Supporting Information

Catalytic asymmetric multicomponent reaction of isocyanide, isothiocyanate and alkylidene malonates

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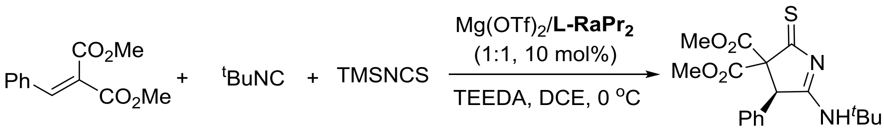
1. General remarks

^{1}H NMR spectra were recorded on bruker ASCEND 400 MHz. Chemical shifts were recorded in ppm relative to tetramethylsilane and with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), integration. $^{13}C\{^{1}H\}$ NMR data were collected on bruker ASCEND 101 MHz with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.16). Enantiomeric excesses were determined by chiral HPLC analysis on Daicel Chiralcel ADH, IA, IB, IC, IE, and Phenomenex Chiralcel Lux 5u Cellulose-2 at 23 °C with UV detector in comparison with the authentic racemates. Optical rotations were determined after flash column chromatography purification and reported as follows: $[\alpha]_D^T$ (*c*: g/100 mL, in CH_2Cl_2, λ = 589 nm). HRMS were recorded on a commercial apparatus (ESI source). IR was recored on Bruker Tensor II spectrometer with Plantium ATR accessory. All the reactions were carried out under an atmosphere of nitrogen in over-dried apparatus. All the solvents were purified by usual methods before use. Chromatography: Qingdao Haiyang silica gel, HG/T2354-92, H CP. Reagents purchased from commercial suppliers were used: *tert*-butyl isocyanide (Aladdin), TMSNCS (Alfa), TMSNCO (TCI), tetraethyl ethylenediamine (3A), magnesium trifluoromethanesulfonate (Alfa). The *N,N'*-dioxide ligands[1], alkylidene malonates[2]and Et_3HNCS[3] were synthesized according to known procedures.

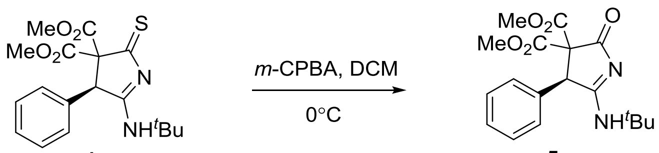
2. Experimental procedures

General procedure 1 for preparation of racemic products **4a**: To an oven-dried tube were added $Mg(OTf)_2$ (0.01 mmol, 10 mol%), Et_3N (0.05 mmol, 50 mol%), dimethyl 2-benzylidenemalonate **1a** (0.10 mmol), *tert*-butyl isocyanide **2a** (0.15 mmol), TMSNCS **3a** (0.15 mmol), and CH_2ClCH_2Cl (1.0 mL). The mixture was stirred in CH_2ClCH_2Cl at 35 °C for 24 h and directly subjected to flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1, v/v) to afford the racemic product **4a** as a yellow solid.



1a **2a** **3a** **4a**

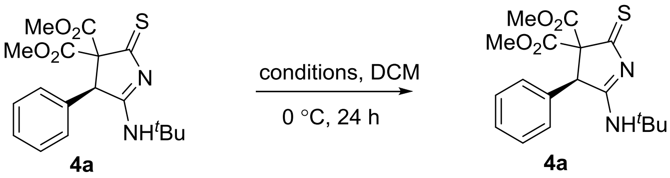
General procedure 2 for preparation of enantioenriched products **4a**: To an oven-dried tube were added $Mg(OTf)_2$ (0.01 mmol, 10 mol%), **L-RaPr$_2$** (0.01 mmol, 10 mol%), tetraethylenediamine (TEEDA) dimethyl 2-benzylidenemalonate (**1a,** 0.10 mmol) and CH_2ClCH_2Cl (1.0 mL). The mixture was stirred in CH_2ClCH_2Cl at 35 °C for 30 min. Then, TMSNCS **3a** (0.15 mmol) and *tert*-butyl isocyanide (**2a**, 0.15 mmol) were added to the mixture at 0 °C. The mixture was stirred in CH_2ClCH_2Cl at 0 °C for 96 h and directly subjected to flash column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 2/1, v/v) to afford the product **4a** as a yellow solid (29.1 mg, 80% yield, 95:5 er).



4a **5a**

General procedure 3 for synthesis of the oxo-product **5a**: To an oven-dried tube were added **4a** and CH_2Cl_2, then, *m*-CPBA (2 equiv) was added to the mixture at 0 °C. The mixture was stirred in CH_2Cl_2 at 0 °C and directly subjected to flash column chromatography on basic Al_2O_3 (upper layer) and silica gel (lower layer) (eluent: petroleum ether/ethyl acetate = 1/1, v/v) to afford the product **5a**.

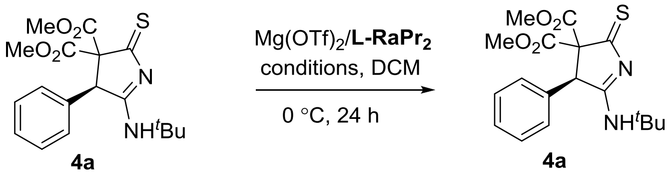
3. Control experiments



4a	conditions	4a
99.5:0.5 er	Li_2CO_3	99.5:0.5 er
99.5:0.5 er	Na_2CO_3	99.5:0.5 er
99.5:0.5 er	K_2CO_3	99.5:0.5 er

Control experiment 1: To an oven-dried tube were added **4a** (**4a** with 99.5:0.5 er could be easily obtained by recrystallization of petroleum ether and ethyl acetate) and CH_2Cl_2, then, base (0.5 equiv) was added to the mixture at 0 °C. The mixture was stirred in CH_2Cl_2 at 0 °C for 24 h and directly subjected to flash column chromatography afforded the product **4a**.

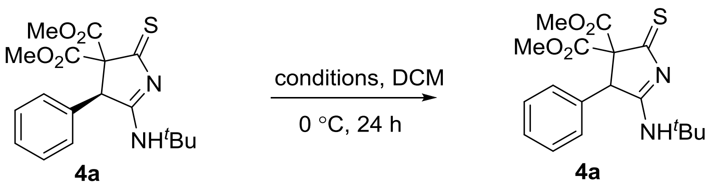
These results indicated the addition of base has no effect on the optical purity of the product.



4a	conditions	4a
99.5:0.5 er	Li_2CO_3	99.5:0.5 er
99.5:0.5 er	Na_2CO_3	99.5:0.5 er
99.5:0.5 er	K_2CO_3	99.5:0.5 er

Control experiment 2: To an oven-dried tube were added $Mg(OTf)_2$ (10 mol%), **L-RaPr₂** (10 mol%), base (0.5 equiv) and CH_2Cl_2, the mixture was stirred in CH_2Cl_2 at 35 °C for 30 min. Then, **4a** was added to the mixture at 0 °C. The mixture was stirred in CH_2Cl_2 at 0 °C for 24 h and directly subjected to flash column chromatography afforded the product **4a**.

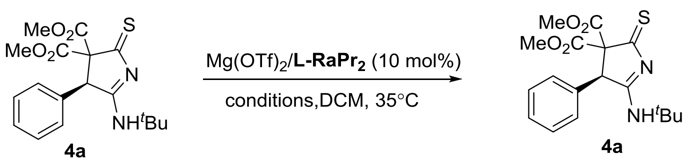
These results indicated that neither base nor chiral *N*,*N'*-dioxide/Mg^{II} can promote the racemization of the product.



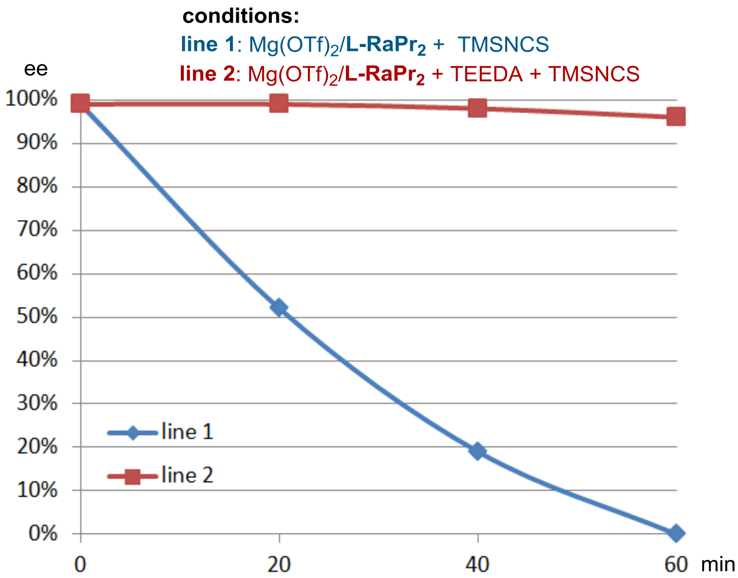
4a	conditions	4a
99.5:0.5 er	TMSNCS	50:50 er

Control experiment 3: To an oven-dried tube were added **4a** and CH_2Cl_2, then, TMSNCS (1 equiv) was added to the mixture at 0 °C. The mixture was stirred in CH_2Cl_2 at 0 °C for 24 h and directly subjected to flash column chromatography afforded the product **4a**.

These results indicated that TMSNCS led to the racemization of the product efficiently, which was also investigated by H-D exchange experiment.

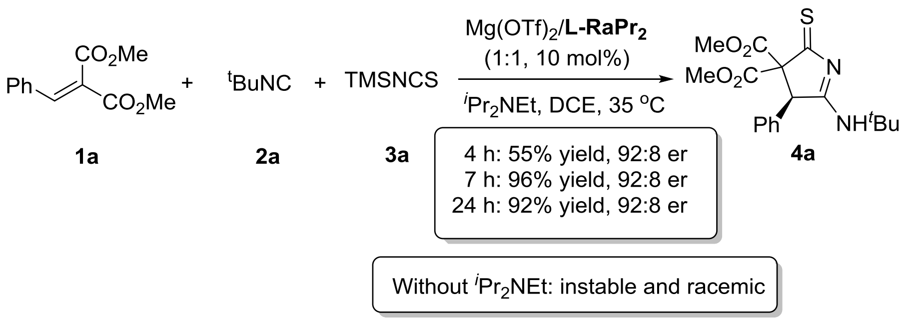


4a	conditions	20 min	40 min	60 min
99.5:0.5 er	TMSNCS	76:24 er	59:40 er	50:50 er
99.5:0.5 er	TMSNCS + TEEDA (0.5 equiv)	99.5:0.5 er	99:1 er	98:2 er
99.5:0.5 er	TMSNCS + TEEDA (1.0 equiv)	99.5:0.5 er	99.5:0.5 er	99.5:0.5 er



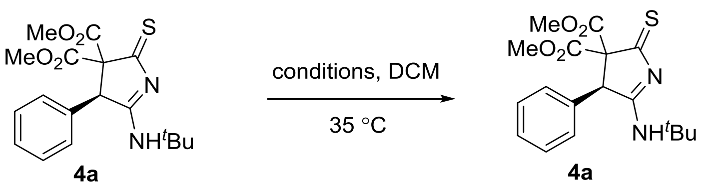
Control experiment 4: To an oven-dried tube were added $Mg(OTf)_2$ (10 mol%), **L-RaPr$_2$** (10 mol%), **4a** (0.5 equiv), TEEDA and CH_2Cl_2, the mixture was stirred in CH_2Cl_2 at 35 °C for 30 min. Then, TMSNCS (1.0 equiv) was added to the mixture at 35 °C and the stock solution was analysed by HPLC every 20 minutes.

It was found that the product underwent racemization quickly. When base additive (0.5 equiv) was added together, the racemization of the product was inhibited efficiently in the presence of chiral *N*,*N*′-dioxide/Mg^{II} (10 mol%).



Control experiment 5: To an oven-dried tube were added $Mg(OTf)_2$ (0.01 mmol, 10 mol%), **L-RaPr$_2$** (0.01 mmol, 10 mol%), $^iPr_3NEt$ (0.05 mmol, 50 mol%), dimethyl 2-benzylidenemalonate **1a** (0.10 mmol), *tert*-butyl isocyanide **2a** (0.15 mmol), TMSNCS **3a** (0.15 mmol), and CH_2ClCH_2Cl (1.0 mL). The mixture was stirred in CH_2ClCH_2Cl at 35 °C.

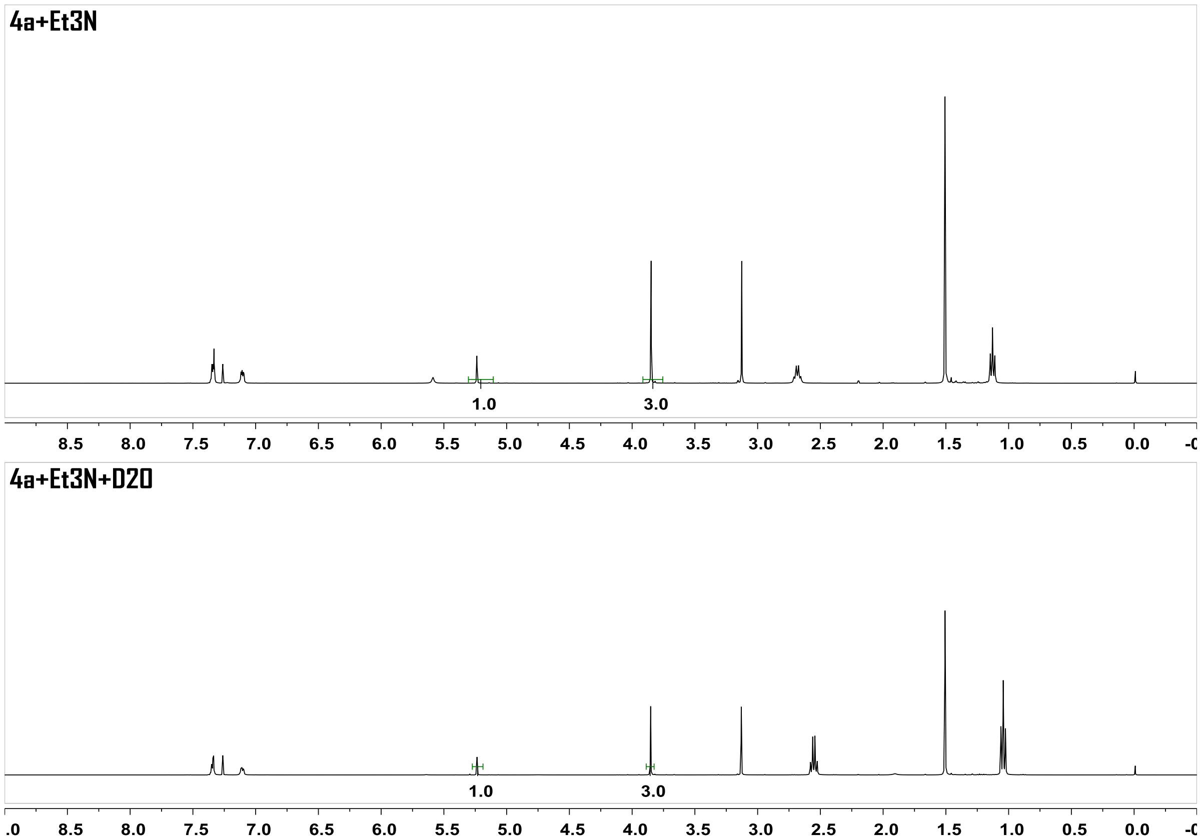
These results indicated that the optical purity of the product was stable during the reaction process. The presence of base additive was crucile for high enantioselectivity. Otherwise, racemic product was afforded.



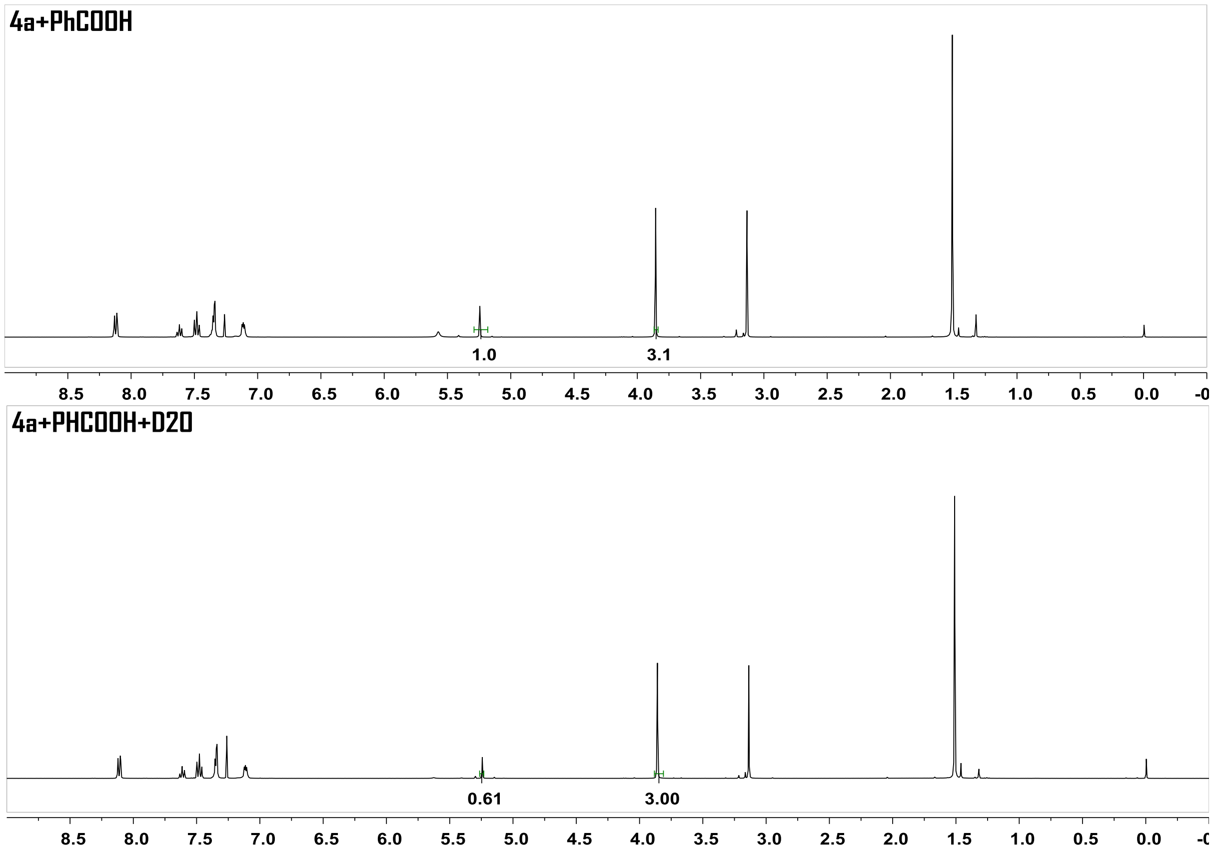
	conditions	20 min	40 min	60 min
99.5:0.5 er	TMSOH	99.5:0.5 er	99.5:0.5 er	99.5:0.5 er
99.5:0.5 er	TMSOH + Et_3N	99.5:0.5 er	99:1 er	99:1 er

Control experiment 6: To an oven-dried tube were added **4a** and CH_2Cl_2, the mixture was stirred in CH_2Cl_2 at 35 °C for 30 min. Then, TMSOH (1.0 equiv) was added to the mixture at 35 °C. The mixture was stirred in CH_2Cl_2 at 35 °C and the stock solution was analysed by HPLC every 20 minutes.

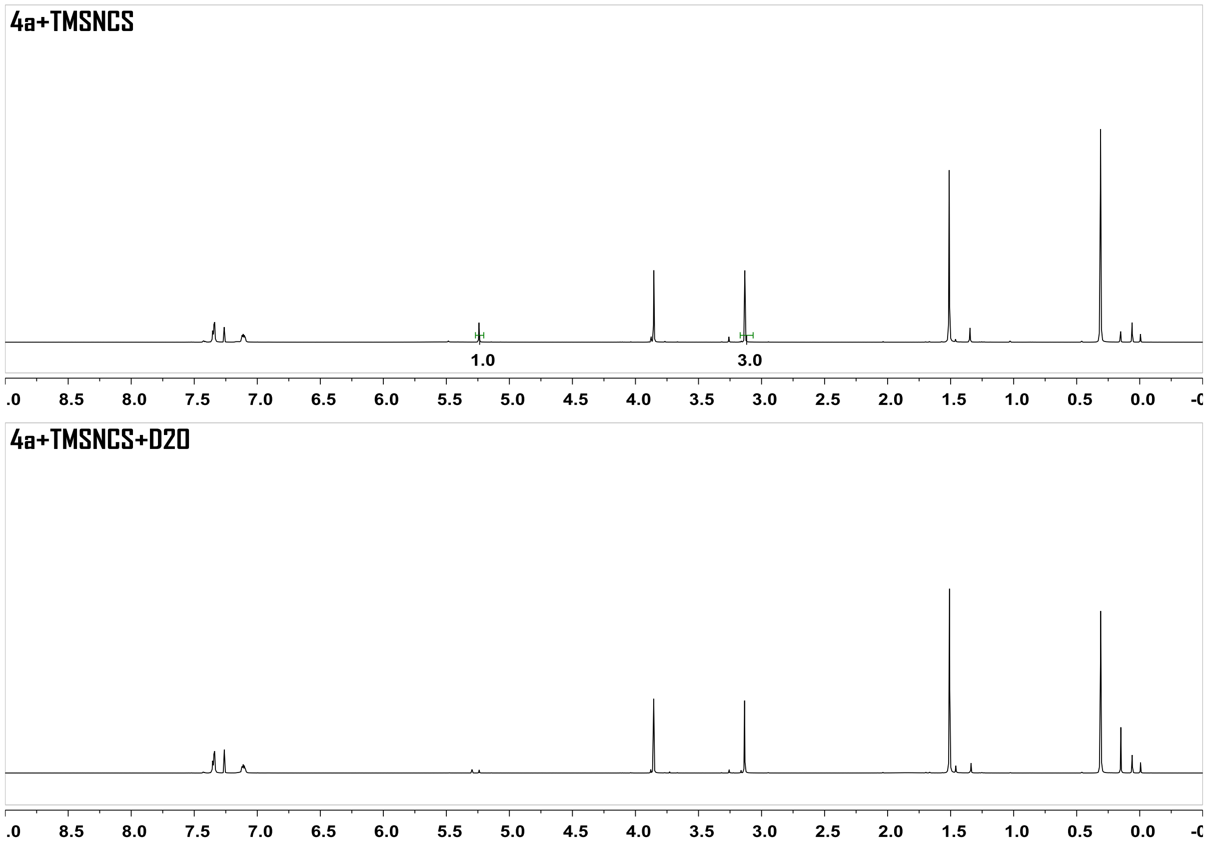
These results indicated that TMSOH has a negligible effect on the optical purity of the product. This control experiment implied that the HNCS generated in-situ was probably responsible for the racemization process.



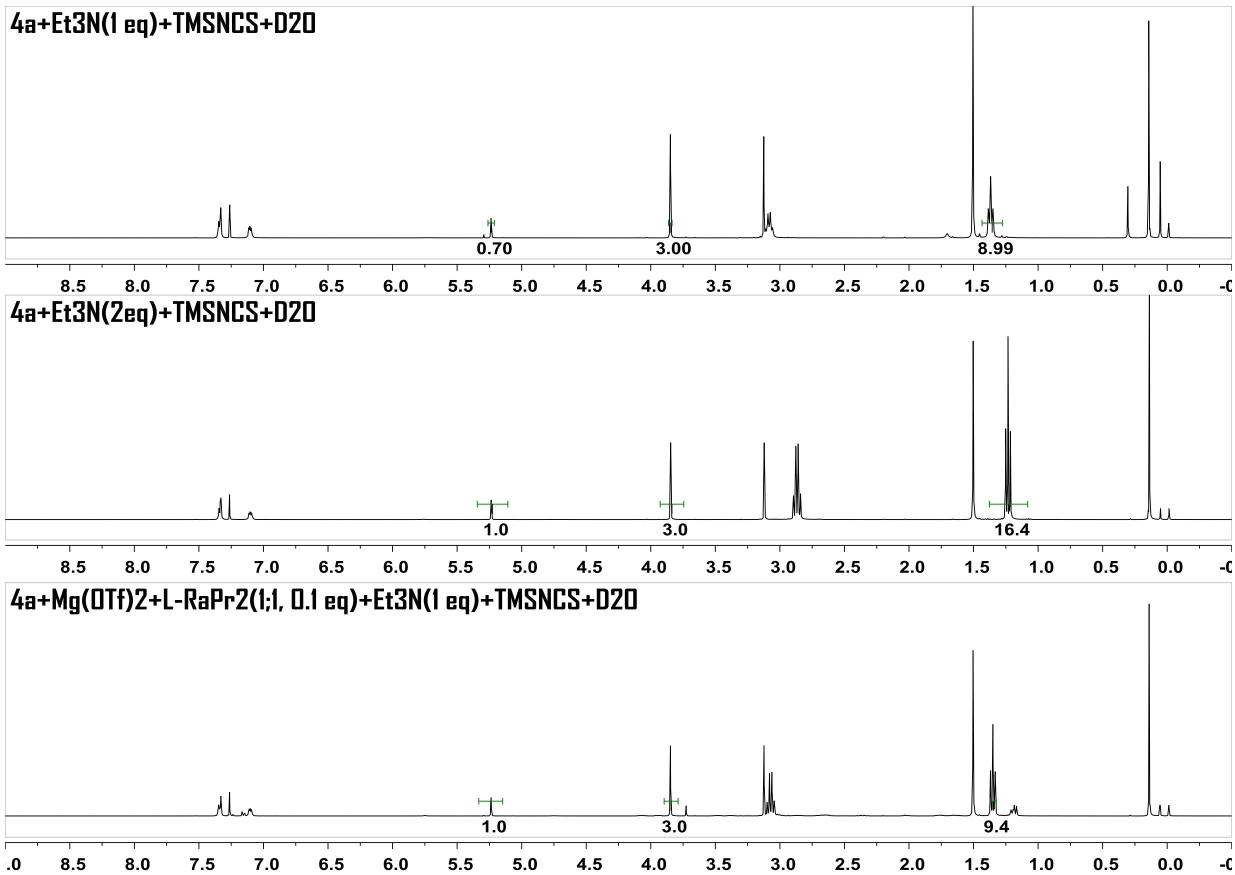
Deuterization experiment 1: To an oven-dried tube were added **4a**, Et_3N(1 equiv) and $CDCl_3$. The mixture was stirred in $CDCl_3$ at 35 °C for 30 min, then, D_2O (5 μL) was added to the mixture at 35 °C. The mixture was stirred for 30 min. The ^1H NMR spectra indicated that EtN_3 is not able to accelerate H-D exchange at α-position of the product.



Deuterization experiment 2: To an oven-dried tube were added **4a**, PhCOOH (1 equiv) and $CDCl_3$. The mixture was stirred in $CDCl_3$ at 35 °C for 30 min, then, D_2O (5 μL) was added to the mixture at 35 °C. The mixture was stirred for 30 min. The ^1H NMR spectra indicated that PhCOOH is able to promote H-D exchange (ca. 40% after 0.5 h) at α-position of the product.

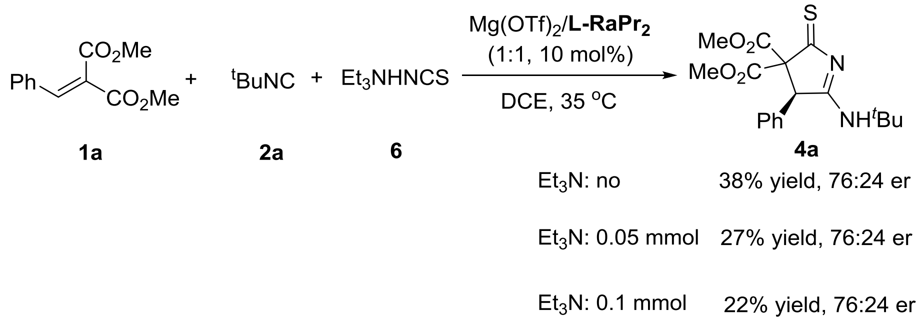


Deuterization experiment 2: To an oven-dried tube were added **4a**, TMSNCS (1 equiv) and $CDCl_3$. The mixture was stirred in $CDCl_3$ at 35 °C for 30 min, then, D_2O (5 μL) was added to the mixture at 35 °C. The mixture was stirred for 30 min. The ^1H NMR spectra indicated that TMSNCS enables to efficiently promote H-D exchange (ca. 100% after 0.5 h) at α-position of the product.

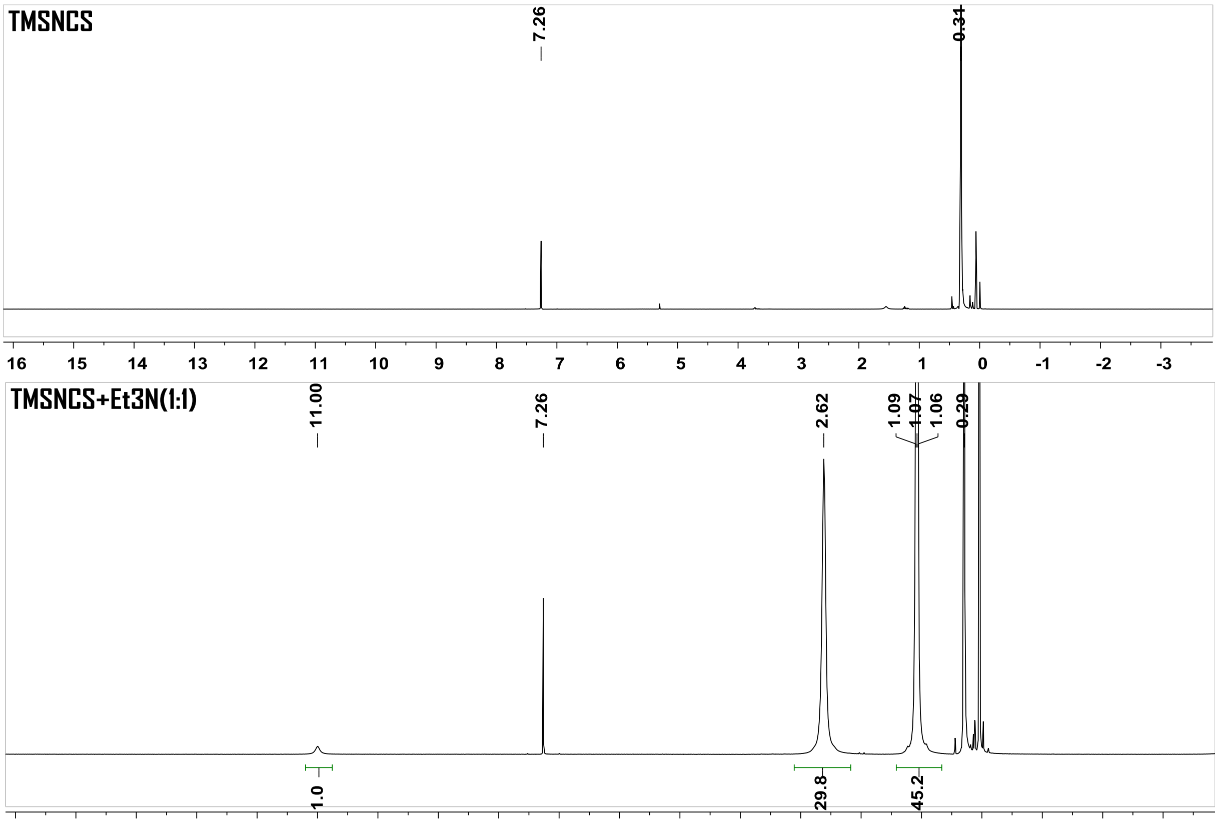


Deuterization experiment 3: To an oven-dried tube were added $Mg(OTf)_2$ (10 mol%), **L-RaPr₂** (10 mol%), **4a**, Et_3N (1 equiv) and $CDCl_3$. The mixture was stirred in $CDCl_3$ at 35 °C for 30 min, then, TMSNCS and D_2O (5 μL) was added to the mixture at 35 °C. Collectively, the ^1H

NMR spectra indicated that EtN_3 can inhibit the TMSNCS-mediated racemization process. Moreover, chiral *N*,*N*'-dioxide/Mg^{II} (10 mol%) could enhance this performance of EtN_3.

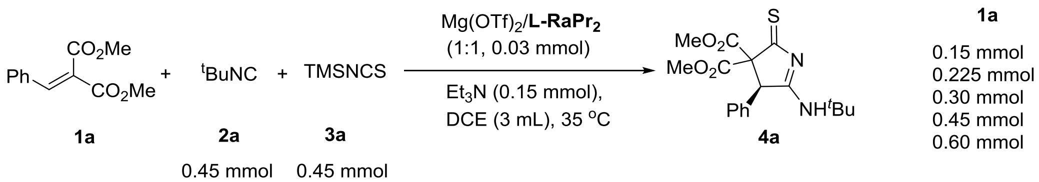


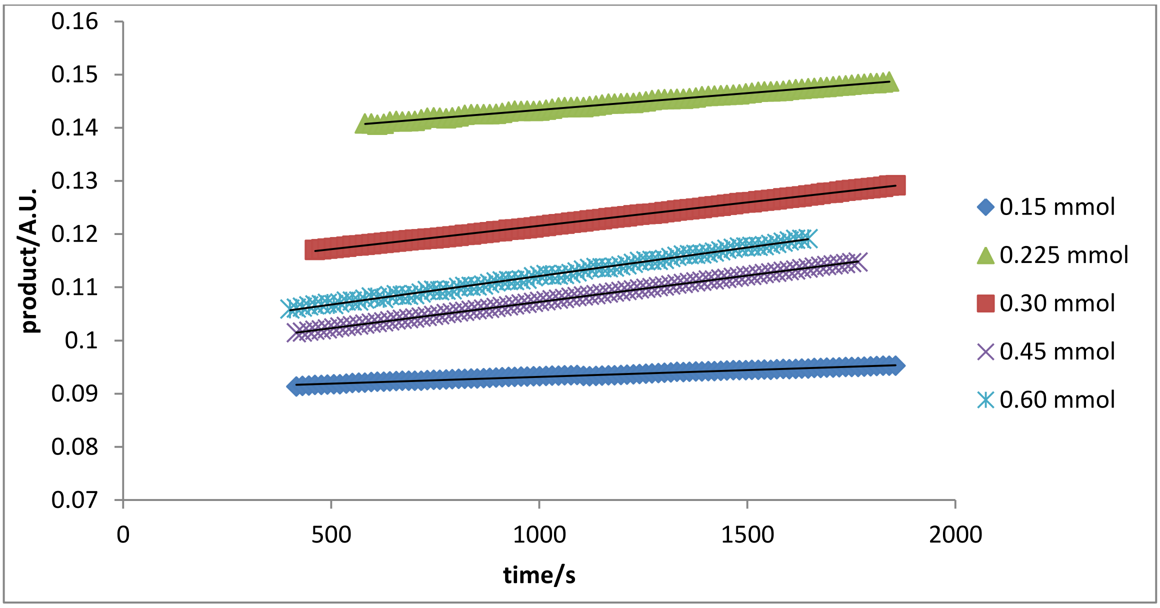
Control experiment 7: To an oven-dried tube were added $Mg(OTf)_2$ (0.01 mmol, 10 mol%), **L-RaPr₂** (0.01 mmol, 10 mol%), dimethyl 2-benzylidenemalonate **1a** (0.10 mmol), *tert*-butyl isocyanide **2a** (0.15 mmol), Et_3N•HNCS (0.10 mmol), Et_3N and CH_2ClCH_2Cl (1.0 mL). The mixture was stirred in CH_2ClCH_2Cl at 35 °C for 24h.

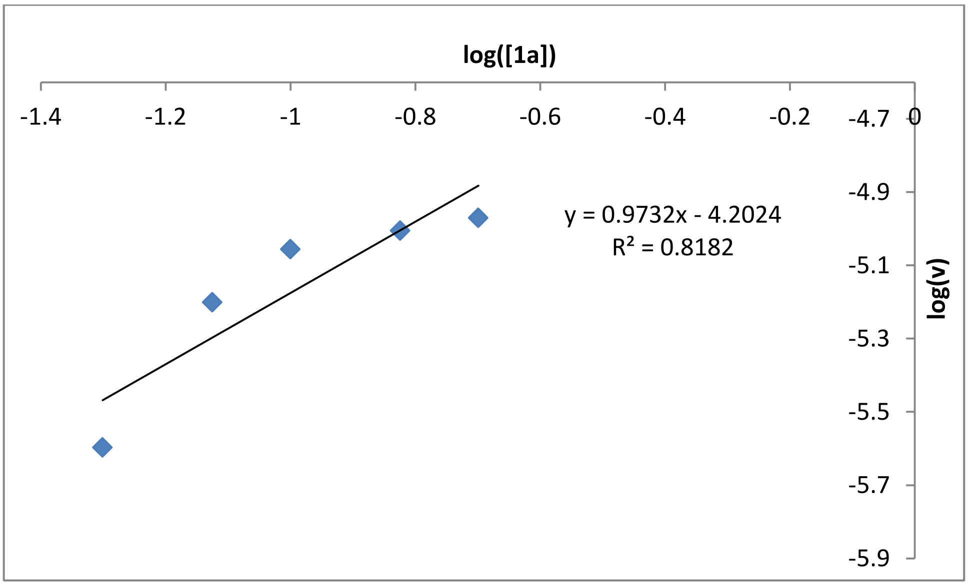


Control experiment 8: Kinetic studies

Kinetic analyses were performed using in situ attenuated total reflectance Fouriertransform infrared (ATR FTIR) spectroscopy to track the formation of product **4a** under synthetically relevant conditions. A Mettler Toledo SW License iC IR 701L instrument was treated as main experiment equipment. All of the kinetic experiments on each plot were performed using a single batch of reagents. Peak at 1335 cm−1 was identified as the characteristic absorption of product **4a**.

