Pentanidium-Catalyzed Direct Assembly of Vicinal All-Carbon Quaternary Stereocenters through C(sp^3)-C(sp^3) Bond Formation

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Supporting Information

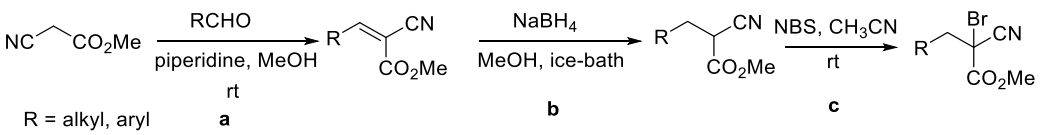
Contents

1. General Information

All reactions were carried out under a nitrogen atmosphere with dry solvents and using anhydrous conditions unless otherwise stated. All reagents were used as received without further purification, unless otherwise stated. THF were distilled over sodium/benzophenone under N_2 atmosphere. Toluene, Acetonitrile and Dichloromethane were distilled over CaH_2 under N_2 atmosphere. Isolated yields were obtained through flash chromatography separations, which were performed on Merck 60 (0.040 - 0.063mm) mesh silica gel, unless otherwise stated. ^1H and ^{13}C NMR spectra were recorded on Bruker AV-300 (300 MHz), BrukerAvance III 400 (400MHz) (100 MHz) spectrometer. Chemical shifts are recorded as δ in units of parts per million (ppm). ^{19}F was performed on a Bruker Avance III 400 (400MHz) spectrometer. 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: $[\alpha]^T_D$ (c g/100 mL, solvent). X-ray crystallography analysis was performed on Bruker X8 APEX X-ray diffractionmeter. Reactions were monitored by analytical thin-layer chromatography (TLC) (Merck 60 F254 silica gel plates). Visualization was performed using a UV lamp or potassium permanganate stain, and heat as developing agents. Melting points were recorded on a Fisher-Johns 12-144 melting point apparatus. All ion-pair catalysts are synthesized according to our previous procedures.

2. General procedure for the synthesis of tertiary bromides

Method A: [1]



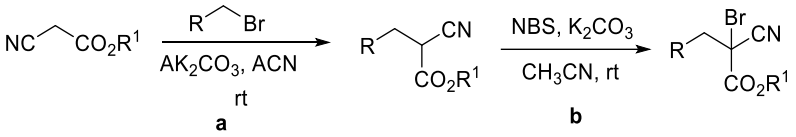
a) To a flame dried flask was added methyl 2-cyanoacetate (1.0 equiv.), the corresponding aldehyde (1.2 equiv.) and MeOH. The solution was stirring for 5min

at room temperature. Piperidine (0.1 mol %) was added and the solution stirred overnight. The precipitation was collected by simply filtration, and washed using MeOH. The pale yellow solid was used directly without further purification for next step.

b) The crude yellow solid alkene residue was dissolved in MeOH. The solution was cooled down using ice-bath. Then $NaBH_4$ (0.3 equiv.) was then added slowly at 0 °C. After stirring for 30 min at 0 °C, the mixture was warmed to room temperature and quenched with saturated NH_4Cl solution. The reaction was partitioned between saturated aqueous NH_4Cl (250 mL) and DCM and the aqueous layer extracted with DCM. The combined organic layers were washed with brine, dried (Na_2SO_4), and the volatiles removed and purified by flash chromatography (hexane: ethyl acetate = 2:1 as the eluent) to get the alkylated methyl 2-cyanoacetate.

c) The alkylated methyl 2-cyanoacetate was dissolved in dry CH_3CN at rt, and then K_2CO_3 (1.5 equiv) was added slowly. After stirring for 30 min, NBS (1.1 equiv) was added. The mixture was stirred for 1 h. Then the mixture was added water (10 mL) and then extracted with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ethyl acetate = 4:1 as the eluent) to get the tertiary bromides.

Method B: [1]

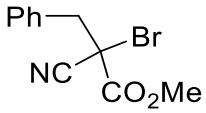


R = alkyl, aryl, H
R^1 = Et, *i*Pr, *t*Bu

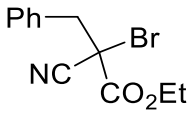
a) Potassium carbonate (2.0 equiv.) was added to a solution of cyanoester (1.0 equiv.) in . After stirring for 30 min, alkyl bromide (0.2 equiv.) was added. The mixture was stirred at rt for 12 h. Then the mixture was added water (20 mL) and then extracted with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by flash chromatography (hexane: ethyl acetate = 5:1 as the eluent) to get the alkylated cyanoester.

b) The alkylated cyanoester was dissolved in anhydrous CH_3CN at rt, and then K_2CO_3 (1.5 CH3CNequiv) was added slowly. After stirring for 30 min, NBS (1.1 equiv) was added. The mixture was stirred for 1 h. Then the mixture was added water (10 mL) and then extracted with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ethyl acetate = 10:1 as the eluent) to get the brominated cyanoester.

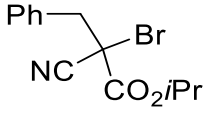
3. Characterization of tertiary bromides



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.

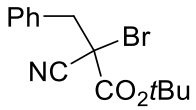


Ethyl 2-bromo-2-cyano-3-phenylpropanoate (1b): method B; colorless oil; 76% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.31; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 5H), 4.53 – 4.17 (m, 2H), 3.75 (d, J = 13.8 Hz, 1H), 3.55 (d, J = 13.8 Hz, 1H), 1.31 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) 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.

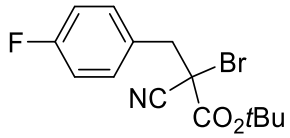


***Iso*propyl 2-cyano-2-iodo-3-phenylpropanoate (1c):** method B; colorless oil; 87% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 5H), 5.09 (dt, J = 12.5, 6.3 Hz, 1H), 3.75 (d, J = 13.9 Hz, 1H), 3.55 (d, J = 13.9 Hz, 1H),

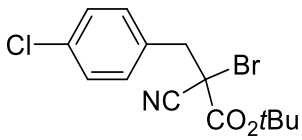
3.50 (q, J = 7.0 Hz, 1H), 1.33 (d, J = 6.3 Hz, 3H), 1.25 – 1.22 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.24, 134.82, 134.18, 130.13, 129.02, 128.77, 128.48, 127.83, 117.73, 72.59, 65.86, 46.76, 43.40, 21.20, 20.81, 15.79, 15.29. HRMS (ESI) calcd for $C_{13}H_{15}BrNO_2$ m/z $[M+H]^+$: 296.0281; found:296.0280.



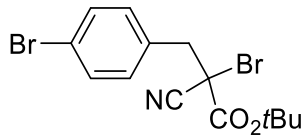
***tert*-Butyl 2-bromo-2-cyano-3-phenylpropanoate (1d)**: method B A; colorless oil; 90% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (t, J = 2.1 Hz, 5H), 3.72 (d, J = 13.8 Hz, 1H), 3.50 (d, J = 13.8 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.55, 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.



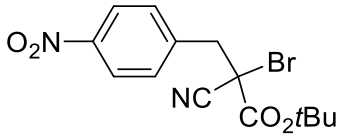
***tert*-Butyl 2-bromo-2-cyano-3-(4-fluorophenyl)propanoate (3d)**: method B; colorless oil; 87% yield; TLC (Hexane:Et_2O, 85:15 v/v): R_f = 0.34; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.39 – 7.29 (m, 2H), 7.04 (t, J = 8.7 Hz, 2H), 3.67 (d, J = 14.0 Hz, 1H), 3.44 (d, J = 14.0 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.48, 161.68, 132.34, 132.25, 128.87, 115.82, 115.69, 115.61, 86.42. ^{19}F NMR (377 MHz, $CDCl_3$) δ -113.01, -113.03, -113.05. HRMS (ESI) calcd for $C_{14}H_{16}BrFNO_2$ m/z $[M+H]^+$:328.0343; found: 328.0340.



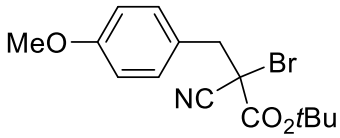
***tert*-Butyl 2-bromo-3-(4-chlorophenyl)-2-cyanopropanoate (4d)**: method B; yellow oil: 90% yield; TLC (Hexane:Et_2O, 85:15 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.30 (s, 4H), 3.66 (d, J = 14.0 Hz, 1H), 3.43 (d, J = 13.9 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 162.47, 134.82, 131.94, 131.55, 129.03, 115.67, 86.60, 44.64, 44.64, 43.54, 43.54, 27.52. HRMS (ESI) calcd for $C_{14}H_{16}BrFNO_2$ m/z $[M+H]^+$:344.0047; found: 344.0040.



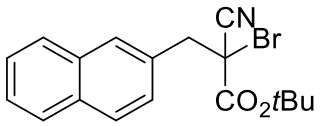
***tert*-Butyl 2-bromo-3-(4-bromophenyl)-2-cyanopropanoate (5d)**: method B; yellow oil; 88% yield; TLC (Hexane:Et_2O, 85:15 v/v): R_f = 0.30; ^1H NMR (400 MHz, Chloroform-d) δ 7.54 (d, J = 8.5 Hz, 2H), 7.34 – 7.24 (m, 2H), 3.69 (d, J = 13.8 Hz, 1H), 3.46 (d, J = 13.9 Hz, 1H), 1.53 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 162.39, 132.19, 132.03, 131.93, 122.96, 115.59, 86.54, 44.66, 43.42, 27.47. HRMS (ESI) calcd for $C_{14}H_{16}Br_2NO_2$ m/z $[M+H]^+$:387.9542; found: 387.9540.



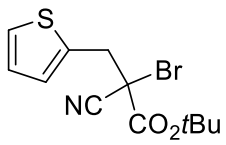
***tert*-Butyl 2-bromo-2-cyano-3-(4-nitrophenyl)propanoate (6d)**: method B; yellow solid; mp: 112–114 °C; 82% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.10; ^1H NMR (400 MHz, Chloroform-d) δ 8.23 (d, J = 8.7 Hz, 2H), 7.57 (d, J = 8.7 Hz, 2H), 3.78 (d, J = 13.9 Hz, 1H), 3.56 (d, J = 13.8 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 162.25, 140.19, 131.75, 123.96, 115.37, 87.14, 44.62, 42.82, 27.57. HRMS (ESI) calcd for $C_{14}H_{16}BrN_2O_4$ m/z $[M+H]^+$: 355.0288; found: 355.0287.



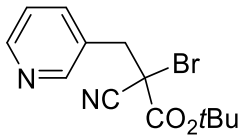
***tert*-Butyl 2-bromo-2-cyano-3-(4-methoxyphenyl)propanoate** (**7d**): method B; colorless oil; 92% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.20; ^1H NMR (400 MHz, Chloroform-d) δ 7.49 – 7.15 (m, 2H), 7.01 – 6.78 (m, 2H), 3.85 (s, 3H), 3.69 (d, J = 13.9 Hz, 1H), 3.45 (d, J = 14.0 Hz, 1H), 1.52 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.65, 159.81, 131.71, 125.13, 115.92, 114.13, 86.12, 76.71, 55.27, 44.75, 27.48. HRMS (ESI) calcd for $C_{15}H_{19}BrNO_3$ m/z $[M+H]^+$: 340.0543; found: 340.0542.



***tert*-Butyl-2-bromo-2-cyano-3-(naphthalen-2-yl)propanoate (8d)**: method B; colorless oil; 90% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.40; ^1H NMR (400 MHz, Chloroform-d) δ 7.84 (dq, J = 7.0, 3.7, 3.2 Hz, 4H), 7.56 – 7.37 (m, 3H), 3.88 (d, J = 13.8 Hz, 1H), 3.63 (d, J = 13.8 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-d) δ 133.26, 133.10, 130.56, 129.99, 128.51, 128.02 , 127.88 , 127.74 , 126.56 , 126.47 , 115.88 , 86.34 , 45.58 , 43.89 , 27.46. HRMS (ESI) calcd for $C_{18}H_{19}BrNO_2$ m/z $[M+H]^+$: 360.0594; found: 360.0598.

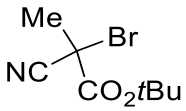


***tert*-Butyl 2-bromo-2-cyano-3-(thiophen-2-yl)propanoate (9d)**: method B; brown oil; 87% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^1H NMR (400 MHz, Chloroform-d) δ 7.28 (dd, J = 5.0, 1.2 Hz, 1H), 7.10 (d, J = 3.4 Hz, 1H), 6.99 (dd, J = 5.1, 3.6 Hz, 1H), 3.92 (d, J = 14.8 Hz, 1H), 3.68 (d, J = 14.8 Hz, 1H), 1.51 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 162.41, 134.17, 129.40, 127.30, 126.65, 115.69, 86.53, 77.12, 76.85, 76.81, 43.18, 39.97, 27.51. HRMS (ESI) calcd for $C_{12}H_{15}BrNO_2S$ m/z $[M+H]^+$: 316.0001; found: 316.0004.

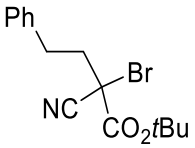


***tert*-butyl 2-bromo-2-cyano-3-(pyridin-3-yl)propanoate (10d)**: method B; colorless oil; 85% yield; TLC (Hexane:Et_2O, 60:40 v/v): R_f = 0.30; ^1H NMR (400 MHz, Chloroform-d) δ 8.68 – 8.51 (m, 2H), 7.77 (dt, J = 7.9, 2.0 Hz, 1H), 7.36 – 7.28 (m, 1H), 3.68 (d, J = 14.1 Hz, 1H), 3.48 (d, J = 14.1 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.25, 151.33, 149.75, 138.18, 129.05, 123.69, 115.46, 86.92, 43.33,

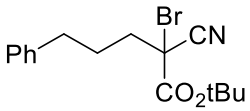
42.52, 27.51. HRMS (ESI) calcd for $C_{13}H_{16}BrN_2O_2$ m/z $[M+H]^+$: 311.0390; found: 311.0381.



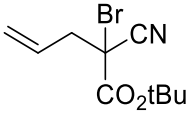
***tert*-butyl 2-bromo-2-cyanopropanoate (11d)**: method B, colorless oil; 90% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.30; ^{1}H NMR (500 MHz, Chloroform-d) δ 2.15 (s, 3H), 1.54 (s, 9H); ^{13}C NMR (126 MHz, Chloroform-d) δ 163.2, 117.1, 86.1, 38.3, 28.0, 27.6; HRMS (ESI) calcd for $C_8H_{13}BrNO_2$ m/z [M+H]+ : 234.0124; found: 234.0120.



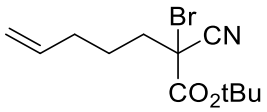
***tert*-Butyl 2-bromo-2-cyano-4-phenylbutanoate (12d)**: method B, colorless oil; 85% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.40; ^{1}H NMR (300 MHz, Chloroformd) δ 7.40 – 7.18 (m, 5H), 3.08 – 2.88 (m, 1H), 2.88 – 2.71 (m, 1H), 2.55 (qdd, J = 14.0, 11.6, 5.0 Hz, 2H), 1.55 (s, 9H); ^{13}C NMR (75 MHz, Chloroform-d) δ 162.8, 138.9, 128.9, 128.6, 126.9, 116.0, 86.3, 43.9, 41.8, 32.8, 27.7; HRMS (ESI) calcd for $C_{15}H_{19}BrNO_2$ m/z [M+H]+ : 324.0594; found: 324.0590.



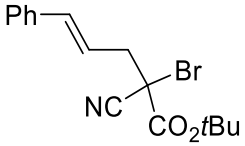
***tert*-Butyl 2-bromo-2-cyano-5-phenylpentanoate (13d)**: method B; colorless oil; 82% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.46 – 7.09 (m, 5H), 2.76 (t, J = 7.4 Hz, 2H), 2.46 – 2.20 (m, 2H), 2.14 – 1.95 (m, 1H), 1.95 – 1.75 (m, 1H), 1.55 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.85, 140.62, 128.72, 128.47, 126.45, 116.08, 86.12, 44.27, 39.43, 34.96, 27.92, 27.60, 27.58. HRMS (ESI) calcd for $C_{16}H_{21}BrNO_2$ m/z [M+H]+ : 338.0750; found: 338.0753.



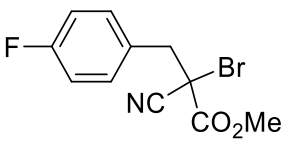
***tert*-Butyl 2-bromo-2-cyanopent-4-enoate (14d)**: method B colorless oil; 88% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-d) δ 5.93 – 5.73 (m, 1H), 5.43 – 5.30 (m, 2H), 3.14 – 3.01 (m, 1H), 3.01 – 2.88 (m, 1H), 1.54 (s, 9H); ^{13}C NMR (101 MHz, Chloroform-d) δ 162.5, 129.7, 122.9, 115.8, 86.3, 44.1, 43.1, 27.7; HRMS (ESI) calcd for $C_{10}H_{15}BrNO_2$ m/z $[M+H]^+$: 260.0281; found: 260.0282.



***tert*-Butyl 2-bromo-2-cyanohept-6-enoate (15d)**: method B; 85% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.24; ^{1}H NMR (400 MHz, Chloroform-d) δ 5.89 – 5.51 (m, 1H), 5.19 – 4.76 (m, 2H), 2.42 – 1.99 (m, 4H), 1.93 – 1.67 (m, 2H), 1.53 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 162.78, 136.85, 116.03, 116.00, 85.98, 44.23, 39.27, 32.65, 27.51, 25.43. HRMS (ESI) calcd for $C_{12}H_{19}BrNO_2$ m/z $[M+H]^+$: 288.0594; found: 288.0592.

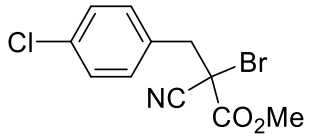


***tert*-butyl (E)-2-bromo-2-cyano-5-phenylpent-4-enoate (16d)**: method B; colorless oil; 90% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.37; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.39 (dt, J = 8.2, 1.6 Hz, 2H), 7.37 – 7.31 (m, 2H), 7.31 – 7.27 (m, 1H), 6.66 (dd, J = 15.8, 1.5 Hz, 1H), 6.28 – 6.09 (m, 1H), 3.23 (ddt, J = 14.0, 7.5, 1.5 Hz, 1H), 3.11 (ddt, J = 14.2, 7.2, 1.4 Hz, 1H), 1.53 (d, J = 1.5 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.56, 137.64, 136.18, 128.82, 128.45, 126.75, 120.48, 115.93, 86.35, 77.16, 76.88, 76.84, 43.48, 27.68. HRMS (ESI) calcd for $C_{16}H_{19}BrNO_2$ m/z $[M+H]^+$: 336.0594; found: 336.0592.

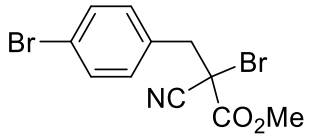


Methyl 2-bromo-2-cyano-3-(4-fluorophenyl)propanoate (3a): method A; colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400 MHz,

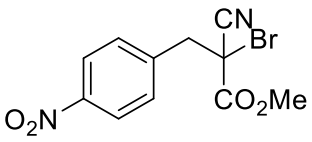
Chloroform-*d*) δ 7.32 (d, *J* = 13.9 Hz, 2H), 7.13 – 6.97 (m, 2H), 3.86 (s, 3H), 3.70 (d, *J* = 14.0 Hz, 1H), 3.49 (d, *J* = 13.9 Hz, 1H). ^{13}C NMR (101 MHz, CHLOROFORM-*D*) δ 164.48, 164.24, 161.77, 132.25, 128.62, 116.05, 115.84, 115.33, 54.92, 44.72, 42.12. ^{19}F NMR (377 MHz, $CDCl_3$) δ -112.72, -112.74. HRMS (ESI) calcd for $C_{11}H_{10}BrFNO_2$ m/z $[M+H]^+$: 285.9873; found: 285.9865.



Methyl 2-bromo-3-(4-chlorophenyl)-2-cyanopropanoate (4a): method A, colorless oil; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.40; ^{1}H NMR (400 MHz, Chloroform-d): δ 7.40 – 7.26 (m, 4H), 3.87 (s, 3H), 3.69 (d, J = 13.9 Hz, 1H), 3.48 (d, J = 13.9 Hz, 1H); ^{13}C NMR (101 MHz, Chloroform-d): δ 164.4, 135.0, 131.9, 131.2, 129.2, 115.3, 55.0, 44.8, 41.9; HRMS (ESI) calcd for $C_{11}H_{10}NO_2ClBr$ m/z $[M+H]^+$: 303.9563; found: 303.9560.

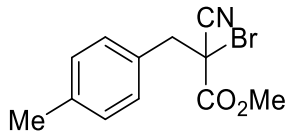


Methyl 2-bromo-3-(4-bromophenyl)-2-cyanopropanoate (5a): method A, yellow oil; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.34; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.33 (dd, J = 8.6, 5.3 Hz, 2H), 7.21 – 6.89 (m, 2H), 3.86 (s, 3H), 3.70 (d, J = 14.0 Hz, 1H), 3.49 (d, J = 14.0 Hz, 1H); ^{13}C NMR (101 MHz, Chloroform-d) δ 164.5, 163.0, 132.3, 128.6, 116.0, 115.4, 54.9, 44.8, 42.2; HRMS (ESI) calcd for $C_{11}H_{10}Br_2NO_2$ m/z [M+H]+ : 345.9073; found: 345.9072.

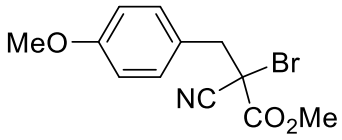


Methyl-2-bromo-2-cyano-3-(4-nitrophenyl)propanoate (6a): method A, yellow oil; TLC (Hexane:Et_2O, 60:40 v/v): R_f = 0.40; ^{1}H NMR (400 MHz, Chloroform-d) δ 8.29 – 8.16 (m, 2H), 7.65 – 7.44 (m, 2H), 3.90 (s, 3H), 3.82 (d, J = 13.9 Hz, 1H), 3.62 (d, J = 14.0 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 164.11, 148.20, 139.66, 131.62,

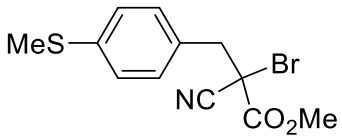
123.97, 114.86, 55.16, 44.65, 41.00. HRMS (ESI) calcd for $C_{11}H_{10}Br_2N_2O_4$ m/z $[M+H]^+$: 312.9818; found: 312.9824.



Methyl 2-bromo-2-cyano-3-(p-tolyl)propanoate (7a): method A; colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 7.9 Hz, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 3.83 (d, *J* = 1.6 Hz, 3H), 3.68 (d, *J* = 13.8 Hz, 1H), 3.47 (d, *J* = 13.8 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.58, 138.59, 130.25, 129.72, 129.58, 115.47, 54.74, 45.28, 42.46, 30.93, 21.20. HRMS (ESI) calcd for $C_{12}H_{13}BrNO_2$ m/z $[M+H]^+$: 282.0124; found: 282.0129.

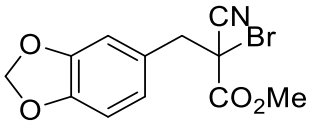


Methyl 2-bromo-2-cyano-3-(4-methoxyphenyl)propanoate (8a): method A; colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.25 (dd, *J* = 8.7, 2.0 Hz, 2H), 6.97 – 6.76 (m, 2H), 3.84 (d, *J* = 2.7 Hz, 3H), 3.79 (d, *J* = 3.1 Hz, 3H), 3.67 (dd, *J* = 14.0, 2.1 Hz, 1H), 3.45 (dd, *J* = 13.9, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.58, 159.90, 131.60, 124.75, 115.53, 114.27, 77.13, 76.86, 76.81, 55.28, 54.75, 44.92, 42.53. HRMS (ESI) calcd for $C_{12}H_{13}BrNO_3$ m/z $[M+H]^+$: 298.0073; found: 298.0089.

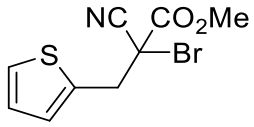


Methyl 2-bromo-2-cyano-3-(4-(methylthio)phenyl)propanoate (9a): method A; colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 (qd, *J* = 9.0, 8.4, 3.6 Hz, 4H), 3.92 – 3.71 (m, 3H), 3.72 – 3.58 (m, 1H), 3.54 – 3.36 (m, 1H), 2.46 (d, *J* = 1.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ

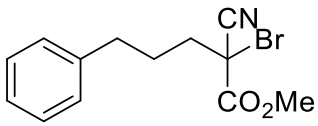
164.48, 139.64, 130.85, 130.80, 129.54, 129.16, 126.87, 126.41, 115.40, 77.50, 76.87, 76.79, 54.84, 45.05, 45.02, 15.38. HRMS (ESI) calcd for $C_{12}H_{13}BrNO_2S$ m/z $[M+H]^+$: 313.9845; found: 313.9852.



Methyl 3-(benzo[d][1,3]dioxol-5-yl)-2-bromo-2-cyanopropanoate (10a): method A; colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.81 (d, *J* = 1.4 Hz, 1H), 6.79 (dd, *J* = 2.9, 1.6 Hz, 2H), 5.97 (s, 2H), 3.87 (s, 3H), 3.65 (d, *J* = 14.0 Hz, 1H), 3.42 (d, *J* = 14.0 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 207.04, 164.66, 149.39, 149.02, 125.12, 122.97, 115.69, 113.35, 111.27, 55.92, 54.82, 45.44, 42.33, 30.99. HRMS (ESI) calcd for $C_{12}H_{11}BrNO_4$ m/z $[M+H]^+$: 311.9866; found: 311.9854.

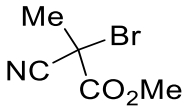


Methyl 2-bromo-2-cyano-3-(thiophen-2-yl)propanoate (11a): method A, yellow oil; TLC (Hexane:Et_2O, 60:40 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.29 (dd, J = 5.2, 1.2 Hz, 1H), 7.10 (dd, J = 3.2, 1.6 Hz, 1H), 7.04 – 6.96 (m, 1H), 3.97 (d, J = 14.6 Hz, 1H), 3.90 (s, 3H), 3.78 – 3.70 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 164.41, 133.76, 129.56, 127.49, 126.92, 115.31, 55.00, 41.52, 40.20. HRMS (ESI) calcd for $C_9H_9BrNO_2S$ m/z $[M+H]^+$: 273.9532; found: 273.9527.

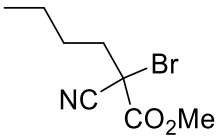


Methyl-2-bromo-2-cyano-5-phenylpentanoate (12a): method A, colorless oil; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 – 7.28 (m, 2H), 7.28 – 7.21 (m, 1H), 7.19 (dt, J = 7.9, 1.7 Hz, 2H), 3.90 (s, 3H), 2.73 (t, J =

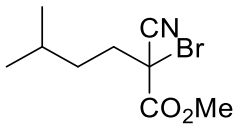
7.5 Hz, 2H), 2.44 – 2.21 (m, 2H), 2.02 (dddd, J = 16.2, 8.7, 4.9, 2.8 Hz, 1H), 1.92 – 1.71 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 164.73, 140.37, 128.65, 128.37, 126.41, 115.59, 54.84, 42.24, 39.37, 34.77, 27.80. HRMS (ESI) calcd for $C_{13}H_{15}BrNO_2$ m/z $[M+H]^+$: 296.0281; found 296.0287.



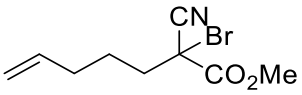
Methyl 2-bromo-2-cyanopropanoate (13a): method A, colorless oil; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.22; ^{1}H NMR (400 MHz, Chloroform-d) δ 3.92 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, Chloroform-d): δ 165.1, 116.6, 55.0, 36.3, 28.1; HRMS (ESI) calcd for $C_7H_5BrNO_2$ m/z $[M+H]^+$: 191.9655; found: 191.9660.



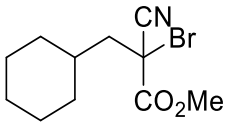
Methyl 2-bromo-2-cyanopentanoate (14a): method A, colorless oil; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.22 ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.98 – 3.84 (m, 3H), 2.42 – 2.13 (m, 2H), 1.77 – 1.54 (m, 1H), 1.51 – 1.35 (m, 3H), 0.93 (tdd, *J* = 8.5, 4.9, 3.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.81, 115.67, 54.76, 42.46, 39.75, 28.32, 21.96, 13.65.; HRMS (ESI) calcd for $C_8H_{13}BrNO_2$ m/z $[M+H]^+$: 234.0124; found: 234.0130.



Methyl 2-bromo-2-cyano-5-methylhexanoate (15a): method A, colorless oil; 82% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.22; ^{1}H NMR (400 MHz, Chloroform-d) δ 3.92 (s, 3H), 2.45 – 2.19 (m, 2H), 1.65 (dt, J = 13.2, 6.6 Hz, 1H), 1.60 – 1.50 (m, 1H), 1.43 – 1.22 (m, 1H), 0.94 (dd, J = 6.6, 1.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.97, 115.79, 54.85, 42.81, 38.35, 35.12, 27.85, 22.38, 22.32. HRMS (ESI) calcd for $C_9H_{15}BrNO_2$ m/z $[M+H]^+$: 248.0281; found 248.0276.

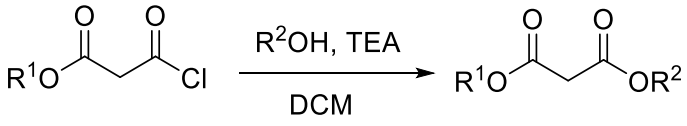


Methyl 2-bromo-2-cyanohept-6-enoate (16a): method A, colorless oil; 82% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.32; ^1H NMR (400 MHz, Chloroform-d) δ 5.76 (dd, J = 17.0, 10.2, 6.7, 1.4 Hz, 1H), 5.14 – 4.89 (m, 2H), 3.91 (d, J = 1.9 Hz, 3H), 2.40 – 2.21 (m, 2H), 2.19 – 2.05 (m, 2H), 1.85 – 1.68 (m, 1H), 1.68 – 1.47 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-d) δ 164.75, 136.75, 116.14, 115.61, 54.83, 42.33, 39.31, 32.58, 25.40. HRMS (ESI) calcd for $C_9H_{13}BrNO_2$ m/z $[M+H]^+$: 246.0124; found 246.0126.



Methyl 2-bromo-2-cyano-3-cyclohexylpropanoate (17a): method A, colorless oil; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.18; 87% yield; ^1H NMR (400 MHz, Chloroform-d) δ 3.91 (s, 3H), 2.47 – 2.10 (m, 2H), 1.87 – 1.61 (m, 6H), 1.42 – 0.91 (m, 5H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.39, 116.13, 54.86, 46.96, 41.45, 36.76, 33.70, 32.68, 26.04, 25.97. HRMS (ESI) calcd for $C_{11}H_{17}BrNO_2$ m/z $[M+H]^+$: 274.0437; found 274.0442.

4. General procedure for the synthesis of malonates



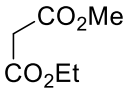
R^1 = Me, Et

R^1 = Et, *i*Pr, *t*Bu

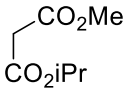
Dissolve alcohol (1.2 equiv.) into dry DCM, cooling down to 0 °C, then triethyl amine (1.2 equiv.) was added to the reaction mixture, followed by alkyl 3-chloro-3-oxopropanoate (1.0 equiv.) dropwise. After stirring for 30 min, the mixture was added water (20 mL) and then extracted with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered and concentrated.

The residue was purified by flash chromatography (hexane: ethyl acetate = 5:1 as the eluent) to get prochiral malonates. [2]

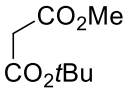
5. Characterization of malonate



Ethyl methyl malonate (18a): colorless oil; 89% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.40; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.13 (q, J = 7.1 Hz, 2H), 3.67 (d, J = 1.5 Hz, 3H), 3.30 (d, J = 1.4 Hz, 2H), 1.21 (td, J = 7.2, 1.5 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.00, 166.44, 61.46, 52.35, 41.30, 13.96. HRMS (ESI) calcd for $C_6H_{11}O_4$ m/z $[M+H]^+$: 147.0652; found: 147.0659.

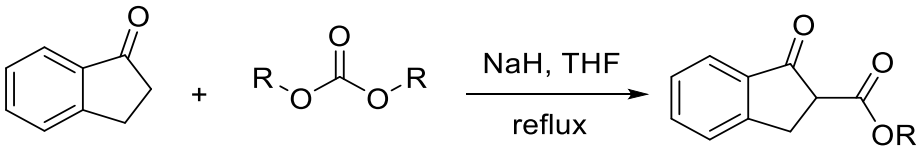


isopropyl methyl malonate (18b): colorless oil; 87% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.36; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.02 (pd, J = 6.3, 1.5 Hz, 1H), 3.71 (d, J = 1.6 Hz, 3H), 3.31 (d, J = 1.5 Hz, 2H), 1.22 (dd, J = 6.3, 1.5 Hz, 7H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.16, 166.03, 69.16, 52.38, 41.68, 21.61. HRMS (ESI) calcd for $C_7H_{13}O_4$ m/z $[M+H]^+$: 161.0808; found: 161.0801.



***tert*-butyl methyl malonate (18c):** colorless oil; 87% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.75 – 3.56 (m, 3H), 3.39 – 3.02 (m, 2H), 1.53 – 1.30 (m, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.41, 165.68, 82.02, 81.98, 52.26, 52.23, 42.60, 42.58, 27.87. HRMS (ESI) calcd for $C_8H_{15}O_4$ m/z $[M+H]^+$: 175.0965; found: 175.0968.

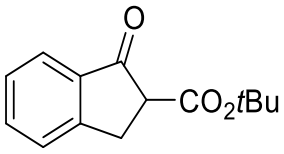
6. General procedure for alkyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate



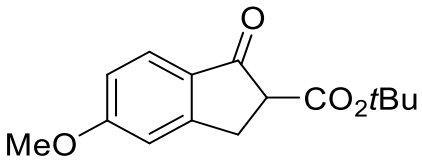
R = Me, Et, *t*Bu

The 2,3-dihydro-1H-inden-1-one (1.0 equiv.) and dimethyl carbonate or di-tert-butyl carbonate (10.0 equiv.) were dissolved in anhydrous THF under N_2 atomasphere, and then NaH (2.5 equiv.) was added slowly. The mixture was brought to reflux for 6 h and cooled to rt. The reaction was quenched with NH_4Cl (1 mL) and then water (10 mL) was added. Separate the organic phase and extract aqueous phase with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ethyl acetate = 5:1 as the eluent) to get the alkyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate.[3]

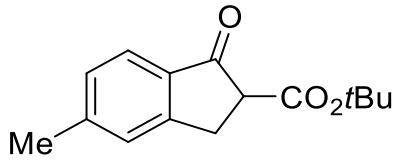
7. Characterization of alkyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate



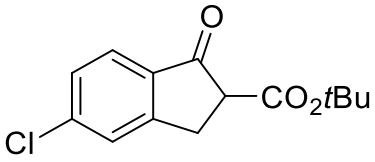
***tert*-butyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21c):** yellow oil; 75% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.60; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 7.7 Hz, 1H), 7.61 (td, *J* = 7.5, 1.3 Hz, 1H), 7.49 (dt, *J* = 7.6, 1.0 Hz, 1H), 7.42 – 7.35 (m, 1H), 3.62 (dd, *J* = 8.2, 4.0 Hz, 1H), 3.47 (d, *J* = 3.6 Hz, 1H), 3.38 – 3.27 (m, 1H), 1.49 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.36, 153.70, 135.52, 135.23, 127.70, 126.54, 124.60, 82.09, 54.41, 30.37, 28.53, 28.06. HRMS (ESI) calcd for $C_{14}H_{17}O_3$ m/z $[M+H]^+$: 233.1172; found: 233.1180.



***tert*-butyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21d)**: yellow solid; mp: 117-119; 76% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.45; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 9.1 Hz, 1H), 6.99 – 6.83 (m, 2H), 3.88 (s, 3H), 3.59 (dd, *J* = 8.1, 3.9 Hz, 1H), 3.43 (dd, *J* = 17.2, 3.9 Hz, 1H), 3.25 (dd, *J* = 17.2, 8.2 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 198.10, 168.67, 165.75, 156.80, 128.72, 126.24, 115.82, 109.57, 81.93, 55.73, 54.60, 30.37, 28.06. HRMS (ESI) calcd for $C_{15}H_{19}O_4$ m/z $[M+H]^+$: 263.1278; found: 263.1270.



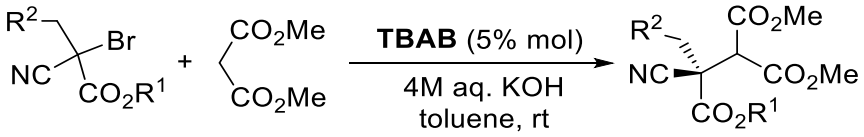
***tert*-butyl 5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21e)**: yellow solid; mp: 110-112 ºC; 70% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.50; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 7.9 Hz, 1H), 7.27 (d, *J* = 6.9 Hz, 1H), 7.18 (d, *J* = 8.1 Hz, 1H), 3.59 (dd, *J* = 8.2, 4.0 Hz, 1H), 3.43 (dd, *J* = 17.0, 4.1 Hz, 1H), 3.26 (dd, *J* = 17.2, 8.2 Hz, 1H), 2.43 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 199.49, 168.56, 154.24, 146.56, 133.26, 128.98, 126.85, 124.40, 81.95, 54.59, 30.21, 28.05, 22.12. HRMS (ESI) calcd for $C_{15}H_{19}O_3$ m/z $[M+H]^+$: 247.1329; found: 247.1334.



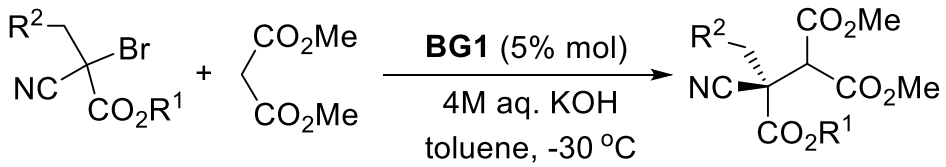
***tert*-butyl 5-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21f):** brown oil; 75% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.45; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 8.2 Hz, 1H), 7.50 (d, *J* = 10.4 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 1H), 3.63 (dd, *J* = 8.2, 3.9 Hz, 1H), 3.54 – 3.42 (m, 1H), 3.30 (dd, *J* = 17.4, 8.3 Hz, 1H), 1.48 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 198.51, 168.02, 155.22, 141.95, 134.13, 128.68, 126.87, 125.77, 82.43, 54.60, 30.20, 28.62, 28.15. HRMS (ESI) calcd for $C_{14}H_{16}ClO_3$ m/z $[M+H]^+$: 267.0782; found: 267.0781.

8. General procedure for the synthesis of isolated all-carbon quaternary stereocenters



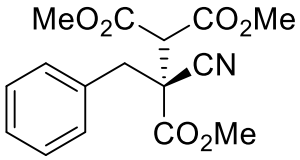
Method A: general procedure for the synthesis of racemic isolated all-carbon quaternary stereocenters: the bromide (1.0 equiv.), dimethyl carbonate (1.2 equiv.) and TBAB (5% mol) were dissolved in Toluene, and then 4M aq. KOH was added slowly. The mixture was stirred at room temperature for 2 h. The reaction was quenched with NH_4Cl (1 mL) and then water (10 mL) was added. Separate the organic phase and extract aqueous phase with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ether = 5:1 as the eluent) to get the racemic isolated all-carbon quaternary stereocenters.



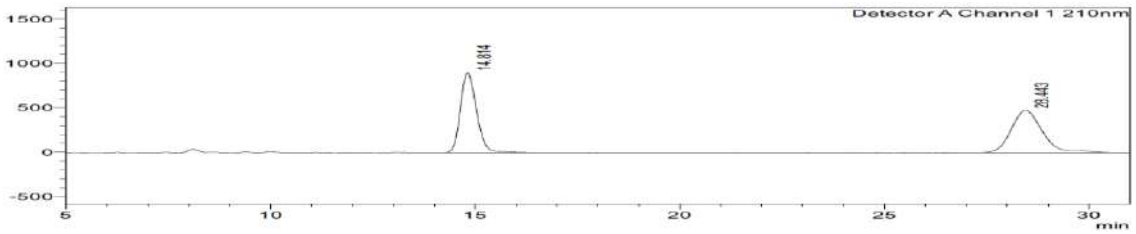
Method B: general procedure for the synthesis of chiral isolated all-carbon quaternary stereocenters: the bromide (1.0 equiv.), dimethyl carbonate (1.2 equiv.) and **BG1** (5% mol) were dissolved in Toluene, cooling down the reaction mixture to –30 °C, and then 4M aq. KOH was added by a micro syringe. The mixture was stirred at -30 °C for 2-3 days until the completion. TLC monitored the process. The reaction was quenched with NH_4Cl (1 mL) and then water (10 mL) was added. Separate the organic phase and extract aqueous phase with DCM. The combined organic phase was washed

with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ether = 5:1 as the eluent) to get the chiral isolated all-carbon quaternary stereocenters.

9. Characterization of isolated all-carbon quaternary stereocenters

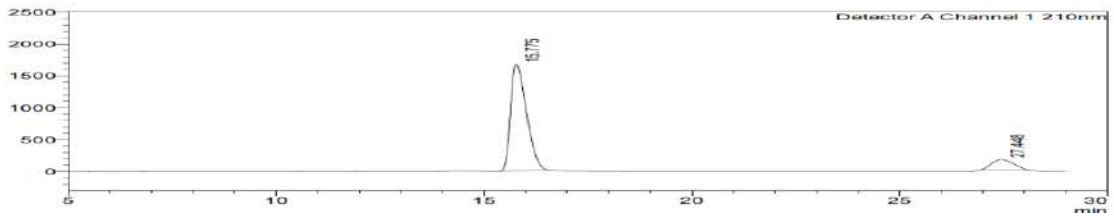


Trimethyl (*R*)-2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2a): Colorless oil; 85% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.25; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 4.9, 1.6 Hz, 3H), 7.30 – 7.22 (m, 2H), 4.17 (s, 1H), 3.91 (s, 3H), 3.80 (d, *J* = 9.1 Hz, 3H), 3.62 (s, 3H), 3.32 (d, *J* = 13.4 Hz, 1H), 3.19 (d, *J* = 13.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.52, 166.21, 165.76, 132.63, 129.91, 128.68, 128.36, 56.19, 53.67, 53.46, 50.24, 41.62. HRMS (ESI) calcd for $C_{16}H_{18}NO_6$ m/z $[M+H]^+$: 320.1129; found: 320.1135; $[a]_D^{22}$= +22.2 (c 0.87, $CHCl_3$); HPLC analysis: Chiralcel OD-H (Hex/IPA = 90/10, 1.0 mL/min, 210 nm, 22°C), 15.7 (major), 27.4 min, 75% ee.



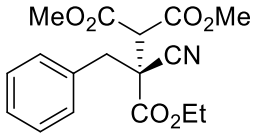
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	14.814	24315560	49.386
2	28.443	24919976	50.614
Total		49235536	100.000

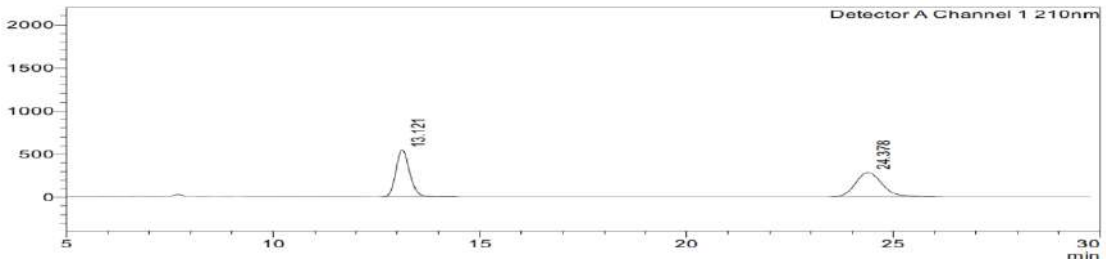


Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	15.775	44361516	87.561
2	27.448	6301907	12.439
Total		50663423	100.000

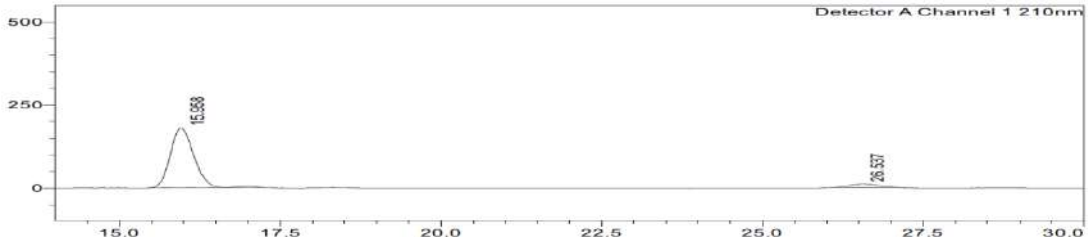


2-ethyl 1,1-dimethyl (*R*)-2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2b): Colorless oil; 84% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.25; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35 (dd, *J* = 4.9, 1.6 Hz, 3H), 7.30 – 7.22 (m, 2H), 4.17 (s, 1H), 3.91 (s, 3H), 3.80 (d, *J* = 9.1 Hz, 3H), 3.62 (s, 3H), 3.32 (d, *J* = 13.4 Hz, 1H), 3.19 (d, *J* = 13.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.52, 166.21, 165.76, 132.63, 129.91, 128.68, 128.36, 56.19, 53.67, 53.46, 50.24, 41.62. HRMS (ESI) calcd for $C_{17}H_{20}NO_6$ m/z $[M+H]^+$: 334.1285; found: 334.1298; $[\alpha]_D^{22}$= +44.0 (c 0.64, $CHCl_3$); HPLC analysis: Chiralcel OD-H (Hex/IPA = 90/10, 1.0 mL/min, 210 nm, 22°C), 15.9 (major), 26.5 min, 86% ee.



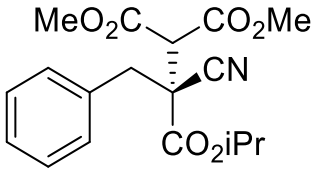
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	13.121	12540538	49.591
2	24.378	12747161	50.409
Total		25287700	100.000



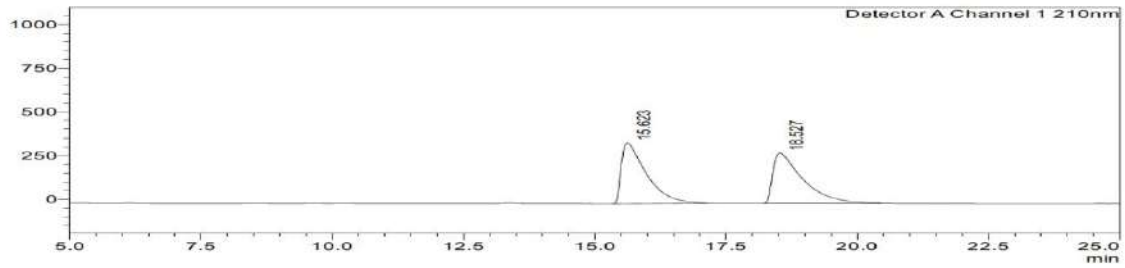
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	15.958	4639621	93.462
2	26.537	324574	6.538
Total		4964195	100.000



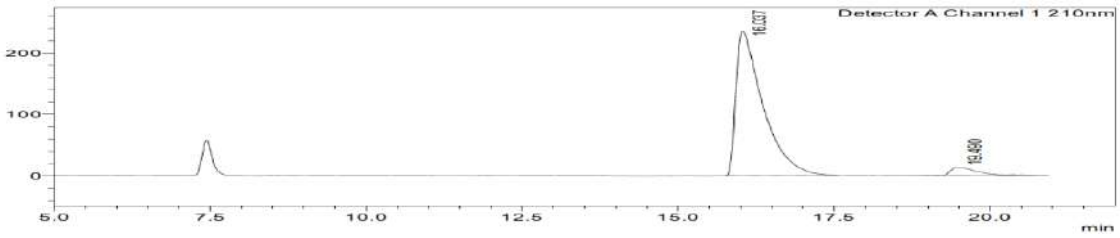
2-isopropyl 1,1-dimethyl (*R*)-2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2c)

Colorless oil; 65% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.25; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41 – 7.20 (m, 6H), 4.98 – 4.72 (m, 1H), 4.17 (s, 1H), 3.91 (s, 3H), 3.81 (s, 3H), 3.32 (d, J = 13.4 Hz, 1H), 3.16 (d, J = 13.4 Hz, 1H), 1.22 (d, J = 6.2 Hz, 3H), 0.89 (d, J = 6.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.29, 166.13, 165.92, 132.81, 130.15, 128.61, 128.19, 116.76, 71.55, 56.42, 53.37, 53.31, 50.17, 41.54, 21.20, 20.92 HRMS (ESI) calcd for $C_{18}H_{22}NO_6$ m/z $[M+H]^+$: 348.1442; found: 348.1442; $[a]_D^{22}$= +9.2 (c 0.51, $CHCl_3$); HPLC analysis: Chiralcel OD-H (Hex/IPA = 90/10, 1.0 mL/min, 210 nm, 22°C), 16.0 (major), 19.5 min, 89% ee.



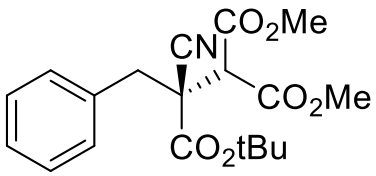
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	15.623	11463496	50.079
2	18.527	11427252	49.921
Total		22890748	100.000

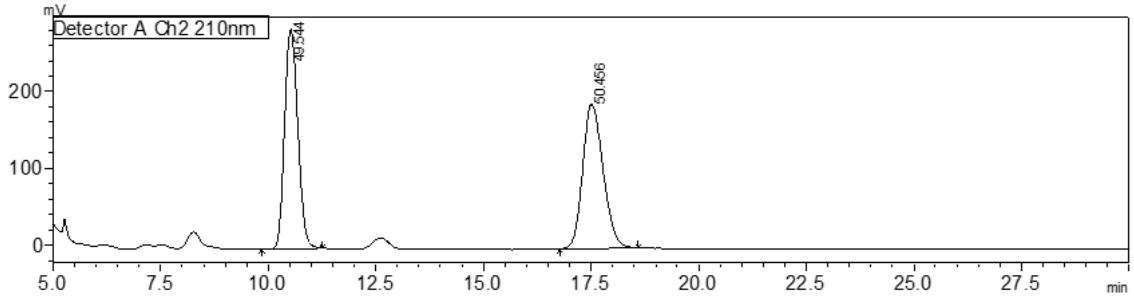


Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	16.037	7112246	94.482
2	19.490	415364	5.518
Total		7527611	100.000

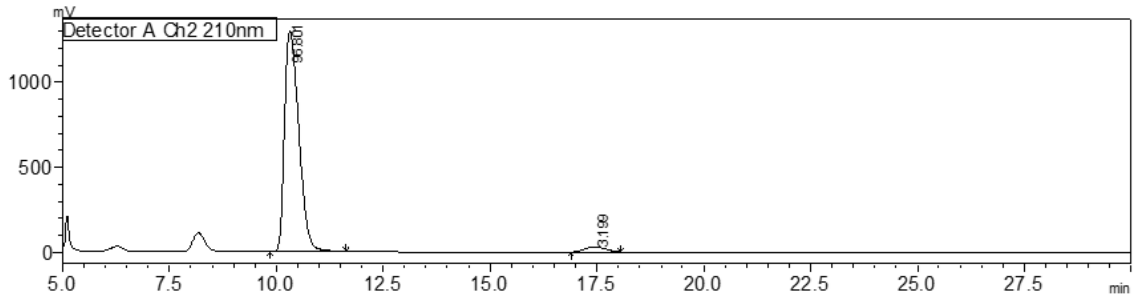


2-(tert-butyl) 1,1-dimethyl (*R*)−2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2d): Colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.28; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (t, *J* = 1.2 Hz, 5H), 4.08 (s, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.31 (d, *J* = 13.5 Hz, 1H), 3.11 (d, *J* = 13.5 Hz, 1H), 1.28 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.33, 166.20, 165.52, 133.10, 130.61, 128.65, 128.25, 127.09, 117.31, 85.18, 56.66, 53.42, 53.33, 50.45, 41.61, 27.58. HRMS (ESI) calcd for $C_{19}H_{24}NO_6$ m/z $[M+H]^+$: 362.1598; found: 362.1590; $[a]_D^{22}$= +22.2 (c 0.17, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 90/10, 1.0 mL/min, 210 nm, 22°C), 10.3 (major), 17.4 min, 94% ee.



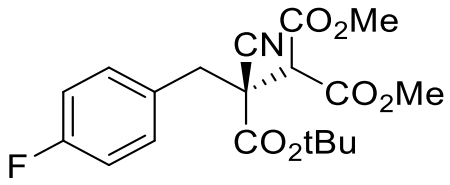
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	10.521	6097418	49.544
2	17.514	6209682	50.456
Total		12307100	100.000

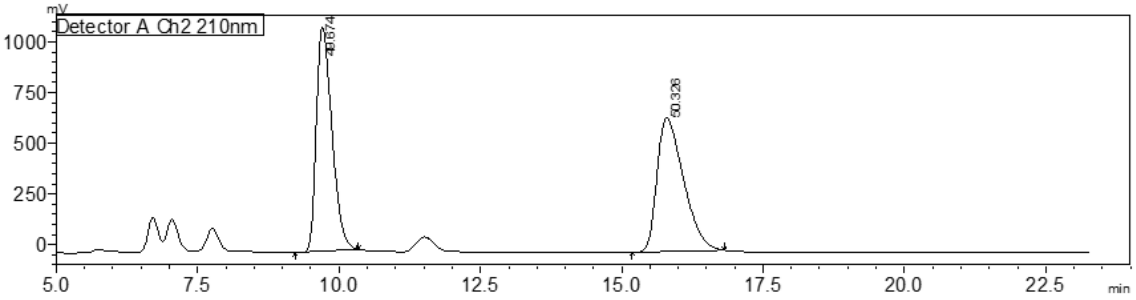


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	10.317	30071637	96.801
2	17.452	993844	3.199
Total		31065482	100.000

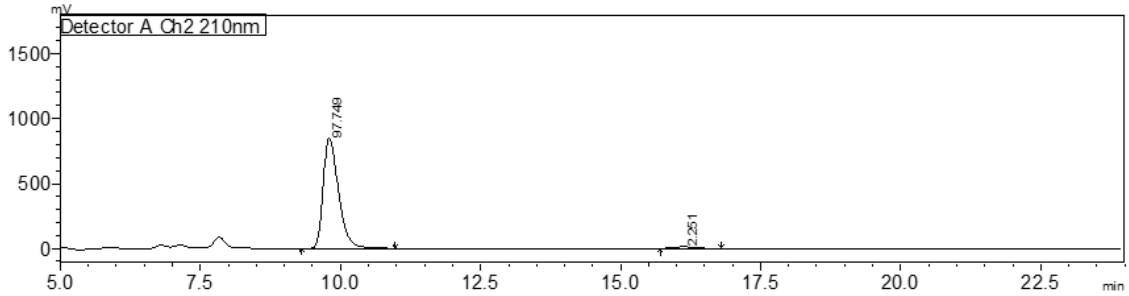


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(4-fluorophenyl)propane-1,1,2-tricarboxylate (2e): Colorless oil; 75% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (d, *J* = 5.3 Hz, 2H), 7.00 (d, *J* = 17.4 Hz, 2H), 4.04 (s, 1H), 3.86 (s, 3H), 3.78 (s, 3H), 3.25 (s, 1H), 3.08 (d, *J* = 13.4 Hz, 1H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 166.13, 165.46, 132.29, 132.21, 128.88, 117.14, 115.68, 115.46, 56.56, 53.51, 53.42, 40.67, 27.59. HRMS (ESI) calcd for $C_{19}H_{23}FNO_6$ m/z $[M+H]^+$: 380.1504; found: 380.1509; $[\alpha]_D^{22}$= +20.1 (c 0.23, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm, 22°C), 9.7 (major), 16.1 min, 96 % ee.



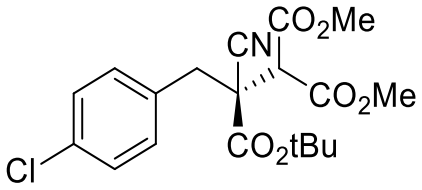
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	9.706	21258069	49.674
2	15.796	21537497	50.326
Total		42795565	100.000

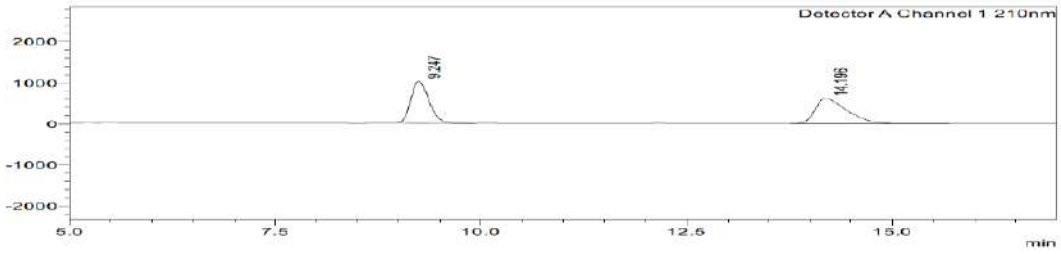


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	9.799	16214202	97.749
2	16.134	373406	2.251
Total		16587608	100.000

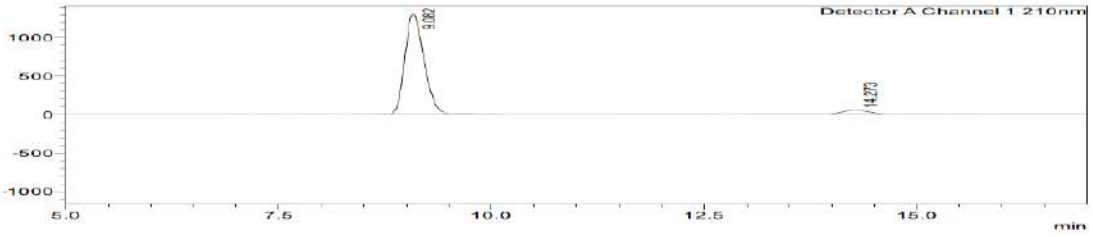


2-(tert-butyl) 1,1-dimethyl 3-(4-chlorophenyl)- (*R*)-2-cyanopropane-1,1,2-tricarboxylate (2f): Colorless oil; 75% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.35; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 2.1 Hz, 4H), 4.08 (s, 1H), 3.87 (s, 3H), 3.78 (s, 3H), 3.31 (d, *J* = 13.5 Hz, 1H), 3.11 (d, *J* = 13.5 Hz, 1H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.21, 166.08, 165.39, 132.92, 130.46, 128.53, 128.14, 117.20, 85.06, 77.38, 77.06, 76.74, 56.51, 53.35, 53.26, 50.29, 41.45, 27.44. HRMS (ESI) calcd for $C_{19}H_{23}ClNO_6$ m/z $[M+H]^+$: 396.1208; found: 396.1214; $[a]_D^{22}$= +16.1 (c 0.63, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm, 22°C), 9.0 (major), 14.2 min, 90 % ee.



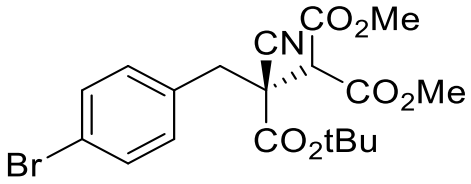
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	9.247	15584213	49.633
2	14.196	15814432	50.367
Total		31398645	100.000



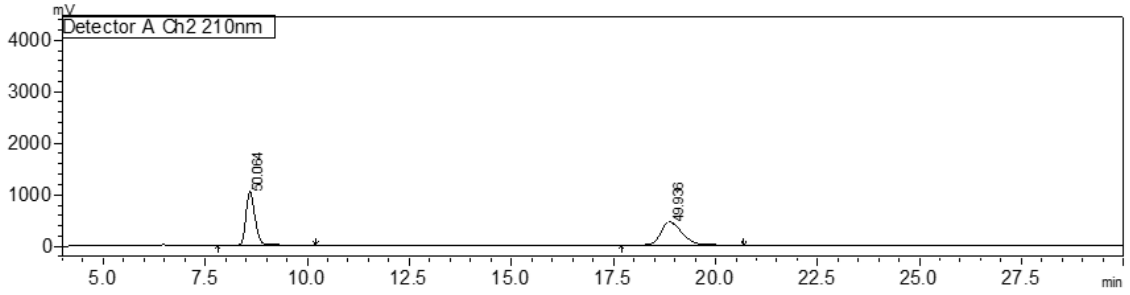
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	9.082	20215631	94.956
2	14.273	1073741	5.044
Total		21289373	100.000



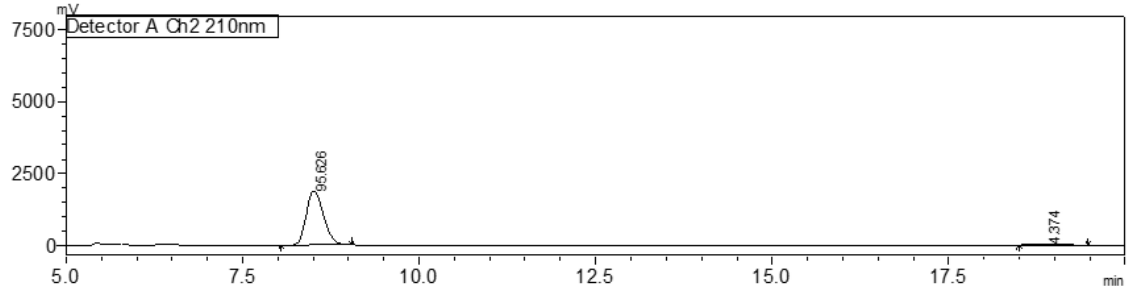
2-(tert-butyl) 1,1-dimethyl 3-(4-bromophenyl)- (*R*)-2-cyanopropane-1,1,2-tricarboxylate (2g): Colorless oil; 77% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.21; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.40 (m, 2H), 7.24 – 7.16 (m, 2H), 4.04 (s, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.26 (d, *J* = 13.6 Hz, 1H), 3.07 (d, *J* = 13.6 Hz, 1H), 1.31 (s, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.04, 165.95, 165.22, 132.14, 132.01, 131.67, 122.39, 116.89, 85.38, 56.42, 53.32, 53.23, 50.18, 40.72, 27.50. HRMS (ESI) calcd for $C_{19}H_{23}BrNO_6$ m/z $[M+H]^+$: 440.0703; found: 440.0710; $[a]_D^{22}$= +13.8 (c 0.15, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm,

22°C), 8.5 (major), 18.8 min, 92 % ee.



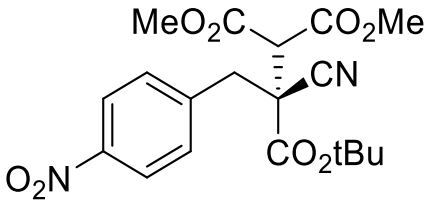
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	8.593	15751416	50.064
2	18.880	15711375	49.936
Total		31462791	100.000



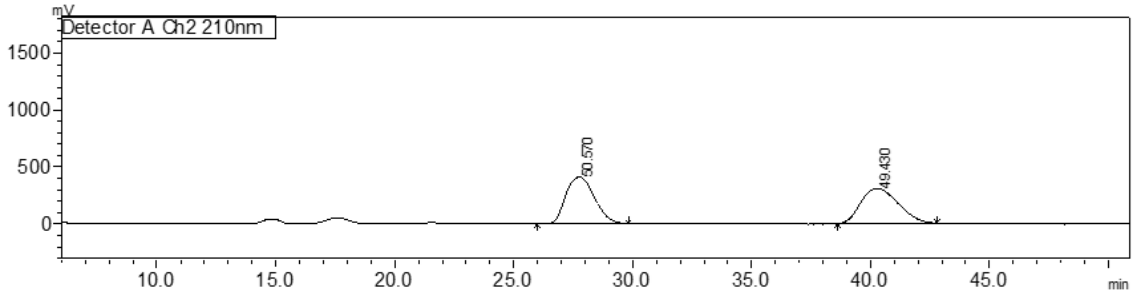
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	8.507	32146937	95.626
2	18.885	1470589	4.374
Total		33617526	100.000



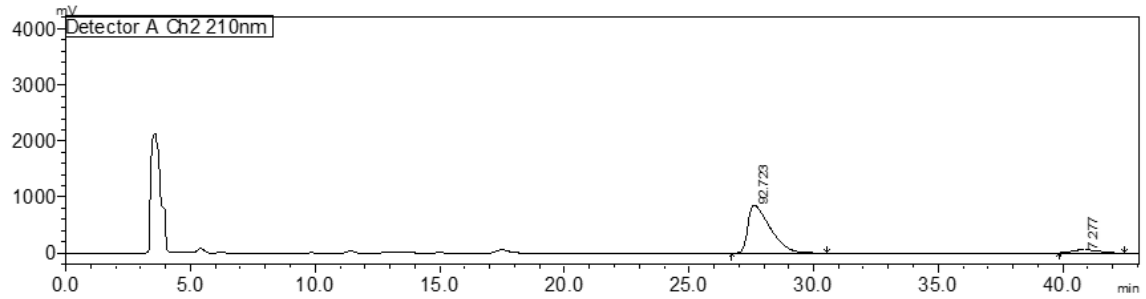
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(4-nitrophenyl)propane-1,1,2-tricarboxylate (2h): Colorless oil; 77% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.18; ^1H NMR (400 MHz, Chloroform-*d*) δ 8.25 (d, *J* = 8.6 Hz, 2H), 7.73 – 7.50 (m, 2H), 4.11 (s, 1H), 3.94 (s, 3H), 3.85 (s, 3H), 3.47 (d, *J* = 13.5 Hz, 1H), 3.28 (d, *J* = 13.4 Hz, 1H), 1.36 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.90, 165.85, 164.97, 147.89,

140.44, 131.55, 123.62, 116.52, 85.89, 76.73, 56.46, 53.53, 53.44, 50.03, 40.64, 27.52. HRMS (ESI) calcd for $C_{19}H_{23}N_2O_8$ m/z $[M+H]^+$: 407.1449; found: 407.1452; $[\alpha]_D^{22}$= +14.5 (c 0.14, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 90/10, 1.0 mL/min, 210 nm, 22℃), 27.6 (major), 40.8 min, 88% ee.



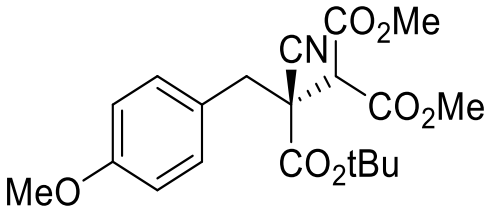
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	27.766	34167468	50.570
2	40.311	33396795	49.430
Total		67564263	100.000



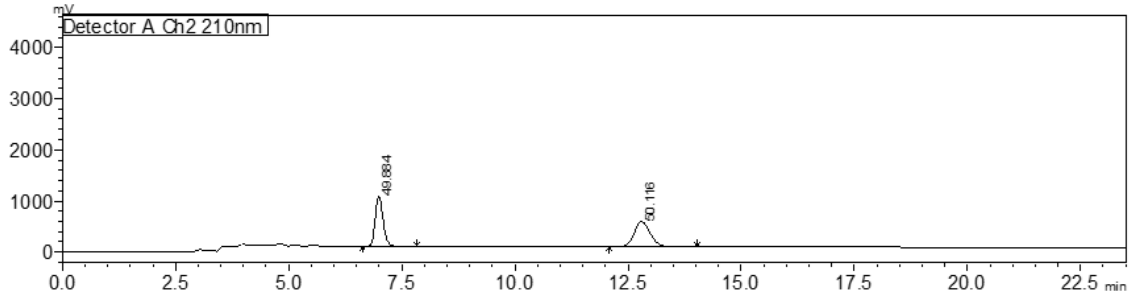
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	27.622	53149406	93.737
2	40.852	3550878	6.263
Total		56700285	100.000



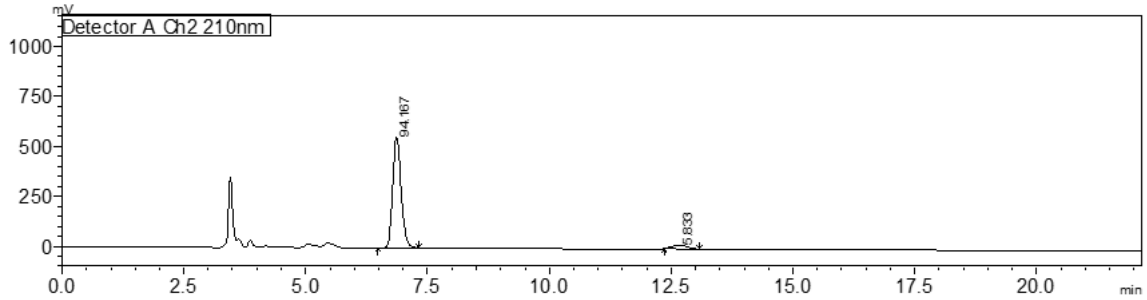
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(4-methoxyphenyl)propane-1,1,2-

tricarboxylate (2i): Colorless oil; 77% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.18; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 – 7.20 (m, 2H), 6.96 – 6.76 (m, 2H), 4.04 (s, 1H), 3.87 (s, 3H), 3.84 – 3.75 (m, 7H), 3.25 (d, *J* = 13.7 Hz, 1H), 3.08 (d, *J* = 13.7 Hz, 1H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.37, 166.23, 165.64, 159.70, 131.71, 128.79, 125.10, 117.40, 114.18, 114.08, 85.11, 76.84, 56.46, 55.45, 53.40, 53.31, 50.69, 40.88, 27.66. HRMS (ESI) calcd for $C_{20}H_{26}NO_7$ m/z $[M+H]^+$: 392.1704; found: 392.1709; $[\alpha]_D^{22}$= +12.2 (c 0.27, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 96/4, 1.0 mL/min, 210 nm, 22°C), 6.8 (major), 12.6 min, 90% ee.



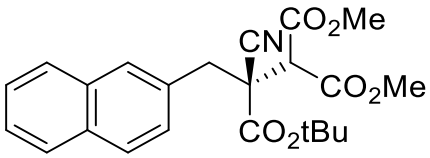
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	6.988	11859973	49.884
2	12.801	11915346	50.116
Total		23775319	100.000

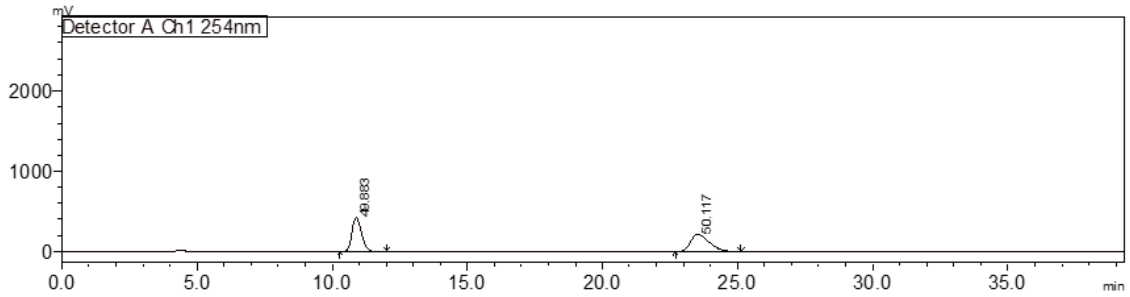


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	6.865	6680758	95.271
2	12.655	331592	4.729
Total		7012350	100.000

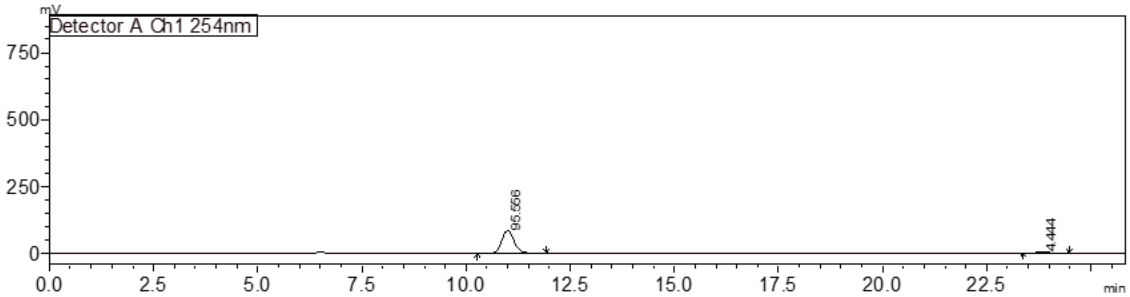


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(naphthalen-2-yl)propane-1,1,2-tricarboxylate (2j): Colorless oil; 72% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.31; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.92 – 7.70 (m, 4H), 7.49 (td, *J* = 7.3, 6.8, 2.6 Hz, 3H), 4.13 (s, 1H), 3.89 (s, 3H), 3.79 (s, 3H), 3.48 (d, *J* = 13.5 Hz, 1H), 3.31 (d, *J* = 13.6 Hz, 1H), 1.20 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.58, 166.34, 166.23, 165.58, 133.33, 133.11, 130.65, 129.81, 128.33, 128.12, 127.97, 127.80, 126.45, 126.38, 117.32, 85.23, 76.84, 56.67, 53.45, 53.34, 53.24, 51.27, 50.57, 41.76, 27.54. HRMS (ESI) calcd for $C_{23}H_{26}NO_6$ m/z $[M+H]^+$: 412.1755; found: 412.1753; $[\alpha]_D^{22}$= +20.9 (c 0.25, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 254 nm, 22°C), 10.9 (major), 23.8 min, 92% ee.



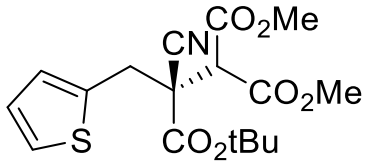
Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	10.887	10227476	49.883
2	23.529	10275369	50.117
Total		20502845	100.000

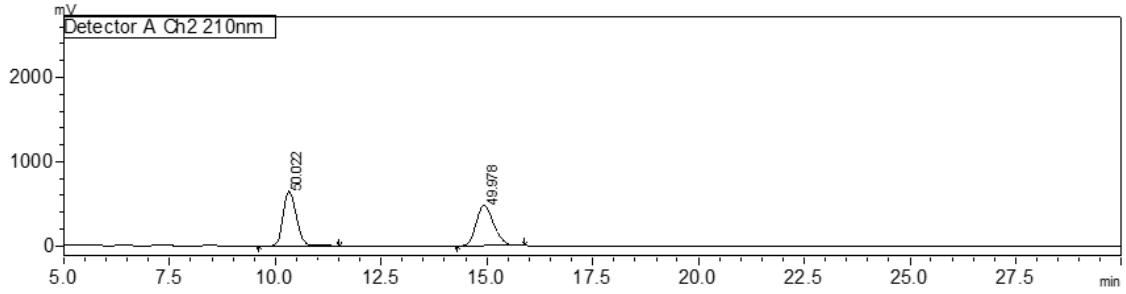


Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	10.996	1740986	95.556
2	23.845	80971	4.444
Total		1821957	100.000

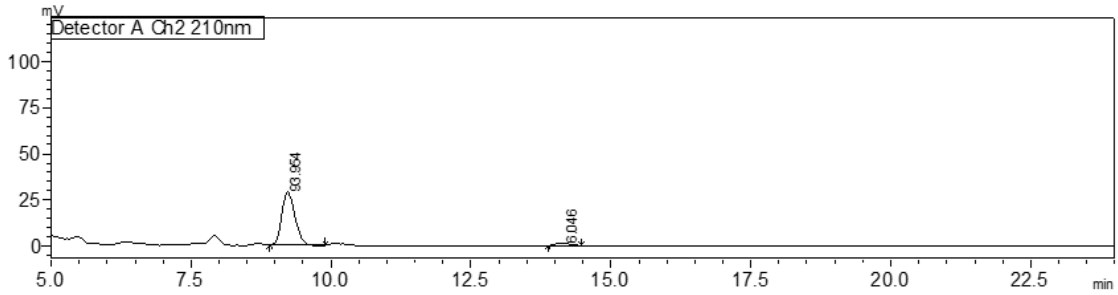


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(thiophen-2-yl)propane-1,1,2-tricarboxylate (2k): Colorless oil; 70% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.21 (m, 1H), 7.02 (d, *J* = 3.1 Hz, 1H), 6.99 – 6.91 (m, 1H), 4.03 (s, 1H), 3.85 (s, 3H), 3.78 (s, 3H), 3.56 (d, *J* = 14.7 Hz, 1H), 3.44 (d, *J* = 14.7 Hz, 1H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 166.39, 166.31, 165.35, 134.17, 129.44, 127.41, 126.46, 117.53, 85.72, 77.80, 55.97, 53.80, 53.74, 53.68, 36.16, 27.92. HRMS (ESI) calcd for $C_{17}H_{22}NO_6S$ m/z $[M+H]^+$: 368.1162; found: 368.1172; $[a]_D^{22}$= +11.1 (c 0.32, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 90/10, 1.0 mL/min, 210 nm, 22°C), 9.2 (major), 14.1 min, 88% ee.



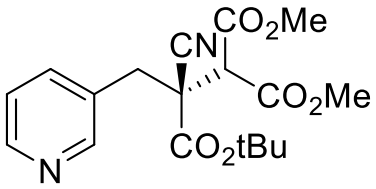
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	10.323	13880505	50.022
2	14.929	13868394	49.978
Total		27748899	100.000

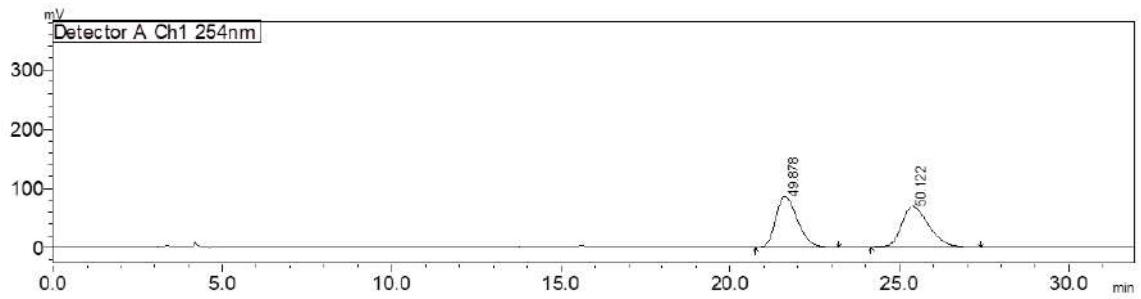


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	9.222	466804	93.954
2	14.160	30037	6.046
Total		496841	100.000

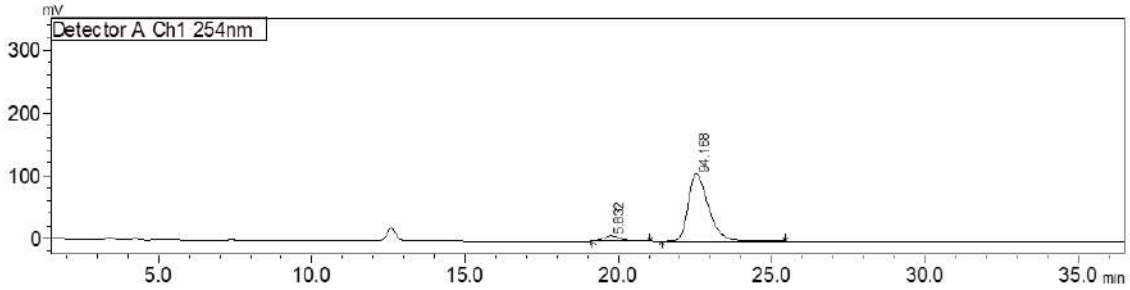


2-(*tert*-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(pyridin-3-yl)propane-1,1,2-tricarboxylate (2l): Colorless oil; 67% yield; TLC (Hexane:Et_2O, 50:50 v/v): R_f = 0.50; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.63 (dd, J = 4.9, 1.6 Hz, 1H), 8.52 (d, J = 2.2 Hz, 1H), 7.85 (d, J = 7.9 Hz, 1H), 7.38 – 7.32 (m, 1H), 4.12 (s, 1H), 3.93 (s, 3H), 3.84 (s, 3H), 3.36 (d, J = 13.7 Hz, 1H), 3.18 (d, J = 13.7 Hz, 1H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.01, 165.93, 165.09, 151.24, 149.61, 137.81, 128.93, 123.41, 116.72, 85.73, 77.37, 77.05, 76.73, 56.43, 53.47, 53.38, 50.15, 38.54, 27.76, 27.44. HRMS (ESI) calcd for $C_{18}H_{23}N_2O_6$ m/z $[M+H]^+$: 363.1551; found: 363.1561; $[\alpha]_D^{22}$= +15.1 (c 0.37, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 70/30, 1.0 mL/min, 254 nm, 22°C), 19.7 min，22.5 (major), 88% ee.



