Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Bisguanidinium-Catalysed Formation of Oxygen-Containing Quaternary Stereogenic Carbon Centres

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Supporting Information

Contents

1. General information

THF were distilled over sodium/benzophenone under N_2 atmosphere. Toluene, Acetonitrile and Dichloromethane were distilled over CaH_2 under N_2 atmosphere. Commercially available materials and other solvents purchased from commercial suppliers were used as received. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV-300 (300 MHz), Bruker Avance III 400 (400MHz) (100 MHz) and JEOL ECA400 NMR spectrometer. Chemical shifts are recorded as δ in units of parts per million (ppm). High resolution mass spectra (HRMS) were obtained on the Q-Tof Premier mass spectrometer (Waters Corporation). HRMS were reported in units of mass of charge ratio (***m/z***). Enantiomeric excess values were determined by HPLC analysis on Shimadzu LC-20AT and LC-2010CHT HPLC workstations. Optical rotations were measured in $CHCl_3$ using a 1 mL cell with a 1 cm path length on a Jasco P-1030 polarimeter with a sodium lamp of wavelength 589 nm and reported as follows: [α]TD (***c*** = g/100 mL, solvent). X-ray crystallography analysis was performed on Bruker X8 APEX X-ray diffractionmeter. Flash chromatography separations were performed on Merck 60 (0.040 - 0.063mm) mesh silica gel. Analytical thin-layer chromatography (TLC) was performed on Merck 60 F254 silica gel plates. Visualization was performed using a UV lamp or potassium permanganate stain. Experiments involving moisture and/or air sensitive components were performed under a positive pressure of nitrogen in ovendried glassware equipped with a rubber septum inlet. All compounds synthesized were stored in a -30 ℃ freezer.

2. Reaction condition optimizations

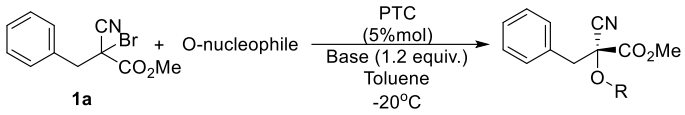


Table S1 Screening of O-nucleophiles (alkyl oxide salts)

Entry	O-nucleophiles	PTC	Result
1	MeONa	**BG1**	Mess reaction
2	EtONa	**BG1**	Mess reaction
3	tBuOK	**BG1**	Mess reaction
4	AcONa	**BG1**	Mess reaction
5	TsOK	**BG1**	No product
6	PhthOK	**PN1**	62% yield 8% ee

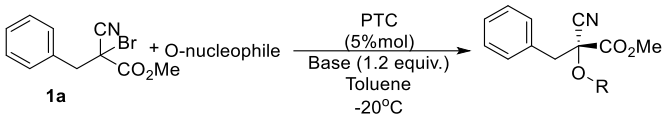
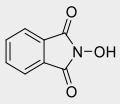
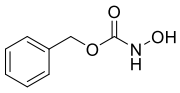
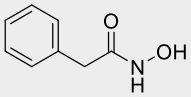
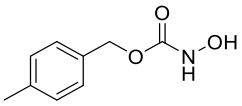
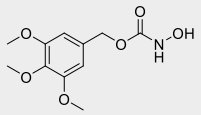
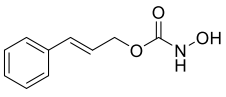
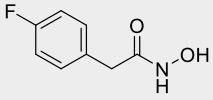
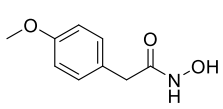
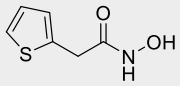
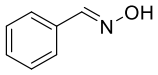
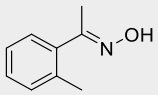
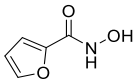
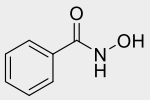
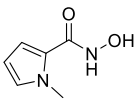
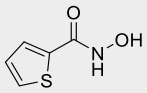
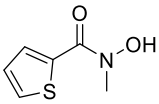
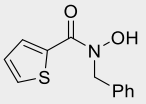
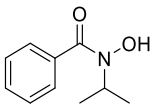
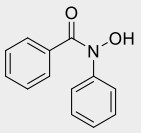
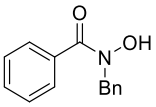


Table S2 Screening of O-nucleophiles (N-hydroxyphthalimide with an inorganic base)

Entry	O-nucleophiles	Base	PTC	Result
1		K_2CO_3	**PN1**	68% yield 12% ee
2		K_2CO_3	**PN1**	59% yield 10% ee
3		K_2CO_3	**PN1**	52% yield 11% ee
4		K_2CO_3	**PN1**	55% yield 8% ee
5		K_2CO_3	**PN1**	52% yield 13% ee
6		K_2CO_3	**PN1**	62% yield 10% ee
7		K_2CO_3	**PN1**	42% yield 7% ee

8		K_2CO_3	**PN1**	30% yield 12% ee
9		K_2CO_3	**PN1**	48% yield 11% ee
10		K_2CO_3	**PN3**	62% yield 0 ee
11		K_2CO_3	**PN3**	70% yield 0 ee
12		K_2CO_3	**PN3**	21% yield 10% ee
13		K_2CO_3	**PN3**	30% yield 9% ee
14		K_2CO_3	**PN3**	57% yield 6% ee
15		K_2CO_3	**PN3**	54% yield 15% ee
16		K_2CO_3	**PN3**	68% yield 13% ee
17		K_2CO_3	**PN3**	70% yield

				15% ee
18		K_2CO_3	**PN3**	No desired product
19		K_2CO_3	**PN3**	70% yield 13% ee
20		K_2CO_3	**PN3**	78% yield 15% ee

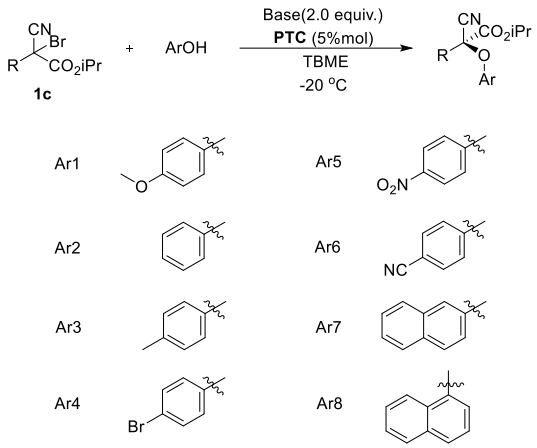


Table S3 Optimizations of Phenols as O-nucleophiles

Entry	1	Ar	Base	PTC	Result
1	1a	Ar-1	K_2CO_3	**BG3**	Elimination product
2	1j	Ar-1	K_2CO_3	**BG3**	85% yield 62% ee
3	1j	Ar-1	K_3PO_4	**BG3**	83% yield 59% ee
4	1j	Ar-1	Cs_2CO_3	**BG3**	88% yield 70% ee
5[a]	1j	Ar-1	-	**BG3**	90% yield 72% ee
6	1j	Ar-1	KOH(aq)	**BG3**	91% yield 73% ee

7[b]	1j	Ar-1	KOH(aq)	**BG3**	82% yield 90% ee
8[b]	1j	Ar-2	KOH(aq)	**BG3**	90% yield 82% ee
9[b]	1j	Ar-3	KOH(aq)	**BG3**	88% yield 89% ee
10[b]	1j	Ar-4	KOH(aq)	**BG3**	52% yield 13% ee
11[b]	1j	Ar-5	KOH(aq)	**BG3**	Trace -
12[b]	1j	Ar-6	KOH(aq)	**BG3**	77% yield 15% ee
13[b]	1j	Ar-7	KOH(aq)	**BG3**	Protonation product
14[b]	1j	Ar-8	KOH(aq)	**BG3**	Protonation product

[a.] Used potassium 4-methoxyphenolate as nucleophile, no base. [b.] Reactions were performed at -60°C

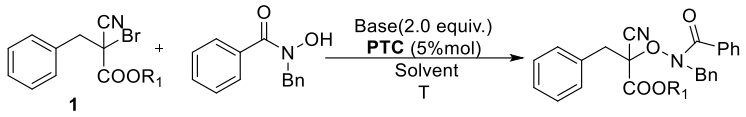


Table S4 Optimization of reaction conditions

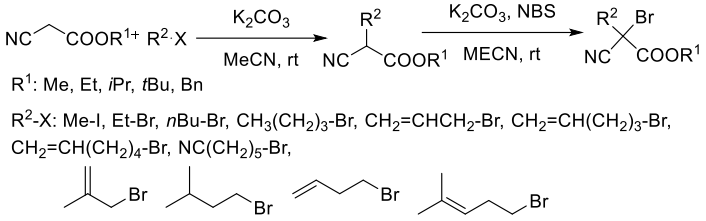
Entry	R1	Base	PTC	Solvent	T	Result
1	Me	Na_2CO_3	**PN3**	Toluene	-20℃	No reaction
2	Me	K_2CO_3	**PN3**	Toluene	-20℃	75% yield 6% ee
3	Me	K_3PO_4	**PN3**	Toluene	-20℃	trace
4	Me	Cs_2CO_3	**PN3**	Toluene	-20℃	80% yield 7% ee
5	Me	KOH(aq)	**PN3**	Toluene	-20℃	82% yield 5% ee
6	Me	Cs_2CO_3	**PN1**	Toluene	-20℃	78% yield 17% ee
7	Me	Cs_2CO_3	**BG1**	Toluene	-20℃	88% yield 21% ee
8	Me	Cs_2CO_3	**BG2**	Toluene	-20℃	85% yield 24% ee
9	Me	Cs_2CO_3	**BG3**	Toluene	-20℃	91% yield

						31% ee
10	Me	Cs_2CO_3	**BG3**	EA	-20℃	95% yield 30% ee
11	Me	Cs_2CO_3	**BG3**	DCM	-20℃	87% yield 27% ee
12	Me	Cs_2CO_3	**BG3**	Hexane	-20℃	trace
13	Me	Cs_2CO_3	**BG3**	Et_2O	-20℃	89% yield 62% ee
14	Me	Cs_2CO_3	**BG3**	TBME	-20℃	93% yield 65% ee
15	Et	Cs_2CO_3	**BG3**	TBME	-20℃	91% yield 71% ee
16	*i*Pr	Cs_2CO_3	**BG3**	TBME	-20℃	80% yield 77% ee
17	*t*Bu	Cs_2CO_3	**BG3**	TBME	-20℃	82% yield 62% ee
18	Bn	Cs_2CO_3	**BG3**	TBME	-20℃	75% yield 71% ee
19	*i*Pr	Cs_2CO_3	**BG3**	TBME	-40℃	85% yield

						90% ee
20	*i*Pr	Cs_2CO_3	**BG3**	TBME	-60°C	78% yield 77% ee

3. Procedures for the preparation of tertiary bromides [1]

Method A



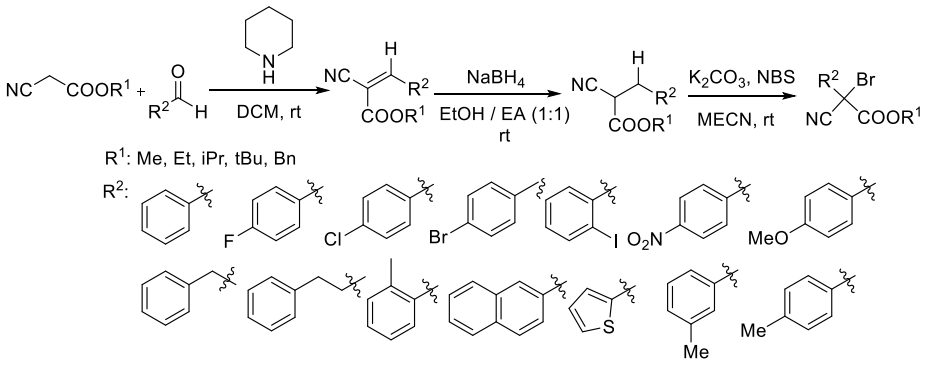
R^1: Me, Et, *i*Pr, *t*Bu, Bn

R^2-X: Me-I, Et-Br, *n*Bu-Br, $CH_3(CH_2)_3$-Br, CH_2=$CHCH_2$-Br, CH_2=$CH(CH_2)_3$-Br, CH_2=$CH(CH_2)_4$-Br, $NC(CH_2)_5$-Br,

Step 1: Potassium carbonate (1.2 equiv.) was added to a solution of cyanoester (3 equiv.) in MeCN (20 mL). After stirring for 30 min, R^2-X (1.0 equiv.) was added to the mixture dropwise. The mixture was stirred at rt for 4 h, TLC monitored the reaction ($KMnO_4$ as the indicator) until the starting material was totally consumed. Brine (15mL) was added to the mixture and then extracted with EA (3 X 20 mL), The combined organic layer was dried by Na_2SO_4, Solvent was removed under reduced pressure and the alkylated cyanoester was obtained by flash chromatography.

Step 2: To the mixture of NBS (1.8 equiv.) and K_2CO_3 (1.5 equiv.) in MeCN (20 mL) was added the alkylated cyanoester dropwise. After stirring for 2 h, TLC monitored the process ($KMnO_4$ as the indicator). Brine (15mL) was added to the mixture and then extracted with EA (3 X 20 mL), The combined organic layer was dried by Na_2SO_4, Solvent was removed under reduced pressure, the residue was purified by flash chromatography to get the brominated cyanoester, which is very unstable, should be kept in -20 ℃ fridge.

Method B



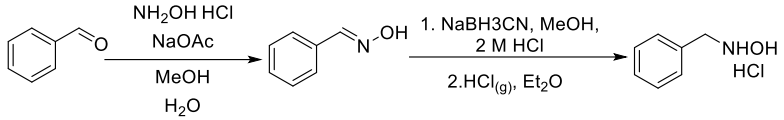
Step 1: To a mixture of cyanoester (1.0 equiv.) and aldehyde (1.1 equiv.) in DCM (20 mL) was added piperidine (0.1 equiv.) dropwise. After stirring for 3-4 h, TLC monitored the reaction ($KMnO_4$ as the indicator) until the starting material was totally consumed. Solvent was removed under vacuum. The obtained residue was taken into 40 mL Et_2O, stand in refrigerator for 2 hrs. Then solid was precipitated, filtered and dried to give the olefin.

Step 2: $NaBH_4$ (0.25 equiv.) was added in portions to a stirred solution of the olefin (1 equiv.) in EtOH/EA (1:1, 20 mL) at room temperature. After stirring for 30 min, TLC analysis showed the complete consumption of the olefin, the reaction mixture was quenched by water, washed with EA (3 X 20 mL), The combined organic layer was dried by Na_2SO_4, Solvent was removed under reduced pressure and the alkylated cyanoester was obtained by flash chromatography.

Step 3: To the mixture of NBS (1.8 equiv.) and K_2CO_3 (1.5 equiv.) in MeCN (20 mL) was added the alkylated cyanoester dropwise. After stirring for 2 h, TLC monitored the process ($KMnO_4$ as the indicator). Brine (15mL) was added to the mixture and then extracted with EA (3 X 20 mL), The combined organic layer was dried by Na_2SO_4, Solvent was removed under reduced pressure, the residue was purified by flash chromatography to get the brominated cyanoester, which is very unstable, should be kept in -20 ℃fridge.

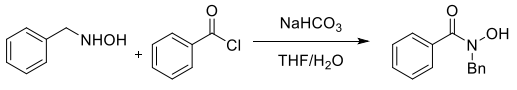
4. Procedures for the preparation of hydroxylamines[2]

1. The synthesis of N-benzyl-N-hydroxybenzamide



Step 1: Aldehyde (50 mmol), hydroxylamine hydrochloride (6 g, 100 mmol), and sodium acetate trihydrate (13.6 g, 100 mmol) were placed in a mixture of methanol (250 ml) and water (50 ml), and stirred at ambient temperature for about 3 h. Upon the completion of reaction, the solvent was removed under reduced pressure and the resulting residue was dissolved in ethyl acetate (50 ml), and then washed with water. The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated in vacuum. Then purification by flash chromatography can give the oxime as a white solid[2].

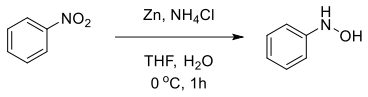
Step 2: To a stirring solution of benzaldehyde oxime (4.85 g, 40 mmol, 1.0 equiv) in MeOH (60 mL) containing an altered pH strip were added solid $NaBH_3CN$ (5.53 g, 88 mmol, 2.2 equiv) and aqueous HCl (2.0 M, about 50 mL) over 15 min in such a way that the pH of the solution stayed within 2–3 during the duration of the addition. The reaction mixture was allowed to stir for an additional 3.5 h, and then was quenched with the addition of aqueous 15% NaOH (until pH = 10). MeOH was removed *in vacuo*. The remaining aqueous solution was extracted with CH_2Cl_2 (3 × 100 mL). The organic layers were combined, washed with brine (100 mL), dried over Na_2SO_4, and filtered. The filtrate was concentrated *in vacuo*. The crude residue was dissolved in Et_2O (75 mL) and gaseous HCl was piped into the solution generating a white precipitate. The precipitate was collected, and then washed with Et_2O and then hexanes to give *N*-benzylhydroxylamine hydrochloride as a white powder[3a,3b].



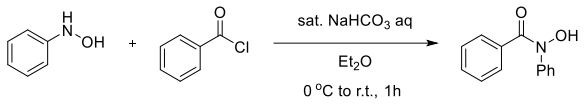
Step 3: To a stirring suspension of *N*-benzylhydroxylamine hydrochloride (20 mmol, 1.0 equiv) and $NaHCO_3$ (40 mmol, 2.0 equiv) in THF/H_2O (22 mL 10:1) under N_2 was added benzoyl chloride (22 mmol, 1.1 equiv) dropwise over 15 min. The reaction

mixture was allowed to stir for 15 h, and was then diluted with H_2O (20 mL). The mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were combined, washed with brine (10 mL), dried over Na_2SO_4, and filtered. The filtrate was concentrated *in vacuo*. Hexanes was added to the residue. The resulting white precipitate was collected and washed with hexanes to give hydroxylamine as a white solid[3a,3c,3d].

2. The synthesis of N-hydroxy-N-phenylbenzamide

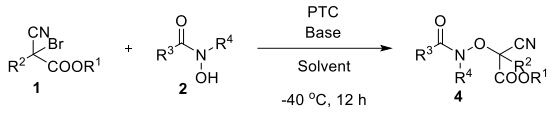


Step 1: To a solution of nitrobenzene (10 mmol, 1.0 equiv), and NH_4Cl (11 mmol, 1.1 equiv) in THF (40 mL) and H_2O (20 mL) was added Zn (20 mmol, 2.0 equiv) at 0 °C. The reaction mixture was stirred at 0 °C for 1 h, then filtered through a short pad of Celite and extracted with Et_2O. The combined organic layers were washed with brine, dried with Na_2SO_4, and solvent was evaporated. Recrystallization from hexane/DCM afforded *N*-phenylhydroxylamine (676 mg, 62%)[4][5].



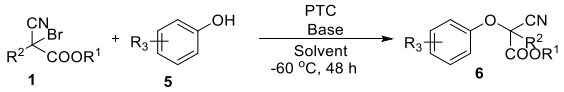
Step 2: To a solution of *N*-phenylhydroxylamine (10 mmol, 1.0 equiv) in ether (15 mL) was added saturated aqueous solution (10 mL) of sodium bicarbonate. After cooling to 0 °C, benzoyl chloride (11 mmol, 1.1 equiv) was added dropwise to the solution. Then, the solution was stirred for 1 hour with allowing the solution to room temperature. The reaction was quenched by saturated aqueous ammonium chloride. After the mixture was extracted with ether, the organic layer was washed by brine and dried over sodium sulfate. After the solvent was removed in vacuo, the crude product was purified by recrystallization (Hexane/DCM) to obtain N-hydroxy-N-phenylbenzamide (1.8 g, 85%)[4][5].

5. Procedure for the coupling of bromides with hydroxylamines



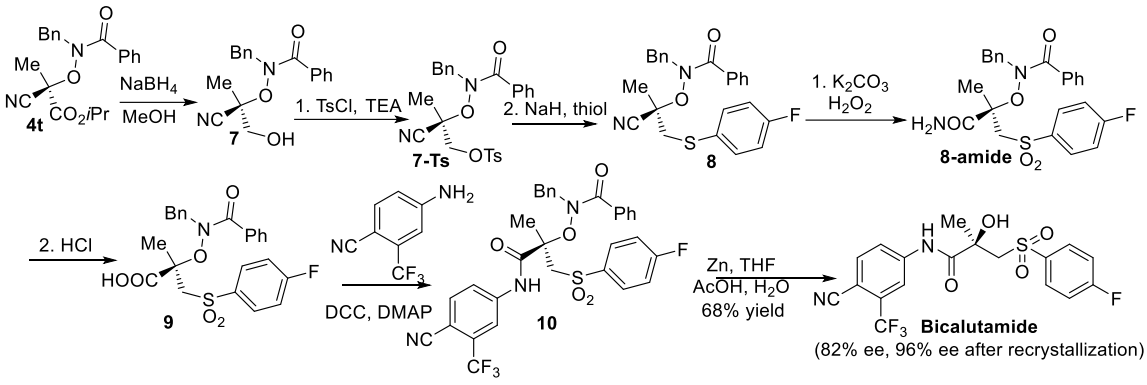
A solution of bromide **1** (1.0 equiv.), hydroxylamine **2** (1.2 equiv.) and PTC (5 mol%) in corresponding solvent (2 mL) was cooled to -40 ℃, and then base (1.2 equiv.) was added in one portion. The mixture was stirred at -40 ℃ for 12 h. After the starting material reacted completely, NH_4Cl was employed to quench the reaction, Et_2O was used to extract the crude product, then purification by short silica gel column to give the desired product **4**.

6. Procedure for the coupling of Bromides with phenol



A solution of bromide **1** (1.0 equiv.), phenol **5** (1.2 equiv.) and PTC (5 mol%) in corresponding solvent (2 mL) was cooled to -60 ℃, and then base (1.2 equiv.) was added in one portion. The mixture was stirred at -60 ℃ for 48 h. After the starting material reacted completely, NH_4Cl was employed to quench the reaction, Et_2O was used to extract the crude product, then purification by short silica gel column to give the desired product **6**.

7. Procedure for the synthesis of Bicalutamid[6]



Step 1: To the solution of **4t** in MeOH was added NaBH4 (2.0 equiv.) by portions, and this mixture was stirred at room temperature for 2 hours, TLC monitored the process. Water was added to the reaction mixture and then washed with Et_2O. The organic layer was separated, concentrated for silica gel column to affored the primary alcohol **7** as a colorless oil.

Step 2: Dissolve the primary alcohol **7** into DCM, and adding Bn_2SnO (0.1 equiv.), TsCl (1.2 equiv.), and TEA (2.0 equiv.) by sequence, then stirred at room temperature for 2 hours. TLC monitored the process, after the completion of this reaction, DCM was added to dilute and then washed using water. The organic layer was separated and concentrated for silica gel column to afford the desired product **7-Ts** as a colorless oil.

To a solution of **7-Ts** in DMF was added the 4-fluorobenzenethiol (2.0 equiv.), and adding NaH (2.5 equiv.) by portions at room temperature, then heat to 50 ºC for overnight. After the completion of the reaction, water was added, Et_2O was employed to extract the mixture and then purification by silica gel column to afford the desired product **8** as a colorless oil.

Step 3: Dissolve **8** into aceton, and added Na_2CO_3 (2.0 equiv.), and then 36% aq. H_2O_2 (10 equiv.) was added, this mixture was stirred overnight. TLC monitored the process, after the completion of the reaction, aceton was removed under depressed pressure, and Et_2O was employed to extract the product. After concentration, the crude amide

was purified by silica gel column to afford the amide **8-amide**.

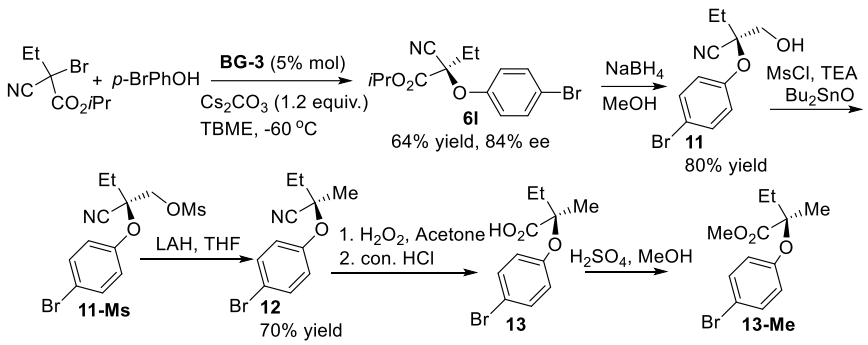
Dissolved the amide into con. HCl, and heated to 50 ºC overnight. Adding water to the reaction mixture, and DCM for extraction. The DCM layer was separated and concentrated to afford the crude free carboxylic acid **9**.

Step 4: To a solution of crude carboxylic acid **9** in dry DCM was added 4-amino-2-(trifluoromethyl)benzonitrile (1.2 equiv.), and then DCC (2.0 equiv.), DMAP (0.1 equiv.). The mixture was stirred under the protection of N_2 for 4 hours. After the completion of the reaction, the solid was removed away by simply filtration, the organic layer was concentrated for column to afforded the product **10**.

Step 5: Activated zinc (10 equiv) was added to a solution of **10** (1.0 equiv) in THF, acetic acid (0.5 mL) and H_2O (0.5 mL). The reaction mixture was then warm to 60 ℃, and stirred for 15 min. Activated zinc (10 equiv) was added to the reaction mixture every 15 min three times. The reaction mixture was quenched with saturated aqueous $NaHCO_3$ (2 mL) at room temperature. The resulting mixture was extracted with EtOAc (2x 5 mL). The combined organic extracts were washed with brine (2 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography.

Activated zinc was prepared as follows. A mixture of zinc powder (25 g) and 3% aqueous HCl (100 mL) was sonicated for 10 min at room temperature. The mixture was filtrated through glass filter, washed with water (2x 100 mL), ethanol (2x 50 mL) and Et_2O (2x 50 mL). The resulting zinc powder was dried under reduced pressure for 2 h.

8. Procedure for the synthesis of fabrate [7]



Step 1: A solution of bromide (1.0 equiv.), phenol (1.2 equiv.) and PTC (5 mol%) in TBME (2 mL) was cooled to -60 ℃, and then Cs_2CO_3 (1.2 equiv.) was added in one portion. The mixture was stirred at -60 ℃for 3 days. After the starting material reacted completely, aq. NH_4Cl was employed to quench the reaction, Et_2O was used to extract the crude product, then purification by short silica gel column to give the desired product **6l**.

Step 2: To the solution of **6l** in MeOH was added NaBH4 (2.0 equiv.) by portions, and this mixture was stirred at room temperature for 2 hours, TLC monitored the process. Water was added to the reaction mixture and then washed with Et_2O. The organic layer was separated, concentrated for silica gel column to affored the primary alcohol **11** as a colorless oil.

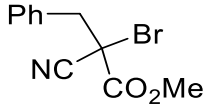
Step 3: Dissolve the primary alcohol **11** into DCM, and adding Bn_2SnO (0.1 equiv.), MsCl (1.2 equiv.), and TEA (2.0 equiv.) by sequence, then stirred at room temperature for 2 hours. TLC monitored the process, after the completion of this reaction, DCM was added to dilute and then washed using water. The organic layer was separated and concentrated for silica gel column to afford the desired product **11-Ms** as a colorless oil.

Step 4: To a solution of the protected alcohol **11-Ms** in dry THF was added LAH (2.0 equiv.), the mixture was reflused under the protection of N_2 for overnight. After the completion of the reaction, the temperature was cooled down to room temperature, *Sat.* NH_4Cl was added to quench LAH, Et_2O was added, and washed with water, the organic

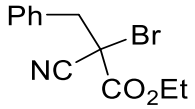
layer was separated and concentrated for column to afforded the product **12** as a colorless oil.

Step 5: Dissolve the **12** into aceton, and added Na_2CO_3 (2.0 equiv.), and then 36% aq. H_2O_2 (10 equiv.) was added, this mixture was stirred overnight. TLC monitored the process, after the completion of the reaction, aceton was removed under depressed pressure, and Et_2O was employed to extract the product. After concentration, the crude amide was used directly without further purification. Dissolved the amide into con. HCl, and heated to 50 ºC overnight. Adding water to the reaction mixture, and DCM for extraction. The DCM layer was separated and concentrated to afford the crude free carboxylic acid. Dissolve the carboxylic acid into MeOH, to this mixture was added 1 ml *con.* H_2SO_4 by dropwise, and stirred at rt overnight. Adding water to the reaction mixture, and Et_2O was employed to extract the desired product, and further purification using silica gel column to afford **13** as a colorless oil.

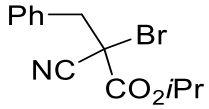
9. Characterization of the substrates and products



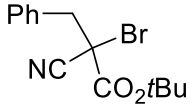
Methyl 2-bromo-2-cyano-3-phenylpropanoate (1a): method A; colorless oil; 87% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroformd): δ 7.41 – 7.31 (m, 5H), 3.85 (s, 3H), 3.73 (d, J = 13.8 Hz, 1H), 3.52 (d, J = 13.8 Hz, 1H); ^{13}C NMR (101 MHz, Chloroform-d): δ 164.6, 132.8, 130.5, 129.0, 128.8, 115.5, 54.9, 45.7, 42.4; HRMS (ESI) calcd for $C_{11}H_{11}NO_2Br$ m/z $[M+H]^+$: 267.9968; found: 267.9967.



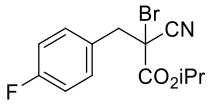
Ethyl 2-bromo-2-cyano-3-phenylpropanoate (1b): method B; colorless oil; 76% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 4.53 – 4.17 (m, 2H), 3.75 (d, J = 13.8 Hz, 1H), 3.55 (d, J = 13.8 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.94, 132.81, 130.42, 128.73, 115.48, 64.43, 45.55, 42.68, 30.89, 13.66. HRMS (ESI) calcd for $C_{12}H_{13}BrNO_2$ m/z $[M+H]^+$:282.0124; found:282.0124.



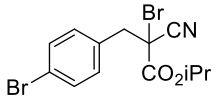
***Iso*propyl 2-cyano-2-iodo-3-phenylpropanoate (1c):** method B; colorless oil; 87% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 5H), 5.09 (dt, J = 12.5, 6.3 Hz, 1H), 3.75 (d, J = 13.9 Hz, 1H), 3.55 (d, J = 13.9 Hz, 1H), 3.50 (q, J = 7.0 Hz, 1H), 1.33 (d, J = 6.3 Hz, 3H), 1.25 – 1.22 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.24, 134.82, 134.18, 130.13, 129.02, 128.77, 128.48, 127.83, 117.73, 72.59, 65.86, 46.76, 43.40, 21.20, 20.81, 15.79, 15.29. HRMS (ESI) calcd for $C_{13}H_{15}BrNO_2$ m/z $[M+H]^+$: 296.0281; found:296.0280.



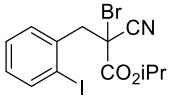
***tert*-Butyl 2-bromo-2-cyano-3-phenylpropanoate (1d)**: method B A; colorless oil; 90% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 2.1 Hz, 5H), 3.72 (d, J = 13.8 Hz, 1H), 3.50 (d, J = 13.8 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.55, 133.05, 130.49, 128.63, 115.81, 86.23, 45.46, 43.96, 27.44. HRMS (ESI) calcd for $C_{14}H_{17}BrNO_2$ m/z $[M+H]^+$:310.0437; found:310.0445.



isopropyl 2-bromo-2-cyano-3-(4-fluorophenyl)propanoate (1e) colorless oil; 66% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.31 (m, 2H), 7.03 (t, *J* = 8.6 Hz, 2H), 5.13 – 5.03 (m, 1H), 3.68 (d, *J* = 14.0 Hz, 1H), 3.48 (d, *J* = 14.0 Hz, 1H), 1.32 (d, *J* = 6.3 Hz, 2H), 1.22 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform- *d*) δ 164.21, 163.36, 161.74, 132.38, 132.29, 128.72, 115.96, 115.74, 73.20, 44.64, 42.92, 21.33, 21.18. ^{19}F NMR (376 MHz, CHLOROFORM-*D*) δ -112.84. HRMS (ESI) calcd for $C_{13}H_{14}BrFNO_2$ *m/z* $[M+H]^+$: 314.0192; found: 314.0159.

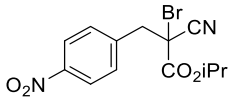


isopropyl 2-bromo-3-(4-bromophenyl)-2-cyanopropanoate: yellow oil; 69% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.3 Hz, 2H), 5.14 – 5.03 (m, 1H), 3.66 (d, *J* = 13.9 Hz, 1H), 3.46 (d, *J* = 14.0 Hz, 1H), 1.33 (d, *J* = 6.3 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.28, 132.21, 132.21, 132.04, 132.04, 131.86, 123.10, 115.40, 73.30, 44.73, 42.54, 21.34, 21.17. HRMS (ESI) calcd for $C_{13}H_{14}Br_2NO_2$ *m/z* $[M+H]^+$: 373.9391; found: 373.9429.

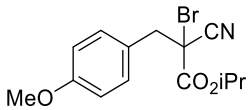


isopropyl 2-bromo-2-cyano-3-(2-iodophenyl)propanoate(1g): yellow oil; 80% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.91 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.33 (t, *J* = 7.6 Hz, 1H), 7.05 – 6.99 (m, 1H), 5.22 – 5.06 (m, 1H), 3.87 (d, *J* = 1.3 Hz,

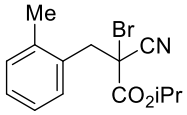
2H), 1.34 – 1.28 (m, 6H). ^{13}C NMR (100 MHz, Chloroform- *d*) δ 163.49, 136.54, 130.17, 130.14, 128.69, 115.36, 102.69, 100.01, 73.41, 48.18, 42.46, 21.37, 21.18. HRMS (ESI) calcd for $C_{13}H_{14}BrINO_2$ m/z $[M+H]^+$: 421.9253; found: 421.9270.



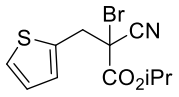
isopropyl 2-bromo-2-cyano-3-(4-nitrophenyl)propanoate (1h): white solid; 87% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.23 (d, *J* = 9.4 Hz, 1H), 7.58 (d, *J* = 9.1 Hz, 1H), 5.18 – 5.07 (m, 1H), 3.80 (d, *J* = 13.8 Hz, 1H), 3.61 (d, *J* = 13.9 Hz, 1H), 1.35 (d, *J* = 6.5 Hz, 1H), 1.28 (d, *J* = 5.3 Hz, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.03, 139.91, 139.91, 131.70, 131.70, 123.96, 123.95, 115.07, 73.68, 44.57, 41.85, 21.37, 21.13. HRMS (ESI) calcd for $C_{13}H_{14}BrN_2O_4$ *m/z* $[M+H]^+$: 341.0137; found: 341.0119.



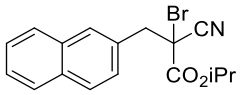
isopropyl 2-bromo-2-cyano-3-(4-methoxyphenyl)propanoate (1i): white solid; 90% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.16 – 4.99 (m, 1H), 3.80 (s, 3H), 3.66 (d, *J* = 13.8 Hz, 1H), 3.44 (d, *J* = 13.9 Hz, 1H), 1.32 (d, *J* = 6.3 Hz, 3H), 1.22 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.54, 159.88, 131.72, 131.72, 124.96, 115.74, 114.22, 114.21, 72.98, 55.34, 44.84, 43.34, 21.33, 21.21. HRMS (ESI) calcd for $C_{14}H_{17}BrNO_3$ *m/z* $[M+H]^+$: 326.0392; found: 326.0384.



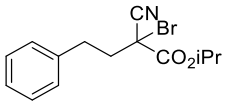
isopropyl 2-bromo-2-cyano-3-(o-tolyl)propanoate (1j): yellow oil; 78% yield; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 7.4 Hz, 1H), 7.28 – 7.12 (m, 3H), 5.19 – 5.03 (m, 1H), 3.79 – 3.60 (m, 2H), 2.45 (s, 3H), 1.32 (d, *J* = 6.2 Hz, 3H), 1.24 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 163.77, 137.68, 131.69, 131.20, 130.13, 128.54, 128.54, 126.25, 73.12, 43.00, 41.63, 21.25, 21.13, 20.05. HRMS (ESI) calcd for $C_{14}H_{17}BrNO_2$ *m/z* $[M+H]^+$: 310.0443; found: 310.0458.



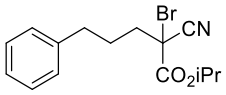
isopropyl 2-bromo-2-cyano-3-(thiophen-2-yl)propanoate (1k): yellow oil; 86% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (dd, *J* = 5.2, 1.3 Hz, 1H), 7.11 – 7.08 (m, 1H), 6.99 (dd, *J* = 5.2, 3.5 Hz, 1H), 5.17 – 5.06 (m, 1H), 3.95 (d, *J* = 14.0 Hz, 1H), 3.72 (d, *J* = 14.1 Hz, 1H), 1.34 (d, *J* = 6.3 Hz, 3H), 1.27 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.30, 133.94, 129.46, 127.36, 126.74, 100.00, 73.29, 42.31, 40.07, 21.33, 21.20. HRMS (ESI) calcd for $C_{11}H_{13}BrNO_2S$ *m/z* $[M+H]^+$: 301.9850; found: 301.9863.



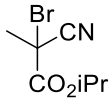
isopropyl 2-bromo-2-cyano-3-(naphthalen-2-yl)propanoate (1l): yellow oil; 86% yield; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.92 – 7.80 (m, 4H), 7.59 – 7.45 (m, 3H), 5.17 – 5.06 (m, 1H), 3.93 (d, *J* = 13.8 Hz, 1H), 3.71 (d, *J* = 13.8 Hz, 1H), 1.35 (d, *J* = 6.3 Hz, 3H), 1.20 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 163.44, 133.23, 133.10, 130.34, 129.96, 128.53, 128.01, 127.75, 127.71, 126.58, 126.47, 115.62, 73.07, 45.60, 43.00, 21.21, 21.13. HRMS (ESI) calcd for $C_{17}H_{17}BrNO_2$ *m/z* $[M+H]^+$: 346.0443; found: 346.0429.



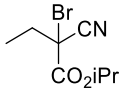
isopropyl 2-bromo-2-cyano-4-phenylbutanoate (1m): yellow oil; 82% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.29 (m, 2H), 7.25 – 7.18 (m, 3H), 5.18 – 5.06 (m, 1H), 3.03 – 2.92 (m, 1H), 2.86 – 2.74 (m, 1H), 2.69 – 2.49 (m, 2H), 1.37 – 1.34 (m, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.48, 138.64, 128.84, 128.84, 128.57, 128.57, 126.90, 115.67, 42.78, 41.63, 32.67, 31.00, 21.39, 21.23. HRMS (ESI) calcd for $C_{14}H_{17}BrNO_2$ *m/z* $[M+H]^+$: 310.0443; found: 310.0446.



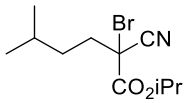
isopropyl 2-bromo-2-cyano-5-phenylpentanoate (1n): yellow oil; 79% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 2H), 7.25 – 7.21 (m, 1H), 7.21 – 7.16 (m, 2H), 5.18 – 5.06 (m, 1H), 2.73 (t, *J* = 7.5 Hz, 2H), 2.40 – 2.22 (m, 2H), 2.07 – 1.94 (m, 1H), 1.89 – 1.75 (m, 1H), 1.36 – 1.30 (m, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.51, 140.40, 128.58, 128.58, 128.32, 128.32, 126.33, 115.69, 72.79, 64.24, 39.27, 34.80, 27.77, 21.29, 21.10. HRMS (ESI) calcd for $C_{15}H_{19}BrNO_2$ *m/z* $[M+H]^+$: 324.0599; found: 324.0626.



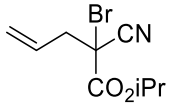
isopropyl 2-bromo-2-cyanopropanoate (1o): yellow oil; 88% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.42 – 4.91 (m, 1H), 2.19 (s, 3H), 1.36 (dd, *J* = 6.3, 3.1 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.84, 116.63, 72.85, 37.10, 27.87, 21.26, 21.06. HRMS (ESI) calcd for $C_7H_{11}BrNO_2$ *m/z* $[M+H]^+$: 219.9973; found: 219.9985.



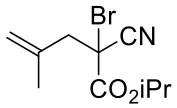
isopropyl 2-bromo-2-cyanobutanoate (1p): colorless oil; 90% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.21 – 5.07 (m, 1H), 2.41 – 2.23 (m, 2H), 1.34 (d, *J* = 6.3 Hz, 6H), 1.18 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.53, 115.57, 72.69, 44.56, 33.66, 21.30, 21.13, 10.58. HRMS (ESI) calcd for $C_8H_{13}BrNO_2$ *m/z* $[M+H]^+$: 234.0130; found: 234.0172.



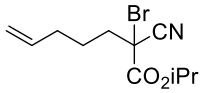
isopropyl 2-bromo-2-cyano-5-methylhexanoate (1q): colorless oil; 80% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.16 – 5.09 (m, 1H), 5.08 (s, 1H), 2.41 – 2.15 (m, 4H), 1.68 (s, 3H), 1.63 (s, 3H), 1.34 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.58, 115.76, 72.65, 43.48, 38.06, 34.97, 27.71, 22.25, 21.29, 21.15, 21.12. HRMS (ESI) calcd for $C_{11}H_{19}BrNO_2$ *m/z* $[M+H]^+$: 276.0559; found: 276.0597.



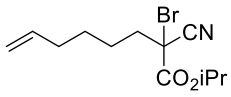
isopropyl 2-bromo-2-cyanopent-4-enoate (1r): colorless oil; 92% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.86 – 5.74 (m, 1H), 5.37 (d, *J* = 1.2 Hz, 1H), 5.35 – 5.31 (m, 1H), 5.17 – 5.06 (m, 1H), 3.12 – 3.03 (m, 1H), 3.01 – 2.92 (m, 1H), 1.33 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.12, 129.40, 122.79, 115.35, 72.95, 72.86, 43.86, 21.31, 21.13. HRMS (ESI) calcd for $C_9H_{13}BrNO_2$ *m/z* $[M+H]^+$: 246.0130; found: 246.0139.



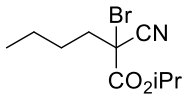
isopropyl 2-bromo-2-cyano-4-methylpent-4-enoate (1s): colorless oil; 75% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.17 – 5.08 (m, 1H), 5.08 – 5.04 (m, 1H), 4.97 (d, *J* = 5.2 Hz, 1H), 3.19 (dd, *J* = 14.0, 5.8 Hz, 1H), 2.96 (dd, *J* = 14.0, 5.7 Hz, 1H), 1.86 (d, *J* = 5.3 Hz, 3H), 1.38 – 1.30 (m, 6H). ^{13}C NMR (100 MHz, Chloroform-d) δ 163.68, 138.40, 117.95, 117.94, 116.03, 73.00, 47.28, 41.45, 23.19, 21.37. HRMS (ESI) calcd for $C_{10}H_{15}BrNO_2$ m/z $[M+H]^+$: 260.0286; found: 260.0312



isopropyl 2-bromo-2-cyanohept-6-enoate (1t) colorless oil; 74% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.83 – 5.71 (m, 1H), 5.17 – 5.10 (m, 1H), 5.10 – 5.01 (m, 2H), 2.37 – 2.21 (m, 2H), 2.20 – 2.13 (m, 2H), 1.83 – 1.71 (m, 1H), 1.64 – 1.51 (m, 1H), 1.35 (dd, *J* = 6.3, 1.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.56, 136.77, 116.04, 115.73, 72.77, 39.22, 32.61, 25.39, 21.31, 21.16, 21.13. HRMS (ESI) calcd for $C_{11}H_{17}BrNO_2$ *m/z* $[M+H]^+$: 274.0437; found: 247.0430.

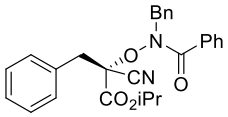


isopropyl 2-bromo-2-cyanooct-7-enoate (1u): colorless oil; 70% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.00 – 5.61 (m, 1H), 5.22 – 5.07 (m, 1H), 5.07 – 4.93 (m, 2H), 2.45 – 2.18 (m, 2H), 2.19 – 1.98 (m, 2H), 1.80 – 1.60 (m, 1H), 1.56 – 1.42 (m, 3H), 1.34 (dd, *J* = 6.3, 1.0 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.60, 137.76, 115.75, 115.19, 72.73, 43.19, 39.74, 33.13, 27.97, 25.66, 21.30, 21.13. HRMS (ESI) calcd for $C_{12}H_{19}BrNO_2$ *m/z* $[M+H]^+$: 288.0599; found: 288.0620.

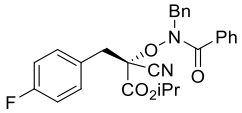


isopropyl 2-bromo-2-cyanohexanoate (1v): colorless oil; 85% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.20 – 5.08 (m, 1H), 2.38 – 2.19 (m, 2H), 1.70 – 1.58 (m, 1H), 1.50 – 1.39 (m, 3H), 1.35 (dd, *J* = 6.3, 1.3 Hz, 6H), 0.95 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 163.66, 115.81, 72.69, 43.31, 39.65, 28.31, 21.99, 21.31, 21.13, 13.64. HRMS (ESI) calcd for $C_{10}H_{17}BrNO_2$ *m/z* $[M+H]^+$: 262.0443; found: 262.0428.

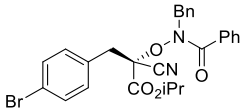
10. Characterization of the products



isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-phenylpropanoate (4g): colorless oil; 85% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.59 (m, 2H), 7.49 (t, *J* = 7.4 Hz, 1H), 7.41 (dd, *J* = 8.3, 6.7 Hz, 2H), 7.31 – 7.21 (m, 8H), 7.09 (dd, *J* = 6.6, 3.0 Hz, 2H), 5.03 – 4.92 (m, 1H), 4.89 – 4.76 (m, 2H), 3.40 – 3.24 (m, 2H), 1.22 (d, *J* = 6.3 Hz, 3H), 1.12 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.77, 164.12, 134.96, 133.84, 131.77, 131.77, 131.45, 131.45, 130.77, 130.77, 128.67, 128.67, 128.63, 128.62, 128.59, 128.22, 128.14, 128.14, 115.28, 100.00, 84.20, 72.34, 57.08, 42.21, 21.56, 21.56, 21.39. HRMS (ESI) calcd for $C_{27}H_{27}N_2O_4$ *m/z* $[M+H]^+$: 443.1971; found: 443.1980. $[\alpha]_D^{22}$= -22.6 (c 0.97, $CHCl_3$); HPLC analysis: Chiralcel IB (Hex/IPA = 95/5, 1.0 mL/min, 254 nm, 22°C), 8.3 (major), 9.9 min, 90% ee.

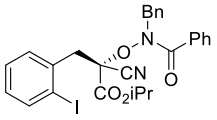


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-fluorophenyl)propanoate (4i): colorless oil; 75% yield; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.65 – 7.59 (m, 2H), 7.54 – 7.47 (m, 1H), 7.46 – 7.39 (m, 2H), 7.32 – 7.26 (m, 3H), 7.20 (dd, J = 8.3, 5.3 Hz, 2H), 7.08 (dd, J = 5.9, 2.9 Hz, 2H), 6.95 (t, J = 8.7 Hz, 2H), 5.06 – 4.95 (m, 1H), 4.89 – 4.74 (m, 2H), 3.40 – 3.22 (m, 2H), 1.24 (d, J = 6.3 Hz, 3H), 1.17 (d, J = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-d) δ 173.81, 164.01, 134.84, 133.72, 132.51, 132.42, 131.84, 128.68, 128.68, 128.64, 128.63, 128.63, 128.48, 128.48, 128.17, 128.17, 127.30, 127.27, 115.64, 115.43, 115.18, 83.91, 72.47, 57.18, 41.32, 21.55, 21.45. ^{19}F NMR (376 MHz, CHLOROFORM-D) δ -112.96. HRMS (ESI) calcd for $C_{27}H_{26}FN_2O_4$ m/z [M+H]+: 461.1877; found: 461.1877. $[\alpha]_D^{22}$= -4.9 (c 0.92, CHCl3); HPLC analysis: Chiralcel IE (Hex/IPA = 70/30, 1.0 mL/min, 254 nm, 22°C), 9.9 (major), 20.9 min, 92% ee.

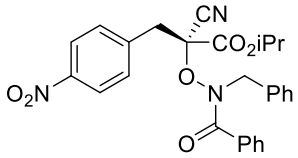


isopropyl (R)-2-((N-benzylbenzamido)oxy)-3-(4-bromophenyl)-2-cyanopropanoate (4j): yellow oil; 82% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.58 (m, 2H), 7.54 – 7.47 (m, 1H), 7.45 – 7.41 (m, 2H), 7.41 – 7.36 (m, 3H), 7.30 – 7.27 (m, 2H), 7.13 – 7.07 (m, 2H), 7.07 – 7.02 (m, 2H), 5.08 – 4.95 (m, 1H), 4.90 – 4.73 (m, 2H), 3.33 (d, *J* = 14.0 Hz, 1H), 3.24 (d, *J* = 14.0 Hz, 1H), 1.24 (d, *J* = 6.3 Hz, 3H), 1.18 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.83, 163.92, 134.77, 133.68, 132.44, 131.85, 131.74, 130.54, 128.70, 128.70, 128.68, 128.64, 128.64, 128.62, 128.62, 128.46, 128.46, 128.18, 128.17, 122.49, 115.12, 83.55, 72.58, 57.22, 41.47, 21.55, 21.47. HRMS (ESI) calcd for $C_{27}H_{26}BrN_2O_4$ *m/z* $[M+H]^+$:

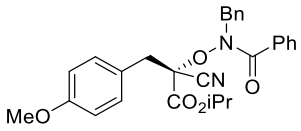
521.1076; found: 521.1075. $[\alpha]_D^{22}$= -6.0 (c 1.05, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 70/30, 1.0 mL/min, 254 nm, 22°C), 10.8 (major), 25.7 min, 89% ee.



isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(2-iodophenyl)propanoate (4k): colorless oil; 75% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (d, *J* = 8.0 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.48 (t, *J* = 7.4 Hz, 1H), 7.40 (t, *J* = 7.6 Hz, 3H), 7.34 – 7.27 (m, 2H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.15 – 7.07 (m, 3H), 6.96 (t, *J* = 7.7 Hz, 1H), 5.13 – 5.01 (m, 1H), 4.85 (q, *J* = 15.8 Hz, 2H), 3.65 (d, *J* = 14.8 Hz, 1H), 3.55 (d, *J* = 14.7 Hz, 1H), 1.25 (t, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.89, 163.98, 140.11, 135.03, 135.03, 133.75, 131.76, 131.42, 129.74, 128.68, 128.68, 128.65, 128.64, 128.51, 128.51, 128.40, 128.40, 128.11, 128.11, 114.85, 102.67, 83.27, 72.69, 57.22, 45.55, 21.53, 21.47. HRMS (ESI) calcd for $C_{27}H_{26}IN_2O_4$ *m/z* $[M+H]^+$: 569.0937; found: 569.0933. $[\alpha]_D^{22}$= -3.4 (c 0.73, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 88/12, 1.0 mL/min, 254 nm, 22°C), 13.7 (major), 15.1 min, 82% ee.

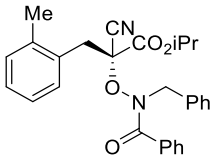


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-nitrophenyl)propanoate (4l): colorless oil; 77% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.10 – 8.05 (m, 2H), 7.64 – 7.59 (m, 2H), 7.54 – 7.47 (m, 1H), 7.45 – 7.35 (m, 4H), 7.29 – 7.24 (m, 3H), 7.00 (dd, *J* = 7.7, 1.7 Hz, 2H), 5.09 – 5.01 (m, 1H), 4.86 (d, *J* = 15.8 Hz, 1H), 4.73 (d, *J* = 15.9 Hz, 1H), 3.51 (d, *J* = 13.9 Hz, 1H), 3.37 (d, *J* = 14.0 Hz, 1H), 1.23 (dd, *J* = 9.6, 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.94, 163.63, 147.84, 139.06, 134.57, 133.46, 132.06, 131.84, 131.84, 130.28, 128.81, 128.70, 128.69, 128.59, 128.29, 128.27, 124.15, 123.61, 114.86, 82.85, 72.93, 57.47, 41.54, 41.54, 28.59, 21.54, 21.53. HRMS (ESI) calcd for $C_{28}H_{29}N_2O_5$ *m/z* $[M+H]^+$: 488.1822; found: 488.1819. $[\alpha]_D^{22}$= -2.3 (c 1.29, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 70/30, 1.0 mL/min, 254 nm, 22°C), 12.8 (major), 28.7 min, 87% ee.

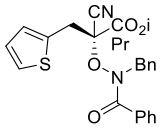


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-methoxyphenyl)propanoate (4m): colorless oil; 78% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 – 7.57 (m, 2H), 7.52 – 7.45 (m, 1H), 7.44 – 7.37 (m, 2H), 7.31 – 7.24 (m, 3H), 7.18 – 7.06 (m, 4H), 6.83 – 6.75 (m, 2H), 5.03 – 4.94 (m, 1H), 4.88 – 4.76 (m, 2H), 3.78 (s, 3H), 3.32 – 3.19 (m, 2H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.14 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.72, 164.20, 159.55, 134.99, 134.99, 133.85, 131.86, 131.86, 131.72, 128.66, 128.65, 128.61, 128.61, 128.60, 128.56, 128.56, 128.11, 123.35, 115.36, 114.00, 100.01, 84.38, 72.27, 57.01, 55.32, 41.44, 21.58, 21.45. HRMS (ESI) calcd for $C_{28}H_{29}N_2O_5$ *m/z* $[M+H]^+$: 473.2076;

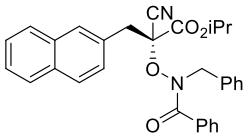
found: 473.2082. $[\alpha]_D^{22}$= -24.3 (c 0.29, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 70/30, 1.0 mL/min, 254 nm, 22°C), 16.7 (major), 39.6 min, 88% ee.



isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(o-tolyl)propanoate (4n): colorless oil; 76% yield. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 – 7.64 (m, 2H), 7.59 – 7.51 (m, 1H), 7.50 – 7.42 (m, 2H), 7.36 – 7.29 (m, 3H), 7.29 – 7.22 (m, 2H), 7.21 – 7.15 (m, 2H), 7.12 – 7.06 (m, 2H), 5.15 – 5.05 (m, 1H), 4.93 – 4.75 (m, 2H), 3.53 (d, *J* = 14.4 Hz, 1H), 3.35 (d, *J* = 14.4 Hz, 1H), 2.28 (s, 3H), 1.28 (dd, *J* = 15.5, 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.61, 164.46, 138.18, 134.96, 133.84, 131.57, 130.97, 130.81, 130.22, 128.60, 128.60, 128.50, 128.50, 128.48, 128.48, 128.45, 128.45, 128.05, 127.96, 125.92, 115.27, 84.08, 72.30, 56.96, 38.54, 21.45, 21.32, 19.83. HRMS (ESI) calcd for $C_{28}H_{29}N_2O_4$ *m/z* $[M+H]^+$: 457.2127; found: 457.2134. $[\alpha]_D^{22}$= -7.0 (c 0.46, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 90/10, 1.0 mL/min, 254 nm, 22°C), 21.3 (major), 31.3 min, 84% ee.

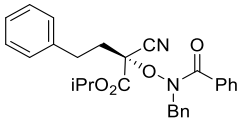


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(thiophen-2-yl)propanoate (4o): yellow oil; 75% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.58 (m, 2H), 7.54 – 7.46 (m, 1H), 7.42 (t, *J* = 7.5 Hz, 2H), 7.30 – 7.26 (m, 3H), 7.23 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.12 (dd, *J* = 6.5, 3.4 Hz, 2H), 7.00 – 6.92 (m, 2H), 5.07 – 4.99 (m, 1H), 4.88 (s, 2H), 3.57 (s, 2H), 1.25 (d, *J* = 6.3 Hz, 3H), 1.20 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.74, 163.73, 134.94, 133.76, 132.19, 131.78, 129.29, 128.67, 128.65, 128.64, 128.64, 128.63, 128.54, 128.53, 128.48, 128.15, 127.21, 126.31, 115.16, 83.78, 72.61, 57.18, 36.49, 21.55, 21.44. HRMS (ESI) calcd for $C_{25}H_{25}N_2O_4S$ *m/z* $[M+H]^+$: 449.1535; found: 449.1530. $[\alpha]_D^{22}$= -13.1 (c 0.29, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 70/30, 1.0 mL/min, 190 nm, 22°C), 14.1 (major), 38.7 min, 90% ee.

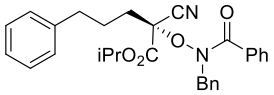


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(naphthalen-2-yl)propanoate (4p): colorless oil; 74% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.79 (m, 1H), 7.77 – 7.68 (m, 3H), 7.63 – 7.58 (m, 2H), 7.51 – 7.44 (m, 3H), 7.41 – 7.34 (m, 3H), 7.24 – 7.17 (m, 3H), 7.05 – 7.00 (m, 2H), 5.03 – 4.94 (m, 1H), 4.88 – 4.74 (m, 2H), 3.50 (q, *J* = 13.9 Hz, 2H), 1.21 (d, *J* = 6.3 Hz, 3H), 1.09 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.82, 164.16, 134.89, 133.82, 133.26, 133.00, 131.75, 130.12, 128.97, 128.66, 128.66, 128.62, 128.61, 128.58,

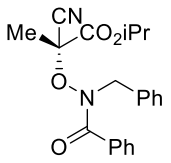
128.57, 128.55, 128.53, 128.28, 128.26, 128.09, 128.02, 127.70, 126.37, 126.30, 115.32, 84.06, 72.43, 57.09, 42.31, 21.55, 21.39. HRMS (ESI) calcd for $C_{31}H_{29}N_2O_4$ *m/z* $[M+H]^+$: 493.2127; found: 493.2130. $[\alpha]_D^{22}$= -25.4 (c 1.09, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 23.5 (major), 55.9 min, 82% ee.



isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-4-phenylbutanoate (4q): colorless oil; 77% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.59 (m, 2H), 7.54 – 7.47 (m, 1H), 7.47 – 7.39 (m, 2H), 7.33 – 7.24 (m, 5H), 7.24 – 7.17 (m, 3H), 7.17 – 7.08 (m, 2H), 5.12 – 5.01 (m, 1H), 4.96 (d, *J* = 5.1 Hz, 2H), 2.87 – 2.60 (m, 2H), 2.41 – 2.22 (m, 2H), 1.30 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.92, 164.45, 139.28, 134.99, 133.84, 131.65, 128.63, 128.63, 128.60, 128.60, 128.59, 128.56, 128.56, 128.51, 128.51, 128.38, 128.38, 128.13, 128.13, 126.57, 115.23, 83.45, 72.32, 57.04, 38.04, 29.92, 21.51, 21.48. HRMS (ESI) calcd for $C_{28}H_{29}N_2O_4$ *m/z* $[M+H]^+$: 457.2127; found: 457.2137. $[\alpha]_D^{22}$= -10.5 (c 1.03, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 90/10, 1.0 mL/min, 254 nm, 22°C), 18.6 (major), 22.6 min, 88% ee.

