Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Palladium-catalyzed enantioselective decarboxylative allylic alkylation of *α*-benzyl cyanoacetates: access to chiral acyclic quaternary carbon stereocenters

Qing Bao,[a,c,#] Ting-Jia Sun,[a,b,#] Yan-Ping Zhang,[a] Zhen-Hua Wang,[a] Yong You,[a] Zhen-Zhen Ge,[a,b] Ming-Qiang Zhou,[a,b] Jian-Qiang Zhao,[a,*] and Wei-Cheng Yuan[a,b,*]

[a]Innovation Research Center of Chiral Drugs, Institute for Advanced Study, Chengdu University, Chengdu, 610106, China

[b]National Engineering Research Center of Chiral Drugs, Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu, 610041, China

[c]School of Pharmacy, Zunyi Medical University, Zunyi, 563006, China

[#]These authors contributed equally.

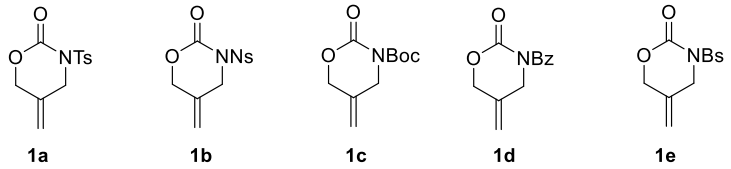
E-mail: zhaojianqiang@cdu.edu.cn;
yuanwc@cioc.ac.cn

Supporting Information

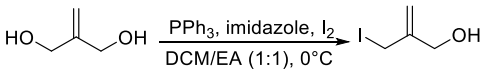
1. General experimental information

Chemical reagents were purchased from commercial sources and were used as received unless mentioned otherwise. Reactions were monitored by thin-layer chromatography (TLC). ^{1}H NMR (400 MHz) and ^{13}C NMR (101 MHz) spectra were recorded in DMSO-d_6. ^{1}H NMR chemical shifts are reported in ppm relative to tetramethylsilane (TMS), with the solvent resonance employed as the internal standard (DMSO-d_6 at 2.50 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, brs = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration. ^{13}C NMR chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard (DMSO-d_6 at 39.51 ppm). Melting points were recorded on a Büchi Melting Point B-545 unit. The HRMS were recorded by The HRMS were recorded by Agilent 6545 LC/Q-TOF mass spectrometer.

2. General experimental procedures for synthesis of alkenyl carbamate 1

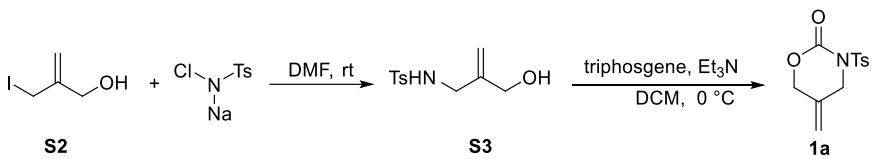


2-(Iodomethyl)-prop-2-en-1-o (S2) [1,2].



To a stirring solution of 2-methylenepropane-1,3-diol (5.7 g, 65 mmol), triphenylphosphine (18.6 g, 71 mmol) and imidazole (4.8 g, 71 mmol) in a 1:1 mixture of dichloromethane/ethyl acetate (100 mL) at 0 ℃ was added iodine (16.4 g, 65 mmol) portion-wise during 1 h. The reaction mixture was left to stir for 9 h at 0 ℃ before being diluted in ethyl acetate (50 mL) followed by washing with water (100 mL). The aqueous layer was extracted with ethyl acetate (25 × 3 mL) and the organic layers combined, dried over anhydrous Na_2SO_4 and concentrated to yield crude material which was purified by flash column chromatography on silica gel (20% ethyl acetate in petroleum ether) to furnish the product **S2** as a colorless oil.

5-methylene-3-tosyl-1,3-oxazinan-2-one (1a)



To a solution of **S2** (5.0 g, 25 mmol) in DMF (80 mL) was added chloramine-T (8.6 g, 37 mmol). And the reaction mixture was stirred for 30 minutes at room temperature. Then the reaction was quenched by aq. $Na_2S_2O_3$ (1 M, 100 mL). The mixture was extracted with ethyl acetate and the

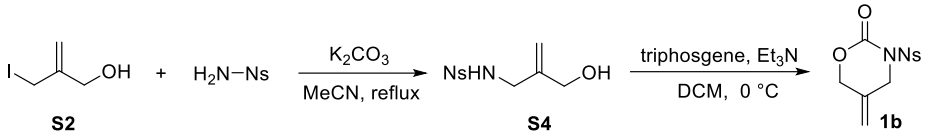
organic layer was washed with water, dried over anhydrous Na_2SO_4. After evaporation of solvent, the obtained crude product **S3** is proceeded directly to the next step without purification.

A solution of triphosgene (7.4 g, 25 mmol) in CH_2Cl_2 (100 mL) was slowly added to a solution of *N*-(2-(hydroxymethyl)allyl)-4-methylbenzenesulfonamide **S3** (4.6 g, 25 mmol) and triethylamine (35 mL, 250 mmol, 10 equiv) in CH_2Cl_2 (100 mL) at 0 °C over 30 min. The resulting mixture was stirred for 1 h. After completion of the reaction, as indicated by TLC, the reaction was quenched with aq. NH_4Cl and extracted with CH_2Cl_2 (80 mL × 3). The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with (PE/EA/DCM = 1:1:1) and the crude product thus obtained was purified by the recrystallization to afford compound **1a** as a white solid.

5-methylene-3-tosyl-1,3-oxazinan-2-one (1a): White solid;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 – 7.78 (m, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 5.35 – 5.29 (m, 1H), 5.30-5.25 (m, 1H), 4.66 (s, 2H), 4.50 (t, *J* = 1.6 Hz, 2H), 2.43 (s, 3H).

5-methylene-3-((4-nitrophenyl)sulfonyl)-1,3-oxazinan-2-one) (1b) [1,2]



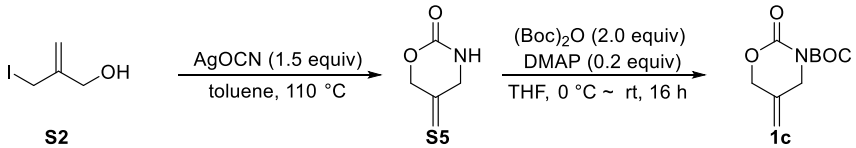
In a reaction tube equipped with a magnetic stirring bar, the solution of **S2** (2.0 g, 10 mmol) in MeCN (40 mL) was at 80 °C, followed by addition of K_2CO_3 (2.8 g, 20 mmol, 2.0 equiv) and $NsNH_2$ (2.0 g, 10 mmol, 1.0 equiv). The resulting mixture was stirred for 1 h, filtered, and thus the filtrate obtained was concentrated in vacuo. Then the residue was purified by column chromatography (PE/EA/CH_2Cl_2 = 1:1:1) to afford the compound **S4** as a white solid (1.2 g, 44% yield).

A solution of triphosgene (445 mg, 1.5 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL) was slowly added to a solution of *N*-(2-(hydroxymethyl)allyl)-4-nitrobenzenesulfonamide **S4** (272 mg, 1.0 mmol) and triethylamine (1.4 mL, 10 mmol, 10 equiv) in CH_2Cl_2 (10 mL) at 0 °C over 30 min. The resulting mixture was stirred for 30 min. After completion of the reaction, as indicated by TLC. The reaction was quenched with aq. NH_4Cl and extracted with CH_2Cl_2 (30 mL × 3). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with (PE/EA = 1:3) and the crude product thus obtained was purified by the recrystallization to afford compound **1b** as a white solid.

5-methylene-3-((4-nitrophenyl)sulfonyl)-1,3-oxazinan-2-one (1b): White solid;

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 – 8.34 (m, 2H), 8.32 – 8.19 (m, 2H), 5.39 (t, *J* = 1.6 Hz, 1H), 5.37 – 5.33 (m, 1H), 4.72 (t, *J* = 0.9 Hz, 2H), 4.55 (t, *J* = 1.6 Hz, 2H).

3-((λ^1-methyl)(λ^1-oxidaneyl)boraneyl)-5-methylene-1,3-oxazinan-2-one)) (1c) [1]



A solution of **S2** (5 g, 25 mmol, 1.0 equiv) in dry toluene (20 mL) was added AgOCN (5.7 g, 11 mmol, 1.5 equiv). the resulting mixture was refluxed in toluene (50 mL) for 14 h. Then, the mixture was filtered and the precipitate was washed with ethyl acetate, and concentrated in vacuo.

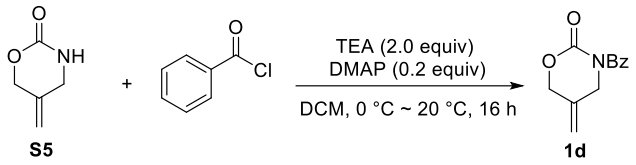
The product was obtained after purification by column chromatography on silica gel (PE/EA = 1:1) to provide **S5** as a white solid.

A solution of **S5** (452 mg, 4 mmol) in THF (10 mL), DMAP (0.98 g, 0.8 mmol) was added, followed by adding dropwise the solution of di(*tert*-butyl) carbonate (1.74 g, 8 mmol) at 0 ℃. After completion of the reaction, as indicated by TLC, the reaction was quenched with aq. NH_4Cl and extracted with ethyl acetate (20 mL × 2). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with petroleum ether / ethyl acetate = 5/1 to afford compound **1c** as a yellow oil.

3-((λ^1-methyl)(λ^1-oxidaneyl)boraneyl)-5-methylene-1,3-oxazinan-2-one)) **(1c):** White solid;

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.18 (d, *J* = 6.1 Hz, 2H), 4.63 (s, 2H), 4.28 (s, 2H), 1.51 (s, 9H).

3-benzoyl-5-methylene-1,3-oxazinan-2-one (1d) [1]



A solution of **S5** (452 mg, 4 mmol) in DCM (10 mL), DMAP (0.12 g, 1.0 mmol) was added, followed by adding dropwise the solution of triethylamine (1.1 mL, 8 mmol) at 0 ℃, After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with HCl (1M, 30 mL), concentrated under reduced pressure, diluted with water, and extracted with DCM (15 mL × 3). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuo. The product was obtained after purification by column chromatography on silica gel (PE/EA = 2:1) to give the desired product **1d** as a white solid. Compound **1e** was prepared by the same method.

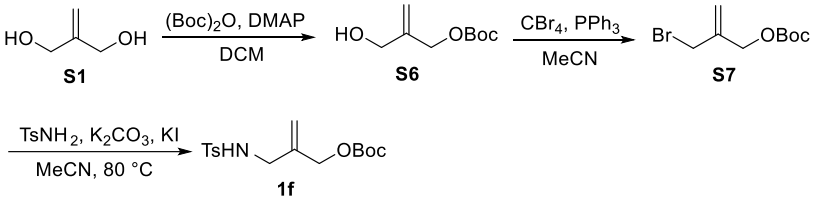
3-benzoyl-5-methylene-1,3-oxazinan-2-one (1d): White solid;

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 7.7 Hz, 2H), 7.53 –7.50 (m, 1H), 7.46 –7.38 (m, 2H), 5.35 – 5.27 (m, 2H), 4.84 (s, 2H), 4.50 (d, *J* = 2.1 Hz, 2H).

5-methylene-3-(phenylsulfonyl)-1,3-oxazinan-2-one (1e): White solid;

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16-7.96 (m, 2H), 7.70 – 7.62 (m, 1H), 7.62 – 7.50 (m, 2H), 5.32 (d, *J* = 1.8 Hz, 1H), 5.30 – 5.25 (m, 1H), 4.67 (s, 2H), 4.52 (t, *J* = 1.7 Hz, 2H);

***tert*-butyl (2-(((4-methylphenyl)sulfonamido)methyl)allyl) carbonate (1f)**)[1,2]



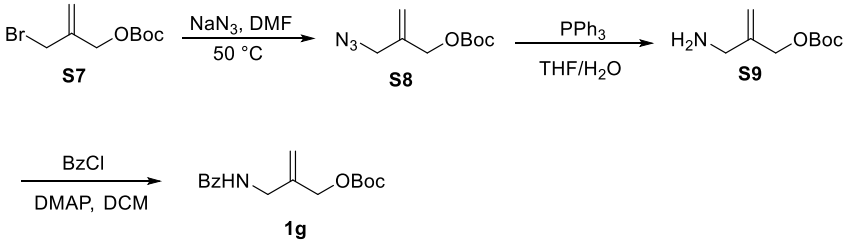
To a solution of **S1** (4.0 g, 45 mmol) in DCM (40 mL) was added DMAP (0.6 g, 5 mmol), followed by adding dropwise the solution of di(*tert*-butyl) carbonate (11.4 mL, 49.5 mmol) in CH_2Cl_2 (50 mL) at 0 ℃. After completion of the reaction, as indicated by TLC, the solution was concentrated under reduced pressure and the mixture was dissolved in MeCN (50 mL) followed by adding CBr_4 (15.7 g) at room temperature. Then the mixture was added PPh_3 in partially. After completion monitored by TLC, the reaction was concentrated in vacuo and purified by column chromatography (PE/EA = 100:1) to afford the product **S7**.

The solution of **S7** (5 mmol, 1.25 g) in CH_3CN (20.0 mL) was heated with oil bath and refluxed

at 82 ℃, followed by addition of K_2CO_3 (1.4 g, 10 mmol, 2.0 equiv), KI (10 mg) and $TsNH_2$ (1.7 g, 10.0 mmol). Maintaining the reaction stirring at the same temperature until **S7** consumed as monitored by TLC. Then, the suspension was filtered through a short of celite column and the filtrate was concentrated, purified by column chromatography (PE/EA = 5:1) to afford the product **1f** as a white solid.

***tert*-butyl (2-(((4-methylphenyl)sulfonamido)methyl)allyl) carbonate (1f):** White solid;
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.8 Hz, 2H), 5.16 (s, 2H), 4.86 (t, *J* = 6.5 Hz, 1H), 4.45 (s, 2H), 3.60 (d, *J* = 6.5 Hz, 2H), 2.42 (s, 3H), 1.46 (s, 9H).

2-(benzamidomethyl)allyl *tert*-butyl carbonate (1g)



To a stirring solution of **S7** (2.0 g, 8 mmol, 1.0 equiv) was dissolved in dry DMF (40 mL), NaN_3 (1.0 g, 16.0 mmol, 2.0 equiv) was added dropwise for 10 min at 0 °C. The reaction was heated at 50 ℃ for 12h. After completion of the reaction (confirmed by TLC analysis), a precipitate mixture formed upon cooling the reaction mixture to room temperature, then quenched by water. The aqueous phase was extracted by ethyl acetate (20 mL × 3), and the combined extracts washed with brine. The organic phase was dried over anhydrous Na_2SO_4 and evaporated in vacuo. The obtained crude product **S8** is proceeded directly to the next step without purification.

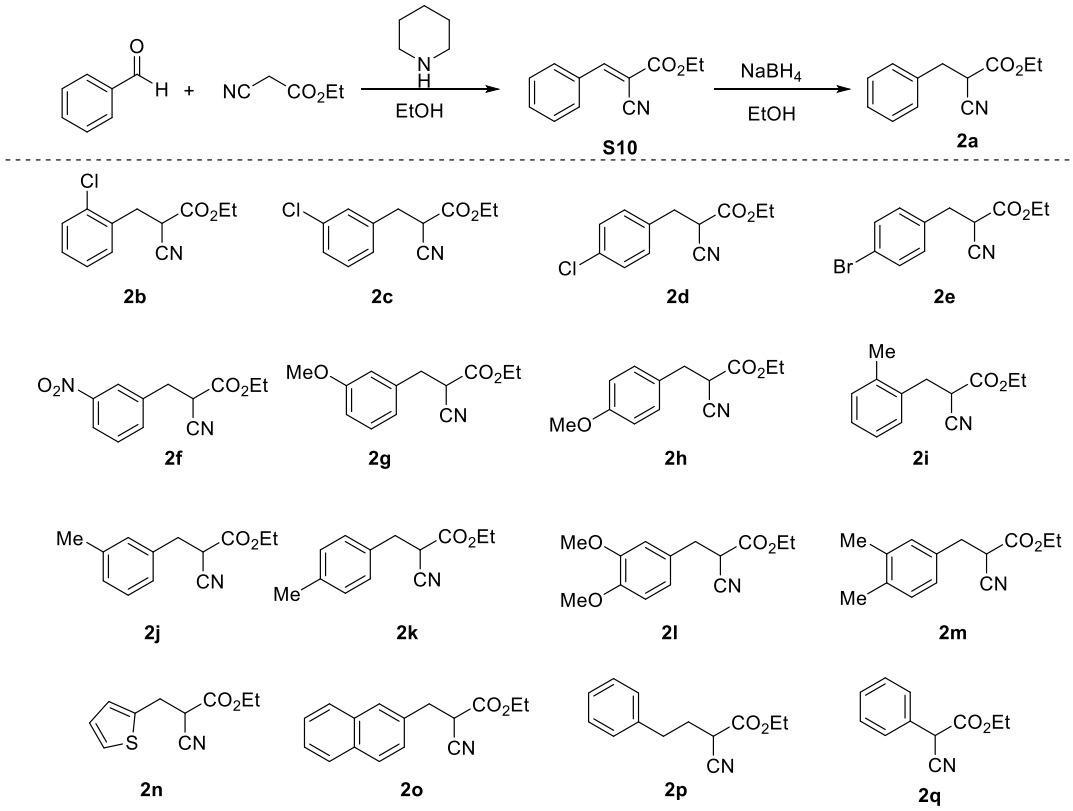
To a solution of **S8** (0.7 g, 3.4 mmol) in THF (20 mL) was heated with oil bath and added PPh_3 (2.52 g, 9.6 mmol) in partially at 50 ℃ for 5 h. The solution was cooled to room temperature and added H_2O (1 mL). Maintaining the reaction stirring at 3 hours until **S8** consumed as monitored by TLC. The solvent was concentrated under reduced pressure. The DCM (40 mL), DMAP (0.6 g, 5 mmol) was added, followed by adding dropwise the solution of benzoyl chloride (0.3 mL, 2.7 mmol) in CH_2Cl_2 (5 mL) at 0 ℃. After completion of the reaction, as indicated by TLC, the solution was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel (PE/EA = 10:1 to 5:1) to give the desired product **1g** as colorless oil. Compound **1h** was prepared by the same method.

2-(benzamidomethyl)allyl *tert*-butyl carbonate (1g): White solid;
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.5 Hz, 2H), 7.65 – 7.31 (m, 3H), 6.61 (d, *J* = 6.3 Hz, 1H), 5.28 (s, 2H), 4.63 (s, 2H), 4.14 (d, *J* = 5.7 Hz, 2H), 1.49 (s, 9H).

***tert*-butyl (2-(((*tert*-butoxycarbonyl)oxy)methyl)allyl)carbamate (1h)**
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.17 (d, J = 11.3 Hz, 2H), 4.77 (s, 1H), 4.56 (s, 2H), 3.78 (d, J = 5.1 Hz, 2H), 1.49 (s, 9H), 1.45 (s, 9H).

3. General experimental procedures synthesis of *α*-substituted cyanoacetates 2

The benzaldehyde are known compounds, which were prepared according to literature **2a-2p** (**2a** as the example)[3,4].



Step 1:

To a stirring solution of benzaldehyde (2.0 mL, 20 mmol, 1.0 equiv), ethyl cyanoacetate (2.2 mL, 21 mmol, 1.05 equiv) in ethanol (10 mL), was added the piperdine (0.1 mL, 1 mmol, 0.05 equiv) dropwise at room temperature. The reaction mixture was stirred for 24 h at room temperature. Then, the mixture was filtered and the precipitate was washed with ethanol to afford pure product **S10** as white solid. The obtained crude product **S10** is proceeded directly to the next step without purification.

Step 2:

To a stirring solution of **S10** (2.3 g, 11 mmol, 1.0 equiv) was dissolved in dry ethanol (15 mL), sodium borohydrate (0.5 g, 13.2 mmol, 1.2 equiv) was slowly added dropwise for 10 min at 0 °C. After completion of the reaction, as indicated by TLC. The reaction was quenched with aq. NH_4Cl and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. Then the residue was purified by column chromatography (PE/EA 10:1) to afford the compound **2a** as a colorless oil.

2a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 1H), 7.34 – 7.23 (m, 4H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.72 (dd, *J* = 8.4, 5.8 Hz, 1H), 3.28 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.19 (dd, *J* = 13.8, 8.4 Hz, 1H), 1.26 (t, *J* = 7.2 Hz, 3H).

2b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.38 (m, 1H), 7.36 – 7.32 (m, 1H), 7.28 – 7.25 (m, 2H), 4.27 (qd, *J* = 7.2, 1.5 Hz, 2H), 3.91 (dd, *J* = 9.5, 6.3 Hz, 1H), 3.52 (dd, *J* = 13.8, 6.3 Hz, 1H), 3.21 (dd, *J* = 13.8, 9.5 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H).

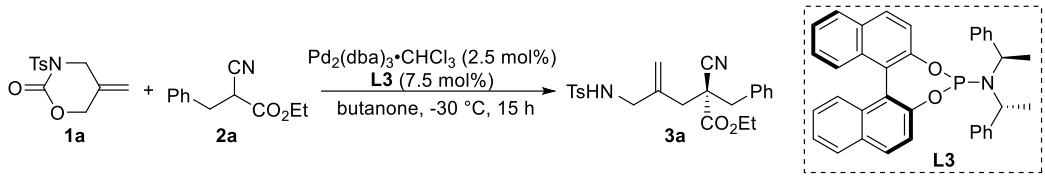
2c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.24 (m, 3H), 7.21 – 7.14 (m, 1H), 4.24 (qd, *J* = 7.1, 0.8 Hz, 2H), 3.73 (dd, *J* = 8.3, 5.9 Hz, 1H), 3.29 – 3.11 (m, 2H), 1.27 (t, *J* = 7.2 Hz, 3H).

2d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.24 – 7.19 (m, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.71 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.20 (qd, *J* = 13.9, 7.0 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H).
2e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.44 (m, 2H), 7.18 – 7.13 (m, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.70 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.19 (qd, *J* = 14.0, 7.0 Hz, 2H), 1.27 (t, *J* = 7.2 Hz, 3H).
2f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 – 8.13 (m, 2H), 7.66 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.81 (dd, *J* = 8.0, 5.9 Hz, 1H), 3.43 – 3.29 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H).
2g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (t, *J* = 7.9 Hz, 1H), 6.87 – 6.80 (m, 3H), 4.28 – 4.19 (m, 2H), 3.80 (s, 3H), 3.72 (dd, *J* = 8.5, 5.8 Hz, 1H), 3.25 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.15 (dd, *J* = 13.8, 8.4 Hz, 1H), 1.27 (t, *J* = 7.2 Hz, 3H).
2h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 – 7.14 (m, 2H), 6.93 – 6.80 (m, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 3.68 (dd, *J* = 8.2, 5.8 Hz, 1H), 3.21 (dd, *J* = 13.9, 5.8 Hz, 1H), 3.14 (dd, *J* = 13.9, 8.2 Hz, 1H), 1.27 (t, *J* = 7.2 Hz, 3H).
2i:^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.16 (m, 4H), 4.26 (qd, *J* = 7.2, 0.8 Hz, 2H), 3.68 (dd, *J* = 9.4, 6.0 Hz, 1H), 3.34 (dd, *J* = 14.1, 6.0 Hz, 1H), 3.19 (dd, *J* = 14.1, 9.4 Hz, 1H), 2.37 (s, 3H), 1.29 (t, *J* = 7.1 Hz, 3H).
2j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (td, *J* = 7.4, 0.9 Hz, 1H), 7.13 – 7.04 (m, 3H), 4.24 (qd, *J* = 7.2, 0.7 Hz, 2H), 3.71 (dd, *J* = 8.5, 5.8 Hz, 1H), 3.24 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.15 (dd, *J* = 13.8, 8.5 Hz, 1H), 2.34 (d, *J* = 0.9 Hz, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).
2k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, *J* = 1.1 Hz, 4H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.69 (dd, *J* = 8.4, 5.8 Hz, 1H), 3.24 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.15 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.33 (s, 3H), 1.28 (t, *J* = 7.1 Hz, 3H).
2l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.81 (dd, *J* = 9.9, 1.3 Hz, 3H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.87 (d, *J* = 5.0 Hz, 6H), 3.69 (dd, *J* = 8.3, 5.7 Hz, 1H), 3.30 – 3.02 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).
2m: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 7.6 Hz, 1H), 7.05 – 6.98 (m, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 3.70 (dd, *J* = 8.5, 5.8 Hz, 1H), 3.25 – 3.08 (m, 2H), 2.25 (d, *J* = 4.1 Hz, 6H), 1.29 (t, *J* = 7.2 Hz, 3H).
2n: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.02 – 6.95 (m, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.76 (dd, *J* = 7.4, 6.0 Hz, 1H), 3.50 – 3.45 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H).
2o: ^{1}H NMR (400 MHz, $CDCl_3$) δ δ 7.87 – 7.77 (m, 3H), 7.74 (s, 1H), 7.52 – 7.44 (m, 2H), 7.38 (dd, *J* = 8.4, 1.8 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.81 (dd, *J* = 8.4, 5.9 Hz, 1H), 3.45 (dd, *J* = 13.9, 5.9 Hz, 1H), 3.36 (dd, *J* = 13.9, 8.4 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H).
2p: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.28 (m, 2H), 7.27 – 7.18 (m, 3H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.44 (dd, *J* = 8.0, 6.5 Hz, 1H), 2.95 – 2.76 (m, 2H), 2.31 – 2.23 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).
2q: **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 – 7.34 (m, 5H), 4.72 (s, 1H), 4.29 – 4.17 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

References:

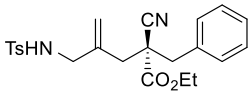
[1] Allen, B. D. W.; Connolly, M. J.; Harrity, J. P. A. *Chem.-Eur*. J. **2016**, 22, 13000.
[2] Yuan S P, Bao Q, Sun T J, et al. Organic Letters, 2022, 24(45): 8348-8353.
[3] Reddy S N, Reddy V R, Dinda S, et al. *Organic Letters*, **2018**, 20(9): 2572-2575.
[4] Zhang D, Lian M, Liu J, et al. *Organic Letters*, **2019**, 21(8): 2597-2601.

4. General experimental procedures for asymmetric synthesis of compounds 3



To a flame-dried reaction tube was added $Pd_2(dba)_3 \cdot CHCl_3$ (2.6 mg, 2.5 mol%), **L3** (4.5 mg, 7.5 mol%), **1a** (26.7 mg, 0.1 mmol) and **2a** (24.3 mg, 0.12 mmol) respectively. Then replaced argon three times quickly, and the reaction mixture was cooled to -30 ºC followed by adding butanone (1.0 mL) for stirring 15 h. After completion of the reaction, as indicated by TLC, then the residue was purified by column chromatography (PE/EA 3:1) to afford the compound **3a** as a colorless oil

ethyl (*R*)-2-benzyl-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3a)



The product **3a** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 47.7 mg, 99% yield; 93% ee; $[\alpha]_D^{20}$ = +12.7 (*c* 1.00, CH_2Cl_2);

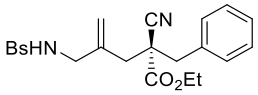
The ee was determined by HPLC (Chiralpak IC, ^{i}PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 19.2 min, t_{minor} = 21.7 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.36 – 7.28 (m, 5H), 7.25 (q, *J* = 4.6, 3.7 Hz, 2H), 5.19 (s, 1H), 5.11 (s, 1H), 4.82 (t, *J* = 6.6 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.65 (dd, *J* = 15.3, 7.0 Hz, 1H), 3.54 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.17 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 13.4 Hz, 1H), 2.77 (d, *J* = 14.7 Hz, 1H), 2.54 (d, *J* = 14.7 Hz, 1H), 2.42 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 143.7, 138.7, 136.8, 133.7, 130.0, 129.9, 128.7, 128.1, 127.3, 119.0, 118.3, 63.1, 50.8, 48.3, 44.0, 40.2, 21.7, 13.9;

HRMS (ESI-TOF) calcd. for $C_{23}H_{27}N_2O_4S$ $[M + H]^+$ 427.1686; found: 427.1696.

ethyl (*R*)-2-benzyl-4-(((4-bromophenyl)sulfonamido)methyl)-2-cyanopent-4-enoate (3b)



The product **3b** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 41.4 mg, 99% yield; 93% ee; $[\alpha]_D^{20}$ = +14.2 (*c* 1.00, CH_2Cl_2);

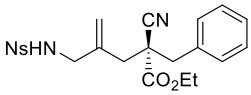
The ee was determined by HPLC (Chiralpak IC, ^{i}PrOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 29.6 min, t_{minor} = 32.5 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.7 Hz, 2H), 7.54 – 7.48 (m, 1H), 7.48 – 7.40 (m, 2H), 7.24 (d, *J* = 5.6 Hz, 3H), 7.17 (d, *J* = 7.8 Hz, 2H), 5.12 (s, 1H), 5.03 (s, 1H), 4.88 (t, *J* = 6.5 Hz, 1H), 4.00 (q, *J* = 7.0 Hz, 2H), 3.60 (dd, *J* = 15.3, 6.0 Hz, 1H), 3.50 (dd, *J* = 15.3, 4.8 Hz, 1H), 3.09 (d, *J* = 13.4 Hz, 1H), 2.96 (d, *J* = 13.4 Hz, 1H), 2.68 (d, *J* = 14.7 Hz, 1H), 2.46 (d, *J* = 14.7 Hz, 1H), 1.03 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 139.9, 138.7, 133.7, 132.9, 130.0, 129.3, 128.7, 128.1, 127.2, 119.0, 118.4, 63.1, 50.8, 48.2, 44.0, 40.2, 13.9;

HRMS (ESI-TOF) calcd. for $C_{22}H_{25}N_2O_4S$ $[M + H]^+$ 413.1530; found: 413.1537.

ethyl (*R*)-2-benzyl-2-cyano-4-(((4-nitrophenyl)sulfonamido)methyl)pent-4-enoate (3c)



The product **3c** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 44.7 mg, 98% yield; 91% ee; $[\alpha]_D^{20}$ = +4.0 (*c* 1.00, CH_2Cl_2);

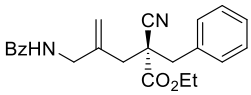
The ee was determined by HPLC (Chiralpak IB EtOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 21.5 min, t_{major} = 22.9 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.3 Hz, 2H), 7.97 (d, *J* = 8.3 Hz, 2H), 7.25 (d, *J* = 5.1 Hz, 3H), 7.19 – 7.12 (m, 2H), 5.13 (s, 1H), 5.08 (t, *J* = 6.7 Hz, 1H), 5.05 (s, 1H), 4.03 (q, *J* = 7.2 Hz, 2H), 3.69 (dd, *J* = 15.7, 6.7 Hz, 1H), 3.58 (dd, *J* = 15.6, 5.7 Hz, 1H), 3.11 (d, *J* = 13.4 Hz, 1H), 2.98 (d, *J* = 13.3 Hz, 1H), 2.69 (d, *J* = 14.5 Hz, 1H), 2.44 (d, *J* = 14.5 Hz, 1H), 1.05 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.2, 150.2, 145.9, 138.3, 133.5, 130.0, 128.8, 128.5, 128.3, 124.6, 119.0, 118.9, 63.2, 50.8, 48.1, 44.0, 40.1, 14.0;

HRMS (ESI-TOF) calcd. for $C_{22}H_{24}N_3O_6S$ $[M + H]^+$ 458.1380; found: 458.1381.

ethyl (*R*)-4-(benzamidomethyl)-2-benzyl-2-cyanopent-4-enoate (3d)



The product **3d** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 31.4 mg, 84% yield; 89% ee; $[\alpha]_D^{20}$ = +12.3 (*c* 1.00, CH_2Cl_2);

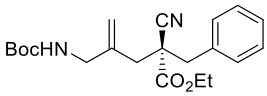
The ee was determined by HPLC (Chiralpak IB EtOH/hexane = 7/93, flow rate 0.8 mL/min, λ = 254 nm, t_{minor} = 15.6 min, t_{major} = 16.7 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.6 Hz, 2H), 7.47 – 7.40 (m, 1H), 7.40 – 7.32 (m, 2H), 7.22 (d, *J* = 6.0 Hz, 5H), 6.52 (t, *J* = 6.0 Hz, 1H), 5.19 (s, 1H), 5.10 (s, 1H), 4.07 (dq, *J* = 14.3, 7.1, 6.6 Hz, 3H), 3.98 (dd, *J* = 15.9, 5.7 Hz, 1H), 3.15 (d, *J* = 13.4 Hz, 1H), 3.03 (d, *J* = 13.4 Hz, 1H), 2.82 (d, *J* = 14.6 Hz, 1H), 2.55 (d, *J* = 14.6 Hz, 1H), 1.05 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 167.4, 139.8, 134.2, 133.7, 131.7, 130.1, 128.7, 128.6, 128.1, 127.1, 119.3, 117.1, 63.1, 51.0, 44.8, 44.1, 40.9, 13.9;

HRMS (ESI-TOF) calcd. for $C_{23}H_{25}N_2O_3$ $[M + H]^+$ 377.1860; found: 377.1861.

ethyl (*R*)-2-benzyl-4-(((tert-butoxycarbonyl)amino)methyl)-2-cyanopent-4-enoate (3e)

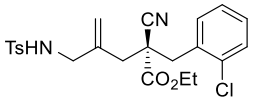


The product **3e** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 34.8 mg, 94% yield; 82% ee; $[\alpha]_D^{20}$ = +15.7 (*c* 1.00, CH_2Cl_2);