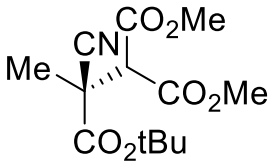
Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	21.618	3841800	49.878
2	25.394	3860563	50.122
Total		7702363	100.000

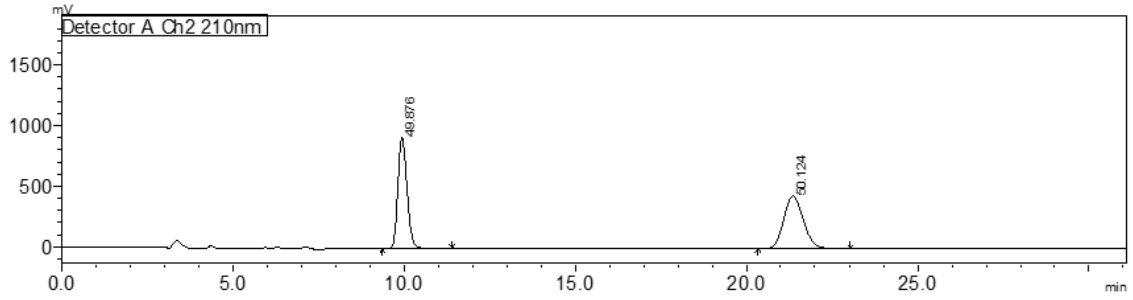


Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	19.744	303004	5.832
2	22.530	4892667	94.168
Total		5195672	100.000

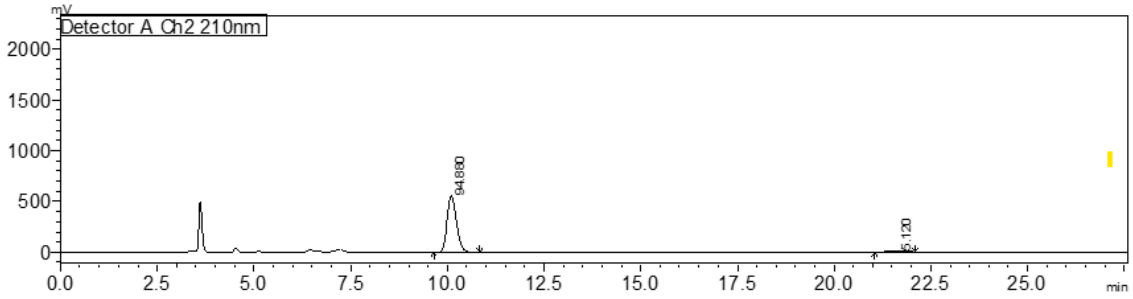


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyanopropane-1,1,2-tricarboxylate (2m): Colorless oil; 78% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.34; ^1H NMR (400 MHz, Chloroform-*d*) δ 3.98 (s, 1H), 3.81 (d, *J* = 13.6 Hz, 7H), 1.68 (s, 3H). ^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 166.74, 166.41, 166.04, 117.92, 85.08, 76.84, 56.52, 53.57, 53.36, 53.34, 53.28, 27.79, 27.70, 22.41. HRMS (ESI) calcd for $C_{13}H_{20}NO_6$ m/z $[M+H]^+$: 286.1285; found: 286.1289; $[\alpha]_D^{22}$= +21.1 (c 0.24, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm, 22°C), 10.1 (major), 21.6 min, 90% ee.



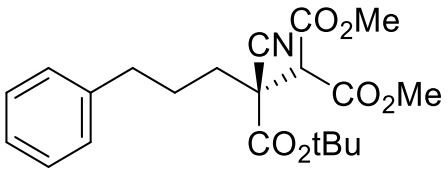
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	9.935	17050878	49.876
2	21.353	17135692	50.124
Total		34186570	100.000



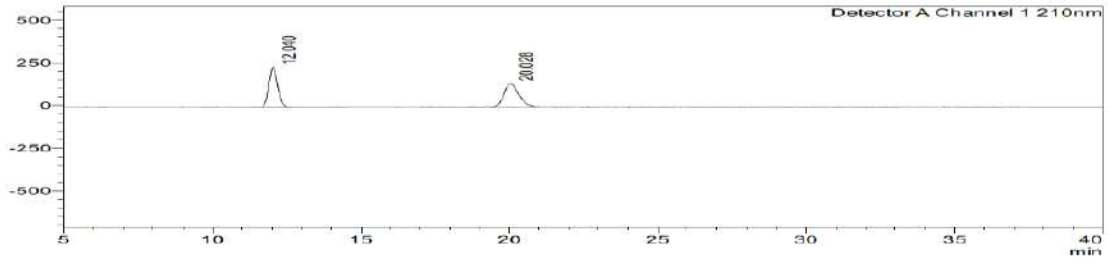
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	10.101	9421203	94.880
2	21.653	508419	5.120
Total		9929622	100.000



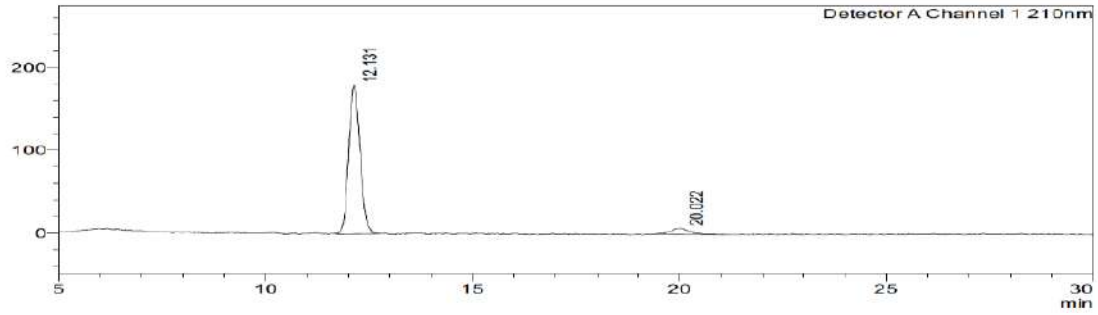
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-5-phenylpentane-1,1,2-tricarboxylate (2n): Colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.35; $CDCl_3$)； ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.26 (m, 2H), 7.20 (d, *J* = 7.3 Hz, 1H), 7.17 – 7.06 (m, 2H), 3.97 (s, 1H), 3.78 (d, *J* = 4.2 Hz, 6H), 2.64 (q, *J* = 7.6 Hz, 2H), 2.03 – 1.81 (m, 3H), 1.79 – 1.63 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (101 MHz, δ 166.36, 166.06, 140.84, 128.66, 128.48, 126.35, 117.18, 85.19, 76.84, 56.34, 53.29, 49.18, 35.46, 35.26, 27.81, 26.38. HRMS (ESI) calcd for $C_{21}H_{28}NO_6$ m/z $[M+H]^+$: 390.1911; found: 390.1908;

$[\alpha]_D^{22}$= +`0.8 (c 0.37, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm, 22°C), 12.1 (major), 20.0 min, 88% ee.



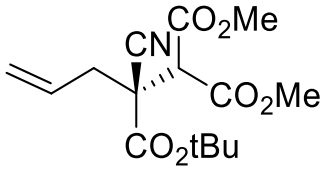
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	12.040	4726851	49.986
2	20.028	4729580	50.014
Total		9456431	100.000



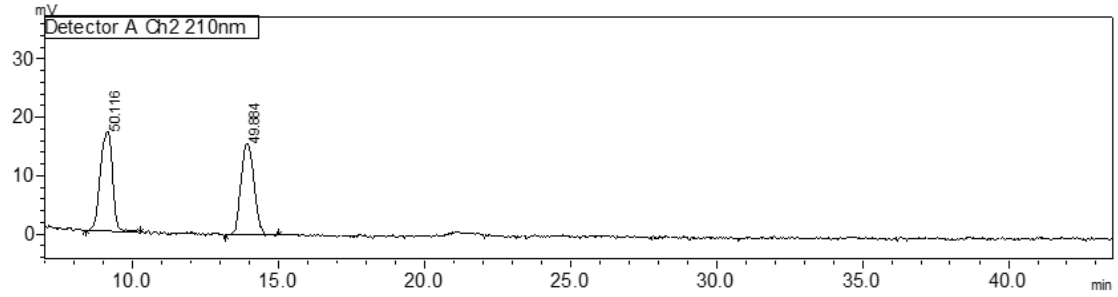
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	12.131	3457004	94.108
2	20.022	216452	5.892
Total		3673456	100.000



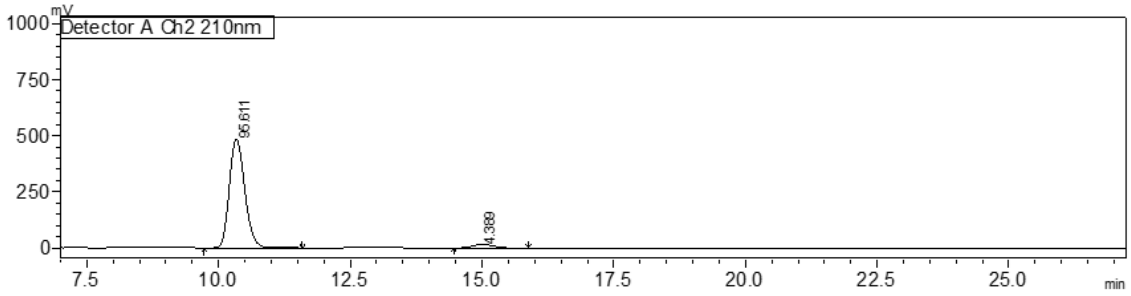
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyanopent-4-ene-1,1,2-tricarboxylate (2o): Colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.28; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.97 – 5.67 (m, 1H), 5.50 – 5.13 (m, 2H), 3.99 (s, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 2.76 (d, *J* = 14.1 Hz, 1H), 2.65 (d, *J* = 9.6 Hz, 1H). ^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 166.30, 165.99, 165.50, 129.54, 121.60, 116.88, 85.28, 55.53,

53.31, 48.75, 40.14, 27.78, 27.75. HRMS (ESI) calcd for $C_{15}H_{22}NO_6$ m/z $[M+H]^+$: 312.1442; found: 312.1432; $[\alpha]_D^{22}$= +20.2 (c 0.32, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 96/4, 1.0 mL/min, 210 nm, 22°C), 10.3 (major), 14.9 min, 92% ee.



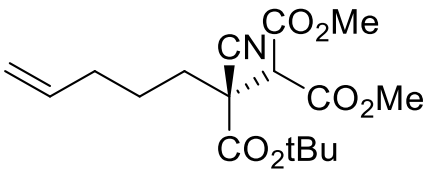
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	9.158	494045	50.116
2	13.920	491752	49.884
Total		985797	100.000



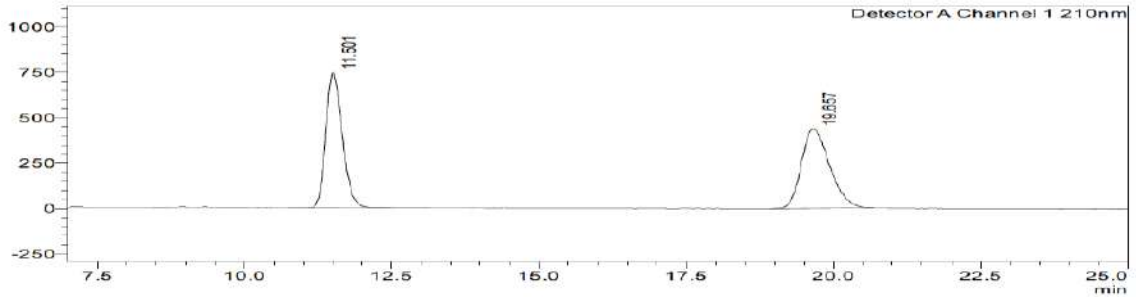
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	10.339	9918349	95.611
2	14.992	455267	4.389
Total		10373616	100.000



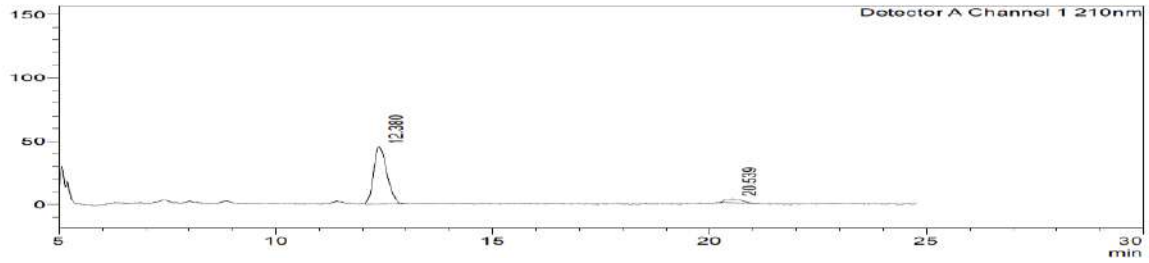
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyanohept-6-ene-1,1,2-tricarboxylate (2p): Colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.37; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.77 (d, *J* = 7.0 Hz, 1H), 5.15 – 4.90 (m, 2H), 3.99 (s, 1H), 3.83 (s, 3H), 3.78 (s, 3H), 2.16 – 2.00 (m, 2H), 2.00 – 1.82 (m, 2H), 1.51 (d, *J* = 11.3 Hz, 10H).

^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 176.08, 172.24, 167.02, 164.64, 150.90, 146.70, 143.62, 123.22, 122.90, 122.58, 114.87, 84.16, 82.84, 62.91, 33.98, 33.90, 33.69. HRMS (ESI) calcd for $C_{17}H_{26}NO_6$ m/z $[M+H]^+$: 340.1755; found: 340.1759; $[\alpha]_D^{22}$= +11.4 (c 0.17, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm, 22°C), 12.3 (major), 19.6 min, 86% ee.



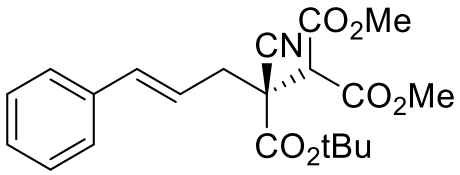
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	11.501	14689522	50.148
2	19.657	14602973	49.852
Total		29292495	100.000



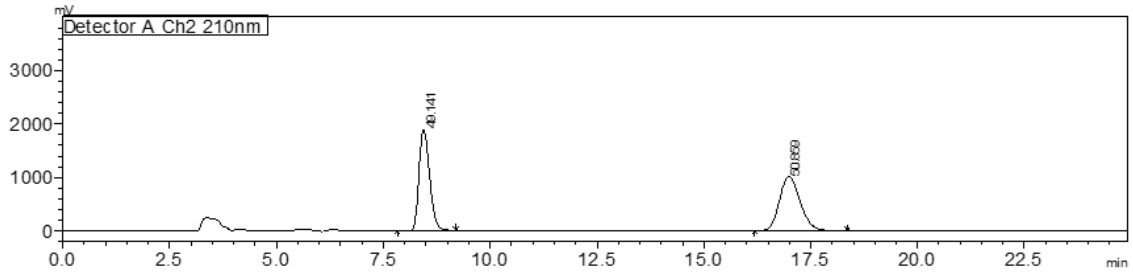
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	12.380	962495	92.992
2	20.539	72533	7.008
Total		1035027	100.000



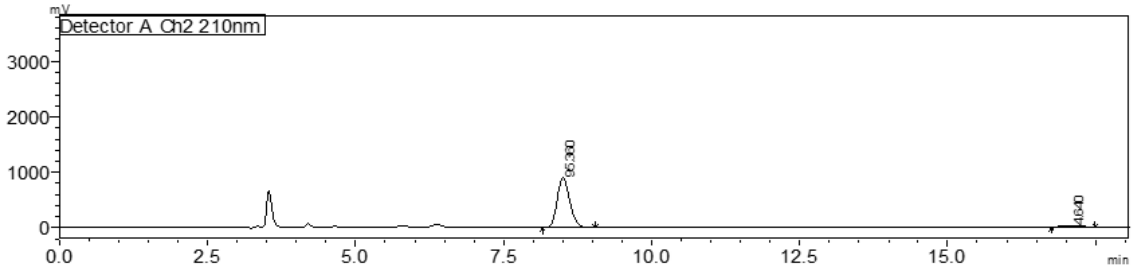
2-(tert-butyl) 1,1-dimethyl (*R*,*E*)-2-cyano-5-phenylpent-4-ene-1,1,2-tricarboxylate (2q): Colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400

MHz, Chloroform-*d*) δ 7.27 (s, 6H), 6.52 (d, *J* = 15.7 Hz, 1H), 6.29 – 6.06 (m, 1H), 4.06 (s, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 2.93 (d, *J* = 14.3 Hz, 1H), 2.88 – 2.70 (m, 1H), 1.45 (s, 9H). ^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 166.02, 165.63, 165.63, 136.12, 128.16, 120.60, 117.01, 76.78, 55.65, 53.39, 53.34, 49.14, 39.60, 27.74. HRMS (ESI) calcd for $C_{21}H_{26}NO_6$ m/z $[M+H]^+$: 388.1755; found: 388.1759; $[\alpha]_D^{22}$= +18.2 (c 0.25, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 96/4, 1.0 mL/min, 210 nm, 22°C), 8.5 (major), 17.0 min, 90% ee.



Detector A Channel 2 210nm

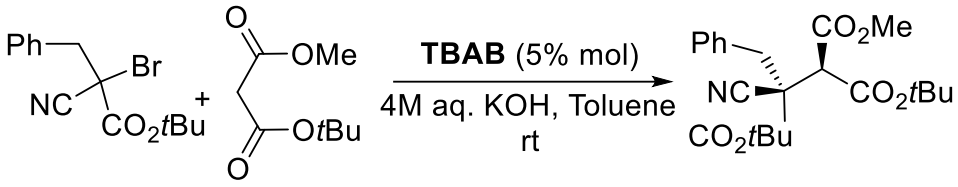
Peak#	Ret. Time	Area	Area%
1	8.441	32752543	49.141
2	16.988	33897269	50.859
Total		66649811	100.000



Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	8.501	13234929	95.360
2	17.095	644014	4.640
Total		13878943	100.000

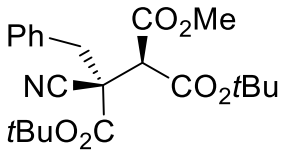
10. General procedure for the synthesis of vicinal tertiary and quaternary stereocenters



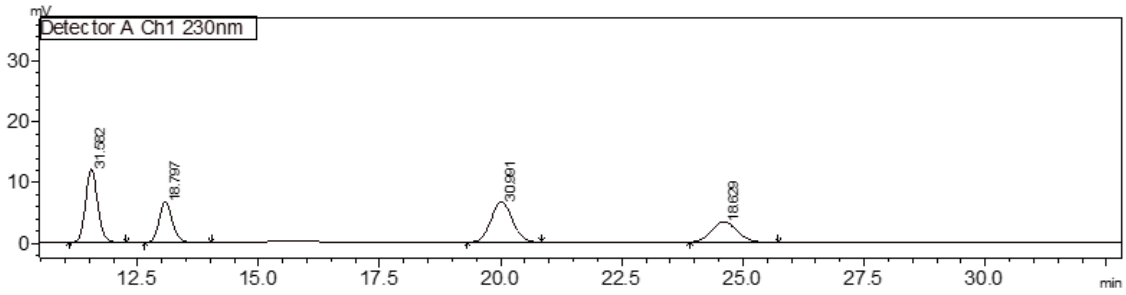
Method A: general procedure for the synthesis of vicinal tertiary and quaternary stereocenters: the bromide (1.0 equiv.), *tert*-butyl methyl malonate (1.2 equiv.) and TBAB (5% mol) were dissolved in Toluene, and then 4M aq. KOH (1.0 equiv.) was added slowly. The mixture was stirred at room temperature for 6 h. The reaction was quenched with NH_4Cl (1 mL) and then water (10 mL) was added. Separate the organic phase and extract aqueous phase with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ether = 5:1 as the eluent) to get the racemic vicinal tertiary and quaternary stereocenters.

Method B: general procedure for the synthesis of vicinal tertiary and quaternary stereocenters: the bromide (1.0 equiv.), dimethyl carbonate (1.2 equiv.) and **PN1** (5% mol) were dissolved in Toluene, cooling down the reaction mixture to – 20 ^oC, and then 4M aq. KOH was added by a micro syringe. The mixture was stirred at -20 ^oC for 3-4 days until the completion. TLC monitored the process. The reaction was quenched with NH_4Cl (1 mL) and then water (10 mL) was added. Separate the organic phase and extract aqueous phase with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ether = 5:1 as the eluent) to get the chiral vicinal tertiary and quaternary stereocenters. One of the chiral centers which bears an acidic proton is not stable, and can be racemized with excess base. After purification, the sample should be kept in – 20 ^oC fridge.

11. Characterization of isolated all-carbon quaternary stereocenters

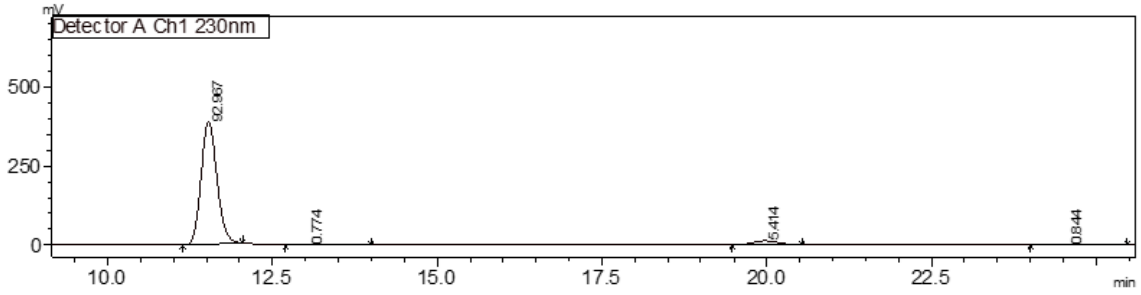


1,2-di-tert-butyl 1-methyl (1S,2R)-2-cyano-3-phenylpropane-1,1,2-tricarboxylate (19k): Colorless oil; 83% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.20; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.28 (m, 5H), 3.94 (s, 1H), 3.78 (s, 3H), 3.33 (d, J = 13.4 Hz, 1H), 3.10 (d, J = 13.5 Hz, 1H), 1.56 (s, 9H), 1.26 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.82, 166.63, 165.69, 165.64, 164.89, 164.59, 133.29, 130.61, 128.59, 128.17, 128.14, 117.40, 84.94, 84.91, 84.23, 83.98, 57.78, 57.68, 53.15, 53.04, 50.50, 50.37, 41.75, 41.64, 27.97, 27.93, 27.85, 27.59, 27.56. HRMS (ESI) calcd for $C_{22}H_{30}NO_6$ m/z $[M+H]^+$: 404.2068; found: 404.2075; $[\alpha]_D^{22}$= -0.03 (c 0.32, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 230 nm, 22°C), 11.5 (major),19.9 min, 90% ee.



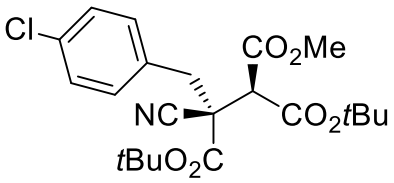
Detector A Channel 1 230nm

Peak#	Ret. Time	Area	Area%
1	11.546	208724	31.582
2	13.074	124232	18.797
3	20.015	204819	30.991
4	24.616	123121	18.629
Total		660895	100.000

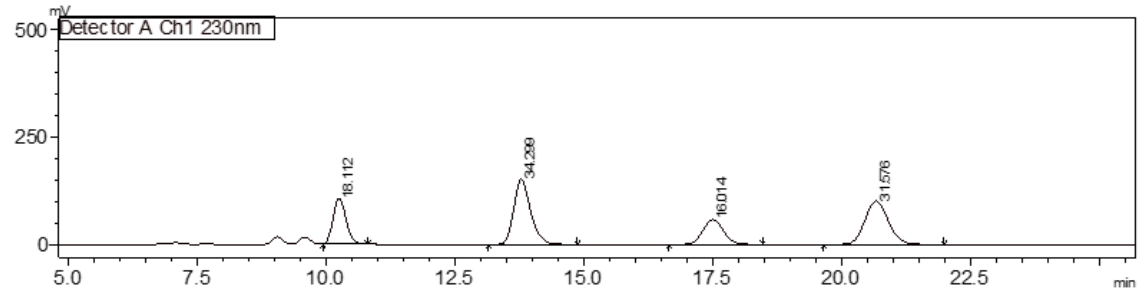


Detector A Channel 1 230nm

Peak#	Ret. Time	Area	Area%
1	11.531	6515210	92.967
2	13.043	54265	0.774
3	19.975	379451	5.414
4	24.552	59126	0.844
Total		7008052	100.000

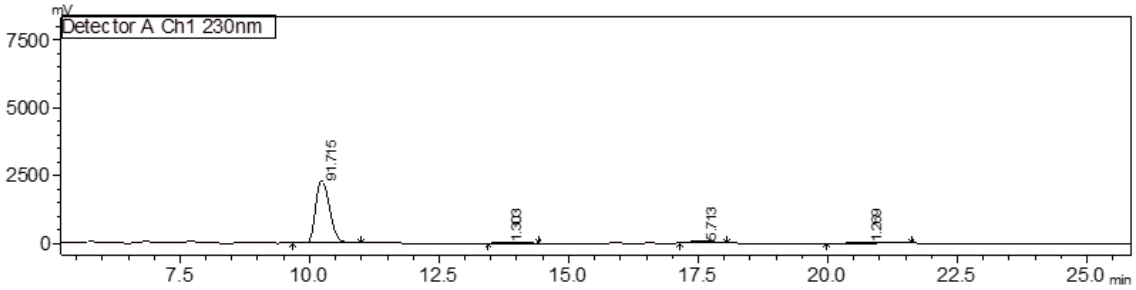


1,2-di-tert-butyl 1-methyl (1S,2R)-3-(4-chlorophenyl)-2-cyanopropane-1,1,2-tricarboxylate (19l): Colorless oil; 79% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.20;^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.29 (m, 5H), 3.94 (s, 1H), 3.78 (s, 3H), 3.33 (d, *J* = 13.5 Hz, 1H), 3.10 (d, *J* = 13.5 Hz, 1H), 1.56 (s, 9H), 1.27 (d, *J* = 8.1 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.83, 165.68, 164.60, 133.24, 130.60, 128.59, 128.17, 117.40, 84.92, 84.24, 57.76, 53.08, 50.48, 41.61, 27.95, 27.92, 27.55. HRMS (ESI) calcd for $C_{22}H_{29}ClNO_6$ m/z $[M+H]^+$: 438.1678; found: 438.1675; $[\alpha]_D^{22}$= -0.03 (c 0.13, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 230 nm, 22°C), 10.2 (major), 17.6 min, 90% ee.



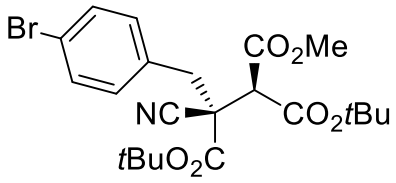
Detector A Channel 1 230nm

Peak#	Ret. Time	Area	Area%
1	10.251	1843528	18.112
2	13.788	3491216	34.299
3	17.506	1629986	16.014
4	20.672	3213979	31.576
Total		10178709	100.000

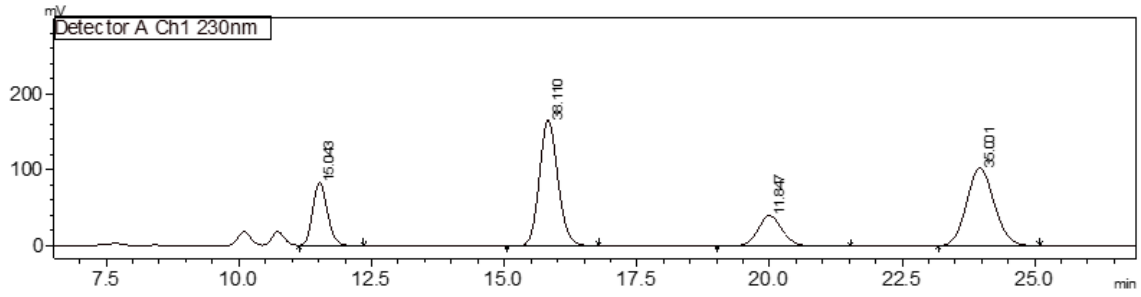


Detector A Channel 1 230nm

Peak#	Ret. Time	Area	Area%
1	10.235	42273427	91.715
2	13.827	600545	1.303
3	17.584	2633399	5.713
4	20.754	584810	1.269
Total		46092182	100.000

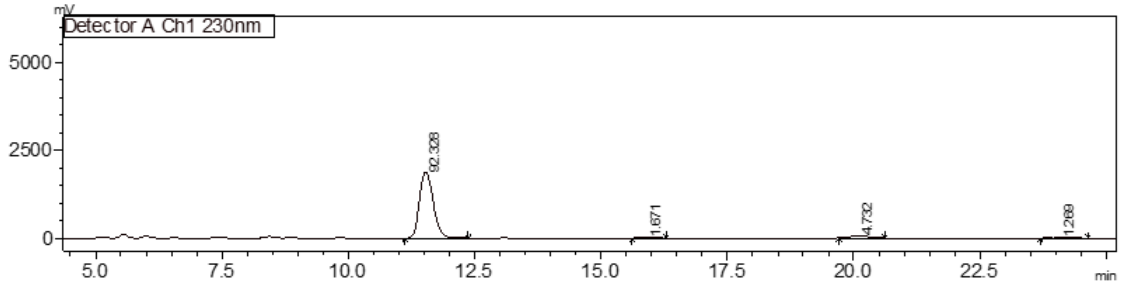


1,2-di-tert-butyl 1-methyl (1S,2R)-3-(4-bromophenyl)-2-cyanopropane-1,1,2-tricarboxylate (19m): Colorless oil; 82% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.25; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.38 (m, 2H), 7.26 – 7.16 (m, 2H), 3.90 (s, 1H), 3.78 (s, 3H), 3.28 (d, J = 13.6 Hz, 1H), 3.07 (d, J = 13.6 Hz, 1H), 1.55 (s, 9H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.54, 165.55, 164.49, 131.75, 129.41, 128.75, 127.05, 85.24, 57.62, 57.54, 53.26, 53.15, 50.27, 40.89, 40.79, 27.94, 27.60. HRMS (ESI) calcd for $C_{22}H_{29}BrNO_6$ m/z $[M+H]^+$: 482.1173; found: 482.1179; $[\alpha]_D^{22}$= -0.03 (c 0.22, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 230 nm, 22°C), 11.5 (major), 20.1 min, 90% ee.



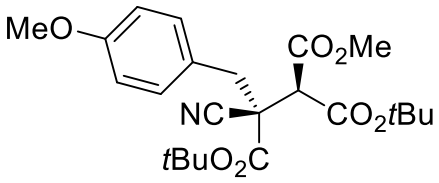
Detector A Channel 1 230nm

Peak#	Ret. Time	Area	Area%
1	11.521	1588405	15.043
2	15.824	4024140	38.110
3	20.003	1250934	11.847
4	23.966	3695884	35.001
Total		10559363	100.000



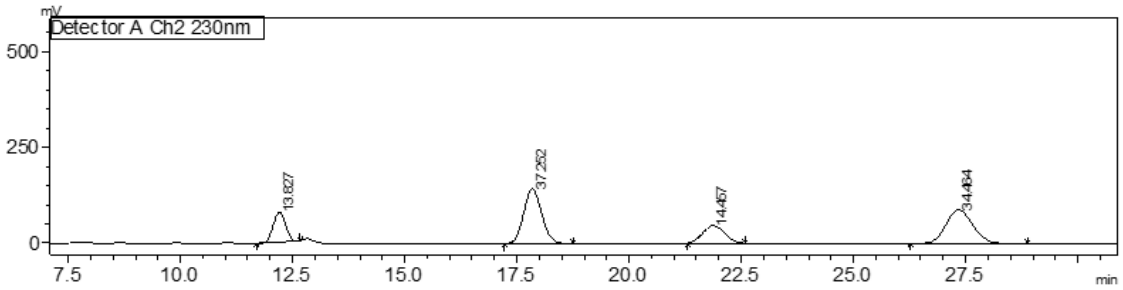
Detector A Channel 1 230nm

Peak#	Ret. Time	Area	Area%
1	11.528	35856241	92.328
2	15.910	649093	1.671
3	20.099	1837811	4.732
4	24.082	492779	1.269
Total		38835924	100.000



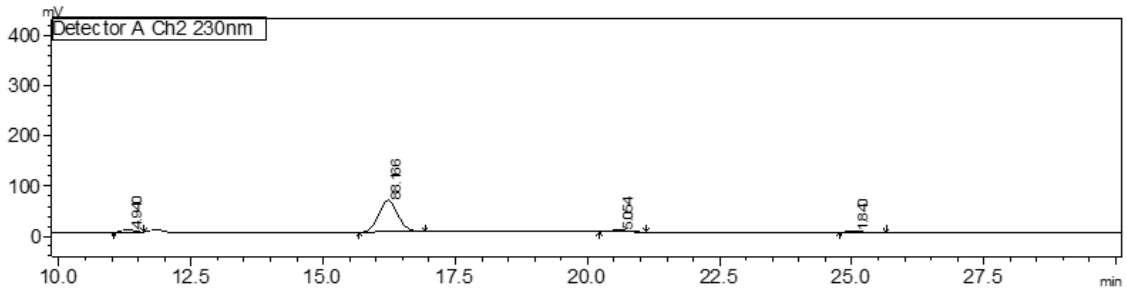
1,2-di-tert-butyl 1-methyl (1S,2R)-2-cyano-3-(4-methoxyphenyl)propane-1,1,2-tricarboxylate (19n): Colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.15; ^1H NMR (400 MHz,) δ 7.24 (d, J = 8.6 Hz, 2H), 6.84 (d, J = 8.6 Hz, 2H), 3.91 (s, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.28 (d, J = 13.7 Hz, 1H), 3.07 (d, J = 13.7 Hz, 1H),

1.55 (s, 9H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.38, 165.16, 164.45, 164.17, 131.95, 131.42, 122.07, 116.92, 116.84, 84.98, 84.95, 84.07, 83.82, 82.61, 76.52, 57.29, 57.21, 52.95, 49.88, 40.62, 40.53, 27.62, 27.58, 27.56, 27.29. HRMS (ESI) calcd for $C_{23}H_{32}NO_7$ m/z $[M+H]^+$: 434.2173; found: 434.2170; $[a]_D^{22}$= -0.02 (c 0.21, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm, 22°C), 16.2 (major), 25.1 min, 96% ee.



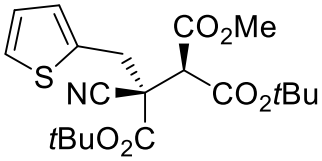
Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	12.207	1490128	13.827
2	17.842	4014484	37.252
3	21.882	1558017	14.457
4	27.347	3714025	34.464
Total		10776655	100.000

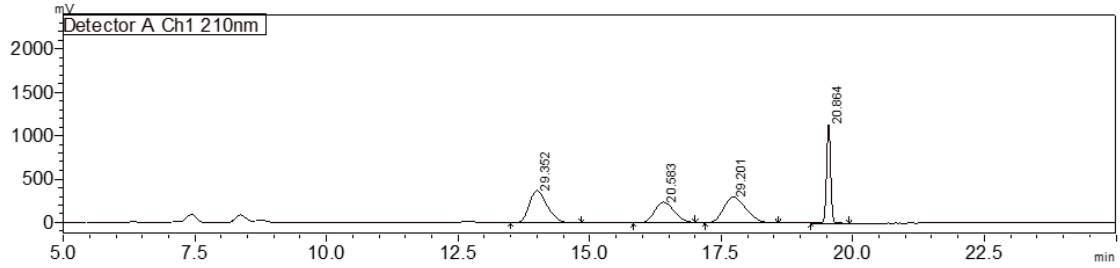


Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	11.301	89110	4.940
2	16.221	1590326	88.166
3	20.605	91162	5.054
4	25.055	33189	1.840
Total		1803787	100.000

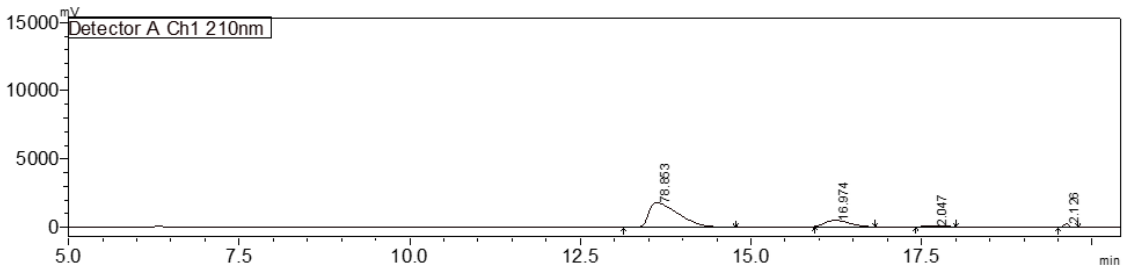


1,2-di-tert-butyl 1-methyl (1S,2R)-2-cyano-3-(thiophen-2-yl)propane-1,1,2-tricarboxylate (19o): Colorless oil; 76% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 – 7.22 (m, 2H), 7.05 (dd, J = 3.5, 1.2 Hz, 2H), 7.00 – 6.94 (m, 2H), 3.78 (s, 1H), 3.59 (d, J = 15.1 Hz, 1H), 3.45 (d, J = 15.0 Hz, 1H), 1.36 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.59, 166.41, 165.26, 165.19, 164.60, 164.35, 134.02, 128.94, 128.91, 126.94, 125.87, 85.06, 85.03, 84.26, 83.91, 56.71, 56.62, 52.90, 50.45, 35.86, 35.82, 27.93, 27.82, 27.77, 27.54, 27.51. HRMS (ESI) calcd for $C_{20}H_{28}NO_6$ m/z $[M+H]^+$: 410.1632; found: 410.1639; $[\alpha]_D^{22}$= -0.01 (c 0.14, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 210 nm, 22°C), 13.6 (major), 17.7 min, 95% ee.



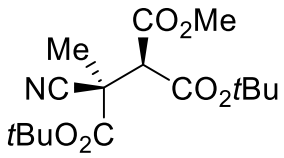
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	14.002	8833397	29.352
2	16.402	6194272	20.583
3	17.725	8787862	29.201
4	19.540	6278879	20.864
Total		30094410	100.000

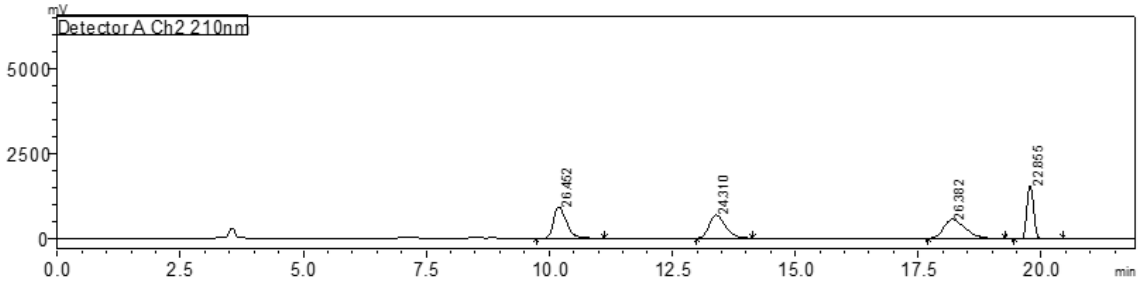


Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	13.619	54760655	78.853
2	16.233	11787766	16.974
3	17.688	1421410	2.047
4	19.620	1476630	2.126
Total		69446461	100.000

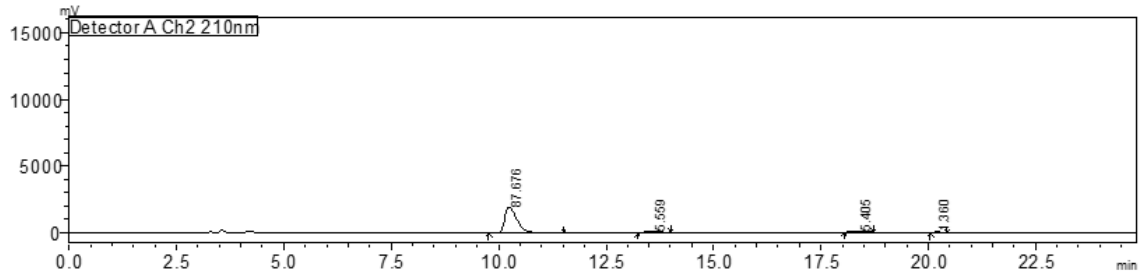


1,2-di-tert-butyl 1-methyl (1S,2R)-2-cyanopropane-1,1,2-tricarboxylate (19p): Colorless oil; 81% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.24;^{1}H NMR (400 MHz, Chloroform-*d*) δ 3.84 (s, 1H), 3.79 (s, 3H), 1.68 (s, 3H), 1.51 (s, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.04, 166.91, 166.00, 164.48, 118.01, 117.03, 85.96, 84.81, 84.08, 57.66, 53.05, 49.02, 44.28, 27.89, 27.74, 27.73, 22.48, 21.59. HRMS (ESI) calcd for $C_{16}H_{26}NO_6$ m/z $[M+H]^+$: 328.1755; found: 328.1759; $[\alpha]_D^{22}$= -0.02 (c 0.19, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 230 nm, 22°C), 10.2 (major), 18.4 min, 89% ee.



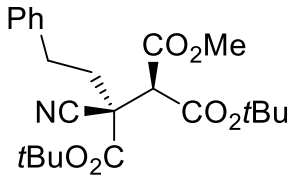
Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	10.193	16861554	26.452
2	13.387	15496424	24.310
3	18.191	16817240	26.382
4	19.775	14568986	22.855
Total		63744204	100.000

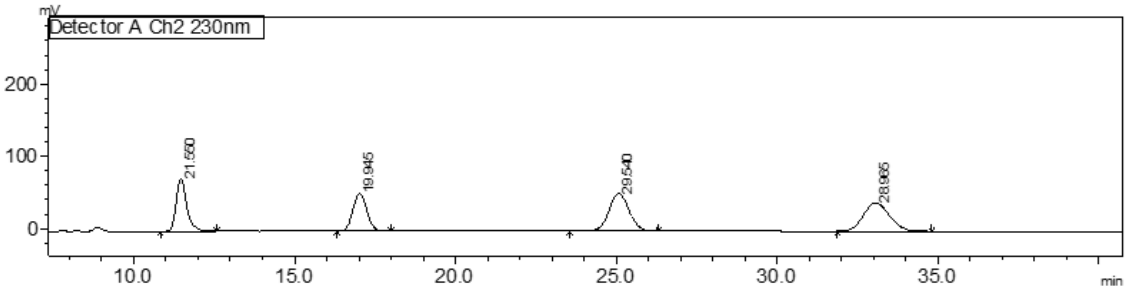


Detector A Channel 2 210nm

Peak#	Ret. Time	Area	Area%
1	10.239	37344781	87.676
2	13.585	2367778	5.559
3	18.384	2302316	5.405
4	20.198	579318	1.360
Total		42594193	100.000

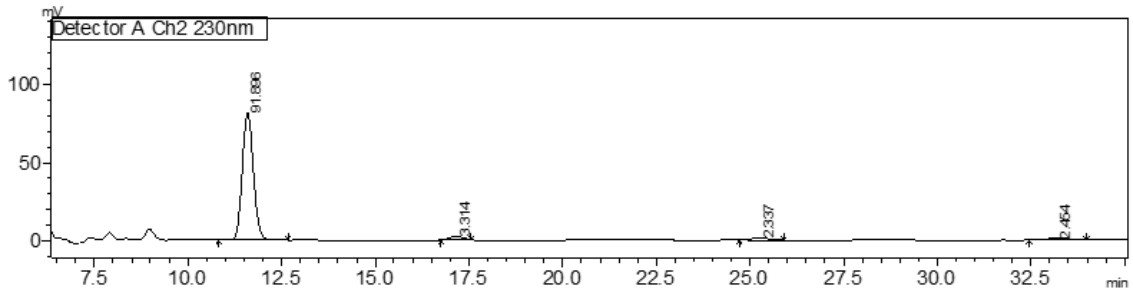


1,2-di-tert-butyl 1-methyl (1S,2R)-2-cyano-4-phenylbutane-1,1,2-tricarboxylate (19q): Colorless oil; 82% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.25; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (t, J = 7.4 Hz, 2H), 7.23 (d, J = 7.3 Hz, 1H), 7.16 (s, 2H), 3.89 (s, 1H), 3.80 (s, 3H), 2.97 – 2.82 (m, 1H), 2.76 – 2.55 (m, 1H), 2.27 (td, J = 13.2, 4.6 Hz, 1H), 2.16 (td, J = 13.2, 5.1 Hz, 1H), 1.56 (s, 9H), 1.50 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.86, 166.44, 166.28, 164.41, 139.76, 128.85, 128.52, 128.45, 126.73, 117.18, 85.17, 84.17, 84.14, 57.38, 57.35, 53.07, 49.32, 37.98, 31.31, 29.84, 27.96, 27.92. HRMS (ESI) calcd for $C_{23}H_{32}NO_6$ m/z $[M+H]^+$: 418.2224; found: 418.2227; $[\alpha]_D^{22}$= -0.03 (c 0.27, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 230 nm, 22°C), 11.6 (major), 17.2 min, 94% ee.



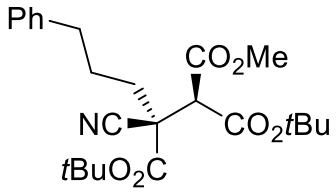
Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	11.466	1683883	21.550
2	17.019	1558522	19.945
3	25.073	2308235	29.540
4	33.060	2263284	28.965
Total		7813924	100.000



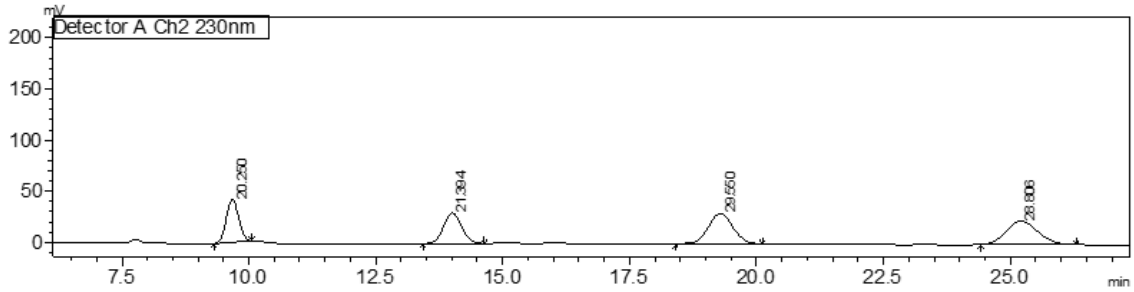
Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	11.591	1684751	91.896
2	17.154	60750	3.314
3	25.260	42839	2.337
4	33.193	44992	2.454
Total		1833332	100.000



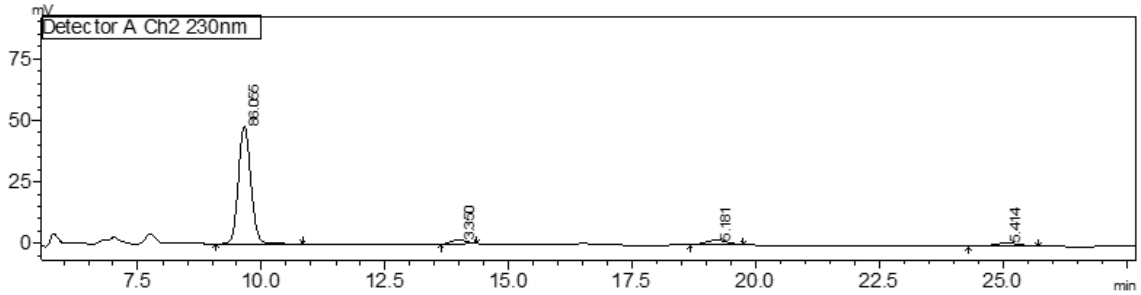
1,2-di-tert-butyl 1-methyl (1S,2R)-2-cyano-5-phenylpentane-1,1,2-tricarboxylate (19r): Colorless oil; 80% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, J = 12.4 Hz, 2H), 7.18 (s, 1H), 7.14 (d, J = 7.5 Hz, 2H), 3.81 (s, 1H), 3.76 (s, 3H), 2.80 – 2.50 (m, 2H), 2.05 – 1.80 (m, 3H), 1.82 – 1.65 (m, 1H), 1.49 (s, 9H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.34, 166.14,

140.79, 128.67, 128.63, 128.50, 126.33, 117.27, 84.93, 84.03, 57.53, 57.32, 53.04, 49.23, 35.51, 35.42, 35.29, 35.24, 28.01, 27.93, 27.83, 26.21. HRMS (ESI) calcd for $C_{24}H_{34}NO_6$ m/z $[M+H]^+$: 432.2381; found: 432.2389; $[\alpha]_D^{22}$= -0.03 (c 0.12, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 230 nm, 22°C), 9.6 (major), 14.0 min, 93% ee.



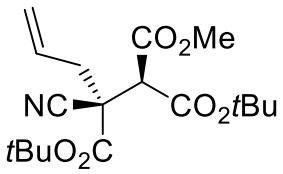
Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	9.677	705714	20.250
2	14.010	745569	21.394
3	19.292	1029832	29.550
4	25.215	1003899	28.806
Total		3485014	100.000

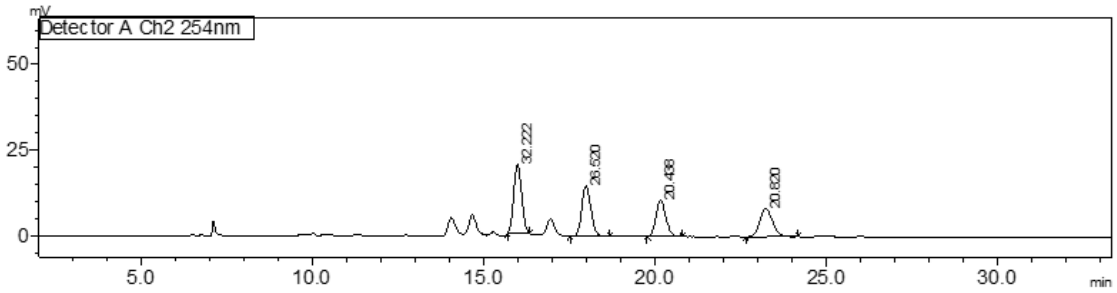


Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	9.652	845631	86.055
2	14.002	32919	3.350
3	19.194	50916	5.181
4	25.071	53199	5.414
Total		982664	100.000

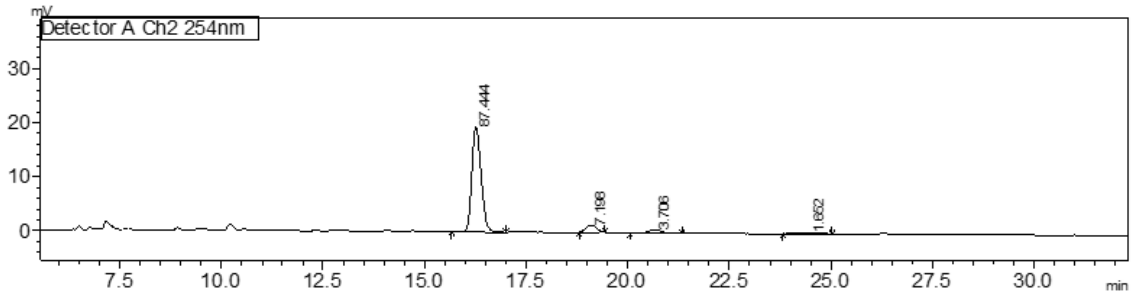


1,2-di-tert-butyl 1-methyl (1S,2R)-2-cyanopent-4-ene-1,1,2-tricarboxylate (19s): Colorless oil; 84% yield; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.27; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.94 – 5.70 (m, 1H), 5.33 – 5.06 (m, 2H), 3.83 (s, 1H), 3.77 (s, 3H), 2.75 (d, J = 5.8 Hz, 1H), 2.71 – 2.48 (m, 1H), 1.50 (d, J = 10.2 Hz, 18H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.54, 165.42, 164.12, 129.48, 121.18, 116.74, 84.77, 83.84, 76.53, 56.38, 56.26, 52.74, 48.59, 39.95, 27.59, 27.55. HRMS (ESI) calcd for $C_{18}H_{28}NO_6$ m/z $[M+H]^+$: 354.1911; found: 354.1918; $[\alpha]_D^{22}$= -0.01 (c 0.12, $CHCl_3$); HPLC analysis: Chiralcel IA-3 linked by Chiralcel IC (Hex/IPA = 98/2, 1.0 mL/min, 230 nm, 22°C), 16.3 (major), 19.1 min, 86% ee.



Detector A Channel 2 254nm

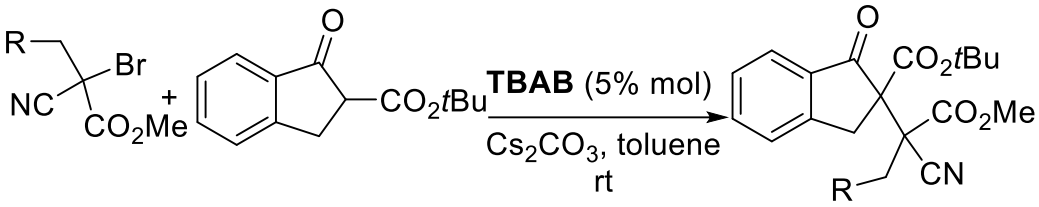
Peak#	Ret. Time	Area	Area%
1	15.981	329717	32.222
2	17.979	271372	26.520
3	20.152	209139	20.438
4	23.221	213040	20.820
Total		1023268	100.000



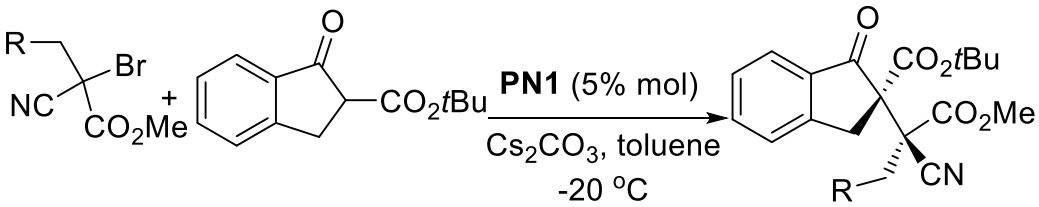
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	16.260	307700	87.444
2	19.096	25327	7.198
3	20.654	13041	3.706
4	24.467	5813	1.652
Total		351881	100.000

12. General procedure for the synthesis of vicinal all-carbon quaternary stereocenters



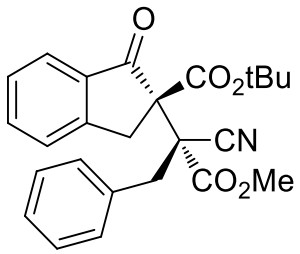
Method A: General procedure for the synthesis of vicinal all-carbon quaternary stereocenters: the bromide (1.0 equiv.), *tert*-butyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (1.2 equiv.) and TBAB (5% mol) were dissolved in Toluene, and then Cs_2CO_3 (1.5 equiv.) was added slowly. The mixture was stirred at room temperature for 4 h. The reaction was quenched with NH_4Cl (1 mL) and then water (10 mL) was added. Separate the organic phase and extract aqueous phase with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ether = 5:1 as the eluent) to get the racemic vicinal all-carbon quaternary stereocenters.



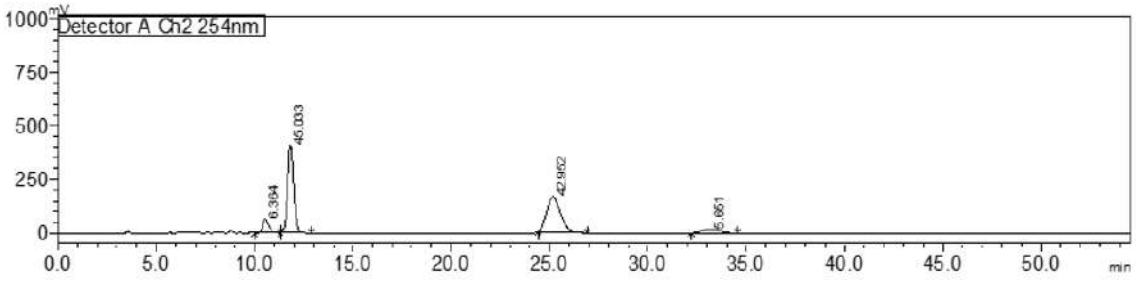
Method B: General procedure for the synthesis of vicinal all-carbon quaternary stereocenters: the bromide (1.0 equiv.), dimethyl carbonate (1.2 equiv.) and **PN1** (5% mol) were dissolved in Toluene, cooling down the reaction mixture to – 20 ^oC, and then

Cs_2CO_3 (1.5 equiv.) was added in one portion. The mixture was stirred at -20 ^oC for 3-4 days until the completion. TLC monitored the process. The reaction was quenched with NH_4Cl (1 mL) and then water (10 mL) was added. Separate the organic phase and extract aqueous phase with DCM. The combined organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated. The residue was purified by flash chromatography (hexane: ether = 5:1 as the eluent) to get the chiral vicinal all-carbon quaternary stereocenters.

13. Characterization of isolated all-carbon quaternary stereocenters

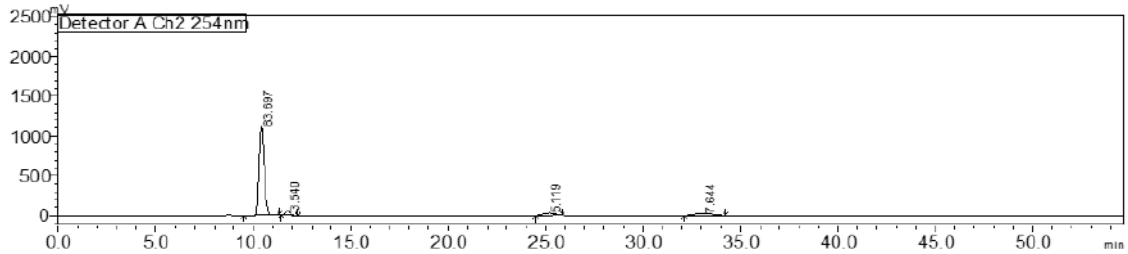


***tert*-butyl (*R*)-2-((R)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22c):** Colorless oil; 83% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.62 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.45 (dd, *J* = 18.3, 7.7 Hz, 2H), 7.30 (s, 5H), 3.91 – 3.66 (m, 3H), 3.50 (s, 4H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.74, 167.13, 166.70, 150.70, 135.33, 135.28, 135.13, 133.91, 130.23, 130.02, 128.75, 128.30, 128.04, 127.93, 127.78, 127.74, 125.85, 124.63, 124.56, 116.72, 84.30, 64.17, 53.98, 53.09, 38.95, 36.18, 27.52. HRMS (ESI) calcd for $C_{25}H_{26}NO_5$ m/z $[M+H]^+$: 420.1805; found: 420.1800; $[a]_D^{22}$= +0.20 (c 0.09, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 10.4 (major), 33.1 min, 84% ee.



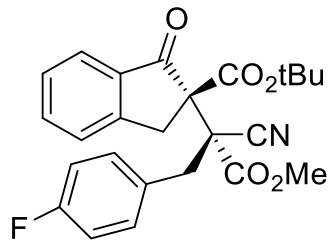
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	10.539	1208412	6.364
2	11.817	8550687	45.033
3	25.155	8155582	42.952
4	33.180	1073005	5.651
Total		18987686	100.000



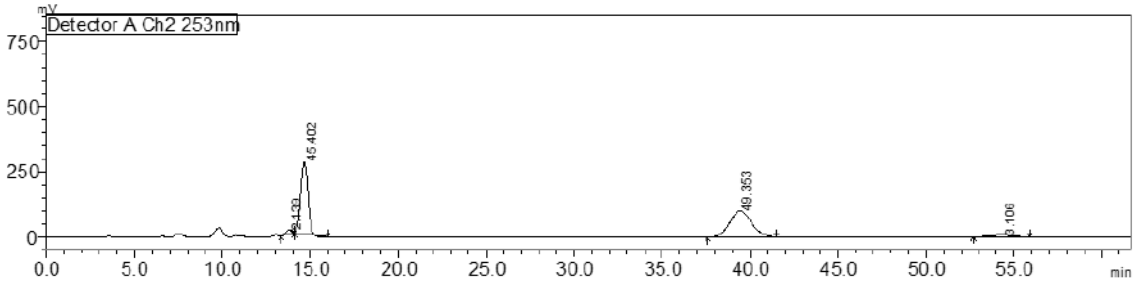
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	10.410	20534834	83.697
2	11.755	868645	3.540
3	25.192	1255872	5.119
4	33.102	1875515	7.644
Total		24534866	100.000



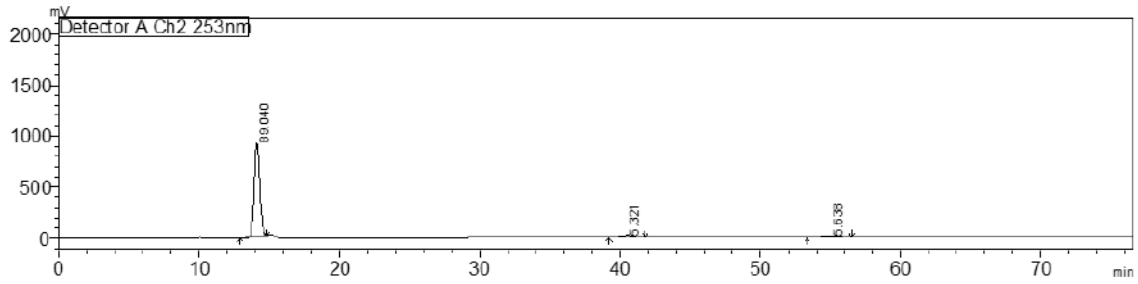
***tert*-butyl (*R*)-2-((*R*)-2-cyano-3-(4-fluorophenyl)-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22d):** Colorless oil; 73% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.28; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.64 (td, *J* = 7.5, 1.3 Hz, 1H), 7.52 – 7.38 (m, 2H), 7.31 – 7.25 (m, 2H), 7.05 – 6.97 (m, 2H), 3.88 – 3.71 (m, 3H), 3.51 (s, 4H), 1.42 (s, 9H). ^{13}C NMR (101

MHz, $CDCl_3$) δ 197.93, 167.30, 150.99, 135.74, 135.36, 132.28, 132.20, 130.90, 130.82, 130.06, 128.31, 126.19, 124.92, 116.90, 116.12, 115.90, 115.67, 115.46, 84.69, 64.34, 53.51, 38.27, 36.45, 27.83. ^{19}F NMR (377 MHz, $CDCl_3$) δ -101.27, -101.29. HRMS (ESI) calcd for $C_{25}H_{25F}NO_5$ m/z $[M+H]^+$: 438.1711; found: 438.1710; $[a]_D^{22}$= +0.08 (c 0.10, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 253 nm, 22°C), 14.1 (major), 55.0 min, 89% ee.



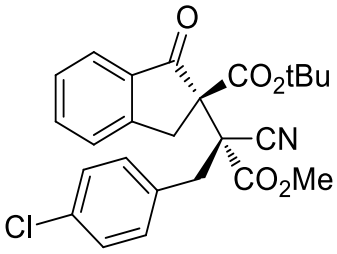
Detector A Channel 2 253nm

Peak#	Ret. Time	Area	Area%
1	13.796	368498	2.139
2	14.659	7820194	45.402
3	39.416	8500712	49.353
4	54.370	535074	3.106
Total		17224478	100.000

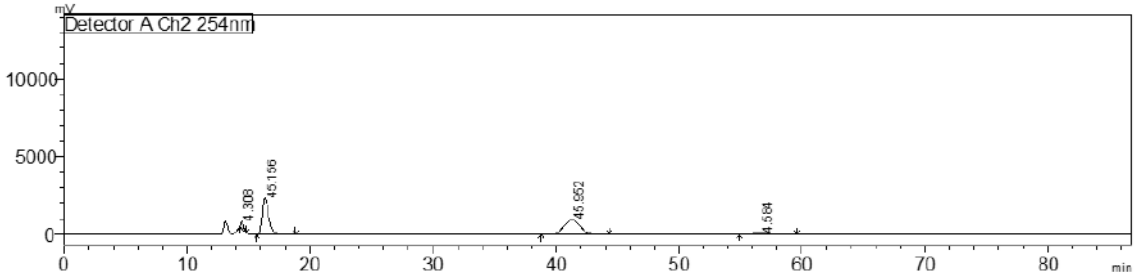


Detector A Channel 2 253nm

Peak#	Ret. Time	Area	Area%
1	14.099	24675614	89.040
2	40.510	1474733	5.321
3	55.067	1562548	5.638
Total		27712895	100.000

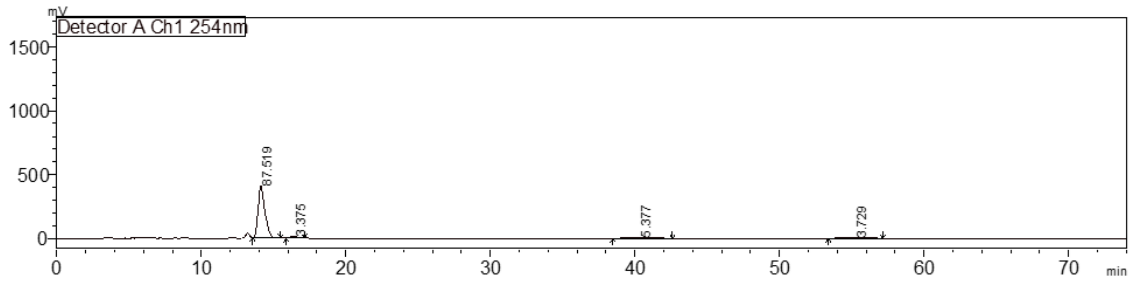


***tert*-butyl (*R*)-2-((*R*)-3-(4-chlorophenyl)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22e):** Colorless oil; 73% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.85 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.63 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.57 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.5 Hz, 1H), 7.36 (td, *J* = 7.5, 1.3 Hz, 1H), 6.98 (td, *J* = 7.7, 1.7 Hz, 1H), 4.13 (d, *J* = 14.1 Hz, 1H), 3.90 (s, 1H), 3.83 – 3.70 (m, 2H), 3.60 (d, *J* = 5.6 Hz, 3H), 1.41 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.76, 150.74, 139.65, 135.25, 131.37, 129.39, 128.28, 127.88, 125.86, 124.54, 101.90, 84.27, 76.53, 64.42, 53.74, 42.06, 36.90, 27.51. HRMS (ESI) calcd for $C_{25}H_{25}ClNO_5$ m/z $[M+H]^+$: 454.1416; found: 454.1427; $[\alpha]_D^{22}$= +0.09 (c 0.12, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 14.1 (major), 55.2 min, 92% ee.



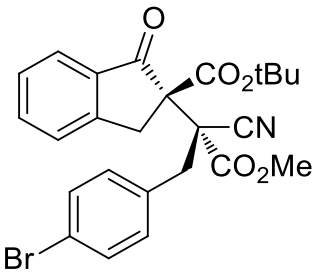
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	14.454	8200784	4.308
2	16.330	85955309	45.156
3	41.338	87470589	45.952
4	56.668	8726674	4.584
Total		190353355	100.000

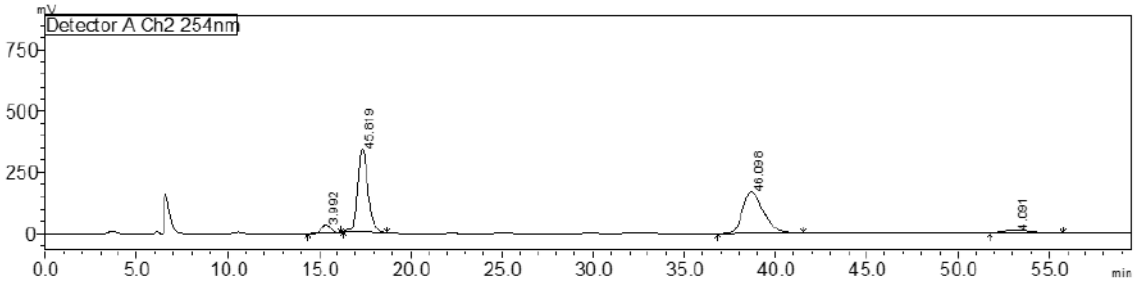


Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	14.127	13254419	87.519
2	16.380	511109	3.375
3	40.319	814301	5.377
4	55.222	564764	3.729
Total		15144592	100.000

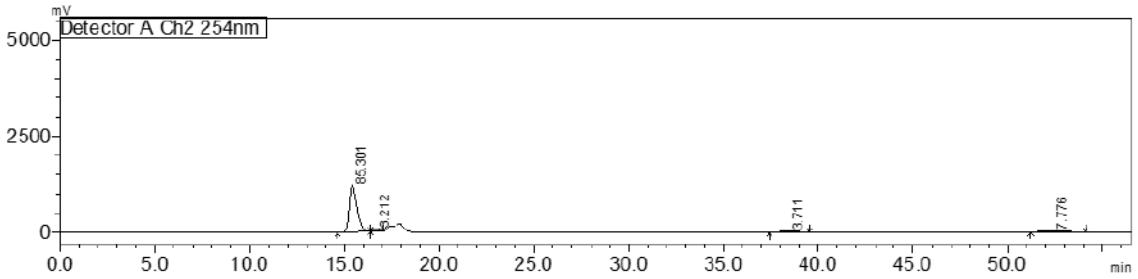


***tert*-butyl (*R*)-2-((*R*)-3-(4-bromophenyl)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22f):** Colorless oil; 81% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.28; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.7 Hz, 1H), 7.64 (td, *J* = 7.5, 1.3 Hz, 1H), 7.53 – 7.38 (m, 4H), 7.23 – 7.10 (m, 2H), 3.96 – 3.58 (m, 4H), 3.49 (d, *J* = 24.8 Hz, 3H), 1.42 (s, 11H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.20, 151.00, 135.79, 135.32, 133.31, 132.30, 132.26, 131.81, 130.91, 128.34, 126.19, 124.96, 122.40, 116.77, 84.74, 76.84, 64.30, 53.58, 38.38, 36.44, 35.24, 30.19, 29.85, 27.84, 22.84, 14.24. HRMS (ESI) calcd for $C_{25}H_{25}BrNO_5$ m/z $[M+H]^+$: 498.0911; found: 498.0916; $[\alpha]_D^{22}$= +0.20 (c 0.17, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 15.4 (major), 52.4 min, 85% ee.



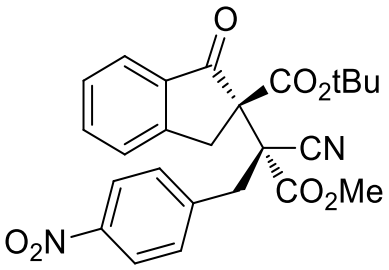
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	15.374	1167710	3.992
2	17.366	13403398	45.819
3	38.662	13485220	46.098
4	53.168	1196832	4.091
Total		29253159	100.000



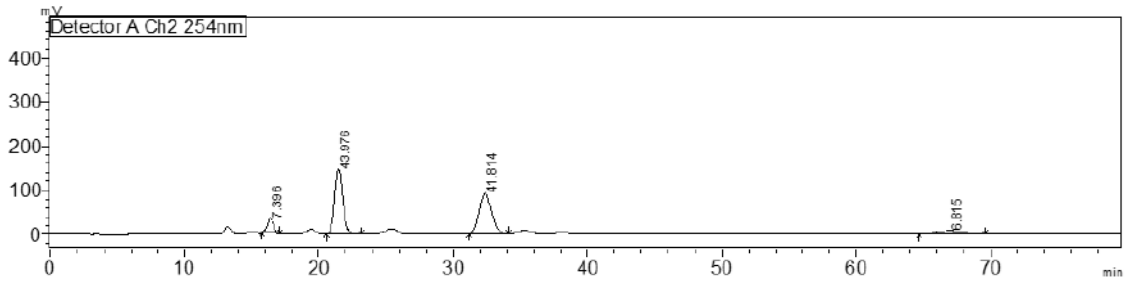
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	15.416	34808885	85.301
2	16.705	1310530	3.212
3	38.459	1514214	3.711
4	52.427	3173340	7.776
Total		40806969	100.000



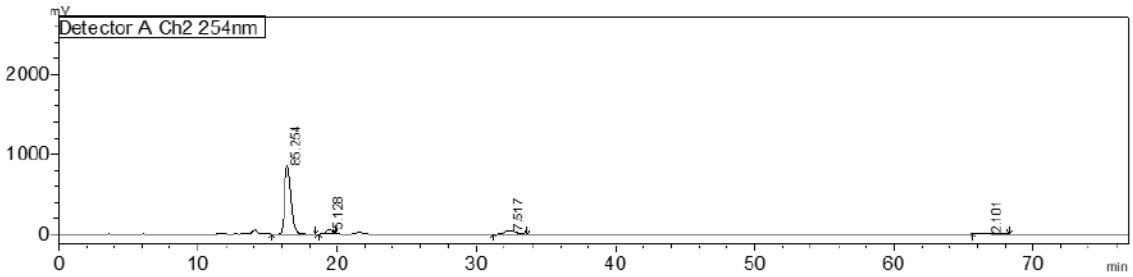
***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-3-(4-nitrophenyl)-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22g):** Colorless oil; 72% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 – 8.12

(m, 2H), 7.82 (dd, *J* = 14.3, 7.7 Hz, 1H), 7.66 (td, *J* = 7.4, 1.2 Hz, 1H), 7.57 – 7.40 (m, 4H), 4.09 – 3.63 (m, 4H), 3.49 (d, *J* = 38.2 Hz, 3H), 1.41 (d, *J* = 12.0 Hz, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.58, 167.48, 166.52, 150.65, 147.63, 141.67, 135.66, 135.49, 134.84, 131.41, 131.11, 128.24, 128.15, 125.90, 124.74, 124.71, 123.46, 123.43, 116.00, 84.63, 84.45, 76.53, 63.78, 53.47, 53.27, 37.88, 37.19, 27.52, 27.49. HRMS (ESI) calcd for $C_{25}H_{25}N_2O_7$ m/z $[M+H]^+$: 465.1656; found: 465.1659; $[\alpha]_D^{22}$= +0.04 (c 0.07, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 16.4 (major), 66.8 min, 95% ee.



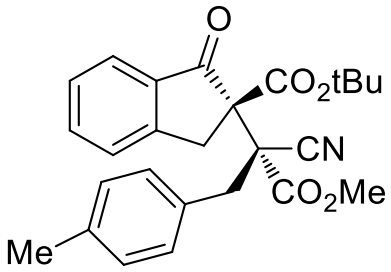
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	16.391	1032779	7.396
2	21.455	6141168	43.976
3	32.377	5839319	41.814
4	66.950	951651	6.815
Total		13964917	100.000

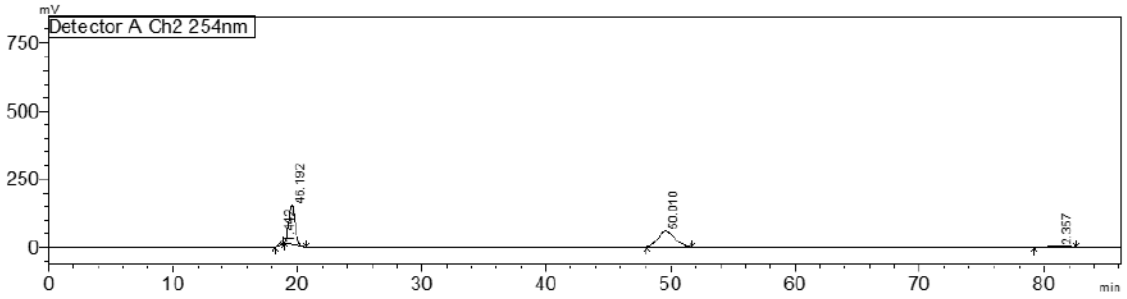


Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	16.414	26542408	85.254
2	19.415	1596526	5.128
3	32.403	2340407	7.517
4	66.802	654044	2.101
Total		31133385	100.000

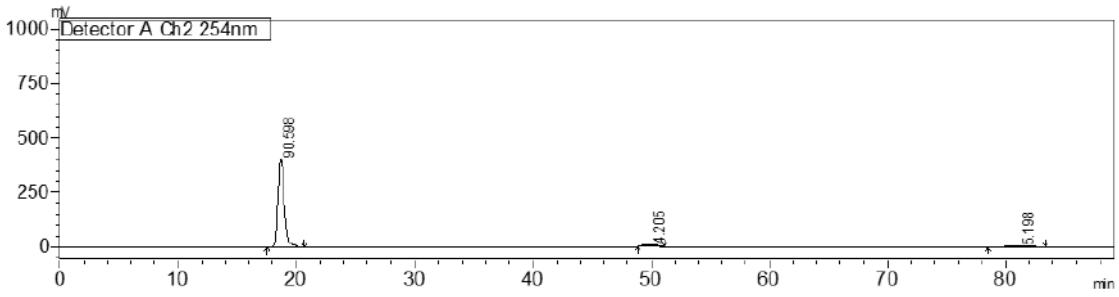


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxo-3-(p-tolyl)propan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22h):** Colorless oil; 72% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.70 – 7.57 (m, 1H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.20 – 7.14 (m, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 3.85 – 3.66 (m, 3H), 3.58 – 3.42 (m, 4H), 2.32 (s, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.30, 167.39, 166.89, 150.91, 137.64, 135.48, 135.34, 130.96, 130.26, 130.22, 129.19, 128.08, 126.03, 124.72, 116.96, 84.43, 64.36, 54.28, 53.25, 38.77, 36.35, 27.70, 21.10. HRMS (ESI) calcd for $C_{26}H_{28}NO_5$ m/z $[M+H]^+$: 434.1962; found: 434.1967; $[\alpha]_D^{22}$= +0.09 (c 0.10, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 18.6 (major), 81.1 min, 91% ee.



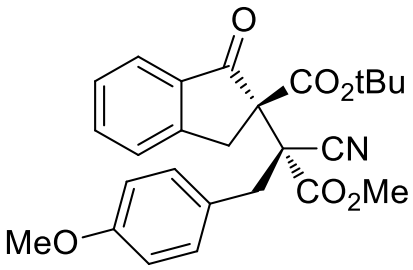
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	18.681	158708	1.442
2	19.529	5085098	46.192
3	49.579	5505487	50.010
4	81.216	259427	2.357
Total		11008720	100.000

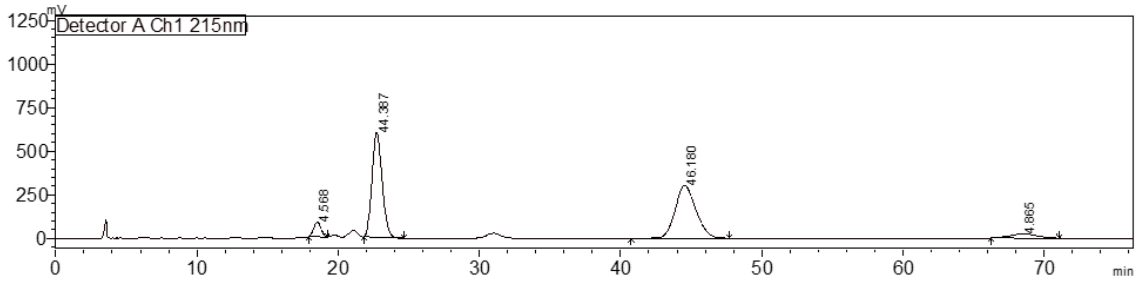


Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	18.663	15019471	90.598
2	49.899	697031	4.205
3	81.169	861652	5.198
Total		16578154	100.000

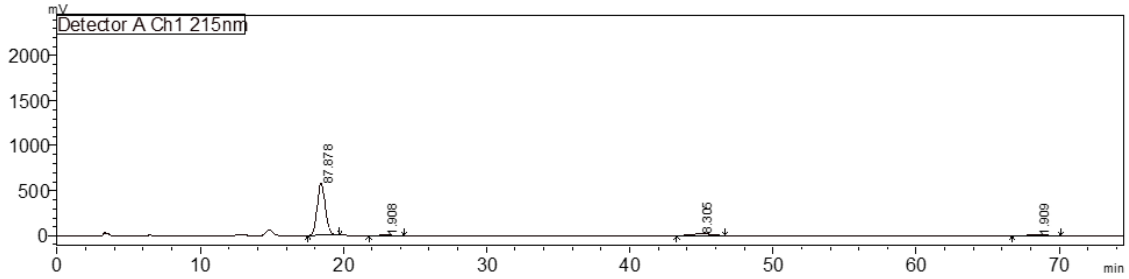


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-3-(4-methoxyphenyl)-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22i):** Colorless oil; 77% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.83 (d, *J* = 7.8 Hz, 1H), 7.64 (s, 1H), 7.46 (dd, *J* = 18.6, 7.8 Hz, 2H), 7.18 (dd, *J* = 8.9, 2.9 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 3.89 – 3.28 (m, 10H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.17, 168.11, 167.79, 159.51, 151.16, 136.32, 135.57, 131.43, 128.32, 126.16, 124.93, 117.25, 114.05, 84.38, 55.33, 53.28, 37.56, 27.82. HRMS (ESI) calcd for $C_{26}H_{28}NO_6$ m/z $[M+H]^+$: 450.1911; found: 450.1917; $[\alpha]_D^{22}$= +0.12 (c 0.10, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 215 nm, 22°C), 18.4 (major), 68.5 min, 95% ee.



