Organocatalytic Enantioselective aza-Henry reaction of Pyrazolone Ketimines

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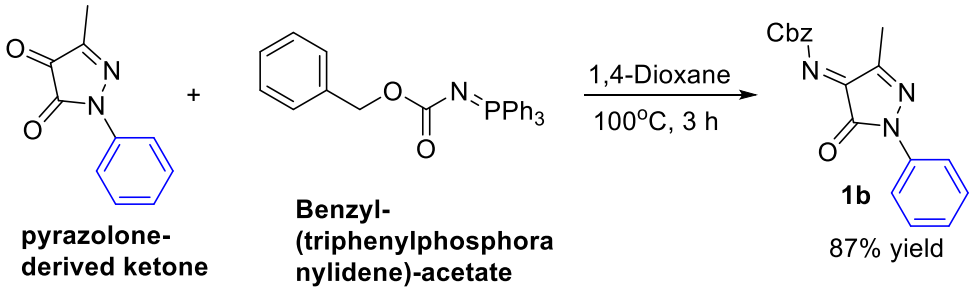
1. General Information

Unless otherwise stated, all commercial reagents and solvents were used without further additional purification. Analytical TLC was visualized with UV light at 254 nm. Thin layer chromatography was carried out on TLC aluminum sheets with silica gel 60 F_{254}. Purification of reaction products was carried out with chromatography on silica gel 60 (200-300 mesh). ^{1}H NMR (400 MHz) spectra was obtained at 25 °C; ^{13}C NMR (126 MHz) and ^{19}F NMR (376 MHz) were recorded on a VARIAN INOVA-400M and AVANCE II 400 spectrometer at 25 °C. Chemical shifts are reported as δ (ppm) values relative to TMS as internal standard and coupling constants (J) in Hz. The enantiomeric excesses (ee) were determined by HPLC. HPLC analyses were performed with Diacel Chiralpak AD-H, IA-H, OD-H and AS-H chiral columns (0.46 cm × 25 cm), using mixtures of n-hexane/isopropyl alcohol as mobile phase, at 25 °C. Mass spectra are reported by using electron ionization and electrospray ionization techniques. Melting points were determined with a hot plate apparatus. Optical rotations were measured on a digital polarimeter with a sodium lamp at 25 °C.

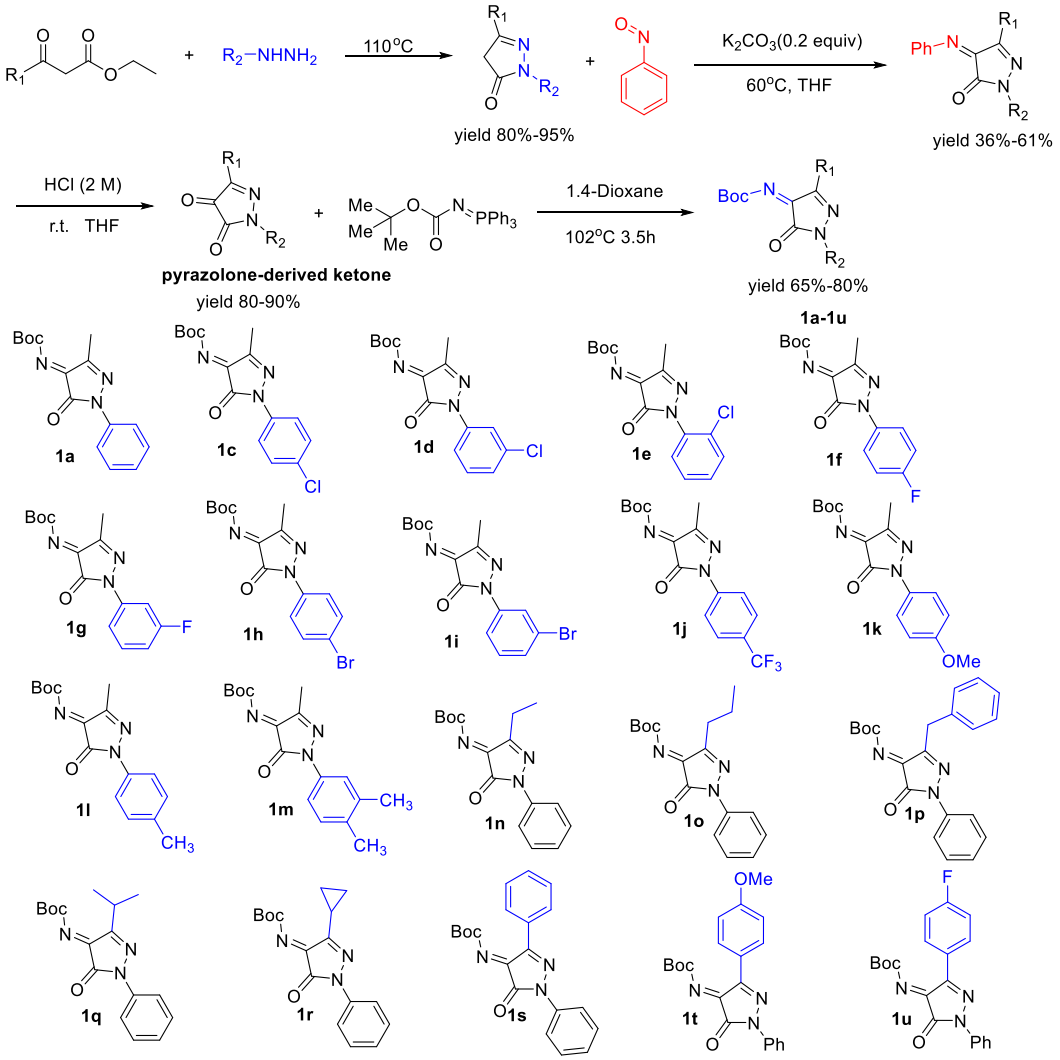
Materials:

Pyrazolone Ketimines:

Pyrazolone ketimine **1b** was prepared from pyrazolone-derived ketone with Benzyl-(triphenylphosphoranylidene)-acetate using 1,4-Dioxane as solvent at 100 °C (Scheme S1). Pyrazolone ketimines **1a, 1c-1u** were prepared partly according to the literature procedures (*Chem. Commun.*, 2017, **53**, 6633; *J. Org. Chem.*, 2017, **82**, 7050) (Scheme S2).



Scheme S1. Preparation of pyrazolone ketimine **1b**

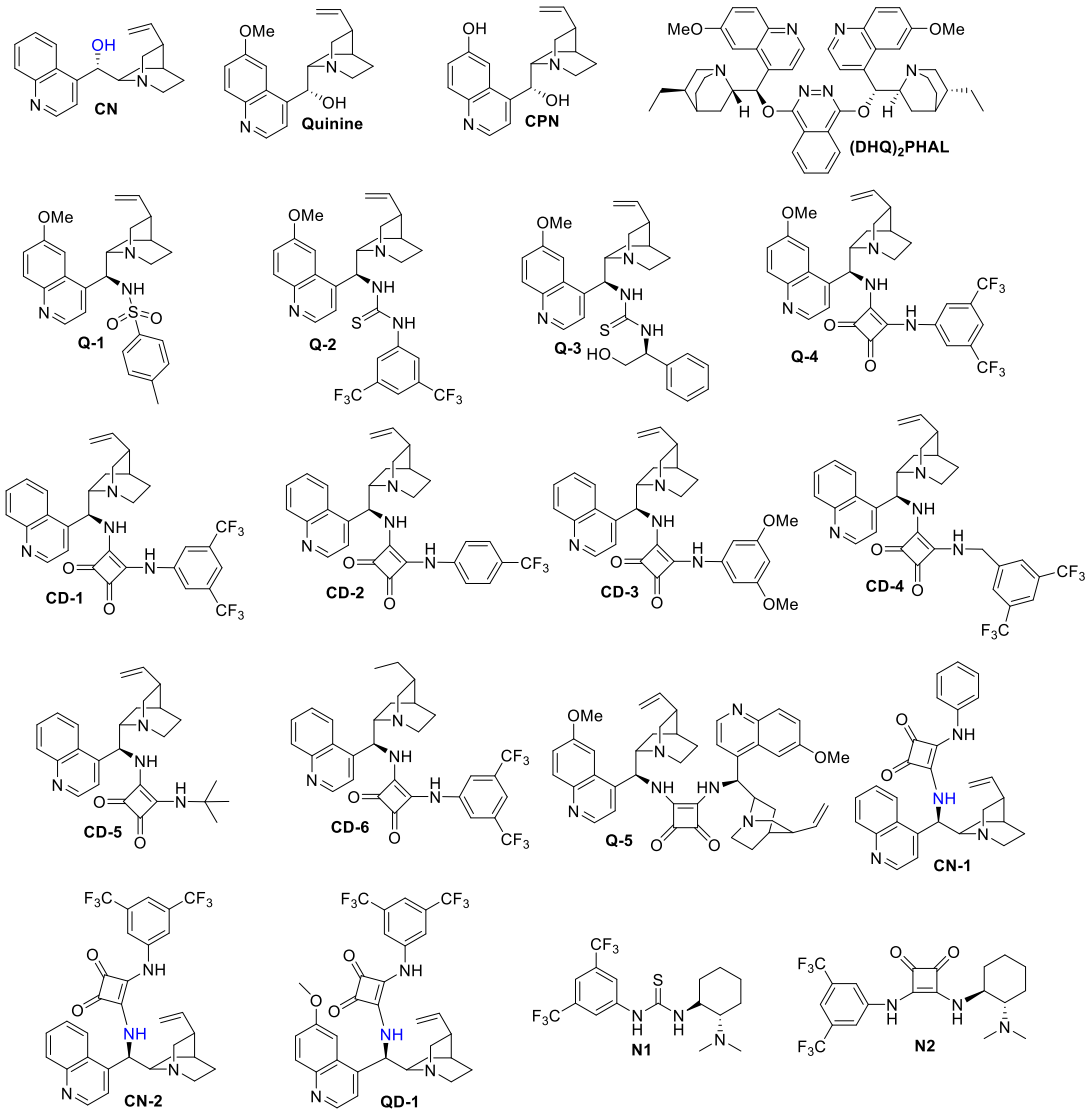


Scheme S2. Preparation of pyrazolone ketimines **1a, 1c-1u.**

Nitroalkanes reagents

CH_3NO_2, $BrCH_2NO_2$, $CH_3CH_2CH_2NO_2$, $PhCH_2NO_2$ were purchased from Innochem and Leyan reagent and used directly without further purification.

Catalysts:



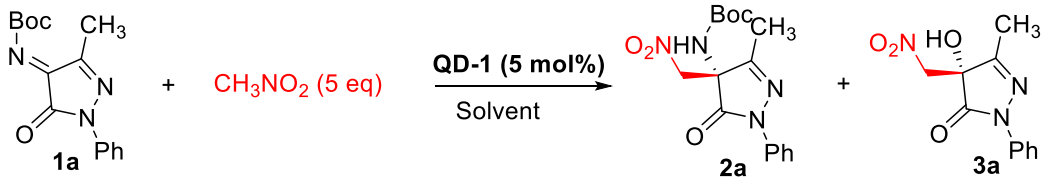
Scheme S3. Screening of organocatalysts for ammetric aza-Henry reaction.

CN, Quinine, CPN, (DHQ)$_2$PHAL, N1 and N2 were purchased from Innochem and Leyan reagent and used directly without further purification. **Q-1-Q5, CD-1-CD-6, CN-1-CN-2, QD-1** were all prepared according to the literatures (*Org. Lett.* **2005**, *7*, 1967; *J. Am. Chem. Soc.* **2008**, *130*, 14416; *J. Org. Chem*. **2024**, *89*, 8011).

2. General proceduce for the enantioselective aza-Henry reaction of pyrazolone ketimines

2.1 Optimization of reaction parameters for the enantioselective aza-Henry reaction

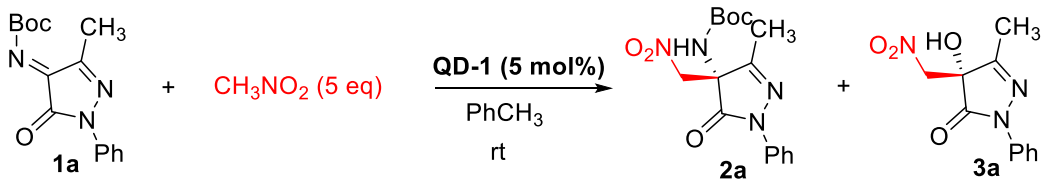
Table S1. Evaluation of different solvents[a]



Entry	Solvent	Tem. [°C]	Time [h]	**2a**/**3a** [c]	Yield[%][b]	ee of **2a** [%][c]
1	DMF	rt	12	Nd	Trace	Nd
2	DMSO	rt	12	Nd	Trace	Nd
3	MeOH	rt	12	14:86	Trace	Nd
4	EtOAc	rt	0.5	72:28	45	83 (R)
5	THF	rt	0.5	63:37	36	81 (R)
6	CH_2Cl_2	rt	0.5	74:26	65	79 (R)
7	*n*-Hexane	rt	2	85:15	75	62 (R)
8	**$PhCH_3$**	**rt**	**0.5**	**75:25**	**58**	**87 (R)**
9	*o*-Xylene	rt	0.5	74:26	55	86 (R)
10	Mesitylene	rt	0.5	74:26	54	85 (R)
11	PhCl	rt	0.5	72:28	54	84 (R)
12	*p*-Xylene	rt	0.5	73:27	55	82 (R)
13	$PhCF_3$	rt	0.5	76:24	61	76 (R)
14	PhF	rt	0.5	74:26	51	83 (R)

[a] Unless specified otherwise, pyrazolone **1a** (0.1 mmol), **QD-1** (0.005 mmol, 5 mol %) dissolved in solvent (2 mL) were added to a test tube equipped with a stirring bar. Then, $MeNO_2$ (0.5 mmol), was added. The mixture was stirred at rt until the reaction was completed. [b]Yields shown are of isolated products. [c]Determined by HPLC analysis (Chiralcel OD-H) with hexane/2-propanol (80:20) as the eluent

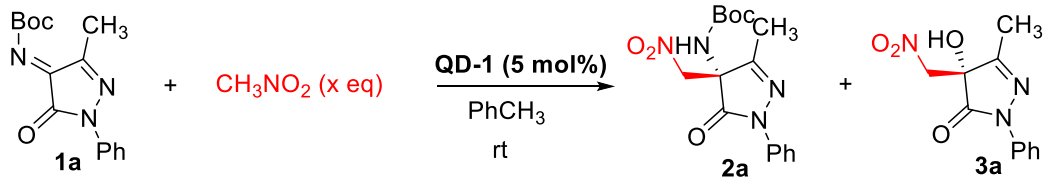
Table S2. Evaluation of the concentration[a]



Entry	**Concentration (mol/L)**	Time [h]	**2a/3a** [c]	Yield[%][b]	ee of **2a** [%][c]
1	0.2	0.5	73:27	53	86 (R)
2	0.1	0.5	75:25	58	87 (R)
3	**0.05**	**1**	**78:22**	**65**	**90 (R)**
4	0.02	6	76:24	59	89 (R)
5	0.01	12	76:24	35	76 (R)

[a] Unless specified otherwise, pyrazolone **1a** (0.1 mmol), **QD-1** (0.005 mmol, 5 mol %) dissolved in toluene (x mL) were added to a test tube equipped with a stirring bar. Then, $MeNO_2$ (0.5 mmol) was added. The mixture was stirred at rt until the reaction was completed. [b]Yields shown are of isolated products. [c]Determined by HPLC analysis (Chiralcel OD-H) with hexane/2-propanol (80:20) as the eluent.

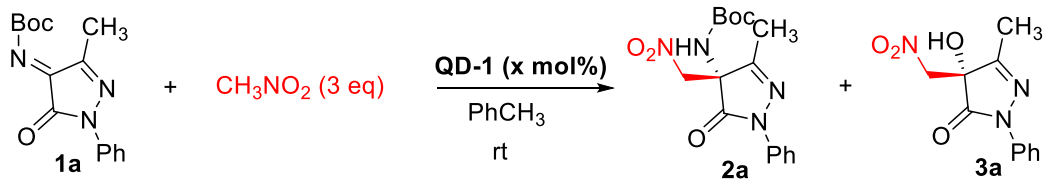
Table S3. Evaluation of the dosage of $MeNO_2$[a]



Entry	**$MeNO_2$ (eq.)**	Time [h]	**2a/3a** [c]	Yield[%][b]	ee of **2a** [%][c]
1	1	6	75:25	27	92 (R)
2	2	6	74:26	45	92(R)
3	**3**	**2**	**74:26**	**59**	**92 (R)**
4	5	2	78:22	65	90 (R)
5	10	1	76:24	63	90 (R)

[a] Unless specified otherwise, pyrazolone **1a** (0.1 mmol) , **QD-1** (5 mol %) dissolved in toluene (2 mL) were added to a test tube equipped with a stirring bar. Then, $MeNO_2$ (x mmol) was added. The mixture was stirred at specified temperature until the reaction was completed. [b]Yields shown are of isolated products. [c]Determined by HPLC analysis (Chiralcel OD-H) with hexane/2-propanol (80:20) as the eluent.

Table S4. Evaluation of the catalyst loading [a]

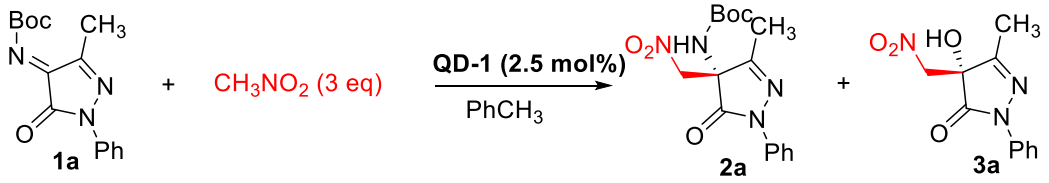


Entry	**QD-1 (mol%)**	Time [h]	**2a/3a** [c]	Yield[%][b]	ee of **2a** [%][c]
1	0.5	8	78:22	35	79 (R)
2	1	4	78:22	48	89 (R)
3	**2.5**	**2**	**78:22**	**61**	**92 (R)**
4	5	2	74:26	59	92 (R)

5	10	2	70:30	51	92 (R)
6	20	1	70:30	52	92 (R)

[a] Unless specified otherwise, pyrazolone **1a** (0.1 mmol), **QD-1** (x mol %) dissolved in toluene (2 mL) were added to a test tube equipped with a stirring bar. Then, $MeNO_2$ (0.3 mmol) was added. The mixture was stirred at rt until the reaction was completed. [b]Yields shown are of isolated products. [c]Determined by HPLC analysis (Chiralcel OD-H) with hexane/2-propanol (80:20) as the eluent.

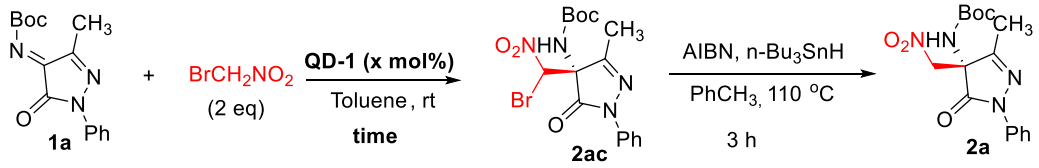
Table S5. Evaluation of different temperatures



Entry	**Temperature**[°C]	Time [h]	**2a**/**3a** [c]	Yield[%][b]	ee of **2a** [%][c]
1	**rt**	**2**	**78:22**	**61**	**92 (R)**
2	35	2	78:22	59	91 (R)
3	20	2	78:22	62	92 (R)
4	0	4	78:22	54	83 (R)
5	-20	4	78:22	51	81 (R)
6	-30	0.5	75:25	53	85 (R)

[a] Unless specified otherwise, pyrazolone **1a** (0.1 mmol), **QD-1** (2.5 mol %) dissolved in toluene (2 mL) were added to a test tube equipped with a stirring bar. Then, $MeNO_2$ (0.3 mmol) was added. The mixture was stirred at specified temperature until the reaction was completed. [b]Yields shown are of isolated products. [c]Determined by HPLC analysis (Chiralcel OD-H) with hexane/2-propanol (80:20) as the eluent.

Table S6. Evaluation of the catalyst loading using $BrCH_2NO_2$ as nucleophile [a]

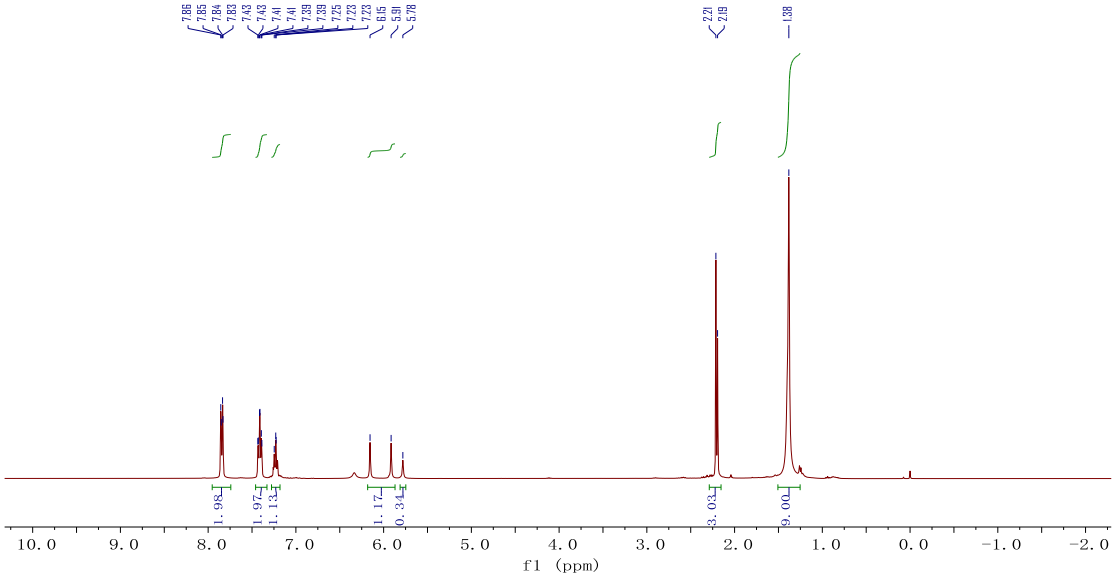


Entry	**QD-1 (mol%)**	Time [h]	Yield of **2a** [%] [b]	ee of **2a** [%][c]
1	0.1	12	78	81 (R)
2	0.5	1	91	92 (R)
3	1	0.5	91	95 (R)
4	**5**	0.5	92	96 (R)
5	**10**	0.5	92	96 (R)

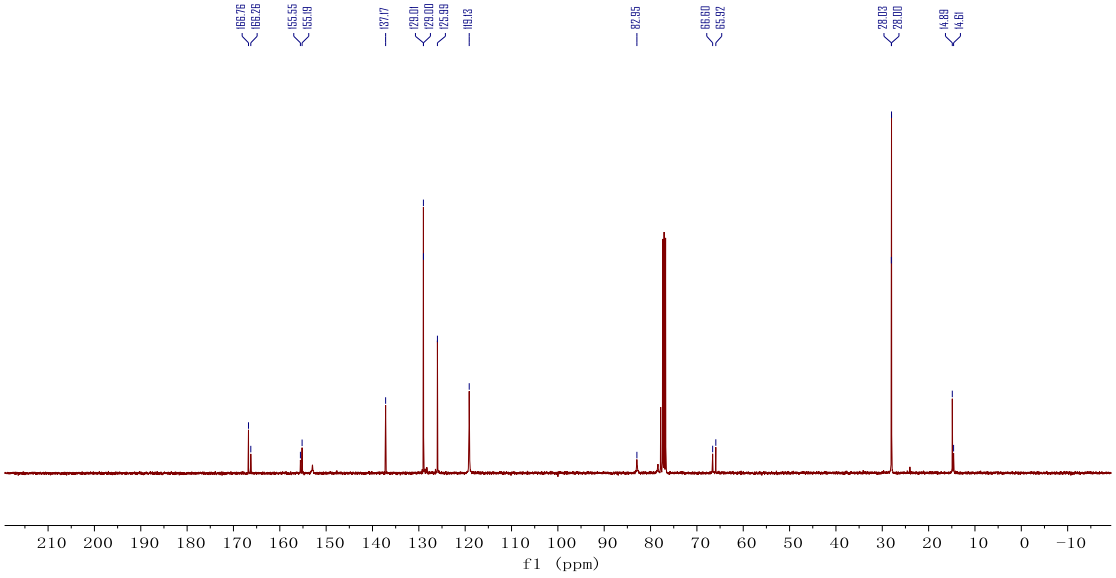
[a] Unless specified otherwise, pyrazolone **1a** (0.1 mmol), **QD-1** (x mol %) dissolved in toluene (2 mL) were added to a test tube equipped with a stirring bar. Then, $BrCH_2NO_2$ (0.2 mmol) was added. The mixture was stirred at specified temperature until the reaction was completed. [b]Yields shown are of isolated products. [c]Determined by HPLC analysis (Chiralcel OD-H) with hexane/2-propanol (80:20) as

the eluent.

Here is the ^{1}H NMR spetra of **2ac**. We can clearly see the diastereoisomers with the 3.5:1 dr.

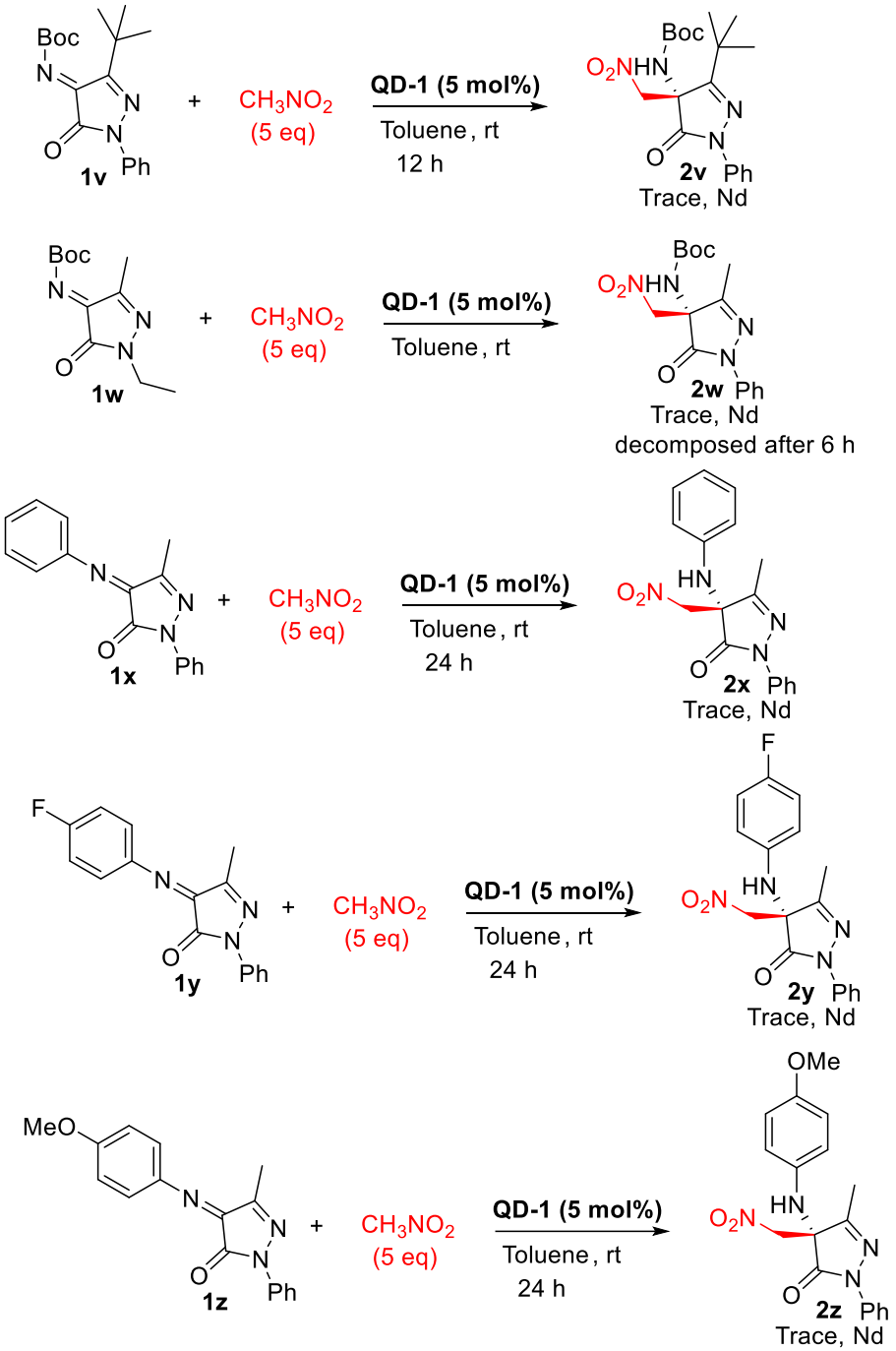


Here is the ^{13}C NMR spetra of **2ac**. We can also clearly see the diastereoisomers.



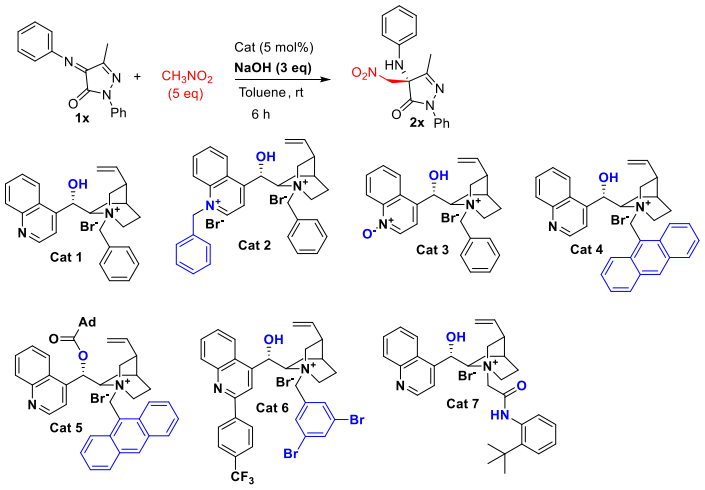
2.2 Other examples for the enantioselective aza-Henry reaction

First, we tested some other pyrazolone ketimines with different structural characteristics. **1v** was texted with the tertiary butyl at C-3 position, but we did not obtain corresponding product **2v** using **QD-1** as chiral catalyst. Then we introduced ethyl at the N-substituents, but **2w** was not obtained, and we can clearly see the **1w** was decomposed under such conditions. The phenyl ketimines **1x, 1y, 1z** were also tested, but corresponding products **2x, 2y, 2z** were not observed under standard conditions. Catalyst **QD-1** had an insufficient alkalinity to activate these inert substrates.



Then we tested the phenyl ketimines **1x** as model substrate under phase transfer catalysis. Different kinds of classical *Cinchona* alkaloid derivatives were screened (**Cat1-Cat7**), such as *N*-benzyl PTC **Cat1**,the biquaternary ammonium salt **Cat 2**, the quinoline-*N*-oxide PTC **Cat 3**, Anthracene-derived **Cat 4** and **Cat 5**, the C-2′-arylated PTC **Cat 6** and the amide-based PTC **Cat 7**. Preliminary results of catalyst screening can be seen in Table S7. We can clearly see the biquaternary ammonium salt **Cat 2** showed promising results, addition product **2x** was obtained with 93% ee after 12 h.

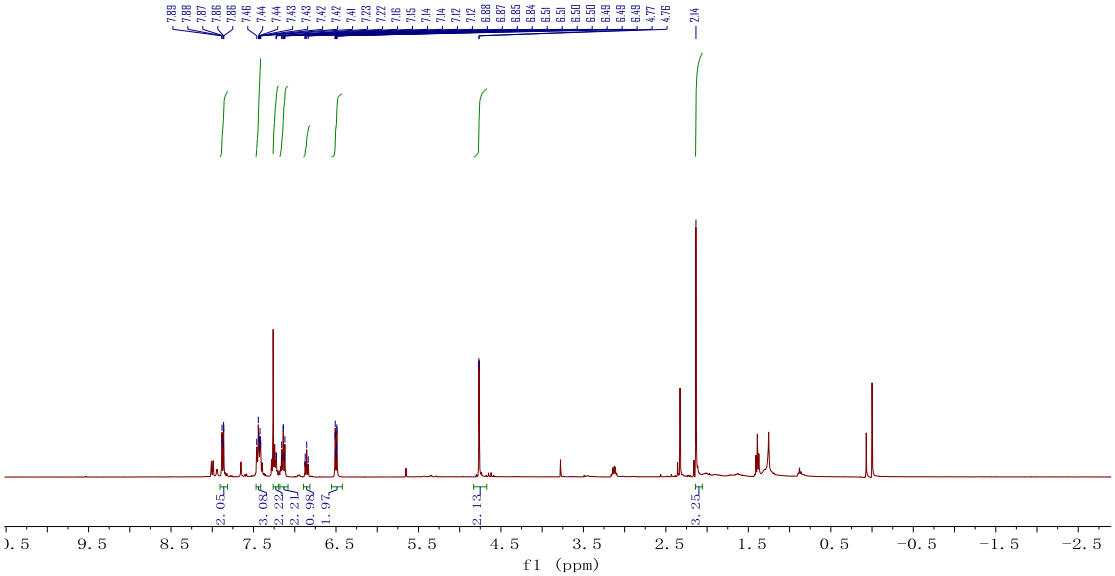
Table S7. Evaluation of the catalyst under phase transfer catalysis [a]

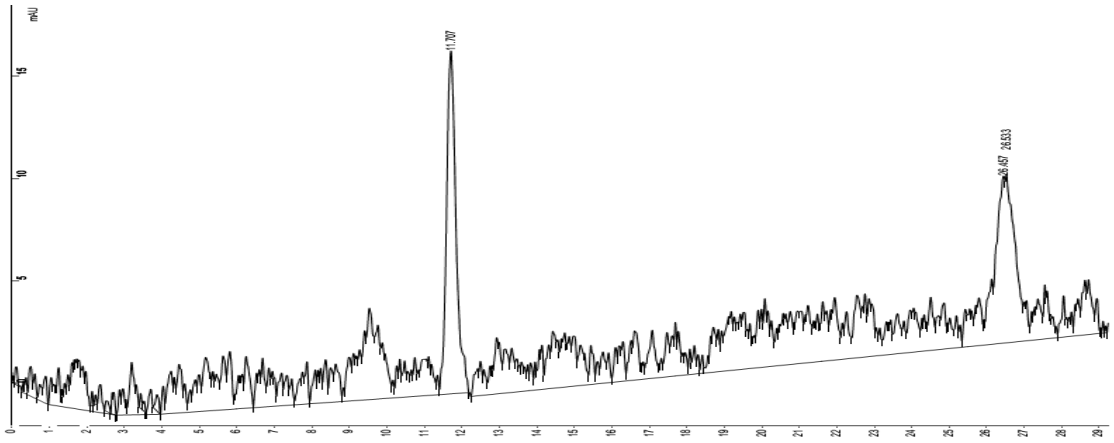


Entry	PTC	ee of **2x** [%][a]
1	**Cat 1**	45 (R)
2	**Cat 2**	93 (R)
3	**Cat 3**	21 (R)
4	**Cat 4**	57 (R)
5	**Cat 5**	14 (R)
6	**Cat 6**	62 (R)
7	**Cat 7**	73 (R)

[a] Unless specified otherwise, pyrazolone **1x**(0.1 mmol), NaOH(0.3 mmol) ,**Cat** (5 mol %) dissolved in toluene (2 mL) were added to a test tube equipped with a stirring bar. Then, CH_3NO_2 (0.5 mmol) was added. The mixture was stirred at specified temperature until the reaction was completed. [c]Determined by HPLC analysis (Chiralcel AD-H) with hexane/2-propanol (80:20) as the eluent.

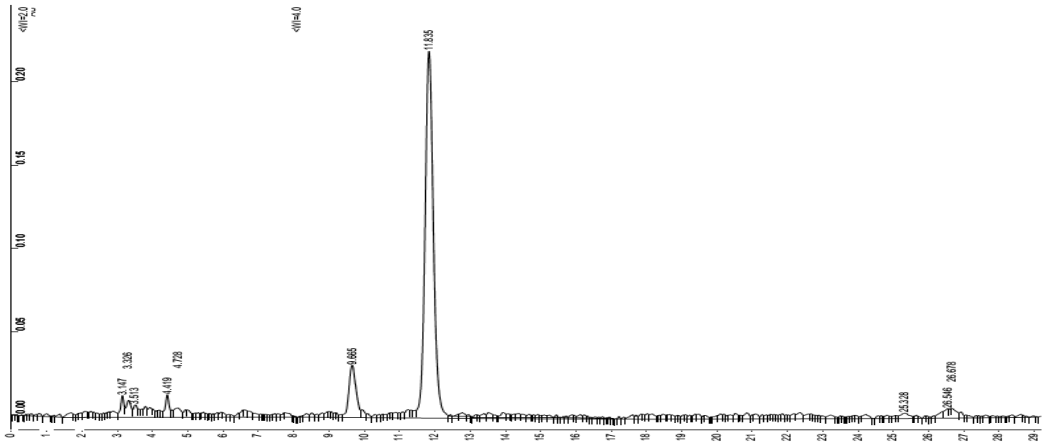
Here is the cruder ^{1}H NMR spetra of **2x** .^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.82 (m, 2H), 7.47 – 7.41 (m, 3H), 7.22 (d, J = 2.8 Hz, 2H), 7.18 – 7.08 (m, 2H), 6.89 – 6.82 (m, 1H), 6.55 – 6.42 (m, 2H), 4.77 (s, 2H), 2.14 (s, 3H). Due to the poor stability of the product, we did not obtain the pure **2x**.





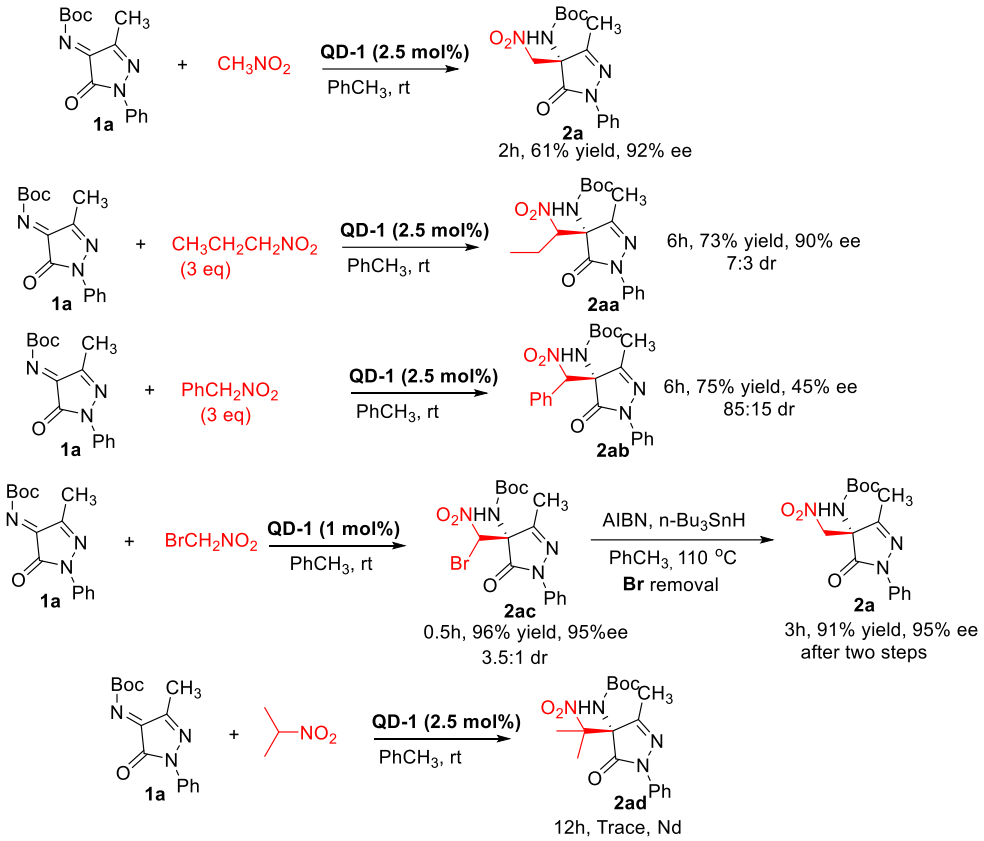
R.Time	Area	Area%
11.707	**2926605**	**50.7850**
26.553	**2836130**	**49.2150**

Racemic product of 2x



R.Time	Area	Area%
11.835	**37859432**	**96.5320**
26.678	**1360134**	**3.4680**

Chiral product of 2x using Cat 2 as PTC

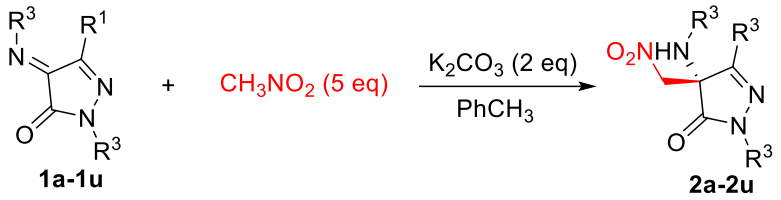


Scheme S5. Screening of nitroalkanes for ammetric aza-Henry reaction.

