Asymmetric Mannich Synthesis of α-Amino Esters by Anion-Binding Catalysis

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Procedures, Materials and Instrumentation

General experimental procedures. All reactions were performed in standard, dry glassware fitted with rubber septa under an inert atmosphere of nitrogen unless otherwise described. Stainless steel syringes or cannulae were used to transfer air- and moisture-sensitive liquids. Reported concentrations refer to solution volumes at room temperature. Evaporation and concentration *in vacuo* was performed using house vacuum (ca. 40 mm Hg). Column chromatography was performed with ZEOprep® 60 (40–63 micron) silica gel from American Scientific. Thin layer chromatography (TLC) was used for reaction monitoring and product

detection using pre-coated glass plates covered with 0.20 mm silica gel with fluorescent indicator; visualization by UV light (λ_{ex} = 254 nm) or $KMnO_4$ stain.

Materials. Reagents were purchased in reagent grade from commercial suppliers and used without further purification, unless otherwise described. α-Chloroglycine esters were prepared according to the procedures reported previously.[1] Anhydrous solvents (toluene, *tert*-butyl methyl ether, Et_2O, CH_2Cl_2, MeOH) were prepared by passing the solvent through an activated alumina column. Triethylamine and diisopropylethylamine were distilled from CaH_2 at atmospheric pressure. H_2O, in synthetic procedures, refers to distilled water; brine refers to satd. aq. NaCl.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) spectra and proton-decoupled carbon nuclear magnetic resonance (^{13}C {^{1}H} NMR) spectra were recorded at 25 °C (unless stated otherwise) on Inova 600 (600 MHz) or Varian Unity/Inova 500 (500 MHz) spectrometers at the Harvard University nuclear magnetic resonance facility. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent. Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent. The solvent peak was referenced to 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C for $CDCl_3$, to 3.31 ppm for ^{1}H and 49.15 ppm for ^{13}C for CD_3OD, to 5.32 ppm for ^{1}H and 54.0 ppm for ^{13}C for CD_2Cl_2, and to 2.09 ppm for ^{1}H and 20.4 ppm for ^{13}C for toluene-d_8. Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sp = septet, m = multiplet), coupling constants in Hertz (Hz). In the case of compounds containing one or more fluorine atom(s), it should be noted that ^{13}C NMR experiments were obtained without ^{19}F decoupling.

Optical rotations were measured using a 1 mL cell with a 5 cm path length on a Jasco P-2000 digital polarimeter.

Infrared spectra were recorded using a Bruker Tensor 27 FT-IR spectrometer. Data are represented as follows: frequency of absorption (cm^{-1}), intensity of absorption (s = strong, m = medium, w = weak, br = broad). In-situ IR kinetic experiments were carried out using a

Mettler Toledo ReactIR™ iC 10 ATR FTIR spectrometer and a 9 mm AgX probe with a SiComp (silicon-based) window.

High-resolution mass spectrometry was measured using a Bruker micrOTOF-QII™ ESI-Qq-TOF mass spectrometer calibrated using an aqueous sodium formate solution (prepared via adding 1 mL of 1 M aq. NaOH in 100 mL of 1% aq. formic acid).

Chiral high performance liquid chromatography (HPLC) analysis was performed using an Agilent 1200 quaternary HPLC system with a commercially available AS-H, AD-H and OD-H chiral columns.

Abbreviations used. Ac = acetyl, Bz = benzyl, TFA = trifluoroacetyl, Boc = *tert*-butoxycarbonyl, *n*-BuLi = *n*-butyllithium, Cbz = carboxybenzyl, DCM = dichloromethane, DIPEA = diisopropylethylamine, DMAP = 4-dimethylaminopyridine, ee = enantiomeric excess, ESI = electrospray ionization, Et_2O = diethyl ether, Et_3N = triethylamine, EtOAc = ethyl acetate, Fmoc = fluorenylmethoxycarbonyl, HR = high-resolution, LC = liquid chromatography, LiHMDS = Lithium bis(trimethylsilyl)amide, MS = mass spectrometry, NA = not applicable, rt = room temperature, TBME = *tert*-butylmethyl ether, THF = tetrahydrofuran, TOCSY = total correlation spectroscopy, TOF = time-of-flight, Troc = 2,2,2-trichloroethoxycarbonyl.

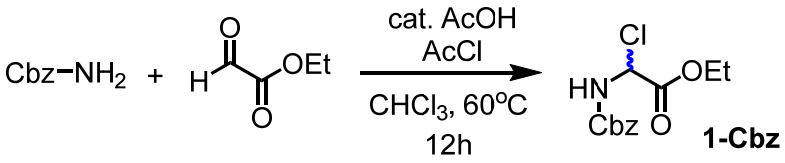
Experimental Section

A. Substrate Preparation

General Procedure for the Preparation of Ethyl 2-(((Benzyloxy)carbonyl)amino)-2-chloroacetate (1-Cbz)

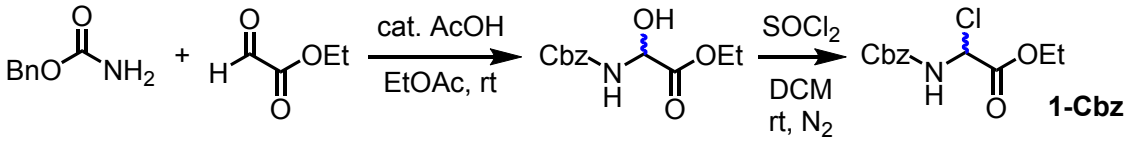
Ethyl 2-(((benzyloxy)carbonyl)amino)-2-chloroacetate (**1-Cbz)** could be prepared by two methods as described by Roche.[1] **1-Cbz** produced by the two methods were identical in quality and gave the Mannich products **3a** and **4a** in nearly equal product yield and ee.

Method 1:



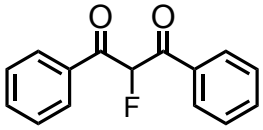
In a 50 mL round-bottom flask, acetic acid (0.5 mmol, 33 µL) was added to a vigorously stirring solution of benzyl carbamate (5.0 mmol, 0.756 g), freshly distilled ethyl 2-oxoacetate (6.5 mmol, 0.65 mL) and acetyl chloride (12.5 mmol, 0.95 mL) in anhydrous chloroform (20 mL). The flask was tightly sealed and the reaction mixture was heated to 60 °C and stirred for 12 h, then concentrated *in vacuo* to yield a colorless solid. The residual acetic acid was co-evaporated twice with anhydrous DCM (20mL) under reduced pressure to give **1-Cbz** in 98% yield (4.9 mmol, 1.359g), which was used in the subsequent Mannich reaction without further purification. The spectroscopic data of **1-Cbz** matched those reported by Roche. [1]

Method 2:



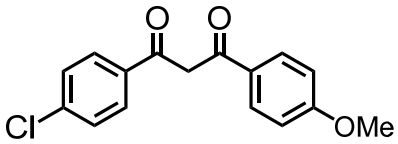
In a 250 mL round-bottom flask equipped with a reflux condenser, acetic acid (6 mmol, 0.36 mL) was added to a vigorously stirring solution of benzyl carbamate (60 mmol, 9.07 g) and ethyl 2-oxoacetate (60 mmol, 15.8 mL of 50% solution in toluene) in ethyl acetate (50 mL). The reaction mixture was heated to reflux and stirred overnight, then concentrated *in vacuo* to yield an off-white slurry. The crude mixture was suspended in 3:7 ethyl acetate/hexane, and cooled in an ice bath. The resulting solid was filtered, washed with hexanes and dried under reduced pressure to give ethyl 2-(((benzyloxy)carbonyl)amino)-2-hydroxyacetate (10.8 g, 71% yield) as a white solid. Treatment of ethyl 2-(((benzyloxy)carbonyl)amino)-2-hydroxyacetate (0.25 mmol) with $SOCl_2$ (0.1 mL) in DCM (0.5 mL) at room temperature under nitrogen atmosphere for 1h, followed by removal of residual $SOCl_2$ and DCM under reduced pressure gave ethyl 2-(((benzyloxy)carbonyl)amino)-2-chloroacetate **1** as a colorless solid in quantitative yield and was used subsequently in the Mannich reaction without further purification. The spectroscopic data of **1-Cbz** matched those reported by Roche. [1]

Procedures for the Preparation of 1,3-Dicarbonyl Compounds



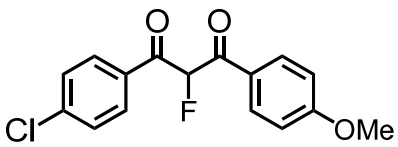
2-Fluoro-1,3-diphenylpropane-1,3-dione

2-Fluoro-1,3-diphenylpropane-1,3-dione was prepared according to a literature procedure[2] at 10 mmol scale. The product was obtained as a yellow solid (2.2 g, 90 %). The NMR spectroscopic data were in agreement with those reported in the literature.[2]



1-(4-Chlorophenyl)-3-(4-methoxyphenyl)propane-1,3-dione

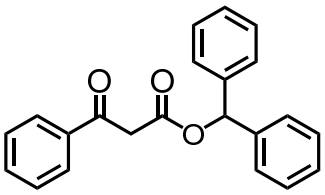
1-(4-Chlorophenyl)-3-(4-methoxyphenyl)propane-1,3-dione was prepared according to a modified literature procedure.[3, 4] To a solution of 1-(4-chlorophenyl)ethan-1-one (7.5 mmol, 0.974 mL) in anhydrous THF (30 mL) was added LiHMDS (30 mmol) and the resulting solution was stirred for 1 h at ‑78°C. The solution was warmed to rt and stirred for 2 h before cooling to -78°C and adding 4-methoxybenzoyl chloride (7.5 mmol, 1.02 mL) dropwise. The solution was warmed to rt and stirred for 16 h. NH_4Cl (saturated solution in water, 30.0 mL) was added, and the pH was adjusted to 7.0. The organic and aqueous layers of the liquid phase were separated and the aqueous layer then extracted three times with EtOAc (40.0 mL). The combined organic layers were washed with brine (100 mL), dried over $MgSO_4$ and then concentrated in vacuo. The crude product was purified by flash chromatography using 5% ethyl acetate in hexanes as eluent to give product as a light yellow solid (1.75g, 81%) yield. The NMR spectroscopic data were in agreement with those reported in the literature.[4]



1-(4-Chlorophenyl)-2-fluoro-3-(4-methoxyphenyl)propane-1,3-dione

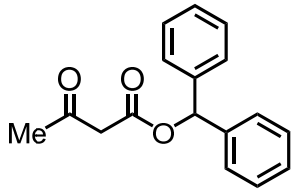
1-(4-Chlorophenyl)-2-fluoro-3-(4-methoxyphenyl)propane-1,3-dione was prepared according to a modified literature procedure.[2] To a solution of 1-(4-Chlorophenyl)—3-(4-

methoxyphenyl)propane-1,3-dione (3.0 mmol, 860 mg) in acetonitrile (30 mL) was added Selectfluor (9.0 mmol, 3.18 g) in one portion. The heterogeneous reaction was stirred vigorously for 2 days at 60 °C. Acetonitrile was removed *in vacuo*, and the crude mixture was redissolved in DCM (100 mL). The solution was washed twice with 50 mL distilled water and purified by flash column chromatography using 10% ether in DCM as eluent, yielding the desired fluorinated diketone (210 mg, 23 %). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.09 (d, J = 8.6 Hz, 2H), 8.06 (d, J = 8.7 Hz, 2H), 7.97 (m, enol tautomer), 7.45 (d, J = 8.7 Hz, 2H), 6.98 (m, enol tautomer), 6.96 (d, J = 8.9 Hz, 2H), 6.45 (d, J = 49.2 Hz, 1H), 3.89 (s, enol tautomer), 3.87 (s, 3H).



Benzhydryl 3-oxo-3-phenylpropanoate

Benzhydryl 3-oxo-3-phenylpropanoate was prepared according to a modified literature procedure.[5] A 250 mL round-bottom flask was equipped with a magnetic stir bar and charged with ethyl 3-oxo-3-phenylpropanoate (80 mmol, 14 mL) and 80 mL of a 1M NaOH solution in distilled water. After stirring overnight, the solution was poured into a separatory funnel and washed four times with 10 mL of DCM each. The aqueous layer was cooled in an ice bath and a 3M solution of HCl was added until the solution was around pH 1. 3-oxo-3-phenylpropanoate was obtained as a light yellow solid (8.0 g, 62%), which was used immediately without further purification. In a 100 mL pear-shaped flask, equipped with a magnetic stir bar, 3-oxo-3-phenylpropanoate (18 mmol, 3.0 g) and benzhydryl alcohol (18 mmol, 3.3 g) were dissolved in 40 mL of acetonitrile. After purging with nitrogen gas, a solution of *N,N'*-dicyclohexyldiimide (18 mmol, 3.7 g) in 20 mL of acetonitrile was added in one portion. The reaction was stirred for 12 h at rt, after which the solvent was removed *in vacuo*. The desired ester (2.2 g, 37%) was obtained as a slightly yellow oil by flash column chromatography, using gradient elution (hexanes → 30% ethyl acetate/hexanes). ^{1}H NMR (600 MHz, $CDCl_3$) δ 12.40 (s, enol tautomer), 7.92 (d, J = 7.2 Hz, 2H), 7.78 (d, J = 7.3 Hz, enol tautomer), 7.58 (t, J = 7.4 Hz, enol tautomer), 7.44 (m, 4H), 7.37 (m, 4H), 7.28 (m, 5H), 7.00 (s, enol tautomer), 6.92 (s, 2H), 4.12 (s, 2H).



Benzhydryl 3-oxobutanoate

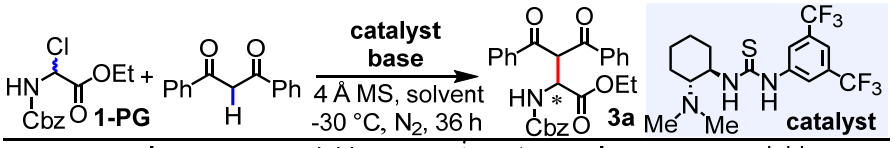
Benzhydryl 3-oxobutanoate was prepared according to a modified literature procedure.[6] In a 100 mL round-bottom flask, equipped with a magnetic stir bar and a reflux condenser, 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (20 mmol, 2.8 g) and benzyl alcohol (20 mmol, 3.6 g) was dissolved in 50 mL xylene. The reaction was heated to vigorous reflux for 2 h, then cooled to room temperature. Xylene was removed *in vacuo*, and the crude reaction mixture was run through a plug of silica (40 g) with 2% ethyl acetate in hexanes as eluent (200 mL). The desired ester was obtained as a yellow oil (2.6 g, 49%) upon concentration *in vacuo*. The NMR spectroscopic data were in agreement with those reported in the literature.[6]

B. Enantioselective Mannich Reaction

Experimental procedure for the optimization of base additives (see Table S1 in SI)

A flame-dried vial equipped with a screw-top septum cap and a magnetic stir bar was charged with 4Å molecular sieves, which was capped with a rubber septum and flame-dried under reduced pressure. After the flask was cooled to room temperature, catalyst (0.005 mmol), nucleophile (0.1 mmol), base (0.05 mmol) and DCM (1 mL) were added. The reaction flask was evacuated and back-filled with N_2 (3-times) and cooled to -78 °C for 20 minutes under stirring. A 0.5M solution of α-chloroglycine ester **1** in DCM (0.1 mL), also cooled to -78 °C, was added by a syringe, and the reaction mixture was transferred to a refrigerator at 0 °C equipped with a magnetic stirrer and stirred for 36 h. Upon completion, the reaction mixture was warned to room temperature, filtered through a pad of Celite, and the filtrate was concentrated *in vacuo*. The product yield was determined by the ^{1}H NMR analysis of the crude product using dibromomethane as the internal standard. The crude product was purified by PTLC using 50% ethyl ether/hexanes as the eluent to give **3a** for the determination of ee by HPLC.

Table S1. Screening of Base

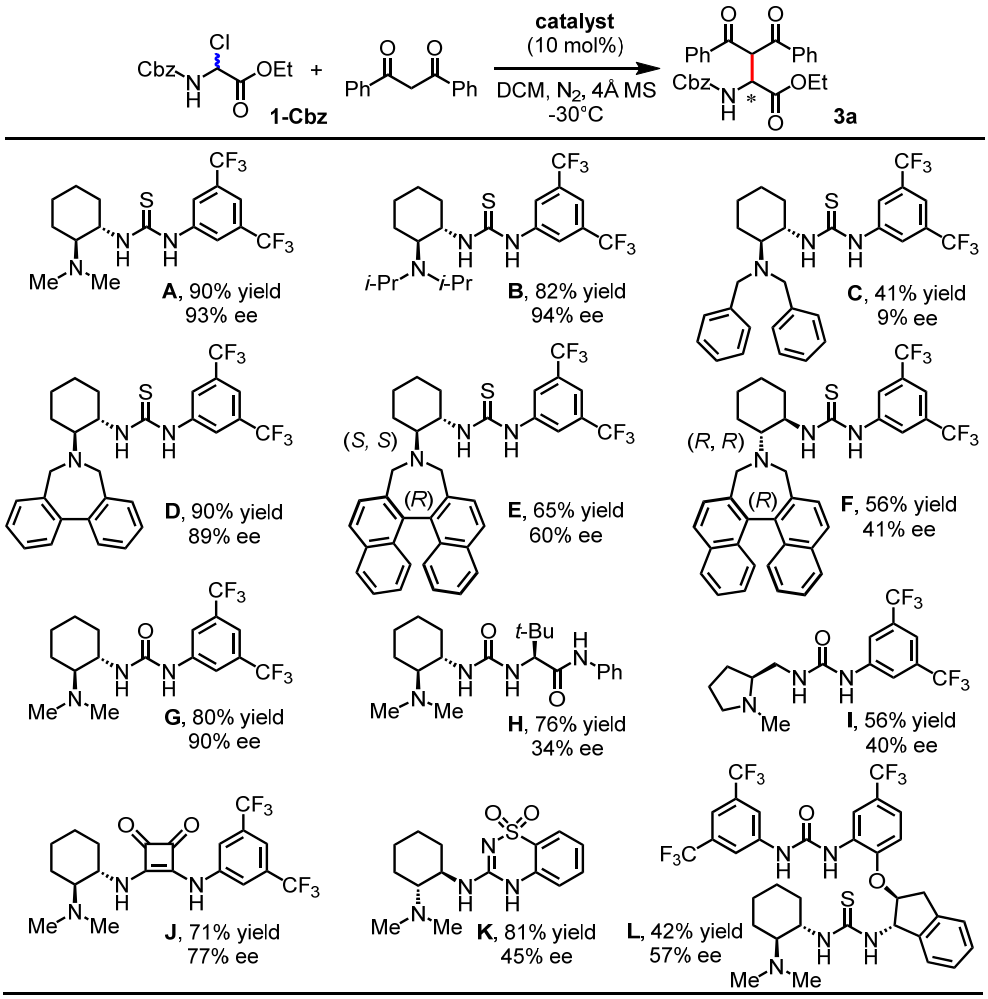


entry	base	yield (%)	ee (%)	entry	base	yield (%)	ee (%)
1	none	90	93	5	K_2CO_3	82	21
2	$NaHCO_3$	77	35	6	Cs_2CO_3	84	74
3	$KHCO_3$	96	30	7	Et_3N	95	99
4	Na_2CO_3	92	33	8	$(i\text{-}Pr)_2EtN$	99	96

Experimental procedure for the evaluation of catalyst (see Table S2 in SI)

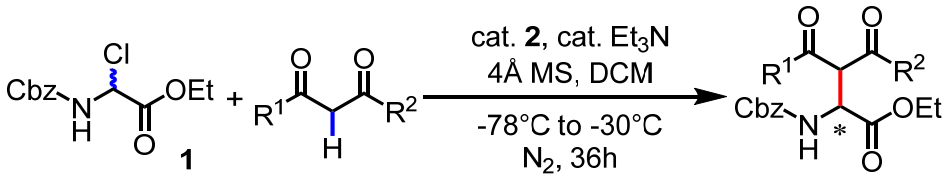
A flame-dried vial equipped with a screw-top septum cap and a magnetic stir bar was charged with 4Å molecular sieves, which was capped with a rubber septum and flame-dried under reduced pressure. After the flask was cooled to room temperature, catalyst (0.005 mmol), dibenzoylmethane (0.1 mmol), and DCM (1 mL) were added. The reaction flask was evacuated and back-filled with N_2 (3-times) and cooled to -78 °C for 20 minutes under stirring. A 0.5 M solution of α-chloroglycine ester **1** in DCM (0.1 mL), also cooled to -78 °C, was added by a syringe, and the reaction mixture was transferred to a cryocool at -30 °C and stirred for 36 h. Upon completion, the reaction mixture was warned to room temperature, filtered through a pad of Celite, and the filtrate was concentrated *in vacuo*. The product yield was determined by the ^{1}H NMR analysis of the crude product using dibromomethane as the internal standard. The crude product was purified by PTLC using 50% ethyl ether/hexanes as the eluent to give **3a** for the determination of ee by HPLC.

Table S2. Evaluation of Catalyst[a]



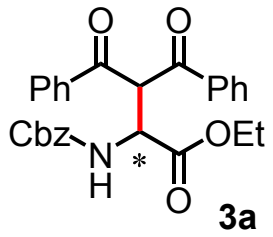
[a] Catalysts **B** to **F** and **H** to **L** were synthesized according to literature procedures, as cited in reference 8.