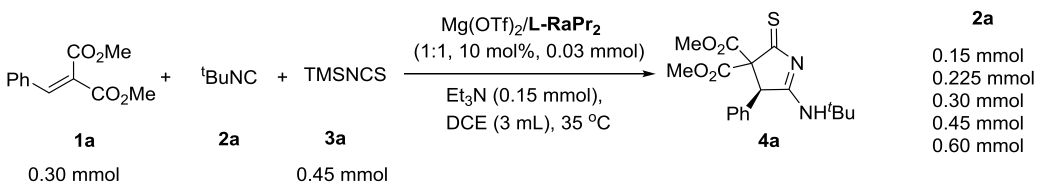


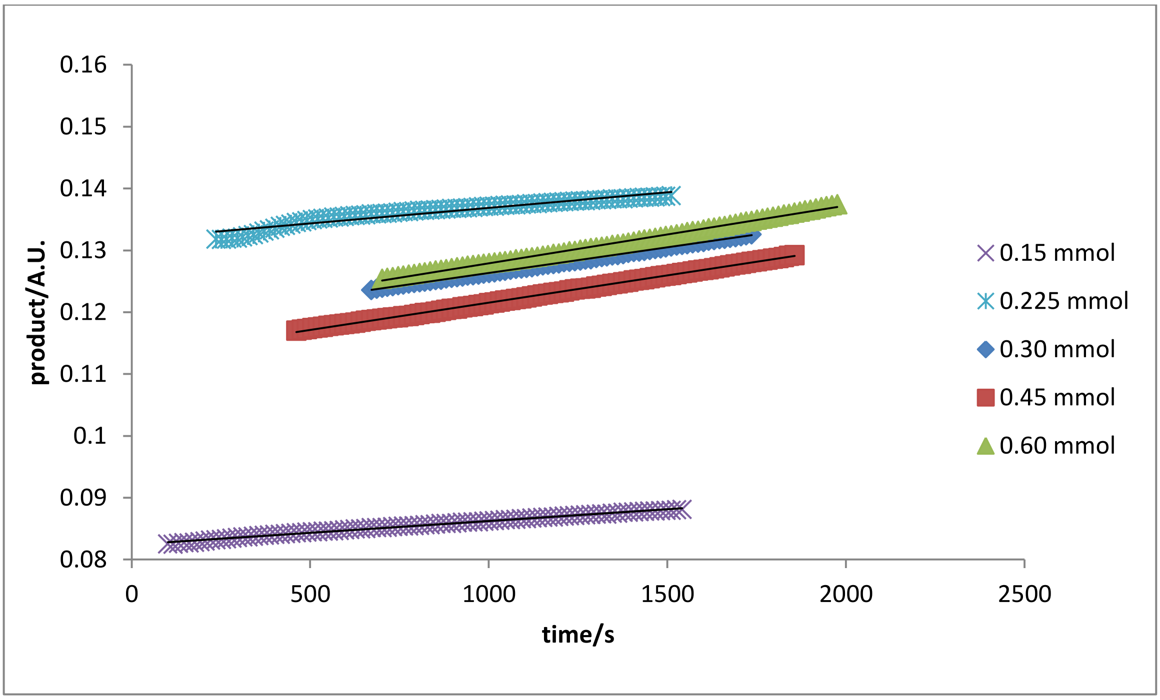


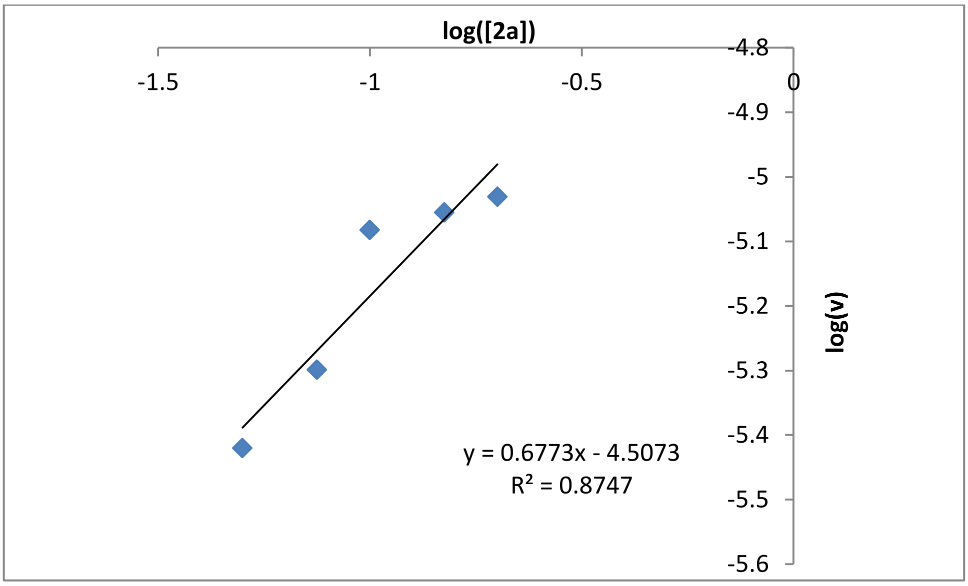


[**1a**]/(M)	reaction rate/(A.U./s)	Log([**1a**])	Log(**v**)
0.05	0.0000025315	-1.301029996	-5.596622068
0.075	0.0000062953	-1.124938737	-5.200983569
0.10	0.0000088052	-1	-5.004671991
0.15	0.0000098930	-0.823908741	-5.004671991
0.20	0.0000107028	-0.698970004	-4.97050259

According to the formula v (Reaction rate) = k[**1a**]$^{\alpha}$ [**2a**]$^{\beta}$ [**3a**]$^{\gamma}$ [**L-RaPr$_2$**/Mg(OTf)$_2$]$^{\lambda}$ [Et$_3$N]$^{\delta}$, we can get the inference that log(v) =αlog([**1a**])+A. Calculating the data by means of excel, α = 0.973 was obtained, which indicates the reaction rate obeys a first order dependence on [**1a**].

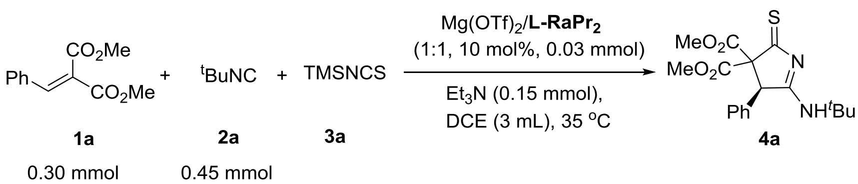






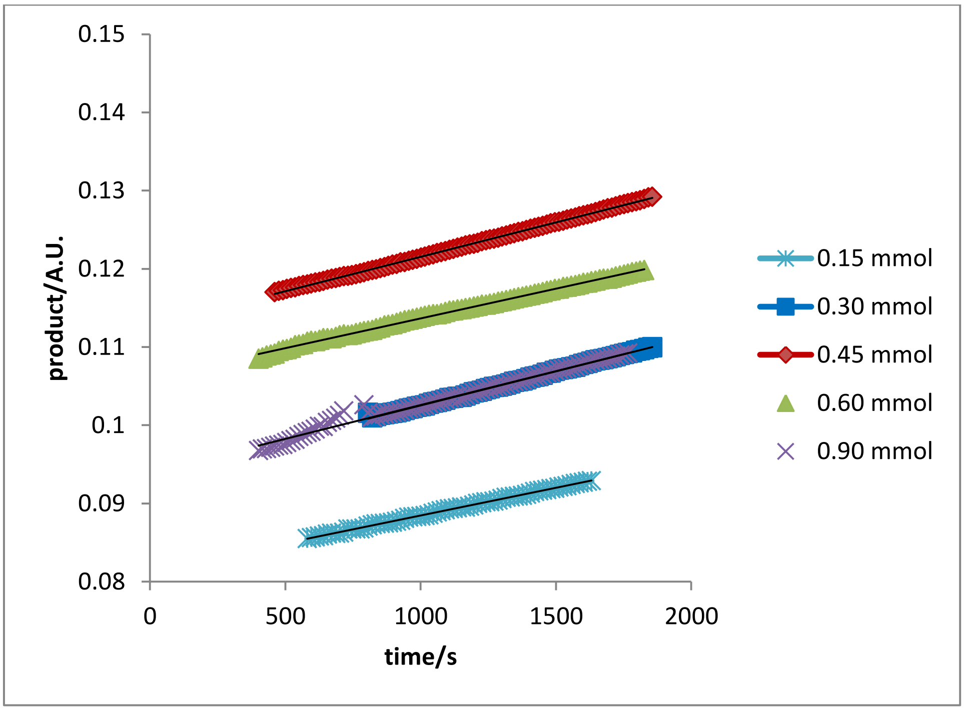
[**2a**]/(M)	reaction rate/(A.U./s)	Log([**2a**])	Log(**v**)
0.05	0.0000037986	-1.301029996	-5.420376436
0.075	0.0000050238	-1.124938737	-5.298967658
0.10	0.0000083253	-1	-5.082541756
0.15	0.0000088052	-0.823908741	-5.055260775
0.20	0.0000093144	-0.698970004	-5.030845116

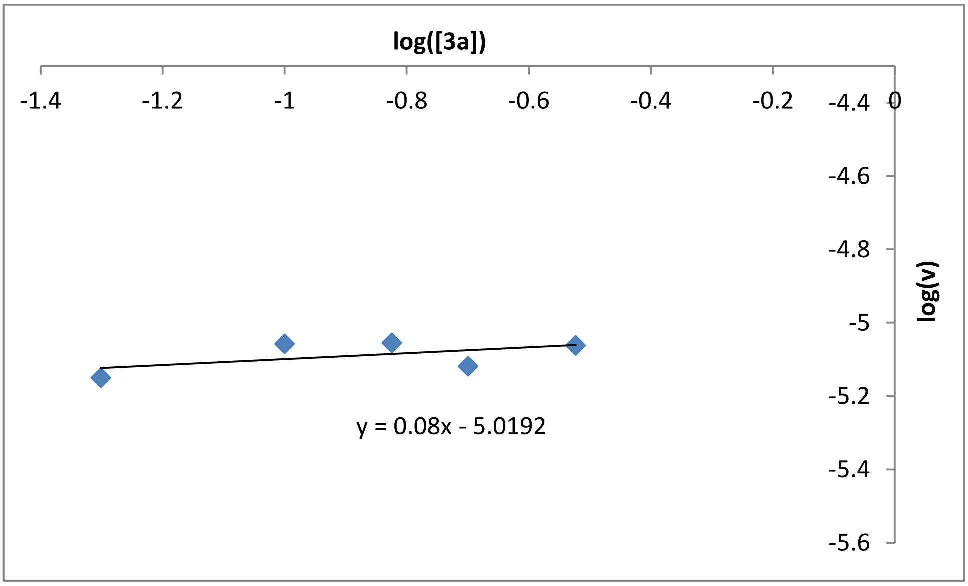
According to the formula v (Reaction rate) = k[**1a**]$^{\alpha}$ [**2a**]$^{\beta}$ [**3a**]$^{\gamma}$ [**L-RaPr$_2$**/Mg(OTf)$_2$]$^{\lambda}$ [Et$_3$N]$^{\delta}$, we can get the inference that log(v) = βlog([**2a**])+B. Calculating the data by means of excel, β = 0.677 was obtained, which indicates the reaction rate obeys a fractional partial order dependence on [**2a**].



3a

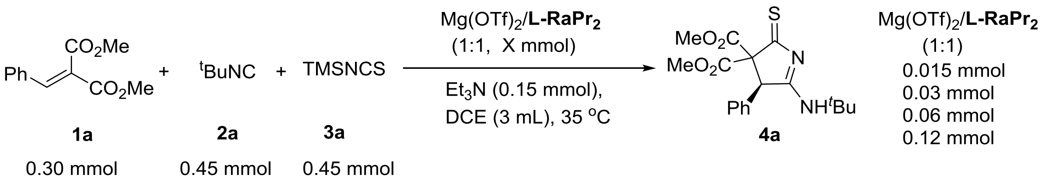
0.15 mmol
0.30 mmol
0.45 mmol
0.60 mmol
0.90 mmol

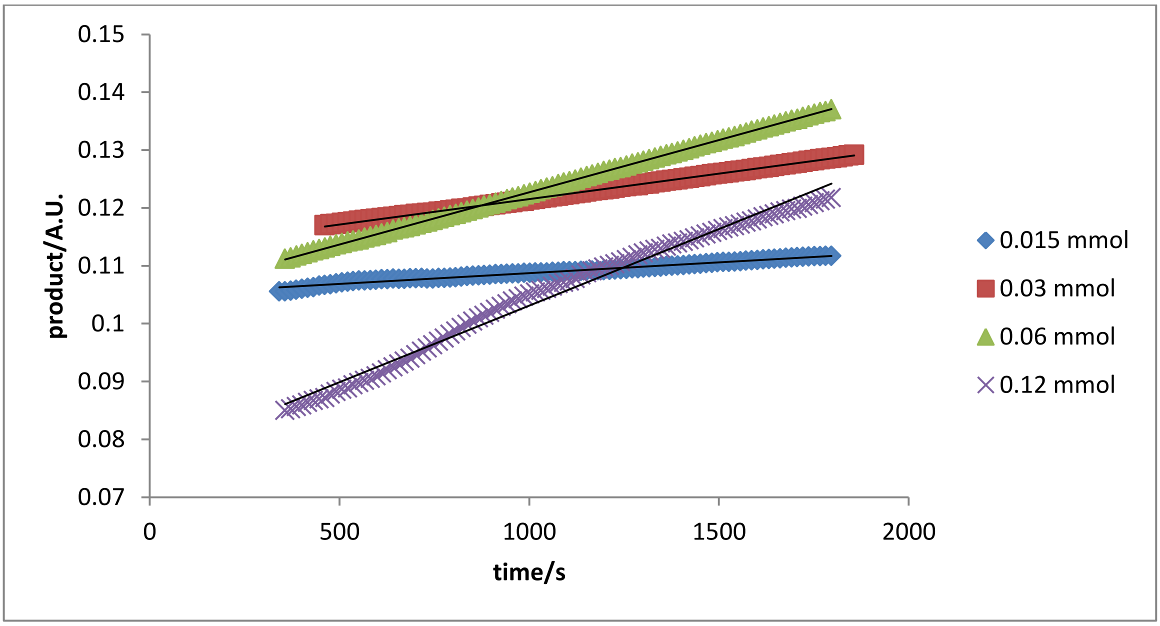


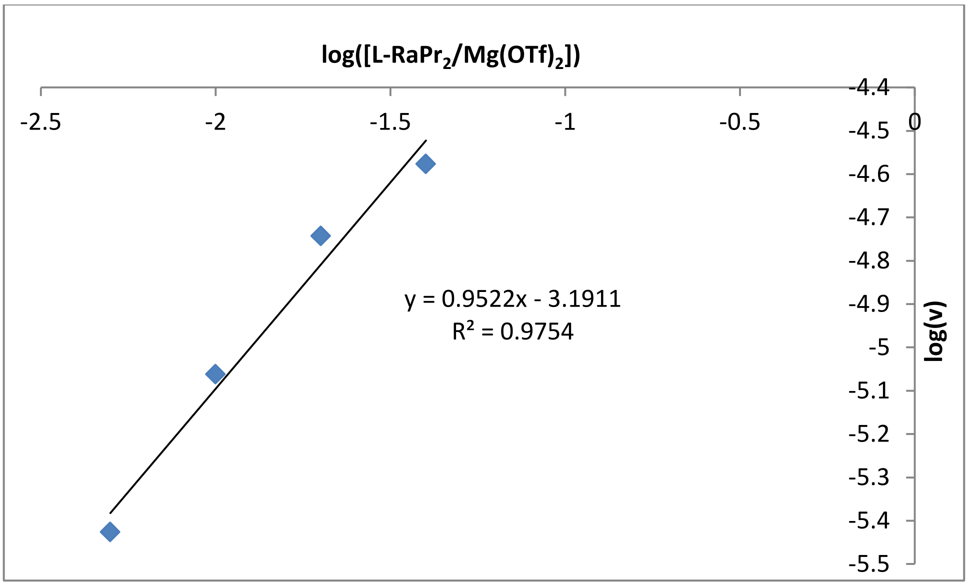


[**3a**]/(M)	reaction rate/(A.U./s)	Log([**3a**])	Log(**v**)
0.05	0.0000070921	-1.301029996	-5.150488454
0.10	0.0000087572	-1	-5.057634732
0.15	0.0000088052	-0.823908741	-5.055260775
0.20	0.0000076095	-0.698970004	-5.118643879
0.30	0.0000086749	-0.522878745	-5.061735523

According to the formula v (Reaction rate) = k[**1a**]$^{\alpha}$ [**2a**]$^{\beta}$ [**3a**]$^{\gamma}$ [**L-RaPr$_2$**/Mg(OTf)$_2$]$^{\lambda}$ [Et$_3$N]$^{\delta}$, we can get the inference that log(v) =γlog([**3a**])+C. Calculating the data by means of excel, γ = 0.08 was obtained, which indicates the reaction rate obeys a zero order dependence on [**3a**].

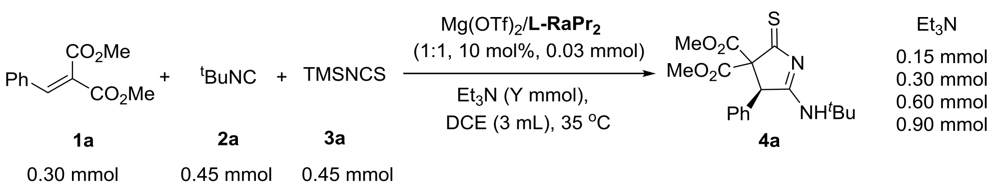


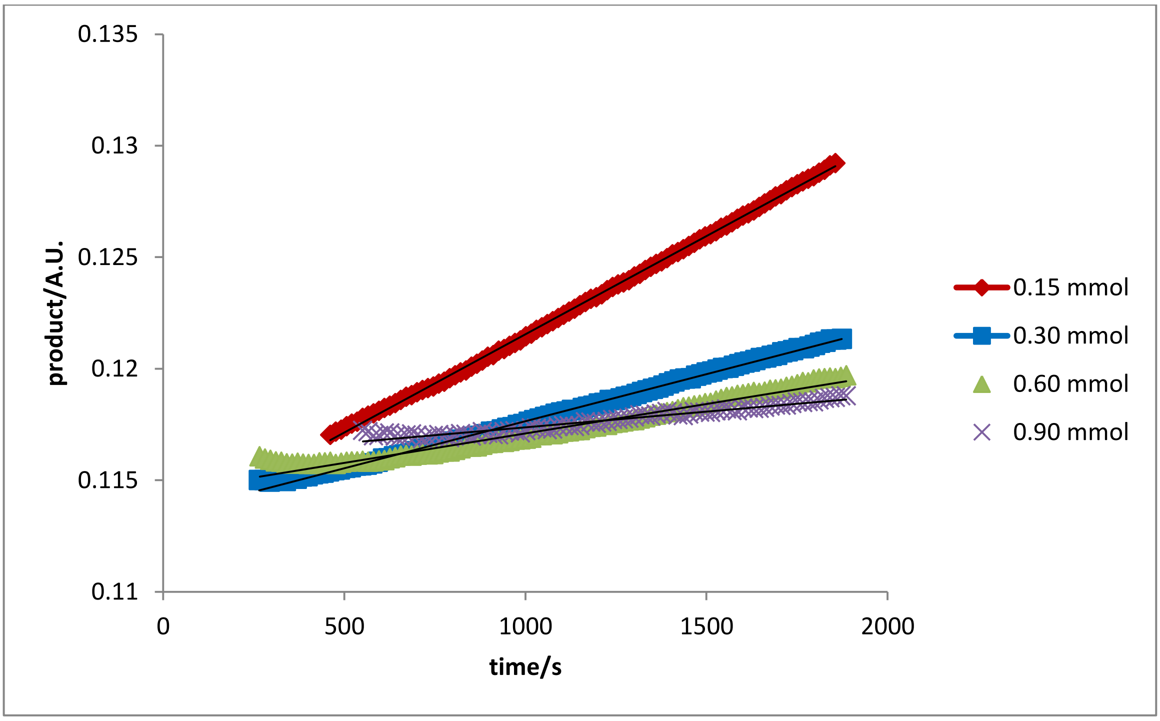


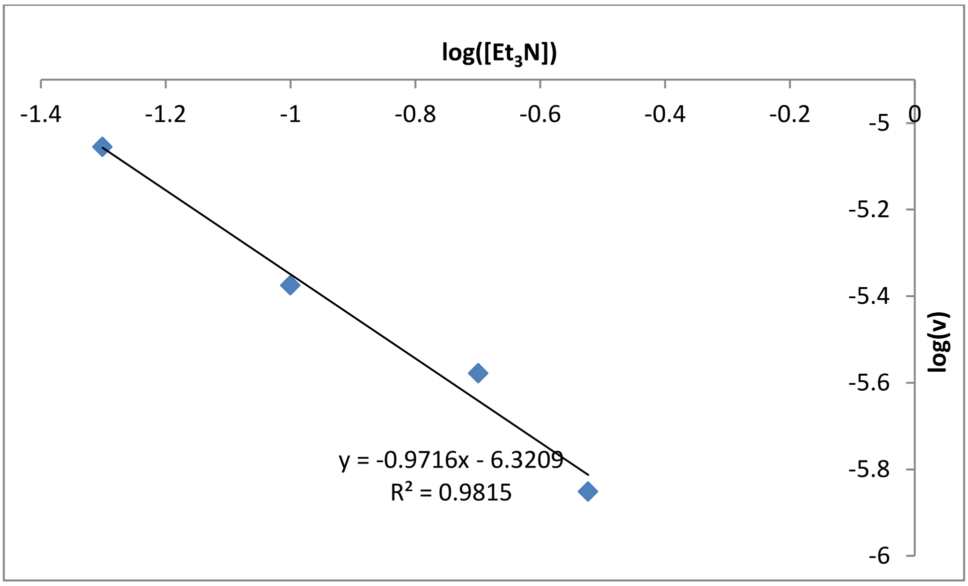


[catalyst]/(M)	reaction rate/(A.U./s)	Log([catalyst])	Log(**v**)
0.005	0.0000037490	-2.301029996	-5.42608456
0.01	0.0000088052	-2	-5.062326672
0.02	0.0000180636	-1.698970004	-4.743195692
0.04	0.0000264860	-1.397940009	-4.576983625

According to the formula v (Reaction rate) = k[**1a**]$^{\alpha}$ [**2a**]$^{\beta}$ [**3a**]$^{\gamma}$ [**L-RaPr$_2$**/Mg(OTf)$_2$]$^{\lambda}$ [Et$_3$N]$^{\delta}$, we can get the inference that log(v) = λlog([**L-RaPr$_2$**/Mg(OTf)$_2$])+D. Calculating the data by means of excel, λ = 0.952 was obtained, which indicates the reaction rate obeys a first order dependence on [**L-RaPr$_2$**/Mg(OTf)$_2$].





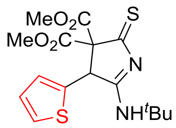


$[Et_3N]$/(M)	reaction rate/(A.U./s)	Log($[Et_3N]$)	Log(**v**)
0.05	0.0000088052	-1.301029996	-5.055260775
0.10	0.0000042119	-1	-5.375521948
0.20	0.0000026410	-0.698970004	-5.578231599
0.30	0.0000014060	-0.522878745	-5.852014679

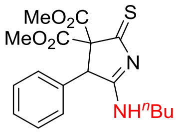
According to the formula v (Reaction rate) = k[**1a**]$^{\alpha}$ [**2a**]$^{\beta}$ [**3a**]$^{\gamma}$ [**L-RaPr$_2$**/Mg(OTf)$_2$]$^{\lambda}$ [Et_3N]$^{\delta}$, we can get the inference that log(v) = δlog([Et_3N])+E. Calculating the data by means of excel, δ = –0.972 was obtained, which indicates the reaction rate obeys a negative first-order dependence on [Et_3N].

To get more insight into the reaction mechanism, kinetic studies via operando IR experiments were performed (for more details, see ESI). Peak at 1335 cm^{-1} was identified as the characteristic absorption of the product **4a**. Kinetic studies exhibited that the initial rate of the reaction was approximate first-order kinetic dependence on the catalyst and alkylidene malonate **1a** and fractional order kinetic dependence on isocyanide **2a**. In contrast, zero-order was observed for TMSNCS. These results imply that catalyst, the initial addition reaction between **1a** and **2a** in the presence of chiral catalyst were involved in the rate-determining step, TMSNCS was not the real reactive species and the addition of NCS group occurred after the rate-determining step. Interestingly, the reaction rate roughly showed negative first-order on base additive, and the presence of base probably generated ammonium thiocyanate to undergo the sequential addition reaction, balancing the initial addition of isocyanide and avoiding the generation of competitive byproducts and racemization process.

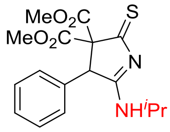
4. Unsuccessful substrate scope



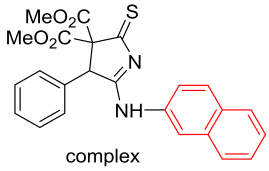
43% yield, 50:50 er



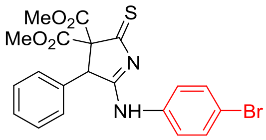
trace



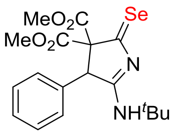
trace



complex

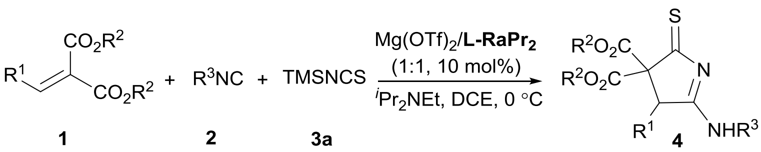


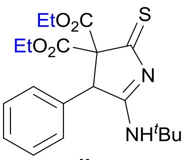
complex



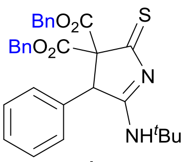
failed

5. Substrate scope with $^{i}Pr_2NEt$

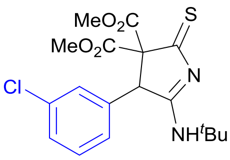




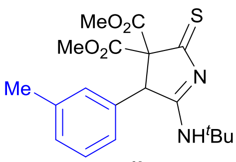
4b
54% yield, 91.5:8.5 er



4c
58% yield, 88:12 er

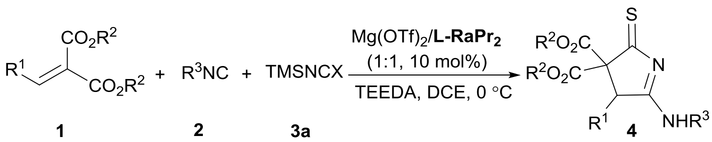


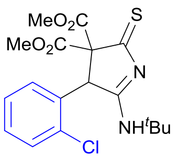
4e
39% yield, 90:10 er



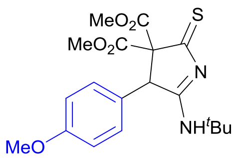
4h
43% yield, 74:26 er

6. Substrate scope with TEEDA at 0 °C

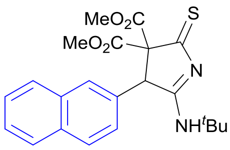




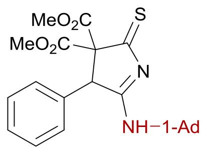
trace



trace



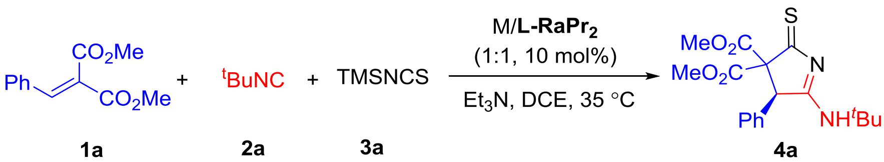
trace



trace

7. Optimization of reaction conditions

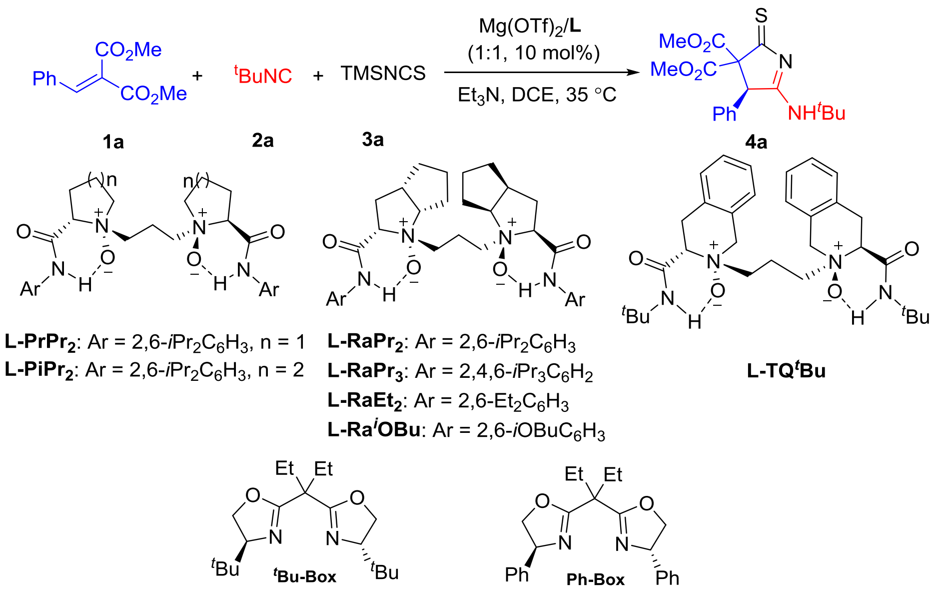
Table S1. Screening of the metal salts [a]



entry	metal salts	yield (%)	er
1	$Mg(OTf)_2$	86	85.5:14.5
2	$Mg(ClO_4)_2$	89	85:15
3	$Mg(NTf)_2$	91	83:17
4	$Zn(OTf)_2$	messy	-
5	$Cu(OTf)_2$	messy	-
6	$Ni(OTf)_2$	messy	-
7	$Sc(OTf)_3$	messy	-
8	$Yb(OTf)_3$	messy	-

[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), M/**L-RaPr₂** (1.0:1.0, 10.0 mol%) and Et_3N (0.5 mmol) in CH_2ClCH_2Cl (1.0 mL) at 35 °C for 24 h. Isolated yield and er was determined by CSP-HPLC analysis.

Table S2. Screening of the ligands [a]

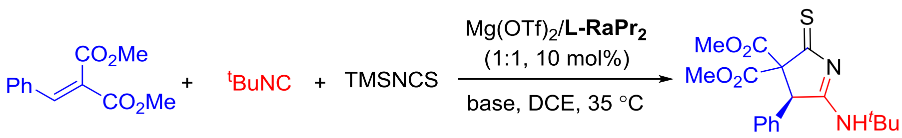


entry	ligands	yield (%)	er
1	**L-PrPr$_2$**	64	81.5:18.5
2	**L-PiPr$_2$**	96	75:25
3	**L-RaPr$_2$**	86	85.5:14.5
4	**L-RaPr$_3$**	90	77:23
5	**L-RaEt$_2$**	87	80:20

6	**L-Ra^{i}OBu$_2$**	35	65:35
7	**L-PrCPh$_3$**	33	63:37
8	**L-TQ^{t}Bu**	81	47:53
9	**^{t}Bu-Box**	93	50:50
10	**Ph-Box**	94	50:50

[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), $Mg(OTf)_2$/**L** (1.0:1.0, 10.0 mol%) and Et_3N in CH_2ClCH_2Cl (1.0 mL) at 35 °C for 24 h. Isolated yield and er was determined by CSP-HPLC analysis.

Table S3. Preliminary screening of the base [a]

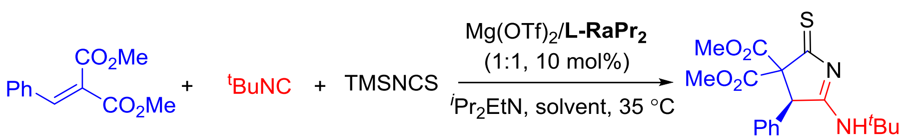


1a 2a 3a 4a

entry	base	yield (%)	er
1	Li_2CO_3	87	50:50
2	Na_2CO_3	70	76:24
3	k_2CO_3	91	87:13
4	Cs_2CO_3	58	66:34
5	Et_2NH	50	82:18
6	Et_3N	86	85.5:14.5
7	$^iPr_2EtN$	88	92:8
8	DMAP	82	53.5:46.5
9	DABCO	95	53:47

[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), $Mg(OTf)_2$/**L-RaPr$_2$** (1:1, 10.0 mol%) and base (0.05 mmol) in CH_2ClCH_2Cl (1.0 mL) at 35 °C for 24 h. Isolated yield and er was determined by CSP-HPLC analysis.

Table S4. Screening of the solvents [a]



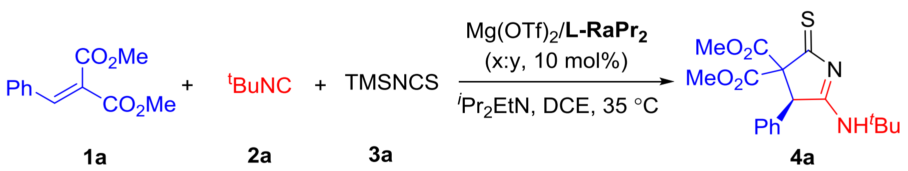
1a 2a 3a 4a

Entry	solvent	yield (%)	er
1	CH_2ClCH_2Cl	88	92:8
2	CH_2Cl_2	56	82:18

3	$CHCl_3$	88	88:12
4	$CHCl_2CHCl_2$	72	85:15
5	Toluene	trace	-
6	Et_2O	69	85:15
7	THF	nr	-
9	PhCl	50	79:21

[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), $Mg(OTf)_2$/**L-RaPr₂** (1.0:1.0, 10.0 mol%) and $^{i}Pr_2EtN$ (0.05 mmol) in solvent (1.0 mL) at 35 °C for 24 h. Isolated yield and er was determined by CSP-HPLC analysis

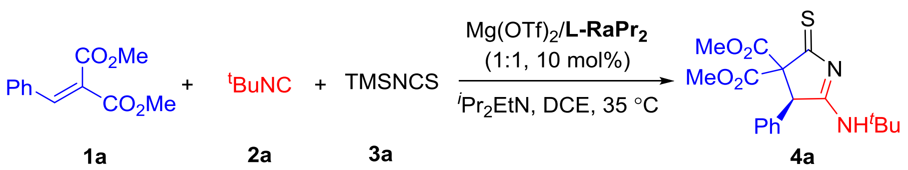
Table S5. Screening of the ratio of metal salt and ligand [a]



entry	M/**L** (x:y)	yield (%)	er
1	1.5:1.0	80	90:10
2	1.2:1.0	93	91:9
3	1.0:1.0	88	92:8
4[b]	1.0:1.5	89	91.5:8.5
5[c]	1.0:2.0	95	91.5:8.5

[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), $Mg(OTf)_2$/**L-RaPr₂** (x:y, 10.0 mol%) and $^{i}Pr_2EtN$ (0.05 mmol) in CH_2ClCH_2Cl (1.0 mL) at 35 °C for 24 h. Isolated yield and er was determined by CSP-HPLC analysis

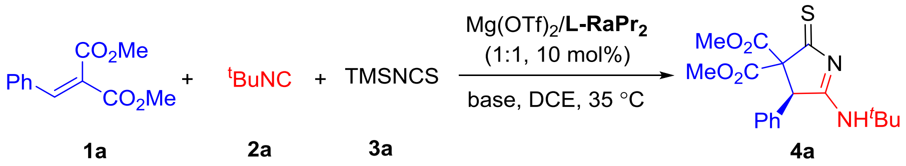
Table S6. Screening of the amount of base [a]

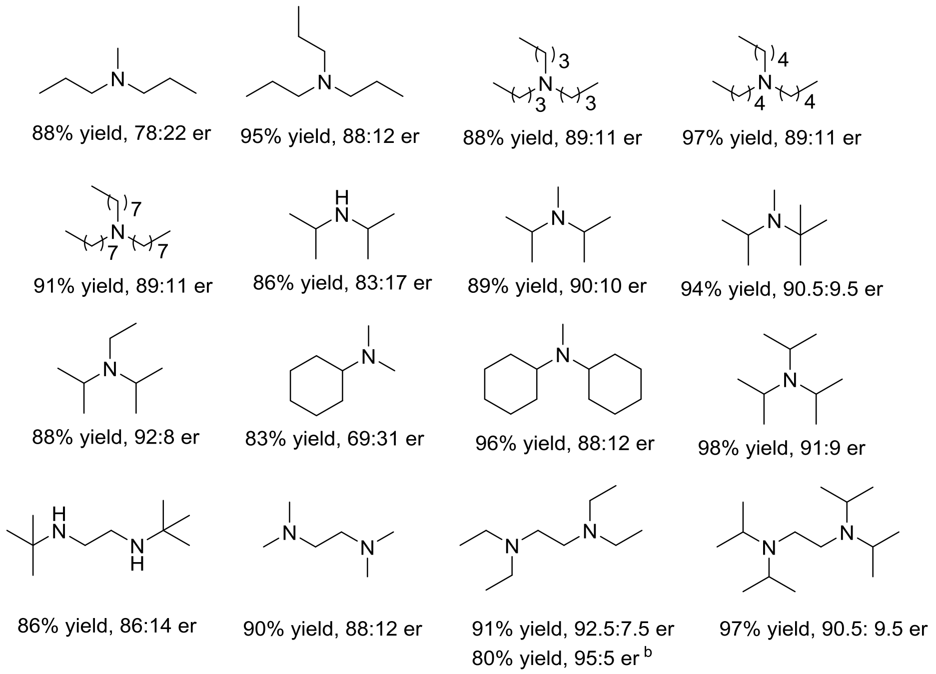


entry	the amount of $^{i}Pr_2EtN$ (x)	yield (%)	er
1	0.25 equiv	83	91:9
2	0.5 equiv	88	92:8
3	1.0 equiv	72	91:9
4	1.5 equiv	51	91:9

[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), $Mg(OTf)_2$/**L-RaPr₂** (1.0:1.0, 10.0 mol%) and $^{i}Pr_2EtN$ (x mmol) in DCE (1.0 mL) at 35 °C for 24 h. Isolated yield and er was determined by CSP-HPLC analysis.

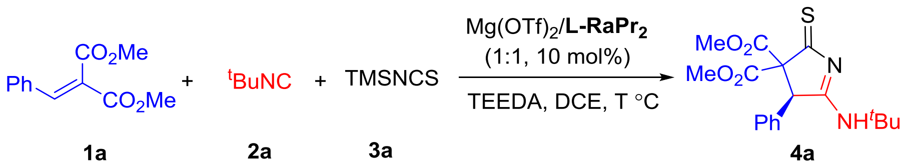
Table S7. Screening of the base [a]





[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), $Mg(OTf)_2$/**L-RaPr₂** (1.0:1.0, 10.0 mol%) and base (0.05 mmol; diamines was 0.025 mmol) in CH_2ClCH_2Cl (1.0 mL) at 35 °C for 24 h. Isolated yield and er was determined by CSP-HPLC analysis. [b] at 0 °C for 96 h.