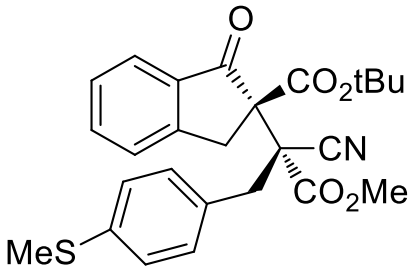
Detector A Channel 1 215nm

Peak#	Ret. Time	Area	Area%
1	18.533	3073560	4.568
2	22.735	29867778	44.387
3	44.549	31074353	46.180
4	68.501	3273369	4.865
Total		67289060	100.000



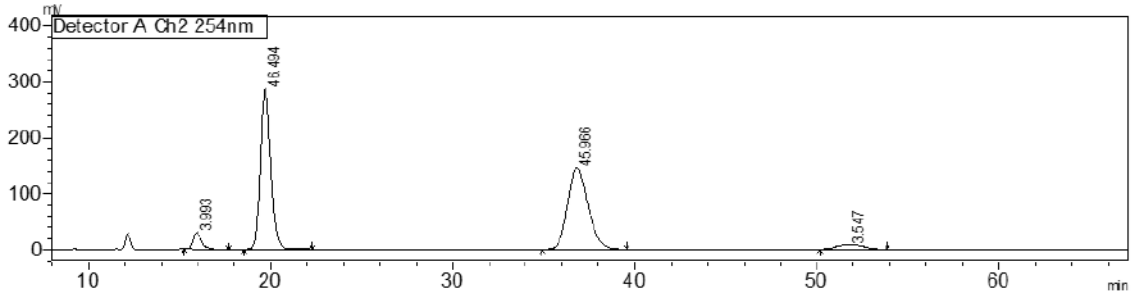
Detector A Channel 1 215nm

Peak#	Ret. Time	Area	Area%
1	18.444	22550613	87.878
2	22.962	489657	1.908
3	44.937	2131143	8.305
4	68.496	489828	1.909
Total		25661241	100.000



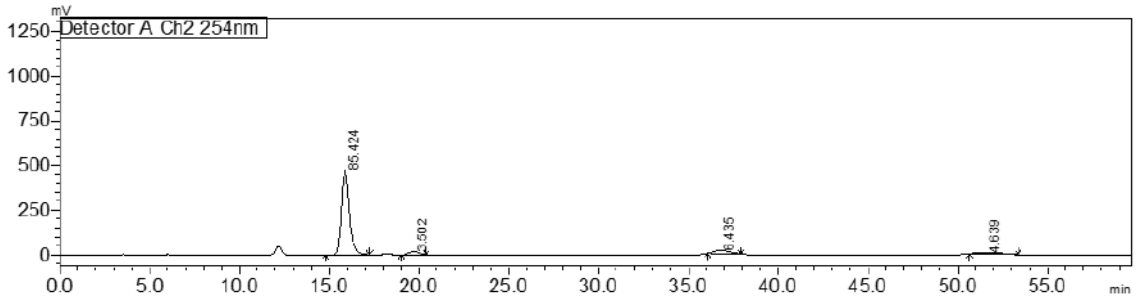
tert-butyl (R)-2-((R)-2-cyano-1-methoxy-3-(4-(methylthio)phenyl)-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22j): Colorless oil; 73% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78

(d, *J* = 7.6 Hz, 1H), 7.69 – 7.55 (m, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.26 – 7.11 (m, 4H), 3.89 – 3.65 (m, 3H), 3.59 – 3.37 (m, 4H), 2.46 (d, *J* = 2.8 Hz, 3H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.07, 150.72, 138.26, 135.37, 130.69, 130.57, 127.96, 126.33, 125.87, 124.60, 84.34, 76.53, 64.08, 53.19, 38.36, 36.15, 27.54, 15.51. HRMS (ESI) calcd for $C_{26}H_{28}NO_5S$ m/z $[M+H]^+$: 466.1683; found: 466.1689; $[\alpha]_D^{22}$= +0.08 (c 0.12, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 15.7 (major), 27.4 min, 90% ee.



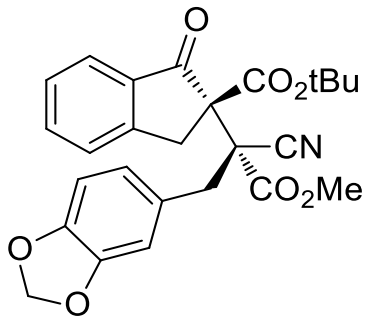
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	15.941	984770	3.993
2	19.699	11466968	46.494
3	36.827	11336800	45.966
4	51.821	874883	3.547
Total		24663421	100.000

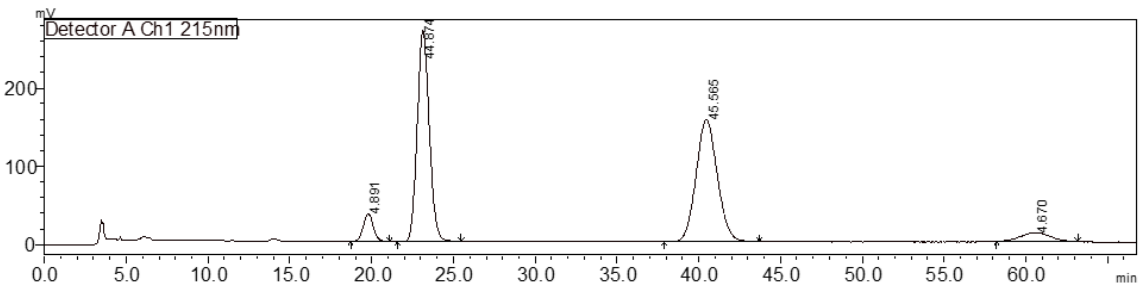


Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	15.874	14760467	85.424
2	19.700	605146	3.502
3	36.815	1111900	6.435
4	51.627	801552	4.639
Total		17279065	100.000

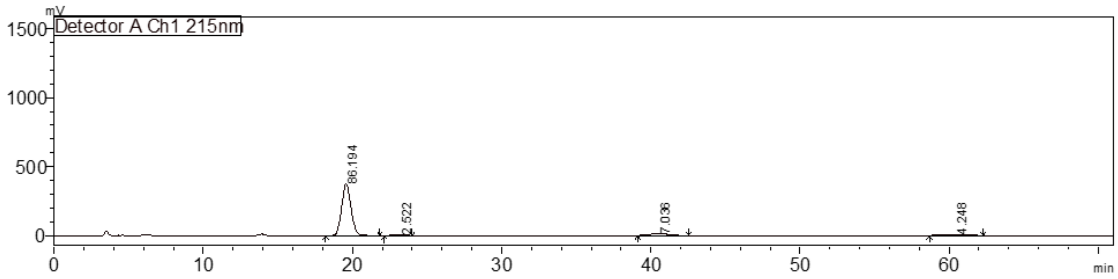


***tert*-butyl (*R*)-2-((*R*)-3-(benzo[d][1,3]dioxol-5-yl)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22k):** Colorless oil; 73% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.80 (dd, *J* = 18.5, 7.6 Hz, 1H), 7.69 – 7.57 (m, 1H), 7.55 – 7.38 (m, 2H), 6.85 – 6.68 (m, 3H), 5.93 (dq, *J* = 3.1, 1.6 Hz, 2H), 3.74 (dd, *J* = 17.7, 12.7 Hz, 2H), 3.55 (s, 3H), 3.52 – 3.42 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.00, 167.48, 151.03, 147.85, 147.56, 135.67, 135.60, 135.40, 128.36, 128.26, 127.77, 126.17, 124.95, 124.89, 124.00, 123.77, 117.02, 110.82, 110.62, 108.39, 101.24, 84.62, 84.44, 64.41, 54.49, 53.53, 53.37, 38.94, 36.43, 30.50, 27.84. HRMS (ESI) calcd for $C_{26}H_{26}NO_7$ m/z $[M+H]^+$: 464.1704; found: 464.1710; $[\alpha]_D^{22}$= +0.10 (c 0.14, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 215 nm, 22°C), 19.5 (major), 60.4 (minor), 91% ee.



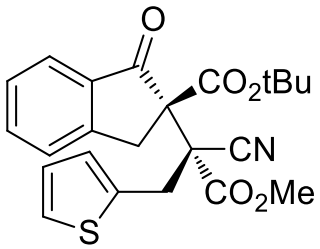
Detector A Channel 1 215nm

Peak#	Ret. Time	Area	Area%
1	19.800	1506620	4.891
2	23.140	13824002	44.874
3	40.466	14036637	45.565
4	60.591	1438703	4.670
Total		30805962	100.000

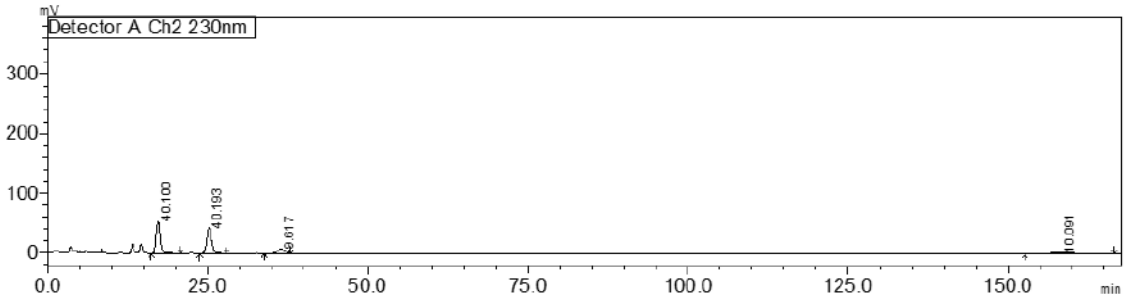


Detector A Channel 1 215nm

Peak#	Ret. Time	Area	Area%
1	19.572	16356103	86.194
2	23.178	478579	2.522
3	40.548	1335094	7.036
4	60.425	806065	4.248
Total		18975840	100.000

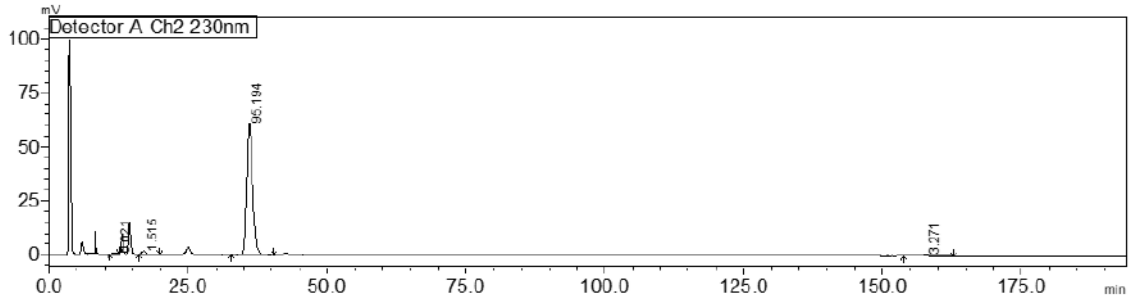


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxo-3-(thiophen-2-yl)propan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22l):** Colorless oil; 72% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.62 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.52 – 7.38 (m, 2H), 7.22 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.05 (dd, *J* = 3.5, 1.1 Hz, 1H), 6.96 (dd, *J* = 5.1, 3.4 Hz, 1H), 4.16 (d, *J* = 14.7 Hz, 1H), 3.89 – 3.74 (m, 2H), 3.64 (d, *J* = 32.4 Hz, 4H), 1.43 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.33, 166.74, 150.84, 135.46, 135.24, 134.85, 128.75, 127.97, 127.18, 126.95, 125.90, 125.87, 125.63, 124.67, 84.47, 76.53, 63.69, 53.46, 36.02, 33.18, 27.53. HRMS (ESI) calcd for $C_{23}H_{24}NO_5$ m/z $[M+H]^+$: 426.1370; found: 426.1374; $[\alpha]_D^{22}$= +0.09 (c 0.17, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 230 nm, 22°C), 35.9 (major), 157.9 min, 93% ee.



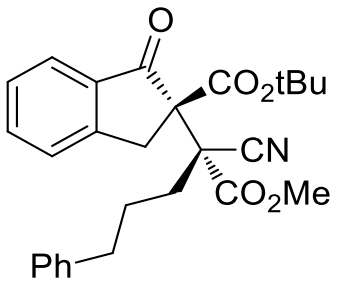
Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	17.195	2282070	40.100
2	25.167	2287391	40.193
3	36.420	547276	9.617
4	158.314	574270	10.091
Total		5691006	100.000



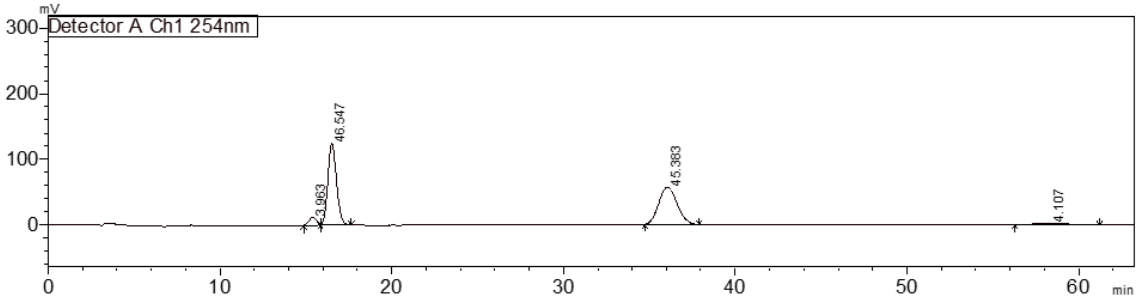
Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	12.079	1016	0.021
2	17.120	74669	1.515
3	35.996	4693219	95.194
4	157.933	161279	3.271
Total		4930184	100.000



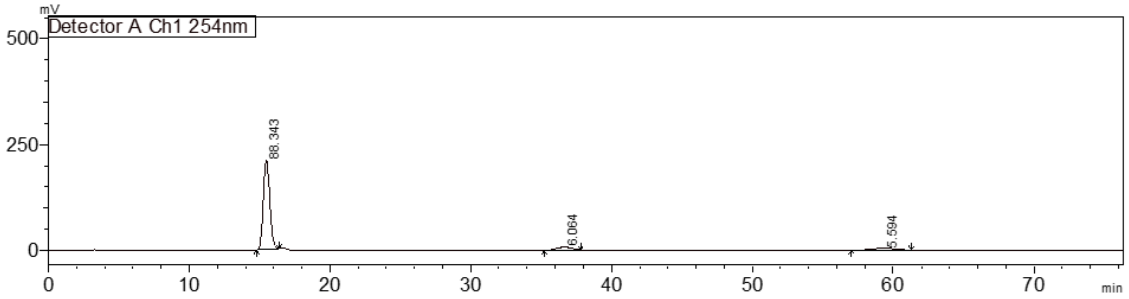
***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxo-5-phenylpentan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22m):** Colorless oil; 76% yield; TLC

(Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 7.6 Hz, 1H), 7.61 (td, *J* = 7.5, 1.2 Hz, 1H), 7.48 – 7.37 (m, 2H), 7.33 – 7.27 (m, 2H), 7.20 – 7.14 (m, 3H), 3.83 (d, *J* = 9.5 Hz, 1H), 3.66 – 3.56 (m, 4H), 2.69 (td, *J* = 7.0, 3.3 Hz, 2H), 2.41 (td, *J* = 12.3, 11.5, 3.2 Hz, 1H), 2.19 – 2.02 (m, 2H), 1.75 – 1.64 (m, 1H), 1.35 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.76, 167.61, 166.83, 151.13, 141.12, 135.62, 135.28, 128.74, 128.61, 128.51, 128.45, 128.22, 126.51, 126.25, 126.17, 124.87, 117.15, 84.54, 76.84, 64.31, 53.62, 52.47, 36.05, 35.53, 32.72, 27.73, 27.46. HRMS (ESI) calcd for $C_{27}H_{30}NO_5$ m/z $[M+H]^+$: 448.2118; found: 448.2110; $[\alpha]_D^{22}$= +0.05 (c 0.09, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 15.4 (major), 59.3 min, 89% ee.



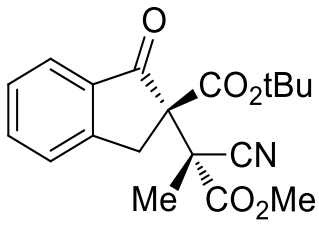
Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	15.395	373107	3.963
2	16.515	4381998	46.547
3	36.053	4272450	45.383
4	58.339	386605	4.107
Total		9414160	100.000

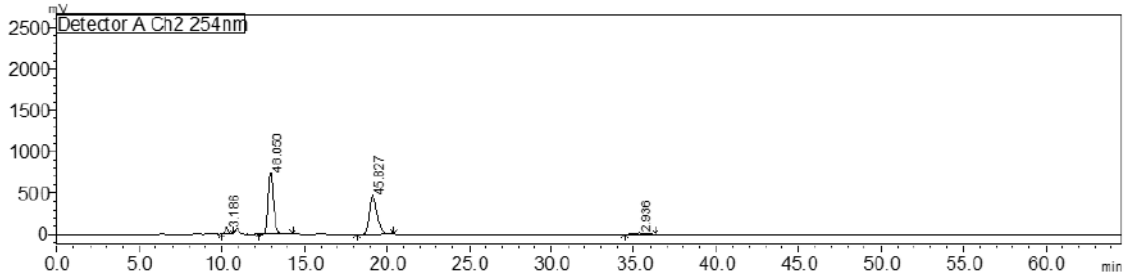


Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	15.475	6728710	88.343
2	36.635	461836	6.064
3	59.373	426038	5.594
Total		7616584	100.000

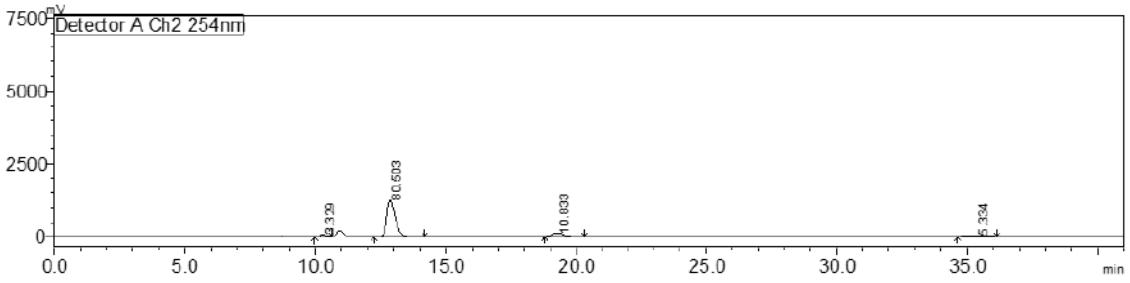


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22n):** Colorless oil; 81% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 7.6 Hz, 1H), 7.62 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.47 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.5 Hz, 1H), 3.90 (d, *J* = 4.2 Hz, 1H), 3.83 – 3.45 (m, 5H), 1.93 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.12, 167.78, 167.24, 151.36, 135.69, 135.65, 128.25, 126.17, 124.93, 118.23, 84.31, 63.27, 54.60, 53.91, 46.97, 37.27, 27.80, 20.60, 20.40. HRMS (ESI) calcd for $C_{19}H_{22}NO_5$ m/z $[M+H]^+$: 344.1492; found: 344.1490; $[\alpha]_D^{22}$= +0.18 (c 0.11, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 12.8 (major), 35.3 min, 78% ee.



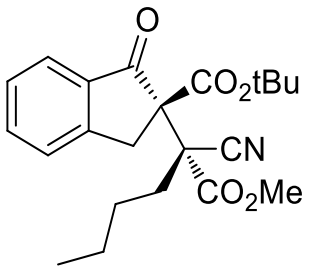
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	10.282	1071590	3.186
2	12.944	16159152	48.050
3	19.145	15411676	45.827
4	35.310	987471	2.936
Total		33629889	100.000



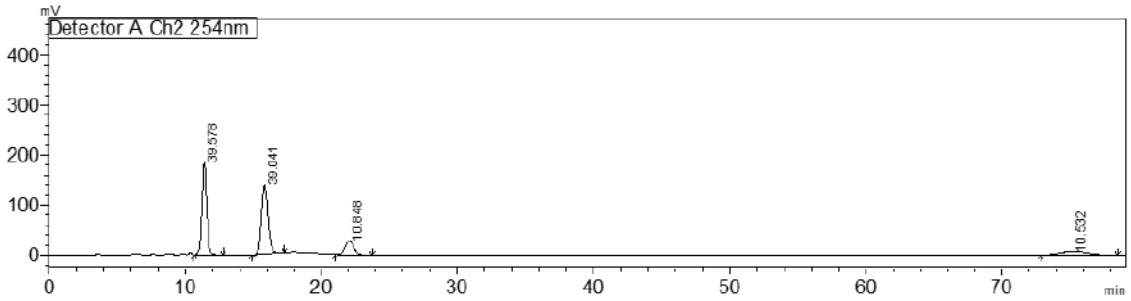
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	10.304	1155023	3.329
2	12.870	27929139	80.503
3	19.277	3758361	10.833
4	35.367	1850609	5.334
Total		34693132	100.000



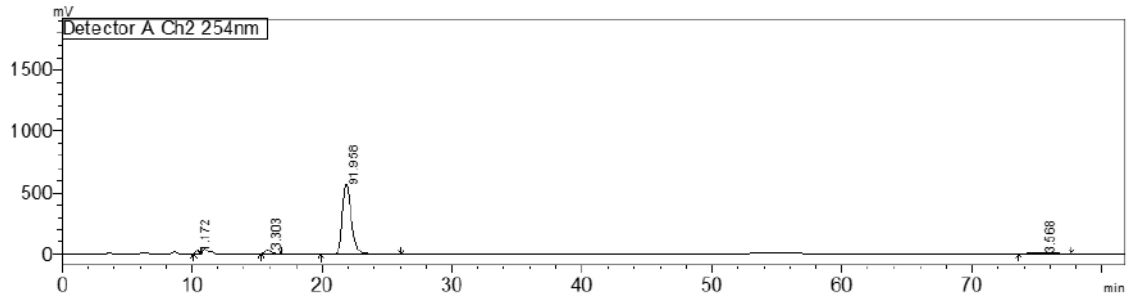
***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxohexan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22o):** Colorless oil; 80% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.27; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 7.7 Hz, 1H), 7.62 (td, *J* = 7.5, 1.2 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.5 Hz, 1H), 3.87 (s, 1H), 3.65 (s, 4H), 2.45 – 2.18 (m, 2H), 2.18 – 1.96 (m, 2H), 1.70 (ddd, *J* = 13.8, 10.5, 5.7 Hz, 2H), 1.40 (s, 9H), 0.93 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.90, 167.86, 151.12, 135.57, 135.41, 128.21, 126.17, 124.85, 117.35, 115.56, 84.45, 64.42, 54.30, 53.58, 52.52, 36.15, 34.47, 33.09, 28.04, 27.80, 22.68, 22.49, 13.89, 13.82. HRMS (ESI) calcd for $C_{23}H_{30}NO_5$ m/z $[M+H]^+$: 400.2118; found: 400.2116; $[\alpha]_D^{22}$=

+0.12 (c 0.11, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 15.7 (major), 27.4 min, 94% ee.



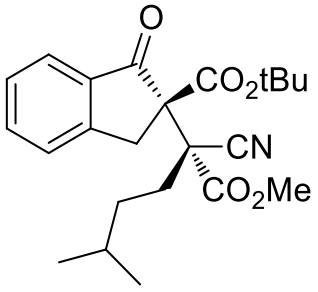
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	11.402	4510681	39.578
2	15.830	4449477	39.041
3	22.052	1236376	10.848
4	75.223	1200359	10.532
Total		11396893	100.000

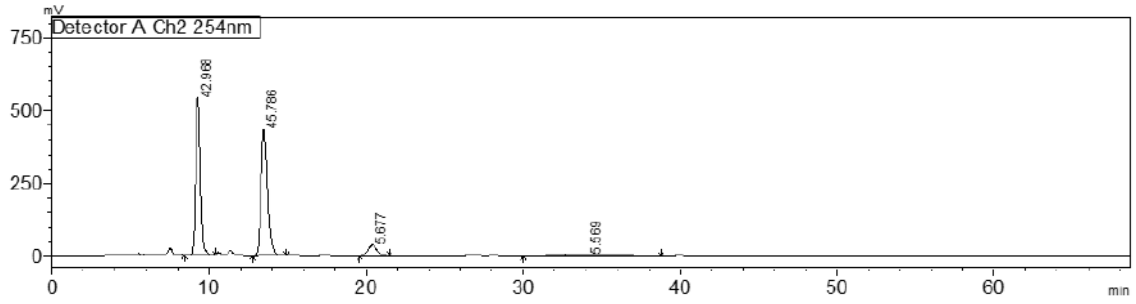


Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	10.350	344294	1.172
2	15.822	970622	3.303
3	21.835	27023404	91.958
4	75.388	1048421	3.568
Total		29386741	100.000

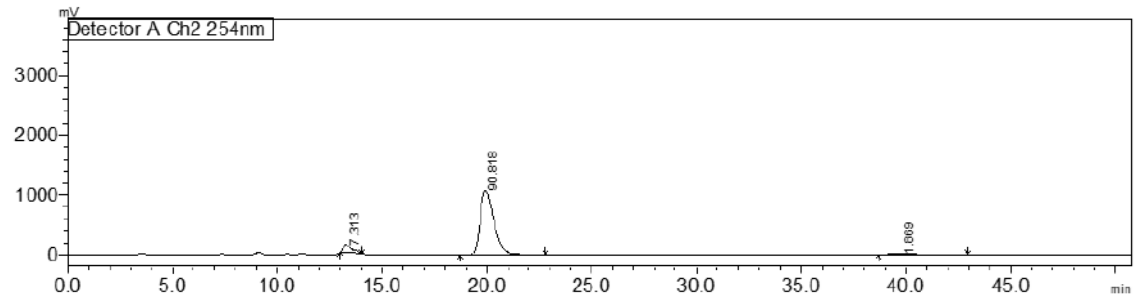


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-5-methyl-1-oxohexan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22p):** Colorless oil; 76% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (d, *J* = 7.7 Hz, 1H), 7.61 (td, *J* = 7.5, 1.2 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.40 (t, *J* = 7.4 Hz, 1H), 3.88 (d, *J* = 15.1 Hz, 1H), 3.65 (d, *J* = 12.3 Hz, 4H), 2.38 (dd, *J* = 13.0, 4.1 Hz, 1H), 2.20 – 2.03 (m, 1H), 1.61 (s, 2H), 1.41 (s, 9H), 1.24 – 1.16 (m, 1H), 0.92 (t, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.85, 167.79, 166.92, 151.15, 135.59, 135.33, 128.20, 126.17, 124.86, 117.32, 84.46, 77.48, 64.44, 53.55, 36.06, 34.69, 31.36, 28.24, 27.81, 22.51, 22.47. HRMS (ESI) calcd for $C_{23}H_{30}NO_5$ m/z $[M+H]^+$: 400.2118; found: 400.2121; $[\alpha]_D^{22}$= +1.10 (c 0.87, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 19.9 (major), 39.7 min, 96% ee.



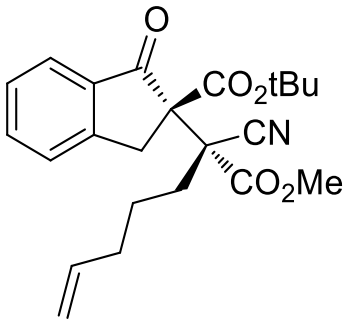
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	9.278	11867629	42.968
2	13.494	12645816	45.786
3	20.393	1567834	5.677
4	34.073	1538209	5.569
Total		27619488	100.000

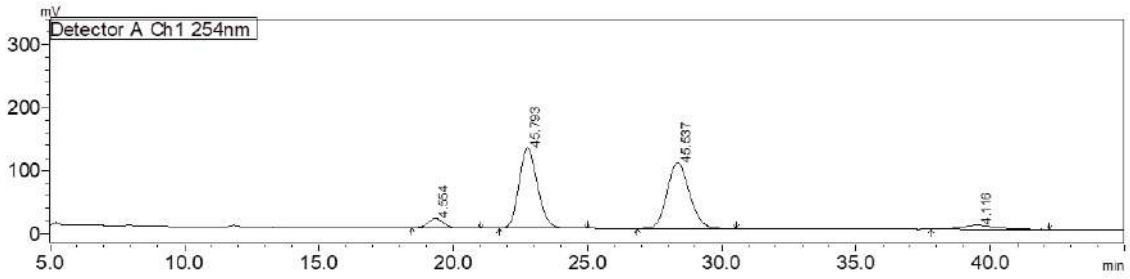


Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	13.295	3894003	7.313
2	19.928	48357220	90.818
3	39.726	995147	1.869
Total		53246369	100.000

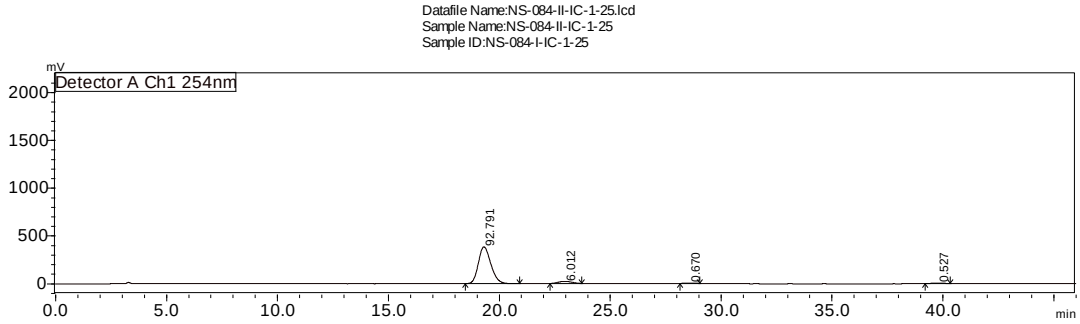


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxohept-6-en-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22q):** Colorless oil; 78% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.36; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (s, 1H), 7.62 (s, 1H), 7.53 – 7.33 (m, 2H), 5.96 – 5.62 (m, 1H), 5.03 (q, *J* = 12.7, 11.6 Hz, 2H), 4.01 – 3.73 (m, 2H), 3.64 (s, 3H), 2.21 (s, 1H), 2.13 (d, *J* = 7.8 Hz, 2H), 2.06 (d, *J* = 15.5 Hz, 1H), 1.83 (s, 1H), 1.48 (d, *J* = 7.6 Hz, 1H), 1.38 (d, *J* = 15.2 Hz, 9H). ^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 197.92, 167.71, 137.50, 136.80, 135.63, 134.06, 128.22, 128.09, 126.18, 125.21, 124.85, 116.28, 115.72, 115.42, 77.48, 54.41, 53.66, 52.36, 39.57, 36.02, 34.01, 33.36, 33.04, 32.67, 29.84, 27.83, 27.77, 27.76, 25.06, 24.84. HRMS (ESI) calcd for $C_{23}H_{28}NO_5$ m/z $[M+H]^+$: 398.1962; found: 398.1967; $[\alpha]_D^{22}$= +0.09 (c 0.24, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 15.7 (major), 27.4 min, 99% ee.



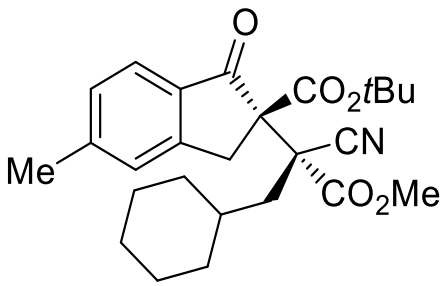
Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	19.340	609182	4.554
2	22.768	6125885	45.793
3	28.352	6091540	45.537
4	39.510	550627	4.116
Total		13377234	100.000



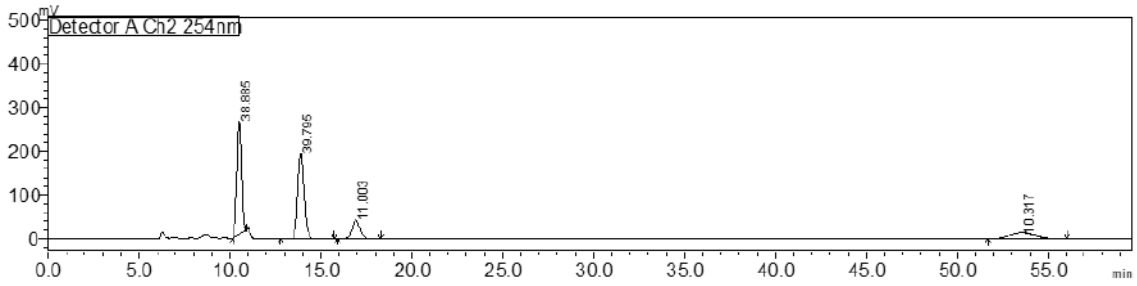
Detector A Channel 1 254nm

Peak#	Ret. Time	Area	Area%
1	19.308	15067428	92.791
2	22.951	976307	6.012
3	28.580	108717	0.670
4	39.777	85641	0.527
Total		16238092	100.000



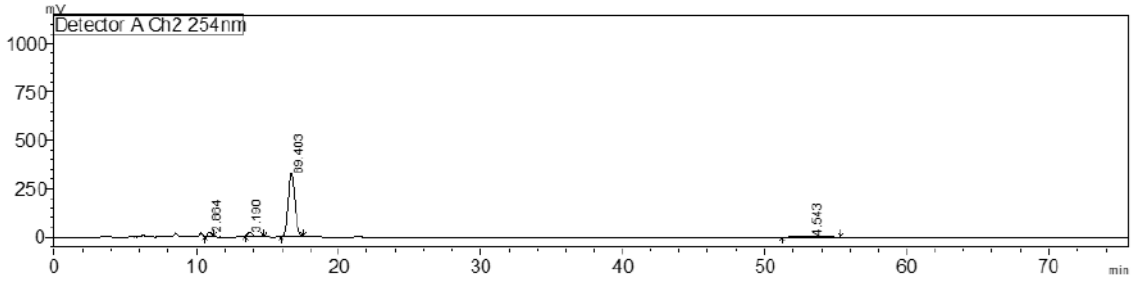
***tert*-butyl (*R*)-2-((*R*)-2-cyano-3-cyclohexyl-1-methoxy-1-oxopropan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22r):** Colorless oil; 74% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 7.8 Hz, 1H), 7.24 – 7.13 (m, 2H), 3.67 – 3.48 (m, 5H), 2.44 (s, 3H), 2.28 (dd, *J* = 13.8, 4.8 Hz, 1H), 2.04 (dd, *J* = 13.8, 7.0 Hz, 1H), 1.95 (d, *J* = 12.7 Hz, 1H), 1.75 – 1.57 (m, 6H), 1.42 (s, 9H), 1.28 (dddd, *J* = 16.1, 13.0, 6.7, 3.4 Hz, 2H), 1.19 – 1.00 (m, 2H), 0.90 (dd, *J* = 12.1, 2.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.14, 166.99, 151.83, 147.08, 132.98, 129.48, 126.51, 124.73, 117.34, 84.36, 77.48, 64.76, 53.61,

51.49, 39.85, 35.70, 35.60, 34.38, 33.38, 27.86, 26.23, 22.30. HRMS (ESI) calcd for $C_{26}H_{34}NO_5$ m/z $[M+H]^+$: 440.2431; found: 440.2438; $[a]_D^{22}$= +0.20 (c 0.21, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 16.6 (major), 53.2 min, 91% ee.



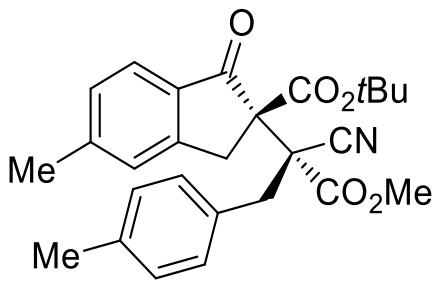
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	10.519	4477913	38.885
2	13.894	4582689	39.795
3	16.930	1267099	11.003
4	53.570	1188044	10.317
Total		11515744	100.000

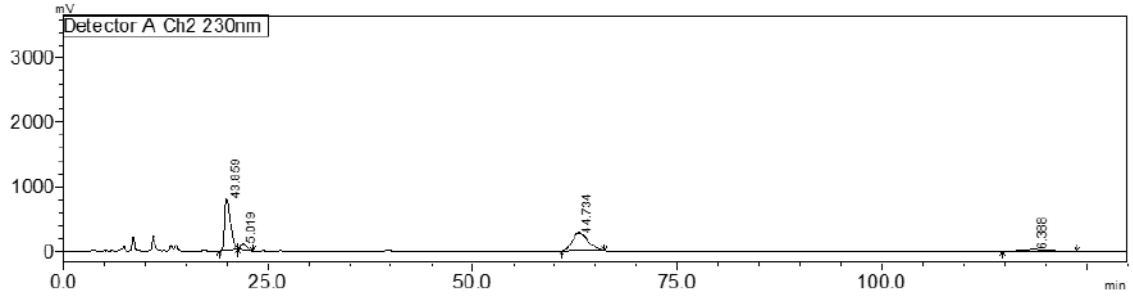


Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	10.902	331749	2.864
2	13.746	369467	3.190
3	16.666	10354526	89.403
4	53.223	526168	4.543
Total		11581909	100.000

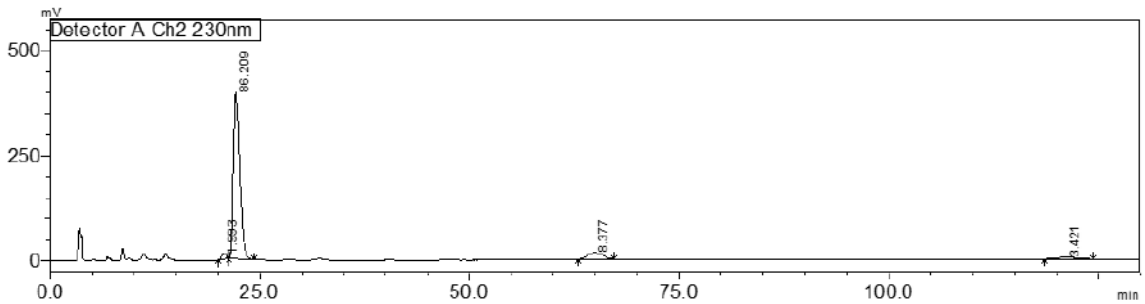


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxo-3-(p-tolyl)propan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22s):** Colorless oil; 73% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 2.1 Hz, 1H), 7.24 – 7.14 (m, 3H), 7.11 (d, *J* = 8.0 Hz, 2H), 3.79 (d, *J* = 13.5 Hz, 1H), 3.72 – 3.65 (m, 2H), 3.48 (d, *J* = 21.1 Hz, 4H), 2.46 (d, *J* = 3.9 Hz, 3H), 2.31 (d, *J* = 4.8 Hz, 3H), 1.44 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.40, 167.50, 151.63, 147.12, 137.73, 133.11, 131.17, 130.40, 130.17, 129.63, 129.51, 129.31, 126.49, 124.75, 117.14, 84.44, 77.48, 64.49, 54.60, 53.38, 38.82, 36.27, 27.86, 22.31, 21.24. HRMS (ESI) calcd for $C_{27}H_{30}NO_5$ m/z $[M+H]^+$: 448.2118; found: 448.2122; $[\alpha]_D^{22}$= +0.08 (c 0.18, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 230 nm, 22°C), 22.1 (major), 121.2 min, 92% ee.



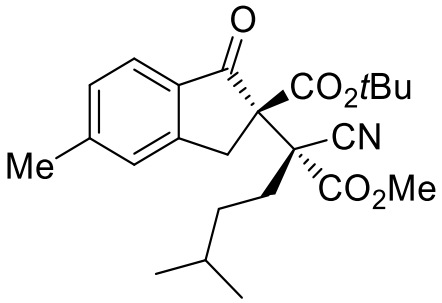
Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	19.949	36909655	43.859
2	21.948	4224040	5.019
3	63.013	37645720	44.734
4	118.601	5376072	6.388
Total		84155487	100.000

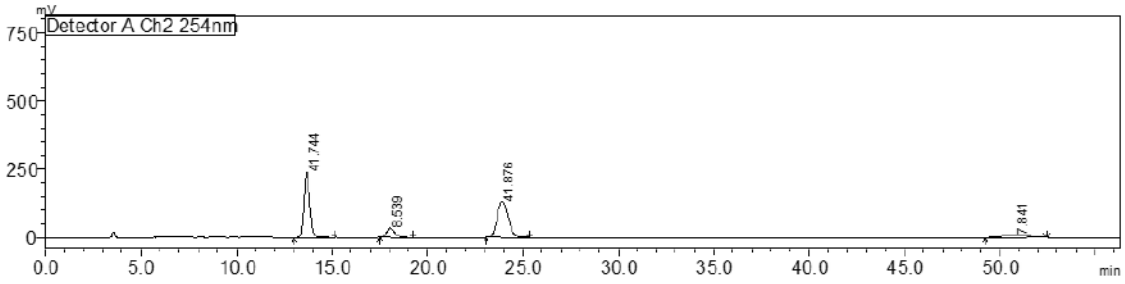


Detector A Channel 2 230nm

Peak#	Ret. Time	Area	Area%
1	20.715	469856	1.993
2	22.147	20324636	86.209
3	64.952	1974952	8.377
4	121.171	806605	3.421
Total		23576049	100.000

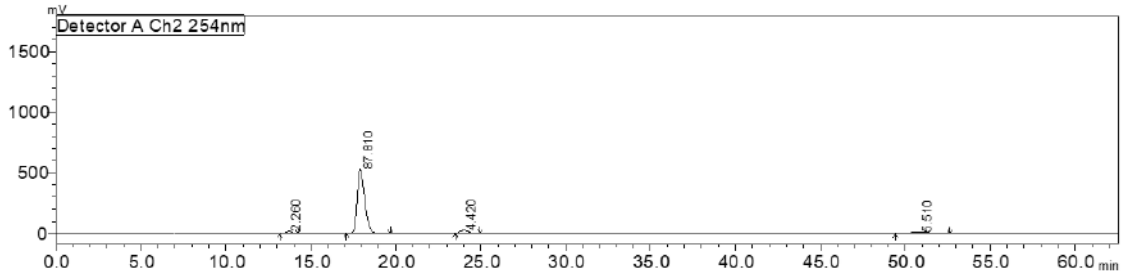


***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-5-methyl-1-oxohexan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22t):** Colorless oil; 73% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.15 (m, 2H), 3.73 – 3.51 (m, 5H), 2.44 (s, 3H), 2.37 (dd, *J* = 13.1, 4.1 Hz, 1H), 2.18 – 2.06 (m, 1H), 1.66 – 1.59 (m, 2H), 1.42 (s, 9H), 1.26 – 1.19 (m, 1H), 0.92 (t, *J* = 6.4 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.18, 167.79, 167.01, 151.71, 147.07, 133.01, 129.50, 126.49, 124.73, 117.37, 84.33, 77.48, 64.46, 53.54, 52.80, 35.88, 34.71, 31.29, 28.24, 27.83, 22.52, 22.48, 22.30. HRMS (ESI) calcd for $C_{24}H_{32}NO_5$ m/z $[M+H]^+$: 414.2275; found: 414.2279; $[a]_D^{22}$= +0.09 (c 0.13, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 15.7 (major), 27.4 min, 88% ee.



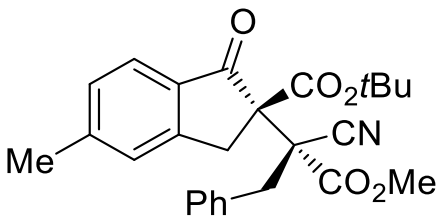
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	13.685	5258734	41.744
2	18.053	1075639	8.539
3	23.932	5275309	41.876
4	50.836	987765	7.841
Total		12597447	100.000



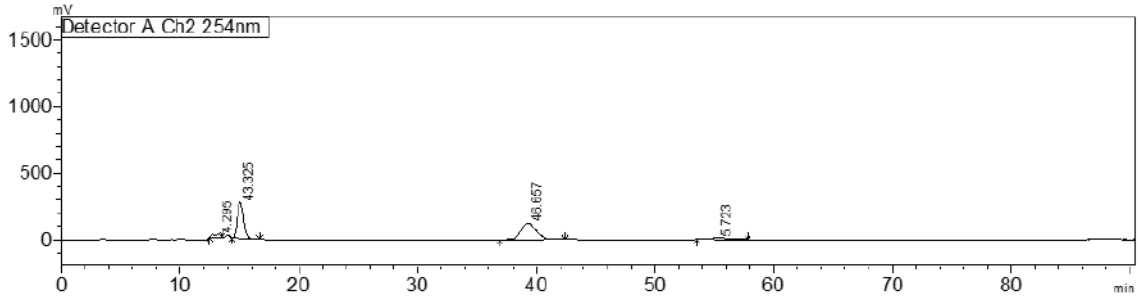
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	13.703	419941	2.260
2	17.900	16319448	87.810
3	24.005	821472	4.420
4	50.861	1024016	5.510
Total		18584878	100.000



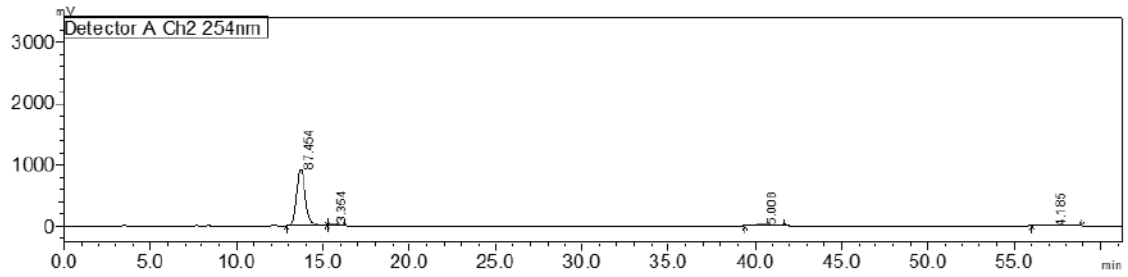
***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22u):** Colorless oil; 81% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 7.9 Hz, 1H), 7.28 (d, *J* = 15.1 Hz, 7H), 7.22 (d, *J* = 8.0 Hz, 1H), 4.04 – 3.62 (m, 4H), 3.50 (s, 4H), 1.44 (s, 11H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.43, 167.07, 151.62, 147.17, 134.35, 133.14, 130.57, 129.55, 128.61, 128.06, 126.51, 124.78, 84.49, 77.48, 64.53, 53.39, 39.20, 36.34, 29.85, 27.88, 27.86, 22.33. HRMS (ESI) calcd for $C_{26}H_{28}NO_5$ m/z $[M+H]^+$: 434.1962; found: 434.1967; $[a]_D^{22}$= +0.09 (c 0.12, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 13.7

(major), 57.2 min, 91% ee.



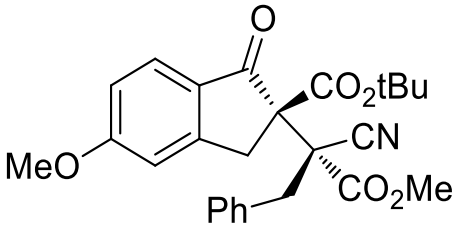
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	13.223	1007880	4.295
2	15.051	10165826	43.325
3	39.313	10947623	46.657
4	55.286	1342782	5.723
Total		23464111	100.000



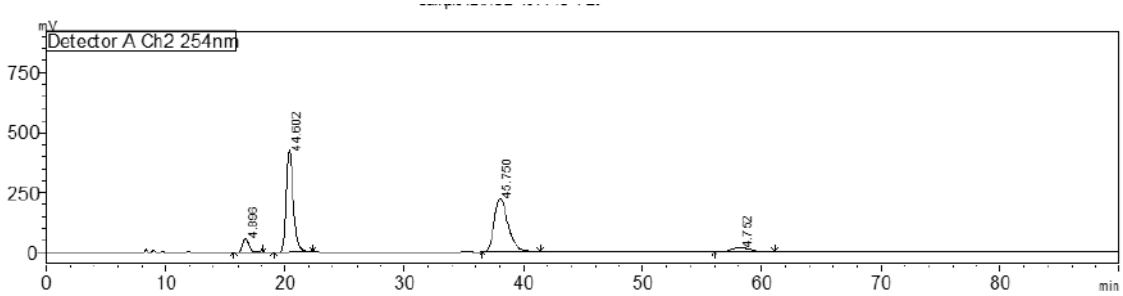
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	13.690	32819205	87.454
2	15.610	1258532	3.354
3	40.463	1879433	5.008
4	57.238	1570359	4.185
Total		37527529	100.000



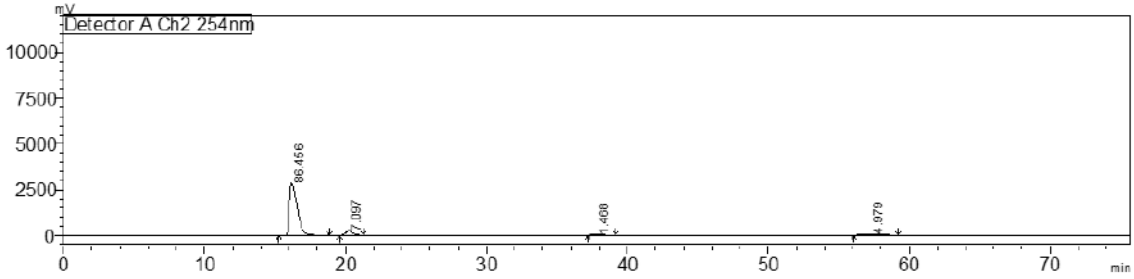
***tert*-butyl (*R*)-2-((*R*)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22v):** Colorless oil; 73% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.20; ^1H NMR (400 MHz, Chloroform-*d*) δ 7.77 (d, *J* = 9.5 Hz, 1H), 7.28 (d, *J* = 11.3 Hz, 5H), 6.96 (d, *J* = 10.8 Hz, 1H), 6.90 (s, 1H), 3.91

(s, 3H), 3.83 – 3.50 (m, 4H), 3.44 (s, 3H), 1.44 (d, *J* = 16.3 Hz, 9H). ^{13}C NMR (100 MHz, CHLOROFORM-*D*) δ 195.89, 165.76, 129.99, 128.27, 127.71, 126.44, 116.05, 109.05, 84.00, 77.16, 55.62, 27.53. HRMS (ESI) calcd for $C_{26}H_{28}NO_6$ m/z $[M+H]^+$: 450.1911; found: 450.1910; $[a]_D^{22}$= +1.01 (c 0.24, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 210 nm, 22°C), 16.1 (major), 57.3 min, 90%.



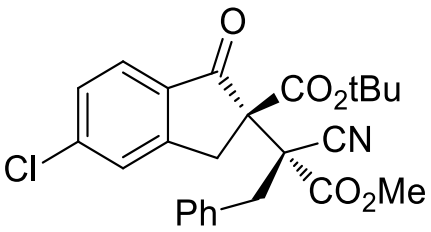
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	16.678	4035076	4.887
2	20.347	37000779	44.808
3	38.031	38048936	46.078
4	58.180	3490763	4.227
Total		82575554	100.000

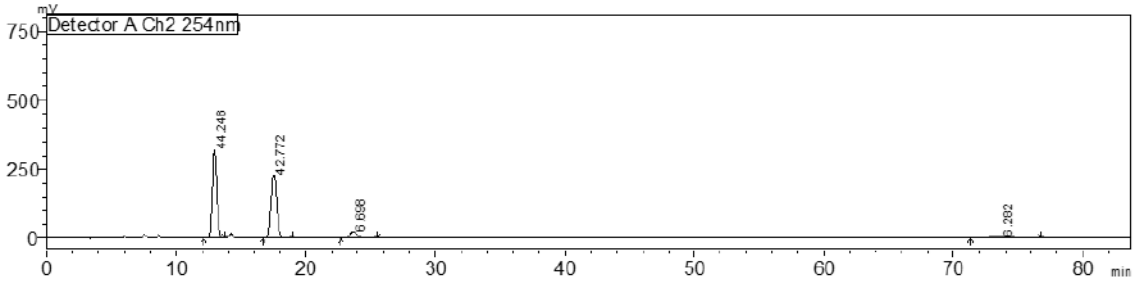


Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	16.178	111850852	86.456
2	20.242	9182064	7.097
3	37.861	1898719	1.468
4	57.325	6440955	4.979
Total		129372591	100.000

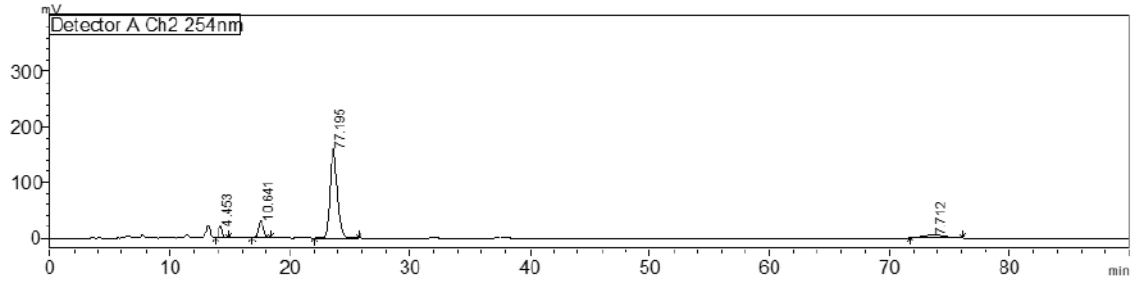


***tert*-butyl (*R*)-5-chloro-2-((*R*)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22w):** Colorless oil; 80% yield; TLC (Hexane:Et_2O, 70:30 v/v): R_f = 0.30; ^{1}H NMR (396 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 8.2 Hz, 1H), 7.46 (s, 1H), 7.37 – 7.27 (m, 5H), 3.89 – 3.59 (m, 4H), 3.52 (s, 3H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 172.29, 163.98, 160.79, 146.56, 135.60, 123.28, 122.95, 122.76, 122.64, 115.14, 74.16, 73.66, 71.92, 71.44, 71.15, 70.98, 69.64, 66.30, 57.81, 47.66, 27.82. HRMS (ESI) calcd for $C_{25}H_{25}ClNO_5$ m/z $[M+H]^+$: 454.1416; found: 454.1423; $[\alpha]_D^{22}$= +0.24 (c 0.37, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 254 nm, 22°C), 23.6 (major), 73.7 min, 83% ee.



Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	12.921	7325215	44.248
2	17.510	7080997	42.772
3	23.665	1108918	6.698
4	73.650	1039950	6.282
Total		16555080	100.000



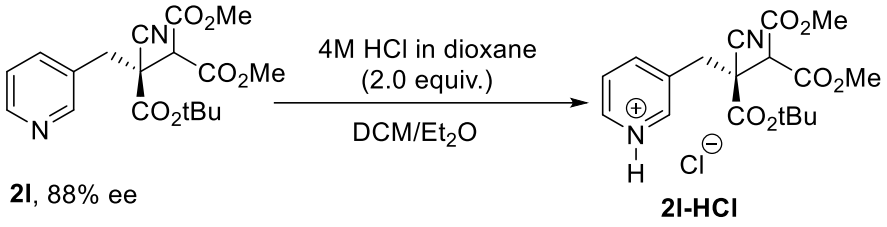
Detector A Channel 2 254nm

Peak#	Ret. Time	Area	Area%
1	14.209	395095	4.453
2	17.573	944147	10.641
3	23.610	6849577	77.195
4	73.713	684318	7.712
Total		8873137	100.000

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

The absolute configurations of **3d**, **5h**, and **9c** are determined by X-ray crystallography. For other products, the absolute configurations are determined by analogy. The supplementary crystallographic data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(A) The absolute configuration of **2l** was determined by the single-crystal structure of **2l**'s salt: **2l-HCl**.



2l, 88% ee

2l-HCl

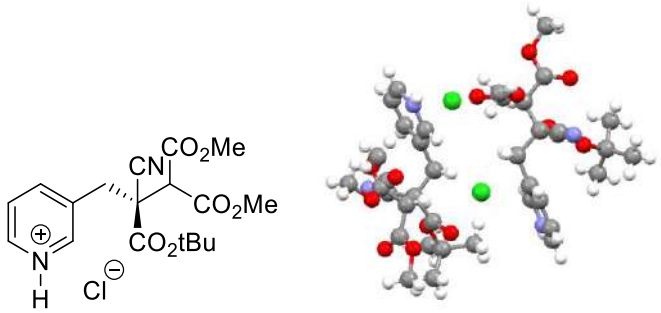
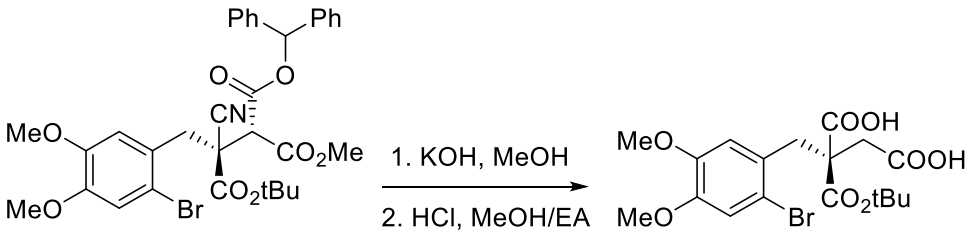


Figure 14.1 Single-crystal structure of **2l-HCl** (CCDC 2034184)

(B) The absolute configuration of the quaternary carbon for the vicinal tertiary-quaternary stereocenters was determined by the single-crystal structure of di-carboxylic acid **ST-2** after hydrolysis of **ST-1**:



ST-1
90% ee, 9:1 dr

ST-2

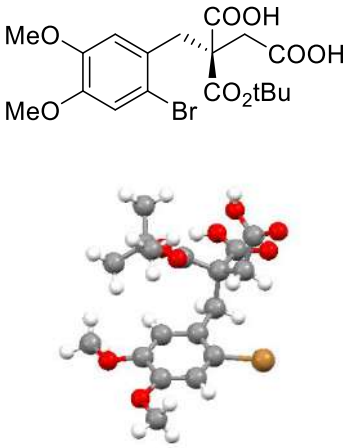


Figure 14.2 Single-crystal structure of **2l-HCl** (CCDC 2053152)

The absolute configuration at the tertiary chiral center was determined with the aid of density functional theory (DFT) calculated isotropic chemical shift. Various attempts to determine the absolute configuration by X-ray crystallography were not successful. From the 1H spectrum of **ST-1**, there is a small difference in chemical shift between the major and minor diastereomer (see Figure 14.3 and Figure). In order to determine if the compound has a R, S or R, R configuration, the order of these peaks that is ascribed to the proton on the tertiary chiral center will be utilized.

Computational Detail

Conformation sampling were performed with CREST[5,6] at GFN2-XTB[7] level of theory with ALPB implicit solvation to model $CHCl_3$. The following command line arguments were used in the CREST calculations:

```
-gfn2 -T 80 -tstep 3 --alpb CHCl3 -ewin 10.0
```

DFT calculations were done with ORCA 4.2.1.[8] Single point calculations on the conformers generated by CREST that are within a window of 6.0 kcal/mol were performed at CPCM/wB97X-V/def2-TZVPP.

```
!wB97X-V def2-tzvpp def2-tzvpp/C def2/J RIJCOSX VeryTightSCF Grid5 GridX7
NoFinalGrid CPCM(Chloroform)
%cpcm     surfacetype vdw_gaussian end
```

Conformers within 2.2 kcal/mol for the RR and 2.1 kcal/mol for the RS were optimized at B97-3c.[9] Vibrational frequencies calculations at the same level of theory were calculated to characterize the stationary points. Vibrational entropy was calculated according to the Quasi RRHO equations[10] The ORCA input for the geometry optimization is:

```
!RKS Opt VeryTightOpt
!B97-3c Grid6 NoFinalGrid
!Numfreq
%Freq
    Temp 253.15
end
```

Further single point calculations at CPCM/DLPNO-revDSD-PBEB86[11]-D3(BJ)/def2-QZVPP[12] were performed. The auxillary basis sets def2/J[13] and def2-QZVPP/C[14] are used. The ORCA input for DLPNO-revDSD-PBEPB86-D3(BJ) calculation:

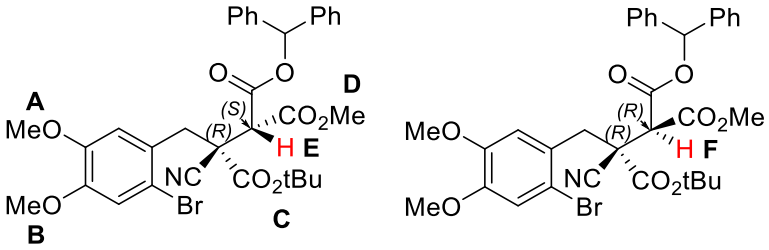
```
!RKS d3bj VeryTightSCF def2-qzvpp def2-qzvpp/C rijcosx def2/j tightPNO Grid6
GridX7 NoFinalGrid CPCM(Chloroform)
%method
    Exchange X_PBE
    Correlation C_P86
    ScalHFX 0.69
    ScalDFX 0.31
    ScalGGAC 0.4296
    ScalLDAC 0.4296
    ScalMP2C 1.0
    D3S6 0.4377
    D3A2 5.5
    D3S8 0.0
    D3A1 0.0
end
%mp2
    DoSCS true
    PS 0.5785
    PT 0.0799
    DLPNO true
end
```

Boltzmann distribution were calculated at 253.15K with the Free energy calculated at CPCM/DLPNO-revDSD-PBEB86-D3(BJ)/ def2-QZVPP //B97-3c with free energy

correction at B97-3c. NMR chemical shift were calculated at CPCM/B3LYP-D3(BJ)/pc-Sseg3[15]//B97-3c. The cc-pwCVQZ/C[16-18] auxillary basis set is used. The relevant ORCA input:

```
!NMR B3LYP D3BJ RIJCOSX VeryTightSCF Grid6 GridX8 NoFinalGrid NoFinalGridX CPCM(Chloroform)
!pcSseg-3 cc-pwCVQZ/C
%MaxCore 16000
%pal nprocs 10
      end
%cpcm    surfacetype vdw_gaussian end
%eprnmr
     giao_2el giao_2el_rijcosx
end
%basis AuxJ "def2/JK" end
%method Z_GridX_RHS 2 end
```

Table 14.1 The Boltzmann weighted isotropic chemical shifts relative to TMS



Proton(s)	Experimental/ppm[a]	Calculated/ppm	Scaled calculated/ppm[b]
A	3.86	4.00[c]	3.91[c]
B	3.83	3.85[c]	3.78[c]
C	1.25	0.92[c]	1.25[c]
D	3.69	3.76[c]	3.70[c]
E	4.30	4.52	4.35
F	4.28	4.46	4.30

[a] In $CDCl_3$ at 253K [b] The average isotropic chemical shifts of all protons is reported. [c] scaled chemical shift = (calculated chemical shift + 0.53) / 1.1599. This is determined by a linear regression of proton A-D.

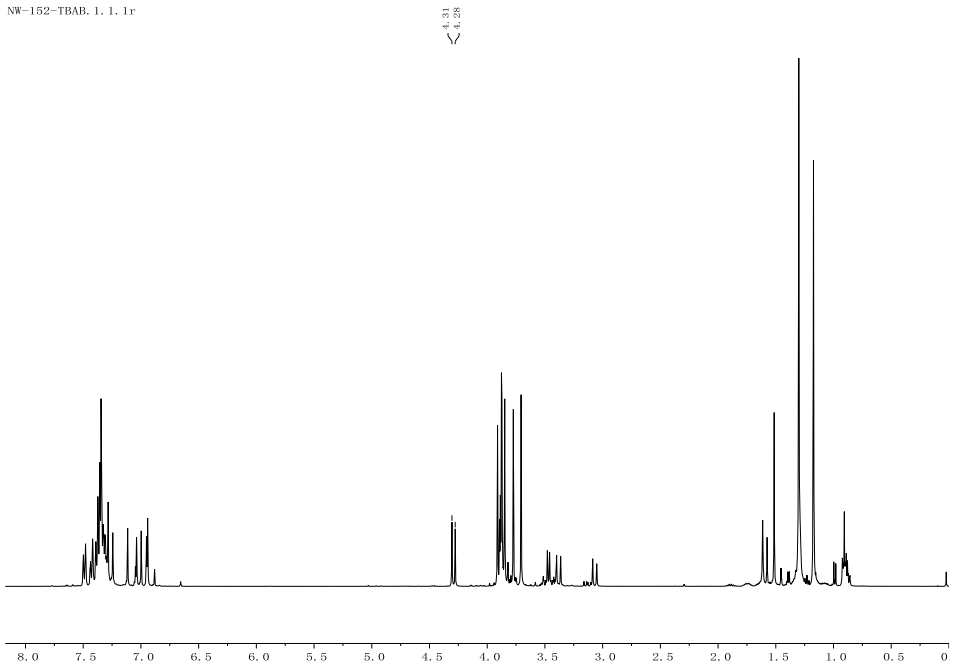


Figure 14.3 Racemic sample (HNMR, $CDCl_3$, room temperature)

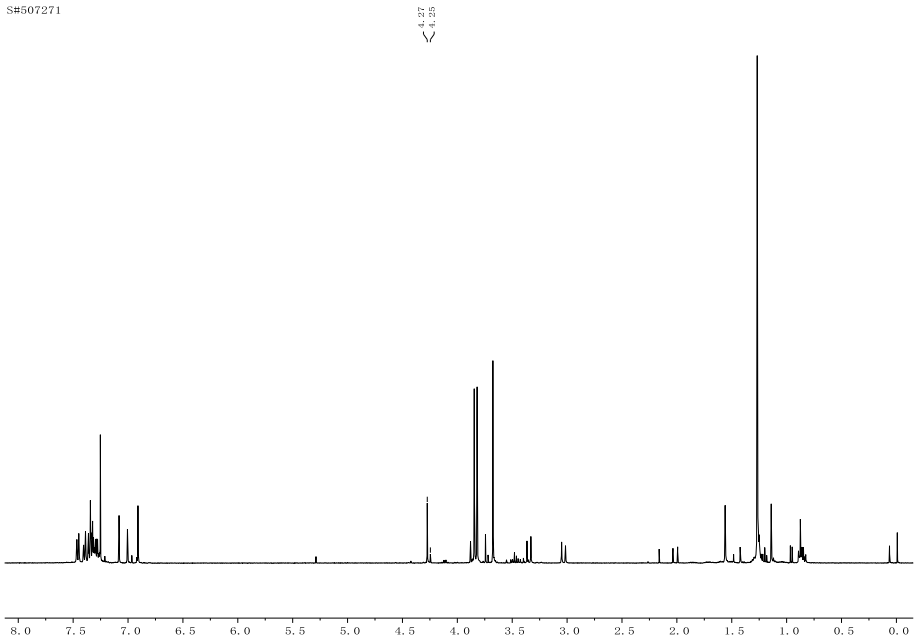


Figure 14.4 Non-racemic sample (NMR, $CDCl_3$, room temperature)

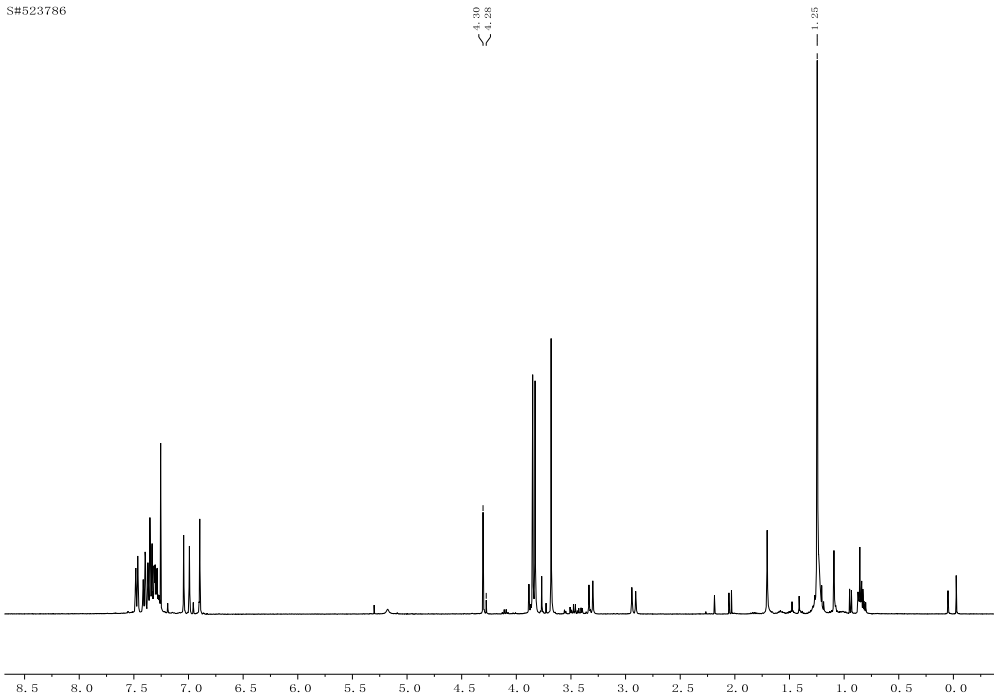
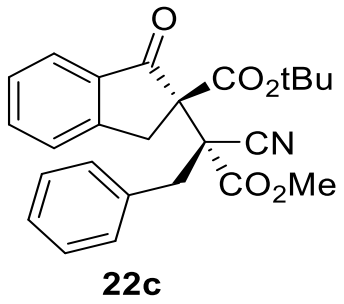


Figure 14.5 Non-racemic sample (NMR, CDCl3, -20°C)

(C) Single-crystal structure of **22c**



22c

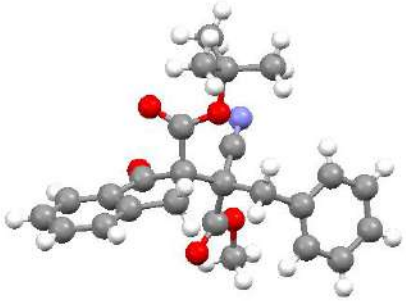
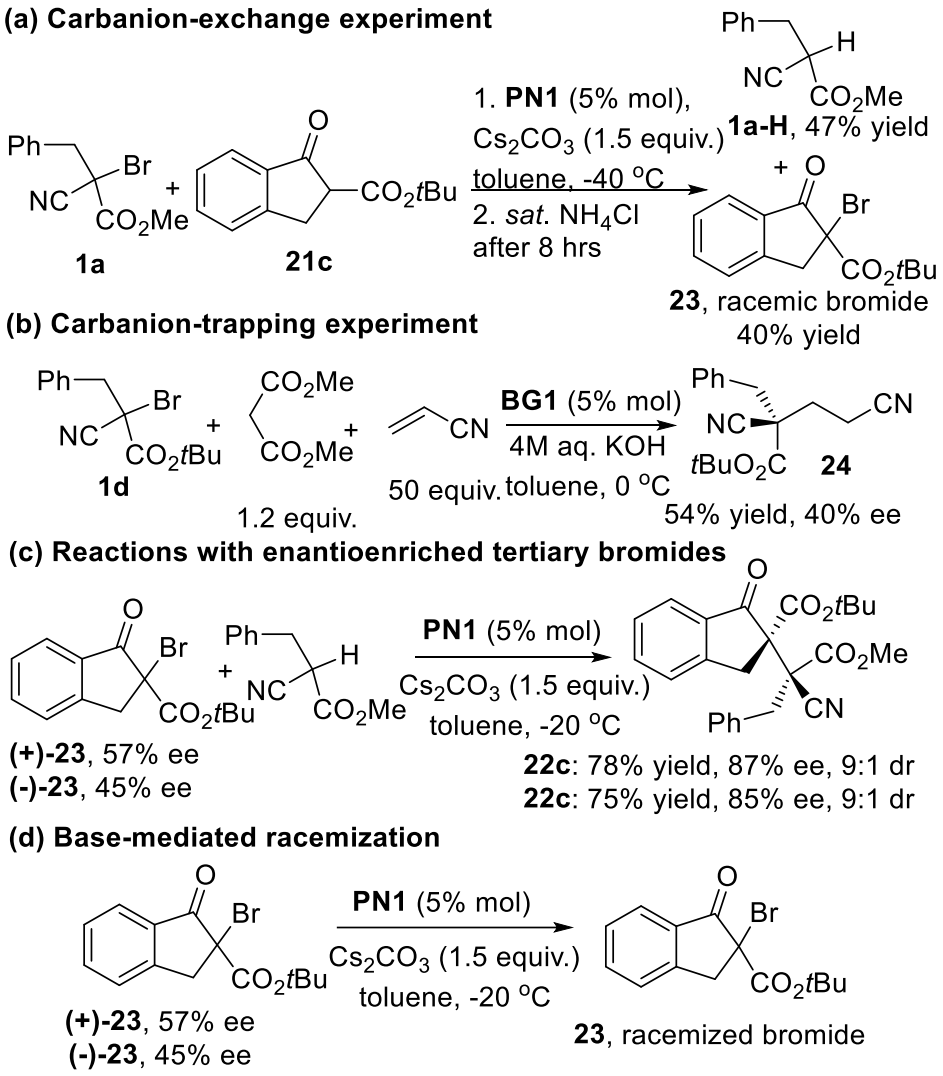


Figure 14.3 Single-crystal structure of **21c** (CCDC 2033879)

15.Control experiments



a) Carbanion-exchange experiment: The mixture of **1a** (1.0 equiv.), **21c** (1.0 equiv.) and **PN1** (1.0 equiv.) in toluene was cooled to -40 °C, and then Cs_2CO_3 was added, stirring continued for 8 hrs, sat. NH_4Cl (aq.) was added to the reaction mixture to quench it. DCM was employed to extract the mixture then washed with water, the organic layer was then separated and concentrated for silica gel column to isolate **1a-H** (54% yield) and **23** (54% yield) in sequence.

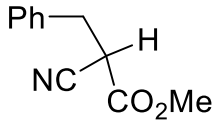
b) Carbanion trapping experiment: The mixture of bromide **1d** (1.0 equiv.), malonate (1.0 equiv.)**,** acrylonitrile (1.0 equiv.) and **BG1** (1.0 equiv.) in toluene was cooled to 0 °C, and the base 4M aq. KOH was added, stirring continued overnight, sat. NH_4Cl (aq.) was added to the reaction mixture to quench it. The organic layer was

then separated for silica gel column to isolate compound **24** (54% yield).

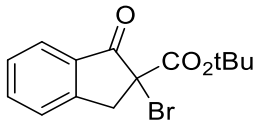
c) Reactions with enantioenriched tertiary bromides: enantioenriched tertiary bromides (+)-**23** (57% ee) and (-)-**23** (45% ee) (prepared from the kinetic resolution of racemic **23**) was added to a solution of 1a-H and PN1 in toluene separately, then cooled them to -20 °C, Cs_2CO_3 was last added. After 3 days, sat. NH_4Cl (aq.) was added to the reaction mixture to quench it. The organic layer was then separated for silica gel column, producing same stereoisomer of **22c**.

d) Base-mediated racemization: enantioenriched tertiary bromides (+)-**23** (57% ee) and (-)-**23** (45% ee) (prepared from the kinetic resolution of racemic **23**) was dissolved into toluene separately, then cooled them to -20 °C, Cs_2CO_3 and **PN1** was added. After 3 days, sat. NH_4Cl (aq.) was added to the reaction mixture to quench it. The organic layer was then separated for silica gel column.

16. Characterization of compounds in control experiments

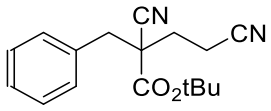


Methyl 2-cyano-3-phenylpropanoate (**1a-H**): 80% yield; colorless oil; TLC (Hexane:Et_2O, 80:20 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.22 (m, 5H), 3.77 (d, *J* = 1.1 Hz, 3H), 3.74 (dd, *J* = 8.4, 5.7 Hz, 1H), 3.27 (dd, *J* = 13.8, 5.8 Hz, 1H), 3.18 (dd, *J* = 13.8, 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.07, 135.31, 129.05, 128.97, 128.94, 127.86, 127.81, 116.09, 77.47, 77.16, 76.84, 53.56, 39.56, 35.77. HRMS (ESI) calcd for $C_{11}H_{12}NO_2$ m/z $[M+H]^+$: 190.0863; found: 190.0875.

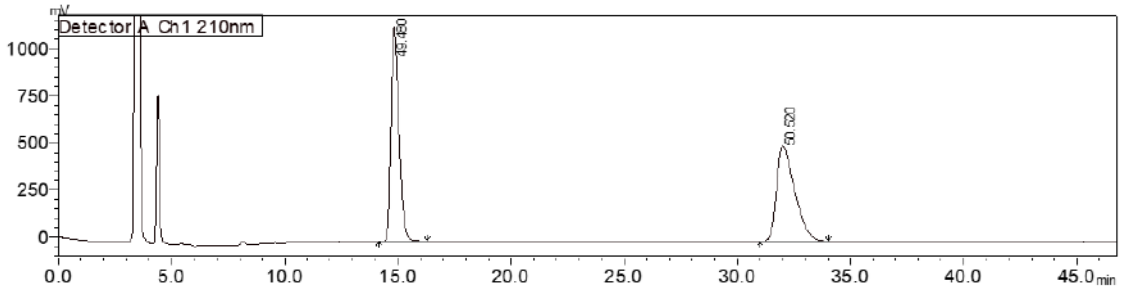


tert-butyl 2-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (23): yellow solid; mp: 123-126 °C; 70% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.40; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.93 – 7.80 (m, 1H), 7.67 (dd, *J* = 7.5, 1.2 Hz, 1H), 7.54 – 7.40

(m, 2H), 4.12 (d, *J* = 18.0 Hz, 1H), 3.65 (d, *J* = 18.0 Hz, 1H), 1.45 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.51, 165.77, 150.23, 136.01, 132.55, 128.42, 126.22, 125.83, 84.41, 77.32, 77.21, 77.00, 76.69, 59.84, 43.98, 27.71. HRMS (ESI) calcd for $C_{14}H_{16}BrO_3$ m/z $[M+H]^+$: 311.0277; found: 311.0284.

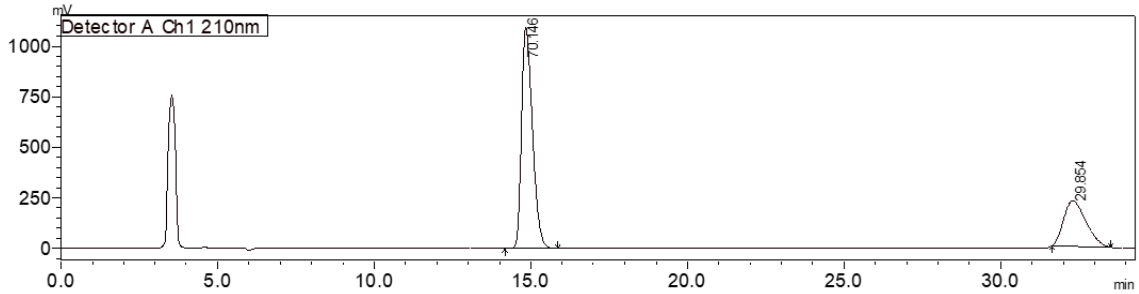


tert-butyl 2-benzyl-2,4-dicyanobutanoate (24): Colorless oil; 78% yield; TLC (Hexane:Et_2O, 90:10 v/v): R_f = 0.30; ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.22 (m, 6H), 3.19 (d, *J* = 13.7 Hz, 1H), 3.06 (d, *J* = 13.4 Hz, 1H), 2.71 – 2.55 (m, 1H), 2.51 – 2.30 (m, 2H), 2.14 (d, *J* = 5.6 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.09, 133.19, 130.20, 128.81, 128.32, 117.75, 85.61, 43.13, 32.48, 27.77. HRMS (ESI) calcd for $C_{17}H_{21}N_2O_2$ m/z $[M+H]^+$: 285.1598; found: 285.1587; $[\alpha]_D^{22}$= +10.2 (c 0.37, $CHCl_3$); HPLC analysis: Chiralcel IC (Hex/IPA = 80/20, 1.0 mL/min, 210 nm, 22°C), 14.8 (major), 32.3 min, 40% ee.



Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	14.830	27740866	49.480
2	32.010	28323603	50.520
Total		56064469	100.000



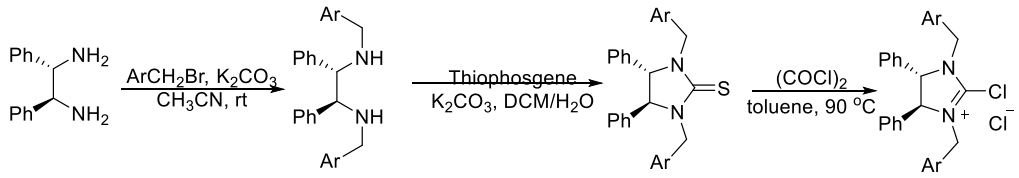
Detector A Channel 1 210nm

Peak#	Ret. Time	Area	Area%
1	14.842	26320228	70.146
2	32.305	11201661	29.854
Total		37521888	100.000

17. Typical procedure for PN and BG catalysts preparation

All the chiral PTCs, including the pentaniduim and bisguanidium salts, are prepared according to our methods reported before.[4]

Synthesis of imidazoline salts



Imidzoline salts

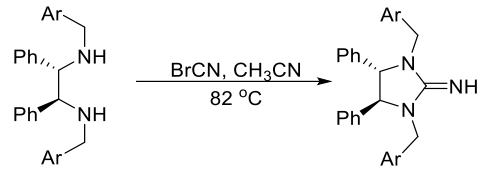
Step a) To a mixture of chiral diamine (1.0 equiv) and K_2CO_3 (2.2 equiv) in dry MeCN was added 2-bromo-3,5-di-tert butylbenzyl bromide (2.05 equiv) by using a syringe pump in 1 h, and then the reaction mixture was stirred overnight at room temperature, TLC monitored the reaction. After substrates was completely consumed, water was added to quench the reaction then extracted with CH_2Cl_2 (30 mL × 3). The combined organic layer was washed by brine and dried by Na_2SO_4 and the solvent was removed under reduced pressure for silica gel column (hexane-ethyl acetate 50:1 to 25:1 as eluent) to afford a white solid.

Step b) To a solution of dialkylated diamine (1.0 equiv) in DCM was added (2.2 equiv) in 1.5 mL H_2O. The resulting mixture was stirred vigorously followed by the dropwise addition of an anhydrous CH_2Cl_2 solution of triphosgene (0.33 equiv) at 0 oC. Then the mixture was warmed to rt and further stirred for 2 h to complete the reaction. The reaction mixture was then extracted with CH_2Cl_2 (5 mL ×3). The combined organic layer was washed by brine and dried by Na_2SO_4. Solvent was removed under reduced pressure for purity by flash chromatograph to afford a white solid.

Step c) To a solution of D (1.0 equiv) in toluene (3 mL) with a condenser under N_2

atmosphere was added $(COCl)_2$ (8.0 equiv) via syringe in one portion. The mixture was refluxed overnight until D was completely reacted. Toluene was removed under reduced pressure and solid imidazoline salt was obtained for the next step with no purification.

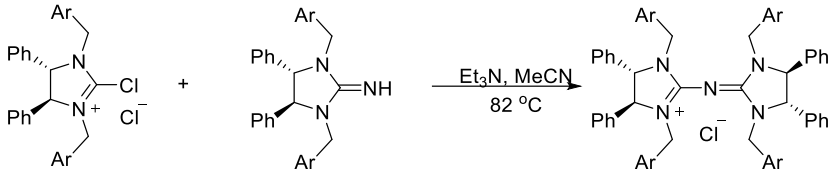
Synthesis of imidazolidine imines



Imidazolidine imines

To a solution of dialkylated diamine (1.0 equiv) in dry MeCN (5 mL) under N_2 was added BrCN (1.0 equiv) in MeCN in one portion. And then the mixture was heated to reflux for 12 h, and then cooled to rt, solvent was removed under reduced pressure for purification by flash chromatography, to afford a white hygroscopic powder.

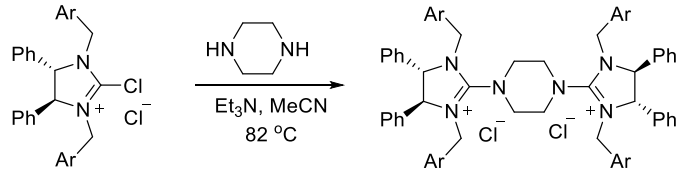
Synthesis of Chiral Pentanidium salts



Imidzoline salts **Imidazolidine imines** **chiral pentanidium salts**

The imidazoline salt (1.0 wquiv.) was dissolved in dry MeCN (3 mL) under N2, and then imidazolidine imine (0.4 equiv) was added, followed by the addition of Et_3N (3.0 equiv). Then the whole solution was heated to reflux for 12 h and cooled to rt. Solvent was removed under reduced pressure and PTC was obtained by flash chromatography (silica gel, DCM-Methanol 100:1-20:1), as a beige powder.

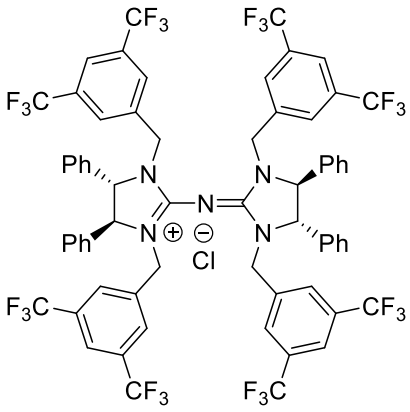
Synthesis of Chiral Bisguanidium salts



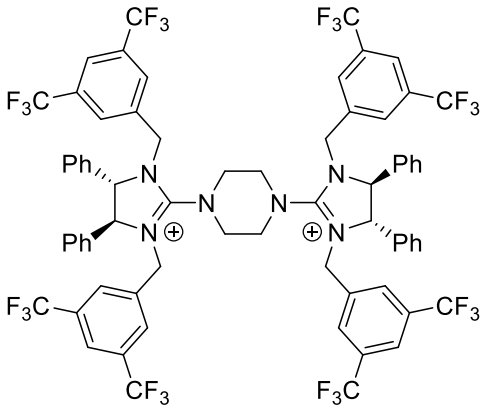
Imidzoline salts **chiral Bisguanidium salts**

The imidazoline salt was dissolved in dry MeCN (3 mL) under N_2, and then piperazine

(0.3 equiv) was added, followed by the addition of Et_3N (6.0 equiv). Then the whole solution was heated to reflux for 12 h and cooled to rt. Solvent was removed under reduced pressure and PTC was obtained by flash chromatography (silica gel, DCM-Methanol 100:1-20:1), as a beige powder.



(4S,5S)-2-(((4S,5S)-1,3-bis(3,5-bis(trifluoromethyl)benzyl)-4,5-diphenylimidazolidin-2-ylidene)amino)-1,3-bis(3,5-bis(trifluoromethyl)benzyl)-4,5-diphenyl-4,5-dihydro-1H-imidazol-3-ium chloride (PN1): white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s, 4H), 7.77 (s, 9H), 7.11 (d, J = 7.2 Hz, 12H), 6.99 (t, J = 7.6 Hz, 9H), 5.13 – 5.00 (m, 4H), 4.92 (s, 8H). ^{19}F NMR (377 MHz, DMSO) δ -61.84, -61.88. ^{13}C NMR (101 MHz, DMSO) δ 159.23, 139.54, 134.99, 130.78, 130.45, 129.58, 129.18, 128.75, 128.65, 124.81, 122.10, 70.47, 49.58, 40.64, 40.43, 40.22, 40.01, 39.80, 39.59, 39.39. HRMS (ESI) calcd for $C_{66}H_{44}N_5F_{24}$ m/z $[M\text{-}Cl]^+$: 1362.3213; found: 1362.3212; $[\alpha]_D^{22}$= +0.29 (c 0.37, $CHCl_3$).



(4S,4'S,5S,5'S)-2,2'-(piperazine-1,4-diyl)bis(1,3-bis(3,5-bis(trifluoromethyl)benzyl)-4,5-diphenyl-4,5-dihydro-1H-imidazol-3-ium)

chloride (BG1): white solid; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.94 (s, 8H), 7.79 (s, 4H), 7.56 (dt, *J* = 8.0, 2.1 Hz, 8H), 7.33 – 7.00 (m, 11H), 5.90 (d, *J* = 17.4 Hz, 4H), 4.95 (s, 4H), 4.72 (d, *J* = 18.3 Hz, 4H), 4.23 (d, *J* = 6.9 Hz, 4H), 3.64 (d, *J* = 7.0 Hz, 4H). ^{19}F NMR (377 MHz, DMSO) δ -61.34. ^{13}C NMR (101 MHz, DMSO) δ 139.93, 135.82, 130.05, 129.71, 129.58, 129.42, 128.79, 128.30, 125.01, 122.29, 74.57, 54.16, 40.43, 40.22, 40.01, 39.80, 39.60. HRMS (ESI) calcd for $C_{70}H_{52}N_6F_{24}$ m/z $[M\text{-}2Cl]^+$: 1432.3859; found: 716.1920; $[\alpha]_D^{22}$= +10.2 (c 0.29, $CHCl_3$)

18. Reference

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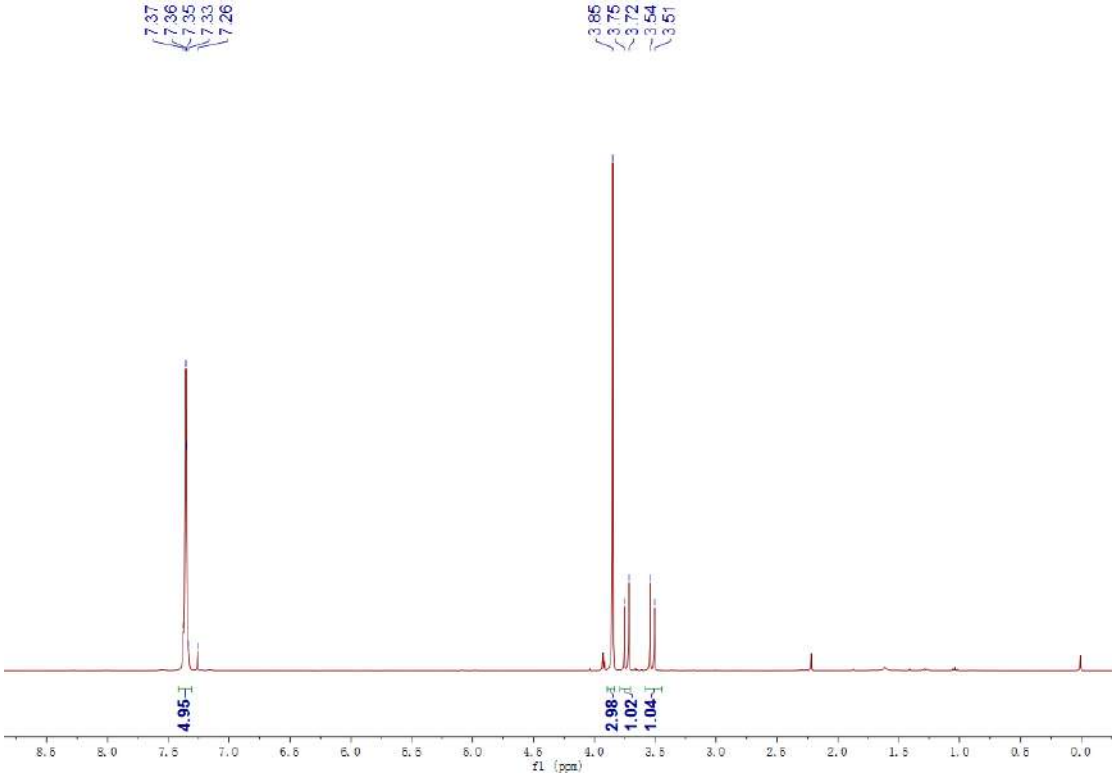
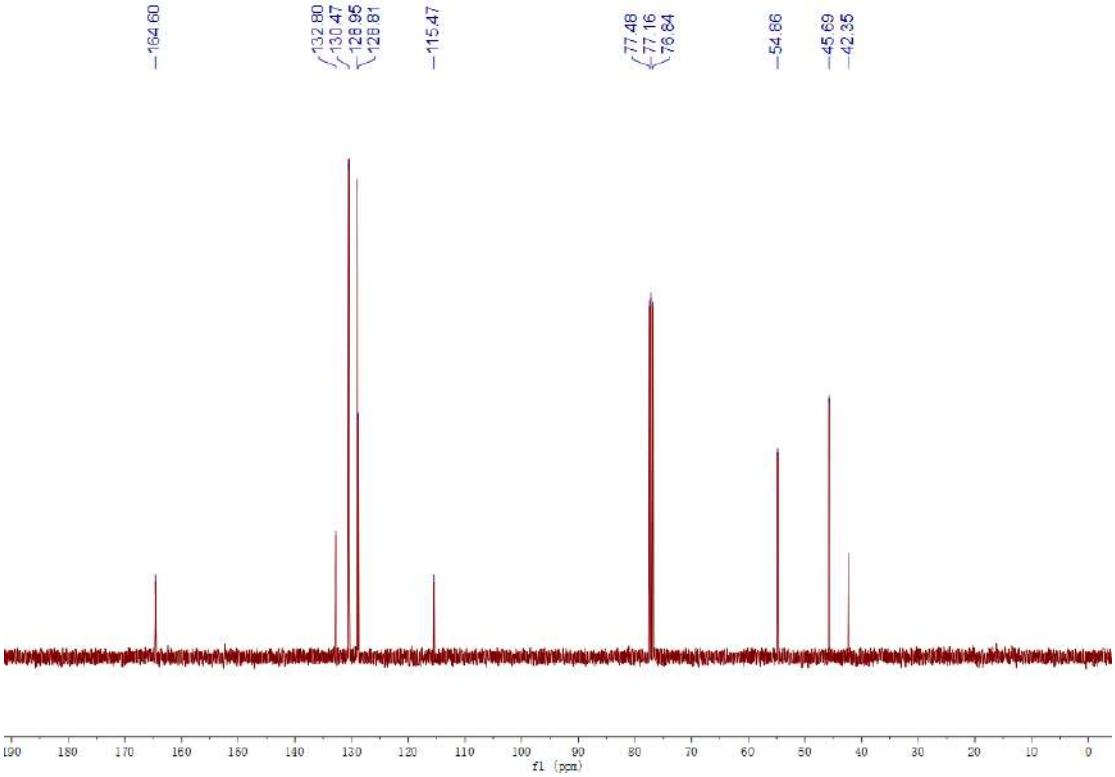
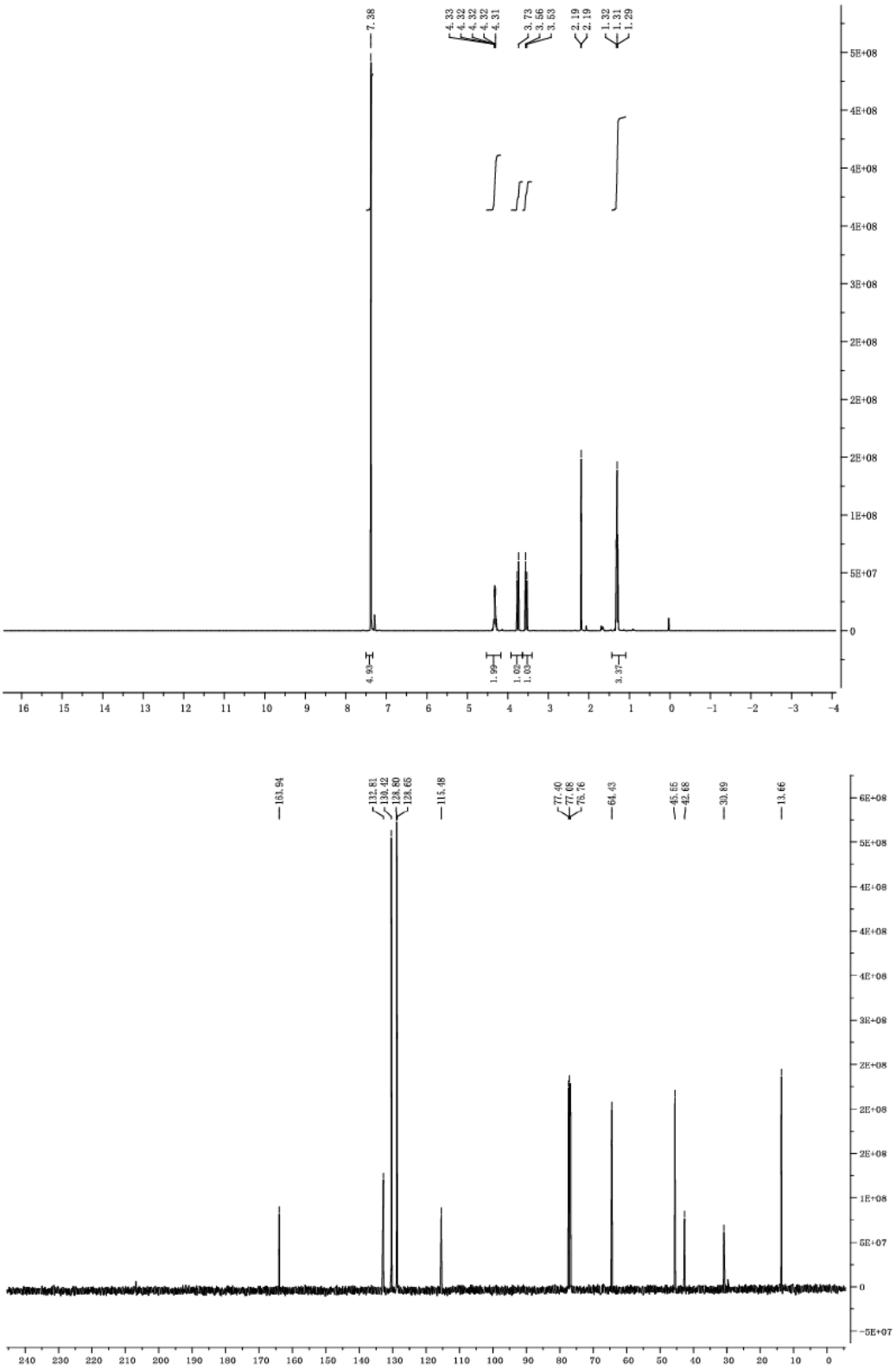
Copy of NMR spectra

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

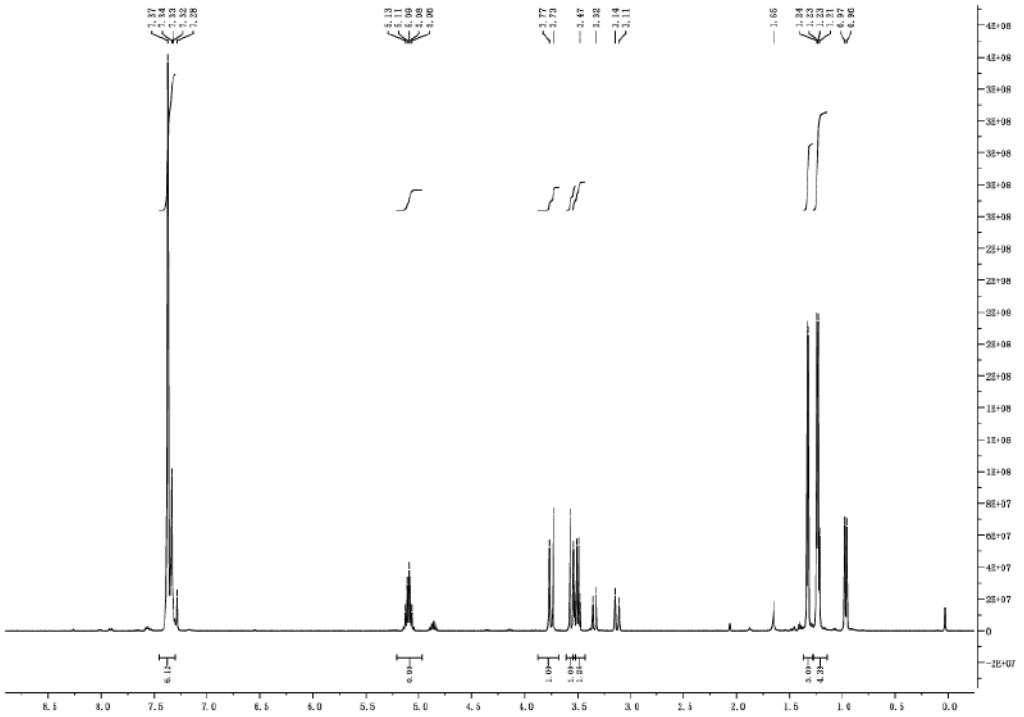


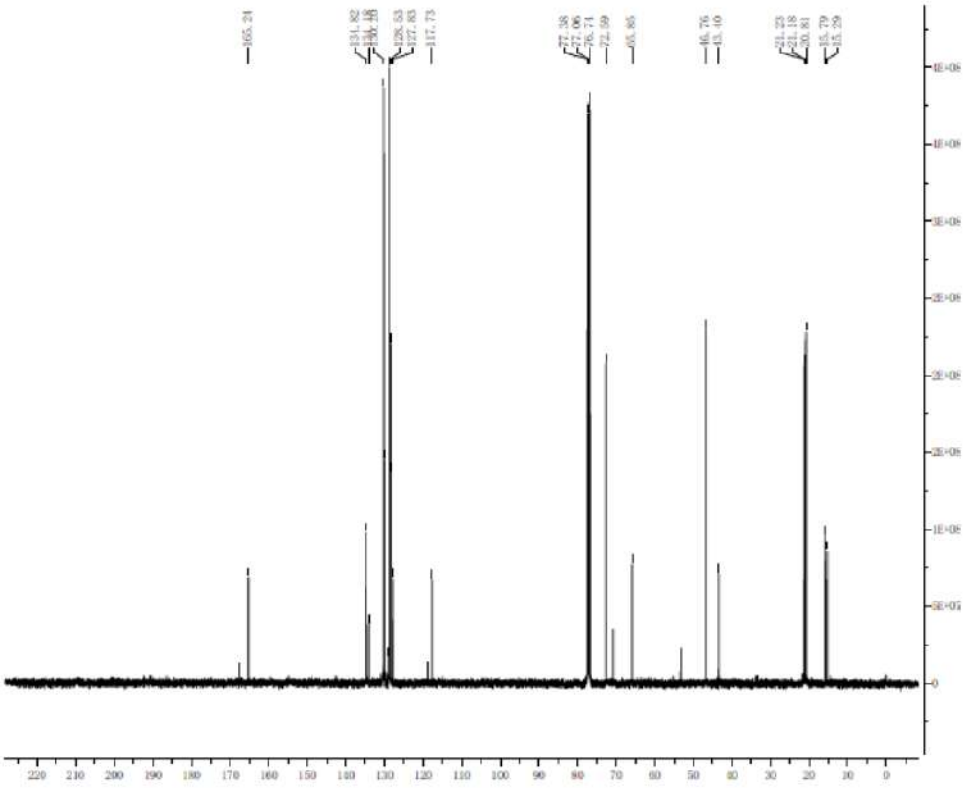


Ethyl 2-bromo-2-cyano-3-phenylpropanoate (1b)

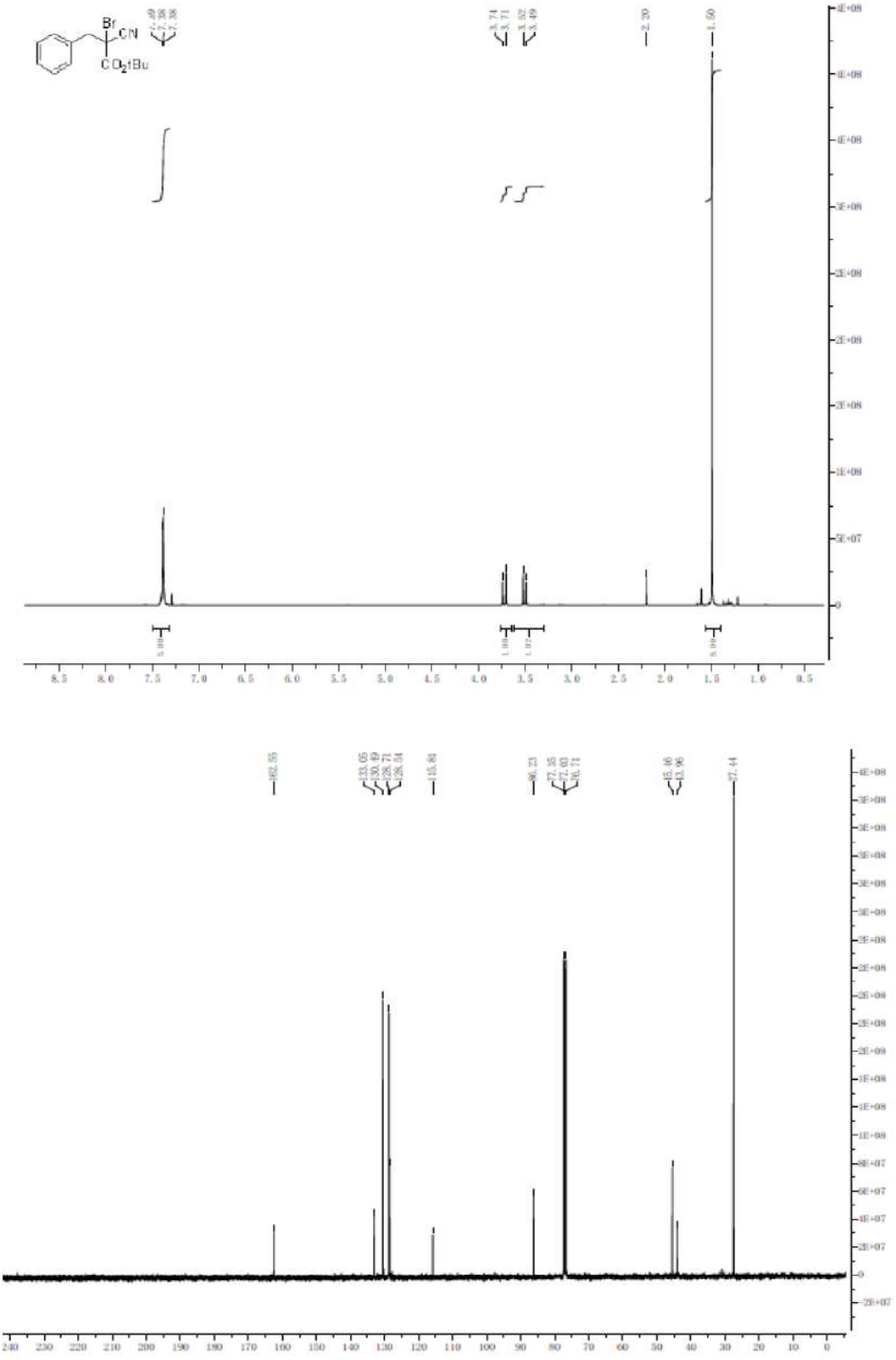


***Iso*propyl 2-cyano-2-iodo-3-phenylpropanoate (1c)**

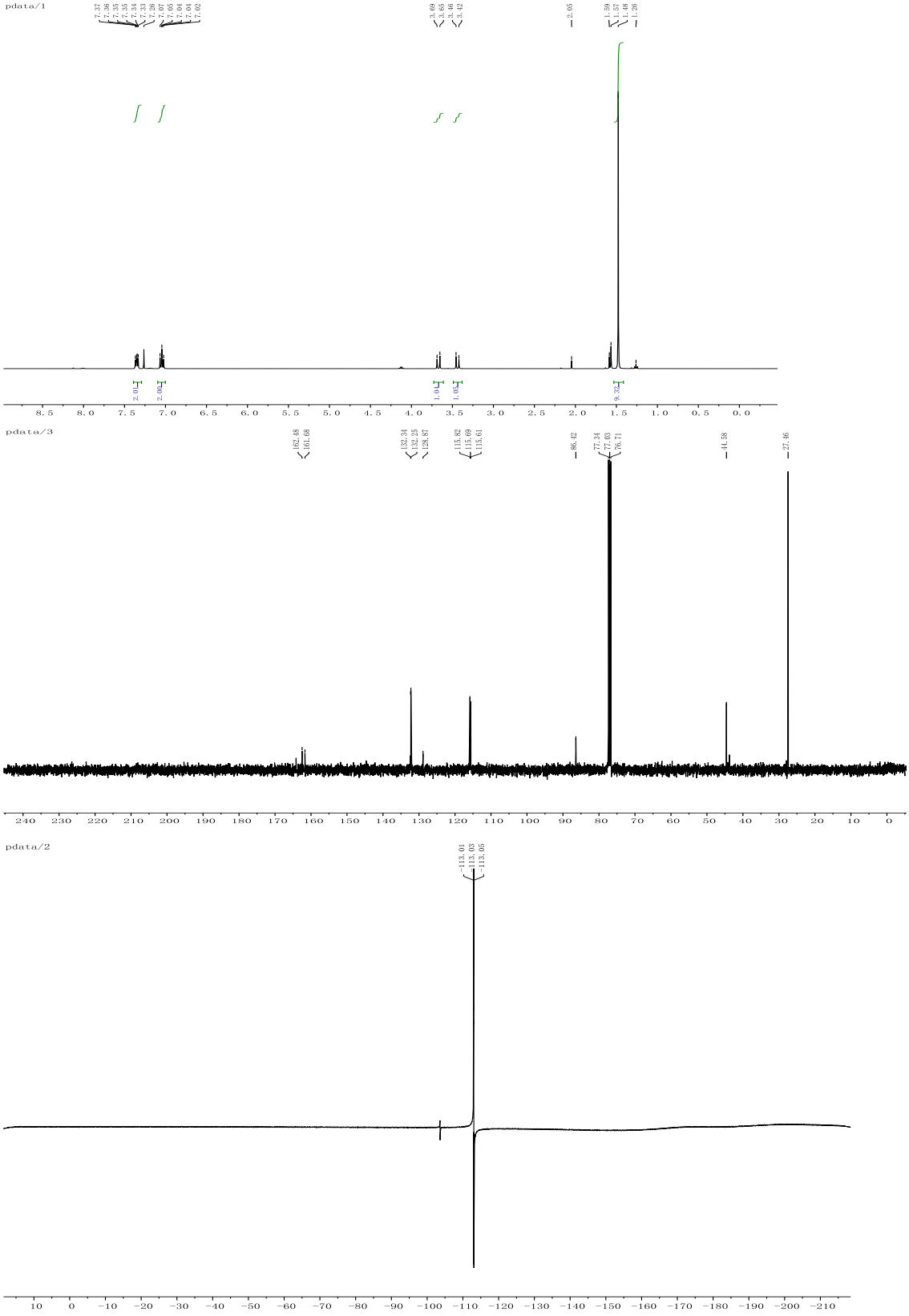




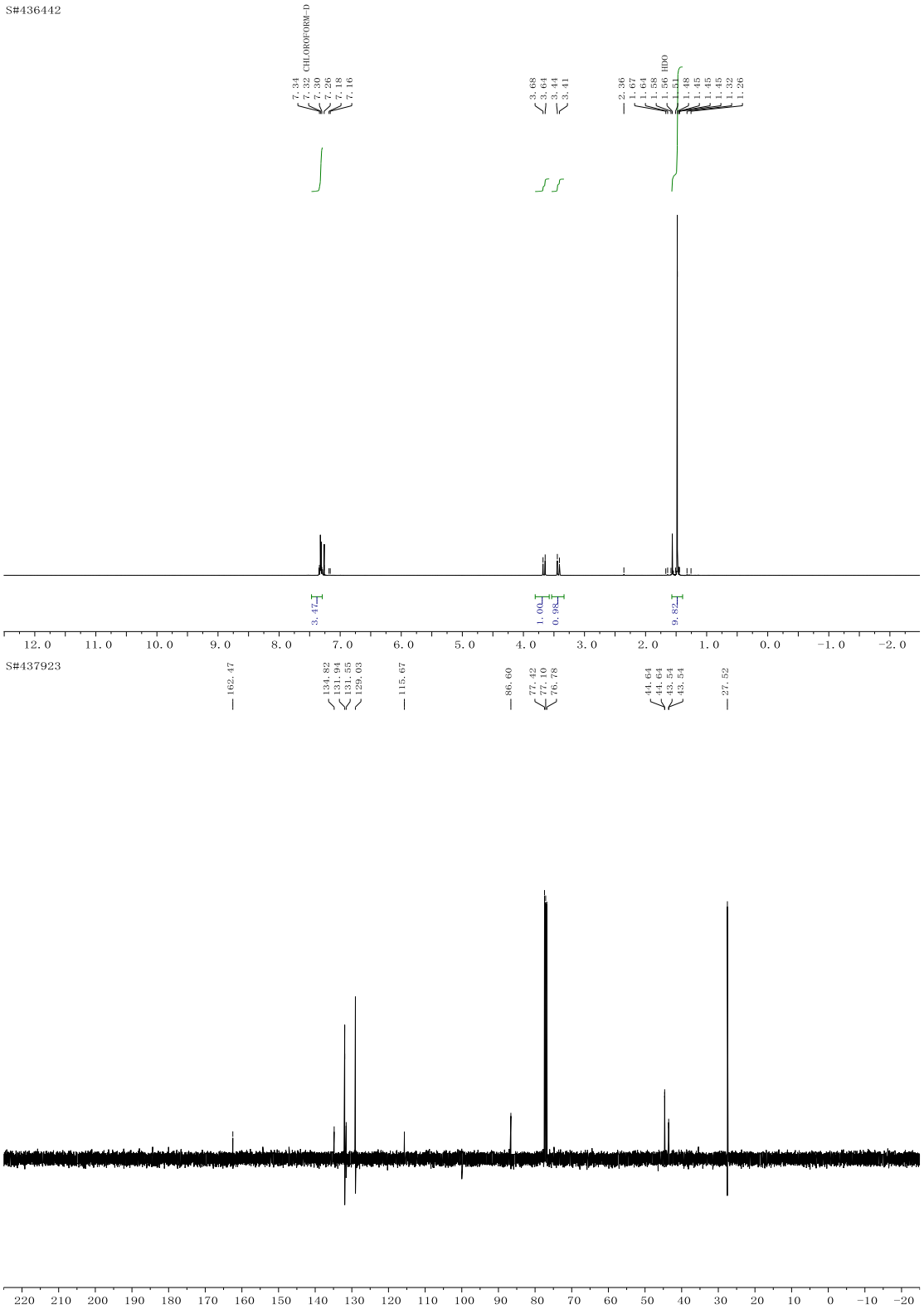
***tert*-Butyl 2-bromo-2-cyano-3-phenylpropanoate (1d)**



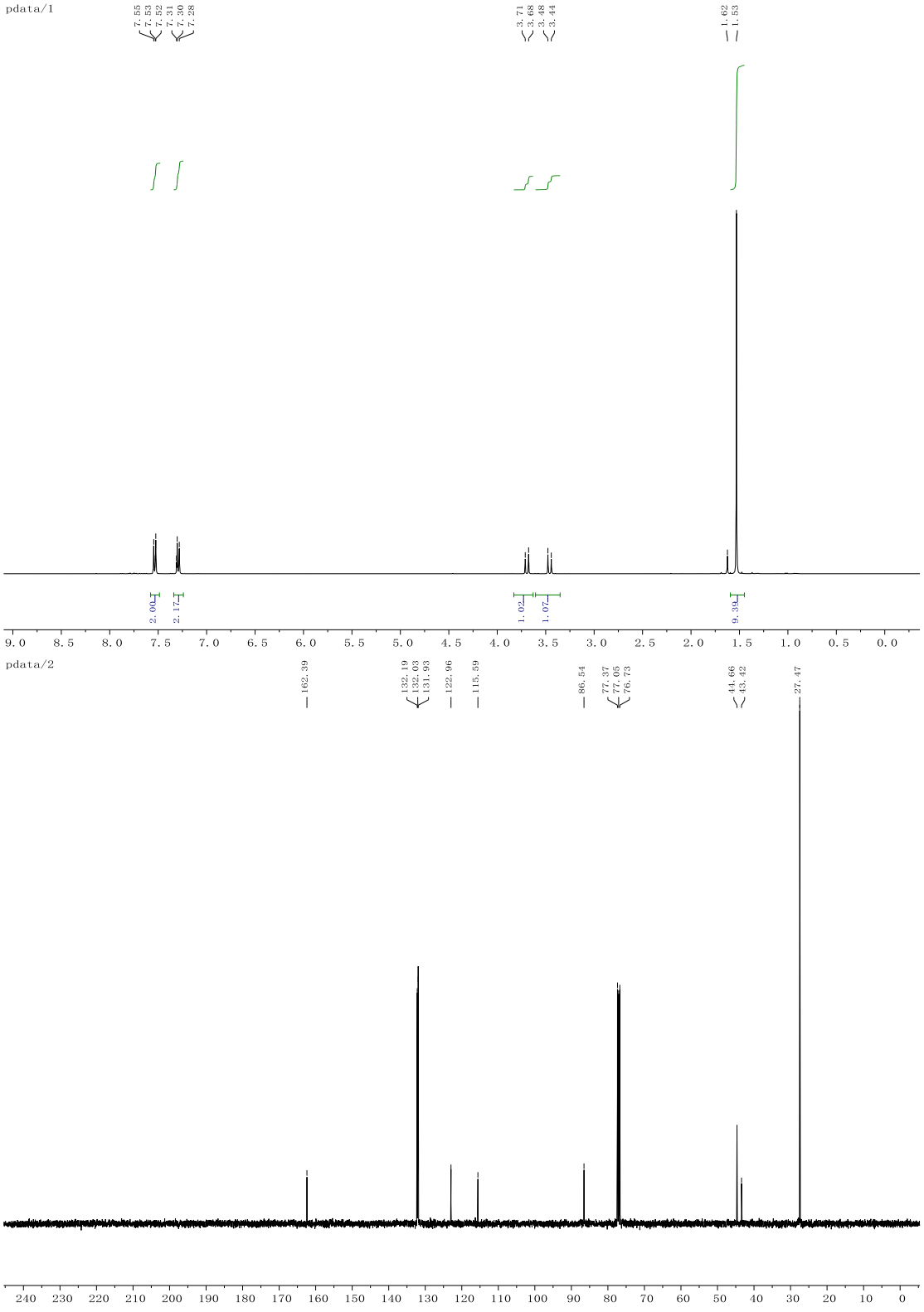
tert-Butyl 2-bromo-2-cyano-3-(4-fluorophenyl)propanoate (3d)



tert-Butyl 2-bromo-3-(4-chlorophenyl)-2-cyanopropanoate (4d)



tert-Butyl 2-bromo-3-(4-bromophenyl)-2-cyanopropanoate (5d)



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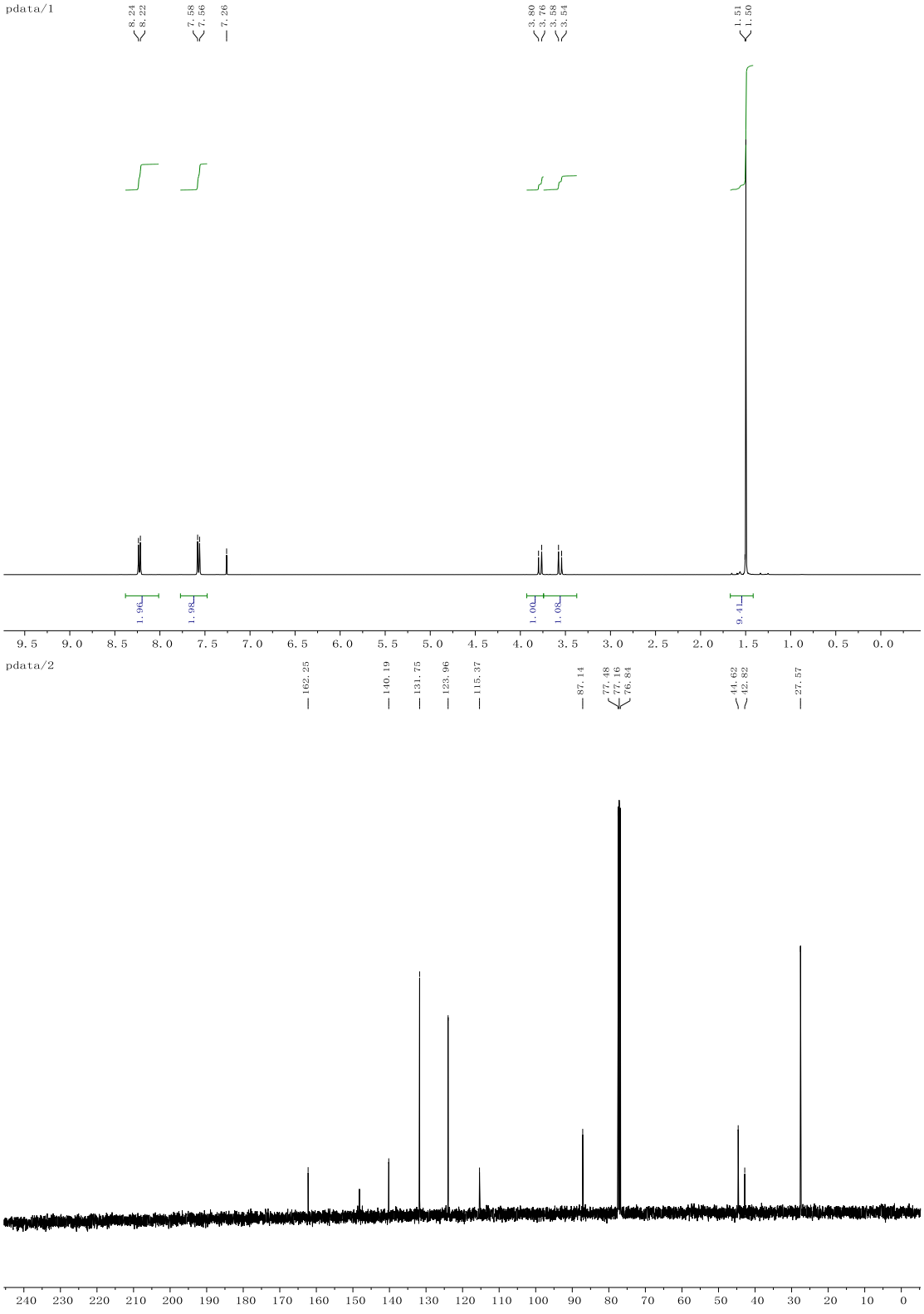

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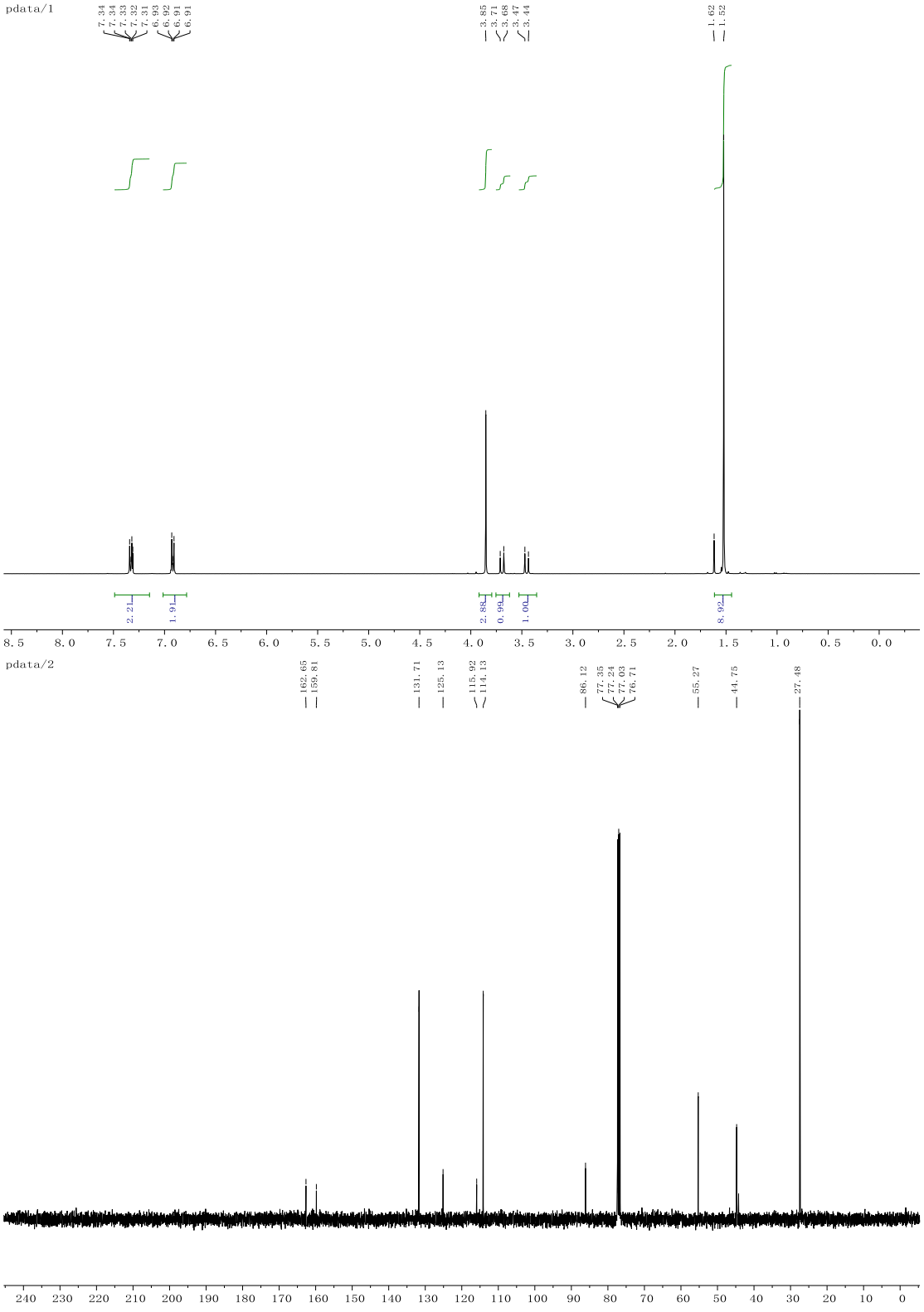
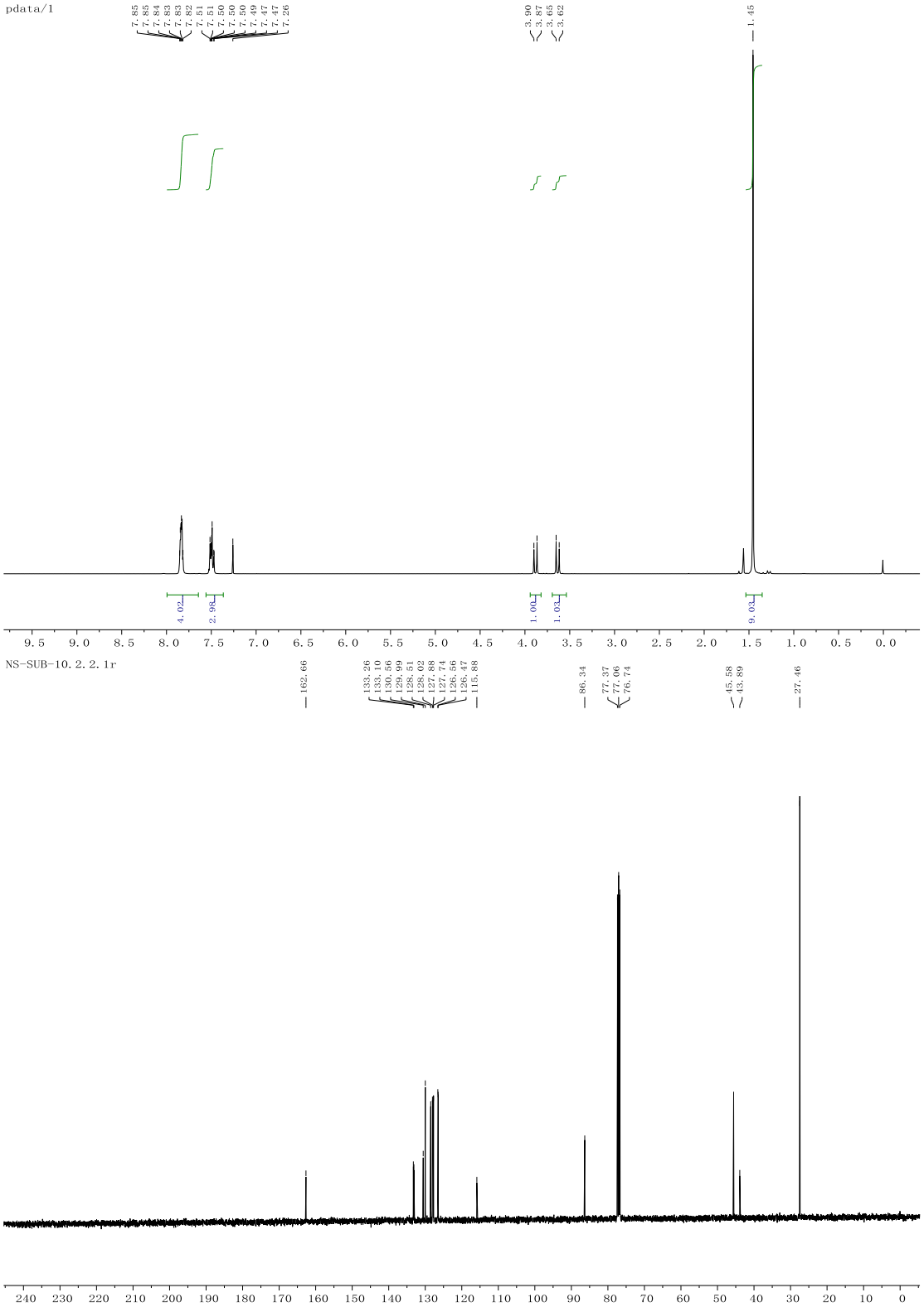
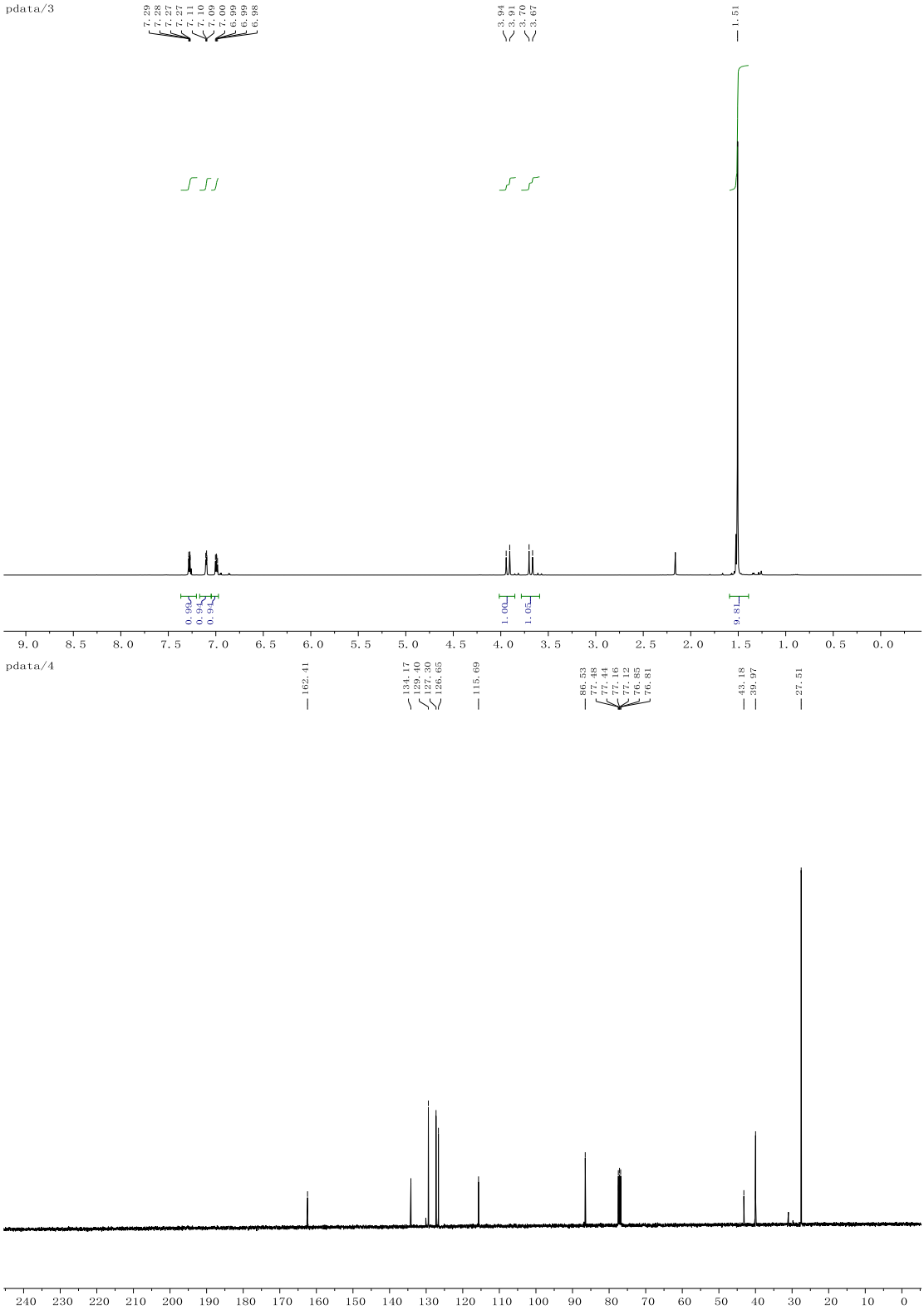


tert-Butyl-2-bromo-2-cyano-3-(naphthalen-2-yl)propanoate(8d)



tert-Butyl 2-bromo-2-cyano-3-(thiophen-2-yl)propanoate (9d)



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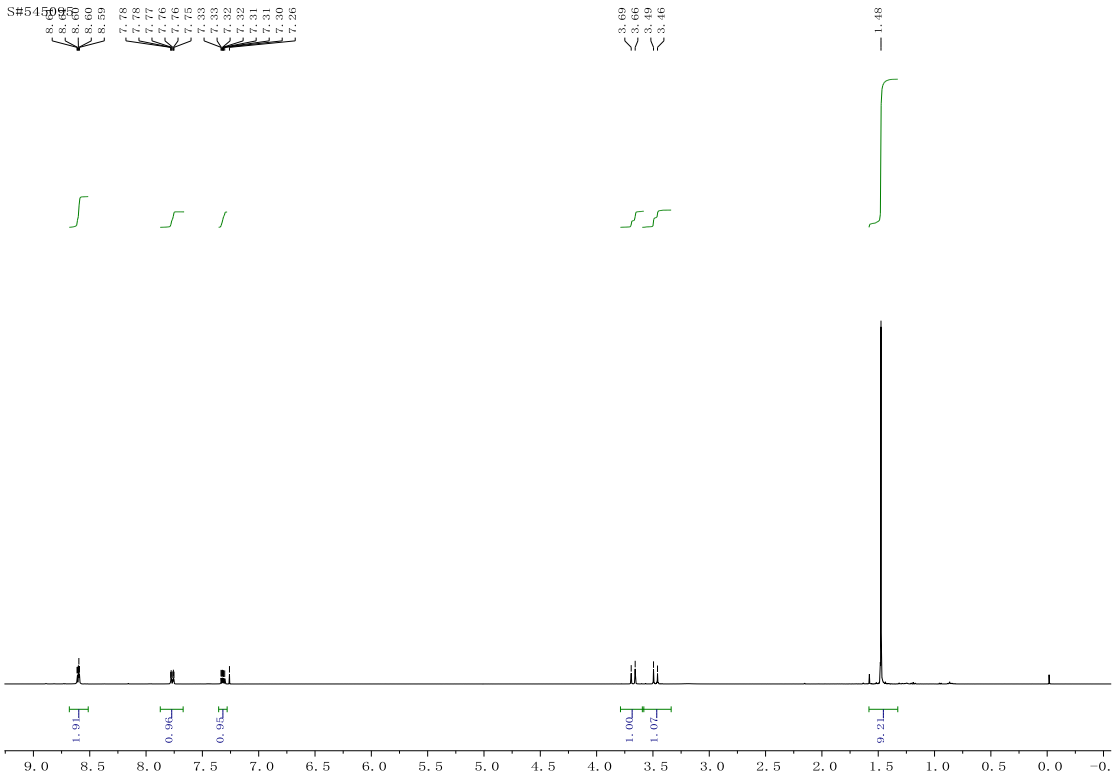
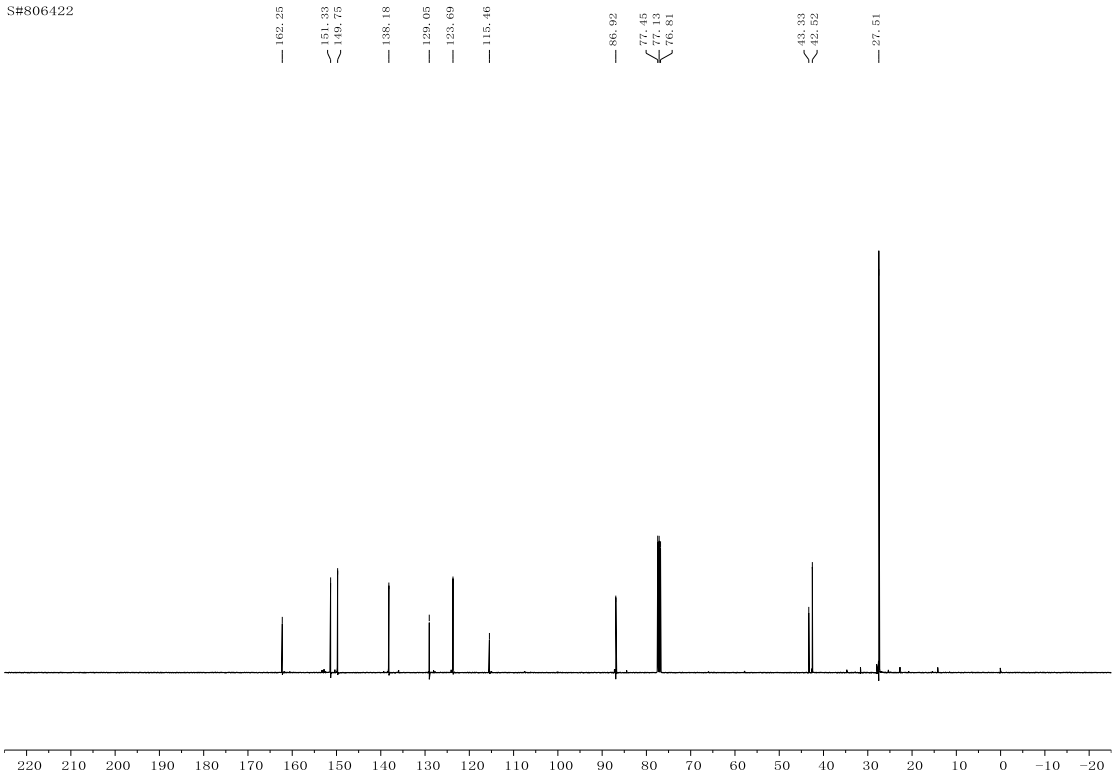
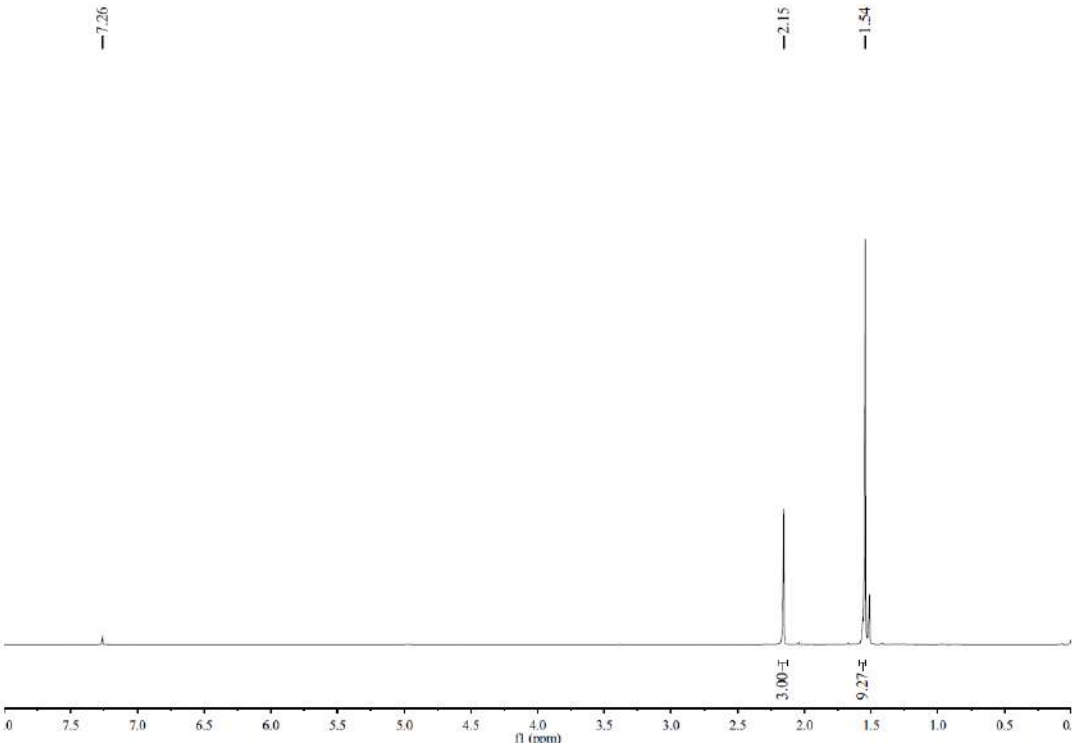
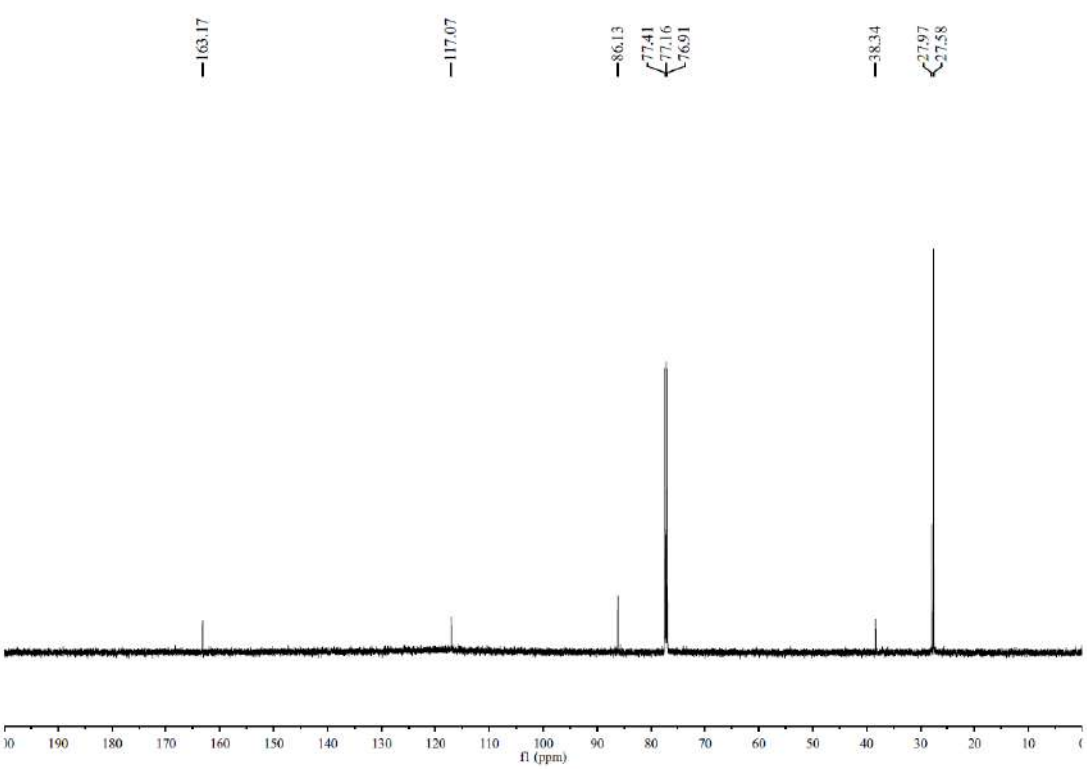


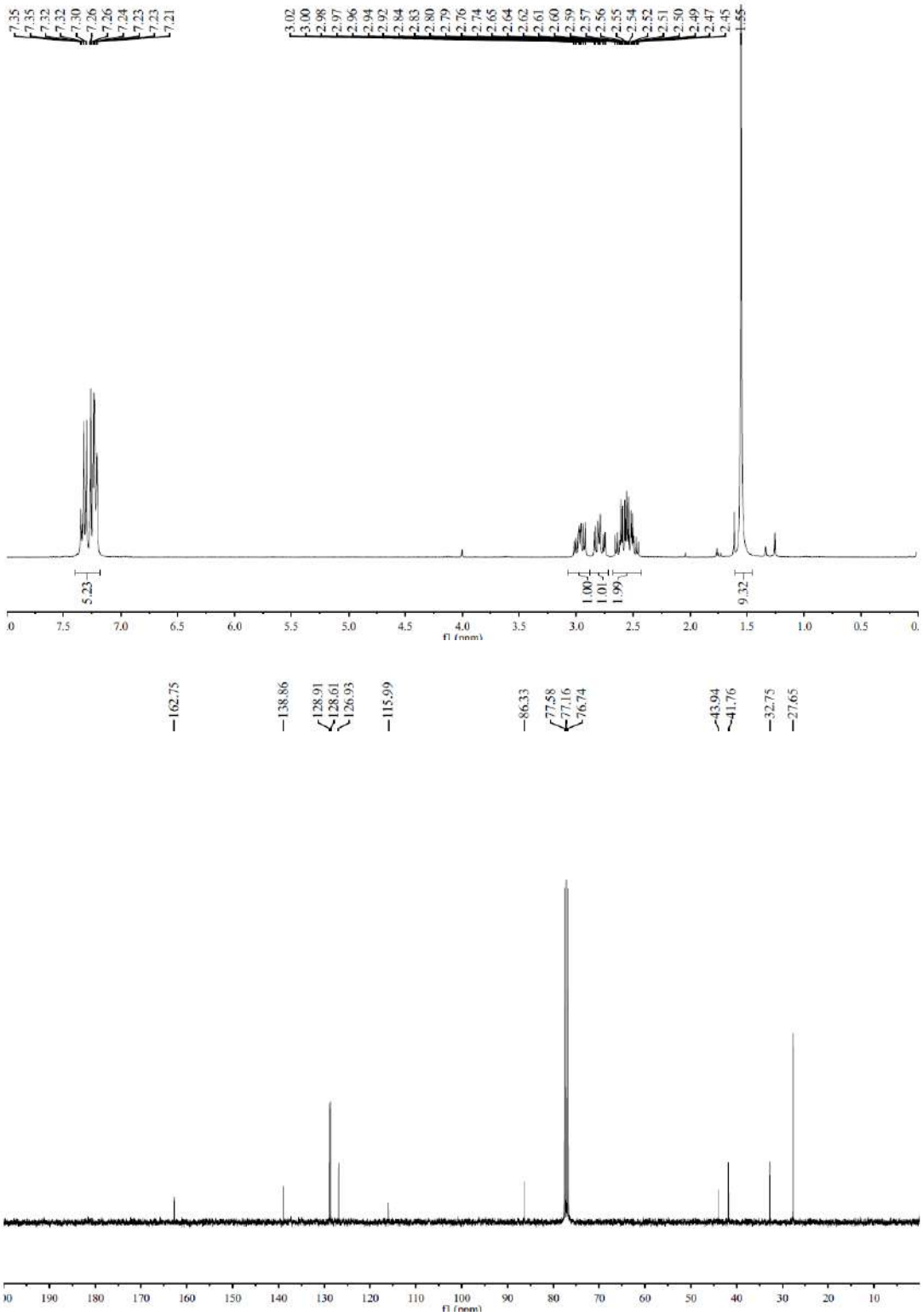


tert-butyl 2-bromo-2-cyanopropanoate (11d)

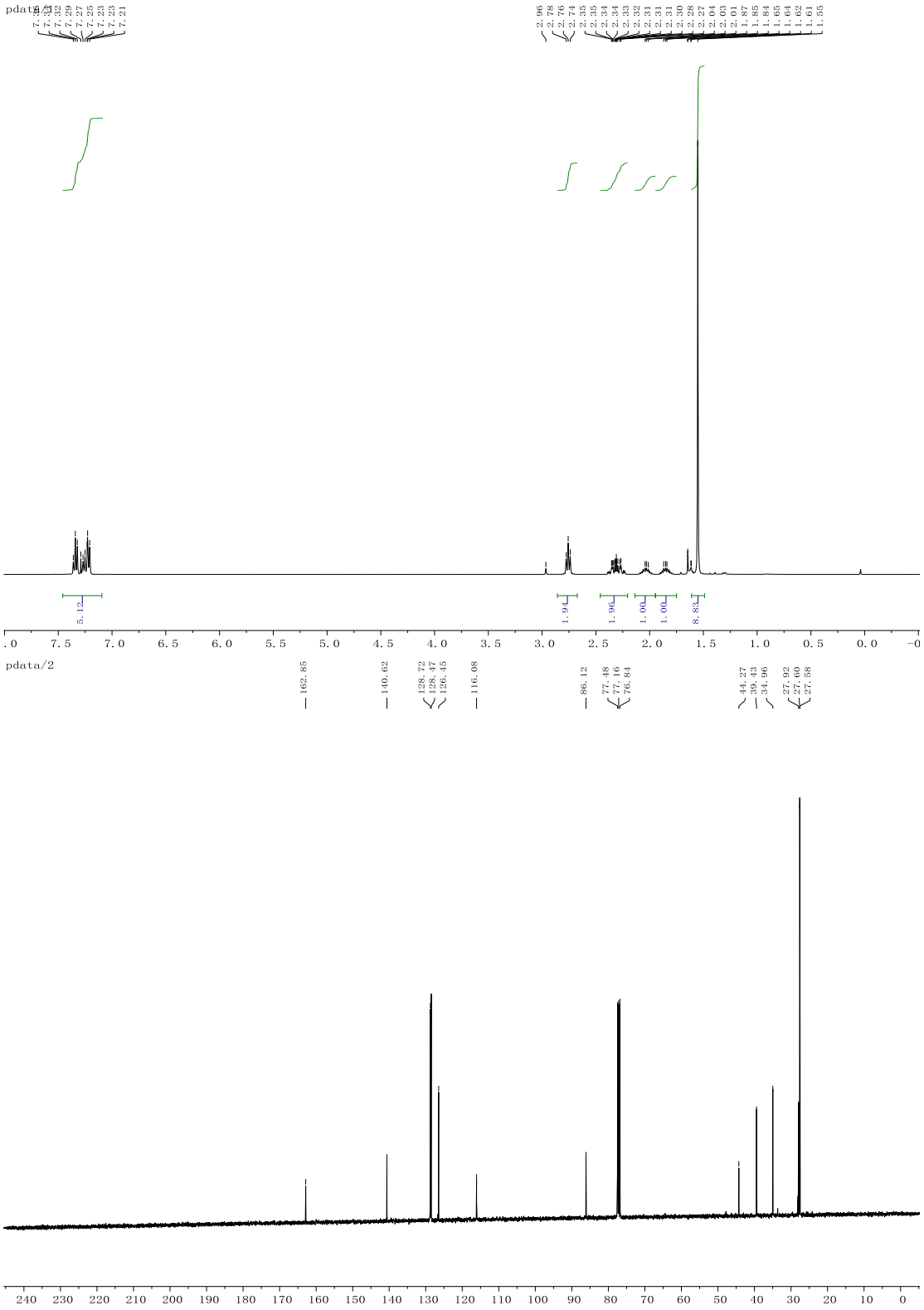

7.26
2.15
1.54
3.00
9.27
f1 (ppm)


163.17
117.07
86.13
77.41
77.16
76.91
38.34
27.97
27.58
f1 (ppm)

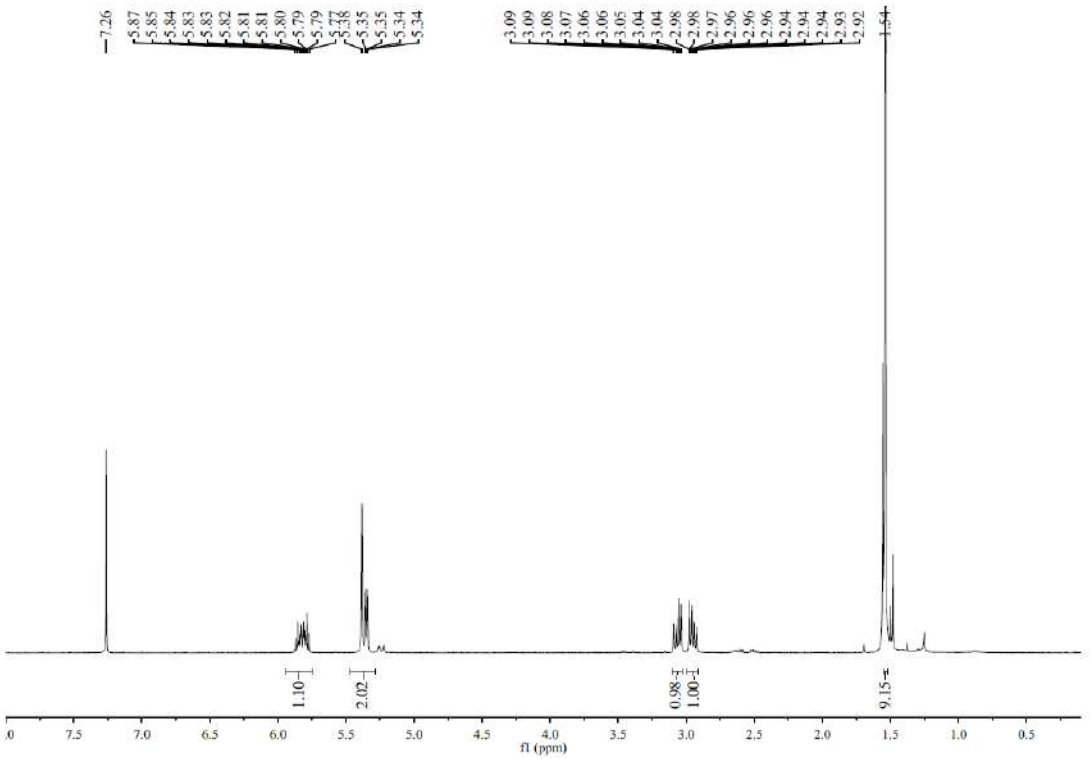
tert-Butyl 2-bromo-2-cyano-4-phenylbutanoate (12d)

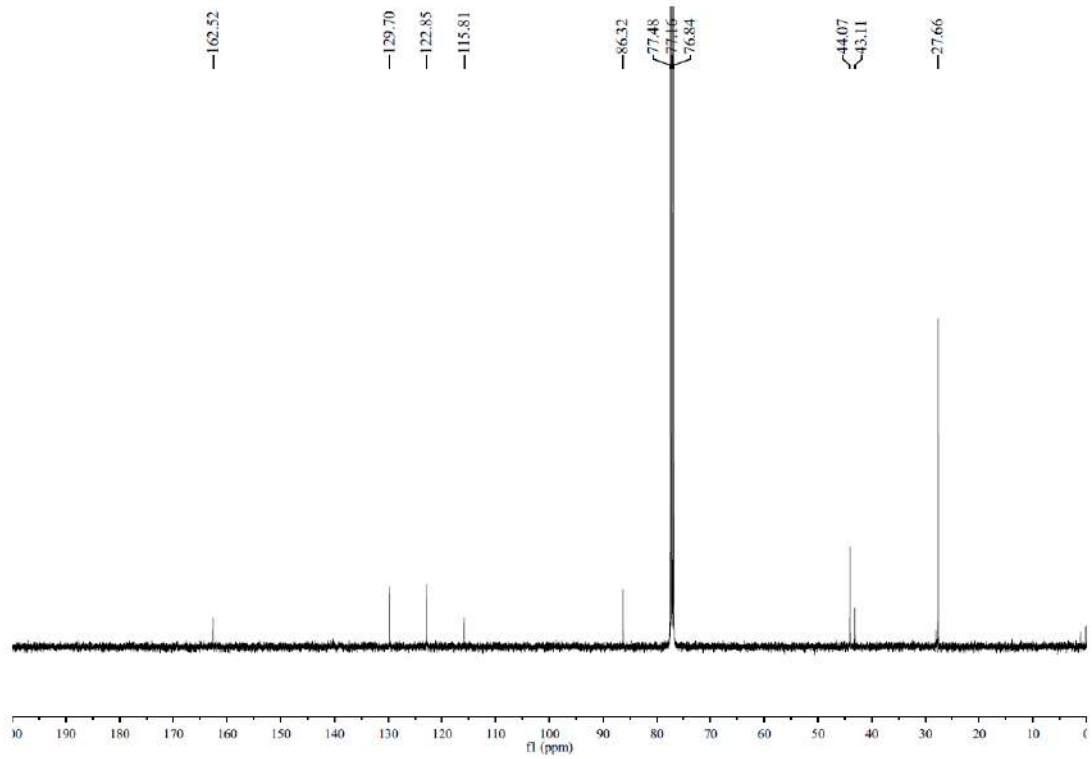


tert-Butyl 2-bromo-2-cyano-5-phenylpentanoate (13d)

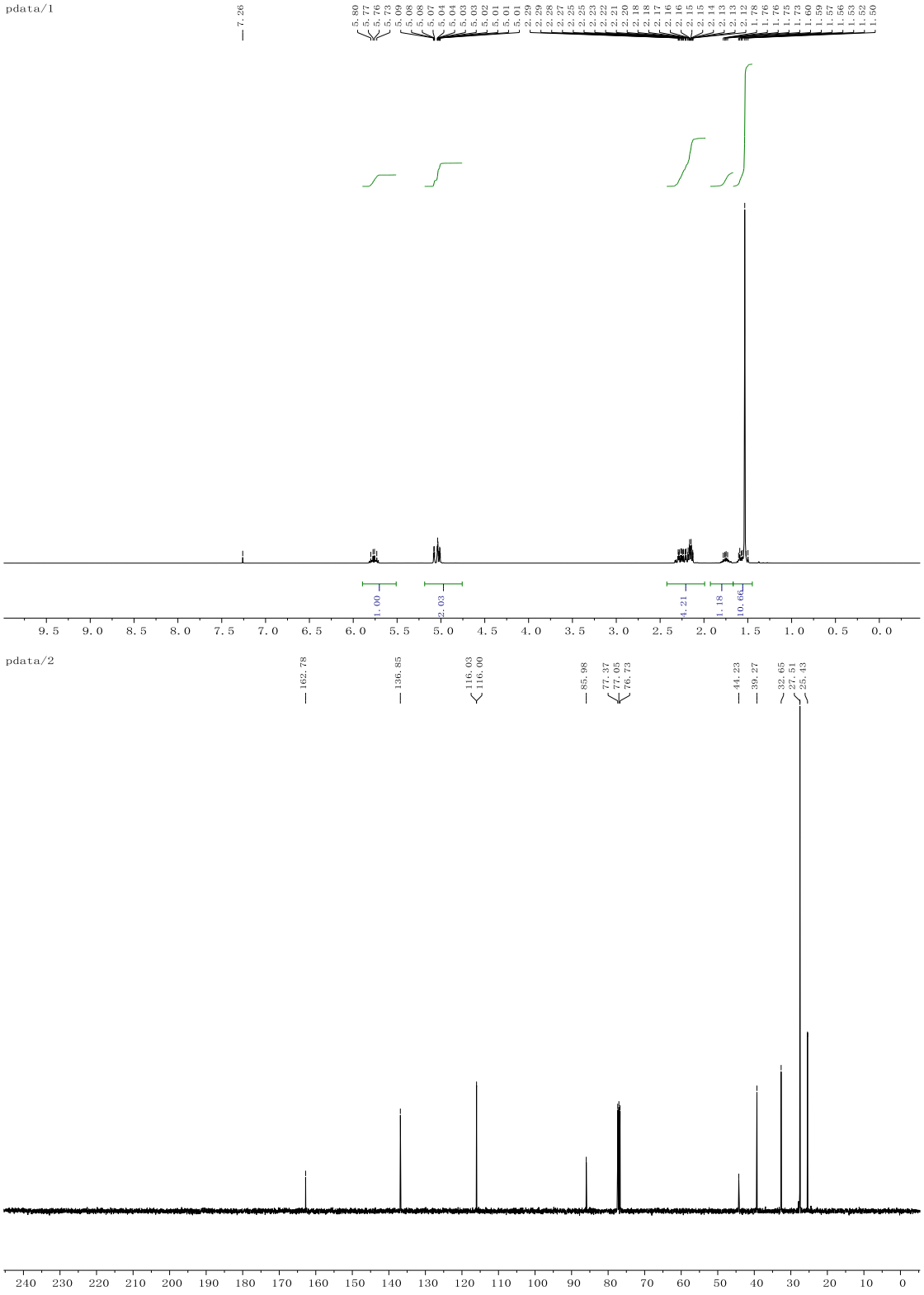


tert-Butyl 2-bromo-2-cyanopent-4-enoate (14d)