General procedure for enantioselective Mannich reaction (See Tables 3 and 4 in manuscript)



A 20 mL pear-shaped flask equipped with a magnetic stir bar was charged with 4Å molecular sieves, which was capped with a rubber septum and flame-dried under reduced pressure. After the flask was cooled to room temperature, catalyst (0.025 mmol), nucleophile (0.5 mmol) and 0.03125M solution of triethylamine in anhydrous DCM (2 mL) were added. The reaction flask was evacuated and back-filled with N_2 (3-times) and cooled to -78 °C for 20 minutes under stirring. A 0.5M solution of α-chloroglycine ester **1** in DCM (0.5 mL), also cooled to -78 °C, was added by a syringe, and the reaction mixture was transferred to a cryocool at -30 °C and stirred for 36 h. Upon completion, the reaction mixture was warmed to room temperature, filtered through a pad of Celite, and the filtrate was concentrated *in vacuo* and purified by a silica gel packed flash chromatography column, typically using ethyl ether/hexanes as the eluent.

The Mannich products were obtained as a mixture of the 1,3-dicarbonyl compounds and the corresponding enols in minor quantity, as observed by ^{1}H NMR. The enol peaks were omitted from the ^{1}H NMR assignment. Products **4a** to **4k** were acquired as the mixtures of diastereomers that separated poorly by flash chromatography. The epimerization of stereocenters α to two carbonyl groups may take place slowly, leading to the gradual erosion in dr. The dr values of the isolated products are provided as the following for **4a** to **4k**.

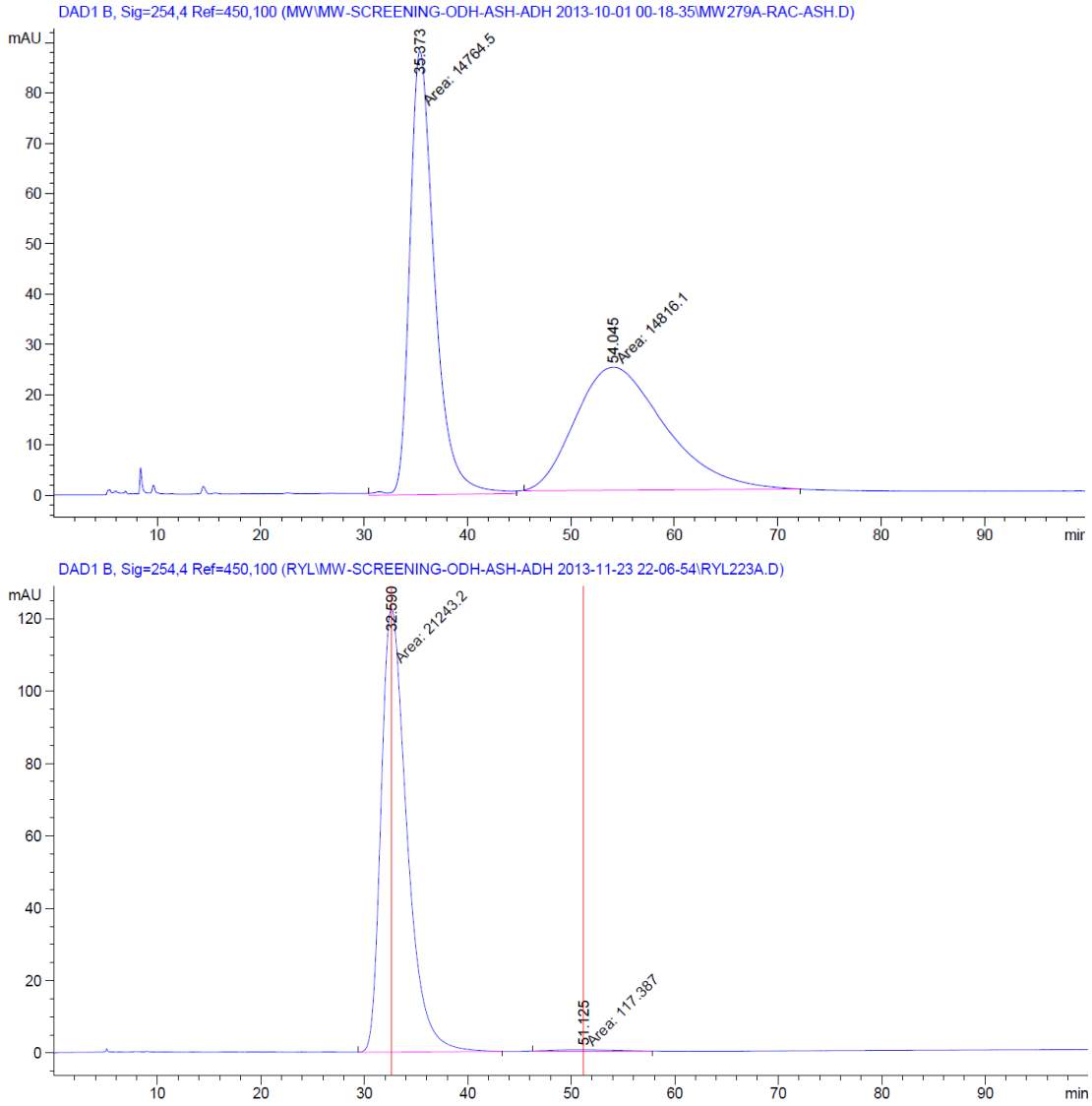


3a

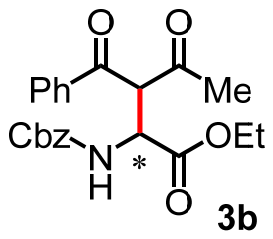
Ethyl 3-benzoyl-2-(((benzyloxy)carbonyl)amino)-4-oxo-4-phenylbutanoate (3a)

Substrate **1-Cbz** was reacted with 1,3-diphenylpropane-1,3-dione following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **3a** was obtained as a colorless solid (109 mg, 95%). $[\alpha]^{25}_{D}$ = 15.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (t, *J* = 6.6 Hz, 4H), 7.63-7.56 (m, 2H), 7.51-7.44 (m, 4H), 7.35-7.29 (m, 5H), 6.22 (d, *J* = 4.2 Hz), 6.14 (d, *J* = 8.4 Hz), 5.17 (q, *J* = 4.2 Hz, 1H), 5.10 (dd, J_1 = 12.6 Hz, J_2 = 17.4 Hz, 2H), 4.24-4.16 (m, 2H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 196.02, 194.80, 170.04, 156.50, 136.01, 135.75, 134.26, 134.07, 129.34, 129.20, 128.79, 128.70, 128.31, 128.01, 67.26, 62.56, 57.68, 54.15, 14.15; IR (neat) ν 3360, 3033, 2983, 1727, 1596, 1505, 1449, 1322, 1269, 1217, 1060, 1027, 727, 667 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{27}H_{25}NO_6$ (MH^+): 460.1775; found: 460.1732.

HPLC (ChiralPak AS-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	32.59	21243.2	99.45
2	51.13	117.387	0.55

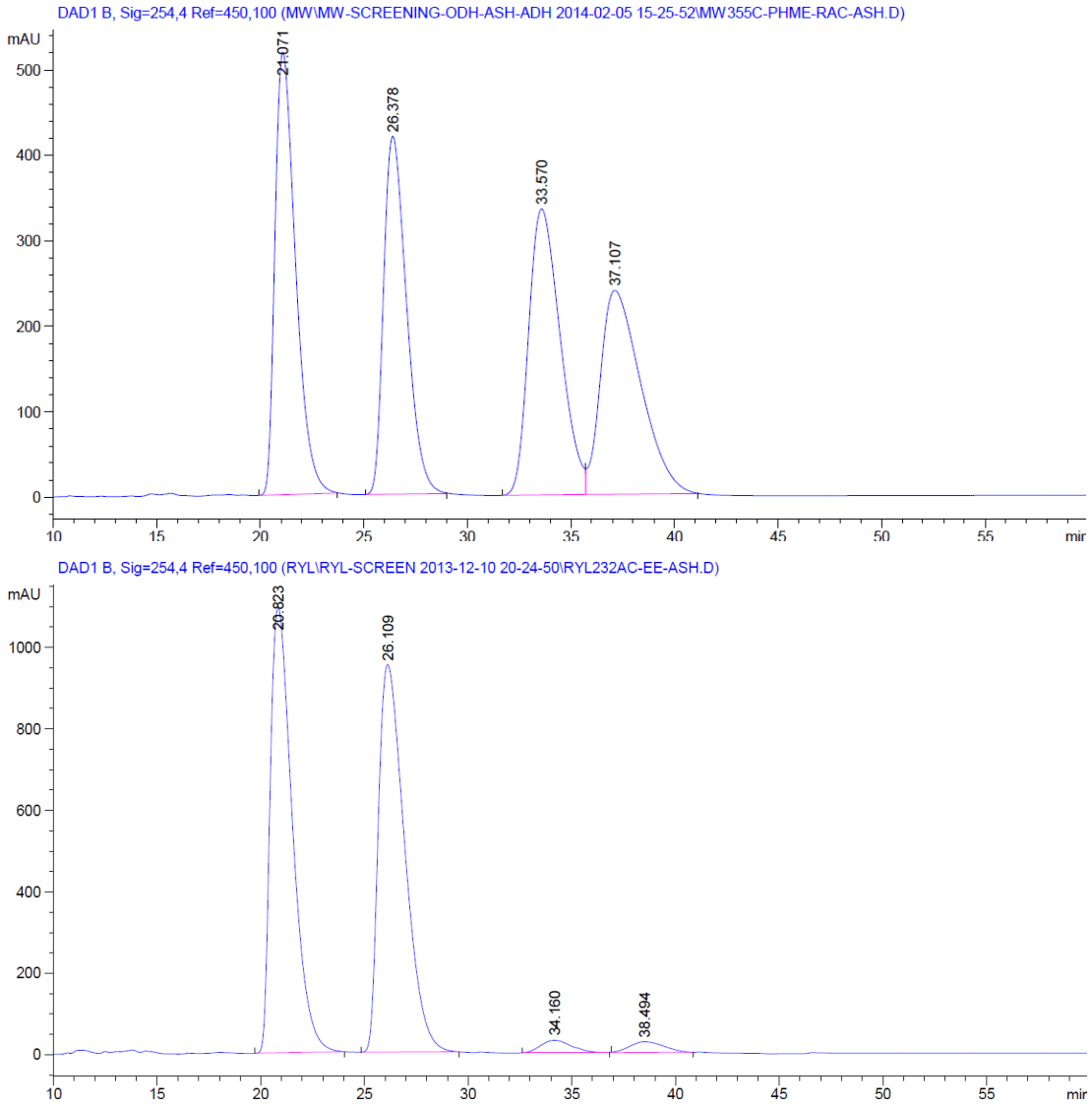


3b

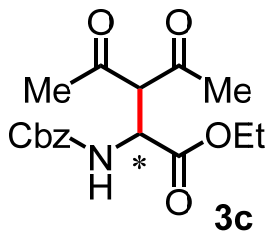
Ethyl 3-benzoyl-2-(((benzyloxy)carbonyl)amino)-4-oxopentanoate (3b)

Substrate **1-Cbz** was reacted with 1-phenylbutane-1,3-dione following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **3b** was obtained as a white solid (80.5 mg, 81%). $[\alpha]^{25}_{D}$ = 26.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.8 Hz, 2H), 7.61 (q, *J* = 7.8 Hz, 1H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.34-7.27 (m, 5H), 6.13 (d, *J* = 9.0 Hz), 5.91 (d, *J* = 9.0 Hz), 5.35 (d, *J* = 5.4 Hz), 5.33 (d, *J* = 4.8 Hz), 5.15-5.00 (m, 3H), 4.19-4.09 (m, 2H), 2.31 (s), 2.21 (s), 1.19 (t, *J* = 6.6 Hz), 1.14 (t, *J* = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.37, 202.66, 196.43, 195.08, 170.17, 169.93, 156.69, 156.36, 136.43, 136.34, 136.03, 137.31, 134.15, 129.26, 129.18, 128.83, 128.74, 128.70, 128.39, 128.34, 128.08, 67.40, 67.28, 62.45, 53.92, 53.73, 30.29, 29.74, 14.17, 14.10; IR (neat) ν 3382, 2988, 2934, 1723, 1679, 1697, 1501, 1449, 1280, 1261, 1215, 1027, 760, 696 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{22}H_{23}NO_6$ (MH^+): 398.1598; found: 398.1586.

HPLC (ChiralPak AS-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	20.82	81150.8	47.40
2	26.11	83670.4	48.88
3	34.16	3233.73	1.889
4	38.49	3140.31	1.834

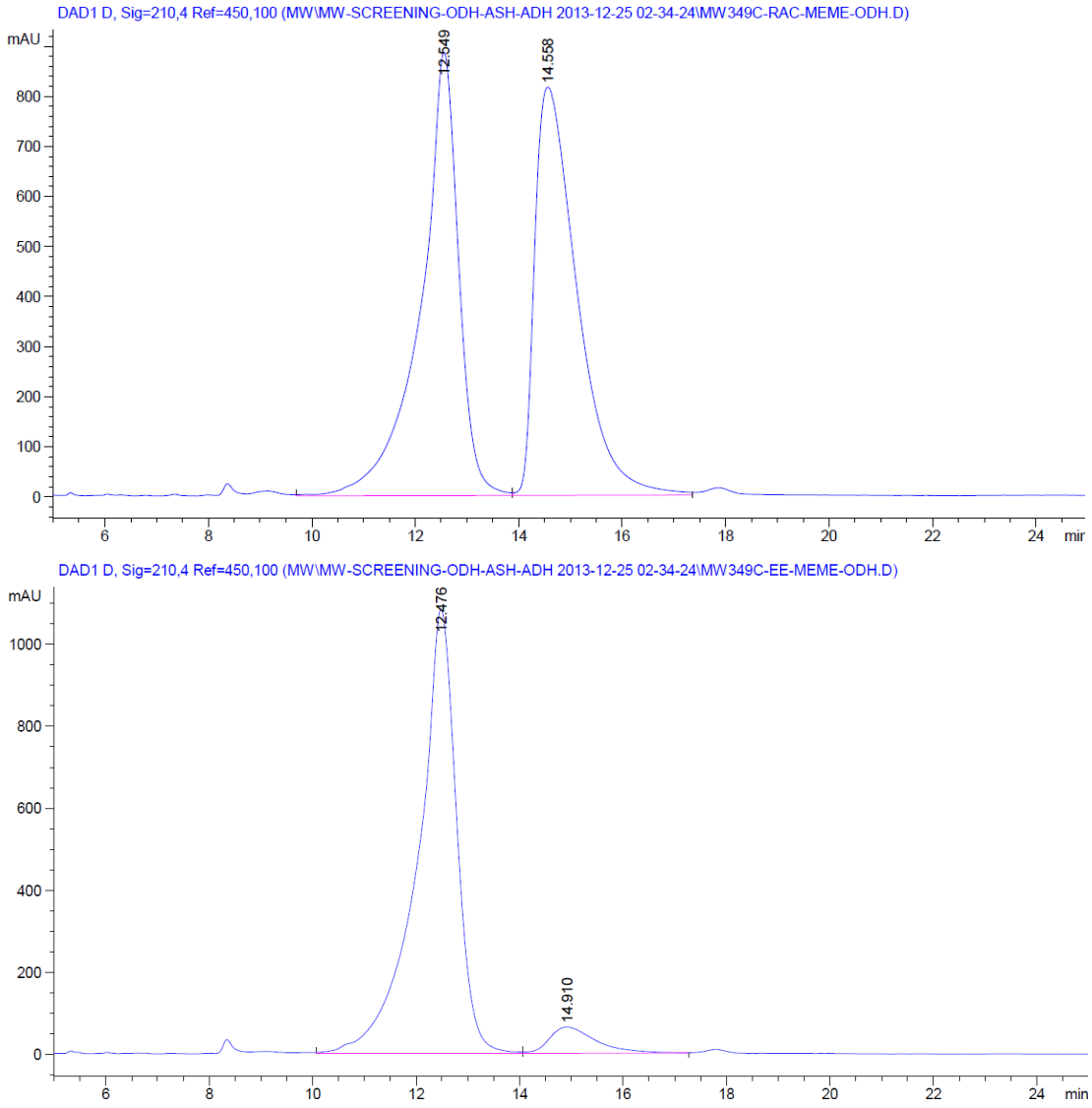


3c

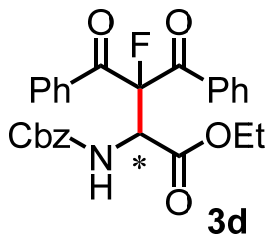
Ethyl 3-acetyl-2-(((benzyloxy)carbonyl)amino)-4-oxopentanoate (3c)

Substrate **1-Cbz** was reacted with pentane-2,4-dione following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **3c** was obtained as a white solid (33.5 mg, 40%). $[\alpha]^{25}_{D}$ = 21.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.31 (m, 5H), 5.83 (d, J = 9.6 Hz, 1H), 5.15 (dd, J_1 = 12.6 Hz, J_2 = 28.2 Hz, 3H), 5.00-4.97 (m, 1H), 4.44 (d, J = 4.2 Hz, 1H), 4.19 (q, J = 7.2 Hz, 2H), 2.32 (s, 3H), 2.23 (s, 3H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 204.34, 203.20, 170.00, 156.70, 136.24, 128.85, 128.76, 128.54, 128.45, 128.13, 67.52, 67. 25, 62.57, 53.00, 30.44, 30.27, 14.17; IR (neat) ν 3376, 2925, 1721, 1518, 1366, 1341, 1215, 1156, 1052, 756, 699 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{17}H_{21}NO_6$ (MH^+): 336.1442; found: 336.1430.

HPLC (ChiralPak OD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 210 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	12.48	57052.4	93.16
2	14.91	4189.64	6.841

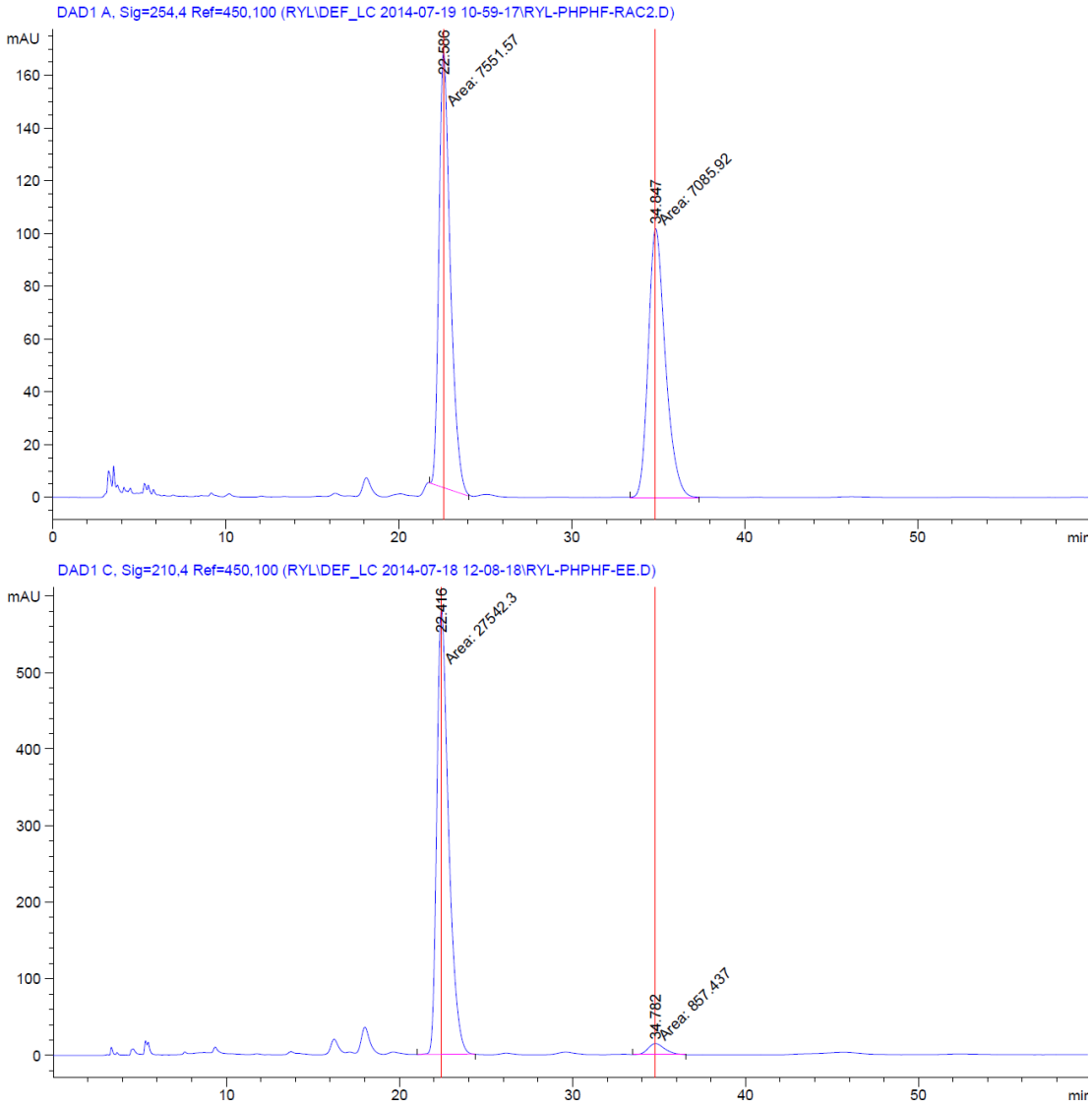


3d

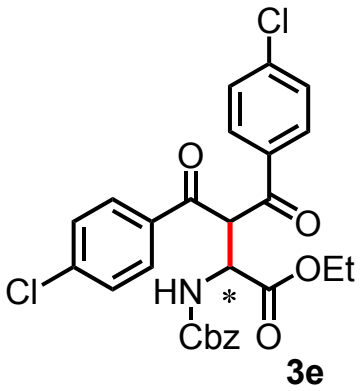
Ethyl 3-benzoyl-2-(((benzyloxy)carbonyl)amino)-3-fluoro-4-oxo-4-phenylbutanoate (3d)

Substrate **1-Cbz** was reacted with 2-fluoro-1,3-diphenylpropane-1,3-dione following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **3d** was obtained as a white solid (110.9 mg, 93%). $[\alpha]^{25}_{D}$ = -28.6° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.8 Hz), 8.03 (d, *J* = 7.8 Hz), 7.59 (t, *J* = 7.8 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 4H), 7.33-7.27 (m, 5H), 5.86-5.77 (m, 2H), 5.11 (q, *J* = 12.6 Hz, 2H), 4.16-4.12 (m, 2H), 1.12 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.69, 187.49, 187.31, 187.12, 162.87, 151.59, 125.49, 125.22, 125.19, 124.40, 124.36, 124.27, 124.15, 124.00, 123.82, 123.68, 123.61, 123.43, 62.94, 57.98, 53.72, 53.54, 9.34, 9.10; IR (neat) ν 3369, 3065, 2987, 2940, 1735, 1597, 1513, 1448, 1308, 1239, 1073, 1045, 1027, 757, 695 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{27}H_{24}FNO_6$ (MH^+): 478.1660; found: 478.1640.

