Organocatalytic enantioselective α-amination of 5-substituted rhodanines: an efficient approach to chiral *N*,*S*-acetals

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1. General information and starting materials

General Information. Unless otherwise noted, materials were purchased from commercial suppliers and used without further purification. Column chromatography was performed on silica gel (100~200 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: $[\alpha]^{T}_{D}$ (c g/100 mL, solvent). ^{1}H and ^{13}C NMR spectra were recorded on either a VARIAN INOVA-400 spectrometer (400 MHz for ^{1}H, 100 MHz for ^{13}C) or a BRUKER AVANCE II-400 spectrometer (400 MHz for ^{1}H, 101 MHz for ^{13}C) with chemical shifts reported as ppm (in $CDCl_3$, TMS as internal standard). High resolution mass spectrometry data were obtained with an HP1100 LC/MSD mass spectrometer and an LC/Q-TOF MS spectrometer.

Starting materials. All solvents and materials were purchased from commercial sources and used without purification unless otherwise noted. Chiral guanidines **G1** and **G2** were prepared from L-tartaric acid according to the literature.[1] Natural cinchona alkaloids and dihydroquinine were purchased from commercial sources and used without further purification. Cinchona alkaloid derived catalysts Q-**4a** and Q-**4b** were prepared according to literature methods.[2] Racemic samples of **3** were prepared with 0.1 equiv. *N*,*N*,*N*′,*N*′-tetramethylguanidine (TMG) as the catalyst in CH_2Cl_2 at room temperature.

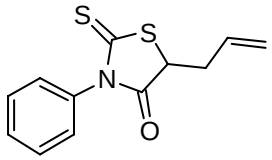
2. Preparation of 5-substituted rhodanines

R= alkyl, aryl

1

The mercapto carboxylic acids other than 2-mercapto-propanoic acid were prepared following the literature procedures.[3] 5-Substituted rhodanines were prepared from the corresponding mercapto carboxylic acids and isothiocyanates according to the literature procedure.[4]

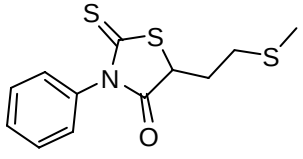
5-allyl-3-phenyl-2-thioxothiazolidin-4-one (**1e**)



1e

Yellow solid; mp: 64.7-65.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.76-2.83 (1H, m), 2.97-3.02 (1H, m), 4.47 (1H, dd, *J* = 4.1, 8.3 Hz), 5.26-5.30 (2H, m), 5.82-5.90 (1H, m), 7.16-7.18 (2H, m), 7.48-7.55 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 33.5, 48.1, 117.4, 125.3, 126.6, 126.7, 132.0, 172.6, 197.6; HRMS (ESI) m/z calcd for $C_{12}H_{11}NOS_2Na^{+}$ ($[M+Na]^{+}$) 272.0180, found 272.0184.

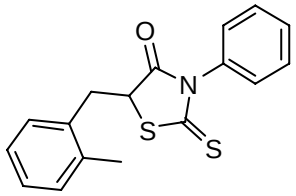
5-(2-(methylthio)ethyl)-3-phenyl-2-thioxothiazolidin-4-one (**1f**)



1f

Yellowish solid; mp: 97.5-99.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.11 (3H, s), 2.37-2.46(1H, m), 2.51-2.59 (1H, m), 2.68-2.82 (2H, m), 4.57 (1H, dd, *J* = 4.8, 7.8 Hz), 7.20-7.22 (2H, m), 7.49-7.53 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.3, 31.0, 31.5, 50.5, 128.4, 129.7, 129.9, 135.3, 176.3, 200.8; HRMS (ESI) m/z calcd for $C_{12}H_{13}NOS_3Na^{+}$ ($[M+Na]^{+}$) 306.0057, found 306.0062.

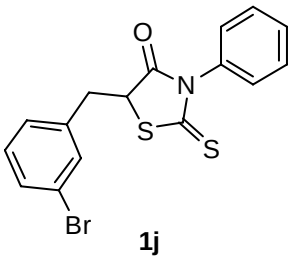
5-(*o*-methylbenzyl)-3-phenyl-2-thioxothiazolidin-4-one (1i)



1i

Yellow solid; mp: 108.5-110.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.40 (3H, s), 3.23 (1H, dd, *J* = 10.3, 14.4 Hz), 3.73 (1H, dd, *J* = 3.9, 10.3 Hz), 4.66 (1H, dd, *J* = 3.9, 14.4 Hz), 7.14-7.25 (6H, m), 7.49-7.55 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 36.1, 52.7, 52.8, 126.6, 128.0, 128.5, 129.4, 129.7, 129.9, 131.1, 134.3, 135.1, 136.7, 175.7, 200.6; HRMS (ESI) m/z calcd for $C_{17}H_{15}NOS_2Na^+$ ($[M+Na]^+$) 336.0493, found 336.0498.

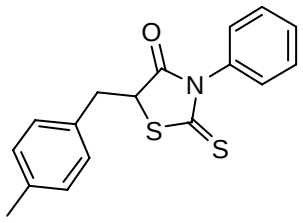
5-(*m*-bromobenzyl)-3-phenyl-2-thioxothiazolidin-4-one (1j)



1j

Yellow solid; mp: 123.9-124.7 °C ; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33 (1H, dd, *J* = 8.3, 14.0 Hz), 3.47 (1H, dd, *J* = 4.0, 14.0 Hz), 4.65 (1H, dd, *J* = 4.0, 8.3 Hz), 7.02-7.03 (2H, m), 7.21-7.25 (2H, m), 7.44-7.53 (5H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 19.8, 36.1, 52.7, 52.8, 126.6, 128.0, 128.5, 129.4, 129.7, 129.9, 131.1, 134.3, 135.1, 136.7, 175.7, 200.6; HRMS (ESI) m/z calcd for $C_{16}H_{12}NOS_2BrNa^+$ ($[M+Na]^+$) 399.9441, found 399.9443.

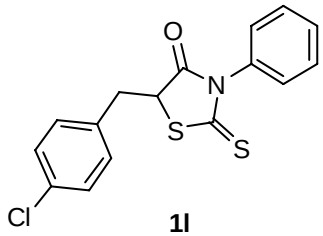
5-(4-methylbenzyl)-3-phenyl-2-thioxothiazolidin-4-one (1k)



1k

Yellow solid; mp: 119.2-120.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.36 (3H, s), 3.30 (1H, dd, *J* = 8.7, 14.0 Hz), 3.50 (1H, dd, *J* = 3.9, 14.0 Hz), 4.66 (1H, dd, *J* = 3.9, 8.7 Hz), 6.99-7.02 (2H, m), 7.14-7.19 (4H, m), 7.46-7.52 (3H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ 21.2, 38.1, 53.5, 128.3, 129.4, 129.6, 129.6, 129.7, 132.1, 135.0, 137.6, 175.5, 200.5; HRMS (ESI) m/z calcd for $C_{17}H_{15}NOS_2Na^+$ ($[M+Na]^+$) 336.0943, found 336.0940.

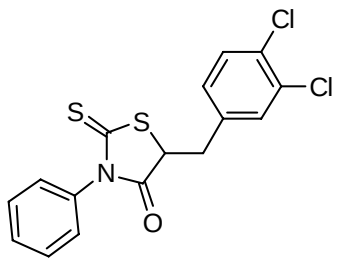
5-(4-chlorobenzyl)-3-phenyl-2-thioxothiazolidin-4-one (1l)



1l

Yellow solid; mp: 148.2-148.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33 (1H, dd, *J* = 8.3, 14.1 Hz), 3.47 (1H, dd, *J* = 3.9, 14.1 Hz), 4.64 (1H, dd, *J* = 4.0, 8.2 Hz), 6.98-6.70 (2H, m), 7.22 (2H, d, *J* = 8.4 Hz), 7.33 (2H, d, *J* = 8.4 Hz), 7.47-7.52 (3H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 37.8, 53.0, 53.1, 128.3, 129.1, 129.8, 131.1, 133.6, 134.0, 134.9, 175.3, 200.0; HRMS (ESI) m/z calcd for $C_{16}H_{12}NOS_2ClNa^+$ ($[M+Na]^+$) 355.9947, found 355.9950.

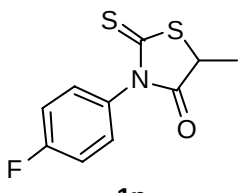
5-(3,4-dichlorobenzyl)-3-phenyl-2-thioxothiazolidin-4-one (1m)



1m

Yellow solid; mp: 122.8-123.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.33 (1H, dd, *J* = 8.2, 14.1 Hz), 3.47 (1H, dd, *J* = 4.1, 14.1 Hz), 4.64 (1H, dd, *J* = 4.1, 8.2 Hz), 6.99-7.15 (3H, m), 7.39 -7.52 (5H, m); ^{13}C NMR (101 MHz, $CDCl_3$): δ 37.4, 52.6, 128.2, 129.0, 129.7, 129.9, 130.8, 131.4, 132.2, 132.9, 134.8, 135.3, 175.1, 199.4; HRMS (ESI) m/z calcd for $C_{16}H_{11}NOS_2Cl_2Na^+$ ($[M+Na]^+$) 389.9557, found 389.9562.

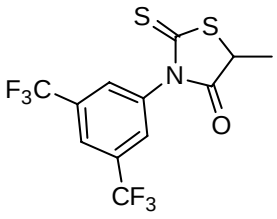
3-(4-fluorophenyl)-5-methyl-2-thioxothiazolidin-4-one (1p)



1p

Yellow solid; mp: 124.5-125.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.78 (3H, d, *J* = 7.3 Hz), 4.39 (1H, q, *J* = 7.3 Hz), 7.17-7.25 (4H, m); ^{19}F NMR (376 MHz, $CDCl_3$): δ -110.57 (1F, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.5, 45.9, 116.8 (d, *J* = 23 Hz), 130.5 (d, *J* = 9 Hz), 130.9 (d, *J* = 3 Hz), 163.0 (d, *J* = 248 Hz), 176.8, 200.5; HRMS (ESI) m/z calcd for $C_{10}H_7NOFS_2^-$ ([M-H]$^-$) 239.9953, found 239.9954.

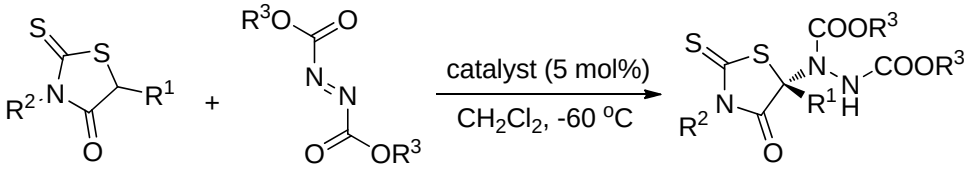
3-(3,5-trifluoromethylphenyl)-5-methyl-2-thioxothiazolidin-4-one (1u)



1u

Yellowish solid; mp: 112.7-113.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.84 (3H, d, *J* = 7.3 Hz), 4.48 (1H, q, *J* = 7.3 Hz), 7.73 (2H, s), 7.99 (1H, s); ^{19}F NMR (376 MHz, $CDCl_3$): δ -62.86 (6F, s); ^{13}C NMR (100 MHz, $CDCl_3$): δ 18.3, 46.1, 122.6 (q, *J* = 272 Hz), 123.6 (2q, *J* = 3 Hz), 129.4 (q, *J* = 3 Hz), 133.0 (q, *J* = 34 Hz), 136.2, 176.1, 199.1; HRMS (ESI) m/z calcd for $C_{12}H_6NOS_2F_6Na^+$ ([M+Na]$^+$) 357.9795, found 357.9788.

3. General procedure for the enantioselective α-amination reaction

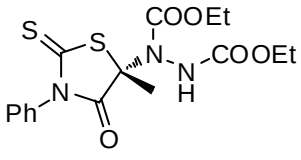


1a-u **2a** **3a-u**

To a solution of 5-substituted rhodanines **1** (0.2 mmol) and catalyst quinine or quinidine (0.01 mmol) in CH_2Cl_2 (2.0 mL) was added **2** (0.22 mmol). The reaction mixture was kept at -60 °C until complete consumption of **1**. Purification of the reaction mixture by chromatography on silica gel afforded the desired product **3**.

4. Analytical data and HPLC analyses of α-aminated products

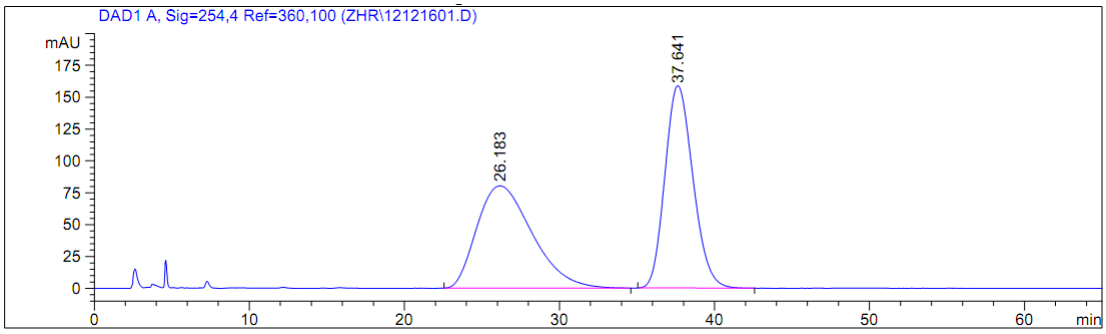
(*S*)-diethyl 1-(5-methyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3a)



3a

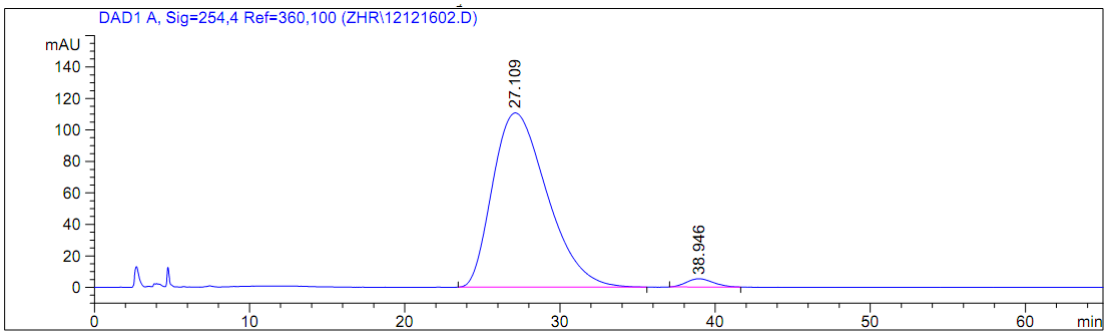
Yellowish solid; mp: 74.2-75.9 °C； 99% yield and 95% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.26-1.37 (6H, m, OCH_2CH_3 rotamers), 1.96 (3H, s), 4.24-4.31 (4H, m, OCH_2CH_3 rotamers), 6.51, 6.77(1H, 2s, NH rotamers), 7.26-7.31 (m, 2H), 7.48-7.53 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 25.6, 63.0, 63.3, 64.1, 75.8, 128.6, 129.5, 129.7, 135.6, 153.8, 154.2, 155.8, 156.7, 174.1, 174.4, 199.7, 200.5; HRMS (ESI) m/z calcd for $C_{16}H_{19}N_3O_5S_2K^+$ ([M+K]$^+$) 436.0403, found 436.0398; $[\alpha]_D^{20}$ = +113.4 (*c* 0.39, CH_2Cl_2). HPLC (chiral AD-H column), hexane /2-propanol = 98/2, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 27.1 min, t_{minor} = 38.9 min.

(*R*)-3a This reaction was catalyzed by quinidine and the product was obtained in 98% yield and 92% ee. HPLC (chiral AD-H column), hexane/2-propanol = 98/2, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 26.5 min, t_{major}= 37.8 min.



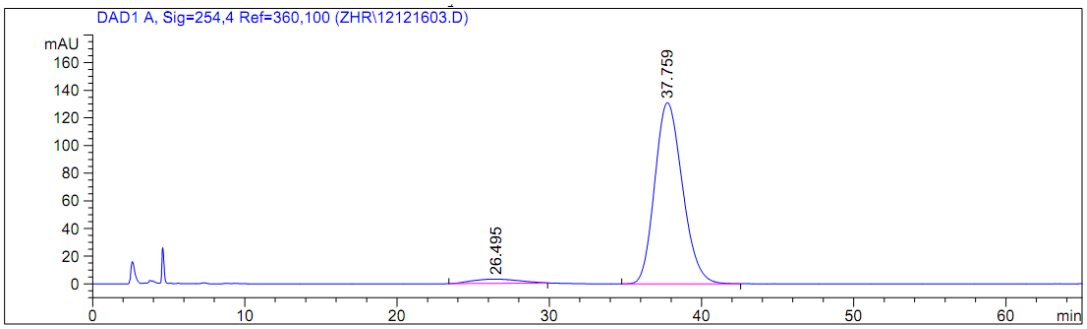
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	26.183	BB	2.9524	1.98716e4	49.8611
2	37.641	BB	1.9143	1.99823e4	50.1389

(racemic **3a**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	27.109	BB	2.9235	2.70146e4	97.7367
2	38.946	BB	1.4792	625.56781	2.2633

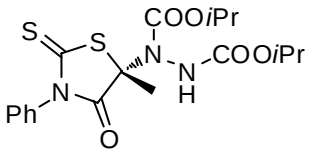
(**3a** catalyzed by quinine)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	26.495	BB	2.7600	634.16522	3.6918
2	37.759	BB	1.9542	1.65434e4	96.3082

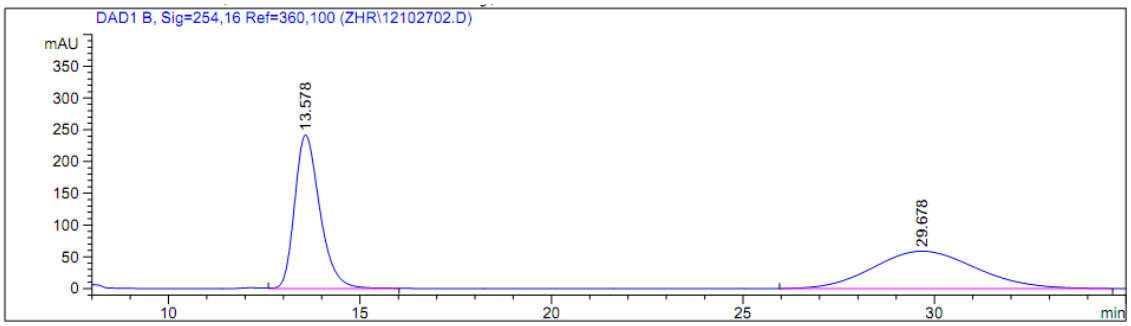
(*ent*-**3a** catalyzed by quinidine)

(*S*)-diisopropyl 1-(5-methyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3a')



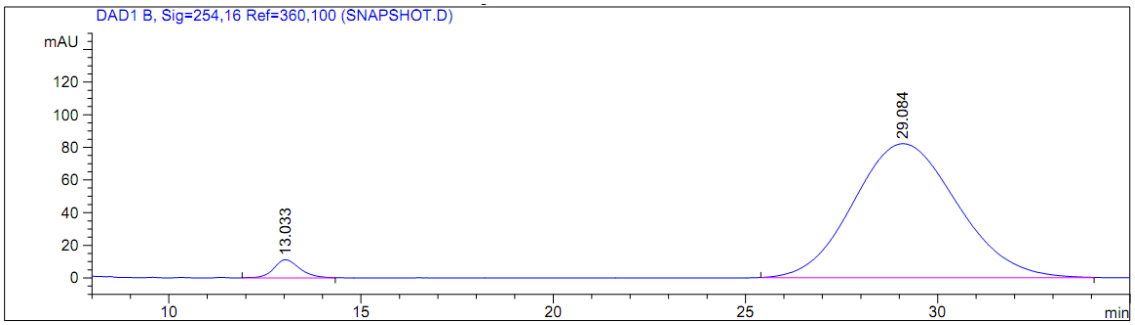
3a'

Yellowish solid; mp: 172.0-172.5 °C; 99% yield and 93% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.26-1.41 (12H, m, OCH(CH_3)$_2$ rotamers), 1.95 (3H, s), 5.01-5.08 (2H, m, OCH(CH_3)$_2$ rotamers), 6.59, 6.74 (1H, 2s, NH rotamers), 7.30-7.31 (m, 2H), 7.47-7.54 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 21.9, 22.0, 22.1, 25.8, 71.2, 72.3, 75.8, 128.6, 129.5, 135.6, 153.3, 153.7, 155.5, 156.4, 174.1, 174.3, 199.8, 200.6; HRMS (ESI) m/z calcd for $C_{18}H_{23}N_3O_5S_2Na^+$ ([M+Na]$^+$) 448.0977, found 448.0982; $[\alpha]_D^{20}$ = +113.2 (*c* 0.43, CH_2Cl_2). HPLC (chiral AS-H column), hexane/2-propanol = 80/20, flow rate 0.6 mL/min, λ = 254 nm, t_{minor} = 13.0 min, t_{major} = 29.1 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.578	VB	0.7026	1.10786e4	241.77968	50.0765
2	29.678	BB	2.9079	1.10448e4	58.78659	49.9235

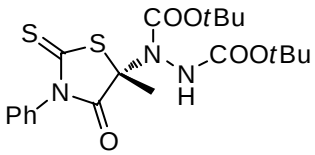
(racemic **3a'**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.033	BB	0.7205	525.33191	11.09334	3.2791
2	29.084	BB	2.5870	1.54951e4	82.20762	96.7209

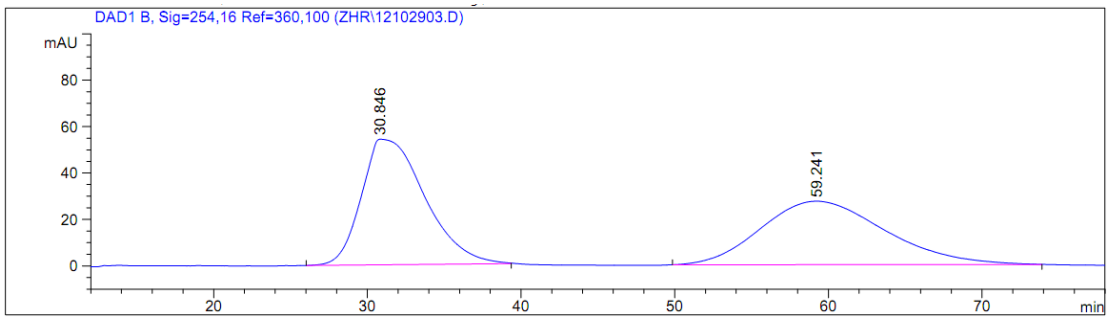
(**3a'** catalyzed by quinine)

(*S*)-di-*tert*-butyl 1-(5-methyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3a")



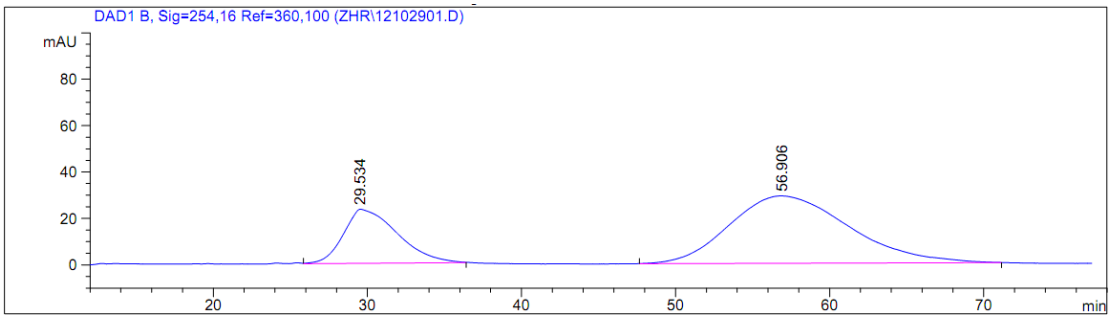
3a"

Yellowish solid; mp: 168.5-169.8 °C; 99% yield and 47% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.47-1.58 (18H, m, $O(CH_3)_3$ rotamers), 1.92 (3H, s), 6.32, 6.58 (1H, 2s, NH rotamers), 7.30-7.32 (m, 2H), 7.46-7.54 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 25.8, 28.1, 28.1, 28.3, 75.6, 82.6, 83.9, 84.1, 128.6, 129.4, 129.5, 135.7, 152.3, 152.9, 155.0, 155.6, 174.4, 200.9; HRMS (ESI) m/z calcd for $C_{20}H_{27}N_3O_5S_2Na^+$ ($[M+Na]^+$) 476.1290, found 476.1281; $[\alpha]_D^{19}$ = +51.4 (*c* 0.45, CH_2Cl_2). HPLC (chiral AS-H column), hexane/2-propanol = 98/2, flow rate 0.6 mL/min, λ = 254 nm, t_{minor} = 29.5 min, t_{major} = 56.9 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.846	BB	3.4913	1.55012e4	54.09212	50.2280
2	59.241	BB	6.5830	1.53605e4	27.30553	49.7720

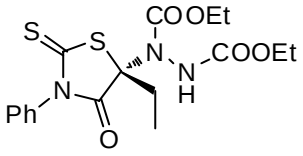
(racemic **3a"**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.534	VB	2.9401	5661.88770	23.29100	26.4981
2	56.906	BB	6.3245	1.57052e4	29.06290	73.5019

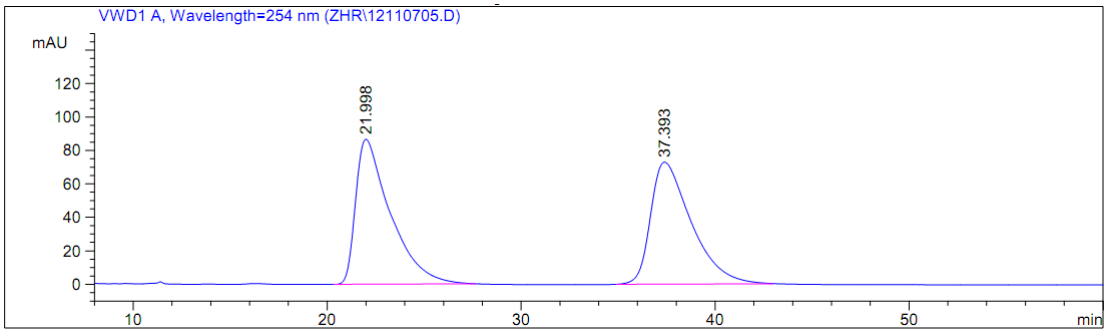
(**3a"** catalyzed by quinine)

(*S*)-diethyl 1-(5-ethyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3b)



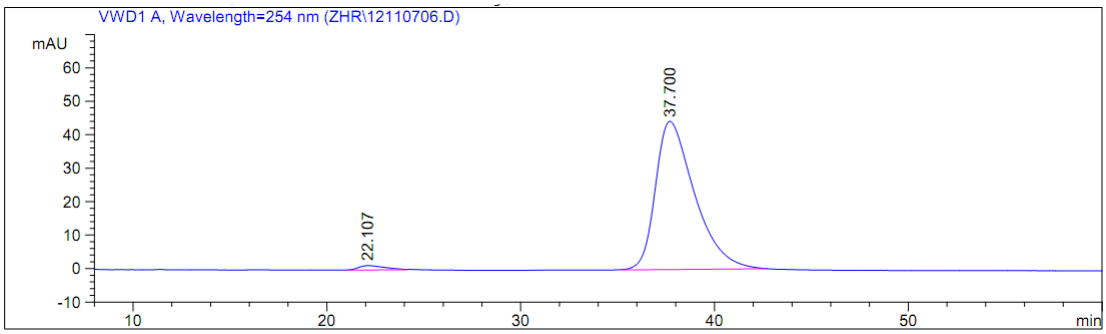
3b

Light yellow solid; mp: 134.7-138.5 °C; 95% yield and 96% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.08-1.15 (3H, m), 1.25-1.37 (6H, m, OCH_2CH_3 rotamers), 2.11-2.29 (2H, m), 4.17-4.32 (4H, m, OCH_2CH_3 rotamers), 6.71, 6.90 (1H, 2s, NH rotamers), 7.26-7.27 (m, 2H), 7.46-7.54 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 30.7, 30.9, 63.1, 63.4, 64.1, 80.5, 80.6, 128.5, 129.6, 129.7, 135.6, 154.2, 155.9, 156.6, 173.3, 173.6, 200.3, 201.0; HRMS (ESI) m/z calcd for $C_{17}H_{21}N_3O_5S_2Na^+$ ($[M+Na]^+$) 434.0820, found 434.0820; $[\alpha]_D^{19}$ = +100.8 (*c* 0.74, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 22.1 min, t_{major} = 37.7 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.998	BB	1.7857	1.07950e4	86.63299	50.3837
2	37.393	BB	2.1393	1.06306e4	72.97308	49.6163

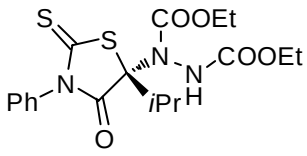
(racemic **3b**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	22.107	BB	1.1313	122.87231	1.29038	1.9392
2	37.700	BB	2.0019	6213.33594	44.25844	98.0608

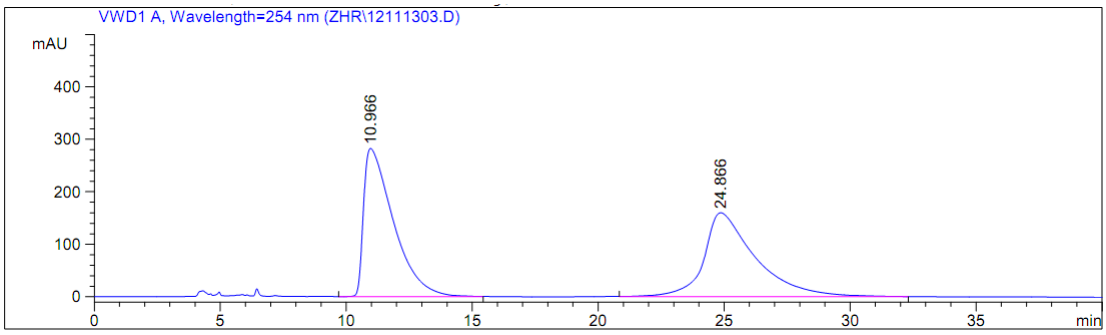
(**3b** catalyzed by quinine)

(*S*)-diethyl 1-(5-isopropyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3c)



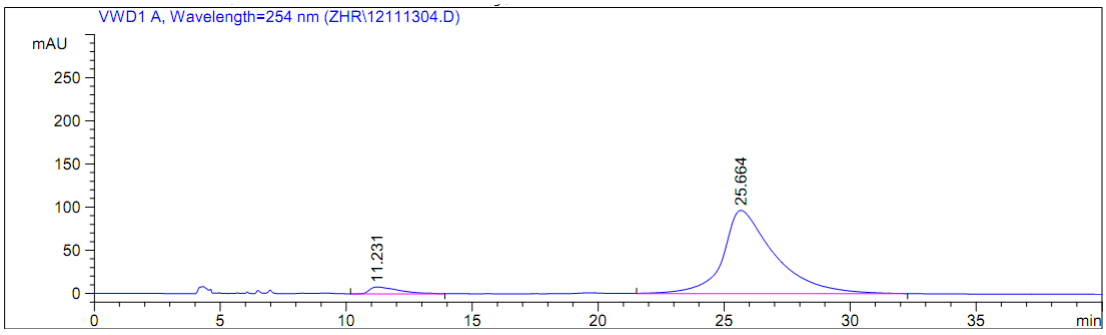
3c

Yellowish solid; mp: 57.5-60.9 °C； 99% yield and 91% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.18-1.34 (12H, m), 2.59-2.64 (1H, m), 4.21-4.30 (4H, m, O*CH*$_2$CH$_3$ rotamers), 6.86, 6.94 (1H, 2s, NH rotamers), 7.20-7.26 (m, 2H), 7.46-7.53 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.4, 14.6, 17.6, 18.0, 35.5, 63.0, 64.0, 84.0, 128.5, 129.5, 135.7, 154.7, 156.9, 172.3, 201.1; HRMS (ESI) m/z calcd for $C_{18}H_{23}N_3O_5S_2Na^+$ ([M+Na]$^+$) 448.0977, found 448.0979; $[\alpha]_D^{18}$ = +100.4 (*c* 0.78, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.7 mL/min, λ = 254 nm, t_{minor} =11.2 min, t_{major} =25.7 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.966	VB	1.2348	2.32783e4	282.56619	50.4266
2	24.866	VB	2.0170	2.28844e4	160.10516	49.5734

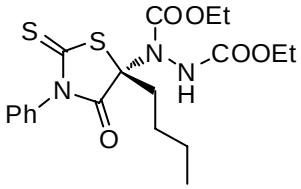
(racemic **3c**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.231	VB	1.1430	625.96564	7.65727	4.3343
2	25.664	BB	2.0161	1.38160e4	96.37558	95.6657

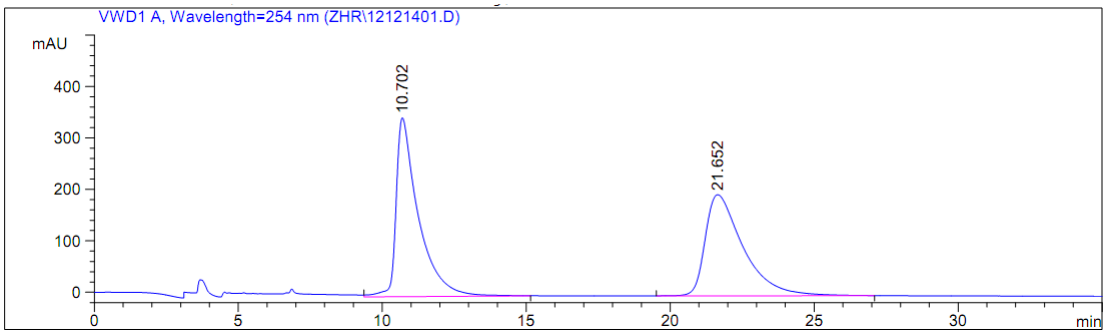
(**3c** catalyzed by quinine)

(*S*)-diethyl 1-(5-butyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3d)



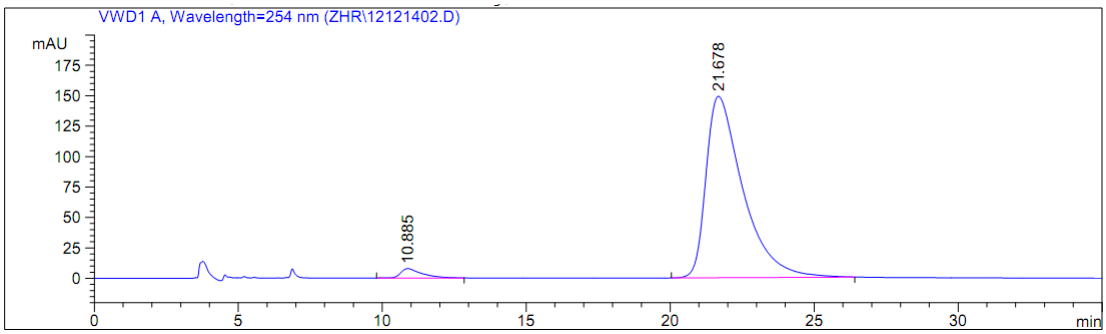
3d

Yellowish solid; mp: 131.4-133.2 °C; 98% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 0.90-0.99 (3H, m), 1.25-1.40 (9H, m), 1.65-1.68 (1H, m), 2.03-2.24 (2H, m), 4.18-4.32 (4H, m, OCH_2CH_3 rotamers), 6.70, 6.89 (1H, 2s, NH rotamers), 7.26-7.27 (m, 2H), 7.46-7.54 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 13.9, 14.4, 14.5, 22.5, 25.0, 37.1, 37.2, 63.0, 63.3, 64.0, 79.8, 79.9, 128.5, 129.5, 129.6, 135.6, 153.8, 154.2, 155.9, 156.6, 173.4, 173.6, 200.2, 200.9; HRMS (ESI) m/z calcd for $C_{19}H_{25}N_3O_5S_2Na^+$ ($[M+Na]^+$) 462.1133, found 462.1127; $[\alpha]_D^{17}$ = +136.3 (*c* 0.82, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 10.9 min, t_{major} = 21.7 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.702	BB	0.7537	1.86585e4	347.14554	50.9560
2	21.652	BB	1.3528	1.79584e4	196.54832	49.0440

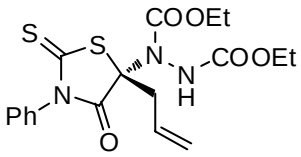
(racemic **3d**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	10.885	BB	0.7355	402.02307	7.79753	2.9332
2	21.678	BB	1.3114	1.33040e4	149.15288	97.0668

(**3d** catalyzed by quinine)

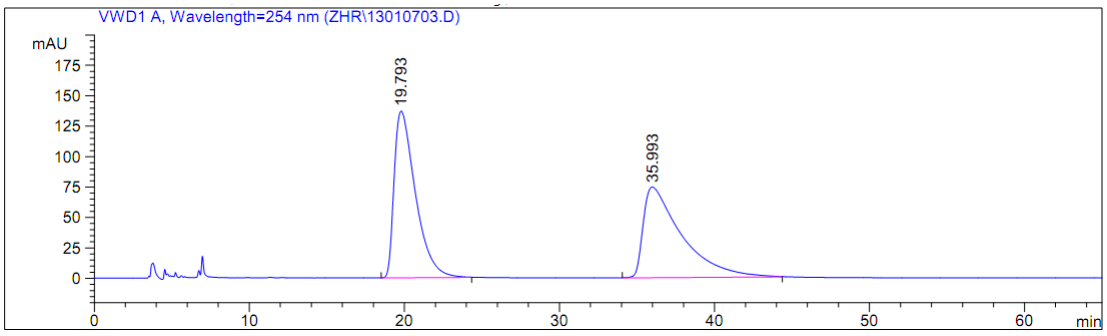
(*S*)-diethyl 1-(5-allyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3e)



3e

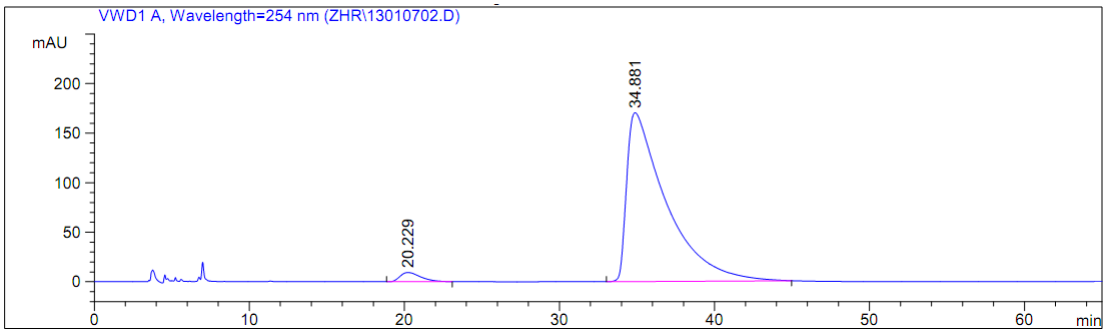
Yellowish solid; mp: 63.2-65.9 °C； 90% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.26-1.37 (6H, m, OCH_2CH_3 rotamers), 2.87-2.97 (2H, m), 4.25-4.31 (4H, m, OCH_2CH_3 rotamers), 5.32-5.36 (2H, m), 5.84-5.90 (1H, m), 6.63, 6.84 (1H, 2s, NH rotamers), 7.22-7.26 (m, 2H), 7.46-7.52 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 15.9, 27.8, 37.3, 63.3, 64.3, 65.7, 79.1, 128.5, 129.0, 129.7, 129.8, 135.5, 153.8, 154.2, 156.6, 173.1, 200.1; HRMS (ESI) m/z calcd for $C_{19}H_{25}N_3O_5S_2Na^+$ ($[M+Na]^+$) 446.0820, found 446.0806; $[\alpha]_D^{16}$ = +175.1 (*c* 0.73, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 20.2 min, t_{major} = 34.9 min.