1-Nitropropane also reacted efficiently with ketimine **1a**, **2aa** was obtained in 73% yield with 90% ee after 6 h, but the diastereoselectivity was low (7:3 dr). Furthermore, (nitromethyl)benzene afforded corresponding product **2ab** in 75% yield with only 45% ee. To our surprise, when Bromonitromethane ($BrCH_2NO_2$) was used as nucleophile, the reaction rate has been significantly increased, the loading of catalyst **QD-1** could be reduced to 1 mol % and we obtained additive product **2ac** with 96% yield in excellent enantioselectivity (95% ee), yet the diastereoselectivity was still unsatisfactory (3.5 :1 dr). Then we tried to remove the bromine group by AIBN and *n*-Bu_3SnH, and the debrominated product **2a** was obtained in 91% yield and 95% ee after two steps. We could not obtain **2ad** using 2-nitropropane as nitroalkane after 12 h. Thus, using $BrCH_2NO_2$ observably accelerated the reaction rate and improved the yield and enantioselectivity compared with $MeNO_2$. To our knowledge, this is the first successful example of aza-Henry reaction of ketimines using $BrCH_2NO_2$ as the nucleophile.

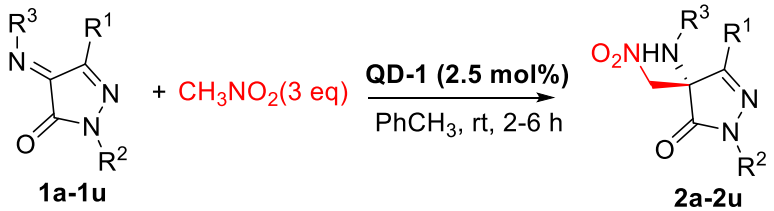
3. Experimental procedures and characterization of chiral products

Achiral aza-Henry reaction of pyrazolone ketimines



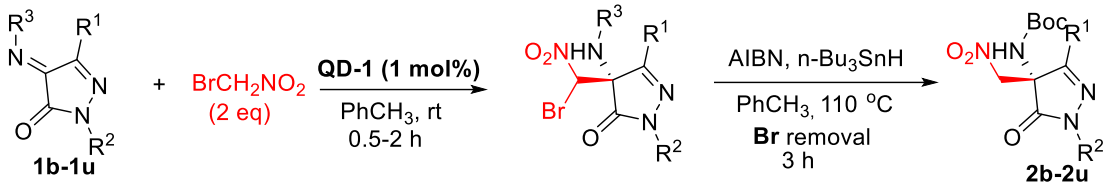
The reaction was conducted with substrate **1** (0.1 mmol) in the presence of CH_3NO_2 (0.5 mmol) in $PhCH_3$ (2 mL). Then K_2CO_3 (0.2 mmol) was added, the reaction was stirred at rt for 2-12 h. After completion of the reaction (confirmed by TLC analysis), the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to provide the corresponding products. The ee of the products were determined by chiral HPLC.

Standard conditions 1: Asymmetric aza-Henry reaction of pyrazolone ketimines using CH_3NO_2 as nucleophile



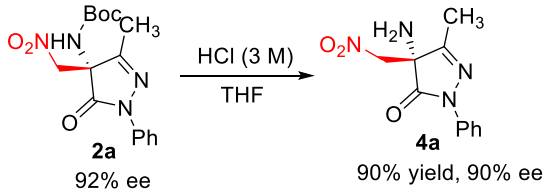
The reaction was conducted with substrate **1** (0.1 mmol) in the presence of CH_3NO_2 (0.3 mmol) in $PhCH_3$ (2 mL). Then **QD-1** (0.0025 mmol) was added, the reaction was stirred at rt for 2-6 h. After completion of the reaction (confirmed by TLC analysis), the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to provide the corresponding products **2a-2u**. The ee of the products were determined by chiral HPLC.

Standard conditions 2: Asymmetric aza-Henry reaction of pyrazolone ketimines using $BrCH_2NO_2$ as nucleophile

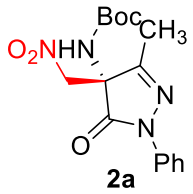


The reaction was conducted with substrate **1** (0.1 mmol) in the presence of $BrCH_2NO_2$ (27.8 mg, 0.2 mmol) in $PhCH_3$ (2 mL). Then **QD-1** (0.001 mmol) was added, the reaction was stirred at rt for 0.5-2 h. After completion of the reaction (confirmed by TLC analysis), AIBN (5 mg, 0.03 mmol) and *n*-Bu_3SnH (58.2 mg, 0.2 mmol) were added directly. The reaction mixture is stirred at 110 °C at an oil bath for 3 h. Then the solvent was removed under reduced pressure and the reside was purified by column chromatography on silica gel (ethyl acetate/petroleum ether) to provide the corresponding products **2a-2u**. The ee of the products were determined by chiral HPLC.

Derivatization of 2a to chira 4-aminopyrazolone 4a

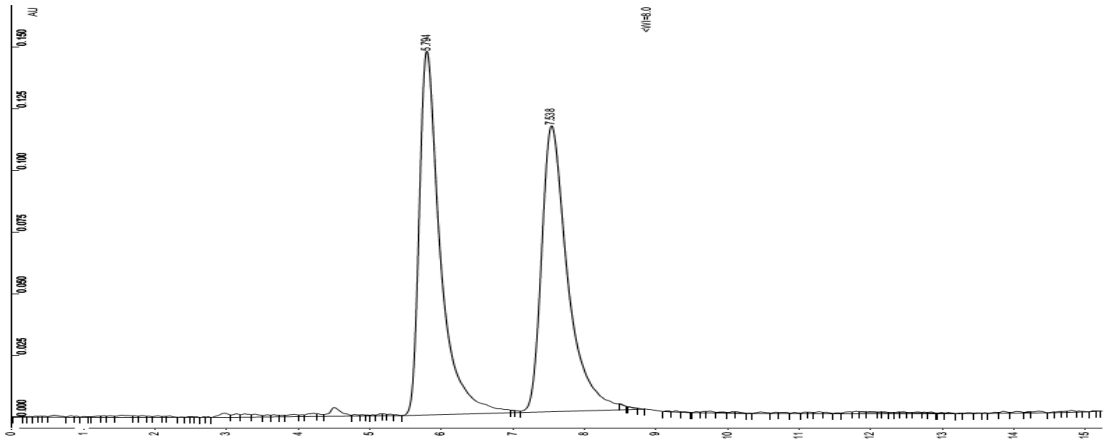


The reaction was conducted with substrate **2a** (0.1 mmol, 92% ee) in $PhCH_3$ (3 mL). Then **HCl** (3 M, 0.1 mL) was added, the reaction was stirred at rt for 3 h. After completion of the reaction (confirmed by TLC analysis), 3 mL saturated $NaHCO_3$ was added, the mixture was diluted with EtOAc (20 mL), washed with water (2×10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (ethyl acetate/petroleum ether = 4:1) to provide the corresponding product **4a**. The ee of the products were determined by chiral HPLC.



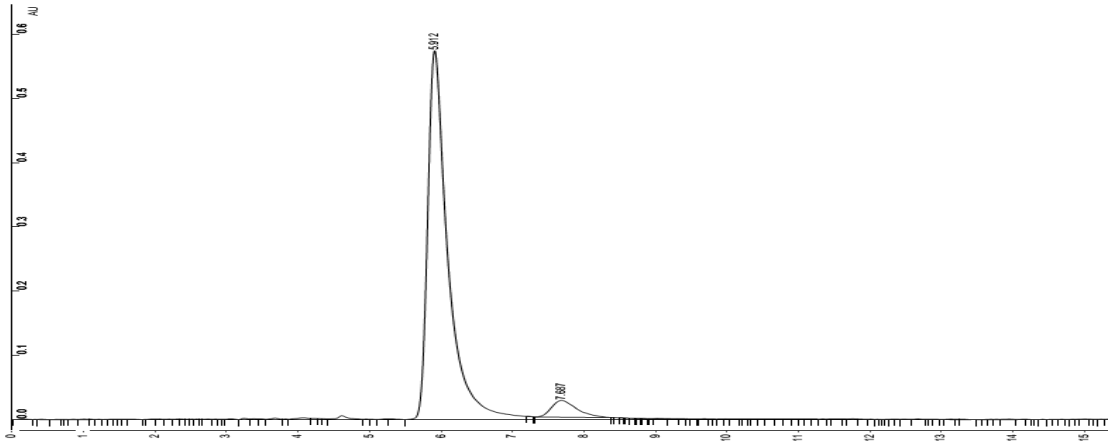
2a

Following the general procedure using **1a** (28.7 mg, 0.1 mmol), **2a** was obtained by flash chromatography (petroleum ether/ethyl acetate: 6/1) as a colourless wax. Standard conditions 1: (21.2 mg, 61% yield, 92% ee). $[\alpha]_D^{25}$ +24.33 (*c* 0.20, $CDCl_3$). Standard conditions 2: (31.6 mg, 91% yield, 95% ee). $[\alpha]_D^{25}$ +26.45 (*c* 0.20, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.1 Hz, 2H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.27 – 7.20 (m, 1H), 6.16 (s, 1H), 4.75 – 4.53 (m, 2H), 2.13 (s, 3H), 1.38 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.34, 157.06, 137.48, 128.99, 125.79, 118.97, 76.03, 63.85, 28.03, 13.86. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.91 min, τR (minor) = 7.68 min. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_{20}N_4O_5Na$: 371.1131; found 371.1135.



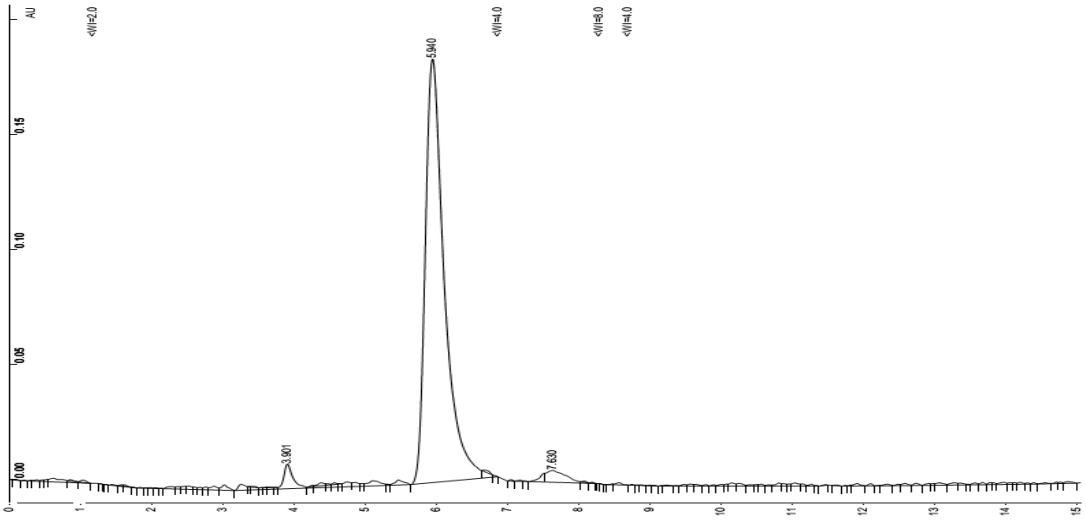
R.Time	Area	Area%
5.794	**30119856**	**50.5346**
7.538	**29482640**	**49.4654**

Racemic product



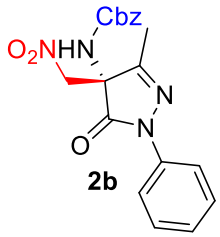
R.Time	Area	Area%
5.912	**118035728**	**95.8782**
7.687	**3843250**	**3.1218**

93% ee ($MeNO_2$ as nucleophile)



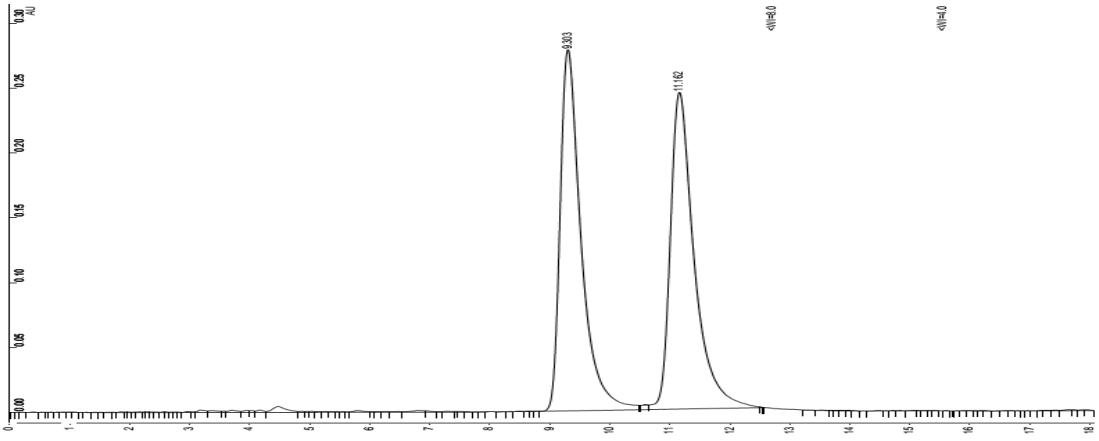
R.Time	Area	Area%
5.940	**34278160**	**97.3916**
7.630	**918058**	**2.6084**

95% ee ($BrCH_2NO_2$ as nucleophile)



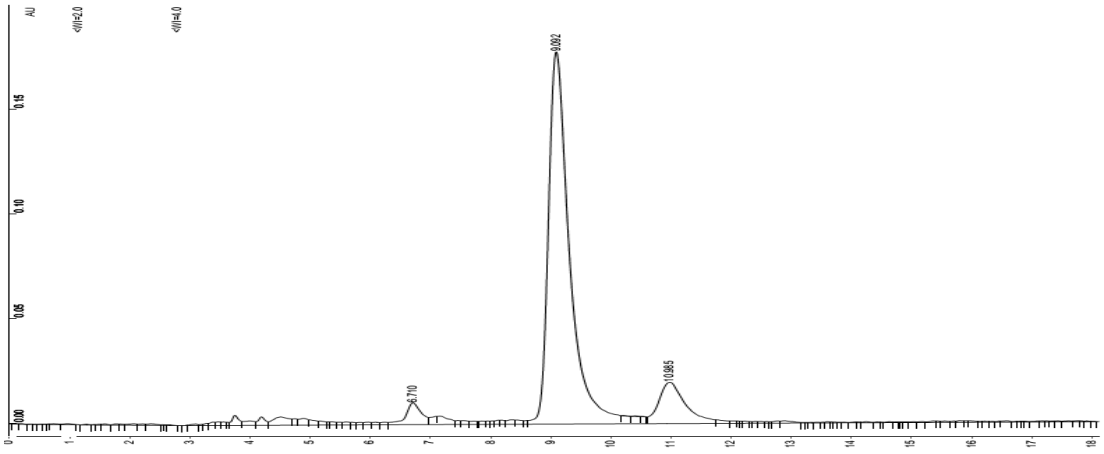
2b

Following the general procedure using **1b** (32.1 mg, 0.1 mmol), **2b** was obtained by flash chromatography (petroleum ether/ethyl acetate: 5/1) as a light yellow solid. Mp 138-140 °C; Standard conditions 1: (24.1 mg, 63% yield, 79% ee). $[\alpha]_D^{25}$ +14.25 (*c* 0.20, $CHCl_3$). Standard conditions 2: (35.5mg, 93% yield, 92% ee). $[\alpha]_D^{25}$ +18.73 (*c* 0.20, $CHCl_3$). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.60 (m, 2H), 7.36 – 7.28 (m, 3H), 7.27 – 7.12 (m, 5H), 6.44 (s, 1H), 5.05 – 4.97 (m, 2H), 4.65 – 4.46 (m, 2H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.08, 137.32, 136.15, 129.01, 128.67, 128.60, 128.40, 128.29, 128.14, 125.98, 119.18, 75.69, 68.27, 67.03, 63.71, 13.84. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 9.29 min, τR (minor) = 10.91 min. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{19}H_{18}N_4O_5Na$: 405.1175; found 405.1172.



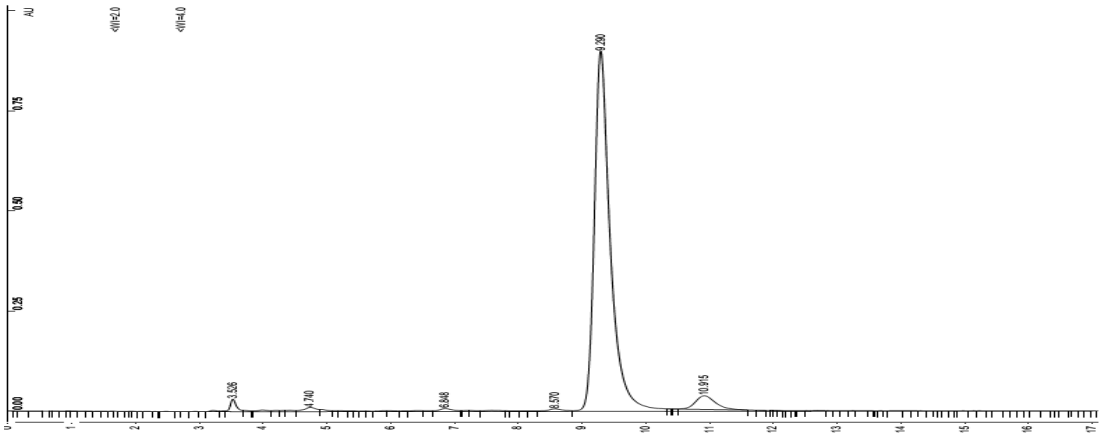
R.Time	Area	Area%
9.303	**67675984**	**50.1229**
11.162	**67344016**	**49.8771**

Racemic product



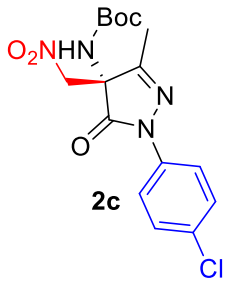
R.Time	Area	Area%
9.092	**43843548**	**89.6878**
10.985	**5041080**	**10.3122**

79% ee ($MeNO_2$ as nucleophile)



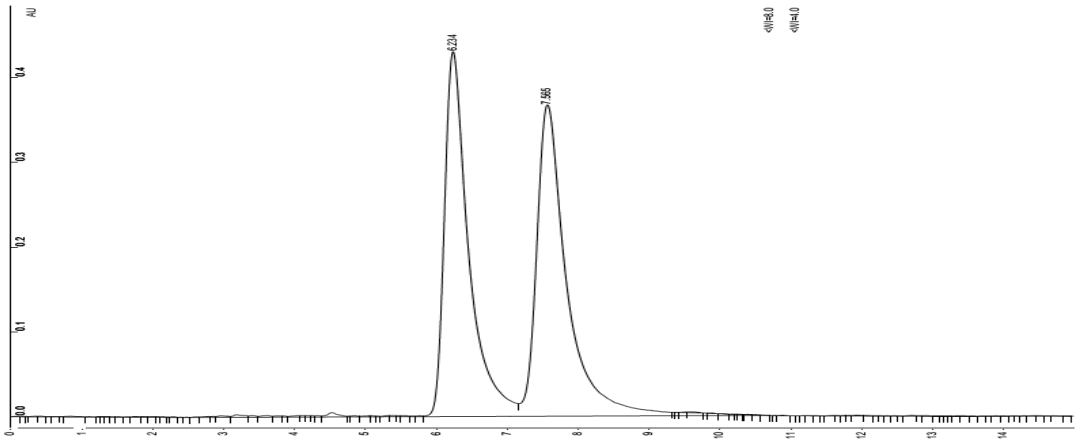
R.Time	Area	Area%
9.290	**162853104**	**95.8940**
10.915	**6973062**	**4.1060**

92% ee ($BrCH_2NO_2$ as nucleophile)



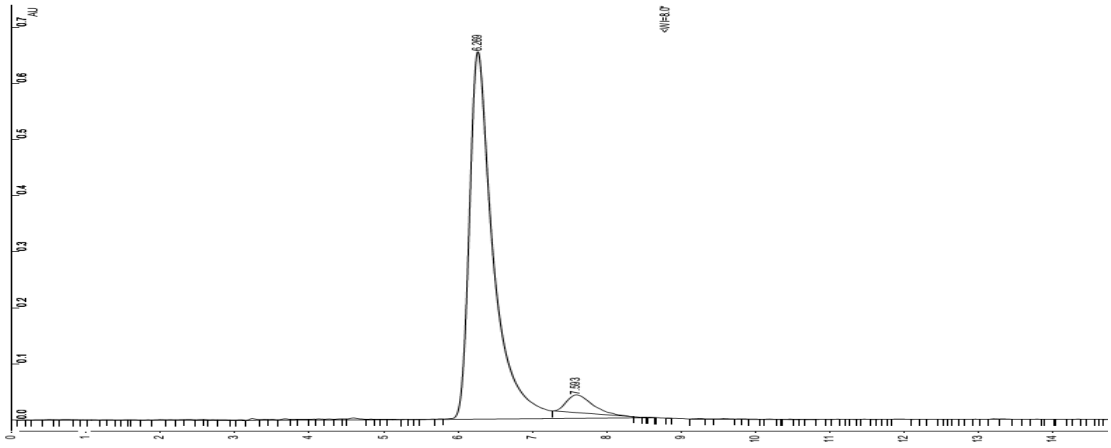
2c

Following the general procedure using **1c** (32.1mg, 0.1 mmol), **2c** was obtained by flash chromatography (petroleum ether/ethyl acetate: 8/1) as light yellow oil; Standard conditions 1: (24.8 mg, 65% yield, 93% ee). $[\alpha]_D^{25}$ +29.53 (*c* 0.25, $CHCl_3$). Standard conditions 2: (35.5 mg, 93% yield, 95% ee). $[\alpha]_D^{25}$ +31.27 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.9 Hz, 2H), 7.30 (d, *J* = 8.9 Hz, 2H), 6.11 (s, 1H), 4.58 (q, *J* = 12.3 Hz, 2H), 2.05 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.31, 156.26, 135.01, 129.83, 127.99, 118.95, 74.84, 62.78, 26.96, 12.75. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 6.23 min, τR (minor) = 7.56 min. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}N_4O_5ClNa$: 405.0942; found 405.0938.



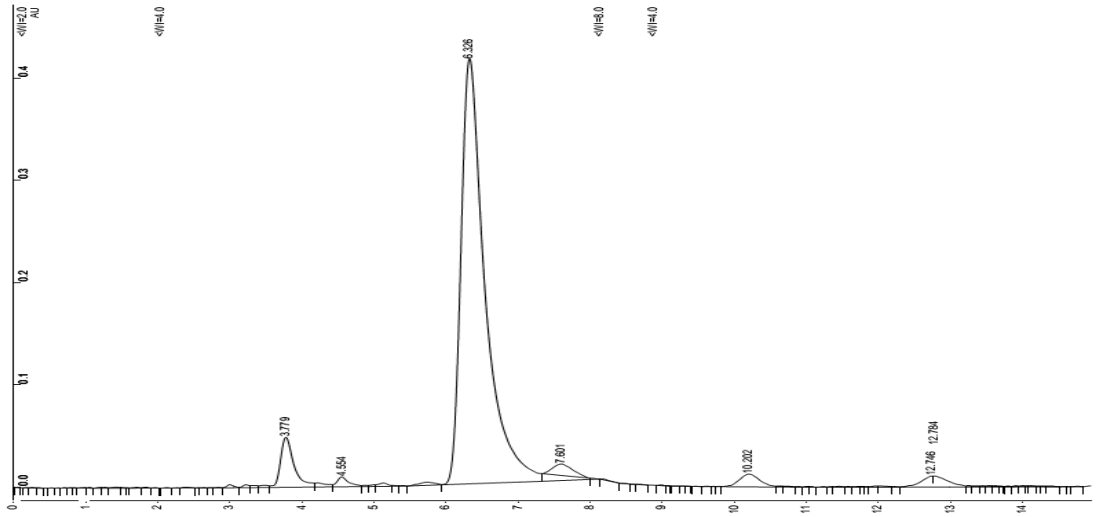
R.Time	Area	Area%
6.234	**102053064**	**49.9834**
7.565	**102120850**	**50.0166**

Racemic product



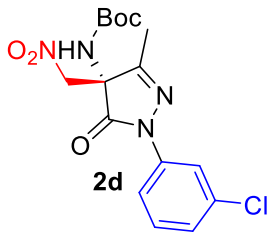
R.Time	Area	Area%
6.269	**150973984**	**96.4158**
7.593	**5612368**	**3.5842**

93% ee ($MeNO_2$ as nucleophile)

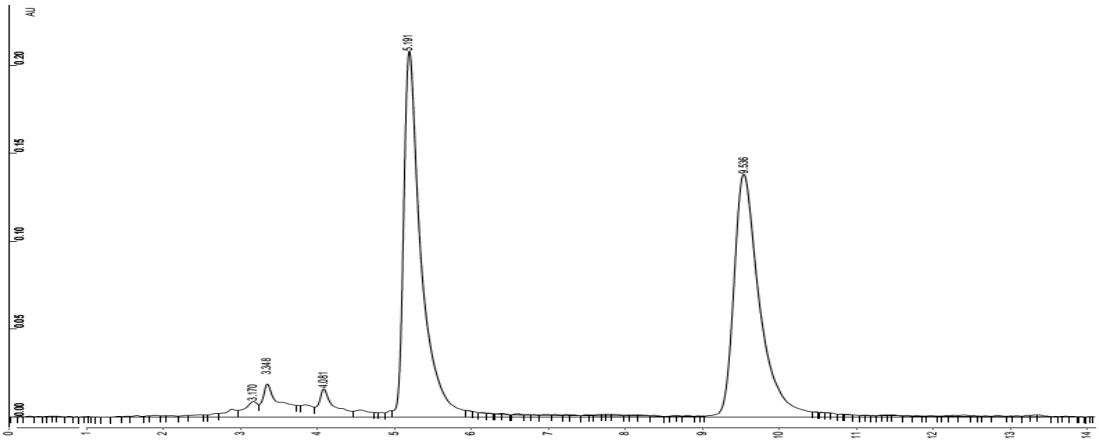


R.Time	Area	Area%
6.326	**98333392**	**97.5031**
7.601	**2518162**	**2.4969**

95% ee ($BrCH_2NO_2$ as nucleophile)

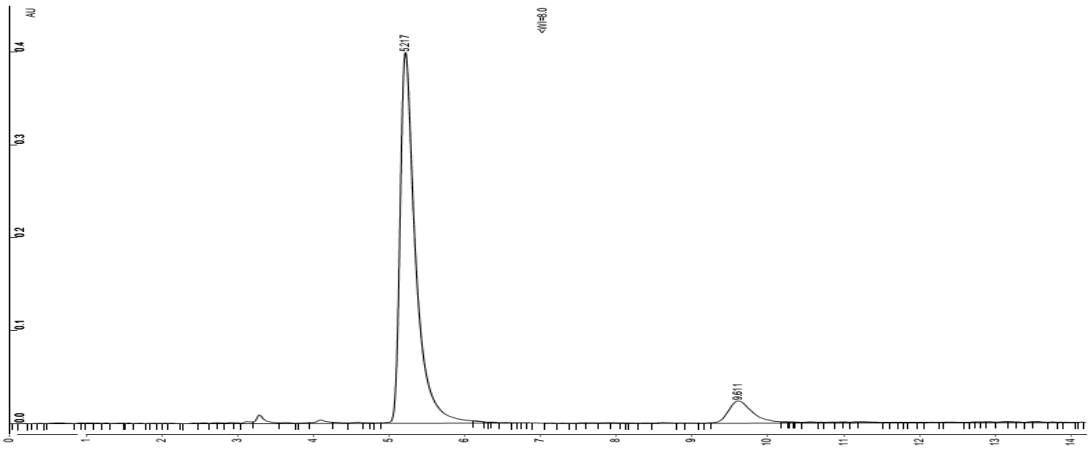


Following the general procedure using **1d** (32.1mg, 0.1 mmol), **2d** was obtained by flash chromatography (petroleum ether/ethyl acetate: 8/1) as colorless oil; Standard conditions 1: (25.9 mg, 68% yield, 87% ee). $[\alpha]_D^{25}$ +24.47 (*c* 0.25, $CHCl_3$). Standard conditions 2: (36.3 mg, 93% yield, 95% ee). $[\alpha]_D^{25}$ +28.71 (*c* 0.25, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 2.2 Hz, 1H), 7.75 (dd, *J* = 8.2, 2.0 Hz, 1H), 7.26 (t, *J* = 8.2 Hz, 1H), 7.11 (dd, *J* = 8.1, 1.9 Hz, 1H), 6.13 (s, 1H), 4.70 – 4.49 (m, 2H), 2.06 (s, 3H), 1.30 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 168.47, 157.36, 138.47, 134.74, 130.07, 125.67, 118.77, 116.63, 75.86, 63.89, 28.02, 13.77. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.19 min, τR (minor) = 9.53 min. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{16}H_{19}N_4O_5ClNa$: 405.0942; found 405.0940.



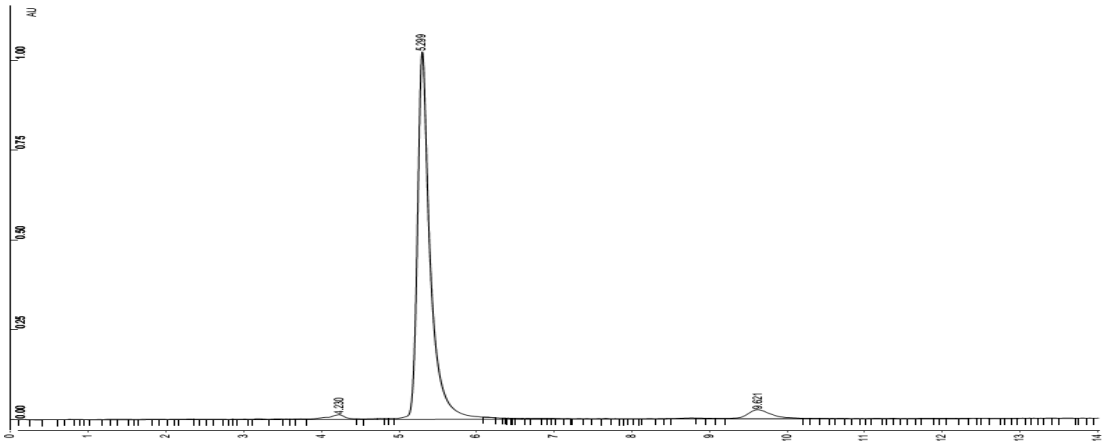
R.Time	Area	Area%
5.191	**34349632**	**50.1050**
9.536	**34205666**	**49.8950**

Racemic product



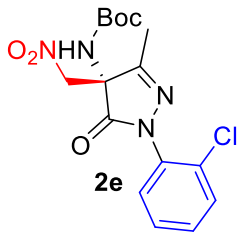
R.Time	Area	Area%
5.217	**56808476**	**93.3427**
9.611	**4051640**	**6.6573**

87% ee ($MeNO_2$ as nucleophile)



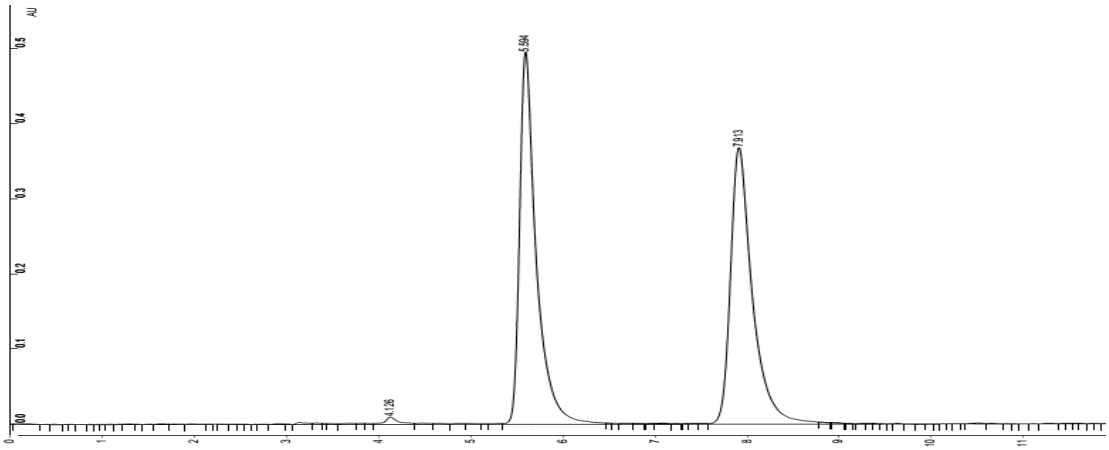
R.Time	Area	Area%
5.299	**119169440**	**97.5458**
9.621	**2998239**	**2.4542**

95% ee ($BrCH_2NO_2$ as nucleophile)



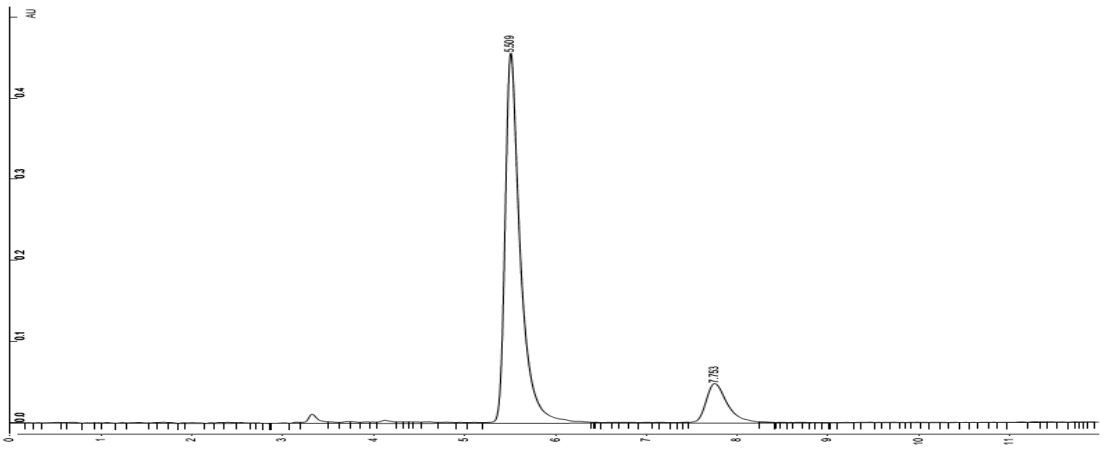
2e

Following the general procedure using **1e** (32.1mg, 0.1 mmol), **2e** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as colorless oil; Standard conditions 1: (24.1 mg, 63% yield, 82% ee). $[\alpha]_D^{25}$ +19.93 (*c* 0.25, $CHCl_3$). Standard conditions 2: (35.9 mg, 94% yield, 91% ee). $[\alpha]_D^{25}$ +23.15 (*c* 0.20, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.46 (m, 2H), 7.42 – 7.28 (m, 2H), 6.15 (s, 1H), 4.70 (q, *J* = 12.4 Hz, 2H), 2.08 (s, 3H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.37, 157.19, 153.59, 134.00, 130.30, 130.21, 128.65, 127.78, 82.29, 75.84, 62.72, 28.11, 13.91. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.59 min, τR (minor) = 7.91 min. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{16}H_{19}N_4O_5ClNa$: 405.0942; found 405.0935.



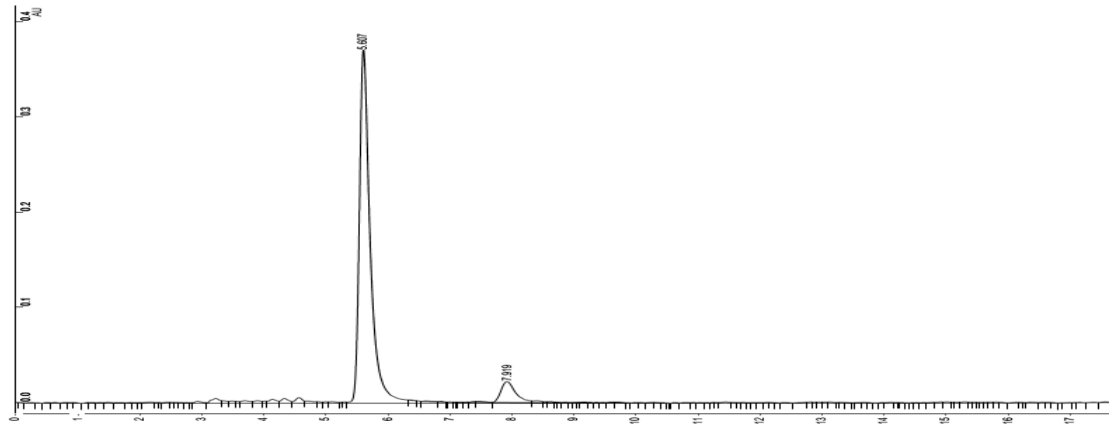
R.Time	Area	Area%
5.594	**62898808**	**50.2274**
7.913	**62329270**	**49.7726**

Racemic product



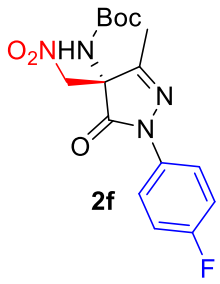
R.Time	Area	Area%
5.509	**53289724**	**90.8889**
7.753	**5536163**	**9.1111**

82% ee ($MeNO_2$ as nucleophile)



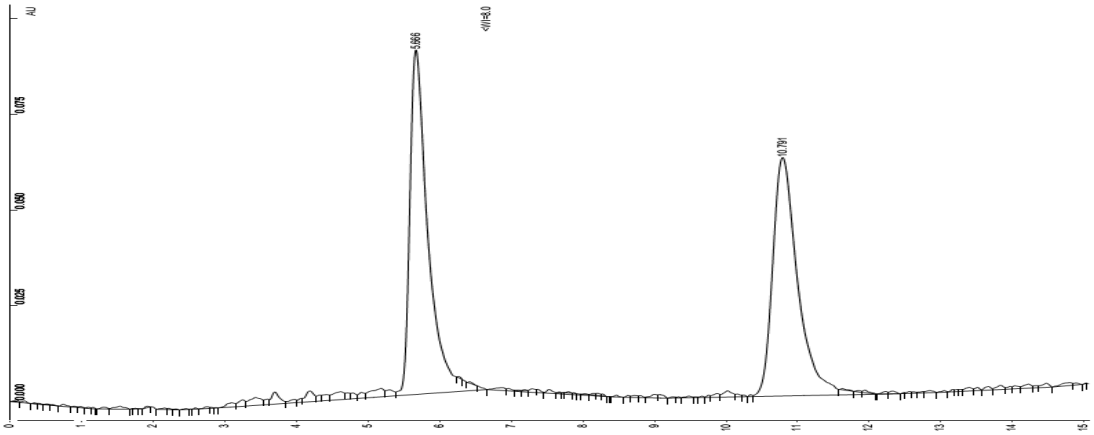
R.Time	Area	Area%
5.607	**47275852**	**95.3234**
7.919	**2423646**	**4.6766**

92% ee ($BrCH_2NO_2$ as nucleophile)



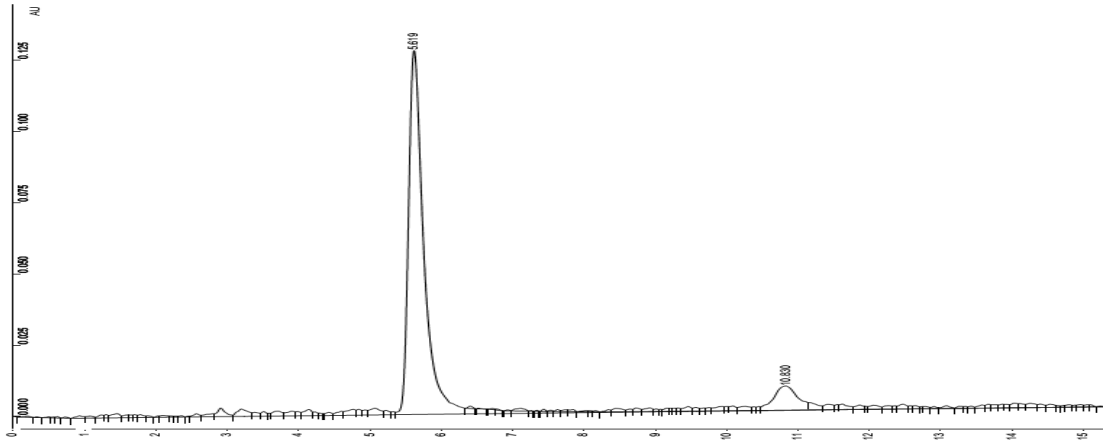
2f

Following the general procedure using **1f** (30.7 mg, 0.1 mmol), **2f** was obtained by flash chromatography (petroleum ether/ethyl acetate: 8/1) as light yellow solid; Mp 122-124 °C; Standard conditions 1: (19.4 mg, 53% yield, 85% ee). $[\alpha]_D^{25}$ +17.63 (*c* 0.20, $CHCl_3$). Standard conditions 2: (32.6mg, 89% yield, 90% ee). $[\alpha]_D^{25}$ +19.28 (*c* 0.20, $CHCl_3$). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.64 (m, 2H), 7.09 – 6.90 (m, 2H), 6.16 (s, 1H), 4.70 – 4.51 (m, 2H), 2.05 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.39, 160.26 (d, *J* = 245.2 Hz), 157.20, 133.64, 133.61, 120.84, 115.85, 115.62, 75.92, 63.79, 28.02, 13.75.^{19}F NMR (376 MHz, $CDCl_3$) δ -116.03 (s, 1F). HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.66 min, τR (minor) = 10.79 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{20}N_4O_5F$: 367.1418; found 367.1425.