HPLC (ChiralPak AD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	22.42	27542.3	96.98
2	34.78	857.437	3.02

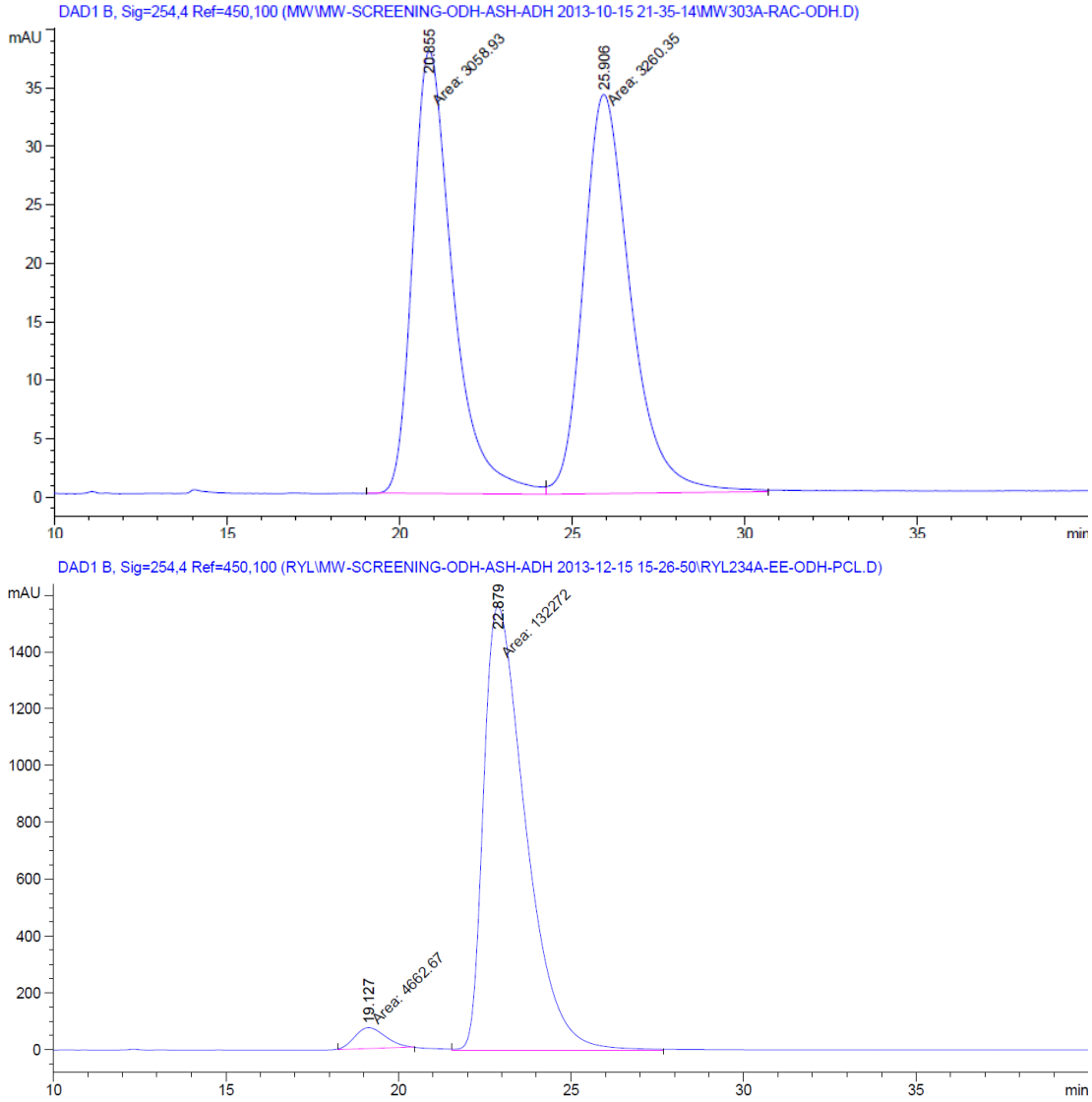


3e

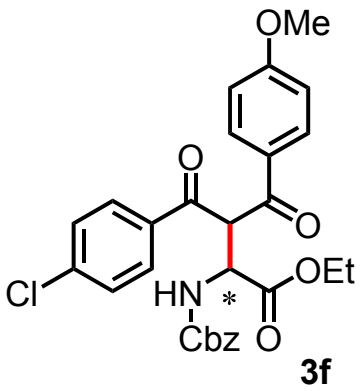
Ethyl 3-benzoyl-2-(((benzyloxy)carbonyl)amino)-3-fluoro-4-oxo-4-phenylbutanoate (3e)

Substrate **1-Cbz** was reacted with 1,3-bis(4-chlorophenyl)propane-1,3-dione following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **3e** was obtained as a white solid (110.7 mg, 84%). $[\alpha]^{25}_{D}$ = 4.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 9.0 Hz, 2H), 7.46-7.42 (m, 4H), 7.32-7.26 (m, 5H), 6.07 (d, *J* = 4.8 Hz), 6.05 (d, *J* = 8.4 Hz), 5.10-5.02 (m, 3H), 4.22-4.16 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.47, 193.44, 169.72, 140.91, 140.74, 136.22, 134.09, 130.15, 130.09, 129.69, 129.60, 128.72, 128.40, 128.06, 67.40, 62.70, 57.75, 54.18, 14.13; IR (neat) ν 3337, 2934, 1713, 1695, 1589, 1499, 1401, 1266, 1216, 1093, 1062, 1012, 840, 752, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{27}H_{23}Cl_2NO_6$ (MH^+): 528.0961; found: 528.0946.

HPLC (ChiralPak OD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	19.13	4662.67	3.405
2	22.88	132272	96.60

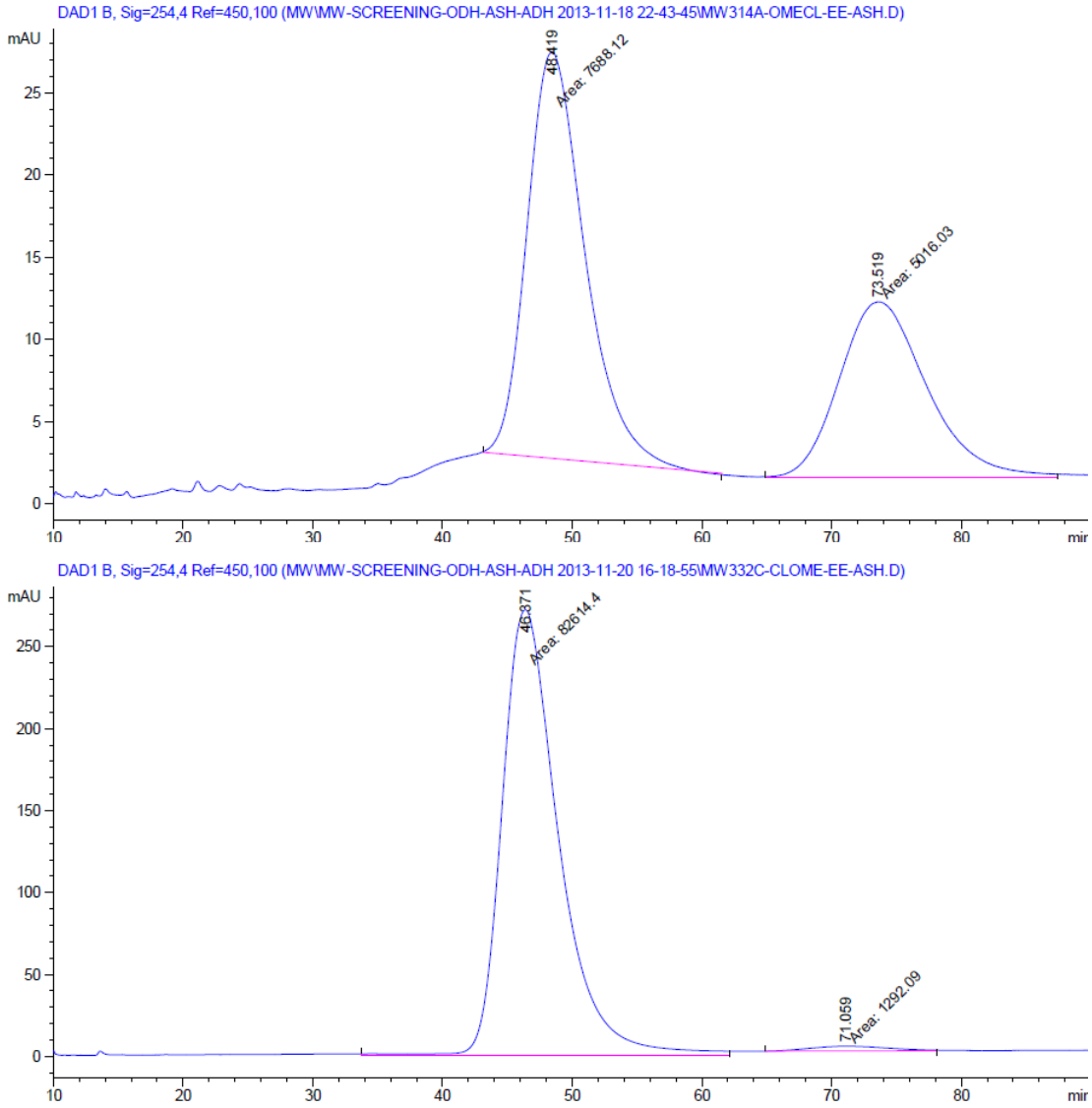


3f

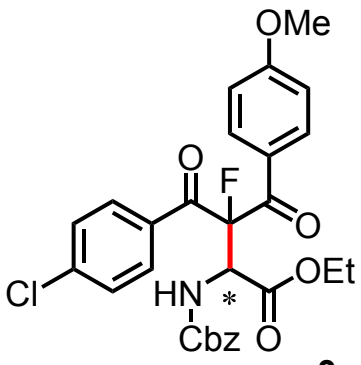
Ethyl 2-(((benzyloxy)carbonyl)amino)-3-(4-chlorobenzoyl)-4-(4-methoxyphenyl)-4-oxobutanoate (3f)

Substrate **1-Cbz** was reacted with 1-(4-chlorophenyl)-3-(4-methoxyphenyl)propane-1,3-dione following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **3f** was obtained as a colorless solid (111.2 mg, 85%). $[\alpha]^{25}_{D}$ = 5.0° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95-7.87 (m, 4H), 7.45-7.40 (m, 2H), 7.33-7.26 (m, 5H), 6.97 (d, *J* = 9.0 Hz), 6.93 (d, *J* = 8.4 Hz), 6.05-6.03 (m, 2H), 5.10-5.00 (m, 3H), 4.22-4.15 (m, 2H), 3.88 (s), 3.85 (s), 1.20 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.41, 169.54, 64.85, 45.24, 36.25, 17.64, 15.01, 14.95, 8.87; IR (neat) ν 3336, 2925, 1699, 1571, 1499, 1411, 1217, 1094, 1026, 1012, 892, 751, 696 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{28}H_{26}ClNO_7$ (MH^+): 524.1476; found: 524.1461.

HPLC (ChiralPak AS-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	46.37	82614.4	98.46
2	71.06	1292.09	1.540

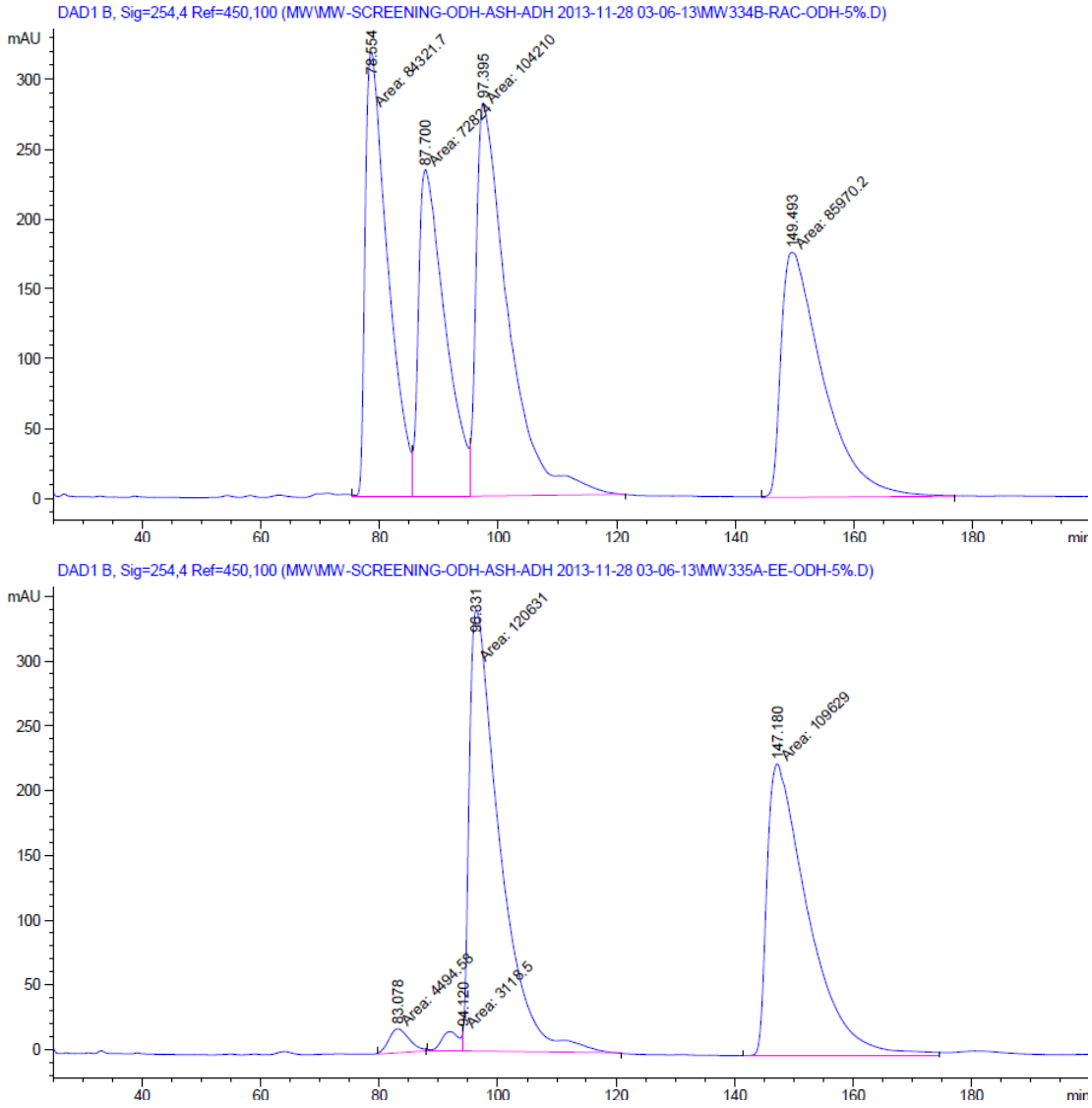


3g

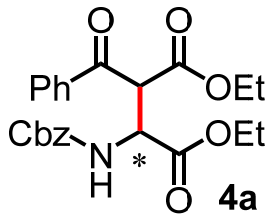
Ethyl 2-(((benzyloxy)carbonyl)amino)-3-(4-chlorobenzoyl)-3-fluoro-4-(4-methoxyphenyl)-4-oxobutanoate (3g)

Substrate **1-Cbz** was reacted with 1-(4-chlorophenyl)-2-fluoro-3-(4-methoxyphenyl)propane-1,3-dione following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **3g** was obtained as a colorless solid (90.6 mg, 67%). $[\alpha]^{25}_{D}$ = 32.2° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01-7.93 (m, 4H), 7.42-7.26 (m, 7H), 6.94-6.92 (m, 2H), 5.74-5.62 (m, 2H), 5.09-5.04 (m, 2H), 4.17-4.12 (m, 2H), 3.87 (s, 3H), 1.14-1.11 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 191.53-190.97 (m), 190.29-189.72 (m), 167.63, 167.48, 164.68, 156.31, 156.24, 140.94, 140.85, 136.08, 132.82, 132.12, 131.62, 131.52, 129.35, 128.57, 128.19, 126.48, 126.45, 114.37, 114.27, 67.71, 62.72, 62.69, 58.40, 58.26, 58.21, 58.06, 55.80, 13.98; IR (neat) ν 3349, 2935, 1733, 1599, 1511, 1370, 1312, 1177, 1094, 1027, 843, 755, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{28}H_{25}ClFNO_7$ (MH^+): 542.1376; found: 524.1349.

HPLC (ChiralPak OD-H, 5% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	83.08	4494.58	1.890
2	94.12	3118.50	1.311
3	96.33	120631	50.71
4	147.2	109629	46.09

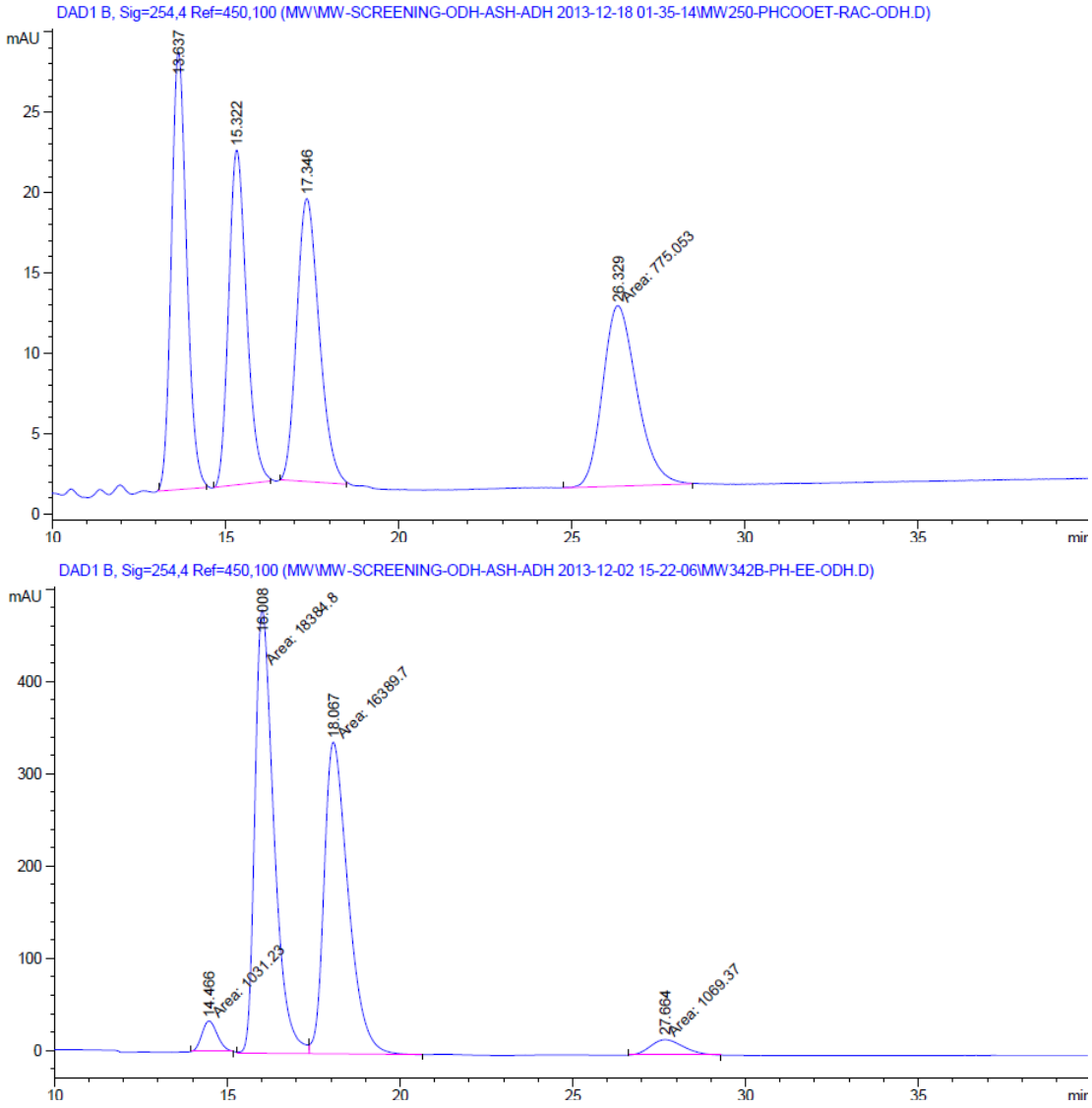


4a

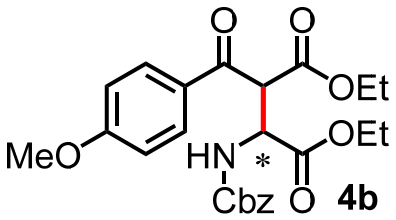
Diethyl 2-benzoyl-3-(((benzyloxy)carbonyl)amino)succinate (4a)

Substrate **1-Cbz** was reacted with ethyl 3-oxo-3-phenylpropanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4a** was obtained as a colorless liquid (85.4 mg, 80%), a mixture of diastereomers (ratio = 1.0 : 0.84). $[\alpha]^{25}_{D}$ = 14.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.8 Hz, major diastereomer), 7.94 (d, *J* = 7.4 Hz, minor diastereomer), 7.60 (td, J_1 = 7.4 Hz, J_2 = 1.2 Hz) 7.49 (q, *J* = 7.9 Hz), 7.35-7.27 (m), 6.15 (d, *J* = 8.4 Hz, major diastereomer), 5.93 (d, *J* = 8.5 Hz, minor diastereomer), 5.20-5.03 (m, 4H), 4.22-4.10 (m, 4H), 1.23-1.13 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.89, 193.47, 170.00, 169.85, 168.34, 167.85, 156.51, 156.22, 136.49, 16.42, 136.14, 135.98, 129.08, 129.07, 128.95, 128.83, 128.71, 128.69, 128.44, 128.34, 128.18, 128.15, 67.31, 67.29, 62.42, 62.40, 62.28, 62.13, 55.65, 55.29, 53.88, 53.77, 29.93, 14.18, 14.16, 14.14, 14.07; IR (neat) ν 3359, 2985, 1713, 1687, 1597, 1503, 1449, 1370, 1269, 1216, 1026, 858, 756, 697 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{23}H_{25}NO_7$ (MH^+): 428.1704; found: 428.1694.