(*R*)-3e This reaction was catalyzed by quinidine and the product was obtained in 99% yield and 92% ee. HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 19.7 min, t_{minor}= 40.4 min



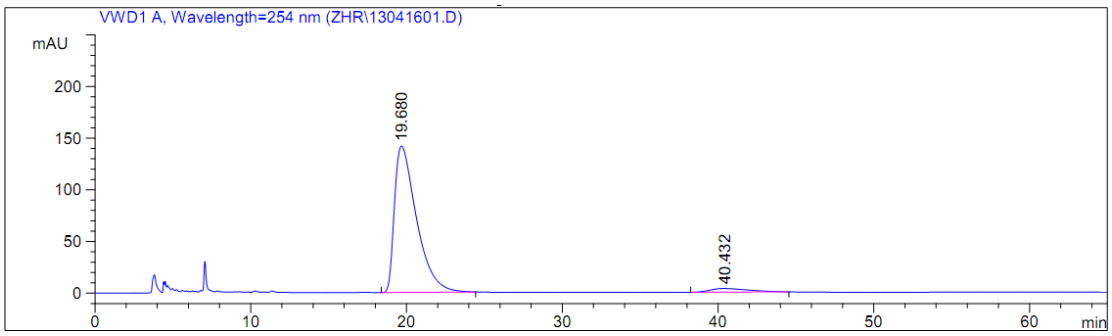
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.793	BB	1.4321	1.30530e4	136.97675	50.5592
2	35.993	BB	2.3307	1.27642e4	74.39719	49.4408

(racemic **3e**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.229	BB	1.3362	885.11456	9.48478	2.8519
2	34.881	BB	2.4319	3.01506e4	170.34077	97.1481

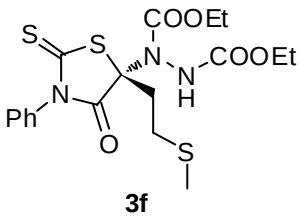
(**3e** catalyzed by quinine)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.680	PB	1.4893	1.39194e4	141.74785	95.7752
2	40.432	BB	2.0237	614.00073	3.56024	4.2248

(*ent*-**3e** catalyzed by quinidine)

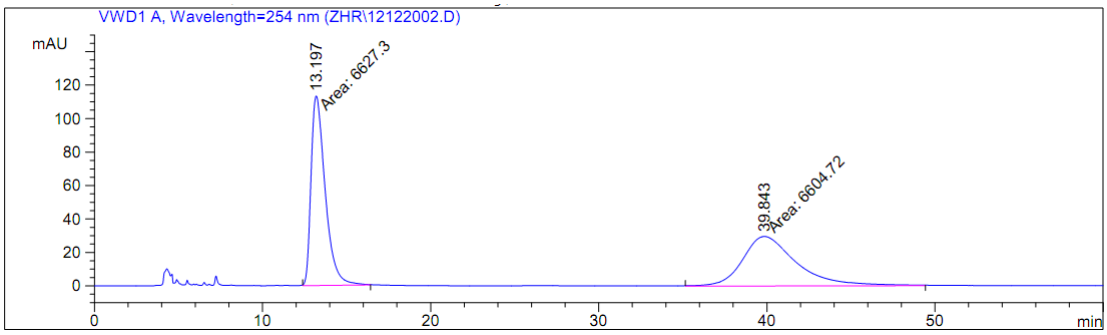
(*S*)-diethyl 1-(5-(2-(methylthio)ethyl)-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2 -dicarboxylate (3f)



3f

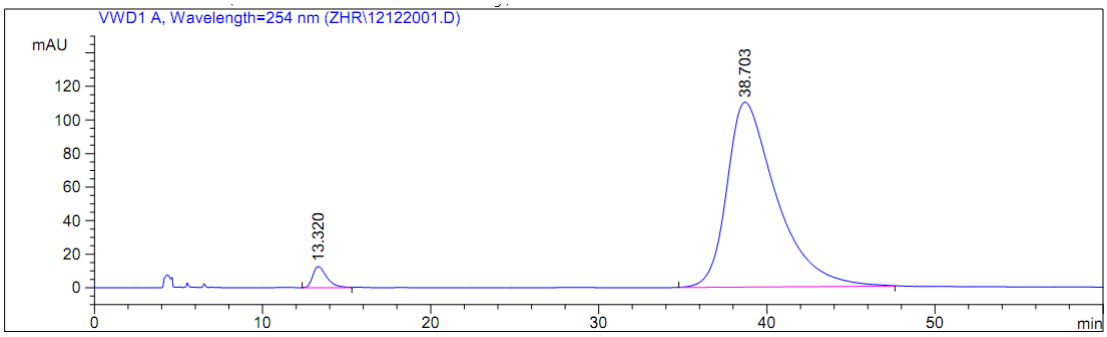
Yellowish solid; mp: 162.1-164.3 ^{o}C; 92% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.26-1.34 (6H, m, OCH_2CH_3 rotamers), 2.12 (3H, s), 2.39-2.53 (3H, m), 2.76-2.82 (1H, m), 4.22-4.32 (4H, m, OCH_2CH_3 rotamers), 6.61, 6.82 (1H, 2s, NH rotamers), 7.26-7.28 (m, 2H), 7.48-7.54 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 15.9, 27.8, 37.3, 63.3, 64.3, 65.7, 79.1, 128.5, 129.0, 129.7, 129.8, 135.5, 153.8, 154.2, 156.6, 173.1, 200.1; HRMS (ESI) m/z calcd for $C_{18}H_{23}N_3O_5S_3Na^+$ ($[M+Na]^+$) 480.0698, found 480.0705; $[\alpha]_D^{16}$ = +123.4 (*c* 0.83, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.7 mL/min, λ=254 nm, t_{minor}= 13.3 min, t_{major} = 38.7 min.

(*R*)-3f This reaction was catalyzed by quinidine and the product was obtained in 99% yield and 91% ee. HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.7 mL/min, λ=254 nm, t_{major} = 12.9 min, t_{minor} = 38.9 min.



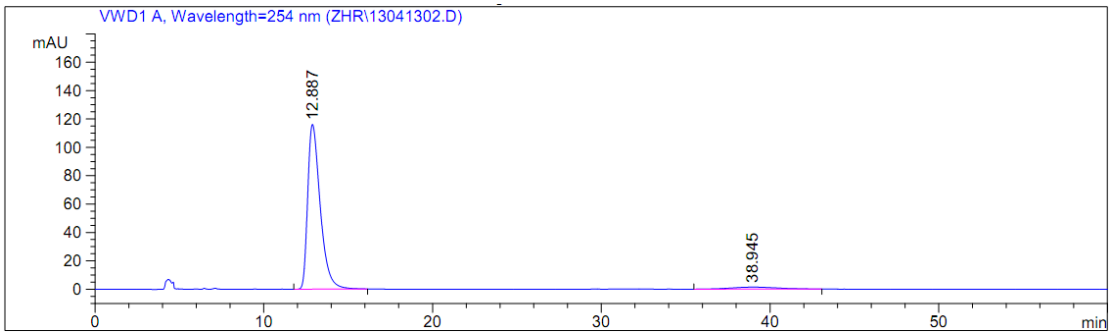
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.197	MM	0.9750	6627.29932	113.29047	50.0853
2	39.843	MM	3.7127	6604.72119	29.64898	49.9147

(racemic **3f**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.320	PB	0.8809	728.68347	12.55657	3.1190
2	38.703	BB	3.0087	2.26340e4	110.15550	96.8810

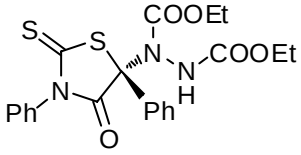
(**3f** catalyzed by quinine)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	12.887	BB	0.7909	5993.97852	116.22984	95.4451
2	38.945	BV	2.3325	286.04785	1.43886	4.5549

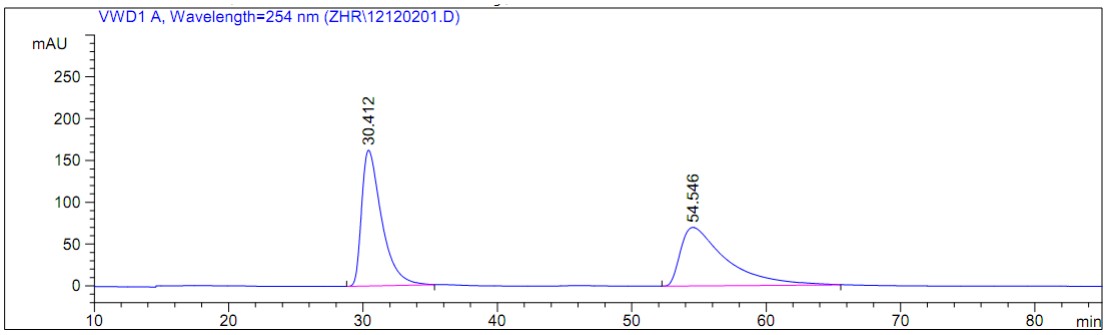
(*ent*-**3f** catalyzed by quinidine)

(*S*)-diethyl 1-(4-oxo-3,5-diphenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3g)



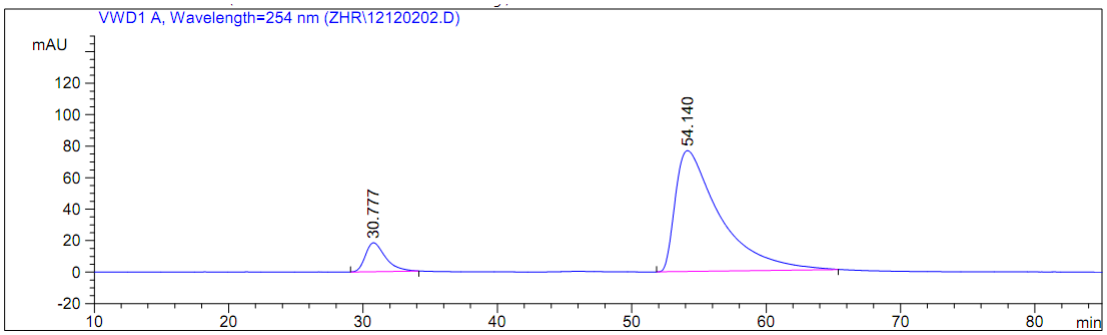
3g

Yellowish solid; mp: 116.1-118.1 °C; 91% yield and 81% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.10-1.40 (6H, 3t, OCH_2CH_3 rotamers), 4.02-4.32 (4H, m, OCH_2CH_3 rotamers), 6.27, 6.49 (1H, 2s, NH rotamers), 7.22-7.25 (m, 2H), 7.40-7.44 (6H, m), 7.84-7.89 (2H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 19.3, 62.7, 64.2, 82.9, 128.6, 129.1, 129.2, 129.5, 129.6, 130.4, 130.6, 132.6, 135.7, 154.8, 155.8, 172.0, 199.7; HRMS (ESI) m/z calcd for $C_{21}H_{21}N_3O_5S_2Na^+$ ($[M+Na]^+$) 482.0820, found 482.0809; $[\alpha]_D^{19}$ = +110.4 (*c* 0.73, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.6 mL/min, λ = 254 nm, t_{minor} = 30.8 min, t_{major} = 54.1 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	30.412	PB	1.5590	1.68489e4	162.32115	50.5927
2	54.546	PB	3.2353	1.64542e4	70.09145	49.4073

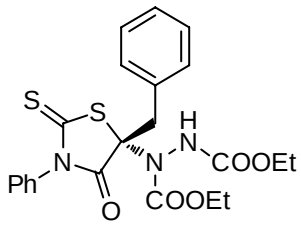
(racemic **3g**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	30.777	BB	1.4973	1907.82080	18.34303	9.6861
2	54.140	PB	3.1458	1.77886e4	76.77496	90.3139

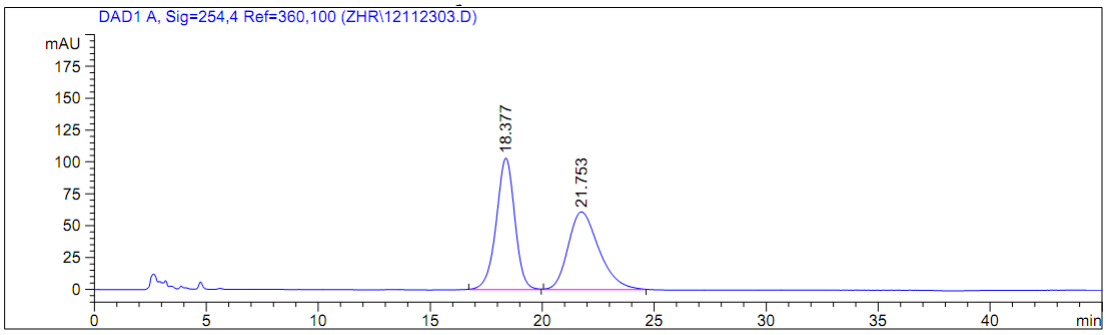
(**3g** catalyzed by quinine)

(*S*)-diethyl 1-(5-benzyl-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3h)



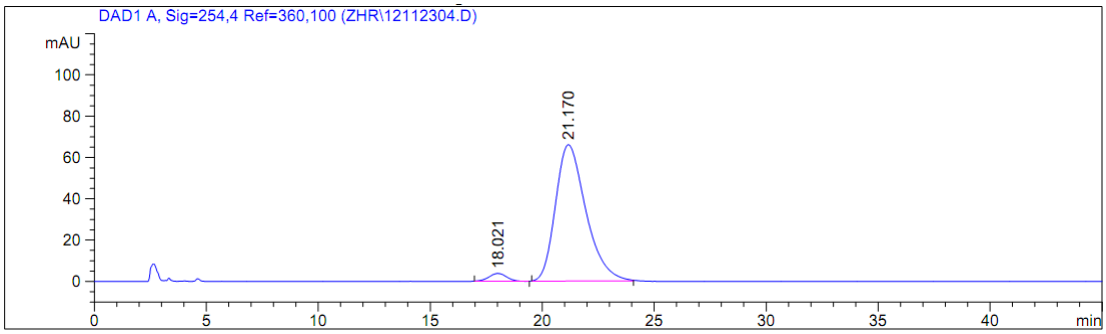
3h

Yellowish solid; mp: 143.7-145.9 °C; 98% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.28-1.45 (6H, m, OCH_2CH_3 rotamers), 3.38 (1H, d, *J*=13.0 Hz), 3.48 (1H, d, *J*=13.0 Hz), 4.27-4.39 (4H, m, OCH_2CH_3 rotamers), 6.64, 6.88 (1H, 2s, NH rotamers), 7.26-7.37 (m, 10H); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 14.8, 42.6, 63.2, 63.5, 64.2, 80.5, 128.3, 128.4, 128.5, 129.3, 129.5, 130.9, 131.1, 131.7, 135.2, 153.8, 154.2, 156.0, 156.8, 172.5, 172.7, 199.2, 199.9; HRMS (ESI) m/z calcd for $C_{22}H_{23}N_3O_5S_2Na^+$ ($[M+Na]^+$) 496.0977, found 496.0971; $[\alpha]_D^{19}$ = +54.3 (*c* 0.88, CH_2Cl_2). HPLC (chiral AD-H column), hexane/2-propanol = 90/10, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 18.0 min, t_{major} = 21.2 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	18.377	BB	0.8818	5955.28418	50.4302
2	21.753	BB	1.4271	5853.67480	49.5698

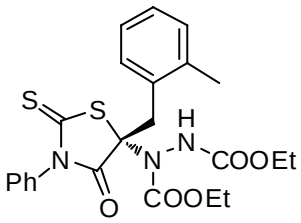
(racemic **3h**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	18.021	BP	0.7031	205.11913	3.1859
2	21.170	BB	1.4299	6233.12549	96.8141

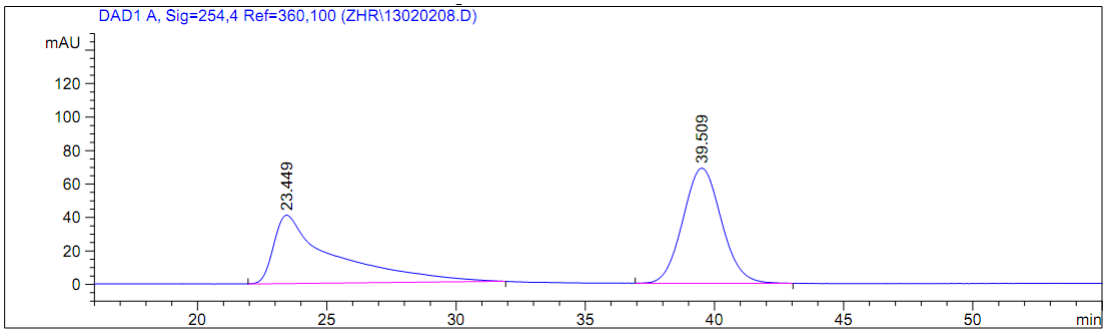
(**3h** catalyzed by quinine)

(*S*)-diethyl 1-(5-(2-methylbenzyl)-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-Dicarboxylate (3i)



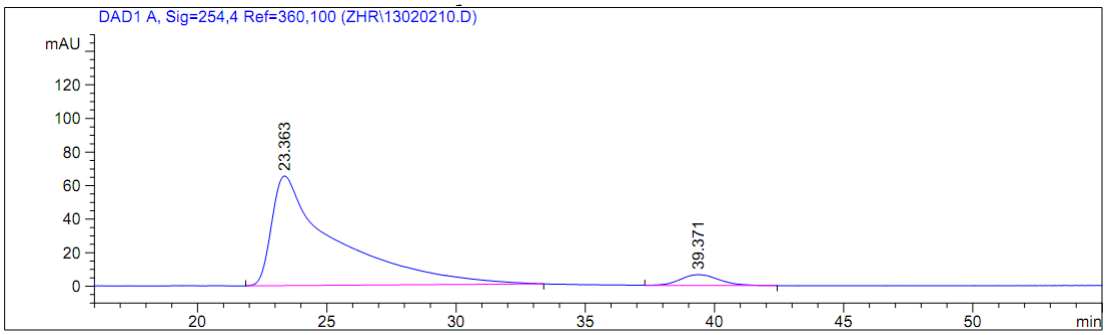
3i

Yellowish solid; mp: 81.3-82.7 °C； 96% yield and 89% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.44 (6H, m, OCH_2CH_3 rotamers), 2.38 (3H, s), 3.48-3.60 (2H, m), 4.26-4.37 (4H, m, OCH_2CH_3 rotamers), 6.76, 6.94 (1H, 2s, NH rotamers), 7.12-7.31 (m, 4H), 7.40-7.42 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 20.6, 38.4, 63.3, 64.2, 80.9, 126.0, 128.4, 129.4, 129.5, 129.9, 131.2, 131.3, 135.5, 138.8, 154.1, 156.8, 173.3, 173.5, 200.3; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_3O_5S_2Na^+$ ($[M+Na]^+$) 510.1133, found 510.1138; $[\alpha]_D^{19}$ = +46.1 (*c* 0.86, CH_2Cl_2). HPLC (chiral AD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 23.3 min, t_{minor}= 39.4 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	23.449	BB	2.1267	6586.49609	47.8932
2	39.509	BV	1.5813	7165.95801	52.1068

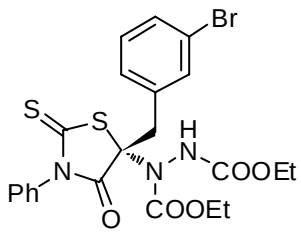
(racemic **3i**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	23.363	BB	2.2567	1.12369e4	94.3687
2	39.371	BB	1.2643	670.53937	5.6313

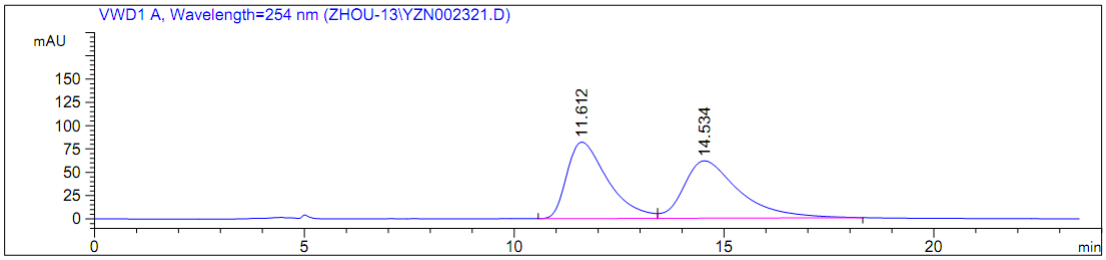
(**3i** catalyzed by quinine)

(*S*)-diethyl 1-(5-(3-bromobenzyl)-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3j)



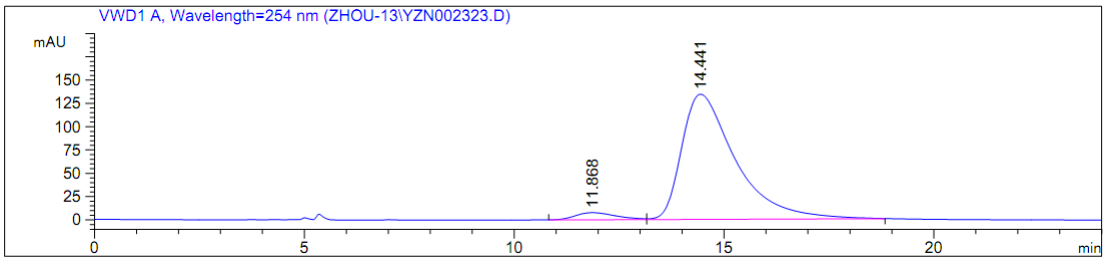
3j

Yellowish solid; mp: 171.4-173.2 °C; 91% yield and 92% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.26-1.44 (6H, m, OCH_2CH_3 rotamers), 3.34 (1H, d, J = 13.0 Hz), 3.45 (1H, d, J = 13.0 Hz), 4.27-4.37 (4H, m, OCH_2CH_3 rotamers), 6.78, 6.98 (1H, 2s, NH rotamers), 7.19-7.32 (4H, m), 7.41-7.52 (5H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.8, 42.1, 63.4, 63.6, 64.3, 80.2, 122.5, 128.3, 129.5, 129.6, 130.0, 130.7, 131.6, 133.5, 134.3, 154.1, 156.8, 172.7, 199.4; HRMS (ESI) m/z calcd for $C_{22}H_{22}N_3O_5S_2BrNa^+$ ($[M+Na]^+$) 574.0082, found 574.0067; $[\alpha]_D^{19}$ = +105.3 (*c* 0.87, CH_2Cl_2). HPLC (chiral OG-H column), hexane/2-propanol = 80/20, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 11.9 min, t_{major} = 14.4 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.612	BB	1.0205	5558.64209	82.04055	49.6148
2	14.534	BB	1.3672	5644.94434	61.53808	50.3852

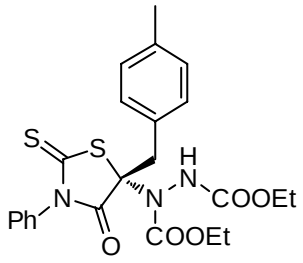
(racemic **3j**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	11.868	BV	0.9779	501.67899	7.60395	4.0224
2	14.441	VB	1.3290	1.19705e4	134.19664	95.9776

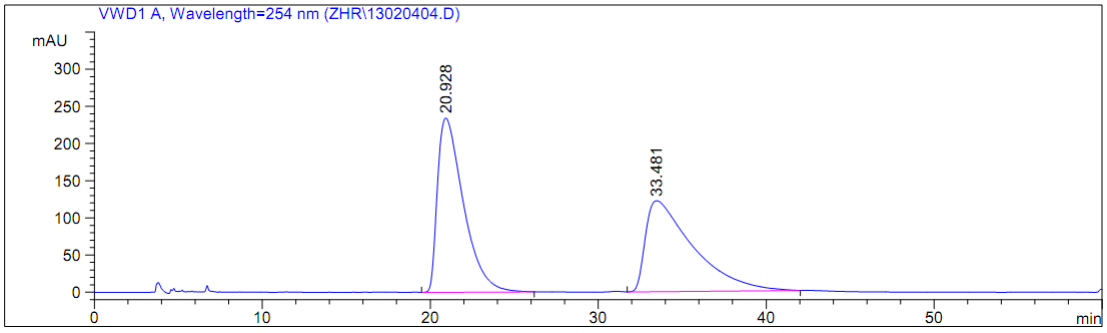
(**3j** catalyzed by quinine)

(*S*)-diethyl 1-(5-(4-methylbenzyl)-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-Dicarboxylate (3k)



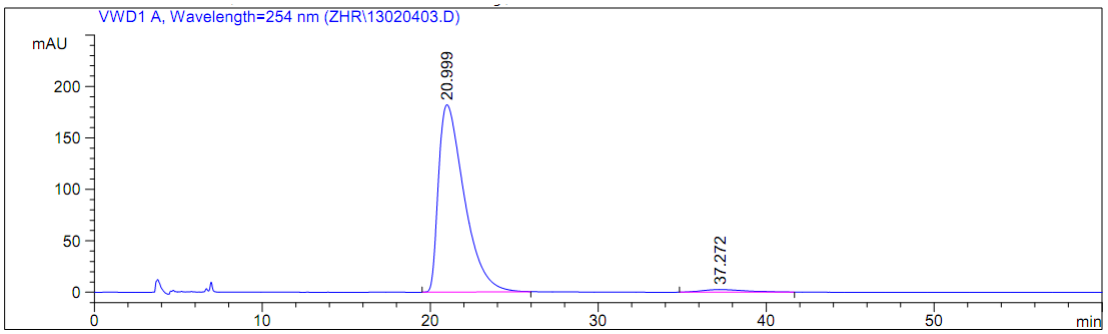
3k

Yellowish solid; mp: 94.7-96.1 °C； 97% yield and 95% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.43 (6H, m, OCH_2CH_3 rotamers), 2.37 (3H, s), 3.34 (1H, d, *J* = 13.1 Hz), 3.44 (1H, d, *J* = 13.1 Hz), 4.26-4.38 (4H, m, OCH_2CH_3 rotamers), 6.74, 6.92 (1H, 2s, NH rotamers), 7.11-7.26 (6H, m), 7.36-7.40 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.8, 21.3, 42.3, 63.2, 63.5, 64.1, 80.6, 127.8, 127.9, 128.3, 129.2, 129.4, 131.6, 135.3, 138.1, 153.9, 154.2, 155.9, 156.8, 172.8, 200.1; HRMS (ESI) m/z calcd for $C_{23}H_{25}N_3O_5S_2Na^+$ ([M+Na]$^+$) 510.1133, found 510.1118; $[\alpha]_D^{19}$ = +69.4 (*c* 0.94, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 21.0 min, t_{minor} = 37.3 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.928	VB	1.6082	2.51290e4	234.26567	51.0892
2	33.481	VB	2.6849	2.40575e4	122.39294	48.9108

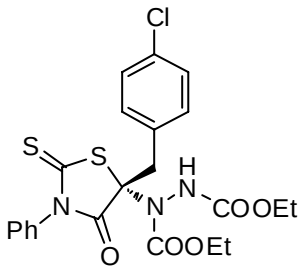
(racemic **3k**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.999	BB	1.6169	1.94165e4	182.07100	97.4840
2	37.272	BB	2.2067	501.12296	2.67406	2.5160

(**3k** catalyzed by quinine)

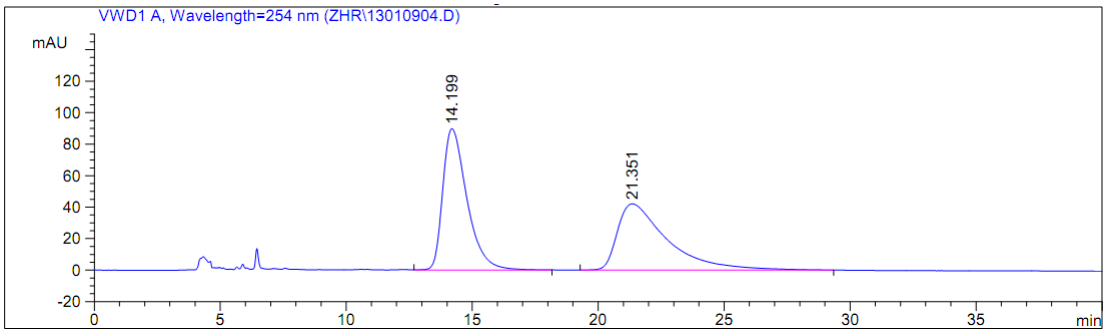
(*S*)-diethyl 1-(5-(4-chlorobenzyl)-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3l)



3l

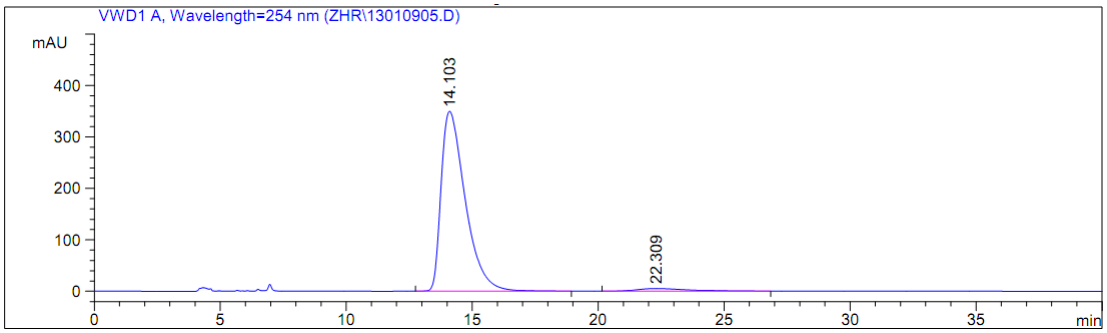
Yellowish solid; mp: 93.4-95.1 °C； 93% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.44 (6H, m, OCH_2CH_3 rotamers), 3.35 (1H, d, *J* = 13.1 Hz), 3.45 (1H, d, *J* = 13.1 Hz), 4.24-4.38 (4H, m, OCH_2CH_3 rotamers), 6.75, 6.93 (1H, 2s, NH rotamers), 7.25-7.32 (6H, m), 7.40-7.41 (3H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.6, 14.7, 29.9, 42.0, 63.4, 63.7, 64.3, 80.3, 128.2, 128.8, 129.5, 129.7, 133.1, 134.7, 135.1, 154.2, 156.9, 172.6, 199.6; HRMS (ESI) m/z calcd for $C_{22}H_{22}N_3O_5S_2ClNa^+$ ($[M+Na]^+$) 530.0587, found 530.0594; $[\alpha]_D^{17}$ = +38.7 (*c* 0.93, CH_2Cl_2). HPLC (chiral AD-H column), hexane/2-propanol = 90/10, flow rate 0.7 mL/min, λ = 254 nm, t_{major} = 14.1 min, t_{minor} = 22.3 min.

(*R*)-3l This reaction was catalyzed by quinidine and the product was obtained in 99% yield and 92% ee. HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 14.0 min, t_{minor}= 21.0 min.