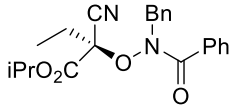


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-5-phenylpentanoate (4r): colorless oil; 88% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.56 (m, 2H), 7.50 – 7.43 (m, 1H), 7.43 – 7.36 (m, 2H), 7.30 – 7.23 (m, 5H), 7.23 – 7.14 (m, 3H), 7.13 – 7.06 (m, 2H), 5.10 – 4.99 (m, 1H), 4.99 – 4.85 (m, 2H), 2.61 (t, *J* = 7.5 Hz, 2H), 2.10 – 1.95 (m, 2H), 1.89 – 1.65 (m, 2H), 1.26 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.95, 164.62, 140.74, 135.09, 133.89, 131.68, 128.65, 128.65, 128.65, 128.58, 128.58, 128.58, 128.56, 128.56, 128.55, 128.54, 128.44, 128.44, 128.16, 126.24, 115.42, 83.80, 72.25, 56.99, 35.79, 35.05, 25.27, 21.55, 21.55. HRMS (ESI) calcd for $C_{29}H_{31}N_2O_4$ *m/z* $[M+H]^+$: 471.2284; found: 471.2281. $[\alpha]_D^{22}$= -1.8 (c 1.47, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 85/15, 1.0 mL/min, 254 nm, 22°C), 11.3 (major), 12.7 min, 90% ee.

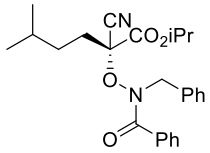


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanopropanoate (4s): colorless oil; 82% yield; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.70 – 7.64 (m, 2H), 7.59 – 7.51 (m, 1H), 7.47 (dd, *J* = 8.2, 6.5 Hz, 2H), 7.33 (dd, *J* = 5.1, 1.9 Hz, 3H), 7.25 (dd, *J* = 6.9, 2.9 Hz, 2H), 5.14 – 5.06 (m, 1H), 5.04 – 4.90 (m, 2H), 1.80 (s, 3H), 1.33 (dd, *J* = 6.3, 4.1 Hz, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 173.79, 164.59, 135.01, 133.77, 131.64, 128.65, 128.65, 128.58, 128.58, 128.53, 128.53, 128.49, 128.49, 128.10, 116.02, 79.52, 72.26, 56.80, 23.10, 21.45, 21.41. HRMS (ESI) calcd for $C_{21}H_{23}N_2O_4$ *m/z* $[M+H]^+$:

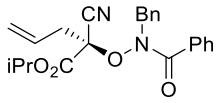
367.1658; found: 367.1673. $[\alpha]_D^{22}$= -5.4 (c 0.42, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 90/10, 1.0 mL/min, 254 nm, 22°C), 16.8 (major), 18.4 min, 83% ee.



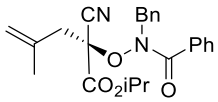
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanobutanoate (4t): colorless oil; 96% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 (dd, *J* = 7.2, 1.7 Hz, 2H), 7.54 – 7.47 (m, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.33 – 7.25 (m, 3H), 7.24 – 7.16 (m, 2H), 5.14 – 5.02 (m, 1H), 5.01 – 4.85 (m, 2H), 2.08 (q, *J* = 7.4 Hz, 2H), 1.30 (dd, *J* = 6.3, 2.3 Hz, 6H), 1.04 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.90, 164.66, 135.12, 135.12, 133.94, 131.66, 131.66, 128.69, 128.68, 128.68, 128.64, 128.57, 128.57, 128.14, 115.37, 84.70, 72.15, 56.94, 30.10, 21.58, 21.56, 8.18. HRMS (ESI) calcd for $C_{22}H_{25}N_2O_4$ *m/z* $[M+H]^+$: 381.1814; found: 381.1819. $[\alpha]_D^{22}$= -1.8 (c 1.2, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 85/15, 1.0 mL/min, 254 nm, 22°C), 10.9 (major), 12.7 min, 92% ee.



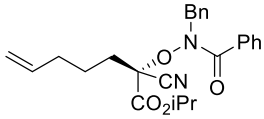
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-5-methylhexanoate (4u): colorless oil; 90% yield; ^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.68 – 7.62 (m, 2H), 7.53 (d, *J* = 7.2 Hz, 1H), 7.46 (dd, *J* = 8.2, 6.5 Hz, 2H), 7.33 (dd, *J* = 5.3, 1.9 Hz, 3H), 7.24 (dd, *J* = 6.9, 2.8 Hz, 2H), 5.16 – 5.06 (m, 1H), 5.06 – 4.89 (m, 2H), 2.04 (dd, *J* = 9.5, 7.5 Hz, 2H), 1.58 – 1.51 (m, 1H), 1.44 – 1.37 (m, 1H), 1.33 (dd, *J* = 6.3, 2.1 Hz, 6H), 1.29 – 1.19 (m, 1H), 0.89 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, Chloroform-*d*) δ 173.75, 164.65, 135.13, 133.97, 131.49, 128.59, 128.59, 128.54, 128.54, 128.50, 128.50, 128.45, 128.44, 128.03, 115.42, 84.17, 72.04, 56.78, 34.45, 32.27, 27.73, 22.19, 22.14, 21.50, 21.46. HRMS (ESI) calcd for $C_{25}H_{31}N_2O_4$ *m/z* $[M+H]^+$: 423.2284; found: 423.2296. $[\alpha]_D^{22}$= -4.3 (c 2.37, $CHCl_3$); HPLC analysis: Chiralcel IE (Hex/IPA = 90/10, 1.0 mL/min, 254 nm, 22°C), 15.3 (major), 21.3 min, 92% ee.



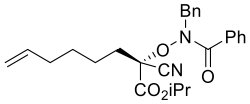
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanopent-4-enoate (4v): colorless oil; 94% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 – 7.59 (m, 2H), 7.55 – 7.48 (m, 1H), 7.47 – 7.40 (m, 2H), 7.32 – 7.25 (m, 3H), 7.23 – 7.17 (m, 2H), 5.78 – 5.64 (m, 1H), 5.26 (d, *J* = 14.0 Hz, 2H), 5.11 – 5.02 (m, 1H), 5.00 – 4.86 (m, 2H), 2.82 – 2.75 (m, 2H), 1.28 (d, *J* = 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.82, 164.04, 135.00, 133.83, 131.72, 128.69, 128.68, 128.64, 128.64, 128.61, 128.61, 128.19, 128.19, 128.16, 128.16, 122.31, 99.99, 83.28, 72.36, 57.04, 40.66, 21.59, 21.59. HRMS (ESI) calcd for $C_{23}H_{25}N_2O_4$ *m/z* $[M+H]^+$: 393.1814; found: 393.1875. $[\alpha]_D^{22}$= -0.7 (c 1.18, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 85/15, 1.0 mL/min, 254 nm, 22°C), 10.4 (major), 11.6 min, 92% ee.



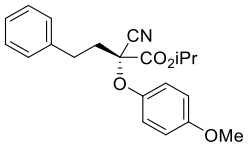
isopropyl 2-((N-benzylbenzamido)oxy)-2-cyano-4-methylpent-4-enoate (4w): colorless oil; 78% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 – 7.59 (m, 2H), 7.53 – 7.47 (m, 1H), 7.42 (t, *J* = 7.4 Hz, 2H), 7.30 – 7.25 (m, 3H), 7.23 – 7.16 (m, 2H), 5.13 – 5.02 (m, 1H), 4.99 (d, *J* = 3.6 Hz, 1H), 4.94 (d, *J* = 9.1 Hz, 1H), 4.90 (d, *J* = 2.6 Hz, 1H), 2.75 (d, *J* = 4.6 Hz, 2H), 1.77 (s, 3H), 1.30 (dd, *J* = 6.4, 2.7 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.94, 164.31, 137.08, 135.13, 133.87, 131.73, 128.71, 128.71, 128.63, 128.62, 128.59, 128.59, 128.50, 128.50, 128.12, 117.98, 115.53, 99.96, 83.46, 72.35, 44.03, 23.42, 21.63, 21.56. HRMS (ESI) calcd for $C_{24}H_{26}N_2O_4$ *m/z* $[M+H]^+$: 407.1971; found: 407.2003. $[\alpha]_D^{22}$= -5.6 (c 0.62, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 85/15, 1.0 mL/min, 254 nm, 22°C), 9.3 (major), 10.3 min, 94% ee.



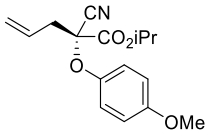
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanohept-6-enoate (4x): colorless oil; 92% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.58 (m, 2H), 7.54 – 7.47 (m, 1H), 7.46 – 7.39 (m, 2H), 7.33 – 7.27 (m, 3H), 7.23 – 7.17 (m, 2H), 5.78 – 5.63 (m, 1H), 5.11 – 5.04 (m, 1H), 5.03 – 4.98 (m, 1H), 4.98 – 4.94 (m, 2H), 4.93 – 4.86 (m, 2H), 2.08 – 1.99 (m, 4H), 1.58 – 1.39 (m, 1H), 1.29 (dd, *J* = 6.2, 1.4 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.95, 164.71, 137.07, 135.10, 135.10, 133.91, 131.68, 128.68, 128.67, 128.64, 128.58, 128.56, 128.56, 128.15, 115.86, 115.45, 100.01, 83.88, 72.22, 56.98, 35.76, 32.90, 22.85, 21.58, 21.54. HRMS (ESI) calcd for $C_{25}H_{29}N_2O_4$ *m/z* $[M+H]^+$: 421.2127; found: 421.2133. $[\alpha]_D^{22}$= -1.6 (c 1.46, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 85/15, 1.0 mL/min, 254 nm, 22°C), 9.4 (major), 10.7 min, 86% ee.



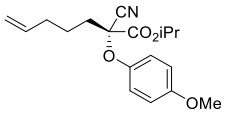
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanooct-7-enoate (4y): colorless oil; 89% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 – 7.58 (m, 2H), 7.50 (t, *J* = 7.4 Hz, 1H), 7.43 (s, 1H), 7.32 – 7.26 (m, 4H), 7.20 (dd, *J* = 6.8, 2.5 Hz, 2H), 5.80 – 5.67 (m, 1H), 5.13 – 5.03 (m, 1H), 5.02 – 4.98 (m, 1H), 4.98 – 4.93 (m, 2H), 4.91 (s, 1H), 2.12 – 1.94 (m, 4H), 1.56 – 1.33 (m, 4H), 1.29 (d, *J* = 6.1 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 173.92, 164.71, 138.05, 135.11, 133.94, 131.66, 128.68, 128.68, 128.68, 128.64, 128.64, 128.58, 128.58, 128.58, 128.15, 115.49, 115.09, 83.93, 72.19, 56.95, 36.23, 33.23, 28.28, 23.11, 21.58, 21.54. HRMS (ESI) calcd for $C_{26}H_{31}N_2O_4$ *m/z* $[M+H]^+$: 435.2284; found: 435.2295. $[\alpha]_D^{22}$= -1.8 (c 1.26, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 85/15, 1.0 mL/min, 254 nm, 22°C), 9.2 (major), 10.4 min, 92% ee.



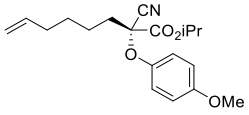
isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)-4-phenylbutanoate (6a): colorless oil; 82% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.28 (m, 2H), 7.28 – 7.20 (m, 3H), 7.12 – 6.99 (m, 2H), 6.89 – 6.78 (m, 2H), 5.15 – 5.01 (m, 1H), 3.78 (s, 3H), 3.14 – 2.98 (m, 1H), 2.98 – 2.83 (m, 1H), 2.62 – 2.37 (m, 2H), 1.27 (d, *J* = 6.3 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.52, 156.40, 148.74, 139.53, 128.79, 128.79, 128.59, 128.59, 126.69, 119.98, 119.98, 116.07, 114.63, 114.62, 79.37, 72.06, 55.69, 40.60, 30.19, 21.56, 21.48. HRMS (ESI) calcd for $C_{21}H_{24}NO_4$ *m/z* $[M+H]^+$: 354.1705; found: 354.1619. $[\alpha]_D^{22}$= +2.5 (c 1.15, $CHCl_3$); HPLC analysis: Chiralcel IG3 (Hex/IPA = 98/2, 1.0 mL/min, 254 nm, 22°C), 17.0, 17.8 (major) min, 90% ee.



isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)pent-4-enoate (6b): colorless oil; 80% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.06 – 7.02 (m, 2H), 6.83 – 6.79 (m, 2H), 5.99 – 5.82 (m, 1H), 5.37 – 5.33 (m, 1H), 5.32 – 5.30 (m, 1H), 5.13 – 5.01 (m, 1H), 3.76 (s, 3H), 3.04 – 2.85 (m, 2H), 1.25 (d, *J* = 6.3 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.05, 156.45, 148.64, 128.58, 122.13, 120.22, 120.21, 115.95, 114.60, 114.60, 79.38, 71.98, 55.67, 43.21, 43.21, 21.54. HRMS (ESI) calcd for $C_{16}H_{20}NO_4$ *m/z* $[M+H]^+$: 290.1392; found: 290.1425. $[\alpha]_D^{22}$= +7.7 (c 0.35, $CHCl_3$); HPLC analysis: Chiralcel IG3 (Hex/IPA = 98/2, 1.0 mL/min, 254 nm, 22°C), 10.9 (major), 11.9 min, 84% ee.

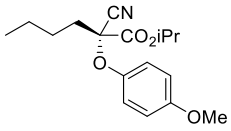


isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)hept-6-enoate (6c): colorless oil; 79% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.03 (d, *J* = 9.1 Hz, 2H), 6.82 (d, *J* = 9.2 Hz, 2H), 5.87 – 5.72 (m, 1H), 5.15 – 5.06 (m, 2H), 5.06 – 5.00 (m, 1H), 3.77 (s, 3H), 2.34 – 2.08 (m, 4H), 1.91 – 1.76 (m, 1H), 1.74 – 1.60 (m, 1H), 1.24 (dd, *J* = 17.6, 6.3 Hz, 6H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.57, 156.26, 148.73, 137.16, 119.86, 116.15, 115.77, 114.51, 114.51, 79.60, 71.75, 55.59, 38.21, 32.90, 22.89, 22.89, 21.47, 21.39. HRMS (ESI) calcd for $C_{18}H_{24}NO_4$ *m/z* $[M+H]^+$: 318.1705; found: 318.1702. $[\alpha]_D^{22}$= +13.2 (c 0.50, $CHCl_3$); HPLC analysis: Chiralcel IG3 (Hex/IPA = 90/10, 1.0 mL/min, 254 nm, 22°C), 5.6 (major), 6.0 min, 88% ee.

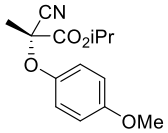


isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)oct-7-enoate (6d): colorless oil; 78% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 – 6.99 (m, 2H), 6.88 – 6.78 (m, 2H),

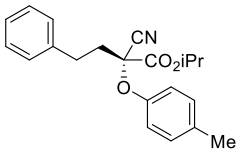
5.89 – 5.72 (m, 1H), 5.14 – 5.03 (m, 2H), 5.03 – 4.94 (m, 1H), 3.77 (s, 3H), 2.30 – 2.03 (m, 4H), 1.82 – 1.65 (m, 1H), 1.63 – 1.57 (m, 1H), 1.56 – 1.45 (m, 2H), 1.26 (d, *J* = 6.2 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.60, 156.25, 148.72, 138.03, 119.86, 116.19, 115.03, 114.51, 114.51, 79.65, 71.72, 55.59, 38.68, 33.28, 28.27, 28.27, 23.12, 21.47, 21.38. HRMS (ESI) calcd for $C_{19}H_{26}NO_4$ *m/z* $[M+H]^+$: 332.1862; found: 332.1874. $[\alpha]_D^{22}$= +10.4 (c 0.24, $CHCl_3$); HPLC analysis: Chiralcel IG3 (Hex/IPA = 98/2, 1.0 mL/min, 254 nm, 22°C), 10.8 (major), 11.8 min, 86% ee.



isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)hexanoate (6e): colorless oil; 75% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.04 (d, *J* = 9.1 Hz, 2H), 6.82 (d, *J* = 9.2 Hz, 2H), 5.16 – 5.03 (m, 1H), 3.77 (s, 3H), 2.30 – 2.10 (m, 2H), 1.79 – 1.63 (m, 1H), 1.54 – 1.49 (m, 1H), 1.43 (q, *J* = 7.1 Hz, 2H), 1.26 (d, *J* = 6.3 Hz, 3H), 1.22 (d, *J* = 6.3 Hz, 3H), 0.96 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.66, 156.24, 119.89, 116.24, 114.51, 114.51, 79.75, 71.66, 55.59, 55.59, 38.58, 25.73, 25.73, 22.22, 21.46, 21.38, 13.72. HRMS (ESI) calcd for $C_{17}H_{24}NO_4$ *m/z* $[M+H]^+$: 306.1705; found: 306.1714. $[\alpha]_D^{22}$= +2.4 (c 0.75, $CHCl_3$); HPLC analysis: Chiralcel IG3 (Hex/IPA = 98/2, 1.0 mL/min, 254 nm, 22°C), 9.2 (major), 10.4 min, 86% ee.

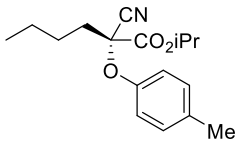


isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)propanoate (6f): colorless oil; 78% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.05 (d, *J* = 9.1 Hz, 2H), 6.83 (d, *J* = 9.1 Hz, 2H), 5.20 – 5.01 (m, 1H), 3.78 (s, 3H), 1.96 (s, 3H), 1.27 (d, *J* = 6.3 Hz, 3H), 1.23 (d, *J* = 6.3 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.78, 156.43, 148.42, 120.33, 116.85, 114.53, 114.53, 75.64, 71.84, 55.59, 55.59, 25.69, 21.41, 21.32. HRMS (ESI) calcd for $C_{14}H_{18}NO_4$ *m/z* $[M+H]^+$: 264.1236; found: 264.1294. $[\alpha]_D^{22}$= +3.1 (c 1.02, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 98/2, 1.0 mL/min, 254 nm, 22°C), 25.4, 32.8 (major) min, 80% ee.

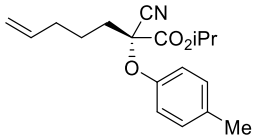


isopropyl (R)-2-cyano-4-phenyl-2-(p-tolyloxy)butanoate (6g): colorless oil; 88% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.28 (m, 2H), 7.25 – 7.16 (m, 4H), 6.94 – 6.83 (m, 3H), 5.14 – 5.06 (m, 1H), 3.14 – 3.01 (m, 1H), 2.98 – 2.85 (m, 1H), 2.61 – 2.40 (m, 2H), 2.34 (s, 3H), 1.28 (d, *J* = 2.6 Hz, 3H), 1.19 (d, *J* = 6.1 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.52, 154.89, 139.91, 139.52, 129.36, 129.36, 128.80, 128.80, 128.59, 128.59, 126.69, 124.67, 118.15, 114.07, 77.70, 72.10, 40.81, 30.18, 21.54, 21.54, 21.39. HRMS (ESI) calcd for $C_{21}H_{24}NO_3$ *m/z* $[M+H]^+$: 338.1756;

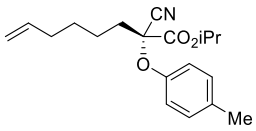
found: 338.1792. $[a]_D^{22}$= +0.4 (c 0.68, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 95/5, 1.0 mL/min, 210 nm, 22°C), 10.5, 18.4 (major) min, 89% ee.



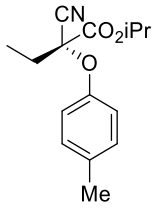
isopropyl (R)-2-cyano-2-(p-tolyloxy)hexanoate (6h): colorless oil; 87% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 7.7 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.87 – 6.81 (m, 2H), 5.15 – 5.07 (m, 1H), 2.32 (s, 3H), 2.29 – 2.13 (m, 2H), 1.80 – 1.66 (m, 1H), 1.63 – 1.55 (m, 1H), 1.48 – 1.40 (m, 2H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.20 (d, *J* = 6.4 Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.78, 154.96, 139.82, 129.30, 129.30, 124.49, 124.49, 118.07, 114.01, 114.01, 78.09, 71.82, 38.88, 25.79, 22.31, 21.40, 13.85. HRMS (ESI) calcd for $C_{17}H_{24}NO_3$ *m/z* $[M+H]^+$: 290.1756; found: 290.1775. $[a]_D^{22}$= +67.1 (c 0.12, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 95/5, 1.0 mL/min, 215 nm, 22°C), 6.0, 12.9 (major) min, 89% ee.



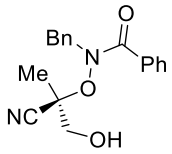
isopropyl (R)-2-cyano-2-(p-tolyloxy)hept-6-enoate (6i): colorless oil; 83% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 7.7 Hz, 1H), 6.92 – 6.87 (m, 1H), 6.86 – 6.80 (m, 2H), 5.88 – 5.72 (m, 1H), 5.15 – 5.07 (m, 1H), 5.07 – 5.00 (m, 2H), 2.32 (s, 3H), 2.27 – 2.15 (m, 4H), 1.92 – 1.80 (m, 1H), 1.75 – 1.64 (m, 1H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.19 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.69, 154.93, 139.84, 137.26, 129.31, 124.53, 118.06, 115.90, 114.00, 100.00, 77.96, 71.91, 38.49, 32.97, 30.28, 22.94, 21.53, 21.40. HRMS (ESI) calcd for $C_{18}H_{24}NO_3$ *m/z* $[M+H]^+$: 302.1756; found: 302.1754. $[a]_D^{22}$= +2.2 (c 0.50, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 95/5, 1.0 mL/min, 210 nm, 22°C), 7.1, 15.3 (major) min, 86% ee.



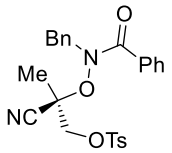
isopropyl (R)-2-cyano-2-(p-tolyloxy)oct-7-enoate (6j): colorless oil; 78% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.18 (t, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.87 – 6.81 (m, 2H), 5.87 – 5.74 (m, 1H), 5.15 – 5.07 (m, 1H), 5.07 – 4.95 (m, 2H), 2.32 (s, 3H), 2.28 – 2.16 (m, 2H), 2.12 (q, *J* = 7.0 Hz, 2H), 1.82 – 1.70 (m, 1H), 1.66 – 1.59 (m, 1H), 1.54 – 1.48 (m, 2H), 1.29 (d, *J* = 1.4 Hz, 3H), 1.20 (d, *J* = 1.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.71, 154.93, 139.83, 138.14, 129.30, 124.52, 118.08, 116.15, 115.14, 114.01, 100.00, 78.01, 71.87, 38.98, 33.38, 28.34, 23.19, 21.53, 21.39. HRMS (ESI) calcd for $C_{19}H_{26}NO_3$ *m/z* $[M+H]^+$: 316.1913; found: 316.1902. $[a]_D^{22}$= +1.5 (c 0.56, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 95/5, 1.0 mL/min, 210 nm, 22°C), 6.5, 13.4 (major) min, 89% ee.



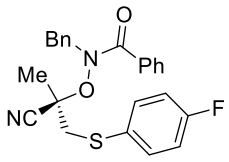
isopropyl (R)-2-cyano-2-(p-tolyloxy)butanoate (6k): colorless oil; 80% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.17 (t, *J* = 7.7 Hz, 1H), 6.88 (d, *J* = 7.7 Hz, 1H), 6.86 – 6.80 (m, 2H), 5.15 – 5.07 (m, 1H), 2.31 (s, 3H), 2.30 – 2.18 (m, 2H), 1.33 – 1.23 (m, 6H), 1.20 (d, *J* = 31.9 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.60, 155.01, 129.64, 129.64, 123.73, 123.73, 117.32, 117.32, 116.00, 78.78, 71.89, 32.83, 21.54, 21.39, 8.19. HRMS (ESI) calcd for $C_{15}H_{20}NO_4$ *m/z* $[M+H]^+$: 262.1443; found: 262.1412. $[\alpha]_D^{22}$= +2.9 (c 1.04, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 95/5, 1.0 mL/min, 210 nm, 22°C), 8.8, 21.4 (major) min, 86% ee.



(R)-N-benzyl-N-((2-cyano-1-hydroxypropan-2-yl)oxy)benzamide (7): colorless oil; 80% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 – 7.62 (m, 2H), 7.61 – 7.54 (m, 1H), 7.53 – 7.46 (m, 2H), 7.34 – 7.29 (m, 3H), 7.11 (dt, *J* = 6.1, 3.4 Hz, 2H), 5.01 (q, *J* = 16.0 Hz, 2H), 4.70 – 4.41 (m, 1H), 3.94 (dd, *J* = 12.9, 3.5 Hz, 1H), 3.60 (dd, *J* = 12.9, 11.0 Hz, 1H), 1.72 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 175.90, 134.66, 133.29, 132.10, 129.40, 128.95, 128.78, 128.74, 128.68, 128.32, 128.22, 128.10, 128.07, 128.02, 118.46, 77.46, 77.14, 76.82, 66.66, 56.78, 20.39. HRMS (ESI) calcd for $C_{18}H_{19}N_2O_3$ *m/z* $[M+H]^+$: 311.1390; found: 311.1382.

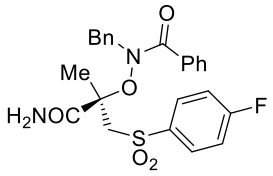


(R)-2-((N-benzylbenzamido)oxy)-2-cyanopropyl 4-methylbenzenesulfonate (7-Ts): colorless oil; 80% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 – 7.72 (m, 2H), 7.61 – 7.54 (m, 2H), 7.54 – 7.48 (m, 1H), 7.44 (dd, *J* = 8.1, 6.8 Hz, 2H), 7.34 (d, *J* = 8.2 Hz, 2H), 7.30 (dp, *J* = 6.6, 2.0 Hz, 3H), 7.15 (dd, *J* = 6.6, 2.9 Hz, 2H), 4.97 (d, *J* = 16.0 Hz, 1H), 4.88 (d, *J* = 15.7 Hz, 1H), 4.15 (d, *J* = 10.3 Hz, 1H), 4.09 (d, *J* = 10.4 Hz, 1H), 2.47 (s, 3H), 1.60 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.03, 173.76, 135.53, 133.84, 131.79, 131.13, 131.04, 128.88, 128.60, 128.29, 128.20, 127.96, 116.45, 116.22, 86.21, 77.35, 77.04, 76.72, 62.93, 58.72, 30.94, 22.15. HRMS (ESI) calcd for $C_{25}H_{25}N_2O_5S$ *m/z* $[M+H]^+$: 465.1479; found: 465.1456.

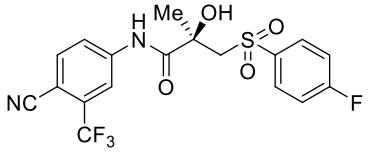


(R)-N-benzyl-N-((2-cyano-1-((4-fluorophenyl)thio)propan-2-yl)oxy)benzamide

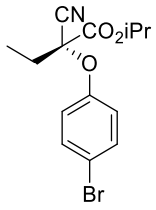
(8): colorless oil; 80% yield; ^{11}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.52 (m, 2H), 7.52 – 7.45 (m, 1H), 7.45 – 7.34 (m, 4H), 7.33 – 7.22 (m, 3H), 7.23 – 7.09 (m, 2H), 7.05 – 6.88 (m, 2H), 5.01 (d, *J* = 13.5 Hz, 2H), 3.27 (d, *J* = 14.2 Hz, 1H), 3.14 (d, *J* = 14.2 Hz, 1H), 1.62 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 174.35, 163.75, 161.28, 135.20, 134.26, 134.18, 133.86, 131.70, 130.09, 130.05, 128.63, 128.60, 128.52, 128.43, 128.10, 118.94, 116.43, 116.21, 80.65, 77.38, 77.07, 76.75, 56.80, 43.94, 29.71, 23.64. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -113.32, -113.34.HRMS (ESI) calcd for $C_{24}H_{22}FN_2O_2S$ *m/z* $[M+H]^+$: 421.1381.; found: 421.1389.



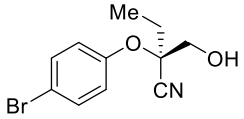
(R)-N-((1-amino-3-((4-fluorophenyl)sulfonyl)-2-methyl-1-oxopropan-2-yl)oxy)-N-benzylbenzamide (8-amide): colorless oil; 80% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.70 (s, 1H), 8.03 – 7.87 (m, 2H), 7.63 – 7.57 (m, 2H), 7.57 – 7.52 (m, 1H), 7.52 – 7.41 (m, 2H), 7.36 – 7.30 (m, 3H), 7.25 (dd, *J* = 7.3, 2.3 Hz, 2H), 7.23 – 7.17 (m, 2H), 5.68 – 5.46 (m, 1H), 5.19 (d, *J* = 16.1 Hz, 1H), 4.90 (d, *J* = 16.1 Hz, 1H), 4.07 (d, *J* = 14.6 Hz, 1H), 3.54 (d, *J* = 14.6 Hz, 1H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.03, 173.76, 135.53, 133.84, 131.79, 131.13, 131.04, 128.88, 128.60, 128.29, 128.20, 127.96, 116.45, 116.22, 86.21, 77.36, 77.04, 76.72, 62.94, 58.71, 22.16. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -108.78, -108.80. HRMS (ESI) calcd for $C_{24}H_{24}FN_2O_5S$ *m/z* $[M+H]^+$: 471.1384; found: 471.1399.



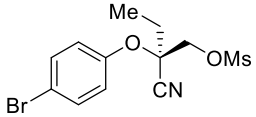
(R)-N-(4-cyano-3-(trifluoromethyl)phenyl)-3-((4-fluorophenyl)sulfonyl)-2-hydroxy-2-methylpropanamide ((R)-Bicalutamide): white solid; 78% yield; M.P.: 176-178 ^{o}C ^{1}H NMR (400 MHz, DMSO-d6): δ 10.35 (s, 1H), 8.43 (s, 1H), 8.20 (d, J = 8.5 Hz, 1H), 8.06 (d, J = 8.5 Hz, 1H), 7.94−7.90 (t, 2H), 7.36−7.30 (m, 2H), 6.39 (s, 1H), 3.95 (d, J = 14.7 Hz, 1H), 3.71 (d, J = 14.7 Hz, 1H), 1.41 (s, 3H). ^{13}C NMR (100 MHz, DMSOd6): δ 173.9, 165.6, 164.1, 143.2, 137.2, 137.2, 136.3, 131.9, 131.6, 131.4, 131.2, 125.3, 123.4, 122.9, 122.8, 121.6, 119.8, 117.6, 116.1, 115.9, 115.8, 102.0, 73.1, 63.5, 27.2. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -62.50, -102.82, -103.40. HRMS (ESI) calcd for $C_{18}H_{15}F_4N2O_4S$ *m/z* $[M+H]^+$: 431.0683; found: 431.0672. $[\alpha]_D^{22}$= +7.9 (c 1.04, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 75/25, 1.0 mL/min, 210 nm, 22°C),16.6 (major), 19.9 min, 82% ee.



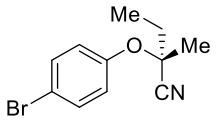
isopropyl (R)-2-(4-bromophenoxy)-2-cyanobutanoate (6l): colorless oil; 65% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.32 (m, 2H), 7.02 – 6.82 (m, 2H), 5.23 – 4.97 (m, 1H), 2.39 – 2.07 (m, 2H), 1.29 (d, *J* = 6.3 Hz, 3H), 1.23 – 1.20 (m, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 165.14, 154.03, 132.51, 119.17, 116.42, 115.58, 78.83, 77.36, 77.04, 76.73, 72.13, 32.70, 21.48, 21.37, 8.09. HRMS (ESI) calcd for $C_{14}H_{17}BrNO_3$ *m/z* $[M+H]^+$: 326.0386; found: 326.0389. $[\alpha]_D^{22}$= +2.2 (c 0.94, $CHCl_3$); HPLC analysis: Chiralcel IG3 (Hex/IPA = 99/1, 1.0 mL/min, 215 nm, 22°C), 15.0, 16.1 (major) min, 84% ee.



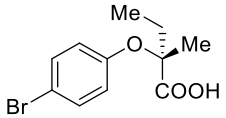
(R)-2-(4-bromophenoxy)-2-(hydroxymethyl)butanenitrile (11): colorless oil; 87% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 – 7.39 (m, 2H), 7.24 – 6.91 (m, 2H), 3.92 (q, *J* = 12.0 Hz, 2H), 2.02 (q, *J* = 7.5 Hz, 2H), 1.12 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.05, 132.74, 123.50, 118.01, 80.95, 77.39, 77.07, 76.76, 64.92, 27.18, 8.18. HRMS (ESI) calcd for $C_{11}H_{13}BrNO_2$ *m/z* $[M+H]^+$: 270.0124; found: 270.0118.



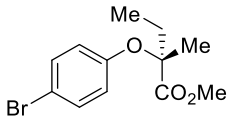
(R)-2-(4-bromophenoxy)-2-cyanobutyl methanesulfonate (11-Ms): colorless oil; 90% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.70 – 7.37 (m, 2H), 7.18 – 6.92 (m, 2H), 2.14 (dd, *J* = 13.9, 7.3 Hz, 1H), 2.08 – 1.87 (m, 1H), 1.72 (s, 3H), 1.32 – 1.18 (m, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.85, 149.20, 132.72, 122.84, 119.80, 119.29, 117.21, 77.36, 77.05, 76.73, 44.83, 31.81, 29.71, 22.89, 9.76. HRMS (ESI) calcd for $C_{12}H_{15}BrNO_4S$ *m/z* $[M+H]^+$: 347.9900; found: 347.9912.



(R)-2-(4-bromophenoxy)-2-methylbutanenitrile (12): colorless oil; 77% yield; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.62 – 7.43 (m, 2H), 7.11 – 6.95 (m, 2H), 2.14 (dd, *J* = 13.9, 7.3 Hz, 1H), 1.97 (dd, *J* = 13.8, 7.5 Hz, 1H), 1.72 (s, 3H), 1.19 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) 149.20, 132.72, 122.84, 119.80, 119.29, 77.36, 77.05, 76.73, 44.83, 31.81, 29.71, 22.89, 9.76. HRMS (ESI) calcd for $C_{11}H_{13}BrNO$ *m/z* $[M+H]^+$: 254.0175; found: 254.0165.



(R)-2-(4-bromophenoxy)-2-methylbutanoic acid (13): colorless pelle; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.9 (b, 1H), δ 7.64 – 7.50 (m, 2H), 7.12 – 6.93 (m, 2H), 2.05 (q, *J* = 7.6 Hz, 2H), 1.57 (s, 3H), 0.95 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) 171.54, 149.60, 133.40, 132.57, 123.39, 123.13, 119.10, 55.43, 51.64, 29.66, 22.43, 9.77. HRMS (ESI) calcd for $C_{11}H_{14}BrO_3$ *m/z* $[M+H]^+$: 273.0121; found: 273.0110.



(R)-2-(4-bromophenoxy)-2-cyanobutyl methanesulfonate (13-Me): colorless oil; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 – 7.37 (m, 2H), 7.06 – 6.78 (m, 2H), 3.79 (s, 3H), 2.03 (q, *J* = 7.6 Hz, 2H), 1.53 (s, 3H), 0.97 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) 170.61, 149.68, 132.50, 132.47, 123.39, 123.13, 119.10, 77.38, 77.06, 76.74, 54.43, 52.64, 28.66, 19.43, 8.77. HRMS (ESI) calcd for $C_{12}H_{16}BrO_3$ *m/z* $[M+H]^+$: 287.0277; found: 287.0270. $[\alpha]_D^{22}$= +4.2 (c 0.34, $CHCl_3$); HPLC analysis: Chiralcel OJH (Hex/IPA = 99/1, 1.0 mL/min, 210 nm, 22°C), 12.1, 23.5 (major) min, 82% ee.

11. Determination of the Absolute Configuration by X-ray Crystallography

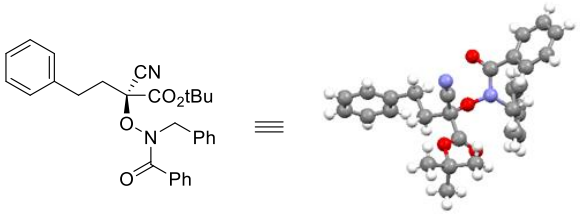


Figure 10.1 X-ray Crystallography of modified **4r** (CDCC 2044133)

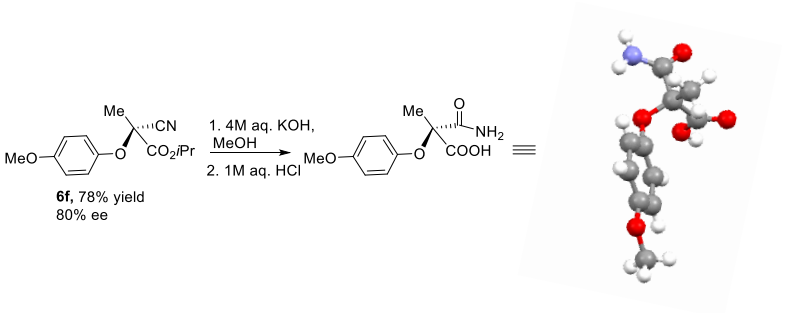
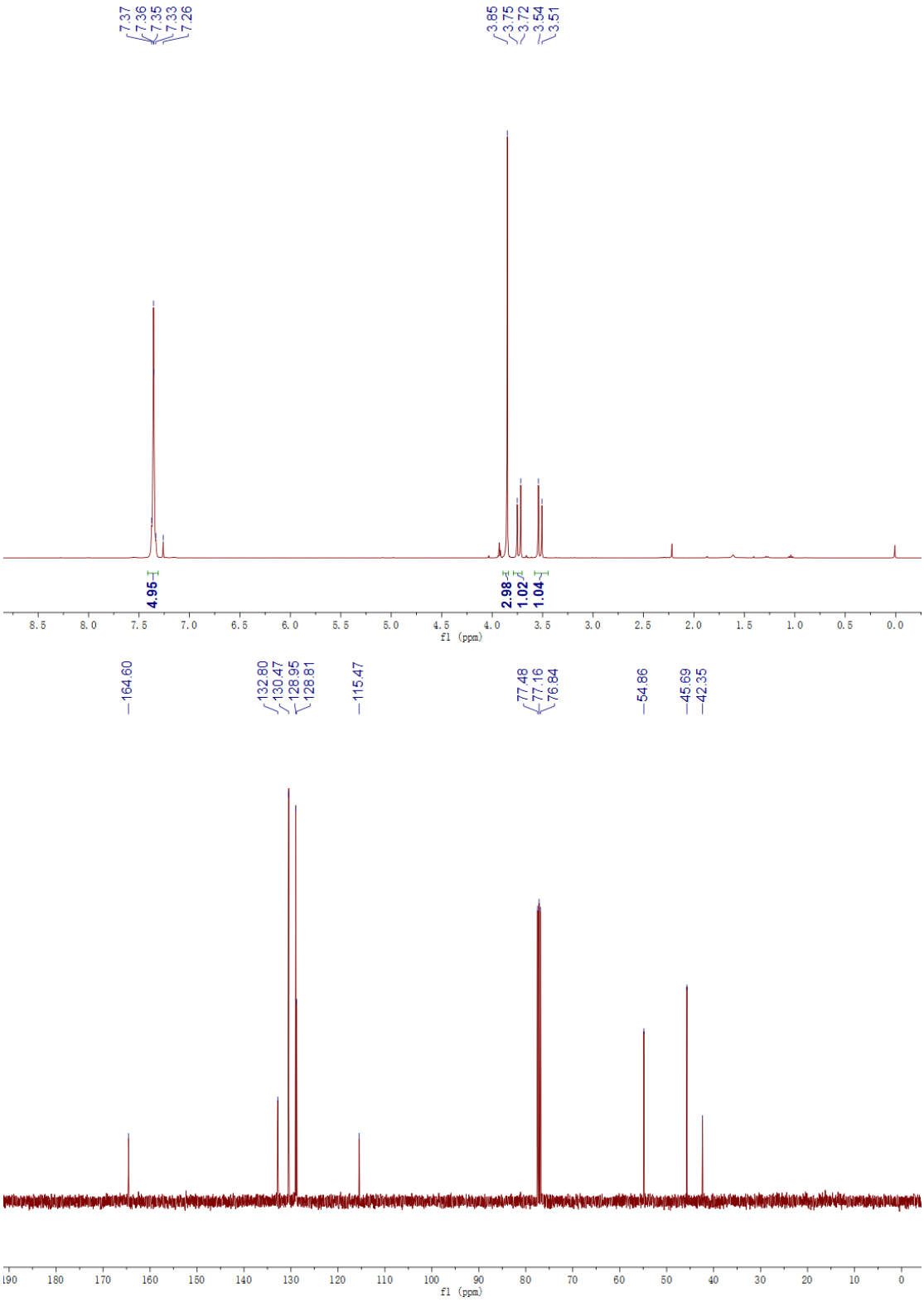


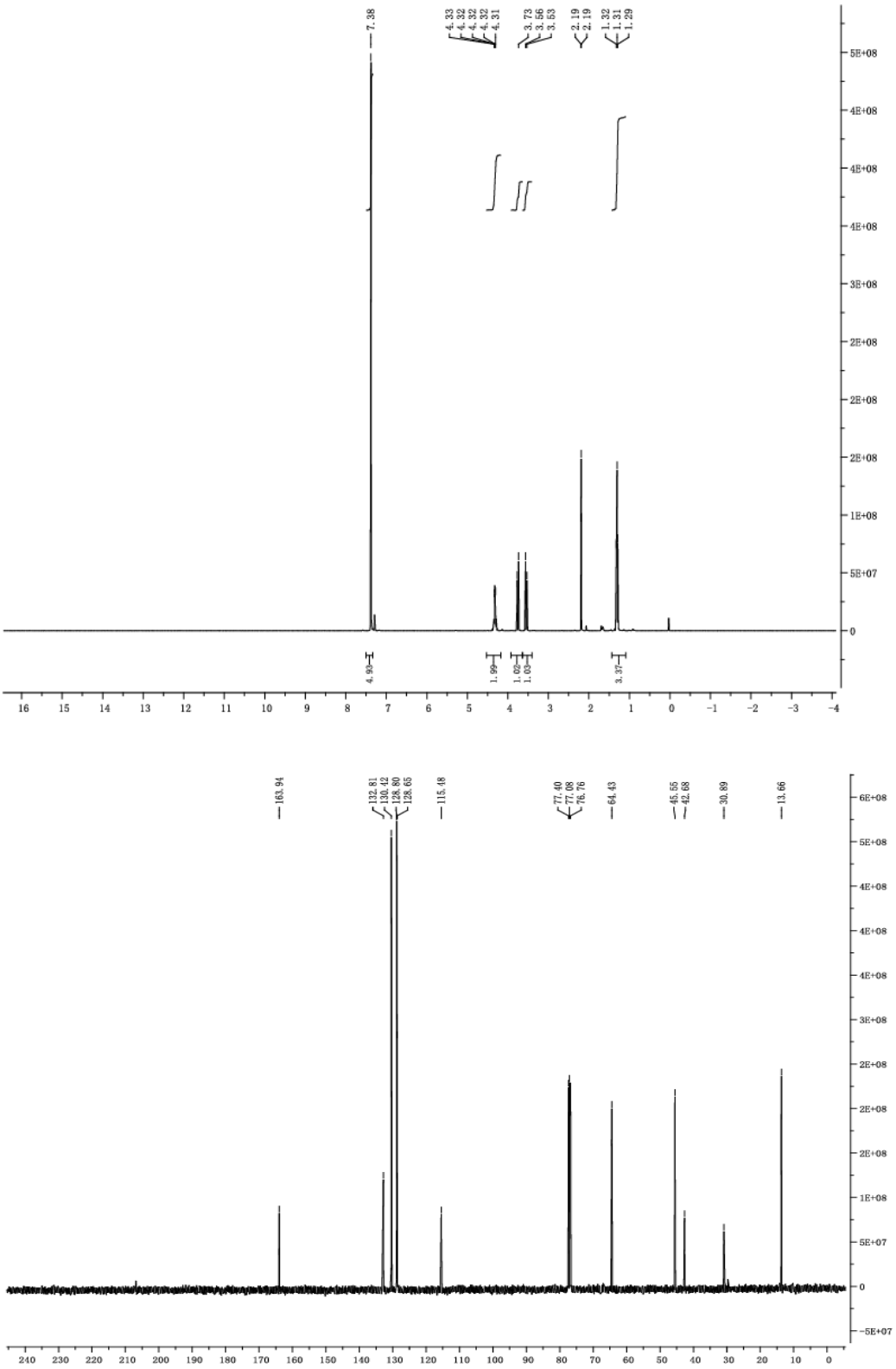
Figure 10.2 X-ray Crystallography of hydrolysis of **6f** (CCDC 2059577)

12. NMR spectra

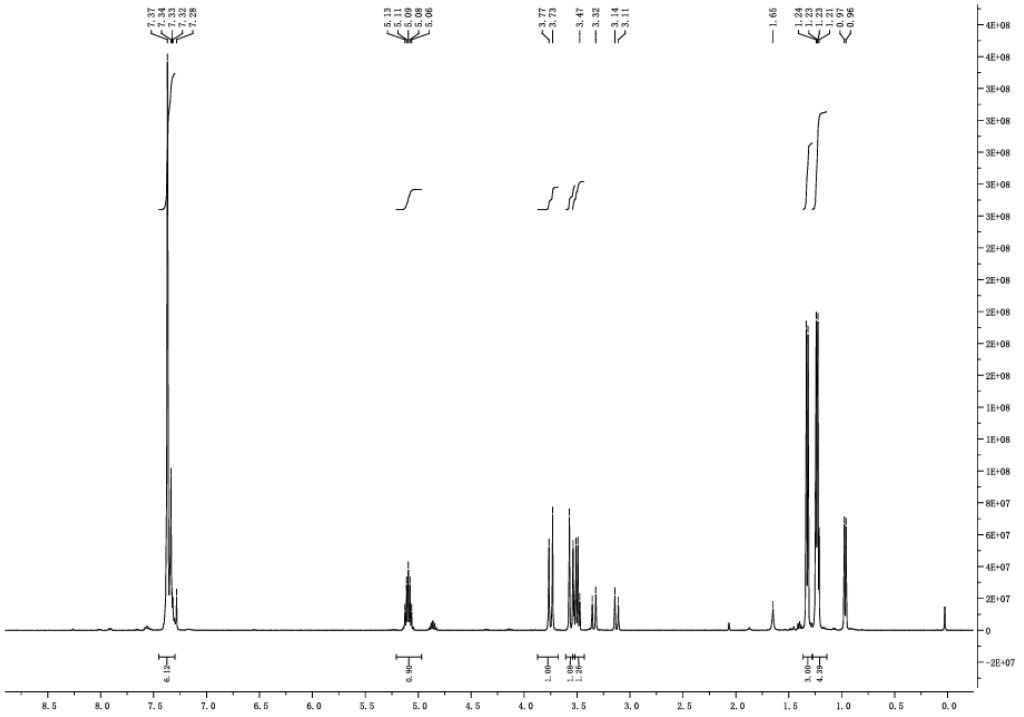
Methyl 2-bromo-2-cyano-3-phenylpropanoate (1a)

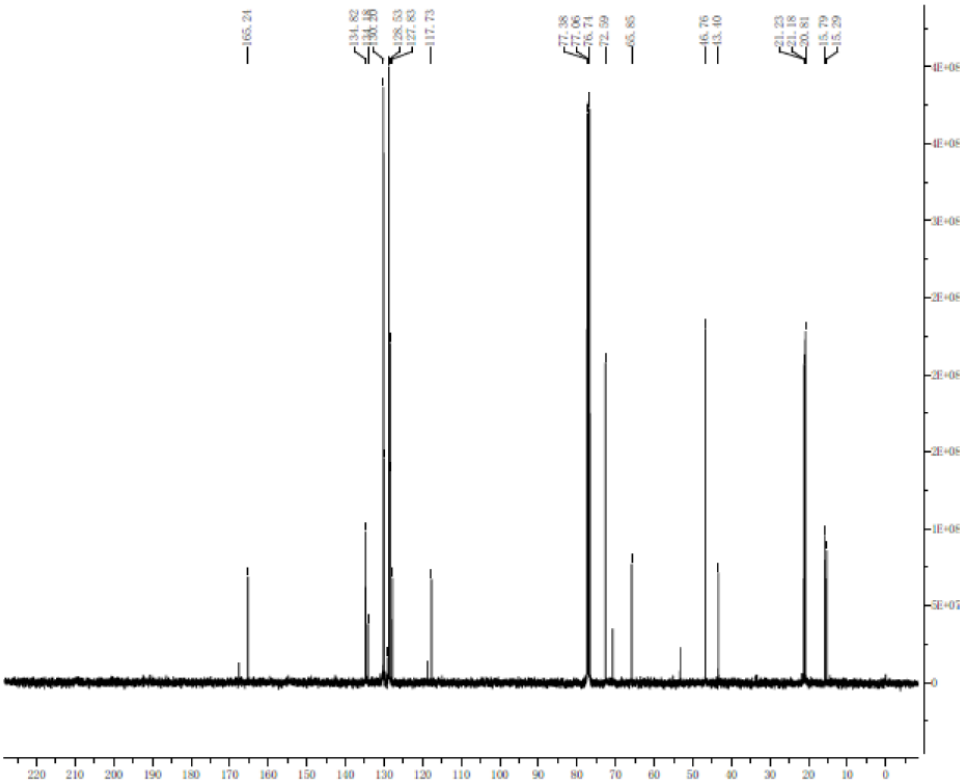


Ethyl 2-bromo-2-cyano-3-phenylpropanoate (1b)

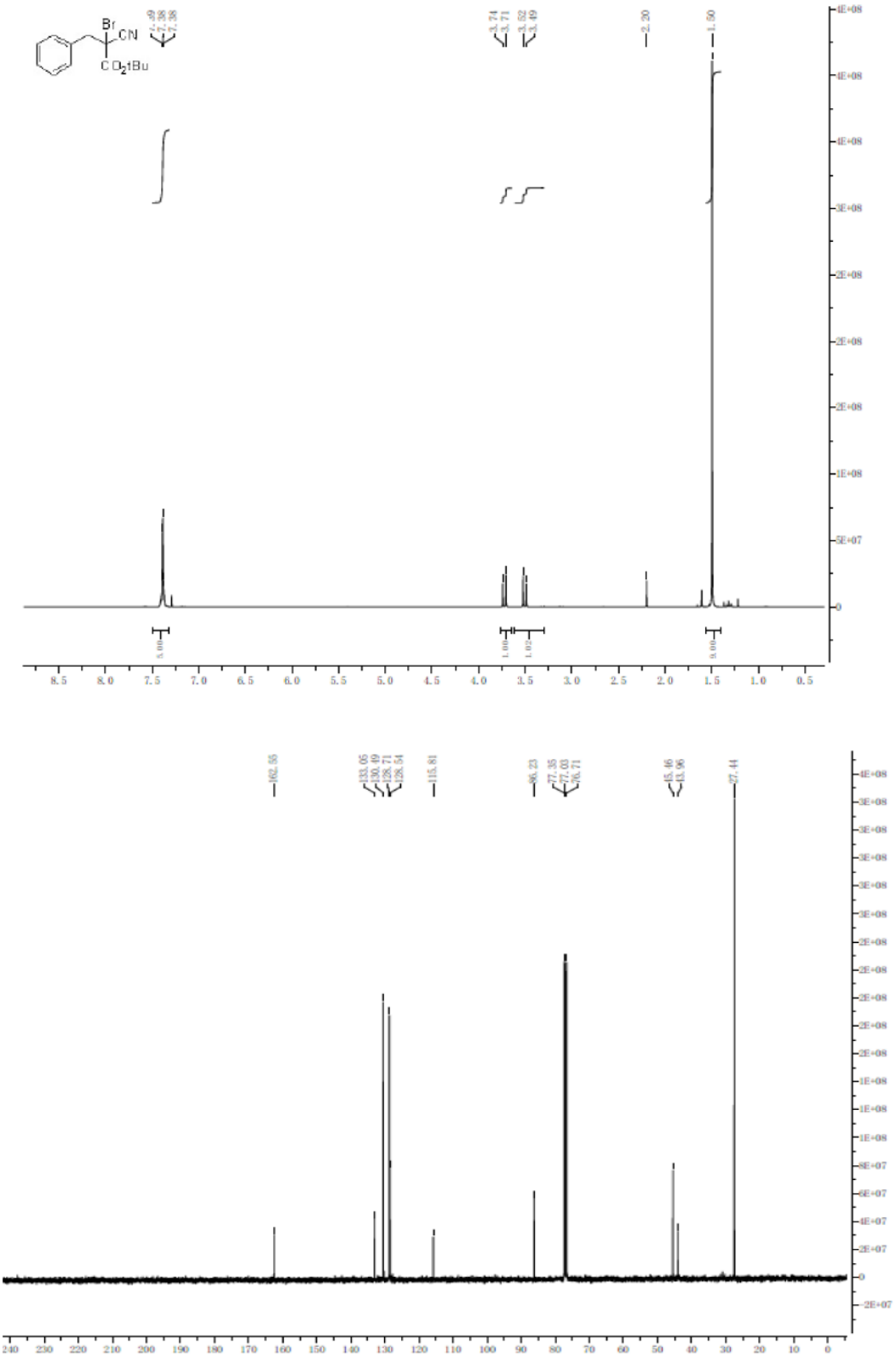


Isopropyl 2-cyano-2-bromo-3-phenylpropanoate (1c)

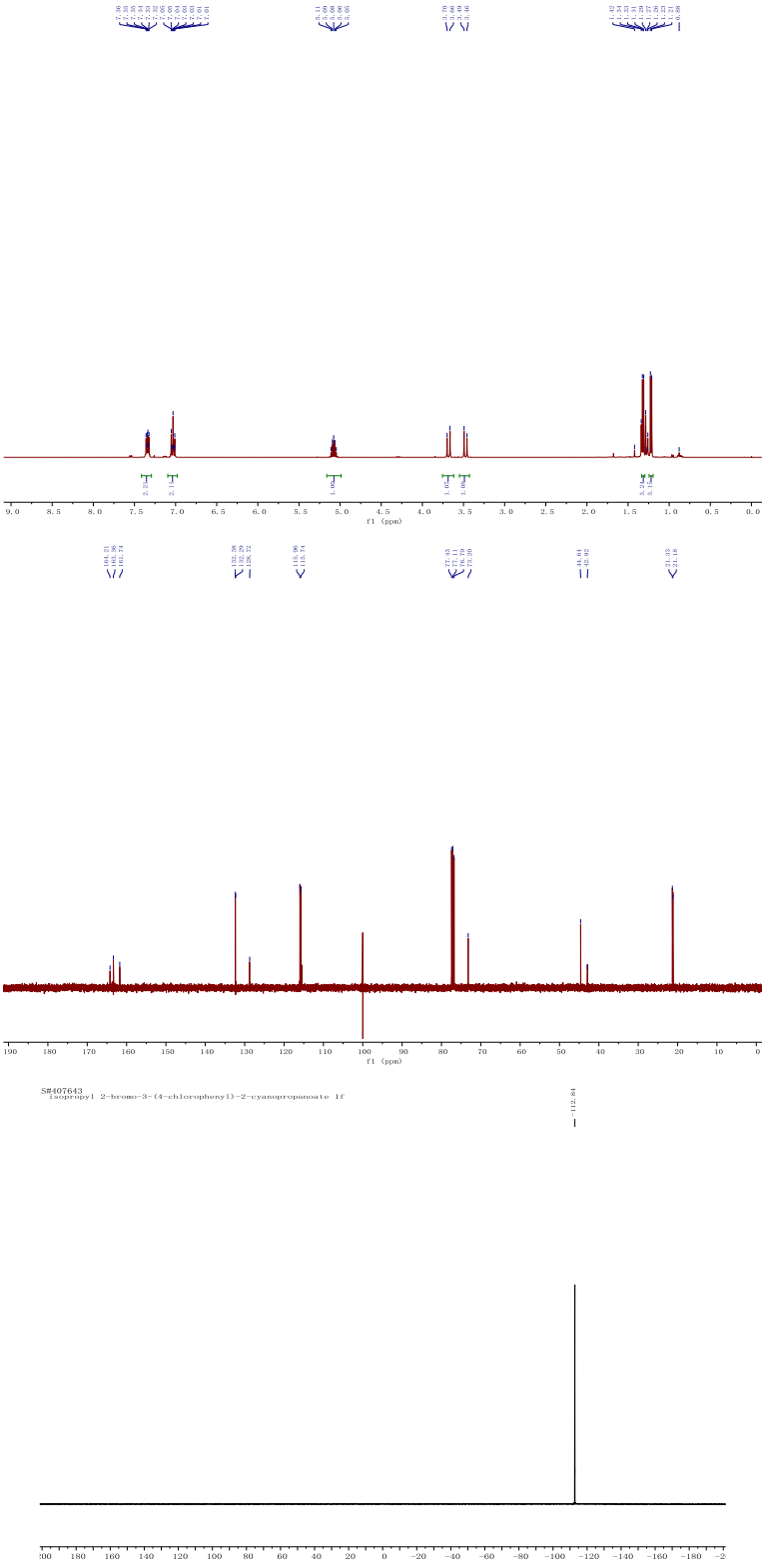




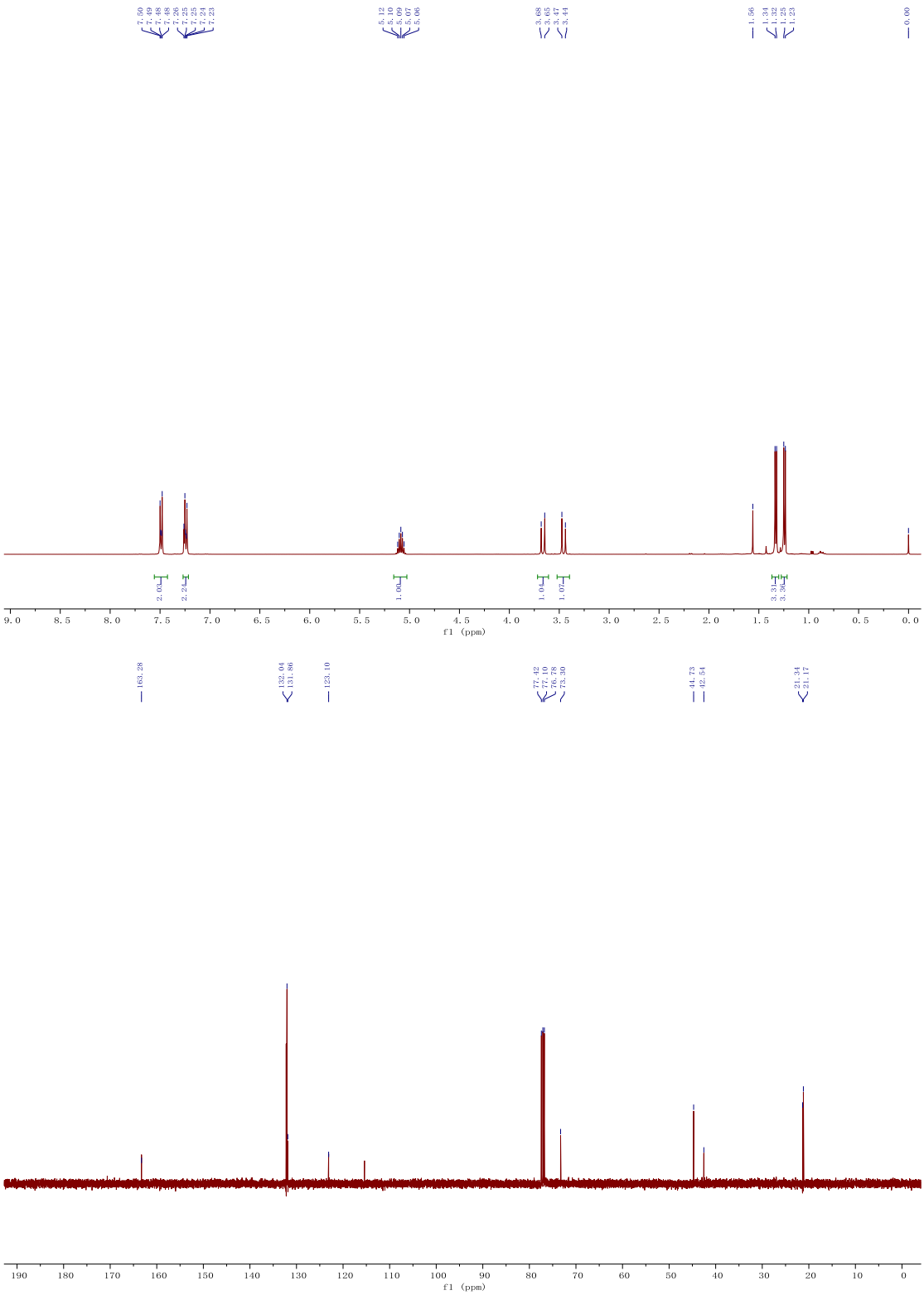
tert-Butyl 2-bromo-2-cyano-3-phenylpropanoate (1d)