The ee was determined by HPLC (Chiralpak IC, ^{i}PrOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 9.2 min, t_{minor} = 10.0 min);

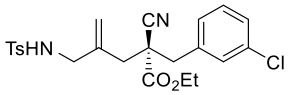
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.19 (m, 5H), 5.12 (s, 1H), 5.04 (s, 1H), 4.72 (s, 1H), 4.05 (d, *J* = 6.8 Hz, 2H), 3.78 – 3.62 (m, 2H), 3.15 (d, *J* = 13.4 Hz, 1H), 3.02 (d, *J* = 13.4 Hz, 1H), 2.76 (d, *J* = 14.6 Hz, 1H), 2.51 (d, *J* = 14.6 Hz, 1H), 1.38 (s, 9H), 1.06 (t, *J* = 7.1 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 155.9, 140.4, 133.9, 130.1, 128.7, 128.1, 119.1, 116.1, 79.7, 77.5, 77.2, 76.8, 63.0, 50.9, 45.5, 44.0, 40.8, 28.5, 14.0;
HRMS (ESI-TOF) calcd. for $C_{21}H_{29}N_2O_4$ $[M + H]^+$ 373.2122; found: 373.2122.

ethyl (*R*)-2-(2-chlorobenzyl)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3f)



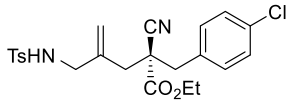
The product **3f** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 48.4 mg, 99% yield; 83% ee; $[\alpha]_D^{20}$ = +19.5 (*c* 1.00, CH_2Cl_2);
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 13.1 min, t_{major} = 16.8 min);
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.9 Hz, 2H), 7.30 (dd, *J* = 15.8, 7.3 Hz, 4H), 7.23 – 7.12 (m, 2H), 5.21 (s, 1H), 5.11 (s, 1H), 4.92 (t, *J* = 6.5 Hz, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.65 (dd, *J* = 15.3, 6.9 Hz, 1H), 3.55 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.15 (d, *J* = 13.4 Hz, 1H), 3.00 (d, *J* = 13.5 Hz, 1H), 2.77 (d, *J* = 14.6 Hz, 1H), 2.57 (d, *J* = 14.6 Hz, 1H), 2.43 (s, 3H), 1.13 (t, *J* = 7.2 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.0, 143.7, 138.6, 136.8, 135.8, 134.4, 130.0 (2C), 129.9 (2C), 128.4, 128.3, 127.3 (2C), 118.6, 118.5, 63.2, 50.7, 48.2, 43.4, 40.3, 21.6, 14.0;
HRMS (ESI-TOF) calcd. for $C_{23}H_{26}ClN_2O_4S$ $[M + H]^+$ 463.1296; found: 463.1304.

ethyl (*R*)-2-(3-chlorobenzyl)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3g)



The product **3g** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 48.6 mg, 99% yield; 91% ee; $[\alpha]_D^{20}$ = +11.3 (*c* 1.00, CH_2Cl_2);
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 15.2 min, t_{major} = 22.6 min);
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.44 – 7.34 (m, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.25 (q, *J* = 4.1 Hz, 2H), 5.21 (s, 1H), 5.11 (s, 1H), 4.90 (t, *J* = 6.5 Hz, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 3.65 (dd, *J* = 15.4, 7.0 Hz, 1H), 3.55 (dd, *J* = 15.4, 6.2 Hz, 1H), 3.38 (d, *J* = 14.0 Hz, 1H), 3.32 (d, *J* = 14.0 Hz, 1H), 2.84 (d, *J* = 14.7 Hz, 1H), 2.52 (d, *J* = 14.7 Hz, 1H), 2.42 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 143.6, 138.7, 136.9, 135.0, 131.9, 131.7, 130.0, 129.8, 129.5, 127.2, 127.1, 118.6, 118.5, 63.4, 49.8, 48.2, 39.8, 39.7, 21.6, 13.9;
HRMS (ESI-TOF) calcd. for $C_{23}H_{26}ClN_2O_4S$ $[M + H]^+$ 461.1296; found: 461.1305.

ethyl (*R*)-2-(4-chlorobenzyl)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3h)



The product **3h** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 38.7 mg, 84% yield; 92% ee; $[\alpha]_D^{20}$ = +17.2 (*c* 1.00, CH_2Cl_2);

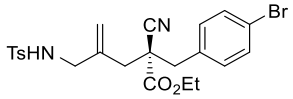
The ee was determined by HPLC (Chiralpak AS-H, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 17.8 min, t_{major} = 26.2 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.34 – 7.27 (m, 4H), 7.19 (d, *J* = 8.0 Hz, 2H), 5.20 (s, 1H), 5.10 (s, 1H), 4.86 (t, *J* = 6.5 Hz, 1H), 4.14 – 4.04 (m, 2H), 3.65 (dd, *J* = 15.4, 6.9 Hz, 1H), 3.54 (dd, *J* = 15.3, 6.1 Hz, 1H), 3.15 (d, *J* = 13.5 Hz, 1H), 3.00 (d, *J* = 13.5 Hz, 1H), 2.76 (d, *J* = 14.6 Hz, 1H), 2.56 (d, *J* = 14.7 Hz, 1H), 2.43 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 143.8, 138.6, 136.8, 134.2, 132.3, 131.4, 129.9, 128.9, 127.3, 118.8, 118.5, 63.2, 50.7, 48.2, 43.1, 40.2, 21.7, 14.0;

HRMS (ESI-TOF) calcd. for $C_{23}H_{26}ClN_2O_4S$ $[M + H]^+$ 461.1296; found: 461.1301.

ethyl (*R*)-2-(4-bromobenzyl)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3i)



The product **3i** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 45.2 mg, 89% yield; 92% ee; $[\alpha]_D^{20}$ = +30.4 (*c* 1.00, CH_2Cl_2);

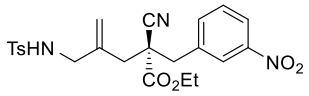
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 15.7 min, t_{major} = 21.5 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 2H), 7.45 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 5.20 (s, 1H), 5.10 (s, 1H), 4.16 – 4.04 (m, 2H), 3.65 (dd, *J* = 15.4, 7.0 Hz, 1H), 3.54 (dd, *J* = 15.4, 6.2 Hz, 1H), 3.14 (d, *J* = 13.5 Hz, 1H), 2.99 (d, *J* = 13.5 Hz, 1H), 2.76 (d, *J* = 14.6 Hz, 1H), 2.56 (d, *J* = 14.7 Hz, 1H), 2.43 (s, 3H), 1.14 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 143.7, 138.6, 136.7, 132.8, 131.9, 131.7, 129.9, 127.2, 122.4, 118.8, 118.5, 63.2, 50.6, 48.2, 43.2, 40.2, 21.7, 14.0;

HRMS (ESI-TOF) calcd. for $C_{23}H_{26}BrN_2O_4S$ $[M + H]^+$ 505.0791; found: 505.0797.

ethyl (*R*)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)-2-(3-nitrobenzyl)pent-4-enoate (3j)



The product **3i** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 49.4 mg, 99% yield; 89% ee; $[\alpha]_D^{20}$ = +30.4 (*c* 1.00, CH_2Cl_2);

The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 40/60, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 16.3 min, t_{major} = 21.1 min);

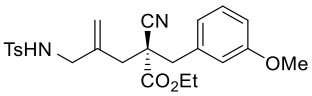
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 – 8.14 (m, 1H), 8.09 (s, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.66 (d, *J* = 7.6 Hz, 1H), 7.57 – 7.50 (m, 1H), 7.32 (d, *J* = 7.9 Hz, 2H), 5.23 (s, 1H), 5.20 – 5.07 (m, 2H), 4.20 – 4.08 (m, 2H), 3.67 (dd, *J* = 15.4, 6.8 Hz, 1H), 3.57 (dd, *J* = 15.4, 6.2 Hz, 1H), 3.33 (d, *J* =

13.7 Hz, 1H), 3.16 (d, *J* = 13.6 Hz, 1H), 2.82 (d, *J* = 14.6 Hz, 1H), 2.67 (d, *J* = 14.6 Hz, 1H), 2.42 (s, 3H), 1.15 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 167.7, 148.3, 143.7, 138.4, 136.7, 136.3, 135.9, 129.8, 129.7, 127.2, 124.8, 123.2, 118.7, 118.3, 63.4, 50.7, 48.2, 42.8, 40.2, 21.6, 13.9;

HRMS (ESI-TOF) calcd. for $C_{23}H_{26}N_3O_6S$ $[M + H]^+$ 472.1537; found: 472.1544.

ethyl (*R*)-2-cyano-2-(3-methoxybenzyl)-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3k)



The product **3k** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 45.7 mg, 99% yield; 88% ee; $[\alpha]_D^{20}$ = +12.3 (*c* 1.00, CH_2Cl_2);

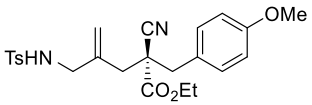
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 15.9 min, t_{major} = 20.3 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.26 – 7.18 (m, 1H), 6.88 – 6.77 (m, 3H), 5.19 (s, 1H), 5.10 (s, 1H), 4.86 (t, *J* = 6.6 Hz, 1H), 4.10 (q, *J* = 7.2 Hz, 2H), 3.79 (s, 3H), 3.65 (dd, *J* = 15.4, 7.0 Hz, 1H), 3.54 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.15 (d, *J* = 13.4 Hz, 1H), 3.00 (d, *J* = 13.4 Hz, 1H), 2.76 (d, *J* = 14.7 Hz, 1H), 2.54 (d, *J* = 14.7 Hz, 1H), 2.43 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 159.7, 143.7, 138.8, 136.9, 135.1, 129.9, 129.7, 127.3, 122.3, 119.0, 118.4, 115.6, 113.7, 63.1, 55.3, 50.8, 48.3, 44.0, 40.2, 21.6, 14.0;

HRMS (ESI-TOF) calcd. for $C_{24}H_{29}N_2O_5S$ $[M + H]^+$ 457.1792; found: 457.1782.

ethyl (*R*)-2-cyano-2-(4-methoxybenzyl)-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3l)



The product **3l** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 46.5 mg, 99% yield; 88% ee; $[\alpha]_D^{20}$ = +13.9 (*c* 1.00, CH_2Cl_2);

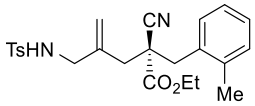
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 16.1 min, t_{major} = 20.9 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.17 (d, *J* = 8.2 Hz, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 5.18 (s, 1H), 5.10 (s, 1H), 4.74 (t, *J* = 6.5 Hz, 1H), 4.16 – 4.05 (m, 2H), 3.79 (s, 3H), 3.65 (dd, *J* = 15.4, 7.0 Hz, 1H), 3.54 (dd, *J* = 15.3, 6.1 Hz, 1H), 3.13 (d, *J* = 13.6 Hz, 1H), 2.97 (d, *J* = 13.6 Hz, 1H), 2.74 (d, *J* = 14.7 Hz, 1H), 2.52 (d, *J* = 14.7 Hz, 1H), 2.43 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 159.5, 143.7, 138.8, 136.9, 131.2, 129.9, 127.3, 125.7, 119.1, 118.3, 114.1, 63.0, 55.4, 51.1, 48.3, 43.3, 40.1, 21.7, 14.0;

HRMS (ESI-TOF) calcd. for $C_{24}H_{29}N_2O_5S$ $[M + H]^+$ 457.1792; found: 457.1797.

ethyl (*R*)-2-cyano-2-(2-methylbenzyl)-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3m)



The product **3m** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1);

Colorless oil; 42.2 mg, 96% yield; 92% ee; $[\alpha]_D^{20}$ = +139 (*c* 1.00, CH_2Cl_2);

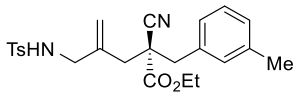
The ee was determined by HPLC (Chiralpak IC, ^{i}PrOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 32.9 min, t_{minor} = 36.4 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.23 – 7.11 (m, 4H), 5.20 (s, 1H), 5.11 (s, 1H), 4.85 (t, *J* = 6.5 Hz, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 3.66 (dd, *J* = 15.3, 7.0 Hz, 1H), 3.54 (dd, *J* = 15.3, 6.1 Hz, 1H), 3.22 (d, *J* = 14.0 Hz, 1H), 3.16 (d, *J* = 14.0 Hz, 1H), 2.82 (d, *J* = 14.6 Hz, 1H), 2.58 (d, *J* = 14.6 Hz, 1H), 2.42 (s, 3H), 2.37 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.7, 143.7, 138.8, 137.3, 136.9, 132.3, 131.1, 130.2, 129.9, 128.1, 127.3, 126.2, 119.2, 118.4, 63.1, 50.1, 48.3, 40.4, 40.1, 21.6, 20.0, 13.9;

HRMS (ESI-TOF) calcd. for $C_{24}H_{29}N_2O_4S$ $[M + H]^+$ 441.1843; found: 441.1847.

ethyl (*R*)-2-cyano-2-(3-methylbenzyl)-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3n)



The product **3n** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1);

Colorless oil; 42.9 mg, 97% yield; 91% ee; $[\alpha]_D^{20}$ = +11.4 (*c* 1.00, CH_2Cl_2);

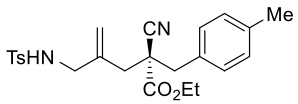
The ee was determined by HPLC (Chiralpak IC, ^{i}PrOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 34.1 min, t_{minor} = 40.0 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.23 – 7.17 (m, 1H), 7.11 (d, *J* = 7.7 Hz, 1H), 7.04 (d, *J* = 6.5 Hz, 2H), 5.19 (s, 1H), 5.10 (s, 1H), 4.86 (t, *J* = 6.6 Hz, 1H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.64 (dd, *J* = 15.3, 7.0 Hz, 1H), 3.54 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.13 (d, *J* = 13.4 Hz, 1H), 2.99 (d, *J* = 13.4 Hz, 1H), 2.76 (d, *J* = 14.7 Hz, 1H), 2.53 (d, *J* = 14.7 Hz, 1H), 2.42 (s, 3H), 2.33 (s, 3H), 1.15 – 1.08 (m, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 143.7, 138.8, 138.3, 136.9, 133.6, 130.7, 129.9, 128.8, 128.6, 127.3, 127.0, 119.0, 118.3, 63.0, 50.8, 48.3, 44.0, 40.2, 21.6, 21.4, 13.9;

HRMS (ESI-TOF) calcd. for $C_{24}H_{29}N_2O_4S$ $[M + H]^+$ 441.1843; found: 441.1850.

ethyl (*R*)-2-cyano-2-(4-methylbenzyl)-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3o)



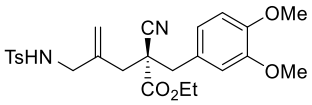
The product **3o** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1);

Colorless oil; 40.4 mg, 92% yield; 91 % ee; $[\alpha]_D^{20}$ = +2.0 (*c* 1.00, CH_2Cl_2);

The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 15/85, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 16.7 min, t_{major} = 20.0 min);

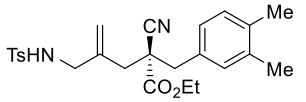
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 7.12 (s, 4H), 5.18 (s, 1H), 5.09 (s, 1H), 4.89 (t, *J* = 6.6 Hz, 1H), 4.14 – 4.04 (m, 2H), 3.63 (dd, *J* = 15.4, 7.0 Hz, 1H), 3.53 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.13 (d, *J* = 13.4 Hz, 1H), 2.98 (d, *J* = 13.5 Hz, 1H), 2.74 (d, *J* = 14.7 Hz, 1H), 2.52 (d, *J* = 14.7 Hz, 1H), 2.42 (s, 3H), 2.32 (s, 3H), 1.12 (t, *J* = 7.2 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 143.7, 138.8, 137.8, 136.9, 130.6, 129.9, 129.8, 129.4, 127.3, 119.0, 118.2, 63.0, 50.9, 48.2, 43.6, 40.1, 21.6, 21.2, 13.9;
HRMS (ESI-TOF) calcd. for $C_{24}H_{29}N_2O_4S$ $[M + H]^+$ 441.1843; found: 441.1851.

ethyl (*R*)-2-cyano-2-(3,4-dimethoxybenzyl)-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3p)



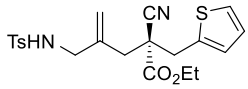
The product **3p** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 43.4 mg, 89% yield; 89% ee; $[\alpha]_D^{20}$ = +2.0 (*c* 1.00, CH_2Cl_2);
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 254 nm, t_{minor} = 11.6 min, t_{major} = 13.7 min);
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.3 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.85 – 6.76 (m, 3H), 5.19 (s, 1H), 5.10 (s, 1H), 5.02 – 4.90 (m, 1H), 4.18 – 4.03 (m, 2H), 3.86 (d, *J* = 2.3 Hz, 6H), 3.64 (dd, *J* = 15.3, 6.8 Hz, 1H), 3.54 (dd, *J* = 15.3, 6.1 Hz, 1H), 3.14 (d, *J* = 13.6 Hz, 1H), 2.99 (d, *J* = 13.6 Hz, 1H), 2.76 (d, *J* = 14.7 Hz, 1H), 2.55 (d, *J* = 14.7 Hz, 1H), 2.42 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.4, 148.8, 148.8, 143.6, 138.8, 136.9, 129.8, 127.2, 126.2, 122.3, 119.2, 118.1, 113.1, 111.1, 63.0, 55.9, 55.8, 51.0, 48.2, 43.7, 40.1, 21.6, 14.0;
HRMS (ESI-TOF) calcd. for $C_{25}H_{31}N_2O_6S$ $[M + H]^+$ 487.1897; found: 487.1902.

ethyl (*R*)-2-cyano-2-(3,4-dimethylbenzyl)-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoate (3q)



The product **3q** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 45.5 mg, 99% yield; 91% ee; $[\alpha]_D^{20}$ = +15.1 (*c* 1.00, CH_2Cl_2);
The ee was determined by HPLC (Chiralpak AS-H, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 13.3 min, t_{major} = 15.4 min);
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.01 – 6.94 (m, 2H), 5.18 (s, 1H), 5.10 (s, 1H), 4.82 (t, *J* = 6.5 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.64 (dd, *J* = 15.4, 6.9 Hz, 1H), 3.54 (dd, *J* = 15.3, 6.1 Hz, 1H), 3.12 (d, *J* = 13.4 Hz, 1H), 2.95 (d, *J* = 13.4 Hz, 1H), 2.74 (d, *J* = 14.7 Hz, 1H), 2.51 (d, *J* = 14.7 Hz, 1H), 2.42 (s, 3H), 2.23 (s, 6H), 1.14 (t, *J* = 7.2 Hz, 3H);
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 143.7, 138.8, 136.9, 136.8, 136.5, 131.2, 131.0, 129.9, 129.8, 127.4, 127.3, 119.0, 118.2, 63.0, 50.9, 48.2, 43.6, 40.1, 21.6, 19.8, 19.5, 14.0;
HRMS (ESI-TOF) calcd. for $C_{25}H_{31}N_2O_4S$ $[M + H]^+$ 455.1999; found: 455.2006.

ethyl (*R*)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)-2-(thiophen-2-ylmethyl)pent-4-enoate (3r)



The product **3r** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 34.5 mg, 80% yield; 89% ee; $[\alpha]_D^{20}$ = +8.7 (*c* 1.00, CH_2Cl_2);

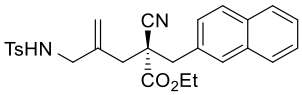
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 15.2 min, t_{major} = 25.5 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 7.9 Hz, 2H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 5.1 Hz, 1H), 7.04 – 6.94 (m, 2H), 5.21 (s, 1H), 5.12 (s, 1H), 4.74 (t, *J* = 6.5 Hz, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 3.66 (dd, *J* = 15.4, 7.0 Hz, 1H), 3.56 (dd, *J* = 15.4, 6.2 Hz, 1H), 3.43 (d, *J* = 14.5 Hz, 1H), 3.27 (d, *J* = 14.5 Hz, 1H), 2.74 (d, *J* = 14.5 Hz, 1H), 2.59 (d, *J* = 14.6 Hz, 1H), 2.43 (s, 3H), 1.20 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 143.8, 138.7, 136.9, 134.9, 129.9, 128.5, 127.3 (2C), 125.9, 118.9, 118.7, 63.3, 51.2, 48.2, 40.0, 38.1, 21.7, 14.0;

HRMS (ESI-TOF) calcd. for $C_{21}H_{25}N_2O_4S_2$ $[M + H]^+$ 433.1250; found: 433.1257.

ethyl (*R*)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)-2-(naphthalen-2-ylmethyl)pent-4-enoate (3s)



The product **3s** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 53.3 mg, 99% yield; 89% ee; $[\alpha]_D^{20}$ = +11.7 (*c* 1.00, CH_2Cl_2);

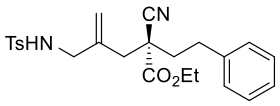
The ee was determined by HPLC (Chiralpak IC, ^{i}PrOH/hexane = 30/70, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 22.5 min, t_{minor} = 25.1 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.77 (m, 3H), 7.76 – 7.68 (m, 3H), 7.47 (dd, *J* = 6.3, 3.2 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 1H), 7.27 (d, *J* = 11.8 Hz, 2H), 5.20 (s, 1H), 5.12 (s, 1H), 4.93 (t, *J* = 6.5 Hz, 1H), 4.12 – 3.99 (m, 2H), 3.65 (dd, *J* = 15.4, 6.9 Hz, 1H), 3.55 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.34 (d, *J* = 13.4 Hz, 1H), 3.19 (d, *J* = 13.4 Hz, 1H), 2.81 (d, *J* = 14.7 Hz, 1H), 2.58 (d, *J* = 14.7 Hz, 1H), 2.40 (s, 3H), 1.04 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.3, 143.7, 138.7, 136.8, 133.3, 132.9, 131.3, 129.8, 129.2, 128.4, 127.9, 127.7, 127.7, 127.2, 126.4, 126.3, 119.0, 118.3, 63.1, 50.9, 48.2, 44.0, 40.3, 21.6, 13.9;

HRMS (ESI-TOF) calcd. for $C_{27}H_{29}N_2O_4S$ $[M + H]^+$ 477.1843; found: 477.1852.

ethyl (*R*)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)-2-phenethylpent-4-enoate (3t)



The product **3t** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 43.0 mg, 98% yield; 81% ee; $[\alpha]_D^{20}$ = +1.6 (*c* 1.00, CH_2Cl_2);

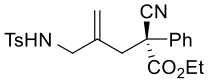
The ee was determined by HPLC (Chiralpak IA, EtOH/hexane = 20/80, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 11.9 min, t_{major} = 20.8 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.72 (m, 2H), 7.33 – 7.27 (m, 4H), 7.23 (d, *J* = 7.2 Hz, 1H), 7.17 (d, *J* = 7.5 Hz, 2H), 5.19 (s, 1H), 5.09 (s, 1H), 4.86 (t, *J* = 6.5 Hz, 1H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.65 (dd, *J* = 15.4, 6.9 Hz, 1H), 3.55 (dd, *J* = 15.4, 6.2 Hz, 1H), 2.88 (td, *J* = 12.8, 4.7 Hz, 1H), 2.69 – 2.51 (m, 3H), 2.40 (s, 3H), 2.21 (td, *J* = 12.7, 5.2 Hz, 1H), 2.03 (td, *J* = 12.8, 4.7 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 143.7, 139.5, 138.8, 136.8, 129.9, 128.7, 128.5, 127.2, 126.7, 119.1, 118.3, 63.2, 49.1, 48.2, 40.3, 39.9, 31.7, 21.6, 14.1;

HRMS (ESI-TOF) calcd. for $C_{24}H_{29}N_2O_4S$ $[M + H]^+$ 441.1843; found: 441.1850.

ethyl (*R*)-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)-2-phenylpent-4-enoate (3u)



The product **3u** was purified by flash column chromatography (ethyl acetate /petroleum ether = 3:1); Colorless oil; 31.1 mg, 75% yield; 23% ee; $[\alpha]_D^{20}$ = -8.1 (*c* 1.00, CH_2Cl_2);

The ee was determined by HPLC (Chiralpak IC EtOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 26.8 min, t_{minor} = 29.3 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.65 (m, 2H), 7.50 (dd, *J* = 7.8, 1.9 Hz, 2H), 7.44 – 7.34 (m, 3H), 7.28 (d, *J* = 8.0 Hz, 2H), 5.18 (s, 1H), 5.09 (s, 1H), 4.76 – 4.68 (m, 1H), 4.29 – 4.14 (m, 2H), 3.47 – 3.30 (m, 2H), 3.10 (d, *J* = 14.8 Hz, 1H), 2.77 (d, *J* = 14.8 Hz, 1H), 2.42 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H);

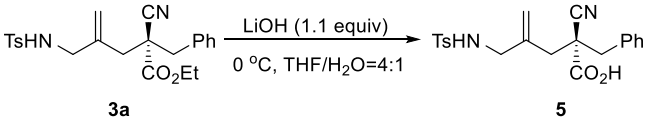
^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 143.6, 138.5, 136.9, 134.2, 129.8, 129.4, 129.2, 127.3, 126.1, 119.1, 118.3, 63.7, 53.7, 48.6, 40.9, 21.6, 13.9;

HRMS (ESI-TOF) calcd. for $C_{22}H_{25}N_2O_4S$ $[M + H]^+$ 413.1530; found: 413.1537.

5. Scale-up experiment

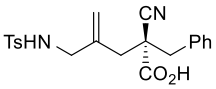
In a flame-dried round bottom flask equipped with a magnetic stirring bar, the solution of 5-methylene-3-tosyl-1,3-oxazinan-2-one **1a** (667mg, 2.5 mmol, 1.0 equiv), ethyl 2-cyano-3-phenylpropanoate **2a** (607 mg, 3 mmol, 1.2 equiv) in butanone (30.0 mL) was stirred at -30 ℃. And then, the mixture was stirred at the same temperature for the specified time (about 15 h). After completion of the reaction, as indicated by TLC, the solvent was concentrated under reduced pressure and the residue was purified by flash chromatography on silica gel with PE/EA = 3:1 to give the desired product **3a** (1.06 g, 99% yield, 92% ee).

6. The procedure for the synthesis of compound 5.



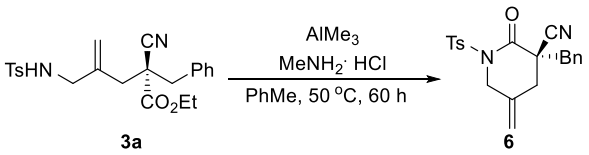
In an ordinary vial equipped with a magnetic stirring bar, **3a** (42.6 mg, 0.1 mmol, 1.0 equiv) was dissolved in THF/H_2O (2 mL/0.5 mL) and the mixture was cooled to 0 ℃. LiOH·H_2O (8.1 mg, 0.39 mmol, 1.1 equiv) was added and the mixture was stirred at 0 ℃ for 30 min. After the reaction was completed, the reaction mixture was added 1M HCl until pH = 2 and then extracted with EA (10 mL × 2). The combined organic extracts were washed with brine, dried over anhydrous Na_2SO_4, and removed under reduced pressure. Then the crude product was purified by flash column chromatography (DCM /MeOH = 20:1) to afford the desired products **5** as a colorless oil (77% yield, 96% ee).

(*R*)-2-benzyl-2-cyano-4-(((4-methylphenyl)sulfonamido)methyl)pent-4-enoic acid (5)



The product **5** was purified by flash column chromatography (DCM /MeOH = 20:1);
Colourless oil; 30.7 mg, 77% yield; 96% ee; $[\alpha]_D^{20}$ = -10.1 (*c* 1.00, CH_2Cl_2);
The ee was determined by HPLC (Chiralpak AD-H, ^{i}PrOH/hexane = 15/85, flow rate 1.0 mL/min, λ = 220 nm, t_{major} = 23.4 min, t_{minor} = 33.7 min);
^{1}H NMR (400 MHz, D_2O) δ 7.73 – 7.61 (m, 2H), 7.42 – 7.28 (m, 5H), 7.25 – 7.15 (m, 2H), 5.11 (s, 1H), 5.02 (s, 1H), 3.63 – 3.44 (m, 2H), 3.03 (d, *J* = 13.4 Hz, 1H), 2.74 (d, *J* = 13.5 Hz, 1H), 2.49 (d, *J* = 14.9 Hz, 1H), 2.32 (s, 3H), 2.13 (d, *J* = 14.9 Hz, 1H);
^{13}C NMR (101 MHz, D_2O) δ 171.0, 142.5, 137.2, 133.3, 133.2, 127.8, 127.7, 126.2, 125.3, 124.6, 120.1, 114.4, 51.8, 45.6, 40.7, 37.0, 18.5;
HRMS (ESI-TOF) calcd. for $C_{21}H_{23}N_2O_4S$ $[M + H]^+$ 399.1373; found: 399.1379.

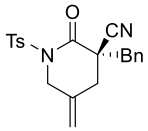
7. The procedure for the synthesis of compound 6.



3a **6**

A freshly prepared stock solution of trimethylaluminum amine complex was prepared by adding trimethylaluminum (0.5 mL, 2M in toluene) to methyl anmine hydrochloride (67.5 mg, 1 mmol) in toluene (4.5 mL) at 0 ºC and allowed to warm to ambient temperature. After the methane evolution ceased (about 1 hour), the aluminum amine complex solution (0.9 mL, 0.18 mmol, 3.0 equiv) was then added to ester **3a** (25.6 mg, 0.06 mmol, 1.0 equiv) in toluene (2 mL) at room temperature and immediately heated to 50 ºC. The reaction was maintained at 50 ºC for three days. After completion of the reaction (confirmed by TLC analysis). The reaction was quenched with aq. NH4Cl and extracted with CH_2Cl_2.The organic layer was dried over Na_2SO_4, filtered, and concentrated under vacuum. The residue was chromatographed on silica gel with (PE/EA 2:1) to afford compound **6** as a white solid (77% yield, 90% ee).

(*R*)-3-benzyl-5-methylene-2-oxo-1-tosylpiperidine-3-carbonitrile (6)



The product **6** was purified by flash column chromatography (ethyl acetate /petroleum ether = 4:1); White solid; 17.6 mg, 77% yield; 90% ee; $[\alpha]_D^{20}$ = +9.2 (*c* 1.00, CH_2Cl_2); m.p. 127.6-128.4 ºC

The ee was determined by HPLC (Chiralpak IC, EtOH/hexane = 10/90, flow rate 1.0 mL/min, λ = 220 nm, t_{minor} = 21.8 min, t_{major} = 23.2 min);

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 – 7.82 (m, 2H), 7.30 (d, *J* = 8.3 Hz, 2H), 7.22 (dd, *J* = 5.0, 2.0 Hz, 3H), 7.12 – 7.06 (m, 2H), 5.26 (s, 1H), 5.10 (s, 1H), 4.58 (dt, *J* = 14.6, 1.5 Hz, 1H), 4.40 (dt, *J* = 14.6, 1.6 Hz, 1H), 3.21 (d, *J* = 13.9 Hz, 1H), 3.02 (d, *J* = 13.9 Hz, 1H), 2.57 (d, *J* = 14.4 Hz, 1H), 2.48 (d, *J* = 14.4 Hz, 1H), 2.40 (s, 3H);

^{13}C NMR (101 MHz, $CDCl_3$) δ 164.9, 145.9, 134.7, 133.3, 132.5, 130.5, 129.8, 129.1, 128.9, 128.2, 117.9, 117.4, 47.9, 41.0, 37.1, 29.8, 21.9;

HRMS (ESI-TOF) calcd. for $C_{21}H_{21}N_2O_3S$ $[M + H]^+$ 381.1267; found: 381.1273.

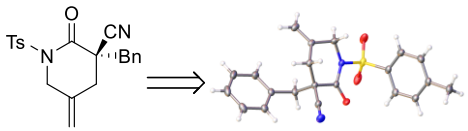
8. X-ray crystal structure of compounds 6

Single crystals of $C_{21}H_{20}N_2O_3S$ **6** was prepared from the mixture solvent of EtOH at room temperature by slow evaporation of solvent. A suitable crystal was selected for structure determination on a SuperNova, Dual, Cu at zero, AtlasS2 diffractometer. The crystal was kept at 170.1(3) K during data collection. Using Olex2 [1], the structure was solved with the SHELXS [2] structure solution program using Direct Methods and refined with the SHELXL [3] refinement package using Least Squares minimisation.

[1] Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J, Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst*. 2009, *42*, 339-341.

[2] Sheldrick, G. M. *Acta Cryst.* 2008, A64, 112-122.

[3] Sheldrick, G. M. *Acta Cryst*. 2015, C71, 3-8.