Table S8. Screening of the temperature [a]

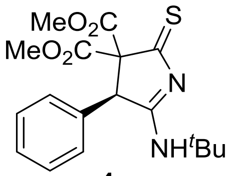


entry	temperature (°C)	yield (%)	er
1[b]	35	91	92.5:7.5
2	0	80	95:5
3	-5	70	95:5
4	-20	trace	-
5[c]	0	48	94.5:5.5
6[d]	0	51	94:6

[a] All reactions were carried out **1a** (0.10 mmol), **2a** (0.15 mmol), **3a** (0.15 mmol), $Mg(OTf)_2$/**L-RaPr₂** (1.0:1.0, 10.0 mol%) and TEEDA (0.025 mmol) in CH_2ClCH_2Cl (1.0 mL) at T °C for 96 h. Isolated yield and er was determined by CSP-HPLC analysis. [b] 35°C for 24 h. [c] 4 Å MS was added as additive. [d] Conducting the reaction in glove box.

8. The analytical and spectral characterization data of products

Dimethyl (*S*)-5-(*tert*-butylamino)-4-phenyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4a)



4a

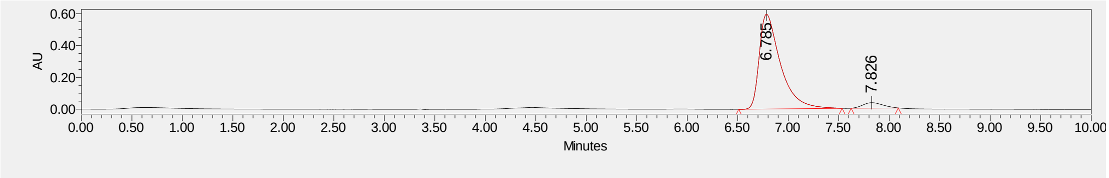
Yellow solid; m.p. 175–179 °C; 29.1 mg, 80% yield, 95:5 er; $[\alpha]^{22}_{D}$ = –15.32 (*c* = 0.44 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IF**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 6.76 min, t_R (minor) = 7.83 min.

IR (neat):3309, 2952, 2361, 1728, 1599, 1531, 1455, 1434, 1322, 1288, 1207, 1124, 1099, 1049, 762 and 701 cm^{-1}.

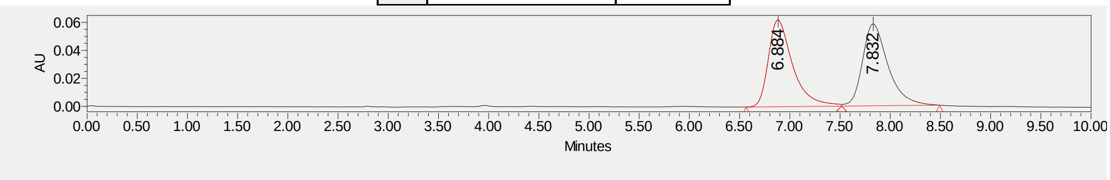
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 – 7.31 (m, 3H), 7.12 – 7.06 (m, 2H), 5.68 (s, 1H), 5.23 (s, 1H), 3.83 (s, 3H), 3.11 (s, 3H), 1.50 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.7, 181.7, 166.9, 165.9, 133.7, 129.6, 129.1, 129.1, 79.4, 59.1, 56.0, 54.0, 52.3, 28.9.

HRMS (ESI-FT) calcd for $C_{18}H_{23}N_2O_4S^+$ ([M+H$^+$]) = 363.1373, Found 363.1365.

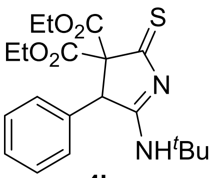


	Retention Time	% Area
1	6.785	94.92
2	7.826	5.08



	Retention Time	% Area
1	6.884	50.28
2	7.832	49.72

Diethyl 5-(*tert*-butylamino)-4-phenyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4b)



4b

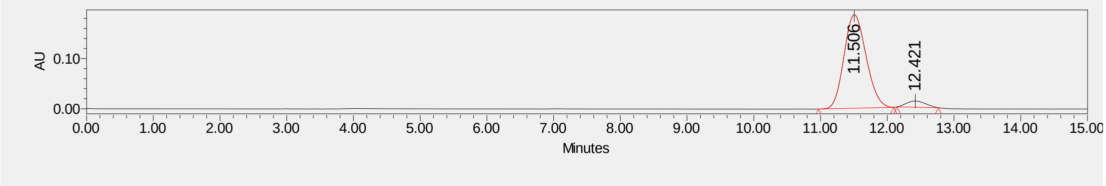
Yellow solid; m.p. 164–168 °C; 25.3 mg, 65% yield, 94.5:5.5 er; $[\alpha]^{22}_{D}$ = –12.16 (*c* = 0.36 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 11.51 min, t_R (minor) = 12.42 min.

IR (neat): 3307, 2978, 2930, 2361, 1724, 1598, 1534, 1456, 1367, 1332, 1228, 1125, 1198, 1048, 762 and 701 cm^{-1}.

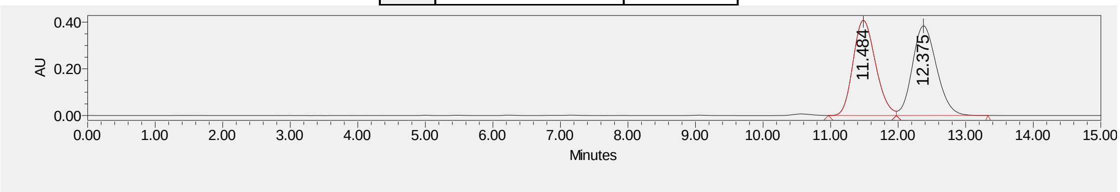
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 – 7.31 (m, 3H), 7.15 – 7.09 (m, 2H), 5.52 (s, 1H), 5.21 (s, 1H), 4.35 – 4.26 (m, 2H), 3.74 – 3.63 (m, 1H), 3.51 – 3.40 (m, 1H), 1.49 (s, 9H), 1.30 (t, *J* = 7.2 Hz, 3H), 0.80 (t, *J* = 7.2 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 218.2, 181.8, 166.5, 165.6, 134.0, 129.7, 129.1, 129.0, 79.1, 63.2, 61.7, 59.1, 55.9, 28.9, 14.0, 13.5.

HRMS (ESI-FT) calcd for $C_{20}H_{27}N_2O_4S^+$ ([M+H$^+$]) = 391.1686, Found 391.1678.

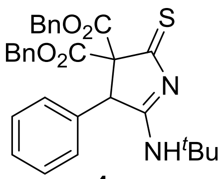


	Retention Time	% Area
1	11.506	94.55
2	12.421	5.45



	Retention Time	% Area
1	11.484	49.70
2	12.375	50.30

Dibenzyl 5-(*tert*-butylamino)-4-phenyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4c)



4c

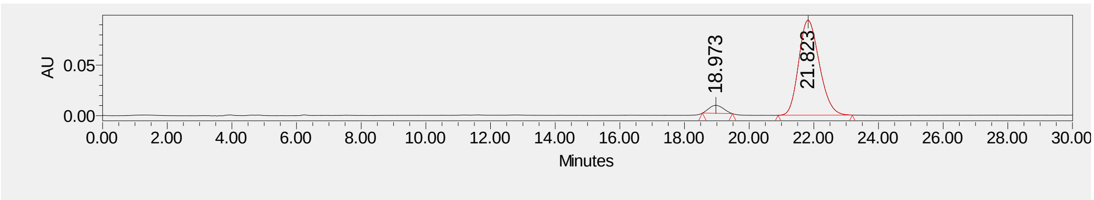
Yellow solid; m.p. 72–76 °C; 34.8 mg, 68% yield, 94.5:5.5 er; $[\alpha]^{22}_{D}$ = –9.85 (*c* = 0.68 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 21.82 min, t_R (minor) = 18.97 min.

IR (neat): 3313, 2926, 2360, 1723, 1597, 1531, 1455, 1369, 1331, 1288, 1207, 1121, 1096, 749 and 697 cm^{-1}.

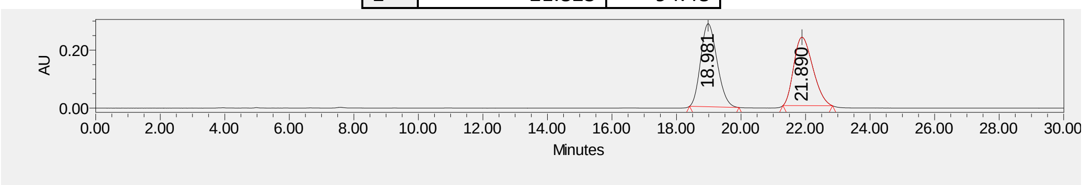
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 – 7.21 (m, 11H), 7.11 – 7.05 (m, 2H), 6.99 – 6.77 (m, 2H), 5.53 (s, 1H), 5.31 – 5.07 (m, 3H), 4.66 (d, *J* = 12.4 Hz, 1H), 4.24 (d, *J* = 12.4 Hz, 1H), 1.48 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.5, 181.7, 166.3, 165.3, 135.2, 134.7, 133.7, 129.7, 129.2, 129.1, 128.5, 128.4, 128.3, 128.2, 79.3, 68.9, 67.5, 59.2, 56.0, 28.9.

HRMS (ESI-FT) calcd for $C_{30}H_{31}N_2O_4S^+$ ([M+H$^+$]) = 515.1999, Found 515.2001.

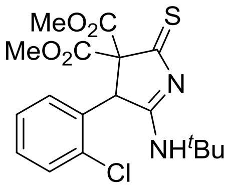


	Retention Time	% Area
1	18.973	5.52
2	21.823	94.48



	Retention Time	% Area
1	18.981	51.13
2	21.890	48.87

Dimethyl 5-(*tert*-butylamino)-4-(2-chlorophenyl)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4d)



4d

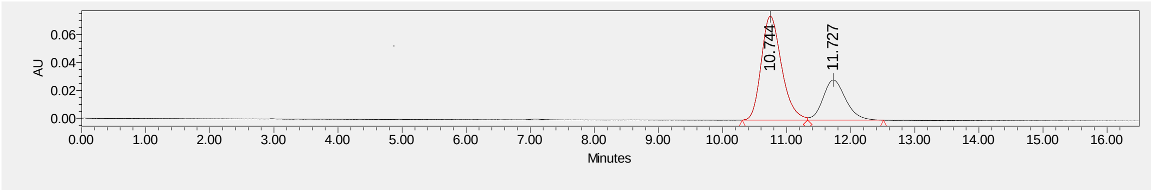
Yellow solid; m.p. 198–202 °C; 22.5 mg, 57% yield, 70:30 er; $[\alpha]^{22}_{D}$ = +53.47 (c = 0.40 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 10.75 min, t_R (minor) = 11.73 min.

IR (neat): 3310, 2953, 1728, 1600, 1532, 1476, 1435, 1338, 1293, 1207, 1124, 1099, 1050 and 760 cm^{-1}.

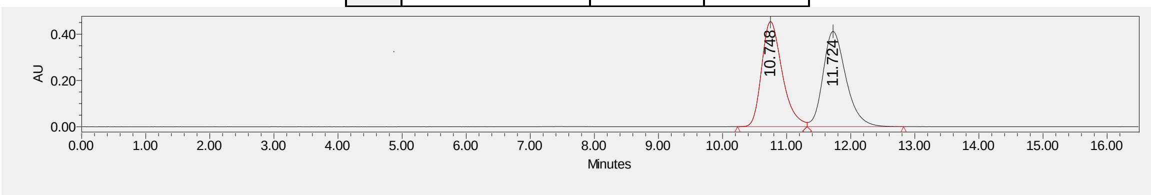
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.47 – 7.40 (m, 1H), 7.31 – 7.22 (m, 2H), 7.00 – 6.89 (d, J = 7.5 Hz, 1H), 5.75 (d, J = 2.4 Hz, 1H), 5.57 (s, 1H), 3.85 (s, 3H), 3.12 (s, 3H), 1.52 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 218.1, 181.7, 166.5, 165.7, 136.2, 132.6, 130.3, 130.0, 129.8, 127.4, 78.4, 56.3, 55.7, 54.2, 52.3, 28.9.

HRMS (ESI-FT) calcd for $C_{18}H_{22}{}^{35}ClN_2O_4S^+$ ([M+H$^+$]) = 397.0983, Found 397.0983; $C_{18}H_{22}{}^{37}ClN_2O_4S^+$ ([M+H$^+$]) = 399.0954, Found 399.0949.

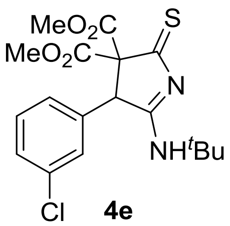


	Retention Time	% Area	Height
1	10.744	69.93	74609
2	11.727	30.07	28816



	Retention Time	% Area
1	10.748	49.80
2	11.724	50.20

Dimethyl 5-(*tert*-butylamino)-4-(3-chlorophenyl)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4e)



4e

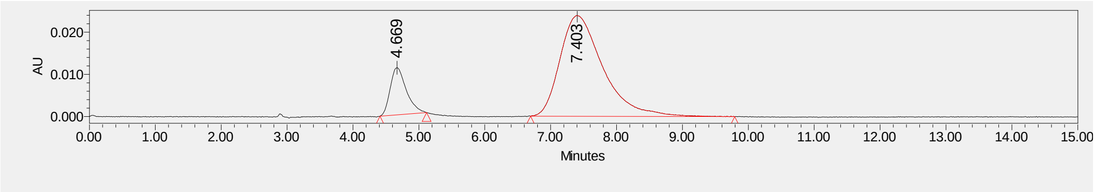
Yellow solid; m.p. 97–101 °C; 20.5 mg, 52% yield, 85:15 er; $[\alpha]^{22}_{D}$ = –4.05 (c = 0.37 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IG**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 7.40 min, t_R (minor) = 4.67 min.

IR (neat): 3309, 2971, 2360, 1729, 1602, 1533, 1476, 1433, 1336, 1288, 1206, 1125, 1099, 1050, 750 and 694 cm^{-1}.

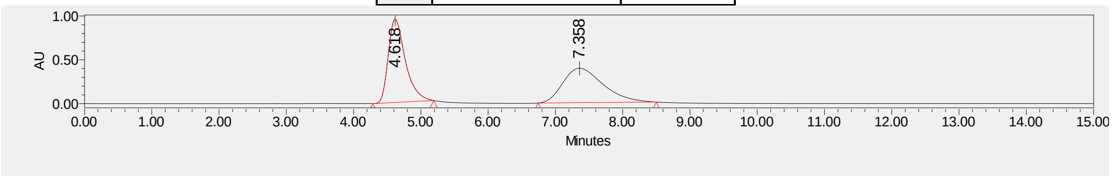
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 – 7.26 (m, 2H), 7.17 – 7.11 (m, 1H), 7.01 – 6.95 (m, 1H), 5.55 (s, 1H), 5.20 (s, 1H), 3.86 (s, 3H), 3.22 (s, 3H), 1.52 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.3, 180.9, 166.8, 165.8, 135.7, 135.0, 130.4, 129.4, 79.3, 58.7, 56.3, 54.2, 52.5, 28.9.

HRMS (ESI-FT) calcd for $C_{18}H_{22}{}^{35}ClN_2O_4S^+$ ([M+H$^+$]) = 397.0983, Found 397.0980; $C_{18}H_{22}{}^{37}ClN_2O_4S^+$ ([M+H$^+$]) = 399.0954, Found 399.0956.

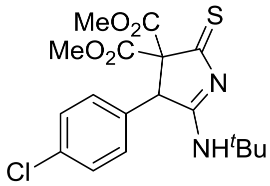


	Retention Time	% Area
1	4.669	14.95
2	7.403	85.05



	Retention Time	% Area
1	4.618	50.67
2	7.358	49.33

Dimethyl 5-(*tert*-butylamino)-4-(4-chlorophenyl)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4f)



4f

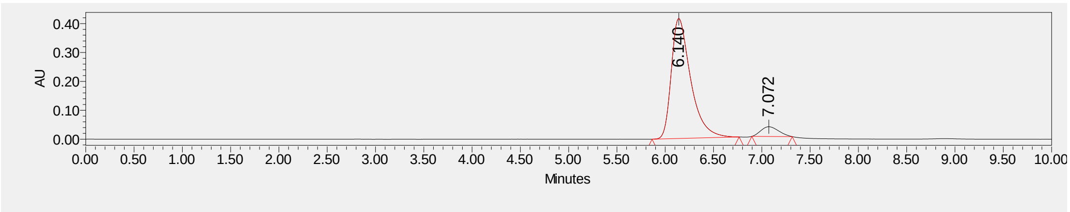
Yellow solid; m.p. 136–140 °C; 33.8 mg, 85% yield, 93:7 er; $[\alpha]^{22}_{D}$ = –27.24 (c = 0.62 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IF**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 6.14 min, t_R (minor) = 7.07 min.

IR (neat): 3312, 2953, 2361, 1729, 1601, 1534, 1492, 1434, 1288, 1207, 1125, 1094, 1050, 1017, 838, 799 and 749 cm^{-1}.

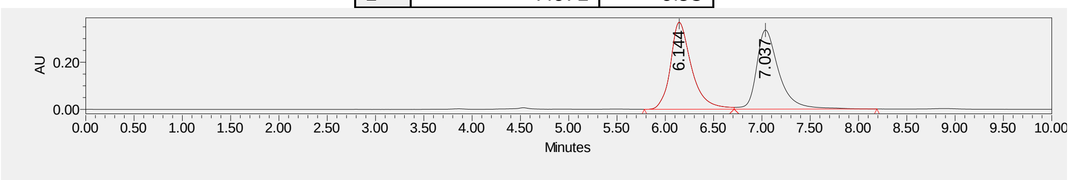
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.39 – 7.26 (m, 2H), 7.08 – 7.00 (m, 2H), 5.67 (s, 1H), 5.20 (s, 1H), 3.84 (s, 3H), 3.19 (s, 3H), 1.49 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.3, 181.2, 166.7, 165.8, 135.2, 132.3, 130.9, 129.3, 79.2, 58.5, 56.2, 54.1, 52.5, 28.9.

HRMS (ESI-FT) calcd for $C_{18}H_{22}{}^{35}ClN_2O_4S^+$ ([M+H$^+$]) = 397.0983, Found 397.0992; $C_{18}H_{22}{}^{37}ClN_2O_4S^+$ ([M+H$^+$]) = 399.0954, Found 399.0961.

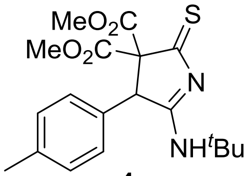


	Retention Time	% Area
1	6.140	93.07
2	7.072	6.93



	Retention Time	% Area
1	6.144	50.99
2	7.037	49.01

Dimethyl 5-(*tert*-butylamino)-2-thioxo-4-(*p*-tolyl)-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4g)



4g

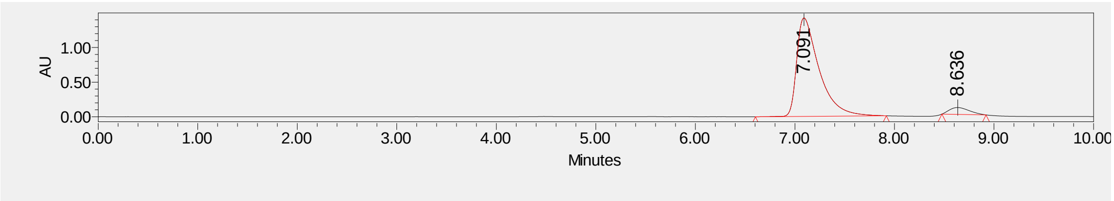
Yellow solid; m.p. 85–89 °C; 25.6 mg, 68% yield, 94:6 er; $[\alpha]^{22}_D$ = –31.06 (*c* = 0.40 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IF**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 7.09 min, t_R (minor) = 8.64 min.

IR (neat): 3311, 2952, 2360, 2341, 1729, 1600, 1533, 1433, 1337, 1288, 1208, 1125, 1099, 940 and 749 cm^{-1}.

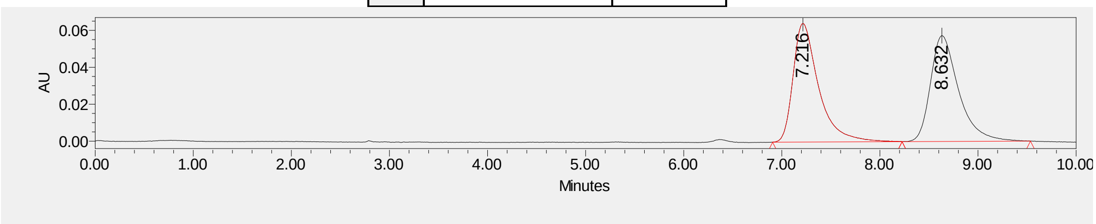
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.21 – 7.12 (m, 2H), 7.03 – 6.92 (m, 2H), 5.58 (s, 1H), 5.20 (s, 1H), 3.84 (s, 3H), 3.17 (s, 3H), 2.33 (s, 3H), 1.50 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 218.0, 182.0, 167.0, 166.0, 139.1, 130.5, 129.8, 129.5, 79.4, 58.9, 56.0, 54.0, 52.4, 28.9, 21.3.

HRMS (ESI-FT) calcd for $C_{19}H_{25}N_2O_4S^+$ ([M+H$^+$]) = 377.1530, Found 377.1528.

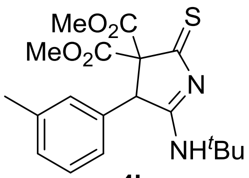


	Retention Time	% Area
1	7.091	94.17
2	8.636	5.83



	Retention Time	% Area
1	7.216	50.44
2	8.632	49.56

Dimethyl 5-(*tert*-butylamino)-2-thioxo-4-(*m*-tolyl)-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4h)



4h

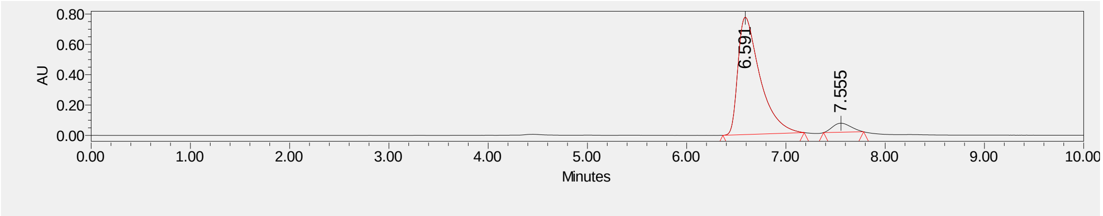
Yellow solid; m.p. 116–120 °C; 21.2 mg, 56% yield, 94:6 er; $[\alpha]^{22}_D$ = –16.48 (*c* = 0.35 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IF**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 6.59 min, t_R (minor) = 7.55 min.

IR (neat): 3310, 2953, 2361, 1729, 1560, 1534, 1433, 1336, 1289, 1207, 1124, 1098, 1050, 748, 750 and 703 cm^{-1}.

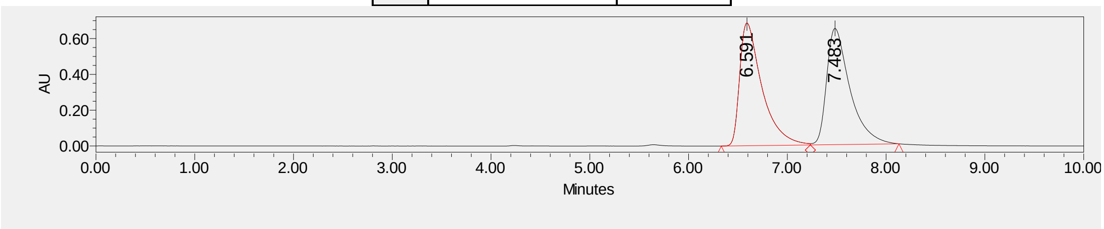
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25 – 7.19 (m, 1H), 7.16 – 7.12 (m, 1H), 6.95 – 6.91 (m, 1H), 6.90 – 6.85 (m, 1H), 5.55 (s, 1H), 5.20 (s, 1H), 3.85 (s, 3H), 3.16 (s, 3H), 2.33 (s, 3H), 1.51 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 218.0, 181.9, 167.0, 165.9, 139.0, 133.6, 130.5, 129.8, 129.0, 126.5, 79.4, 59.2, 56.0, 54.1, 54.0, 52.3, 29.0, 21.4.

HRMS (ESI-FT) calcd for $C_{19}H_{25}N_2O_4S^+$ ([M+H$^+$]) = 377.1530, Found 377.1526.

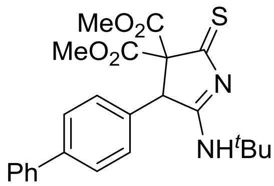


	Retention Time	% Area
1	6.591	94.01
2	7.555	5.99



	Retention Time	% Area
1	6.591	50.27
2	7.483	49.73

Dimethyl 4-([1,1'-biphenyl]-4-yl)-5-(*tert*-butylamino)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4i)



4i

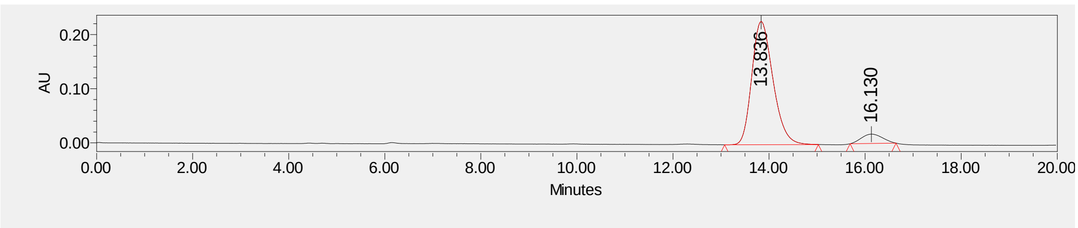
Yellow solid; m.p. 157–161 °C; 20.6 mg, 47% yield, 93:7 er; $[\alpha]^{22}_{D}$ = –63.55 (c = 0.31 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 13.84 min, t_R (minor) = 16.13 min.

IR (neat): 3309, 2971, 2360, 2341, 1729, 1560, 1533, 1487, 1434, 1337, 1288, 1207, 1124, 1098, 765, 750 and 699 cm^{-1}.

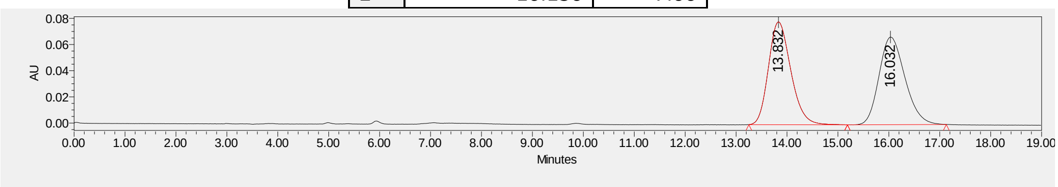
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.61 – 7.55 (m, 4H), 7.48 – 7.42 (m, 2H), 7.40 – 7.35 (m, 1H), 7.21 – 7.14 (m, 2H), 5.63 (s, 1H), 5.29 (s, 1H), 3.87 (s, 3H), 3.17 (s, 3H), 1.53 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.8, 181.7, 167.0, 166.0, 141.9, 139.9, 132.6, 130.1, 129.1, 128.1, 127.7, 127.2, 127.1, 79.5, 58.9, 56.1, 54.1, 52.5, 29.0.

HRMS (ESI-FT) calcd for $C_{24}H_{27}N_2O_4S^+$ ($[M+H^+]$) = 439.1686, Found 439.1687.



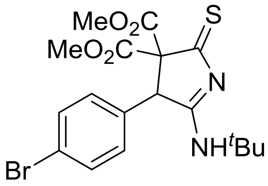
	Retention Time	% Area
1	13.836	93.00
2	16.130	7.00



	Retention Time	% Area

1	13.832	50.29
2	16.032	49.71

Dimethyl 4-(4-bromophenyl)-5-(*tert*-butylamino)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4j)



4j

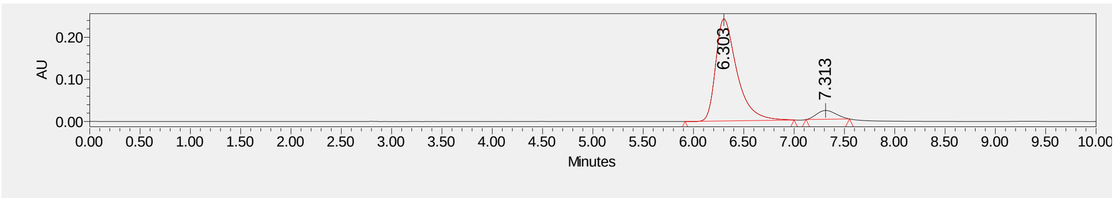
Yellow solid; m.p. 177–181 °C; 22.4 mg, 51% yield, 93:7 er; $[\alpha]^{22}_{D}$ = –33.58 (c = 0.55 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IF**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 6.30 min, t_R (minor) = 7.31 min.

IR (neat): 3311, 2952, 2360, 1728, 1600, 1532, 1488, 1434, 1407, 1335, 1286, 1207, 1125, 1099, 1049,1012, 836, 798 and 748 cm^{-1}.

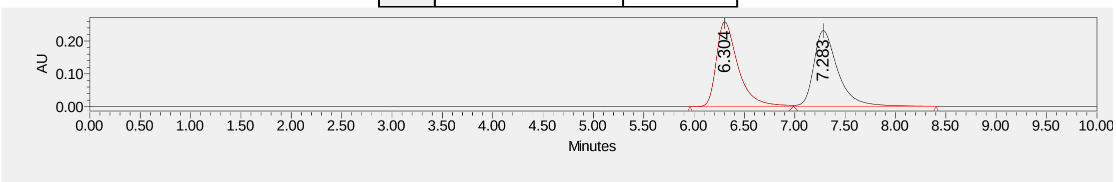
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 – 7.42 (m, 2H), 7.06 – 6.93 (m, 2H), 5.64 (s, 1H), 5.18 (s, 1H), 3.84 (s, 3H), 3.19 (s, 3H), 1.50 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.3, 181.1, 166.7, 165.8, 132.8, 132.3, 131.2, 123.4, 79.1, 58.5, 56.2, 54.1, 52.5, 28.9.

HRMS (ESI-FT) calcd for $C_{18}H_{22}{}^{79}BrN_2O_4S^+$ ([M+H$^+$]) = 441.0478, Found 441.0485; $C_{18}H_{22}{}^{81}BrN_2O_4S^+$ ([M+H$^+$]) = 443.0458, Found 443.0462.

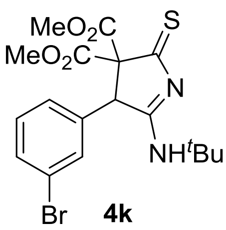


	Retention Time	% Area
1	6.303	92.74
2	7.313	7.26



	Retention Time	% Area
1	6.304	50.23
2	7.283	49.77

Dimethyl 4-(3-bromophenyl)-5-(*tert*-butylamino)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4k)



4k

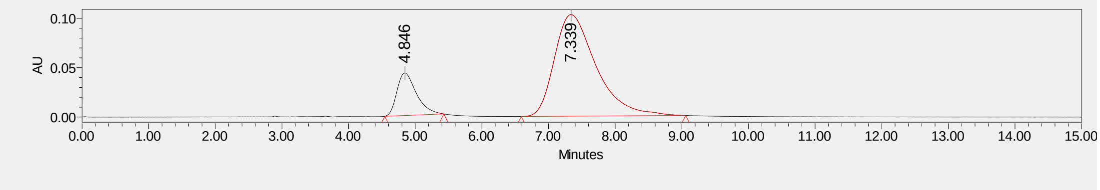
Yellow solid; m.p. 84–88 °C; 30.2 mg, 68% yield, 84:16 er; $[\alpha]^{22}_{D}$ = –5.16 (c = 0.50 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IG**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 7.34 min, t_R (minor) = 4.85 min.

IR (neat): 3309, 2952, 2360, 1729, 1601, 1532, 1475, 1433, 1335, 1287, 1206, 1125, 1099, 1049, 479 and 694 cm^{-1}.

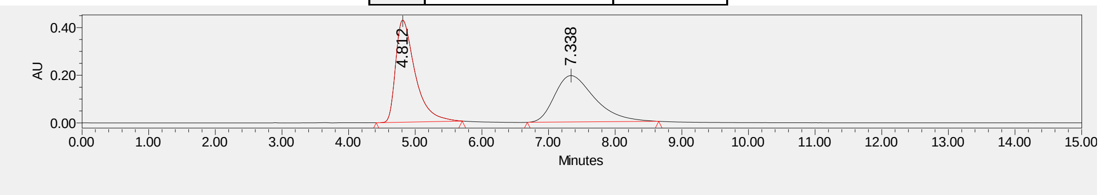
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.51 – 7.42 (m, 2H), 7.06 – 6.93 (m, 2H), 5.64 (s, 1H), 5.18 (s, 1H), 3.84 (s, 3H), 3.19 (s, 3H), 1.50 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.2, 181.0, 166.7, 165.7, 136.0, 132.3, 130.7, 123.0, 121.1, 79.3, 58.6, 56.2, 54.2, 52.5, 28.9.

HRMS (ESI-FT) calcd for $C_{18}H_{22}{}^{79}BrN_2O_4S^+$ ([M+H$^+$]) = 441.0478, Found 441.0479; $C_{18}H_{22}{}^{81}BrN_2O_4S^+$ ([M+H$^+$]) = 443.0458, Found 443.0458.

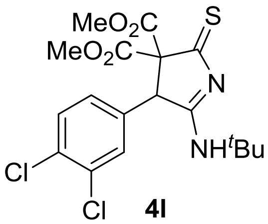


	Retention Time	% Area
1	4.846	16.34
2	7.339	83.66



	Retention Time	% Area
1	4.812	51.62
2	7.338	48.38

Dimethyl 5-(*tert*-butylamino)-4-(3,4-dichlorophenyl)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4l)



4l

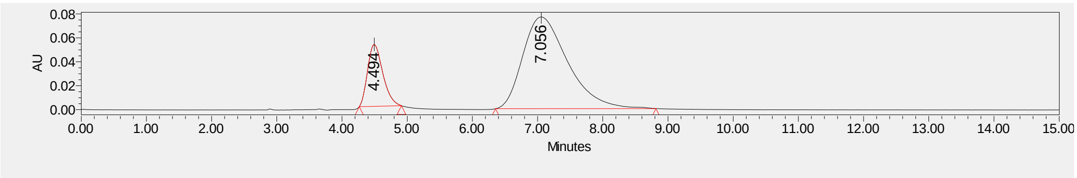
Yellow solid; m.p. 66–70 °C; 30.3 mg, 70% yield, 81.5:18.5 er; $[\alpha]^{22}_{D}$ = –19.11 (c = 0.65 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IG**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 7.06 min, t_R (minor) = 4.49 min.

IR (neat): 3310, 2953, 1728, 1599, 1531, 1470, 1434, 1398, 1331, 1283, 1203, 1130, 1099, 1033, 946, 896, 737 and 677 cm^{-1}.

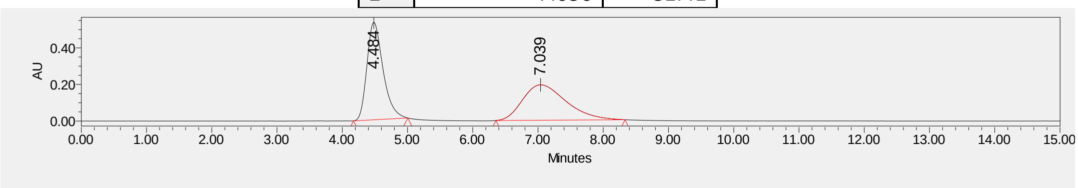
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.46 – 7.40 (m, 1H), 7.26 – 7.22 (m, 1H), 6.98 – 6.87 (m, 1H), 5.66 (s, 1H), 5.18 (s, 1H), 3.85 (s, 3H), 3.26 (s, 3H), 1.51 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 216.9, 180.5, 166.6, 165.7, 133.9, 133.6, 133.3, 131.7, 131.1, 128.6, 79.1, 58.1, 56.3, 54.3, 52.6, 28.9.

HRMS (ESI-FT) calcd for $C_{18}H_{21}{}^{35}Cl_2N_2O_4S^+$ ([M+H$^+$]) = 431.0594, Found 431.0599; $C_{18}H_{21}{}^{35}Cl^{37}ClN_2O_4S^+$ ([M+H$^+$]) = 433.0564, Found 433.0567; $C_{18}H_{21}{}^{37}Cl_2N_2O_4S^+$ ([M+H$^+$]) = 435.0535, Found 435.0534.

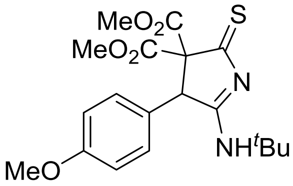


	Retention Time	% Area
1	4.494	18.59
2	7.056	81.41



	Retention Time	% Area
1	4.484	50.46
2	7.039	49.54

Dimethyl 5-(*tert*-butylamino)-4-(4-methoxyphenyl)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4m)



4m

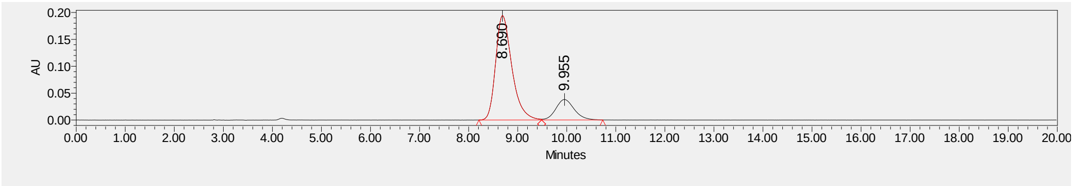
Yellow solid; m.p. 105–109 °C; 30.9 mg, 79% yield, 82:18 er; $[\alpha]^{22}_D$ = –33.74 (*c* = 0.49 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IF**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 8.69 min, t_R (minor) = 9.96 min.

IR (neat): 3310, 2957, 1728, 1603, 1514, 1435, 1333, 1287, 1207, 1098, 1033, 839 and 753 cm^{-1}.

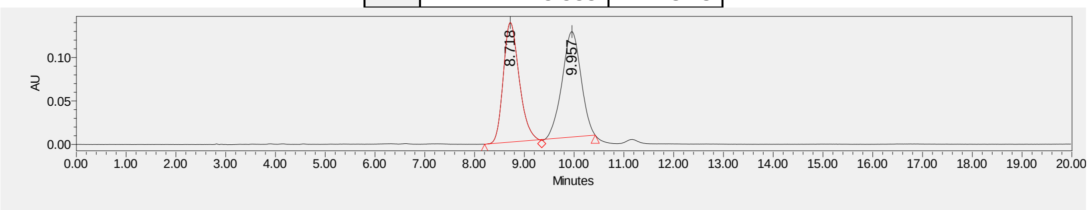
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.05 – 6.98 (m, 2H), 6.90 – 6.80 (m, 2H), 5.63 (s, 1H), 5.19 (s, 1H), 3.84 (s, 3H), 3.79 (s, 3H), 3.19 (s, 3H), 1.50 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.9, 182.0, 167.0, 166.0, 160.0, 130.8, 125.3, 114.5, 79.3, 58.5, 56.0, 55.4, 54.0, 52.5, 28.9.