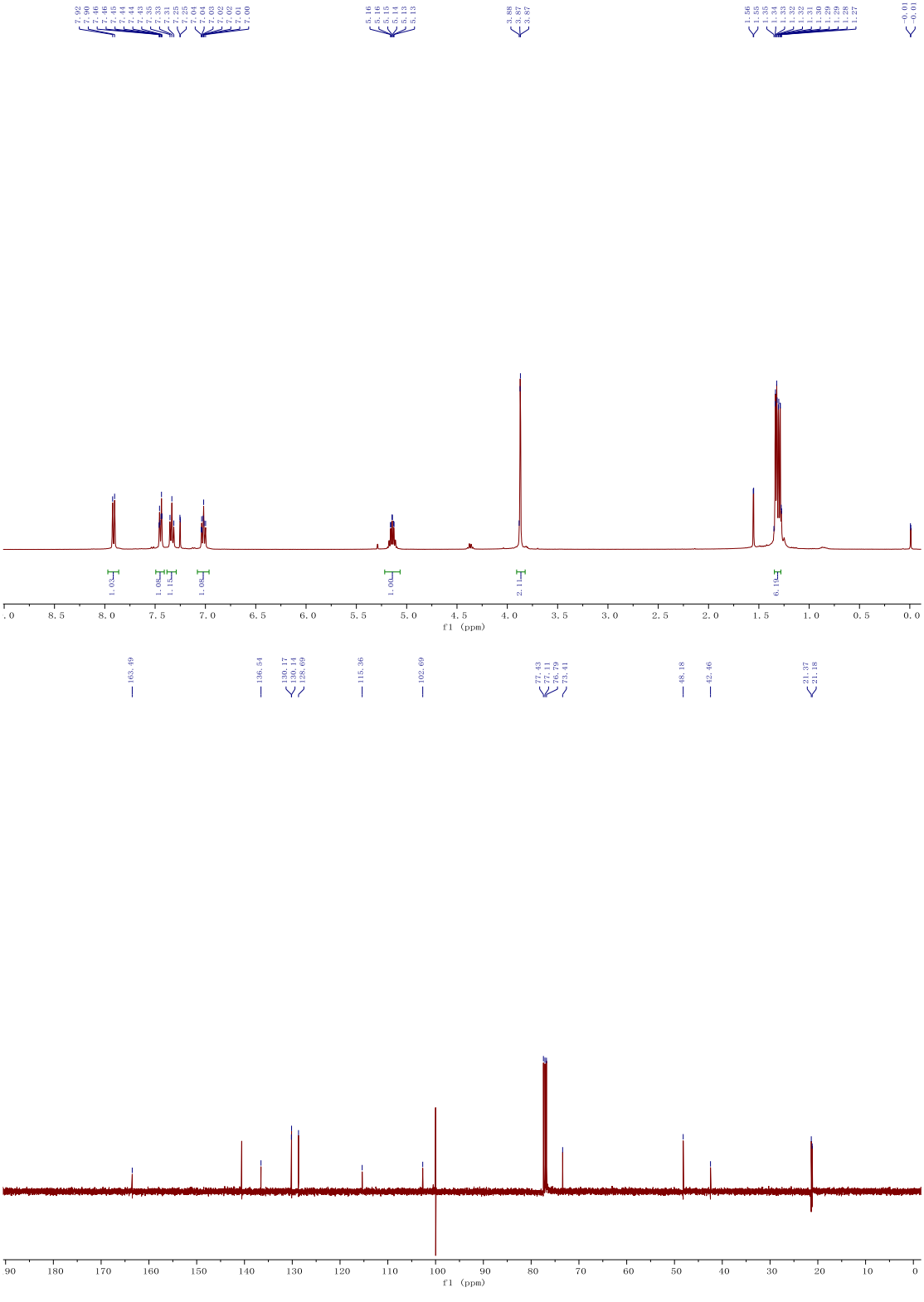
Isopropyl 2-bromo-2-cyano-3-(4-fluorophenyl)propanoate (1e)



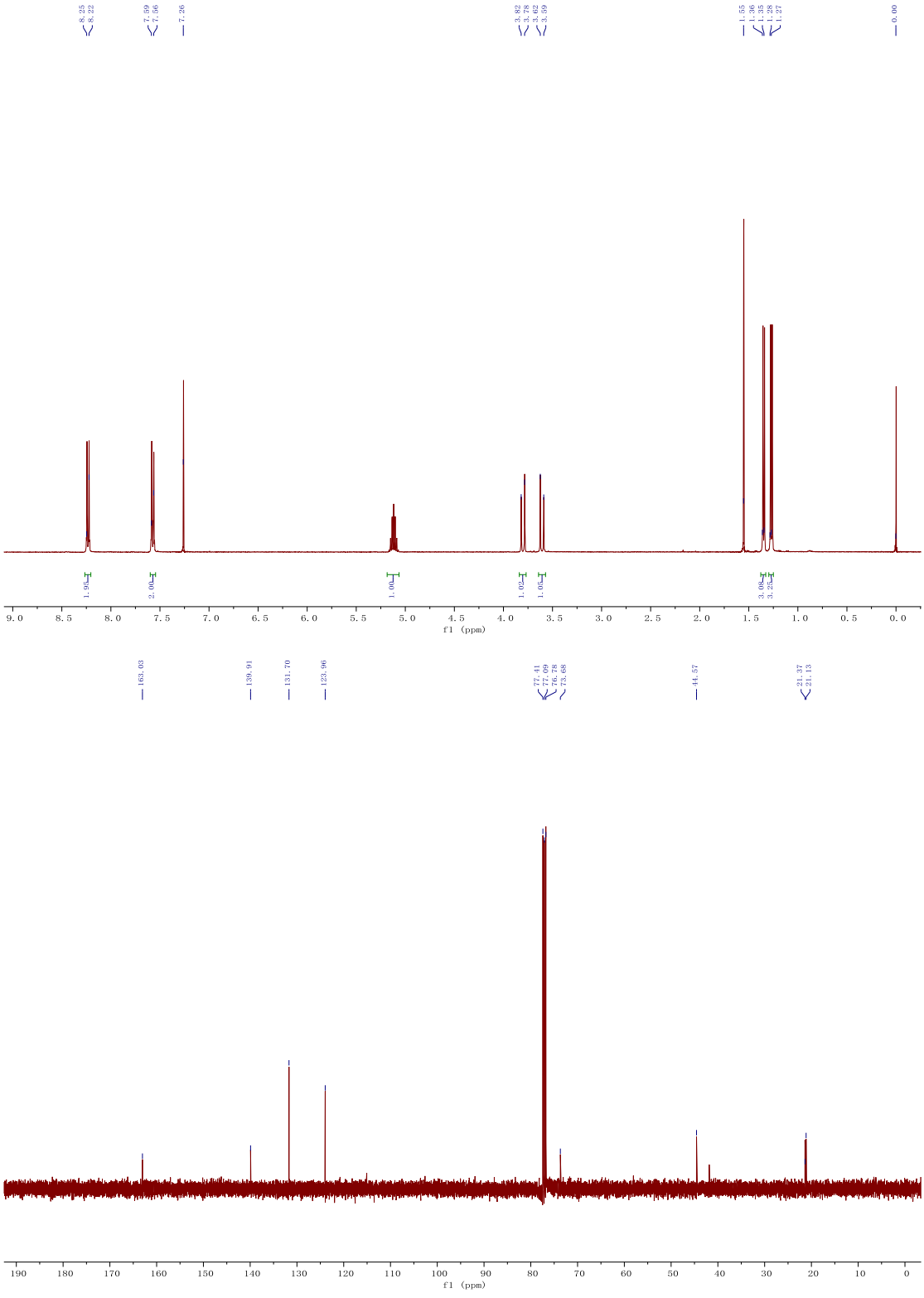
Isopropyl 2-bromo-3-(4-bromophenyl)-2-cyanopropanoate (1f)



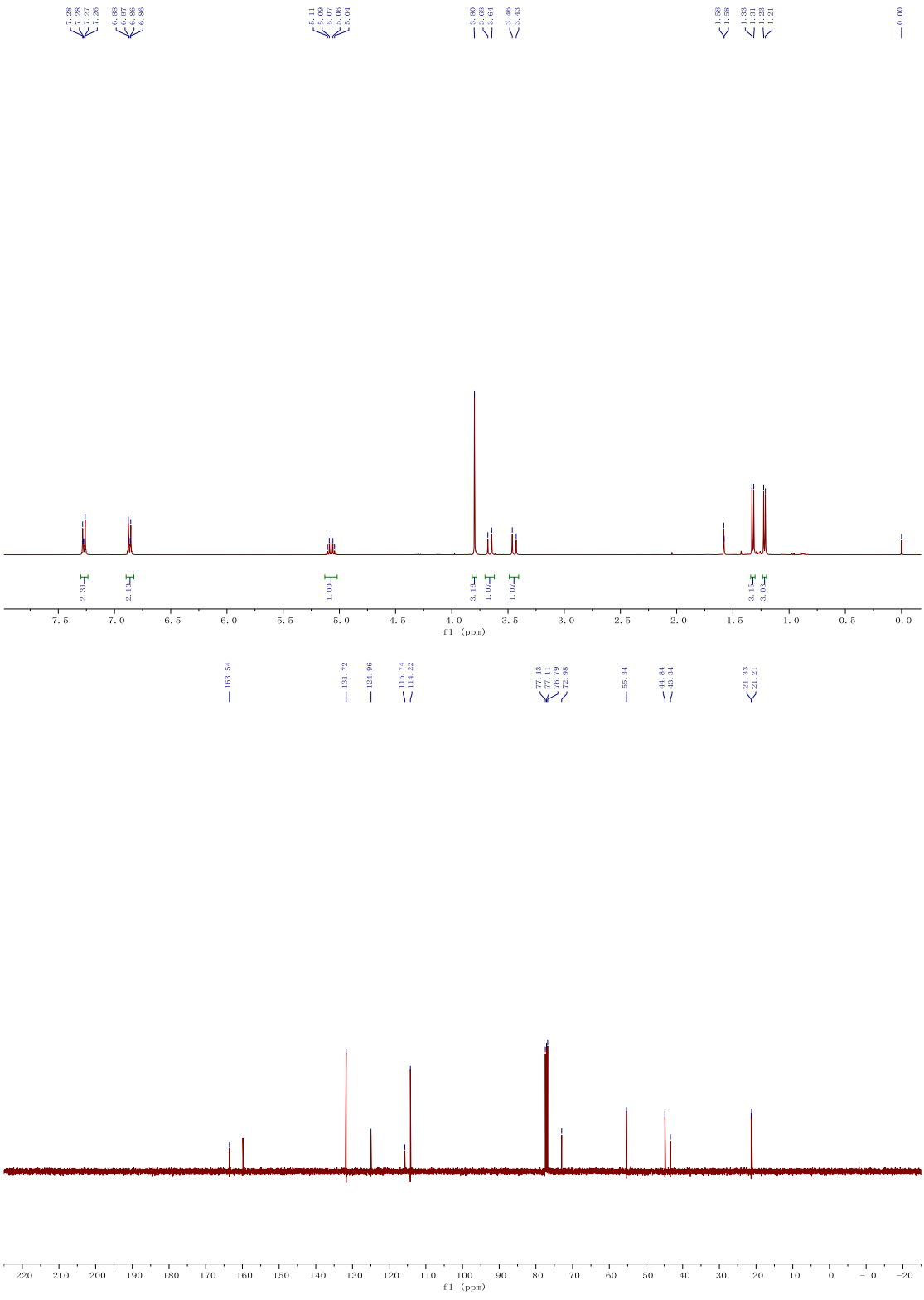
Isopropyl 2-bromo-2-cyano-3-(2-iodophenyl)propanoate (1g)



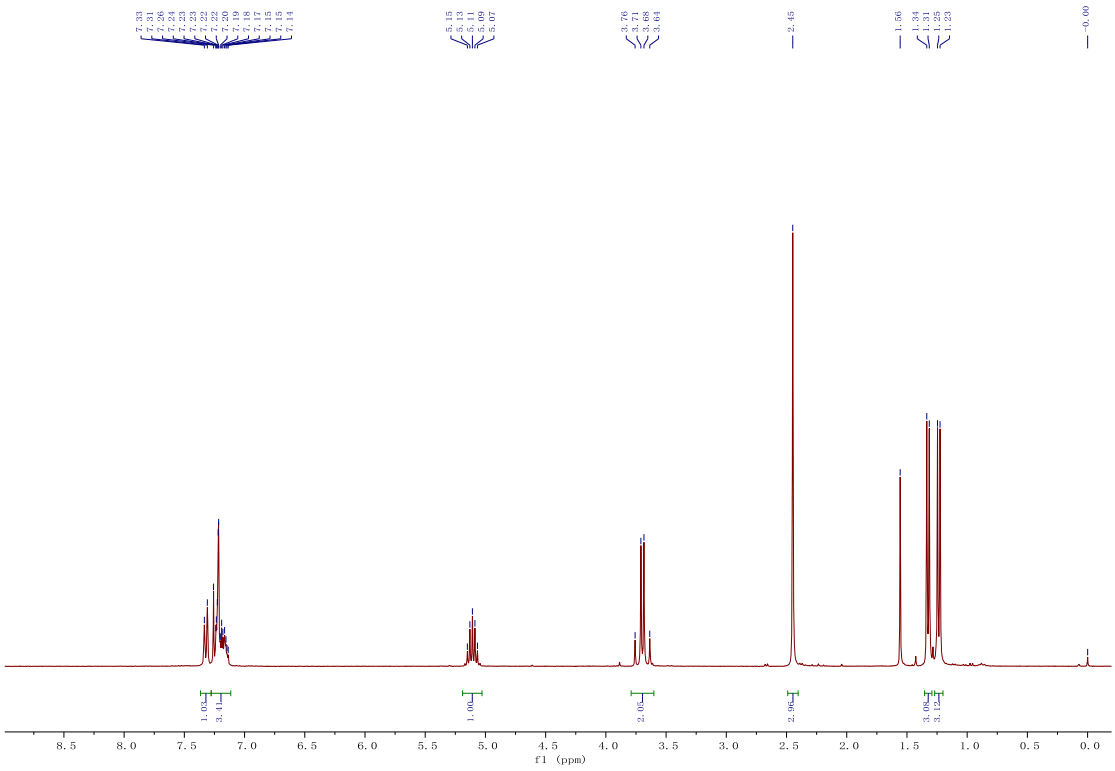
Isopropyl 2-bromo-2-cyano-3-(4-nitrophenyl)propanoate (1h)

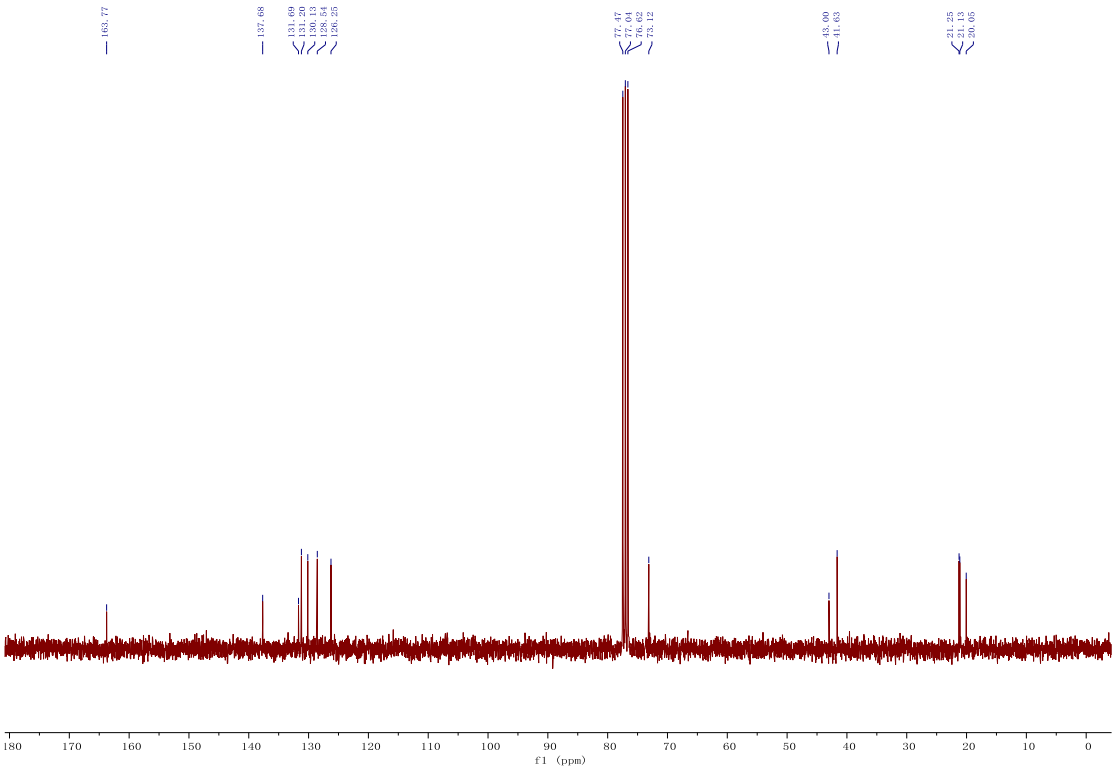


Isopropyl 2-bromo-2-cyano-3-(4-methoxyphenyl)propanoate (1i)

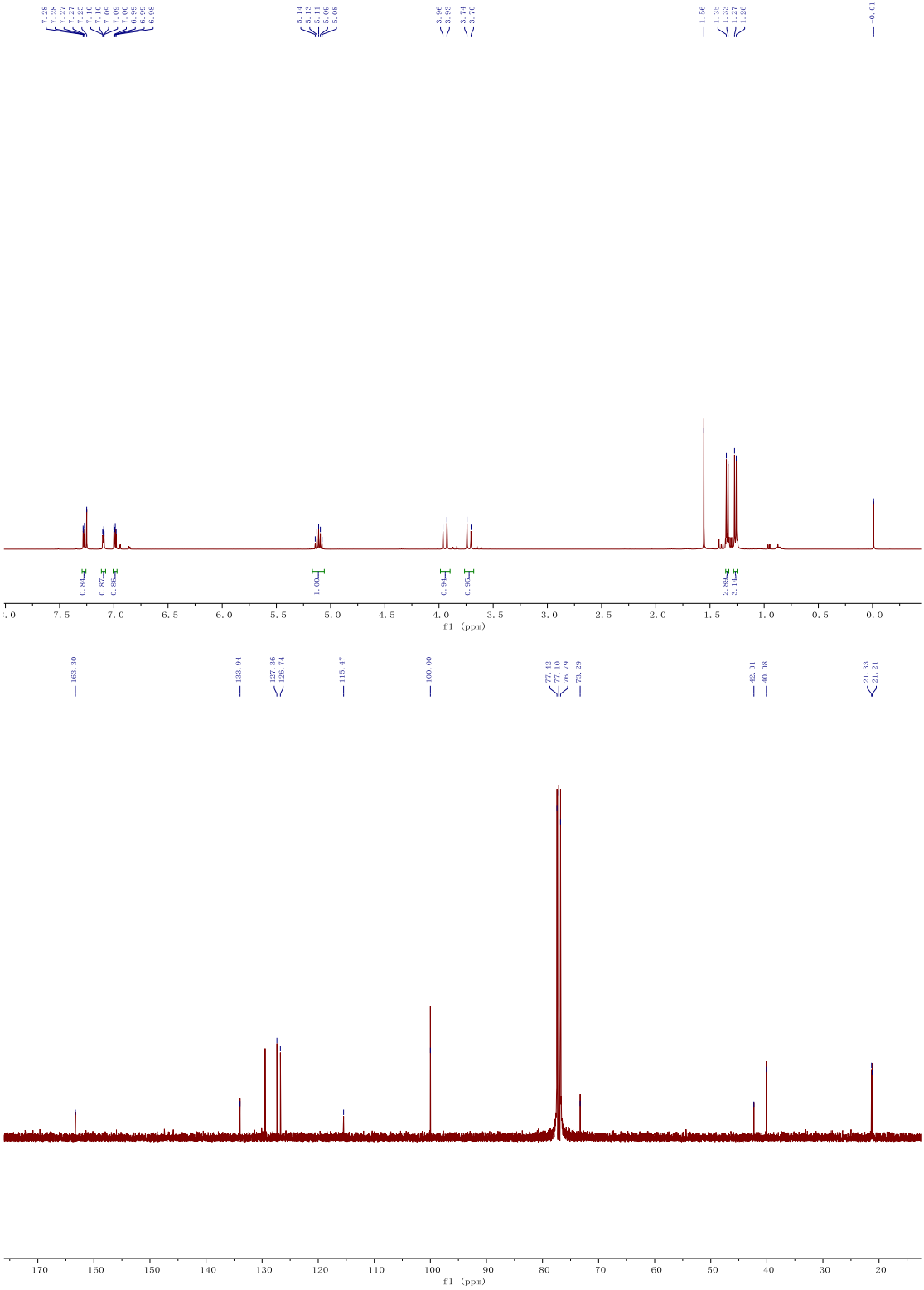


Isopropyl 2-bromo-2-cyano-3-(o-tolyl)propanoate (1j)

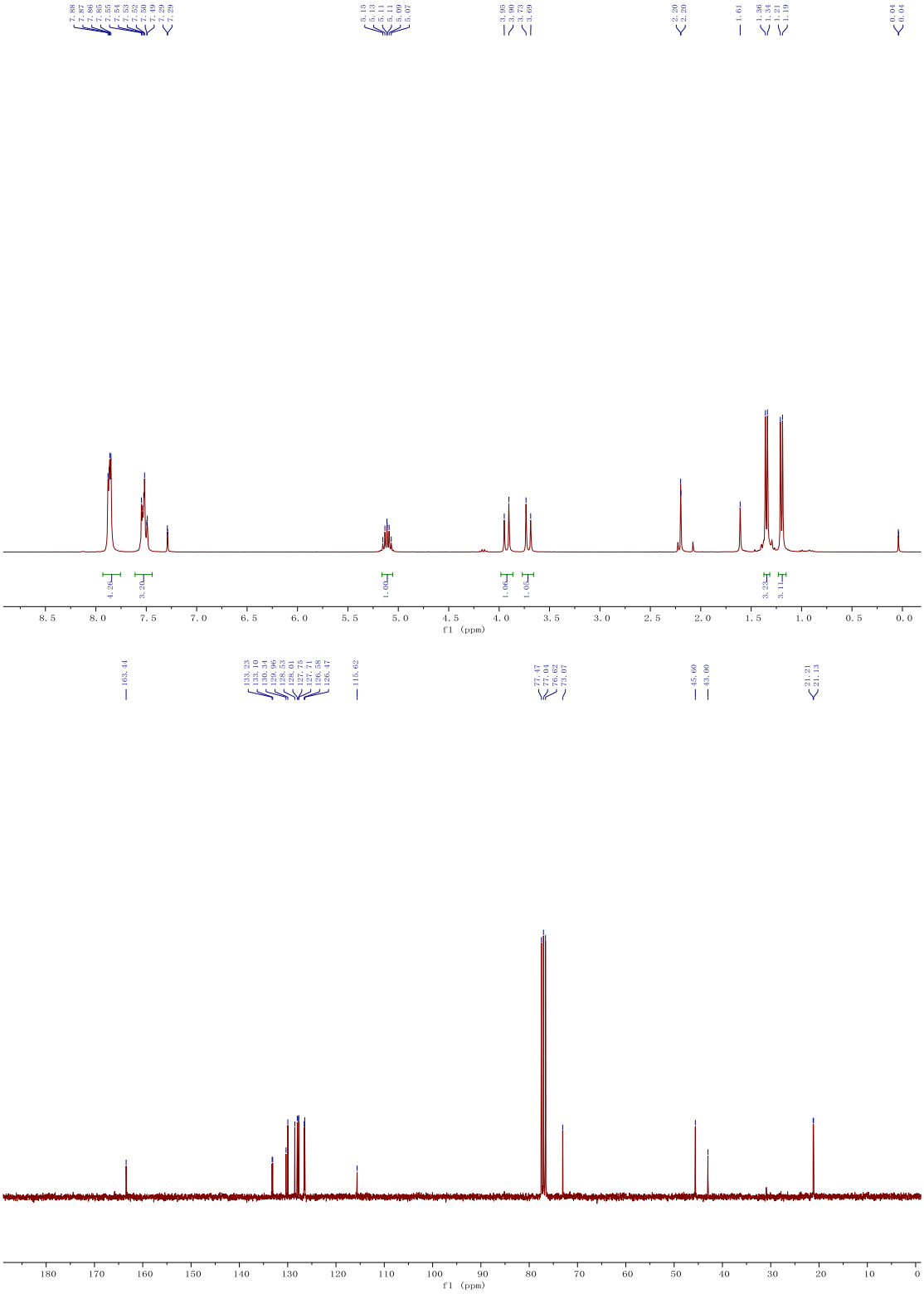




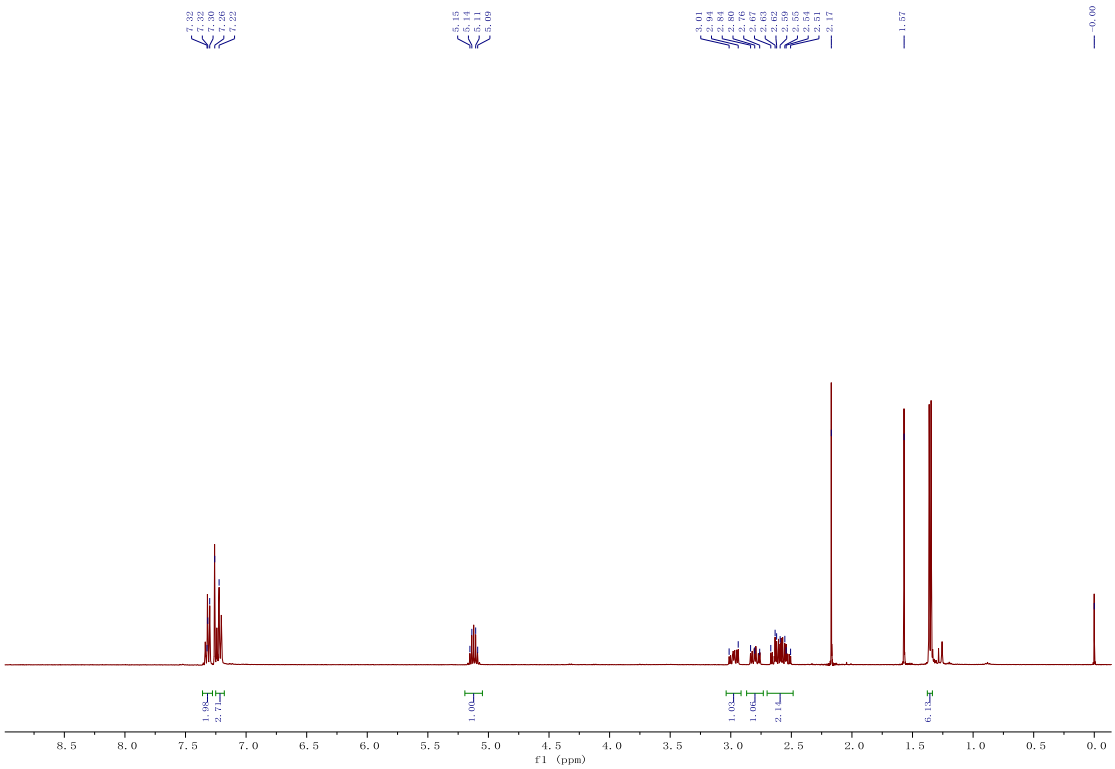
Isopropyl 2-bromo-2-cyano-3-(thiophen-2-yl)propanoate (1k)

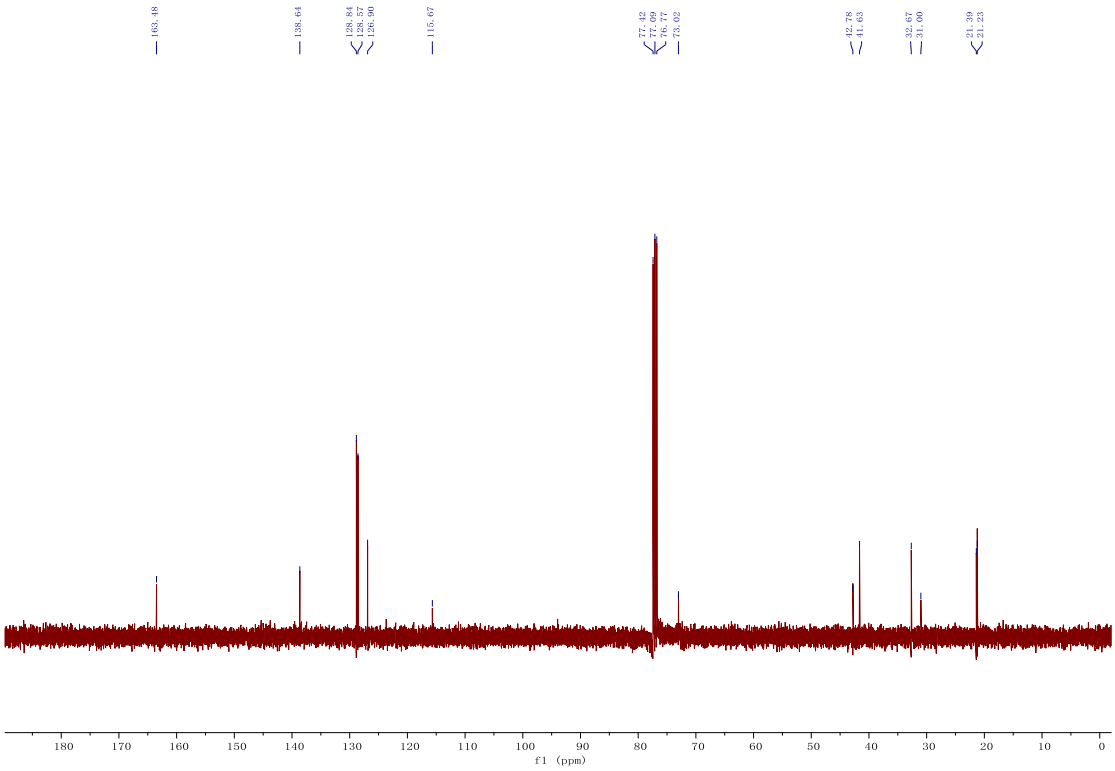


Isopropyl 2-bromo-2-cyano-3-(naphthalen-2-yl)propanoate (1l)

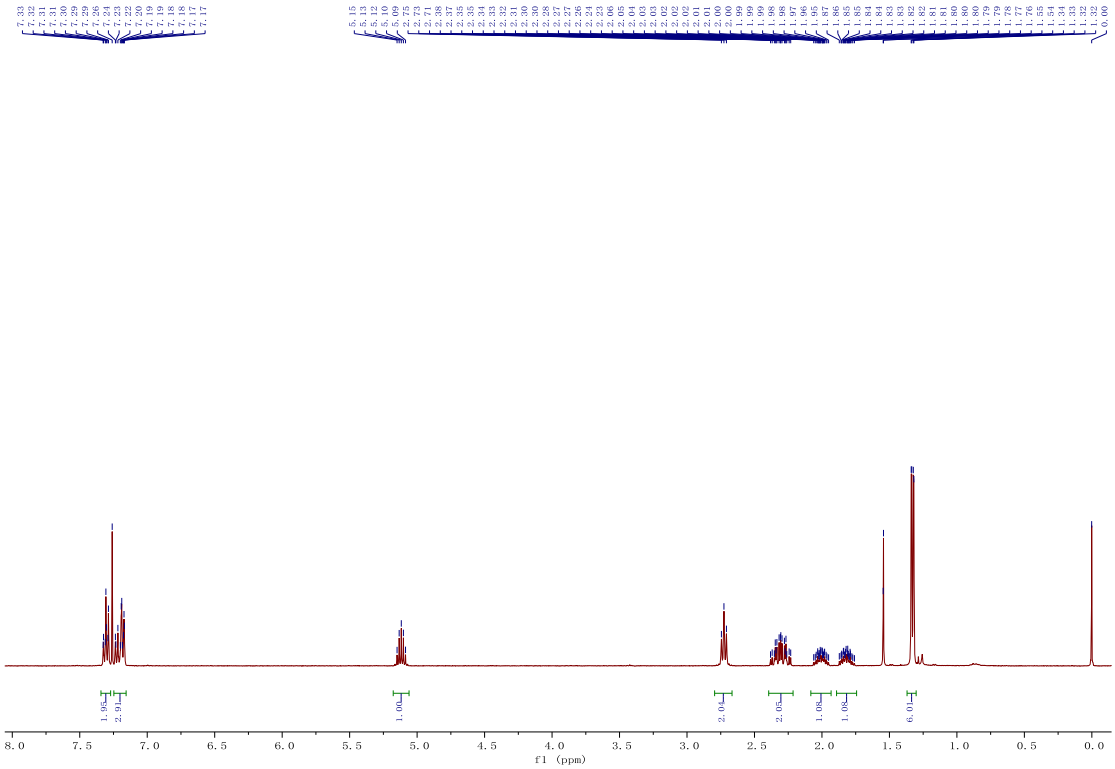


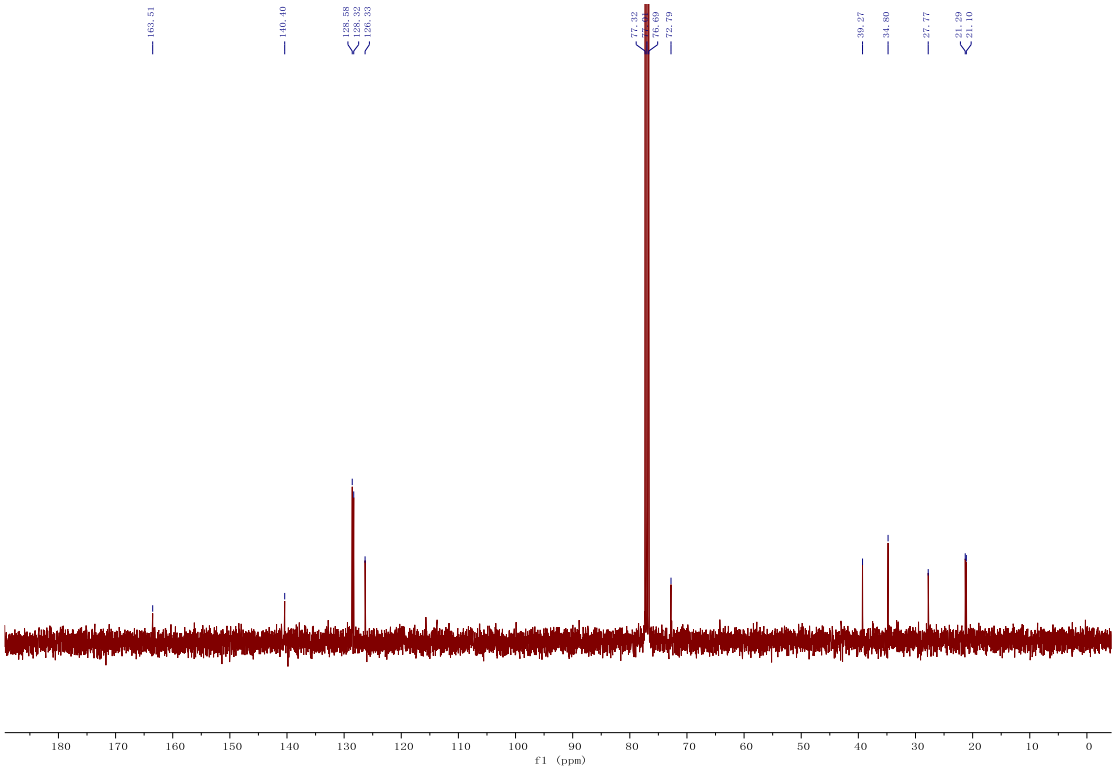
Isopropyl 2-bromo-2-cyano-4-phenylbutanoate (1m)



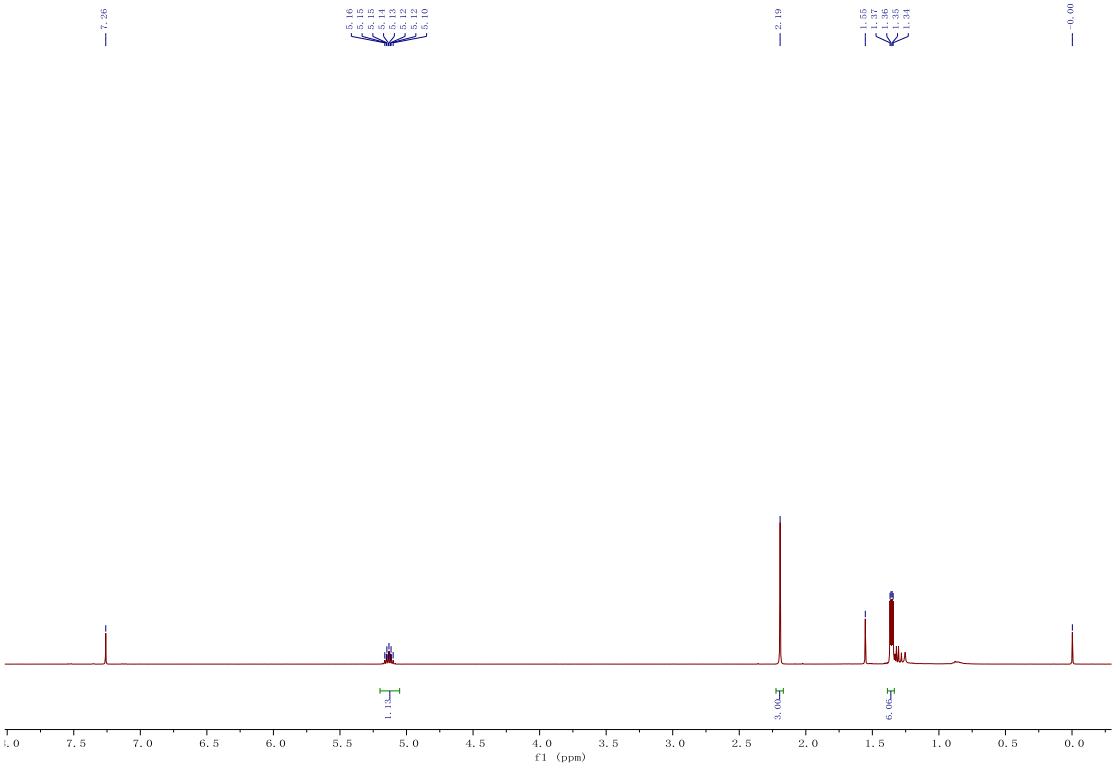


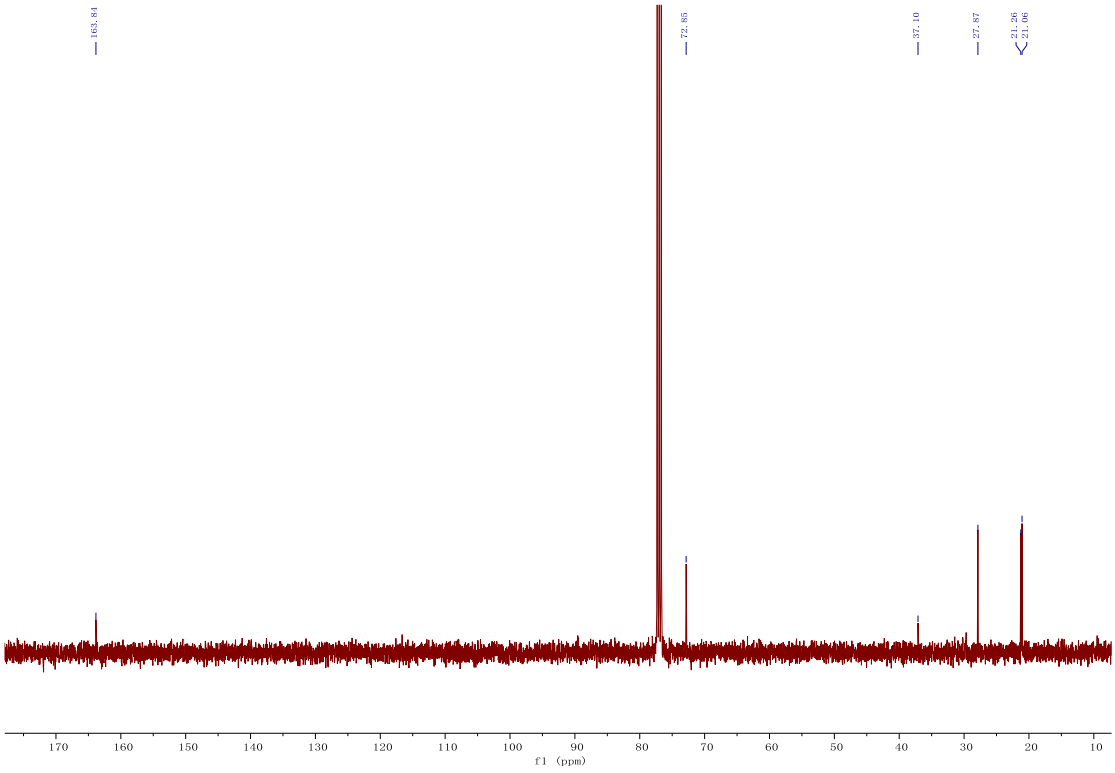
Isopropyl 2-bromo-2-cyano-5-phenylpentanoate (1n)



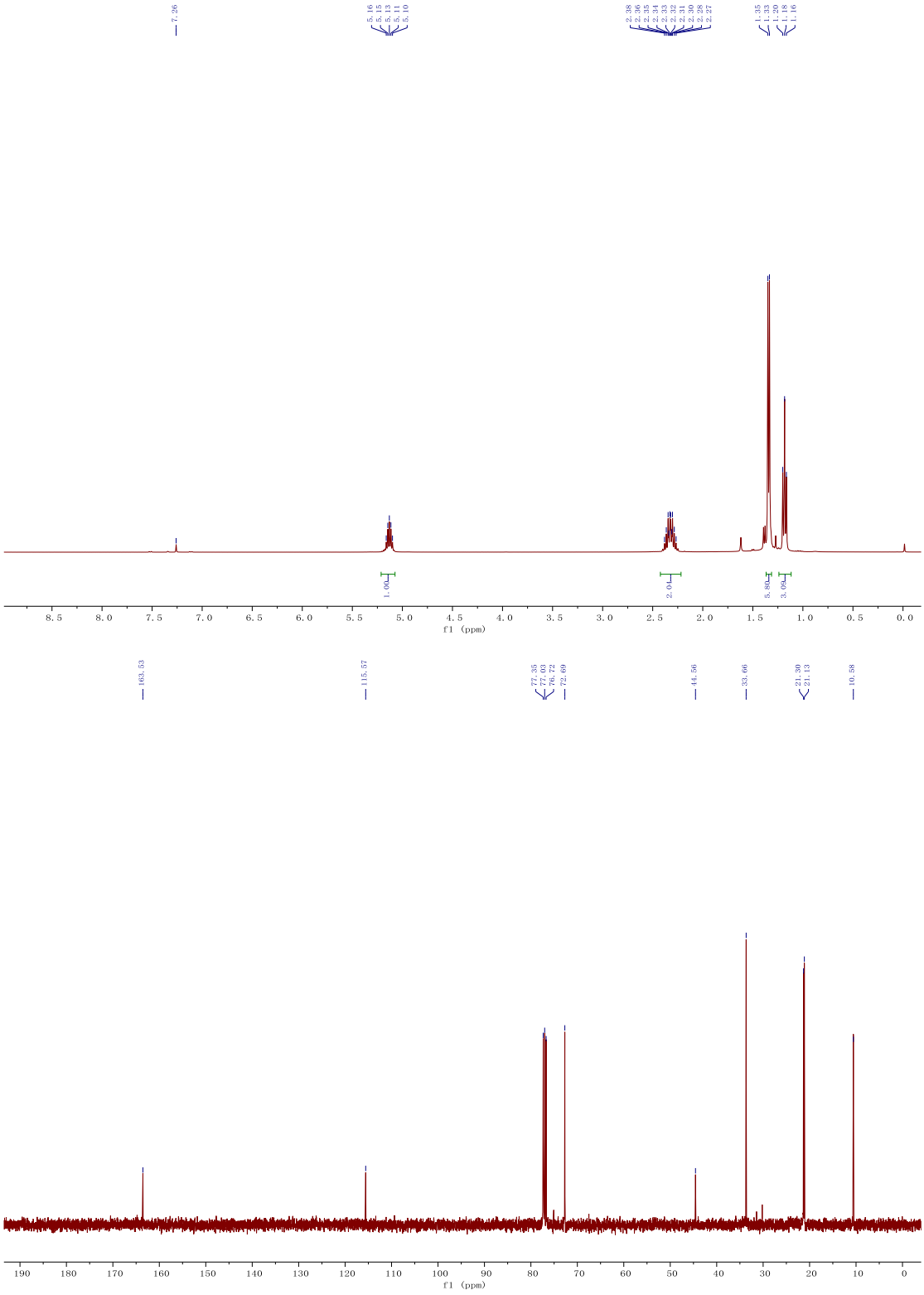


Isopropyl 2-bromo-2-cyanopropanoate (1o)

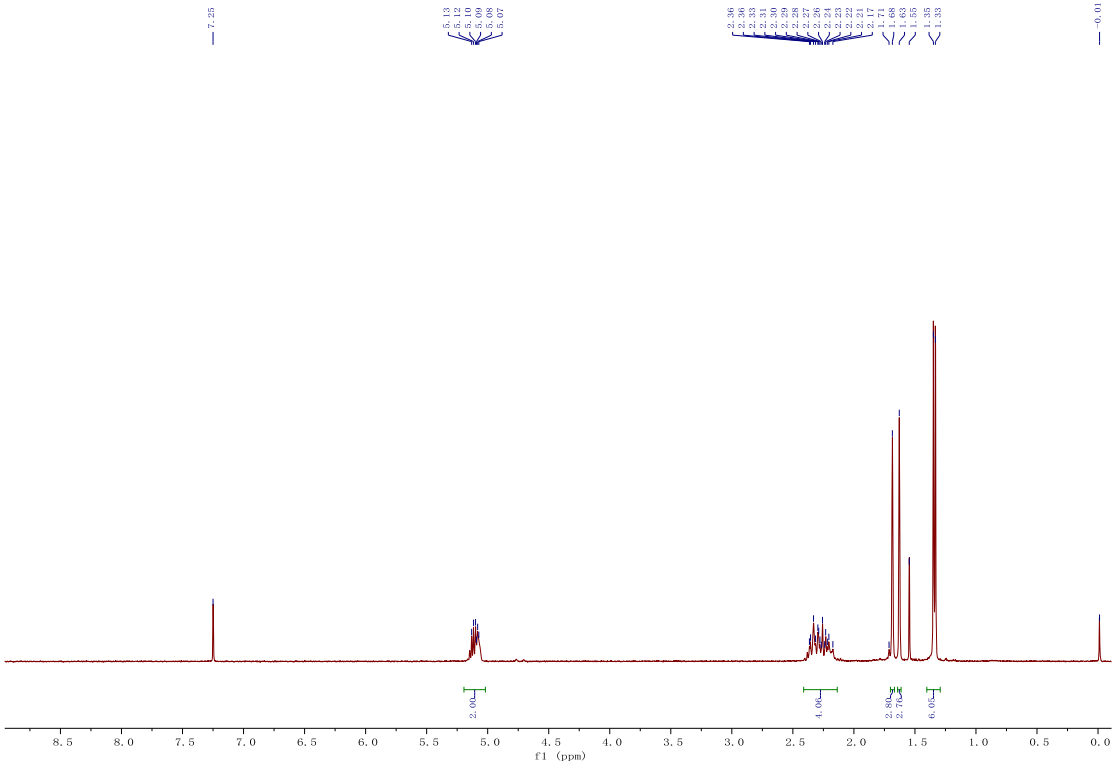


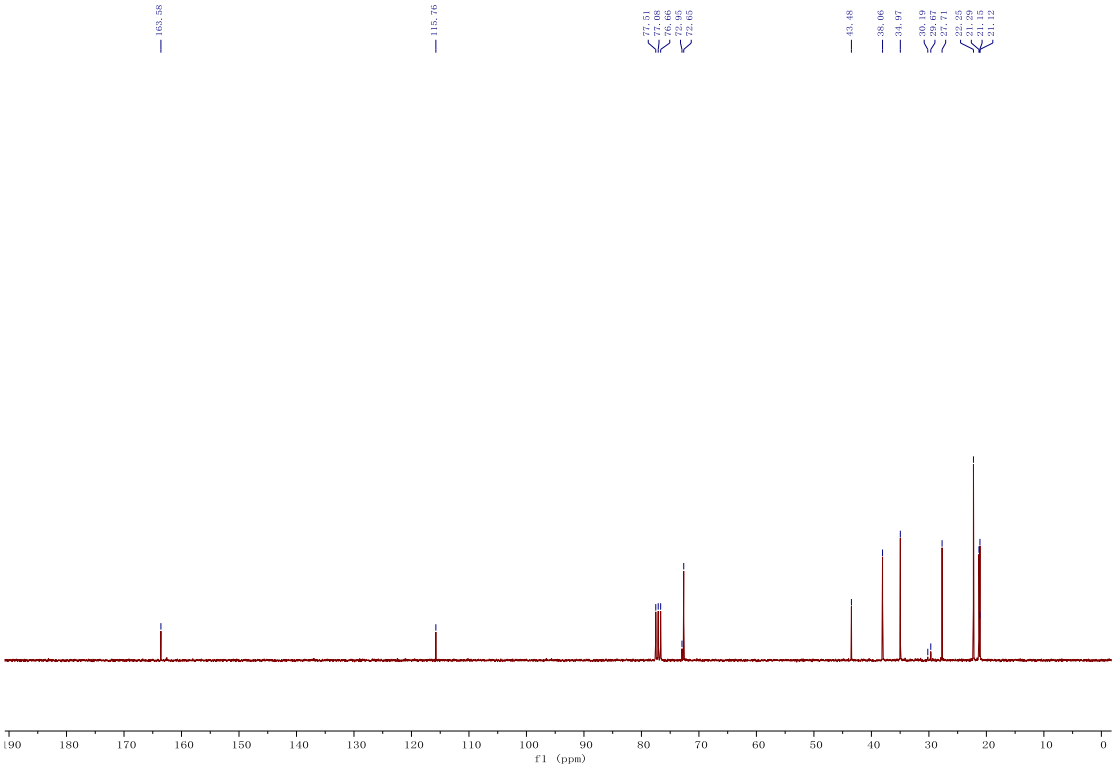


Isopropyl 2-bromo-2-cyanobutanoate (1p)

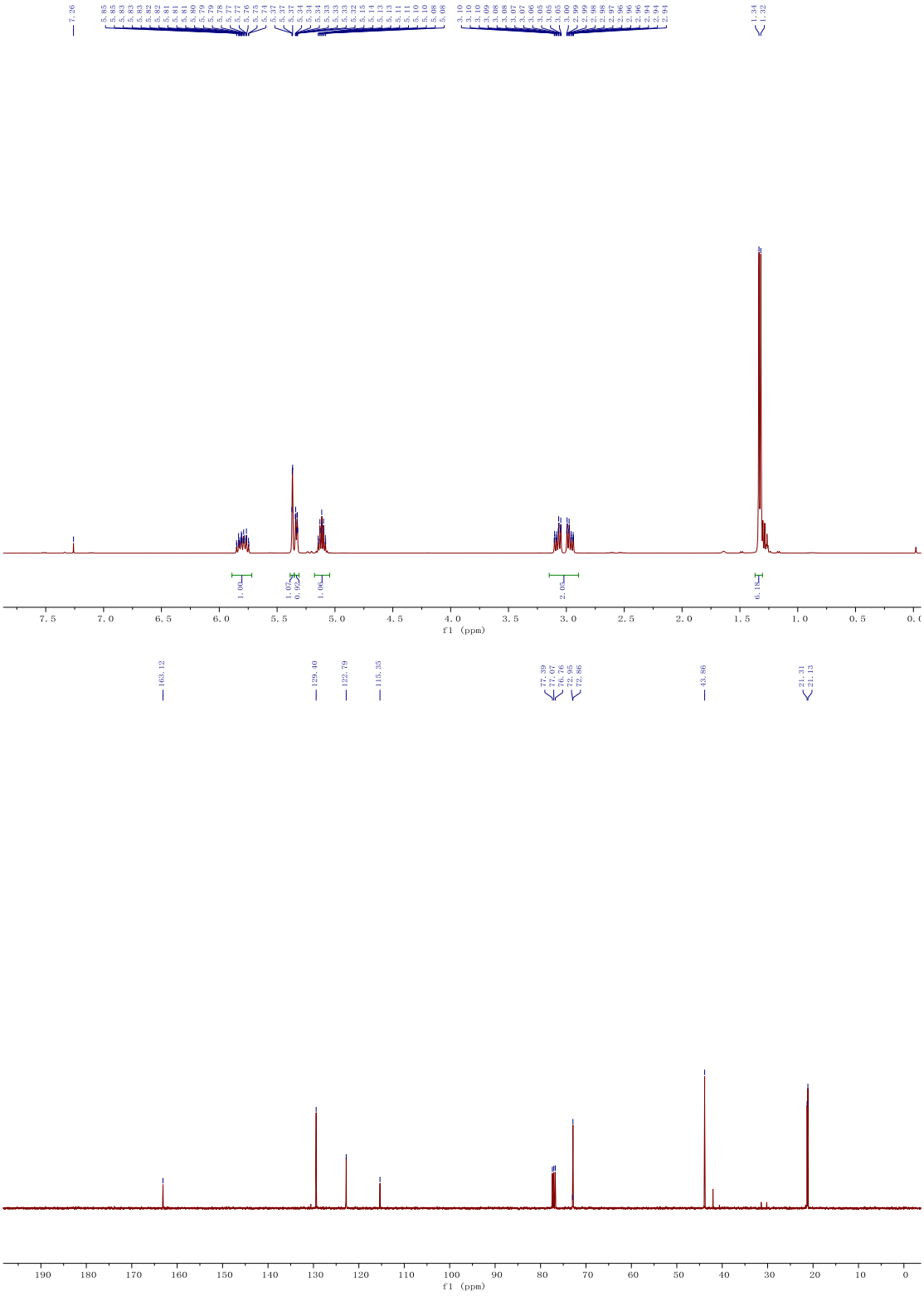


Isopropyl 2-bromo-2-cyano-5-methylhexanoate (1q)





isopropyl 2-bromo-2-cyanopent-4-enoate (1r)



