Supporting Information

Asymmetric synthesis of (*R*)-baclofen and (3*S*,4*S*)-tetflupyrolimet via "on water" organocatalytic addition reactions: a tip on catalysts screening

Bingfu Wang,[a,b] Jian Liu,[b] Tianxing Li,[b] Hui Jin,[b,*] and Lixin Zhang[a,b,*]

[a] School of Chemical Engineering, University of Science and Technology Liaoning, Anshan 110031, People's Republic of China

[b] Institute of Functional Molecules, Shenyang University of Chemical Technology; National-Local Joint Engineering Laboratory for Development of Boron and Magnesium Resources and Fine Chemical Technology; Liaoning Province Key Laboratory of Green Functional Molecular Design and Development, Shenyang 110142, People's Republic of China
E-mail: hjin@syuct.edu.cn, zhanglixin@syuct.edu.cn

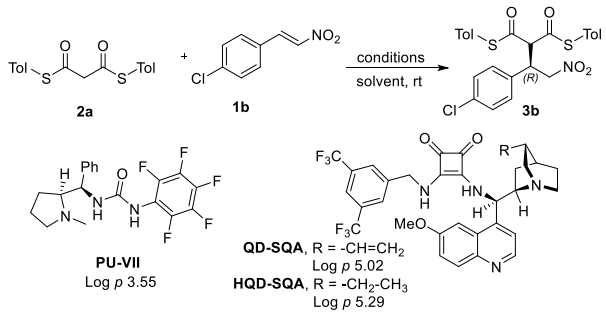
Table of contents:

1. General information S1
2. Catalyst evaluation for access to **3b** S1
3. Further optimization for access to **3b** S2
4. Optimization for access to *ent*-**3c** S3
5. Gram-scale synthesis of **3b**, **3c** and *ent*-**3c** S5
6. Synthesis of (*R*)-baclofen S5
7. Synthesis of tetflupyrolimet S6
8. Addition reactions between diverse dithiomalonates and nitroolefins catalyzed by **QD-SQA** or **QN-SQA** S7
9. Catalyst evaluation in the Michael addition of dimethyl malonate to nitrostyrene S16
10. References S17
11. Copies of ^{1}**H** and ^{13}**C NMR** spectra S18
12. Copies of **HPLC** chromatograms S41

1. General information

Unless stated otherwise, reagents were used directly as obtained commercially. Reactions were monitored by TLC using silica gel GF254 plates. Flash column chromatography was performed using silica gel. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker AV III 400 MHz NMR spectrometers. Chemical shifts are reported in ppm using tetramethylsilane or the residual solvent peak as a reference. Analytical high performance liquid chromatography (HPLC) was performed on Elite EClassical 3100 HPLC system using the indicated chiral column (4.6 mm×25 cm). Specific rotations were measured by WZZ/2S automatic polarimeter at 589 nm. Melting points were determined using WRS-2 microcomputer melting point instrument. The compounds used in the experiment were weighed with Mettler Toledo Electronic balance XSR205DU/AC. Infrared spectra were recorded on a Nicolet iS50 FT-IR. HRMS were recorded on a Waters Xevo G2-XS TOF mass spectrometer. The organocatalysts (**PU-VII**,[1,2] **QN-SQA**,[3] **HQN-SQA**,[3] **QD-SQA**,[3] and **HQD-SQA**[3]), dithiomalonates[1,2] and nitroolefins examined in this study were obtained according to the published procedures.

2. Catalyst evaluation for access to 3b[a]



General Procedure A

To a 3 mL dried vial equipped with a Teflon-coated magnetic stirring bar, *p*-chloronitroolefin **1b** (44 mg, 0.24 mmol, 1.5 equiv.) and solvent (1.5 mL) were added. The catalyst (5 mol %) and *S*,*S'*-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol, 1.0 equiv.) were added to the reaction mixture successively. The reaction mixture was vigorously stirred at room temperature for 1.5 hours. Upon completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure and the resulting residue was purified via column chromatography on silica gel to yield white solid products **3b**. The ee values of **3b** was determined by chiral HPLC (with COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm).

The yields and ee values of **3b** are shown in **Table S1**. And plotting % ee of **3b** vs different reaction conditions graph using Microsoft Excel are shown in **Figure S1**.

Table S1. Catalyst evaluation for access to the key intermediate **3b**.

entry	cat.	condition	cat. (mol %)	**3b** yield (%)[b]	**3b** ee (%)[c]
1	**PU-VII**	toluene	5	95	87
2	**PU-VII**	H_2O	5	80	73
3	**PU-VII**	brine	5	90	83
4[d]	**PU-VII**	brine/toluene	5	95	86
5[d]	**PU-VII**	brine/toluene	0.5	93	87
6	**QD-SQA**	toluene	5	90	92
7	**QD-SQA**	H_2O	5	85	72
8	**QD-SQA**	brine	5	91	72

9[d]	**QD-SQA**	brine/toluene	5	95	92
10[d]	**QD-SQA**	brine/toluene	0.5	96	97
11	**HQD-SQA**	toluene	5	91	86
12	**HQD-SQA**	H_2O	5	81	80
13	**HQD-SQA**	brine	5	90	91
14[d]	**HQD-SQA**	brine/toluene	5	89	88
15[d]	**HQD-SQA**	brine/toluene	0.5	93	92

[a]Unless otherwise noted, all reactions were conducted using **2a** (0.16 mmol, 1 equiv.), **1b** (0.24 mmol, 1.5 equiv.), and cat. (0.5~5 mol %) in different solvents. [b]Isolated yield. [c]ee was determined using HPLC. [d]10 equiv. of toluene was added.

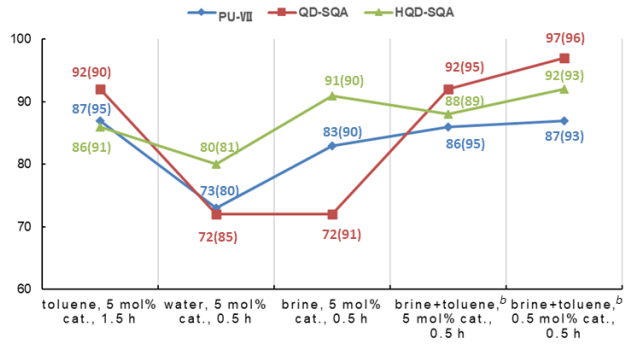
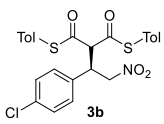


Figure S1. Catalysts evaluation for access to the key intermediate **3b**.

(*R*)-2-(1-(4-chlorophenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3b)**



Following the general procedure with **QD-SQA** (0.50 mg, 0.5 mol %) and toluene (10 equiv.) in 1.5 mL brine, **3b** was obtained as a white solid (76 mg, 96% yield, 97% ee).

R_f =0.40 (petroleum ether/ethyl acetate (*v*/*v*), 10/1).

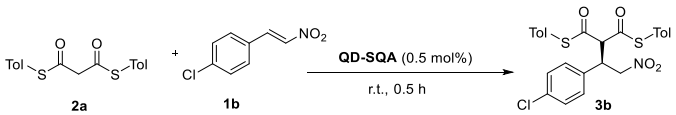
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dt, *J* = 24.3, 8.2 Hz, 6H), 7.22-7.16 (m, 4H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.80 (d, *J* = 6.5 Hz, 2H), 4.44-4.33 (m, 2H), 2.39 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 190.0, 140.8, 140.7, 134.6, 134.2, 134.2, 133.9, 130.4, 130.3, 129.8, 129.3, 122.5, 122.4, 76.9, 68.9, 43.7, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 15.55 min (minor), t_R= 13.71 min (major).

[α]$^{20}_D$ = -101.4(c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -92.2 (c = 1.0, $CHCl_3$; 87% ee)].

3. Further optimization for access to 3b



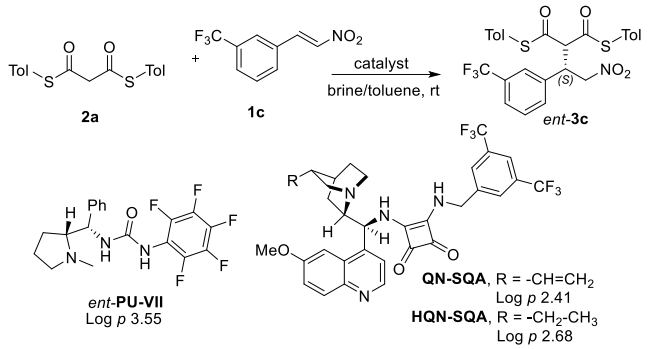
Following the general procedure A (page S1), a comprehensive optimization study for the "on water" addition reaction of **2a** with **1b** was conducted to investigate the reaction media and catalyst loading of **QD-SQA**. The data of yields and ee values are shown in **Table S2**.

Table S2. Further optimization for the enantioselective access to the key intermediate **3b**.[a]

entry	additive	cat. (mol%)	yield (%)[b]	ee (%)[c]
1	toluene	0.5	96	97
2[d]	toluene	0.5	95	93
3[d]	toluene	0.25	93	95
4	PhCl	0.5	94	93
5	xylene	0.5	93	92
6	mesitylene	0.5	90	91
7[e]	toluene	0.1	92	89
8[e]	toluene	0.2	95	94
9[e]	toluene	2	95	92
10[e]	toluene	5	95	92

[a]These reactions were conducted using **2a** (0.16 mmol, 1 equiv.), **1b** (0.24 mmol, 1.5 equiv.), cat. (0.5 mol %), and toluene (10 equiv.) in 1.5 mL of brine. [b]Isolated yield. [c]ee was determined using HPLC. [d]5 equiv. of toluene was added. [e]These reactions were conducted using **2a** (0.16 mmol, 1 equiv.), **1b** (0.24 mmol, 1.5 equiv.), cat. (0.1-5 mol %), and toluene (10 equiv.) in 1.5 mL of brine.

4. Optimization for access to *ent*-3c



General Procedure B

To a 3 mL dried vial equipped with a Teflon-coated magnetic stirring bar, *m*-trifluoromethyl nitroolefin **1c** (52 mg, 0.24 mmol) and brine (1.5 mL)/toluene (10 equiv.) were added. The catalyst (0.2-2 mol %) and *S,S'*-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol, 1.0 equiv.) were added to the reaction mixture successively. The reaction mixture was vigorously stirred at room temperature for 30-50 min. Upon completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure and the resulting residue was purified via column chromatography on silica gel to yield white solid products *ent*-**3c**. The ee values of *ent*-**3c** was determined by chiral HPLC (with COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm).

The data of yields and ee values are shown in **Table S3**.

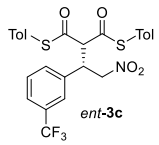
Table S3. Optimization for access to the key intermediate *ent*-**3c**.[a]

entry	cat.	cat (mol%)	time (min)	yield (%)[b]	ee (%)[c]
1	*ent*-**PU-VII**	0.5	30	94	82
2	**QN-SQA**	0.5	30	96	97
3	**HQN-SQA**	0.5	50	92	84

4	**QN-SQA**	0.2	50	90	66
5	**QN-SQA**	2	30	94	95
6[d]	**QD-SQA**	0.5	30	95	96

[a]These reactions were conducted using **2a** (0.16 mmol, 1 equiv.), **1c** (0.24 mmol, 1.5 equiv.), cat. (0.2-2 mol %), and toluene (10 equiv.) in 1.5 mL of brine. [b]Isolated yield. [c]ee was determined using HPLC. [d](*R*)-**3c** was obtained as the major product.

(*S*)-2-(1-(3-(trifluoromethyl-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(*ent*-3c)**



ent-**3c**

Following the general procedure with **QN-SQA** (0.5 mol %) and toluene (10 equiv.) in 1.5 mL brine, the reaction was completed in 30 min at r.t., *ent*-**3c** was obtained as a white solid (80.8 mg, 96% yield, 97% ee).

New Compound, $\mathbf{R_f}$ =0.35 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

mp: 137-140 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.59 (m, 1H), 7.54-7.46 (m, 3H), 7.31-7.28 (m, 2H), 7.28-7.25 (m, 2H), 7.19-7.16 (m, 2H), 7.05-7.01 (m, 2H), 4.87 (dd, *J* = 4.0, 2.4 Hz, 2H), 4.49-4.45 (m, 1H), 4.45-4.42 (m, 1H), 2.40 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 190.0, 140.9, 140.7, 136.7, 134.2, 134.1, 131.6, 131.3, 130.8 (q, *J* = 223.3 Hz), 130.4, 130.3 125.5 (q, *J* = 3.6 Hz), 125.2 (q, *J* = 3.9 Hz), 122.4 (q, *J* = 3.9 Hz), 76.6, 68.6, 44.0, 21.4, 21.4 ppm.

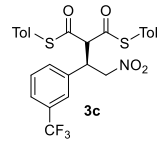
IR (KBr) 2924, 1912, 1698, 1617, 1549, 1492, 1453, 1399, 1335, 1317, 1261, 1167, 1075, 980, 810, 706 cm^{-1}.

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{22}F_3NO_4S_2Na$ 556.0845, found 556.0840.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 15.49 min (minor), t_R= 19.97 min (major).

[α]$^{20}_D$ = +64.8 (c = 1.0, $CHCl_3$).

(*R*)-2-(1-(3-(trifluoromethyl-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(3c)**



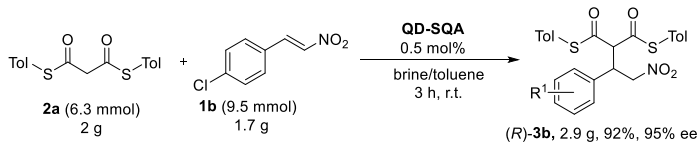
3c

Following the general procedure with **QD-SQA** (0.5 mol %) and toluene (10 equiv.) in 1.5 mL brine, the reaction was completed in 30 min at r.t., **3c** was obtained as a white solid (80 mg, 95% yield, 96% ee). Analytical data are consistent with that of *ent*-**3c.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 18.86 min (minor), t_R= 14.77 min (major). **[α]$^{20}_D$** = -64.5 (c = 1.0, $CHCl_3$).

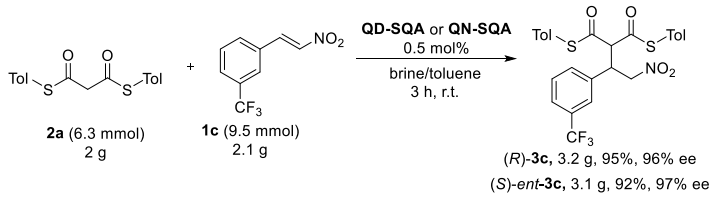
5. Gram-scale synthesis of 3b, 3c and *ent*-3c

5.1 Gram-scale synthesis of 3b



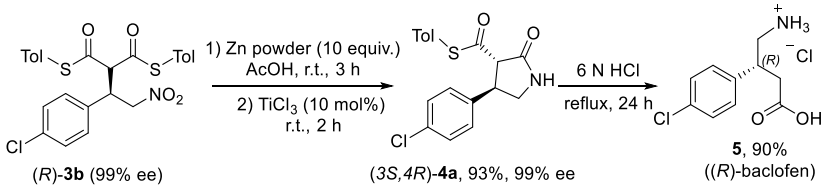
To a stirred solution of catalyst **QD-SQA** (0.5 mol %) and *β*-nitroolefin **1b** (1.7 g, 9.5 mmol, 1.5 equiv.) in brine (20 mL) and toluene (10 equiv.), *S,S'*-bis (4-methylphenyl) dithiomalonate **2a** (2 g, 6.3 mmol, 1.0 equiv.) was added. The reaction mixture was vigorously stirred for 3 h at r.t.. After the reaction was completed (monitored by TLC), the reaction mixture was extract with CH_2Cl_2 (20 mL×3) and washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified through column chromatography on silica gel to provide the desired products **3b** as a white solid (2.9 g, 92% yield, 95% ee). Analytical data are consistent with above values.

5.2 Gram-scale synthesis of 3c and *ent*-3c



To a stirred solution of catalyst **QD-SQA** or **QN-SQA** (0.5 mol %) and *β*-nitroolefin **1c** (2.1 g, 9.5 mmol, 1.5 equiv.) in brine (20 mL) and toluene (10 equiv.), *S,S'*-bis (4-methylphenyl) dithiomalonate **2a** (2 g, 6.3 mmol, 1.0 equiv.) was added. The reaction mixture was vigorously stirred for 3 h at r.t.. After the reaction was completed (monitored by TLC), the reaction mixture was extract with CH_2Cl_2 (20 mL×3) and washed with brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified through column chromatography on silica gel to provide the desired products **3c** (3.2 g, 95% yield, 96% ee) and *ent*-**3c** (3.1 g, 92% yield, 97% ee) as a white solid, respectively. Analytical data are consistent with above values.

6. Synthesis of (*R*)-baclofen



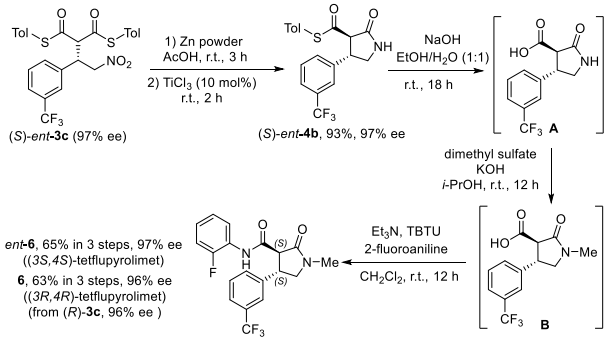
6.1 Synthesis of 4a

To a 50 mL dried round-bottom flask equipped with a Teflon-coated magnetic stirring bar, adduct **3b** (99% ee) (150 mg, 0.28 mmol, 1.0 equiv) was dissolved in 5.0 mL of AcOH. A freshly activated zinc powder (185 mg, 2.8 mmol, 10 equiv.) was added and the mixture was stirred at r.t. under an argon atmosphere for 3 hours. After this period, $TiCl_3$ (30 μL, 0.028 mmol, 0.1 equiv; 12% solution in 5% HCl) was added and the resulting mixture was stirred for additional 2 h. The mixture was filtered through a pad of Celite, the filter cake was washed with EtOAc and the obtained solution was concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica gel to obtain the product **4a** as a white solid (96 mg, 93% yield, 99% ee); $\mathbf{R_f}$ =0.24 (petroleum ether:ethyl acetate (*v*/*v*), 1/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.29 (m, 4H), 7.23-7.19 (m, 4H), 6.38 (s, 1H), 4.11 (dd, *J* = 15.4, 7.9 Hz, 1H), 3.86-3.73 (m, 2H), 3.41 (dd, *J* = 9.7, 7.1 Hz, 1H), 2.37 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.0, 171.4, 140.2, 138.7, 134.4, 130.1, 129.3, 128.4, 123.4, 62.2, 47.5, 43.5, 21.4 ppm; **IR** (KBr) 2921, 1722, 1684, 1597, 1560, 1494, 1445, 1324, 1281, 1091, 1053, 1013, 821 cm^{-1}; **HRMS** (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{16}ClNO_2SNa$ 368.0488, found 368.0485; **HPLC** COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 12.91 min (minor), t_R= 9.05 min (major); **$[\alpha]^{20}_D$** = -60.0 (c = 1.0, $CHCl_3$); **mp**: 127-130 °C.

6.2 Synthesis of (*R*)-baclofen 5

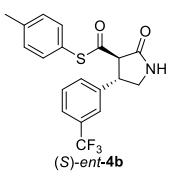
To a 10 mL dried round-bottom flask equipped with a Teflon-coated magnetic stirring bar, the lactam **4a** (96 mg, 0.31 mmol) was refluxed in 6 N HCl (1.0 mL) for 24 h. After cooling, the reaction mixture was washed with EtOAc. The volatile components were removed under reduced pressure to give (*R*)-baclofen (**5**) in HCl salt form as a white solid (60 mg, 90% yield). Analytical data are consistent with reported values.[4] **^{1}H NMR** (400 MHz, D_2O) δ 7.41-7.37 (m, 2H), 7.31-7.27 (m, 2H), 3.42-3.30 (m, 2H), 3.22-3.15 (m, 1H), 2.81 (dd, *J* = 16.1, 5.9 Hz, 1H), 2.69 (dd, *J* = 16.1, 8.8 Hz, 1H) ppm; **^{13}C NMR** (101 MHz, D_2O) δ 175.3, 137.0, 133.4, 129.4, 129.3, 43.6, 39.4, 38.2 ppm; **MS** (ESI) m/z 214.1; **$[\alpha]^{20}_D$** = -4.23 (c = 0.65, H_2O). [lit.[4] **$[\alpha]^{20}_D$** = -3.79 (c = c = 0.65, H_2O)].

7. Synthesis of tetflupyrolimet



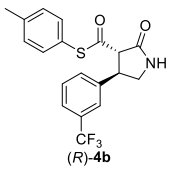
7.1 Synthesis of *ent*-4b

To a 50 mL dried round-bottom flask equipped with a Teflon-coated magnetic stirring bar, adduct *ent*-**3c** (97% ee) (500 mg, 1.1 mmol, 1.0 equiv.) and AcOH (25 mL) were added. Then, freshly activated zinc powder (754 mg, 11 mmol, 10 equiv.) was added and the mixture was stirred at r.t. under an argon atmosphere for 3 h. After this period, $TiCl_3$ (127 μL, 1.1 mmol, 0.1 equiv; 12% solution in 5% HCl) was added and the resulting mixture was stirred for additional 2 h. The mixture was filtered through a pad of Celite, the filter cake was washed with EtOAc and the obtained solution was concentrated *in vacuo*. The crude material was purified by flash column chromatography on silica gel to obtain the product *ent*-**4b** as a white solid (332.5 mg, 93% yield, 97% ee).


(*S*)-*ent*-**4b**

R_f =0.24 (petroleum ether/ethyl acetate (*v*/*v*), 1/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36-7.29 (m, 4H), 7.23-7.19 (m, 4H), 6.38 (s, 1H), 4.11 (dd, *J* = 15.4, 7.9 Hz, 1H), 3.86-3.73 (m, 2H), 3.41 (dd, *J* = 9.7, 7.1 Hz, 1H), 2.37 (s, 3H) ppm; **^{13}C NMR** (101 MHz, $CDCl_3$) δ 194.0, 171.4, 140.2, 138.7, 134.4, 130.1, 129.3, 128.4, 123.4, 62.2, 47.5, 43.5, 21.4 ppm; **IR** (KBr) 2921, 1722, 1684, 1597, 1560, 1494, 1445, 1324, 1281, 1091, 1053, 1013, 821 cm^{-1}; **HRMS** (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{16}F_3NO_2SNa$ 402.0752, found 402.0751; **HPLC** COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 6.11 min (minor), t_R= 7.22 min (major); **$[\alpha]^{20}_D$** = +72.8 (c = 1.0, $CHCl_3$); **mp**: 89-94 °C.

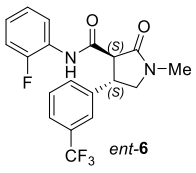
7.2 Synthesis of 4b


(*R*)-**4b**

Following the above procedure (for *ent*-**4b)** with **3c** (500 mg, 1.1 mmol, 96% ee), **4b** (336 mg, 94% yield, 96% ee) was obtained as a white solid. Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**, **IR** and **mp**) are consistent with that of *ent*-**4b**. **$[\alpha]^{20}_D$** = -72.3 (c = 0.9, $CHCl_3$, 96% ee).

7.3 Synthesis of (3*S*,4*S*)-tetflupyrolimet *ent*-6

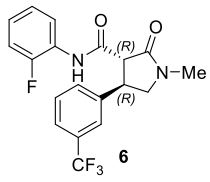
To a 25 mL dried round-bottom flask equipped with a Teflon-coated magnetic stirring bar, lactam *ent*-**4b** (200 mg, 0.53 mmol) was added to a solution of ethanol (5 mL), sodium hydroxide aqueous solution (50%, 63.3 mg, 1.59 mmo1) was added, and stirred at r.t. for 18 h. The reaction mixture was then diluted with water (5 mL) and extracted with ethyl ether (2 x 5 mL). The aqueous phase was acidified to pH 2 with concentrated hydrochloric acid and extracted with methylene chloride (3×5mL). The combined methylene chloride extract was washed with brine, dried (Na_2SO_4), and concentrated under pressure to obtain a white solid carboxylic acid **A**. Carboxylic acid **A** was added to a solution of potassium hydroxide (148 mg, 2.65 mol) in isopropyl alcohol (5 mL) at 20 °C, then dimethyl sulfate (150 μL, 2.65 mol) was added dropwise into the reaction mixture, and stirred for 16 h at 20 °C. After this period, the mixture was quenched with water (2 mL). The resulting solution was concentrated under reduced pressure to remove excess isopropyl alcohol, then acidified with concentrated hydrochloric acid and extracted with methylene chloride (2×20 mL), dried (Na_2SO_4), and concentrated under pressure to obtain a white solid *N*-methylated carboxylic acid **B**. To a solution of *N*-methylated carboxylic acid **B** in methylene chloride, was added 2-fluoroaniline (100 μL, 1.06 mol) and triethylamine (220 μL, 1.59 mol) dropwise at room temperature. Then, a solution of TBTU (371 mg, 1.17 mmol) in CH_2Cl_2 was added dropwise to the above reaction mixture and stirred overnight at room temperature. The reaction mixture was extract with CH_2Cl_2 and the combined CH_2Cl_2 extract was washed in brine, dried (Na_2SO_4), and concentrated under pressure. The crude material was purified by flash column chromatography on silica gel to obtain a brown solid (3*S*,4*S*)-tetflupyrolimet *ent*-**6** (130 mg, 65% yield, 97% ee).


ent-**6**

R_f =0.3 (petroleum ether/ethyl acetate (*v*/*v*), 1/1); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.25-8.19 (m, 1H), 7.55 (ddd, *J* = 26.2, 14.1, 6.4 Hz, 4H), 7.12-6.99 (m, 3H), 4.19 (dd, *J* = 17.3, 9.0 Hz, 1H), 3.86-3.62 (m, 2H), 3.47 (dd, *J* = 10.1, 8.0 Hz, 1H), 3.01 (s, 3H); **^{13}C NMR** (101 MHz, CDCl3) δ 170.4, 165.0, 152.9 (d, *J* = 245.0 Hz), 142.6, 131.4 (q, *J* = 32.4 Hz), 129.6, 128.0, 126.2, 126.1, 124.5 (d, *J* = 7.6 Hz), 124.3 (q, 3.7 Hz), 124.1 (q, *J* = 3.8 Hz), 124.0 (q, *J* = 272.4 Hz), 121.8, 115.0 (d, *J* = 19.1 Hz), 54.7, 54.7, 39.0, 30.2, 29.7 ppm; **IR** (KBr) 3065, 2924, 1703, 1617, 1597, 1548, 1492, 1456, 1395, 1325, 1259, 1175, 1116, 1072, 902, 802, 757, 701 cm^{-1}; **HRMS** (ESI-QTOF) m/z: [M + Na]+ Calcd for $C_{19}H_{16}F_4N_2O_2Na$ 403.1050, found 403.1046; **HPLC**

COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 6.82 min (minor), t_R= 9.95 min (major); **[α]$^{20}_D$** = +22.5 (c = 0.9, $CHCl_3$, 97% ee); **mp**: 116-120 ℃.

7.4 Synthesis of (3*R*,4*R*)-tetflupyrolimet 6



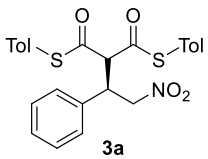
Following the above procedure (for *ent*-**6)** with **4b** (200 mg, 0.53 mmol, 96% ee), (3*R*,4*R*)-tetflupyrolimet **6** (126 mg, 63% yield, 96% ee) was obtained as a brown solid. Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**, **IR** and **mp**) are consistent with *ent*-**6**. **[α]$^{20}_D$** = -22.2 (c = 0.9, $CHCl_3$, 96% ee).

8. Addition reactions between diverse dithiomalonates and nitroolefins catalyzed by QD-SQA or QN-SQA

General Procedure C

To a 3 mL vial equipped with a Teflon-coated magnetic stirring bar, *β*-nitroolefin **1** (0.24 mmol, 1.5 equiv.), brine (1.5 mL) and toluene (10 equiv.) were added. Then, 0.5 mol % of catalyst (**QD-SQA** or **QN-SQA**) and dithiomalonate **2** (0.16 mmol, 1.0 equiv.) were subsequently introduced into the reaction mixture. The reaction mixture was stirred at room temperature for 0.5-6 hours until the reaction was completed, which was monitored by TLC. The reaction mixture was extract with CH_2Cl_2 (3×5 mL) and washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified through column chromatography on silica gel to provide the desired products **3a**-**3r**.

(*R*)-2-(2-nitro-1-phenylethyl)-malonic acid bis-4-methylphenyl dithioester **(3a)**



Following the general procedure C with nitroolefin **1a** (35.7 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (70 mg, 95% yield, 90% ee). Analytical data are consistent with reported values.[2]

R_f =0.40 (petroleum ether/ethyl acetate (*v*/*v*), 10/1).

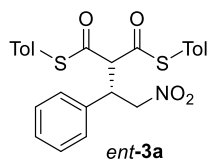
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.27 (m, 7H), 7.26-7.23 (m, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.1 Hz, 2H), 4.90-4.80 (m, 2H), 4.45 (d, *J* = 9.4 Hz, 1H), 4.38 (td, *J* = 8.9, 5.0 Hz, 1H), 2.39 (s, 3H), 2.34 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9, 190.1, 140.7, 140.5, 135.3, 134.2, 134.2, 130.3, 130.2, 129.1, 128.6, 128.4, 122.6, 122.6, 69.2, 44.3, 29.7, 21.4, 21.3 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 11.88 min (minor), t_R= 14.90 min (major).

[α]$^{20}_D$ = -71.4(c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -75.6 (c = 1.0, $CHCl_3$; 95% ee)].

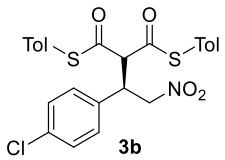
(*S*)-2-(2-nitro-1-phenylethyl)-malonic acid bis-4-methylphenyl dithioester **(***ent*-**3a)**



Following the general procedure C with nitroolefin **1a** (35.7 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.5 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (70 mg, 95% yield, 80% ee). Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of *ent*-**3a**.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 11.28 min (mijor), t_R= 14.18 min (manor).

(*R*)-2-(1-(4-chlorophenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3b)**



Following the general procedure C with nitroolefin **1b** (44 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (76 mg, 96% yield, 97% ee). Analytical data are consistent with reported values.[2]

R$_f$ =0.40 (petroleum ether/ethyl acetate (*v*/*v*), 10/1).

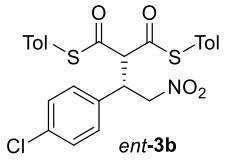
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dt, *J* = 24.3, 8.2 Hz, 6H), 7.22-7.16 (m, 4H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.80 (d, *J* = 6.5 Hz, 2H), 4.44-4.33 (m, 2H), 2.39 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 190.0, 140.8, 140.7, 134.6, 134.2, 134.2, 133.9, 130.4, 130.3, 129.8, 129.3, 122.5, 122.4, 76.9, 68.9, 43.7, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 15.55 min (minor), t_R= 13.71 min (major).

[α]$^{20}_D$ = -101.4(c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -92.2 (c = 1.0, $CHCl_3$; 87% ee)].

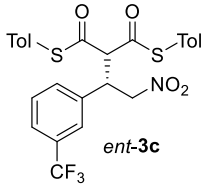
(*S*)-2-(1-(4-chlorophenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3b)**



Following the general procedure C with nitroolefin **1b** (44 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (68 mg, 93% yield, 85% ee). Analytical data (**R**$_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3b**.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 14.08 min (minor), t_R= 15.93 min (major).

(*S*)-2-(1-(3-(trifluoromethyl-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(*ent*-3c)**



Following the general procedure C with nitroolefin **1c** (52 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and **QN-SQA** (0.5 mol %) and toluene (10 equiv.) in 1.5 mL brine, the reaction was completed in 30 min at r.t., *ent*-**3c** was obtained as a white solid (81 mg, 96% yield, 97% ee).

New Compound, **R**$_f$ =0.35 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

mp: 137-140 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63-7.59 (m, 1H), 7.54-7.46 (m, 3H), 7.31-7.28 (m, 2H), 7.28-7.25 (m, 2H), 7.19-7.16 (m, 2H), 7.05-7.01 (m, 2H), 4.87 (dd, *J* = 4.0, 2.4 Hz, 2H), 4.49-4.45 (m, 1H), 4.45-4.42 (m, 1H), 2.40 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 190.0, 140.9, 140.7, 136.7, 134.2, 134.1, 131.6, 131.3, 130.8 (q, *J* = 223.3 Hz), 130.4, 130.3 125.5 (q, *J* = 3.6 Hz), 125.2 (q, *J* = 3.9 Hz), 122.4 (q, *J* = 3.9 Hz), 76.6, 68.6, 44.0, 21.4, 21.4 ppm.

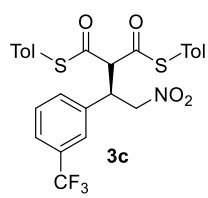
IR (KBr) 2924, 1912, 1698, 1617, 1549, 1492, 1453, 1399, 1335, 1317, 1261, 1167, 1075, 980, 810, 706 cm^{-1}.

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{22}F_3NO_4S_2Na$ 556.0845, found 556.0840.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 15.49 min (minor), t_R= 19.97 min (major).

[α]$^{20}_D$ = +64.8 (c = 1.0, $CHCl_3$).

(*R*)-2-(1-(3-(trifluoromethyl-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(3c)**



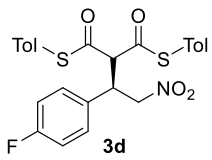
Following the general procedure C with nitroolefin **1c** (52 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and **QD-SQA** (0.5 mol %) and toluene (10 equiv.) in 1.5 mL brine, the reaction was completed in 30 min at r.t., **3c** was obtained as a white solid (80 mg, 95% yield, 96% ee).

New Compound

Analytical data (**R**$_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of *ent*-**3c**.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 18.86 min (minor), t_R= 14.77 min (major); **[α]$^{20}_D$** = -64.5 (c = 1.0, $CHCl_3$).

(*R*)-2-(1-(4-fluorophenyl)-2-nitro-ethyl)-malonic acid bis-4methylphenyl dithioester **(3d)**



3d

Following the general procedure C with nitroolefin **1d** (40 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (73 mg, 95% yield, 96% ee). Analytical data are consistent with reported values.[2]

R_f =0.40 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

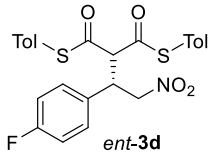
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.2 Hz, 2H), 7.27-7.22 (m, 4H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.08-7.02 (m, 4H), 4.81 (d, *J* = 6.3 Hz, 2H), 4.44-4.34 (m, 2H), 2.40 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 190.0, 162.7 (d, *J* = 248.1 Hz), 140.8, 140.6, 134.2, 134.1, 131.1 (d, *J* = 3.3 Hz), 130.4, 130.3, 130.2, 130.1, 122.5 (d, *J* = 4.3 Hz), 116.1 (d, *J* = 21.7 Hz), 77.4, 69.1, 43.6, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/n-hexane = 30/70, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 14.14min (minor), t_R= 12.51 min (major).

[α]$^{20}_D$ = -75.0 (c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -72.4 (c = 1.0, $CHCl_3$; 92% ee)].

(*S*)-2-(1-(4-fluorophenyl)-2-nitro-ethyl)-malonic acid bis-4methylphenyl dithioester **(*ent*-3d)**

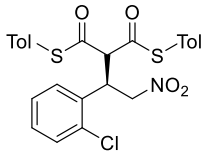


ent-**3d**

Following the general procedure with nitroolefin **1d** (40 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t.,to give the desired product as a white solid (68.4 mg, 89% yield, 57% ee). Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3d**.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 12.50 min (minor), t_R= 14.03 min (major).

(*R*)-2-(1-(2-chlorophenyl)-2-nitroethyl)-malonic acid bis-4-methylphenyl dithioester **(3e)**



3e

Following the general procedure C with nitroolefin **1e** (44 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (73 mg, 92% yield, 96% ee). Analytical data are consistent with reported values.[2]

R_f =0.40 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

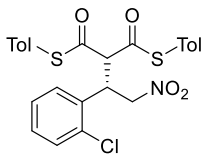
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-.42 (m, 1H), 7.30-7.26 (m, 3H), 7.24 (s, 4H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 7.9 Hz, 2H), 5.11 (dd, *J* = 13.7, 8.9 Hz, 1H), 4.96-4.81 (m, 2H), 4.76 (d, *J* = 8.0 Hz, 1H), 2.38 (s, 3H), 2.34 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.2, 190.2, 140.7, 140.6, 134.2, 134.2, 132.8, 130.7, 130.4, 130.3, 129.8, 127.4, 122.7, 122.5, 75.0, 66.6, 41.1, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 12.04 min (minor), t_R=8.88 min (major).

[α]$^{20}_D$ = -31.4(c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -31.8 (c = 1.0, $CHCl_3$; 96% ee)].

(*S*)-2-(1-(2-chlorophenyl)-2-nitroethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3e)**

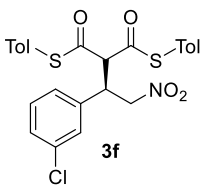


ent-**3e**

Following the general procedure C with nitroolefin **1e** (44 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t.,to give the desired product as a white solid (71.4 mg, 90% yield, 89% ee). Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3e.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 9.00 min (minor), t_R=12.14 min (major).

(*R*)-2-(1-(3-chlorophenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3f)**



Following the general procedure C with nitroolefin **1f** (44 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (71 mg, 90% yield, 95% ee). Analytical data are consistent with reported values.[2]

R*f* =0.36 (petroleum ether:ethyl acetate (*v*/*v*), 10/1)

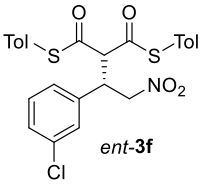
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.28 (m, 4H), 7.28-7.24 (m, 3H), 7.21-7.14 (m, 3H), 7.08 (d, *J* = 8.0 Hz, 2H), 4.84 (d, *J* = 6.5 Hz, 2H), 4.42-4.32 (m, 2H), 2.39 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 190.0, 140.8, 140.7, 137.5, 135.0, 134.3, 134.2, 130.4, 130.4, 130.3, 128.9, 128.6, 126.5, 122.4, 122.4, 76.6, 68.7, 43.9, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 10.21 min (minor), t_R= 8.87 min (major).

[α]$^{20}_D$ = -80.0(c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -77.8 (c = 1.0, $CHCl_3$; 92% ee)].

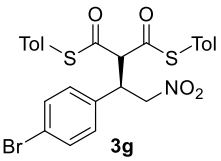
(*S*)-2-(1-(3-chlorophenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3f)**



Following the general procedure C with nitroolefin **1f** (44 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (69.4 mg, 88% yield, 91% ee). Analytical data (**R*f*, ^{1}H NMR**, **^{13}C NMR**) are consistent with that of *ent*-**3f.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 8.76 min (minor), t_R= 9.98 min (major).

(*R*)-2-(1-(4-bromo-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(3g)**



Following the general procedure C with nitroolefin **1g** (54 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (82 mg, 95% yield, 98% ee). Analytical data are consistent with reported values.[2]

R*f* =0.40 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

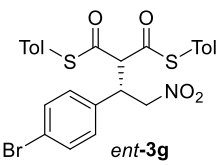
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 7.4 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 4.81 (d, *J* = 6.7 Hz, 2H), 4.41 (d, *J* = 9.4 Hz, 1H), 4.38-4.31 (m, 1H), 2.40 (s, 3H), 2.35 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.8, 189.9, 140.8, 140.6, 134.4, 134.2, 134.1, 132.2, 130.4, 130.3, 130.0, 122.7, 122.4, 122.4, 76.8, 68.8, 43.7, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25°C, 1.0 mL/min, λ= 254 nm, t_R= 15.45 min (minor), t_R= 13.42 min (major).

[α]$^{20}_D$ = -68.5 (c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -61.0 (c = 1.0, $CHCl_3$; 87% ee)].

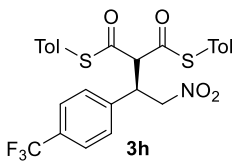
(*S*)-2-(1-(4-bromo-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(*ent*-3g)**



Following the general procedure C with nitroolefin **1g** (54 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (77.6 mg, 90% yield, 50% ee). Analytical data (**R*f*, ^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3g.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25°C, 1.0 mL/min, λ= 254 nm, t_R= 13.35 min (minor), t_R= 15.30 min (major).

(*R*)-2-(1-(4-(trifluoromethyl-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(3h)**.



Following the general procedure C with nitroolefin **1h** (52 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (82 mg, 97% yield, 95% ee). Analytical data are consistent with reported values.[2]

R*f* =0.42 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

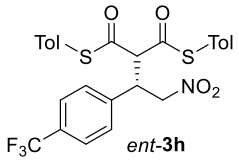
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.32-7.25 (m, 4H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.1 Hz, 2H), 4.87-4.82 (m, 2H), 4.47-4.43 (m, 2H), 2.40 (s, 3H), 2.34 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.7, 189.9, 140.9, 140.7, 139.5, 134.2, 134.1, 131.2 (q, *J* = 32.5 Hz), 130.4, 130.3, 129.0, 126.0 (q, *J* = 3.7 Hz), 123.8 (q, *J* = 272.2 Hz), 122.4, 122.2, 76.6, 68.6, 43.9, 21.4, 21.3 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 12.25 min (minor), t_R= 10.76 min (major).

[α]^{20}D = -58.0 (c = 1.0, $CHCl_3$). [lit.[2] **[α]^{20}D** = -50.8 (c = 1.0, $CHCl_3$; 82% ee)].

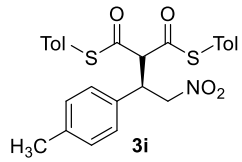
(*S*)-2-(1-(4-(trifluoromethyl-phenyl)-2-nitro-ethyl)-malonic acid diphenyl dithioester **(*ent*-3h)**.



Following the general procedure C with nitroolefin **1h** (52 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (79.5 mg, 94% yield, 92% ee). Analytical data (**R*f***, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3h.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 10.77 min (minor), t_R= 12.21 min (major).

