Access to Arylurazoles Bearing Both Central and C-N Axial Chirality *via* Asymmetric Desymmetrization Catalyzed by Chiral Phosphoric Acid

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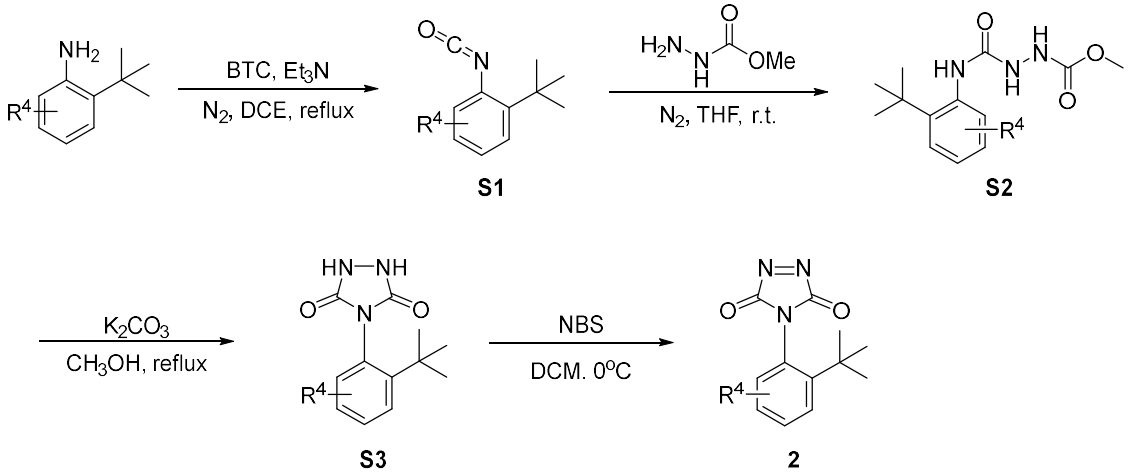
Contents

1. General information

Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Column chromatography was performed on silica gel (200~300 mesh). Enantiomeric excesses (ee) were determined by HPLC using corresponding commercial chiral columns as stated at 30 °C with UV detector at 254 nm. Optical rotations were reported as follows: $[\alpha]_D^T$ (c g/100 mL, solvent). All ^{1}H NMR spectra were recorded on Bruker Avance Ⅱ 400 MHz or Bruker Avance III 500 MHz, ^{13}C NMR spectra were recorded on Bruker Avance Ⅱ 101 MHz, ^{19}F NMR spectra were recorded on Bruker Avance Ⅱ 377 MHz with chemical shifts reported as ppm (in $CDCl_3$ or DMSO-d_6, TMS as an internal standard). Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, br = broad singlet, dd = double doublet, ddd = doublet of doublet of doublets, dt = doublet of triplets, coupling constants in Hz, integration). HRMS (ESI) was obtained with a HRMS/MS instrument (LTQ Orbitrap XL TM). The absolute configuration of **3xa** was assigned by the X-ray analysis.

Allyl pyrazolones **1** were prepared according to literature methods[1].

2. Experimental procedures of compounds 2[2]



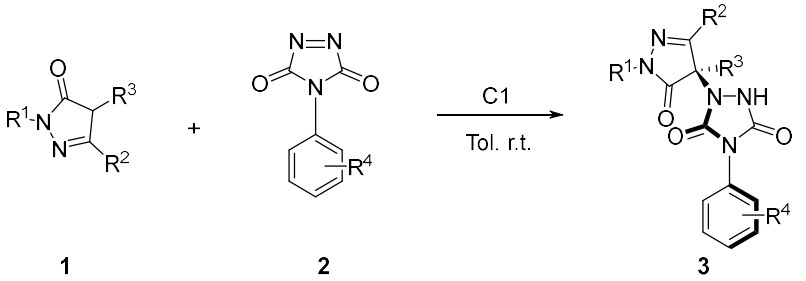
Aryl isocyanate **S1**: Et_3N (0.03 mL, 0.01 equiv) was added to a stirring solution of triphosgene (2.97 g, 10.0 mmol, 0.5 equiv) in dry DCE (50 mL) at 0 °C. After stirring 5 minutes, aromatic amine (20.0 mmol) in dry DCE (50 mL) was added slowly over 2 h. The reaction mixture was then refluxed and stirred under nitrogen for 4 h. After cooling to room temperature, the mixture was evaporated under reduced pressure to afford **S1** as a yellow liquid.

4-Ar-1-carbethoxysemicarbazide **S2**: To a solution of methyl carbazate (1.8 g, 20.0 mmol) in anhydrous THF under argon atmosphere, aryl isocyante **S1** (20.0 mmol, 1.0 equiv.) was added over 1-2 minutes. The resulting mixture was stirred at room temperature for 1 h. After the reaction completion (monitored by TLC), the white solid product was collected by filtration or by simple evaporation to dryness.

4-Ar-urazole **S3**: To a solution of intermediate **S2** in methanol, potassium carboxylate (2.0 equiv.) was added and the reaction mixture was refluxed overnight. After the reaction completion (monitored by TLC), the resulting mixture was condensed and re-dissolved with small amount of water. The pH of resulting mixture was adjusted to the range of 3~4 with the drop-wise addition of 1N aqueous HCl. The desired product **S3** was collected by simple filtration and washed with cold deionized water prior to drying.

4-aryl-l,2,4-triazoline-3,5-diones **2**: *N*-Bromosuccinimide (20 mmol) was added to an ice-cold suspension of urazoles (10 mmol) in 150 mL of CH_2C1_2. After being stirred for 30 min, the resulting red solution was extracted five times with water. The CH_2Cl_2 layer was then dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purple or dark red solid of various triazolinediones were obtained.

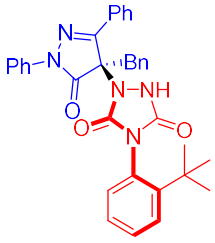
3. Experimental procedures and characterization of compound 3



1 2 3

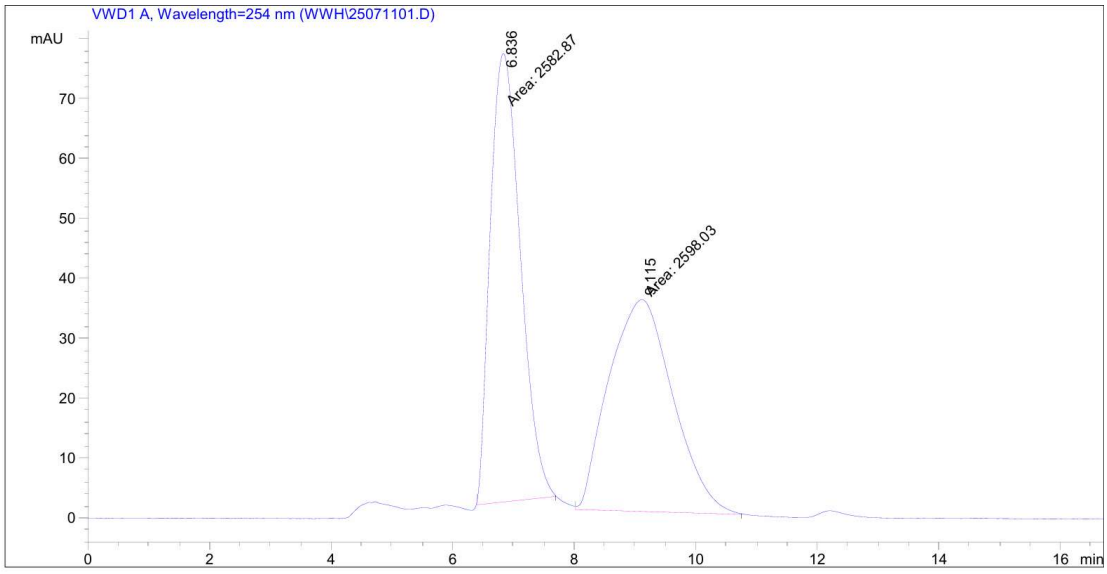
To a tube charged with compound **1** (0.2 mmol), **C1** (0.01 mmol)followed with Tol (2 mL), compound **2** (0.24 mmol) were then added in one portion. The reaction mixture was stirred at 25 °C for 0.2 hours. When compound **1** was consumed as checked by TLC, then the reaction was stopped and purified by column chromatography on silica gel directly to give the product **3**.

1-(4-benzyl-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dion (3aa)



3aa

White solid, mp 131-133 ℃, 80% yield, 98% ee, dr = 13:1. $[\alpha]_D^{25}$ = -1.205 (c = 0.2, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.33 (s, 1H), 8.10 - 8.03 (m, 2H), 7.57 - 7.45 (m, 6H), 7.39 - 7.34 (m, 1H), 7.31 - 7.27 (m, 2H), 7.23 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.20 - 7.04 (m, 4H), 6.98 (ddd, *J* = 11.2, 8.1, 1.6 Hz, 3H), 4.01 - 3.84 (m, 2H), 1.16 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 156.1, 153.3, 152.6, 148.9, 136.6, 132.5, 131.4, 130.5, 130.0, 128.8, 128.6, 128.6, 128.3, 128.3, 128.2, 128.1, 127.7, 126.4, 125.5, 120.4, 71.7, 39.6, 35.3, 31.3. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{31}N_5NaO_3$, 580.2325; Found 580.2316. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 7:3, flow rate = 0.8 mL/min., λ = 240 nm, t_R = 8.3 min. (minor), 5.5 min. (major).



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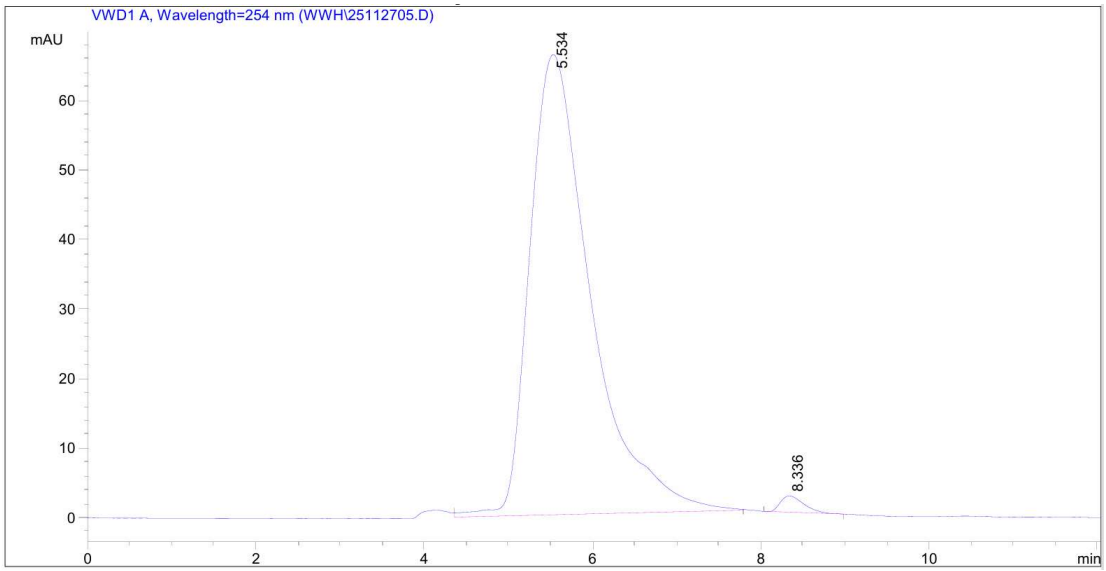

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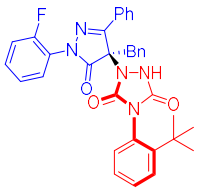
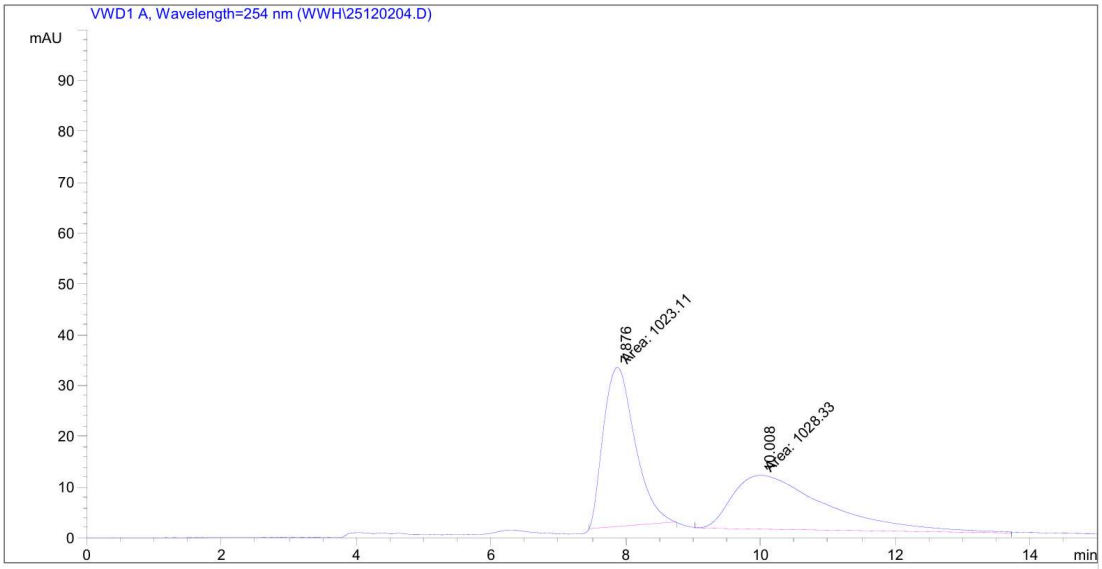
1	5.534	VB	0.7492	3333.26831	66.18851	98.6511
2	8.336	PB	0.2954	45.57866	2.34242	1.3489

1-(4-benzyl-1-(2-fluorophenyl)-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ba)



3ba

White solid, mp 174-1176 ℃, 87% yield, 98% ee, dr = 13:1. $[\alpha]_D^{25}$ = +1.835 (c = 0.4, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 - 8.06 (m, 2H), 7.53 (dd, *J* = 11.8, 7.2 Hz, 4H), 7.43 -7.34 (m, 1H), 7.34 -6.98 (m, 12H), 3.88 (d, *J* = 5.7 Hz, 2H), 1.13 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 154.7 (d, *J* = 243.6 Hz), 153.3, 149.2, 135.7, 133.5, 131.5, 131.5, 131.1, 130.7, 130.6, 130.3, 130.2, 129.7, 129.3, 129.0, 128.6 (d, *J* = 8.5 Hz), 128.5, 128.1(d, *J* = 17.7 Hz), 127.6 (d, *J* = 2.6 Hz), 126.7, 121.9 (d, *J* = 28.9 Hz), 121.1, 116.4 (d, *J* = 24.1 Hz), 71.1, 39.1, 35.3, 31.2. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -117.78. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}FN_5NaO_3$, 598.2230; Found 598.2223. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 6.7 min. (minor), 8.2 min. (major).



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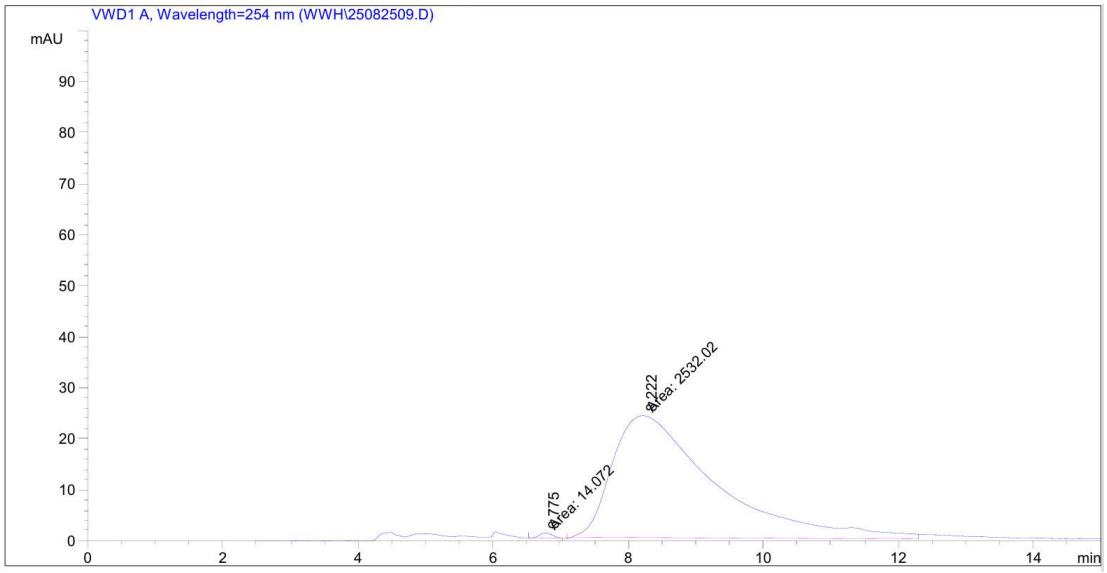
2	10.008	MM	1.6155	1028.33496	10.60889	50.1274



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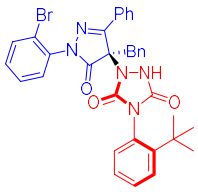
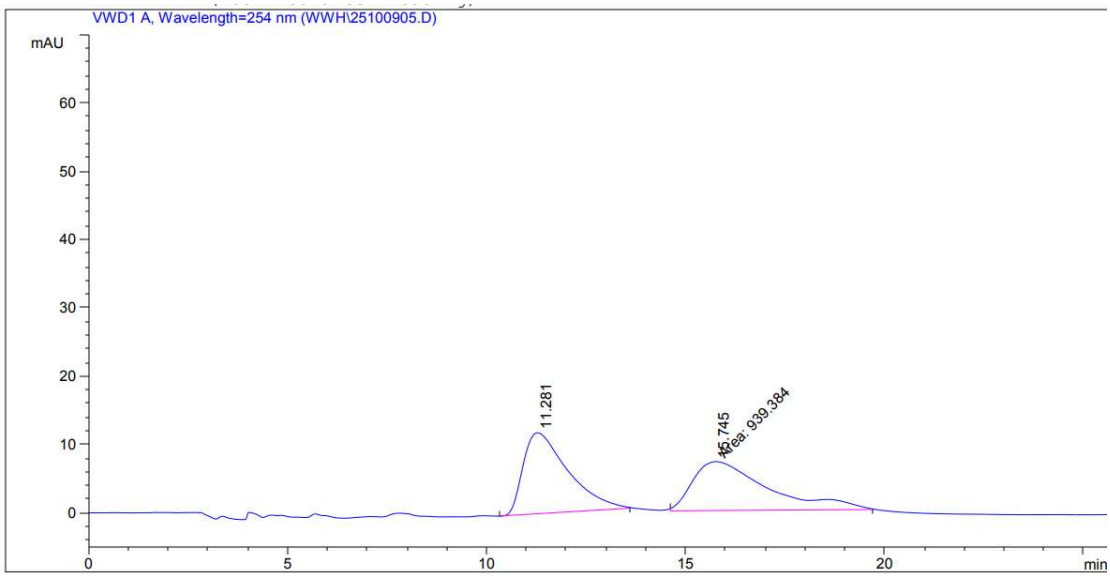
1	6.775	MM	0.2269	14.07197	1.03359	0.5527
2	8.222	MM	1.7654	2532.01978	23.90362	99.4473

1-(4-benzyl-1-(2-bromophenyl)-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dion (3ca)



3ca

White solid, mp 160-162 °C, 70% yield, > 99% ee, dr = 14:1. $[\alpha]_D^{25}$ = -0.855 (c = 0.1, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.09 (s, 1H), 8.08 -8.02 (m, 2H), 7.56 -7.42 (m, 5H), 7.36 (ddd, *J* = 10.2, 5.8, 2.1 Hz, 1H), 7.25 - 7.12 (m, 6H), 7.08 -6.93 (m, 4H), 3.88 (d, *J* = 6.9 Hz, 2H), 1.12 (s, 9H) **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.1, 156.0, 153.4,150.1, 149.1, 136.6, 133.5, 131.4, 130.4, 130.1, 130.0, 129.9, 129.7, 129.0, 128.7, 128.6, 128.4, 128.2, 128.1, 127.8, 127.6, 126.3, 120.5, 72.0, 39.7, 35.3, 31.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}BrN_5NaO_3$, 658.1430; Found 658.1423. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 7:3, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 11.3 min. (major).



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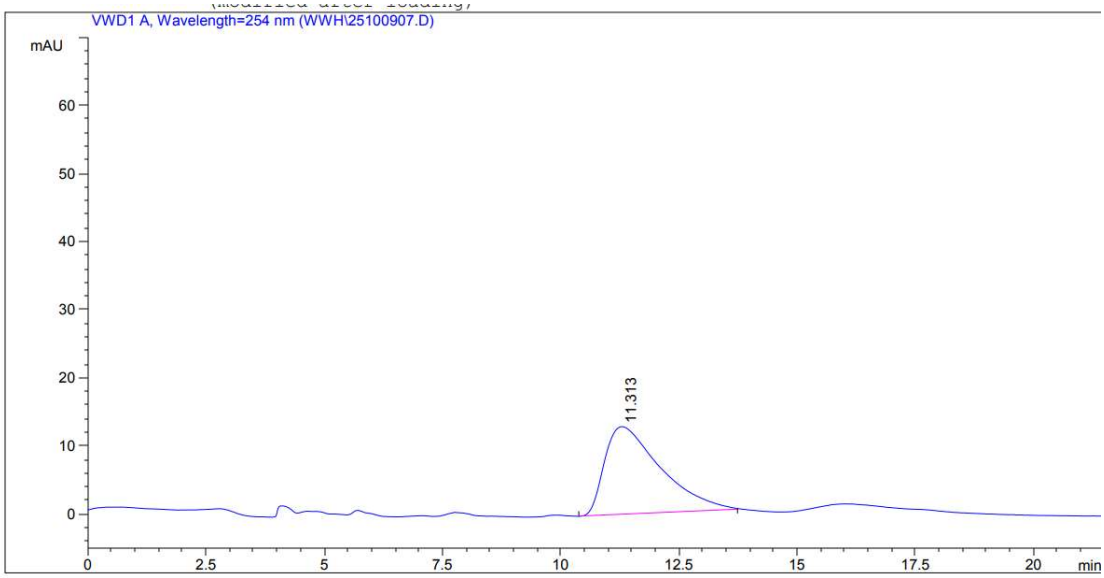
1	11.281	PB	1.0551	928.00977	11.86554	49.6954
2	15.745	MM	2.1856	939.38409	7.16353	50.3046



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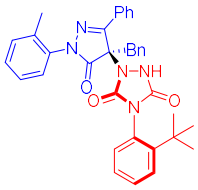
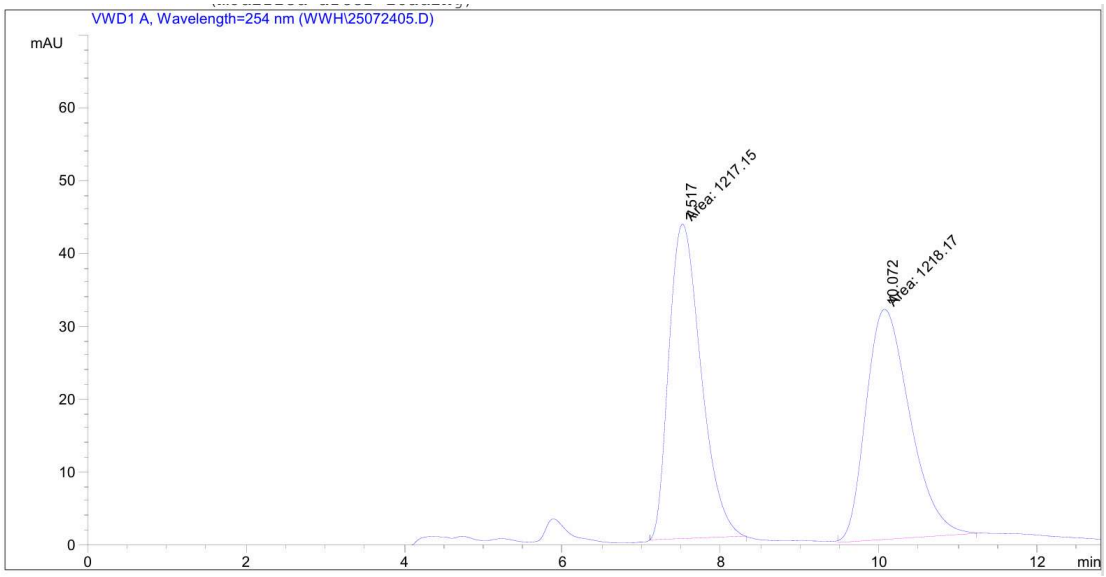
1	11.313	PB	0.9779	1059.08801	12.86499	100.0000

1-(4-benzyl-5-oxo-3-phenyl-1-(o-tolyl)-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3da)



3da

White solid, mp 163-165 ℃, 68% yield, > 99% ee, dr = 10:1. $[\alpha]_D^{25}$ = -1.389 (c = 0.1, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 -7.92 (m, 2H), 7.51 (ddd, *J* = 8.2, 3.6, 1.4 Hz, 3H), 7.37 (ddd, *J* = 8.1, 6.0, 1.5 Hz, 1H), 7.31 - 7.27 (m, 5H), 7.17 - 7.05 (m, 5H), 6.98 (ddd, *J* = 11.9, 7.3, 1.6 Hz, 3H), 3.98 (d, *J* = 12.6 Hz, 1H), 3.94 -3.82 (m, 1H), 2.46 (s, 3H), 1.17 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 155.8, 153.5, 149.2, 141.6, 136.9, 131.4, 130.4, 130.4, 130.1, 130.0, 128.7, 128.6, 128.3, 128.1, 127.5, 126.9, 126.6, 126.1, 120.2, 39.6, 35.4, 31.3, 21.7. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2473. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 7.4 min. (major).



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1	7.517	MM	0.4699	1217.15259	43.17379	49.9792
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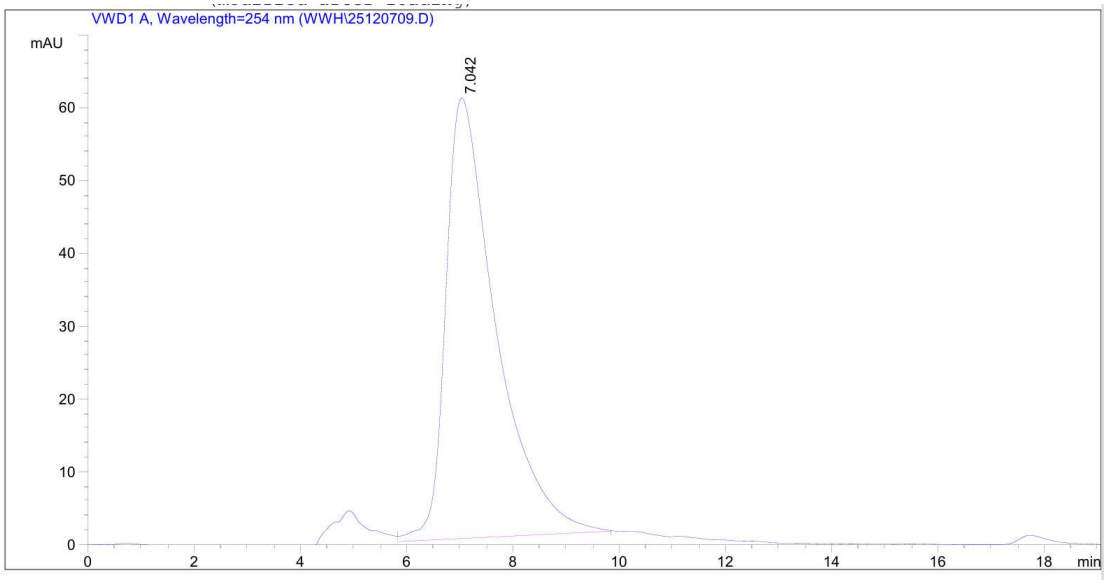

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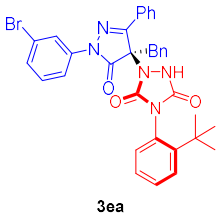
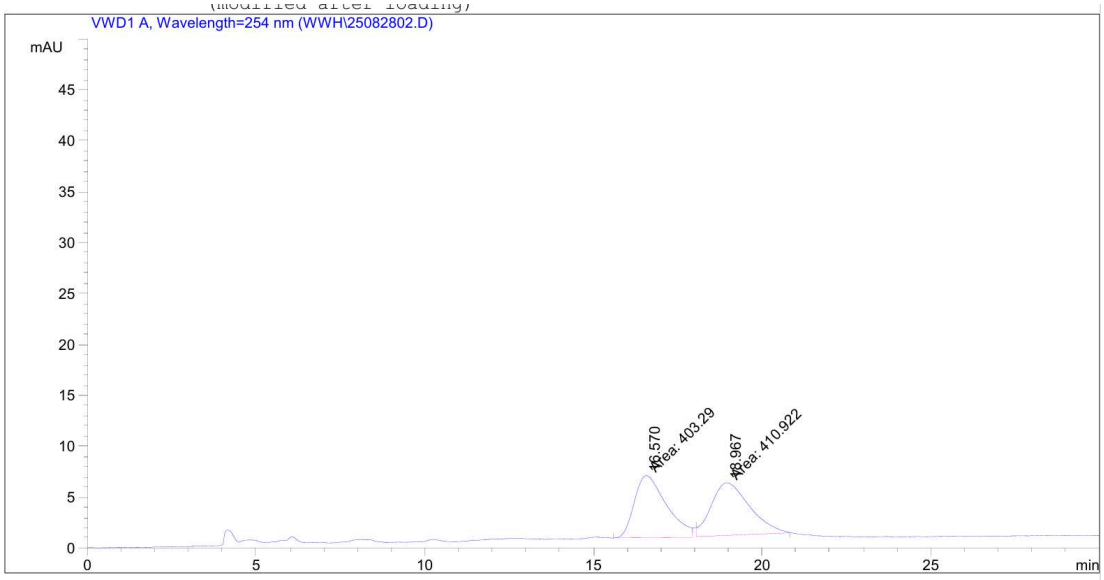
1-(4-benzyl-1-(3-bromophenyl)-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ea)

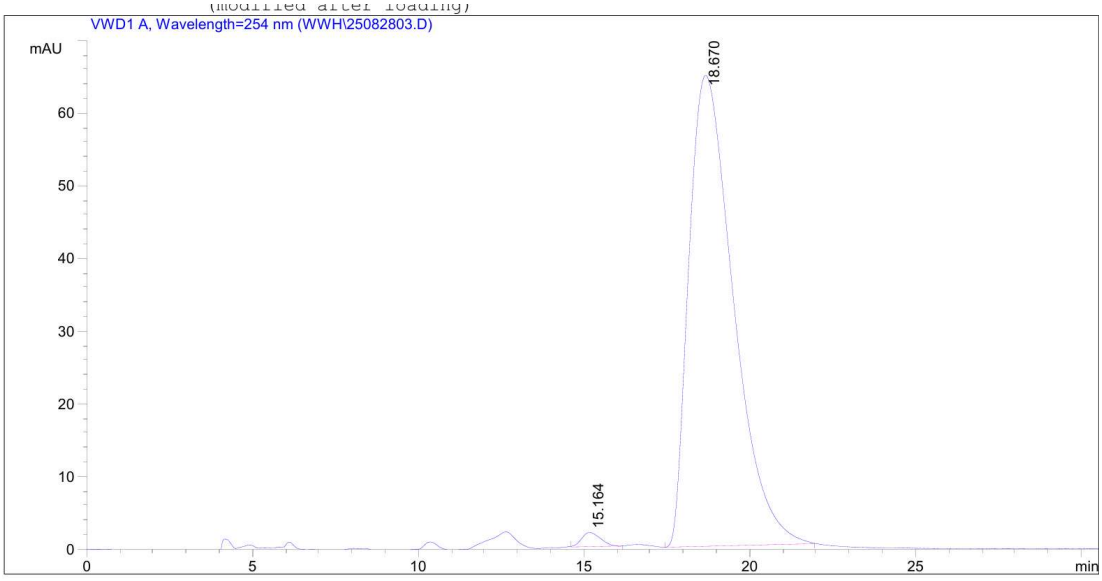


3ea

White solid, mp 163-165 °C, 71% yield, 98% ee, dr = 10:1. $[\alpha]_D^{25}$ = +14.921 (c = 0.1, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 -8.02 (m, 2H), 7.71 - 7.69 (m, 1H), 7.58 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.55 -7.43 (m, 4H), 7.41 -7.27 (m, 2H), 7.24 -6.98 (m, 7H), 6.90 (d, *J* = 7.5 Hz, 2H), 3.87 - 3.77 (m, 2H), 1.10 (d, *J* = 3.3 Hz, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.2, 156.1, 153.4, 150.1, 149.1, 136.6, 133.5, 131.5, 130.4, 130.1, 130.0, 129.8, 129.7, 129.0, 128.7, 128.5, 128.4, 128.2, 128.1, 127.6, 126.3, 120.6, 107.1, 100.0, 71.9, 39.7, 35.3, 31.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}BrN_5NaO_3$, 658.1430; Found 658.1418. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 15:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 15.2 min. (minor), 18.7 min. (major).

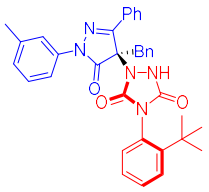


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	16.570	MM	1.1019	403.29037	6.09982	49.5314
2	18.967	MM	1.3226	410.92160	5.17820	50.4686



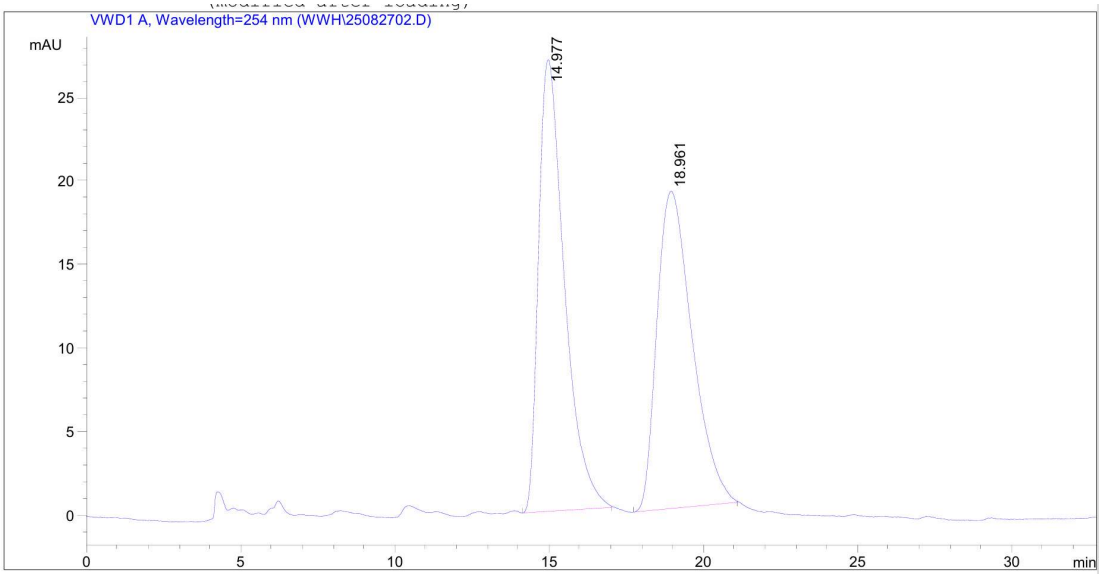
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	15.164	BP	0.4840	76.95125	1.96088	1.2574
2	18.670	PB	1.3772	6042.91602	64.74623	98.7426

1-(4-benzyl-5-oxo-3-phenyl-1-(m-tolyl)-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dion (3fa)



3fa

White solid, mp 170-172 ℃, 76% yield, 96% ee, dr = 12:1. $[\alpha]_D^{25}$ = +12.871 (c = 0.1, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 -8.03 (m, 2H), 7.56 -7.43 (m, 4H), 7.39 -7.07 (m, 9H), 7.07 -6.90 (m, 4H), 3.96 -3.81 (m, 2H), 2.29 (s, 3H), 1.13 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 156.0, 153.4, 153.1, 149.1, 138.7, 136.7, 131.5, 131.0, 130.3, 130.1, 129.7, 129.2, 128.5, 128.4, 128.3, 128.2, 127.5, 127.1, 126.7, 121.1, 117.7, 72.0, 39.6, 35.3, 31.2, 21.4. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2476. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 15:2, flow rate = 0.8 mL/min., λ = 232 nm, t_R = 14.5 min. (minor), 18.3 min. (major).



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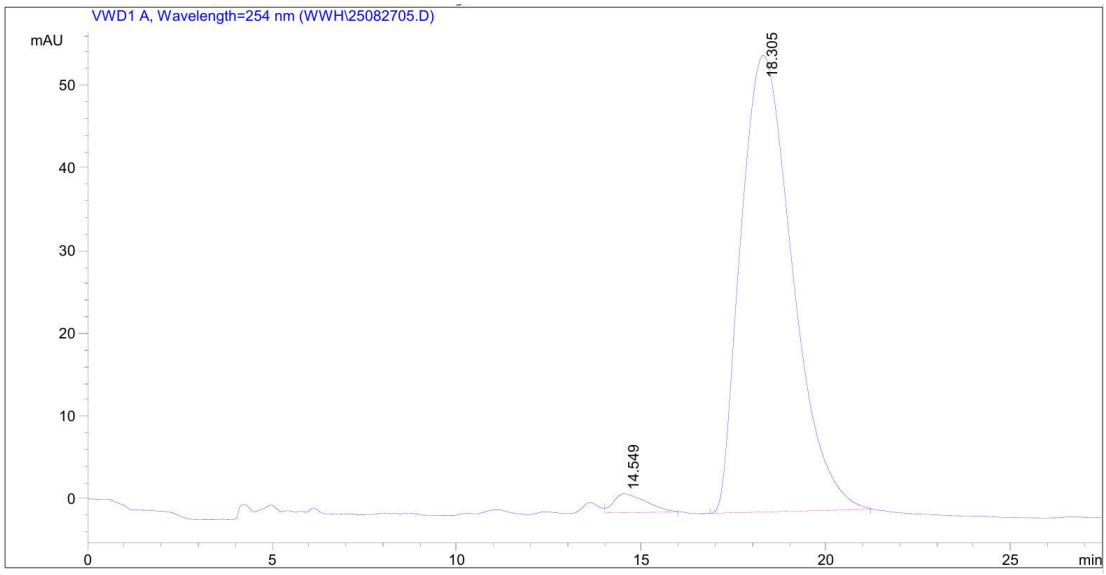
2	18.961	MM	1.3750	1588.36145	19.25307	50.1691



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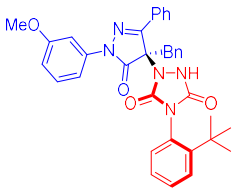
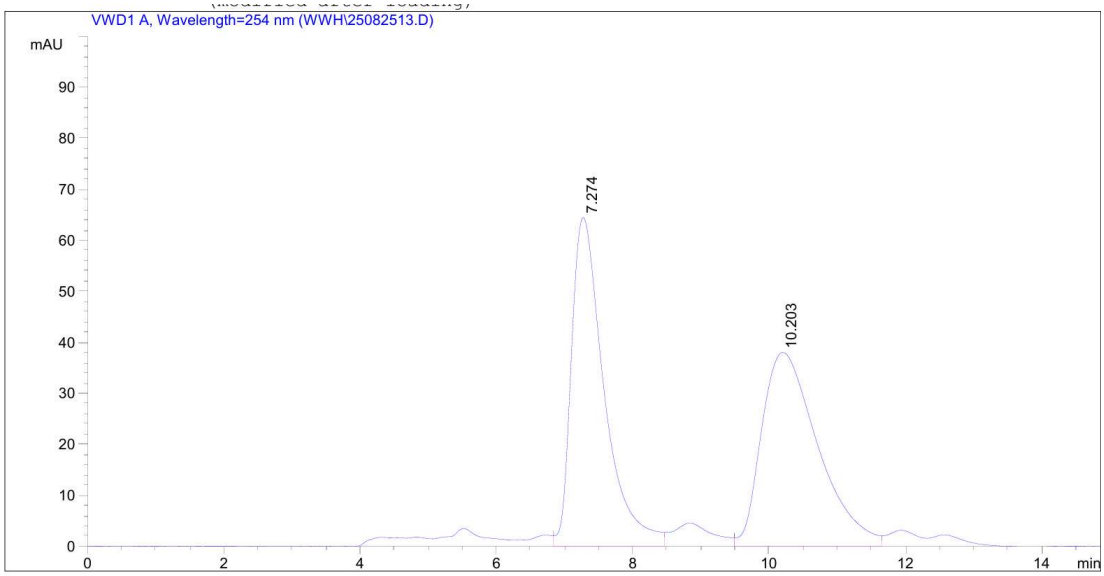
1	14.549	VB	0.7331	141.56720	2.28457	2.5724
2	18.305	BB	1.4263	5361.66504	55.18008	97.4276

1-(4-benzyl-1-(3-methoxyphenyl)-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dion (3ga)

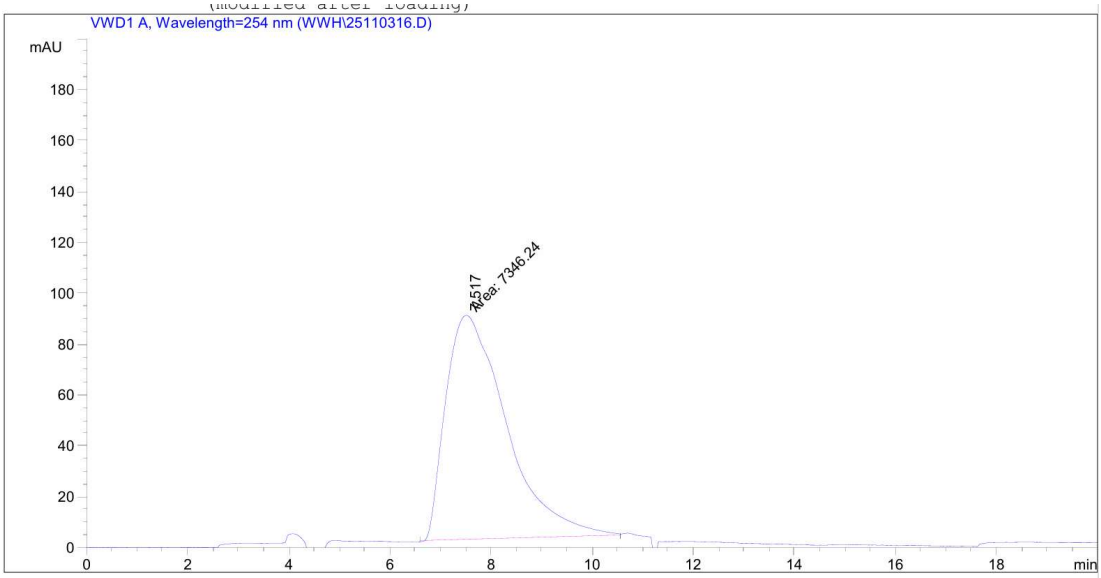


3ga

White solid, mp 159-161 °C, 87% yield, > 99% ee, dr = 12:1. $[\alpha]_D^{25}$ = +0.645 (c = 0.3, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.10 -8.02 (m, 2H), 7.48 (ddd, *J* = 9.7, 7.3, 5.4 Hz, 4H), 7.37 - 7.33 (m, 1H), 7.24 -6.99 (m, 8H), 6.97 -6.87 (m, 2H), 6.99 - 6.73 (m, 1H), 3.92 (dd, *J* = 12.5, 1.9 Hz, 1H), 3.84 (d, *J* = 12.5 Hz, 1H), 3.75 (s, 3H), 1.14 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 159.8, 153.2, 137.9, 131.5, 131.1, 130.3, 130.1, 129.6, 129.5, 129.2, 128.5, 128.4, 128.3, 128.2, 127.5, 126.7, 112.6, 112.1, 105.9, 72.1, 55.4, 39.7, 35.3, 31.2. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_4$, 610.2430; Found 610.2421. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 7:3, flow rate = 0.8 mL/min., λ = 232 nm, t_R = 7.5 min. (major).