HPLC (ChiralPak OD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	14.47	1031.23	2.797
2	16.01	18384.8	49.86
3	18.07	16389.7	44.45
4	27.66	1069.37	2.900

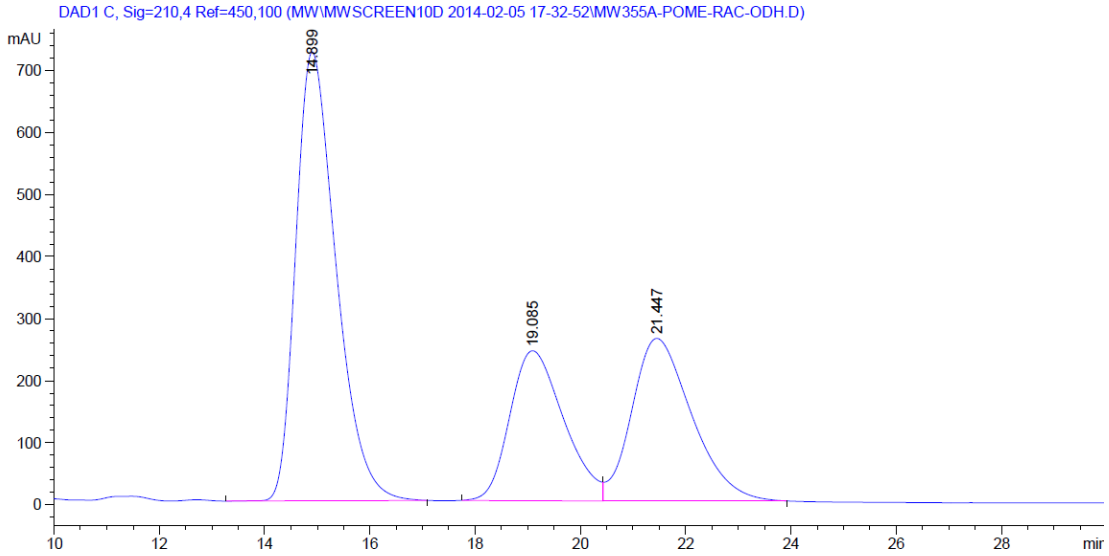


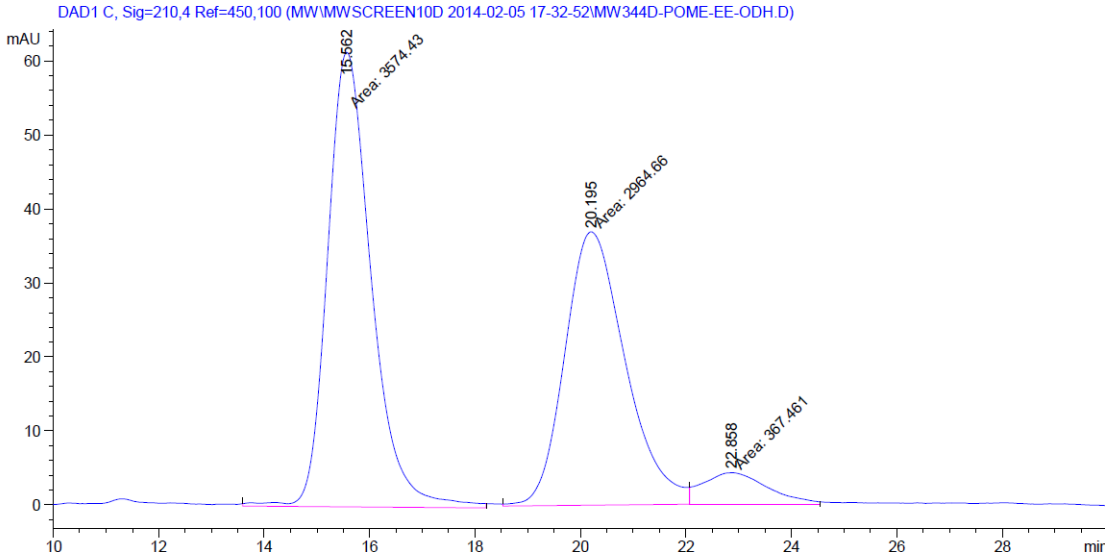
4b

Diethyl 2-(((benzyloxy)carbonyl)amino)-3-(4-methoxybenzoyl)succinate (4b)

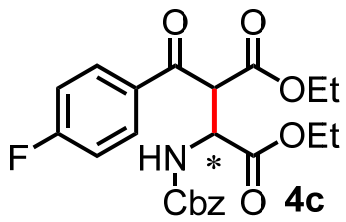
Substrate **1-Cbz** was reacted with ethyl 3-(4-methoxyphenyl)-3-oxopropanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4b** was obtained as a colorless liquid (48.0 mg, 42%), a mixture of diastereomers (ratio = 1 : 0.75). $[\alpha]^{25}_{D}$ = 14.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.93 (d, *J* = 9.0 Hz, major diastereomer), 7.91 (d, *J* = 9.0 Hz, minor diastereomer), 7.34-7.26 (m), 6.93 (d, *J* = 9.0 Hz, major diastereomer), 6.92 (d, *J* = 8.9 Hz, minor diastereomer), 6.19 (d, *J* = 8.6 Hz, major diastereomer), 5.94 (d, *J* = 8.4 Hz, minor diastereomer), 5.14-5.02 (m, 4H), 4.20-4.09 (m, 4H), 3.83 (s, 3H), 1.19-1.14 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.69, 191.29, 169.70, 169.55, 168.14, 167.61, 163.99, 163.94, 156.11, 155.84, 136.12, 136.04, 130.83, 130.74, 128.70, 128.25, 127.87, 127.70, 127.68, 113.87, 66.81, 61.92, 61.88, 61.78, 61.24, 55.34, 54.76, 54.61, 53.54, 53.43, 29.50, 13.76, 13.71, 13.68; HRMS (ESI-TOF) Calcd for $C_{24}H_{27}NO_8$ (MH^+): 458.1809; found: 458.1800.

HPLC (ChiralPak OD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 210 nm)





Peak	Retention time (min)	Area (mAU*s)	Area %
1	15.56	3574.43	51.76
2	20.20	2964.66	42.93
3	22.86	367.461	5.321

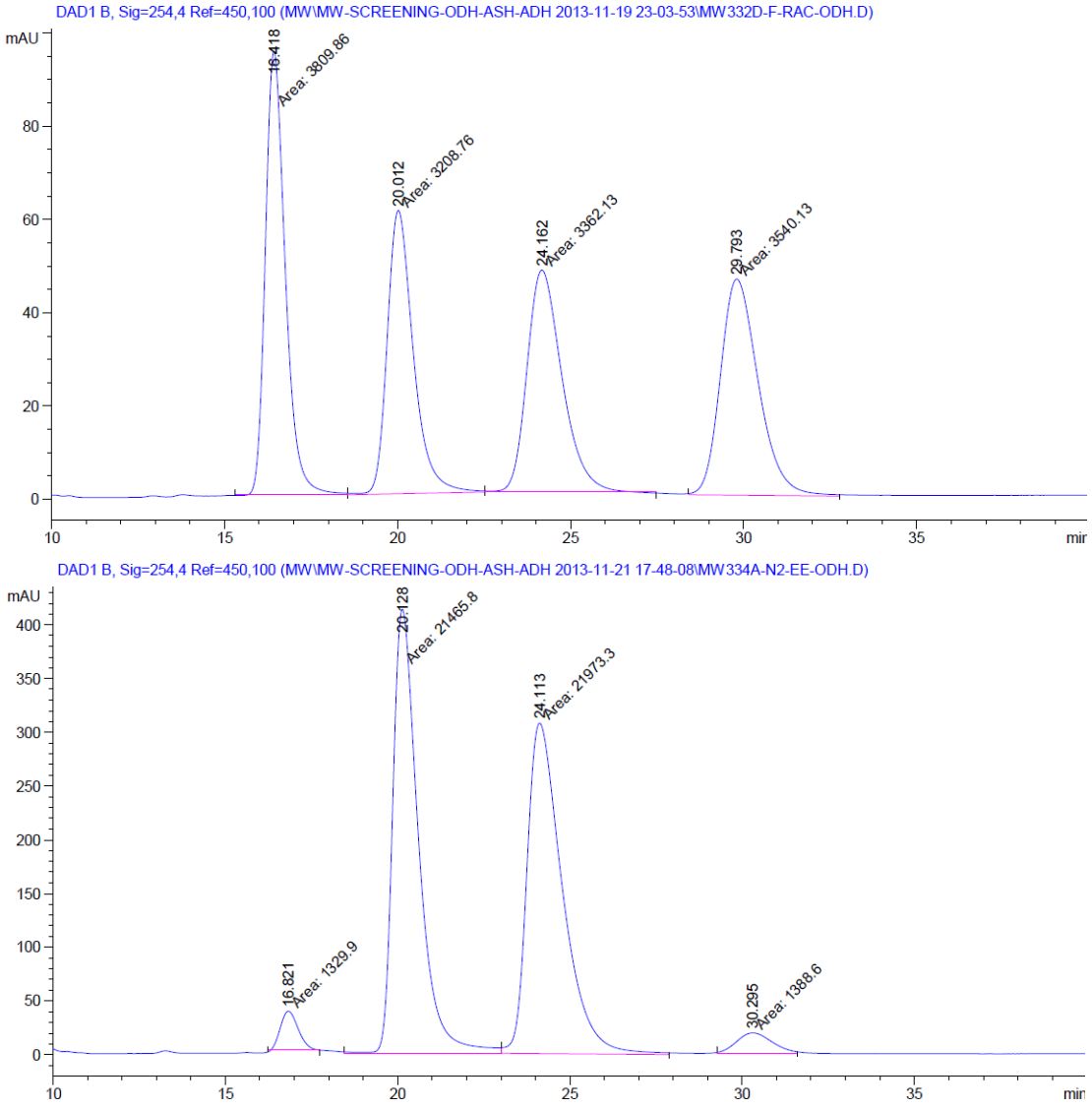


4c

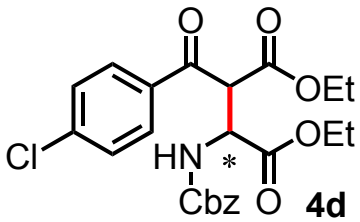
Diethyl 2-(((benzyloxy)carbonyl)amino)-3-(4-fluorobenzoyl)succinate (4c)

Substrate **1-Cbz** was reacted with ethyl 3-(4-fluorophenyl)-3-oxopropanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4c** was obtained as a colorless liquid (90.1 mg, 81%), a mixture of diastereomers (ratio = 1.0 : 0.74). $[\alpha]^{25}_{D}$ = 15.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (dd, J_1 = 9.0 Hz, J_2 = 5.4 Hz, major diastereomer), 7.95 (dd, J_1 = 9.0 Hz, J_2 = 5.4 Hz, minor diastereomer), 7.34-7.27 (m), 7.13 (q, J = 8.8 Hz), 6.12 (d, J = 8.5 Hz, major diastereomer), 5.91 (d, J = 8.5 Hz, minor diastereomer), 5.16-5.03 (m, 4H), 4.22-4.10 (m, 4H), 1.21-1.13 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.91, 191.52, 169.53, 169.41, 167.72, 167.32, 167.01, 166.97, 164.96, 156.10, 155.82, 136.05, 136.99, 132.21, 132.19, 132.11, 131.24, 131.16, 131.08, 128.31, 127.98, 127.79, 115.99, 115.94, 115.81, 115.77, 66.95, 62.07, 62.05, 71.97, 61.81, 55.20, 53.51, 53.41, 29.54, 13.77, 13.74, 13.69; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.74 (m, major diastereomer), -104.90 (m, minor diastereomer); IR (neat) ν 3356, 2982, 1735, 1687, 1599, 1508, 1370, 1269, 1234, 1159, 1026, 848, 755, 699 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{23}H_{24}FNO_7$ (MH^+): 446.1610; found: 446.1599.

HPLC (ChiralPak OD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	16.82	1329.90	2.881
2	20.13	21465.8	46.51
3	24.11	21973.3	47.61
4	30.30	1388.60	3.008

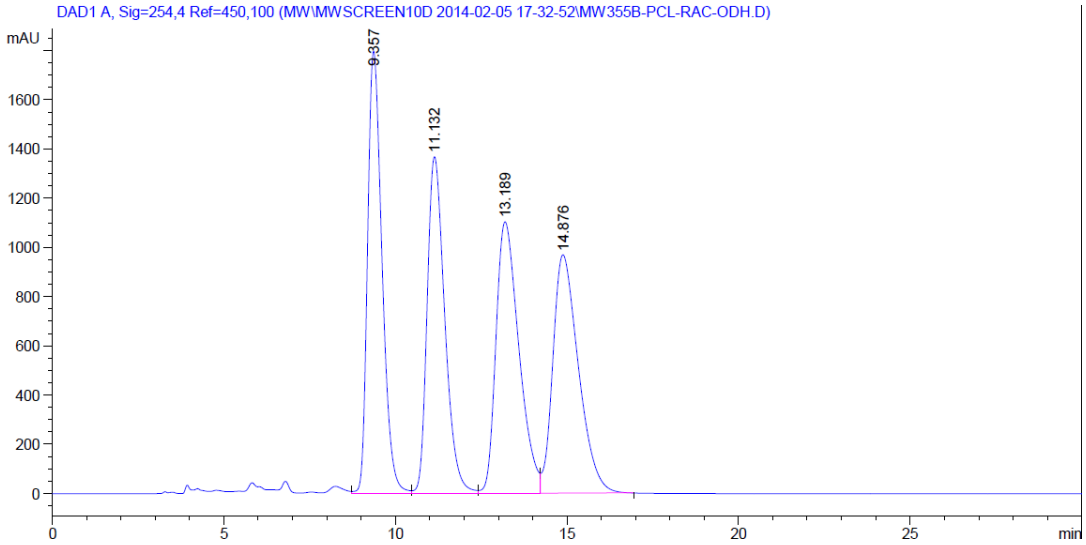


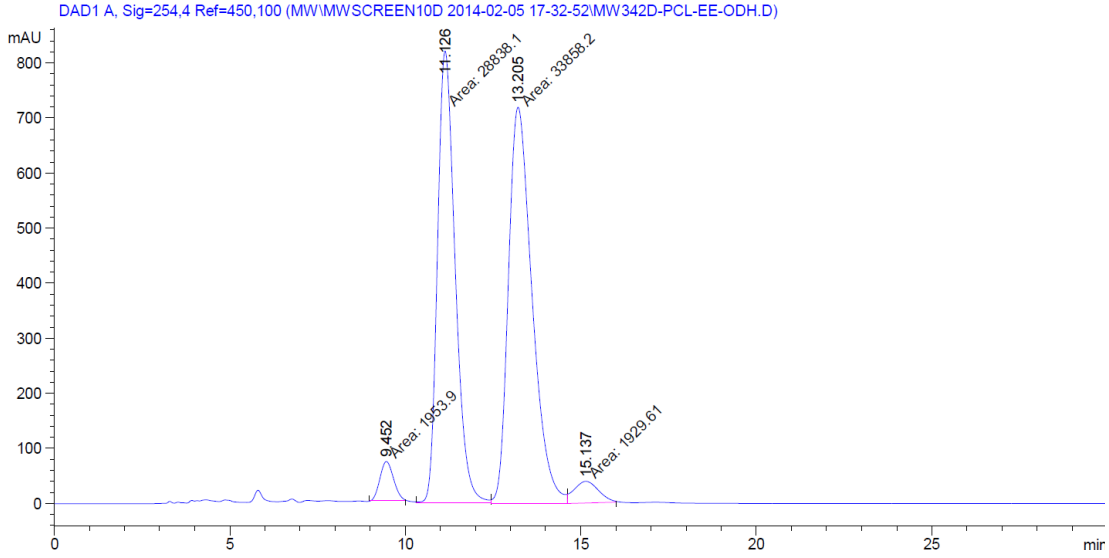
4d

Diethyl 2-(((benzyloxy)carbonyl)amino)-3-(4-chlorobenzoyl)succinate (4d)

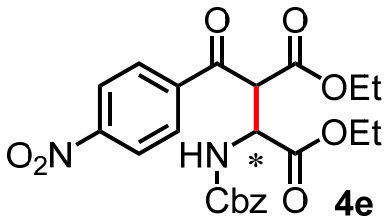
Substrate **1-Cbz** was reacted with ethyl 3-(4-chlorophenyl)-3-oxopropanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4d** was obtained as a colorless liquid (94.5 mg, 82%), a mixture of diastereomers (ratio = 1.0 : 0.96). $[\alpha]^{25}_{D}$ = 13.8° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.6 Hz, major diastereomer), 7.86 (d, *J* = 8.5 Hz, minor diastereomer), 7.43 (d, *J* = 8.6 Hz, major diastereomer), 7.42 (d, *J* = 8.7 Hz, minor diastereomer), 7.34-7.28 (m), 6.12 (d, *J* = 8.5 Hz, major diastereomer), 5.91 (d, *J* = 8.5 Hz, minor diastereomer), 5.16-5.03 (m, 4H), 4.20-4.10 (m, 4H), 1.22-1.14 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.73, 192.34, 169.87, 169.75, 168.00, 167.64, 156.47, 156.20, 140.65, 140.57, 136.42, 136.46, 134.49, 134.42, 130,24. 130.15, 129.43, 129.38, 128.46, 128.38, 67.35, 62.47, 62.39, 62.23, 55.64, 55.25, 53.87, 53.80, 29.93, 14.16, 14.14, 14.08; IR (neat) ν 3358, 2981, 1735, 1687, 1589, 1504, 1401, 1370, 1269, 1216, 1093, 1026, 844, 755, 699 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{23}H_{24}ClNO_7$ (MH^+): 462.1314; found: 462.1305.