(*R*)-2-(1-(4-methyl-phenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3i)**



Following the general procedure C with nitroolefin **1i** (39 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (71 mg, 94% yield, 94% ee). Analytical data are consistent with reported values.[2]

R*f* =0.39 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

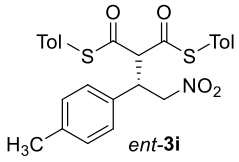
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, *J* = 8.1 Hz, 2H), 7.25 (d, *J* = 7.7 Hz, 2H), 7.19-7.11 (m, 6H), 7.05 (d, *J* = 8.1 Hz, 2H), 4.87-4.78 (m, 2H), 4.43 (d, *J* = 9.4 Hz, 1H), 4.34 (td, *J* = 8.8, 5.3 Hz, 1H), 2.39 (s, 3H), 2.33 (d, *J* = 1.7 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.1, 190.1, 140.7, 140.4, 138.3, 134.3, 134.2, 132.3, 130.4, 130.2, 129.7, 128.2, 122.7, 122.7, 77.2, 69.3, 44.1, 21.4, 21.4, 21.2 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 10.76 min (minor), t_R= 9.72 min (major).

[α]^{20}D = -81.0 (c = 1.0, $CHCl_3$). [lit.[2] **[α]^{20}D** = -82.2 (c = 1.0, $CHCl_3$; 95% ee)].

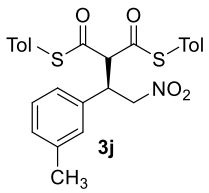
(*S*)-2-(1-(4-methyl-phenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3i)**



Following the general procedure C with nitroolefin **1i** (39 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (67.9 mg, 90% yield, 84% ee). Analytical data (**R*f***, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3i.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 9.80 min (minor), t_R= 10.79 min (major).

(*R*)-2-(1-(3-methyl-phenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3j)**



Following the general procedure C with nitroolefin **1j** (39 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 3 h at r.t.. After column chromatography, the desired product was obtained as a white solid (63 mg, 83% yield, 92% ee).

New Compound, $\mathbf{R}_f$ =0.38 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

mp: 121-127 ℃.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.22 (m, 5H), 7.14 (dd, *J* = 16.4, 7.7 Hz, 3H), 7.07-7.02 (m, 4H), 4.89-4.79 (m, 2H), 4.43 (d, *J* = 9.3 Hz, 1H), 4.33 (td, *J* = 8.9, 5.2 Hz, 1H), 2.39 (s, 3H), 2.34 (s, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 190.2, 140.7, 140.5, 138.8, 135.3, 134.3, 134.2, 130.4, 130.2, 129.3, 129.2, 128.9, 125.2, 122.7, 77.0, 69.2, 44.3, 21.5, 21.4, 21.4 ppm.

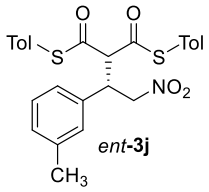
IR (KBr) 2922, 1742, 1698, 1548, 1492, 1376, 1261, 1180, 1017, 982, 810, 725 cm^{-1}.

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{25}NO_4S_2Na$ 502.1128, found 502.1123.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 ℃, 1.0 mL/min, λ= 254 nm, t_R= 9.72 min (minor), t_R= 8.50 min (major).

[α]$^{20}_D$ = -46.5(c = 1.0, $CHCl_3$).

(*S*)-2-(1-(3-methyl-phenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3j)**

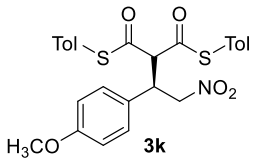


Following the general procedure C with nitroolefin **1j** (39 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 3 h at r.t., to give the desired product as a white solid (60.7 mg, 80% yield, 80% ee).

Analytical data ($\mathbf{R}_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3j.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 8.56 min (minor), t_R= 9.75 min (major).

(*R*)-2-(1-(4-methoxy-phenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3k)**



Following the general procedure C with nitroolefin **1k** (43 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (73 mg, 93% yield, 99% ee). Analytical data are consistent with reported values.[2]

$\mathbf{R}_f$ =0.38 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

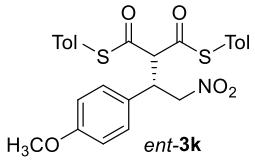
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.28 (m, 2H), 7.26-7.23 (m, 2H), 7.20-7.15 (m, 4H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.90-6.85 (m, 2H), 4.82-4.78 (m, 2H), 4.42 (d, *J* = 9.5 Hz, 1H), 4.37-4.29 (m, 1H), 3.80 (s, 3H), 2.39 (s, 3H), 2.34 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.0, 190.1, 159.6, 140.7, 140.5, 134.2, 134.2, 130.3, 130.2, 129.5, 127.2, 122.7, 122.7, 114.5, 77.3, 69.4, 55.3, 43.8, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 14.81 min (minor), t_R= 15.66 min (major).

[α]$^{20}_D$ = -84.4 (c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -81.4 (c = 1.0, $CHCl_3$; 95% ee)].

(*S*)-2-(1-(4-methoxy-phenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3k)**



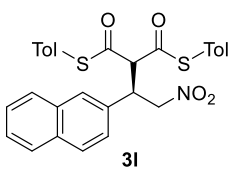
Following the general procedure C with nitroolefin **1k** (43 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (68.3 mg, 87% yield, 64% ee).

Analytical data ($\mathbf{R}_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3k.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 14.18min (minor), t_R= 15.06

min (major).

(*R*)-2-(1-(2-naphthyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3l)**



3l

Following the general procedure C with nitroolefin **1l** (47 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (73 mg, 90% yield, 86% ee). Analytical data are consistent with reported values.[2]

R$_f$ =0.37 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

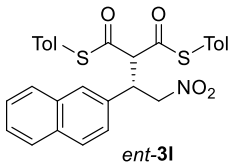
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89-7.80 (m, 3H), 7.72 (s, 1H), 7.55-7.48 (m, 2H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.31-7.26 (m, 4H), 7.10 (d, *J* = 7.6 Hz, 2H), 6.94 (d, *J* = 7.8 Hz, 2H), 5.03-4.89 (m, 2H), 4.59-4.52 (m, 2H), 2.40 (s, 3H), 2.31 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.1, 190.1, 140.7, 140.5, 134.3, 134.2, 133.3, 133.1, 132.8, 130.4, 130.1, 129.1, 128.0, 127.9, 127.7, 126.6, 125.4, 122.6, 122.5, 76.9, 69.2, 44.5, 21.4, 21.3 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 16.48 min (minor), t_R= 13.17 min (major).

[α]$^{20}_D$ = -50.1 (c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -45.0 (c = 1.0, $CHCl_3$; 77% ee)].

(*S*)-2-(1-(2-naphthyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3l)**

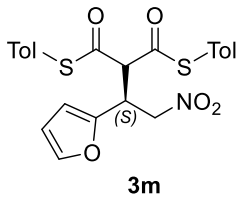


ent-**3l**

Following the general procedure C with nitroolefin **1l** (47 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (67.8 mg, 86% yield, 61% ee). Analytical data (**R**$_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3l.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 13.00 min (minor), t_R= 16.20 min (major).

(*S*)-2-(1-(2-furyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3m)**



3m

Following the general procedure C with nitroolefin **1m** (33 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (65 mg, 90% yield, 92% ee). Analytical data are consistent with reported values.[2]

R$_f$ =0.38 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

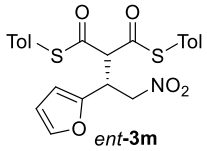
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.41 (m, 1H), 7.31-7.27 (m, 2H), 7.26-7.17 (m, 6H), 6.33 (dd, *J* = 3.3, 1.9 Hz, 1H), 6.25 (d, *J* = 3.3 Hz, 1H), 4.88-4.77 (m, 2H), 4.59 (d, *J* = 8.8 Hz, 1H), 4.49 (td, *J* = 8.6, 4.4 Hz, 1H), 2.38 (s, 3H), 2.36 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.6, 190.2, 148.7, 143.1, 140.7, 140.6, 134.3, 134.3, 130.4, 130.3, 122.6, 122.6, 110.7, 109.4, 75.1, 66.8, 38.1, 21.4, 21.4.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 9.89 min (minor), t_R= 11.00 min (major).

[α]$^{20}_D$ = -50.3 (c = 1.0, $CHCl_3$). [lit.[2] **[α]$^{20}_D$** = -51.6 (c = 1.0, $CHCl_3$; 94% ee)].

(*R*)-2-(1-(2-furyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3m)**

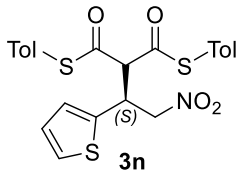


ent-**3m**

Following the general procedure C with nitroolefin **1m** (33 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (65.7 mg, 91% yield, 92% ee). Analytical data (**R**$_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3m.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 9.82 min (minor), t_R= 10.84 min (major).

(*S*)-2-(1-(2-thiophenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3n)**



3n

Following the general procedure C with nitroolefin **1n** (37.2 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 30 min at r.t.. After column chromatography, the desired product was obtained as a white solid (63 mg, 85% yield, 96% ee). Analytical data are consistent with reported values.[2]

R_f =0.42 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

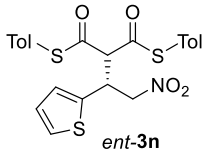
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.27 (m, 4H), 7.25-7.23 (m, 1H), 7.22-7.13 (m, 4H), 6.99-6.96 (m, 2H), 4.90-4.80 (m, 2H), 4.67 (td, *J* = 8.2, 5.1 Hz, 1H), 4.52 (d, *J* = 8.7 Hz, 1H), 2.39 (s, 3H), 2.36 (s, 3H) ppm;

^{13}C NMR (101 MHz, $CDCl_3$) δ 190.9, 190.1, 140.7, 140.6, 137.8, 134.3, 130.4, 130.3, 127.5, 127.2, 125.8, 122.6, 122.6, 77.7, 69.6, 39.8, 21.4, 21.4 ppm.

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 23.32 min (minor), t_R= 20.76 min (major).

$[\alpha]^{20}_D$ = -24.9(c = 1.0, $CHCl_3$). [lit.[2] **$[\alpha]^{20}_D$** = -23.6 (c = 1.0, $CHCl_3$; 91% ee)].

(*R*)-2-(1-(2-thiophenyl)-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3n)**

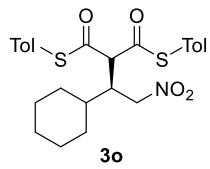


ent-**3n**

Following the general procedure C with nitroolefin **1n** (37.2 mg, 0.24 mmol), *S*,*S*'-bis(4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 50 min at r.t., to give the desired product as a white solid (65.2 mg, 88% yield, 95% ee). Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3n.**

HPLC COSMOSIL 5A column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 20.38 min (minor), t_R= 22.62 min (major).

(*S*)-2-(1-cyclohexyl-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3o)**



3o

Following the general procedure C with nitroolefin **1o** (37 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (0.50 mg, 0.5 mol %), the reaction was completed in 4 h at r.t.. After column chromatography, the desired product was obtained as a white solid (61 mg, 82% yield, 90% ee). Analytical data are consistent with reported values.[2]

R_f =0.37 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

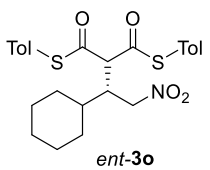
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.1 Hz, 2H), 7.29 (d, *J* = 8.1 Hz, 2H), 7.27 (s, 1H), 7.24 (d, *J* = 7.9 Hz, 3H), 4.81 (dd, *J* = 14.8, 3.0 Hz, 1H), 4.59 (dd, *J* = 14.8, 7.2 Hz, 1H), 4.40 (d, *J* = 5.3 Hz, 1H), 3.03-2.96 (m, 1H), 2.38 (d, *J* = 2.6 Hz, 6H), 1.84-1.67 (m, 5H), 1.30-1.00 (m, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 191.7, 140.6, 140.6, 134.4, 134.3, 130.4, 130.3, 122.9, 122.8, 75.0, 65.4, 44.3, 40.0, 30.6, 29.8, 26.3, 26.3, 26.0, 21.4 ppm.

HPLC COSMOSIL 5C column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 8.86 min (minor), t_R= 8.36 min (major).

$[\alpha]^{20}_D$ = -63.7(c = 1.0, $CHCl_3$). [lit.[2] **$[\alpha]^{20}_D$** = -58.4 (c = 1.0, $CHCl_3$; 82% ee)].

(*R*)-2-(1-cyclohexyl-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3o)**

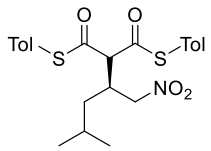


ent-**3o**

Following the general procedure C with nitroolefin **1o** (37 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (0.51 mg, 0.5 mol %), the reaction was completed in 4 h at r.t., to give the desired product as a white solid (63.2 mg, 85% yield, 90% ee). Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3o.**

HPLC COSMOSIL 5C column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 7.63 min (minor), t_R= 8.45 min (major).

(*S*)-2-(1-isobutyl-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(3p)**



3p

Following the general procedure C with nitroolefin **1p** (31 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QD-SQA** (2.0 mg, 2.0 mol %), the reaction was completed in 6 h at r.t.. After column chromatography, the desired product was obtained as a white oil (45 mg, 64% yield, 90% ee).

New Compound, $\mathbf{R}_f$ =0.36 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.29 (m, 4H), 7.27-7.22 (m, 4H), 4.61 (ddd, *J* = 20.0, 13.7, 5.2 Hz, 2H), 4.32 (d, *J* = 6.6 Hz, 1H), 3.11-3.01 (m, 1H), 2.39 (s, 6H), 1.78-1.67 (m, 1H), 1.38 (td, *J* = 7.2, 3.0 Hz, 2H), 0.94 (dd, *J* = 6.4, 5.4 Hz, 6H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 191.6, 191.6, 140.6, 140.6, 134.3, 134.3, 130.4, 130.3, 122.9, 122.8, 76.4, 67.2, 38.9, 36.6, 25.2, 22.5, 22.3, 22.1, 21.4 ppm.

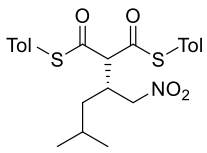
IR (KBr) 2922, 1702, 1547, 1492, 1468, 1388, 1261, 1208, 1017, 984, 806, 775 cm^{-1}.

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{27}NO_4S_2Na$ 468.1280, found 468.1279.

HPLC COSMOSIL 5C column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R=6.03 min (minor), t_R= 6.34 min (major).

$[\alpha]^{20}_D$ = -25.9(c = 2.0, $CHCl_3$).

(*R*)-2-(1-isobutyl-2-nitro-ethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3p)**



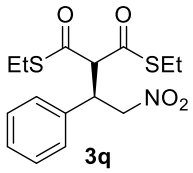
ent-**3p**

Following the general procedure C with nitroolefin **1p** (31 mg, 0.24 mmol), *S*,*S*'-bis (4-methylphenyl) dithiomalonate **2a** (50 mg, 0.16 mmol) and catalyst **QN-SQA** (2.1 mg, 2.0 mol %), the reaction was completed in 4 h at r.t., to give the desired product as a white solid (56.3 mg, 80% yield, 92% ee).

Analytical data ($\mathbf{R}_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3p.**

HPLC COSMOSIL 5C column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 6.34 min (minor), t_R= 6.03 min (major).

(*R*)-2-(2-nitro-1-phenylethyl)-malonic acid diethyl dithioester **(3q)**



3q

Following the general procedure C with nitroolefin **1a** (35.7 mg, 0.24 mmol), *S*,*S*'-diethyl dithiomalonate **2b** (30.7 mg, 0.16 mmol) and catalyst **QD-SQA** (2.0 mg, 2 mol %), the reaction was completed in 1 h at r.t.. After column chromatography, the desired product was obtained as a white solid (49.1 mg, 90% yield, 81% ee). Analytical data are consistent with reported values.[1]

$\mathbf{R}_f$ =0.41 (petroleum ether:ethyl acetate (*v*/*v*), 20/1).

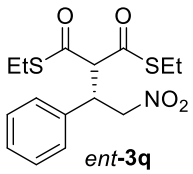
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.25 (m, 3H), 7.23-7.19 (m, 2H), 4.77-4.72 (m, 2H), 4.38 (ddd, *J* = 10.0, 8.2, 5.7 Hz, 1H), 4.25 (d, *J* = 10.1 Hz, 1H), 2.97 (q, *J* = 7.4 Hz, 2H), 2.82-2.65 (m, 2H), 1.28 (t, *J* = 7.4 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 192.1, 191.1, 135.4, 128.9, 128.4, 128.2, 77.4, 70.3, 44.2, 24.5, 24.2, 14.2, 14.1 ppm.

HPLC Chiracel OD-H column, *i*-PrOH/*n*-hexane = 5/95, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 13.62 min (major), t_R= 12.73 min (minor).

$[\alpha]^{20}_D$ = -31.1 (c = 1.0, $CHCl_3$). [lit.[1] **$[\alpha]^{20}_D$** = -34.3 (c = 1.0, $CHCl_3$; 89% ee)].

(*S*)-2-(2-nitro-1-phenylethyl)-malonic acid diethyl dithioester **(*ent*-3q)**



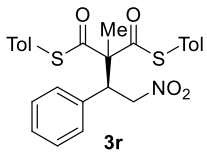
ent-**3q**

Following the general procedure C with nitroolefin **1a** (35.7 mg, 0.24 mmol), *S*,*S*'-diethyl dithiomalonate **2b** (30.7 mg, 0.16 mmol) and catalyst **QN-SQA** (2.0 mg, 2 mol %), the reaction was completed in 1 h at r.t., to give the desired product as a white solid (48.5 mg, 89% yield, 77% ee).

Analytical data ($\mathbf{R}_f$, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3q.**

HPLC Chiracel OD-H column, *i*-PrOH/*n*-hexane = 5/95, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 13.12 min (major), t_R= 13.77 min (minor).

(*S*)-2-methyl-2-(2-nitro-1-phenylethyl)-malonic acid bis-4-methylphenyl dithioester **(3r)**



3r

Following the general procedure C with nitroolefin **1a** (35.7 mg, 0.24 mmol), *S*,*S*'-2-methyl-bis (4-methylphenyl) dithiomalonate **2c** (52.8 mg, 0.16 mmol) and catalyst **QD-SQA** (5.2 mg, 5 mol %), the reaction was completed in 3 days at r.t.. After column chromatography, the desired product was obtained as a white solid (65.9 mg, 86% yield, 74% ee). Analytical data are consistent with reported values.[2]

R_f : 0.41 (petroleum ether:ethyl acetate (*v*/*v*), 20/1).

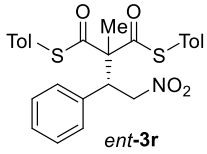
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.31 (m, 3H), 7.30-7.27 (m, 4H), 7.26-.22 (m, 6H), 5.05 (dd, *J* = 13.7, 11.2 Hz, 1H), 4.89 (dd, *J* = 13.8, 3.1 Hz, 1H), 4.32 (dd, *J* = 11.1, 3.0 Hz, 1H), 2.39 (d, *J* = 10.9 Hz, 6H), 1.72 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.8, 197.1, 140.6, 140.5, 134.8, 134.6, 134.4, 130.5, 130.3, 129.7, 128.8, 128.6, 122.9, 122.4, 77.1, 69.8, 49.9, 21.4, 21.4, 20.2 ppm.

HPLC Chiracel OD-H column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 6.23 min (minor), t_R= 7.31 min (major).

$[\alpha]^{20}_D$ = -27.7 (c = 1.0, $CHCl_3$). [lit.[2] **$[\alpha]^{20}_D$** = -23.9 (c = 1.0, $CHCl_3$; 63% ee)].

(*R*)-2-methyl-2-(2-nitro-1-phenylethyl)-malonic acid bis-4-methylphenyl dithioester **(*ent*-3r)**



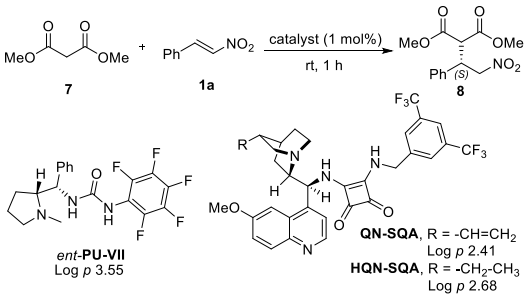
ent-**3r**

Following the general procedure C with nitroolefin **1a** (35.7 mg, 0.24 mmol), *S*,*S*'-2-methyl-bis (4-methylphenyl) dithiomalonate **2c** (52.8 mg, 0.16 mmol) and catalyst **QN-SQA** (5.1 mg, 5 mol %), the reaction was completed in 6 h at r.t., to give the desired product as a white solid (68.9 mg, 90% yield, 60% ee).

Analytical data (**R_f**, **^{1}H NMR**, **^{13}C NMR**) are consistent with that of **3r**.

HPLC Chiracel OD-H column, *i*-PrOH/*n*-hexane = 30/70, 25 °C, 1.0 mL/min, λ= 254 nm, t_R= 7.51 min (minor), t_R= 6.08 min (major).

9. Catalyst evaluation in the Michael addition of dimethyl malonate to nitrostyrene



General Procedure D

To a 3 mL vial equipped with a Teflon-coated magnetic stirring bar, nitroolefin **1a** (35.7 mg, 0.24 mmol, 1.5 equiv.), brine (1.5 mL) and toluene (10 equiv.) were added. The catalyst (1 mol %) and dimethyl malonate **7** (18.3 μL, 0.16 mmol, 1.0 equiv.) were added to the reaction mixture successively. The reaction mixture was vigorously stirred at room temperature for 1 h. Upon completion of the reaction (monitored by TLC), the solvent was evaporated under reduced pressure and the resulting residue was purified via column chromatography on silica gel to yield white solid products **8**.

The data of yields and ee values are shown in **Table S4**.

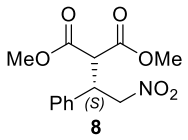
Table S4. Catalyst evaluation in the Michael addition of dimethyl malonate to nitrostyrene.[a]

entry	additive	cat.(mol%)	yield (%)[b]	ee (%)[c]
1[d]	-	**QN-SQA**	34	90
2[d]	-	**HQN-SQA**	99	92
3	toluene	*ent*-**PU-VII**	NR	-
4	toluene	**QN-SQA**	90	96

5	toluene	**HQN-SQA**	86	94

[a]The reactions were conducted using **7** (0.16 mmol, 1 equiv.), **1c** (0.24 mmol, 1.5 equiv.), cat. (1 mol%), and toluene (10 equiv.) in 1.5 mL of brine. [b]Isolated yield. [c]ee was determined using HPLC. [d]The data are collected from ref. 5.

dimethyl (*S*)-2-(2-nitro-1-phenylethyl)malonate **(8)**



8

Following the general procedure D with catalyst **QN-SQA** (1.0 mg, 1 mol%), the reaction was completed in 1 h at r.t.. After column chromatography, the desired product was obtained as a white solid (40.5 mg, 90% yield, 96% ee). Analytical data are consistent with reported values.[5,6]

$\mathbf{R}_f$ =0.2 (petroleum ether:ethyl acetate (*v*/*v*), 10/1).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 3H), 7.24-7.20 (m, 2H), 4.90 (qd, *J* = 13.2, 7.0 Hz, 2H), 4.24 (td, *J* = 9.0, 5.2 Hz, 1H), 3.87 (d, *J* = 9.1 Hz, 1H), 3.75 (s, 3H), 3.55 (s, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 167.3, 136.2, 129.0, 128.4, 127.9, 77.4, 54.8, 53.0, 52.8, 43.0 ppm.

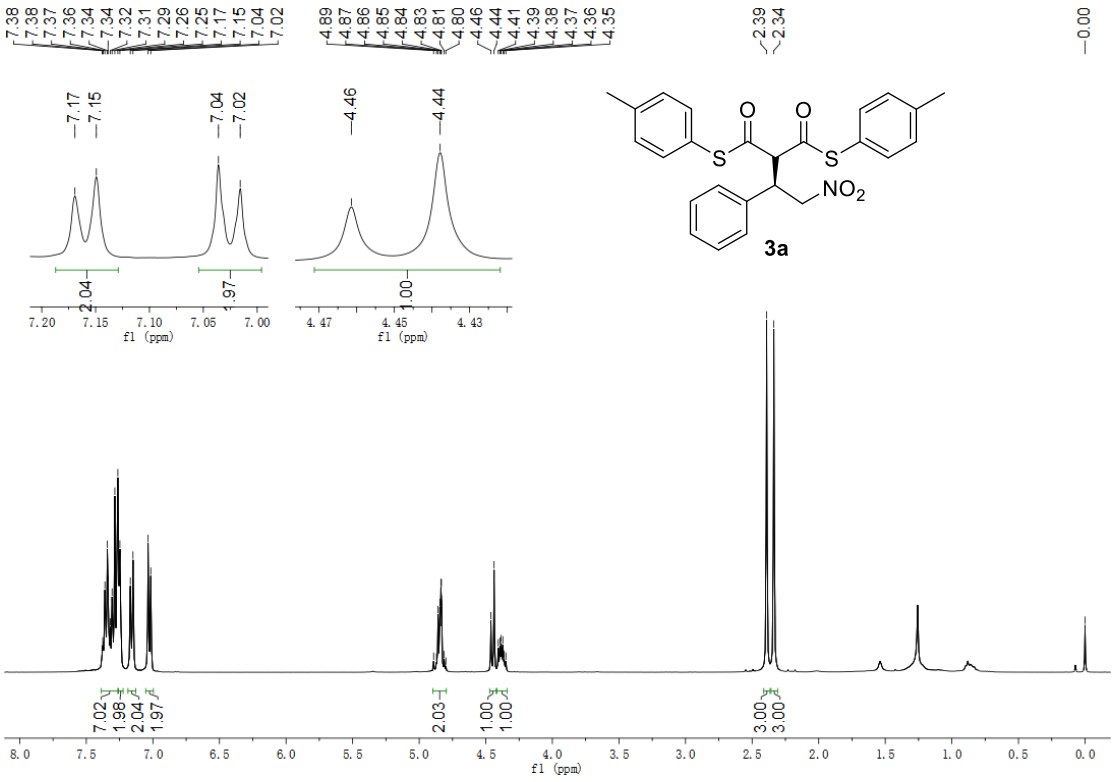
HPLC Chiracel OD-H column, *i*-PrOH/*n*-hexane = 10/90, 25 °C, 1.0 mL/min, λ= 220 nm, t_R= 27.21 min (major), t_R= 30.78 min (minor).

$[\alpha]^{20}_D$ = +5.8 (c = 1.0, $CHCl_3$; 96% ee). [lit.[6] **$[\alpha]^{20}_D$** = + 5.58 (c = 1.0, $CHCl_3$; 95% ee)].

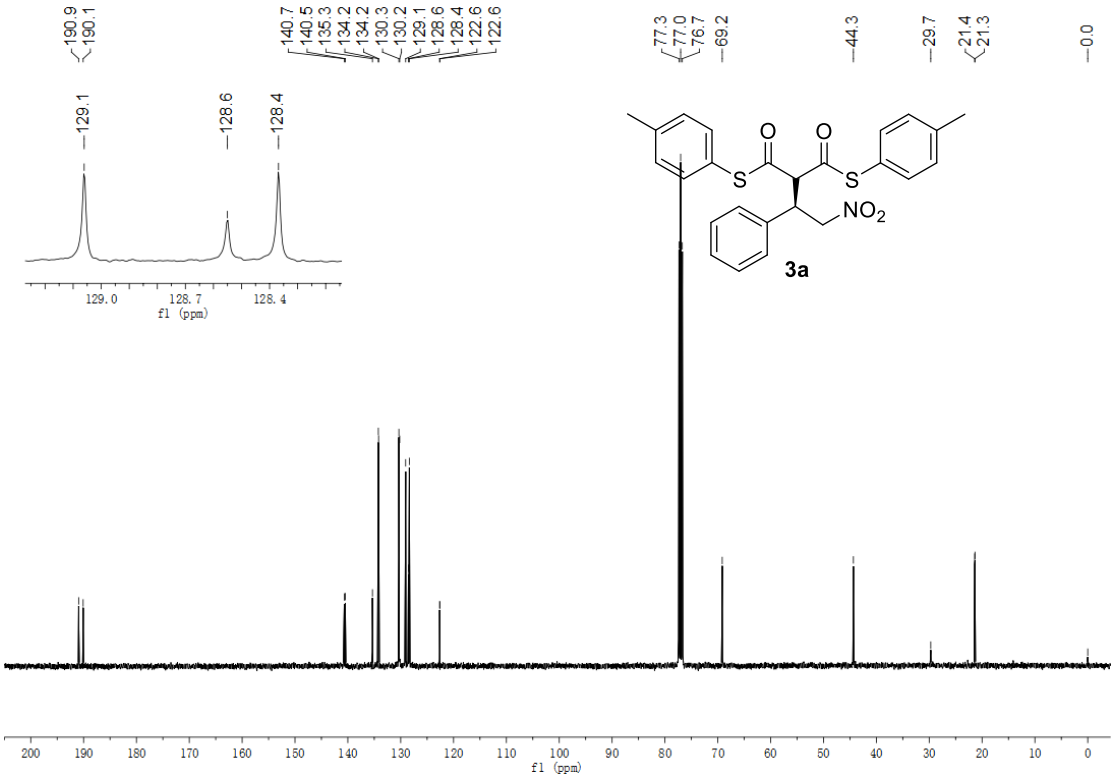
10. References

1. Jin, H.; Kim, S. T.; Hwang, G. S.; Ryu, D. H. *L*-Proline Derived Bifunctional Organocatalysts: Enantioselective Michael Addition of Dithiomalonates to trans-*β*-Nitroolefifins. *J. Org. Chem*. **2016**, *81*, 3263-3274.
2. Wang, B.; Li, T.; Liu, J.; Wang, S.; Shi, H.; Jin, H.; Ryud, D. H.; Zhang, L. Pentafluorophenyl-substituted Proline-derived Chiral Urea for "on Water" Asymmetric Hydrogen-bonding Catalysis. *Adv. Synth. Catal.* **2023**, *365*, 4155-4162.
3. Malerich, J. P.; Hagihara, K.; Rawal, V. H. Chiral squaramide derivatives are excellent hydrogen bond donor catalysts. *J. Am. Chem. Soc.* **2008**, *130*, 14416-14417.
4. Okino, T.; Hoashi, Y.; Furukawa, T.; Xu, X. N.; Takemoto, Y. Enantio- and Diastereoselective Michael Reaction of 1,3-Dicarbonyl Compounds to Nitroolefins Catalyzed by a Bifunctional Thiourea. *J. Am. Chem. Soc.* **2005**, *127*, 119-125.
5. Bae, H. Y.; Song, E. S. Unprecedented Hydrophobic Amplification in Noncovalent Organocatalysis "on Water": Hydrophobic Chiral Squaramide Catalyzed Michael Addition of Malonates to Nitroalkenes. *ACS Catal.* **2015**, *5*, 3613-3619.
6. Zhang, L.; Lee, M.-M.; Lee, S.-M.; Lee, J.; Cheng, M.; Jeong, B.-S.; Park, H.-G.; Jew, S.-S. Novel Cinchona-Aminobenzimidazole Bifunctional Organocatalysts. *Adv. Synth. Catal*. **2009**, *351*, 3063-3066.

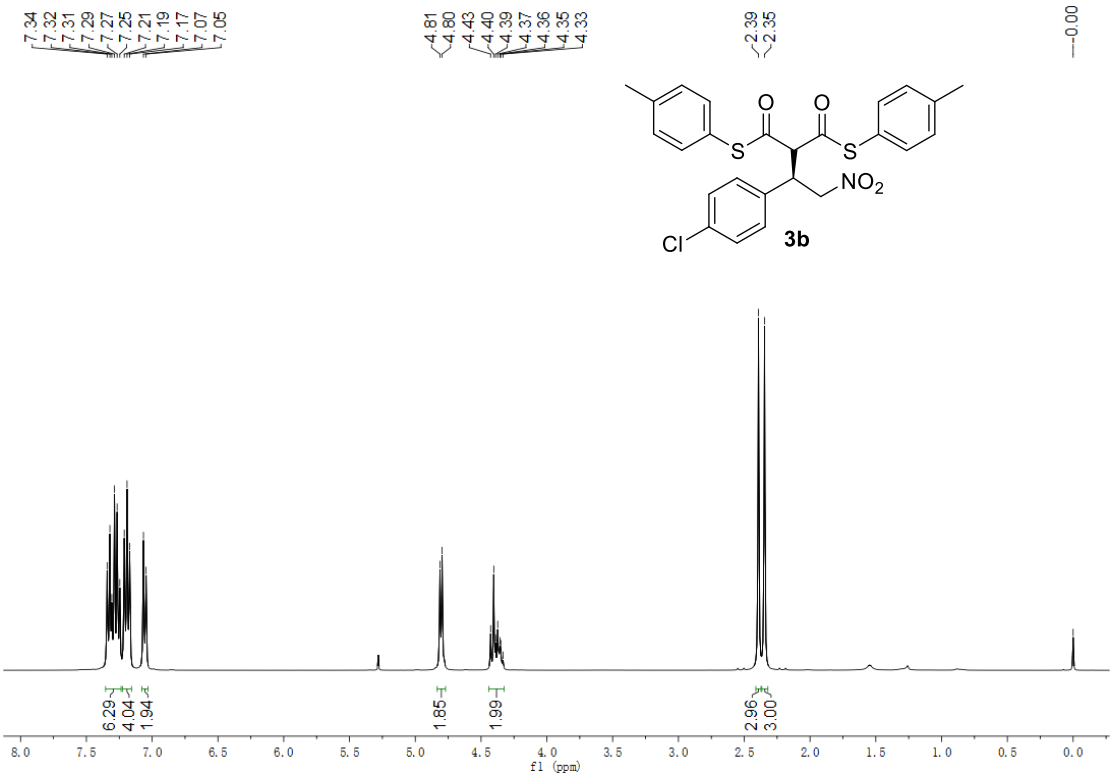
11. Copies of ^{1}H and ^{13}C NMR spectra



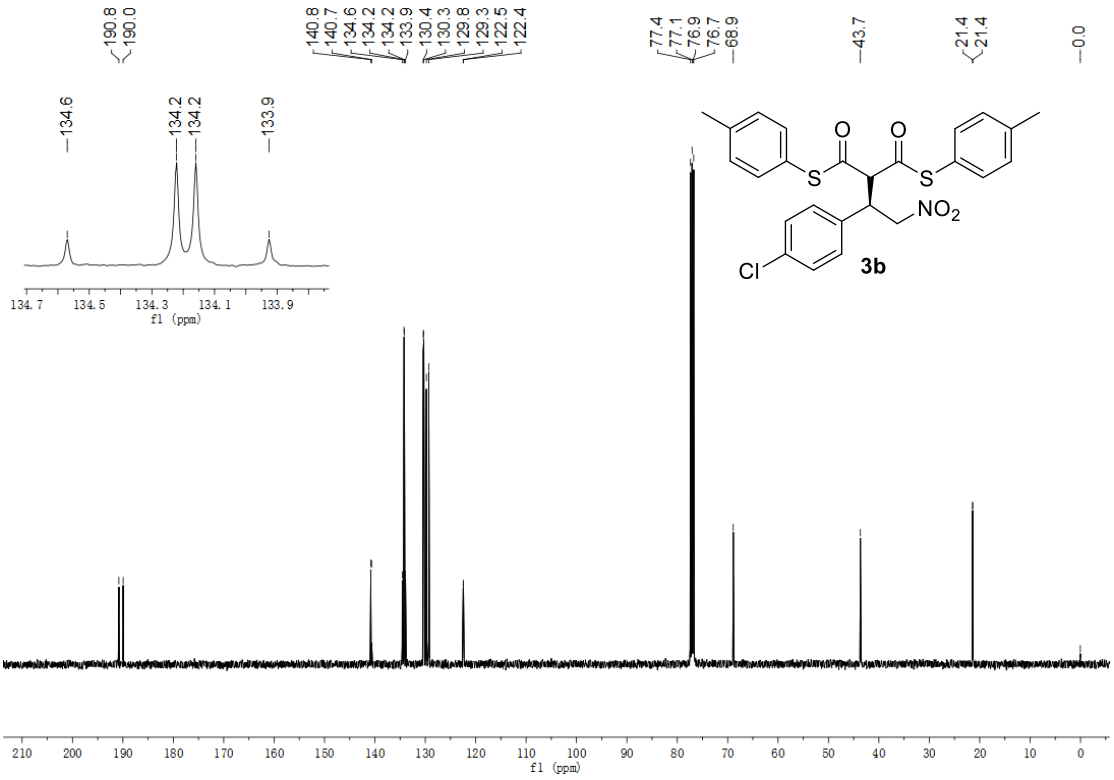
^{1}H NMR spectrum of compound **3a** (400 MHz, $CDCl_3$)



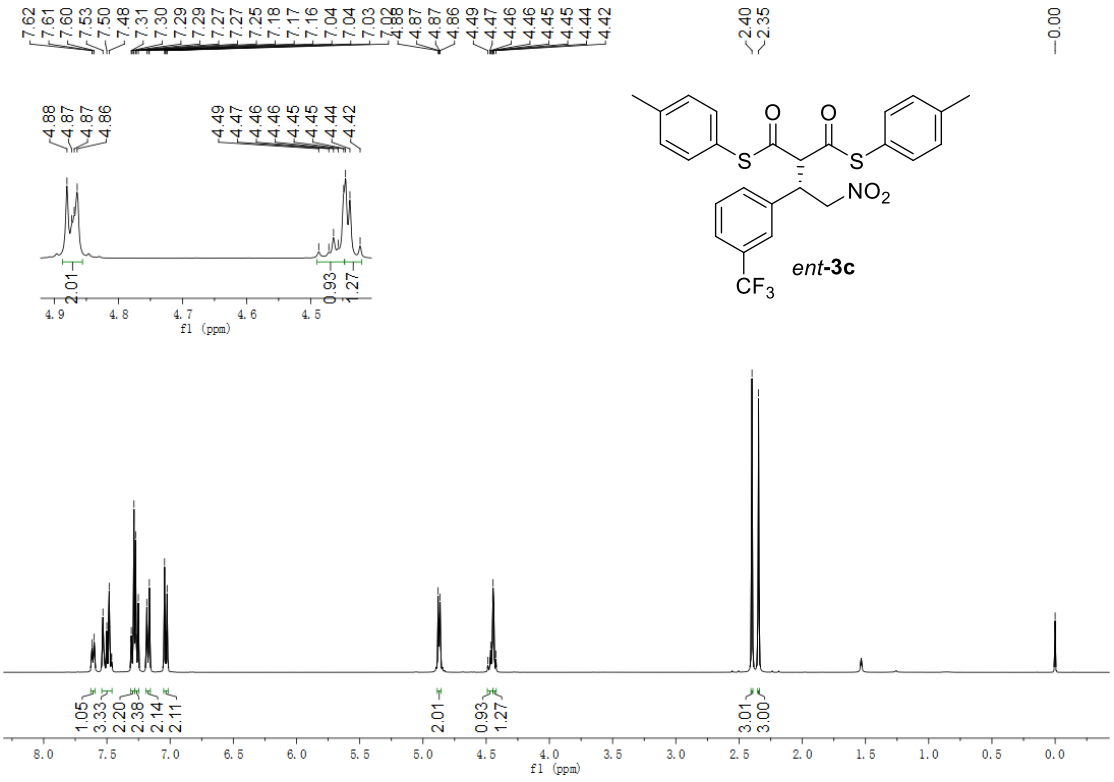
^{13}C NMR spectrum of compound **3a** (101 MHz, $CDCl_3$)



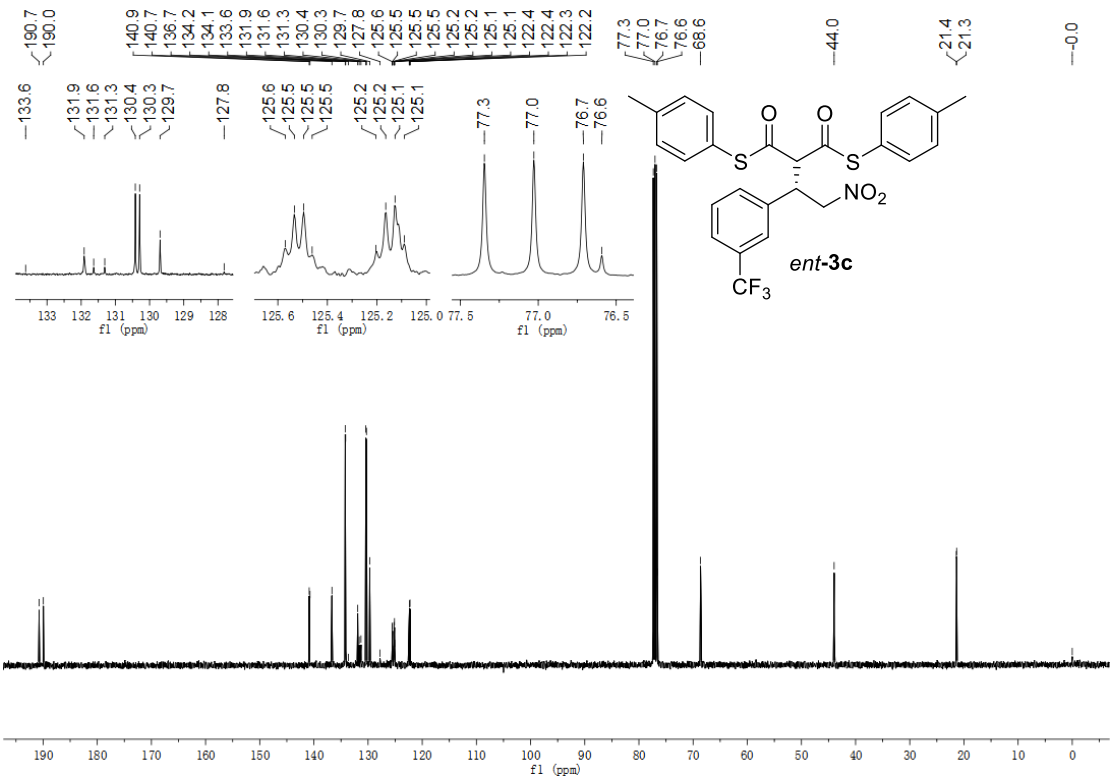
^{1}H NMR spectrum of compound **3b** (400 MHz, $CDCl_3$)