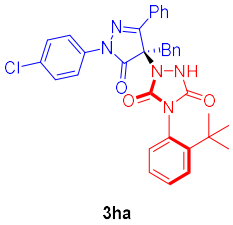


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.274	VB	0.5005	2153.91577	64.45762	49.5814
2	10.203	VV	0.8657	2190.28320	38.02136	50.4186



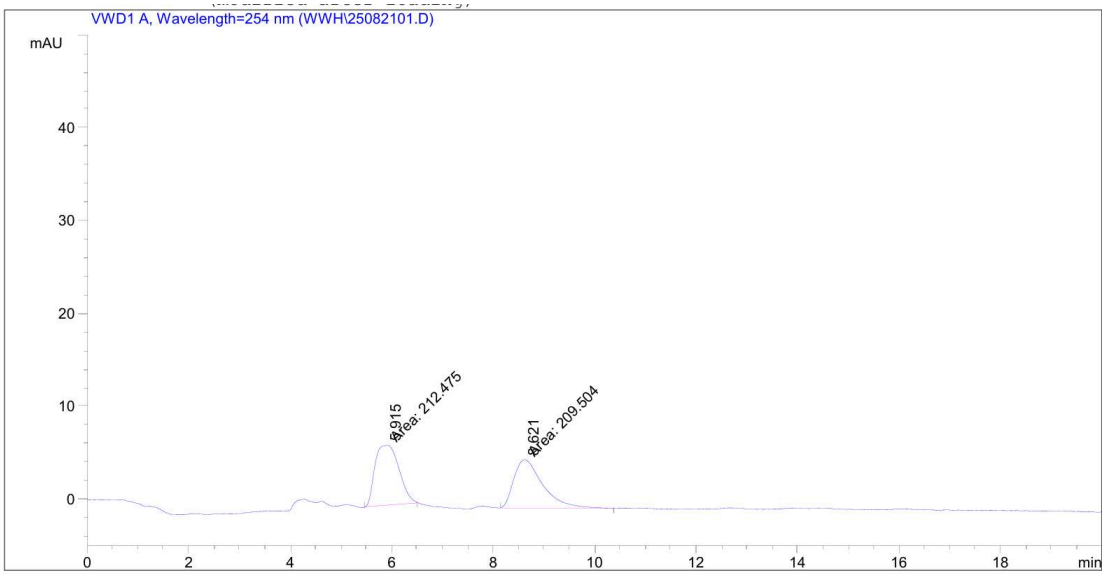
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.517	MM	1.3903	7346.24219	88.06552	100.0000

1-(4-benzyl-1-(4-chlorophenyl)-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ha)

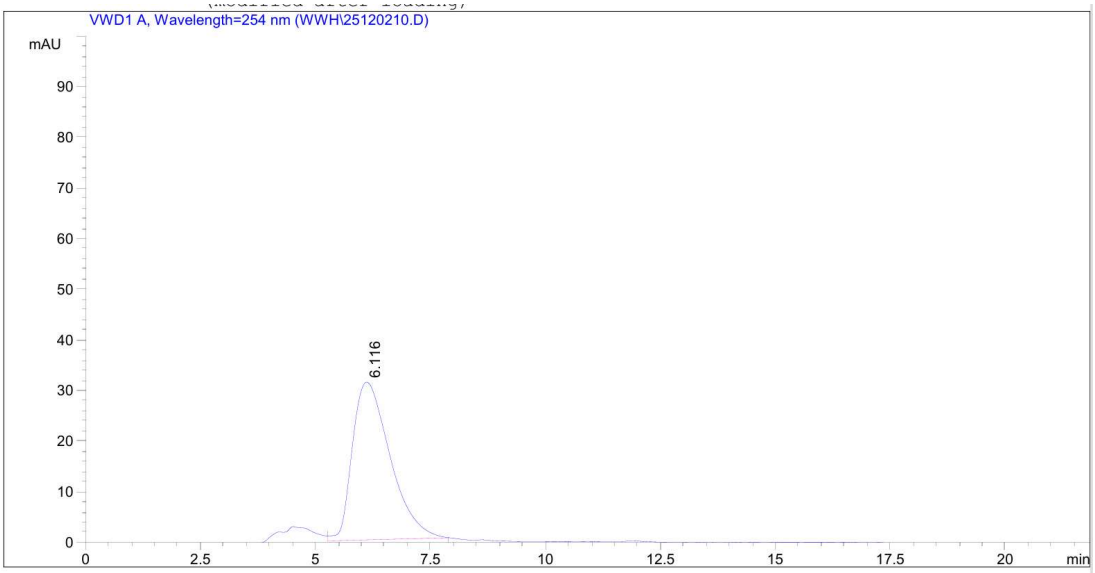


3ha

White solid, mp 152-154 °C, 77% yield, > 99% ee, 13:1. $[\alpha]_D^{25}$ = +15.76 (c = 0.6, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.30 -7.12 (m, 5H), 7.08 -6.92 (m, 4H), 6.86 - 6.82 (m, 2H), 6.79 - 6.75 (m, 2H), 6.72 -6.67 (m, 1H), 6.63 -6.53 (m, 2H), 3.62 -3.47 (m, 1H), 3.42 (d, *J* = 12.6 Hz, 1H), 0.83 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 156.1, 153.3, 152.6, 148.9, 136.6, 132.5, 131.4, 130.5, 130.0, 128.8, 128.6, 128.6, 128.4, 128.3, 128.3, 128.1, 127.7, 126.4, 125.5, 120.4, 71.7, 39.6, 35.4, 31.3, 31.3. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}ClN_5NaO_3$, 614.1935; Found 614.1930. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 6.1 min. (major).

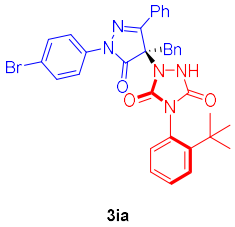


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.915	MM	0.5483	212.47543	6.45885	50.3521
2	8.621	MM	0.6680	209.50403	5.22715	49.6479



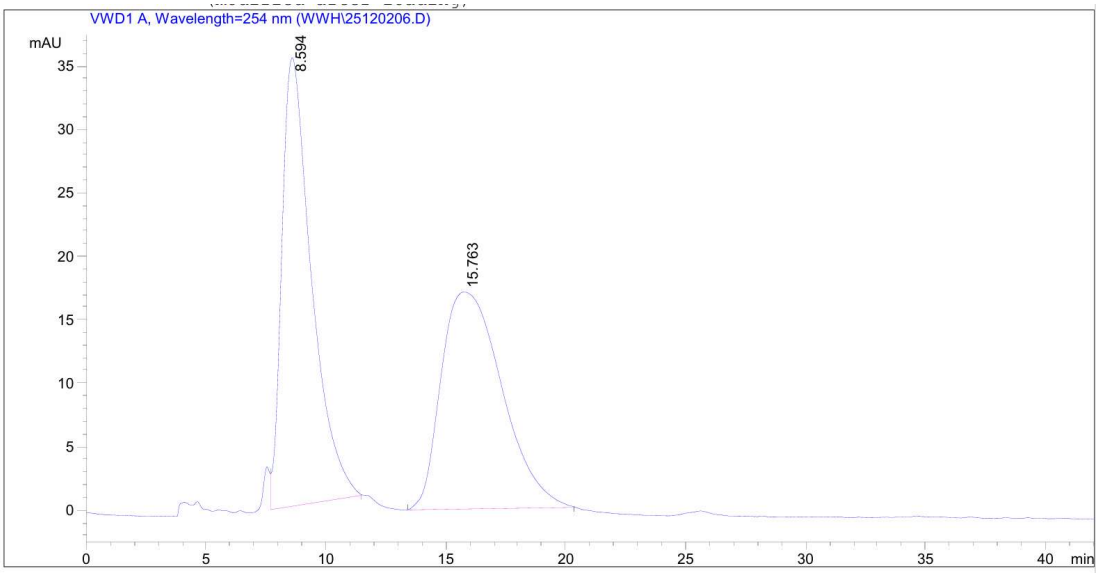
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.116	VB	0.8626	1784.41882	31.18735	100.0000

1-(4-benzyl-1-(4-bromophenyl)-5-oxo-3-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ia)

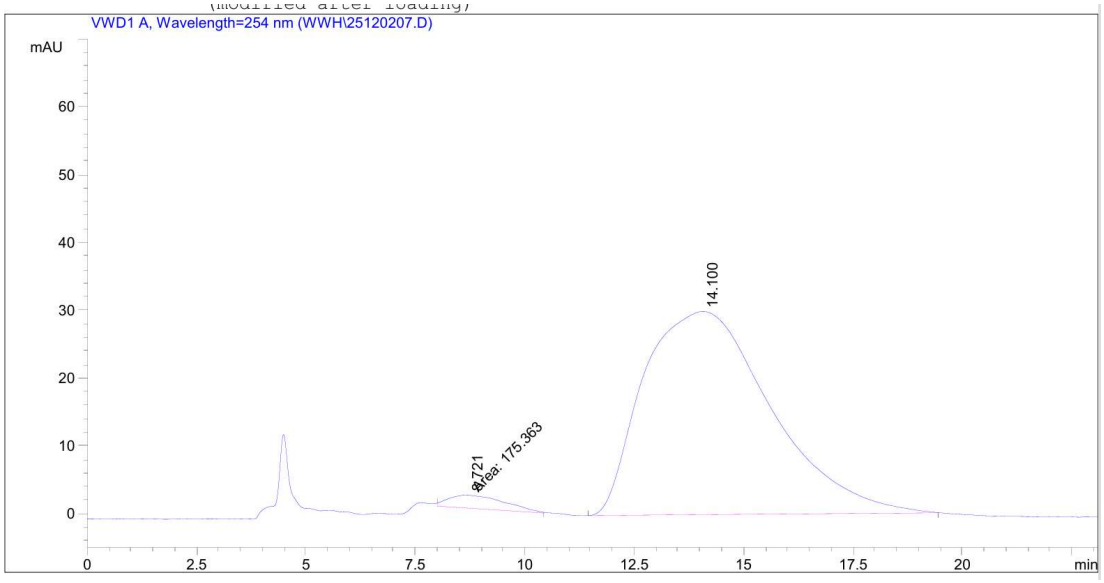


3ia

White solid, mp 153-155 ℃, 73% yield, 94% ee, dr = 13:1. $[\alpha]_D^{25}$ = +23.810 (c = 0.4, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 -8.01 (m, 2H), 7.57 -7.32 (m, 10H), 7.25 -6.96 (m, 5H), 6.95 -6.86 (m, 2H), 3.91 - 3.82 (m, 2H), 1.12 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 155.9, 153.5, 153.3, 149.2, 135.7, 133.5, 131.5, 131.1, 130.7, 130.4, 130.2, 129.7, 129.3, 129.0, 128.7, 128.6, 128.2, 128.0, 127.6, 126.8, 121.1, 71.1, 39.1, 35.3, 31.2. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}BrN_5NaO_3$, 658.1430; Found 658.1426. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 232 nm, t_R = 8.7 min. (minor), 14.1 min. (major).

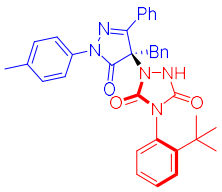


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.594	VB	1.2408	3044.78833	35.34923	50.1320
2	15.763	BB	2.0843	3028.75928	17.12042	49.8680



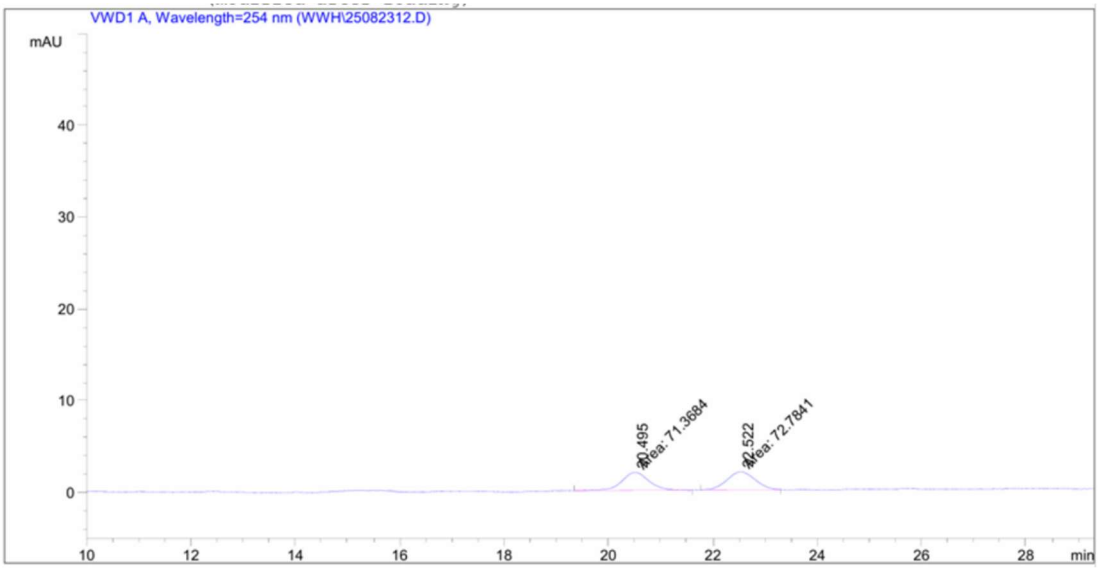
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.721	MM	1.5294	175.36275	1.91101	2.8020
2	14.100	BB	2.3852	6083.02832	29.95485	97.1980

1-(4-benzyl-5-oxo-3-phenyl-1-(p-tolyl)-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ja)

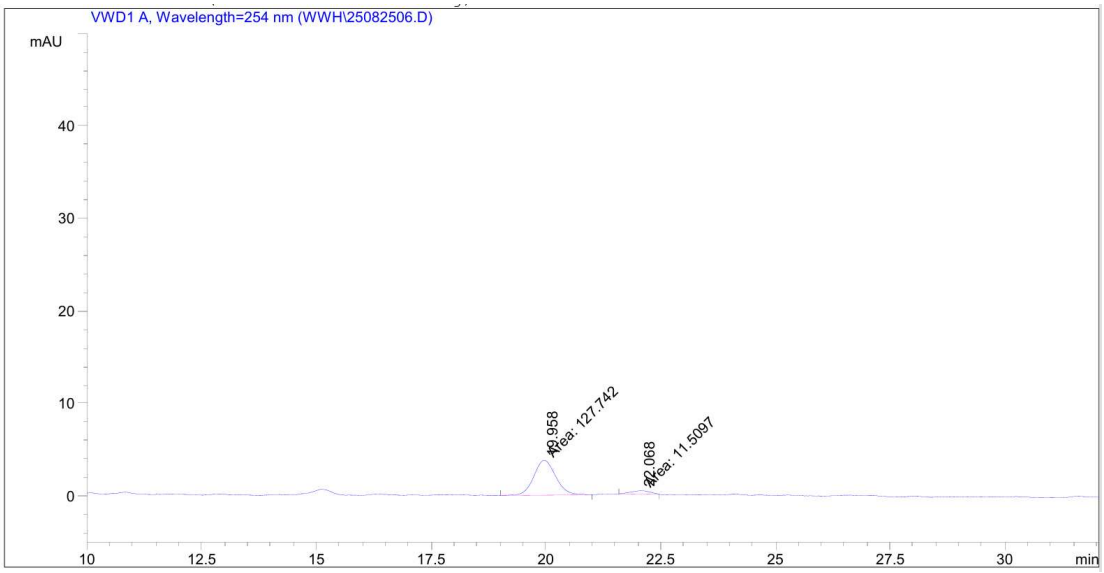


3ja

White solid, mp 167-169 ℃, 73% yield, 84% ee, dr = 15:1. $[\alpha]_D^{25}$ = +16.956 (c = 0.4, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.53 (s, 1H), 8.11 -8.02 (m, 2H), 7.52 - 7.44 (m, 4H), 7.38 - 7.32 (m, 3H), 7.24 -7.13 (m, 2H), 7.11 - 7.01 (m, 5H), 6.94 (dd, *J* = 11.5, 7.6 Hz, 2H), 3.86 (m, 2H), 2.29 (d, *J* = 6.3 Hz, 3H), 1.11 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 156.1, 153.5, 153.1, 149.1, 136.1, 134.3, 131.6, 130.9, 130.3, 130.3, 130.1, 129.7, 129.3, 129.2, 128.5, 128.3, 128.2, 127.6, 126.7, 120.7, 71.8, 39.7, 35.3, 31.2, 21.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2468. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 3:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 22.1 min. (minor), 20.0 min. (major).

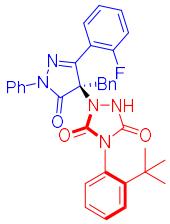


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.495	MM	0.6057	71.36836	1.96367	49.5089
2	22.522	MM	0.6201	72.78415	1.95637	50.4911



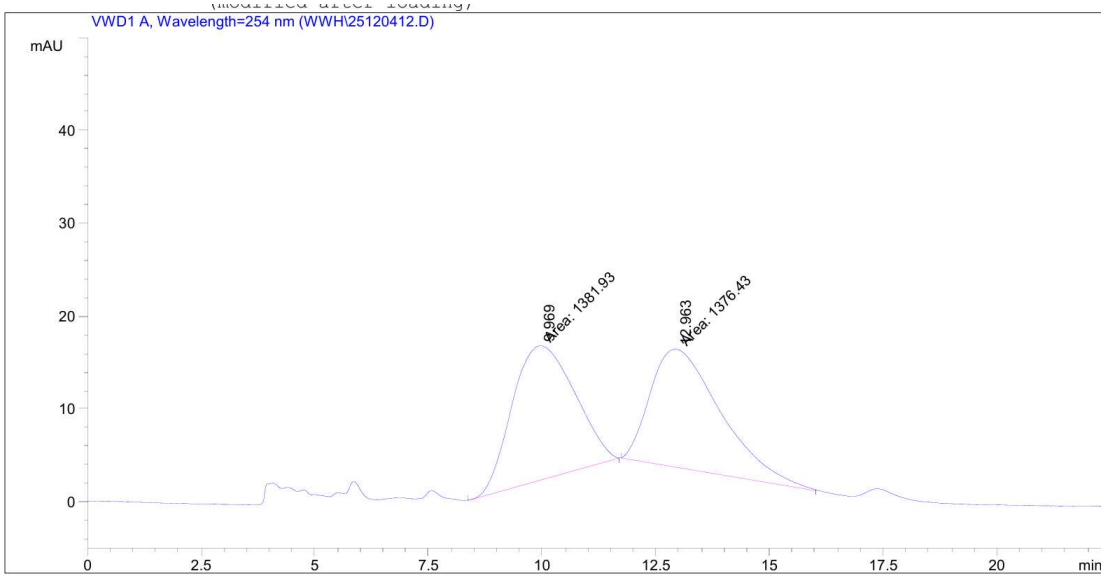
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.958	MM	0.5619	127.74215	3.78914	91.7346
2	22.068	MM	0.5102	11.50971	3.75967e-1	8.2654

1-(4-benzyl-3-(2-fluorophenyl)-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ka)

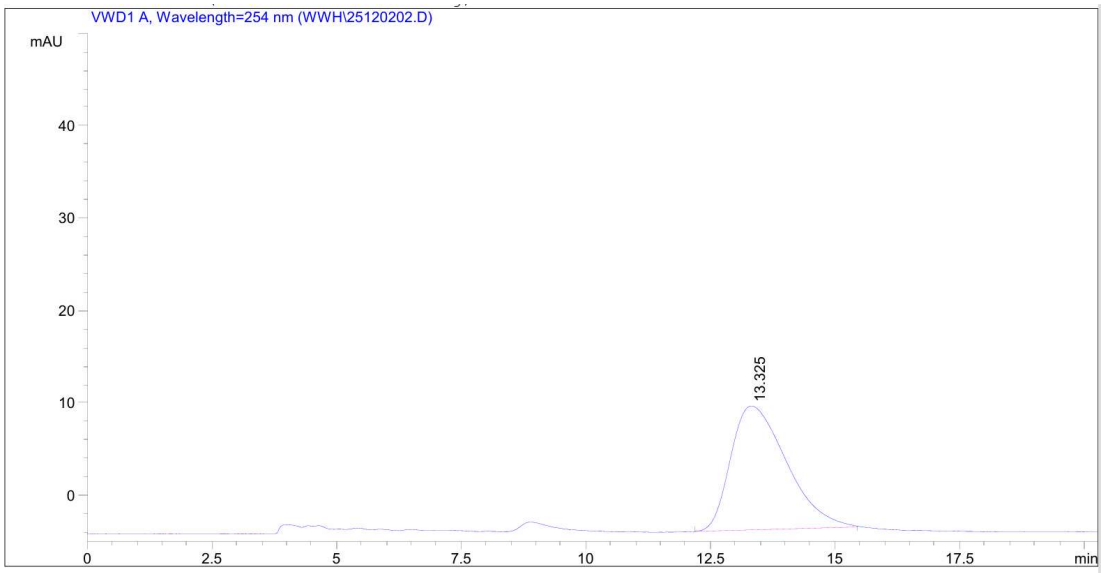


3ka

White solid, mp 266-268 °C, 71% yield, > 99% ee, dr = 12:1. $[\alpha]_D^{25}$ = +5.556 (c = 0.05, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.12 - 8.08 (m, 1H), 7.57 - 7.54 (m, 4H), 7.43 -7.27 (m, 6H), 7.25 -7.15 (m, 4H), 7.09 (d, *J* = 7.4 Hz, 3H), 4.01 (d, *J* = 12.5 Hz, 1H), 3.88 (d, *J* = 12.5 Hz, 1H), 1.25 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 161.4, 154.1 (d, *J* = 291.1 Hz), 151.0, 149.8, 149.0, 136.7, 132.6, 131.5, 130.4 (d, *J* = 7.5 Hz), 130.1, 129.8 (d, *J* = 7.0 Hz), 128.7, 128.6, 128.3, 128.2,127,7, 127.5, 126.2, 125.0 (d, *J* = 3.1 Hz), 120.2, 118.0 (d, *J* = 21.2 Hz), 117.0 (d, *J* = 23.0 Hz), 71.9, 38.9, 35.5, 31.3. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -107.47. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}FN_5NaO_3$, 598.2230; Found 598.2219. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 15:2, flow rate = 0.8 mL/min., λ = 232 nm, t_R = 13.3 min. (major).

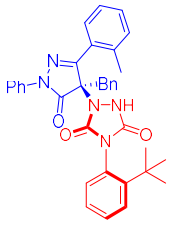


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.969	MM	1.5900	1381.92615	14.48521	50.0996
2	12.963	MM	1.8028	1376.43359	12.72490	49.9004



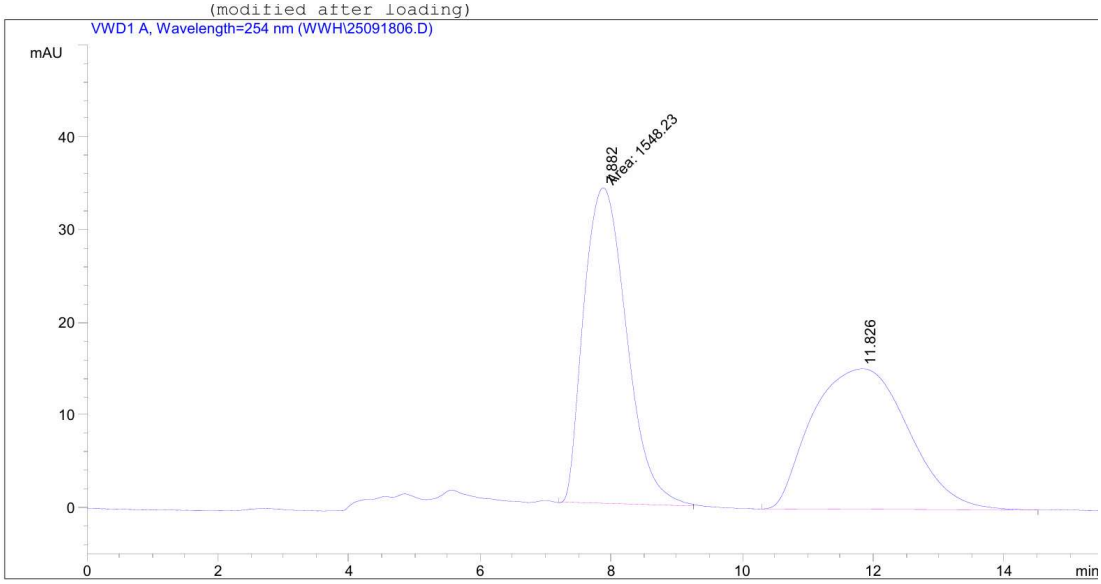
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.325	BB	1.1177	1046.78723	13.42755	100.0000

1-(4-benzyl-5-oxo-1-phenyl-3-(o-tolyl)-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3la)

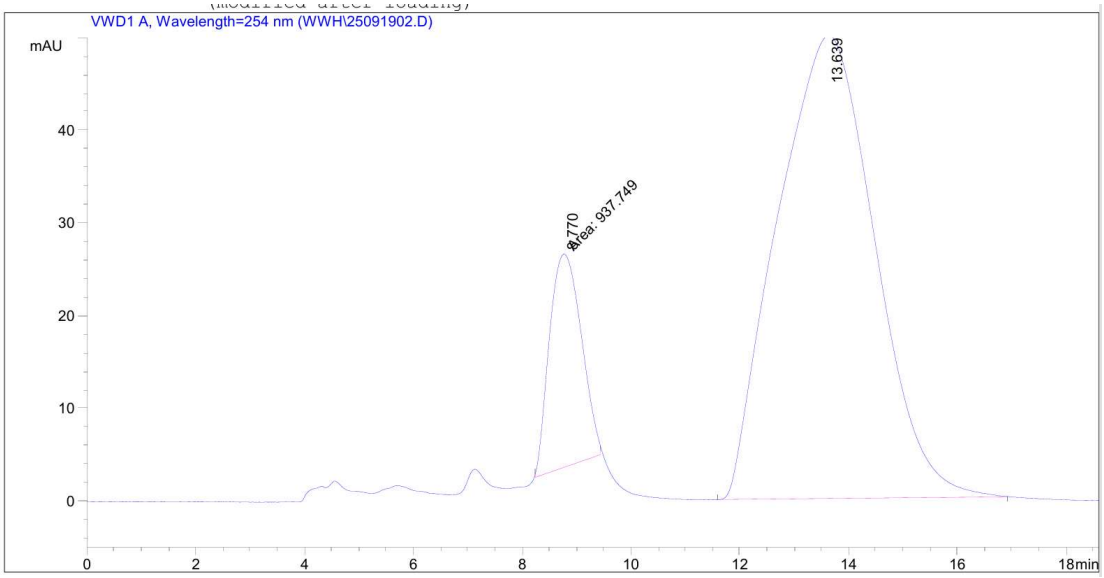


3la

White solid, mp 127-129 °C, 68% yield, 96% ee, dr = 15:1. $[\alpha]_D^{25}$ = +2.333 (c = 0.3, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.11 -8.02 (m, 2H), 7.52 - 7.44 (m, 4H), 7.38 - 7.32 (m, 3H), 7.26 -6.99 (m, 8H), 6.94 (dd, *J* = 11.5, 7.6 Hz, 2H), 3.92 - 3.82 (m, 2H), 2.29 (s, 3H), 1.11 (d, *J* = 4.5 Hz, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.6, 156.1, 154.2, 149.0, 131.5, 131.0, 130.3, 130.1, 129.8, 129.8, 129.6, 129.2, 128.5, 128.4, 128.2, 127.6, 127.2, 126.7, 124.3, 116.7, 100.0, 70.9, 39.3, 35.3, 31.1, 29.6. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2473. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 232 nm, t_R = 8.8 min (minor), 13.6 min. (major).

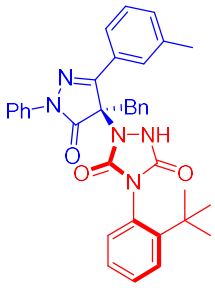


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.882	MM	0.7574	1548.23181	34.07030	49.9535
2	11.826	BP	1.2016	1551.11499	15.17085	50.0465



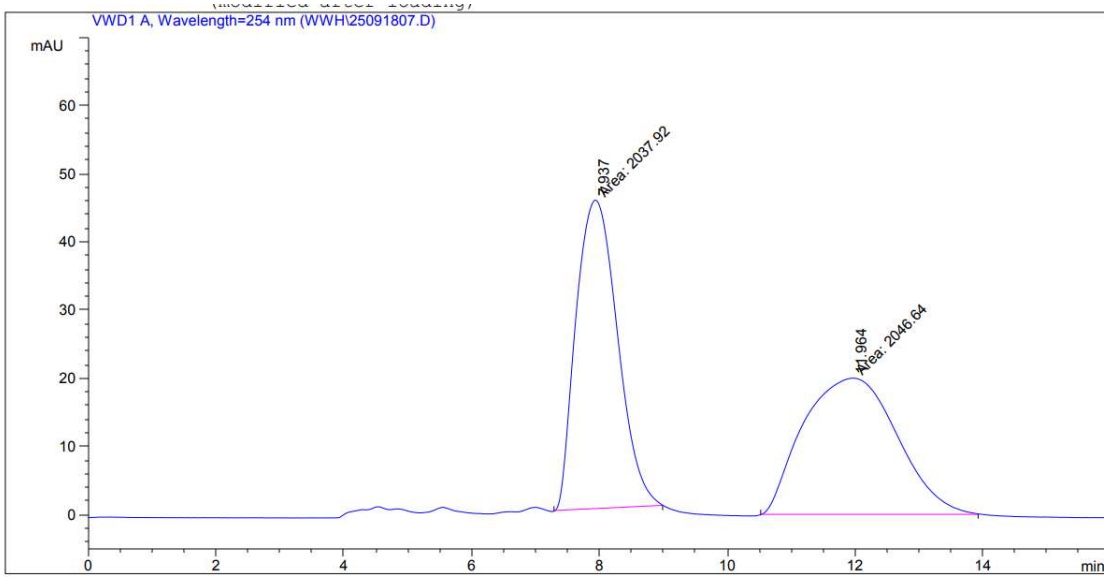
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.770	MM	0.6785	937.74854	23.03412	13.1348
2	13.639	BB	1.6442	6201.66016	49.98106	86.8652

1-(4-benzyl-5-oxo-1-phenyl-3-(m-tolyl)-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dion (3ma)

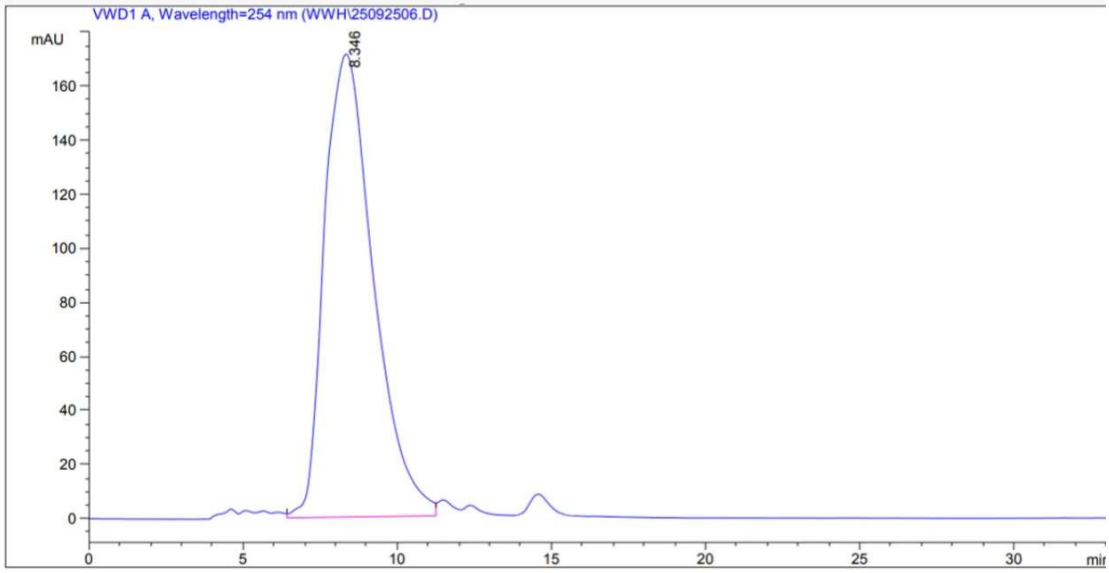


3ma

White solid, mp 130-132 °C, 78% yield, 84% ee, dr = 11:1. $[\alpha]_D^{25}$ = +6.215 (c = 0.3, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 7.3 Hz, 2H), 7.67 -7.53 (m, 6H), 7.47 -7.28 (m, 6H), 7.12 (dd, *J* = 16.9, 7.9 Hz, 3H), 6.96 (d, *J* = 8.3 Hz, 2H), 3.97 (d, *J* = 12.8 Hz, 1H), 3.91 (d, *J* = 11.9 Hz, 1H), 2.83 (s, 3H), 1.20 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.0, 155.7, 154.3, 153.9, 149.2, 135.7, 133.6, 131.3, 131.1, 130.7, 130.4, 130.3, 129.8, 129.3, 129.0, 128.7, 128.2, 128.1, 128.0, 127.5, 126.6, 121.2, 72.1, 39.0, 35.8, 31.7, 31.2. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2473. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 232 nm, t_R = 8.3 min (major).

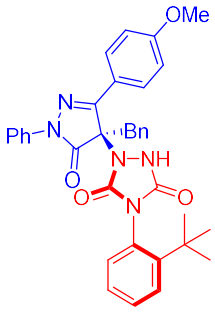


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.937	MM	0.7514	2037.92310	45.20157	49.8932
2	11.964	MM	1.7077	2046.64392	19.97480	50.1068



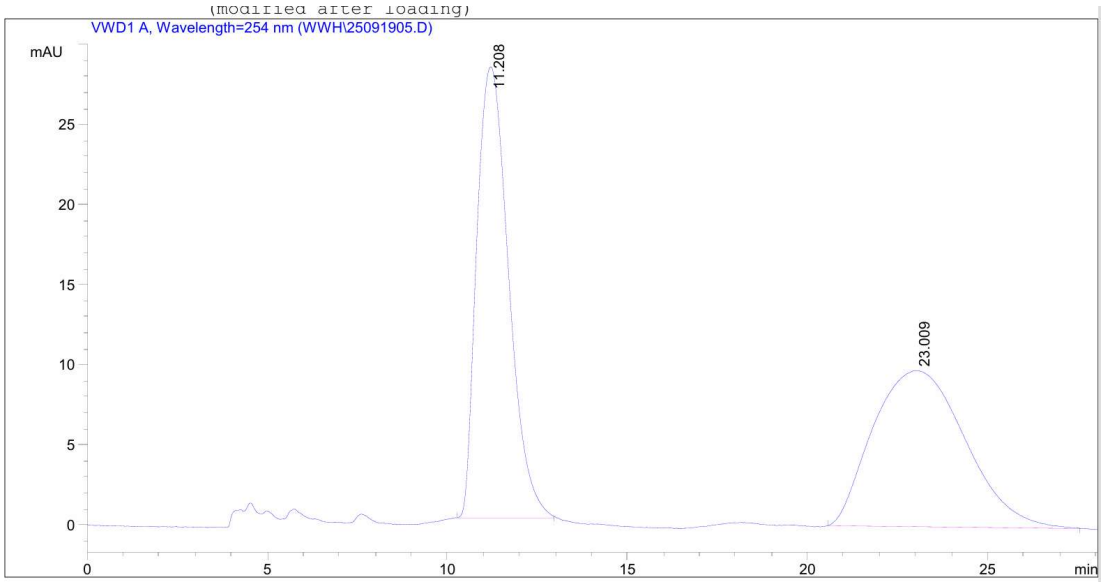
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.346	VV	1.5727	1.89919e4	171.34476	100.0000

1-(4-benzyl-3-(4-methoxyphenyl)-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3na)

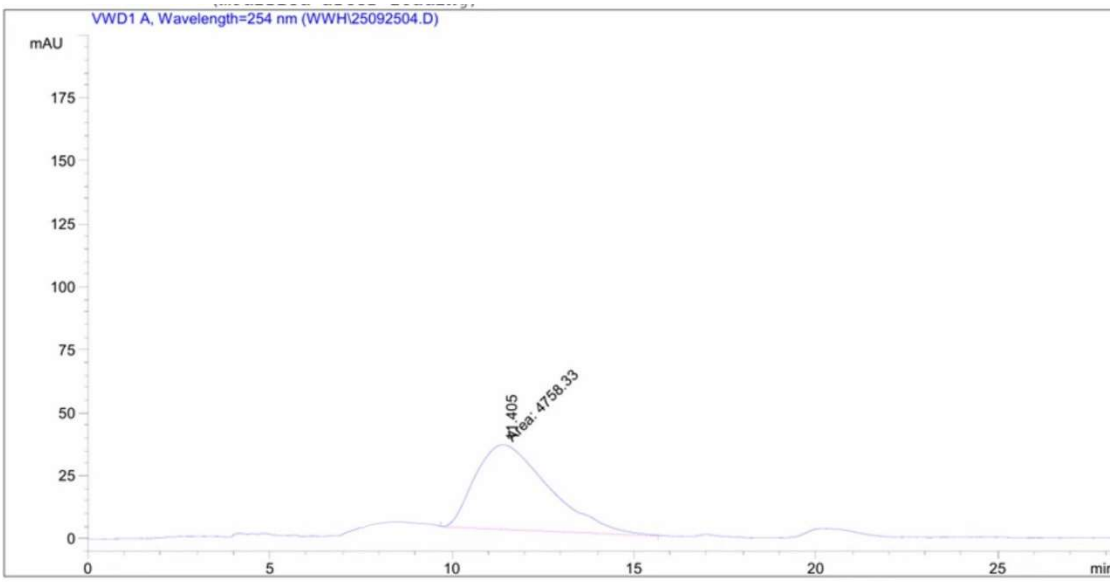


3na

White solid, mp 145-147 °C, 86% yield, 90% ee, dr = 15:1. $[\alpha]_D^{25}$ = +1.431 (c = 0.4, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (s, 1H), 8.11 -8.03 (m, 2H), 7.57 -7.45 (m, 4H), 7.39 - 7.35 (m, 1H), 7.25 -7.17 (m, 2H), 7.17 -7.12 (m, 2H), 7.12 - 7.05 (m, 3H), 7.05 -6.99 (m, 1H), 6.96 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 2H), 6.73 - 6.70 (m, 1H), 3.97 (d, *J* = 12.5 Hz, 1H), 3.93 -3.83 (m, 1H), 3.77 (s, 3H), 1.17 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 156.0, 153.9, 153.0, 149.0, 135.9, 131.7, 131.5, 131.2, 130.4, 130.0, 129.4, 129.3, 128.5, 128.4, 128.3, 127.6, 126.8, 121.5, 119.1, 71.8, 39.7, 35.3, 31.2, 29.7. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_4$, 610.2430; Found 610.2421. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 232 nm, t_R = 11.4 min. (major).

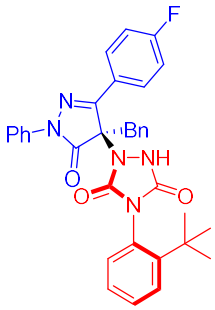


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.208	BB	0.9807	1734.54077	28.16127	49.8882
2	23.009	BB	2.0953	1742.31787	9.74866	50.1118



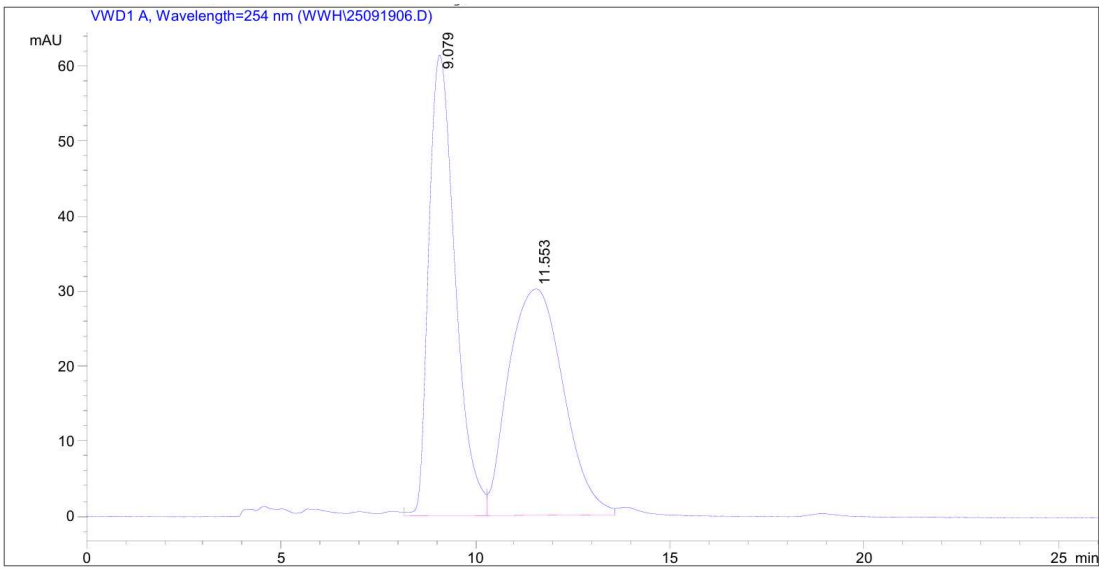
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.405	MM	2.3601	4758.32764	33.60316	100.0000

1-(4-benzyl-3-(4-fluorophenyl)-5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3oa)

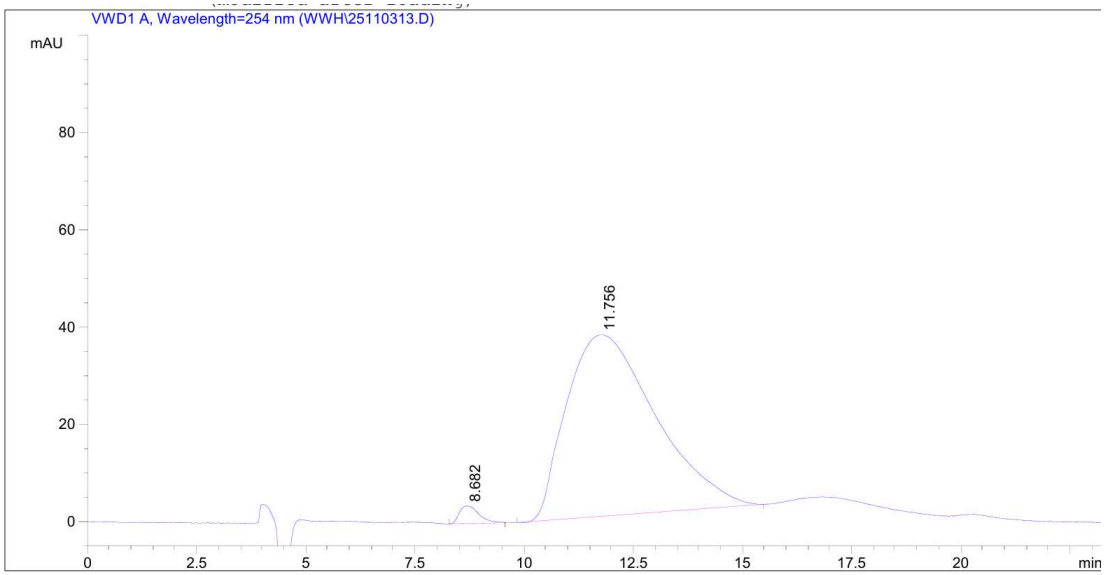


3oa

White solid, mp 147-149 °C, 68% yield, 96% ee, dr = 12:1. $[\alpha]_D^{25}$ = +5.993 (c = 0.3, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.17 (s, 1H), 7.84 (d, *J* = 3.7 Hz, 1H), 7.55 -7.42 (m, 4H), 7.37 - 7.33 (m, 1H), 7.29 -7.17 (m, 4H), 7.17 -7.08 (m, 5H), 7.05 - 6.99 (m, 3H), 3.84 (d, *J* = 12.4 Hz, 1H), 3.76 (d, *J* = 12.3 Hz, 1H), 1.14 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.2, 158.9, 154.7 (d, *J* = 271.7 Hz), 150.2, 150.1, 149.1, 136.6, 133.5, 131.5, 130.4 (d, *J* = 3.5 Hz), 130.0 (d, *J* = 7.2 Hz), 129.7, 129.0, 128.7, 128.6, 128.4, 128.3, 128.1, 127.6, 126.3, 120.6, 116.6 (d, *J* = 22.0 Hz), 107.1, 72.0, 39.7, 35.3, 31.1. **^{19}F NMR** (377 MHz, DMSO) δ -109.22. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}FN_5NaO_3$, 598.2230; Found 598.2225. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 8.7 min. (minor), 11.8 min. (major).

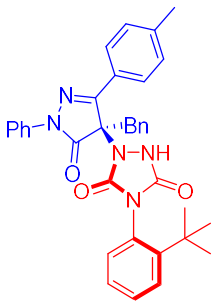


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.079	VV	0.7411	2913.03979	61.42910	49.5574
2	11.553	VV	1.1860	2965.07764	30.20660	50.4426



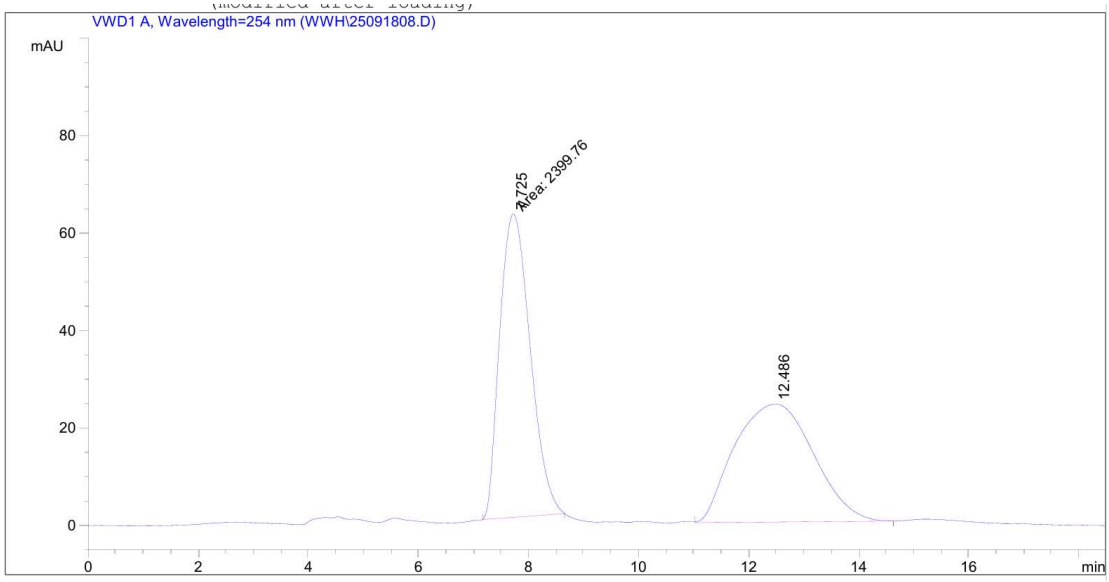
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.682	PB	0.4029	114.63318	3.62004	2.1163
2	11.756	PP	1.7024	5301.91895	37.35766	97.8837

1-(4-benzyl-5-oxo-1-phenyl-3-(p-tolyl)-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3pa)

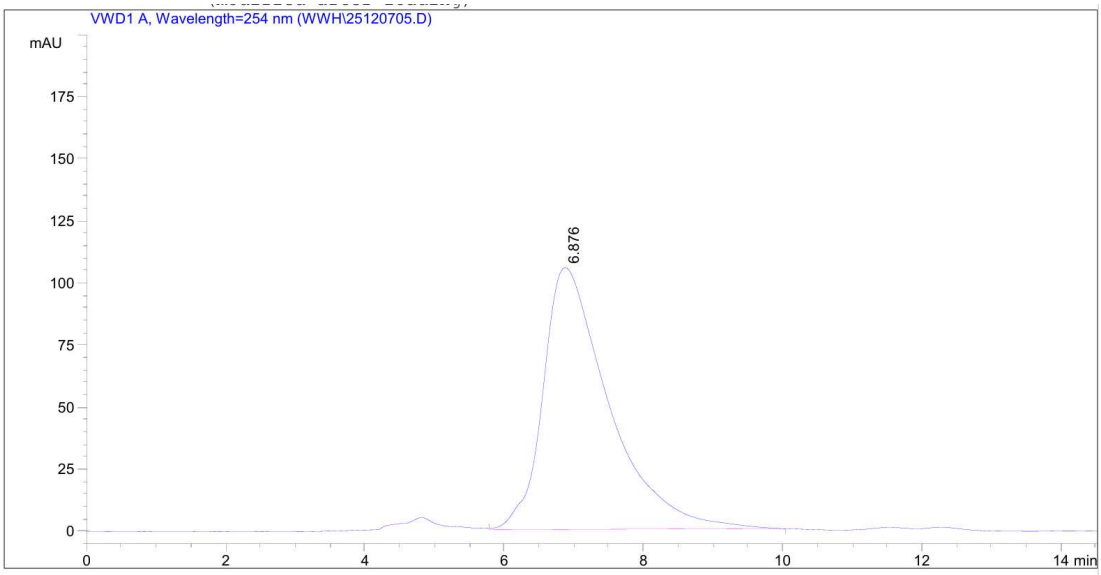


3pa

White solid, mp 140-142 °C, 68% yield, > 99% ee, dr = 13:1. $[\alpha]_D^{25}$ = +6.977 (c = 0.3, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 8.4, 3.2 Hz, 2H), 7.50 (ddd, *J* = 10.1, 7.5, 1.5 Hz, 3H), 7.40 -6.90 (m, 14H), 3.96 -3.79 (m, 2H), 2.45 (s, 3H), 1.15 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.5, 131.5, 130.3, 130.1, 130.0, 128.7, 128.5, 128.2, 128.1, 127.5, 126.9, 126.7, 126.1, 120.3, 72.2, 39.7, 35.3, 31.3, 21.6. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2473. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 6.9 min. (major).