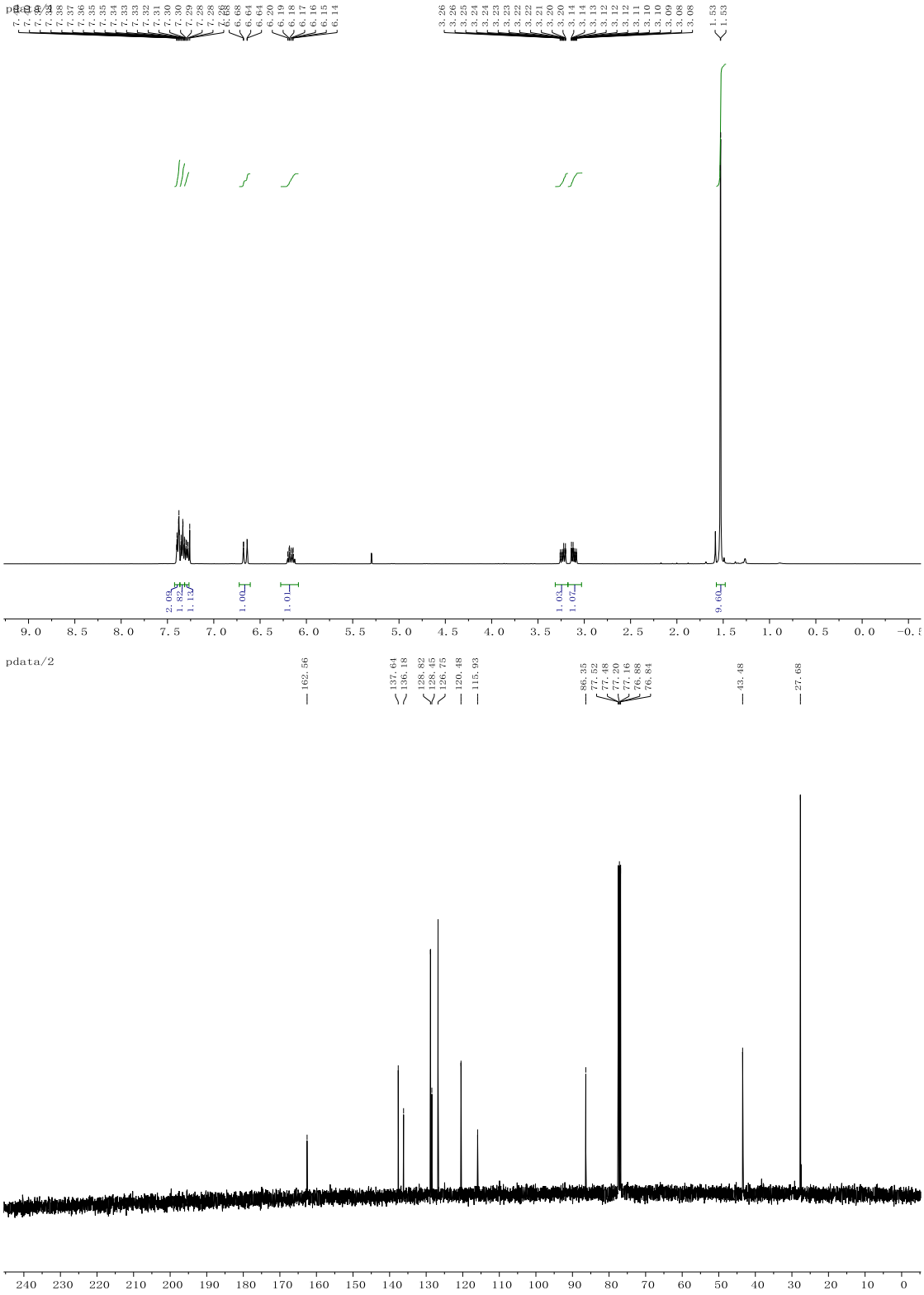




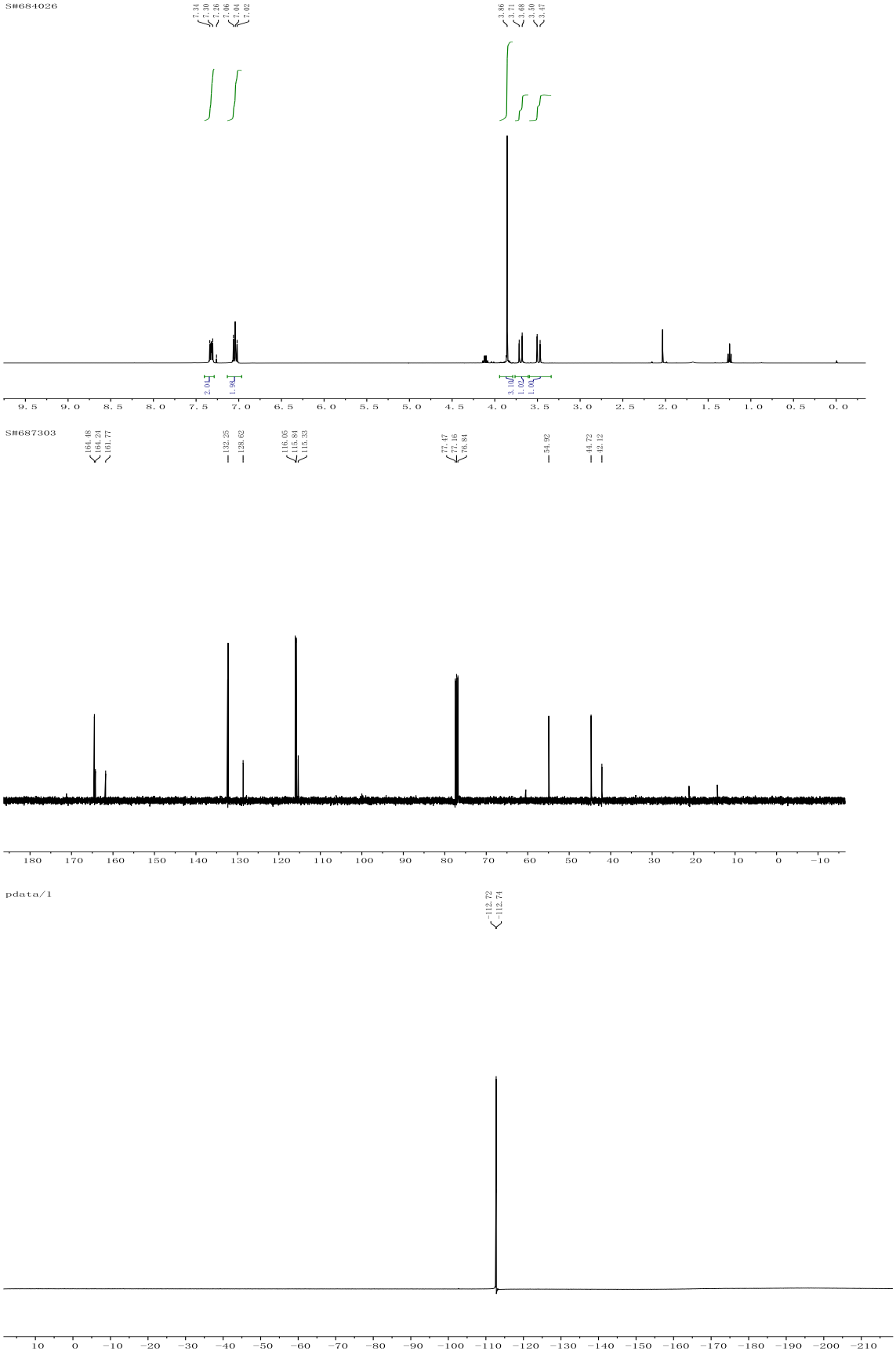
tert-Butyl 2-bromo-2-cyanohept-6-enoate (15d)



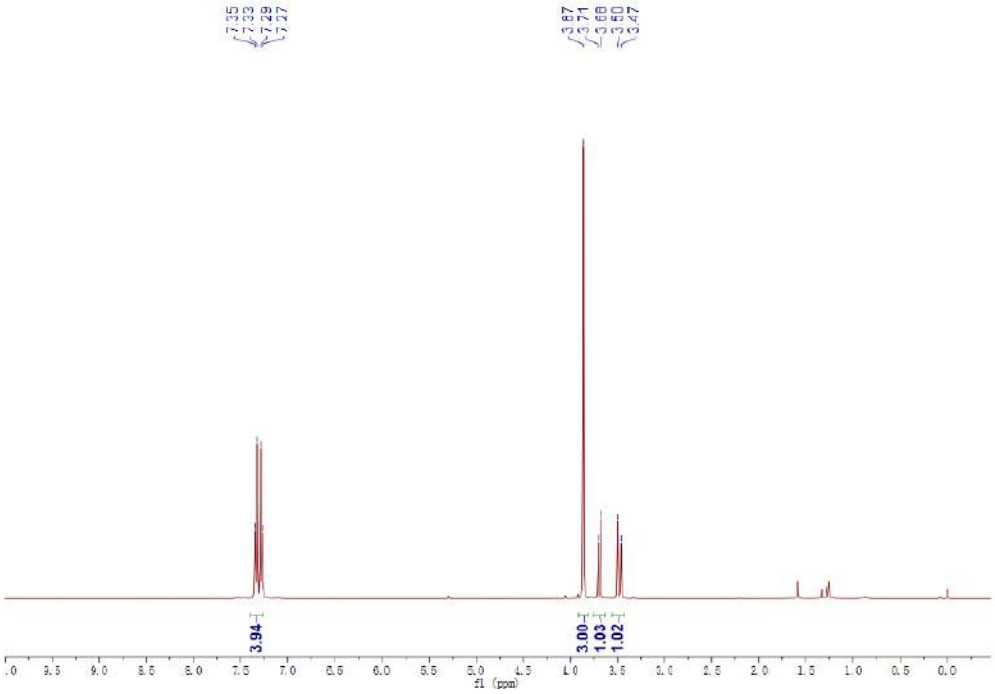
tert-butyl (E)-2-bromo-2-cyano-5-phenylpent-4-enoate (16d)

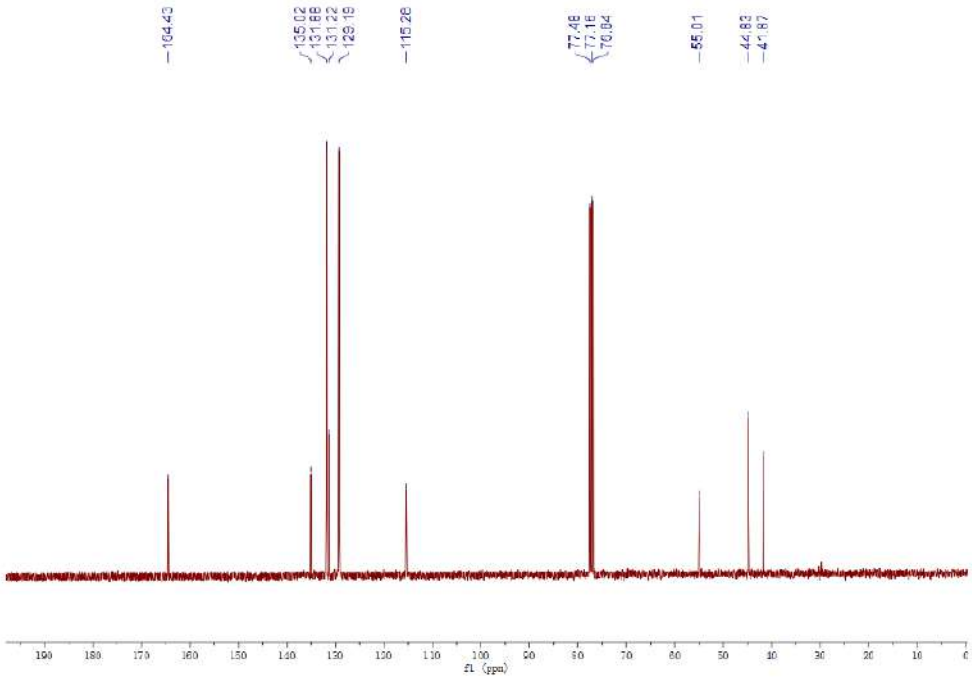


Methyl 2-bromo-2-cyano-3-(4-fluorophenyl)propanoate (3a)

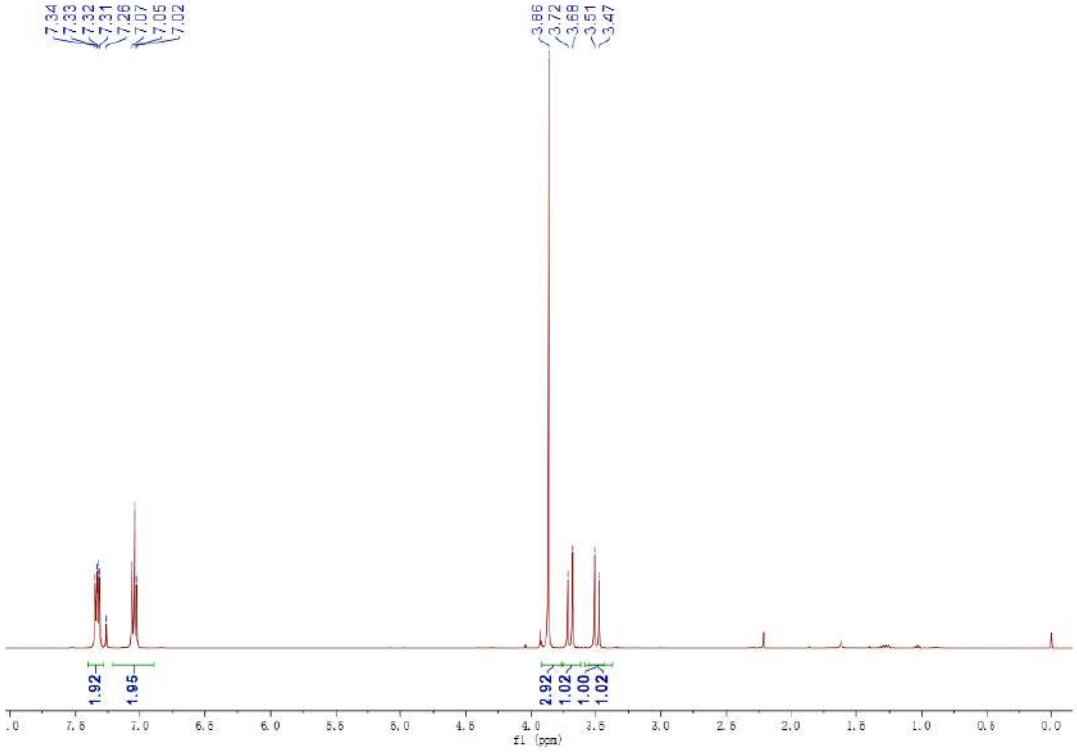


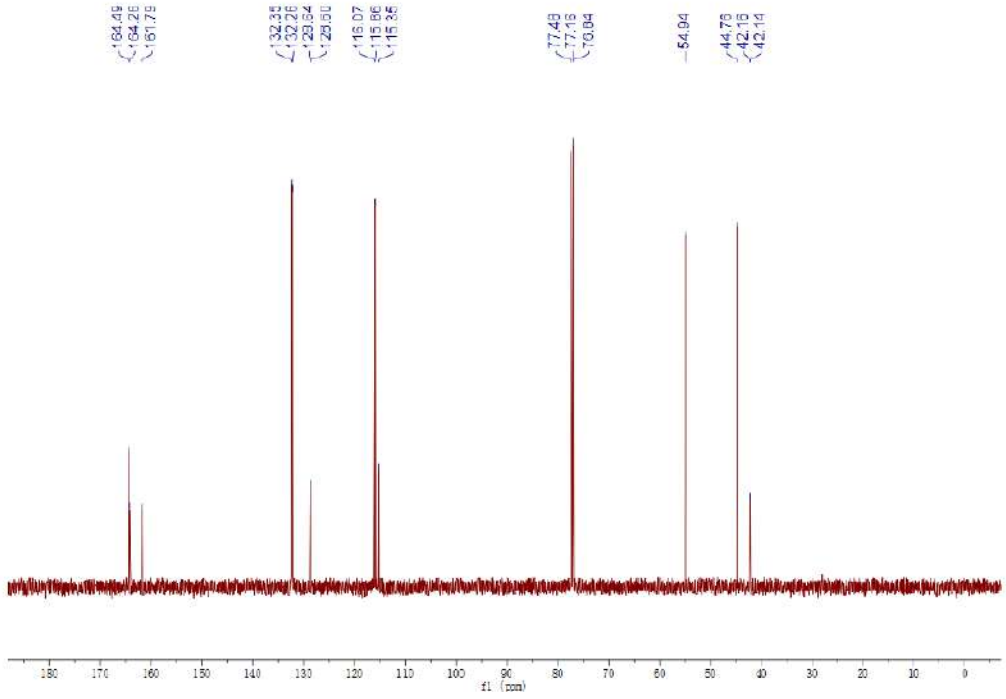
Methyl 2-bromo-3-(4-chlorophenyl)-2-cyanopropanoate (4a)



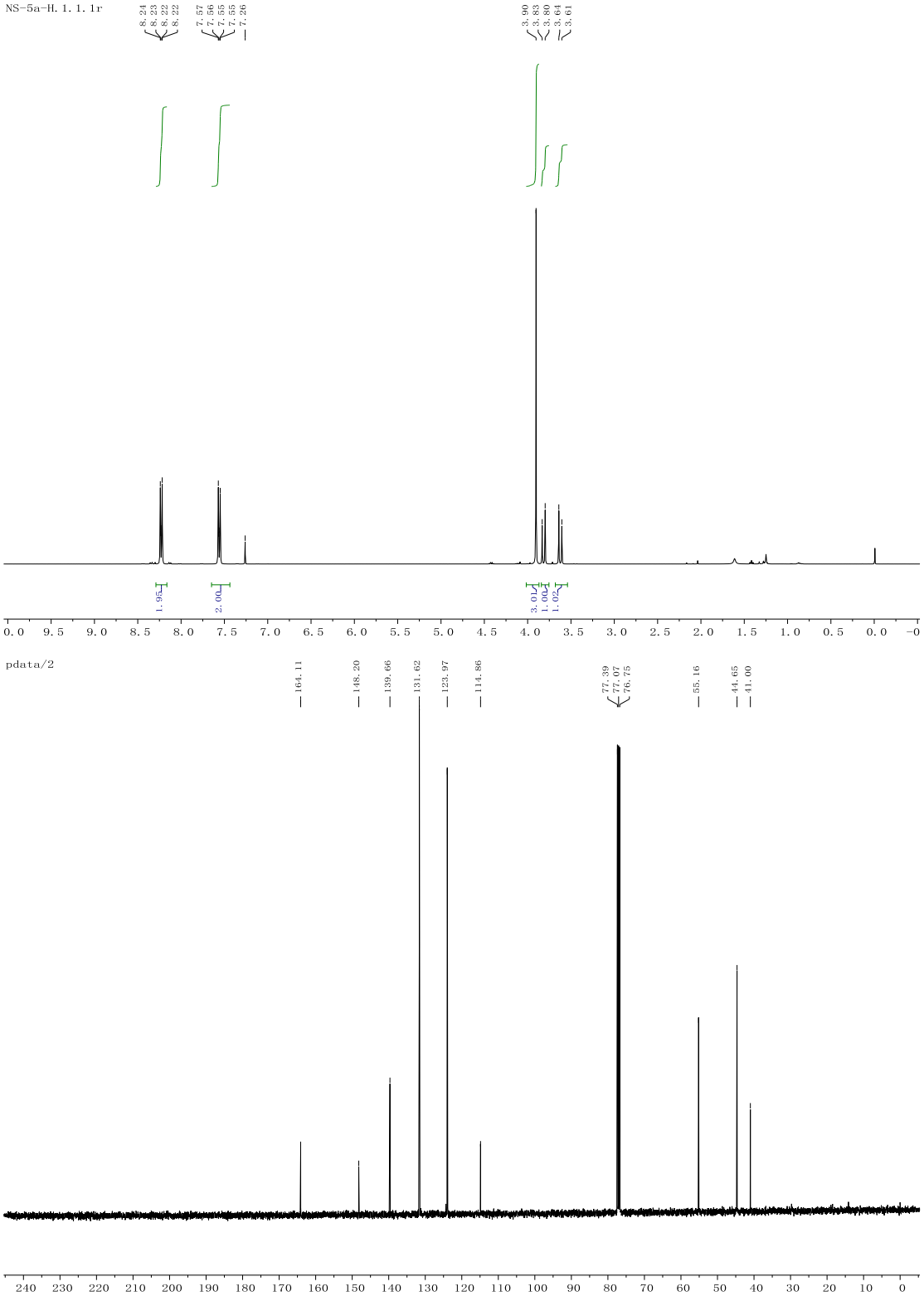


Methyl 2-bromo-3-(4-bromophenyl)-2-cyanopropanoate (5a)

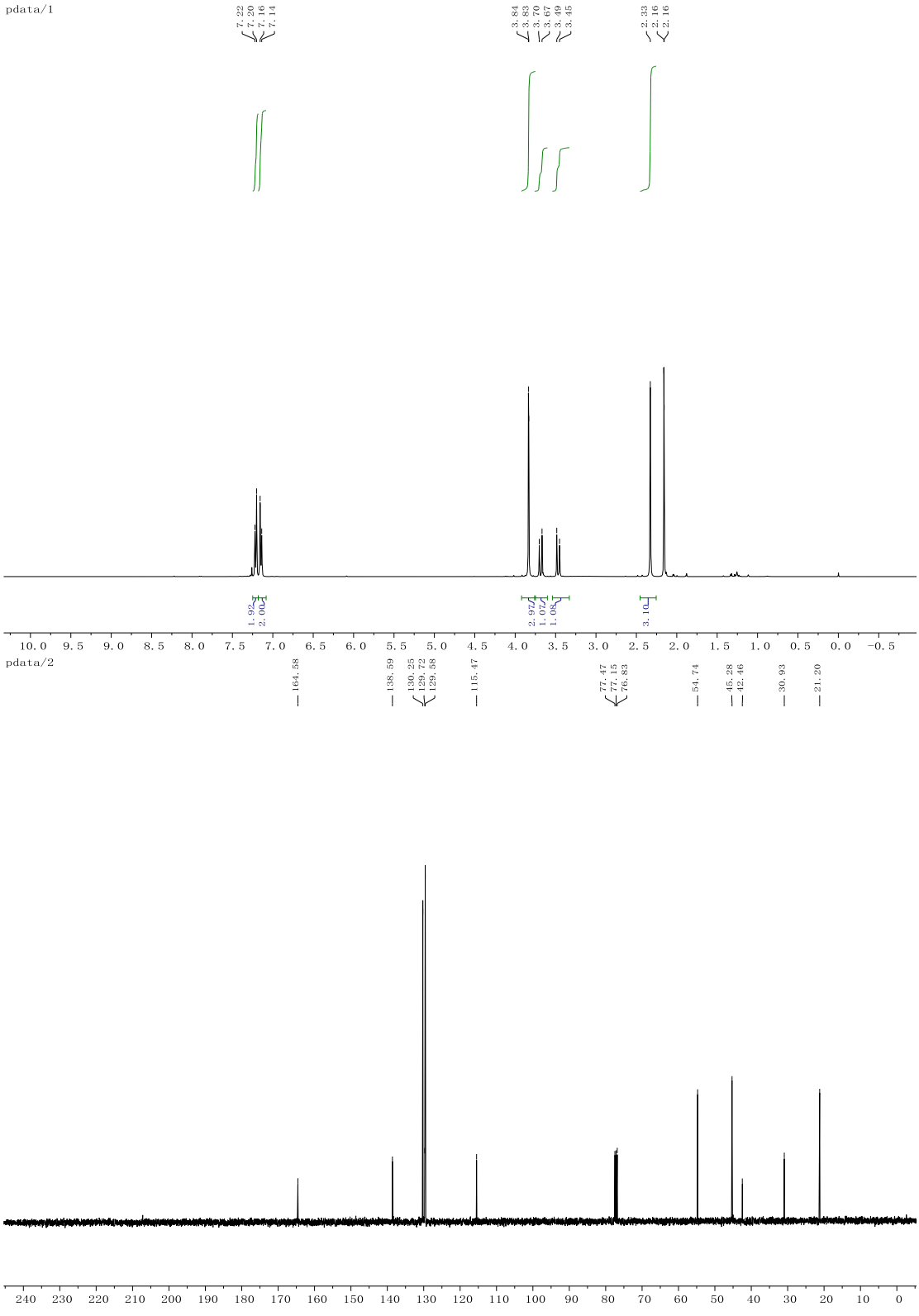




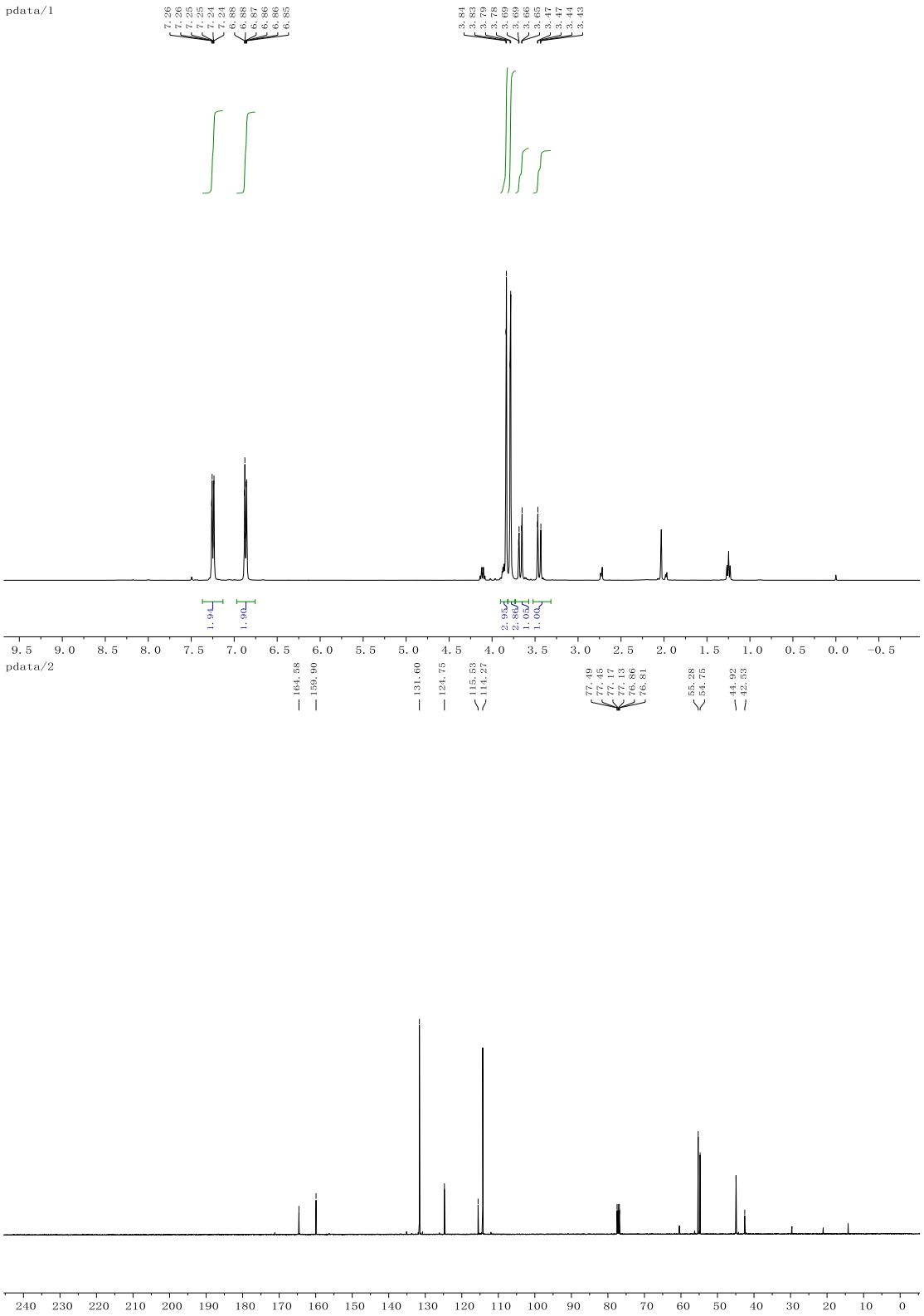
Methyl-2-bromo-2-cyano-3-(4-nitrophenyl)propanoate (6a)



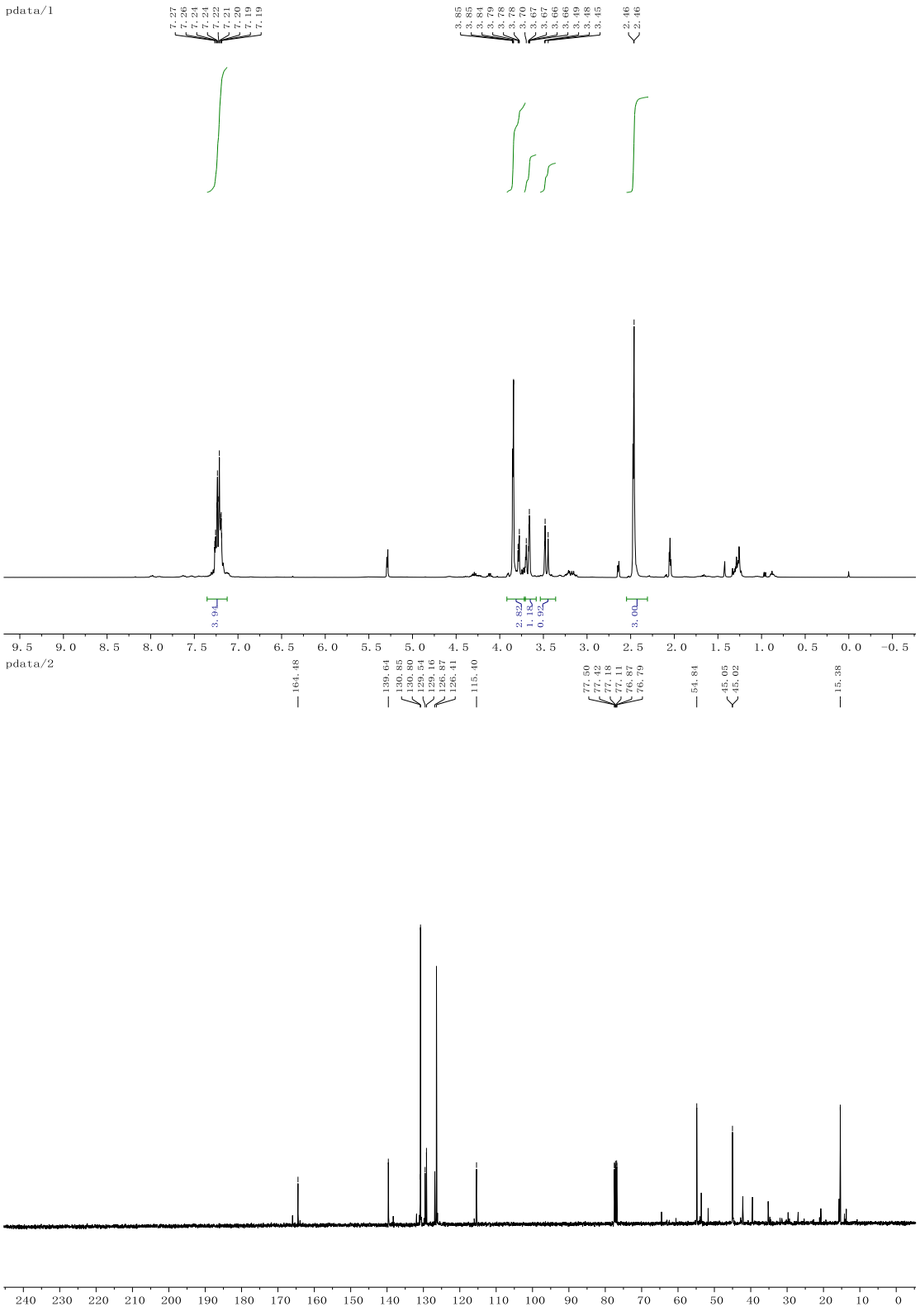
Methyl 2-bromo-2-cyano-3-(p-tolyl)propanoate (7a)



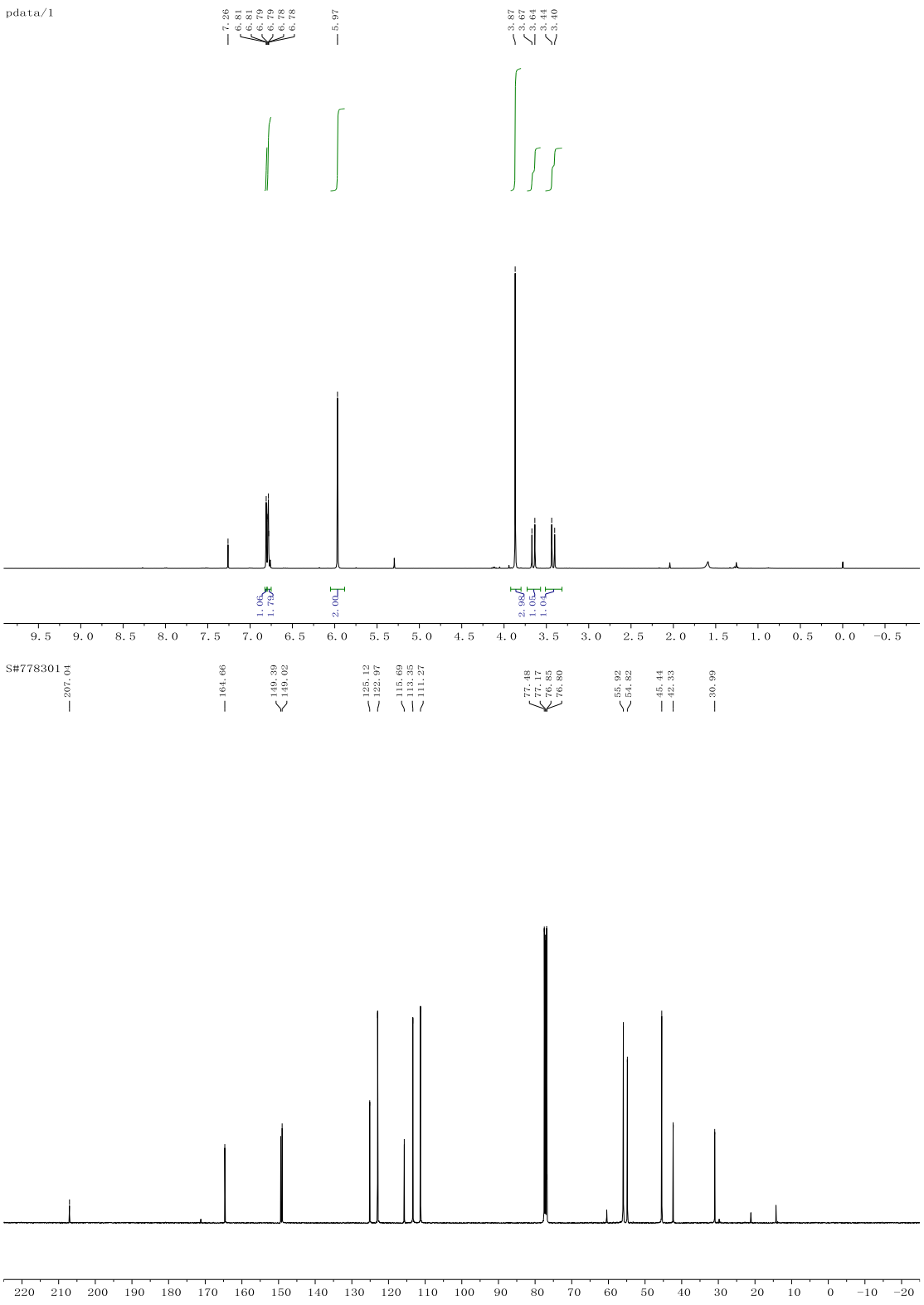
Methyl 2-bromo-2-cyano-3-(4-methoxyphenyl)propanoate (8a)



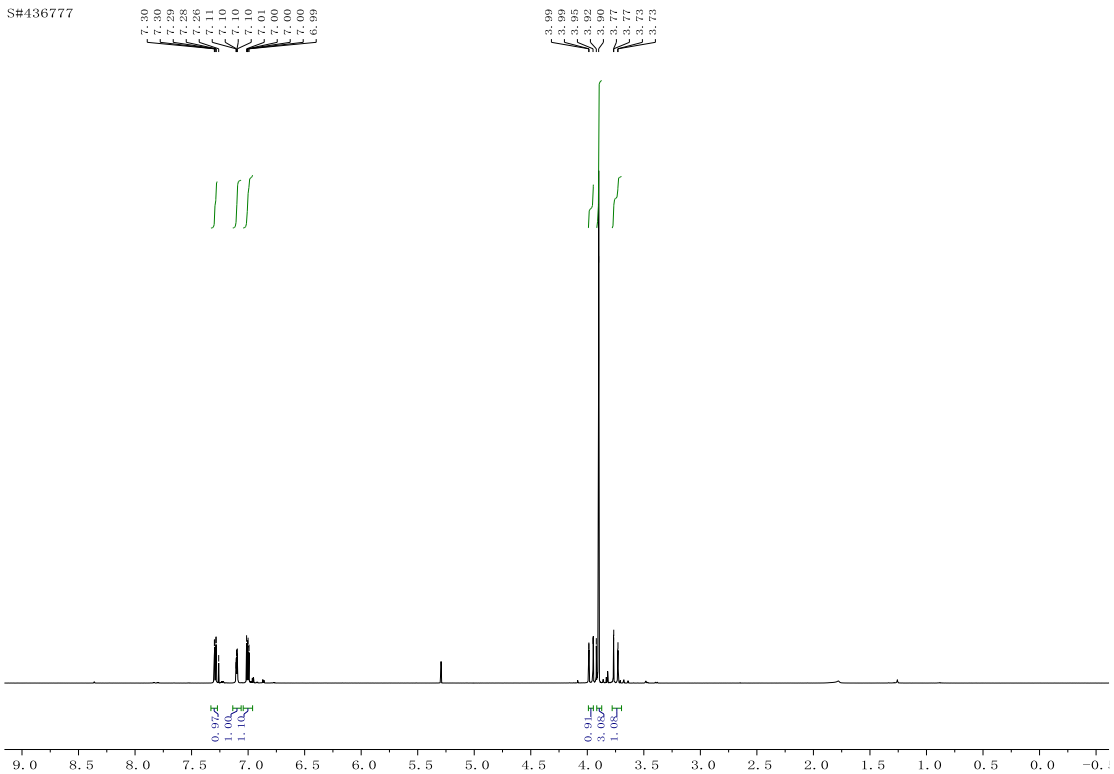
Methyl 2-bromo-2-cyano-3-(4-(methylthio)phenyl)propanoate (9a)



Methyl 3-(benzo[d][1,3]dioxol-5-yl)-2-bromo-2-cyanopropanoate (10a)



Methyl 2-bromo-2-cyano-3-(thiophen-2-yl)propanoate (11a)


S#436777
7.30
7.30
7.29
7.28
7.26
7.11
7.10
7.10
7.01
7.00
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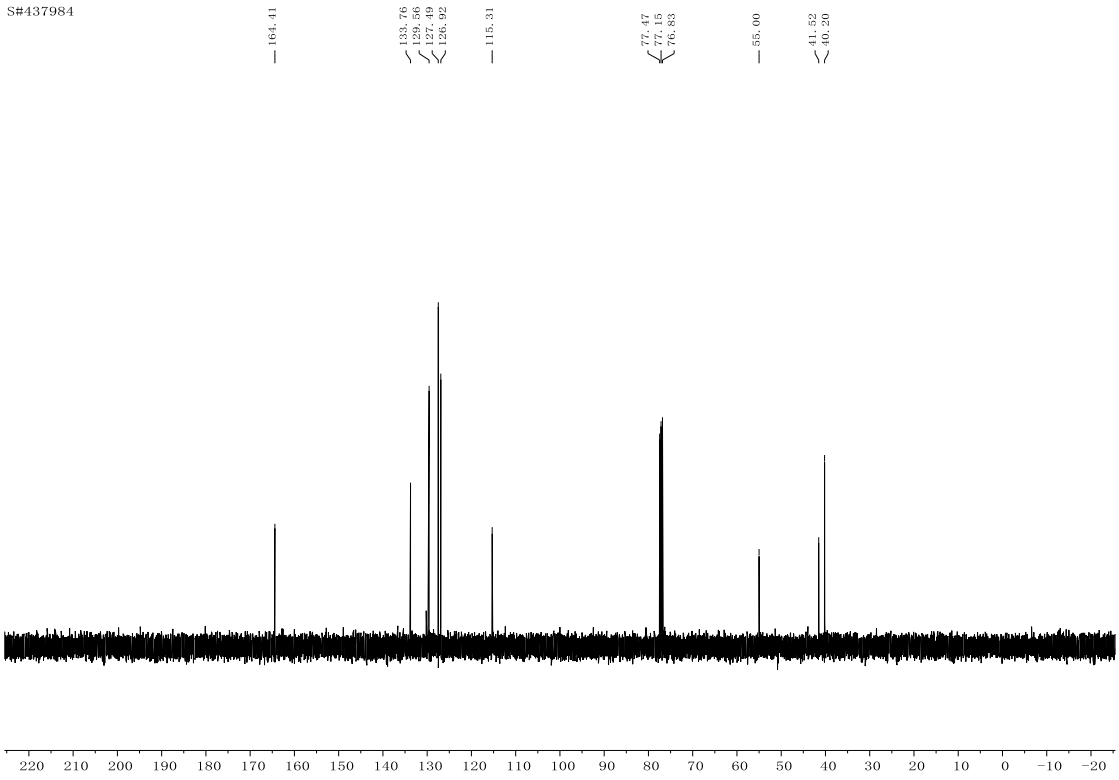
7.00
6.99
3.99
3.99
3.95
3.92
3.90
3.77
3.77
3.73
3.73
0.97
1.00
1.10
0.91
3.02
1.08
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


S#437984
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129.56
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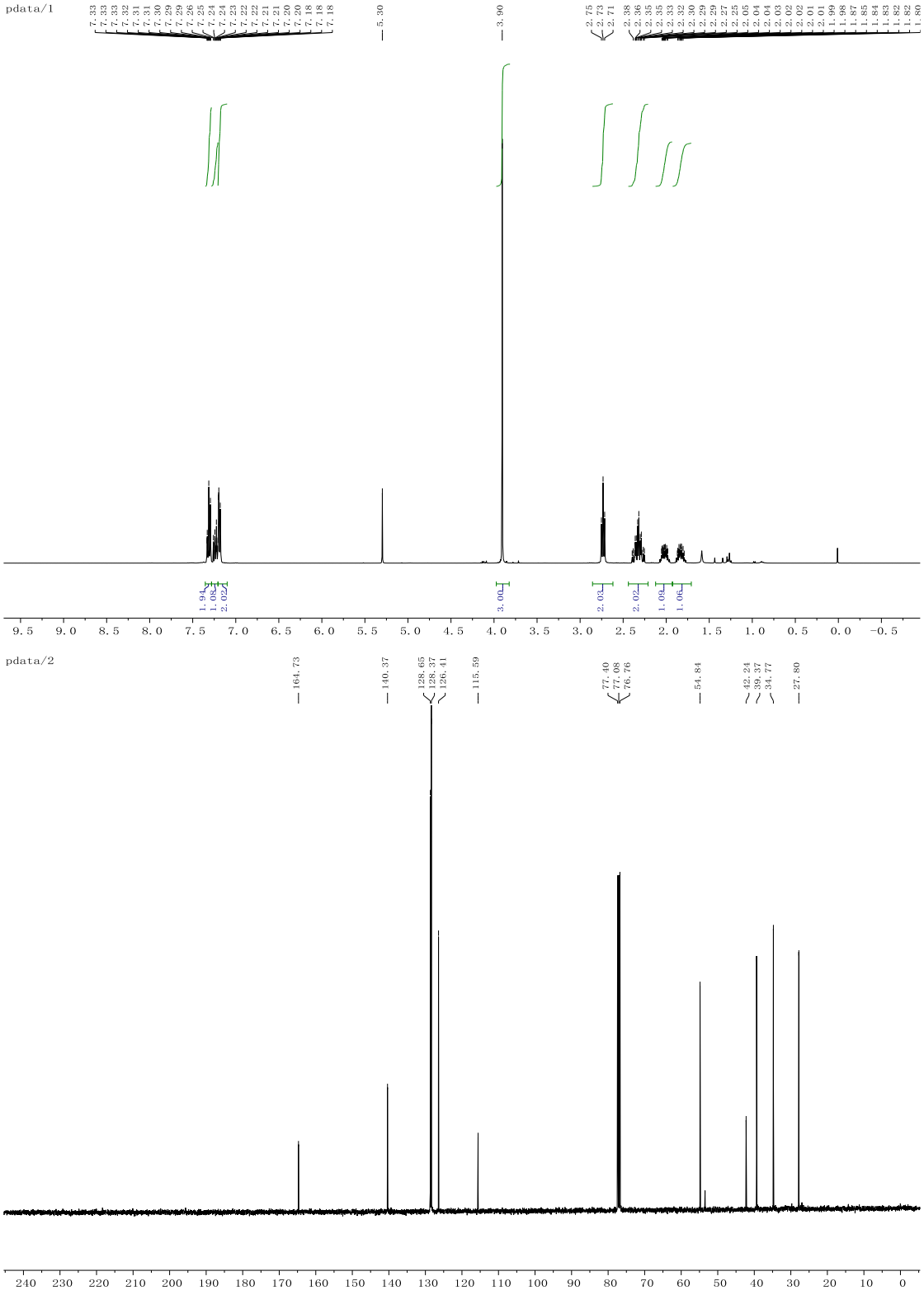
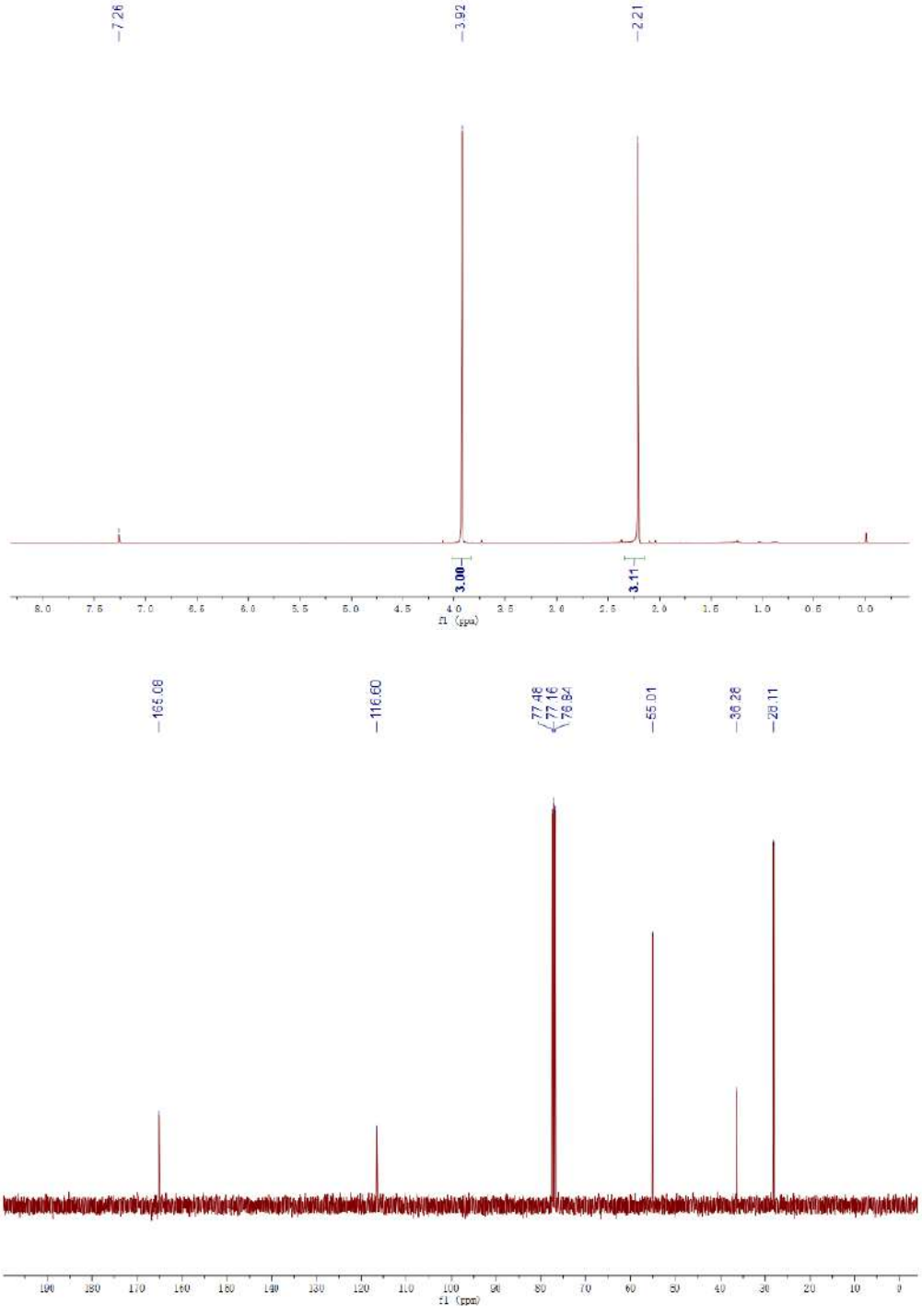
126.92
115.31
77.47
77.15
76.83
55.00
41.52
40.20
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20

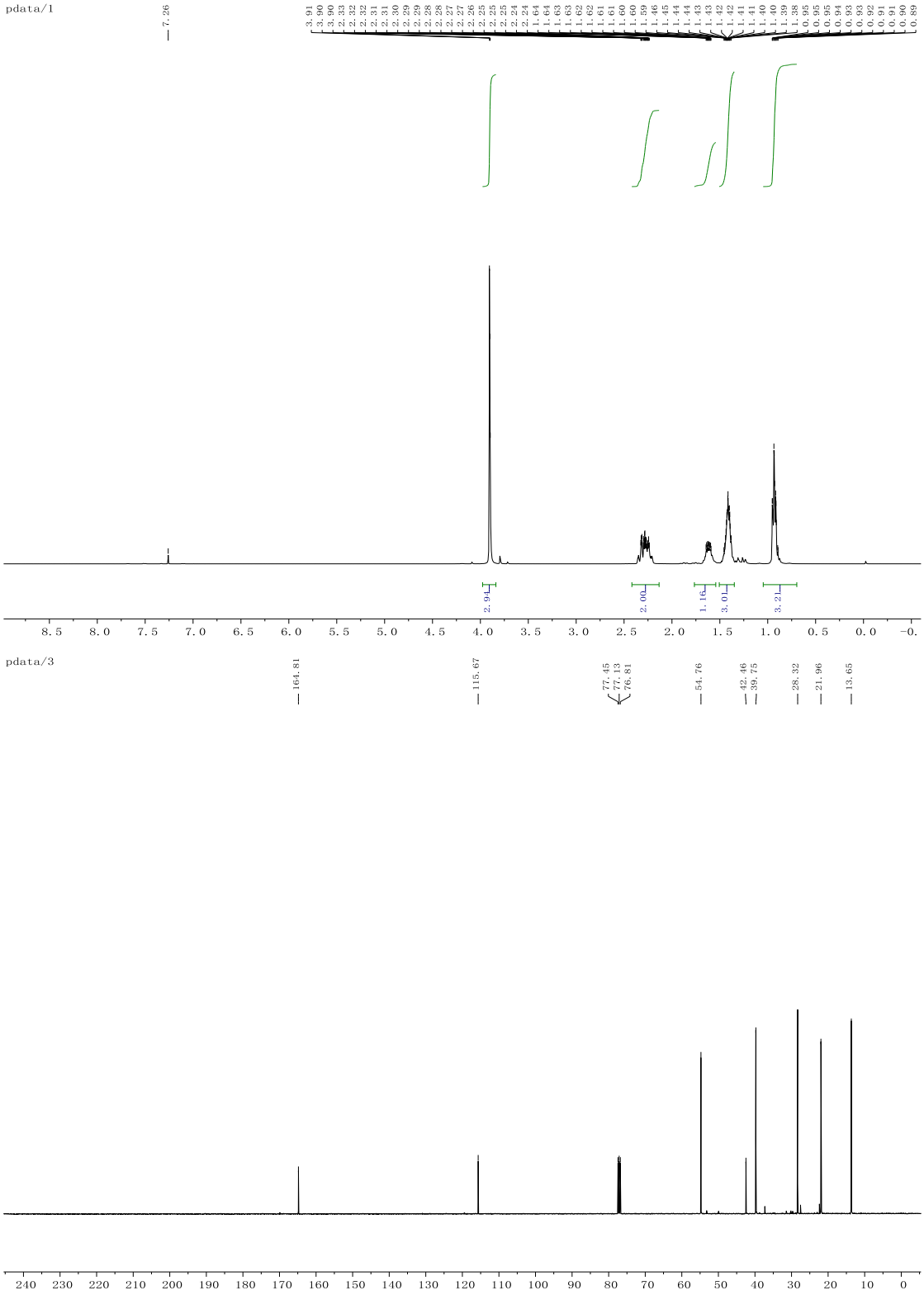
Methyl-2-bromo-2-cyano-5-phenylpentanoate (12a)



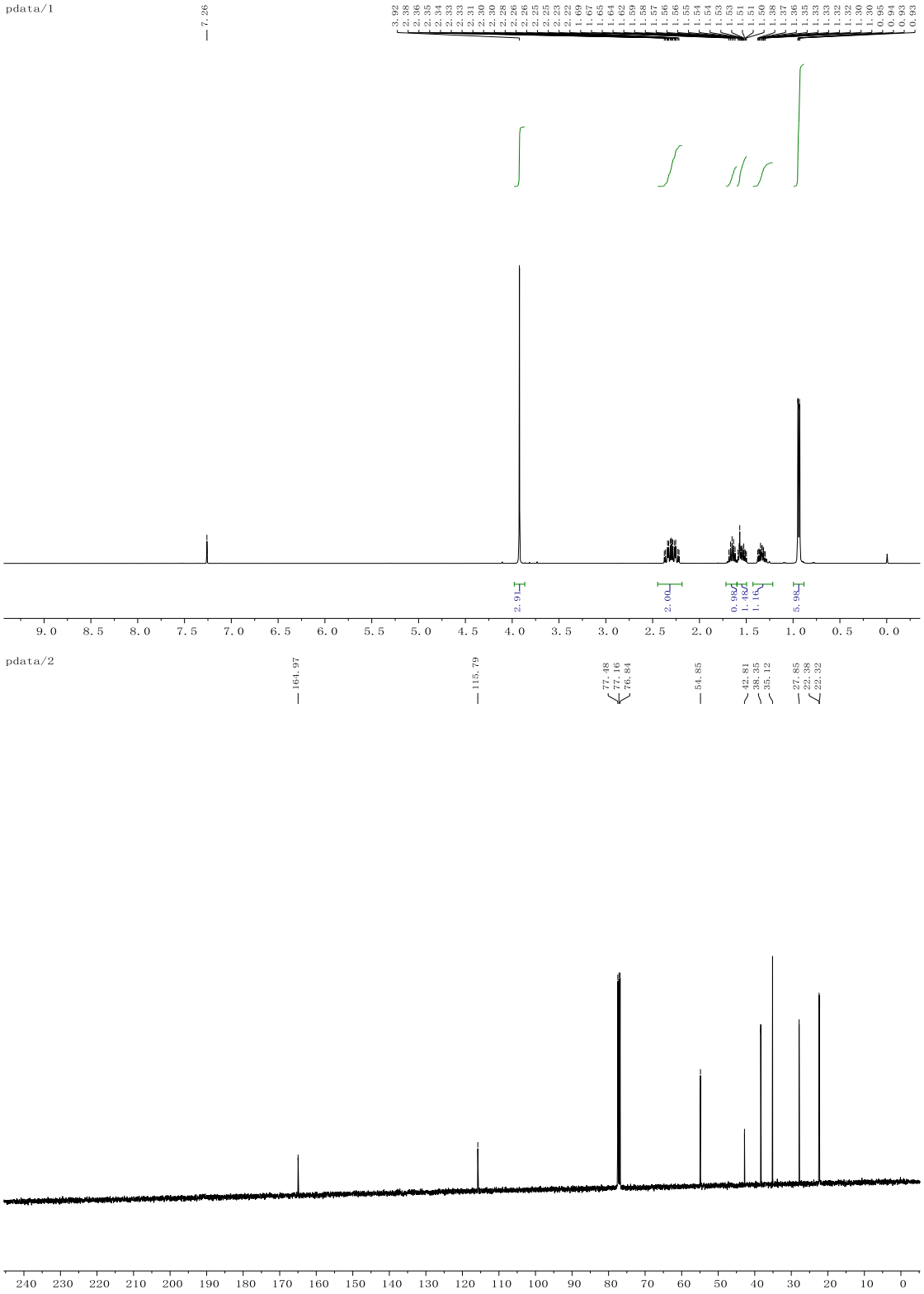
Methyl 2-bromo-2-cyanopropanoate (13a)



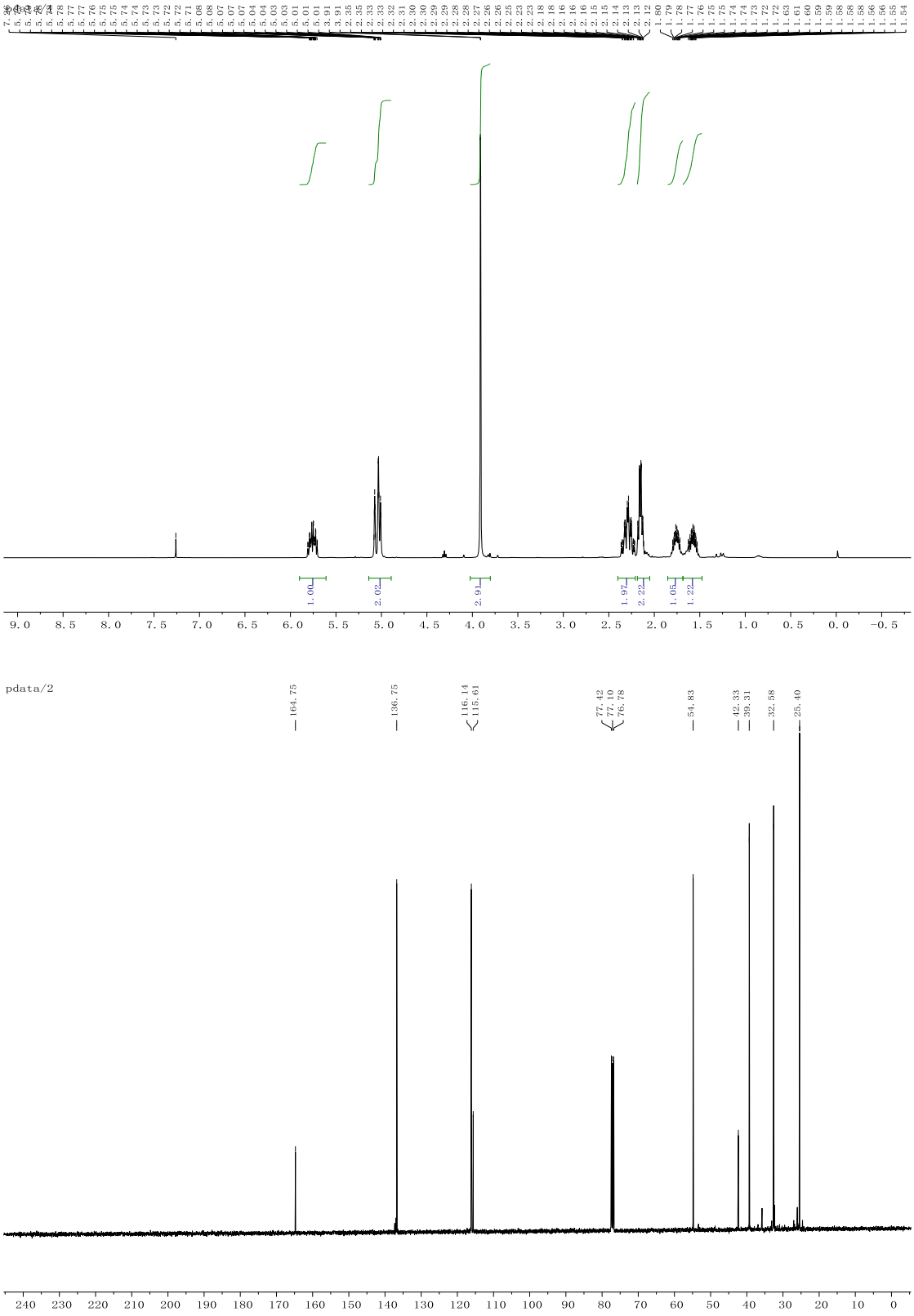
Methyl 2-bromo-2-cyanopentanoate (14a)



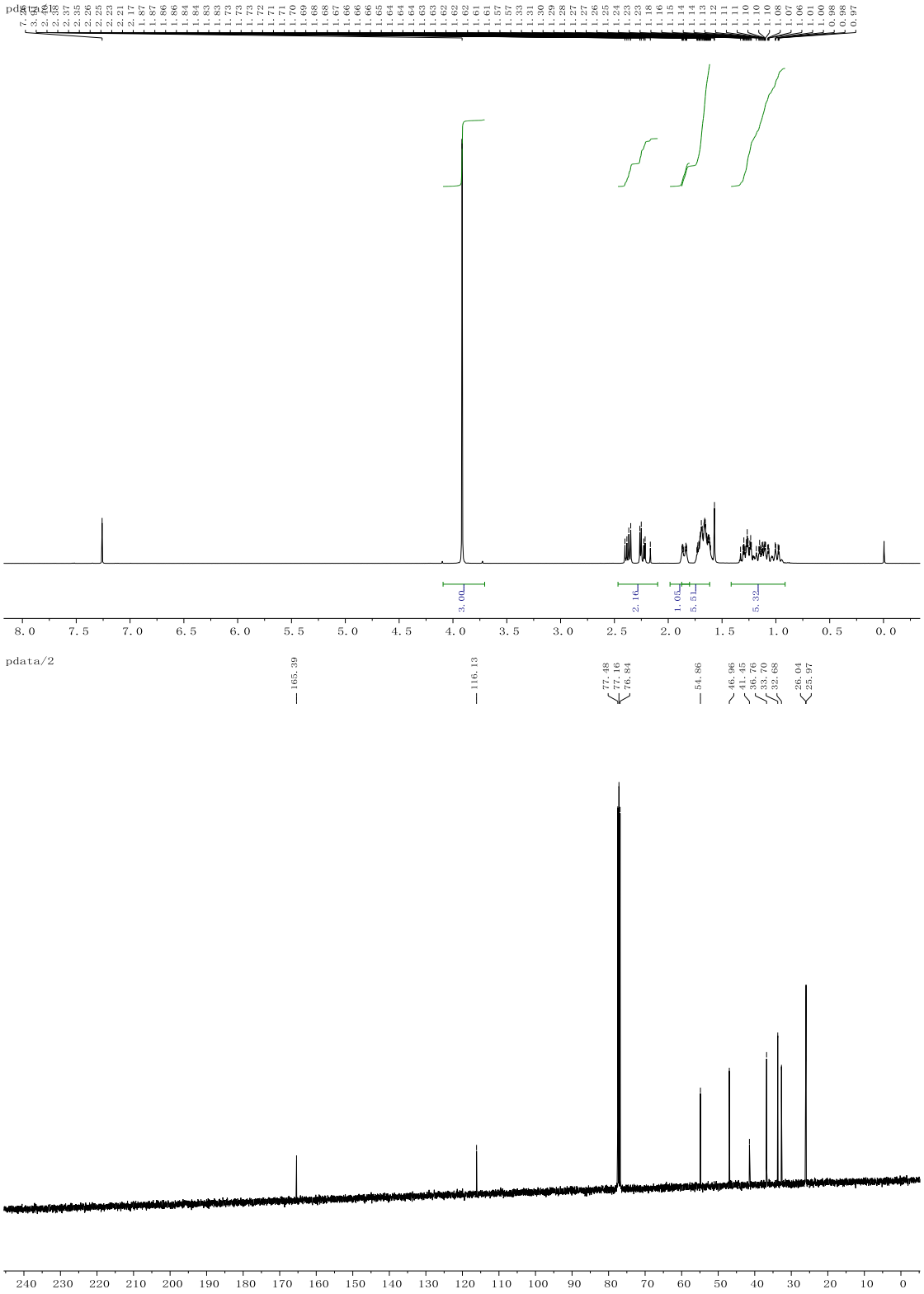
Methyl 2-bromo-2-cyano-5-methylhexanoate (15a)



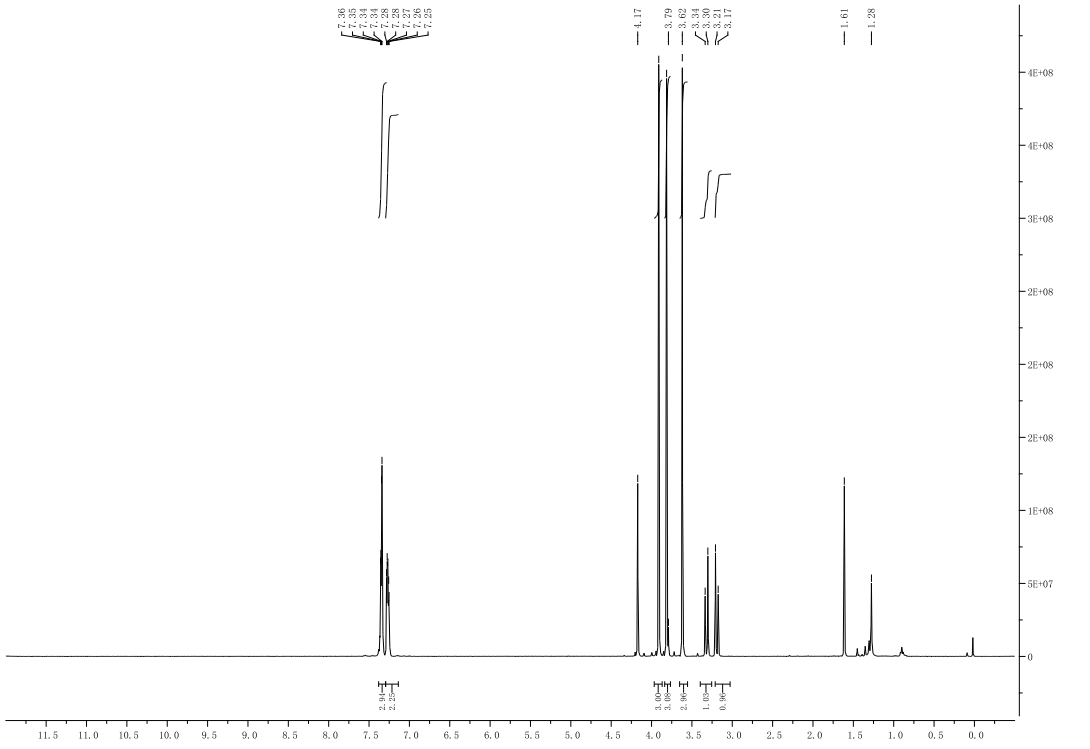
Methyl 2-bromo-2-cyanohept-6-enoate (16a)

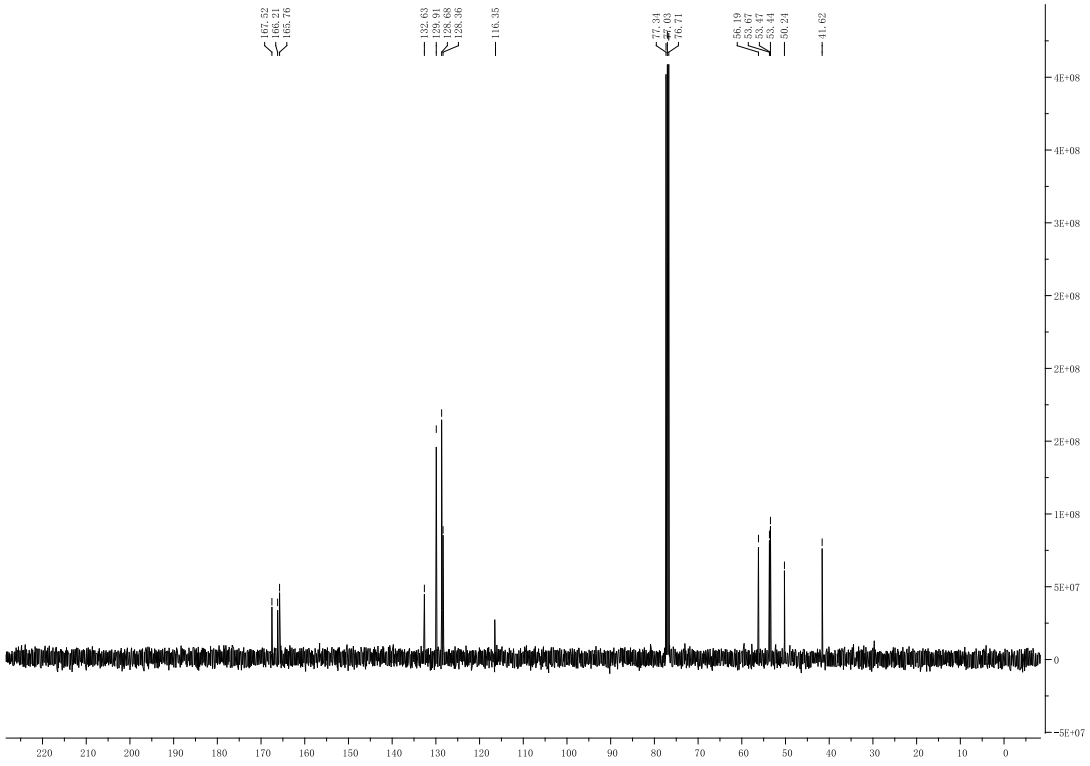


Methyl 2-bromo-2-cyano-3-cyclohexylpropanoate (17a)

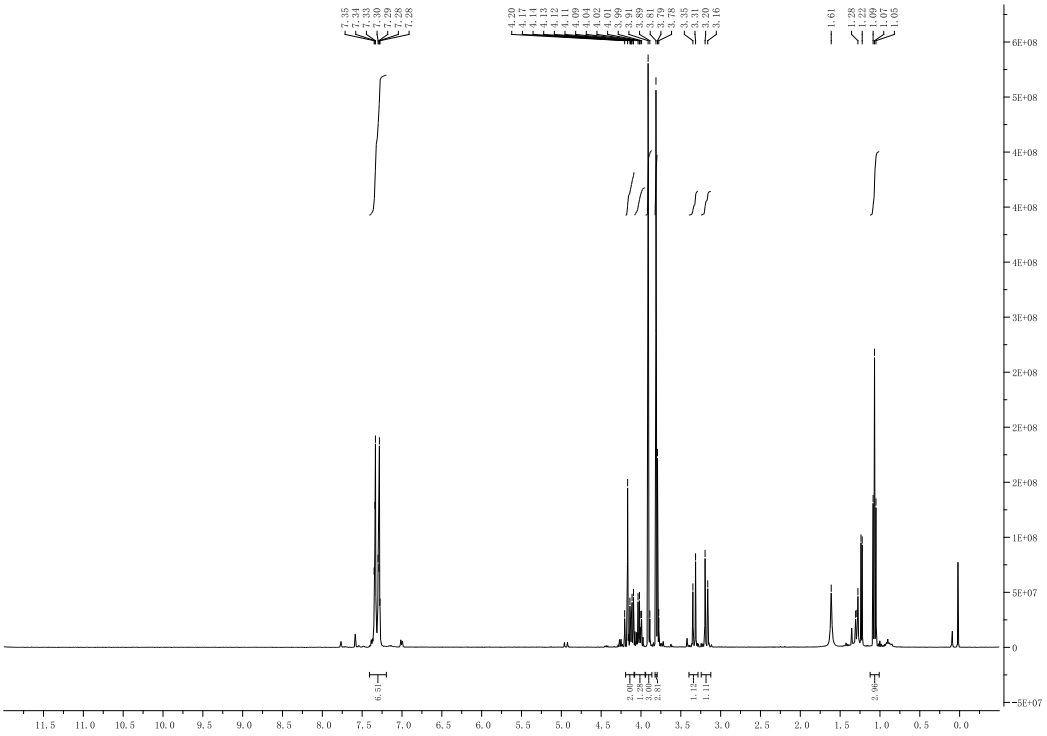


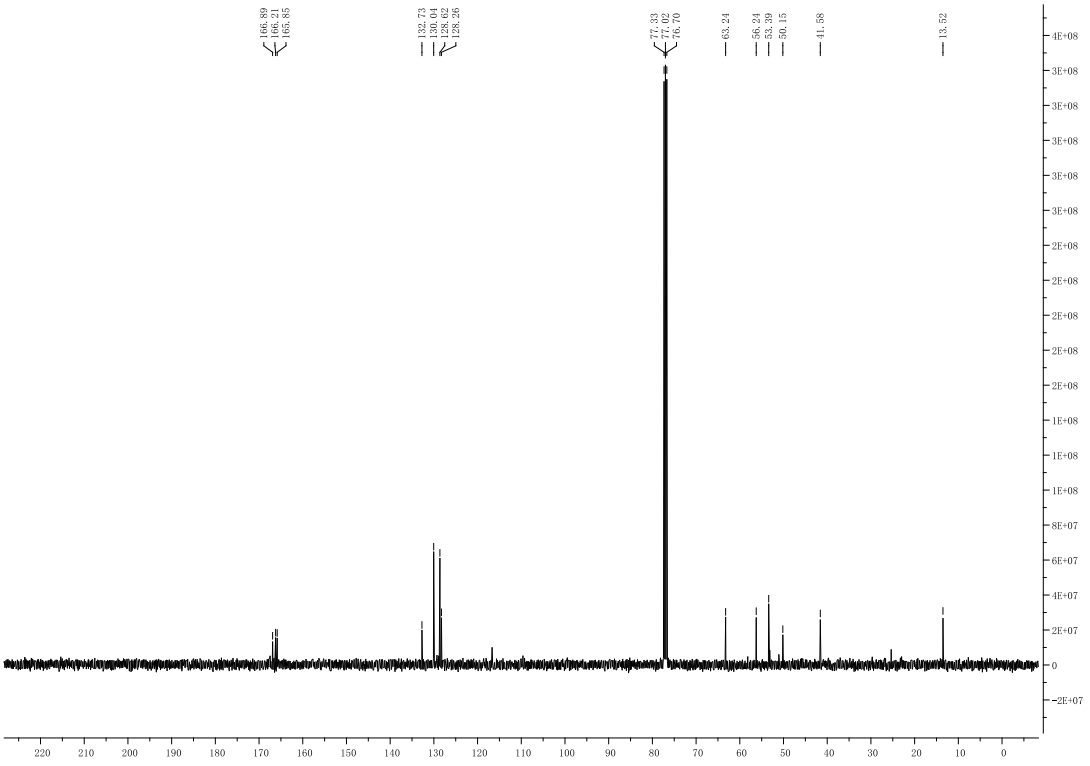
Trimethyl (*R*)-2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2a)


7.36
7.35
7.34
7.28
7.28
7.27
7.26
7.25
4.17
3.79
3.62
3.34
3.30
3.21
3.17
1.61
1.28
2.94
2.25
3.00
3.00
2.96
1.05
0.96

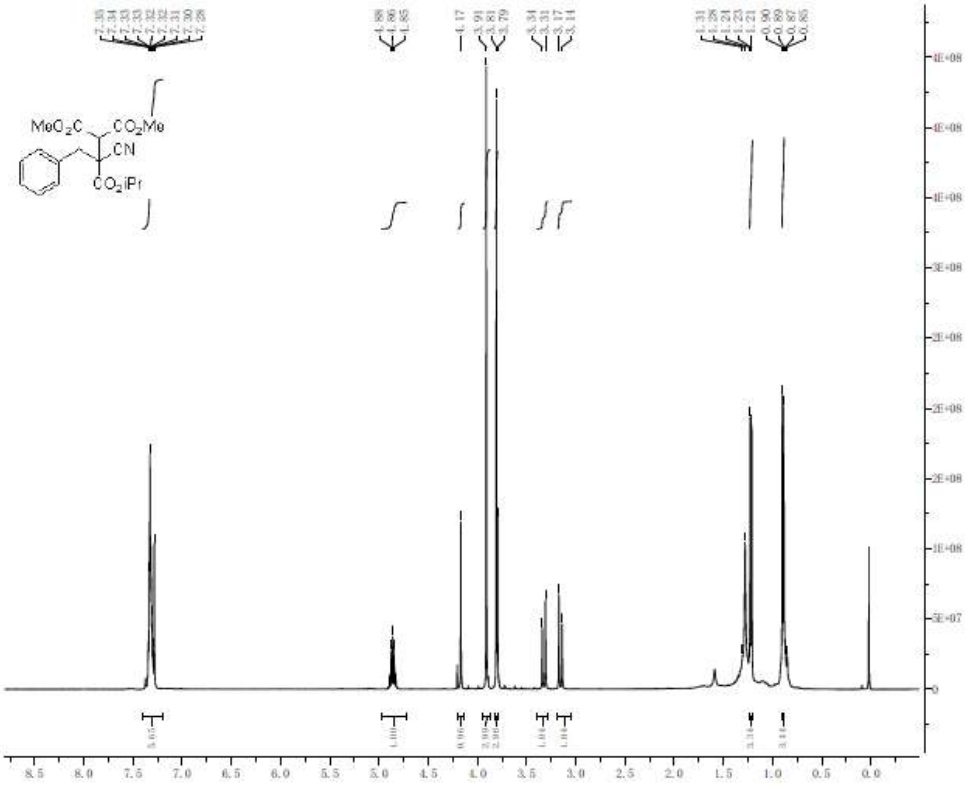

167.52
166.21
165.76
132.63
129.91
128.68
128.36
116.35
77.34
77.03
76.71
56.19
53.67
53.47
53.44
50.24
41.62