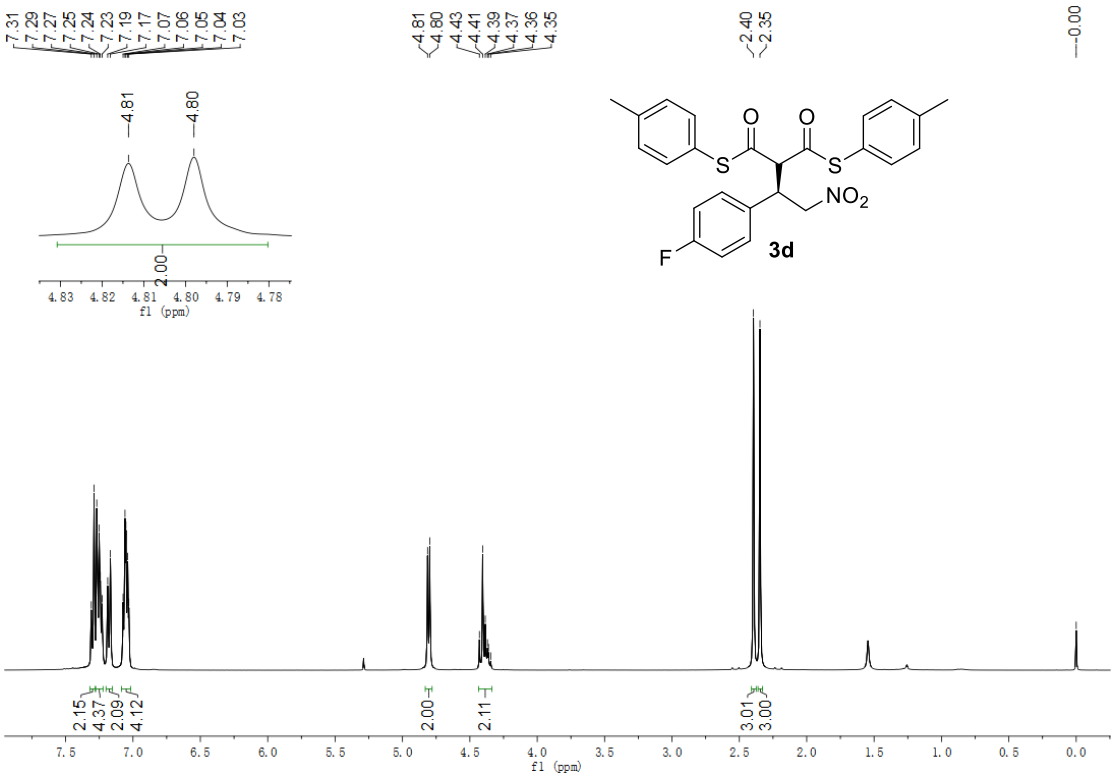
^{13}C NMR spectrum of compound **3b** (101 MHz, $CDCl_3$)



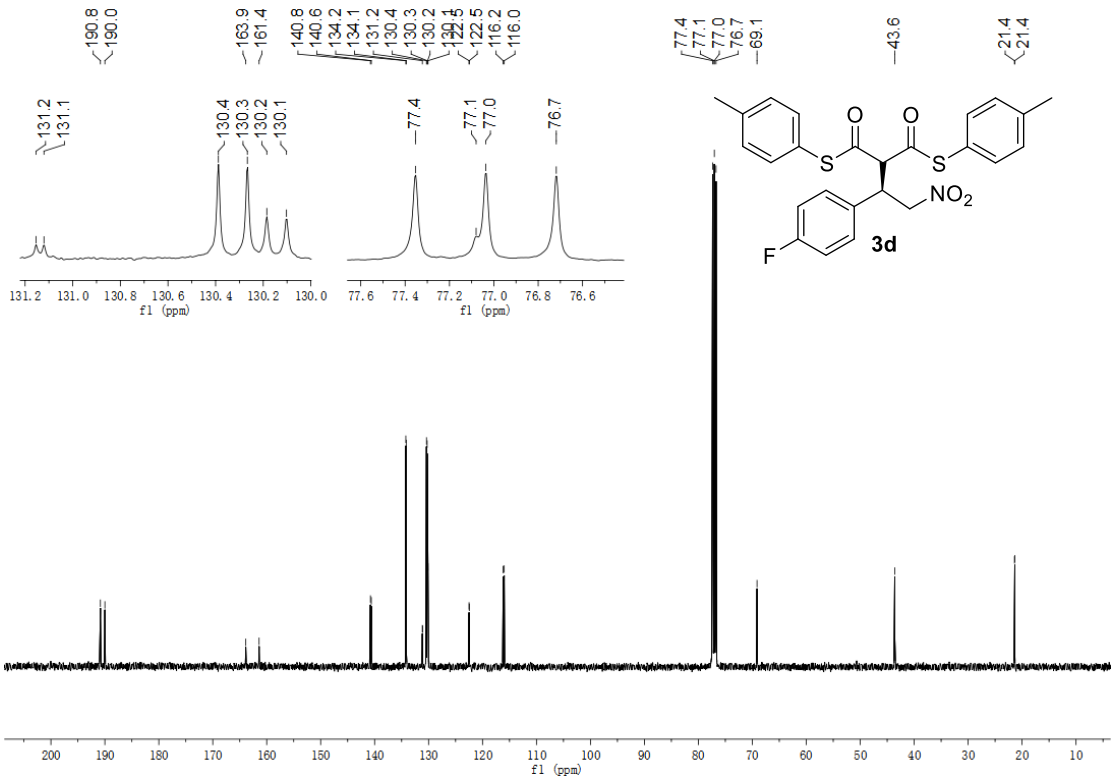
^{1}H NMR spectrum of compound **3c** (400 MHz, $CDCl_3$)



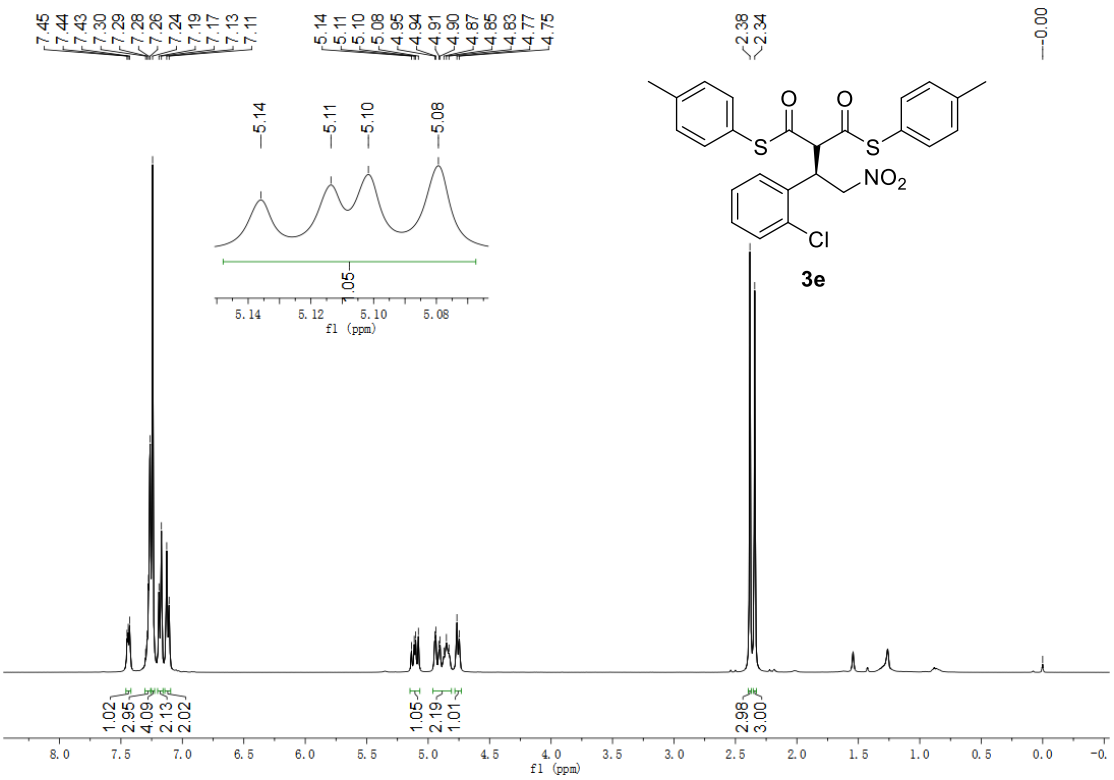
^{13}C NMR spectrum of compound **3c** (101 MHz, $CDCl_3$)



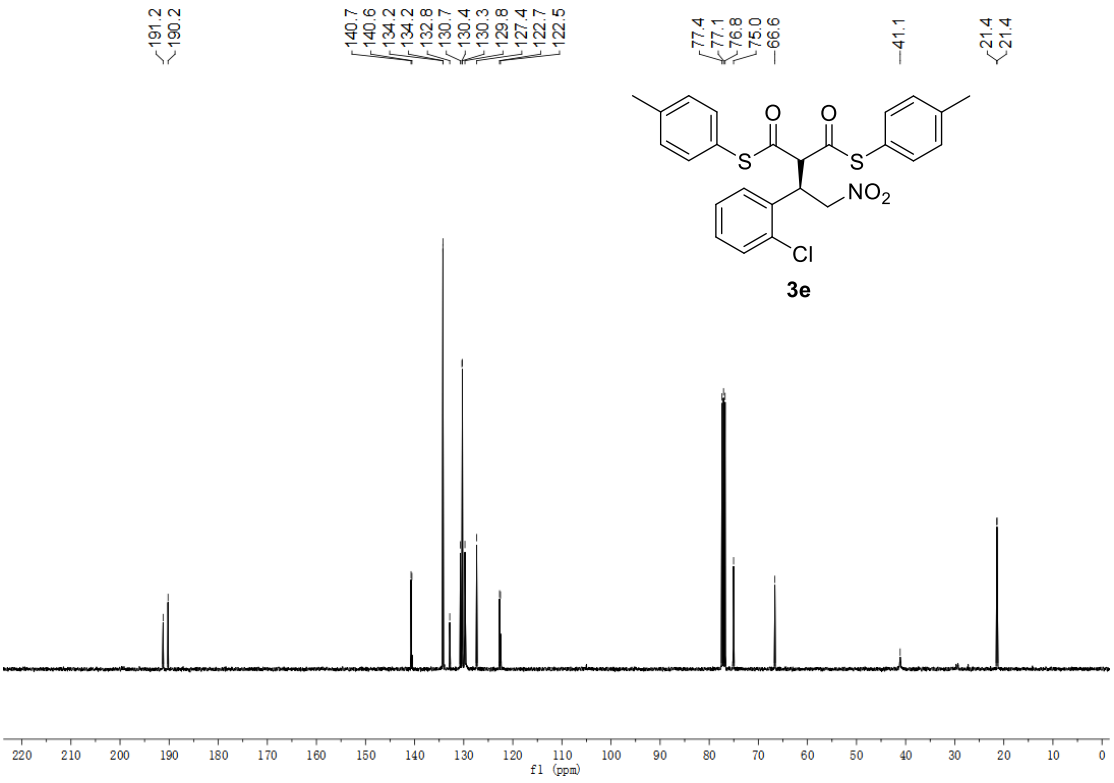
^{1}H NMR spectrum of compound **3d** (400 MHz, $CDCl_3$)



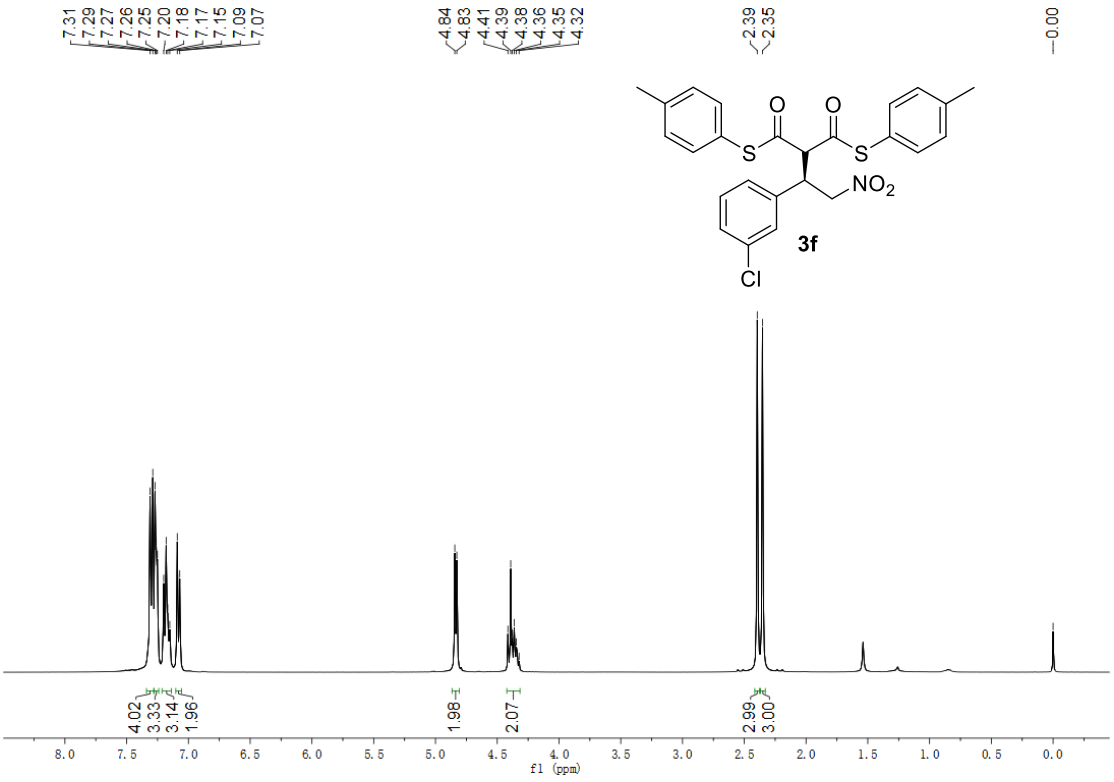
^{13}C NMR spectrum of compound **3d** (101 MHz, $CDCl_3$)



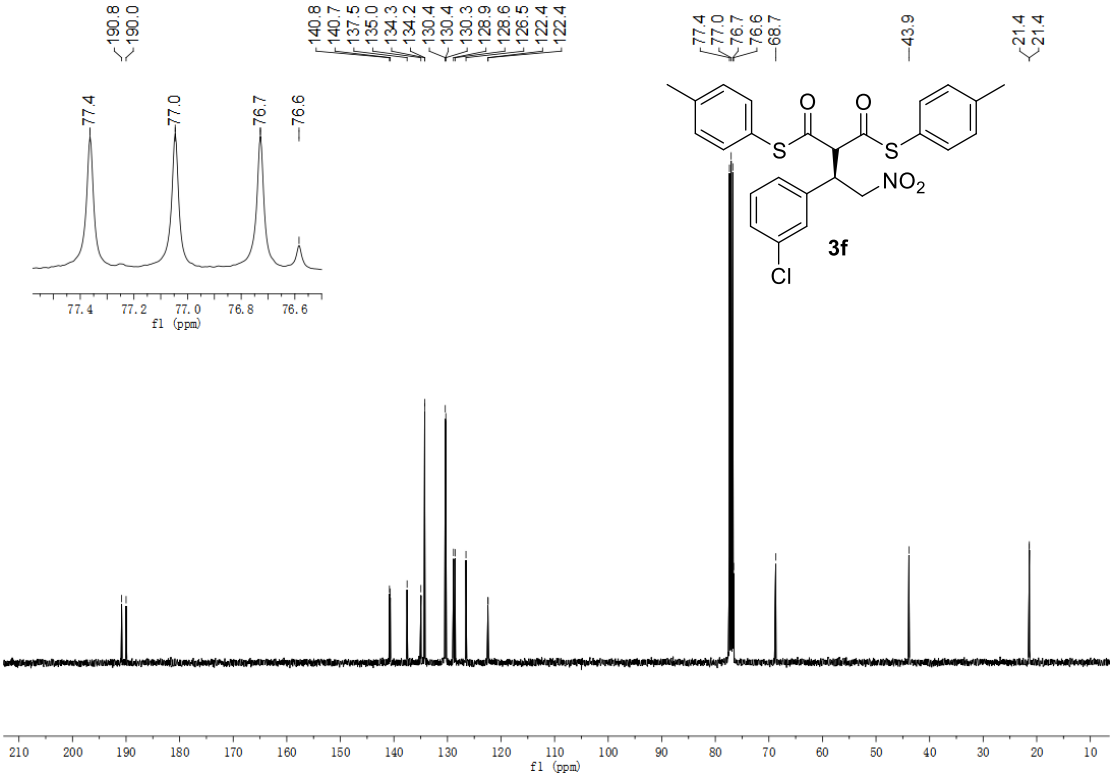
^{1}H NMR spectrum of compound **3e** (400 MHz, $CDCl_3$)



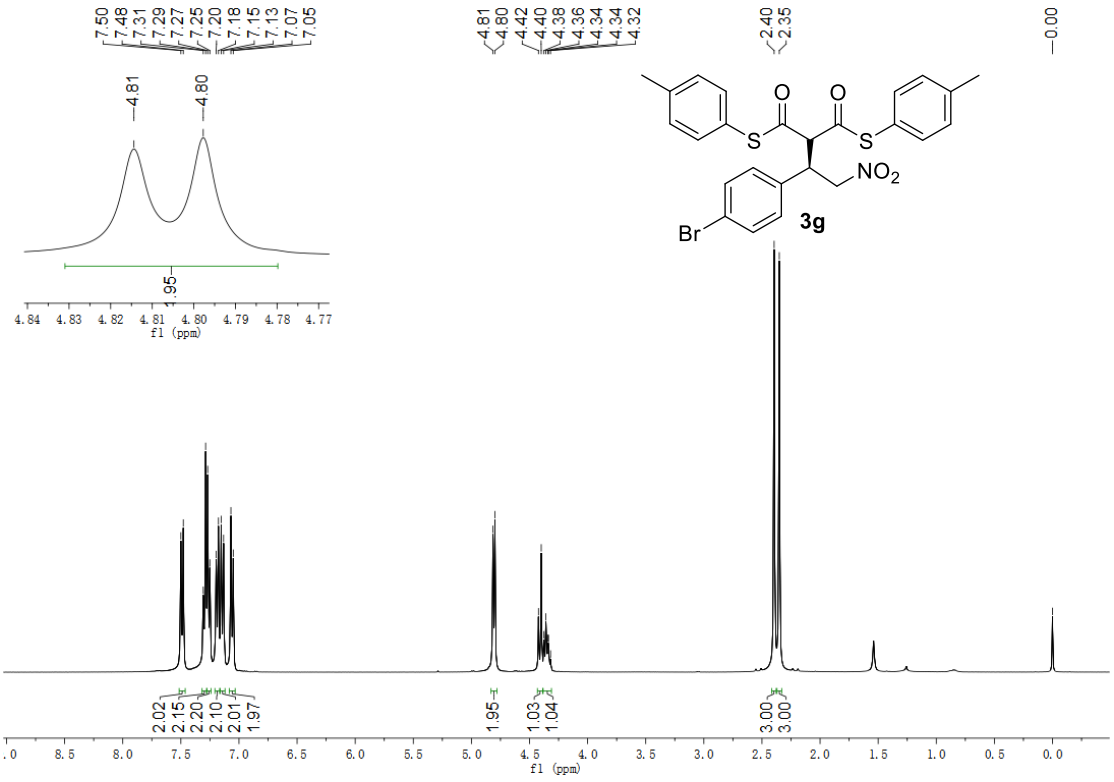
^{13}C NMR spectrum of compound **3e** (101 MHz, $CDCl_3$)



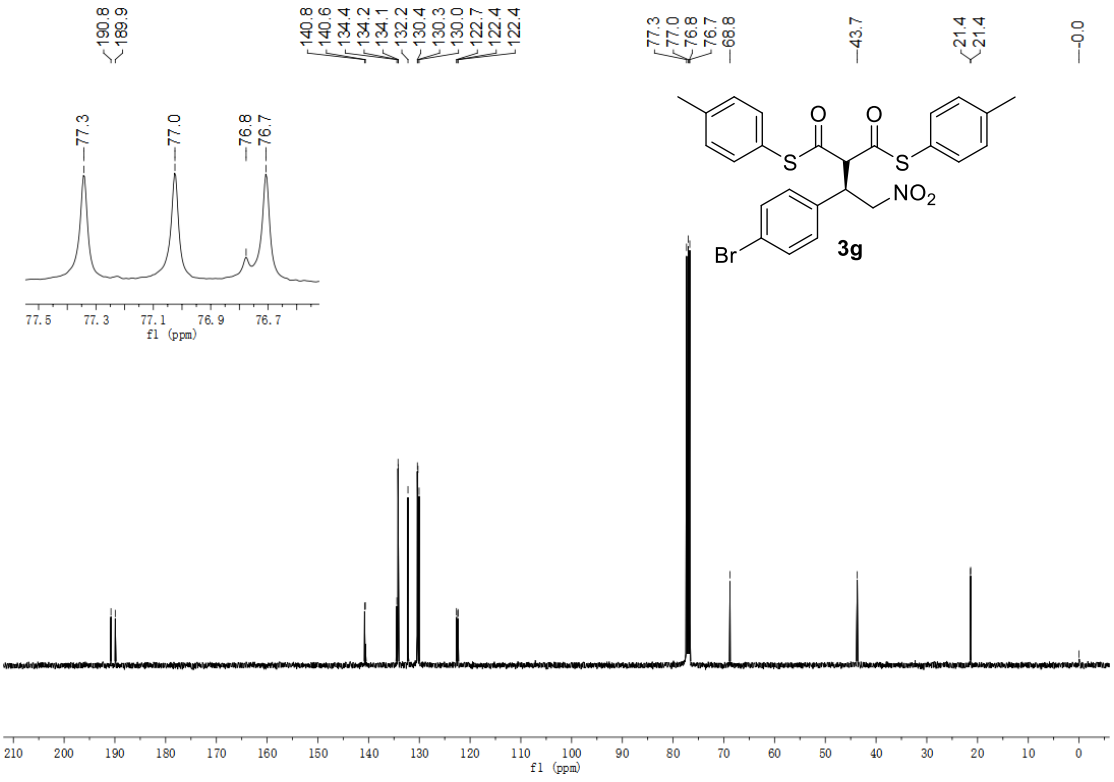
^{1}H NMR spectrum of compound **3f** (400 MHz, $CDCl_3$)



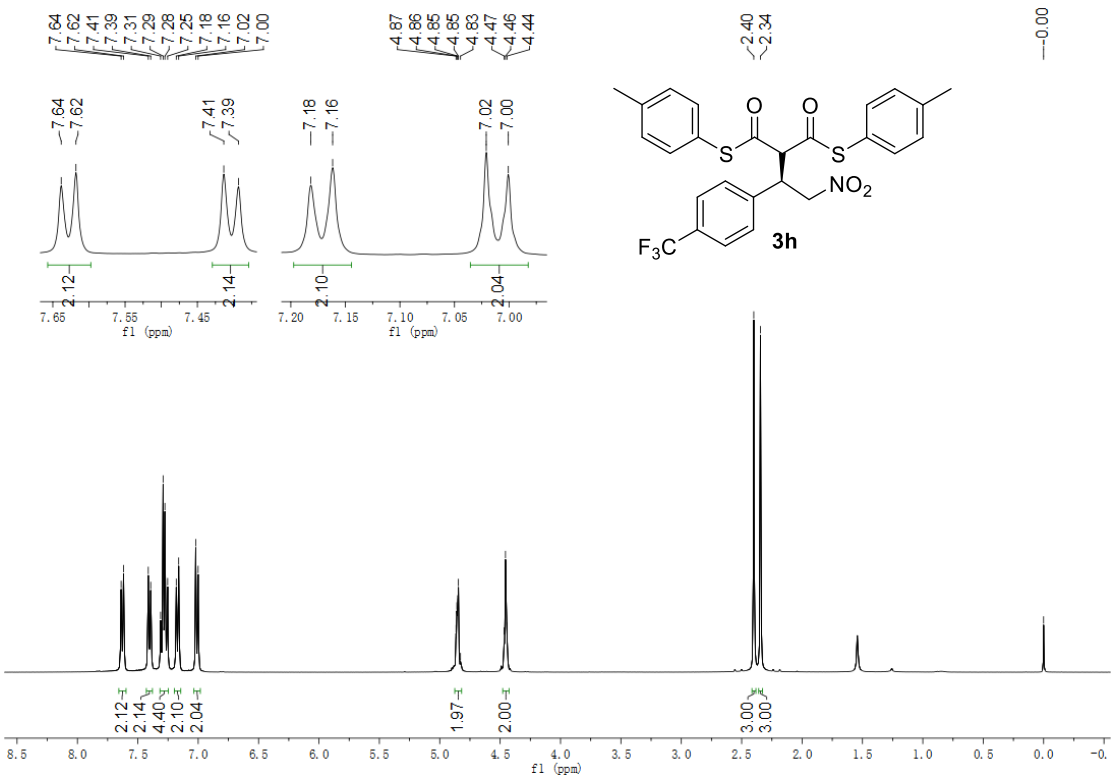
^{13}C NMR spectrum of compound **3f** (101 MHz, $CDCl_3$)



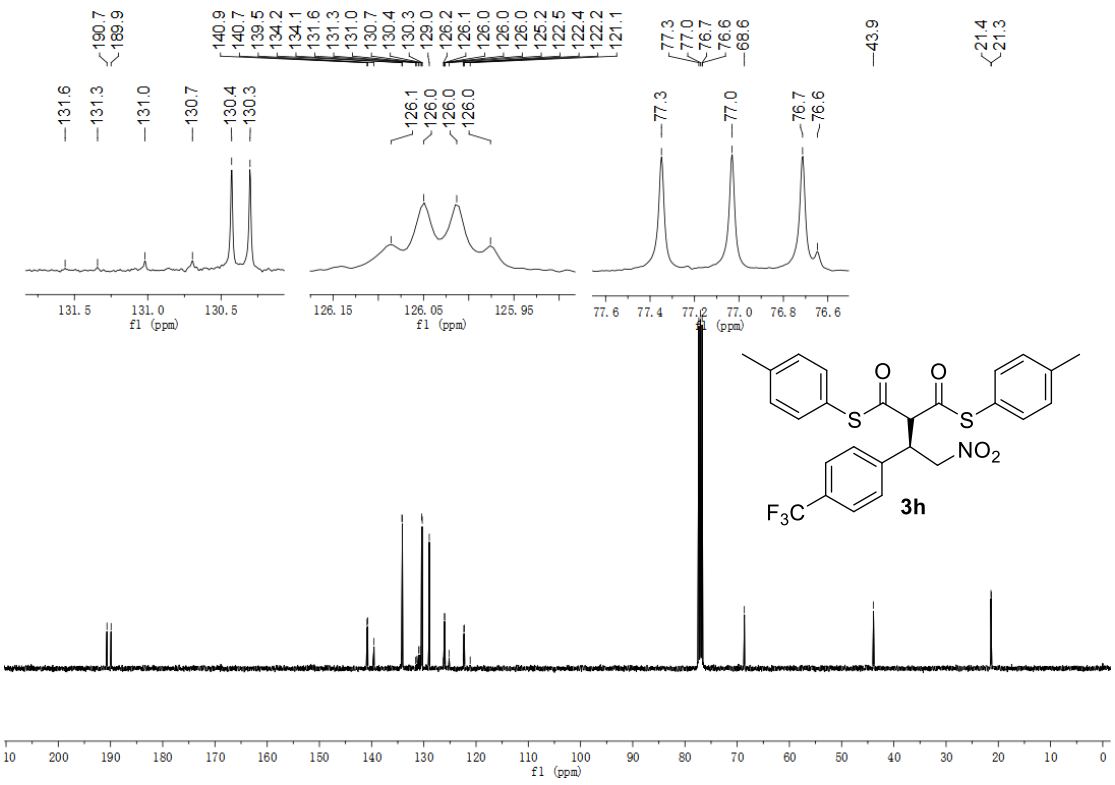
^{1}H NMR spectrum of compound **3g** (400 MHz, $CDCl_3$)



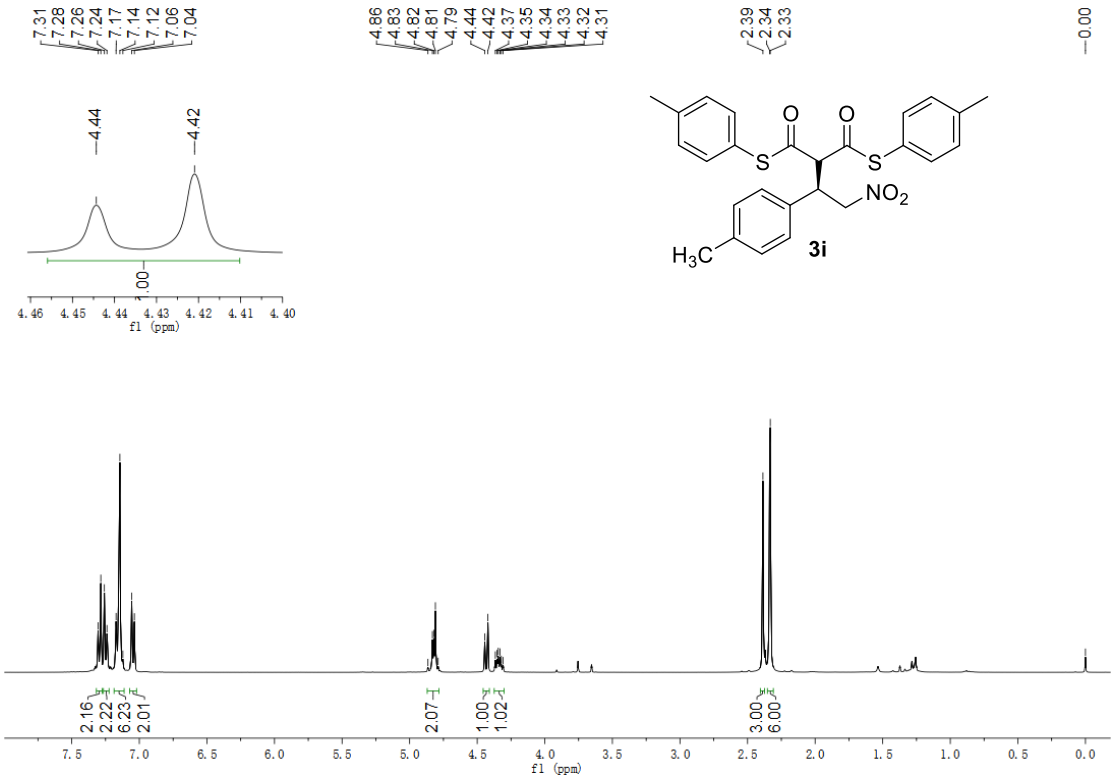
^{13}C NMR spectrum of compound **3g** (101 MHz, $CDCl_3$)



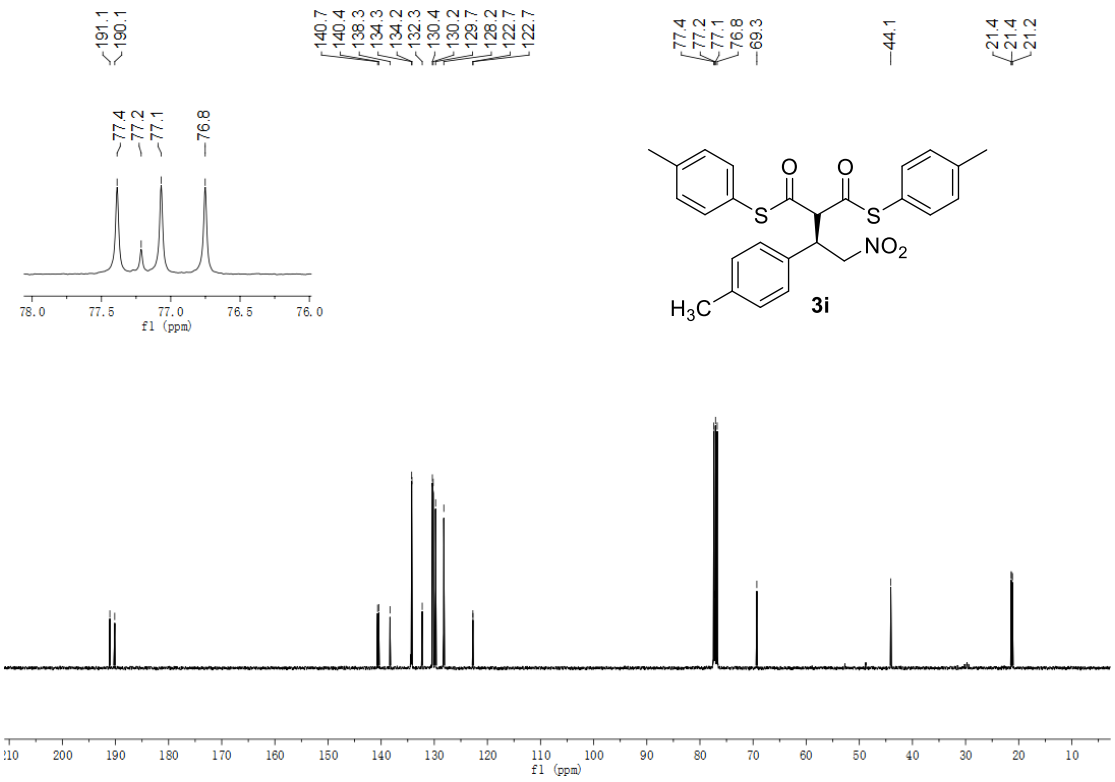
^{1}H NMR spectrum of compound **3h** (400 MHz, $CDCl_3$)



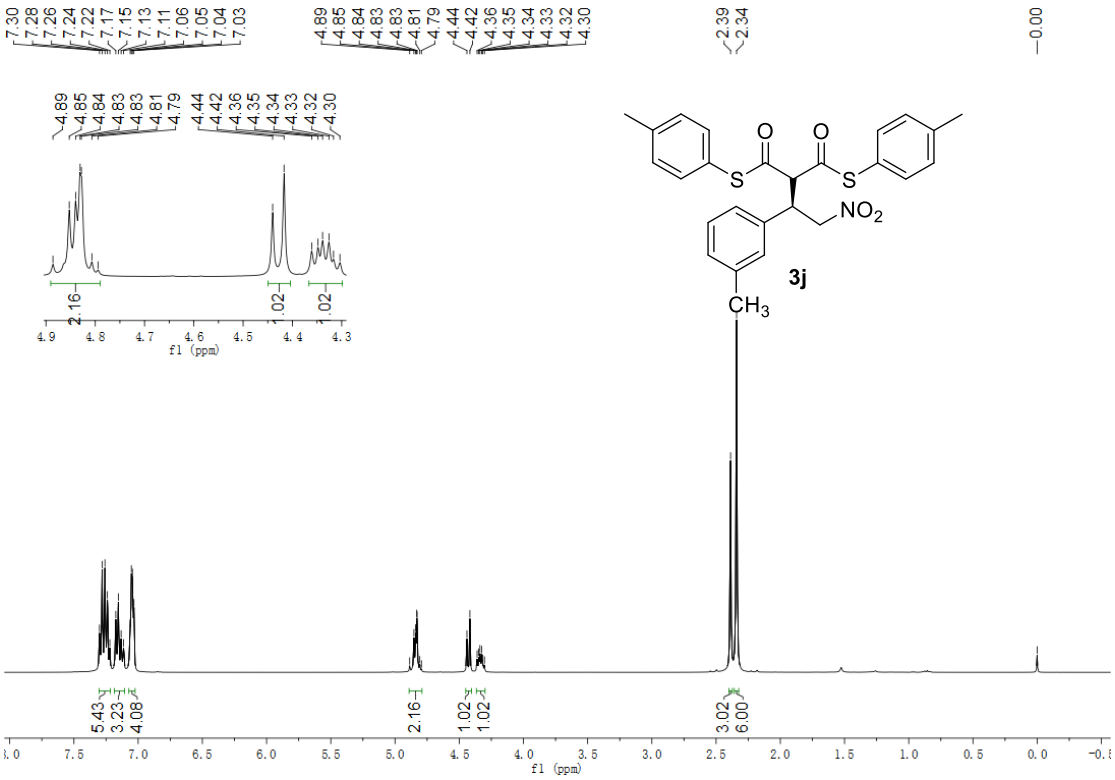
^{13}C NMR spectrum of compound **3h** (101 MHz, $CDCl_3$)



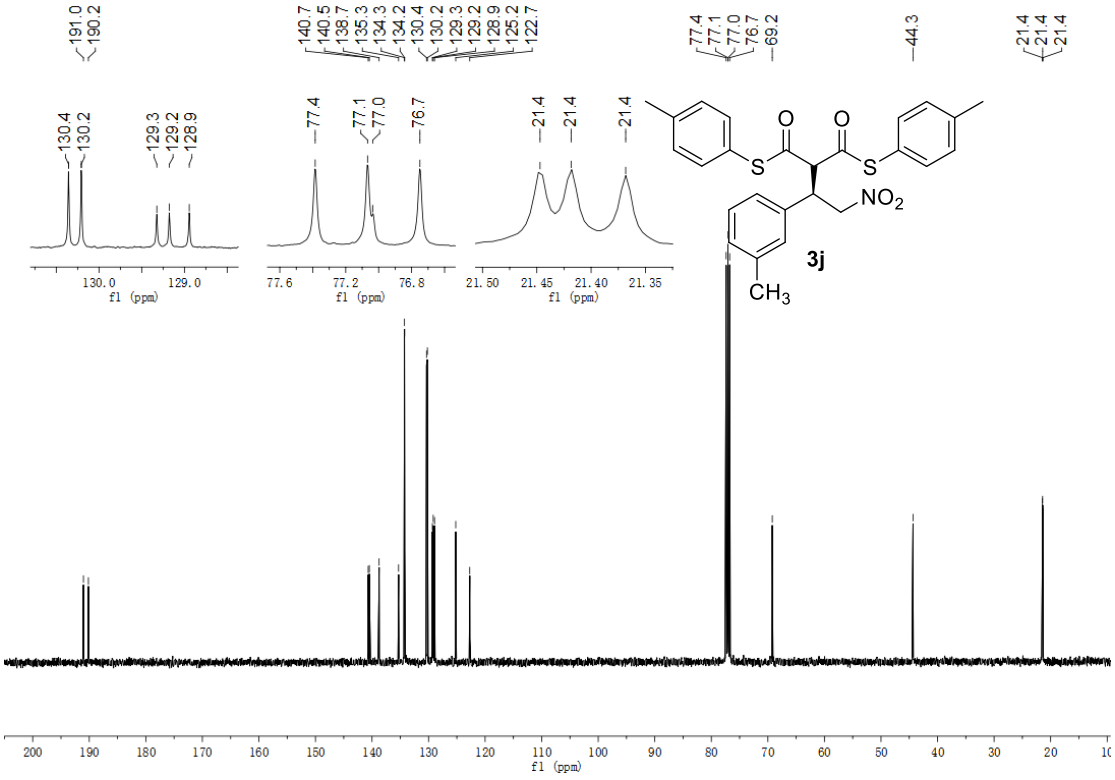
^{1}H NMR spectrum of compound **3i** (400 MHz, $CDCl_3$)



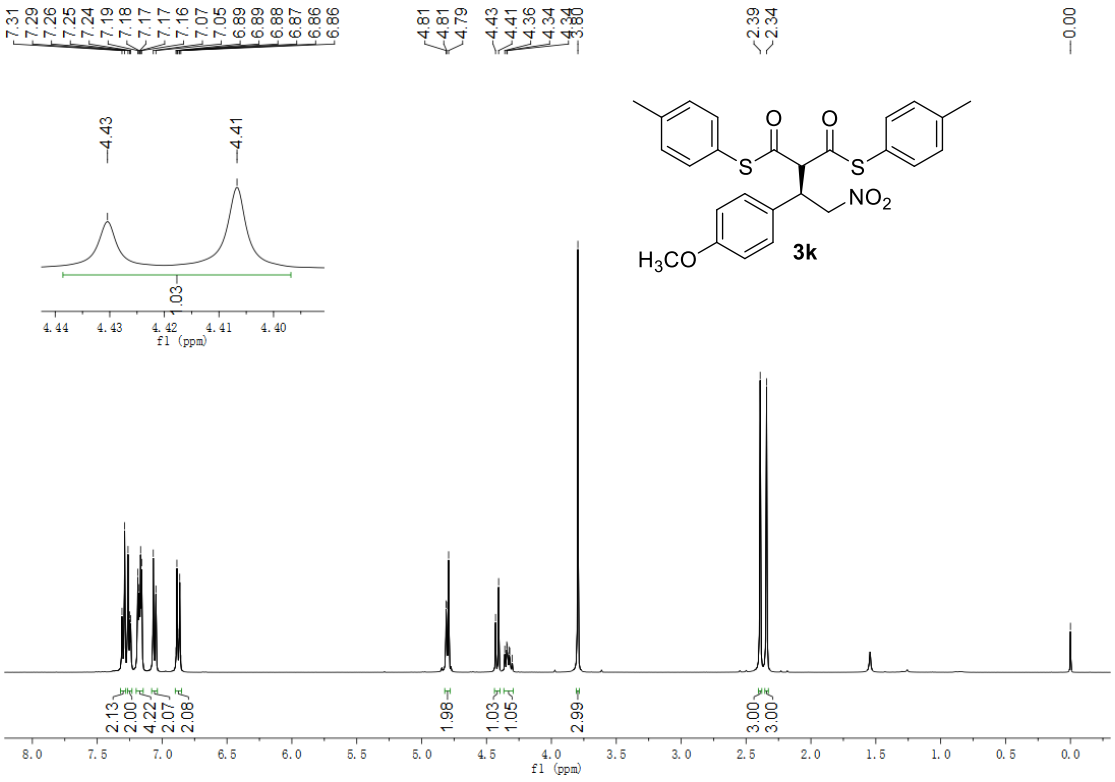
^{13}C NMR spectrum of compound **3i** (101 MHz, $CDCl_3$)