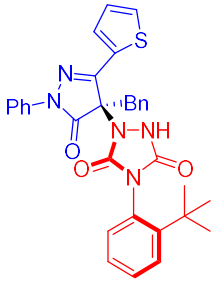


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.725	MM	0.6428	2399.76025	62.21721	49.8556
2	12.486	BP	1.2066	2413.66455	24.21463	50.1444



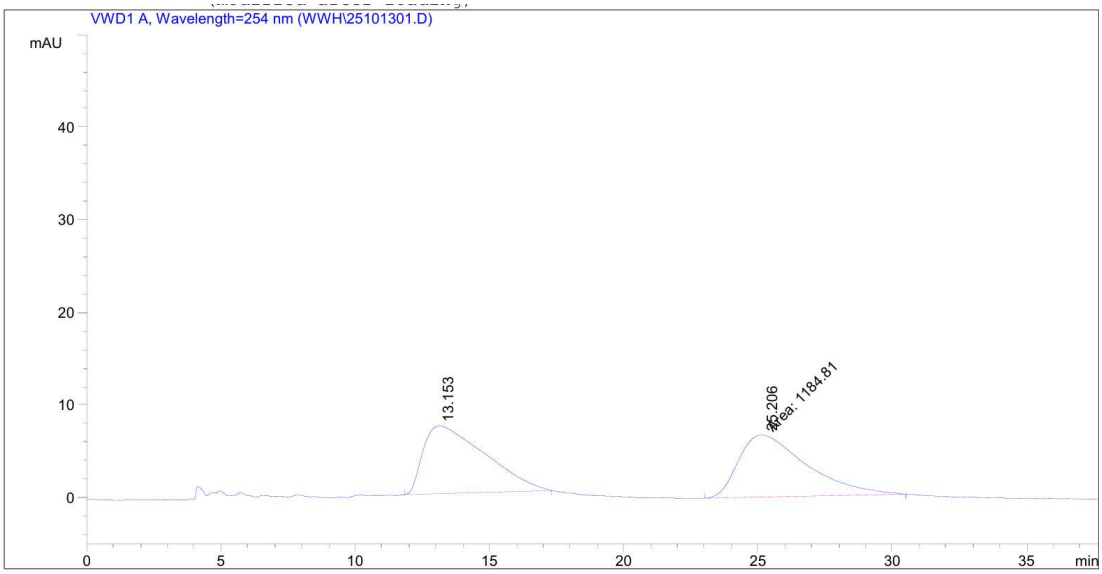
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.876	BB	0.9485	6967.37207	105.44959	100.0000

1-(4-benzyl-5-oxo-1-phenyl-3-(thiophen-2-yl)-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3qa)

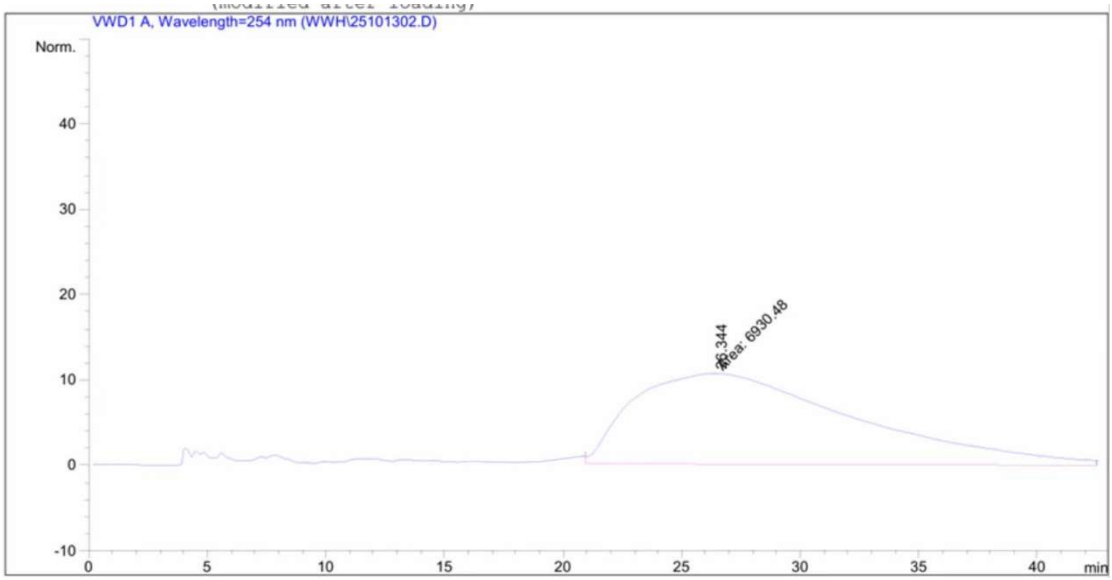


3qa

White solid, mp 134-136 °C, 76% yield, > 99% ee, dr = 10:1. $[\alpha]_D^{25}$ = +5.242 (c = 0.2, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.12 (s, 1H), 7.87 - 7.82 (m, 1H), 7.55 - 7.41 (m, 4H), 7.38 - 7.34 (m, 1H), 7.32 - 7.17 (m, 4H), 7.17 - 7.08 (m, 5H), 7.07 - 6.94 (m, 3H), 3.85 (d, *J* = 12.4 Hz, 1H), 3.77 (d, *J* = 12.4 Hz, 1H), 1.14 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.2, 156.0, 153.4, 150.1, 149.1, 136.6, 133.5, 131.5, 130.4, 130.1, 130.0, 129.7, 129.0, 128.7, 128.6, 128.4, 128.3, 128.1, 127.6, 126.3, 120.5, 77.3, 72.0, 39.7, 35.3, 31.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{32}H_{29}N_5O_3NaS$, 586.1889; Found 586.1884. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 15:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 26.3 min. (major).

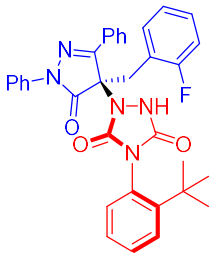


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.153	BB	1.8773	1173.48059	7.34410	49.7598
2	25.206	MM	2.9474	1184.80994	6.69977	50.2402



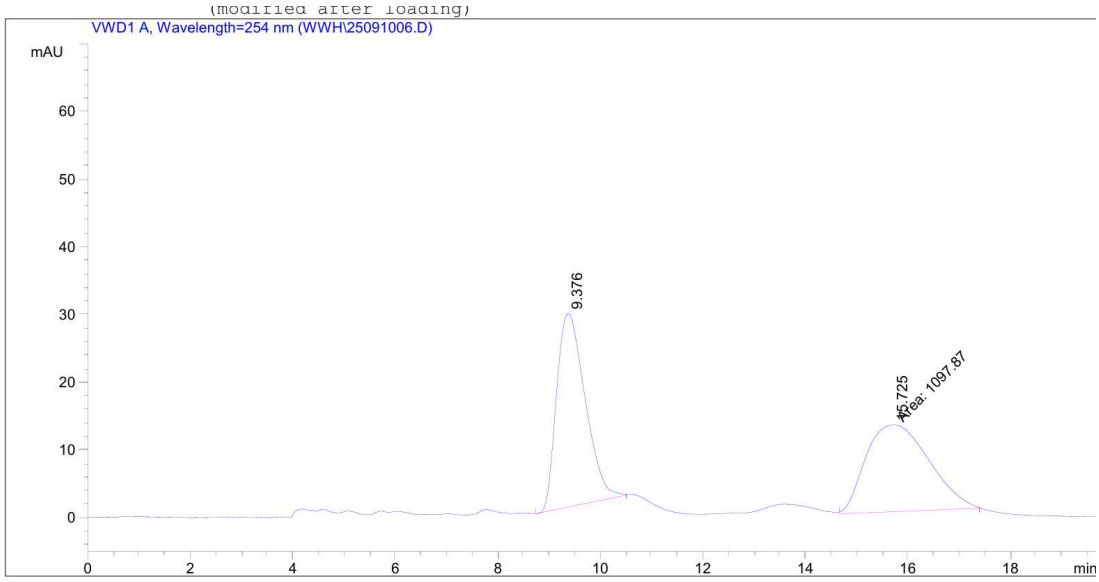
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.344	MM	10.8405	6930.47852	10.65521	100.0000

4-(2-(tert-butyl)phenyl)-1-(4-(2-fluorobenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-1,2,4-triazolidine-3,5-dion (3ra)

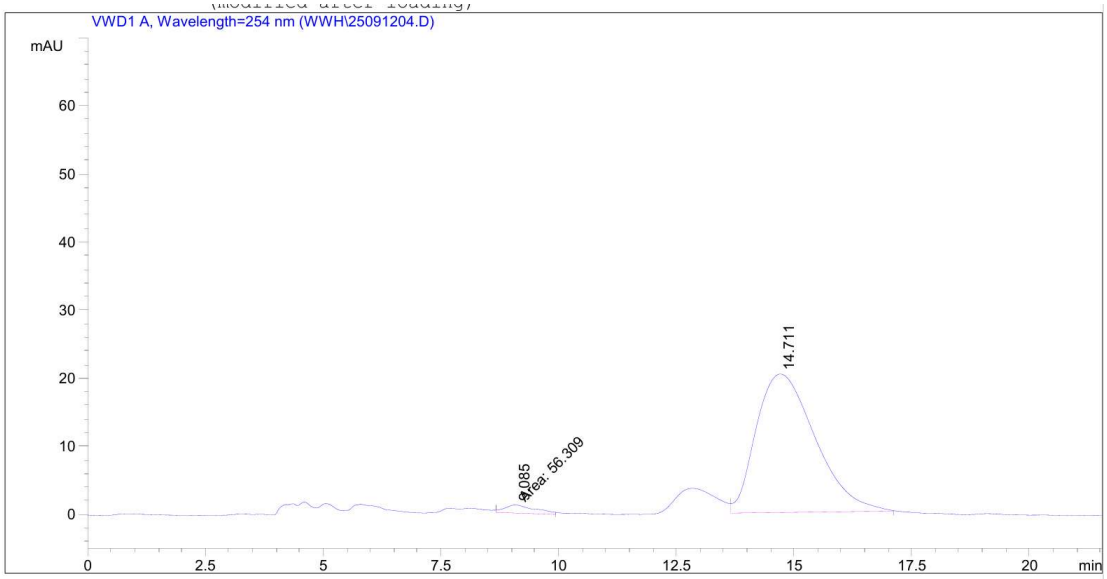


3ra

White solid, mp 249-251 °C, 73% yield, 94% ee, dr = 12:1. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.08 -8.01 (m, 2H), 7.61 -7.40 (m, 6H), 7.38 -7.24 (m, 3H), 7.24 -7.03 (m, 4H), 6.99 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.91 -6.81 (m, 2H), 4.04 (d, *J* = 12.9 Hz, 1H), 4.00 -3.89 (m, 1H), 1.11 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 160.1 (d, *J* = 253.7 Hz), 155.5, 152.6, 151.0 (d, *J* = 3.6 Hz), 148.9, 136.7, 132.6 (d, *J* = 8.8 Hz), 131.5, 130.4, 130.3, 130.1, 130.1, 129.8, 129.8, 128.7 (d, *J* = 9.2 Hz), 128.3, 128.2, 127.5, 126.2, 125.0, 125.0, 122.6 (d, *J* = 25.5 Hz), 120.2, 118.1, 117.0 (d, *J* = 23.0 Hz), 71.9, 35.5 , 31.3 . **^{19}F NMR** (377 MHz, $CDCl_3$) δ -113.71. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}FN_5NaO_3$, 598.2230; Found 598.2224. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 9.1 min. (minor), 14.7 min. (major).

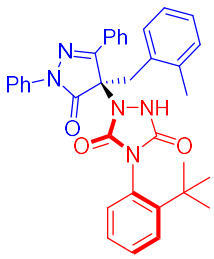


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.376	PB	0.5898	1106.36414	28.58725	50.1926
2	15.725	MM	1.4241	1097.87158	12.84876	49.8074



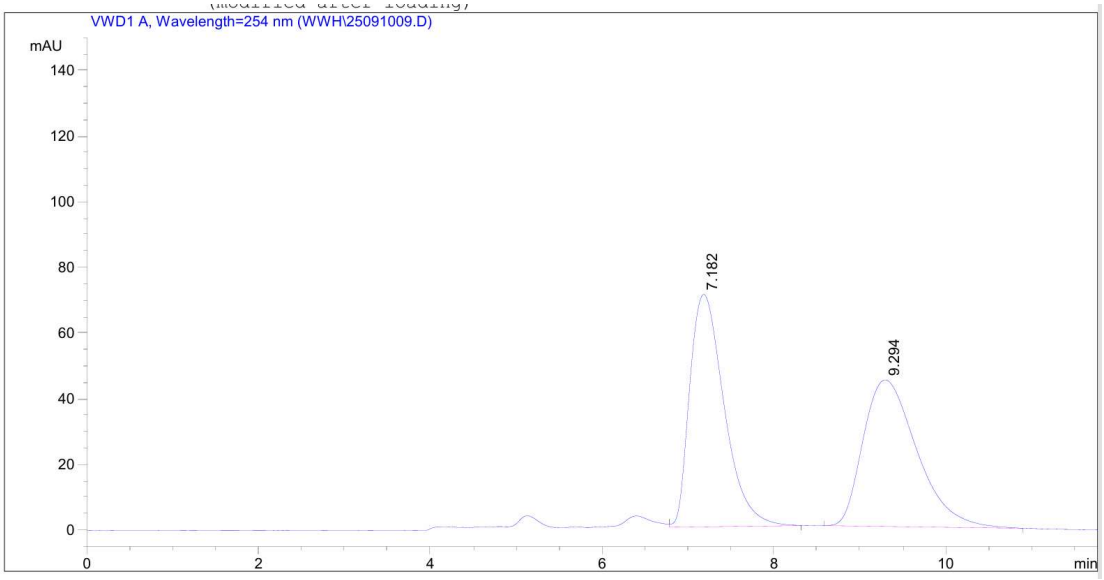
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	9.085	MM	0.7657	56.30904	1.22557	3.0673
2	14.711	VB	1.0641	1779.48267	20.34599	96.9327

4-(2-(tert-butyl)phenyl)-1-(4-(2-methylbenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-1,2,4-triazolidine-3,5-dione (3sa)

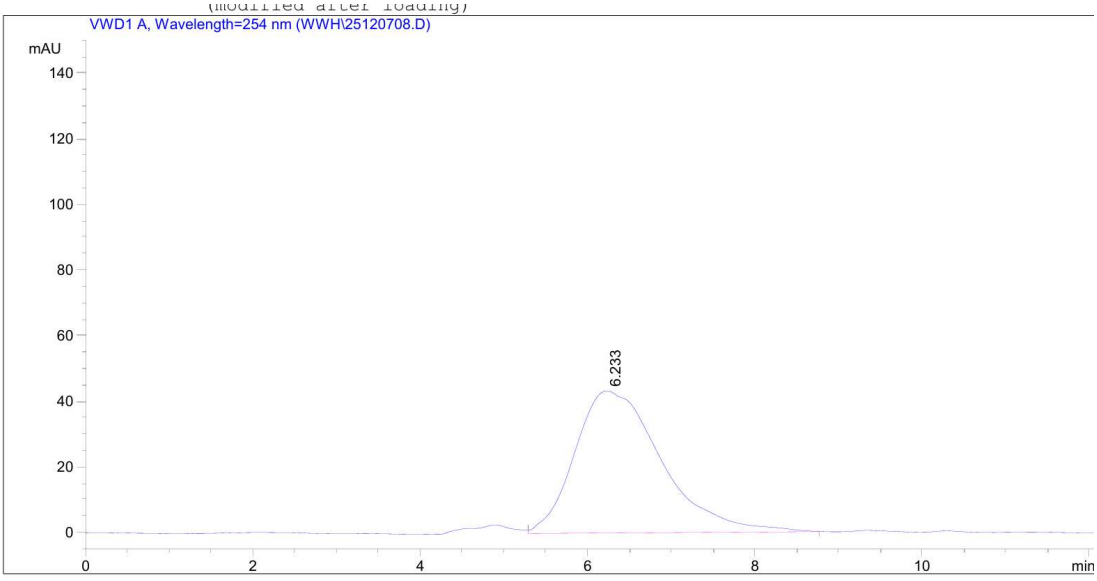


3sa

White solid, mp 150-152 ℃, 85% yield, > 99% ee, dr = 10:1. $[\alpha]_D^{25}$ = +0.8 (c = 0.8, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.87 (d, J = 7.3 Hz, 2H), 7.55 - 7.45 (m, 3H), 7.44 - 7.26 (m, 5H), 7.25 - 6.90 (m, 8H), 4.01 - 3.85 (m, 2H), 2.43 (s, 3H), 1.15 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.7, 169.8, 156.0, 153.3, 149.1, 136.7, 134.2, 131.4, 131.3, 130.4, 129.5, 129.4, 128.8, 128.6, 128.5, 128.3, 127.6, 126.6, 126.4, 120.2, 71.8, 38.9, 35.3, 31.2, 29.6. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2473. The enantiomeric ratio was determined by HPLC analysis on a chiral IF-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 6.2 min. (major).

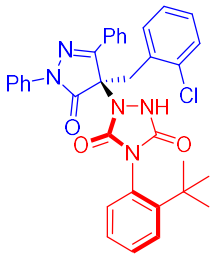


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.182	VB	0.4365	1977.64282	70.80798	50.4170
2	9.294	BB	0.6725	1944.92480	44.66753	49.5830



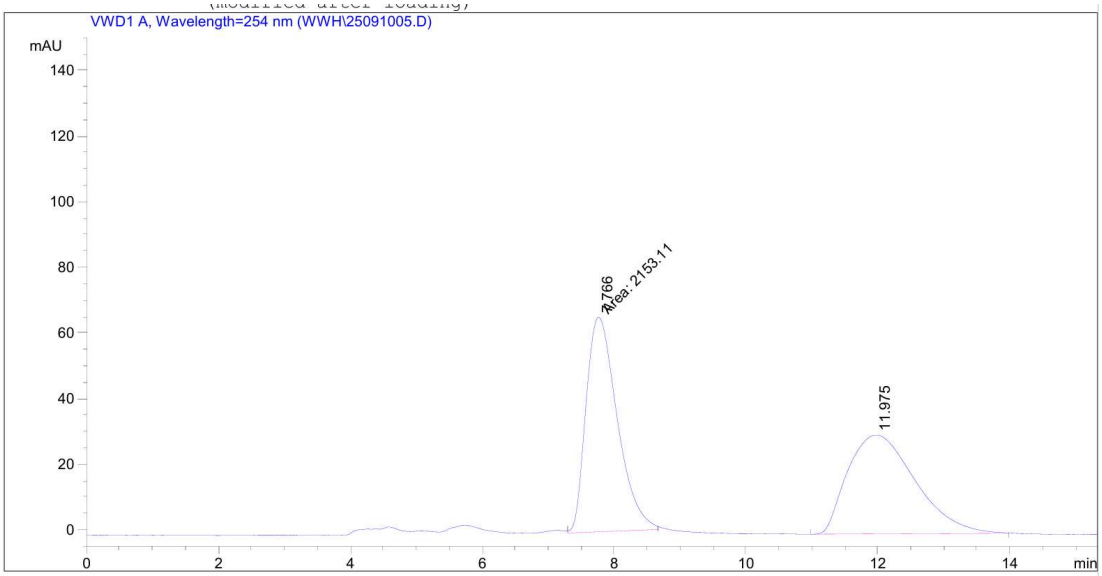
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.233	VB	0.9922	3130.54761	43.36574	100.0000

4-(2-(tert-butyl)phenyl)-1-(4-(2-chlorobenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-1,2,4-triazolidine-3,5-dione(3ta)

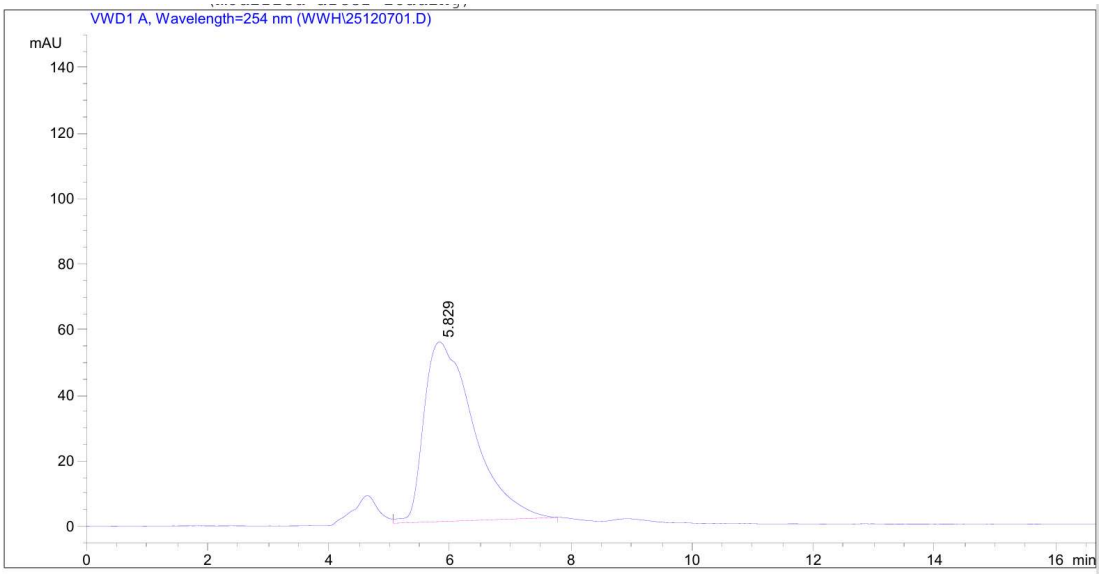


3ta

White solid, mp 245-247 ℃, 85% yield, > 99% ee, dr = 10:1. $[\alpha]_D^{25}$ = +3.917 (c = 0.4, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.20 (s, 1H), 8.13 - 8.06 (m, 2H), 7.67 - 7.57 (m, 2H), 7.57 - 7.44 (m, 4H), 7.42 - 7.16 (m, 6H), 7.15 - 7.10 (m, 1H), 7.03 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.94 - 6.88 (m, 2H), 4.09 (d, *J* = 12.9 Hz, 1H), 4.05 - 3.94 (m, 1H), 1.17 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.2, 156.1, 153.4, 153.3, 150.1, 149.1, 136.6, 131.5, 130.4, 130.1, 130.0, 129.7, 129.0, 128.7, 128.5, 128.4, 128.2, 128.1, 127.6, 126.3, 120.6, 71.9, 39.7, 35.3, 31.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}ClN_5NaO_3$, 614.1935; Found 614.1921. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 7:3, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 8.2 min. (major).

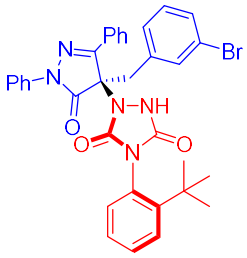


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.766	MM	0.5482	2153.10596	65.46516	50.1117
2	11.975	PB	1.1193	2143.50879	30.14425	49.8883



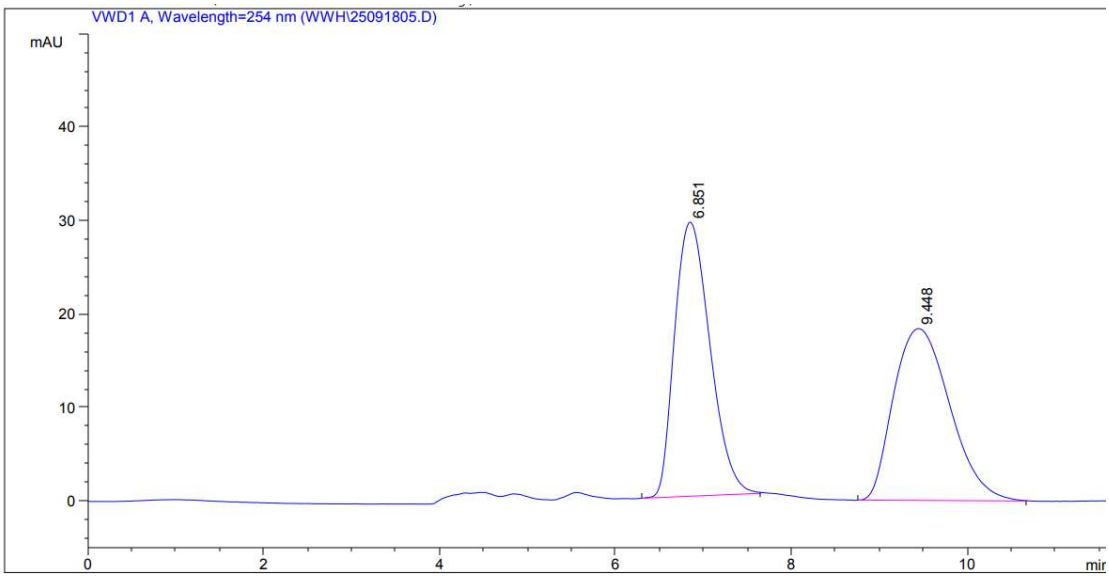
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.829	VB	0.7890	3131.16943	54.79317	100.0000

1-(4-(3-bromobenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione(3ua)

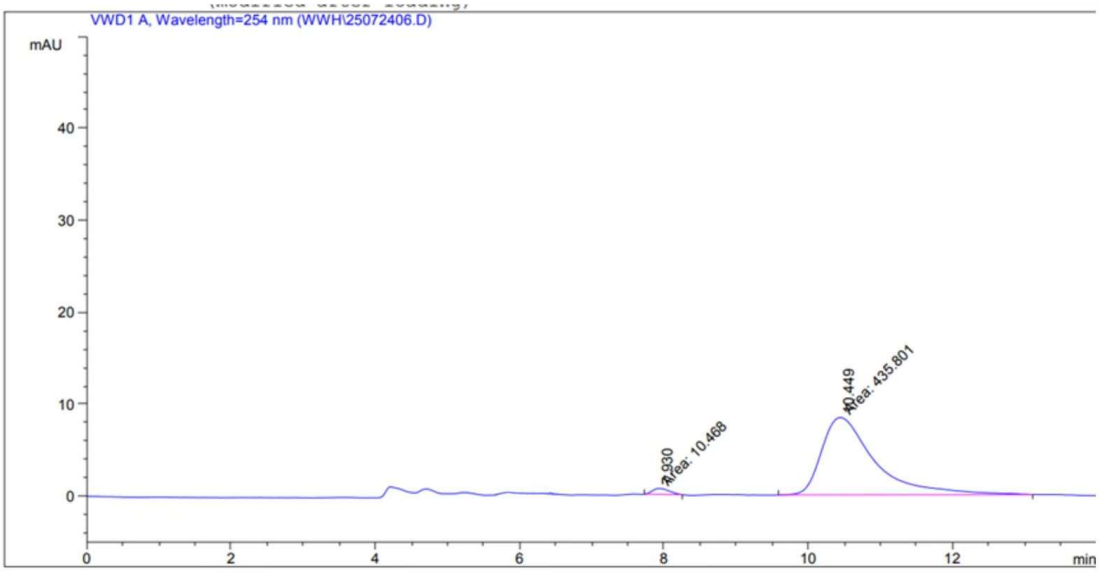


3ua

White solid, mp 151-153 ℃, 83% yield, > 99% ee, dr = 10:1. $[\alpha]_D^{25}$ = +0.725 (c = 0.1, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 8.15 -8.11 (m, 2H), 7.65 (ddd, *J* = 7.7, 4.4, 1.6 Hz, 2H), 7.57 (ddd, *J* = 14.6, 7.9, 6.3 Hz, 3H), 7.50 -7.44 (m, 1H), 7.41 -7.31 (m, 3H), 7.29 -7.22 (m, 3H), 7.15 -7.08 (m, 2H), 6.95 (dd, *J* = 7.5, 2.0 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 4.11 -3.98 (m, 2H), 1.48 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 156.1, 152.6, 148.9, 132.5, 131.4, 130.5, 130.0, 129.9, 128.8, 128.8, 128.6, 128.6, 128.3, 128.3, 128.2, 128.1, 127.7, 126.4, 125.5, 120.4, 71.7, 39.6, 35.3, 31.3, 31.3. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}BrN_5NaO_3$, 658.1430; Found 658.1423. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 15:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 7.9 min. (minor), 10.5 min. (major).

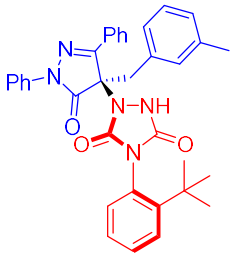


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.851	BB	0.4450	822.62286	29.34192	50.1283
2	9.448	PB	0.7028	818.41113	18.38618	49.8717



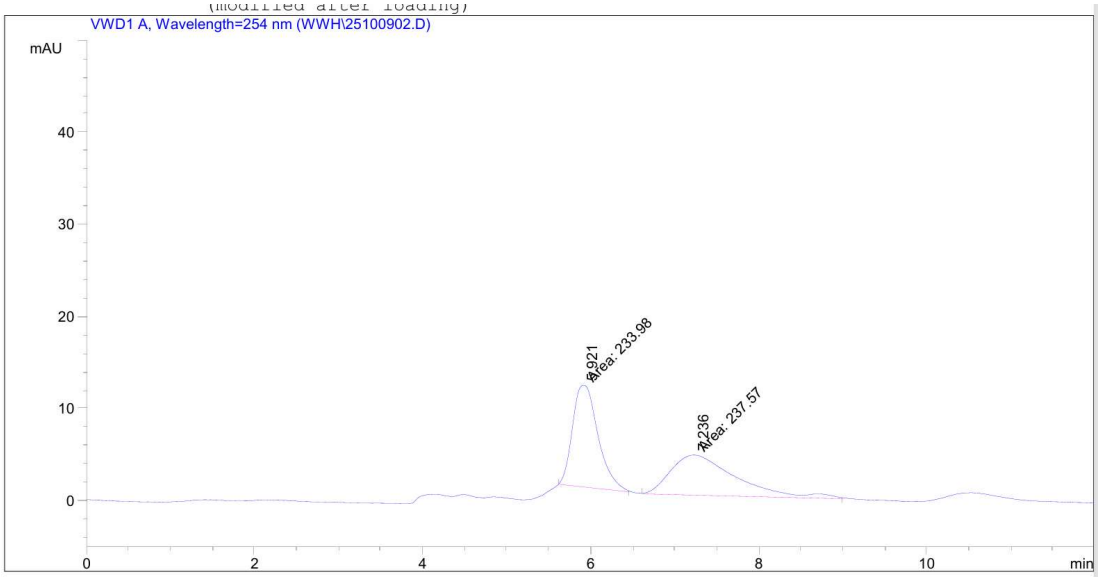
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	7.930	MM	0.2725	10.46797	6.40325e-1	2.3457
2	10.449	MM	0.8613	435.80139	8.43319	97.6543

4-(2-(tert-butyl)phenyl)-1-(4-(3-methylbenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1H-pyrazol-4-yl)-1,2,4-triazolidine-3,5-dione (3va)

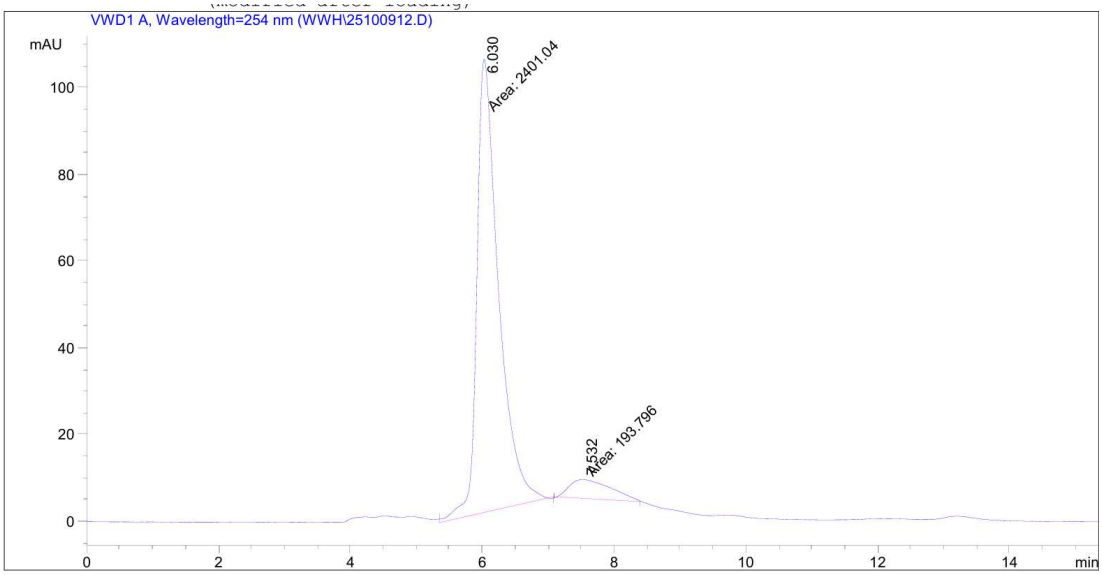


3va

White solid, mp 152-154 ℃, 80% yield, 86% ee, dr = 12:1. $[\alpha]_D^{25}$ = +5.067 (c = 0.7, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.40 (s, 1H), 8.12 -8.03 (m, 2H), 7.53 - 7.45 (m, 4H), 7.29 (d, *J* = 7.0 Hz, 2H), 7.26 -6.90 (m, 10H), 3.92 - 3.83 (m, 2H), 2.28 (s, 3H), 1.12 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 156.1, 153.5, 153.1, 149.1, 138.7, 136.7, 131.5, 131.0, 130.4, 130.2, 130.1, 129.7, 129.2, 128.5, 128.4, 128.3, 128.2, 127.6, 127.1, 126.7, 121.1, 117.8, 71.9, 39.6, 35.3, 31.2, 21.4. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}BrN_5NaO_3$, 658.1430; Found 658.1423. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 9.0 min. (major).

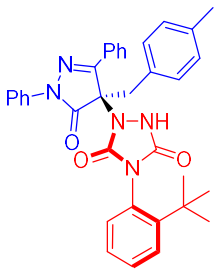


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.921	MM	0.3520	233.98009	11.07988	49.6194
2	7.236	MM	0.9065	237.56998	4.36778	50.3806



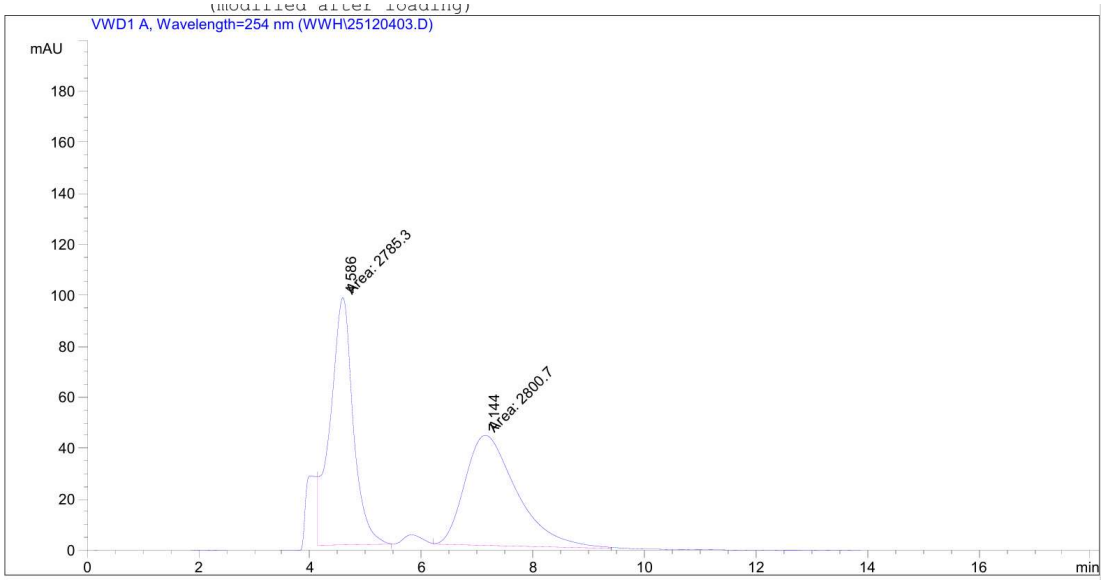
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.030	MM	0.3826	2401.04053	104.58047	92.5315
2	7.532	MM	0.7399	193.79587	4.36530	7.4685

4-(2-(tert-butyl)phenyl)-1-(4-(4-methylbenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-1,2,4-triazolidine-3,5-dione (3wa)

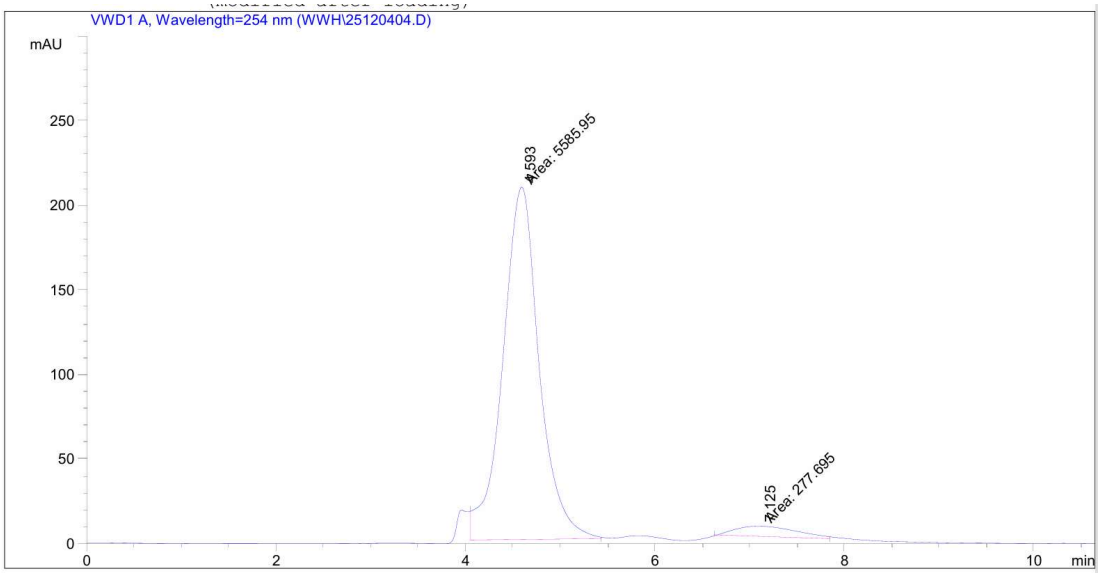


3wa

White solid, mp 145-147 °C, 85% yield, 90% ee, dr = 13:1. $[\alpha]_D^{25}$ = -0.585 (c = 0.4, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.14 - 8.06 (m, 2H), 7.57 - 7.48 (m, 4H), 7.41 - 7.36 (m, 3H), 7.31 - 7.02 (m, 8H), 6.98 (dd, *J* = 11.5, 7.5 Hz, 2H), 3.92 (d, *J* = 12.5 Hz, 1H), 3.87 (d, *J* = 12.3 Hz, 1H), 2.33 (d, *J* = 6.2 Hz, 3H), 1.15 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 178.1, 169.9, 156.1, 153.8, 153.0, 149.0, 135.4, 131.4, 131.3, 131.2, 130.4, 130.0, 129.4, 129.3, 128.8, 128.5, 128.3, 128.3, 128.3, 127.6, 126.8, 121.3, 71.8, 39.7, 35.3, 31.2, 29.6. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{35}H_{33}N_5NaO_3$, 594.2481; Found 594.2473. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 3:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 7.1 min. (minor), 4.6 min. (major).

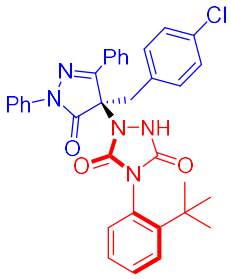


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.586	MM	0.4782	2785.30420	97.07089	49.8622
2	7.144	MM	1.0792	2800.69971	43.25322	50.1378



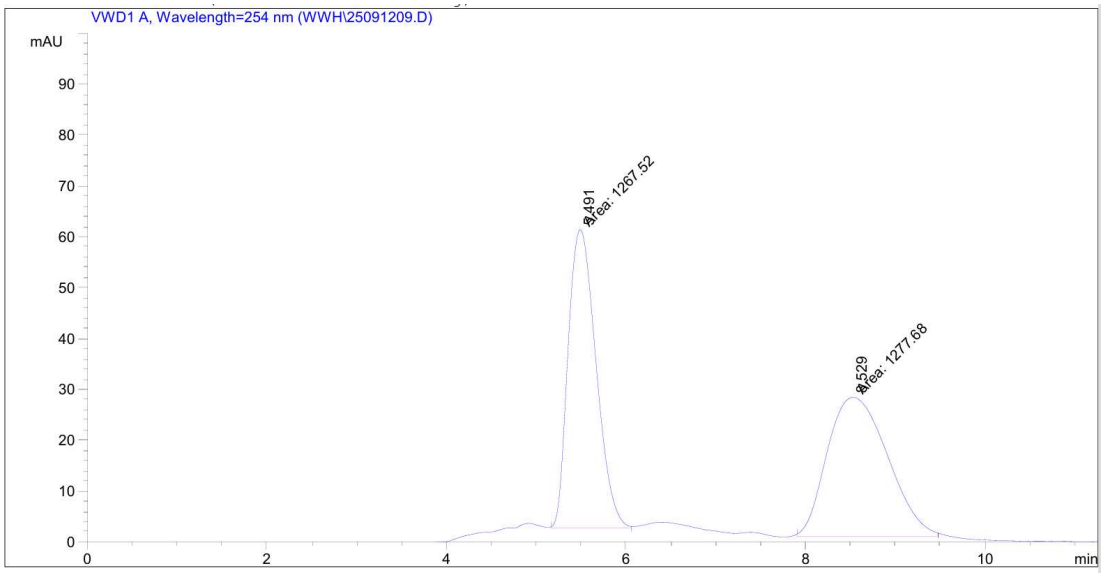
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.593	MM	0.4471	5585.95361	208.21674	95.2641
2	7.125	MM	0.7565	277.69528	6.11781	4.7359

4-(2-(tert-butyl)phenyl)-1-(4-(4-chlorobenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-1,2,4-triazolidine-3,5-dione (3xa)

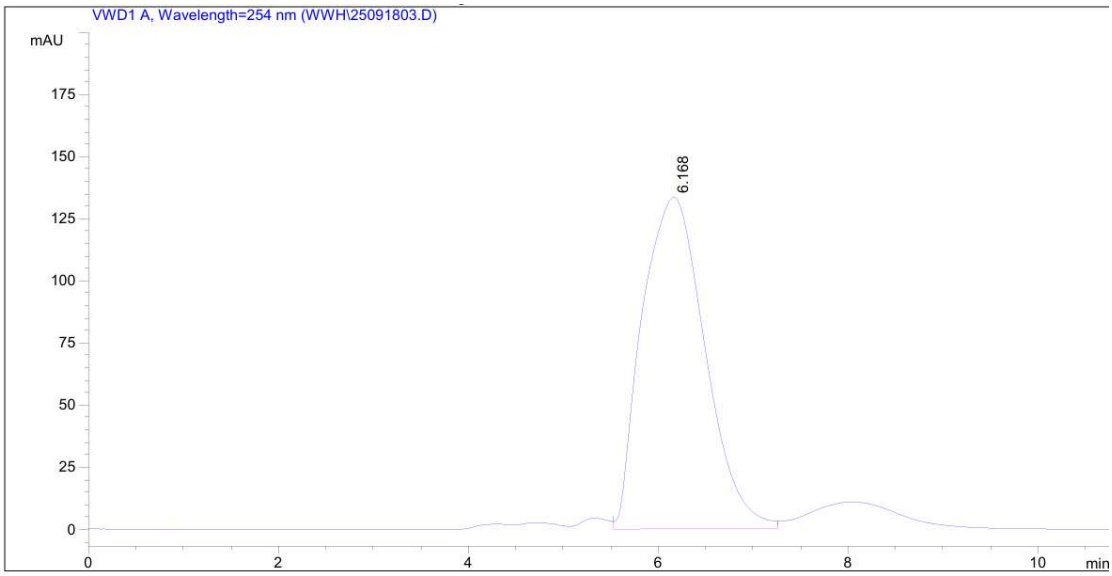


3wa

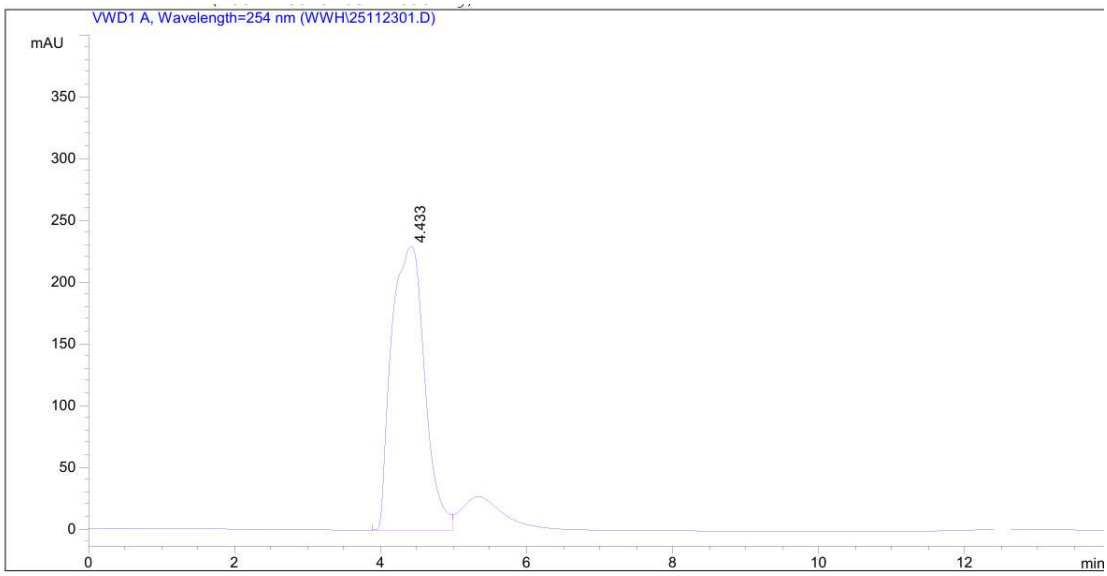
White solid, mp 125-127 °C, 85% yield, > 99% ee, dr = 12:1. $[\alpha]_D^{25}$ = +8.931 (c = 0.5, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 -7.97 (m, 2H), 7.55 -7.39 (m, 6H), 7.38 -7.09 (m, 6H), 7.06 -6.93 (m, 3H), 6.86 -6.75 (m, 2H), 3.91 -3.79 (m, 1H), 3.75 (d, *J* = 12.7 Hz, 1H), 1.10 (s, 9H) **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 156.0, 153.3, 153.2, 149.1, 136.7, 134.2, 131.4, 131.4, 131.2, 130.4, 129.5, 129.3, 128.8, 128.6, 128.5, 128.4, 127.6, 126.6, 126.4, 120.2, 71.8, 38.9, 35.3, 31.2. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}ClN_5NaO_3$, 614.1935; Found 614.1927. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 3:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 6.2 min. (major).