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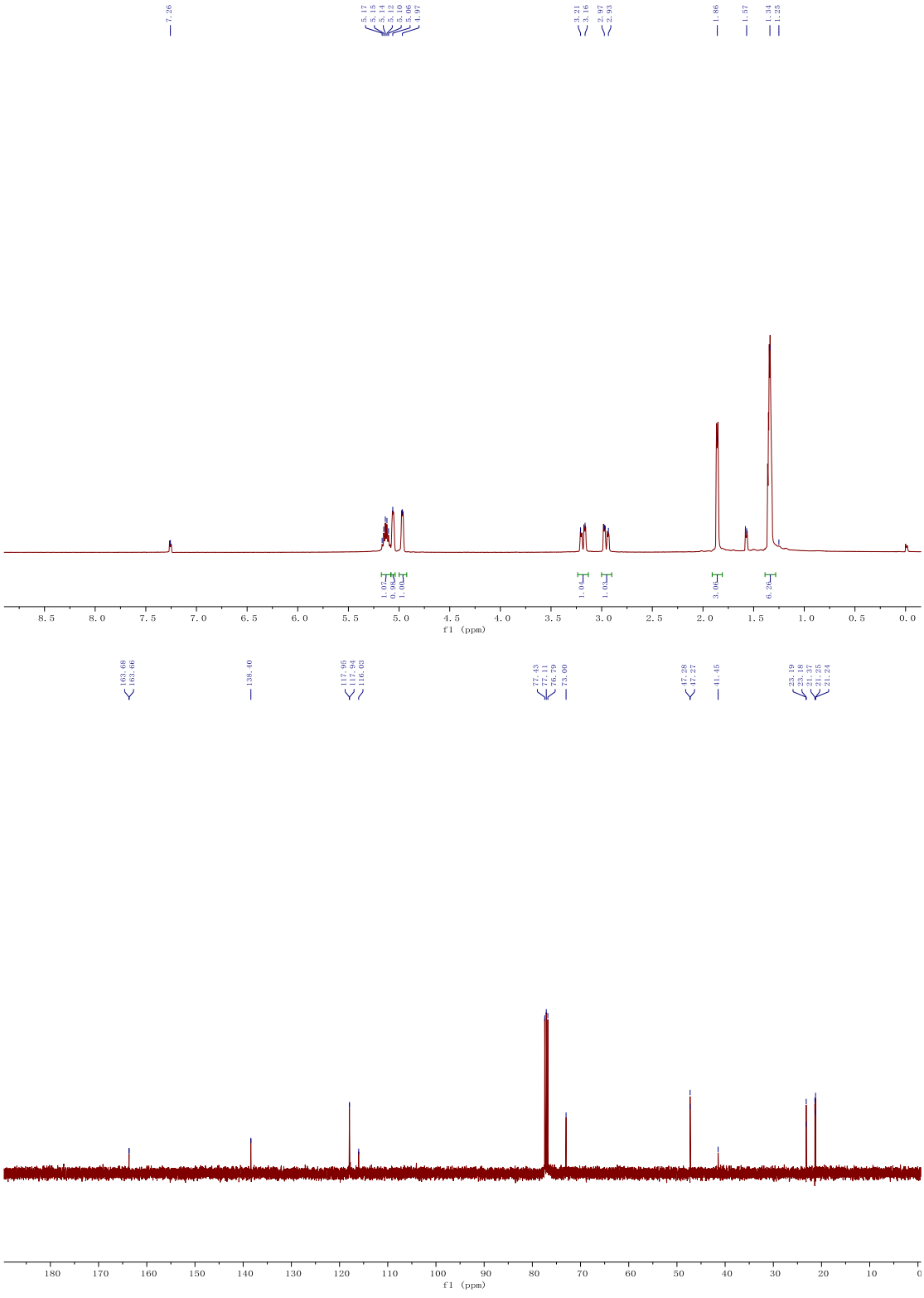
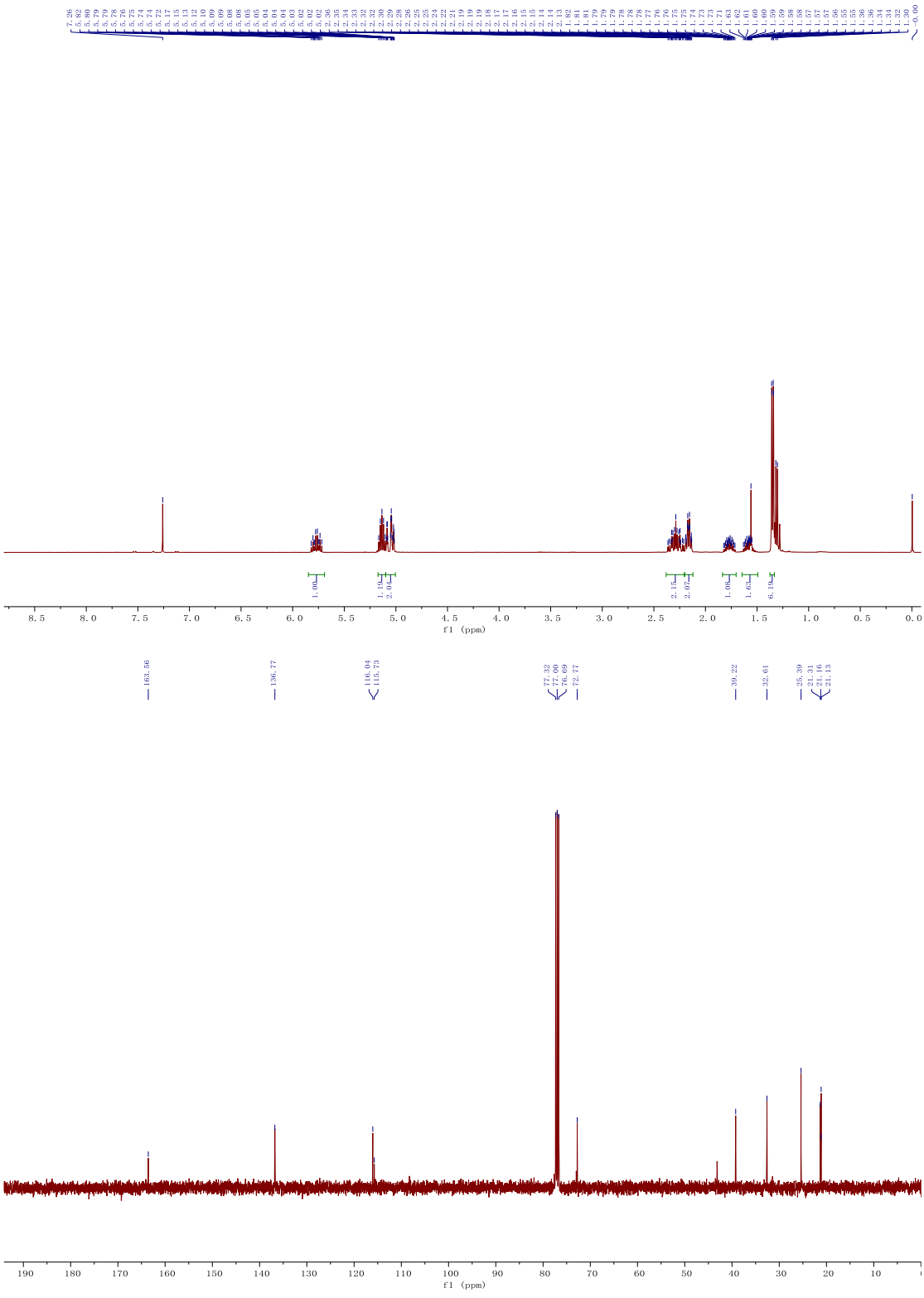
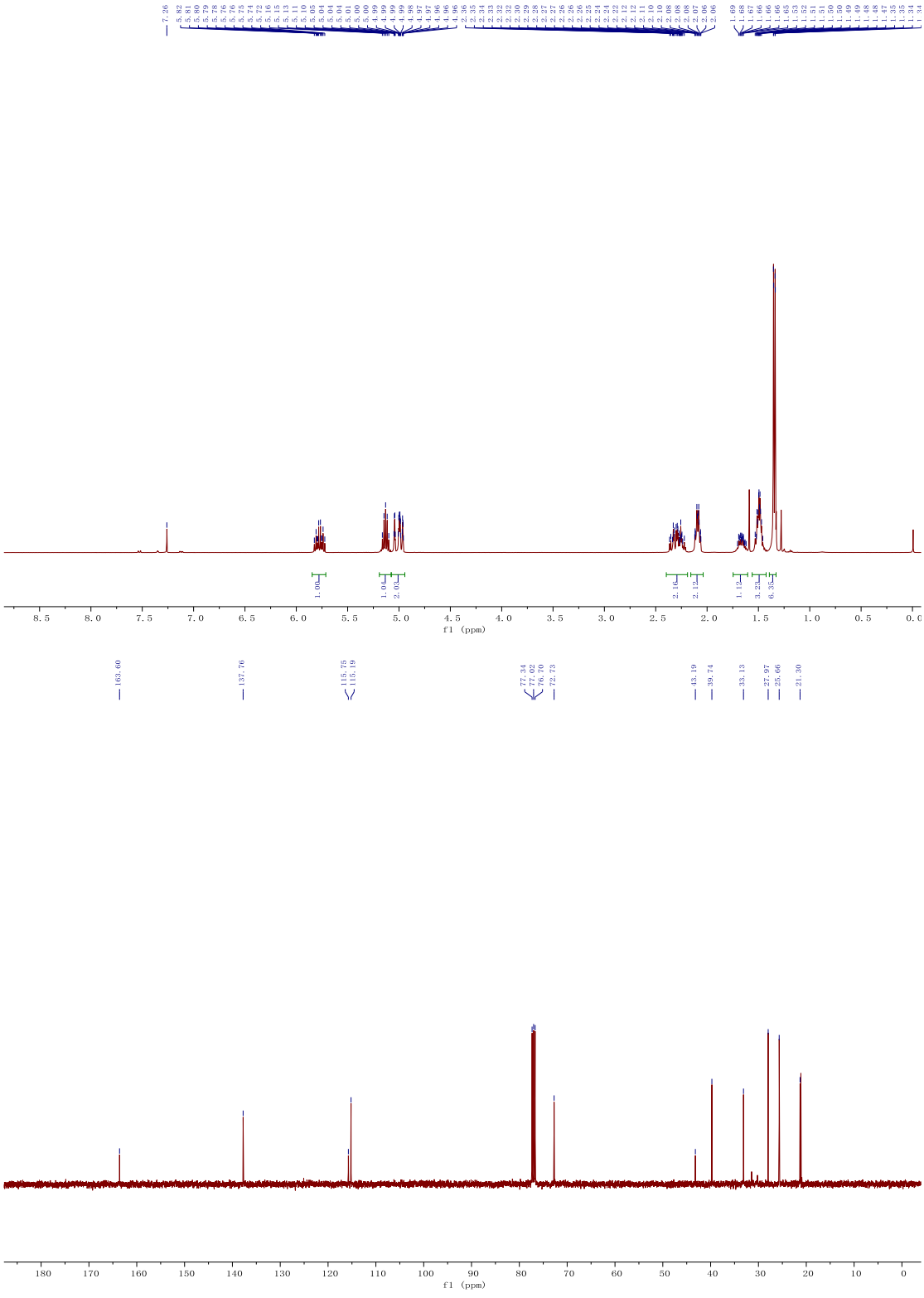


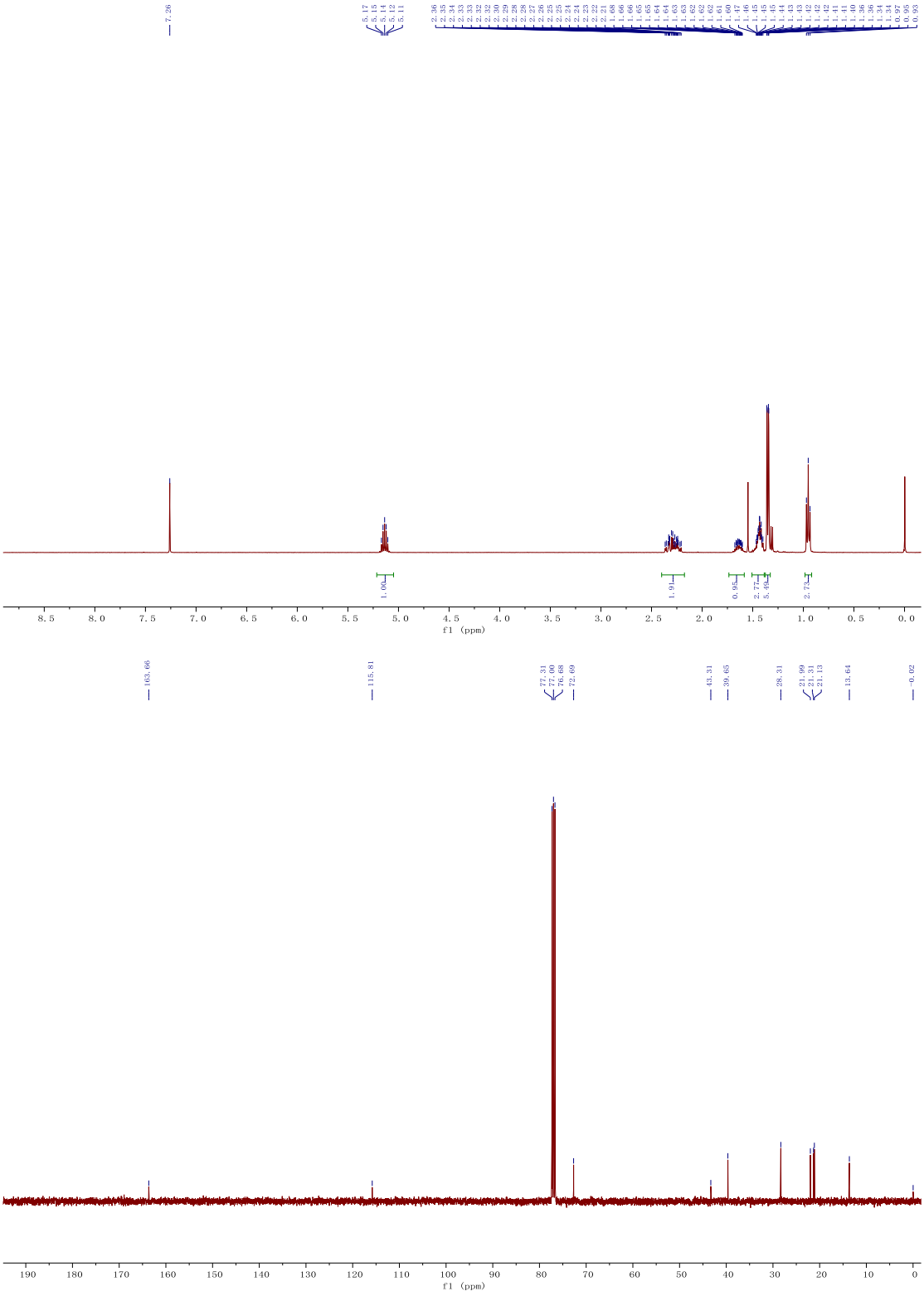
Isopropyl 2-bromo-2-cyanohept-6-enoate (1t)



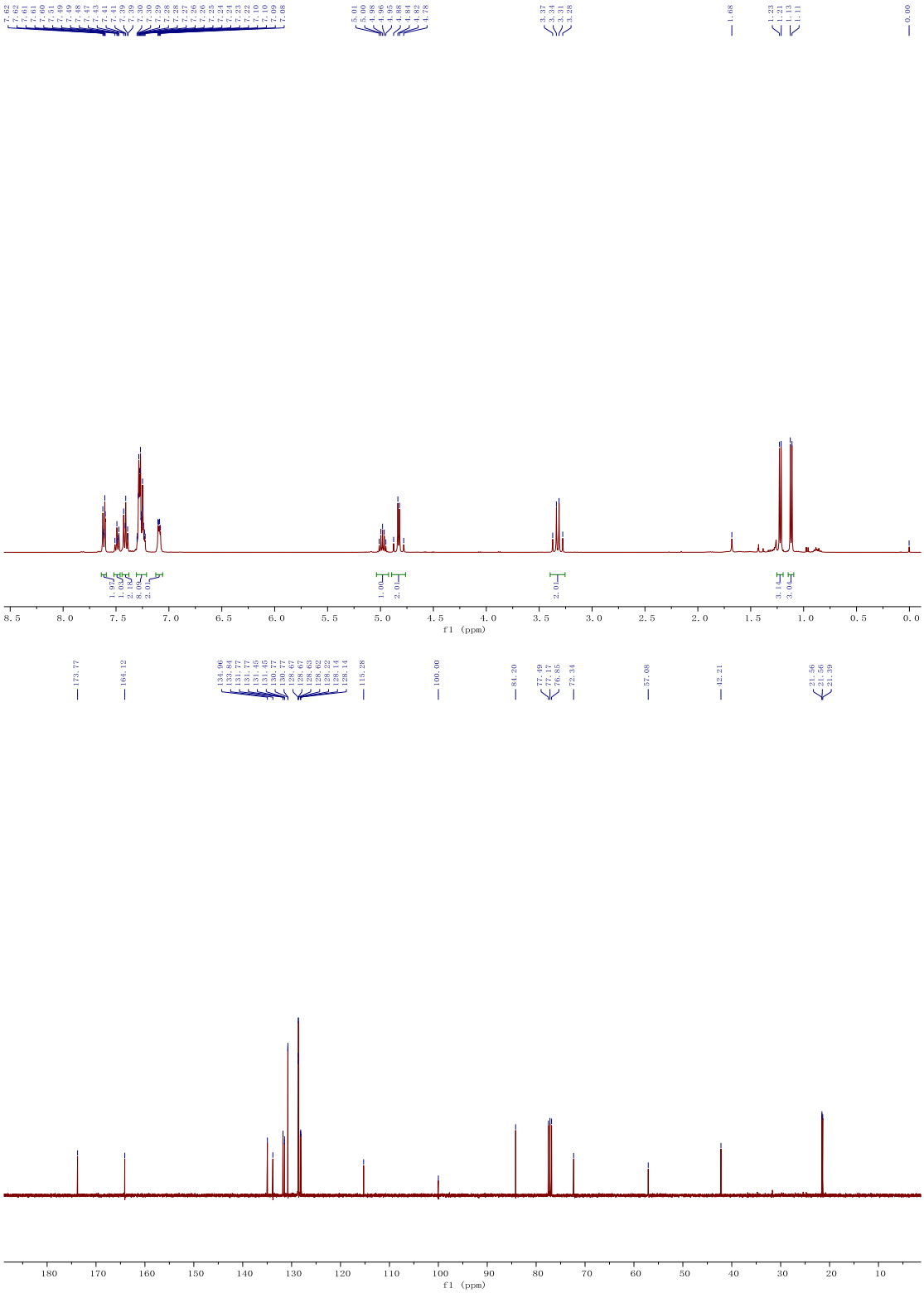
Isopropyl 2-bromo-2-cyanooct-7-enoate (1u)



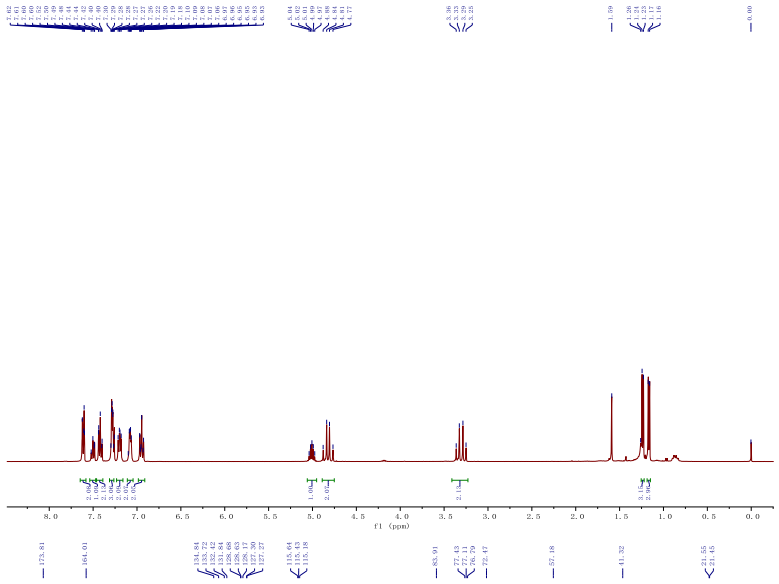
Isopropyl 2-bromo-2-cyanohexanoate (1v)

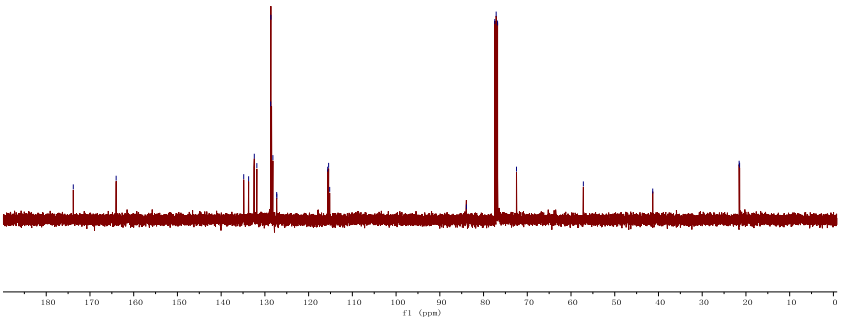


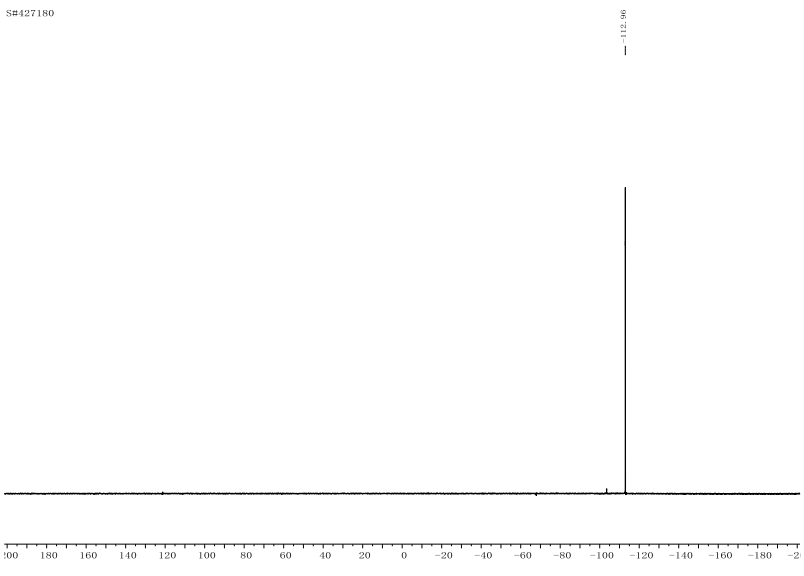
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-phenylpropanoate (4g)



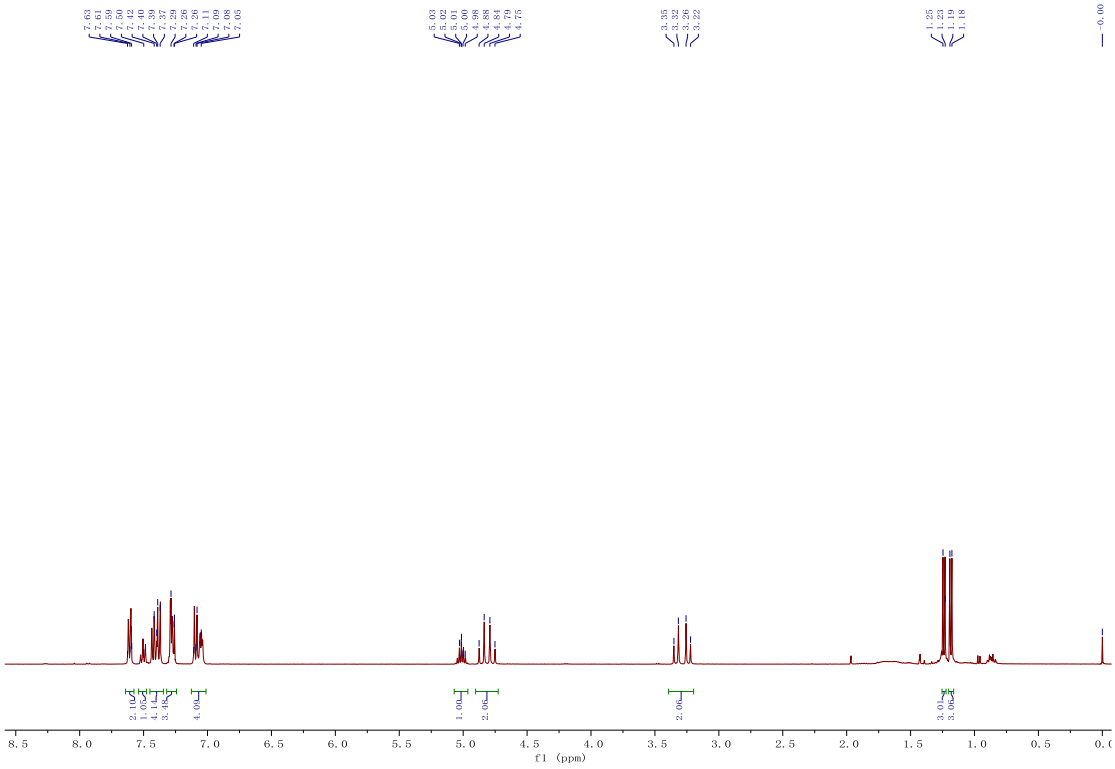
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-fluorophenyl)propanoate (4i)

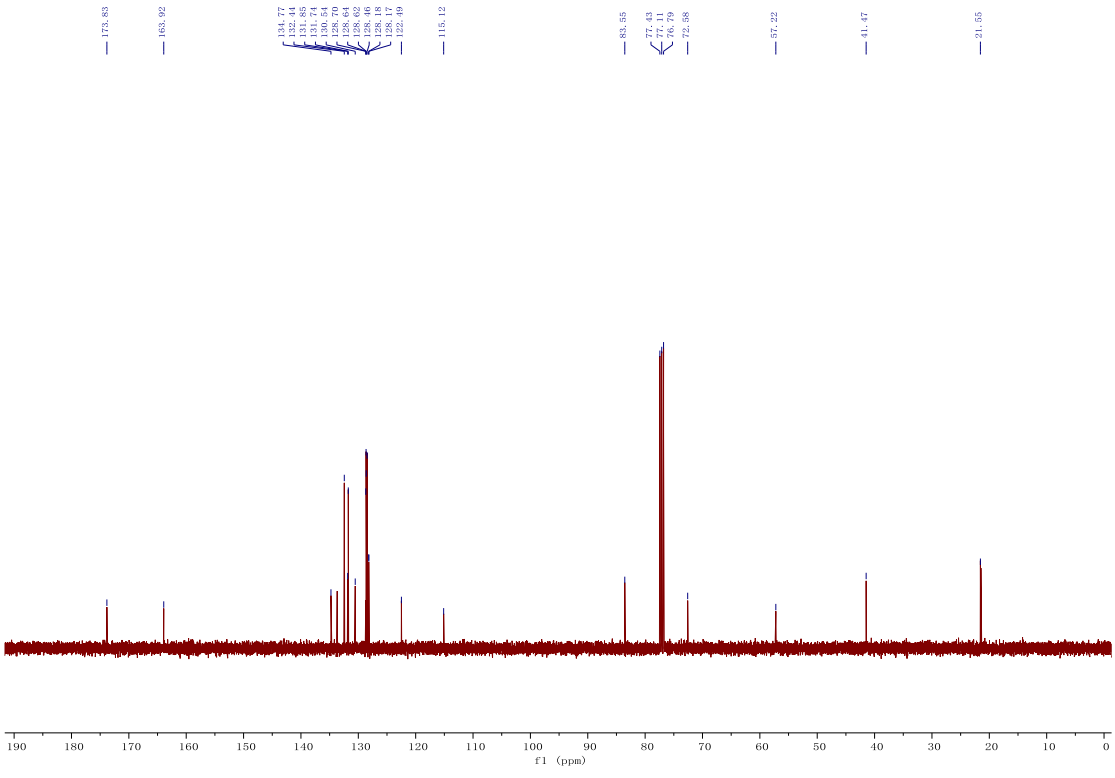




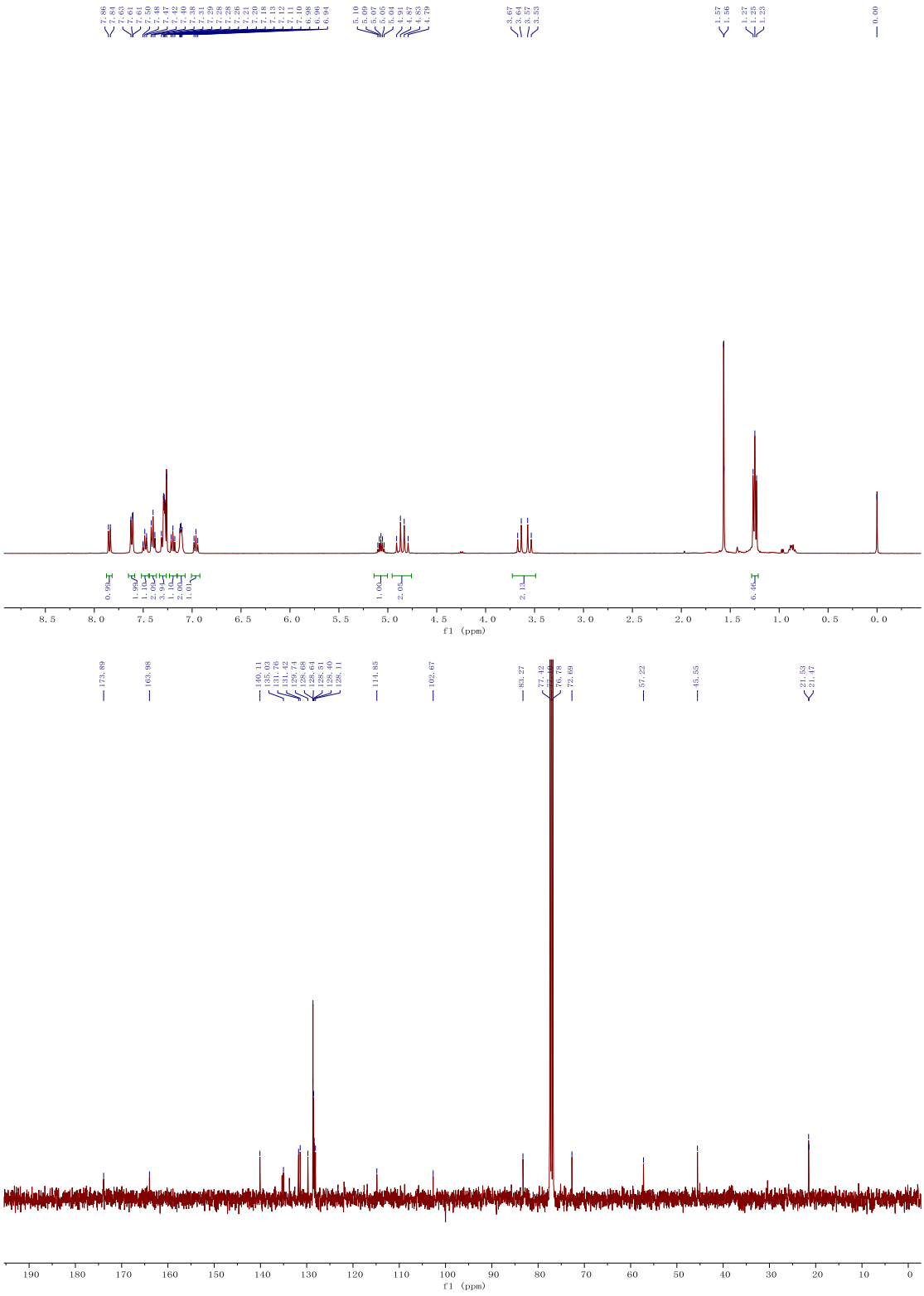


isopropyl (R)-2-((N-benzylbenzamido)oxy)-3-(4-bromophenyl)-2-cyanopropanoate (4j)





isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(2-iodophenyl)propanoate (4k)



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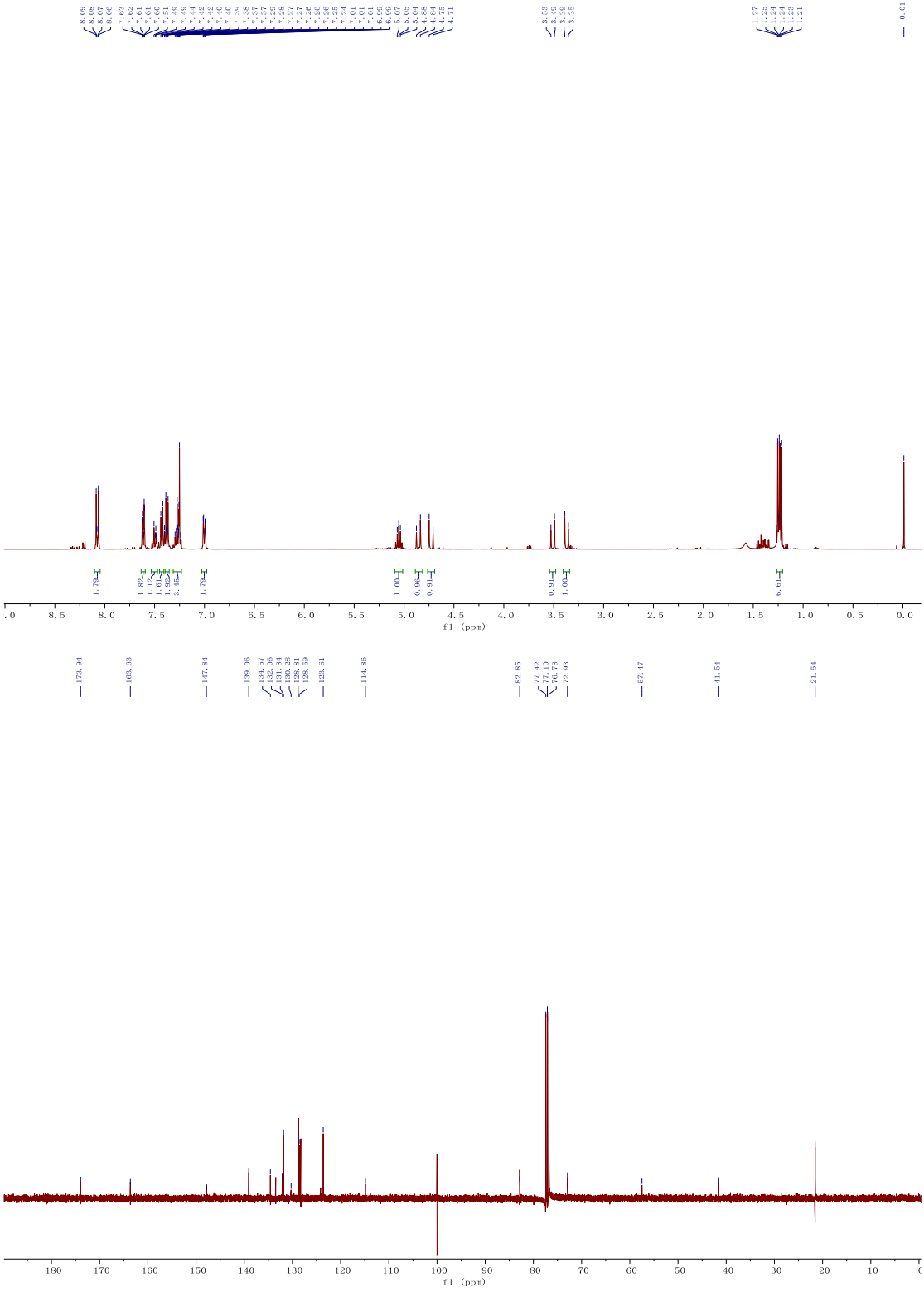
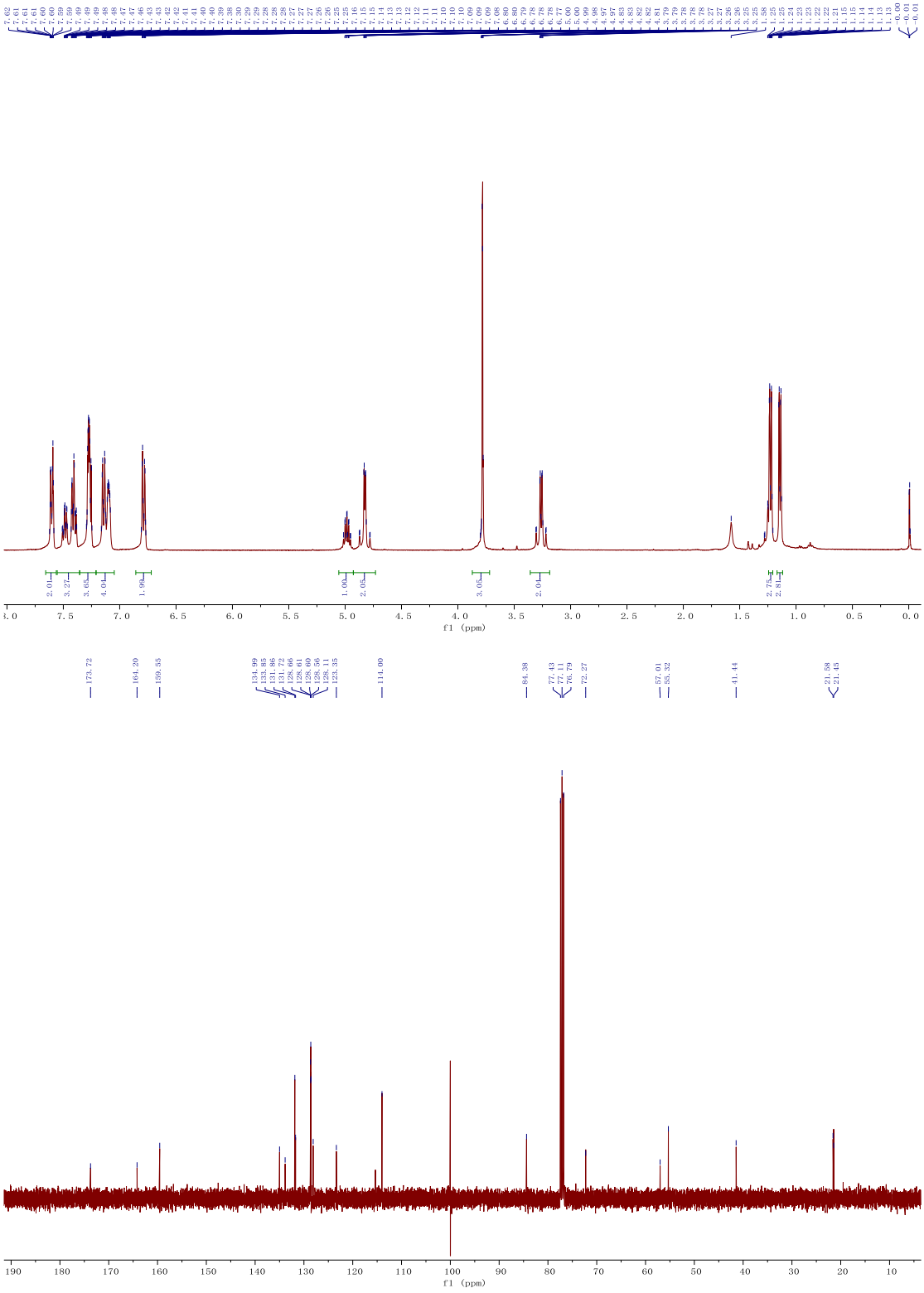
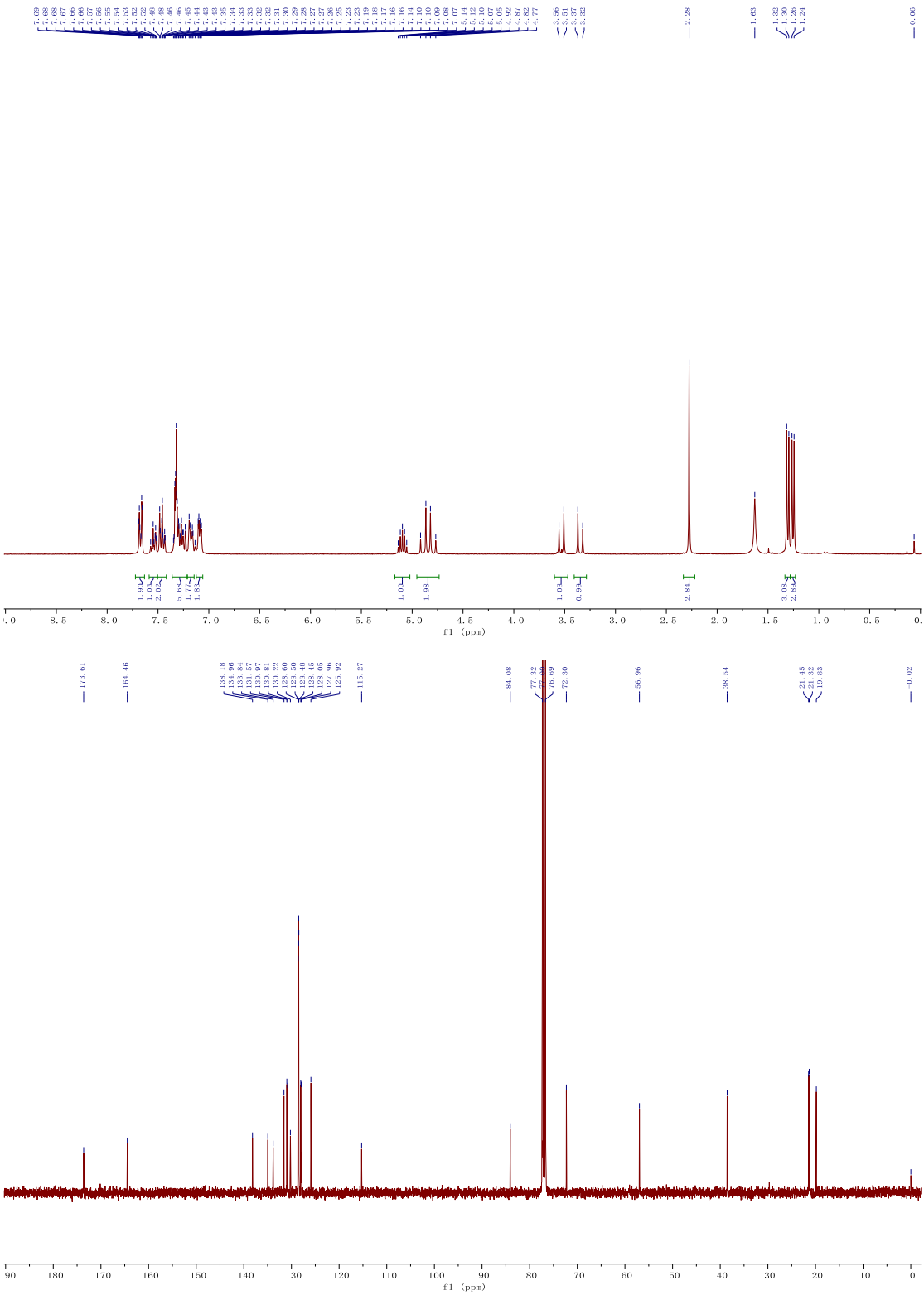


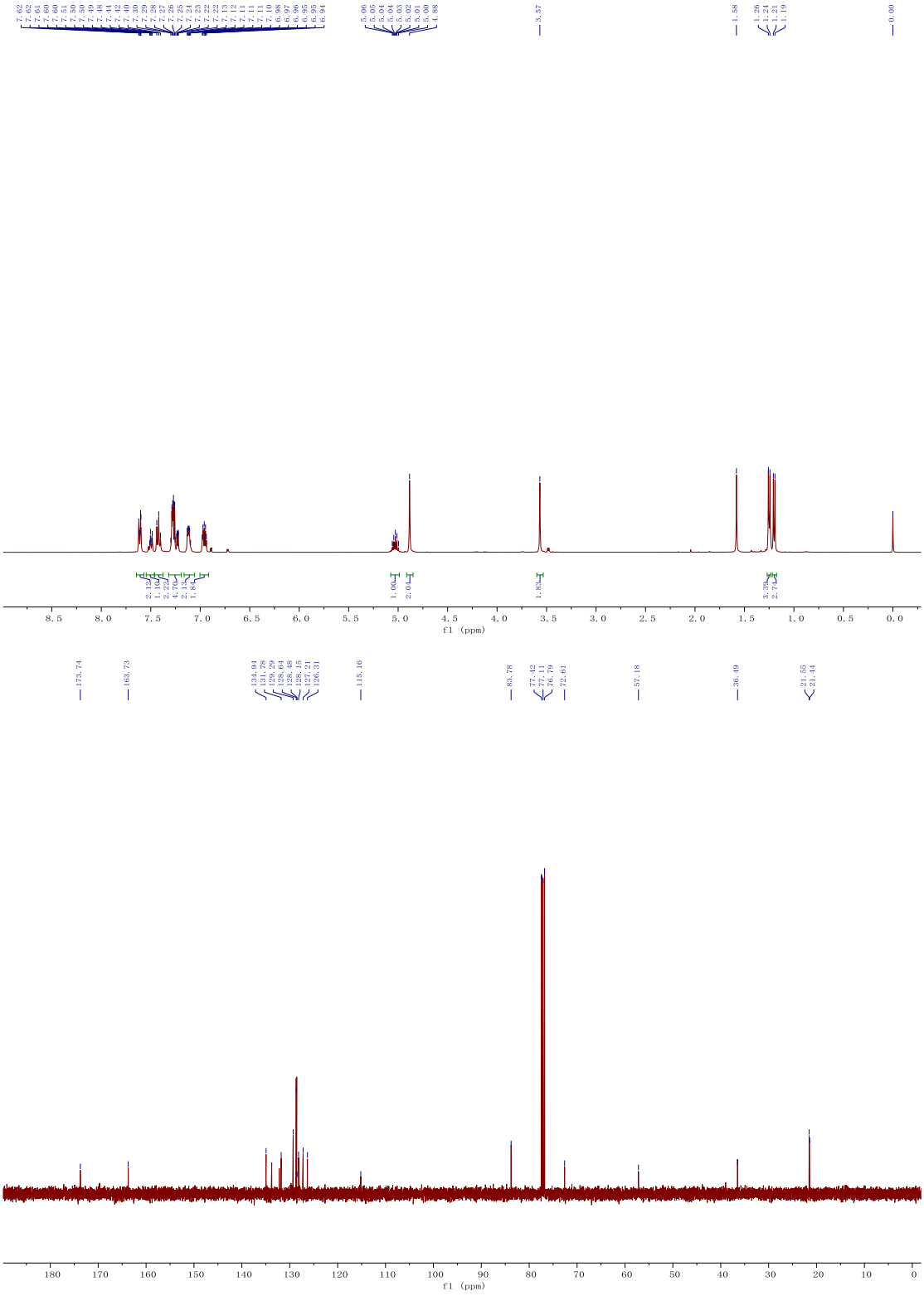
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-methoxyphenyl)propanoate (4m)



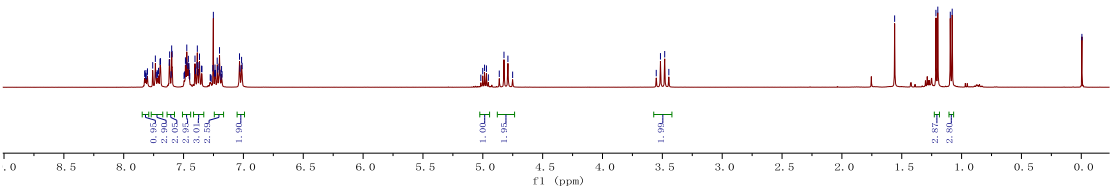
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(o-tolyl)propanoate (4n)

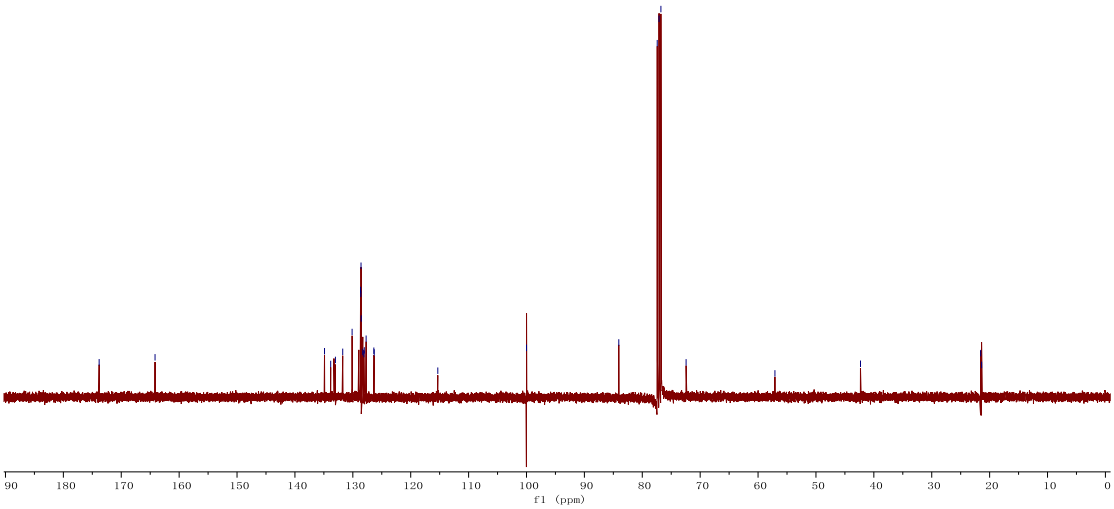


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(thiophen-2-yl)propanoate (4o)

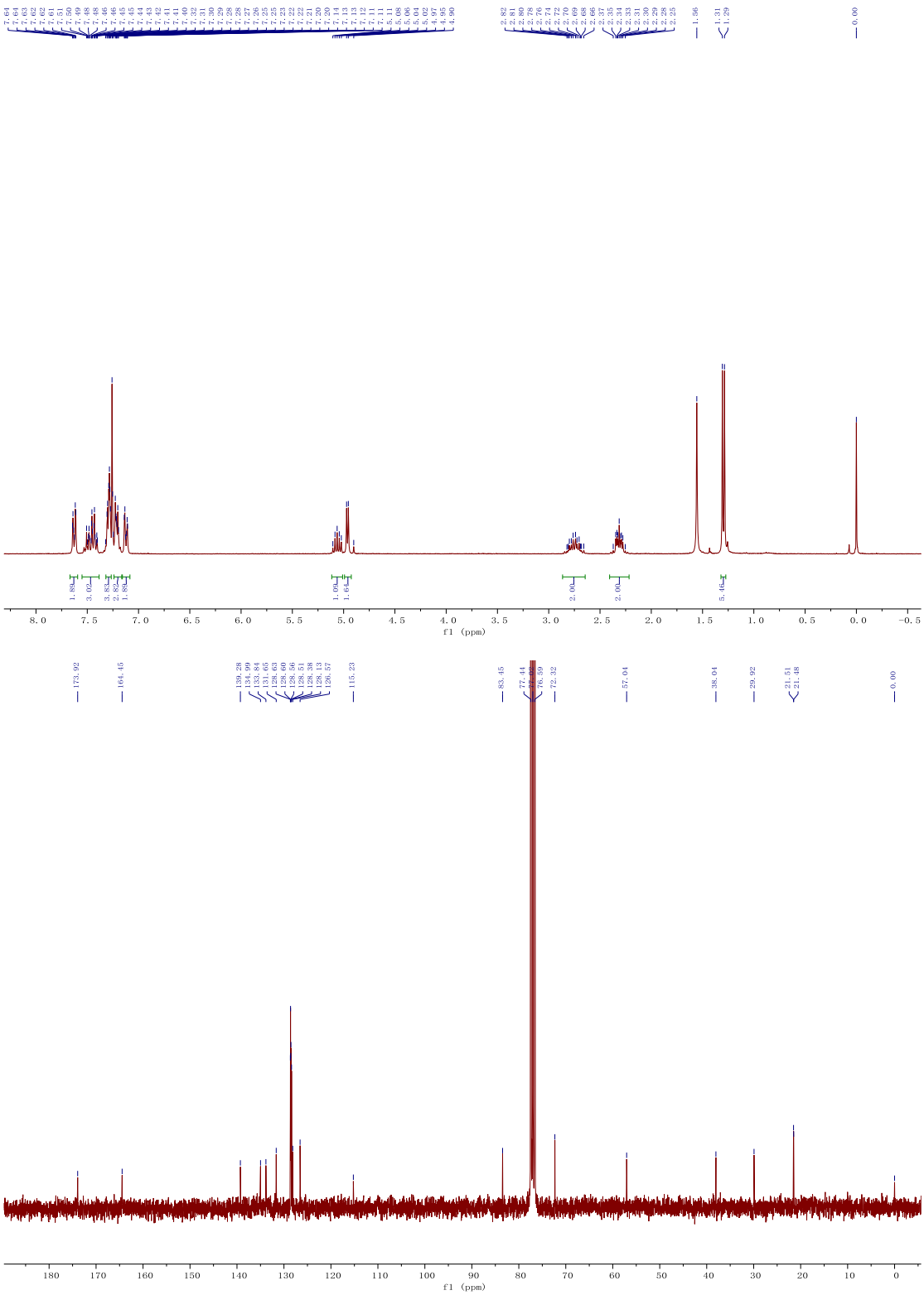


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(naphthalen-2-yl)propanoate (4p)

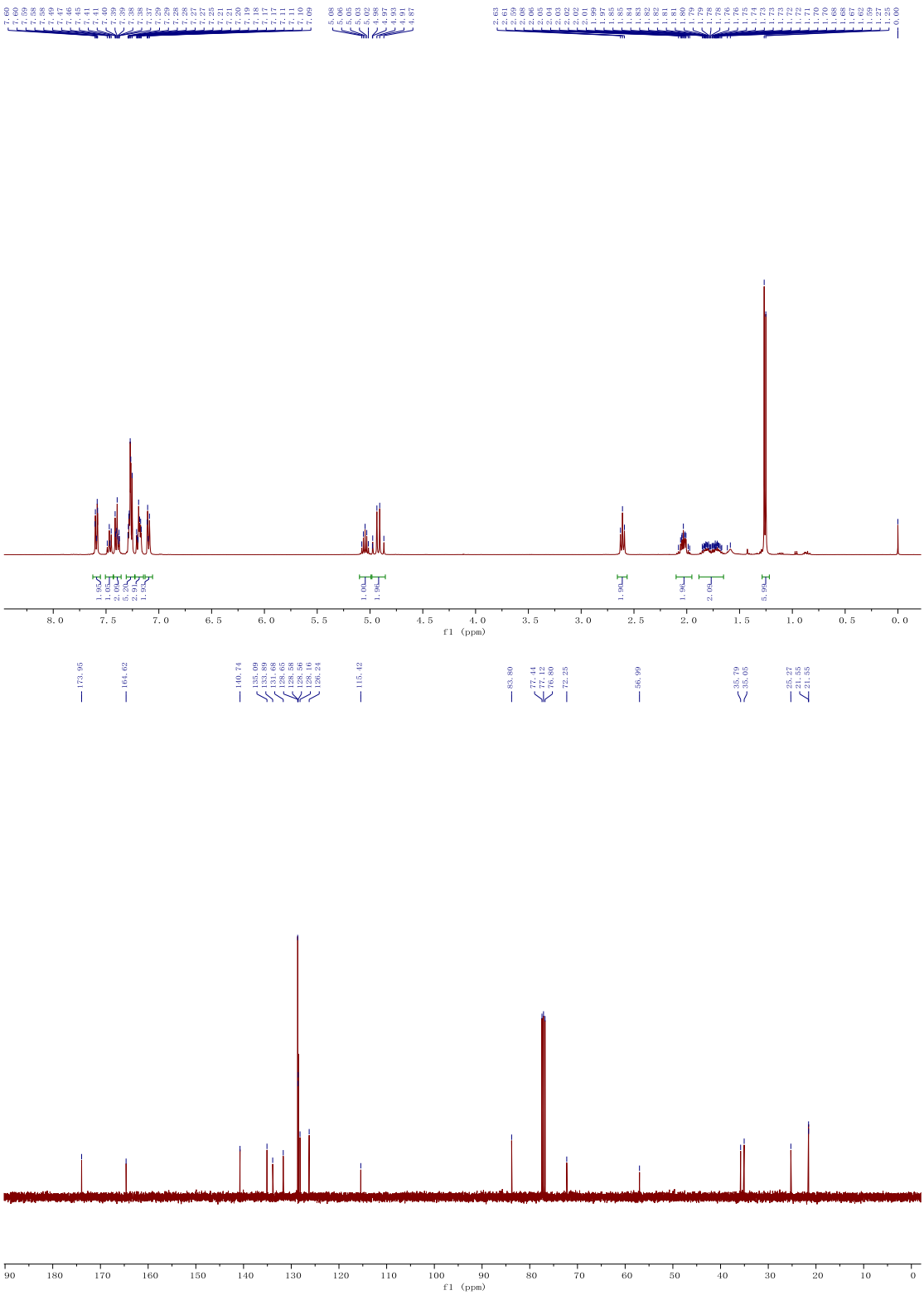




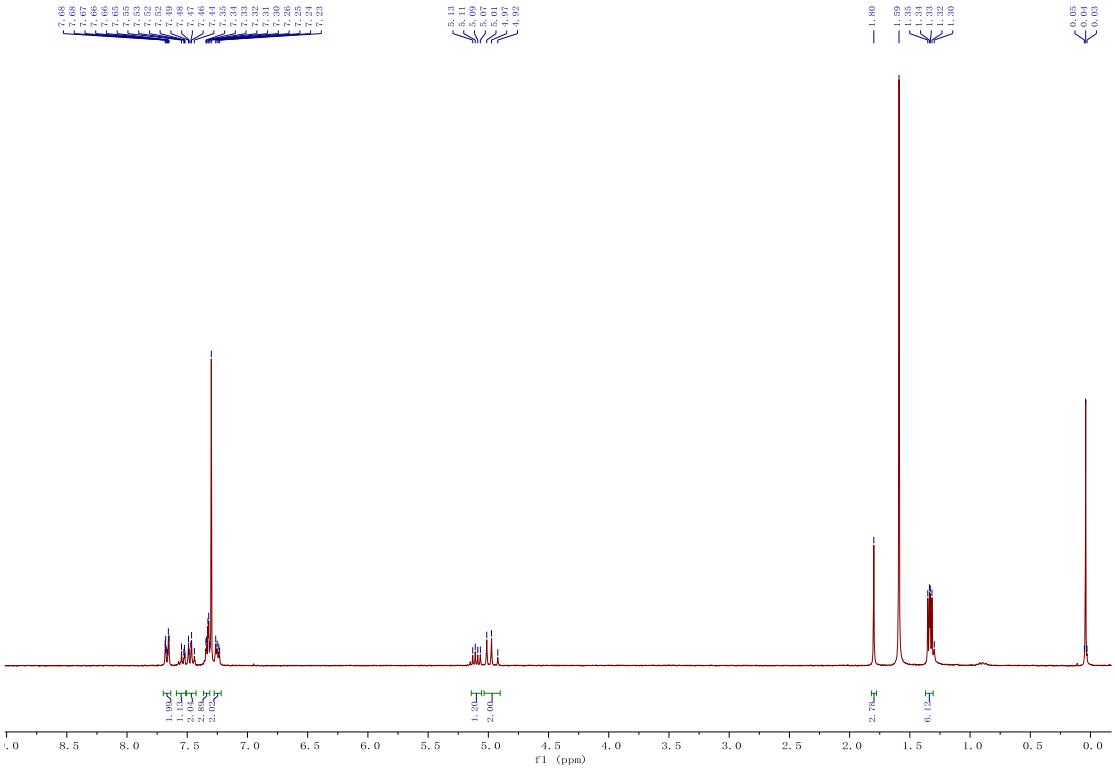
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-4-phenylbutanoate (4q)