HRMS (ESI-FT) calcd for $C_{19}H_{25}N_2O_5S^+$ ([M+H$^+$]) = 393.1479, Found 393.1479.

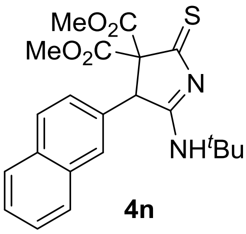


	Retention Time	% Area
1	8.690	81.82
2	9.955	18.18



	Retention Time	% Area
1	8.718	48.80
2	9.957	51.20

Dimethyl 5-(*tert*-butylamino)-4-(naphthalen-2-yl)-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4n)



4n

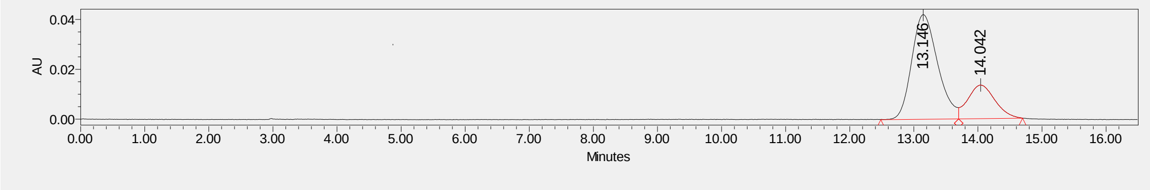
Yellow solid; m.p. 214–218 °C; 34.4 mg, 83% yield, 75:25 er; $[\alpha]^{22}_D$ = –22.63 (*c* = 0.55 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 13.15 min, t_R (minor) = 14.04 min.

IR (neat): 3310, 2971, 1729, 1601, 1531, 1435, 1335, 1287, 1207, 1125, 1098, 1051 and 752 cm^{-1}.

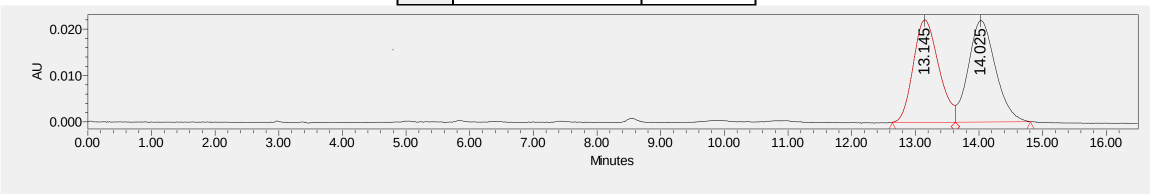
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.88 – 7.60 (m, 3H), 7.68 – 7.59 (m, 1H), 7.56 – 7.49 (m, 2H), 7.18 – 7.09 (m, 1H), 5.62 (s, 1H), 5.41 (s, 1H), 3.87 (s, 3H), 3.02 (s, 3H), 1.51 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.9, 181.8, 167.0, 166.0, 133.2, 131.0, 129.0, 128.0, 127.9, 127.2, 127.0, 79.4, 59.4, 56.1, 54.1, 52.4, 28.9.

HRMS (ESI-FT) calcd for $C_{22}H_{25}N_2O_4S^+$ ([M+H$^+$]) = 413.1530, Found 413.1531.

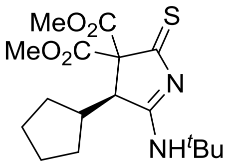


	Retention Time	% Area
1	13.146	74.87
2	14.042	25.13



	Retention Time	% Area
1	13.145	48.74
2	14.025	51.26

Dimethyl (*S*)-5-(*tert*-butylamino)-4-cyclopentyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4o)



4o

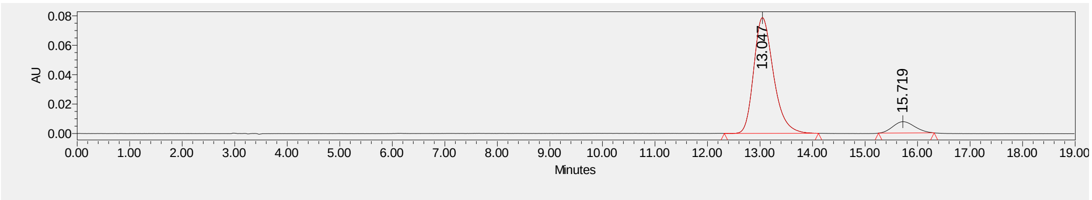
Yellow solid; m.p. 158–162 °C; 16.0 mg, 45% yield, 90:10 er; $[\alpha]^{22}_{D}$ = –81.94 (c = 0.31 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 13.05 min, t_R (minor) = 15.72 min.

IR (neat): 3342, 2957, 2872, 1730, 1597, 1526, 1435, 1332, 1294, 1207, 1103, 934 and 753 cm^{-1}.

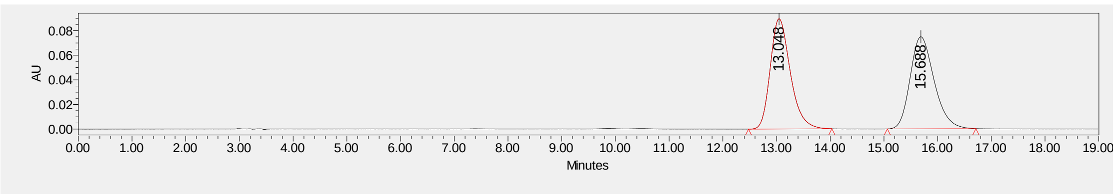
^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.03 (s, 1H), 3.85 – 3.79 (m, 4H), 3.75 (s, 3H), 2.18 – 2.07 (m, 1H), 1.91 – 1.79 (m, 2H), 1.71 – 1.66 (m, 2H), 1.63 – 1.56 (m, 2H), 1.53 (s, 9H), 1.29 – 1.20 (m, 2H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 218.0, 182.6, 167.5, 166.5, 77.9, 58.7, 56.0, 53.8, 53.0, 39.0, 32.3, 31.0, 29.0, 25.7, 24.8.

HRMS (ESI-FT) calcd for $C_{17}H_{27}N_2O_4S^+$ ([M+H$^+$]) = 355.1686, Found 355.1685.

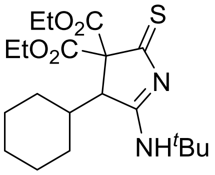


	Retention Time	% Area
1	13.047	90.21
2	15.719	9.79



	Retention Time	% Area
1	13.048	50.09
2	15.688	49.91

Diethyl 5-(*tert*-butylamino)-4-cyclohexyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4p)



4p

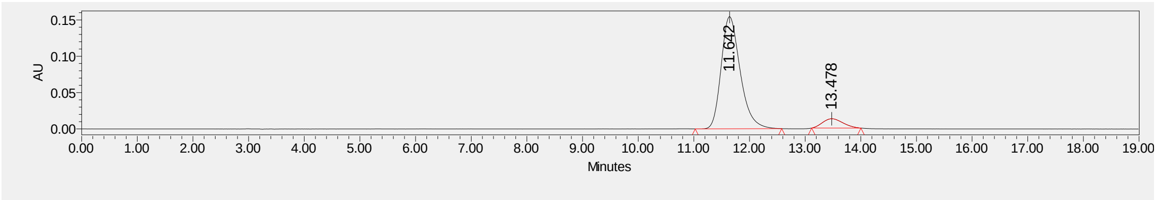
Yellow solid; m.p. 72–76 °C; 27.2 mg, 67% yield, 92:8 er; $[\alpha]^{22}_{D}$ = +101.9 (c = 0.55 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 11.64 min, t_R (minor) = 13.48 min.

IR (neat): 3345, 2929, 2855, 1727, 1594, 1529, 1451, 1340, 1284, 1208, 1123, 1098, 1032, 860 and 756 cm^{-1}.

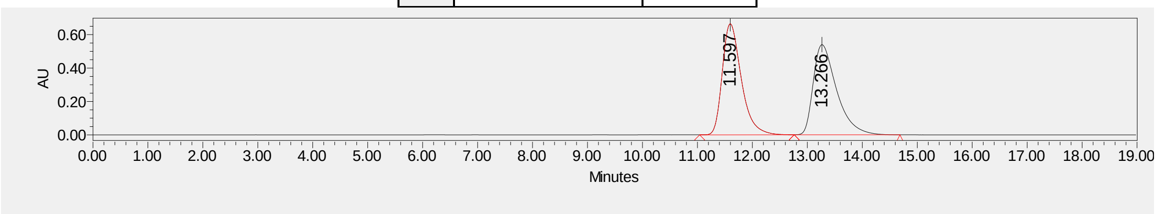
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.90 (s, 1H), 4.32 – 4.09 (m, 4H), 3.49 (d, J = 2.4 Hz, 1H), 1.82 – 1.74 (m, 2H), 1.71 – 1.61 (m, 4H), 1.53 (s, 9H), 1.31 – 1.21 (m,8H), 1.11 – 0.98 (m, 2H), 0.80 – 0.69 (m, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.7, 181.8, 166.7, 166.0, 63.1, 61.8, 59.3, 55.9, 39.0, 33.0, 29.1, 29.0, 27.2, 26.3, 26.2, 14.2, 13.8.

HRMS (ESI-FT) calcd for $C_{20}H_{33}N_2O_4S^+$ ([M+H$^+$]) = 397.2156, Found 397.2158.

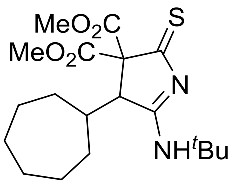


	Retention Time	% Area
1	11.642	91.83
2	13.478	8.17



	Retention Time	% Area
1	11.597	50.02
2	13.266	49.98

Dimethyl 5-(*tert*-butylamino)-4-cycloheptyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4q)



4q

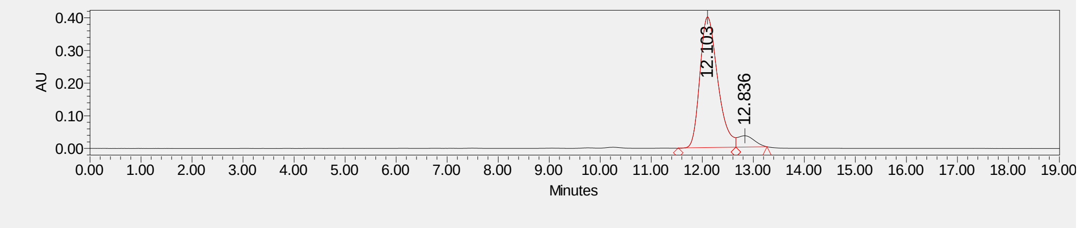
Yellow solid; m.p. 156–160 °C; 20.0 mg, 52% yield, 92.5:7.5 er; $[\alpha]^{22}_{D}$ = +37.13 (c = 0.40 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 12.10 min, t_R (minor) = 12.84 min.

IR (neat): 3344, 2925, 2857, 1730, 1593, 1526, 1436, 1340, 1286, 1207, 1122, 1066 and 751 cm^{-1}.

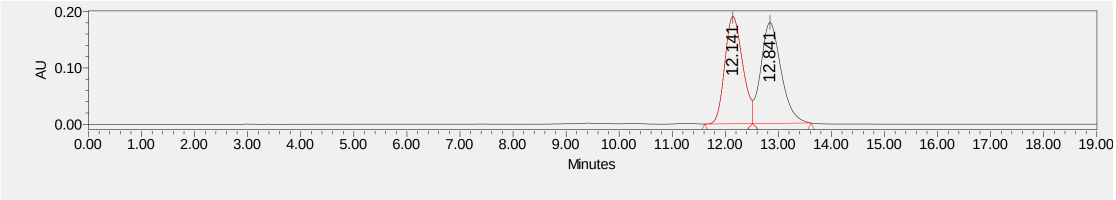
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.80 (s, 1H), 3.79 – 3.74 (m, 7H), 1.84 – 1.61 (m, 6H), 1.53 (s, 9H), 1.49 – 1.37 (m, 5H), 1.35 – 1.33 (m, 2H), 1.11 – 0.99 (m, 1H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 218.1, 181.9, 167.3, 166.7, 60.3, 55.9, 54.1, 52.8, 52.8, 39.6, 35.6, 30.2, 29.1, 27.8, 27.2, 27.0.

HRMS (ESI-FT) calcd for $C_{19}H_{31}N_2O_4S^+$ ([M+H$^+$]) = 383.1999, Found 383.1996.

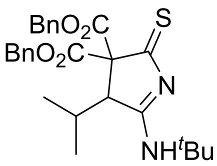


	Retention Time	% Area
1	12.103	92.54
2	12.836	7.46



	Retention Time	% Area
1	12.141	48.46
2	12.841	51.54

Dibenzyl 5-(*tert*-butylamino)-4-isopropyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4r)



4r

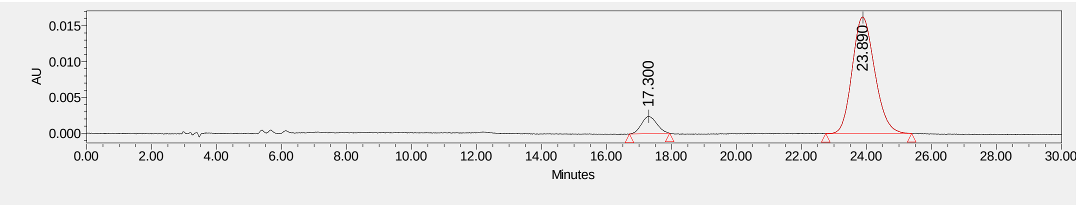
Yellow solid; m.p. 98–102 °C; 20.1 mg, 42% yield, 91:9 er; $[\alpha]^{22}_D$ = +97.78 (c = 0.40 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 23.89 min, t_R (minor) = 17.30 min.

IR (neat): 3345, 2968, 2326, 1728, 1596, 1525, 1459, 1365, 1312, 1287, 1207, 1131, 1046, 751 and 698 cm^{-1}.

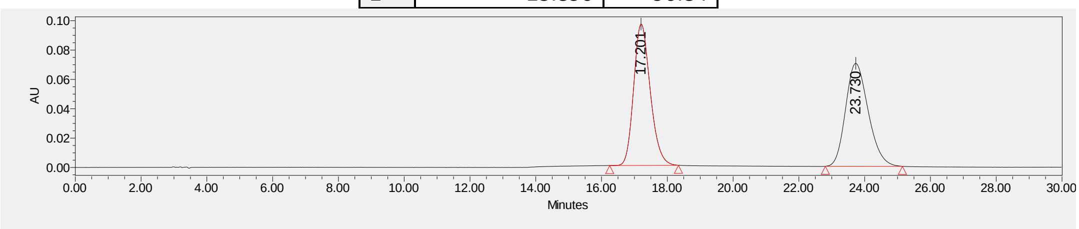
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.31 – 7.24 (m, 10H), 5.74 (s, 1H), 5.27 – 5.01 (m, 4H), 3.56 (d, J = 2.6 Hz, 1H), 1.86 – 1.77 (m, 1H), 1.50 (s, 9H), 1.01 (d, J = 6.8 Hz, 3H), 0.73 (d, J = 6.8 Hz, 3H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.1, 181.5, 166.4, 165.7, 135.1, 135.0, 128.7, 128.6, 128.6, 128.5, 128.3, 128.1, 68.7, 67.6, 59.5, 56.0, 29.1, 28.3, 22.4, 17.9.

HRMS (ESI-FT) calcd for $C_{27}H_{33}N_2O_4S^+$ ([M+H$^+$]) = 481.2156, Found 481.2155.

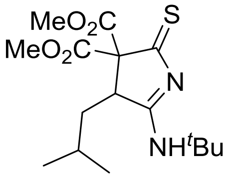


	Retention Time	% Area
1	17.300	9.16
2	23.890	90.84



	Retention Time	% Area
1	17.201	50.14
2	23.730	49.86

Dimethyl 5-(*tert*-butylamino)-4-isobutyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4s)



4s

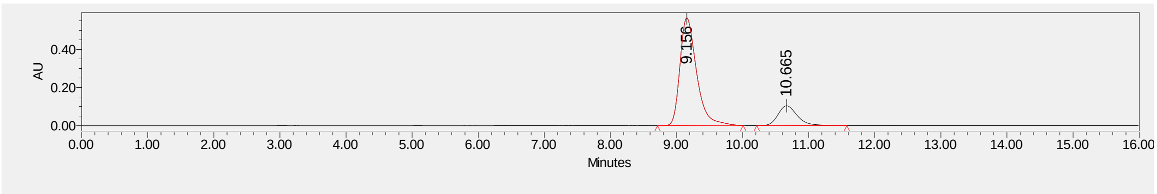
Yellow solid; m.p. 200–204 °C; 25.1 mg, 70% yield, 82:18 er; $[\alpha]^{22}_{D}$ = –109.64 (*c* = 0.28 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 9.16 min, t_R (minor) = 10.67 min.

IR (neat): 3329, 2958, 1729, 1597, 1520, 1435, 1335, 1298, 1204, 1119, 1074, 1045, 981 and 754 cm^{-1}.

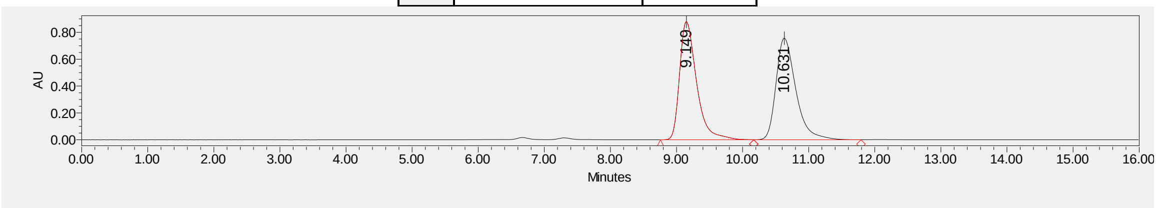
^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.73 (s, 1H), 4.00 (dd, *J* = 10.0, 5.2 Hz, 1H), 3.84 (s, 3H), 3.74 (s, 3H), 1.54 (m, 10H), 1.35 – 1.23 (m, 2H), 0.93 (dd, *J* = 13.2, 6.4 Hz, 6H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 218.5, 183.4, 167.4, 166.4, 77.3, 56.1, 53.7, 53.1, 51.2, 38.0, 29.0, 26.4, 23.4, 21.8.

HRMS (ESI-FT) calcd for $C_{16}H_{27}N_2O_4S^+$ ([M+H$^+$]) = 343.1686, Found 343.1686.

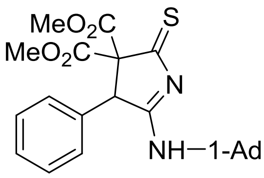


	Retention Time	% Area
1	9.156	82.46
2	10.665	17.54



	Retention Time	% Area
1	9.149	49.95
2	10.631	50.05

Dimethyl 5-(adamantan-1-ylamino)-4-phenyl-2-thioxo-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (4t)



4t

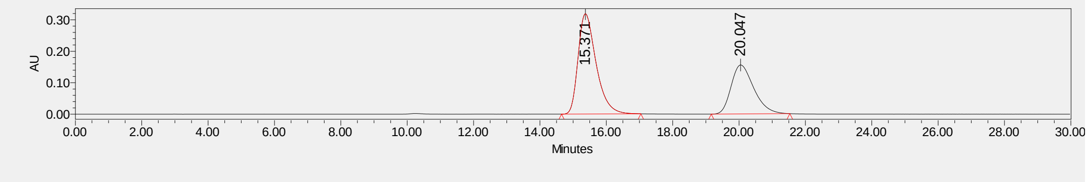
Yellow solid; m.p. 226–230 °C; 28.1 mg, 64% yield, 62:38 er; $[\alpha]^{22}_{D}$ = –6.44 (*c* = 0.40 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 320 nm, t_R (major) = 15.37 min, t_R (minor) = 20.05 min.

IR (neat): 2911, 2853, 1728, 1600, 1529, 1453, 1333, 1289, 1084, 755 and 701 cm^{-1}.

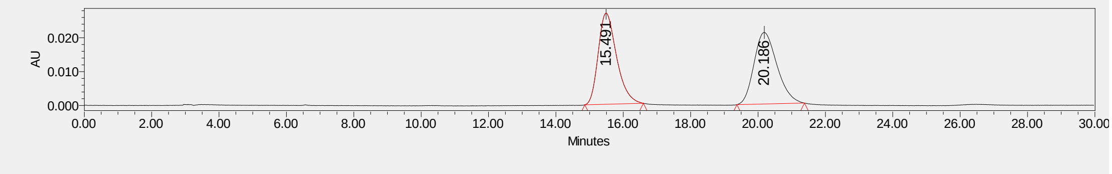
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 – 7.30 (m 3H), 7.17 – 7.05 (m, 2H), 5.48 (s, 1H), 5.25 (s, 1H), 3.85 (s, 3H), 3.13 (s, 3H), 2.15 – 2.10 (m, 8H), 1.77 – 1.60 (m, 7H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 217.8, 181.6, 167.0, 165.9, 133.8, 129.7, 129.1, 129.1, 79.3, 59.2, 59.2, 56.7, 54.1, 54.0, 52.4, 41.5, 35.9, 29.5.

HRMS (ESI-FT) calcd for $C_{24}H_{29}N_2O_4S^+$ ([M+H$^+$]) = 441.1843, Found 441.1847.

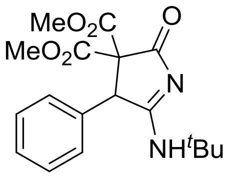


	Retention Time	% Area
1	15.371	61.93
2	20.047	38.07



	Retention Time	% Area
1	15.491	50.35
2	20.186	49.65

Dimethyl 5-(*tert*-butylamino)-2-oxo-4-phenyl-2,4-dihydro-3*H*-pyrrole-3,3-dicarboxylate (5a)



5a

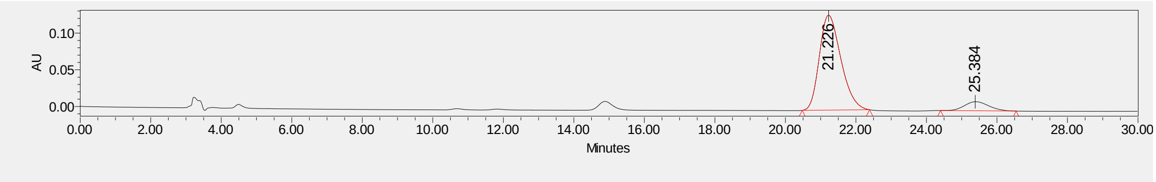
White solid; m.p. 210–214 °C; 3.9 mg, 11% yield, 89:11 er; $[\alpha]^{22}_{D}$ = –102.14 (c = 0.47 in CH_2Cl_2). HPLC DAICEL CHIRALCEL **IE**, *n*-hexane/2-propanol = 70/30, flow rate = 1.0 mL/min, λ = 254 nm, t_R (major) = 21.23 min, t_R (minor) = 25.38 min.

IR (neat): 3264, 3072, 2959, 1731, 1584, 1543, 1455, 1367, 1333, 1263, 1200, 1111, 1061, 759 and 701 cm^{-1}.

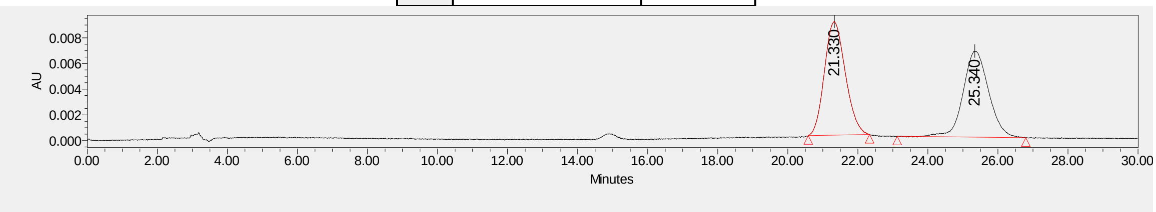
^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.35 – 7.30 (m, 3H), 7.16 – 7.09 (m, 2H), 5.53 (s, 1H), 5.13 (s, 1H), 3.84 (s, 3H), 3.14 (s, 3H), 1.45 (s, 9H).

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ = 181.3, 166.8, 165.8, 133.8, 129.8, 129.6, 129.0, 129.0, 71.0, 56.2, 55.3, 54.0, 54.0, 52.4, 28.5, 28.5.

HRMS (ESI-FT) calcd for $C_{18}H_{23}N_2O_5^+$ ([M+H$^+$]) = 347.1601, Found 347.1600.



