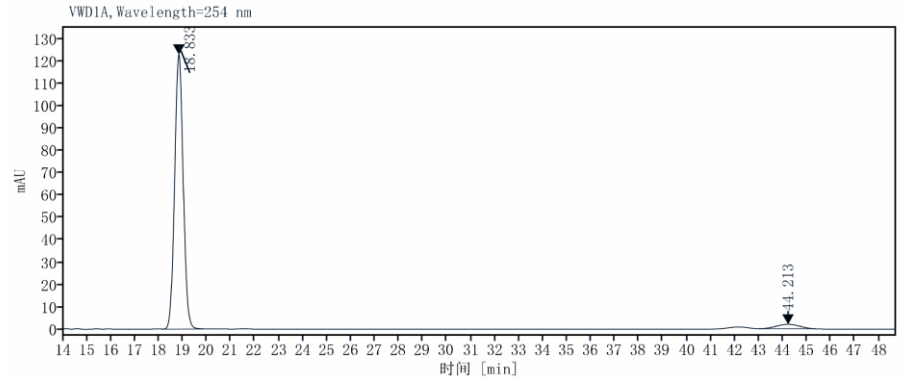
(R)-(3-(4-methoxyphenyl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ab)



Purification by flash column chromatography (PE/EA = 7:1) generated **3ab** (12.9 mg, 63% yield); 95.9:4.1 er; white solid; **m.p.** 173 – 175 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -15 (c = 0.16, MeOH).
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.86 (m, 2H), 7.50 – 7.45 (m, 2H), 7.37 – 7.32 (m, 2H), 7.30 – 7.24 (m, 4H), 7.05 – 7.01 (m, 2H), 6.77 (d, *J* = 6.0 Hz, 1H), 6.72 – 6.68 (m, 2H), 5.00 (d, *J* = 6.0 Hz, 1H), 4.07 – 4.01 (m, 2H), 3.76 (s, 3H), 1.58 (s, 1H) ppm.
^{13}C NMR (75 MHz, $CDCl_3$) δ 159.6, 148.6, 147.9, 146.0, 138.6, 138.2, 129.8, 129.1, 128.7, 127.2, 127.0, 126.5, 126.0, 121.1, 113.5, 110.6, 97.7, 66.7, 55.2, 45.8 ppm.
HRMS (ESI) *m/z* Calcd for $[C_{26}H_{22}N_2O_3 + H]^+$ 411.1703, found 411.1703.
HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 ml/min, uv-vis λ = 254nm, t_{R1} = 18.8 min (major), t_{R2} = 44.2 min (minor).

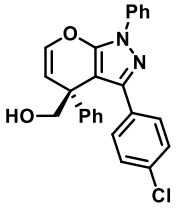


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
18.844	BB	1.4050	111.1344	4.5154	51.8130
44.186	MM m	0.8318	103.3567	1.4549	48.1870



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
18.833	BB	2.3650	3045.1098	122.9860	95.8511
44.213	BM m	0.7828	131.8083	2.0003	4.1489

(R)-(3-(4-chlorophenyl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ac)



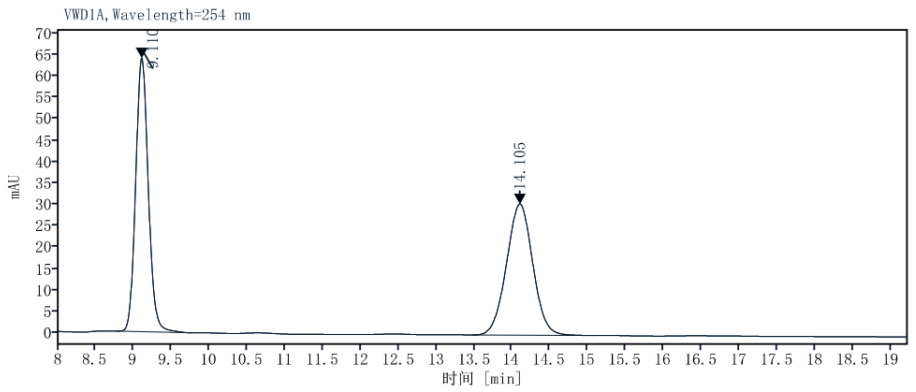
Purification by flash column chromatography (PE/EA = 7:1) generated **3ac** (15.4 mg, 74% yield); 96:4 er; white solid; **m.p.** 155 – 157 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -13 (c = 0.15, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.5 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.37 – 7.24 (m, 6H), 7.17 – 7.12 (m, 2H), 7.05 – 7.00 (m, 2H),6.76 (d, *J* = 5.9 Hz, 1H), 4.99 (d, *J* = 6.0 Hz, 1H), 4.08 – 3.95 (m, 2H), 1.51 (s, 1H) ppm;

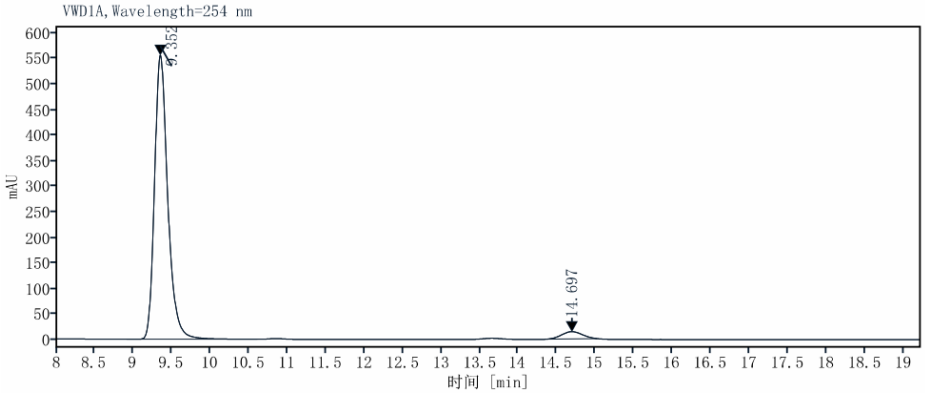
^{13}C NMR (75 MHz, $CDCl_3$) δ 147.9, 147.5, 145.7, 138.5, 137.9, 134.1, 132.0, 129.8, 129.1, 128.8, 128.2, 127.1, 126.7, 121.1, 110.4, 98.2, 66.7, 45.6 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{19}ClN_2O_2 + H]^+$ 415.1208, found 415.1206.

HPLC: Daicel Chiralcel IA-H, *n*-hexane/isopropanol 50/50, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 9.4 min (major), t_{R2} = 14.7 min (minor).

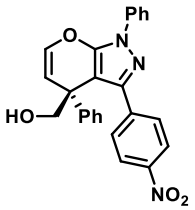


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
9.110	BB	0.9967	739.4417	63.9524	49.8039
14.105	BB	1.6233	745.2653	30.6685	50.1961



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
9.352	MB m	0.1807	6612.9915	556.1309	96.1015
14.697	MM m	0.2970	268.2675	14.2278	3.8985

(R)-(3-(4-nitrophenyl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ad)



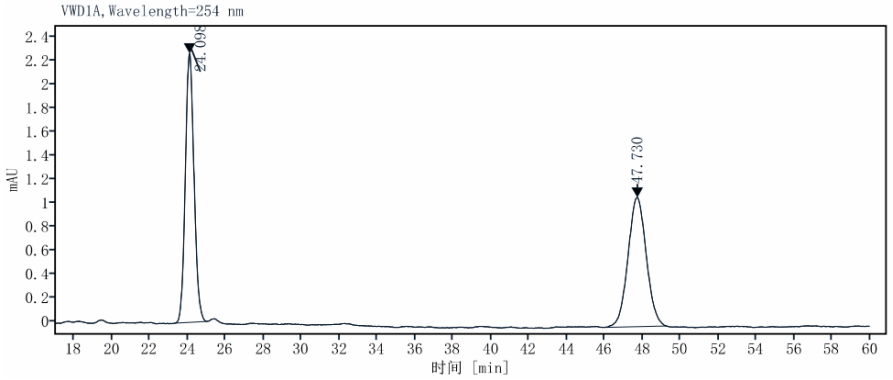
Purification by flash column chromatography (PE/EA = 6:1) generated **3ad** (11.3 mg, 53% yield); 94:6 er; white solid; **m.p.** 185 – 187 °C; R_f = 0.2 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -12 (c = 0.13, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 – 7.97(m, 2H), 7.89 – 7.86 (m, 2H), 7.53 – 7.48 (m, 2H), 7.40 – 7.25 (m, 8H), 6.77 (d, *J* = 6.0 Hz, 1H), 5.00 (d, *J* = 6.0 Hz, 1H), 4.10 (d, *J* = 10.8 Hz, 1H), 3.97 (d, *J* = 10.7 Hz, 1H), 1.64 (s, 1H) ppm;

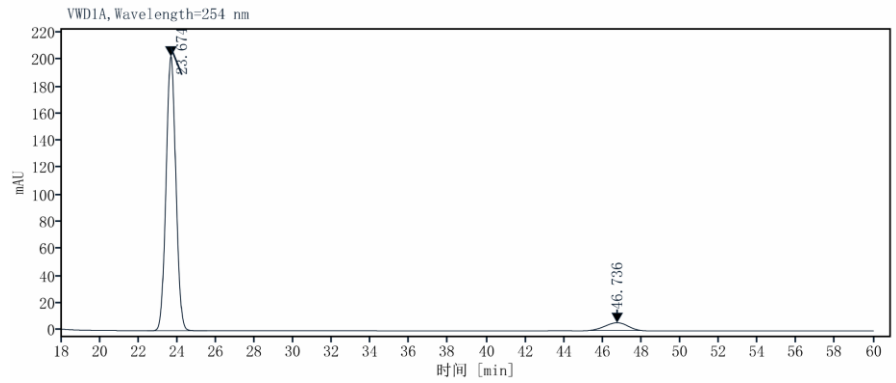
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 147.3, 146.3, 145.6, 140.1, 138.5, 137.8, 129.3, 129.1, 129.0, 127.4, 127.1, 123.3, 121.3, 110.4, 98.9, 66.9, 45.7 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{19}N_3O_4 + H]^+$ 426.1448, found 426.1446;

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 23.7 min (major), t_{R2} = 46.7 min (minor).

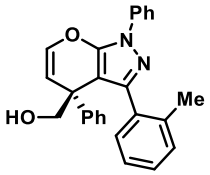


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
24.098	BB	1.6333	72.2582	2.2639	49.7292
47.730	MM m	0.7977	73.0452	1.0889	50.2708



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
23.674	BB	3.0800	7140.2924	203.2191	94.0172
46.736	MM m	1.0778	454.3765	5.7075	5.9828

(R)-(1,4-diphenyl-3-(o-tolyl)-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ae)



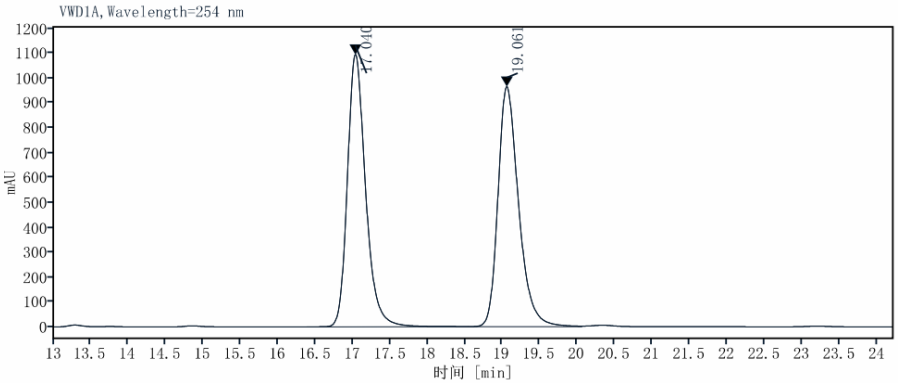
Purification by flash column chromatography (PE/EA = 7:1) generated **3ae** (13.7 mg, 70% yield); 93.5:6.5 er; white solid; **m.p.** 80 – 82 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = 2 (c = 0.10, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.84 – 7.80 (m, 2H), 7.46 – 7.39 (m, 2H), 7.29 – 7.21 (m, 1H), 7.19 – 7.13 (m, 4H), 7.07 – 7.00 (m, 2H), 6.97 – 6.93 (m, 2H), 6.89 (d, *J* = 6.1 Hz, 1H), 6.78 (dd, *J* = 7.5, 1.4 Hz, 1H), 4.99 (d, *J* = 6.1 Hz, 1H), 3.95 (dd, *J* = 10.6, 6.9 Hz, 1H), 3.87 (dd, *J* = 10.7, 6.0 Hz, 1H), 1.74 – 1.70 (m, 4H) ppm.

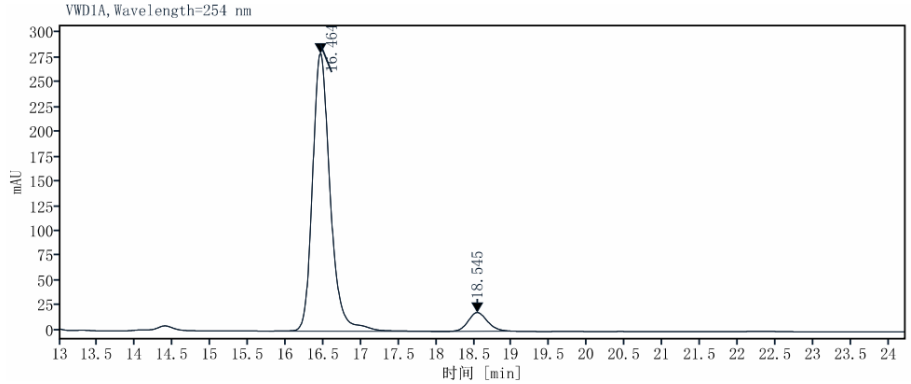
^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 146.5, 144.3, 140.0, 138.2, 132.9, 130.2, 129.8, 129.1, 128.6, 128.2, 127.3, 126.7, 126.4, 125.0, 120.9, 109.2, 100.1, 67.0, 45.0, 19.3 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{26}H_{22}N_2O_2 + H]^+$ 395.1754, found 395.1754.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 16.5 min (major), t_{R2} = 18.5 min (minor).

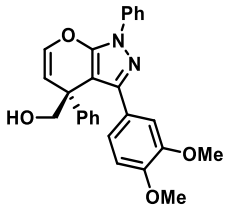


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
17.040	BB	2.1553	18456.5075	1094.3884	50.0459
19.061	BV	1.5220	18422.6329	965.0296	49.9541



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
16.464	BM m	0.2472	4567.0850	280.1963	93.2633
18.545	MM m	0.2695	329.8956	18.8249	6.7367

(R)-(3-(3,4-dimethoxyphenyl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3af)



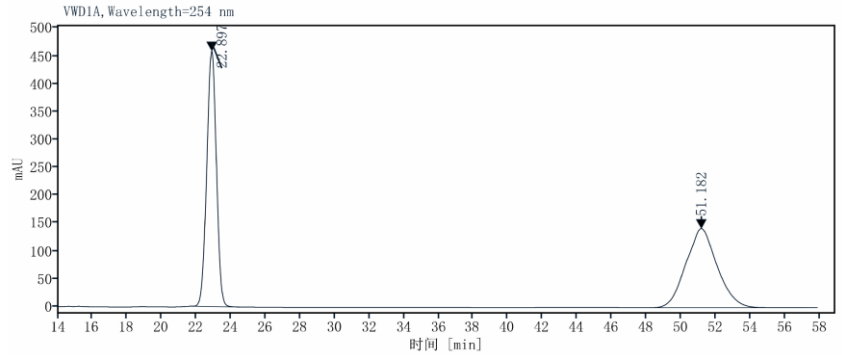
Purification by flash column chromatography (PE/EA = 7:1) generated **3af** (16.1 mg, 73% yield); 95:5 er; light yellow solid; **m.p.** 152 – 154 ºC; R_f = 0.4 (PE/EA = 2/1); $[\alpha]_D^{20}$ = -23.3 (c = 0.42, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.51 – 7.44 (m, 2H), 7.38 – 7.21 (m, 6H), 6.89 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.73 – 6.70 (m, 2H), 6.60 (d, *J* = 2.0 Hz, 1H), 4.97 (d, *J* = 6.0 Hz, 1H), 4.07 (dd, *J* = 10.7, 7.7 Hz, 1H), 4.00 (dd, *J* = 10.7, 5.5 Hz, 1H), 3.83 (s, 3H), 3.40 (s, 3H), 1.60 – 1.51 (m, 1H) ppm.

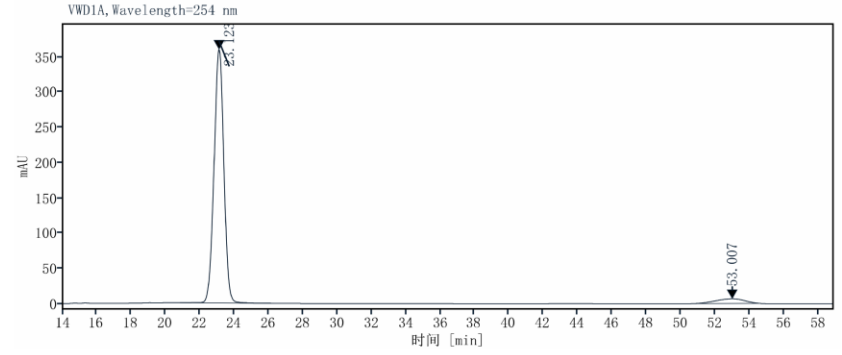
^{13}C NMR (75 MHz, $CDCl_3$) δ 149.0, 148.5, 148.3, 148.0, 146.3, 138.2, 138.1, 129.2, 128.9, 127.2, 127.0, 126.5, 126.2, 121.1, 116.4, 111.6, 110.9, 110.8, 97.5, 66.6, 55.8, 55.3, 45.9 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{27}H_{24}N_2O_4 + H]^+$ 441.1809, found 441.1817;

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 23.1 min (major), t_{R2} = 53.0 min (minor).

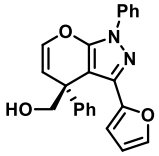


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
22.897	BB	2.8500	17712.7831	458.3316	49.8402
51.182	BB	9.0933	17826.3807	141.9982	50.1598



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
23.123	BB	5.4400	14292.6895	359.6775	95.0755
53.007	MM m	1.3373	740.2949	6.5215	4.9245

(R)-(3-(furan-2-yl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ag)



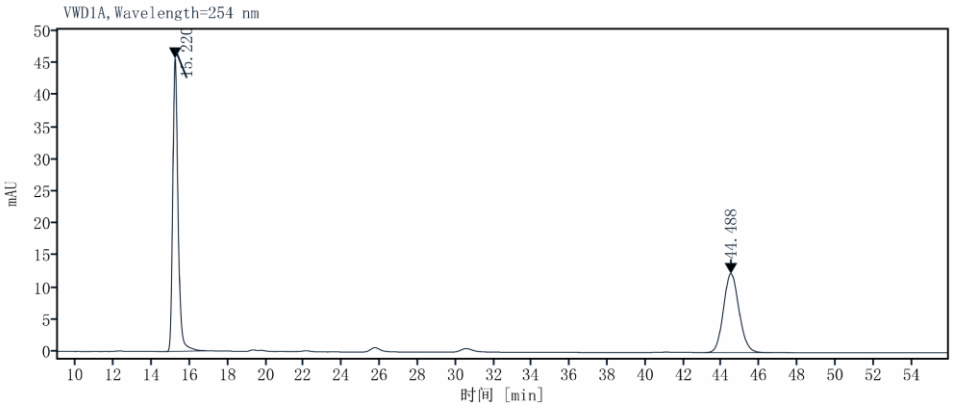
Purification by flash column chromatography (PE/EA = 7:1) generated **3ag** (10.7 mg, 58% yield); 95:5 er; white solid; **m.p.** 287 – 290 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -10 (c = 0.18, MeOH).

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.80 – 7.76 (m, 2H), 7.53 – 7.48 (m, 3H), 7.36 – 7.30 (m, 2H), 7.28 – 7.22 (m, 2H), 7.16 – 7.10 (m, 1H), 6.88 (d, *J* = 6.1 Hz, 1H), 6.34 (dd, *J* = 3.4, 1.8 Hz, 1H), 6.04 (d, *J* = 3.3 Hz, 1H), 5.06 (d, *J* = 6.1 Hz, 1H), 4.89 (t, *J* = 5.4 Hz, 1H), 4.13 (dd, *J* = 10.5, 5.7 Hz, 1H), 4.03 (dd, *J* = 10.4, 5.3 Hz, 1H) ppm.

^{13}C NMR (75 MHz, DMSO-d_6) δ 147.9, 147.8, 146.1, 143.0, 140.2, 138.1, 138.0, 129.9, 128.7, 127.7, 127.2, 126.8, 121.3, 111.8, 111.7, 108.9, 98.9, 66.3, 45.6 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{23}H_{18}N_2O_3 + H]^+$ 371.1390, found 371.1398.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ=254nm, t_{R1} = 14.9 min (major), t_{R2} = 44.0 min (minor).



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
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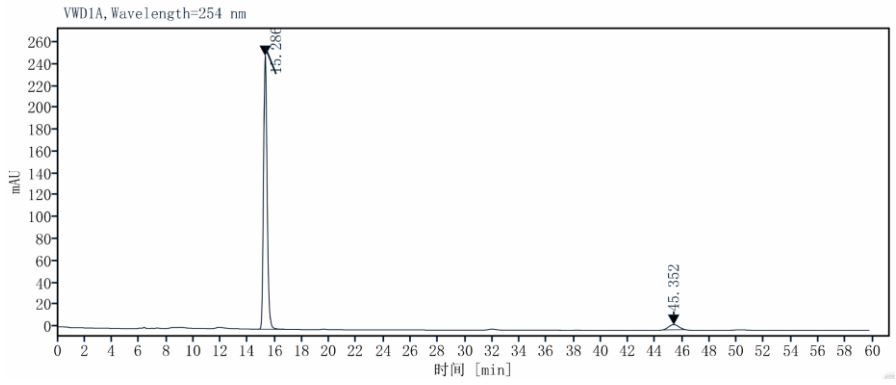
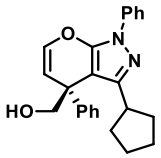
44.488	BB	3.5433	881.1514	12.3223	49.9727



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
15.286	BB	3.0533	4561.5390	250.3312	94.9967
45.352	MM m	0.7792	240.2495	4.7250	5.0033

(R)-(3-cyclopentyl-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol(3ah)



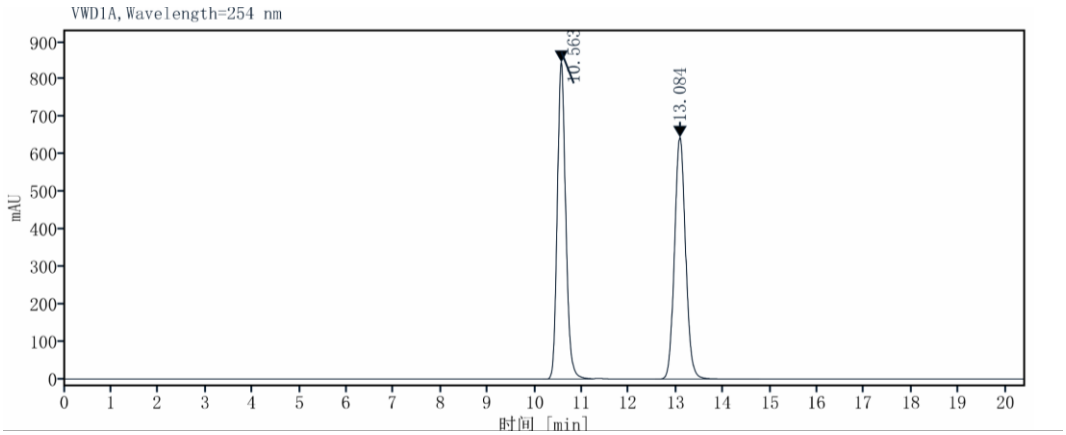
Purification by flash column chromatography (PE/EA = 7:1) generated **3ah** (13.1 mg, 70% yield); 83:17 er; white solid; **m.p.** 167–169 °C; R_f = 0.3 (PE/EA = 5/1); $[\alpha]_D^{20}$ = -0.10 (c=0.60, MeOH)。

^{1}H NMR (300 MHz, DMSO-d_6) δ 7.64 (d, J = 8.0 Hz, 2H), 7.40 – 7.35 (m, 2H), 7.29 – 7.07 (m, 6H), 6.81 (d, J = 6.0 Hz, 1H), 4.97 (d, J = 6.1 Hz, 1H), 4.93 (d, J = 5.2 Hz, 1H), 4.02 (dd, J = 10.6, 5.5 Hz, 1H), 3.87 (dd, J = 10.6, 5.0 Hz, 1H), 1.73 – 1.19 (m, 8H), 1.04 – 0.96 (m, 1H) ppm.

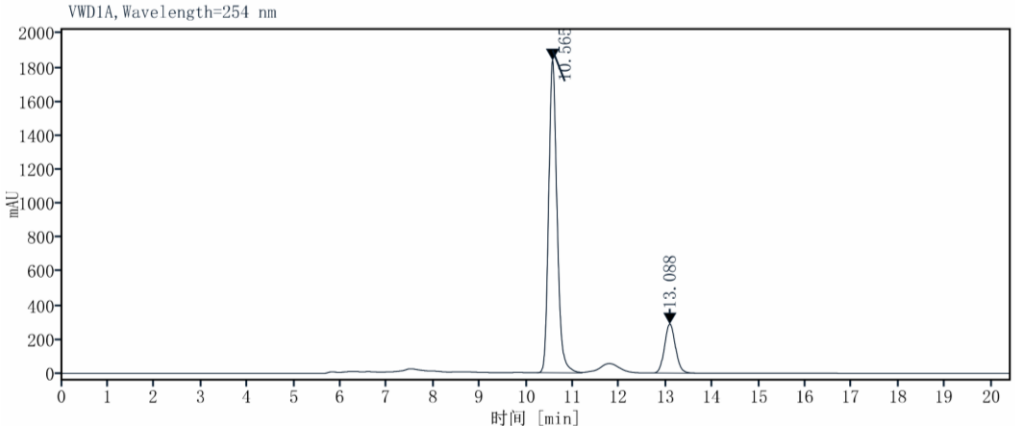
^{13}C NMR (75 MHz, DMSO-d_6) δ 153.8, 146.5, 146.2, 138.7, 138.6, 129.7, 128.5, 128.0, 126.7, 126.2, 120.3, 111.0, 100.1, 67.3, 44.8, 38.4, 32.7, 32.5, 25.6, 25.5 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{24}H_{24}N_2O_2 + H]^+$ 373.1911 found 373.1913.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 10.6 min (major), t_{R2} = 13.1 min (minor).

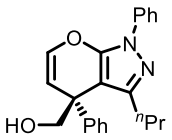


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
10.563	BV	1.0637	10574.0388	847.3369	49.9731
13.084	BB	2.2050	10585.4286	646.1215	50.0269

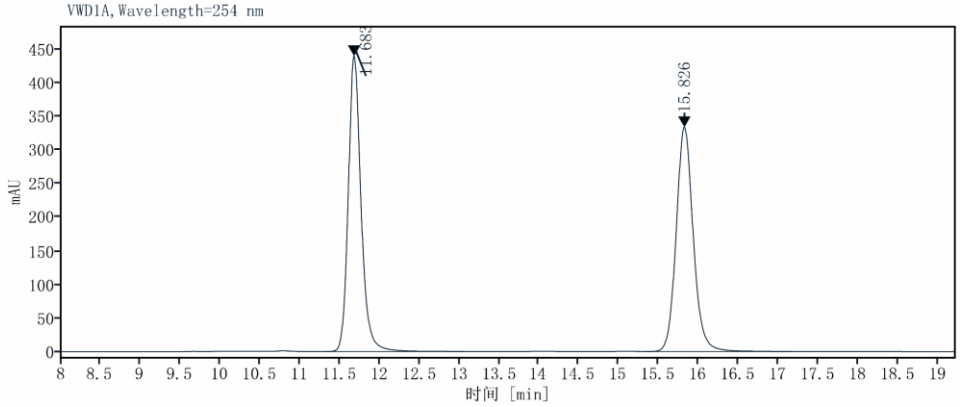


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
10.565	BV	0.9794	23150.1487	1839.1161	83.1476
13.088	BM m	0.2518	4692.0784	288.3827	16.8524

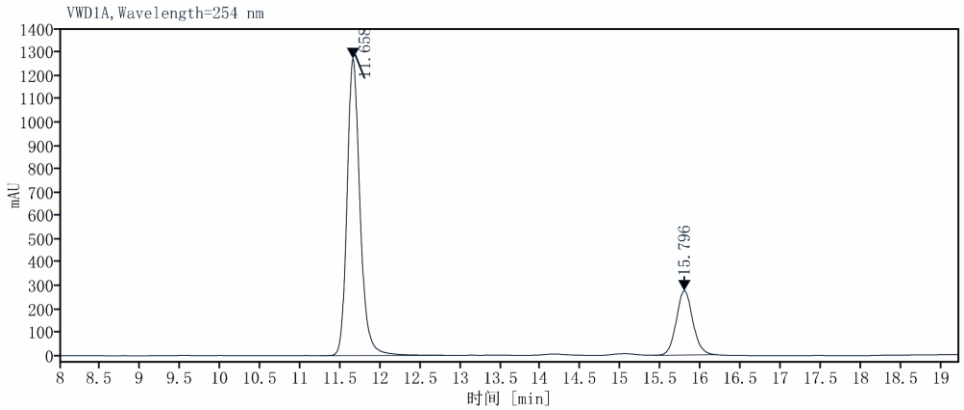
(R)-(1,4-diphenyl-3-propyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ai)



Purification by flash column chromatography (PE/EA = 7:1) generated **3ai** (6.8 mg, 39% yield); 78:22 er; white solid; **m.p.** 100 – 102 ºC; R_f = 0.3 (PE/EA = 5/1); $[\alpha]_D^{20}$ = -3.1 (c = 0.36, MeOH);
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 8.0, 1.7 Hz, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.41 – 7.20 (m, 6H), 6.77 (d, *J* = 6.1 Hz, 1H), 4.99 (d, *J* = 6.1 Hz, 1H), 4.23 – 4.03 (m, 2H), 2.36 – 2.13 (m, 2H), 1.97 (t, 1H), 1.60 – 1.22 (m, 2H), 0.81 (t, *J* = 7.3 Hz, 3H) ppm.
^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 147.3, 144.7, 139.3, 138.4, 129.2, 128.7, 127.2, 127.0, 126.2, 120.9, 110.0, 97.6, 67.7, 45.4, 30.4, 21.7, 14.2 ppm.
HRMS (ESI) *m/z* Calcd for $[C_{22}H_{22}N_2O_2 + H]^+$ 347.1754, found 347.1755.
HPLC: Daicel Chiralcel IA-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 11.7 min (major), t_{R2} = 15.8 min (minor).

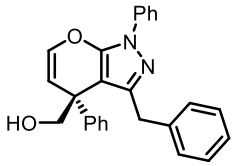


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
11.683	BB	1.7300	4969.0864	439.9630	50.0564
15.826	BB	1.8333	4957.8914	334.2199	49.9436

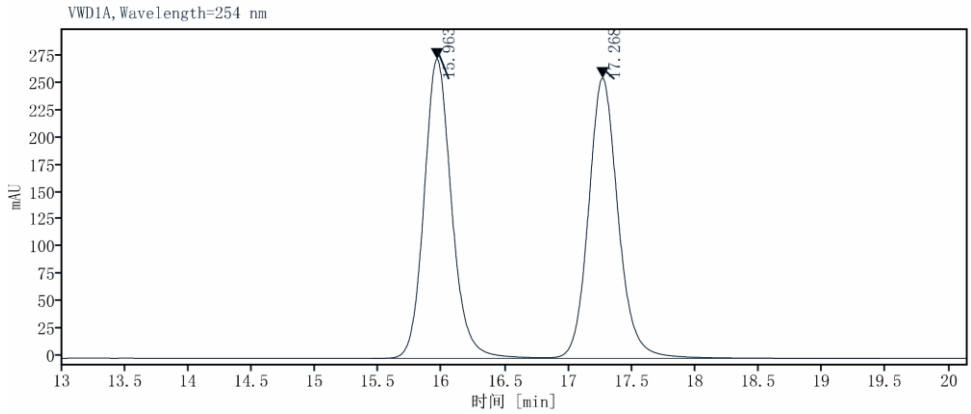


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
11.658	BB	1.7088	14276.2819	1271.8721	78.1433
15.796	VM m	0.2227	3993.0866	276.1173	21.8567

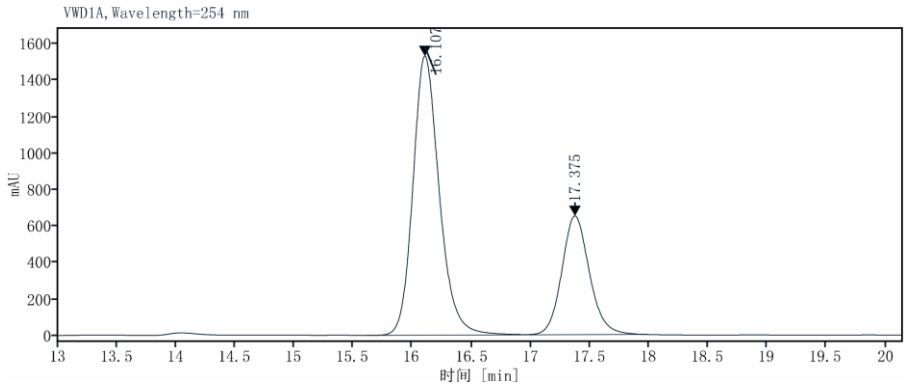
(R)-(1-(tert-butyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3aj)



Purification by flash column chromatography (PE/EA = 7:1) generated **3aj** (8.9 mg, 45% yield); 69.5:30.5 er; white solid; **m.p.** 114 – 116 °C; R_f = 0.4 (PE/EA = 5/1); $[\alpha]_D^{20}$ = +6.2 (c = 0.36, MeOH); **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.89 – 7.78 (m, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.37 – 7.17 (m, 9H), 7.08 – 6.98 (m, 2H), 6.74 (d, *J* = 6.1 Hz, 1H), 4.90 (d, *J* = 6.1 Hz, 1H), 3.86 (d, *J* = 15.5 Hz, 1H), 3.78 (dd, *J* = 10.9, 7.3 Hz, 1H), 3.59 (dd, *J* = 11.1, 4.0 Hz, 1H), 3.34 (d, *J* = 15.6 Hz, 1H) ppm.
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3, 147.8, 144.3, 139.0, 138.6, 138.2, 129.1, 128.6, 128.5, 128.4, 127.1, 127.0, 126.5, 126.3, 120.8, 110.2, 97.9, 67.3, 45.2, 34.2 ppm.
HRMS (ESI) *m/z* Calcd for $[C_{26}H_{22}N_2O_2 + H]^+$ 395.1754, found 395.1754.
HPLC: Daicel Chiralcel IA-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 16.1 min (major), t_{R2} = 17.3 min (minor).

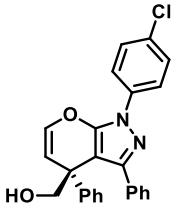


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
15.963	BV	1.3664	4151.7436	274.4228	49.7897
17.268	VB	2.6436	4186.8189	257.0382	50.2103



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
16.107	BM m	0.2358	23753.4902	1532.6621	69.1367
17.375	MM m	0.2486	10603.7855	652.5210	30.8633

(R)-(1-(4-chlorophenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ak)



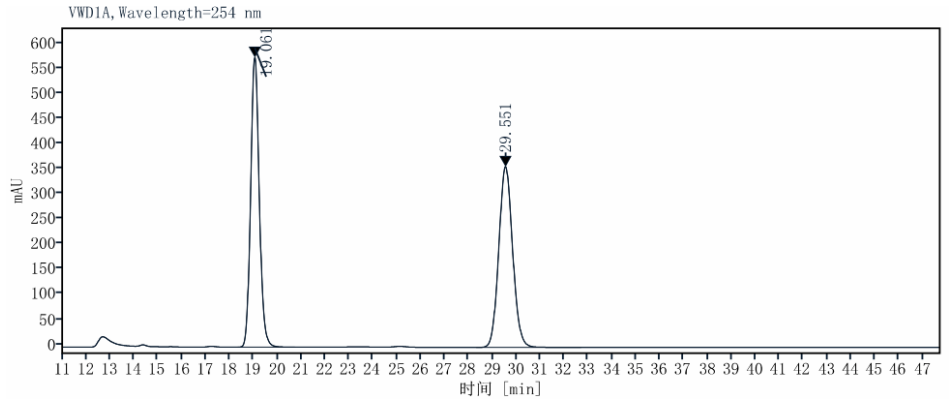
Purification by flash column chromatography (PE/EA = 7:1) generated **3ak** (15.7 mg, 76% yield); 94.5:5.5 er; white solid; **m.p.** 163 – 165 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -14 (c = 0.18, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 – 7.81 (m, 2H), 7.47 – 7.39 (m, 2H), 7.37 – 7.30 (m, 2H), 7.28 – 7.22 (m, 4H), 7.20 – 7.14 (m, 2H), 7.11 – 7.06 (m, 2H), 6.77 (d, *J* = 6.1 Hz, 1H), 5.01 (d, *J* = 6.1 Hz, 1H), 4.02 – 3.96 (m, 2H), 1.51 (s, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.2, 147.8, 145.7, 138.6, 136.8, 133.3, 131.9, 129.2, 128.7, 128.6, 128.4, 128.1, 127.2, 127.1, 122.0, 110.7, 98.5, 66.7, 45.7 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{19}ClN_2O_2 + H]^+$ 415.1208, found 415.1209;

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 19.2 min (major), t_{R2} = 29.9 min (minor).



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
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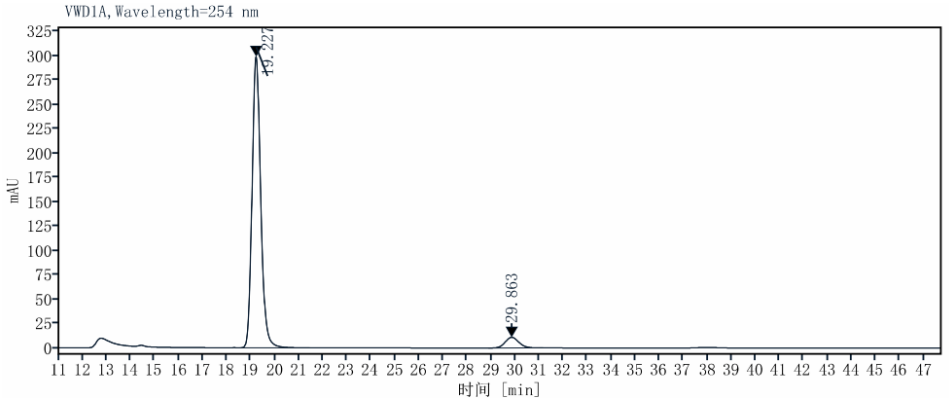
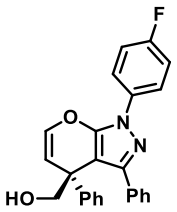
29.551	BB	4.3767	14484.2291	359.8902	50.0354



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
19.227	BB	2.8867	7503.3521	299.3719	94.5432
29.863	BB	2.2650	433.0735	10.9581	5.4568

(R)-(1-(4-fluorophenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3al)



Purification by flash column chromatography (PE/EA = 7:1) generated **3al** (14.5mg, 73% yield); 93.5:6.5 er; white solid; **m.p.** 175 – 176 ºC; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -14 (c = 0.13, MeOH).

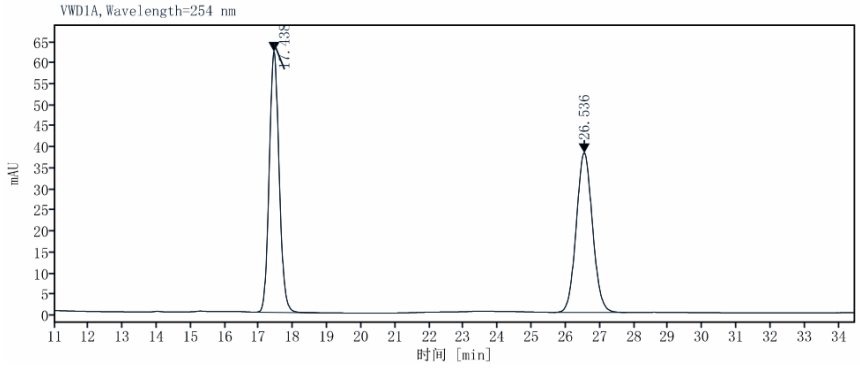
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 – 7.82 (m, 2H), 7.37 – 7.31 (m, 2H), 7.29 – 7.22 (m, 4H), 7.21 – 7.14 (m, 4H), 7.11 – 7.07 (m, 2H), 6.77 (d, J = 6.1 Hz, 1H), 5.02 (d, J = 6.0 Hz, 1H), 4.08 – 3.99 (m, 2H), 1.44 (s, 1H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.0 (d, $^1J_{C\text{-}F}$ = 246.9 Hz), 148.9, 147.7, 145.8, 138.6, 134.3 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 133.4, 128.7, 128.6, 128.3, 128.1, 127.2, 127.1, 122.9 (d, $^3J_{C\text{-}F}$ = 8.3 Hz), 115.9 (d, $^2J_{C\text{-}F}$ = 22.9 Hz) ppm, 110.7, 98.2, 66.8, 45.7 ppm.

^{19}F NMR (282 MHz, $CDCl_3$) δ -122.61 ppm.

HRMS (ESI) *m*/*z* Calcd for $[C_{25}H_{19}FN_2O_2 + H]^+$ 399.1503, found 399.1503.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 16.7 min (major), t_{R2} = 25.9 min (minor).



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
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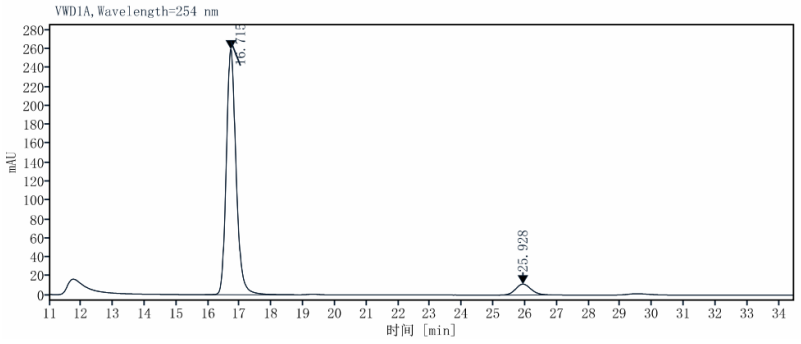
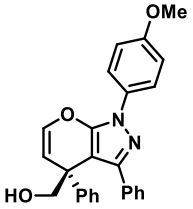
26.536	BB	2.1367	1254.3868	37.8735	49.9922



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
16.715	BB	2.9400	5560.5531	259.4004	93.5109
25.928	MM m	0.5185	385.8706	11.4975	6.4891

(R)-(1-(4-methoxyphenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3am)



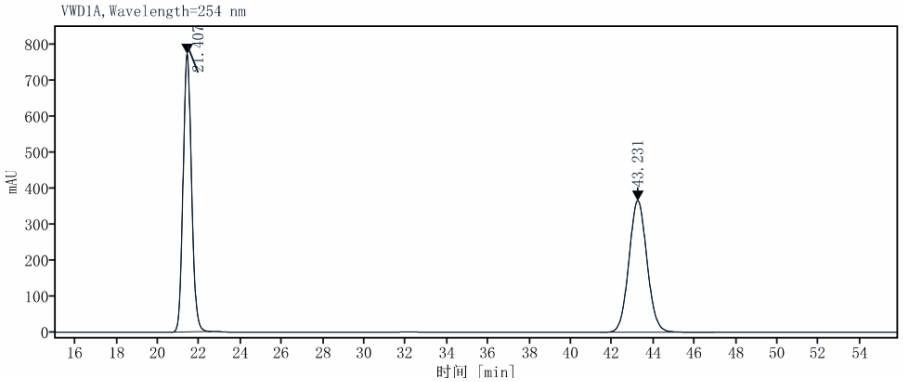
Purification by flash column chromatography (PE/EA = 7:1) generated **3am** (15.1mg, 74% yield); 95:5 er; white solid; **m.p.** 125 – 127 °C; R_f = 0.4 (PE/EA = 4/1); $[\alpha]_D^{20}$ = - 12 (c = 0.10, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.80 – 7.70 (m, 2H), 7.37 – 7.31 (m, 2H), 7.28 – 7.21 (m, 4H), 7.18 – 7.13 (m, 2H), 7.12 – 7.08 (m, 2H), 7.02 – 6.97 (m, 2H), 6.74 (d, *J* = 6.0 Hz, 1H), 4.99 (d, *J* = 6.1 Hz, 1H), 4.06 – 3.98 (m, 2H), 3.85 (s, 3H), 1.47 (s, 1H) ppm.

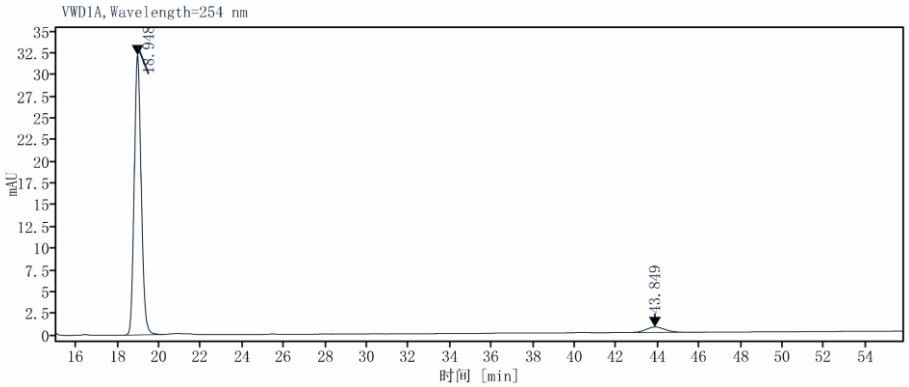
^{13}C NMR (75 MHz, $CDCl_3$) δ 158.3, 148.3, 147.6, 146.0, 138.6, 133.7, 131.4, 128.7, 128.6, 128.14, 128.08, 127.2, 127.0, 123.0, 114.3, 110.6, 97.6, 66.8, 55.6, 45.8 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{26}H_{22}N_2O_3 + H]^+$ 411.1703, found 411.1707.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 18.9 min (major), t_{R2} = 43.8 min (minor).