6

X-ray of **6**
CCDC 2294266

ORTEP of **6** (at 50% level)

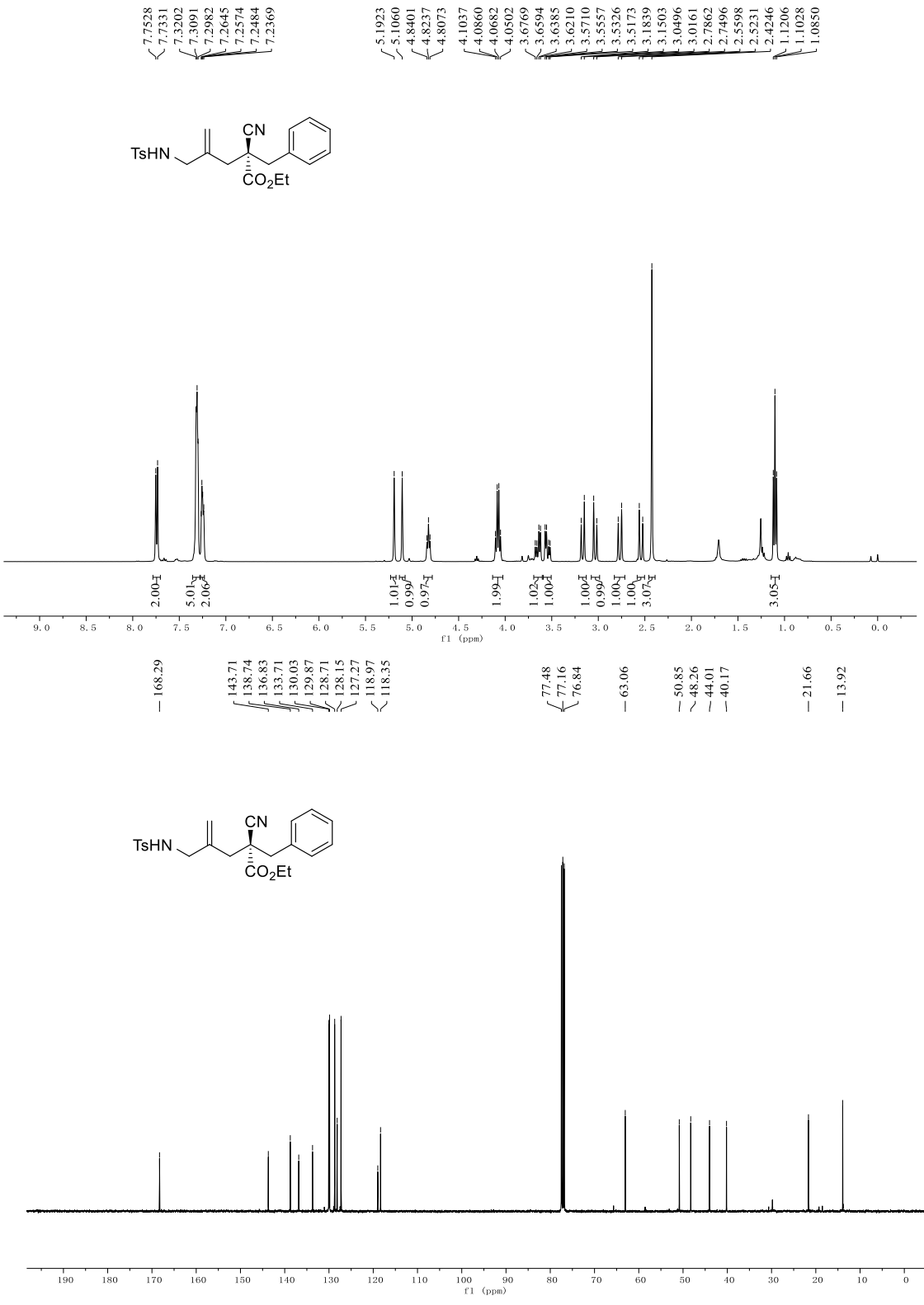
Crystal data and structure refinement for 6

Identification code	**6**
Empirical formula	$C_{21}H_{20}N_2O_3S$
Formula weight	380.45
Temperature/K	99.96(16)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	7.46283(5)
b/Å	13.94255(10)
c/Å	18.09638(13)
α/°	90
β/°	90
γ/°	90

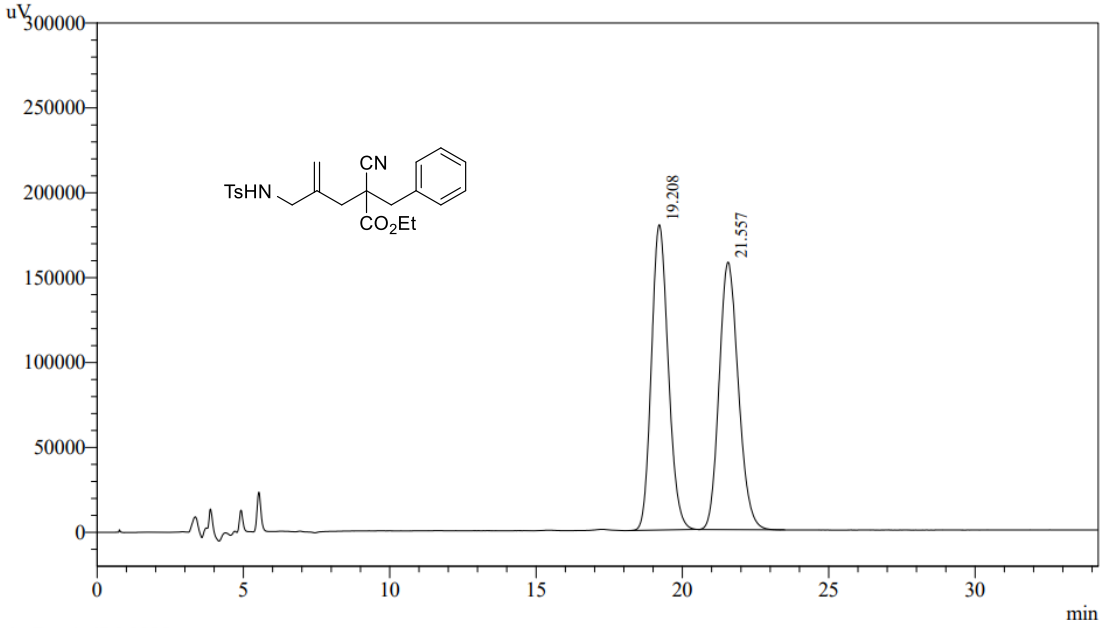
Volume/Å^3	1882.94(2)
Z	4
ρ_{calc}g/cm^3	1.342
μ/mm^{-1}	1.727
F(000)	800.0
Crystal size/mm^3	0.16 × 0.12 × 0.1
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.006 to 148.658
Index ranges	-9 ≤ h ≤ 4, -16 ≤ k ≤ 17, -22 ≤ l ≤ 15
Reflections collected	9403
Independent reflections	3718 [R_{int} = 0.0136, R_{sigma} = 0.0135]
Data/restraints/parameters	3718/0/254
Goodness-of-fit on F^2	1.051
Final R indexes [I>=2σ (I)]	R_1 = 0.0230, wR_2 = 0.0620
Final R indexes [all data]	R_1 = 0.0231, wR_2 = 0.0621
Largest diff. peak/hole / e Å^{-3}	0.21/-0.23
Flack/Hooft parameter	0.009(5)/-0.005(3)

9. The copies of ^{1}H NMR, ^{13}C NMR and HPLC spectra for compounds 3, 5, 6

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3a



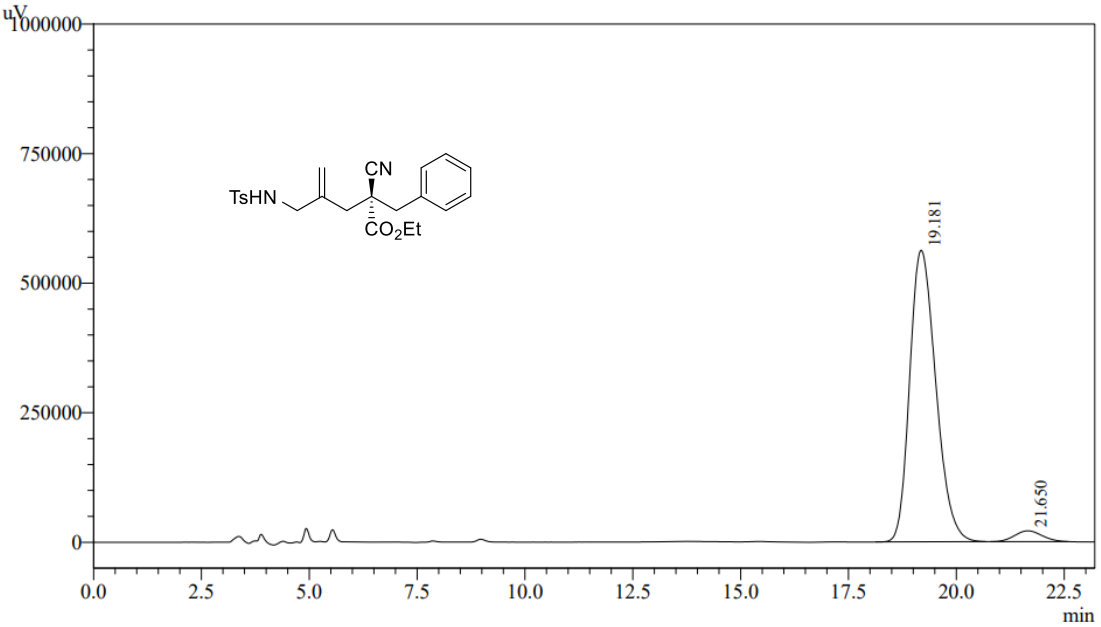
HPLC spectra of 3a



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.208	7201606	179866	49.974	53.304
2	21.557	7209198	157568	50.026	46.696
Total		14410804	337435	100.000	100.000

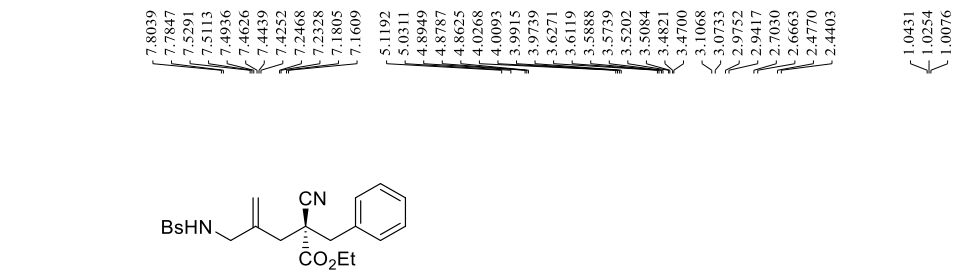


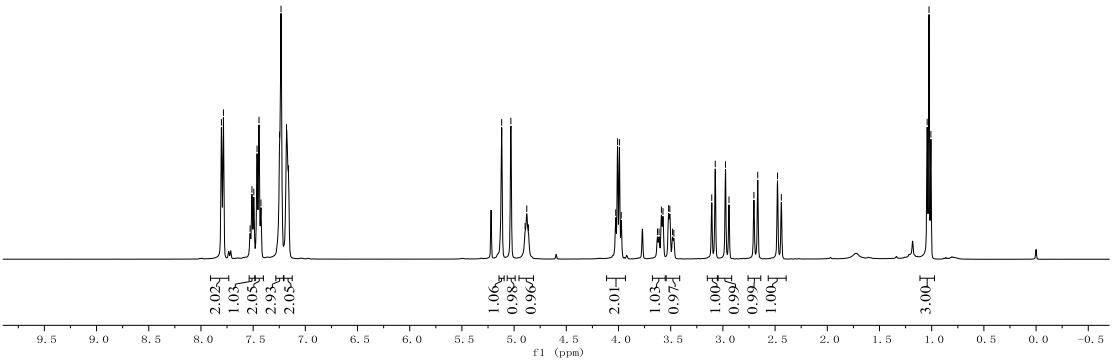
1 Det.A Ch1 / 220nm

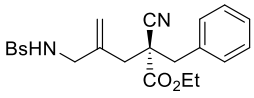
Detector A Ch1 220nm

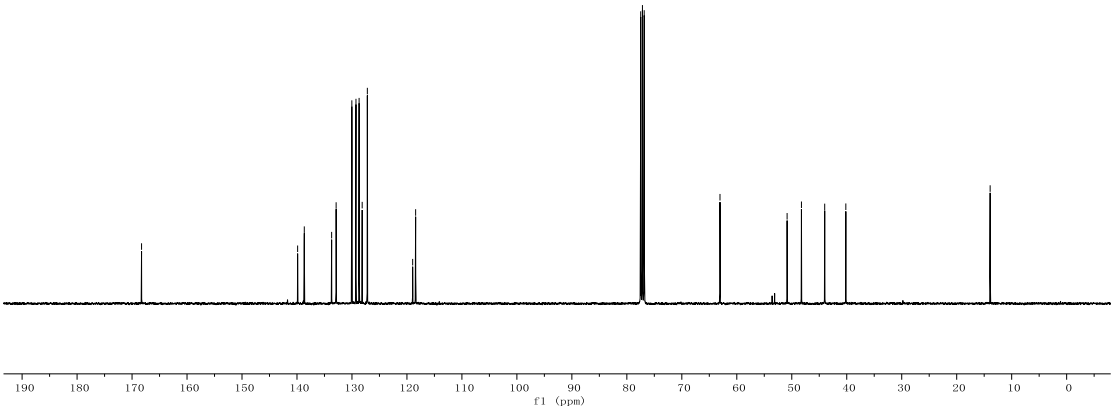
Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.181	23710053	562554	96.281	96.432
2	21.650	915844	20812	3.719	3.568
Total		24625898	583365	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3b

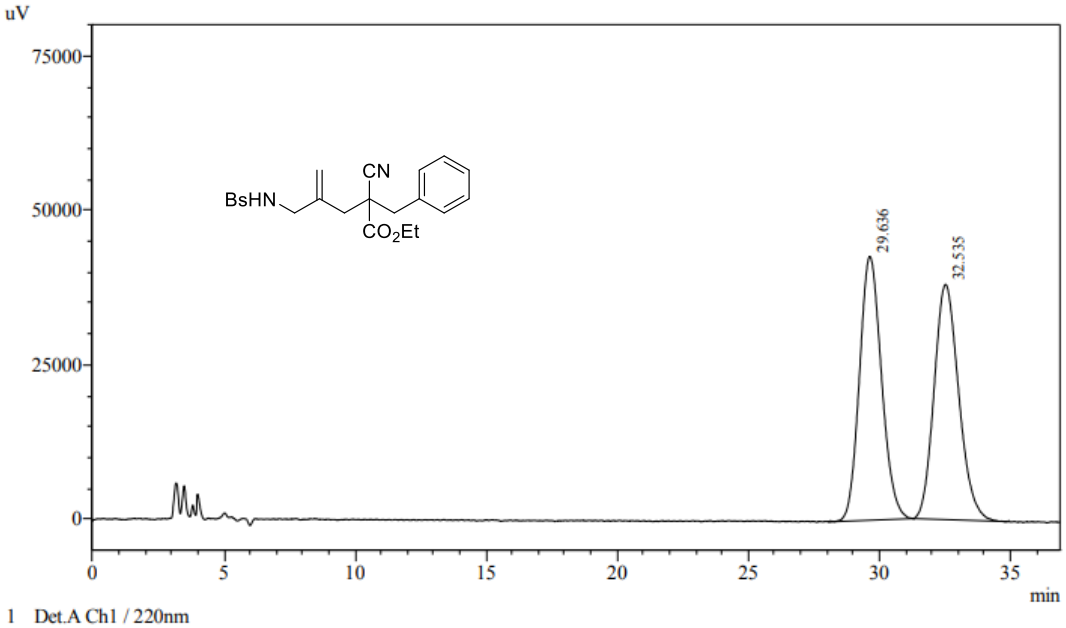








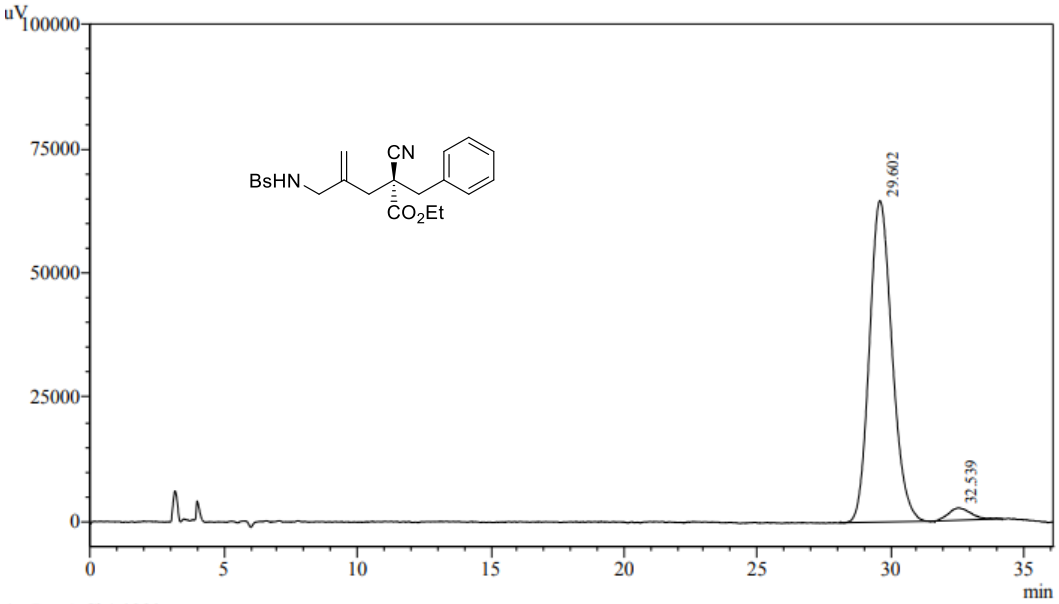
HPLC spectra of 3b



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.636	2500643	42706	50.118	52.872
2	32.535	2488913	38067	49.882	47.128
Total		4989556	80773	100.000	100.000

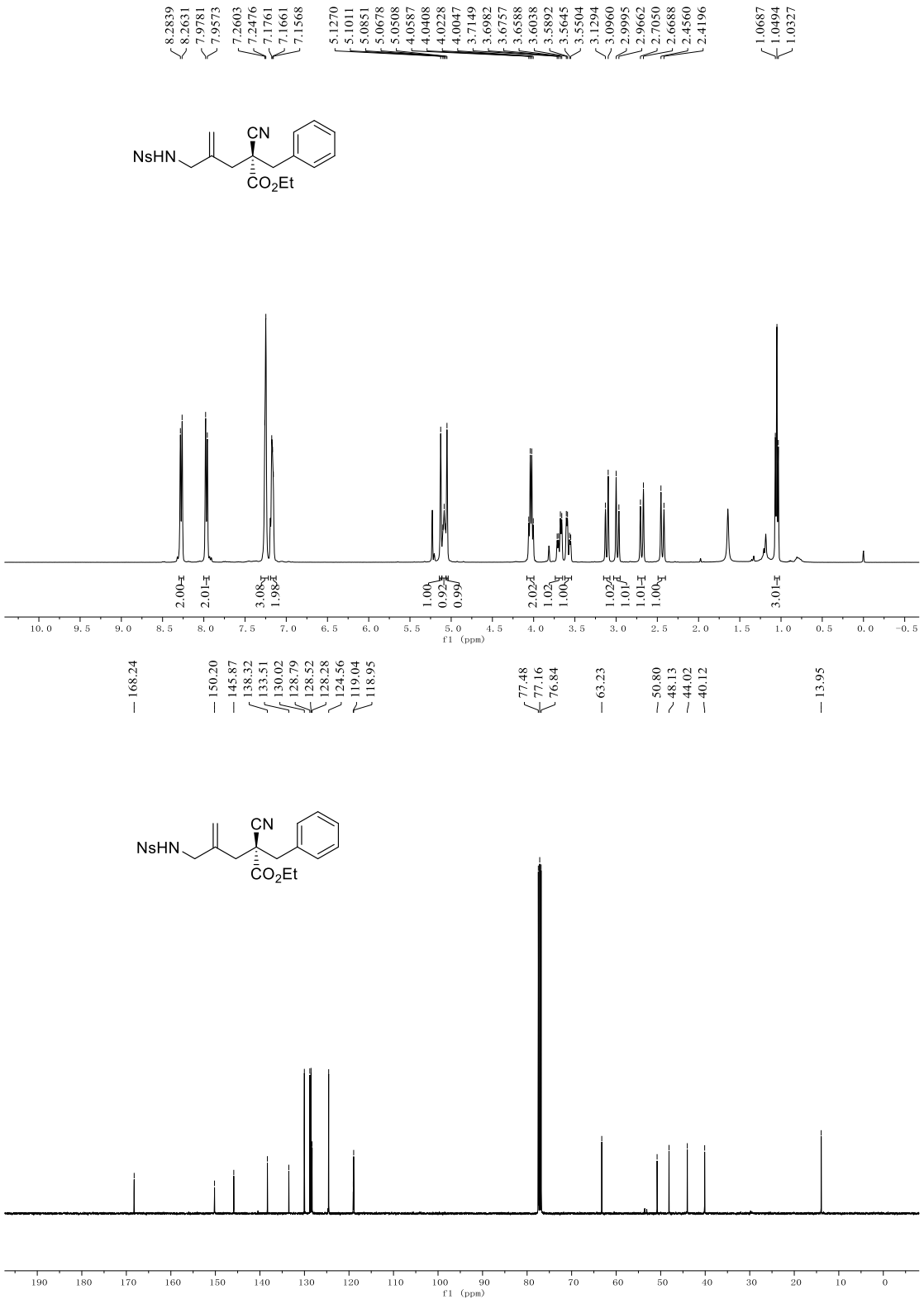


1 Det.A Ch1 / 220nm

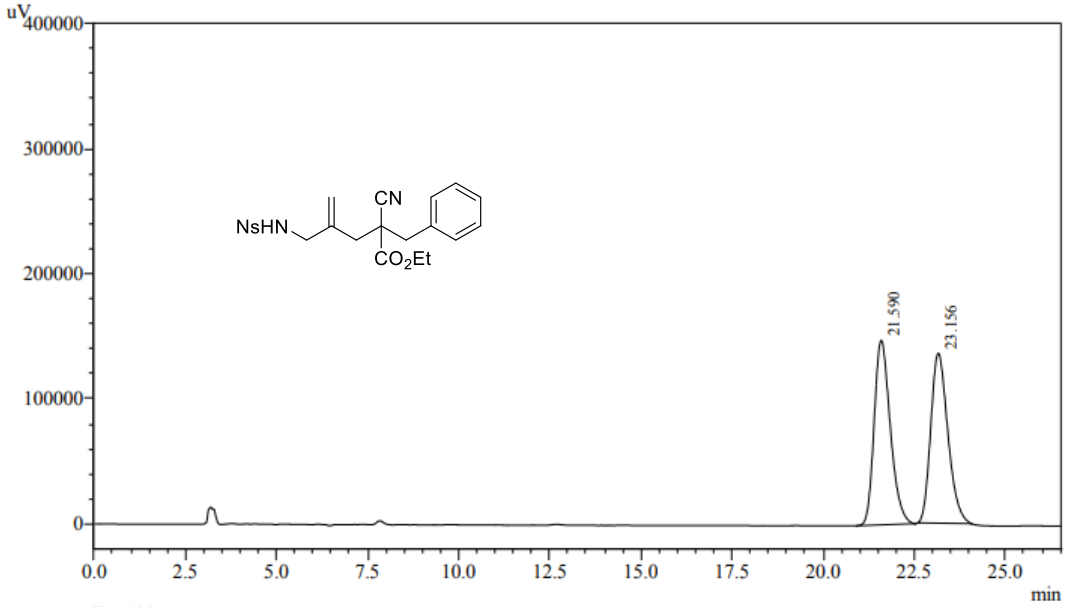
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.602	3821516	64644	96.386	96.331
2	32.539	143283	2462	3.614	3.669
Total		3964799	67106	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3c



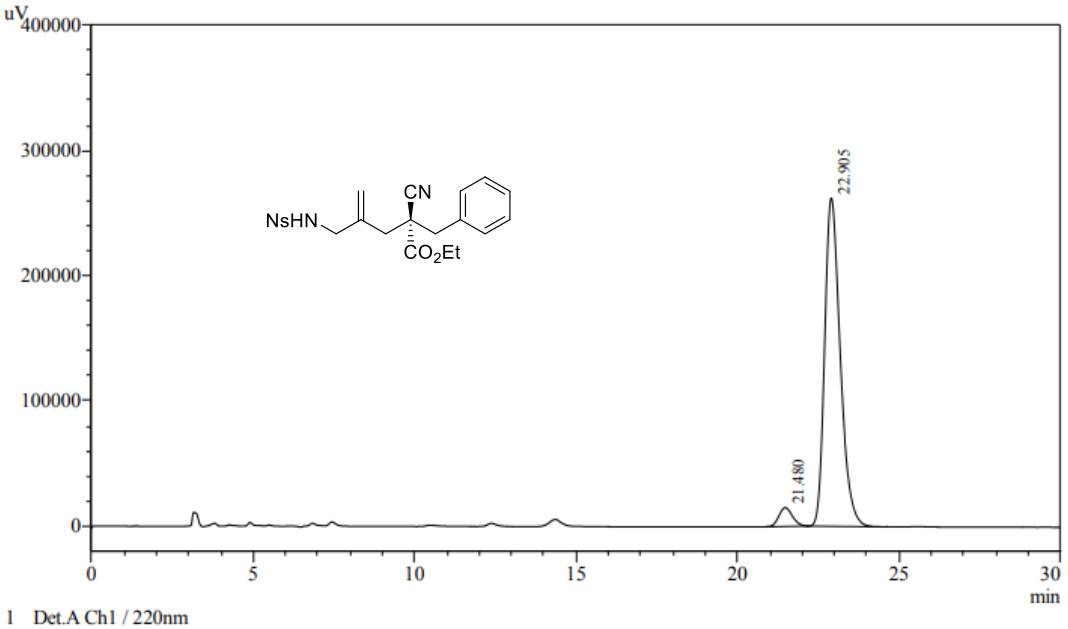
HPLC spectra of 3c



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.590	4547190	147614	50.583	52.080
2	23.156	4442299	135823	49.417	47.920
Total		8989489	283436	100.000	100.000

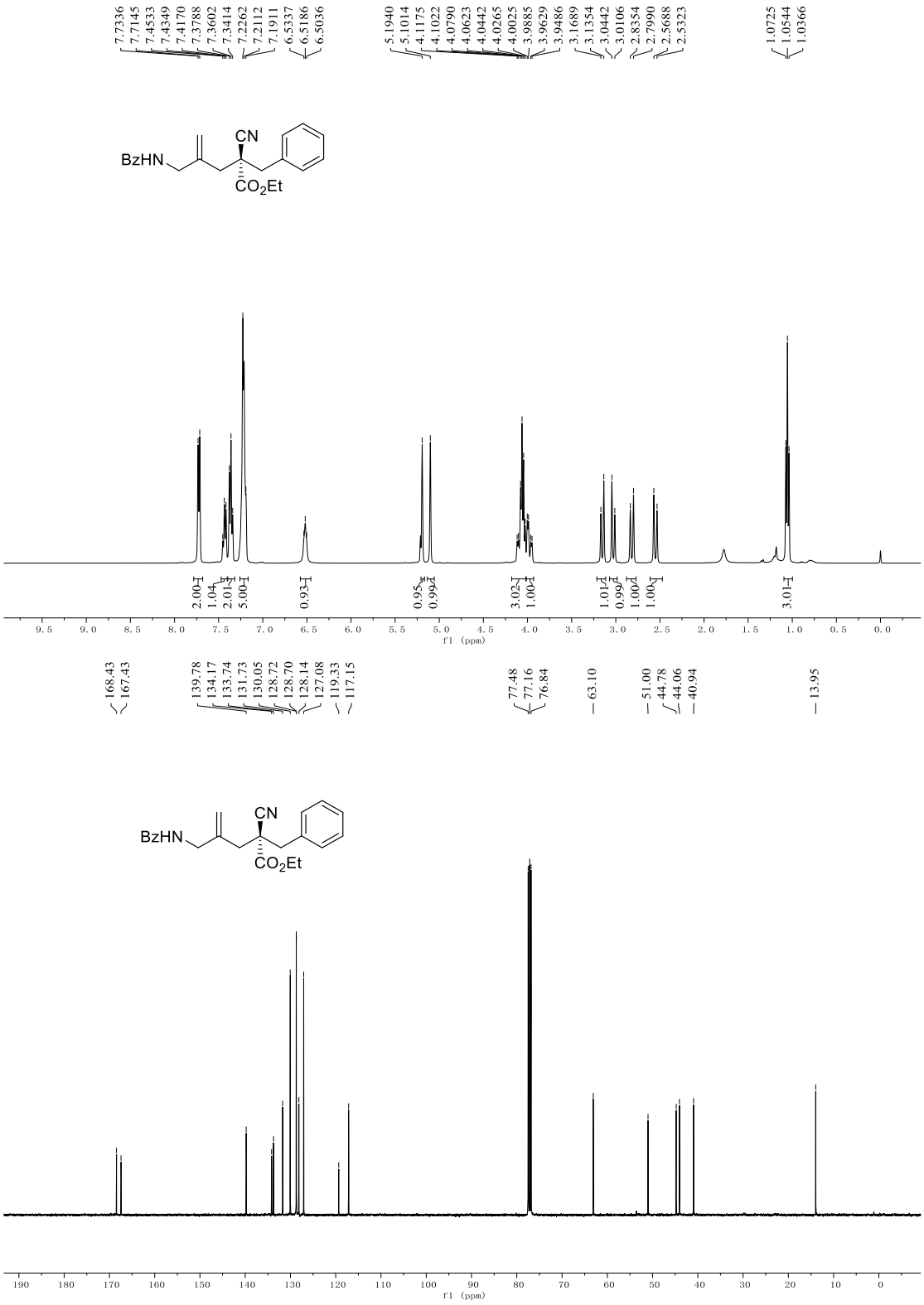


1 Det.A Ch1 / 220nm

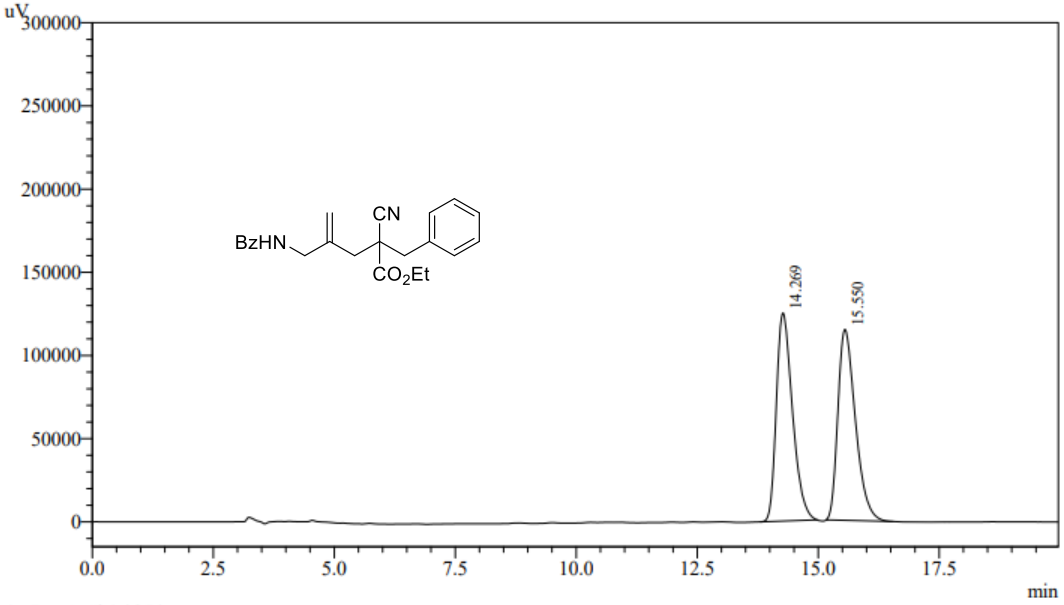
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.480	431654	15003	4.700	5.413
2	22.905	8752835	262178	95.300	94.587
Total		9184489	277181	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3d



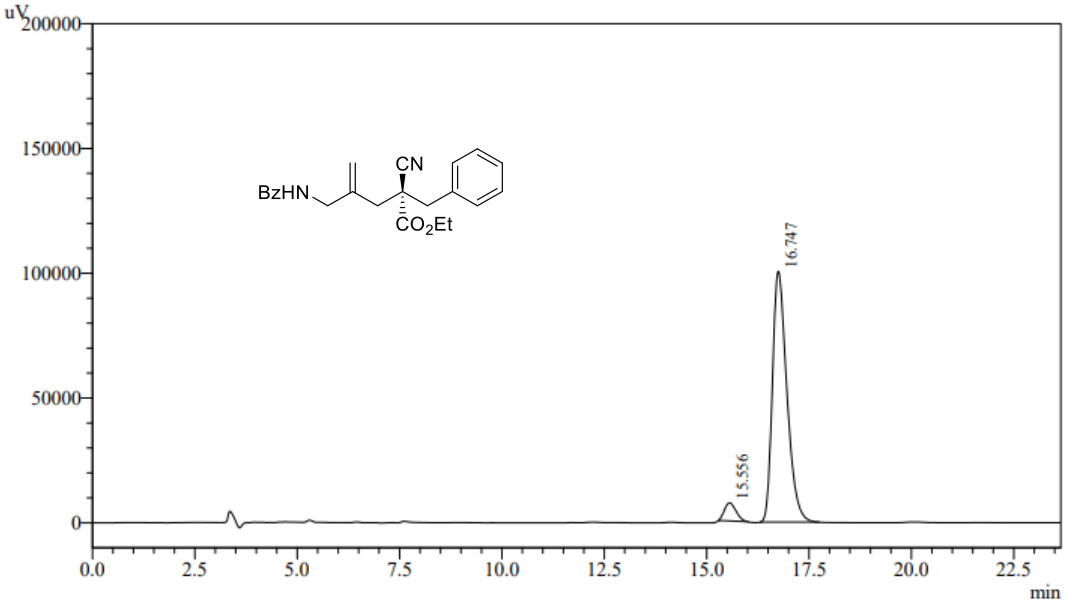
HPLC spectra of 3d



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.269	2897619	125117	49.994	52.162
2	15.550	2898265	114743	50.006	47.838
Total		5795884	239861	100.000	100.000