	Retention Time	% Area
1	21.226	89.72
2	25.384	10.28



	Retention Time	% Area
1	21.330	51.90
2	25.340	48.10

9. Copies of NMR spectra

Figure S1. ^{1}H NMR of 4a

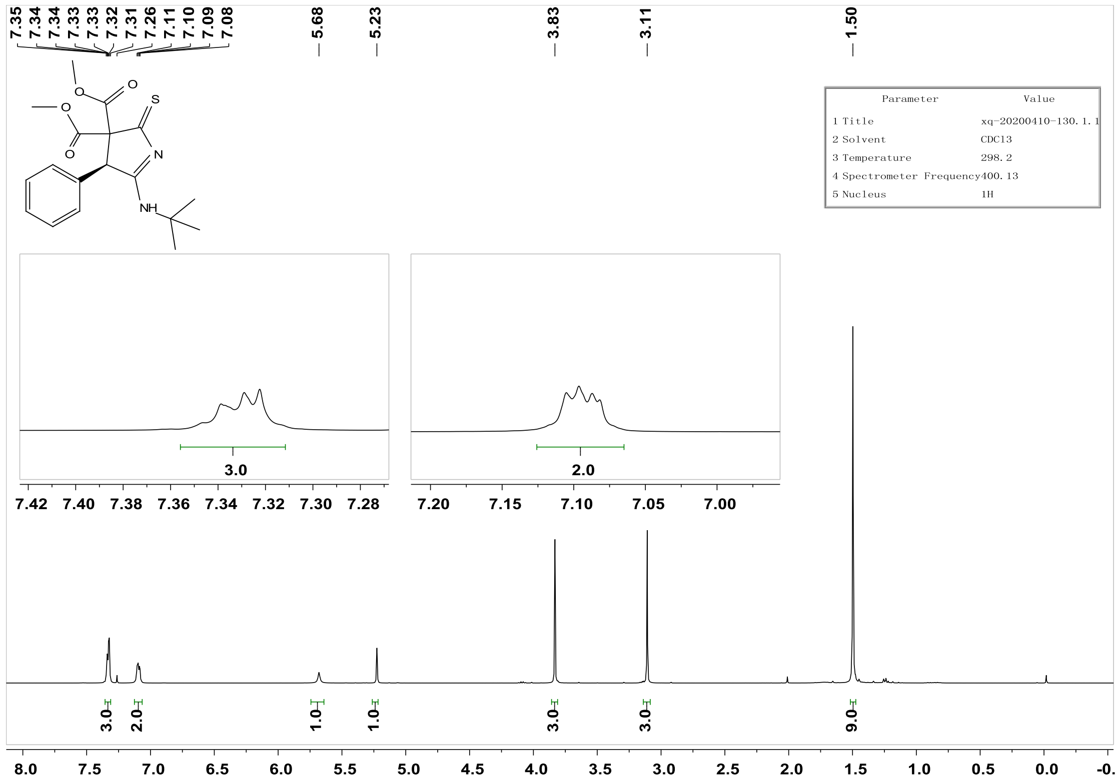


Figure S2. $^{13}C\{^{1}H\}$ NMR of 4a

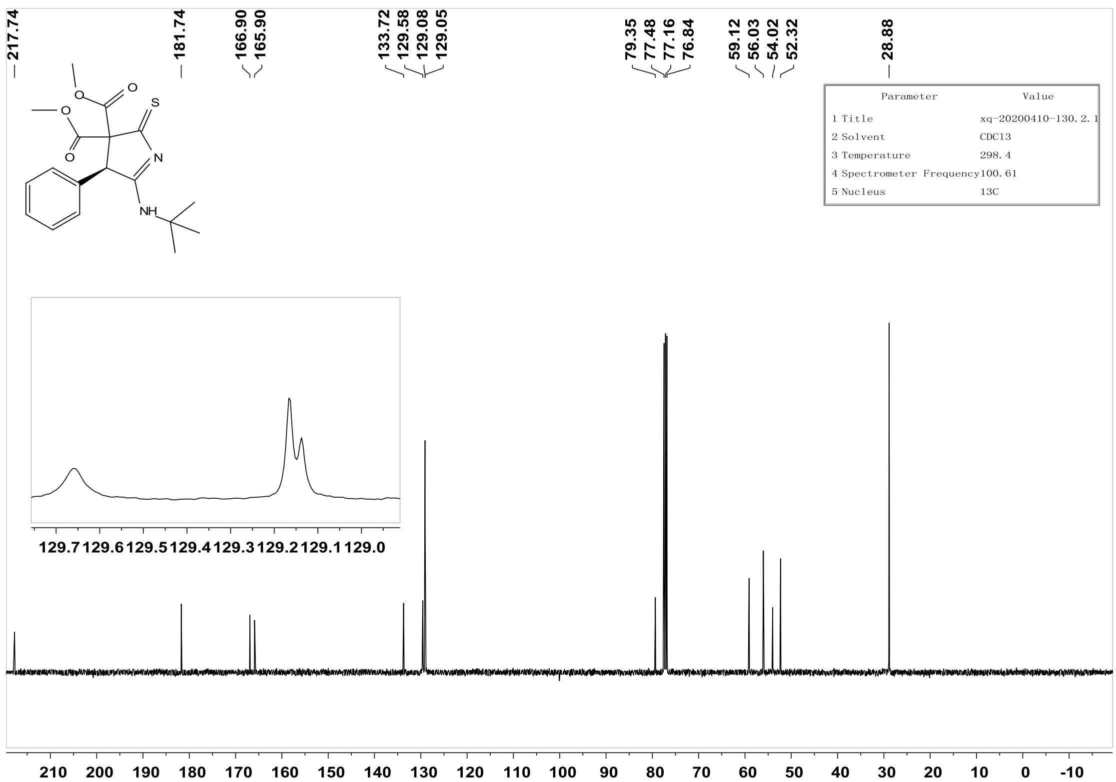


Figure S3. ^{1}H **NMR of 4b**

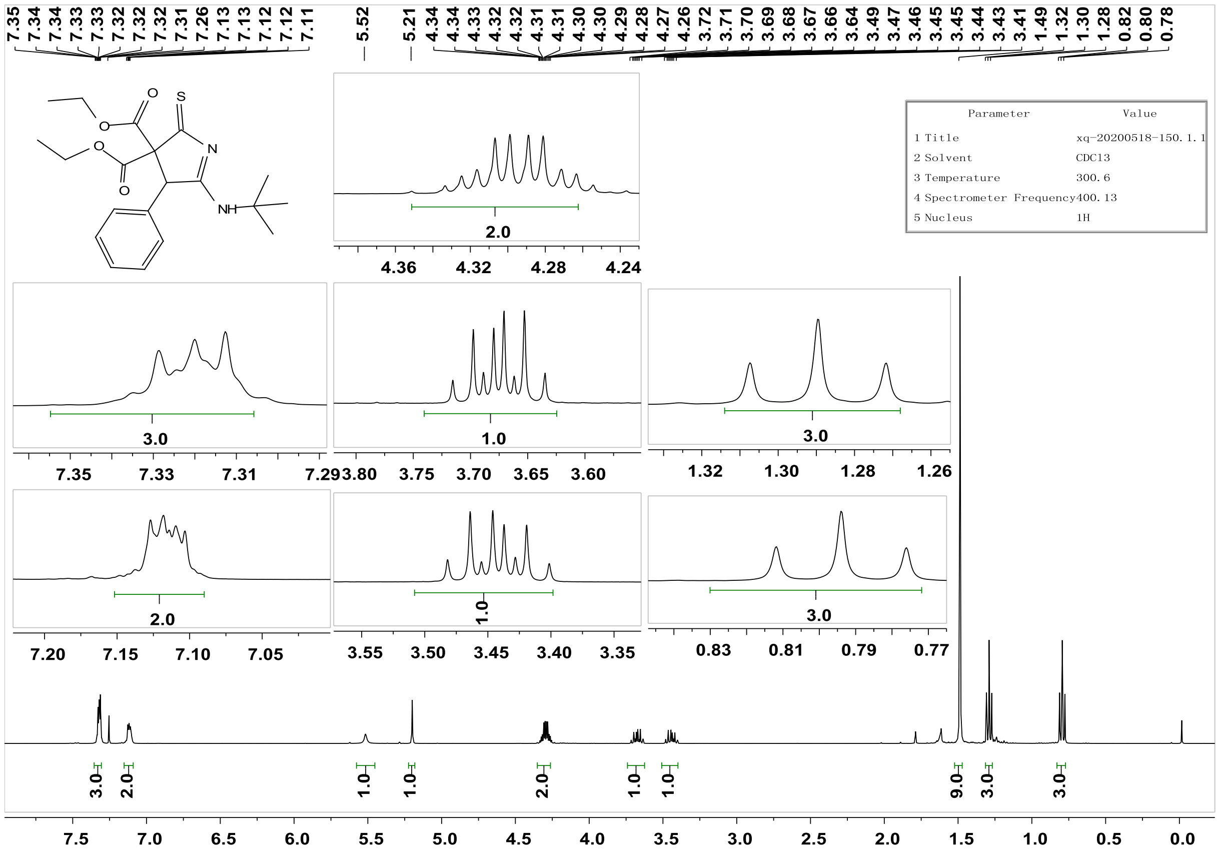


Figure S4. ^{13}C{^{1}H} **NMR of 4b**

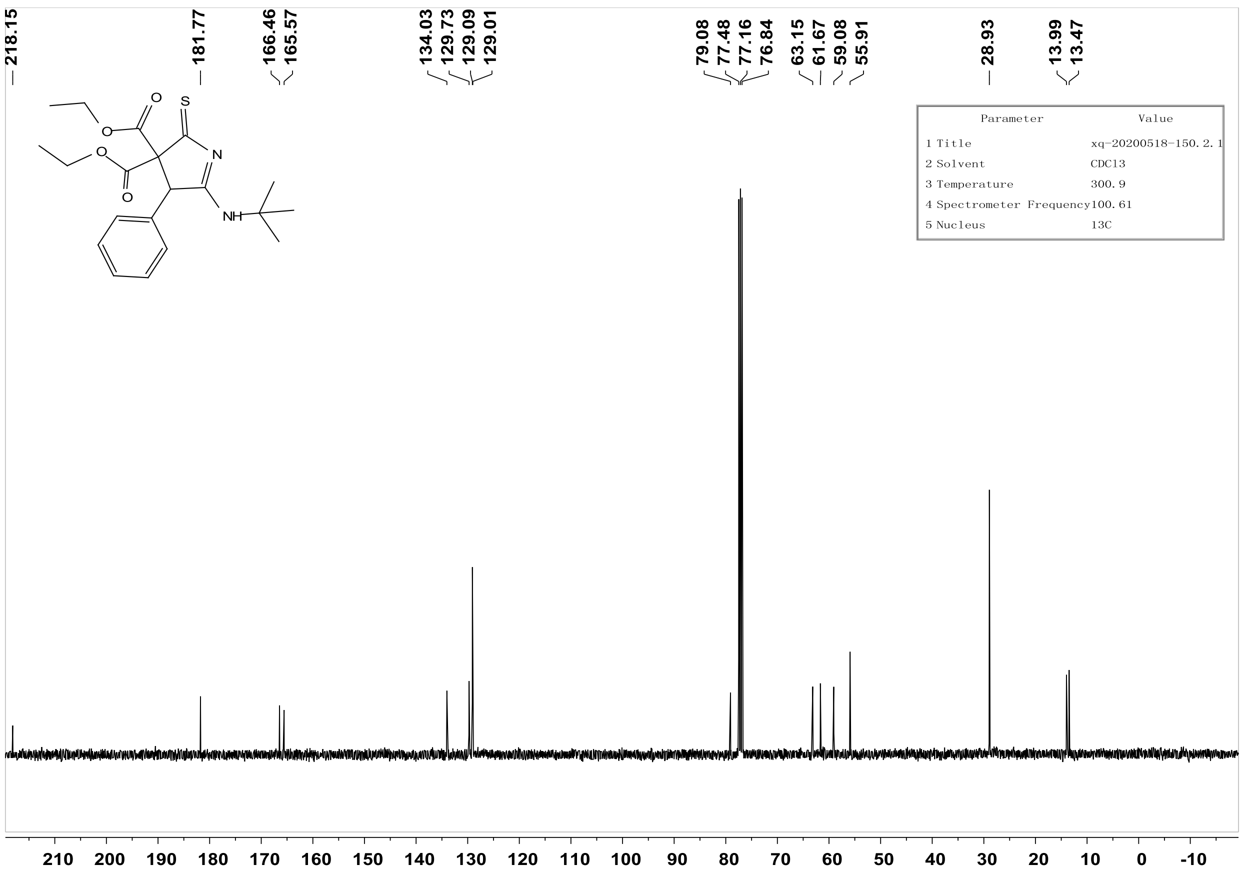


Figure S5. ^{1}H NMR of 4c

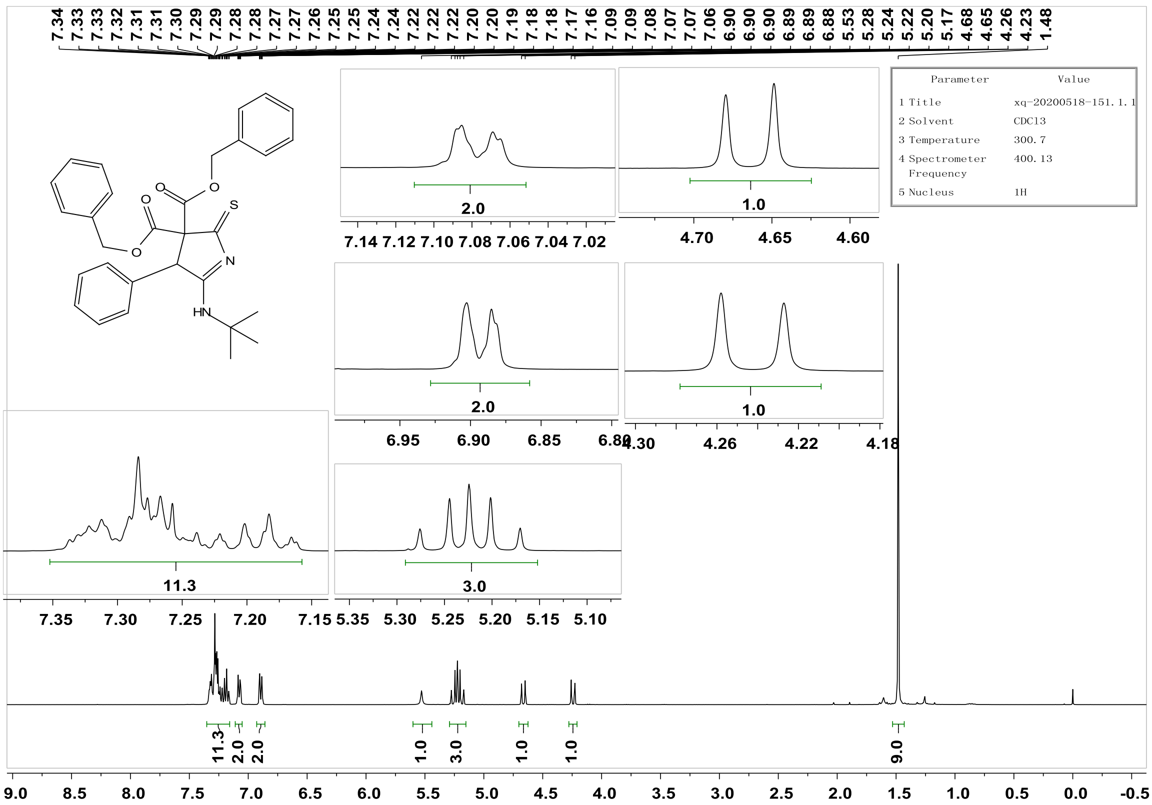


Figure S6. $^{13}C\{^{1}H\}$ NMR of 4c

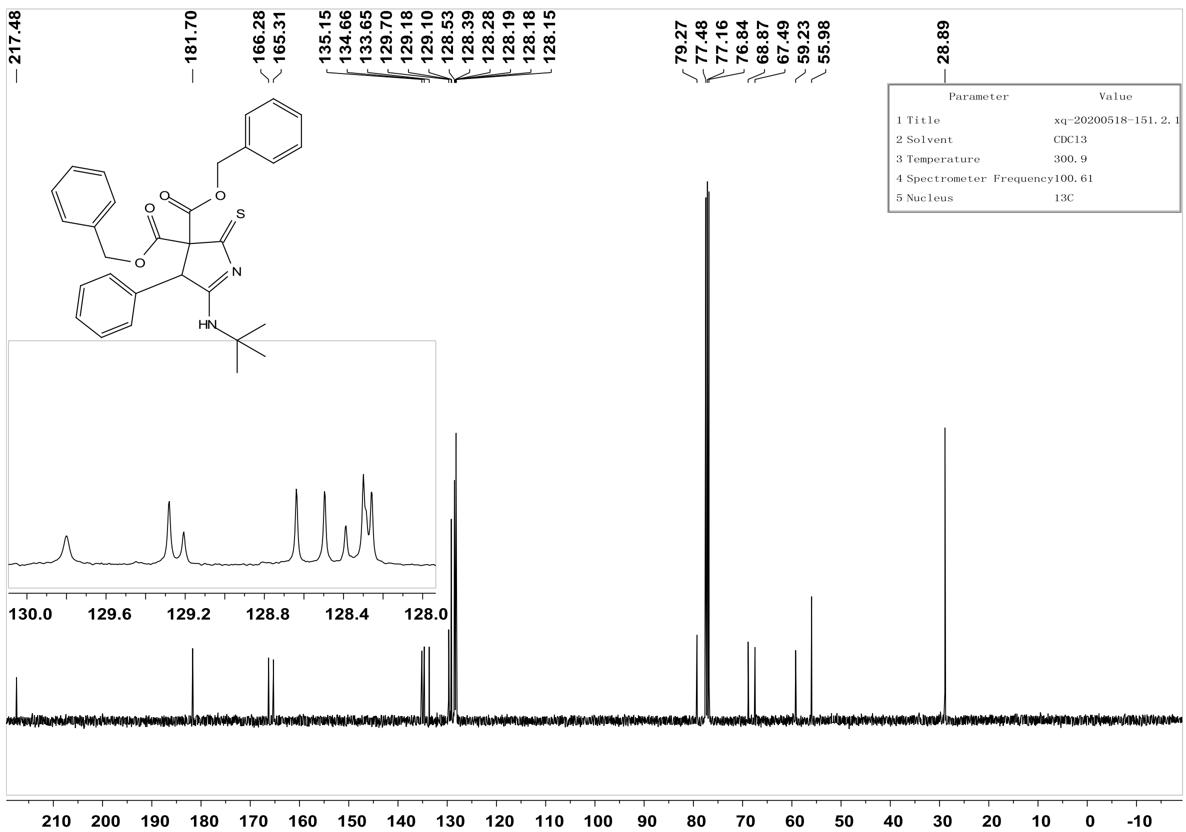


Figure S7. ^{1}H NMR of 4d

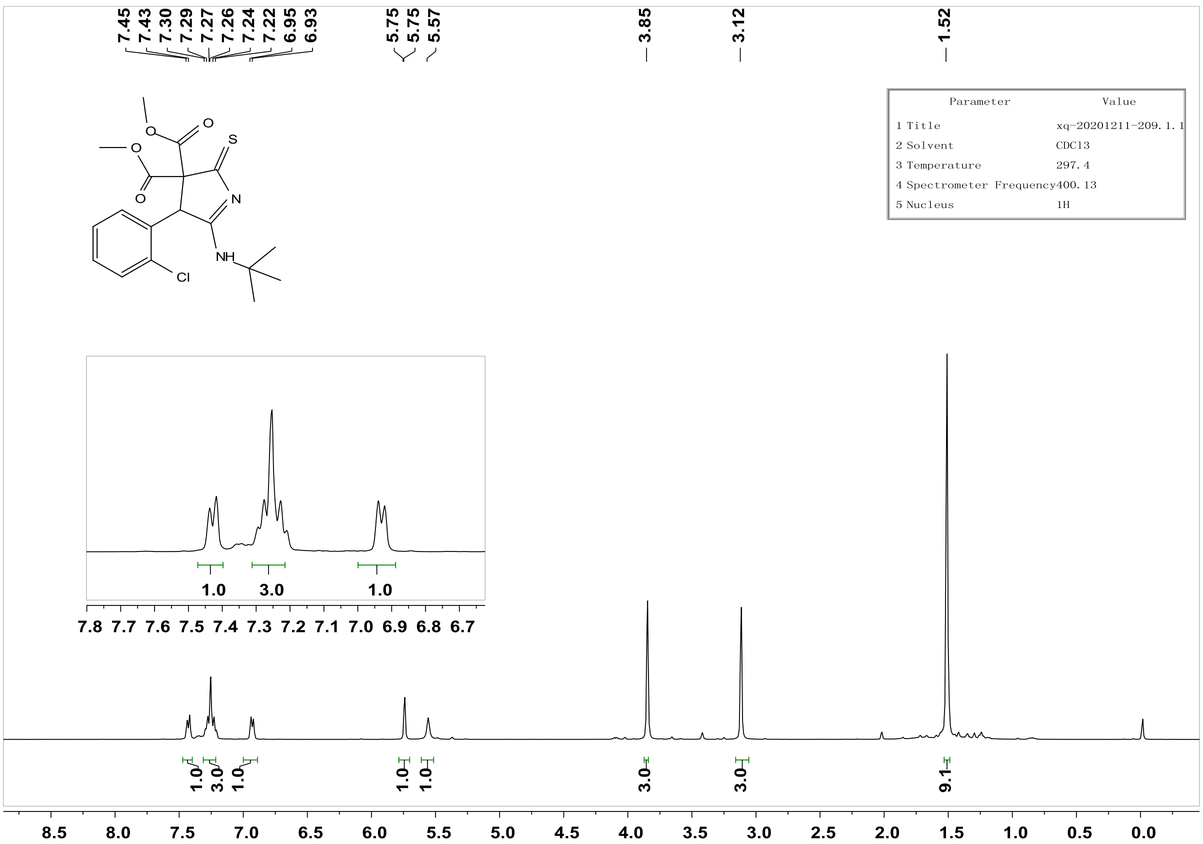


Figure S8. ^{13}C{^{1}H} NMR of 4d

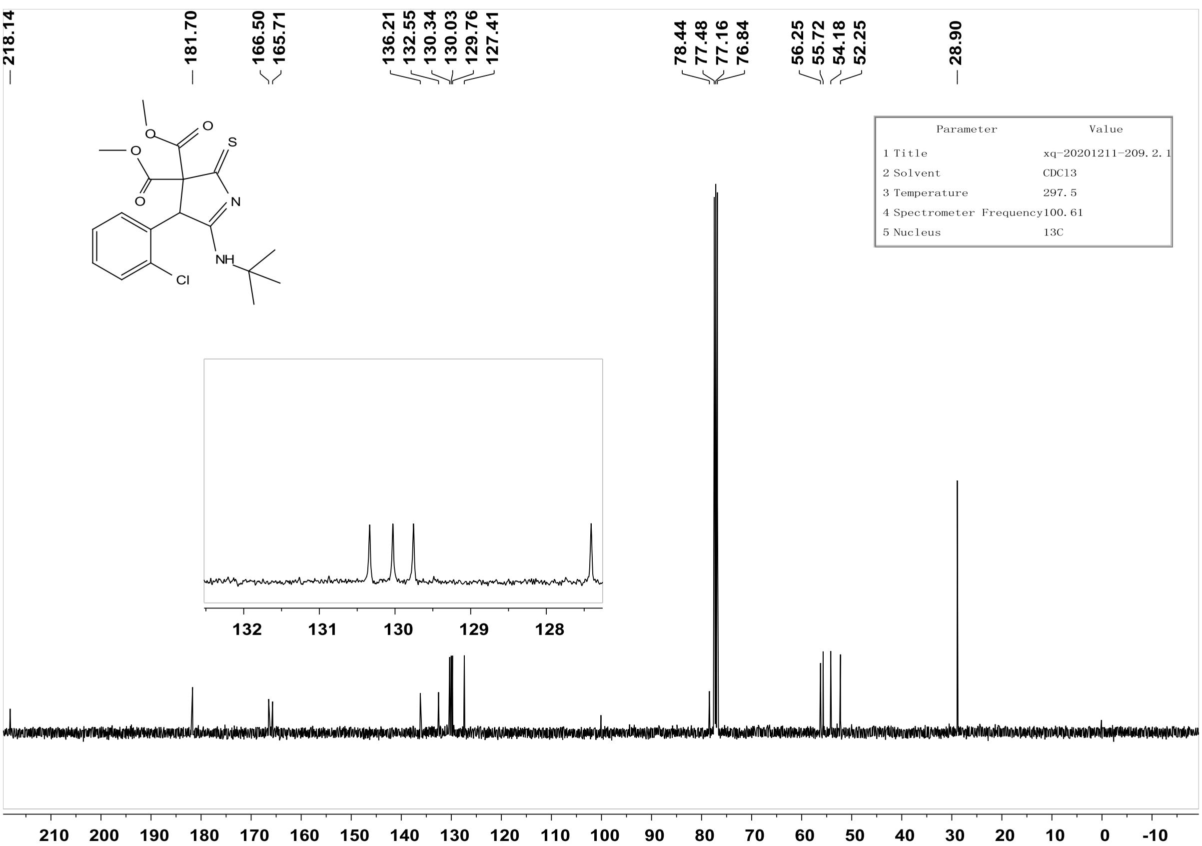


Figure S9. ^{1}H NMR of 4e

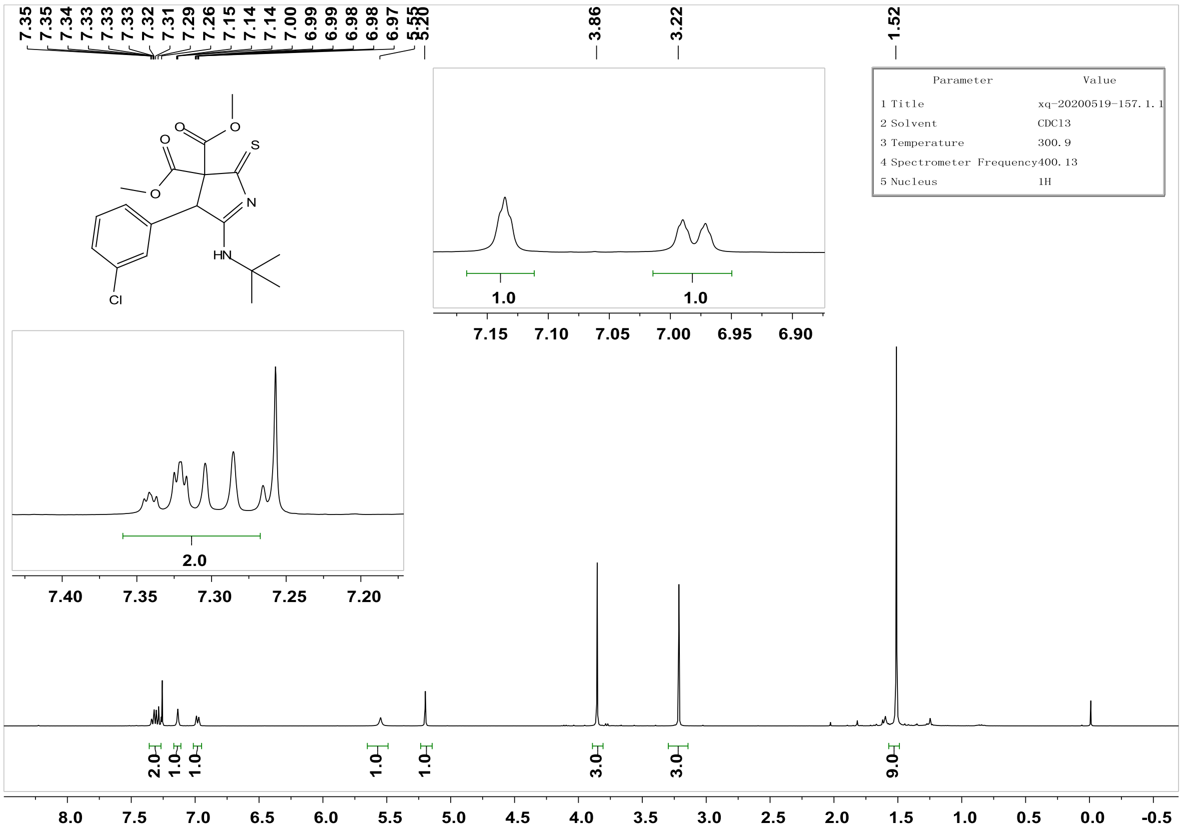


Figure S10. ^{13}C{^{1}H} NMR of 4e

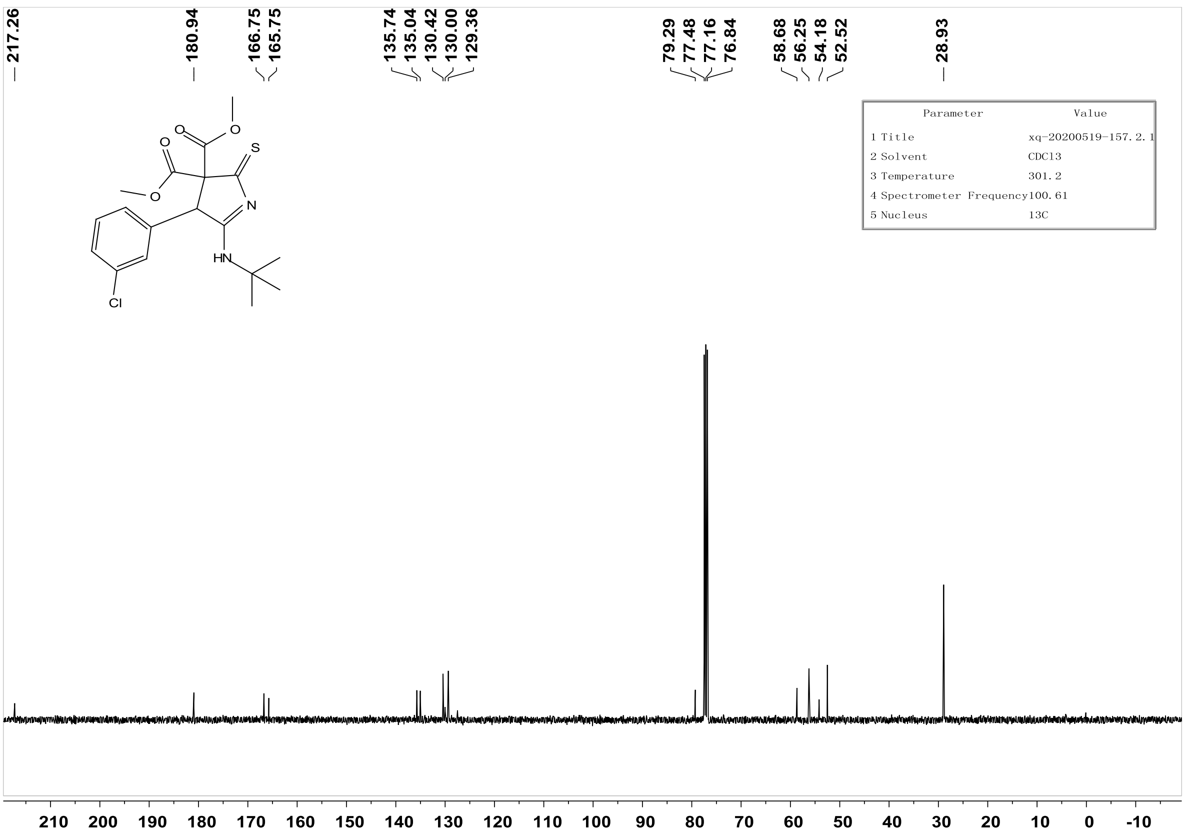


Figure S11. ^{1}H NMR of 4f

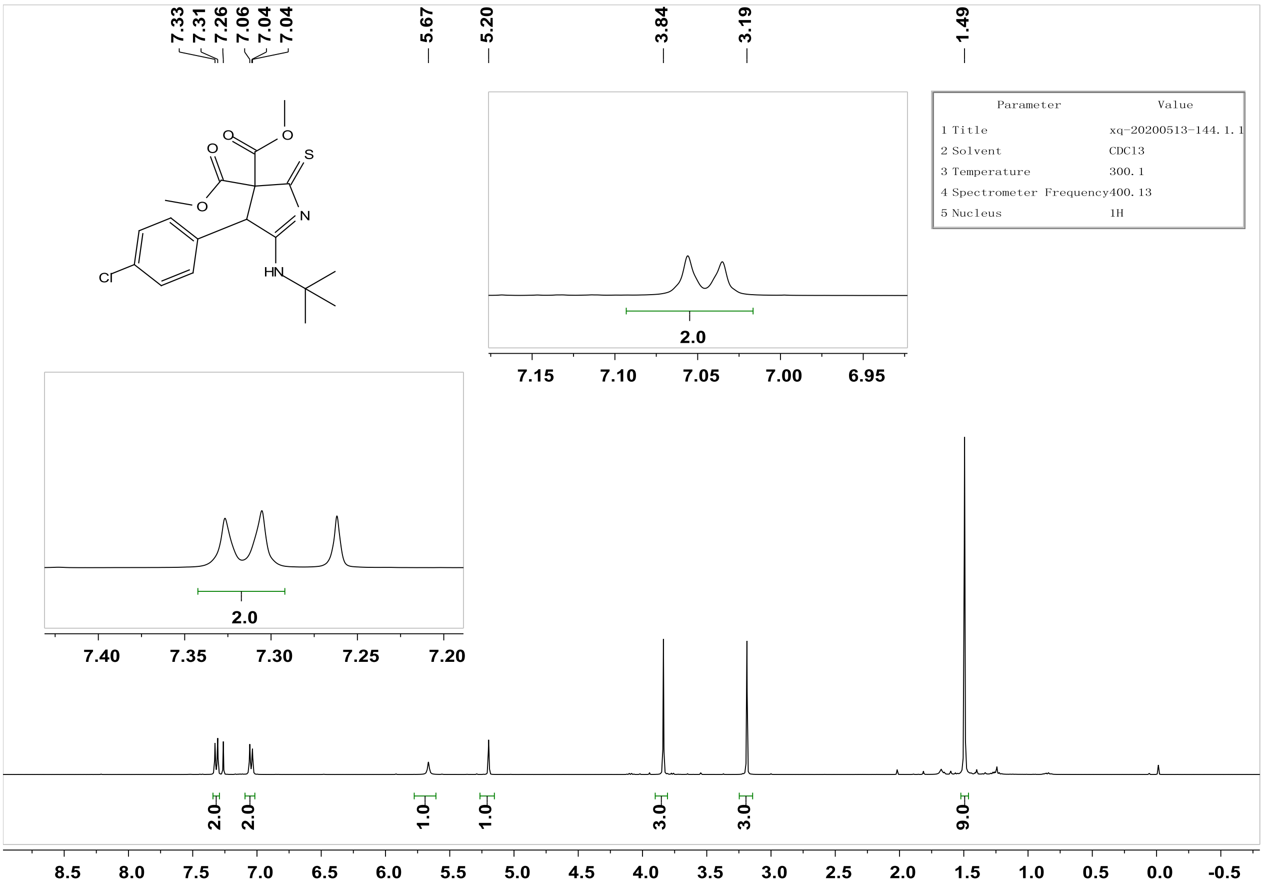


Figure S12. ^{13}C{^{1}H} NMR of 4f

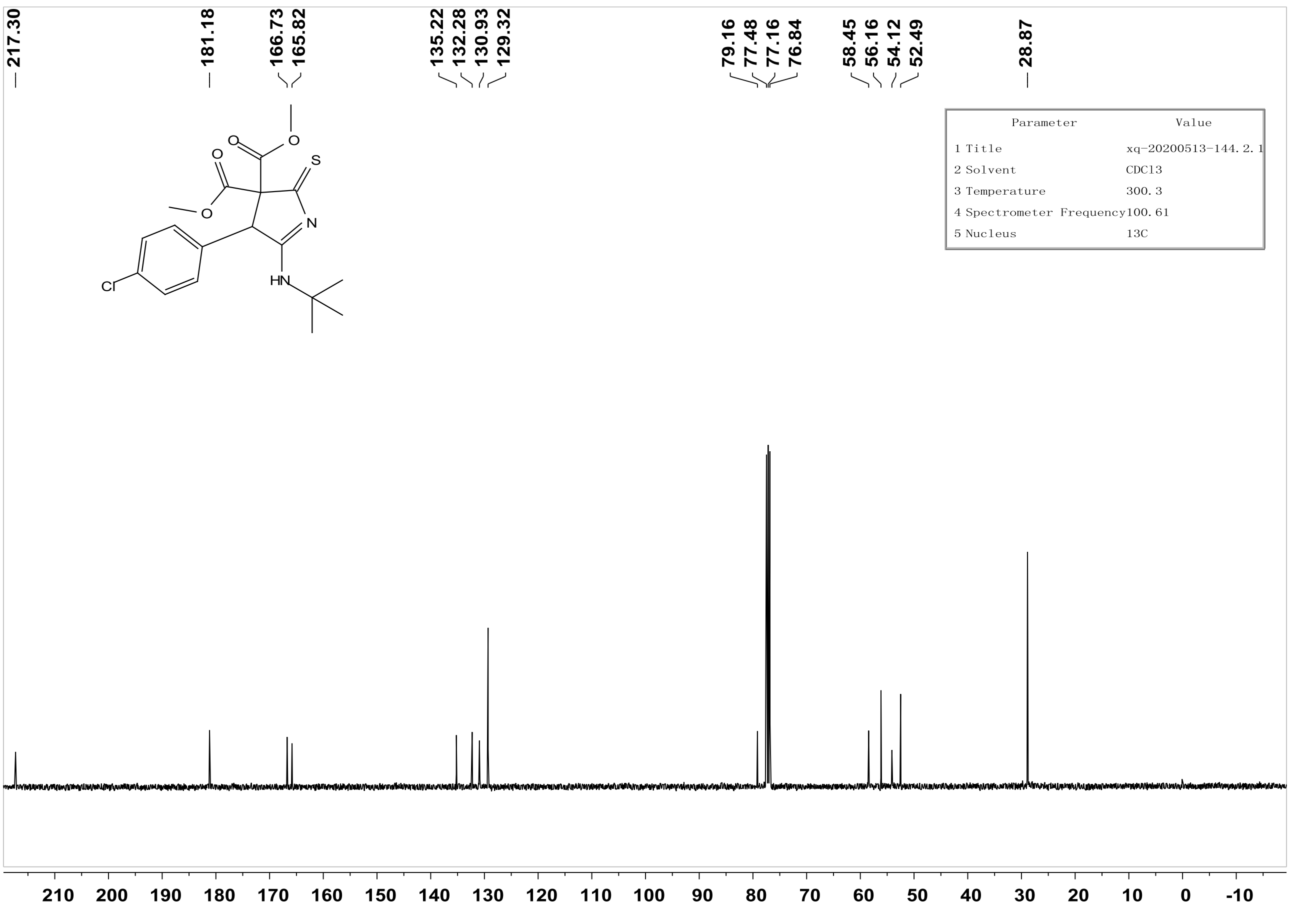


Figure S13. ^{1}**H NMR of 4g**

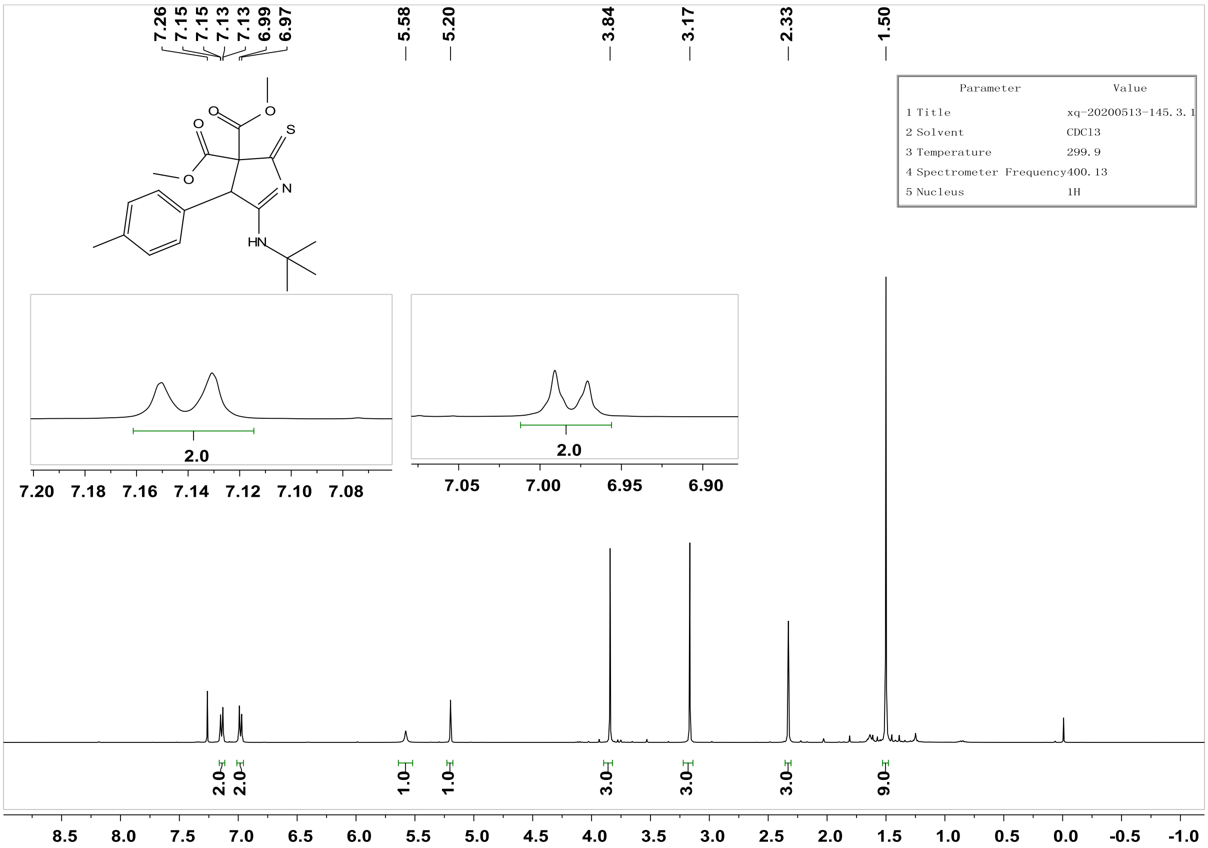


Figure S14. ^{13}**C{**^{1}**H} NMR of 4g**

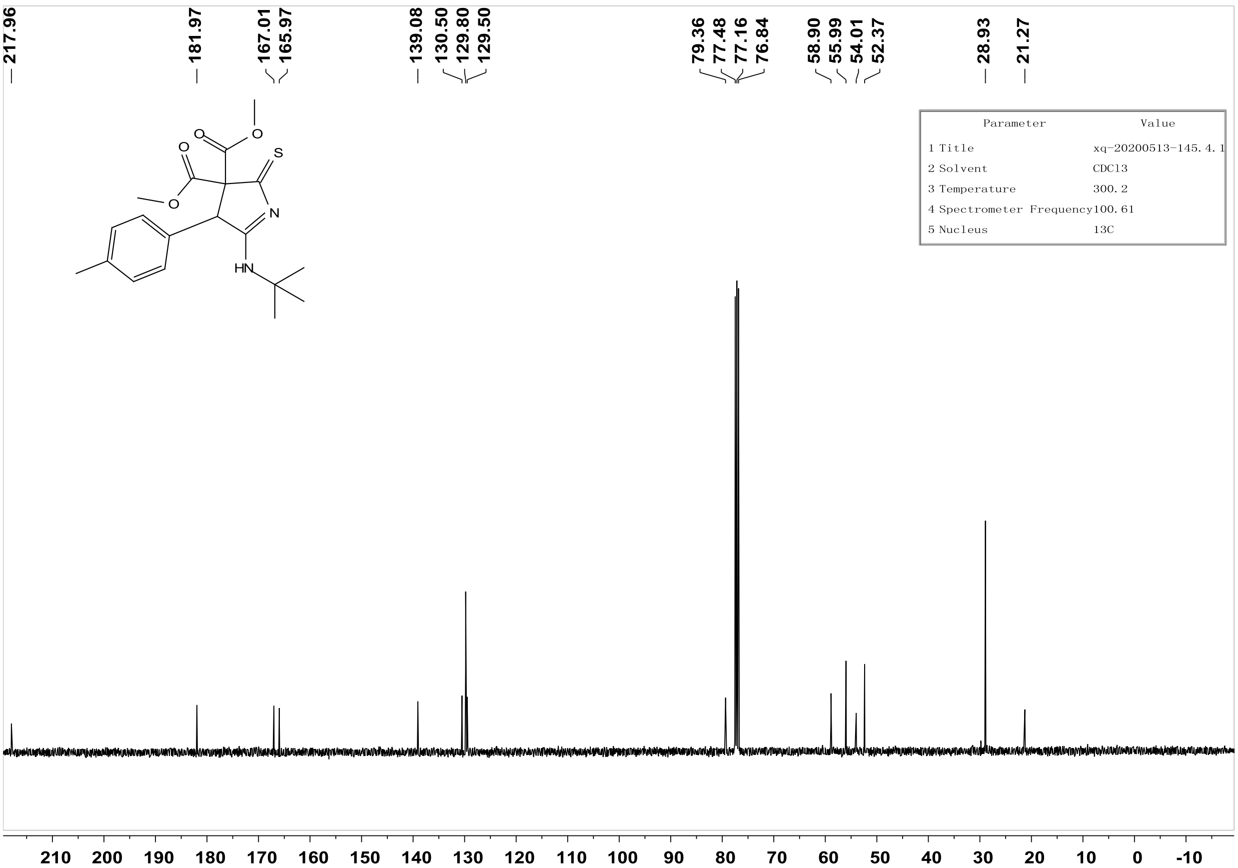


Figure S15. ^{1}H NMR of 4h

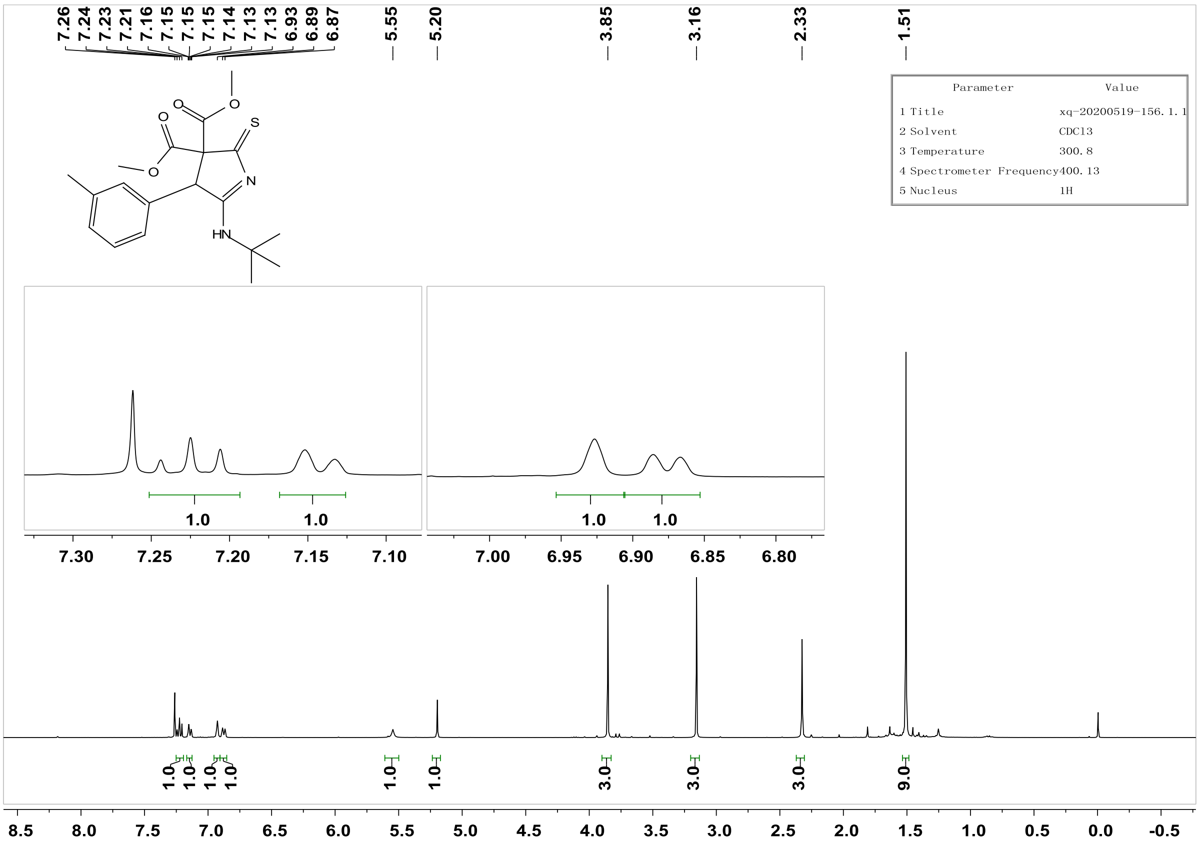


Figure S16. ^{13}C{^{1}H} NMR of 4h

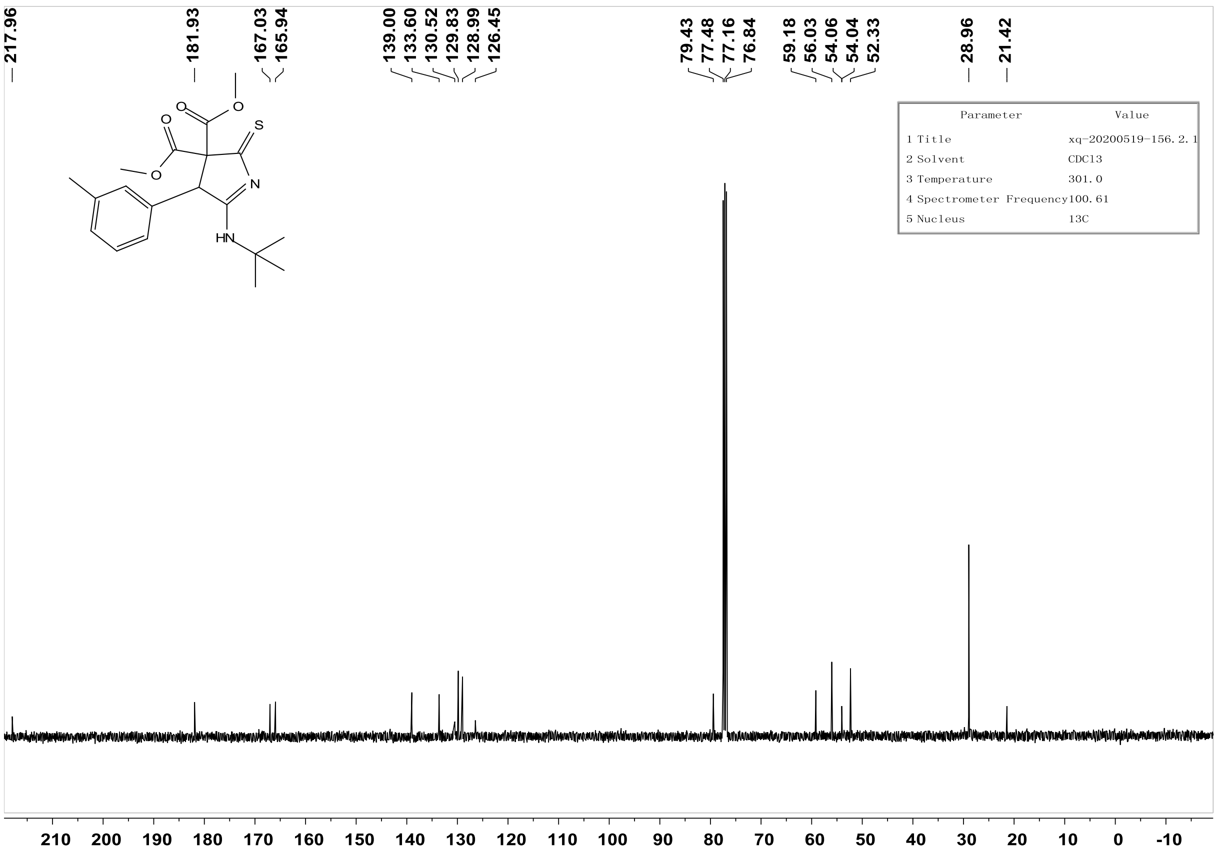


Figure S17. [1]H NMR of 4i

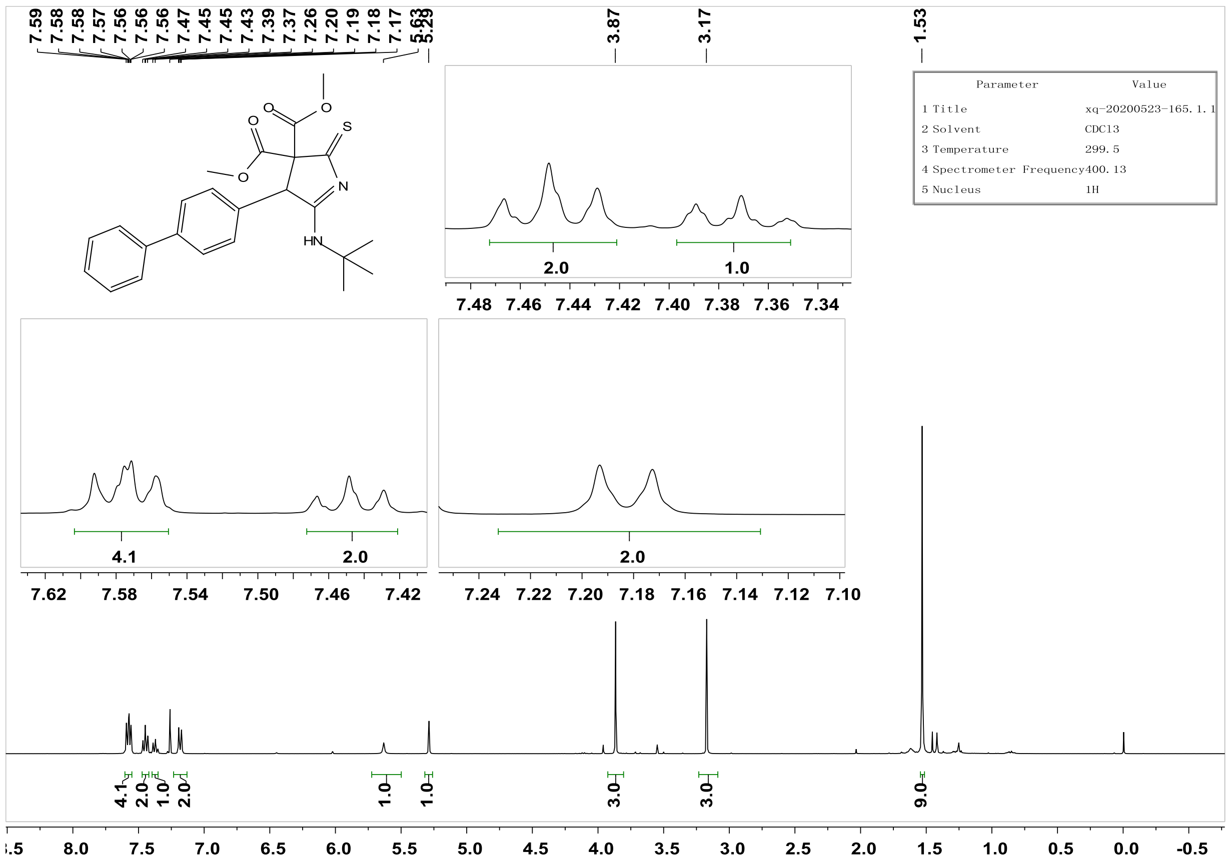