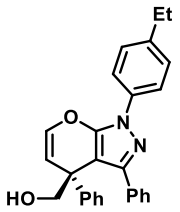


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
21.407	BB	1.9489	21985.6198	773.2803	49.7012
43.231	BB	5.5200	22249.9492	365.7353	50.2988



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
18.948	BB	1.8567	754.1313	32.2198	95.2075
43.849	MM m	0.7275	37.9610	0.6189	4.7925

(R)-(1-(4-ethylphenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3an)



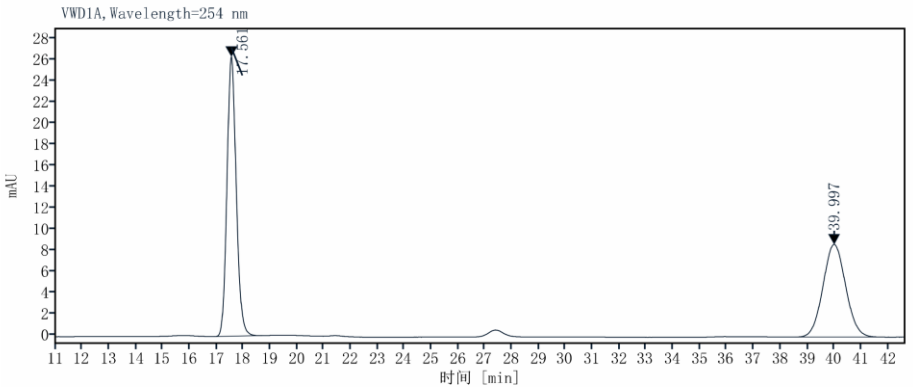
Purification by flash column chromatography (PE/EA = 7:1) generated **3an** (17.3 mg, 85% yield); 90.5:9.5 er; white solid; **m.p.** 193 – 195 °C; R_f = 0.3 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -13 (c = 0.12, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.79 – 7.74 (m, 2H), 7.37 – 7.31 (m, 3H), 7.29 – 7.21 (m, 6H), 7.19 – 7.08 (m, 4H), 6.76 (d, *J* = 6.0 Hz, 1H), 5.00 (d, *J* = 6.1 Hz, 1H), 4.02 (s, 2H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.44 (d, *J* = 6.5 Hz, 1H), 1.27 (t, *J* = 7.6 Hz, 3H) ppm.

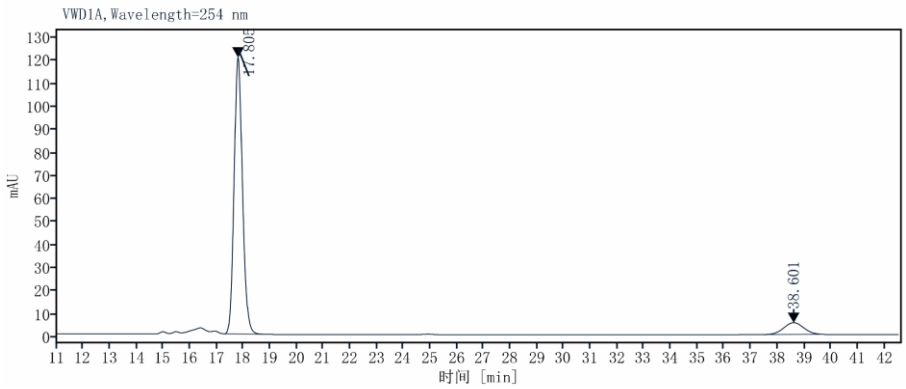
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.5, 147.7, 145.9, 142.9, 138.6, 135.8, 133.6, 128.7, 128.6, 128.5, 128.15, 128.05, 127.2, 127.0, 121.3, 110.6, 97.8, 66.8, 45.8, 28.5, 15.6 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{27}H_{24}N_2O_2 + H]^+$ 409.1911, found 409.1914.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ=254nm, t_{R1} = 17.8 min (major), t_{R2} = 38.6 min (minor).

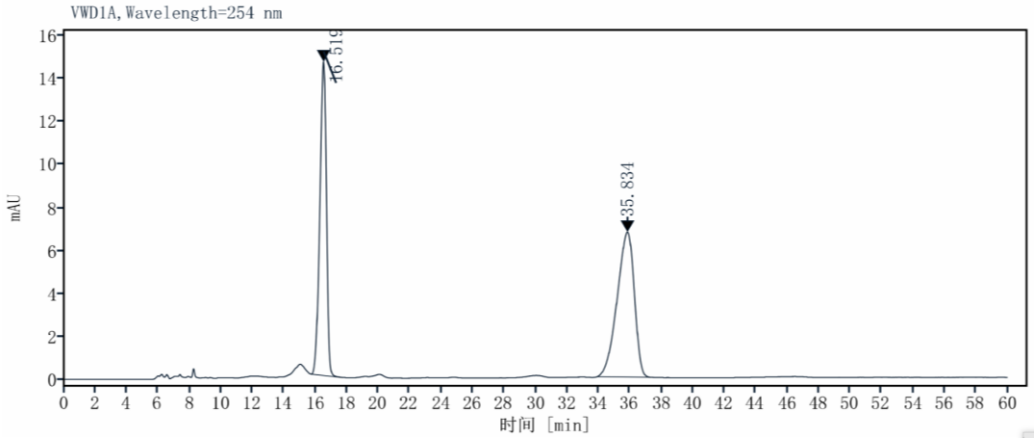


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
17.561	BB	1.5817	532.5001	26.3548	50.9138
39.997	BB	3.2767	513.3860	8.7404	49.0862

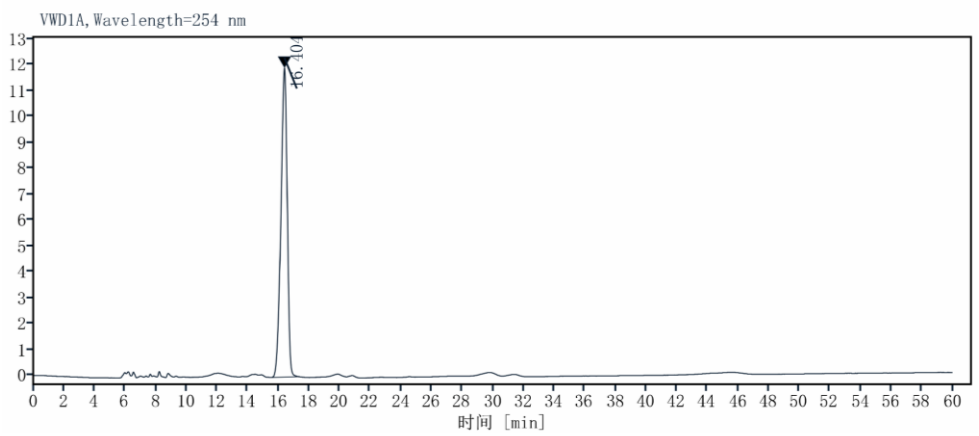


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
17.805	BB	1.8117	2627.2920	120.1274	90.8228
38.601	MM m	0.7847	265.4739	5.1048	9.1772

After recrystallization

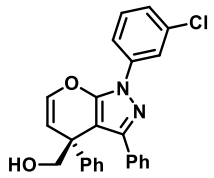


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
16.519	BB	1.9467	422.6811	14.5961	49.8821
35.834	MM m	1.0532	424.6787	6.7441	50.1179



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
16.404	BB	1.8017	343.9449	11.9524	100.0000

(R)-(1-(3-chlorophenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ao)



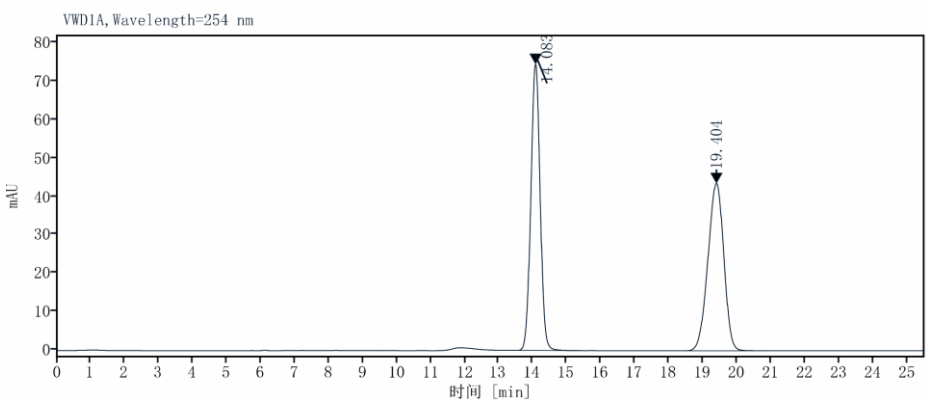
Purification by flash column chromatography (PE/EA = 7:1) generated **3ao** (15.7 mg, 76% yield); 93:7 er; light yellow solid; **m.p.** 147 – 149 °C; R_f = 0.3 (PE/EA = 5/1); $[\alpha]_D^{20}$ = -15.2 (c = 0.42, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (t, *J* = 2.1 Hz, 1H), 7.82 – 7.78 (m, 1H), 7.39 – 7.28 (m, 3H), 7.26 – 7.20 (m, 5H), 7.18 – 7.12 (m, 2H), 7.09 – 7.05 (m, 2H), 6.74 (d, *J* = 6.1 Hz, 1H), 4.98 (d, *J* = 6.1 Hz, 1H), 4.02 – 3.91 (m, 2H), 1.66 (t, *J* = 6.4 Hz, 1H) ppm.

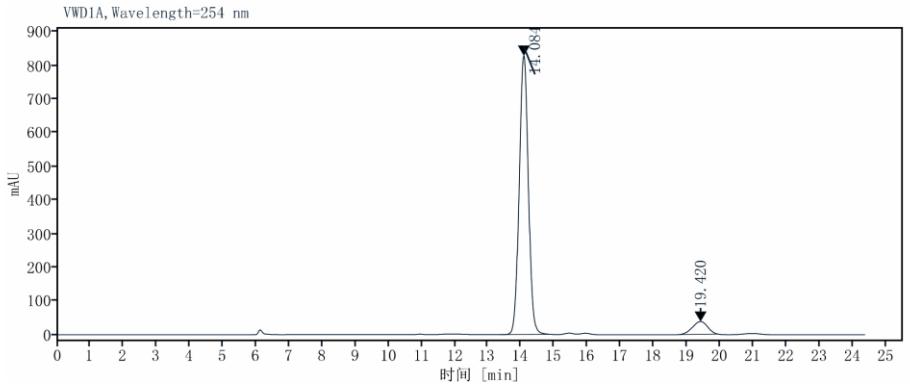
^{13}C NMR (75 MHz, $CDCl_3$) δ 149.4, 148.0, 145.7, 139.2, 138.5, 134.9, 133.3, 130.2, 128.8, 128.6, 128.4, 128.1, 127.2, 127.1, 126.4, 120.9, 118.7, 110.7, 98.8, 66.7, 45.6 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{19}ClN_2O_2 + H]^+$ 415.1208, found 415.1214.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 14.1 min (major), t_{R2} = 19.4 min (minor).

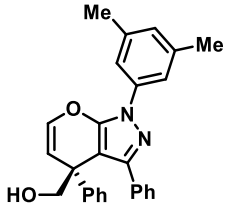


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
14.083	BB	2.0200	1416.7507	74.5550	49.9688
19.404	BB	2.5067	1418.5196	43.6029	50.0312



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
14.084	BM m	0.2975	15872.7170	828.4658	93.0476
19.420	MM m	0.4955	1185.9897	37.8532	6.9524

(R)-(1-(3,5-dimethylphenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ap)



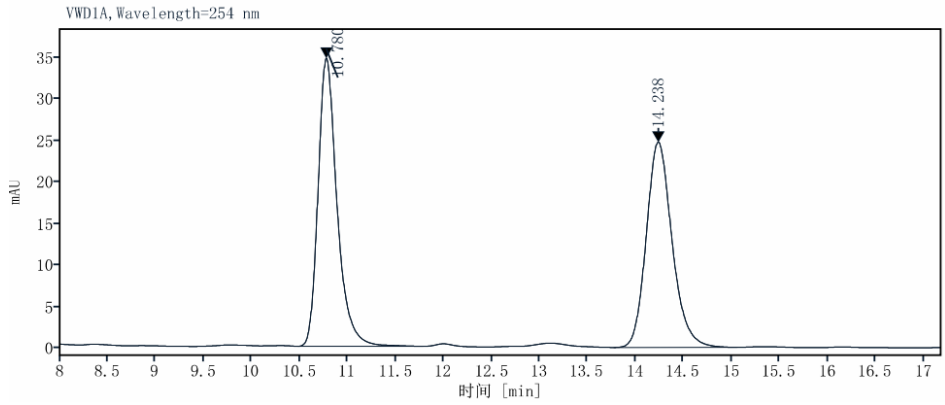
Purification by flash column chromatography (PE/EA = 7:1) generated **3ap** (18.0 mg, 88% yield); 94.5:5.5 er; white solid; **m.p.** 176 – 178 °C; R_f = 0.5 (PE/EA = 4/1); $[\alpha]_D^{20}$ = -17 (c = 0.16, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (s, 2H), 7.36 – 7.31 (m, 2H), 7.27 – 7.21 (m, 5H), 7.19 – 7.13 (m, 2H), 7.10 – 7.07 (m, 2H), 6.96 (s, 1H), 6.77 (d, *J* = 6.0 Hz, 1H), 4.99 (d, *J* = 6.0 Hz, 1H), 4.03 – 4.00 (m, 2H), 2.39 (s, 6H), 1.45 (t, *J* = 6.6 Hz, 1H) ppm.

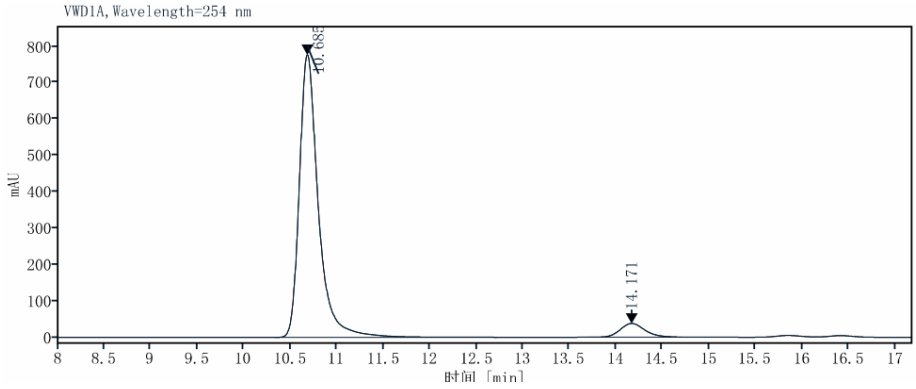
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 147.8, 146.0, 138.9, 138.7, 137.9, 133.6, 128.7, 128.6, 128.4, 128.2, 128.1, 127.2, 127.0, 119.2, 110.5, 97.9, 66.8, 45.7, 21.5 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{27}H_{24}N_2O_2 + H]^+$ 409.1911, found 409.1907.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 10.7 min (major), t_{R2} = 14.2 min (minor).

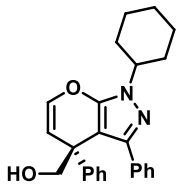


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
10.780	BB	1.3033	477.0157	34.6721	50.8175
14.238	BB	1.2817	461.6676	24.7096	49.1825



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
10.685	BM m	0.2136	11022.1925	776.5131	94.1317
14.171	MM m	0.2813	687.1438	37.5923	5.8683

(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3aq)



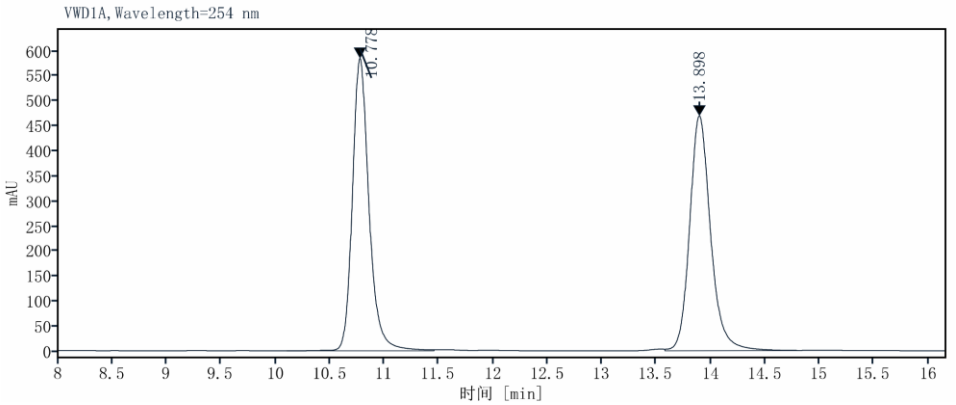
Purification by flash column chromatography (PE/EA = 7:1) generated **3aq** (12.5 mg, 65% yield); 88:12 er; white solid; **m.p.** 92 – 94 °C; R_f = 0.4 (PE/EA = 5/1); $[\alpha]_D^{20}$ = -25 (c = 0.7, MeOH);

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 2H), 7.26 – 7.10 (m, 6H), 7.08 – 7.00 (m, 2H), 6.67 (d, *J* = 6.1 Hz, 1H), 4.92 (d, *J* = 6.1 Hz, 1H), 4.20 (tt, *J* = 10.5, 4.8 Hz, 1H), 4.03 – 3.91 (m, 2H), 2.14 – 2.02 (m, 3H), 2.01 – 1.87 (m, 3H), 1.74 – 1.65 (m, 1H), 1.53 – 1.26 (m, 4H) ppm.

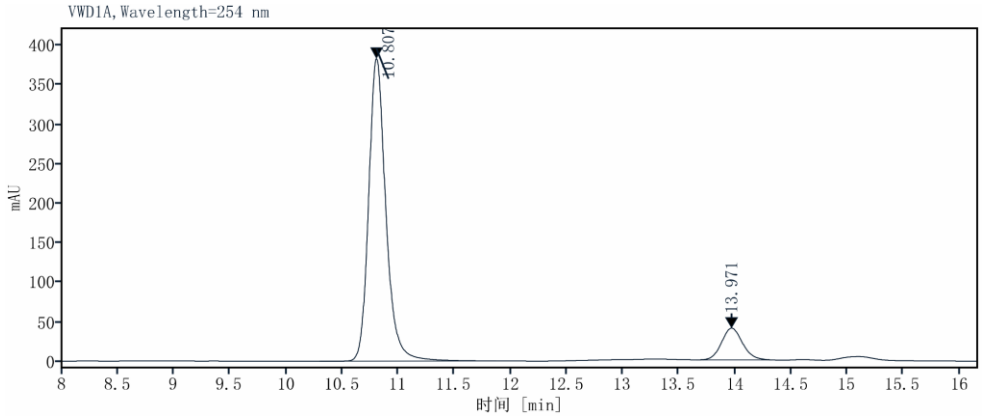
^{13}C NMR (75 MHz, $CDCl_3$) 147.4, 146.5, 146.3, 138.4, 134.3, 128.7, 128.4, 128.0, 127.7, 127.1, 126.8, 110.7, 95.6, 66.9, 57.4, 45.9, 32.3, 31.9, 25.7, 25.3 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{26}N_2O_2 + H]^+$ 387.2067, found 387.2067.

HPLC: Daicel Chiralcel IA-H, *n*-hexane/isopropanol 80/20, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 10.8 min (major), t_{R2} = 13.9 min (minor).



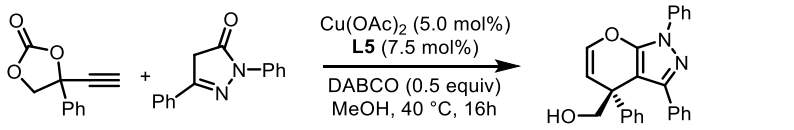
RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
10.778	BV	1.3546	6210.6801	583.7505	49.7399
13.898	VB	1.2379	6275.6213	468.5168	50.2601



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
10.807	BB	1.5661	4101.0410	383.5557	88.7103
13.971	MM m	0.1992	521.9156	40.2809	11.2897

5. Synthetic Applications

5.1. Procedure for 2.0 mmol Experiment



1a
6.0 mmol
1.130 g

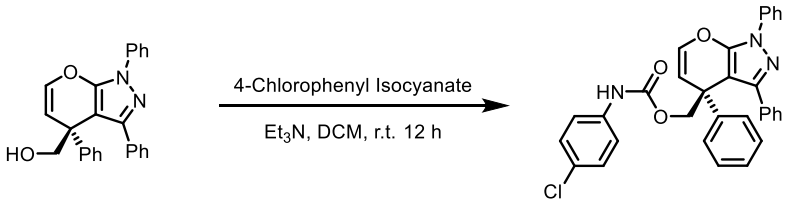
2a
2.0 mmol
0.472 g

3aa
593.4 mg, 78% yield, 93.5:6.5 er
(541.7 mg, 71% yield, 99.5:0.5 er
after recrystallization)

To an oven-dried 100-mL schlenk tube equipped with a tefloncoated magnetic stir bar was added $Cu(OAc)_2$ (18.1 mg, 0.1 mmol, 5.0 mol%), **L5** (174.0 mg, 0.15 mmol, 7.5 mol%), **2a** (0.472 g, 2.0 mmol, 1.0 equiv), DABCO (112.2 mg, 1.0 mmol, 0.5 equiv). Then the schlenk tube was evacuated and filled with argon for three times. After that, **1a** (1.130 g, 6.0 mmol, 3.0 equiv) and MeOH (20.0 mL) was added to the tube via a syringe under argon atmosphere. The reaction mixture was stirred at 40 °C for 18 h. After completion of the reaction, the reaction mixture was concentrated in vacuum and the crude product was purified by flash chromatography on silica gel (PE/EA, 20:1 to 5:1) to afford the desired product **3aa** (593.4 mg, 78% yield, 541.7 mg, 71% yield, 99.5:0.5 er after recrystallization).

5.2. Transformations of 4-10

Synthesis of (R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methyl (4-chlorophenyl)carbamate (4)

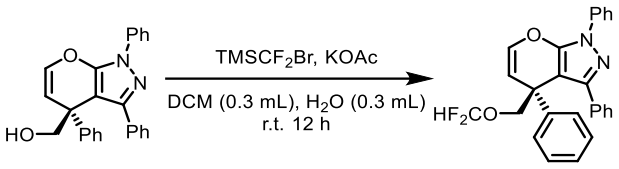


3aa

4
94% yield, 99.5:0.5 er

To a solution of **3aa** (77.0 mg, 0.2 mmol, 1.0 equiv) in DCM (2.0 mL) was added the 4-chlorophenyl isocyanate (39.9 mg, 0.26 mmol, 1.3 equiv), Et_3N (0.3 mL, 2.0 mmol, 10.0 equiv). The solution was stirred at room temperature for 30 min. After removal of the solvent in vacuo, the resultant crude product **4** was purified by flash column chromatography on silica gel using PE/EA 7:1, delivering product **4** (100.2 mg, 94% yield, 99.5:0.5 er).

Synthesis of (R)-4-((difluoromethoxy)methyl)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole (5)

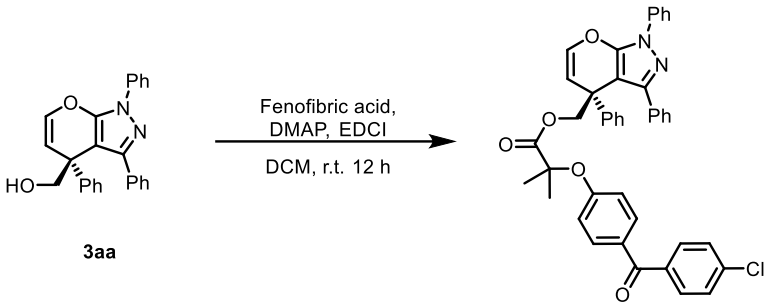


3aa **5**

60% yield, 99.5:0.5 er

The product **5** was prepared according to the literature procedure[4]. To a 10 mL plastic tube equipped with a cap was added **3aa** (77 mg, 0.2 mmol, 1.0 equiv) and KOAc (117.6 mg, 1.2 mmol, 6.0 equiv). Then DCM (0.3 mL) and H_2O (0.3 mL) were added. The reaction mixture was stirred at room temperature and $TMSCF_2Br$ (203 mg, 1.0 mmol, 3.0 equiv) was added. After 10 h, the reaction mixture was treated with water (20 mL) and extracted with DCM (20.0 mL ×3). The organic layer was combined and dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by flash column chromatography on silica gel using PE:EA (20:1) to afford **5** (51.6 mg, 60% yield, 99.5:0.5 er).

Synthesis of (R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (6)

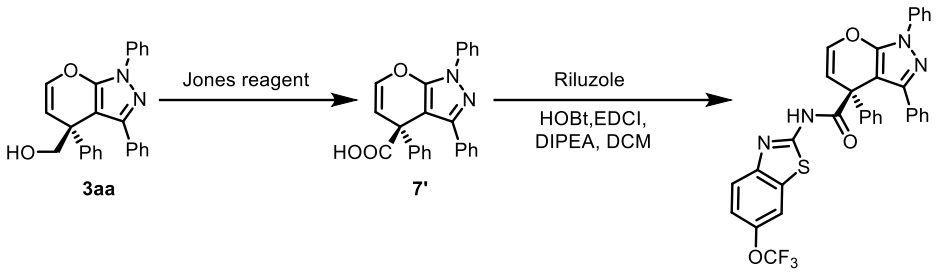


3aa **6**

88% yield, 99:1 er

To a solution of **3aa** (38.5 mg, 0.1 mmol, 1.0 equiv) in DCM (1.5 mL) was added the fenofibric acid (48.0 mg, 0.15 mmol, 1.5 equiv), DMAP (1.3 mg, 0.01 mmol, 0.1 equiv), EDCI (48.0 mg, 0.25 mmol, 2.5 equiv). The solution was stirred at r.t. for 12h. The resultant crude product **6** was purified by flash column chromatography on silica gel using PE:EA (15:1), delivering product **6** (59.8 mg, 88% yield, 99:1 er).

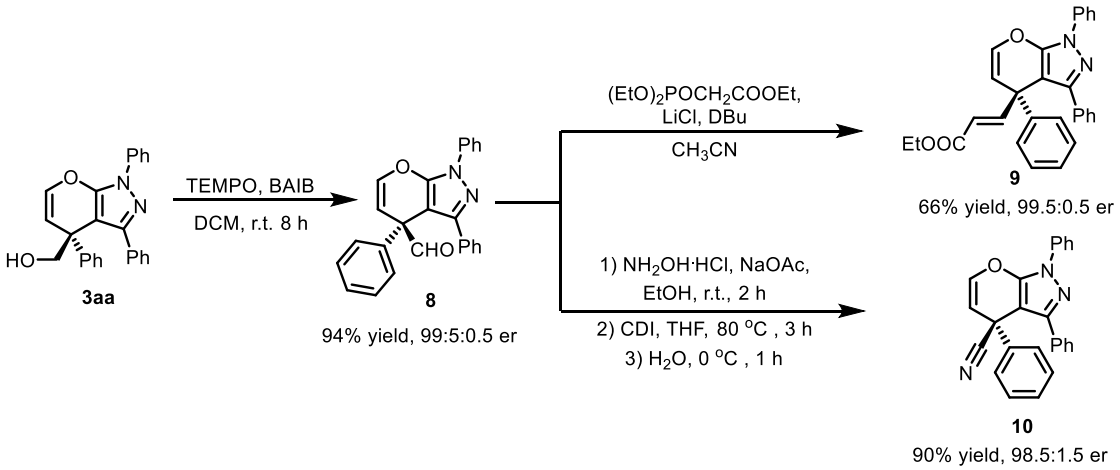
Synthesis of 1,3,4-triphenyl-N-(6-(trifluoromethoxy)benzo[d]thiazol-2-yl)-1,4 dihydropyrano[2,3-c]pyrazole-4-carboxamide(7)



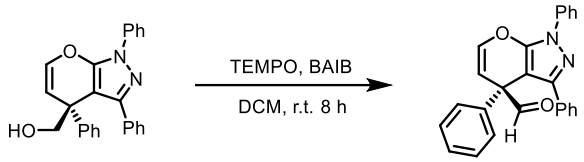
To a solution of **3aa** (79.0 mg, 0.2 mmol, 1.0 equiv) in acetone (2.0 mL), Jones reagent (77.0 μL, 1.0 mmol, 5.0 equiv) was added dropwise at 0 ºC. The resulting solution was stirred at 0 ºC till almost full conversion of **3aa** to **7'** by TLC analysis. Then the reaction mixture was quenched by isopropanol, and filtered through a plug of Celite. The filter cake was washed with acetone for 3 times. The mixture was then concentrated in vacuo and the crude residue was dissolved in EA (5.0 mL) and diluted with aqueous $NaHCO_3$ and the aqueous phase was washed with EA (3 x 5.0 mL). Concentrated aqueous HCl was added to the aqueous phase followed by extraction with EA (3 x 10.0 mL), the combined organic phases were dried over Na_2SO_4, filtered and concentrated in vacuo. The crude product **7'** was used next step directly without further purification.

The product **7** was prepared according to the literature procedure [5]. A mixture of compound **7'** (0.2 mmol, 1.0 equiv), EDCI (46.0 mg, 0.24 mmol, 1.2 equiv), HOBt (32.4 mg, 0.24 mmol, 1.2 equiv), DIPEA (42.0 μL, 0.24 mmol, 1.2 equiv), Riluzole (56.2 mg, 0.24 mmol, 1.2 equiv) in DCM (1.5 mL) was stirred at room temperature for 24 h. When the reaction was complete, H_2O was added. The organic phase was separated and the aqueous phase was extracted with DCM for 3 times. The combined organic phase was washed with brine, dried over Na_2SO_4, evaporated in vacuum and was purified by chromatography on silica gel using PE:EA (10:1) to afford **7** (74.4 mg, 61% yield, 99.3:0.7 er).

Synthesis of 8, 9,10



Synthesis of (R)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole-4-carbaldehyde (8)

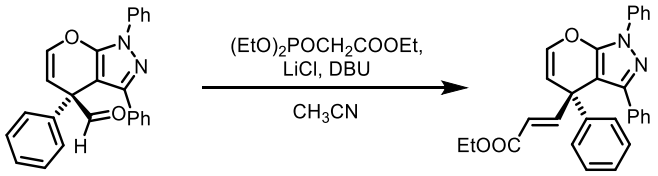


3aa **8**

94% yield, 99.5:0.5 er

The product **8** was prepared according to the literature procedure [6]. To a stirred solution of **3aa** (154.0 mg, 0.4 mmol, 1.0 equiv) in DCM (3.0 mL) was added TEMPO (12.8 mg, 0.08 mmol, 0.2 equiv), BAIB (312.0 mg, 0.96 mmol, 2.4 equiv). The reaction mixture was stirred for 8 h at room temperature. After that, the reaction mixture was added H_2O (20.0 mL) and extracted with DCM (20.0 mL × 3). The combined organic layers were washed with saturated solution of $NaHCO_3$ and dried over Na_2SO_4, and concentrated in vacuum. The crude product was purified by flash chromatography on silica gel using PE:EA (30/1) to afford the desired product **8** (142.1 mg, 94% yield, 99.5:0.5 er).

Synthesis of ethyl (S,E)-3-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)acrylate (9)

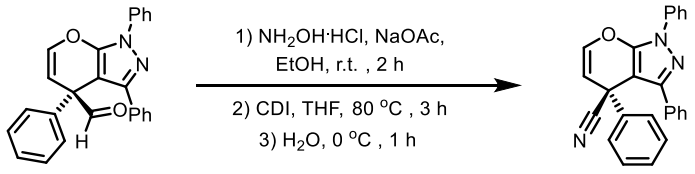


8 **9**

66% yield, 99.5:0.5 er

The product **9** was prepared according to the literature procedure [7]. To a solution of $(EtO)_2P(O)CH_2CO_2Et$ (41.0 μL, 0.2 mmol, 1.0 equiv) and LiCl (9.0 mg, 0.2 mmol, 1.0 equiv) in CH_3CN (0.5 mL) was added DBU (30.0 μL, 0.2 mmol, 1.0 equiv) and the reaction was stirred for 1 h at room temperature. Next, **8** (79.0 mg, 0.2 mmol, 1.0 equiv) in CH_3CN (1.0 mL) was added dropwise over 0.5 h at room temperature. After being stirred at room temperature overnight, the mixture was evaporated under reduced pressure. The residue was purified through flash column chromatography on silica gel using PE:EA (20:1 – 10:1) to give **9** (59.2 mg, 66% yield, 99.5:0.5 er)

Synthesis of (R)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole-4-carbonitrile (10)



8 **10**

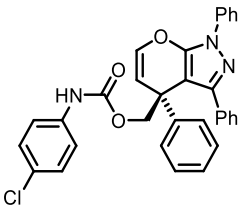
90% yield, 98.5:1.5 er

The reaction to synthesis **10** was adapted a literature procedure[7]. Sodium acetate (44.8 mg, 0.56 mmol, 2.8 equiv) and NH_2OH•HCl (38.4 mg, 0.56 mmol, 2.8 equiv) were added to the solution of **8** (79.0 mg, 0.2 mmol, 1.0 equiv) in ethanol (1.5 mL). The mixture was stirred at room temperature for 3 h and concentrated *in vacuo*. The residue was diluted with EA (10.0 mL), added H_2O (10.0 mL), and extracted with EA (20.0 mL × 3). After that, the combined organic layers were washed

with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was then dissolved in anhydrous THF (1.5 mL) and treated with N,N'-carbonyldiimidazole (CDI) (0.26 g, 1.6 mmol, 8.0 equiv) before refluxing for 2.5 h under argon. The reaction was then cooled to 0 °C and added H_2O (1.0 mL) slowly. After that the resulting mixture was stirred for an additional hour. The reaction was added H_2O (20.0 mL), and extracted with EA (20.0 mL × 3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified through flash column chromatography on silica gel using PE:EA (20:1) to give **10** (67.5 mg, 90% yield, 98.5:1.5 er).

5.3 Characterization of the products 4-11

(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methyl (4-chlorophenyl)carbamate (4)



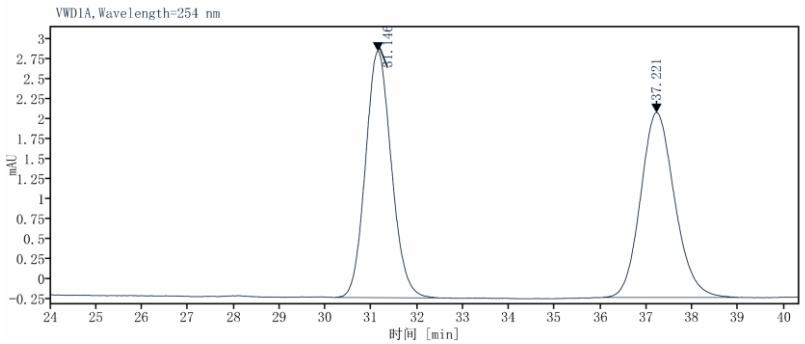
4 (100.2 mg, 94% yield); 99.5:0.5 er; white solid; **m.p.** 182 – 185 °C; R_f = 0.4 (PE/EA = 5/1); $[\alpha]_D^{20}$ = -26.8 (c = 0.07, MeOH).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.86 (m, 2H), 7.49 – 7.45 (m, 2H), 7.40 – 7.24 (m, 7H), 7.20 – 7.14 (m, 6H), 7.03 – 7.00 (m, 2H), 6.67 (d, *J* = 6.1 Hz, 1H), 5.79 (s, 1H), 4.95 (d, *J* = 6.1 Hz, 1H), 4.61 (s, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 152.8, 149.5, 146.7, 145.6, 138.1, 137.8, 136.3, 134.8, 129.2, 129.0, 128.9, 128.8, 128.3, 127.9, 127.9, 127.5, 127.1, 126.6, 121.2, 119.6, 109.3, 99.5, 68.8, 43.5 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{32}H_{24}ClN_3O_3 + H]^+$ 534.1579, found 534.1582.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate =0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 30.8 min (major), t_{R2} = 36.8 min (minor).



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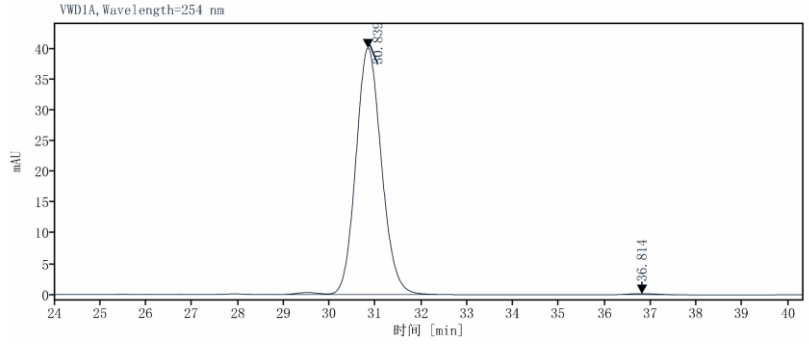
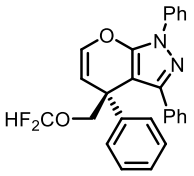
37.221	BB	2.9883	119.5685	2.3132	49.6481



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
30.839	MB m	0.6012	1566.7182	40.2461	99.5628
36.814	MM m	0.4759	6.8795	0.1697	0.4372

(R)-4-((difluoromethoxy)methyl)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole (5)



5 (51.6 mg, 60% yield); 99.5:0.5 er; white solid; **m.p.** 137 – 139 °C; R_f = 0.4 (PE/EA = 20/1); $[\alpha]_D^{20}$ = -30.8 (c = 0.12, MeOH).

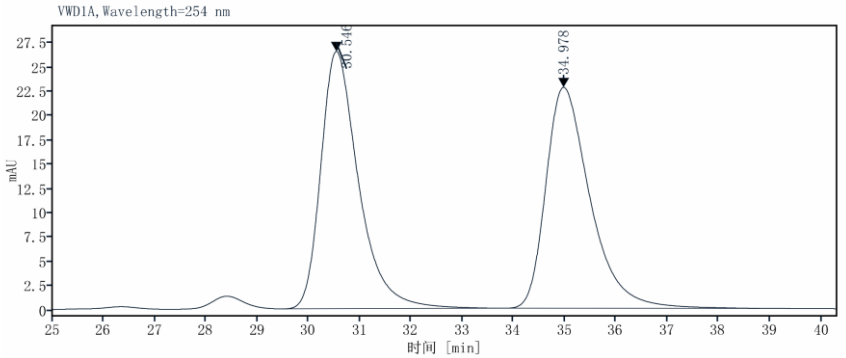
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.91 – 7.86 (m, 2H), 7.50 – 7.44 (m, 2H), 7.37 – 7.22 (m, 7H), 7.19 – 7.13 (m, 2H), 7.02 – 6.98 (m, 2H), 6.73 (d, *J* = 6.1 Hz, 1H), 6.08 (t, *J* = 74.2 Hz, 1H), 5.06 (d, *J* = 6.1 Hz, 1H), 4.33 (d, *J* = 9.5 Hz, 1H), 4.16 (d, *J* = 9.5 Hz, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 149.1, 146.9, 145.3, 138.2, 138.0, 133.6, 129.1, 128.7, 128.6, 128.2, 128.0, 127.3, 127.1, 126.5, 121.1, 115.8 (t, $^1J_{C\text{-}F}$ = 260.5 Hz), 109.6, 99.0, 66.8 (t, $^3J_{C\text{-}F}$ = 4.4 Hz), 43.0 ppm.

^{19}F NMR (282 MHz, $CDCl_3$) δ -84.33 (dd, *J* = 156.8, 188.5 Hz, 2F)

HRMS (ESI) *m/z* Calcd for $[C_{26}H_{20}F_2N_2O_2 + H]^+$ 431.1566, found 431.1569.

HPLC: Daicel Chiralcel OD-H, *n*-hexane/isopropanol 99/1, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 31.4 min (major), t_{R2} = 36.3 min (minor).



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
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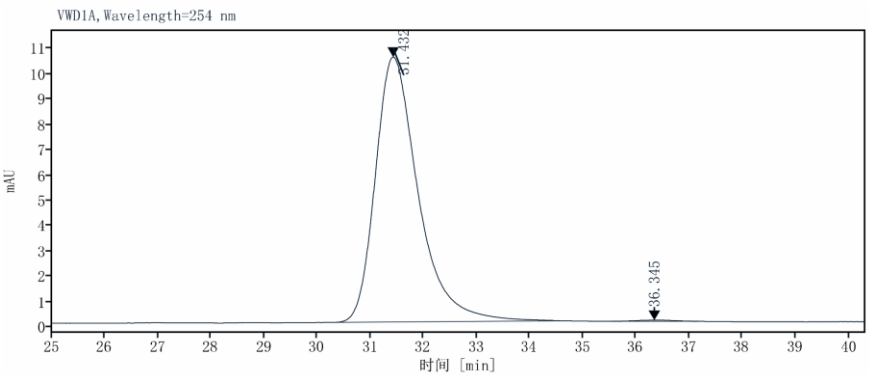
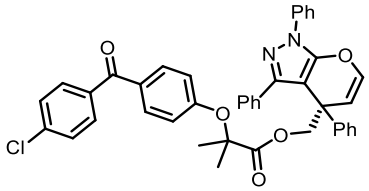
34.978	BB	4.9867	1364.3458	22.7205	50.1353



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
31.432	MM m	0.8376	587.3246	10.4834	99.6193
36.345	MM m	0.5597	2.2448	0.0470	0.3807

(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (6)



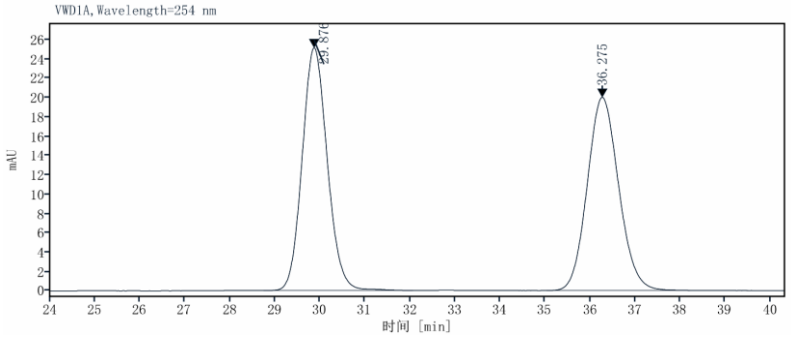
6 (59.8 mg, 88% yield); 99:1 er; white solid; **m.p.** 79 – 81 °C; R_f = 0.5 (PE/EA = 10/1); $[\alpha]_D^{20}$ = -25.0 (c = 0.07, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 – 7.79 (m, 2H), 7.69 – 7.60 (m, 4H), 7.47 – 7.39 (m, 4H), 7.34 – 7.26 (m, 3H), 7.25 – 7.18 (m, 4H), 7.14 – 7.08 (m, 2H), 6.98 – 6.95 (m, 2H), 6.73 – 6.68 (m, 2H), 6.59 (d, *J* = 6.1 Hz, 1H), 4.87 (d, *J* = 6.1 Hz, 1H), 4.70 (d, *J* = 10.6, 1H), 4.48 (d, *J* = 10.7, 1H), 1.53 (s, 6H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1, 173.2, 159.6, 149.0, 147.0, 145.1, 138.4, 138.1, 138.0, 136.4, 133.4, 132.0, 131.2, 130.3, 129.1, 128.7, 128.6, 128.5, 128.2, 128.0, 127.2, 127.1, 126.6, 121.0, 117.3, 109.8, 98.6, 79.3, 68.6, 43.3, 25.4, 25.3 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{42}H_{33}ClN_2O_5 + K]^+$ 719.1710, found 719.1708.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 29.4 min (major), t_{R2} = 35.6 min (minor).



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
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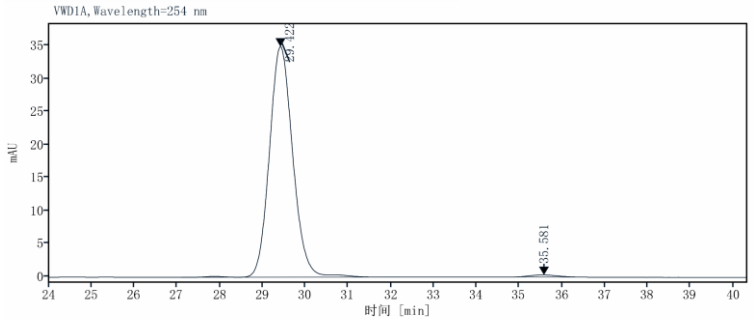
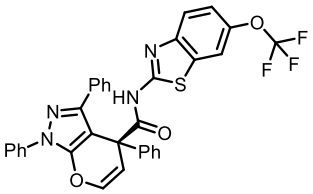
36.275	BB	3.1717	966.9079	19.9609	49.8802



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
29.422	MM m	0.5866	1327.7799	34.9207	99.0320
35.581	MM m	0.4932	12.9789	0.3115	0.9680

1,3,4-triphenyl-N-(6-(trifluoromethoxy)benzo[d]thiazol-2-yl)-1,4-dihydropyrano[2,3-c]pyrazole-4-carboxamide (7)



7 (74.4 mg, 61% yield, over 2 steps); 99.3:0.7 er; white solid; **m.p.** 106 – 108 °C; R_f = 0.3 (PE/EA = 10/1); $[\alpha]_D^{20}$ = 20.8 (c = 0.07, MeOH).

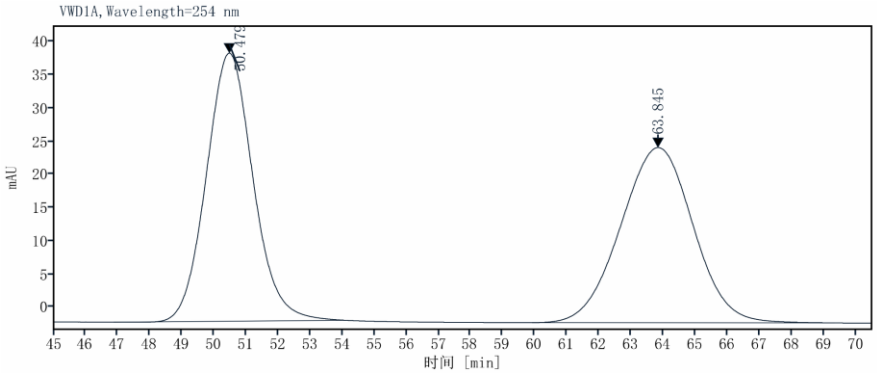
^{1}H NMR (300 MHz, $CDCl_3$) δ 9.18 (s, 1H), 7.89 – 7.85 (m, 2H), 7.66 – 7.63 (m, 2H), 7.54 – 7.47 (m, 2H), 7.38 – 7.35 (m, 1H), 7.33 – 7.24 (m, 8H), 7.23 – 7.13 (m, 3H), 6.79 (d, *J* = 6.0 Hz, 1H), 5.44 (d, *J* = 6.0 Hz, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 158.1, 148.9, 147.0, 146.6, δ 145.5 (q, $^3J_{C\text{-}F}$ = 2.0 Hz), 141.5, 138.6, 137.6, 133.1, 132.3, 129.3, 128.7, 128.7, 128.5, 128.4, 128.2, 127.8, 127.2, 121.8, 121.5, δ 120.6 (q, $^1J_{C\text{-}F}$ = 255.6 Hz), 120.2, 114.2, 108.0, 96.0, 52.2 ppm.

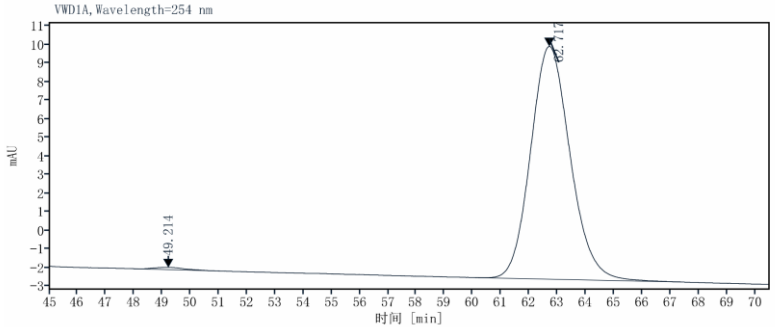
^{19}F NMR (282 MHz, $CDCl_3$) δ -58.04 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{33}H_{21}F_3N_4O_3S + H]^+$ 611.1359, found 611.1361.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 49.2 min (minor), t_{R2} = 62.7 min (major).