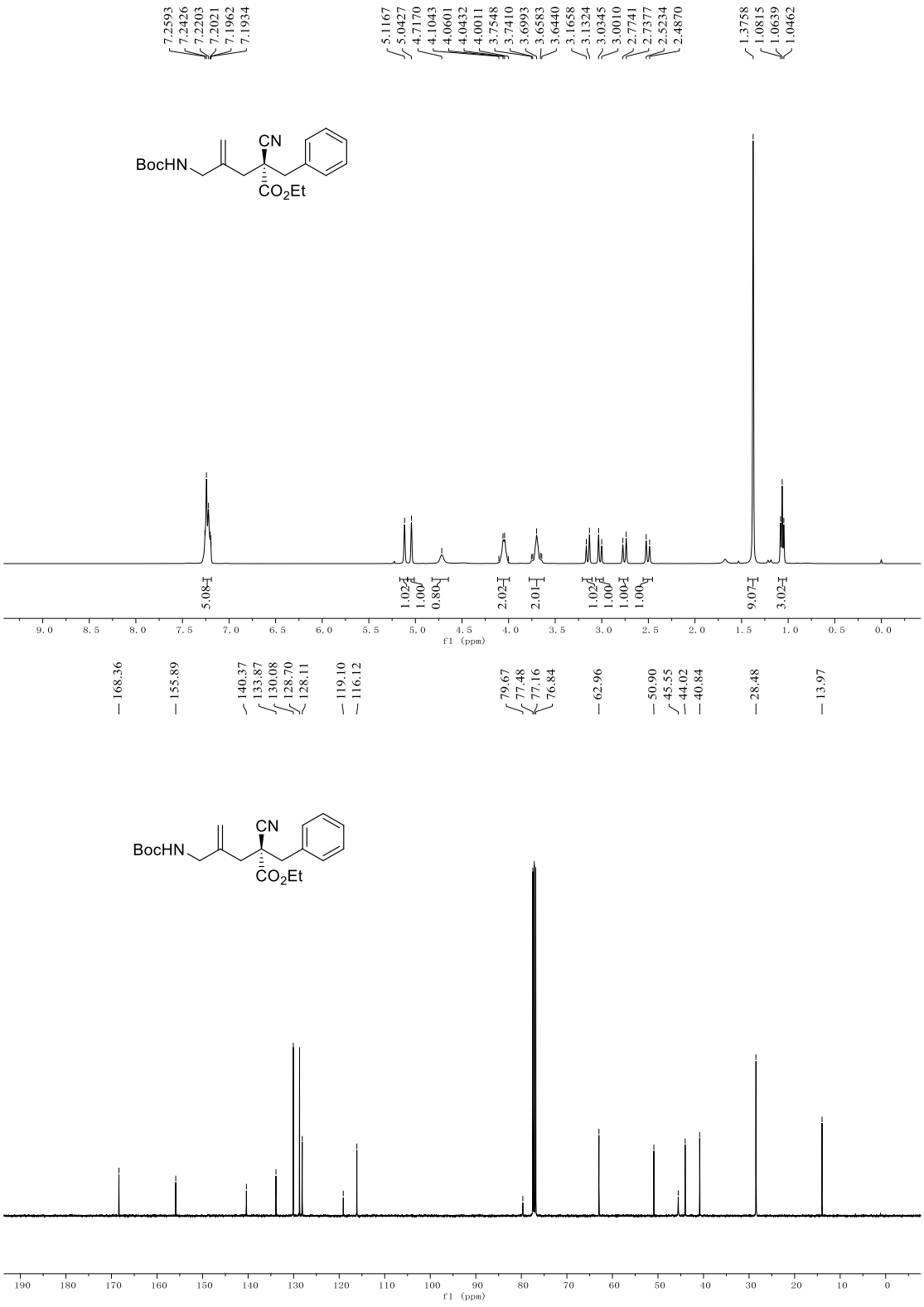


1 Det.A Ch1 / 254nm

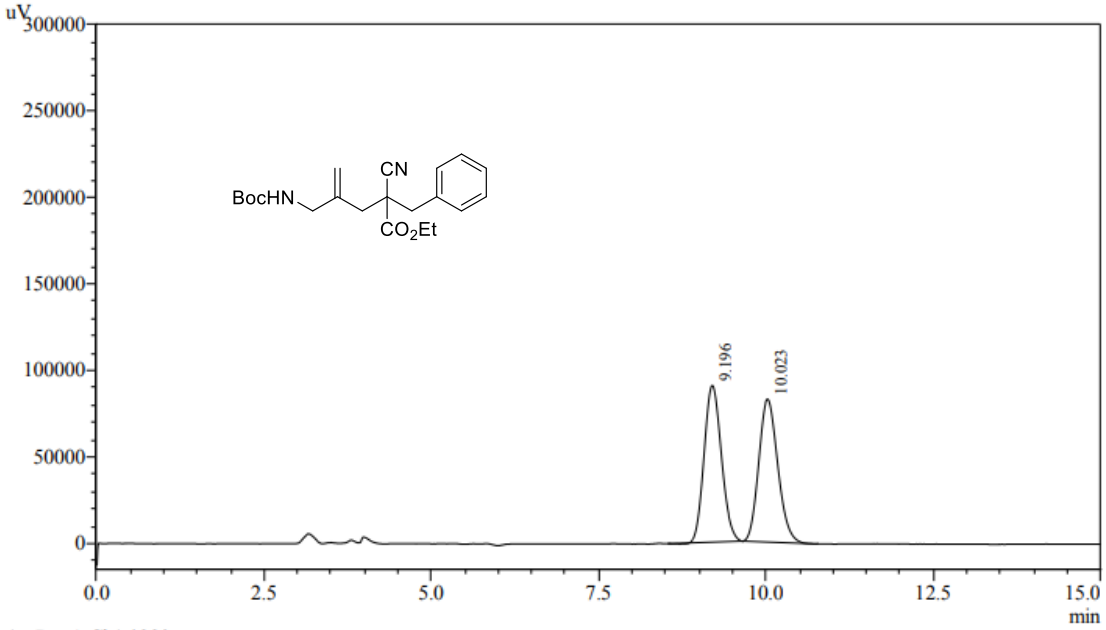
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.556	141871	7246	5.426	6.727
2	16.747	2472612	100461	94.574	93.273
Total		2614484	107706	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3e



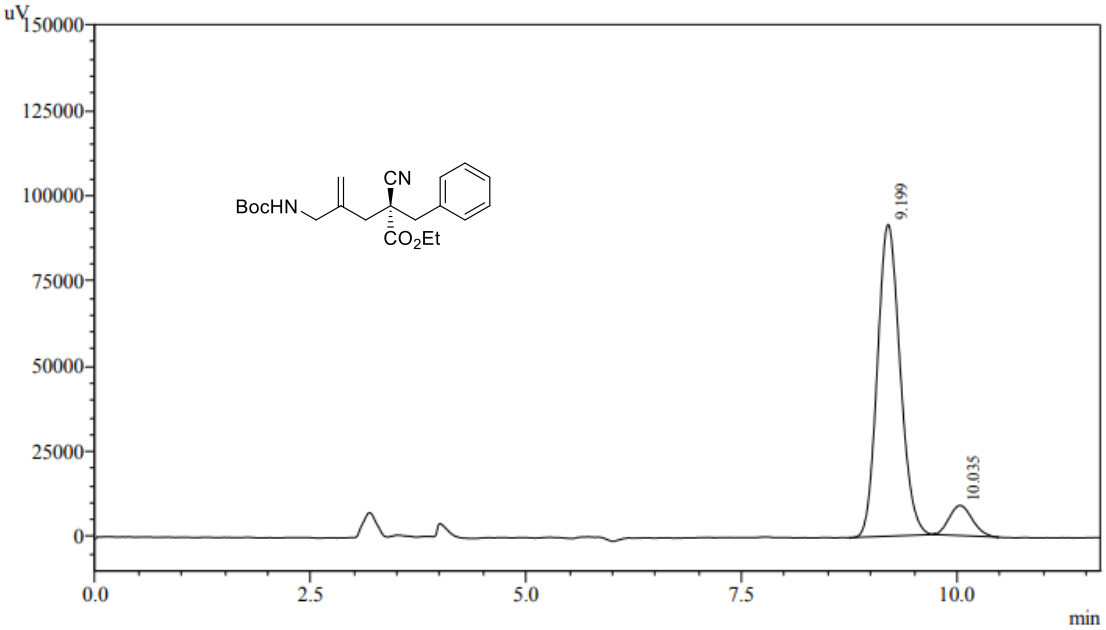
HPLC spectra of 3e



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.196	1620350	90634	49.696	52.297
2	10.023	1640172	82671	50.304	47.703
Total		3260522	173305	100.000	100.000

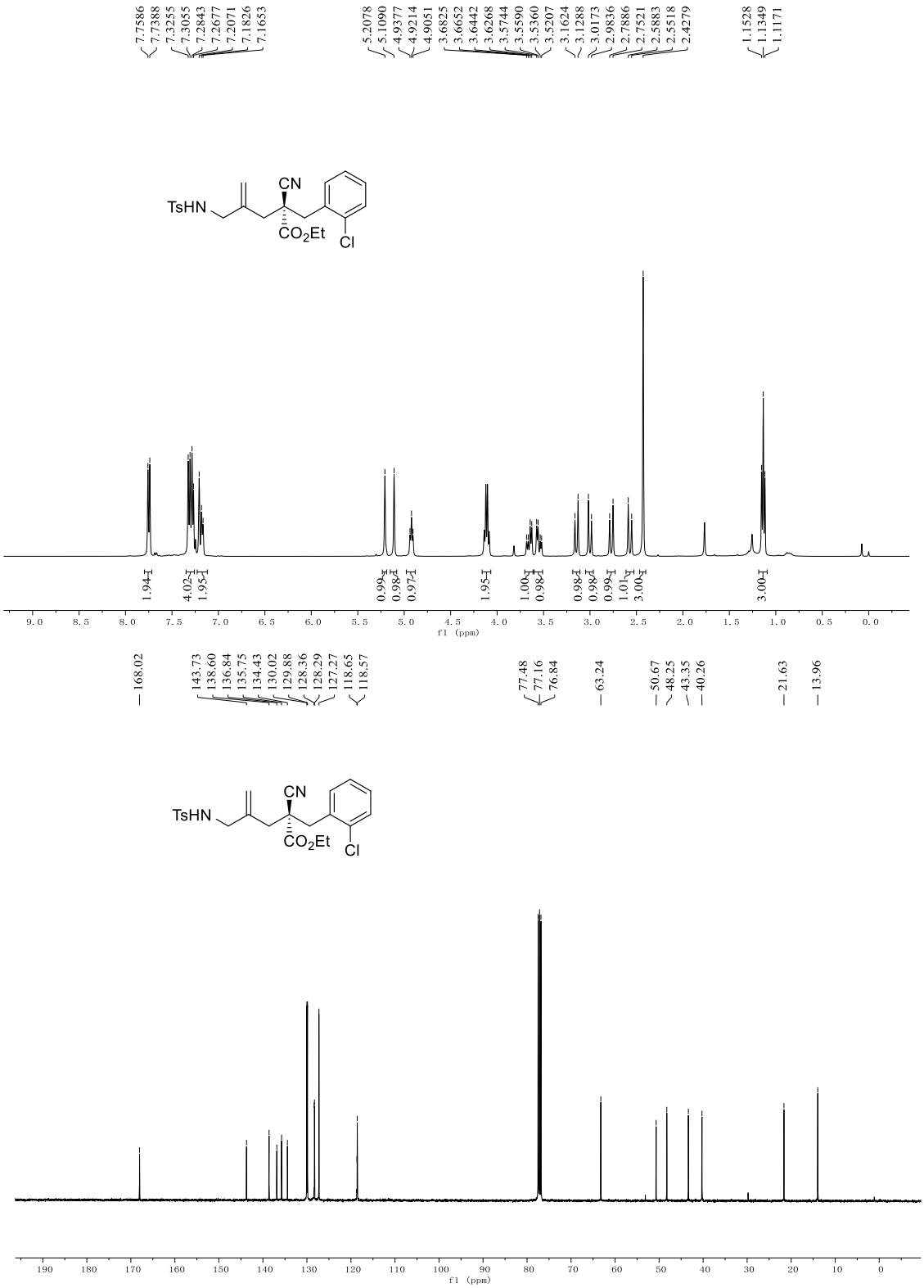


1 Det.A Ch1 / 220nm

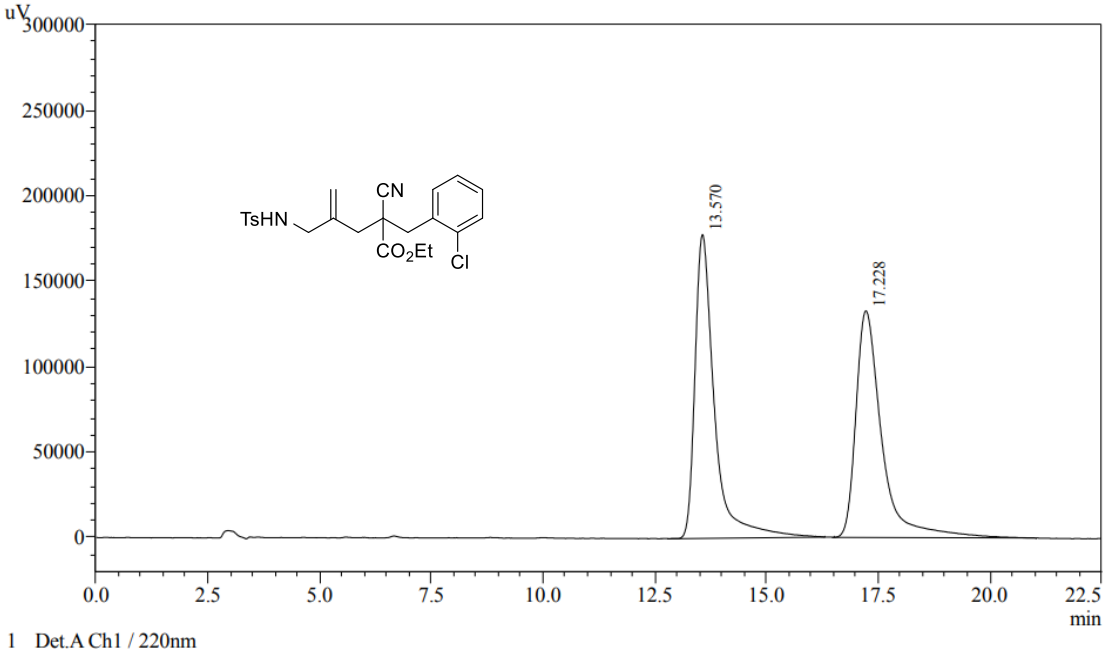
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.199	1673505	91361	91.046	91.201
2	10.035	164589	8814	8.954	8.799
Total		1838094	100176	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3f



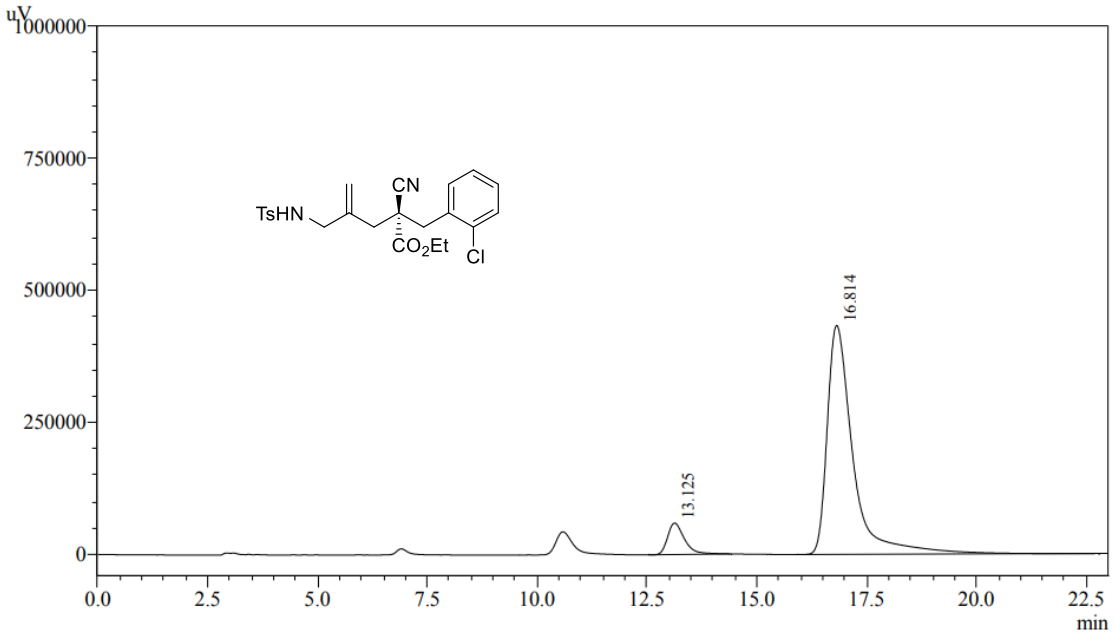
HPLC spectra of 3f



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.570	5398472	177735	50.245	57.268
2	17.228	5345857	132621	49.755	42.732
Total		10744329	310356	100.000	100.000

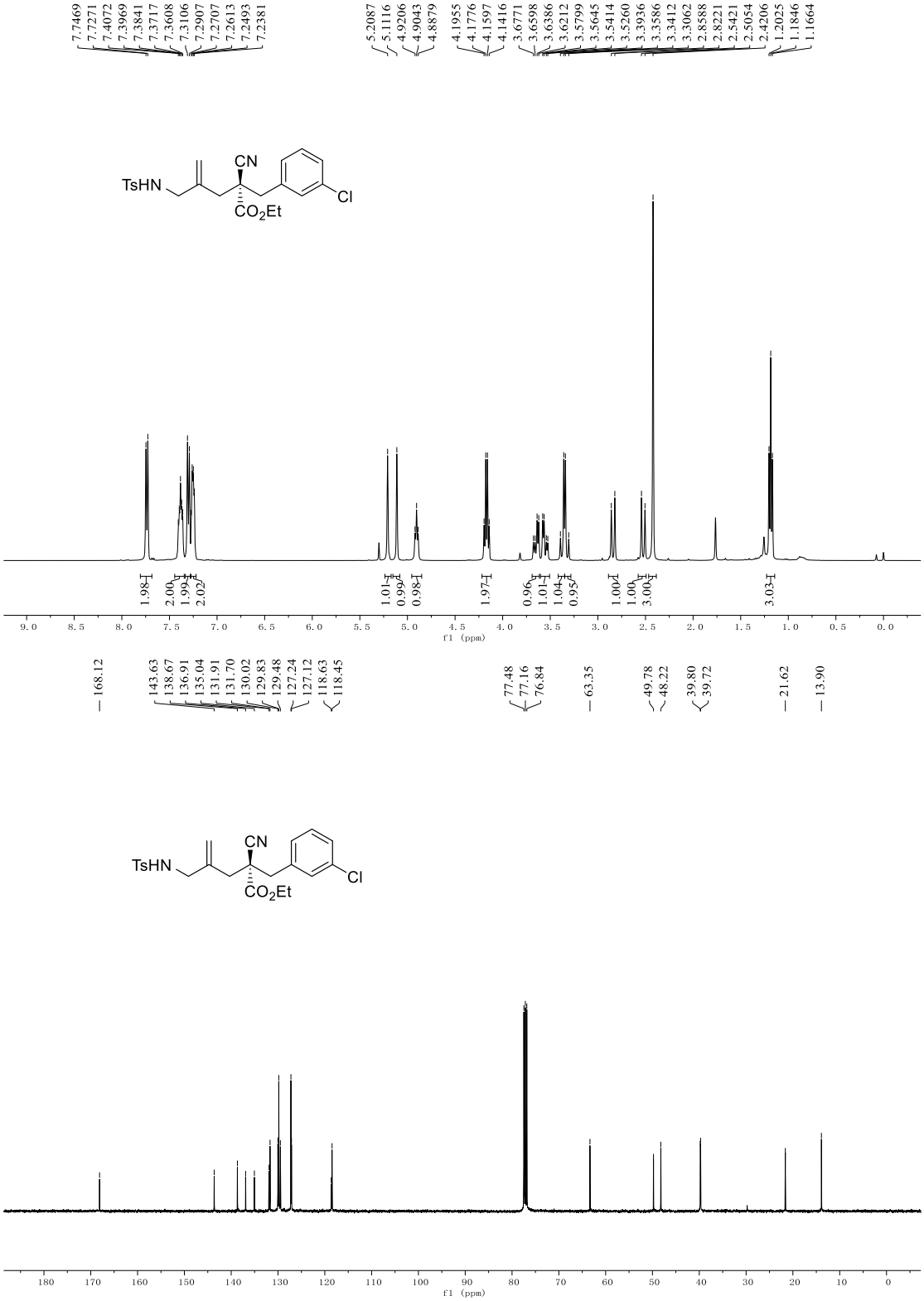


1 Det.A Ch1 / 220nm

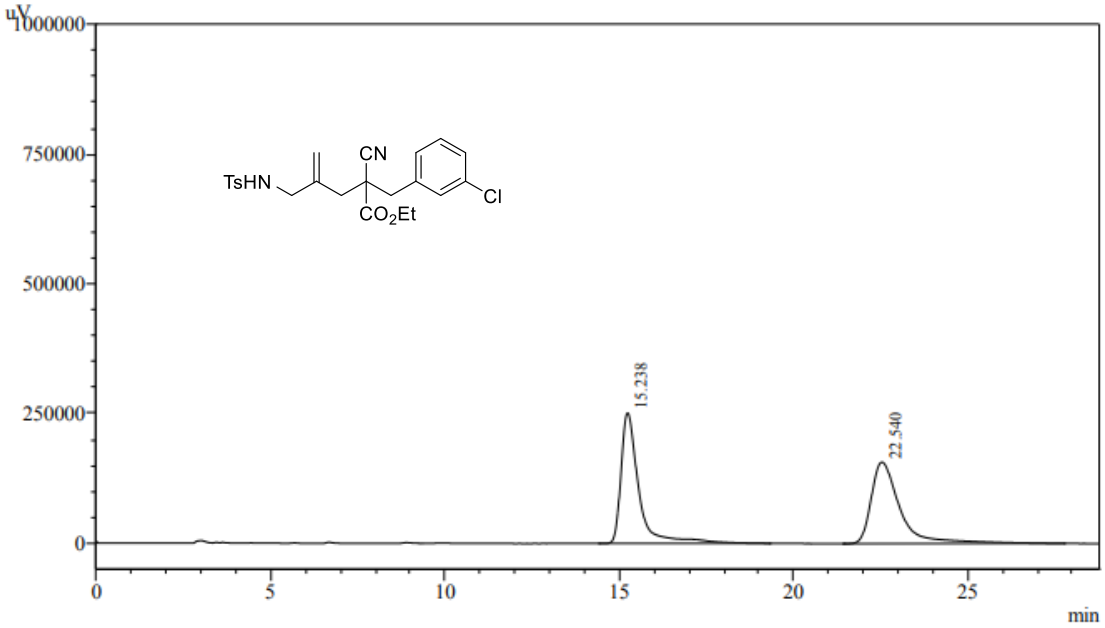
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.125	1597926	59701	8.270	12.110
2	16.814	17724268	433281	91.730	87.890
Total		19322194	492982	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3g



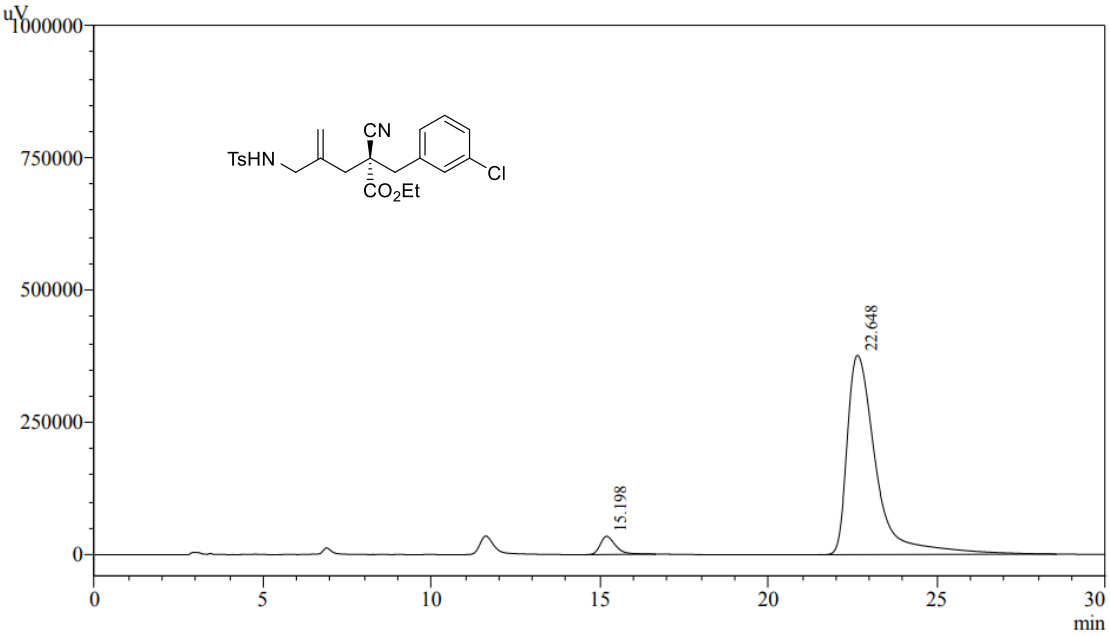
HPLC spectra of 3g



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.238	9001603	251257	49.874	61.537
2	22.540	9046940	157047	50.126	38.463
Total		18048543	408304	100.000	100.000

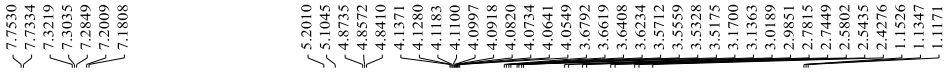


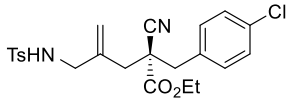
1 Det.A Ch1 / 220nm

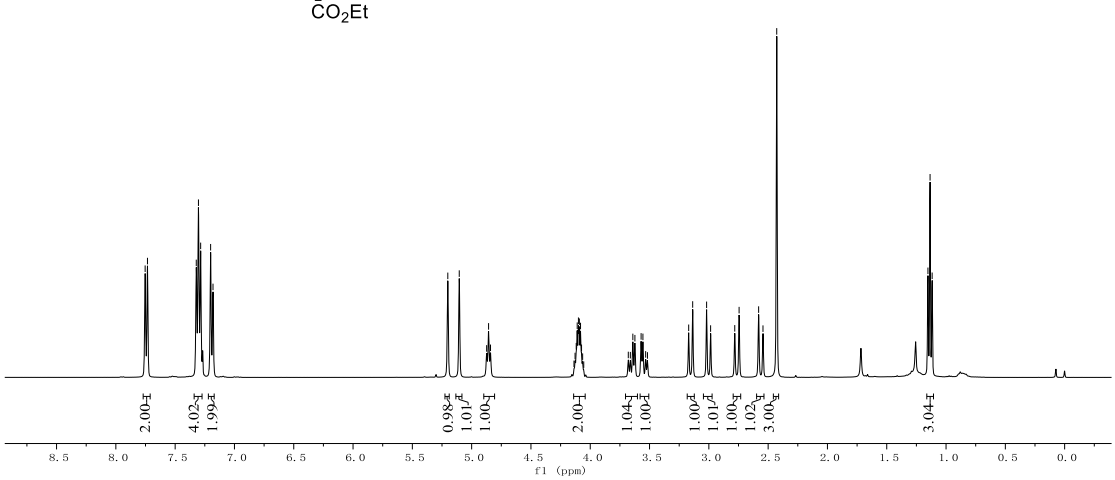
Detector A Ch1 220nm

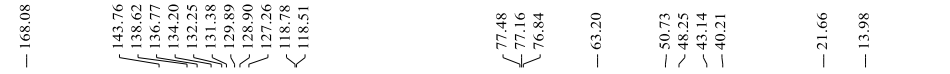
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.198	1076455	34331	4.554	8.349
2	22.648	22560384	376864	95.446	91.651
Total		23636839	411196	100.000	100.000

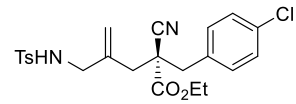
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3h

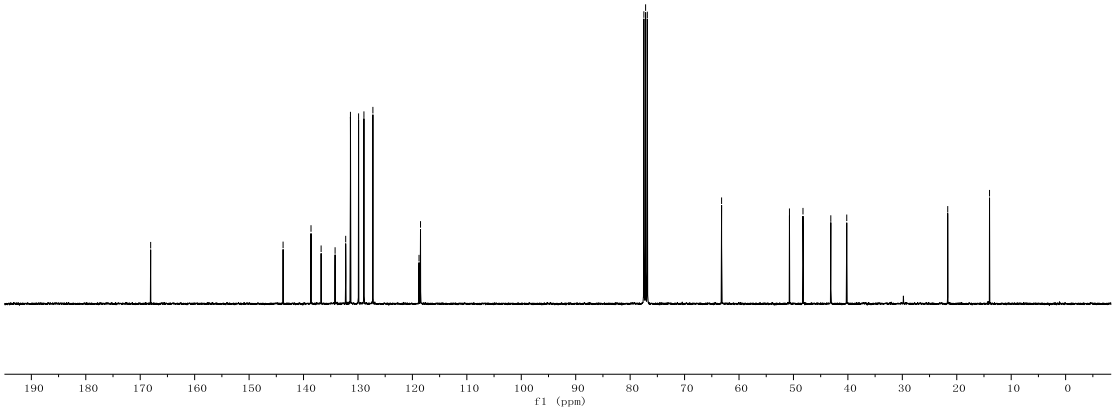




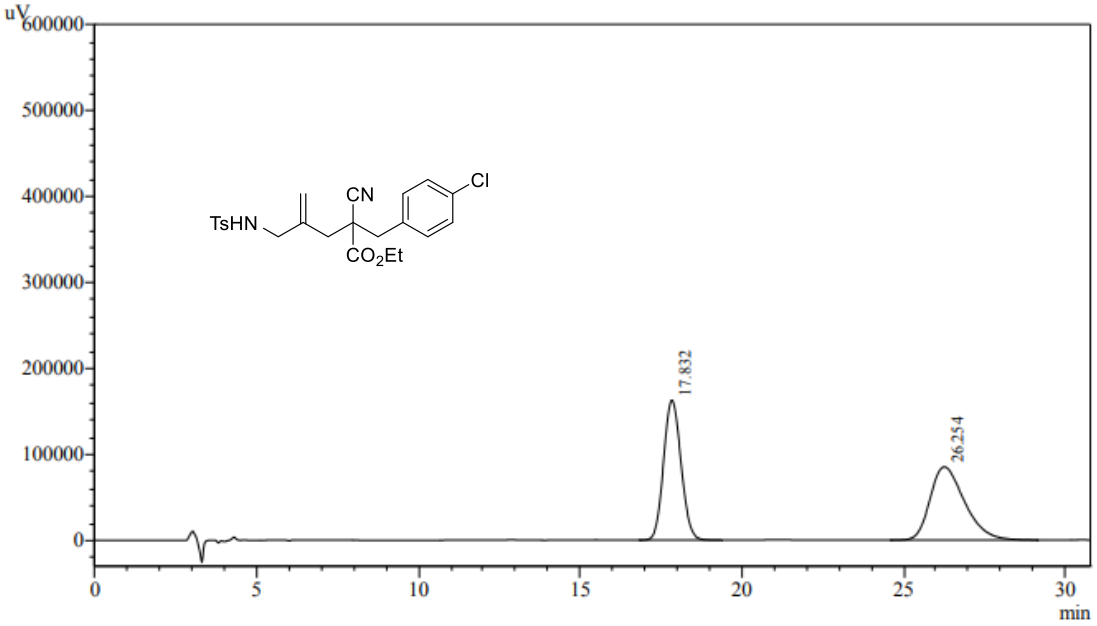








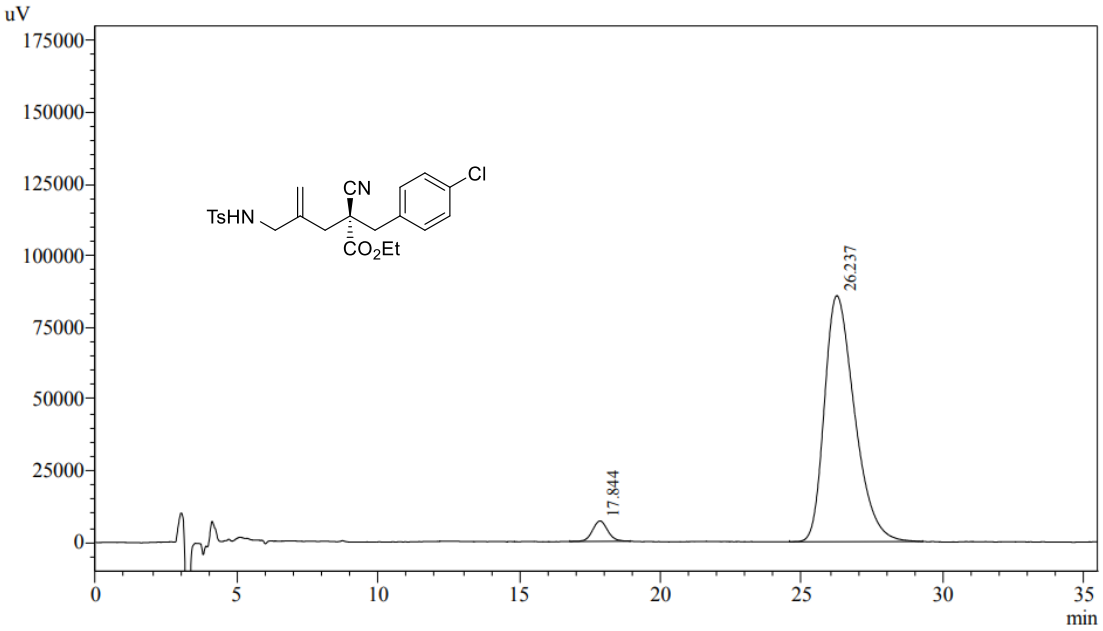
HPLC spectra of 3h



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.832	6117205	162843	49.228	65.648
2	26.254	6309120	85213	50.772	34.352
Total		12426324	248056	100.000	100.000