Figure S18. [13]C{[1]H} NMR of 4i

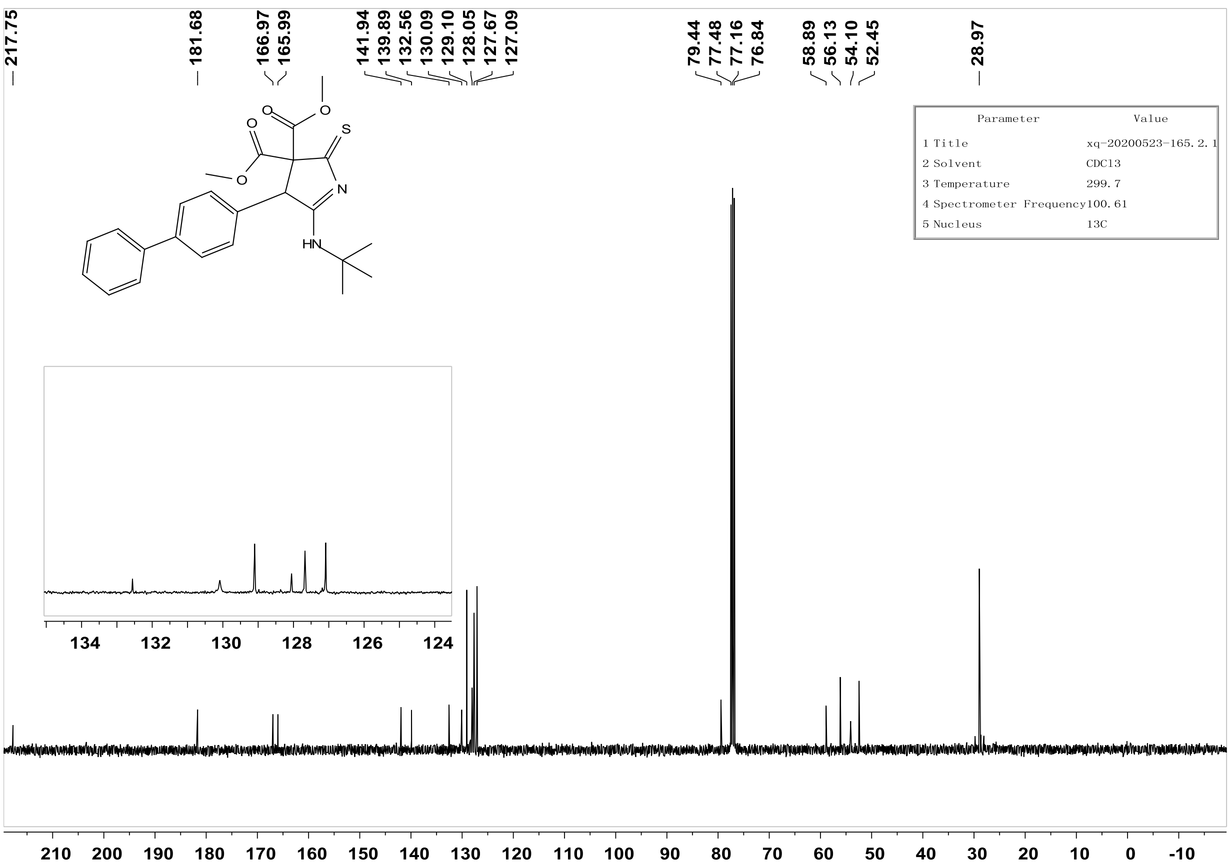


Figure S19. ^{1}H NMR of 4j

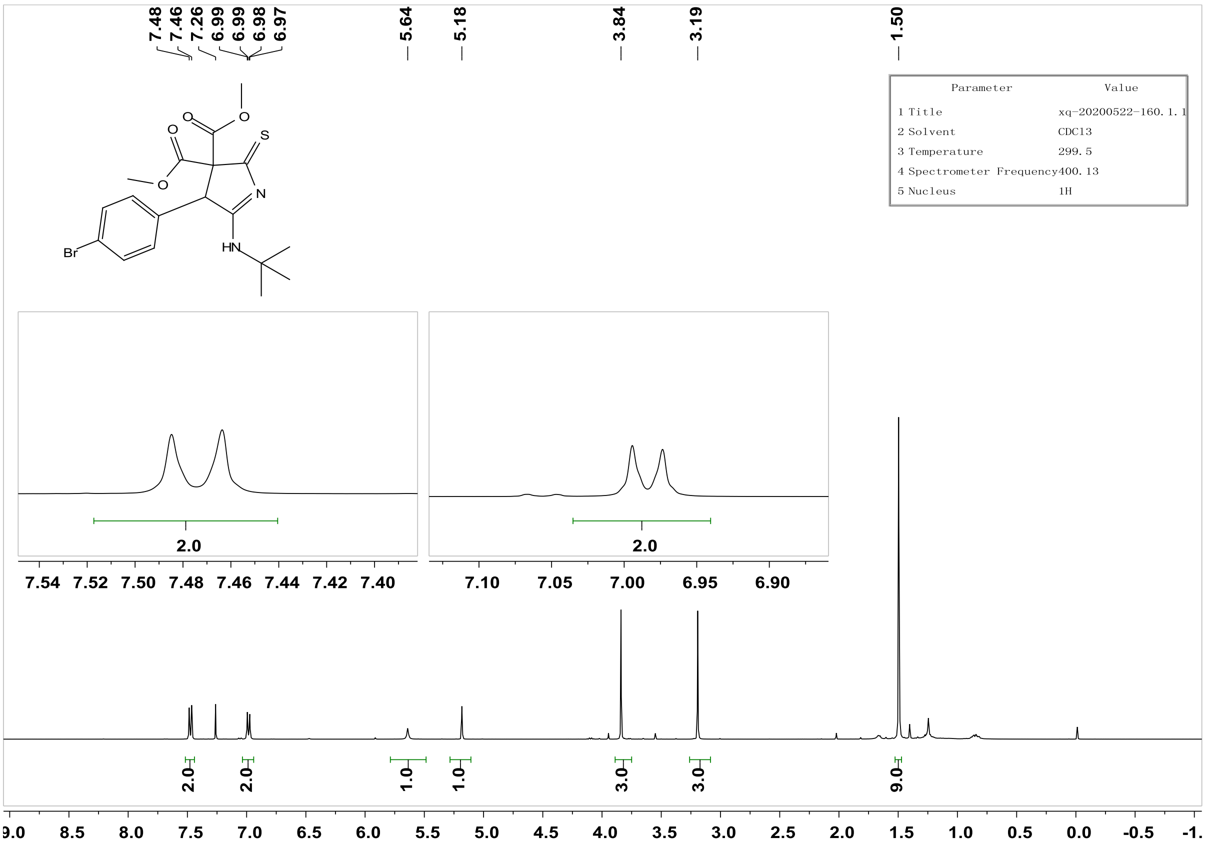


Figure S20. ^{13}C{^{1}H} NMR of 4j

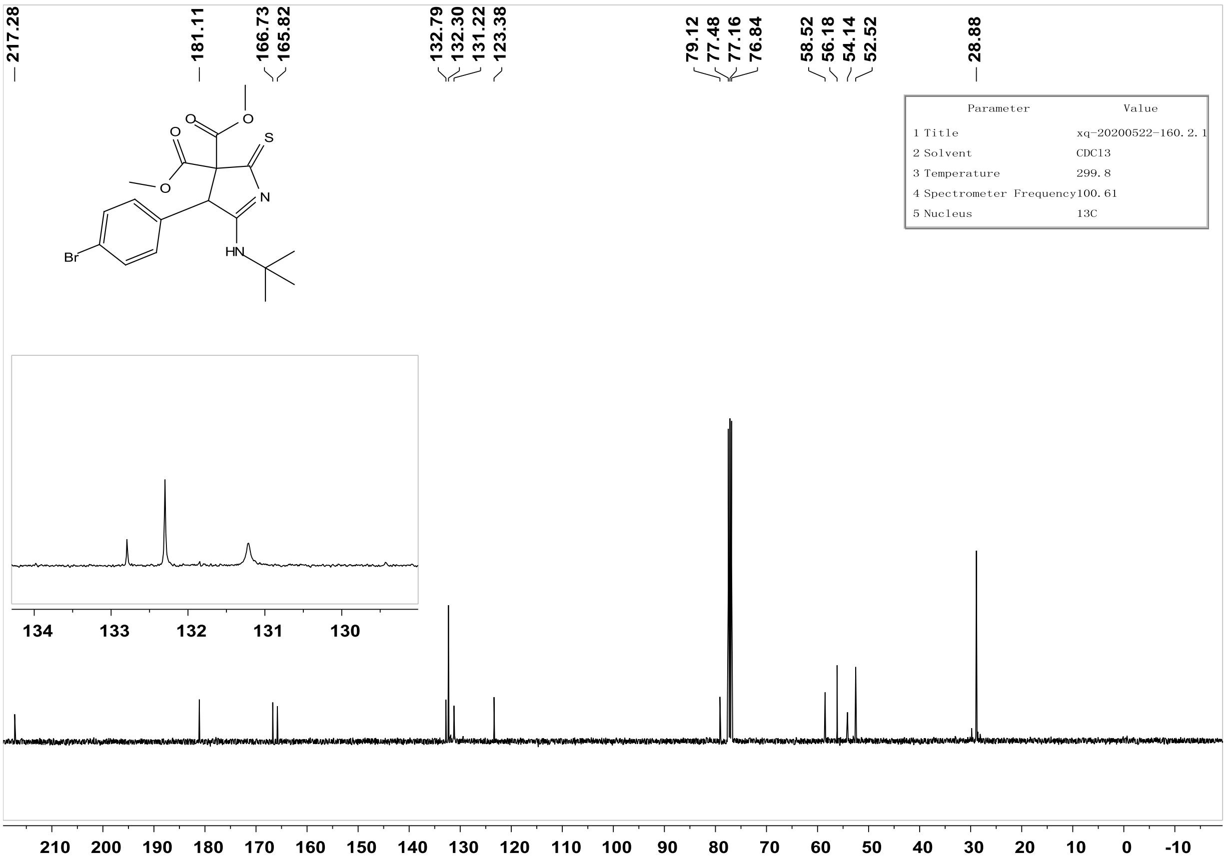


Figure S21. ^{1}H NMR of 4k

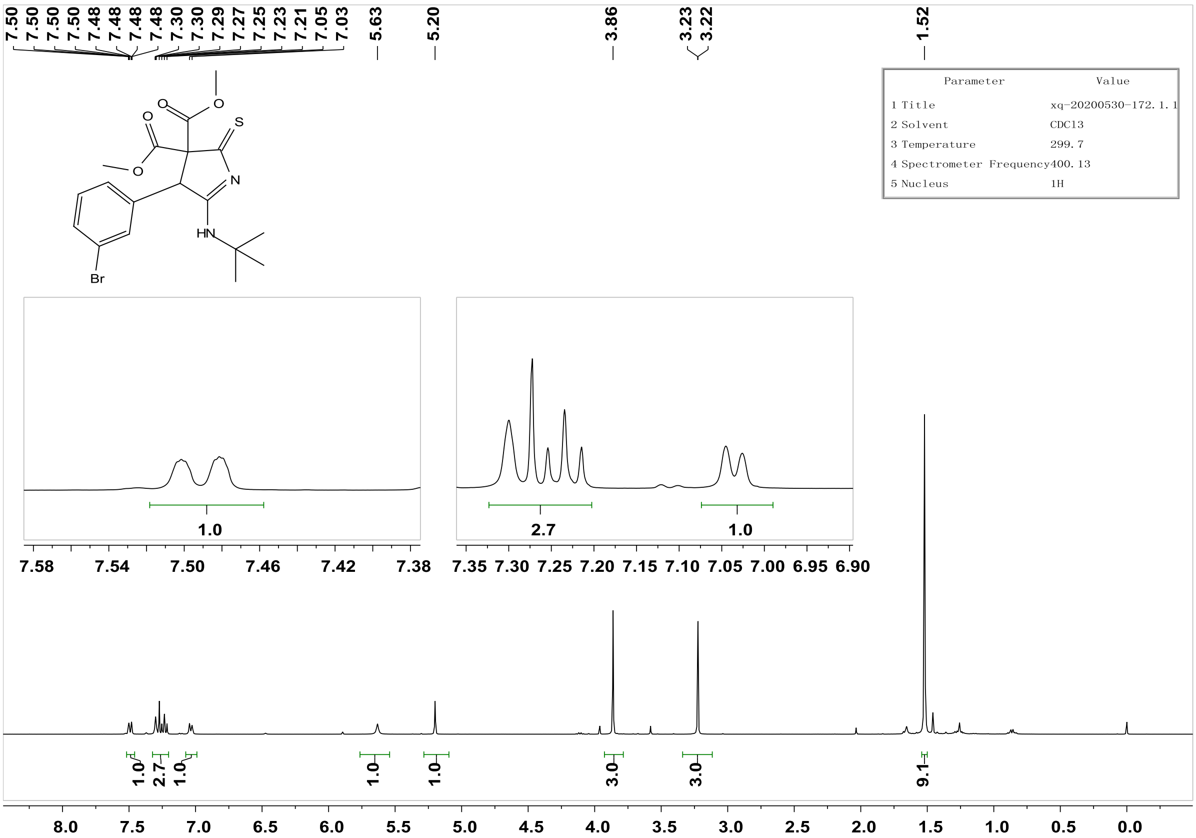


Figure S22. ^{13}C{^{1}H} NMR of 4k

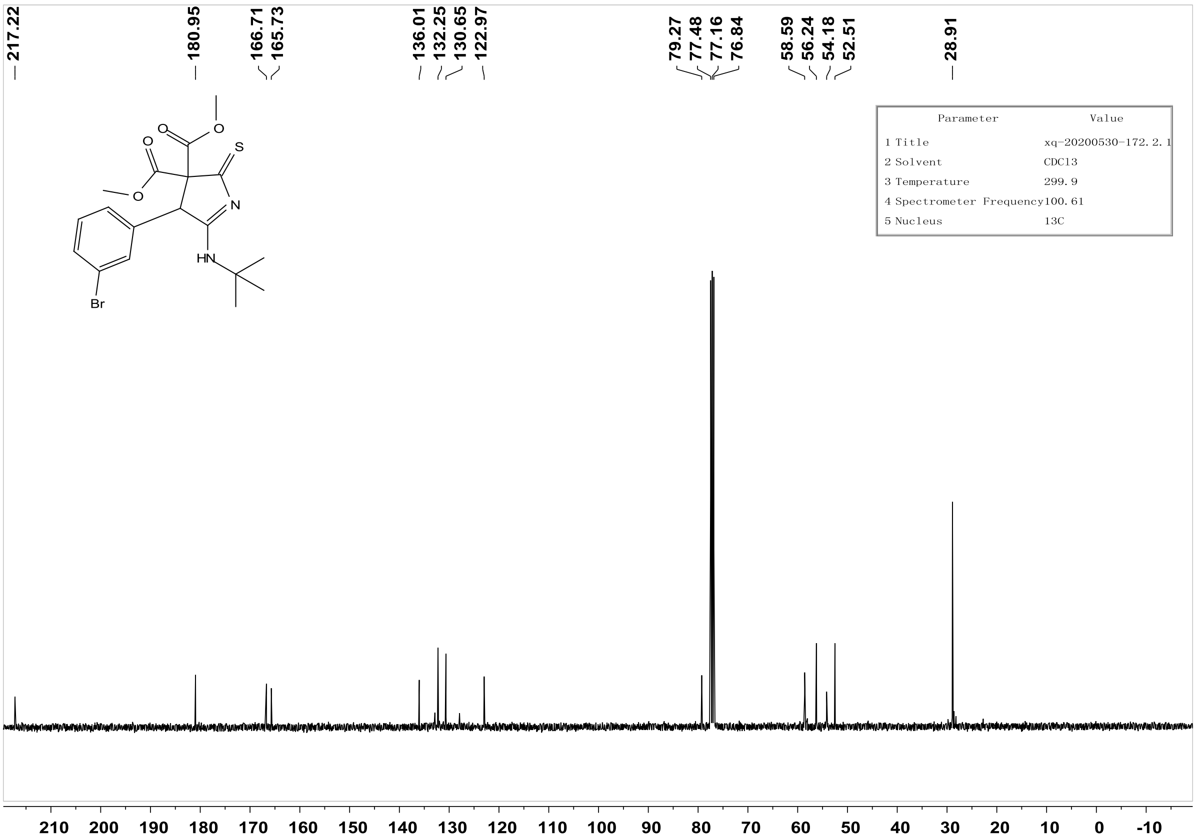


Figure S23. ^{1}H NMR of 4l

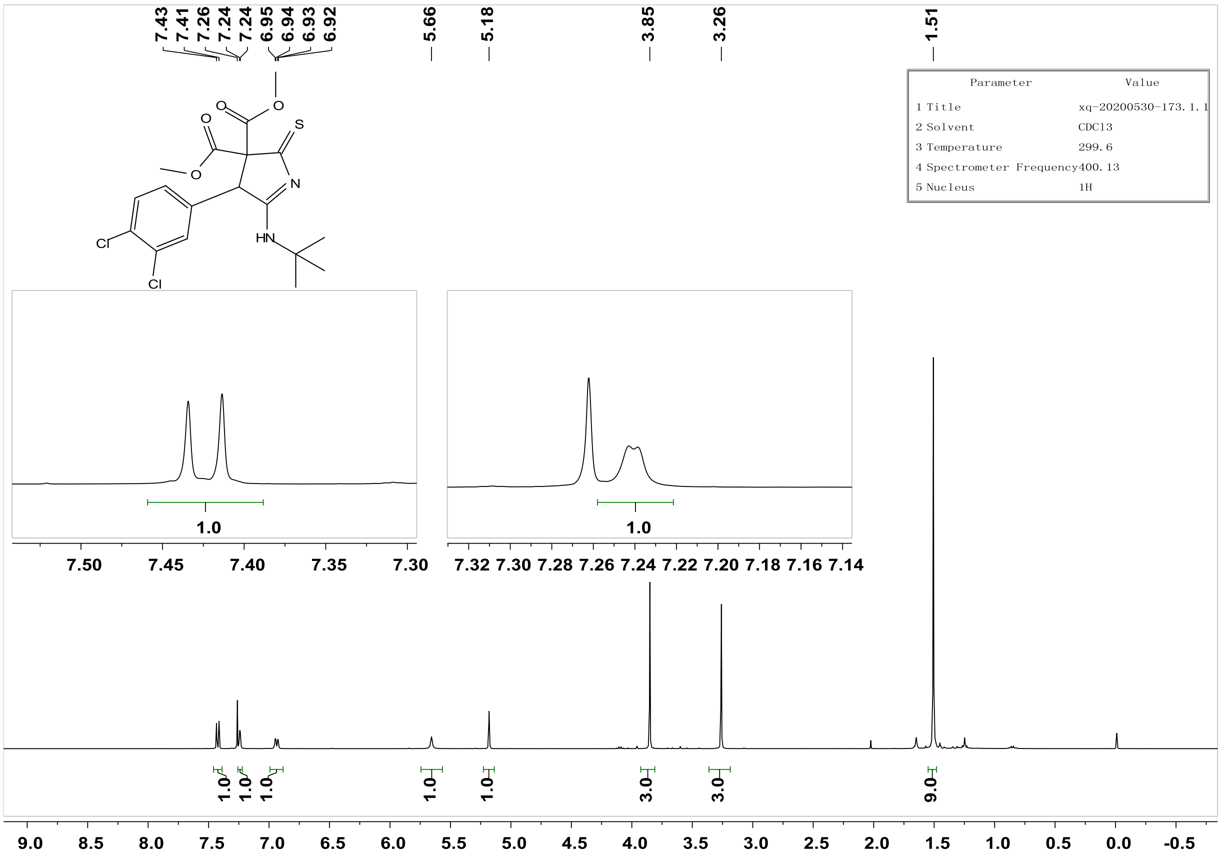


Figure S24. ^{13}C{^{1}H} NMR of 4l

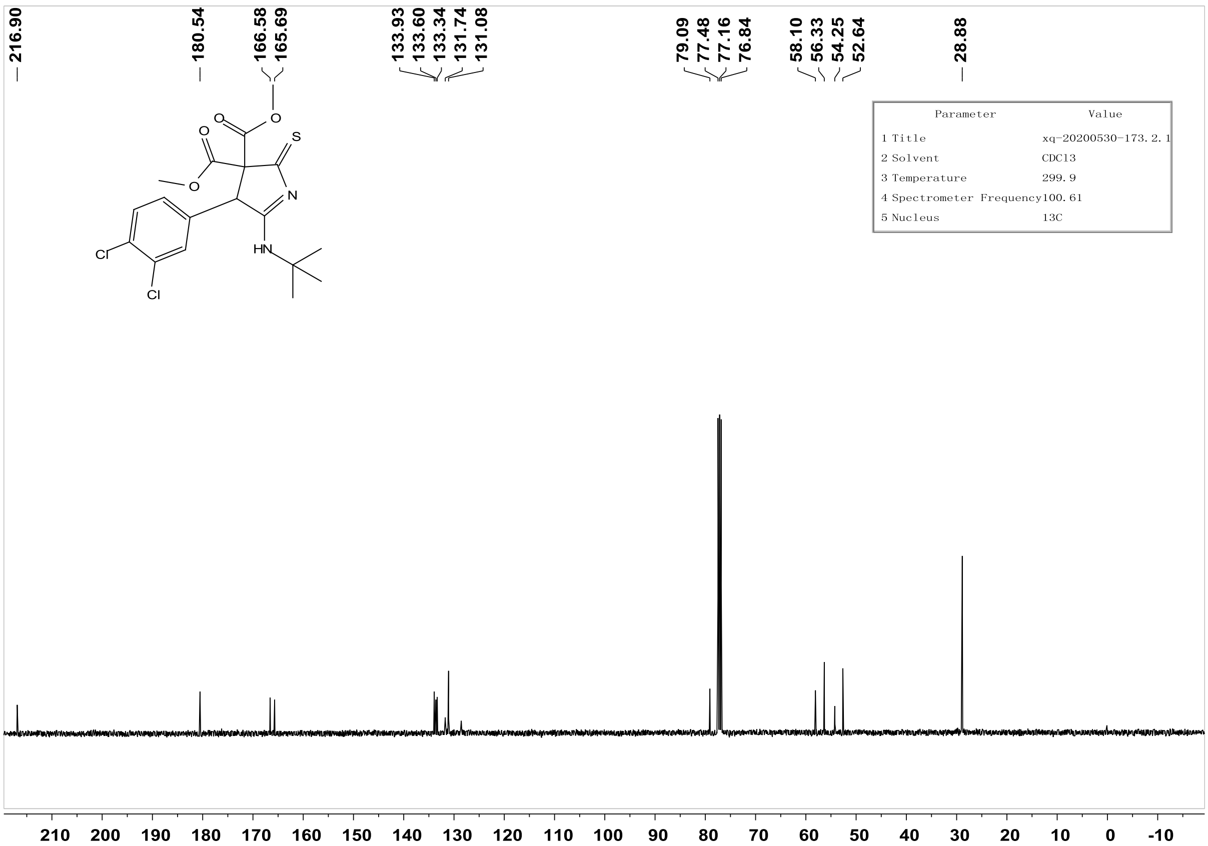


Figure S25. ^{1}H NMR of 4m

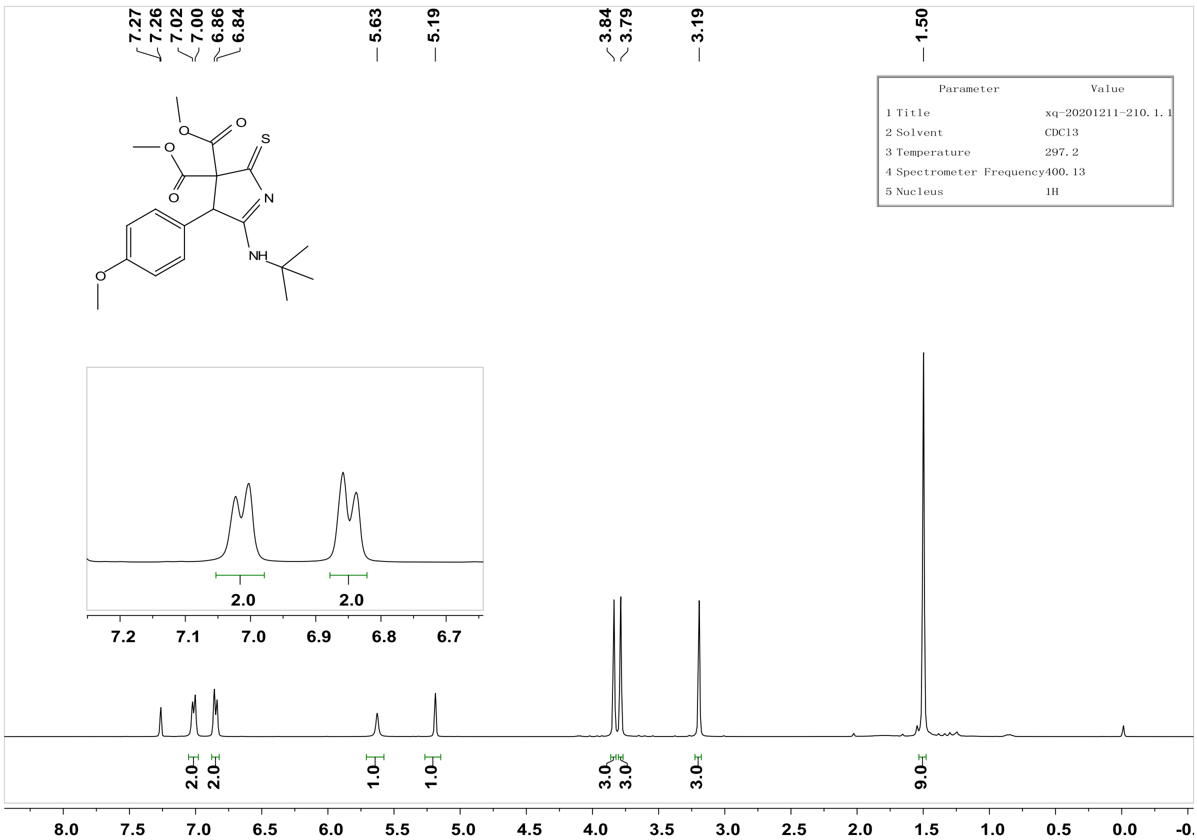


Figure S26. ^{13}C{^{1}H} NMR of 4m

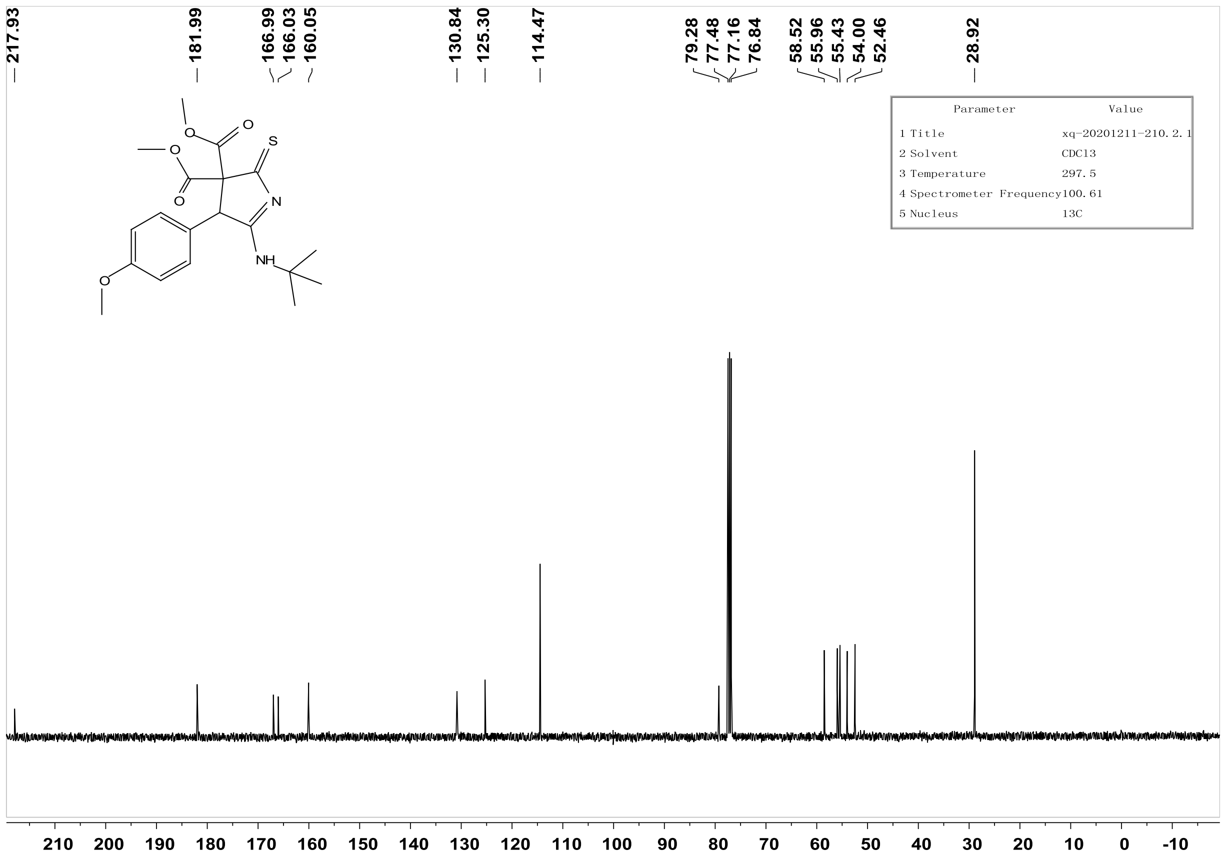


Figure S27. 1H NMR of 4n

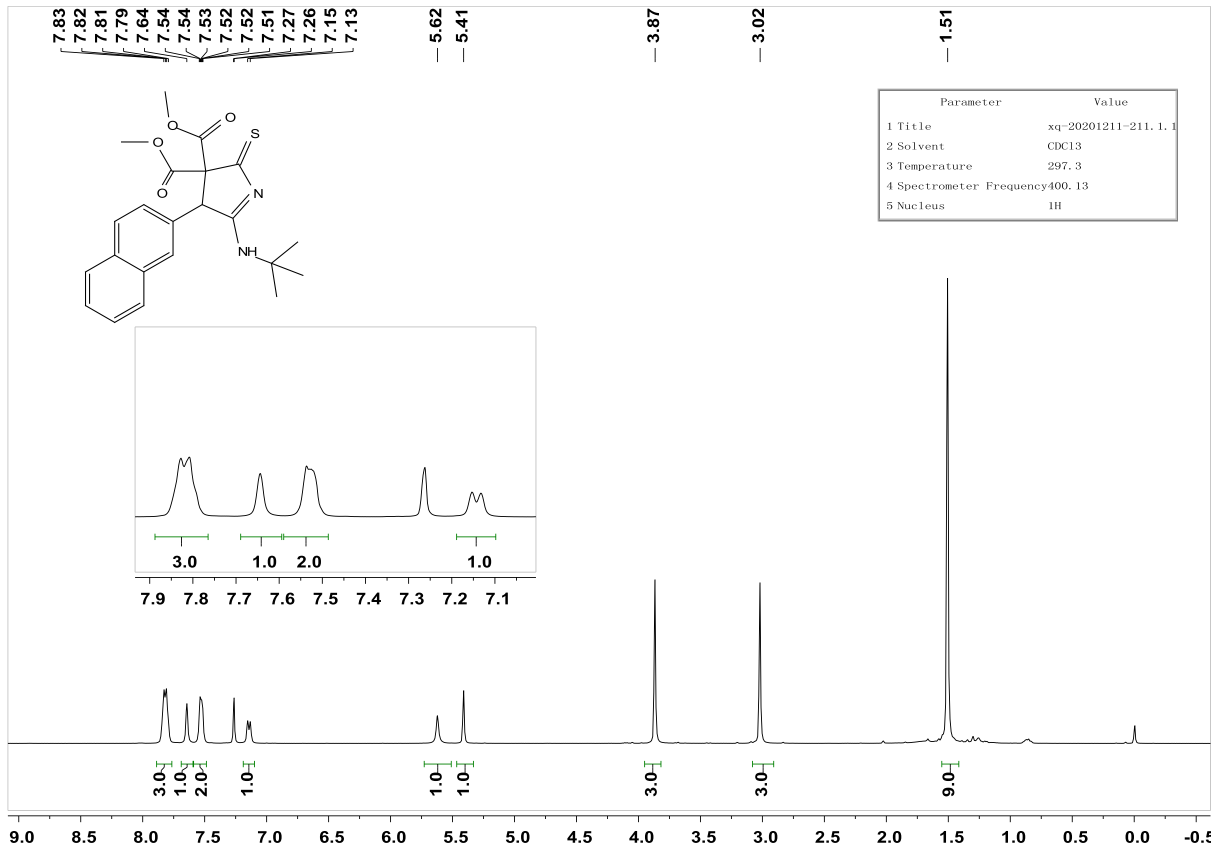


Figure S28. 13C{1H} NMR of 4n

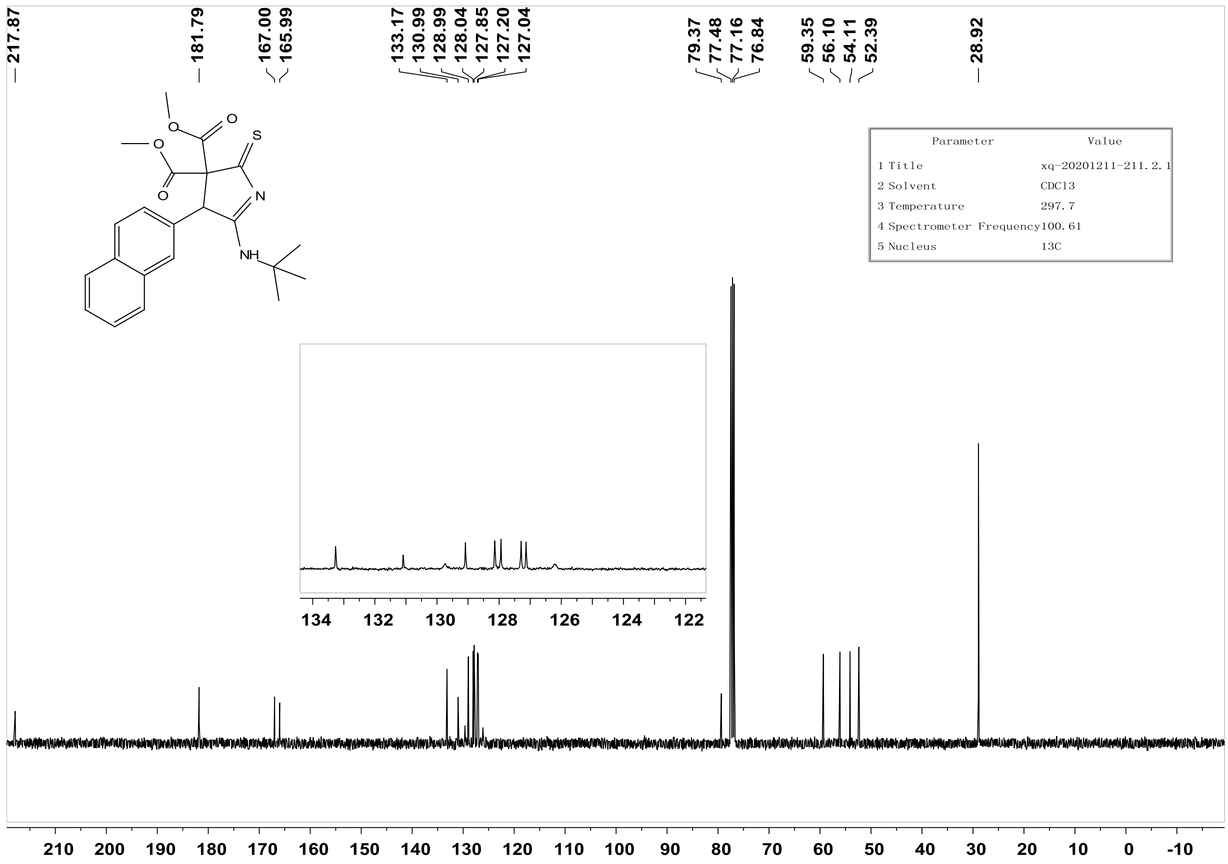


Figure S29. ^{1}H NMR of 4o

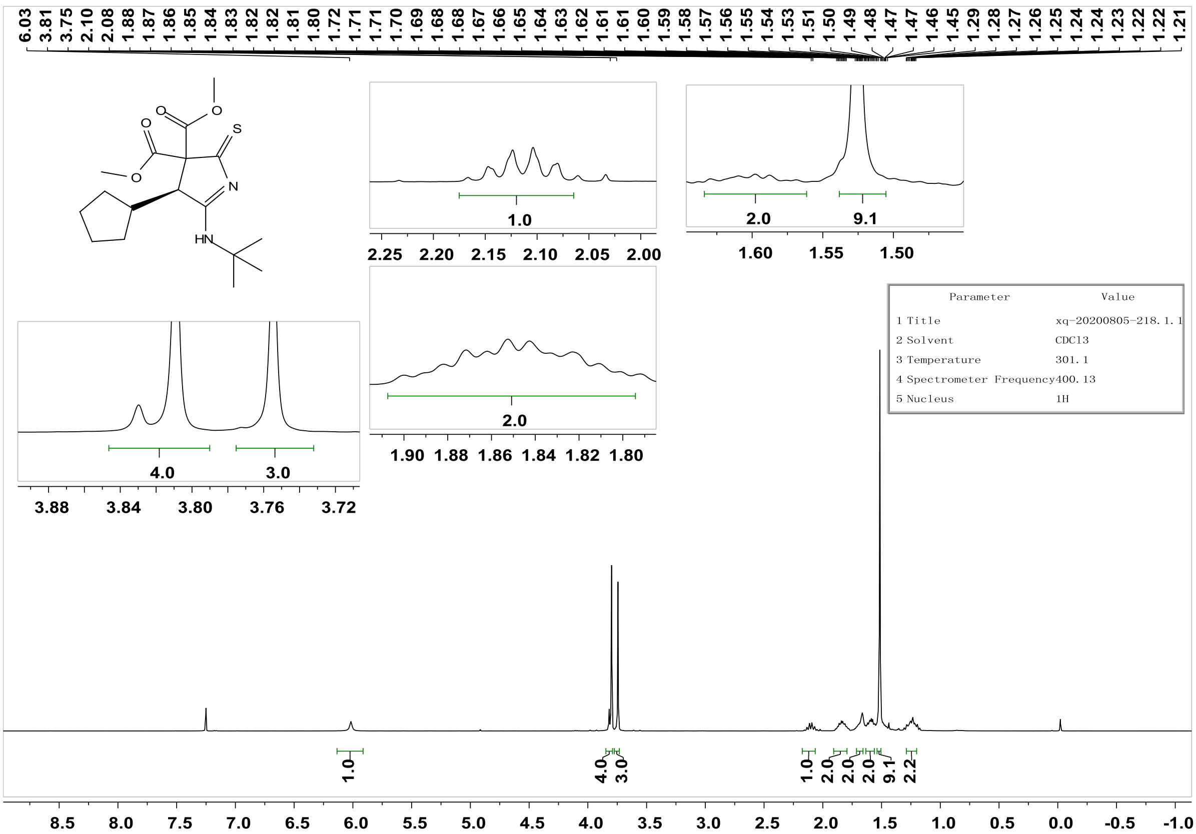


Figure S30. ^{13}C{^{1}H} NMR of 4o

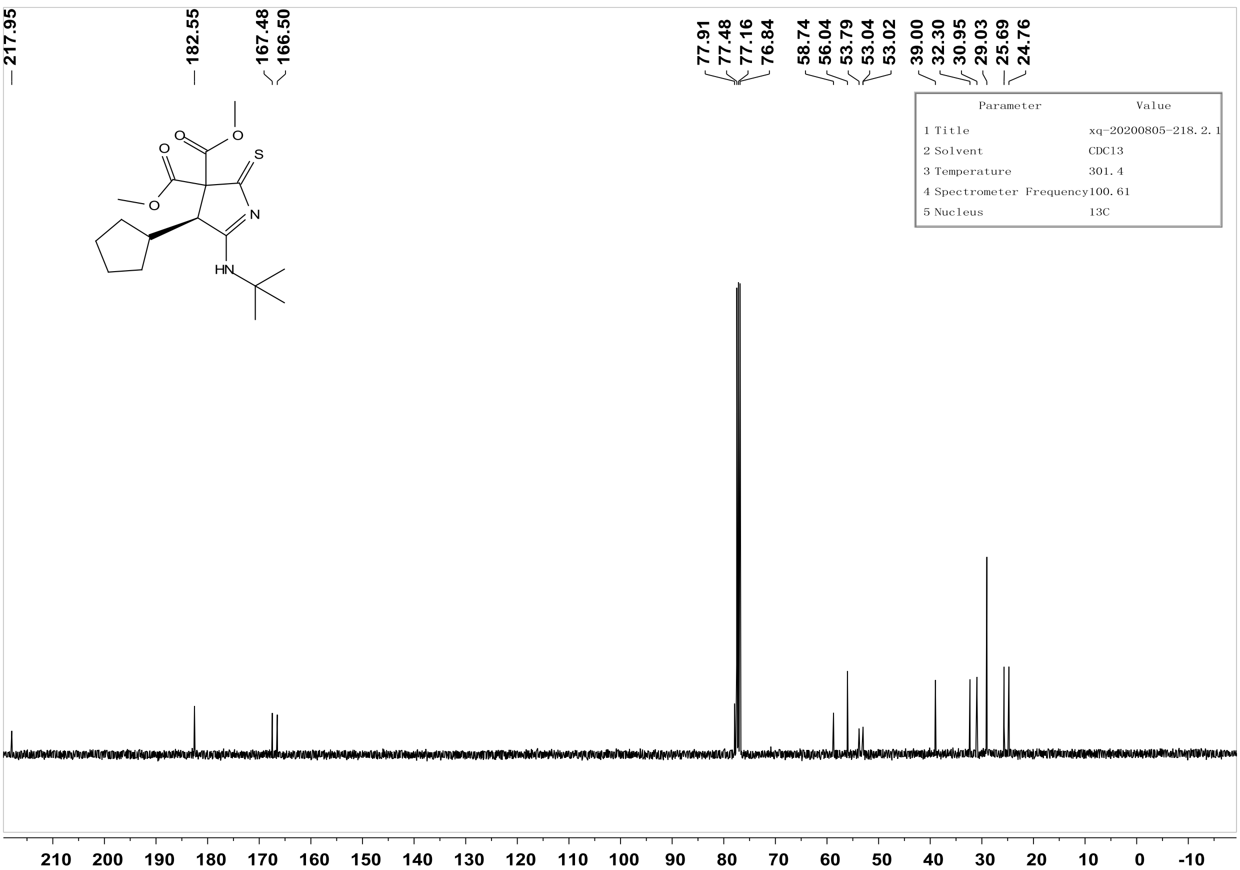


Figure S31. ^{1}H NMR of 4p

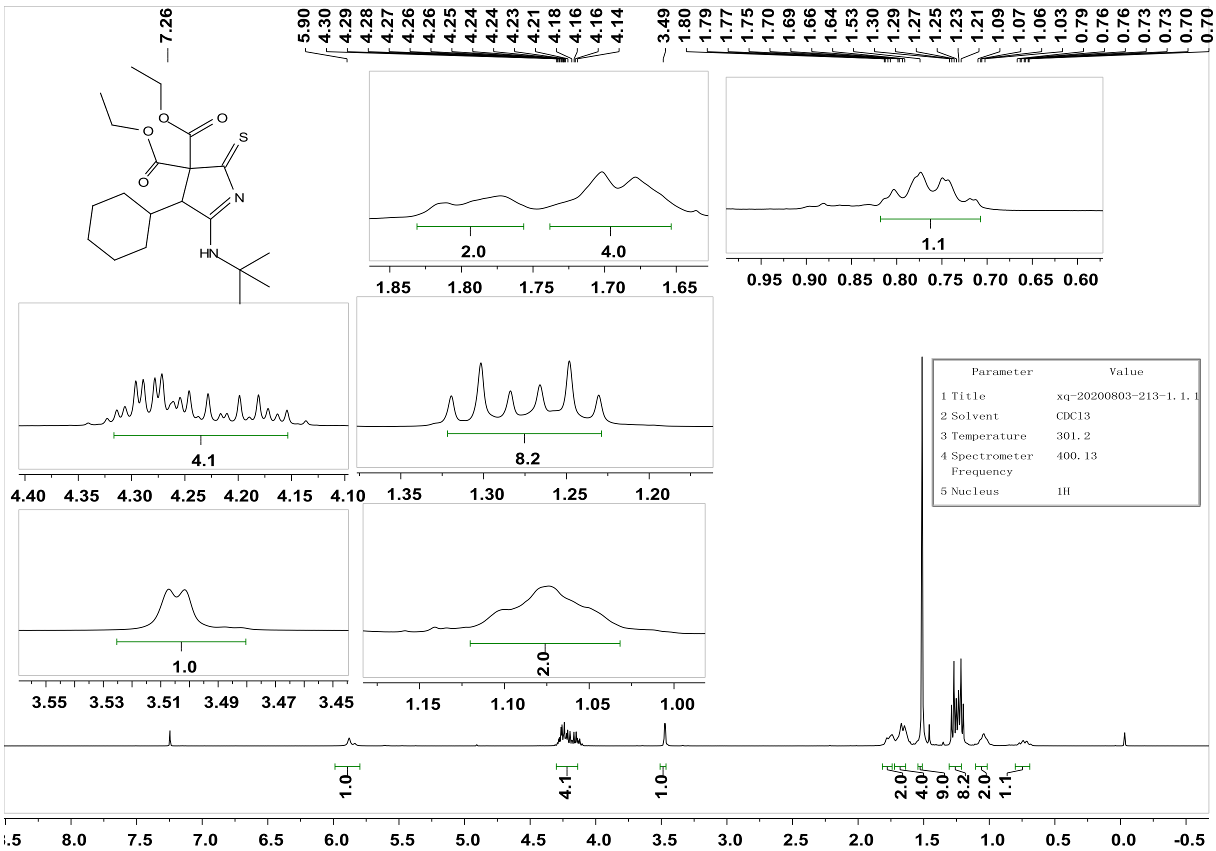


Figure S32. ^{13}C{^{1}H} NMR of 4p

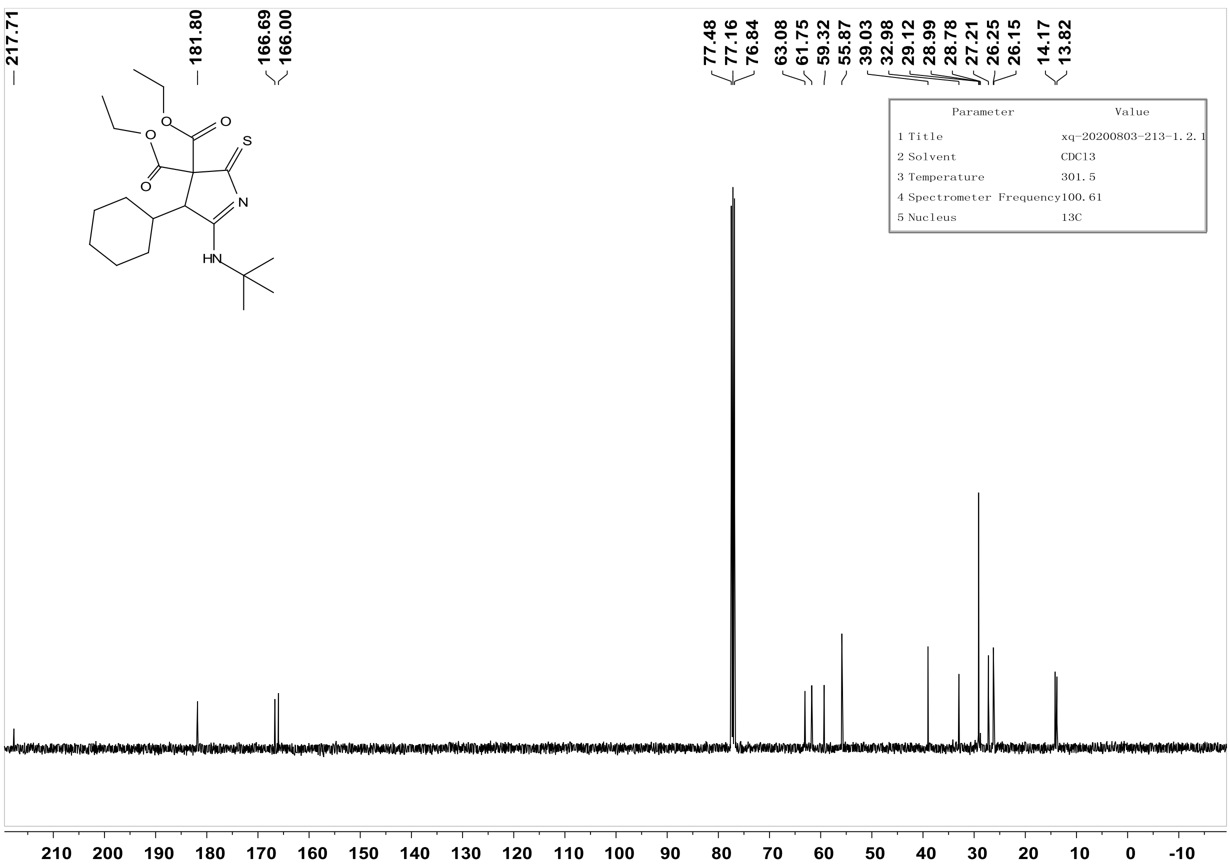


Figure S33. ^{1}H NMR of 4q

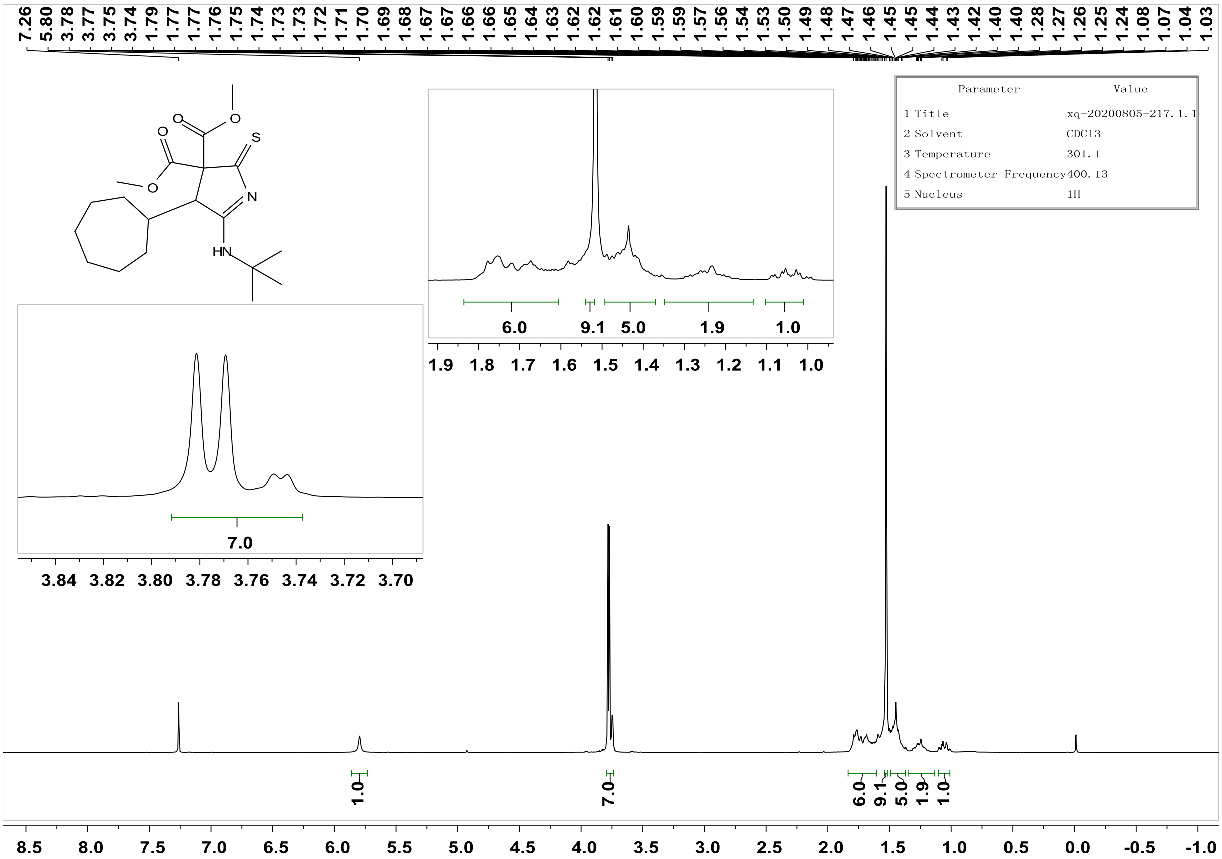


Figure S34. ^{13}C{^{1}H} NMR of 4q

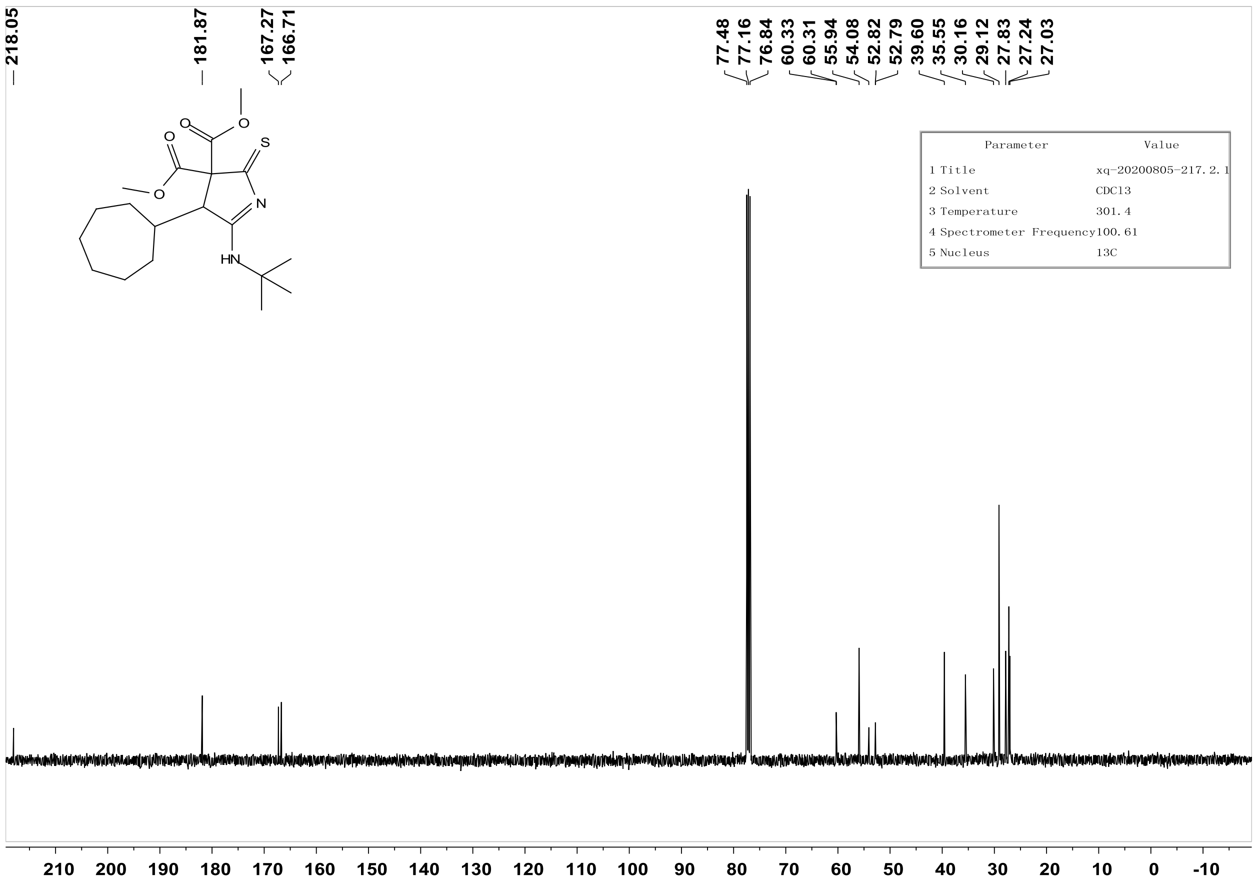


Figure S35. ^{1}H **NMR of 4r**

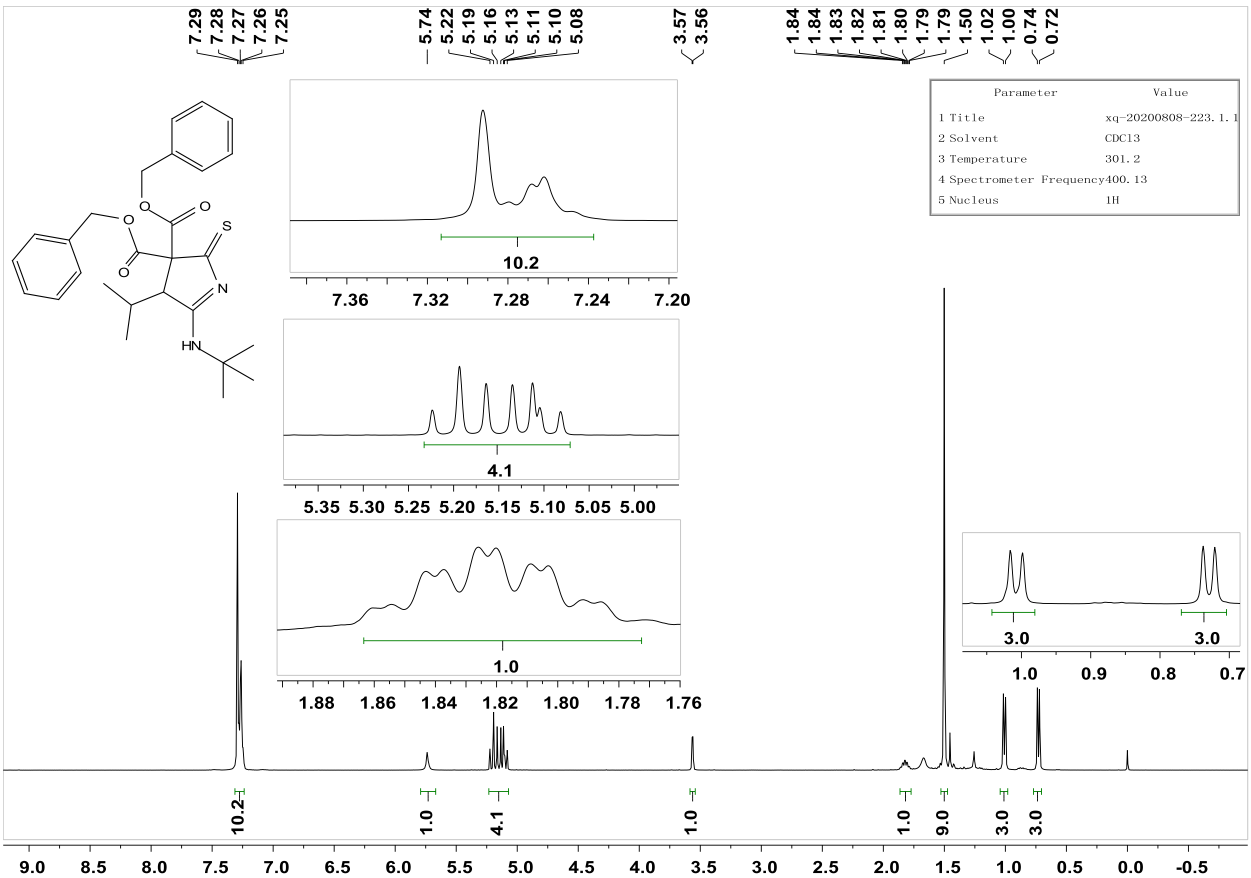


Figure S36. ^{13}C{^{1}H} **NMR of 4r**

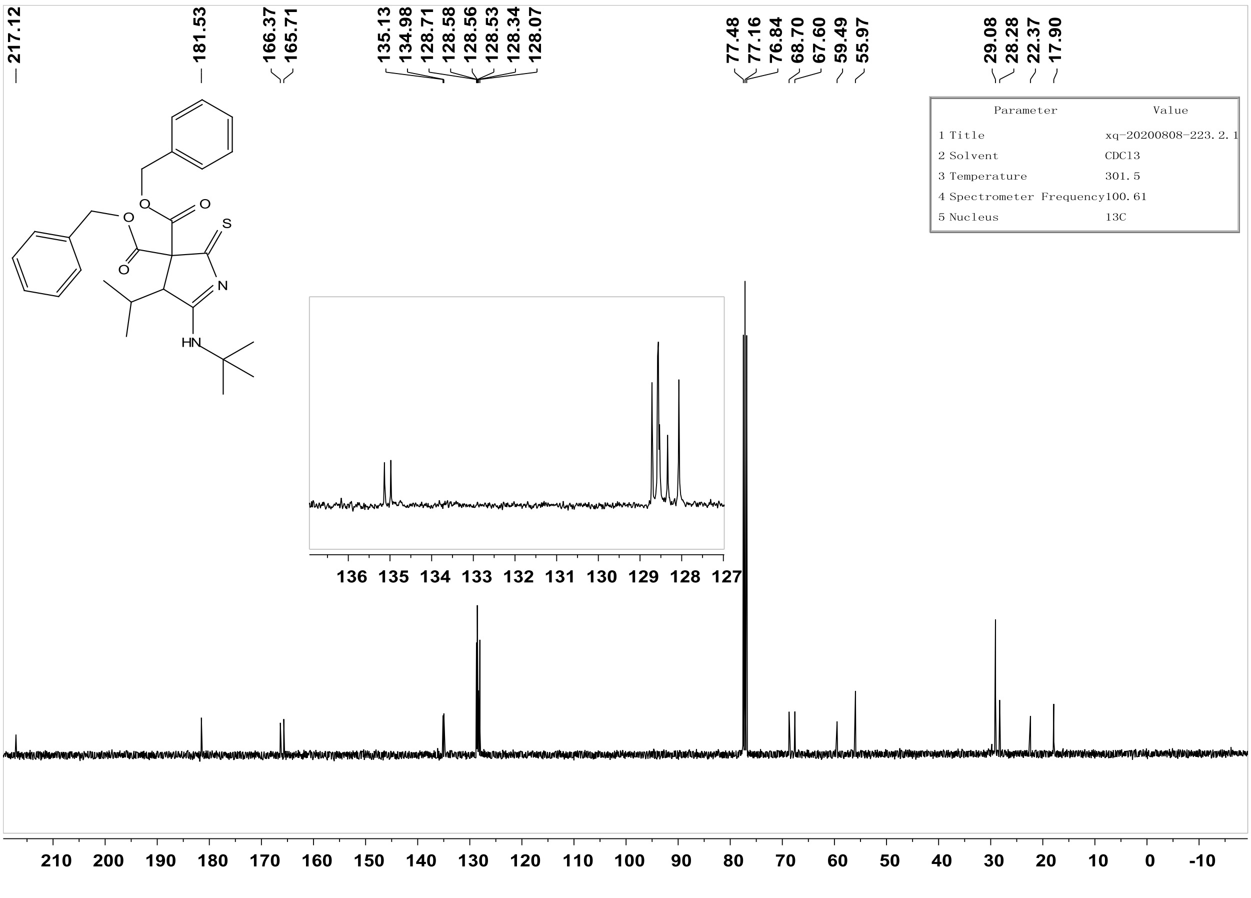


Figure S37. ^{1}H NMR of 4s