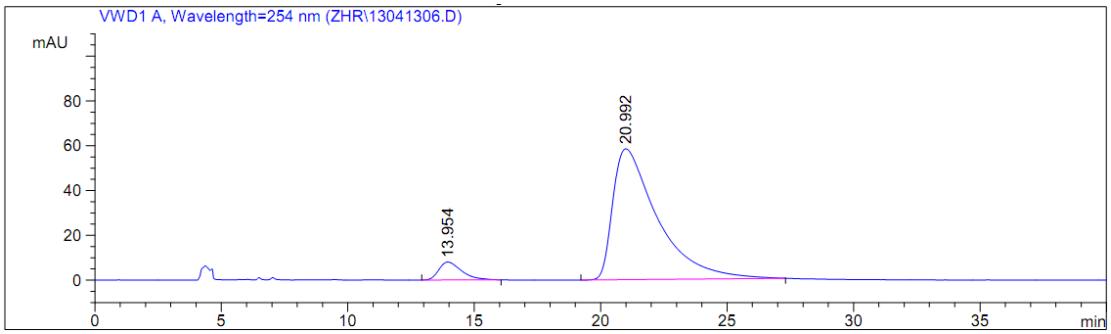
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.199	VB	1.0178	5993.77197	89.76215	50.9640
2	21.351	BB	1.9274	5767.01318	41.98018	49.0360

(racemic **3l**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.103	VB	1.0186	2.33343e4	349.74011	96.8257
2	22.309	PB	1.7096	764.97375	5.31553	3.1743

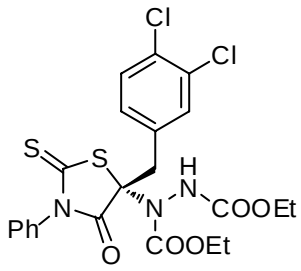
(**3l** catalyzed by quinine)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.954	BB	0.9378	499.92703	7.99400	6.4806
2	20.992	BB	1.7485	7214.31787	58.45473	93.5194

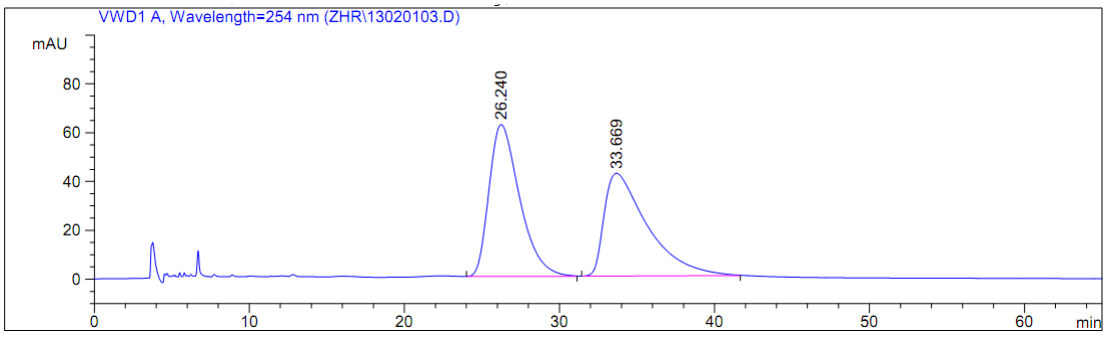
(*ent*-**3l** catalyzed by quinidine)

(*S*)-diethyl 1-(5-(3,4-dichlorobenzyl)-4-oxo-3-phenyl-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3m)



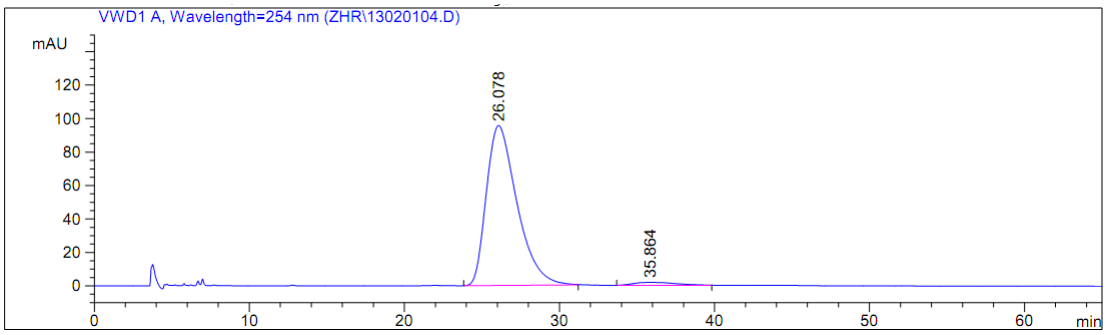
3m

Yellowish solid; mp: 93.9-95.5 °C； 90% yield and 95% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.44 (6H, m, OCH_2CH_3 rotamers), 3.33 (1H, d, *J* = 13.1 Hz), 3.44 (1H, d, *J* = 13.1 Hz), 4.24-4.38 (4H, m, OCH_2CH_3 rotamers), 6.75, 6.93 (1H, 2s, NH rotamers), 7.16-7.26 (3H, m), 7.39-7.42 (5H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 41.6, 63.4, 63.7, 64.4, 80.0, 128.2, 129.6, 129.7, 130.4, 131.3, 131.5, 132.6, 133.3, 135.0, 154.1, 156.8, 172.6, 199.1; HRMS (ESI) m/z calcd for $C_{22}H_{21}N_3O_5S_2Cl_2Na^+$ ($[M+Na]^+$) 564.0197, found 564.0191; $[\alpha]_D^{19}$ = +58.1 (*c* 0.88, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 26.1 min, t_{minor} = 35.9 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.240	PB	2.0144	8540.13086	62.23820	51.0614
2	33.669	PB	2.6961	8185.10205	42.10423	48.9386

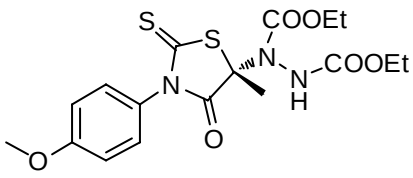
(racemic **3m**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	26.078	BB	2.0491	1.31300e4	95.61602	97.4616
2	35.864	BB	2.1150	341.96857	1.89545	2.5384

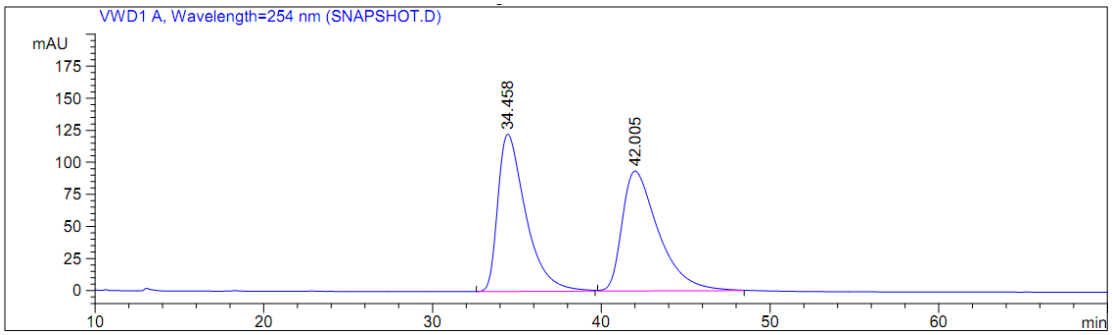
(**3m** catalyzed by quinine)

(*S*)-diethyl 1-(3-(4-methoxyphenyl)-5-methyl-4-oxo-2-thioxothiazolidin-5-yl)hydrazine-1,2-Dicarboxylate (3n)



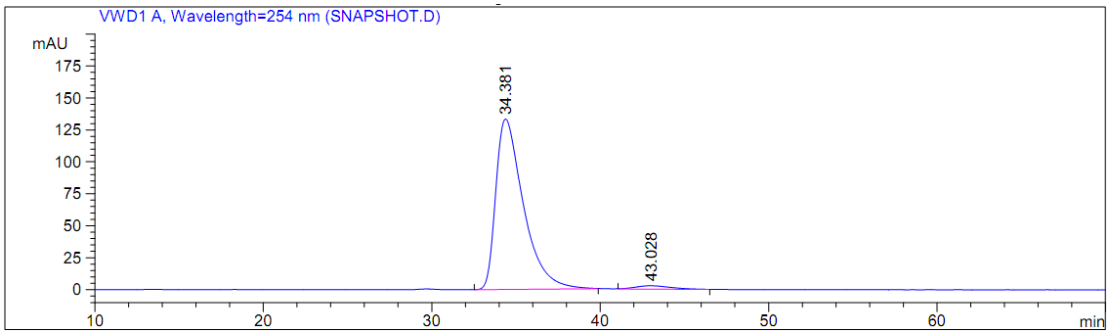
3n

Yellowish solid; mp: 133.1-134.9 °C； 98% yield and 95% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.38 (6H, m, OCH_2CH_3 rotamers), 1.94 (3H, s), 3.84 (3H, s), 4.24-4.31 (4H, m, OCH_2CH_3 rotamers), 6.70, 6.92 (1H, 2s, NH rotamers), 7.02 (2H, d, J = 8.5 Hz), 7.21 (2H, m, d, J = 8.5 Hz); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 25.6, 55.6, 63.2, 63.4, 64.1, 75.6, 114.9, 128.1, 129.6, 153.8, 154.1, 155.9, 156.6, 160.3, 174.5, 200.9; HRMS (ESI) m/z calcd for $C_{17}H_{21}N_3O_6S_2Na^+$ ([M+Na]$^+$) 450.0769, found 450.0767; $[\alpha]_D^{18}$ = +110.0 (*c* 0.84, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.6 mL/min, λ = 254 nm, t_{major} = 34.4 min, t_{minor} = 43.0 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	34.458	BB	1.7321	1.40957e4	122.55011	50.1853
2	42.005	BB	2.2141	1.39916e4	93.37518	49.8147

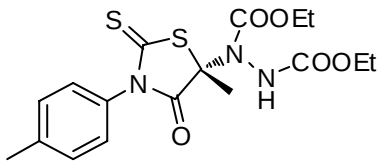
(racemic **3n**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	34.381	PB	1.6997	1.51937e4	133.29356	97.6813
2	43.028	BB	1.6710	360.66177	2.54014	2.3187

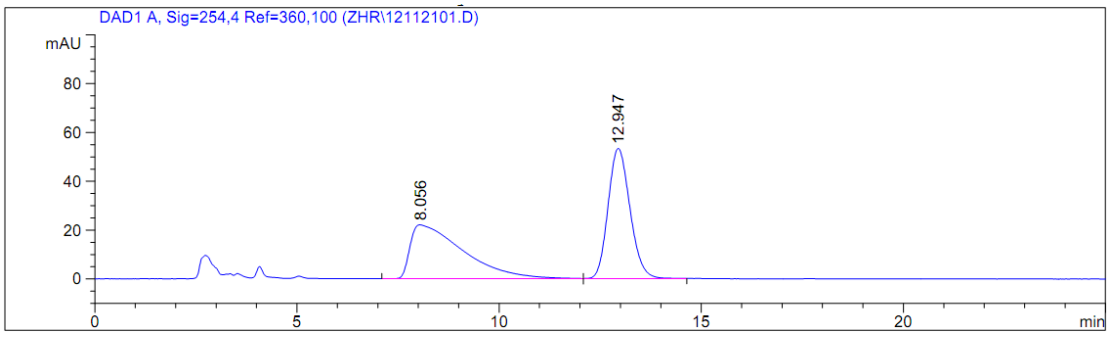
(**3n** catalyzed by quinine)

(*S*)-diethyl 1-(5-methyl-4-oxo-2-thioxo-3-p-tolylthiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3o)



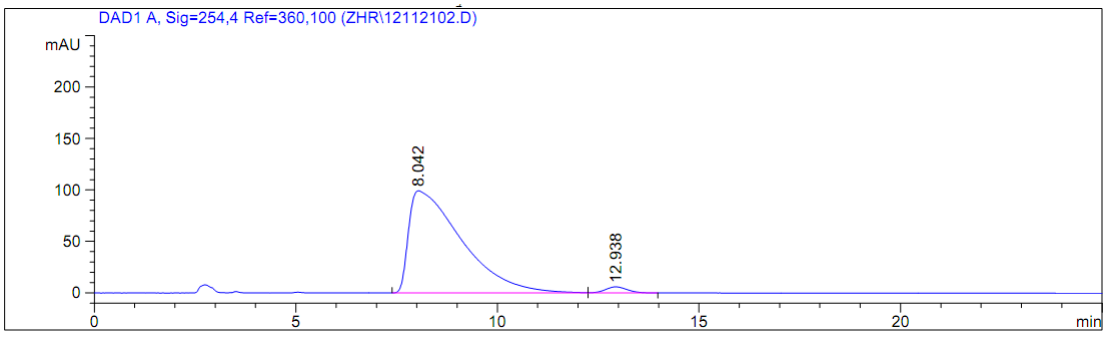
3o

Yellowish solid; mp: 137.4-139.8 °C； 95% yield and 95% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.24-1.35 (6H, m, OCH_2CH_3 rotamers), 1.93 (3H, s), 2.40 (3H, s), 4.24-4.25 (4H, m, OCH_2CH_3 rotamers), 6.93, 7.10 (1H, 2s, NH rotamers), 7.16 (2H, d, J = 7.0 Hz), 7.31 (2H, m, d, J = 7.0 Hz); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 21.4, 21.5, 25.6, 62.7, 63.3, 64.0, 75.6, 75.7, 128.1, 130.2, 132.8, 139.7, 153.7, 154.0, 155.8, 156.5, 174.3, 200.6; HRMS (ESI) m/z calcd for $C_{17}H_{21}N_3O_5S_2Na^+$ ($[M+Na]^+$) 434.0820, found 434.0804; $[\alpha]_D^{18}$ = +114.8 (*c* 0.63, CH_2Cl_2). HPLC (chiral AD-H column), hexane/2-propanol = 90/10, flow rate 0.8 mL/min, λ = 254 nm, t_{major} =8.0 min, t_{minor} =12.9 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	8.056	BV	1.3736	2004.13586	49.9344
2	12.947	PB	0.5903	2009.40308	50.0656

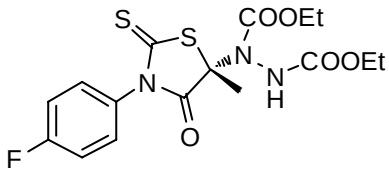
(racemic **3o**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	8.042	BV	1.1748	9047.35937	97.6432
2	12.938	VB	0.5709	218.37042	2.3568

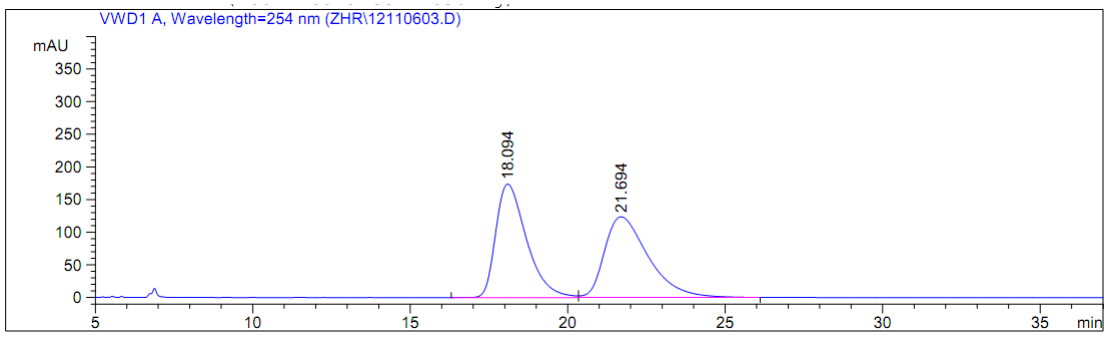
(**3o** catalyzed by quinine)

(*S*)-diethyl 1-(3-(4-fluorophenyl)-5-methyl-4-oxo-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3p)



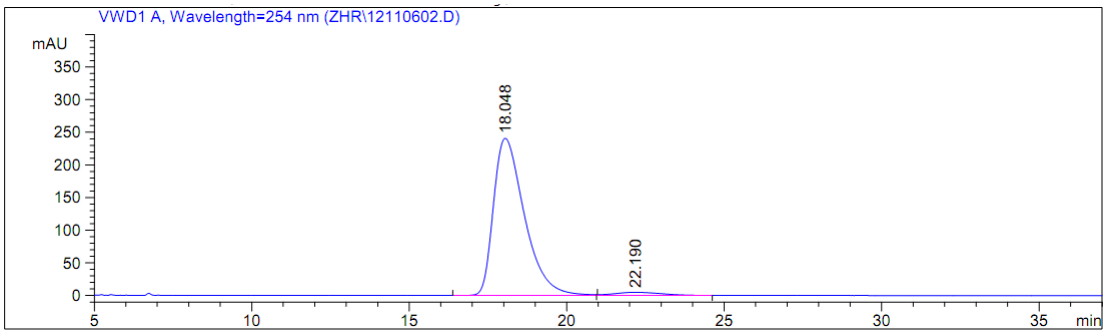
3p

Yellowish solid; mp: 135.1-137.8 °C； 99% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.24-1.37 (6H, m, OCH_2CH_3 rotamers), 1.93 (3H, s), 4.23-4.30 (4H, m, OCH_2CH_3 rotamers), 6.88, 7.03 (1H, 2s, NH rotamers), 7.17-7.21 (2H, m), 7.27-7.28 (2H, m); ^{19}F NMR for rotamers (376 MHz, $CDCl_3$): δ -111.48, -111.28 (1F, 2s); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.4, 14.5, 14.6, 25.4, 63.2, 63.4, 64.1, 75.7, 75.7, 116.6 (d, J = 22 Hz), 130.5 (d, J = 8 Hz), 131.3, 154.1, 155.8, 156.5, 163.0 (d, J = 248 Hz), 174.0, 174.3, 199.7, 200.4; HRMS(ESI) m/z calcd for $C_{16}H_{18}N_3O_5S_2FNa^+$ ([M+Na]$^+$) 438.0570, found 438.0575; $[\alpha]_D^{18}$ = +104.3 (*c* 0.40, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 18.0 min, t_{minor} = 22.2 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.094	BV	1.0408	1.18534e4	173.99632	49.8108
2	21.694	VB	1.4766	1.19434e4	123.78430	50.1892

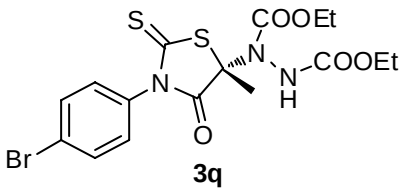
(racemic **3p**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	18.048	BB	1.0454	1.64673e4	240.78320	96.9367
2	22.190	BB	1.2766	520.37573	4.91253	3.0633

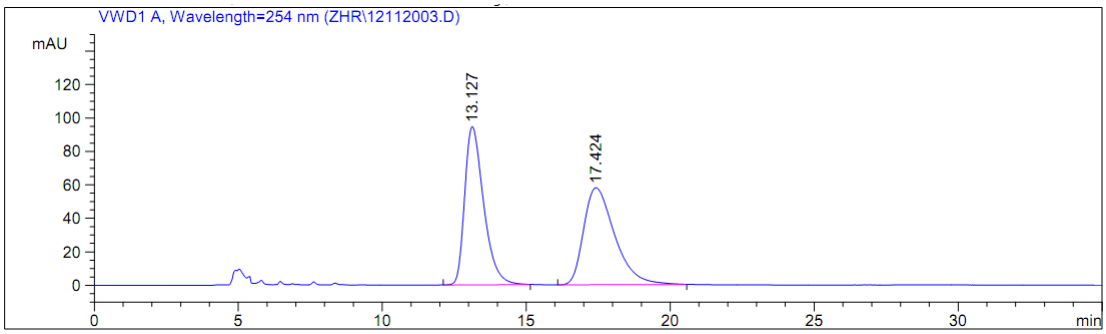
(**3p** catalyzed by quinine)

(*S*)-diethyl 1-(3-(4-bromophenyl)-5-methyl-4-oxo-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3q)



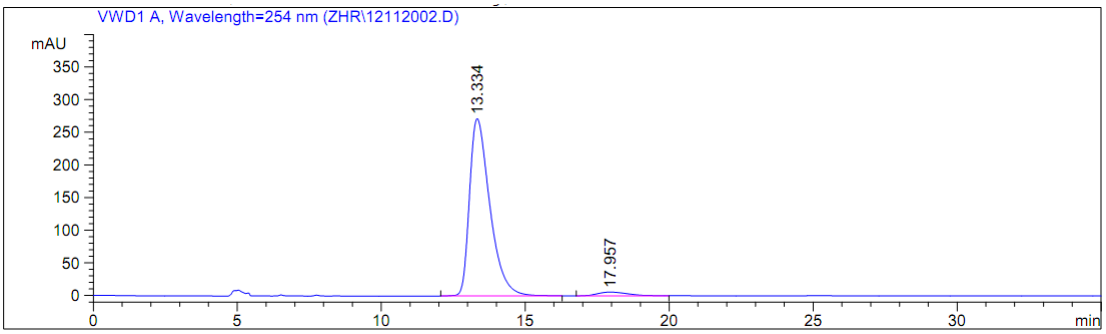
3q

Yellowish solid; mp: 148.4-151.6 °C; 96% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.33 (6H, m, OCH_2CH_3 rotamers), 1.94 (3H, s), 4.23-4.30 (4H, m, OCH_2CH_3 rotamers), 6.78, 6.97 (1H, 2s, NH rotamers), 7.18 (2H, d, J = 8.3 Hz), 7.64 (2H, d, J = 8.3 Hz); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.4, 14.5, 14.6, 25.4, 63.1, 63.4, 64.1, 75.7, 75.8, 123.8, 123.9, 130.3, 132.8, 134.5, 153.8, 154.1, 155.8, 156.5, 173.7, 174.0, 199.3, 200.0; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_3O_5S_2BrNa^+$ ([M+Na]$^+$) 497.9769, found 497.9762; $[\alpha]_D^{19}$ = +100.2 (*c* 0.82, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.6 mL/min, λ = 254 nm, t_{major} = 13.3 min, t_{minor} = 18.0 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.127	BB	0.7013	4337.62500	94.52998	49.9033
2	17.424	PB	1.1475	4354.43018	57.94844	50.0967

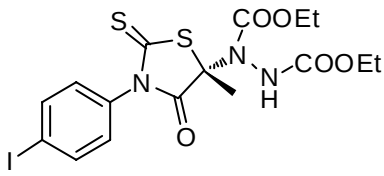
(racemic **3q**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.334	BB	0.7496	1.33902e4	271.74689	96.9113
2	17.957	PB	1.0128	426.76834	5.79977	3.0887

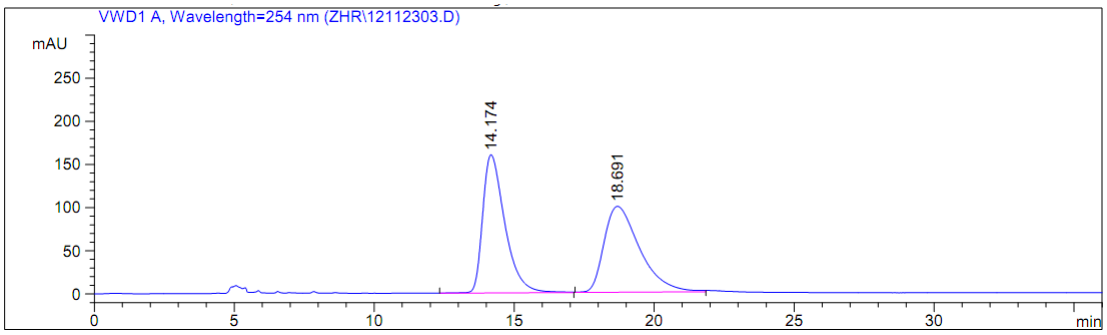
(**3q** catalyzed by quinine)

(*S*)-diethyl 1-(3-(4-iodophenyl)-5-methyl-4-oxo-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3r)



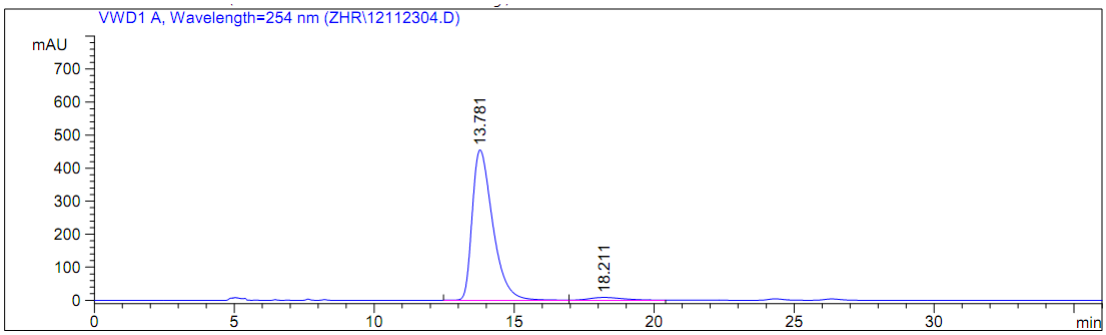
3r

Yellowish solid; mp: 143.1-145.2 °C； 98% yield and 94% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.38 (6H, m, OCH_2CH_3 rotamers), 1.94 (3H, s), 4.23-4.30 (4H, m, OCH_2CH_3 rotamers), 6.74, 6.77 (1H, 2s, NH rotamers), 7.04 (2H, d, J = 8.2 Hz), 7.84 (2H, d, J = 8.2 Hz); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.4, 14.6, 25.5, 63.2, 63.4，64.2, 75.8, 95.7, 130.5, 135.2, 138.8, 153.8, 154.1, 155.8, 156.5, 174.0, 200.0; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_3O_5S_2INa^+$ ($[M+Na]^+$) 545.9630, found 545.9644; $[\alpha]_D^{18}$ = +95.4 (*c* 1.00, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 90/10, flow rate 0.6 mL/min, λ = 254 nm, t_{major} = 13.8 min, t_{minor} = 18.2 min.



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	14.174	PB	0.8348	8809.02246	159.93634	49.8935
2	18.691	BB	1.3577	8846.62012	99.49430	50.1065

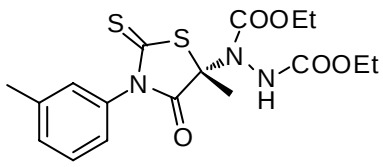
(racemic **3r**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	13.781	BB	0.7811	2.31853e4	454.85193	96.9077
2	18.211	BB	1.3231	739.84814	8.38836	3.0923

(**3r** catalyzed by quinine)

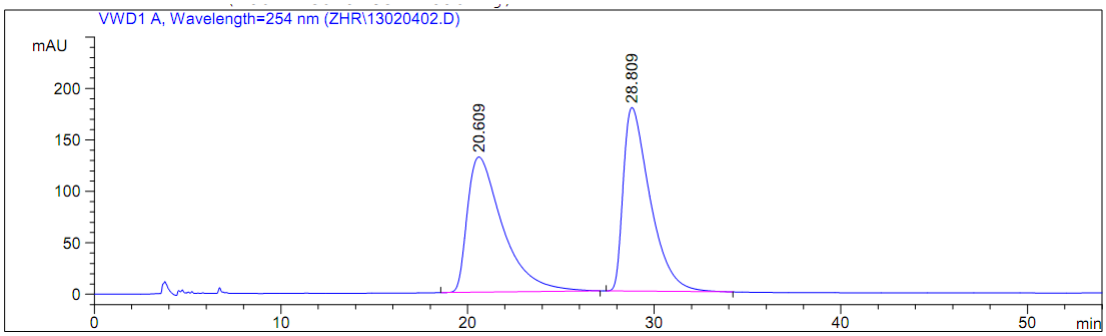
(*S*)-diethyl 1-(5-methyl-4-oxo-2-thioxo-3-m-tolylthiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3s)



3s

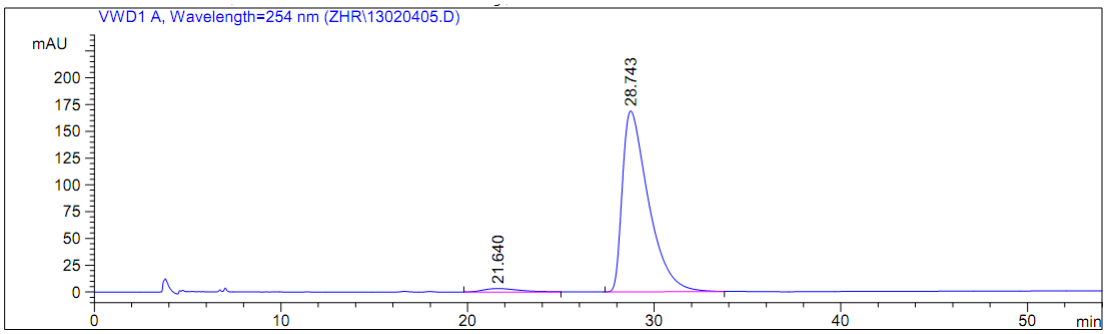
Yellowish solid; mp: 80.5-81.9 °C； 95% yield and 95% ee; ^{1}H NMR for rotamers (500 MHz, $CDCl_3$): δ 1.26-1.38 (6H, m, OCH_2CH_3 rotamers), 1.95 (3H, s), 2.41(3H, s), 4.22-4.31 (4H, m, OCH_2CH_3 rotamers), 6.59, 6.83 (1H, 2s, NH rotamers), 7.05-7.13 (2H, m), 7.26-7.30 (1H, m), 7.39-7.42 (1H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.4, 14.5, 21.4, 25.5, 63.0, 63.3, 64.0, 75.7, 125.4, 128.9, 135.4, 139.6, 153.7, 154.1, 155.8, 156.6, 174.0, 174.3, 199.7, 200.4; HRMS (ESI) m/z calcd for $C_{17}H_{21}N_3O_5S_2Na^+$ ($[M+Na]^+$) 434.0820, found 434.0835; $[\alpha]_D^{19}$= +186.3 (*c* 0.75, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 21.6 min, t_{major} = 28.7 min.

(*R*)-3s This reaction was catalyzed by quinidine and the product was obtained in 99% yield and 87% ee. HPLC (chiral OD-H column), hexane/2-propanol = 95/5, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 19.6 min, t_{minor}= 31.4 min.



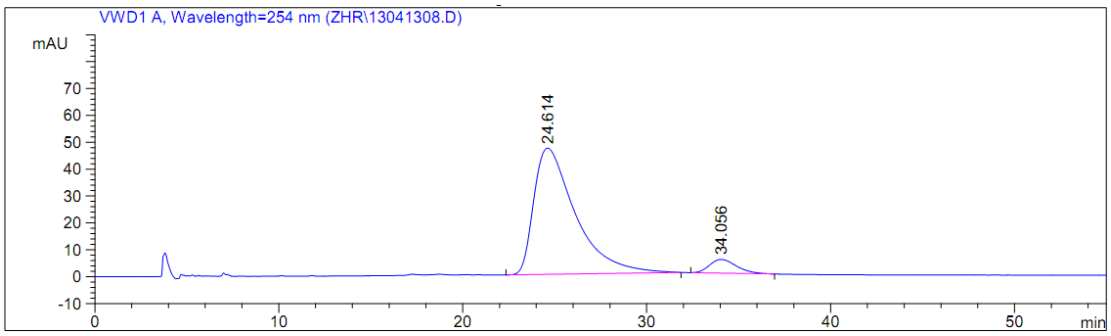
Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	20.609	BB	1.9527	1.72920e4	131.31322	49.2561
2	28.809	PB	1.4977	1.78143e4	178.28233	50.7439

(racemic **3s**)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	21.640	BB	1.5977	449.29095	3.30178	2.6586
2	28.743	BB	1.4459	1.64500e4	168.97298	97.3414

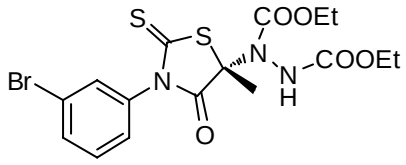
(**3s** catalyzed by quinine)



Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	19.578	VB	1.8799	1.69548e4	137.34311	93.3108
2	31.438	BB	1.5611	1215.44116	11.37459	6.6892

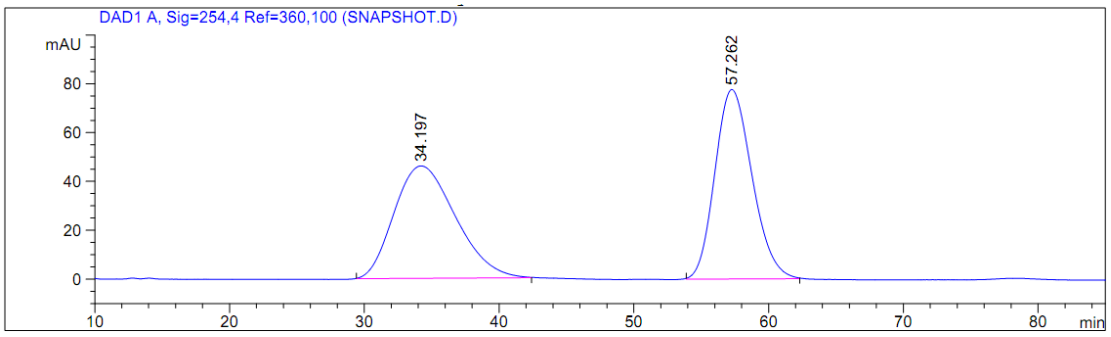
(*ent*-**3s** catalyzed by quinidine)

(*S*)-diethyl 1-(3-(3-bromophenyl)-5-methyl-4-oxo-2-thioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (3t)



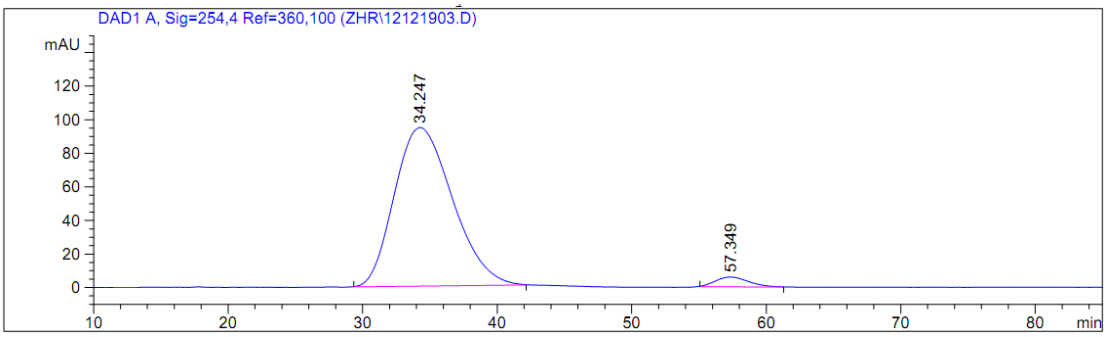
3t

Yellowish solid; mp: 80.9-84.1 °C； 96% yield and 93% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.26-1.39 (6H, m, OCH_2CH_3 rotamers), 1.95 (3H, s), 4.21-4.32 (4H, m, OCH_2CH_3 rotamers), 6.65, 6.87 (1H, 2s, NH rotamers), 7.25-7.26 (1H, m), 7.38-7.46 (2H, m), 7.60-7.62 (1H, m); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.5, 14.6, 25.5, 63.2, 63.5, 64.3, 75.9, 122.8, 127.6, 130.7, 136.7, 154.1, 155.7, 156.6, 174.0, 199.9; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_3O_5S_2BrNa^+$ ($[M+Na]^+$) 497.9769, found 497.9762; $[\alpha]_D^{17}$= +150.6 (*c* 0.90, CH_2Cl_2). HPLC (chiral OD-H column), hexane/2-propanol = 98/2, flow rate 0.8 mL/min, λ = 254 nm, t_{major} = 34.2 min, t_{minor} = 57.3 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	34.197	BB	3.7178	1.45841e4	49.5268
2	57.262	BB	2.3153	1.48628e4	50.4732

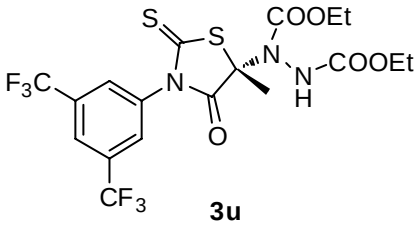
(racemic **3t**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	34.247	BB	3.5282	2.84079e4	96.6502
2	57.349	BB	2.0143	984.59607	3.3498

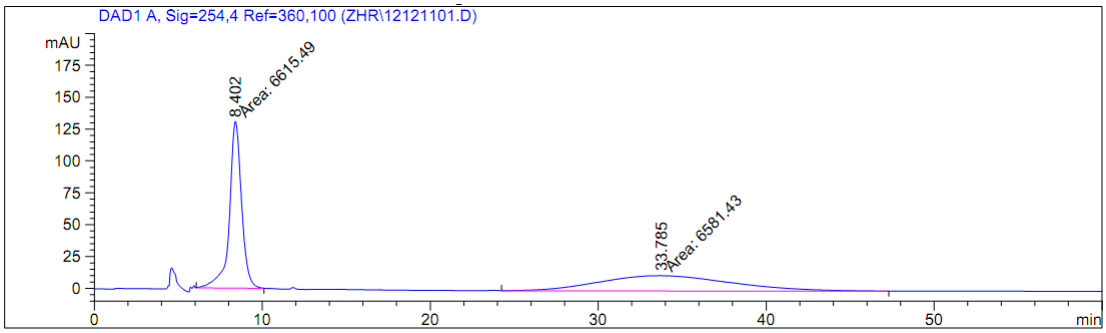
(*ent*-**3t** catalyzed by quinine)

(S)-diethyl 1-(3-(3,5-bis(trifluoromethyl)phenyl)-5-methyl-4-oxo-2-thioxothiazolidin-5-yl) hydrazine-1,2-dicarboxylate (3u)



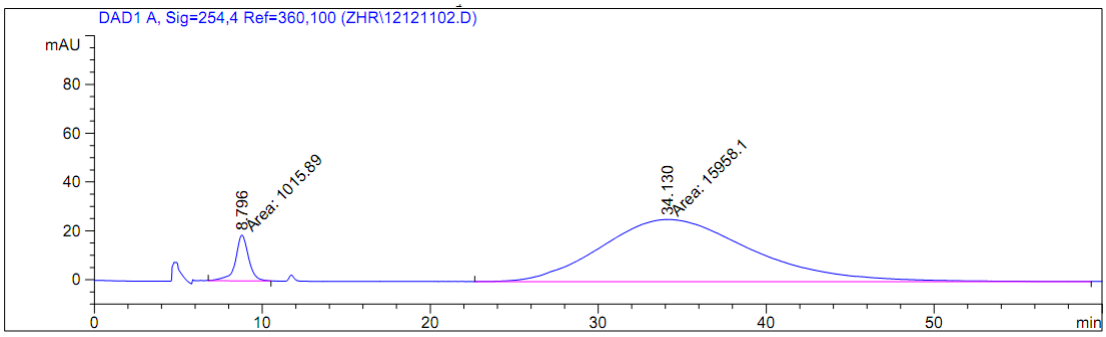
3u

Yellowish solid; mp: 114.8-116.5 °C； 99% yield and 88% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.28-1.38 (6H, m, OCH_2CH_3 rotamers), 1.98 (3H, s), 4.23-4.33 (4H, m, OCH_2CH_3 rotamers), 6.53, 6.79 (1H, 2s, NH rotamers), 7.79 (2H, s), 7.98 (1H, s); ^{19}F NMR for rotamers (376 MHz, $CDCl_3$): δ -62.79 (6F, s); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.4, 14.5, 25.3, 25.5, 63.3, 63.6, 64.5, 76.1, 122.9 (q, J = 271 Hz), 123.6 (q, J = 3 Hz), 129.7 (q, J = 3 Hz), 133.0 (q, J = 34 Hz), 137.0, 154.0, 154.3, 155.7, 156.6, 173.6, 173.9, 198.6, 199.4; HRMS (ESI) m/z calcd for $C_{18}H_{17}N_3O_5F_6S_2BrNa^+$ ([M+Na]$^+$) 556.0412, found 556.0405; $[\alpha]_D^{17}$= +90.8 (*c* 0.97, CH_2Cl_2). HPLC (chiral AS-H column), hexane/2-propanol = 95/5, flow rate 0.7 mL/min, λ = 254 nm, t_{minor} = 8.8 min, t_{major} = 34.1 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	8.402	MM	0.8429	6615.49316	50.1291
2	33.785	MM	9.2236	6581.42676	49.8709

(racemic **3u**)

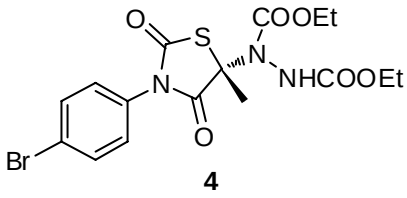


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	8.796	MM	0.9044	1015.88599	5.9850
2	34.130	MM	10.4272	1.59581e4	94.0150

(**3u** catalyzed by quinine)

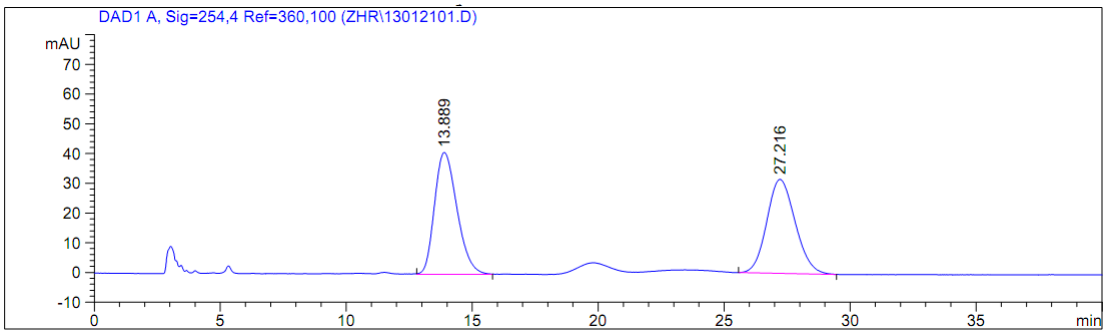
5. Derivatization of the Amination Products[5]

(S)-diethyl 1-(3-(4-bromophenyl)-5-methyl-2,4-dioxothiazolidin-5-yl)hydrazine-1,2-dicarboxylate (4)



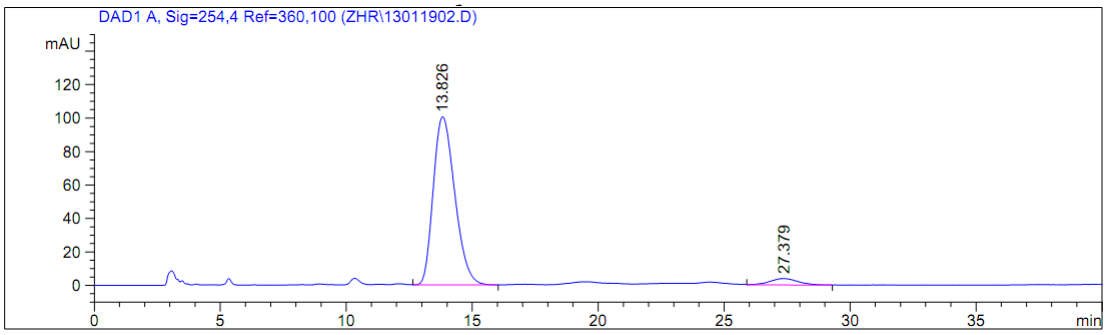
4

White solid; mp: 129.7-131.3 °C; 81% yield and 91% ee; ^{1}H NMR for rotamers (400 MHz, $CDCl_3$): δ 1.25-1.36 (6H, m, OCH_2CH_3 rotamers), 1.97 (3H, s), 4.23-4.32 (4H, m, OCH_2CH_3 rotamers), 6.56, 6.80 (1H, 2s, NH rotamers), 7.23 (2H, d, J = 8.5 Hz), 7.62 (2H, d, J = 8.5 Hz); ^{13}C NMR for rotamers (100 MHz, $CDCl_3$): δ 14.3, 14.5, 26.5, 63.0, 63.3, 64.0, 74.8, 123.2, 129.1, 132.1, 132.5, 153.9, 155.7, 156.4, 169.9, 173.0; HRMS (ESI) m/z calcd for $C_{16}H_{18}N_3O_6SBrNa^+$ ($[M+Na]^+$) 481.9997, found 481.9992; $[\alpha]_D^{20}$= +69.5 (*c* 0.34, CH_2Cl_2). HPLC (chiral AD-H column), hexane/2-propanol = 9/1, flow rate 0.7 mL/min, λ = 254 nm, t_{major} = 13.8 min, t_{minor} = 27.4 min.