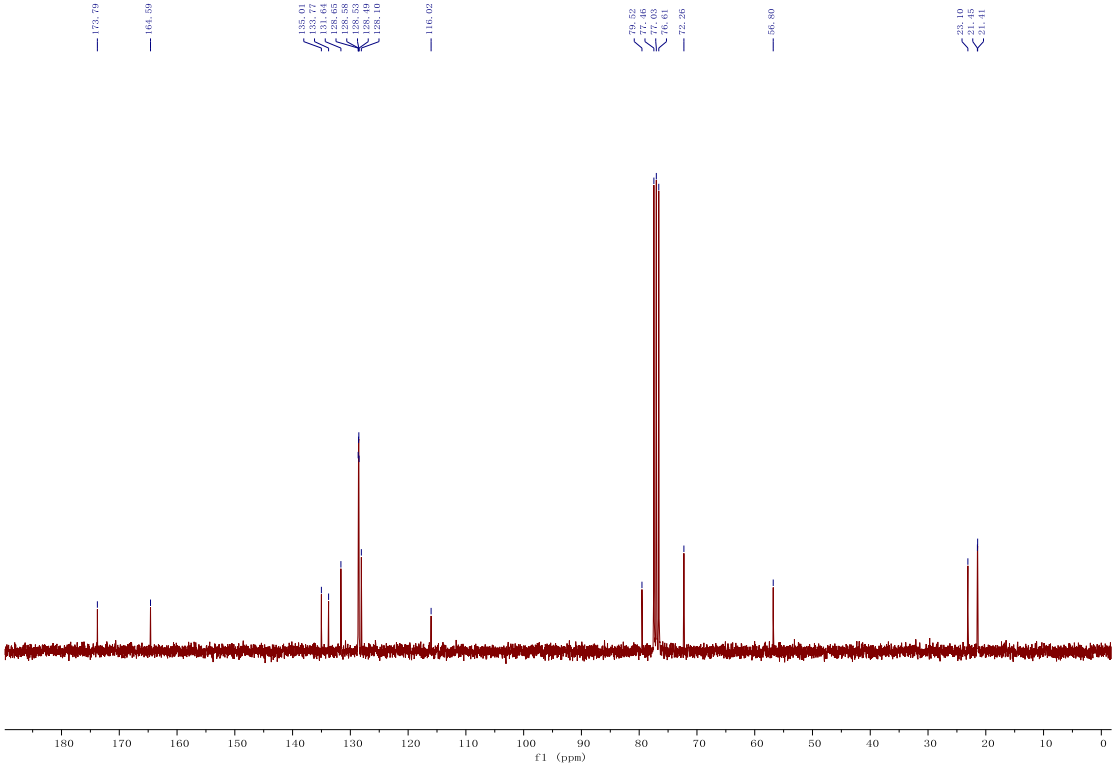


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-5-phenylpentanoate (4r)

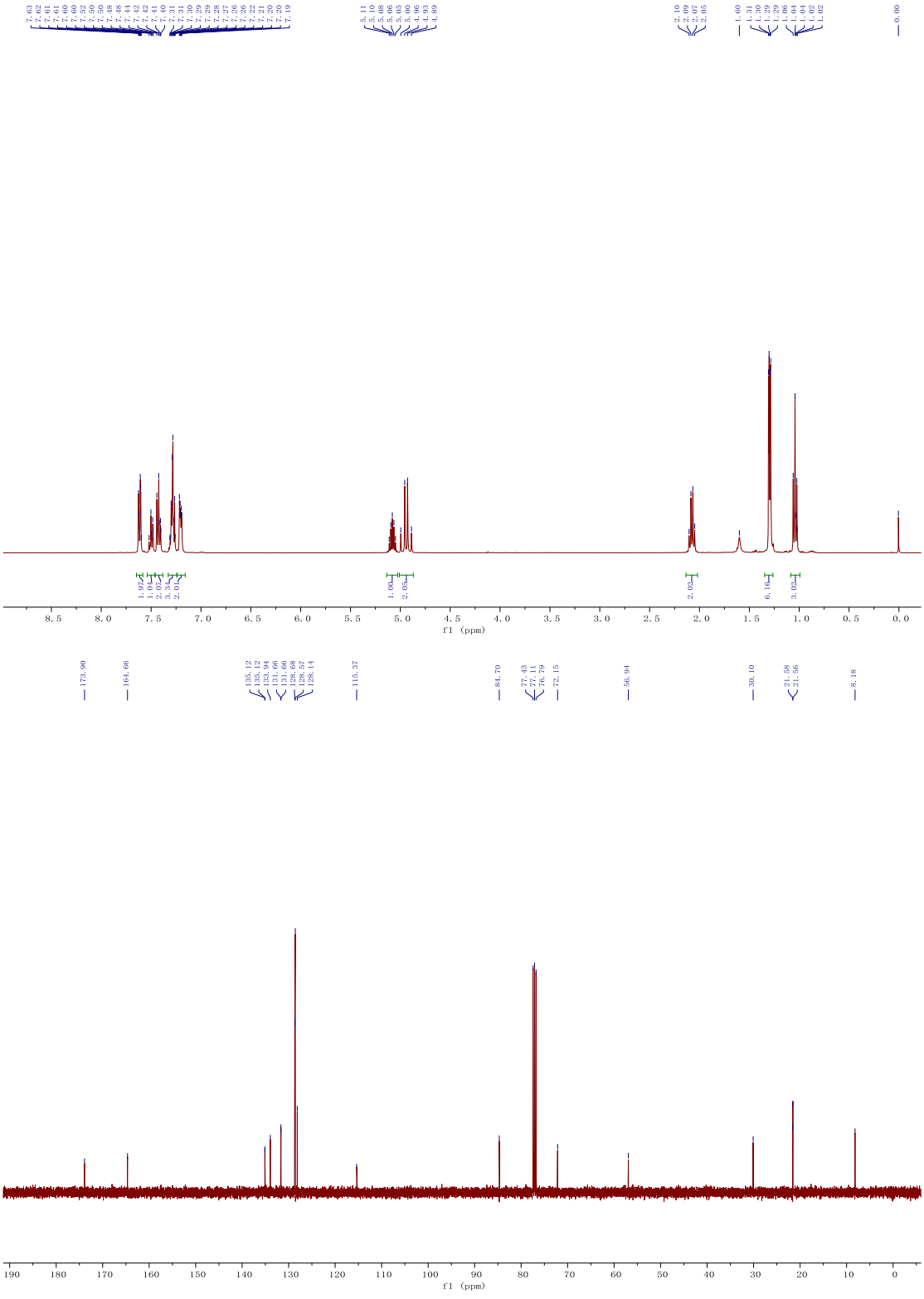


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanopropanoate (4s)

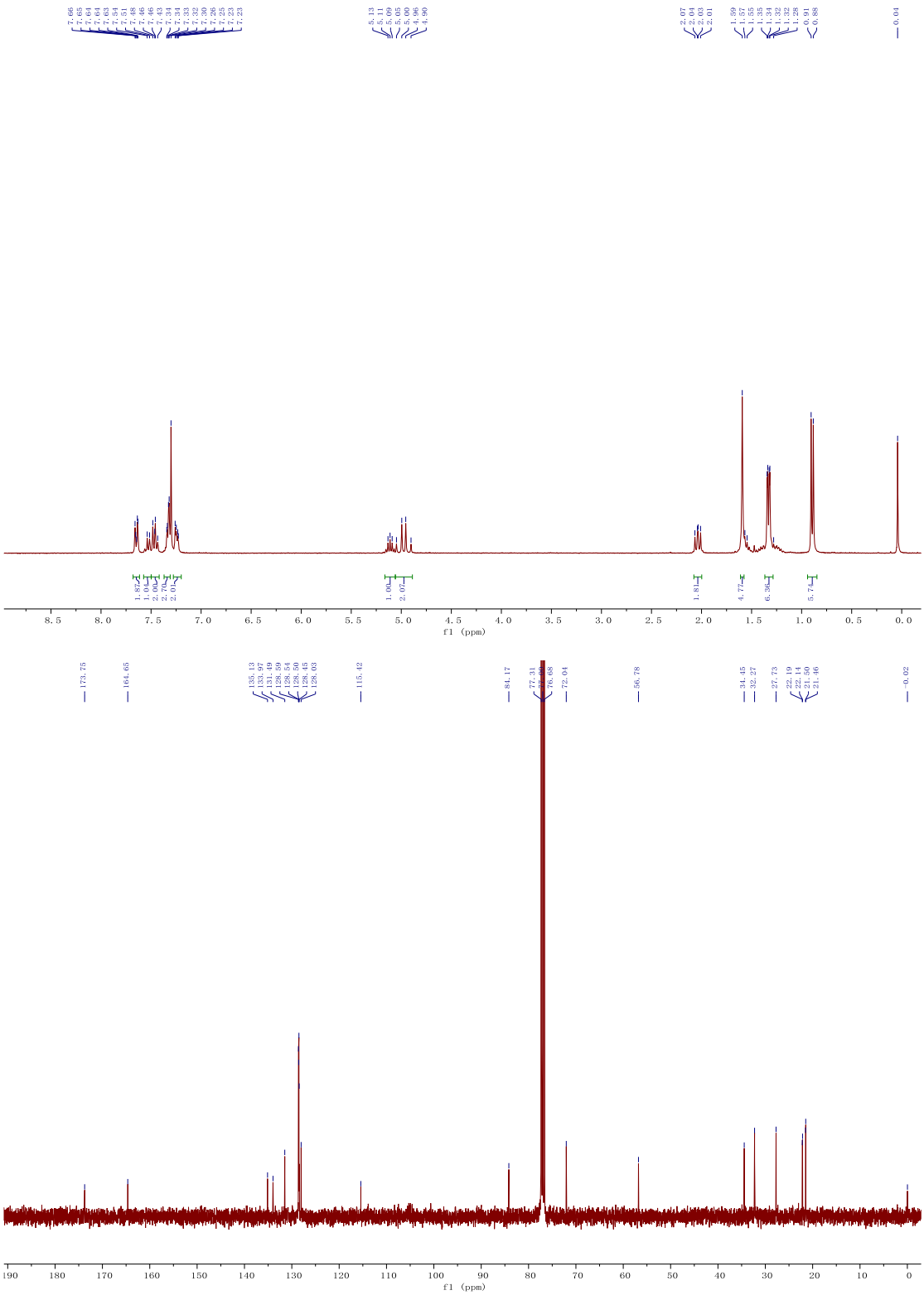




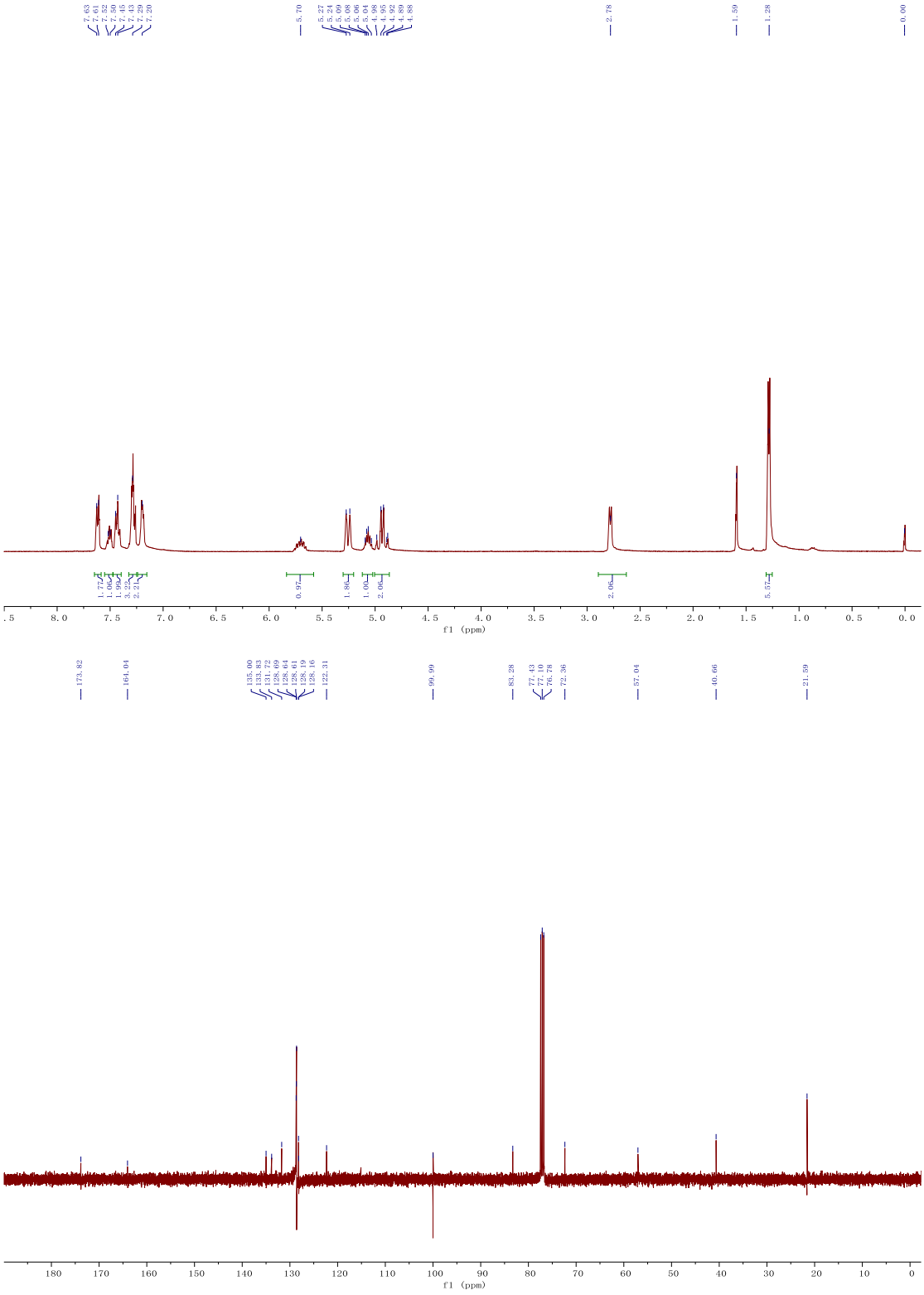
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanobutanoate (4t)



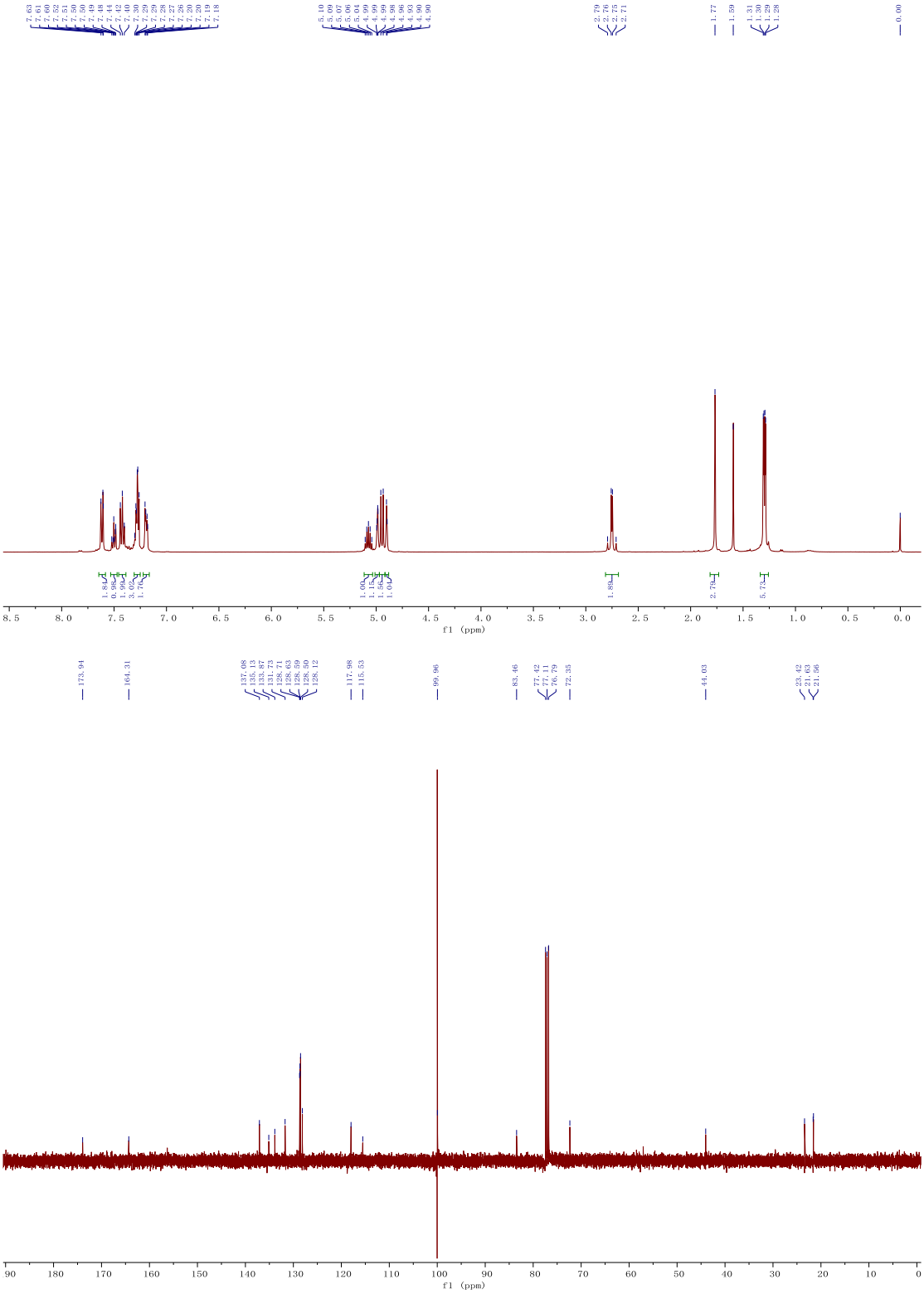
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-5-methylhexanoate (4u)



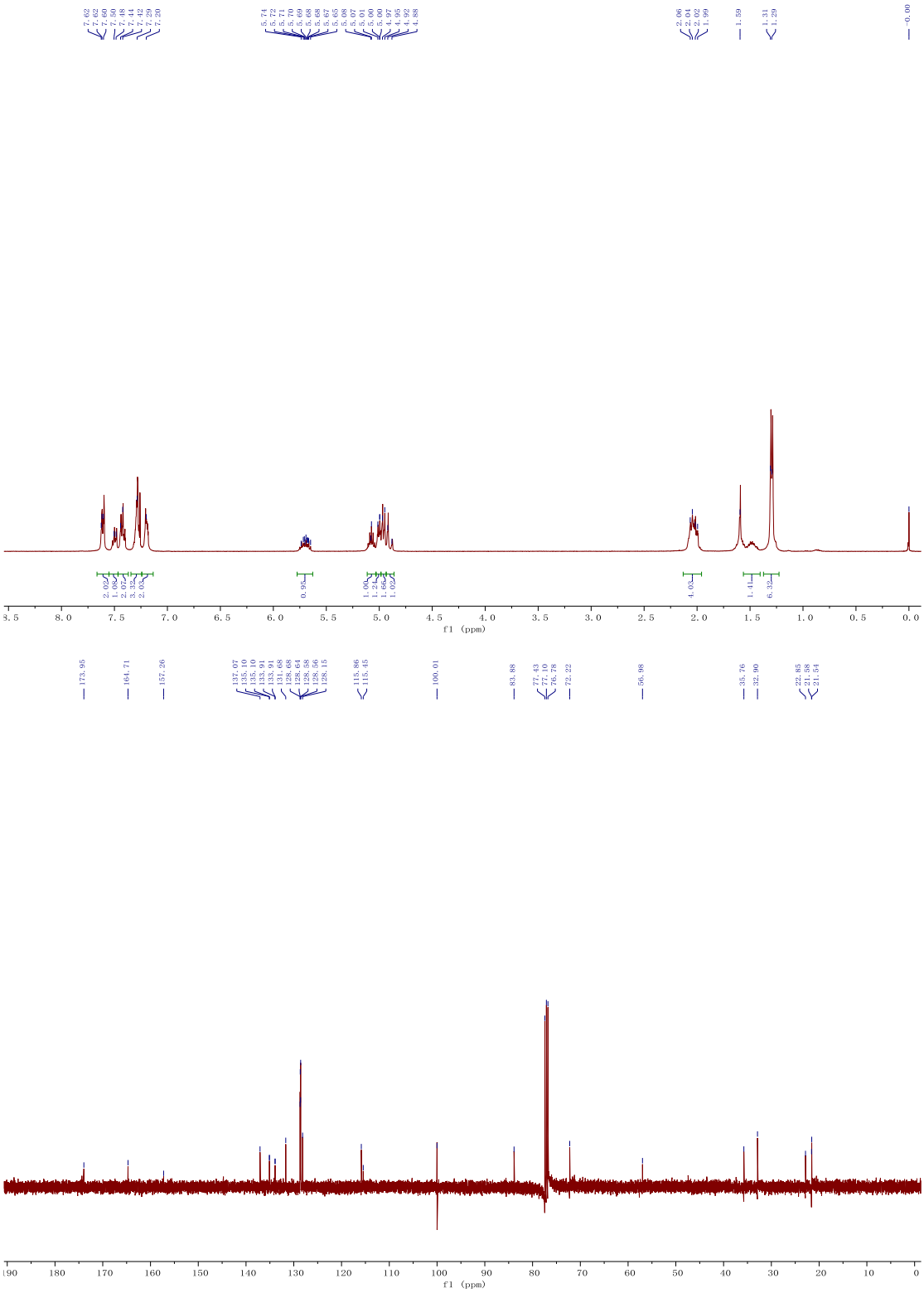
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanopent-4-enoate (4v)



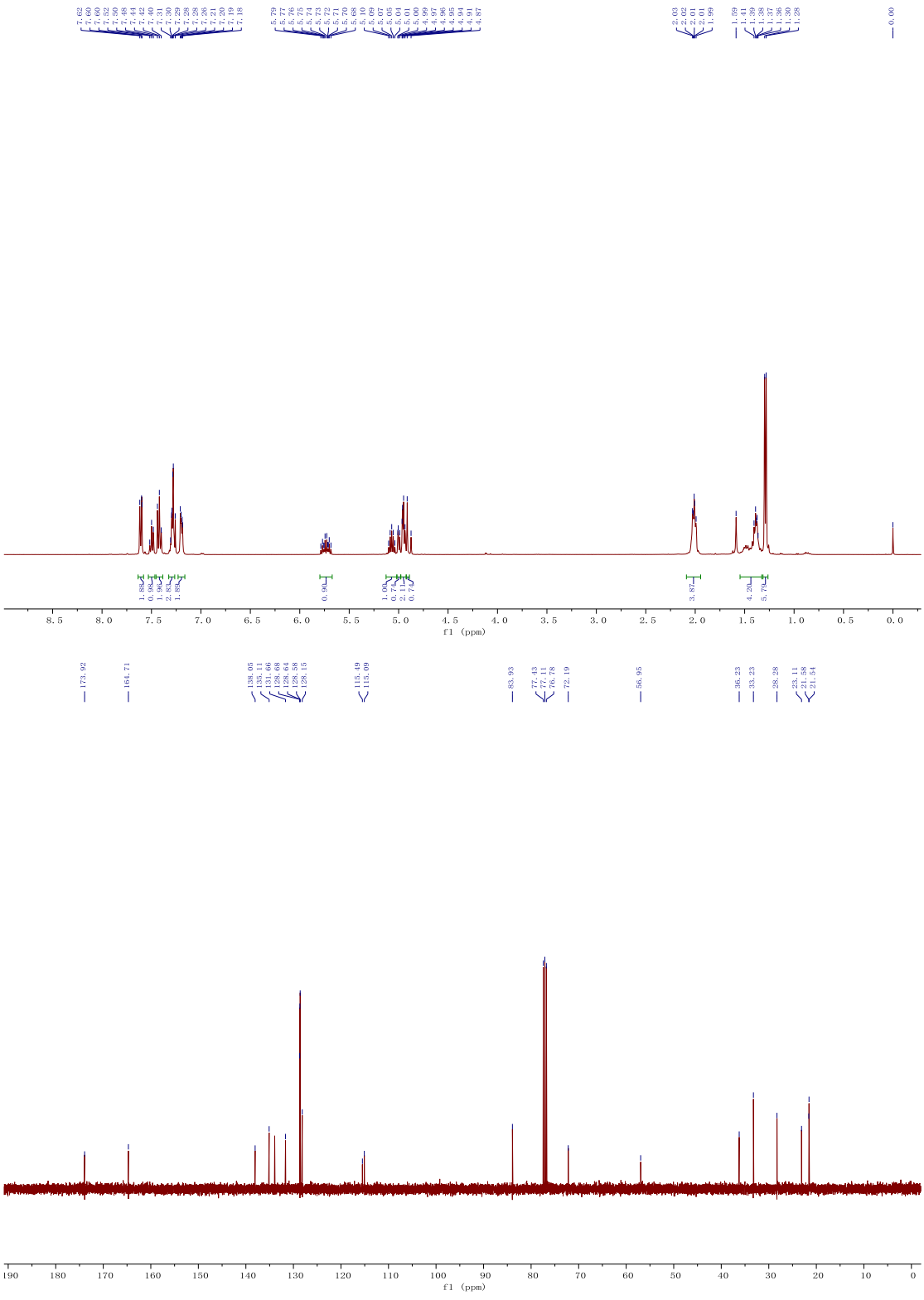
isopropyl 2-((N-benzylbenzamido)oxy)-2-cyano-4-methylpent-4-enoate (4w)



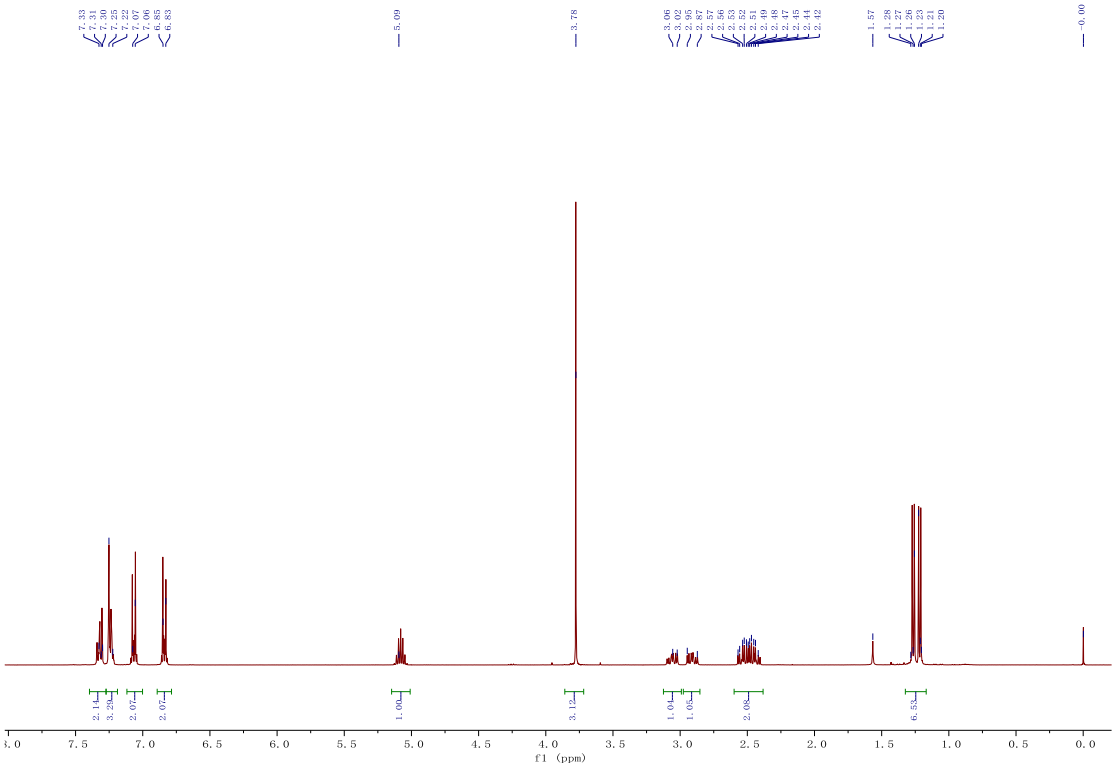
isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanohept-6-enoate (4x)

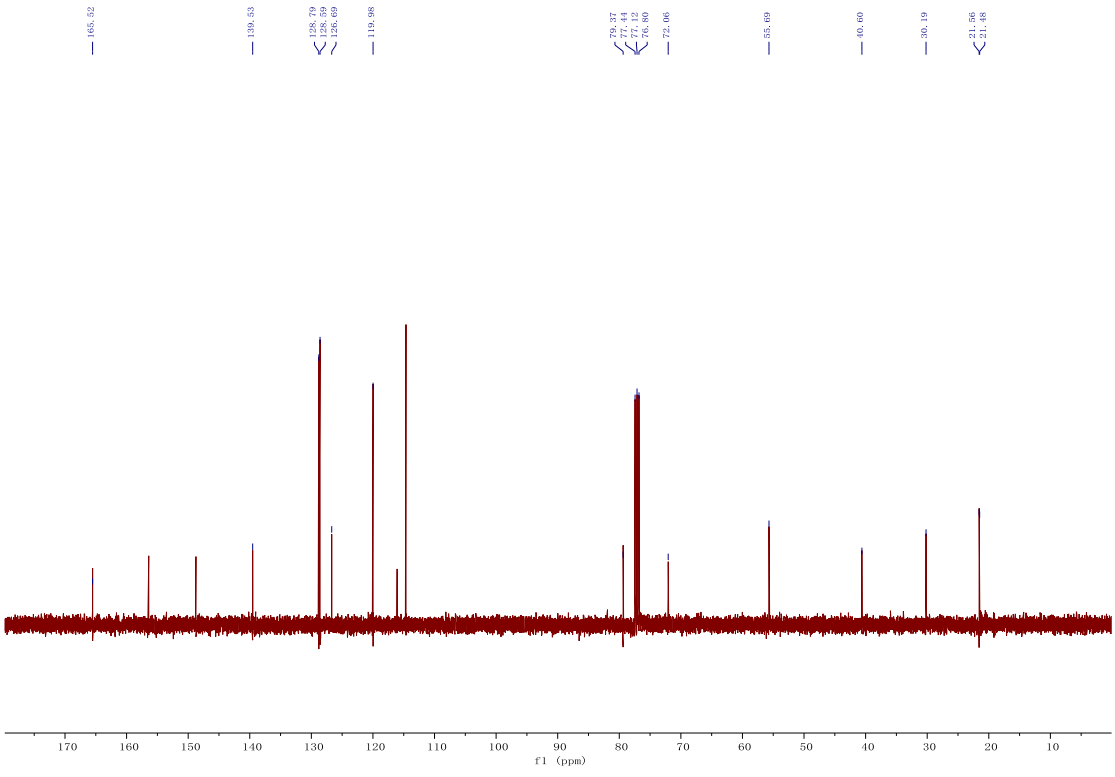


isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanooct-7-enoate (4y)

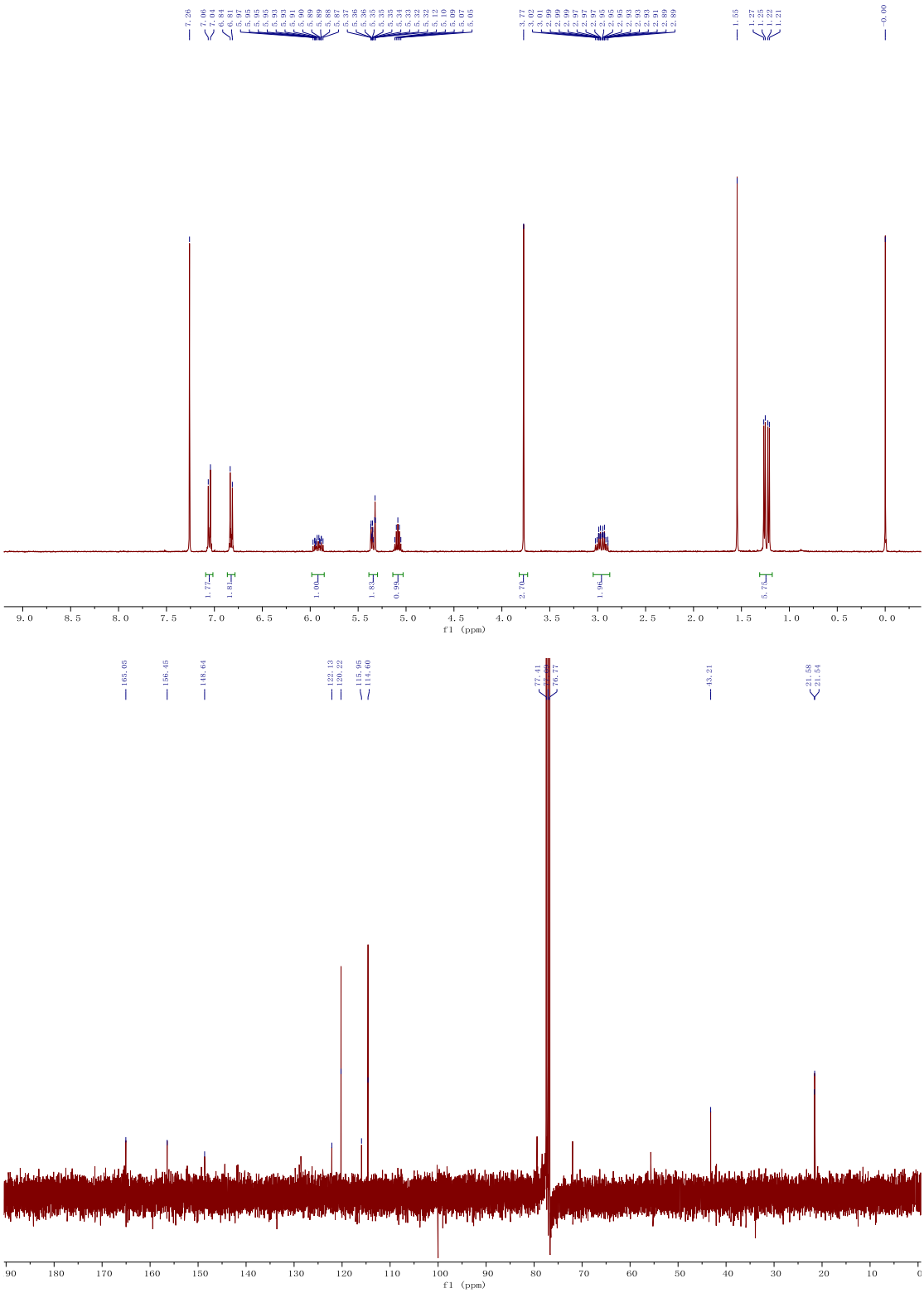


isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)-4-phenylbutanoate (6a)

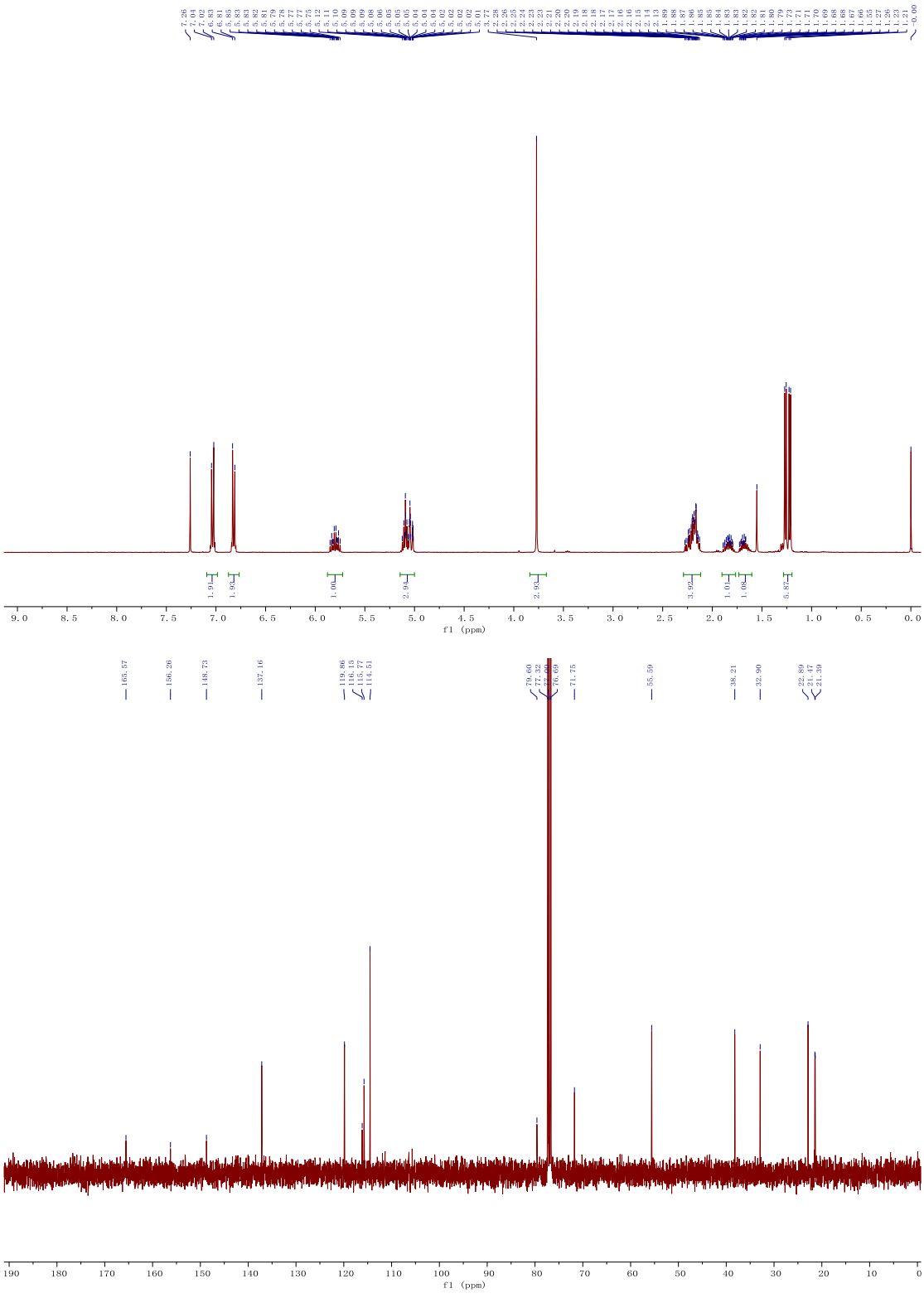




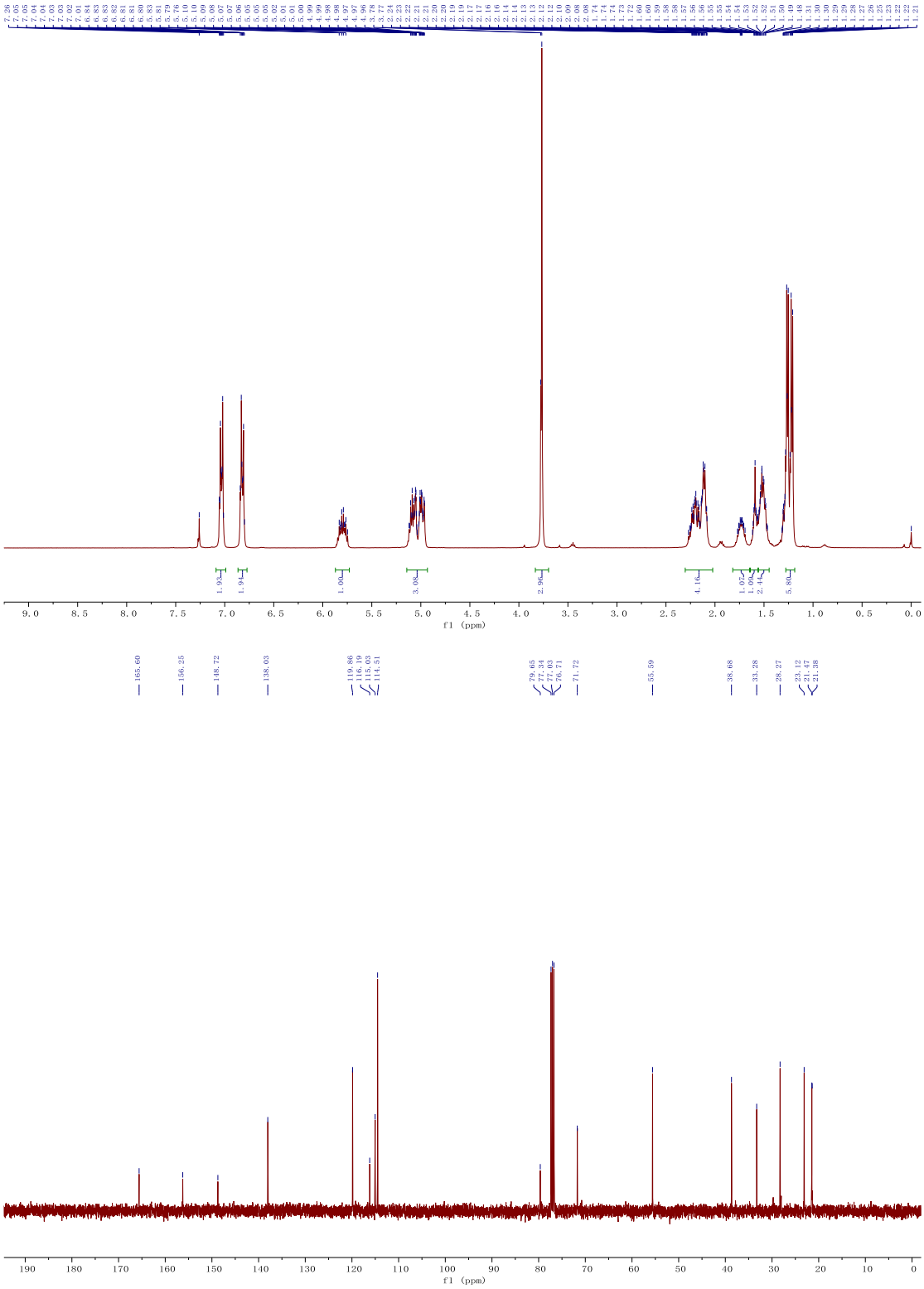
isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)pent-4-enoate (6b)



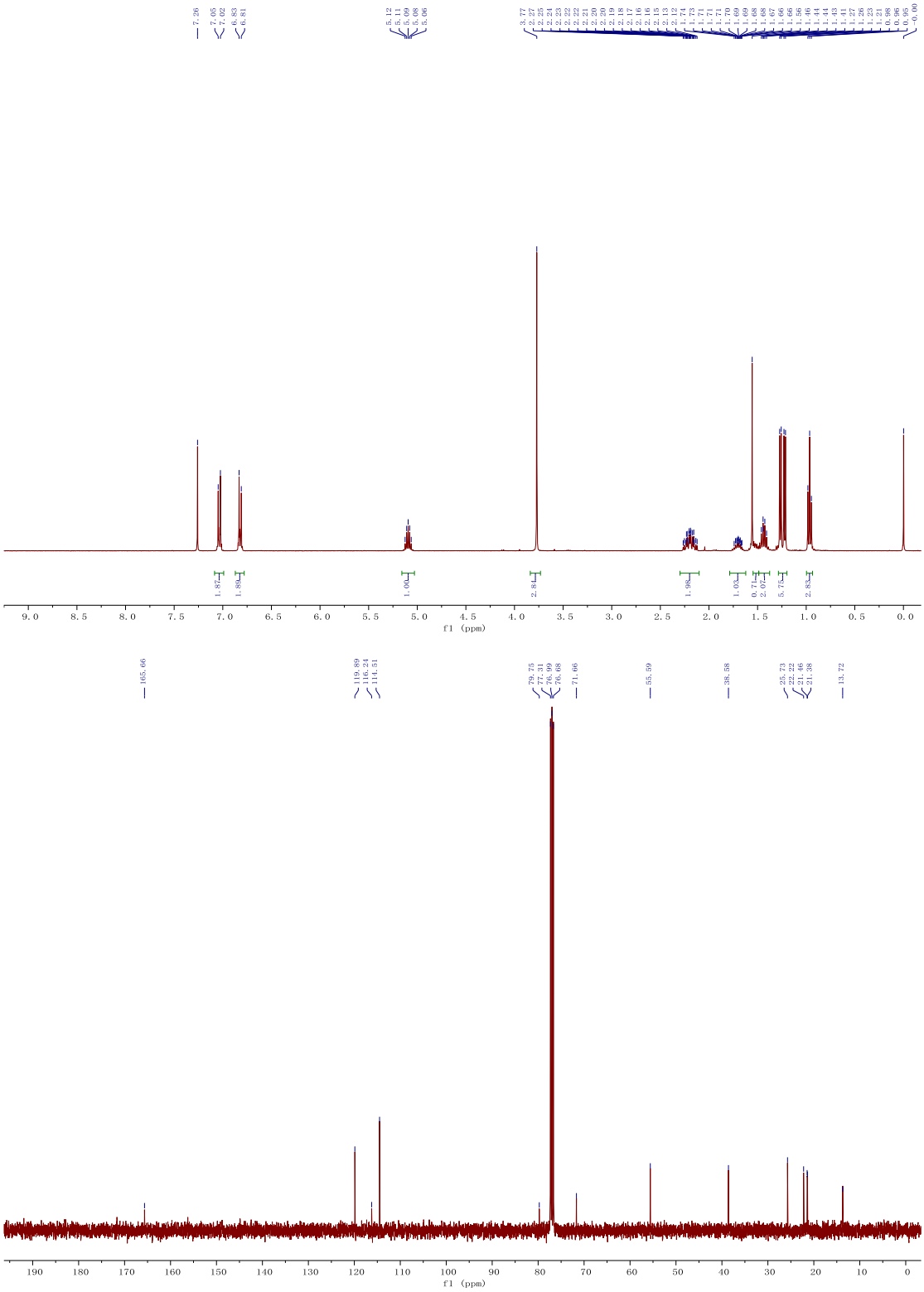
isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)hept-6-enoate (6c)



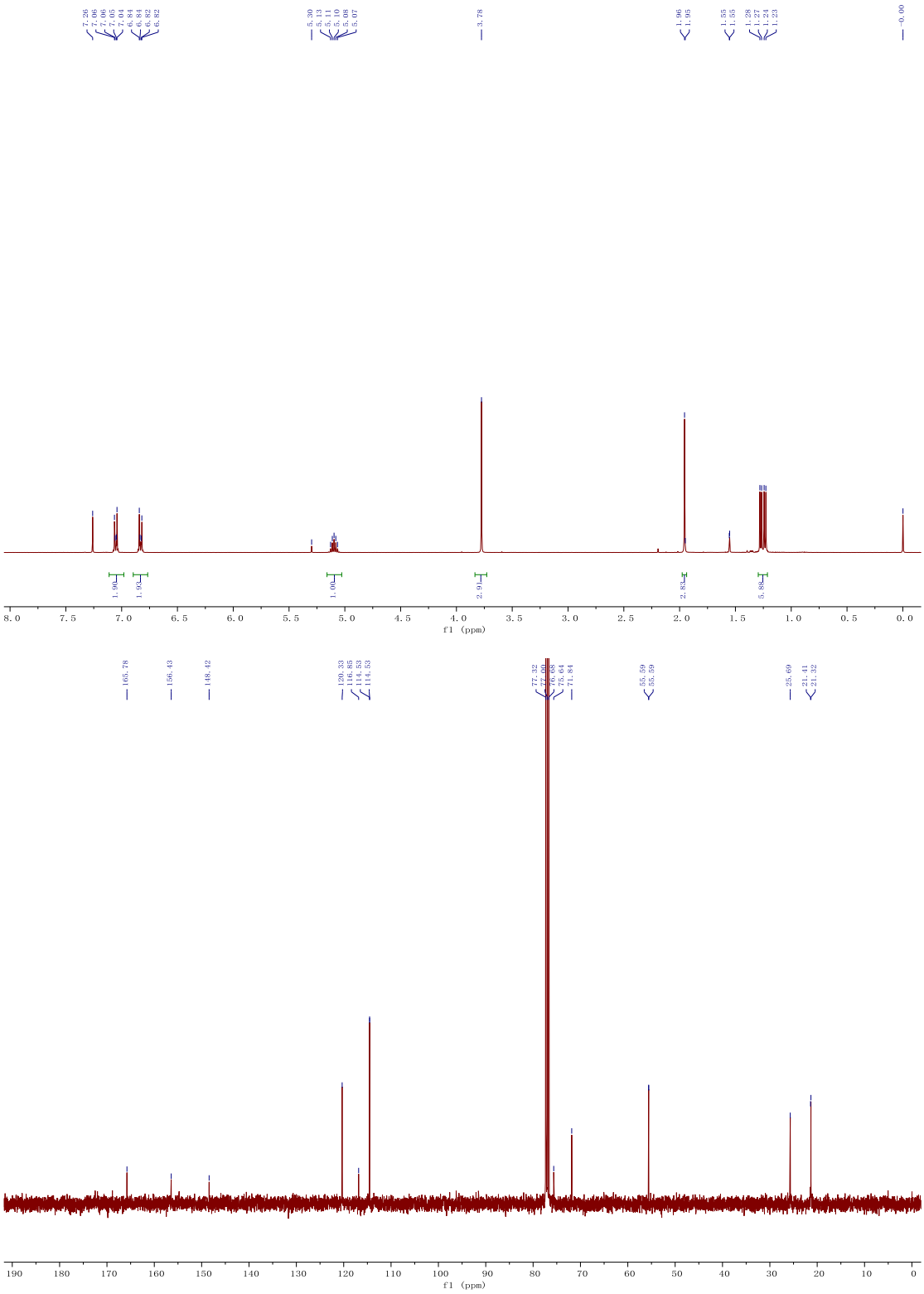
isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)oct-7-enoate (6d)



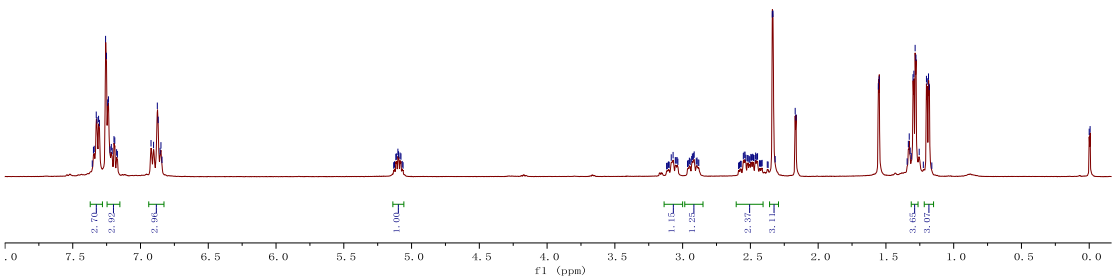
isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)hexanoate (6e)

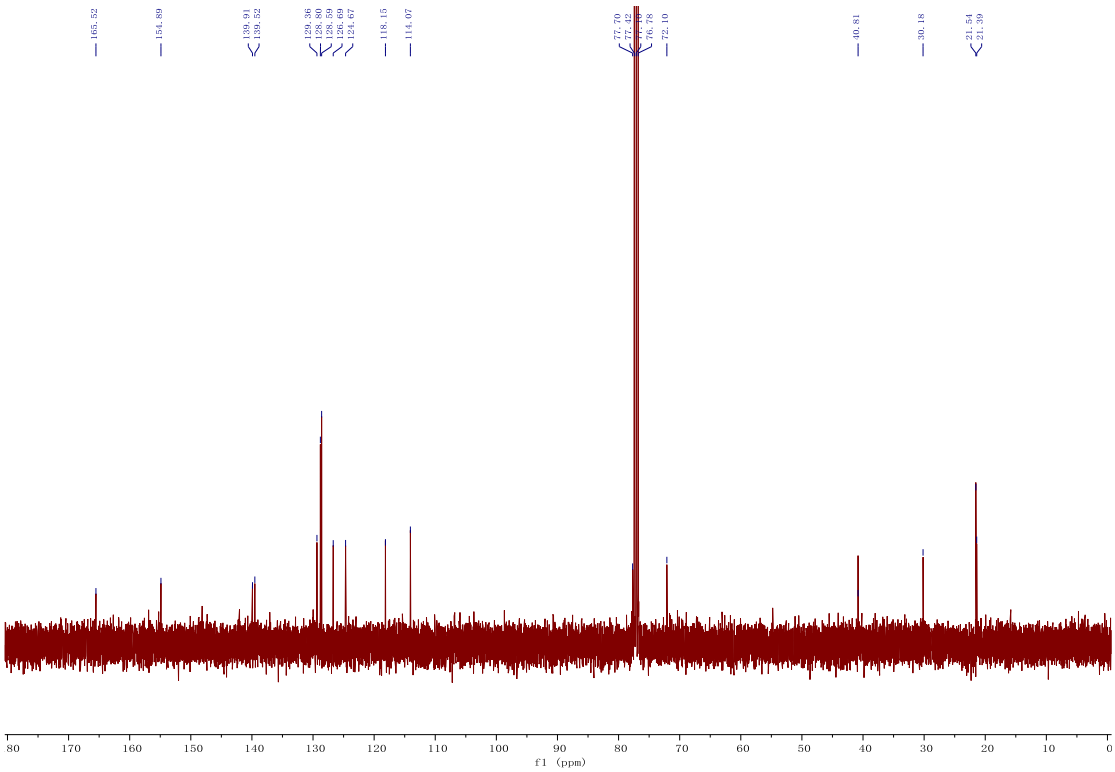


isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)propanoate (6f)

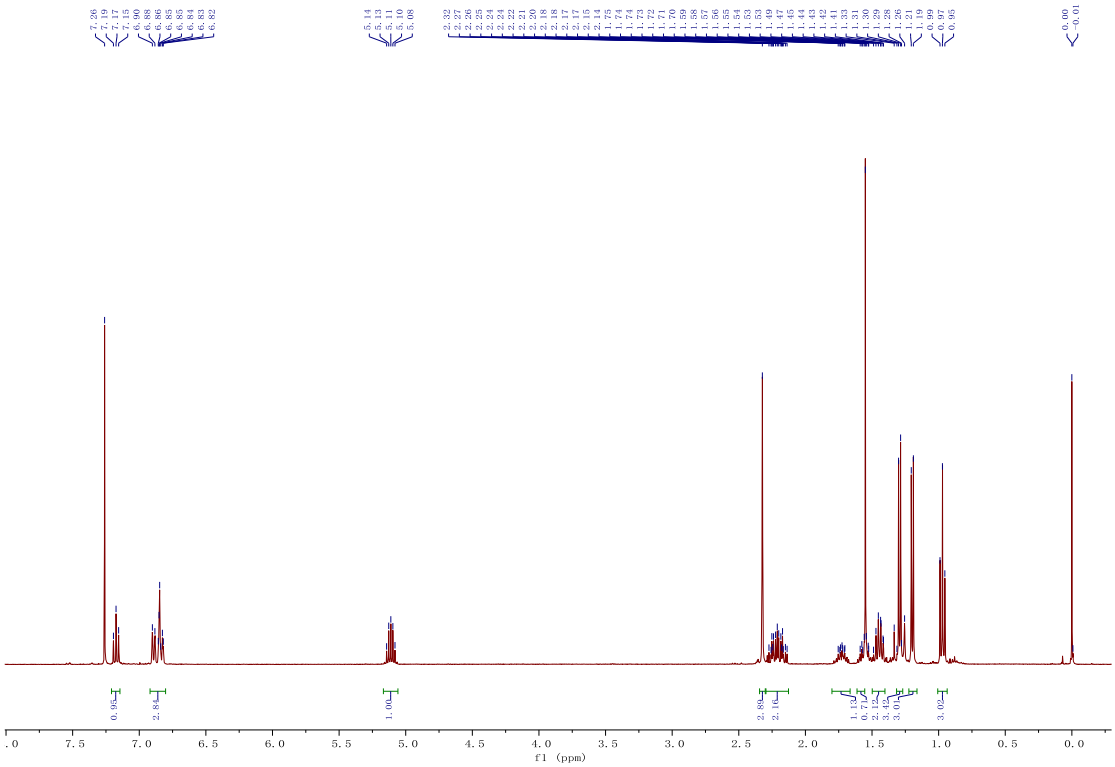


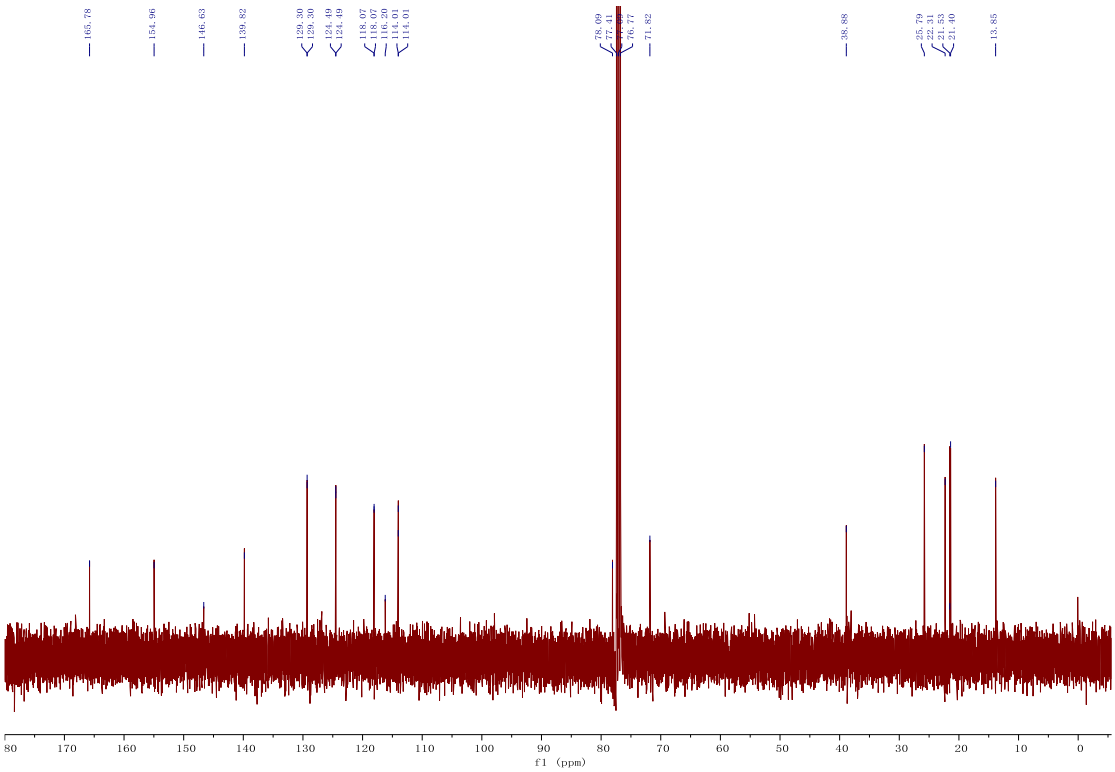
isopropyl (R)-2-cyano-4-phenyl-2-(p-tolyloxy)butanoate (6g)