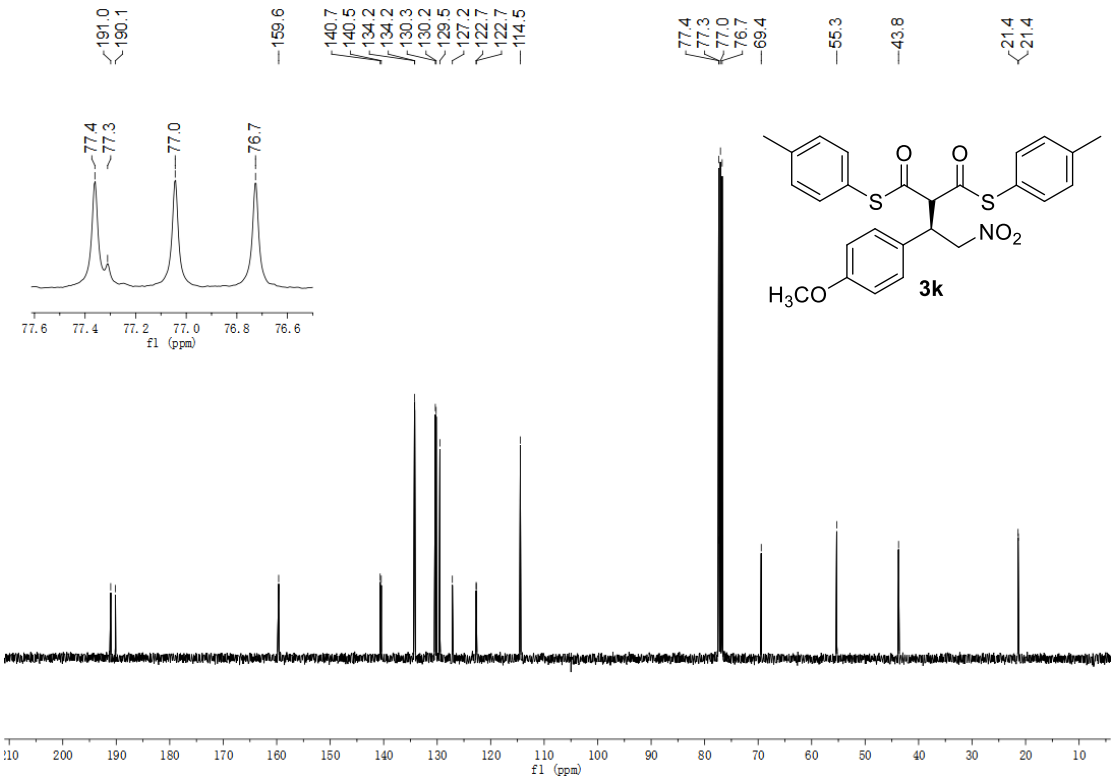
^{1}H NMR spectrum of compound **3j** (400 MHz, $CDCl_3$)



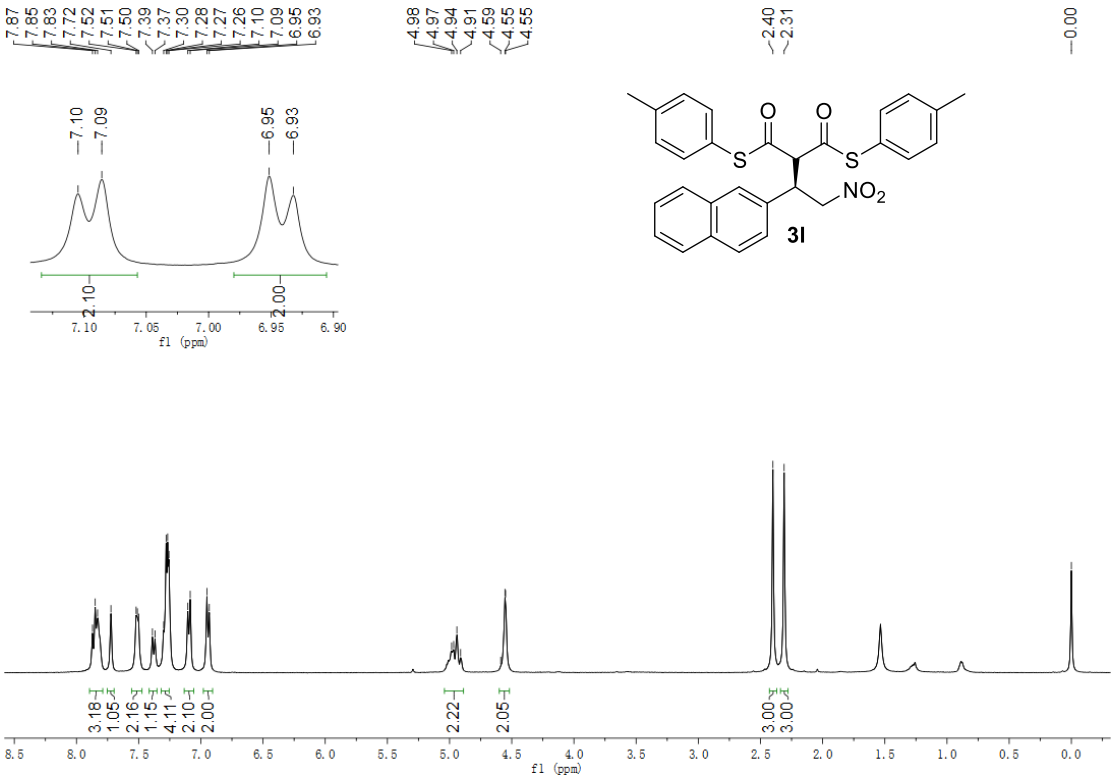
^{13}C NMR spectrum of compound **3j** (101 MHz, $CDCl_3$)



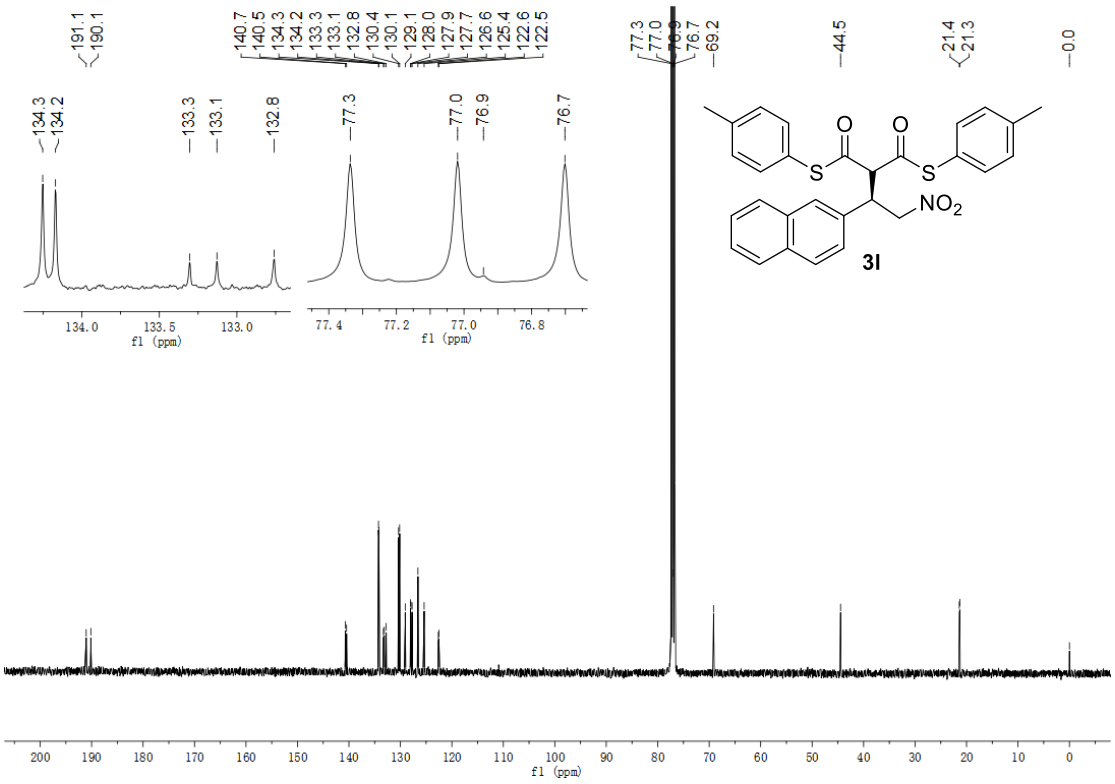
^{1}H NMR spectrum of compound **3k** (400 MHz, $CDCl_3$)



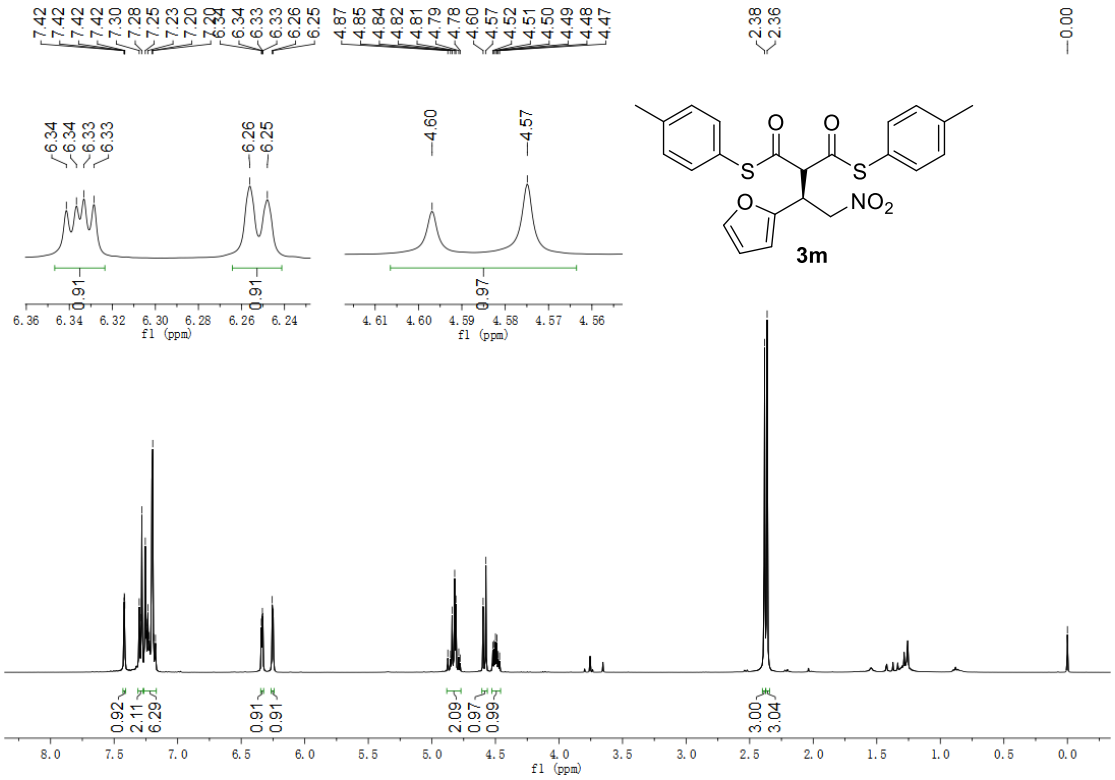
^{13}C NMR spectrum of compound **3k** (101 MHz, $CDCl_3$)



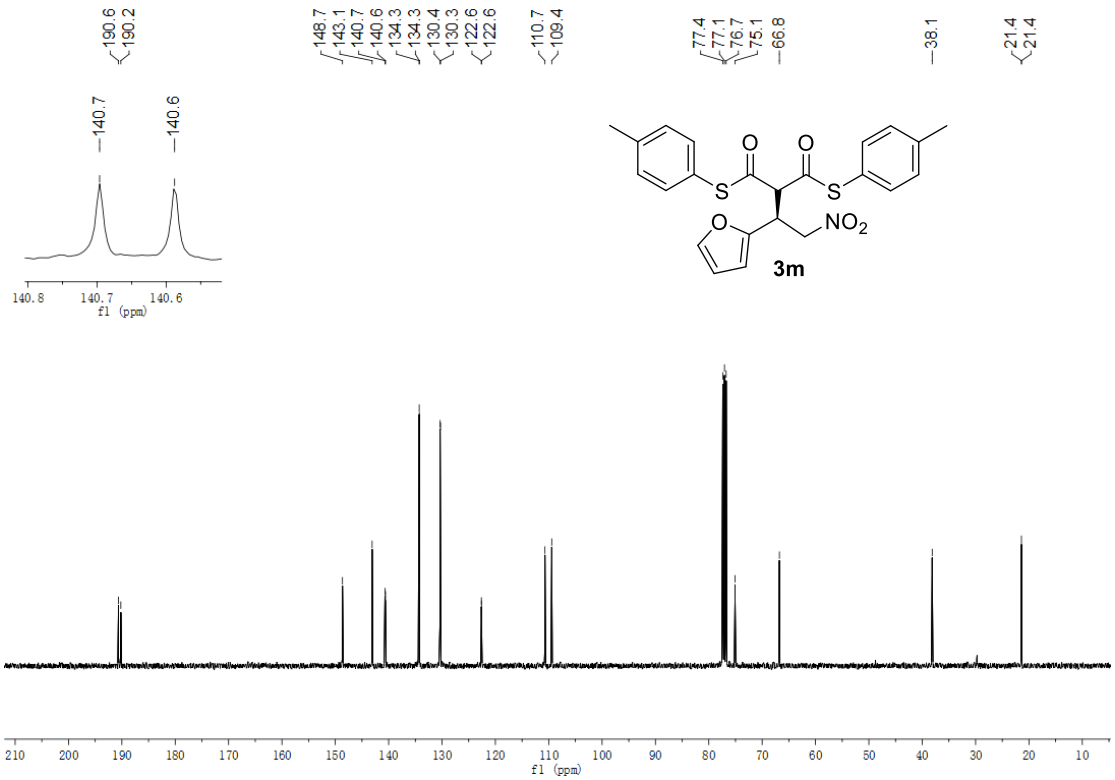
^{1}H NMR spectrum of compound **3l** (400 MHz, $CDCl_3$)



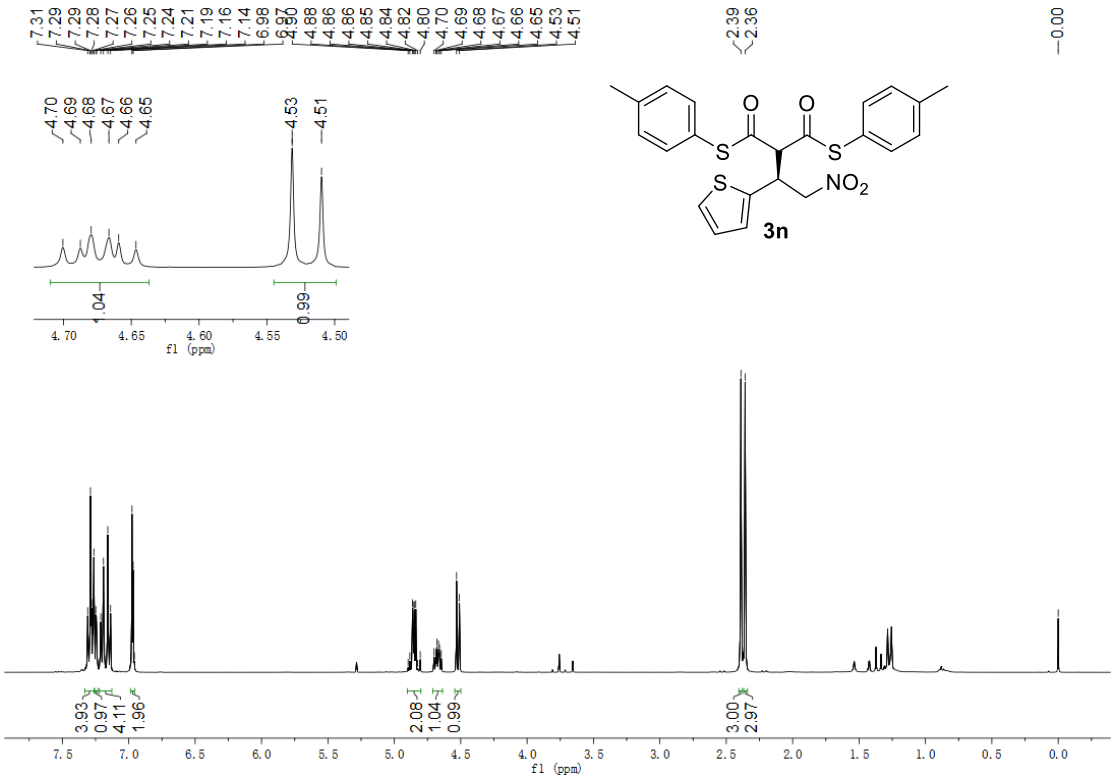
^{13}C NMR spectrum of compound **3l** (101 MHz, $CDCl_3$)



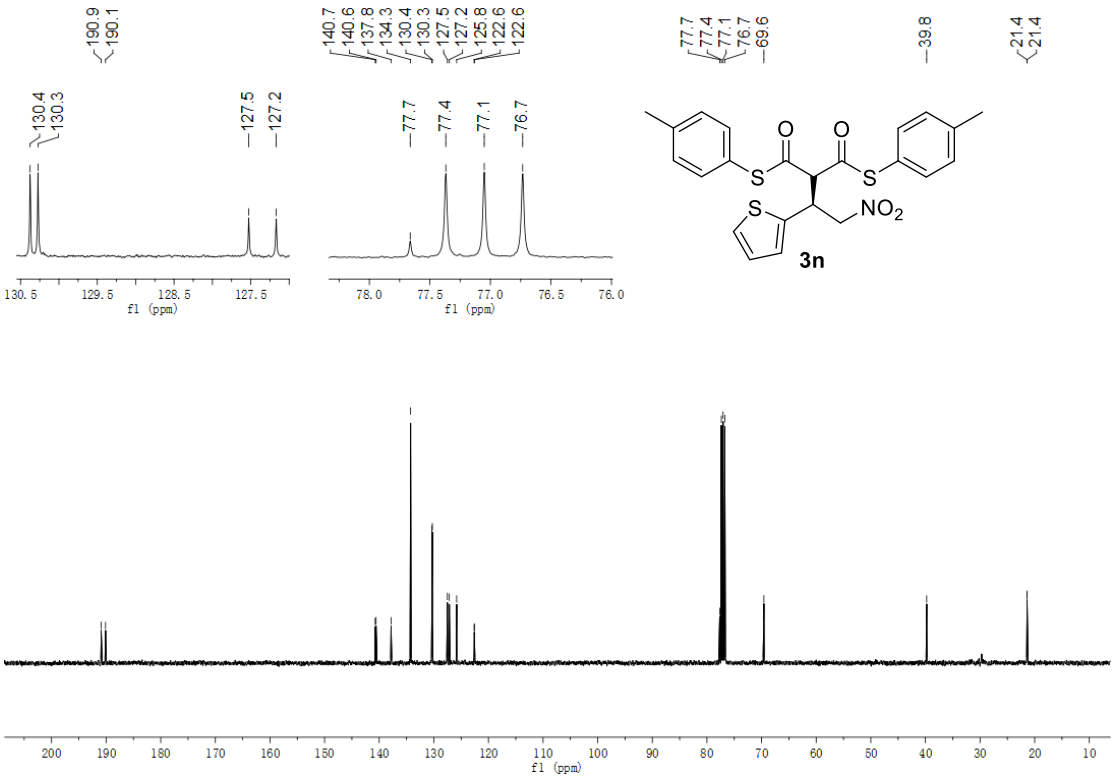
^{1}H NMR spectrum of compound **3m** (400 MHz, $CDCl_3$)



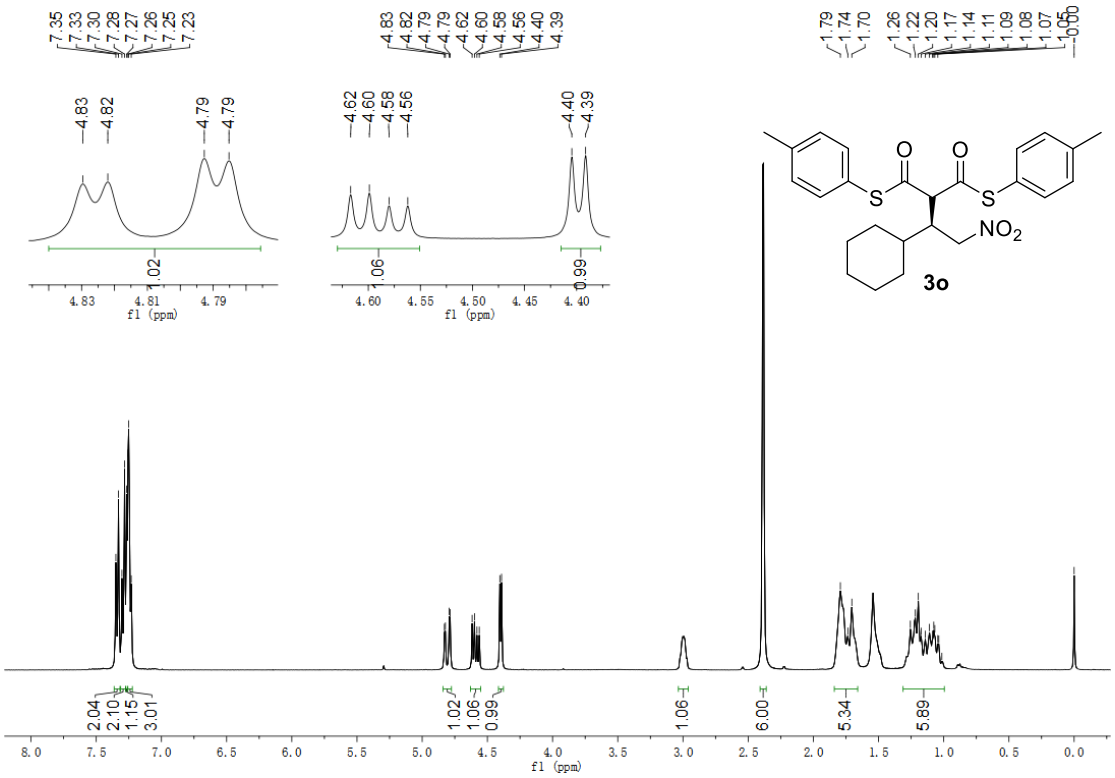
^{13}C NMR spectrum of compound **3m** (101 MHz, $CDCl_3$)



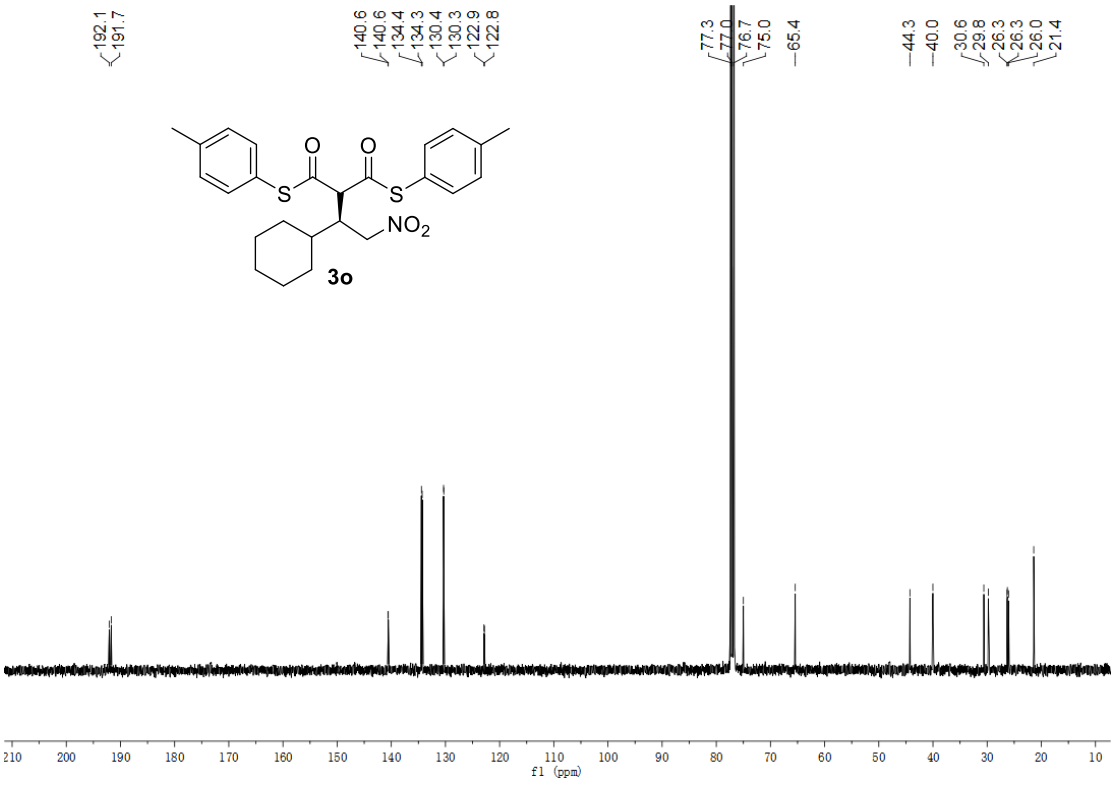
^{1}H NMR spectrum of compound **3n** (400 MHz, $CDCl_3$)



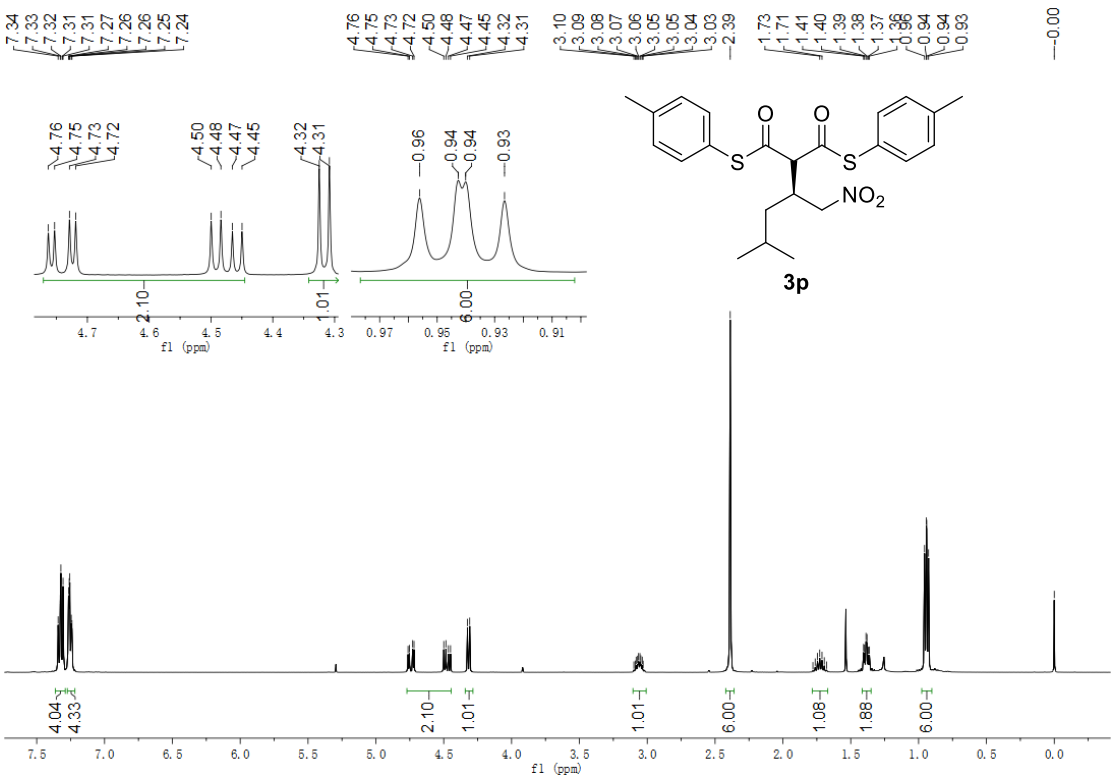
^{13}C NMR spectrum of compound **3n** (101 MHz, $CDCl_3$)



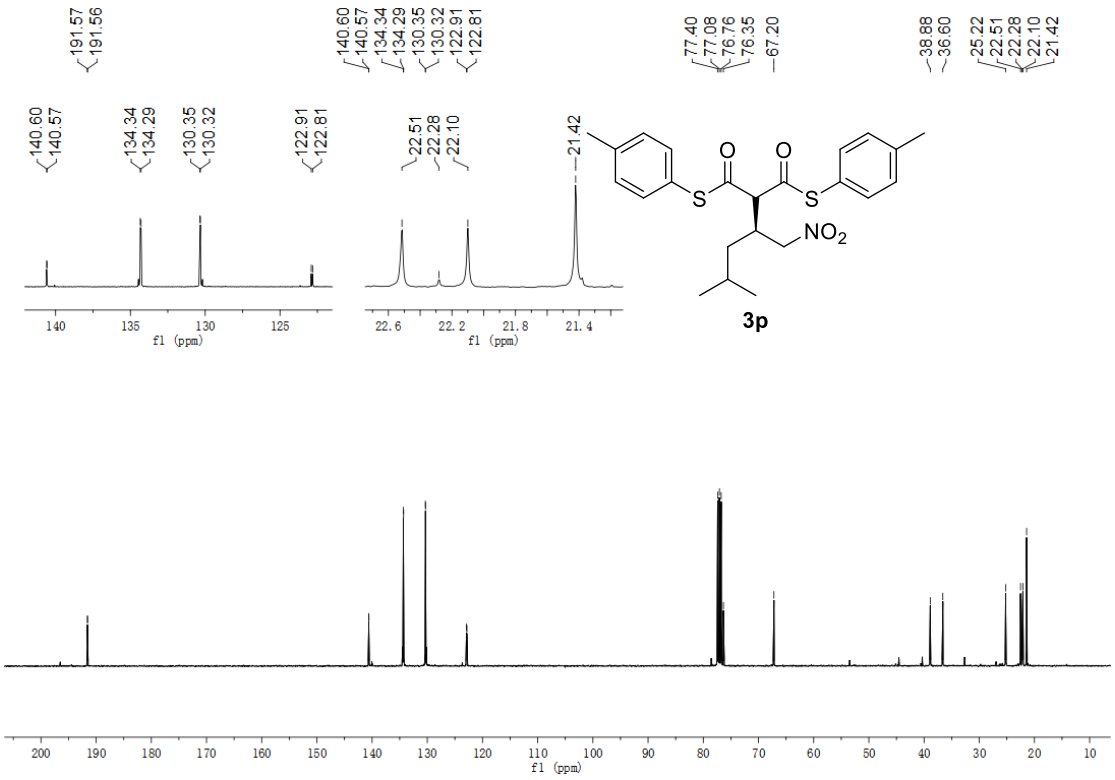
^{1}H NMR spectrum of compound **3o** (400 MHz, $CDCl_3$)



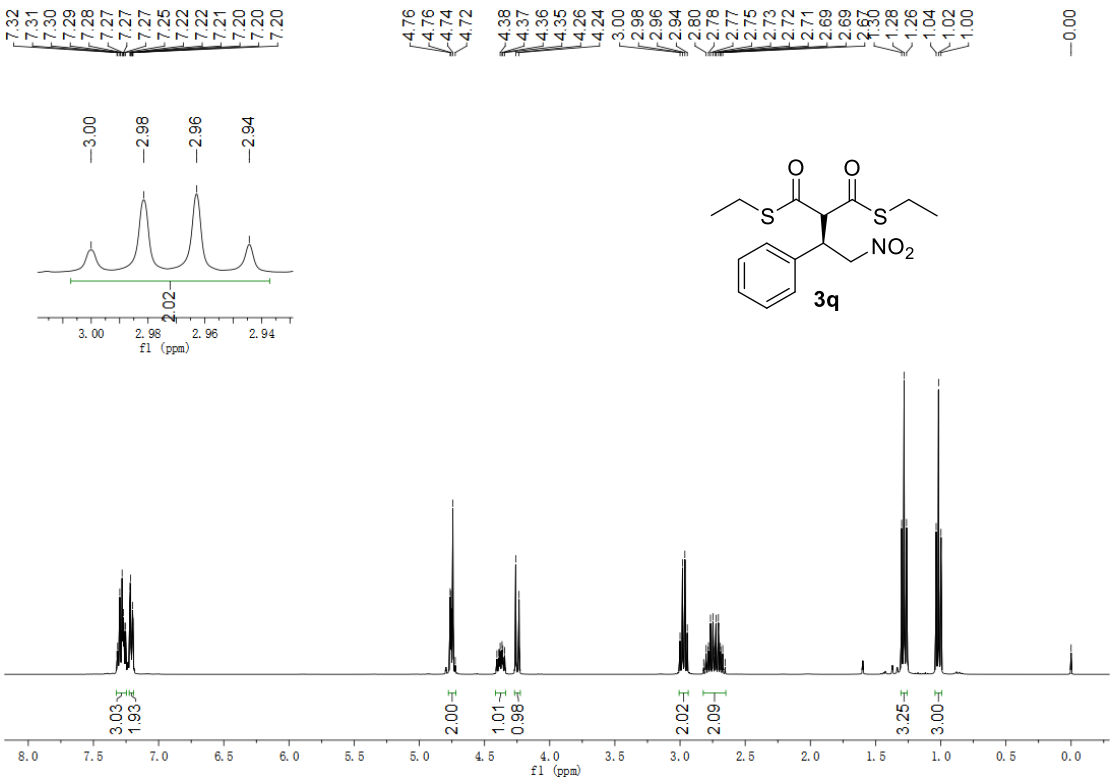
^{13}C NMR spectrum of compound **3o** (101 MHz, $CDCl_3$)



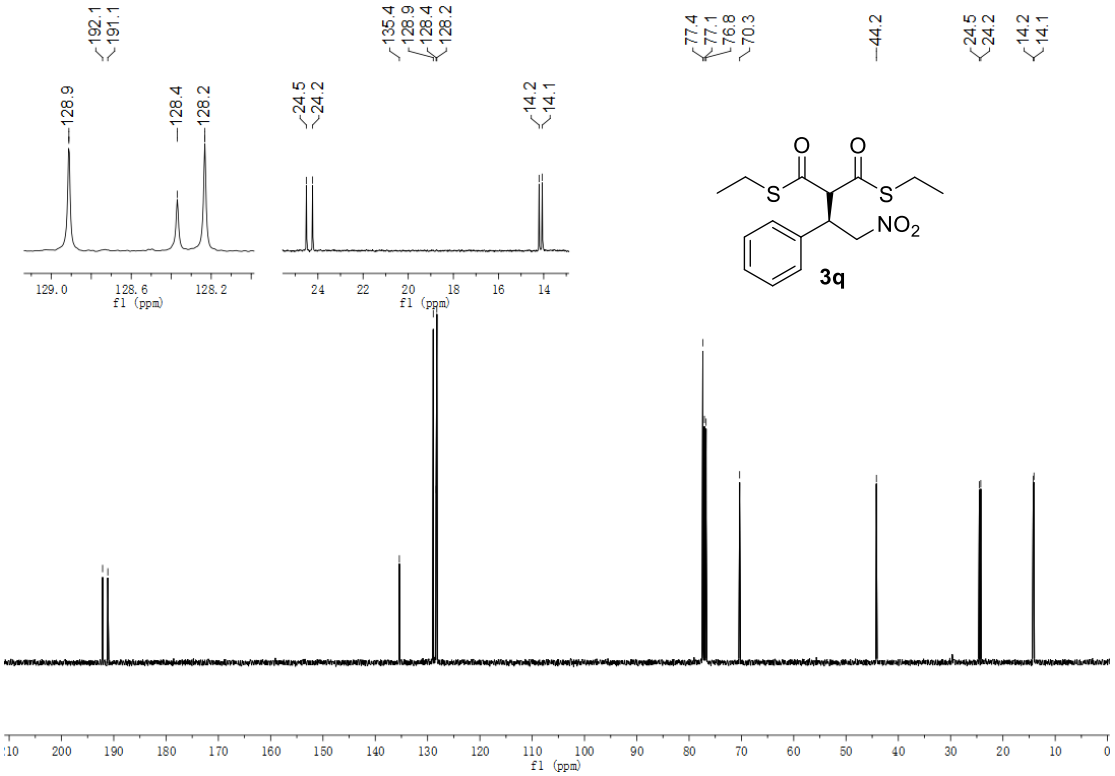
^{1}H NMR spectrum of compound **3p** (400 MHz, $CDCl_3$)



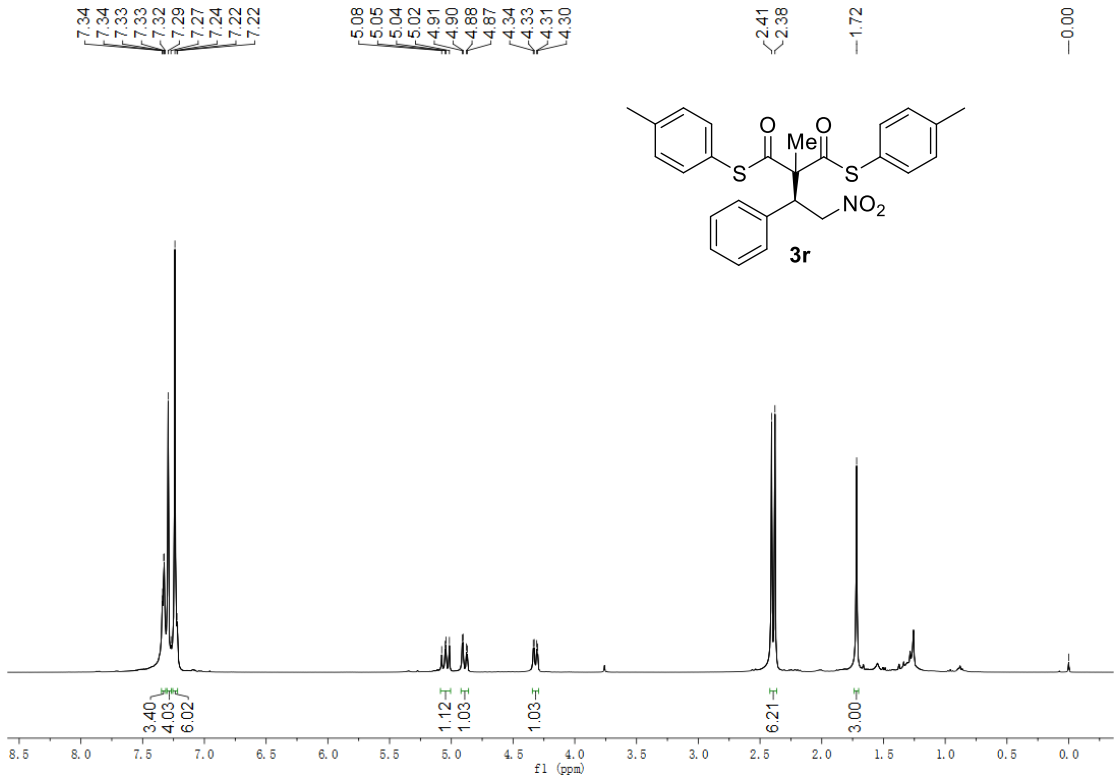
^{13}C NMR spectrum of compound **3p** (101 MHz, $CDCl_3$)



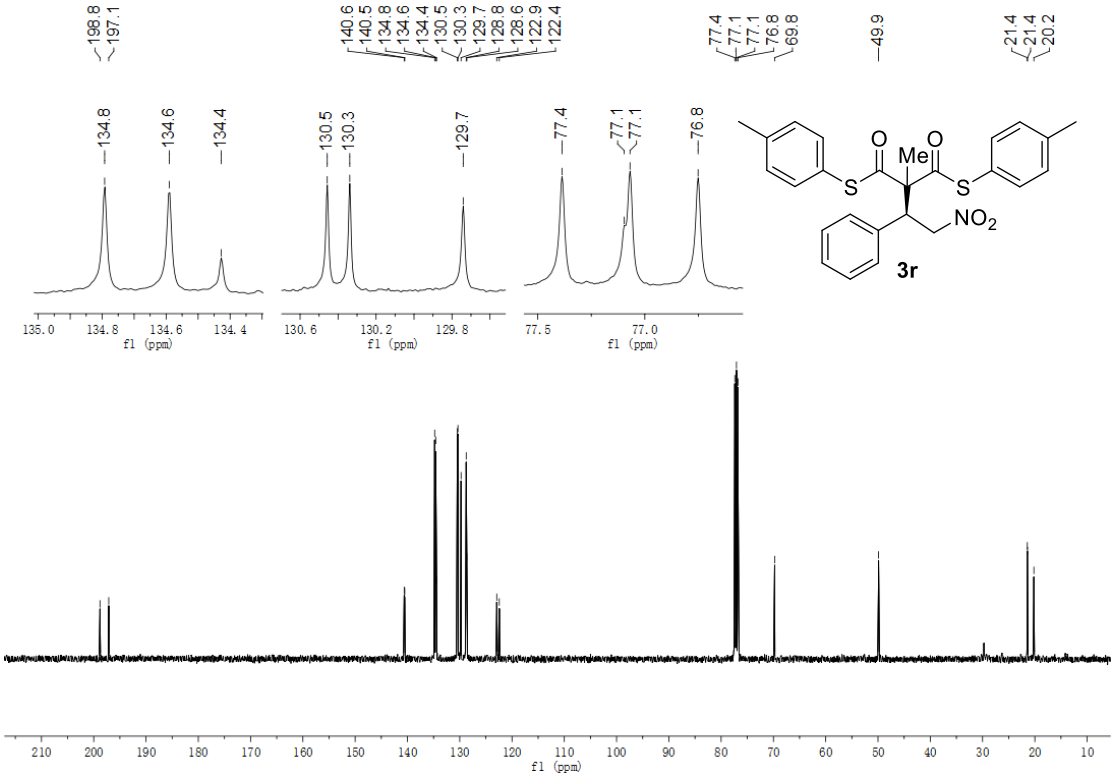
^{1}H NMR spectrum of compound **3q** (400 MHz, $CDCl_3$)