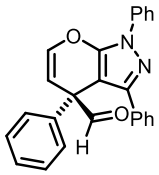


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
50.479	MM m	1.5293	4086.2042	40.3573	49.6247
63.845	BB	9.4267	4148.0055	26.3736	50.3753



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
49.214	MM m	0.8756	9.1160	0.1222	0.7408
62.717	MM m	1.4320	1221.4231	12.5335	99.2592

(R)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole-4-carbaldehyde (8)



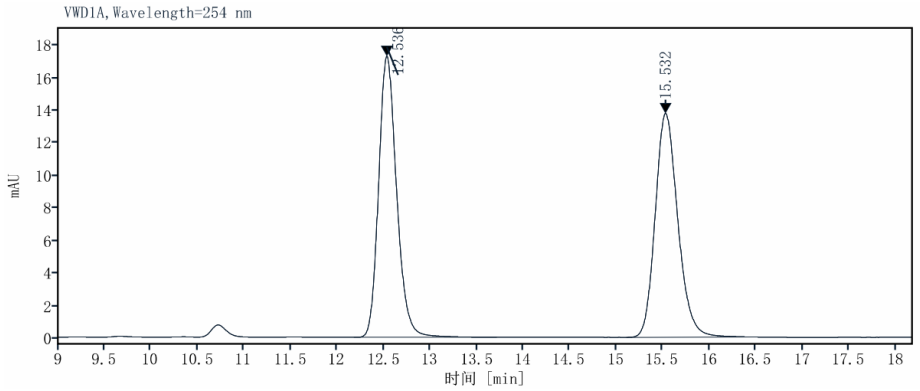
8 (142.1 mg, 94% yield); 99.5:0.5 er; white solid; **m.p.** 130 – 132 °C; R_f = 0.4 (PE/EA = 20/1). $[\alpha]_D^{20}$ = - 14.3 (c = 0.22, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.74 (s, 1H), 7.89 – 7.85 (m, 2H), 7.49 – 7.43 (m, 2H), 7.38 – 7.28 (m, 6H), 7.26 – 7.13 (m, 5H), 6.69 (d, *J* = 6.1 Hz, 1H), 5.19 (d, *J* = 6.1 Hz, 1H) ppm.

^{13}C NMR (75 MHz, $CDCl_3$) δ 196.8, 148.8, 147.3, 141.9, 138.3, 138.0, 133.3, 129.3, 128.4, 128.34, 128.27, 127.8, 127.4, 127.0, 121.4, 106.3, 94.7, 55.5 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{18}N_2O_2 + H]^+$ 379.1441, found 379.1443.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate =0.5 mL/min, uv-vis λ=254nm, t_{R1} = 12.4 min (major), t_{R2} = 15.2 min (minor).



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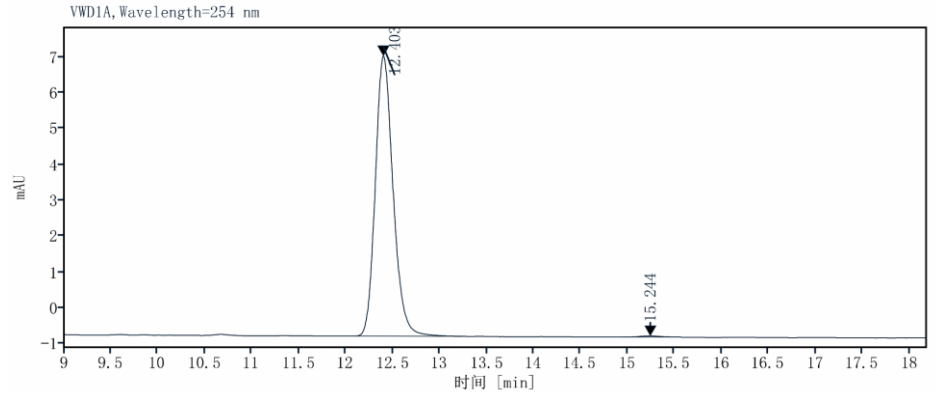
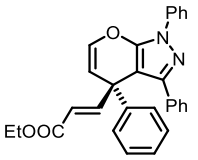


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
12.403	BB	1.1467	103.3213	7.8310	99.5267
15.244	MM m	0.1773	0.4913	0.0347	0.4733

Ethyl (S,E)-3-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)acrylate(9)



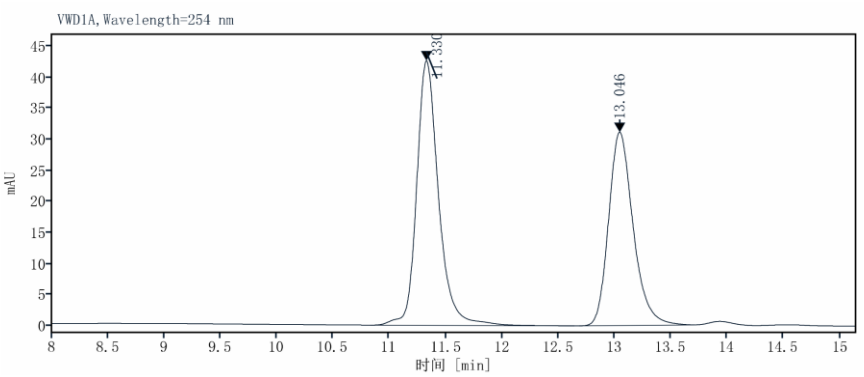
9 (59.2 mg, 66% yield, over 2 steps); 99.5:0.5 er; white solid; **m.p.** 99 – 101 °C; R_f = 0.3 (PE/EA = 10/1); $[\alpha]_D^{20}$ = -48.3 (c = 0.06, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 – 7.85 (m, 2H), 7.50 – 7.42 (m, 2H), 7.40 (d, *J* = 15.7 Hz, 1H), 7.35 – 7.22 (m, 6H), 7.22 – 7.10 (m, 5H), 6.66 (d, *J* = 6.1 Hz, 1H), 5.91 (d, *J* = 15.7 Hz, 1H), 5.02 (d, *J* = 6.0 Hz, 1H), 4.21 – 4.05 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H) ppm.

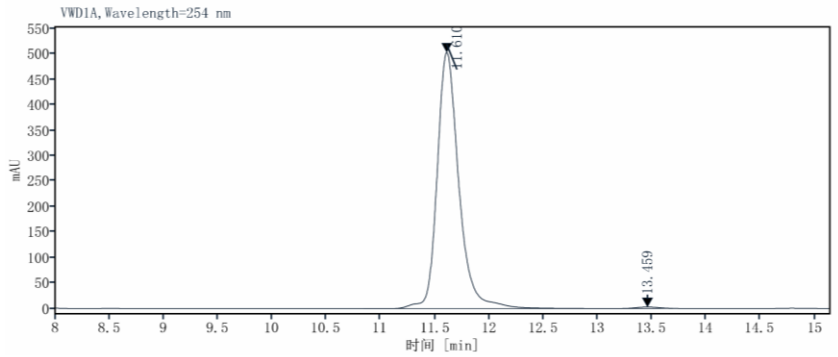
^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5, 150.7, 148.9, 146.3, 138.1, 136.9, 133.3, 129.2, 128.8, 128.4, 128.1, 128.0, 127.4, 127.2, 126.7, 123.2, 121.2, 109.6, 99.4, 60.5, 45.5, 14.2 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{29}H_{24}N_2O_3 + H]^+$ 449.1860, found 449.1864.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate =0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 11.6 min (major), t_{R2} = 13.5 min (minor).

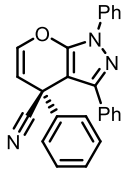


RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
11.330	BB	1.7800	471.4543	42.6434	49.9900
13.046	BB	1.0221	471.6421	31.1325	50.0100



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
11.610	BM m	0.2105	7006.8143	503.0588	99.4466
13.459	MM m	0.2173	38.9890	2.8551	0.5534

(R)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole-4-carbonitrile (10)



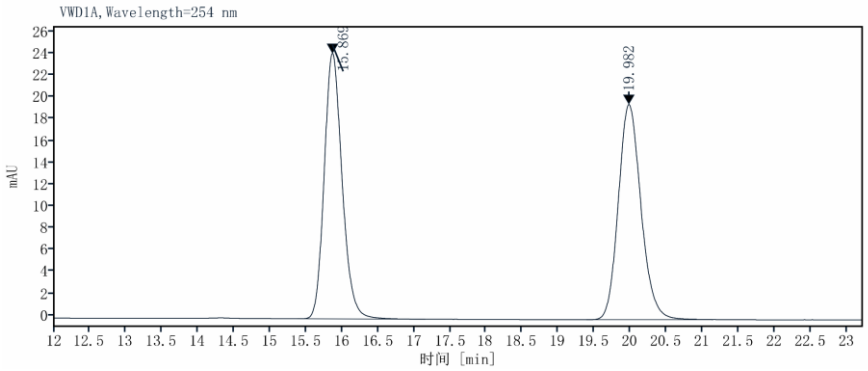
10 (67.5 mg, 90% yield, over 2 steps); 98.5:1.5 er; white solid; **m.p.** 113 – 115 ºC; R_f = 0.3 (PE/EA = 20/1); $[\alpha]_D^{20}$ = -42.1 (c = 0.15, MeOH).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.88 – 7.83 (m, 2H), 7.52 – 7.39 (m, 2H), 7.44 – 7.39 (m, 4H), 7.37 – 7.26 (m, 3H), 7.25 – 7.16 (m, 4H), 6.70 (d, *J* = 6.0 Hz, 1H), 5.19 (d, *J* = 6.0 Hz, 1H) ppm.

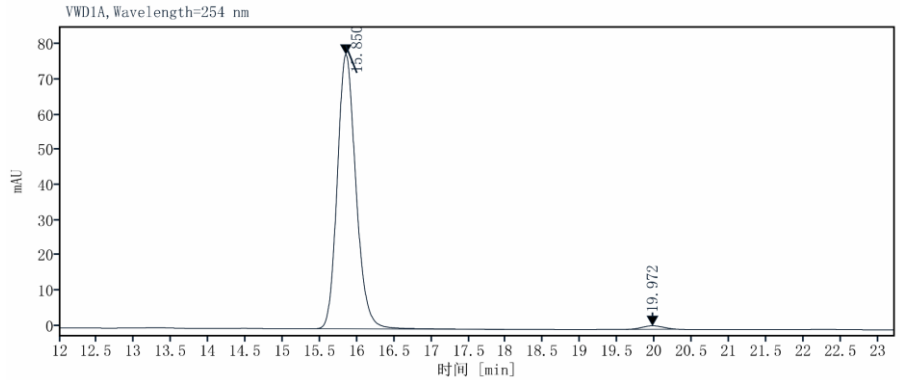
^{13}C NMR (75 MHz, $CDCl_3$) δ 148.6, 146.1, 140.4, 138.2, 137.7, 131.8, 129.3, 129.0, 128.5, 128.4, 128.2, 128.1, 127.2, 126.5, 121.5, 119.7, 106.2, 94.8, 40.6 ppm.

HRMS (ESI) *m/z* Calcd for $[C_{25}H_{17}N_3O + H]^+$ 376.1444, found 376.1453.

HPLC: Daicel Chiralcel AD-H, *n*-hexane/isopropanol 90/10, flow rate = 0.5 mL/min, uv-vis λ = 254nm, t_{R1} = 15.9 min (major), t_{R2} = 20.0 min (minor).



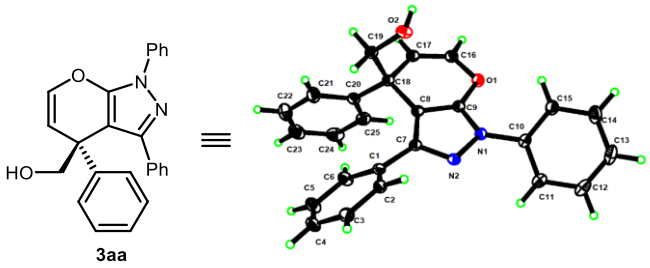
RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
15.869	BB	1.7700	420.2962	24.3444	49.3240
19.982	BB	1.7517	431.8175	19.7356	50.6760



RetTime[min]	Type	Width[min]	Area[mAU*s]	Height[mAU]	Area%
15.850	BB	2.6100	1358.6242	78.0385	98.5642
19.972	MM m	0.3062	19.7909	0.9988	1.4358

6. Crystal Structure of 3aa

Procedure for recrystallization of the compound **3aa**: the hexane was slowly added into the solution of product **3aa** in dichloromethane, then the dichloromethane was evaporated from the mixed solvent system at room temperature under dark and the crystals were obtained after a few days.



ORTEP plot of the crystal structure of **3aa**, and thermal ellipsoid is set at 50% probability.

Table S4 X-ray Crystallographic Data of 3aa

CCDC number	2054833
Bond precision	C-C = 0.0035 A Wavelength=1.54178
Cell	a=9.8692 (3) b=10.1814 (4) c=19.2471 (7) alpha=90 beta=90 gamma=90
Temperature	170 K
Volume	1933.99 (12)
Space group	P 21 21 21
Hall group	P 2ac 2ab
Sum formula	$C_{25}H_{20}N_2O_2$
Mr	380.43
Dx, g cm-3	1.307
Z	4
Mu (mm-1)	0.665
F000	800.0
F000’	802.32
h, k, lmax	12, 12, 24
Nref	3941
Tmin, Tmax	0.628, 0.745
Tmin’	0.899
Correction method	# Reported T Limits: Tmin=0.628 Tmax=0.754
AbsCorr	MULTI-SCAN
Data completeness	1.73/0.99
Theta(max)	74.690
R(reflections)	0.0373 (3721)
wR2(reflections)	0.0916 (3941)
S	1.059
Npar	266
Ellipsoid contour % probability levels	50

7. References

[1] Zhang, Y.-C.; Zhang, B.-W.; Geng, R.-L.; Song, J. *Org. Lett.* **2018**, *20*, 7907-7911.

[2] Gómez, J. E.; Cristòfol, À.; Kleij, A. W. *Angew. Chem. Int. Ed.* **2019**, *58,* 3903-3907.

[3] Li, L.; Liu, Z.-T.; Hu, X.-P. *Chem. Commun.,* **2018***, 54,* 12033-12036.

[4] Xie, Q.-Q.; Ni, C.-F.; Zhang, R.-Y.; Li, L.-C.; R, J.; Hu, J.-B. *Angew. Chem. Int. Ed.* **2017***, 56,* 3206-3210.

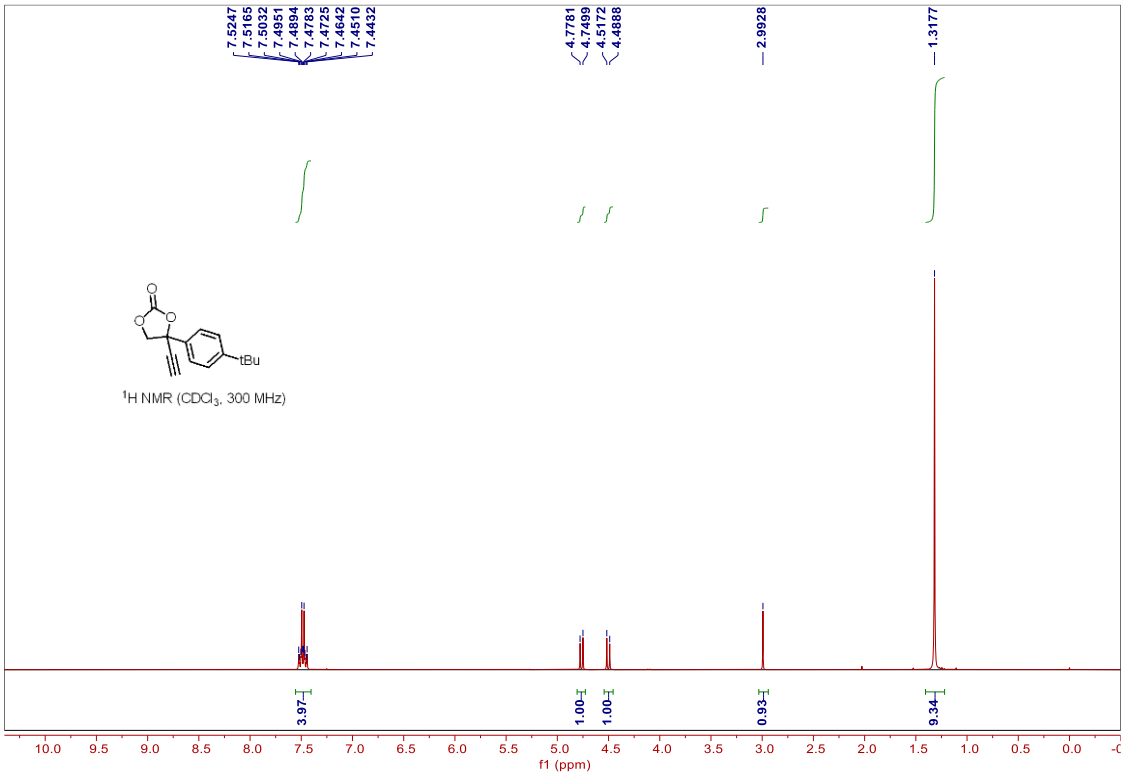
[5] Yuan, Z.-B.; F, Z.-W.; Zeng, Y.-Y.; Zhao, X.-B.; Lin, A.-J.; Yao, H.-Q. *Angew. Chem. Int. Ed.* **2019**, 58, 2884-2888.

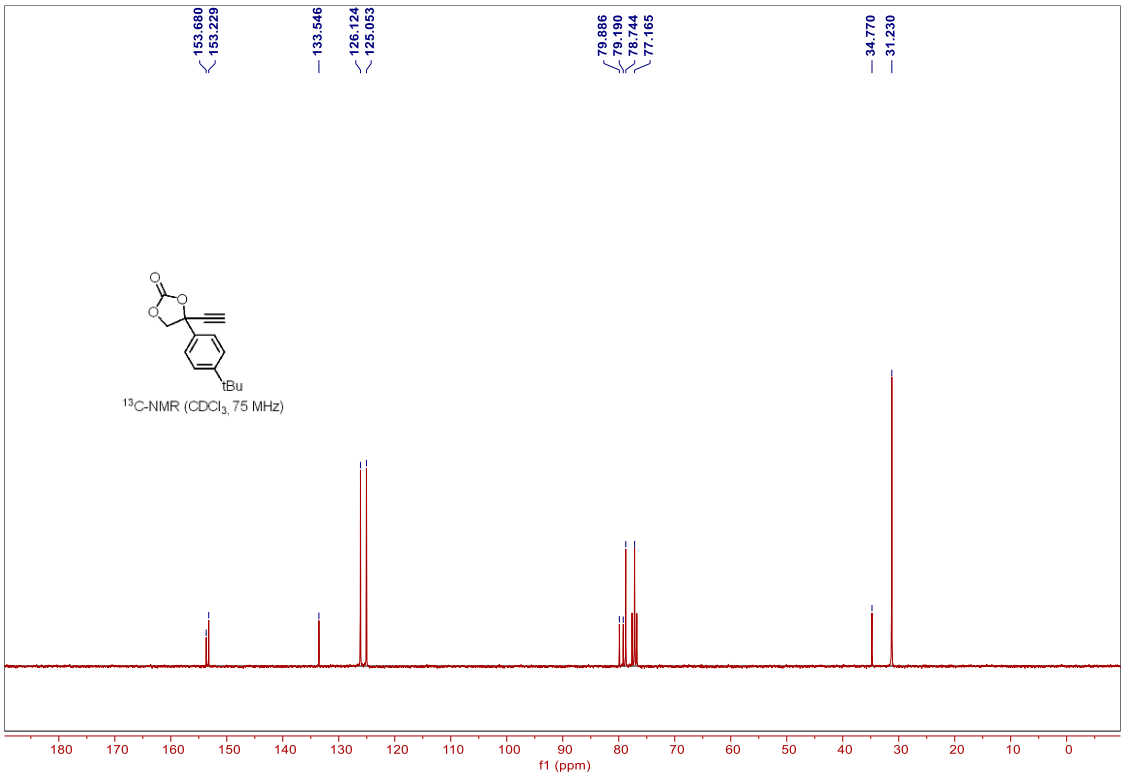
[6] Kumaraswamy, G.; Ramakrishna, G.; Sridhar, B. *Tetrahedron Lett.* **2011**, *52*, 1778-1782.

[7] Meng, J.; Fan, L.-F.; Han, Z.-Y. Gong, L.-Z. *Chem.* **2018**, *4*, 931-933.

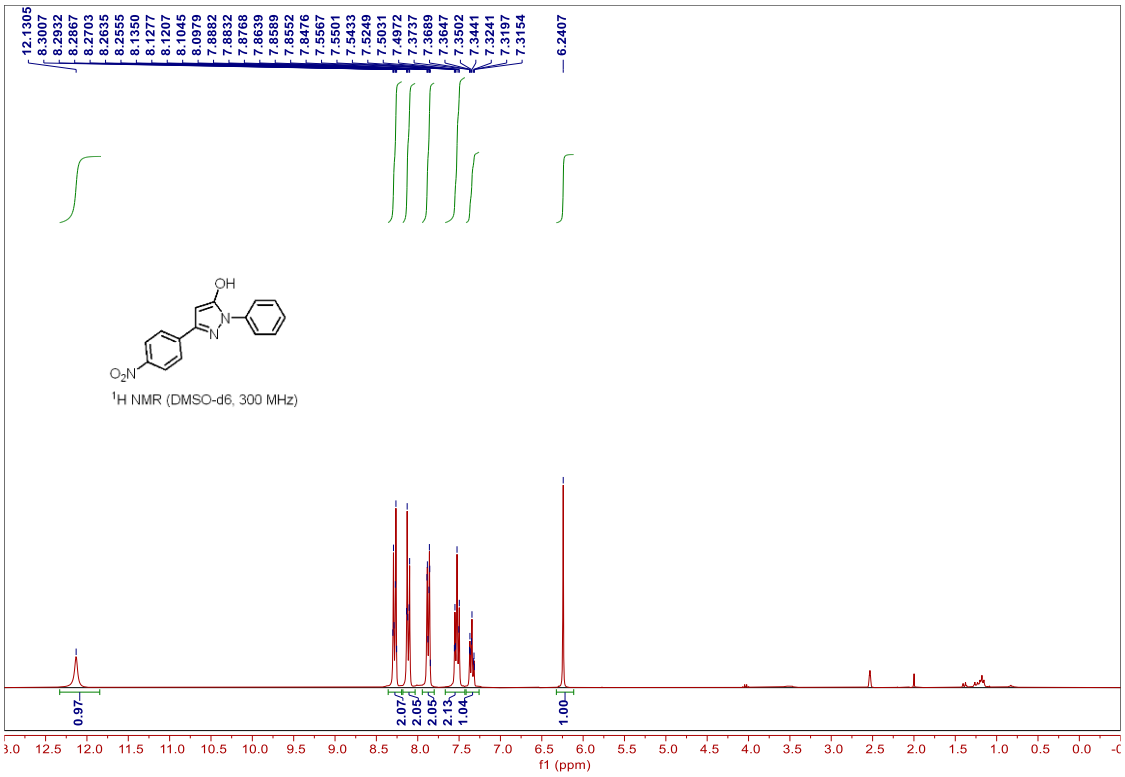
8. ^{1}H and ^{13}C NMR Spectra of the Title Compounds

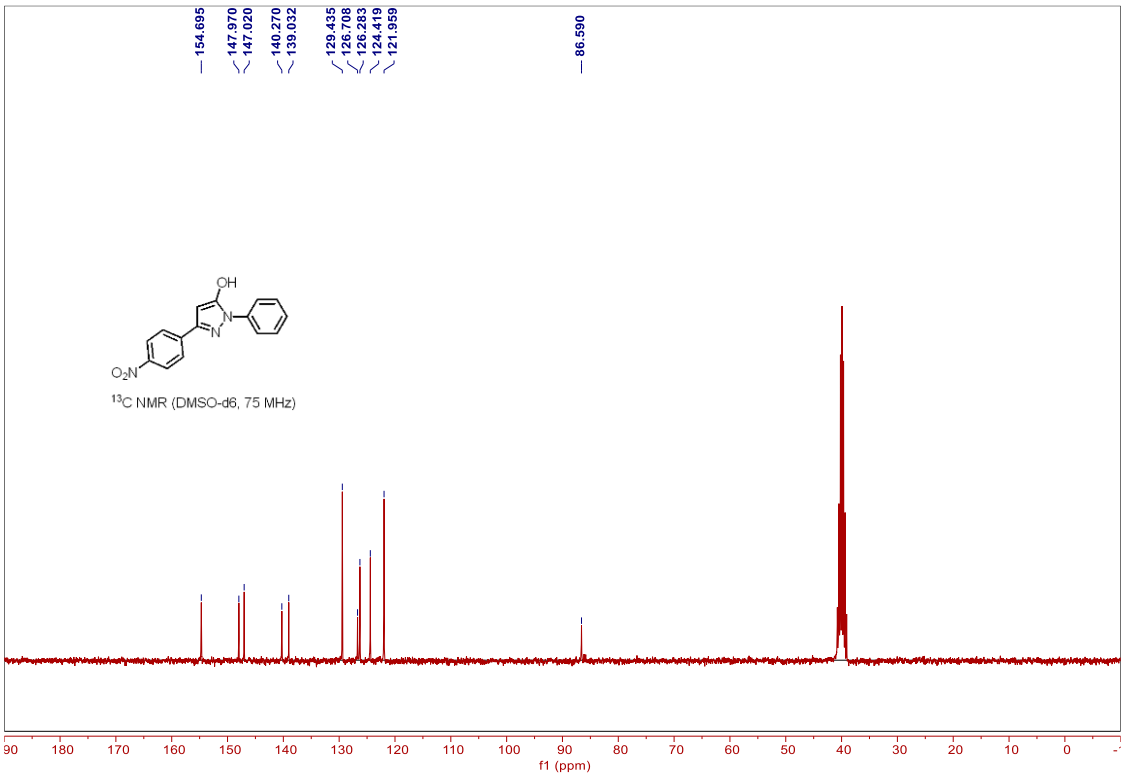
4-(4-(tert-butyl)phenyl)-4-ethynyl-1,3-dioxolan-2-one (1e)



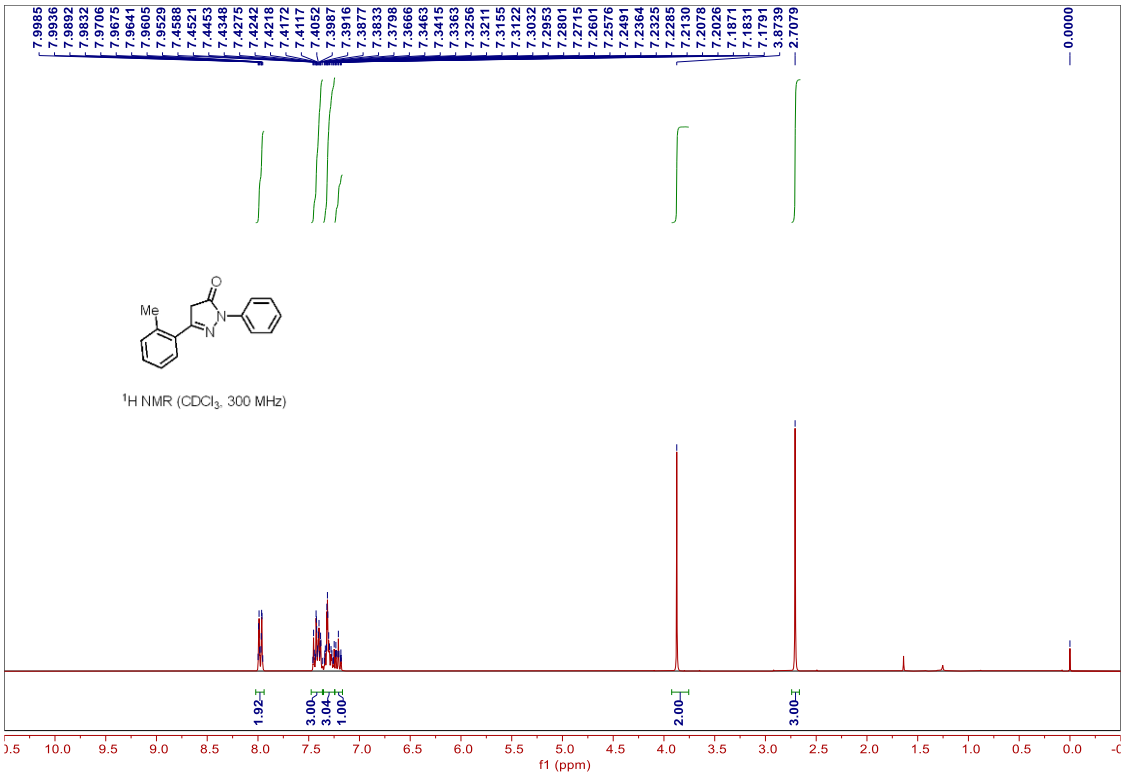


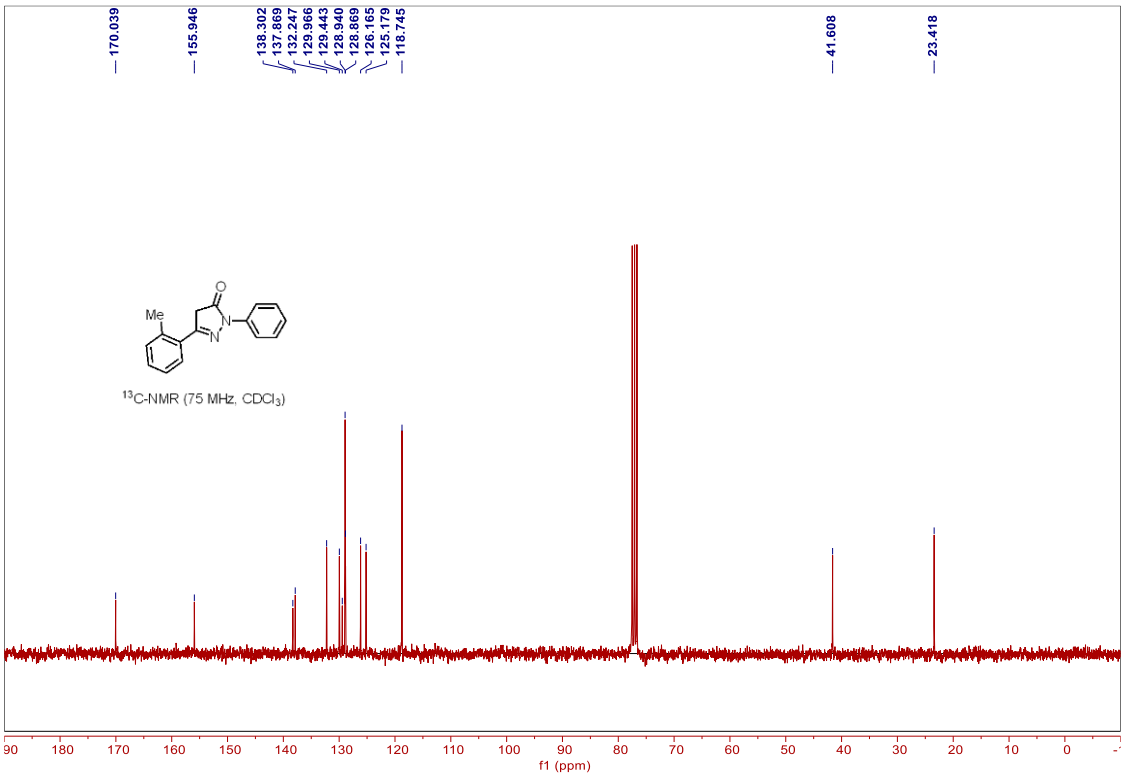
5-(4-nitrophenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2d)



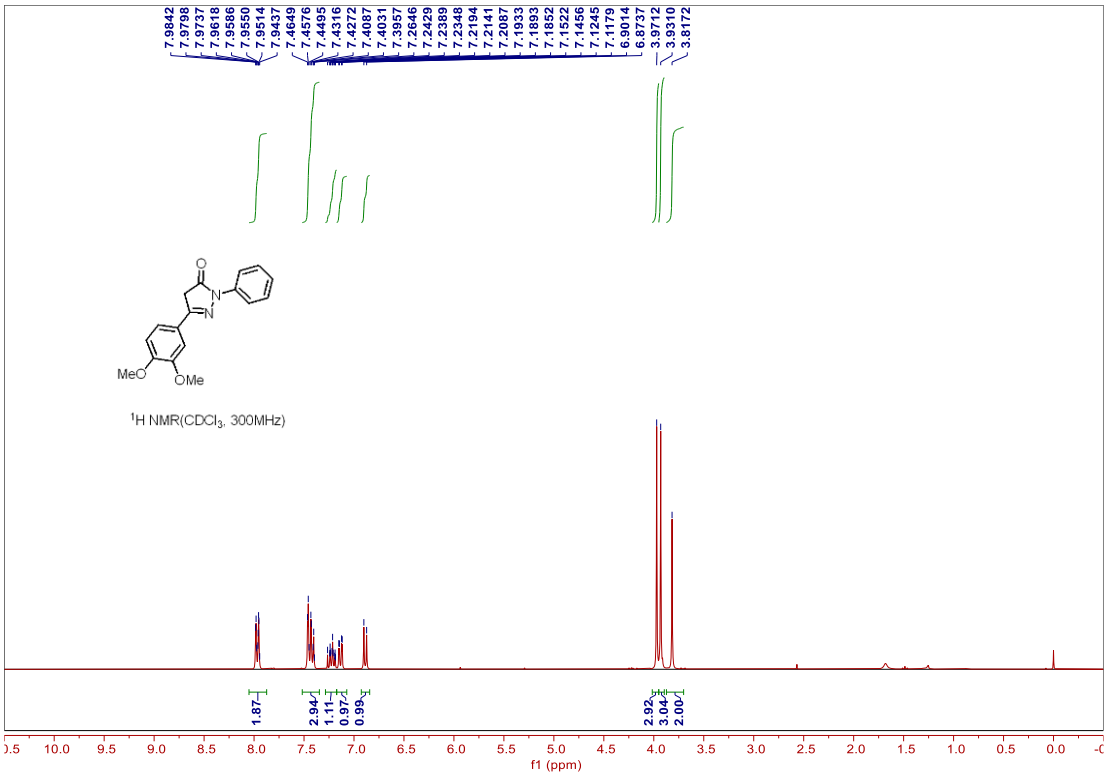


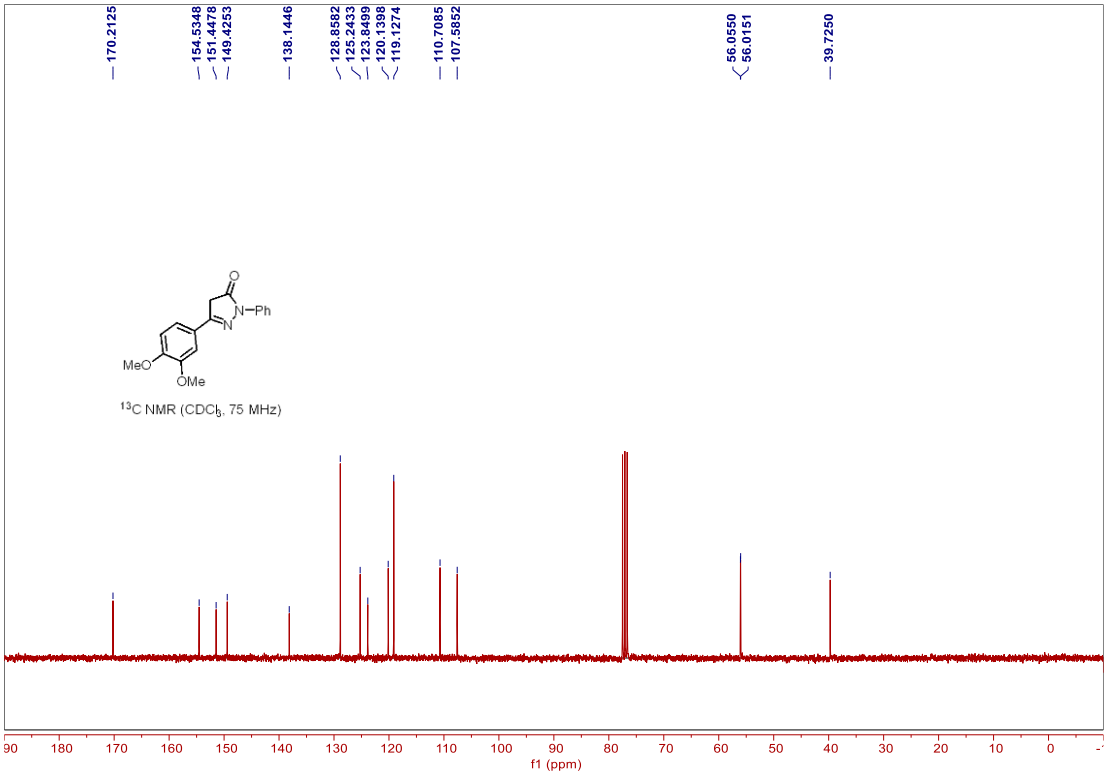
2-phenyl-5-(o-tolyl)-2,4-dihydro-3H-pyrazol-3-one (2e)



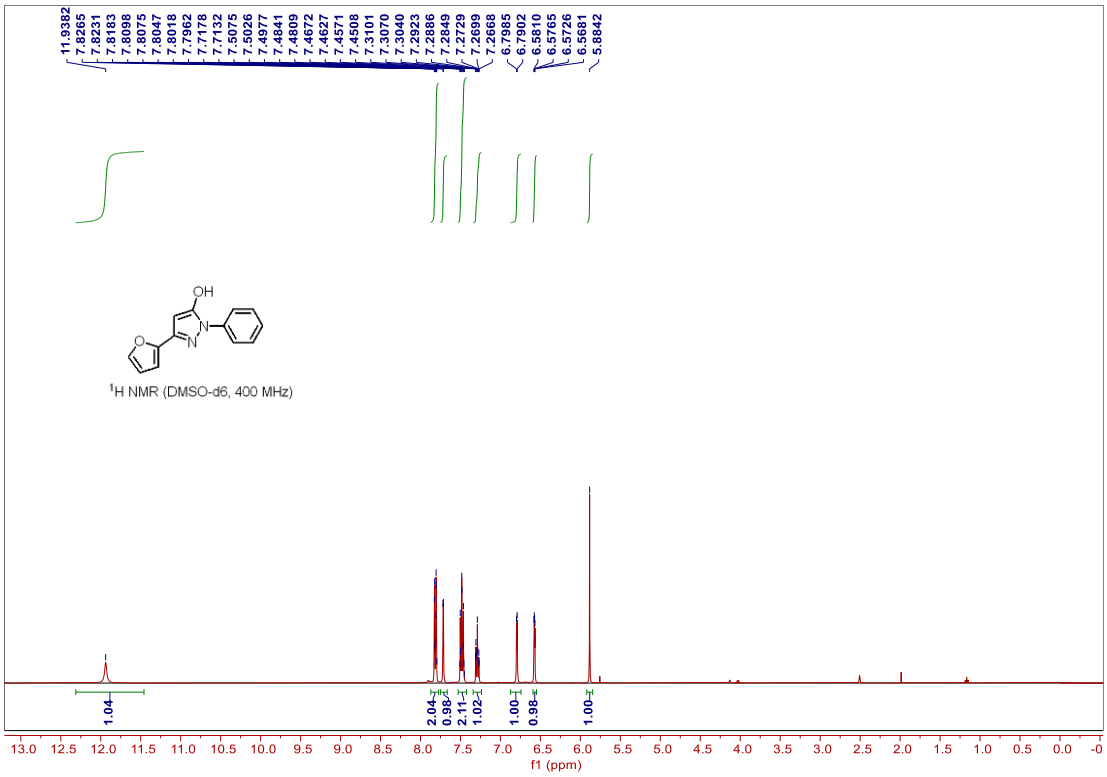


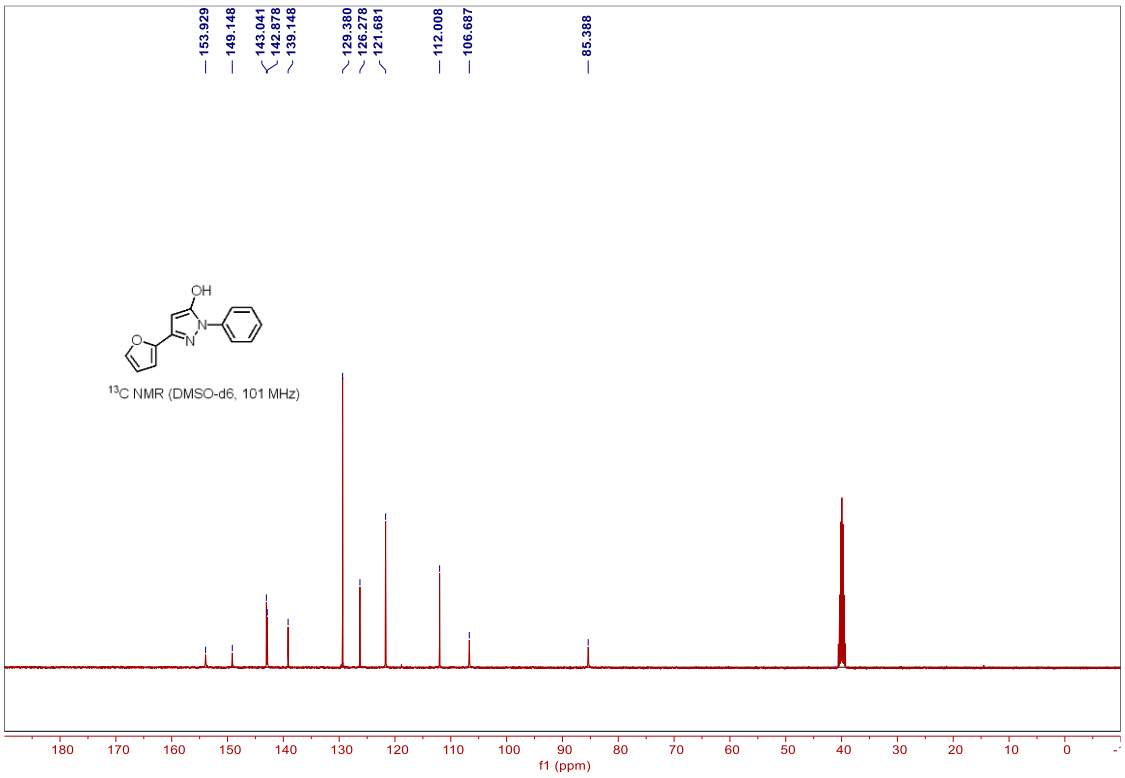
5-(3,4-dimethoxyphenyl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2f)



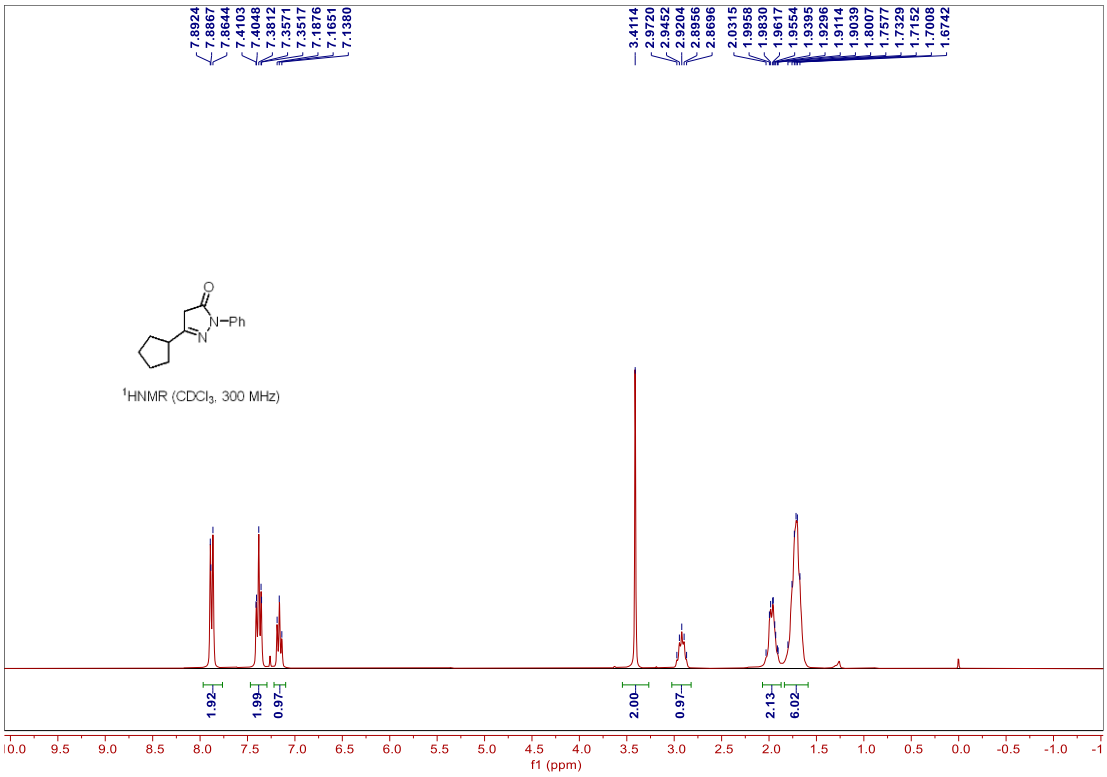


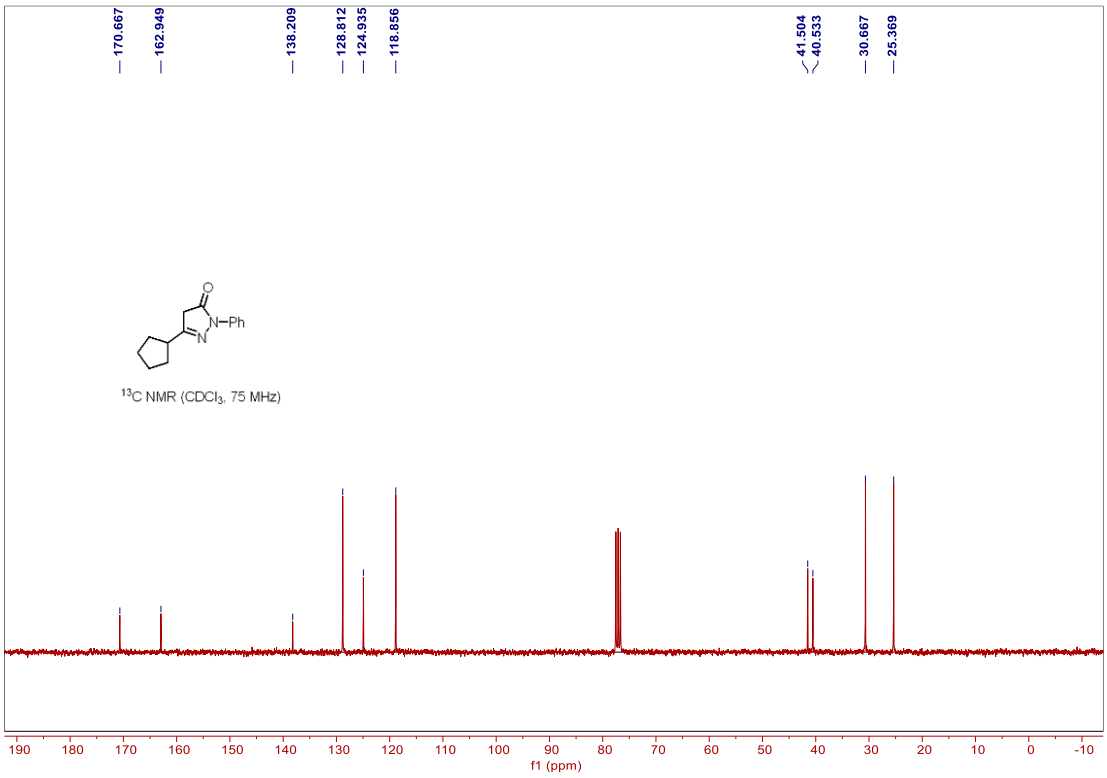
5-(furan-2-yl)-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2g)