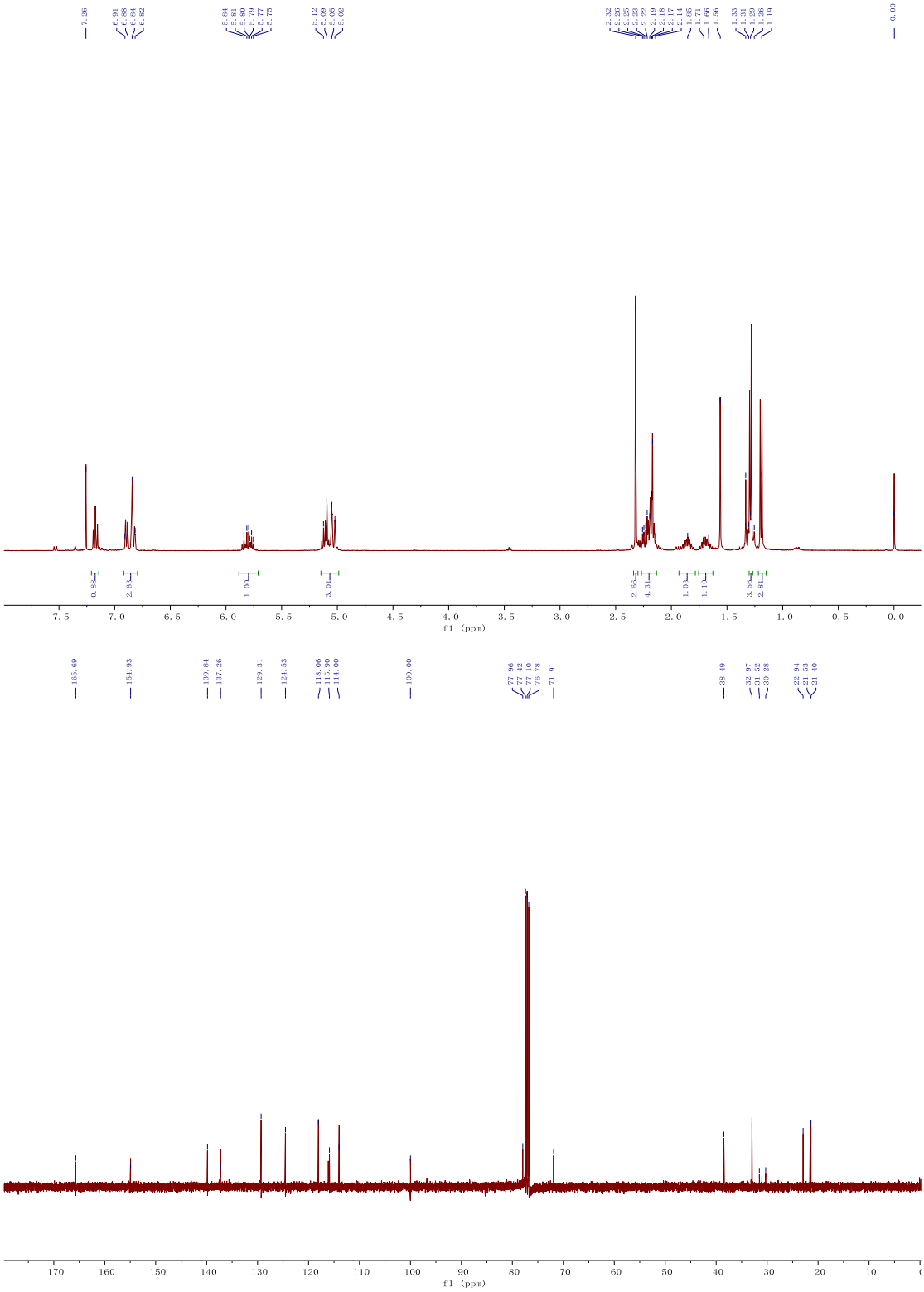


isopropyl (R)-2-cyano-2-(p-tolyloxy)hexanoate (6h)

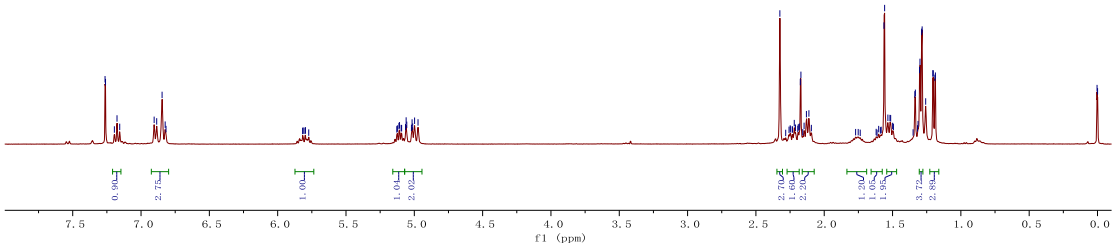


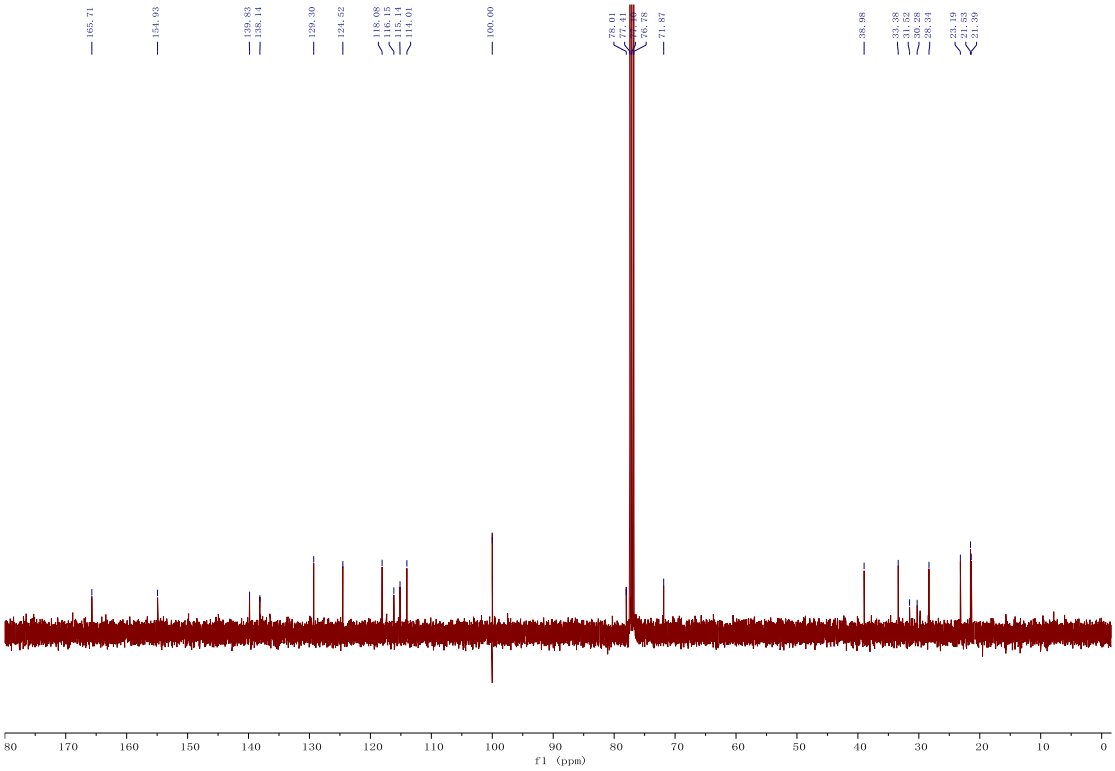


isopropyl (R)-2-cyano-2-(p-tolyloxy)hept-6-enoate (6i)

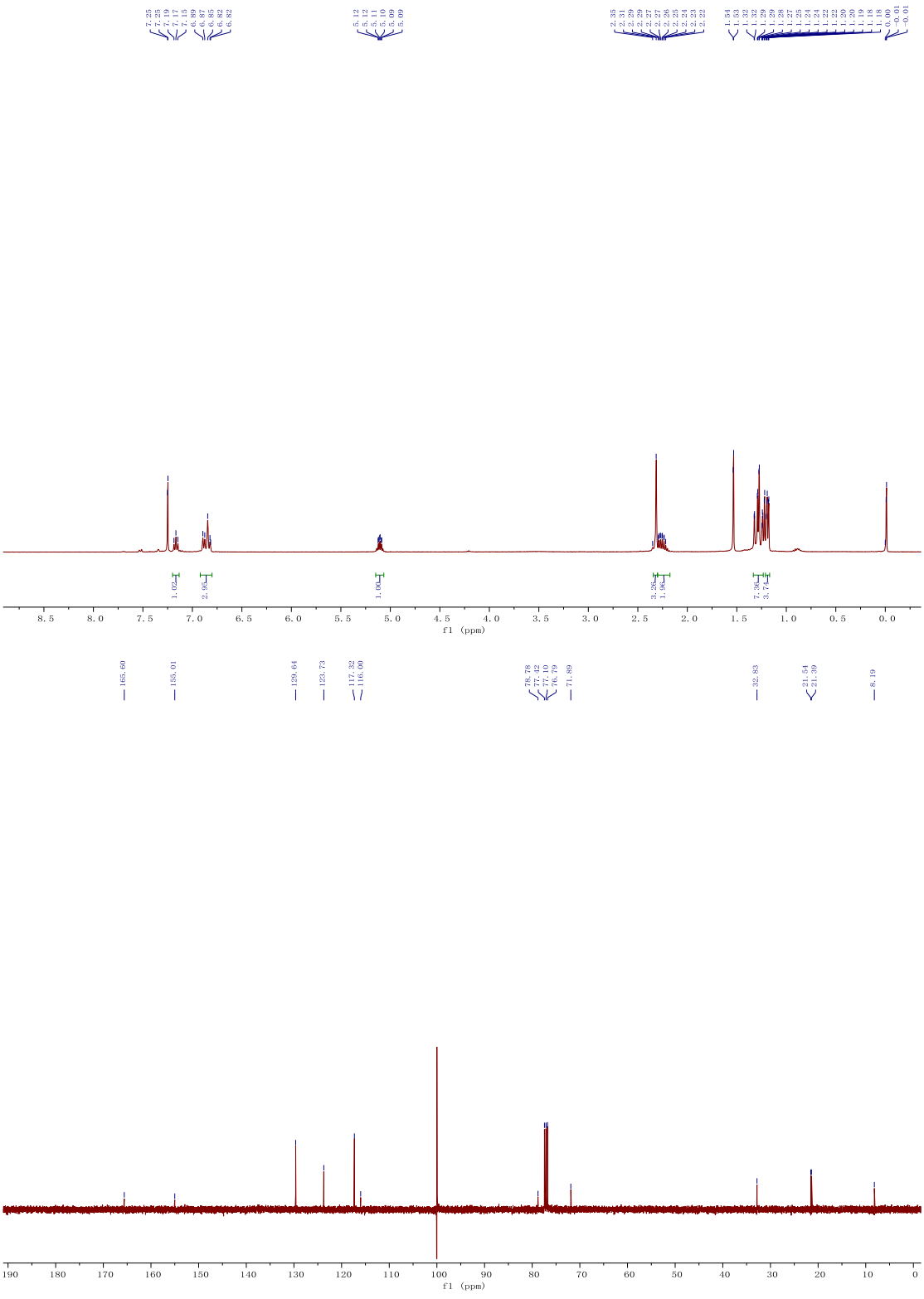


isopropyl (R)-2-cyano-2-(p-tolyloxy)oct-7-enoate (6j)

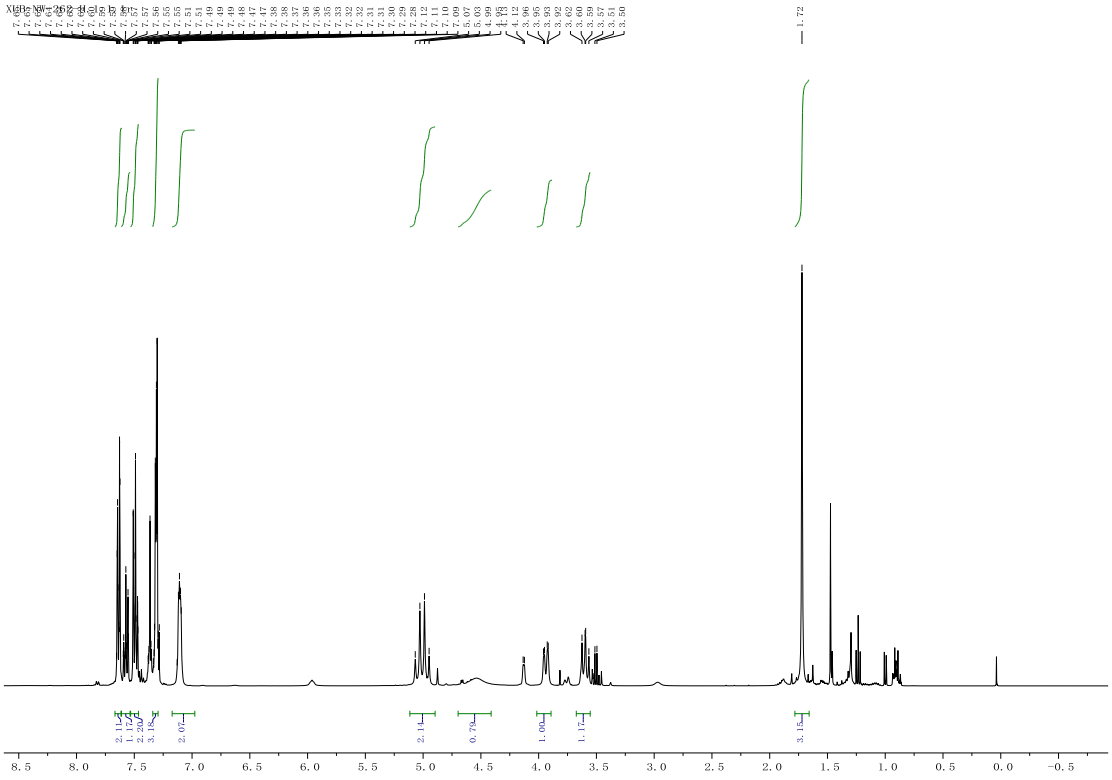


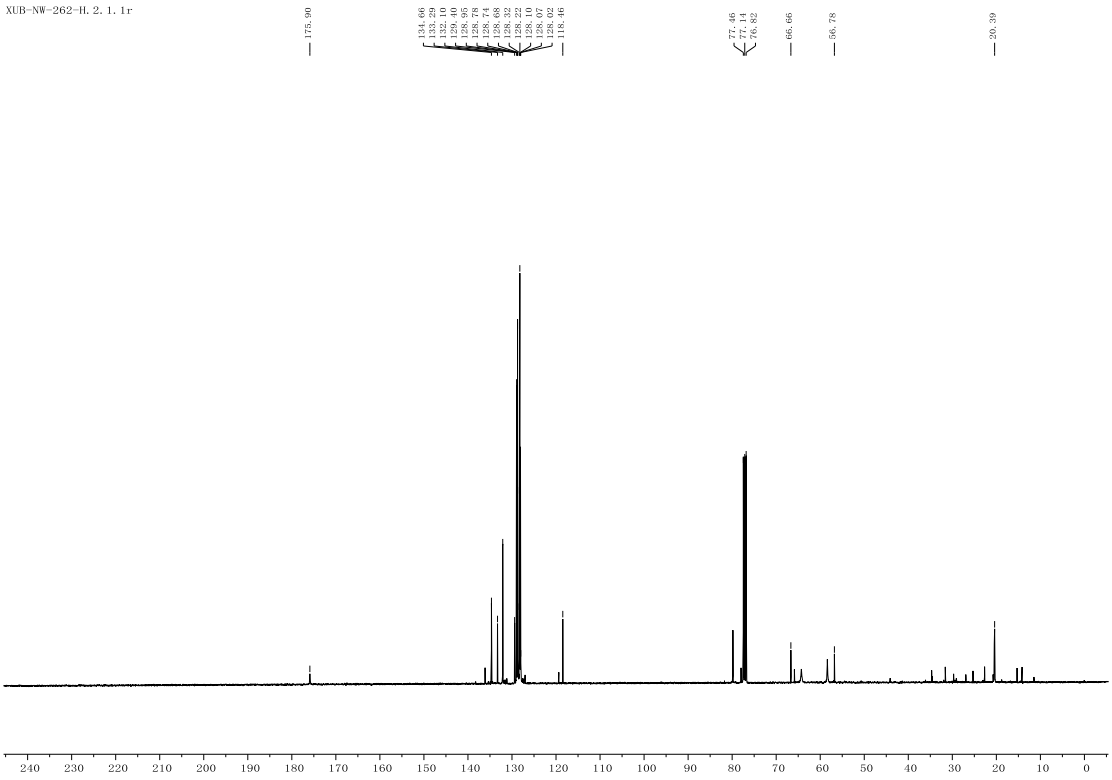


isopropyl (R)-2-cyano-2-(p-tolyloxy)butanoate (6k)

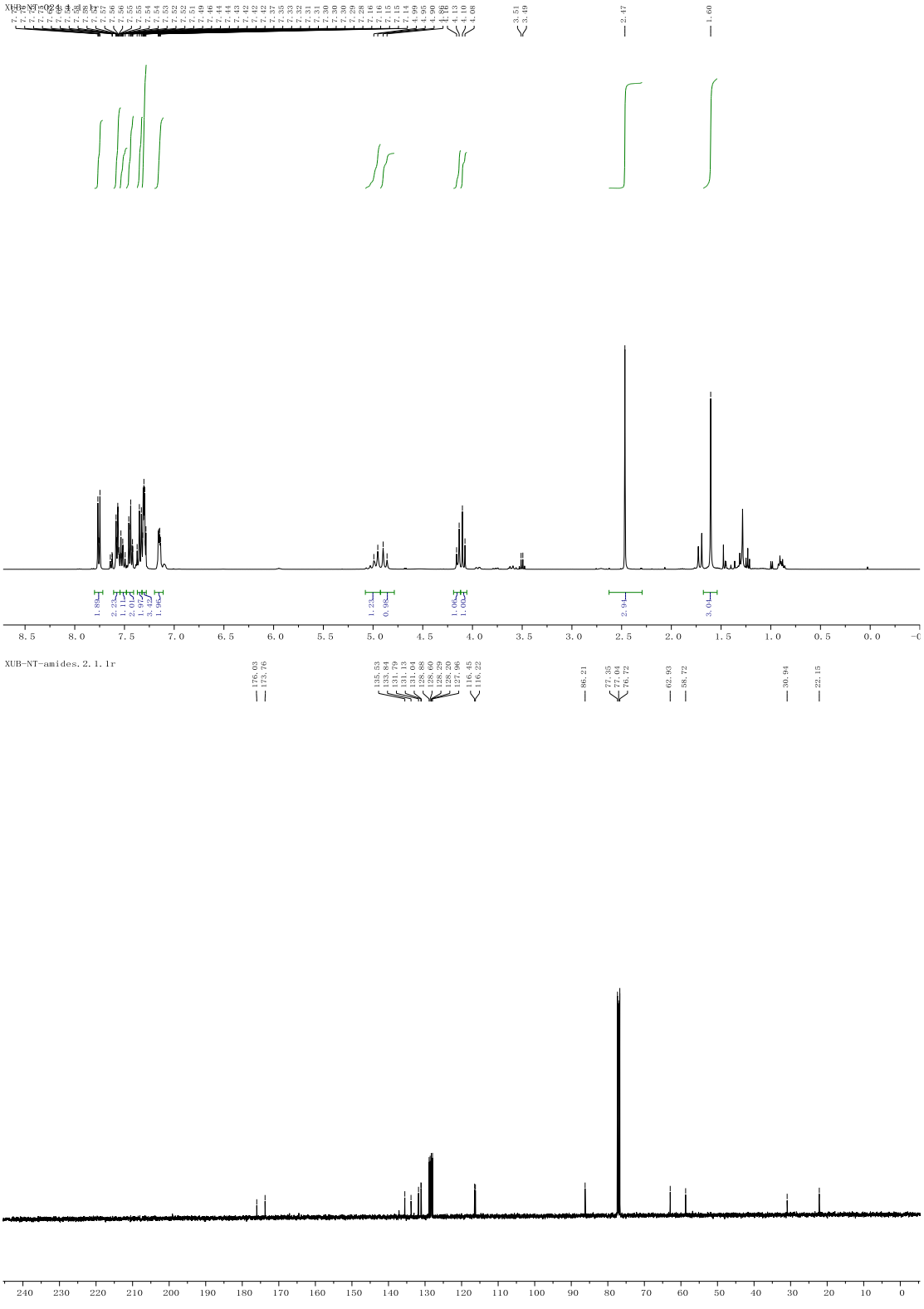


(R)-N-benzyl-N-((2-cyano-1-hydroxypropan-2-yl)oxy)benzamide (7)

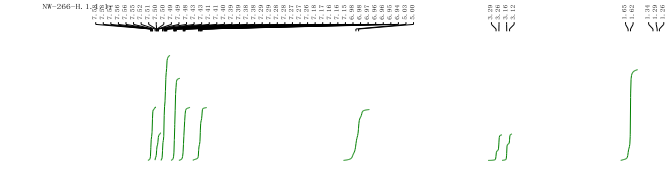


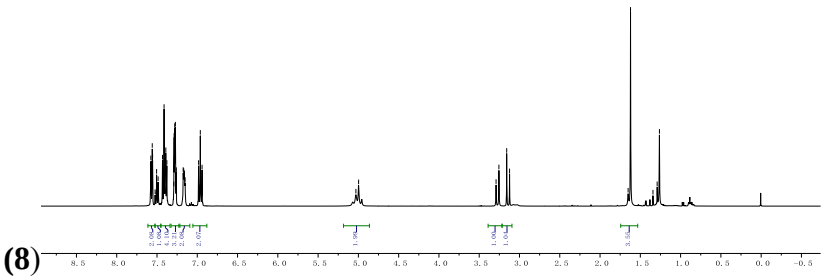


(R)-2-((N-benzylbenzamido)oxy)-2-cyanopropyl 4-methylbenzenesulfonate (7-Ts)

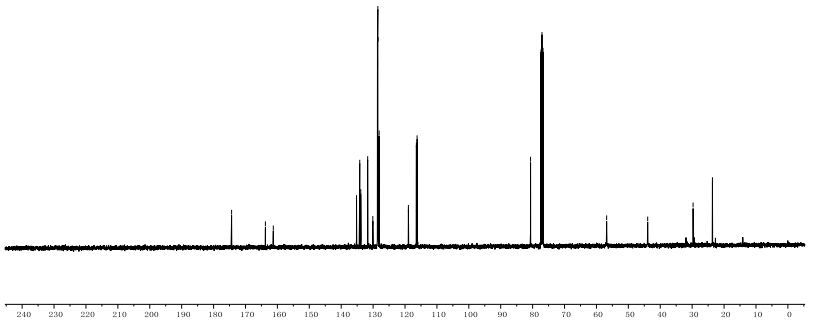


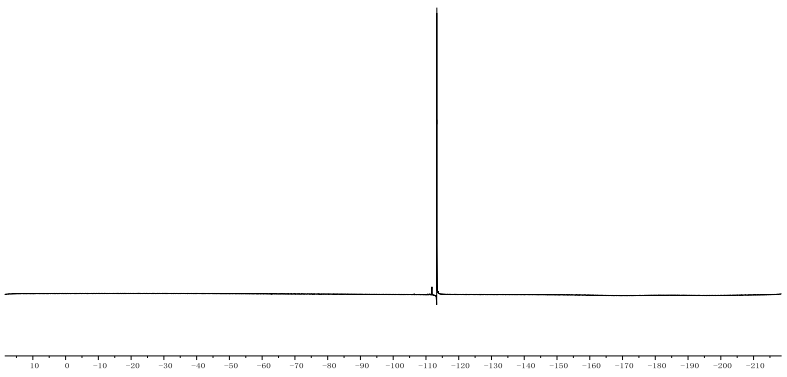
(R)-N-benzyl-N-((2-cyano-1-((4-fluorophenyl)thio)propan-2-yl)oxy)benzamide



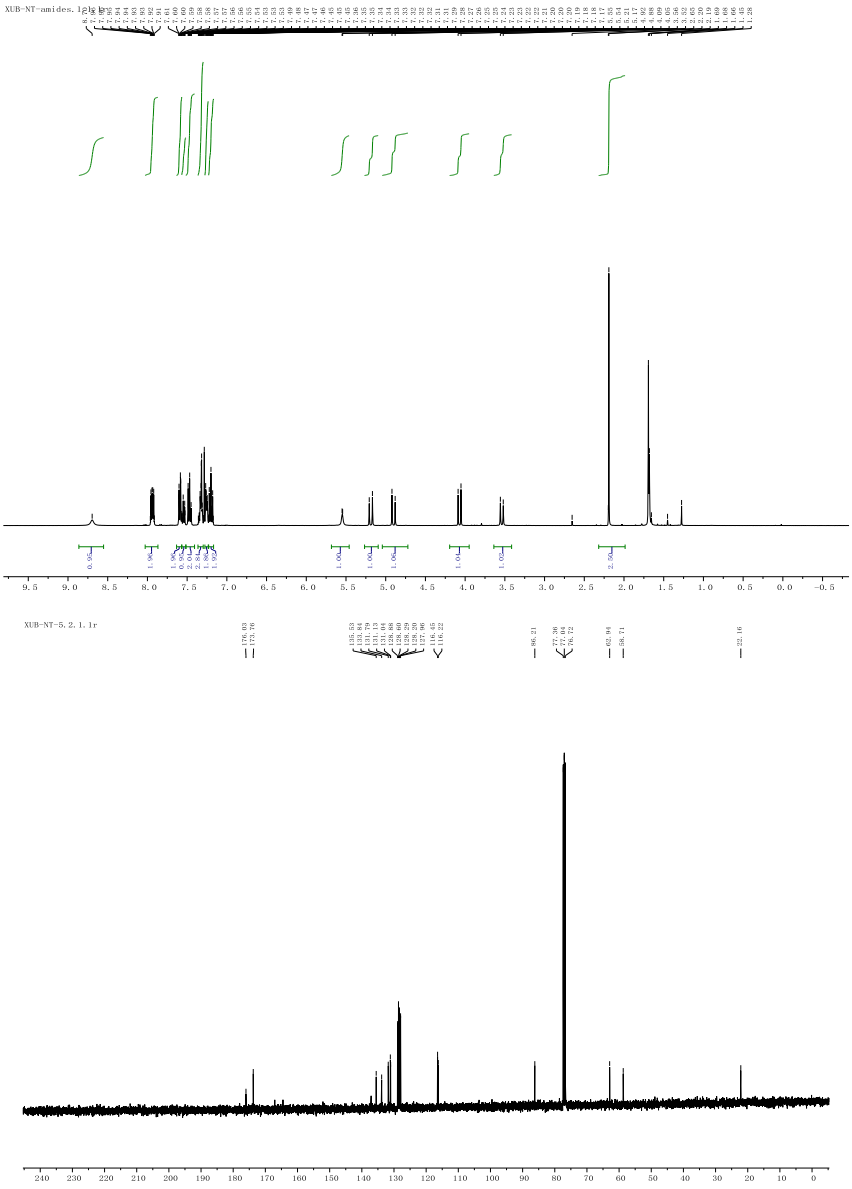


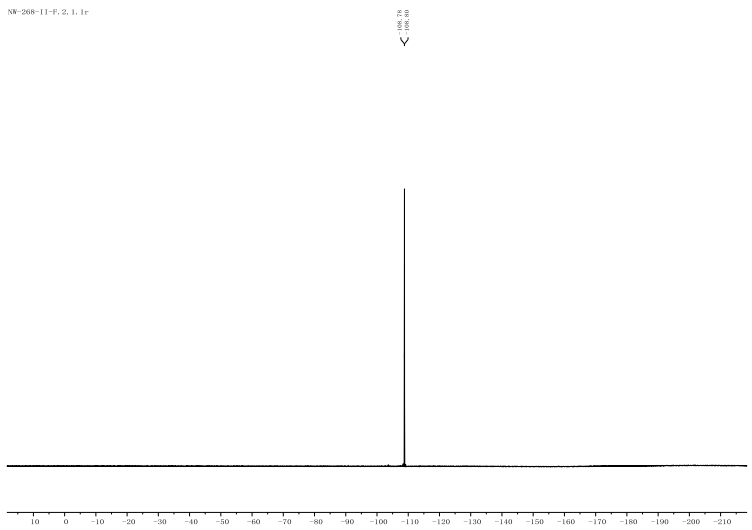
(8)



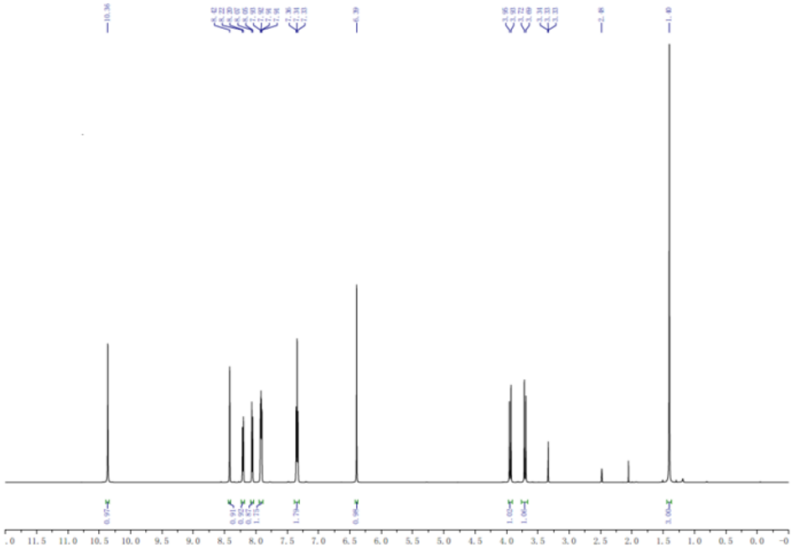


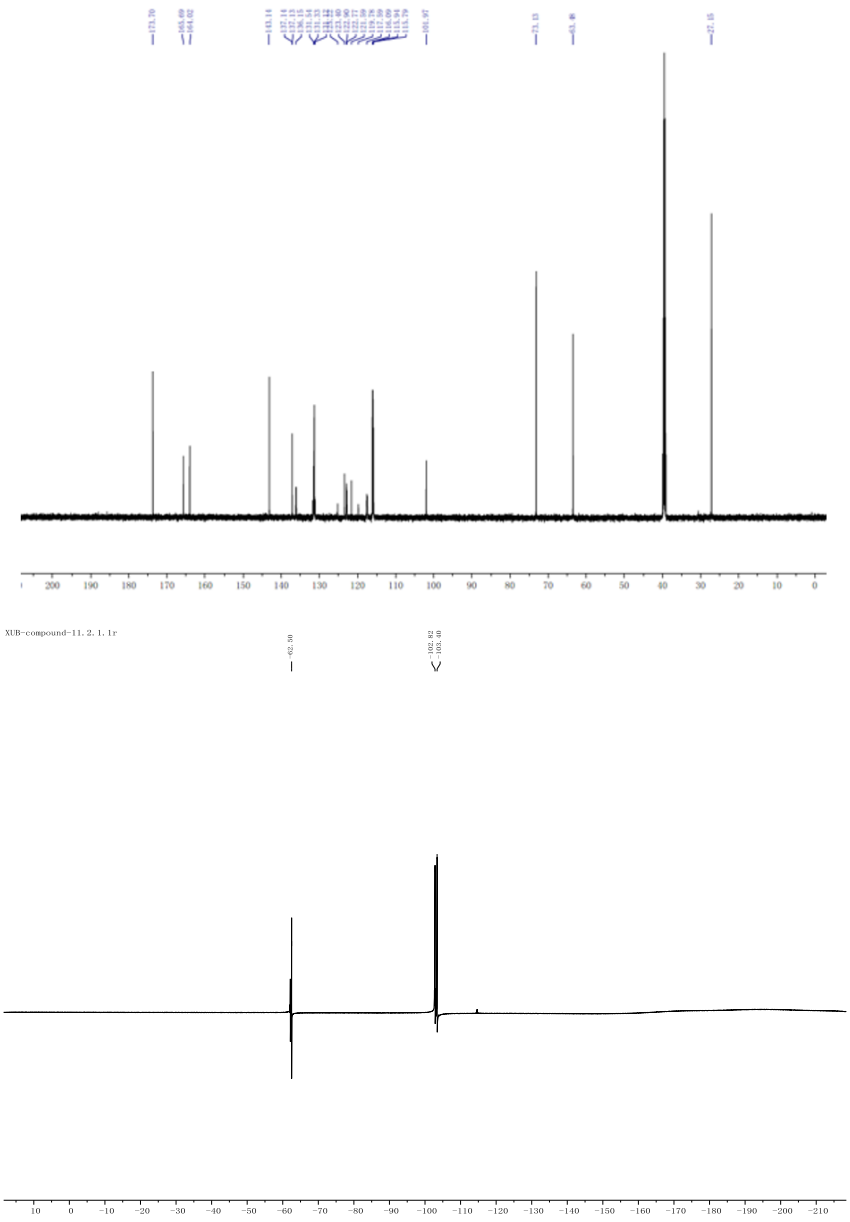
(R)-N-((1-amino-3-((4-fluorophenyl)sulfonyl)-2-methyl-1-oxopropan-2-yl)oxy)-N-benzylbenzamide (8-amide)



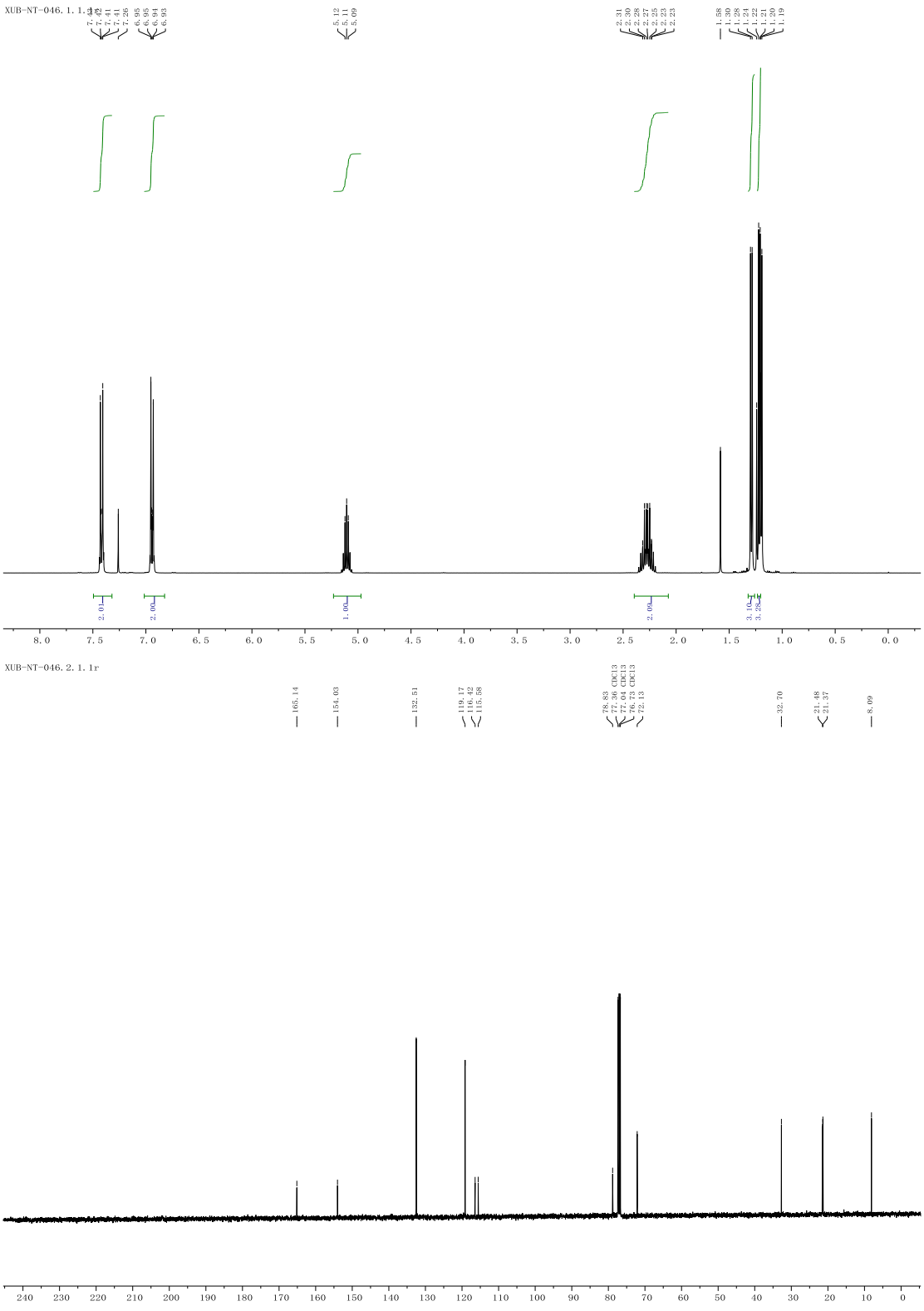


(R)-N-(4-cyano-3-(trifluoromethyl)phenyl)-3-((4-fluorophenyl)sulfonyl)-2-hydroxy-2-methylpropanamide ((R)-Bicalutamide)

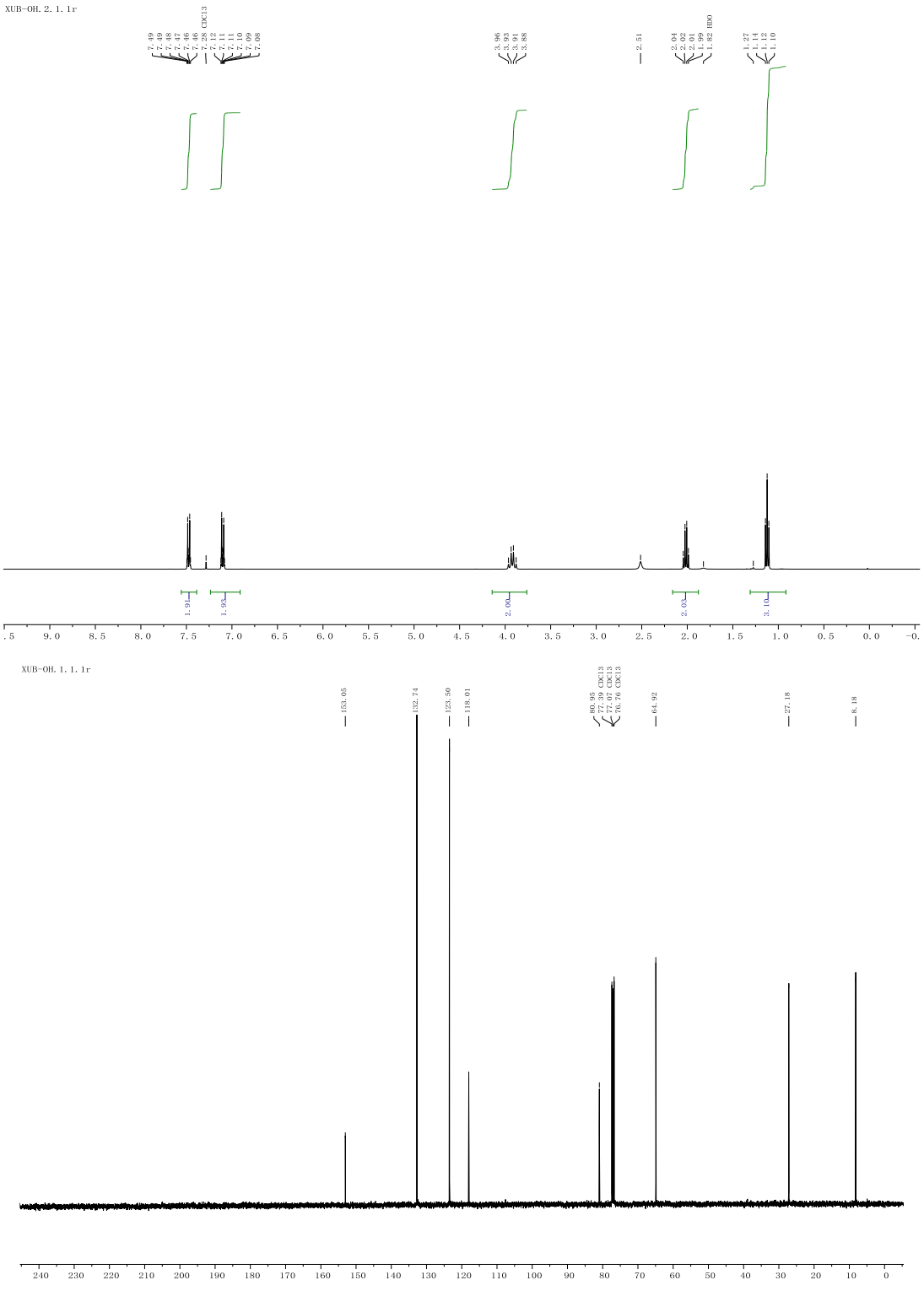




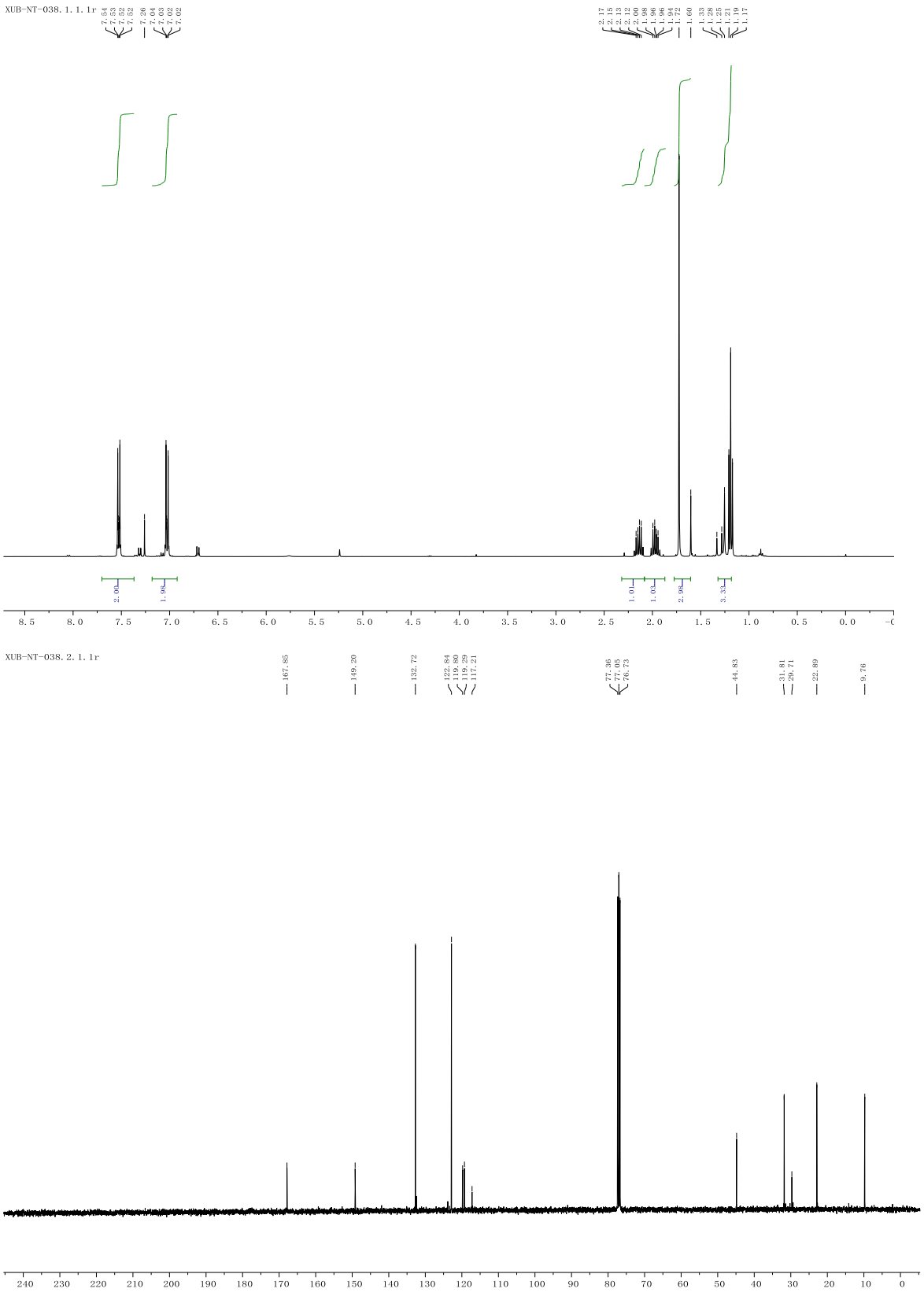
isopropyl (R)-2-(4-bromophenoxy)-2-cyanobutanoate (6l)



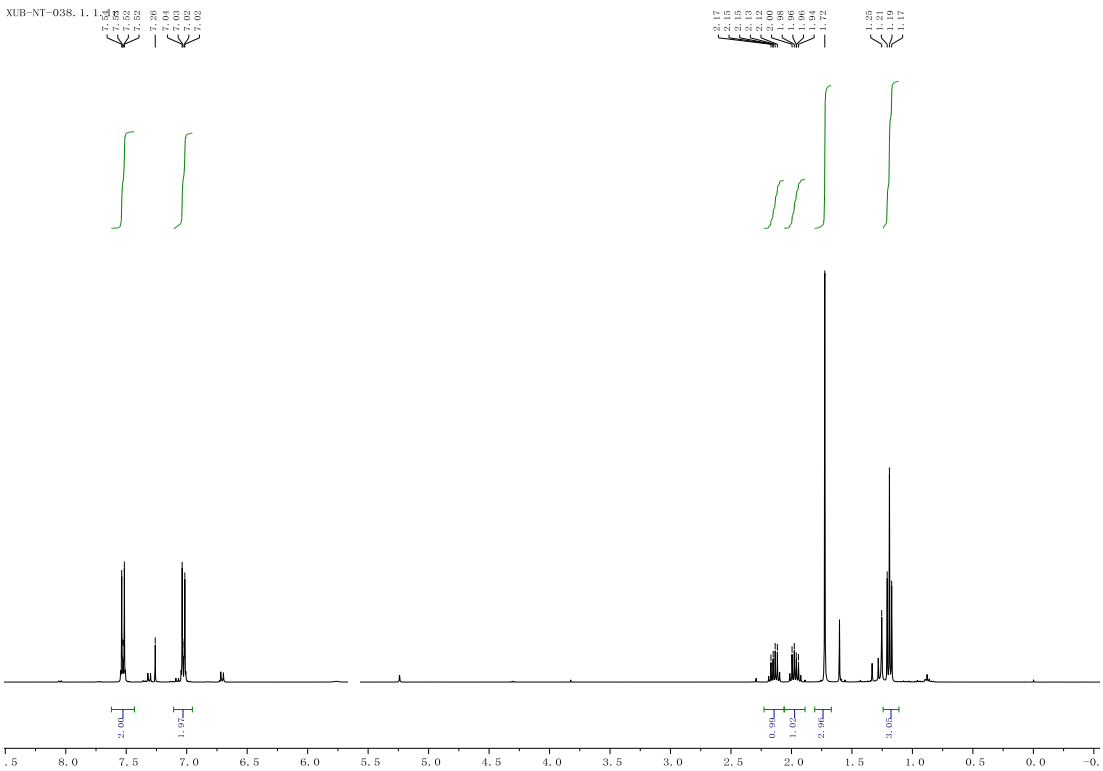
(R)-2-(4-bromophenoxy)-2-(hydroxymethyl)butanenitrile (11)

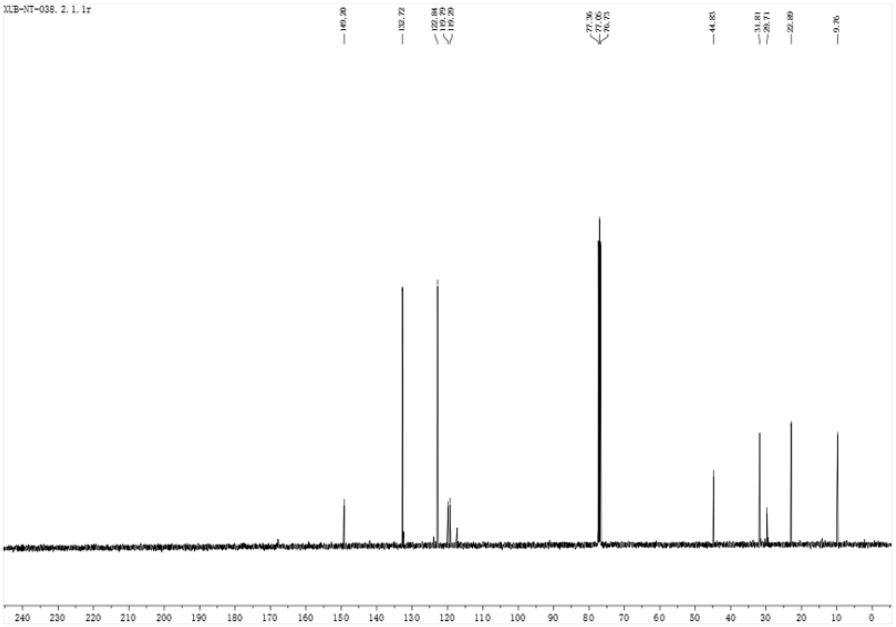


(R)-2-(4-bromophenoxy)-2-cyanobutyl methanesulfonate (11-Ms)

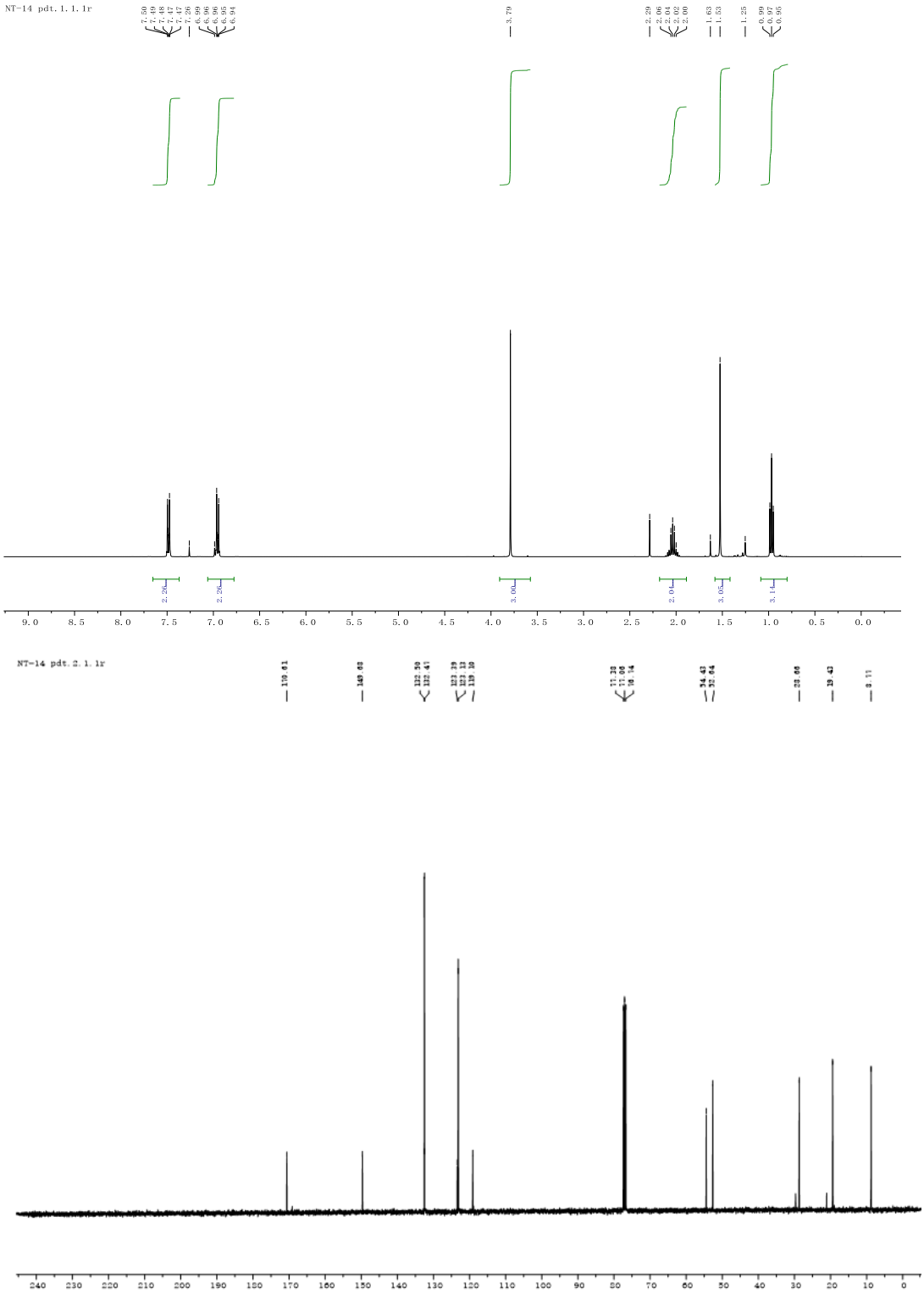


(R)-2-(4-bromophenoxy)-2-methylbutanenitrile (12)


XUB-NT-038. 1. 1. 1r
7.64
7.63
7.52
7.52
7.26
7.04
7.00
7.02
7.02
2.17
2.15
2.15
2.13
2.12
2.00
1.98
1.96
1.94
1.72
1.25
1.21
1.19
1.17
2.00
1.97
0.99
1.02
2.96
3.05

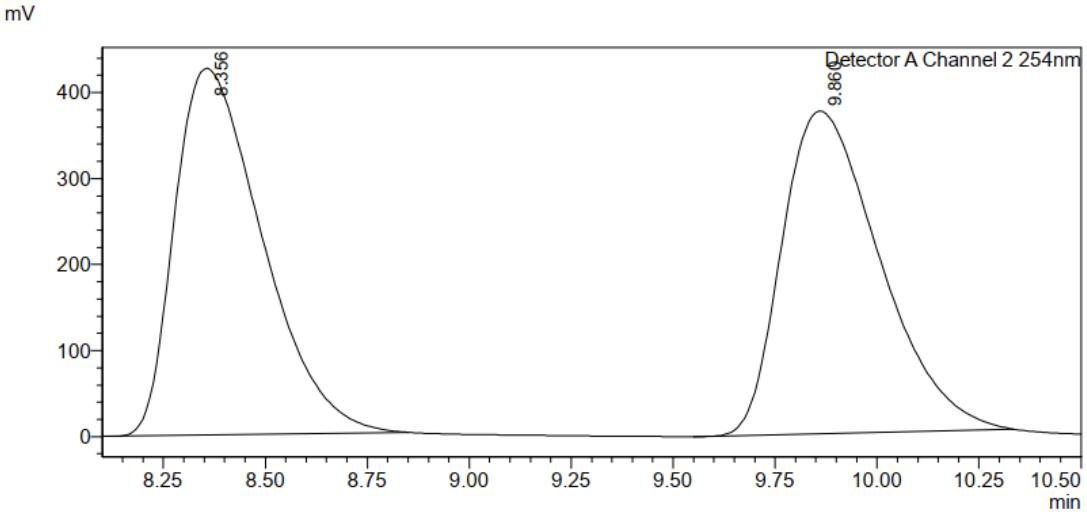

XUB-NT-038. 2. 1. 1r
140.20
132.72
122.84
119.79
118.29
77.36
77.05
76.73
44.83
33.81
29.71
22.89
9.96

(R)-2-(4-bromophenoxy)-2-cyanobutyl methanesulfonate (13-Me)



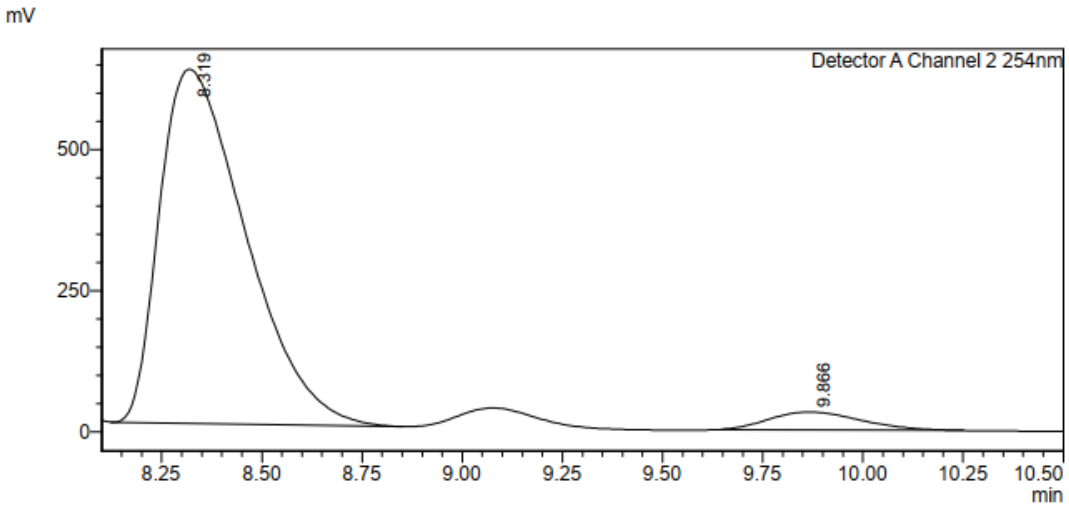
13. HPLC charts

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-phenylpropanoate (4g)



Detector A Channel 2 254nm

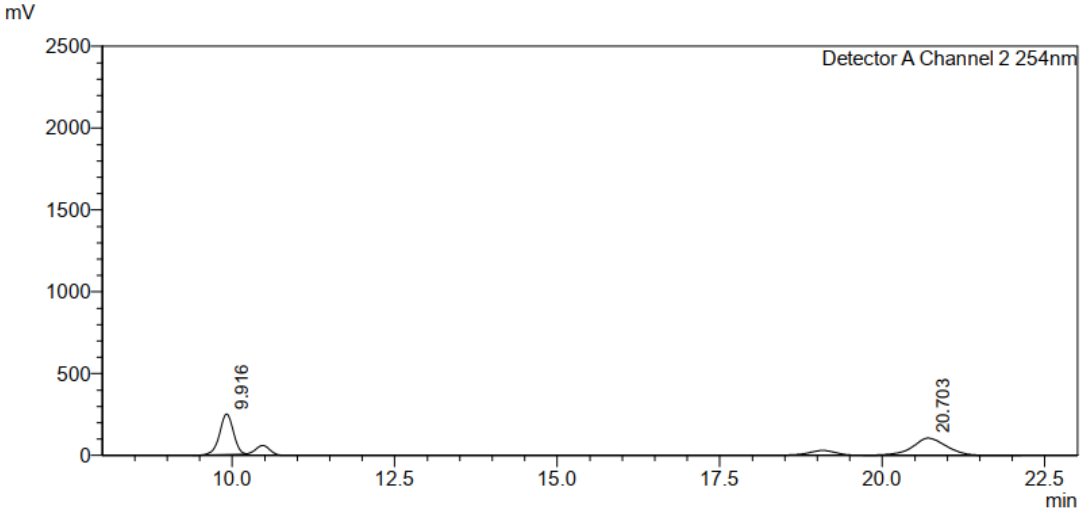
Peak#	Ret. Time	Area	Area%
1	8.356	6376833	50.420
2	9.860	6270499	49.580
Total		12647332	100.000