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	13.889	VB	0.8800	2541.19141	50.6458
2	27.216	VB	1.0508	2476.38452	49.3542

(racemic **4**)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Area %
1	13.826	BB	0.9348	5982.47461	95.5196
2	27.379	BB	1.0369	280.61176	4.4804

(**4**)

6. References

(1) L. Zou, B. Wang, H. Mu, H. Zhang, Y. Song and J. Qu, *Org. Lett*., 2013, **15**, 3106.

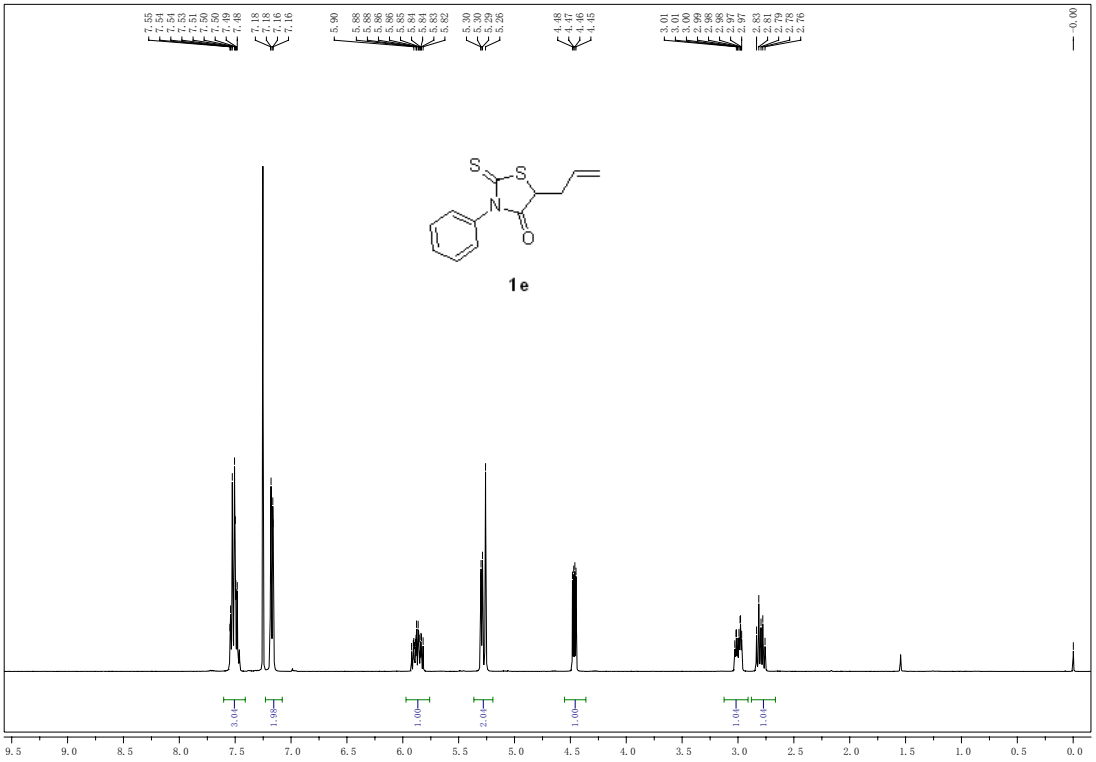
(2) H. Li, Y.-Q. Wang and L. Deng, *Org. Lett.*, 2006, **8**, 4063.

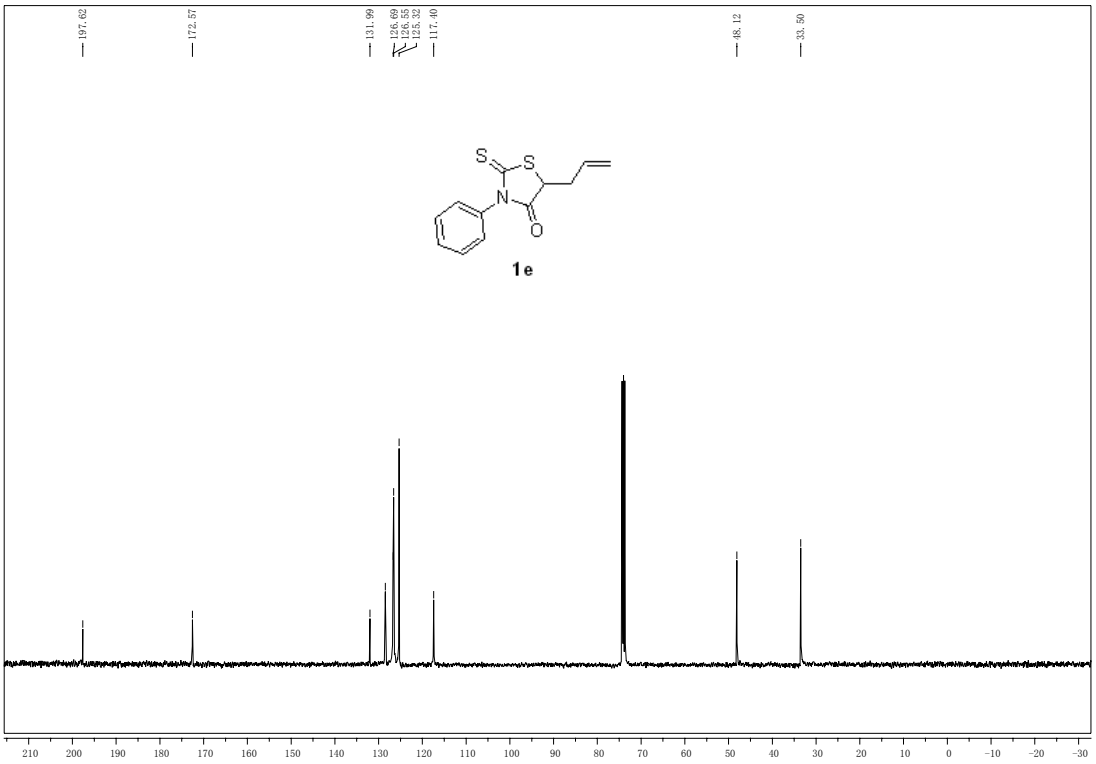
(3) For the preparation of the mercapto carboxylic acids, see: (a) N. T. Pokhodylo, V. S. Matiychuk and M. D. Obushak, *Phosphorus, Sulfur, and Silicon*, 2012, **187**, 850; (b) A. Kudelko, *Tetrahedron*, 2012, **68**, 3616; (c) S.-C. J. Fu, S. M. Birnbaum and J. P. Greenstein, *J. Am. Chem. Soc*., 1954, **76**, 5385; R. Moumne, S. Lavielle and P. Karoyan, *J. Org. Chem*., 2006, **71**, 3332; (d) A. M. Elgeshi, V. Maslak and R. N. SAIČIĆ, *J. Serb. Chem. Soc*., 2007, **72**, 1173.

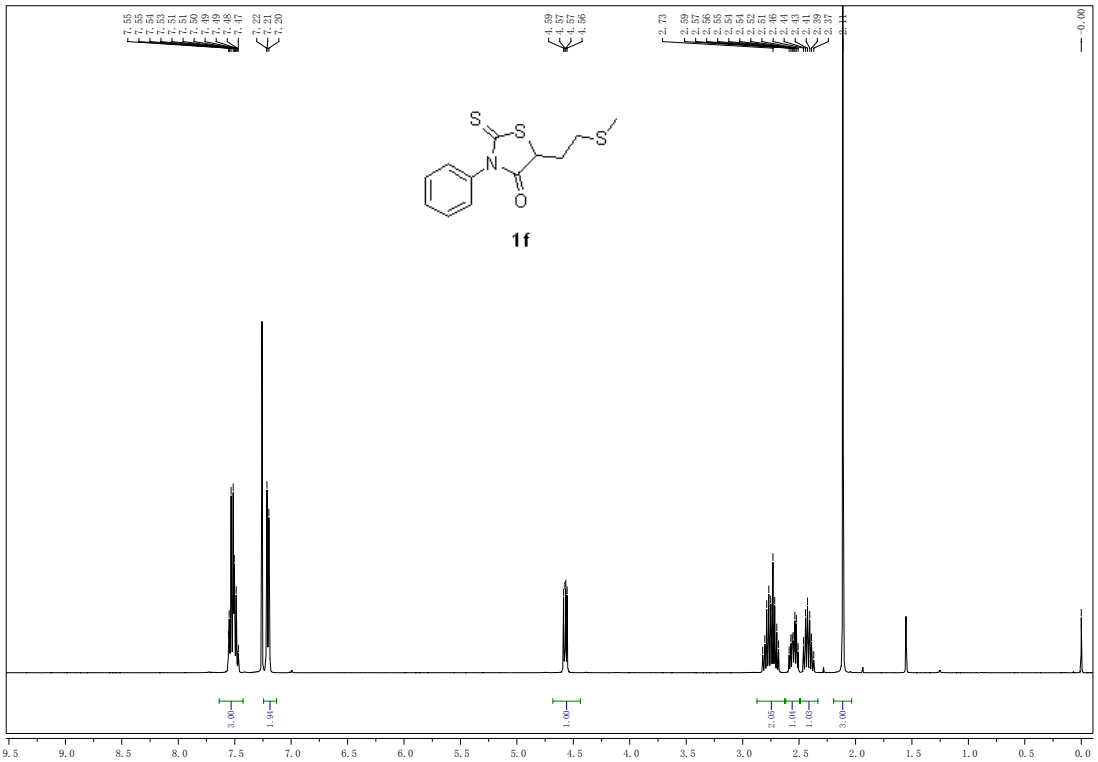
(4) F. Yu, H. X. Hu, X. D. Gu and J. X. Ye, *Org. Lett*., 2012, **14**, 2038.

(5) N. K. El-Aasar and K. F. Saied, *J. Sulfur Chem*., 2008, **29**, 43.

7. Copies of the NMR spectra



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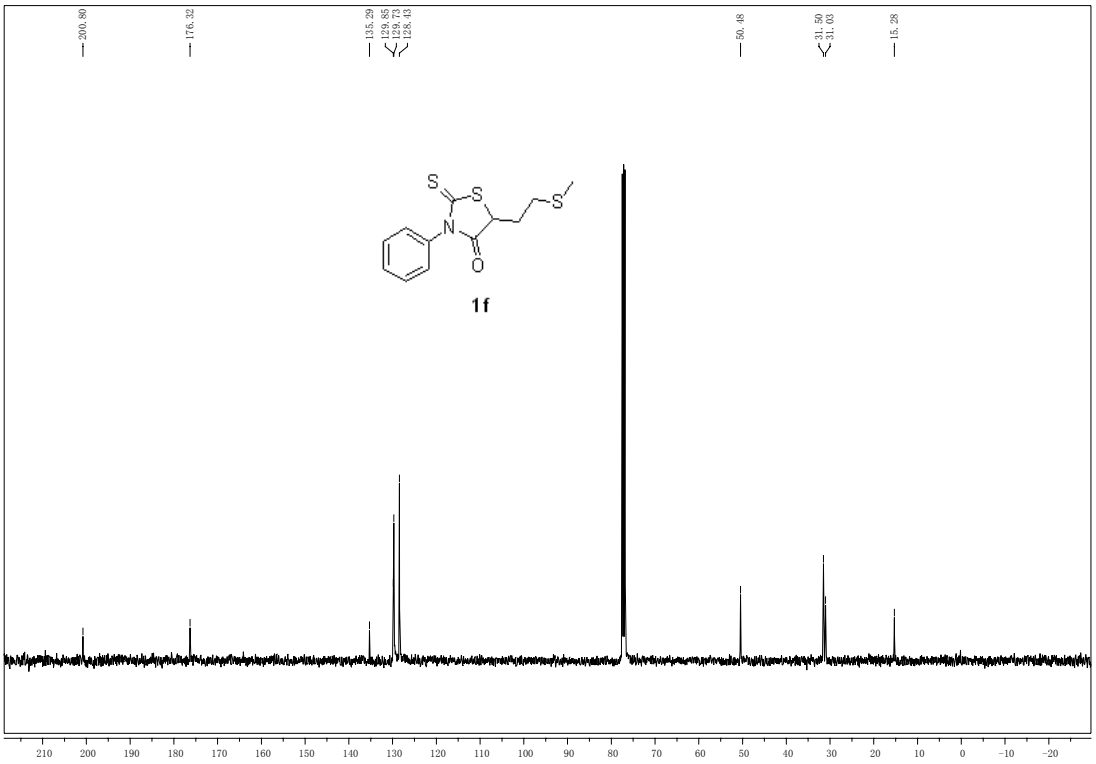
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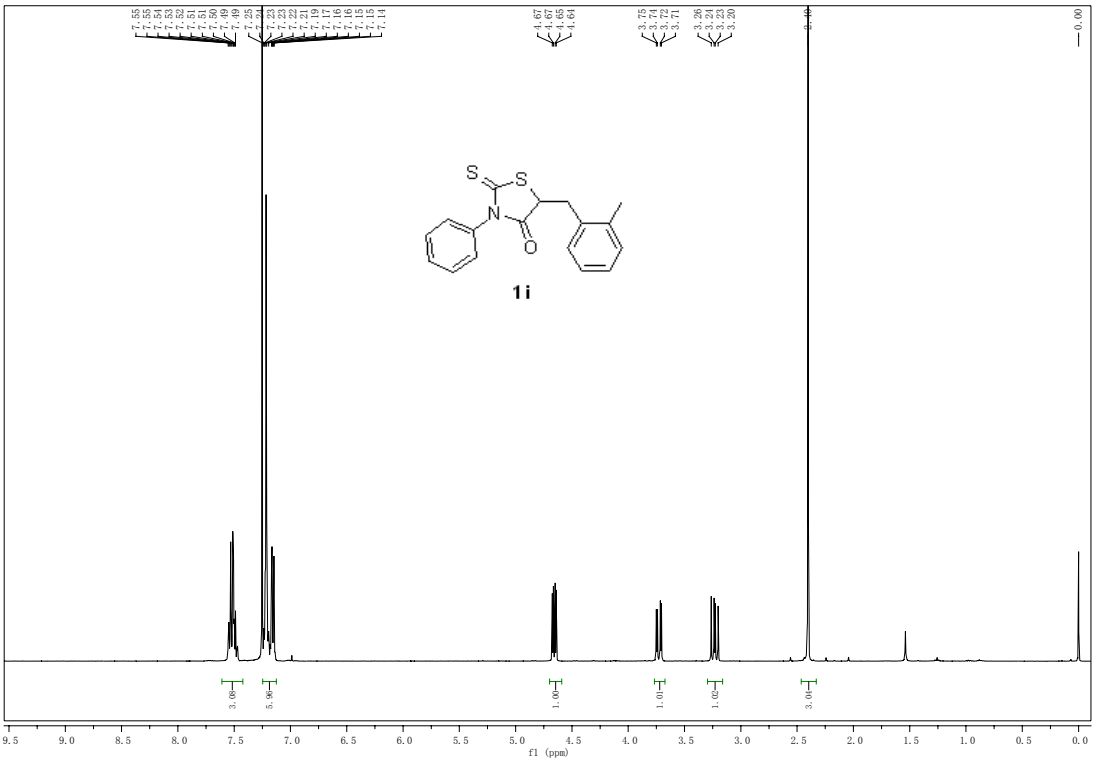
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3.24
3.23
3.20
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3.08
5.96
1.00
1.01
1.02
3.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
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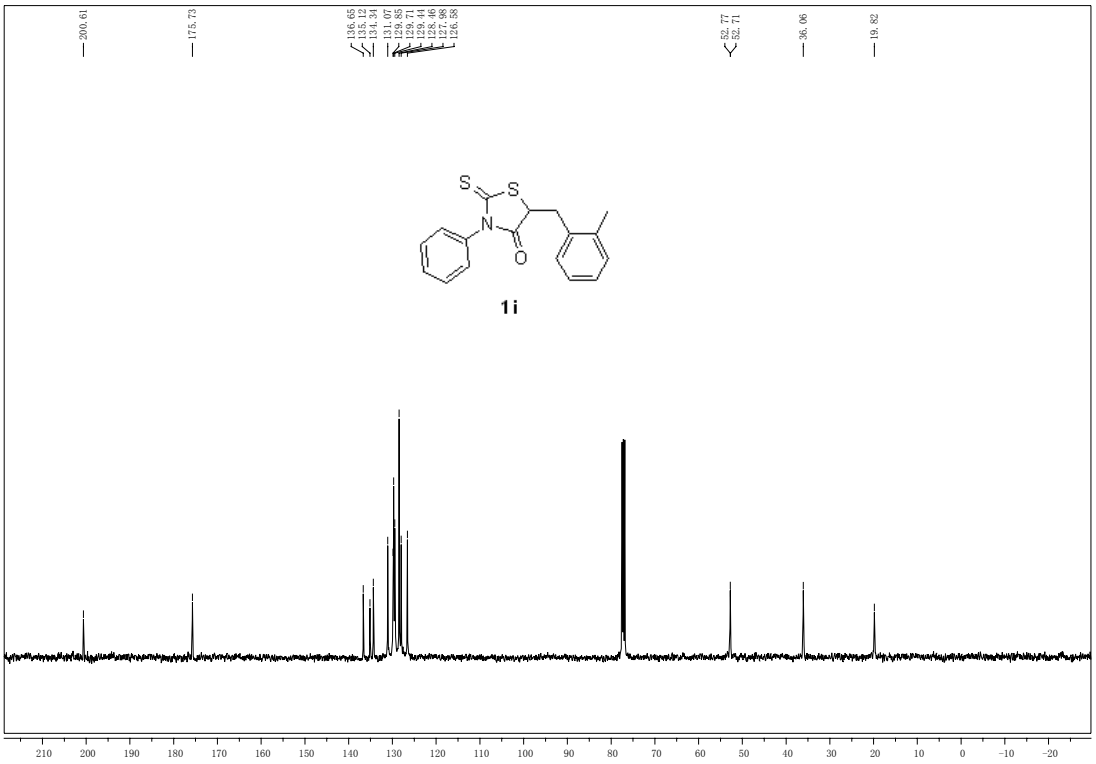
O
1i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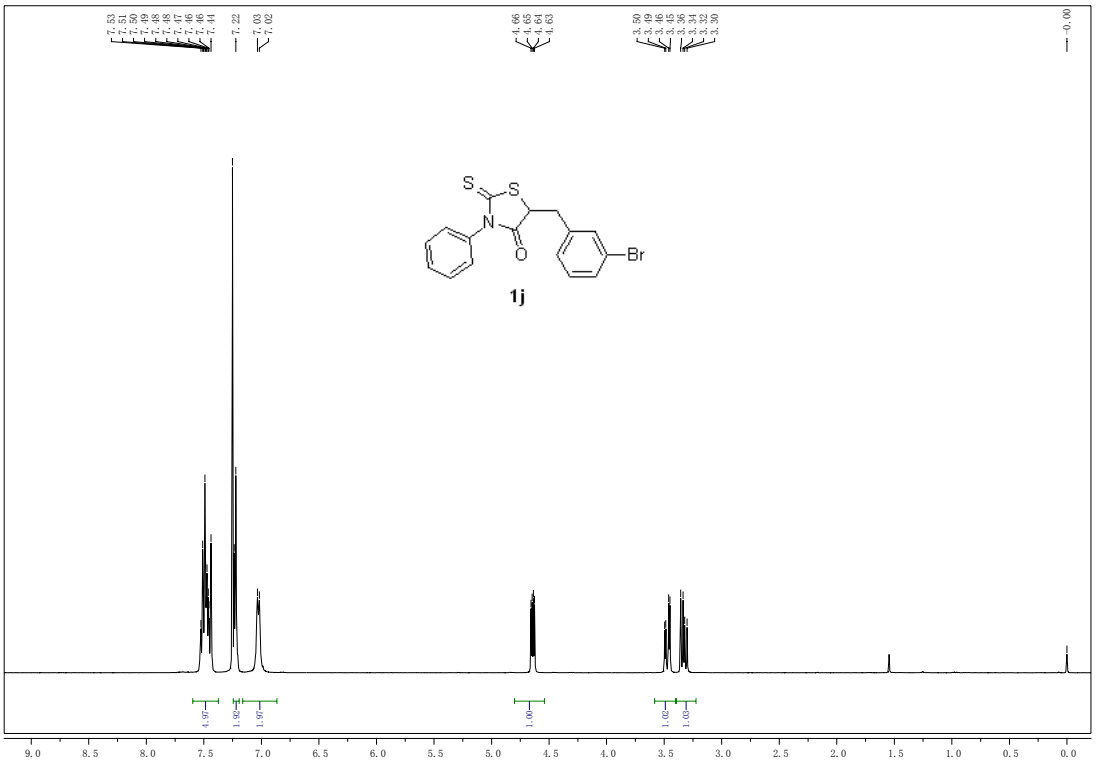
N
O
1i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3.46
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3.36
3.31
3.32
3.30
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S
N
O
Br
1j
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1.00
1.02
1.03
9.0
8.5
8.0
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7.0
6.5
6.0
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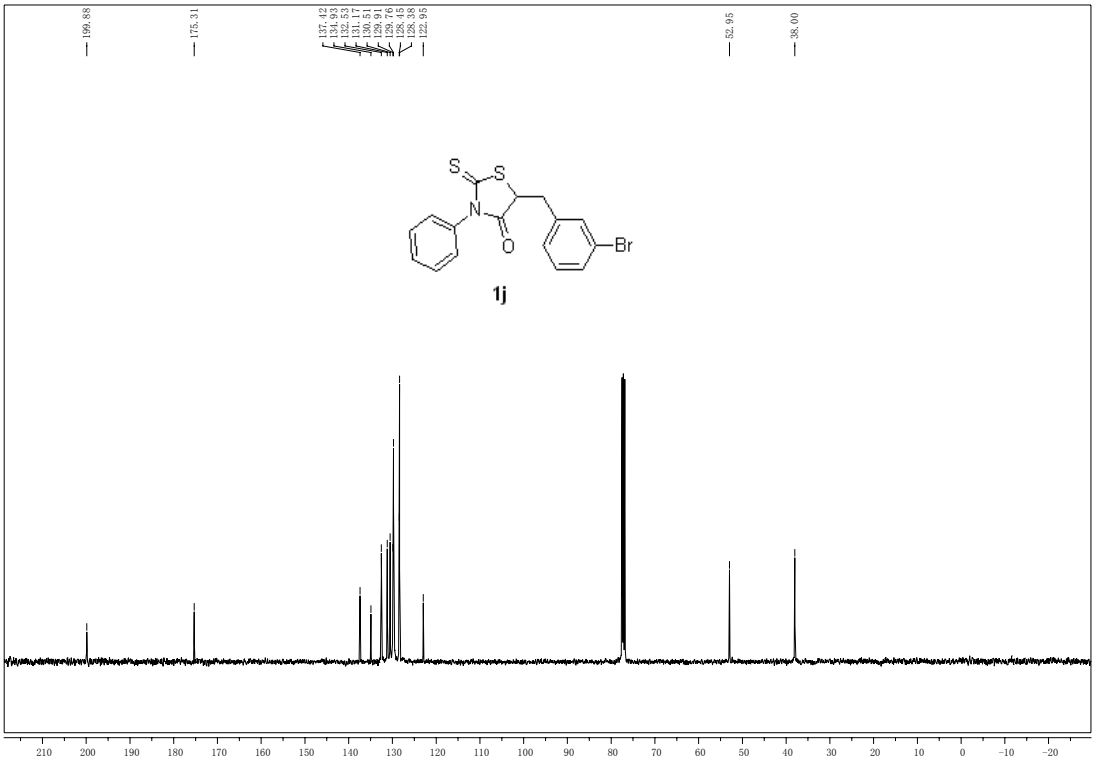
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O
Br
1j
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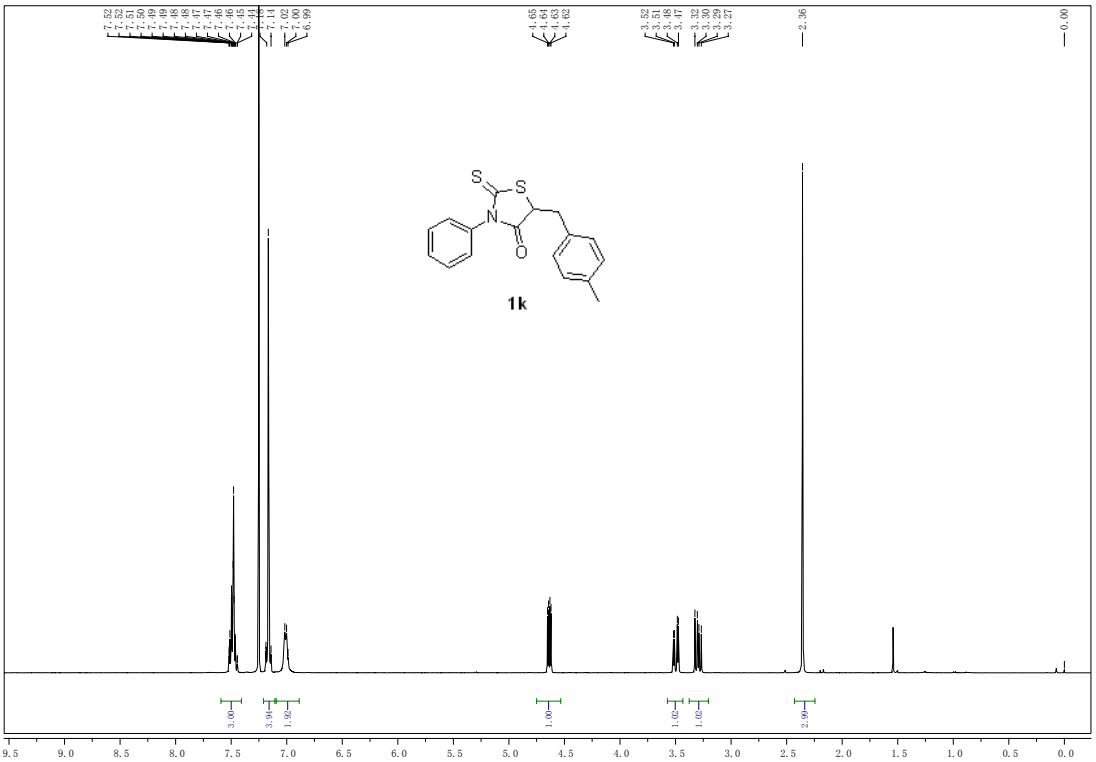
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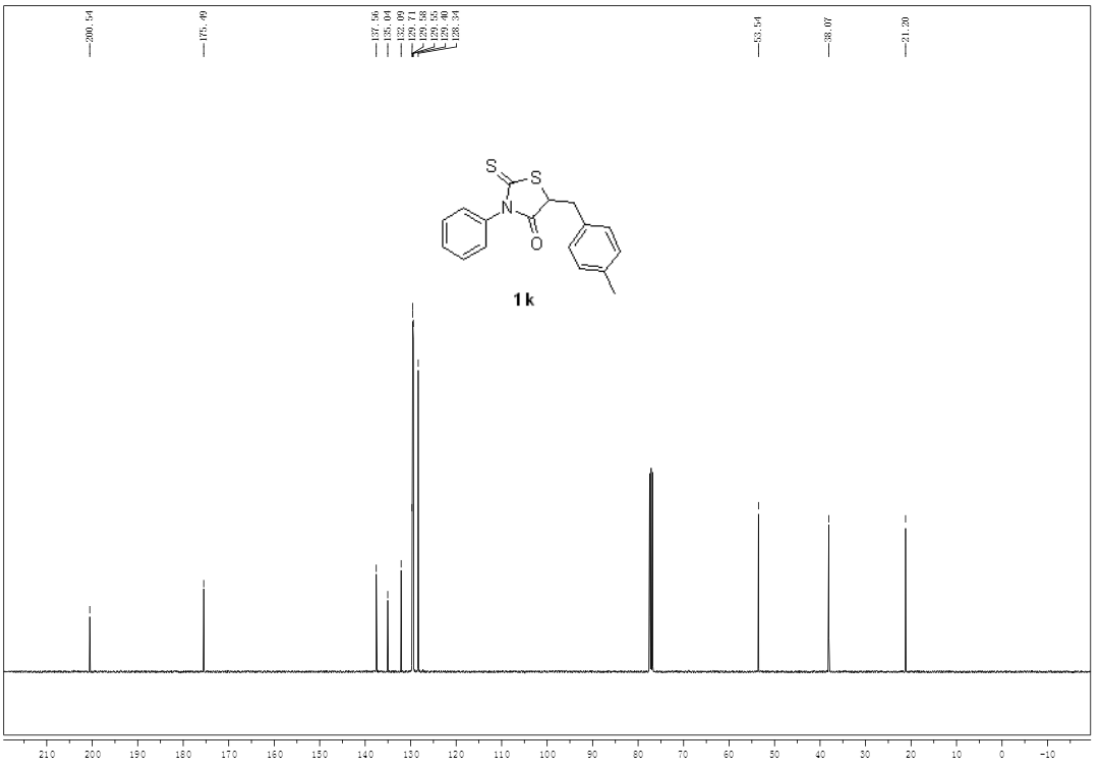
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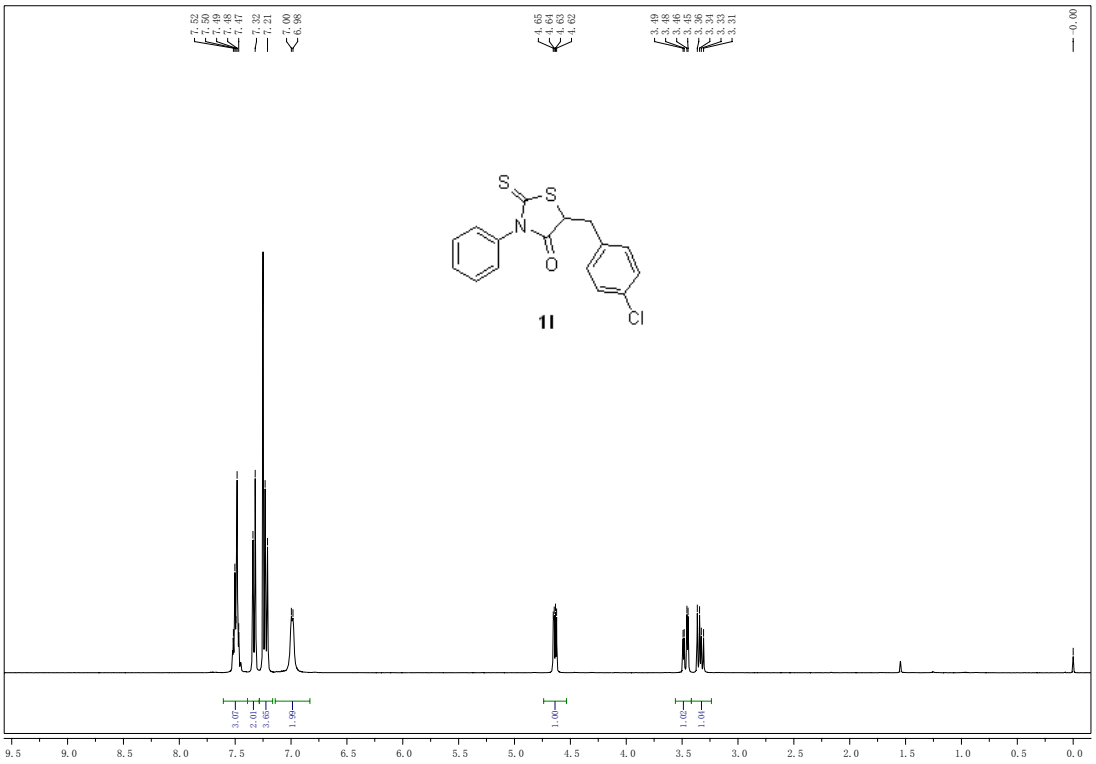
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3.48
3.46
3.45
3.36
3.34
3.33
3.31
0.00
S
S
N
O
Cl
1l
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2.01
3.65
1.99
1.00
1.02
1.01
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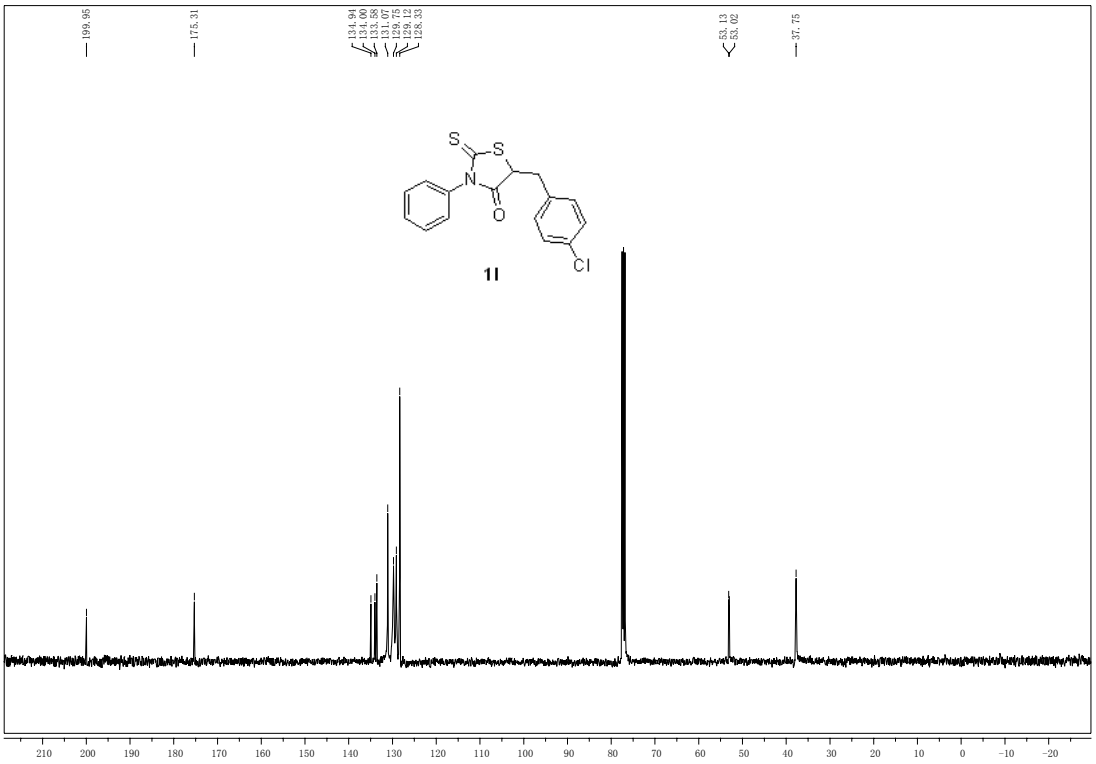
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O
Cl
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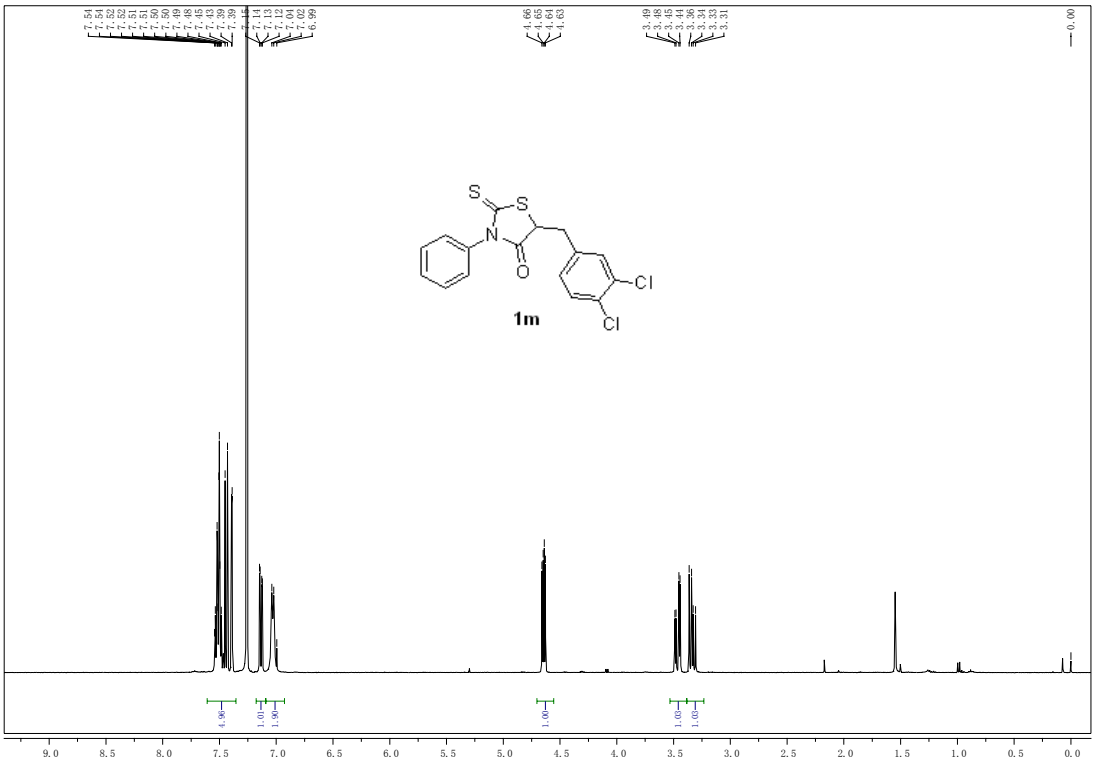
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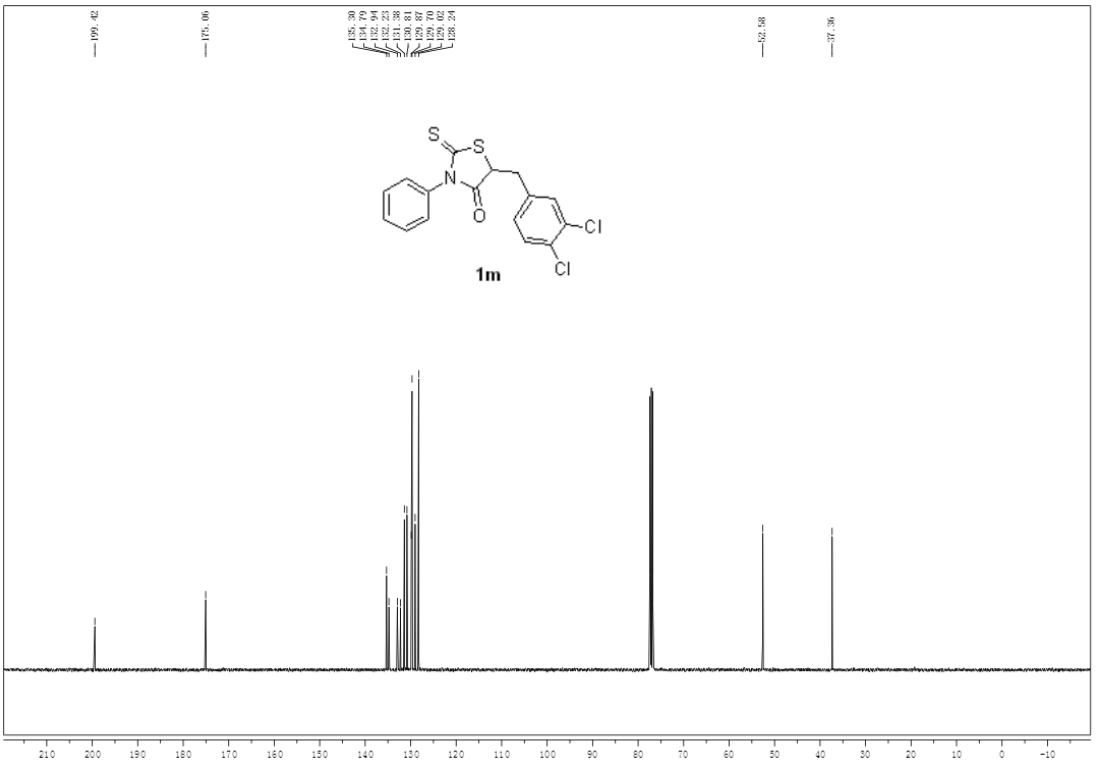
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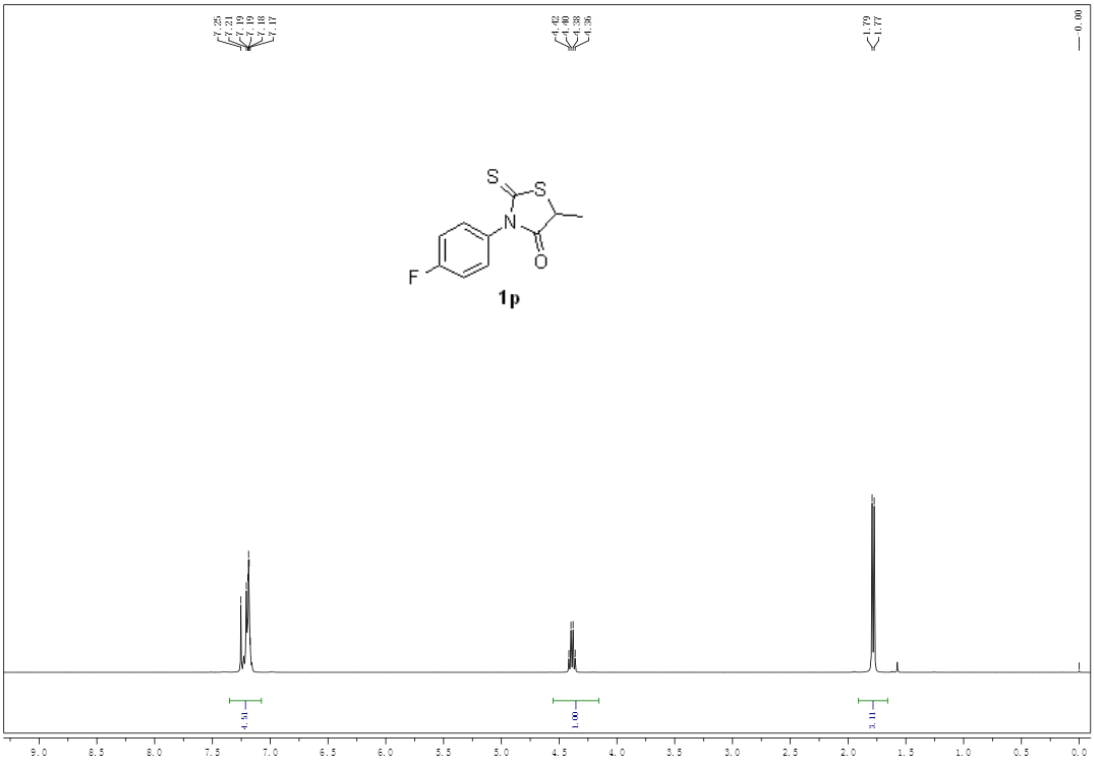
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N
O
F
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1.00
3.11
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8.0
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6.0
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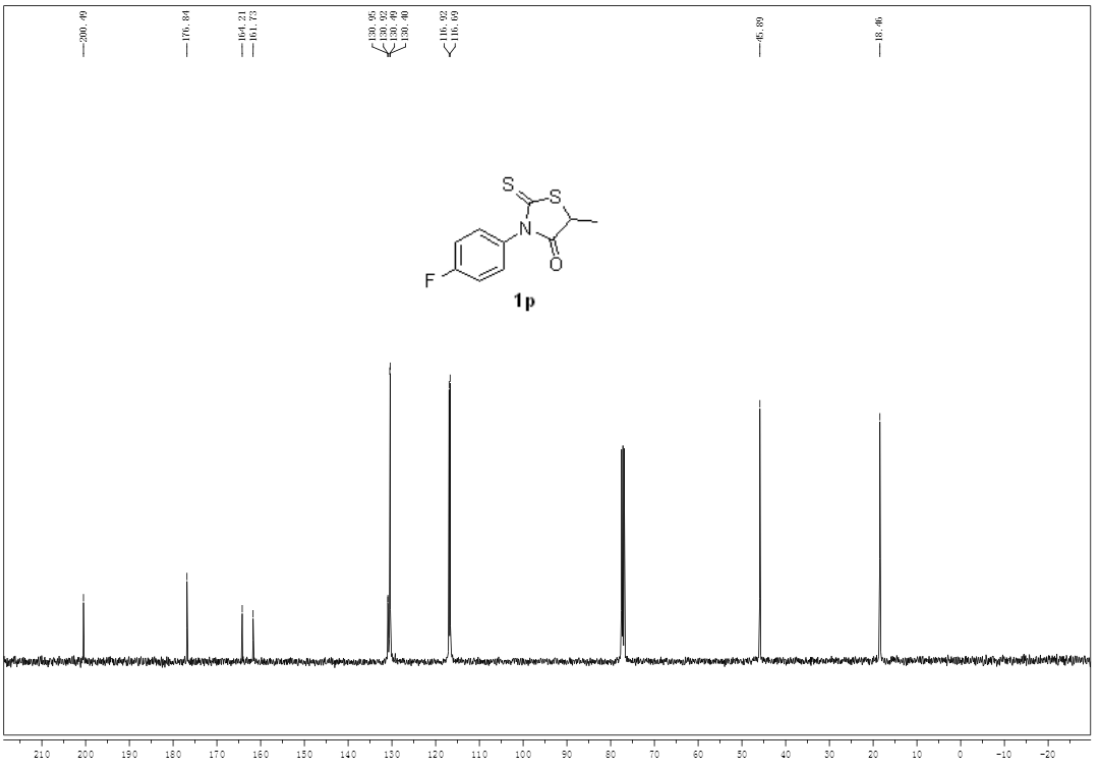
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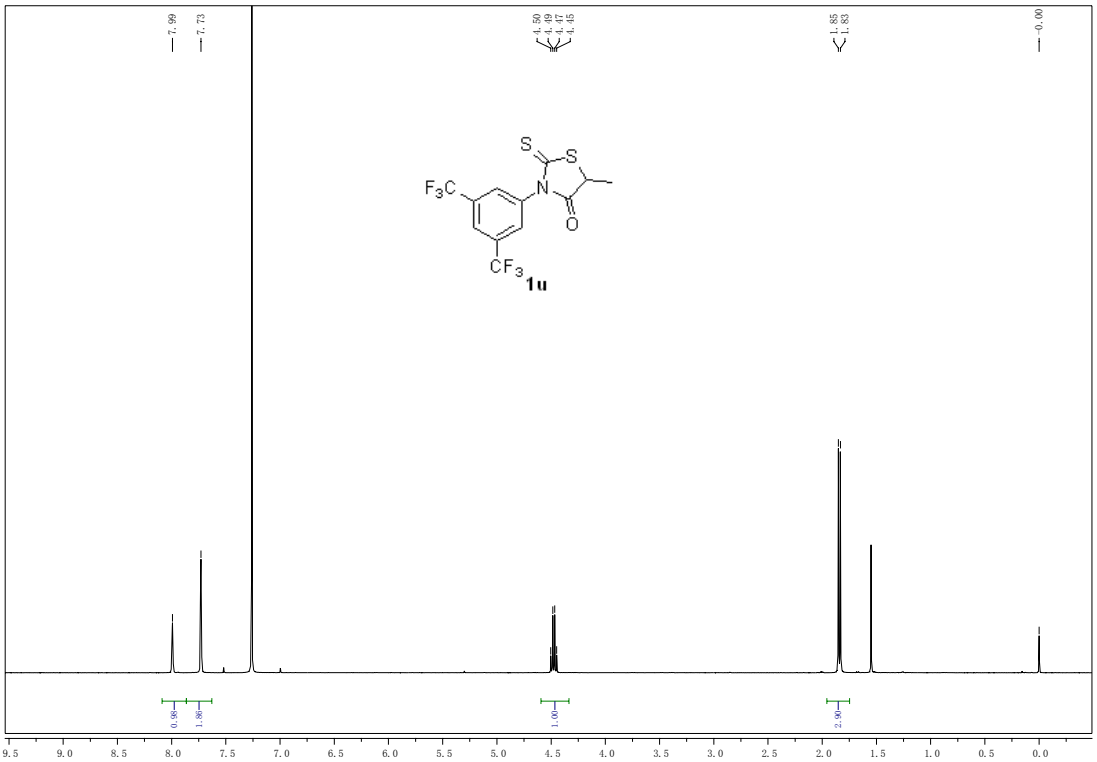
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CF3
1u
0.69
1.38
1.00
2.90
9.5
9.0
8.5
8.0
7.5
7.0
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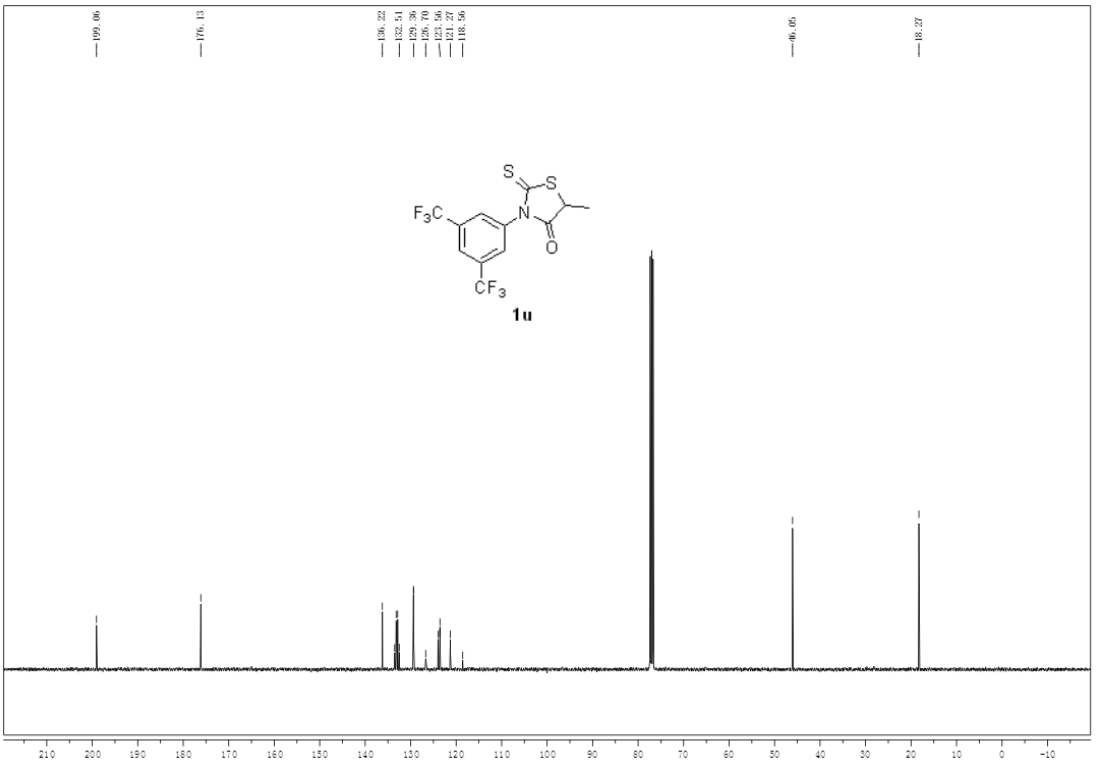
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S
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O
F3C
CF3
1u
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200
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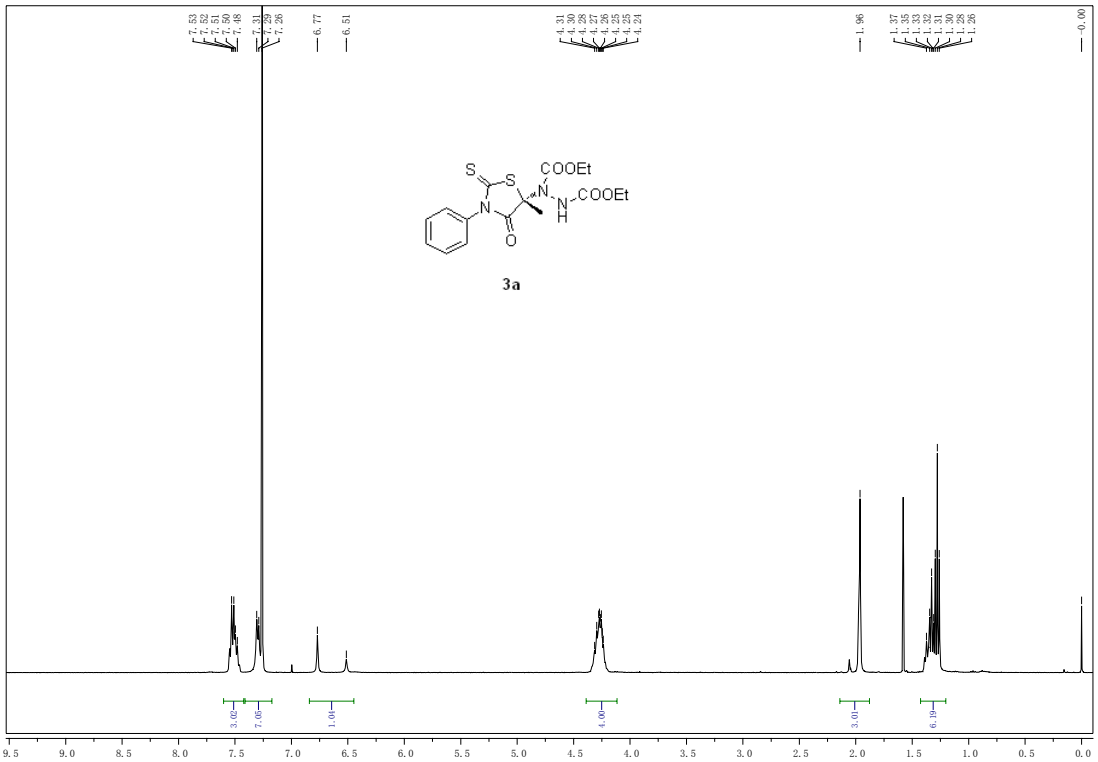
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4.24
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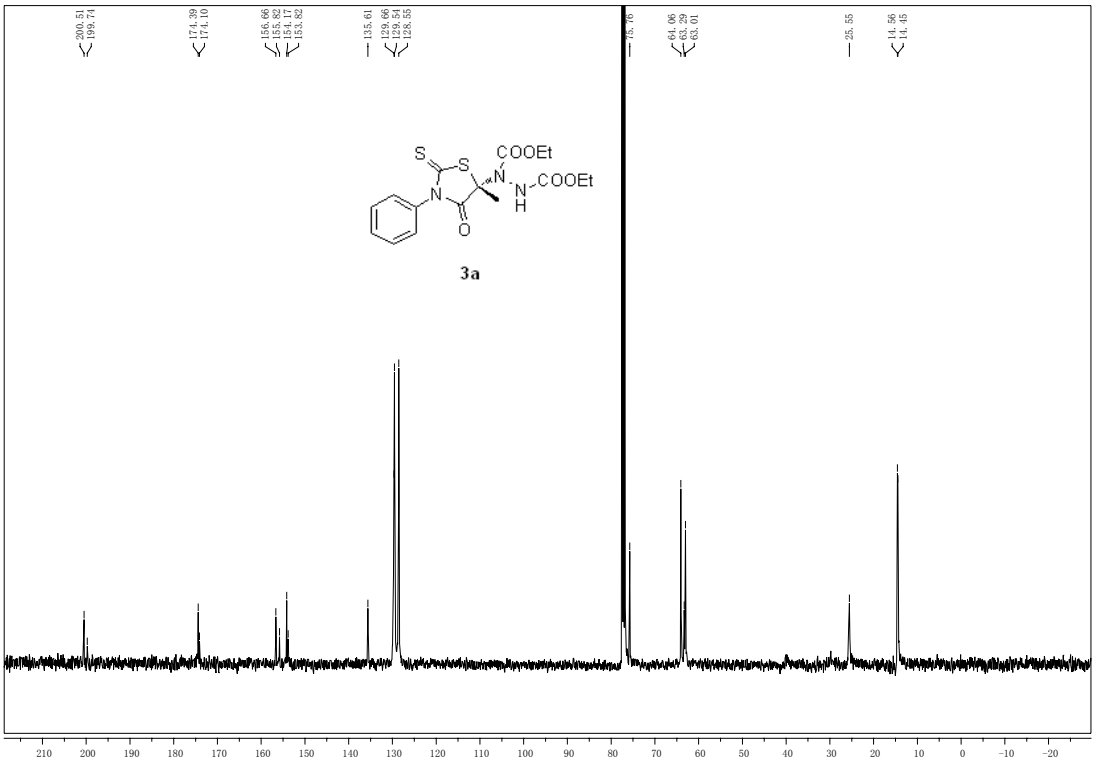
1.37
1.35
1.33
1.32
1.31
1.30
1.28
1.26
-0.00
3.02
7.05
1.00
4.00
3.01
6.19
S
S
N
N
H
O
COOEt
COOEt
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