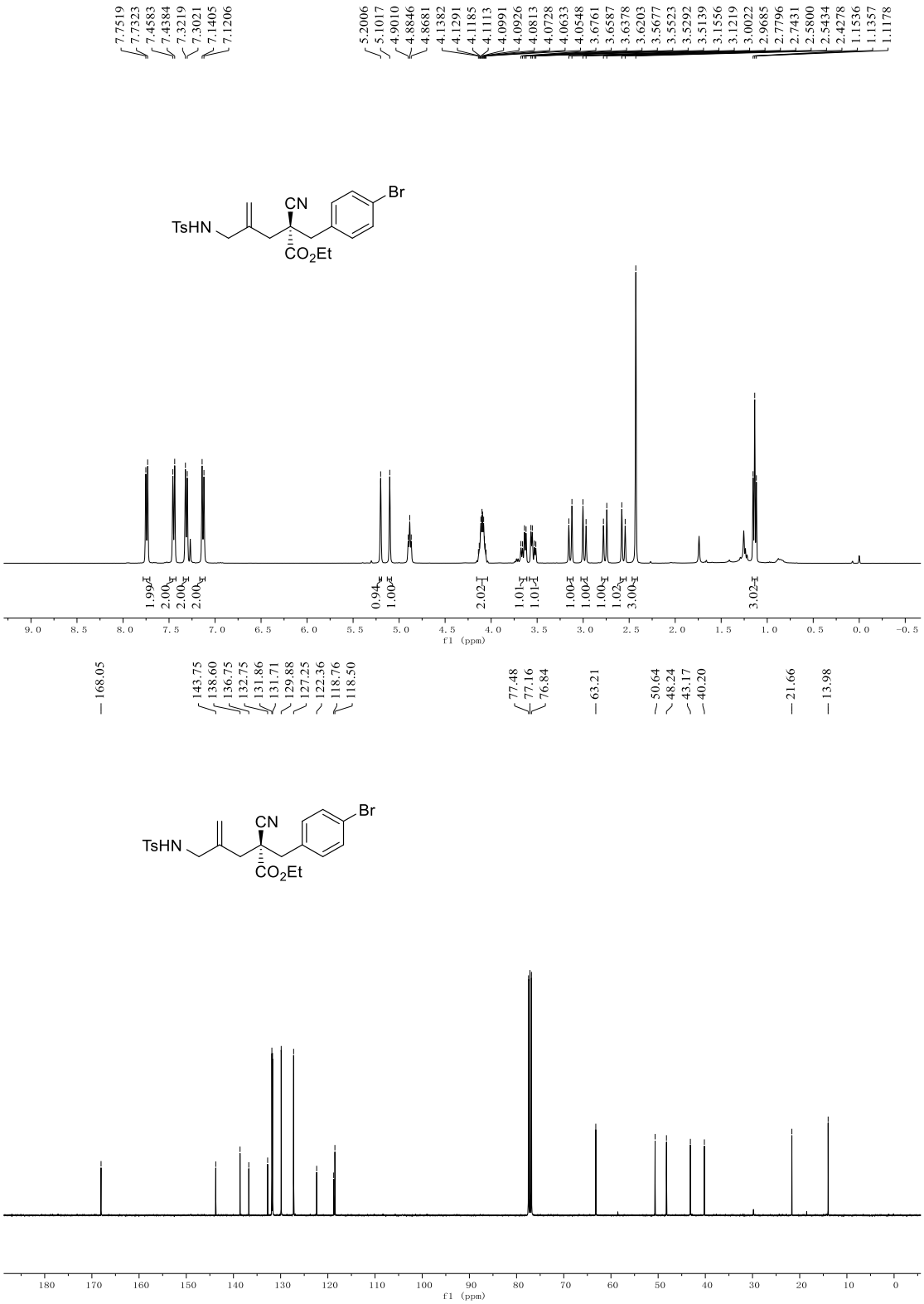


1 Det.A Ch1 / 220nm

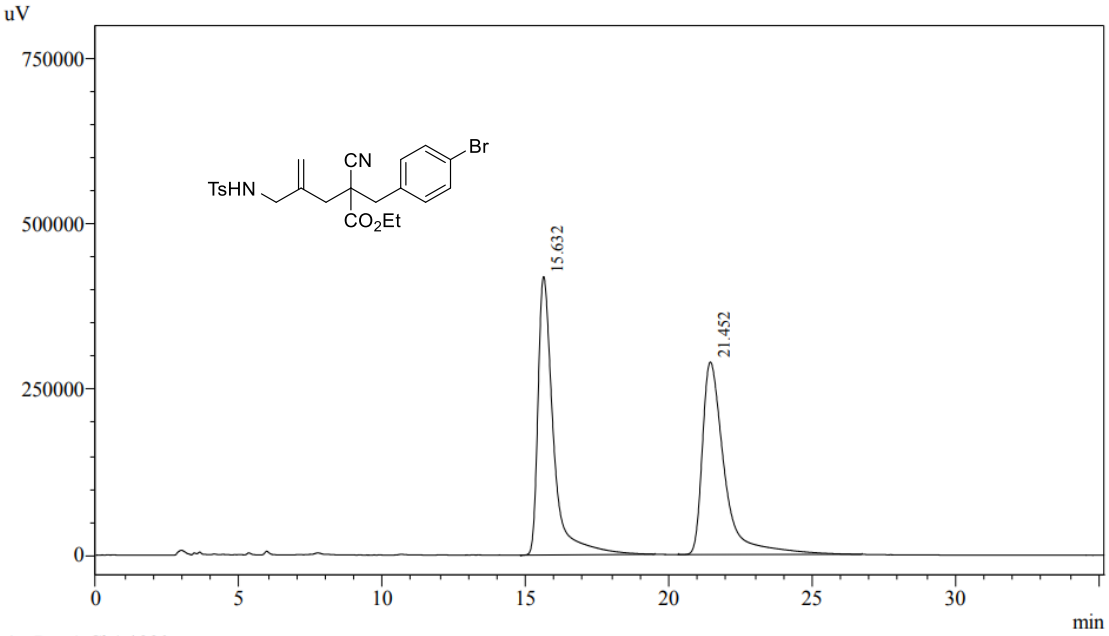
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	17.844	264684	7107	3.980	7.648
2	26.237	6386421	85815	96.020	92.352
Total		6651105	92922	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3i



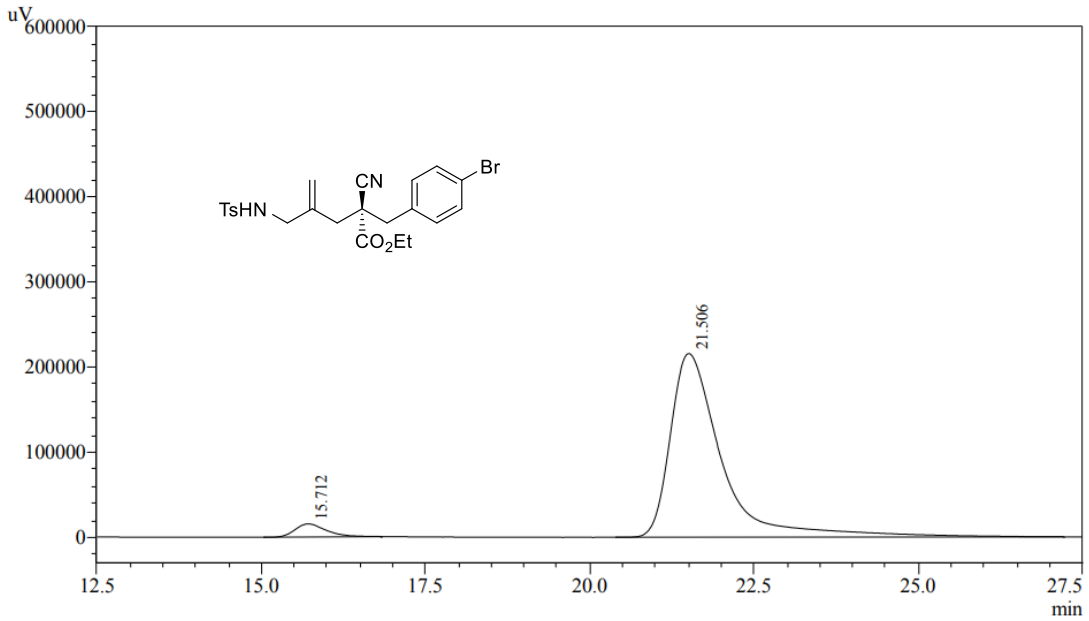
HPLC spectra of 3i



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.632	15795580	421147	50.088	59.116
2	21.452	15740195	291266	49.912	40.884
Total		31535775	712412	100.000	100.000

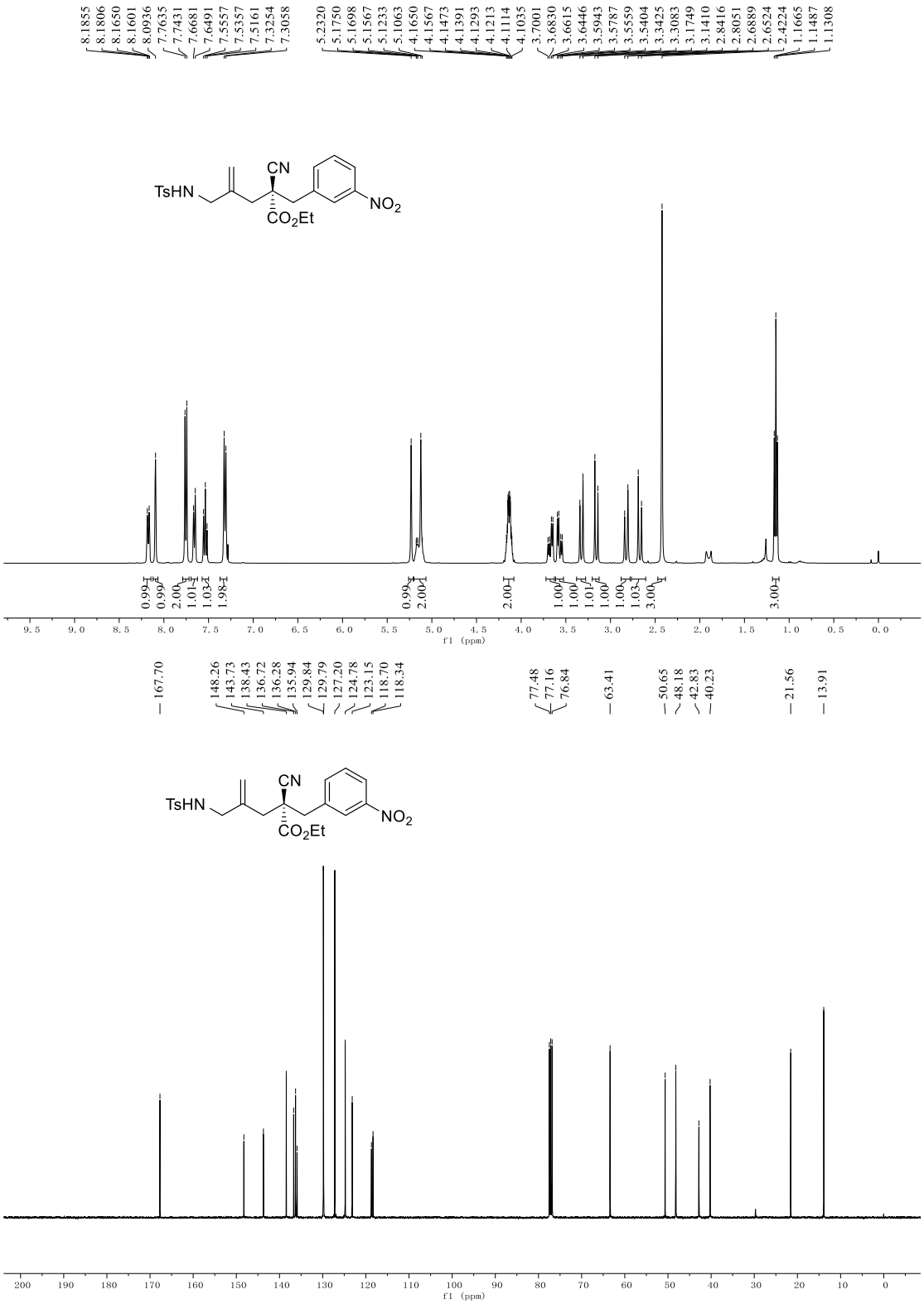


1 Det.A Ch1 / 220nm

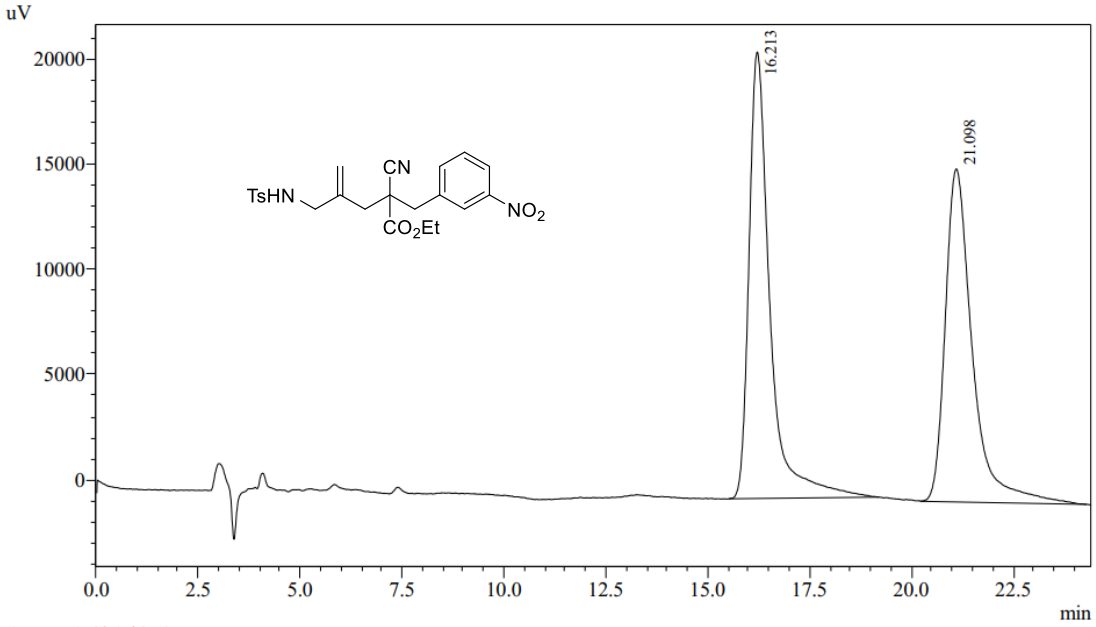
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.712	508554	15353	4.152	6.643
2	21.506	11740598	215769	95.848	93.357
Total		12249153	231122	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3j



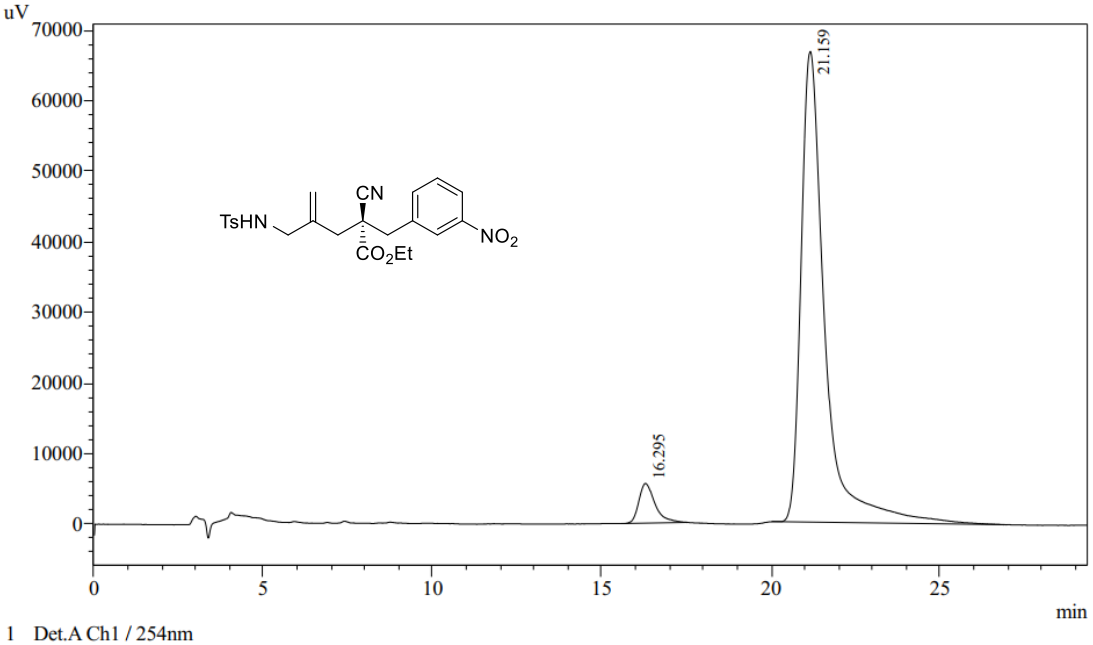
HPLC spectra of 3j



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.213	759701	21212	50.967	57.279
2	21.098	730863	15820	49.033	42.721
Total		1490564	37032	100.000	100.000

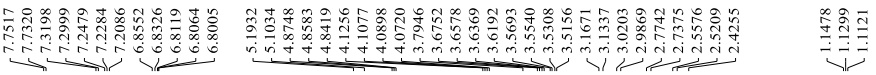


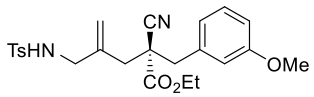
1 Det.A Ch1 / 254nm

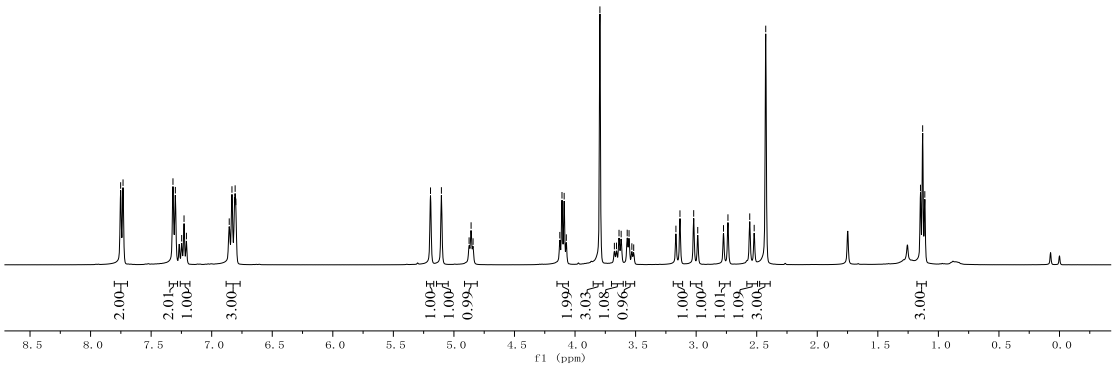
Detector A Ch1 254nm

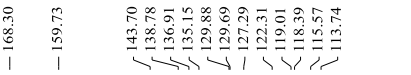
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.295	185913	5612	5.381	7.763
2	21.159	3268852	66672	94.619	92.237
Total		3454765	72283	100.000	100.000

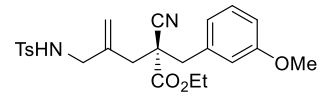
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3k

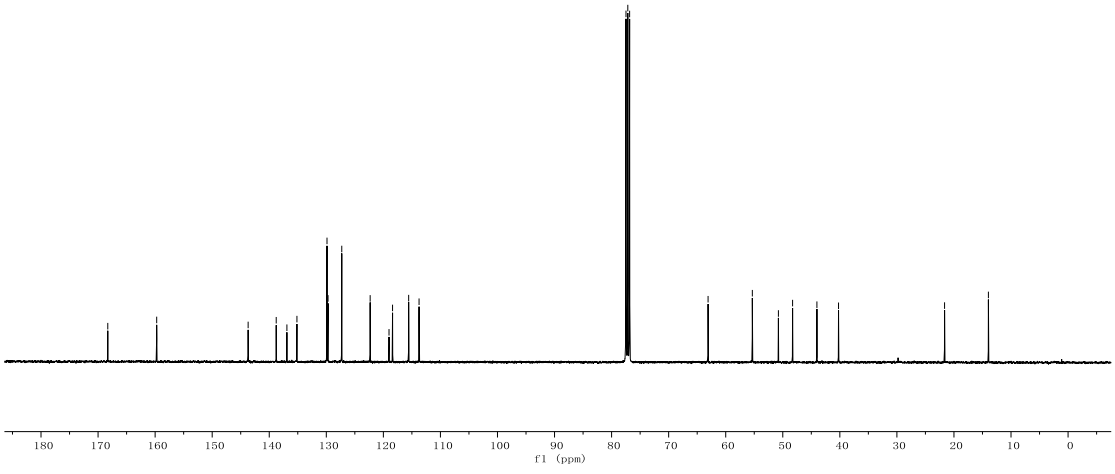

7.7517
7.7320
7.3198
7.2999
7.2479
7.2284
7.2086
6.8552
6.8326
6.8119
6.8064
6.8005
5.1932
5.1034
4.8748
4.8583
4.8419
4.1256
4.1077
4.0898
4.0720
3.7946
3.6752
3.6578
3.6369
3.6192
3.5693
3.5540
3.5308
3.5156
3.1671
3.1337
3.0203
2.9869
2.7742
2.7375
2.5576
2.5209
2.4255
1.1478
1.1299
1.1121


CN
TsHN
OMe
CO2Et

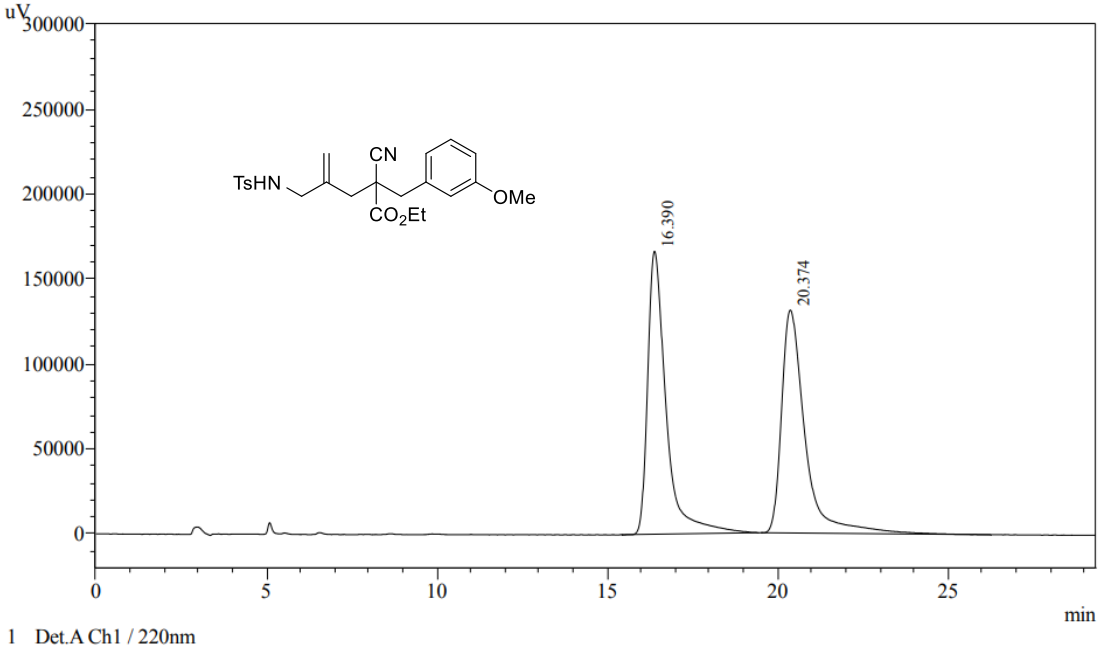

2.00
2.01
1.00
3.00
1.00
1.00
0.99
1.99
3.03
1.08
0.96
1.00
1.00
1.01
1.09
3.00
3.00
f1 (ppm)


168.30
159.73
143.70
138.78
136.91
135.15
129.88
129.69
127.29
122.31
119.01
118.39
115.57
113.74
77.48
77.16
76.84
63.09
55.34
50.77
48.28
44.02
40.23
21.65
13.96


CN
TsHN
OMe
CO2Et


f1 (ppm)

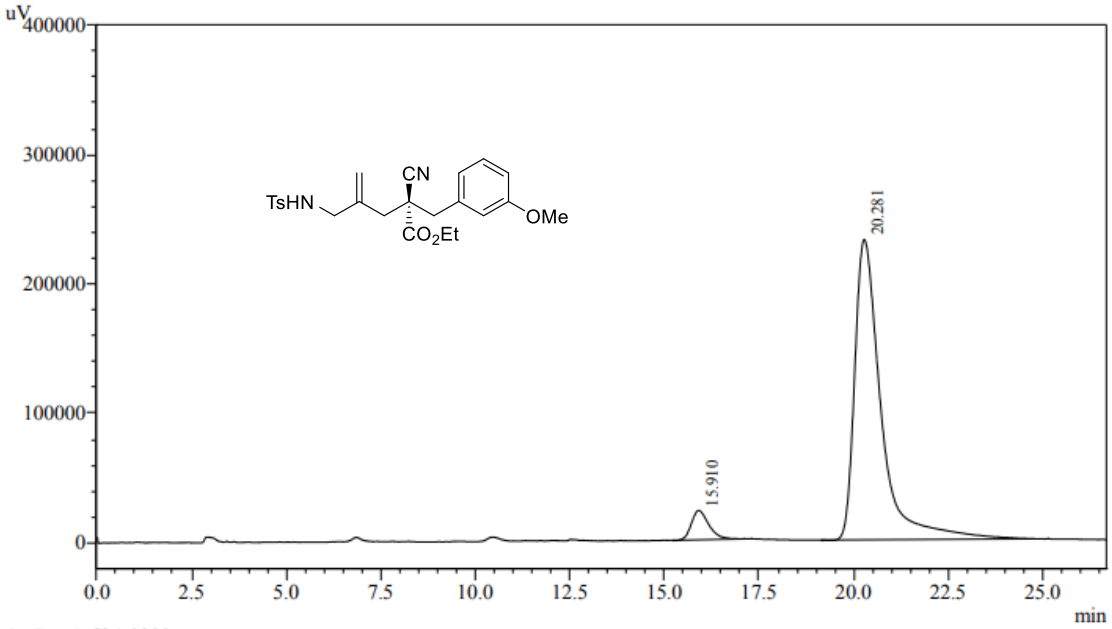
HPLC spectra of 3k



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.390	6271503	166496	49.871	55.933
2	20.374	6303917	131174	50.129	44.067
Total		12575420	297669	100.000	100.000

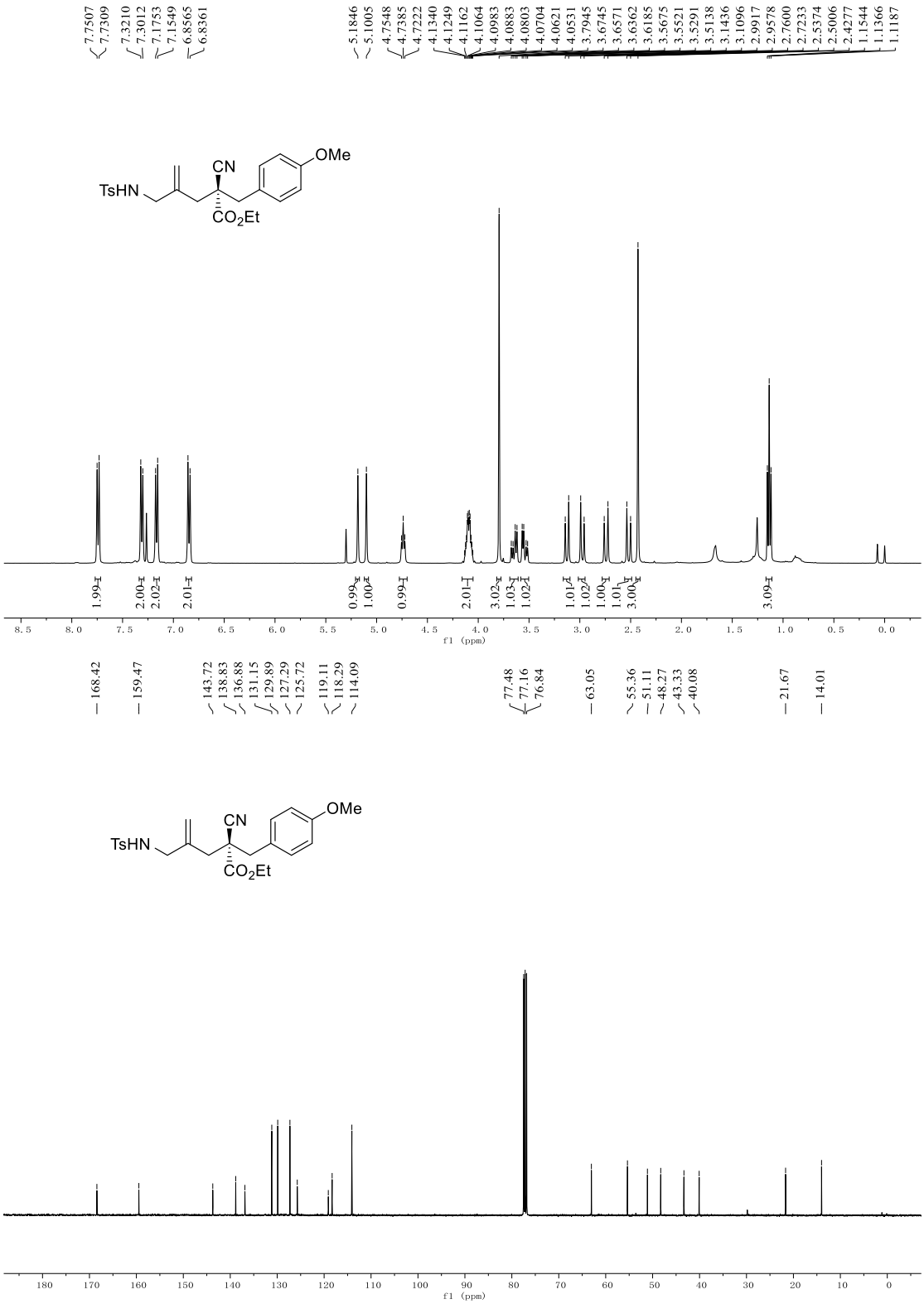


1 Det.A Ch1 / 220nm

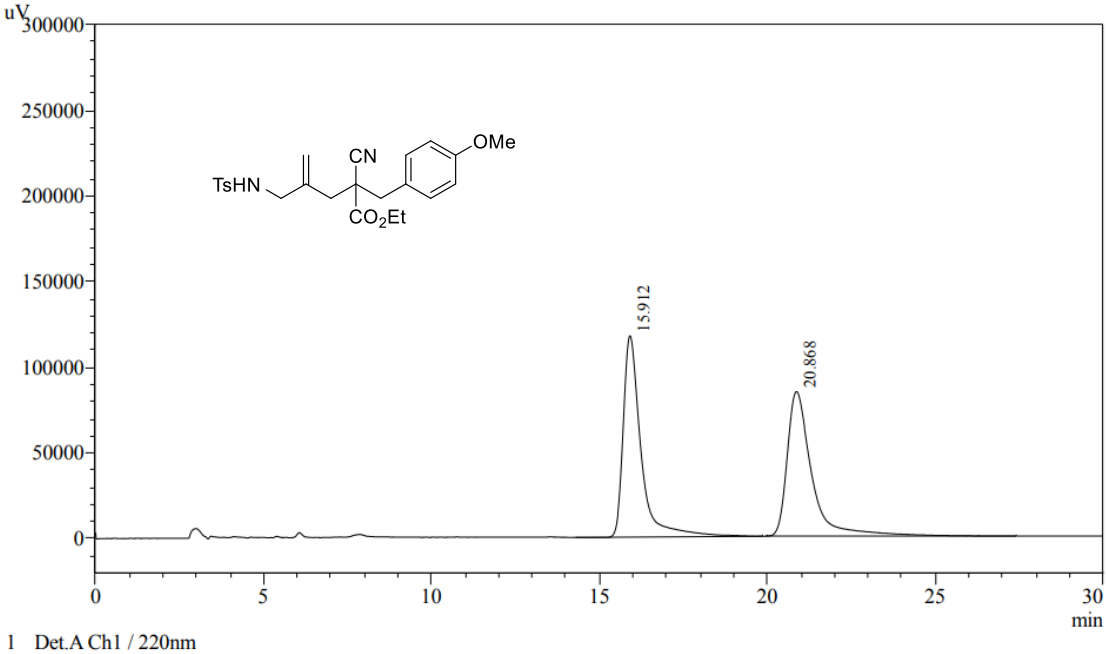
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.910	734597	22745	6.106	8.928
2	20.281	11297085	232025	93.894	91.072
Total		12031682	254770	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3l