Detector A Channel 2 254nm

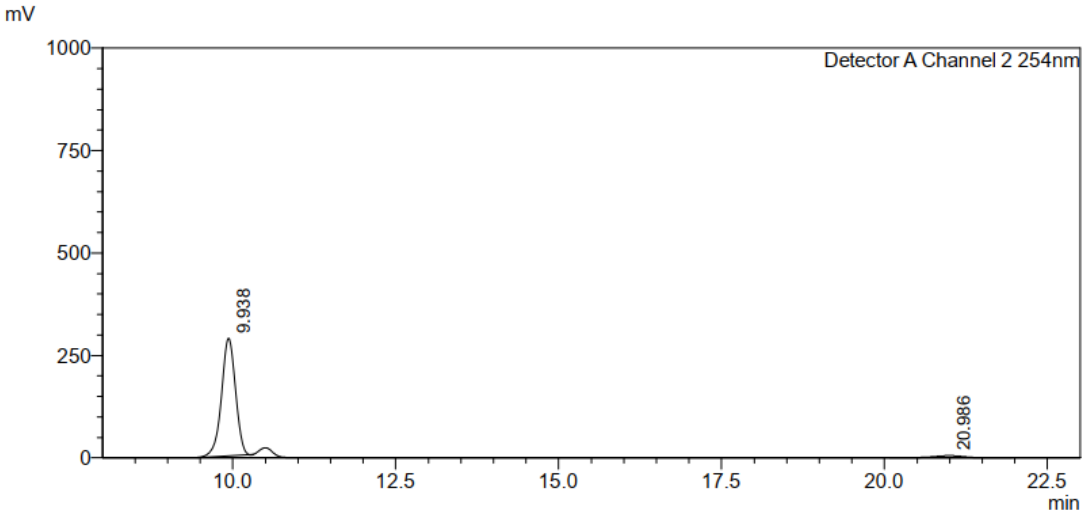
Peak#	Ret. Time	Area	Area%
1	8.319	9392012	94.746
2	9.866	520871	5.254
Total		9912882	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-fluorophenyl)propanoate (4i)



Detector A Channel 2 254nm

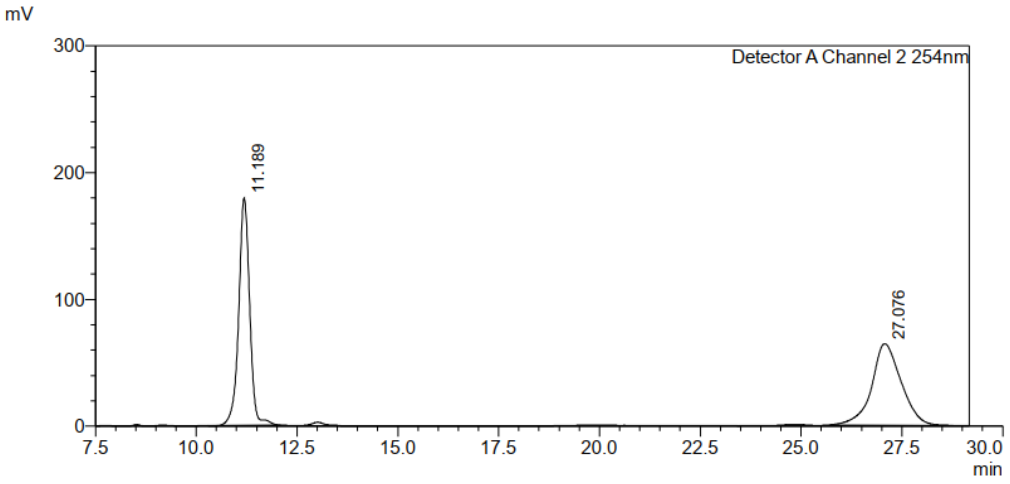
Peak#	Ret. Time	Area	Area%
1	9.916	3760216	49.523
2	20.703	3832591	50.477
Total		7592808	100.000



Detector A Channel 2 254nm

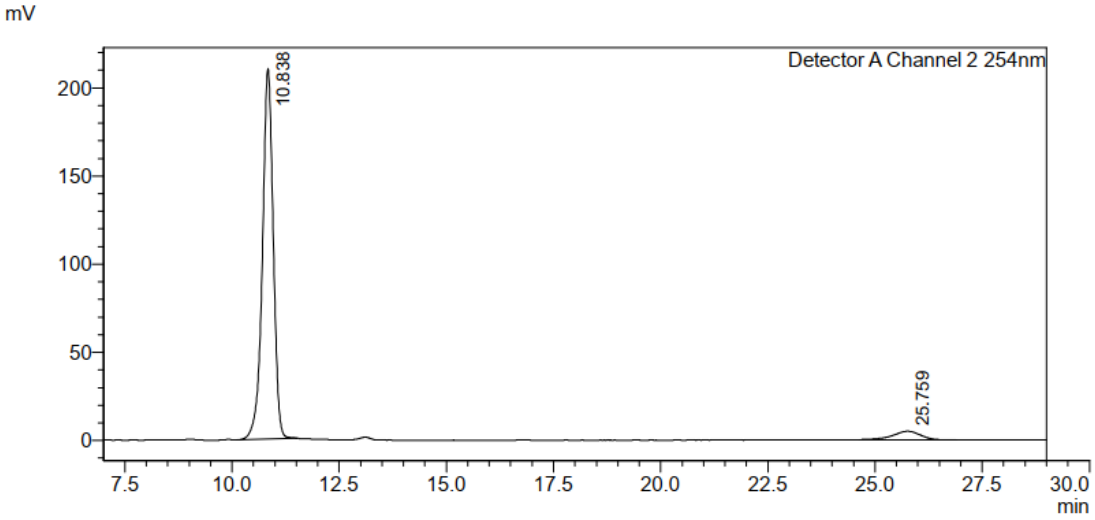
Peak#	Ret. Time	Area	Area%
1	9.938	4309654	95.639
2	20.986	196534	4.361
Total		4506187	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-3-(4-bromophenyl)-2-cyanopropanoate (4j)



Detector A Channel 2 254nm

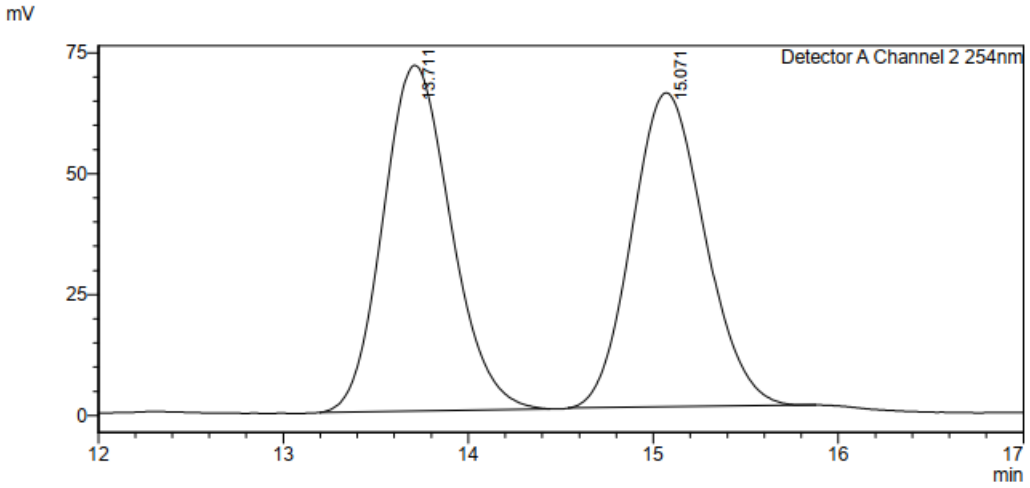
Peak#	Ret. Time	Area	Area%
1	11.189	3373414	50.831
2	27.076	3263141	49.169
Total		6636555	100.000



Detector A Channel 2 254nm

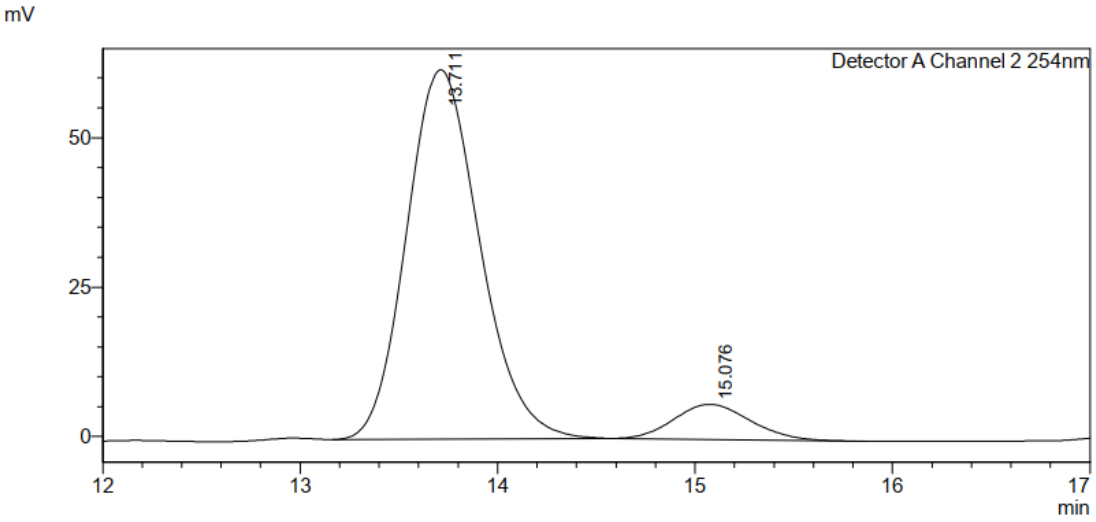
Peak#	Ret. Time	Area	Area%
1	10.838	3699048	94.512
2	25.759	214793	5.488
Total		3913841	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(2-iodophenyl)propanoate (4k)



Detector A Channel 2 254nm

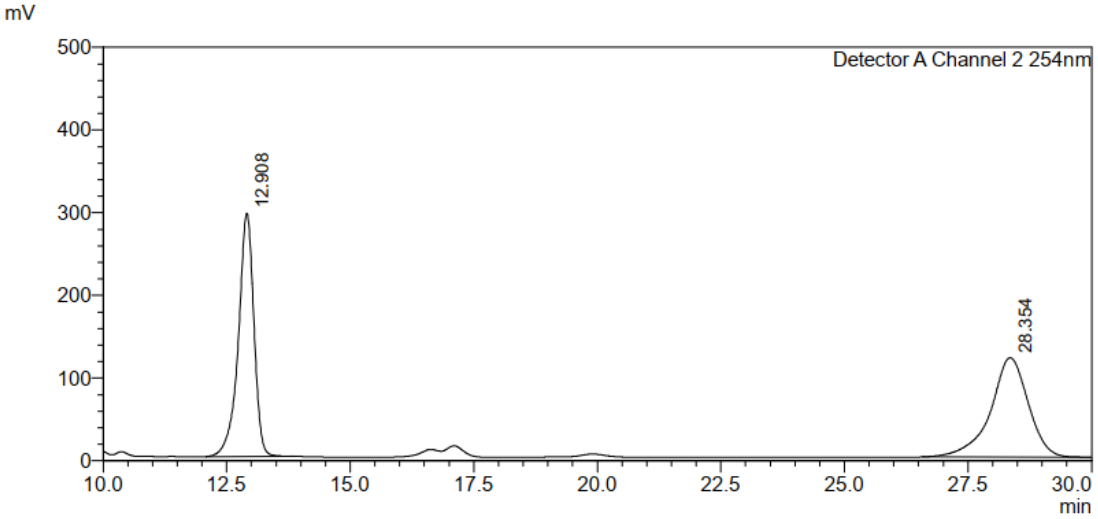
Peak#	Ret. Time	Area	Area%
1	13.711	1819436	50.517
2	15.071	1782197	49.483
Total		3601633	100.000



Detector A Channel 2 254nm

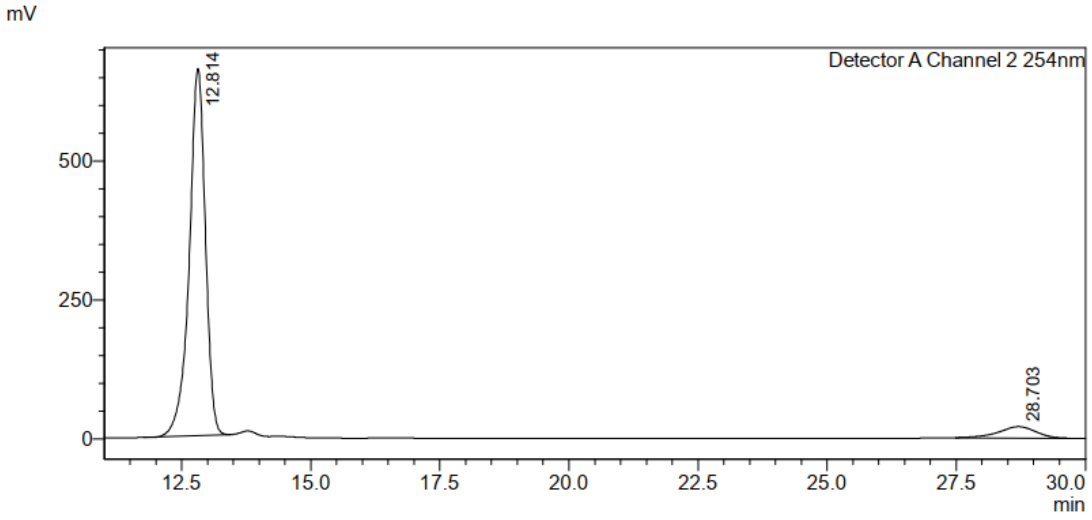
Peak#	Ret. Time	Area	Area%
1	13.711	1589754	90.856
2	15.076	159992	9.144
Total		1749747	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-nitrophenyl)propanoate (4l)



Detector A Channel 2 254nm

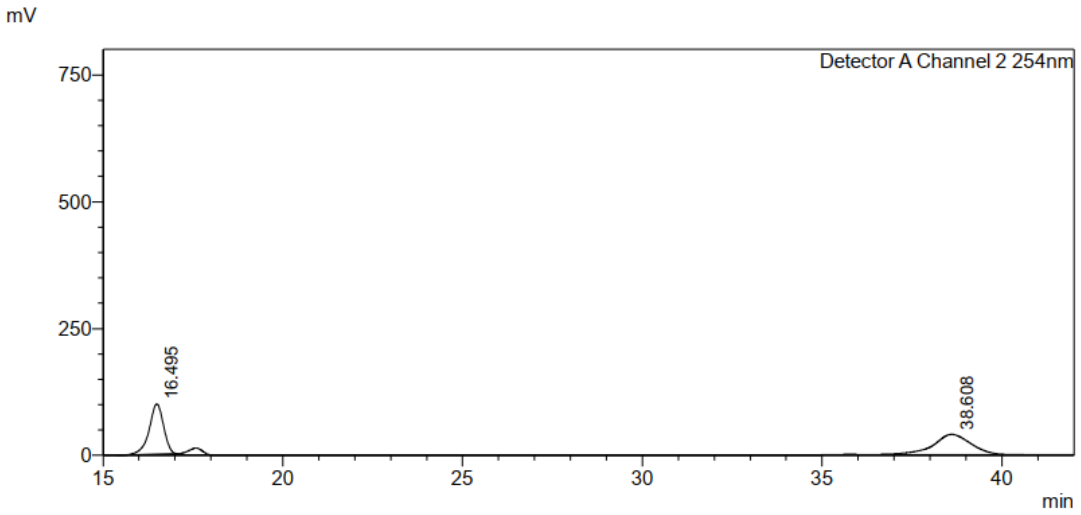
Peak#	Ret. Time	Area	Area%
1	12.908	6461306	50.260
2	28.354	6394552	49.740
Total		12855858	100.000



Detector A Channel 2 254nm

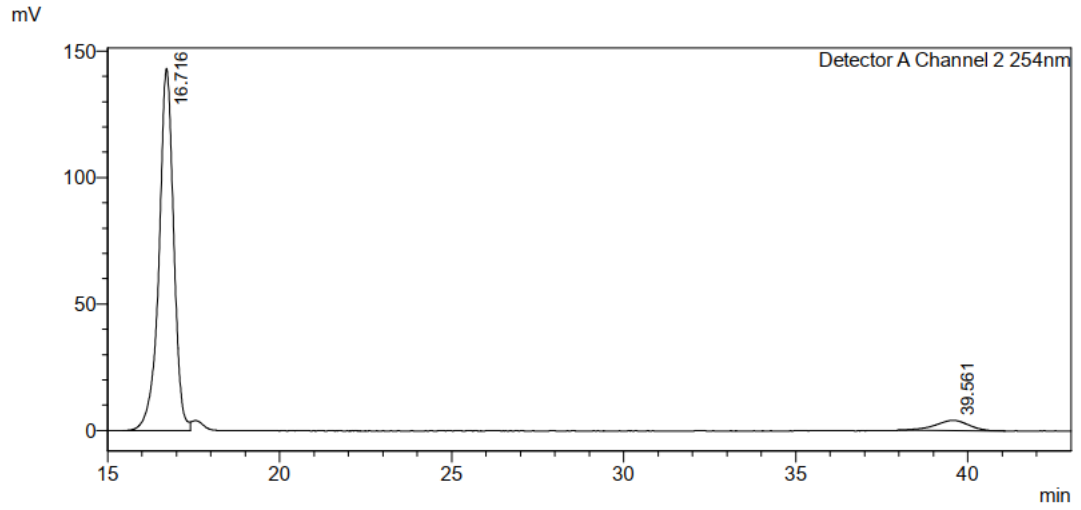
Peak#	Ret. Time	Area	Area%
1	12.814	14370542	93.320
2	28.703	1028676	6.680
Total		15399219	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(4-methoxyphenyl)propanoate (4m)



Detector A Channel 2 254nm

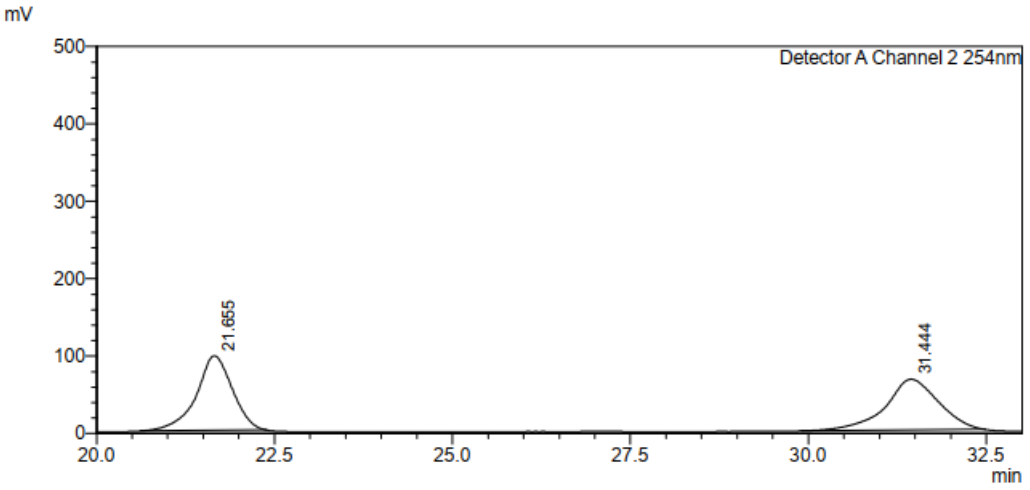
Peak#	Ret. Time	Area	Area%
1	16.495	2781329	49.050
2	38.608	2889034	50.950
Total		5670363	100.000



Detector A Channel 2 254nm

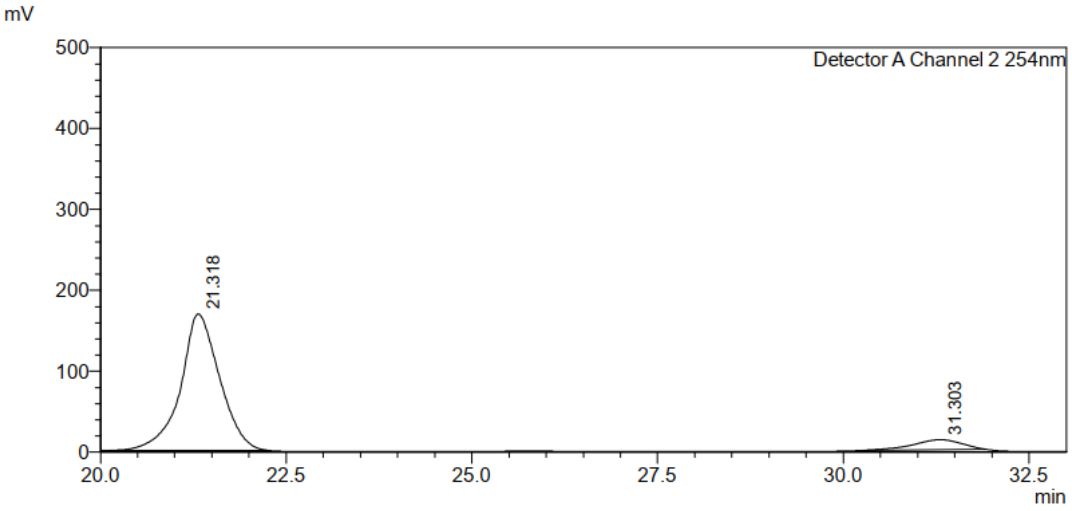
Peak#	Ret. Time	Area	Area%
1	16.716	4253771	93.961
2	39.561	273372	6.039
Total		4527143	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(o-tolyl)propanoate (4n)



Detector A Channel 2 254nm

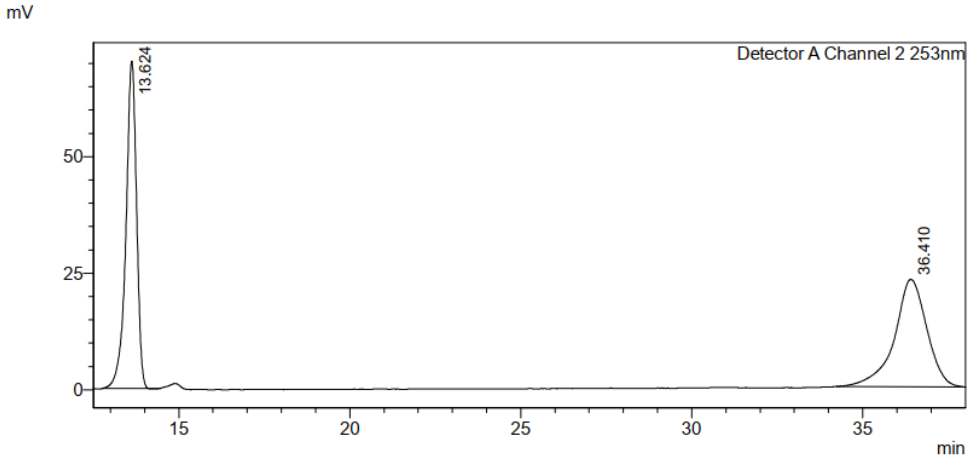
Peak#	Ret. Time	Area	Area%
1	21.655	3410157	49.887
2	31.444	3425593	50.113
Total		6835750	100.000



Detector A Channel 2 254nm

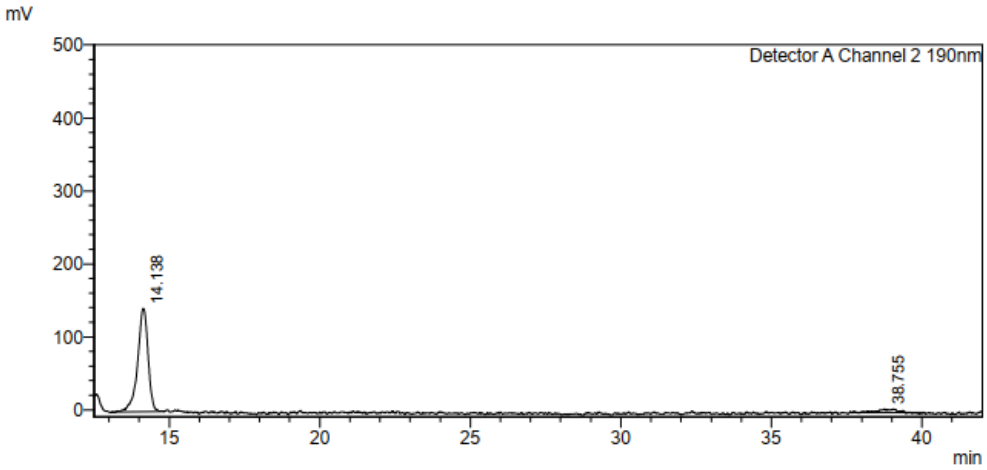
Peak#	Ret. Time	Area	Area%
1	21.318	6172005	91.791
2	31.303	551949	8.209
Total		6723953	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(thiophen-2-yl)propanoate (4o)



Detector A Channel 2 253nm

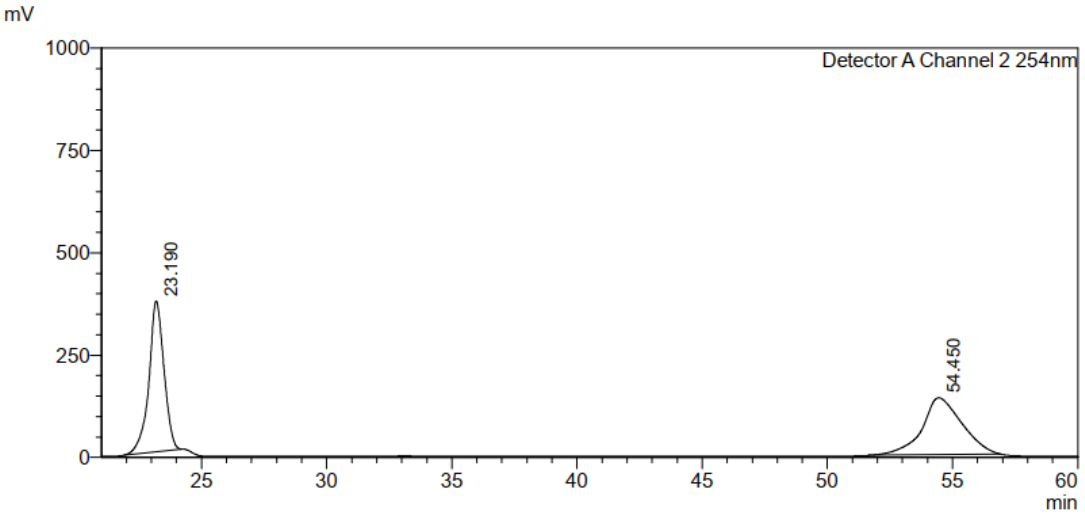
Peak#	Ret. Time	Area	Area%
1	13.624	1516810	49.950
2	36.410	1519844	50.050
Total		3036654	100.000



Detector A Channel 2 190nm

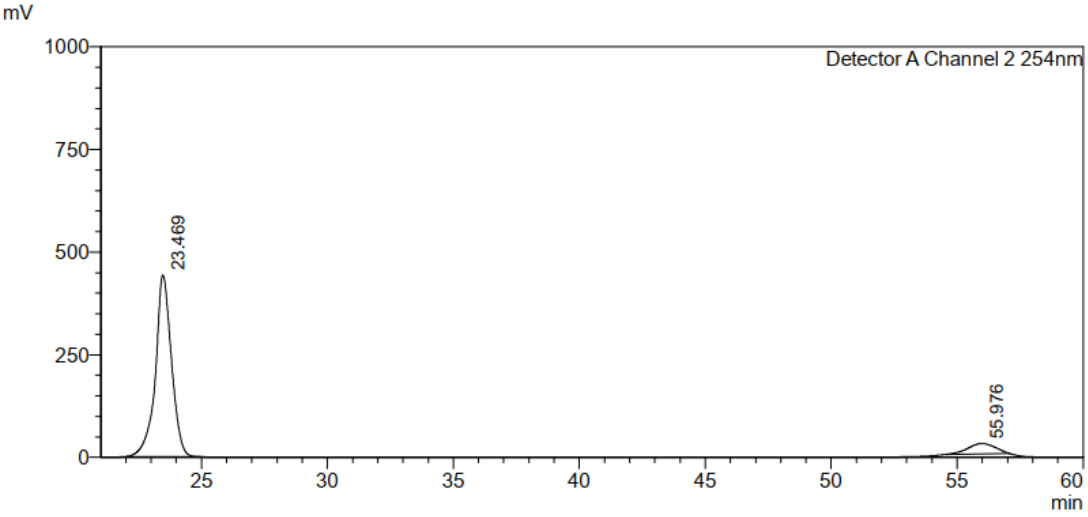
Peak#	Ret. Time	Area	Area%
1	14.138	3407936	94.777
2	38.755	187810	5.223
Total		3595746	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-3-(naphthalen-2-yl)propanoate (4p)



Detector A Channel 2 254nm

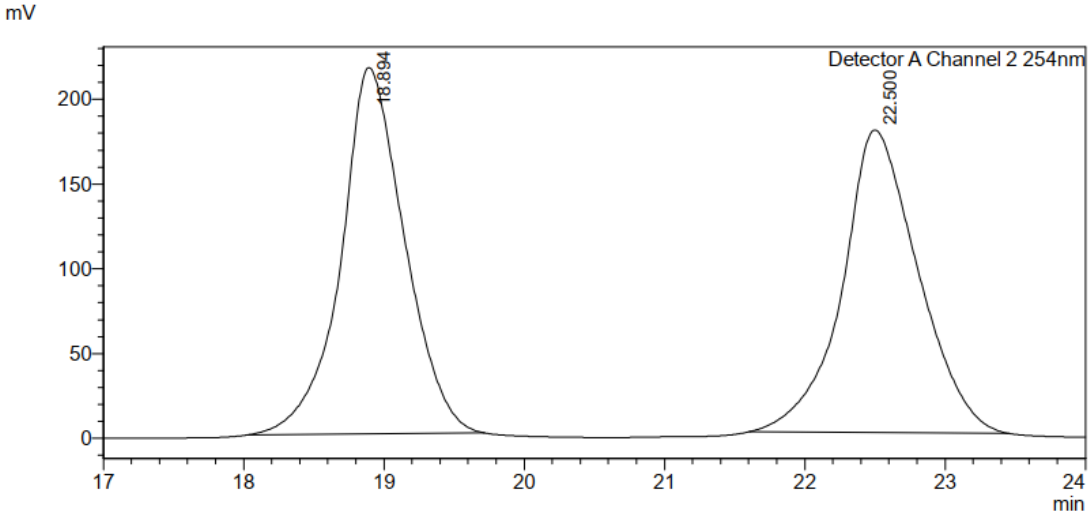
Peak#	Ret. Time	Area	Area%
1	23.190	15424686	49.938
2	54.450	15463045	50.062
Total		30887731	100.000



Detector A Channel 2 254nm

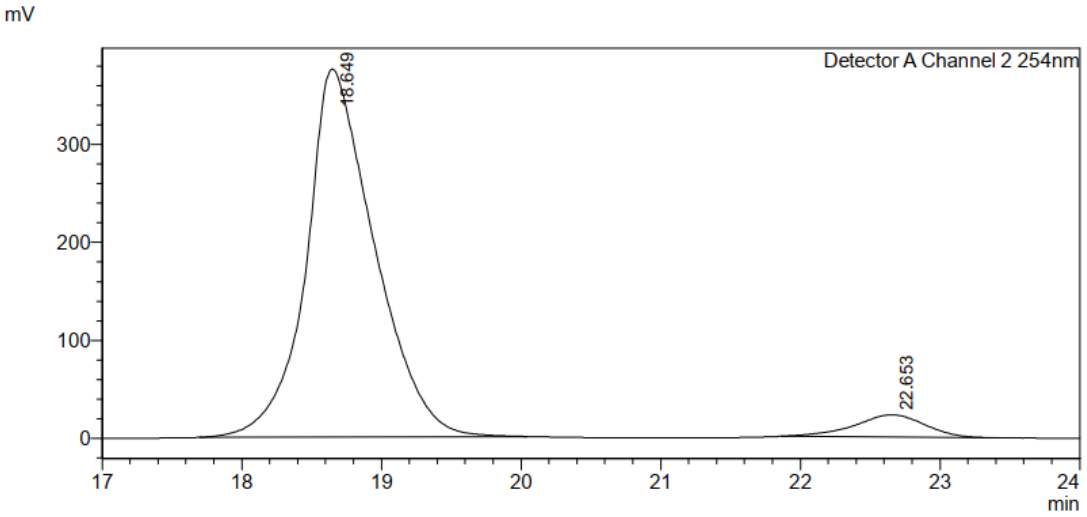
Peak#	Ret. Time	Area	Area%
1	23.469	19625602	91.234
2	55.976	1885575	8.766
Total		21511177	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-4-phenylbutanoate (4q)



Detector A Channel 2 254nm

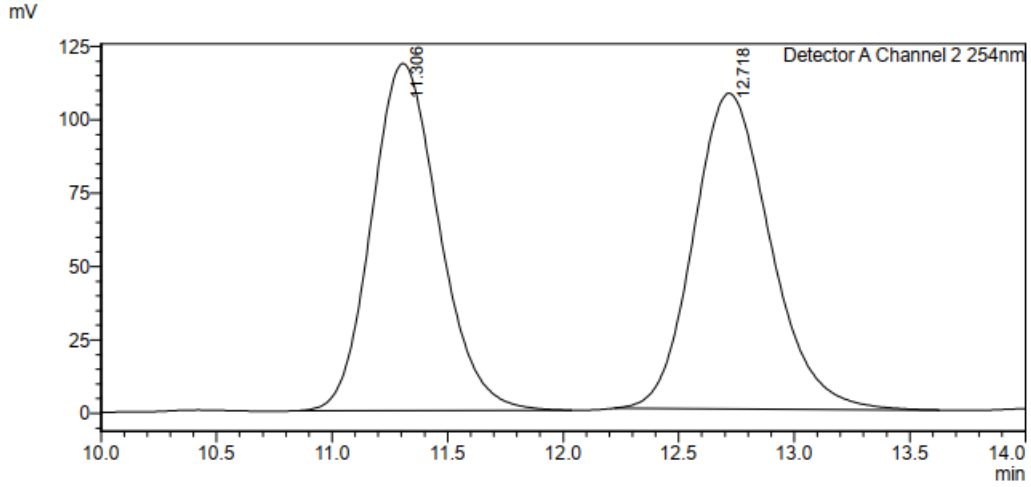
Peak#	Ret. Time	Area	Area%
1	18.894	6838942	50.448
2	22.500	6717375	49.552
Total		13556317	100.000



Detector A Channel 2 254nm

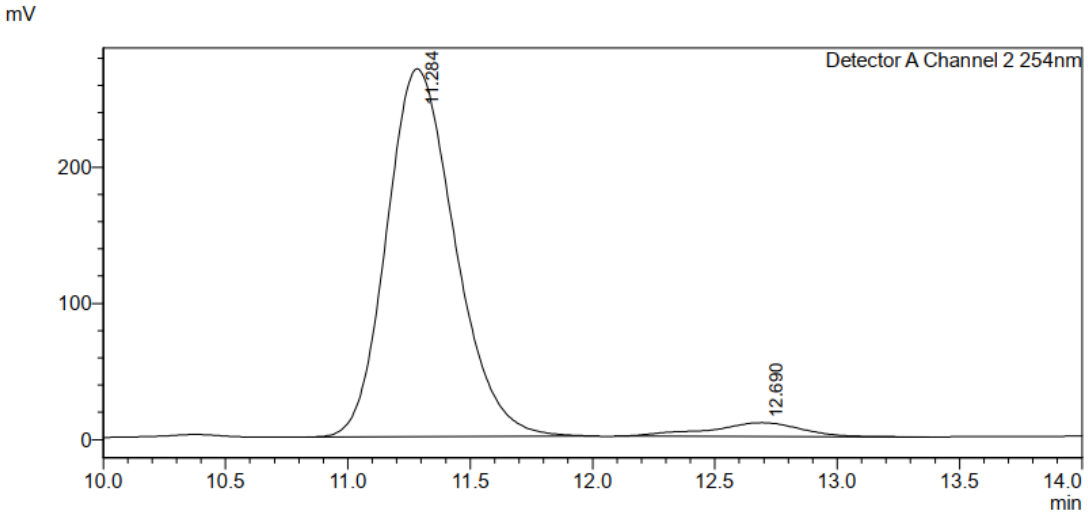
Peak#	Ret. Time	Area	Area%
1	18.649	12794043	94.114
2	22.653	800172	5.886
Total		13594215	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-5-phenylpentanoate (4r)



Detector A Channel 2 254nm

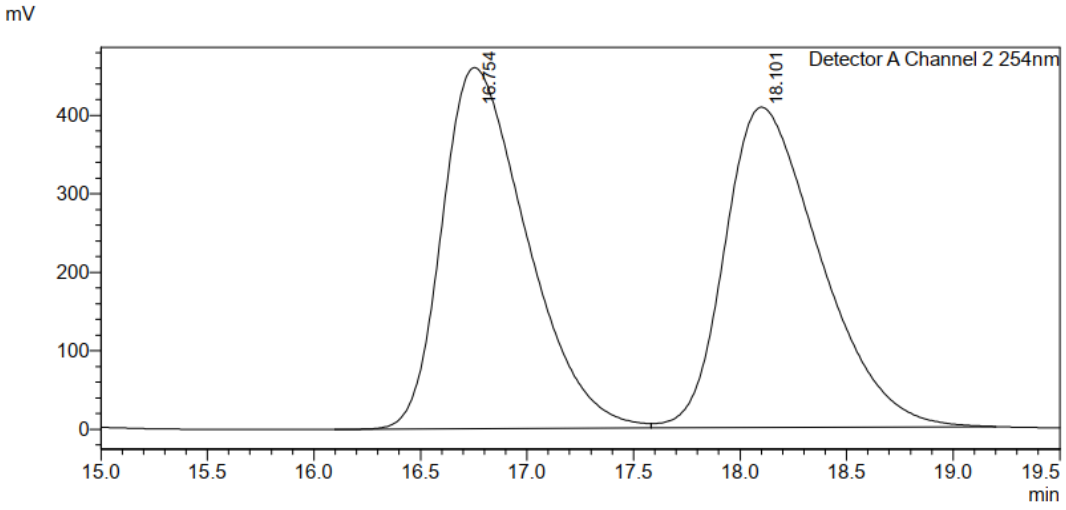
Peak#	Ret. Time	Area	Area%
1	11.306	2397292	49.064
2	12.718	2488751	50.936
Total		4886043	100.000



Detector A Channel 2 254nm

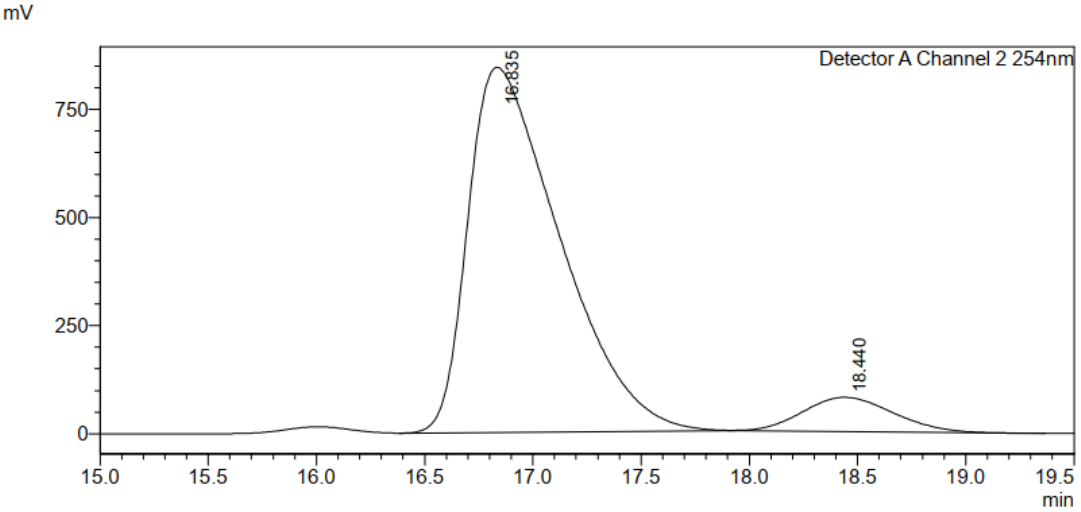
Peak#	Ret. Time	Area	Area%
1	11.284	5245658	95.166
2	12.690	266433	4.834
Total		5512091	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanopropanoate (4s)



Detector A Channel 2 254nm

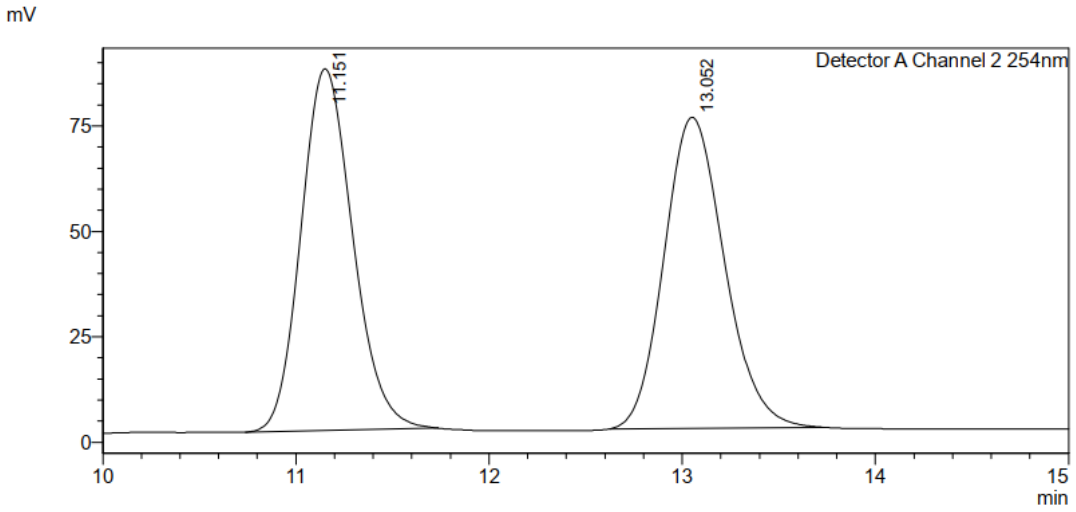
Peak#	Ret. Time	Area	Area%
1	16.754	12717097	49.980
2	18.101	12727212	50.020
Total		25444310	100.000



Detector A Channel 2 254nm

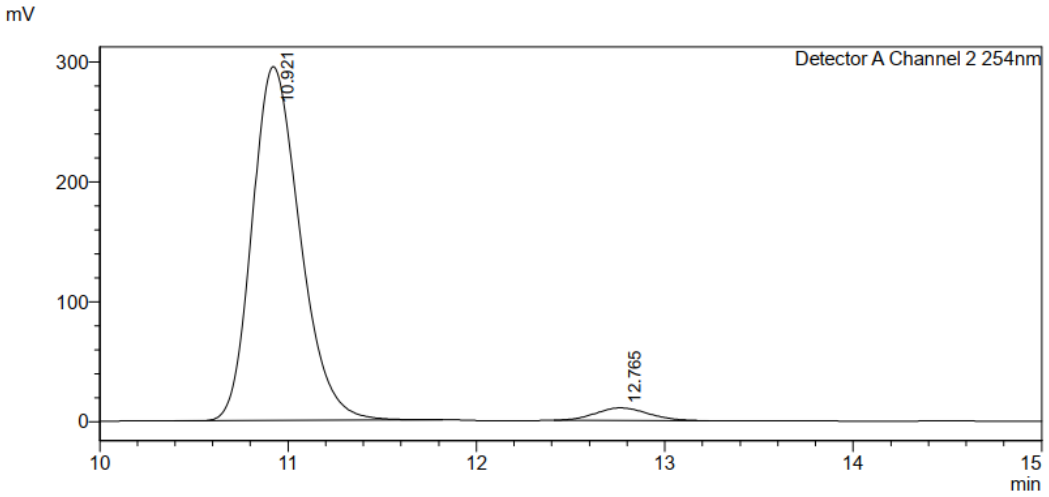
Peak#	Ret. Time	Area	Area%
1	16.835	24912260	91.584
2	18.440	2289242	8.416
Total		27201502	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanobutanoate (4t)



Detector A Channel 2 254nm

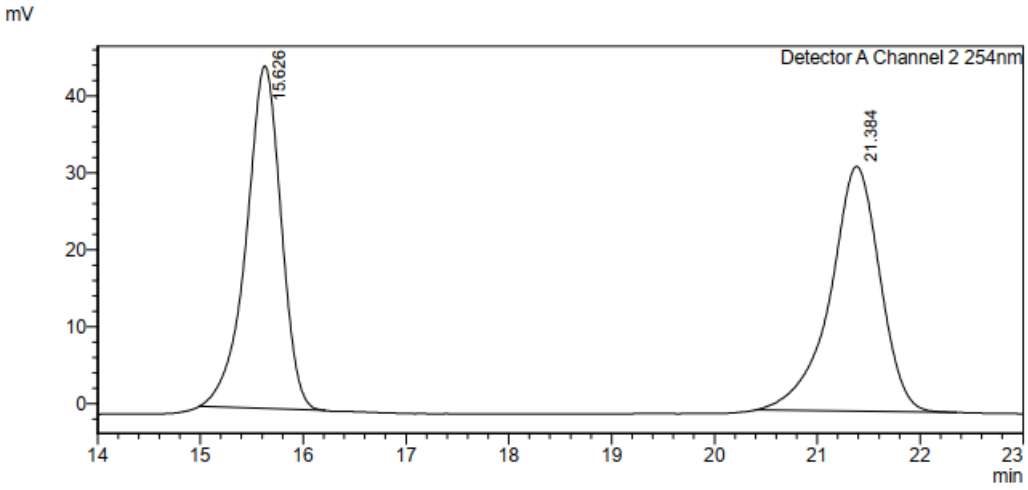
Peak#	Ret. Time	Area	Area%
1	11.151	1605123	49.995
2	13.052	1605475	50.005
Total		3210598	100.000



Detector A Channel 2 254nm

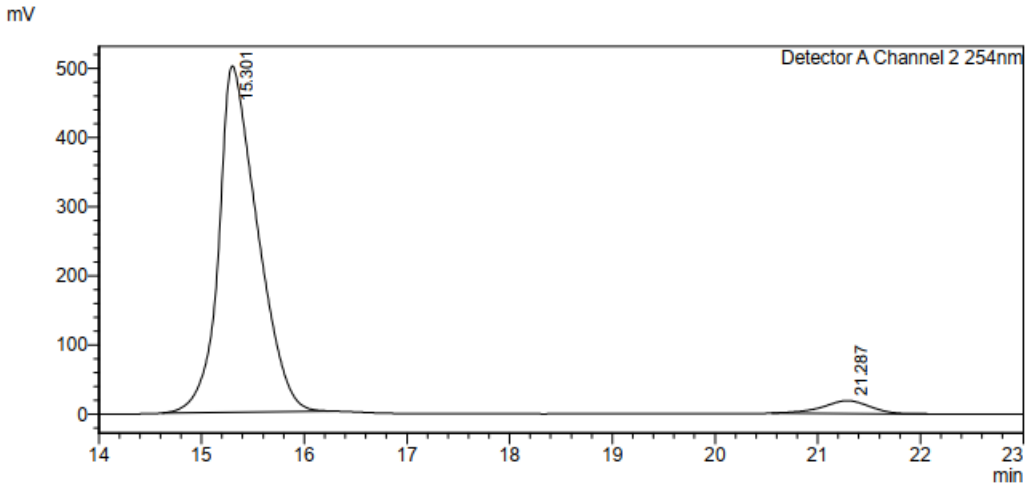
Peak#	Ret. Time	Area	Area%
1	10.921	5192102	96.214
2	12.765	204292	3.786
Total		5396395	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyano-5-methylhexanoate (4u)



Detector A Channel 2 254nm

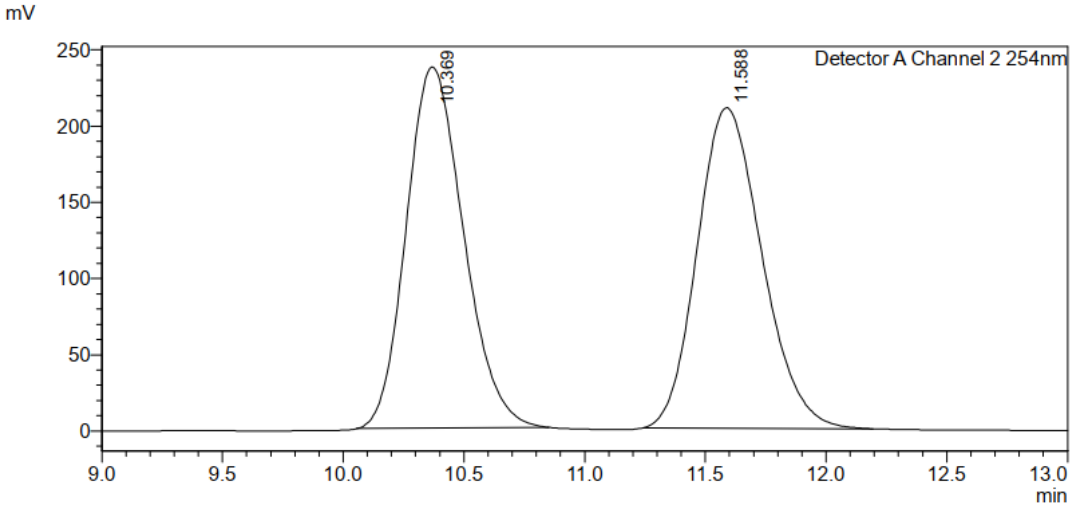
Peak#	Ret. Time	Area	Area%
1	15.626	1050773	49.586
2	21.384	1068298	50.414
Total		2119071	100.000



Detector A Channel 2 254nm

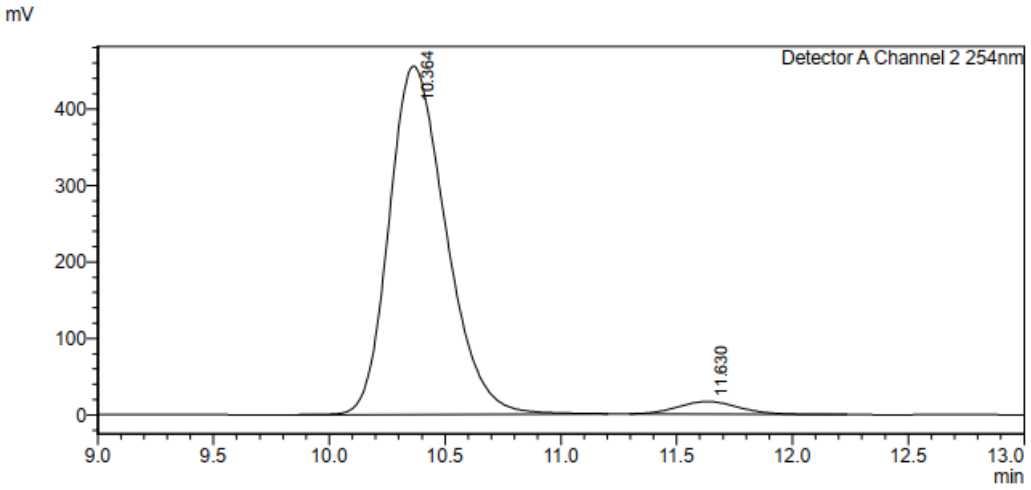
Peak#	Ret. Time	Area	Area%
1	15.301	13199608	95.731
2	21.287	588618	4.269
Total		13788226	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanopent-4-enoate (4v)



Detector A Channel 2 254nm

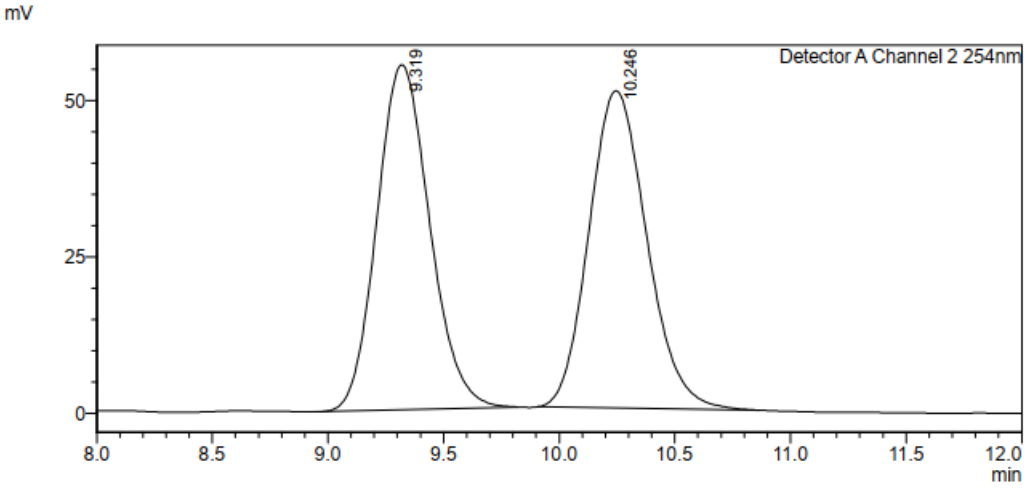
Peak#	Ret. Time	Area	Area%
1	10.369	3911251	49.902
2	11.588	3926535	50.098
Total		7837786	100.000



Detector A Channel 2 254nm

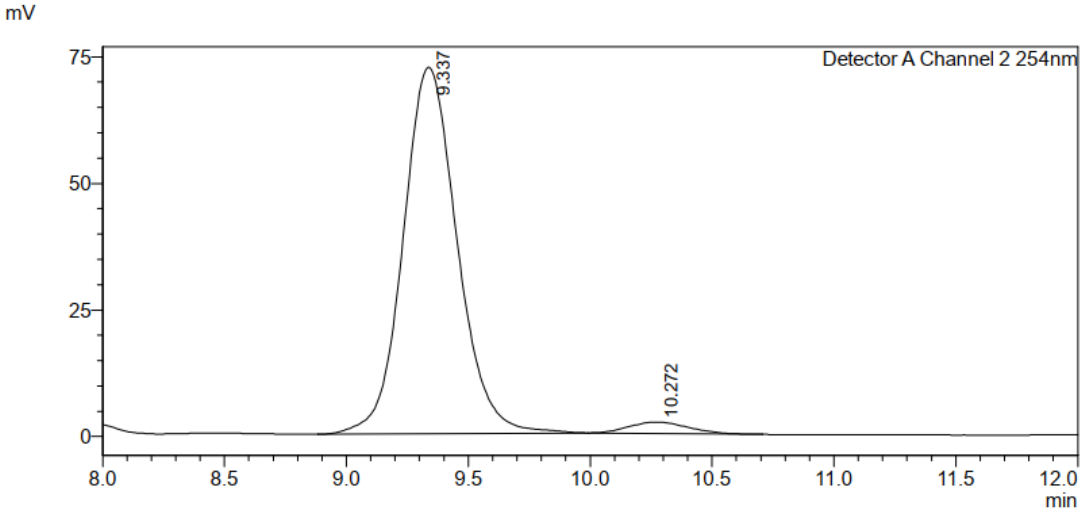
Peak#	Ret. Time	Area	Area%
1	10.364	7762672	96.308
2	11.630	297599	3.692
Total		8060271	100.000

isopropyl 2-((N-benzylbenzamido)oxy)-2-cyano-4-methylpent-4-enoate (4w)



Detector A Channel 2 254nm

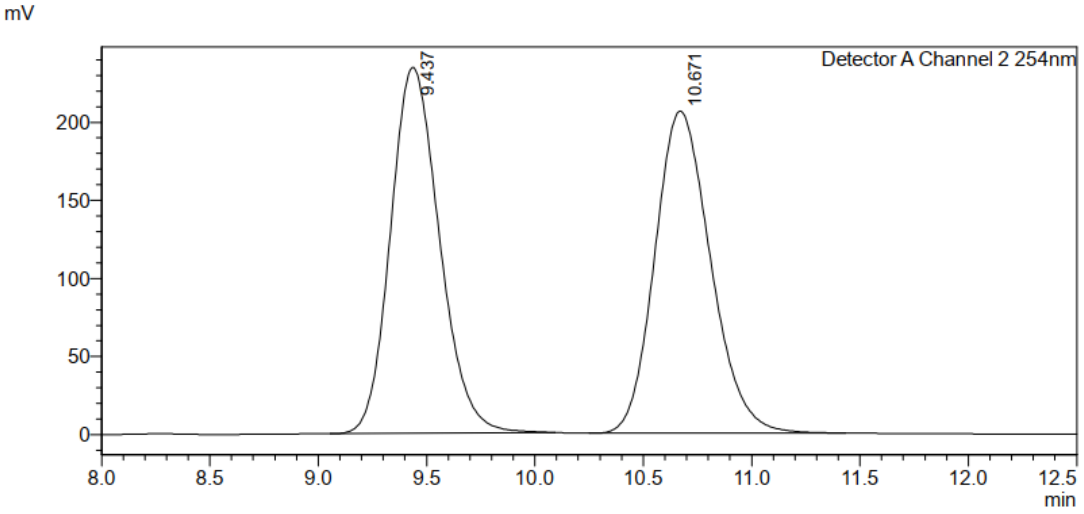
Peak#	Ret. Time	Area	Area%
1	9.319	875933	49.786
2	10.246	883467	50.214
Total		1759399	100.000



Detector A Channel 2 254nm

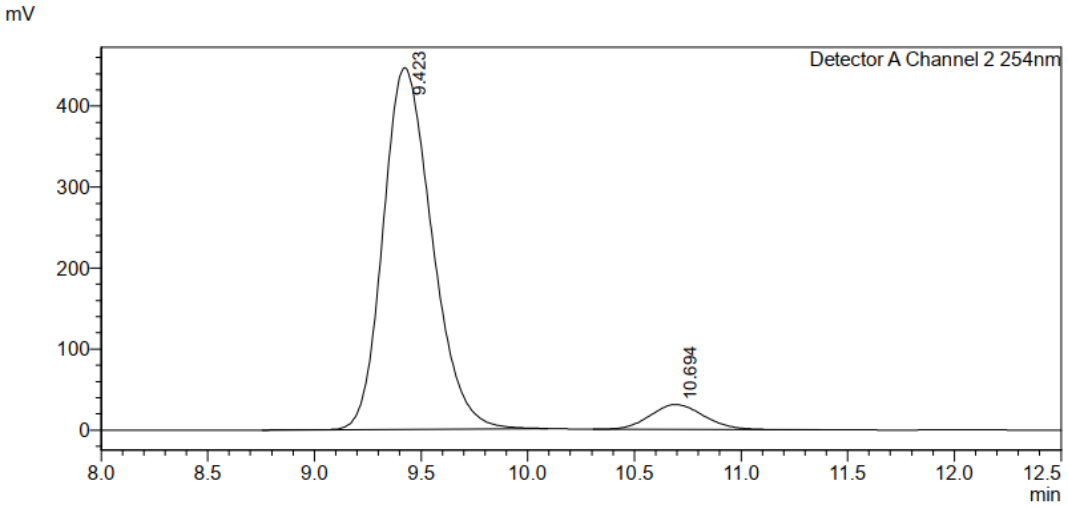
Peak#	Ret. Time	Area	Area%
1	9.337	1115410	96.729
2	10.272	37714	3.271
Total		1153124	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanohept-6-enoate (4x)