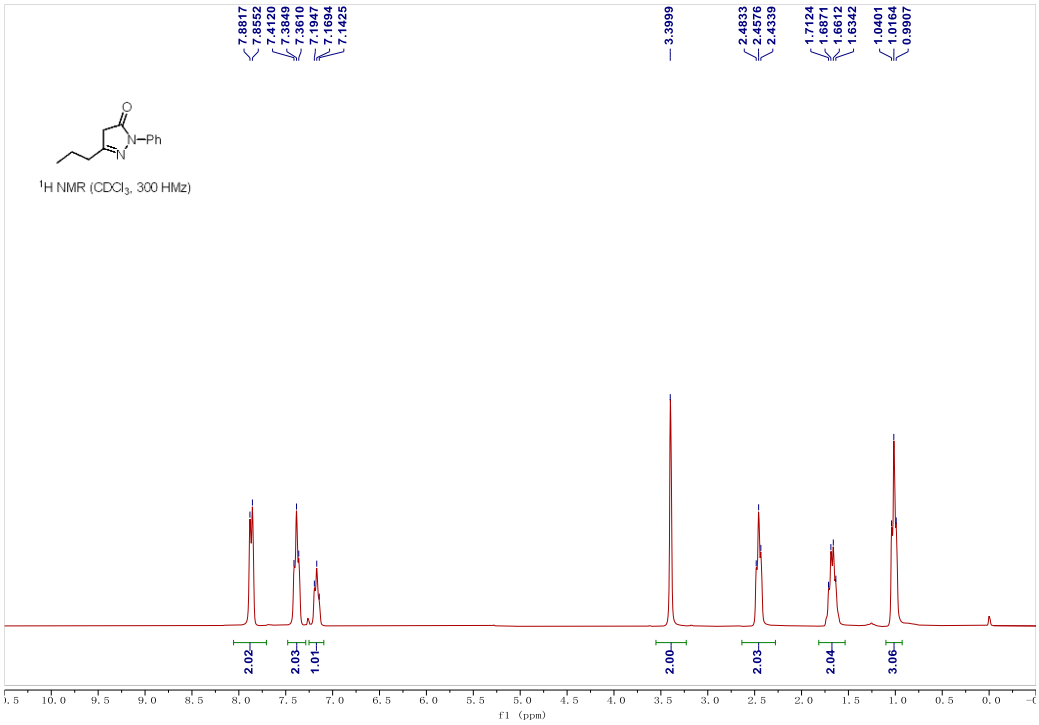


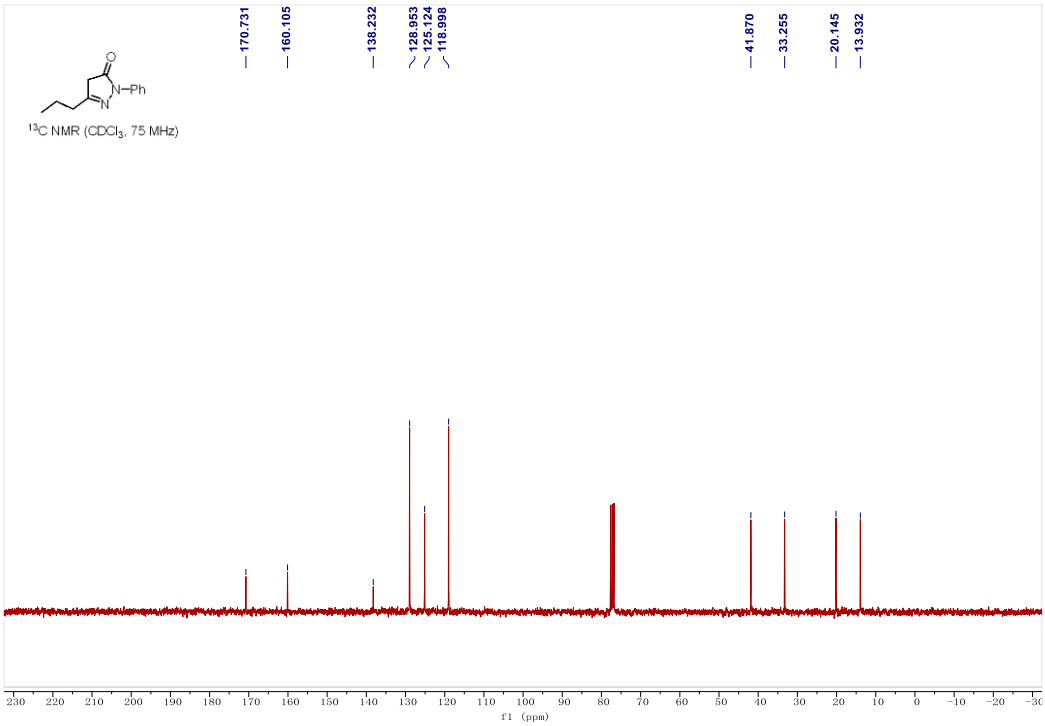
4-cyclopentyl-1-phenyl-1,3-dihydro-2H-pyrrol-2-one (2h)



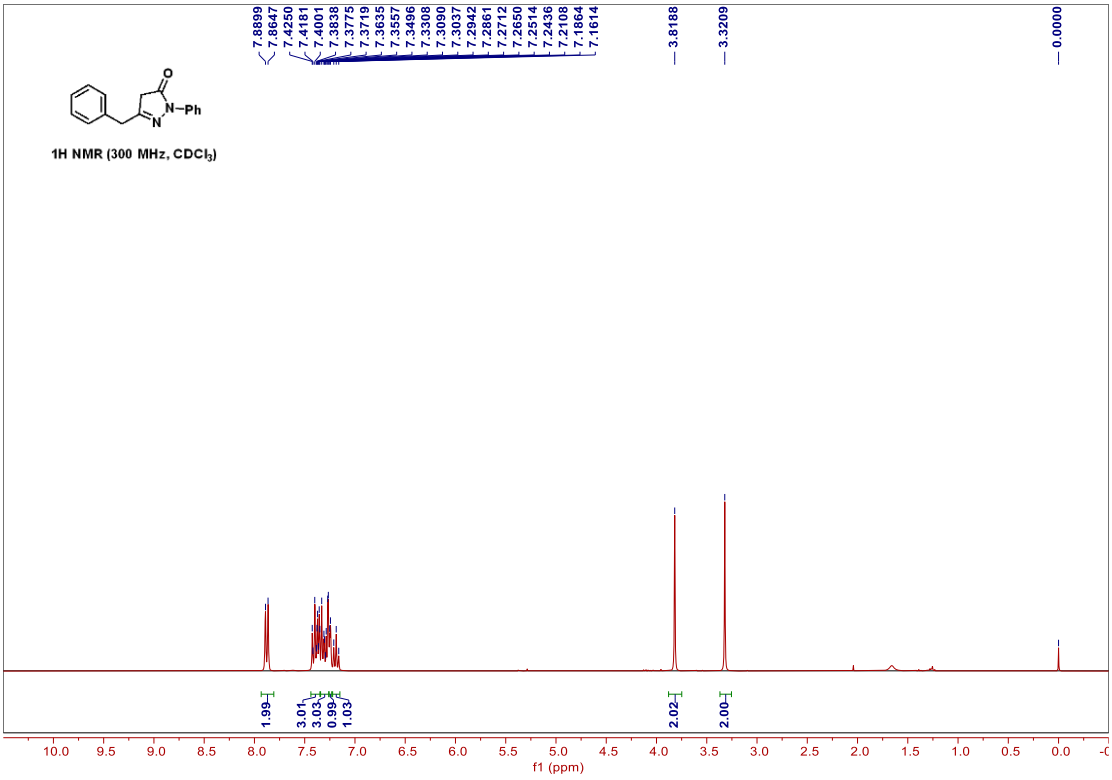


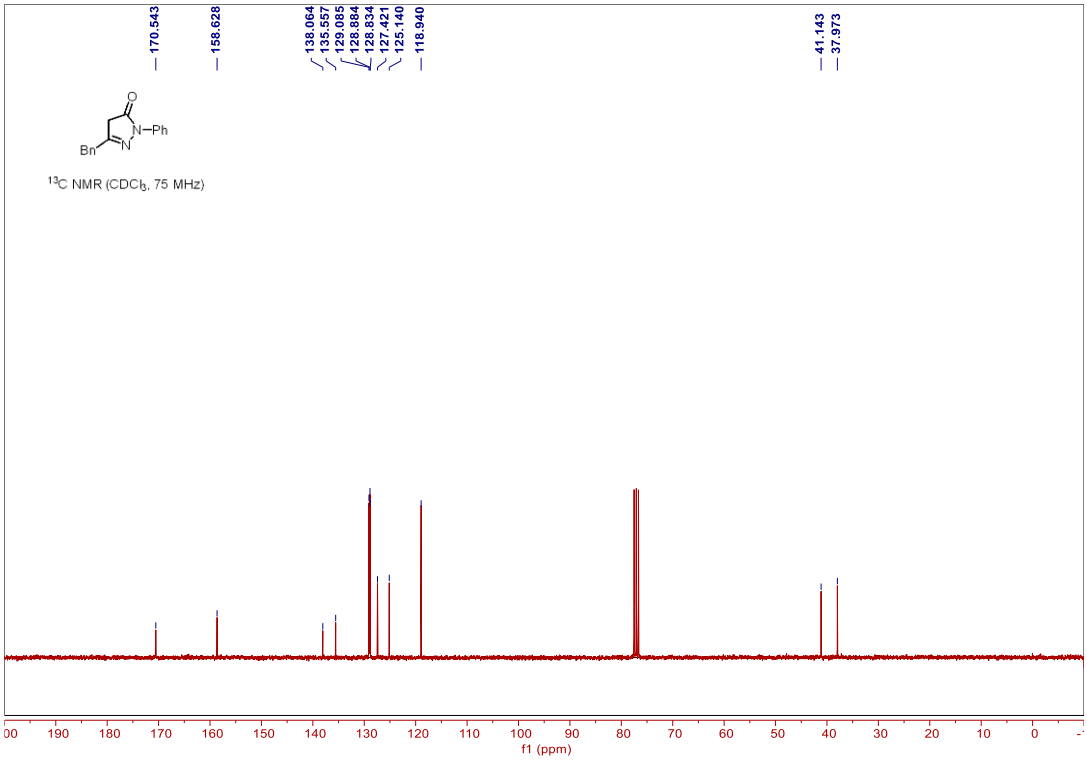
2-phenyl-5-propyl-2,4-dihydro-3H-pyrazol-3-one (2i)



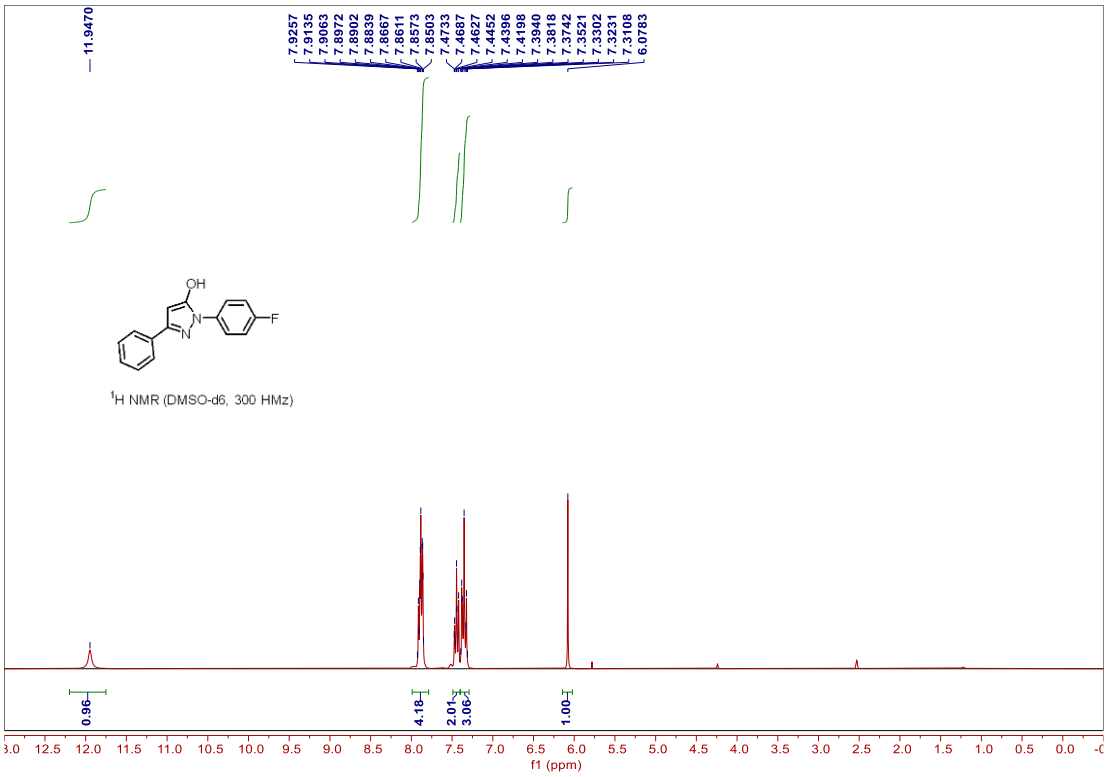


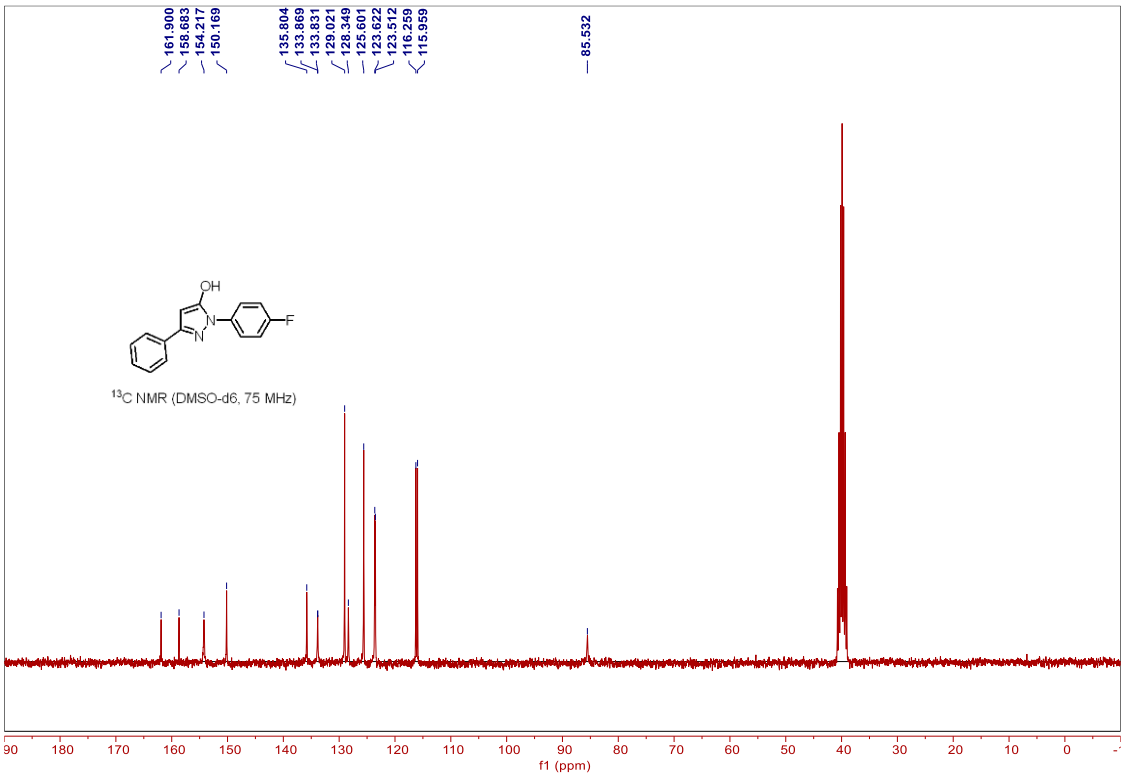
5-benzyl-2-phenyl-2,4-dihydro-3H-pyrazol-3-one (2j)

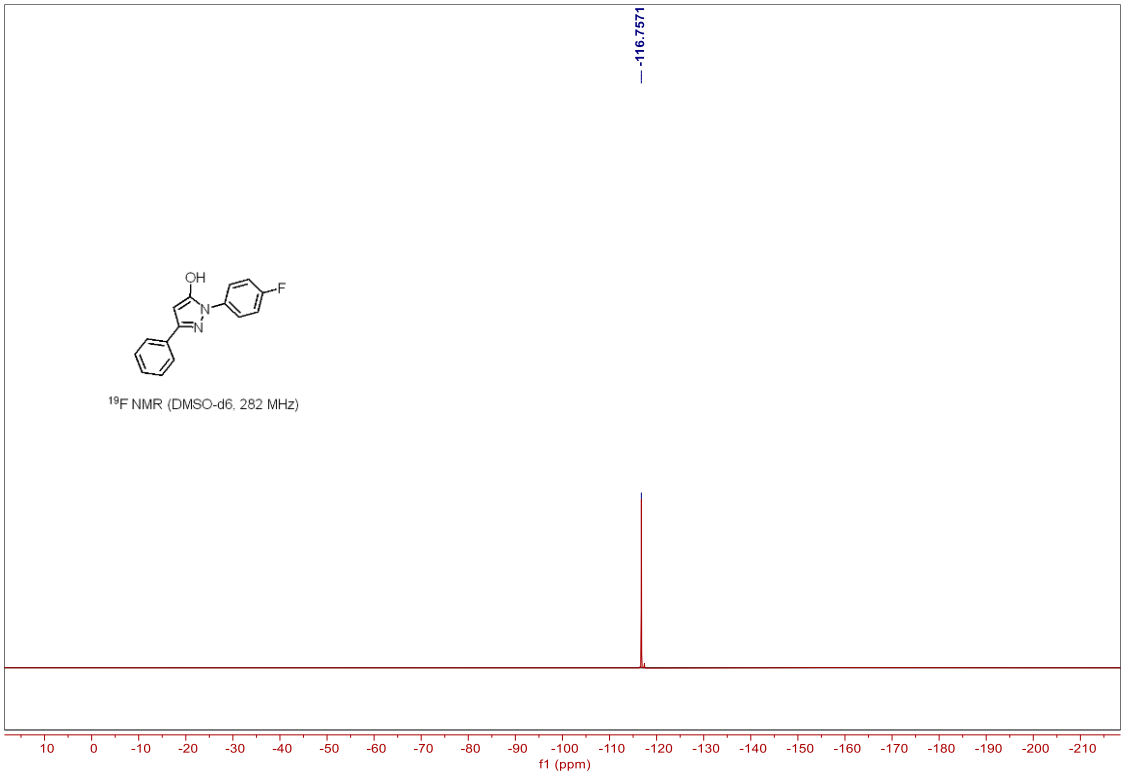




2-(4- fluorophenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (2l)

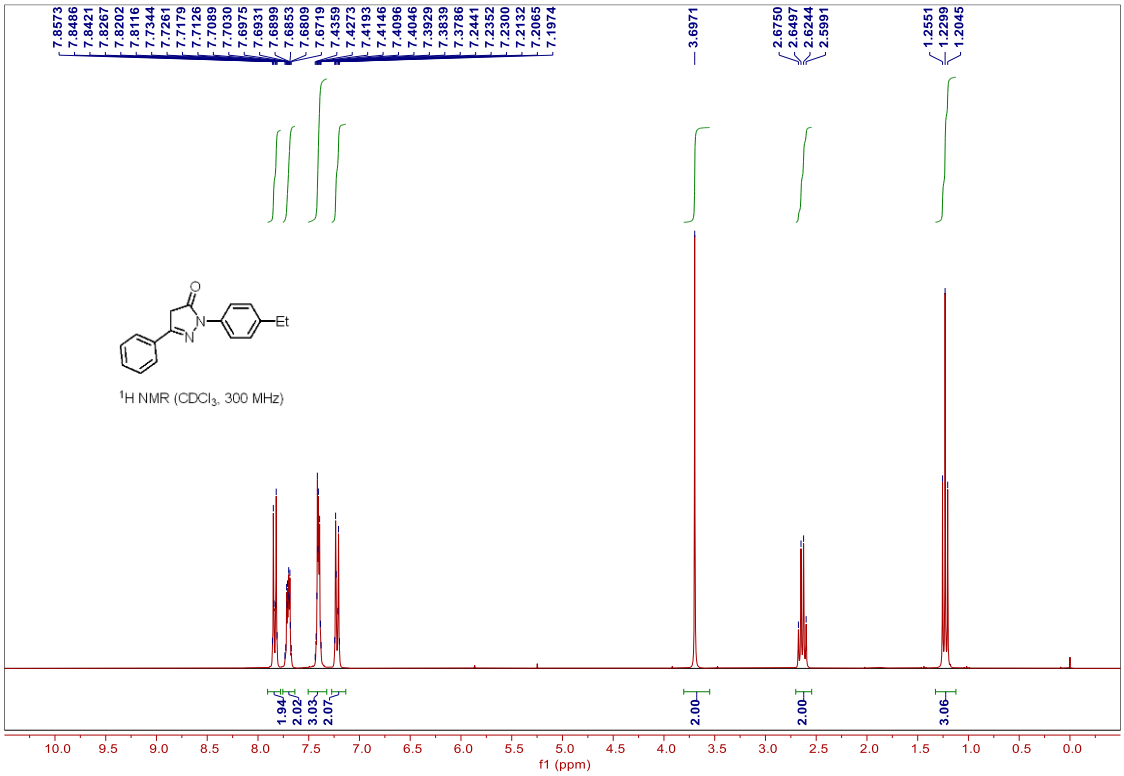


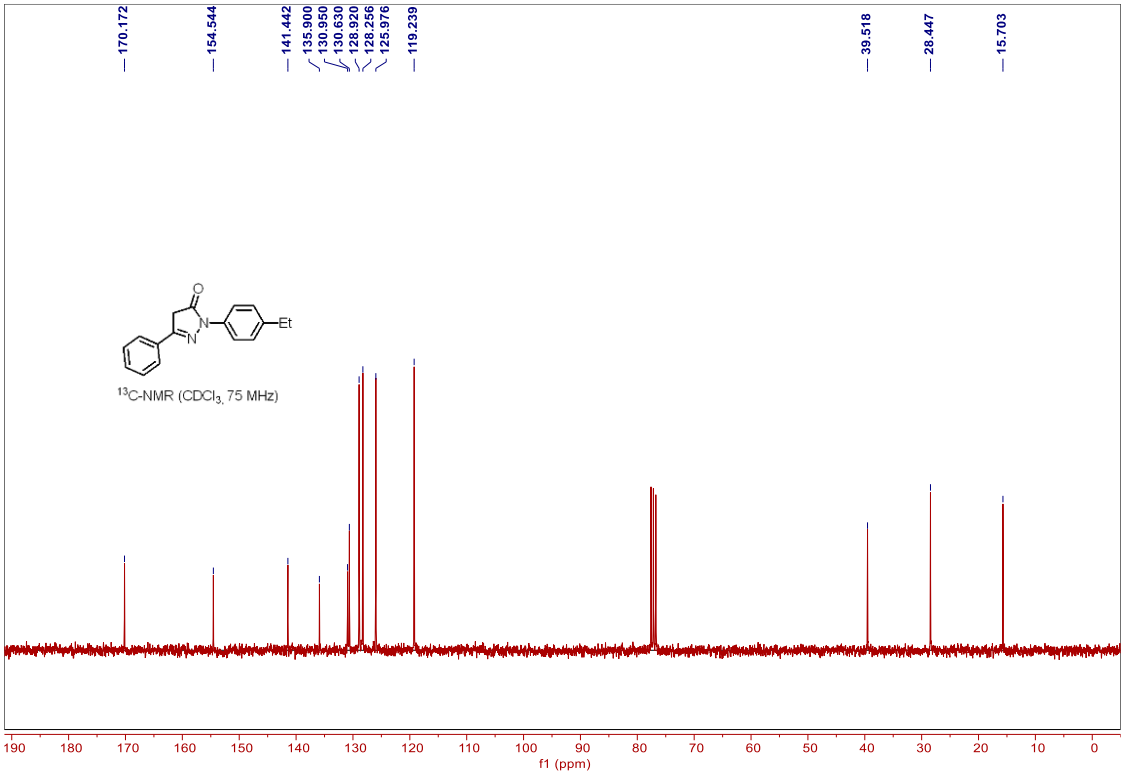




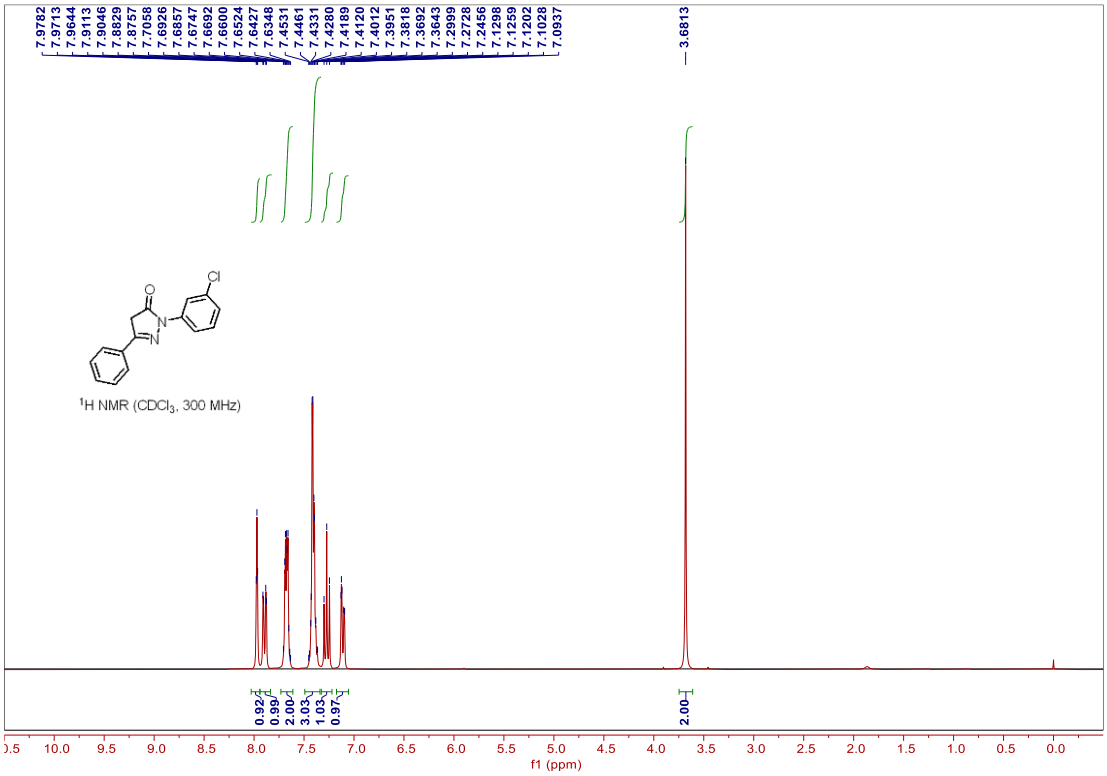
^{19}F NMR (DMSO-d6, 282 MHz)

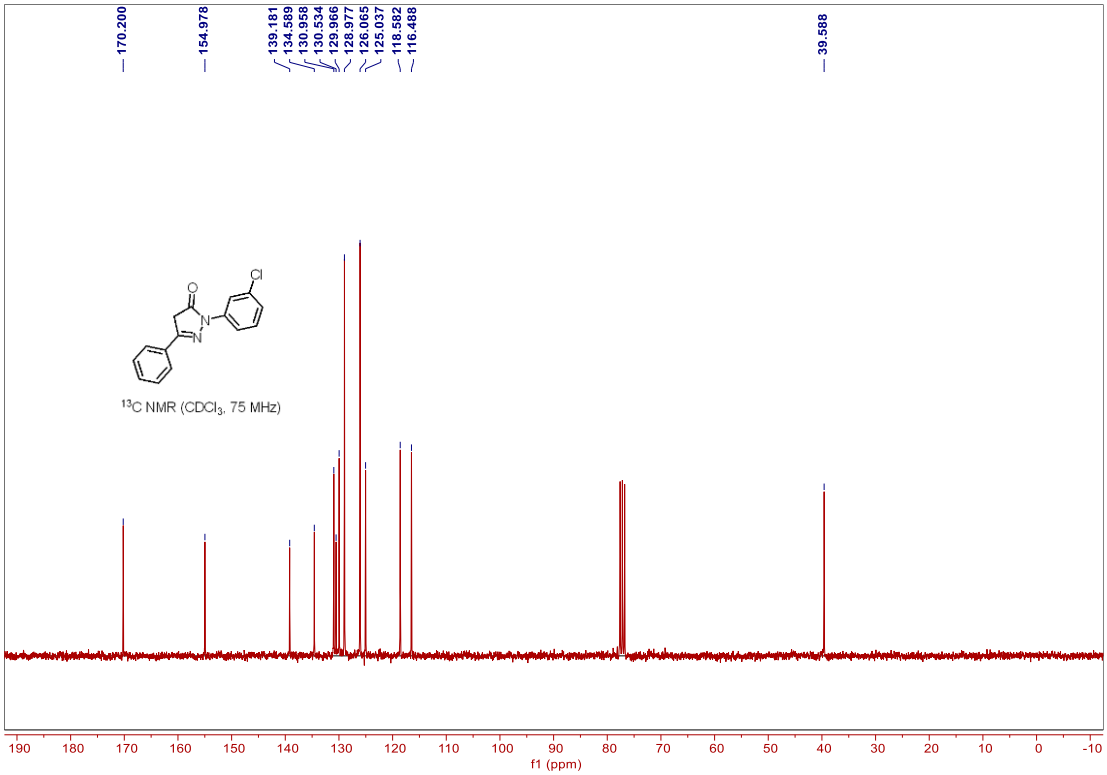
2-(4-ethylphenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (2n)



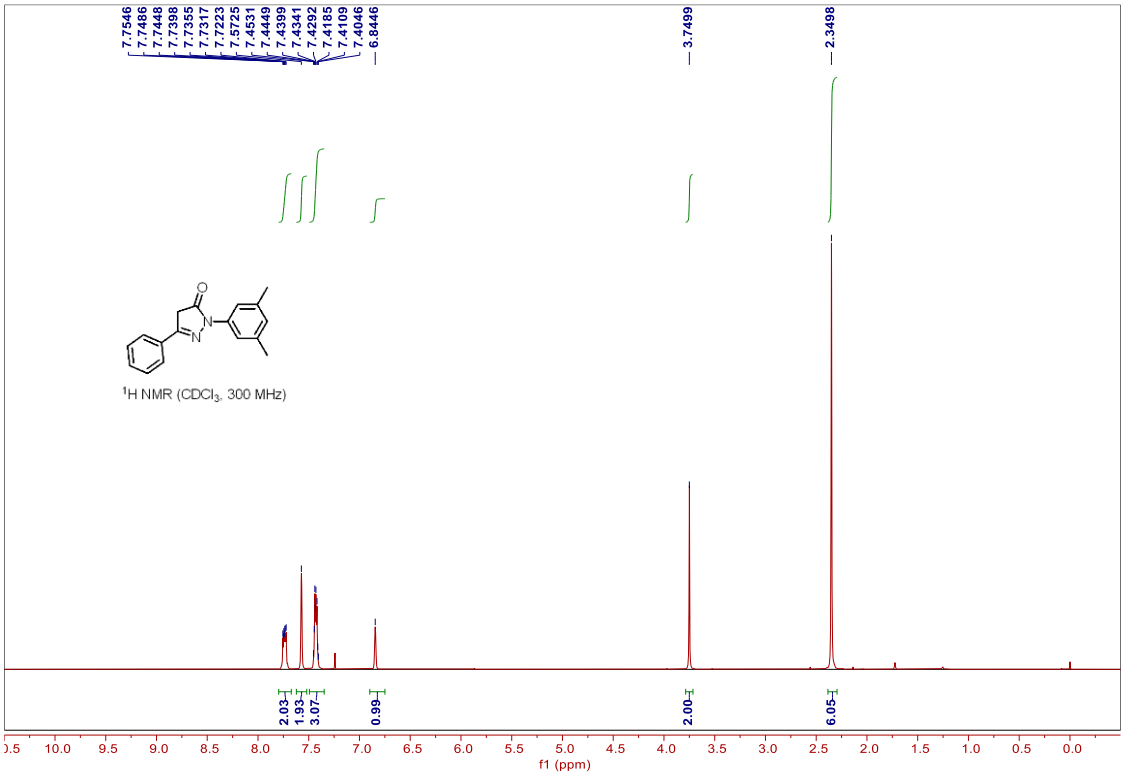


1-(3-chlorophenyl)-4-phenyl-1,3-dihydro-2H-pyrrol-2-one (2o)

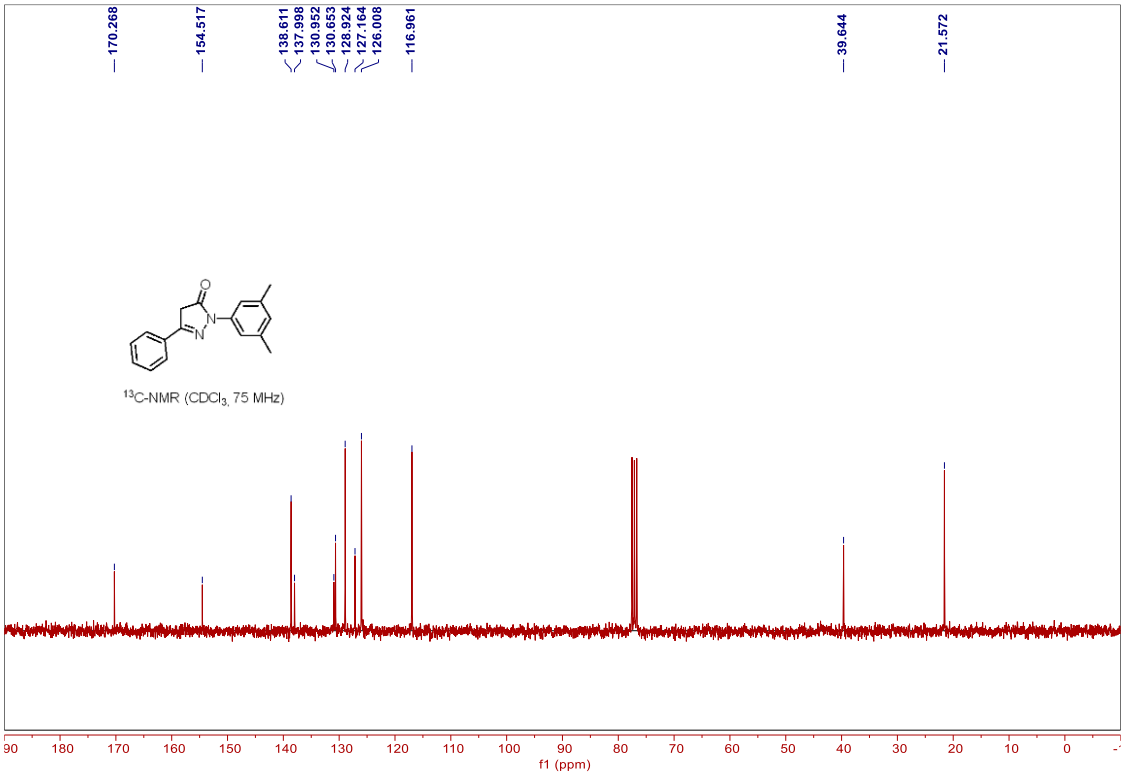




2-(3,5-dimethylphenyl)-5-phenyl-2,4-dihydro-3H-pyrazol-3-one (2p)

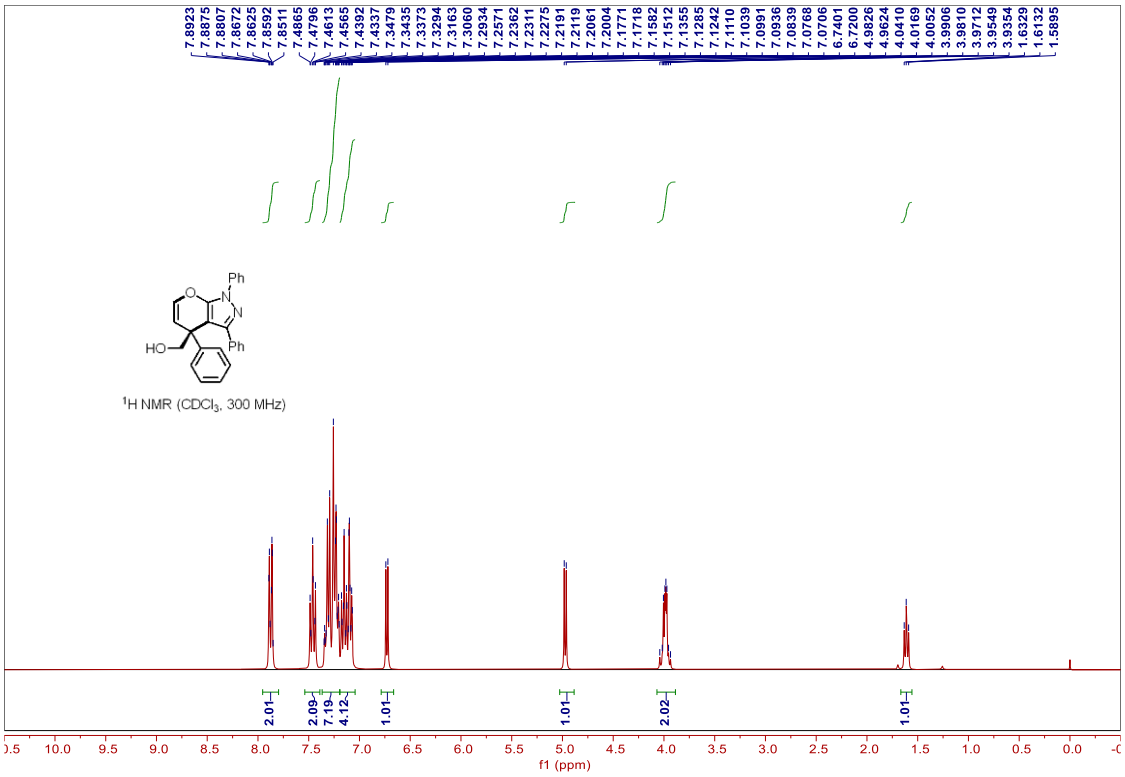


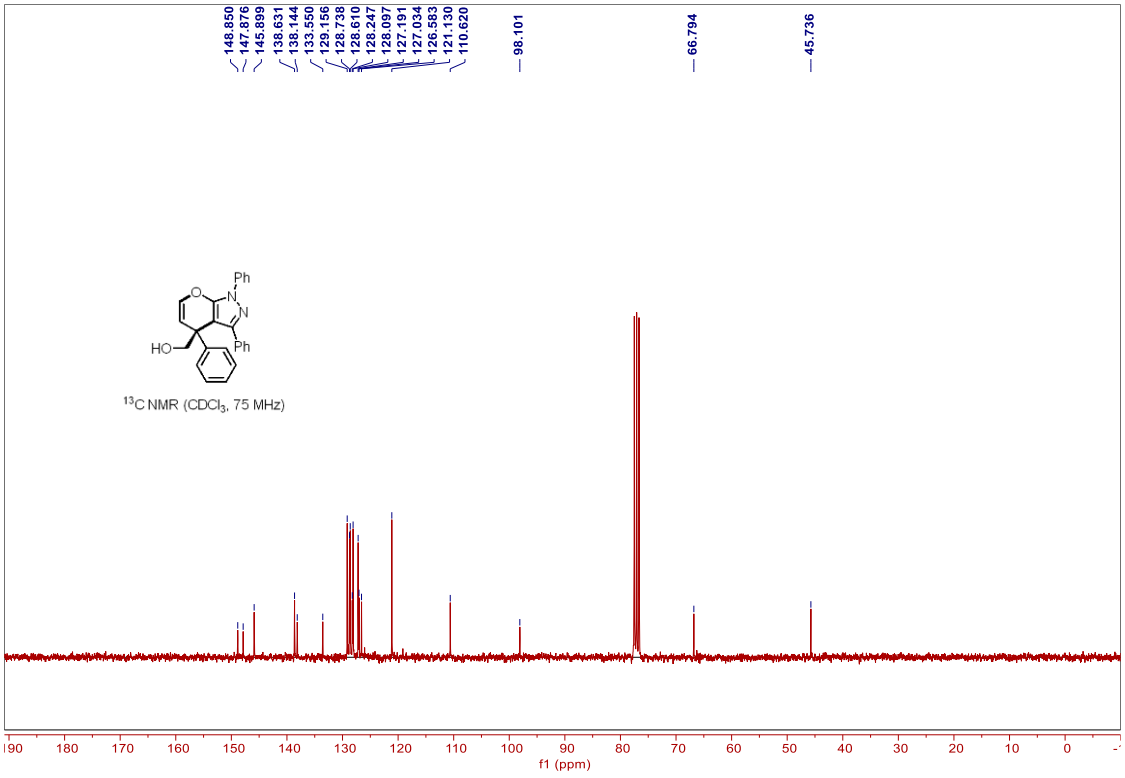
^{1}H NMR ($CDCl_3$, 300 MHz)



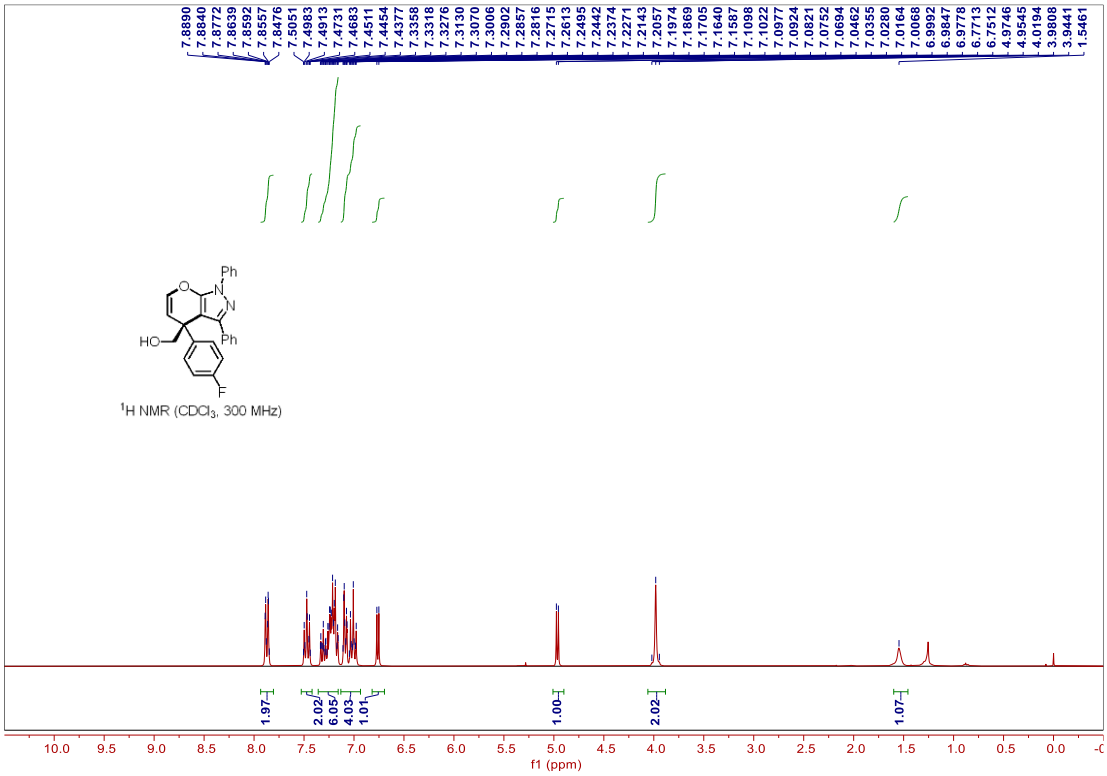
^{13}C-NMR ($CDCl_3$, 75 MHz)

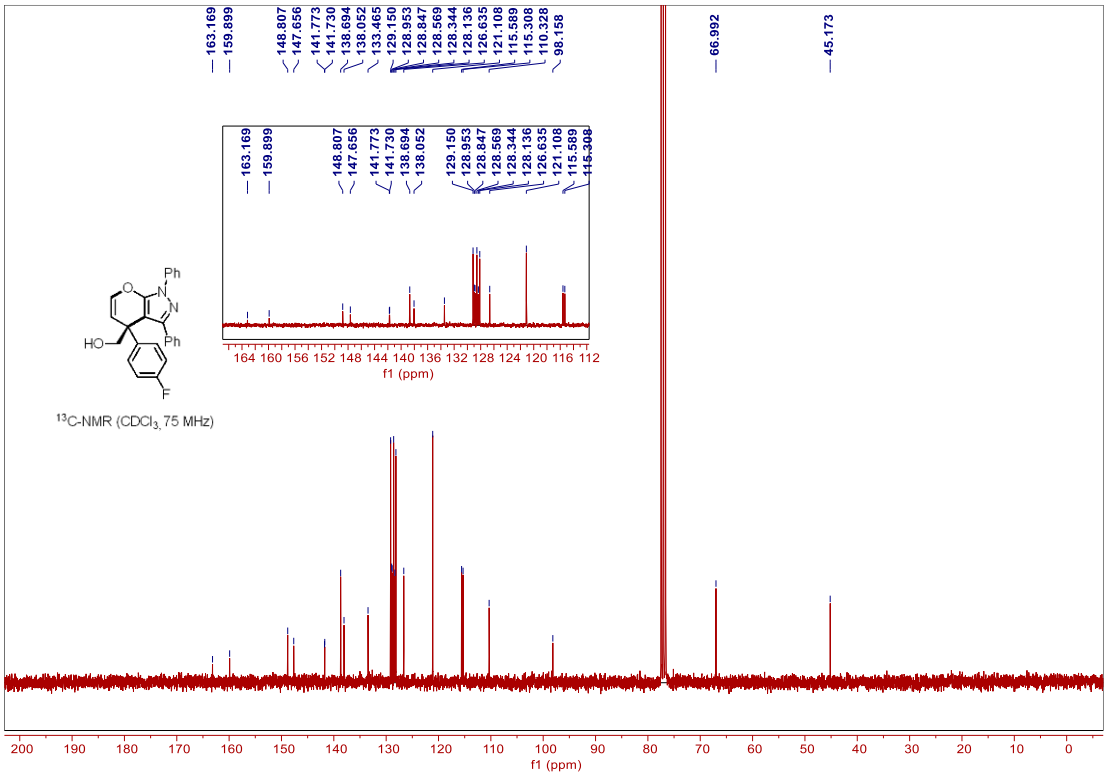
(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3aa)