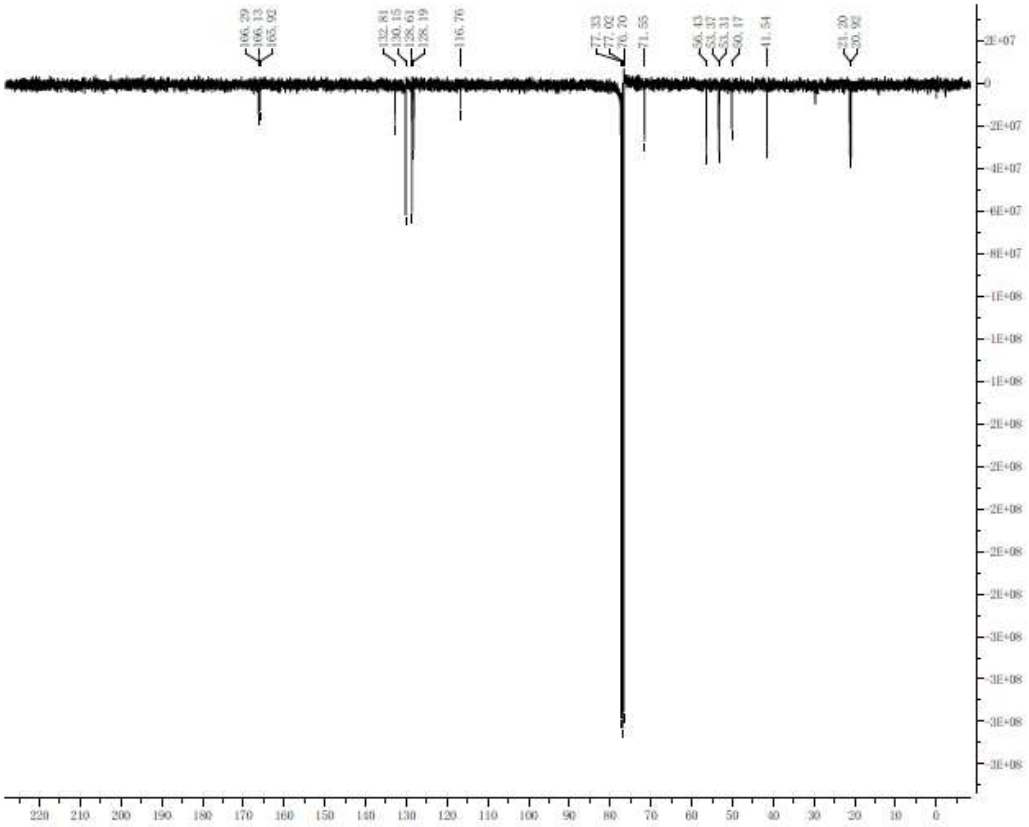
2-ethyl 1,1-dimethyl (*R*)-2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2b)



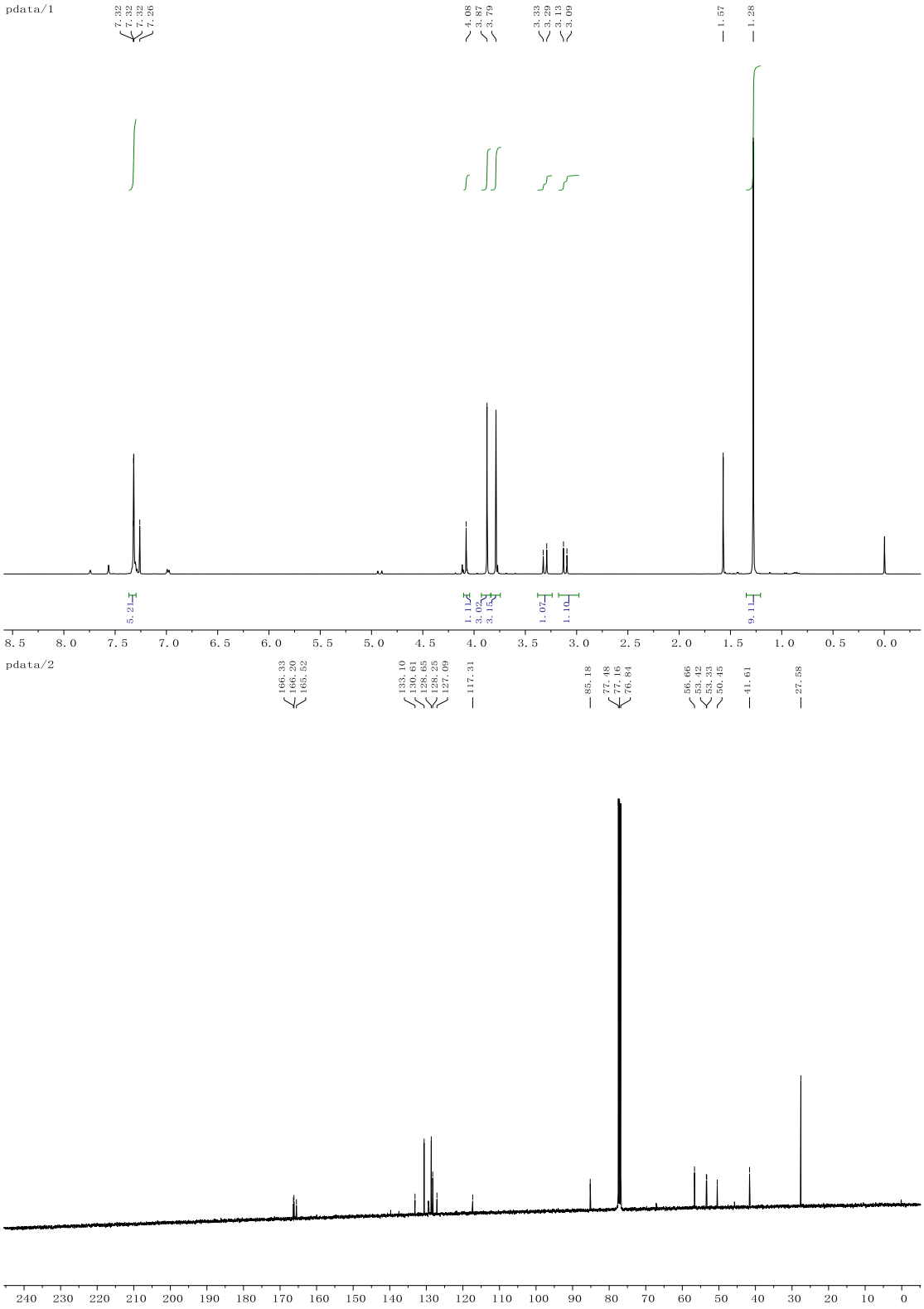


2-isopropyl 1,1-dimethyl (*R*)-2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2c)

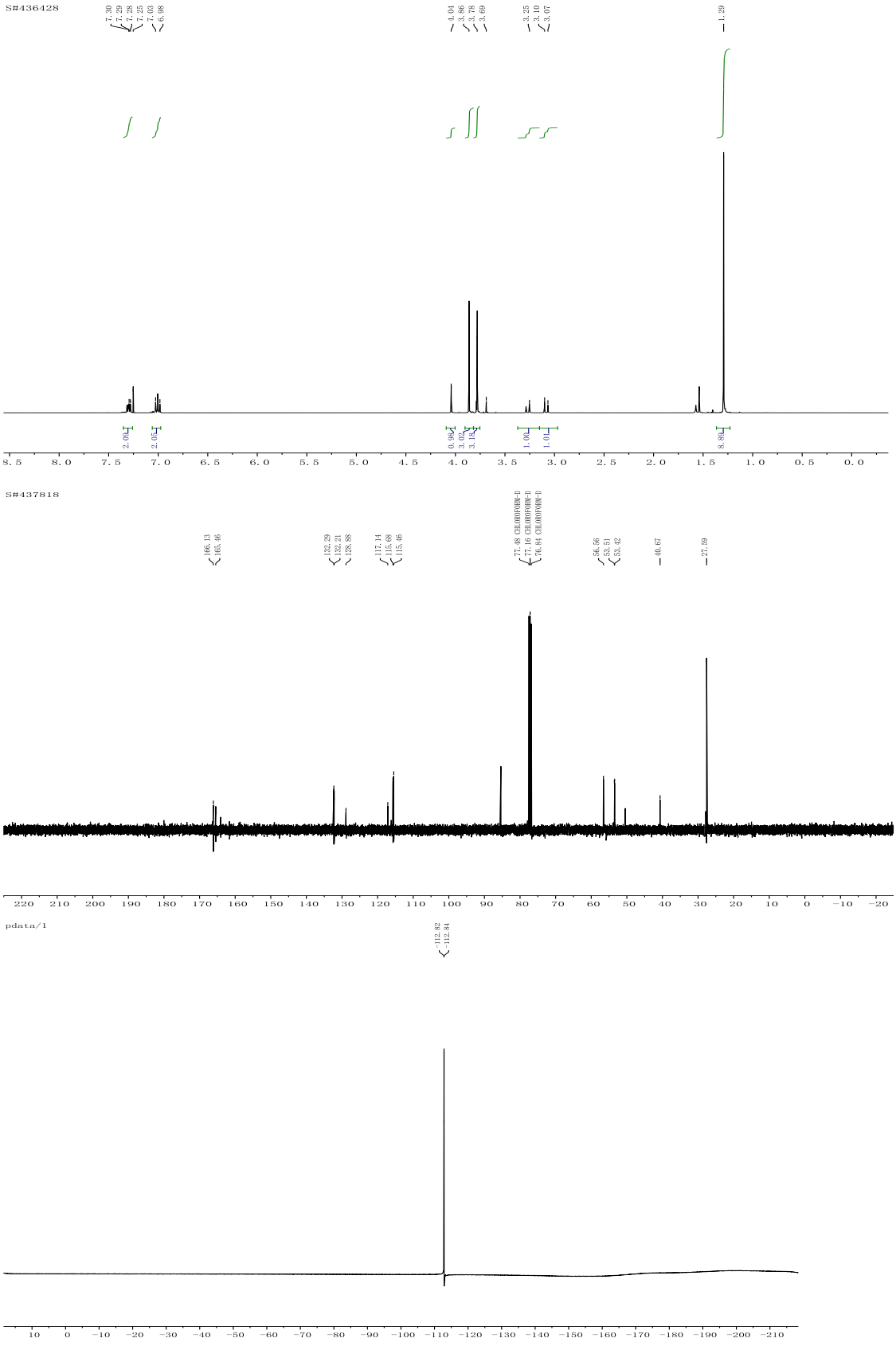




2-(tert-butyl) 1,1-dimethyl (*R*)−2-cyano-3-phenylpropane-1,1,2-tricarboxylate (2d)

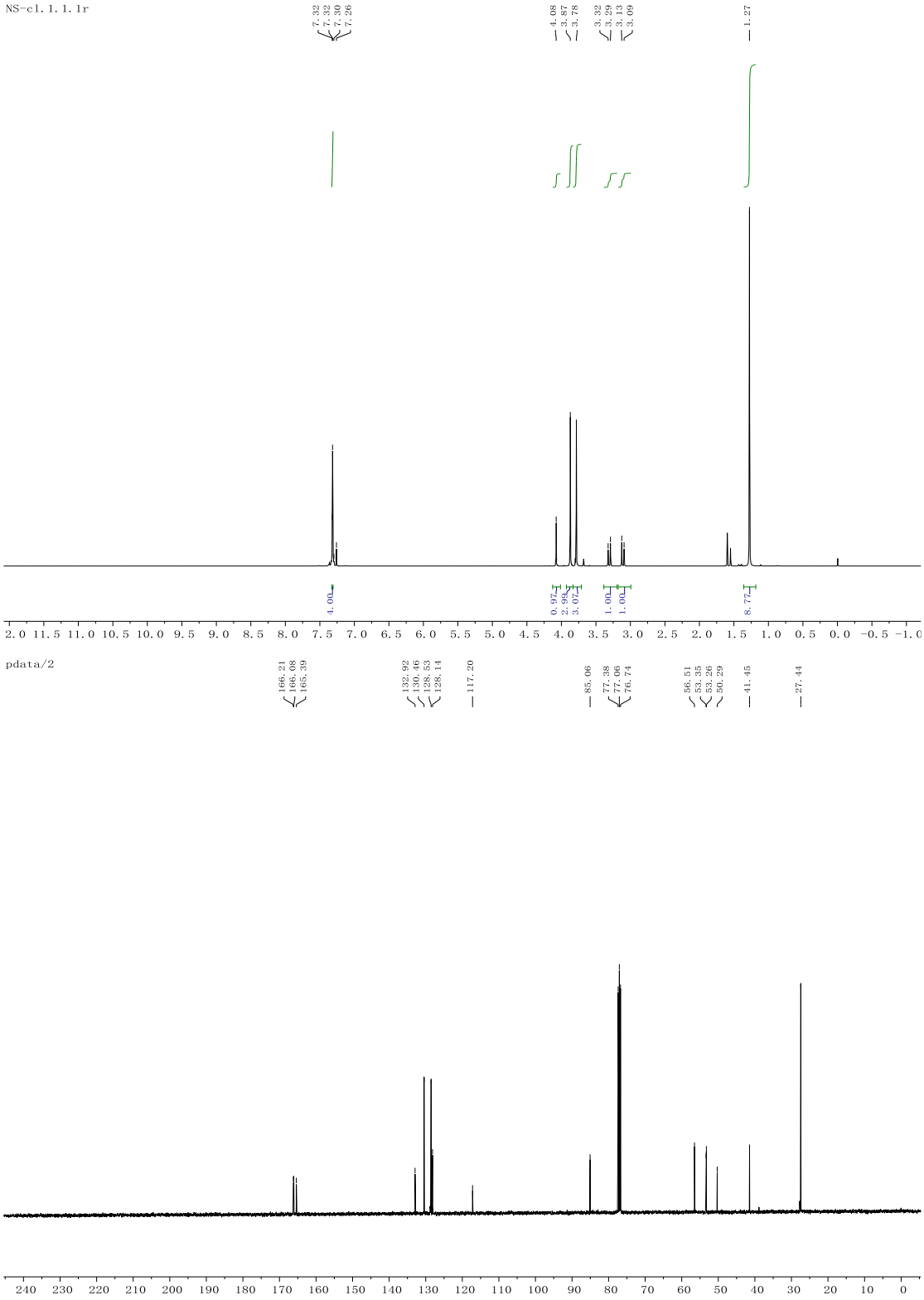


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(4-fluorophenyl)propane-1,1,2-tricarboxylate (2e)

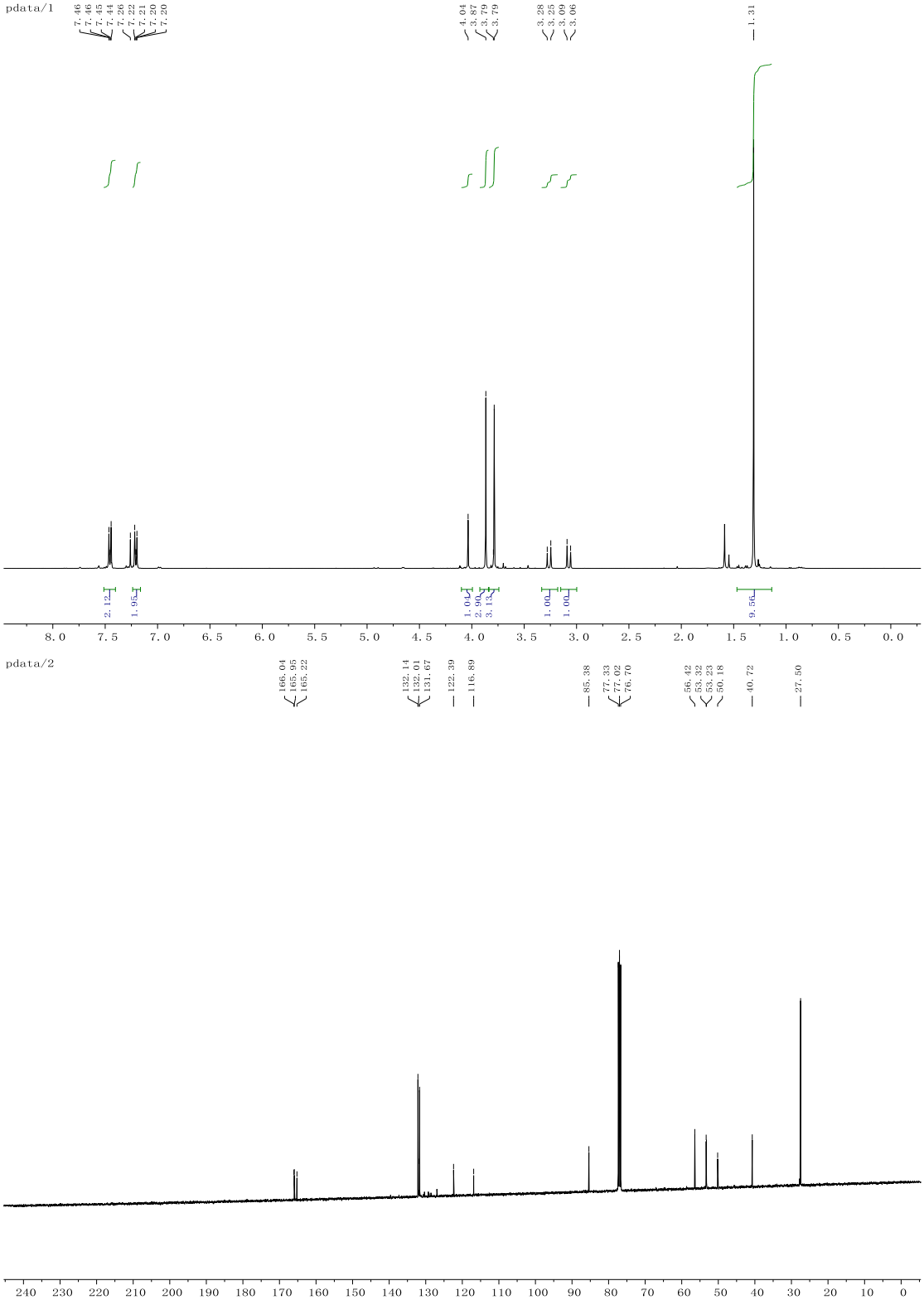


2-(tert-butyl) 1,1-dimethyl 3-(4-chlorophenyl)- (*R*)-2-cyanopropane-1,1,2-

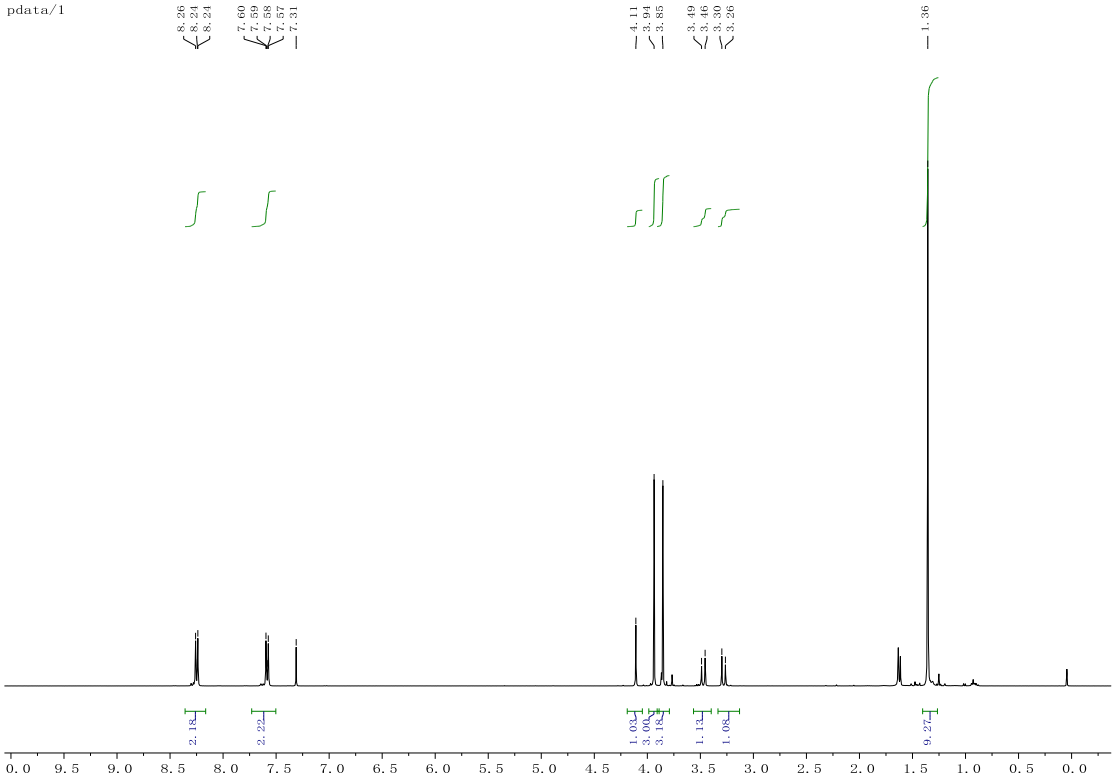
tricarboxylate (2f)

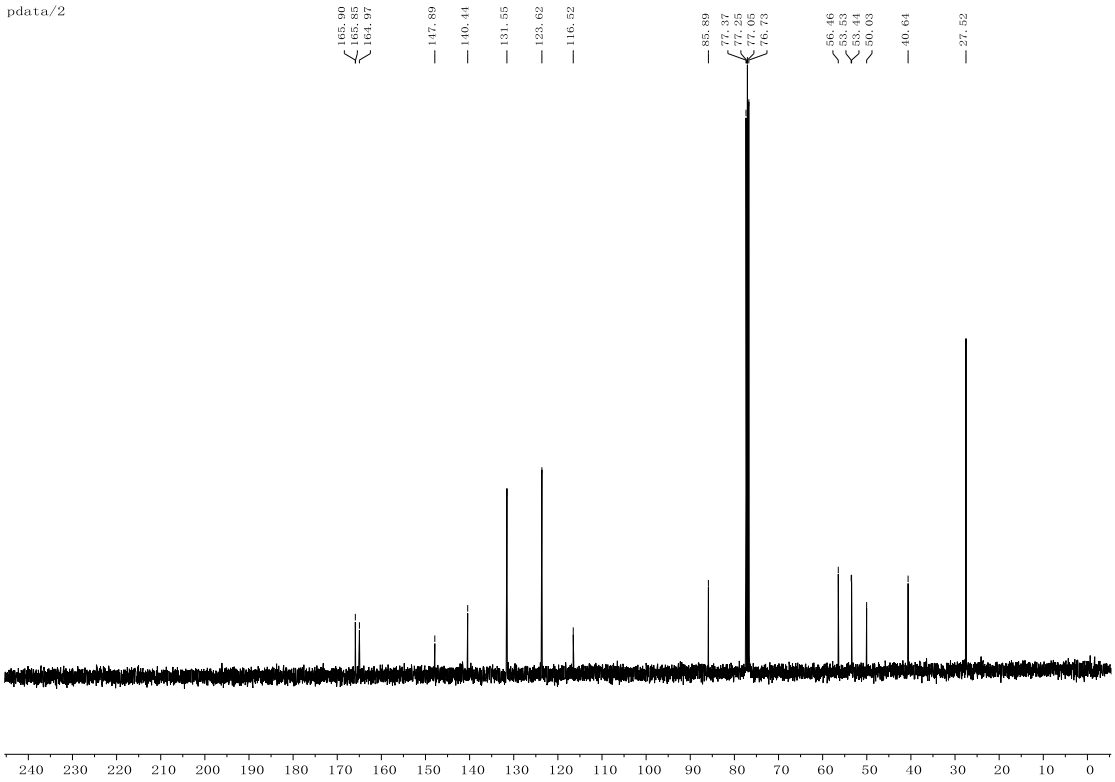


2-(tert-butyl) 1,1-dimethyl 3-(4-bromophenyl)- (*R*)-2-cyanopropane-1,1,2-tricarboxylate (2g)

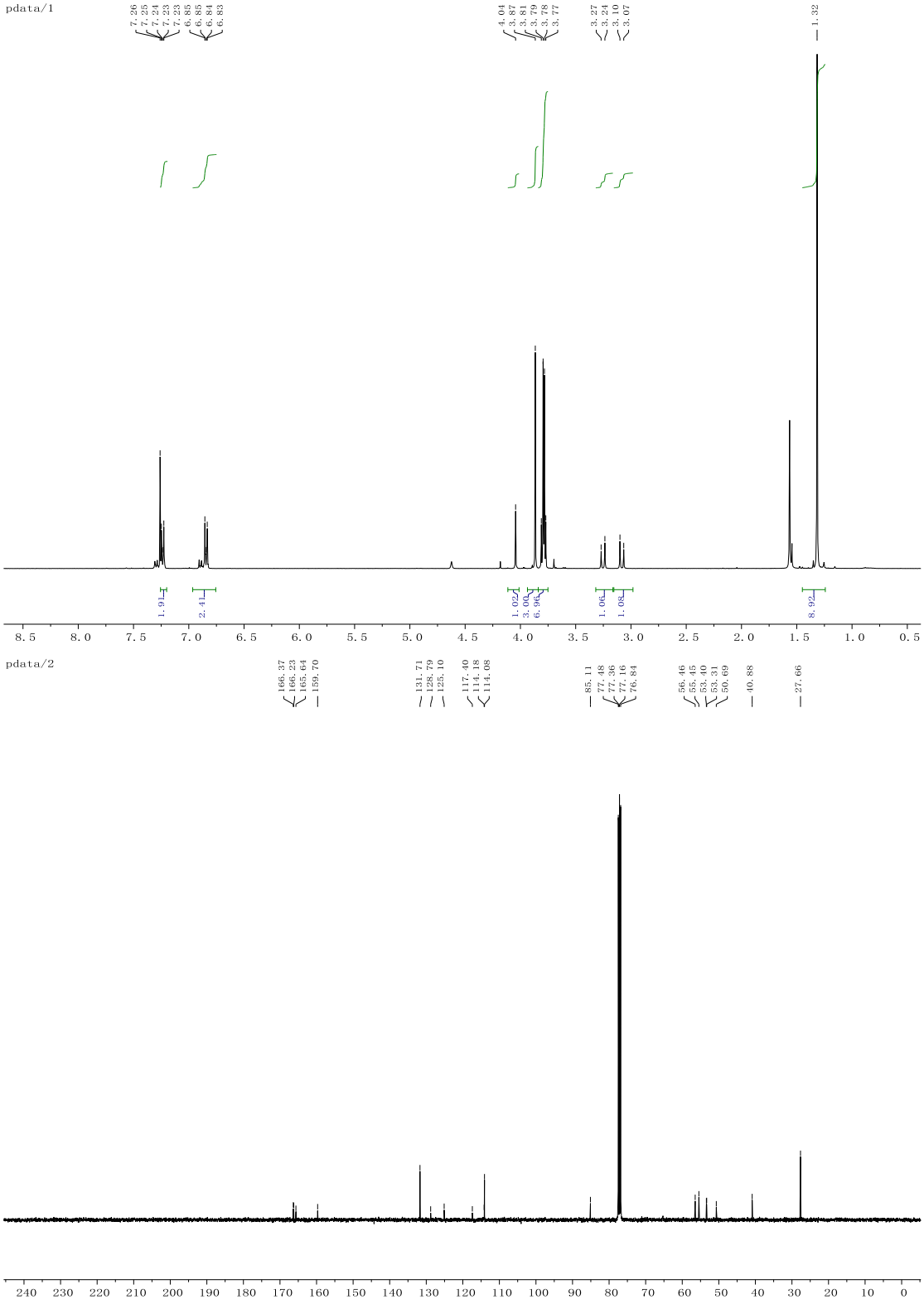


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(4-nitrophenyl)propane-1,1,2-tricarboxylate (2h)

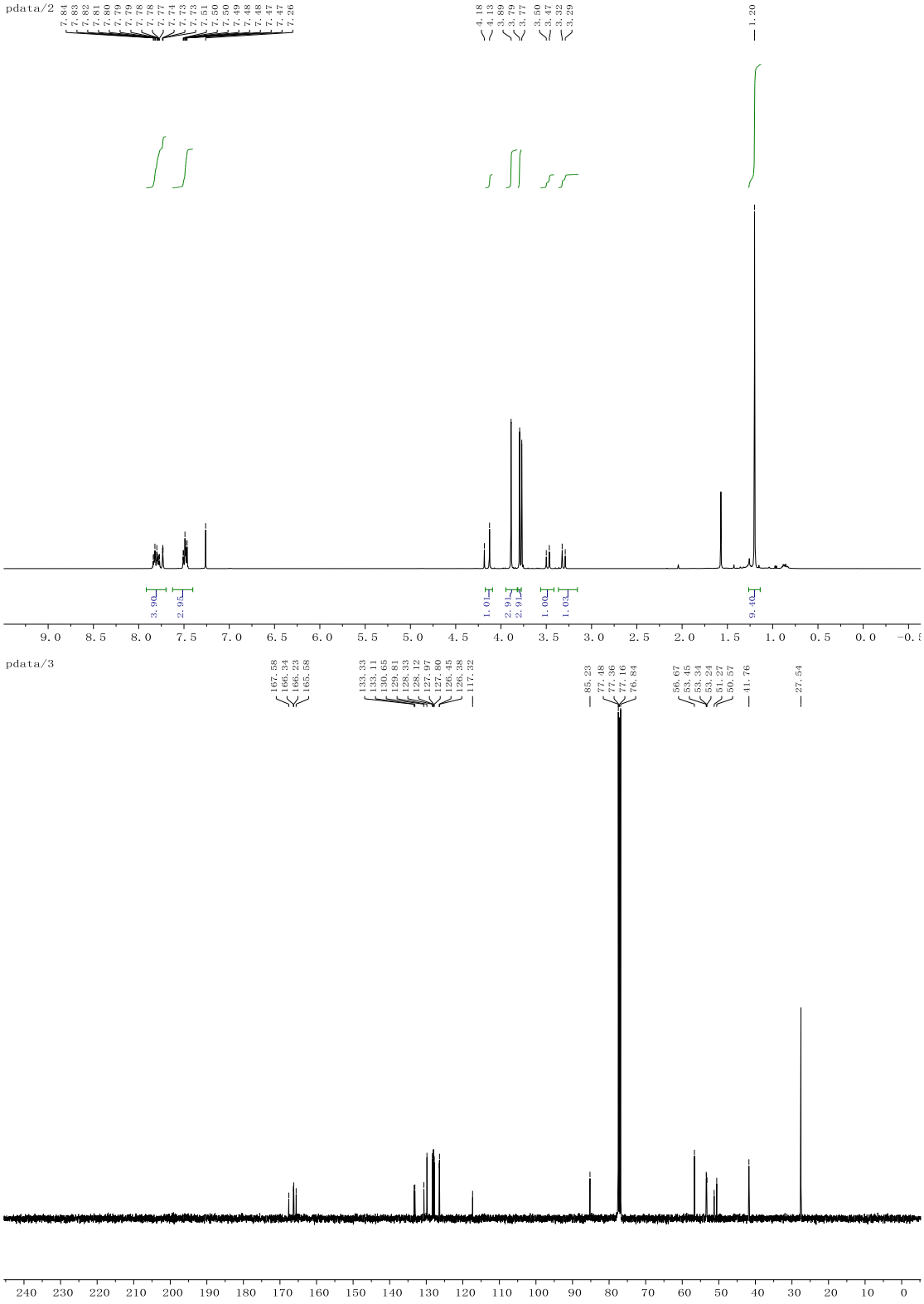




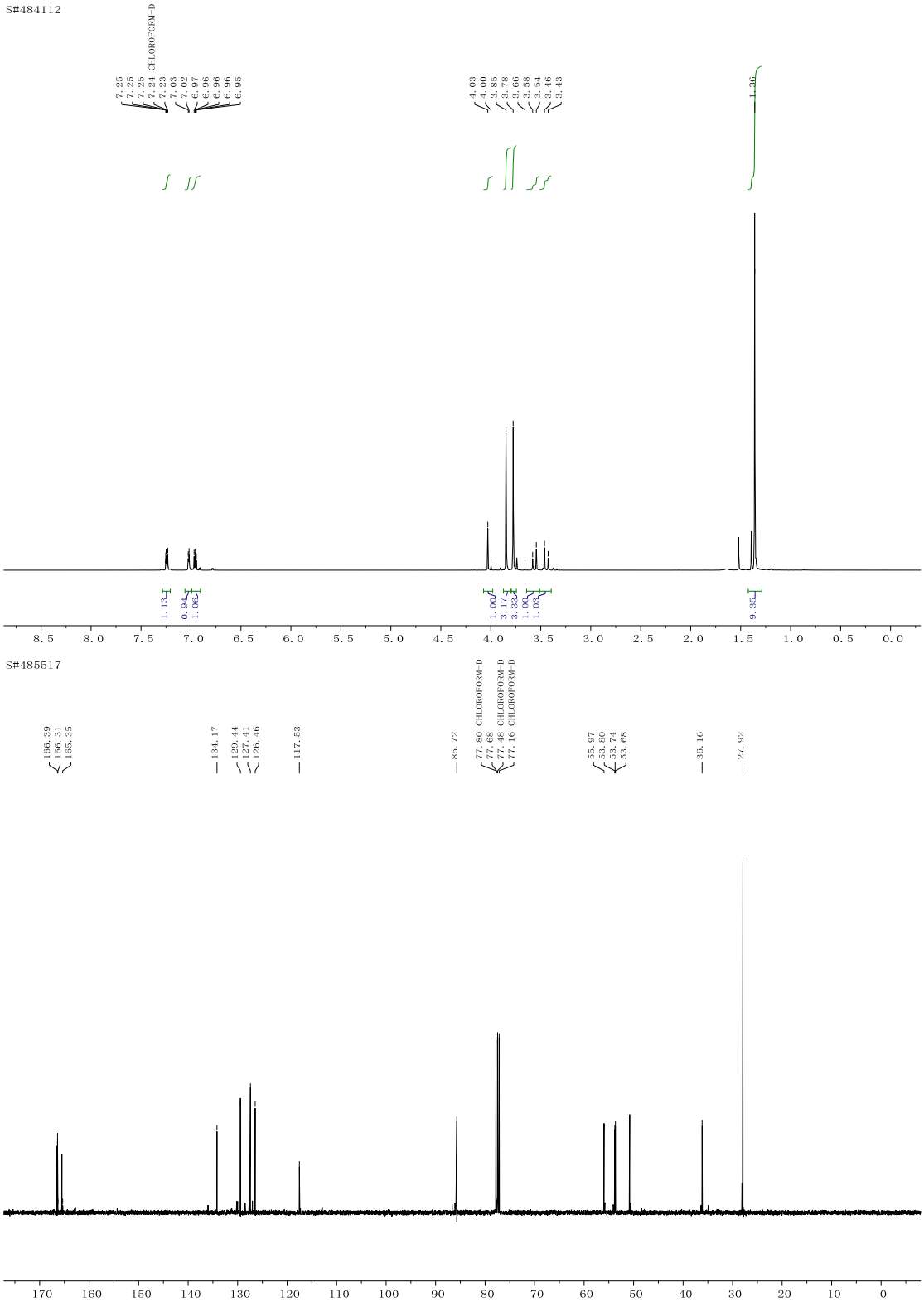
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(4-methoxyphenyl)propane-1,1,2-tricarboxylate (2i)



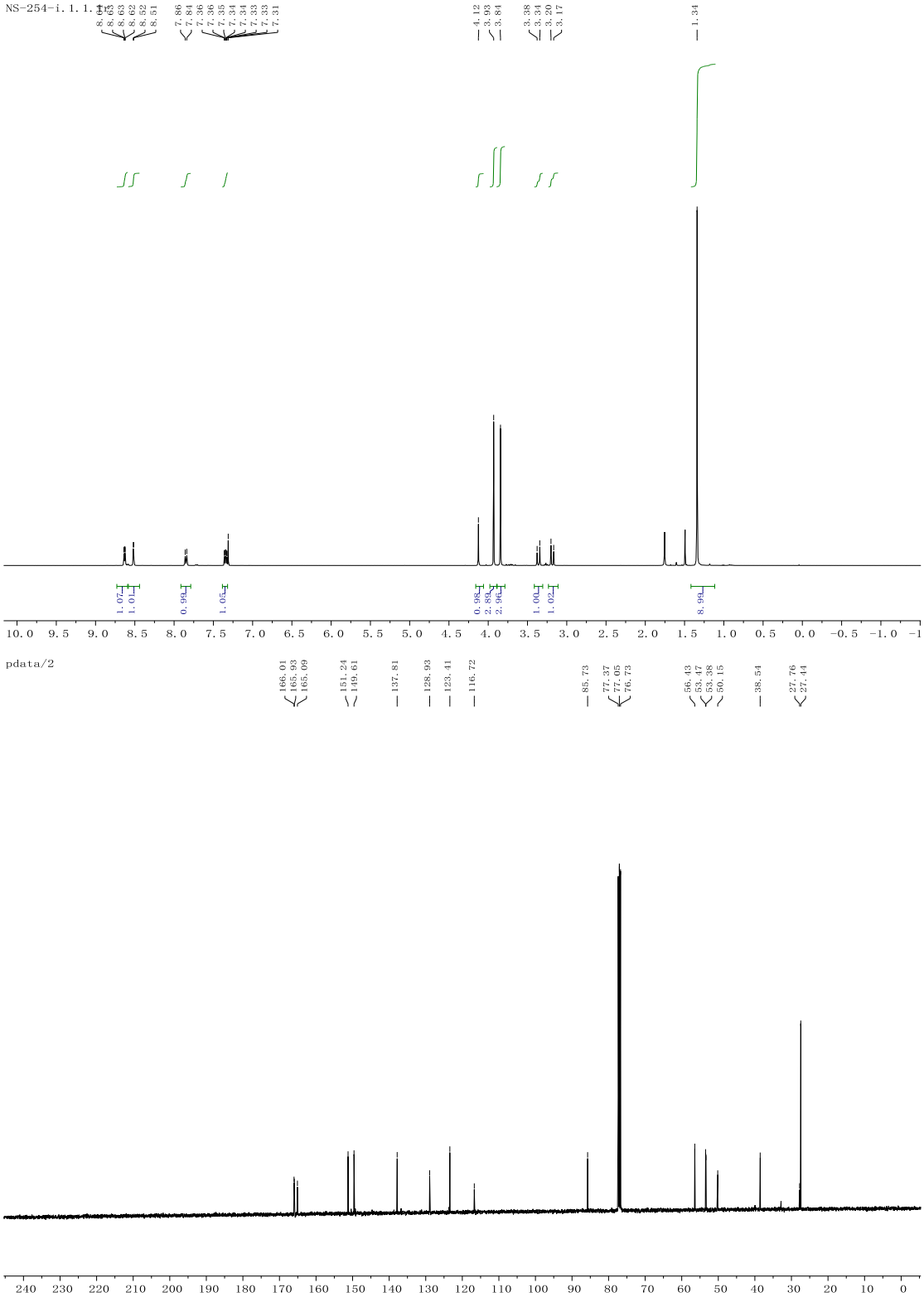
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(naphthalen-2-yl)propane-1,1,2-tricarboxylate (2j)



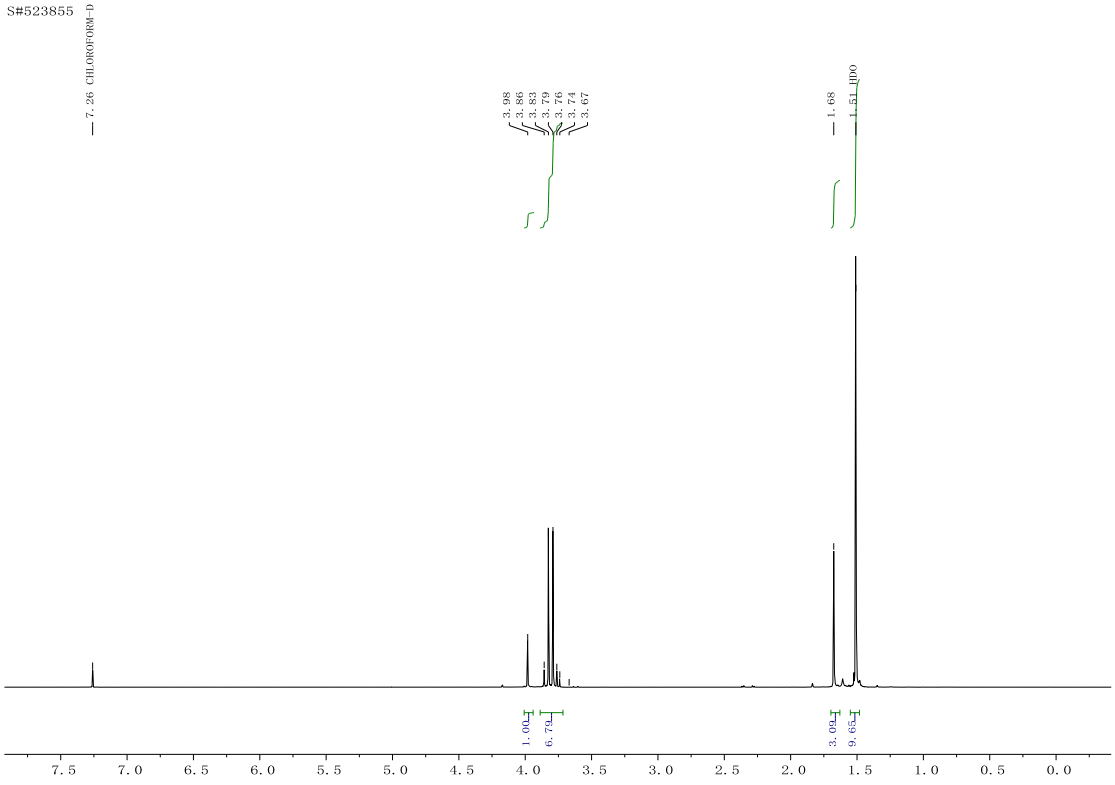
2-(tert-butyl) 1,1-dimethyl 2-cyano-3-(thiophen-2-yl)propane-1,1,2-tricarboxylate (2k)

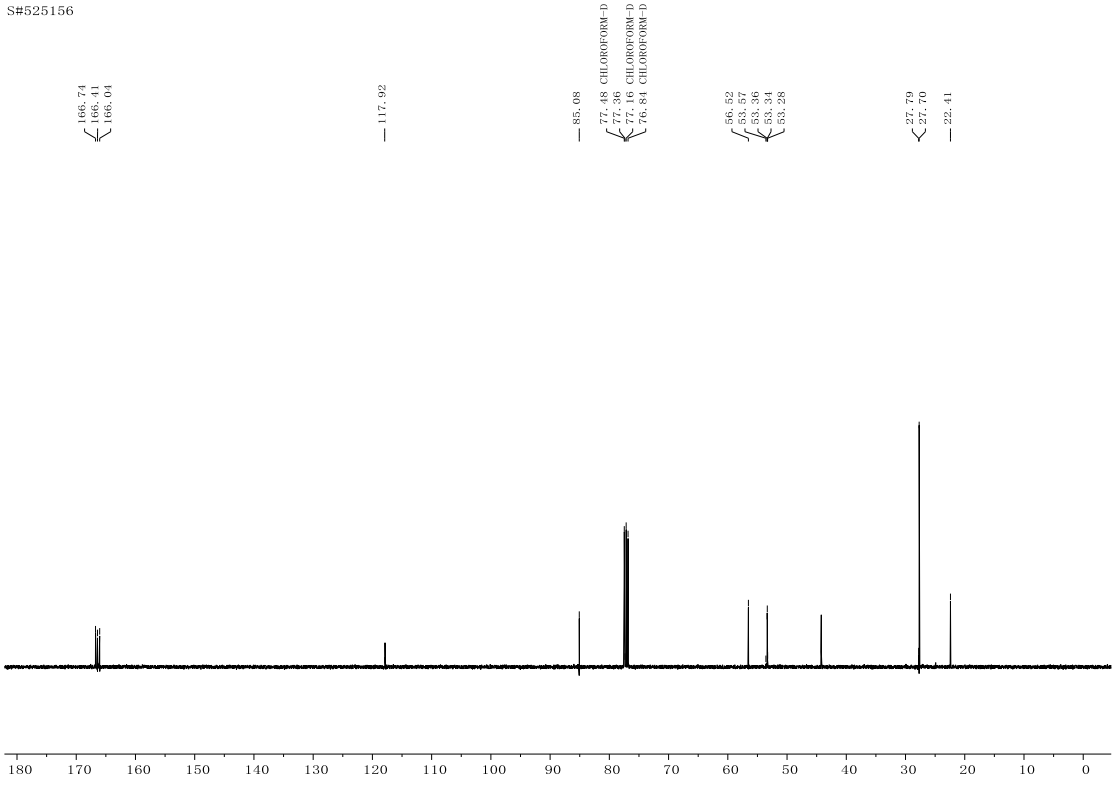


2-(*tert*-butyl) 1,1-dimethyl (*R*)-2-cyano-3-(pyridin-3-yl)propane-1,1,2-tricarboxylate (2l)

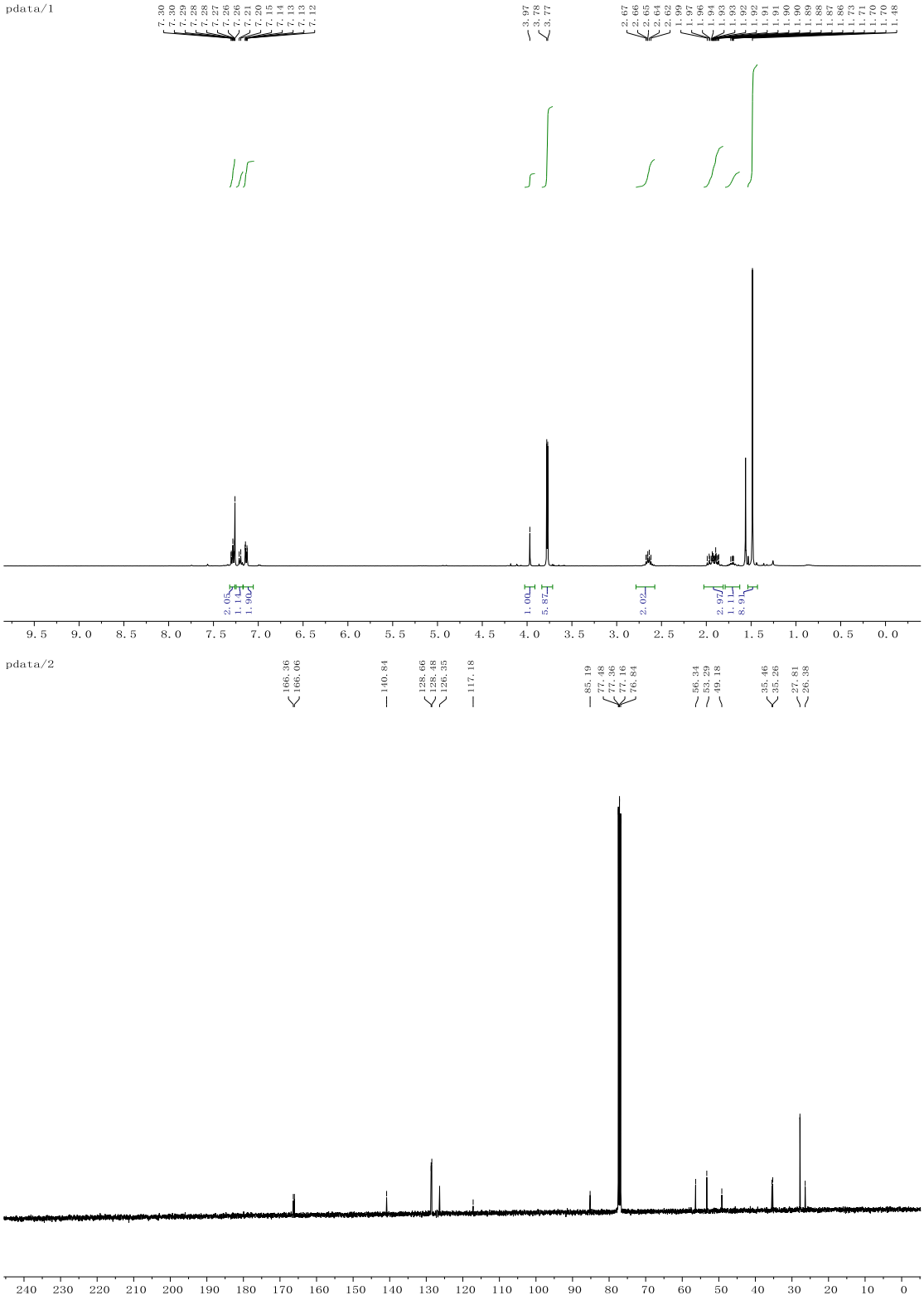


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyanopropane-1,1,2-tricarboxylate (2m)

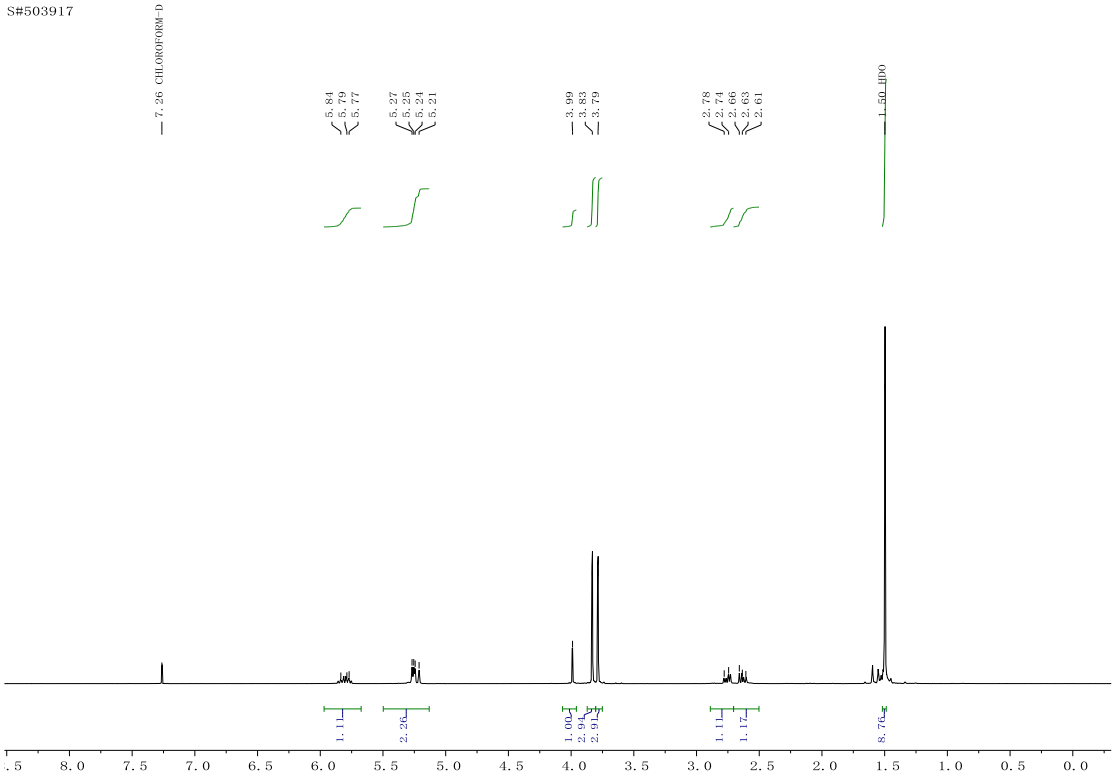


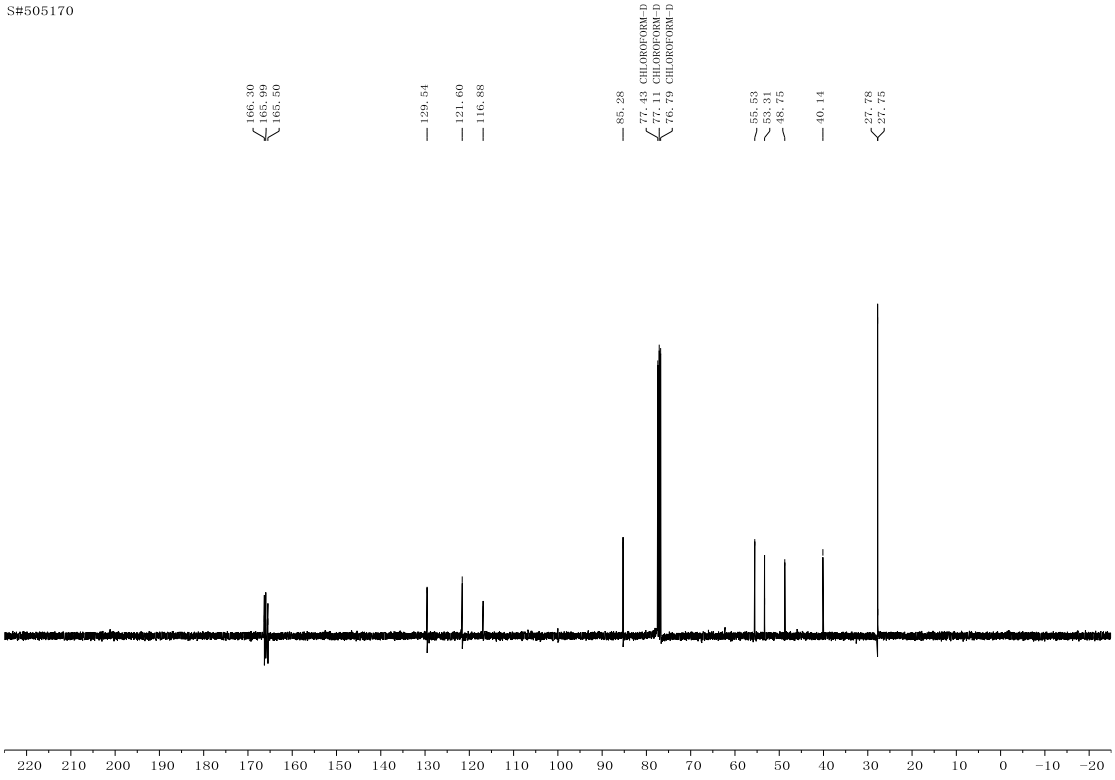


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyano-5-phenylpentane-1,1,2-tricarboxylate (2n)

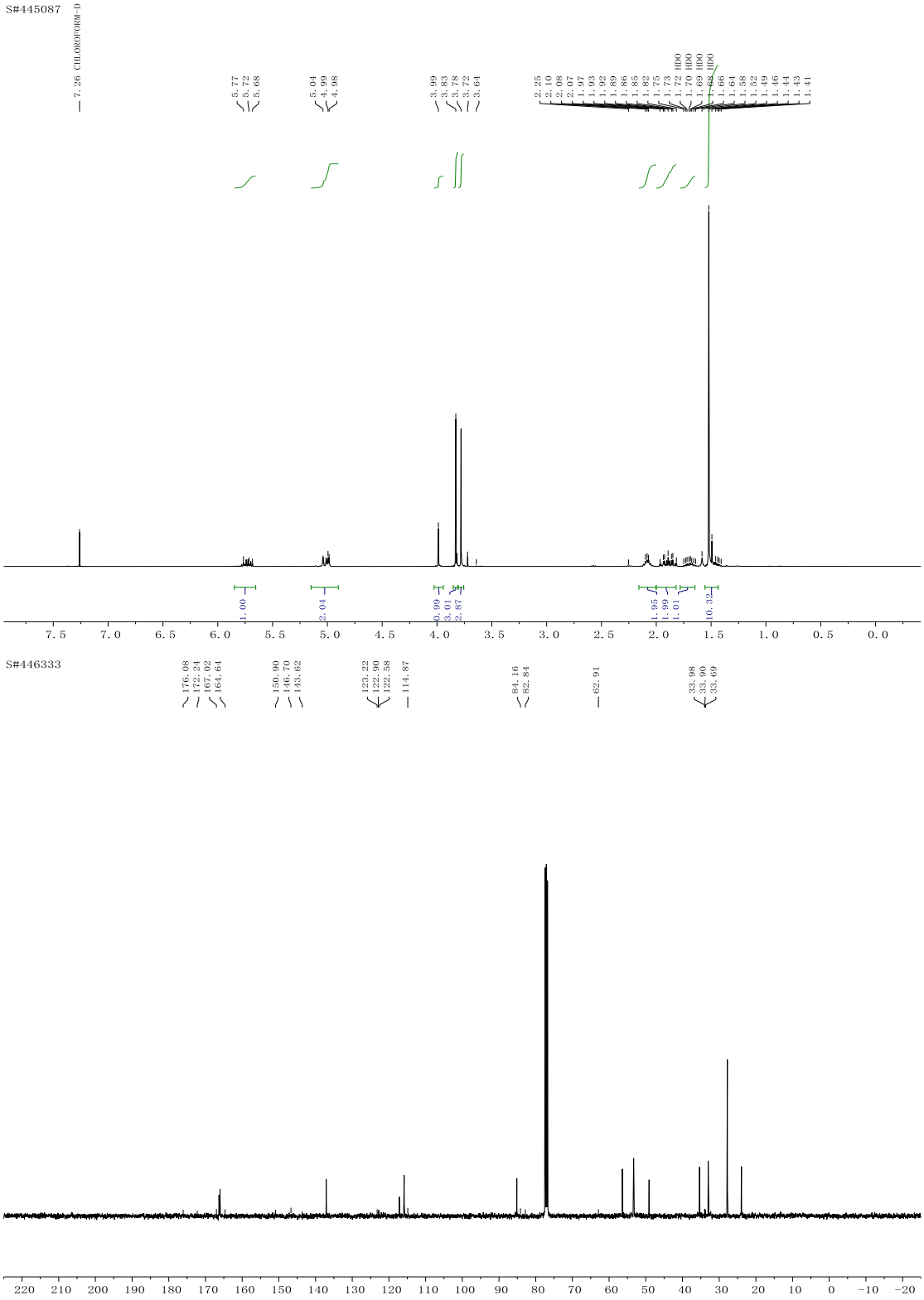


2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyanopent-4-ene-1,1,2-tricarboxylate (2o)

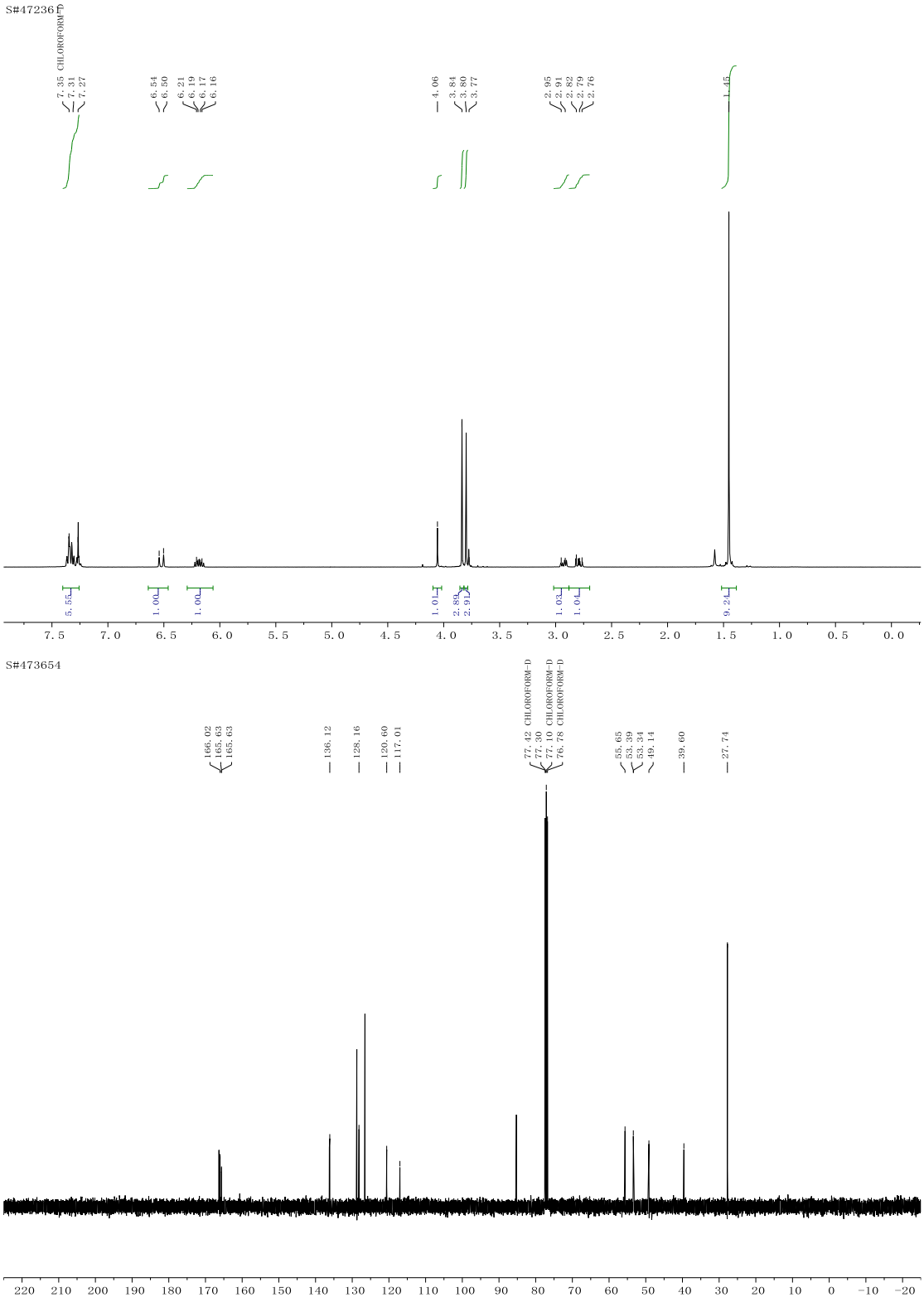




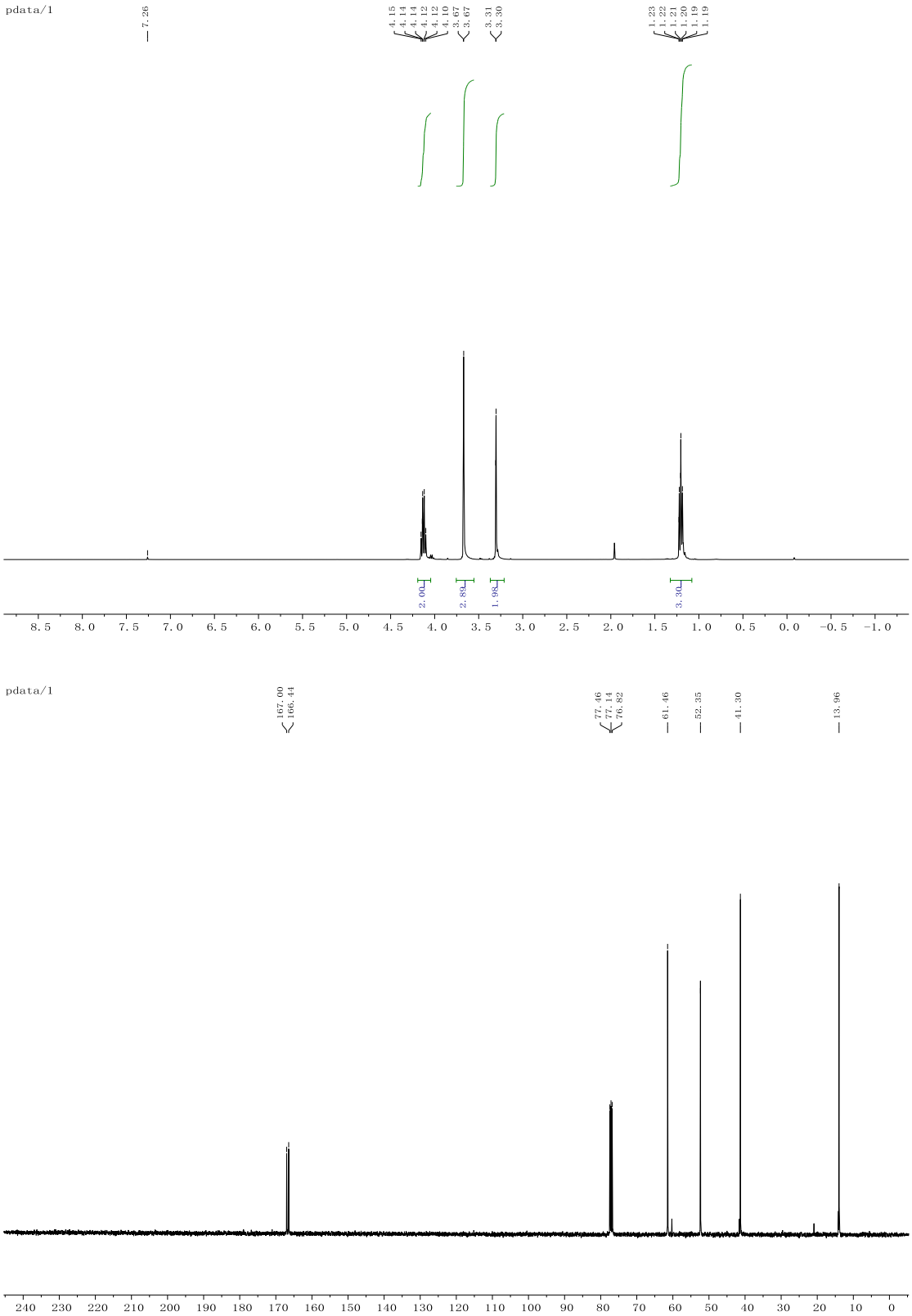
2-(tert-butyl) 1,1-dimethyl (*R*)-2-cyanohept-6-ene-1,1,2-tricarboxylate (2p)



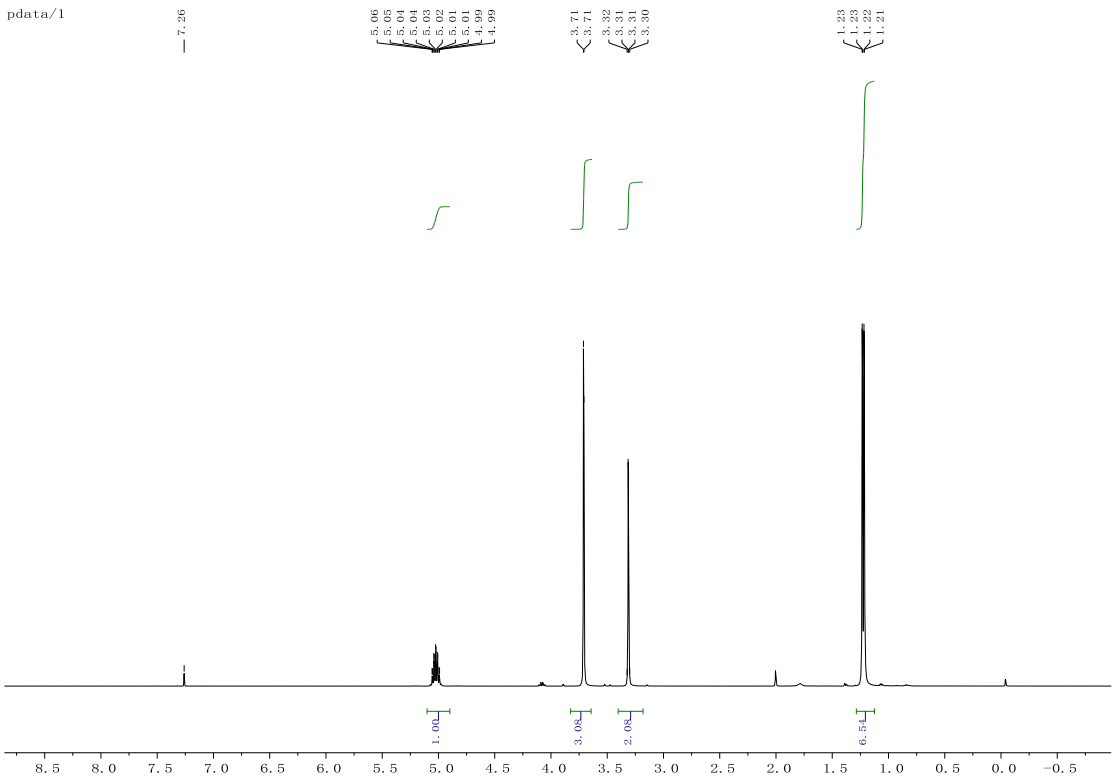
2-(tert-butyl) 1,1-dimethyl (*R*,*E*)-2-cyano-5-phenylpent-4-ene-1,1,2-tricarboxylate (2q)



Ethyl methyl malonate (18a)



isopropyl methyl malonate (18b)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5.02
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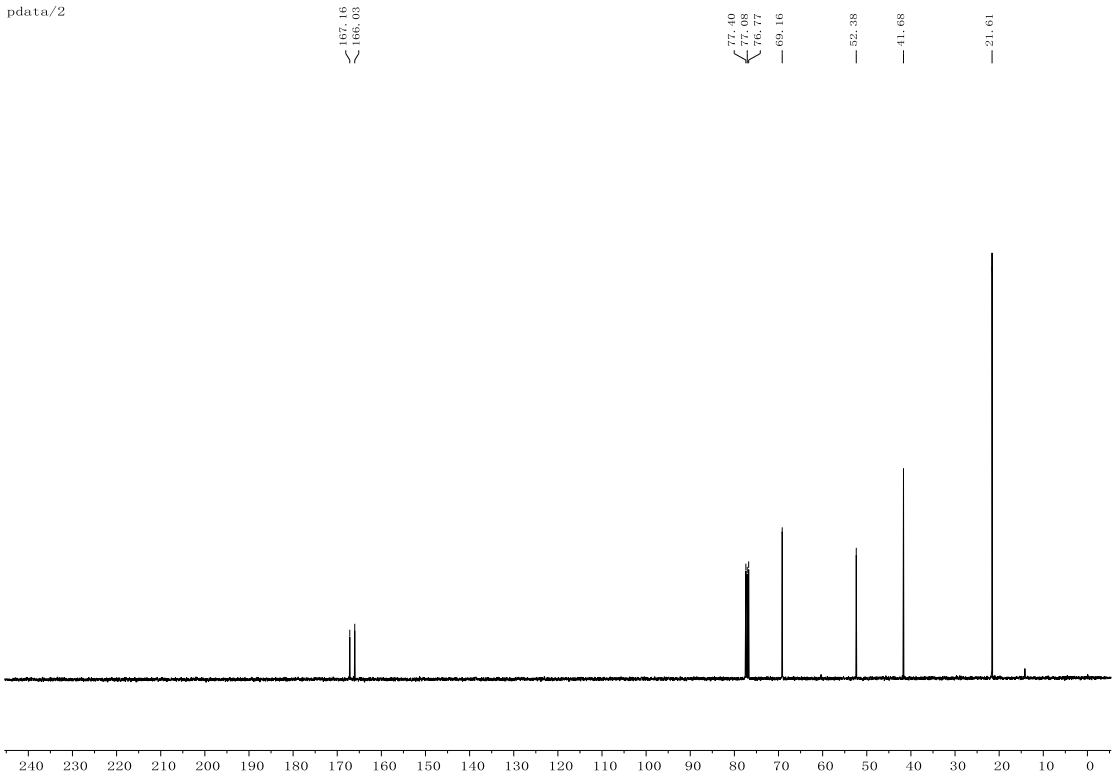
3.71
3.32
3.31
3.31
3.30
1.23
1.23
1.22
1.21
1.00
3.08
2.08
6.54
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5


pdata/2
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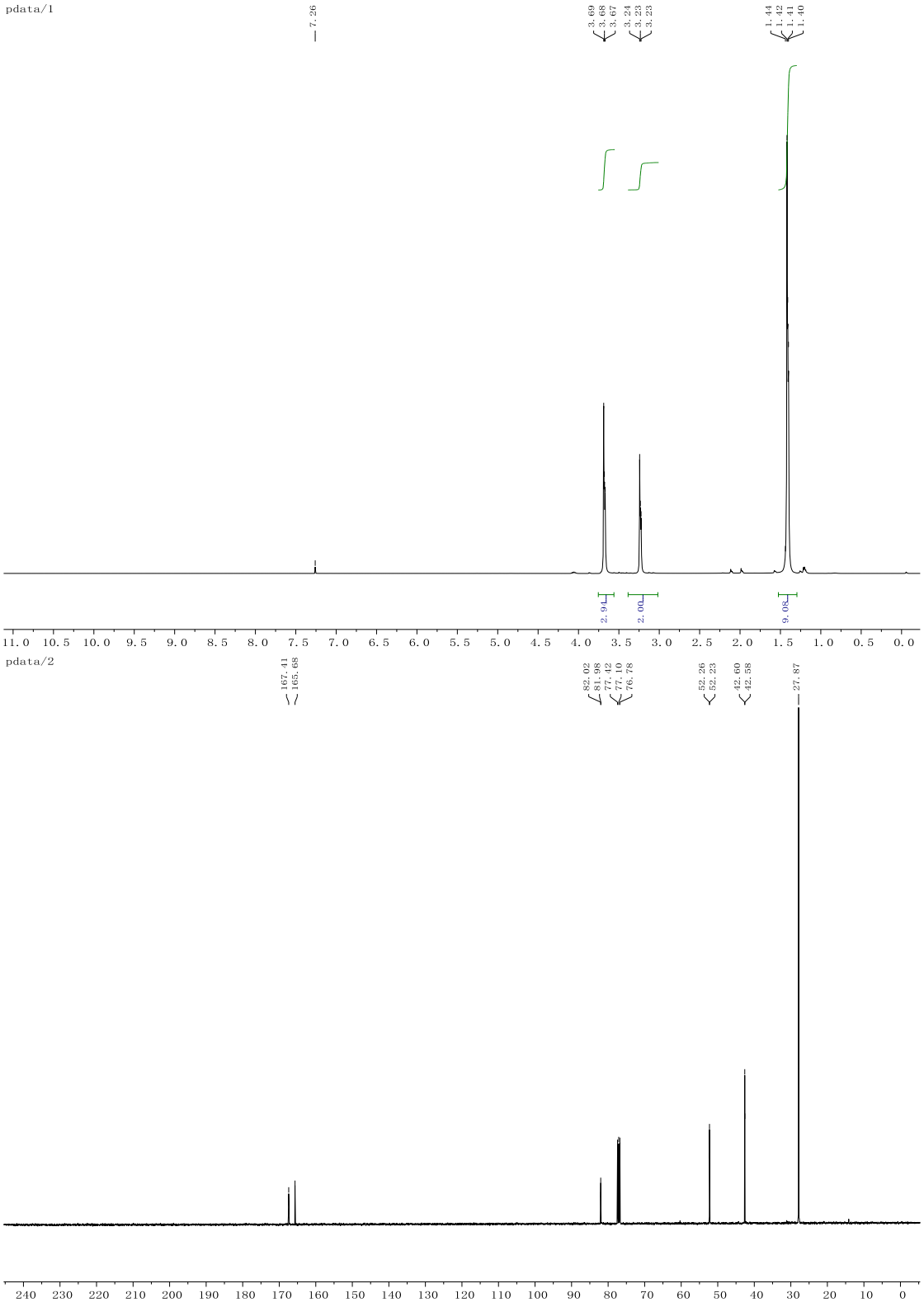
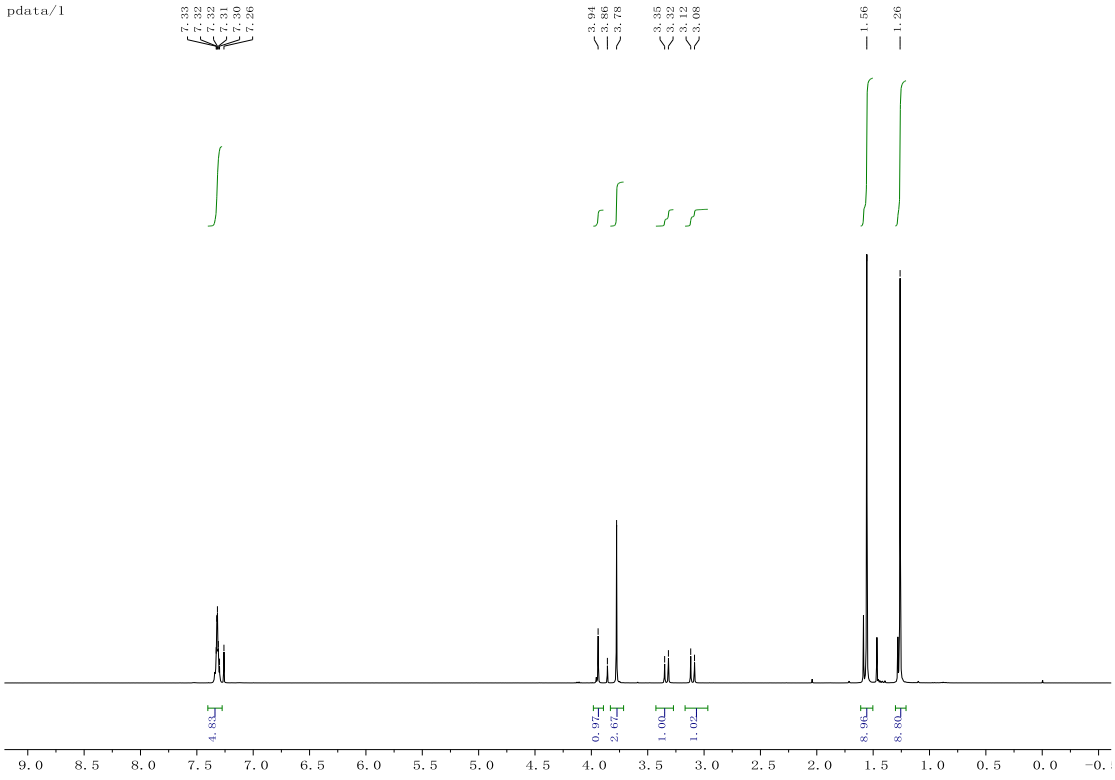
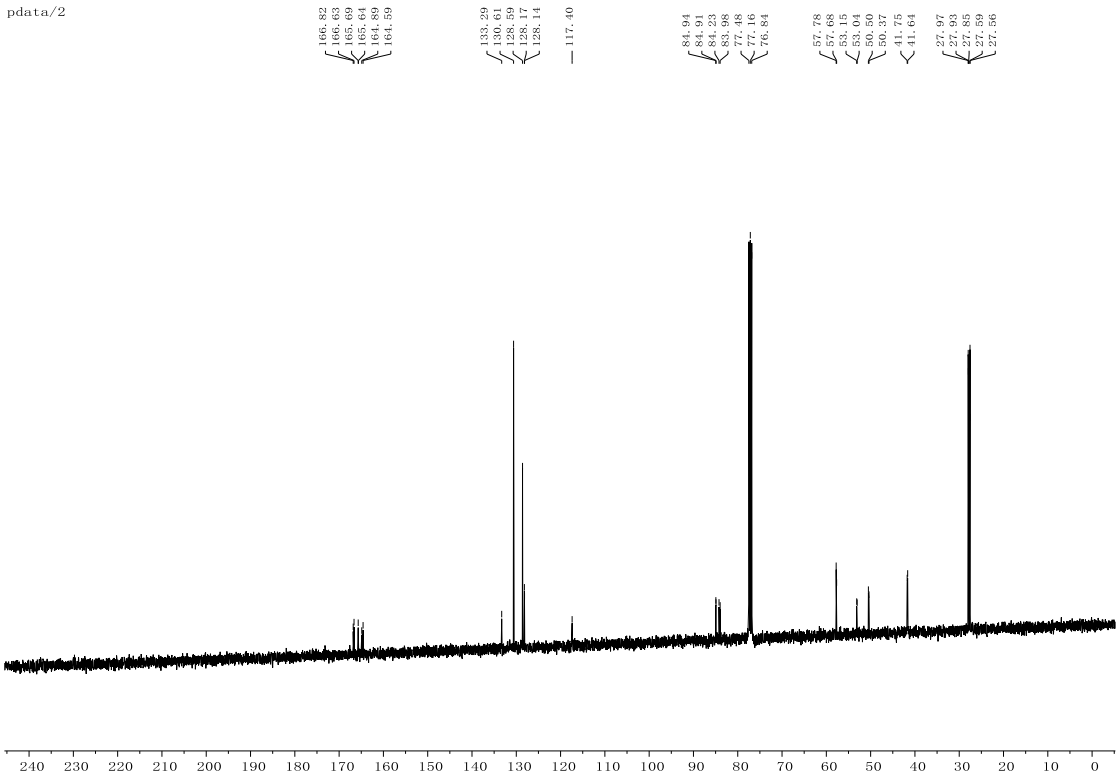
166.03
77.40
77.08
76.77
69.16
52.38
41.68
21.61
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

tert-butyl methyl malonate (18d):