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	5.491	MM	0.3600	1267.51648	58.67917	49.8003
2	8.529	MM	0.7786	1277.68384	27.35143	50.1997

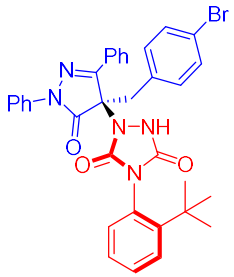


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.168	VV	0.7608	6154.94971	133.45183	100.0000



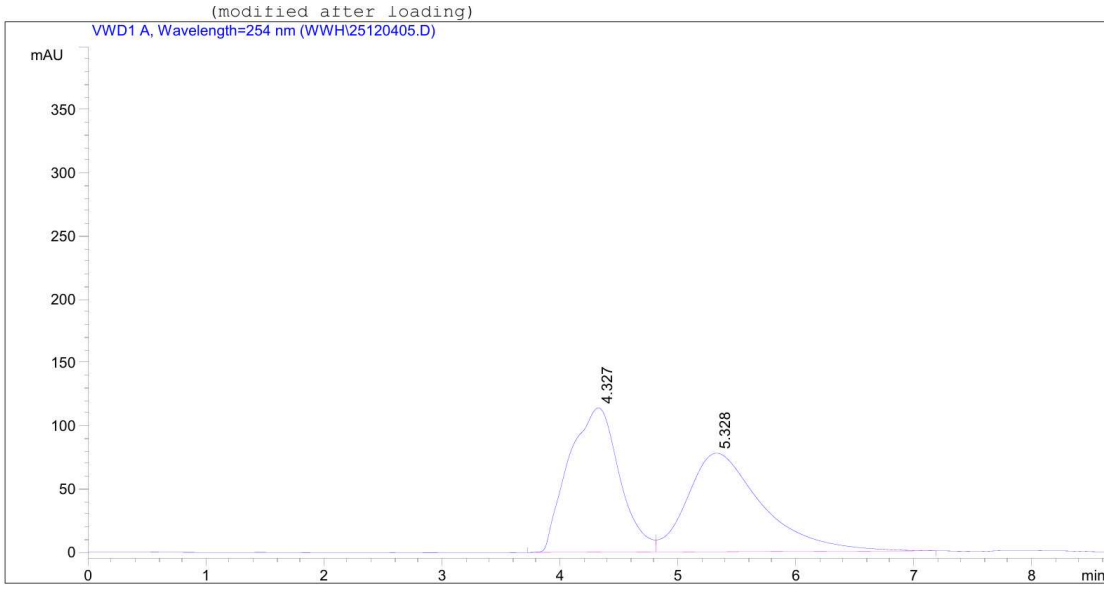
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.433	BV	0.4343	7193.96875	229.41437	100.0000

1-(4-(4-bromobenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ya)

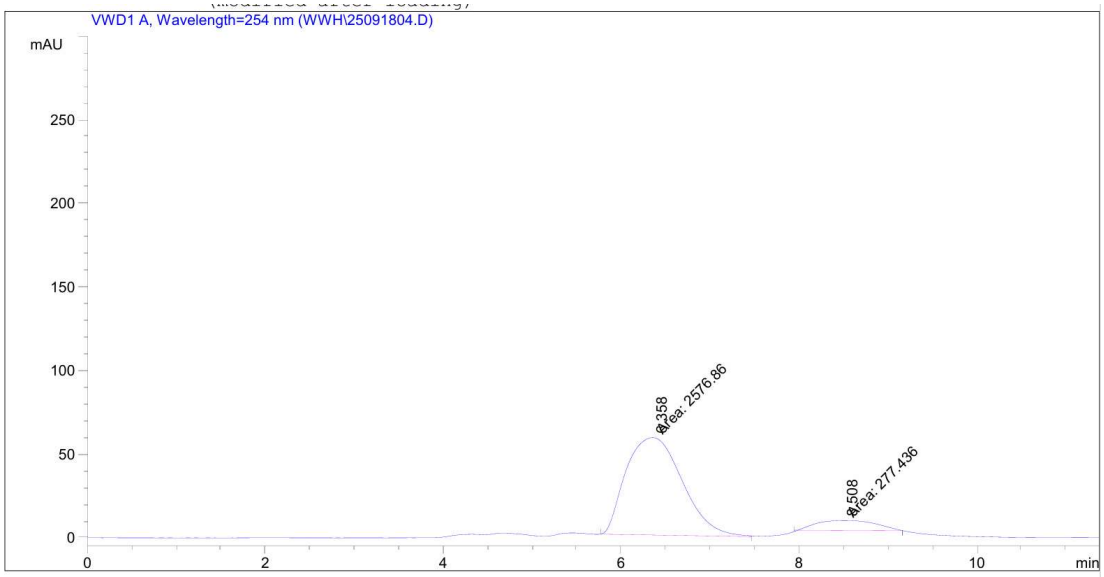


3ya

White solid, mp 134-136 ℃, 83% yield, 80% ee, dr = 13:1. $[\alpha]_D^{25}$ = +2 (c = 0.1, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.11 - 8.04 (m, 2H), 7.58 - 7.50 (m, 6H), 7.41 - 7.34 (m, 3H), 7.28 (d, *J* = 2.9 Hz, 1H), 7.23 (dd, *J* = 7.8, 4.5 Hz, 3H), 7.04 (d, *J* = 7.8 Hz, 1H), 6.81 (d, J = 8.1 Hz, 2H), 3.90 (d, *J* = 12.7 Hz, 1H), 3.81 (d, *J* = 12.6 Hz, 1H), 1.16 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 170.0, 156.2, 153.4, 153.2, 149.0, 136.7, 131.7, 131.4, 131.3, 130.5, 129.3, 129.2, 128.9, 128.6, 128.2, 127.6, 126.6, 126.4, 122.4, 120.3, 71.7, 38.9, 35.3, 31.2. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}BrN_5NaO_3$, 658.1430; Found 658.1428. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 3:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 8.5 min. (minor), 6.4 min. (major).

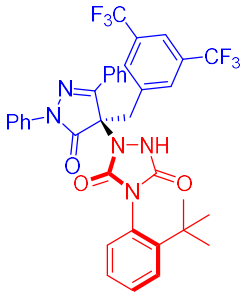


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.327	BV	0.4144	3417.57080	114.29707	49.9766
2	5.328	VB	0.6470	3420.77734	78.00625	50.0234



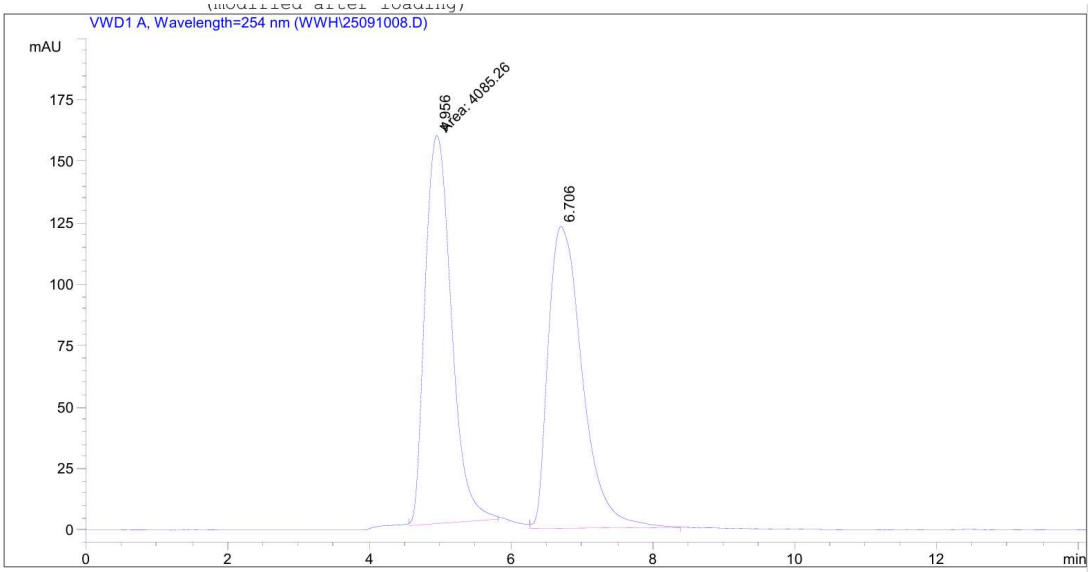
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	6.358	MM	0.7358	2576.85596	58.36792	90.2800
2	8.508	MM	0.7804	277.43579	5.92484	9.7200

1-(4-(3,5-bis(trifluoromethyl)benzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1H-pyrazol-4-yl)-4-(2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3za)

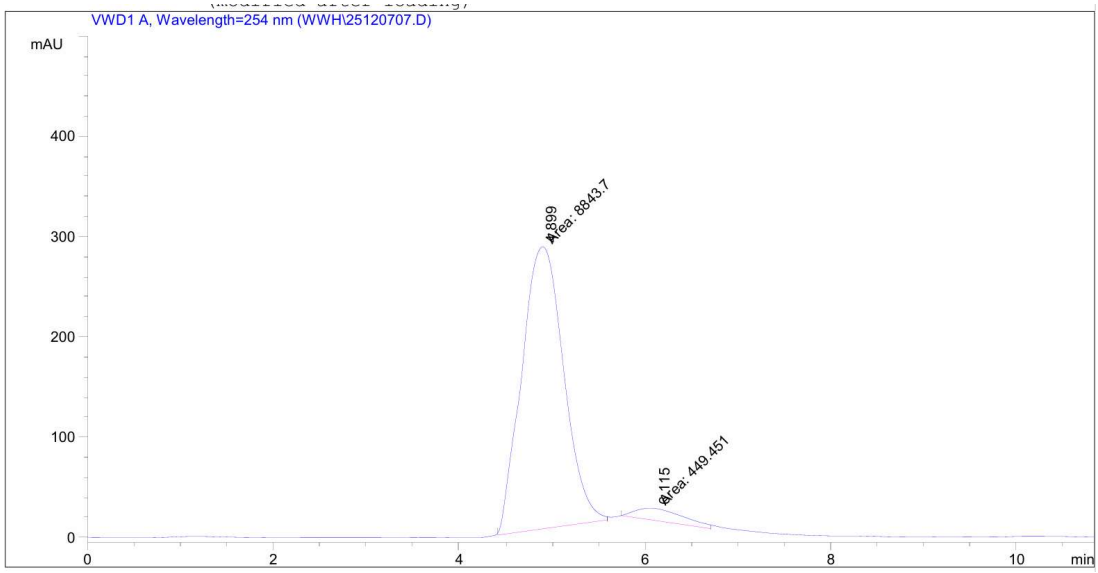


3za

White solid, mp 148-150 °C, 85% yield, 90% ee, dr = 10:1. $[\alpha]_D^{25}$ = +30.963 (c = 0.5, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.95 (d, *J* = 7.5 Hz, 2H), 7.61 (s, 1H), 7.51 - 7.43 (m, 6H), 7.36 - 7.32 (m, 1H), 7.26 (s, 6H), 7.16 - 7.12 (m, 1H), 6.98 (d, *J* = 7.7 Hz, 1H), 4.10 (d, *J* = 12.9 Hz, 1H), 3.82 (d, *J* = 12.8 Hz, 1H), 1.21 (s, 9H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 170.1, 154.0, 149.0, 136.7, 134.6, 132.1, 132.1, 132.0, 131.9, 131.2, 131.2, 131.2, 131.1, 130.9, 130.6, 130.5, 130.2, 129.8, 129.4, 129.3, 129.0 (d, *J* = 28.1 Hz), 127.9 (q, *J* = 3.5 Hz), 127.3, 126.5, 125.7 (d, *J* = 222.0 Hz), 124.0, 122.5 (q, *J* = 4.2 Hz), 121.9, 119.0, 40.9, 38.8, 35.4, 31.4. **^{19}F NMR** (377 MHz, $CDCl_3$) δ -63.14. HRMS (ESI) m/z: [M + Na]$^+$ Calcd for $C_{36}H_{29}F_6N_5NaO_3$, 716.2072; Found 716.2062. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 8:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 6.1 min. (minor), 4.9 min. (major).

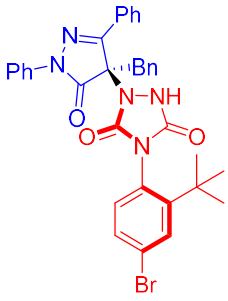


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.956	MM	0.4310	4085.26245	157.99005	49.7688
2	6.706	VB	0.5283	4123.22607	122.90296	50.2312



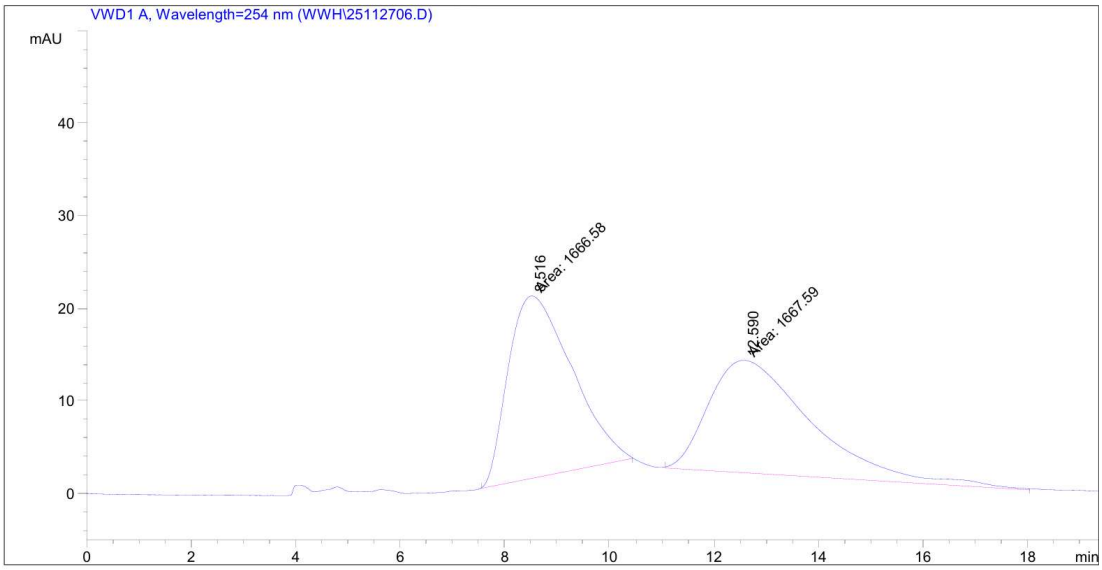
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.899	MM	0.5241	8843.70117	281.24863	95.1636
2	6.115	MM	0.6189	449.45132	12.10271	4.8364

1-(4-benzyl-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(4-bromo-2-(tert-butyl)phenyl)-1,2,4-triazolidine-3,5-dione (3ab)

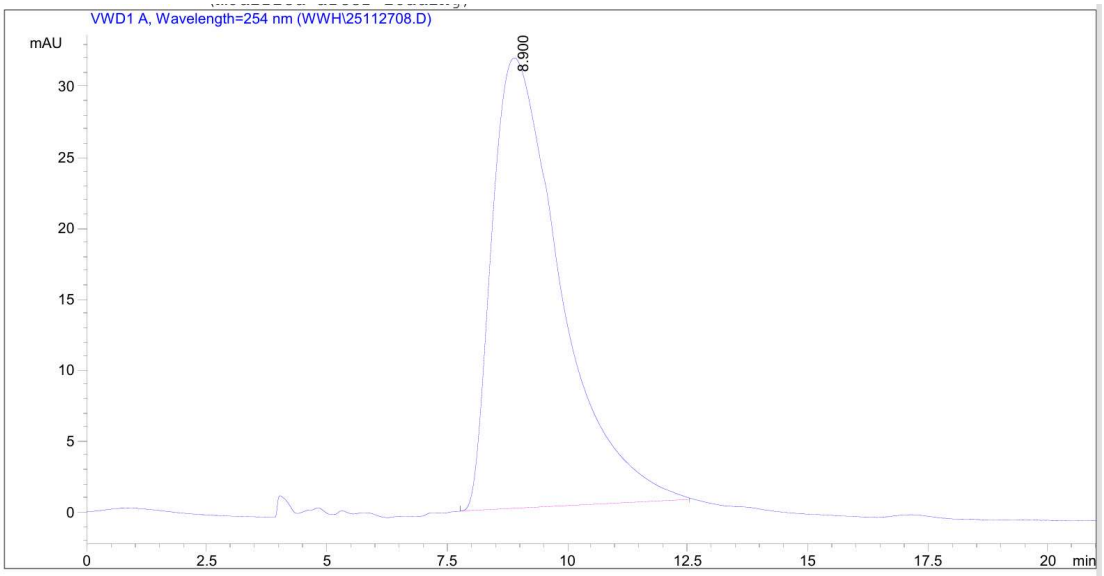


3ab

White solid, mp 151-153 ℃, 85% yield, 99% ee, dr = 18:1. $[\alpha]_D^{25}$ = +0.917 (c = 0.1, CH_2Cl_2).. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.07 - 8.01 (m, 2H), 7.60 (d, *J* = 2.3 Hz, 1H), 7.53 - 7.45 (m, 5H), 7.33 - 7.26 (m, 3H), 7.18 - 7.13 (m, 2H), 7.09 - 7.06 (m, 2H), 6.95 (d, *J* = 7.2 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 1H), 3.92 (d, *J* = 12.6 Hz, 1H), 3.85 (d, *J* = 12.7 Hz, 1H), 1.11 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.9, 155.6, 153.5, 152.7, 151.4, 136.7, 133.1, 131.9, 131.1, 130.8, 130.0, 129.5, 129.3, 128.8, 128.3, 128.3, 127.6, 126.7, 126.3, 124.8, 120.5, 72.0, 39.7, 35.5, 30.9. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}BrN_5NaO_3$, 658.1430; Found 658.1427. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 15:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 8.9 min. (major).

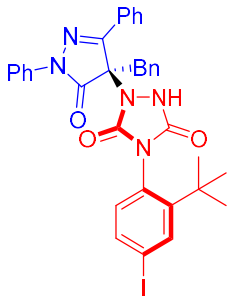


Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.516	MM	1.4101	1666.58044	19.69799	49.9848
2	12.590	MM	2.2858	1667.59143	12.15881	50.0152



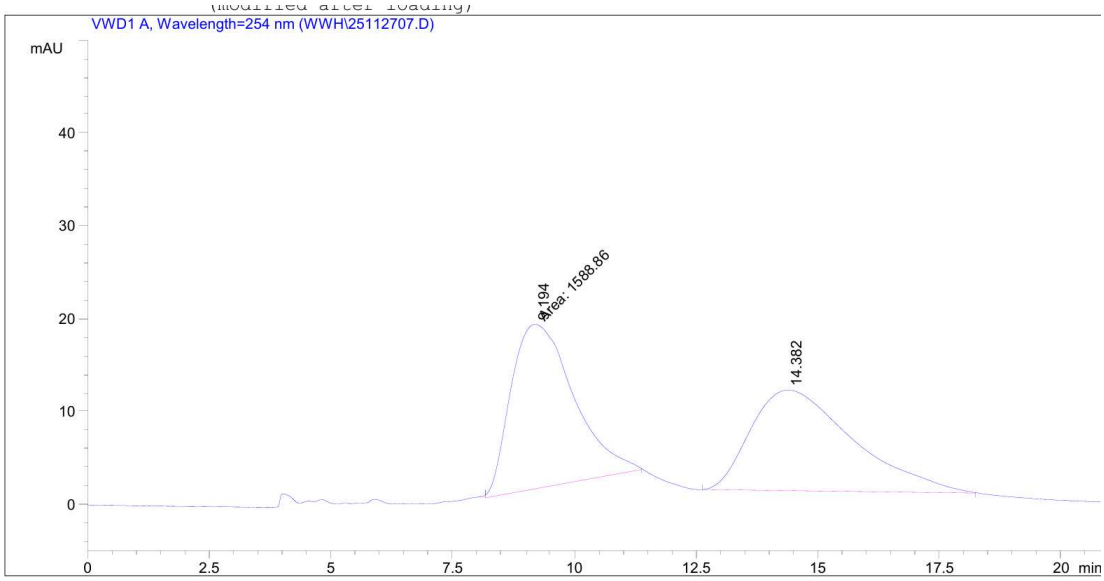
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	8.900	PB	1.4167	3156.36182	31.73330	100.0000

1-(4-benzyl-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-4-(2-(tert-butyl)-4-iodophenyl)-1,2,4-triazolidine-3,5-dione(3ac)



3ac

White solid, mp 142-144 °C, 83% yield, 99% ee, dr = 18:1. $[\alpha]_D^{25}$ = +3.047 (c = 0.2, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.50 (s, 1H), 8.06 (d, *J* = 7.5 Hz, 2H), 7.57 - 7.48 (m, 6H), 7.40 - 7.33 (m, 3H), 7.28 (s, 1H), 7.23 (dd, *J* = 8.3, 3.6 Hz, 3H), 7.05 (d, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 7.9 Hz, 2H), 3.92 - 3.76 (m, 2H), 1.13 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.2, 156.1, 153.4, 150.2, 149.1, 136.6, 133.5, 131.5, 130.4, 130.1, 129.7, 129.0, 128.7, 128.6, 128.4, 128.3, 128.1, 127.6, 126.3, 120.6, 72.0, 39.7, 35.3, 31.1. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{34}H_{30}IN_5NaO_3$, 706.1291; Found 706.1280. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 15:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 9.2 min. (major).



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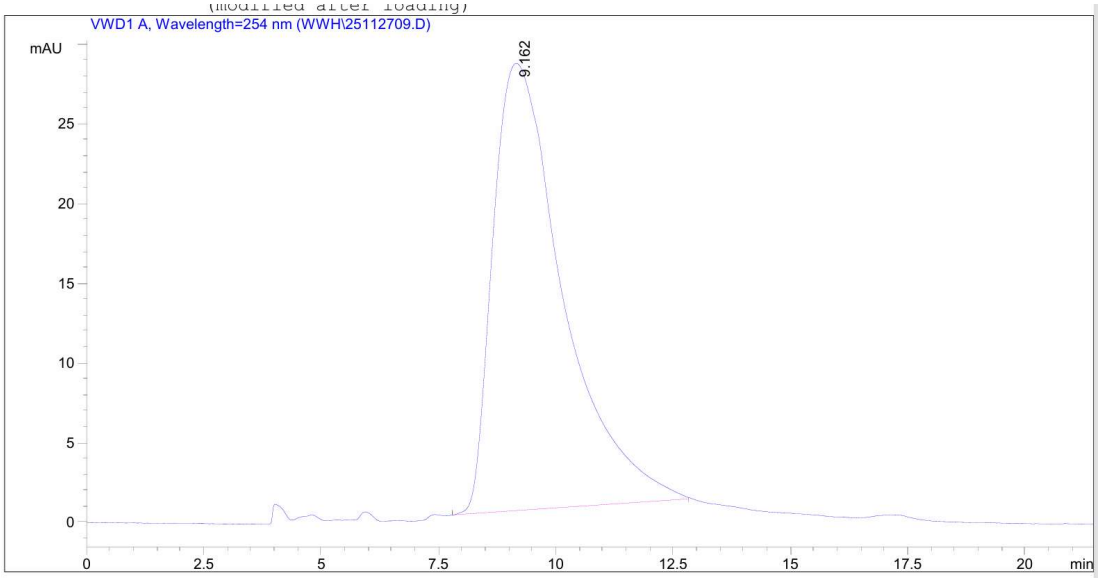
2	14.382	BB	1.7164	1585.49512	10.84133	49.9470



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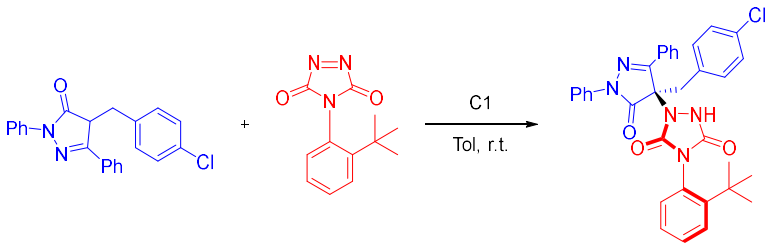
1	9.162	BB	1.4713	2917.15356	28.07757	100.0000

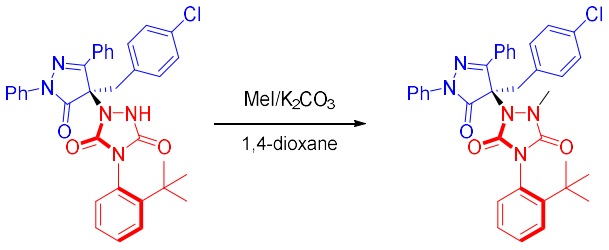
Gram scale synthesis of the product 3xa



1x, 2.5 mmol　　**2a**, 3 mmol　　**3xa**, 1.22 g
83% yield, >99% ee, 12:1 dr

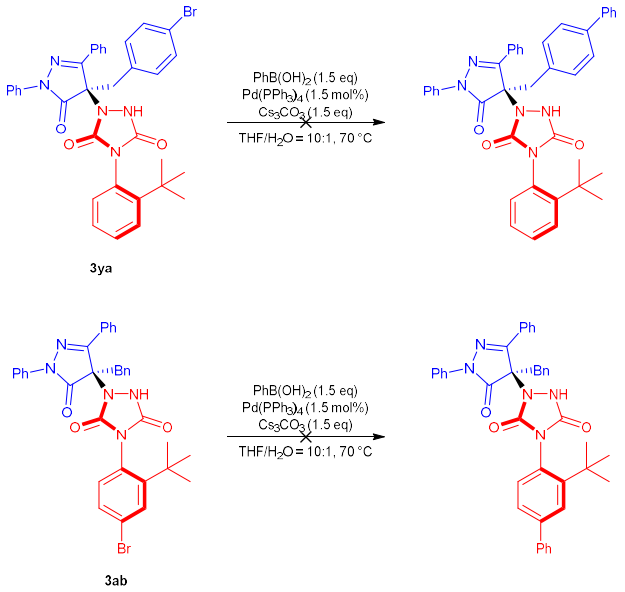
A tube was charged with **1x** (900 mg, 2.5 mmol, 1.0 eq.), **2a** (693 mg, 3 mmol, 1.2 eq.), **C1** (160 mg, 0.25 mmol, 0.1 eq.), followed with Tol (25 mL). The reaction mixture was stirred at 25 °C for 1 h. When compound **1x** was consumed as checked by TLC, the reaction was stopped and purified by column chromatography on silica gel directly to give the product **3xa** as white solid (yield 83%, > 99% ee, dr = 12:1).

Synthesis of the products 4



3xa　　**4**, 67% yield
92% ee, > 20:1 dr

Potassium carbonate (0.4 mmol, 2.0 equiv) was added to a solution of products **3xa** (0.2 mmol, 1.0 equiv) and iodomethane (2.0 mmol, 10 equiv) in dioxane (1 mL) at room temperature. The solution was stirred at room temperature for 5 h. When compound **3xa** was consumed as checked by TLC, the reaction was stopped and purified by column chromatography on silica gel directly to give the product **4** as white solid (yield 67%, ee 92%, dr > 20:1).

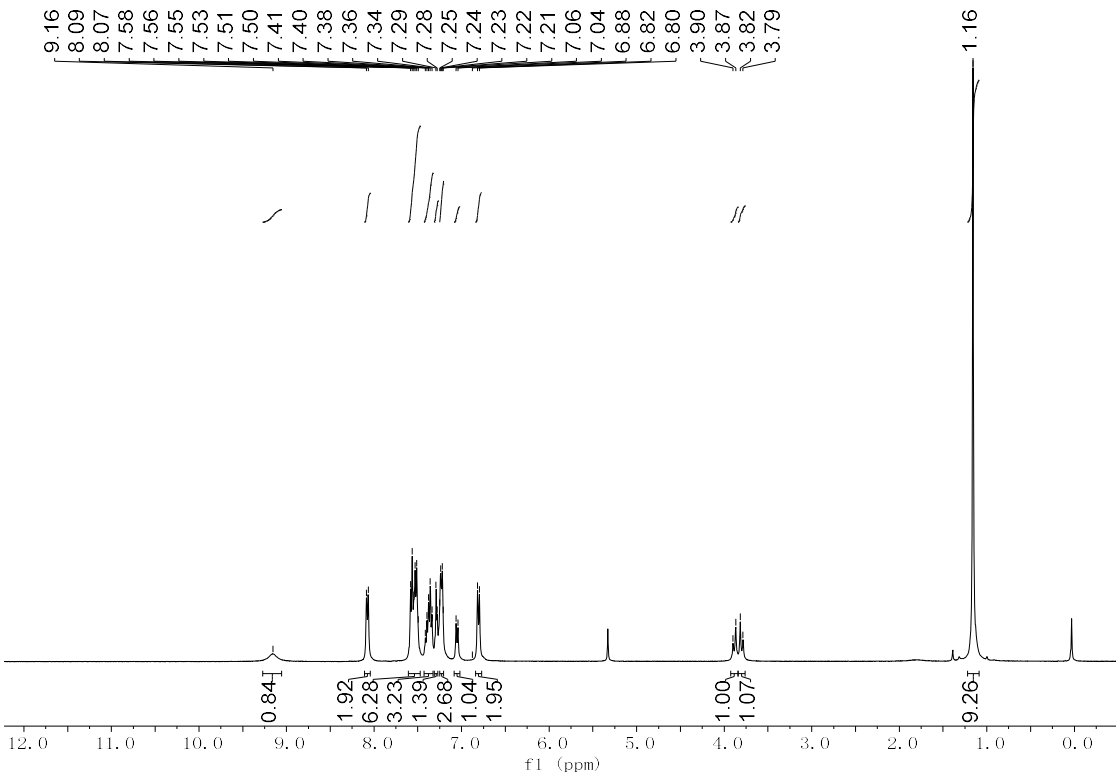


To a solution of **3ya/3ab** (1.0 equiv, 0.1 mmol) in 2.0 mL THF/H_2O (10:1) was added phenylboronic acid (1.5 equiv, 0.15 mmol), $Pd(PPh_3)_4$ (0.15 equiv, 0.015 mmol), Cs_2CO_3 (1.5 equiv, 0.15 mmol). Then, the reaction system was degassed and filled with nitrogen for three times. The reaction mixture was stirred under N_2 at 70 °C for 14 h. TLC monitoring showed no significant change in the spot corresponding to the starting material. Subsequently, the reaction mixture was purified by silica gel column chromatography, and the isolated product was analyzed by ^{1}H NMR spectroscopy, which confirmed its identity to be consistent with that of the starting material.

3ya

isolated product

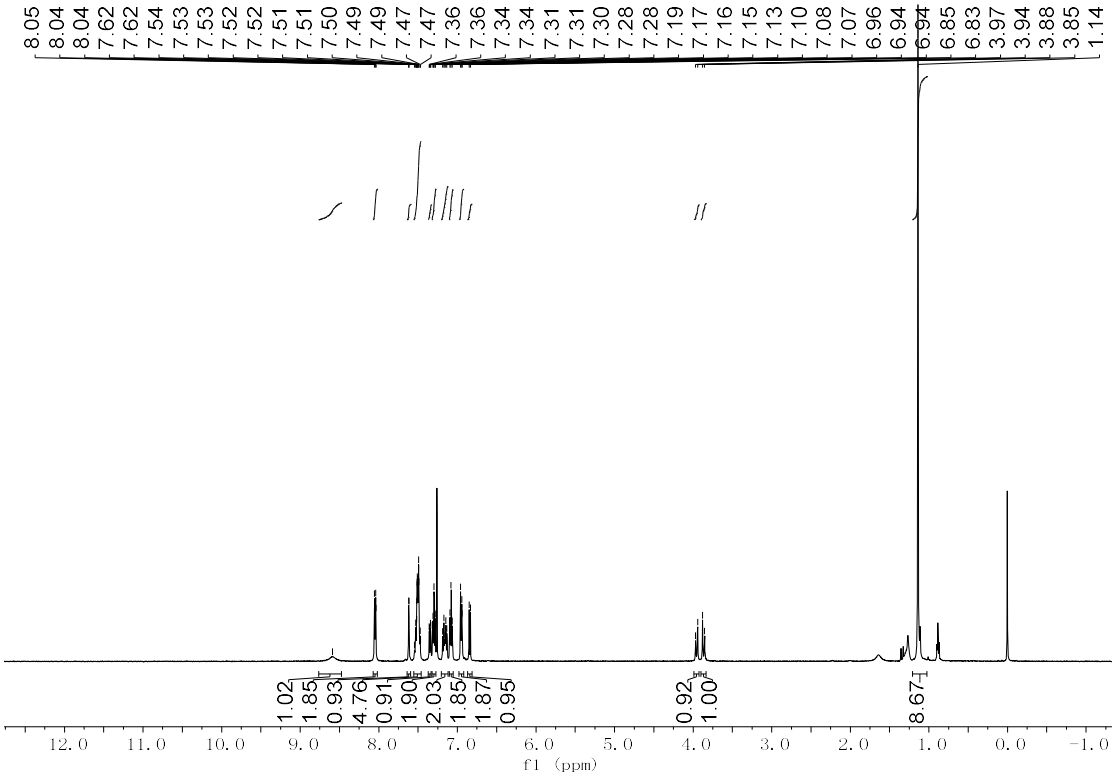
^{1}H NMR (400 MHz, $CDCl_3$) δ 9.16 (s, 1H), 8.08 (d, *J* = 7.5 Hz, 2H), 7.61 - 7.47 (m, 6H), 7.41 - 7.34 (m, 3H), 7.28 (d, *J* = 5.6 Hz, 1H), 7.23 (dd, *J* = 7.9, 3.9 Hz, 3H), 7.05 (d, *J* = 7.8 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 2H), 3.88 (d, *J* = 12.7 Hz, 1H), 3.80 (d, *J* = 12.6 Hz, 1H), 1.16 (s, 9H).

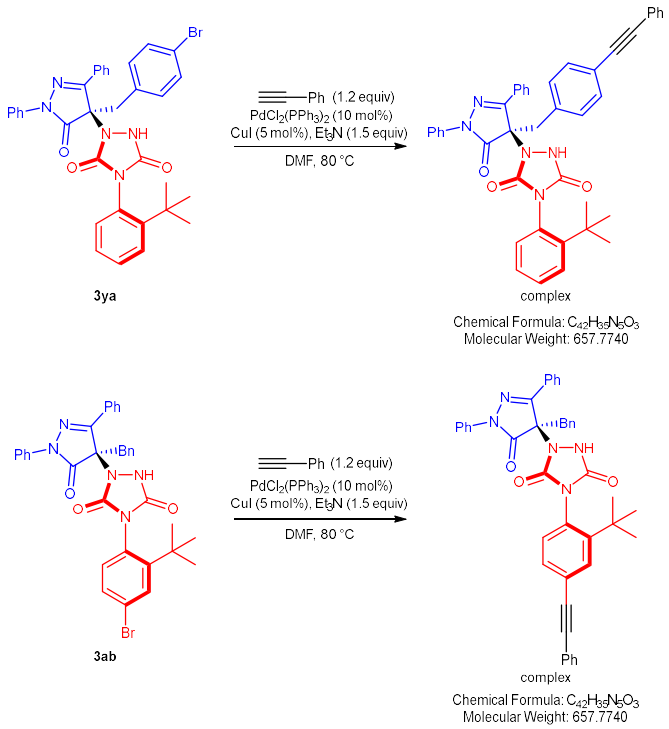


3ab

isolated product

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.05 (d, *J* = 7.1 Hz, 2H), 7.62 (d, *J* = 2.2 Hz, 1H), 7.55 - 7.46 (m, 5H), 7.35 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.31 - 7.28 (m, 2H), 7.20 - 7.12 (m, 2H), 7.10 - 7.07 (m, 2H), 6.95 (d, *J* = 7.2 Hz, 2H), 6.84 (d, *J* = 8.3 Hz, 1H), 3.96 (d, *J* = 12.6 Hz, 1H), 3.87 (d, *J* = 12.5 Hz, 1H), 1.14 (s, 9H).

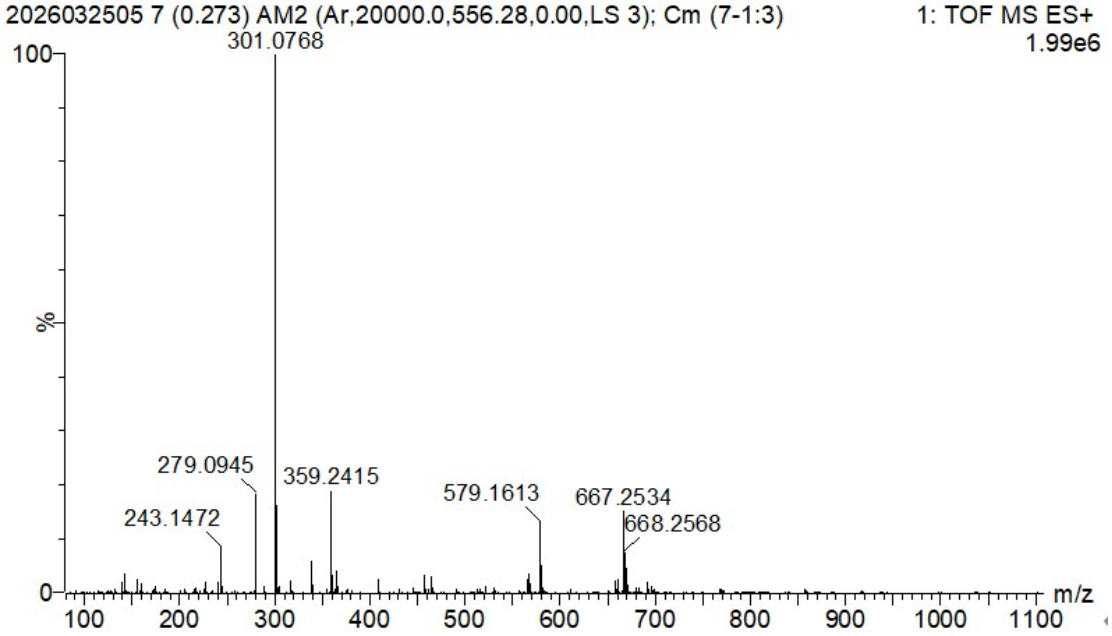


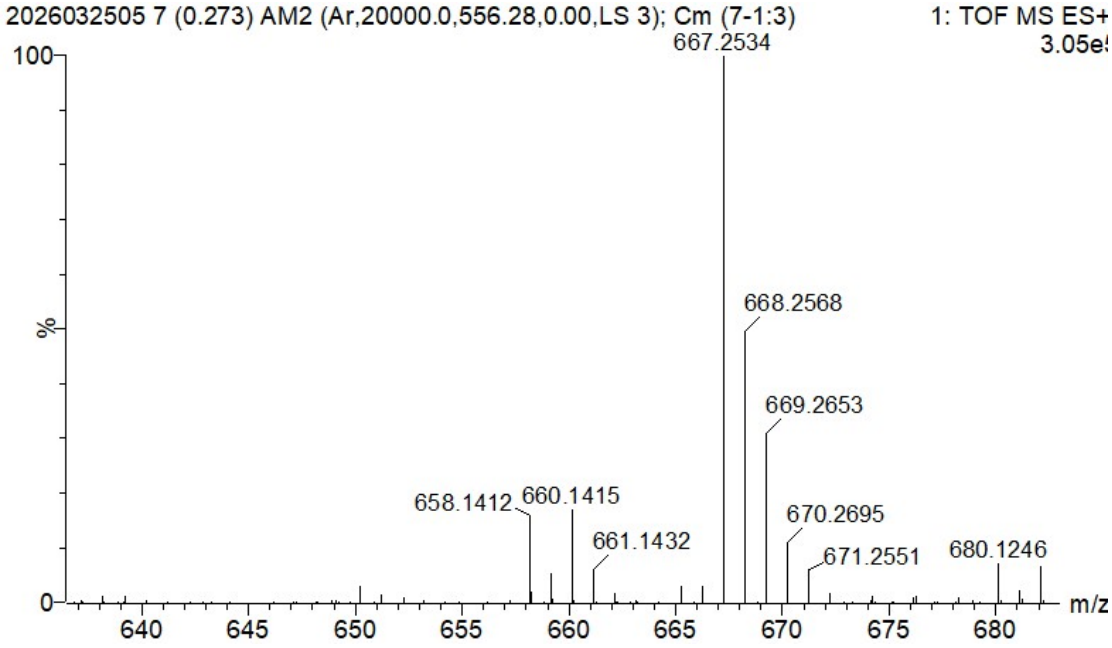


To a solution of **3ya/3ab** (1.0 equiv, 0.1 mmol), Et_3N (0.07 mL) in 1.0 mL DMF was added ethynylbenzene (2.5 equiv, 0.25 mmol), CuI (5.0 mol%), $PdCl_2(PPh_3)_2$ (10 mol%). Then, the reaction system was degassed and filled with nitrogen for three times. The reaction mixture was stirred under N_2 at 80 °C for 17 h. TLC analysis revealed a complex reaction mixture with multiple product spots. Subsequent HRMS analysis of the crude reaction mixture indicated the absence of the desired compound.

3ya

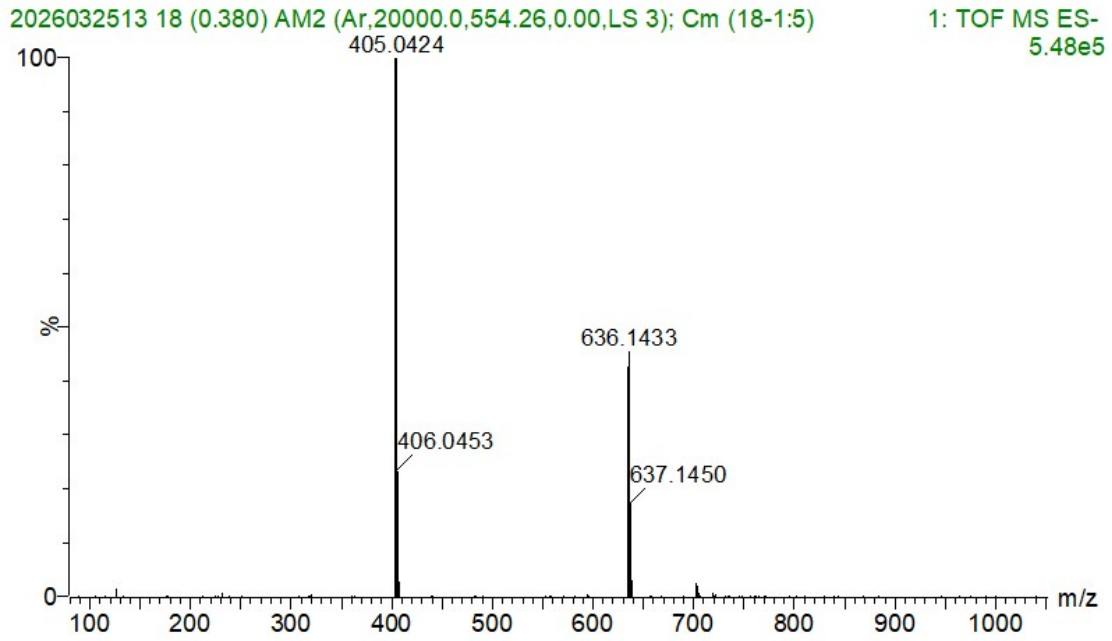
reaction system

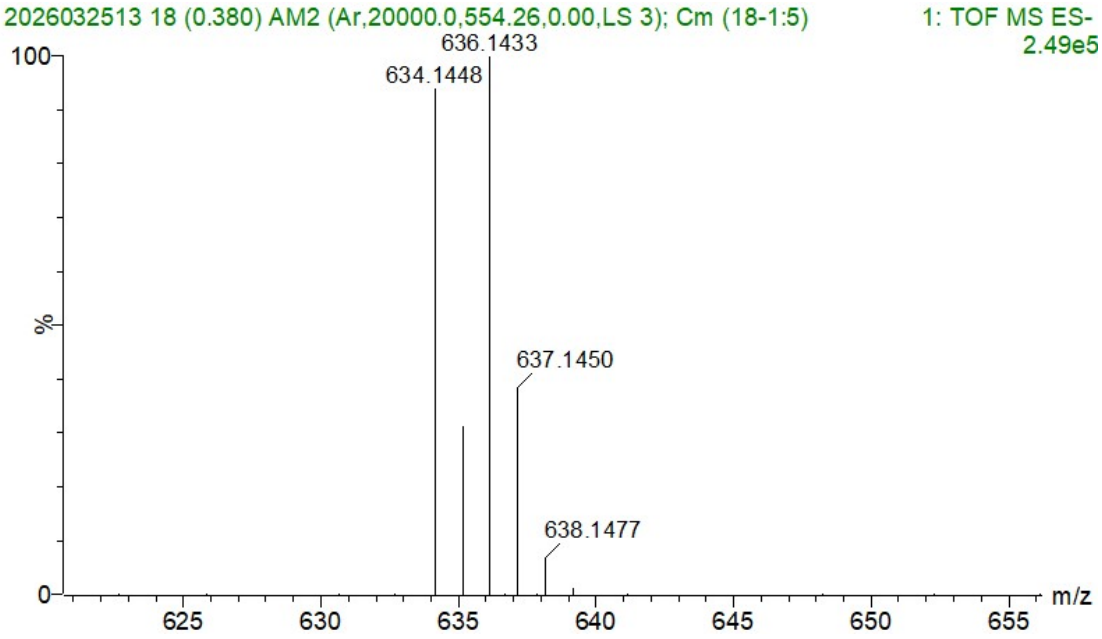




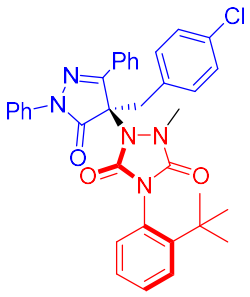
3ab

reaction system



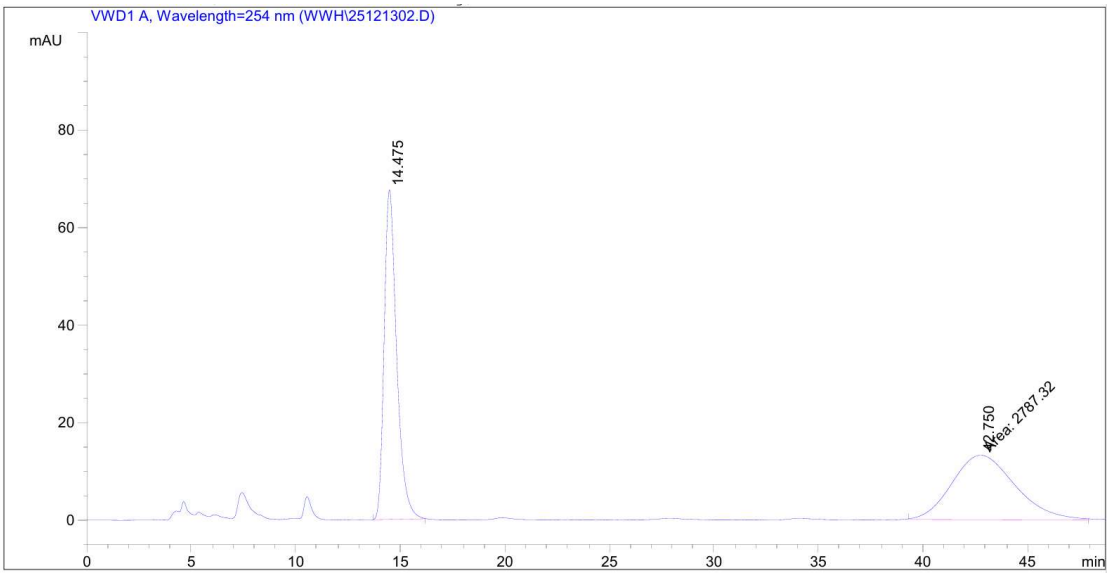

2026032513 18 (0.380) AM2 (Ar,20000.0,554.26,0.00,LS 3); Cm (18-1:5)
1: TOF MS ES-
2.49e5
636.1433
634.1448
637.1450
638.1477
100
%
0
625
630
635
640
645
650
655
m/z

4-(2-(tert-butyl)phenyl)-1-(4-(4-chlorobenzyl)-5-oxo-1,3-diphenyl-4,5-dihydro-1*H*-pyrazol-4-yl)-2-methyl-1,2,4-triazolidine-3,5-dione (4):



4

White solid, mp 135-137 °C, 67% yield, 92% ee, dr > 20:1. $[\alpha]_D^{25}$ = +20.972 (c = 0.2, CH_2Cl_2). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 - 8.09 (m, 2H), 7.67 - 7.52 (m, 6H), 7.51 - 7.41 (m, 1H), 7.40 - 7.36 (m, 2H), 7.32 - 7.28 (m, 1H), 7.25 - 7.21 (m, 1H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.99 - 6.92 (m, 1H), 6.81 (d, *J* = 8.0 Hz, 2H), 4.05 (s, 2H), 3.21 (s, 3H), 1.38 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.8, 155.3, 149.5, 136.7, 134.1, 131.5, 131.4, 131.2, 130.4, 129.9, 129.5, 129.1, 129.0, 128.7, 128.4, 127.6, 126.6, 126.3, 119.7, 75.0, 39.3, 35.6, 31.4, 29.7. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{32}ClN_5NaO_3$, 628.2091; Found 628.2088. The enantiomeric ratio was determined by HPLC analysis on a chiral AD-H column. *n*-Hexane/*i*-PrOH = 3:2, flow rate = 0.8 mL/min., λ = 254 nm, t_R = 14.5 min. (minor), 42.7 min. (major).