3a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64.06
63.29
63.01
25.55
14.58
14.45
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H
O
COOEt
COOEt
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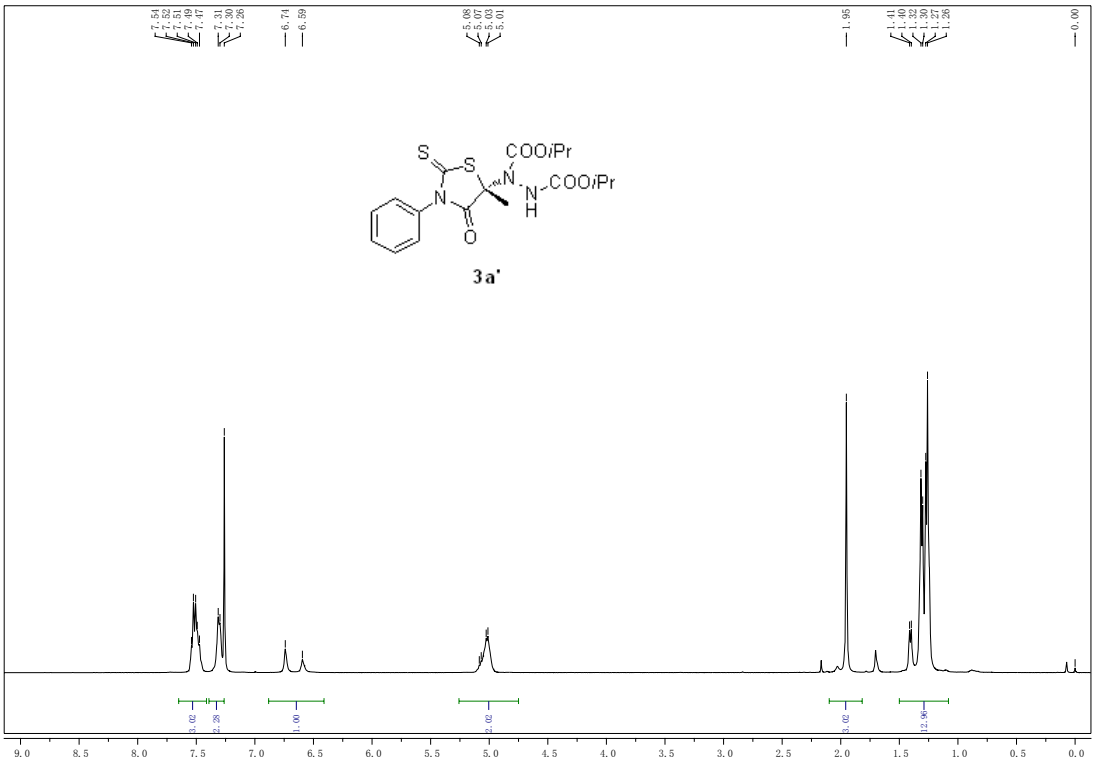
3a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5.01
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1.40
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1.30
1.27
1.26
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S
S
N
O
COO*i*Pr
N
N
H
COO*i*Pr
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2.28
1.00
2.02
3.02
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8.5
8.0
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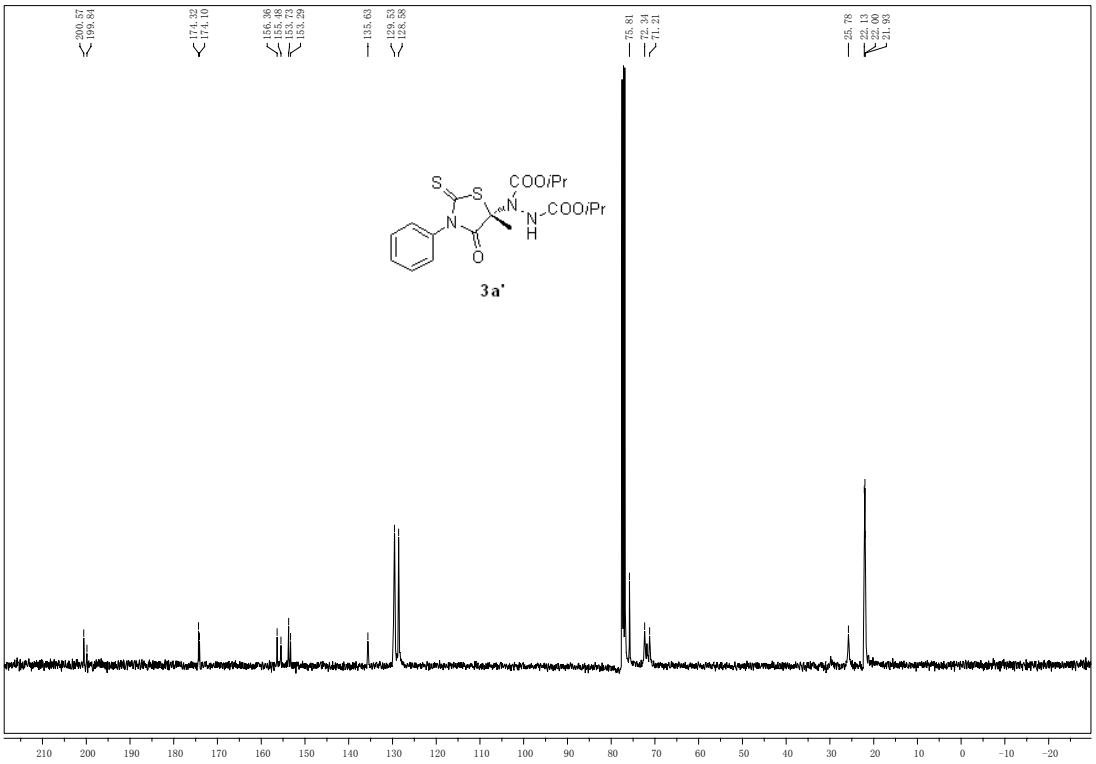
3a'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22.00
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S
S
N
O
COO*i*Pr
N
N
H
COO*i*Pr
210
200
190
180
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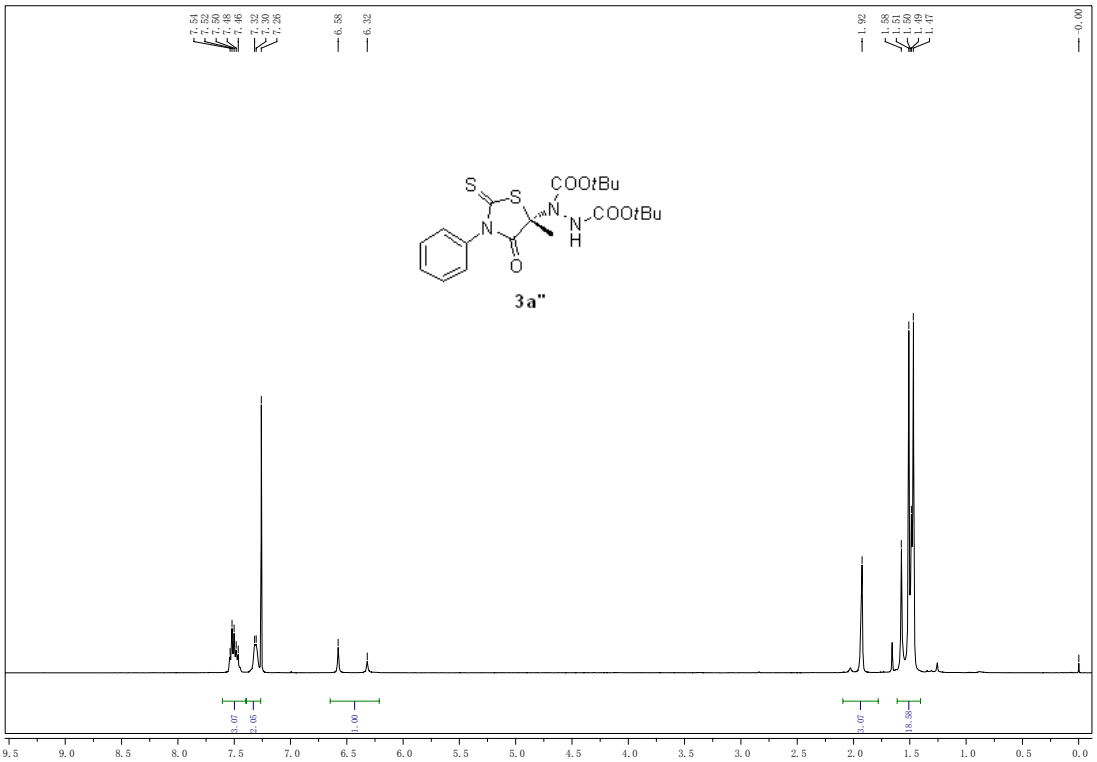
3a'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1.49
1.47
0.00
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S
N
N
H
O
COOtBu
COOtBu
3a"
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2.05
1.00
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18.88
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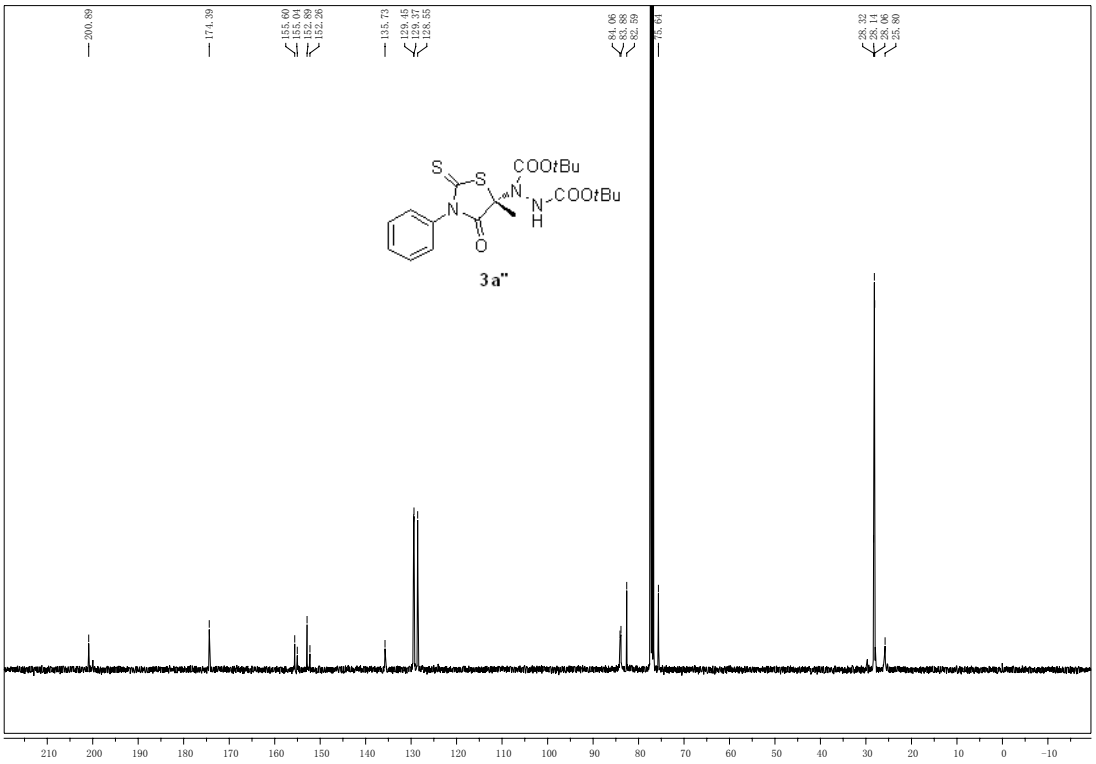
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76.64
28.32
28.11
28.06
25.80
S
S
N
N
H
O
COOtBu
COOtBu
3a"
210
200
190
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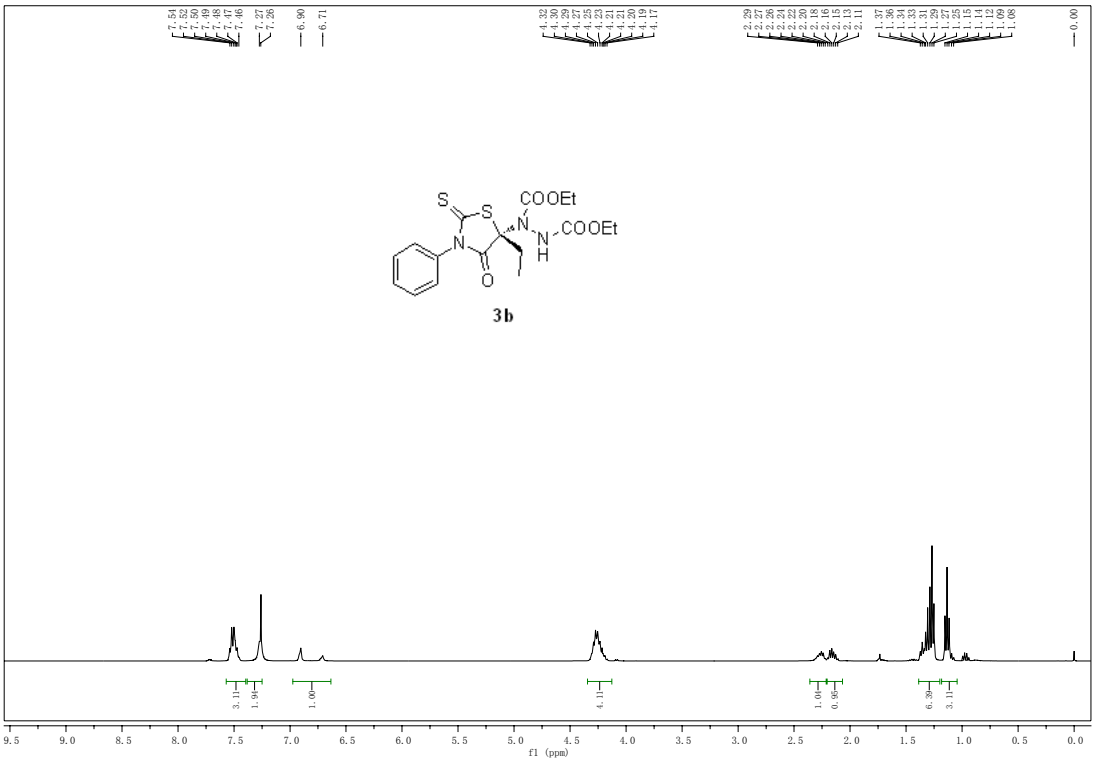
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2.27
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2.24
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2.15
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N
COOEt
H
O
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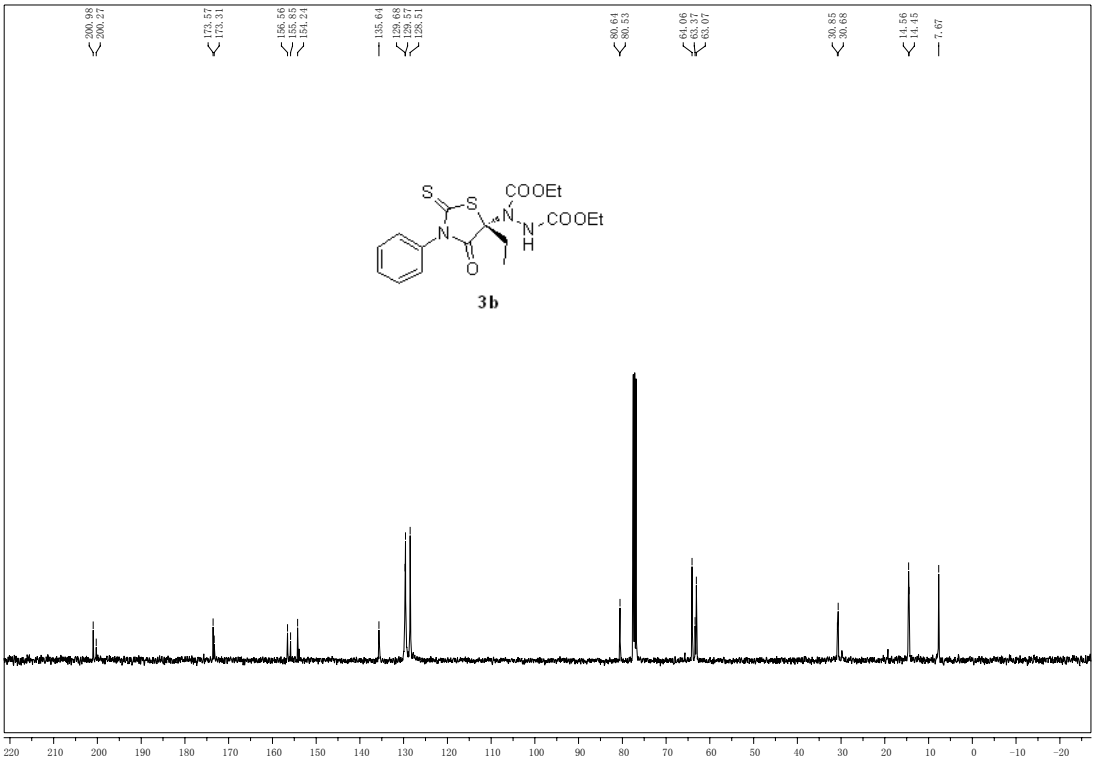
1.00
4.11
1.04
0.95
6.39
3.11
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