HPLC (ChiralPak OD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)





Peak	Retention time (min)	Area (mAU*s)	Area %
1	9.45	1953.90	2.935
2	11.13	28838.1	43.31
3	13.21	33858.2	50.86
4	15.14	1929.61	2.898

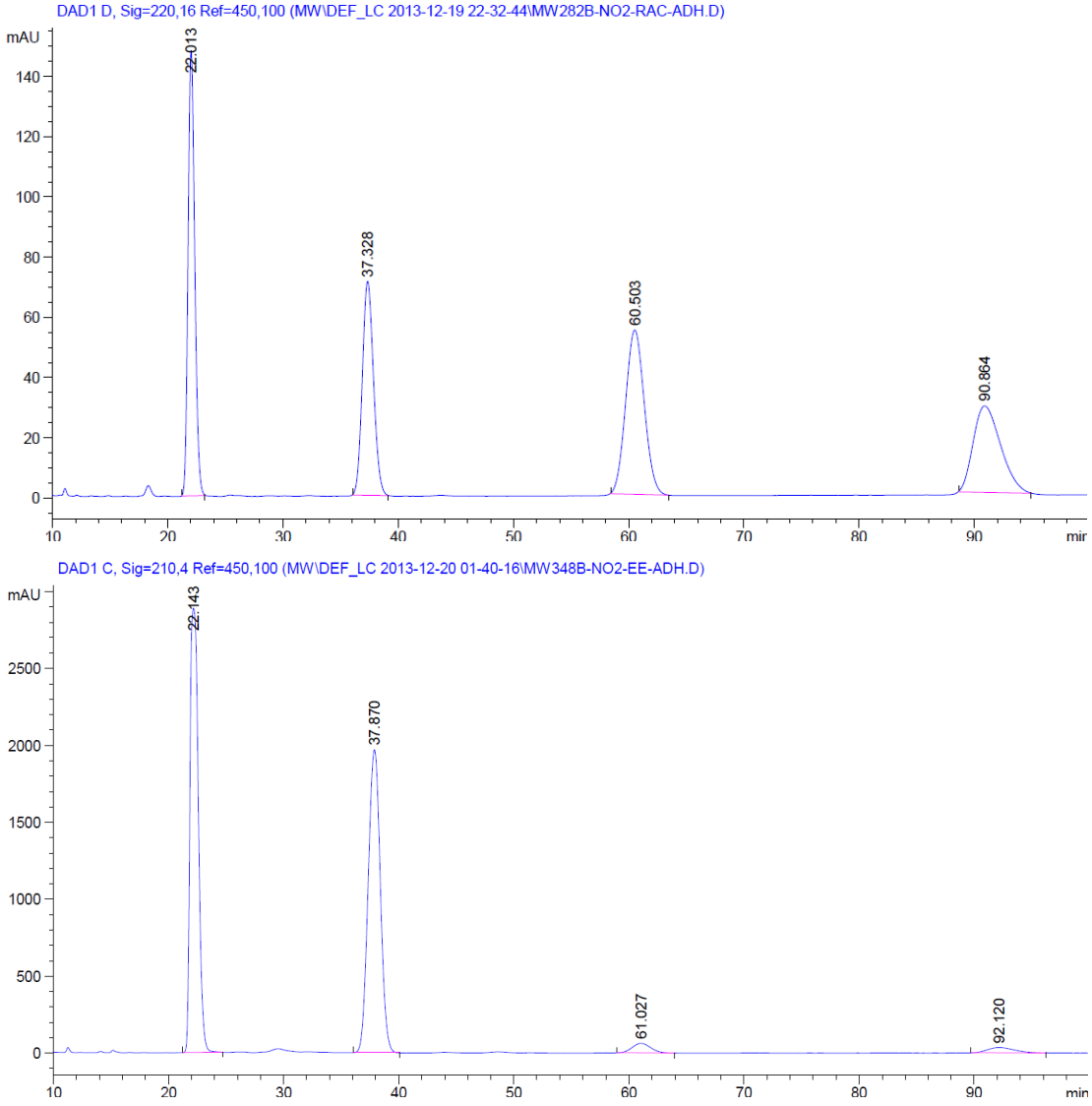


4e

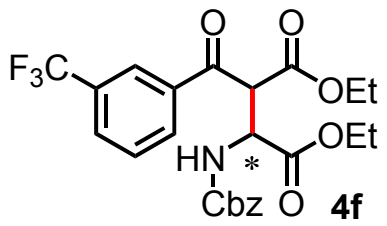
Diethyl 2-(((benzyloxy)carbonyl)amino)-3-(4-nitrobenzoyl)succinate (4e)

Substrate **1-Cbz** was reacted with ethyl 3-(4-nitrophenyl)-3-oxopropanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4e** was obtained as a colorless liquid (85.0 mg, 72%), a mixture of diastereomers (ratio = 1.0 : 0.87). $[\alpha]^{25}_{D}$ = 9.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.29 (d, *J* = 9.0 Hz, major diastereomer), 8.26 (d, *J* = 9.0 Hz, minor diastereomer), 8.12 (d, *J* = 8.6 Hz, major diastereomer), 8.05 (d, *J* = 8.9 Hz, minor diastereomer), 7.32-7.26 (m), 6.07 (d, *J* = 8.6 Hz, major diastereomer), 5.94 (d, *J* = 8.2 Hz, minor diastereomer), 5.21 (minor diastereomer, *J* = 5.4 Hz), 5.14-5.10 (m), 5.06-5.03 (m), 4.20-4.11 (m, 4H), 1.25-1.14 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.39, 192.04, 169.25, 169.14, 167.08, 166.89, 156.02, 155.76, 150.43, 150.33, 140.32, 140.23, 135.89, 135.86, 129.44, 129.37, 128.31, 128.12, 128.04, 127.81, 123.85, 123.76, 67.06, 67.03, 65.63, 62.22, 62.21, 55.82, 55.27, 53.45, 53.40, 29.50, 15.09, 13.75, 13.73; IR (neat) ν 3392, 2962, 2927, 1734, 1528, 1393, 1269, 1217, 1064, 1026, 853, 757, 699 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{23}H_{24}N_2O_9$ (MH^+): 473.1555; found: 473.1543.

HPLC (ChiralPak AD-H, 30% *i*-PrOH in hexanes, 1 mL/min, 220 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	22.14	145134	48.00
2	37.87	144333	47.74
3	61.03	7011.53	2.319
4	92.12	5839.56	1.932

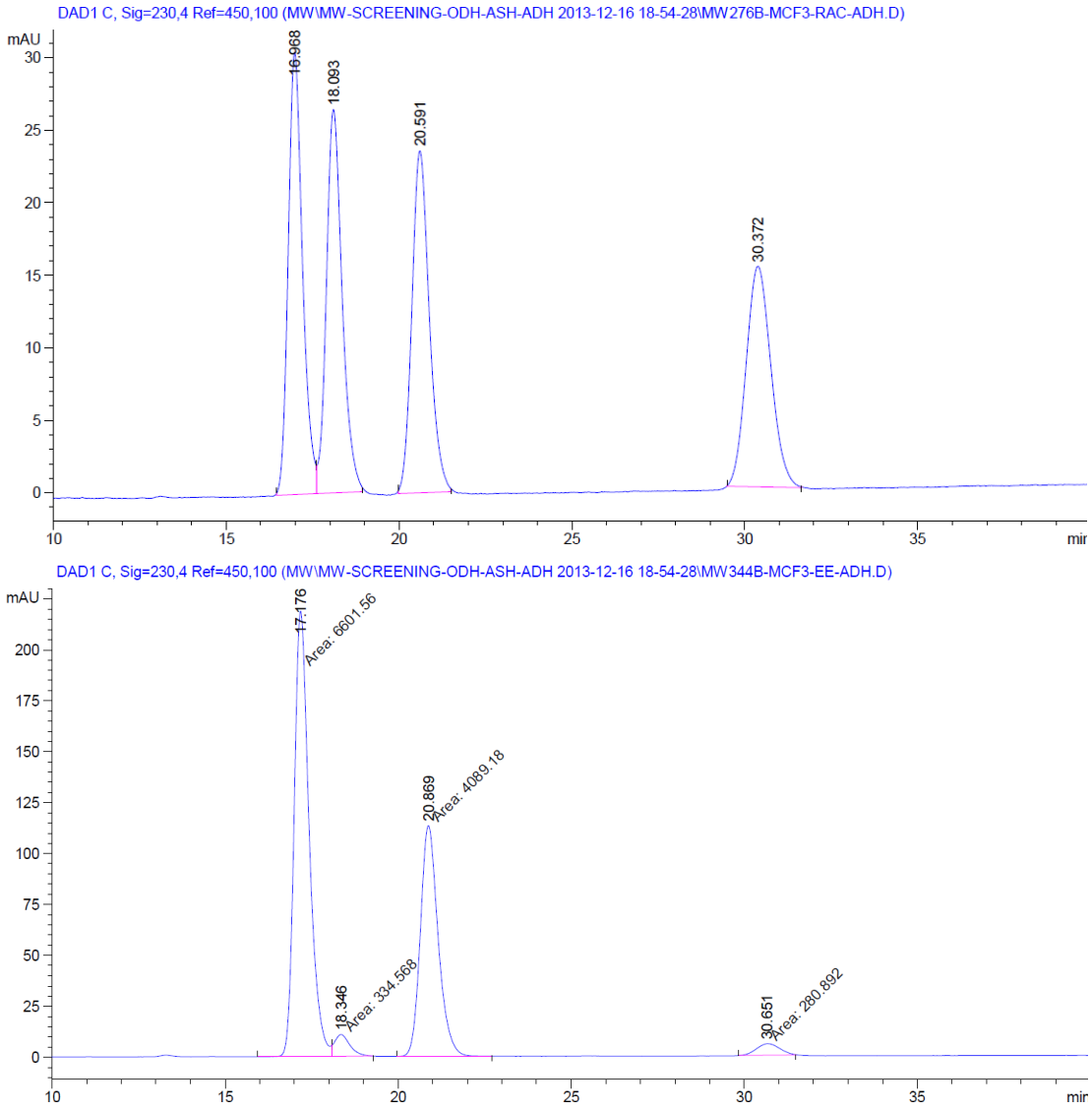


4f

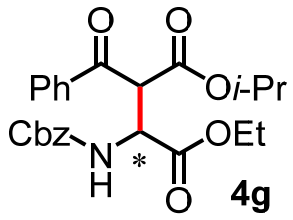
Diethyl 2-(((benzyloxy)carbonyl)amino)-3-(3-(trifluoromethyl)benzoyl)succinate (4f)

Substrate **1-Cbz** was reacted with ethyl 3-oxo-3-(3-(trifluoromethyl)phenyl)propanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4f** was obtained as a colorless liquid (79.4 mg, 72%), a mixture of diastereomers (ratio = 1.0 : 0.20). $[\alpha]^{25}_{D}$ = 14.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.21 (s), 8.16 (d, *J* = 8.6 Hz), 8.11 (d, *J* = 7.7 Hz), 7.84 (d, *J* = 7.6 Hz), 7.61 (t, *J* = 7.6 Hz), 7.34-7.27 (m), 6.11 (d, *J* = 9.0 Hz), 5.93 (d, *J* = 8.6 Hz), 5.20 (d, *J* = 5.4 Hz), 5.15 (d, *J* = 4.0 Hz), 5.14 (s), 5.09-5.03 (m, 2H), 4.24-4.12 (m, 4H), 1.27-1.15 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 193.44, 191.92, 169.39, 169.33, 169.31, 167.06, 156.08, 155.80, 136.32, 136.00, 135.90, 131.64, 131.40, 131.14, 129.97, 129.94, 129.43, 129.35, 128.31, 128.02, 127.80, 125.23, 125.20, 124.48, 122.31, 67.02, 62.15, 62.12, 61.97, 55.38, 55.00, 5.41, 29.53, 13.73, 13.68, 13.62; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.86 (s), -62.93 (s); IR (neat) ν 3359, 2984, 1736, 1612, 1506, 1370, 1332, 1217, 1170, 1073, 1026, 807, 755, 696 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{24}H_{24}F_3NO_7$ (MH^+): 496.1578; found: 496.1574.

HPLC (ChiralPak AD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



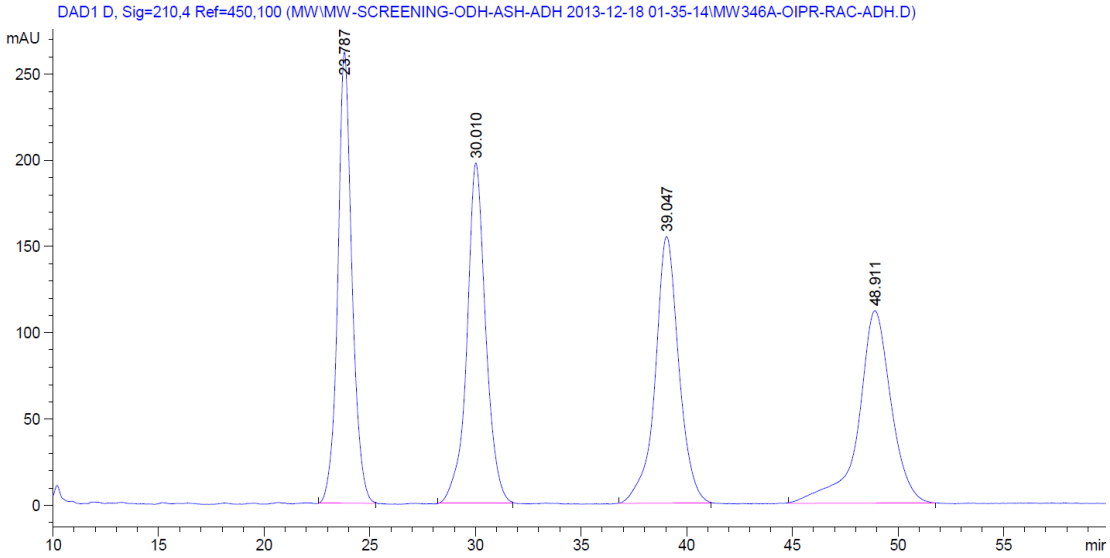
Peak	Retention time (min)	Area (mAU*s)	Area %
1	17.18	6601.56	58.39
2	18.35	334.568	2.959
3	20.87	4089.18	36.17
4	30.65	280.892	2.484

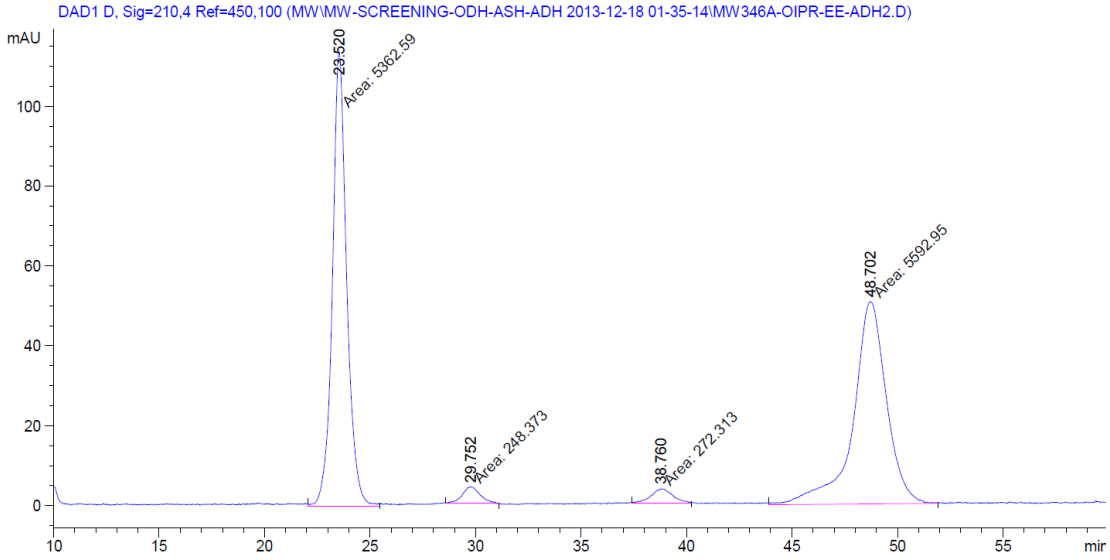


4-Ethyl 1-isopropyl 2-benzoyl-3-(((benzyloxy)carbonyl)amino)succinate (4g)

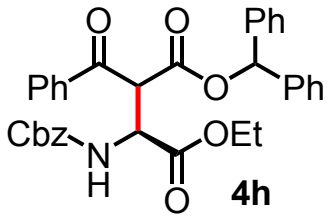
Substrate **1-Cbz** was reacted with isopropyl 3-oxo-3-phenylpropanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4g** was obtained as a colorless solid (79.4 mg, 72%), a mixture of diastereomers (ratio = 1.0 : 0.73). $[\alpha]^{25}_{D}$ = 20.0° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95-7.92 (m, 2H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.49-7.46 (m, 2H), 7.35-7.29 (m, 5H), 6.13 (d, *J* = 9.0 H, major diastereomer), 5.89 (d, *J* = 8.4 H, minor diastereomer), 5.15-4.97 (m, 5H), 4.23-4.11 (m, 2H), 1.23-1.06 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.07, 193.54, 170.04, 169.96, 167.87, 167.31, 156.51, 156.22, 136.42, 136.04, 134.02, 129.03, 128.69, 128.65, 128.43, 128.19, 128.14, 70.16, 70.01, 67.30, 62.36, 55.80, 55.51, 53.81, 53.69, 29.94, 21.43, 14.22, 14.15; IR (neat) ν 3350, 2963, 2927, 1732, 1686, 1503, 1450, 1270, 1215, 1104, 1064, 1027, 753, 696 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{24}H_{27}NO_7$ (MH^+): 442.1860; found: 442.1862.

HPLC (ChiralPak AD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 210 nm)





Peak	Retention time (min)	Area (mAU*s)	Area %
1	23.52	5362.59	46.73
2	29.75	248.373	2.164
3	38.76	272.313	2.373
4	48.70	280.892	48.74

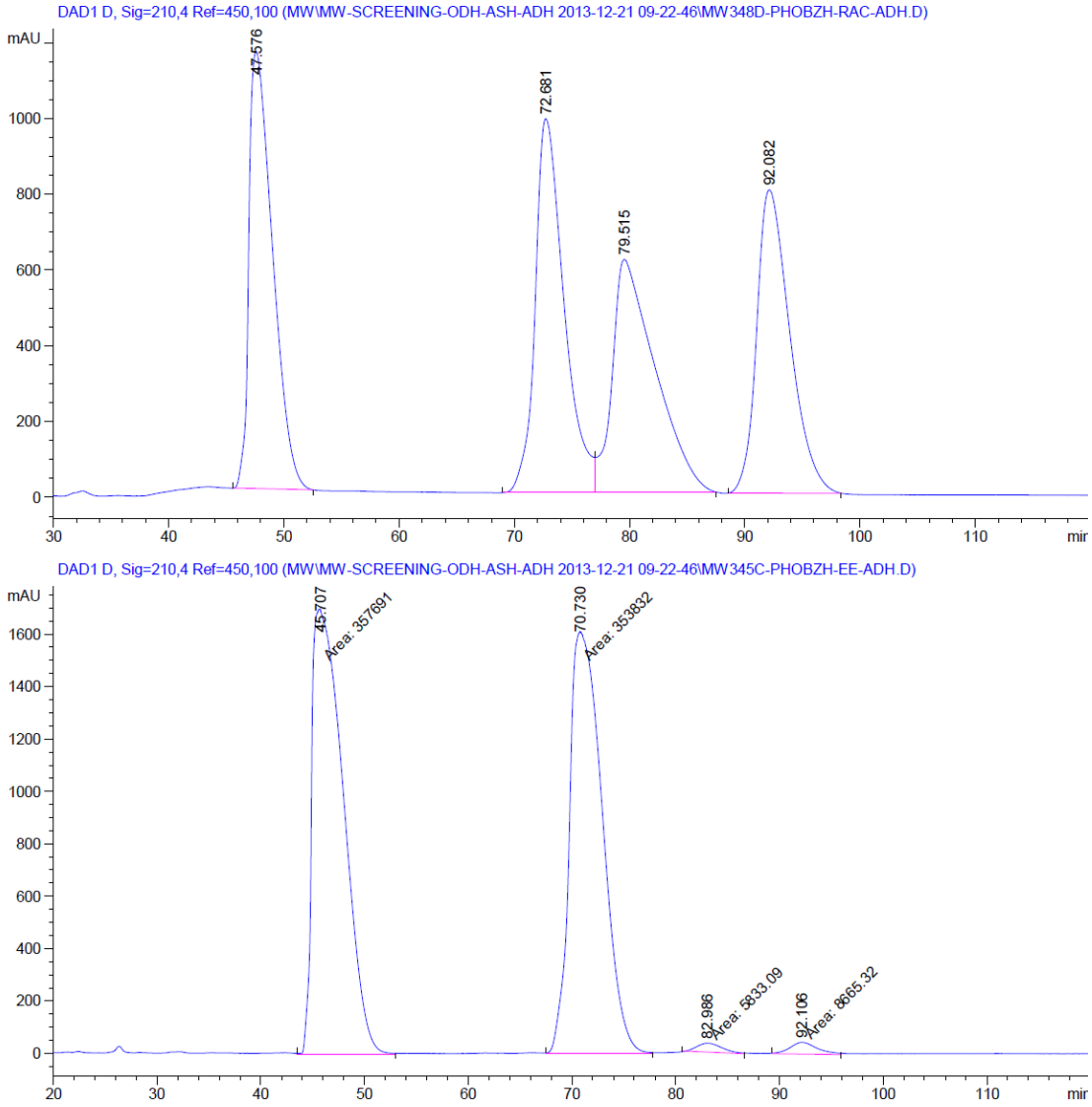


4h

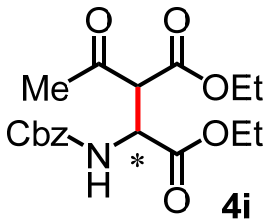
1-Benzhydryl 4-ethyl (3S)-2-benzoyl-3-(((benzyloxy)carbonyl)amino)succinate (4h)

Substrate **1-Cbz** was reacted with benzhydryl 3-oxo-3-phenylpropanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4h** was obtained as a colorless solid (124.3 mg, 88%), a mixture of diastereomers (ratio = 1.0 : 0.96). $[\alpha]^{25}_{D}$ = 13.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.2 Hz), 7.92 (d, *J* = 7.2 Hz), 7.61-7.57 (m, 1H), 7.46 (t, *J* = 7.8 Hz), 7.42 (t, *J* = 7.8 Hz), 7.37-7.10 (m), 6.93 (s), 6.87 (s), 6.07 (d, *J* = 9.0 Hz), 5.79 (d, *J* = 8.4 Hz), 5.35-4.93 (m, 5H), 4.15-4.03 (m, 2H), 1.16 (t, *J* = 7.2 Hz), 1.05 (t, *J* = 7.2 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 194.74, 193.19, 169.88, 169.85, 167.24, 166.80, 156.57, 156.19, 139.56, 139.47, 139.38, 139.33, 136.47, 136.15, 134.16, 134.10, 128.72, 128.37, 128.31, 128.22, 128.13, 127.27, 79.11, 78.81, 67.33, 67.31, 62.49, 62.46, 55.71, 55.50, 53.97, 53.86, 14.16, 14.02; IR (neat) ν 3428, 3032, 2739, 1737, 157, 1498, 1450, 1217, 1027, 758, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{34}H_{31}NO_7$ (MH^+): 566.2173; found: 566.2147.