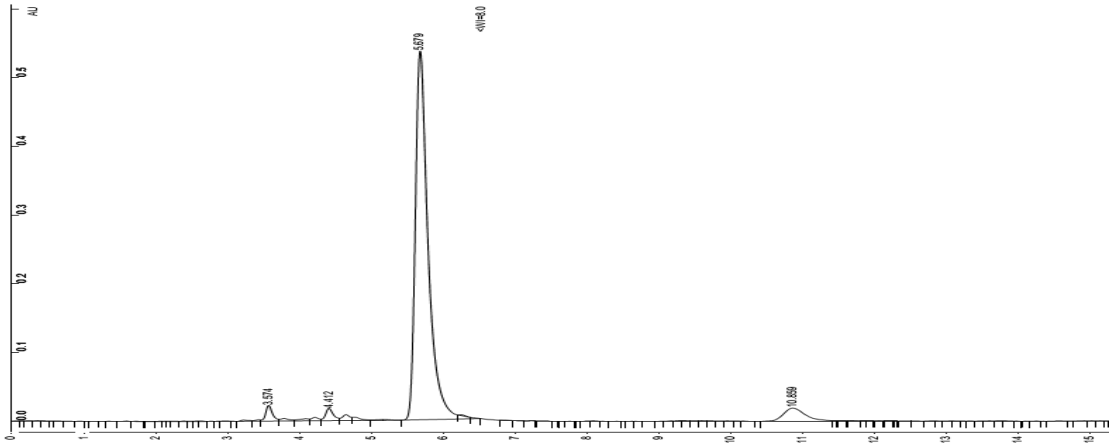
R.Time	Area	Area%
5.666	**15901312**	**51.1245**
10.791	**15201813**	**48.8755**

Racemic product



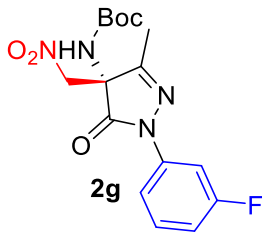
R.Time	Area	Area%
5.619	**20150660**	**92.5120**
10.830	**1631012**	**7.4880**

85% ee ($MeNO_2$ as nucleophile)



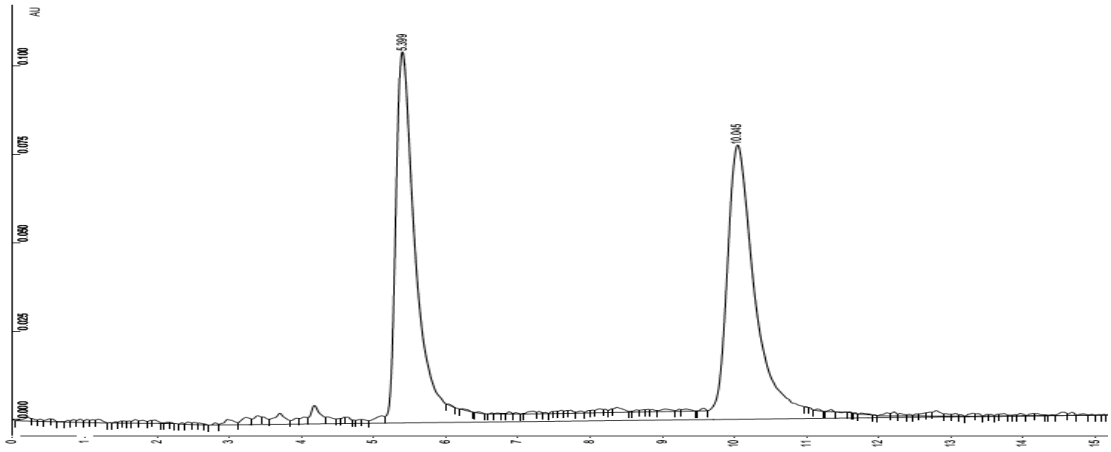
R.Time	Area	Area%
5.679	**66353884**	**95.0158**
10.859	**3480695**	**4.9842**

90% ee ($BrCH_2NO_2$ as nucleophile)



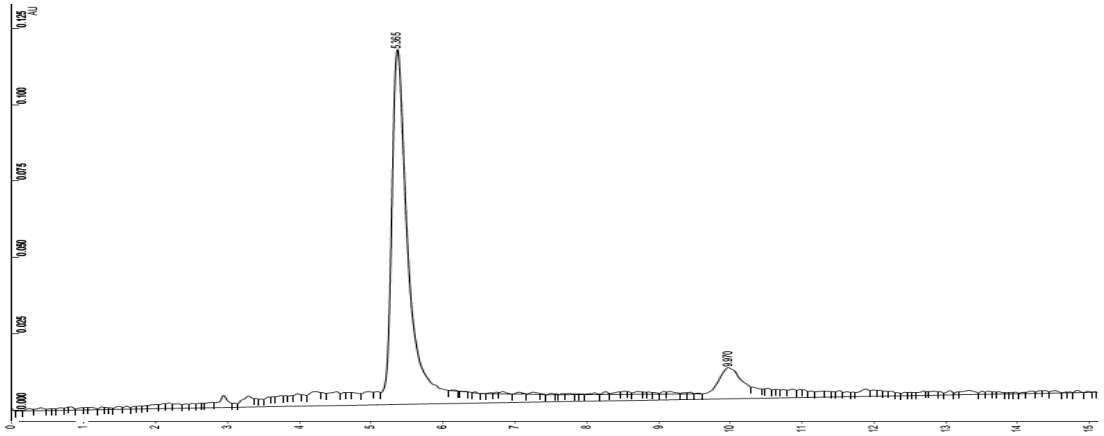
2g

Following the general procedure using **1g** (30.7 mg, 0.1 mmol), **2g** was obtained by flash chromatography (petroleum ether/ethyl acetate: 8/1) as light yellow solid; Mp 112-114 ºC; Standard conditions 1: (19.5 mg, 53% yield, 84% ee). $[\alpha]_D^{25}$ +17.63 (*c* 0.20, $CHCl_3$). Standard conditions 2: (33.2 mg, 91% yield, 91% ee). $[\alpha]_D^{25}$ +21.59 (*c* 0.20, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.54 (m, 2H), 7.41 – 7.24 (m, 1H), 6.95 – 6.74 (m, 1H), 6.11 (s, 1H), 4.58 (q, *J* = 12.3 Hz, 2H), 2.06 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.41, 162.84 (d, *J* = 245.3 Hz), 157.29, 138.86, 138.76, 130.34, 130.25, 114.05, 112.51, 112.30, 106.22 (d, *J* = 26.4 Hz), 63.93, 28.01, 13.78. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.03 (s, 1F). HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.39 min, τR (minor) = 10.04 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{20}N_4O_5F$: 367.1418; found 367.1421.



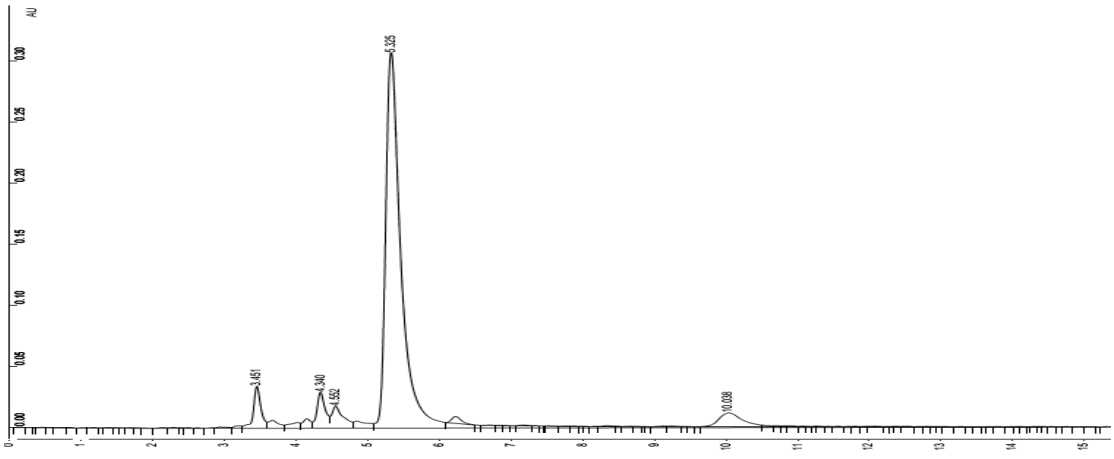
R.Time	Area	Area%
5.399	**24541364**	**50.8519**
10.045	**23719102**	**49.1481**

Racemic product



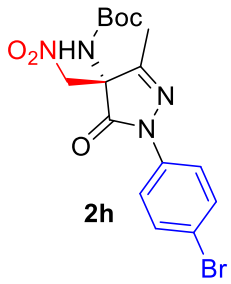
R.Time	Area	Area%
5.365	**23356434**	**91.8288**
9.970	**2078325**	**8.1712**

84% ee ($MeNO_2$ as nucleophile)



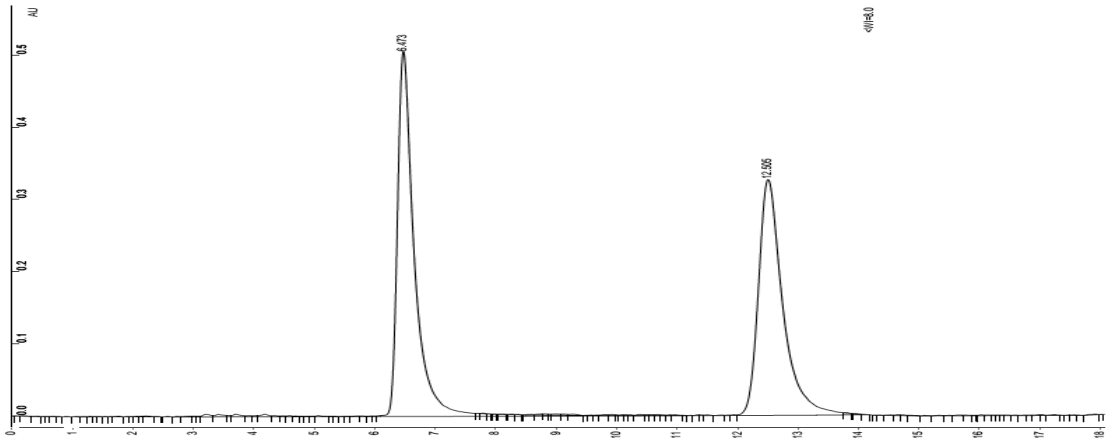
R.Time	Area	Area%
5.325	**48813840**	**95.5180**
10.038	**2290496**	**4.4820**

91% ee ($BrCH_2NO_2$ as nucleophile)



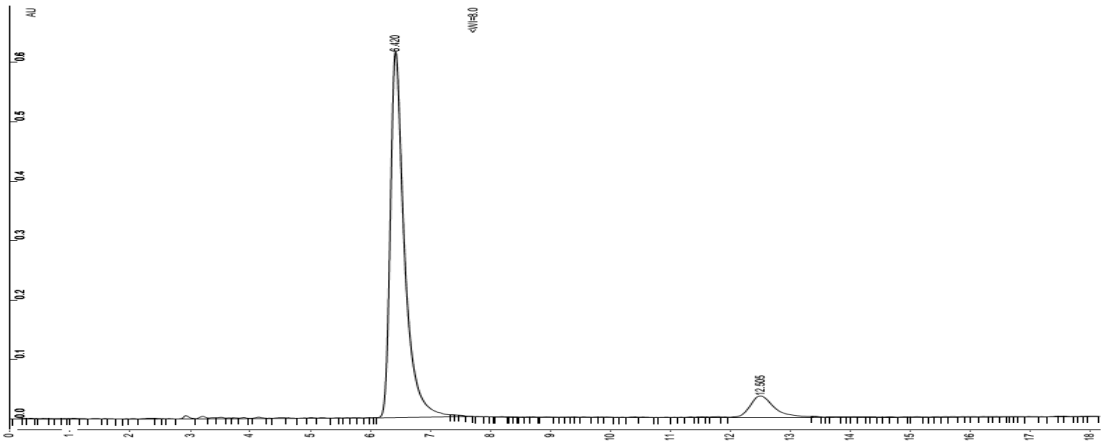
2h

Following the general procedure using **1h** (36.5 mg, 0.1 mmol), **2g** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow oil; Standard conditions 1: (26.0 mg, 61% yield, 84% ee). $[\alpha]_D^{25}$ +26.72 (*c* 0.20, $CHCl_3$). Standard conditions 2: (40.4 mg, 95% yield, 90% ee). $[\alpha]_D^{25}$ +31.25 (*c* 0.20, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.9 Hz, 2H), 7.44 (d, *J* = 8.9 Hz, 2H), 6.11 (s, 1H), 4.70 – 4.34 (m, 2H), 2.05 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.32, 135.51, 130.94, 119.22, 117.62, 62.79, 26.97, 16.32. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 6.47 min, τR (minor) = 12.50 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{20}N_4O_5Br$: 427.0617; found 427.0613.



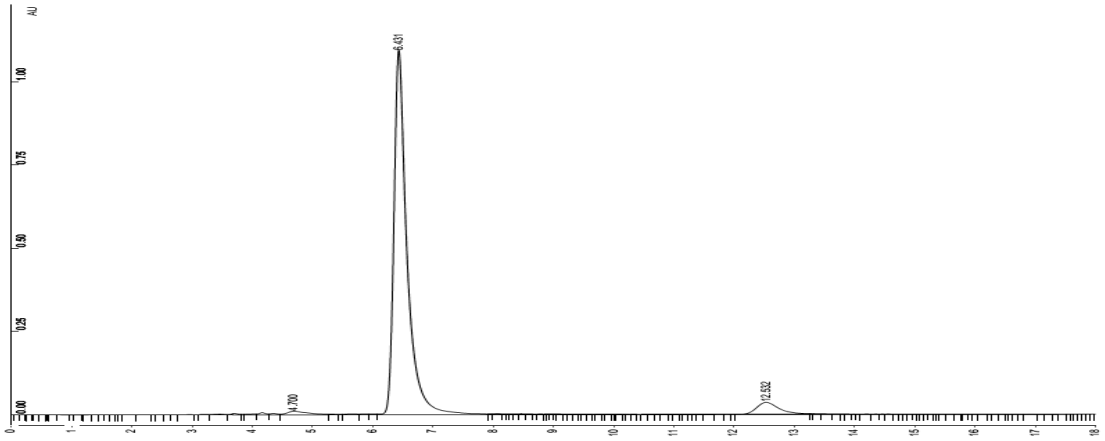
R.Time	Area	Area%
6.473	**98951840**	**50.0228**
12.505	**98861637**	**49.9772**

Racemic product



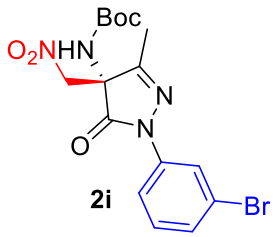
R.Time	Area	Area%
6.420	**100709016**	**91.8542**
12.505	**8931061**	**8.1458**

84% ee ($MeNO_2$ as nucleophile)



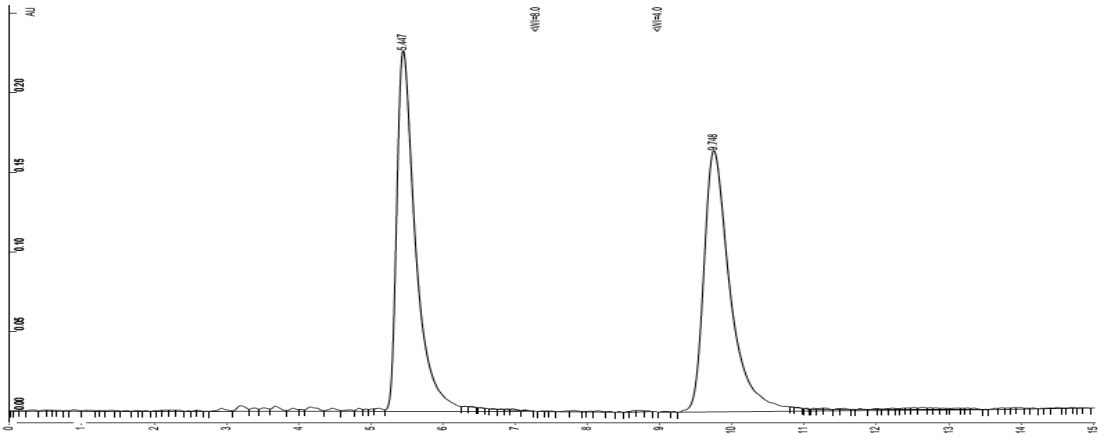
R.Time	Area	Area%
6.431	**167986176**	**94.9934**
12.53	**8853663**	**5.0066**

90% ee ($BrCH_2NO_2$ as nucleophile)



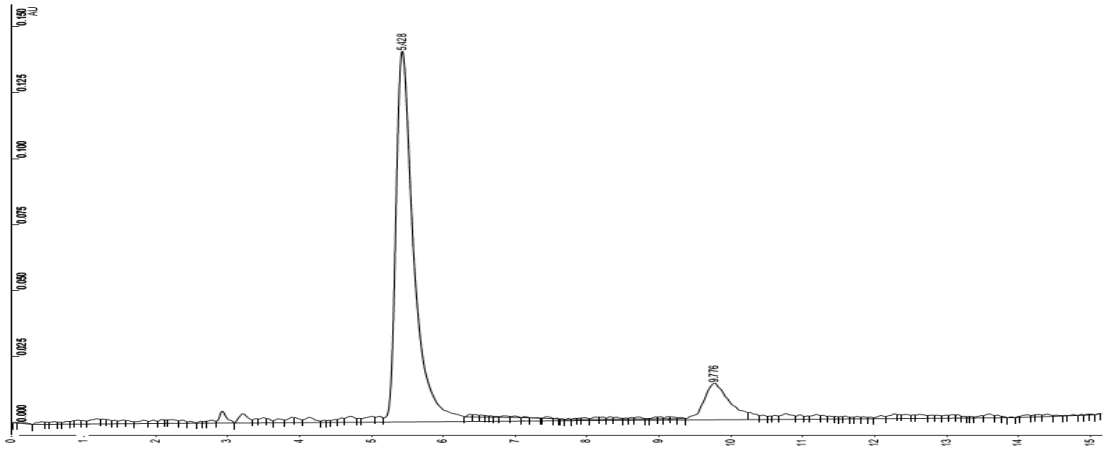
2i

Following the general procedure using **1i** (36.5 mg, 0.1 mmol), **2i** was obtained by flash chromatography (petroleum ether/ethyl acetate: 12/1) as light yellow wax; Standard conditions 1: (26.8 mg, 63% yield, 79% ee). $[\alpha]_D^{25}$ +18.05 (*c* 0.20, $CHCl_3$). Standard conditions 2: (40.5 mg, 95% yield, 90% ee). $[\alpha]_D^{25}$ +23.67 (*c* 0.20, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (t, *J* = 2.0 Hz, 1H), 7.89 – 7.71 (m, 1H), 7.33 – 7.10 (m, 2H), 6.06 (s, 1H), 4.57 (q, *J* = 12.3 Hz, 2H), 2.06 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.31, 156.29, 137.51, 129.27, 127.56, 121.62, 120.53, 116.03, 74.84, 62.78, 26.98, 12.59. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.44 min, τR (minor) = 9.74 min. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{16}H_{20}N_4O_5Br$: 427.0617; found 427.0620.



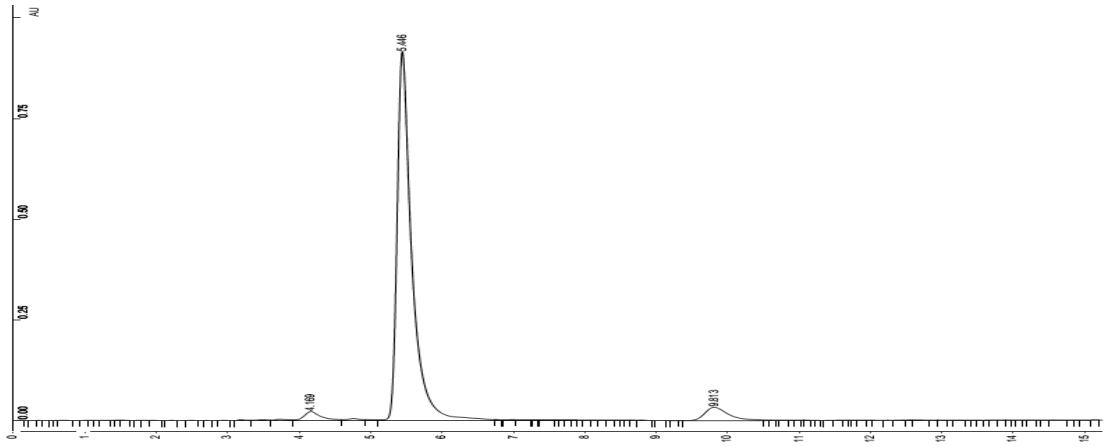
R.Time	Area	Area%
5.447	**41554840**	**49.6707**
9.748	**42105829**	**50.3293**

Racemic product



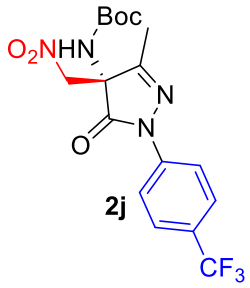
R.Time	Area	Area%
5.428	**25683384**	**89.4256**
9.776	**3037009**	**10.5744**

84% ee ($MeNO_2$ as nucleophile)

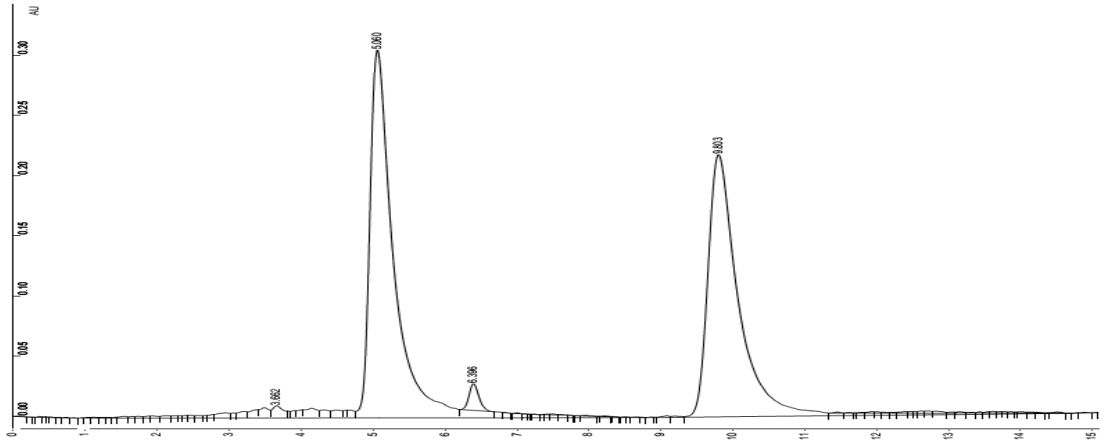


R.Time	Area	Area%
5.446	**131779296**	**95.1073**
9.813	**6779254**	**4.8927**

90% ee ($BrCH_2NO_2$ as nucleophile)

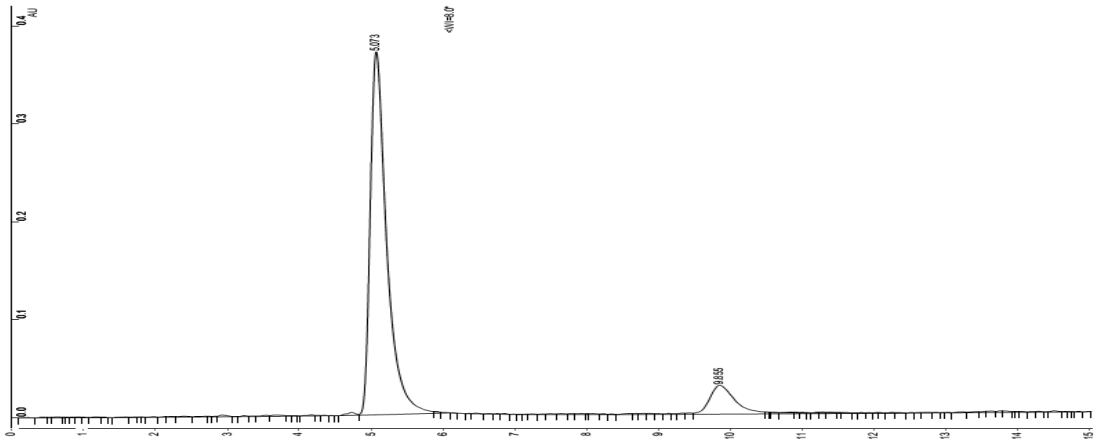


Following the general procedure using **1j** (35.5 mg, 0.1 mmol), **2j** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow oil; Standard conditions 1: (21.2 mg, 51% yield, 80% ee). $[\alpha]_D^{25}$ +31.21 (*c* 0.25, $CHCl_3$). Standard conditions 2: (37.8 mg, 91% yield, 89% ee). $[\alpha]_D^{25}$ +37.63 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 6.15 (s, 1H), 4.68 – 4.50 (m, 2H), 2.07 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.82, 157.57, 153.35, 140.21, 126.25, 126.22, 123.98 (q, *J* = 271.8 Hz), 127.26 (q, *J* = 32.8 Hz), 118.33, 63.92, 27.98, 13.74. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.22 (s, 3F). HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.06 min, τR (minor) = 9.08 min. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{17}H_{19}N_4O_5F_3$: 439.1205; found 439.1211.



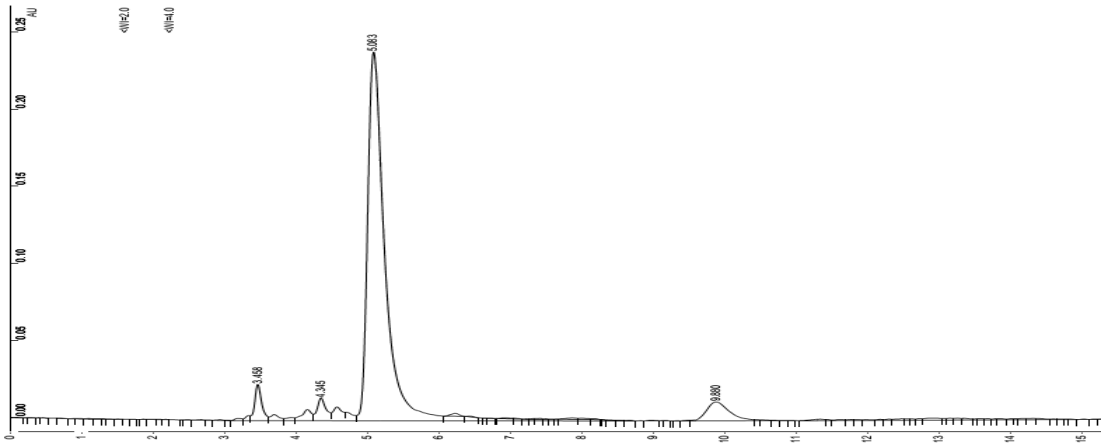
R.Time	Area	Area%
5.060	**72501744**	**50.3732**
9.803	**71427456**	**49.6268**

Racemic product



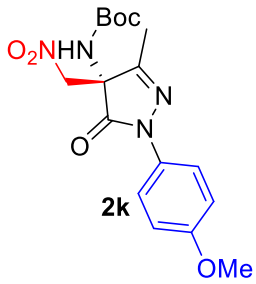
R.Time	Area	Area%
5.073	**58485632**	**90.0700**
9.855	**6447900**	**9.9300**

80% ee ($MeNO_2$ as nucleophile)

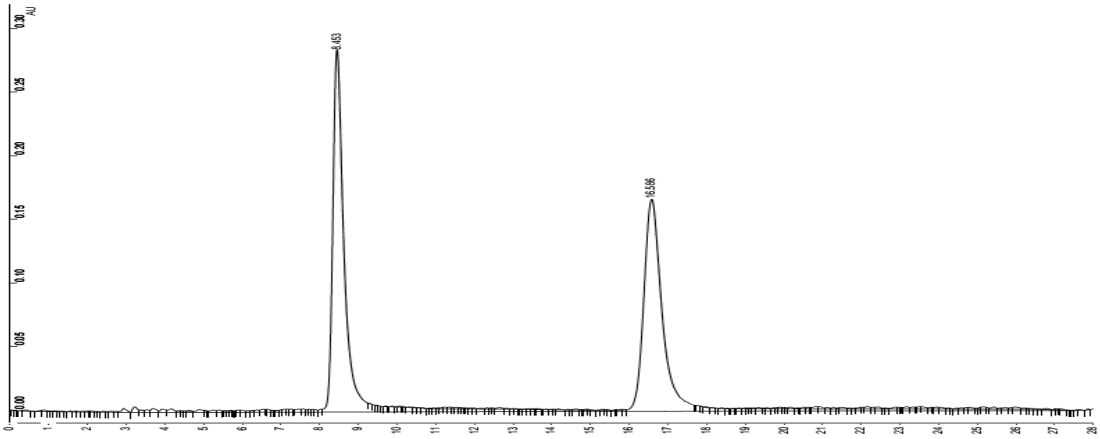


R.Time	Area	Area%
5.083	**41340596**	**94.4506**
9.880	**2428947**	**5.5494**

89% ee ($BrCH_2NO_2$ as nucleophile)

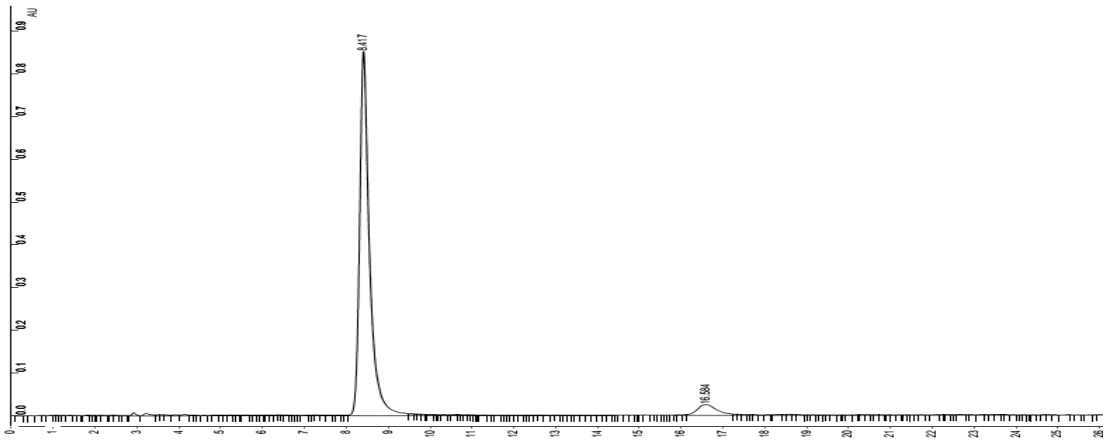


Following the general procedure using **1k** (31.7 mg, 0.1 mmol), **2k** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow oil; Standard conditions 1: (27.9 mg, 74% yield, 92% ee). $[\alpha]_D^{25}$ +35.18 (*c* 0.25, $CHCl_3$). Standard conditions 2: (36.6 mg, 97% yield, 95% ee). $[\alpha]_D^{25}$ +38.64 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 9.1 Hz, 2H), 6.86 (d, *J* = 9.1 Hz, 2H), 6.01 (s, 1H), 4.68 – 4.40 (m, 2H), 3.75 (s, 3H), 2.04 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.97, 156.46, 155.87, 129.73, 119.93, 113.05, 75.03, 54.46, 27.00, 12.59. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 8.45 min, τR (minor) = 16.58 min. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{17}H_{23}N_4O_6$: 379.1618; found 379.1623.



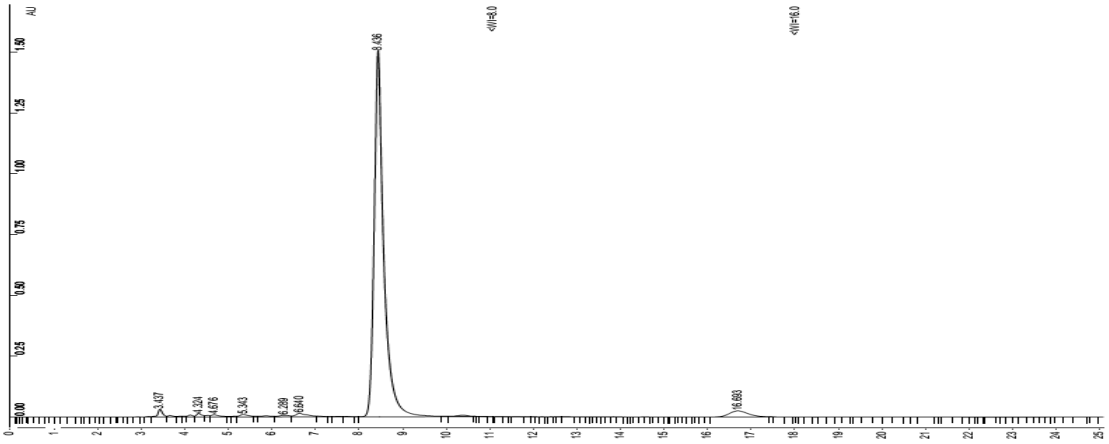
R.Time	Area	Area%
8.453	**64719952**	**50.4537**
16.586	**63555916**	**49.5463**

Racemic product



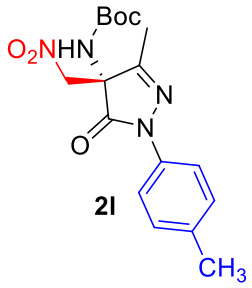
R.Time	Area	Area%
8.417	**141553248**	**96.0580**
16.584	**5809021**	**3.9420**

92% ee ($MeNO_2$ as nucleophile)



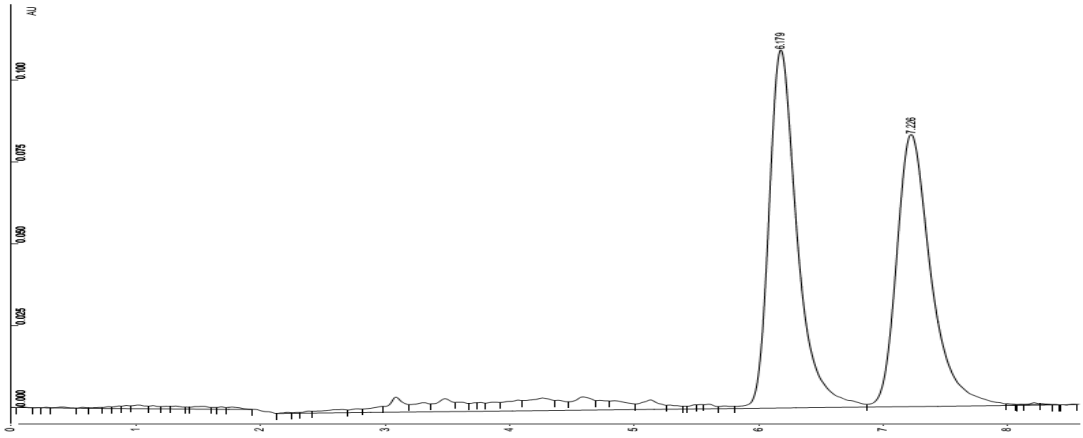
R.Time	Area	Area%
8.436	**226853408**	**97.4610**
16.693	**5909859**	**2.5390**

95% ee ($BrCH_2NO_2$ as nucleophile)



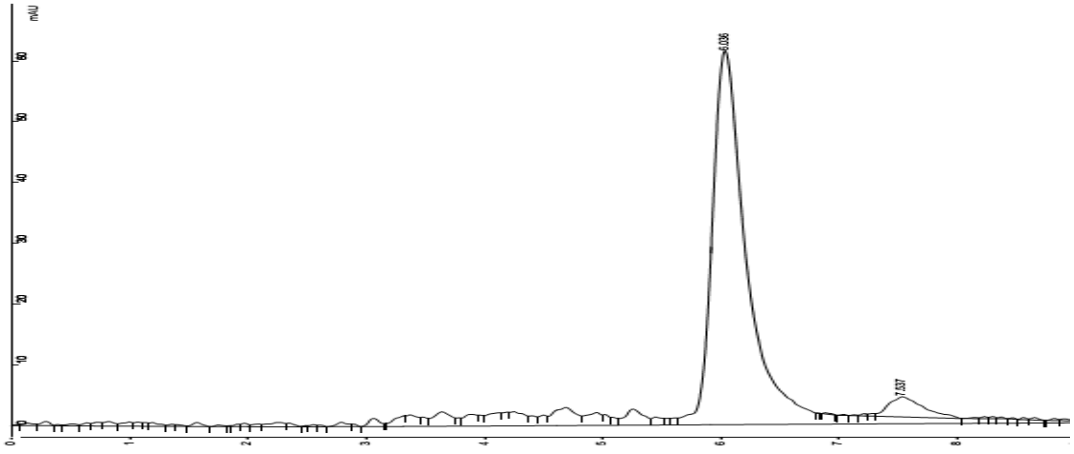
2l

Following the general procedure using **1l** (30.1 mg, 0.1 mmol), **2l** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow solid; Mp 112-114 °C; Standard conditions 1: (25.7 mg, 71% yield, 93% ee). $[\alpha]_D^{25}$ +18.83 (*c* 0.25, $CHCl_3$). Standard conditions 2: (34.7 mg, 96% yield, 95% ee). $[\alpha]_D^{25}$ +21.16 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.2 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.14 (s, 1H), 4.67 – 4.41 (m, 2H), 2.27 (s, 3H), 2.04 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.32, 156.99, 153.32, 135.57, 135.04, 119.05, 76.00, 63.83, 28.03, 21.02, 13.80. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 6.03 min, τR (minor) = 7.53 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{23}N_4O_5$: 363.1668; found 363.1671.