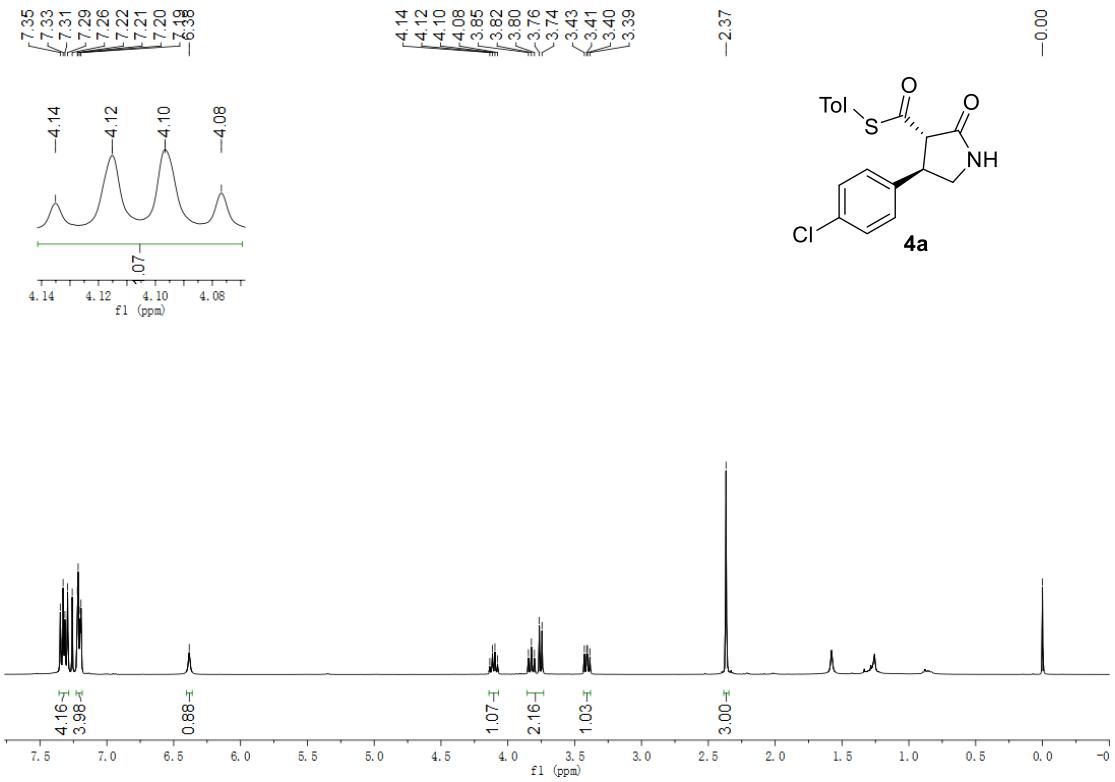
^{13}C NMR spectrum of compound **3q** (101 MHz, $CDCl_3$)



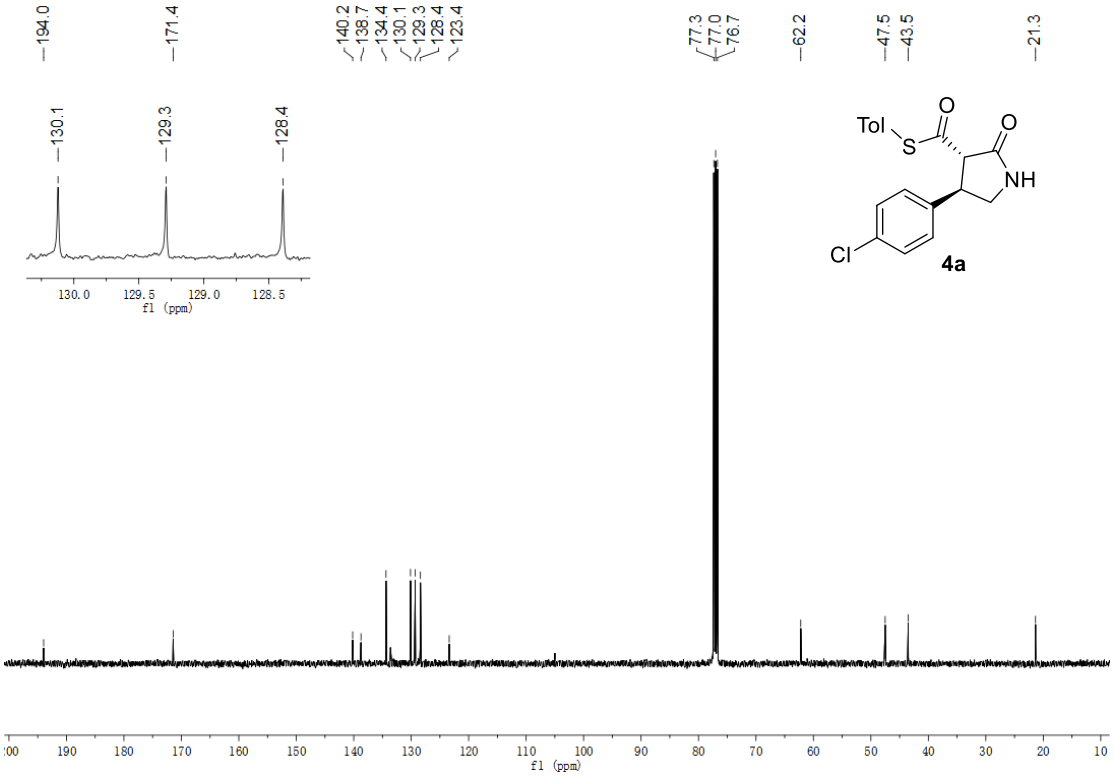
^{1}H NMR spectrum of compound **3r** (400 MHz, $CDCl_3$)



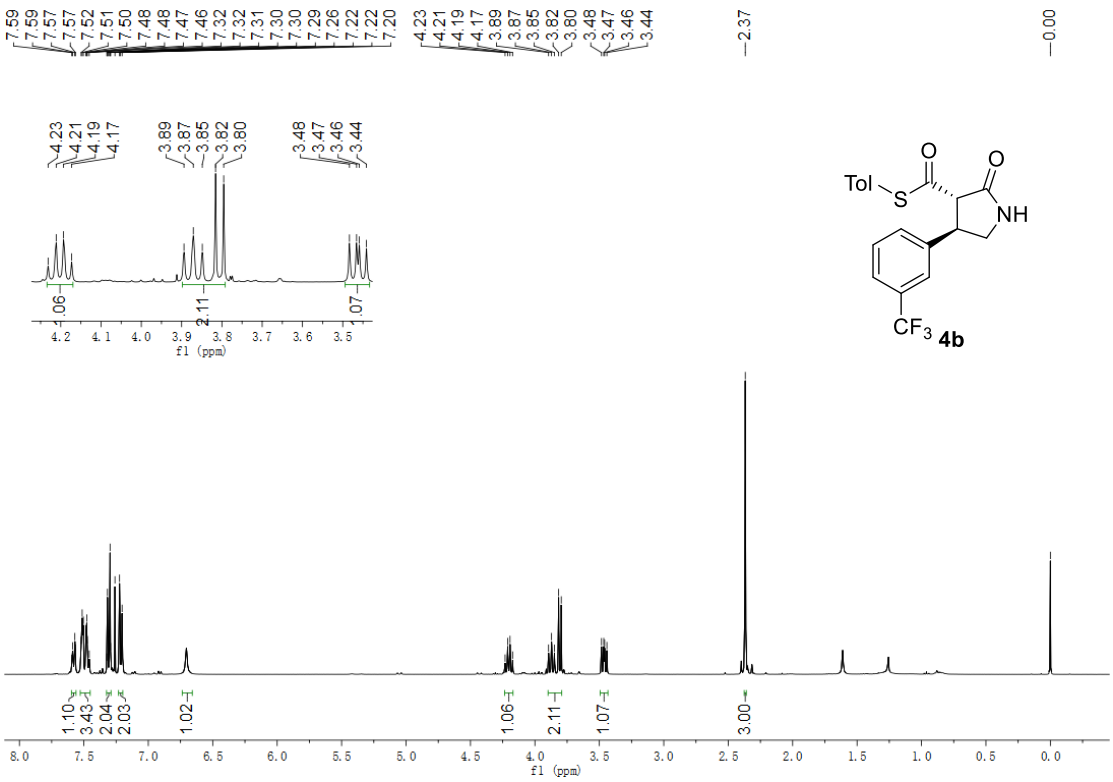
^{13}C NMR spectrum of compound **3r** (101 MHz, $CDCl_3$)



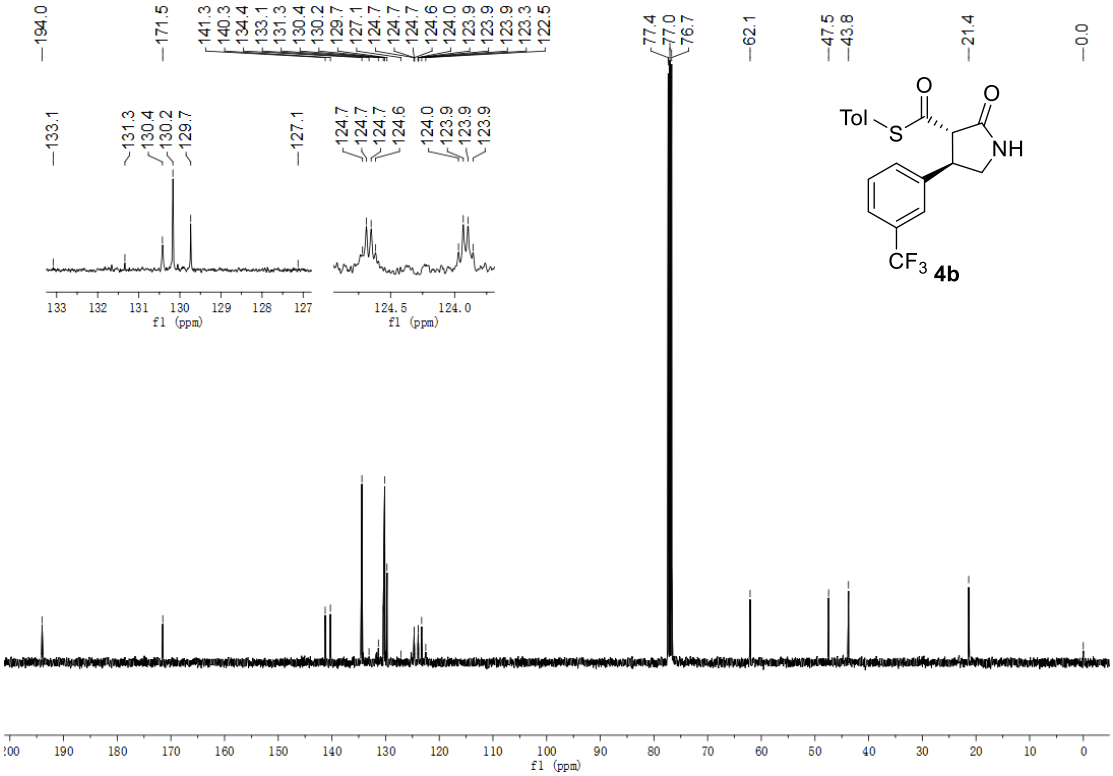
^{1}H NMR spectrum of compound **4a** (400 MHz, $CDCl_3$)



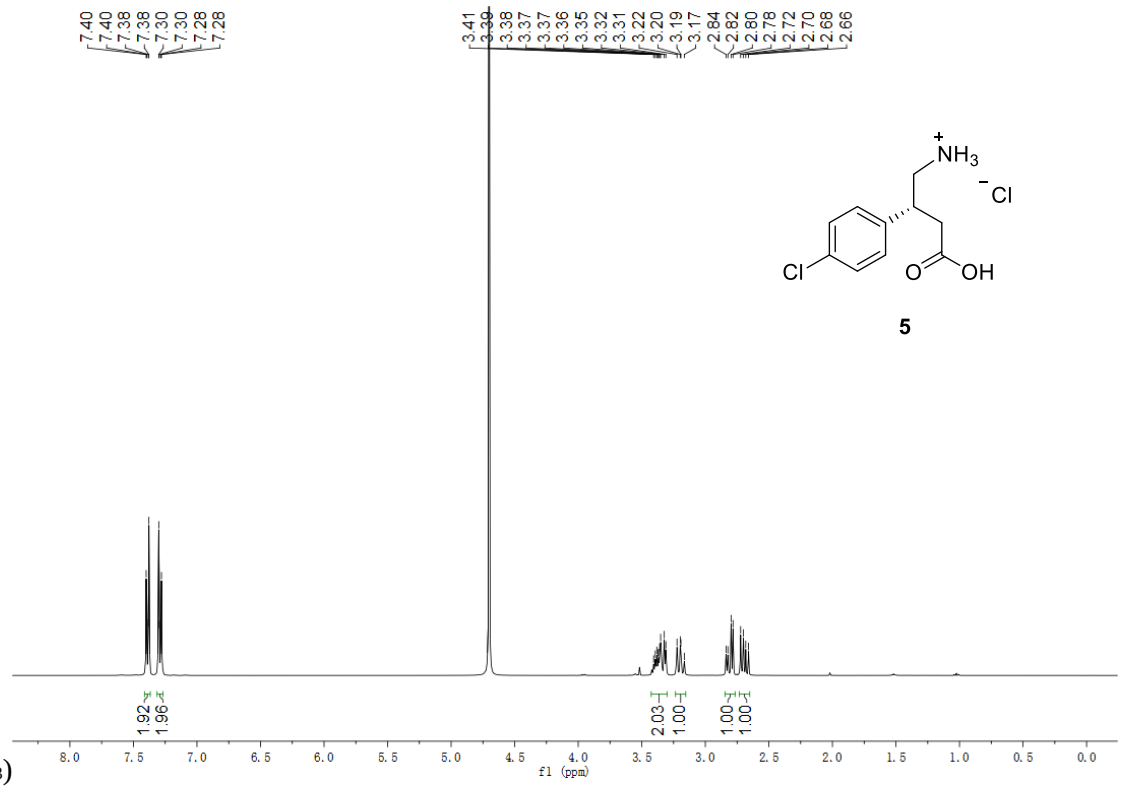
^{13}C NMR spectrum of compound **4a** (101 MHz, $CDCl_3$)



^{1}H NMR spectrum of compound **4b** (400 MHz, $CDCl_3$)

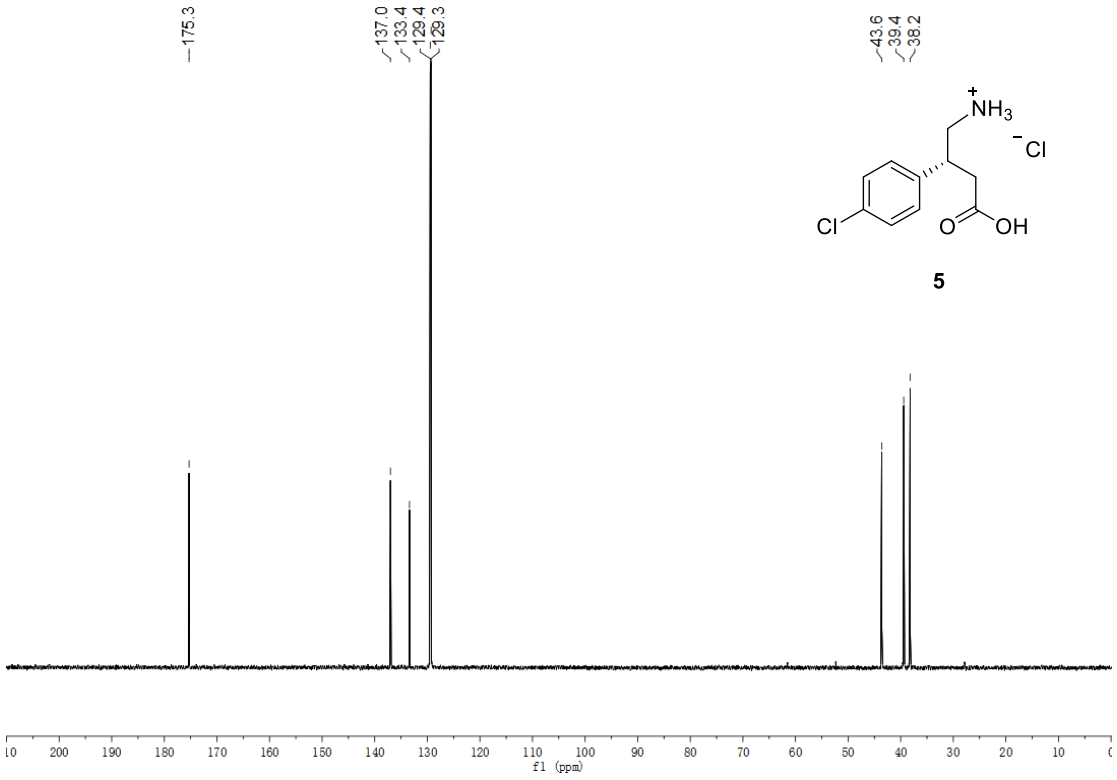


^{13}C NMR spectrum of compound **4b** (101 MHz, $CDCl_3$)

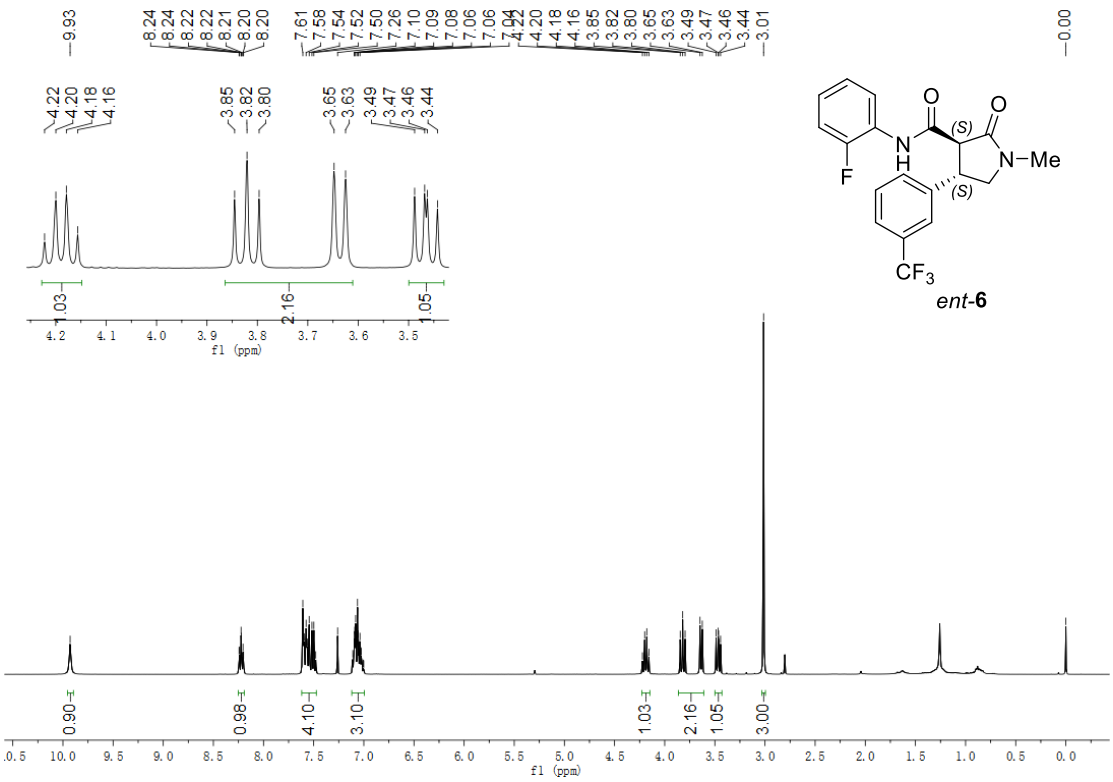


CDCl3)

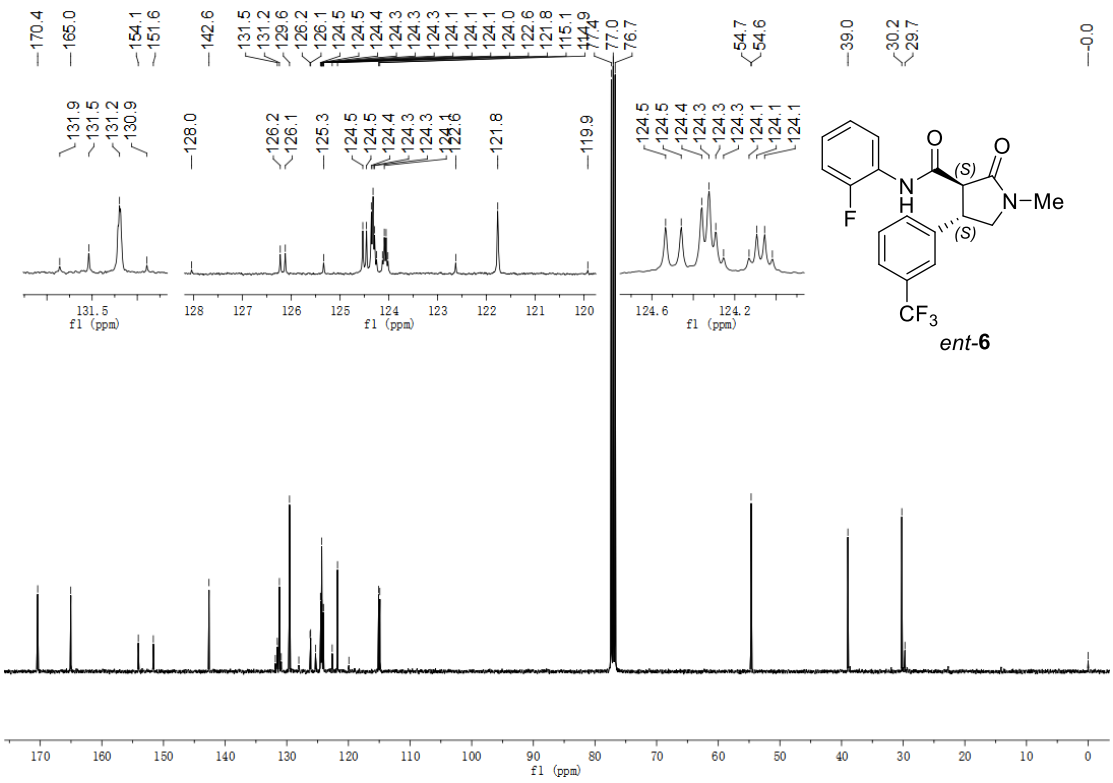
[1]H NMR spectrum of compound **5** (400 MHz, $CDCl_3$)



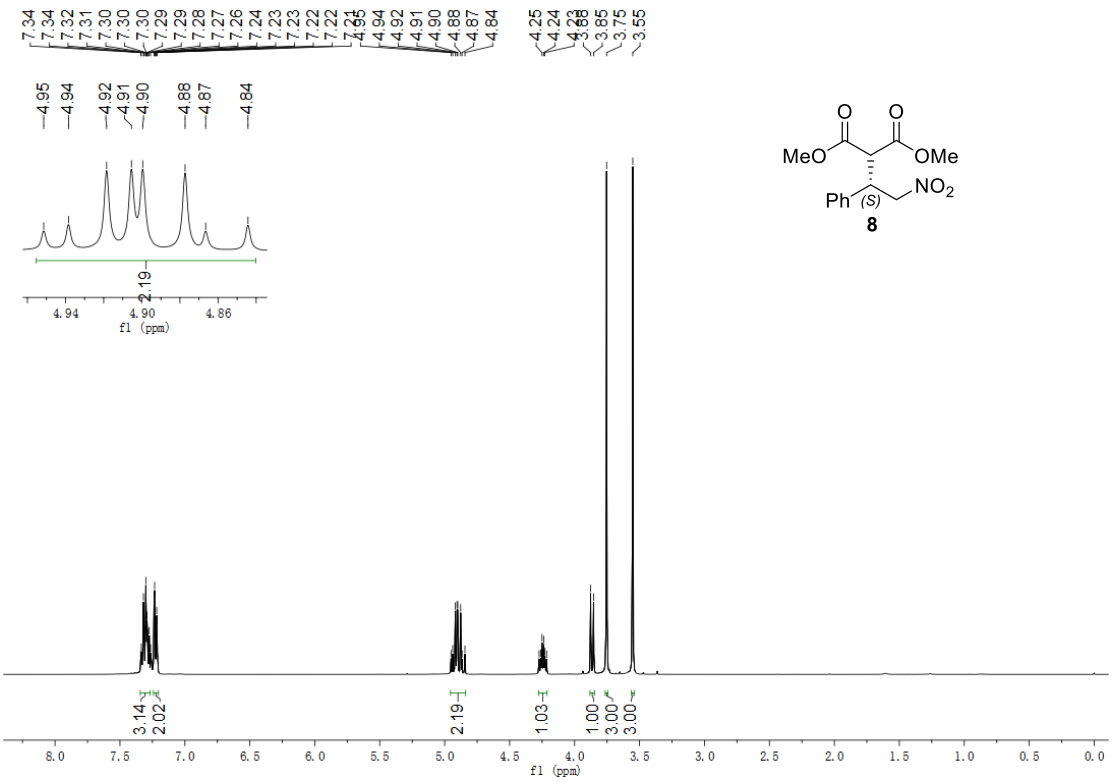
[13]C NMR spectrum of compound **5** (101 MHz, $CDCl_3$)



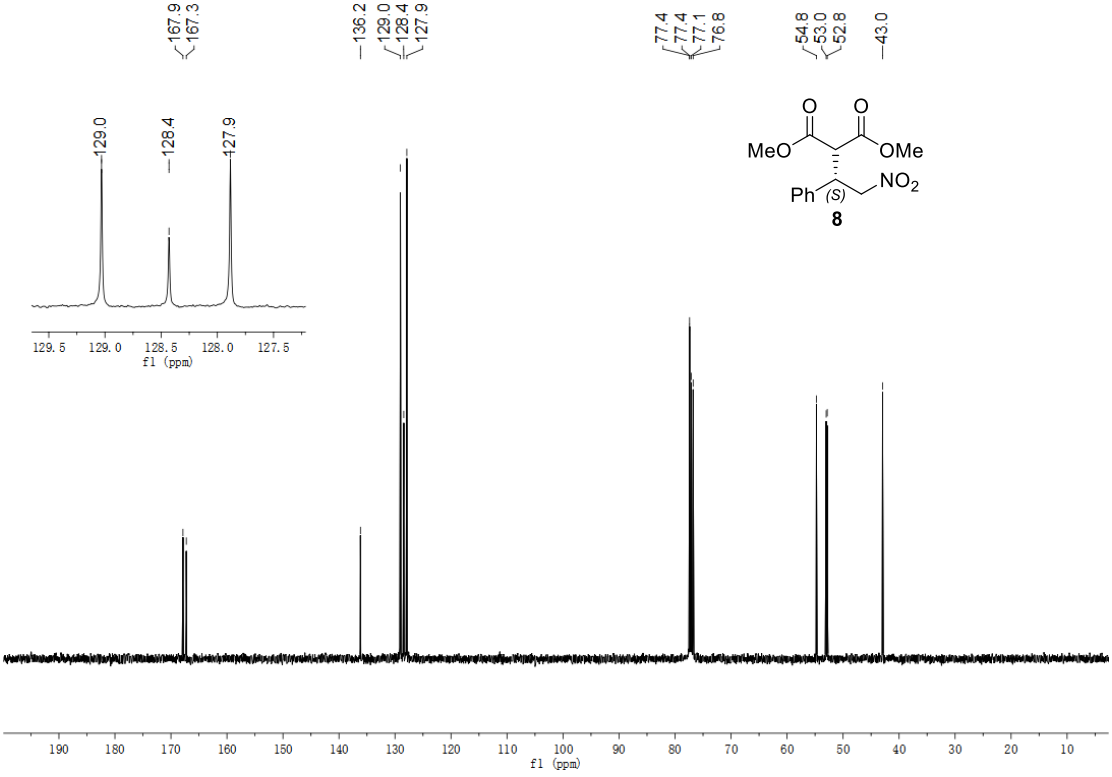
^{1}H NMR spectrum of compound *ent*-**6** (400 MHz, $CDCl_3$)



^{13}C NMR spectrum of compound *ent*-**6** (101 MHz, $CDCl_3$)

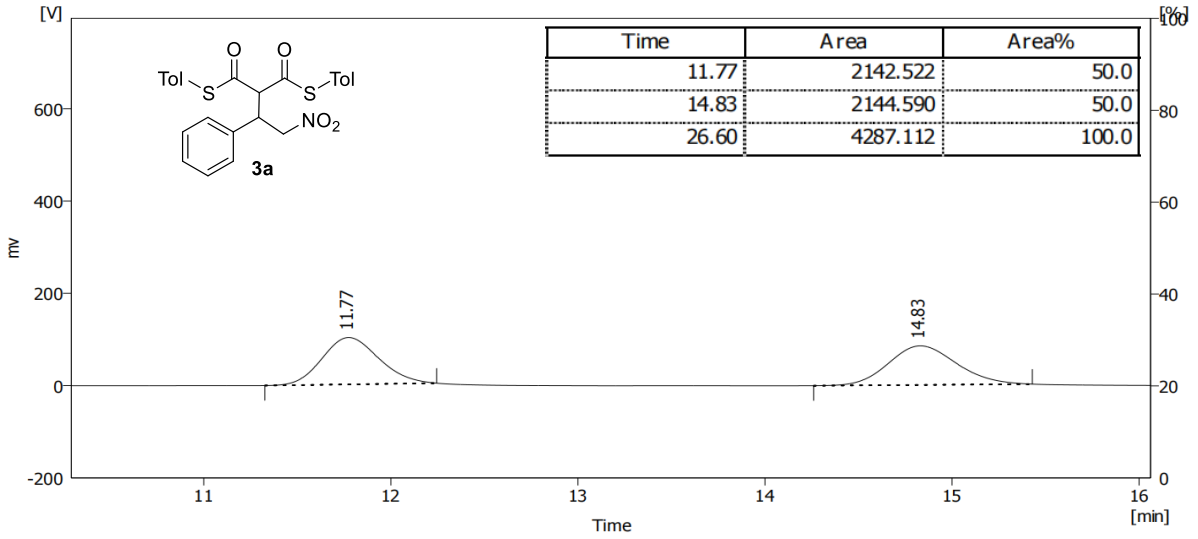


^{1}H NMR spectrum of compound **8** (400 MHz, $CDCl_3$)

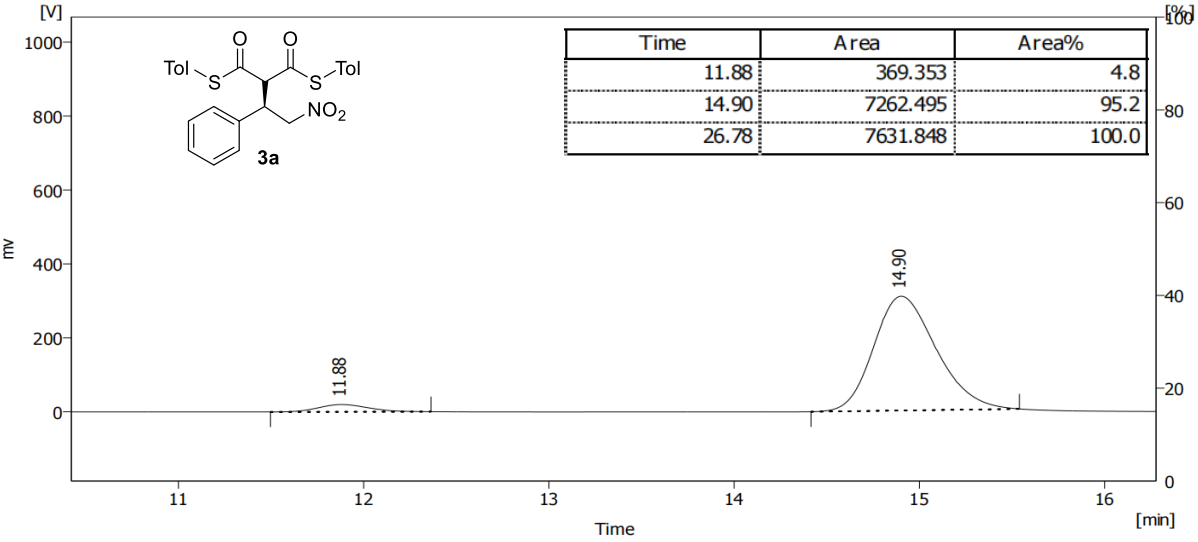


^{13}C NMR spectrum of compound **8** (101 MHz, $CDCl_3$)

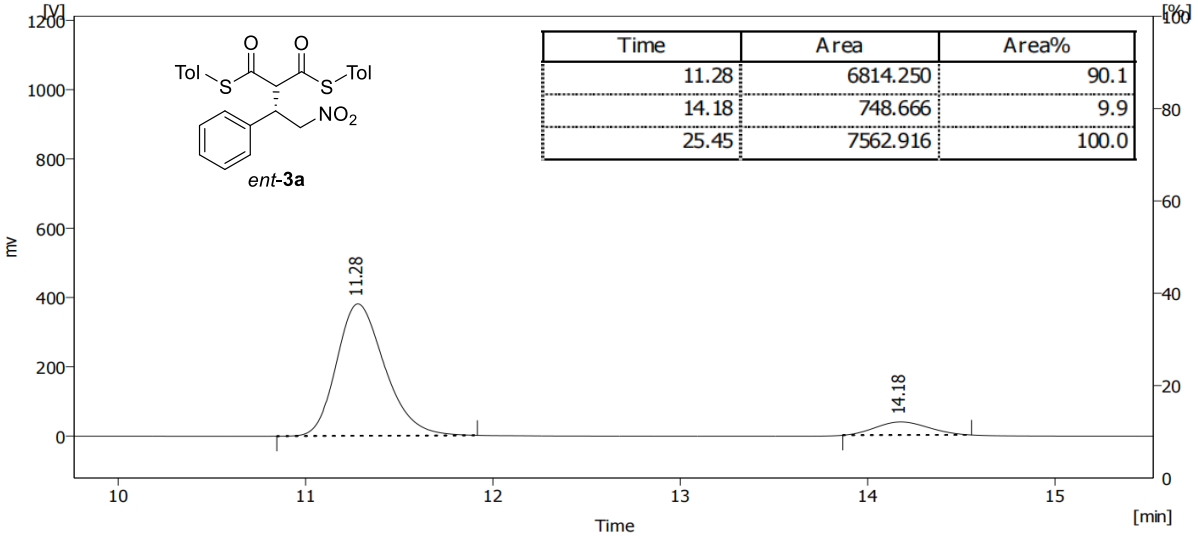
12. Copies of HPLC chromatograms



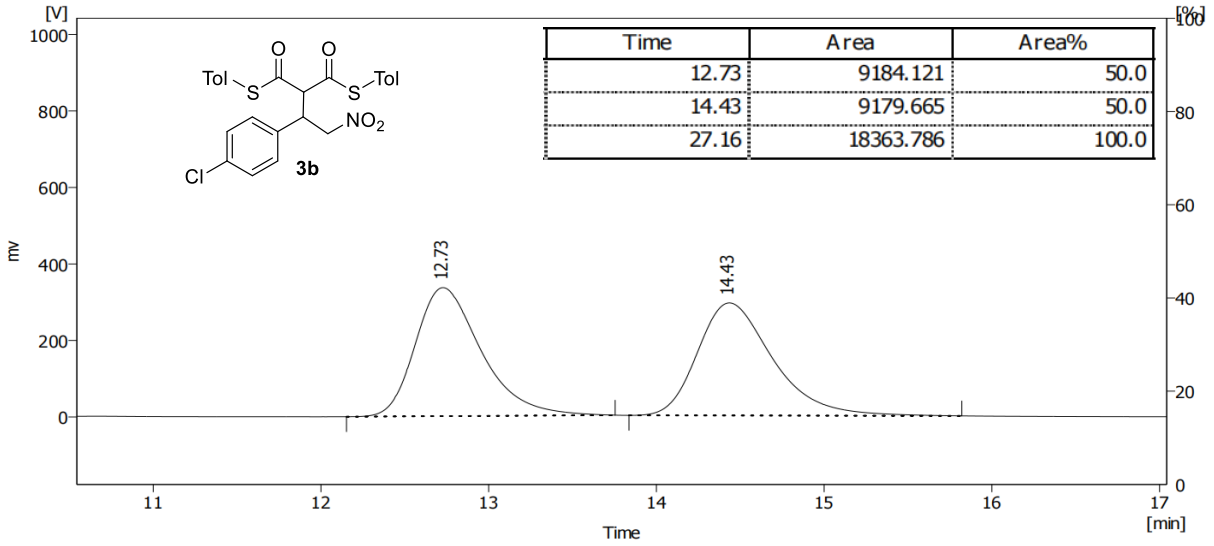
HPLC spectrum of racemic mixture **3a**



HPLC spectrum of **3a** with 0.5 mol % **QD-SQA**

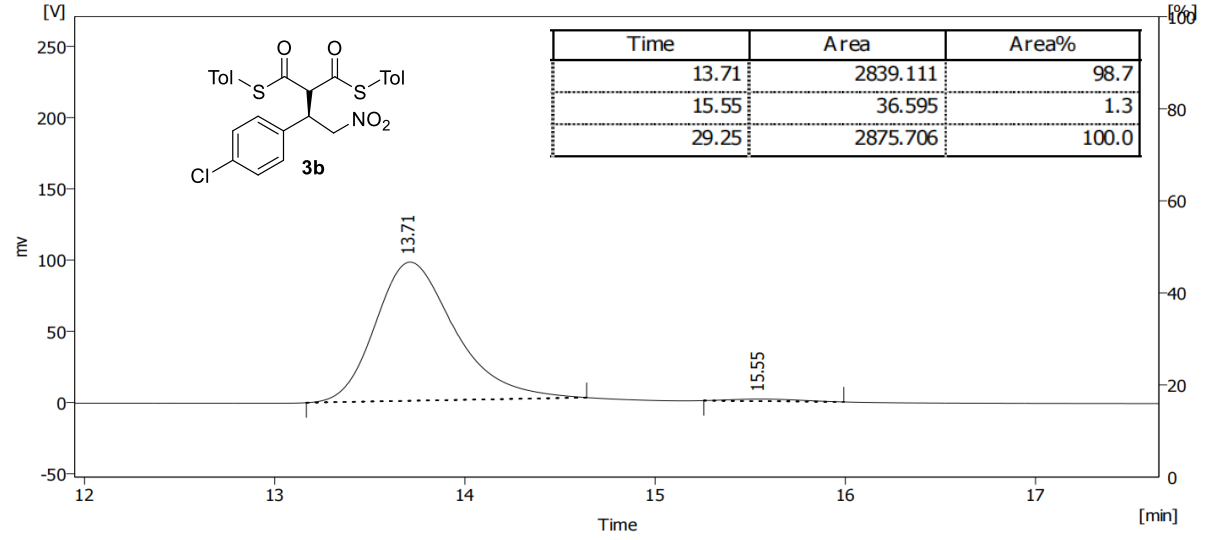


HPLC spectrum of *ent*-**3a** with 0.5 mol % **QN-SQA**



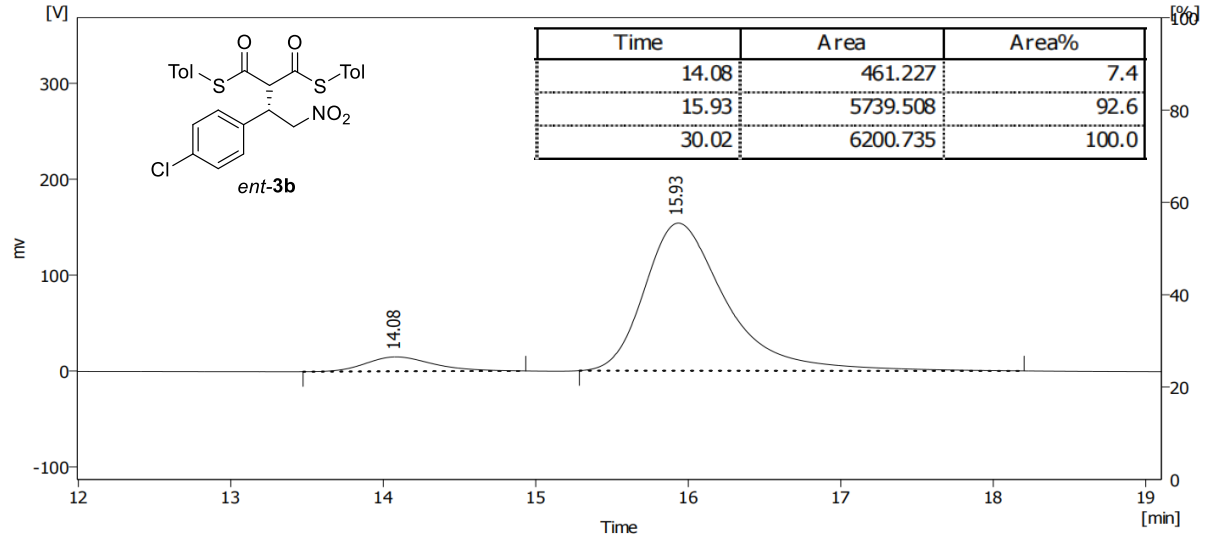
Time	Area	Area%
12.73	9184.121	50.0
14.43	9179.665	50.0
27.16	18363.786	100.0

HPLC spectrum of racemic mixture **3b**



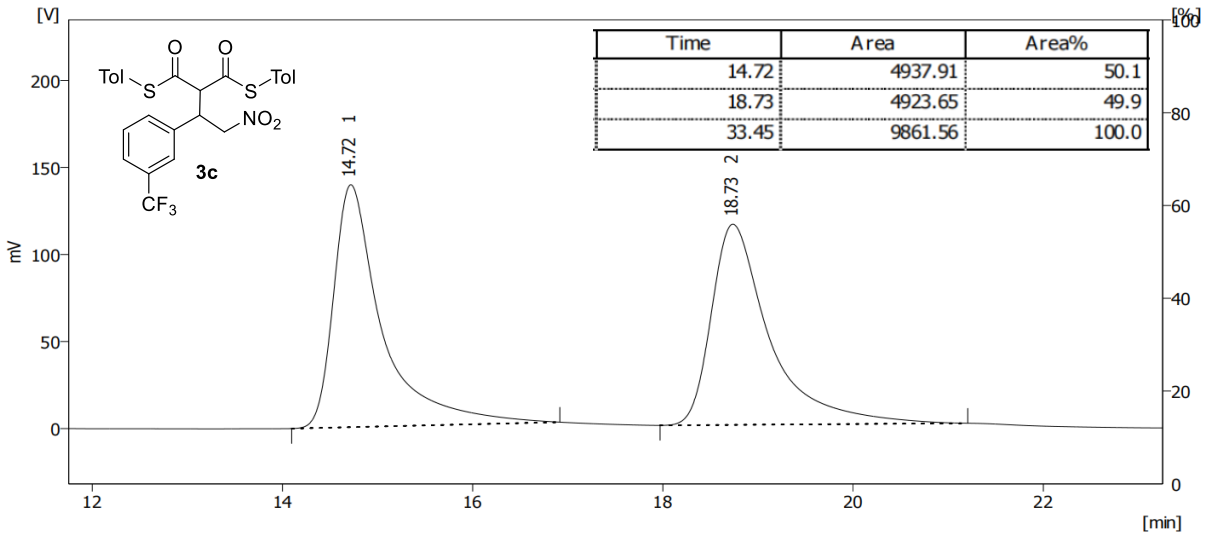
Time	Area	Area%
13.71	2839.111	98.7
15.55	36.595	1.3
29.25	2875.706	100.0