HPLC (ChiralPak AD-H, 50% *i*-PrOH in hexanes, 0.5 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	45.71	357691	49.27
2	70.73	353832	48.74
3	82.99	5833.09	0.803
4	92.11	8665.32	1.194

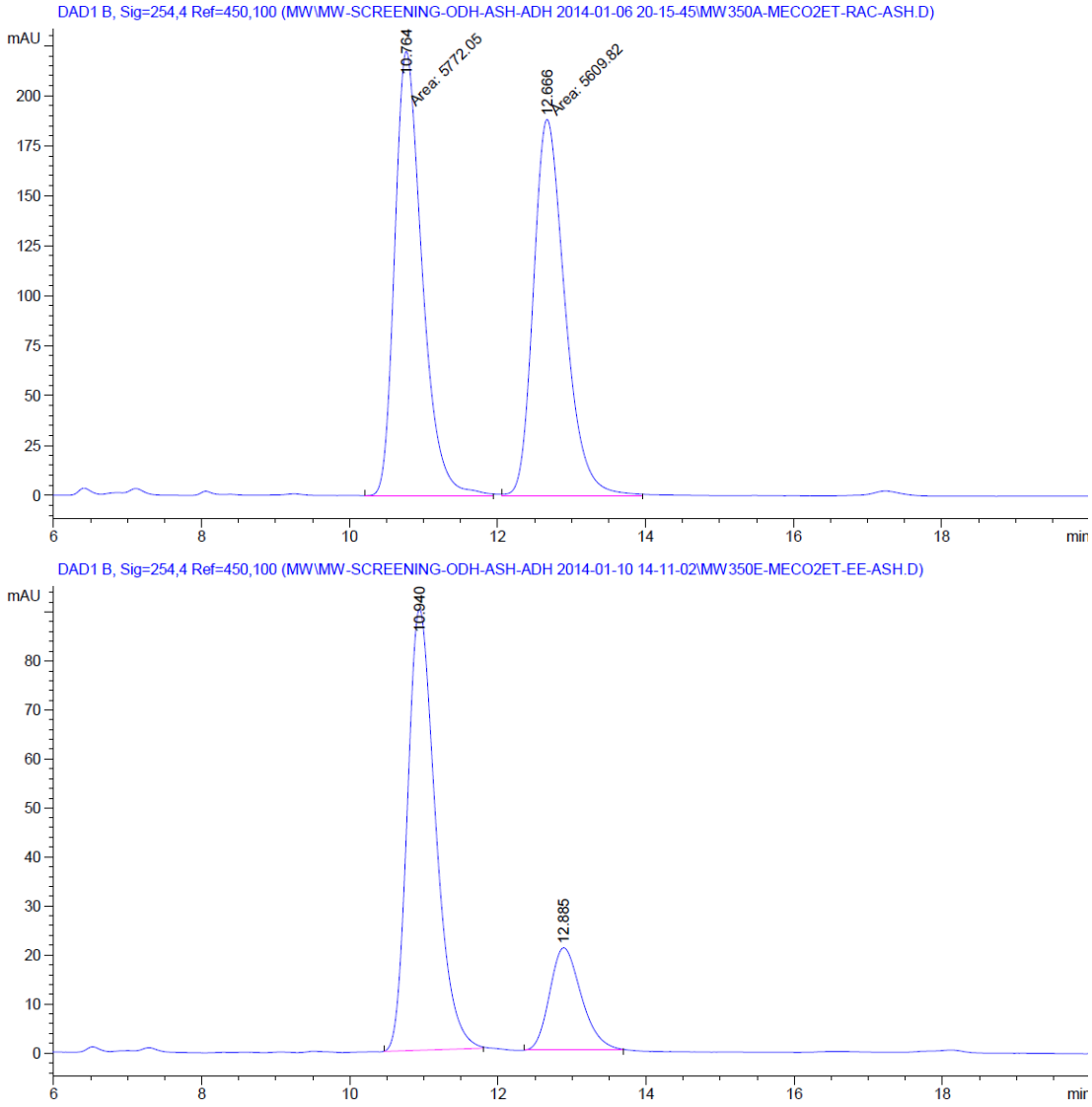


4i

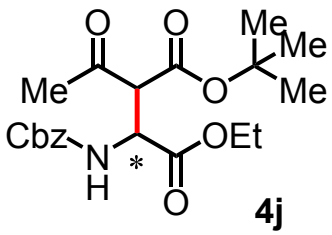
Diethyl 2-acetyl-3-(((benzyloxy)carbonyl)amino)succinate (4i)

Substrate **1-Cbz** was reacted with ethyl 3-oxobutanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4i** was obtained as a colorless liquid (29.2 mg, 32%), a mixture of diastereomers (ratio = 1.0 : 1.0). $[\alpha]^{25}_{D}$ = 14.8° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.29 (m, 5H), 5.85 (d, J = 8.4 Hz, 1H), 5.14-5.08 (m, 2H), 5.10-4.98 (m, 1H), 4.27-4.15 (m, 4H), 2.31 (s), 2.29 (s), 1.28-1.21 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.85, 201.38, 170.05, 169.87, 168.26, 167.71, 156.44, 156.39, 136.45, 136.30, 128.80, 128.75, 128.71, 128.48, 128.43, 128.38, 128.21, 67.46, 67.34, 60.03, 53.43, 53.00, 30.11, 30.02, 29.93, 14.23, 14.19, 14.14; IR (neat) ν 3370, 2927, 1722, 1504, 1215, 1027, 860, 754, 699 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{18}H_{13}NO_7$ (MH^+): 366.1563; found: 366.1552.

HPLC (ChiralPak AS-H, 5% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	10.94	2373.77	79.17
2	12.89	624.460	20.83

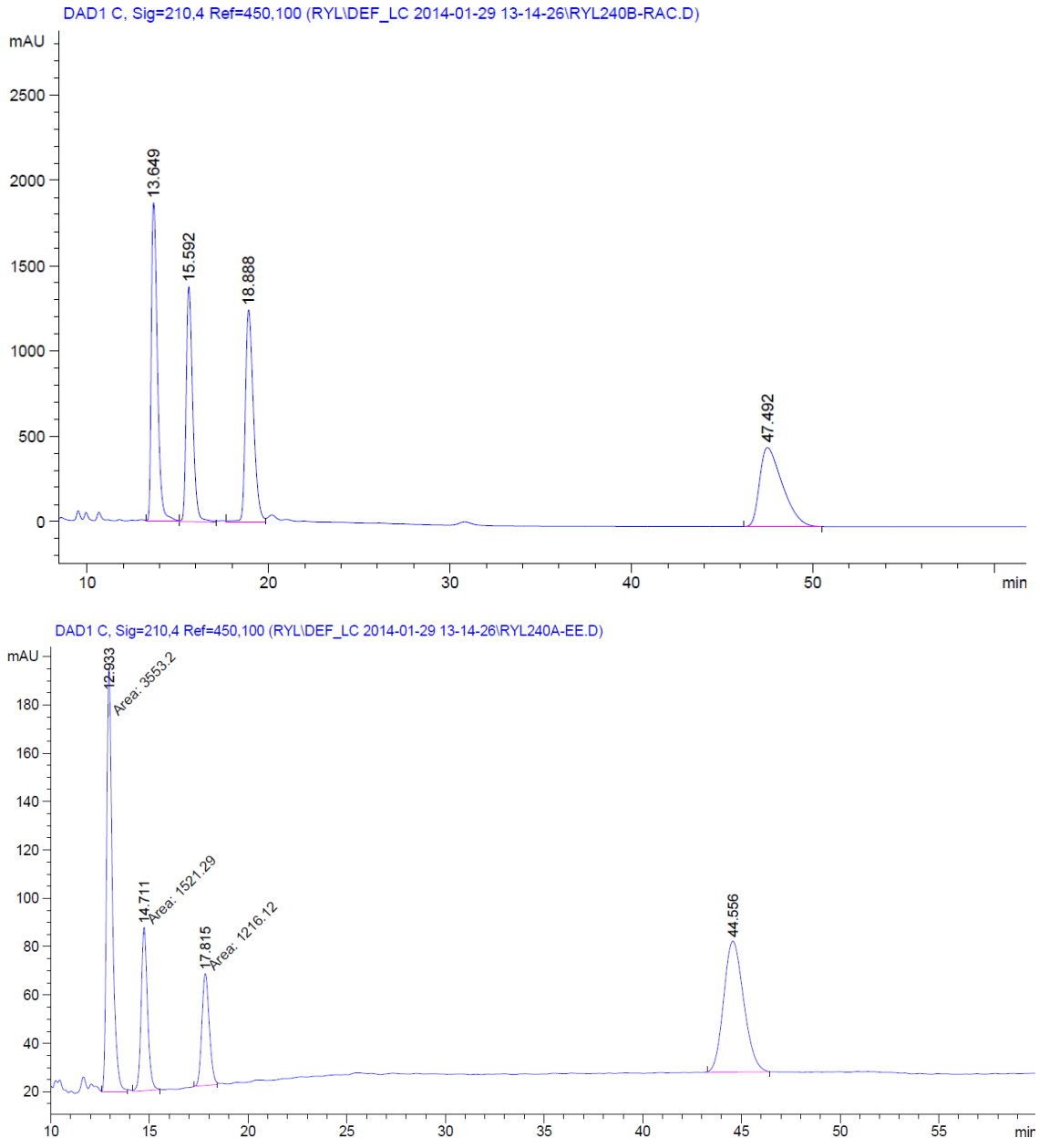


4j

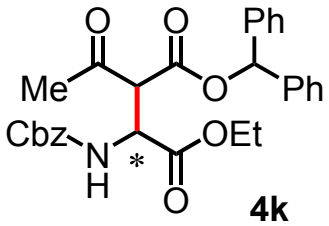
1-(*tert*-Butyl) 4-Ethyl 2-acetyl-3-(((benzyloxy)carbonyl)amino)succinate (4j)

Substrate **1-Cbz** reacted was *tert*-butyl 3-oxobutanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4j** was obtained as a colorless liquid (60.0 mg, 61%), a mixture of diastereomers (ratio = 1.0 : 0.81). $[\alpha]^{25}_{D}$ = 2.8° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.29 (m, 5H), 5.87 (d, *J* = 9.7 Hz, minor diastereomer), 5.82 (d, *J* = 9.1 Hz, major diastereomer), 5.15-5.07 (m, 2H), 4.96 (ddd, *J* = 12.9, 9.2, 4.0 Hz, 1H), 4.23-4.15 (m, 3H), 2.27 (m, 3H), 1.46 (s), 1.40 (s), 1.27-1.21 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.47, 201.34, 170.12, 169.81, 167.16, 166.44, 156.23, 136.26, 136.13, 128.50, 128.46, 128.15, 128.11, 128.03, 127.94, 83.34, 83.06, 82.91, 67.15, 67.05, 62.08, 62.039, 60.95, 60.41, 53.31, 52.78, 30.08, 29.68, 28.24, 27.86, 27.72, 14.02, 13.98; IR (neat) ν 2924, 2853, 1717, 1503, 1456, 1368, 1213, 1149, 1049, 757, 698 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{20}H_{27}NO_7$ (MH^+): 394.1860; found: 394.1846.

HPLC (ChiralPak AD-H, 20% *i*-PrOH in hexanes, 1 mL/min, 254 nm)



Peak	Retention time (min)	Area (mAU*s)	Area %
1	12.93	3553.24	37.08
2	14.71	1521.29	15.01
3	17.81	1216.12	12.01
4	44.56	3841.54	37.91

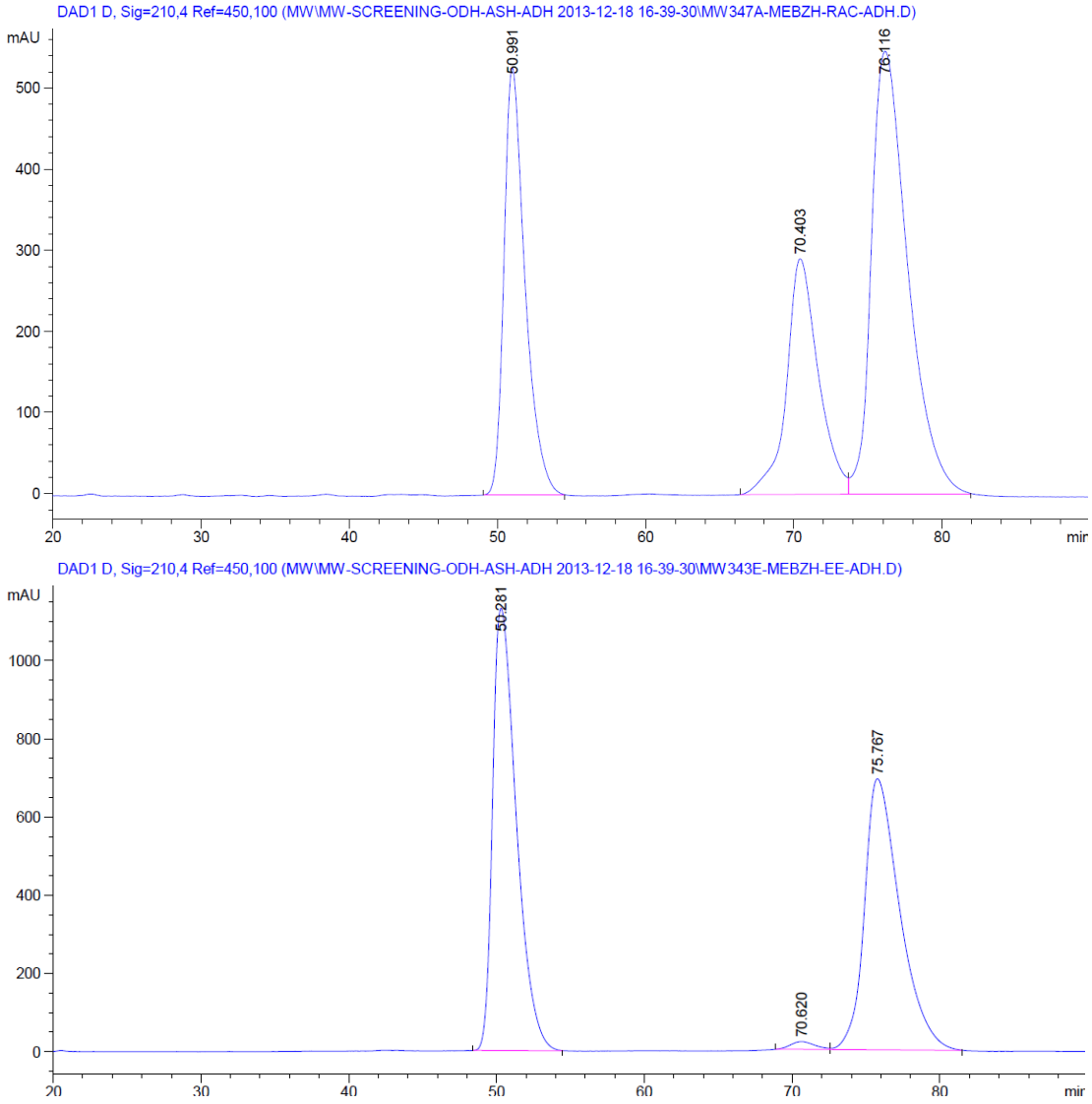


4k

1-Benzhydryl 4-ethyl 2-acetyl-3-(((benzyloxy)carbonyl)amino)succinatee (4k)

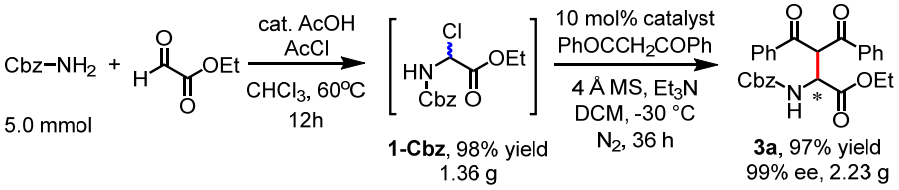
Substrate **1-Cbz** was reacted with benzhydryl 3-oxobutanoate following the general procedure. After purification by column chromatography (30% ethyl ether in hexanes), **4k** was obtained as a colorless solid (100.6 mg, 80%), a mixture of diastereomers (ratio = 1.0 : 0.61). $[\alpha]^{25}_{D}$ = 21.4° (c = 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.37-7.29 (m, 15H), 6.95 (s, major diastereomer), 6.93 (s, minor diastereomer), 5.86 (t, *J* = 6.0 Hz, 1H), 5.14-4.98 (m, 3H), 4.42-4.40 (m, 1H), 4.17-4.01 (m, 2H), 2.30 (s, major diastereomer), 2.26 (s, minor diastereomer), 1.20 (t, *J* = 6.0 Hz, minor diastereomer), 1.06 (t, *J* = 6.0 Hz, major diastereomer); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.24, 200.60, 169.66, 169.34, 167.16, 166.42, 156.13, 156.09, 139.15, 139.03, 139.01, 138.99, 136.08, 135.96, 128.75, 128.52, 128.48, 128.47, 128.42, 128.39, 128.28, 128.08, 128.03, 127.95, 127.83, 127.81, 127.71, 127.68, 127.34, 127.25, 127.17, 127.13, 127.07, 127.01, 126.87, 78.84, 78.51, 67.11, 67.00, 62.15, 62.12, 60.16, 59.70, 53.20, 52.76, 29.97, 29.71, 29.62, 13.86, 13.82, 13.66; IR (neat) ν 3429, 3033, 2924, 2853, 1721, 1498, 1455, 1215, 1049, 1028, 862, 757, 699 cm^{-1}; HRMS (ESI-TOF) Calcd for $C_{29}H_{29}NO_7$ (MH^+): 504.2017; found: 504.1995.