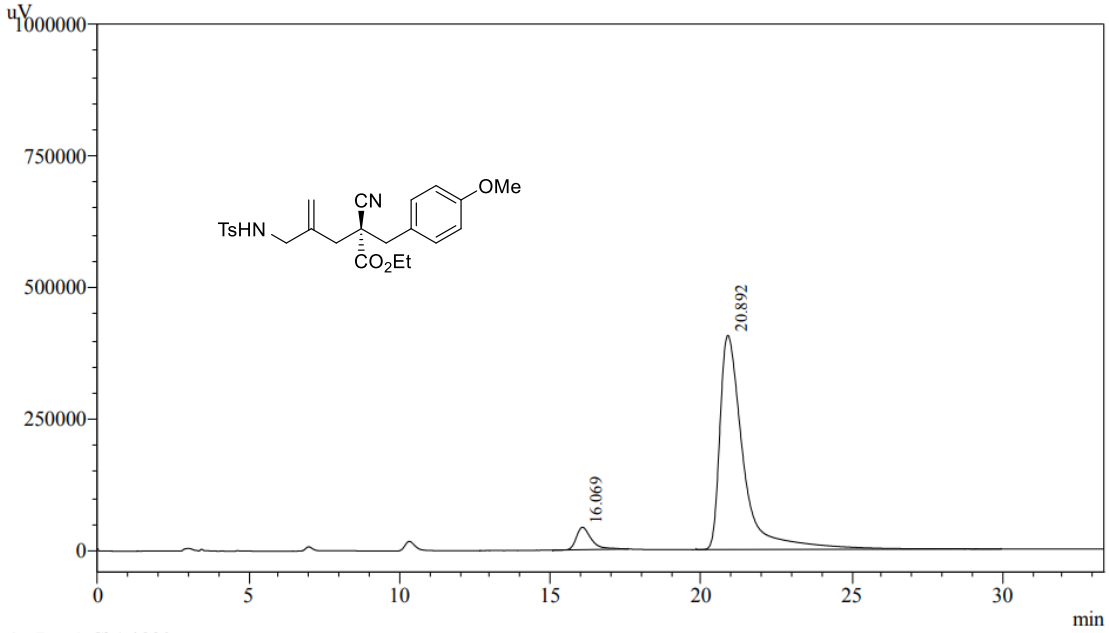
HPLC spectra of 3l



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.912	4311445	117516	50.047	58.200
2	20.868	4303385	84403	49.953	41.800
Total		8614830	201918	100.000	100.000

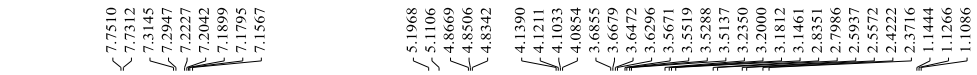


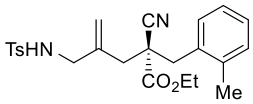
1 Det.A Ch1 / 220nm

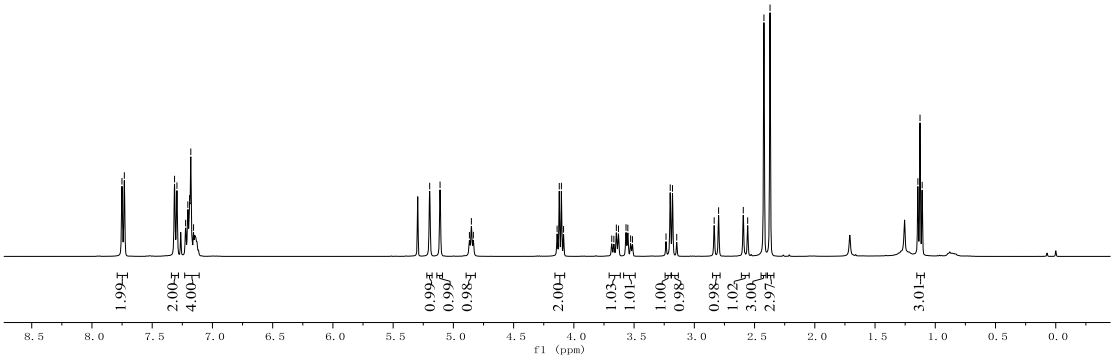
Detector A Ch1 220nm

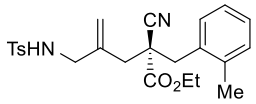
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.069	1472187	42669	6.220	9.489
2	20.892	22196615	406985	93.780	90.511
Total		23668803	449655	100.000	100.000

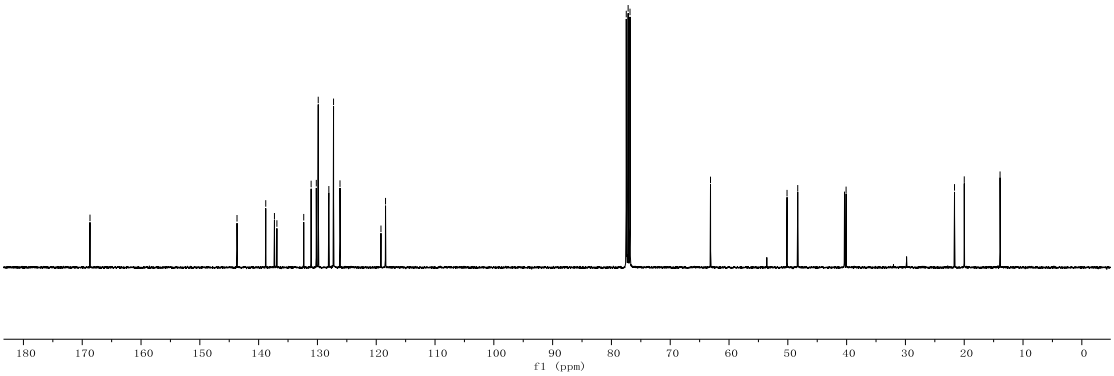
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3m



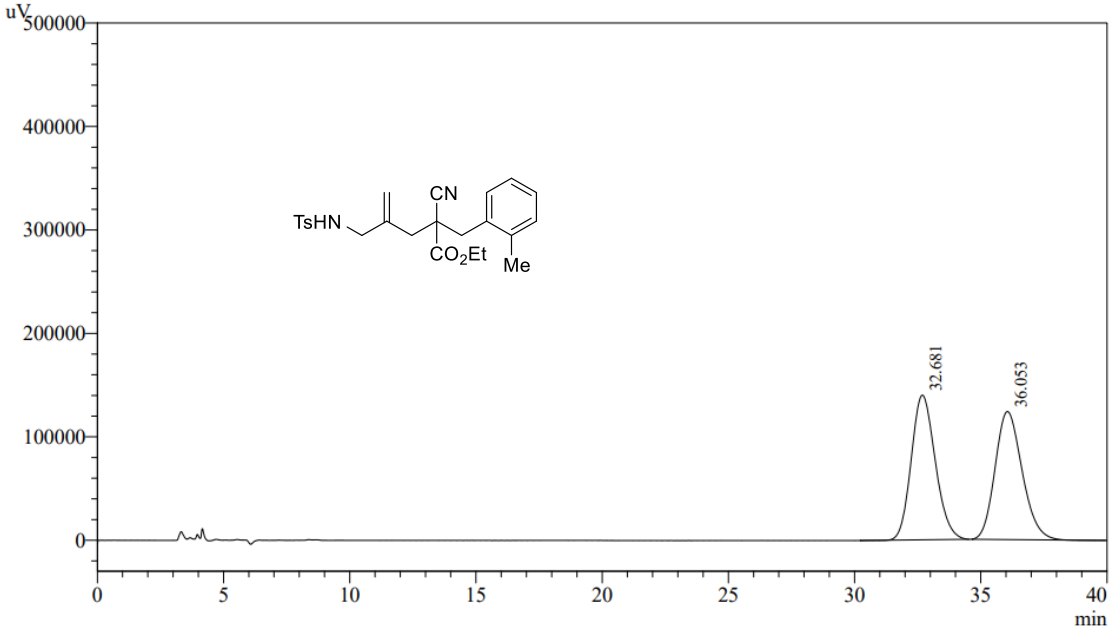








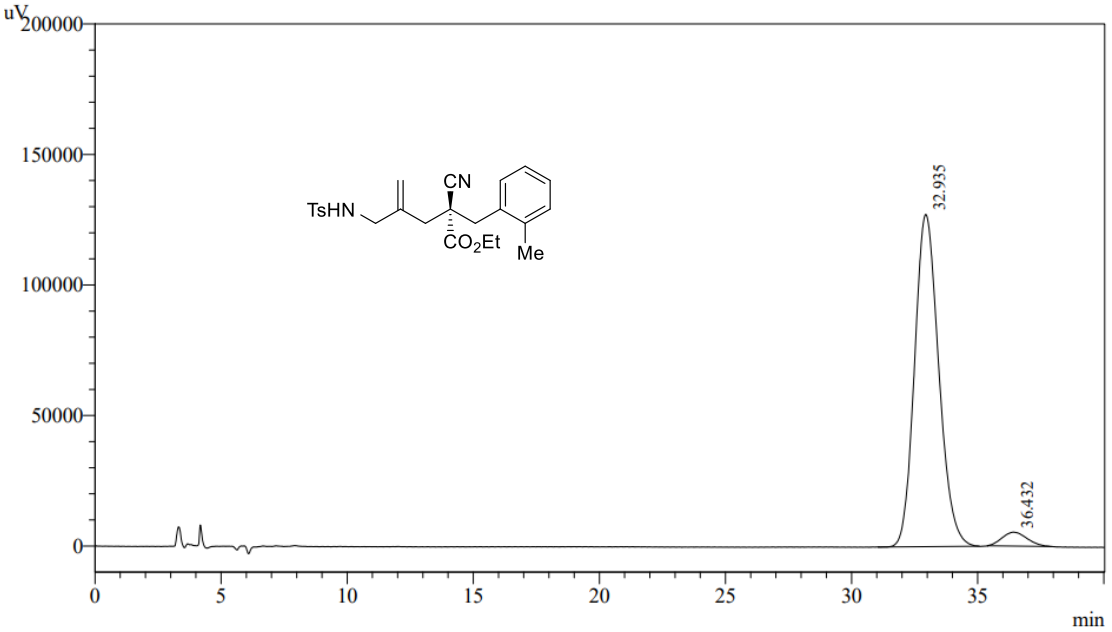
HPLC spectra of 3m



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.681	9271417	139919	50.108	53.069
2	36.053	9231593	123737	49.892	46.931
Total		18503010	263655	100.000	100.000

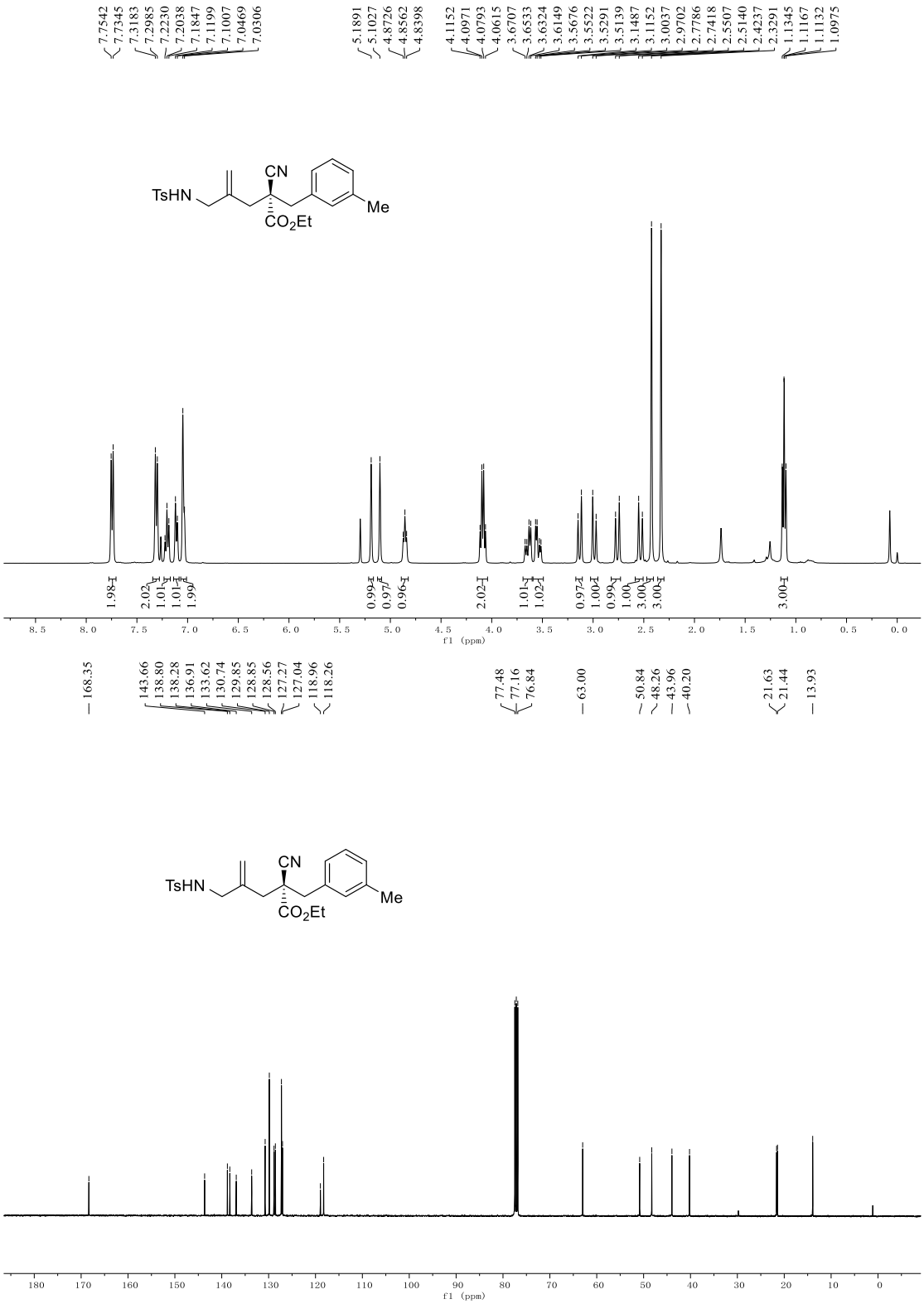


1 Det.A Ch1 / 220nm

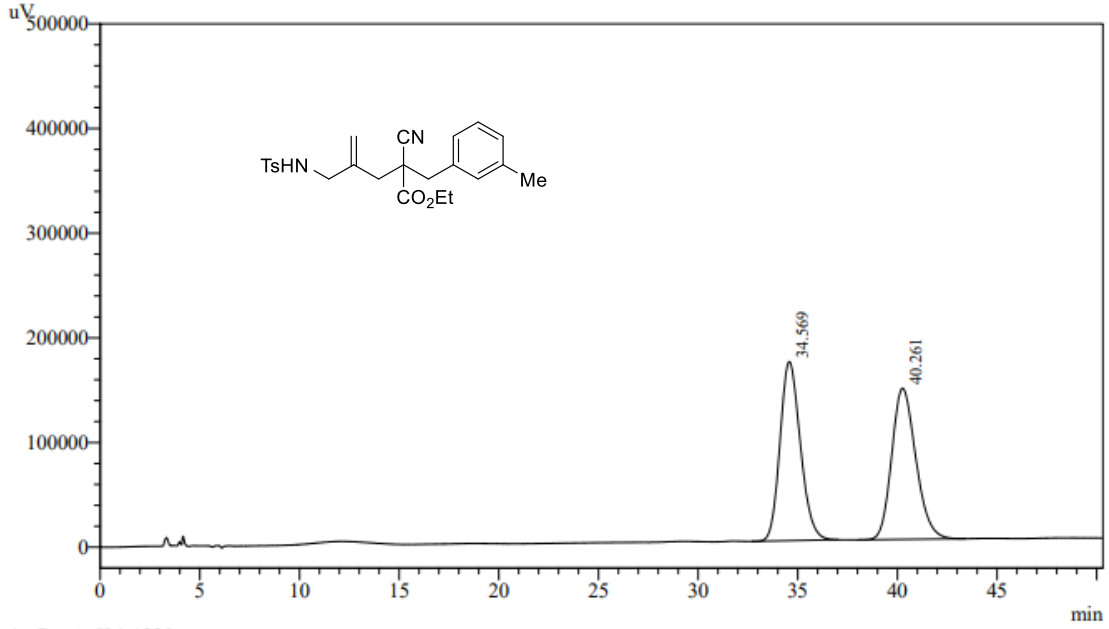
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	32.935	8472304	127283	95.843	95.959
2	36.432	367426	5360	4.157	4.041
Total		8839730	132643	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3n



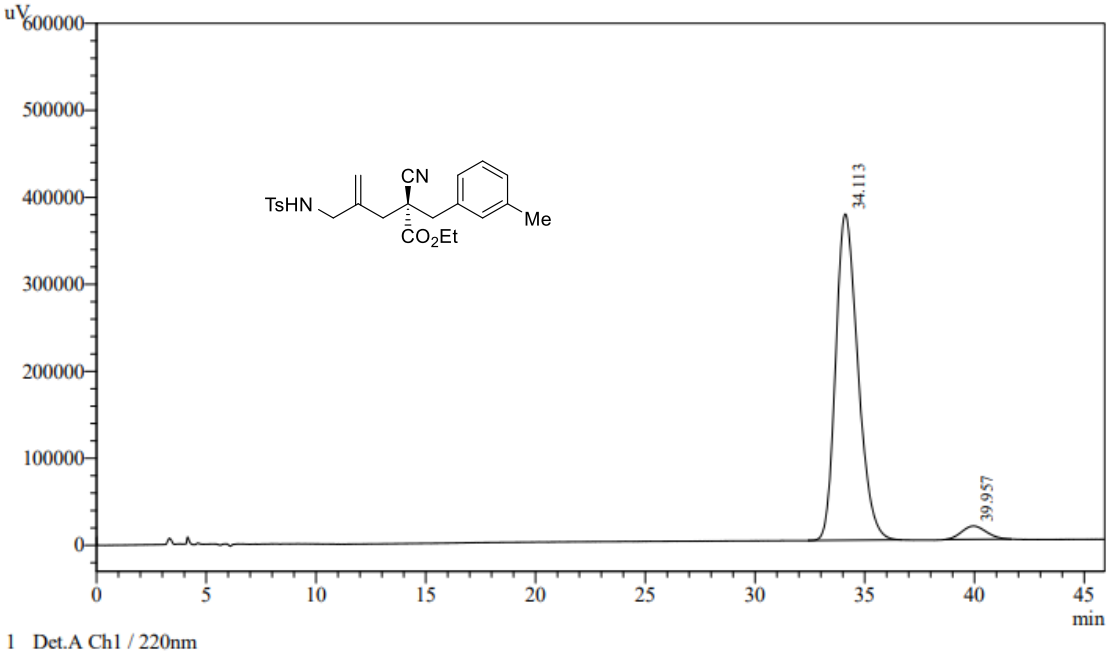
HPLC spectra of 3n



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.569	12162241	171079	49.948	54.227
2	40.261	12187729	144409	50.052	45.773
Total		24349971	315488	100.000	100.000

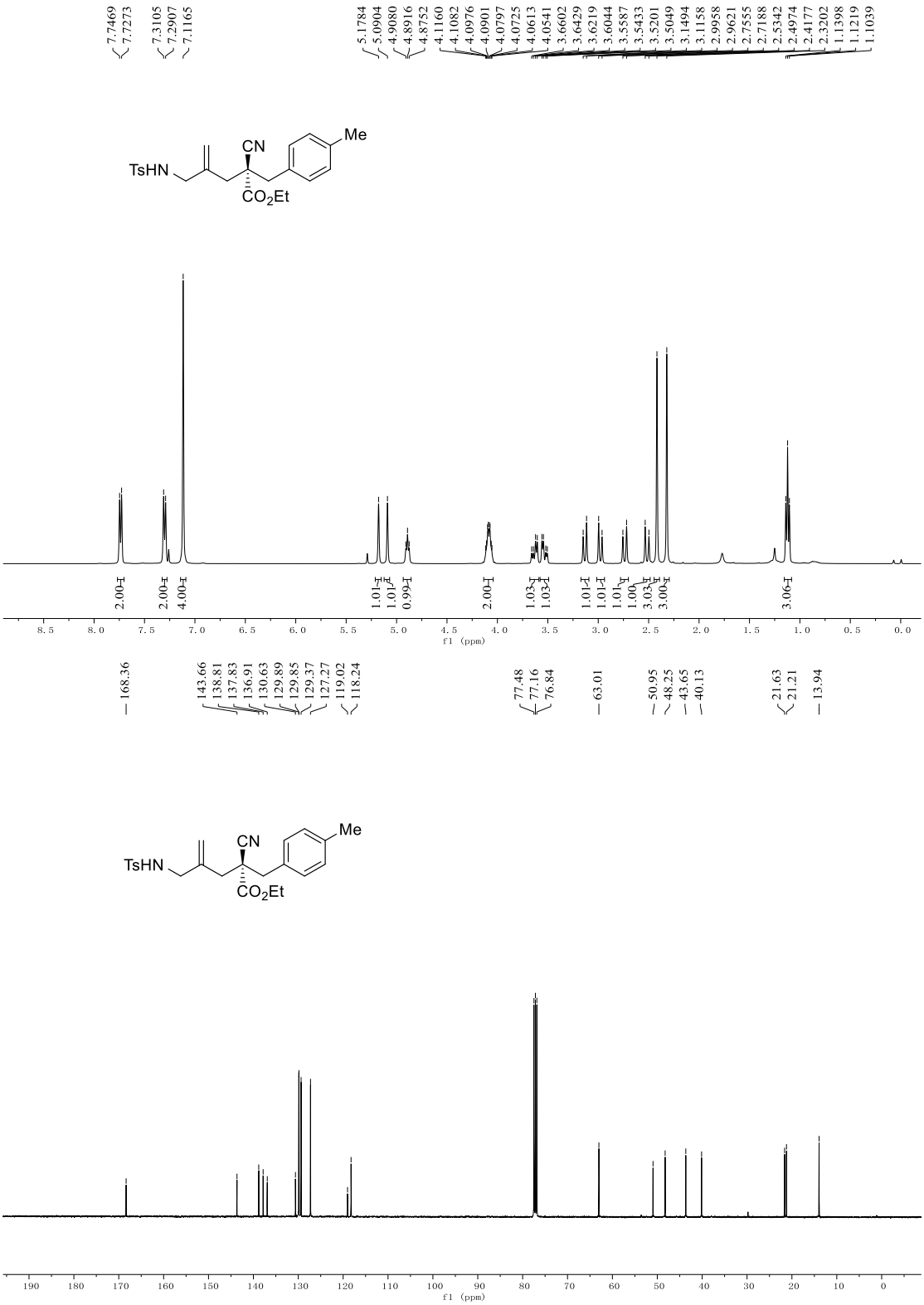


1 Det.A Ch1 / 220nm

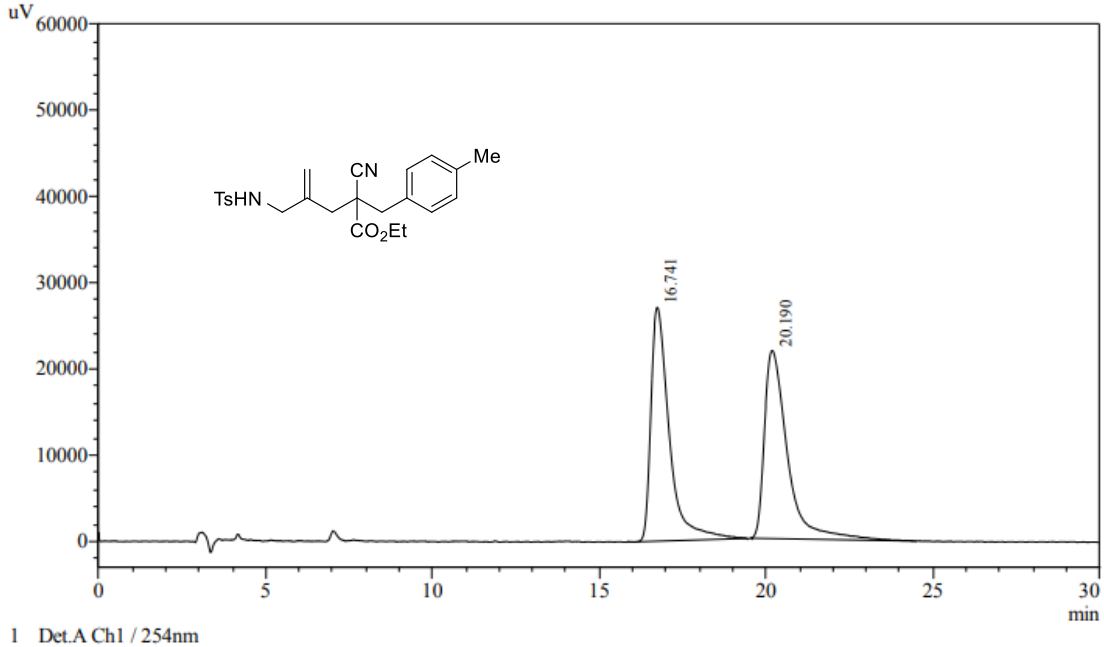
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	34.113	26363635	375058	95.711	96.096
2	39.957	1181375	15236	4.289	3.904
Total		27545010	390294	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3o



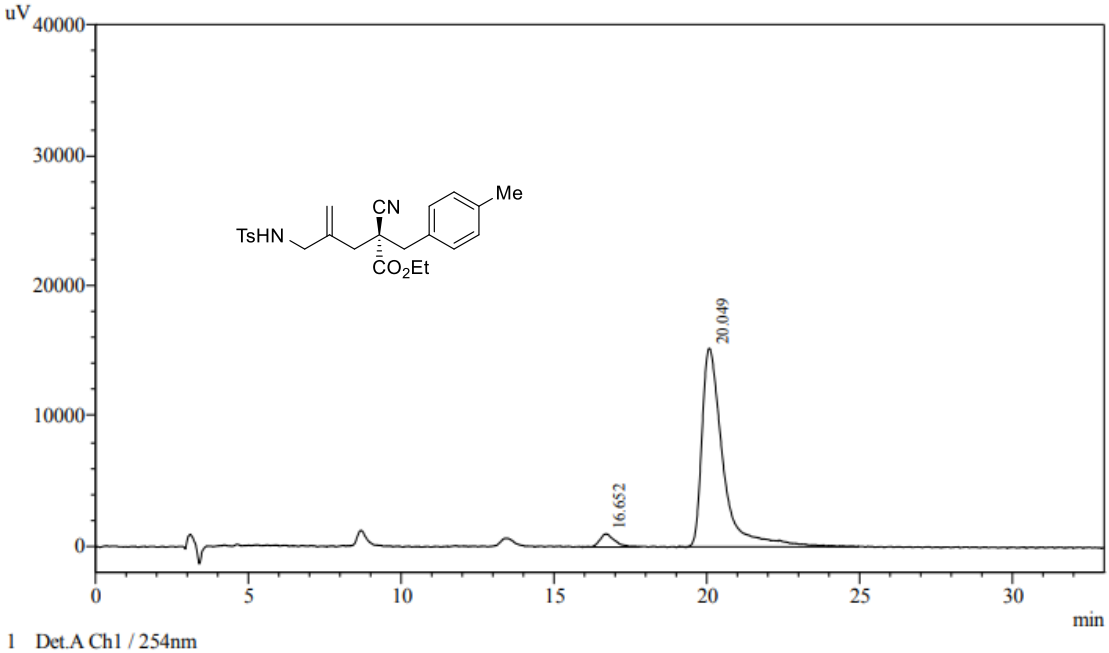
HPLC spectra of 3o



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.741	1045289	27108	49.844	55.420
2	20.190	1051847	21806	50.156	44.580
Total		2097136	48914	100.000	100.000

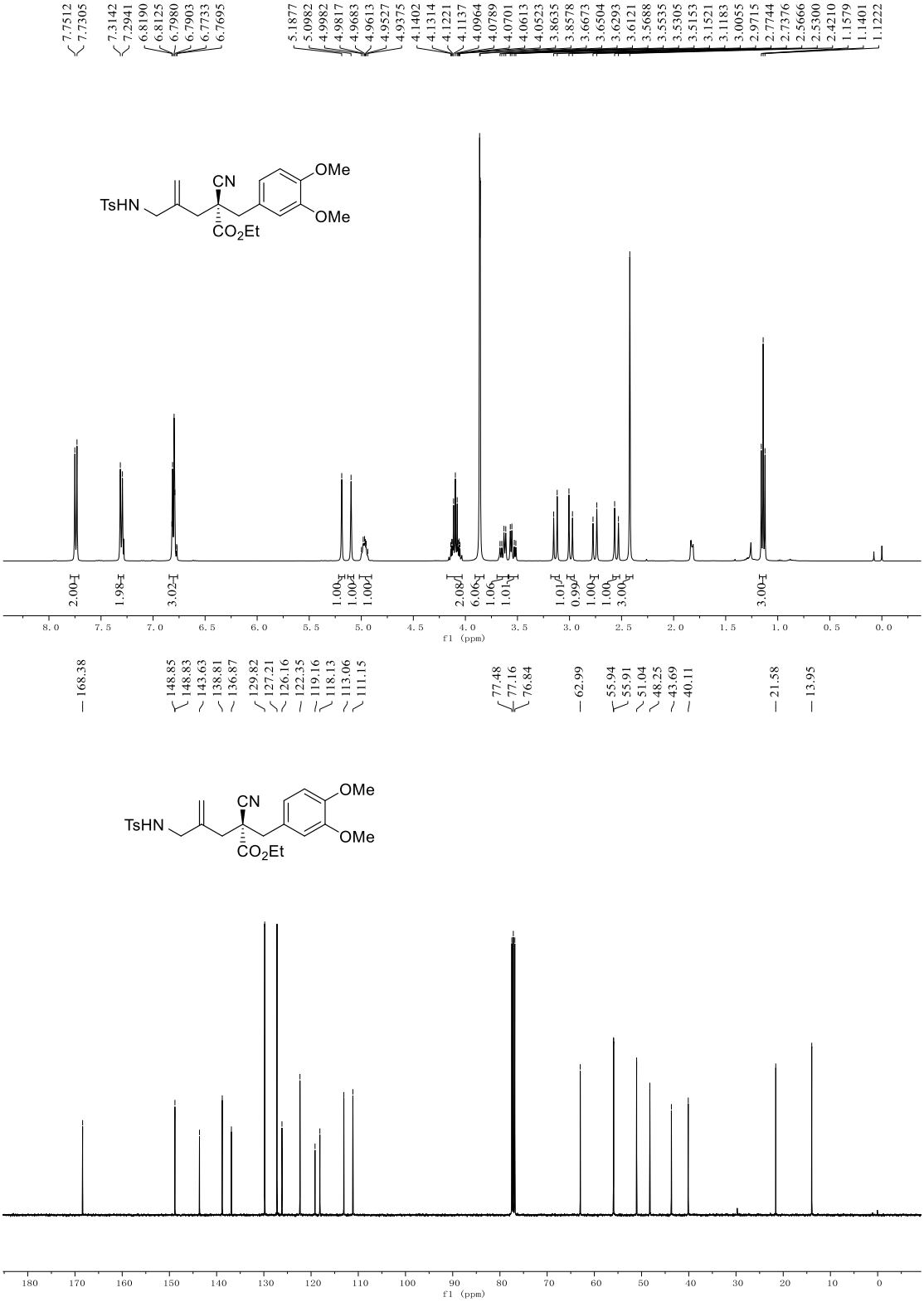


1 Det.A Ch1 / 254nm

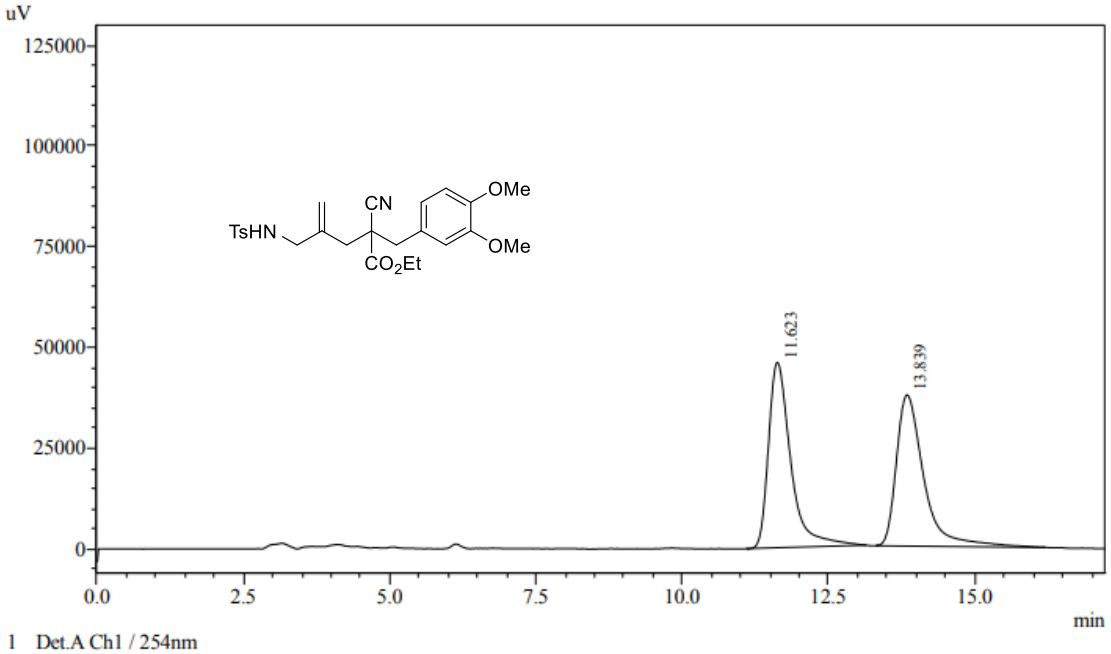
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.652	34692	1012	4.527	6.232
2	20.049	731572	15224	95.473	93.768
Total		766264	16236	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3p