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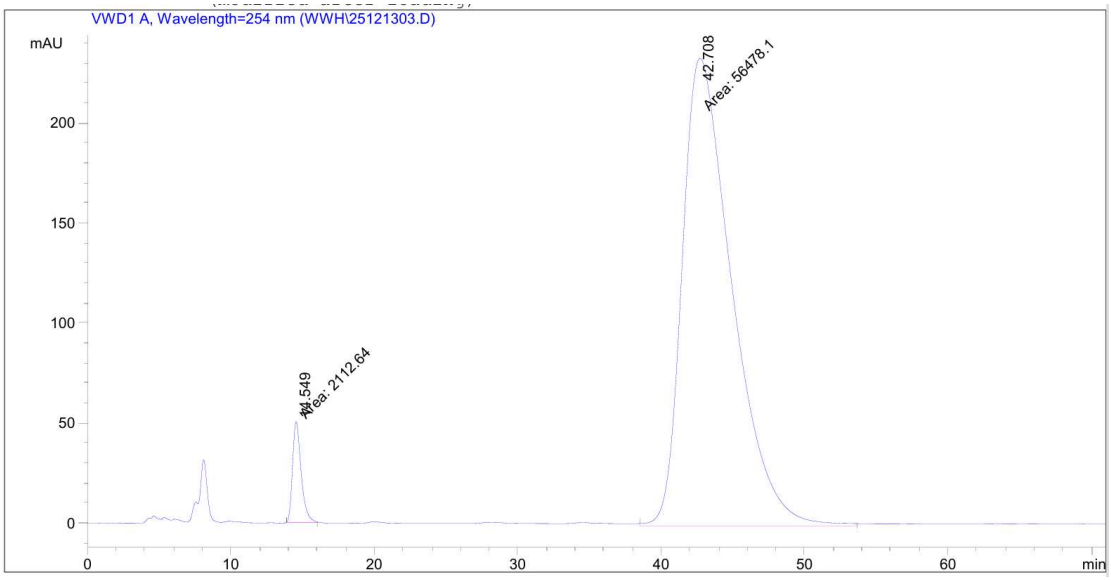
2	42.750	MM	3.5130	2787.32422	13.22387	49.8213



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.549	MM	0.6993	2112.63550	50.35394	3.6057
2	42.708	MM	4.0230	5.64781e4	233.97910	96.3943

4. The racemization experiment[3]

The enantiomerisation barrier was obtained by kinetic of racemization of an enantiomer[3e]. The slope of the first order kinetic line gives the racemization ($k_{ent} = \frac{1}{2}\, k_{rac}$). Erying equation gives the enantiomerisation barrier ($\Delta G_T^{\neq}$) from enantiomerisation constant (k_{ent}), R = 8.31451 J·K^{-1}mol^{-1}, h = 6.62608×10^{-34} J·s, $k_B = 1.38066 \times 10^{-23}$ J·K^{-1}. Enantiomeric excess values were determined by HPLC.

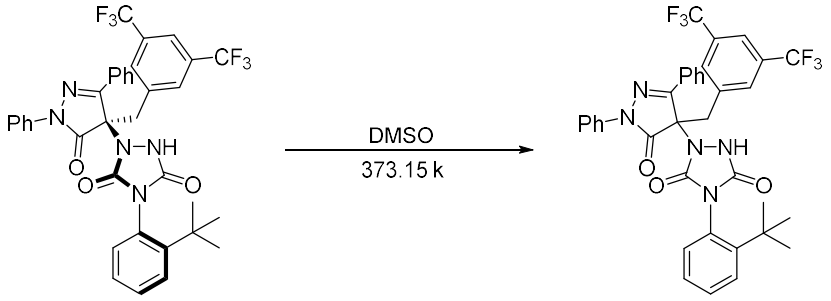


Table S1. Racemization of **3za** in mesitylene at 100 ℃.

t/h	dr	de	t (s)	ln(de$_0$/de$_t$)
0		1	0	0
1	39	0.95	3600	0.051293294
1.5	36	0.945945946	5400	0.055569851
2	29	0.933333333	7200	0.068992871
2.5	19	0.9	9000	0.105360516
3	14	0.866666667	10800	0.143100844
3.5	11	0.833333333	12600	0.182321557
4.5	9	0.8	16200	0.223143551
5.5	8	0.777777778	19800	0.251314428

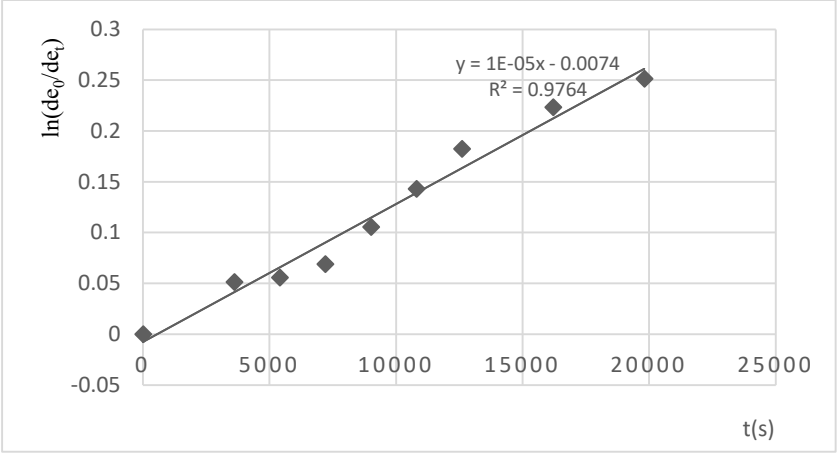


Figure S1. The plot of ln[(de$_0$/de$_t$)] vs time of **3za** at 100 ℃

T = 100 ℃ (DMSO); $k_{ent} = \frac{1}{2}\, k_{rac} = \frac{1}{2} slope = 5 \times 10^{-6}$; $t_{1/2} = \ln 2 / k_{rac} = 19$ h;

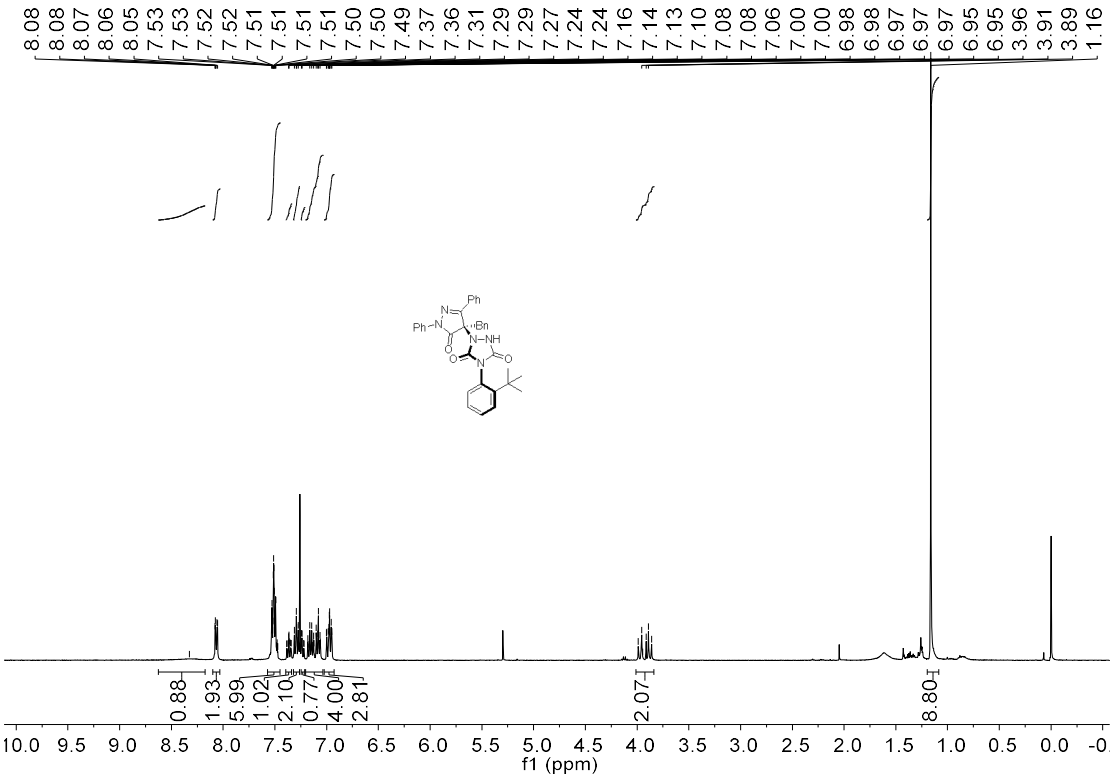
$\Delta G_T^{\neq} = \ln(\frac{k_B T}{h \times k_{ent}})$ RT = 129.96 kJ·mol^{-1} = 31.1 kcal·mol^{-1}

5. References

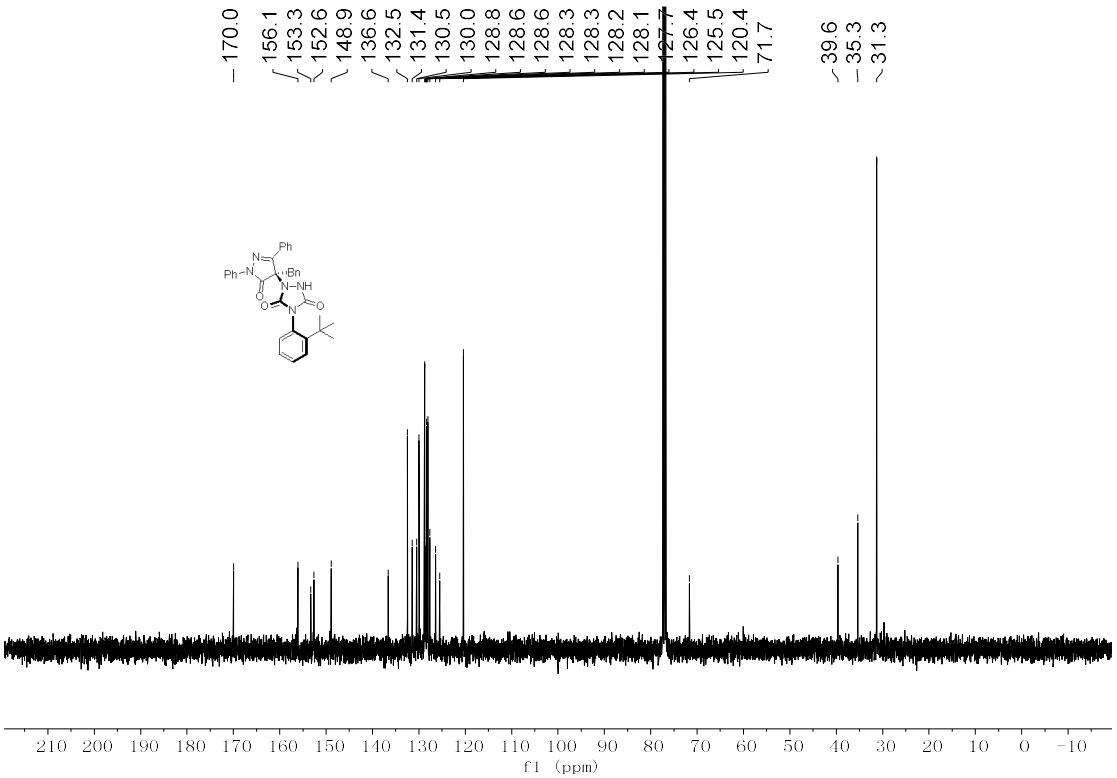
1. J. Geng, X. Wei, B. He, Y. Hao, J. Qu and B. Wang, *Molecules*, 2023, **28**, 4279.
2. L. L. Zhang, J. W. Zhang, S. H. Xiang, Z. Guo and B. Tan, *Org Lett*, 2018, **20**, 6022-6026.
3. (a) S. Barik, S. S. Ranganathappa and A. T. Biju, *Nat. Commun.*, 2024, **15**, 5755; (b) S. Barik, S. Shee, S. Das, R. G. Gonnade, G. Jindal, S. Mukherjee and A. T. Biju, *Angew. Chem. Int. Ed.*, 2021, **60**, 12264-12268; (c) A. Luc and J. Wencel-Delord, *Chem. Commun.*, 2023, **59**, 8159-8167; (d) G.-J. Mei, J. J. Wong, W. Zheng, A. A. Nangia, K. N. Houk and Y. Lu, *Chem*, 2021, **7**, 2743-2757; (e) H.-Q. Wang, S.-F. Wu, J.-R. Yang, Y.-C. Zhang and F. Shi, *J. Org. Chem.*, 2022, **88**, 7684-7702.

6. NMR spectra copies

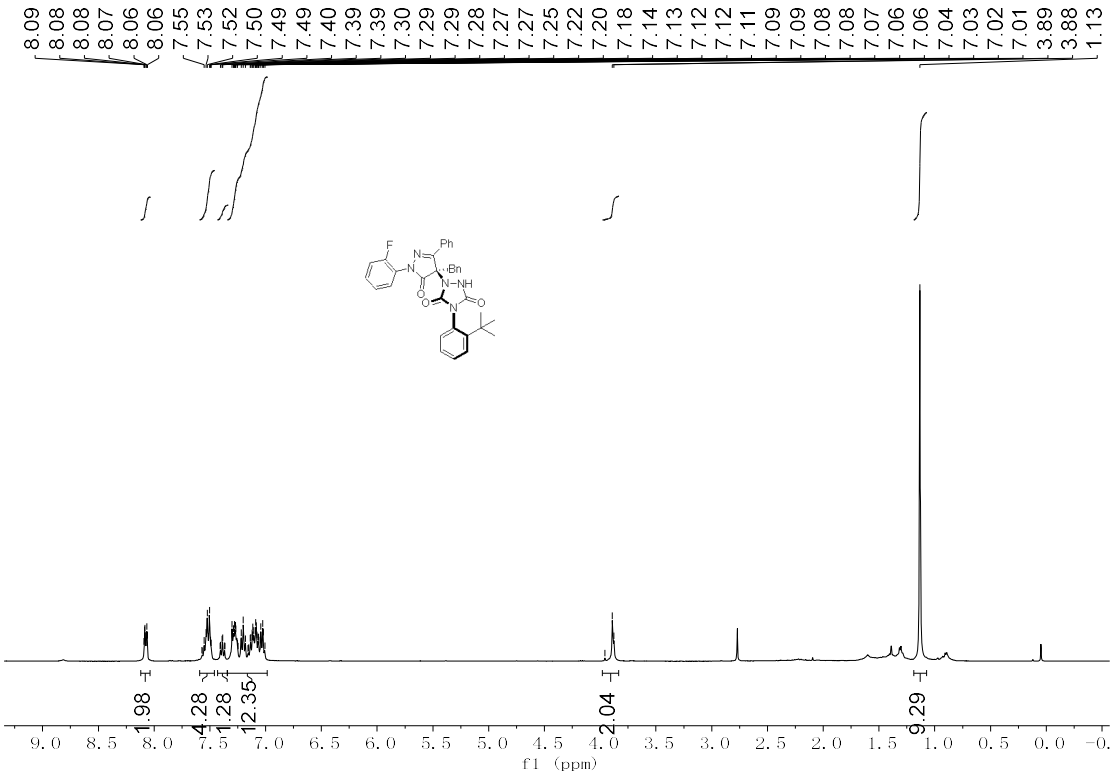
^{1}H NMR spectra of **3aa**



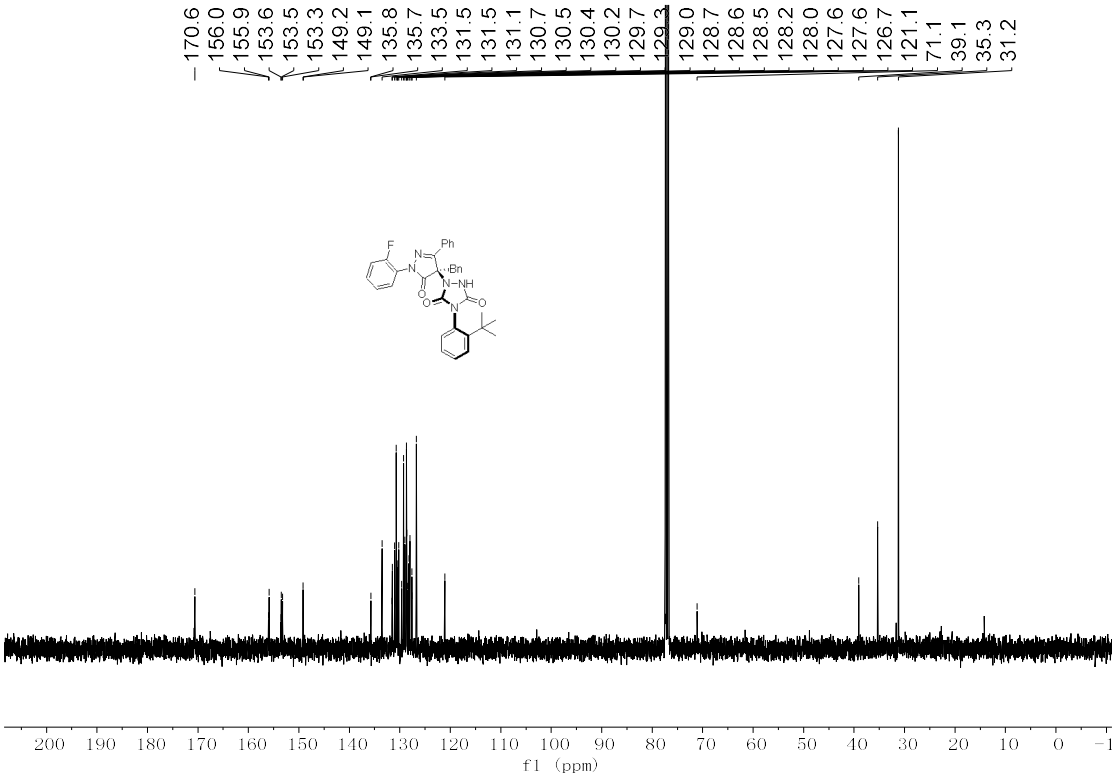
^{13}C NMR spectra of **3aa**



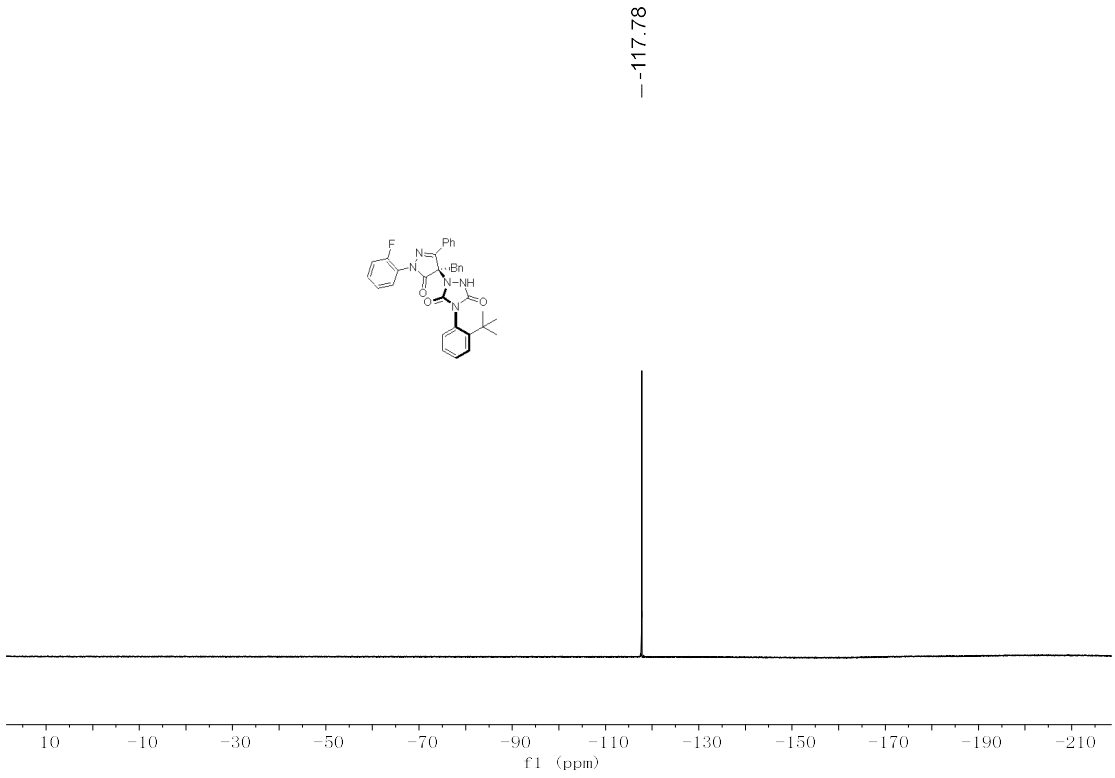
^{1}H NMR spectra of **3ba**



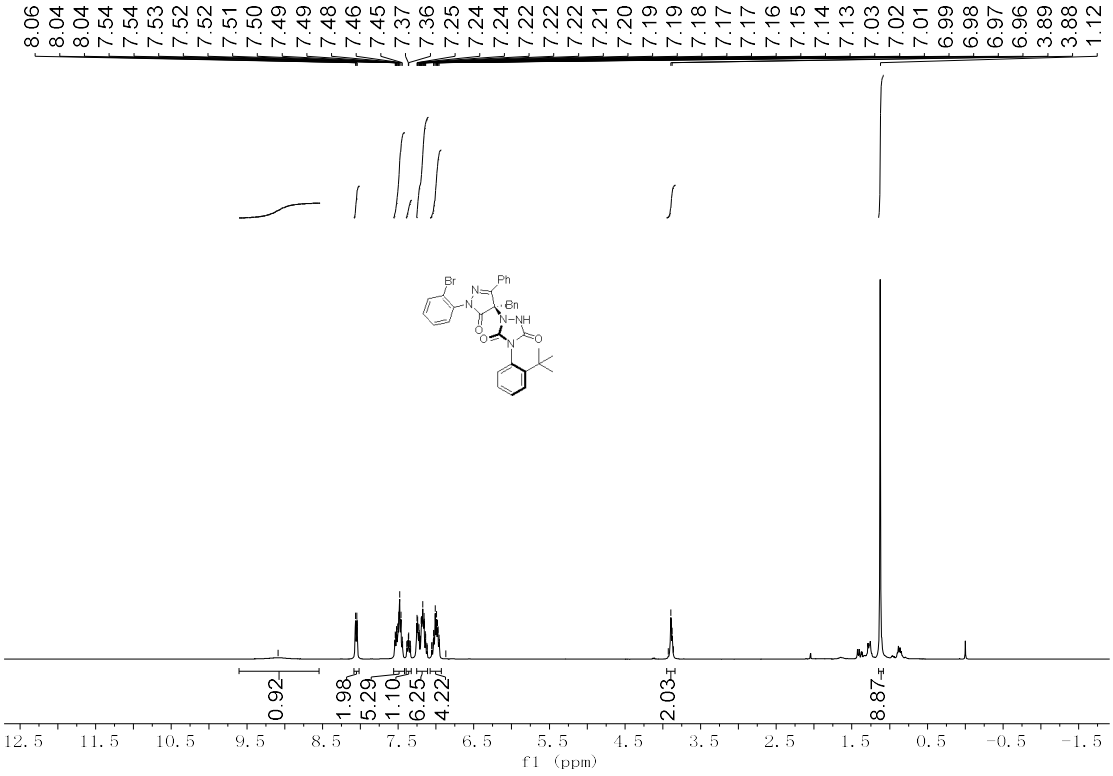
^{13}C NMR spectra of **3ba**



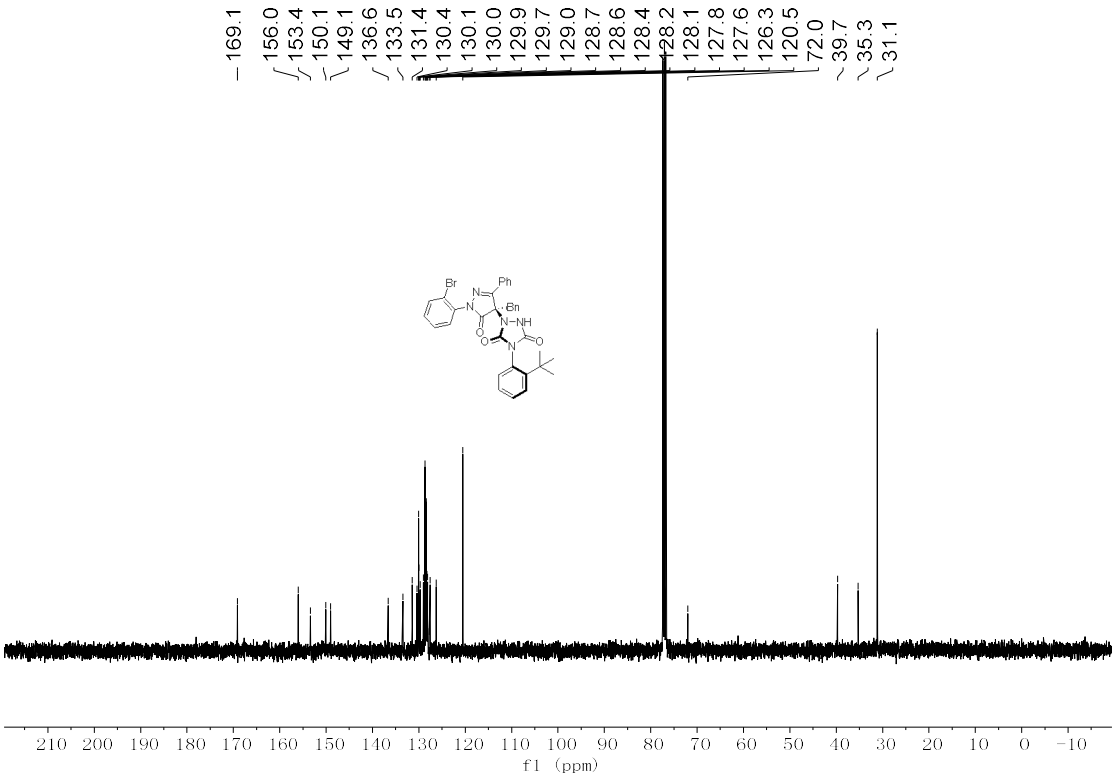
^{19}F NMR spectra of **3ba**


-117.78
F
Ph
N
N
Bn
N
NH
O
O
N
O
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