HPLC (ChiralPak AD-H, 10% *i*-PrOH in hexanes, 1 mL/min, 210 nm)



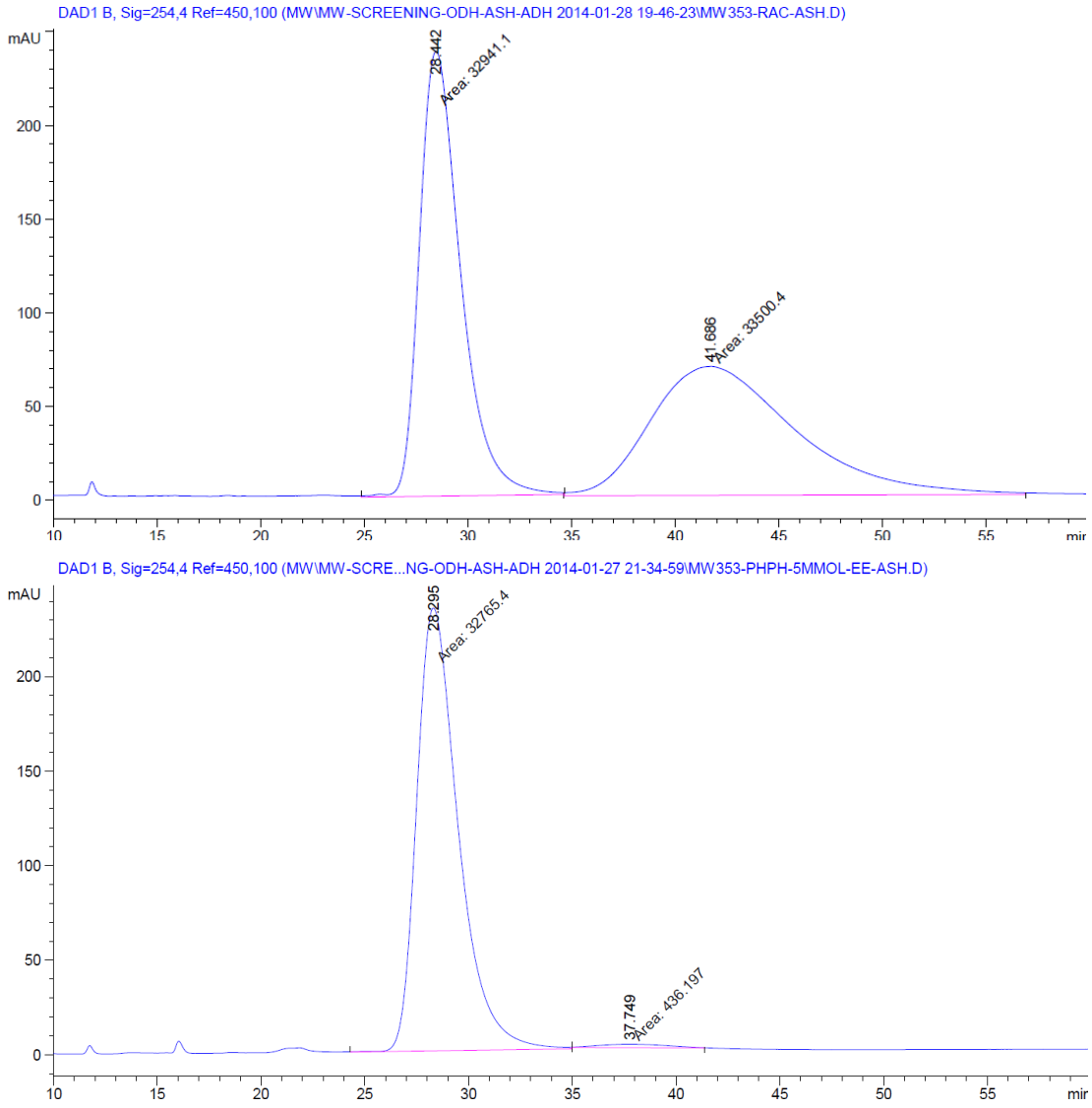
Peak	Retention time (min)	Area (mAU*s)	Area %
1	50.28	126238	51.58
2	70.62	2421.97	0.99
3	75.77	116097	47.43

C. One-Pot Preparation of α-Chloro Glycine Ester and Mannich Reaction



Ethyl 2-(((benzyloxy)carbonyl)amino)-2-chloroacetate **1-Cbz** was prepared according to a modified literature procedure by Roche.[1] In a 50 mL round-bottom flask, acetic acid (0.5 mmol, 33 μL) was added to a vigorously stirring solution of benzyl carbamate (5.0 mmol, 0.756 g), freshly distilled ethyl 2-oxoacetate (6.5 mmol, 0.65 mL) and acetyl chloride (12.5 mmol, 0.95 mL) in anhydrous chloroform (20 mL). The flask was tightly sealed and the reaction mixture was heated to 60°C and stirred for 12h, then concentrated *in vacuo* to yield a colorless solid. The residual acetic acid was co-evaporated twice with anhydrous DCM (20mL) under reduced pressure to give **1-Cbz** in 98% yield (4.9 mmol, 1.359g), which was used in the subsequent Mannich reaction without further purification. Flame-dried 4Å molecular sieves (0.5g) and anhydrous DCM (10 mL) was added to the flask containing **1-Cbz** (4.9 mmol), which was then cooled to -30°C. A solution of catalyst (0.5 mmol, 0.207g), dibenzoyl methane (10 mmol, 2.243g), and triethylamine (1.25 mmol, 0.127g) in anhydrous DCM (7.5 mL) was precooled to -30°C, which was added to the flask containing **1-Cbz** by cannula. Additional 2.5 mL of DCM was necessary to dissolve and transfer the remaining solid. The resulting reaction mixture was stirred for 36h at -30°C under nitrogen atmosphere, and then warmed to room temperature. The crude product mixture was filtered through a pad of celite, washed twice with DCM (10 mL each), and dried under reduced pressure to give a yellow solid, which was purified by flash chromatography using diethyl ether and hexanes (1:3) as eluent. The Mannich product **3a** was obtained in 97% yield (4.85 mmol, 2.229g) based on the amount of benzyl carbamate used (5.0 mml) as a white solid, and its enantiomeric excess was determined to be 97%.

HPLC (ChiralPak AS-H, 20% *i*-PrOH/ hexanes, 1 mL/min, 254 nm).



Peak	Retention time (min)	Area (mAU*s)	Area %
1	28.44	32768.4	98.69
2	37.75	436.197	1.314