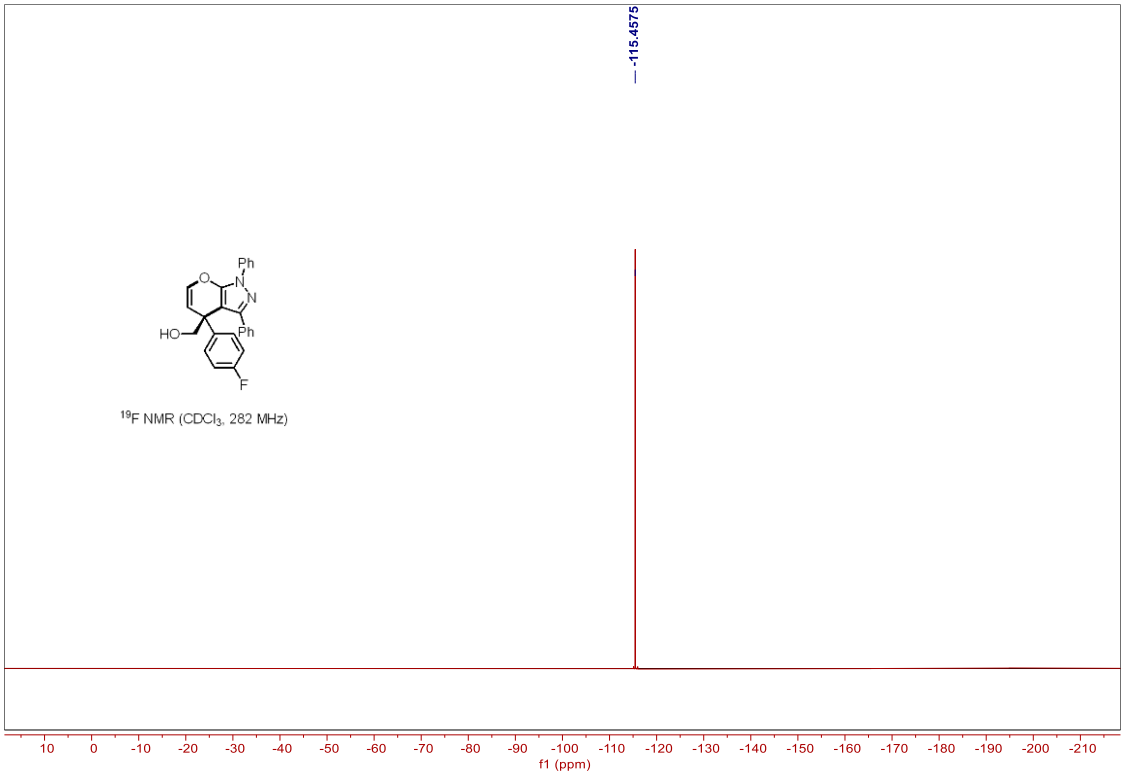




(R)-(4-(4-fluorophenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ba)

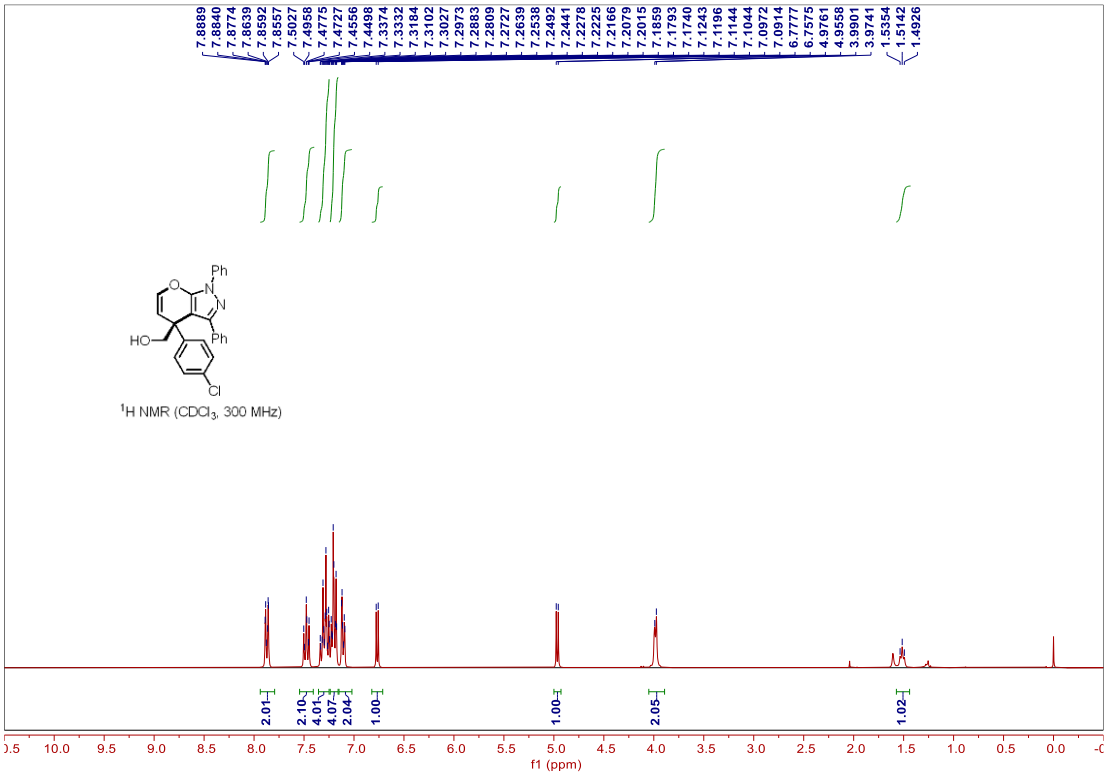


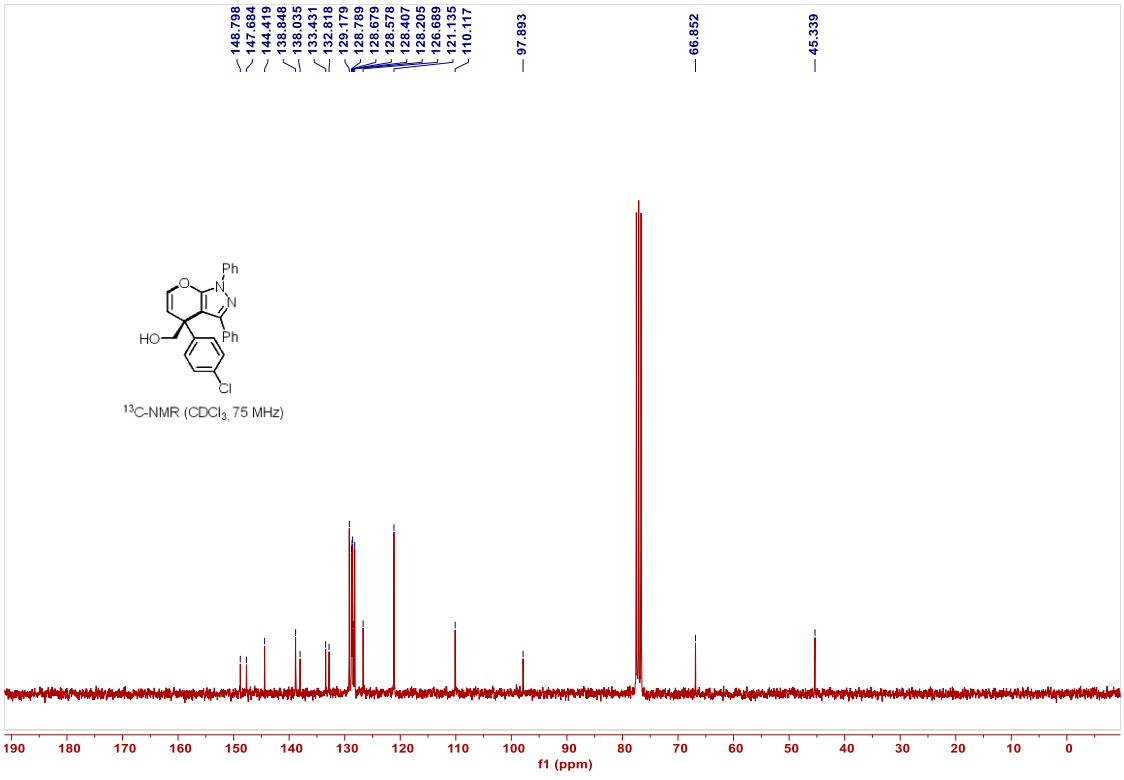




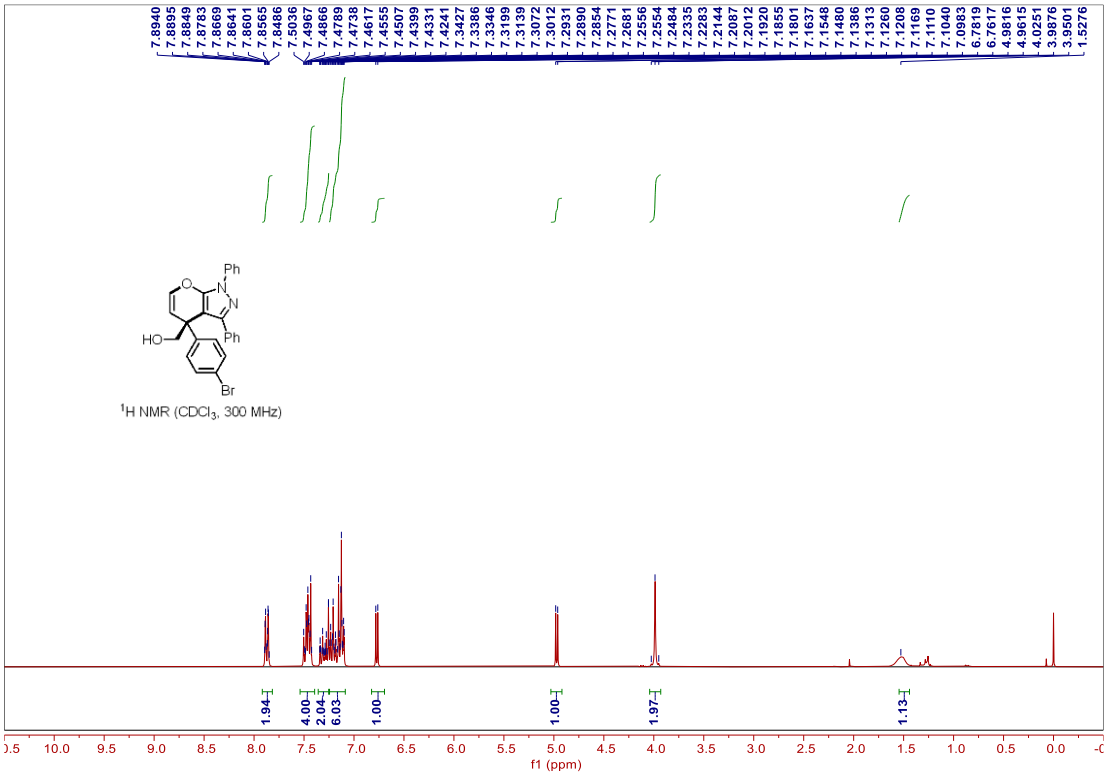
^{19}F NMR ($CDCl_3$, 282 MHz)

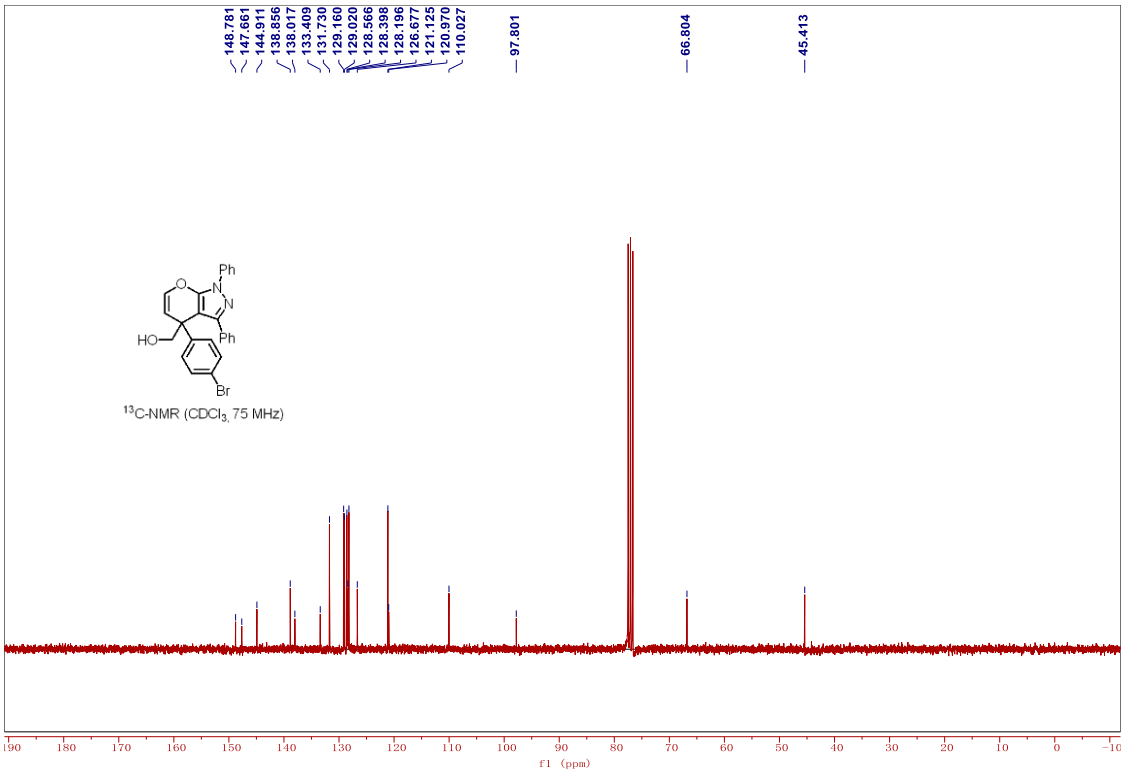
(R)-(4-(4-chlorophenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ca)



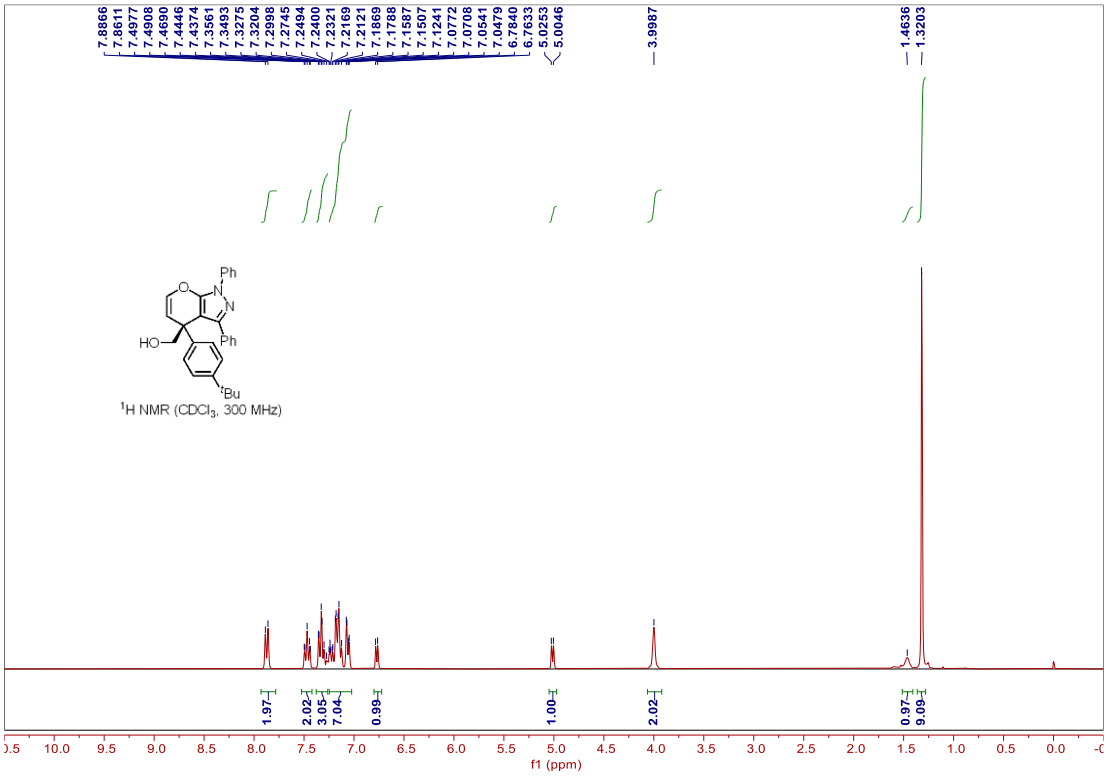


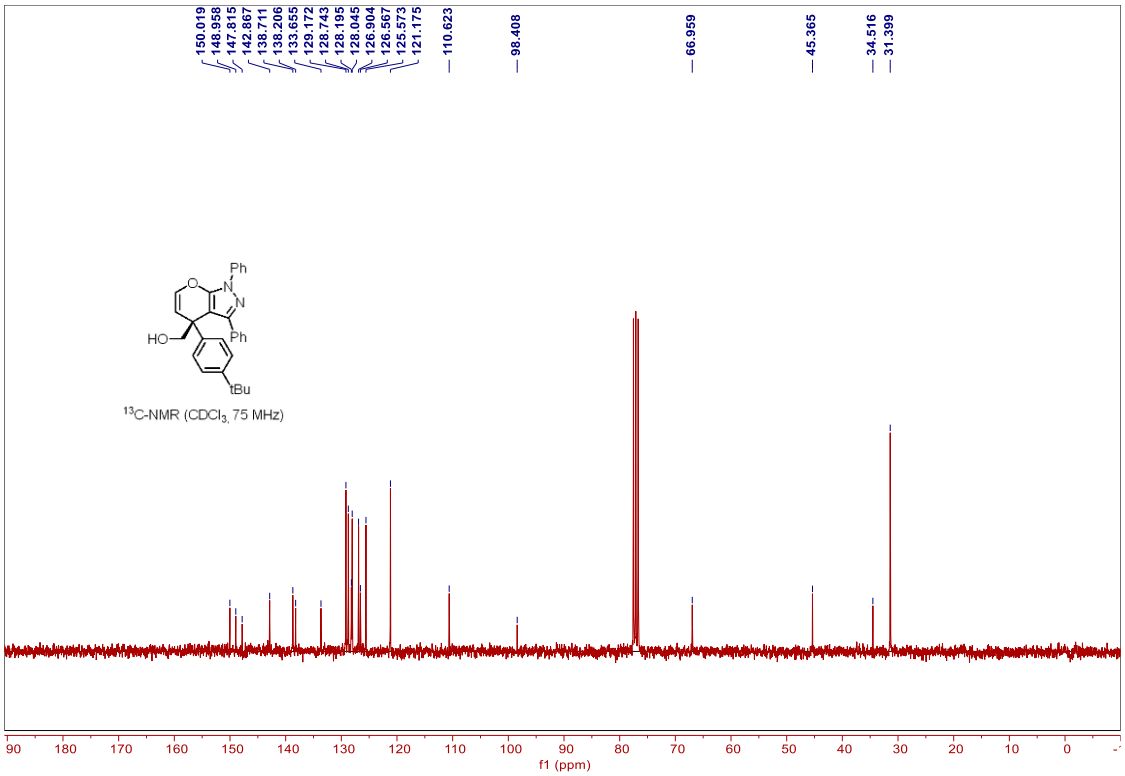
(R)-(4-(4-bromophenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3da)



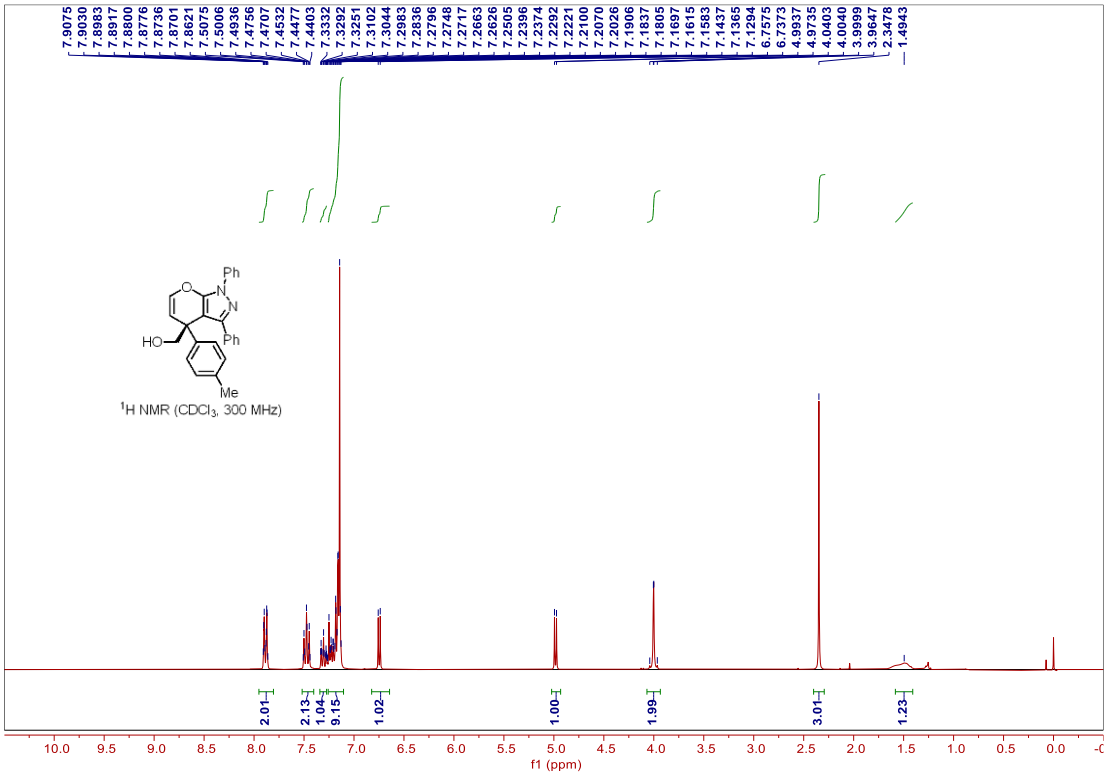


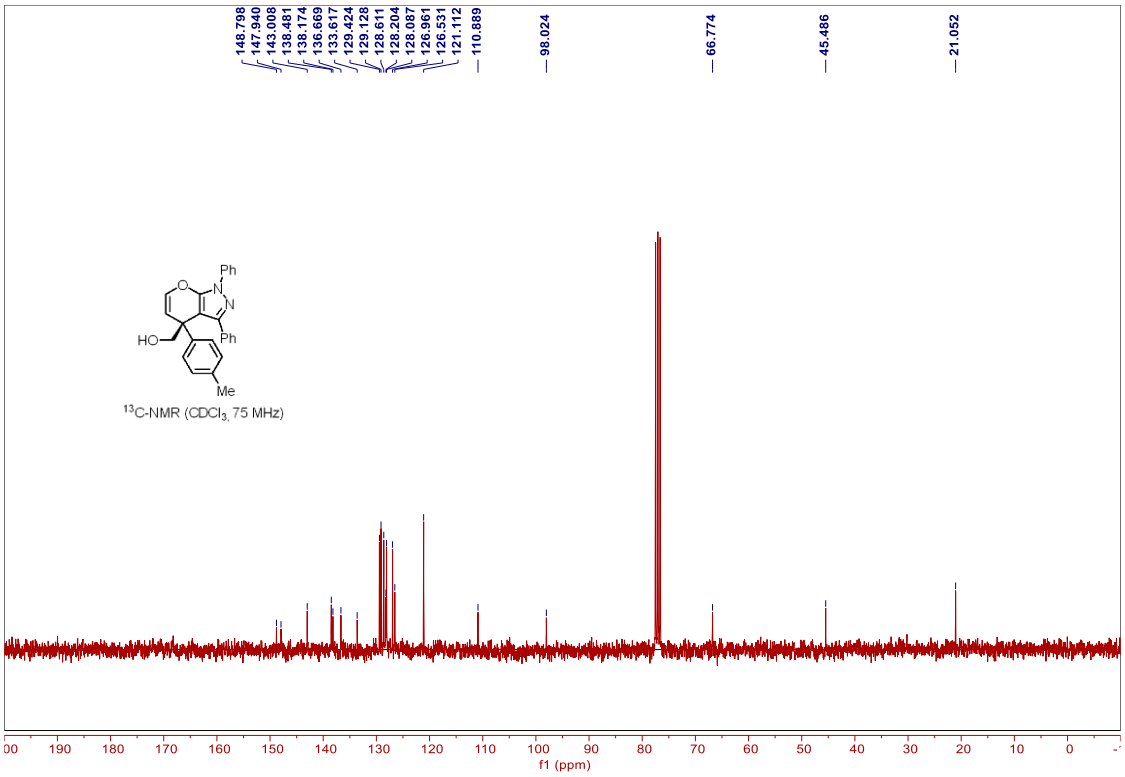
(R)-(4-(4-(tert-butyl)phenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ea)



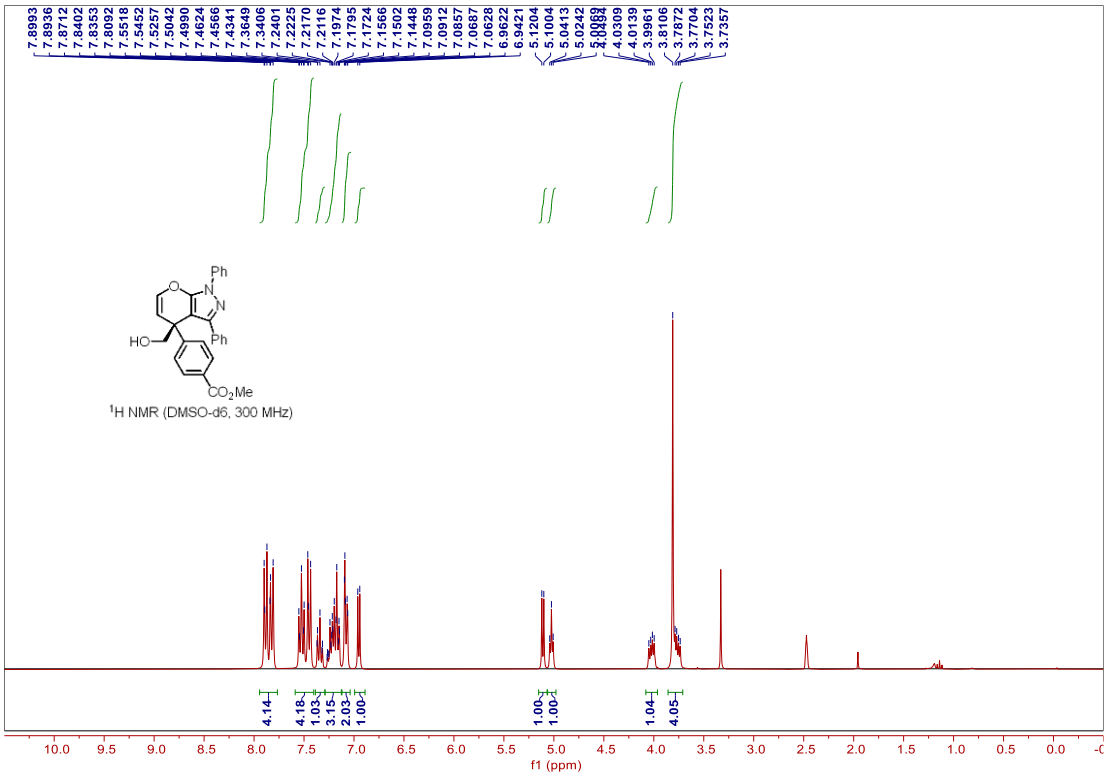


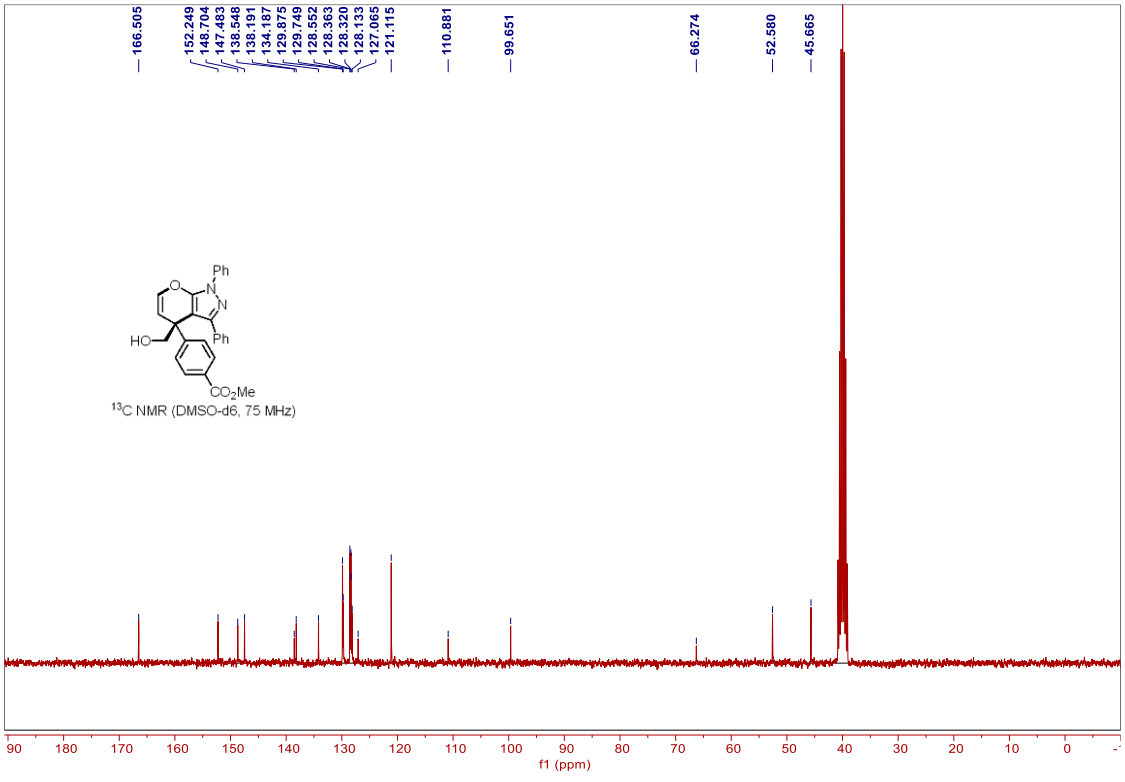
(R)-(1,3-diphenyl-4-(p-tolyl)-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3fa)



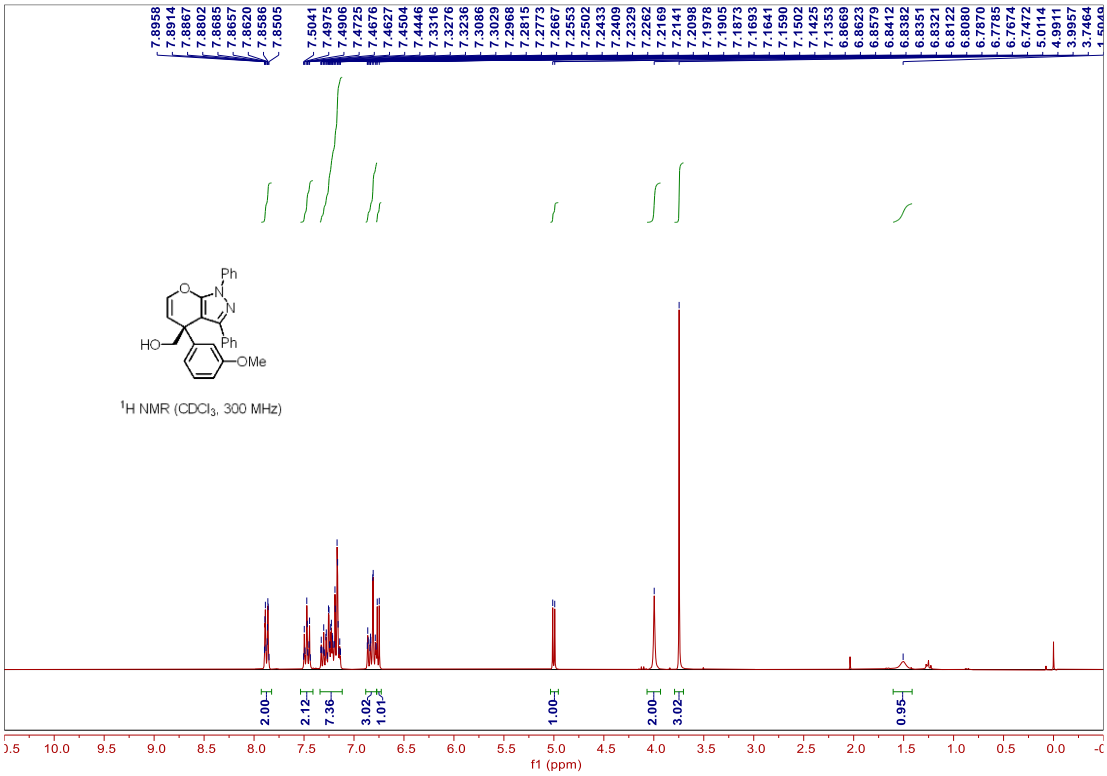


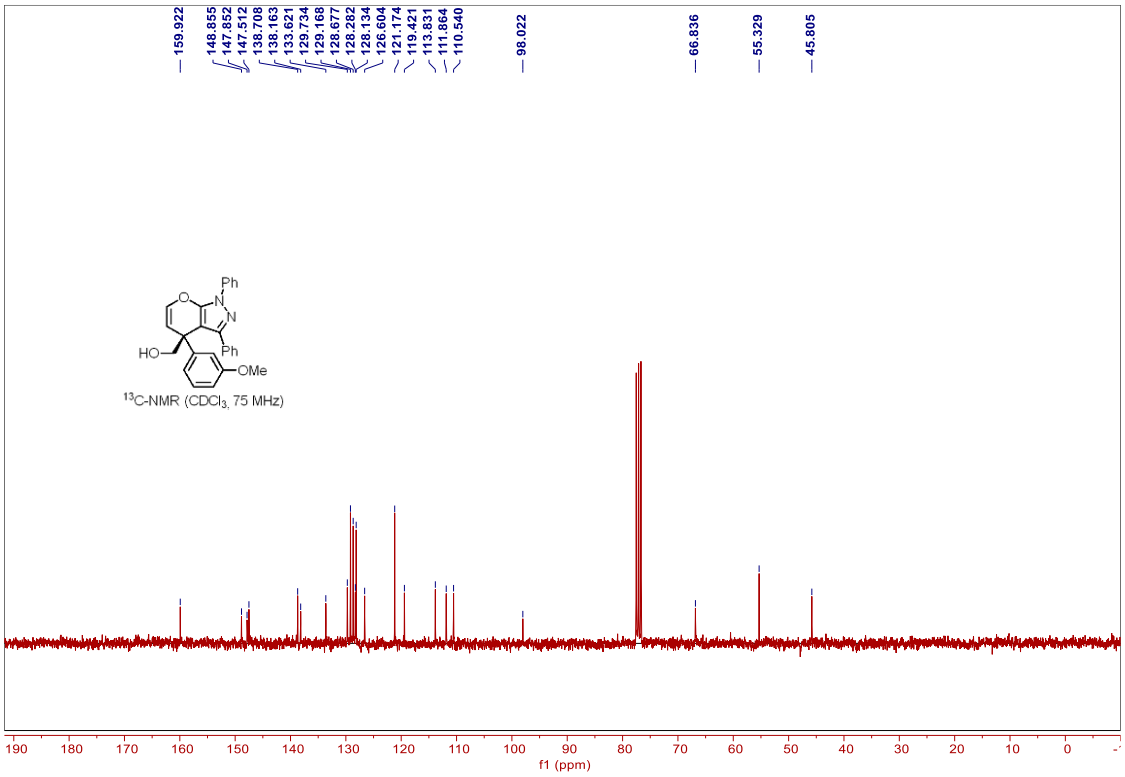
methyl (R)-4-(4-(hydroxymethyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)benzoate (3ga)



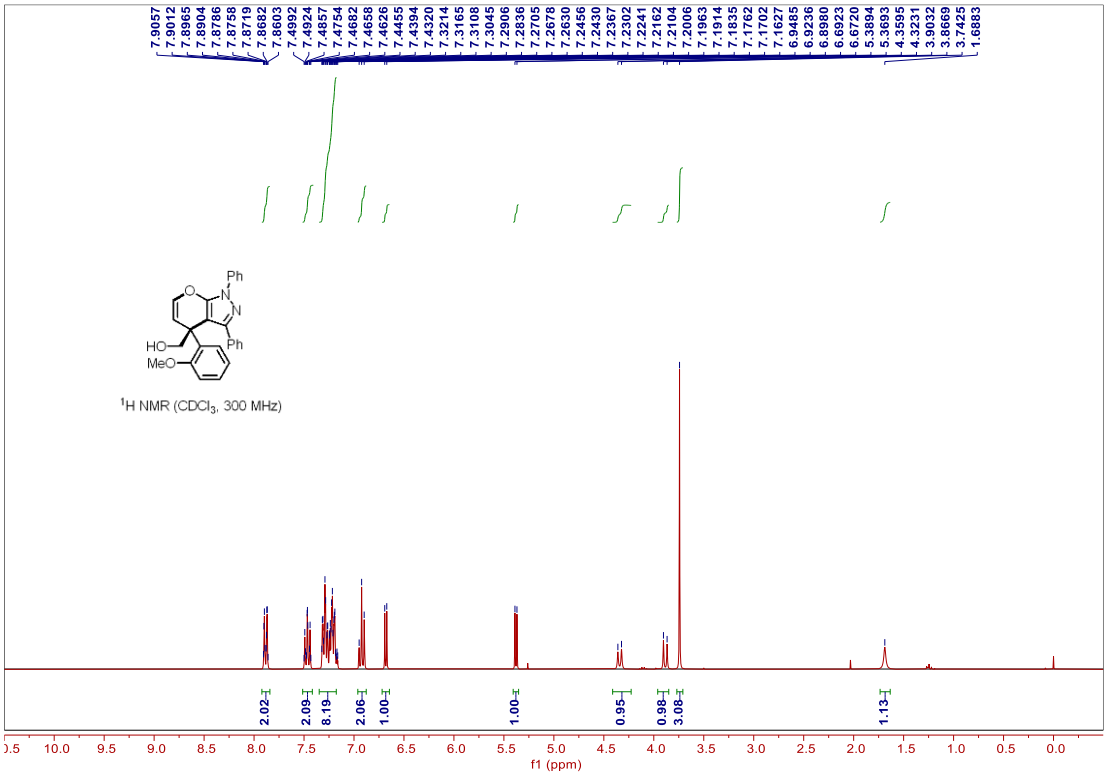


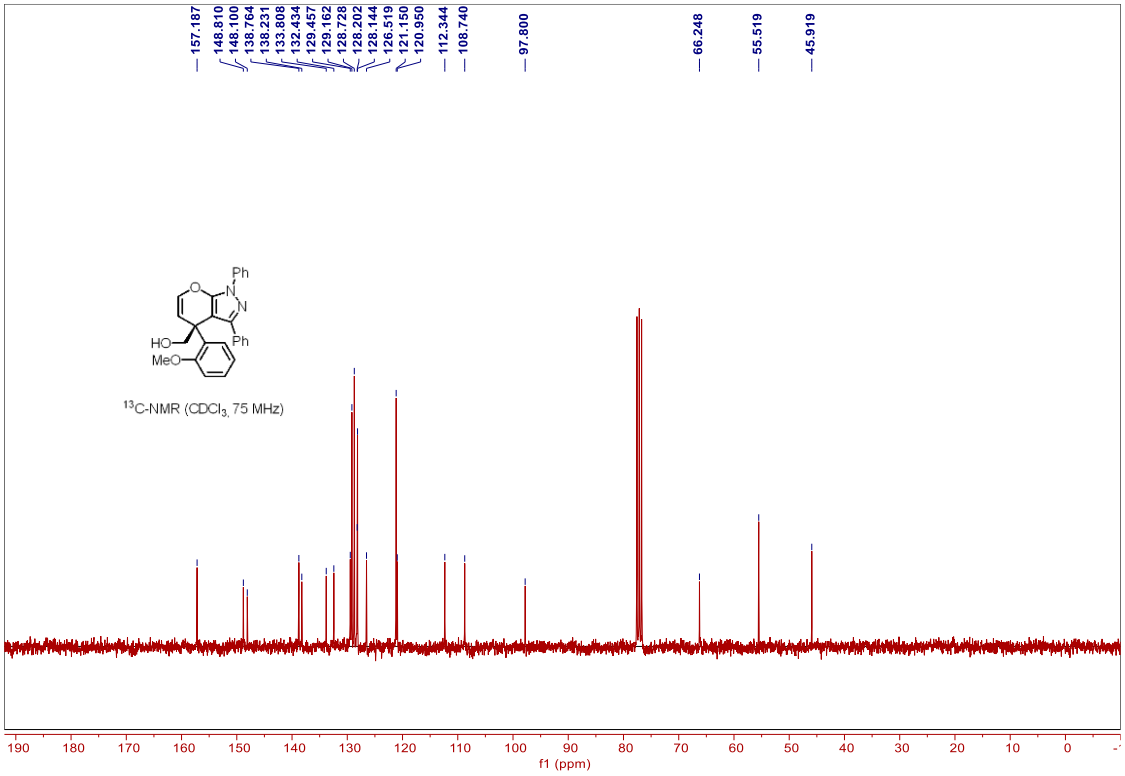
(R)-(4-(3-methoxyphenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ha)



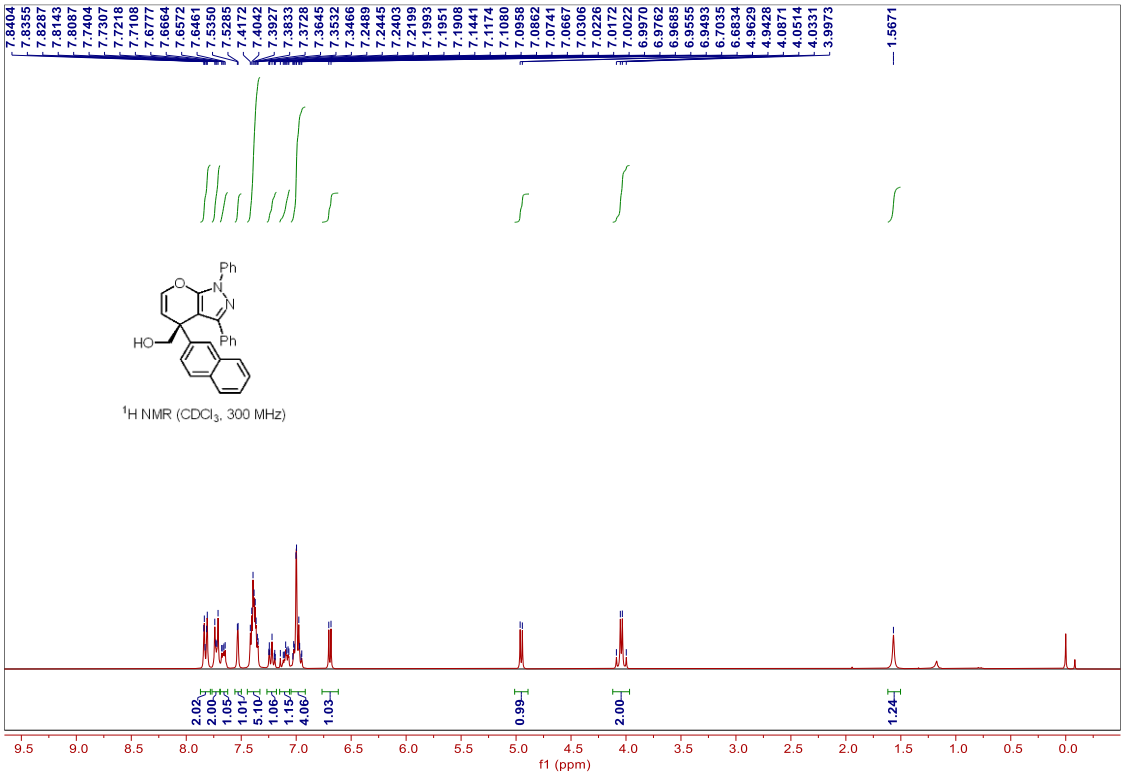


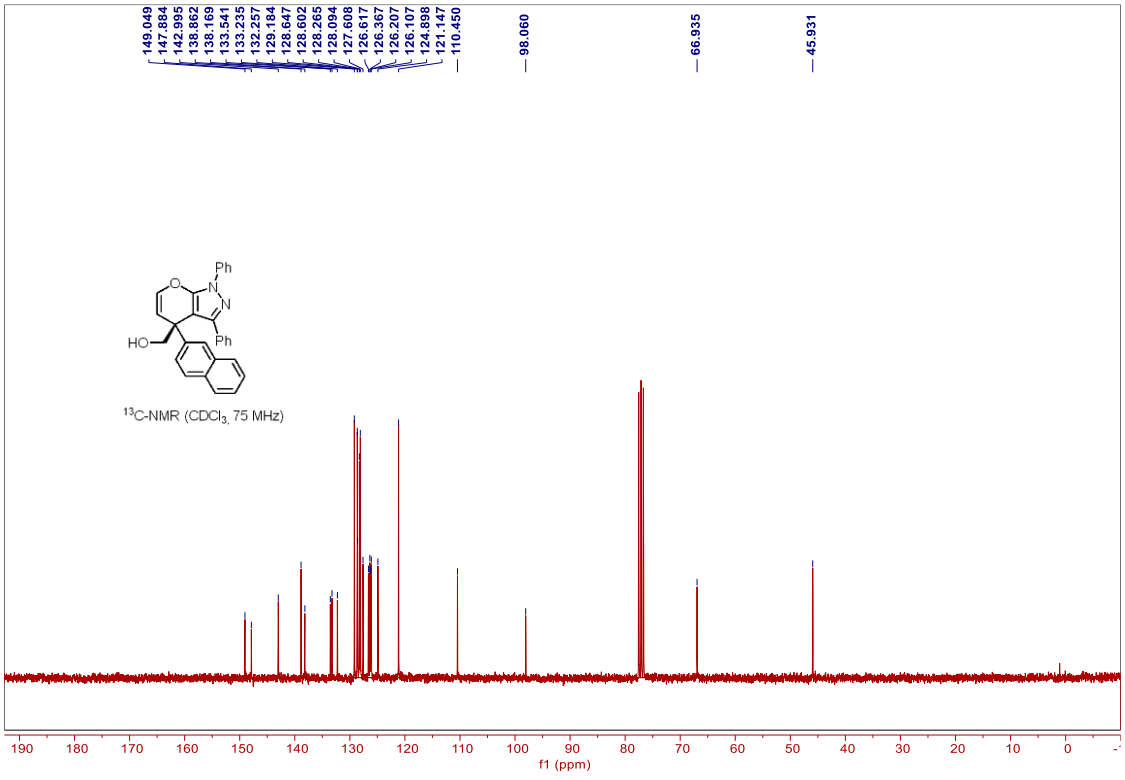
(R)-(4-(2-methoxyphenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ia)