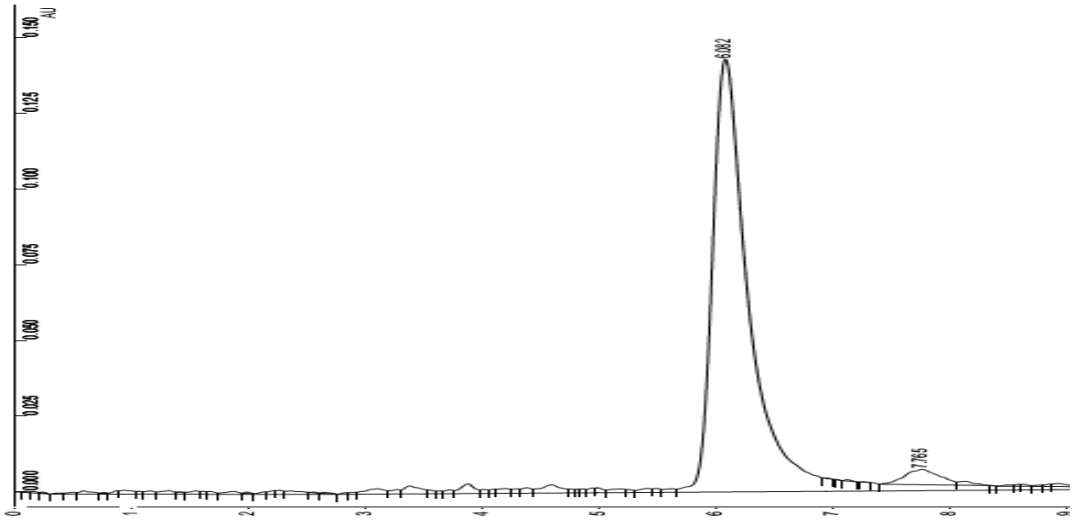
R.Time	Area	Area%
6.179	**17187692**	**50.8712**
7.266	**16598992**	**49.1288**

Racemic product



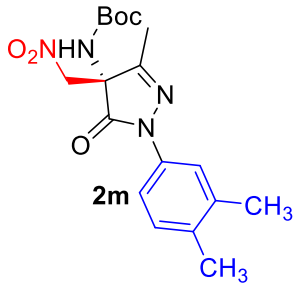
R.Time	Area	Area%
6.036	**13623414**	**96.2725**
7.537	**527474**	**3.7275**

92% ee ($MeNO_2$ as nucleophile)

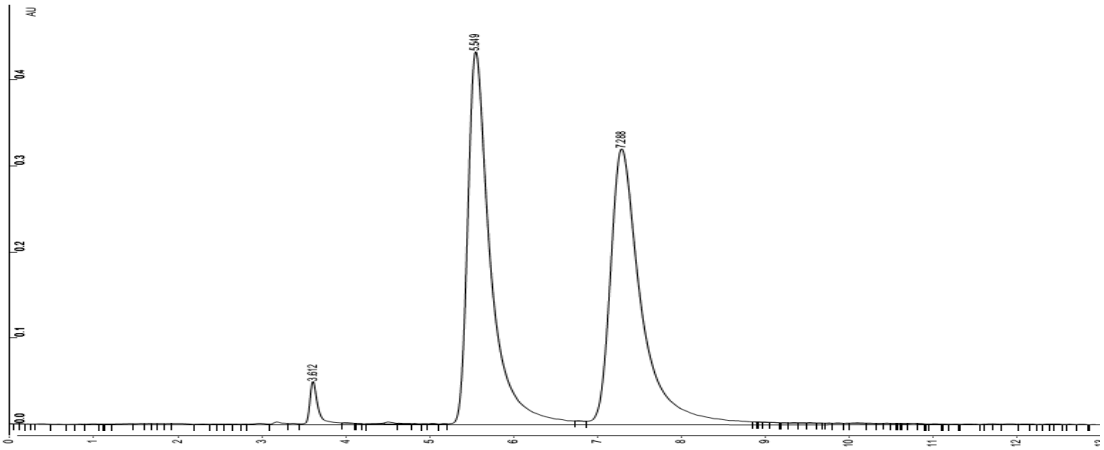


R.Time	Area	Area%
6.082	**33652804**	**97.5050**
7.765	**861122**	**2.4950**

95% ee ($BrCH_2NO_2$ as nucleophile)

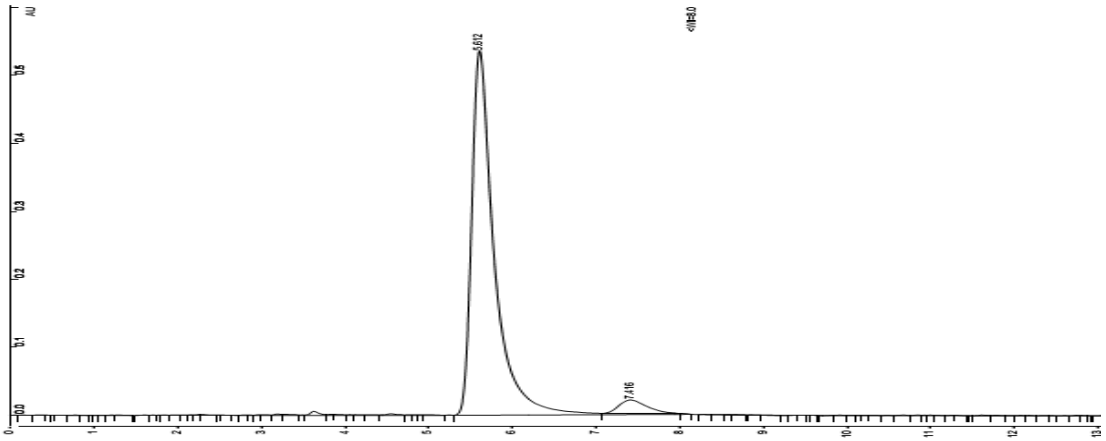


Following the general procedure using **1m** (31.5 mg, 0.1 mmol), **2m** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as white solid; Mp 155-158 °C; Standard conditions 1: (25.2mg, 67% yield, 92% ee). $[\alpha]_D^{25}$ +21.25 (*c* 0.25, $CHCl_3$). Standard conditions 2: (35.7 mg, 95% yield, 96% ee). $[\alpha]_D^{25}$ +24.92 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 2.2 Hz, 1H), 7.48 (dd, *J* = 8.2, 2.3 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 1H), 6.14 (s, 1H), 4.67 – 4.43 (m, 2H), 2.21 (s, 3H), 2.17 (s, 3H), 2.04 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.32, 156.94, 153.35, 137.36, 135.23, 134.35, 129.95, 120.27, 116.68, 76.01, 63.81, 28.04, 20.01, 19.37, 13.79. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.54 min, τR (minor) = 7.29 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{25}N_4O_5$: 377.1825; found 377.1828.



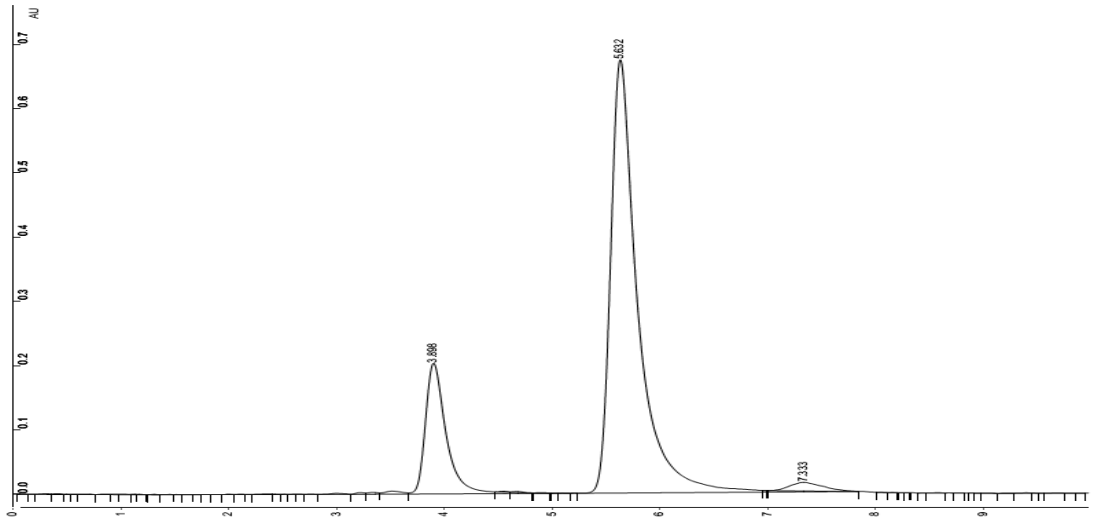
R.Time	Area	Area%
5.549	**82185080**	**50.5350**
7.288	**80444939**	**49.4650**

Racemic product



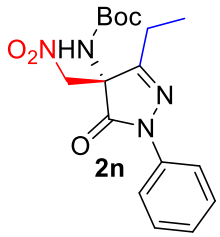
R.Time	Area	Area%
5.612	**101089368**	**96.0098**
7.416	**4201308**	**3.9902**

92% ee ($MeNO_2$ as nucleophile)

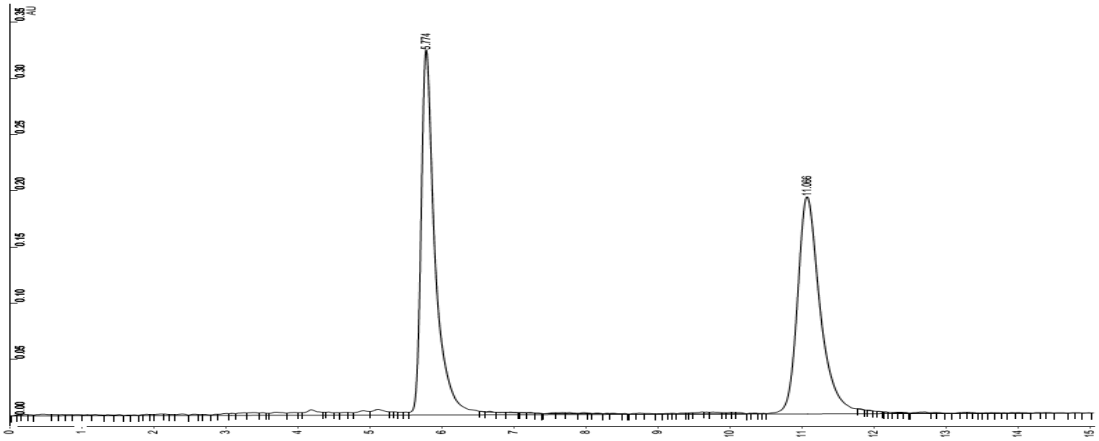


R.Time	Area	Area%
5.622	**118362848**	**98.0135**
7.333	**2405013**	**1.9865**

96% ee ($BrCH_2NO_2$ as nucleophile)

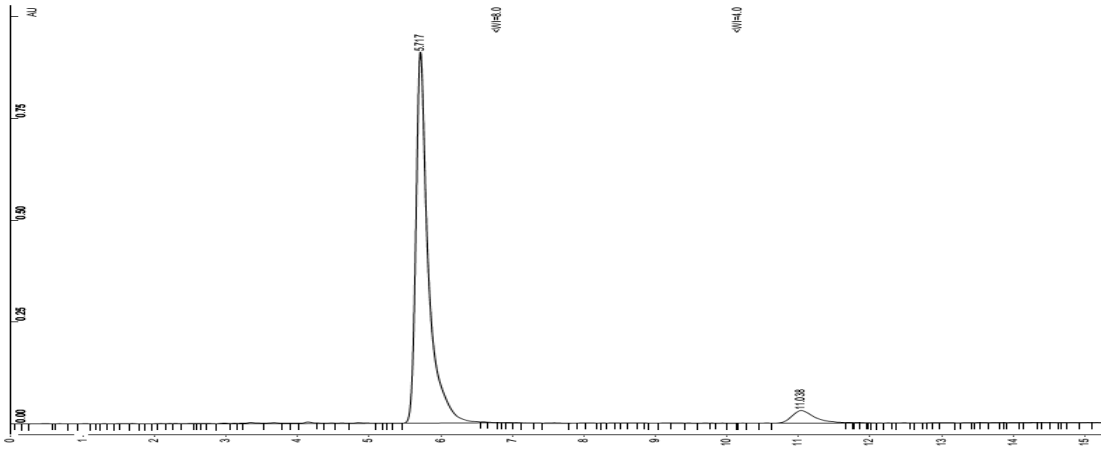


Following the general procedure using **1n** (30.1 mg, 0.1 mmol), **2n** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow solid; Mp 148-150 °C; Standard conditions 1: (20.3 mg, 56% yield, 89% ee). $[\alpha]_D^{25}$ +19.43 (*c* 0.25, $CHCl_3$). Standard conditions 2: (33.4 mg, 94% yield, 95% ee). $[\alpha]_D^{25}$ +22.79 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.20 (s, 1H), 4.58 (d, *J* = 2.7 Hz, 2H), 2.44 – 2.17 (m, 2H), 1.41 – 1.13 (m, 12H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.74, 160.82, 153.33, 137.64, 128.96, 125.69, 118.96, 76.09, 64.06, 28.01, 21.34, 9.41. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.77 min, τR (minor) =11.07 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{23}N_4O_5$: 363.1668; found 363.1671.



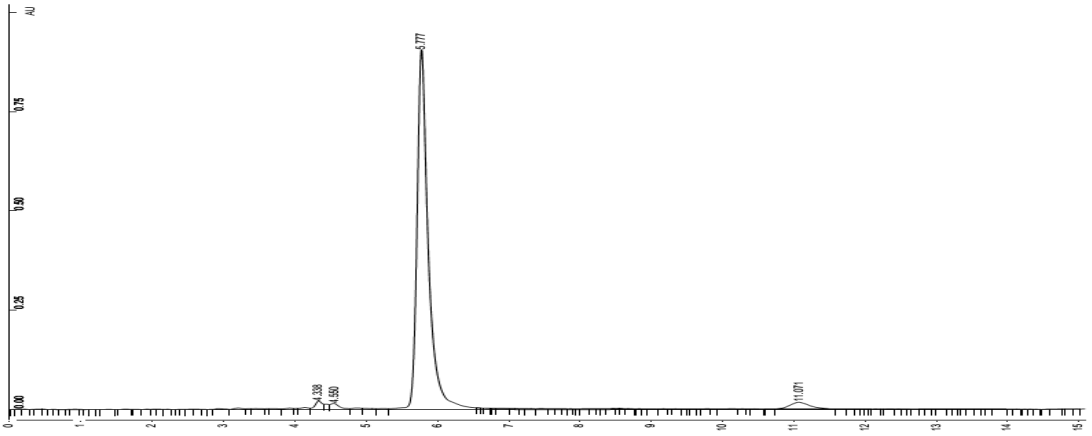
R.Time	Area	Area%
5.774	**45225660**	**51.3906**
11.066	**42778052**	**48.6094**

Racemic product



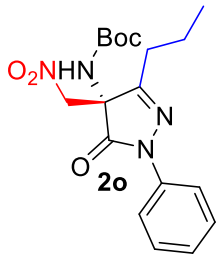
R.Time	Area	Area%
5.717	**109937448**	**94.5943**
11.038	**6282502**	**5.4057**

89% ee ($MeNO_2$ as nucleophile)

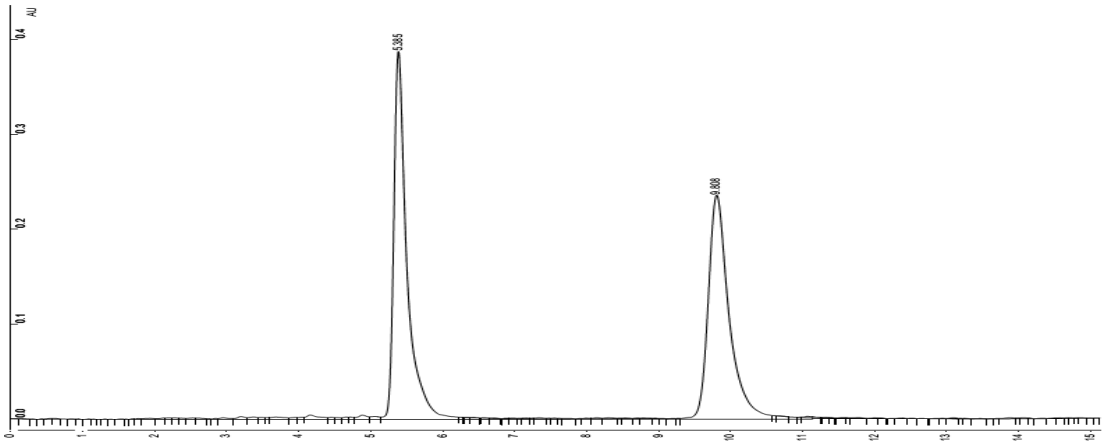


R.Time	Area	Area%
5.777	**105278400**	**97.1806**
11.071	**3054333**	**2.8194**

95% ee ($BrCH_2NO_2$ as nucleophile)

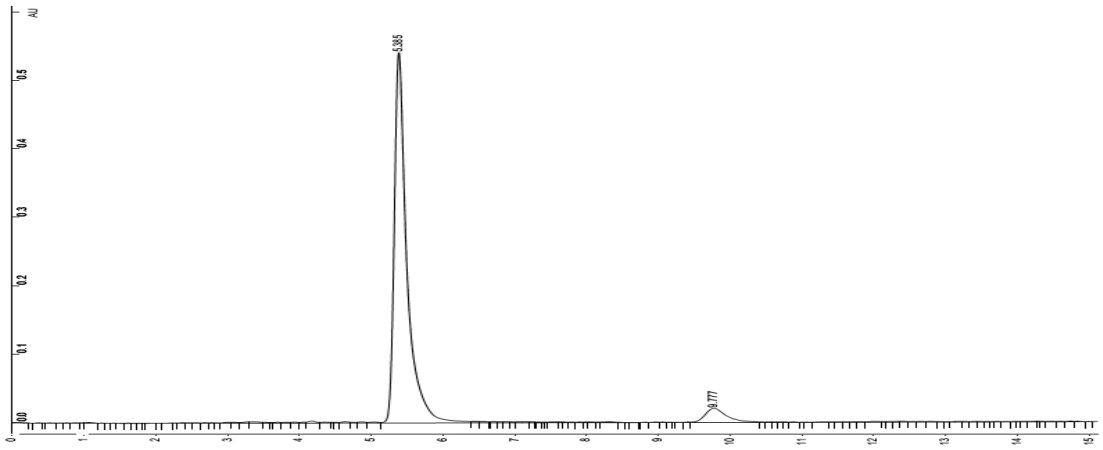


Following the general procedure using **1o** (31.5 mg, 0.1 mmol), **2o** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow solid; Mp 155-157 °C; Standard conditions 1: (20.3 mg, 54% yield, 90% ee). $[\alpha]_D^{25}$ +17.51 (*c* 0.25, $CHCl_3$). Standard conditions 2: (35.3 mg, 94% yield, 91% ee). $[\alpha]_D^{25}$ +17.73 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.41 (t, *J* = 7.9 Hz, 2H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.24 (s, 1H), 4.74 – 4.54 (m, 2H), 2.34 (q, *J* = 7.0 Hz, 2H), 1.81 (q, *J* = 7.4 Hz, 2H), 1.36 (s, 9H), 1.04 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.57, 159.64, 153.29, 137.65, 128.96, 125.67, 118.93, 76.10, 64.02, 28.02, 18.58, 13.90. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.38 min, τR (minor) =9.80 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{25}N_4O_5$: 377.1825; found 377.1831.



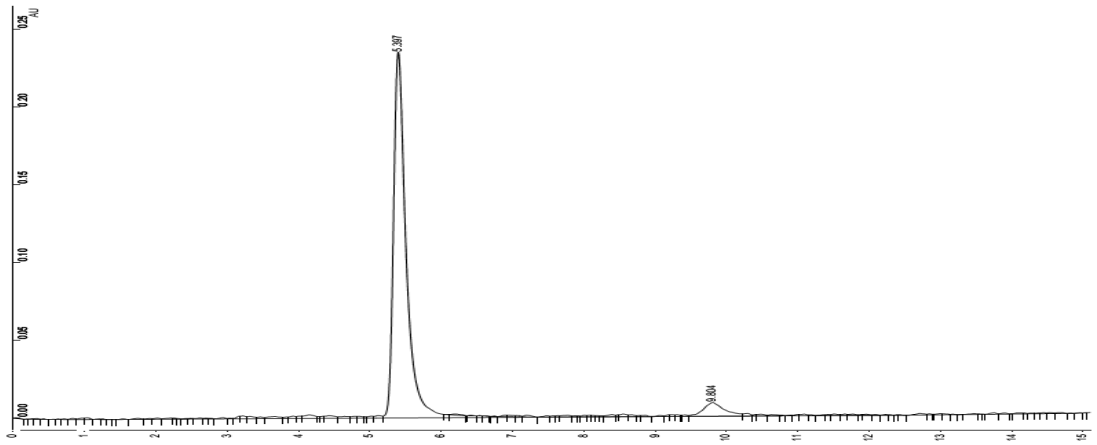
R.Time	Area	Area%
5.385	**49805624**	**50.6324**
9.808	**48561536**	**49.3676**

Racemic product



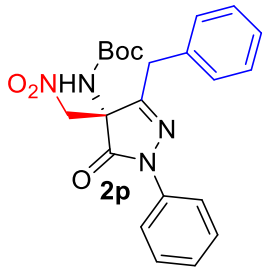
R.Time	Area	Area%
5.385	**67002792**	**94.9288**
9.777	**3579362**	**5.0712**

90% ee ($MeNO_2$ as nucleophile)

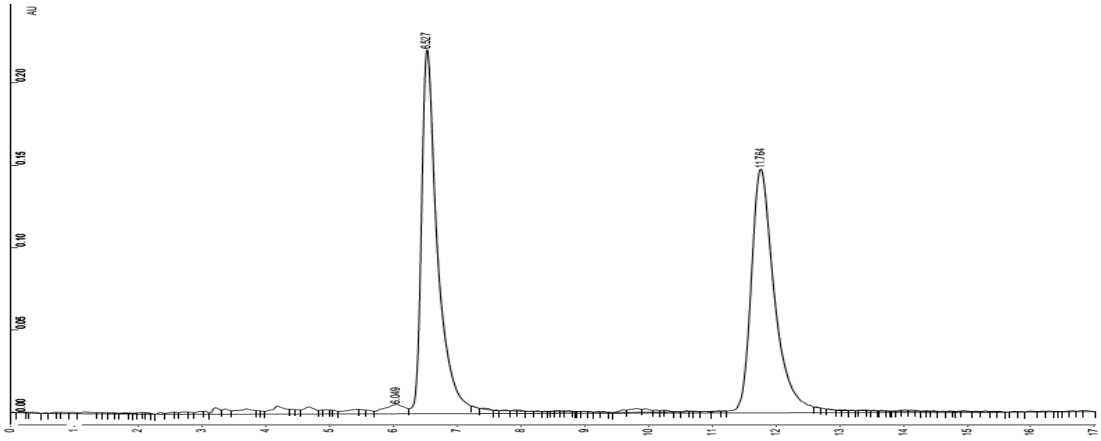


R.Time	Area	Area%
5.397	**29255060**	**95.5944**
9.804	**1348260**	**4.4056**

91% ee ($BrCH_2NO_2$ as nucleophile)

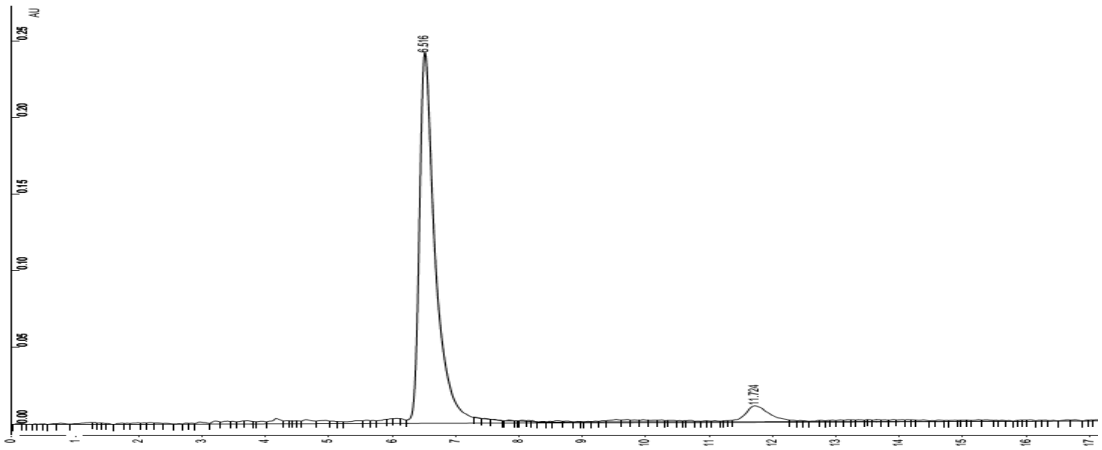


Following the general procedure using **1p** (36.3 mg, 0.1 mmol), **2p** was obtained by flash chromatography (petroleum ether/ethyl acetate: 12/1) as light yellow oil; Standard conditions 1: (25.0 mg, 59% yield, 90% ee). $[\alpha]_D^{25}$ +14.38 (*c* 0.25, $CHCl_3$). Standard conditions 2: (39.4 mg, 93% yield, 95% ee). $[\alpha]_D^{25}$ +17.62 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.9 Hz, 2H), 7.37 – 7.26 (m, 5H), 7.21 (t, *J* = 7.4 Hz, 1H), 6.16 (s, 1H), 4.42 – 4.20 (m, 2H), 3.95 – 3.66 (m, 2H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.59, 157.72, 153.39, 137.55, 133.84, 129.39, 129.05, 128.99, 127.67, 125.75, 119.01, 75.72, 63.73, 34.98, 28.02. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 6.53 min, τR (minor) =11.76 min. HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ calcd for $C_{22}H_{24}N_4O_5Na$: 447.1644; found 447.1641.



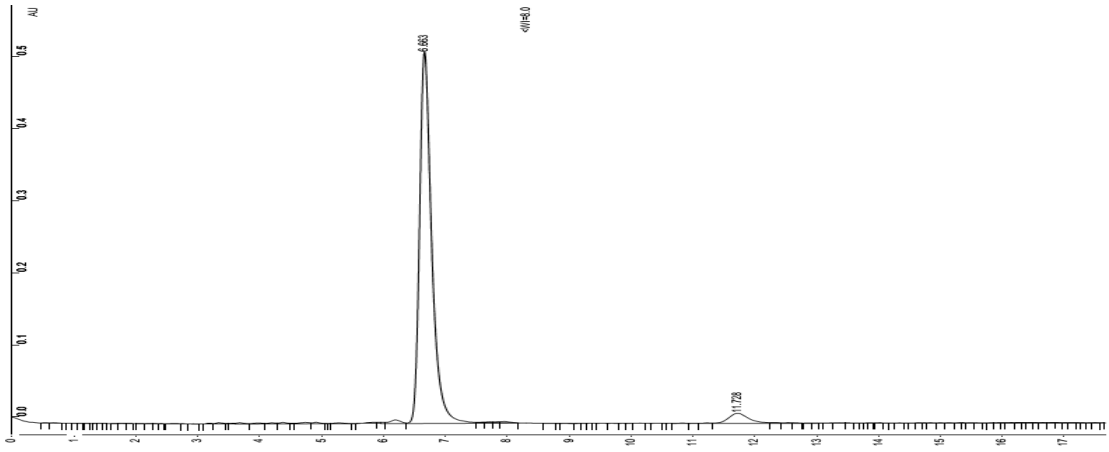
R.Time	Area	Area%
6.527	**40710068**	**50.4194**
11.764	**40032797**	**49.5806**

Racemic product



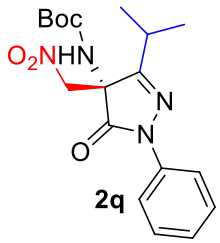
R.Time	Area	Area%
6.516	**44335488**	**95.0235**
11.724	**2321905**	**4.9765**

90% ee ($MeNO_2$ as nucleophile)



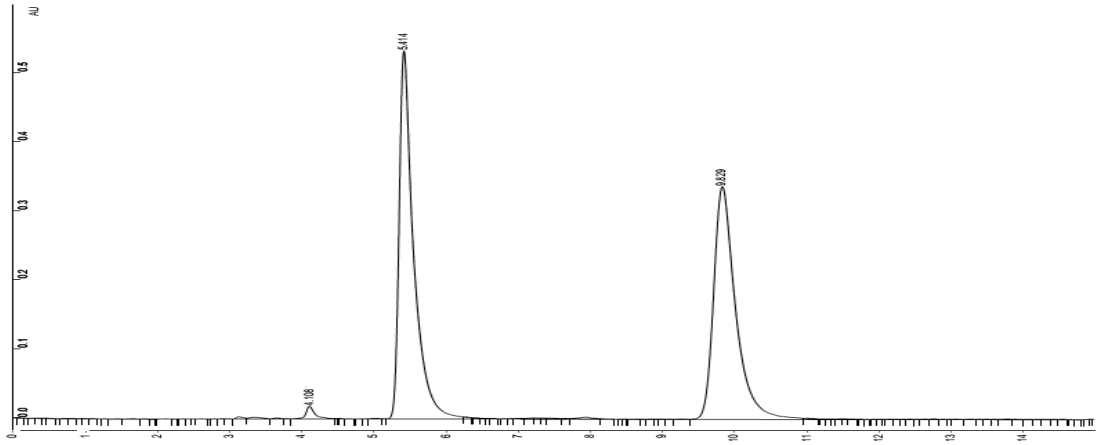
R.Time	Area	Area%
6.663	**70035904**	**97.4150**
11.728	**2154895**	**2.5850**

95% ee ($BrCH_2NO_2$ as nucleophile)



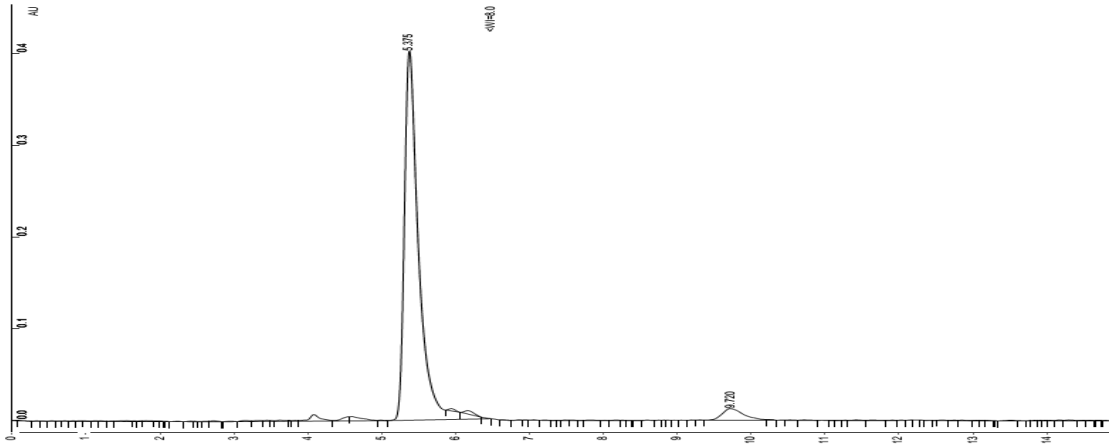
2q

Following the general procedure using **1q** (31.7 mg, 0.1 mmol), **2p** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as white solid; Mp 156-158 °C; Standard conditions 1: (21.8 mg, 58% yield, 92% ee). $[\alpha]_D^{25}$ +14.38 (*c* 0.25, $CHCl_3$). Standard conditions 2: (35.7 mg, 95% yield, 94% ee). $[\alpha]_D^{25}$ +16.41 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.1 Hz, 2H), 7.33 (t, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.4 Hz, 1H), 6.21 (s, 1H), 4.60 (s, 2H), 2.72 – 2.40 (m, 1H), 1.36 – 1.00 (m, 15H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.55, 163.43, 153.37, 137.69, 128.93, 125.62, 77.40, 77.08, 76.76, 76.17, 28.52, 28.02, 20.36. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 5.41 min, τR (minor) =9.82 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{25}N_4O_5$: 377.1825; found 377.1823.



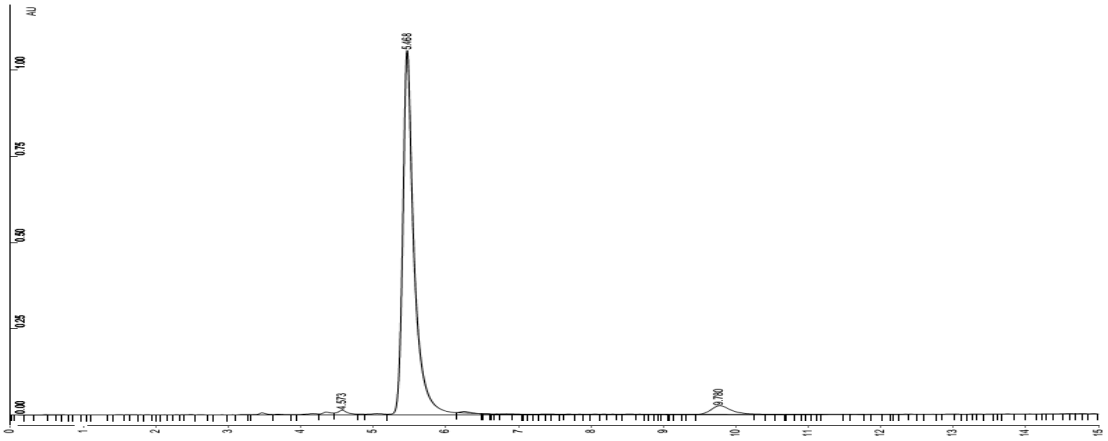
R.Time	Area	Area%
5.414	**75085032**	**50.4399**
9.829	**73775358**	**49.5601**

Racemic product



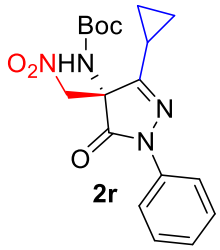
R.Time	Area	Area%
5.375	**54431212**	**96.0824**
9.720	**2219342**	**3.9176**

92% ee ($MeNO_2$ as nucleophile)

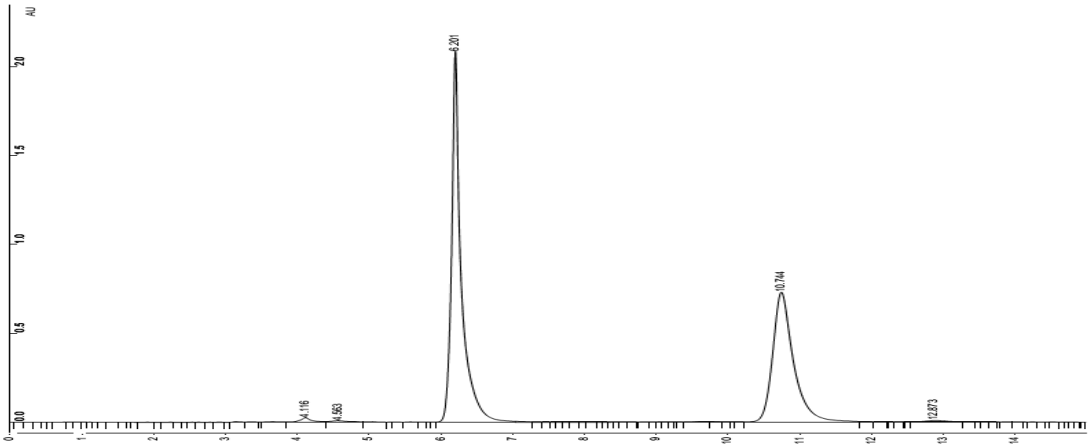


R.Time	Area	Area%
5.468	**56534429**	**97.1067**
9.780	**1684447**	**2.8933**

94% ee ($BrCH_2NO_2$ as nucleophile)

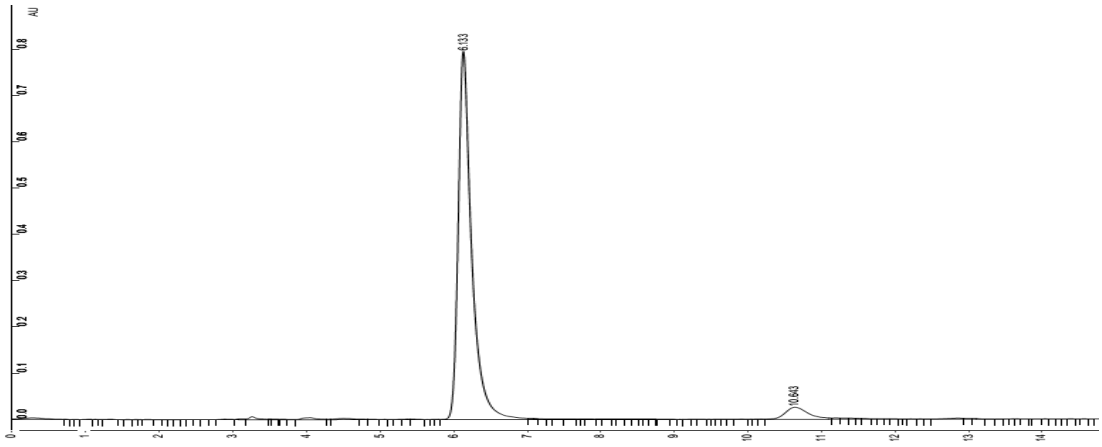


Following the general procedure using **1r** (31.3 mg, 0.1 mmol), **2r** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as white solid; Mp 183-185 °C; Standard conditions 1: (20.5 mg, 55% yield, 93% ee). $[\alpha]_D^{25}$ +17.38 (*c* 0.25, $CHCl_3$). Standard conditions 2: (35.1 mg, 94% yield, 94% ee). $[\alpha]_D^{25}$ +21.42 (*c* 0.25, $CHCl_3$).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.31 (t, *J* = 7.9 Hz, 2H), 7.12 (t, *J* = 7.4 Hz, 1H), 6.25 (s, 1H), 4.70 – 4.49 (m, 2H), 1.50 – 1.42 (m, 1H), 1.31 (s, 9H), 1.12 – 0.85 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.25, 137.66, 128.90, 125.57, 118.84, 76.74, 76.18, 28.04, 9.05, 8.31. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 6.20 min, τR (minor) = 10.74 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{23}N_4O_5$: 375.1668; found 375.1663.