3b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64.06
63.37
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30.68
14.56
14.46
7.67
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COOEt
H
O
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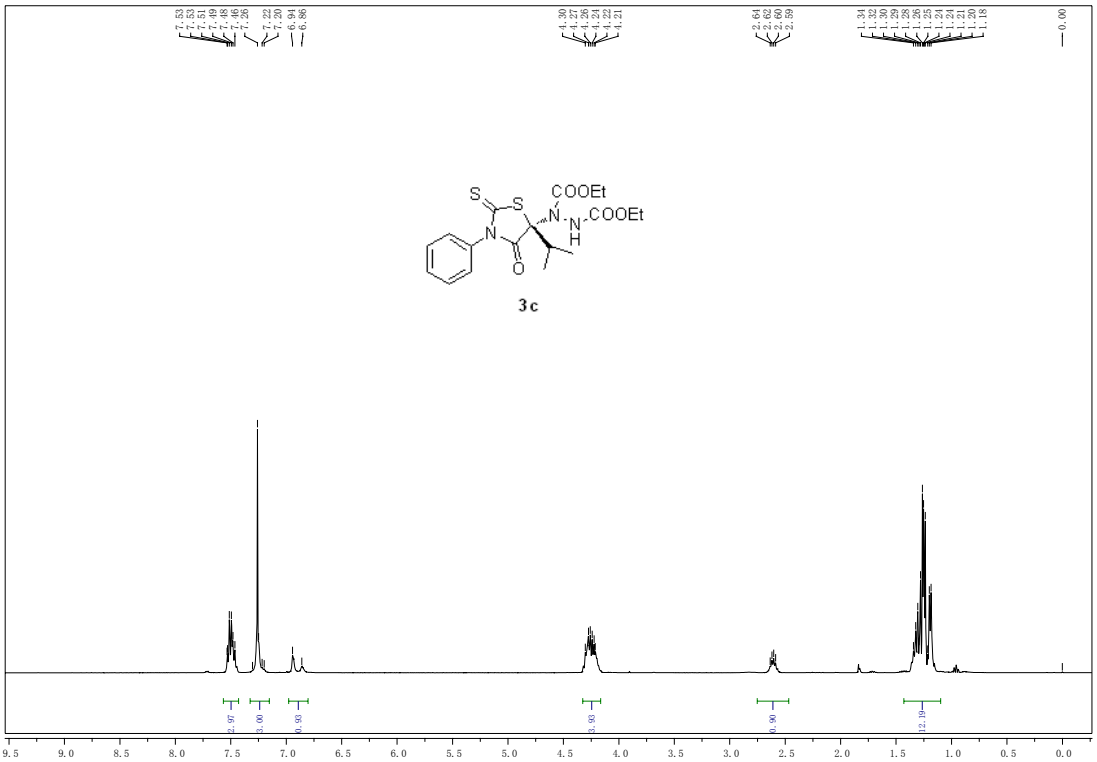
3b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4.24
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2.60
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1.32
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1.29
1.28
1.26
1.25
1.24
1.24
1.21
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COOEt
COOEt
3c
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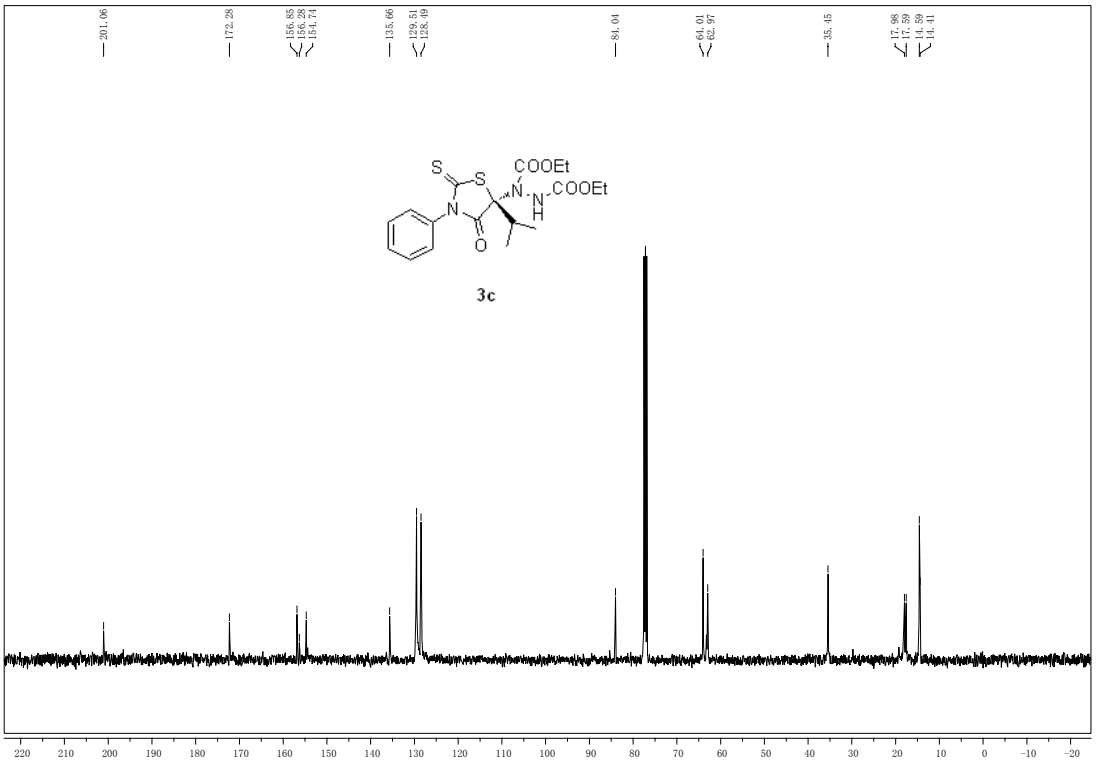
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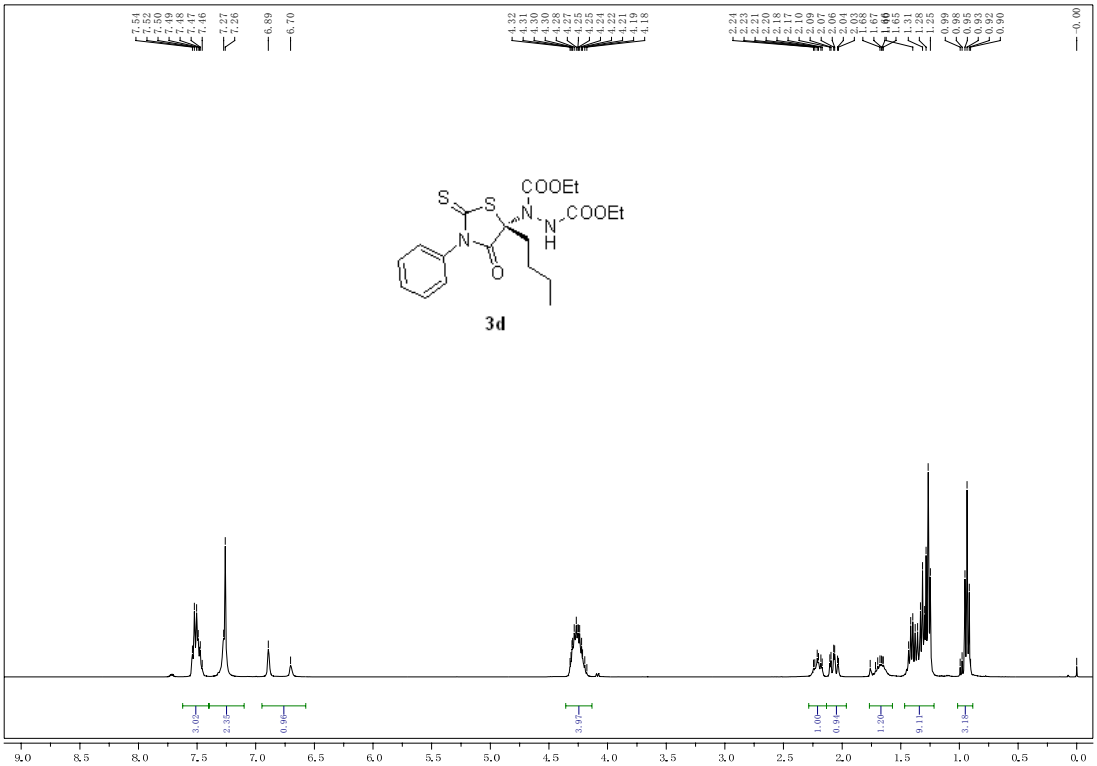
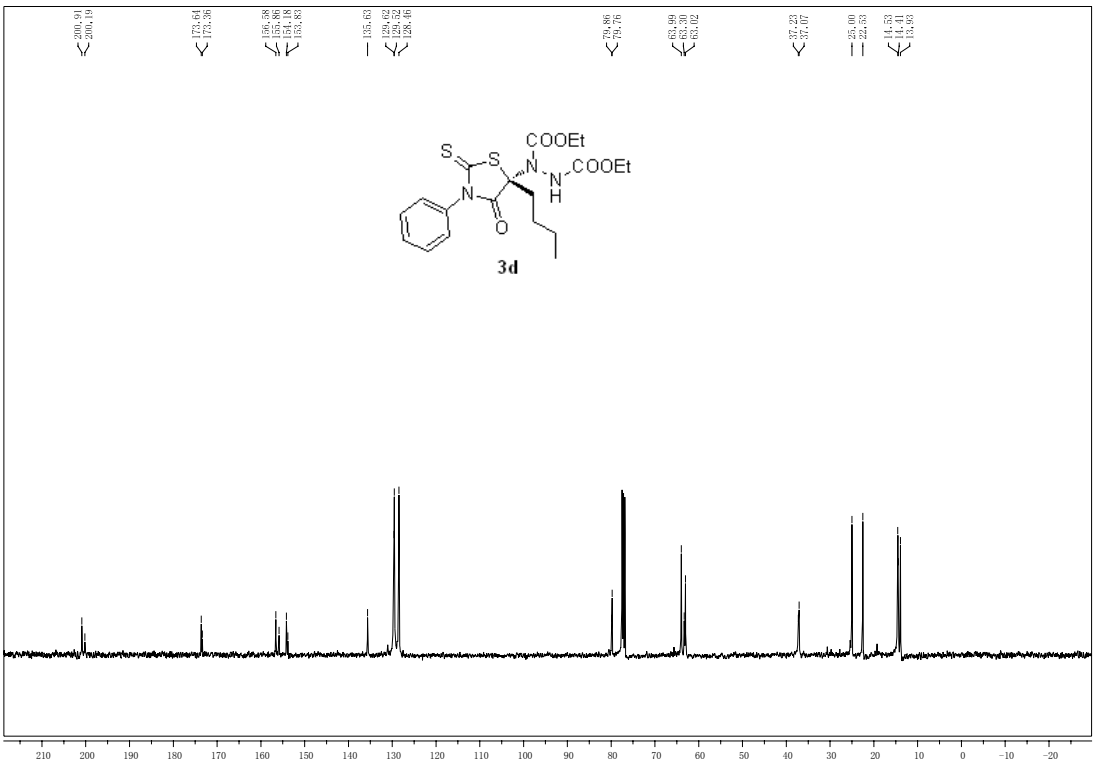
COOEt
3c