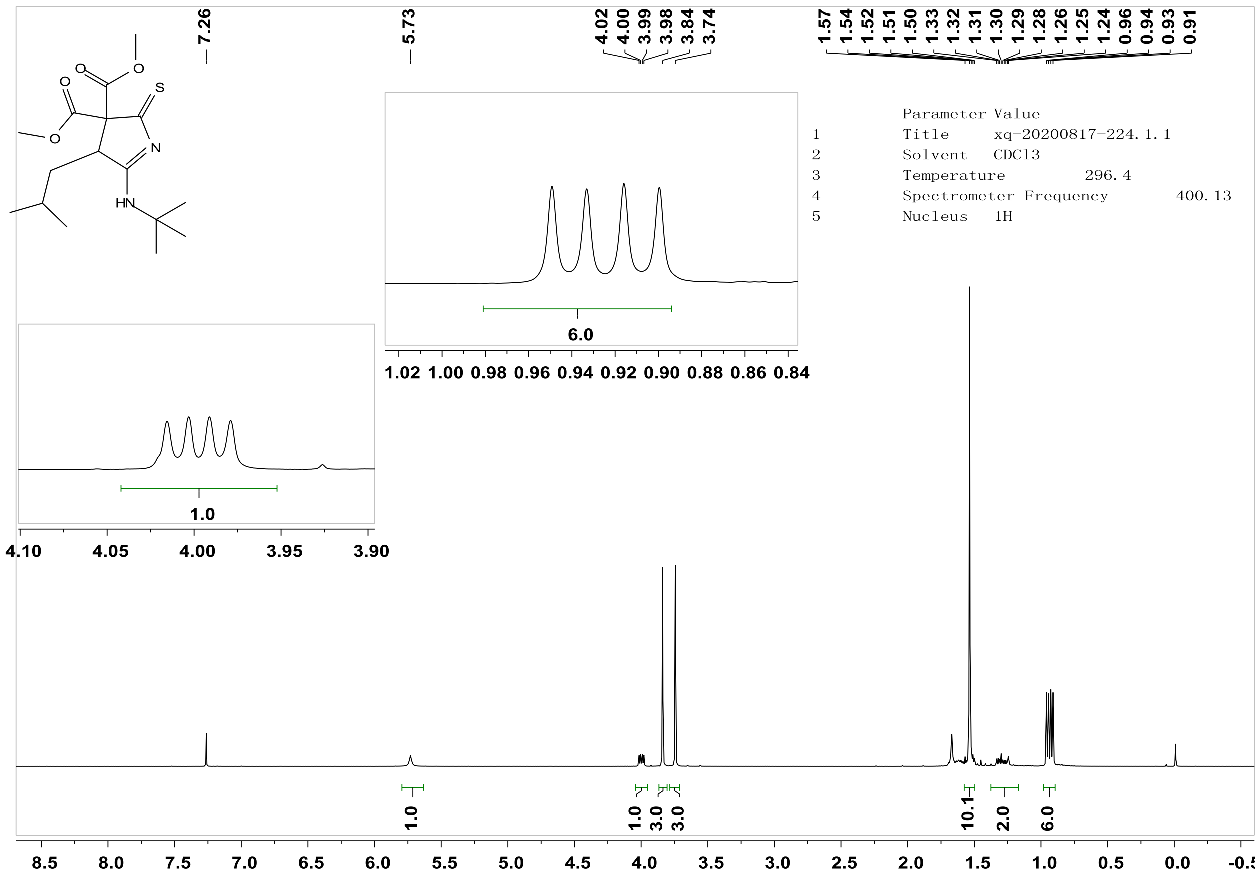


Figure S38. $^{13}C\{^1H\}$ NMR of 4s

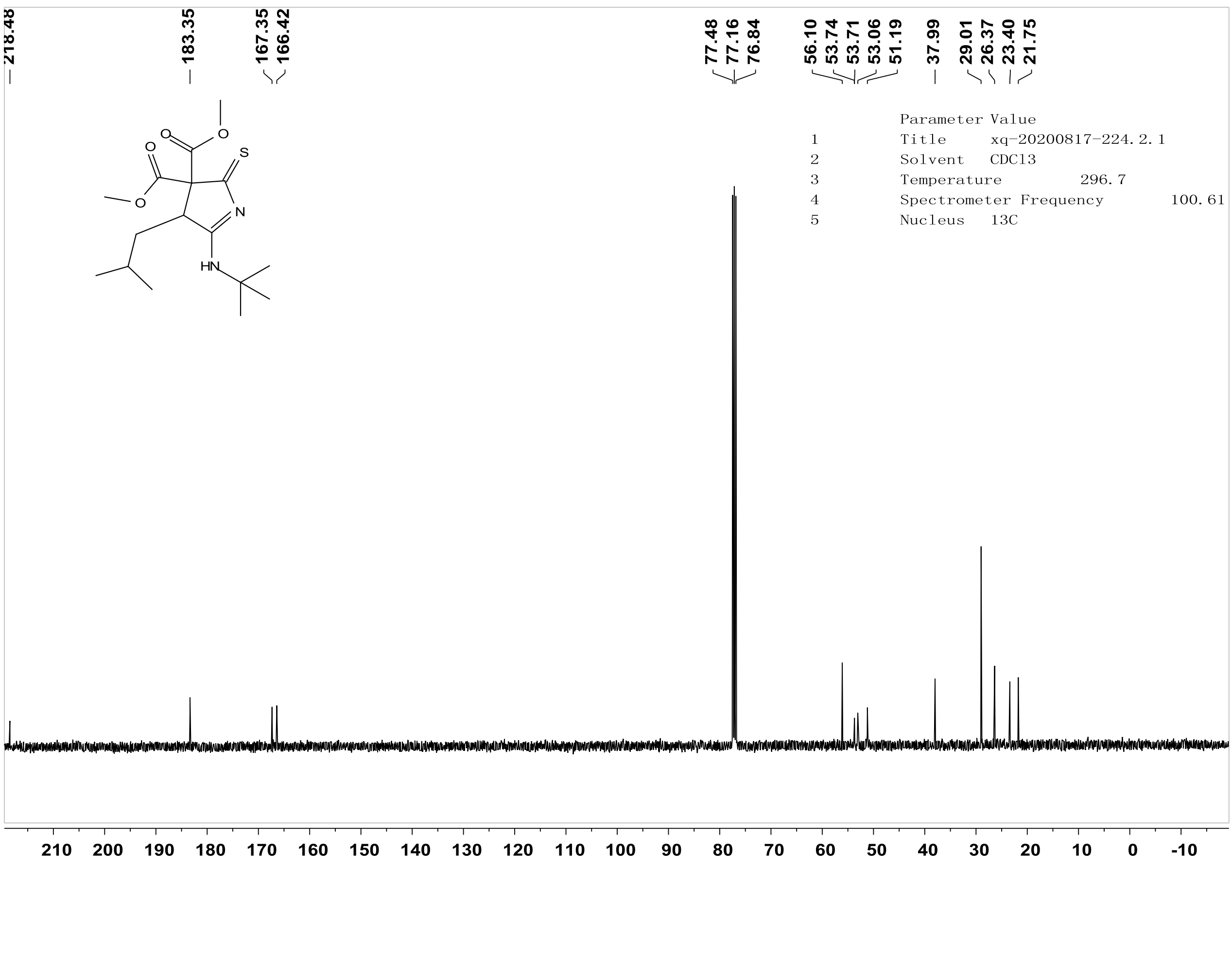


Figure S39. ^{1}H NMR of 4t

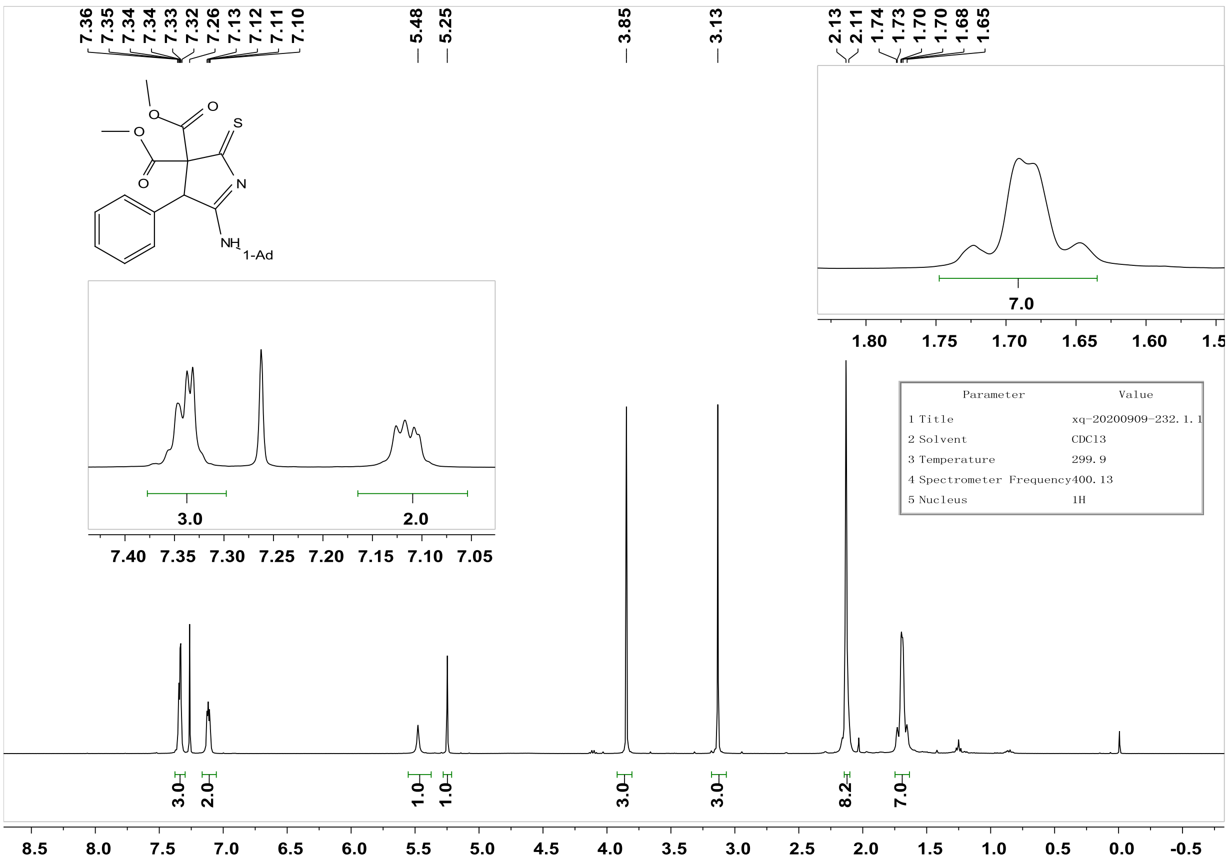


Figure S40. ^{13}C{^{1}H} NMR of 4t

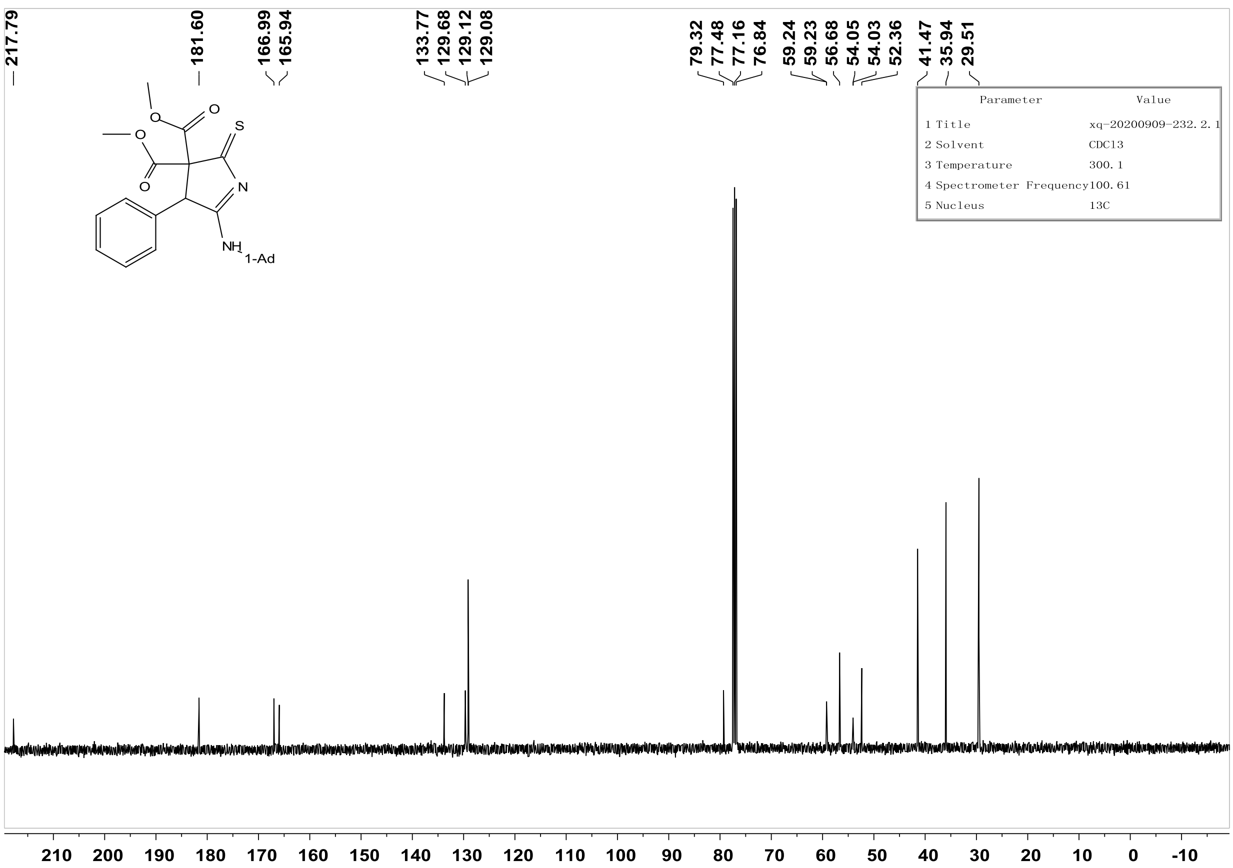


Figure S41. ^{1}H NMR of 5a

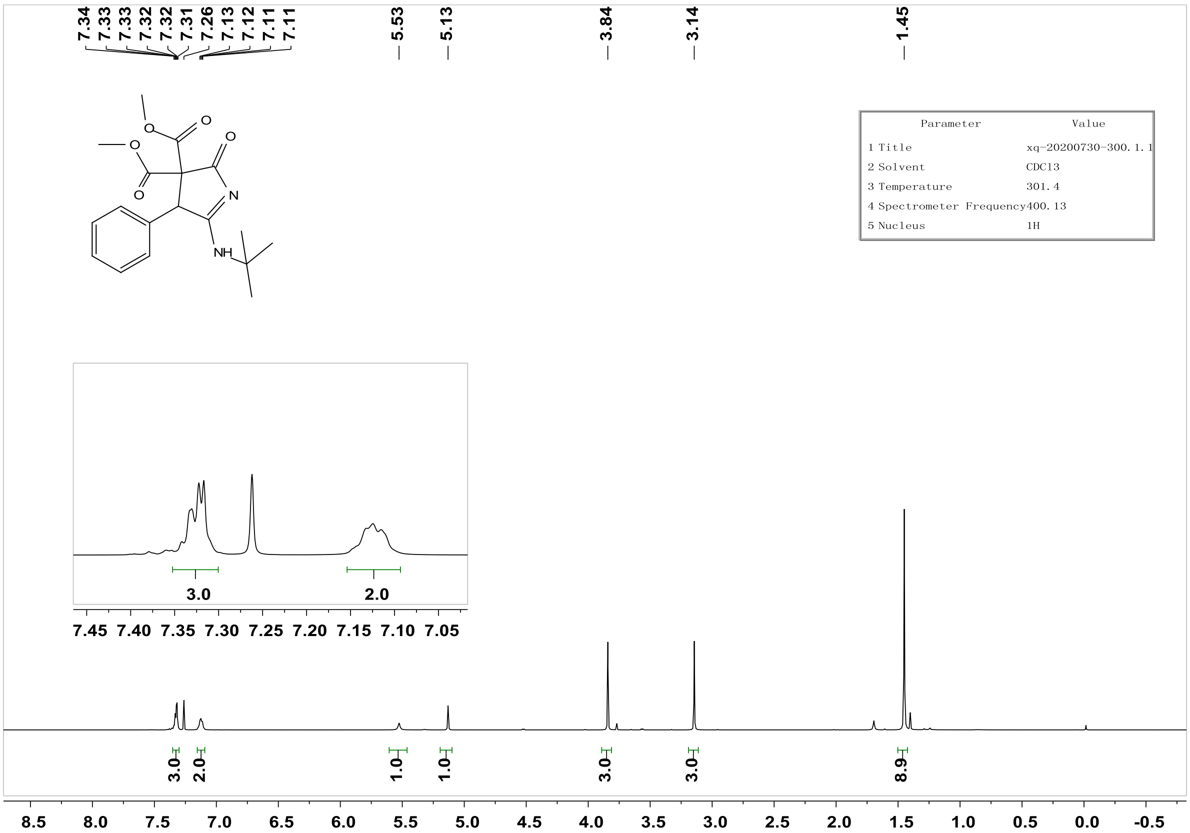


Figure S42. ^{13}C{^{1}H} NMR of 5a

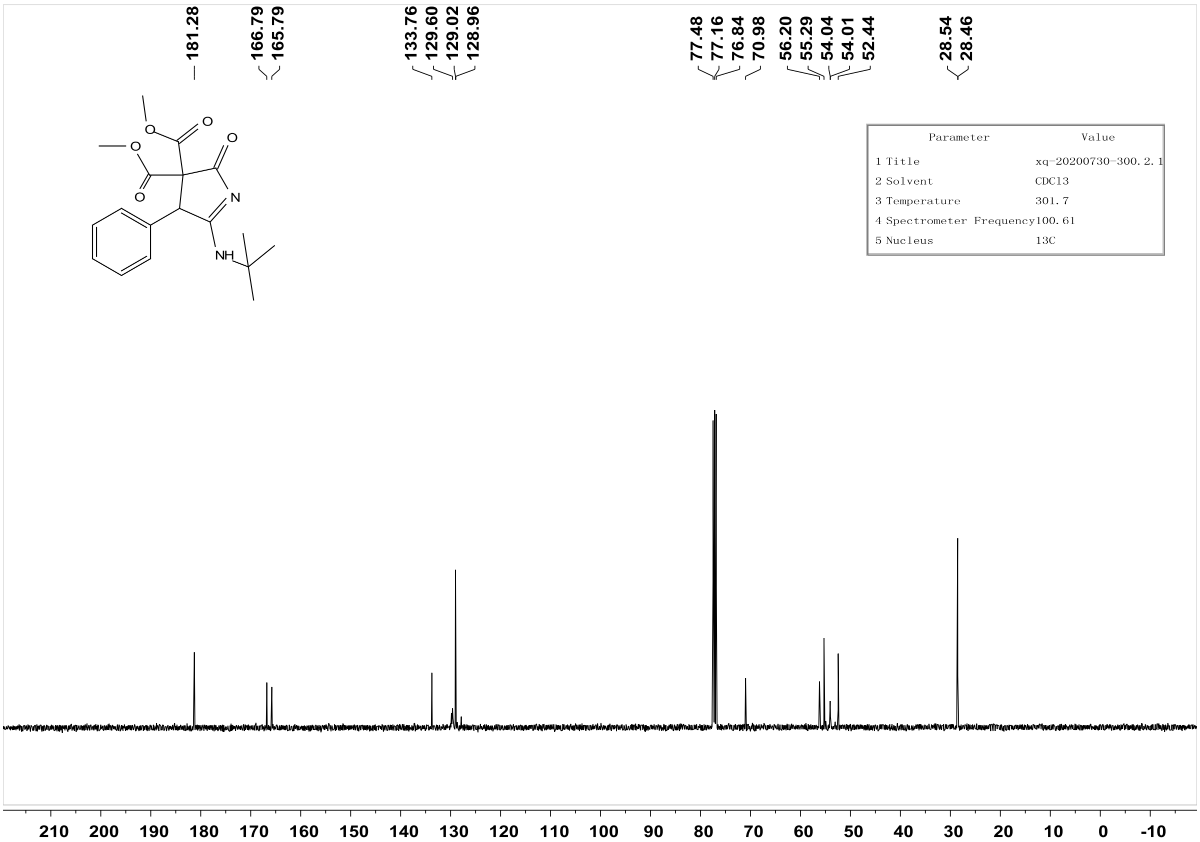


Figure S44. Cosy of 4a

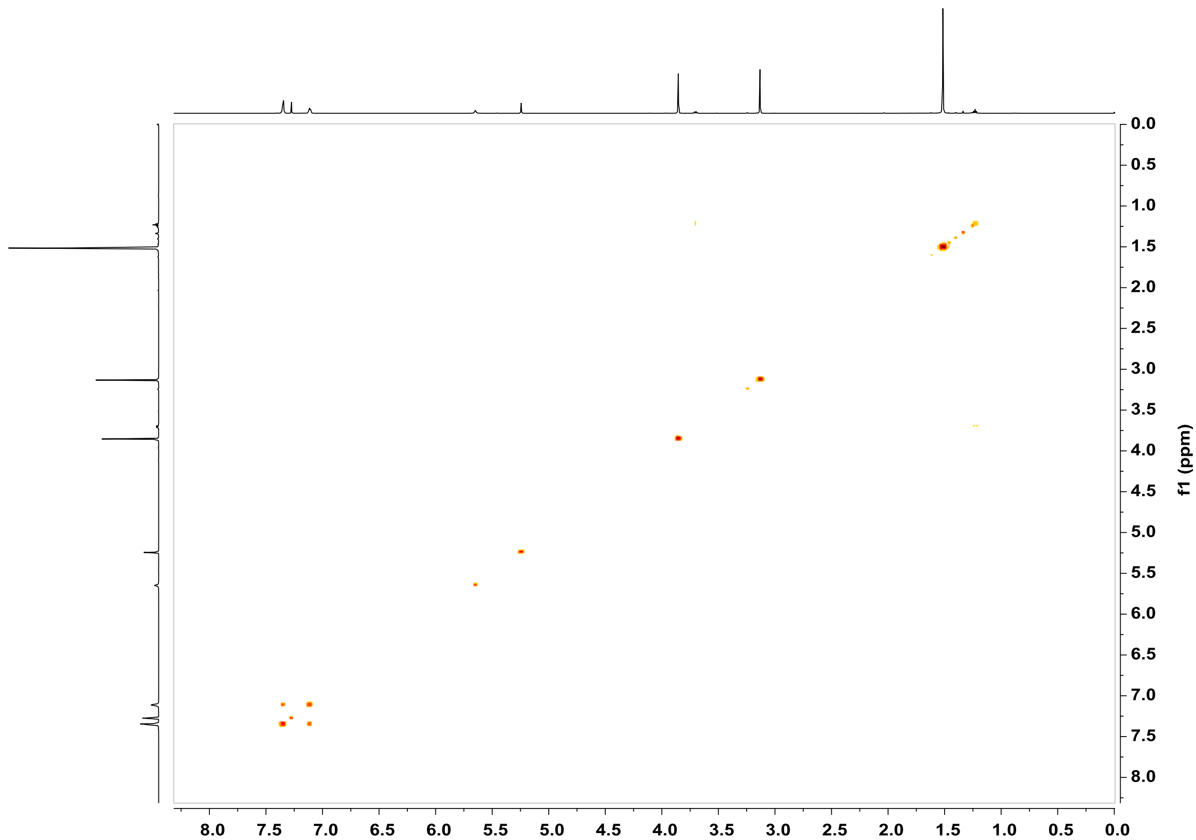


Figure S45. HSQCGP of 4a

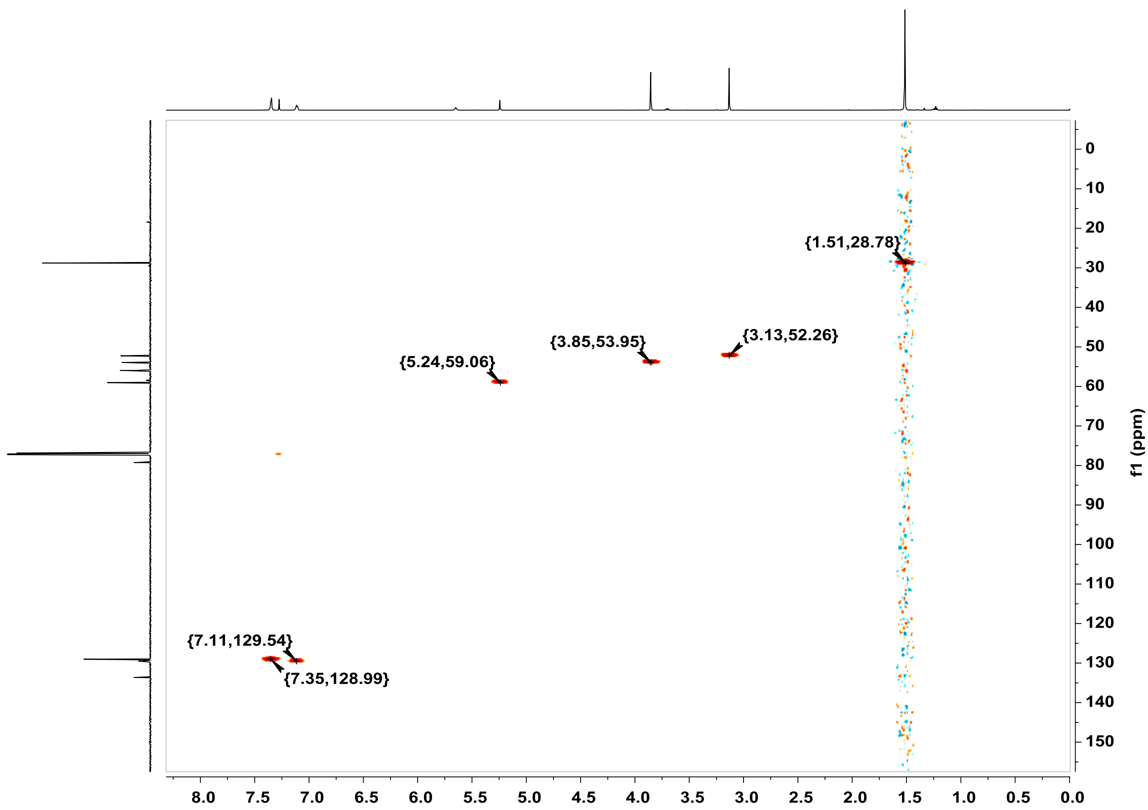


Figure S46. HSQCGP of 4a

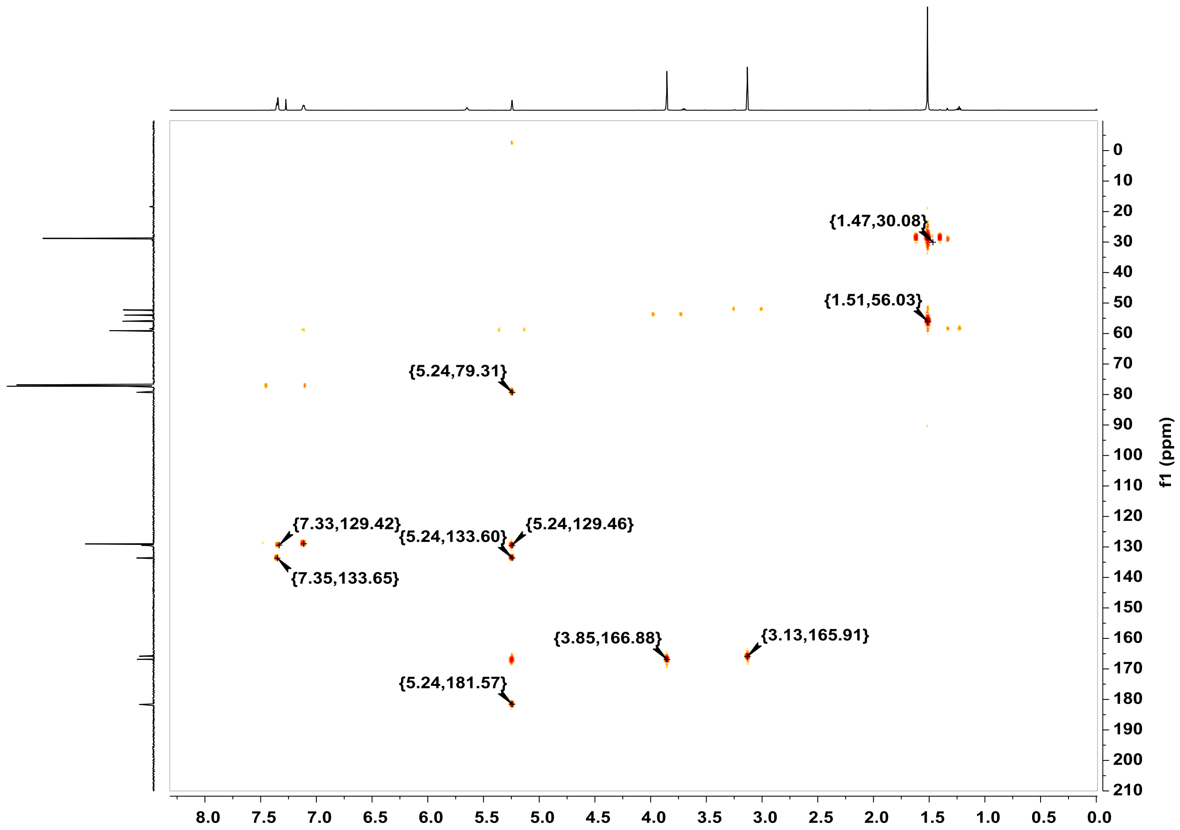
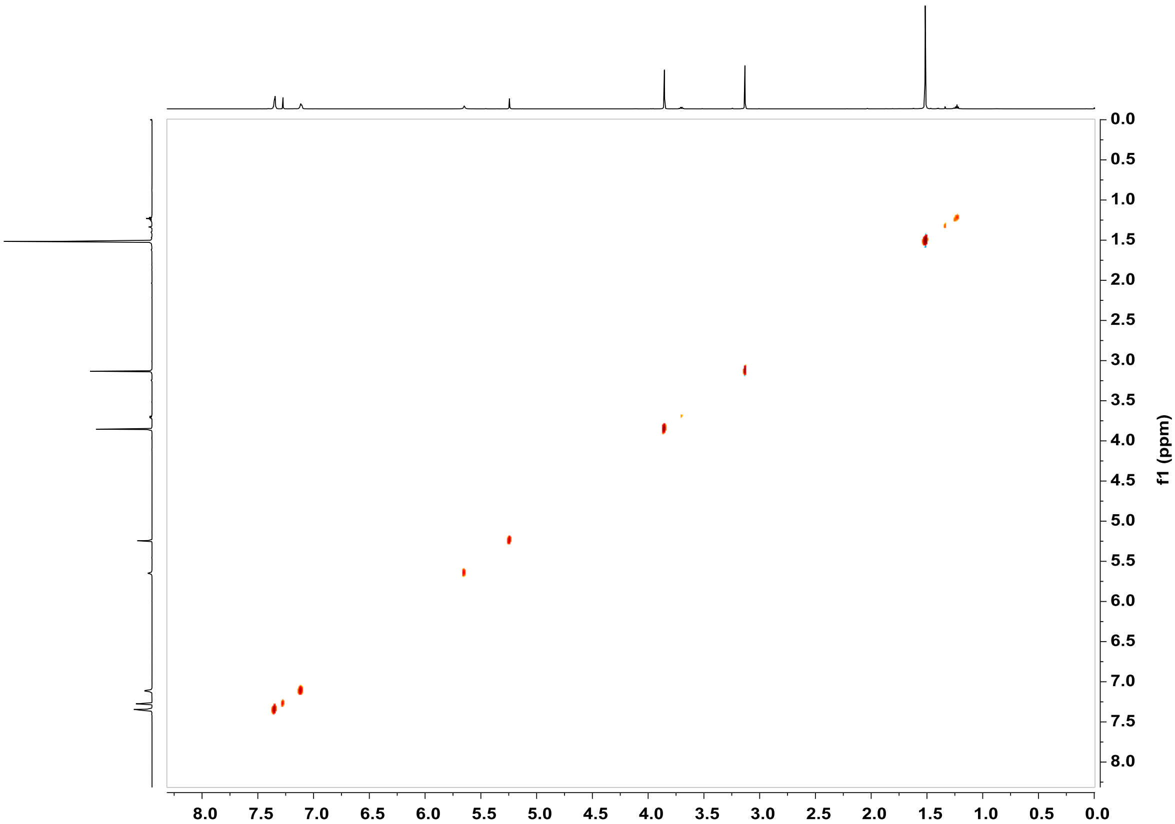
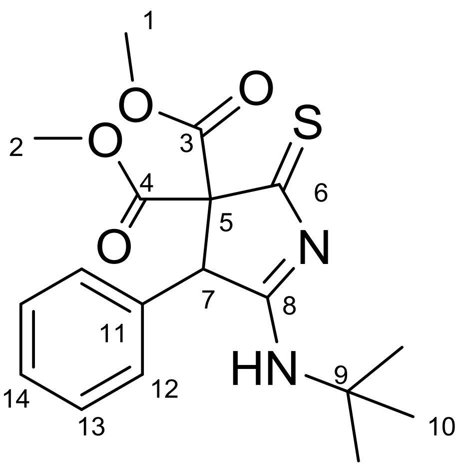


Figure S47. NOE of 4a





1, 3H (3.85, 53.95) 2, 3H (3.13, 52.26) 3, (166.88) 4, (165.91) 5, (79.31) 6, (181.57) 7, 1H (5.24, 59.06) 8, (129.46) 9, (56.03) 10, 9H (1.51, 28.78) 11, 1H (133.60) 12, 1H (7.32, 128.99) 13, 1H (7.11, 129.54) 14, 1H (7.35, 128.99)

Figure S48. ^{1}**H NMR of** Et_3NHNCS

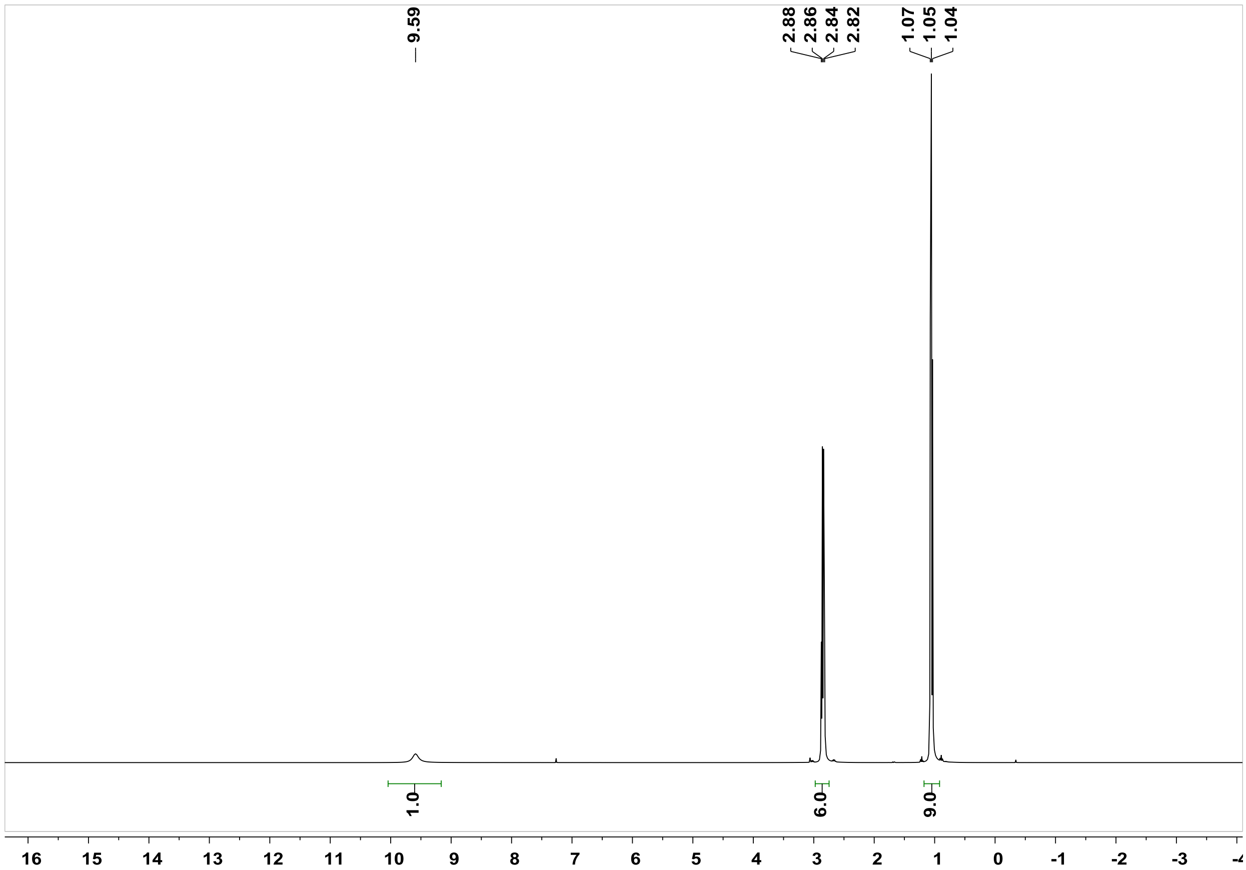
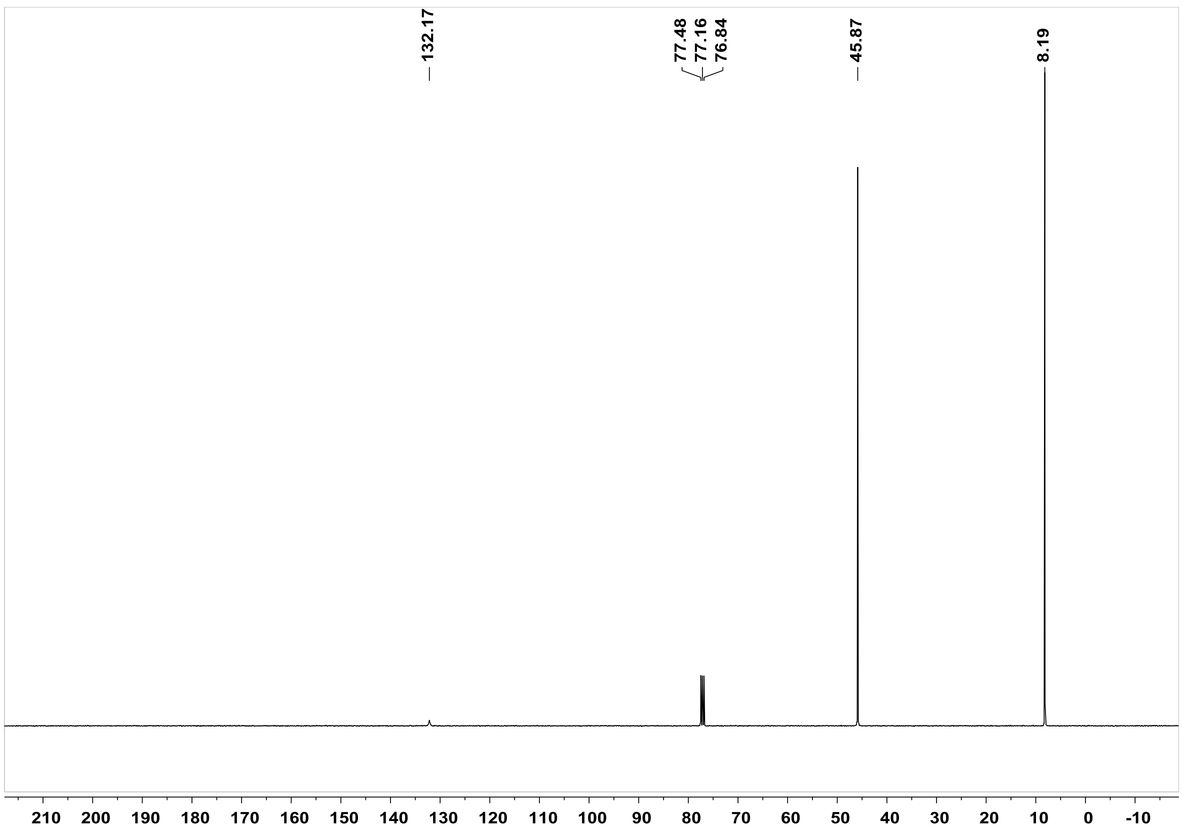


Figure S49. ^{13}**C NMR of** Et_3NHNCS



10. Absolute configuration of 4a and 4o

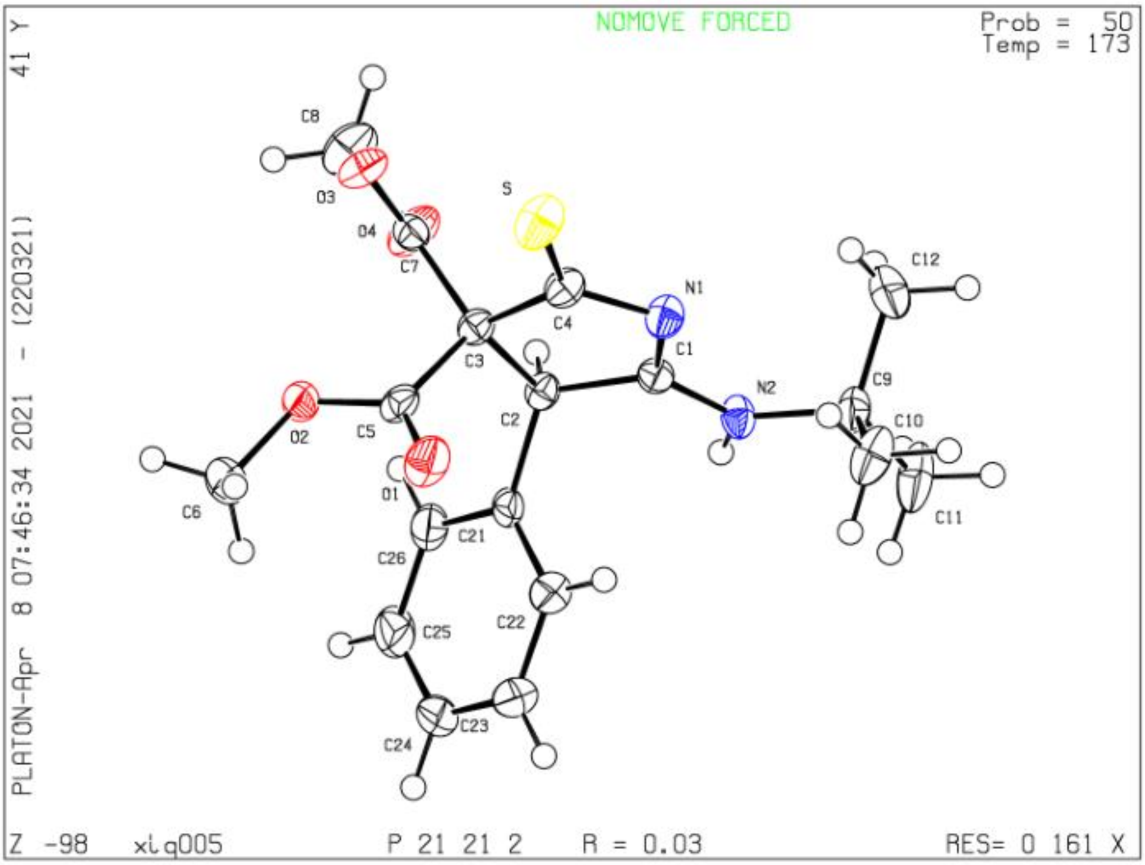


Figure S50. X-ray structure of 4a

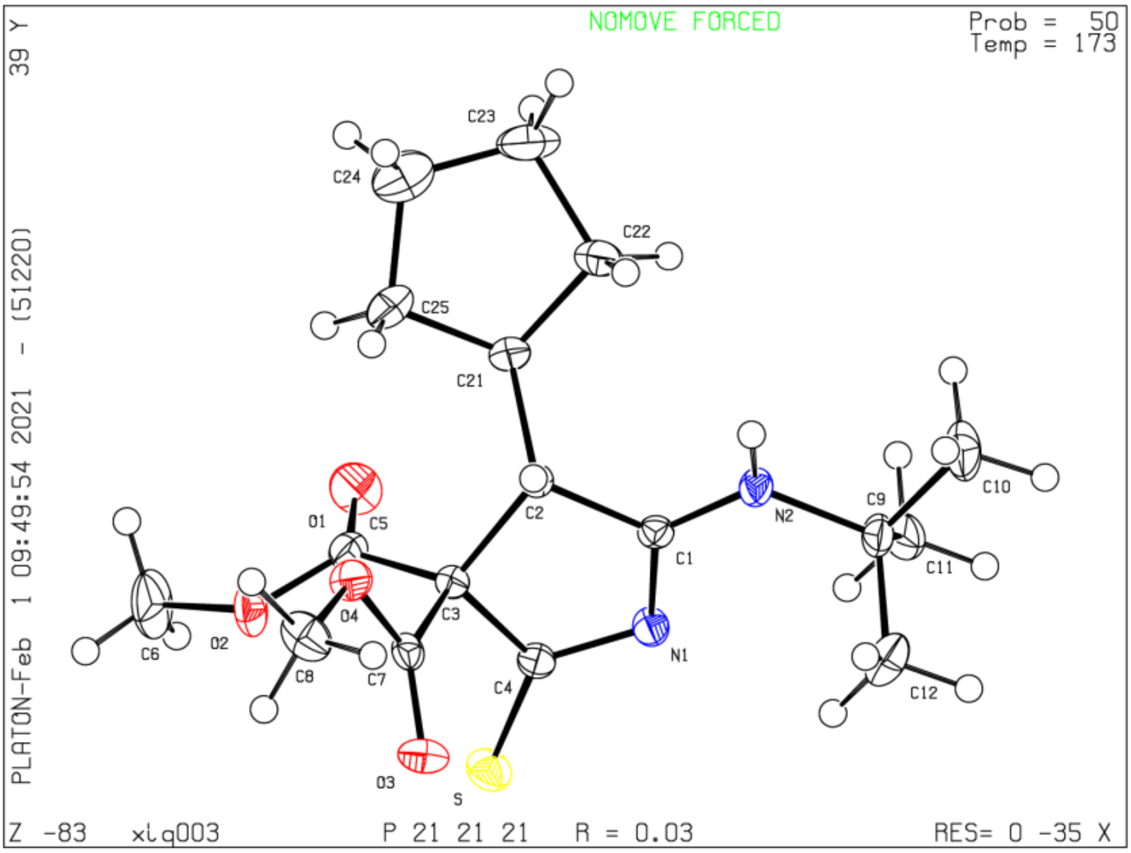


Figure S51. X-ray structure of 4o

Crystallographic Data for **4a** and **4o**.

	4a	**4o**
Formula	C18 H22 N2 O4 S	C17 H26 N2 O4 S