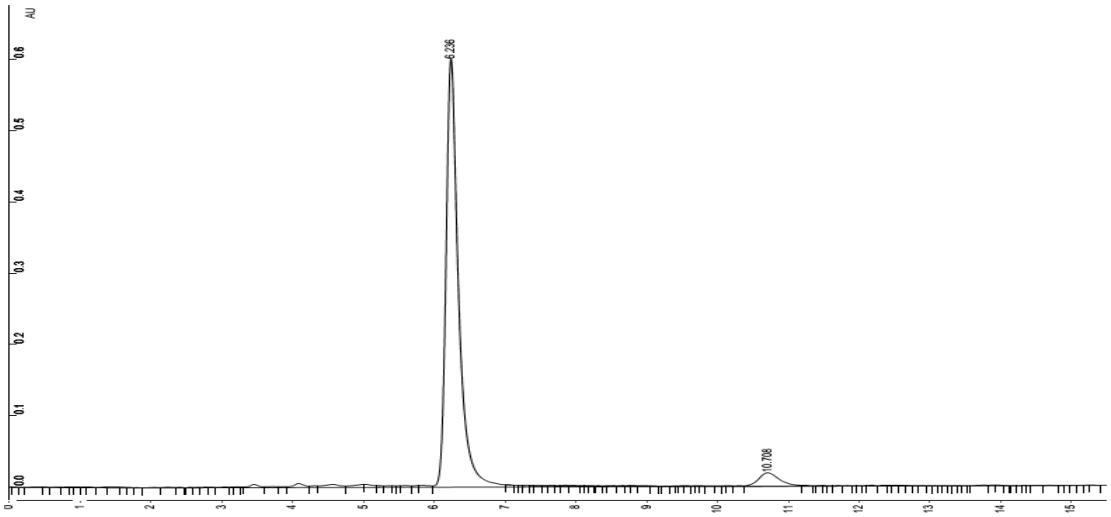
R.Time	Area	Area%
6.201	**19797963360**	**51.9244**
10.744	**183304762**	**48.0756**

Racemic product



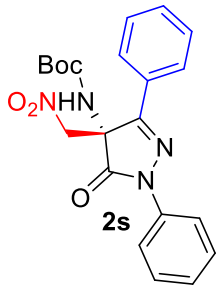
R.Time	Area	Area%
6.133	**101584200**	**96.6071**
10.643	**3567698**	**3.3929**

93% ee ($MeNO_2$ as nucleophile)

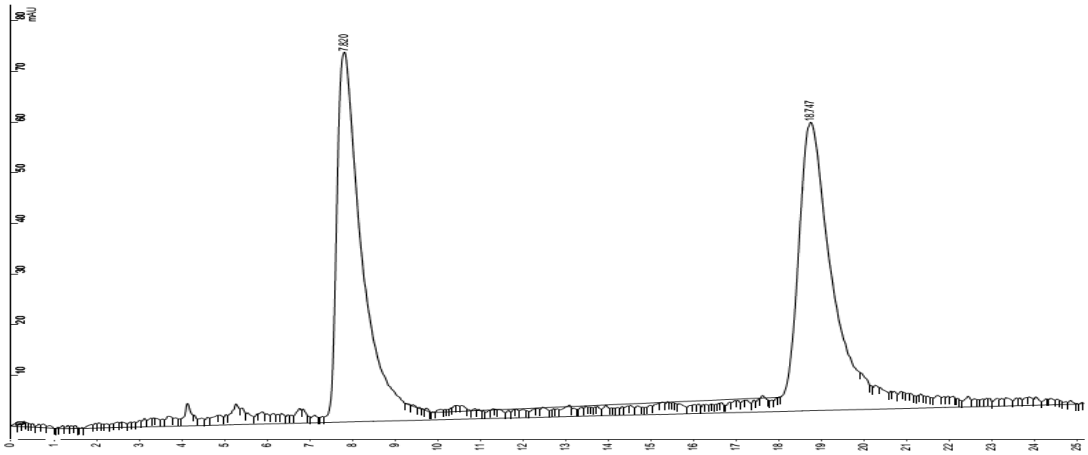


R.Time	Area	Area%
6.236	**75625176**	**96.8820**
10.708	**2433881**	**3.1180**

94% ee ($BrCH_2NO_2$ as nucleophile)

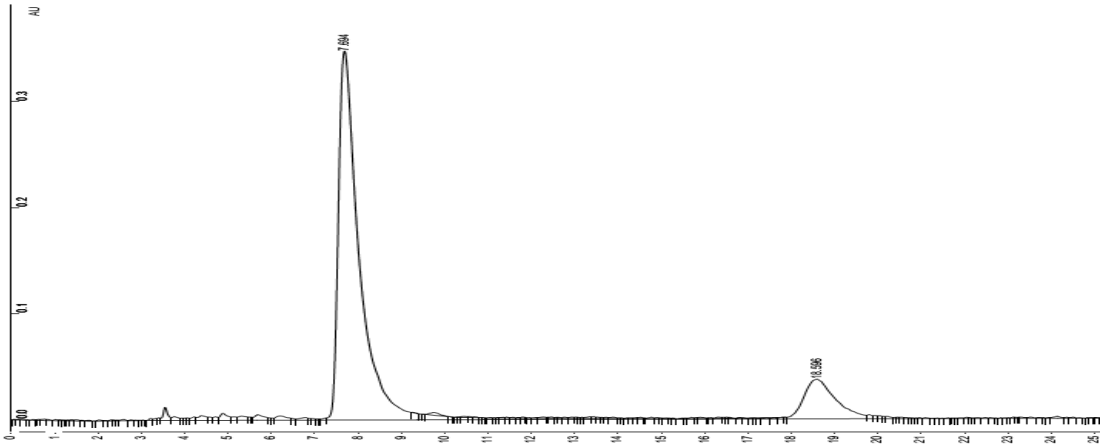


Following the general procedure using **1s** (34.9 mg, 0.1 mmol), **2s** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow solid; Mp 161-164 °C; Standard conditions 1: (21.3 mg, 52% yield, 77% ee). $[\alpha]_D^{25}$ +18.42 (*c* 0.25, $CHCl_3$). Standard conditions 2: (38.1 mg, 93% yield, 81% ee). $[\alpha]_D^{25}$ +20.17 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, Chloroform-*d*) δ 8.00 – 7.83 (m, 4H), 7.44 – 7.33 (m, 5H), 7.22 – 7.14 (m, 1H), 4.79 (d, *J* = 12.5 Hz, 1H), 4.62 (d, *J* = 12.5 Hz, 1H), 1.21 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.03, 153.55, 137.58, 131.34, 129.19, 129.06, 126.10, 125.98, 119.13, 63.43, 27.97. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 7.82 min, τR (minor) = 18.75 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{23}N_4O_5$: 411.1668; found 411.1671.



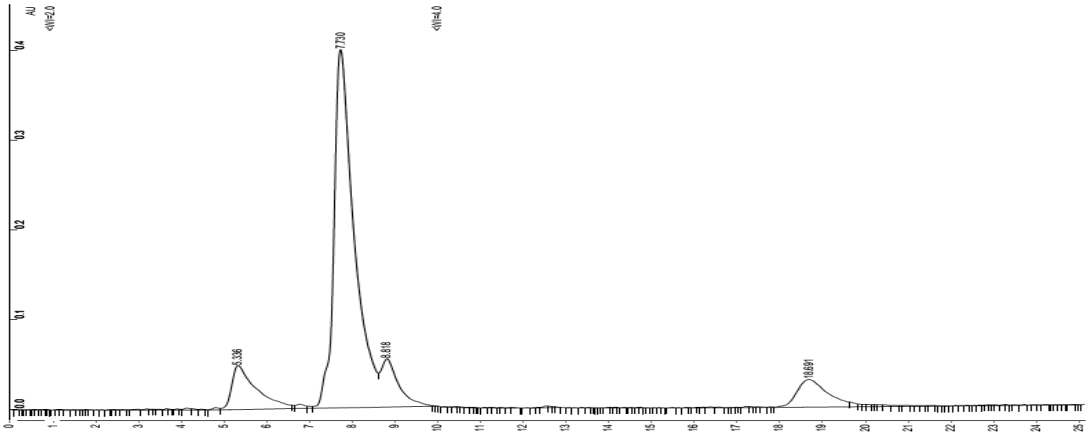
R.Time	Area	Area%
7.820	**37946108**	**50.3279**
18.747	**37451649**	**49.6721**

Racemic product



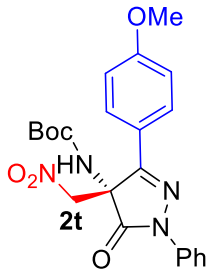
R.Time	Area	Area%
7.694	**121260304**	**88.6067**
18.596	**15591993**	**11.3933**

77% ee ($MeNO_2$ as nucleophile)

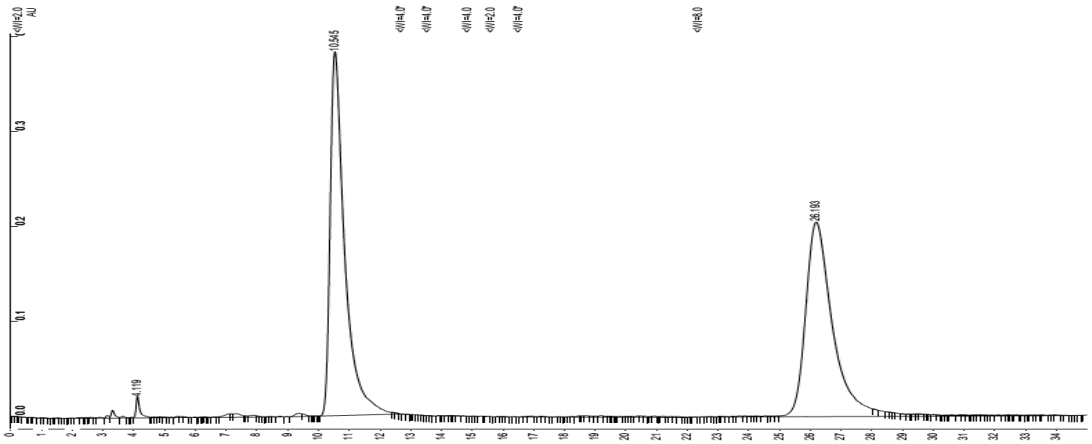


R.Time	Area	Area%
7.730	**130574664**	**90.4530**
18.691	**13781702**	**9.5470**

81% ee ($BrCH_2NO_2$ as nucleophile)

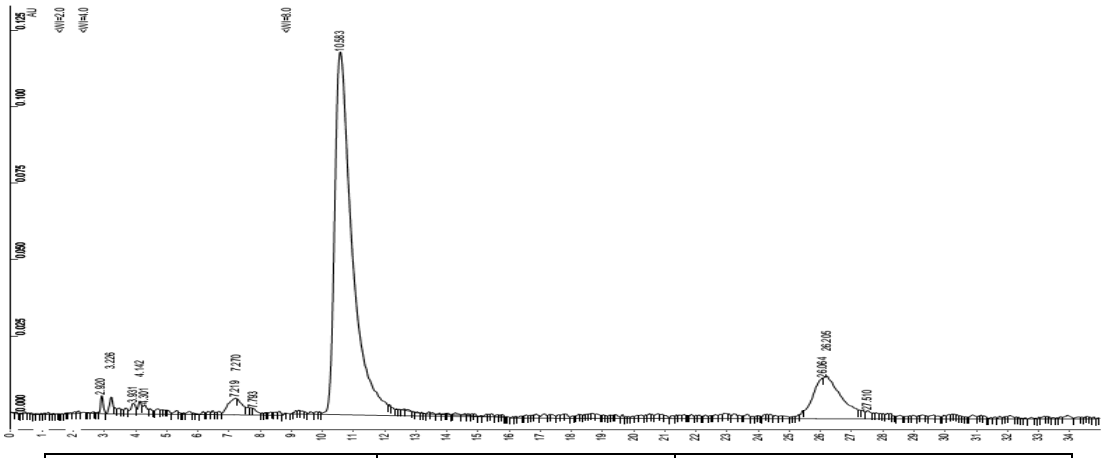


Following the general procedure using **1t** (37.9 mg, 0.1 mmol), **2t** was obtained by flash chromatography (petroleum ether/ethyl acetate: 8/1) as light yellow solid; Mp 168-170 °C; Standard conditions 1: (27.7 mg, 63% yield, 79% ee). $[\alpha]_D^{25}$ +18.42 (*c* 0.25, $CHCl_3$). Standard conditions 2: (41.8 mg, 95% yield, 81% ee). $[\alpha]_D^{25}$ +21.39 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, Chloroform-*d*) δ 8.09 – 7.87 (m, 4H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.4 Hz, 1H), 7.00 – 6.90 (m, 2H), 6.74 (s, 1H), 4.83 (d, *J* = 12.3 Hz, 1H), 4.68 (d, *J* = 12.3 Hz, 1H), 3.85 (s, 3H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.76, 161.95, 153.48, 153.26, 137.68, 129.01, 127.80, 125.81, 121.70,, 119.05, 114.57, 63.52, 55.44, 27.97. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 10.54 min, τR (minor) = 26.19 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{25}N_4O_6$: 441.1774; found 441.1778.



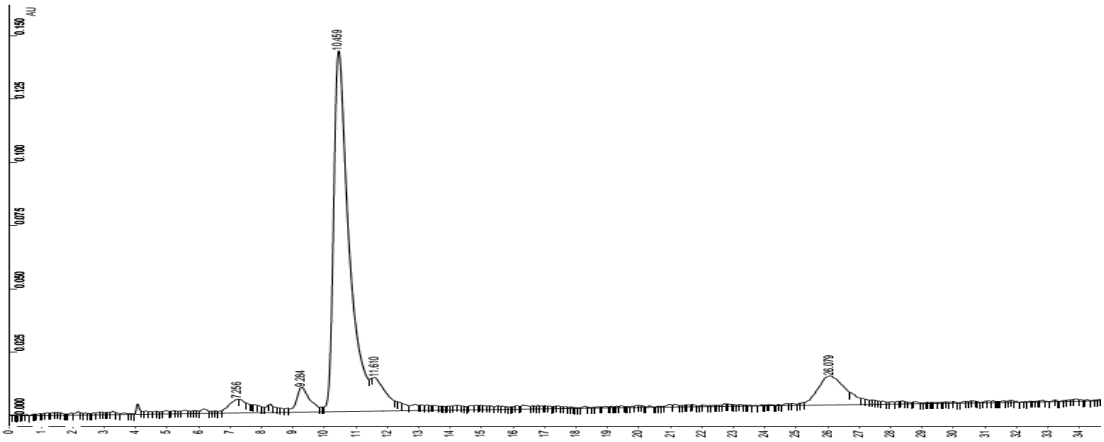
R.Time	Area	Area%
10.545	**125728128**	**49.8820**
26.193	**126322969**	**50.1180**

Racemic product



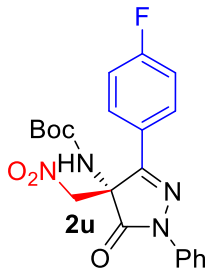
R.Time	Area	Area%
10.583	**48534583**	**89.5531**
26.064	**5661847**	**10.4469**

79% ee ($MeNO_2$ as nucleophile)

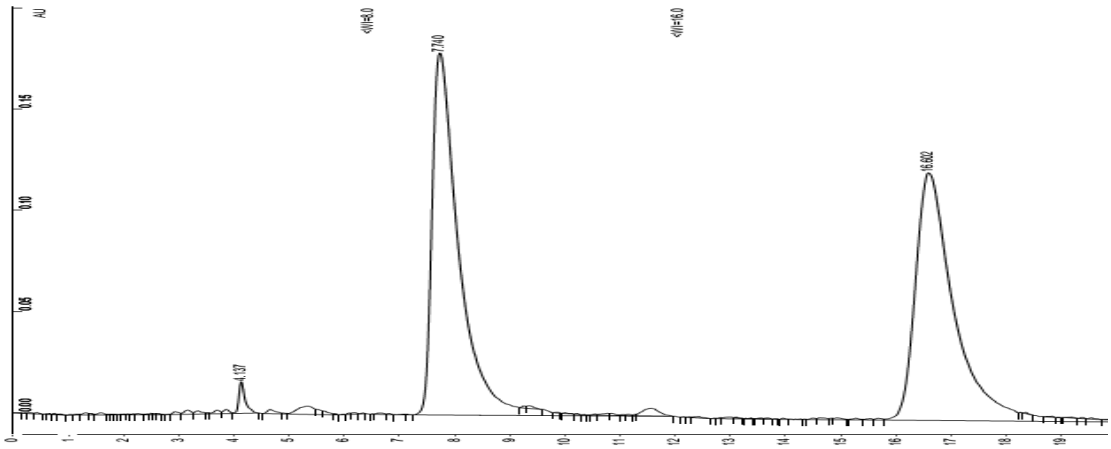


R.Time	Area	Area%
10.459	**47630600**	**90.5430**
26.079	**497546**	**9.4570**

81% ee ($BrCH_2NO_2$ as nucleophile)

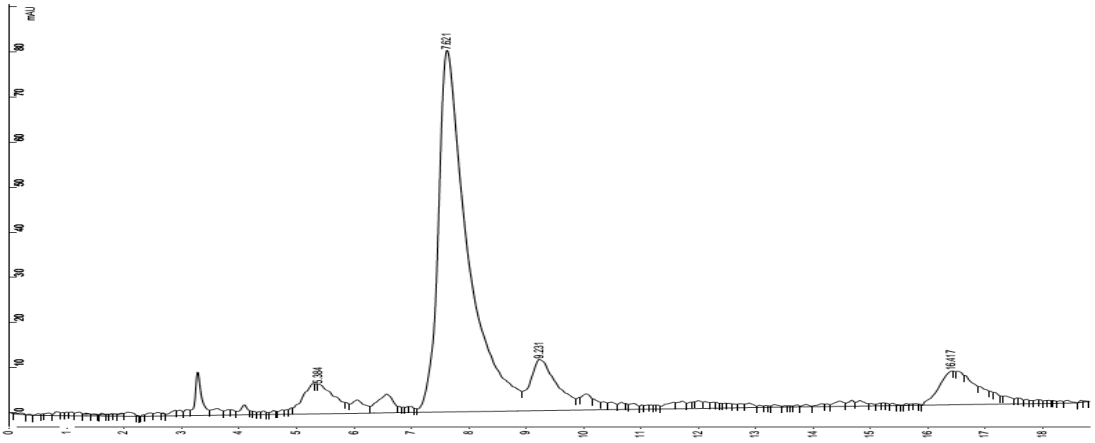


Following the general procedure using **1u** (36.7 mg, 0.1 mmol), **2u** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow oil; Standard conditions 1: (20.5 mg, 48% yield, 75% ee). $[\alpha]_D^{25}$ +14.73 (*c* 0.25, $CHCl_3$). Standard conditions 2: (37.7 mg, 88% yield, 80% ee). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.98 (dd, *J* = 8.6, 4.8 Hz, 4H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.27 (t, *J* = 5.9 Hz, 1H), 7.15 (t, *J* = 8.5 Hz, 2H), 6.69 (s, 1H), 4.89 – 4.59 (m, 2H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.73, 163.16, 153.45, 152.54, 137.47, 129.08, 128.32, 128.23, 126.08, 125.48, 119.11, 116.46 (d, *J* = 22.0 Hz), 63.41, 27.97. HPLC conditions: Chiralcel IA-H column (250 × 4.6 mm), hexane /*i*-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 7.74 min, τR (minor) = 16.60 min. HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{22}N_4O_5F$: 429.1574; found 429.1576.



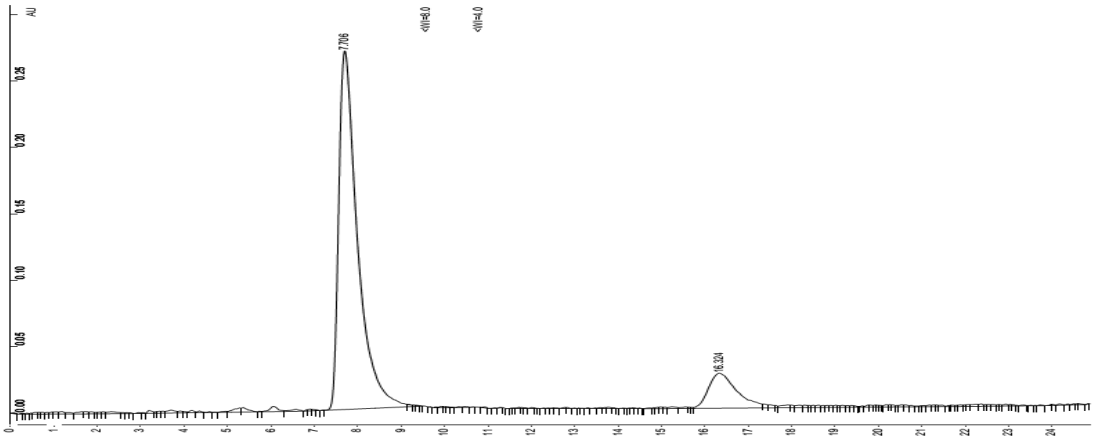
R.Time	Area	Area%
7.740	**60471996**	**49.7870**
16.602	**61164628**	**50.2130**

Racemic product



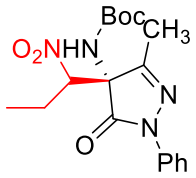
R.Time	Area	Area%
7.621	**28630199**	**87.1541**
16.417	**4219899**	**12.8459**

75% ee ($MeNO_2$ as nucleophile)



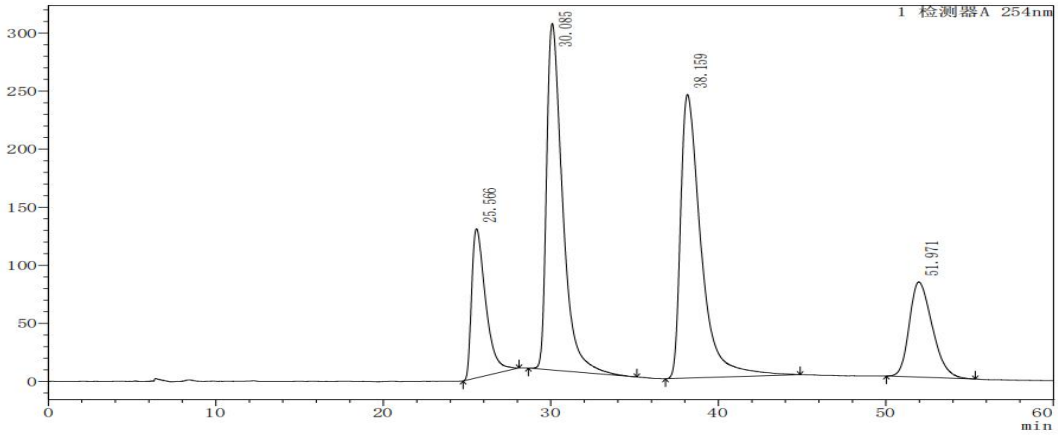
R.Time	Area	Area%
7.706	**80841925**	**89.8970**
16.324	**9085352**	**10.1030**

80% ee ($BrCH_2NO_2$ as nucleophile)



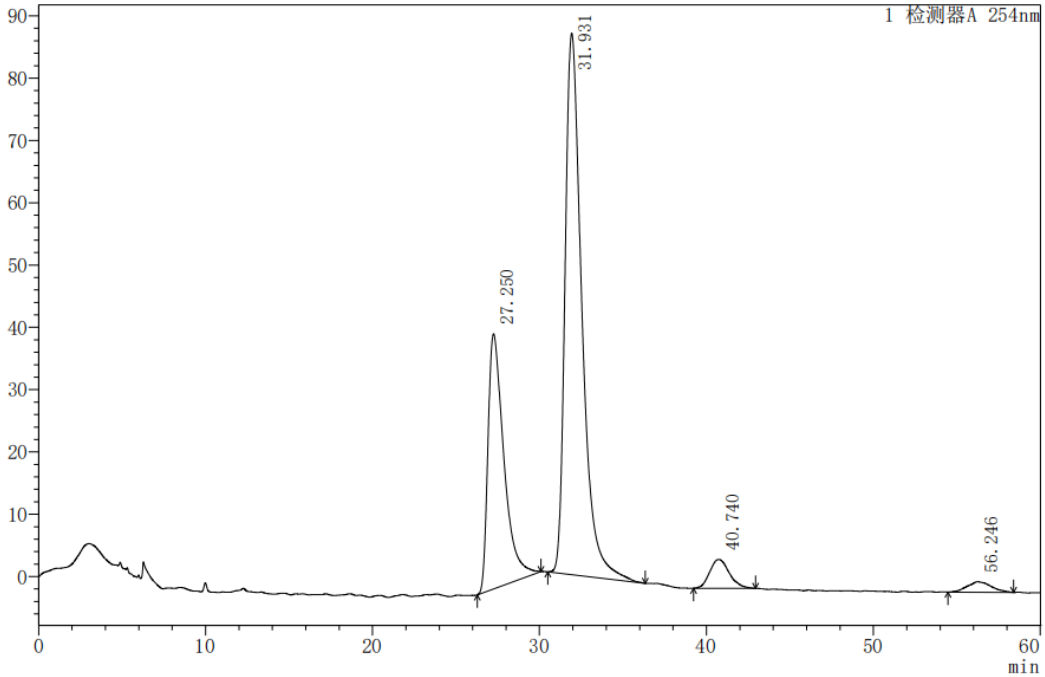
2aa

Following the general procedure using **1a** (26.8 mg, 0.1 mmol), **2aa** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as light yellow wax; Standard conditions 1: (27.4 mg, 73% yield, 90% ee, 7:3 dr). $[\alpha]_D^{25}$ +21.23 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.69 (m, 2H), 7.34 (dd, *J* = 8.7, 7.3 Hz, 2H), 7.15 (t, *J* = 7.4 Hz, 1H), 6.03 (s, 1H), 4.67 – 4.45 (m, 2H), 2.06 (s, 3H), 1.31 (s, 9H), 1.18 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.21, 155.98, 136.43, 127.93, 124.73, 117.90, 75.02, 62.77, 28.68, 26.98, 12.84. HPLC conditions: Chiralcel OD-H column (250 × 4.6 mm), hexane /i-PrOH = 99 / 1, 0.6 mL / min, 254 nm, τR (major) = 31.93 min, τR (minor) = 40.74 min. HRMS (ESI-TOF) m/z: [M + H]+ calcd for $C_{18}H_{25}N_4O_5$: 377.1825; found 377.1828.



R.Time	Area	Area%
25.566	**7491356**	**13.418**
30.085	**19815339**	**35.491**
38.159	**20725293**	**37.121**
10.985	**7799860**	**13.970**

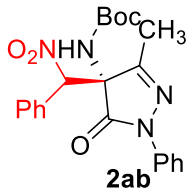
Racemic product (73:27 dr)



R.Time	Area	Area%
27.250	**2725917**	**29.111**
31.931	**6116107**	**65.316**
40.740	**346650**	**3.702**
56.246	**172830**	**1.871**

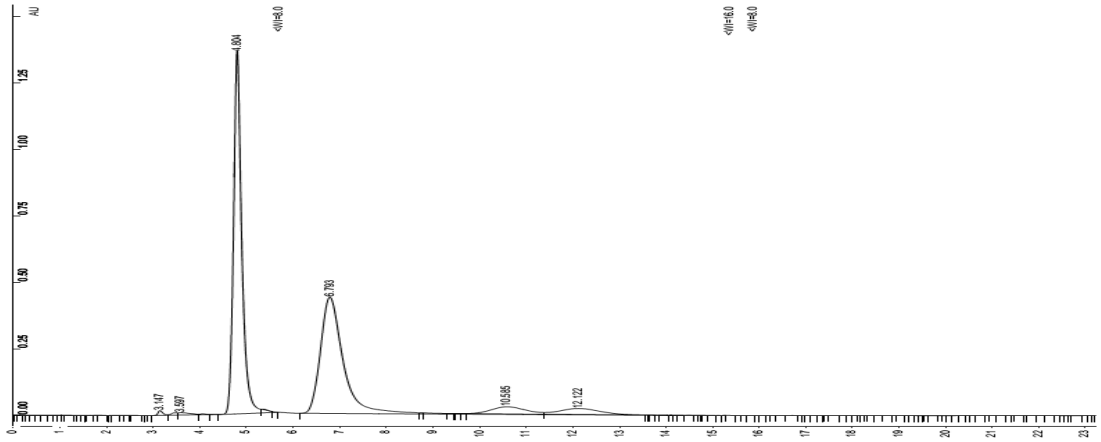
90% ee (69:31 dr)

($CH_3CH_2CH_2NO_2$ as nucleophile)



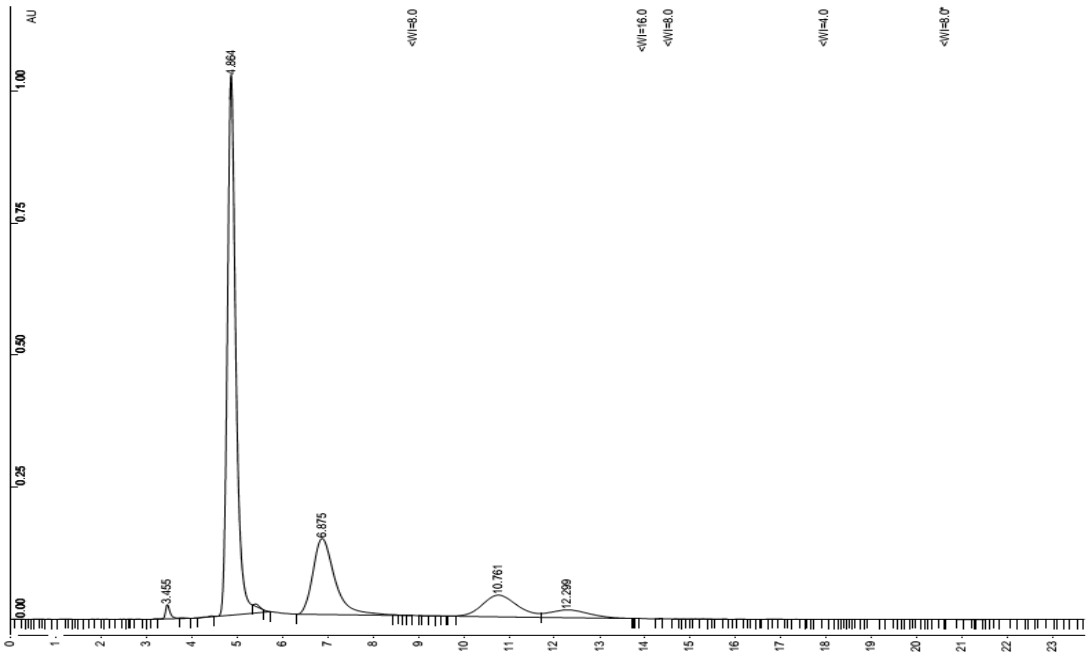
2ab

Following the general procedure using **1a** (26.8 mg, 0.1 mmol), **2aa** was obtained by flash chromatography (petroleum ether/ethyl acetate: 10/1) as colourless oil; Standard conditions 1: (31.8 mg, 75% yield, 45% ee, 85:15 dr). $[\alpha]_D^{25}$ +14.26 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.33 (m, 4H), 7.34 – 7.23 (m, 3H), 7.23 – 7.17 (m, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 5.87 (s, 1H), 5.69 (s, 1H), 2.21 (s, 3H), 1.31 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.54, 136.88, 131.23, 129.09, 128.81, 128.68, 126.68, 125.76, 119.41, 91.97, 28.05, 15.46. HPLC conditions: Chiralcel AS-H column (250 × 4.6 mm), hexane /i-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 31.93 min, τR (minor) = 40.74 min. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{25}N_4O_5$: 425.1825; found 425.1821.



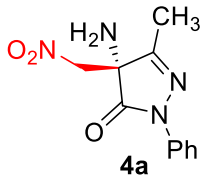
R.Time	Area	Area%
4.804	**162152976**	**46.8580**
6.793	**155390740**	**44.4908**
3.9398	**13760338**	**3.9398**
3.8813	**13556256**	**3.8813**

Racemic product (91:9 dr)



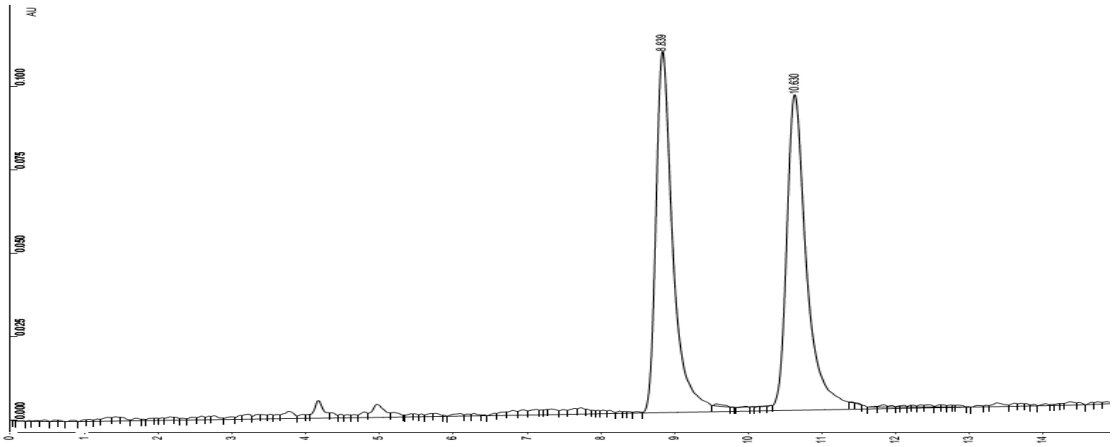
R.Time	Area	Area%
4.864	**133355368**	**61.6248**
6.875	**50564841**	**23.3665**
10.761	**22295142**	**10.3028**
12.299	**10187842**	**4.7079**

45% ee (85:15 dr)



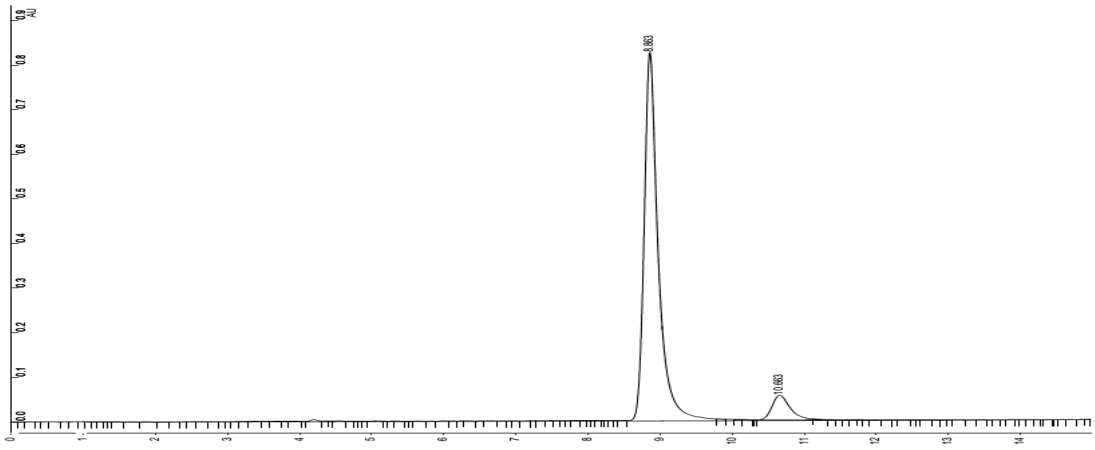
4a

Following the general procedure using **2a** (34.8 mg, 0.1 mmol), **4a** was obtained by flash chromatography (petroleum ether/ethyl acetate: 4/1) as light yellow oil (22.3 mg, 90% yield, 90% ee) ; $[\alpha]_D^{25}$ -34.26 (*c* 0.25, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.76 (m, 2H), 7.42 (dd, *J* = 8.6, 7.4 Hz, 2H), 7.27 – 7.19 (m, 1H), 4.78 (d, *J* = 13.6 Hz, 1H), 4.66 (d, *J* = 13.6 Hz, 1H), 2.22 (s, 3H), 1.88 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.82, 158.64, 137.39, 129.03, 125.77, 118.96, 63.04, 13.50. HPLC conditions: Chiralcel AD-H column (250 × 4.6 mm), hexane /i-PrOH = 80 / 20, 1 mL / min, 254 nm, τR (major) = 8.86 min, τR (minor) = 10.66 min. HRMS (ESI-TOF) m/z: [M + Na]$^+$ calcd for $C_{11}H_{12}N_4O_3Na$: 271.0807; found 271.0802.



R.Time	Area	Area%
8.839	**1773760**	**49.6422**
10.630	**18030008**	**50.3578**

Racemic product



R.Time	Area	Area%
8.863	**114247624**	**95.1532**
10.663	**5819409**	**4.8468**

90% ee

4. Single Crystal data

CCDC 24695580 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.The thermal ellipsoids are 30% probability level.

In this study, CH_2Cl_2/Et_2O were selected for single crystal culture through natural solvent volatilization. The Xcalibur, Eos, Gemini diffractometer was used for the crystal measurement.

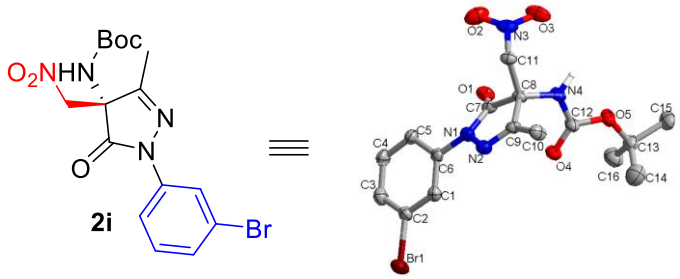


Table S6 Crystal data and structure refinement for CCDC 24695580.

Identification code	202508ZT
Empirical formula	$C_{16}H_{19}BrN_4O_5$
Formula weight	427.26
Temperature/K	293(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	6.11553(9)
b/Å	12.3395(2)
c/Å	25.2572(4)
α /°	90
β /°	90
γ /°	90
Volume/Å^3	1905.97(6)
Z	4
ρ_{calc}g/cm^3	1.489
μ /mm^{-1}	3.245
F(000)	872.0
Crystal size/mm^3	0.16 × 0.12 × 0.1
Radiation	Cu K α （λ = 1.54184)

2Θ range for data collection/°	7 to 141.59
Index ranges	$-7 \leqslant h \leqslant 3$, $-14 \leqslant k \leqslant 11$, $-28 \leqslant l \leqslant 30$
Reflections collected	7547
Independent reflections	3592 [R_{int} = 0.0321, R_{sigma} = 0.0453]
Data/restraints/parameters	3592/40/274
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0510, wR_2 = 0.1317
Final R indexes [all data]	R_1 = 0.0581, wR_2 = 0.1387
Largest diff. peak/hole / e Å^{-3}	0.52/-0.30
Flack parameter	-0.021(17)

Table S7 Anisotropic Displacement Parameters (Å^2×10^3) for CCDC 24695580**. The Anisotropic displacement factor exponent takes the form: -2 π ^{2}[h^{2}a*^{2}U$_{11}$+2hka*b*U$_{12}$+⋯].**

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
Br1	73.9(4)	89.6(5)	78.7(4)	-12.4(4)	-10.8(4)	-23.5(4)
O1	53(2)	77(3)	58(2)	-20(2)	8.4(18)	-1.6(19)
O2	112(5)	163(7)	62(3)	13(4)	-2(3)	11(5)
O3	77(4)	127(6)	110(4)	-57(4)	-13(3)	2(3)
O4	52(2)	59(3)	108(4)	-4(2)	-27(2)	-1(2)
O5	58(3)	50(2)	137(5)	6(3)	-22(3)	-1(2)
N1	45(2)	50(2)	51(2)	-7.2(19)	4.4(19)	3(2)
N2	47(2)	64(3)	50(2)	-6(2)	3.5(19)	-2(2)
N3	46(3)	111(5)	70(3)	-19(4)	-10(2)	5(3)
N4	40(2)	53(3)	93(3)	-11(2)	-15(2)	-1(2)
C1	51(3)	48(3)	51(3)	-1(2)	5(2)	2(2)
C2	51(3)	52(3)	62(3)	-3(2)	-1(3)	-2(3)
C3	62(3)	64(4)	80(4)	6(3)	8(3)	-13(3)
C4	78(4)	70(4)	65(4)	18(3)	5(3)	-10(3)
C5	64(3)	60(4)	56(3)	11(3)	-3(3)	-1(3)
C6	50(3)	41(3)	55(3)	0(2)	0(2)	6(2)
C7	41(2)	55(3)	52(3)	-7(2)	-5(2)	9(2)
C8	36(2)	53(3)	61(3)	-8(2)	-7(2)	1(2)
C9	39(2)	60(3)	51(3)	0(2)	-3(2)	0(2)
C10	61(3)	90(5)	55(3)	1(3)	8(3)	-24(4)

Table S7 Anisotropic Displacement Parameters ($Å^2 \times 10^3$) for CCDC 24695580**. The Anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2a^{*2}U_{11}+2hka^*b^*U_{12}+\cdots]$.**

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C11	37(2)	65(4)	57(3)	-8(3)	-3(2)	5(2)
C12	43(3)	50(3)	81(4)	-1(3)	-7(3)	-2(2)
C13	61(4)	57(4)	93(5)	5(3)	-10(3)	2(3)
C14	120(20)	110(20)	120(20)	13(16)	-5(18)	10(20)
C14A	115(15)	85(10)	113(12)	-1(8)	-44(11)	23(11)
C15	65(14)	56(12)	120(20)	0(13)	-6(17)	18(10)
C15A	91(11)	60(7)	102(12)	12(7)	21(9)	-6(7)
C16	79(15)	97(18)	130(20)	-4(17)	-7(16)	-10(13)
C16A	83(10)	66(8)	108(12)	1(7)	11(9)	-8(7)

Table S8 Bond Lengths for CCDC 24695580.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
Br1	C2	1.908(6)	C1	C6	1.382(8)
O1	C7	1.194(7)	C2	C3	1.375(10)
O2	N3	1.198(10)	C3	C4	1.367(11)
O3	N3	1.232(10)	C4	C5	1.386(10)
O4	C12	1.201(8)	C5	C6	1.380(8)
O5	C12	1.321(8)	C7	C8	1.537(8)
O5	C13	1.457(9)	C8	C9	1.519(8)
N1	N2	1.410(7)	C8	C11	1.541(7)
N1	C6	1.414(8)	C9	C10	1.481(8)
N1	C7	1.377(7)	C13	C14	1.51(2)
N2	C9	1.273(8)	C13	C14A	1.503(15)
N3	C11	1.486(8)	C13	C15	1.53(2)
N4	C8	1.438(7)	C13	C15A	1.521(14)
N4	C12	1.371(8)	C13	C16	1.46(2)
C1	C2	1.371(9)	C13	C16A	1.494(15)

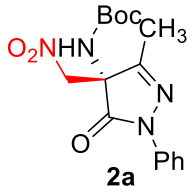
Table S9 Bond Angles for CCDC 24695580.