COOEt
COOEt
S
S
N
N
H
O
3d


COOEt
COOEt
S
S
N
N
H
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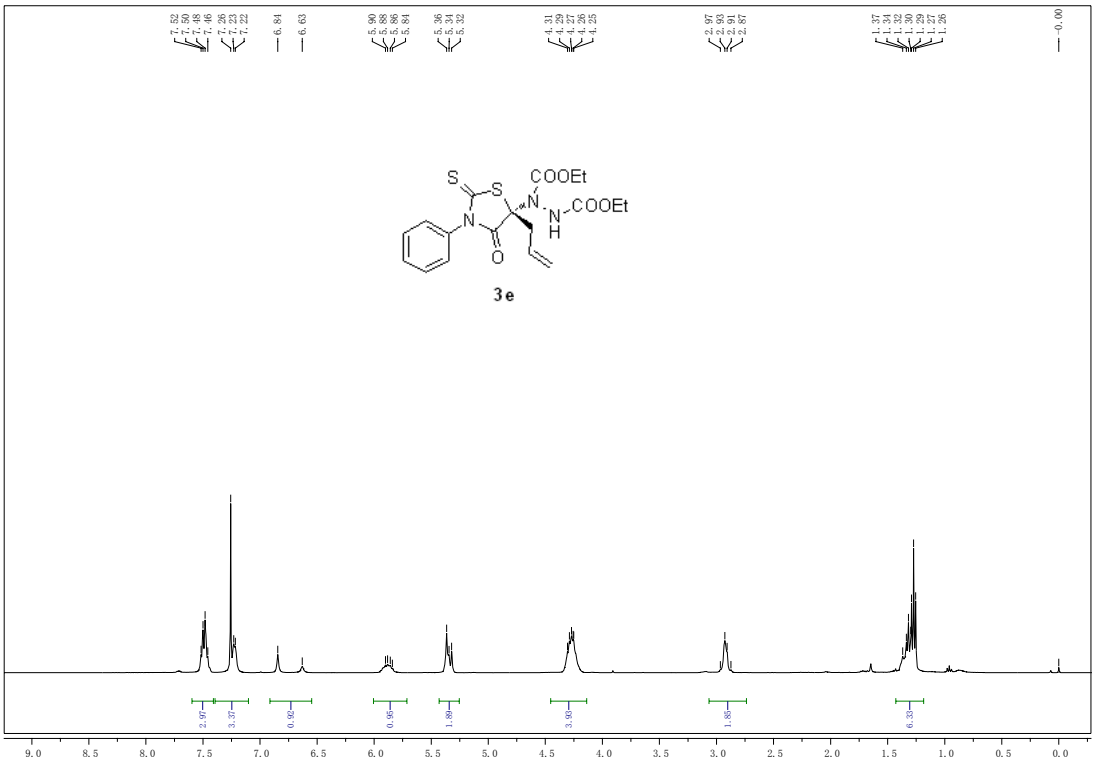
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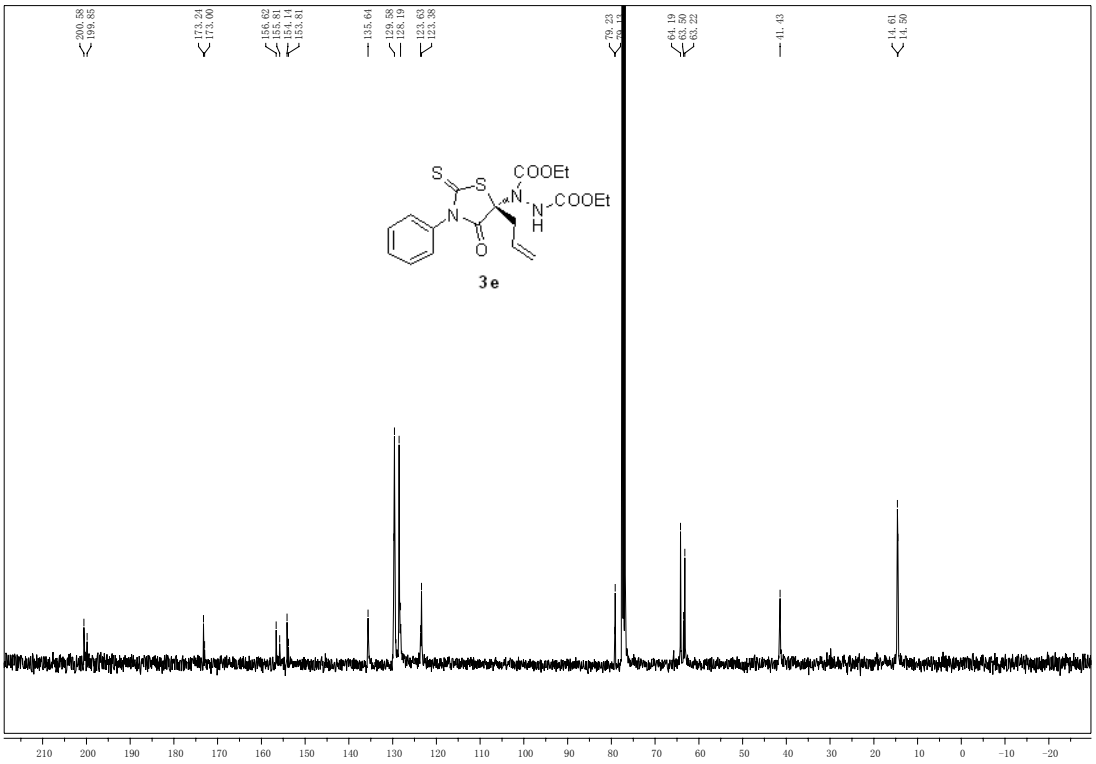
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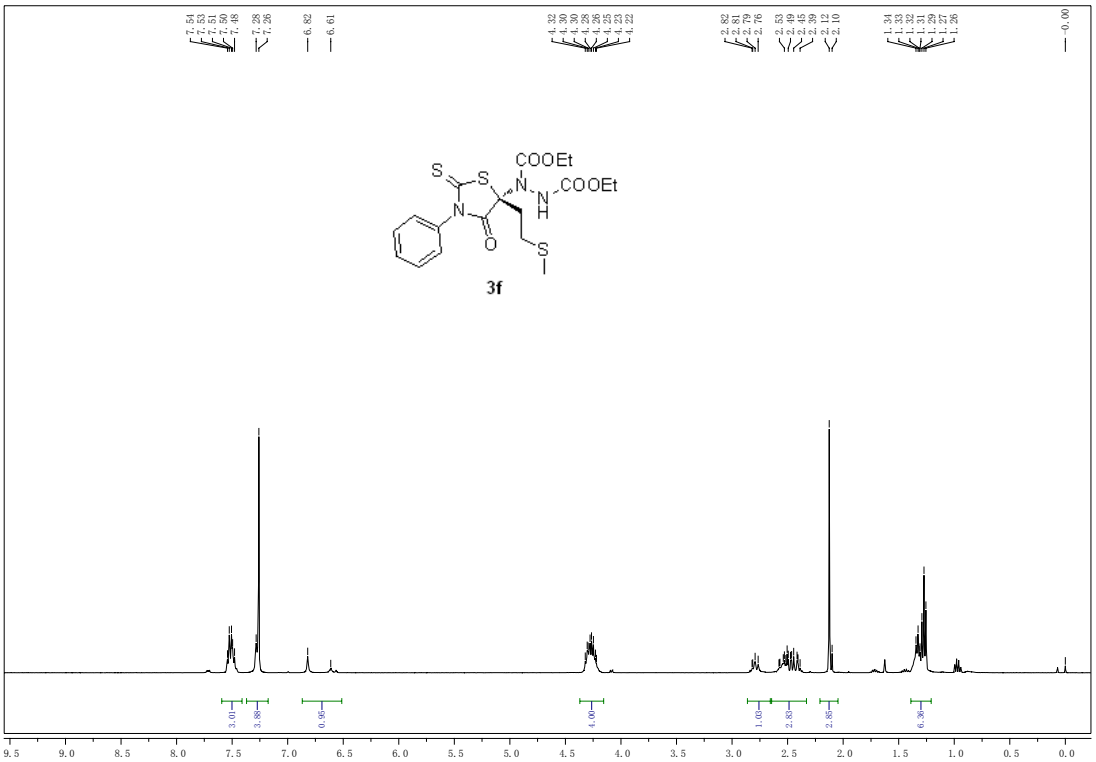
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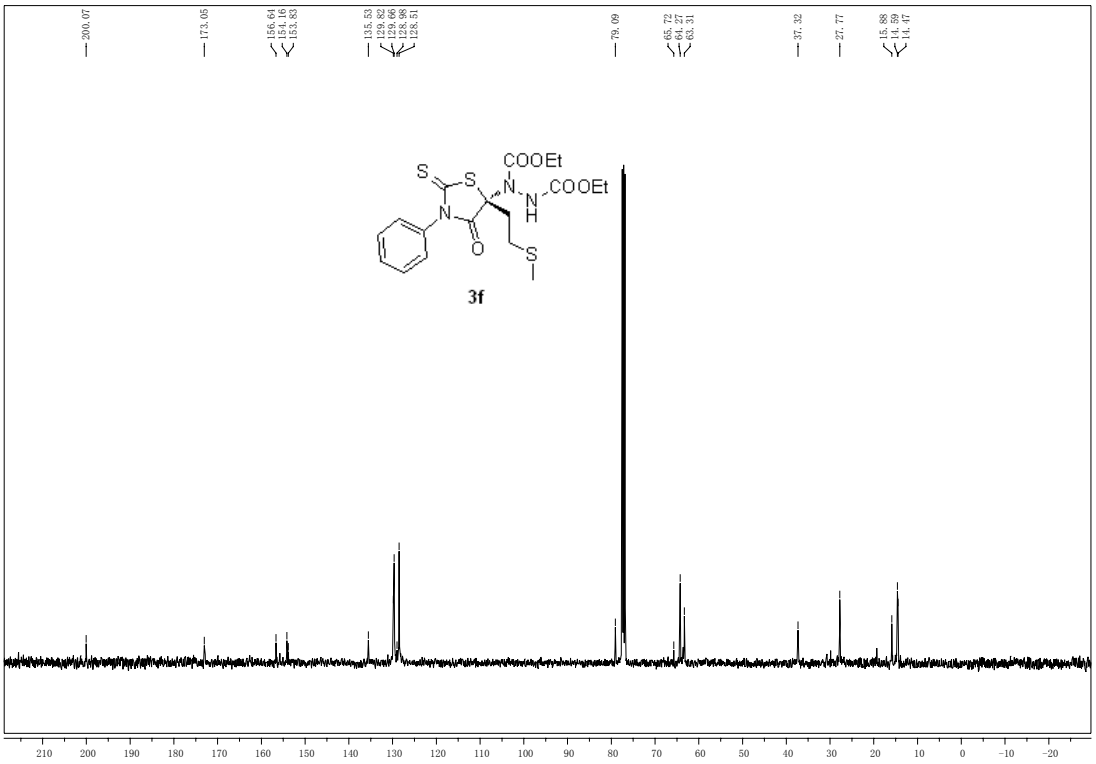
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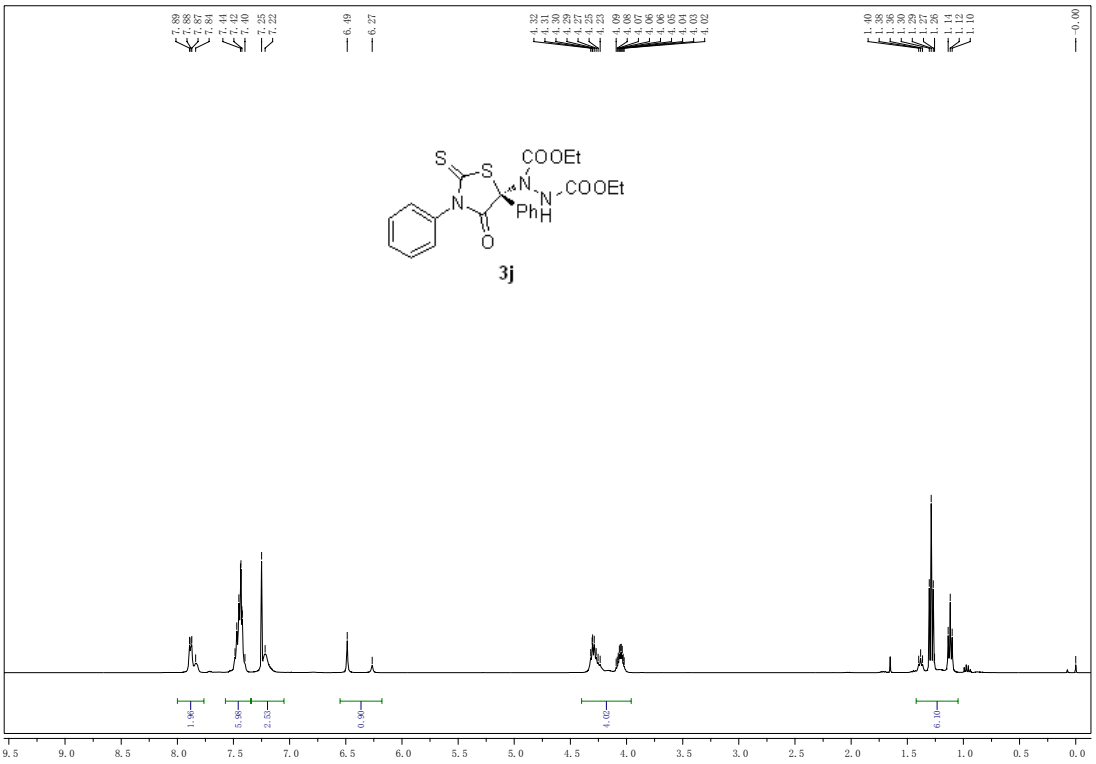
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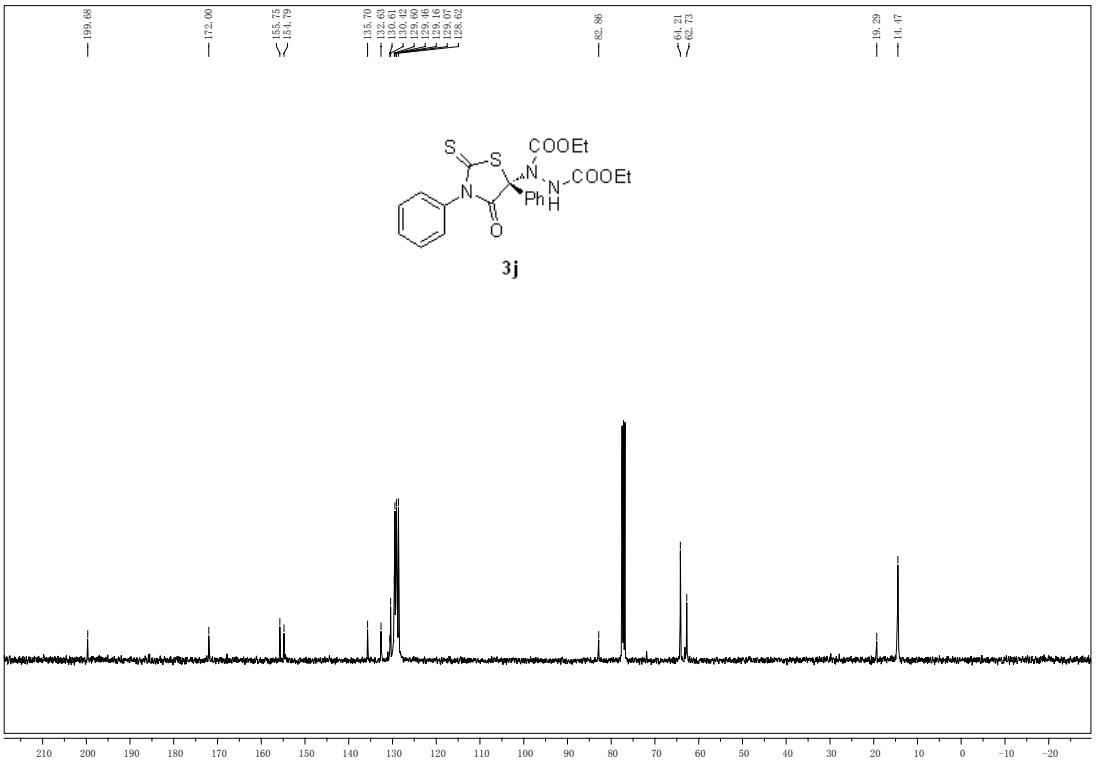
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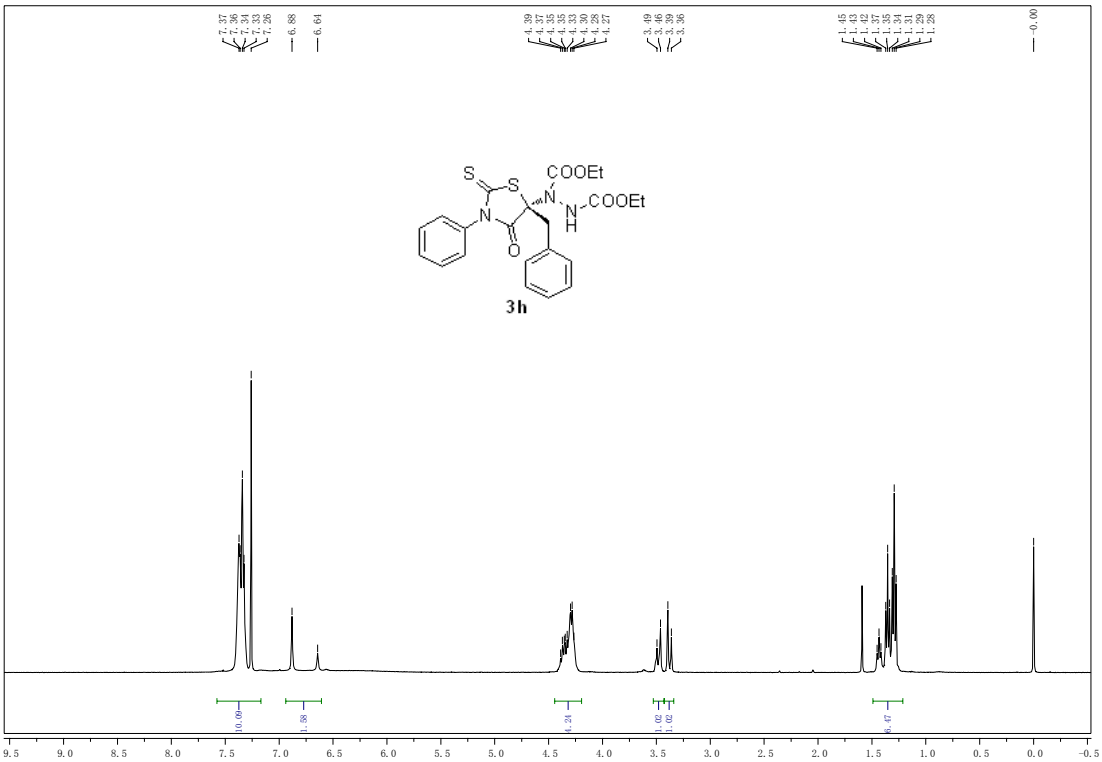
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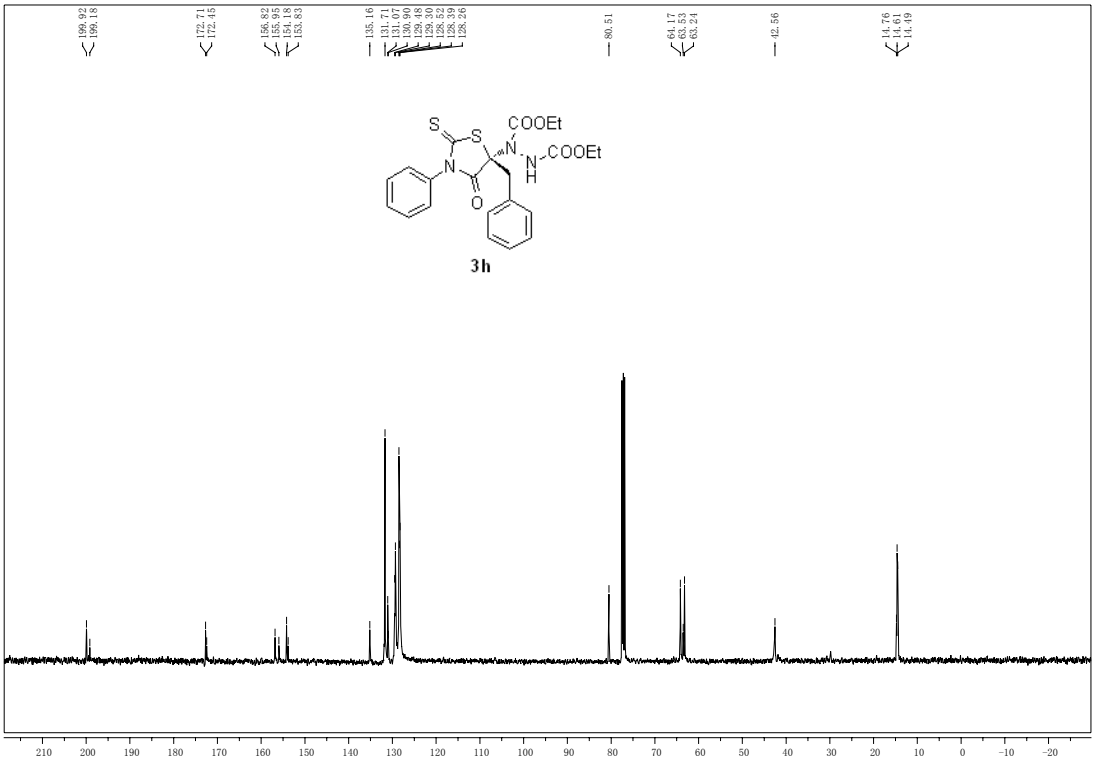
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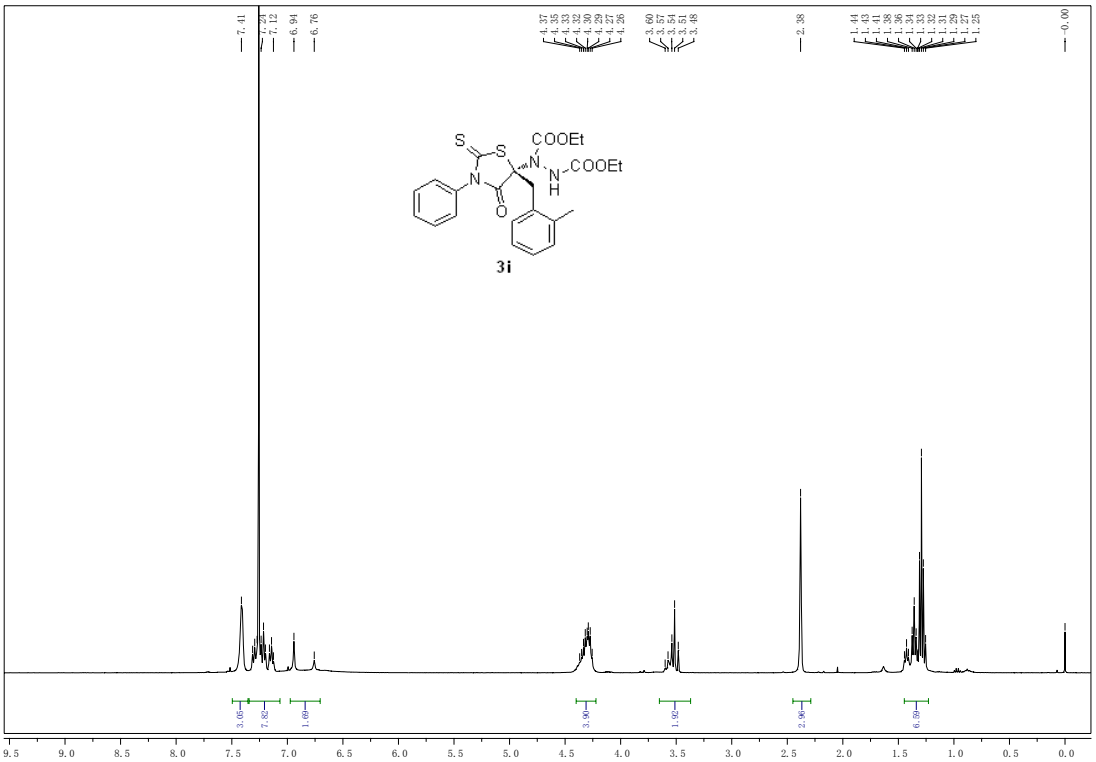
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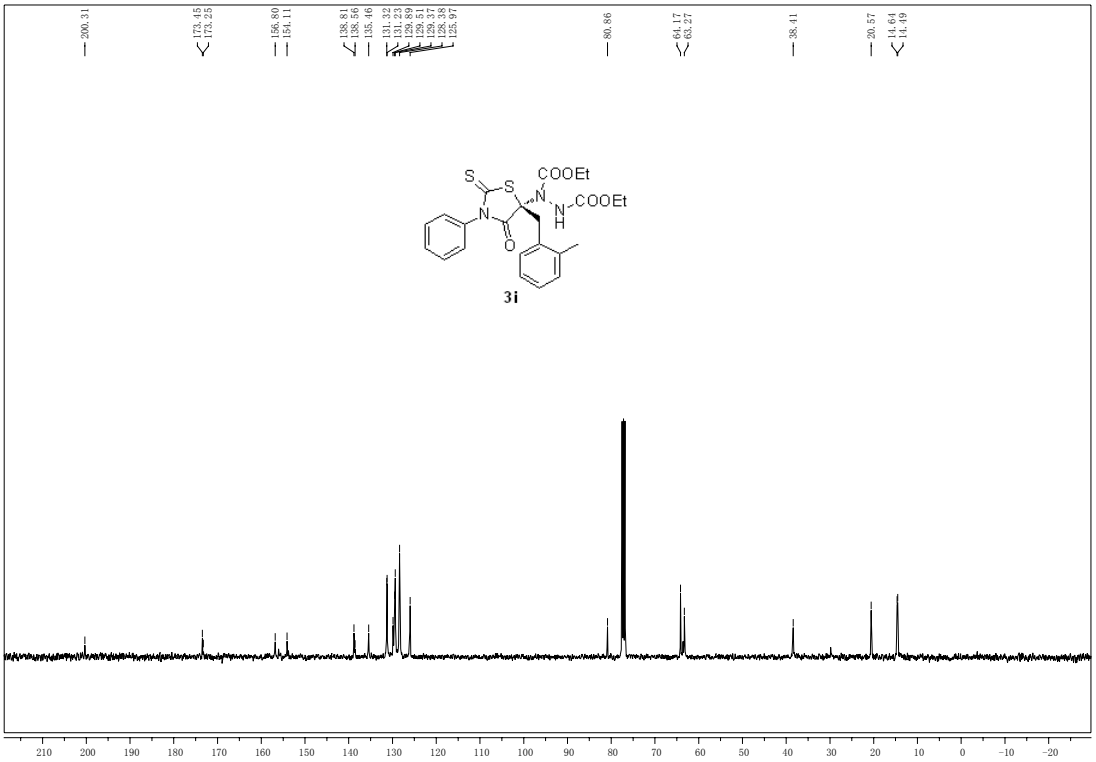
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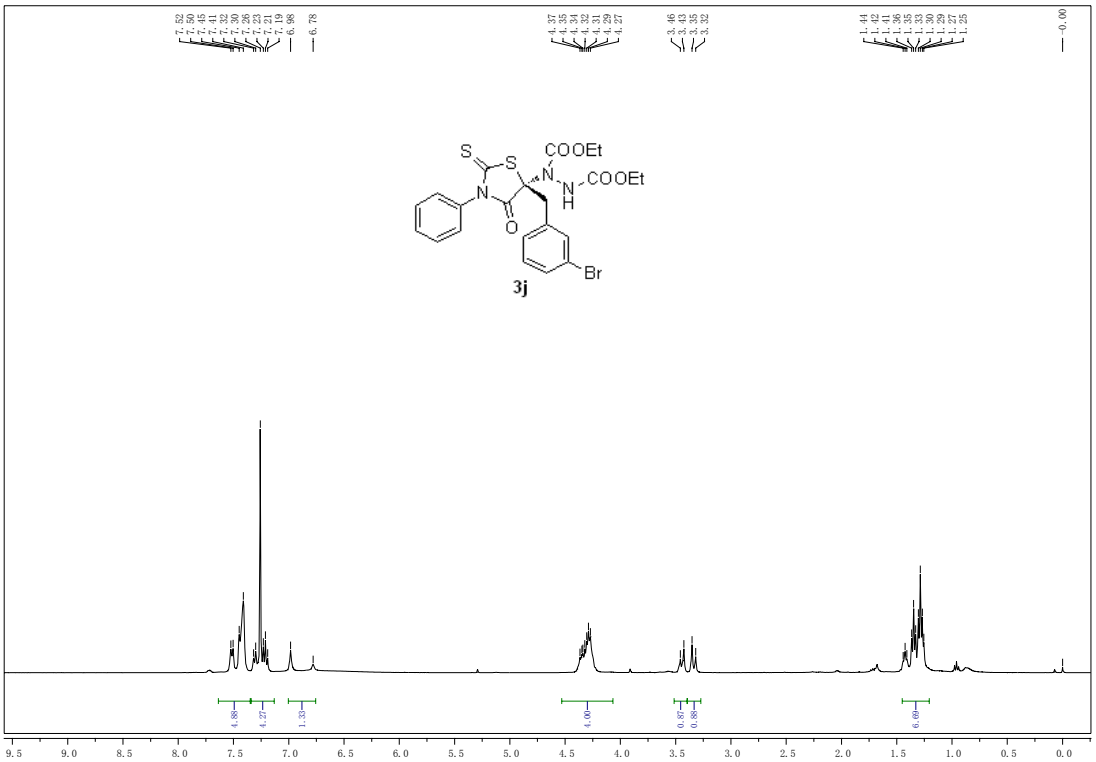
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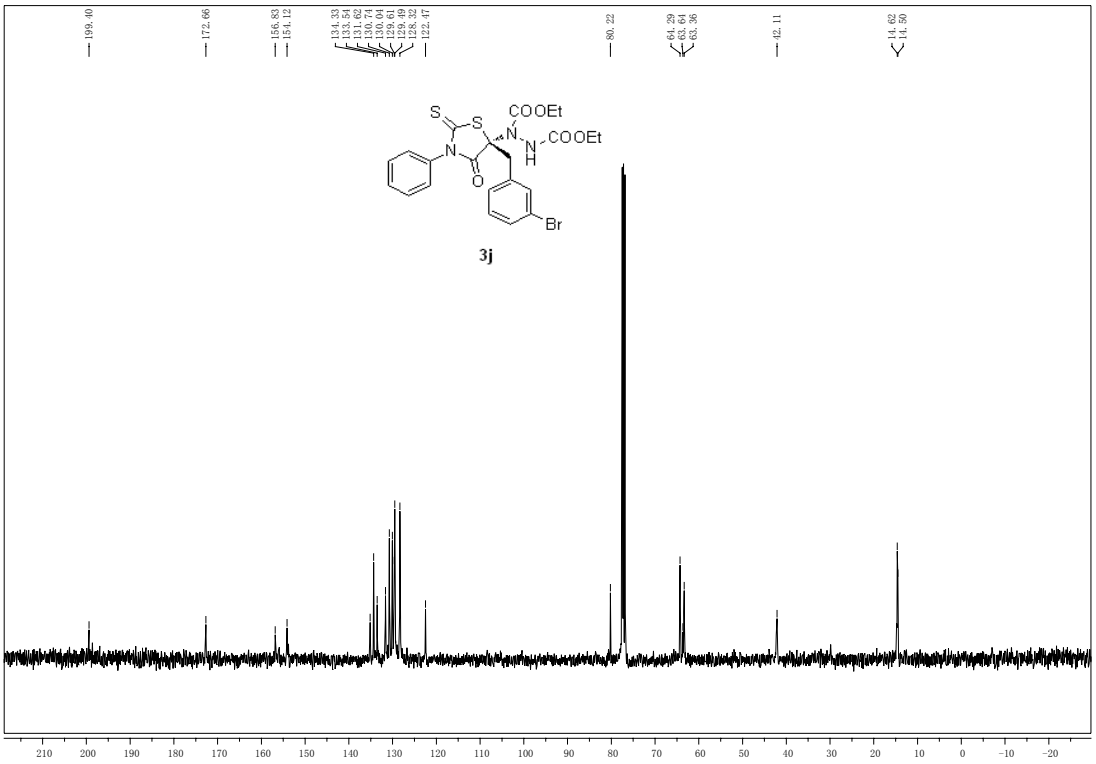
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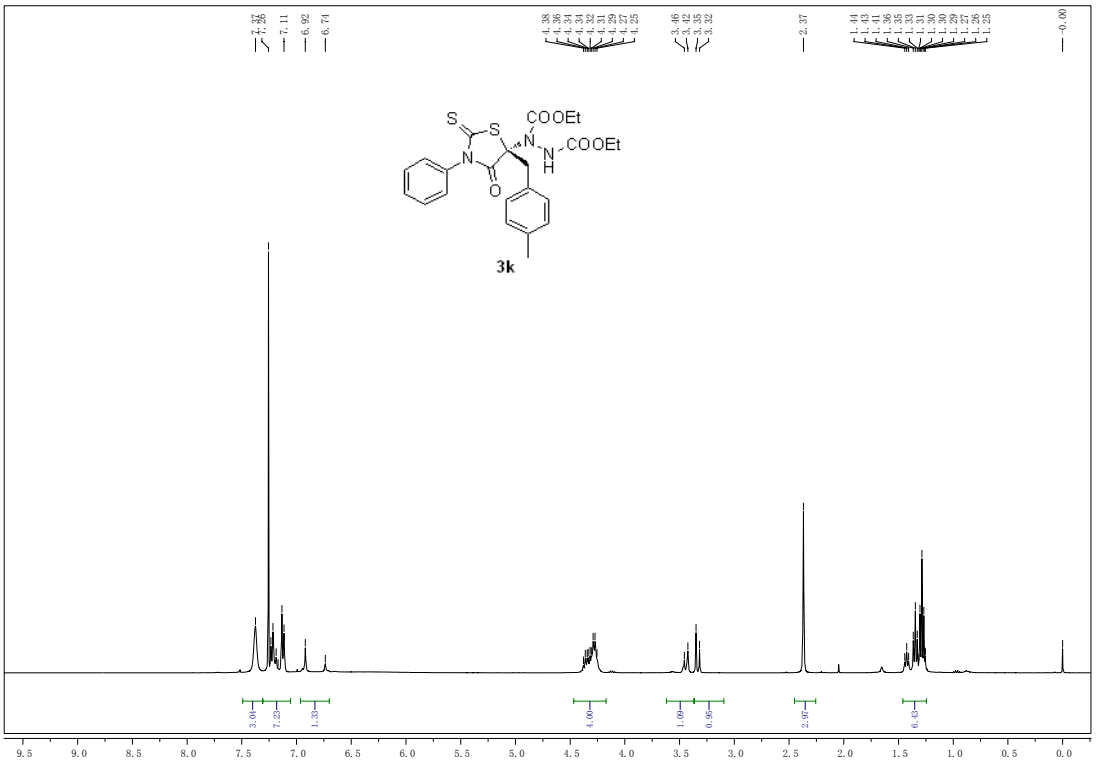
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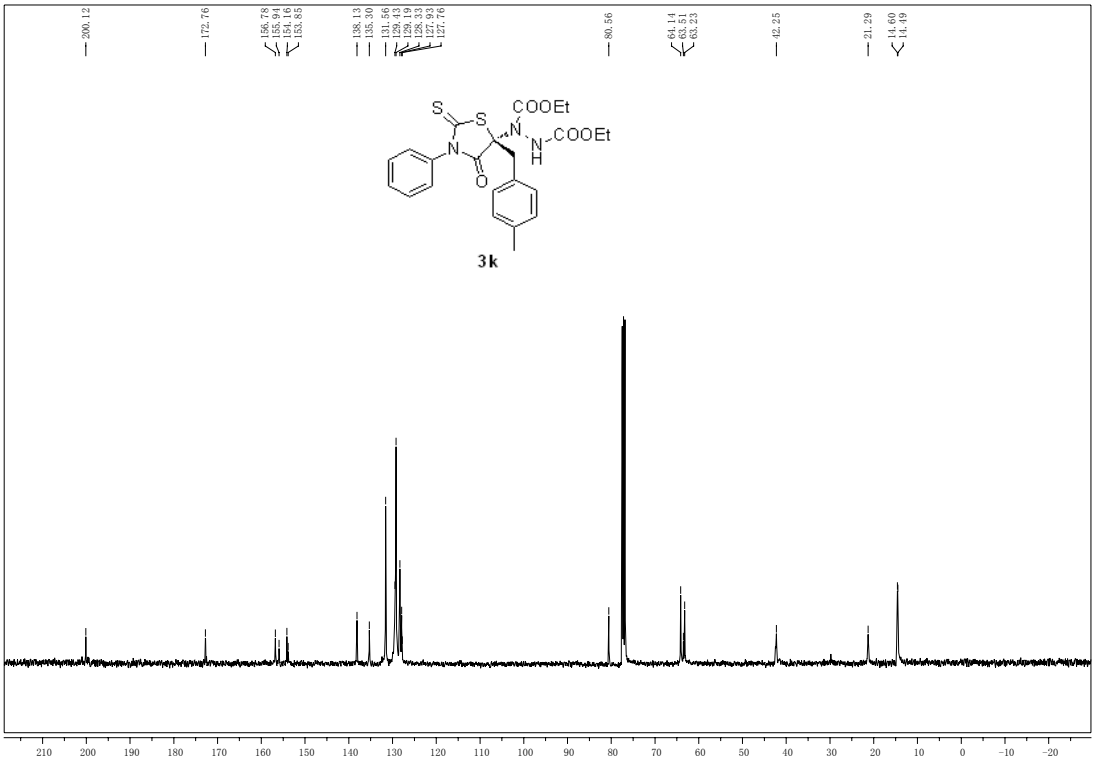
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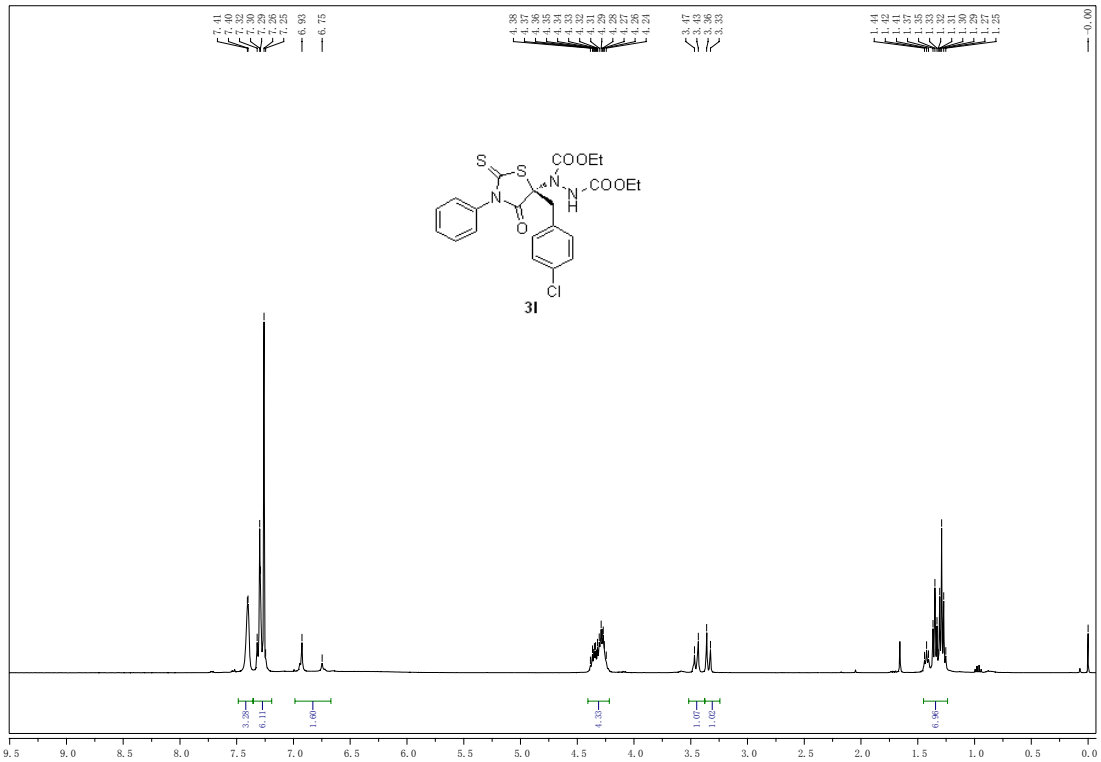
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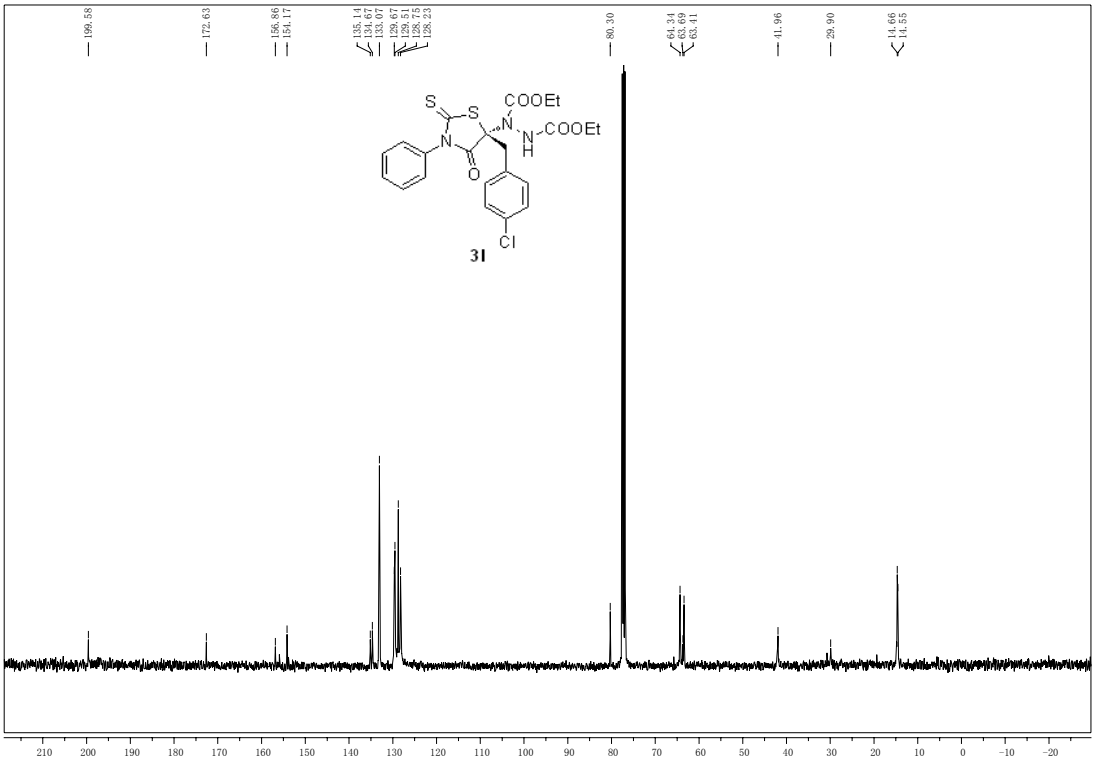
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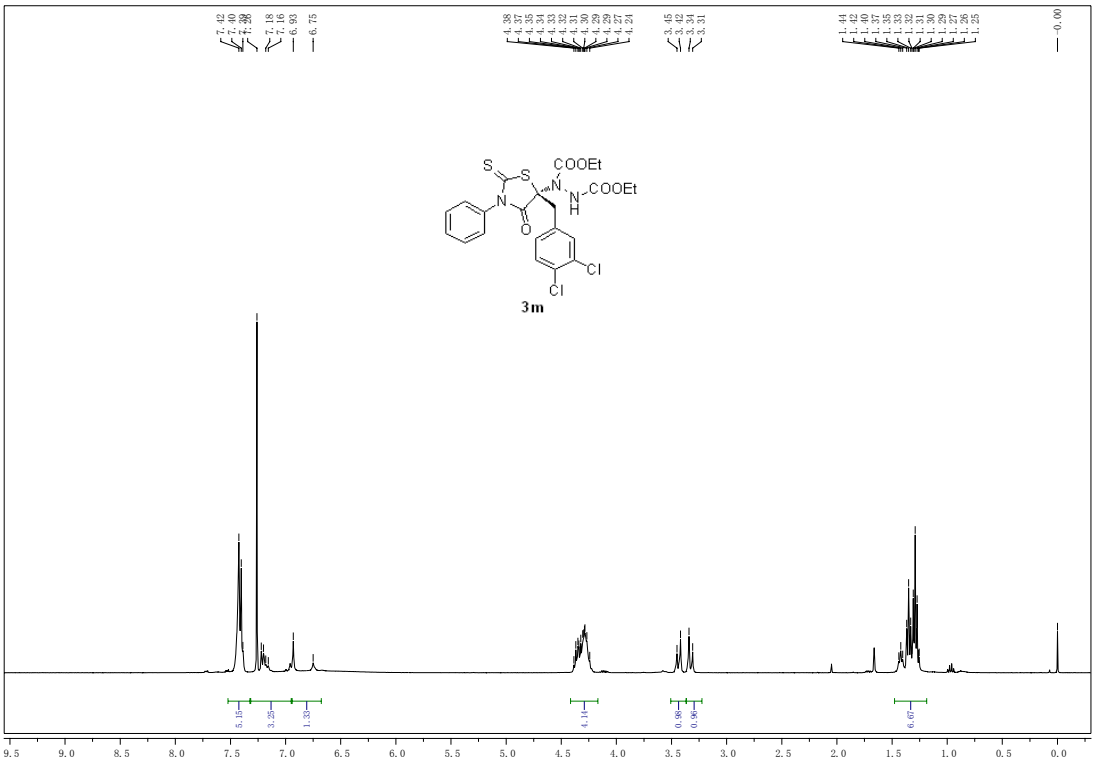
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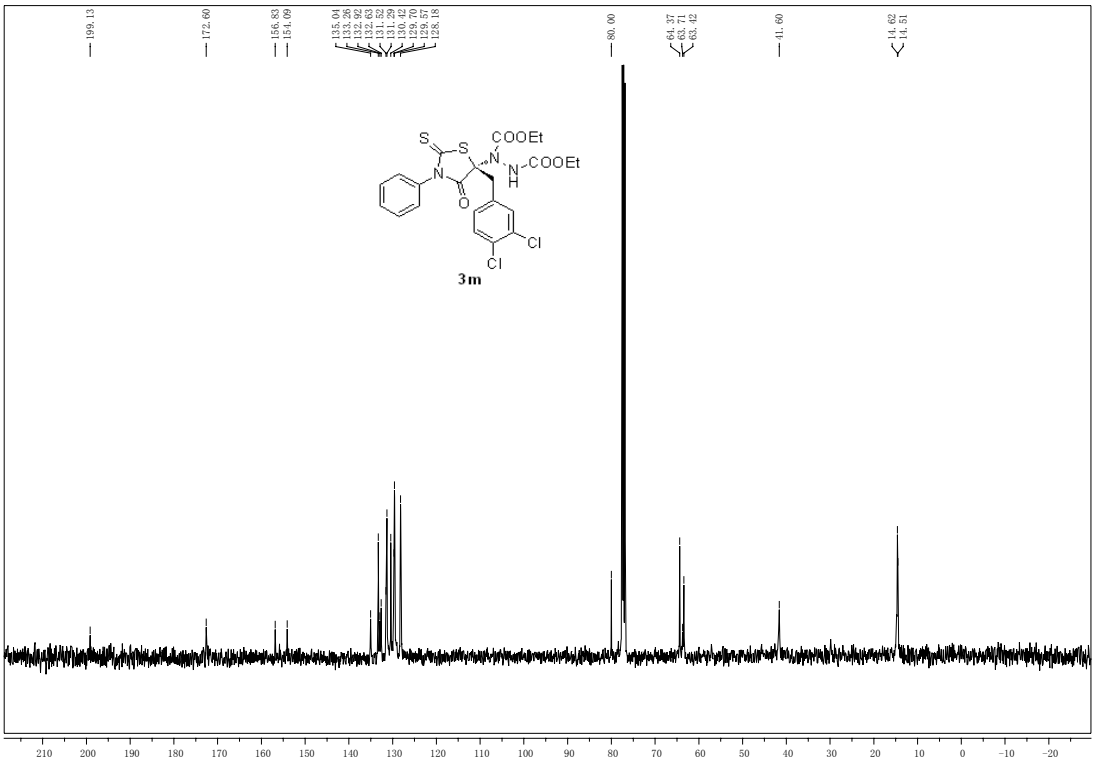
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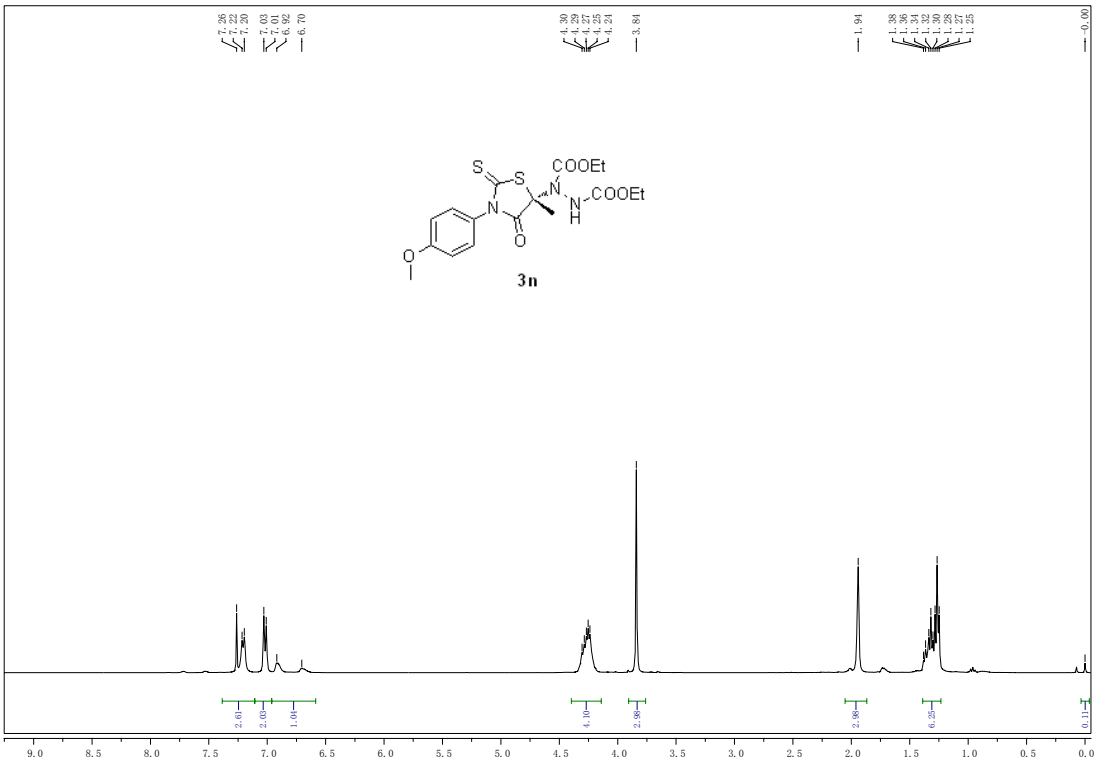