Detector A Channel 2 254nm

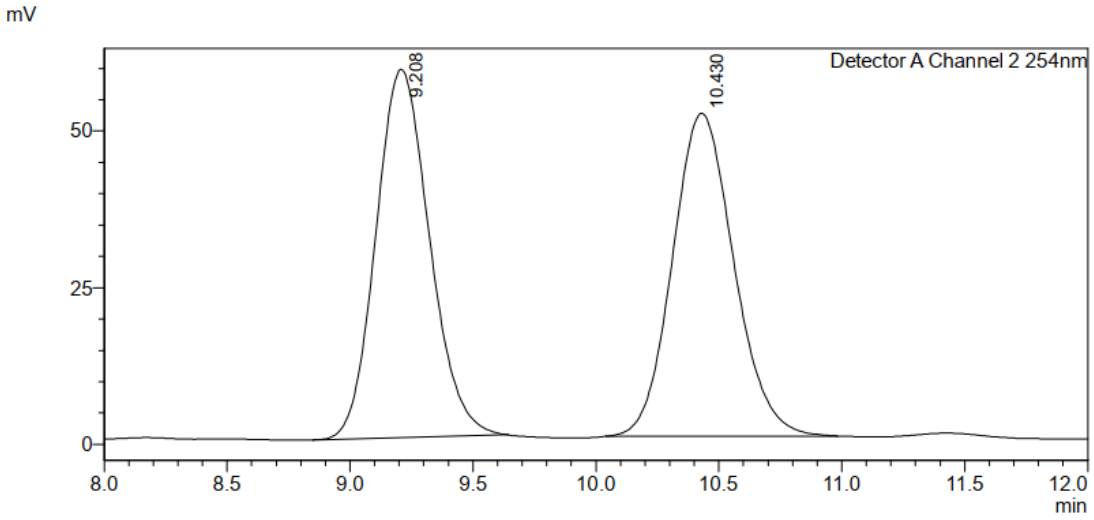
Peak#	Ret. Time	Area	Area%
1	9.437	3685664	49.928
2	10.671	3696343	50.072
Total		7382006	100.000



Detector A Channel 2 254nm

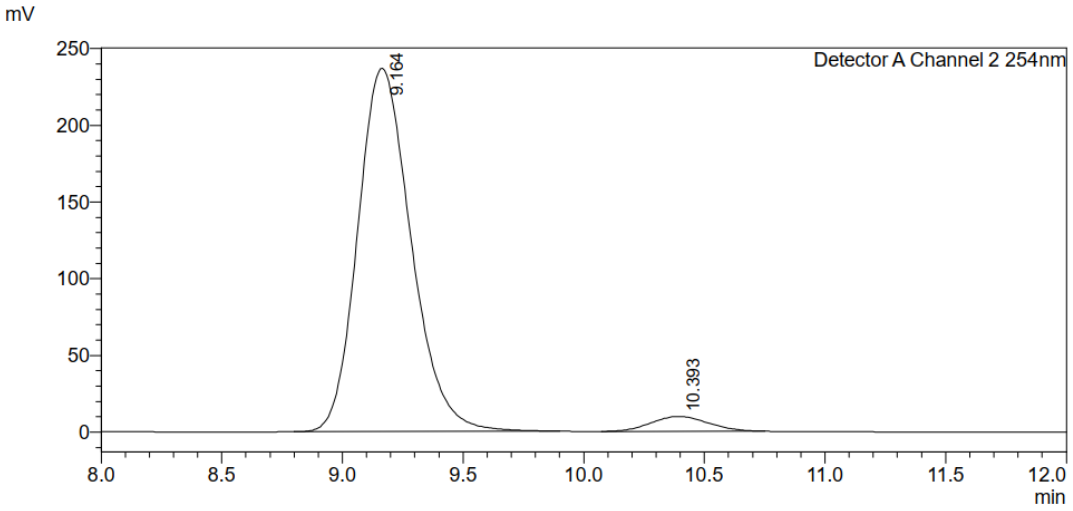
Peak#	Ret. Time	Area	Area%
1	9.423	7125249	92.961
2	10.694	539558	7.039
Total		7664808	100.000

isopropyl (R)-2-((N-benzylbenzamido)oxy)-2-cyanooct-7-enoate (4y)



Detector A Channel 2 254nm

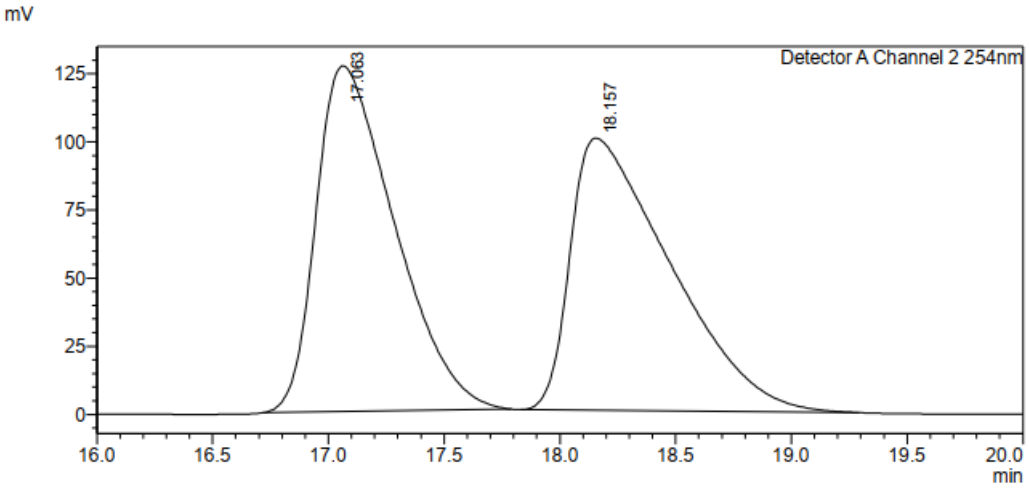
Peak#	Ret. Time	Area	Area%
1	9.208	891966	49.942
2	10.430	894037	50.058
Total		1786003	100.000



Detector A Channel 2 254nm

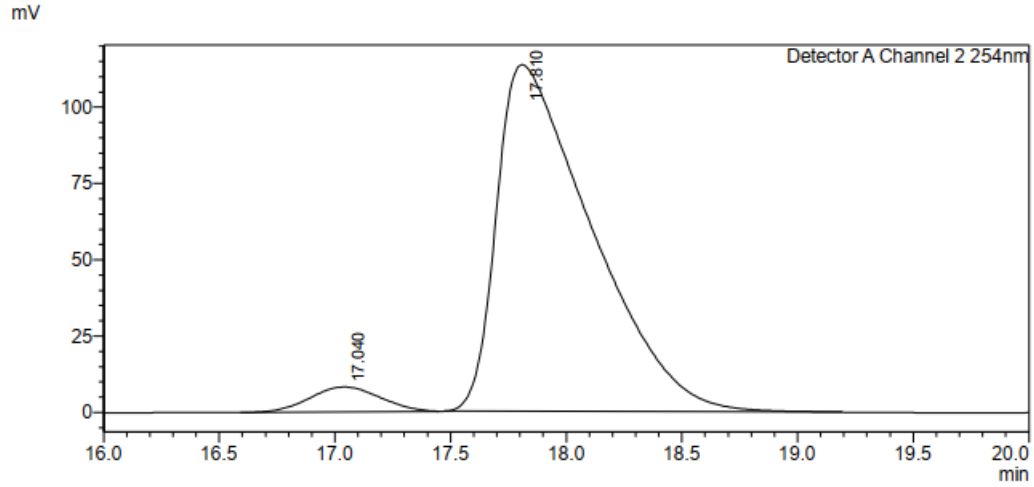
Peak#	Ret. Time	Area	Area%
1	9.164	3640851	95.750
2	10.393	161605	4.250
Total		3802456	100.000

isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)-4-phenylbutanoate (6a)



Detector A Channel 2 254nm

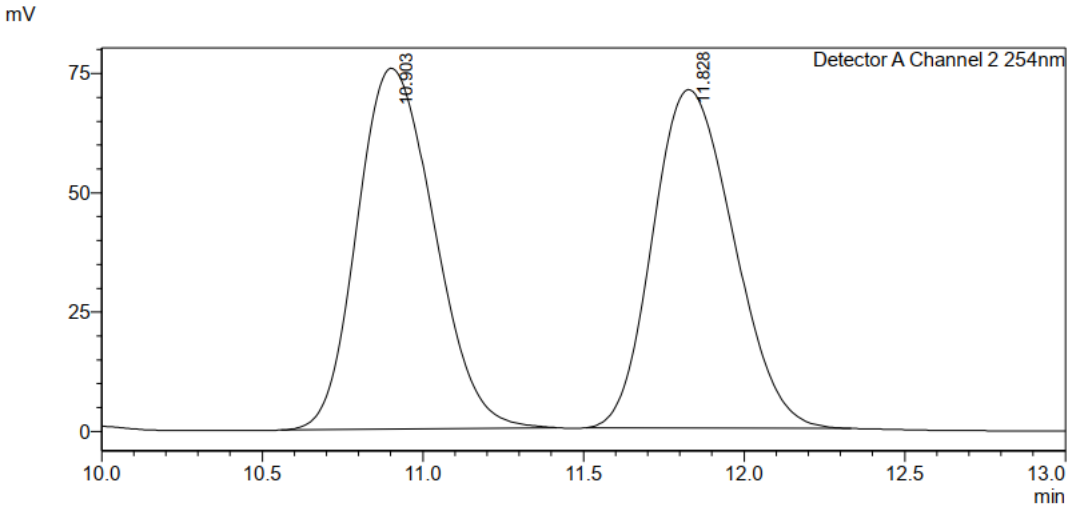
Peak#	Ret. Time	Area	Area%
1	17.063	2996419	49.971
2	18.157	2999923	50.029
Total		5996342	100.000



Detector A Channel 2 254nm

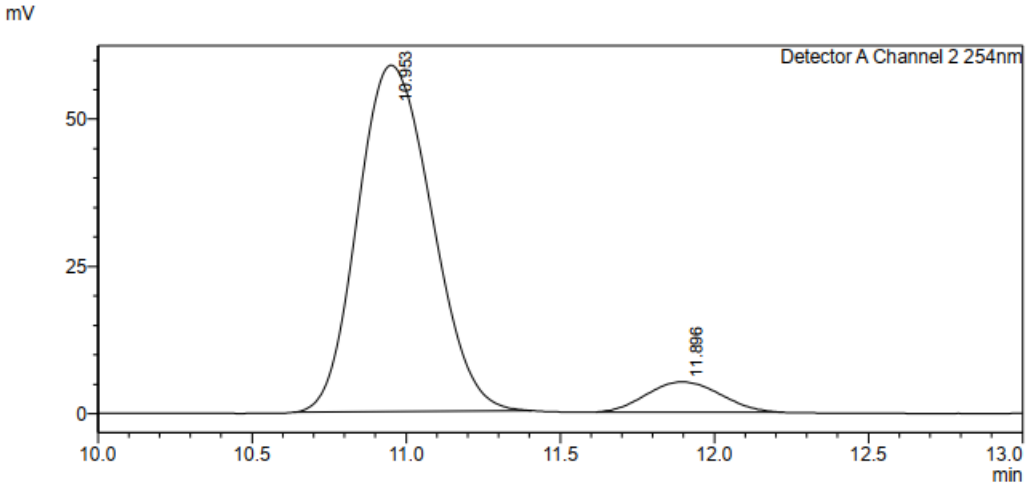
Peak#	Ret. Time	Area	Area%
1	17.040	172519	5.043
2	17.810	3248118	94.957
Total		3420637	100.000

isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)pent-4-enoate (6b)



Detector A Channel 2 254nm

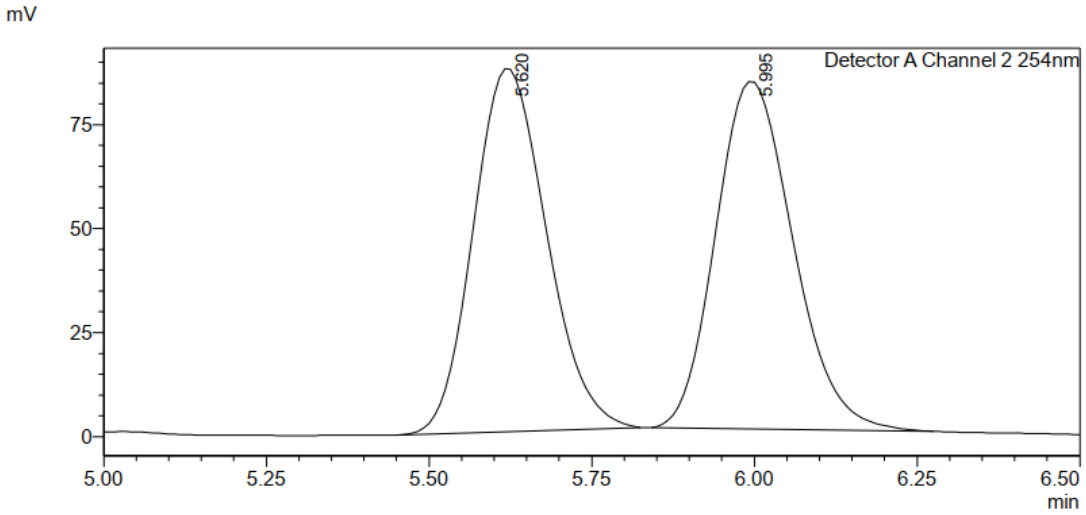
Peak#	Ret. Time	Area	Area%
1	10.903	1260413	50.396
2	11.828	1240628	49.604
Total		2501042	100.000



Detector A Channel 2 254nm

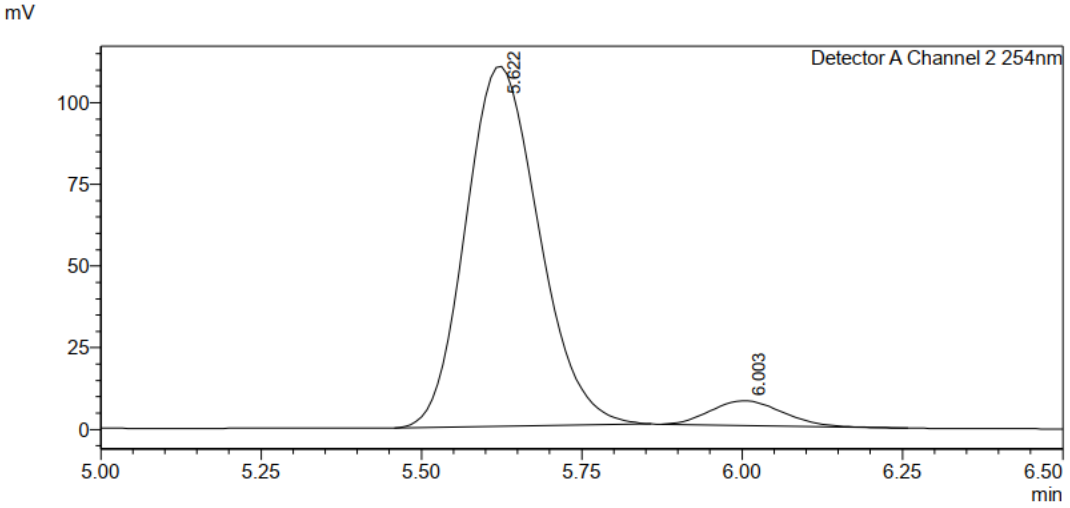
Peak#	Ret. Time	Area	Area%
1	10.953	982521	91.960
2	11.896	85897	8.040
Total		1068418	100.000

isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)hept-6-enoate (6c)



Detector A Channel 2 254nm

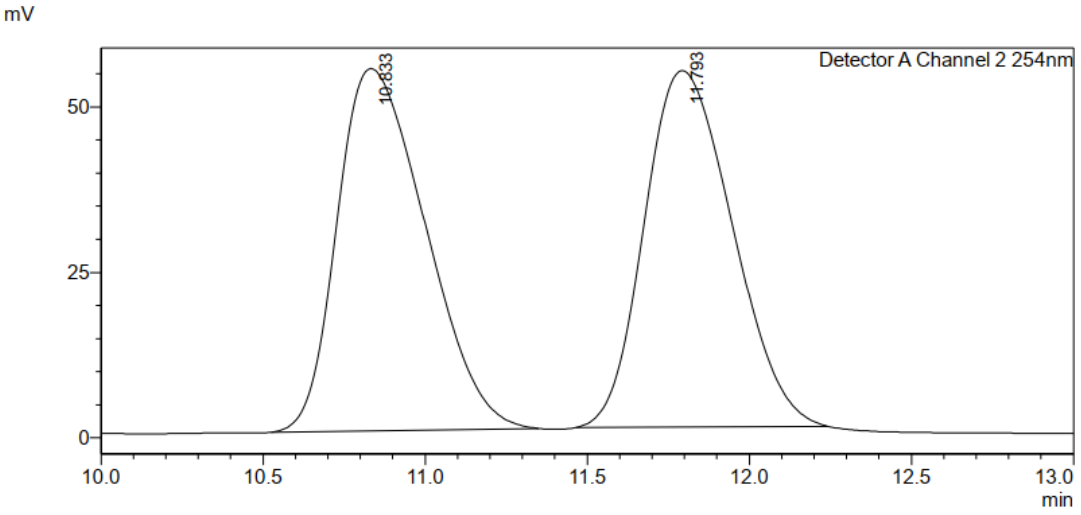
Peak#	Ret. Time	Area	Area%
1	5.620	685253	49.839
2	5.995	689679	50.161
Total		1374932	100.000



Detector A Channel 2 254nm

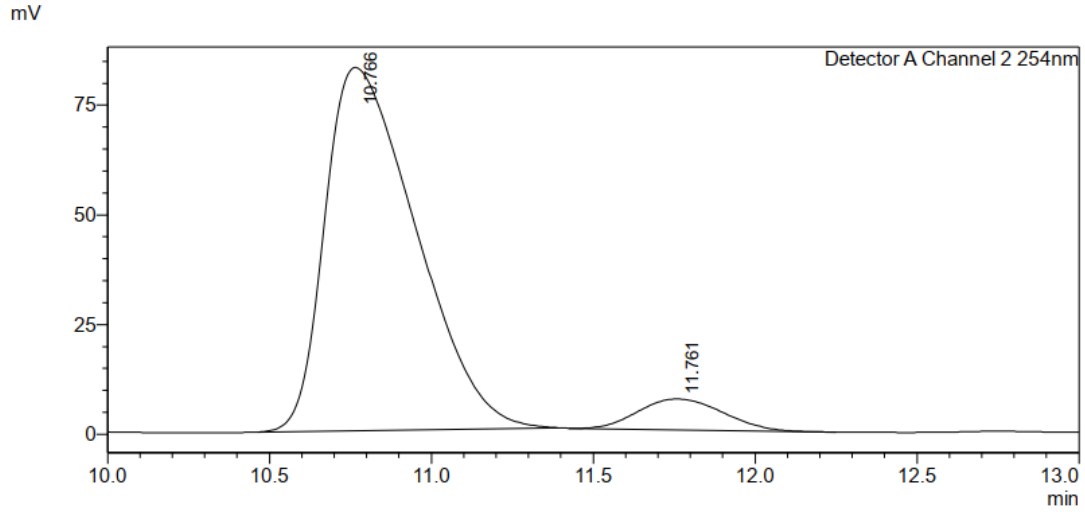
Peak#	Ret. Time	Area	Area%
1	5.622	879156	93.749
2	6.003	58619	6.251
Total		937775	100.000

isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)oct-7-enoate (6d)



Detector A Channel 2 254nm

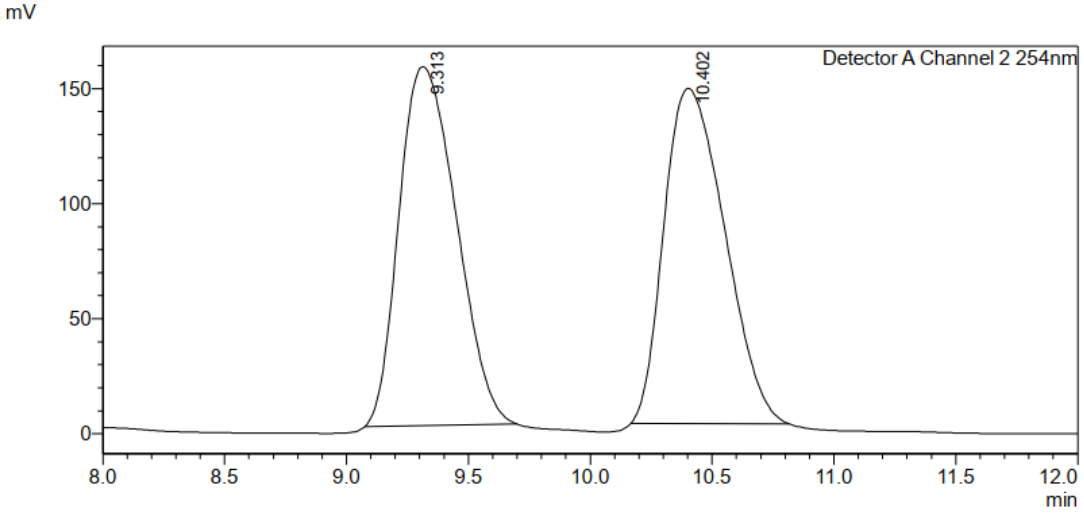
Peak#	Ret. Time	Area	Area%
1	10.833	1035872	50.460
2	11.793	1017001	49.540
Total		2052873	100.000



Detector A Channel 2 254nm

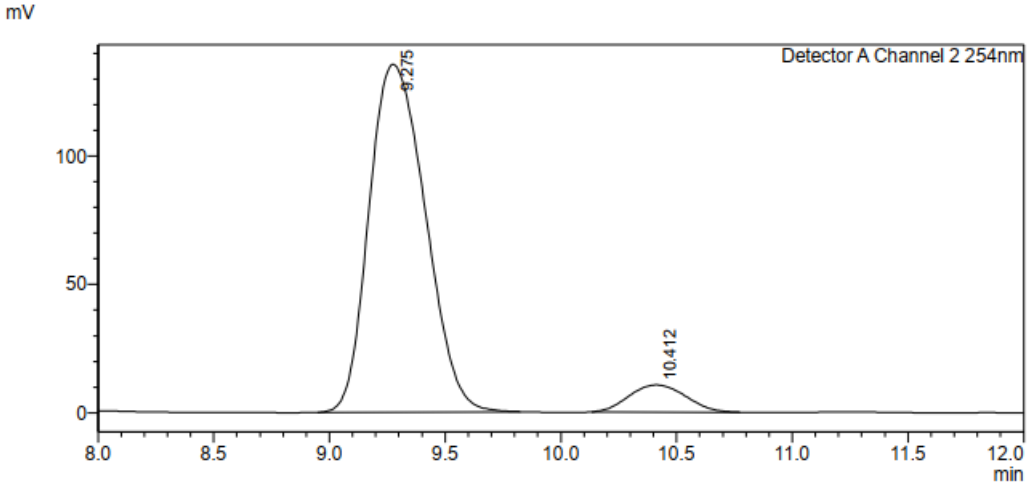
Peak#	Ret. Time	Area	Area%
1	10.766	1618604	92.683
2	11.761	127791	7.317
Total		1746395	100.000

isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)hexanoate (6e)



Detector A Channel 2 254nm

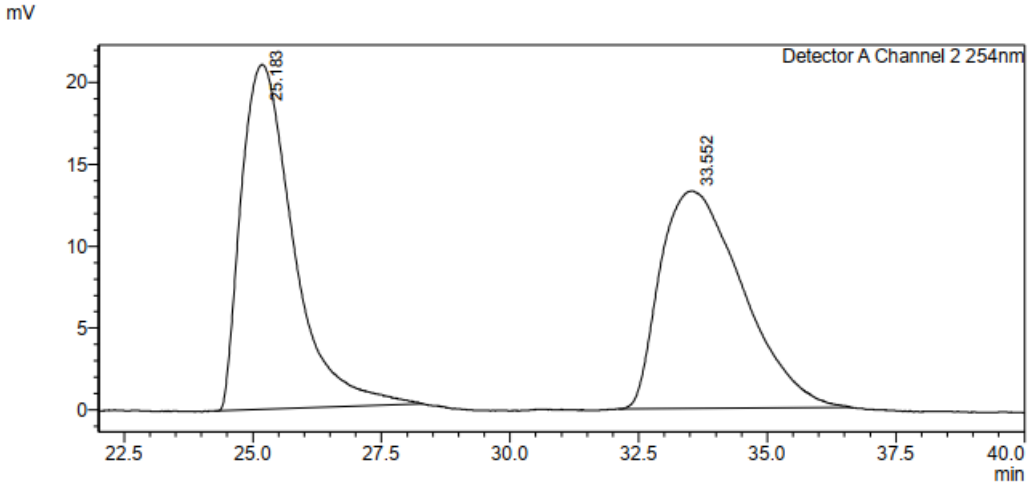
Peak#	Ret. Time	Area	Area%
1	9.313	2551408	50.223
2	10.402	2528711	49.777
Total		5080119	100.000



Detector A Channel 2 254nm

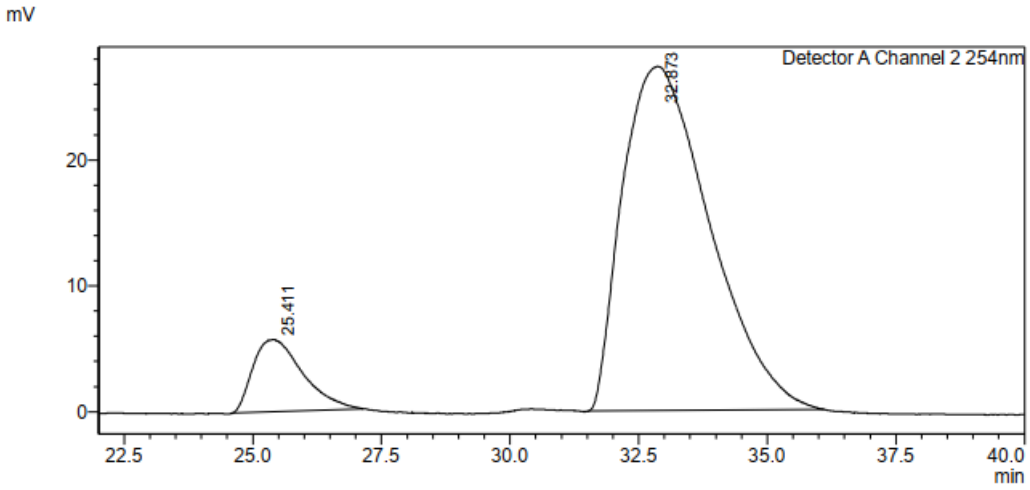
Peak#	Ret. Time	Area	Area%
1	9.275	2292171	92.736
2	10.412	179559	7.264
Total		2471730	100.000

isopropyl (R)-2-cyano-2-(4-methoxyphenoxy)propanoate (6f)



Detector A Channel 2 254nm

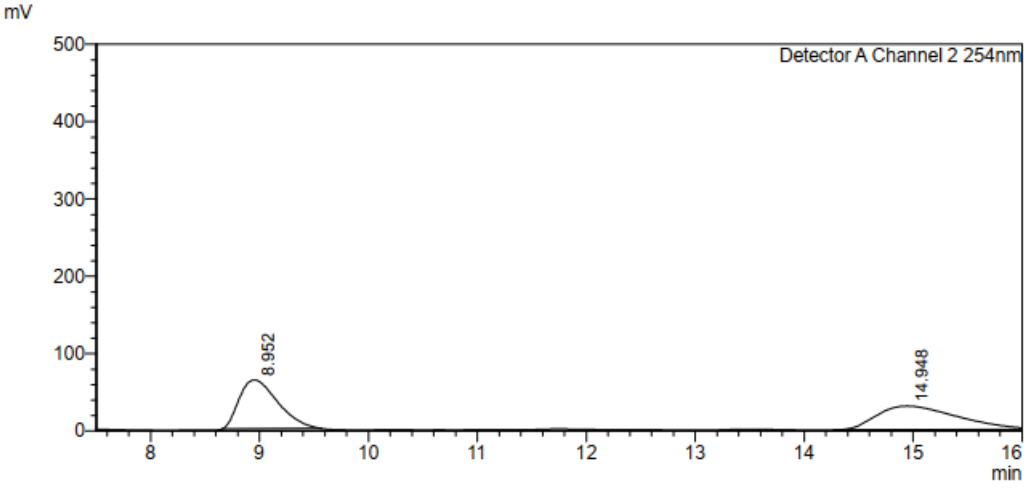
Peak#	Ret. Time	Area	Area%
1	25.183	1489927	50.127
2	33.552	1482370	49.873
Total		2972296	100.000



Detector A Channel 2 254nm

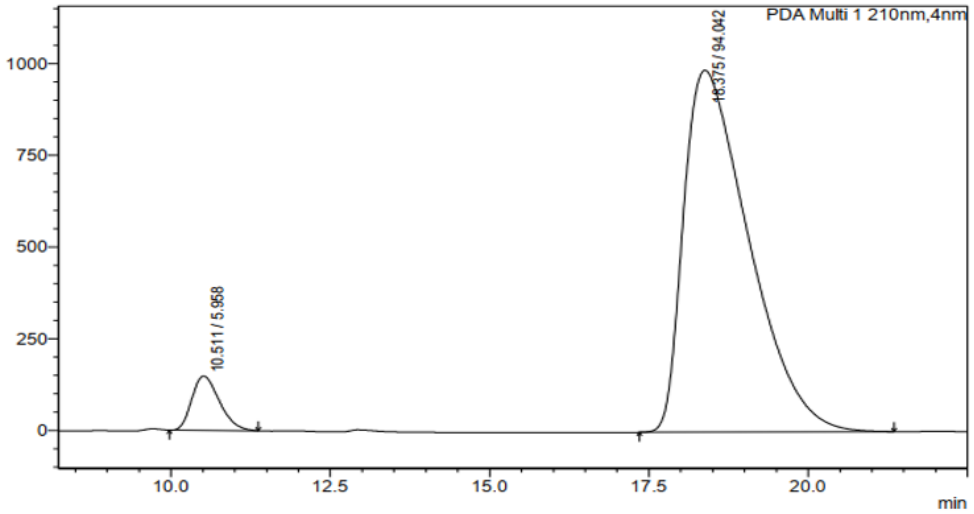
Peak#	Ret. Time	Area	Area%
1	25.411	384777	10.639
2	32.873	3231831	89.361
Total		3616608	100.000

isopropyl (R)-2-cyano-4-phenyl-2-(p-tolyloxy)butanoate (6g)



Detector A Channel 2 254nm

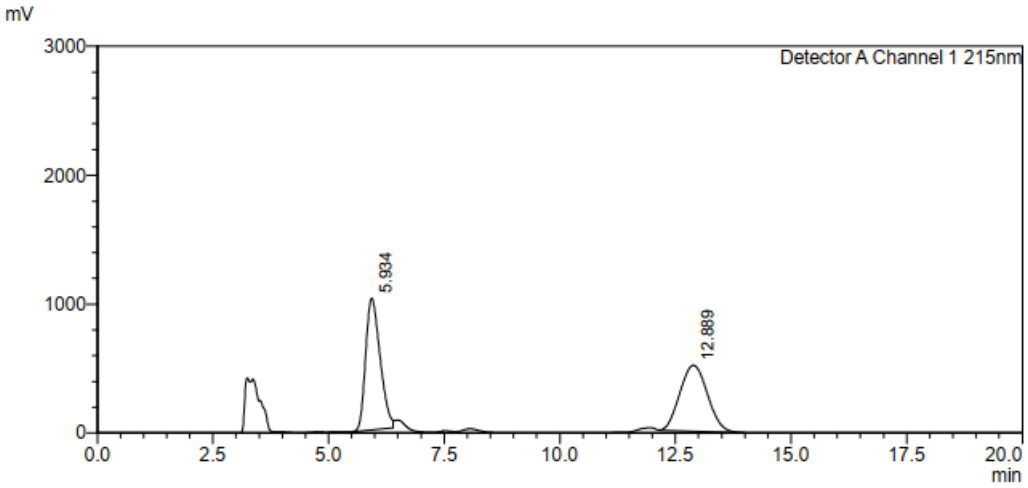
Peak#	Ret. Time	Area	Area%
1	8.952	1554171	49.101
2	14.948	1611056	50.899
Total		3165226	100.000



Detector A Channel 2 254nm

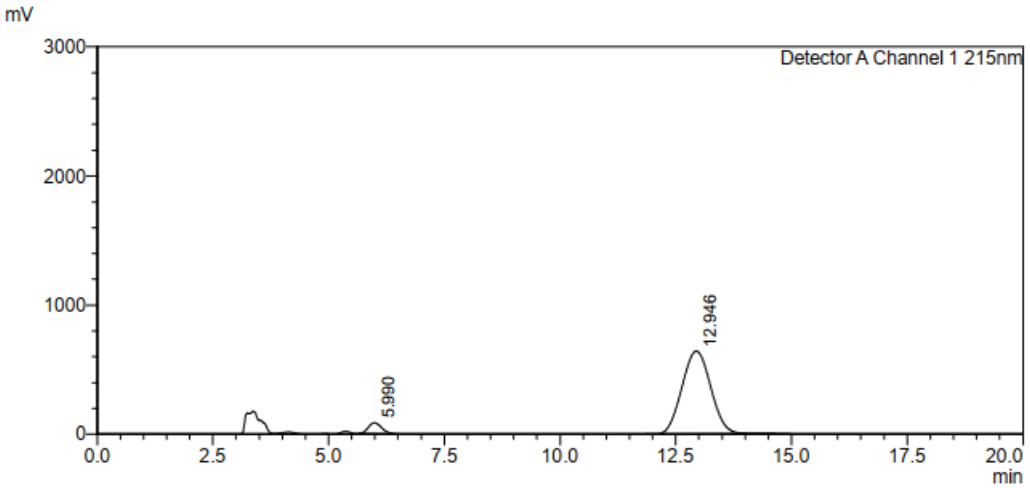
Peak#	Ret. Time	Area	Area%
1	10.517	125225	5.607
2	18.382	2108216	94.393
Total		2233442	100

isopropyl (R)-2-cyano-2-(p-tolyloxy)hexanoate (6h)



Detector A Channel 2 254nm

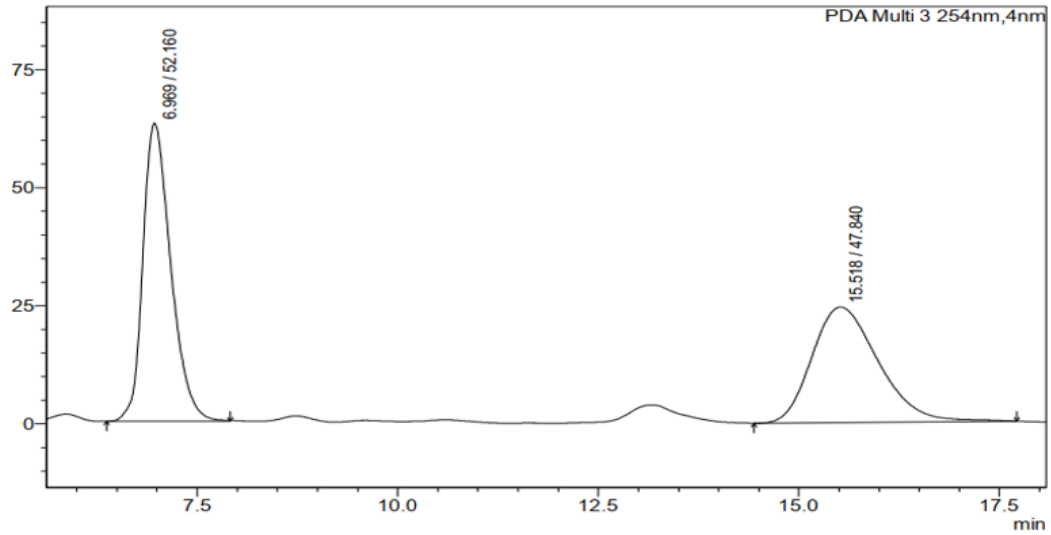
Peak#	Ret. Time	Area	Area%
1	5.933	747972	49.898
2	12.887	751044	50.102
Total		1499016	100.000



Detector A Channel 2 254nm

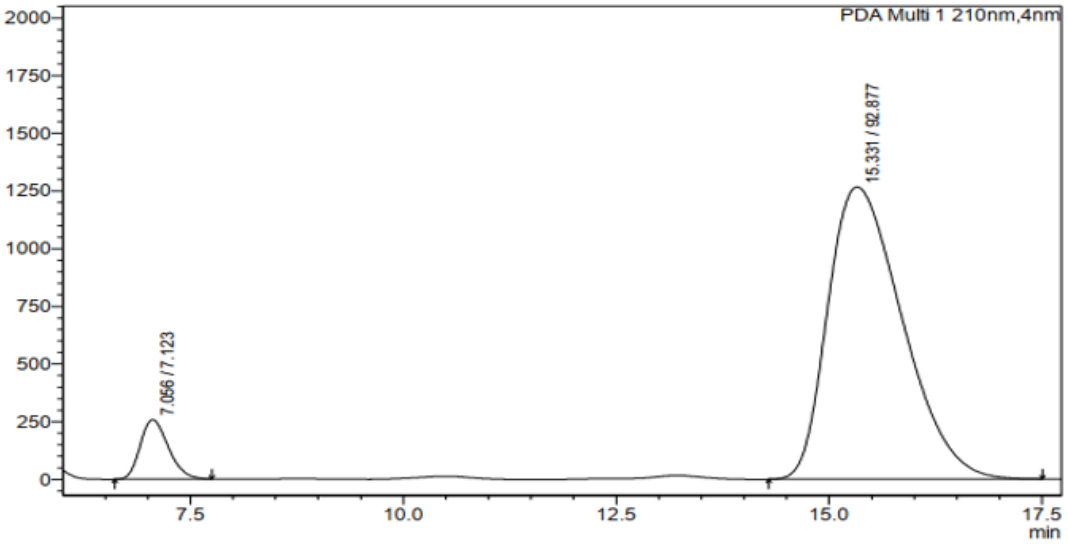
Peak#	Ret. Time	Area	Area%
1	5.982	62037	5.534
2	12.945	1059060	94.466
Total		1121097	100.000

isopropyl (R)-2-cyano-2-(p-tolyloxy)hept-6-enoate (6i)



Detector A Channel 2 254nm

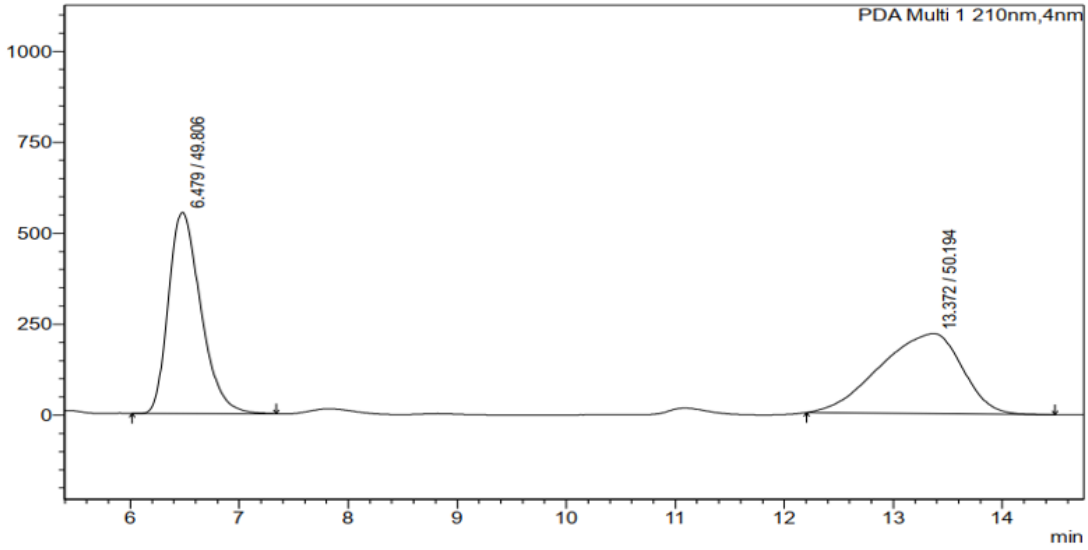
Peak#	Ret. Time	Area	Area%
1	6.971	5013997	50348
2	15.517	4750674	49.652
Total		9764671	100



Detector A Channel 2 254nm

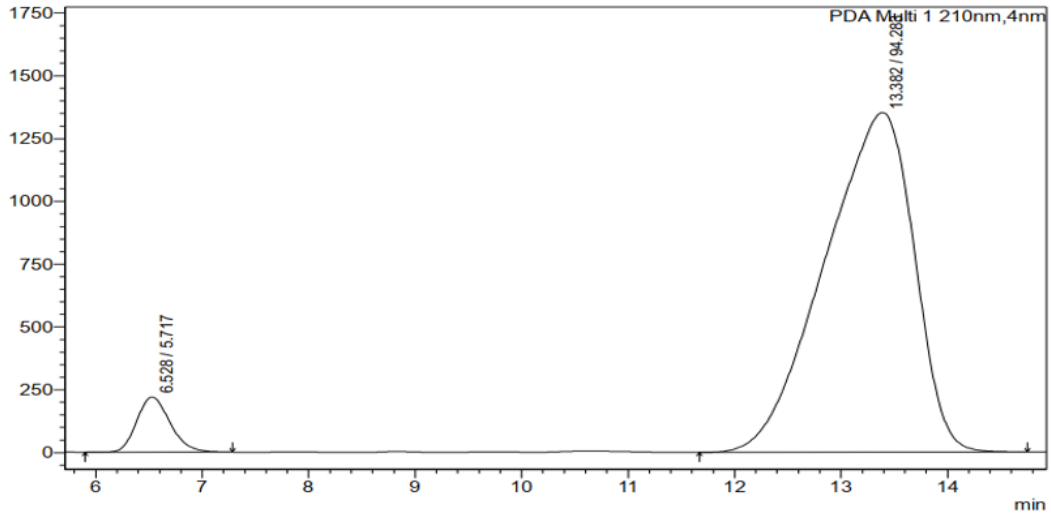
Peak#	Ret. Time	Area	Area%
1	7.063	859566	7.146
2	15.328	11168278	92.854
Total		12027843	100

isopropyl (R)-2-cyano-2-(p-tolyloxy)oct-7-enoate (6j)



Detector A Channel 2 254nm

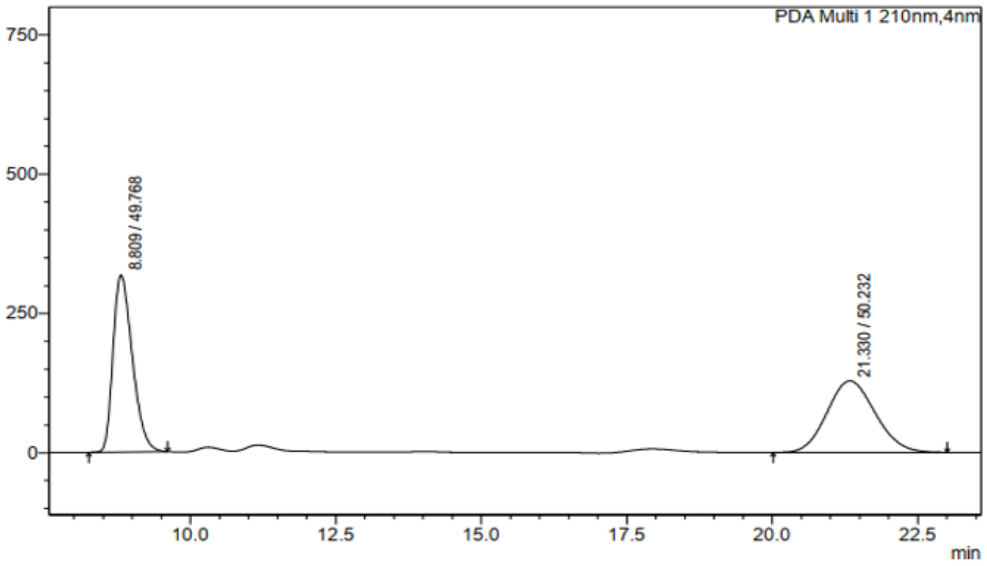
Peak#	Ret. Time	Area	Area%
1	6.479	11445646	49.806
2	13.372	11534973	50.194
Total		22980619	100



Detector A Channel 2 254nm

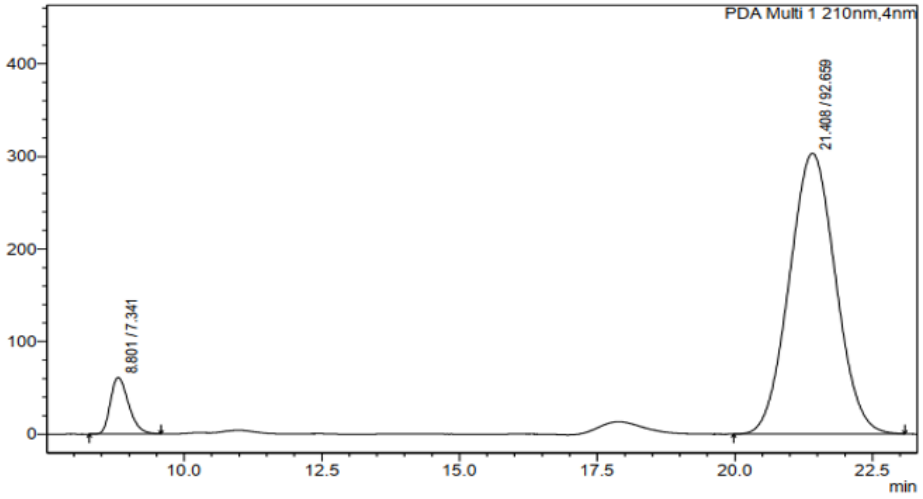
Peak#	Ret. Time	Area	Area%
1	6.528	4783409	5.717
2	13.382	78884007	94.283
Total		83667416	100

isopropyl (R)-2-cyano-2-(p-tolyloxy)butanoate (6k)



Detector A Channel 2 254nm

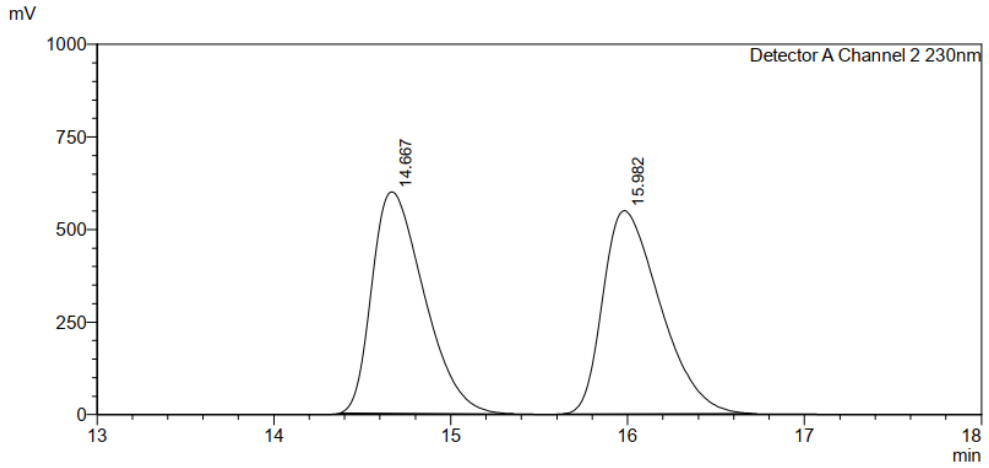
Peak#	Ret. Time	Area	Area%
1	8.809	7348775	49.768
2	21.33	7417383	50.232
Total		14766157	100



Detector A Channel 2 254nm

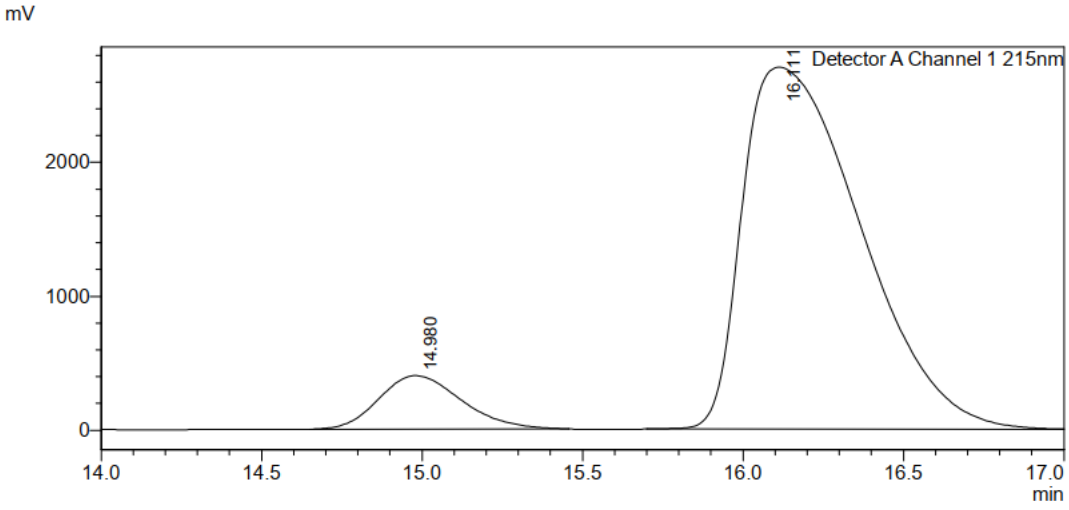
Peak#	Ret. Time	Area	Area%
1	8.801	1401468	7.341
2	21.408	17690278	92.659
Total		19091745	100

isopropyl (R)-2-(4-bromophenoxy)-2-cyanobutanoate (6l)



Detector A Channel 2 230nm

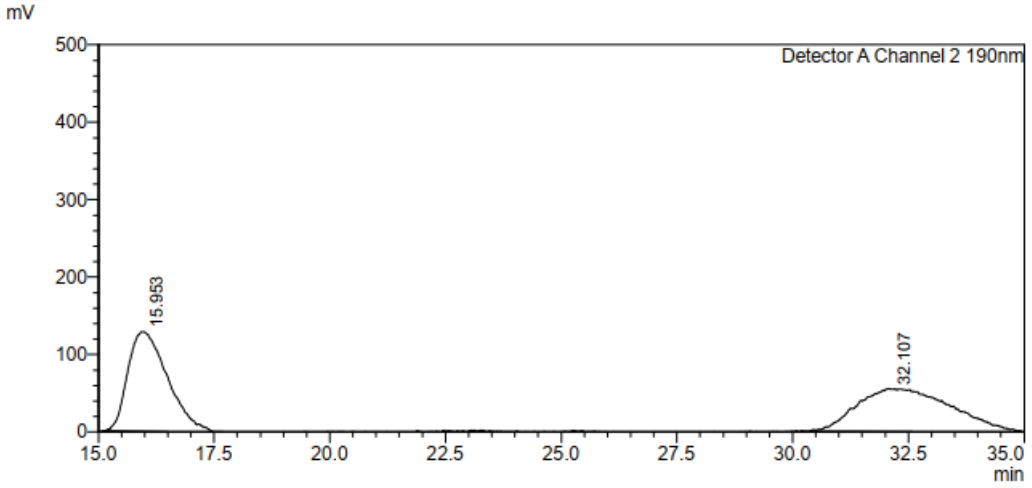
Peak#	Ret. Time	Area	Area%
1	14.667	12189269	49.619
2	15.982	12376333	50.381
Total		24565602	100.000



Detector A Channel 2 254nm

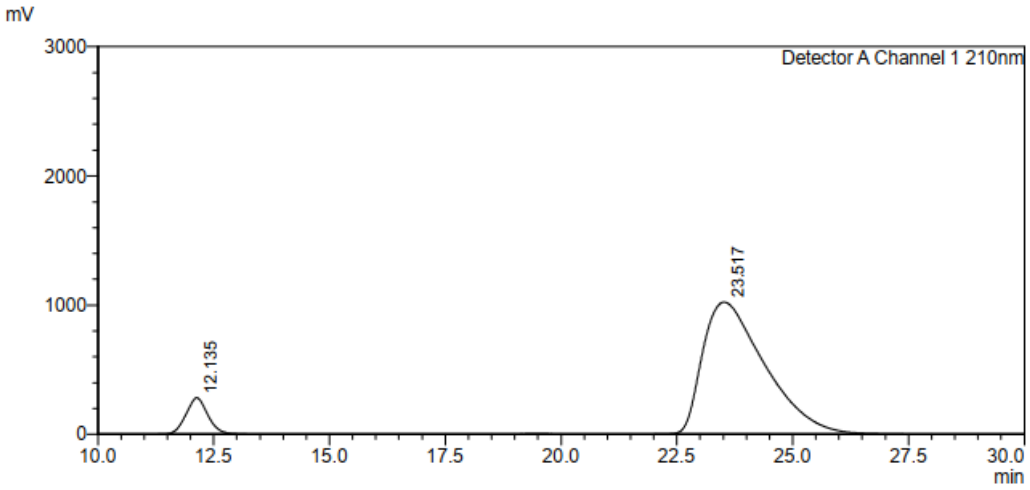
Peak#	Ret. Time	Area	Area%
1	14.980	312938	8.051
2	16.111	3574139	91.949
Total		3887076	100.000

(R)-2-(4-bromophenoxy)-2-cyanobutyl methanesulfonate (13-Me)



Detector A Channel 2 190nm

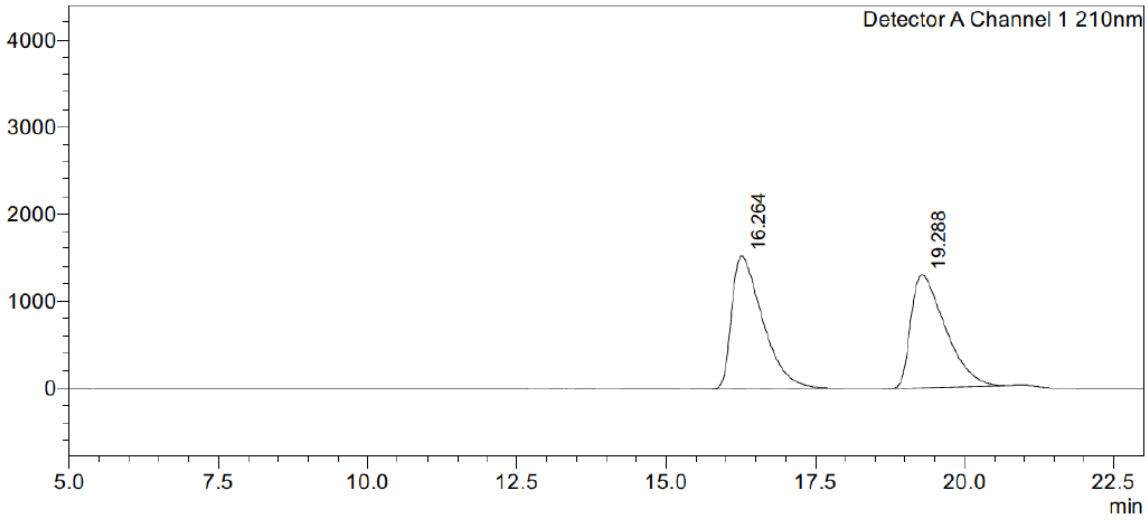
Peak#	Ret. Time	Area	Area%
1	15.953	7782356	49.614
2	32.107	7903578	50.386
Total		15685934	100.000



Detector A Channel 2 230nm

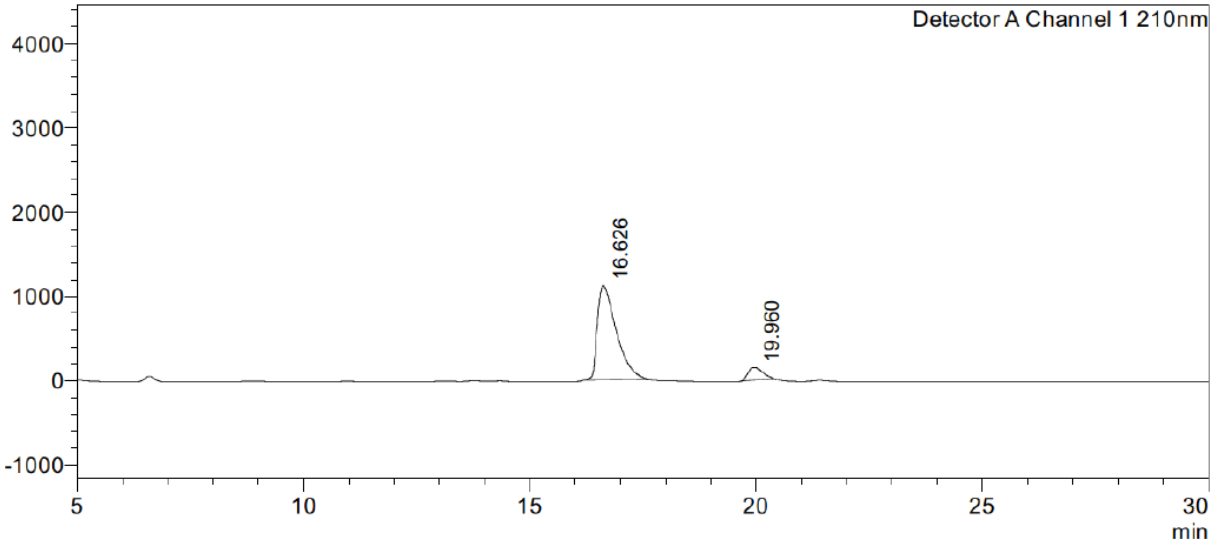
Peak#	Ret. Time	Area	Area%
1	12.147	568539	9.242
2	23.516	5583045	90.758
Total		6151584	100.000

(R)-N-(4-cyano-3-(trifluoromethyl)phenyl)-3-((4-fluorophenyl)sulfonyl)-2-hydroxy-2-methylpropanamide ((R)-Bicalutamide)



Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	16.264	55085883	51.343
2	19.288	52204192	48.657
Total		107290074	100.000



Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	16.626	32658952	90.379
2	19.960	3476752	9.621
Total		36135704	100.000

14. References

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[6]. a) I Colomer, R C Barcelos, K E. Christensen, T J. Donohoe *Org. Lett*. 2016, **18**, 5880; b) Y. Li, A. Studer *Angew. Chem. Int. Ed.* 2012, **51**, 8221.

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