HPLC spectrum of **3b** with 0.5 mol % **QD-SQA**

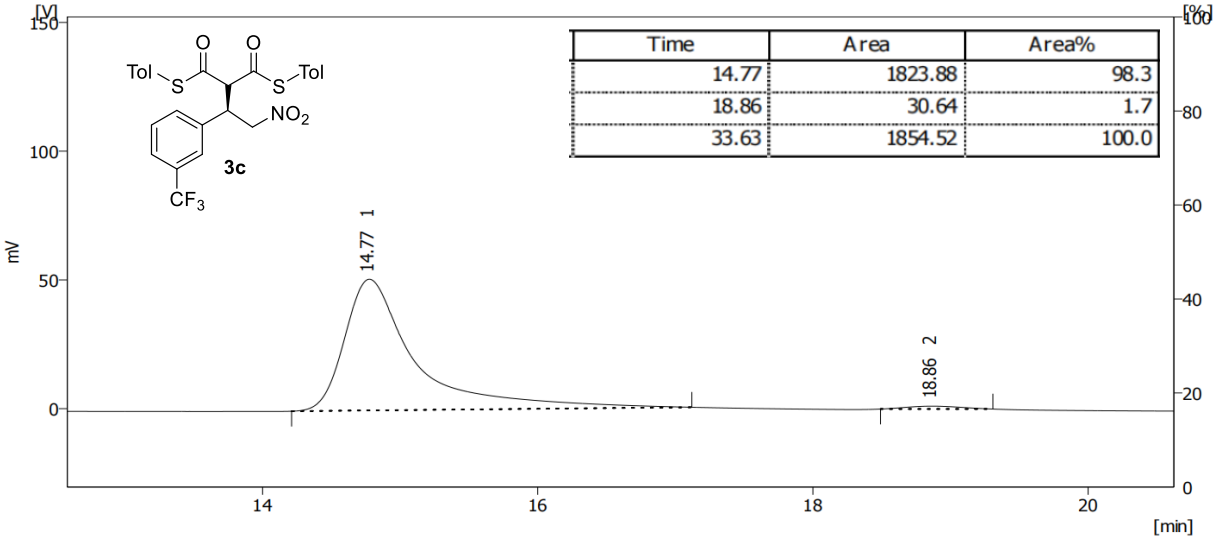


Time	Area	Area%
14.08	461.227	7.4
15.93	5739.508	92.6
30.02	6200.735	100.0

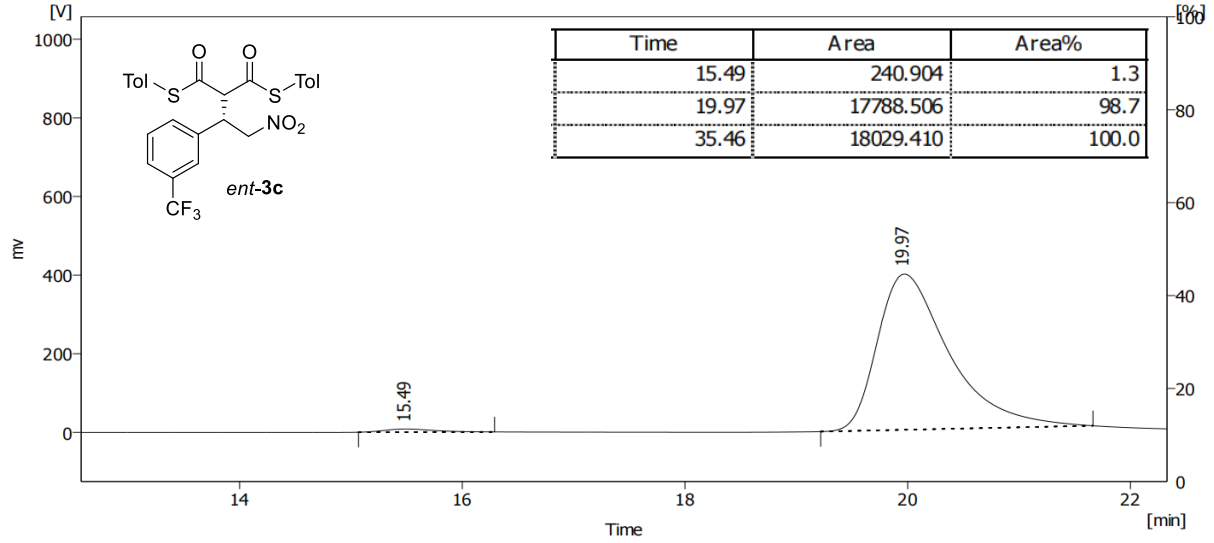
HPLC spectrum of *ent*-**3b** with 0.5 mol % **QN-SQA**



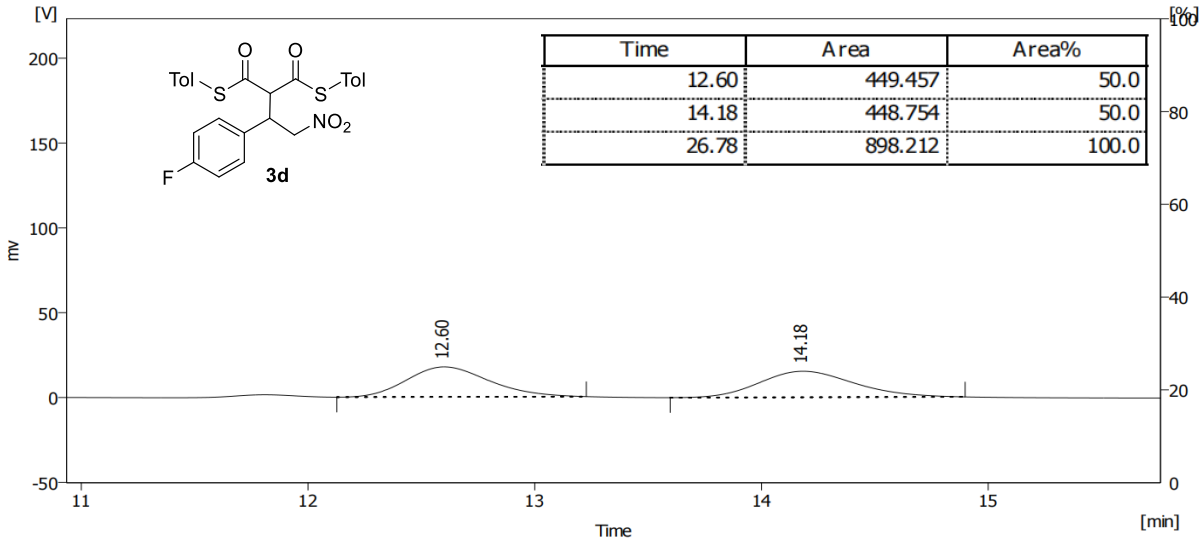
HPLC spectrum of racemic mixture **3c**



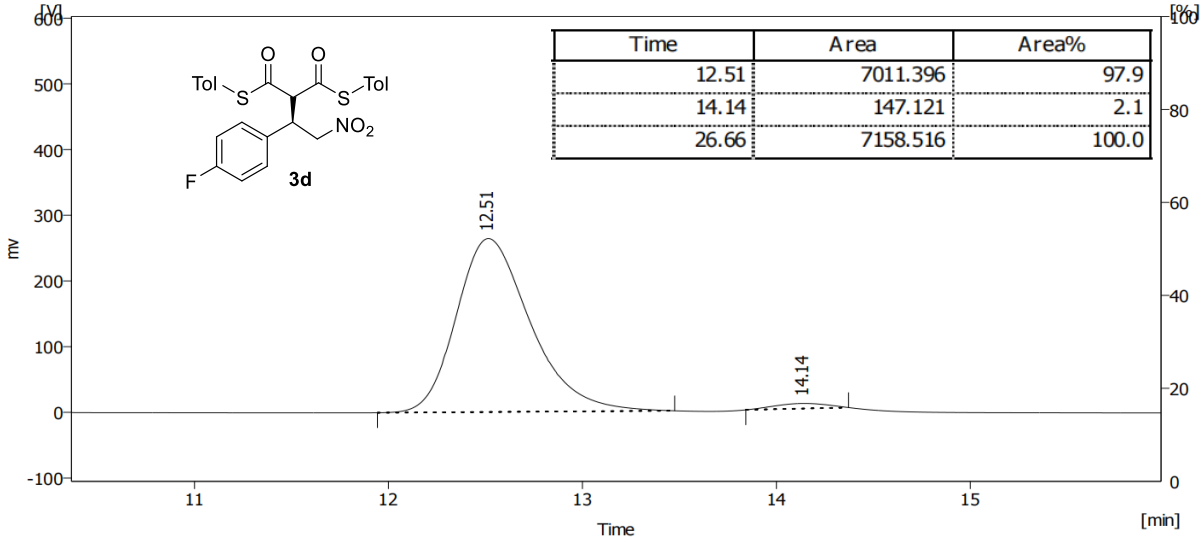
HPLC spectrum of **3c** with 0.5 mol % **QD-SQA**



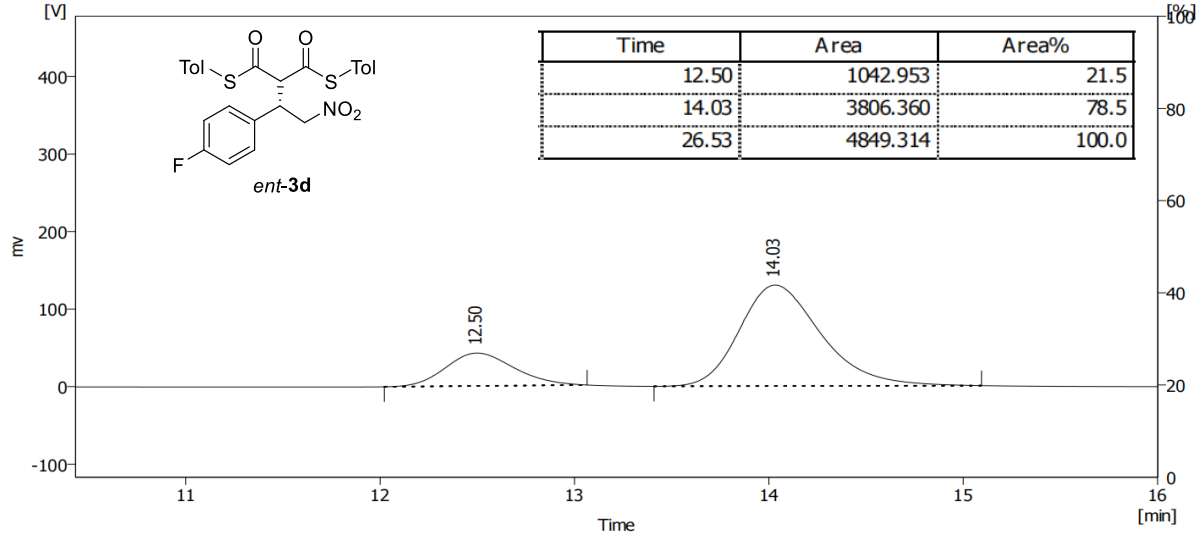
HPLC spectrum of *ent*-**3c** with 0.5 mol % **QN-SQA**



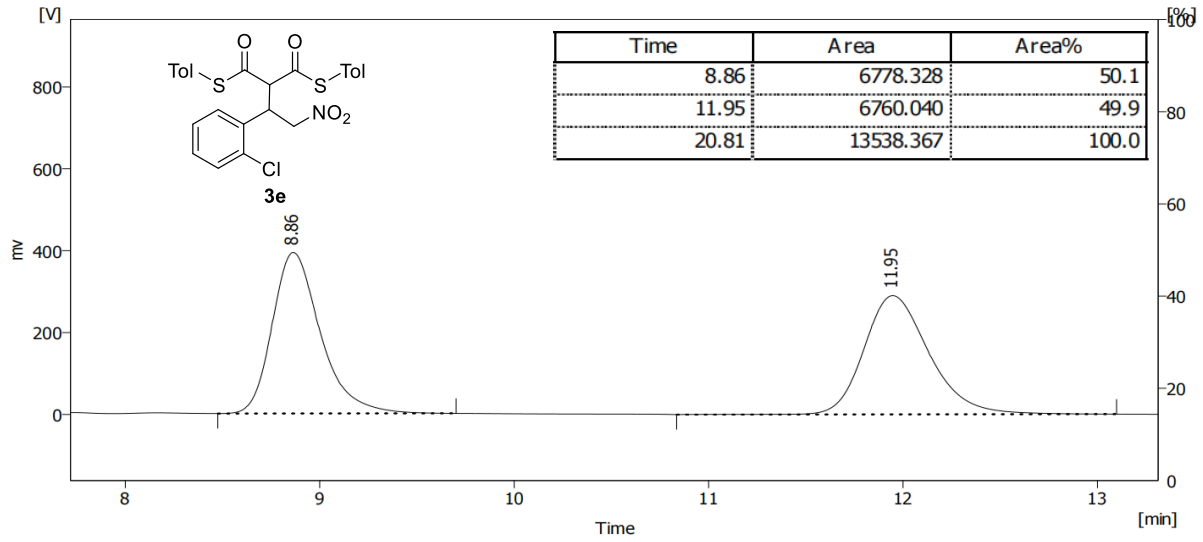
HPLC spectrum of racemic mixture **3d**



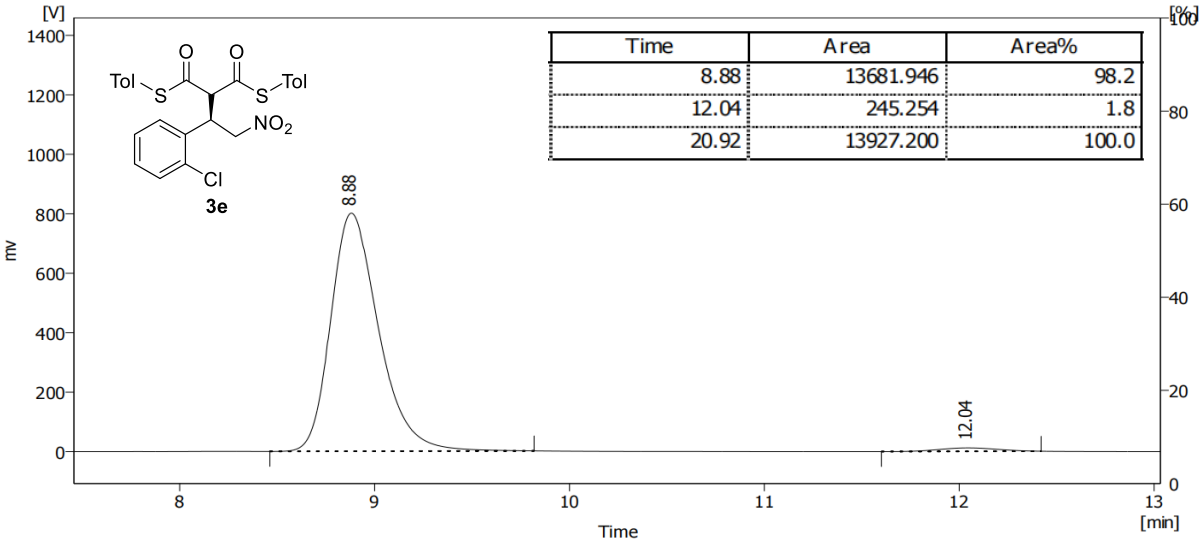
HPLC spectrum of **3d** with 0.5 mol % **QD-SQA**



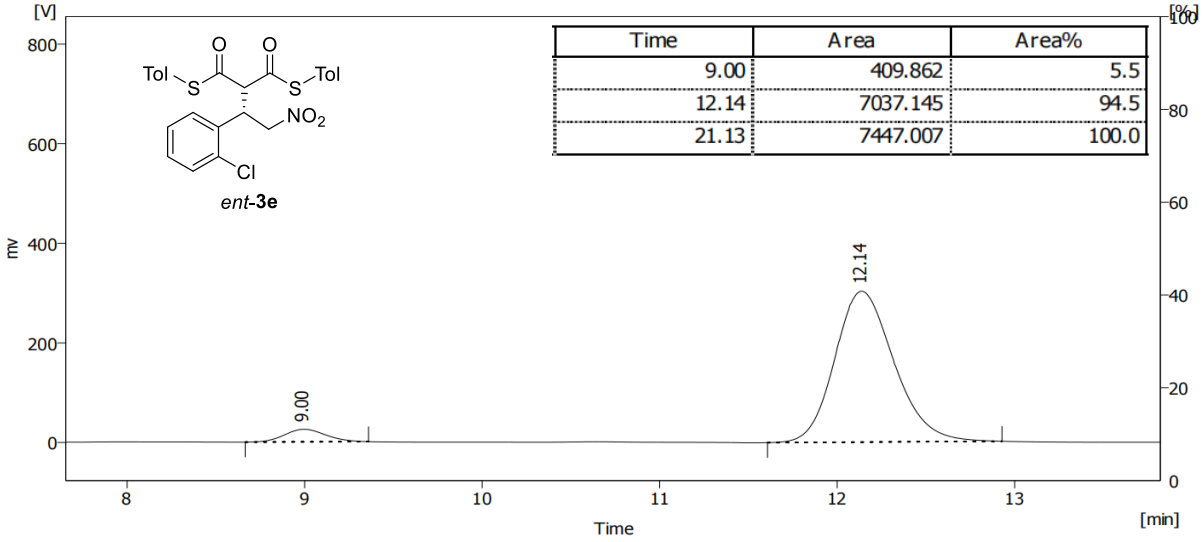
HPLC spectrum of *ent*-**3d** with 0.5 mol % **QN-SQA**



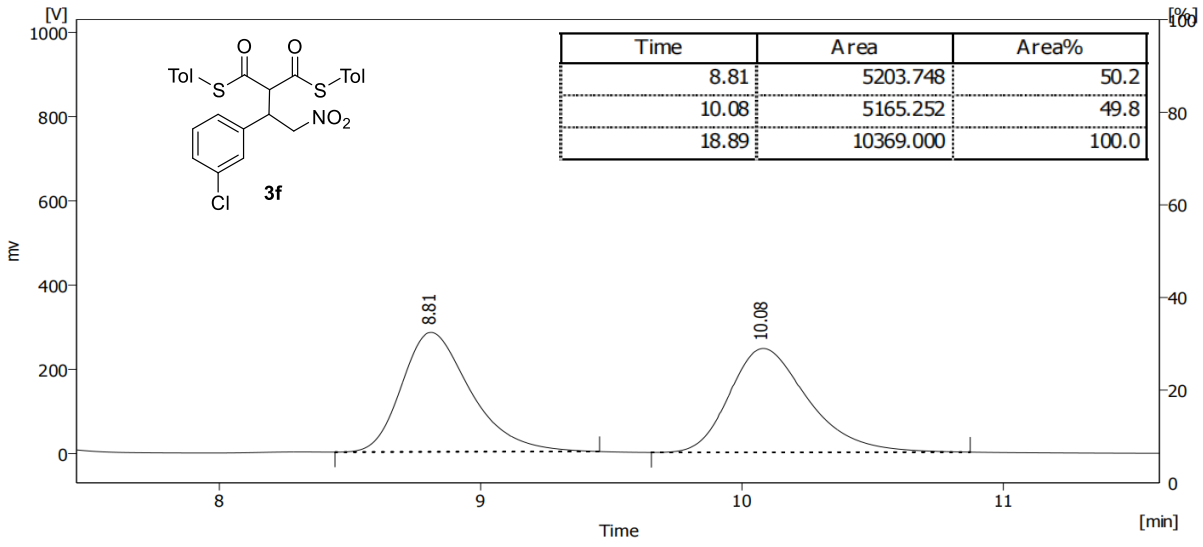
HPLC spectrum of racemic mixture **3e**



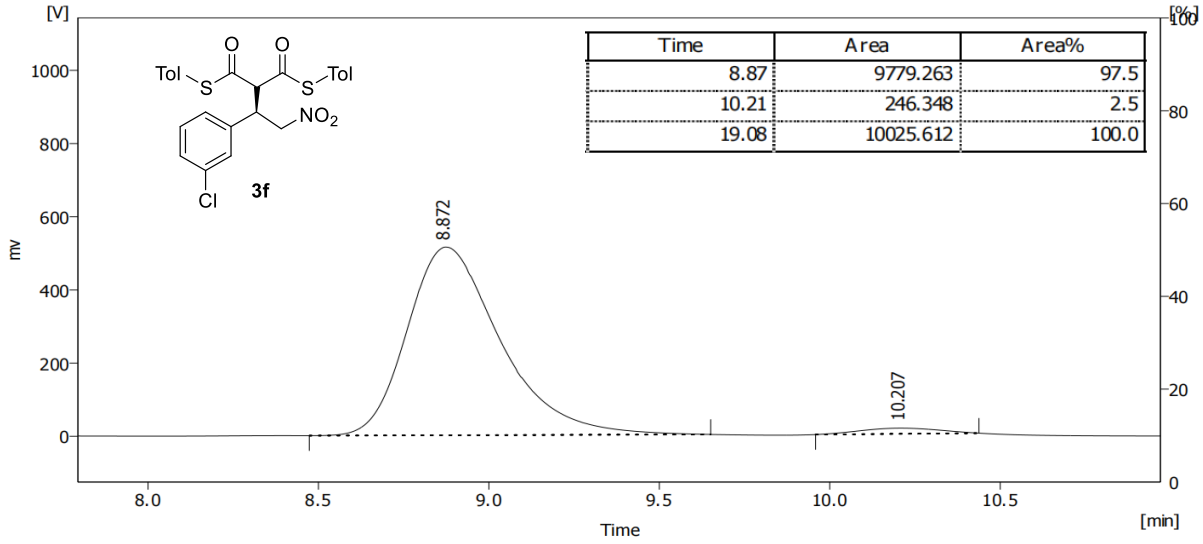
HPLC spectrum of **3e** with 0.5 mol % **QD-SQA**



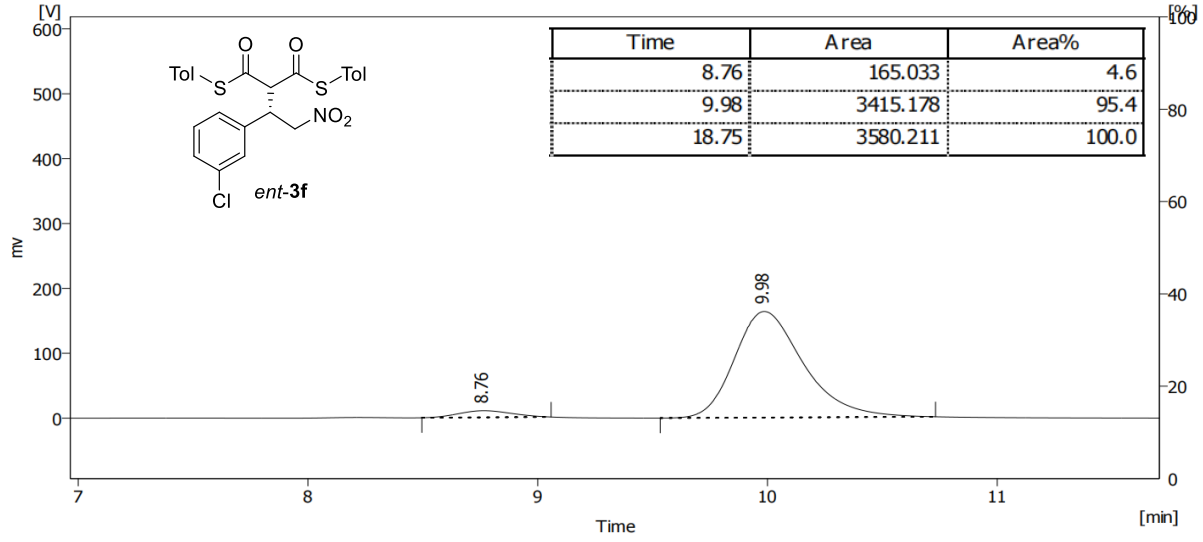
HPLC spectrum of *ent*-**3e** with 0.5 mol % **QN-SQA**



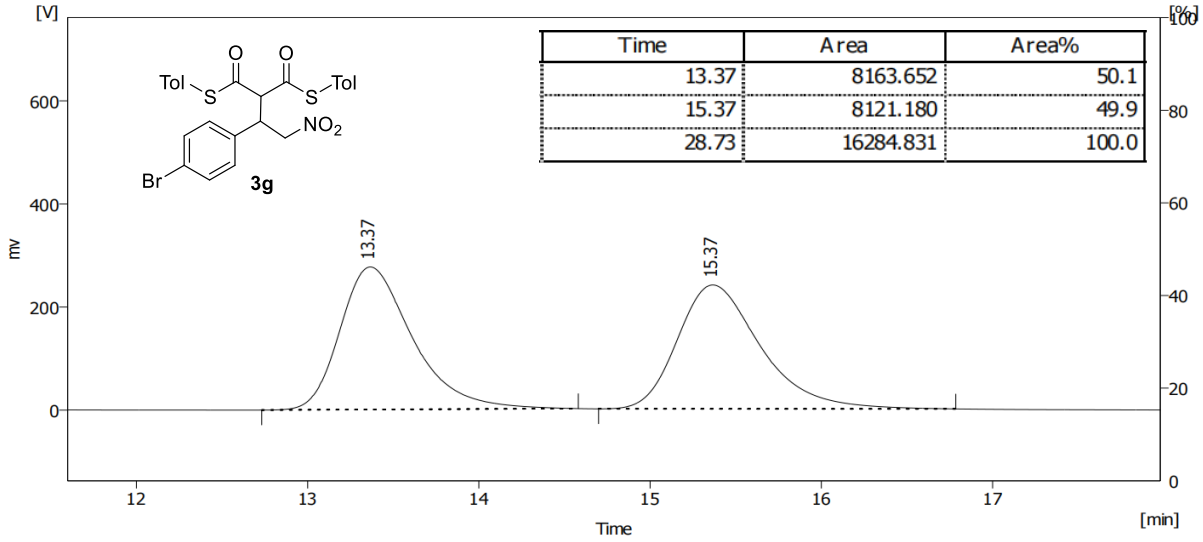
HPLC spectrum of racemic mixture **3f**



HPLC spectrum of **3f** with 0.5 mol % **QD-SQA**

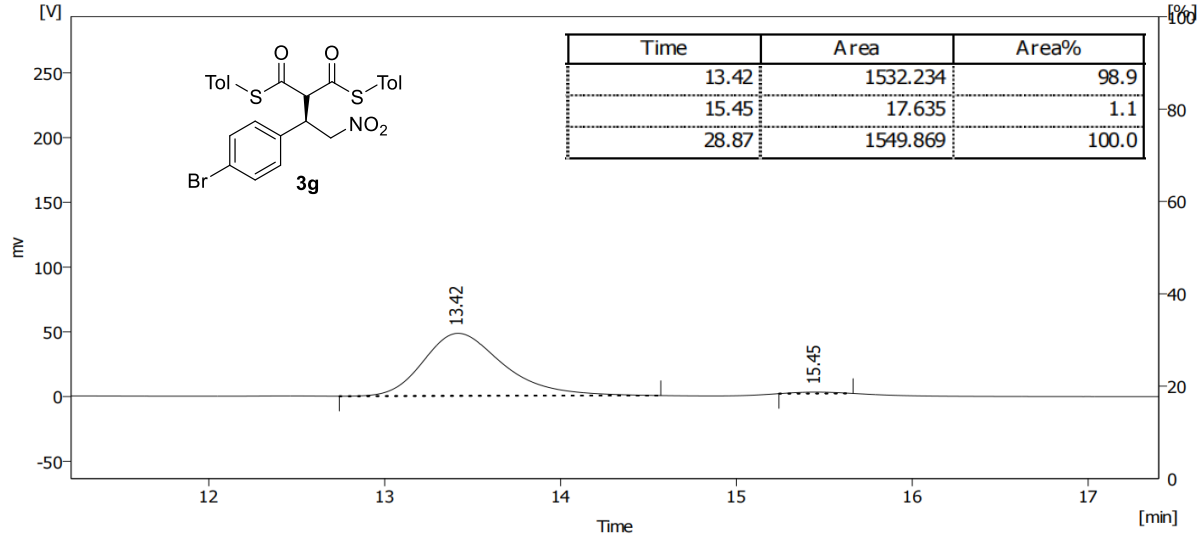


HPLC spectrum of *ent*-**3f** with 0.5 mol % **QN-SQA**



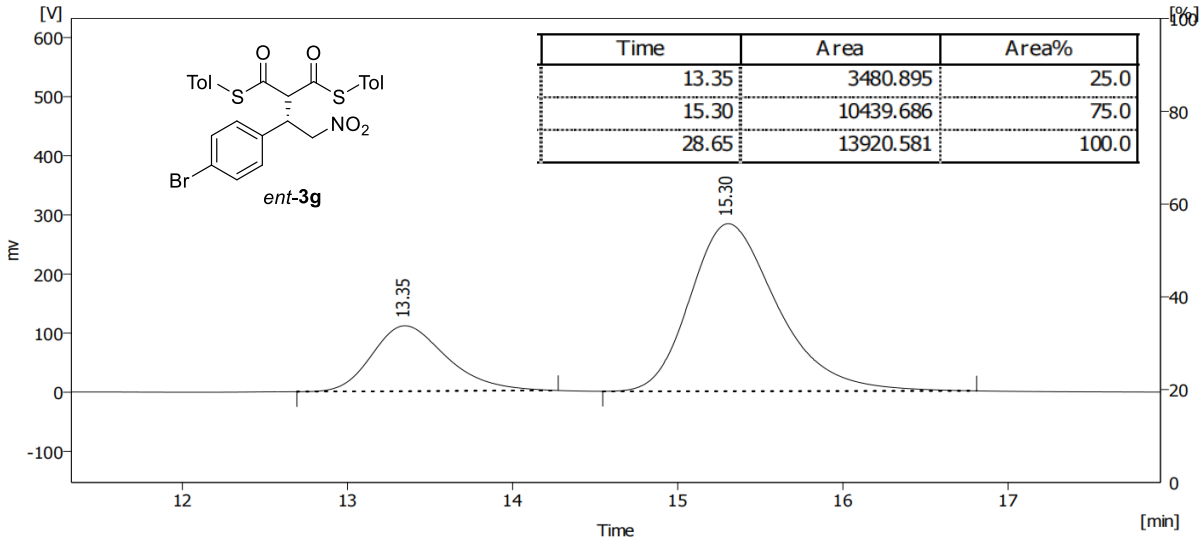
Time	Area	Area%
13.37	8163.652	50.1
15.37	8121.180	49.9
28.73	16284.831	100.0

HPLC spectrum of racemic mixture **3g**



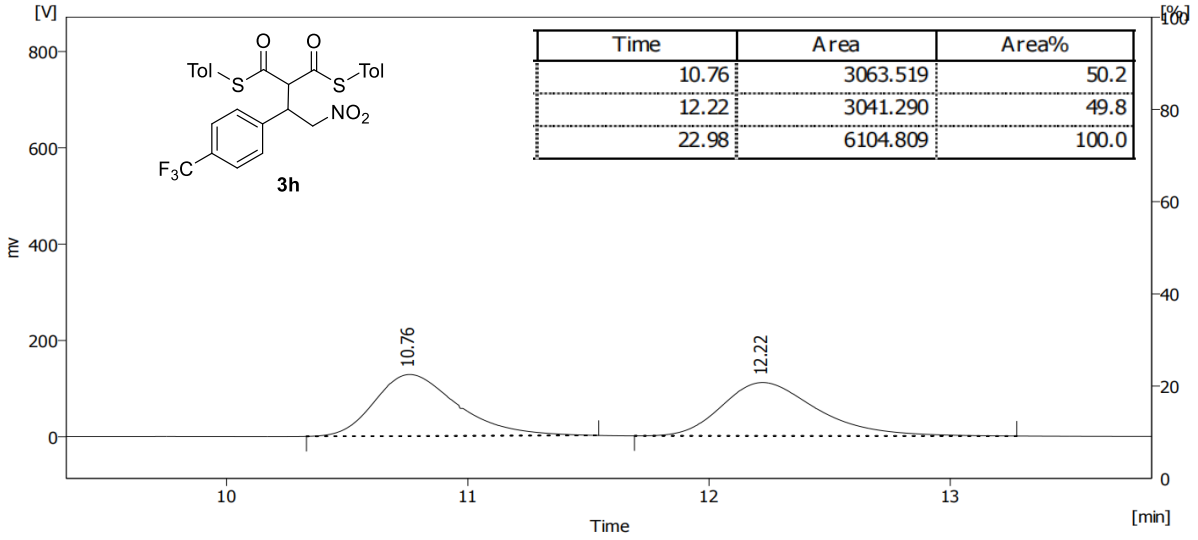
Time	Area	Area%
13.42	1532.234	98.9
15.45	17.635	1.1
28.87	1549.869	100.0

HPLC spectrum of **3g** with 0.5 mol % **QD-SQA**

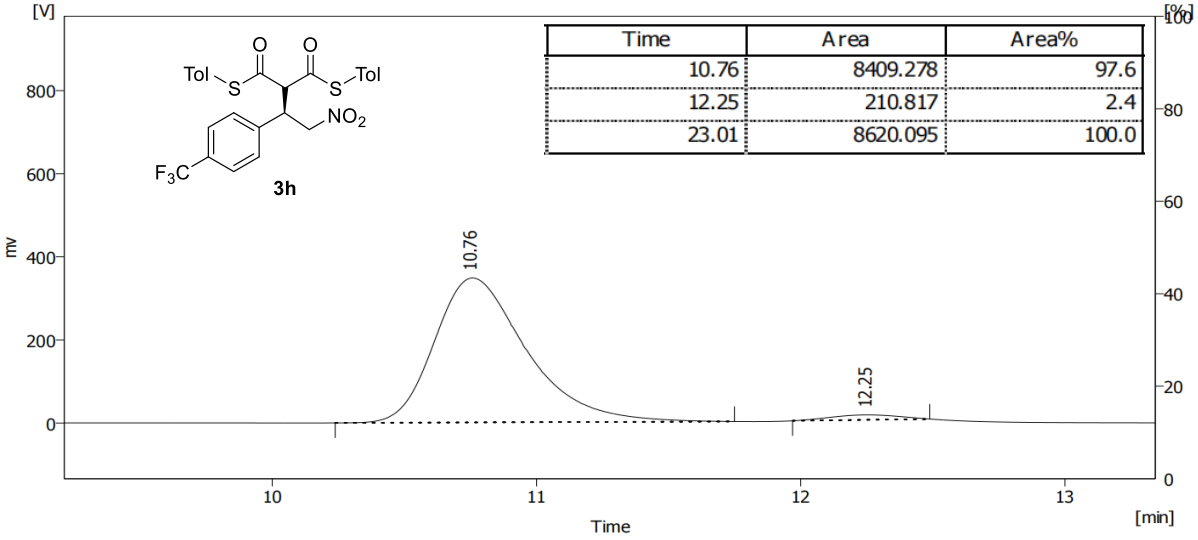


Time	Area	Area%
13.35	3480.895	25.0
15.30	10439.686	75.0
28.65	13920.581	100.0

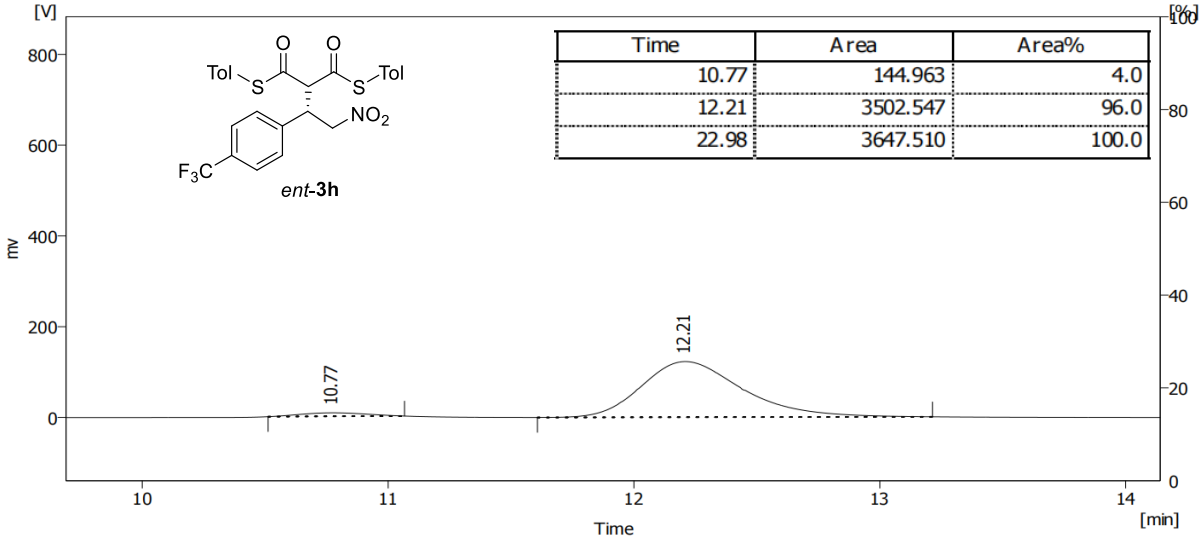
HPLC spectrum of *ent*-**3g** with 0.5 mol % **QN-SQA**



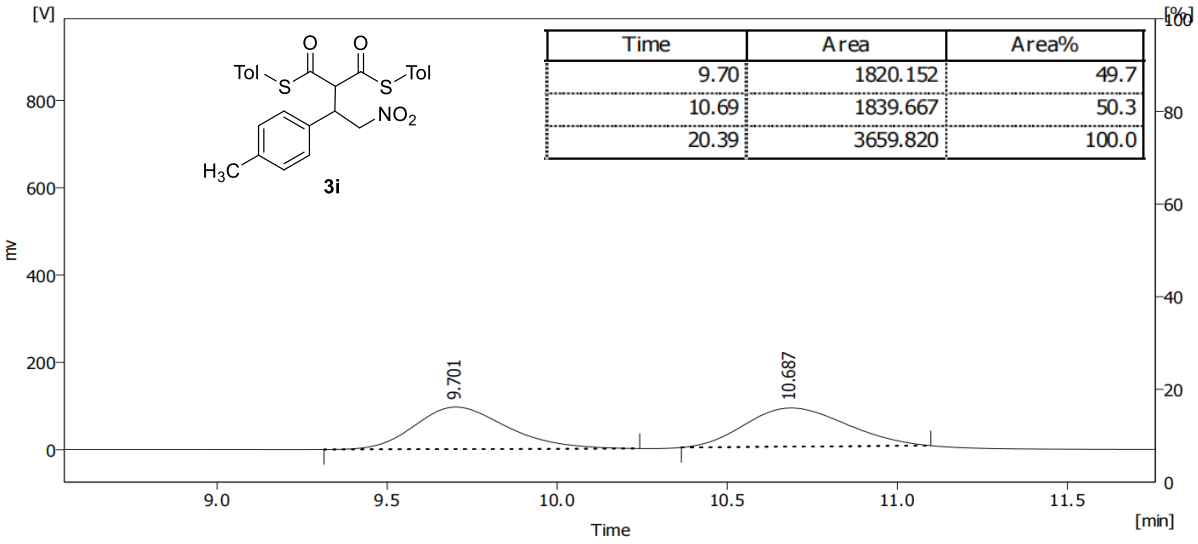
HPLC spectrum of racemic mixture **3h**



HPLC spectrum of **3h** with 0.5 mol % **QD-SQA**

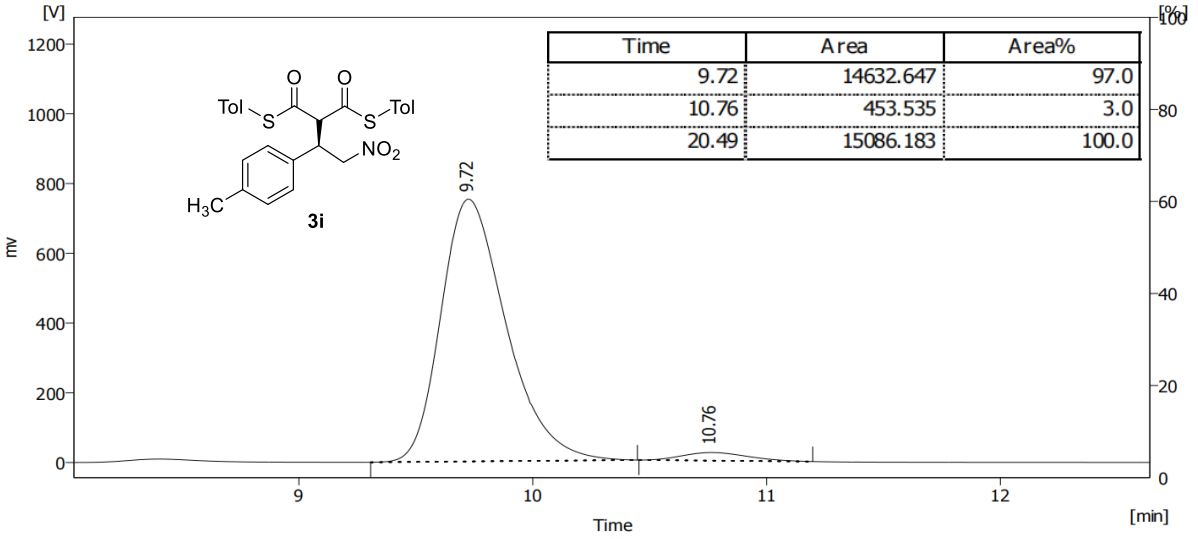


HPLC spectrum of *ent*-**3h** with 0.5 mol % **QN-SQA**



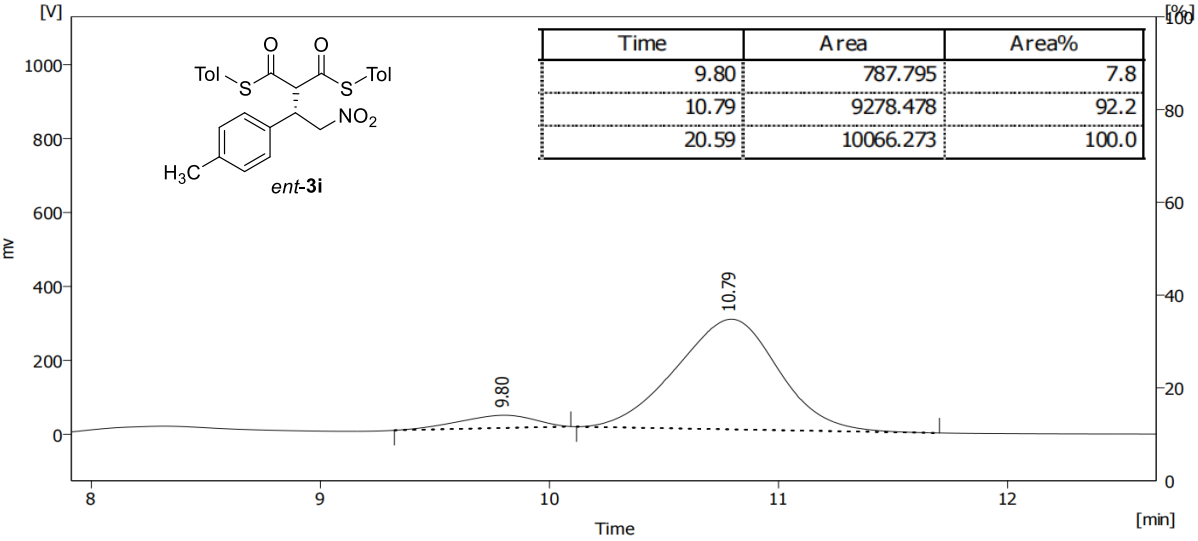
Time	Area	Area%
9.70	1820.152	49.7
10.69	1839.667	50.3
20.39	3659.820	100.0