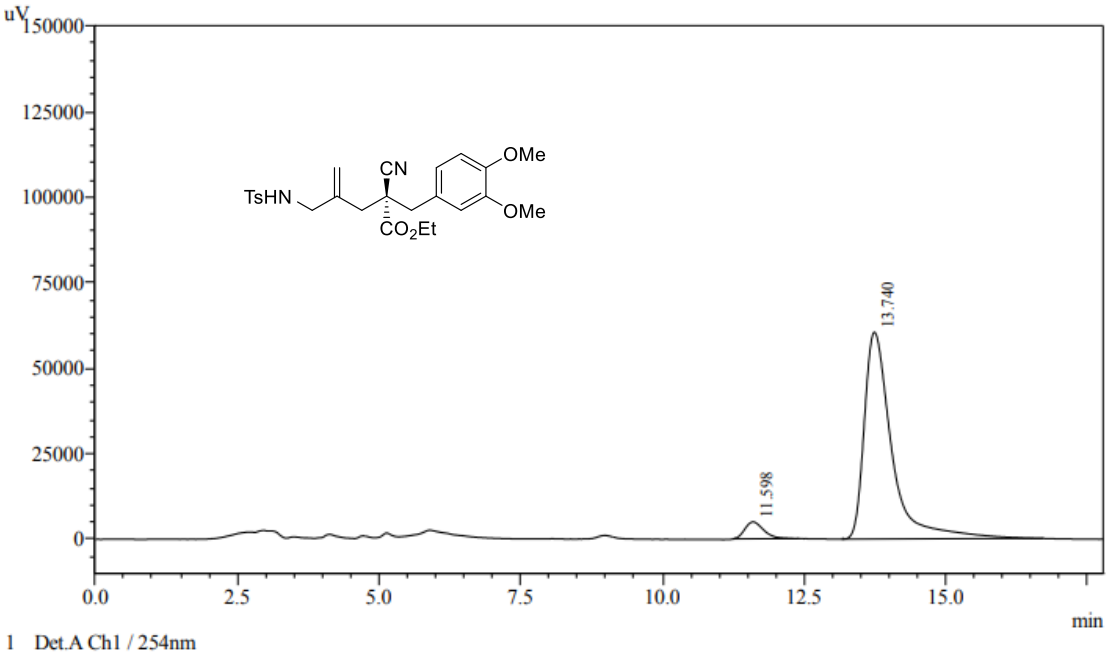
HPLC spectra of 3p



1 Det.A Ch1 / 254nm

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.623	1221089	46049	49.863	55.066
2	13.839	1227813	37577	50.137	44.934
Total		2448902	83627	100.000	100.000

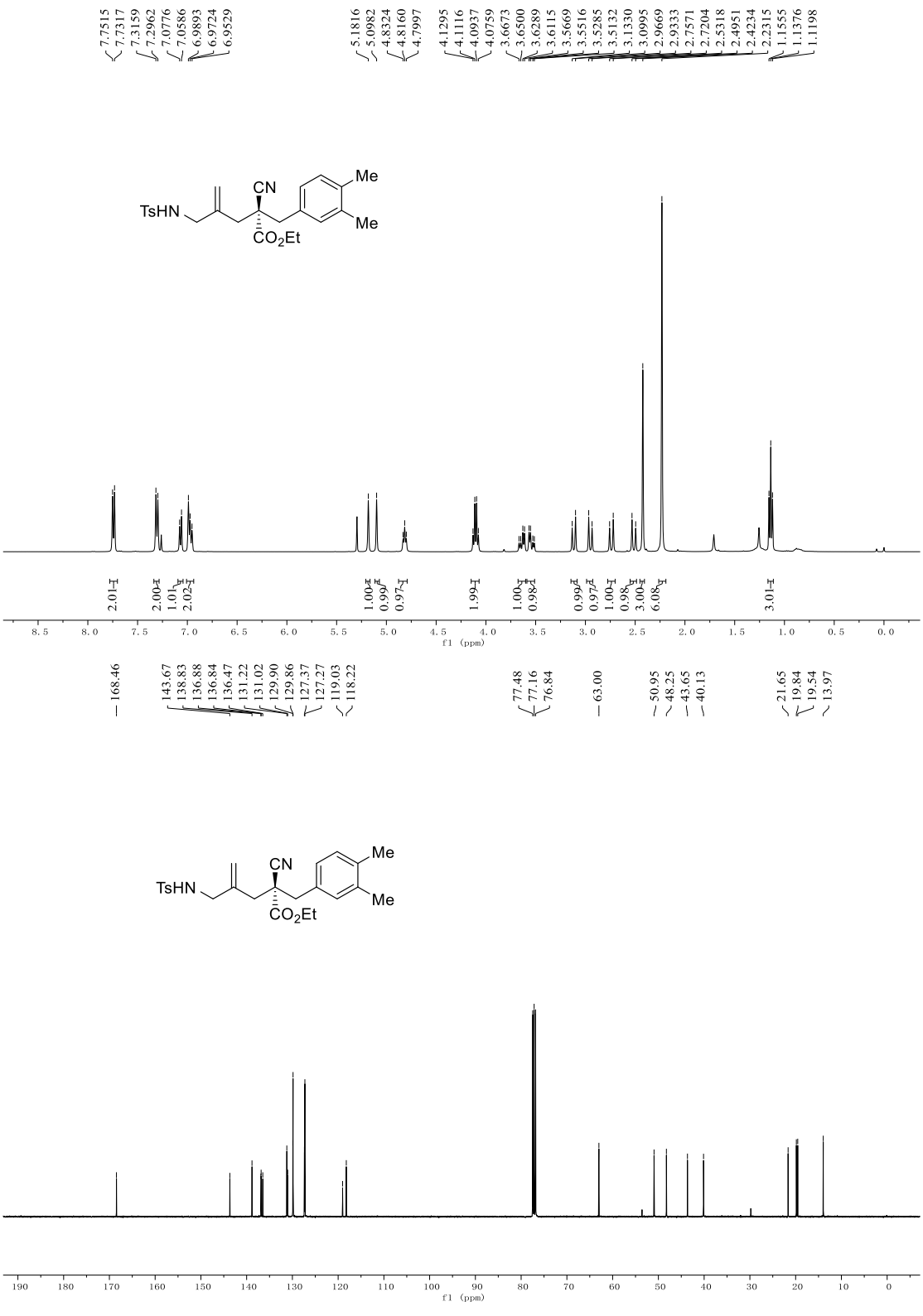


1 Det.A Ch1 / 254nm

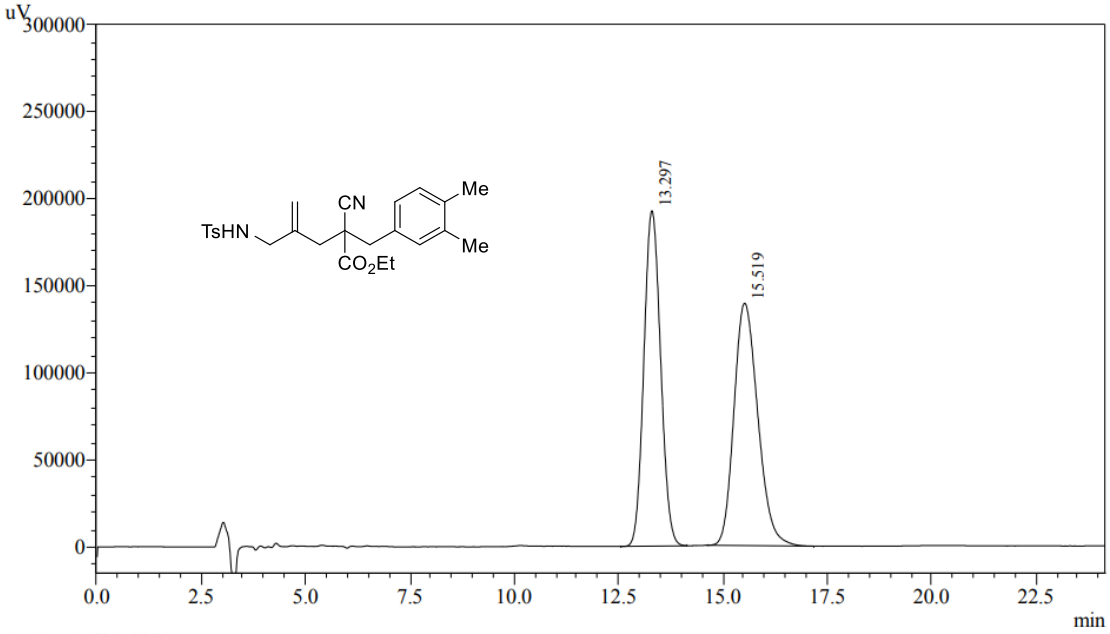
Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.598	115301	4984	5.314	7.617
2	13.740	2054549	60443	94.686	92.383
Total		2169850	65427	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3q


7.7515
7.7317
7.3159
7.2962
7.0776
7.0586
6.9893
6.9724
6.9529
5.1816
5.0982
4.8324
4.8160
4.7997
4.1295
4.1116
4.0937
4.0759
3.6673
3.6500
3.6289
3.6115
3.5669
3.5516
3.5285
3.5132
3.1330
3.0995
2.9669
2.9333
2.7571
2.7204
2.5318
2.4951
2.4234
2.2315
1.1555
1.1376
1.1198
TsHN
CN
CO2Et
Me
Me
2.01
2.00
1.01
2.02
1.00
0.99
0.97
1.99
1.00
0.98
0.99
0.97
1.00
0.98
3.00
6.08
3.01
f1 (ppm)
168.46
143.67
138.83
136.88
136.84
136.47
131.22
131.02
129.90
129.86
127.37
127.27
119.03
118.22
77.48
77.16
76.84
63.00
50.95
48.25
43.65
40.13
21.65
19.84
19.54
13.97
f1 (ppm)

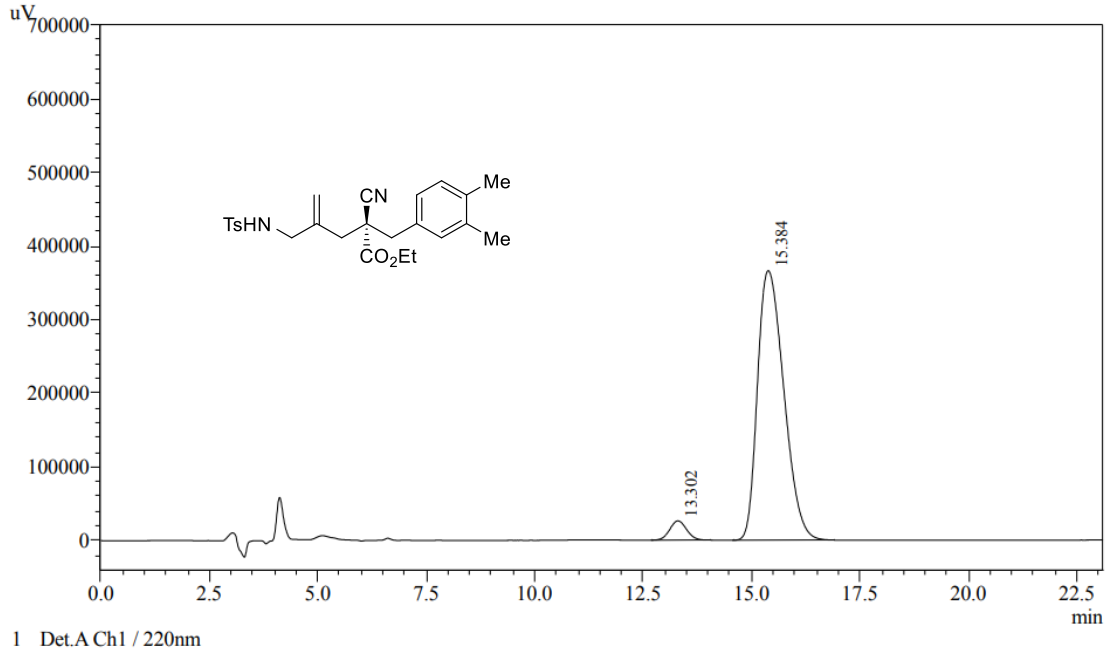
HPLC spectra of 3q



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.297	5377928	192660	49.243	58.038
2	15.519	5543201	139295	50.757	41.962
Total		10921129	331955	100.000	100.000

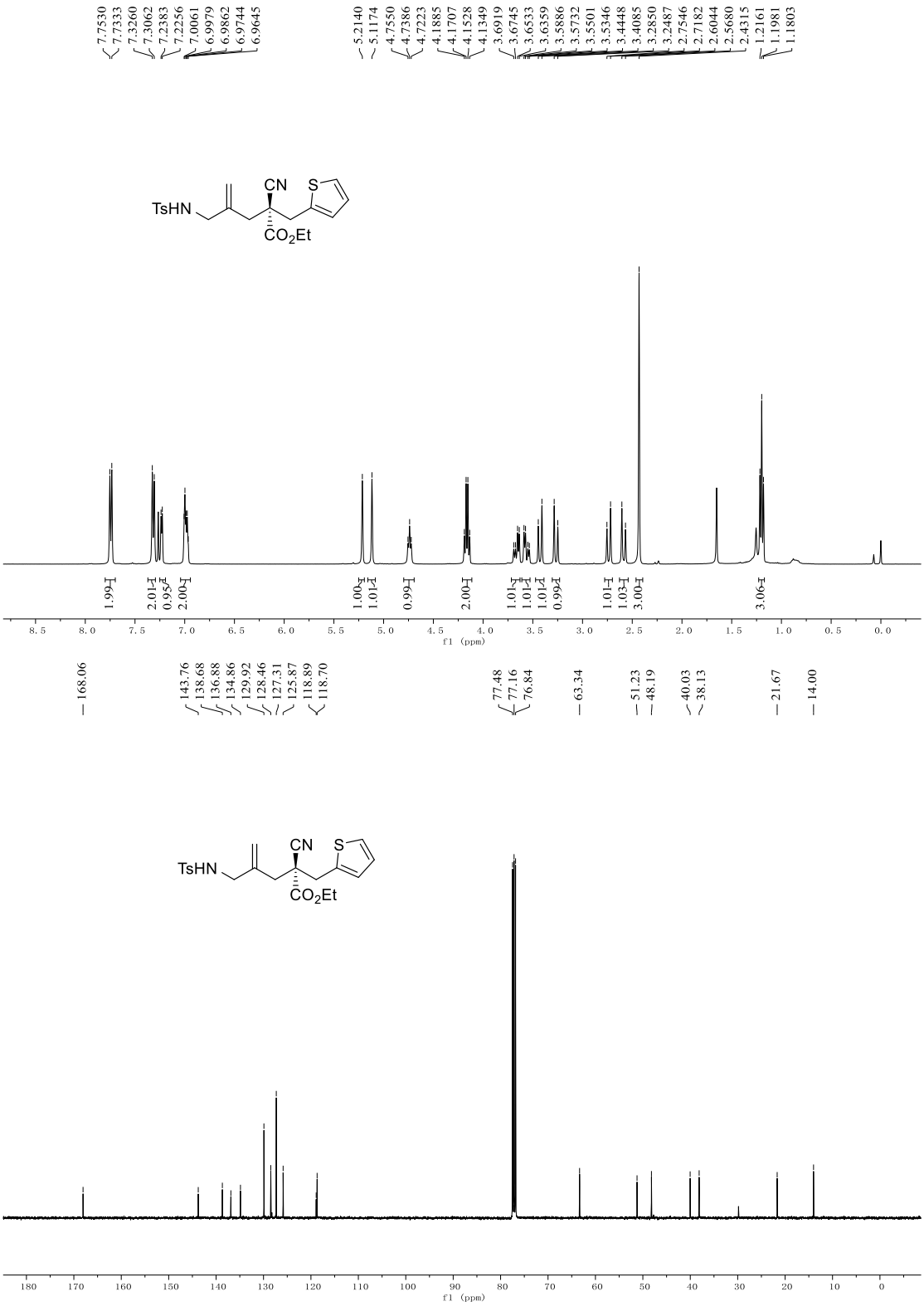


1 Det.A Ch1 / 220nm

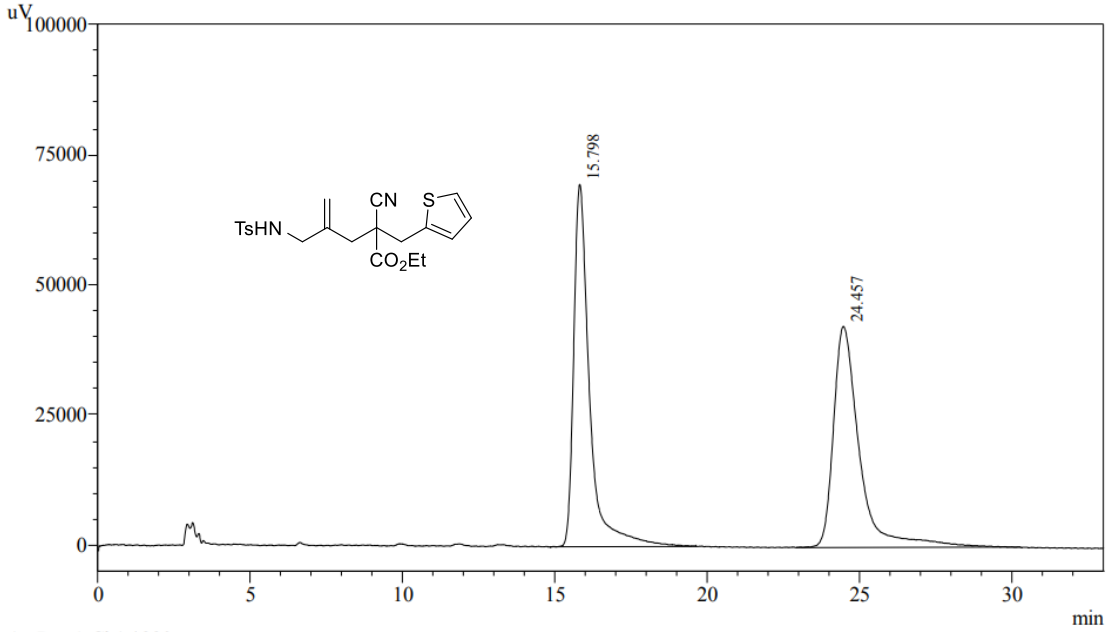
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.302	702035	26066	4.337	6.650
2	15.384	15486907	365925	95.663	93.350
Total		16188942	391991	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3r


7.7530
7.7333
7.3260
7.3062
7.2383
7.2256
7.0061
6.9979
6.9862
6.9744
6.9645
5.2140
5.1174
4.7550
4.7386
4.7223
4.1885
4.1707
4.1528
4.1349
3.6919
3.6745
3.6533
3.6359
3.5886
3.5732
3.5501
3.5346
3.4448
3.4085
3.2850
3.2487
2.7546
2.7182
2.6044
2.5680
2.4315
1.2161
1.1981
1.1803
CN
S
TsHN
CO2Et
1.99
2.01
0.95
2.00
1.00
1.01
0.99
2.00
1.01
1.01
1.01
0.99
1.01
1.03
3.00
3.06
f1 (ppm)
168.06
143.76
138.68
136.88
134.86
129.92
128.46
127.31
125.87
118.89
118.70
77.48
77.16
76.84
63.34
51.23
48.19
40.03
38.13
21.67
14.00
CN
S
TsHN
CO2Et
f1 (ppm)

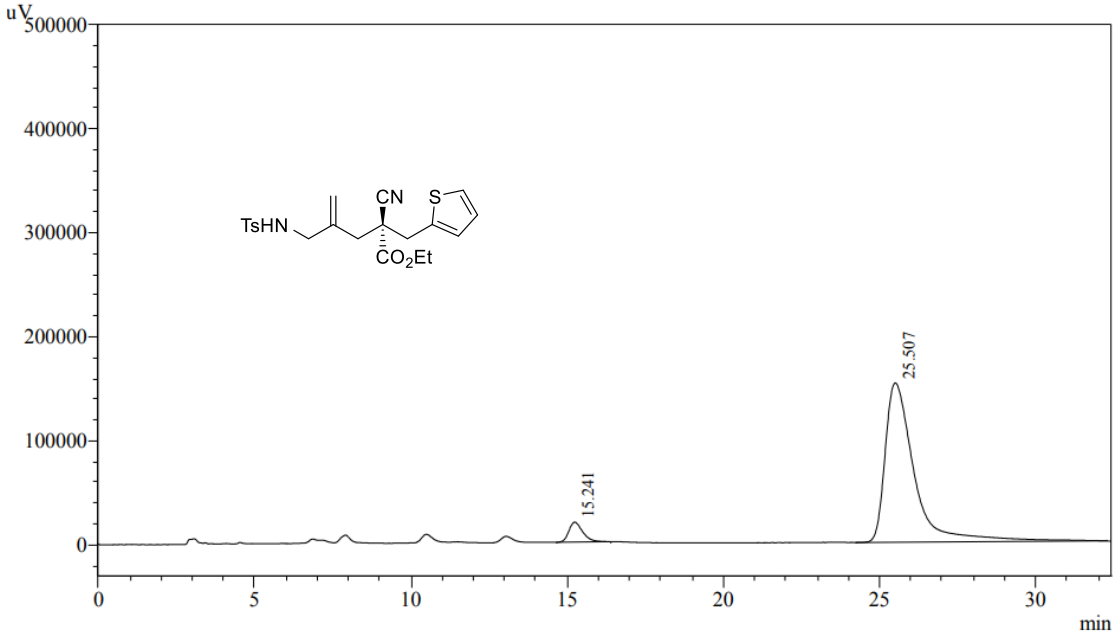
HPLC spectra of 3r



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.798	2525576	69600	49.993	62.110
2	24.457	2526305	42459	50.007	37.890
Total		5051881	112060	100.000	100.000



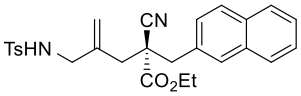
1 Det.A Ch1 / 220nm

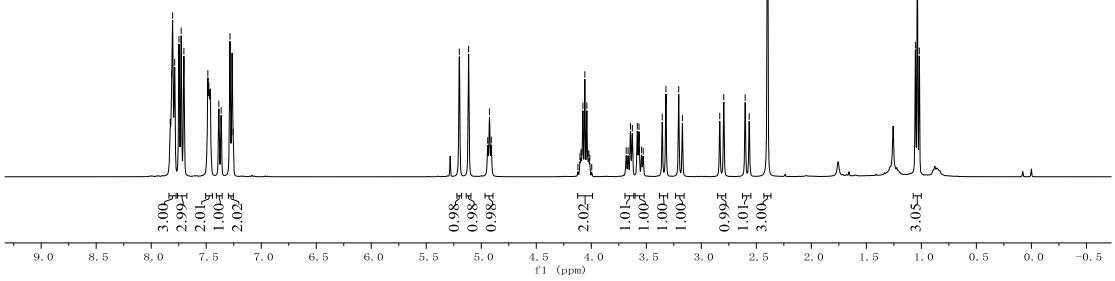
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.241	587678	19109	5.559	11.092
2	25.507	9984005	153166	94.441	88.908
Total		10571683	172275	100.000	100.000

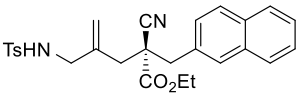
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3s

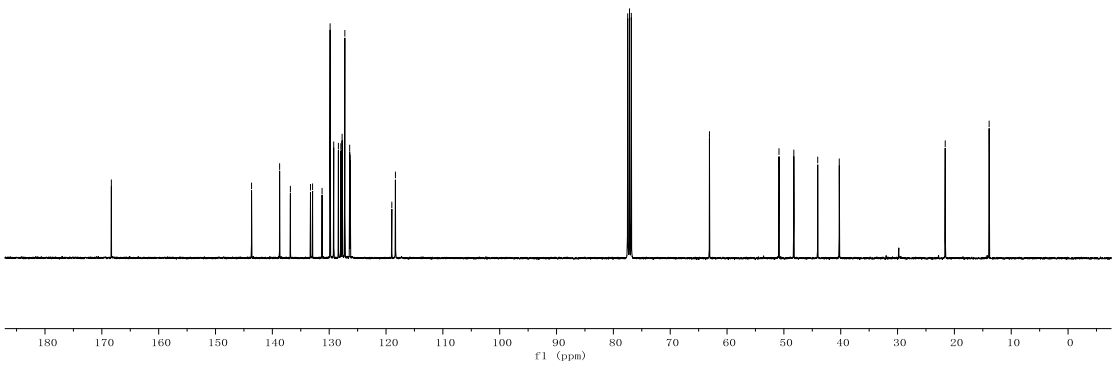

7.8272
7.8138
7.8052
7.7865
7.7474
7.7277
7.7031
7.4852
7.4765
7.4688
7.4614
7.3853
7.3643
7.2841
7.2545
5.1994
5.1150
4.9415
4.9252
4.9091
4.1215
4.1032
4.0941
4.0860
4.0764
4.0586
4.0407
4.0304
4.0226
4.0135
3.9959
3.6827
3.6654
3.6443
3.6270
3.5817
3.5664
3.5433
3.5279
3.3552
3.3217
3.2057
3.1721
2.8325
2.7959
2.6016
2.5647
2.3983
1.0544
1.0366
1.0187


CN
TsHN
CO2Et

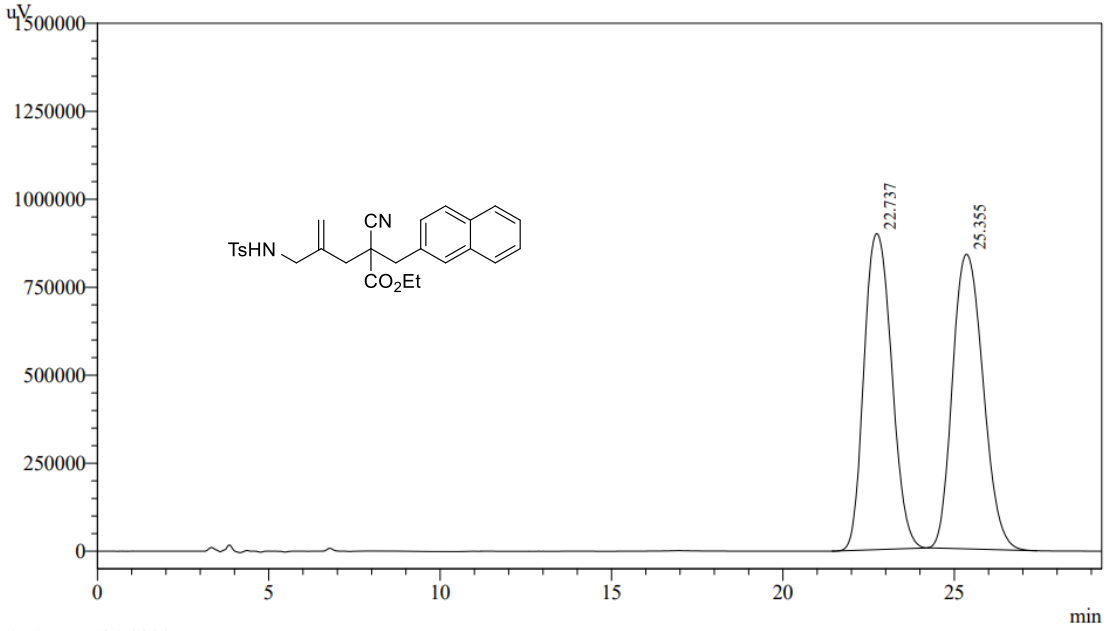

3.00
2.99
2.01
1.00
2.02
0.98
0.98
0.98
2.02
1.01
1.00
1.00
1.00
0.99
1.01
3.00
3.05
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


168.33
143.66
138.72
136.82
133.29
132.92
131.25
129.84
129.20
128.38
127.95
127.73
127.70
127.24
126.39
126.30
118.98
118.35
77.48
77.16
76.84
63.10
50.86
48.25
44.04
40.25
21.61
13.89


CN
TsHN
CO2Et


180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

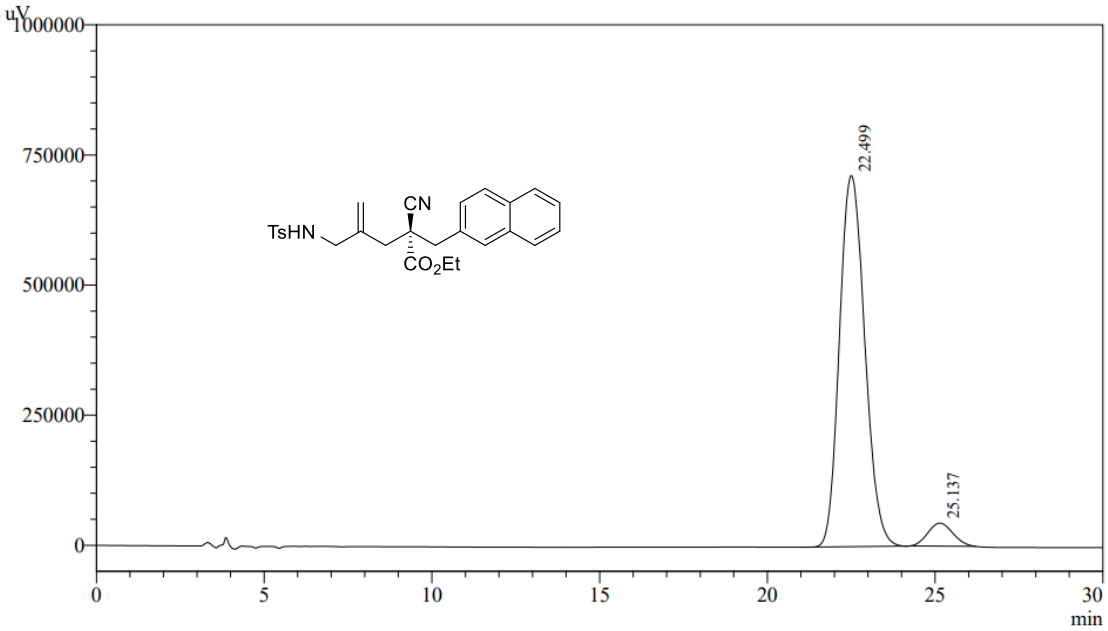
HPLC spectra of 3s



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.737	50448071	897963	49.208	51.747
2	25.355	52071016	837328	50.792	48.253
Total		102519087	1735291	100.000	100.000

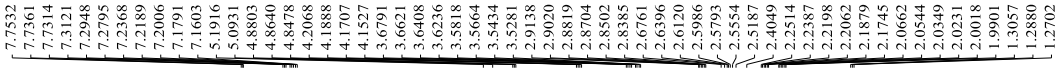


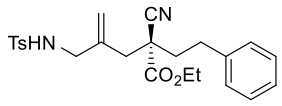
1 Det.A Ch1 / 220nm

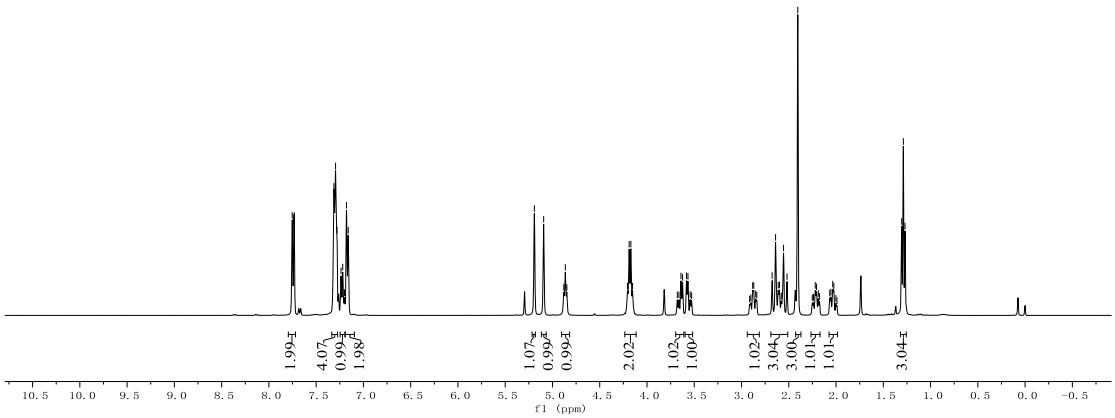
Detector A Ch1 220nm

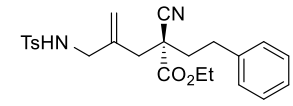
Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.499	37429411	713036	94.243	94.177
2	25.137	2286579	44089	5.757	5.823
Total		39715990	757125	100.000	100.000

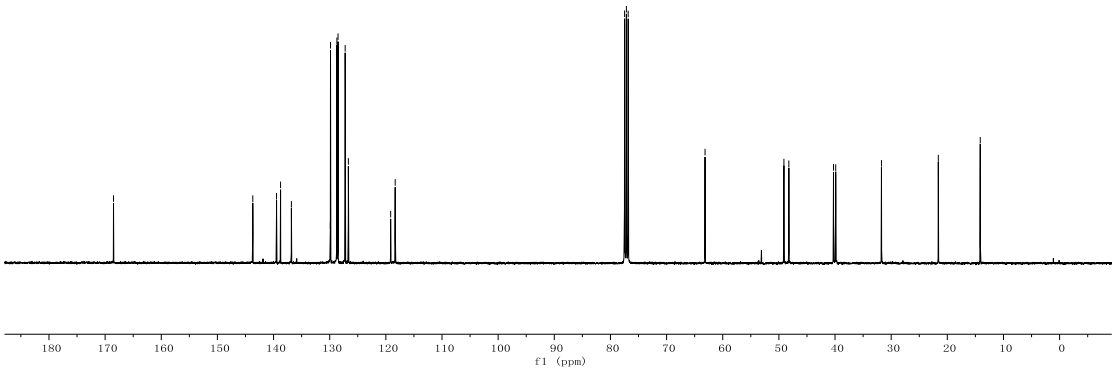
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3t