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C12	O5	C13	123.1(6)	N4	C8	C11	110.8(5)

Table S9 Bond Angles for CCDC 24695580.

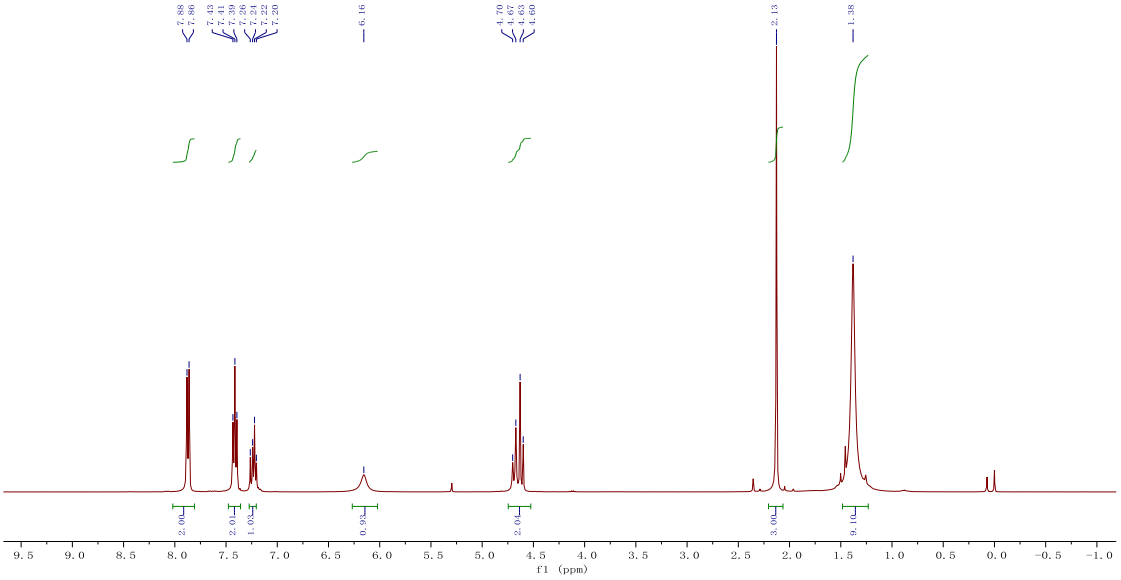
Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
N2	N1	C6	119.3(4)	C7	C8	C11	109.4(5)
C7	N1	N2	112.7(5)	C9	C8	C7	100.7(4)
C7	N1	C6	126.1(5)	C9	C8	C11	106.4(4)
C9	N2	N1	108.6(5)	N2	C9	C8	112.4(5)
O2	N3	O3	124.6(7)	N2	C9	C10	123.7(5)
O2	N3	C11	118.9(7)	C10	C9	C8	123.9(5)
O3	N3	C11	116.4(8)	N3	C11	C8	111.8(5)
C12	N4	C8	119.2(5)	O4	C12	O5	128.2(6)
C2	C1	C6	118.2(5)	O4	C12	N4	122.8(6)
C1	C2	Br1	118.7(5)	O5	C12	N4	109.0(5)
C1	C2	C3	122.4(6)	O5	C13	C14	98(2)
C3	C2	Br1	118.9(5)	O5	C13	C14A	114.9(11)
C4	C3	C2	118.6(6)	O5	C13	C15	103.9(14)
C3	C4	C5	120.7(6)	O5	C13	C15A	102.2(11)
C6	C5	C4	119.4(6)	O5	C13	C16	118.8(17)
C1	C6	N1	119.9(5)	O5	C13	C16A	104.8(11)
C5	C6	N1	119.5(5)	C14	C13	C15	113(3)
C5	C6	C1	120.6(6)	C14A	C13	C15A	109.5(13)
O1	C7	N1	128.4(6)	C16	C13	C14	110(2)
O1	C7	C8	127.3(5)	C16	C13	C15	112(2)
N1	C7	C8	104.3(5)	C16A	C13	C14A	111.6(12)
N4	C8	C7	114.1(5)	C16A	C13	C15A	113.5(11)
N4	C8	C9	114.8(5)				

5. NMR spectra for chiral products

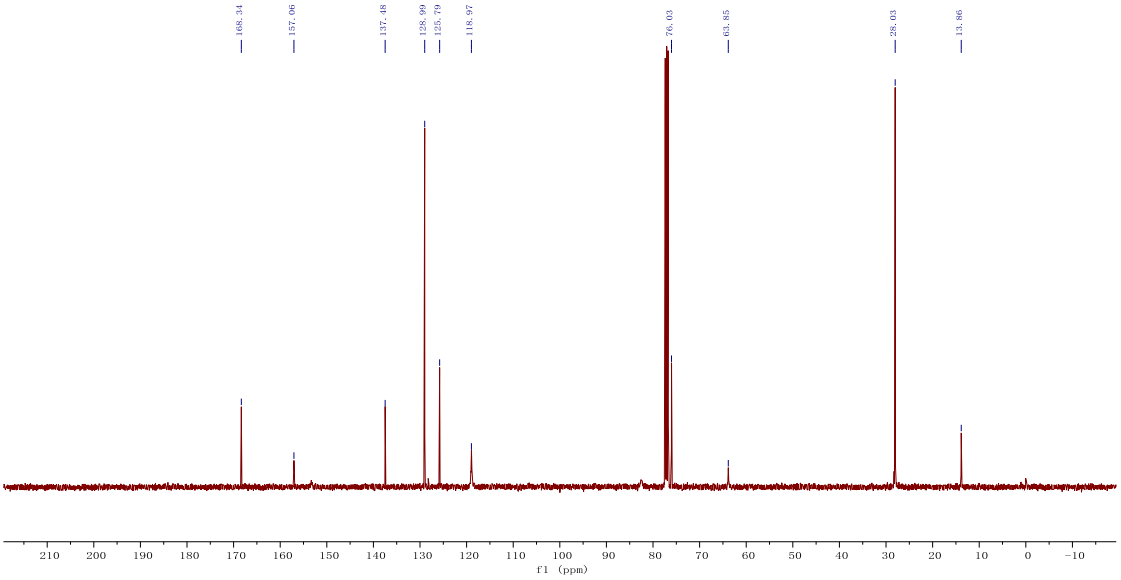


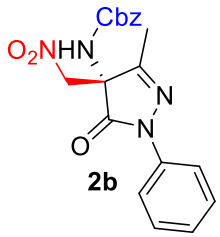
2a

[1] H NMR Spectra of compound **2a** in $CDCl_3$ (400 MHz)

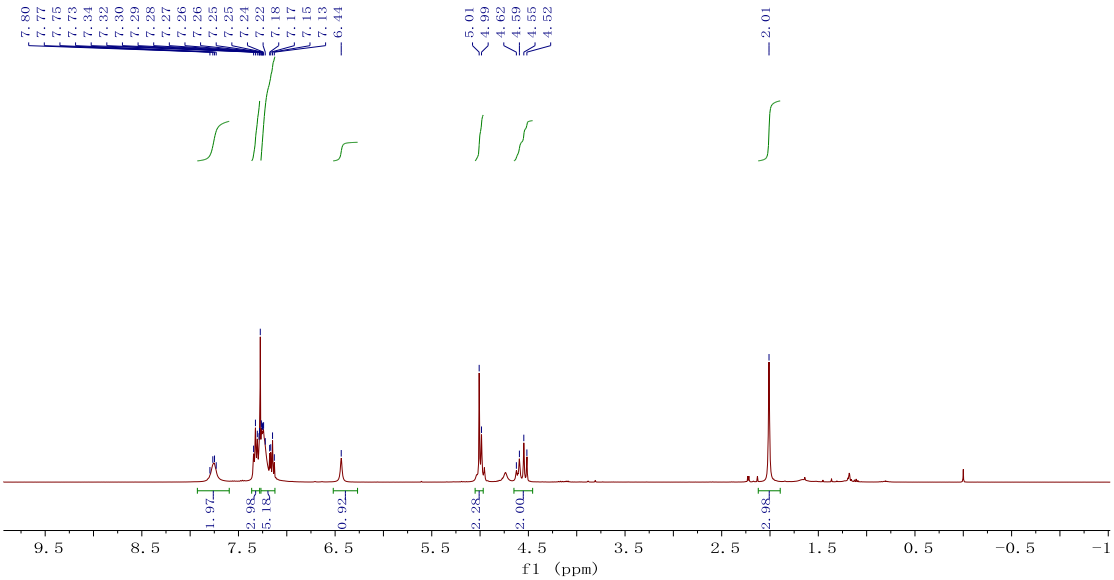


[13] C NMR Spectra of compound **2a** in $CDCl_3$ (101 MHz)

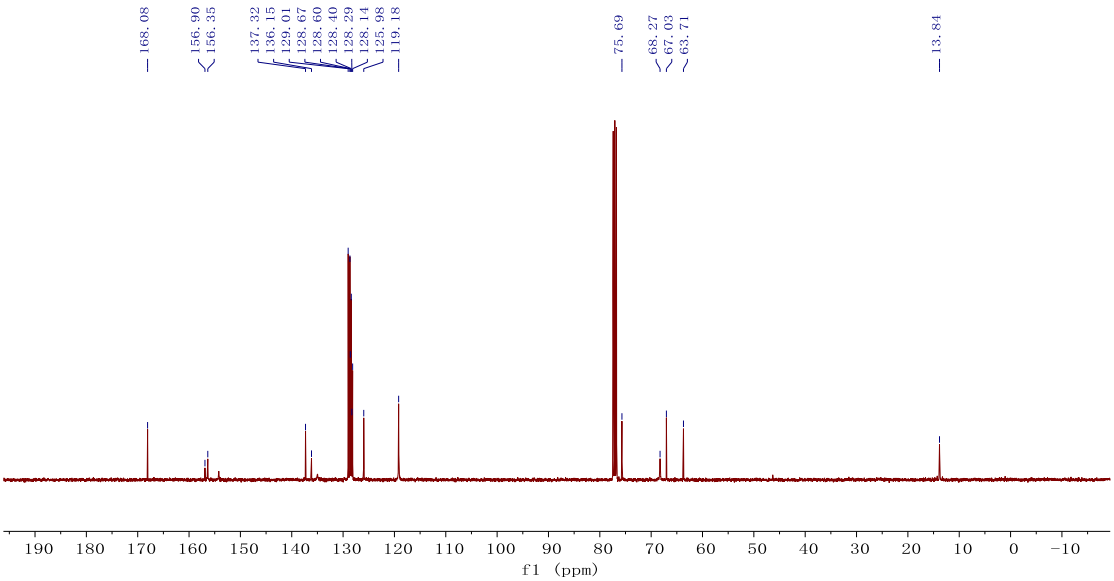


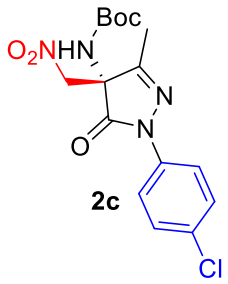


[1] H NMR Spectra of compound **2b** in $CDCl_3$ (400 MHz)



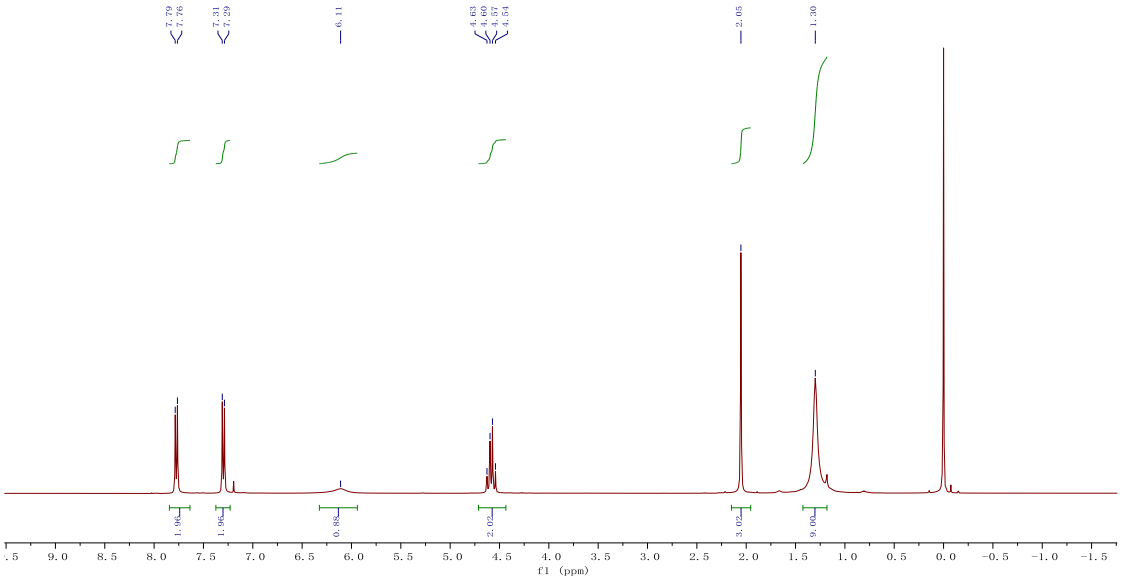
[13] C NMR Spectra of compound **2b** in $CDCl_3$ (101 MHz)



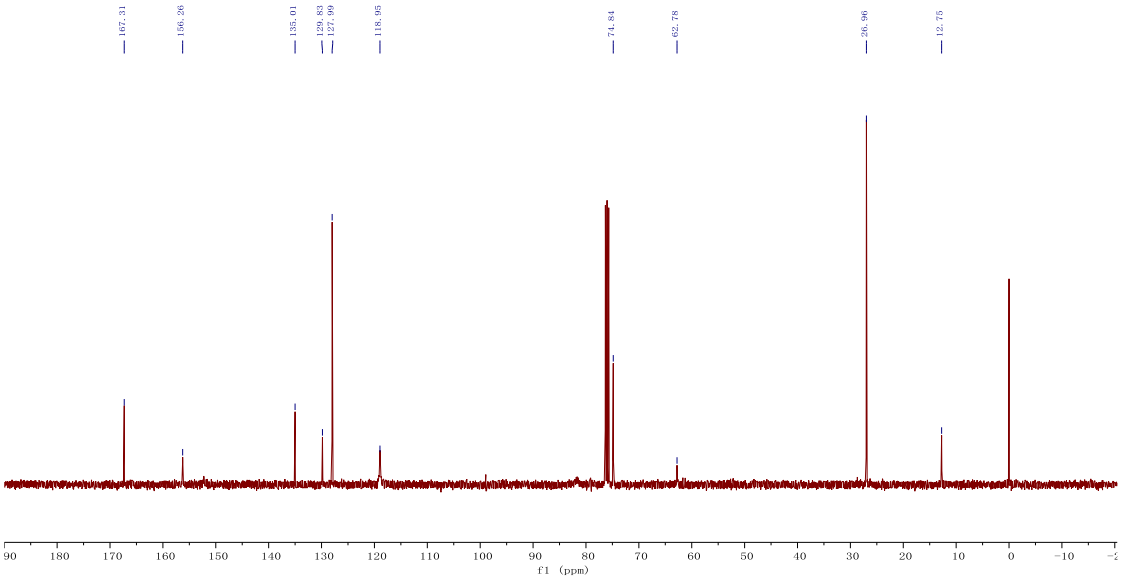


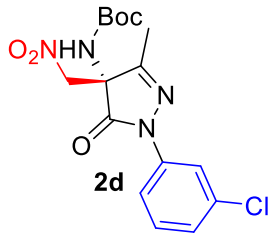
2c

^{1}H NMR Spectra of compound **2c** in $CDCl_3$ (400 MHz)

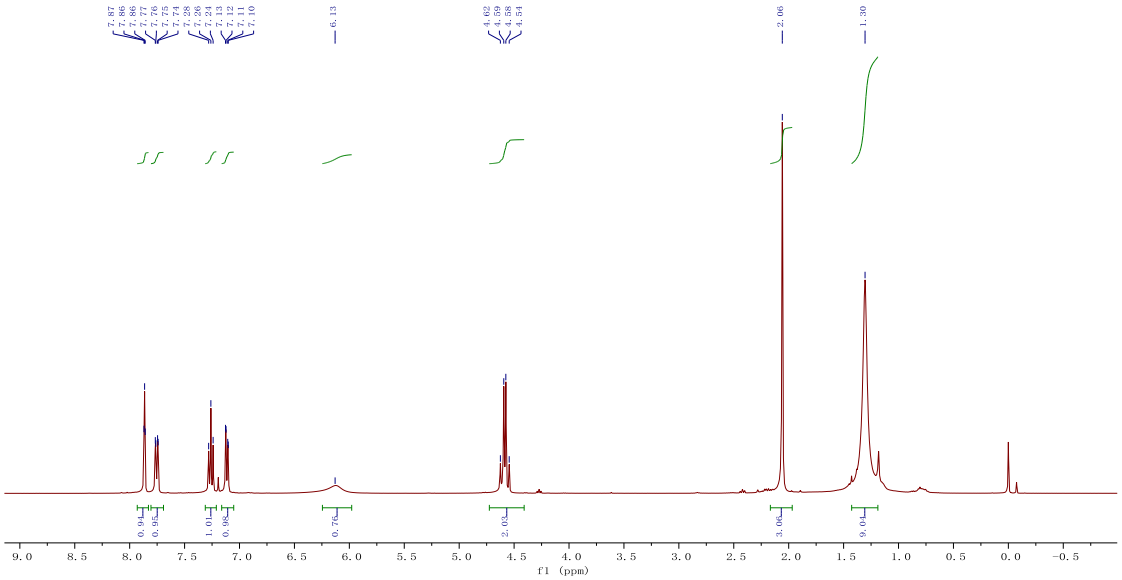


^{13}C NMR Spectra of compound **2c** in $CDCl_3$ (101 MHz)

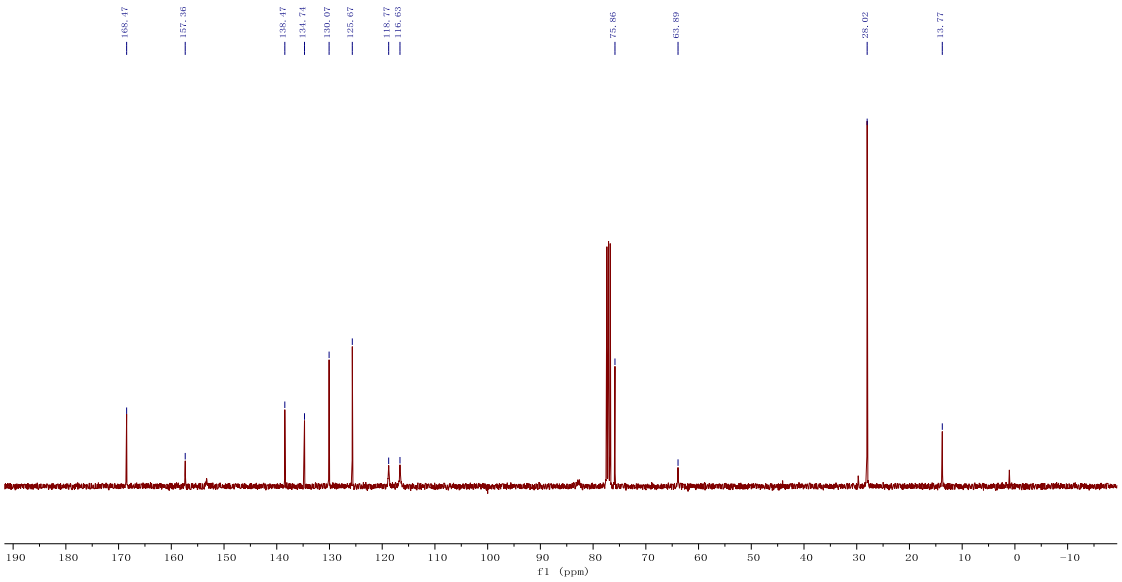


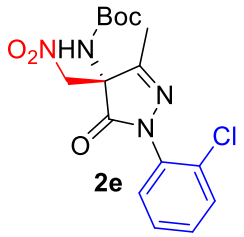


[1] H NMR Spectra of compound **2d** in $CDCl_3$ (400 MHz)

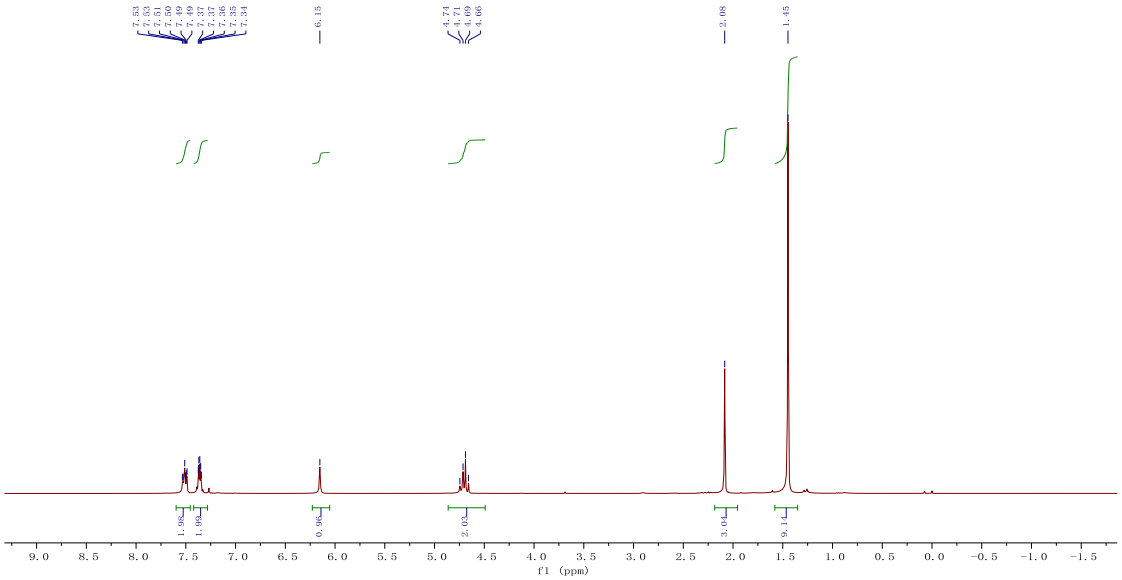


[13] C NMR Spectra of compound **2d** in $CDCl_3$ (101 MHz)

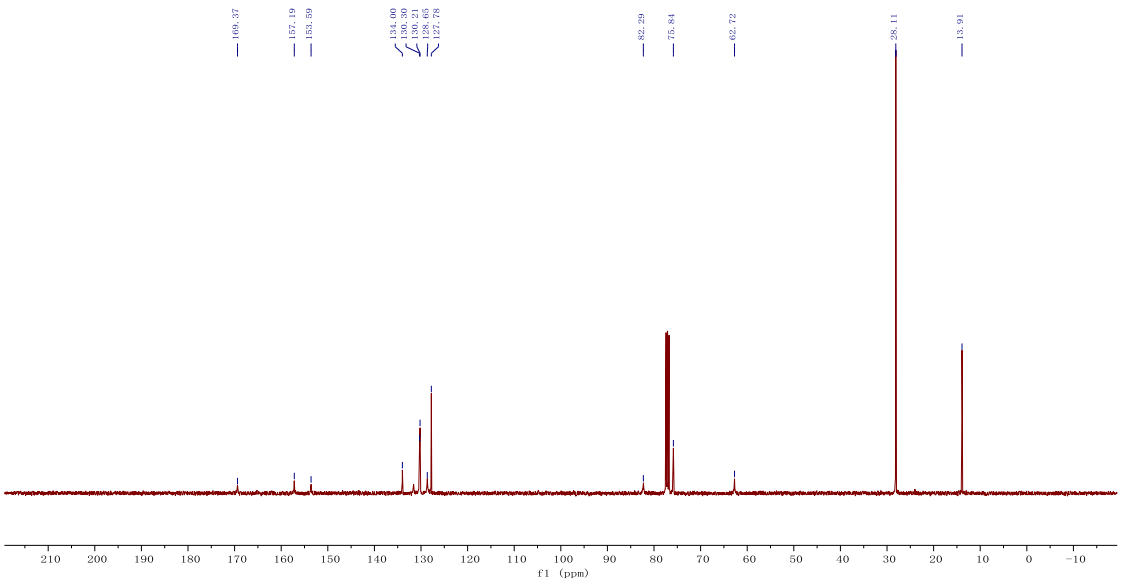


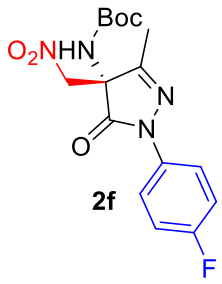


[1] H NMR Spectra of compound **2e** in $CDCl_3$ (400 MHz)



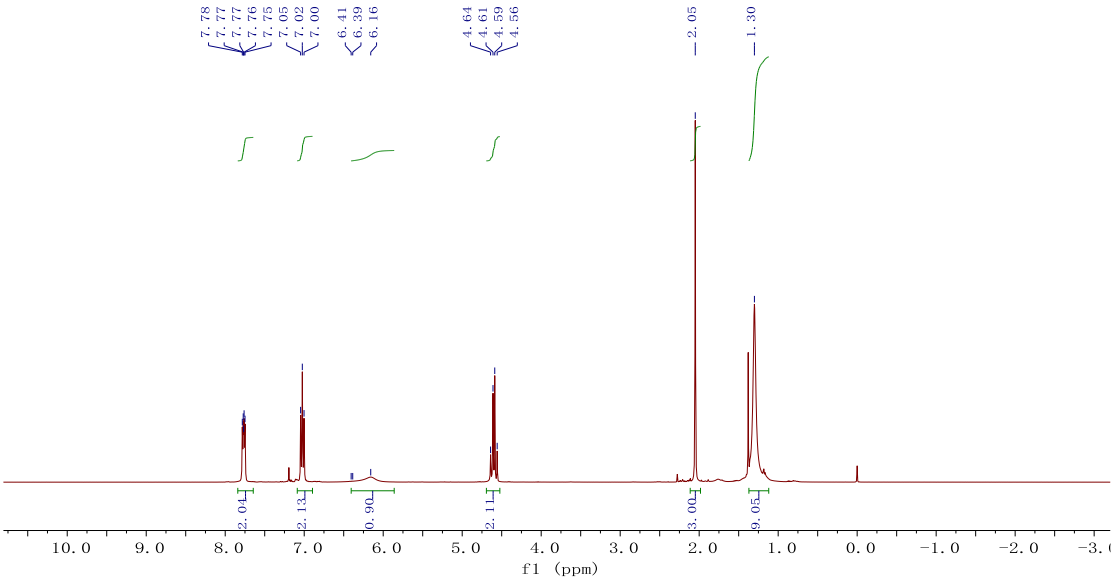
[13] C NMR Spectra of compound **2e** in $CDCl_3$ (101 MHz)



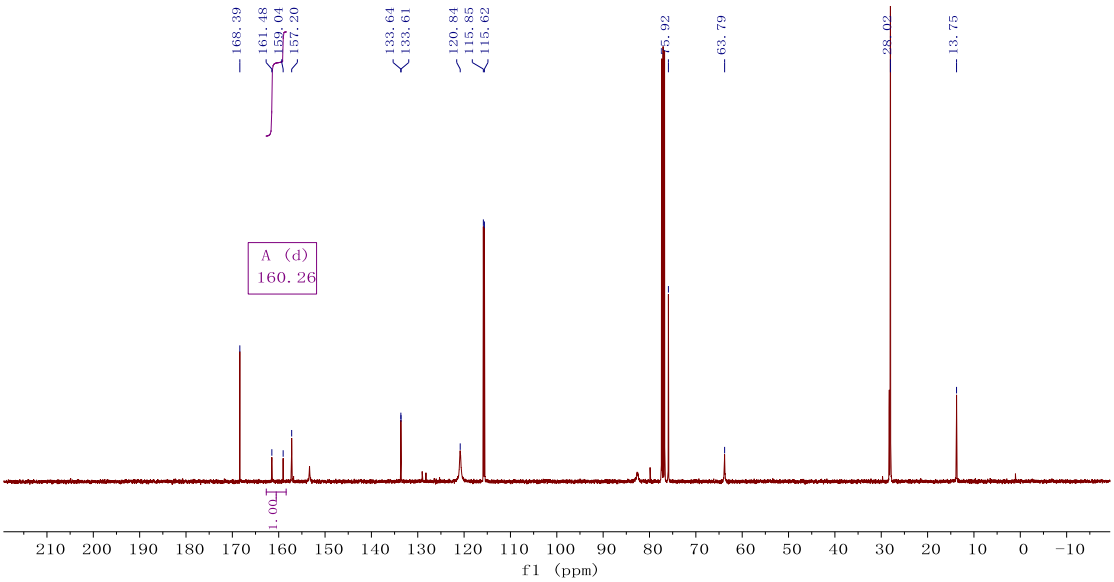


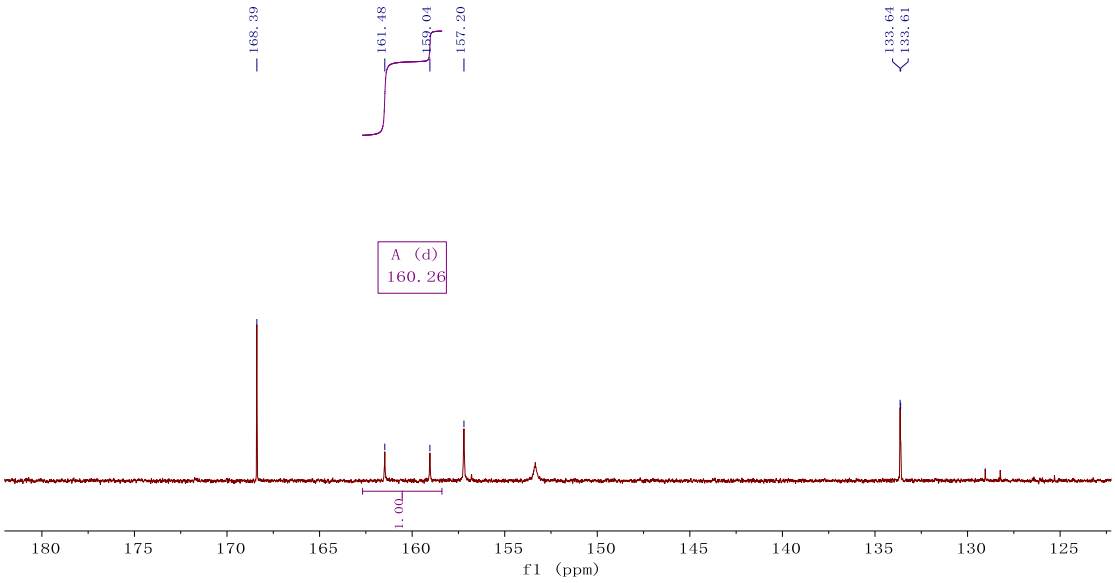
2f

^{1}H NMR Spectra of compound **2f** in $CDCl_3$ (400 MHz)

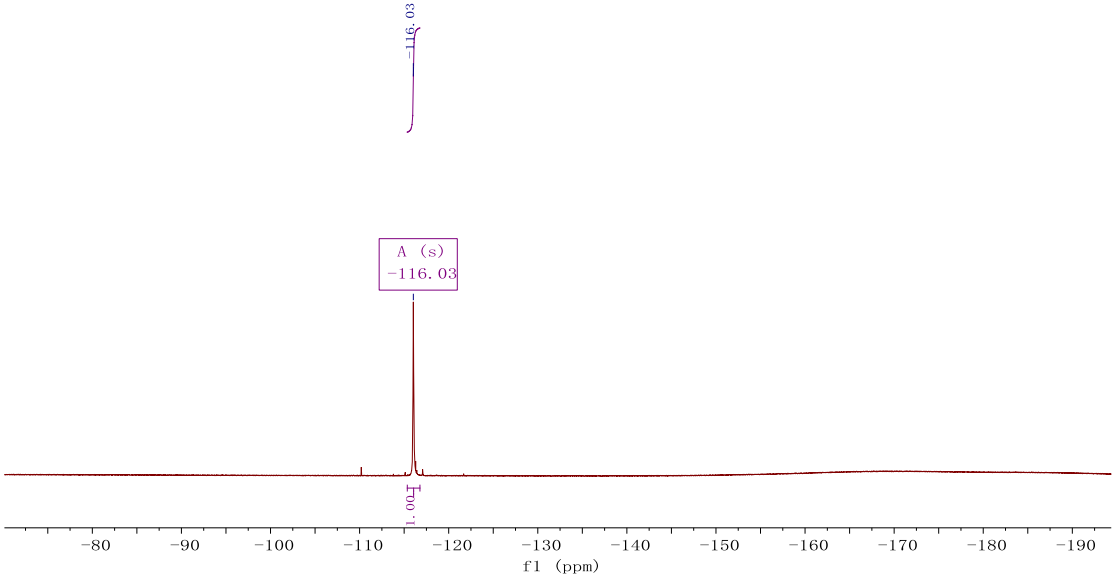


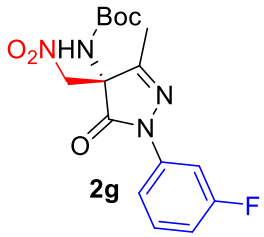
^{13}C NMR Spectra of compound **2f** in $CDCl_3$ (101 MHz)



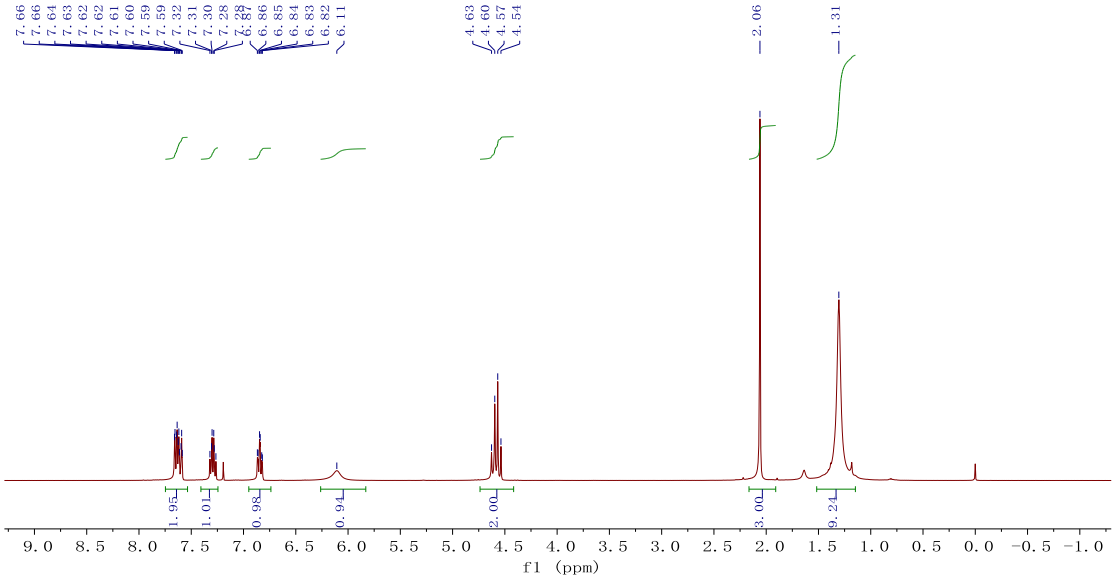


^{19}F NMR Spectra of compound **2f** in $CDCl_3$ (376 MHz)

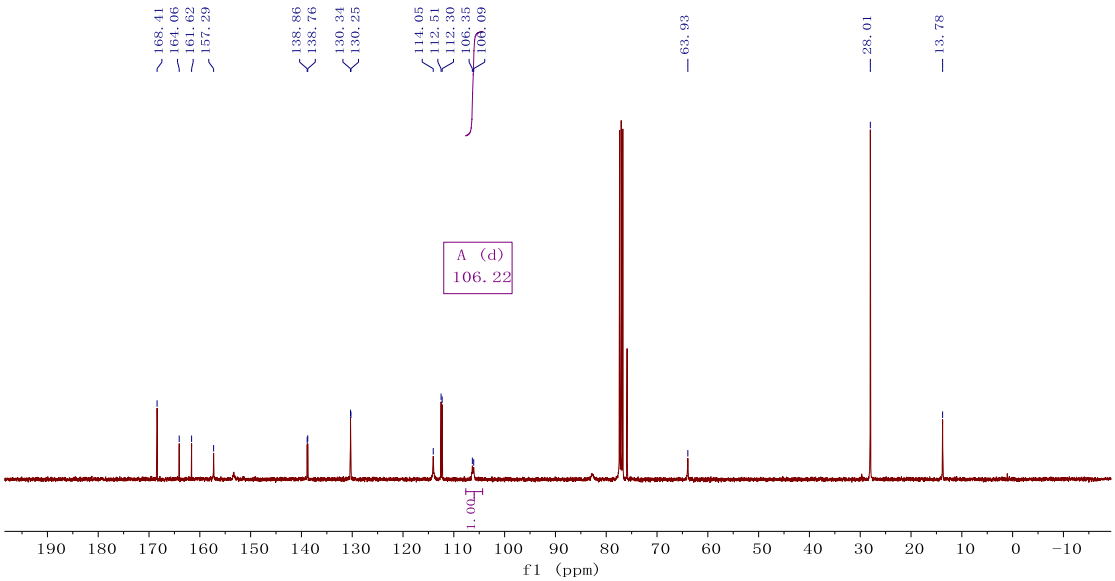


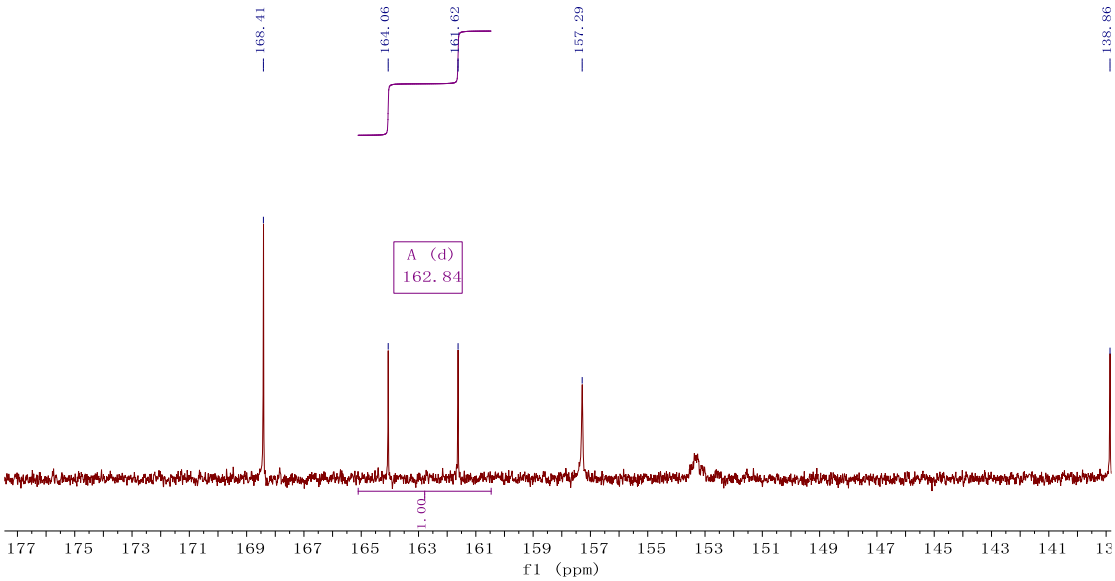


[1] H NMR Spectra of compound **2g** in $CDCl_3$ (400 MHz)