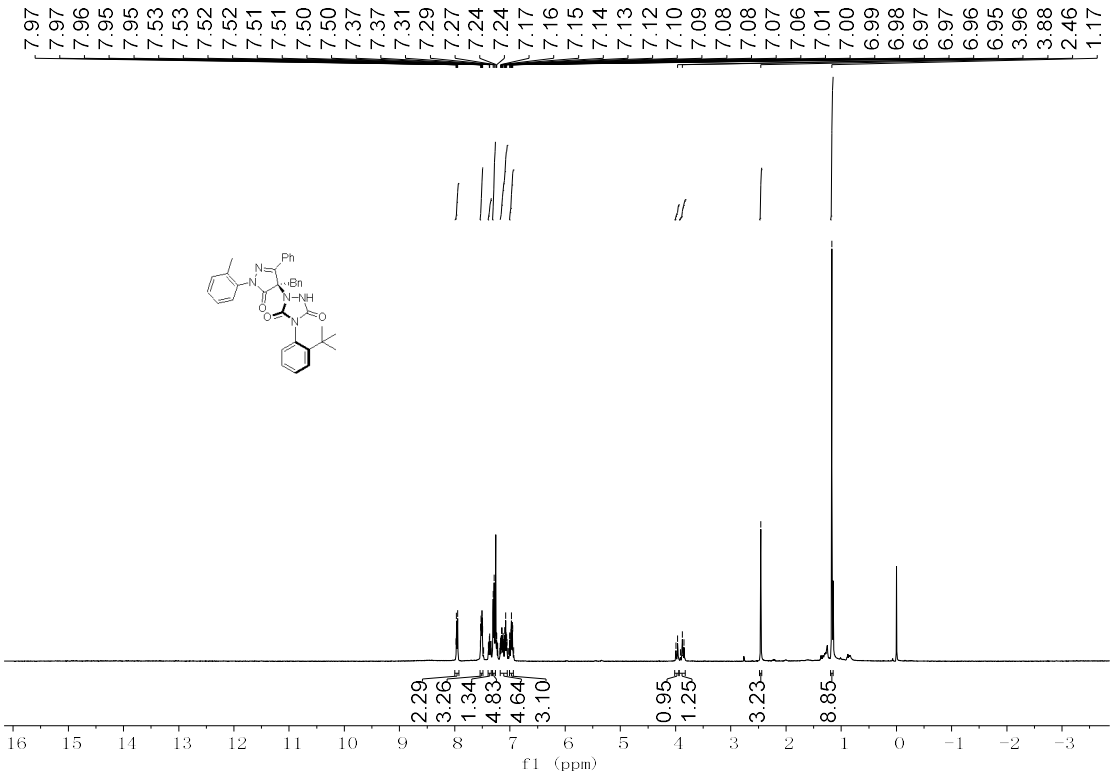
^{1}H NMR spectra of **3ca**



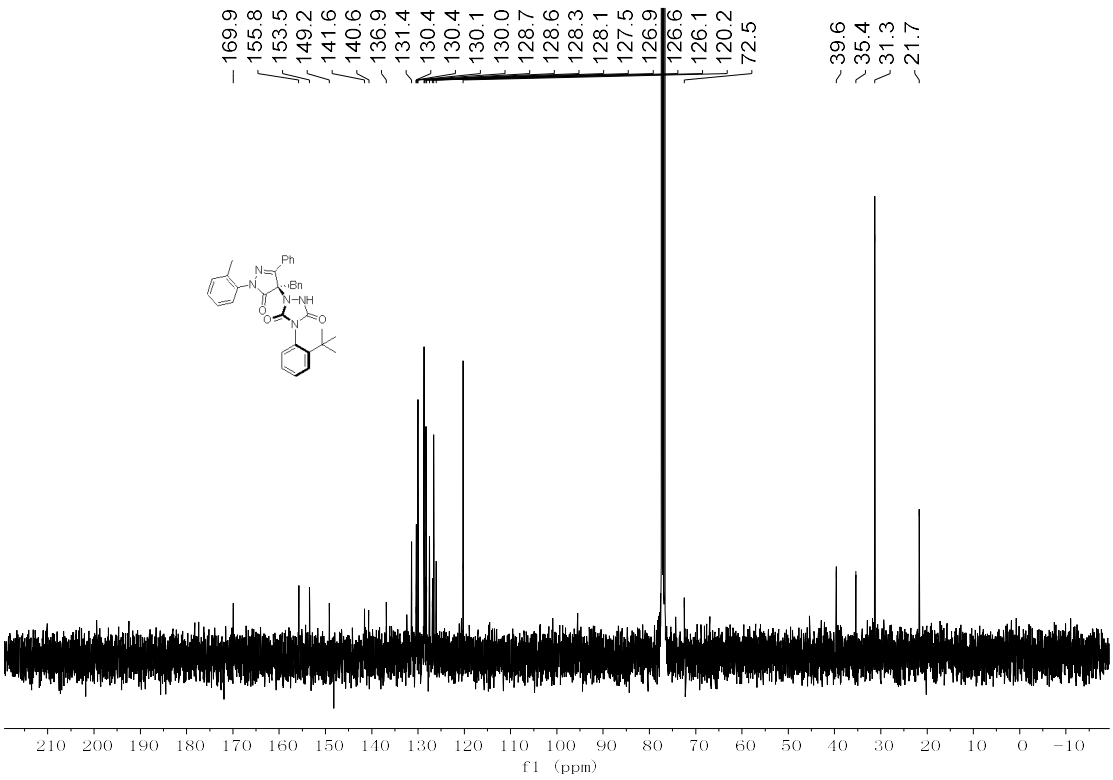
^{13}C NMR spectra of **3ca**



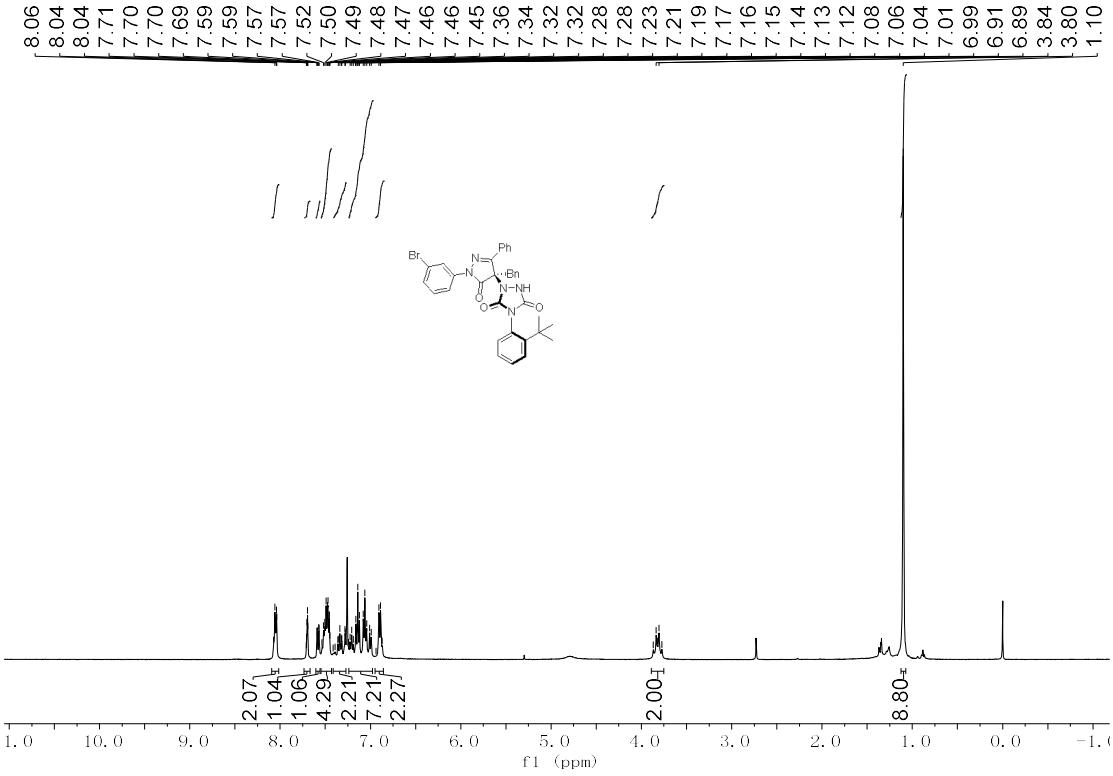
^{1}H NMR spectra of **3da**



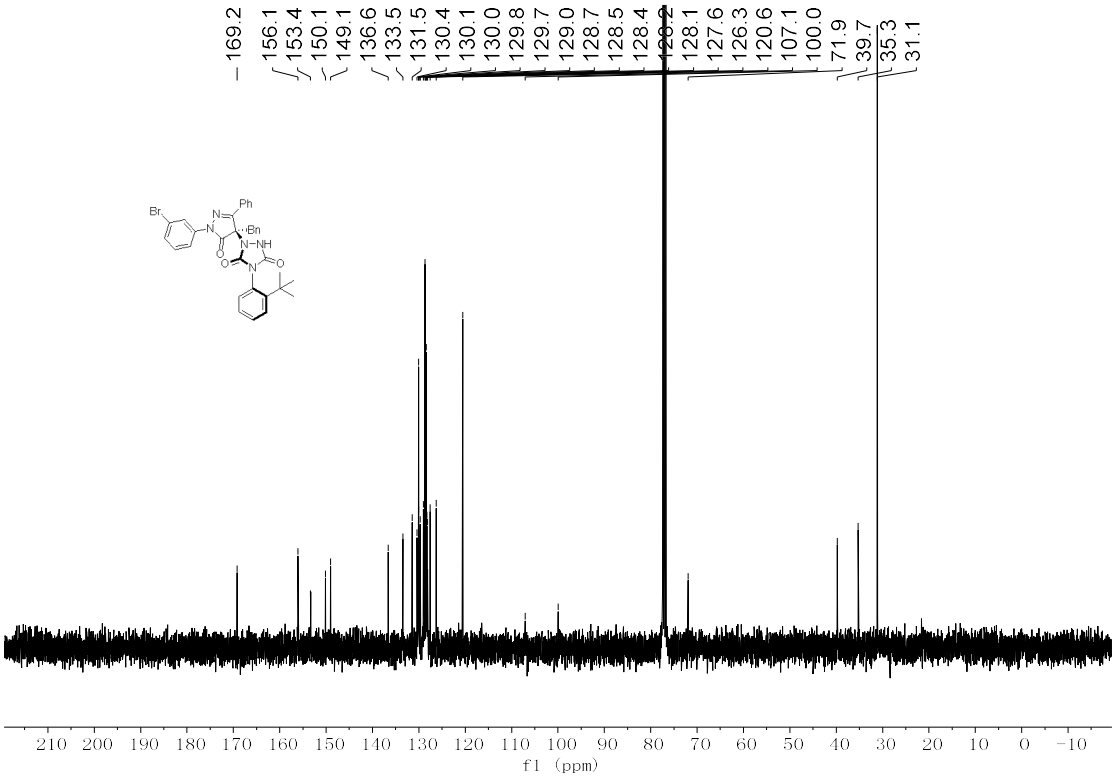
^{13}C NMR spectra of **3da**



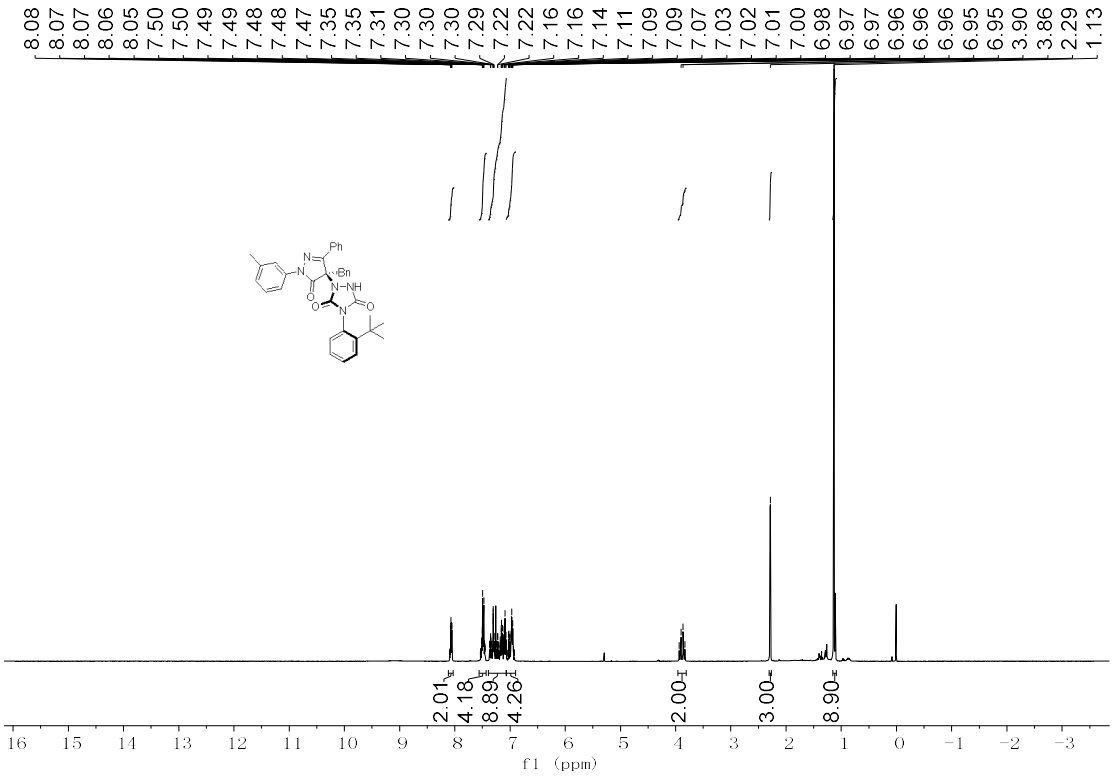
^{1}H NMR spectra of **3ea**



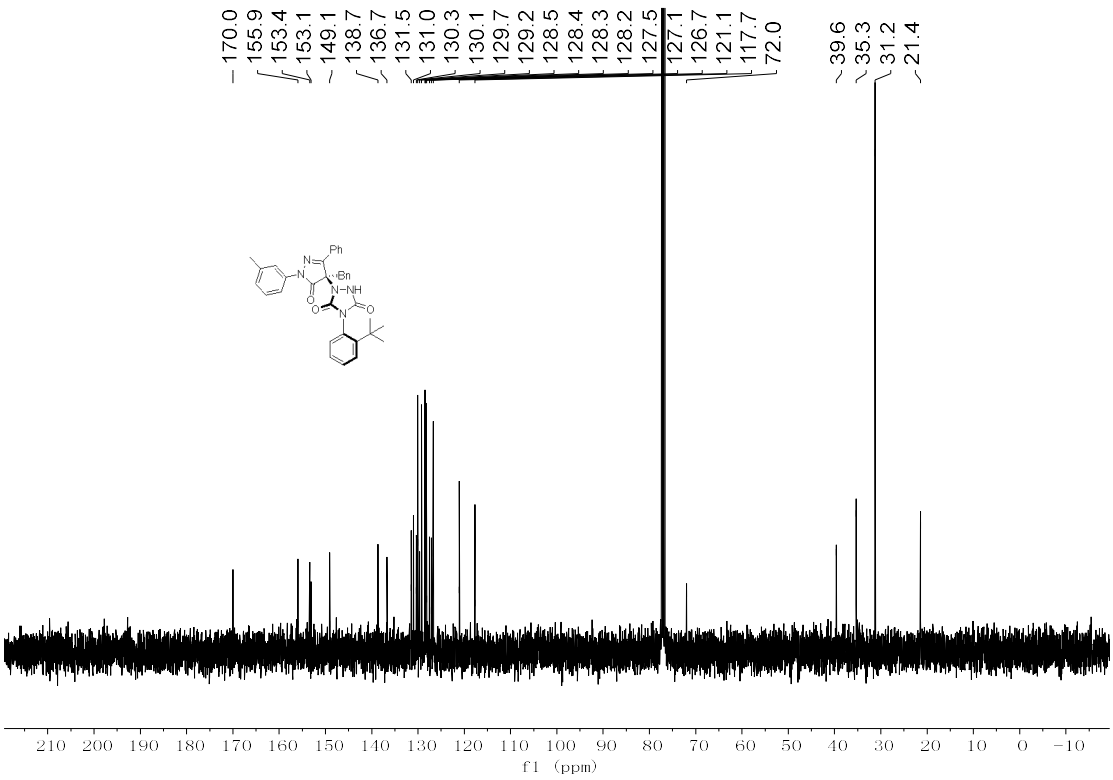
^{13}C NMR spectra of **3ea**



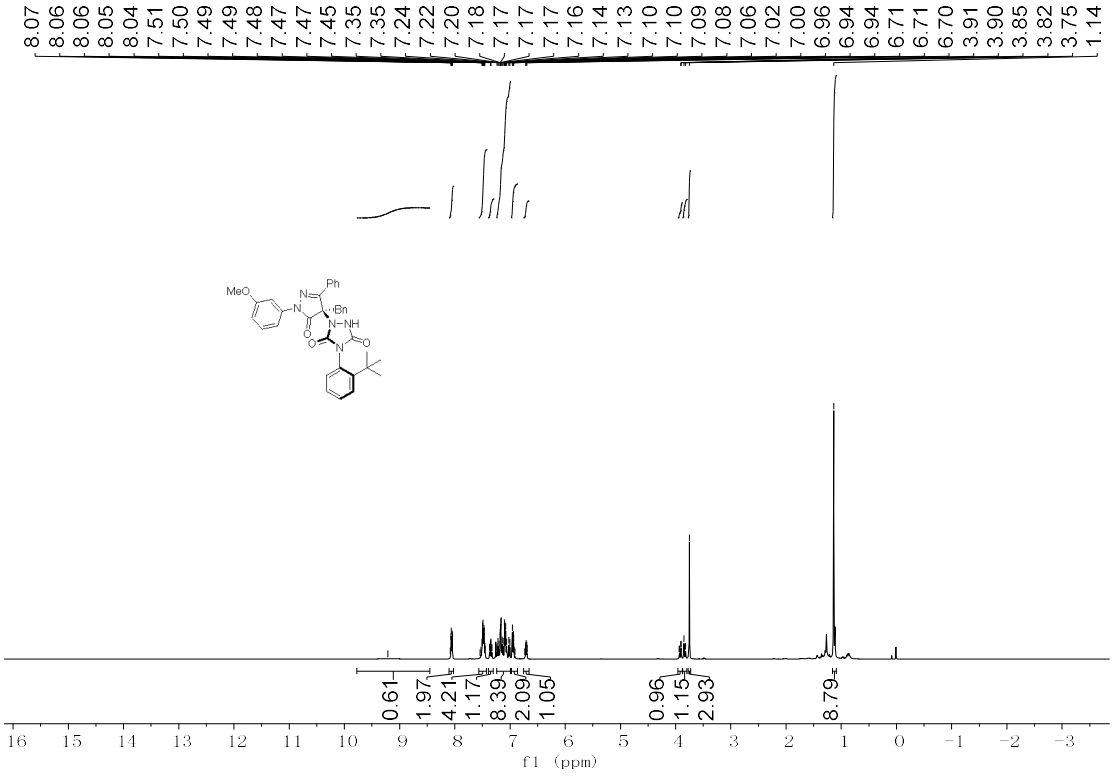
^{1}H NMR spectra of **3fa**



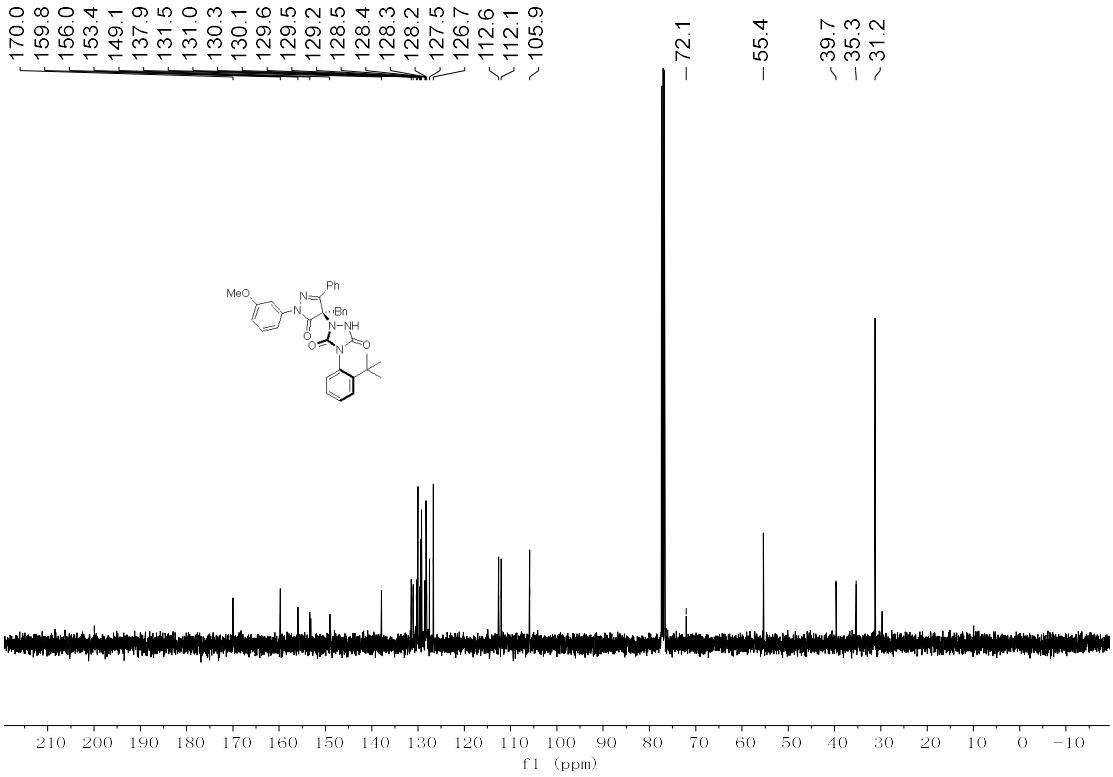
^{13}C NMR spectra of **3fa**



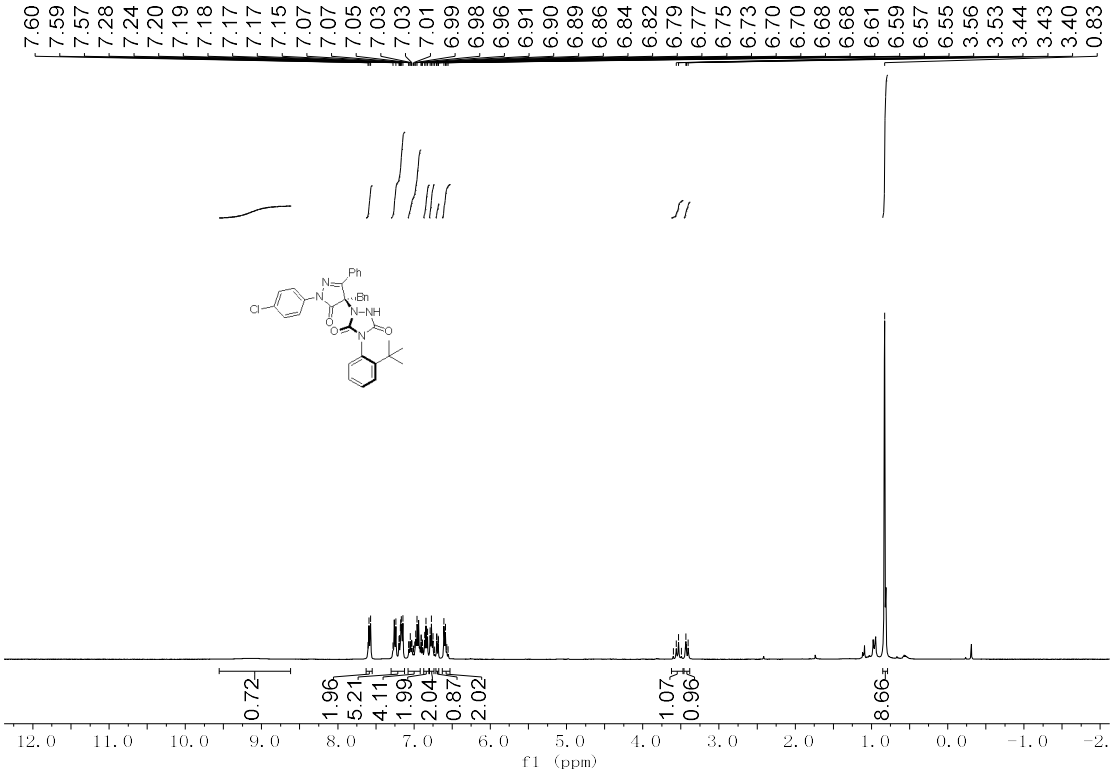
^{1}H NMR spectra of **3ga**



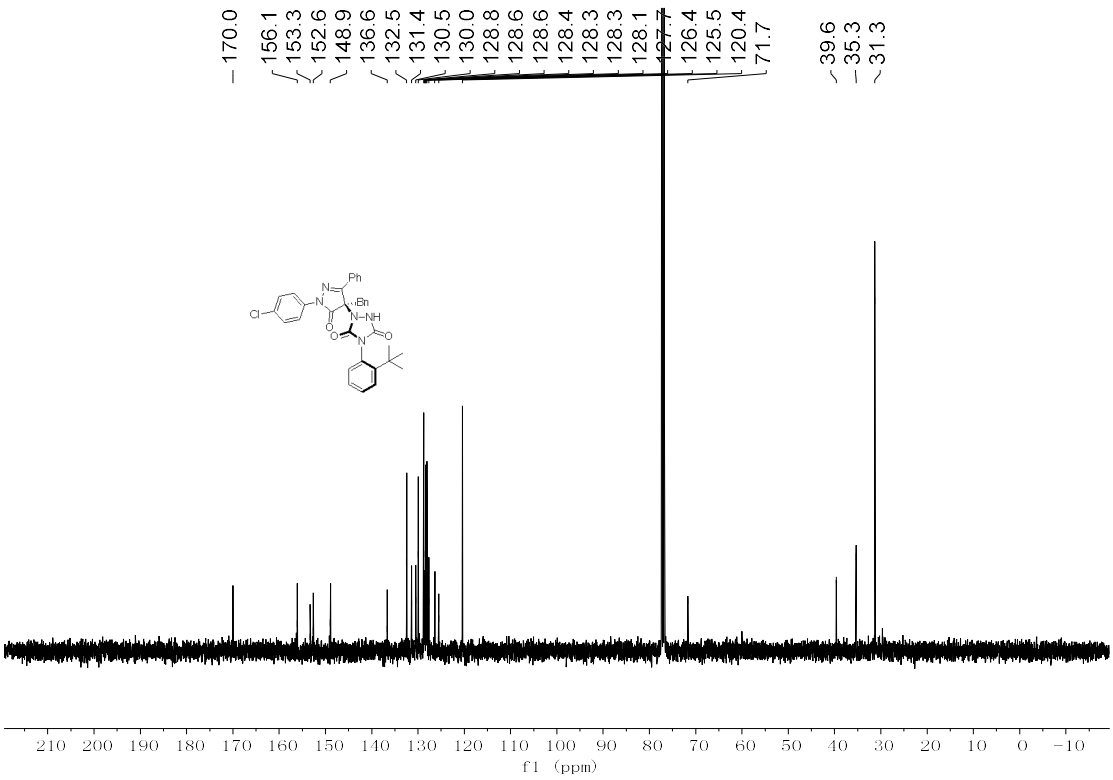
^{13}C NMR spectra of **3ga**



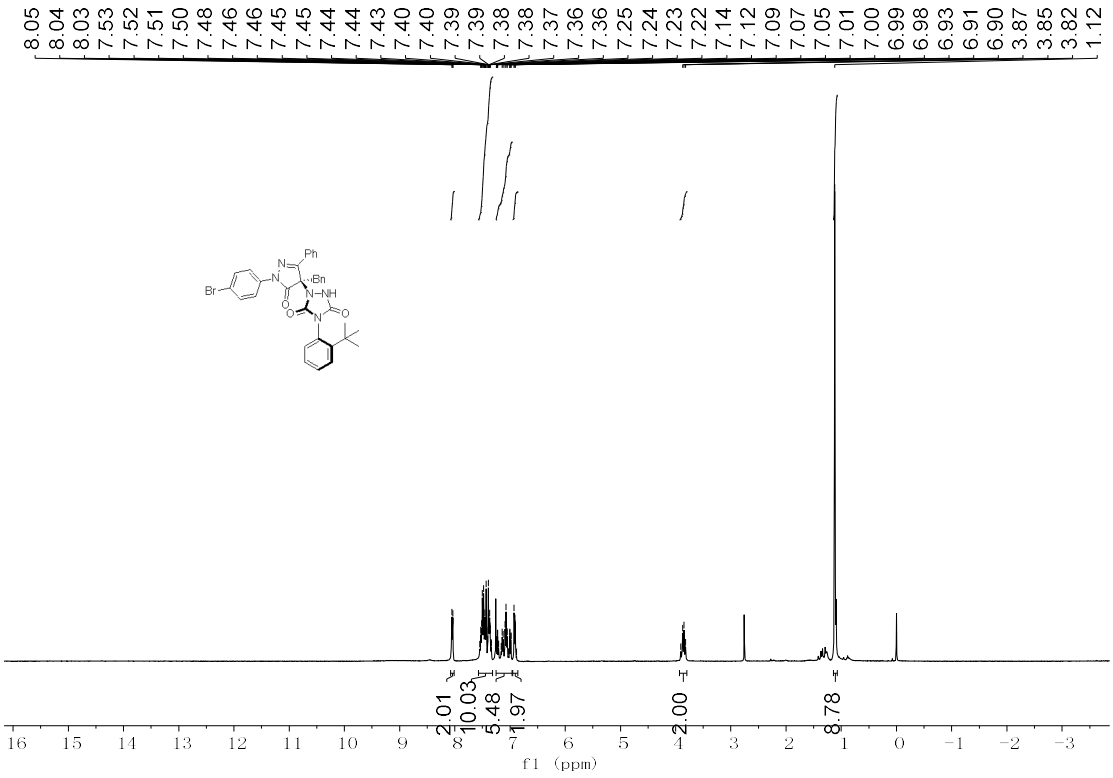
^{1}H NMR spectra of **3ha**



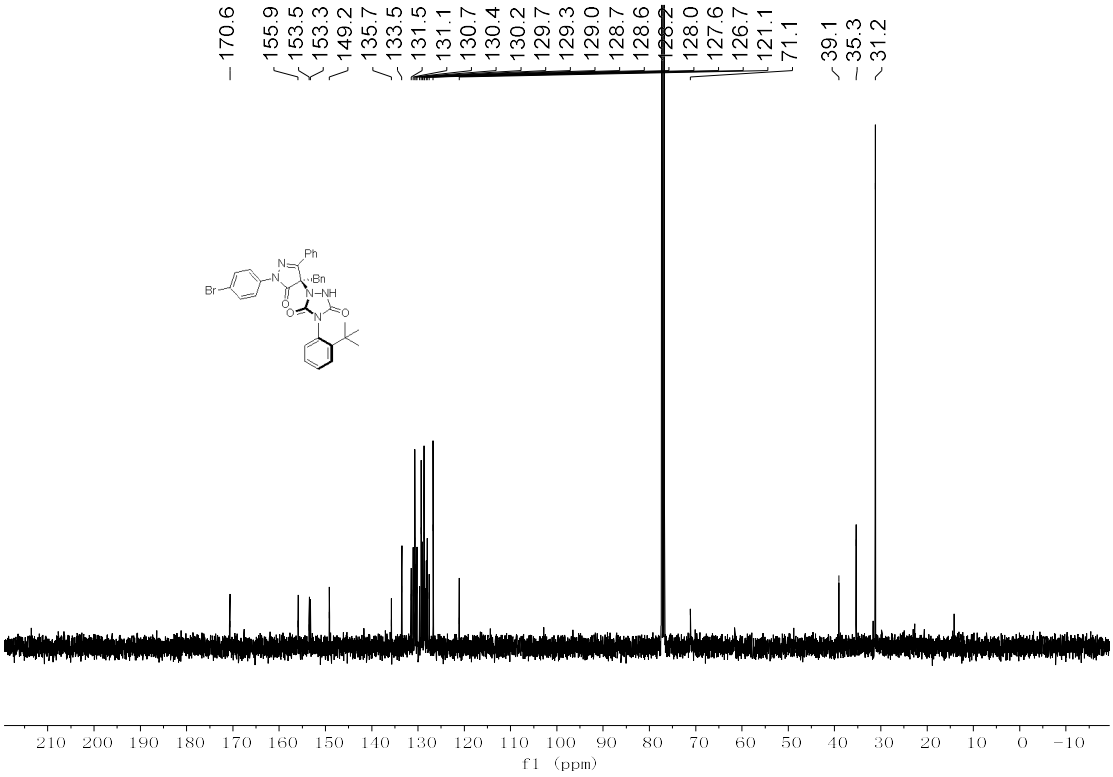
^{13}C NMR spectra of **3ha**



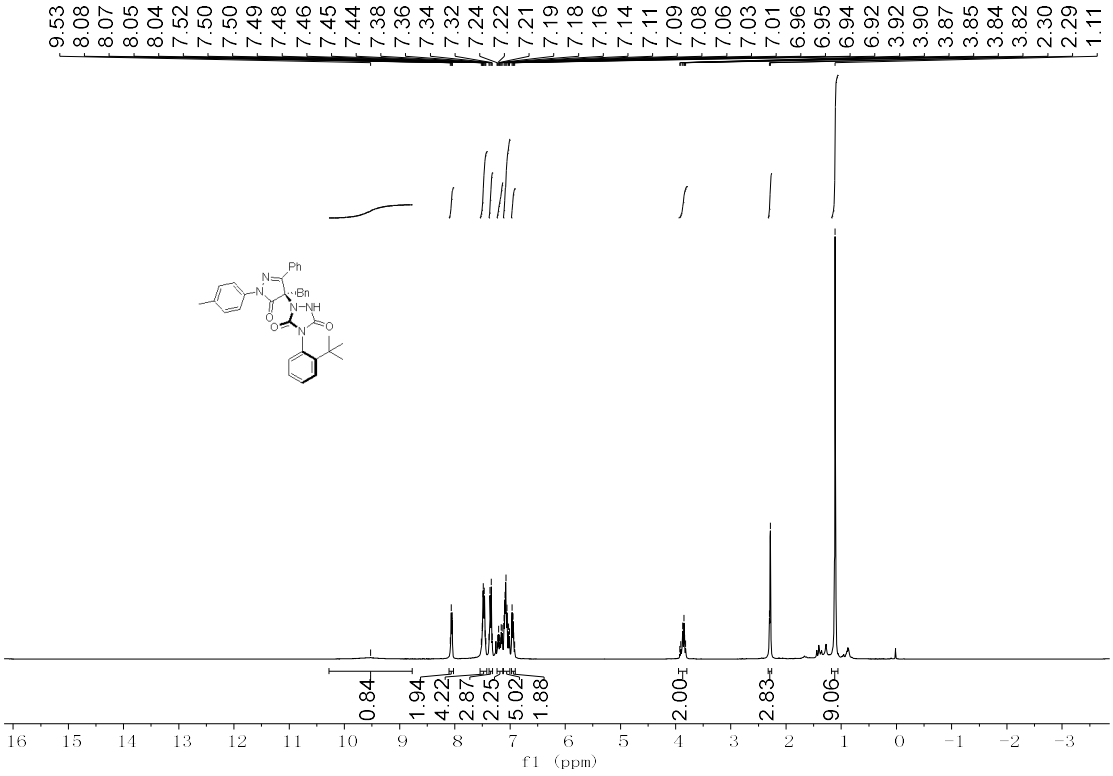
^{1}H NMR spectra of **3ia**



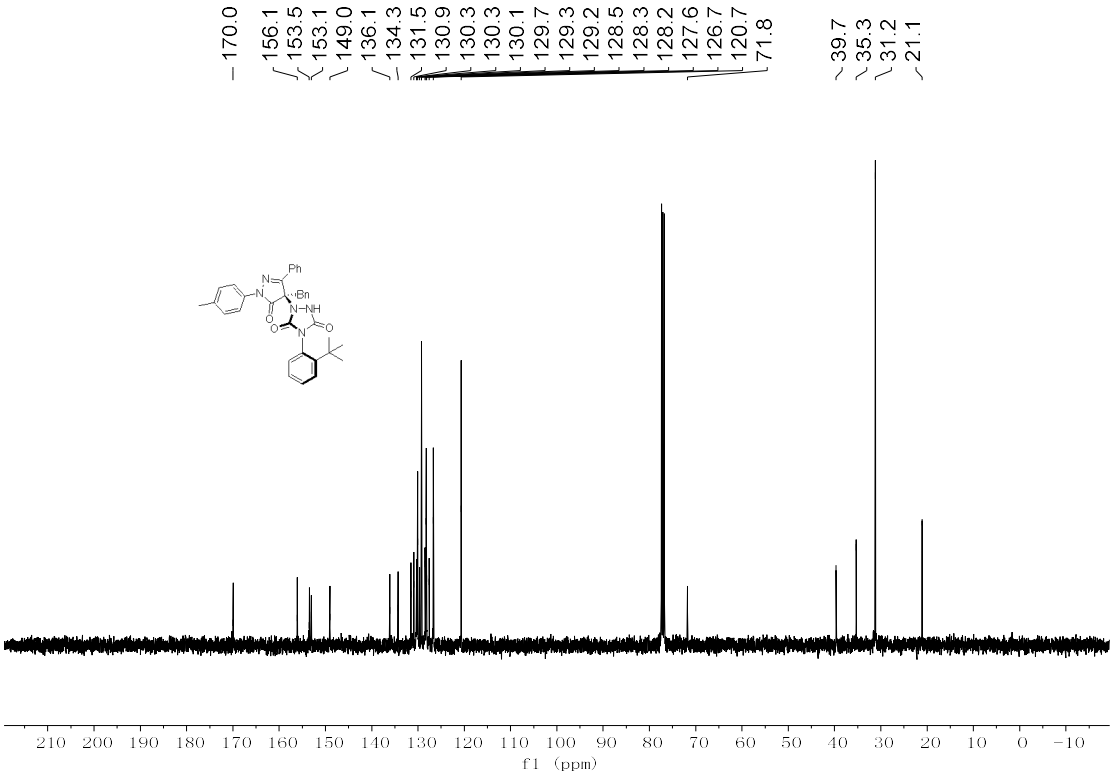
^{13}C NMR spectra of **3ia**



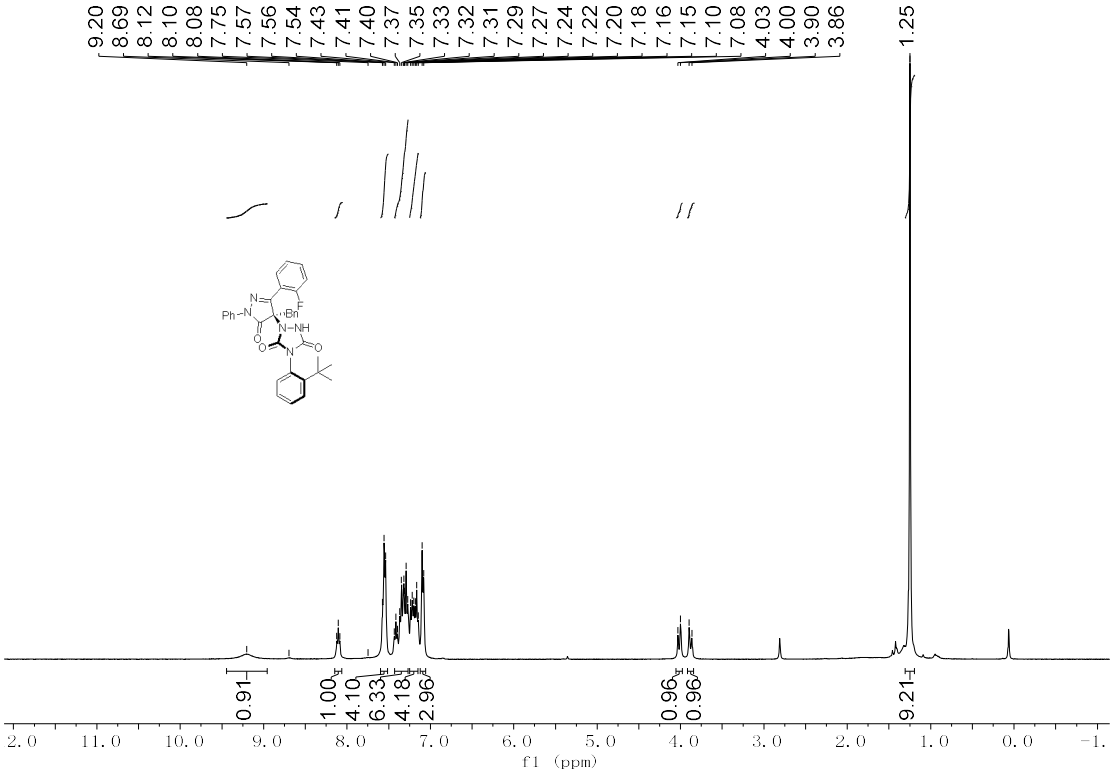
^{1}H NMR spectra of **3ja**



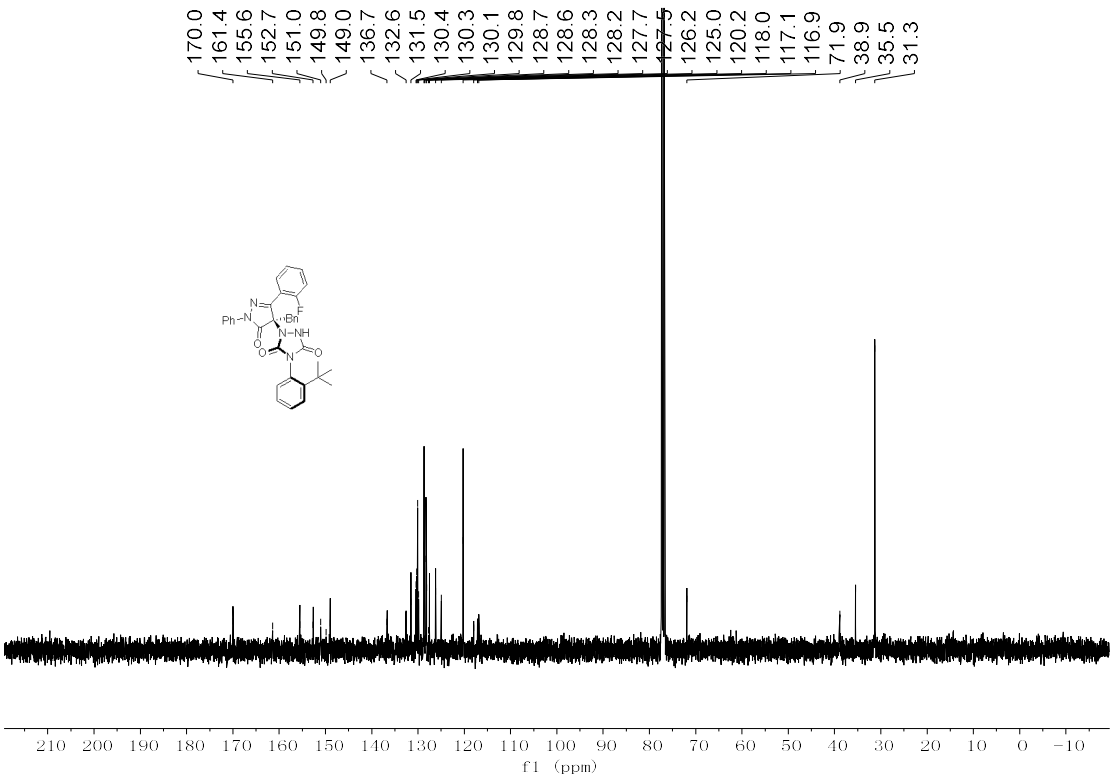
^{13}C NMR spectra of **3ja**



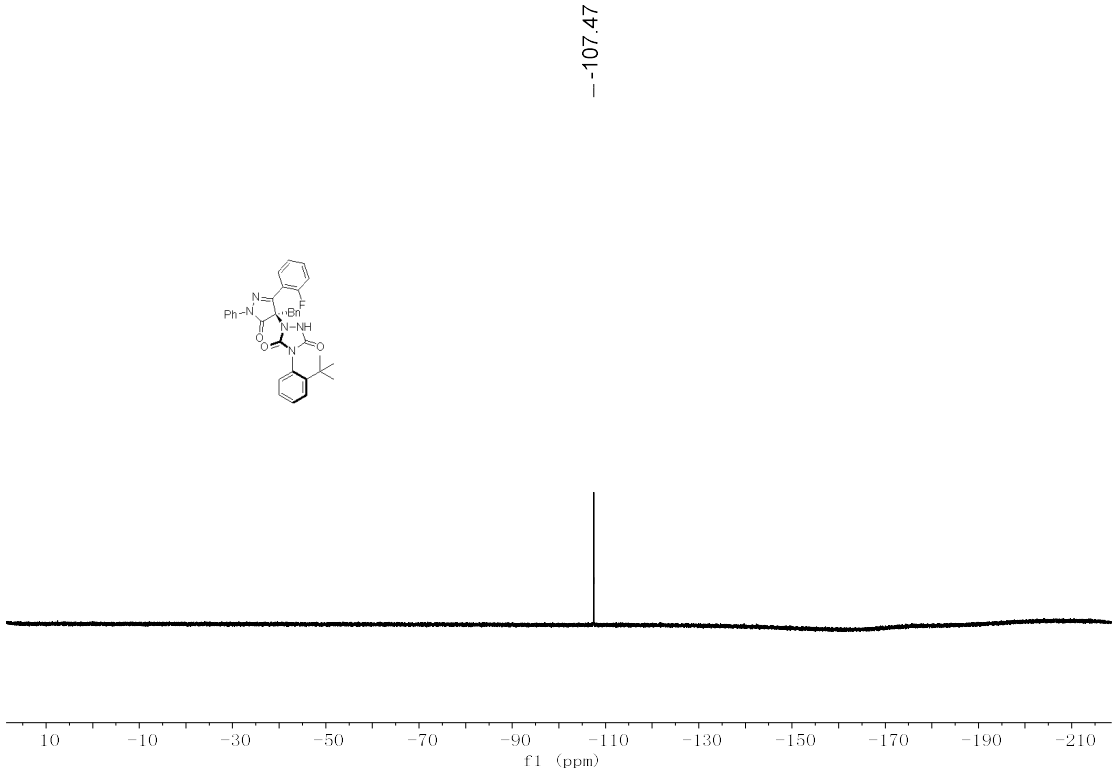
^{1}H NMR spectra of **3ka**



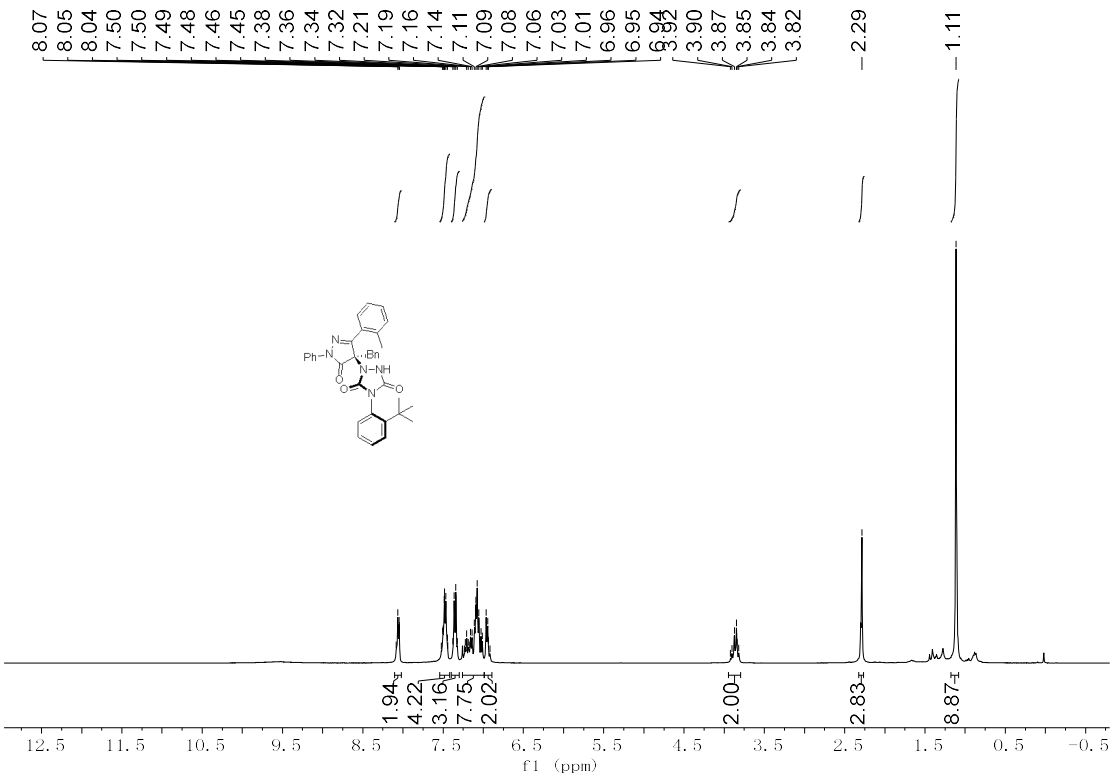
^{13}C NMR spectra of **3ka**



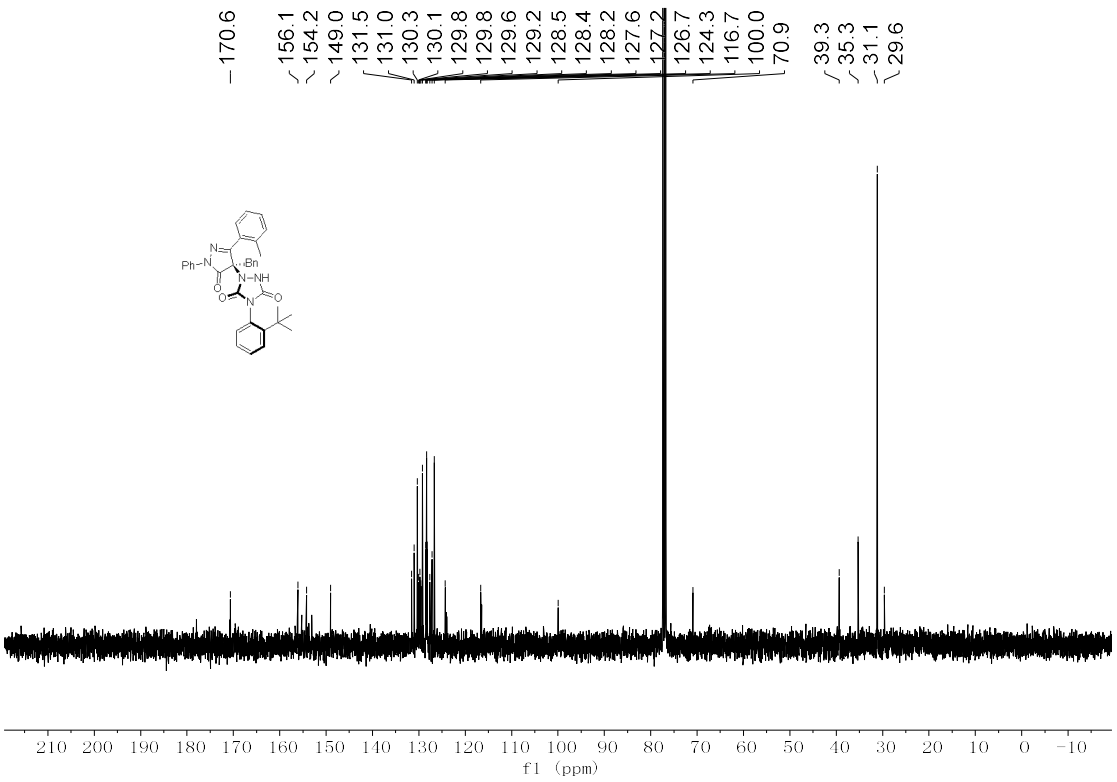
^{19}F NMR spectra of **3ka**


-107.47
Ph
N
N
F
Bn
N
NH
O
O
O
N
O
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