Formula mass (amu)	362.43	354.46
Space group	P 21 21 2	P 21 21 21
a (Å)	12.4981(5)	9.7300(2)
b (Å)	17.3226(8)	11.7702(3)
c (Å)	8.4593(4)	16.4807(4)
α (deg)	90	90
β (deg)	90	90
γ (deg)	90	90
V (Å^3)	1831.44(14)	1887.44(8)
Z	4	4
λ (Å)	0.71073	1.54178
T (K)	173 K	173 K
ρ_{calcd} (g cm^{-3})	1.314	1.247
μ (mm^{-1})	0.201	1.712
Transmission factors	0.898–0.989	0.637–0.781
θ_{max} (deg)	25.430	68.307
No. of unique data, including $F_o^2 < 0$	3366	3442
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	3139	3401
No. of variables	235	226
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ [a]	0.0308	0.0252
$R_w(F_o^2)$ [b]	0.0678	0.0704
Goodness of fit	1.066	1.101

[a] $R(F) = \sum||F_o| - |F_c|| / \sum|F_o|$.

[b] $R_w(F_o^2) = [\sum[w(F_o^2 - F_c^2)^2] / \sum wF_o^4]^{1/2}$; $w^{-1} = [\sigma^2(F_o^2) + (Ap)^2 + Bp]$, where $p = [\max(F_o^2,0) + 2F_c^2] / 3$.

11. References

(1) (a) Y. H. Wen, X. Huang, J. L. Huang, Y. Xiong, B. Qin, X. M. Feng, *Synlett* 2005, 2445. (b) Z. P. Yu, X. H. Liu, Z. H. Dong, M. S. Xie, X. M. Feng, *Angew. Chem. Int. Ed.* 2008, **47**, 1308.

(2) (a) J. Wang, Y. Zhou, L. Zhang, Z. Li, X. Chen, H. Liu, *Org. Lett.* 2013, **15**, 1508. (b) Y. Guan, J. W. Attard, Visco, M. D. Fisher, T. J. Mattson, *Chem. Eur. J.* 2018, **24**, 7123.

(3) I. A. Andreev, N. K. Ratmanova, A. U. Augustin, O. A. Ivanova, I. I. Levina, V. N. Khrustalev, D. B. Werz, I. V. Trushkov, *Angew. Chem. Int. Ed.* 2021, **60**, 7927.