HPLC spectrum of racemic mixture **3i**



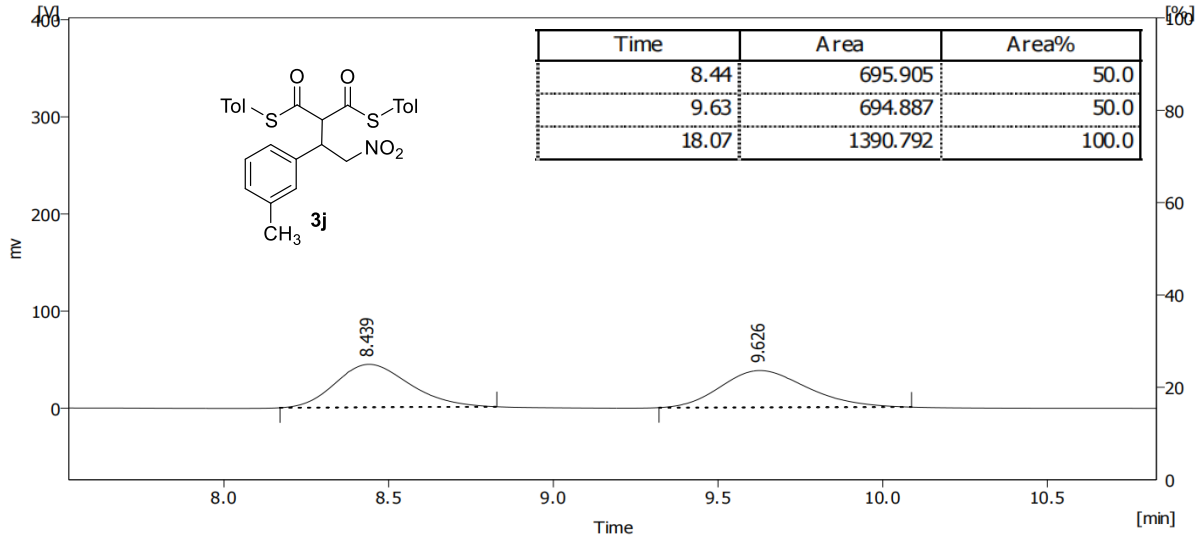
Time	Area	Area%
9.72	14632.647	97.0
10.76	453.535	3.0
20.49	15086.183	100.0

HPLC spectrum of **3i** with 0.5 mol % **QD-SQA**

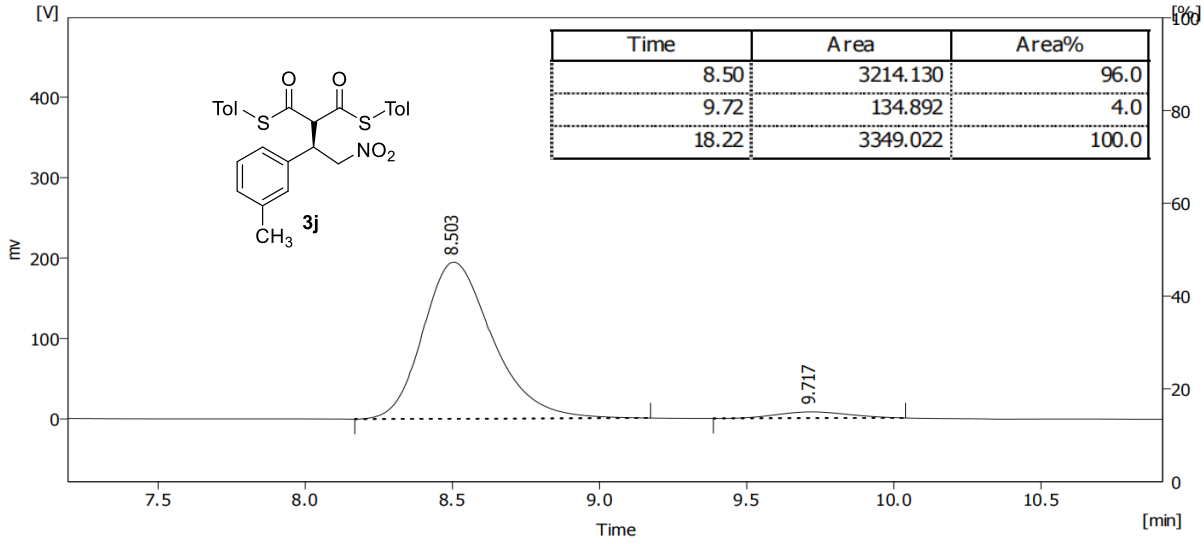


Time	Area	Area%
9.80	787.795	7.8
10.79	9278.478	92.2
20.59	10066.273	100.0

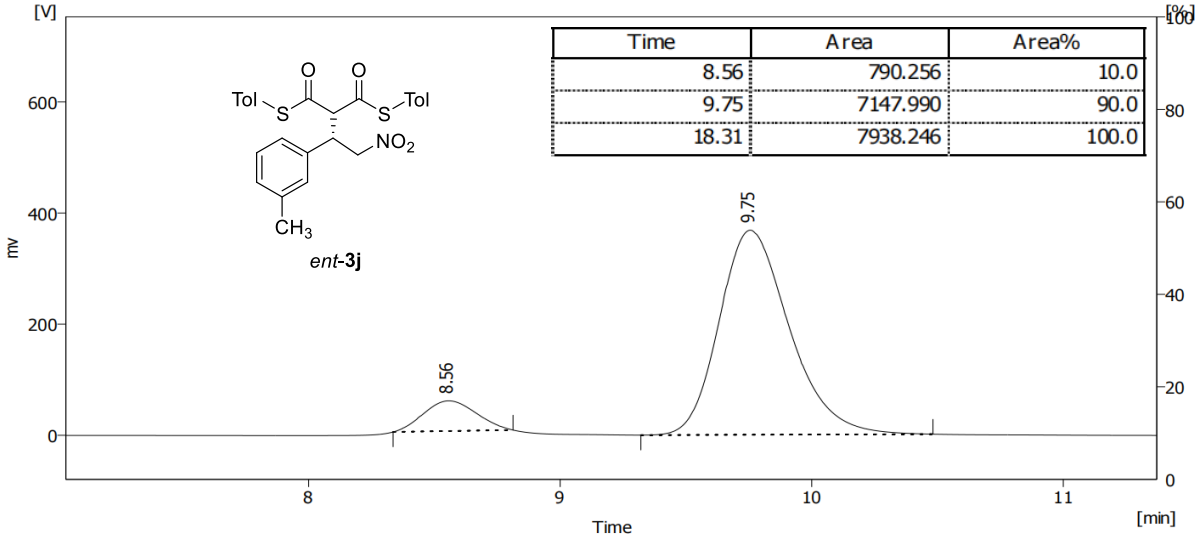
HPLC spectrum of *ent*-**3i** with 0.5 mol % **QN-SQA**



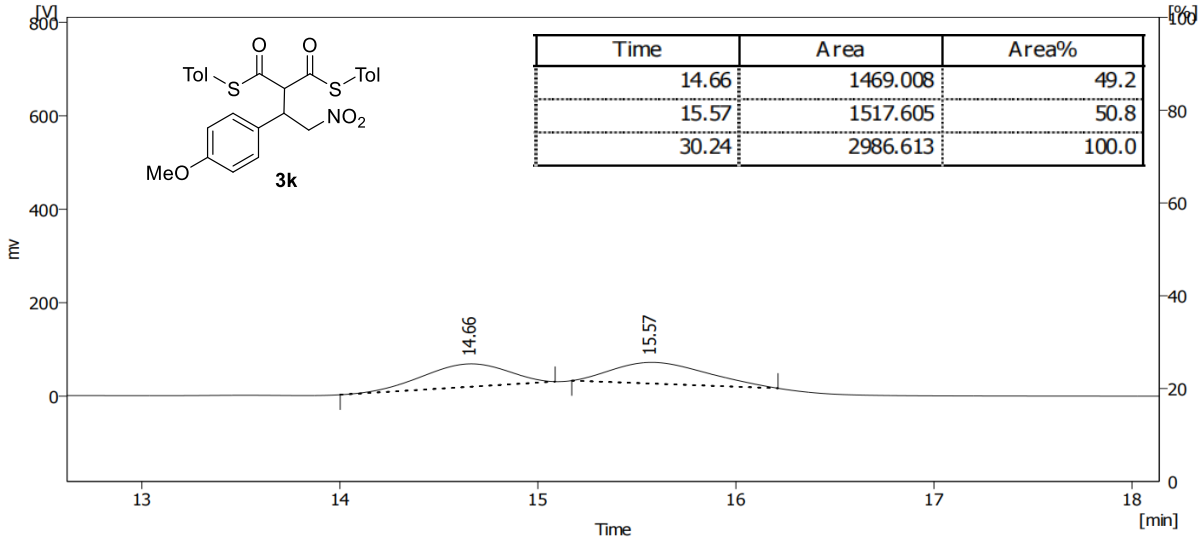
HPLC spectrum of racemic mixture **3j**



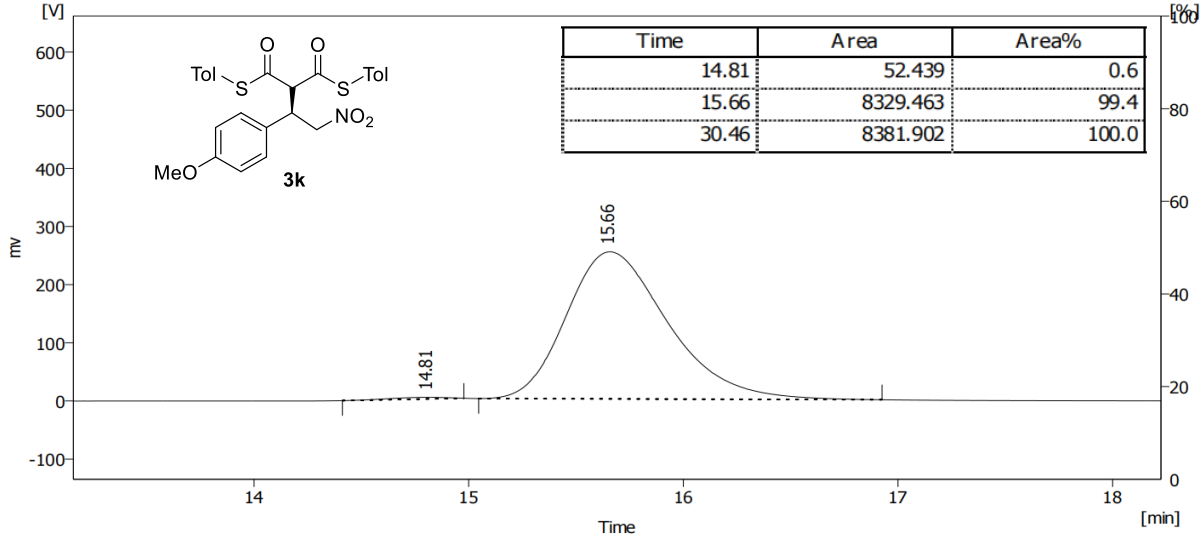
HPLC spectrum of **3j** with 0.5 mol % **QD-SQA**



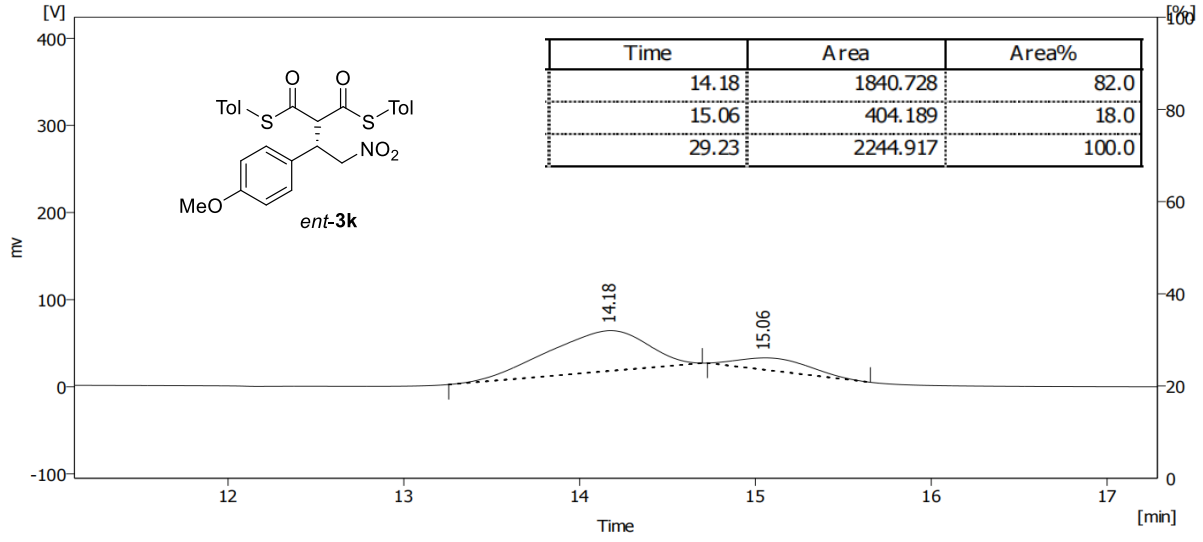
HPLC spectrum of *ent*-**3j** with 0.5 mol % **QN-SQA**



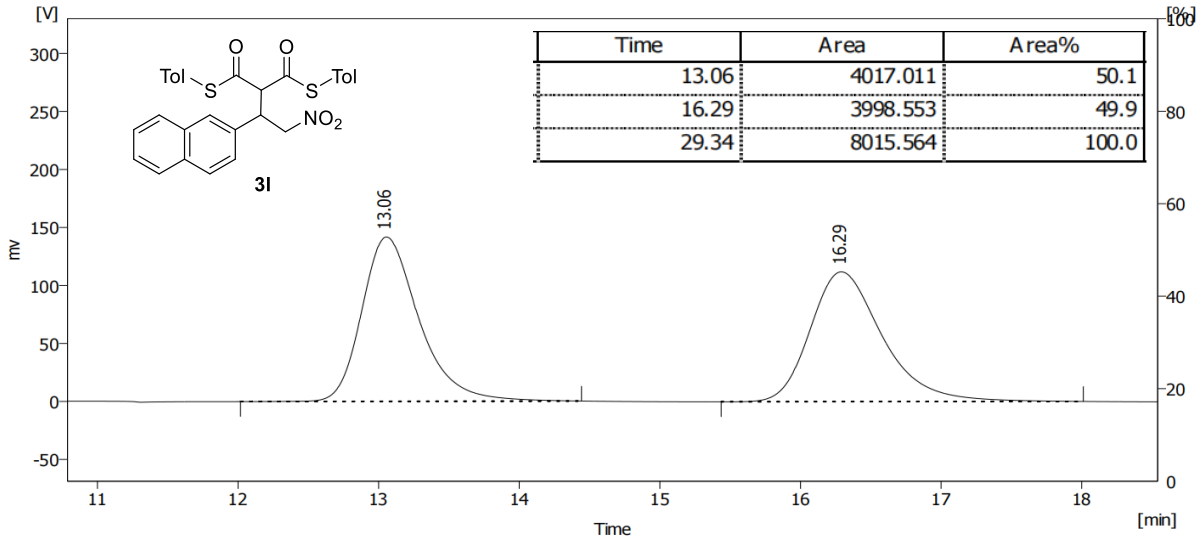
HPLC spectrum of racemic mixture **3k**



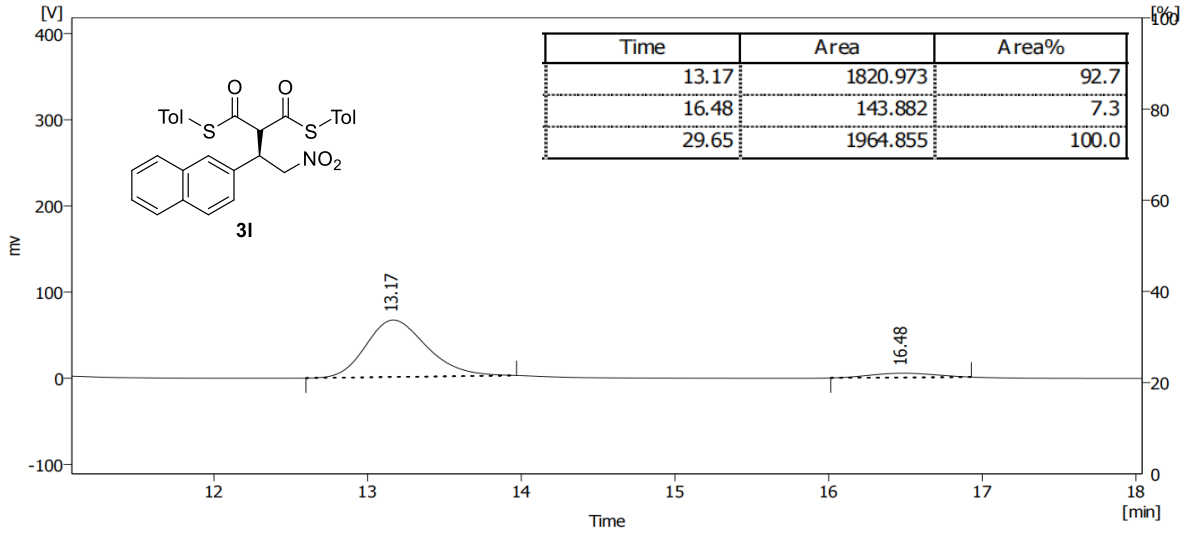
HPLC spectrum of **3k** with 0.5 mol % **QD-SQA**



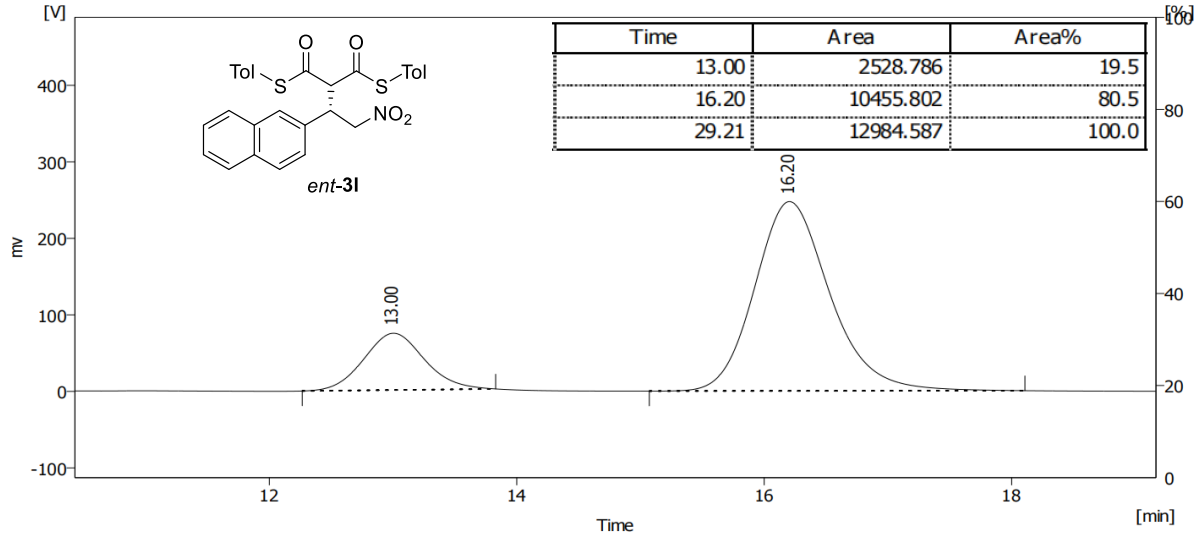
HPLC spectrum of *ent*-**3k** with 0.5 mol % **QN-SQA**



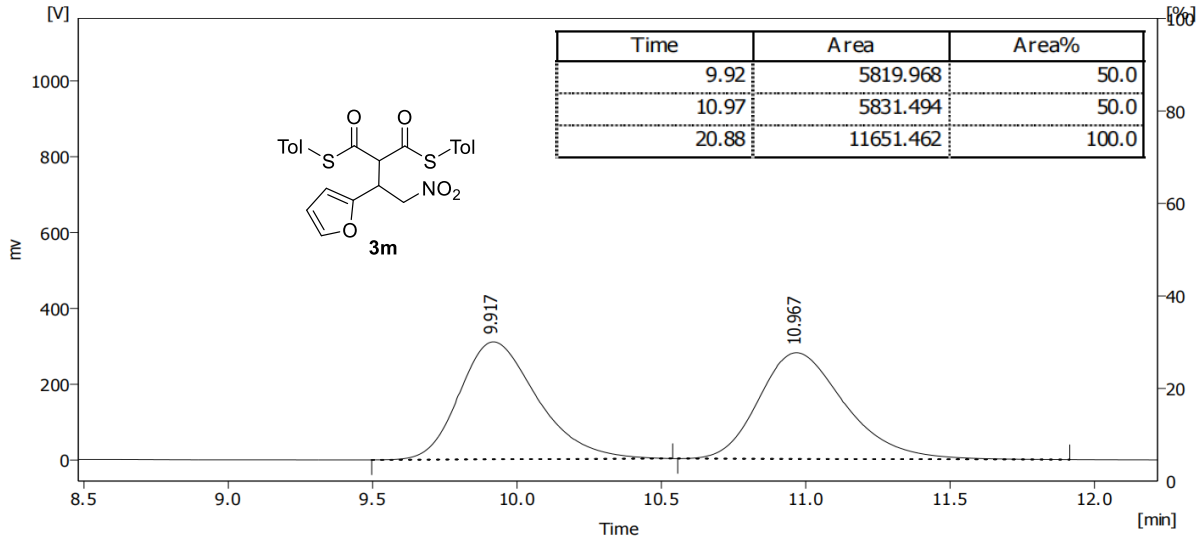
HPLC spectrum of racemic mixture **3l**



HPLC spectrum of **3l** with 0.5 mol % **QD-SQA**

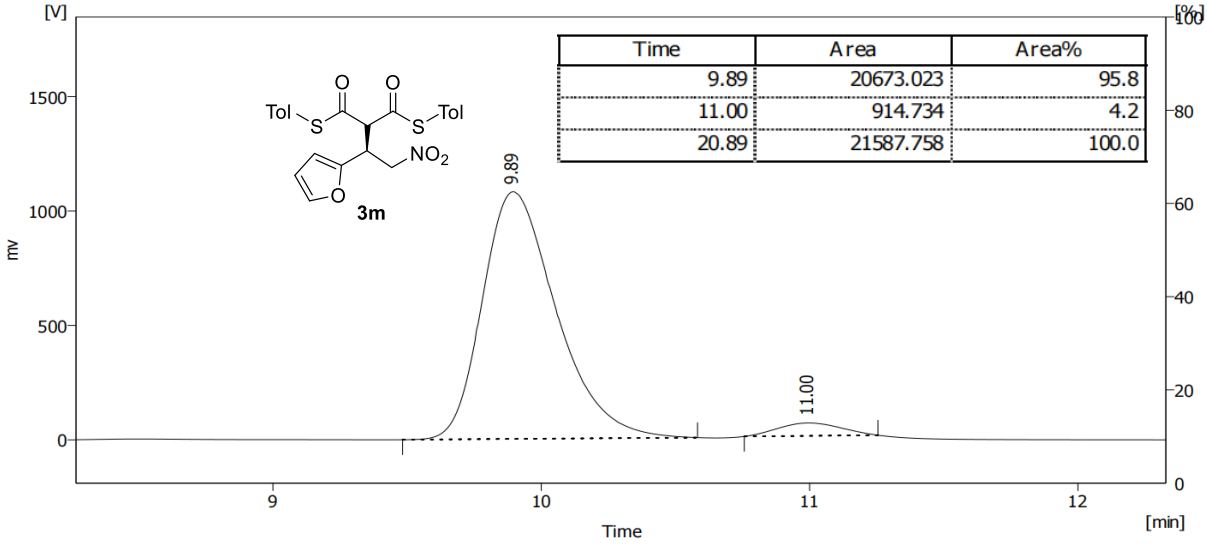


HPLC spectrum of *ent*-**3l** with 0.5 mol % **QN-SQA**



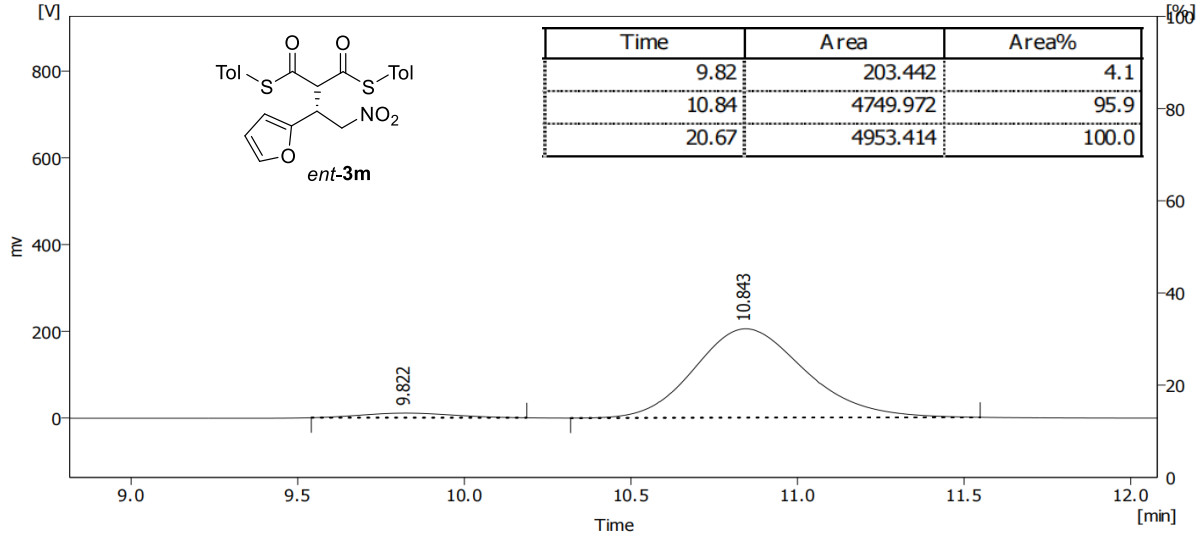
Time	Area	Area%
9.92	5819.968	50.0
10.97	5831.494	50.0
20.88	11651.462	100.0

HPLC spectrum of racemic mixture **3m**



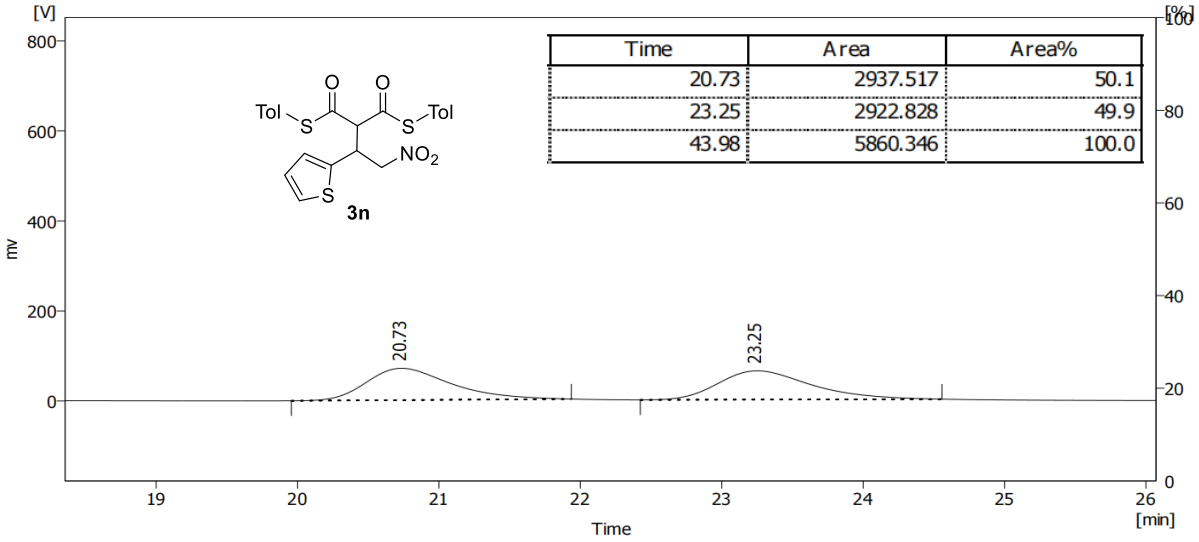
Time	Area	Area%
9.89	20673.023	95.8
11.00	914.734	4.2
20.89	21587.758	100.0

HPLC spectrum of **3m** with 0.5 mol % **QD-SQA**

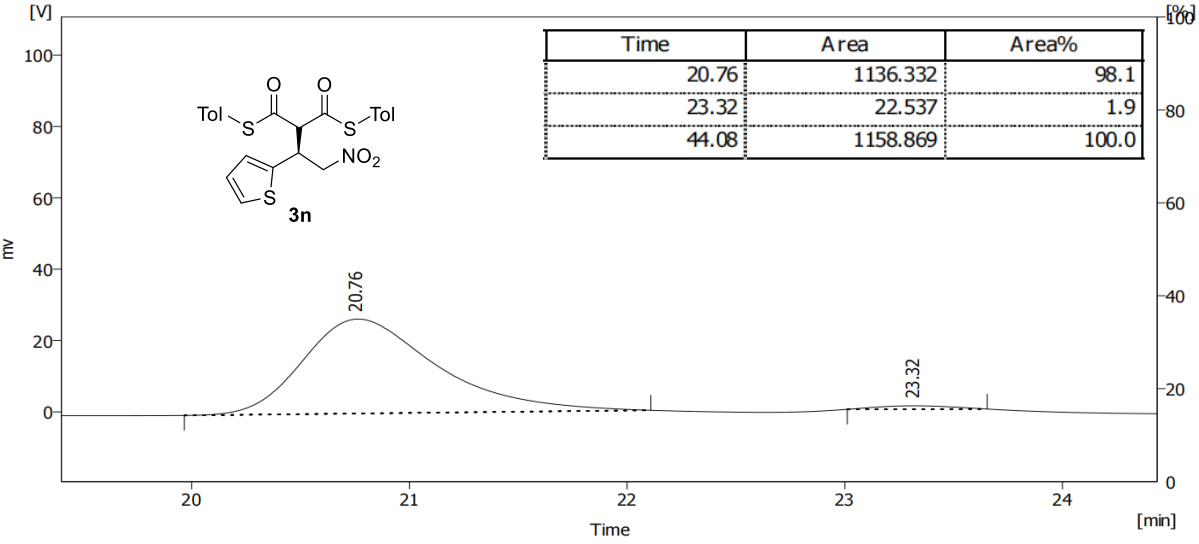


Time	Area	Area%
9.82	203.442	4.1
10.84	4749.972	95.9
20.67	4953.414	100.0

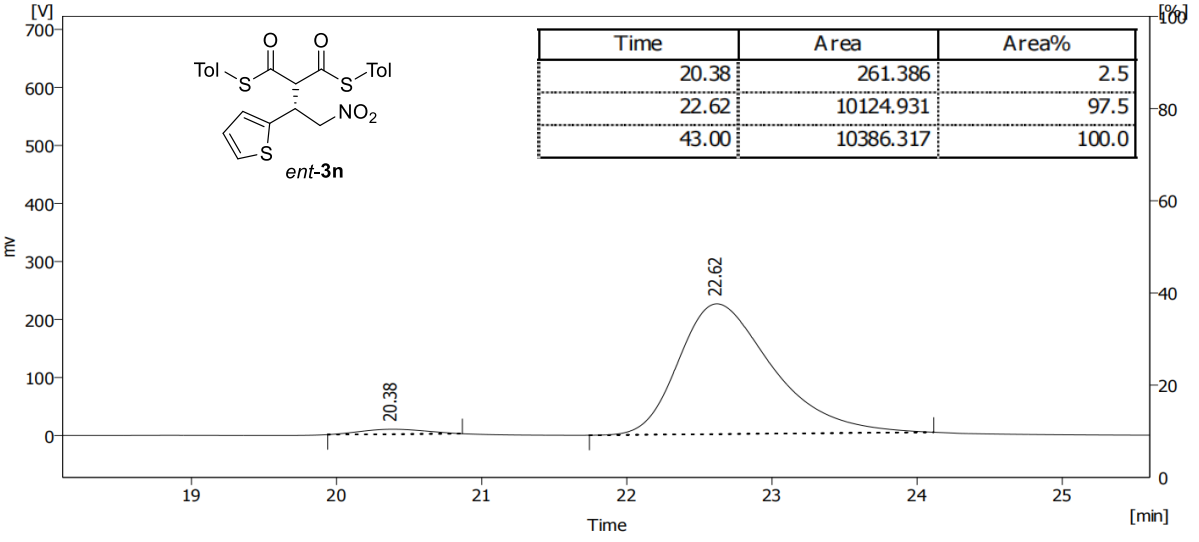
HPLC spectrum of *ent*-**3m** with 0.5 mol % **QN-SQA**



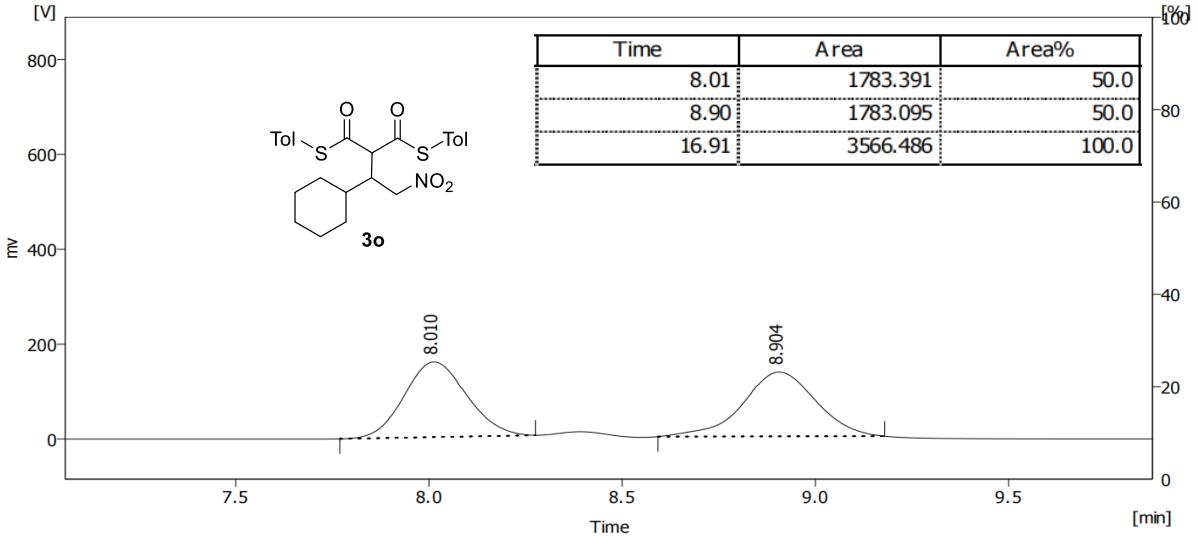
HPLC spectrum of racemic mixture **3n**



HPLC spectrum of **3n** with 0.5 mol % **QD-SQA**

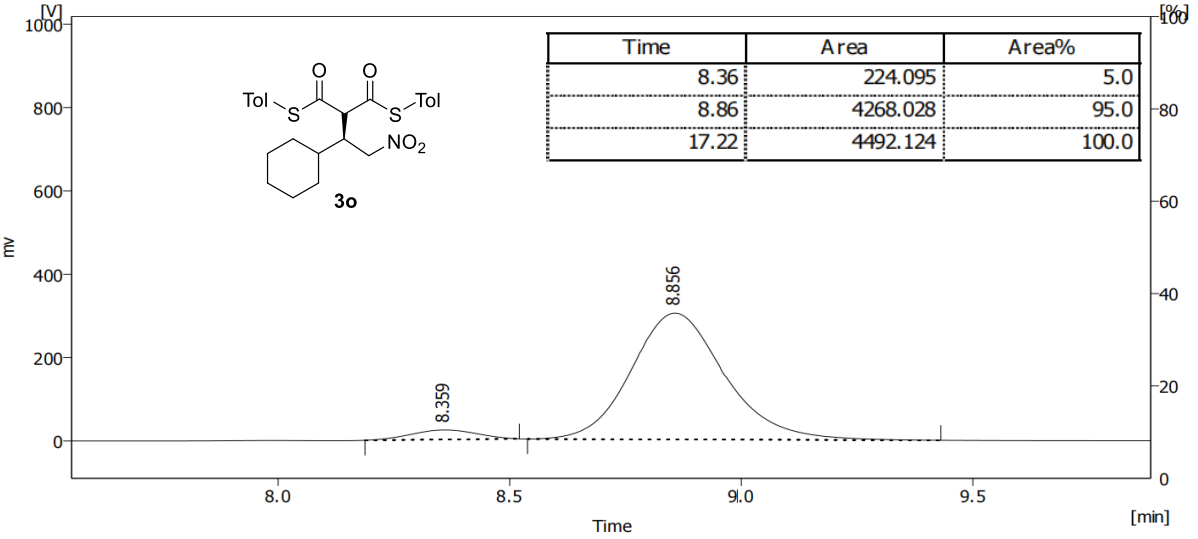


HPLC spectrum of *ent*-**3n** with 0.5 mol % **QN-SQA**



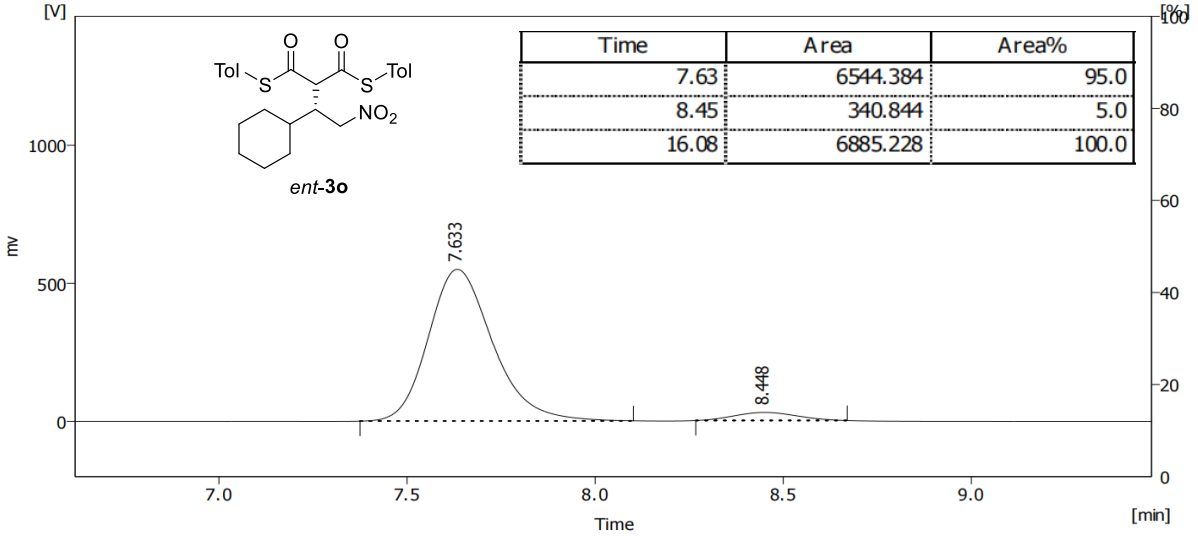
Time	Area	Area%
8.01	1783.391	50.0
8.90	1783.095	50.0
16.91	3566.486	100.0

HPLC spectrum of racemic mixture **3o**



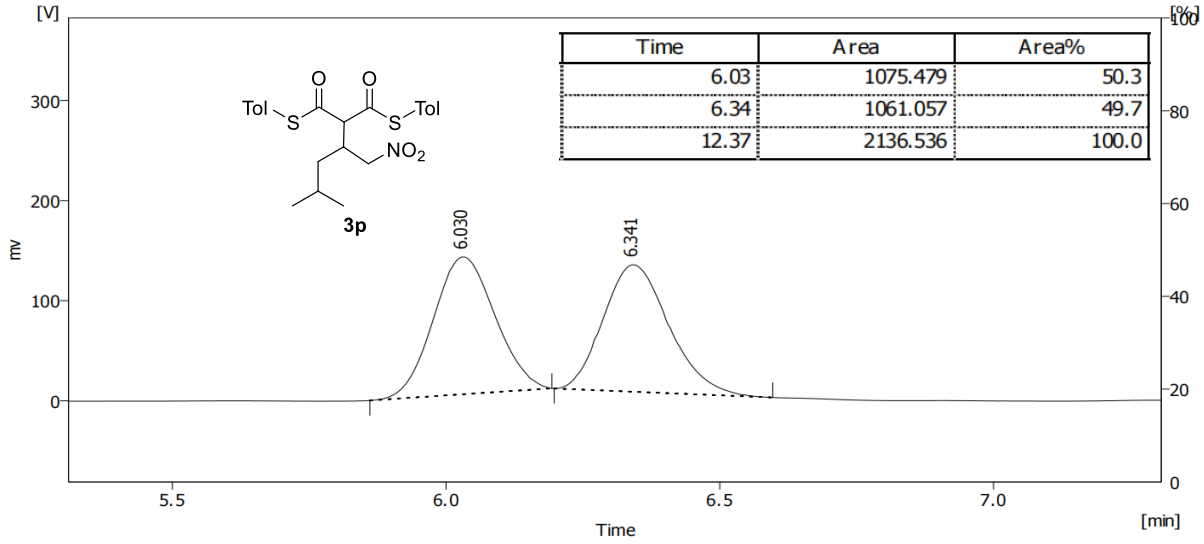
Time	Area	Area%
8.36	224.095	5.0
8.86	4268.028	95.0
17.22	4492.124	100.0