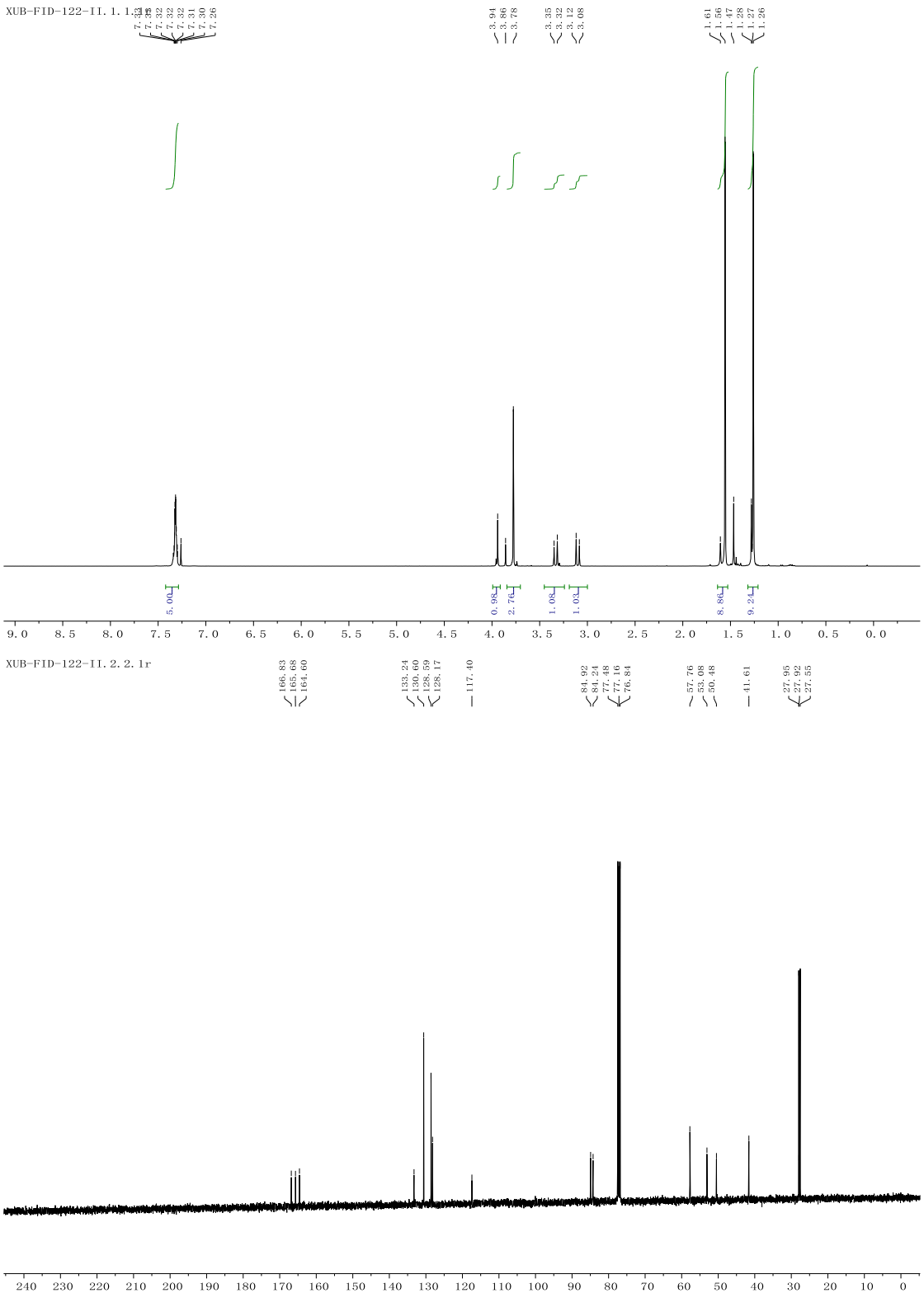


1,2-di-tert-butyl 1-methyl 2-cyano-3-phenylpropane-1,1,2-tricarboxylate（19k）

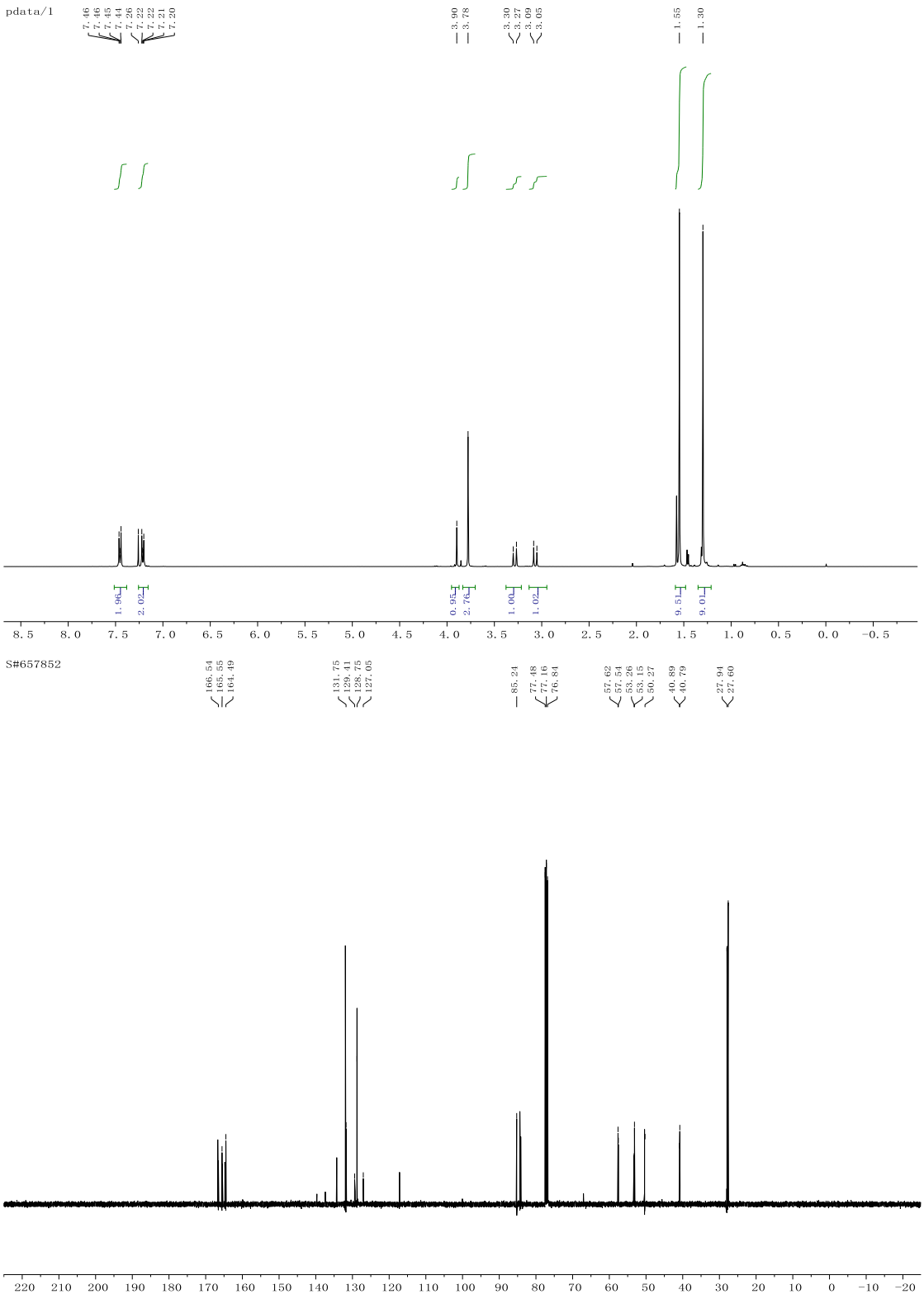




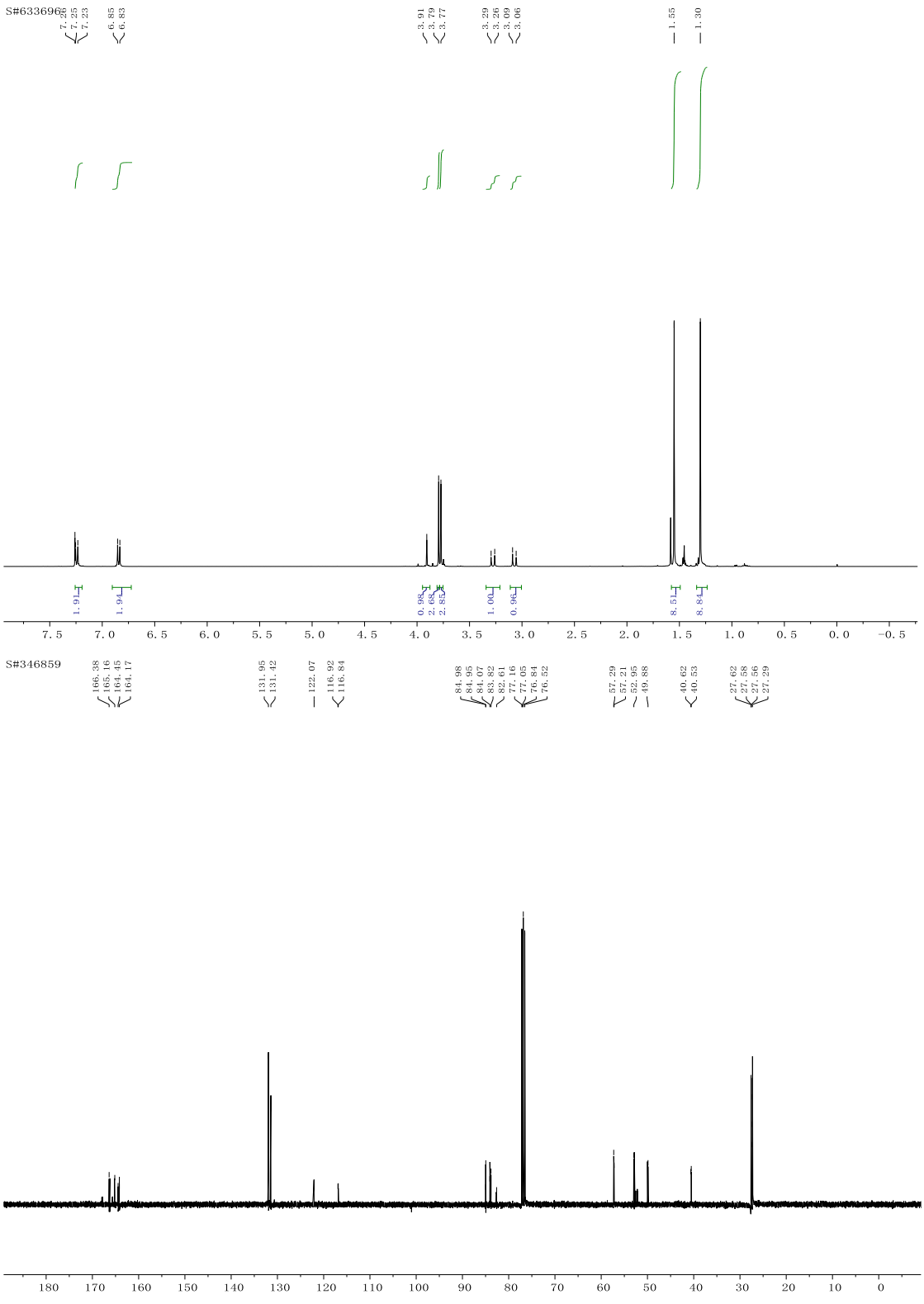
1,2-di-tert-butyl 1-methyl 3-(4-chlorophenyl)-2-cyanopropane-1,1,2-tricarboxylate (19l)



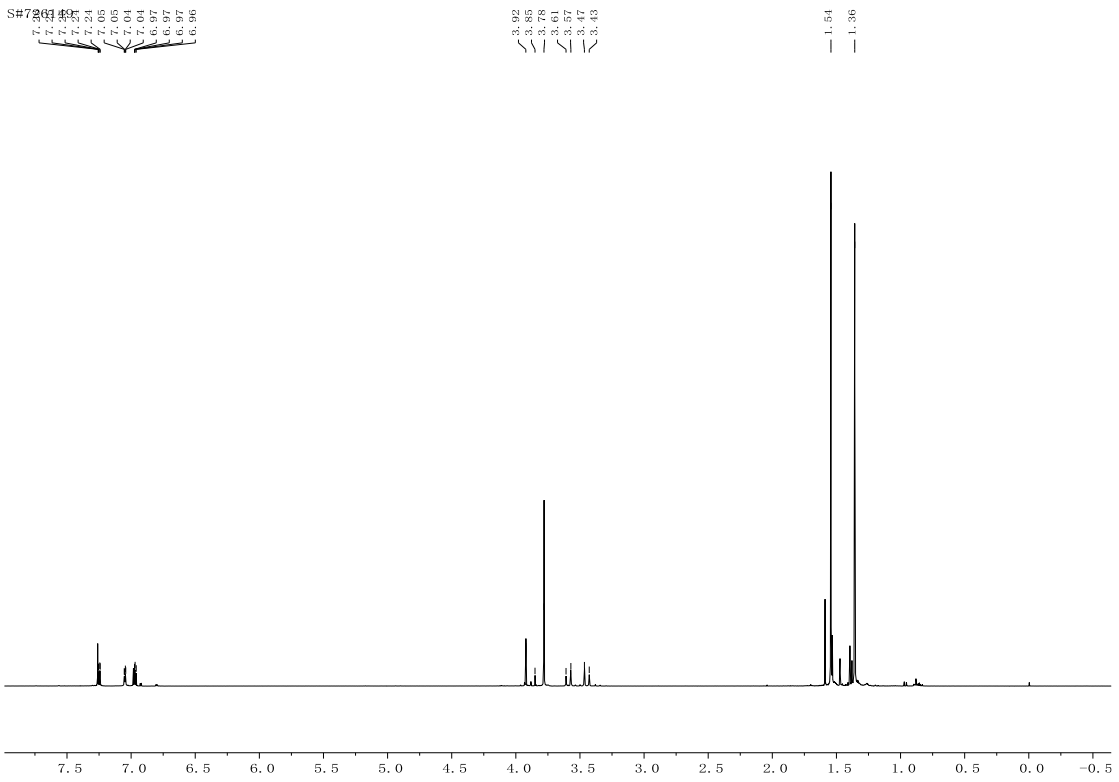
1,2-di-tert-butyl 1-methyl 3-(4-bromophenyl)-2-cyanopropane-1,1,2-tricarboxylate (19m)

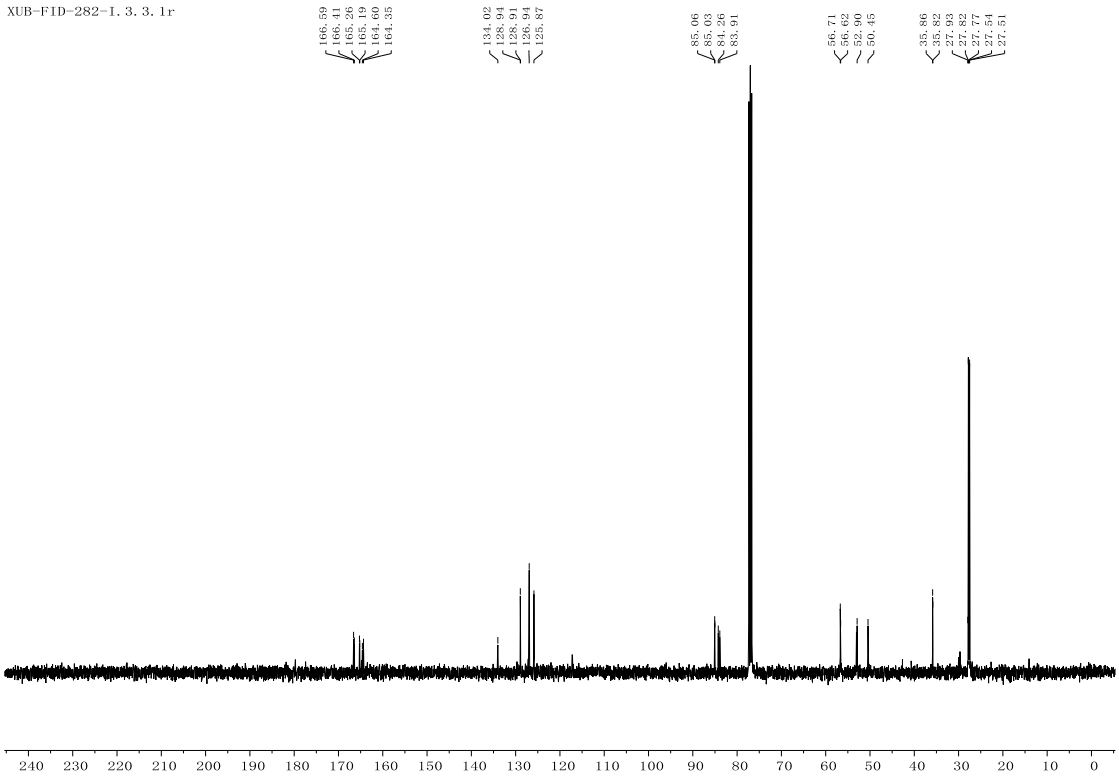


1,2-di-tert-butyl 1-methyl 2-cyano-3-(4-methoxyphenyl)propane-1,1,2-tricarboxylate (19n)

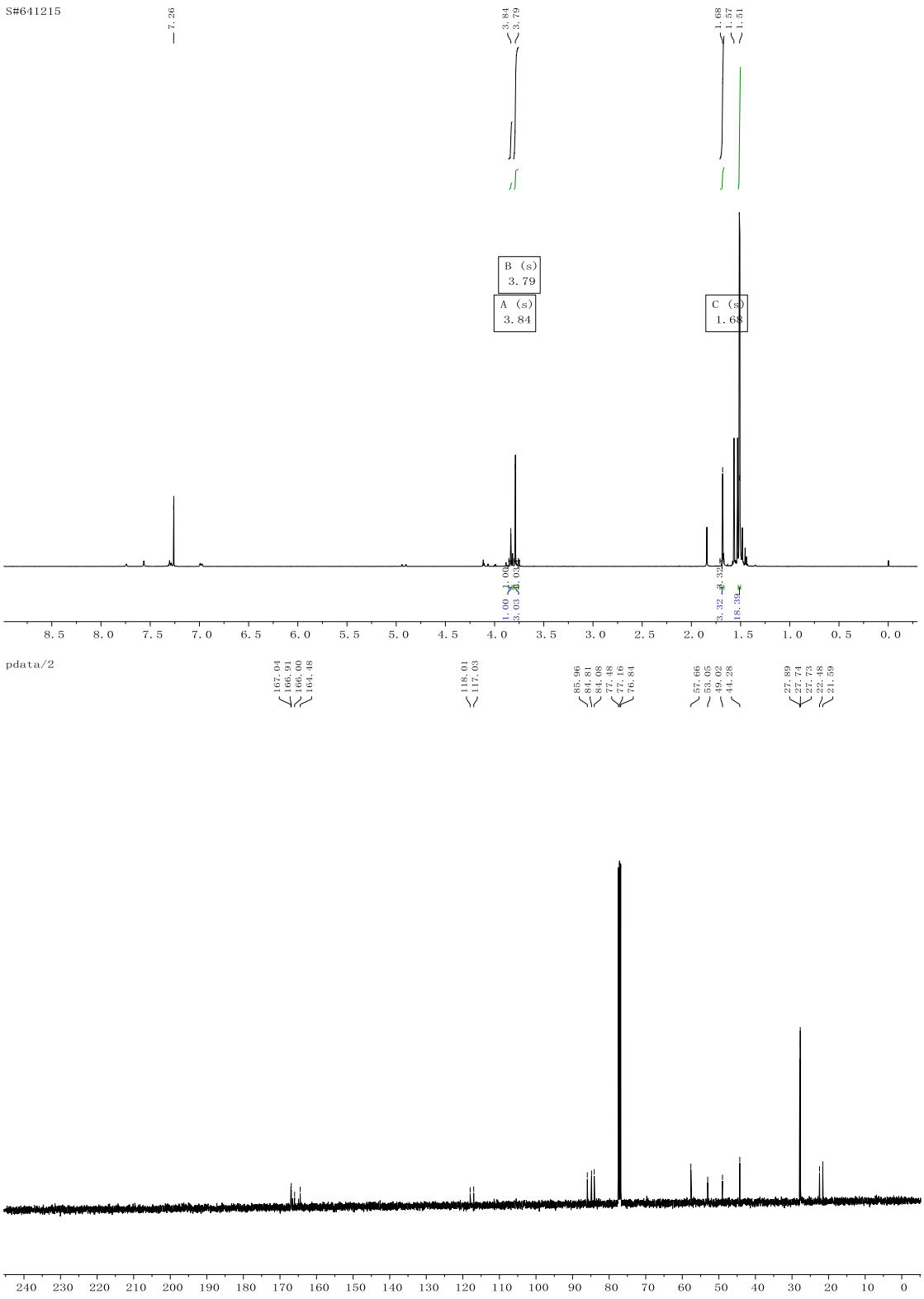


1,2-di-tert-butyl 1-methyl 2-cyano-3-(thiophen-2-yl)propane-1,1,2-tricarboxylate (19o)

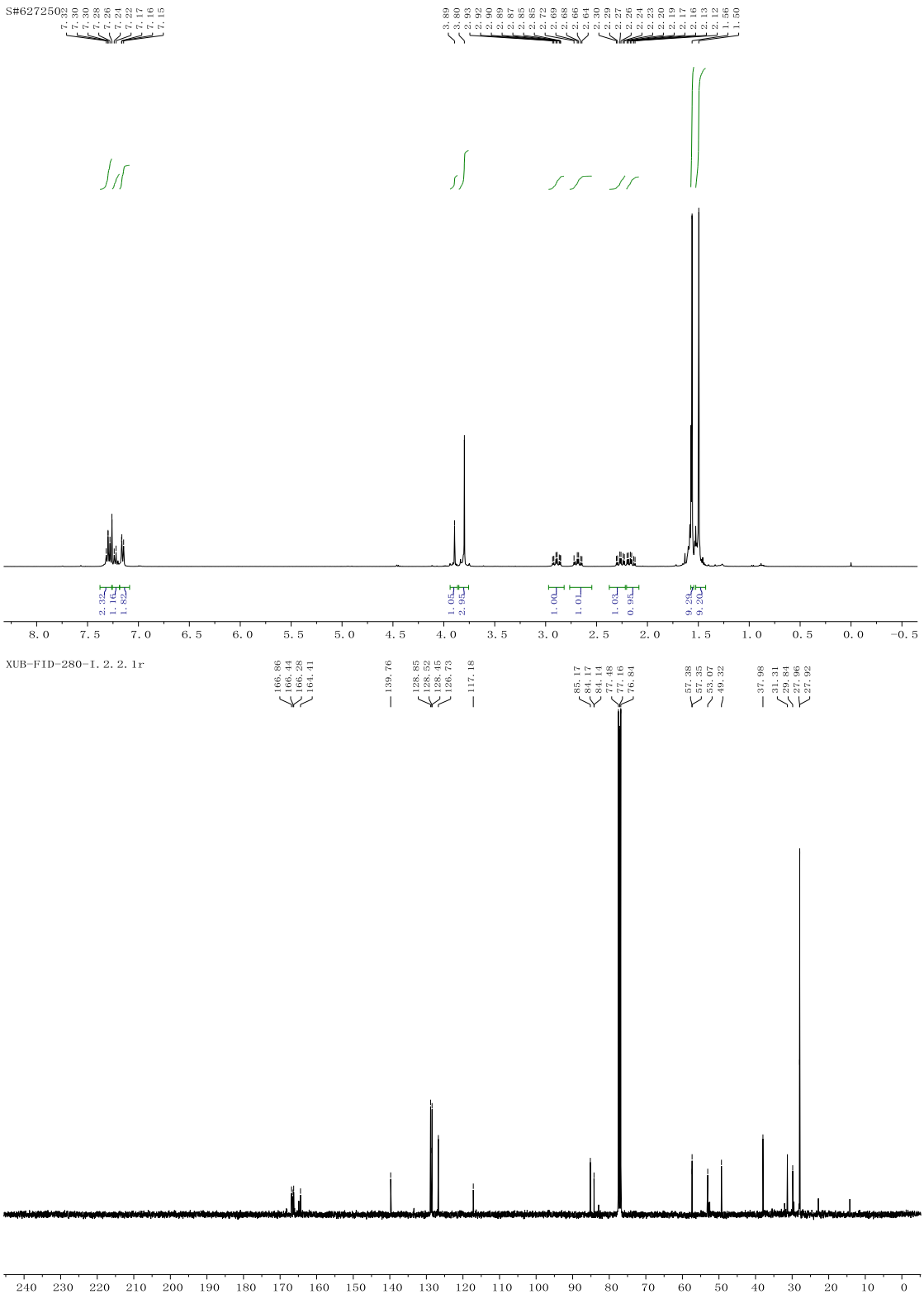




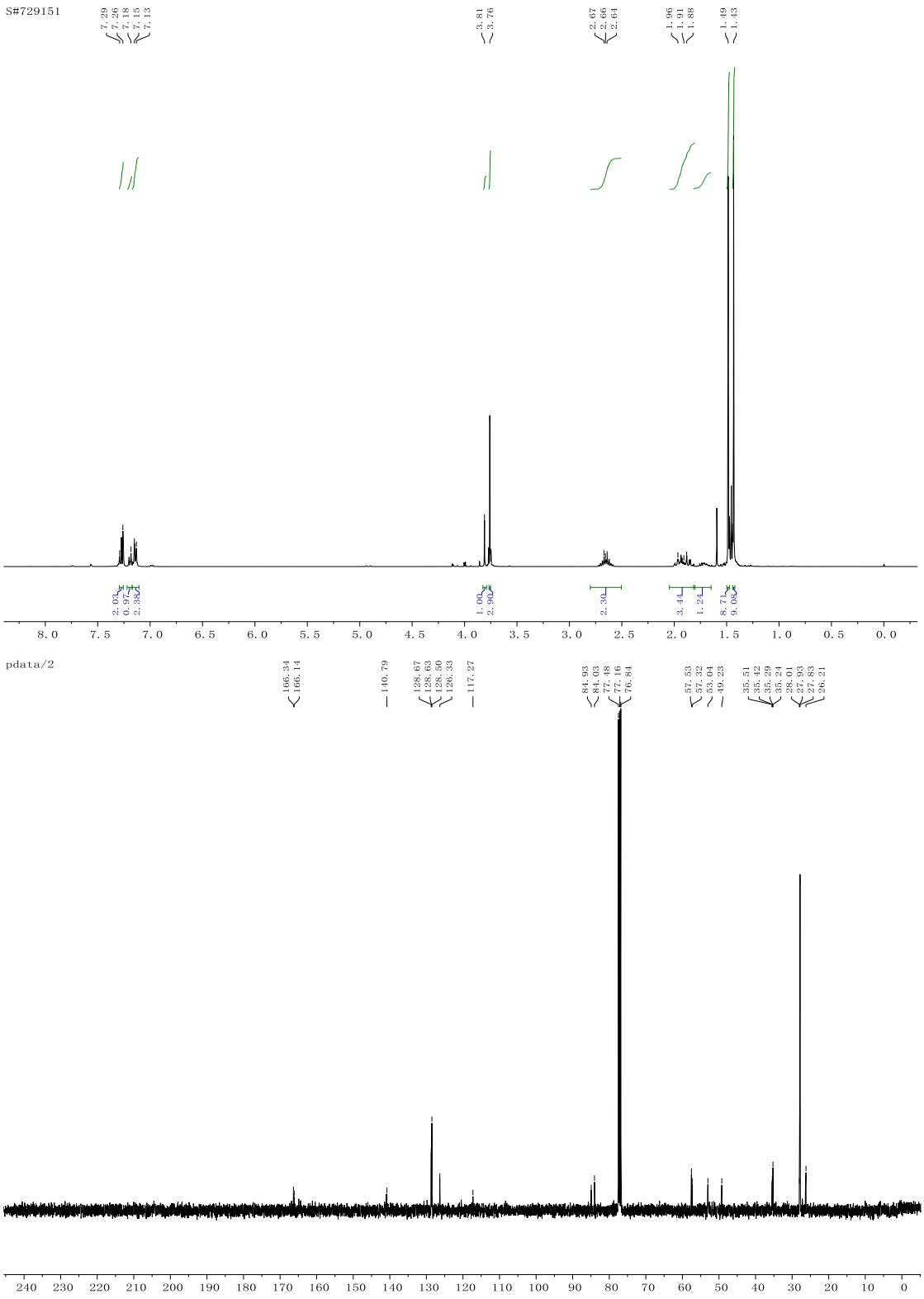
1,2-di-tert-butyl 1-methyl 2-cyanopropane-1,1,2-tricarboxylate (19p)



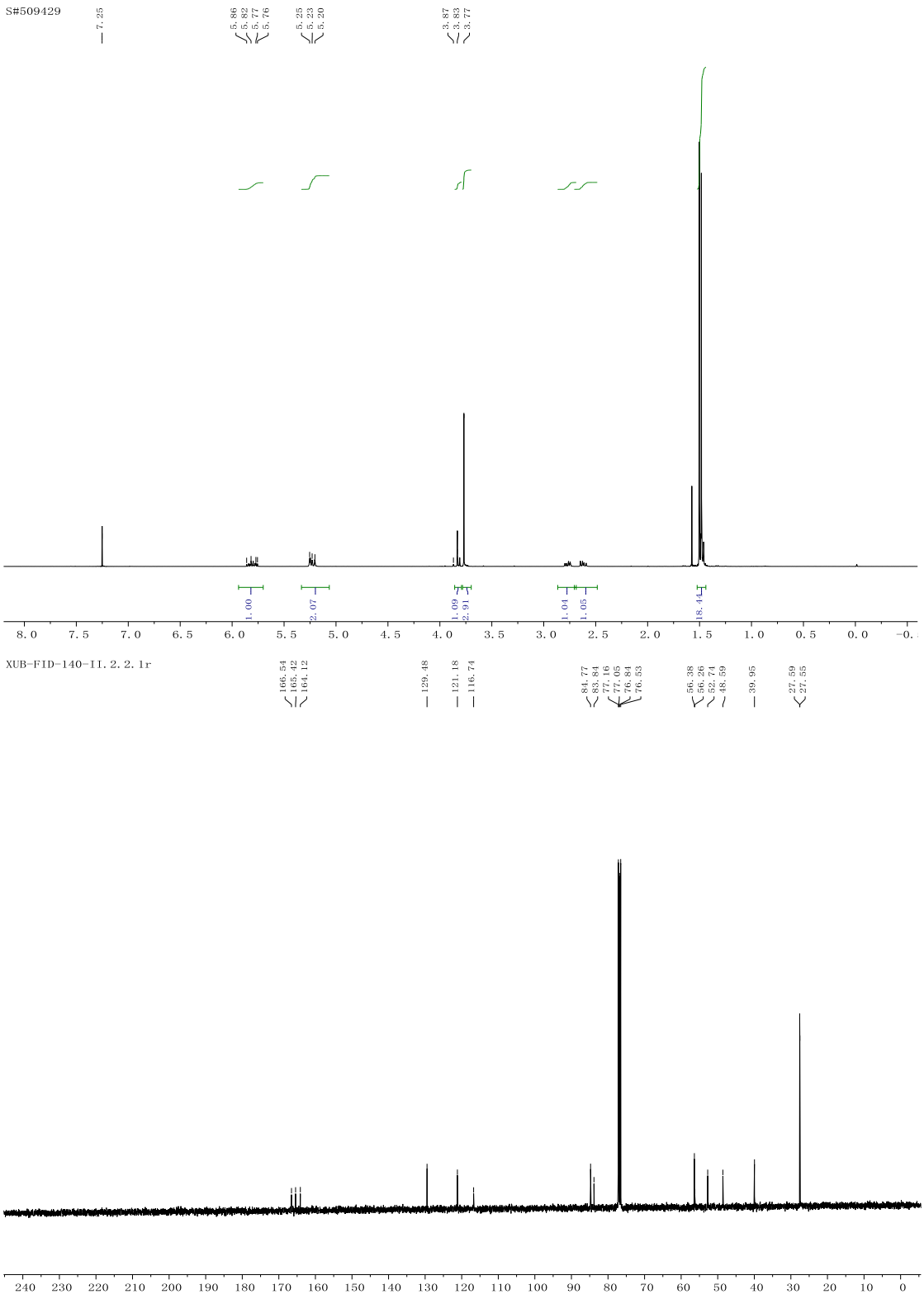
1,2-di-tert-butyl 1-methyl 2-cyano-4-phenylbutane-1,1,2-tricarboxylate (19q)



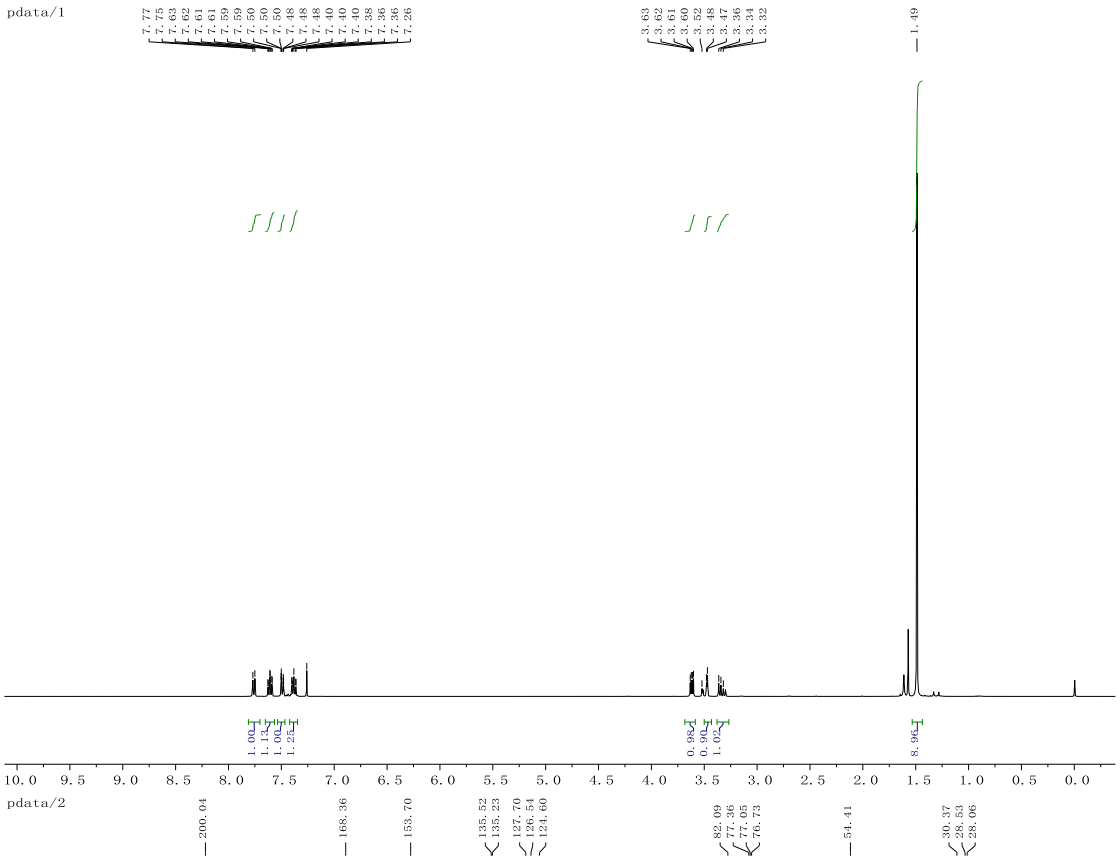
1,2-di-tert-butyl 1-methyl 2-cyano-5-phenylpentane-1,1,2-tricarboxylate (19r)



1,2-di-tert-butyl 1-methyl 2-cyanopent-4-ene-1,1,2-tricarboxylate (19s)



***tert*-butyl 1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21c)**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3.62
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3.52
3.48
3.47
3.36
3.34
3.32
1.49
1.00
1.13
1.06
1.25
0.98
0.96
1.05
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10.0
9.5
9.0
8.5
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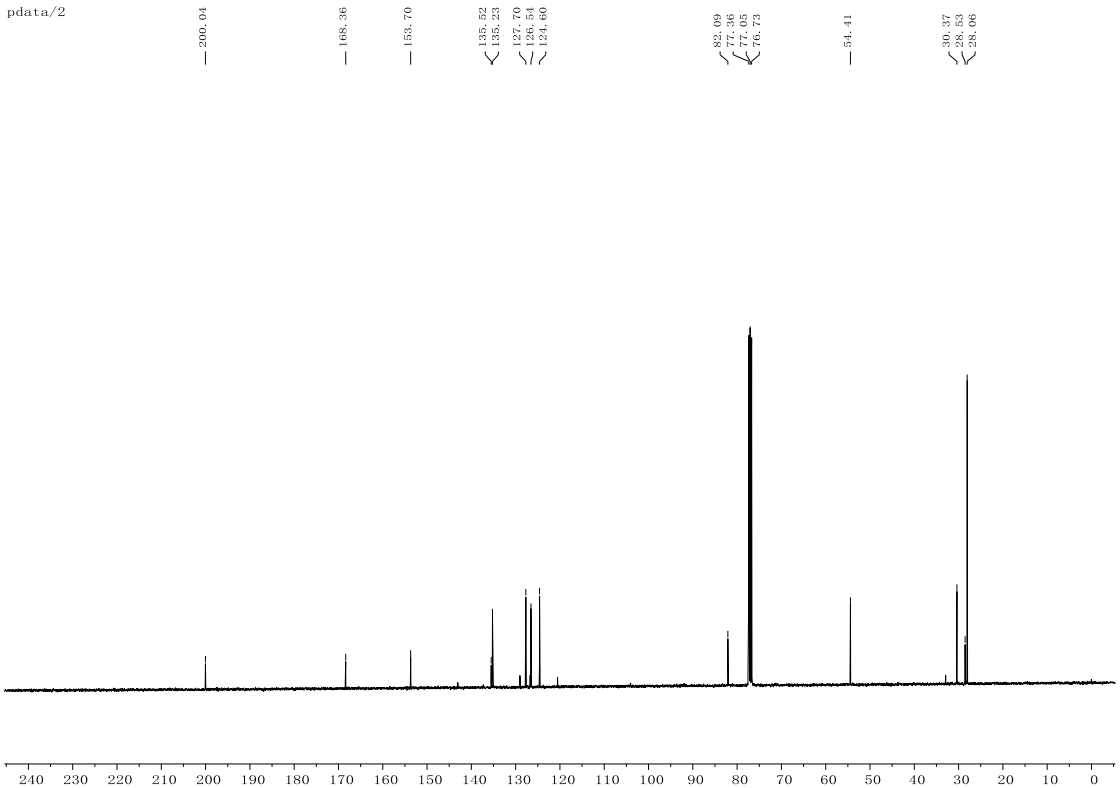
0.5
0.0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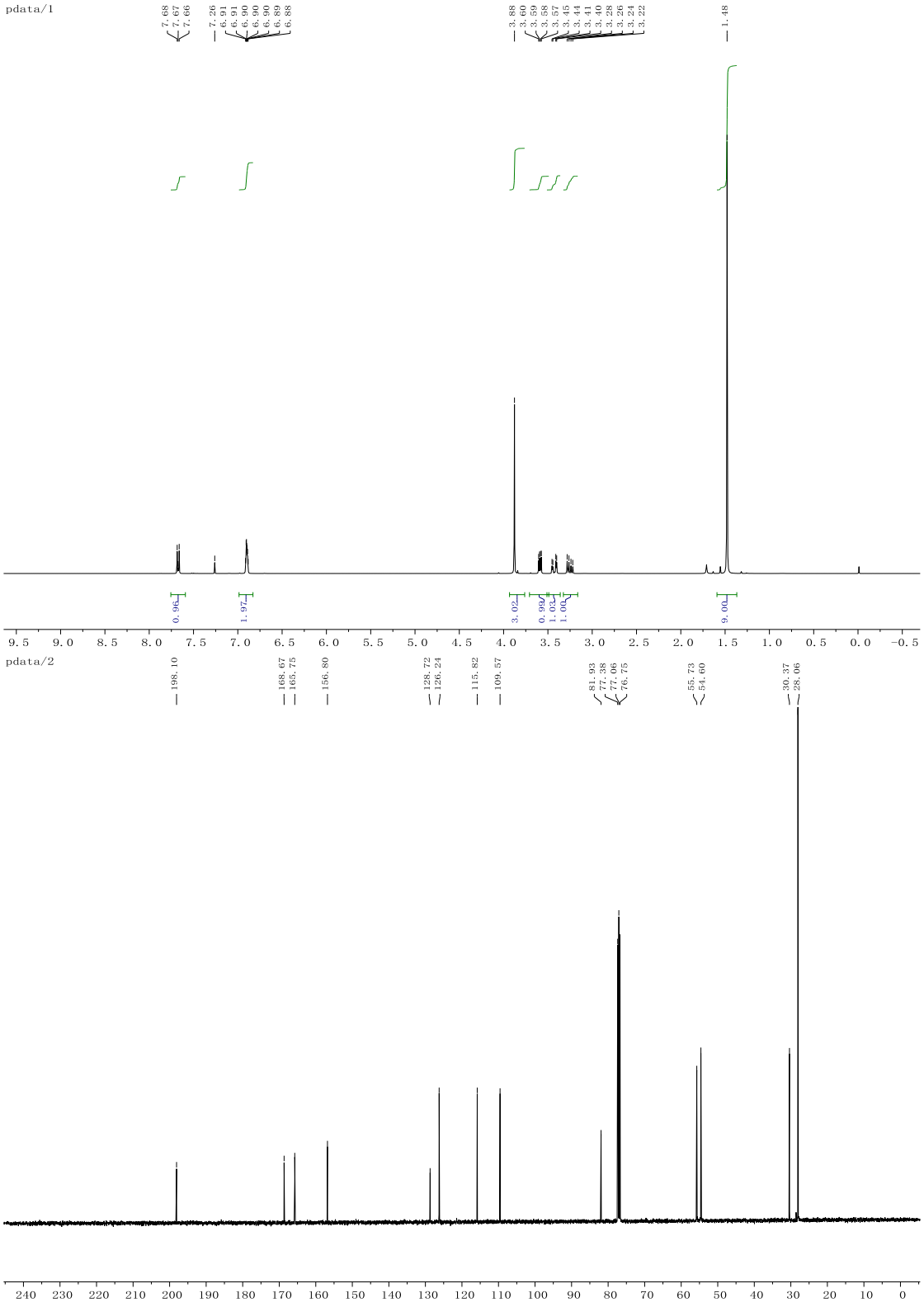
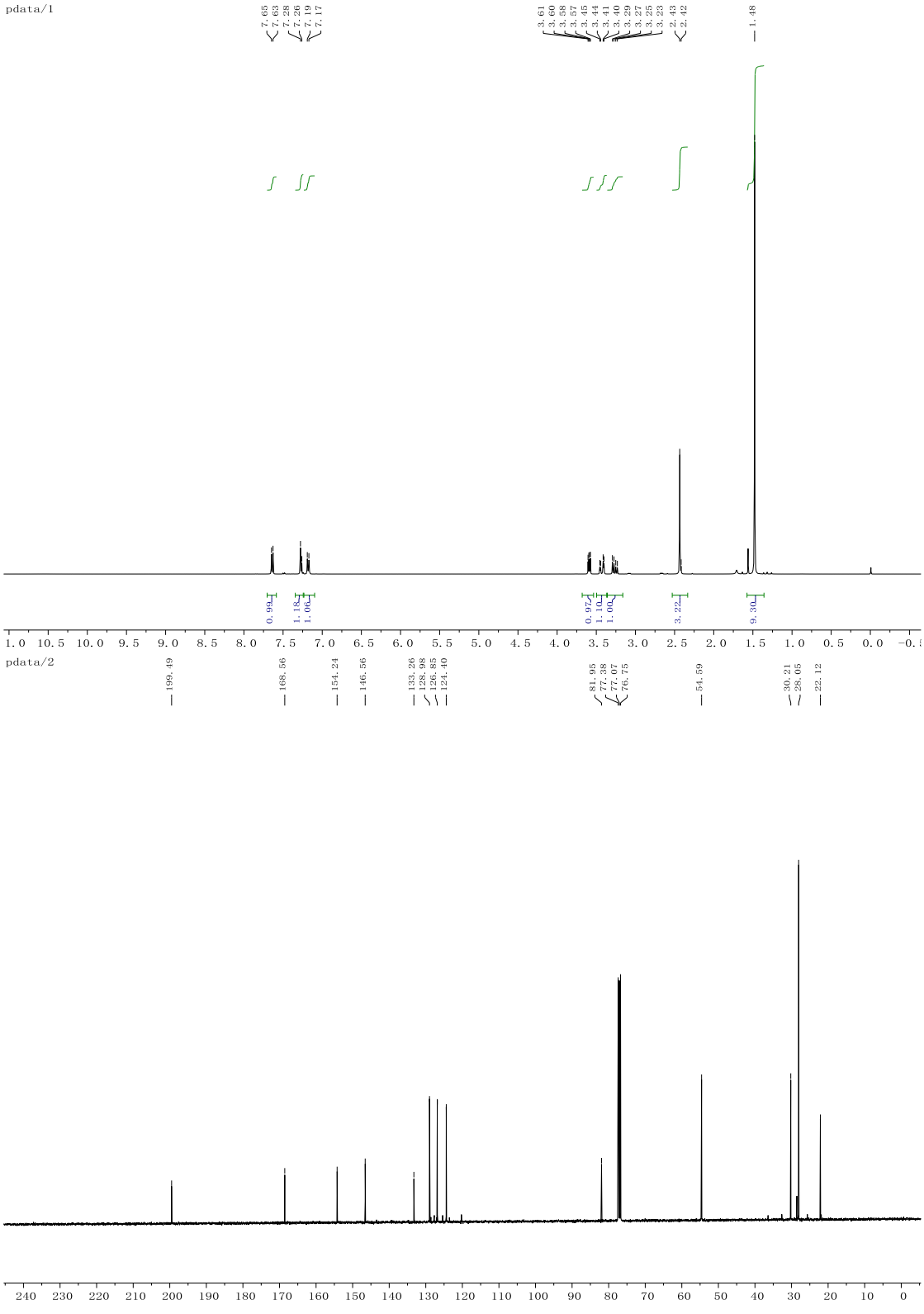
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

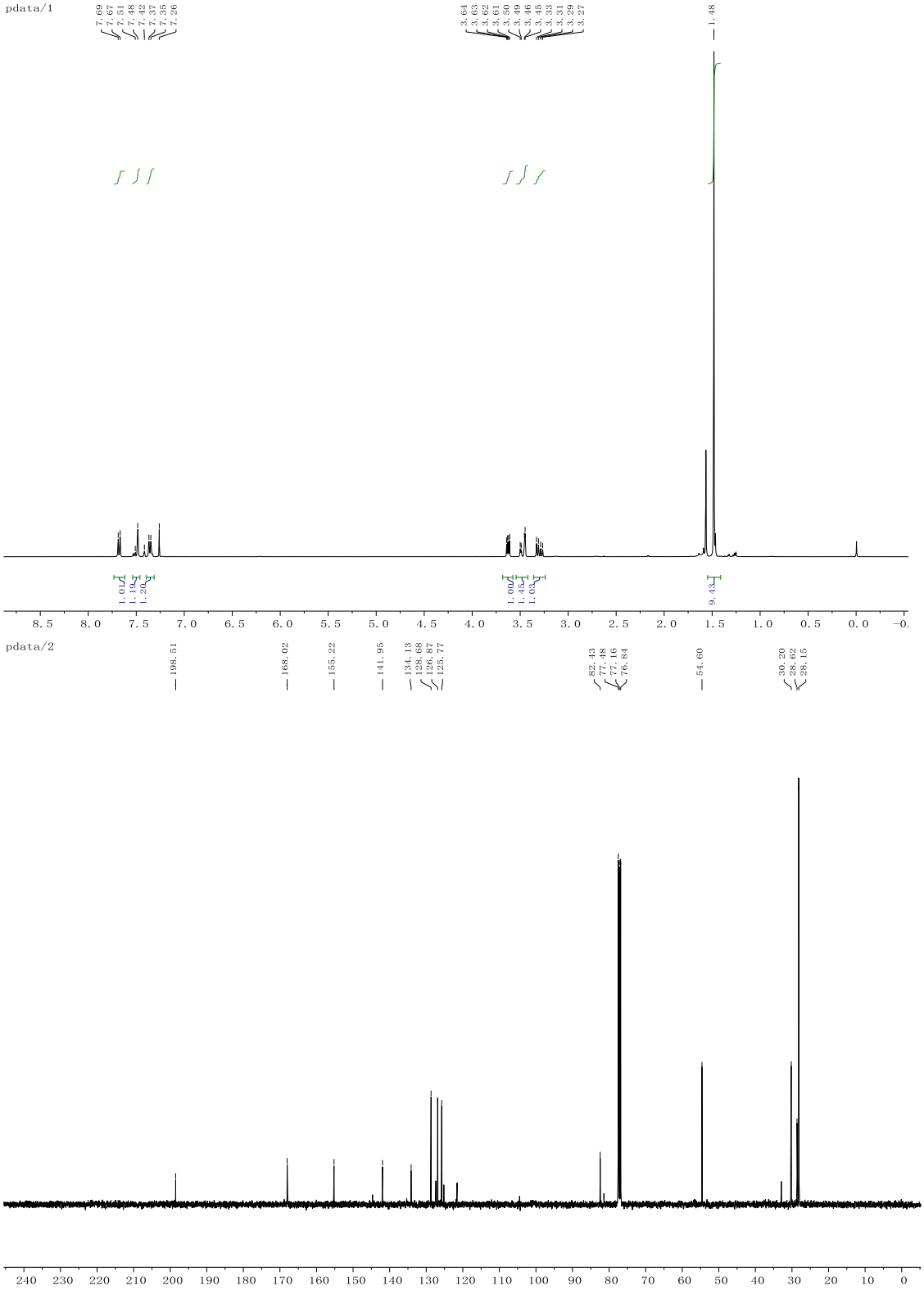
tert-butyl 5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21d)



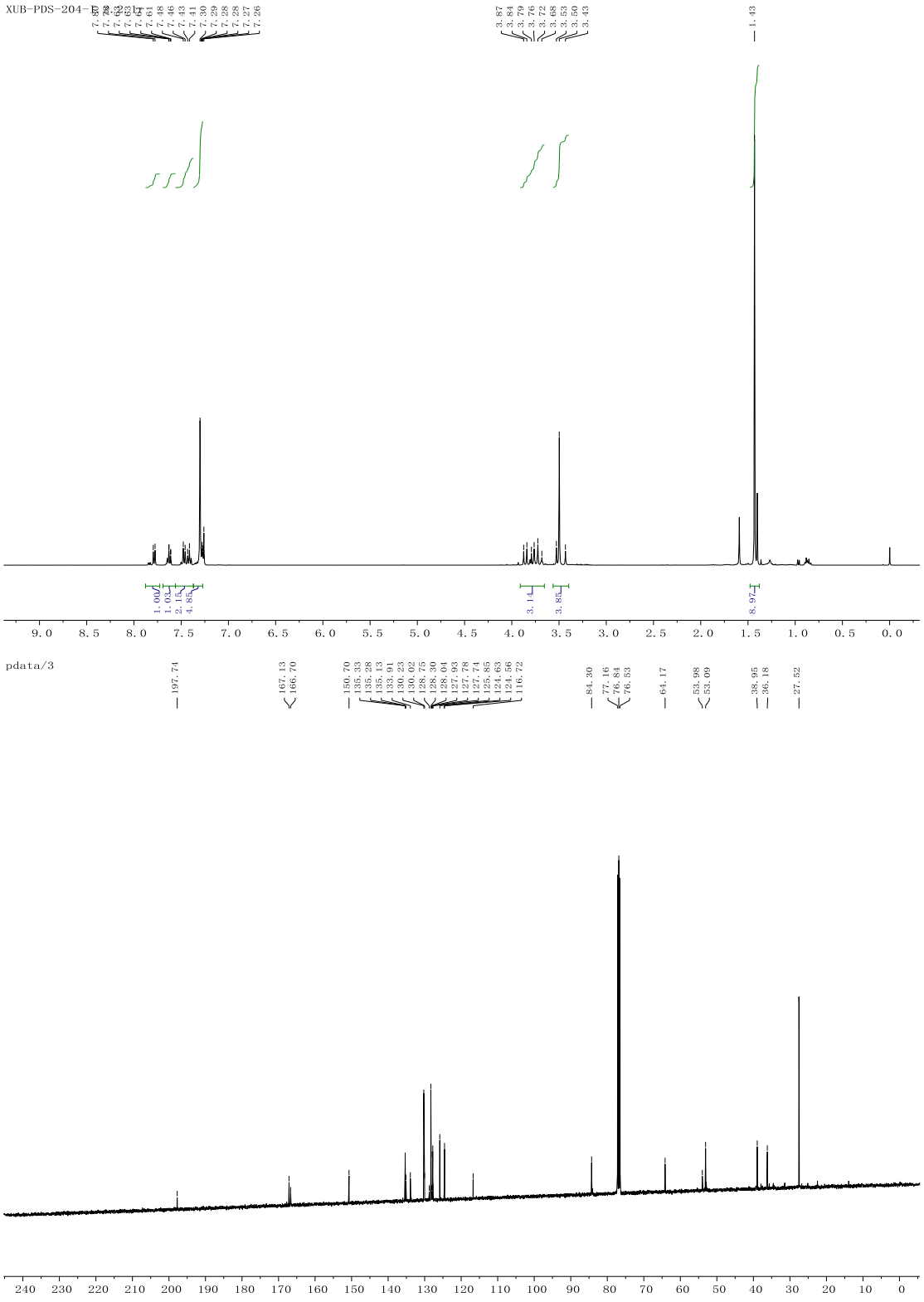
tert-butyl 5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21e)



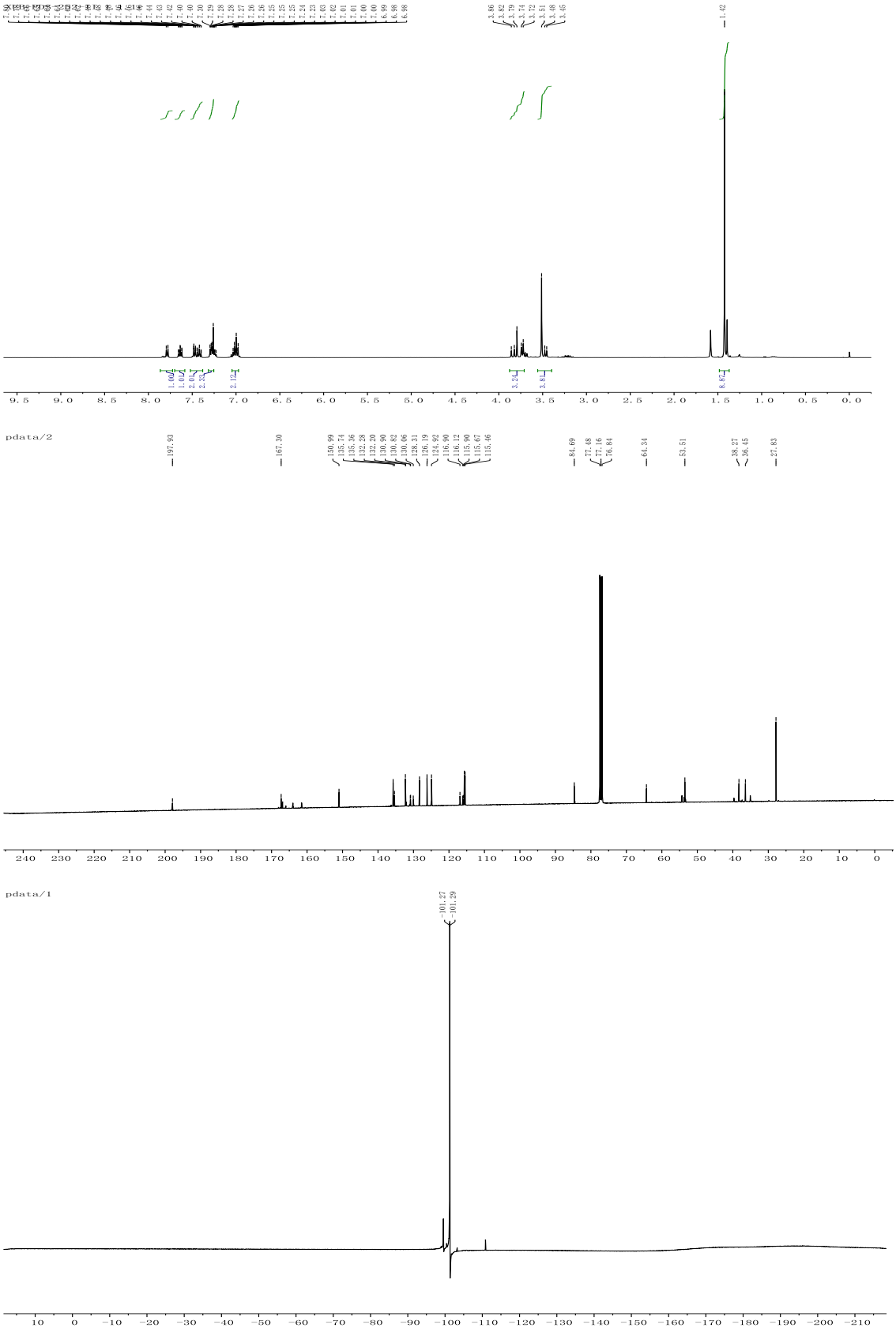
***tert*-butyl 5-chloro-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (21f)**



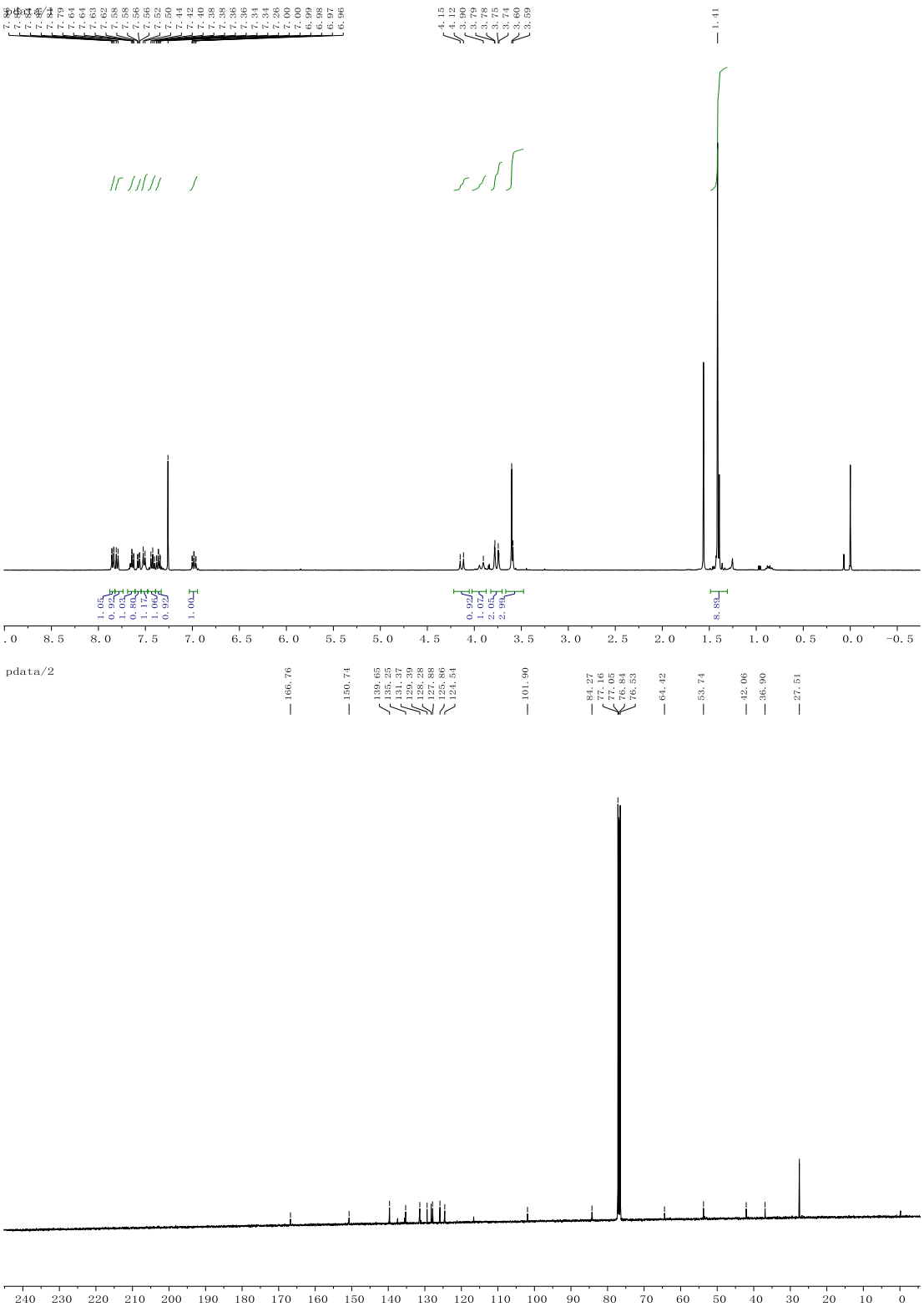
***tert*-butyl (*R*)-2-((R)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22c)**



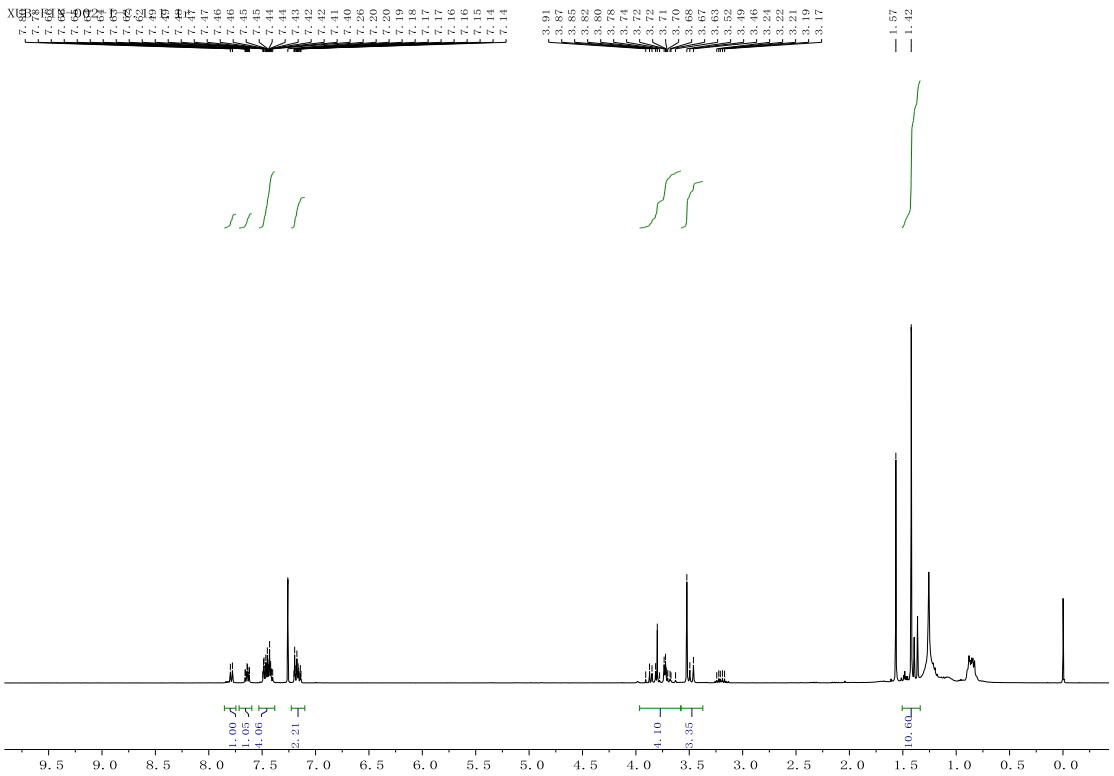
***tert*-butyl (*R*)-2-((*R*)-2-cyano-3-(4-fluorophenyl)-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22d)**

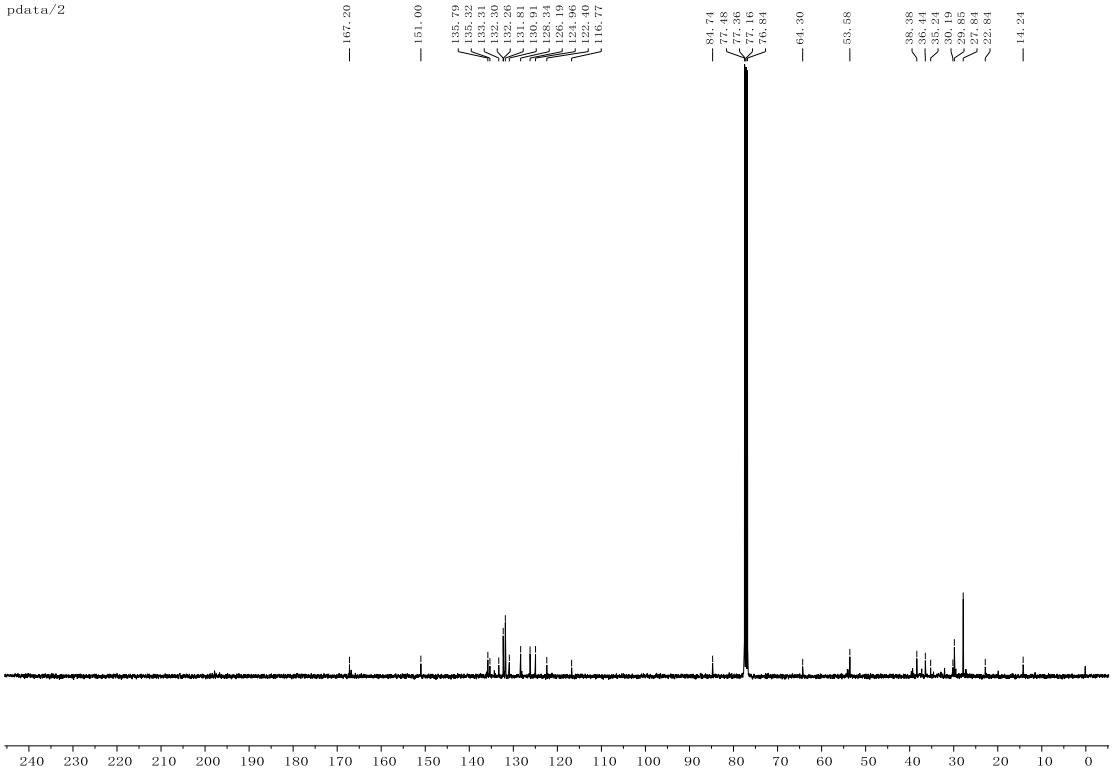


***tert*-butyl (*R*)-2-((*R*)-3-(4-chlorophenyl)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22e)**

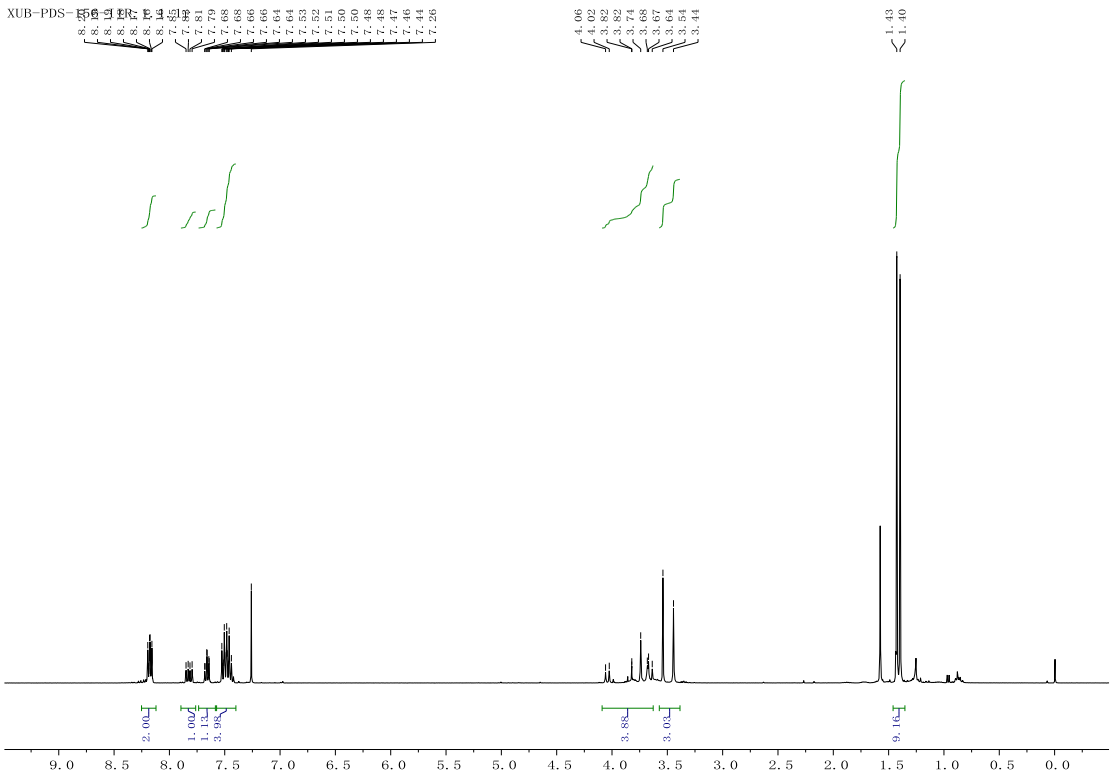


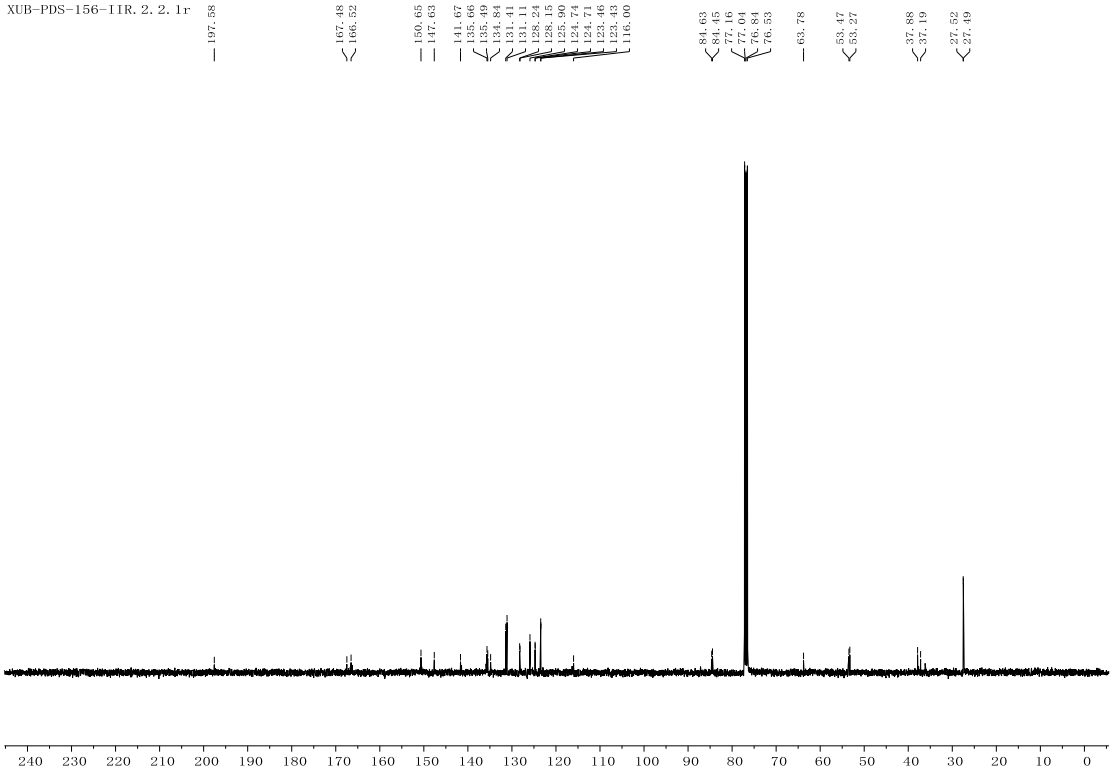
***tert*-butyl (*R*)-2-((*R*)-3-(4-bromophenyl)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22f)**



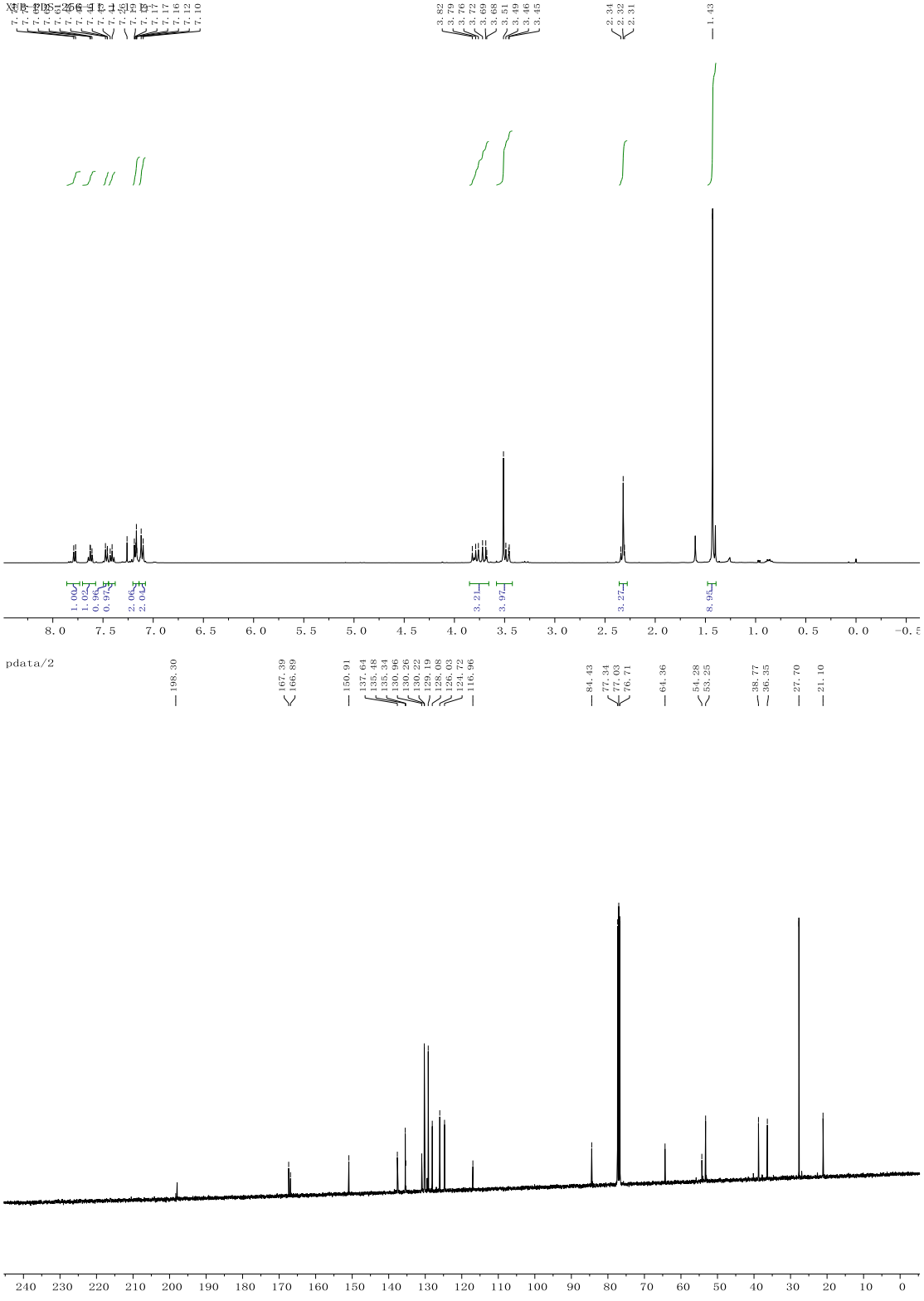


tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-3-(4-nitrophenyl)-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22g)

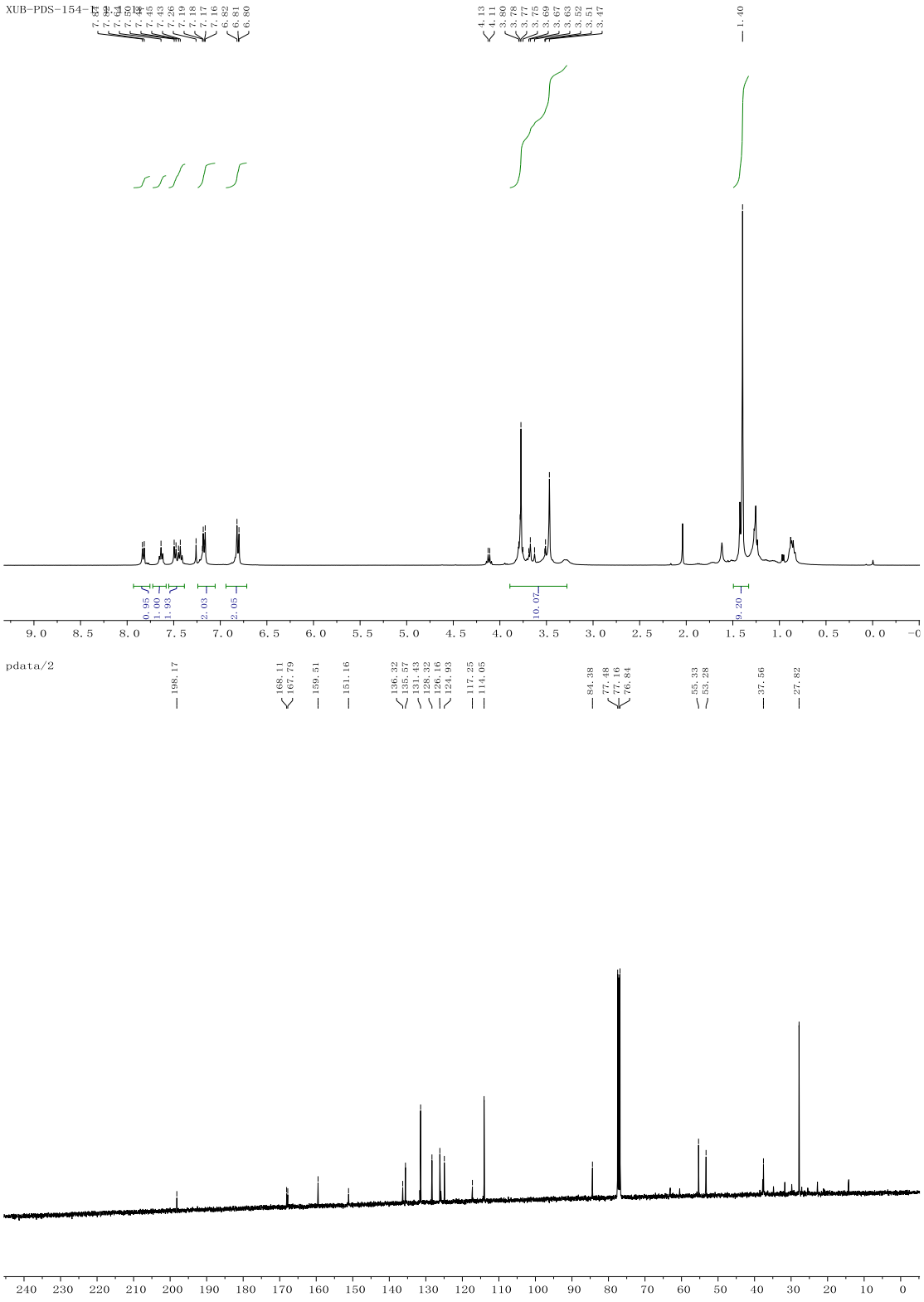




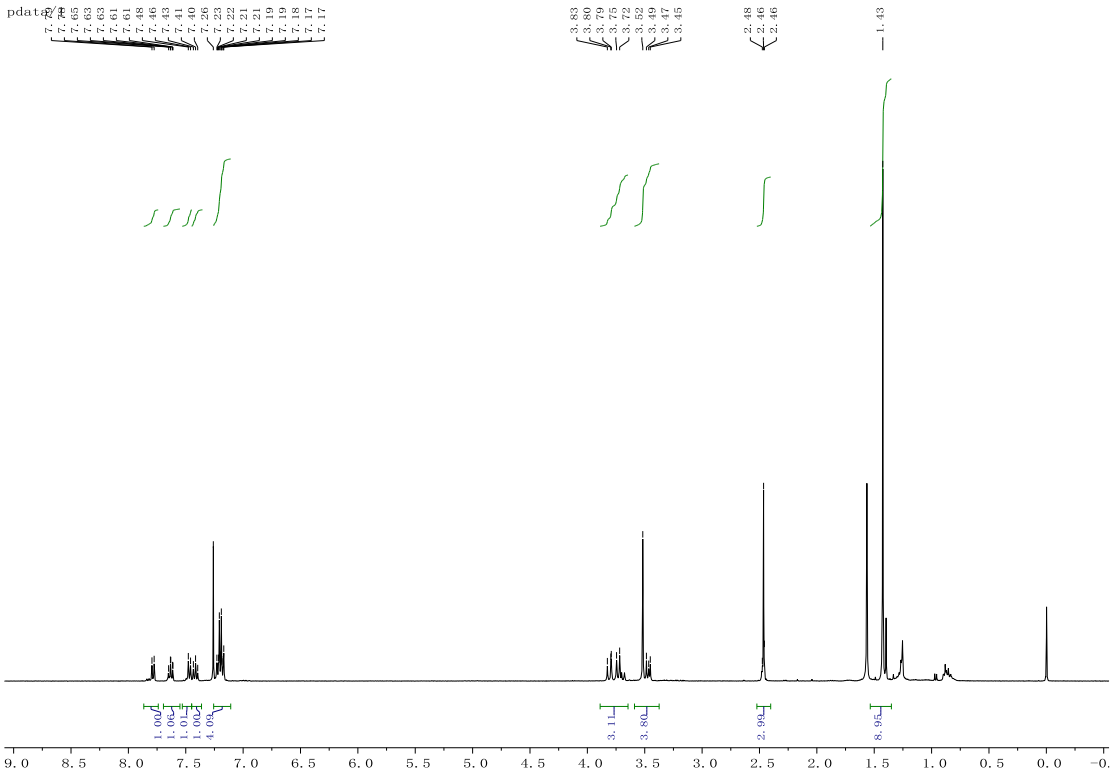
tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxo-3-(p-tolyl)propan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22h)