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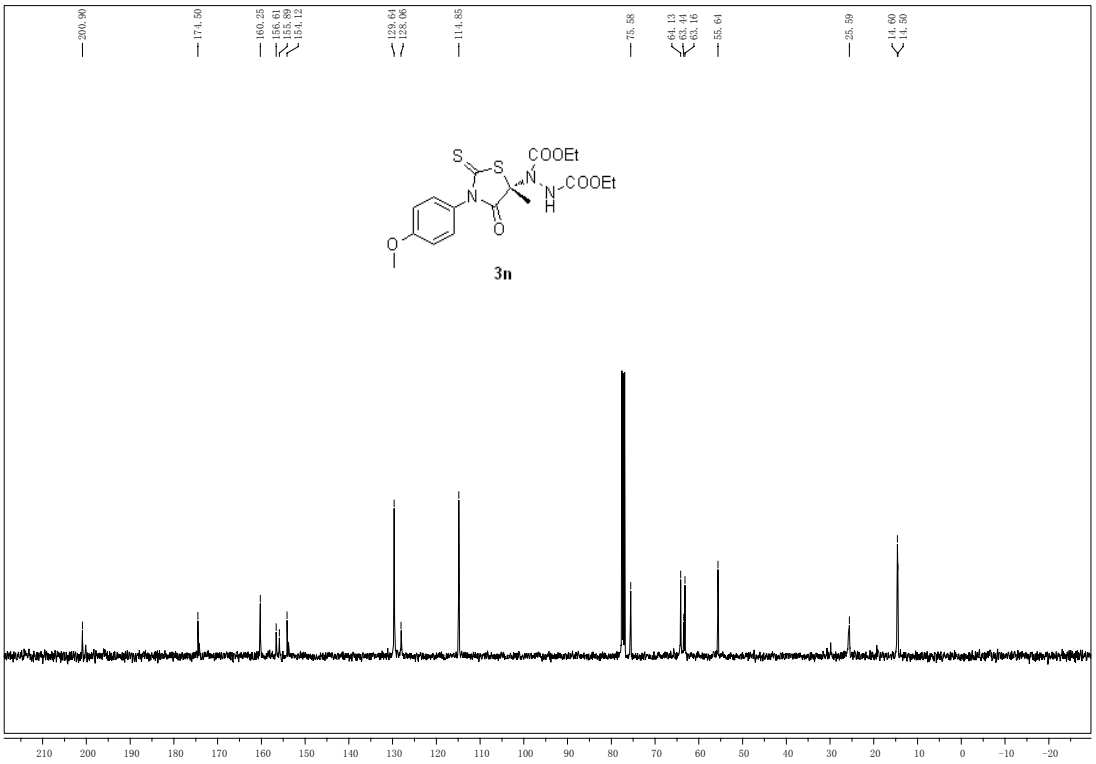
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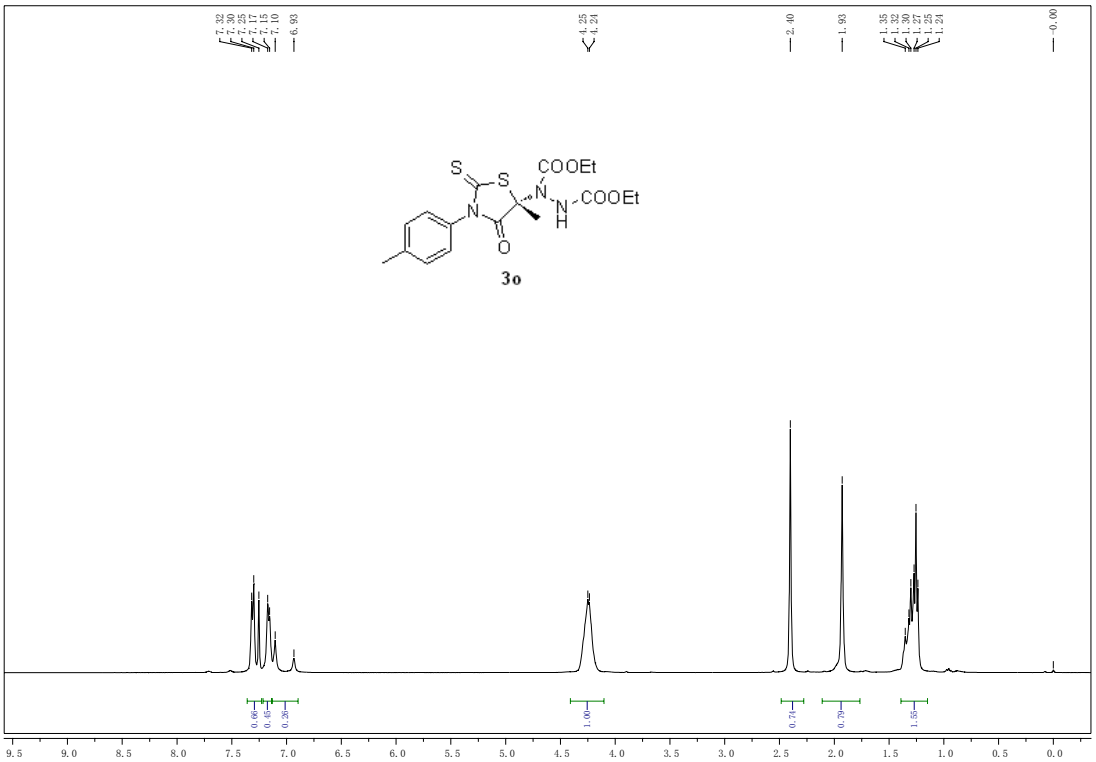
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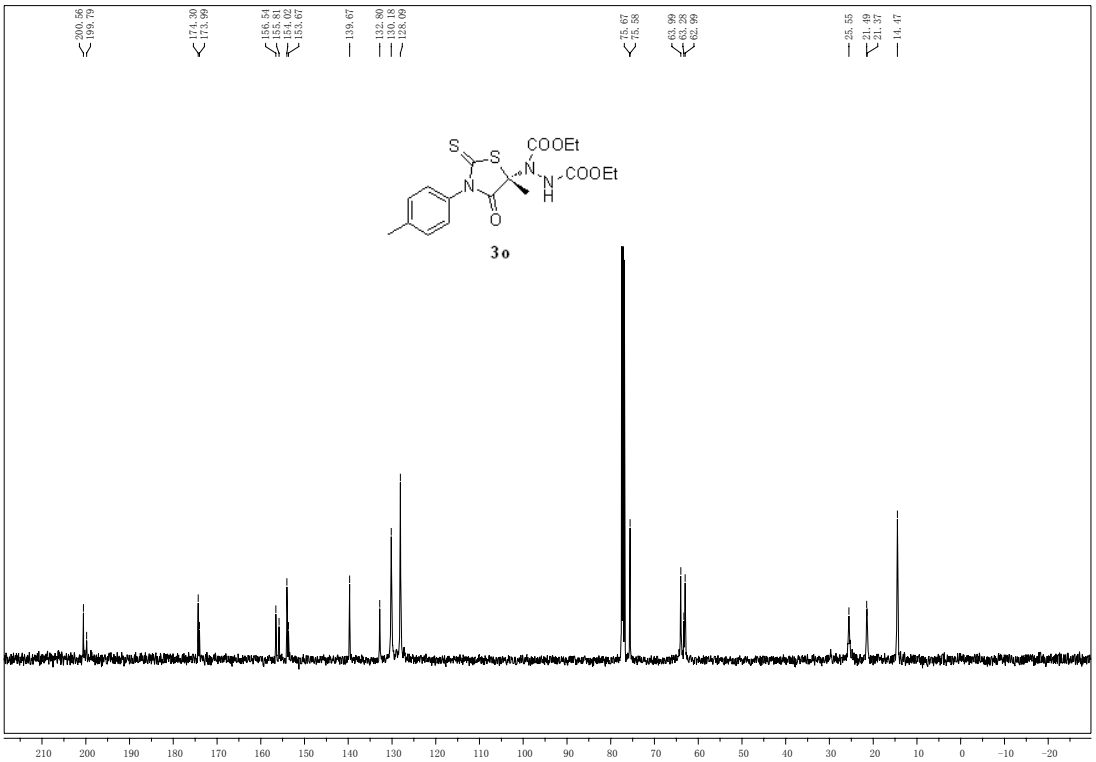
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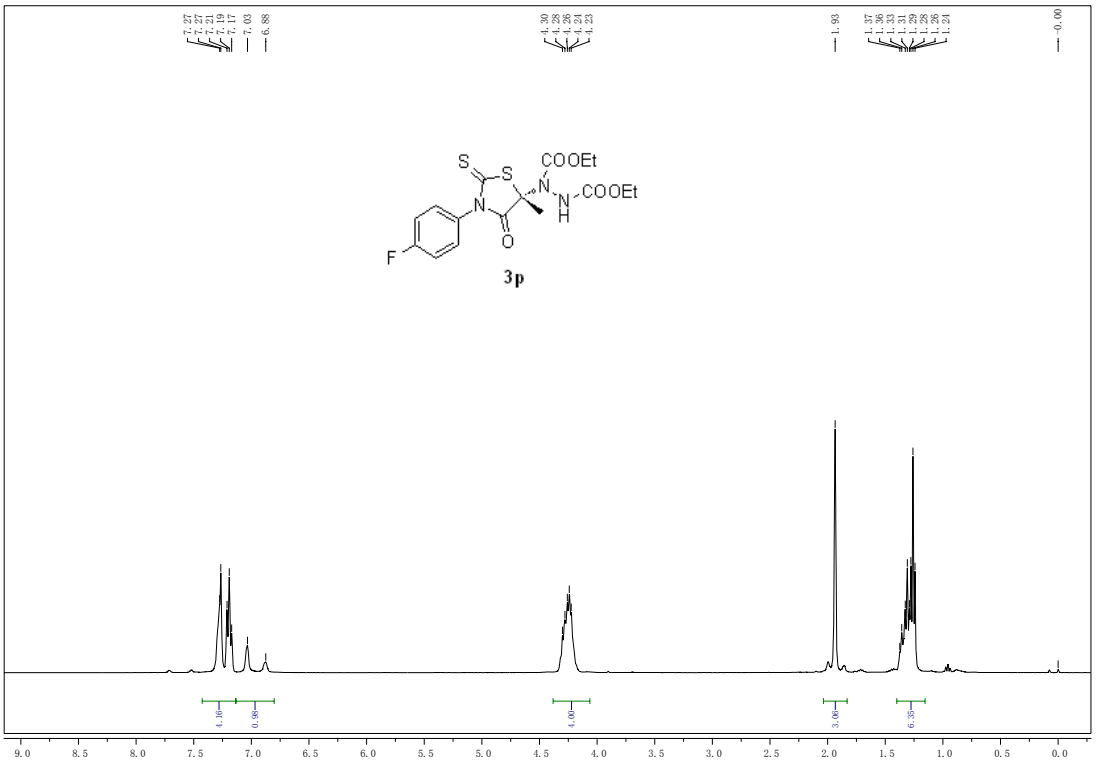
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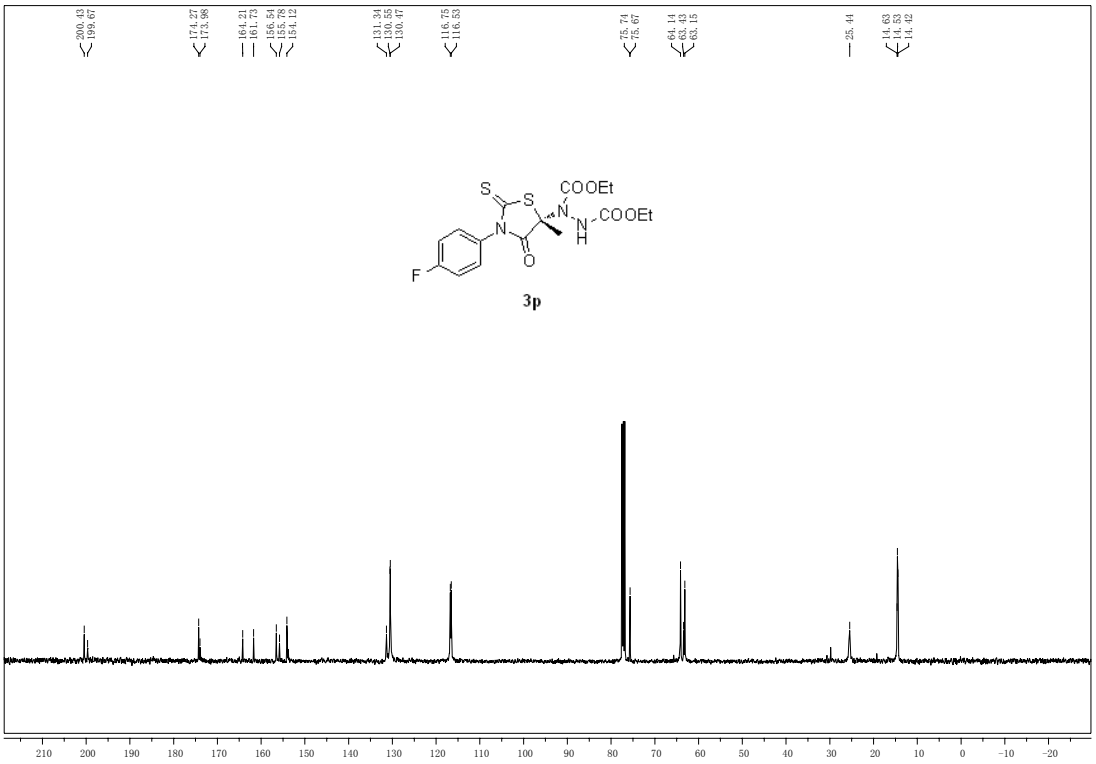
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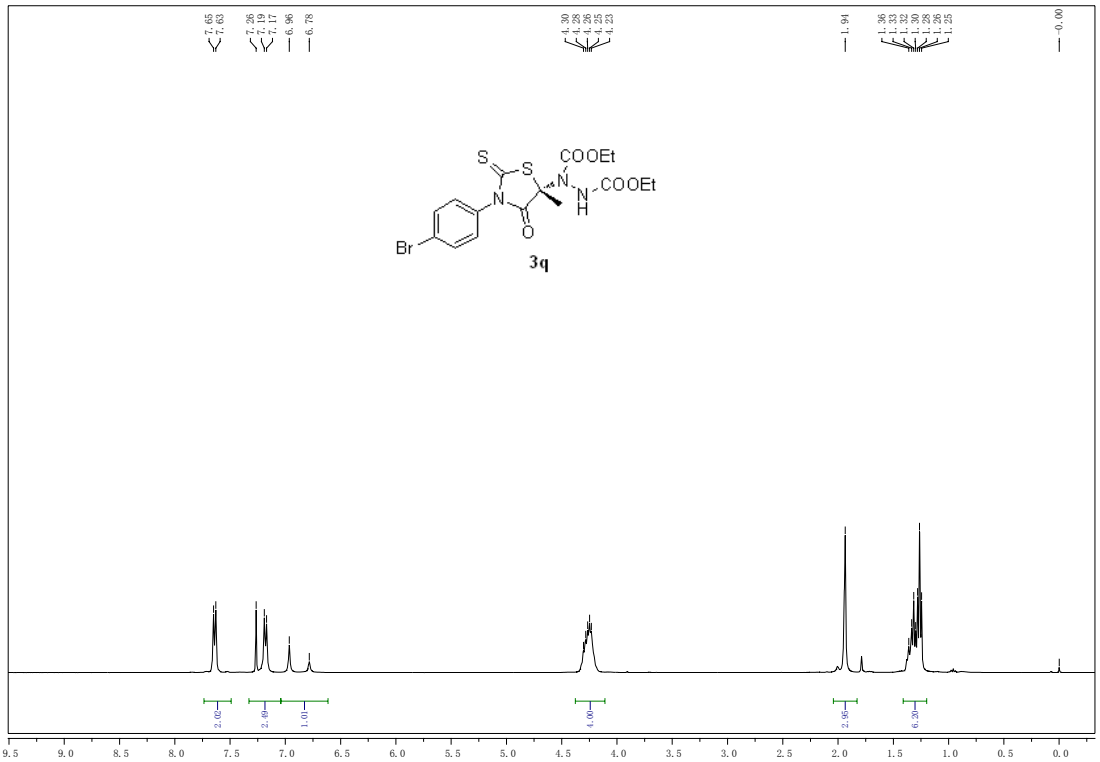
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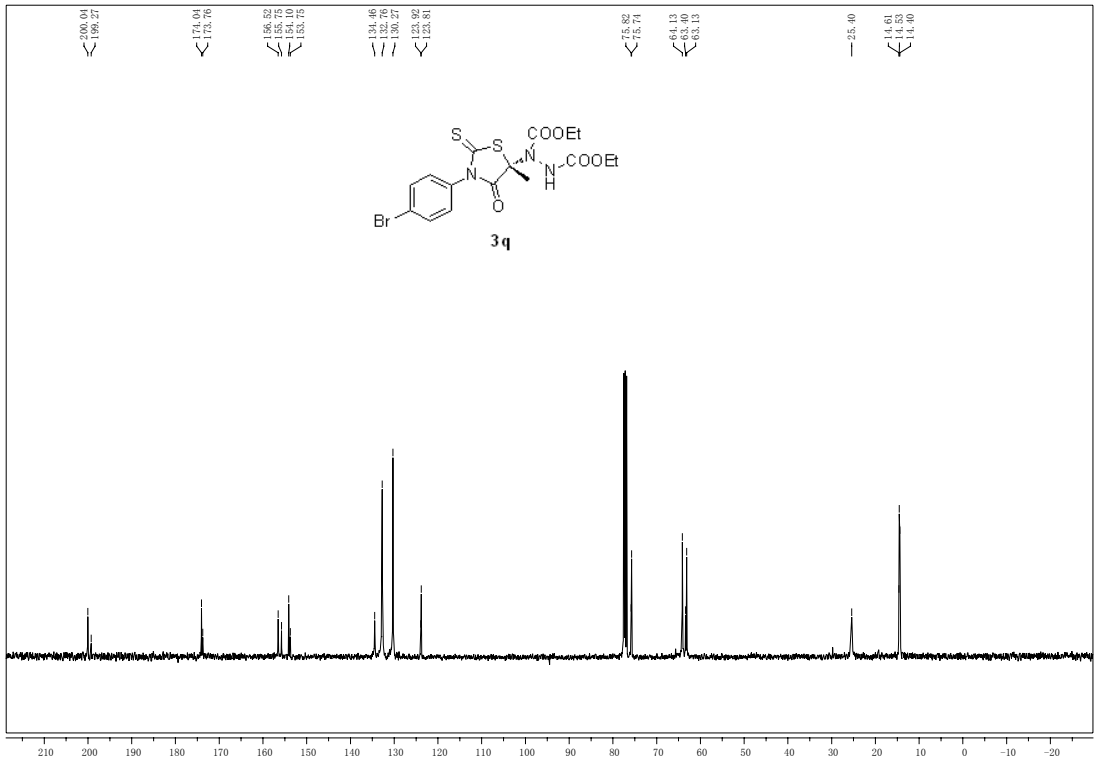
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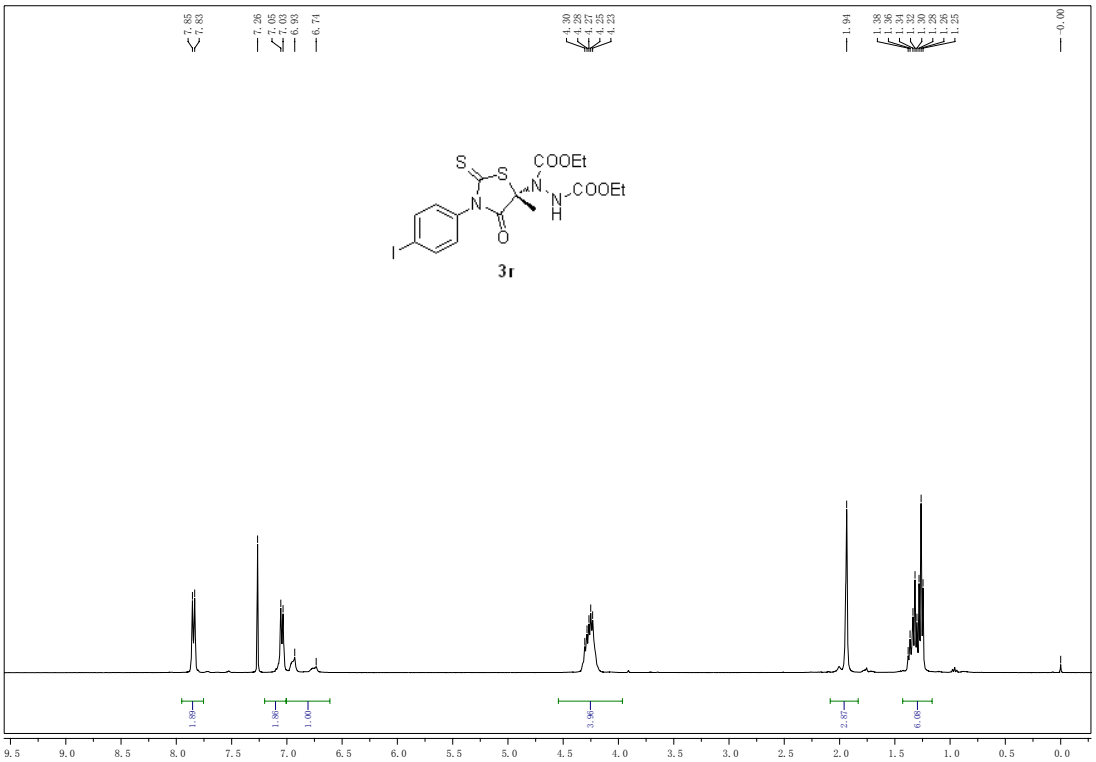
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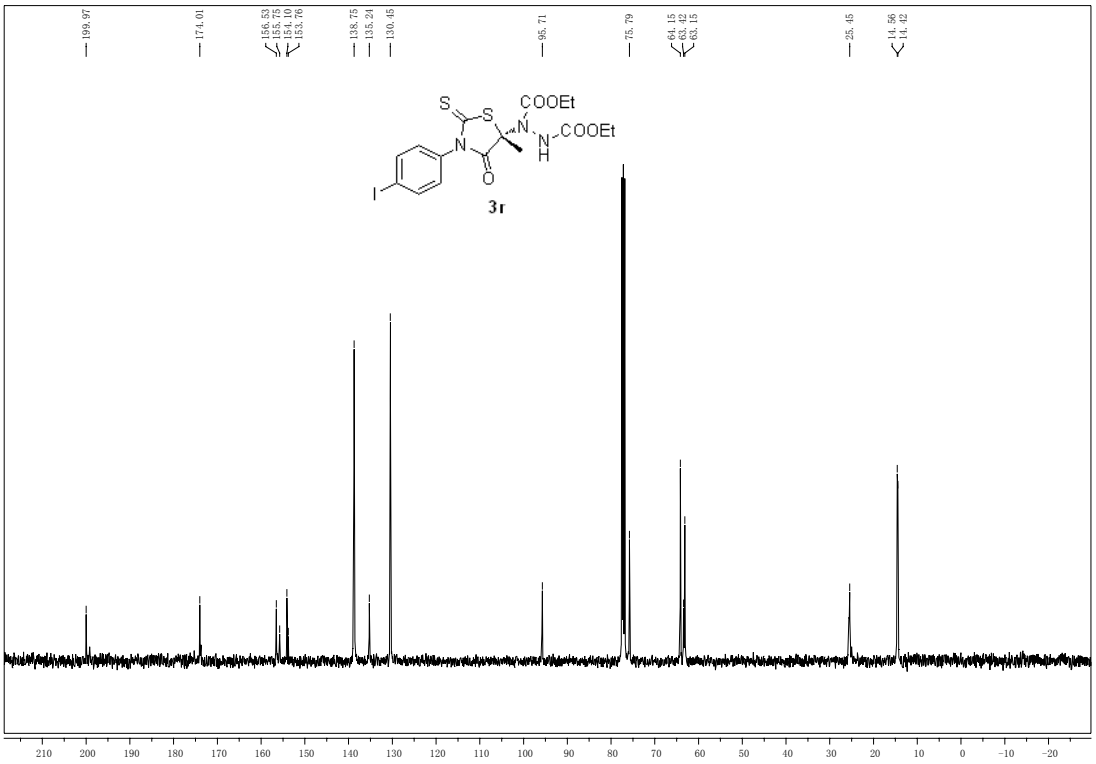
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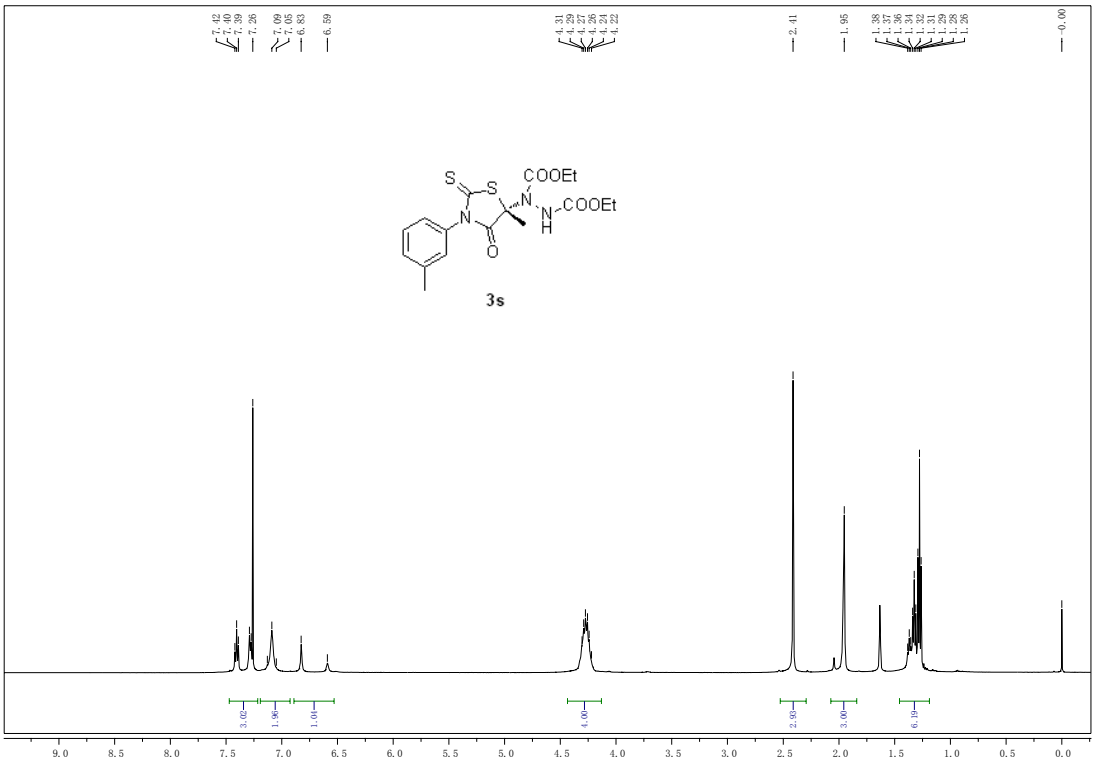
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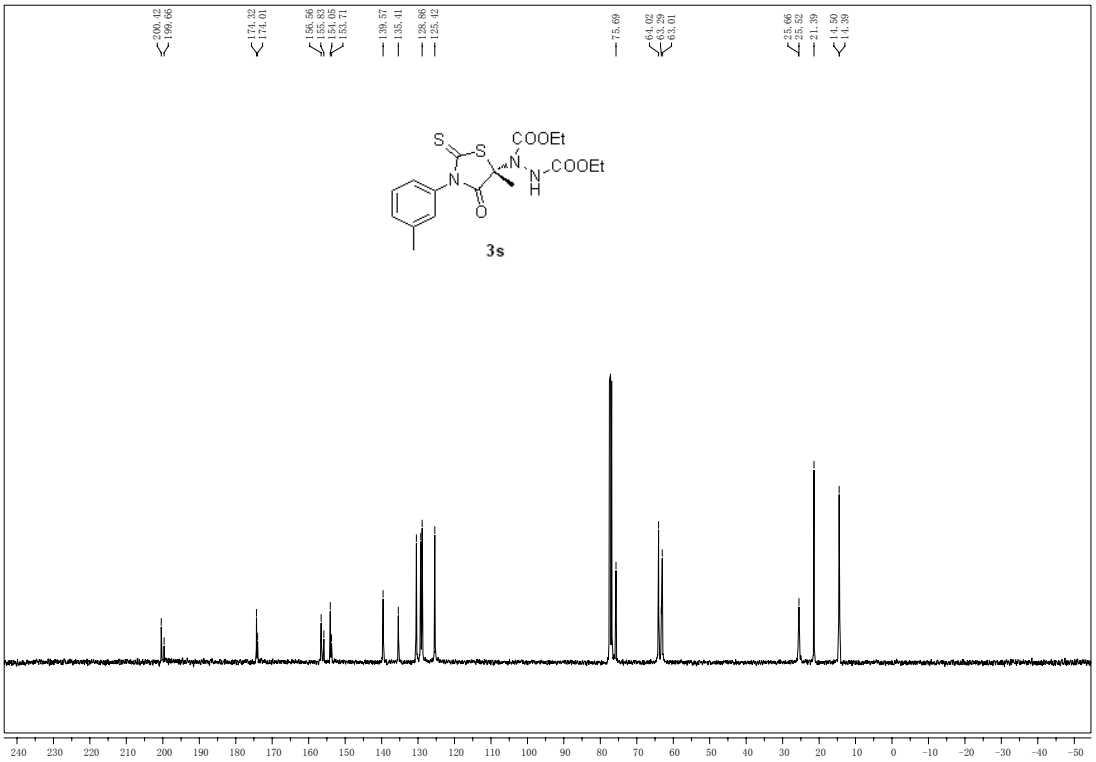
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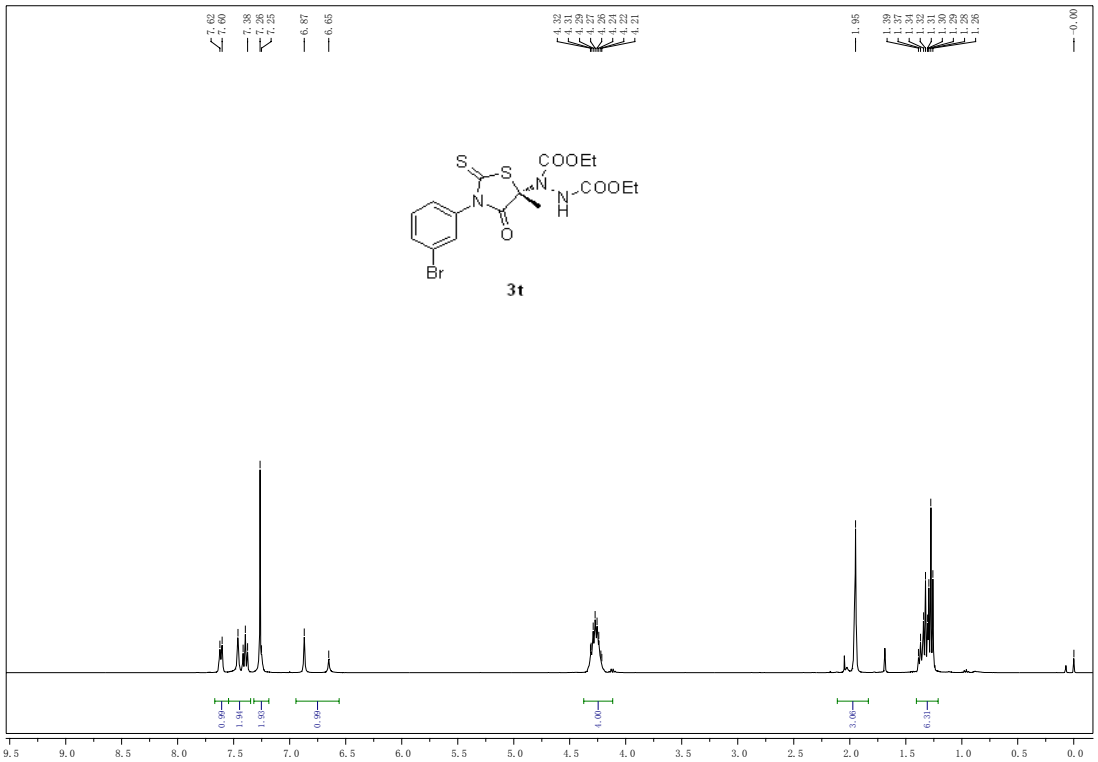
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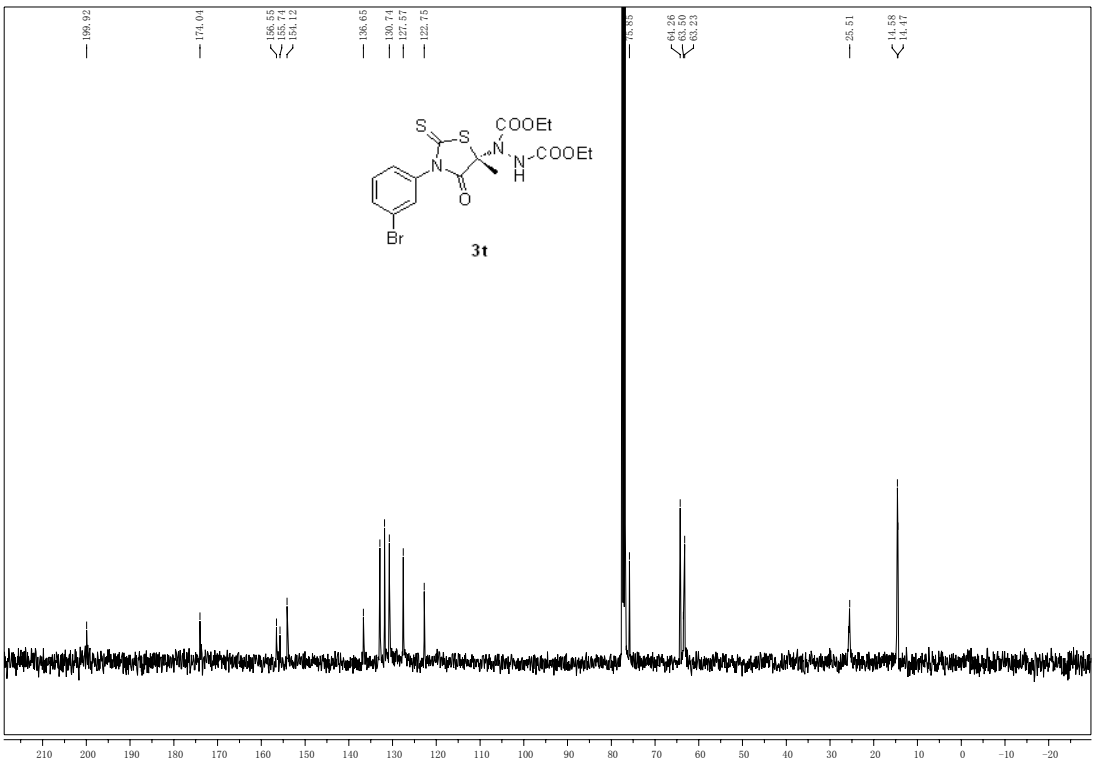
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H
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Br
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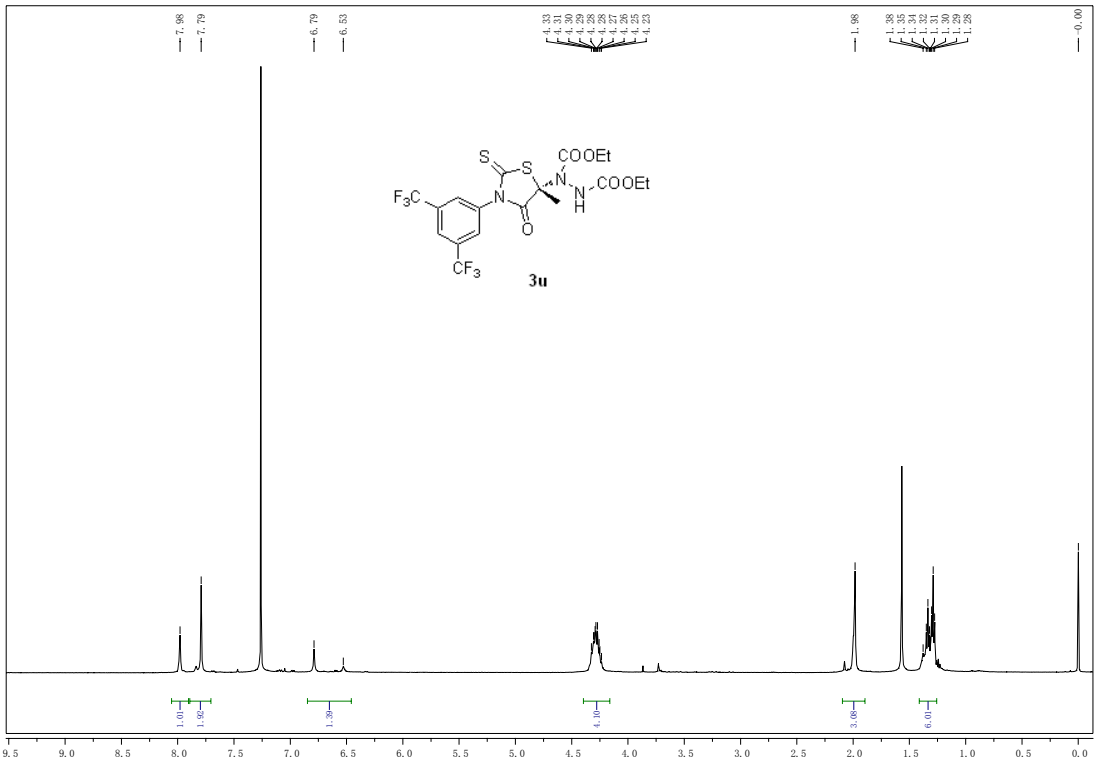
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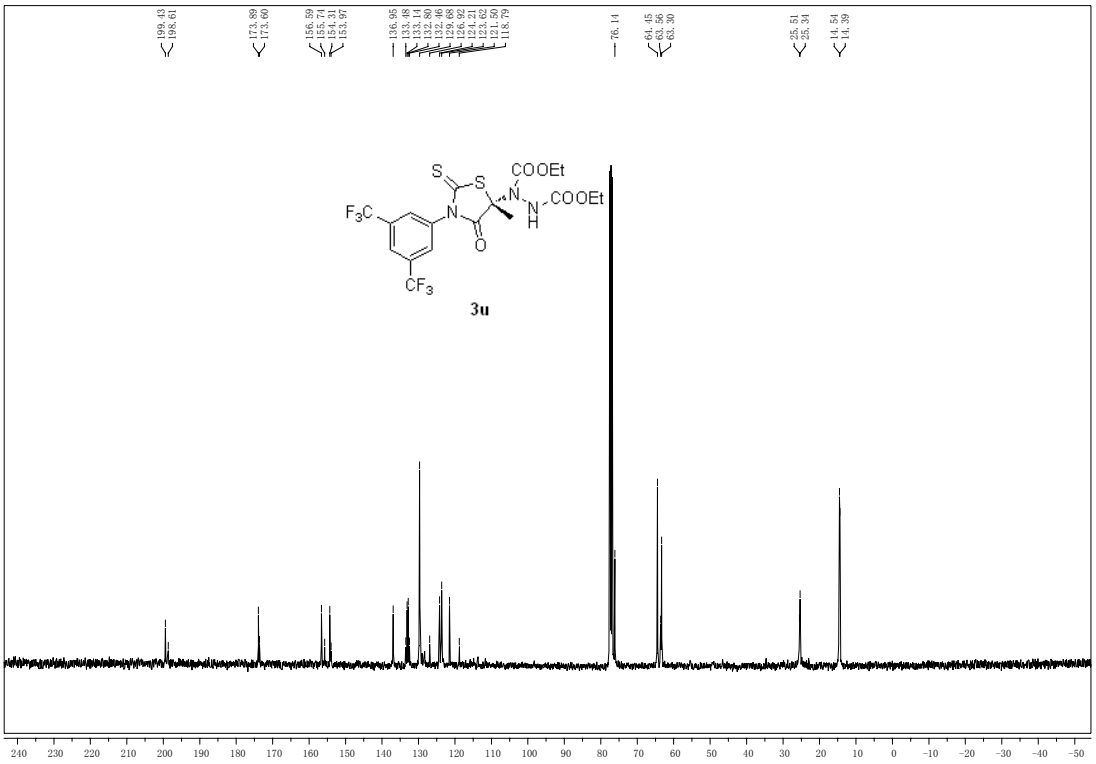
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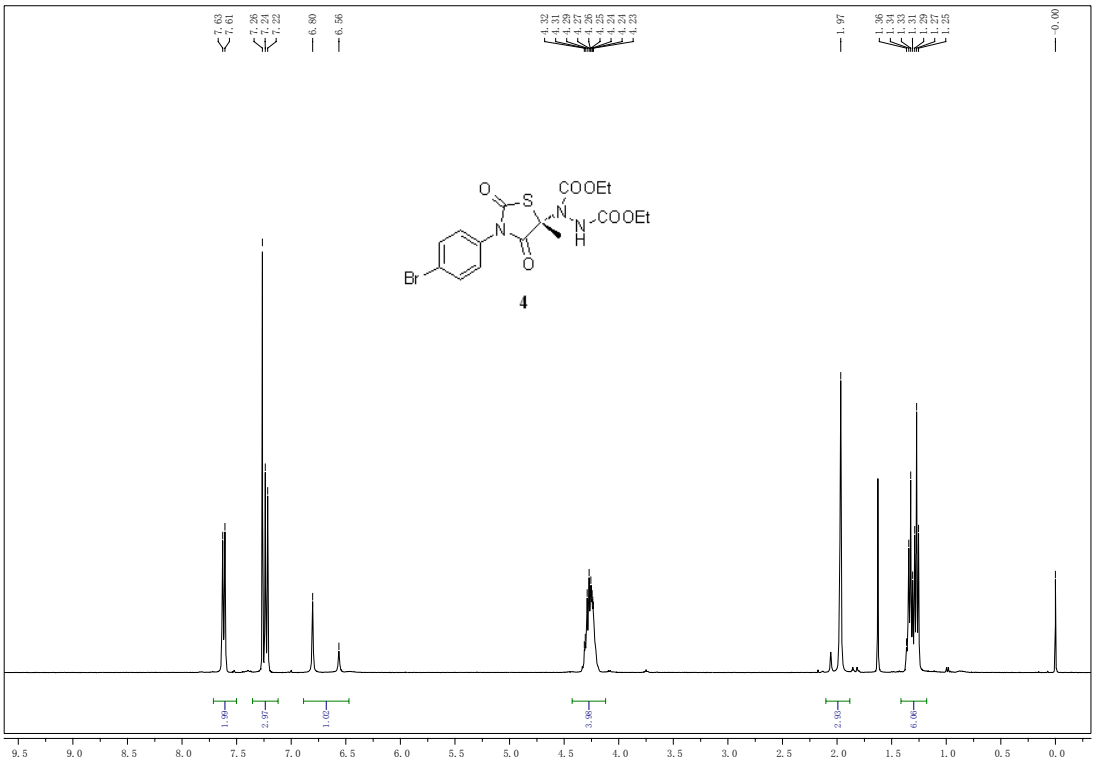
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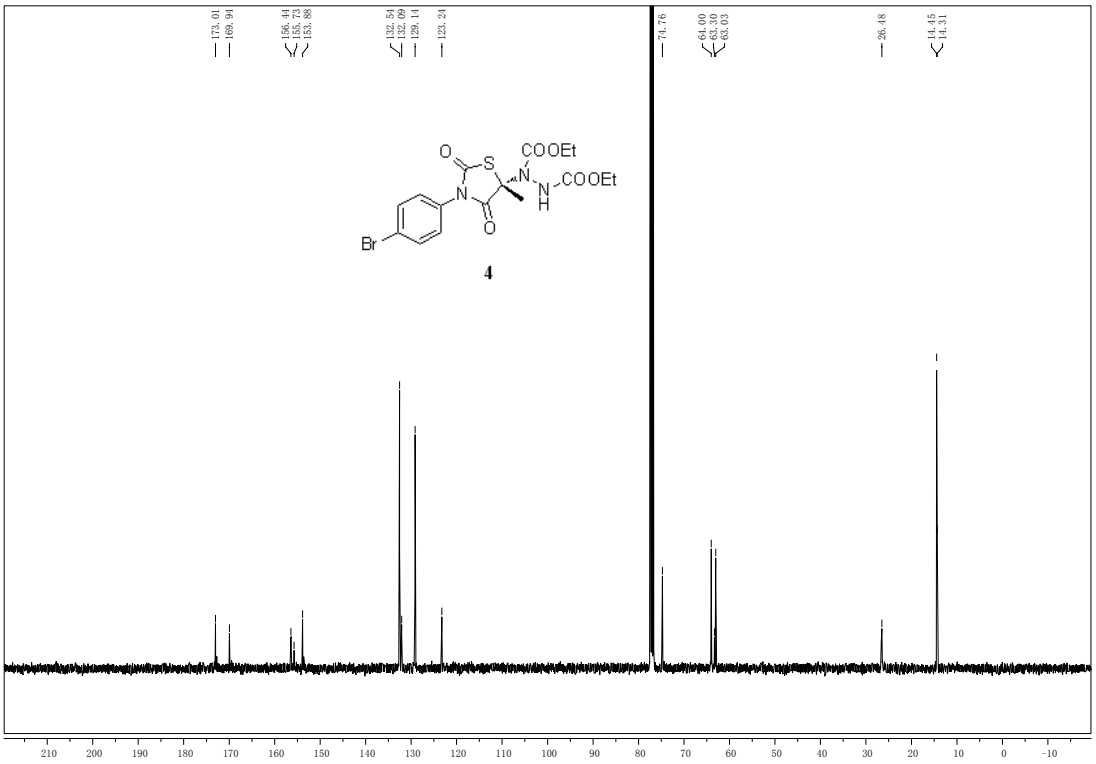
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