HPLC spectrum of **3o** with 0.5 mol % **QD-SQA**

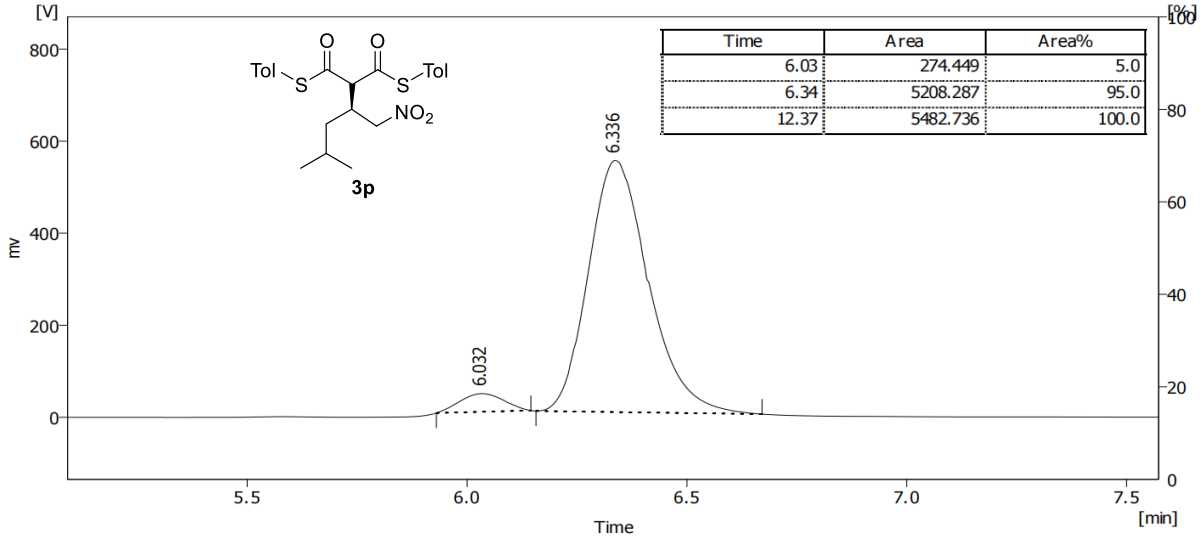


Time	Area	Area%
7.63	6544.384	95.0
8.45	340.844	5.0
16.08	6885.228	100.0

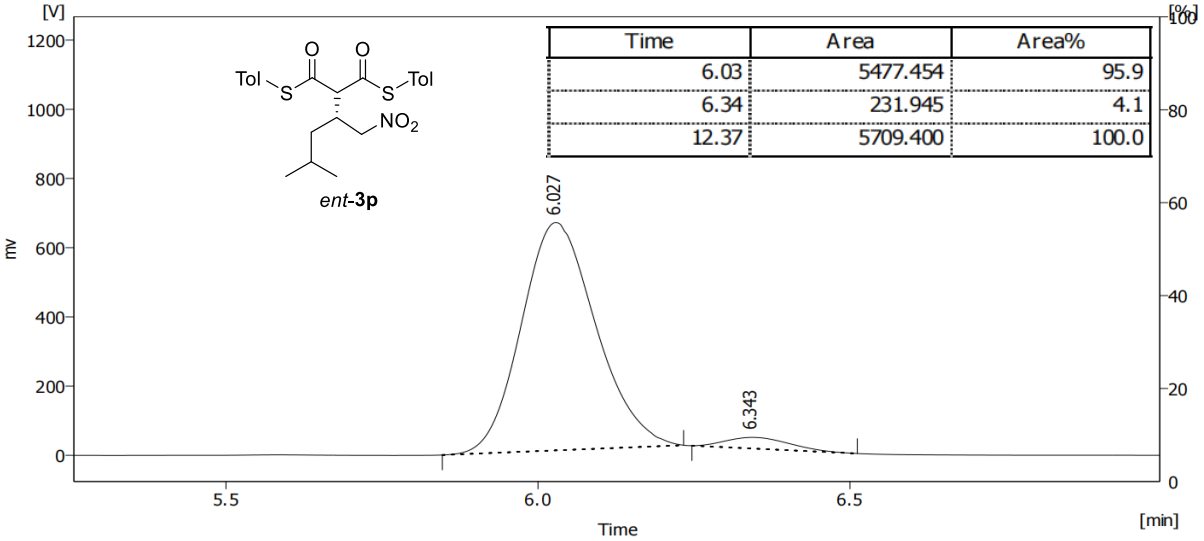
HPLC spectrum of *ent*-**3o** with 0.5 mol % **QN-SQA**



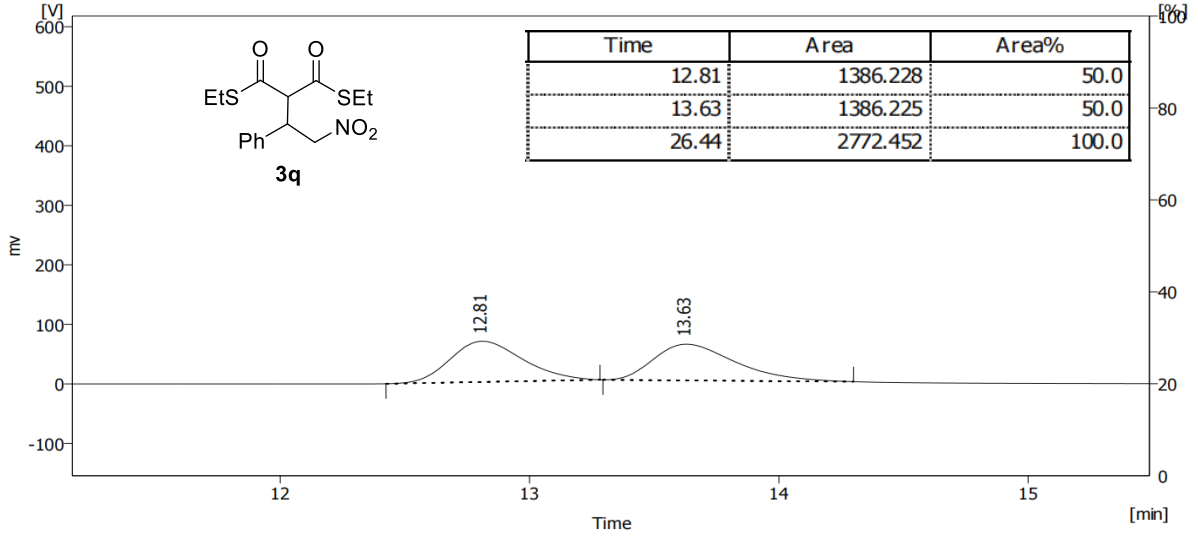
HPLC spectrum of racemic mixture **3p**



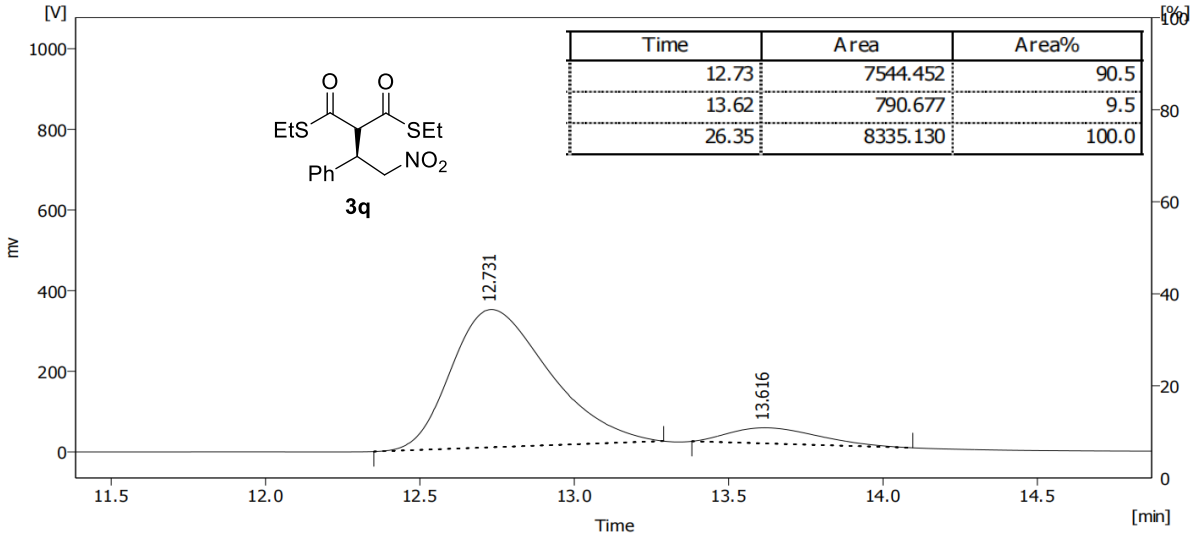
HPLC spectrum of **3p** with 2 mol % **QD-SQA**



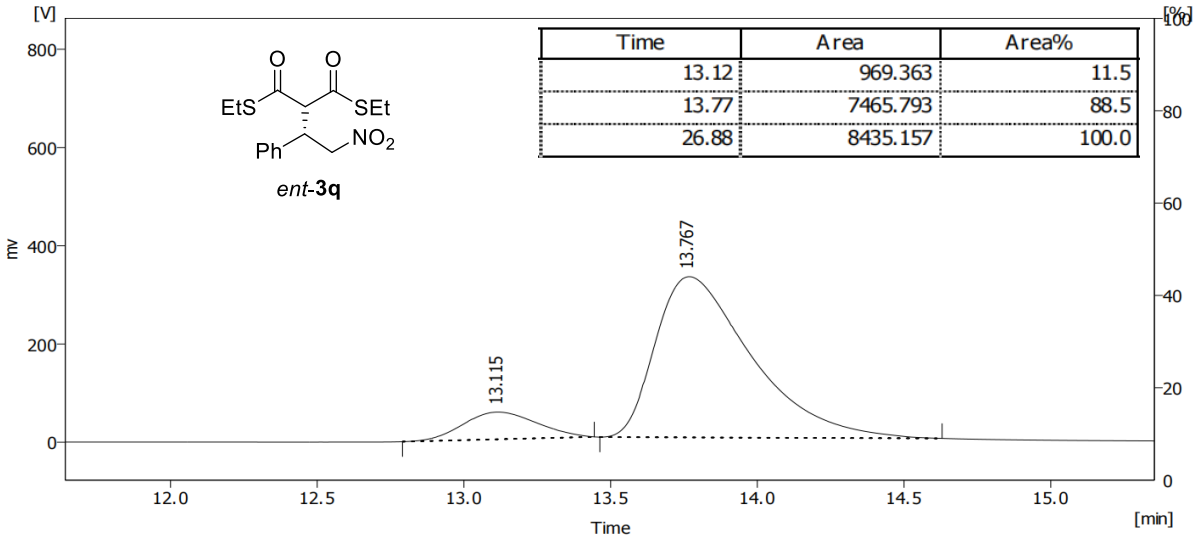
HPLC spectrum of *ent*-**3p** with 2 mol % **QN-SQA**



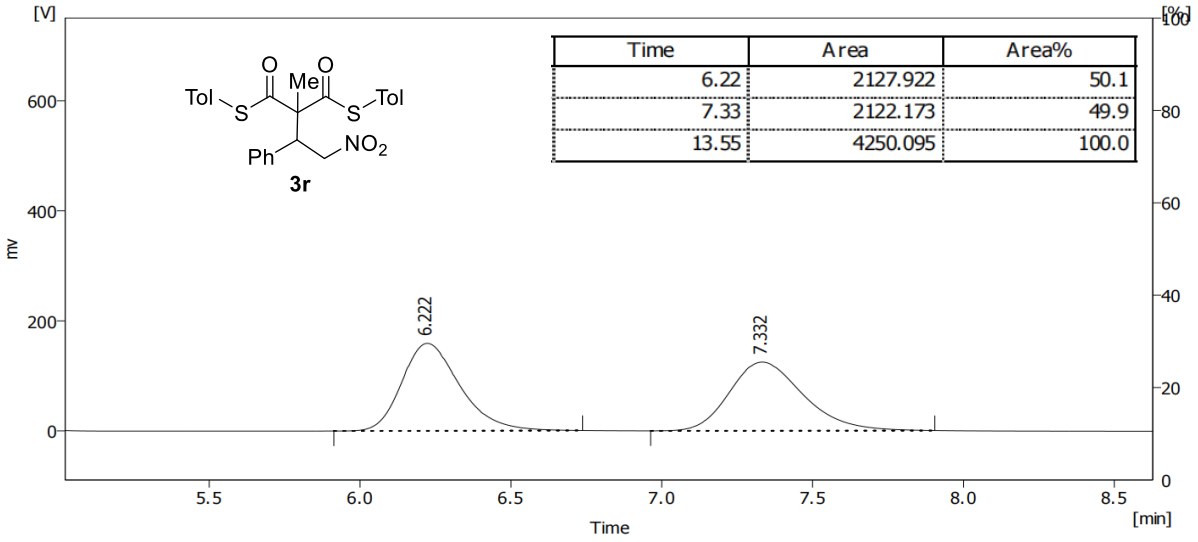
HPLC spectrum of racemic mixture **3q**



HPLC spectrum of **3p** with 2 mol % **QD-SQA**

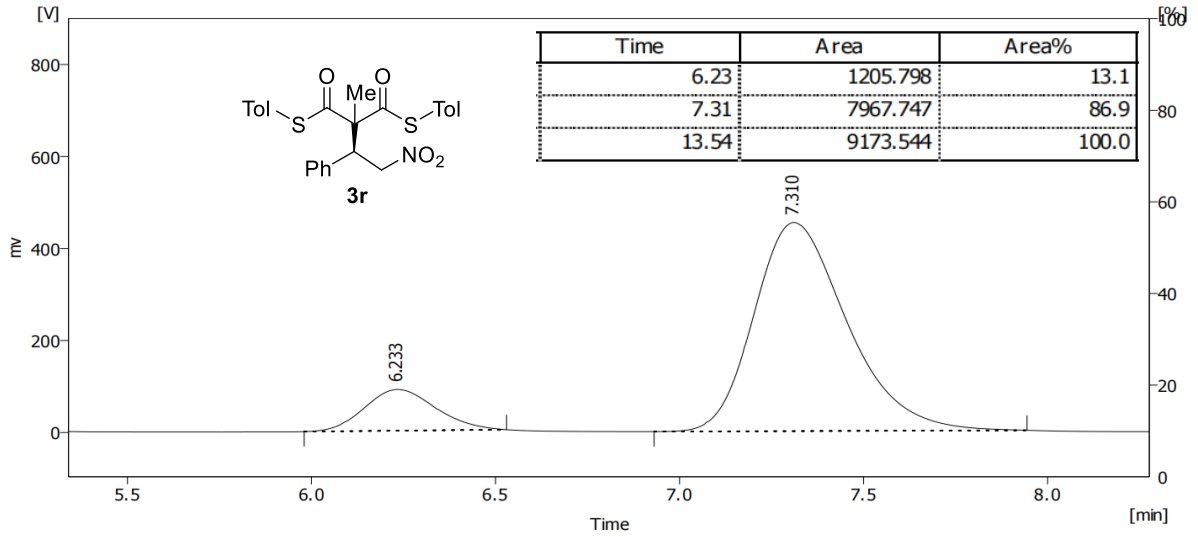


HPLC spectrum of *ent*-**3q** with 2 mol % **QN-SQA**



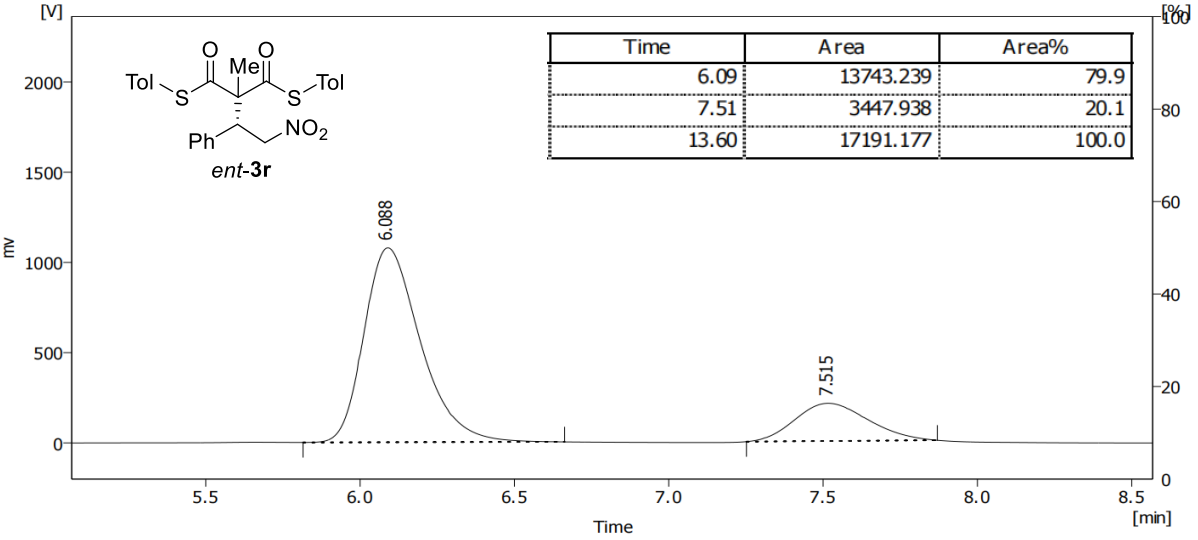
Time	Area	Area%
6.22	2127.922	50.1
7.33	2122.173	49.9
13.55	4250.095	100.0

HPLC spectrum of racemic mixture **3r**



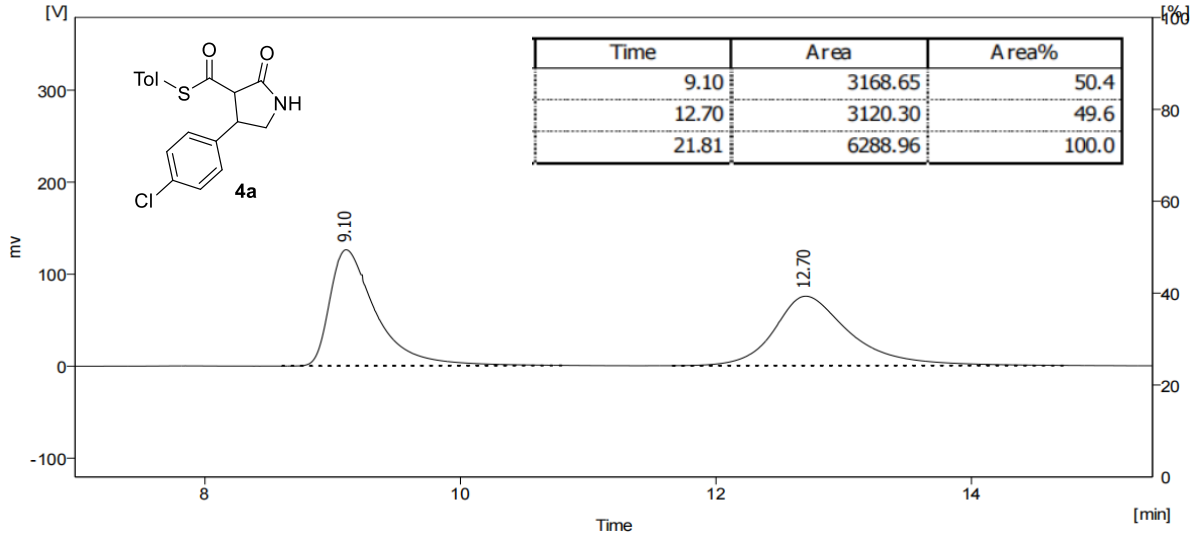
Time	Area	Area%
6.23	1205.798	13.1
7.31	7967.747	86.9
13.54	9173.544	100.0

HPLC spectrum of **3p** with 5 mol % **QD-SQA**

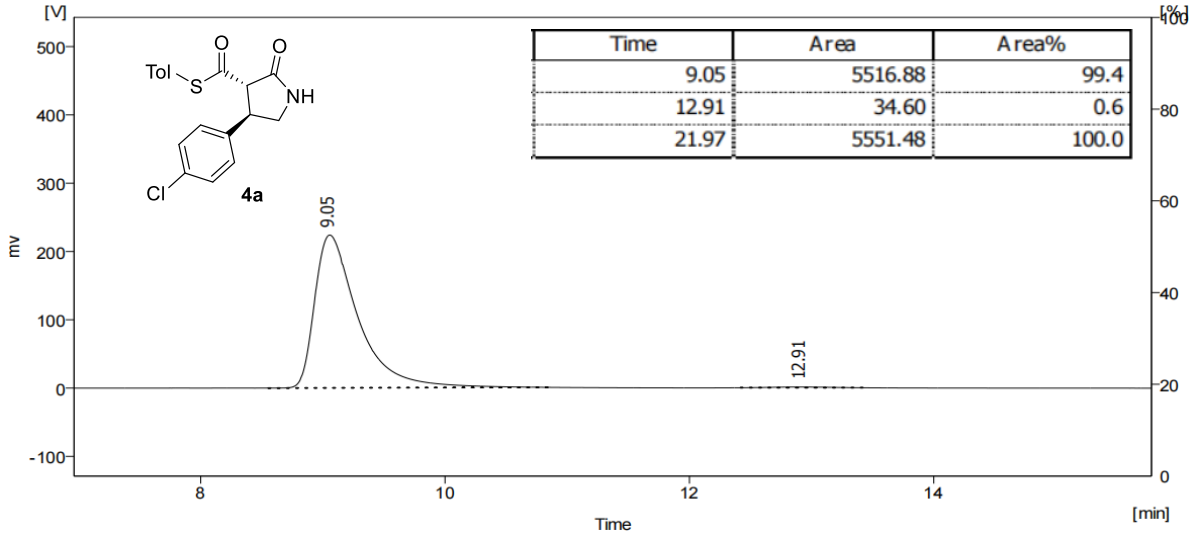


Time	Area	Area%
6.09	13743.239	79.9
7.51	3447.938	20.1
13.60	17191.177	100.0

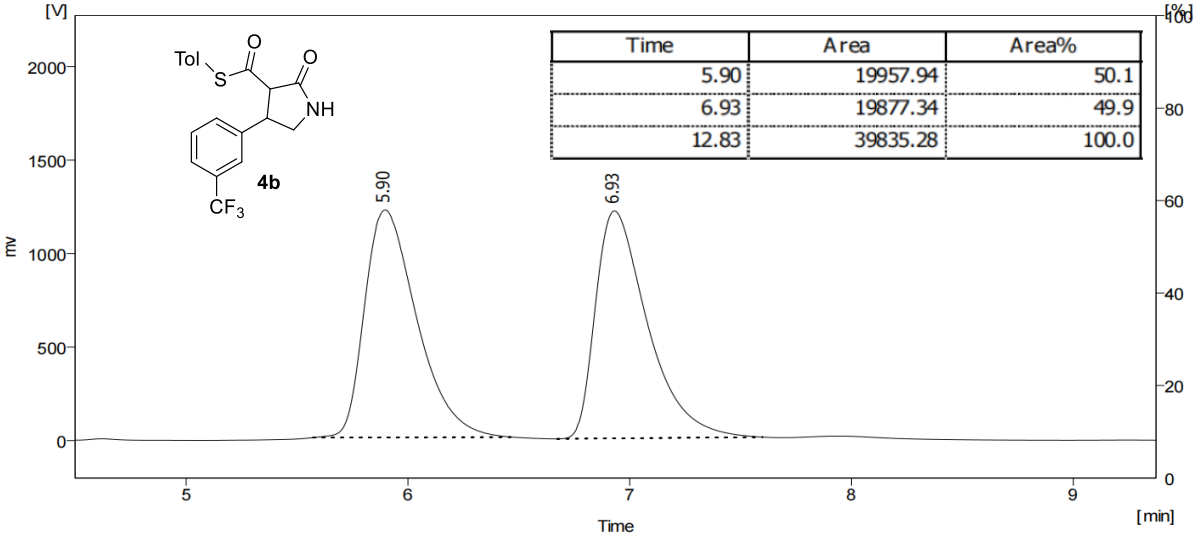
HPLC spectrum of *ent*-**3r** with 5 mol % **QN-SQA**



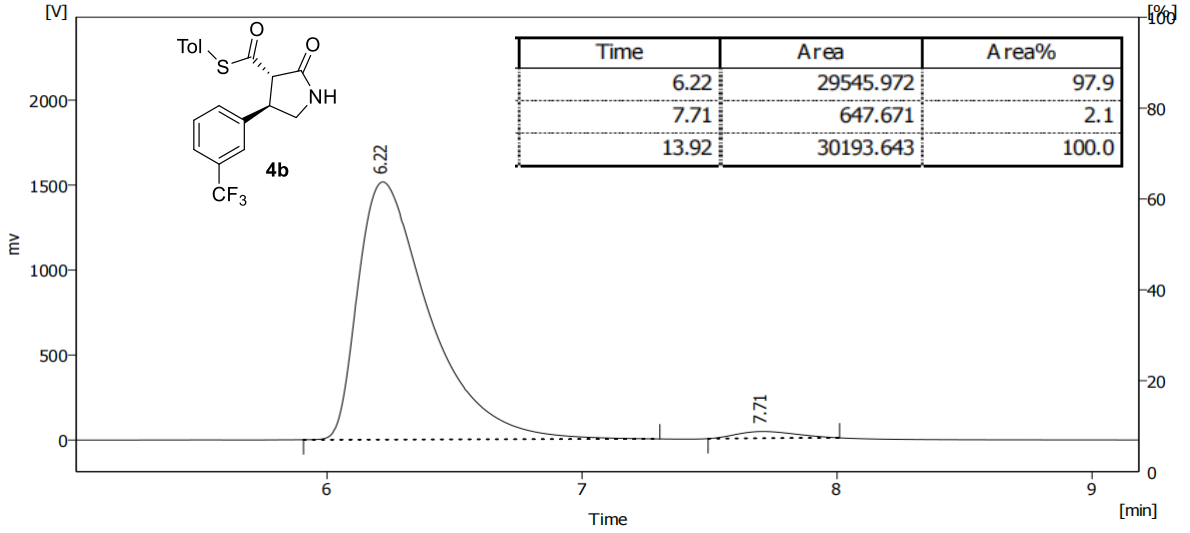
HPLC spectrum of racemic mixture **4a**



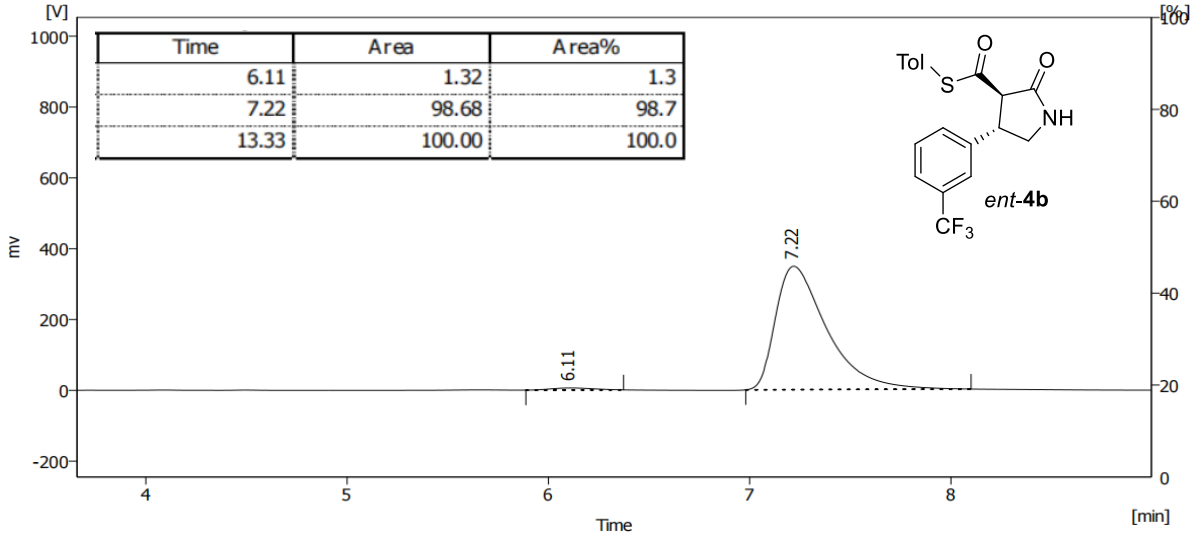
HPLC spectrum of **4a**



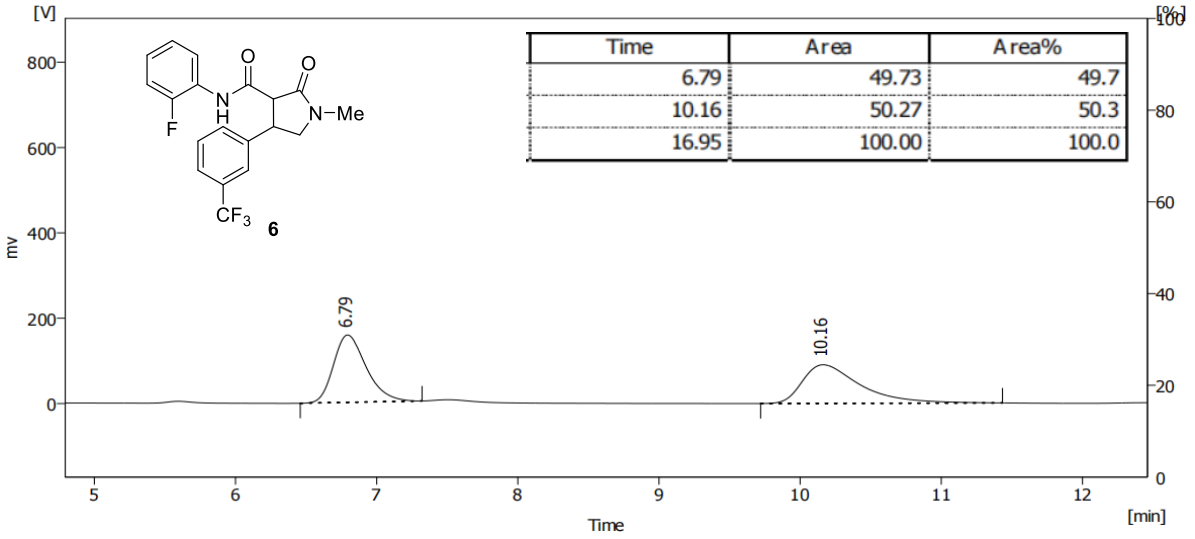
HPLC spectrum of racemic mixture **4b**



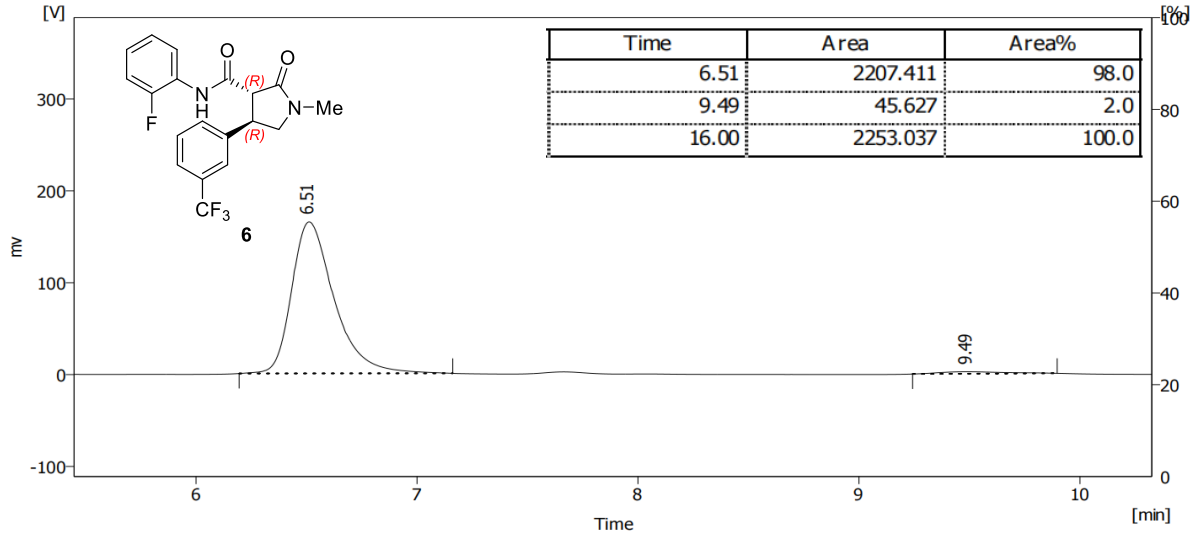
HPLC spectrum of **4b**



HPLC spectrum of *ent*-**4b**

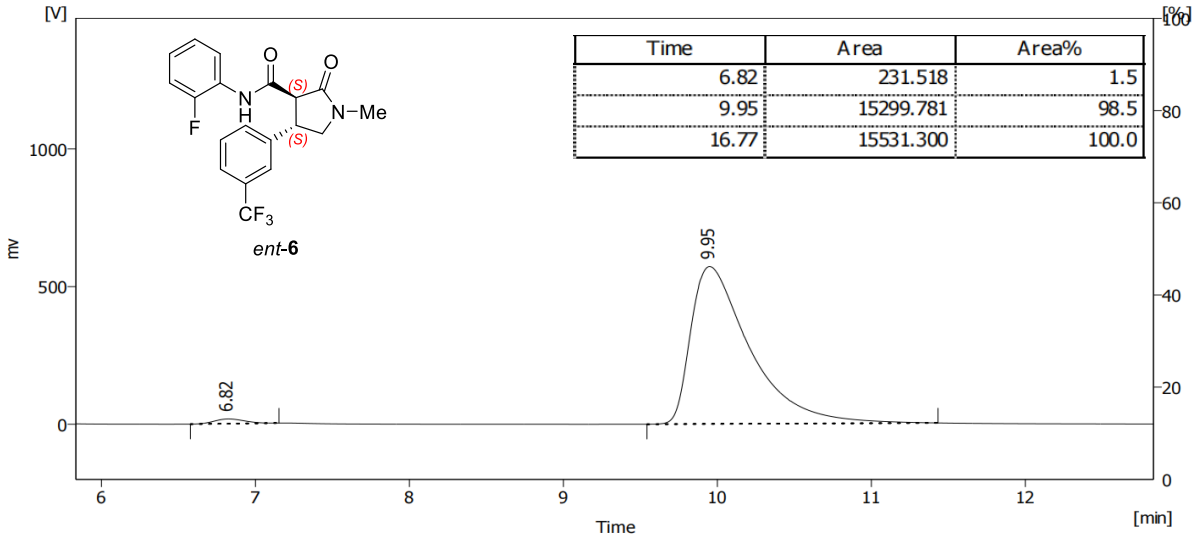


HPLC spectrum of racemic mixture **6**



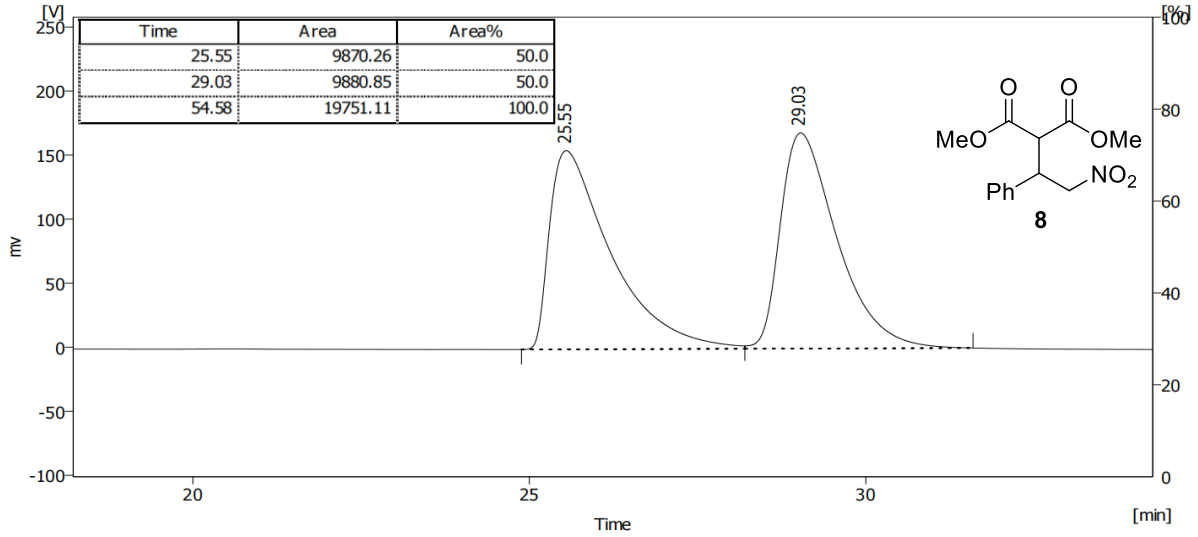
Time	Area	Area%
6.51	2207.411	98.0
9.49	45.627	2.0
16.00	2253.037	100.0

HPLC spectrum of **6**



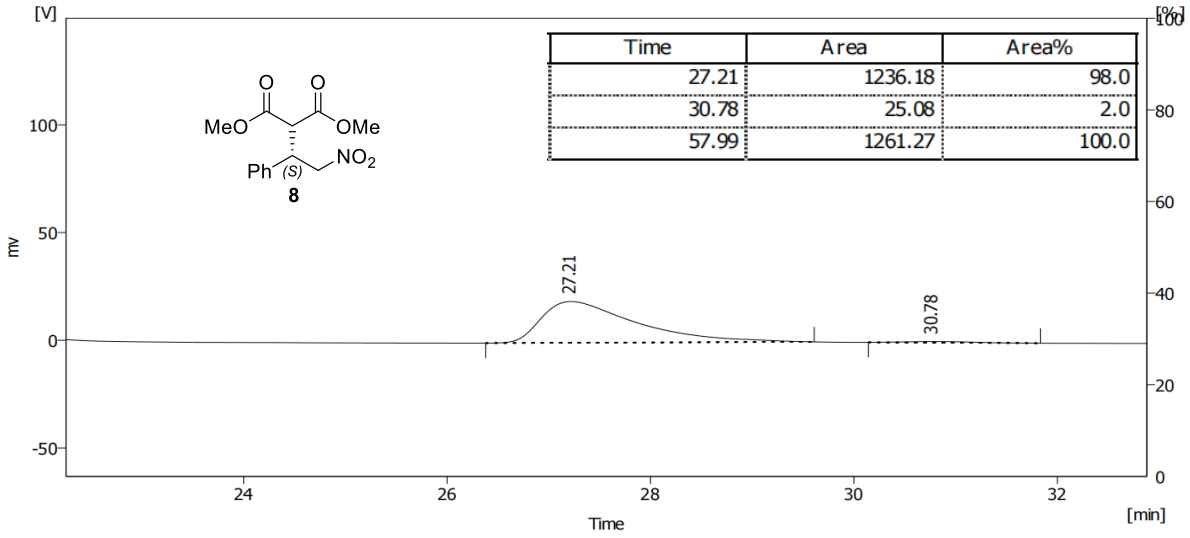
Time	Area	Area%
6.82	231.518	1.5
9.95	15299.781	98.5
16.77	15531.300	100.0

HPLC spectrum of *ent*-**6**

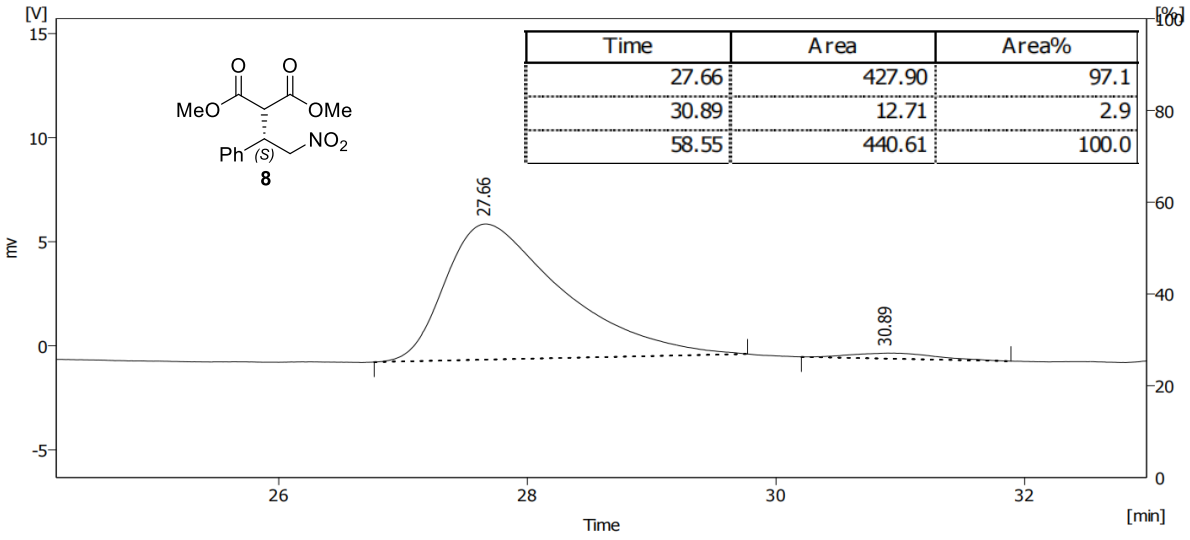


Time	Area	Area%
25.55	9870.26	50.0
29.03	9880.85	50.0
54.58	19751.11	100.0

HPLC spectrum of racemic mixture **8**



HPLC spectrum of **8** with 1 mol % **QN-SQA**



HPLC spectrum of **8** with 1 mol % **HQN-SQA**