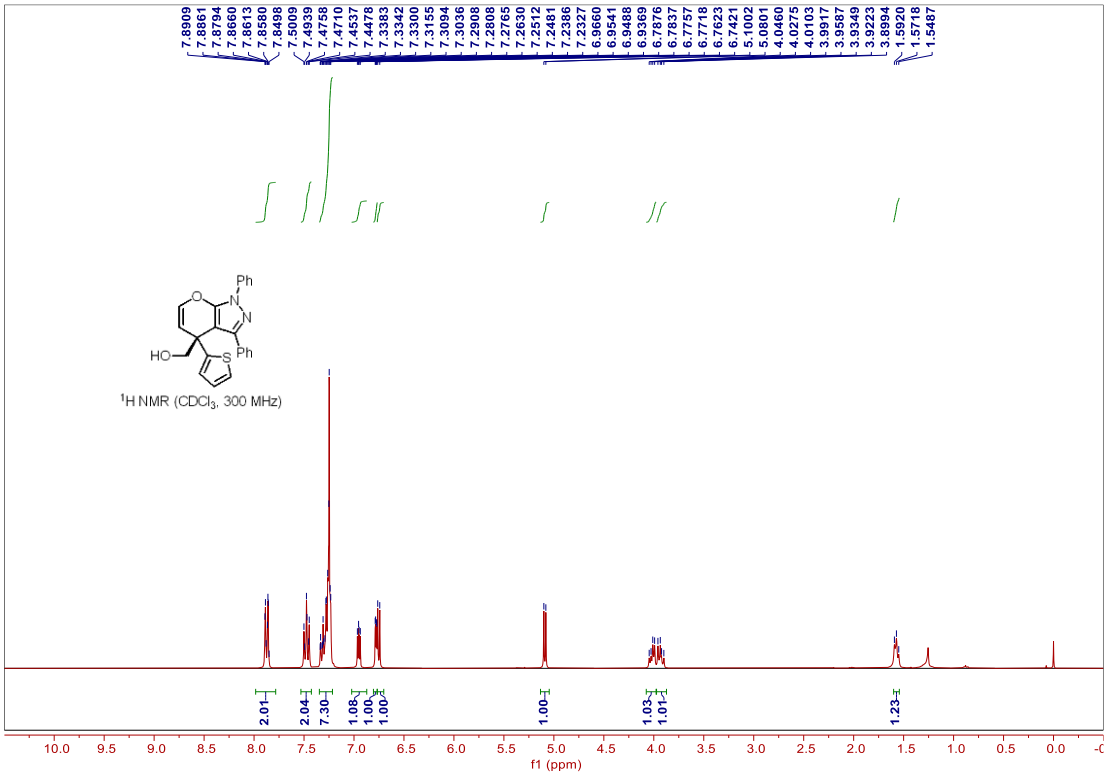


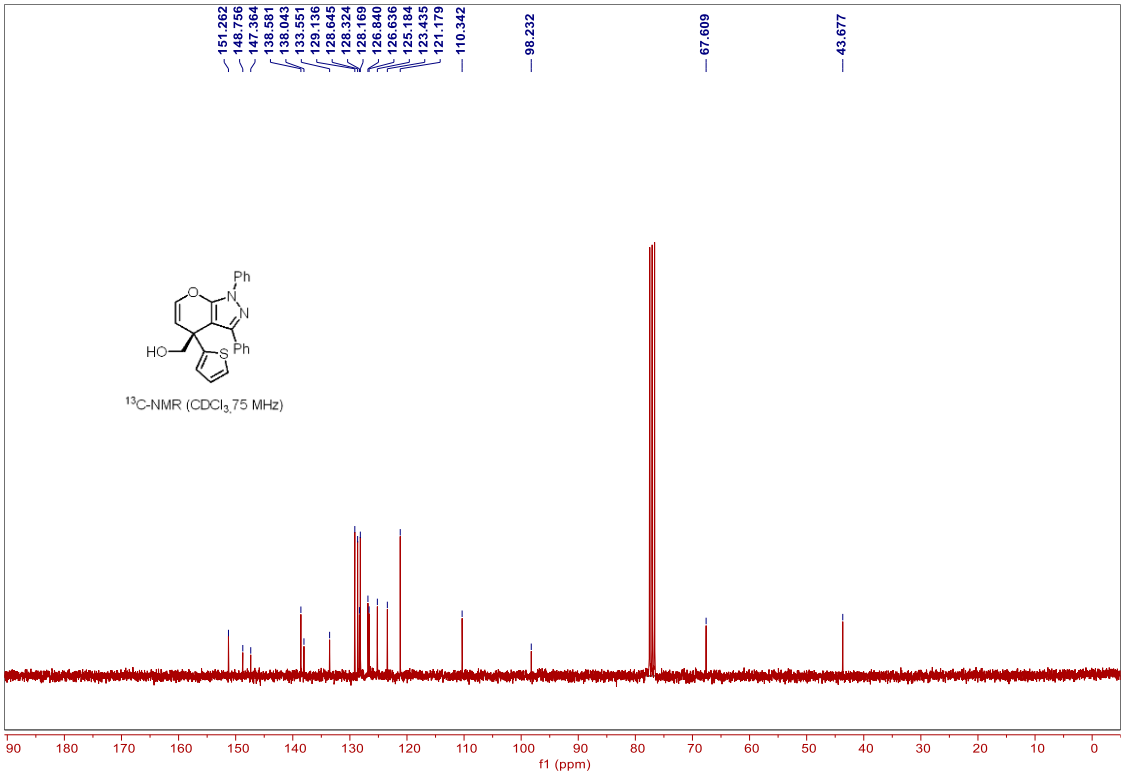
(R)-(4-(naphthalen-2-yl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ja)



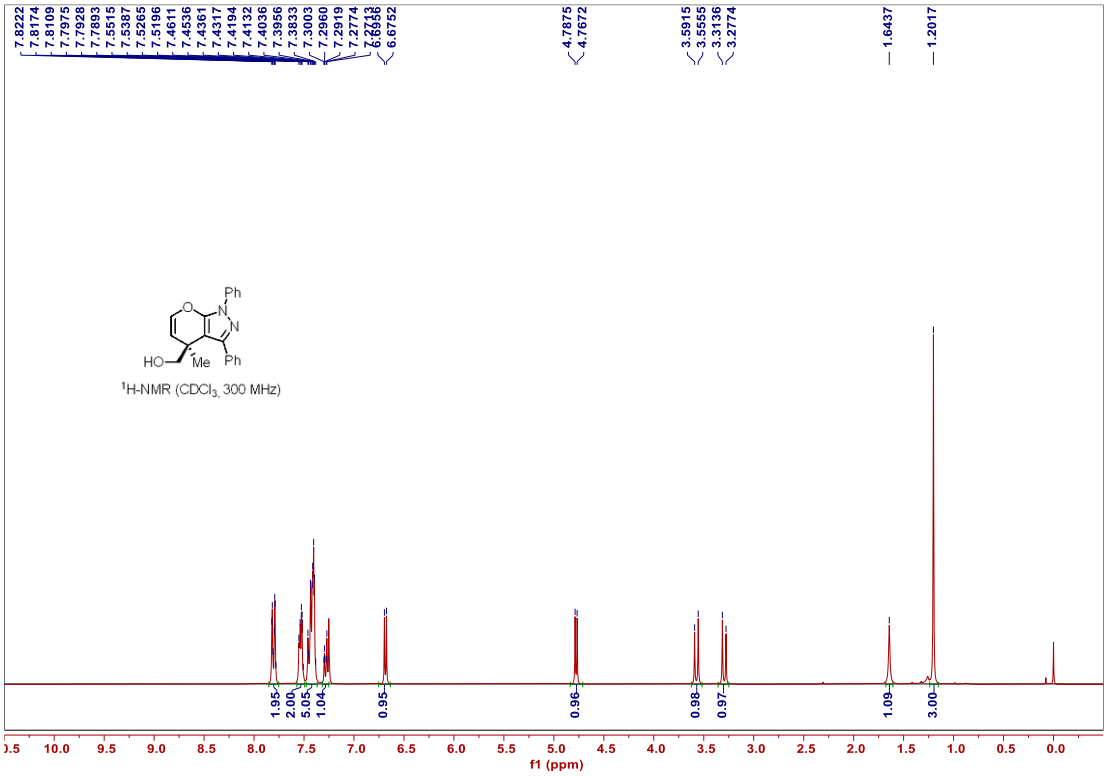


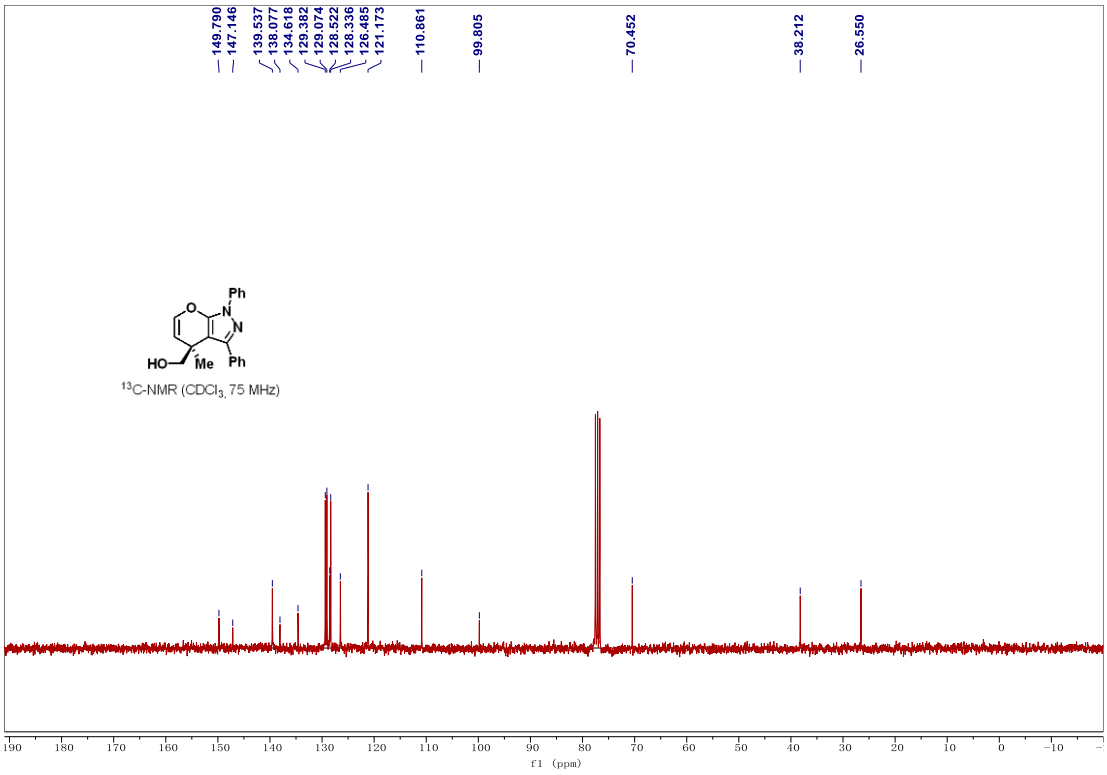
(R)-(1,3-diphenyl-4-(thiophen-2-yl)-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ka)



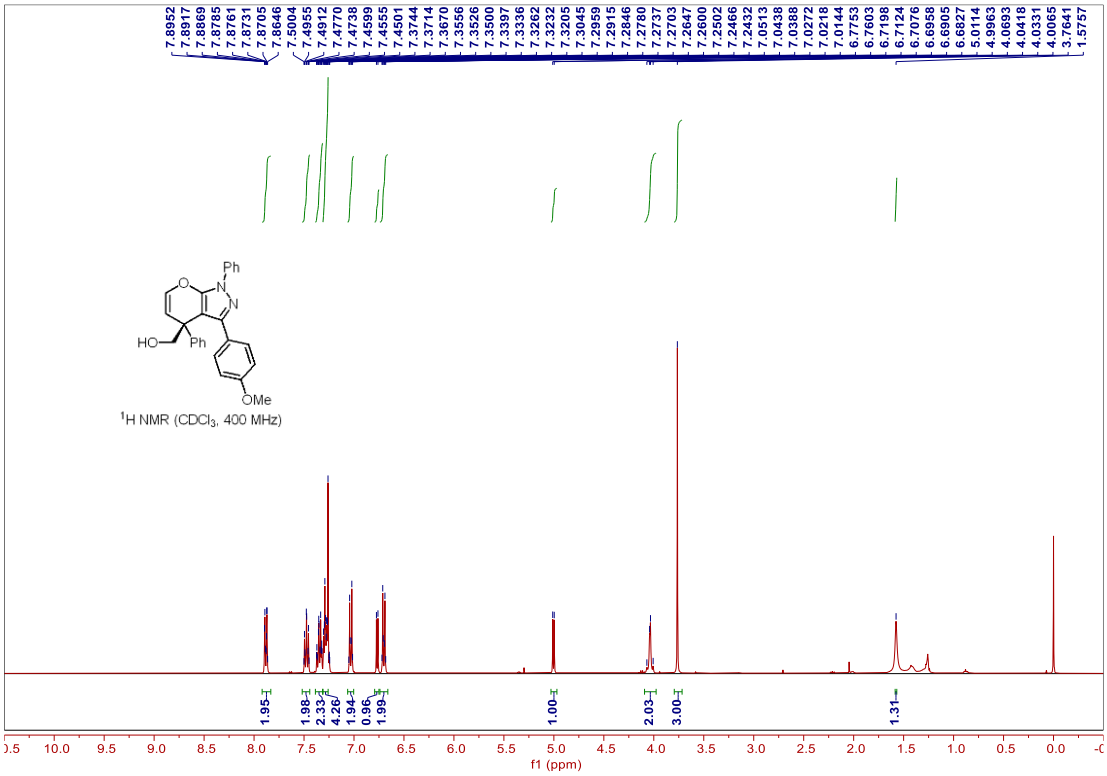


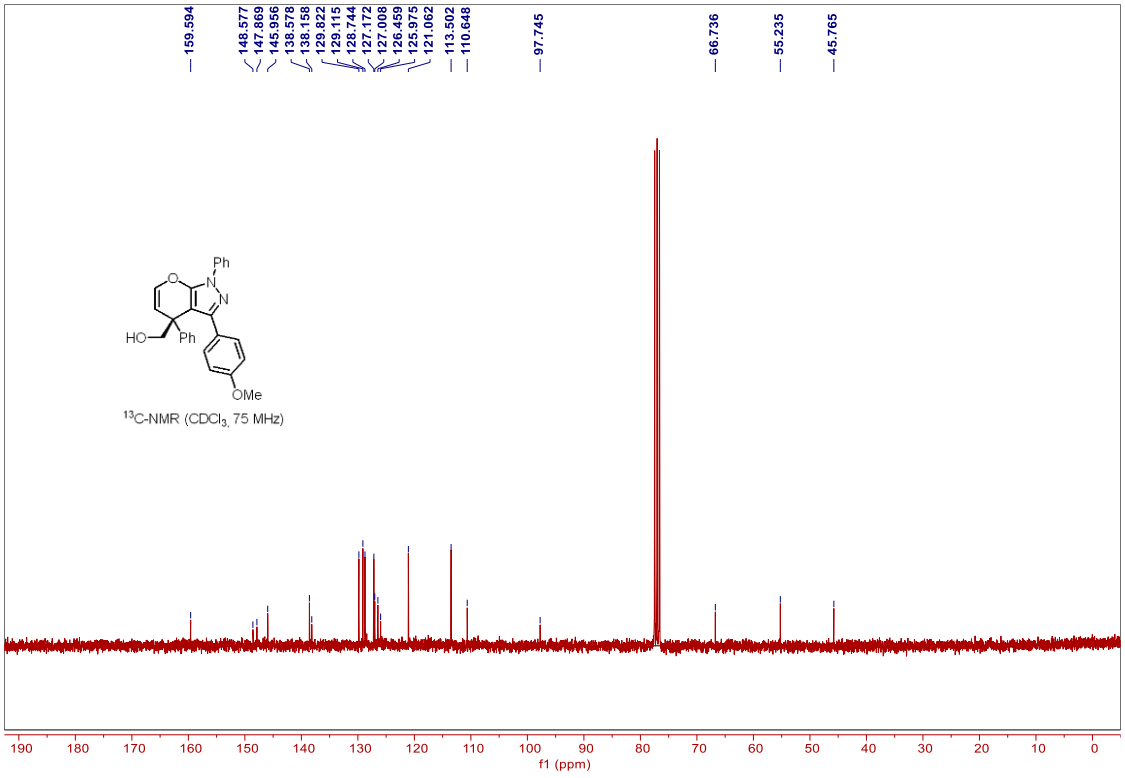
R-(4-methyl-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3la)



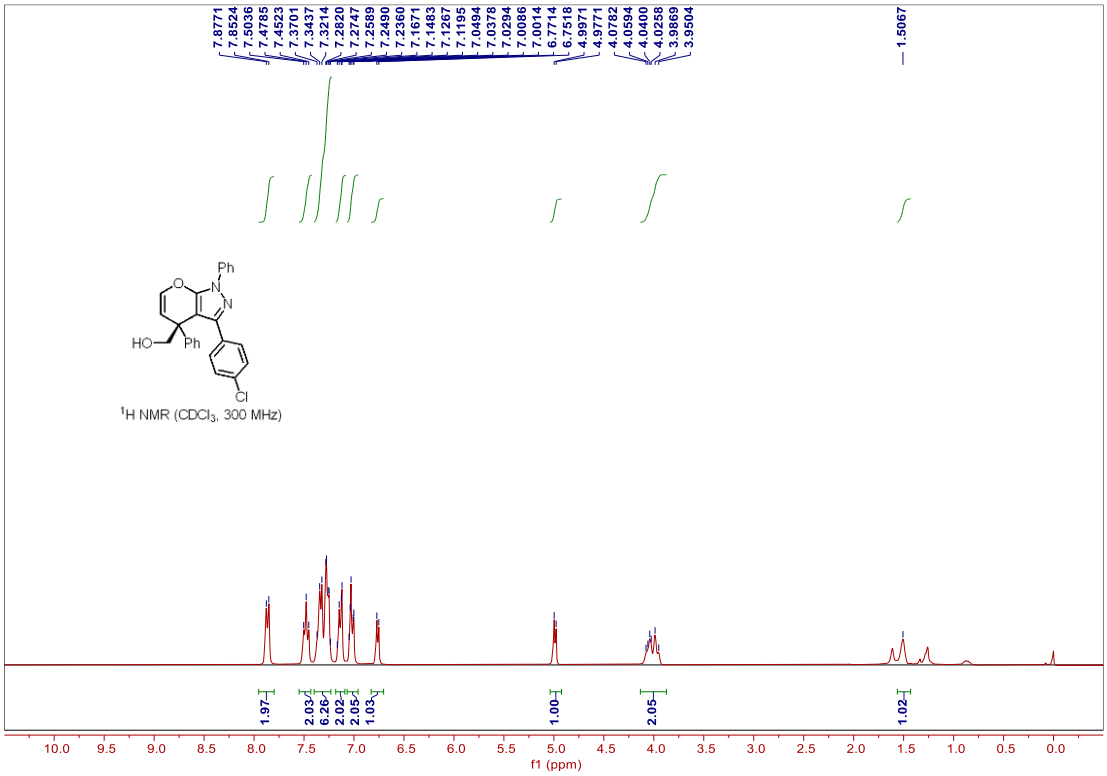


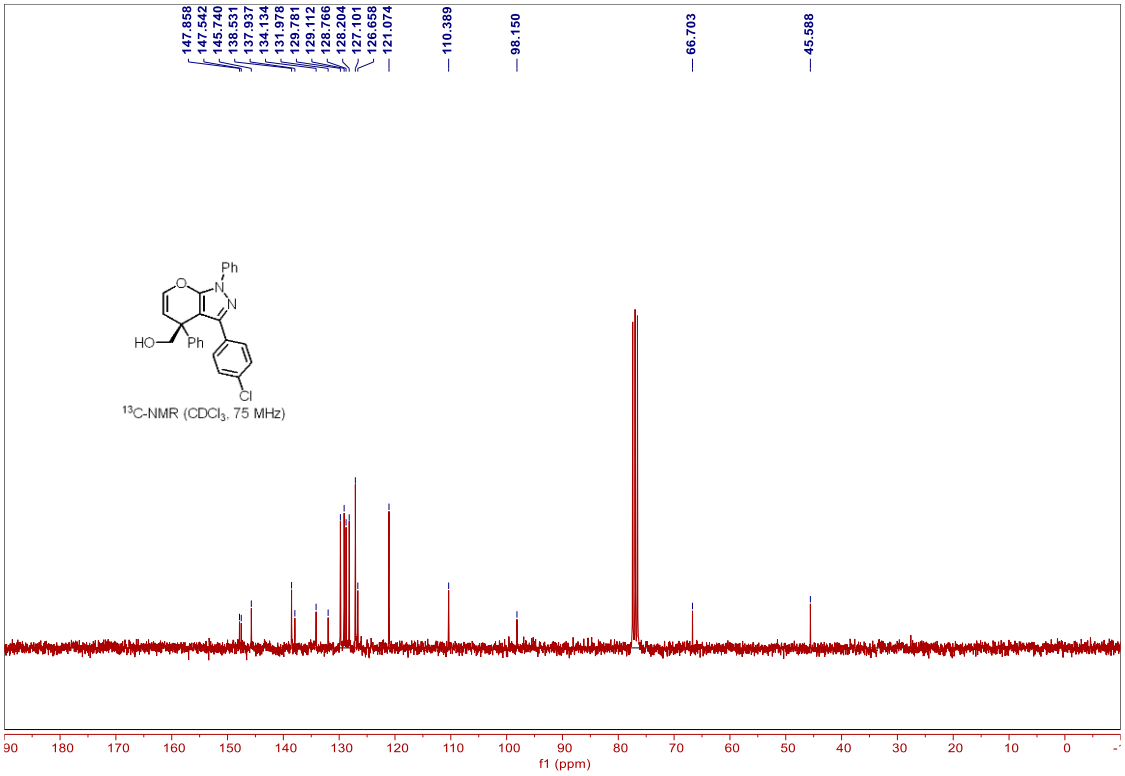
(R)-(3-(4-methoxyphenyl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ab)



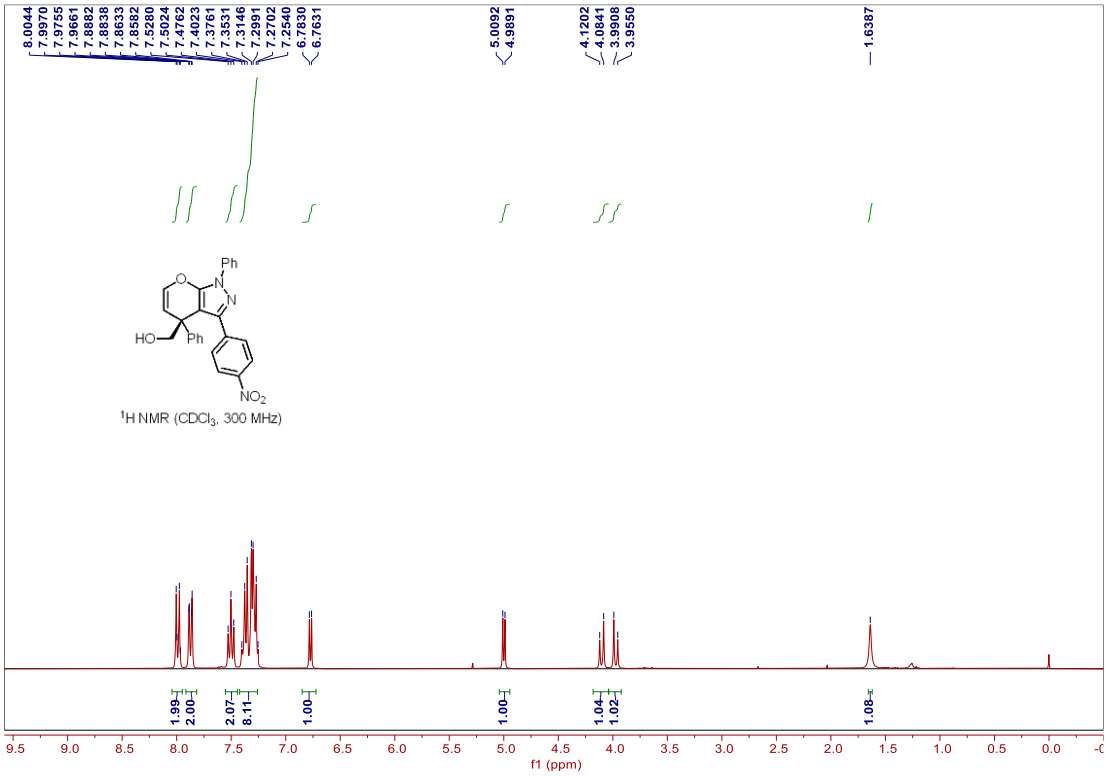


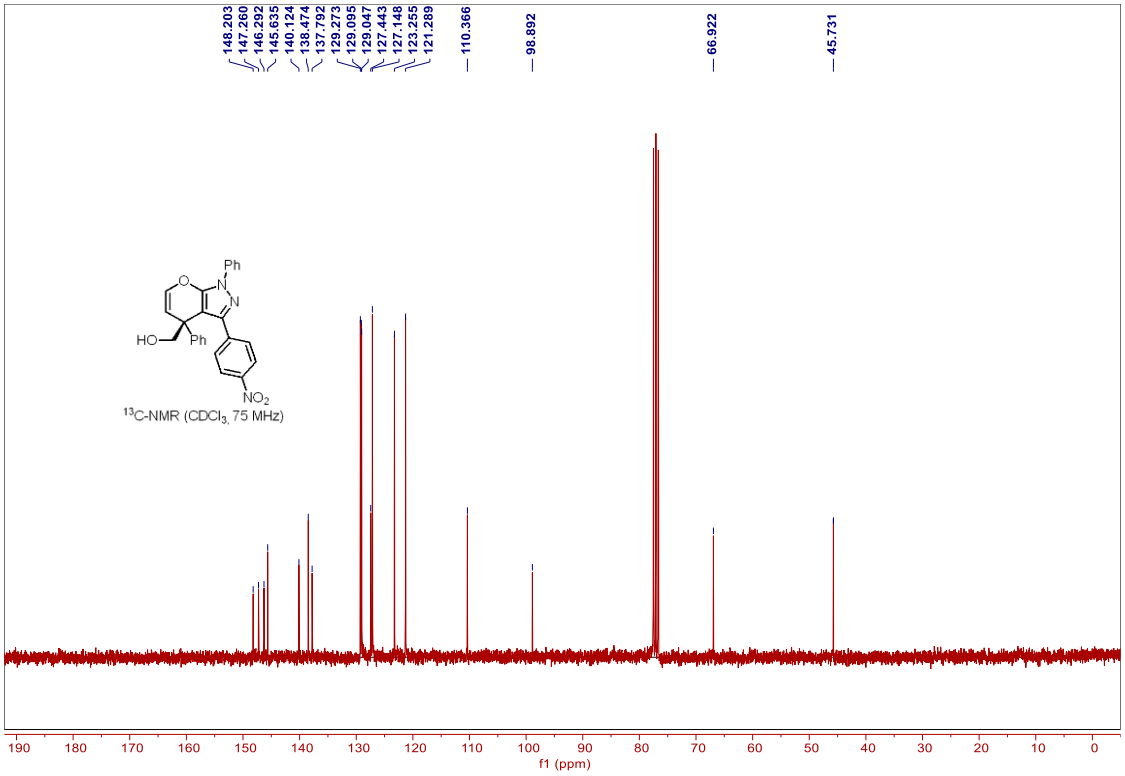
(R)-(3-(4-chlorophenyl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ac)



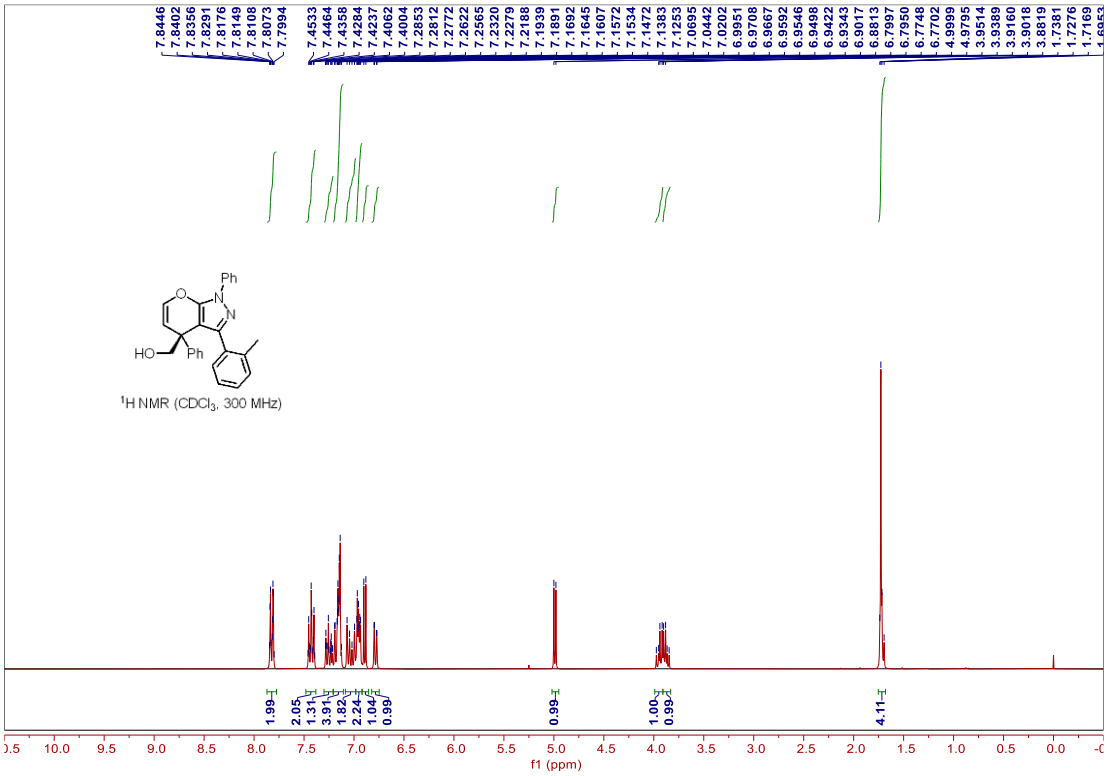


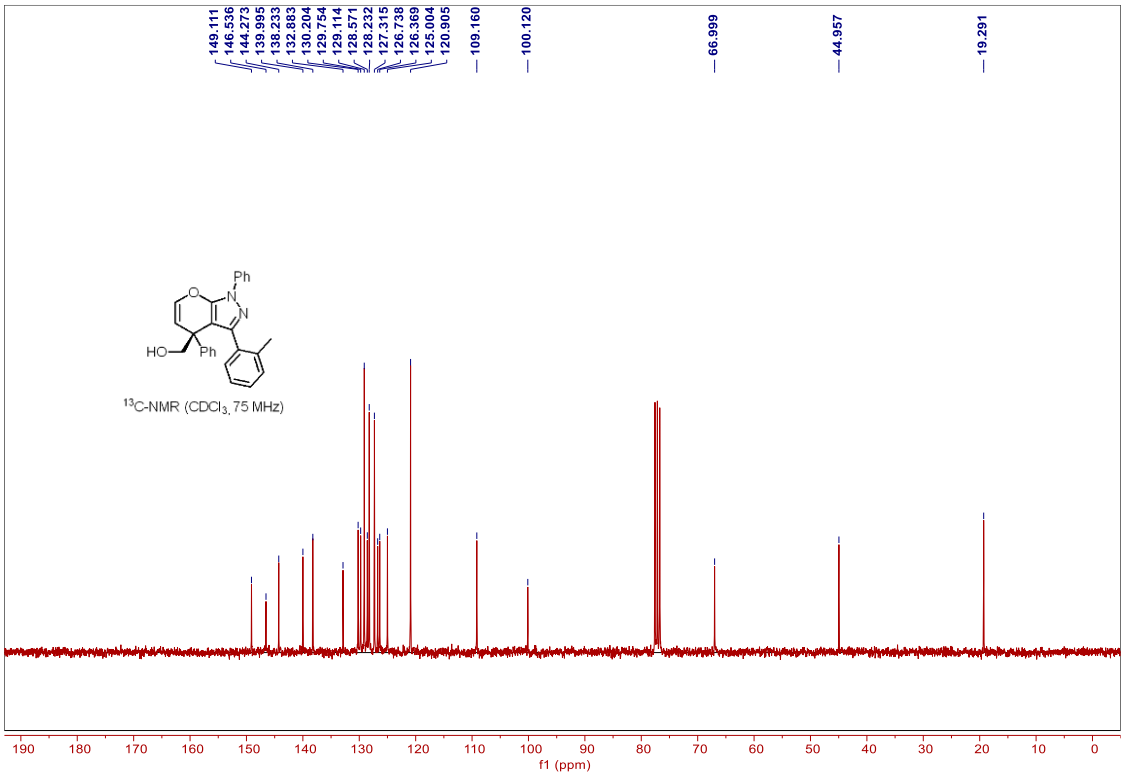
(R)-(3-(4-nitrophenyl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ad)



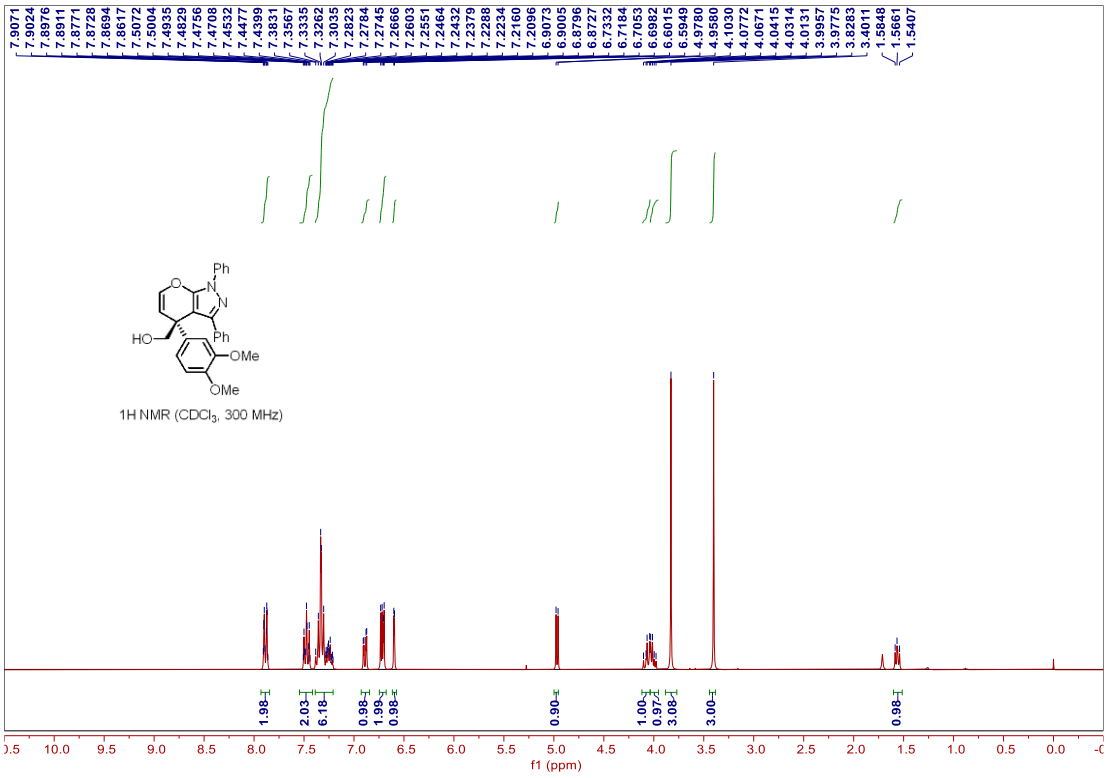


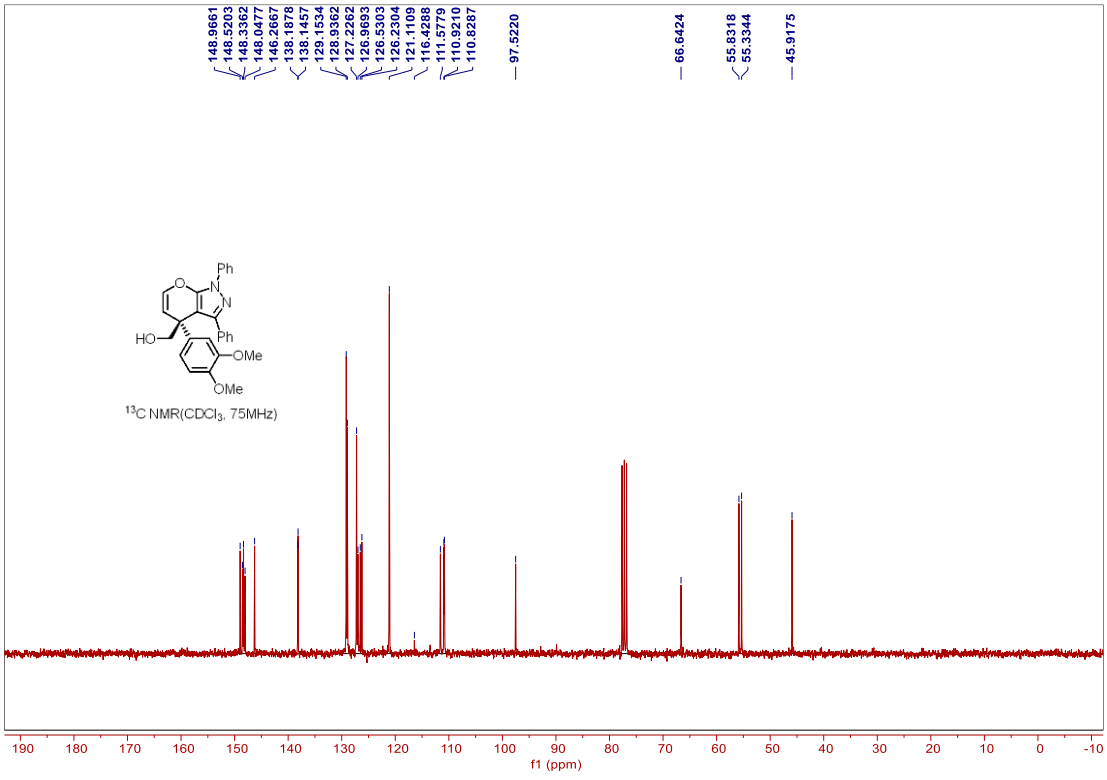
(R)-(1,4-diphenyl-3-(o-tolyl)-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ae)



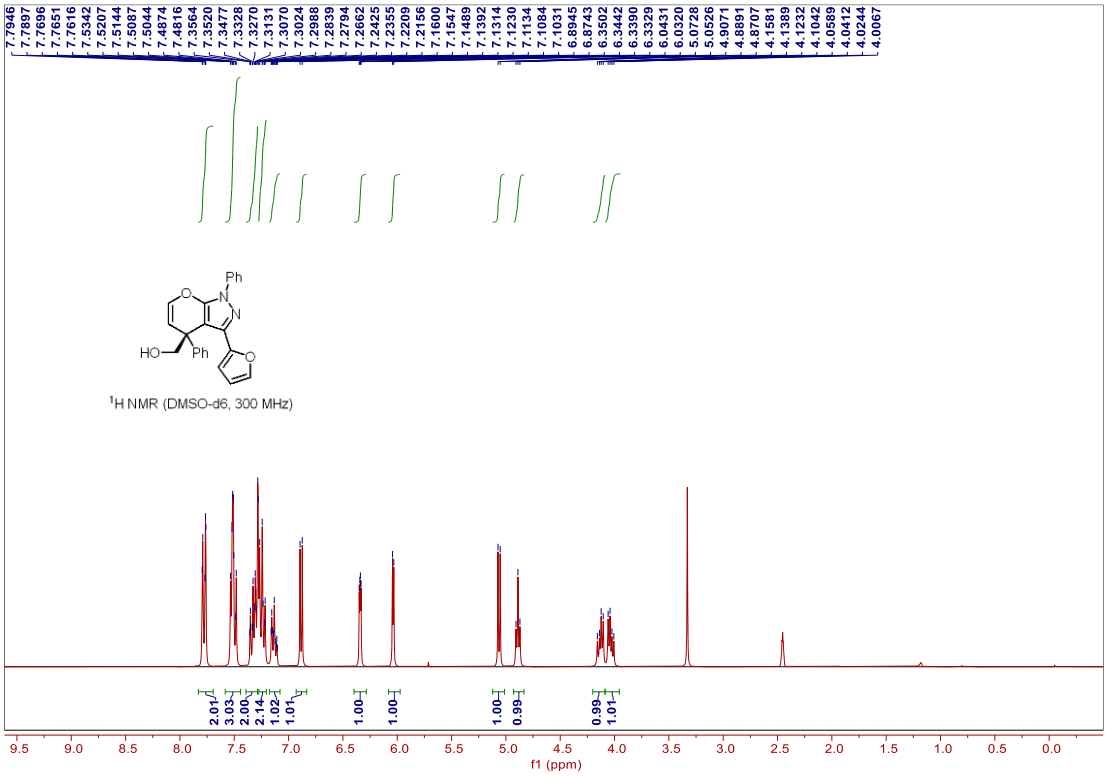


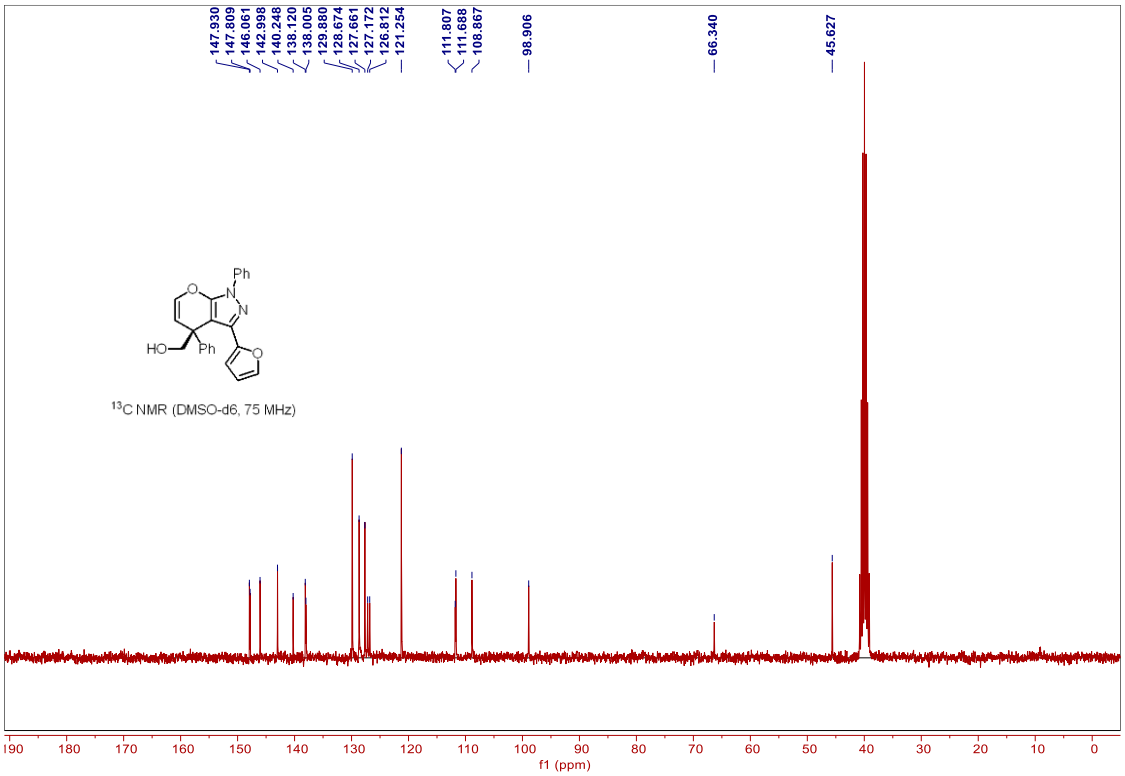
(R)-(4-(3,4-dimethoxyphenyl)-1,3-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3af)



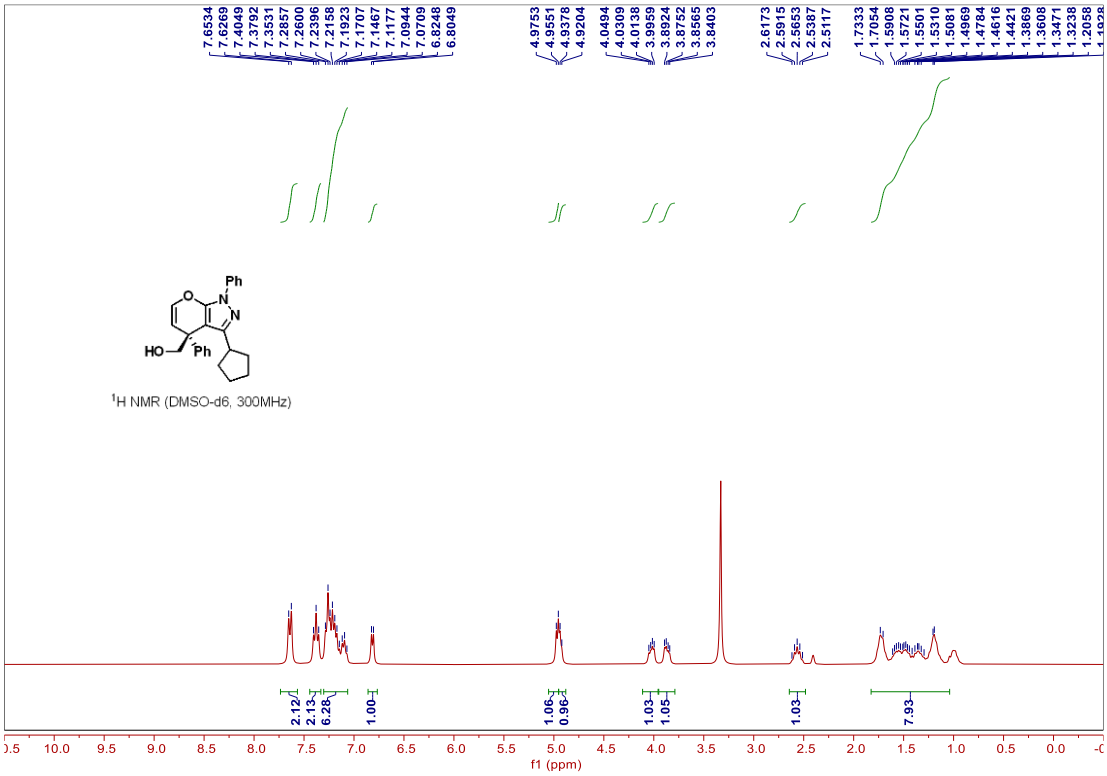


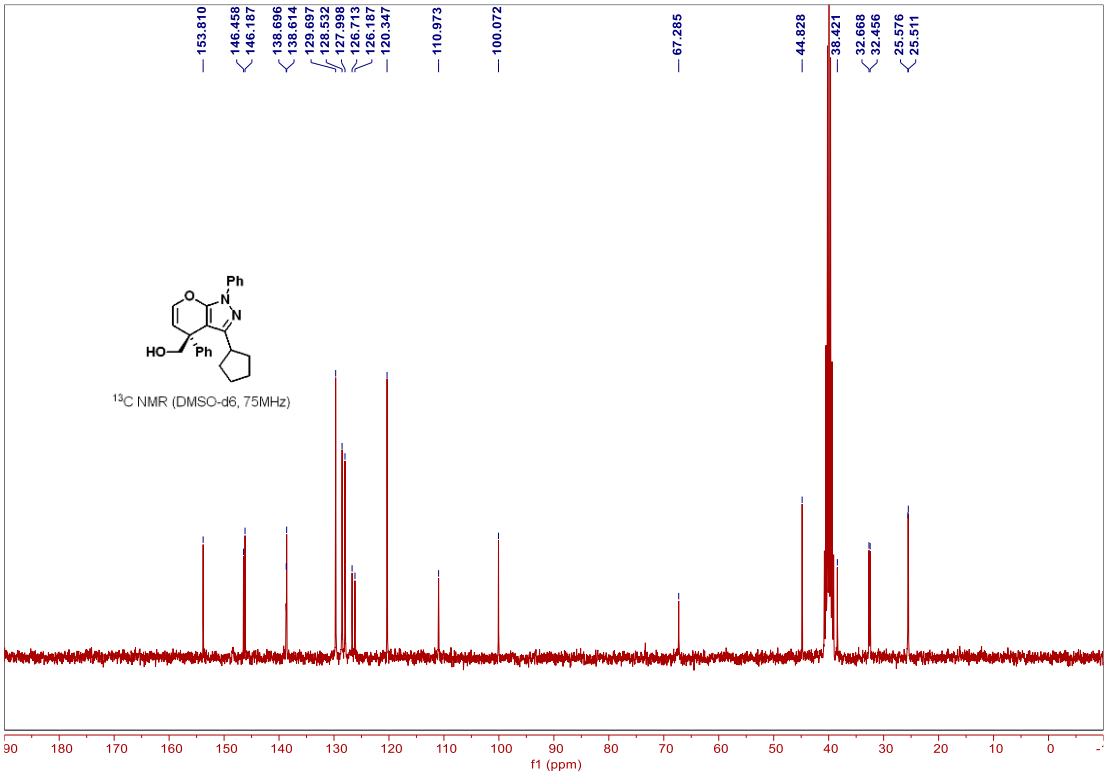
(R)-(3-(furan-2-yl)-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ag)