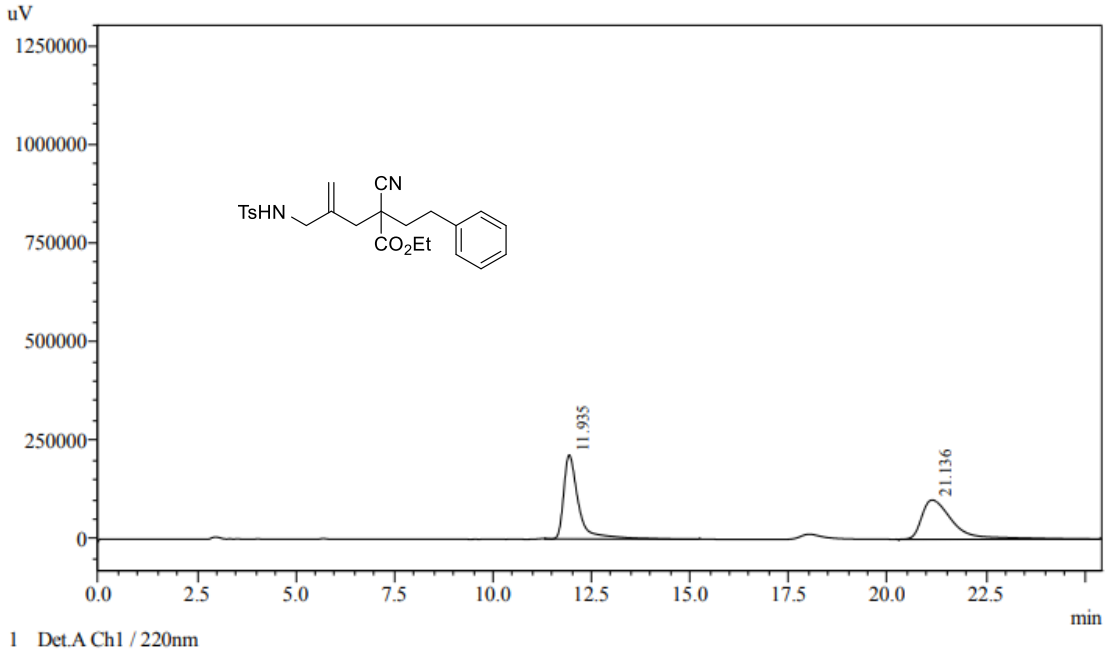








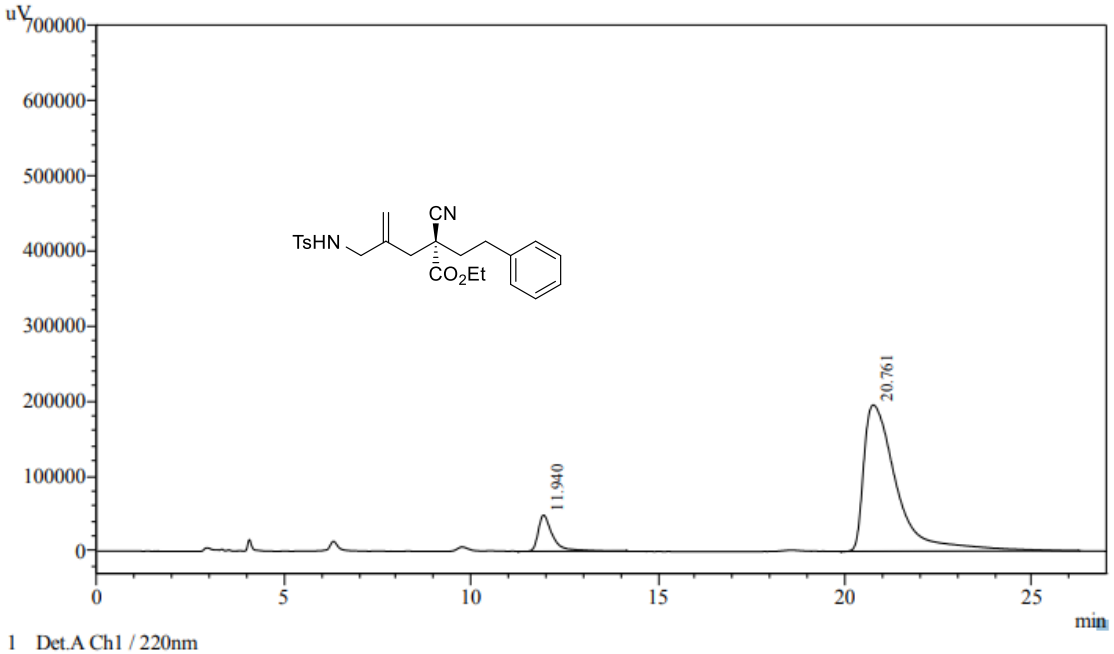
HPLC spectra of 3t



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.935	5529647	212237	50.363	68.091
2	21.136	5449963	99461	49.637	31.909
Total		10979610	311698	100.000	100.000

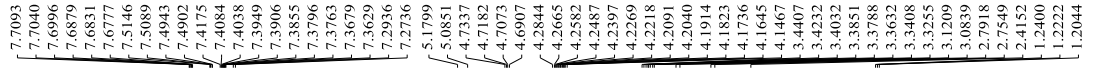


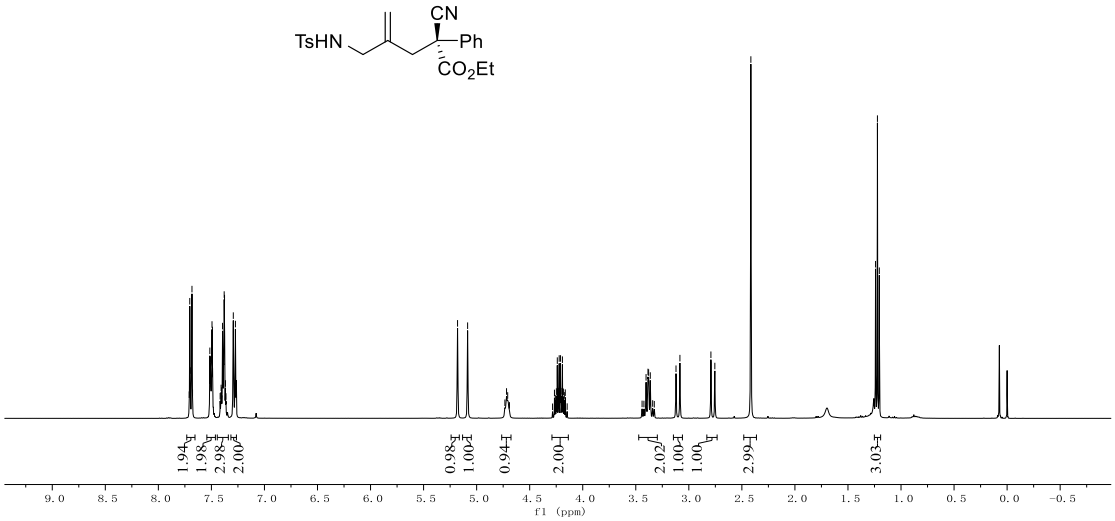
1 Det.A Ch1 / 220nm

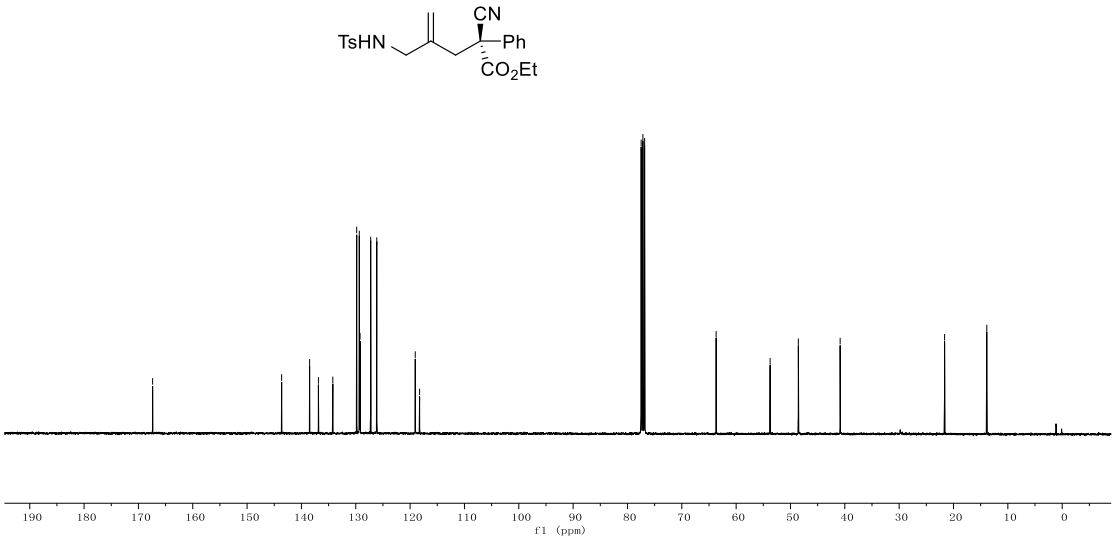
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.940	1283714	48054	9.653	19.758
2	20.761	12015199	195164	90.347	80.242
Total		13298914	243218	100.000	100.000

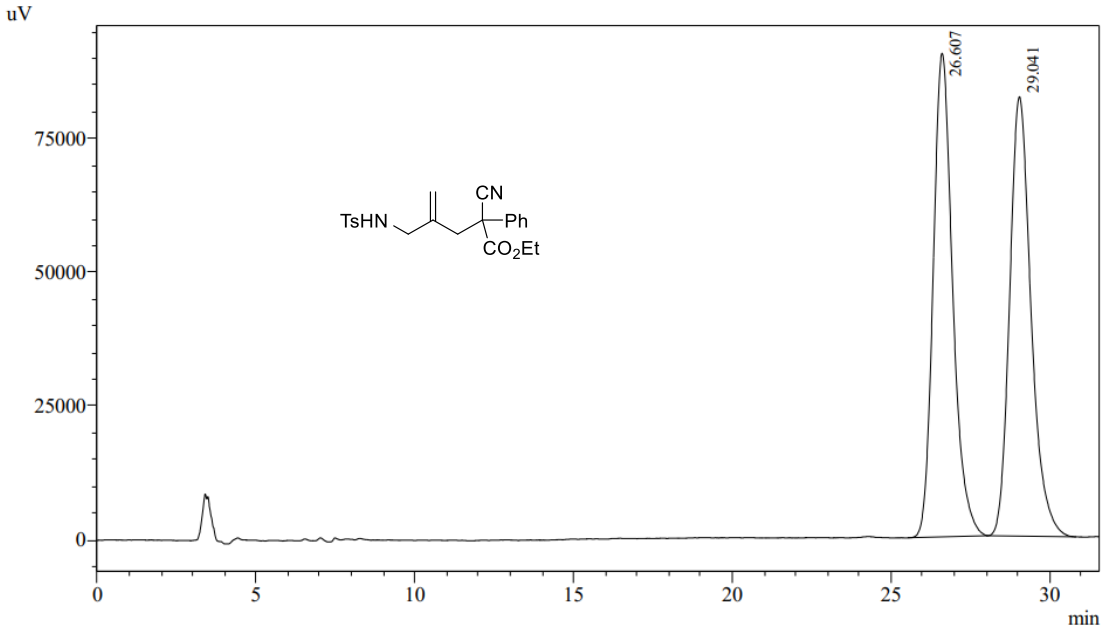
^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 3u







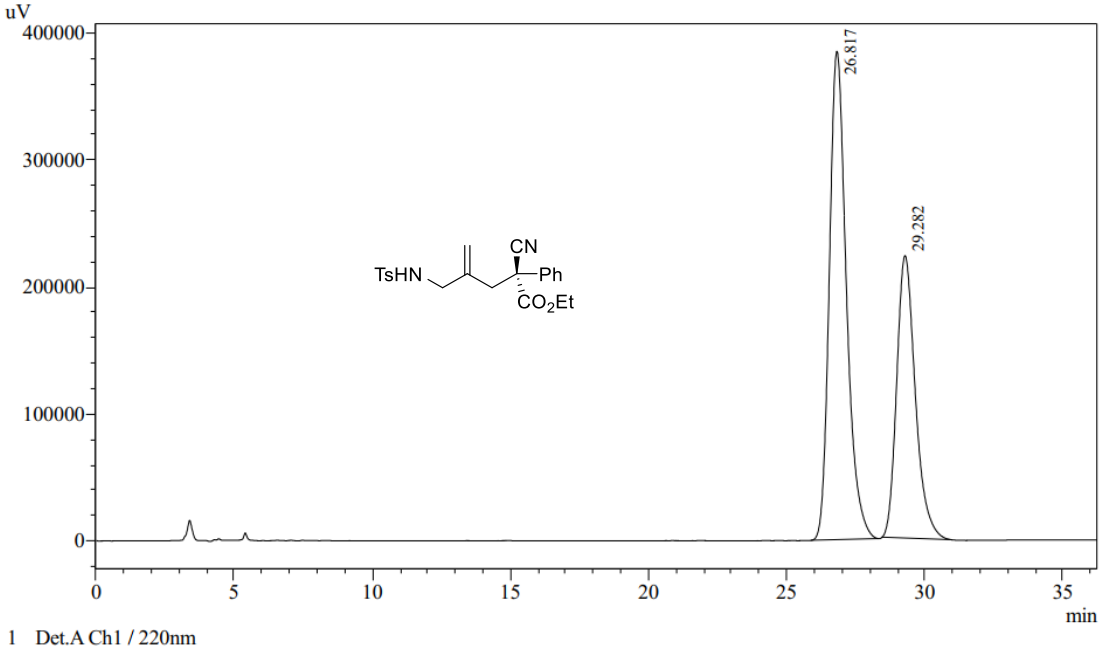
HPLC spectra of 3u



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.607	3850711	90380	50.007	52.398
2	29.041	3849609	82107	49.993	47.602
Total		7700320	172487	100.000	100.000

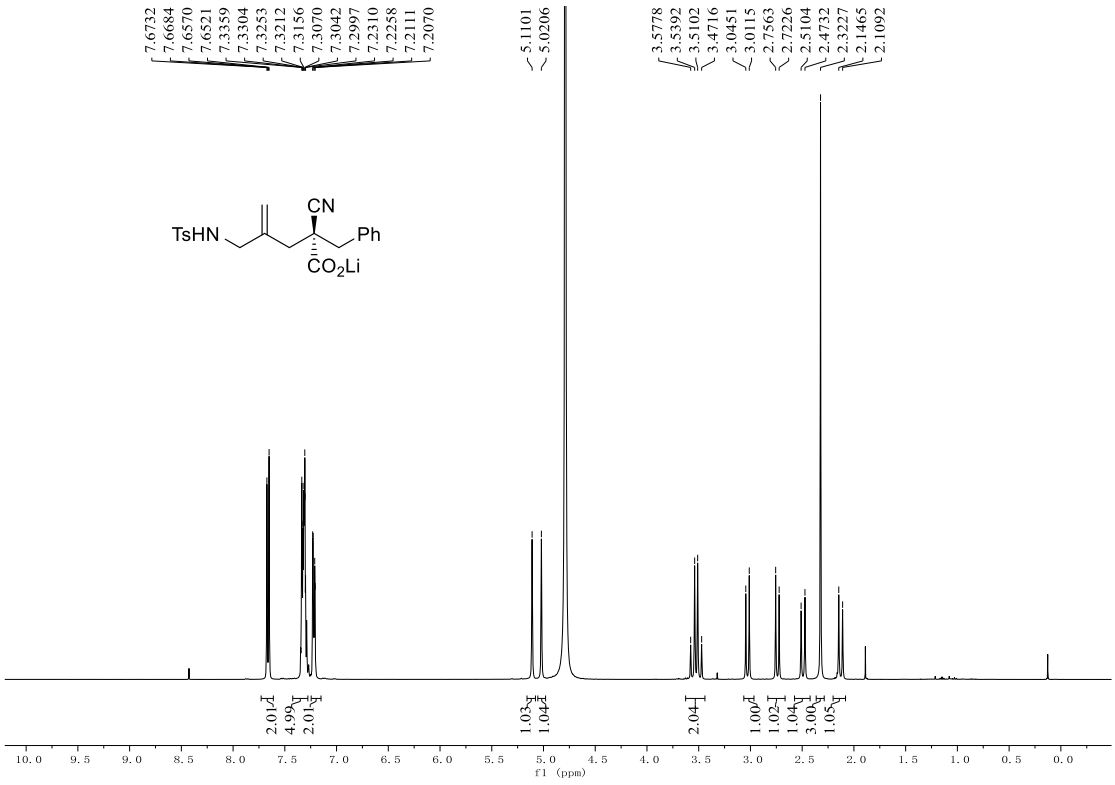


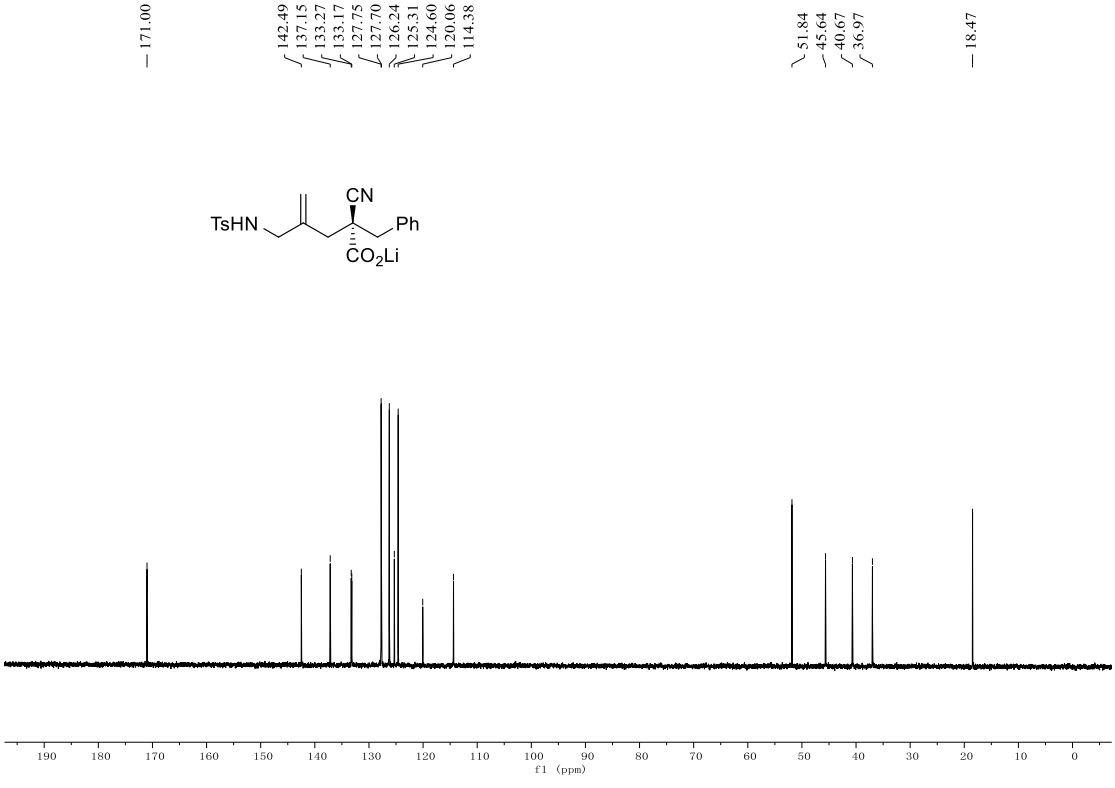
1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

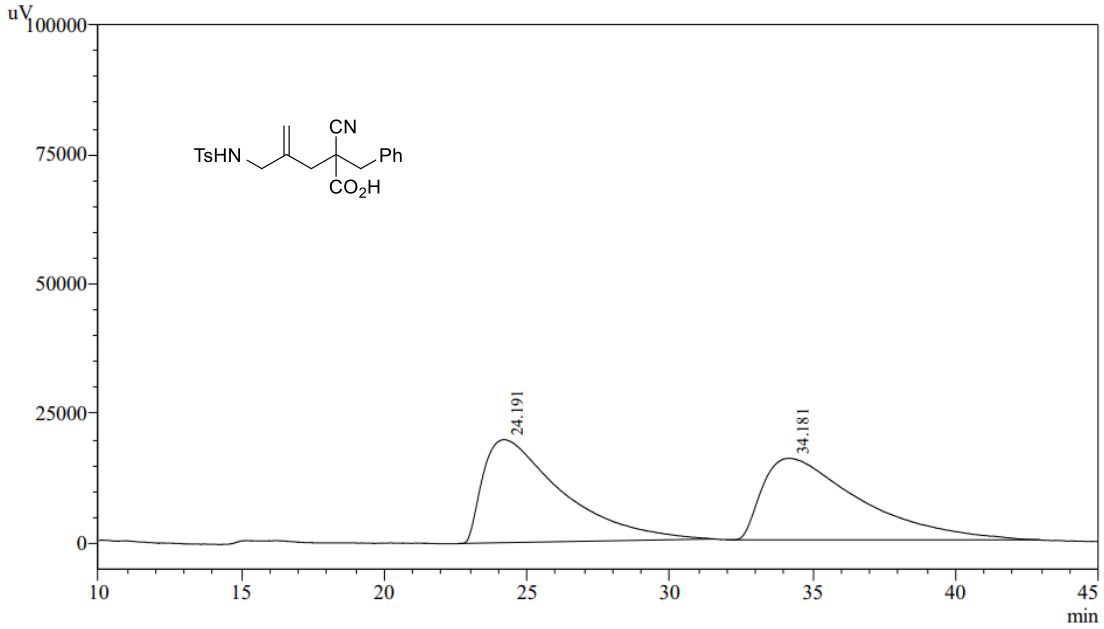
Peak#	Ret. Time	Area	Height	Area %	Height %
1	26.817	16525680	384628	61.369	63.364
2	29.282	10402732	222381	38.631	36.636
Total		26928412	607009	100.000	100.000

^{1}H NMR (400 MHz, D_2O) and ^{13}C NMR (101 MHz, D_2O) of 5





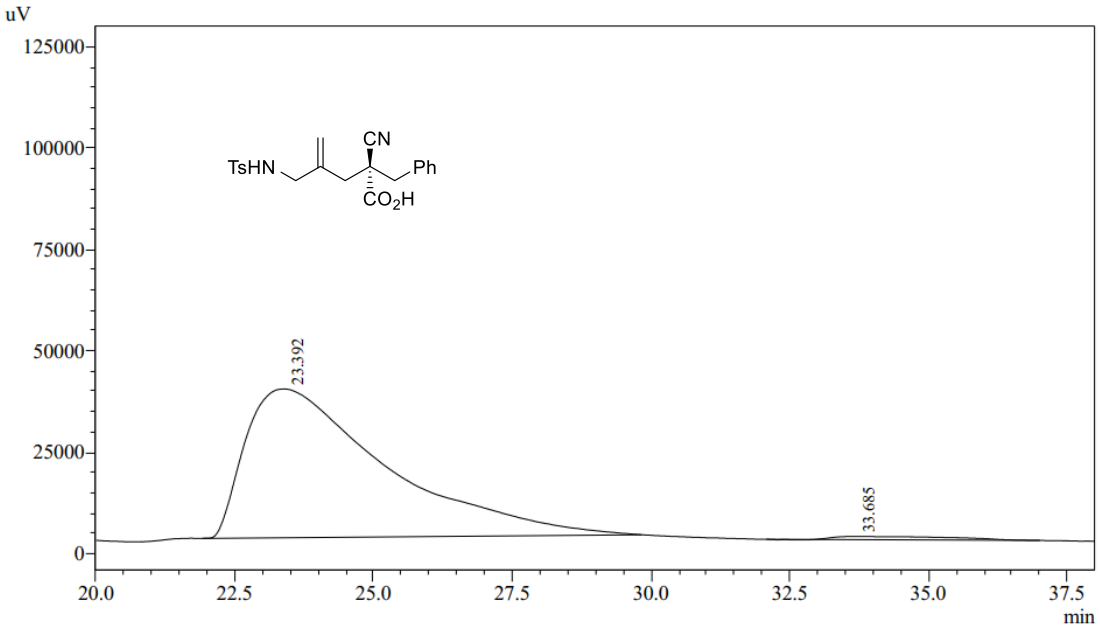
HPLC spectra of 5



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	24.191	3837259	19910	50.660	55.895
2	34.181	3737205	15711	49.340	44.105
Total		7574463	35621	100.000	100.000

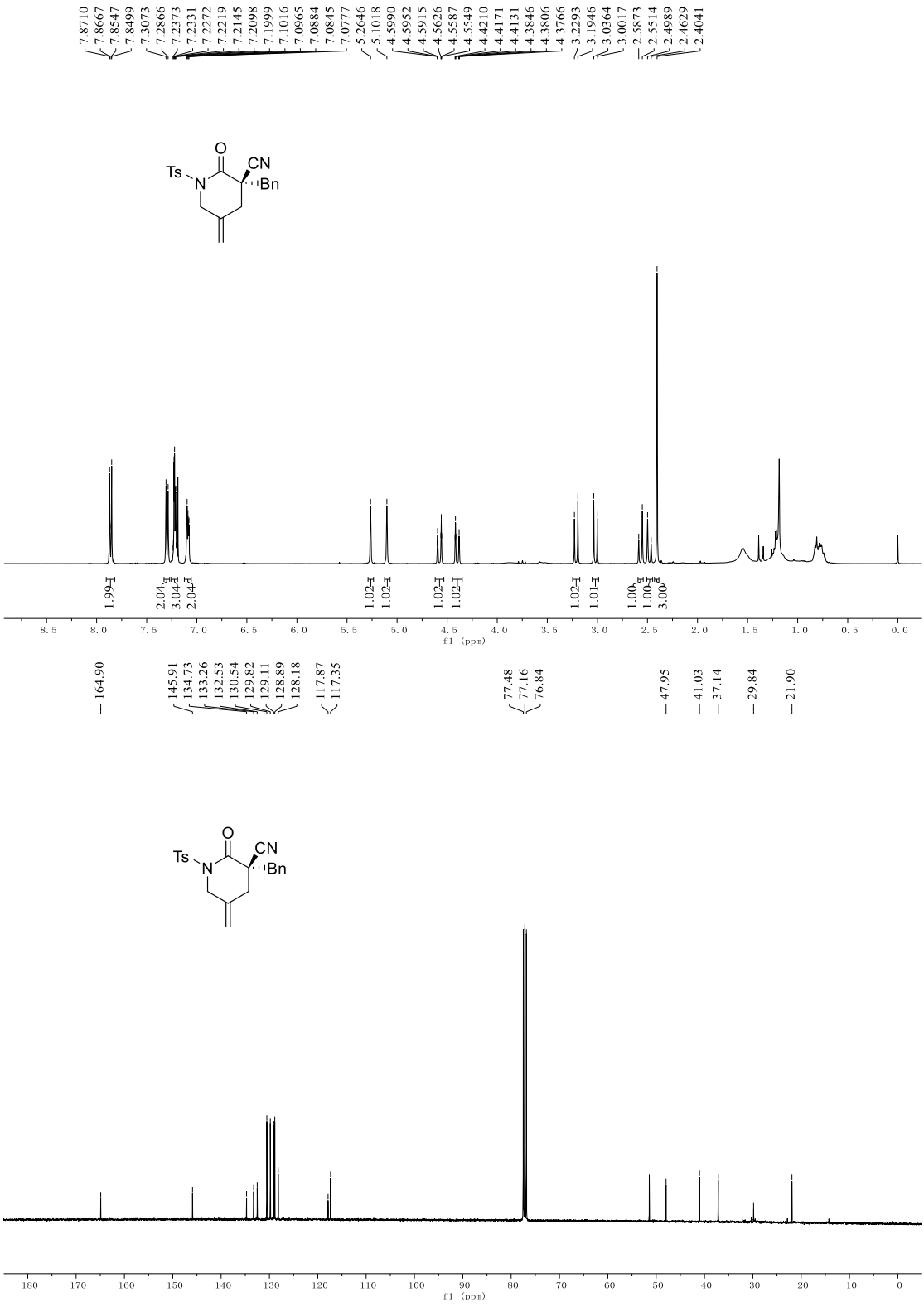


1 Det.A Ch1 / 220nm

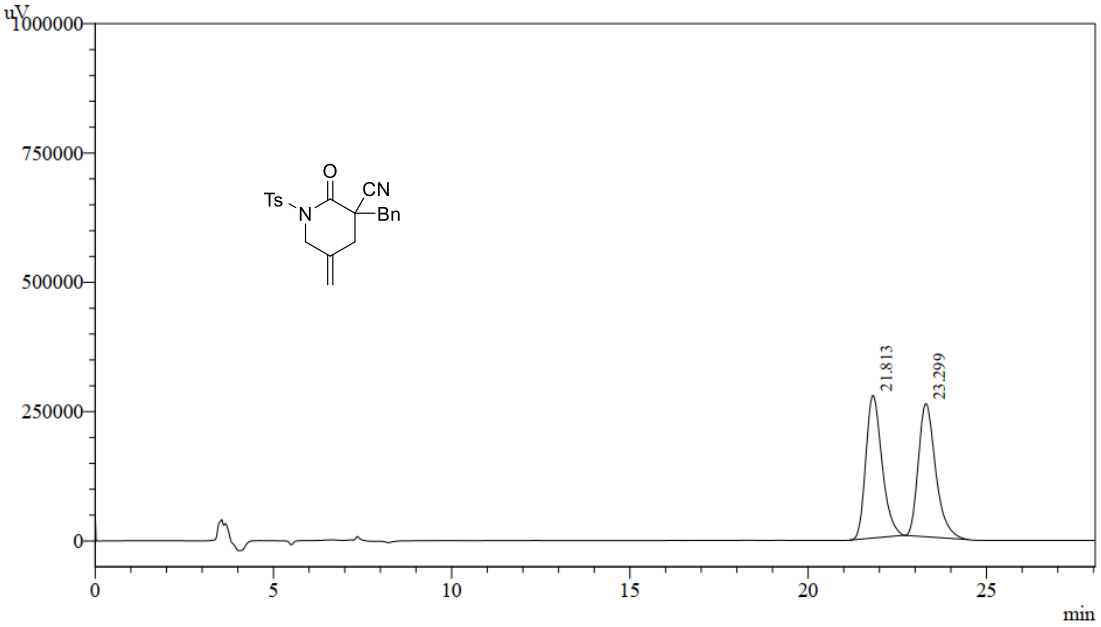
Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	23.392	6442667	36662	98.174	97.824
2	33.685	119800	816	1.826	2.176
Total		6562467	37477	100.000	100.000

^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (101 MHz, $CDCl_3$) of 6



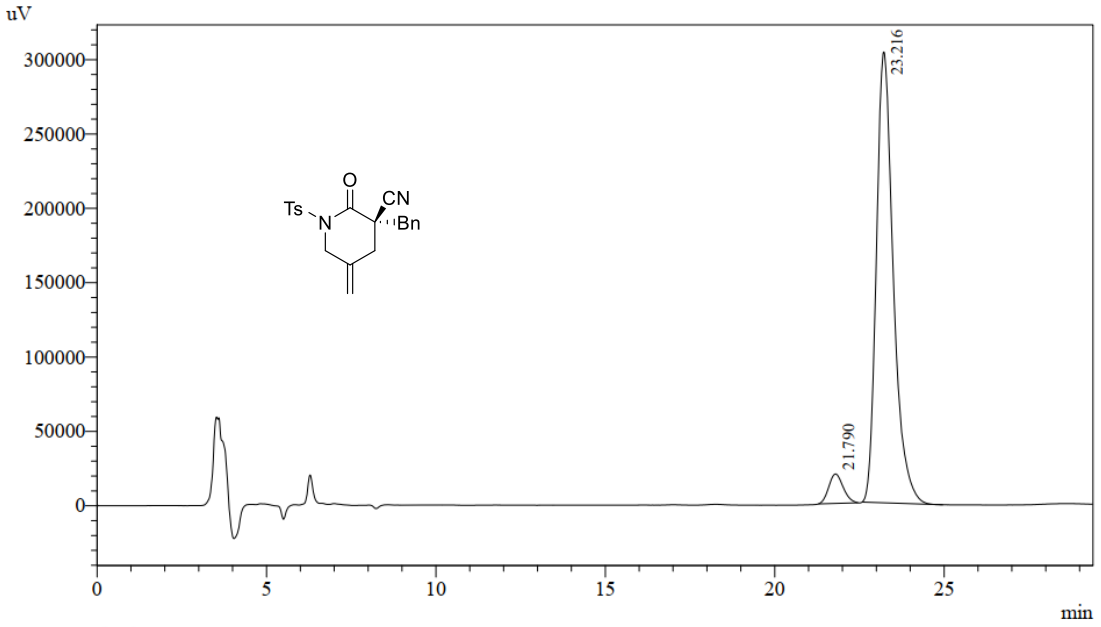
HPLC spectra of 6



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.813	8706508	275862	49.996	51.730
2	23.299	8707851	257407	50.004	48.270
Total		17414359	533269	100.000	100.000



1 Det.A Ch1 / 220nm

Detector A Ch1 220nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	21.790	583646	19785	5.246	6.127
2	23.216	10541408	303154	94.754	93.873
Total		11125054	322939	100.000	100.000