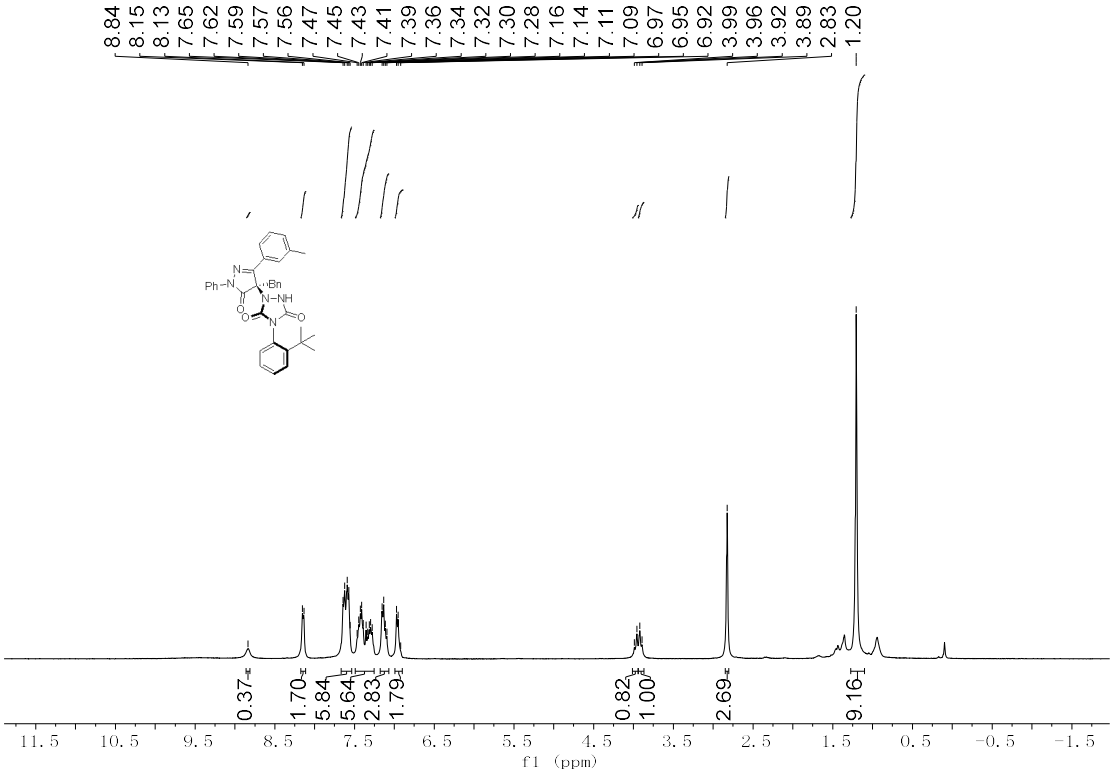
^{1}H NMR spectra of **3la**



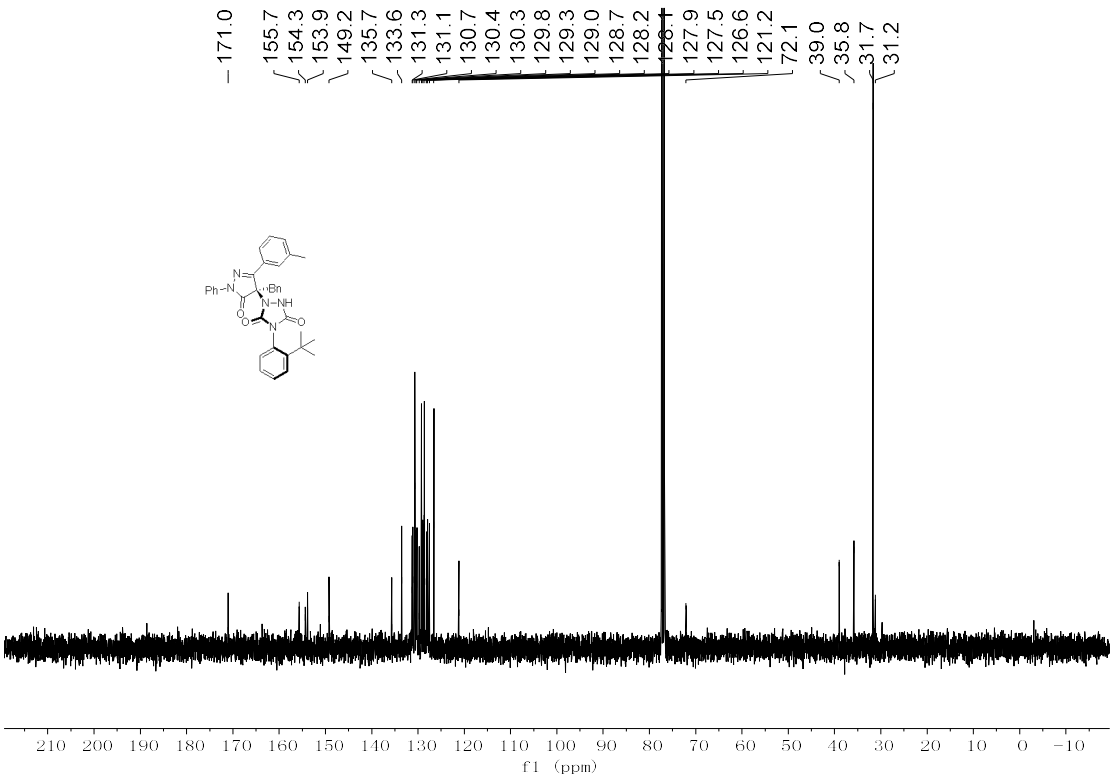
^{13}C NMR spectra of **3la**



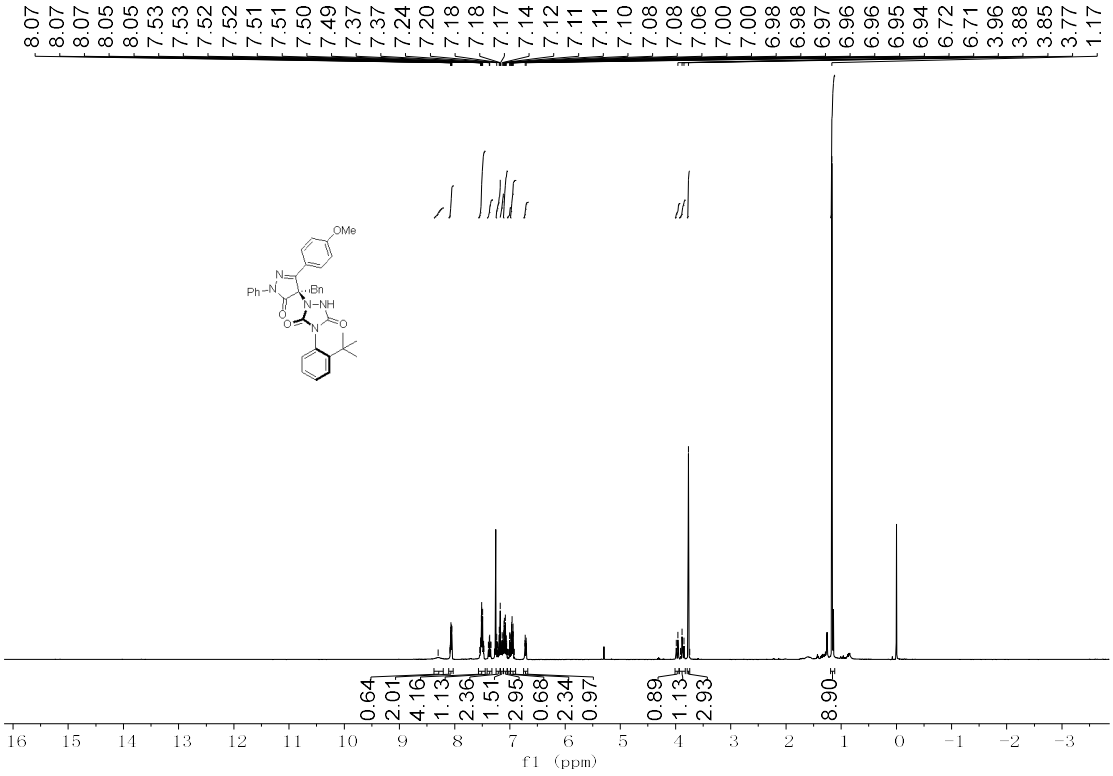
^{1}H NMR spectra of **3ma**



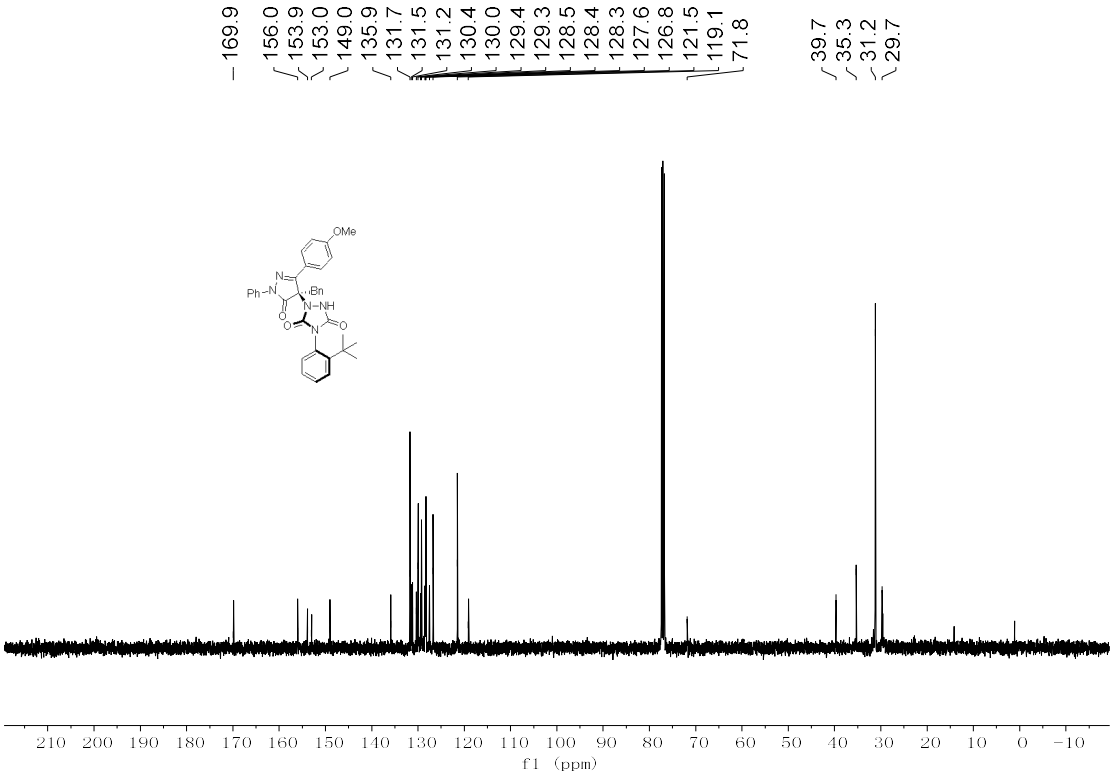
^{13}C NMR spectra of **3ma**



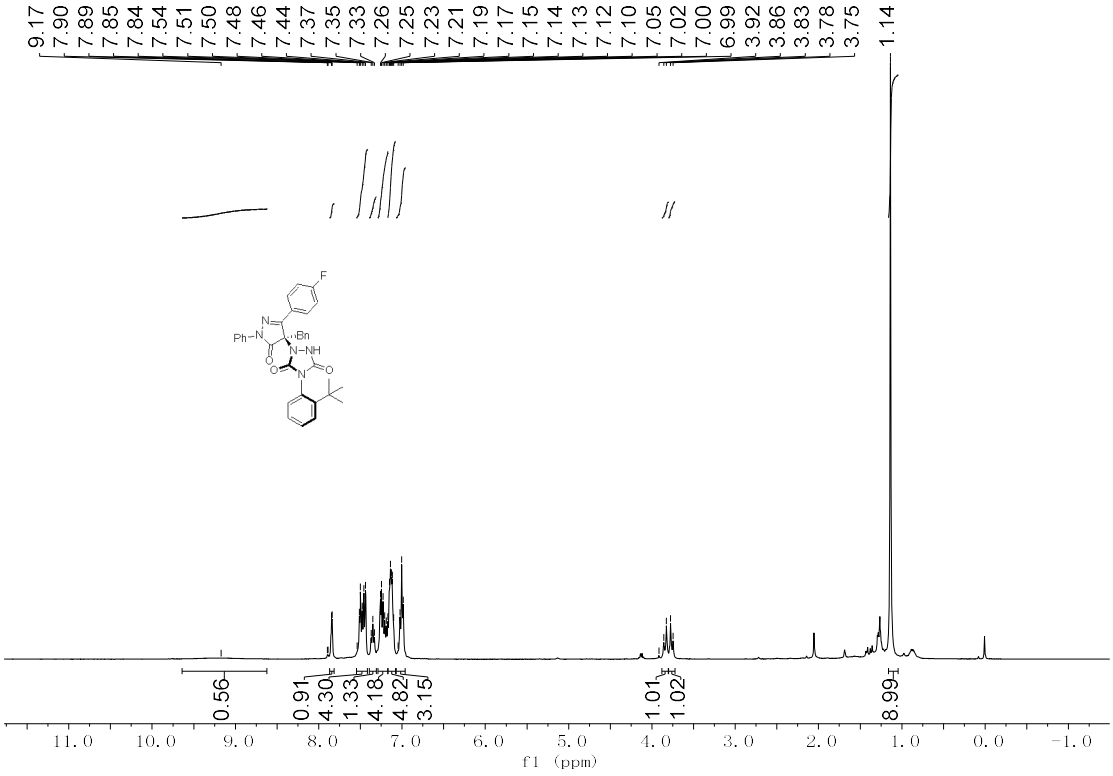
^{1}H NMR spectra of **3na**



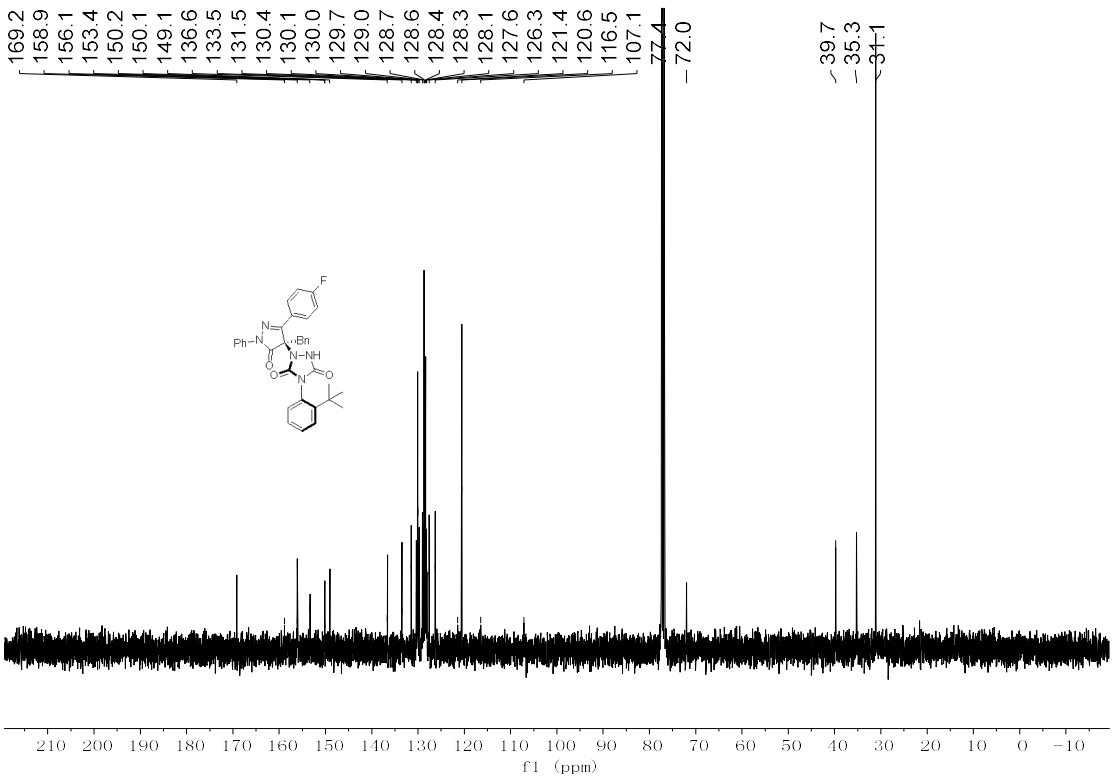
^{13}C NMR spectra of **3na**



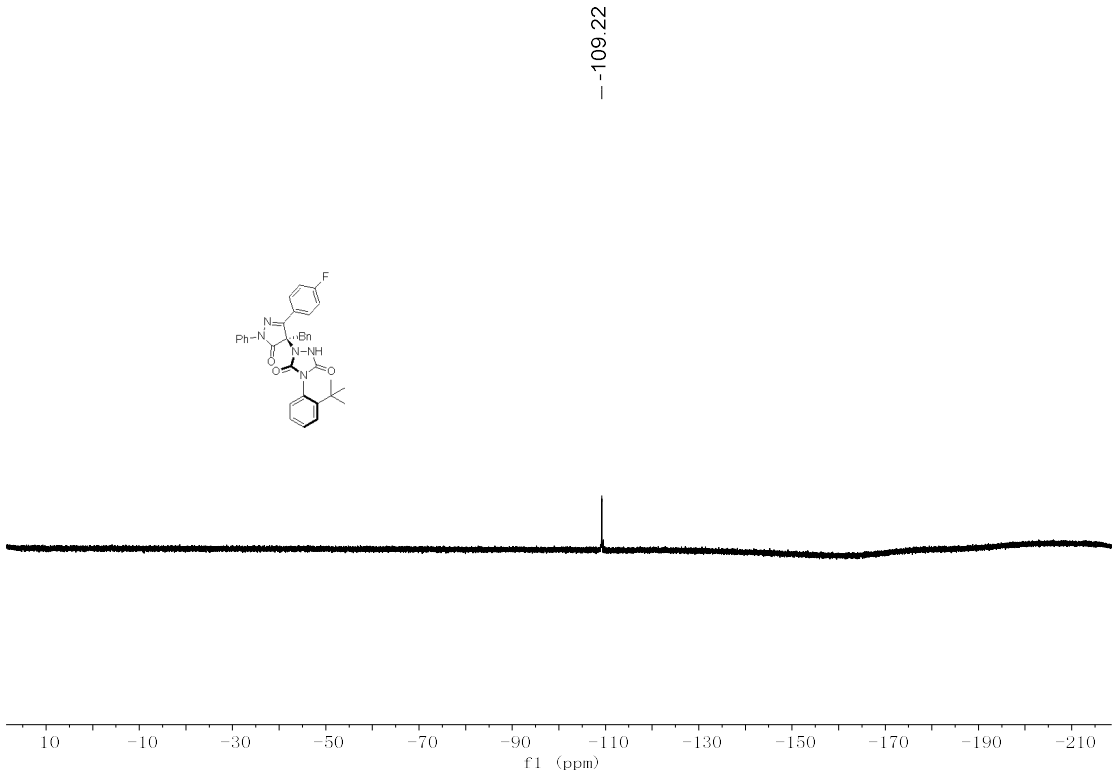
^{1}H NMR spectra of **3oa**



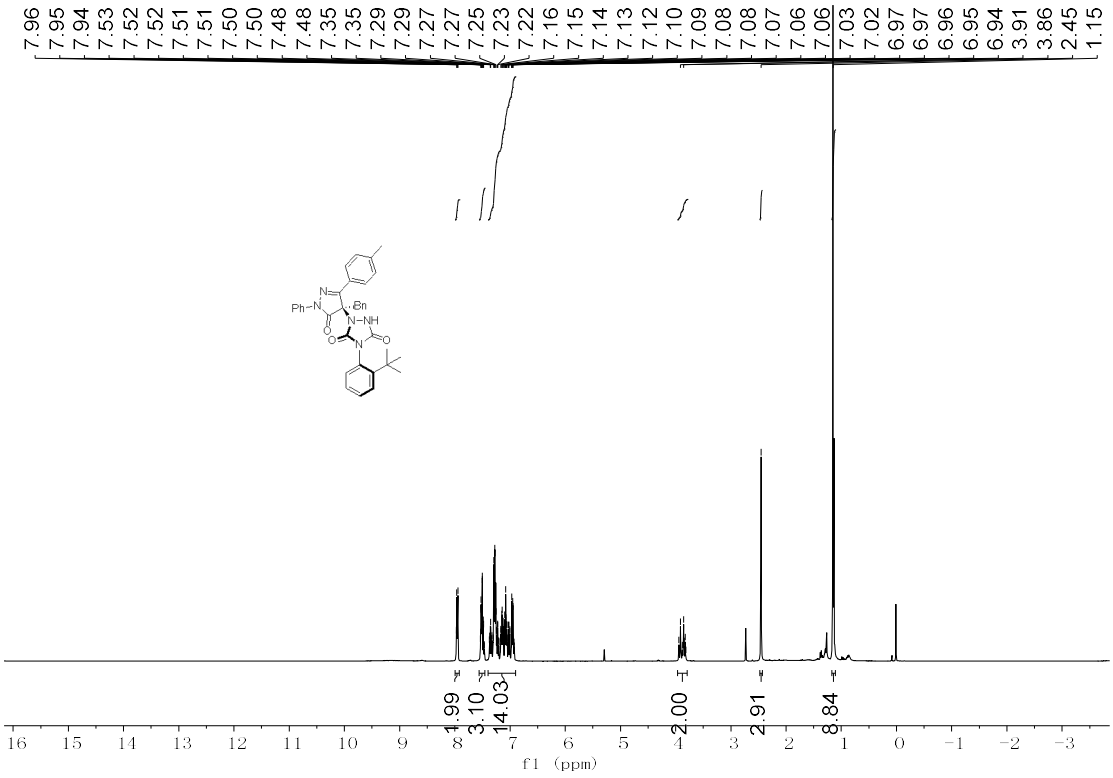
^{13}C NMR spectra of **3oa**



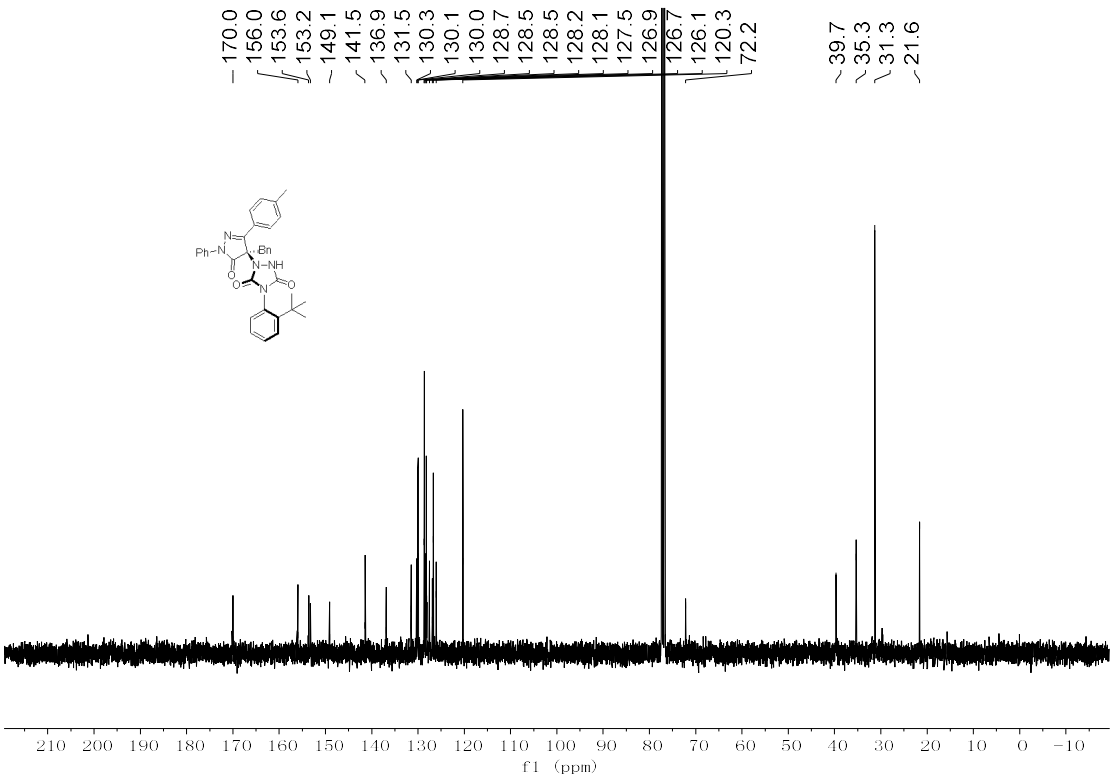
^{19}F NMR spectra of **3oa**


-109.22
F
Ph
N
Bn
N-NH
O
O
O
N
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

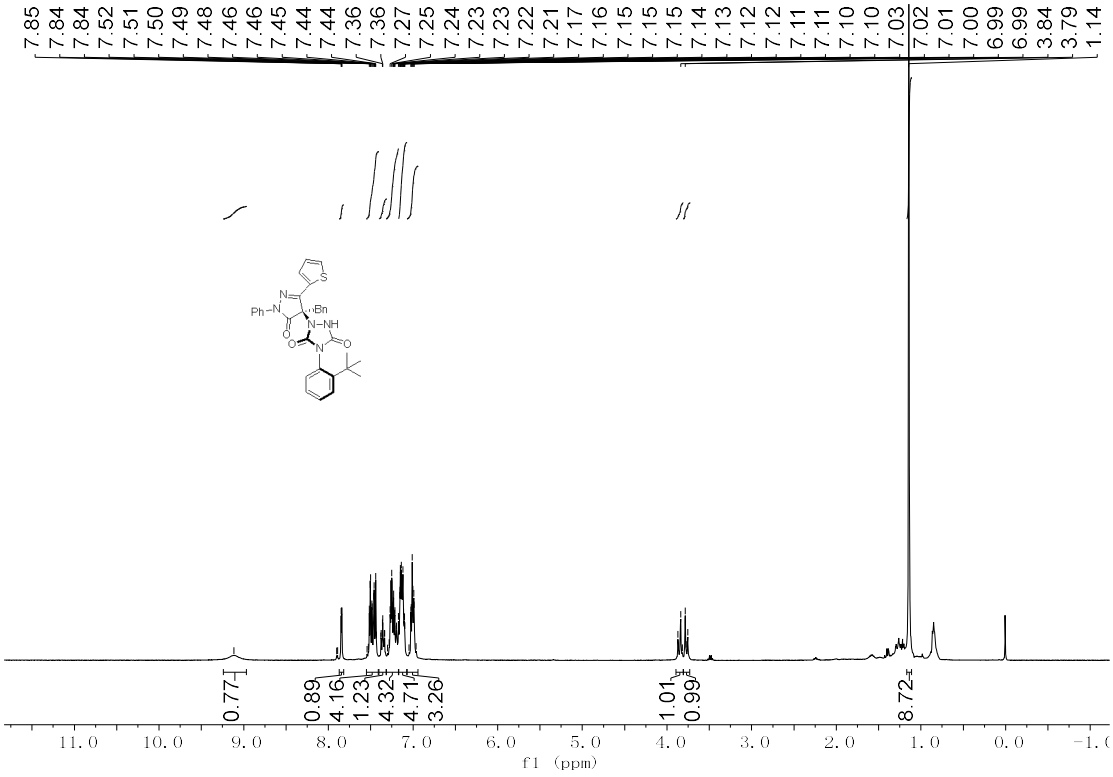
^{1}H NMR spectra of **3pa**



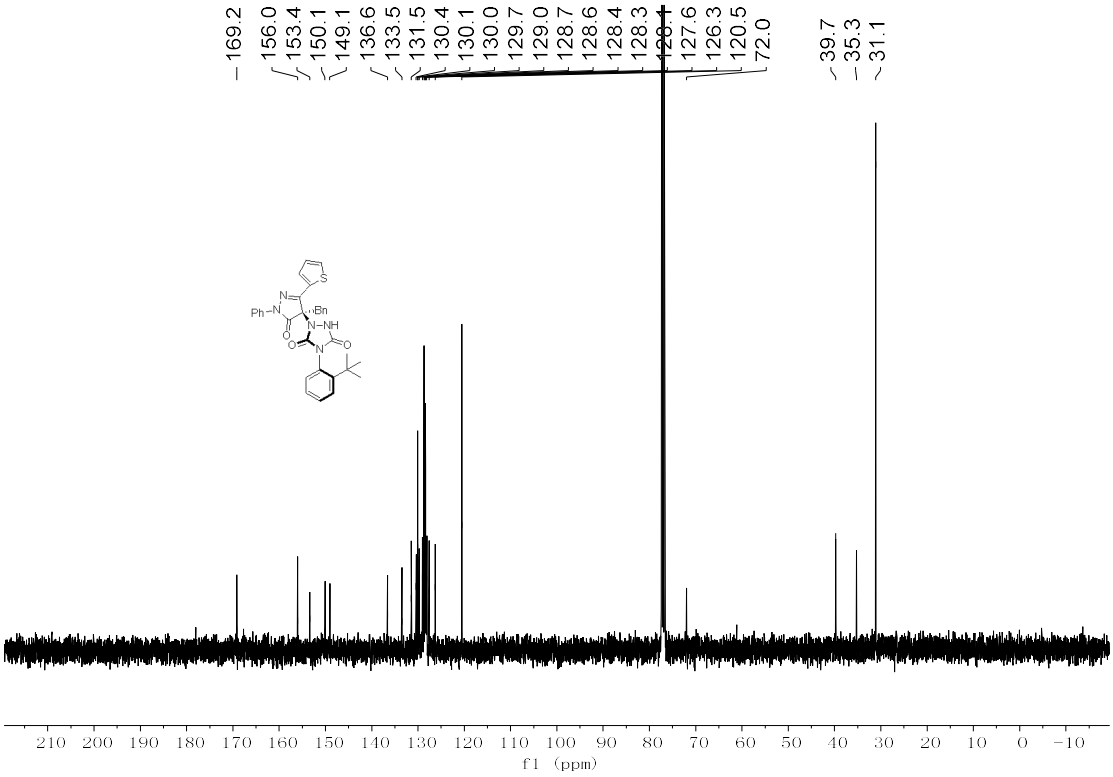
^{13}C NMR spectra of **3pa**



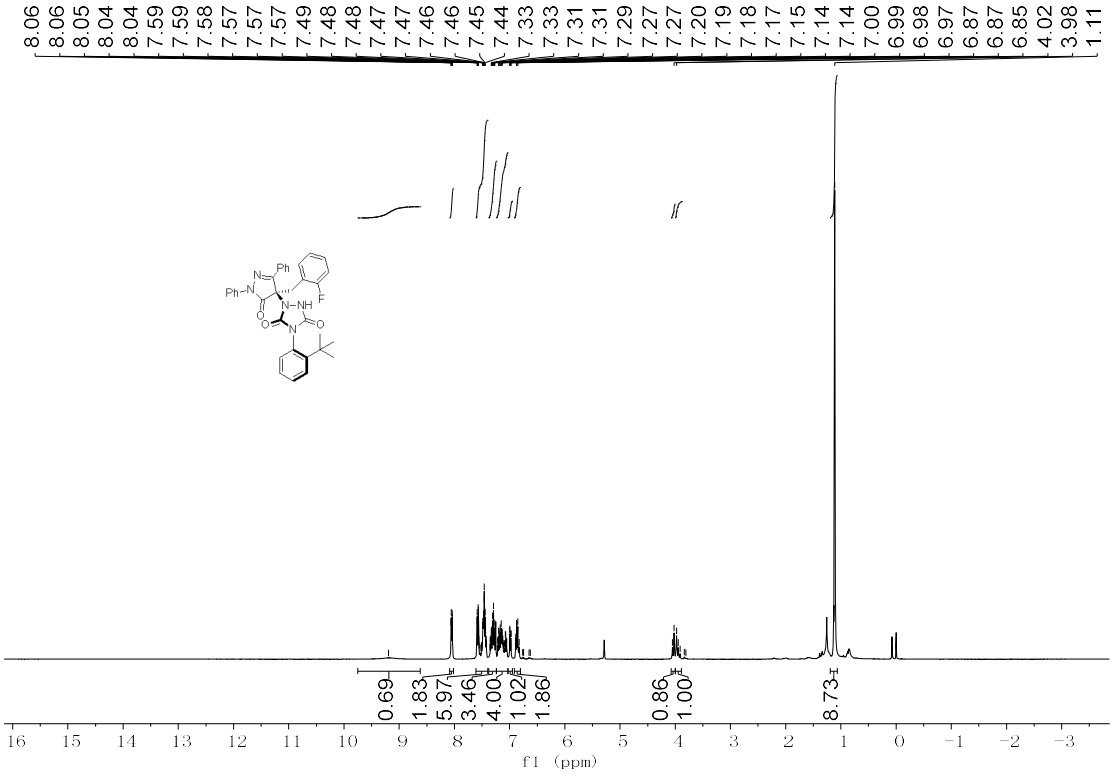
^{1}H NMR spectra of **3qa**



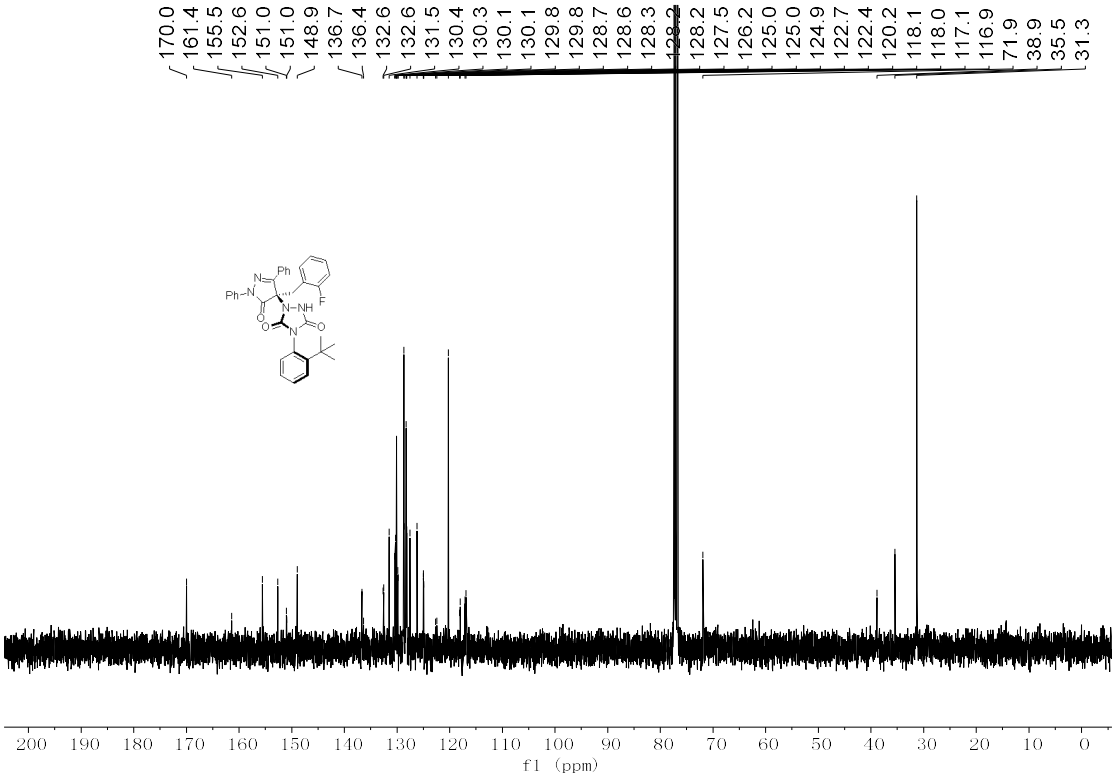
^{13}C NMR spectra of **3qa**



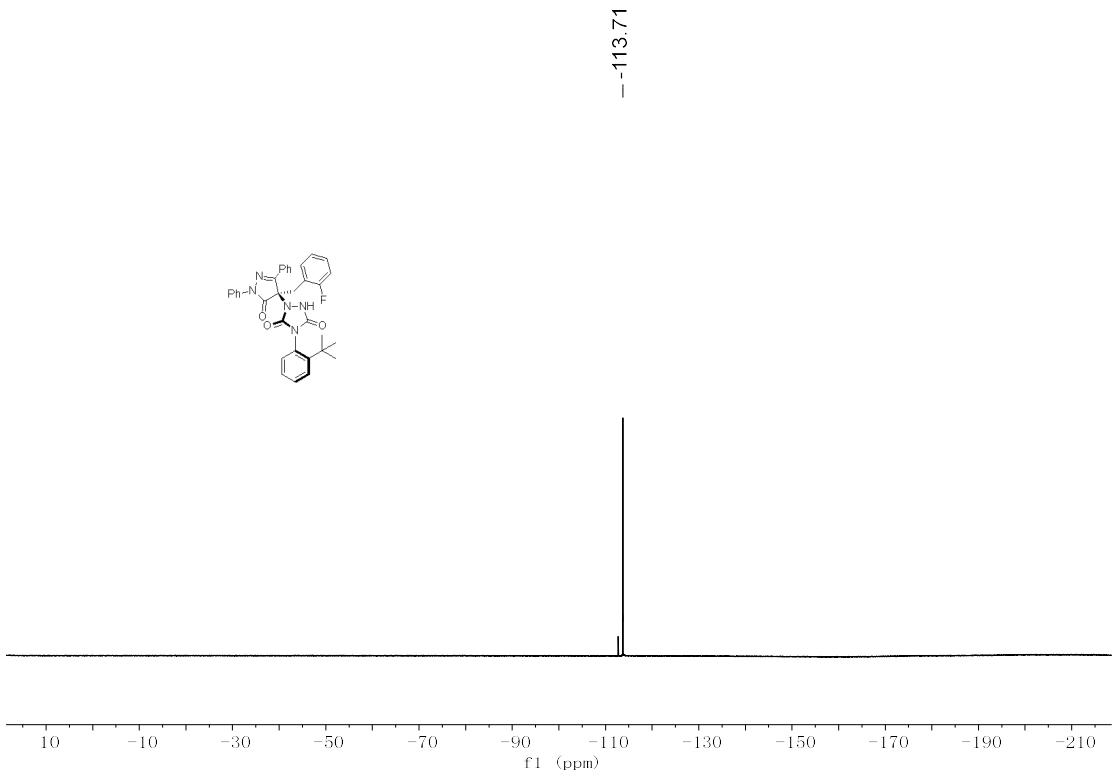
^{1}H NMR spectra of **3ra**



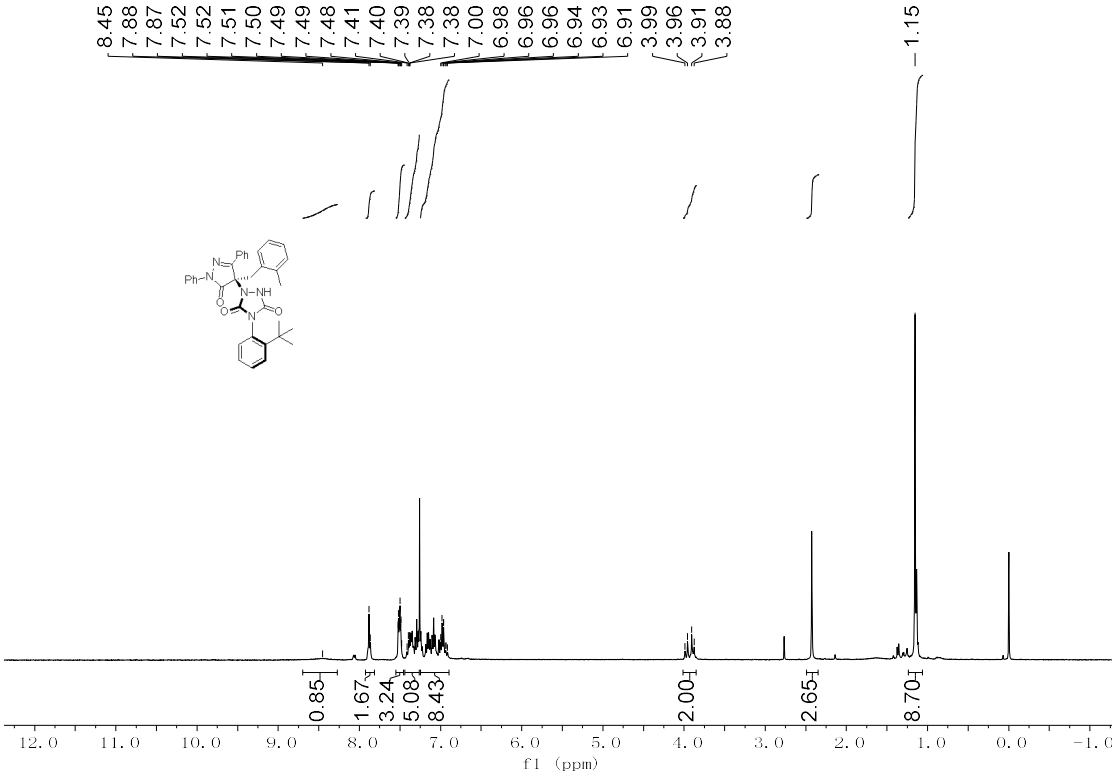
^{13}C NMR spectra of **3ra**



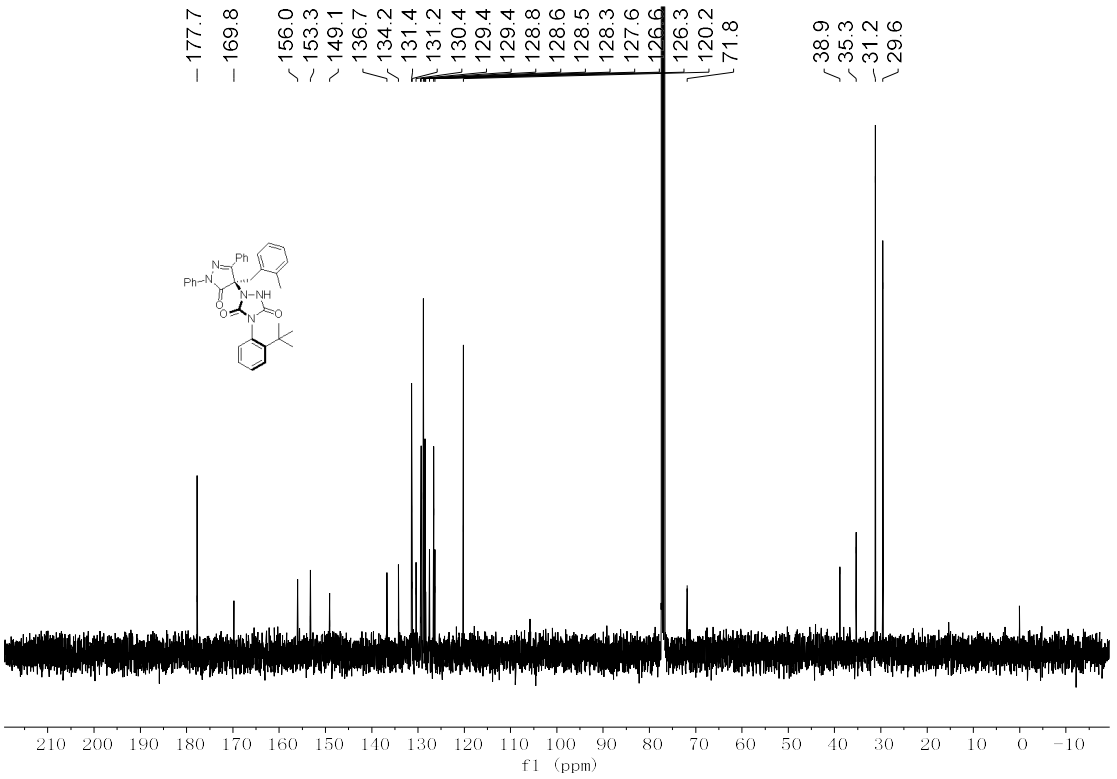
^{19}F NMR spectra of **3ra**


-113.71
Ph
N
Ph-N
O
N-NH
F
O
N
O
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