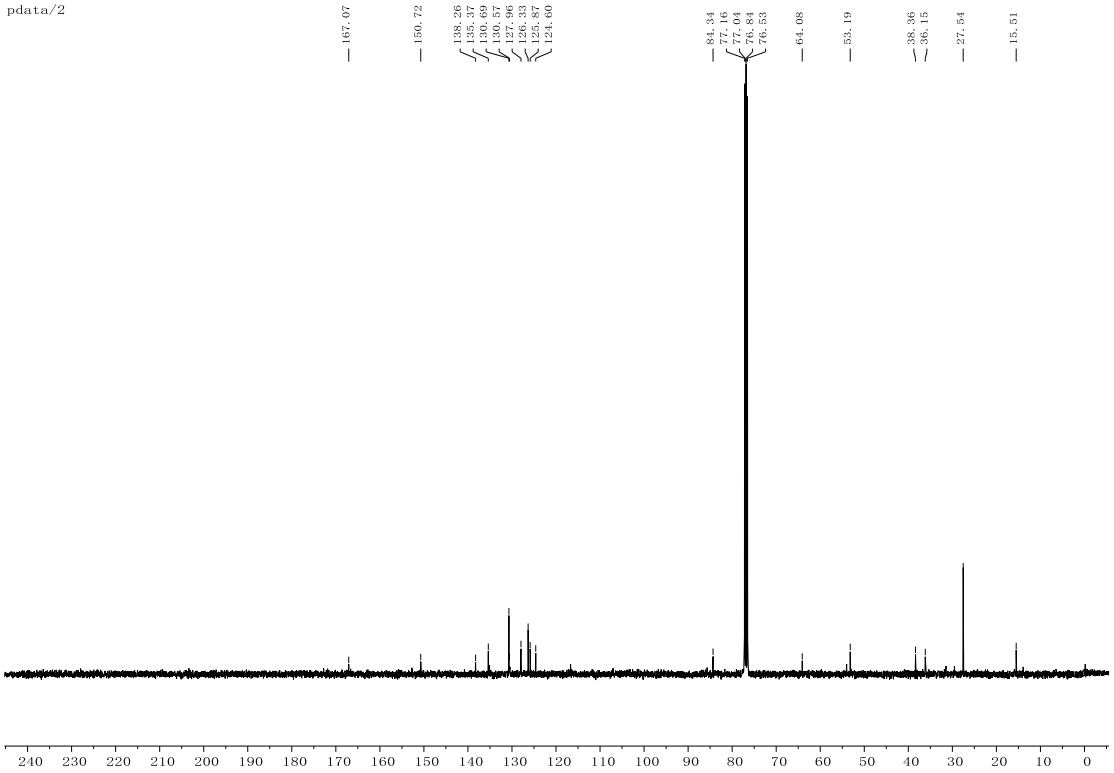


tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-3-(4-methoxyphenyl)-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22i)

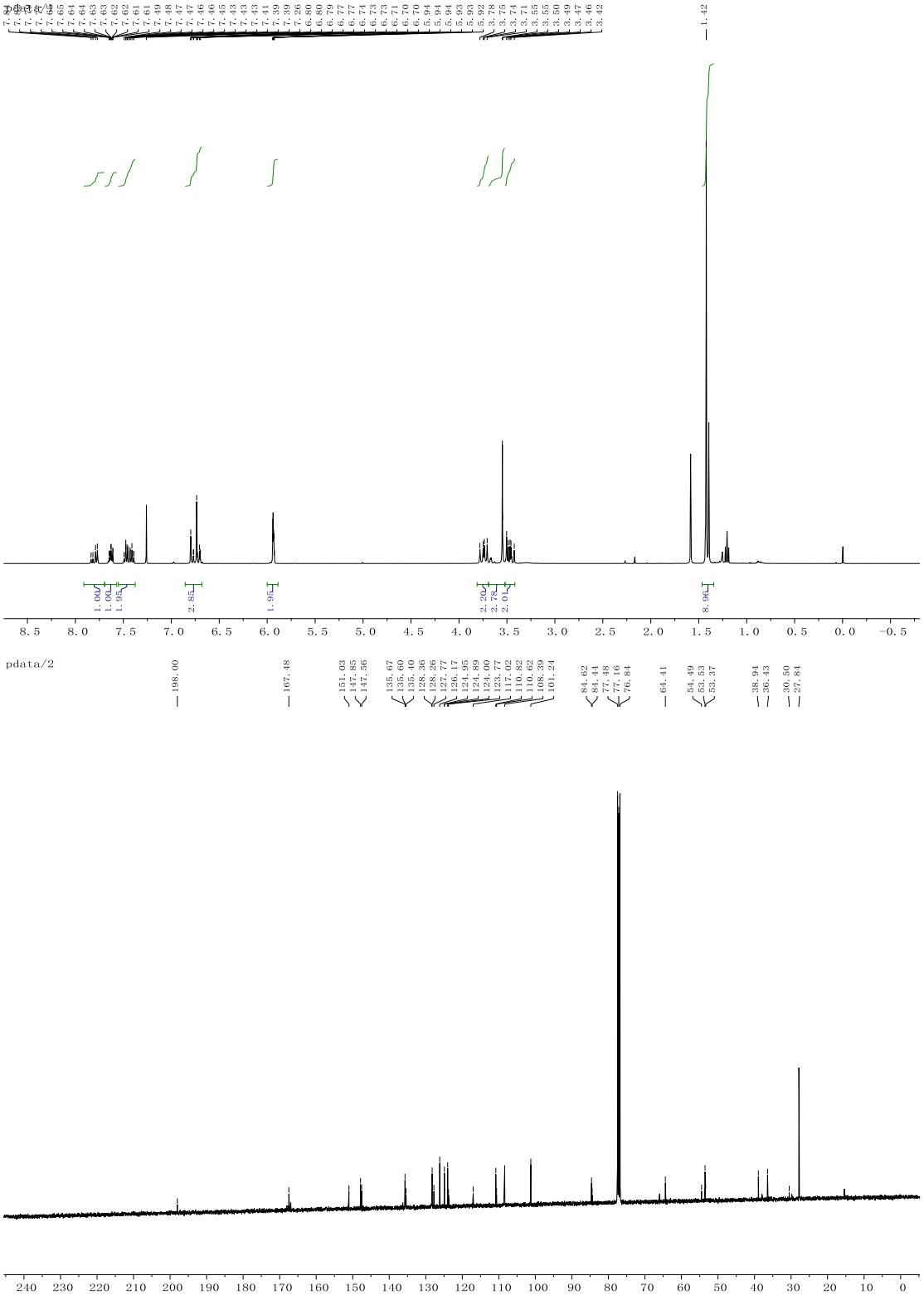


***tert*-butyl (R)-2-((R)-2-cyano-1-methoxy-3-(4-(methylthio)phenyl)-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22j)**

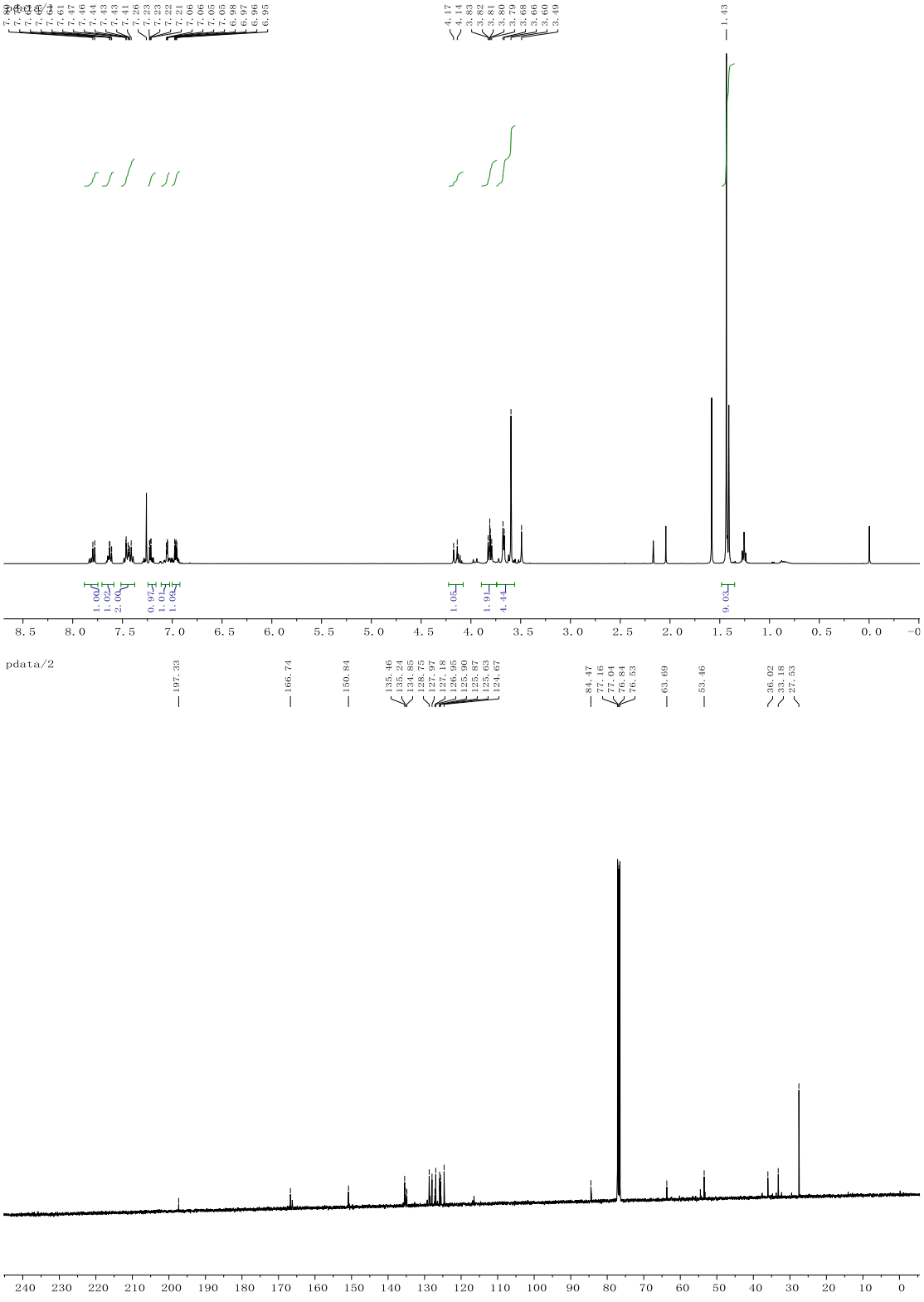




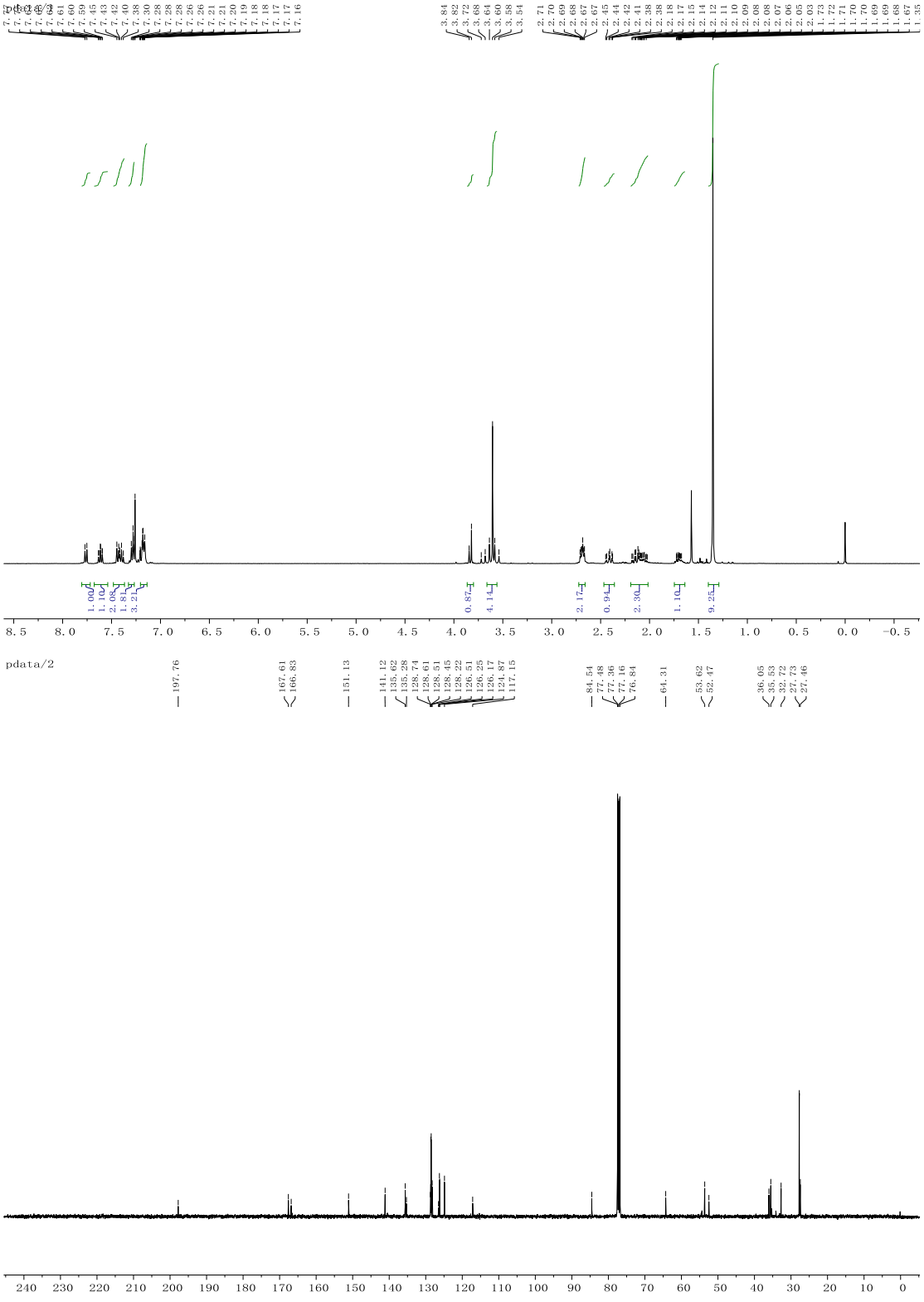
tert-butyl (_R_)-2-((_R_)-3-(benzo[d][1,3]dioxol-5-yl)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22k)



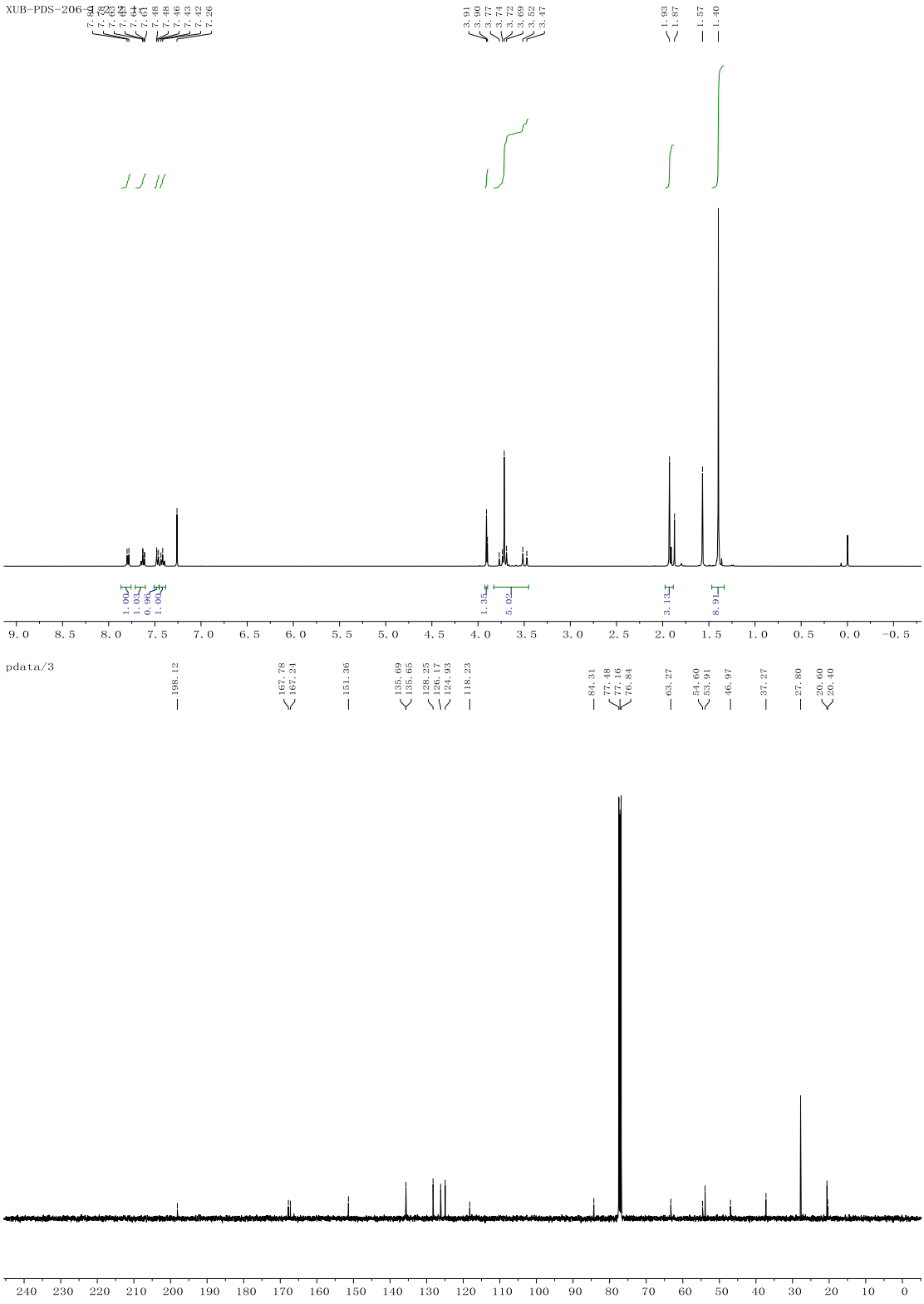
tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxo-3-(thiophen-2-yl)propan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22l)



tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxo-5-phenylpentan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22m)

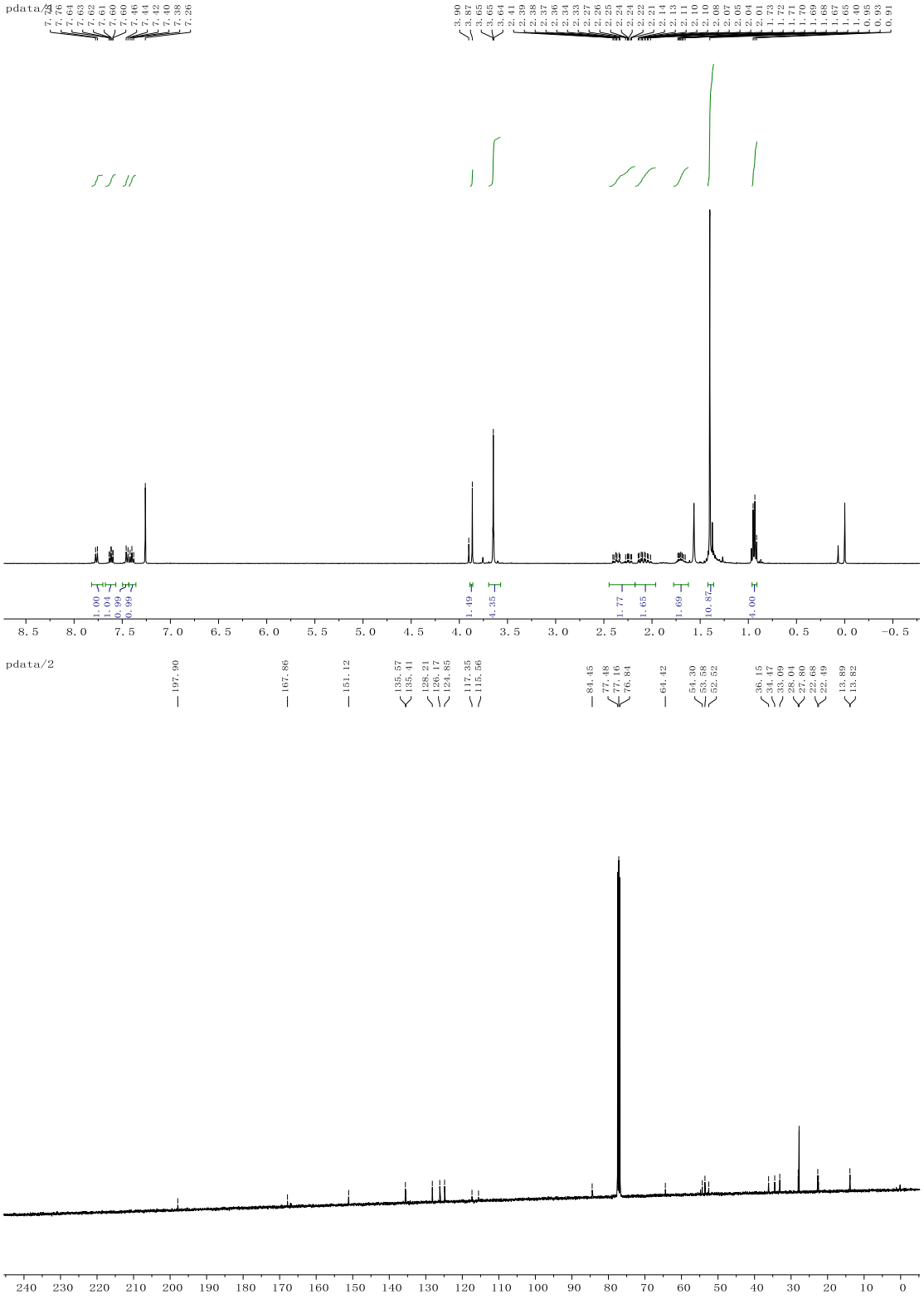


tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxopropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22n)

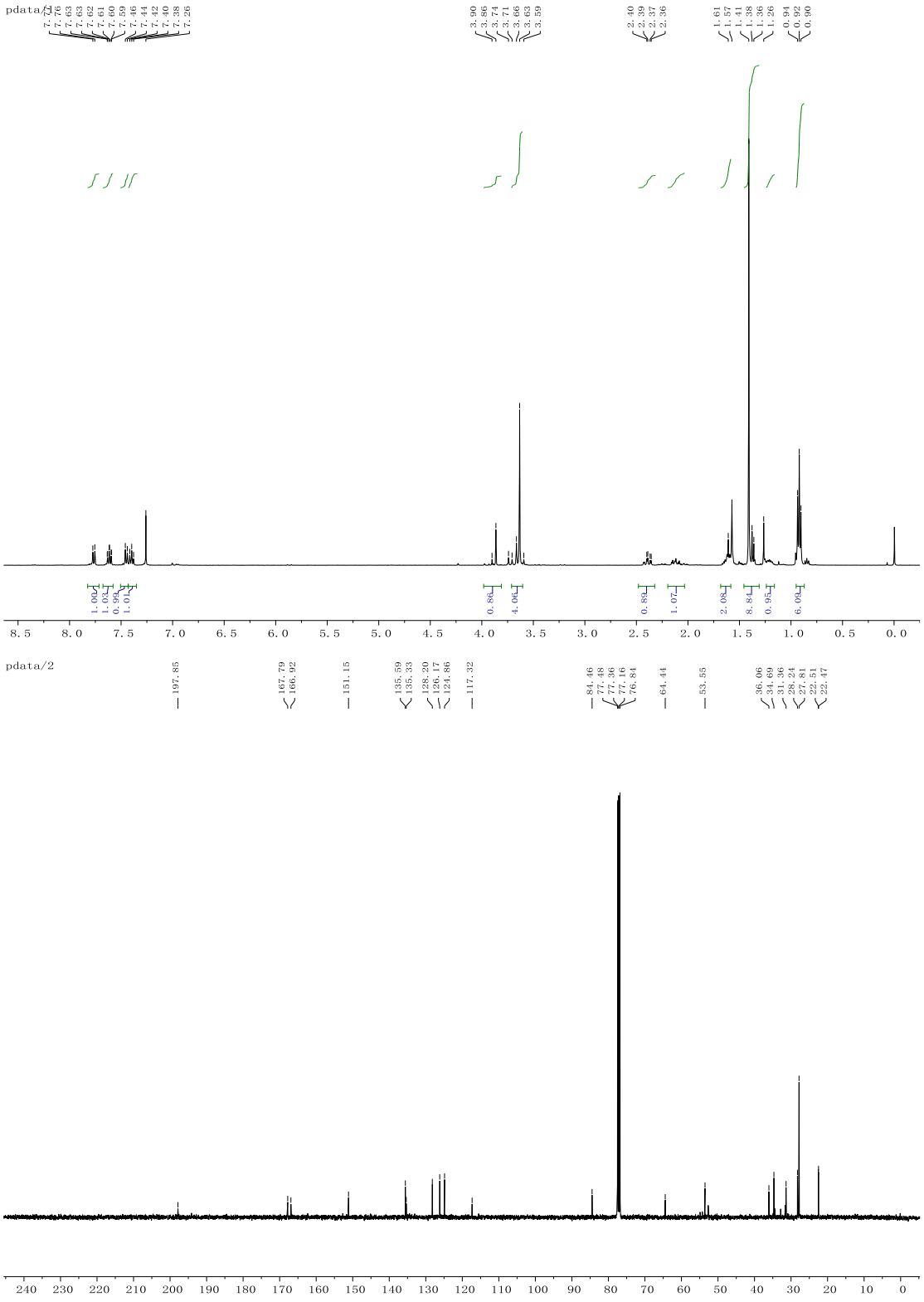


tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxohexan-2-yl)-1-oxo-2,3-dihydro-1H-

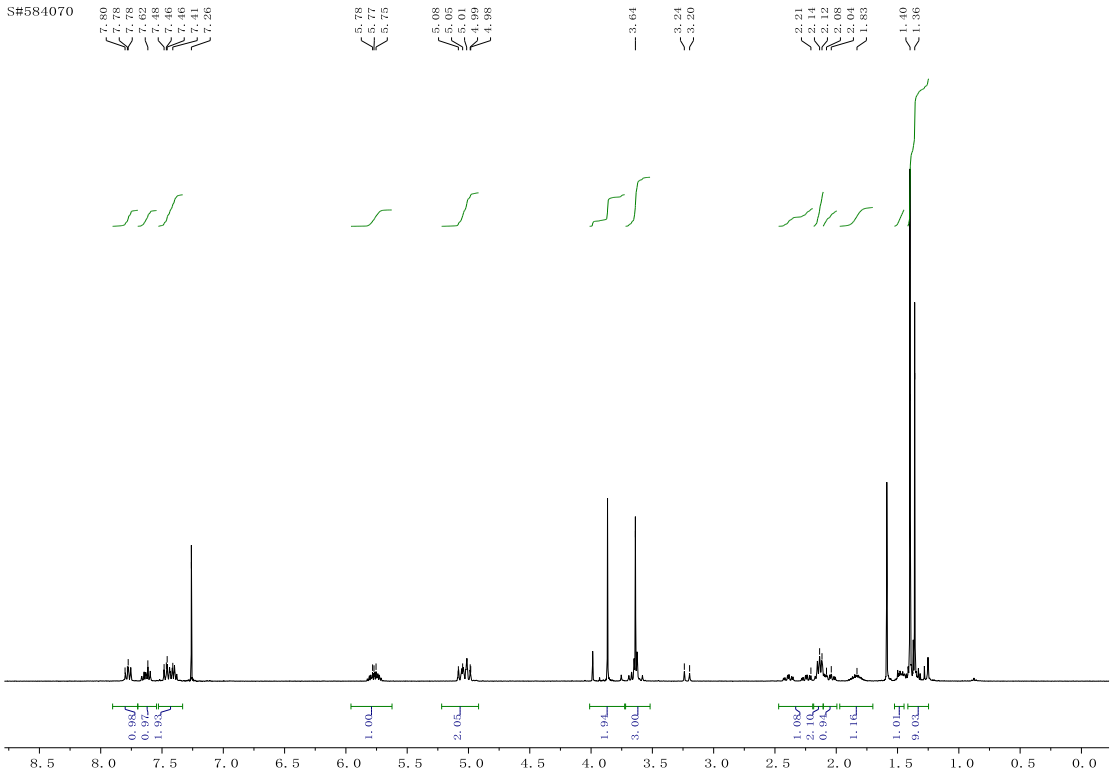
indene-2-carboxylate (22o):

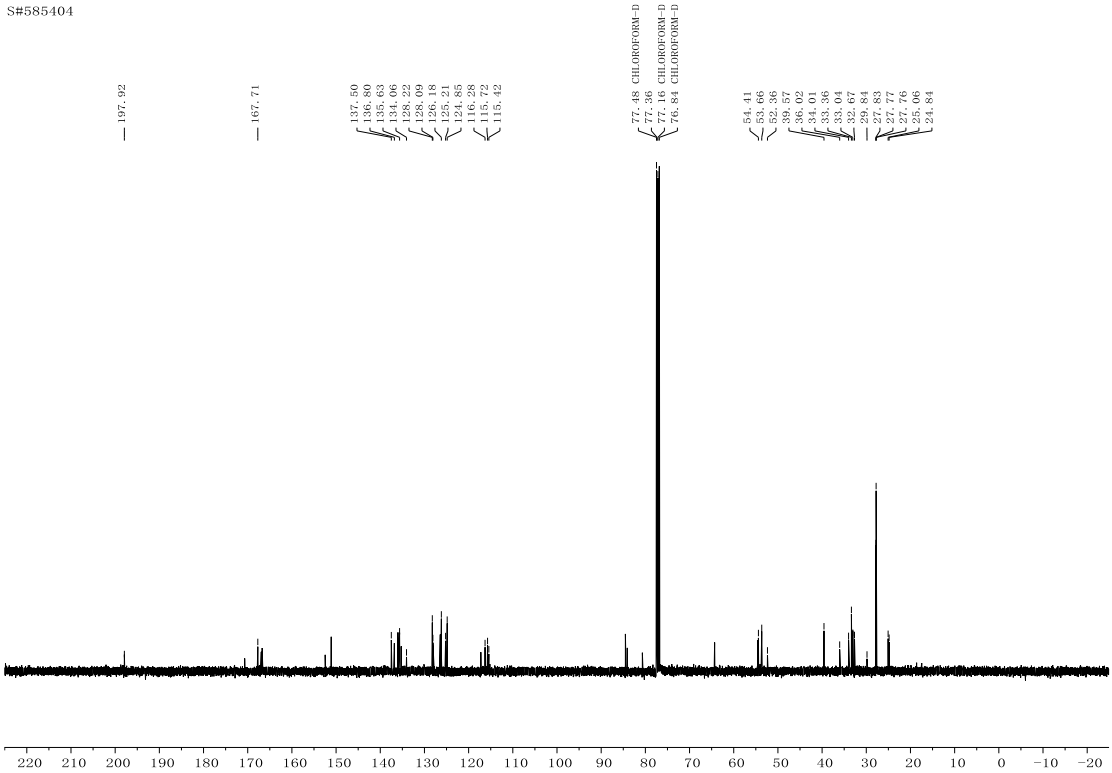


tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-5-methyl-1-oxohexan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22p)

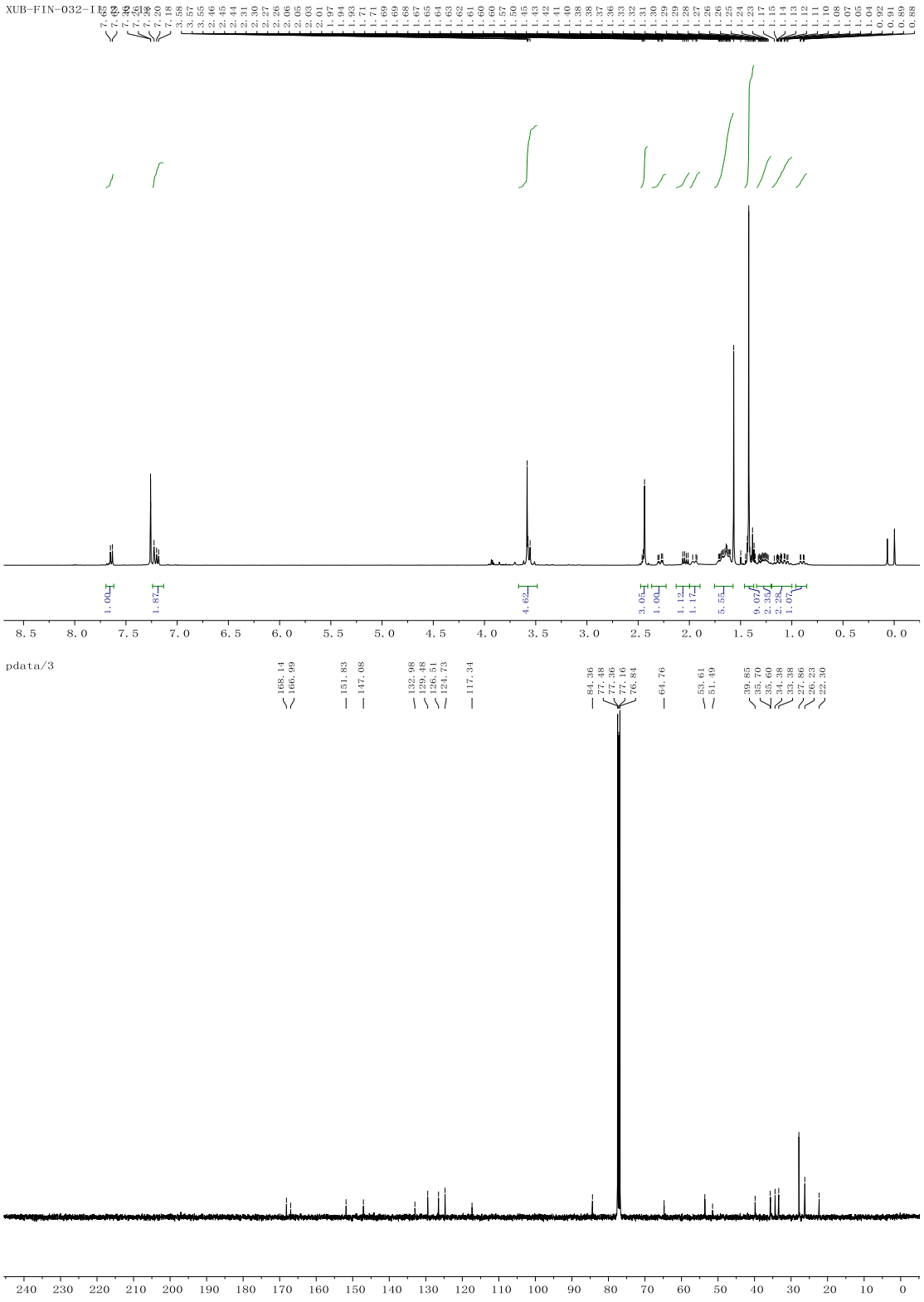


tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxohept-6-en-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22q)

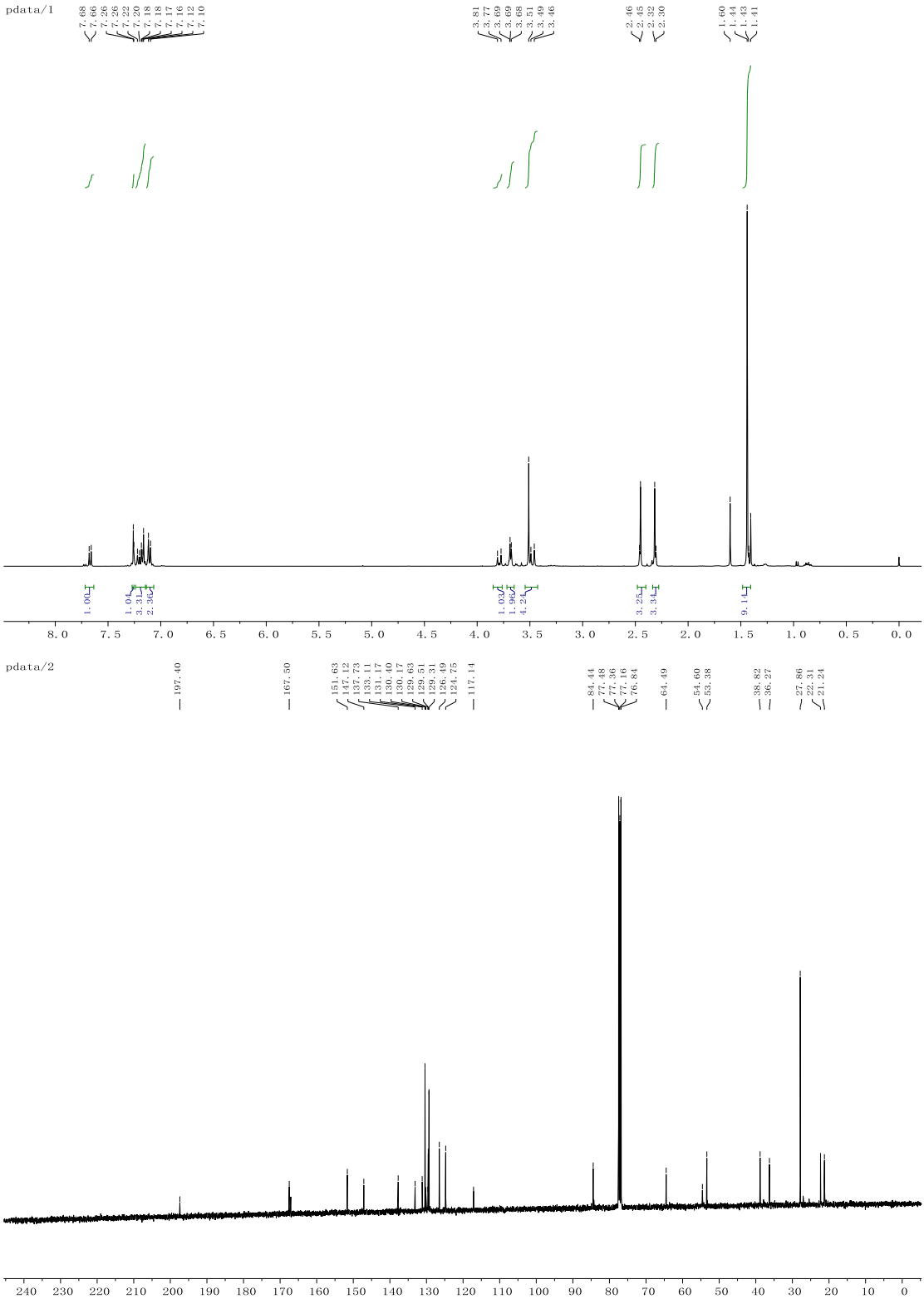




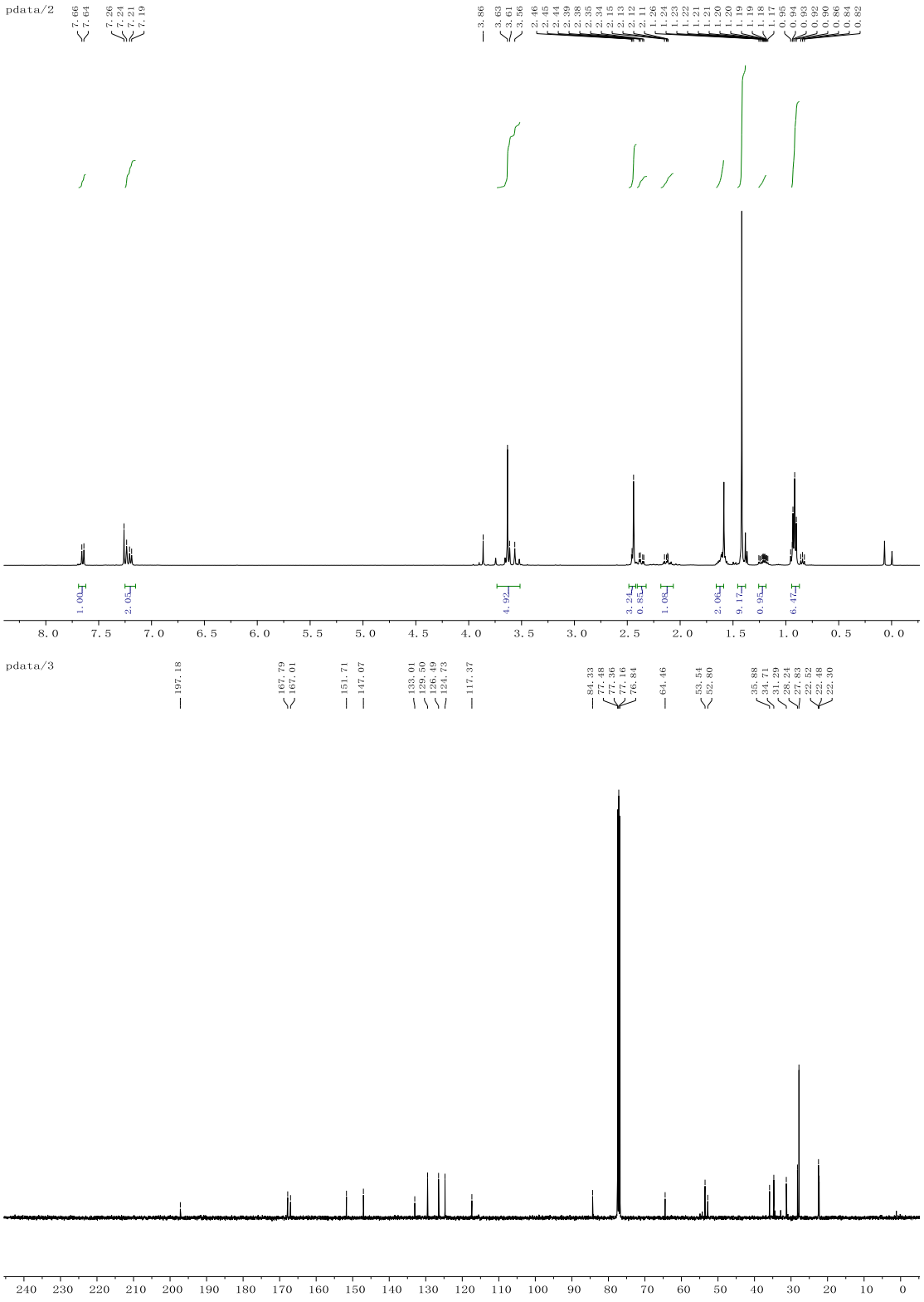
tert-butyl (_R_)-2-((_R_)-2-cyano-3-cyclohexyl-1-methoxy-1-oxopropan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22r)



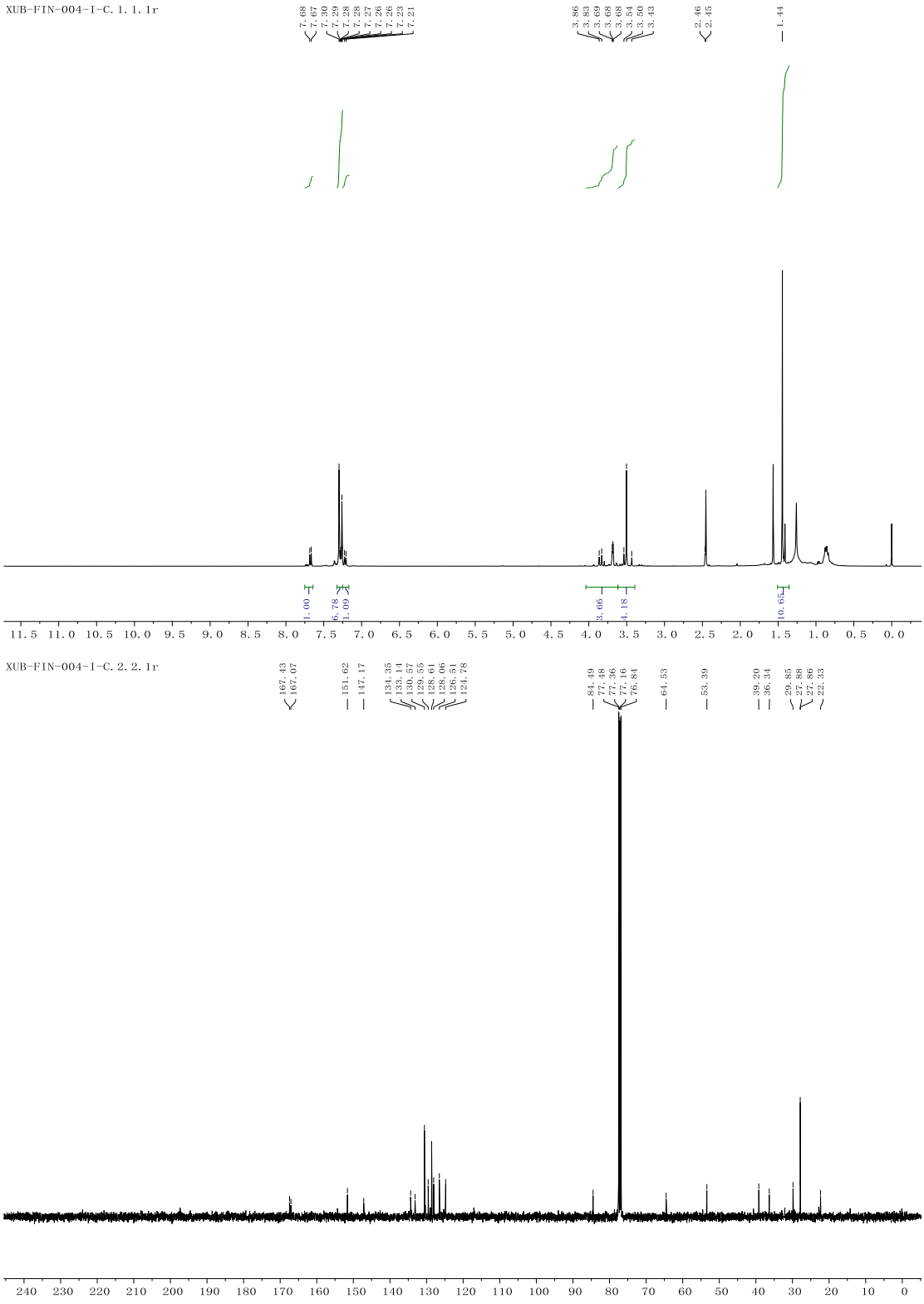
tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxo-3-(p-tolyl)propan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22s)



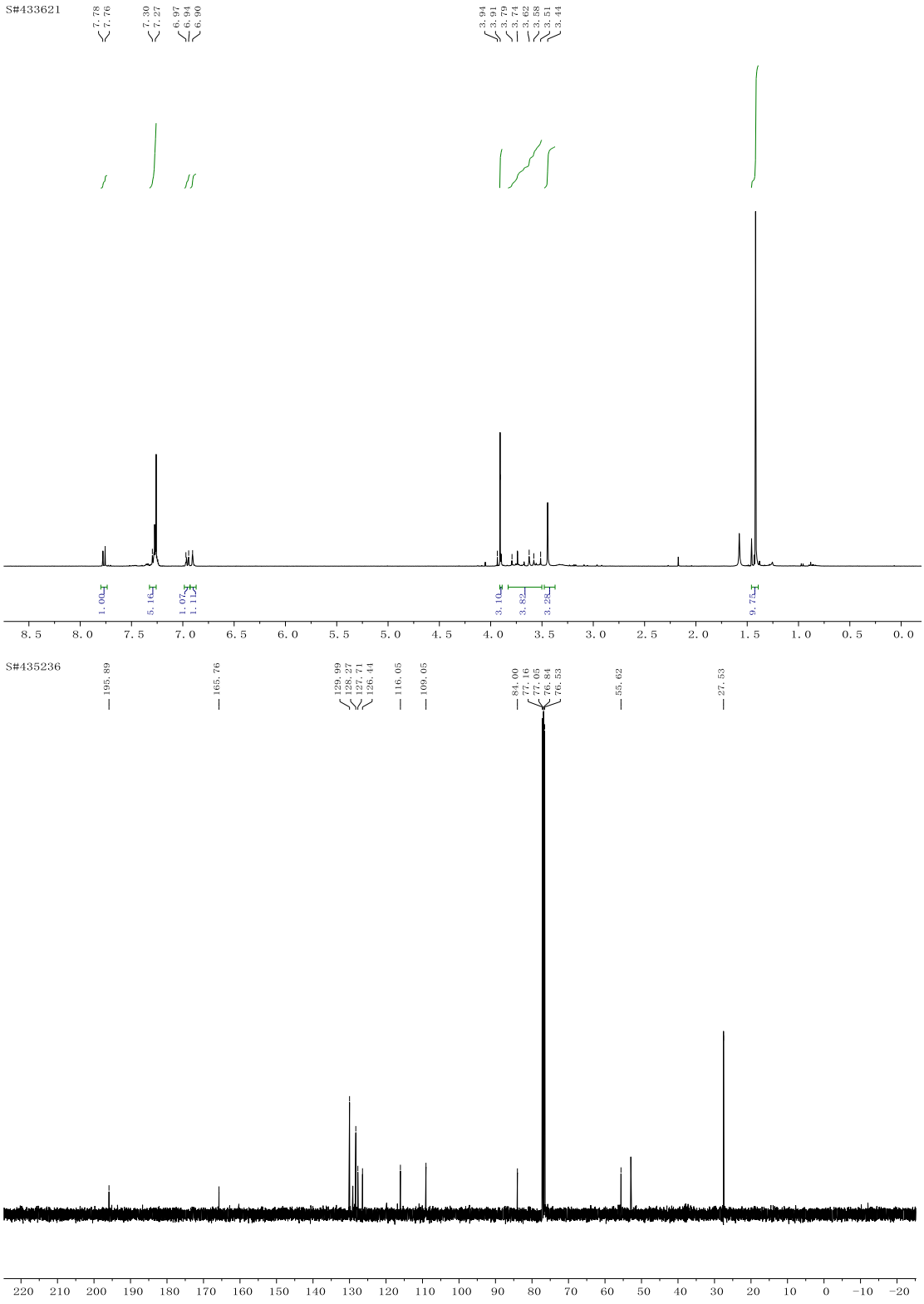
tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-5-methyl-1-oxohexan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22t)



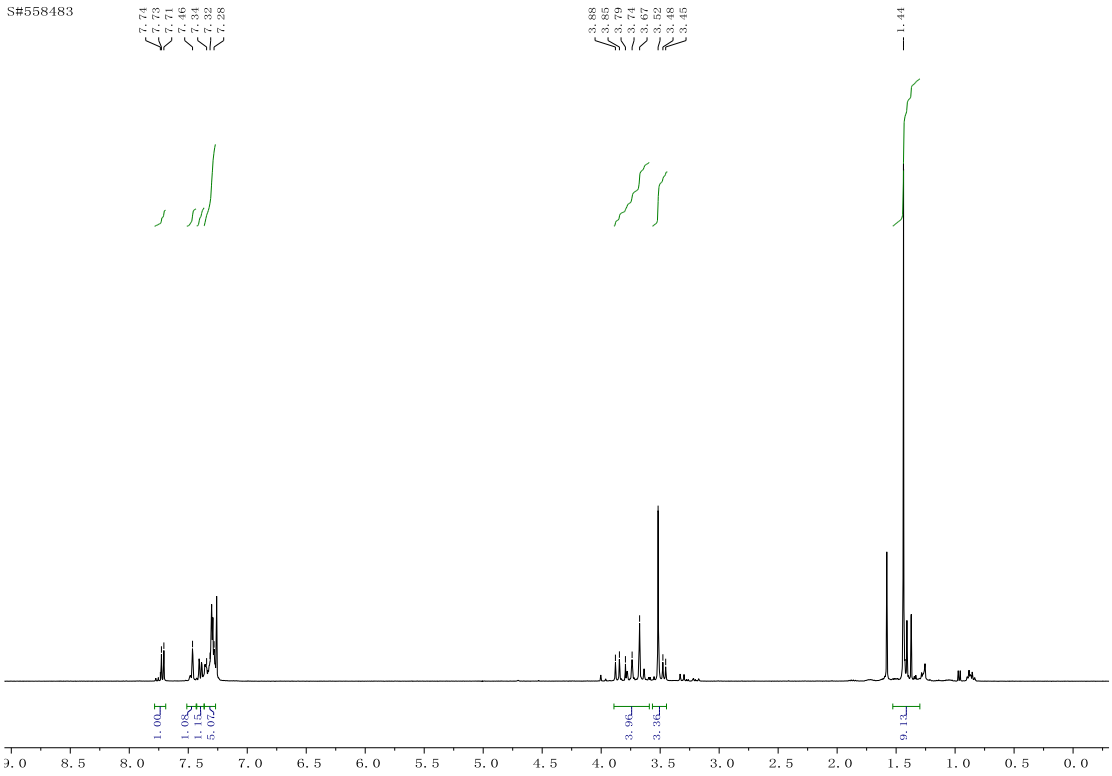
tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-5-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22u)

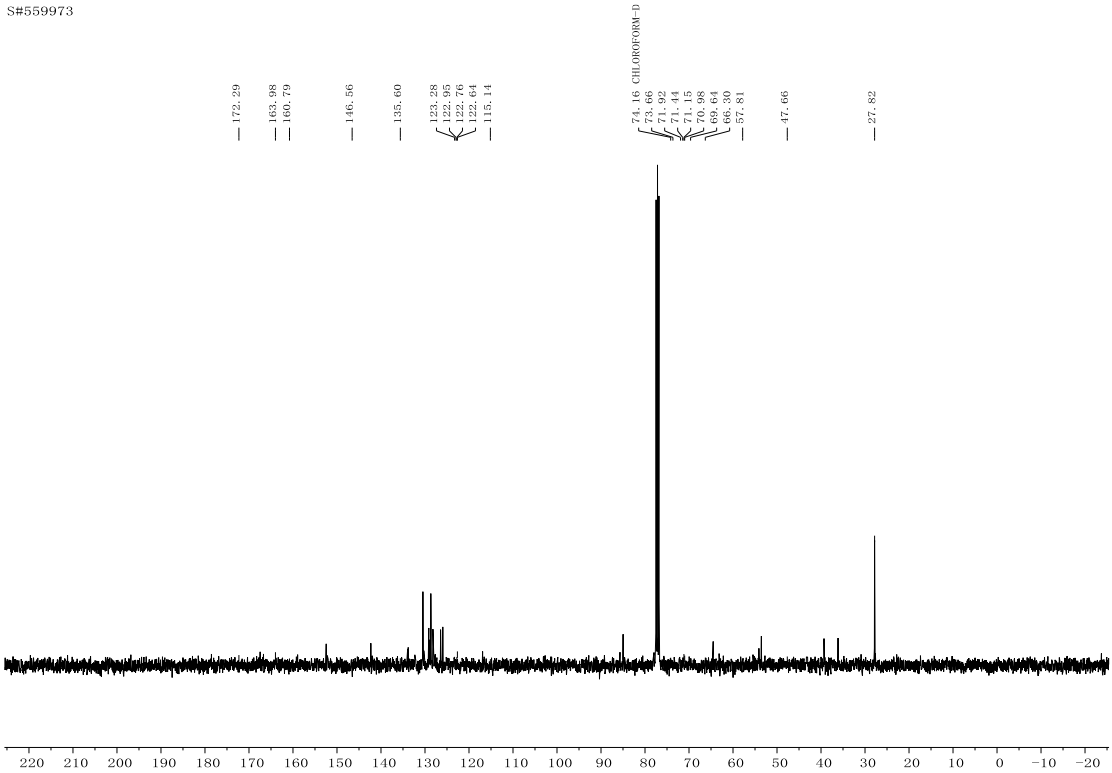


tert-butyl (_R_)-2-((_R_)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-5-methoxy-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22v)

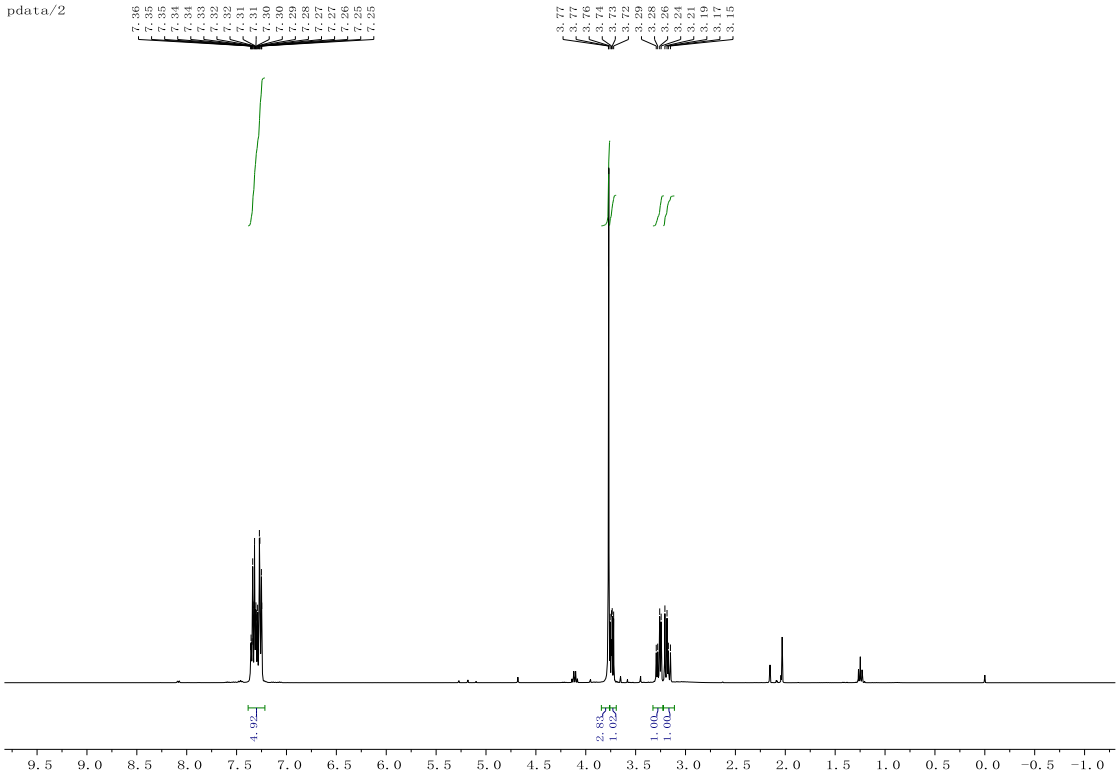


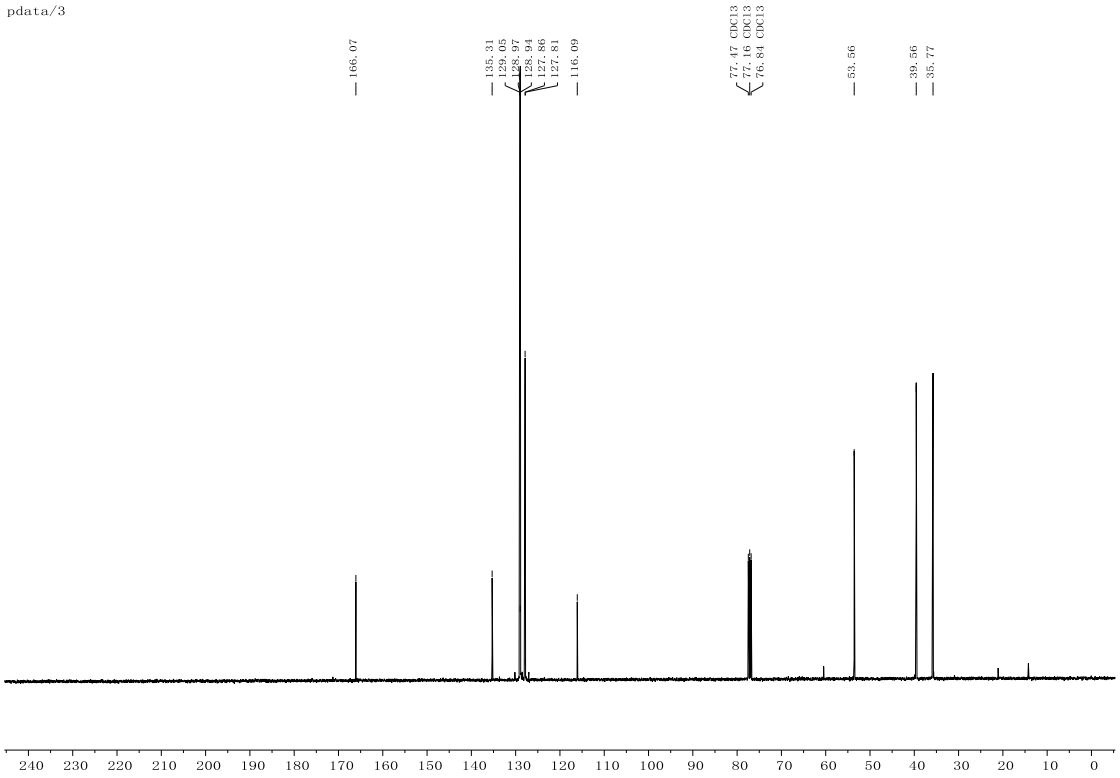
tert-butyl (_R_)-5-chloro-2-((_R_)-2-cyano-1-methoxy-1-oxo-3-phenylpropan-2-yl)-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (22w)



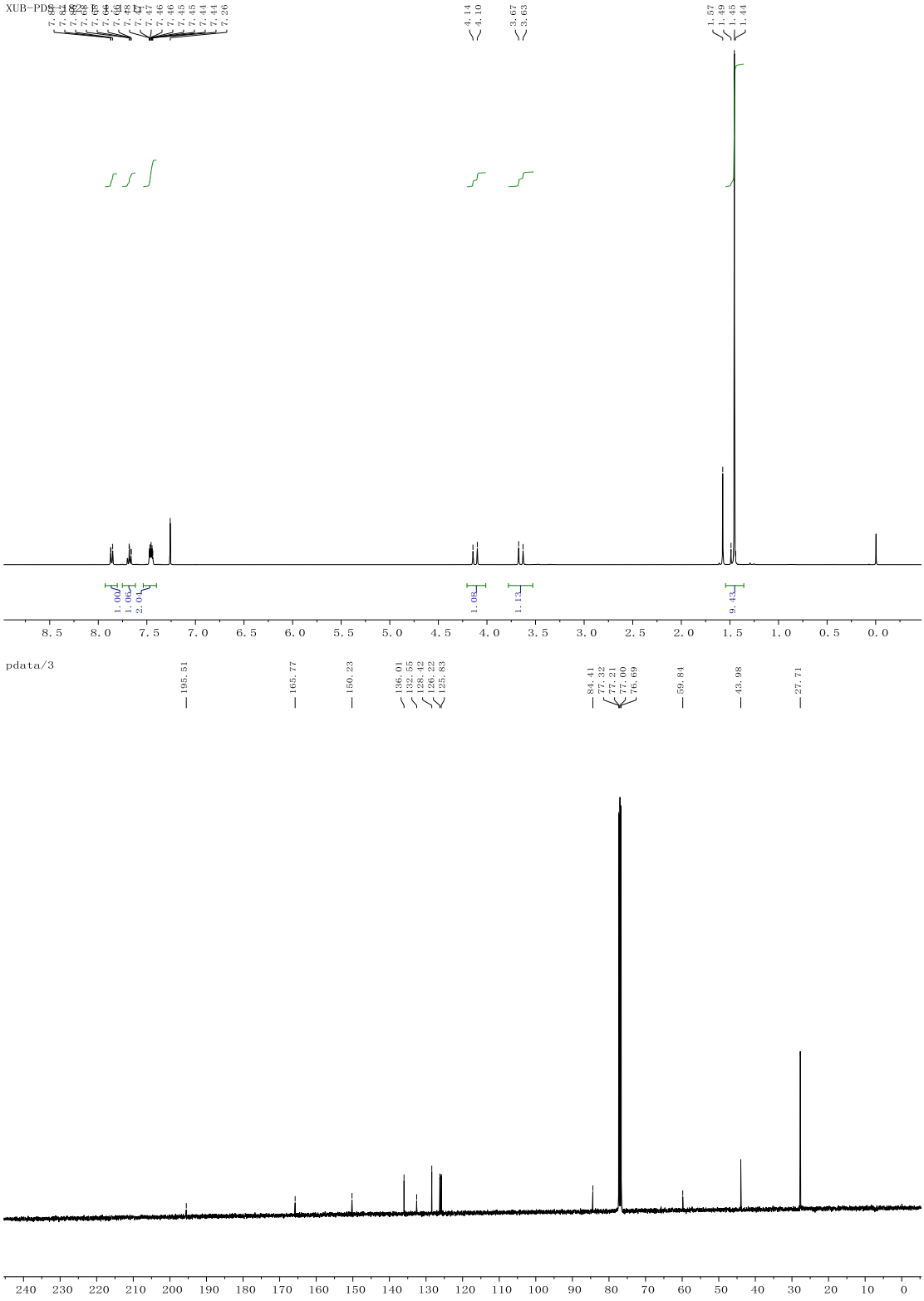


Methyl 2-cyano-3-phenylpropanoate (1a-H)

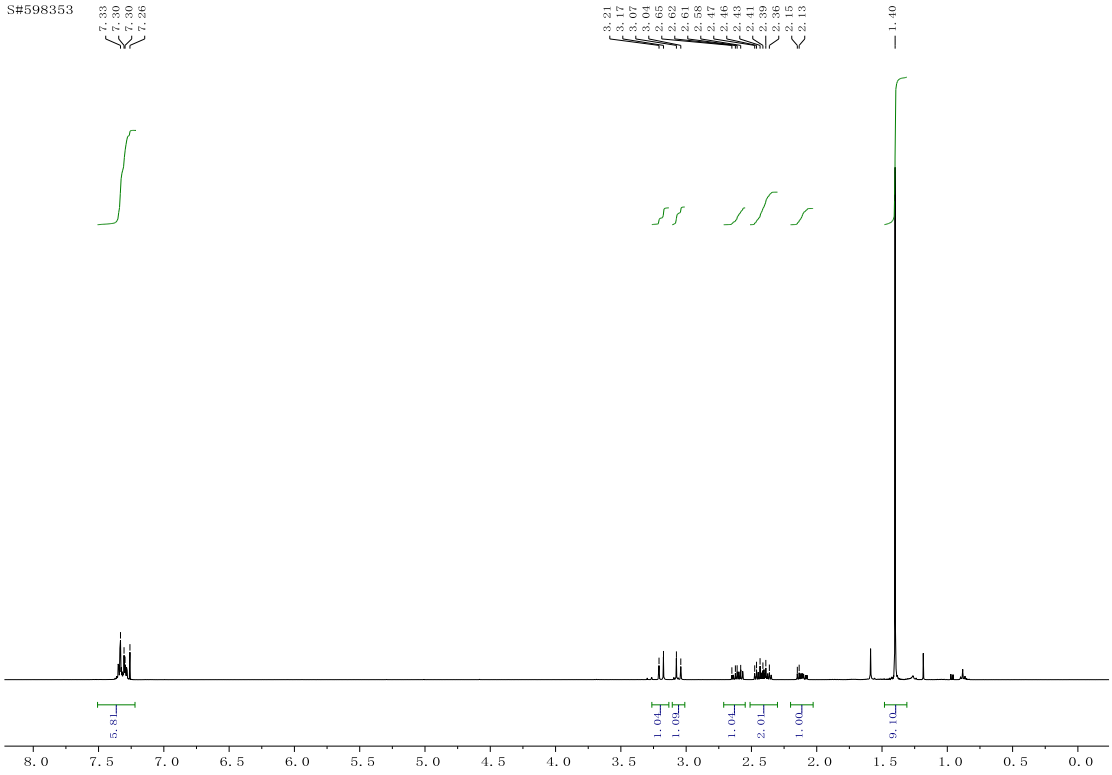


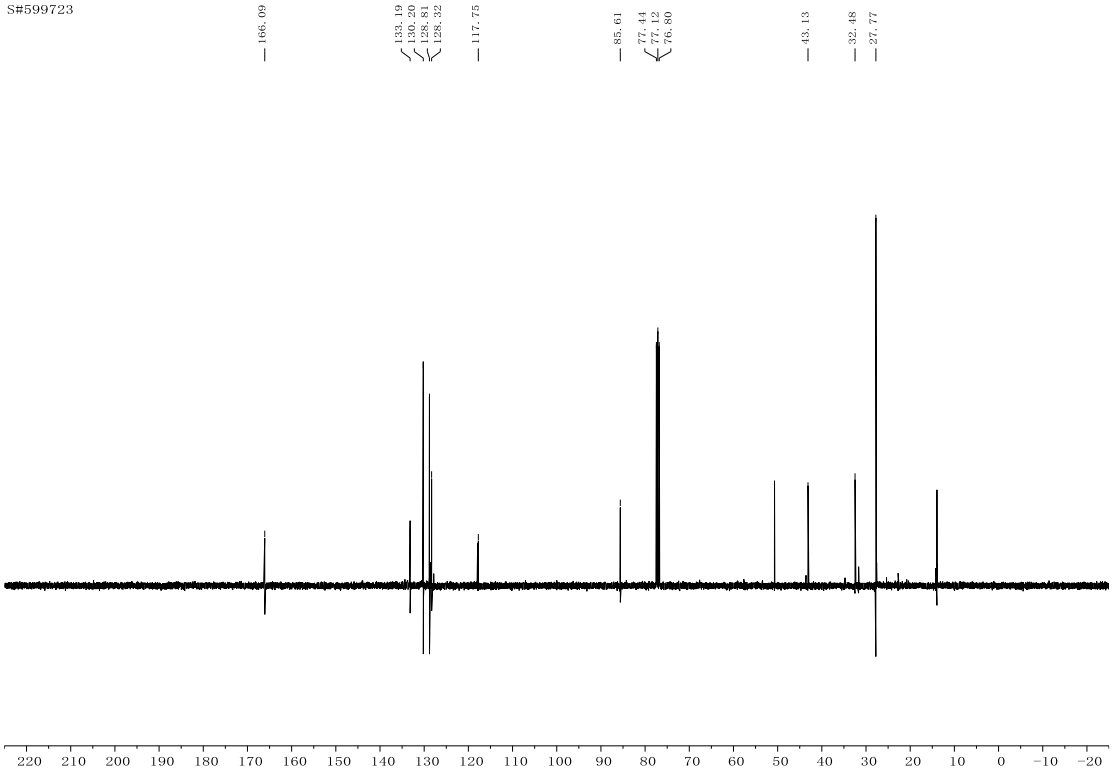


tert-butyl 2-bromo-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (23)

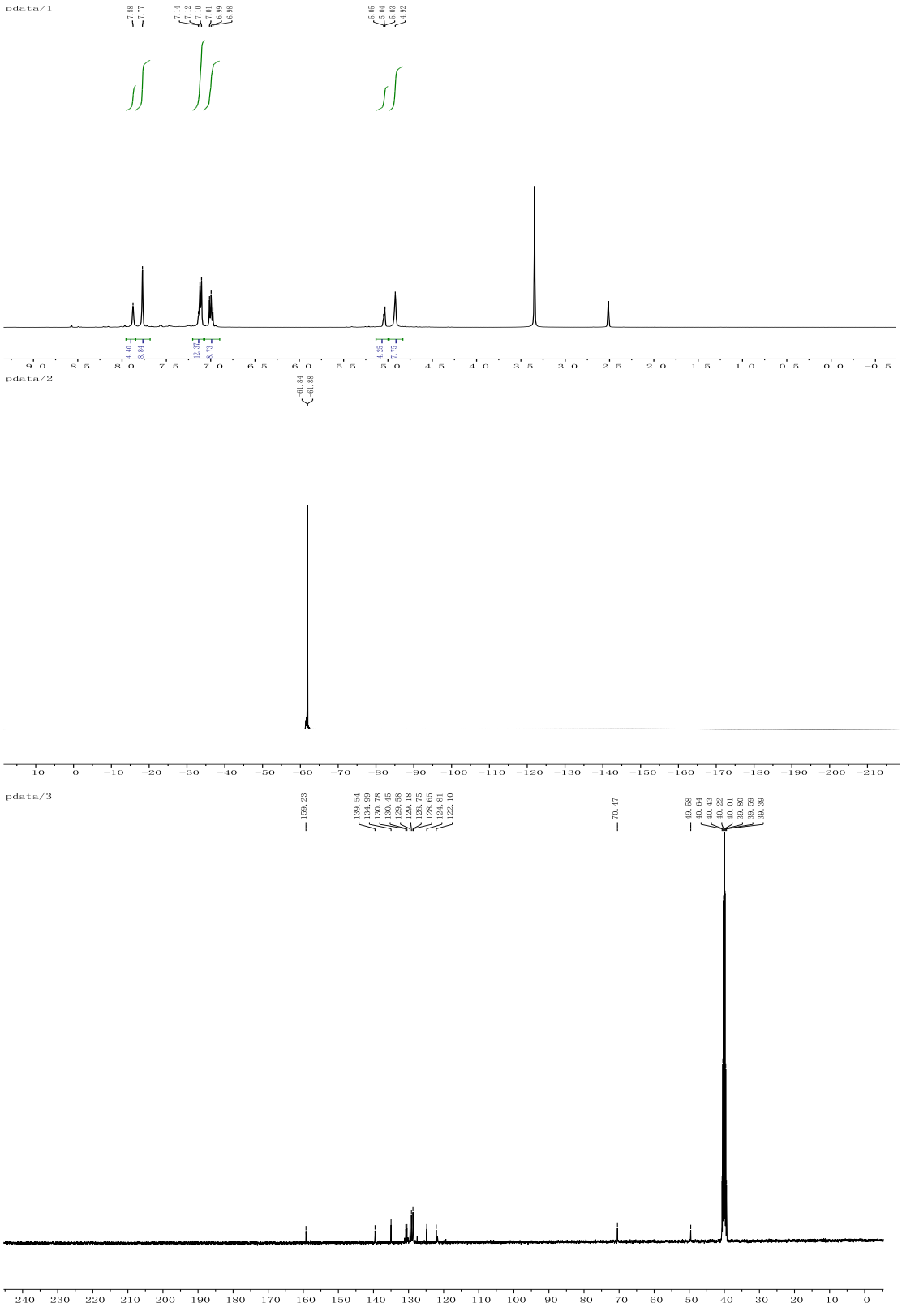


tert-butyl 2-benzyl-2,4-dicyanobutanoate (24)

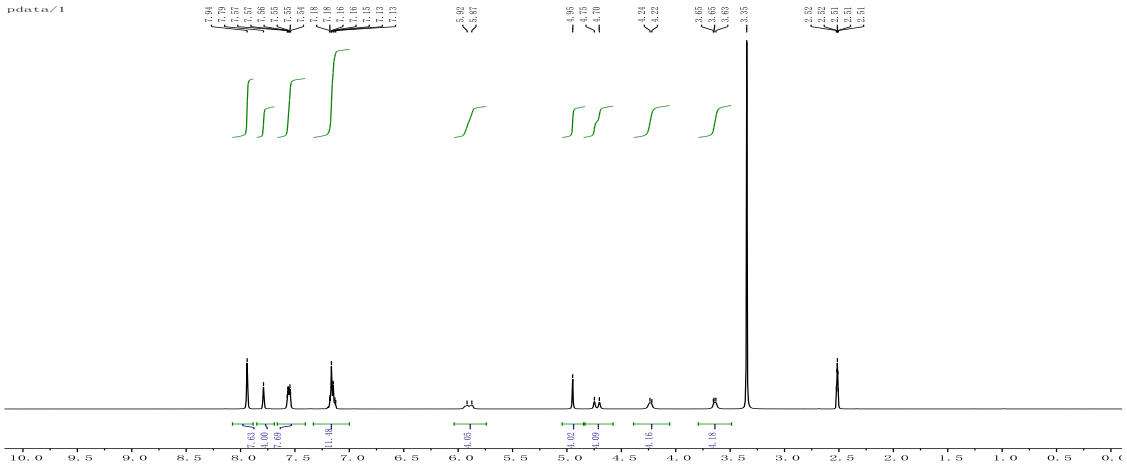




PN1



BG1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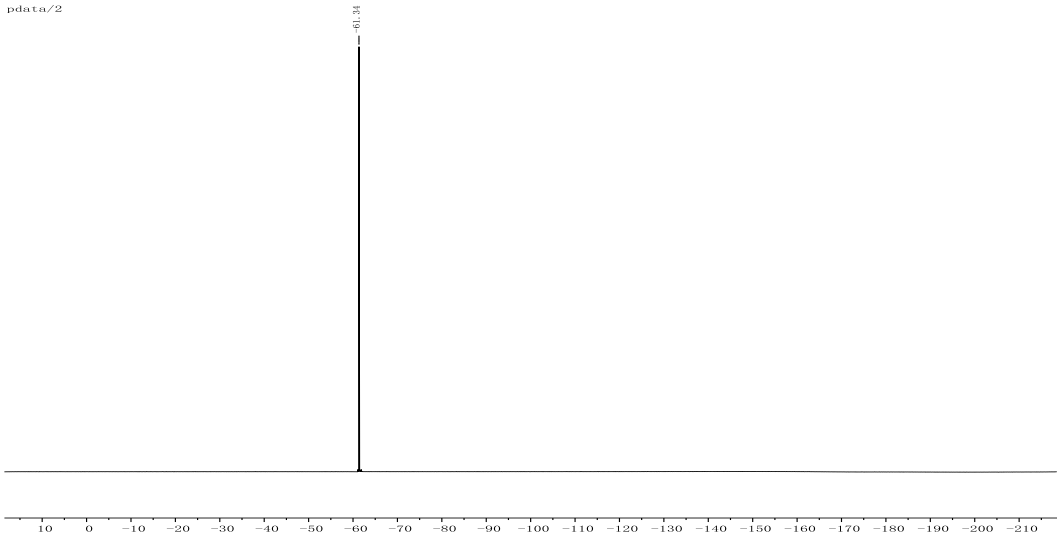
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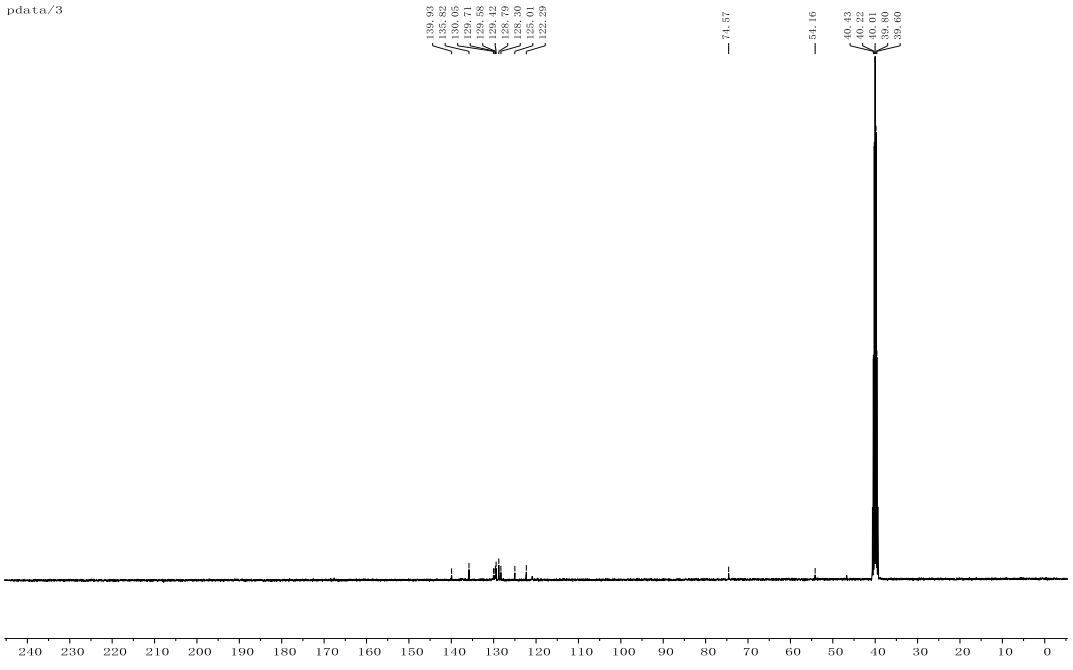
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