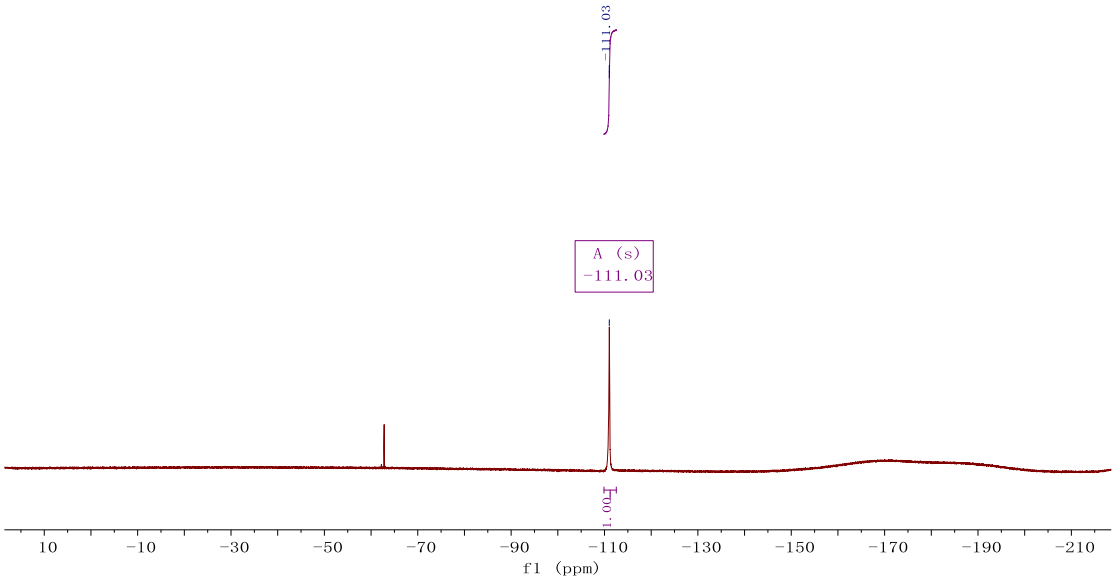


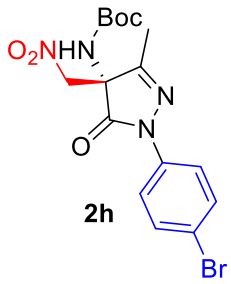
[13] C NMR Spectra of compound **2g** in $CDCl_3$ (101 MHz)





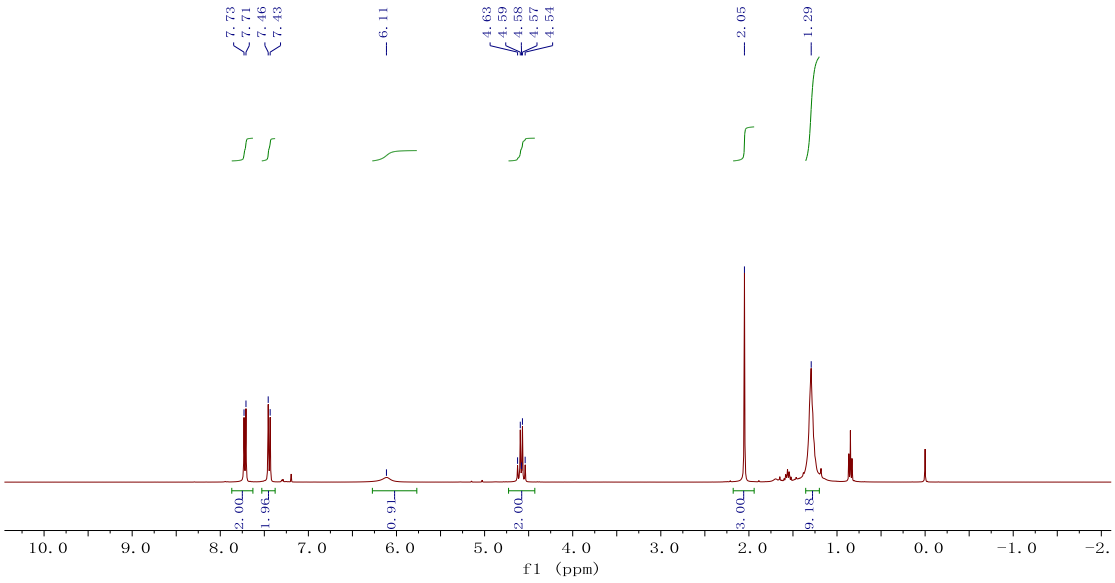
^{19}F NMR Spectra of compound **2g** in $CDCl_3$ (376 MHz)



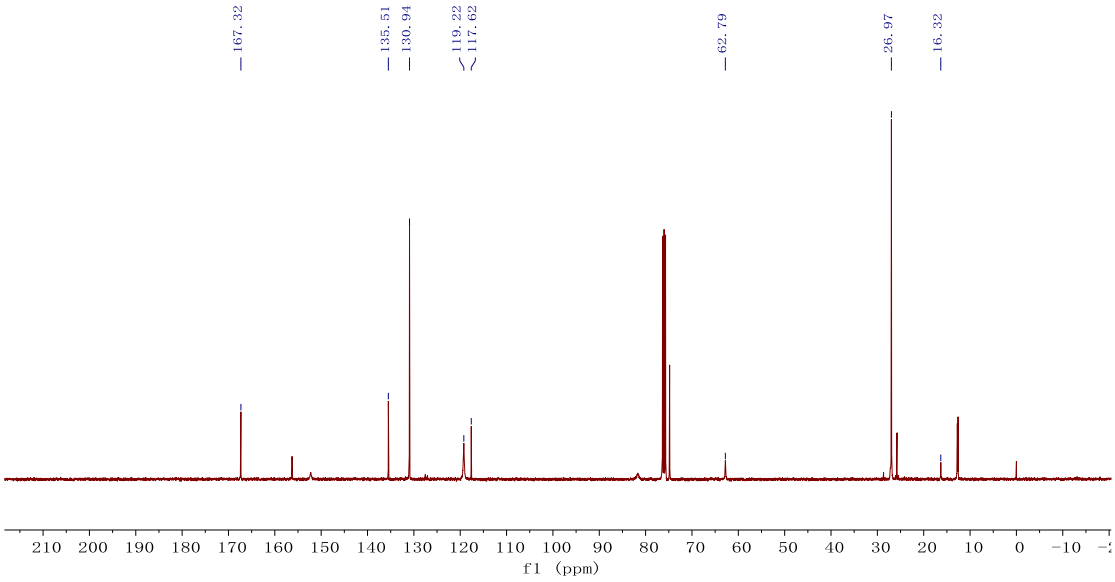


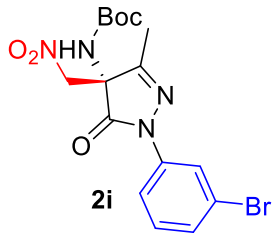
2h

[1] H NMR Spectra of compound **2h** in $CDCl_3$ (400 MHz)



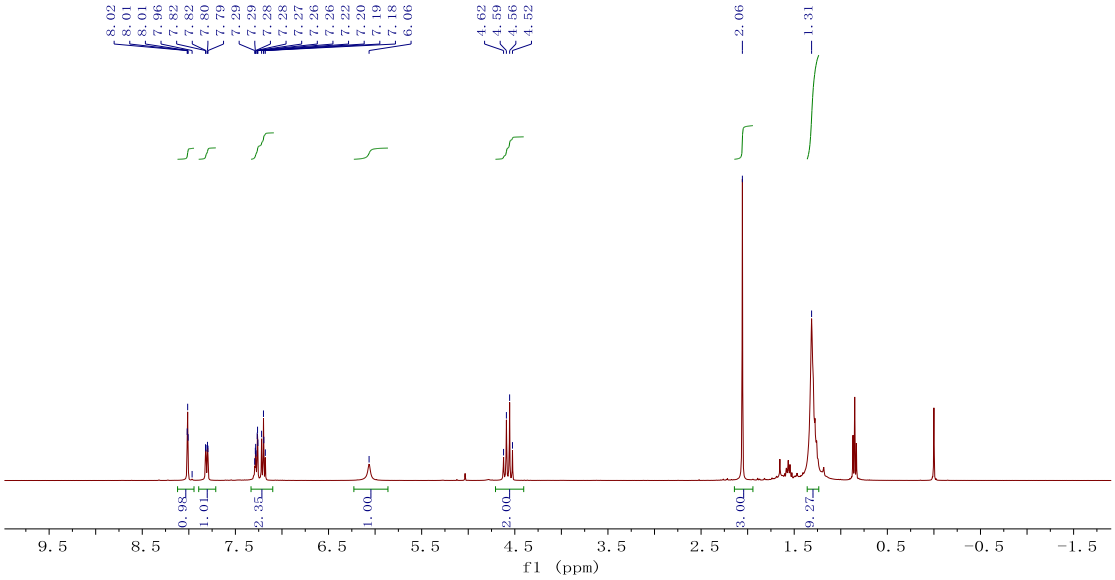
[13] C NMR Spectra of compound **2h** in $CDCl_3$ (101 MHz)



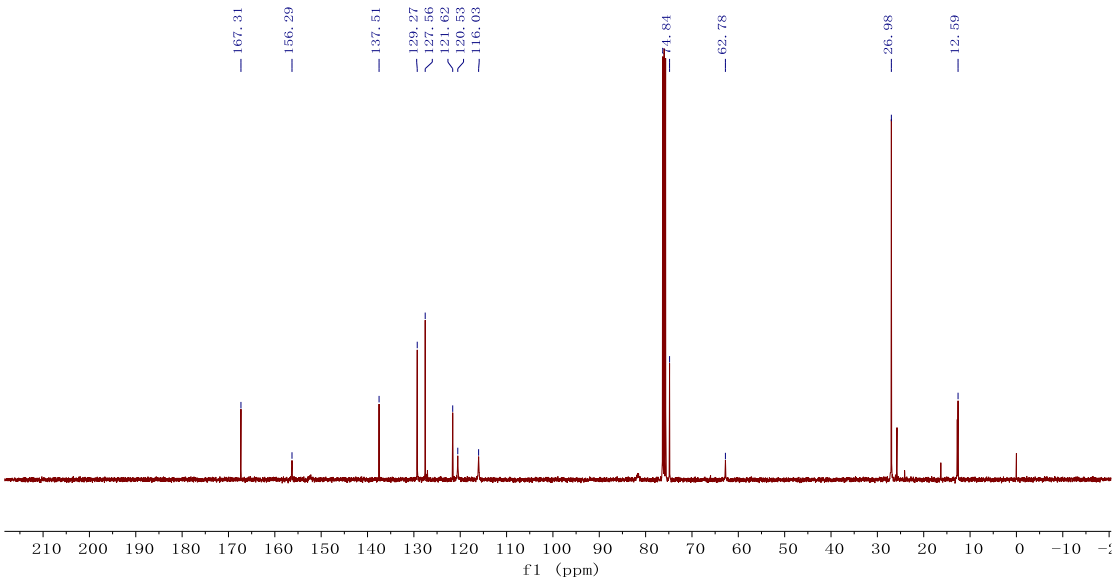


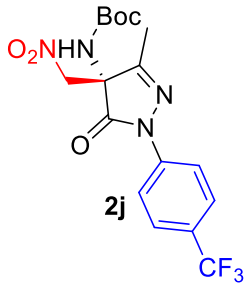
2i

[1] H NMR Spectra of compound **2i** in $CDCl_3$ (400 MHz)

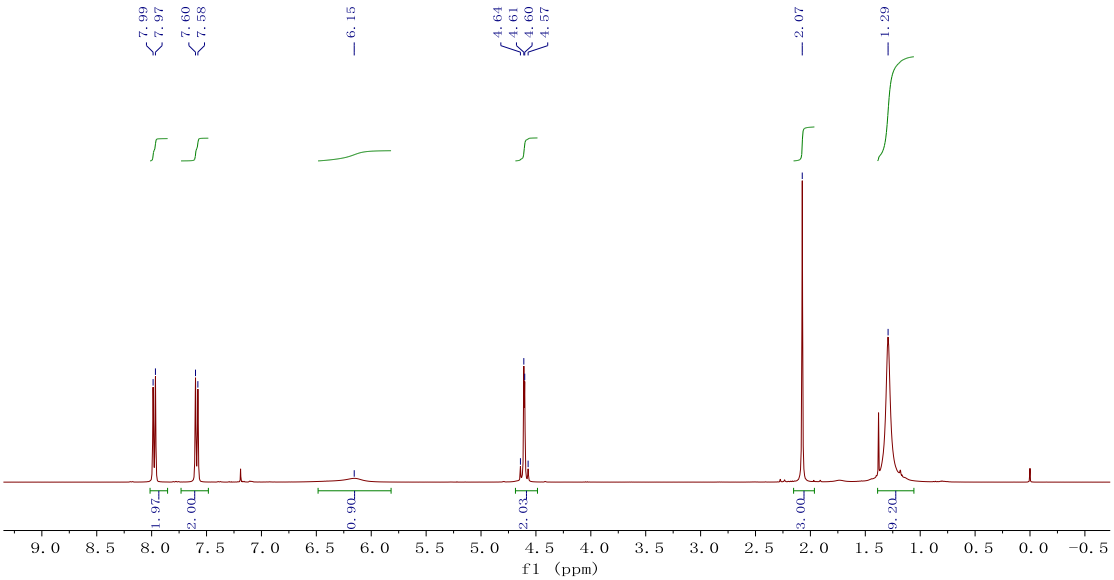


[13] C NMR Spectra of compound **2i** in $CDCl_3$ (101 MHz)

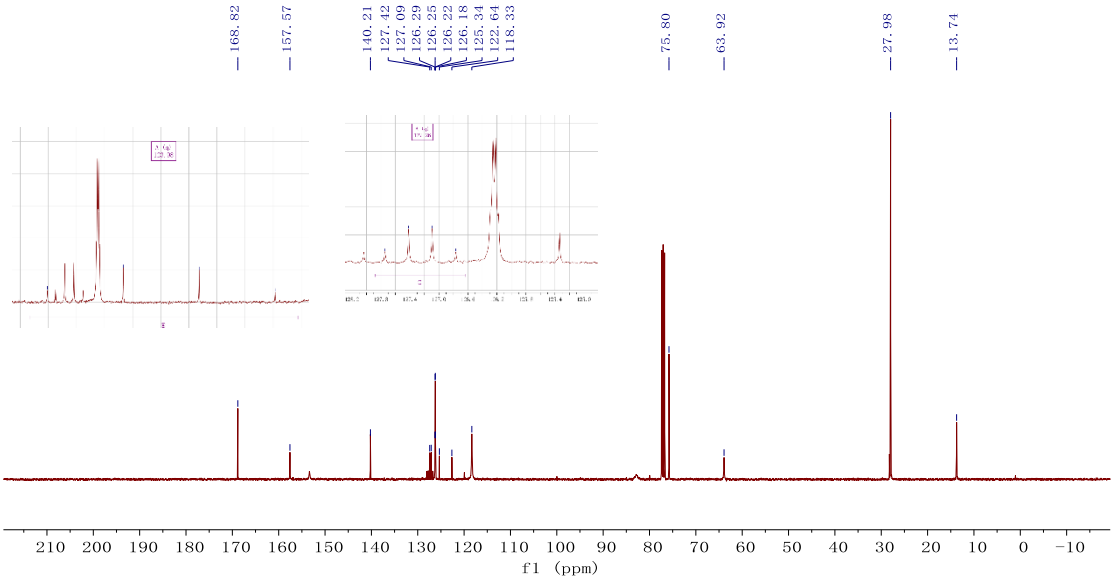




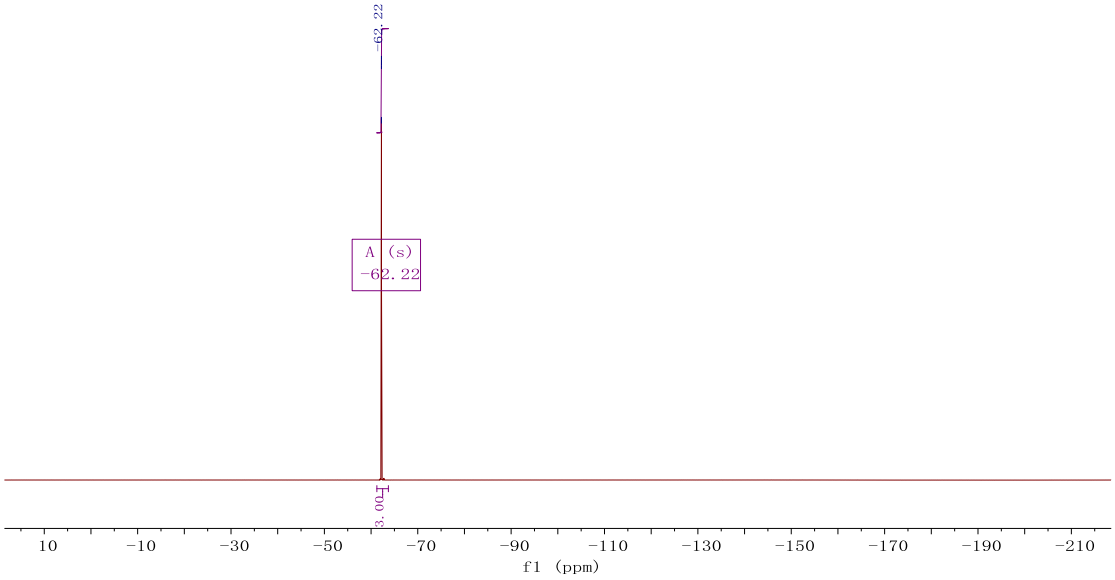
[1] H NMR Spectra of compound **2j** in $CDCl_3$ (400 MHz)

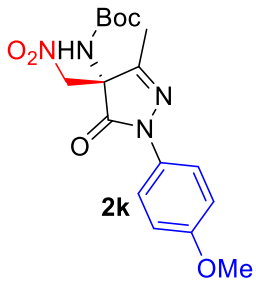


[13] C NMR Spectra of compound **2j** in $CDCl_3$ (101 MHz)

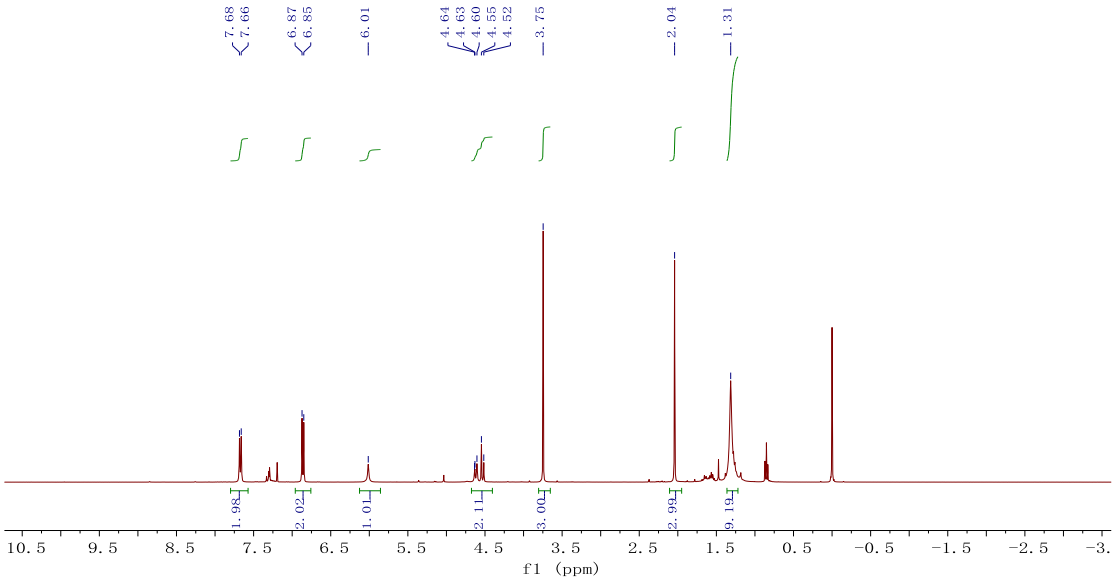


^{19}F NMR Spectra of compound **2j** in $CDCl_3$ (376 MHz)

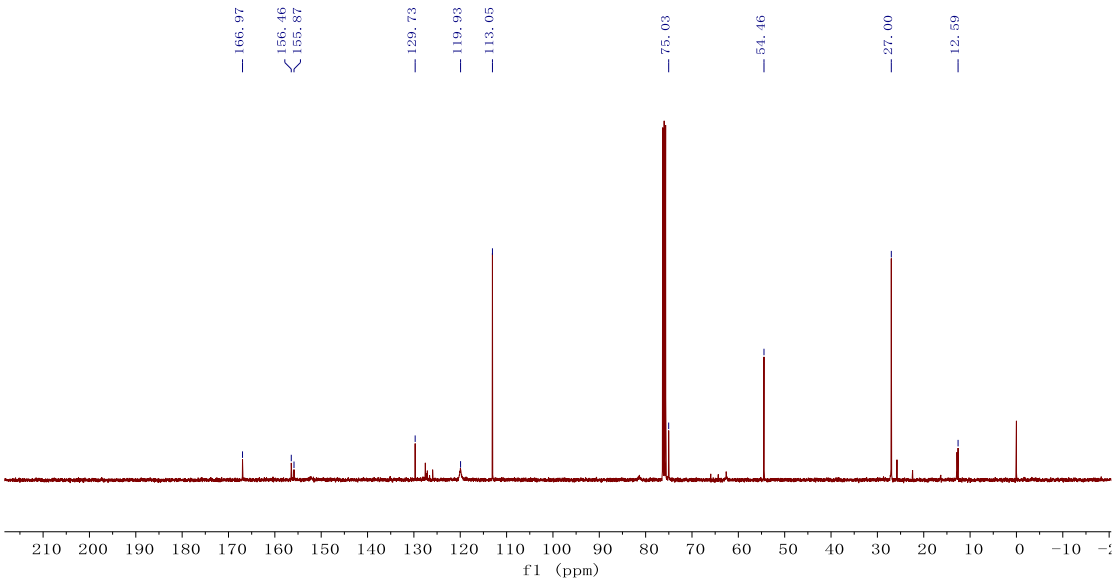


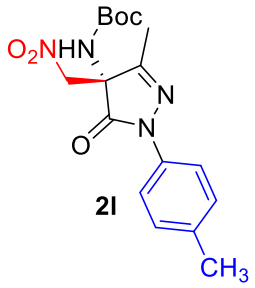


[1] H NMR Spectra of compound **2k** in $CDCl_3$ (400 MHz)



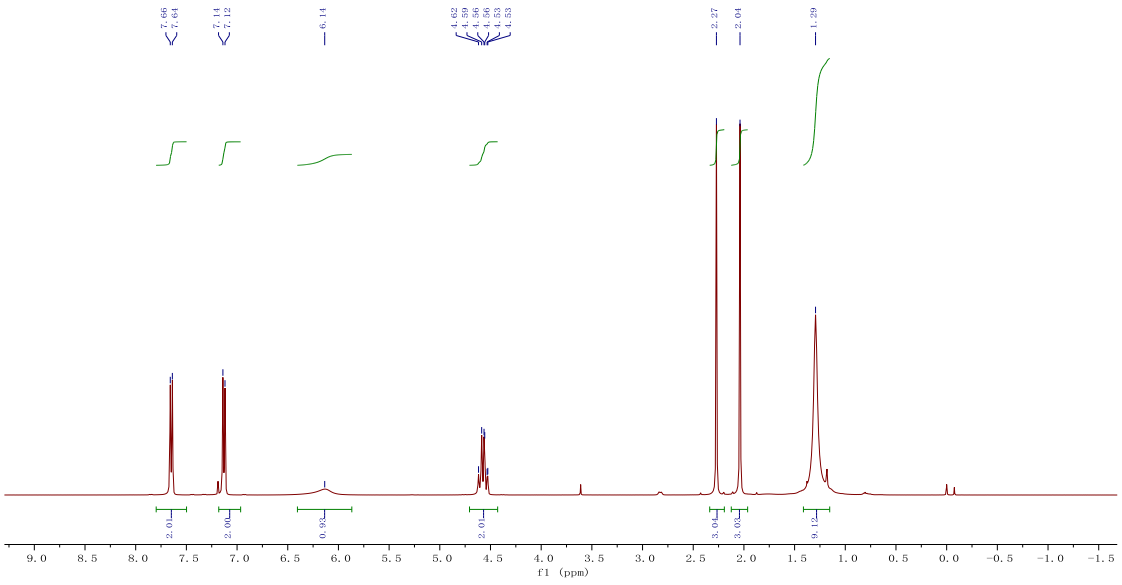
[13] C NMR Spectra of compound **2k** in $CDCl_3$ (101 MHz)



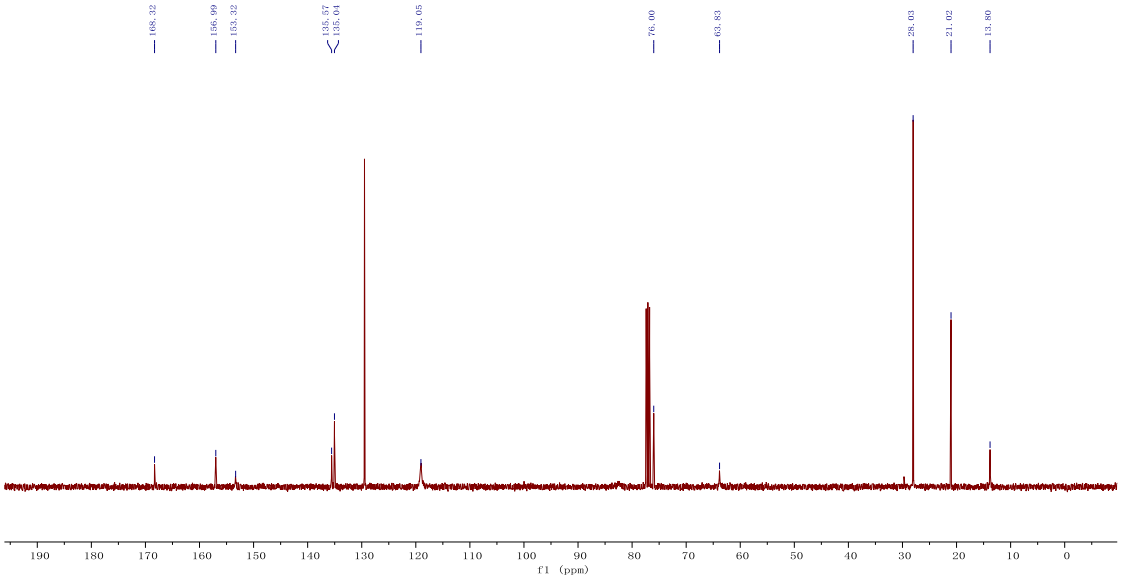


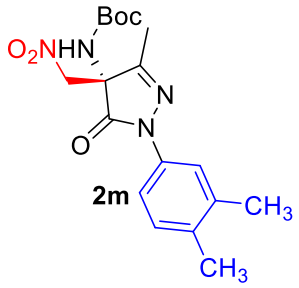
2l

[1] H NMR Spectra of compound **2l** in $CDCl_3$ (400 MHz)

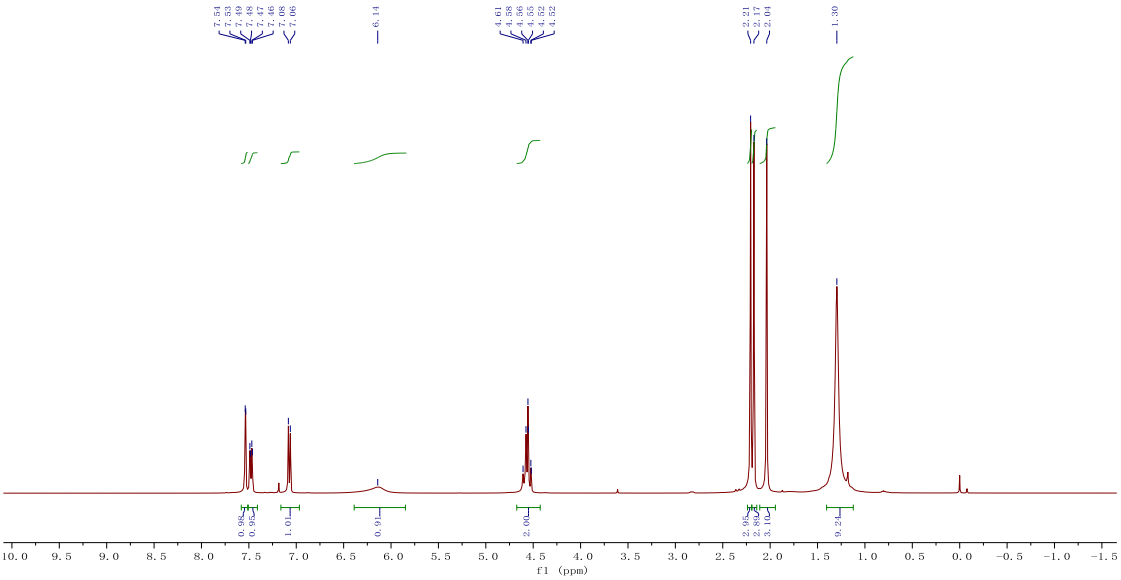


[13] C NMR Spectra of compound **2l** in $CDCl_3$ (101 MHz)

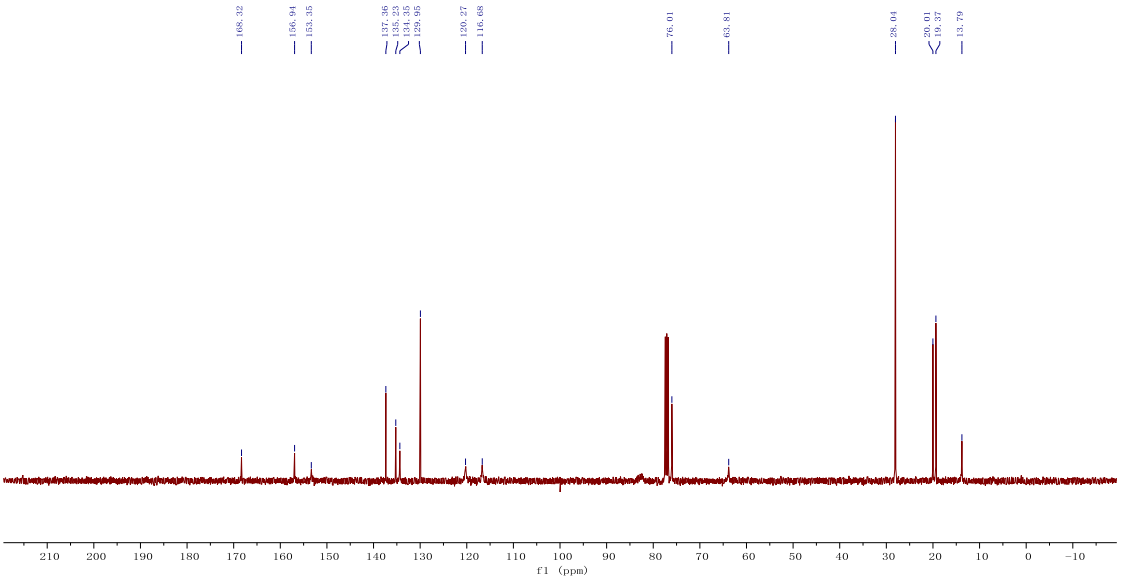


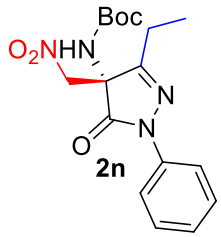


[1] H NMR Spectra of compound **2m** in $CDCl_3$ (400 MHz)

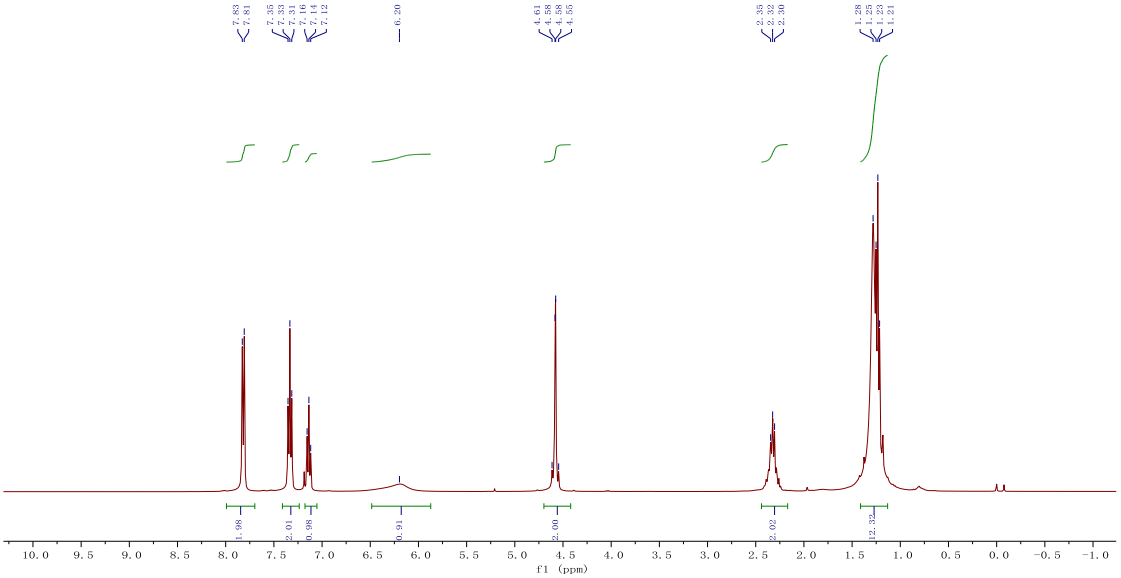


[13] C NMR Spectra of compound **2m** in $CDCl_3$ (101 MHz)

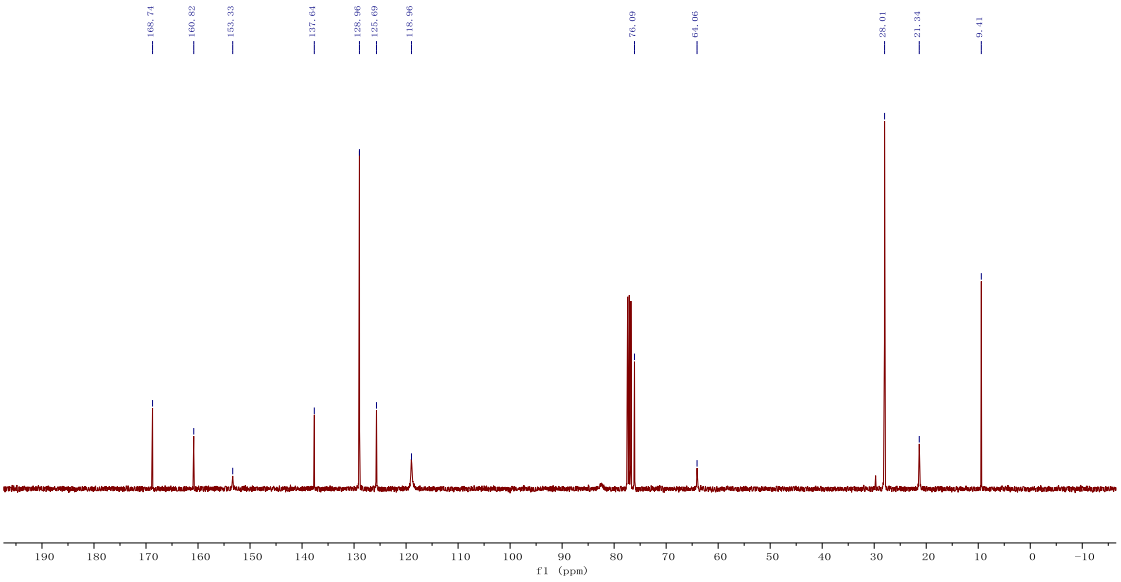


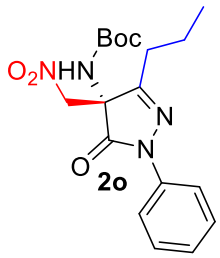


[1] H NMR Spectra of compound **2n** in $CDCl_3$ (400 MHz)

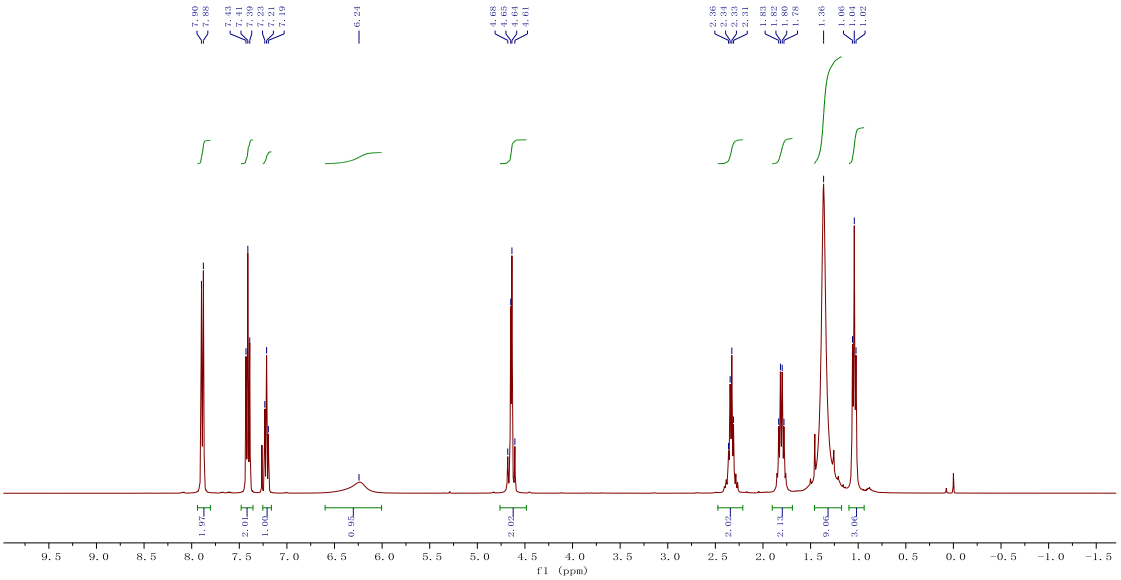


[13] C NMR Spectra of compound **2n** in $CDCl_3$ (101 MHz)