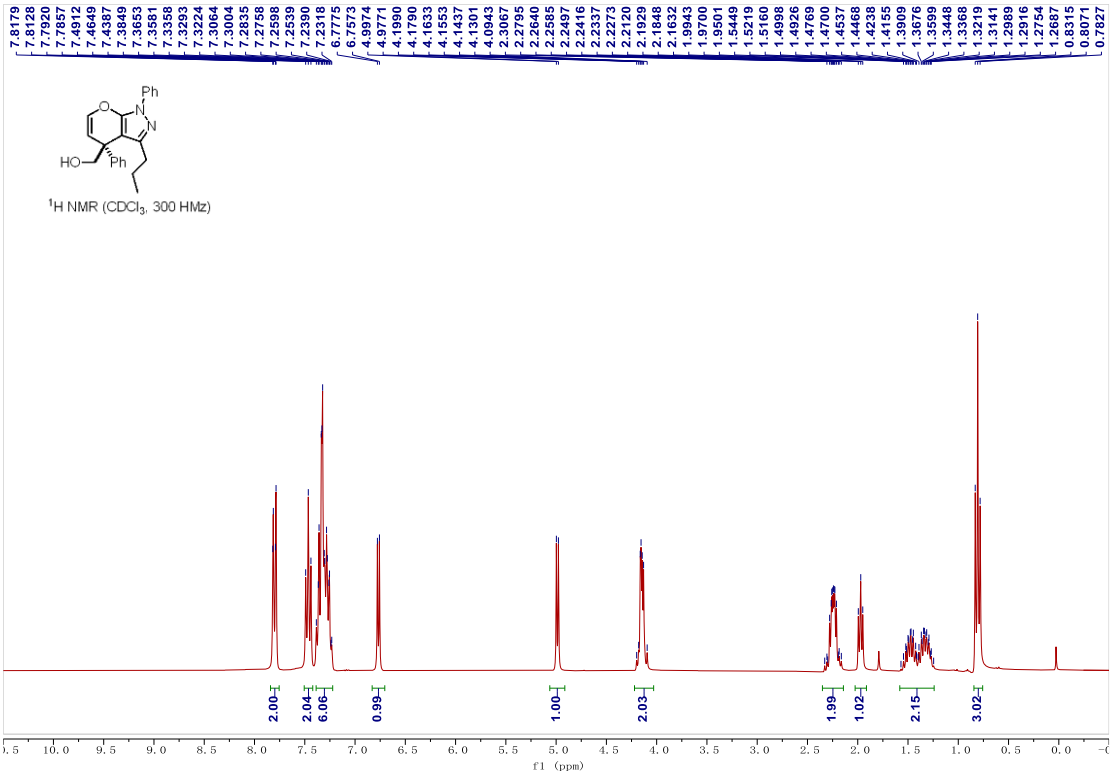


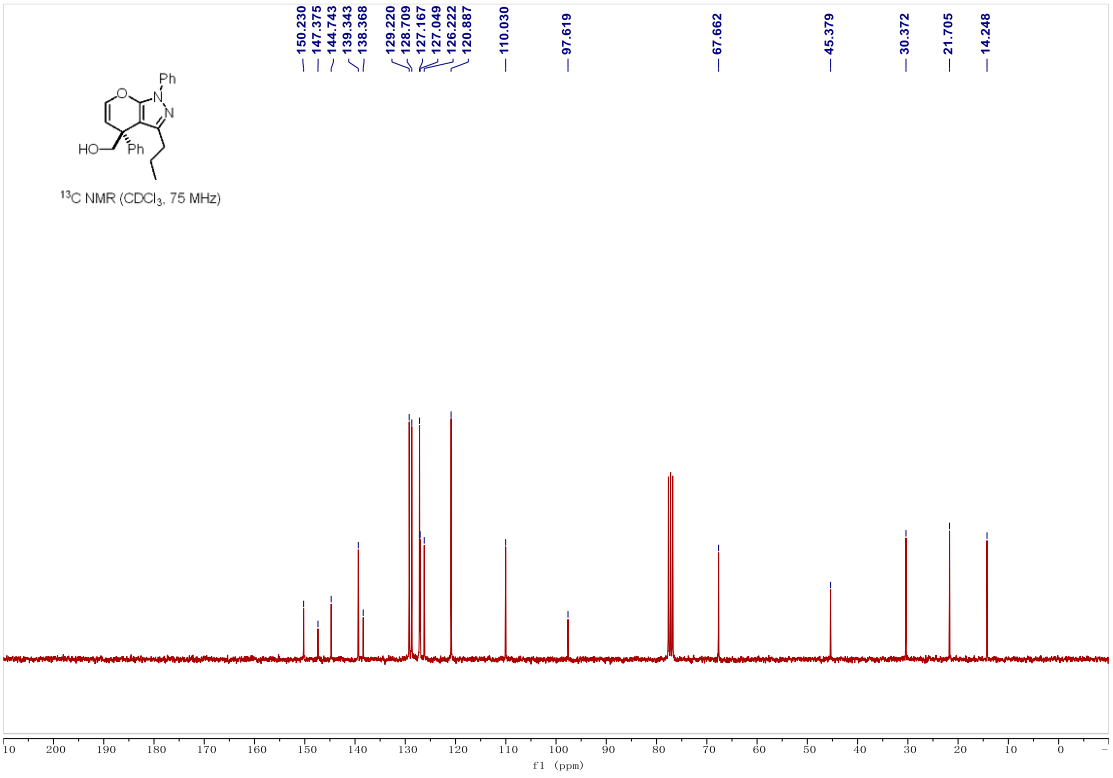
(R)-(3-cyclopentyl-1,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ah)



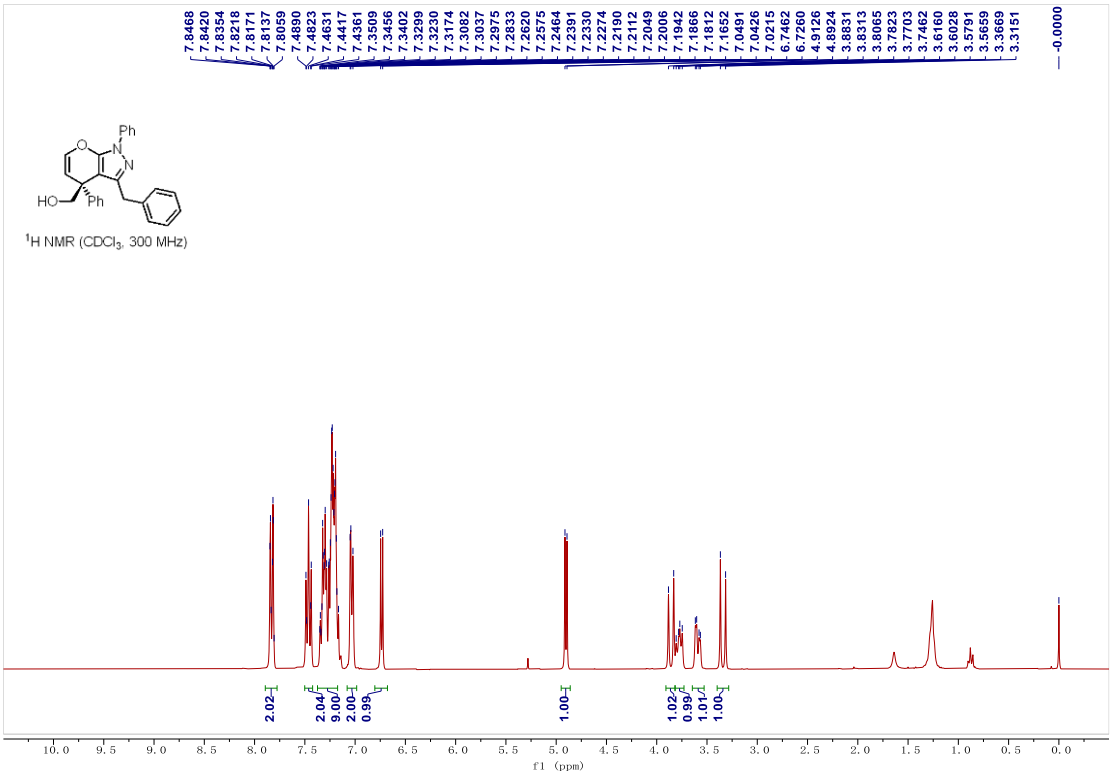


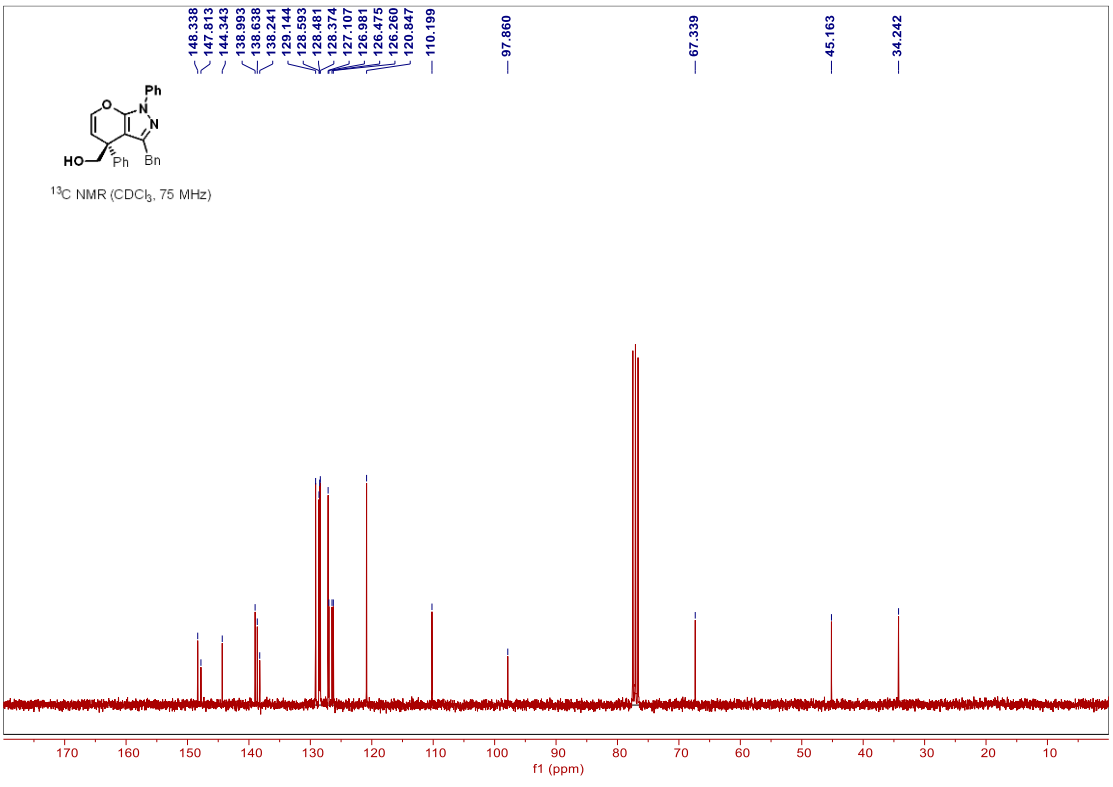
(R)-(1,4-diphenyl-3-propyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ai)



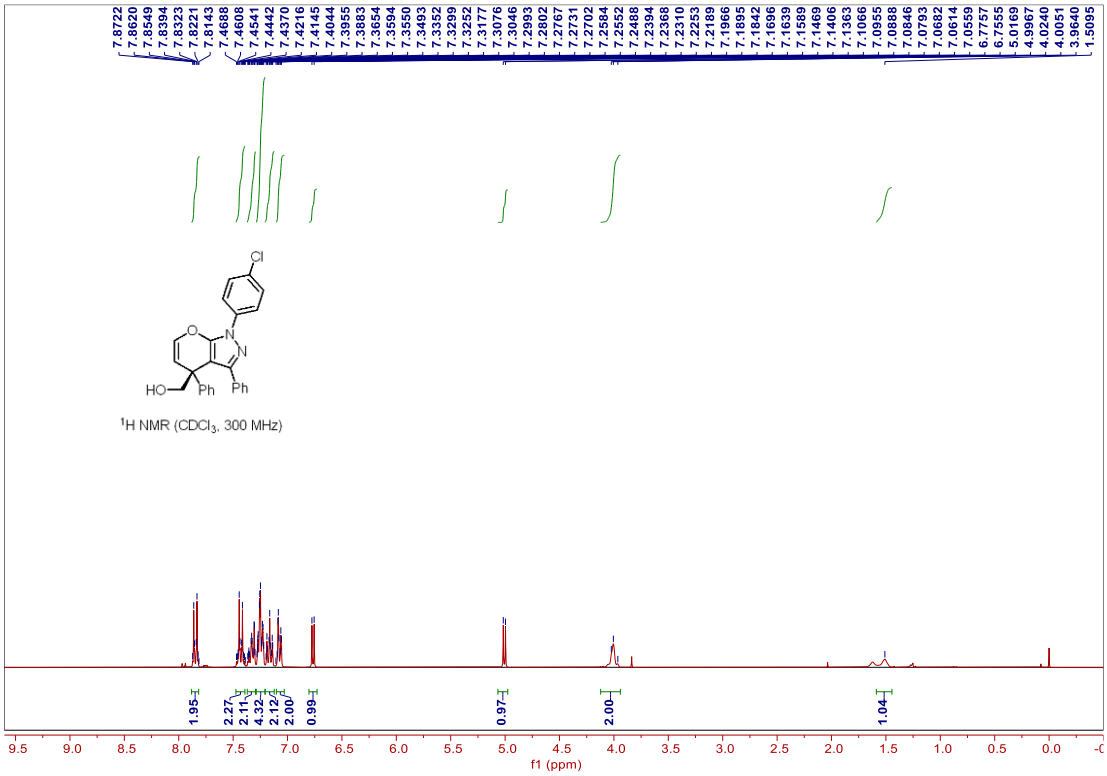


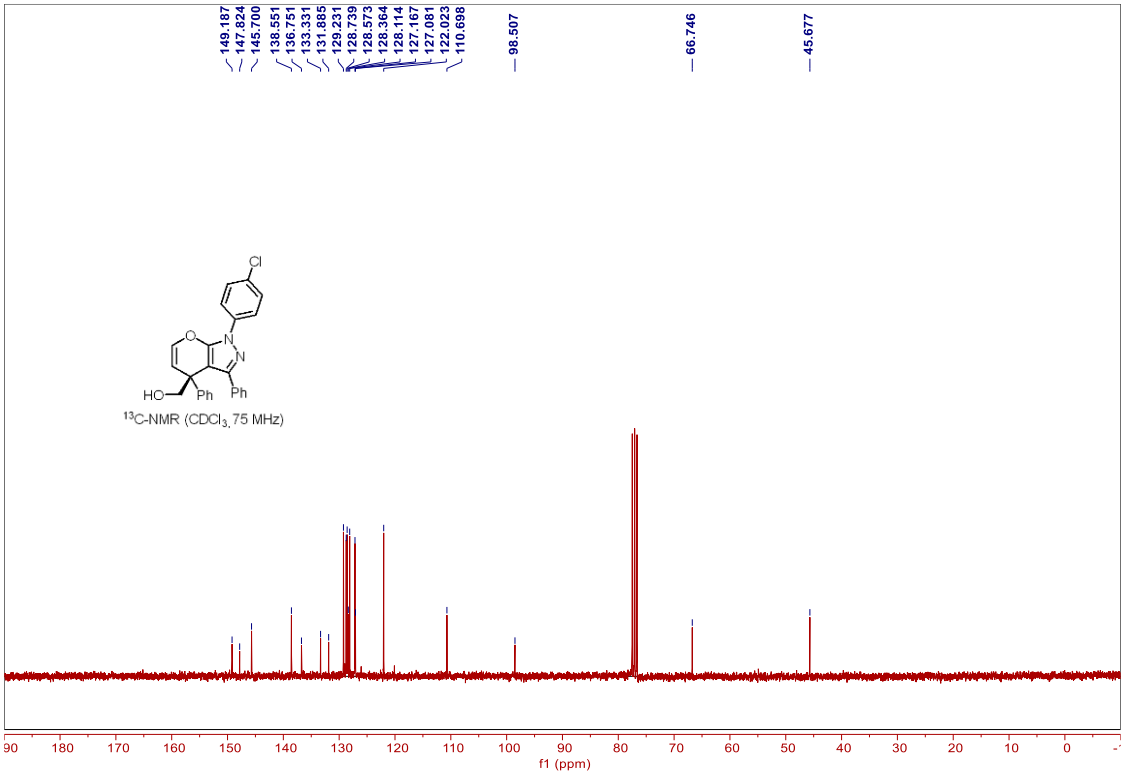
(R)-(1-(tert-butyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3aj)



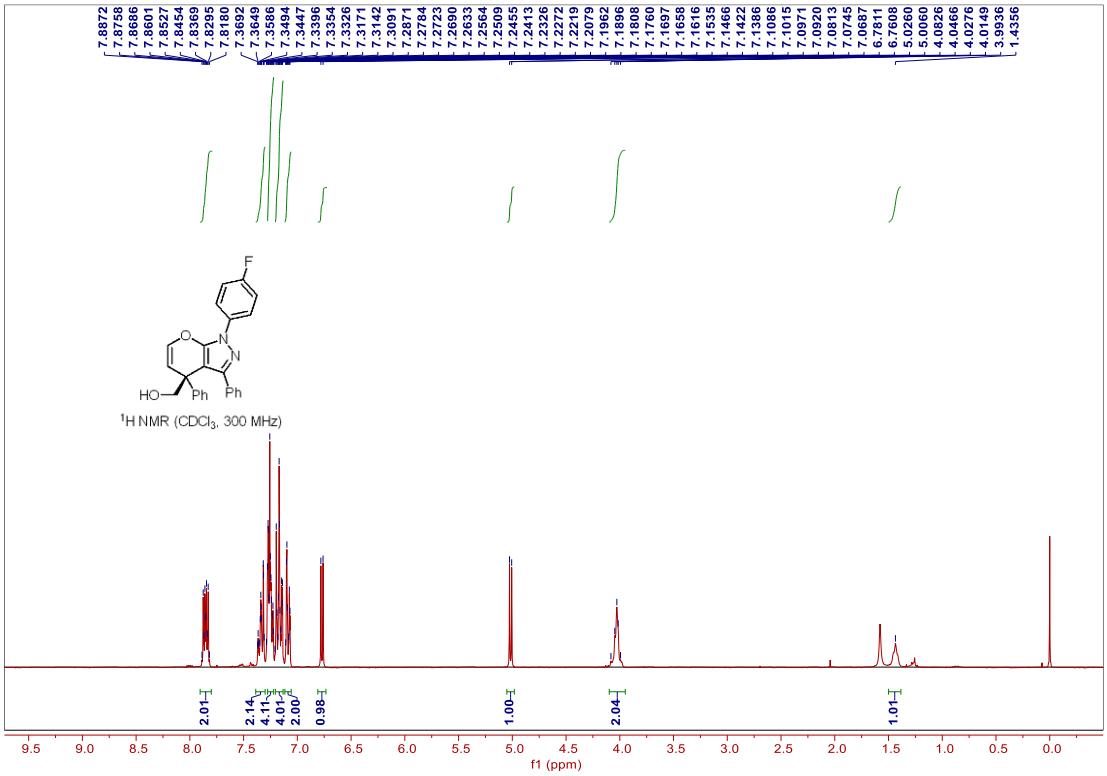


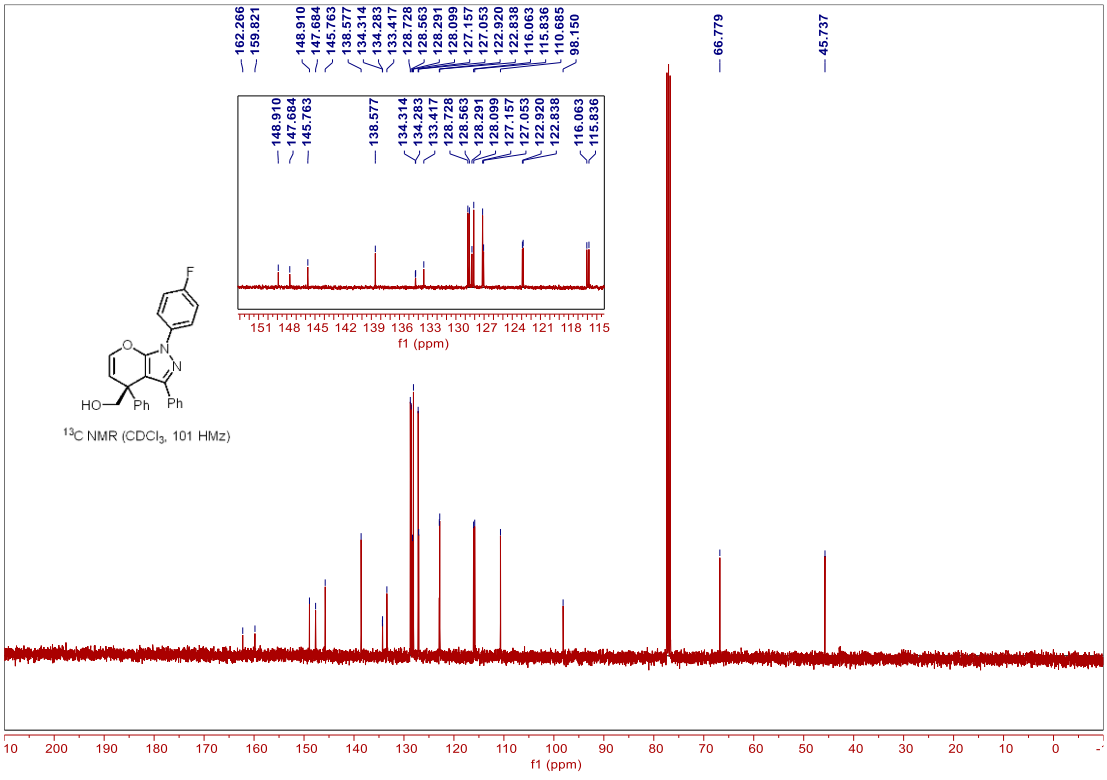
(R)-(1-(4-chlorophenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ak)

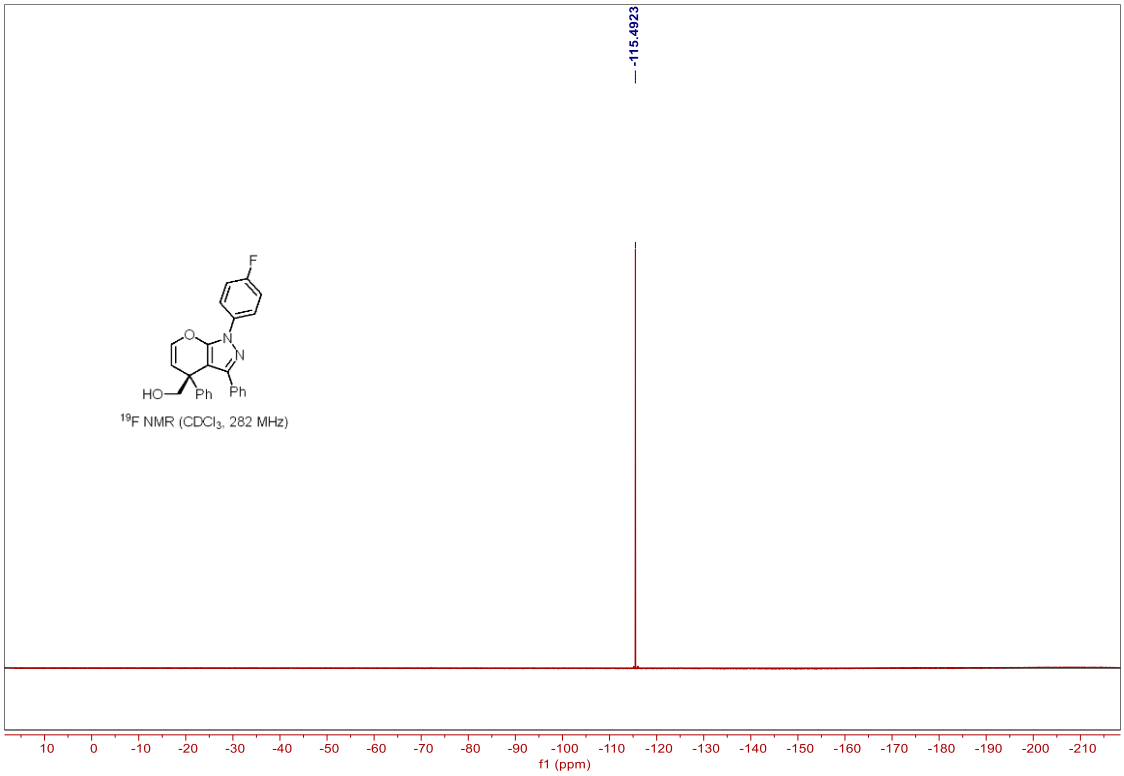




(R)-(1-(4-fluorophenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3al)

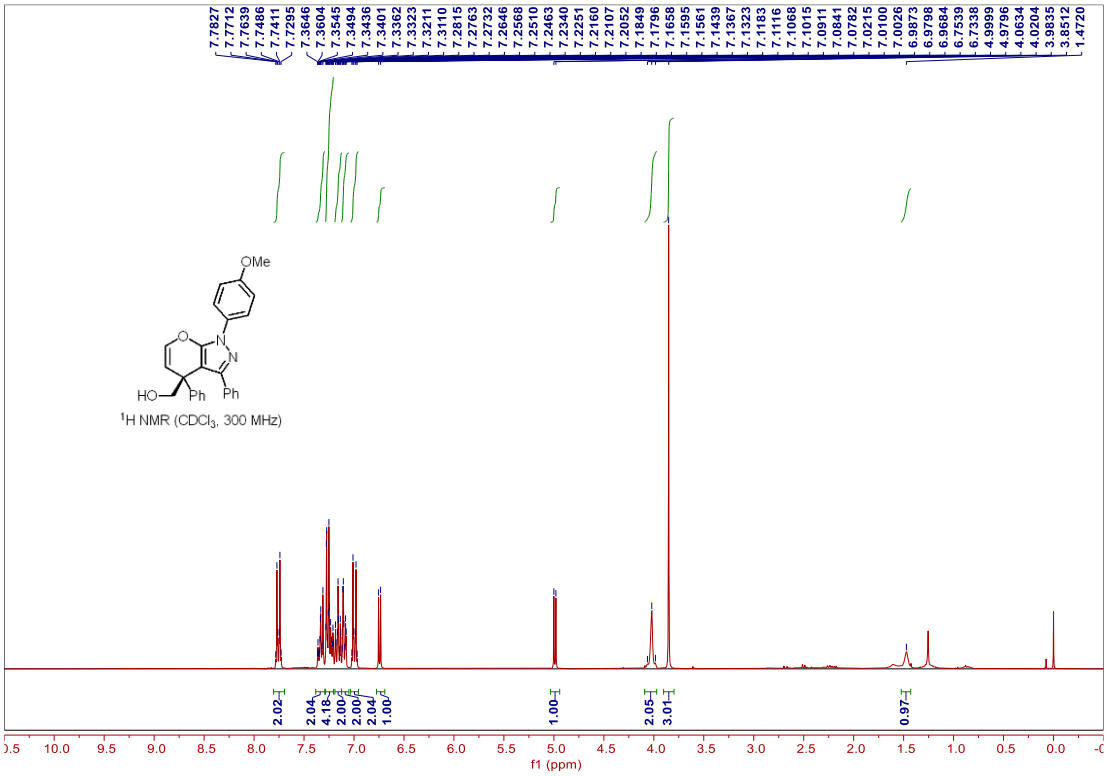


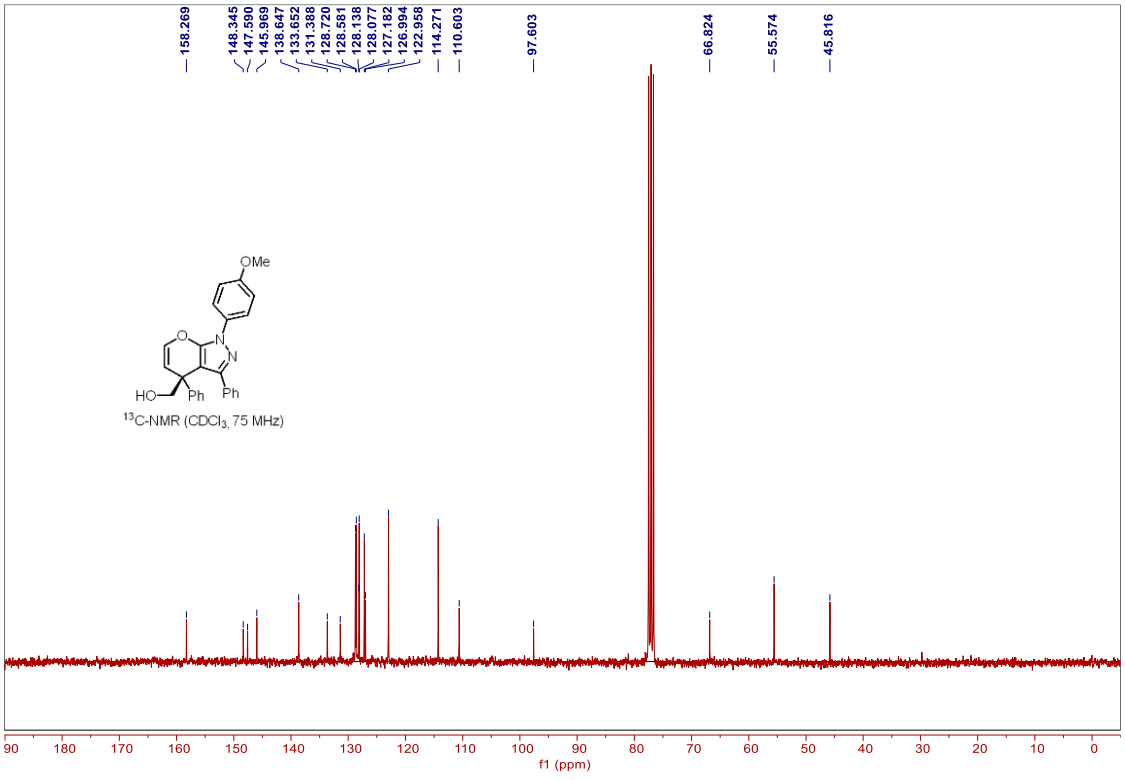




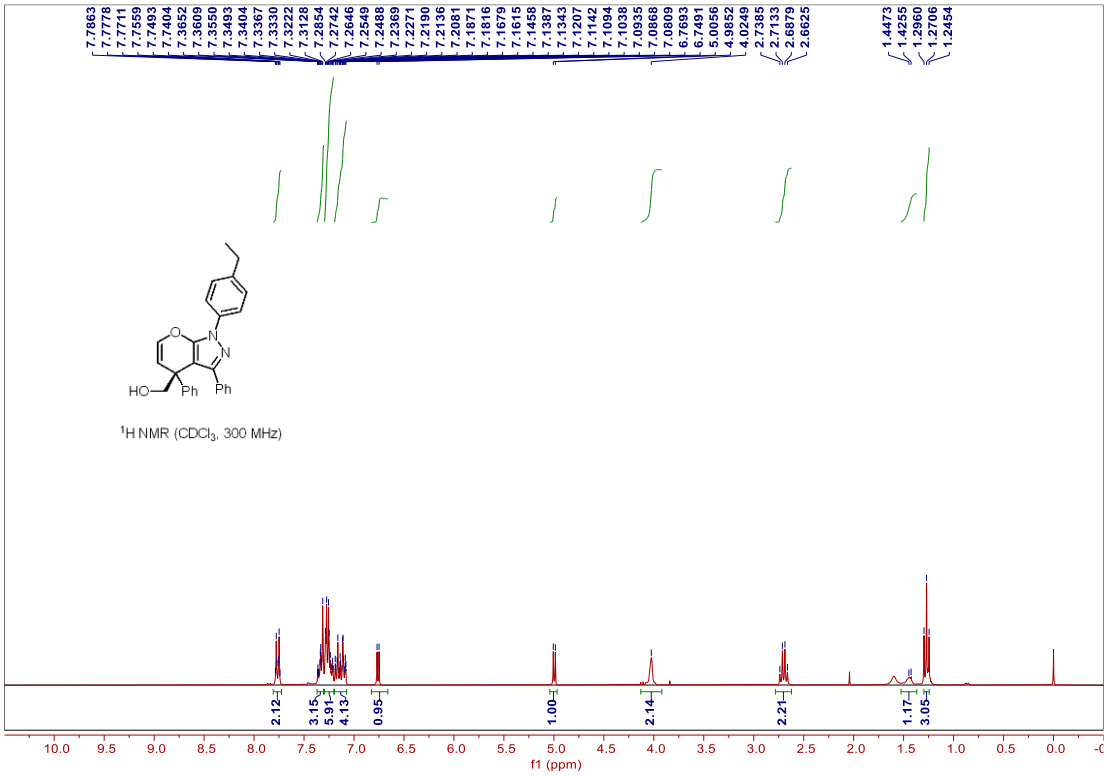
^{19}F NMR ($CDCl_3$, 282 MHz)

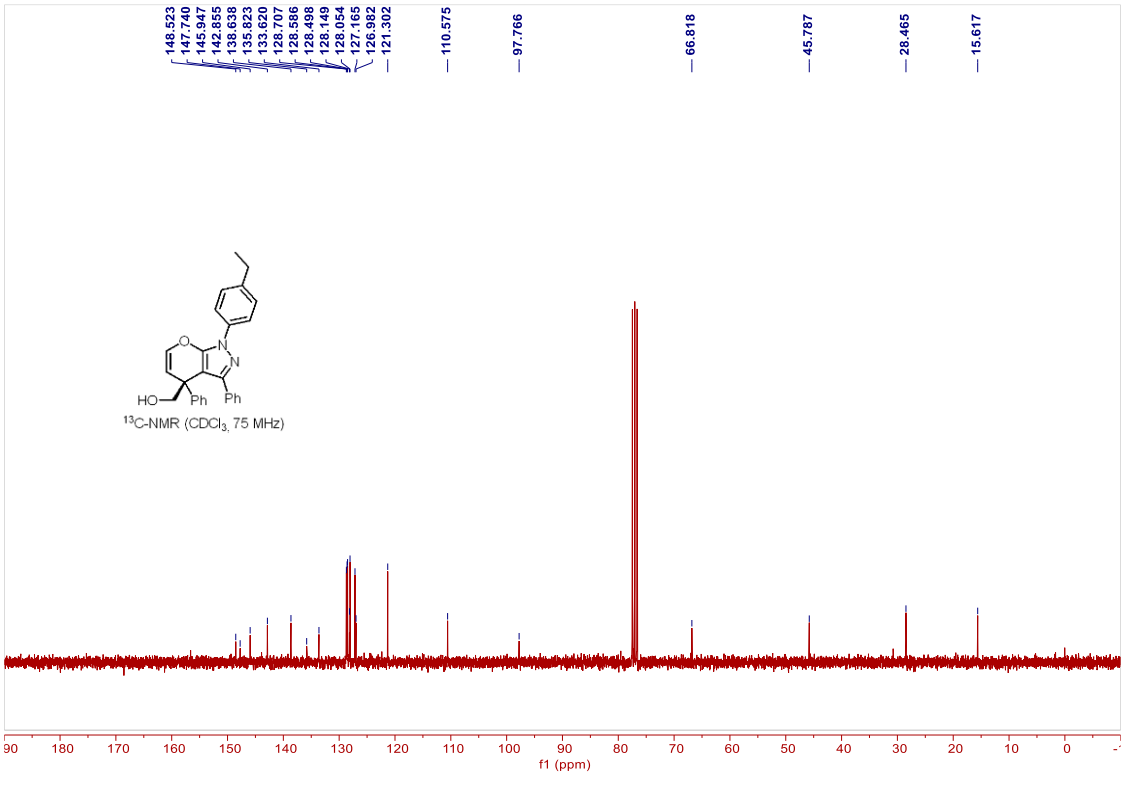
(R)-(1-(4-methoxyphenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3am)



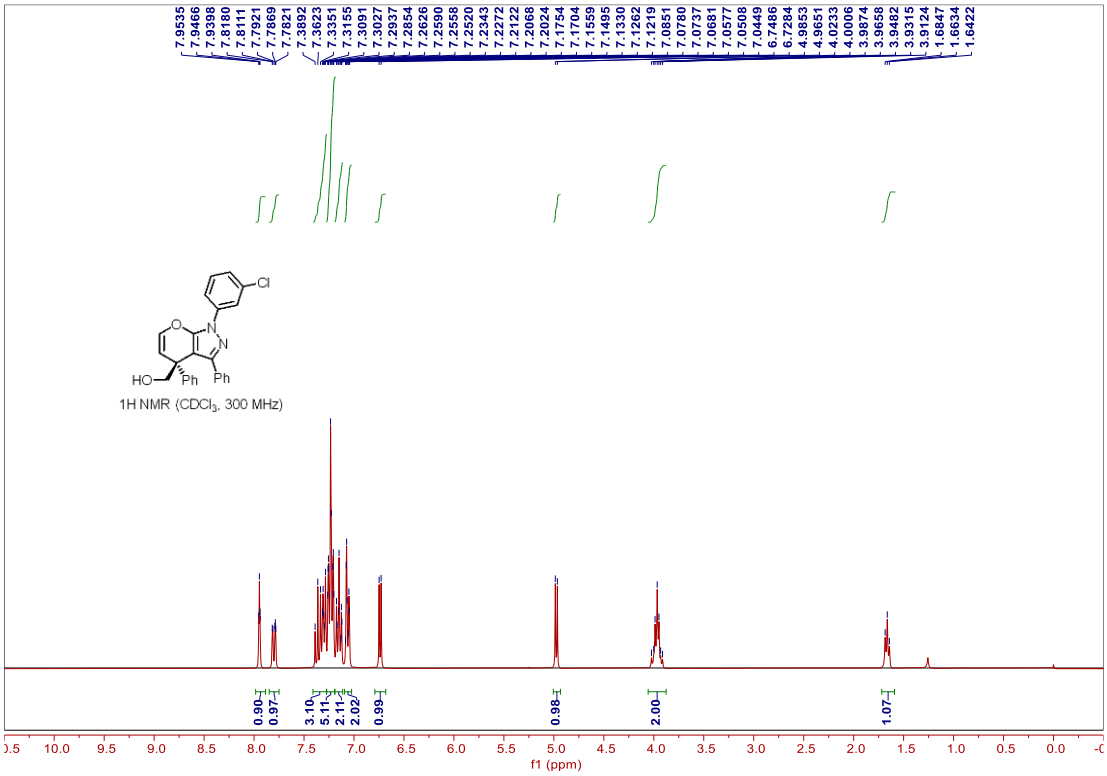


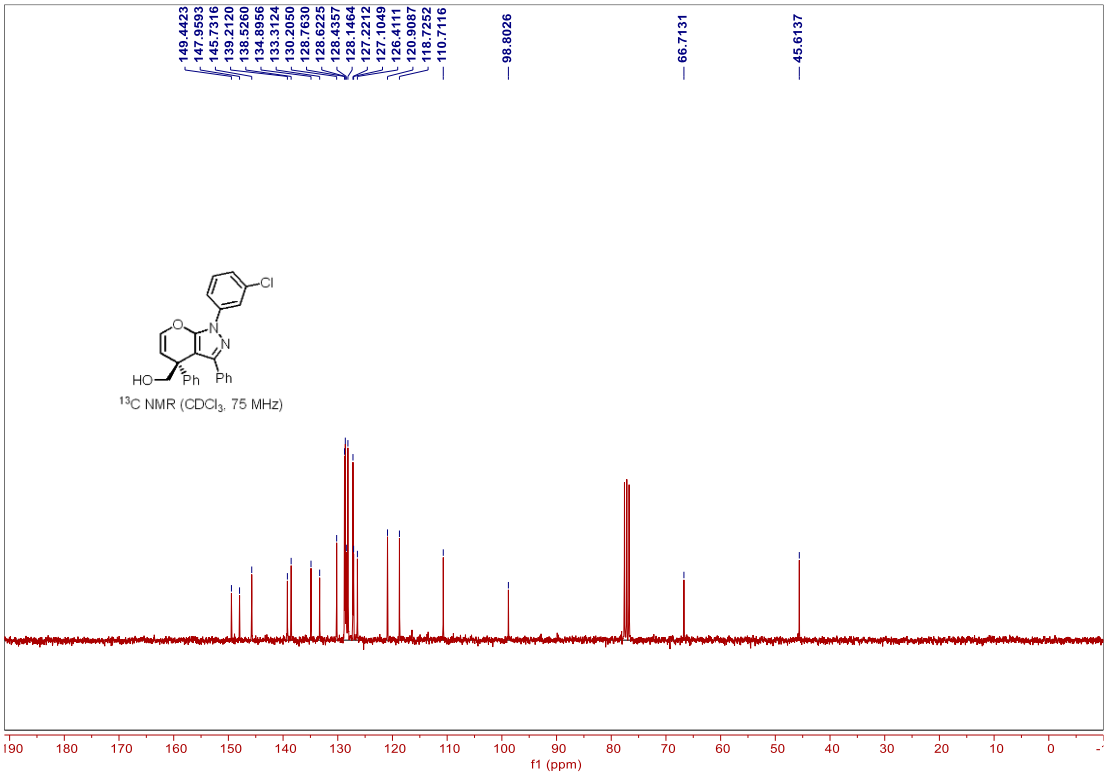
(R)-(1-(4-ethylphenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3an)



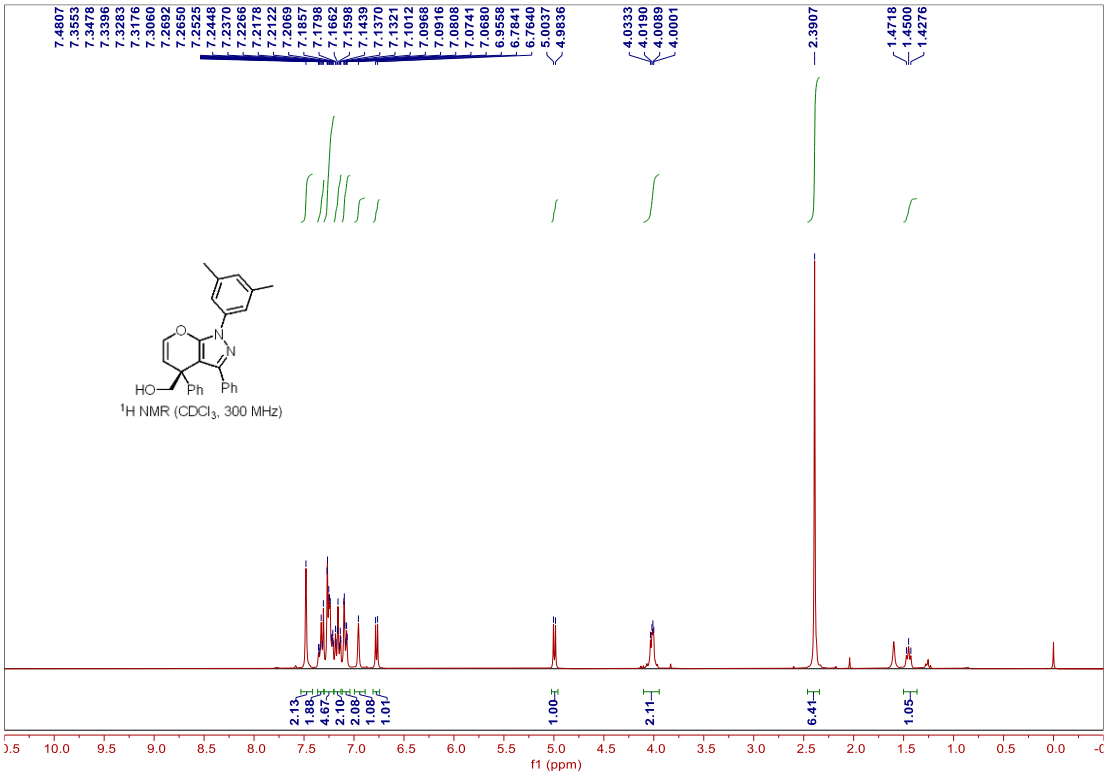


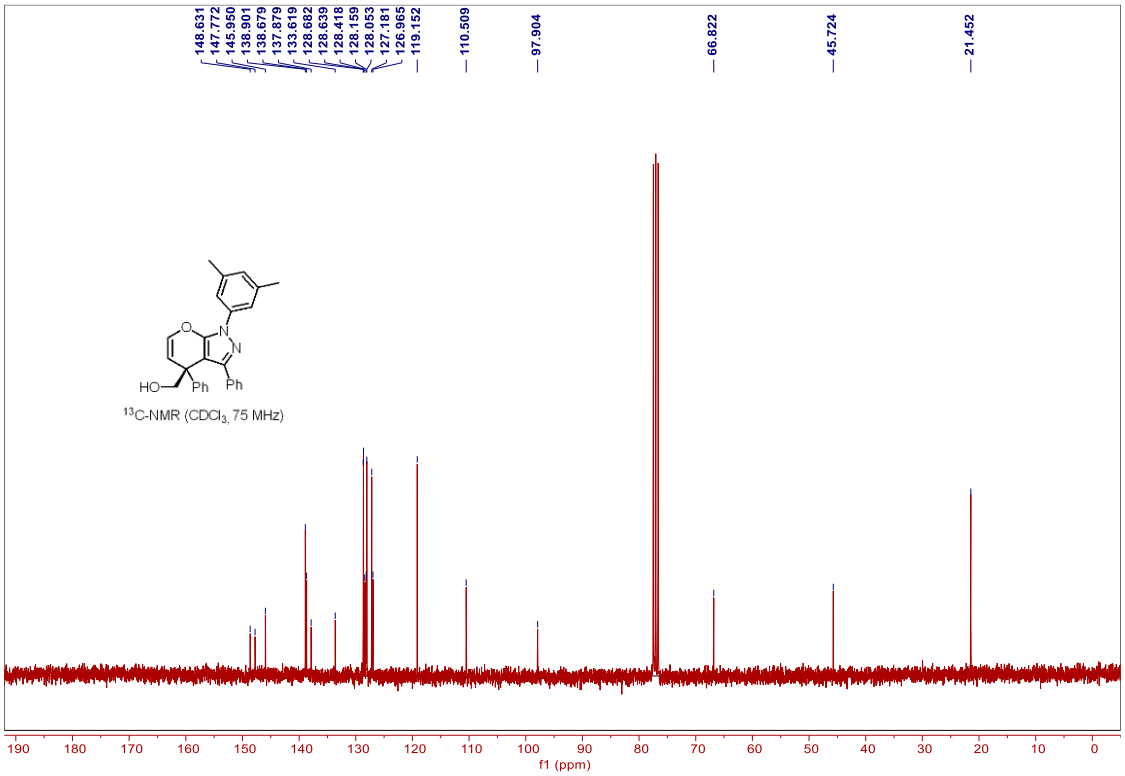
R-(1-(3-chlorophenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ao)