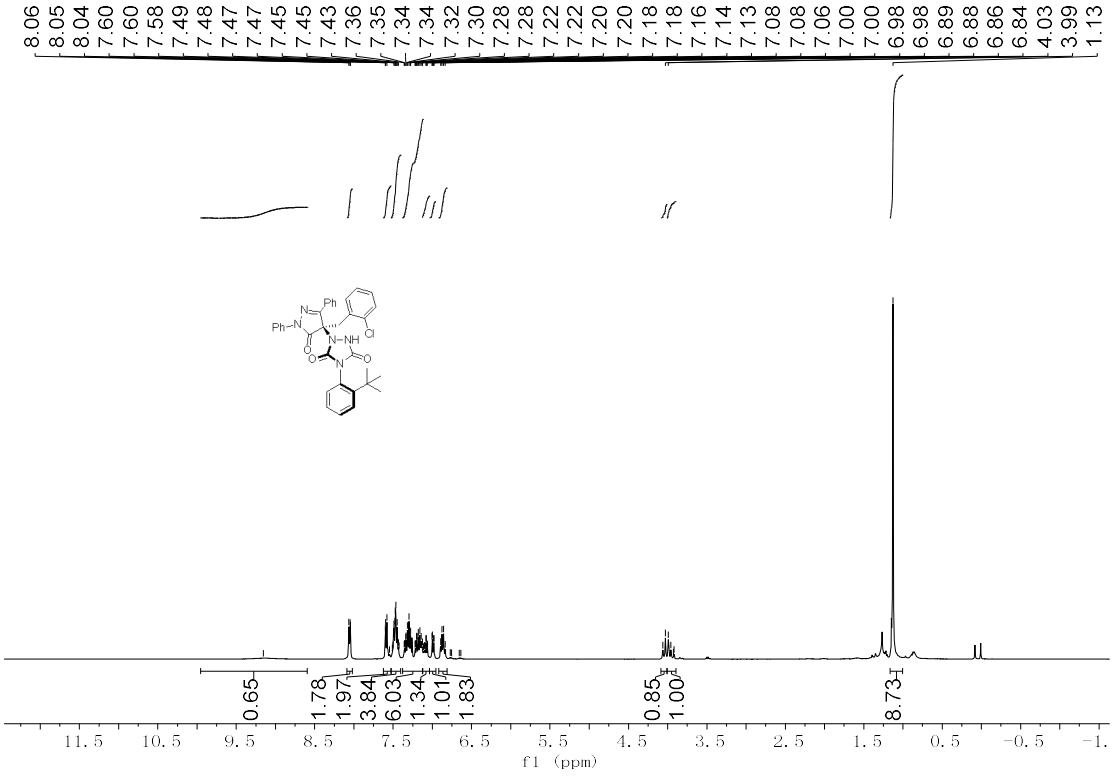
^{1}H NMR spectra of **3sa**



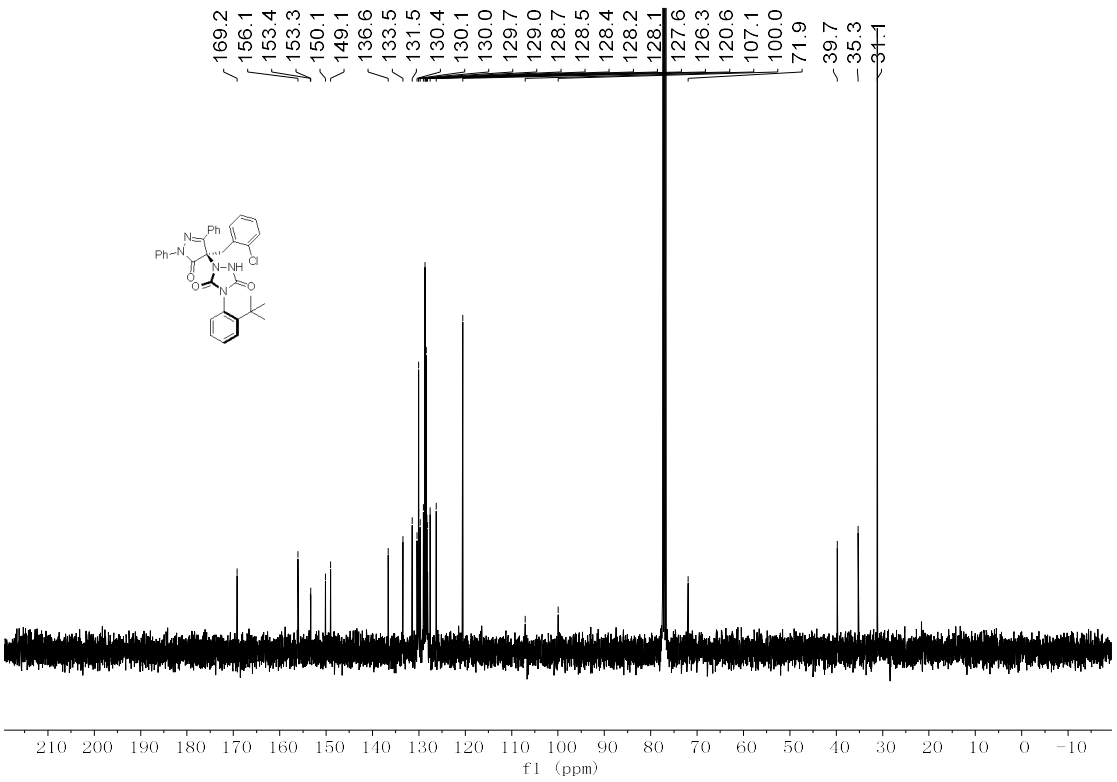
^{13}C NMR spectra of **3sa**



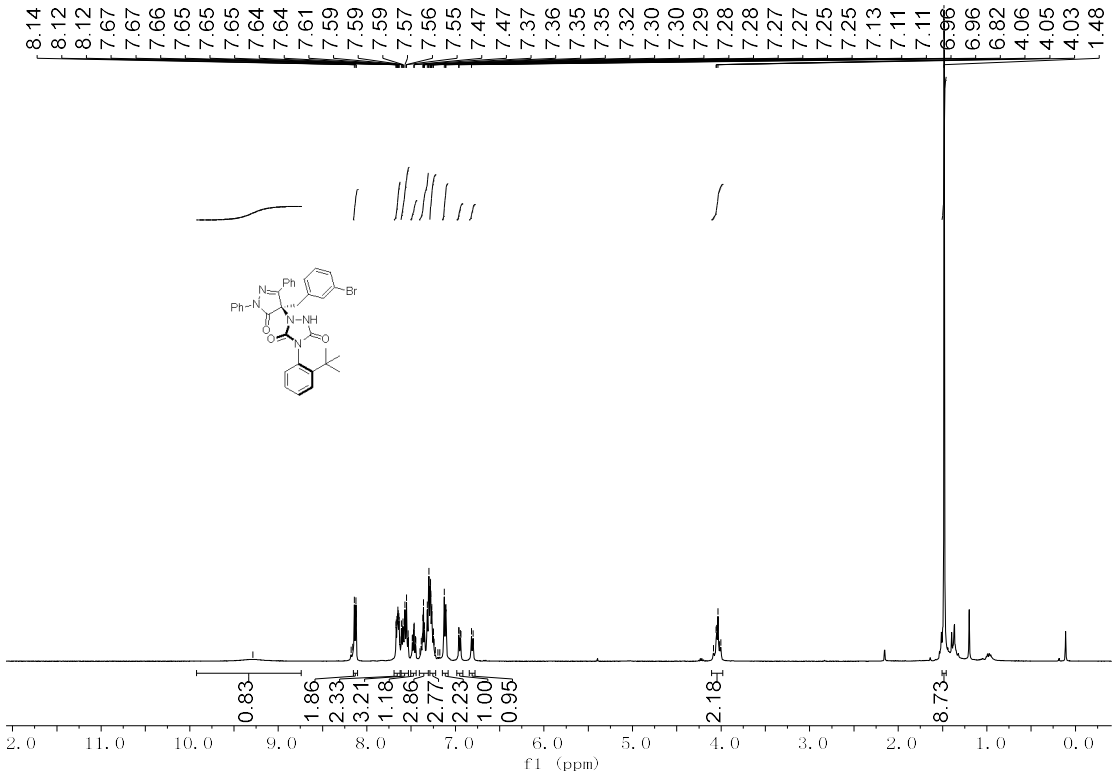
^{1}H NMR spectra of **3ta**



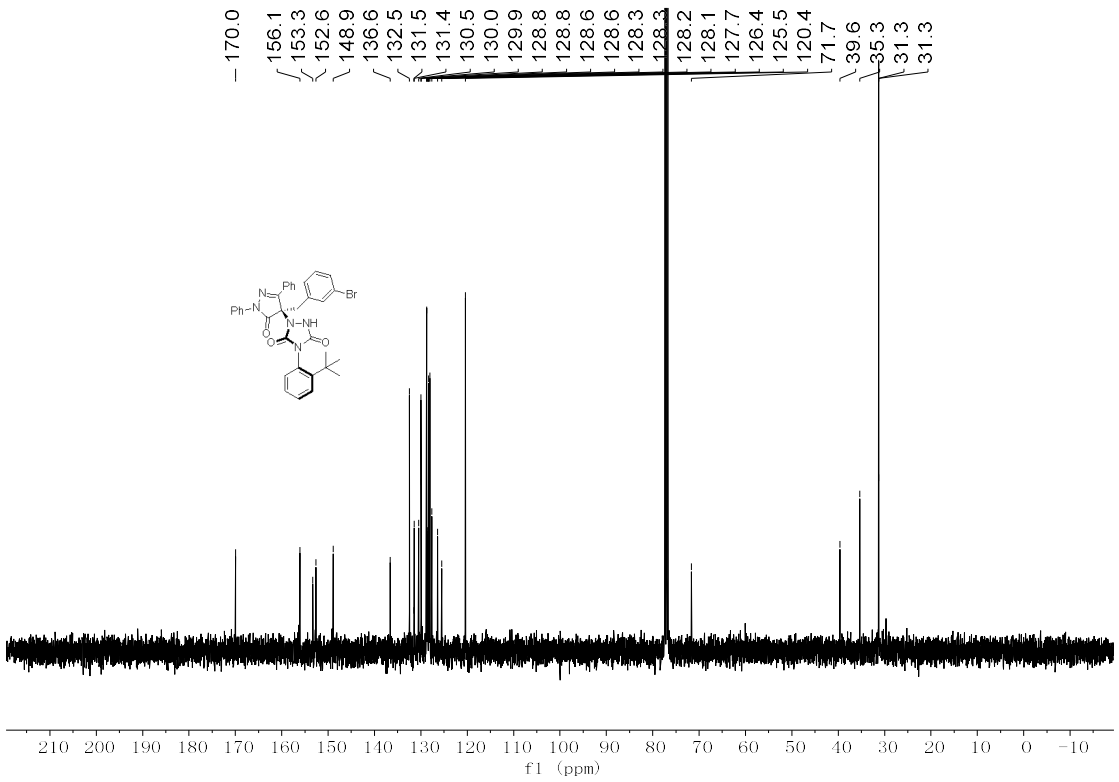
^{13}C NMR spectra of **3ta**



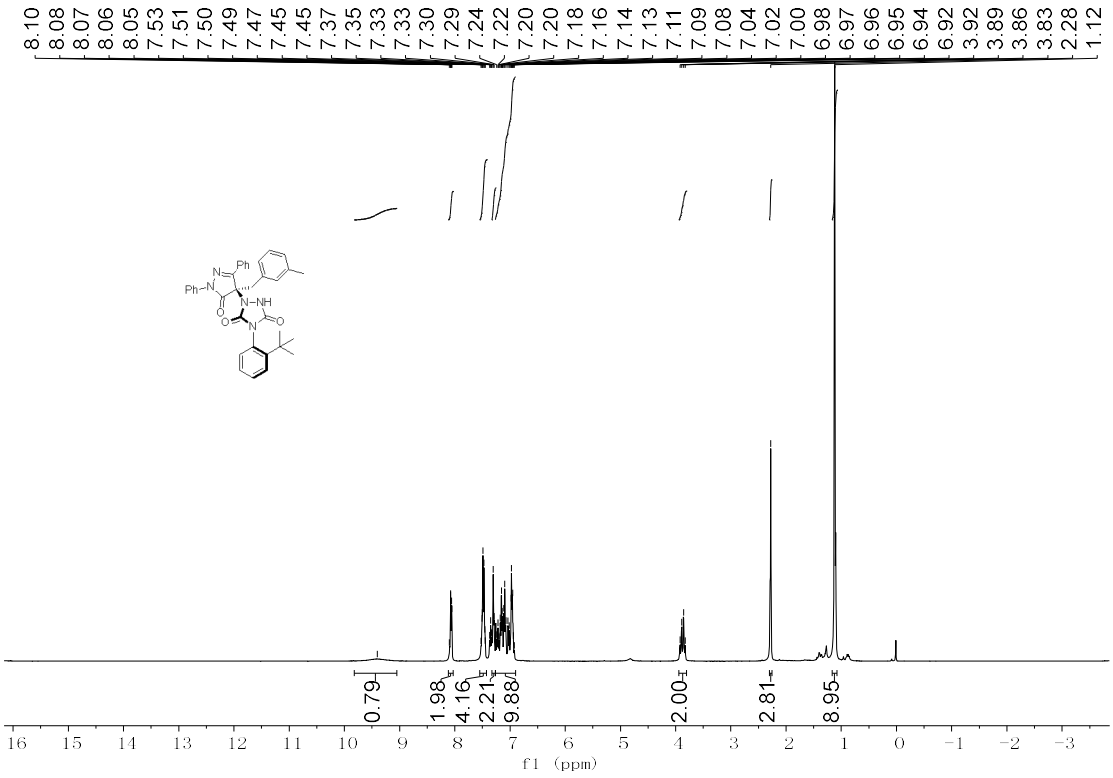
^{1}H NMR spectra of **3ua**



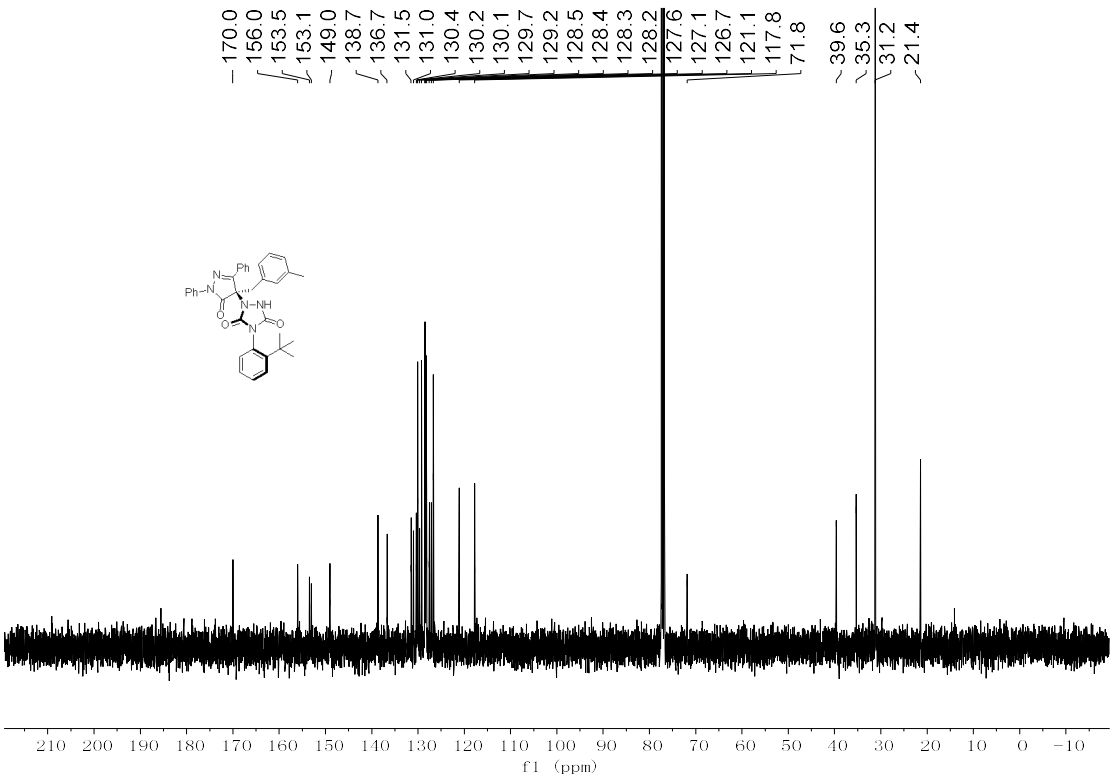
^{13}C NMR spectra of **3ua**



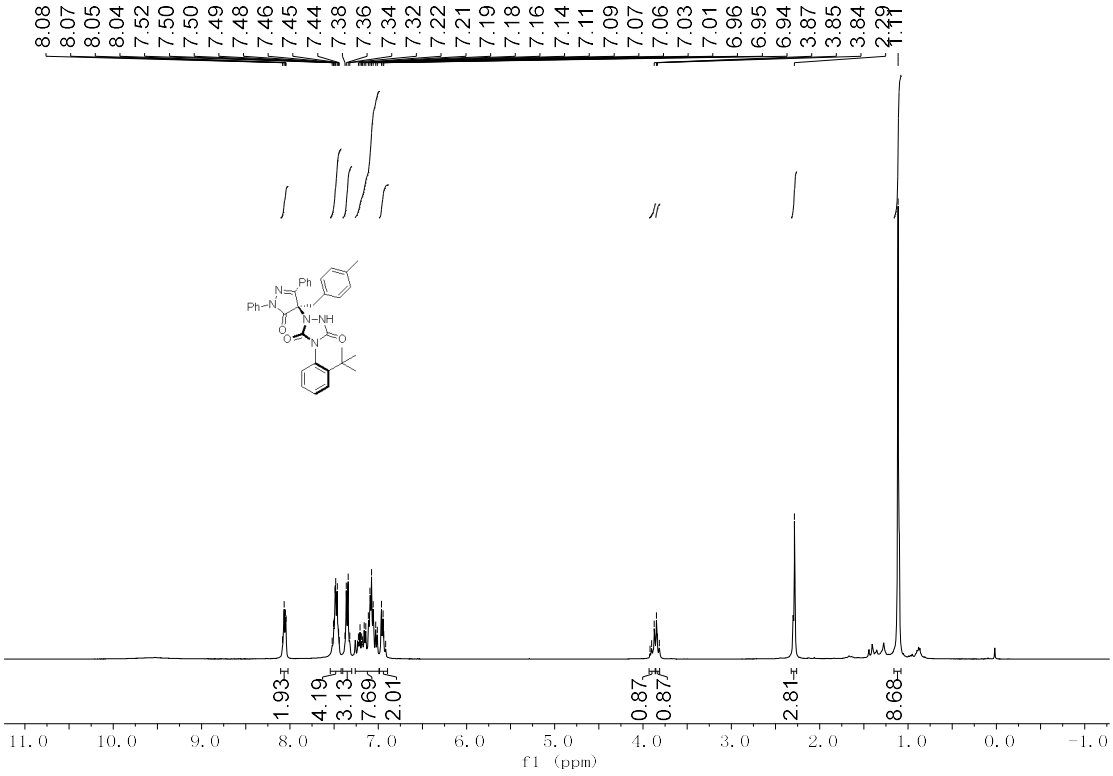
^{1}H NMR spectra of **3va**



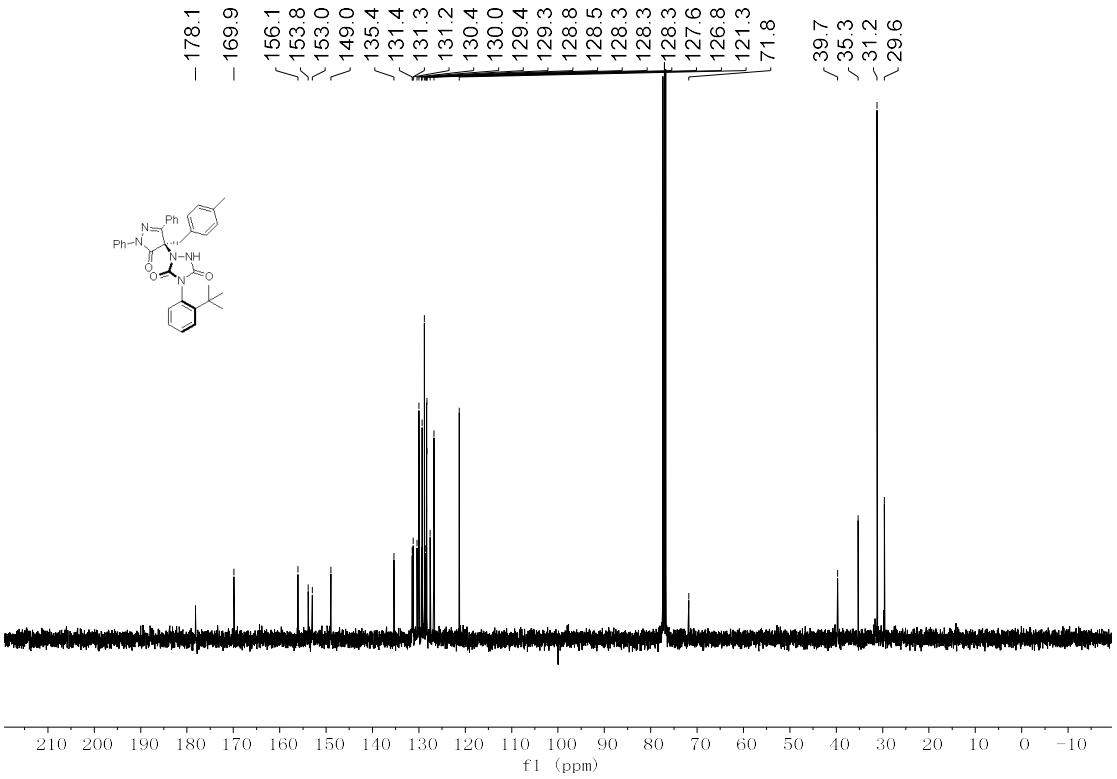
^{13}C NMR spectra of **3va**



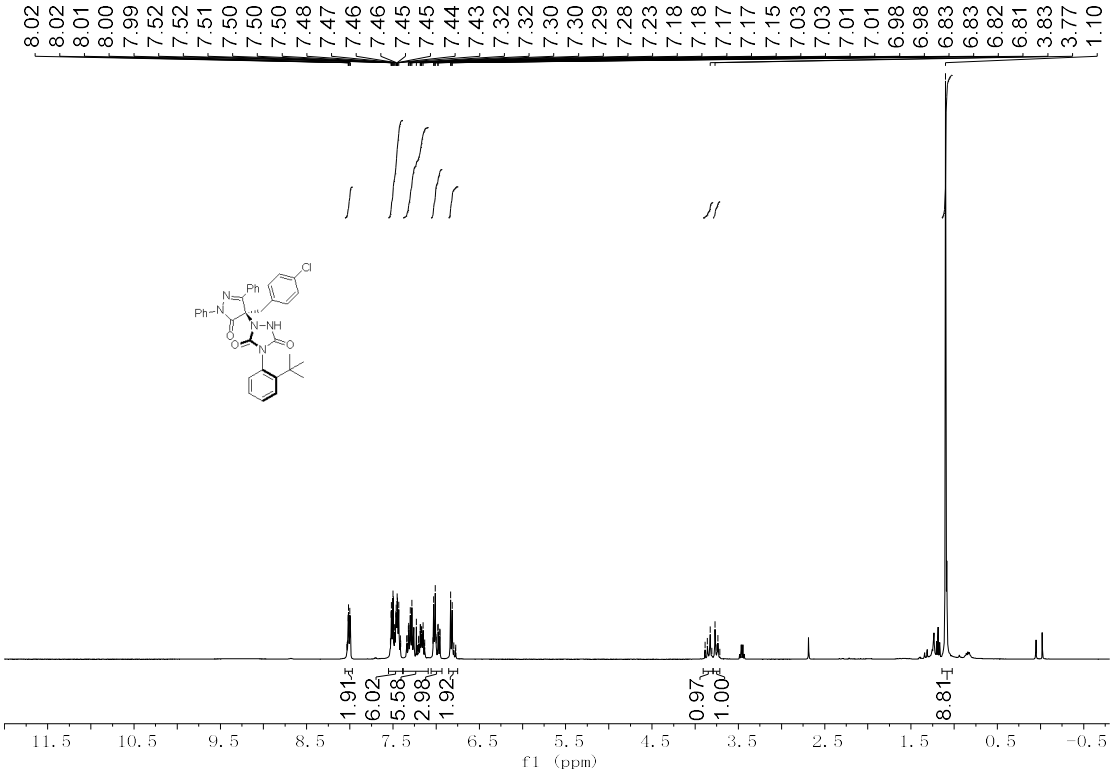
^{1}H NMR spectra of **3wa**



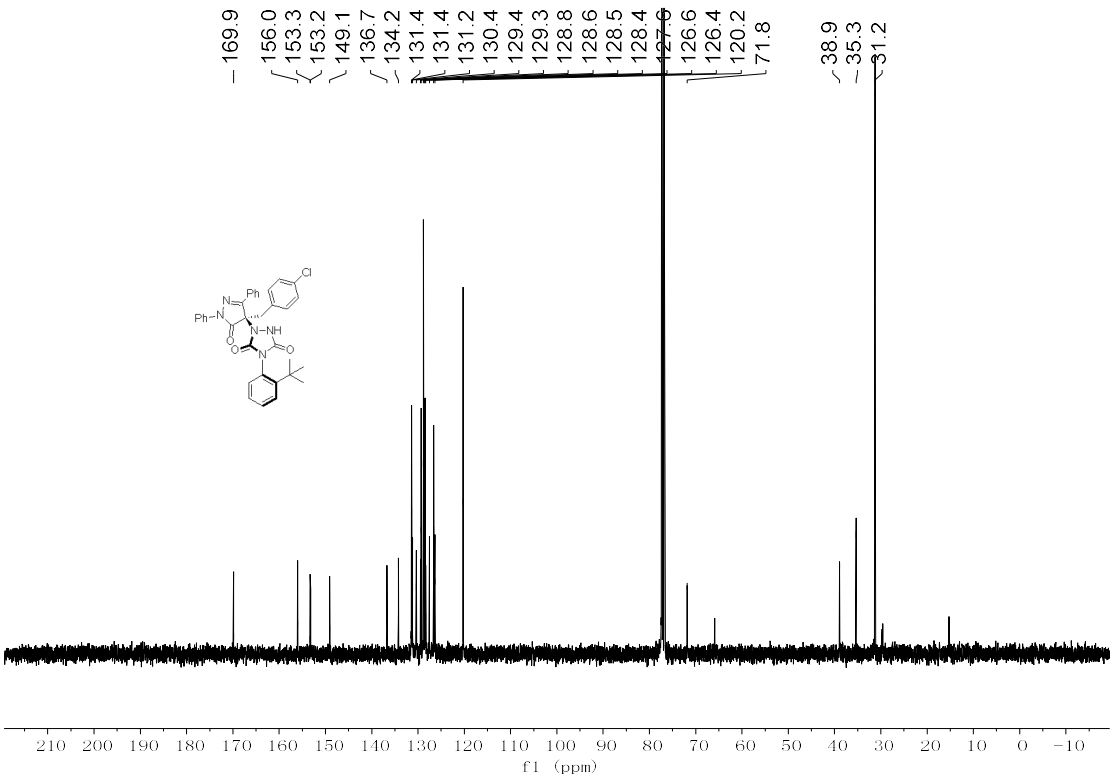
^{13}C NMR spectra of **3wa**



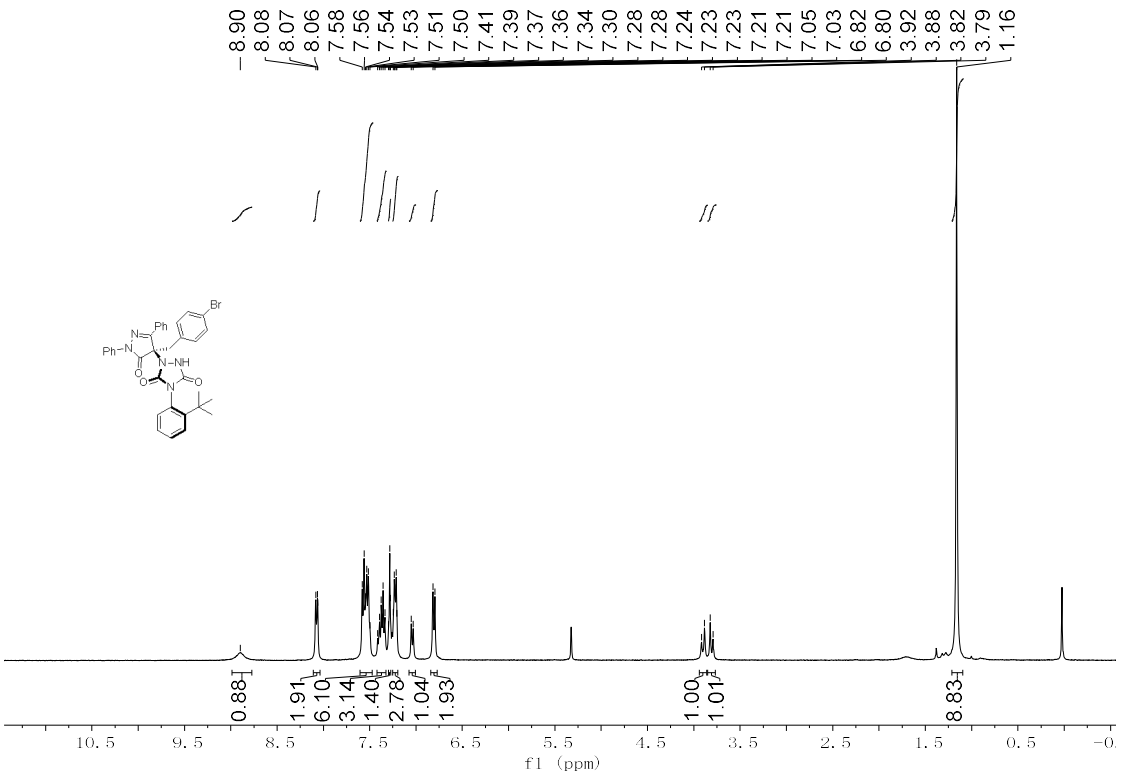
^{1}H NMR spectra of **3xa**



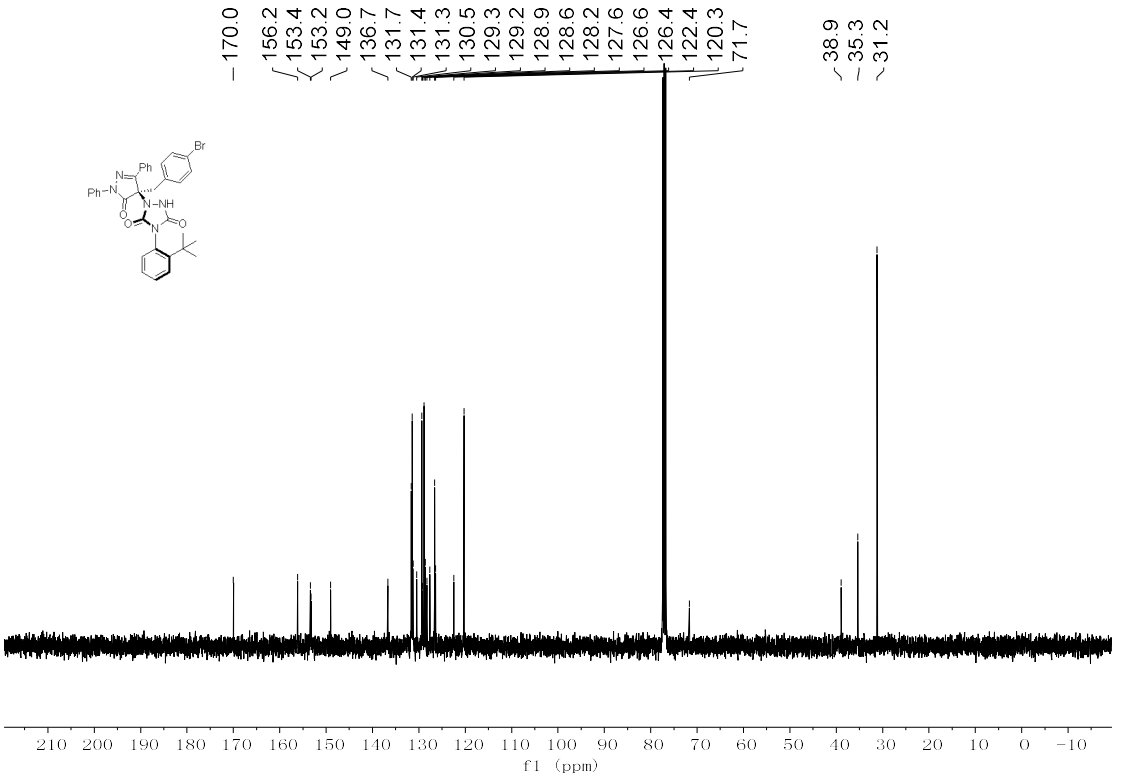
^{13}C NMR spectra of **3xa**



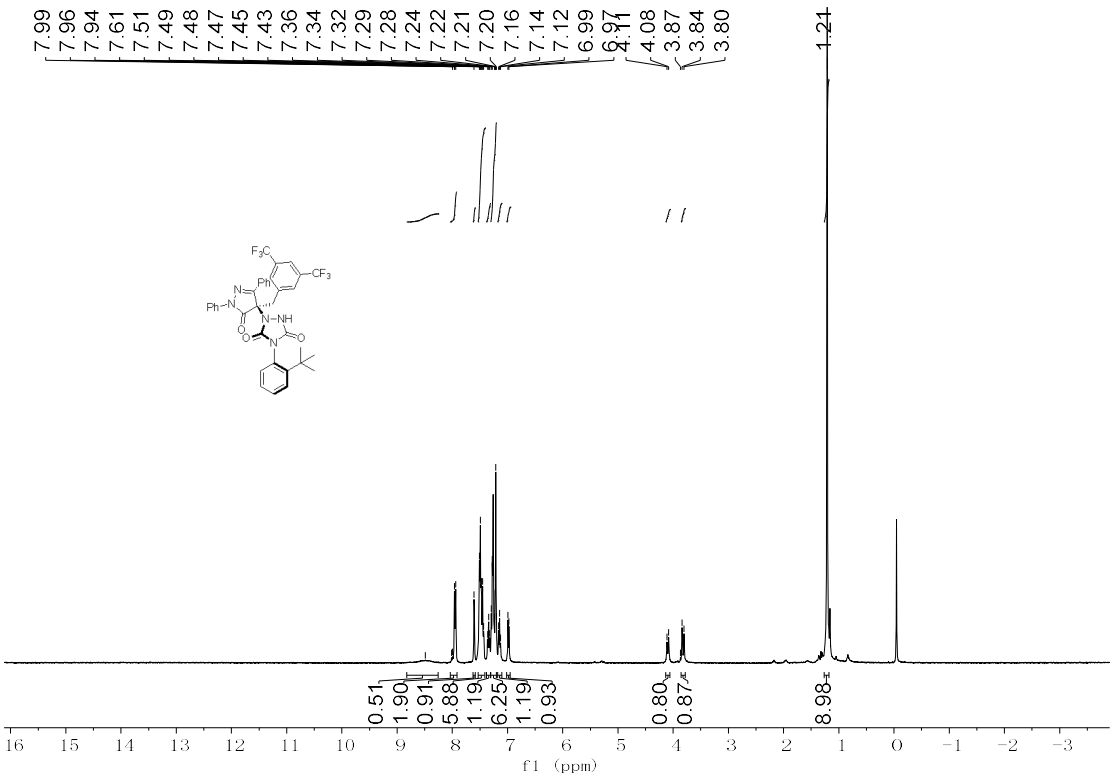
^{1}H NMR spectra of **3ya**



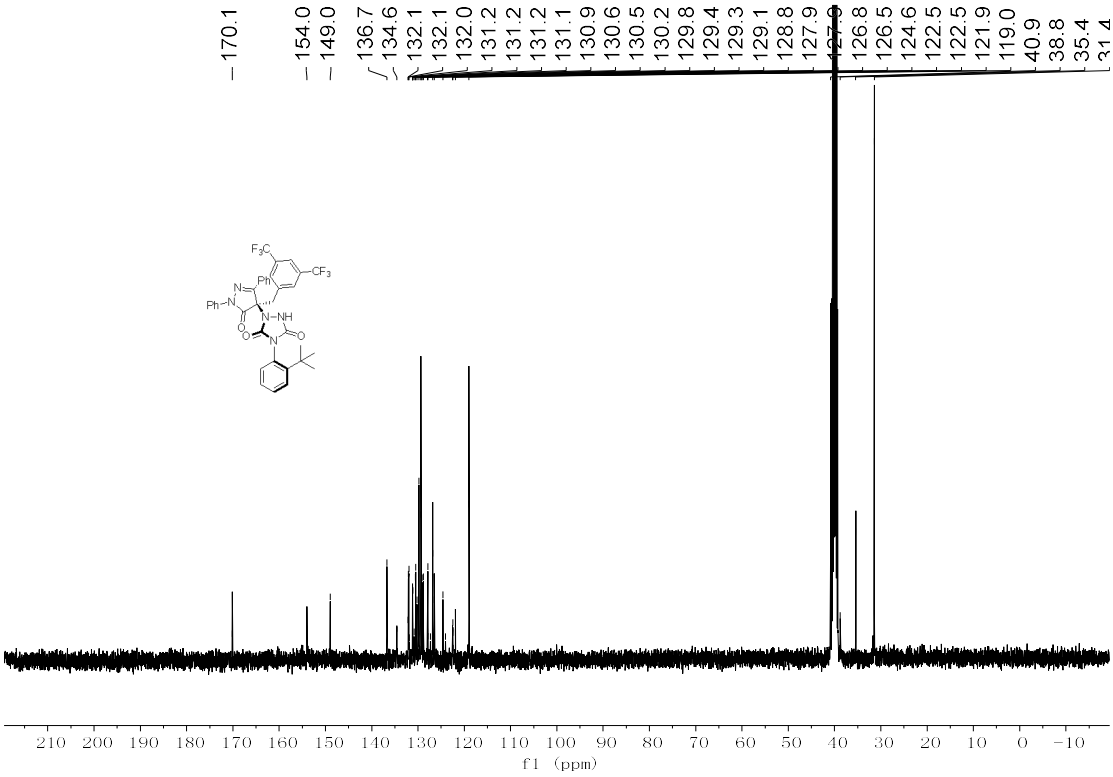
^{13}C NMR spectra of **3ya**



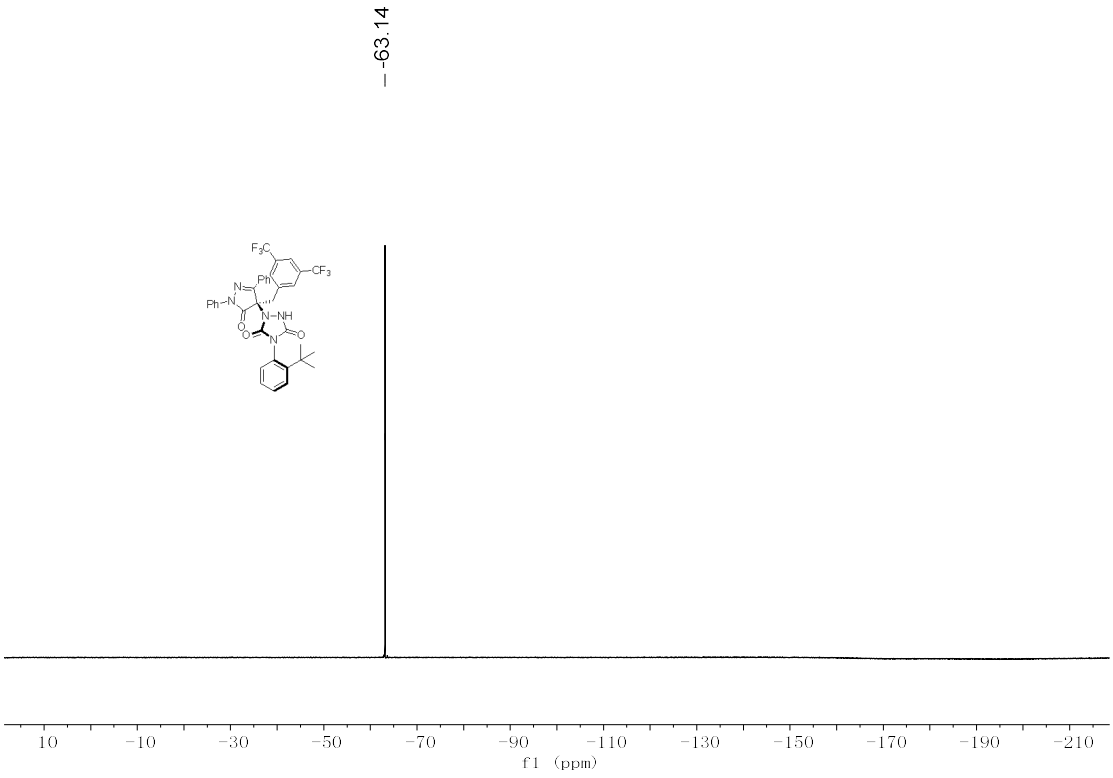
^{1}H NMR spectra of **3za**



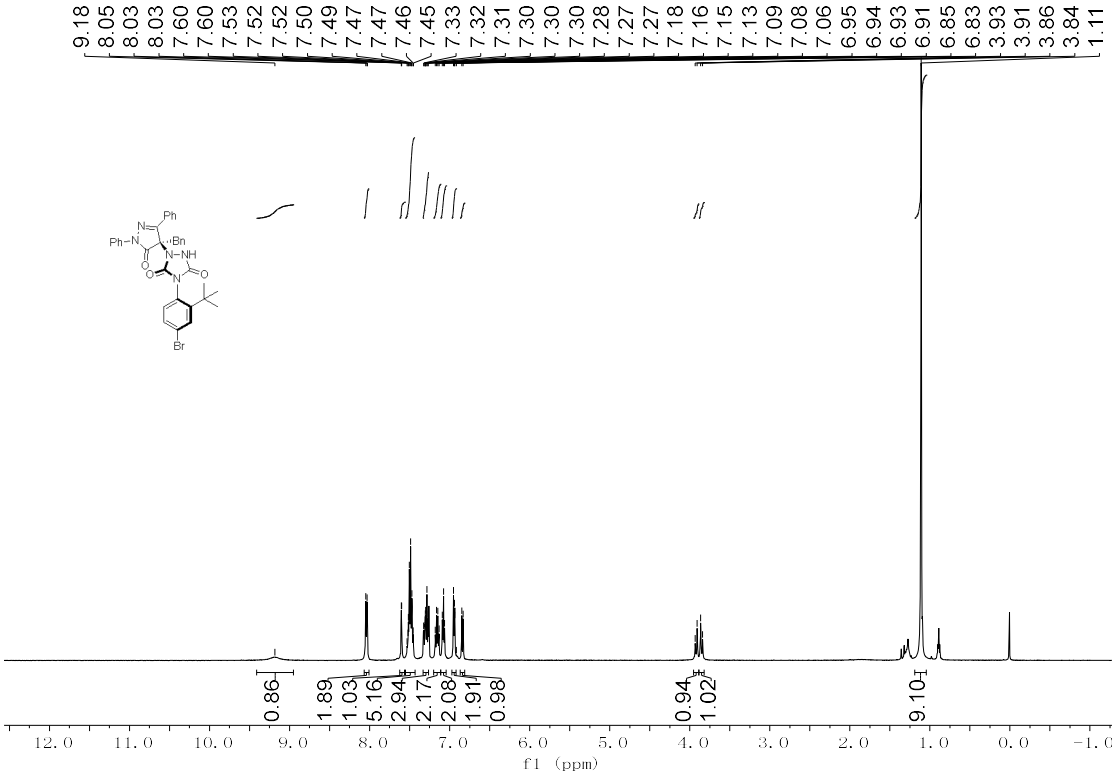
^{13}C NMR spectra of **3za**



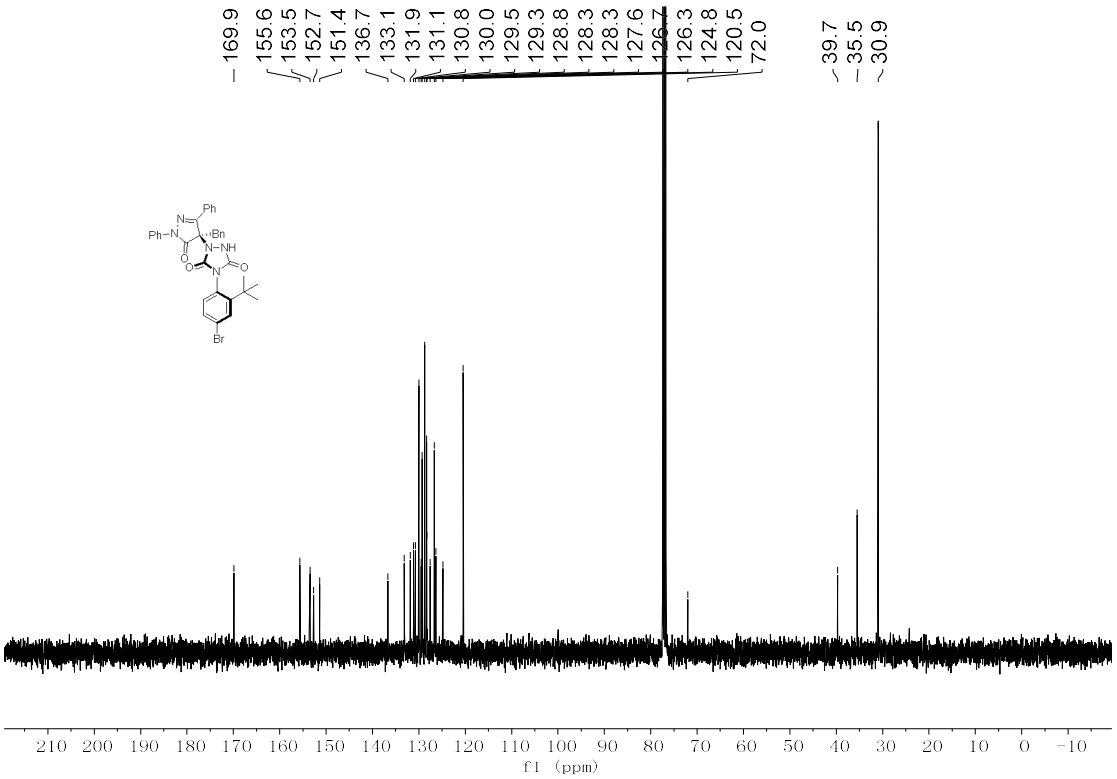
^{19}F NMR spectra of **3za**


-63.14
F3C
CF3
Ph
Ph-N
N
O
N-NH
O
O
N
O
10
-10
-30
-50
-70
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

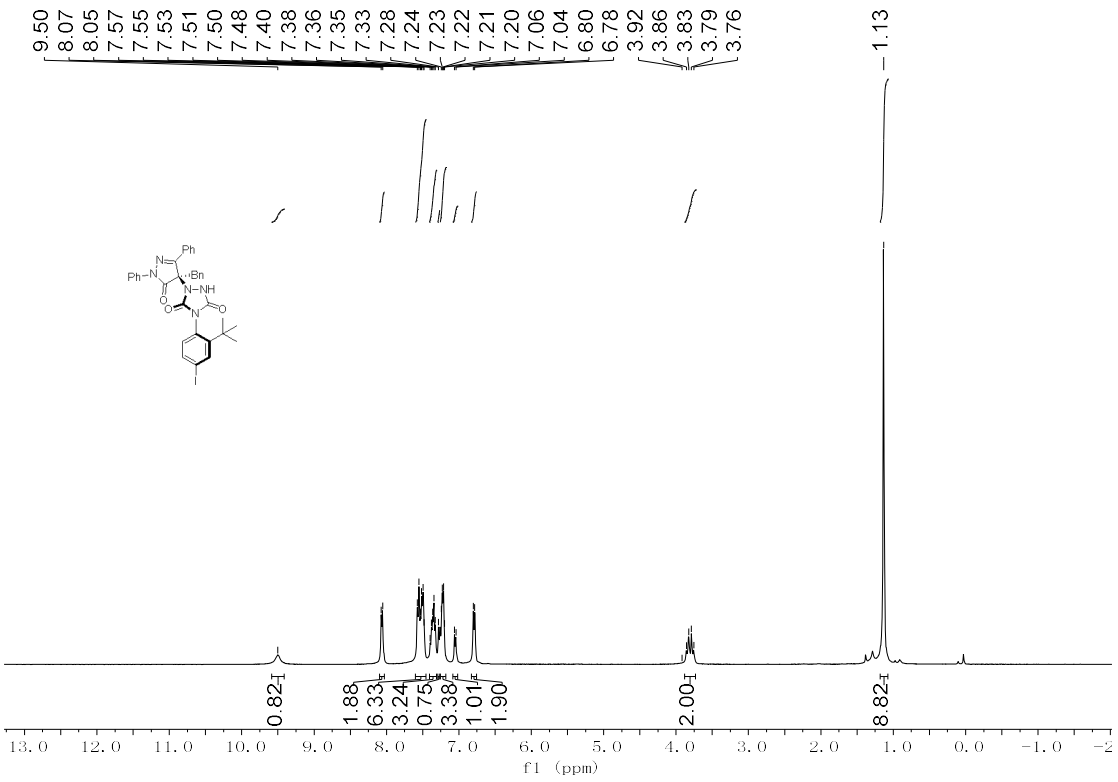
^{1}H NMR spectra of **3ab**



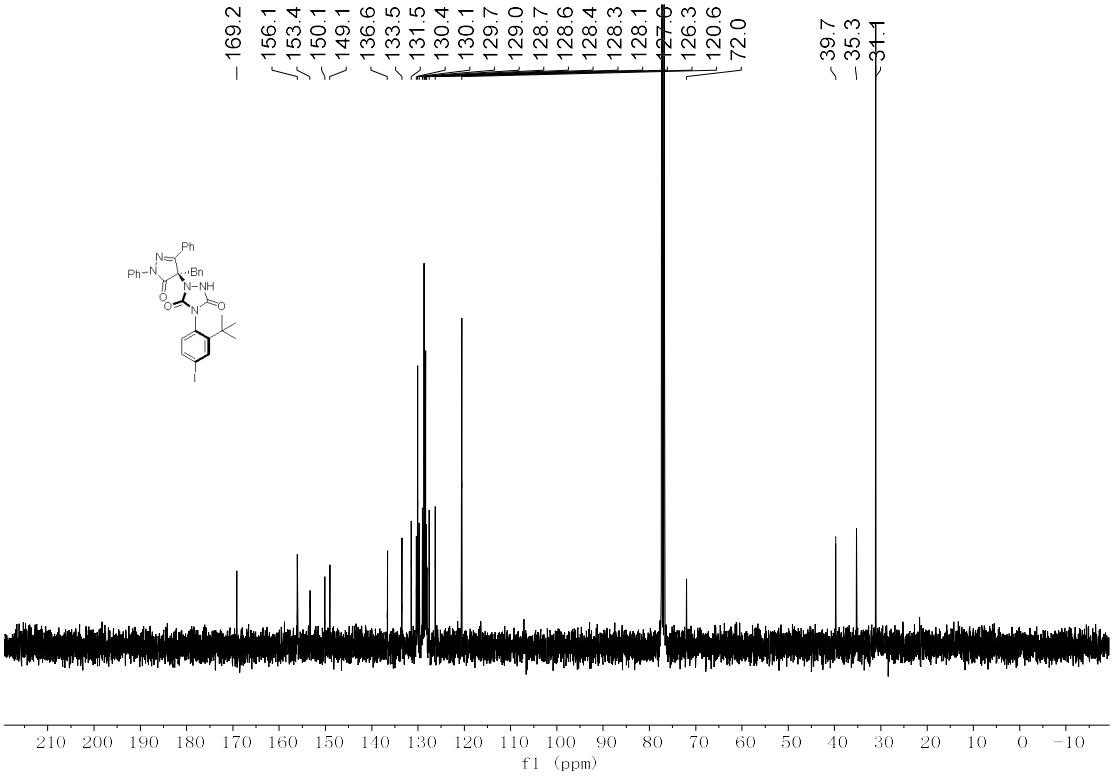
^{13}C NMR spectra of **3ab**



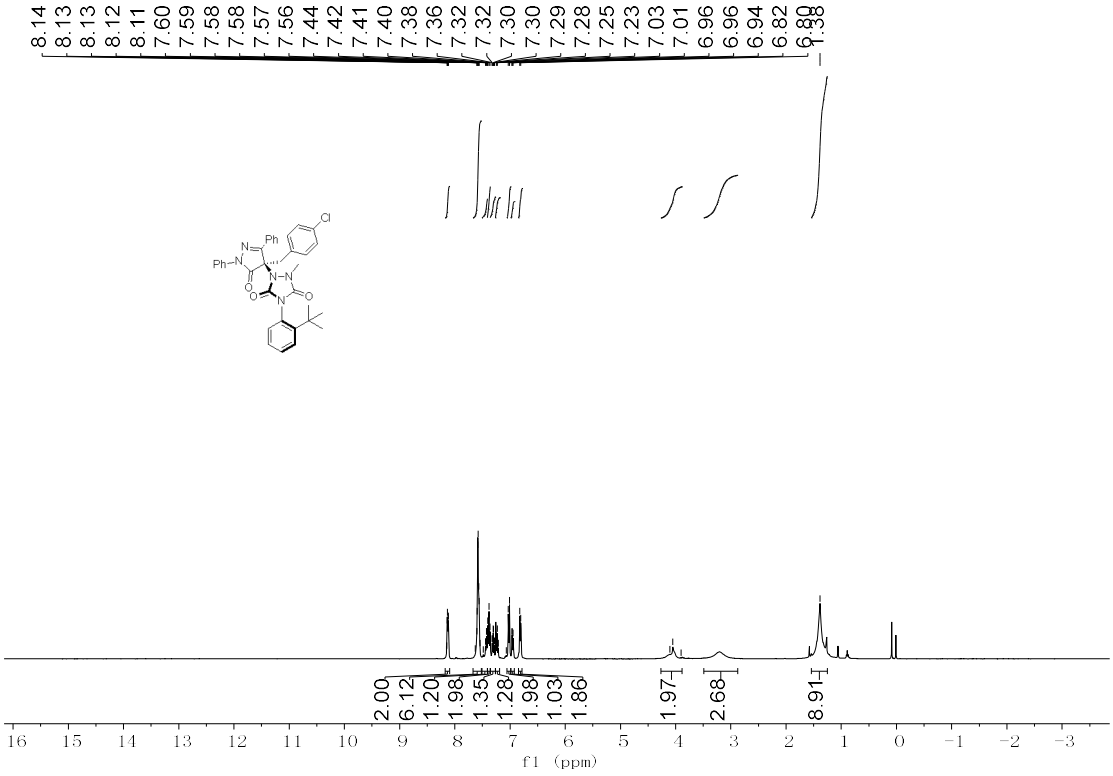
^{1}H NMR spectra of **3ac**



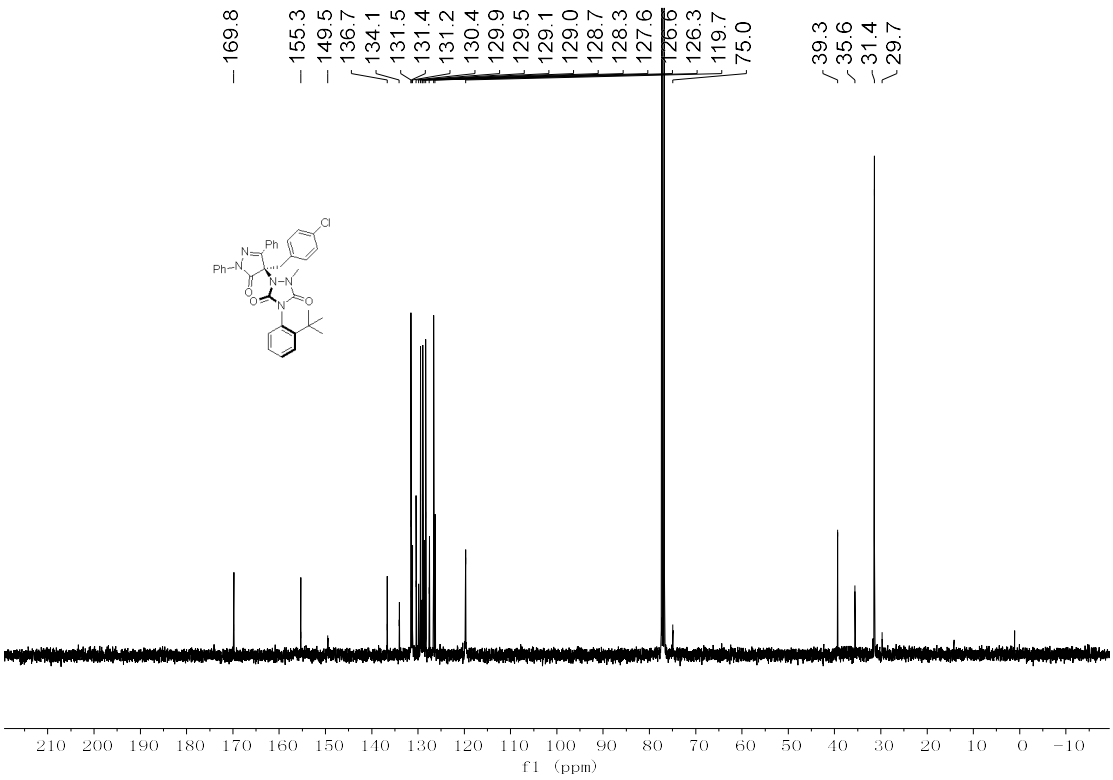
^{13}C NMR spectra of **3ac**



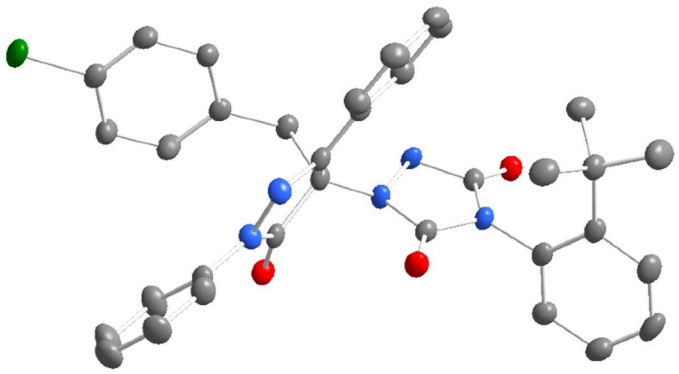
^{1}H NMR spectra of **4**



^{13}C NMR spectra of **4**



7. X-ray crystal structure of 3xa.



CCDC： 2526445

Bond precision: C-C = 0.0038 A Wavelength=0.71073

Cell: a=8.5157(11) b=12.5173(16) c=13.9114(17)
alpha=90.342(3) beta=91.011(4) gamma=97.382(4)

Temperature: 120 K

	Calculated	Reported
Volume	1470.3(3)	1470.3(3)
Space group	P -1	P-1
Hall group	-P 1	-P 1
Moiety formula	C34 H31 Cl N5 O3	C34 H31 Cl N5 O3
Sum formula	C34 H31 Cl N5 O3	C34 H31 Cl N5 O3
Mr	593.09	593.09
Dx, g cm-3	1.340	1.340
Z	2	2
Mu (mm-1)	0.175	0.175
F000	622.0	622.0
F000'	622.53	
h, k, lmax	10, 15, 17	10, 15, 17
Nref	6126	6038
Tmin, Tmax	0.983, 0.983	0.604, 0.745
Tmin'	0.983	

Correction method= # Reported T Limits: Tmin=0.604 Tmax=0.745 AbsCorr = NONE

Data completeness= 0.986 Theta(max)= 26.543

R(reflections)= 0.0576(4326) wR2(reflections)= 0.1554(6038)

S = 1.051 Npar= 391