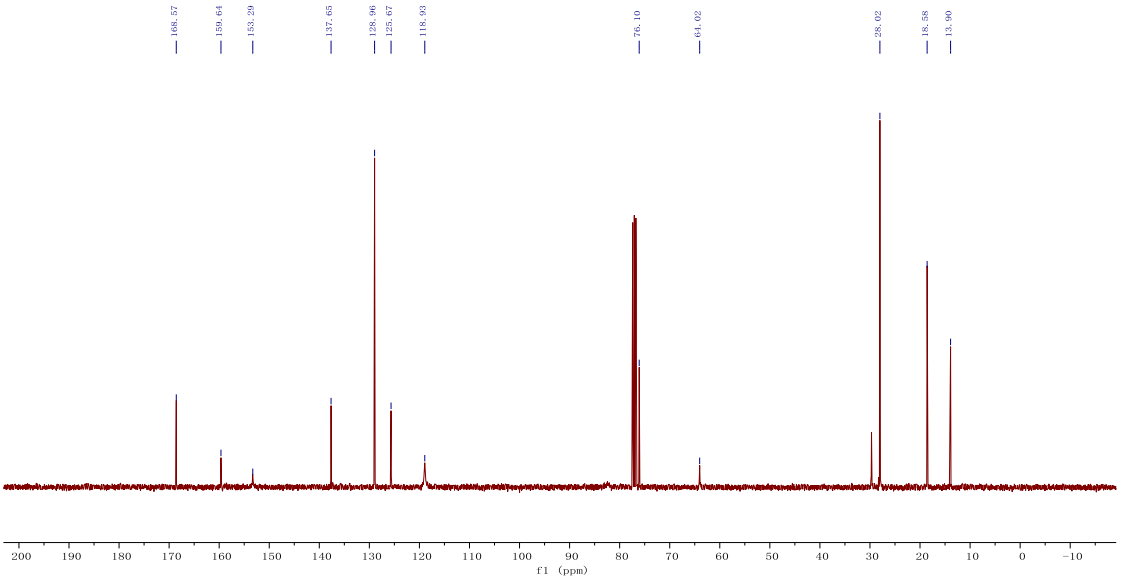


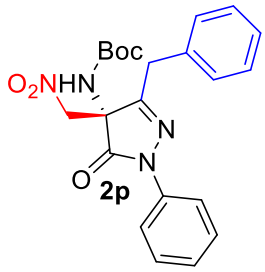


[1] H NMR Spectra of compound **2o** in $CDCl_3$ (400 MHz)

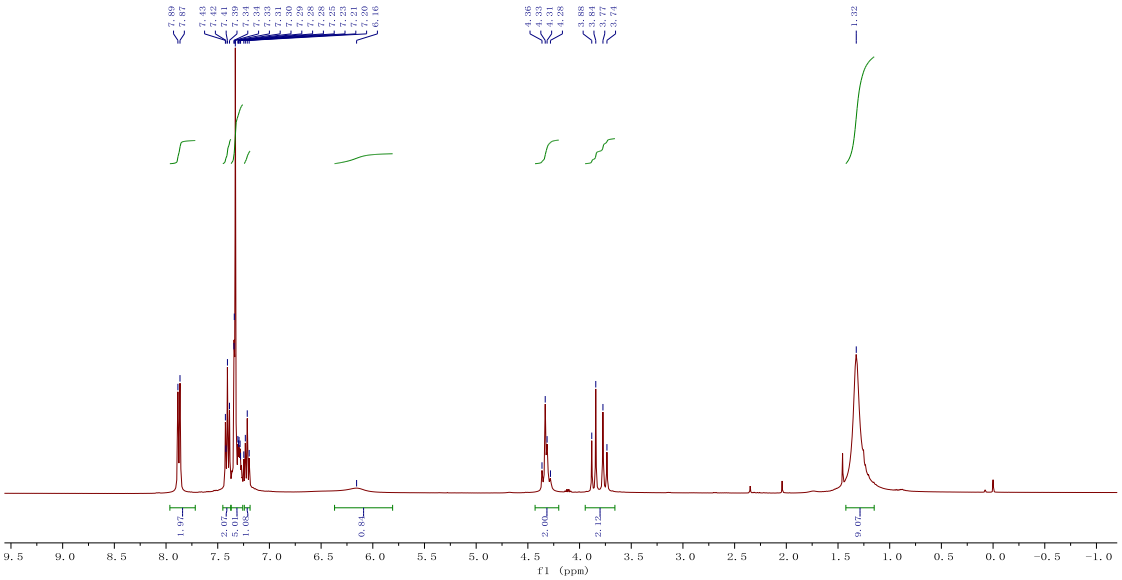


[13] C NMR Spectra of compound **2o** in $CDCl_3$ (101 MHz)

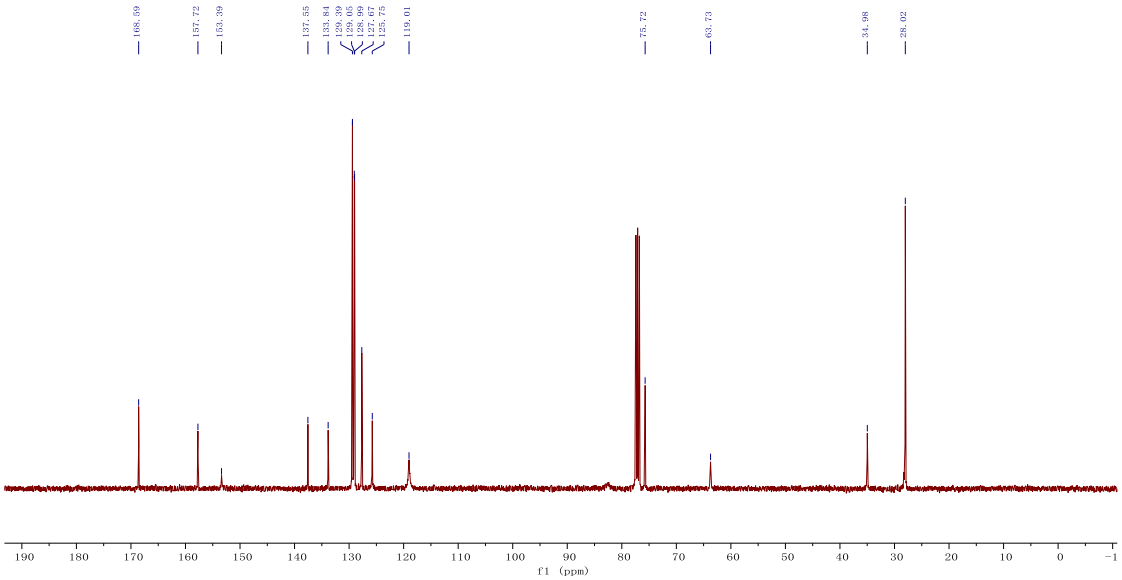


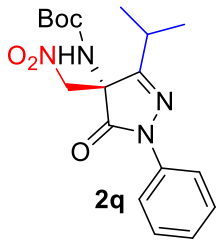


[1] H NMR Spectra of compound **2p** in $CDCl_3$ (400 MHz)

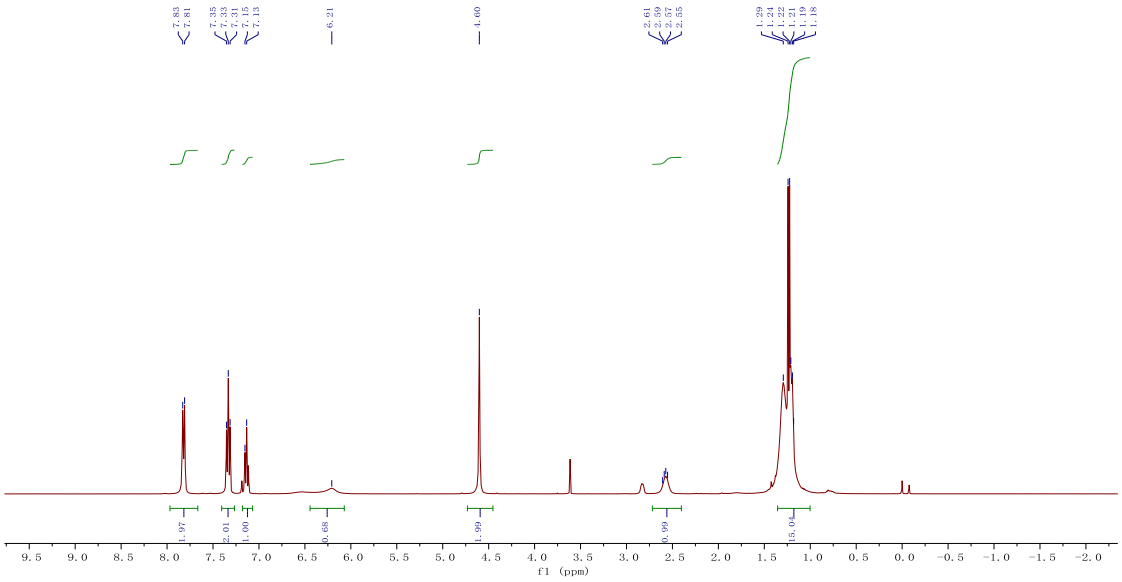


[13] C NMR Spectra of compound **2p** in $CDCl_3$ (101 MHz)

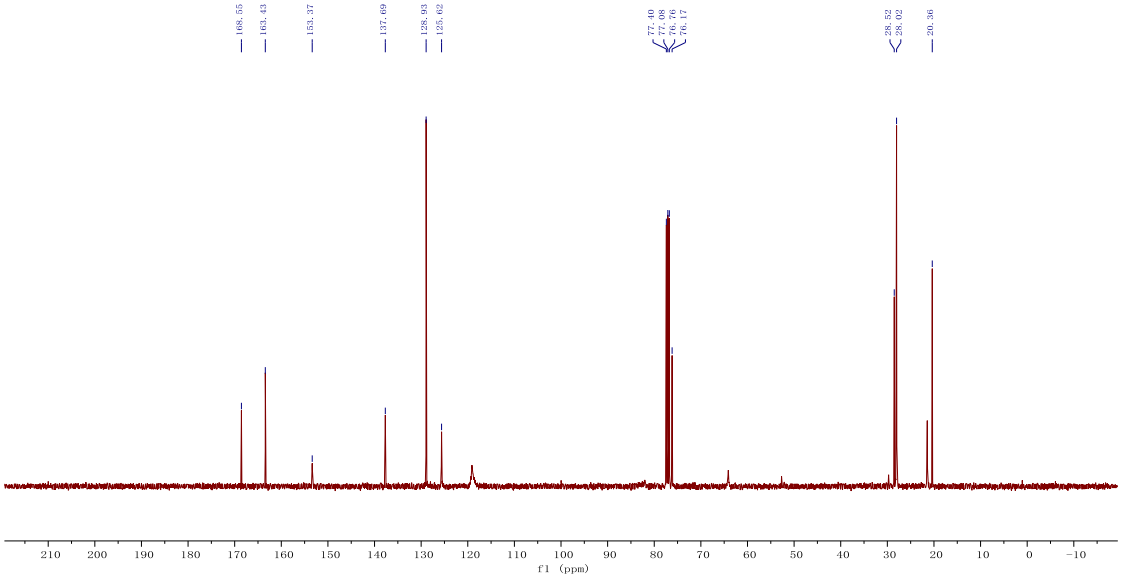


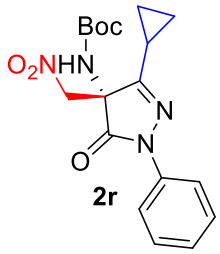


[1] H NMR Spectra of compound **2q** in $CDCl_3$ (400 MHz)

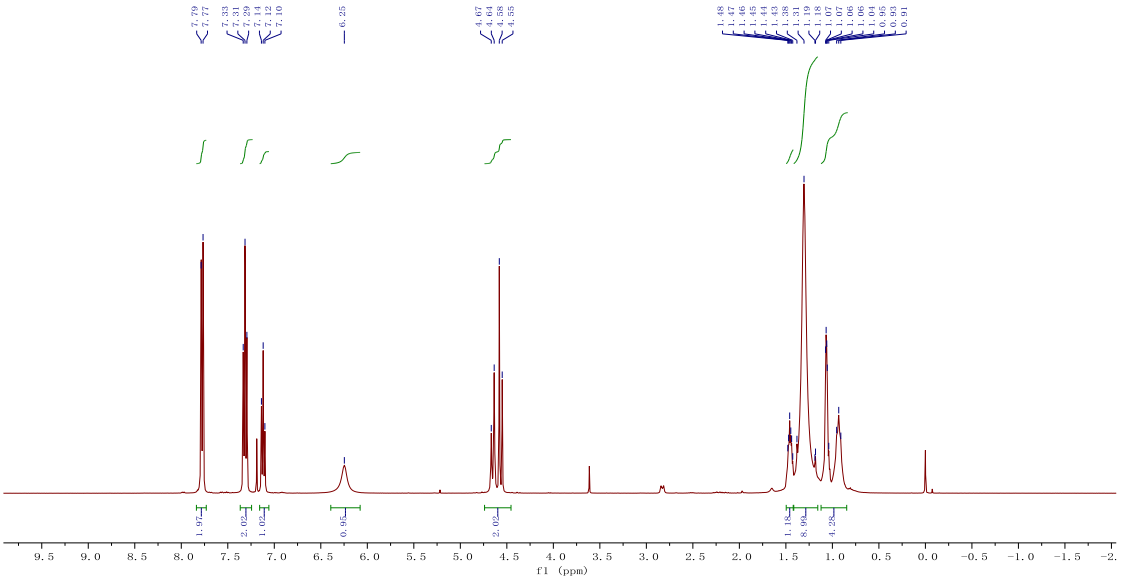


[13] C NMR Spectra of compound **2q** in $CDCl_3$ (101 MHz)

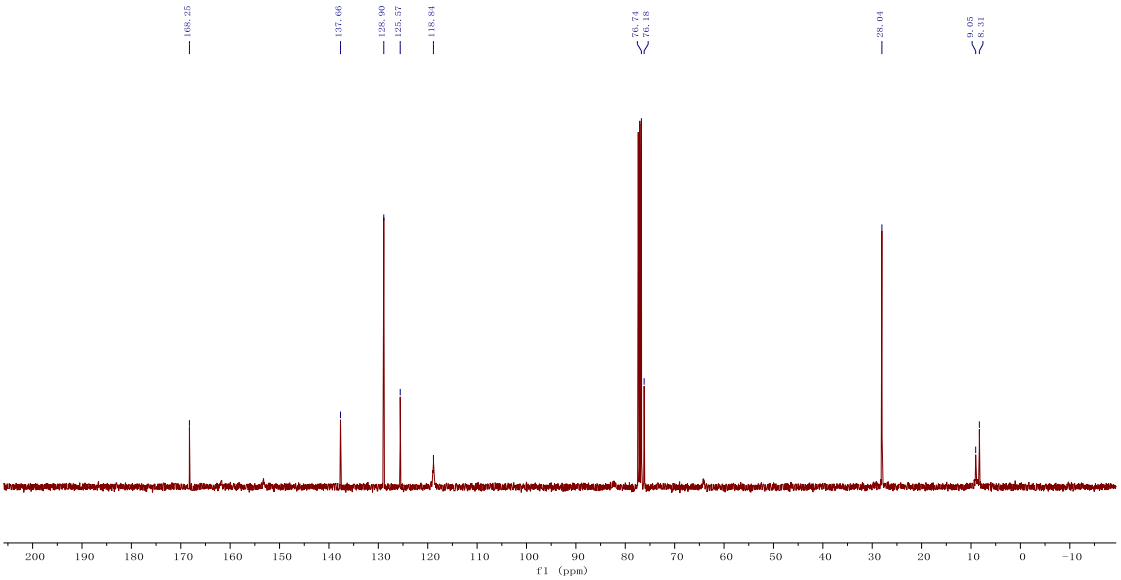


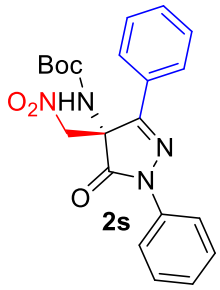


[1] H NMR Spectra of compound **2r** in $CDCl_3$ (400 MHz)

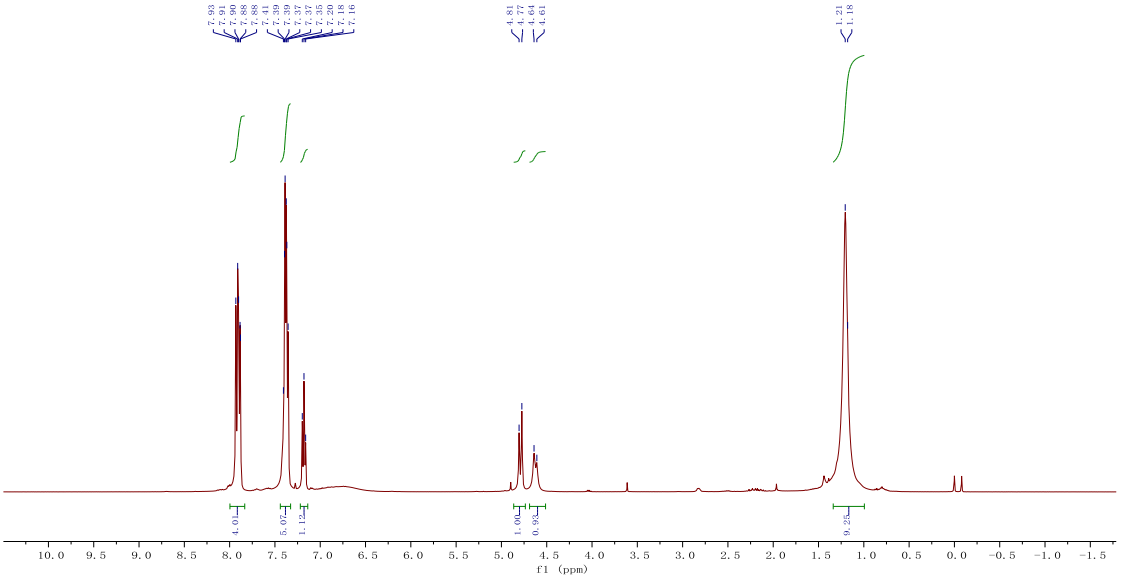


[13] C NMR Spectra of compound **2r** in $CDCl_3$ (101 MHz)

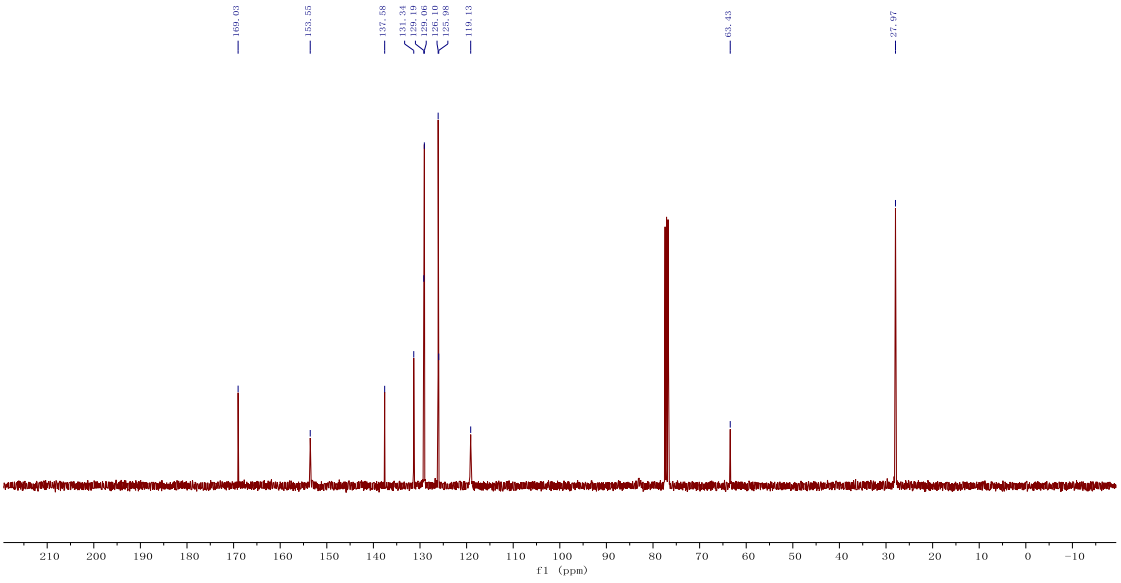


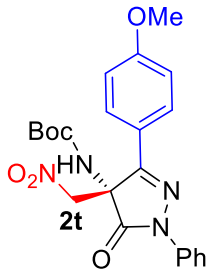


[1] H NMR Spectra of compound **2s** in $CDCl_3$ (400 MHz)

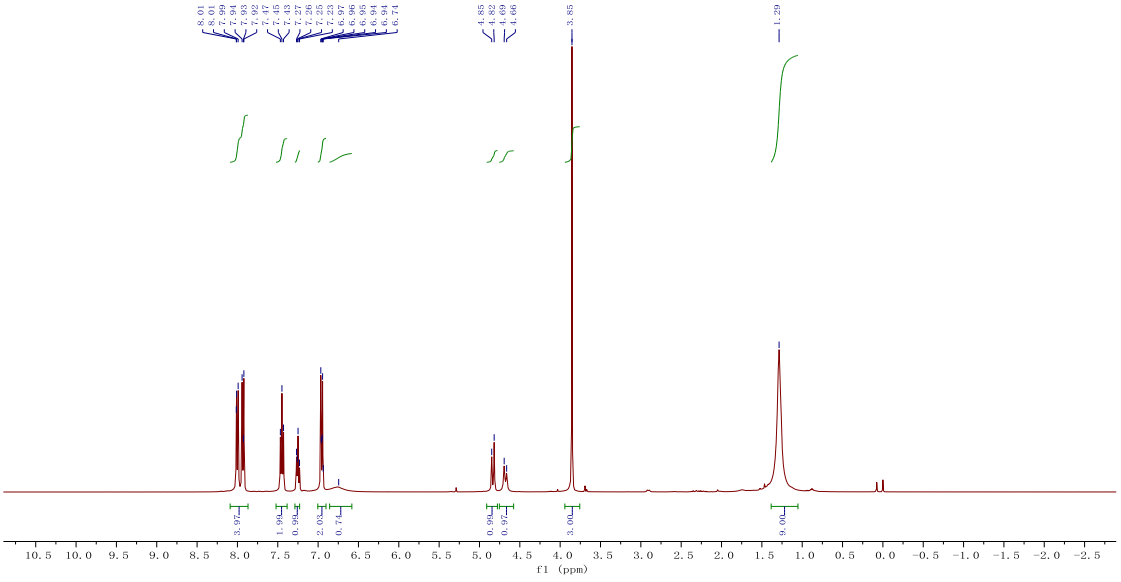


[13] C NMR Spectra of compound **2s** in $CDCl_3$ (101 MHz)

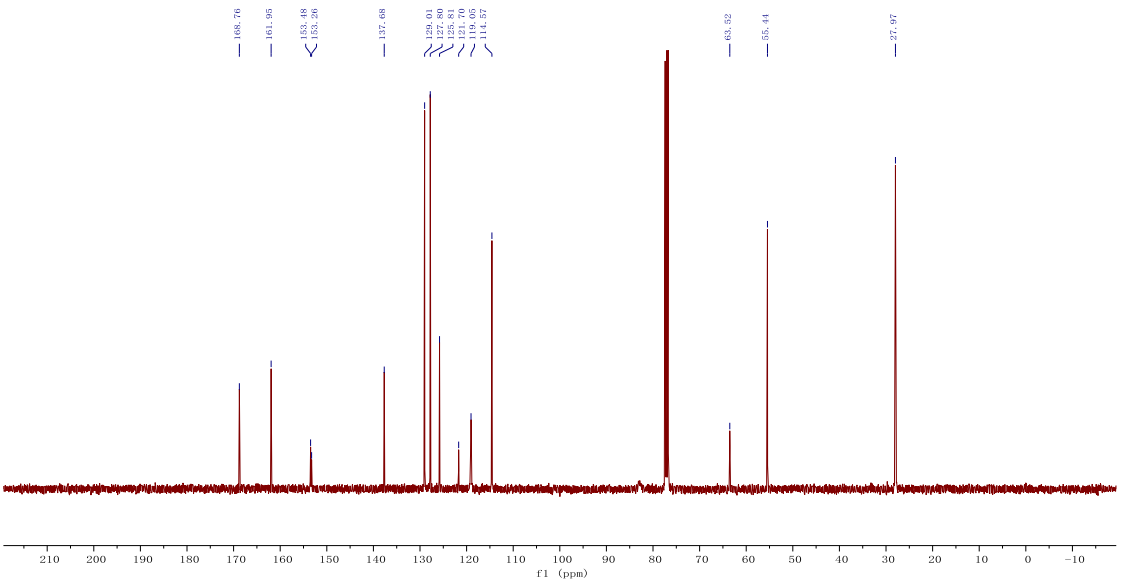


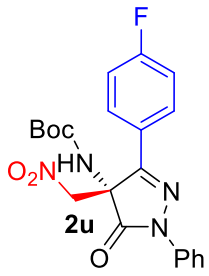


[1] H NMR Spectra of compound **2t** in $CDCl_3$ (400 MHz)

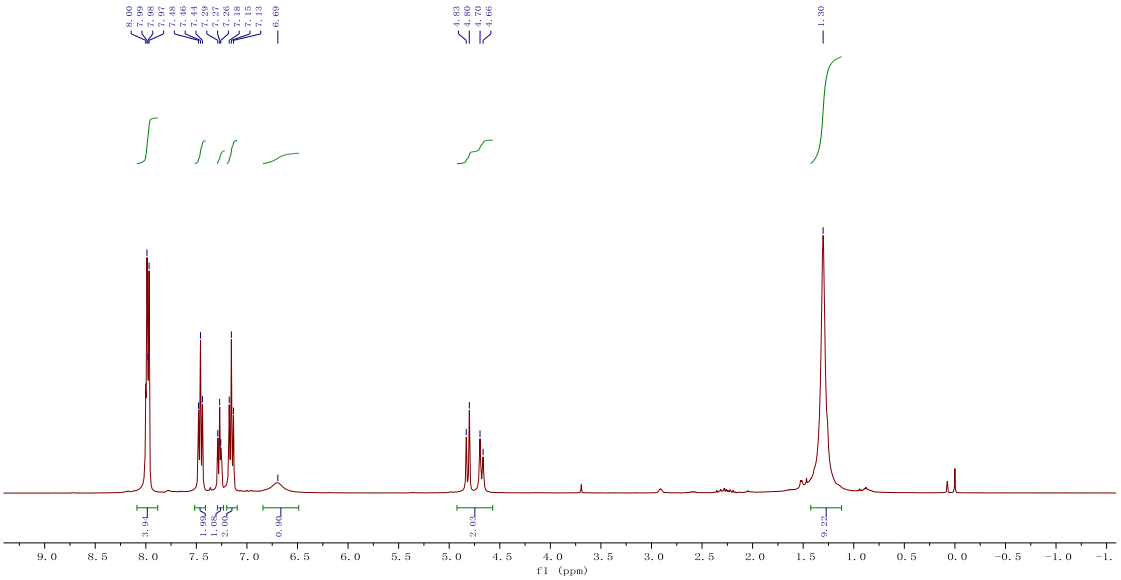


[13] C NMR Spectra of compound **2t** in $CDCl_3$ (101 MHz)

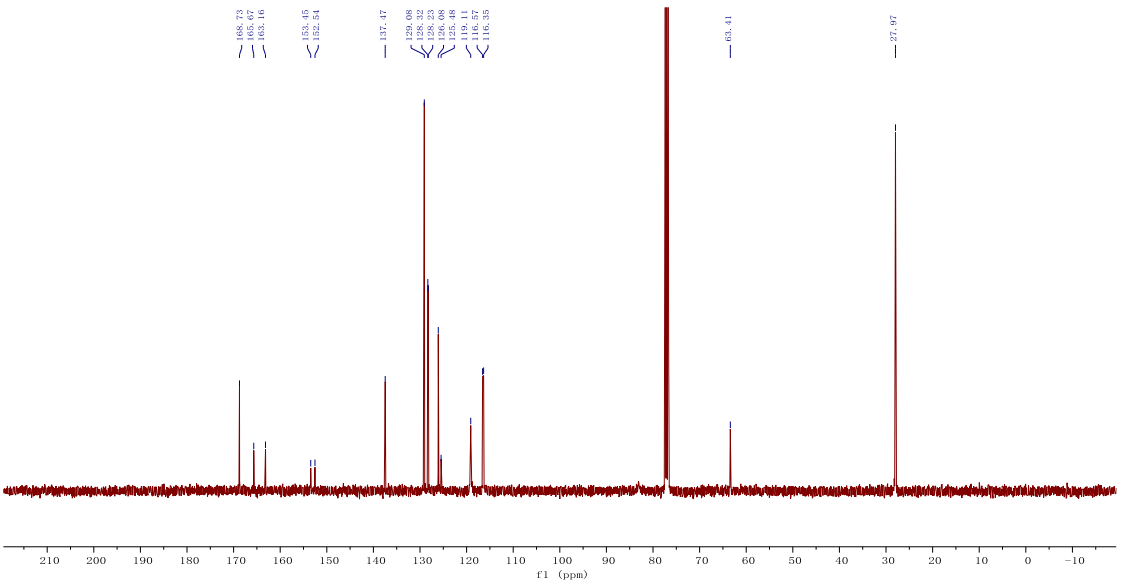


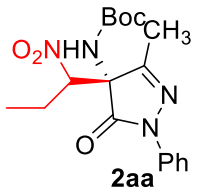


[1] H NMR Spectra of compound **2u** in $CDCl_3$ (400 MHz)



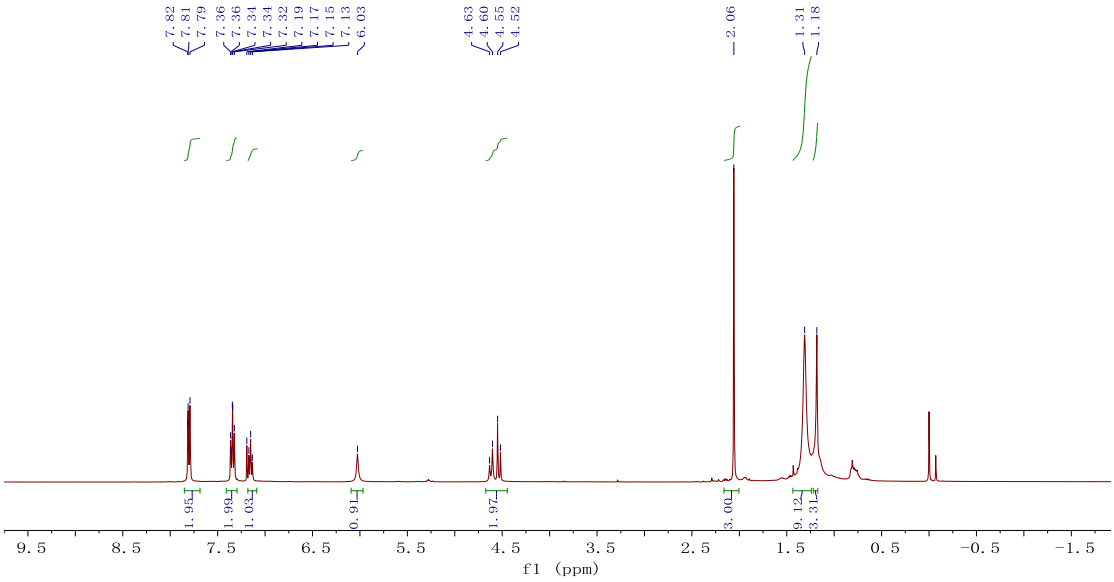
[13] C NMR Spectra of compound **2u** in $CDCl_3$ (101 MHz)



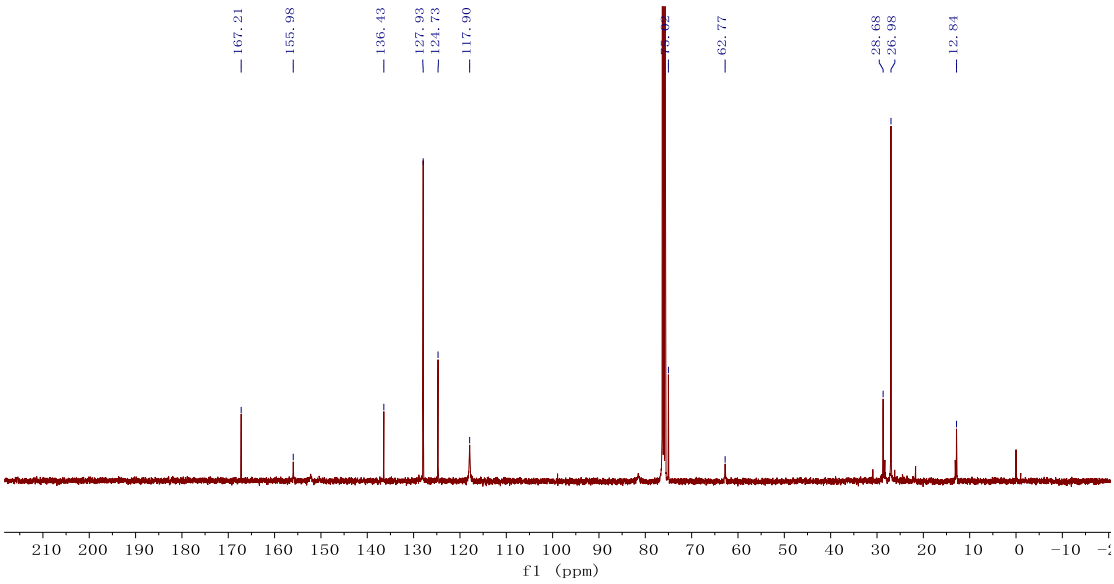


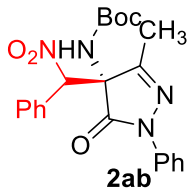
2aa

[1] H NMR Spectra of compound **2aa** in $CDCl_3$ (400 MHz)



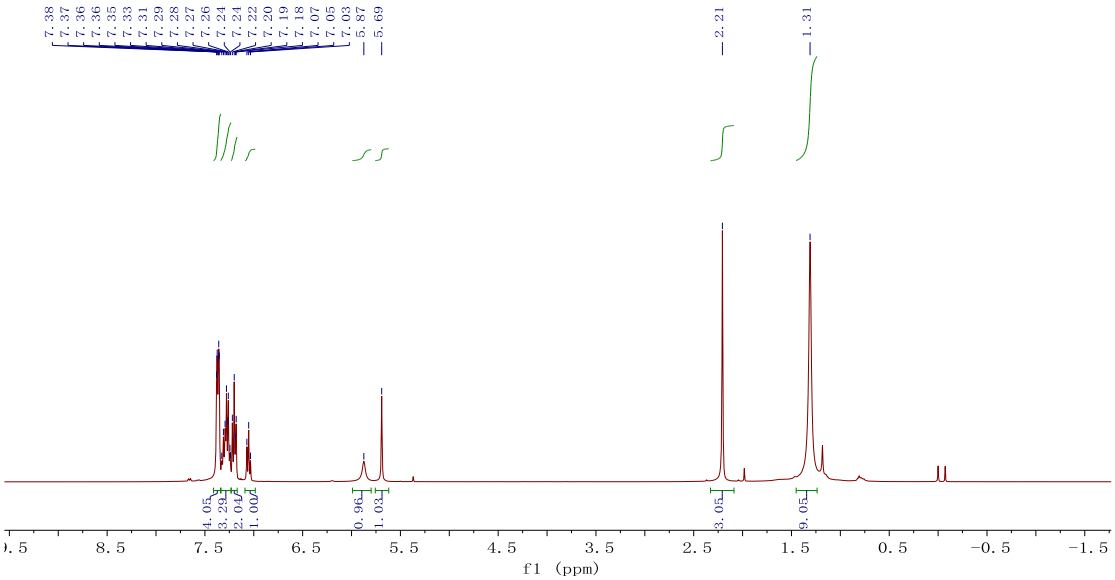
[13] C NMR Spectra of compound **2aa** in $CDCl_3$ (101 MHz)



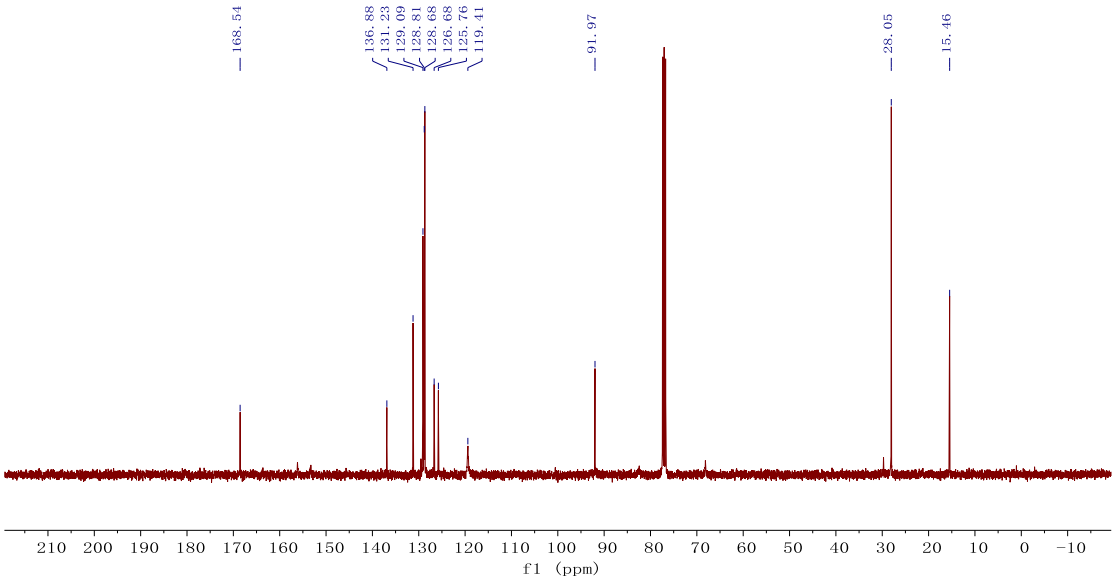


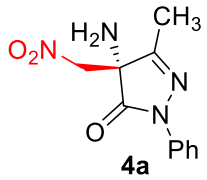
2ab

[1] H NMR Spectra of compound **2ab** in $CDCl_3$ (400 MHz)



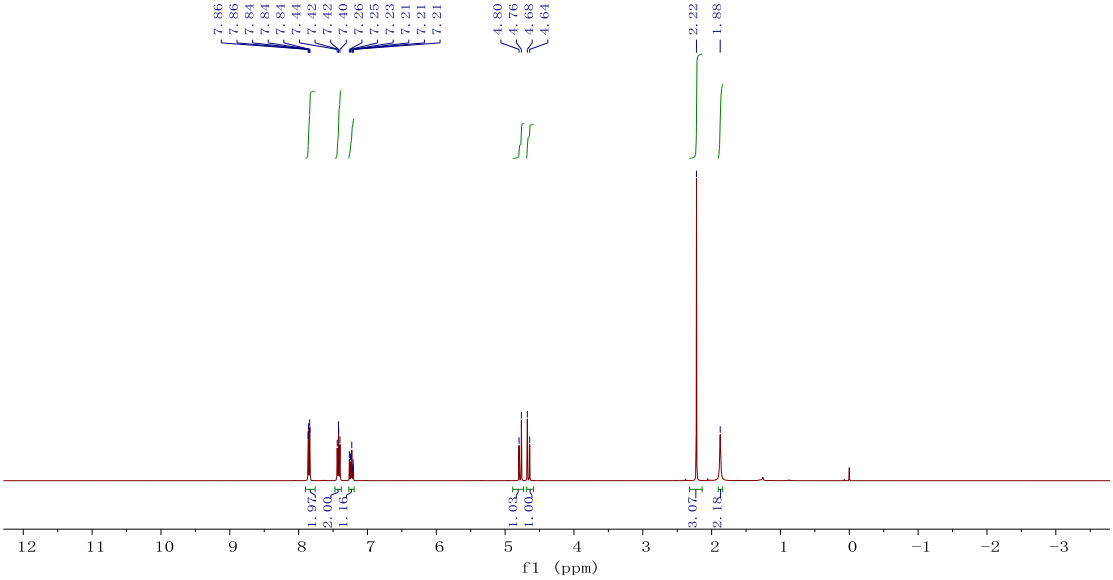
[13] C NMR Spectra of compound **2ab** in $CDCl_3$ (101 MHz)





4a

^{1}H NMR Spectra of compound **4a** in $CDCl_3$ (400 MHz)



^{13}C NMR Spectra of compound **4a** in $CDCl_3$ (101 MHz)