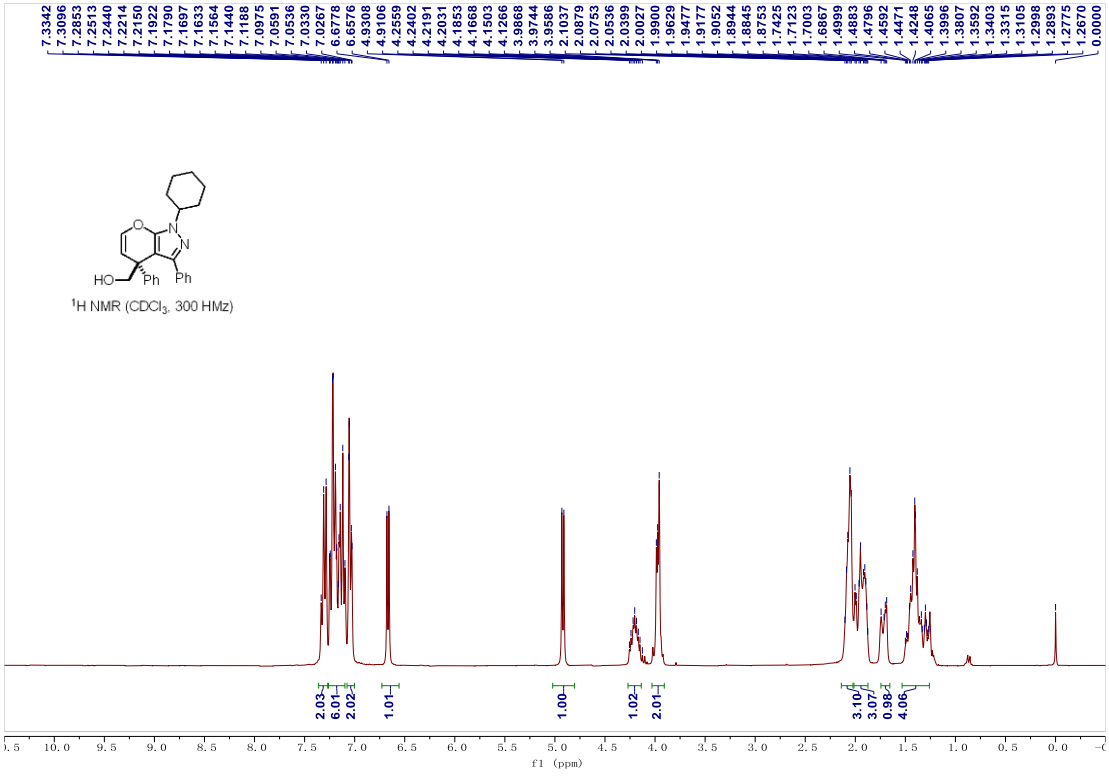


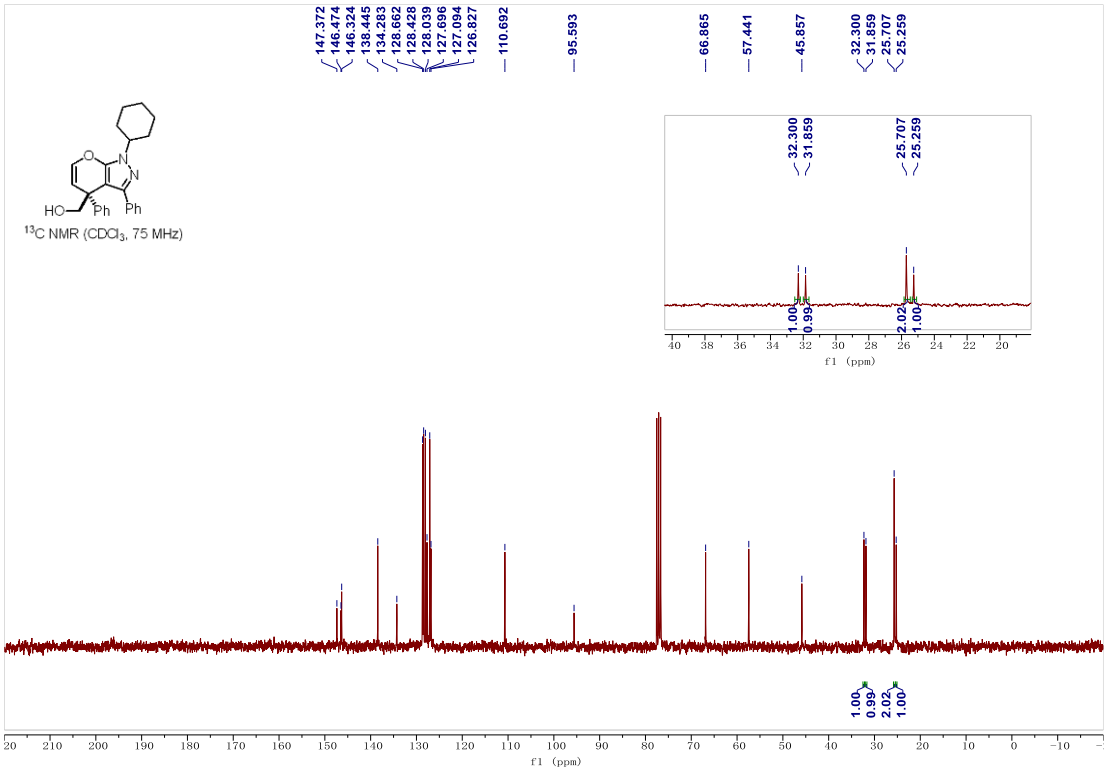
(R)-(1-(3,5-dimethylphenyl)-3,4-diphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3ap)



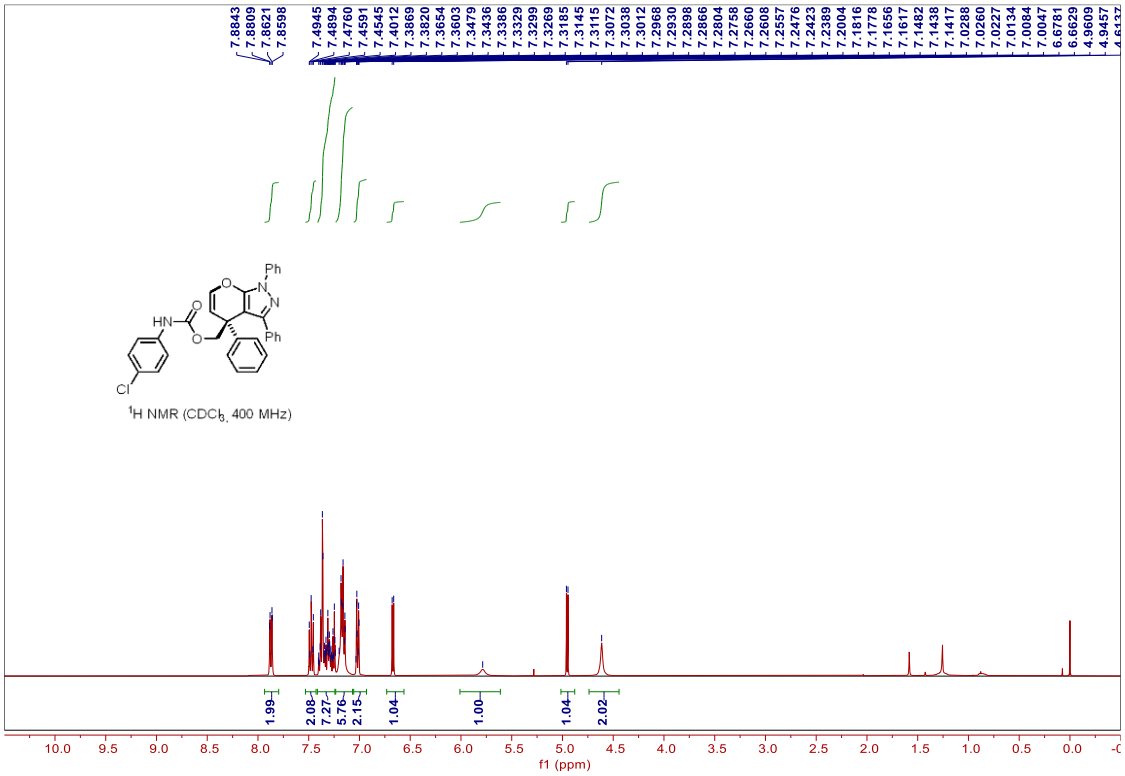


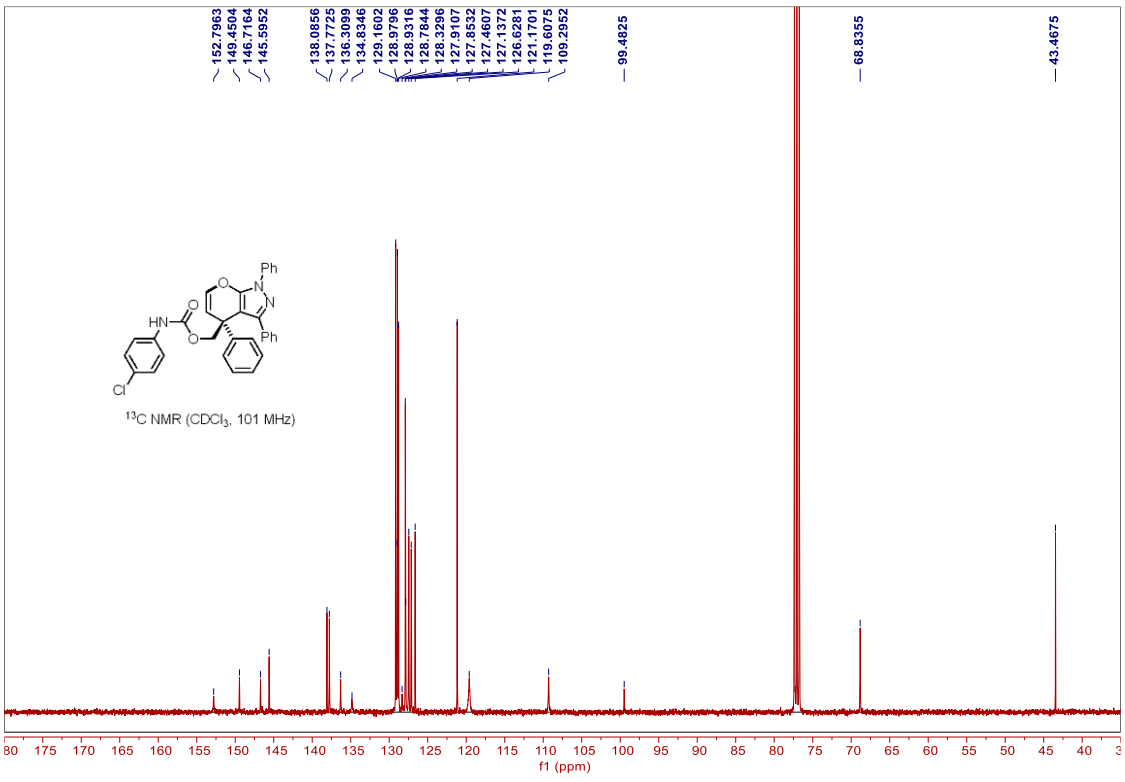
(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methanol (3aq)



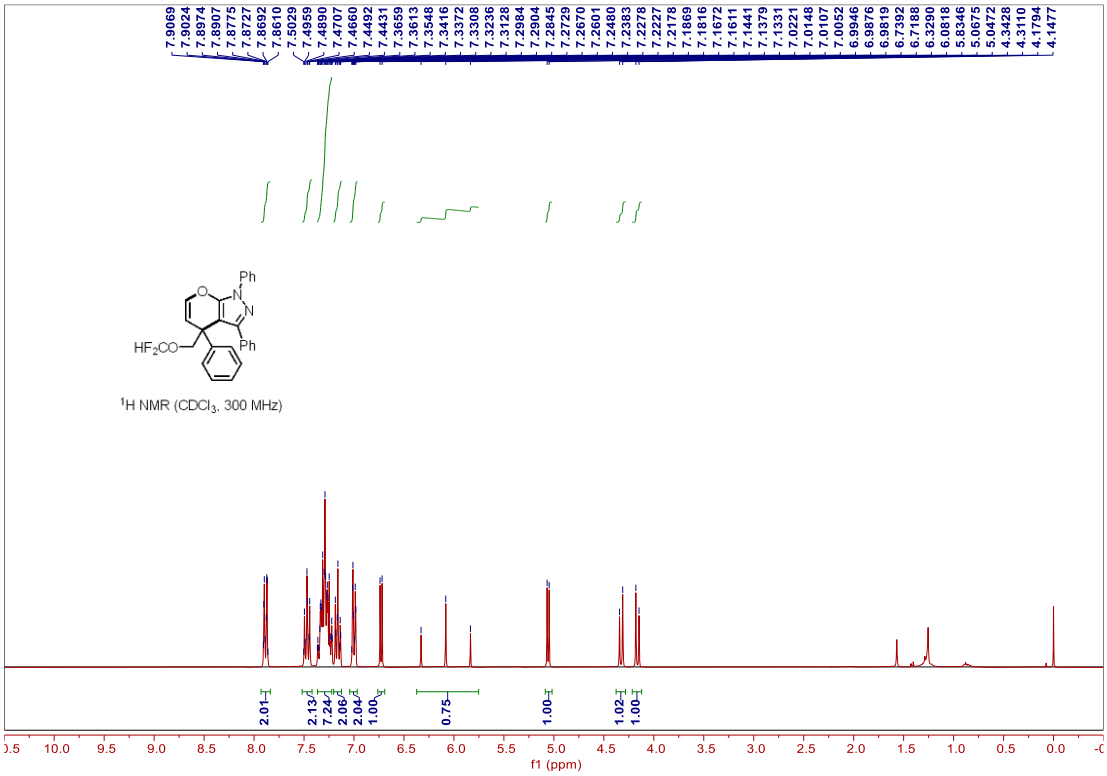


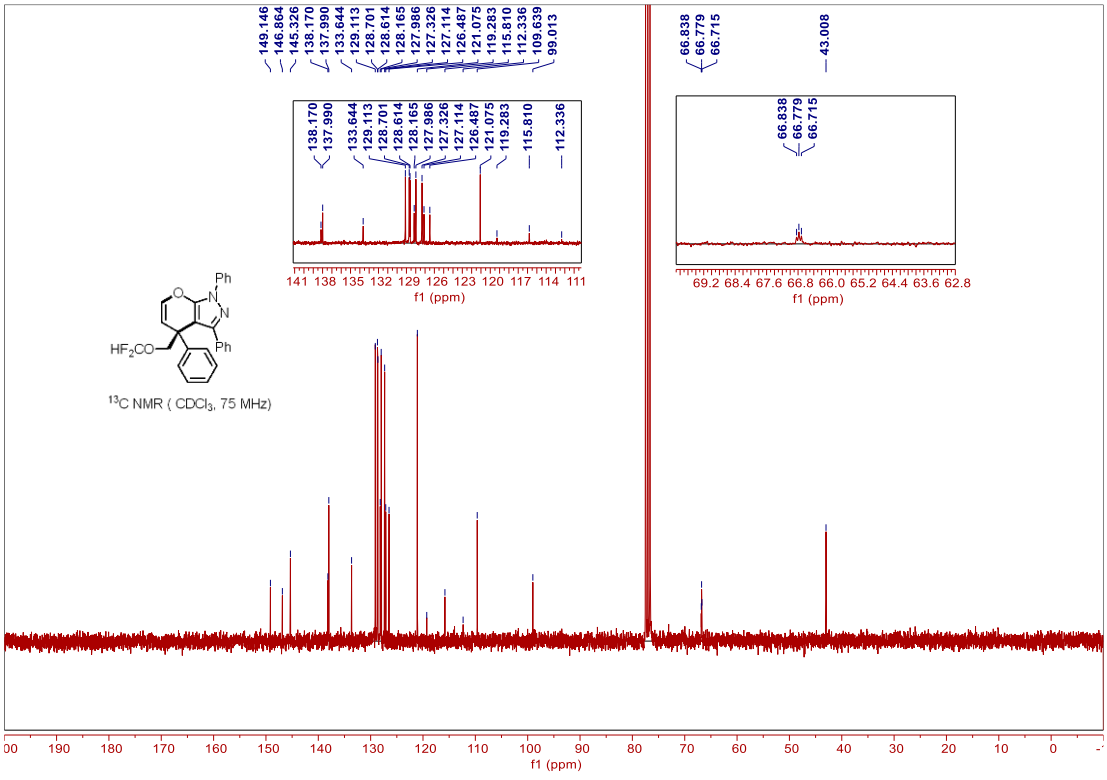
(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methyl (4-chlorophenyl)carbamate (4)

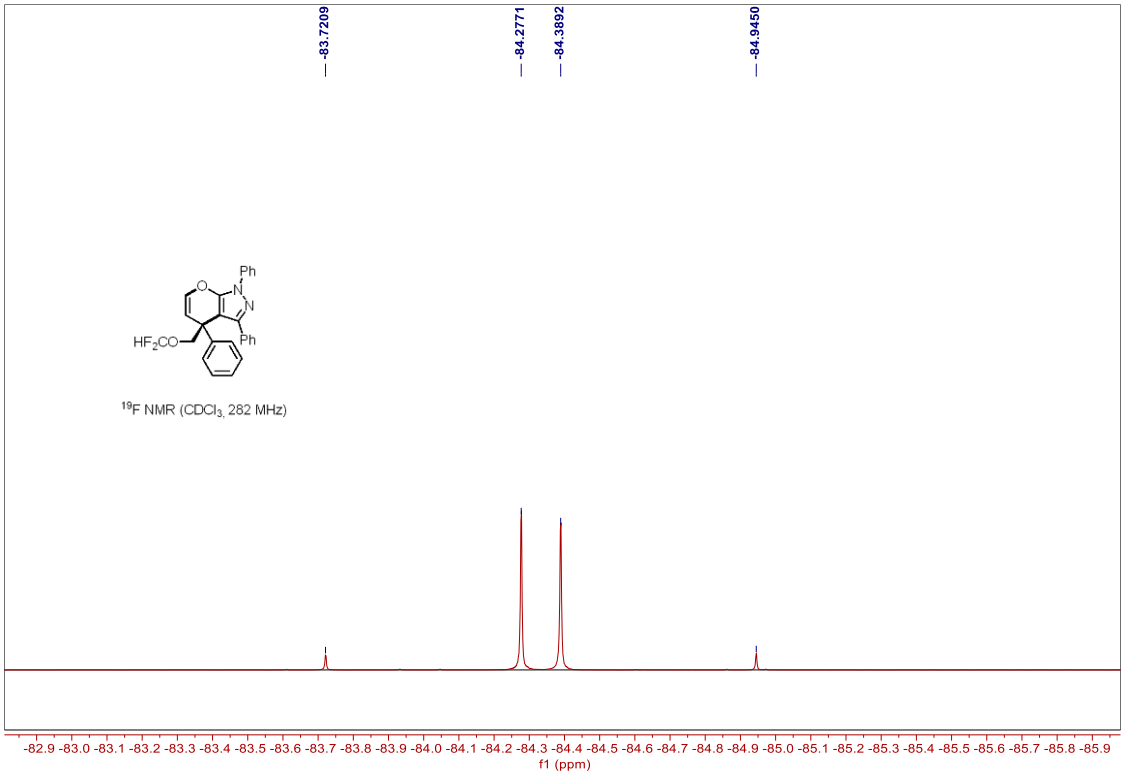




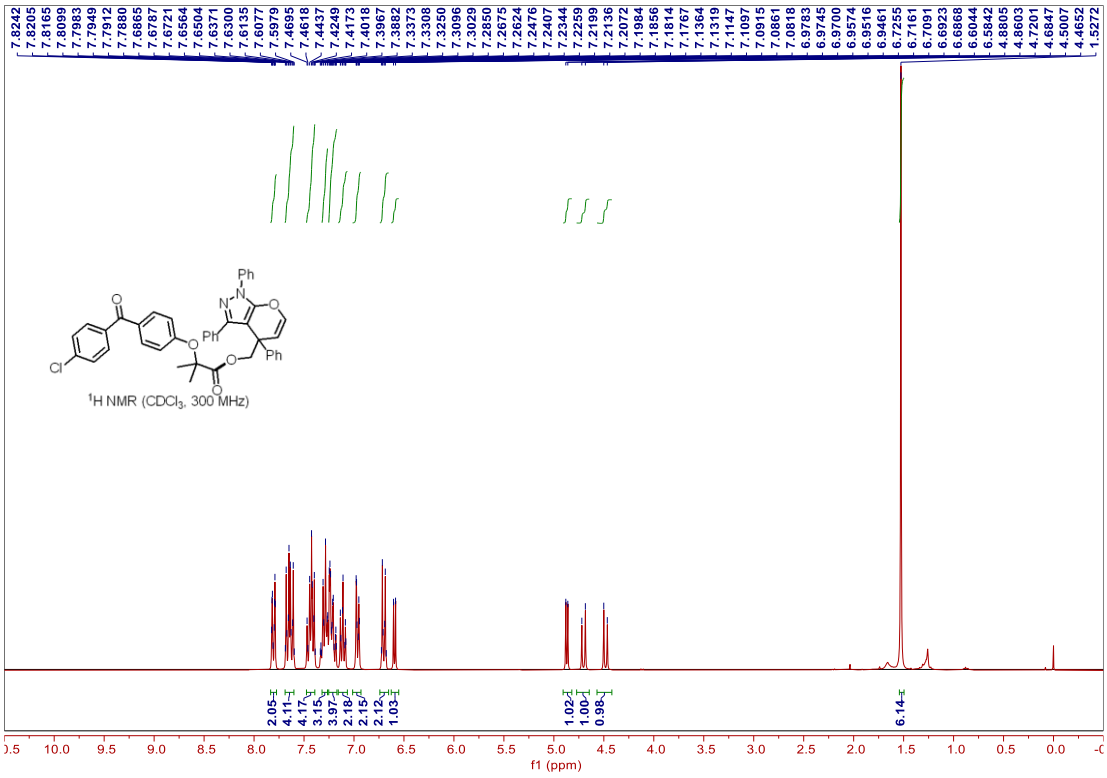
(R)-4-((difluoromethoxy)methyl)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole (5)

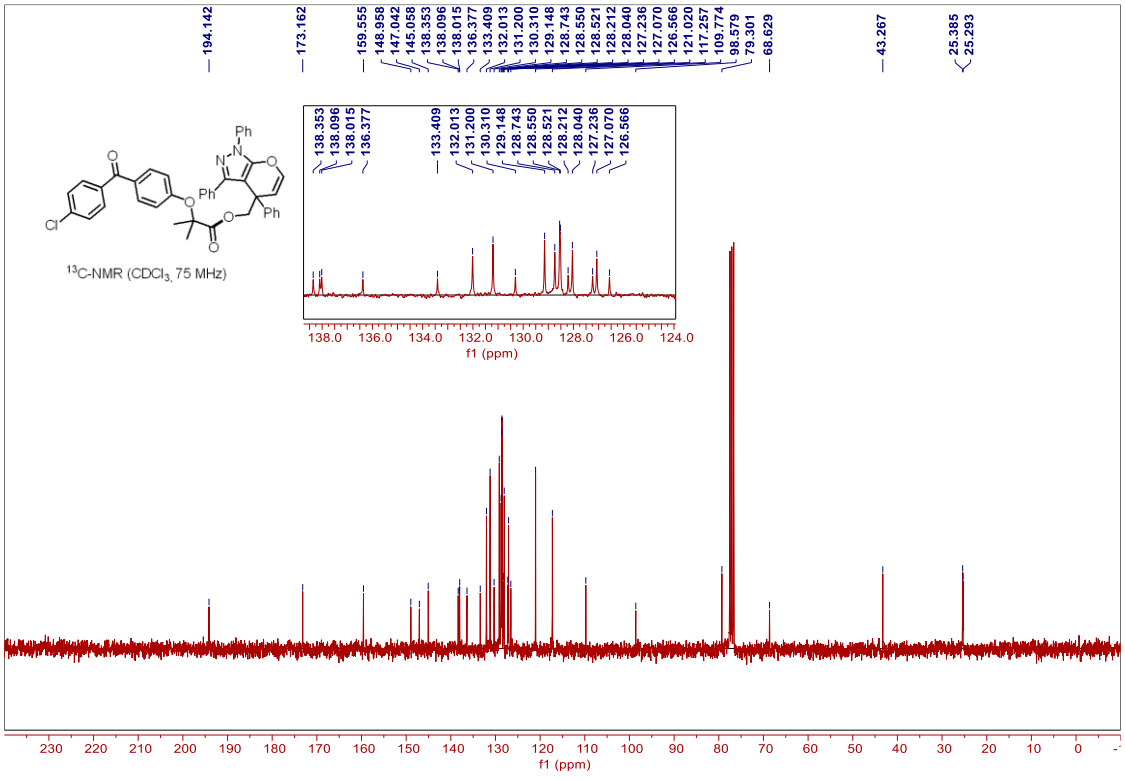




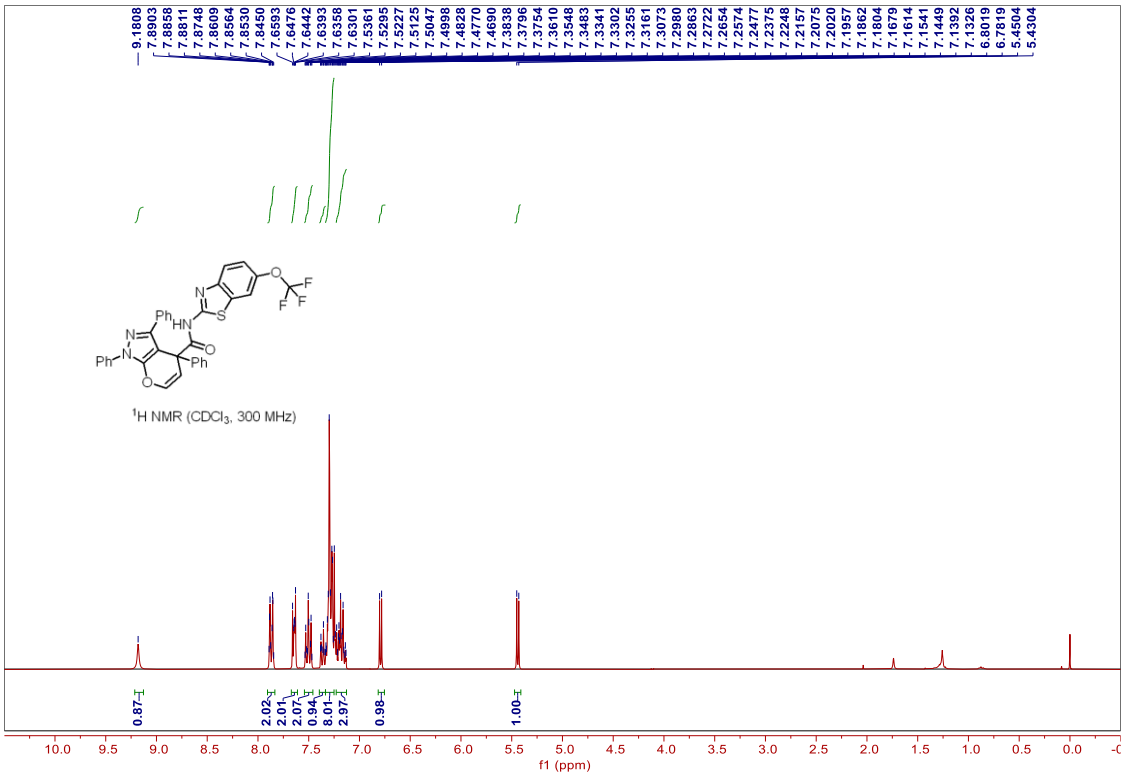

-83.7209
-84.2771
-84.3892
-84.9450
Ph
N
N
O
HF2CO
Ph
19F NMR (CDCl3, 282 MHz)
-82.9 -83.0 -83.1 -83.2 -83.3 -83.4 -83.5 -83.6 -83.7 -83.8 -83.9 -84.0 -84.1 -84.2 -84.3 -84.4 -84.5 -84.6 -84.7 -84.8 -84.9 -85.0 -85.1 -85.2 -85.3 -85.4 -85.5 -85.6 -85.7 -85.8 -85.9
f1 (ppm)

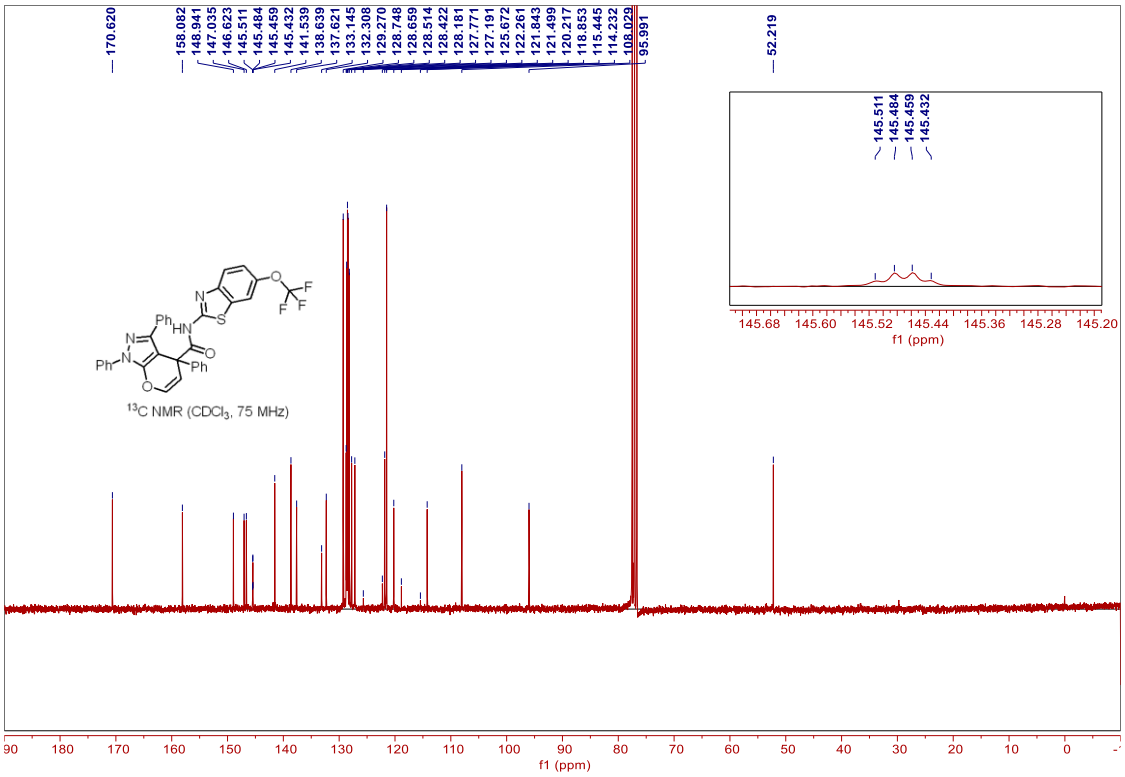
(R)-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)methyl 2-(4-(4-chlorobenzoyl)phenoxy)-2-methylpropanoate (6)

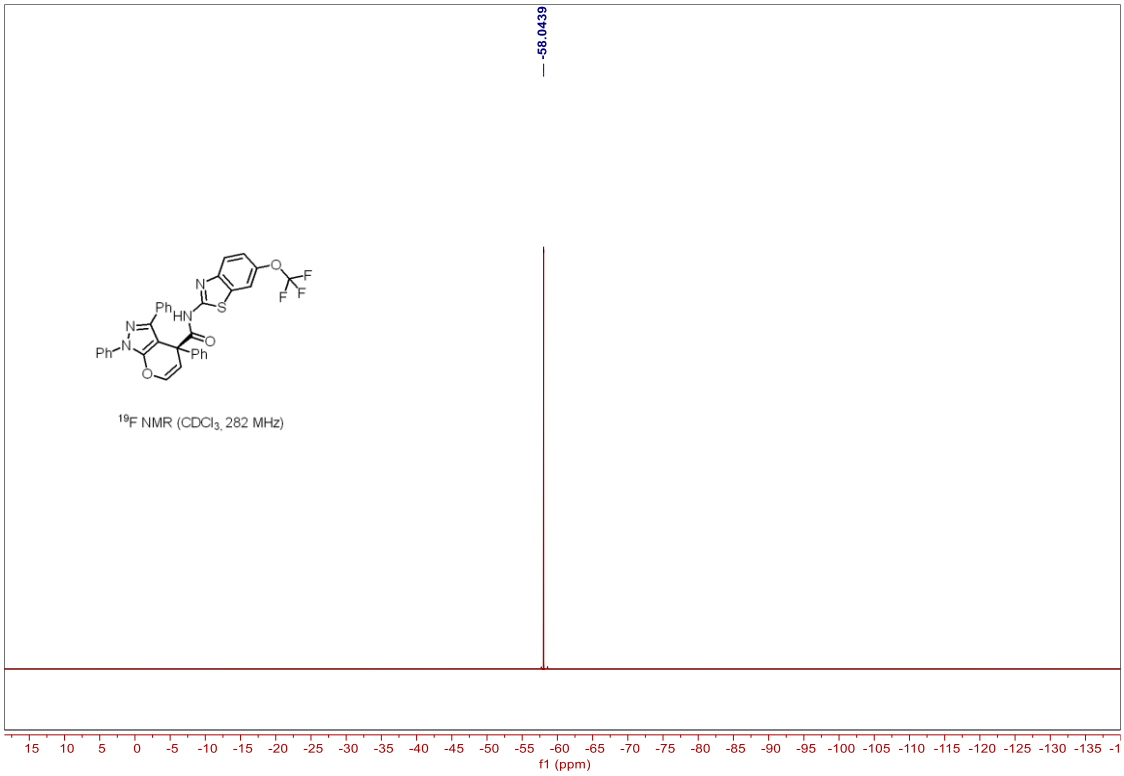




1,3,4-triphenyl-N-(6-(trifluoromethoxy)benzo[d]thiazol-2-yl)-1,4-dihydropyrano[2,3-c]pyrazole-4-carboxamide (7)

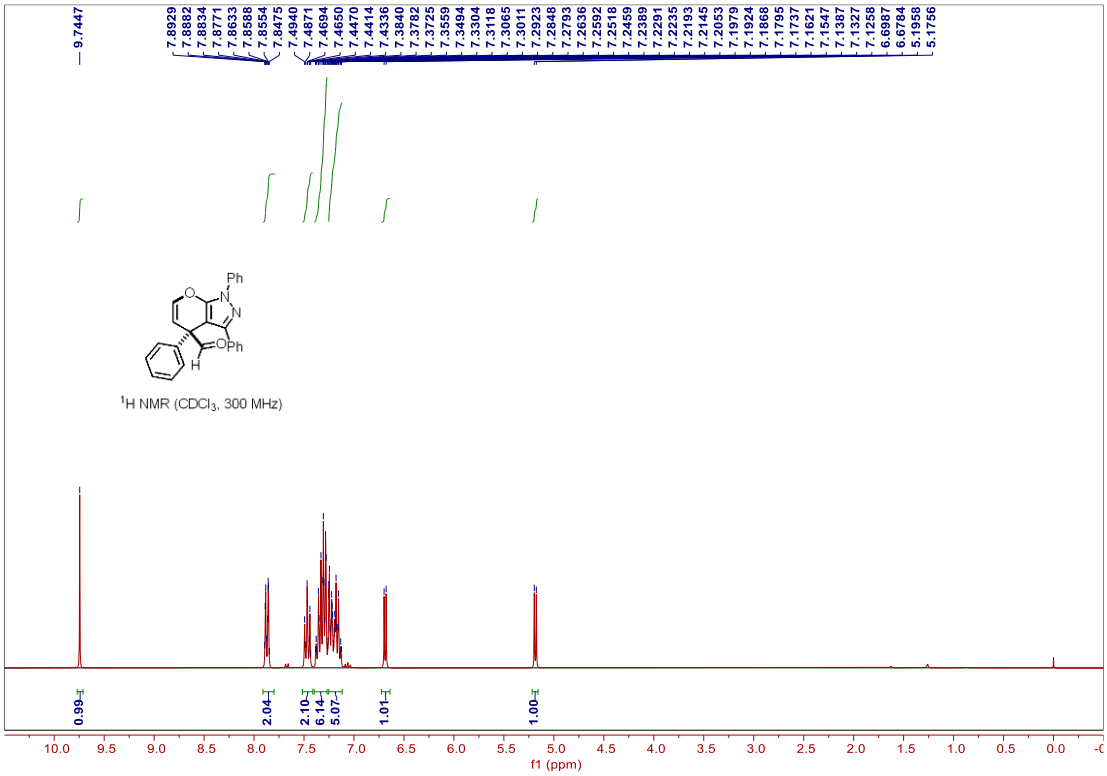


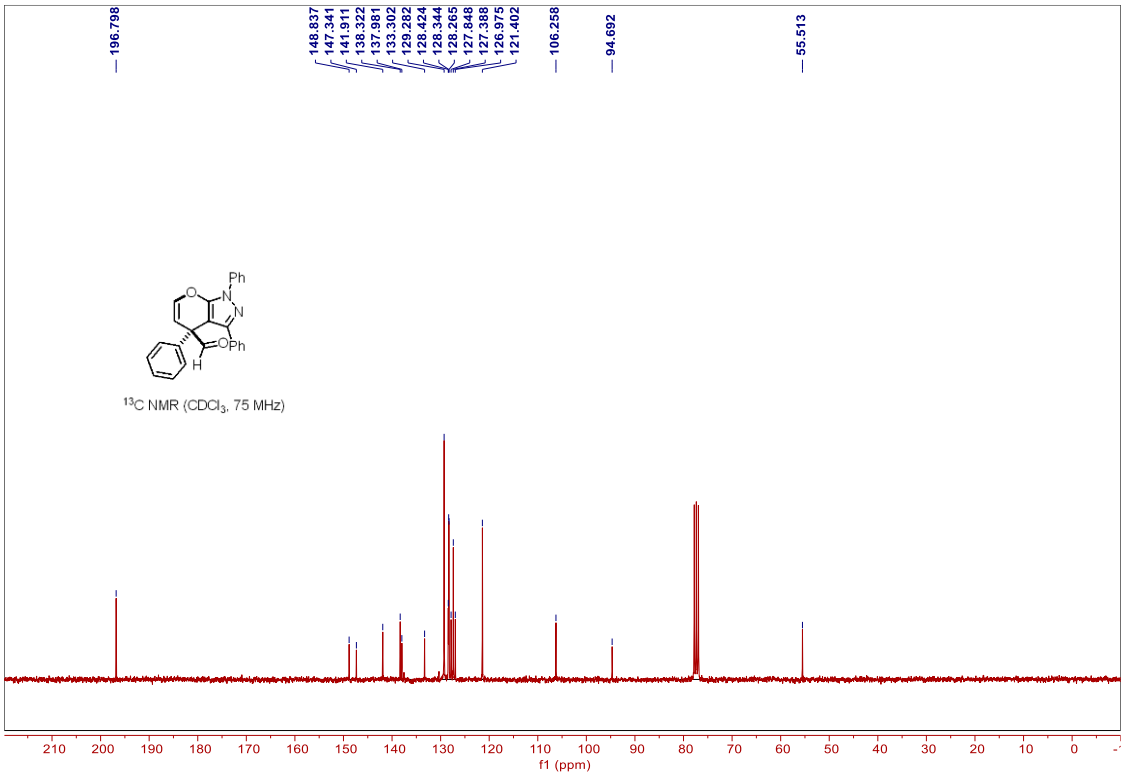




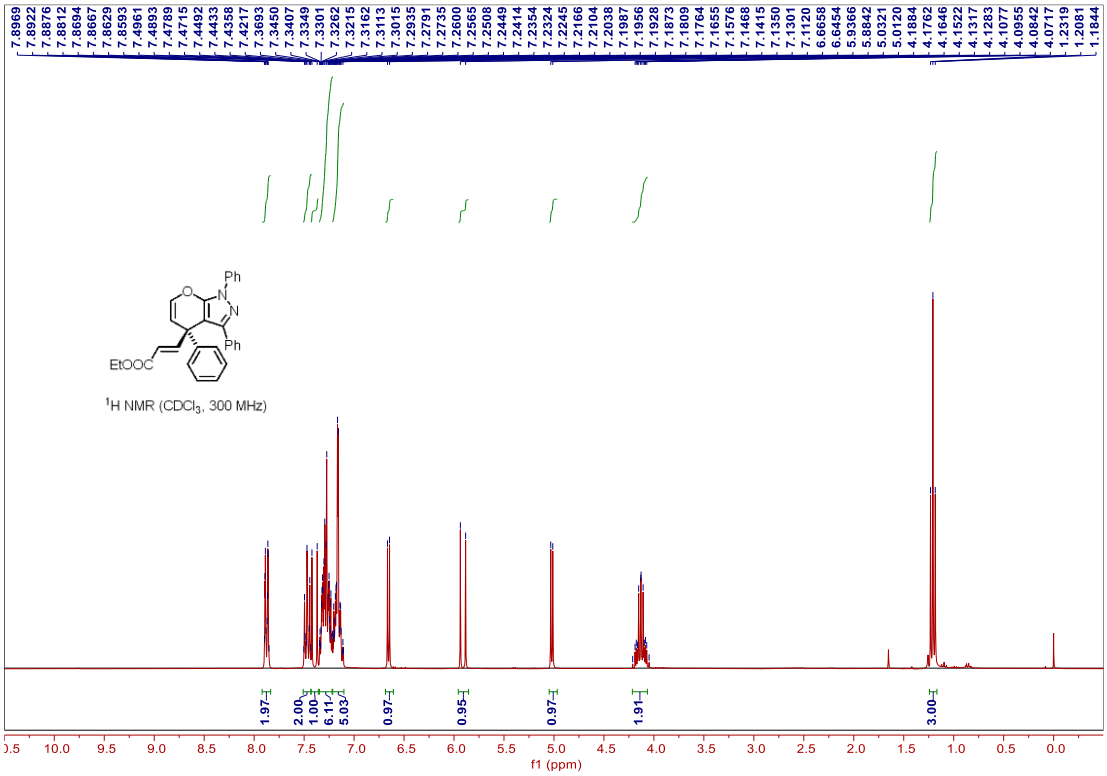
^{19}F NMR ($CDCl_3$, 282 MHz)

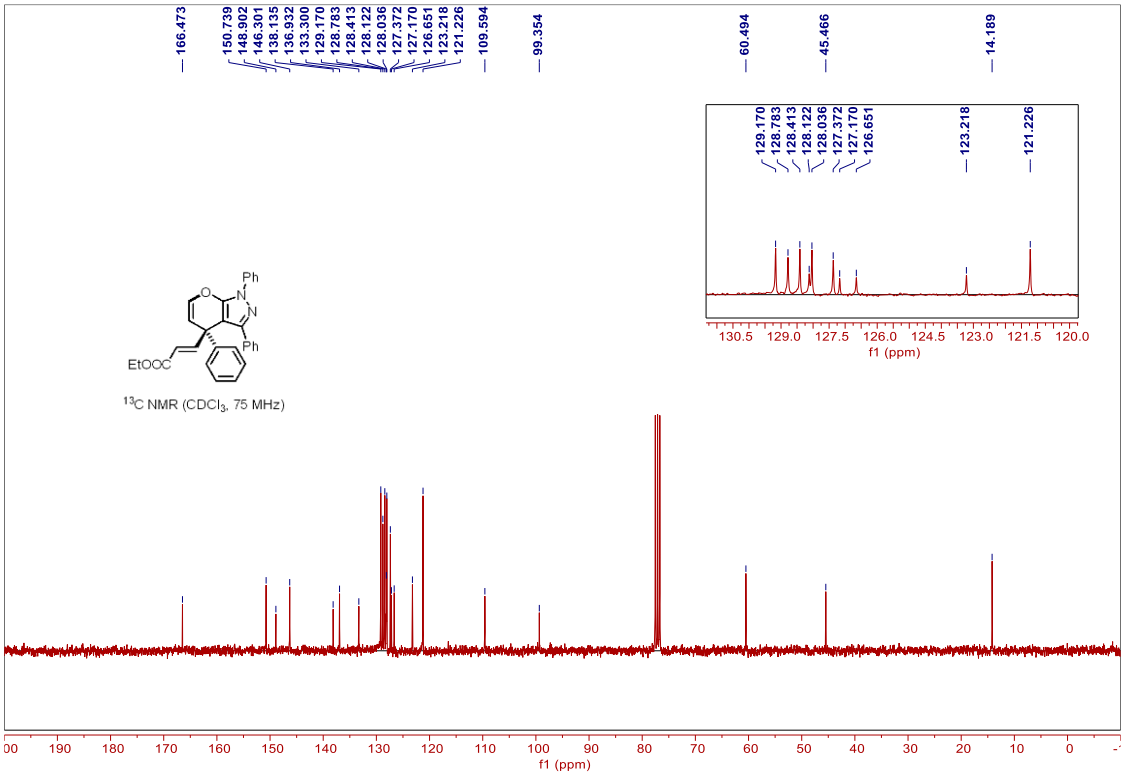
(R)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole-4-carbaldehyde (8)





Ethyl (S,E)-3-(1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazol-4-yl)acrylate (9)





(R)-1,3,4-triphenyl-1,4-dihydropyrano[2,3-c]pyrazole-4-carbonitrile (10)