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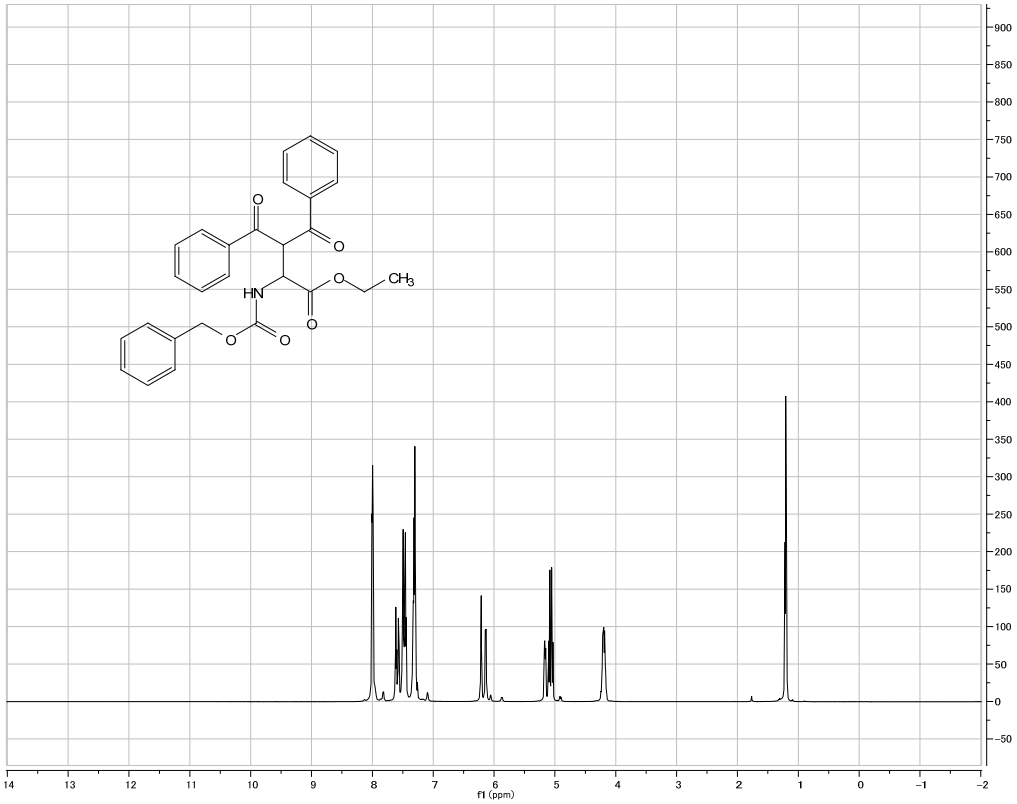
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CH3
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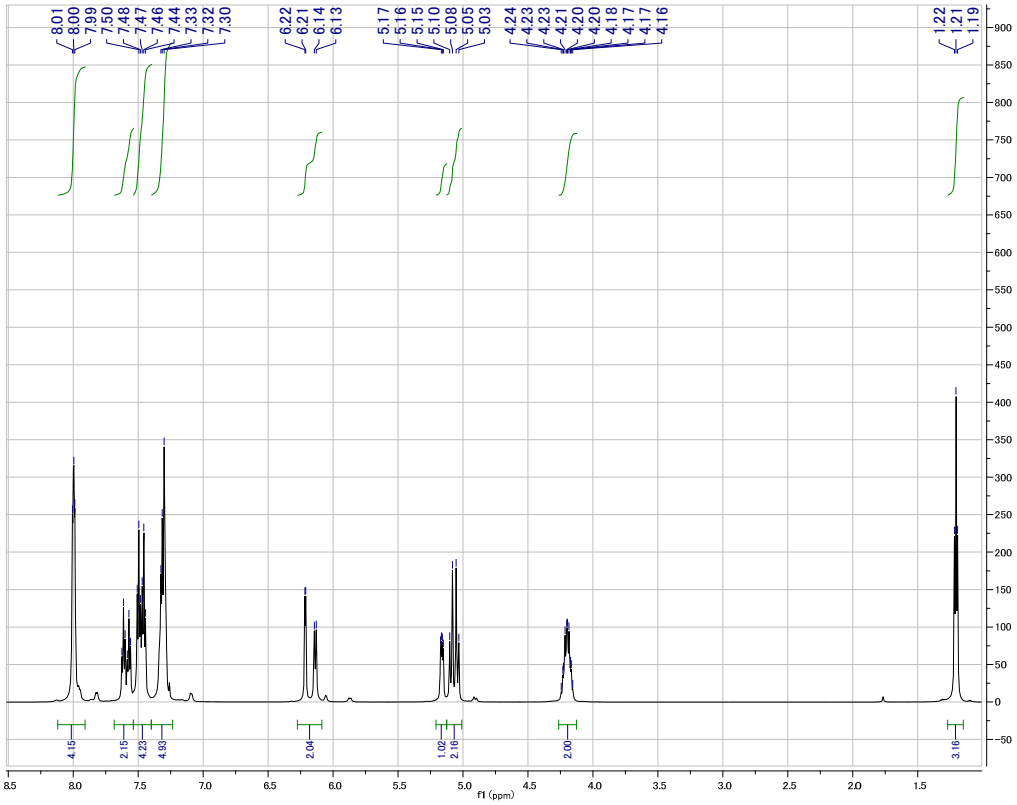
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7.47
7.46
7.44
7.33
7.32
7.30
6.22
6.21
6.14
6.13
5.17
5.16
5.15
5.10
5.08
5.05
5.03
4.24
4.23
4.23
4.21
4.20
4.20
4.18
4.17
4.17
4.16
1.22
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2.16
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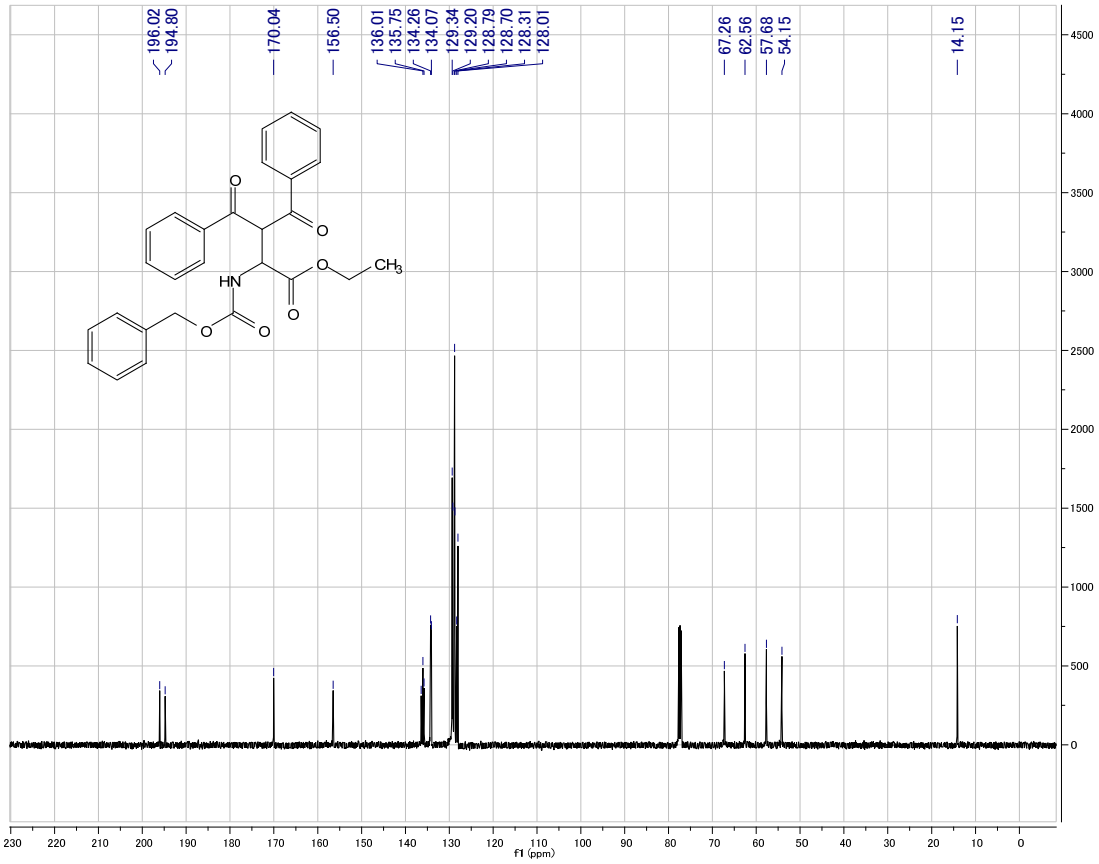
f1 (ppm)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134.07
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128.70
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128.01
67.26
62.56
57.68
54.15
14.15
O
O
O
HN
O
O
O
CH3
4500
4000
3500
3000
2500
2000
1500
1000
500
0
230
220
210
200
190
180
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50
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10
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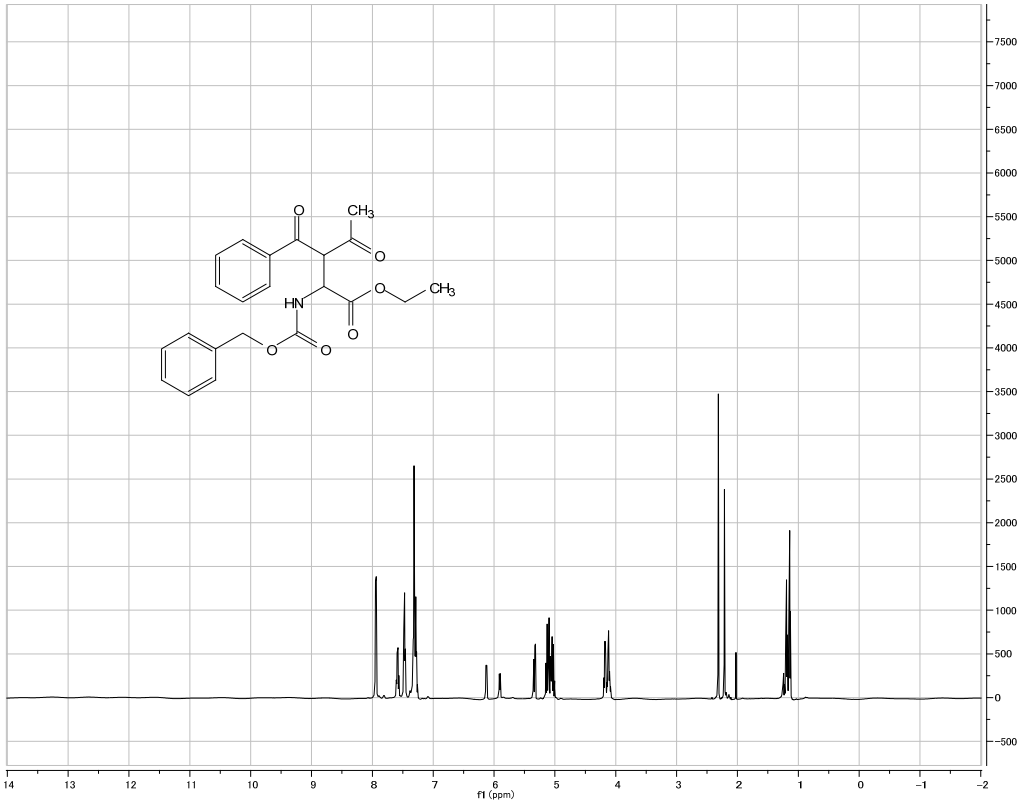
f1 (ppm)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CH3
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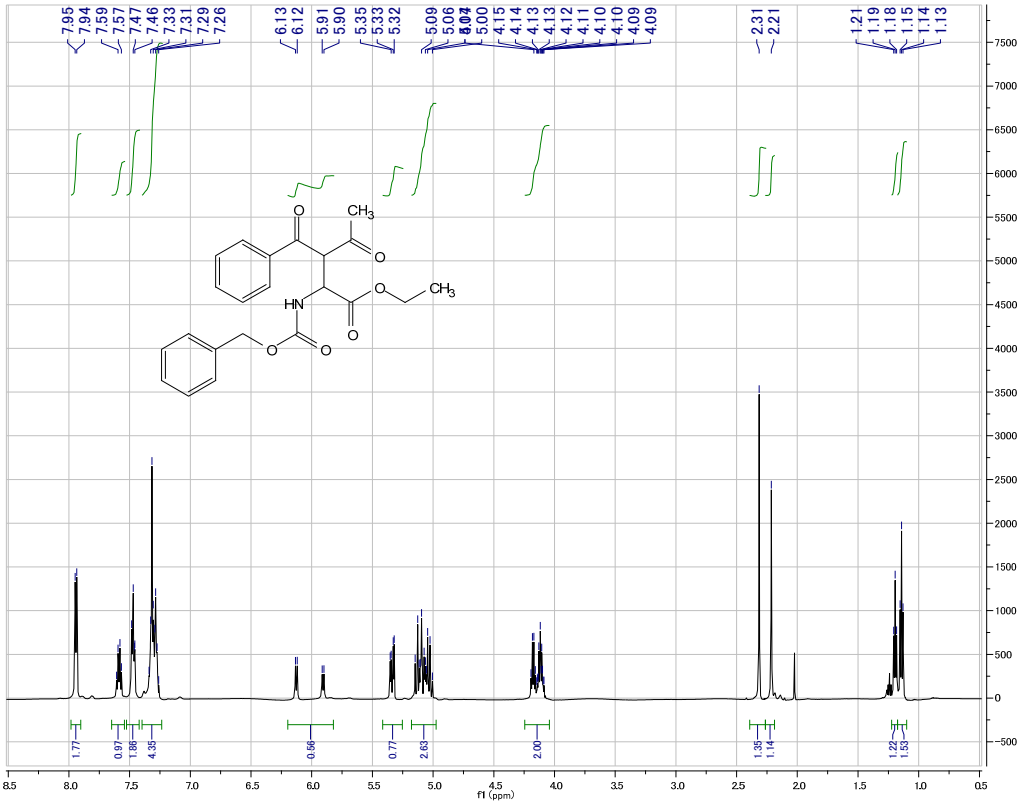
f1 (ppm)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5.90
5.35
5.33
5.32
5.09
5.06
5.00
4.15
4.14
4.13
4.12
4.11
4.10
4.09
4.09
2.31
2.21
1.21
1.19
1.18
1.15
1.14
1.13
O
CH3
O
HN
O
CH3
O
O
O
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0.77
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1.14
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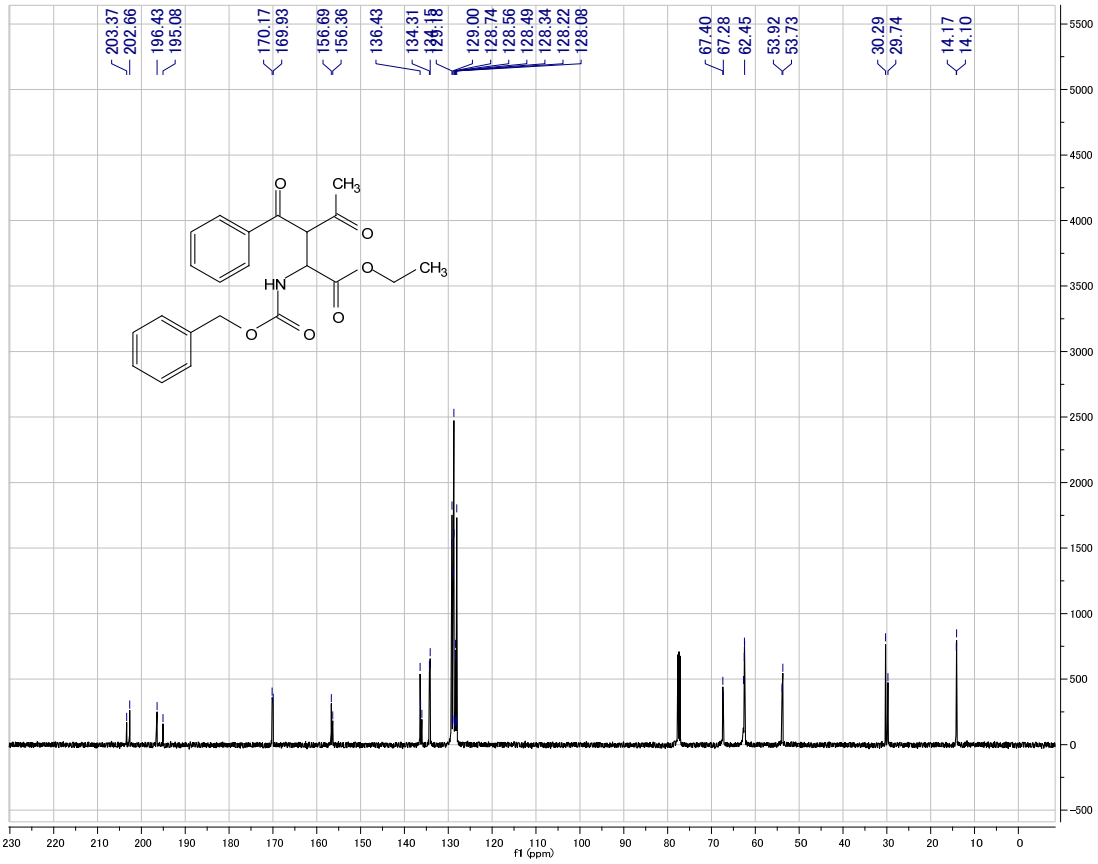
1.53
f1 (ppm)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156.36
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134.31
134.15
134.18
129.00
128.74
128.56
128.49
128.34
128.22
128.08
67.40
67.28
62.45
53.92
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14.10
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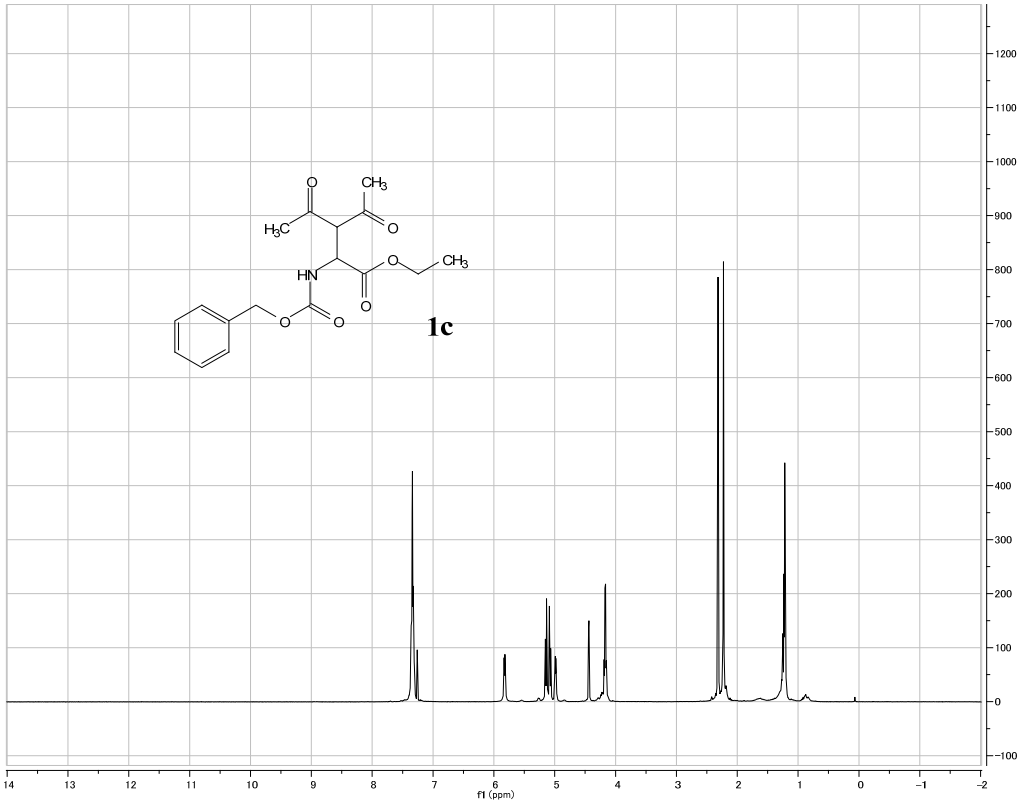
CH3
O
O
CH3
HN
O
O
O
f1 (ppm)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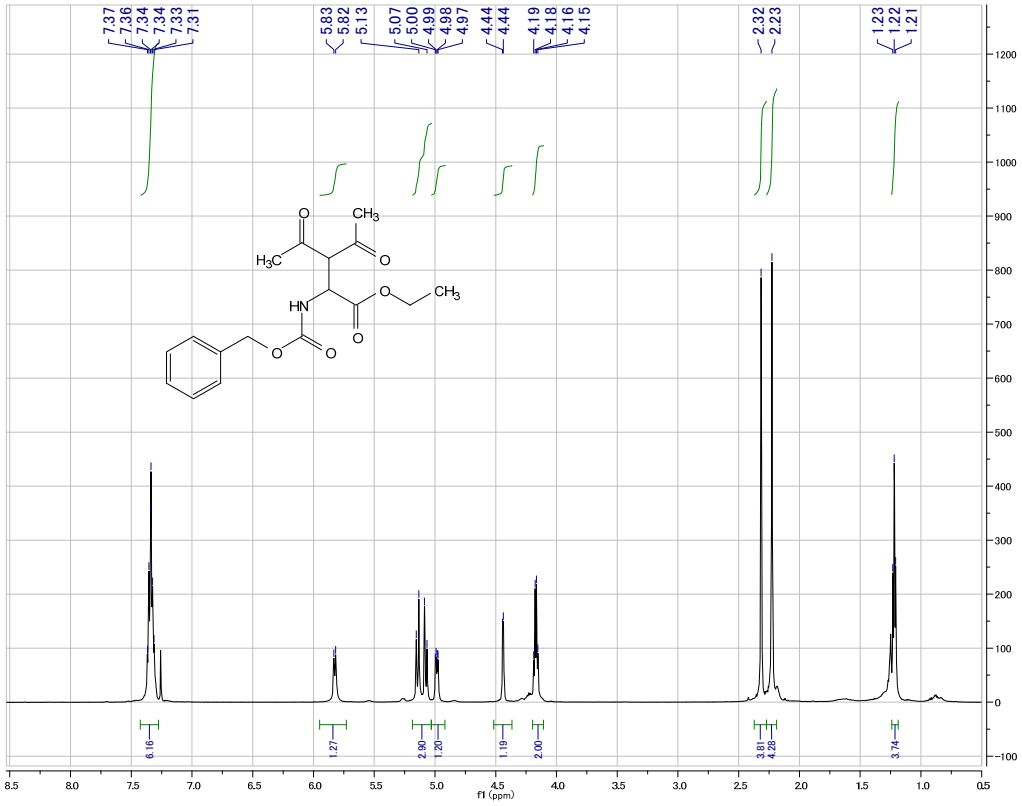
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5.07
5.00
4.99
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4.97
4.44
4.44
4.19
4.18
4.16
4.15
2.32
2.23
1.23
1.22
1.21
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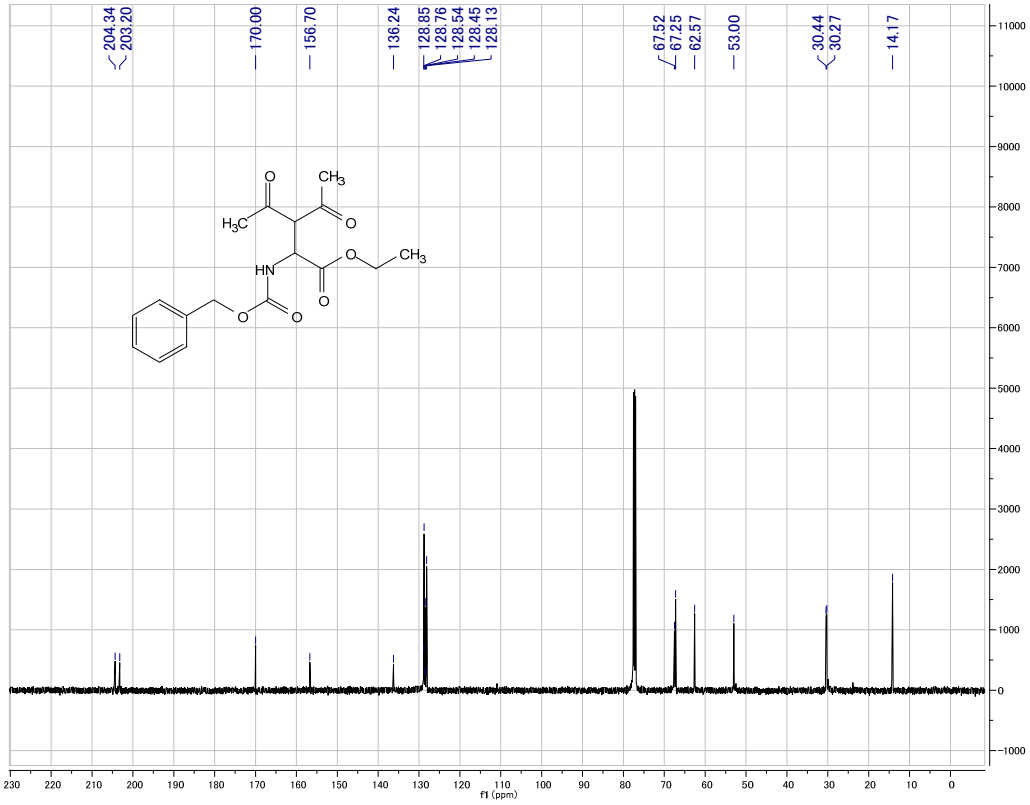
1.27
2.90
1.20
1.19
2.00
3.81
4.28
3.74
f1 (ppm)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136.24
128.85
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128.13
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67.25
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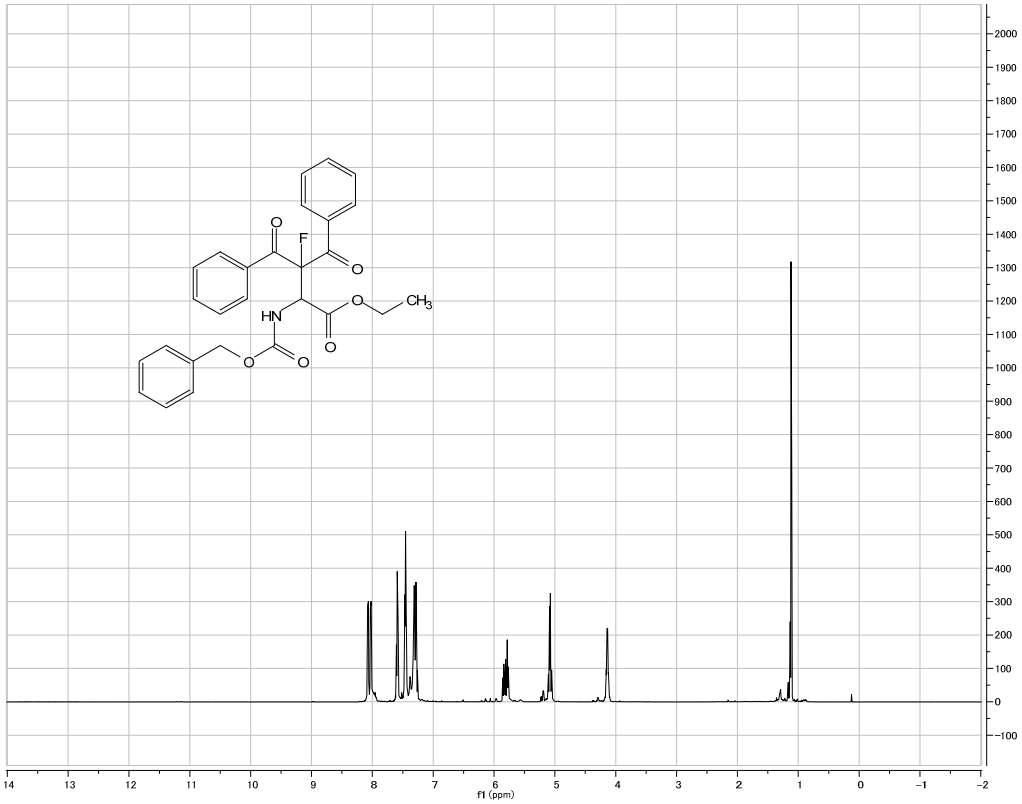
53.00
30.44
30.27
14.17
f1 (ppm)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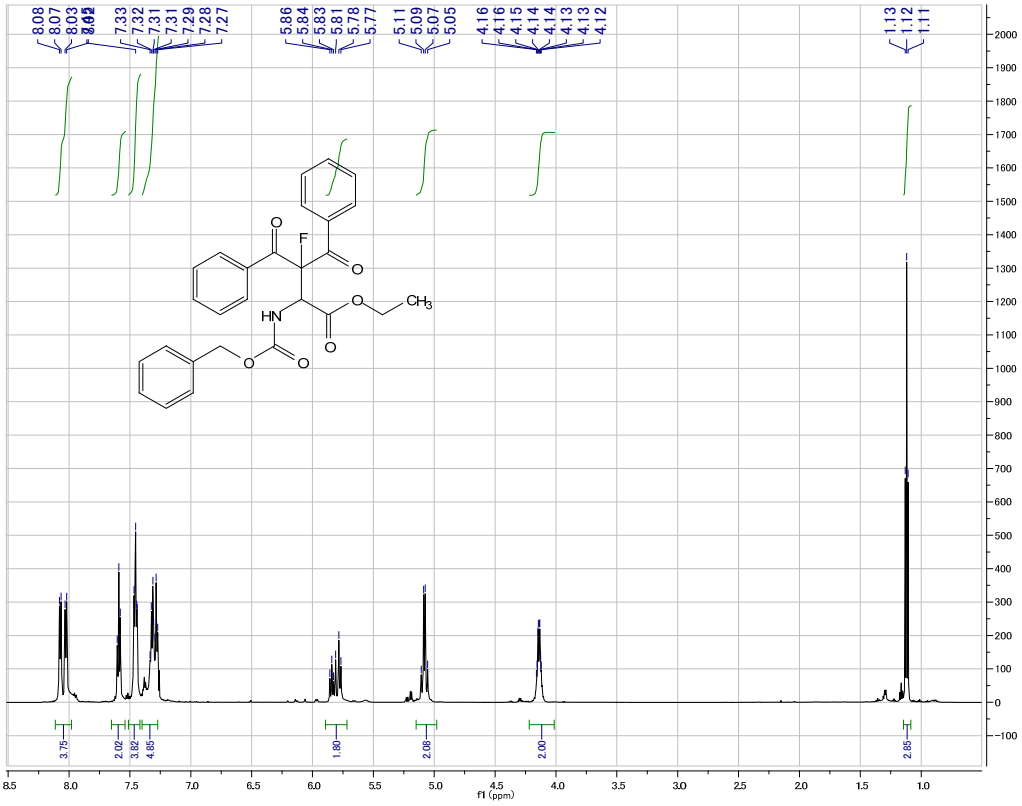
HN
O
O
O
CH3
O
O
f1 (ppm)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7.27
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5.84
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5.77
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5.09
5.07
5.05
4.16
4.16
4.15
4.14
4.14
4.13
4.13
4.12
1.13
1.12
1.11
O
F
O
HN
O
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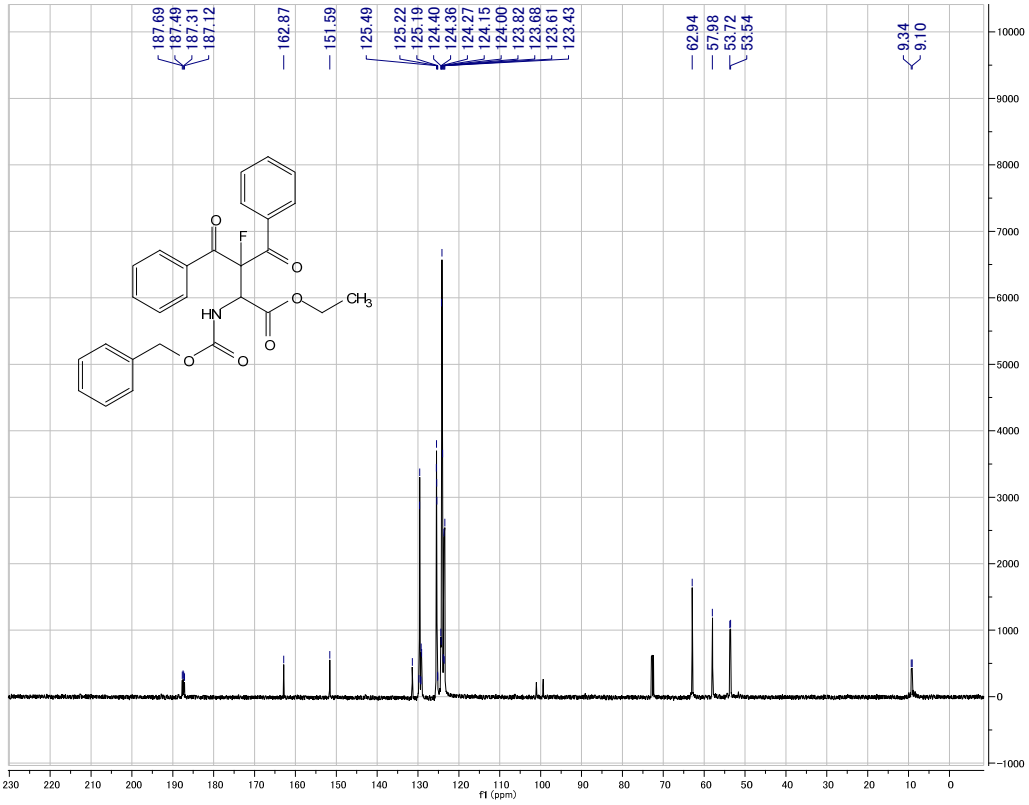
3.82
4.85
1.80
2.08
2.00
2.85
f1 (ppm)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124.36
124.27
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124.00
123.82
123.68
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123.43
62.94
57.98
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53.54
9.34
9.10
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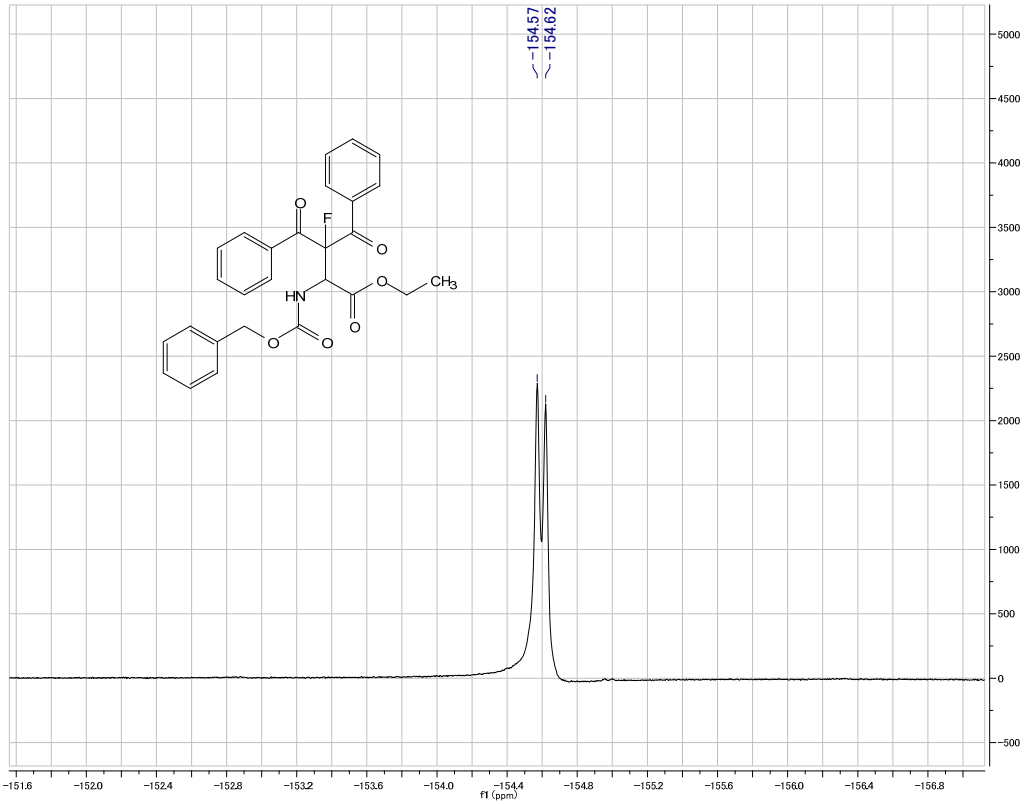
O
HN
CH3
f1 (ppm)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CH3
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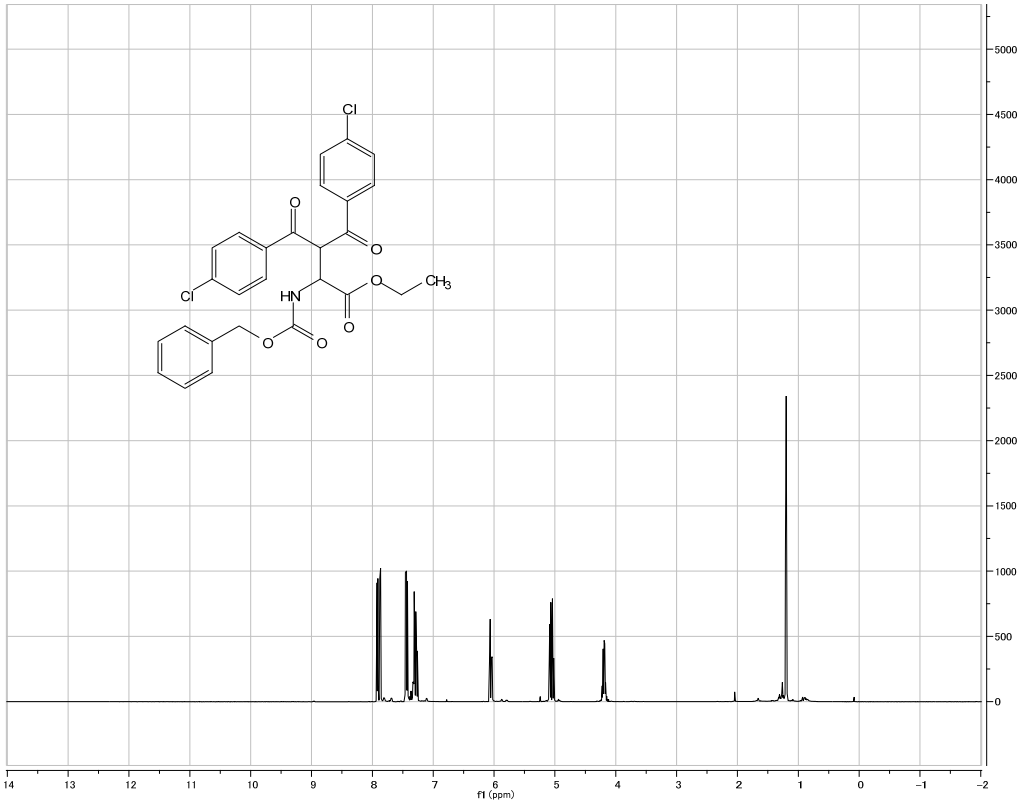
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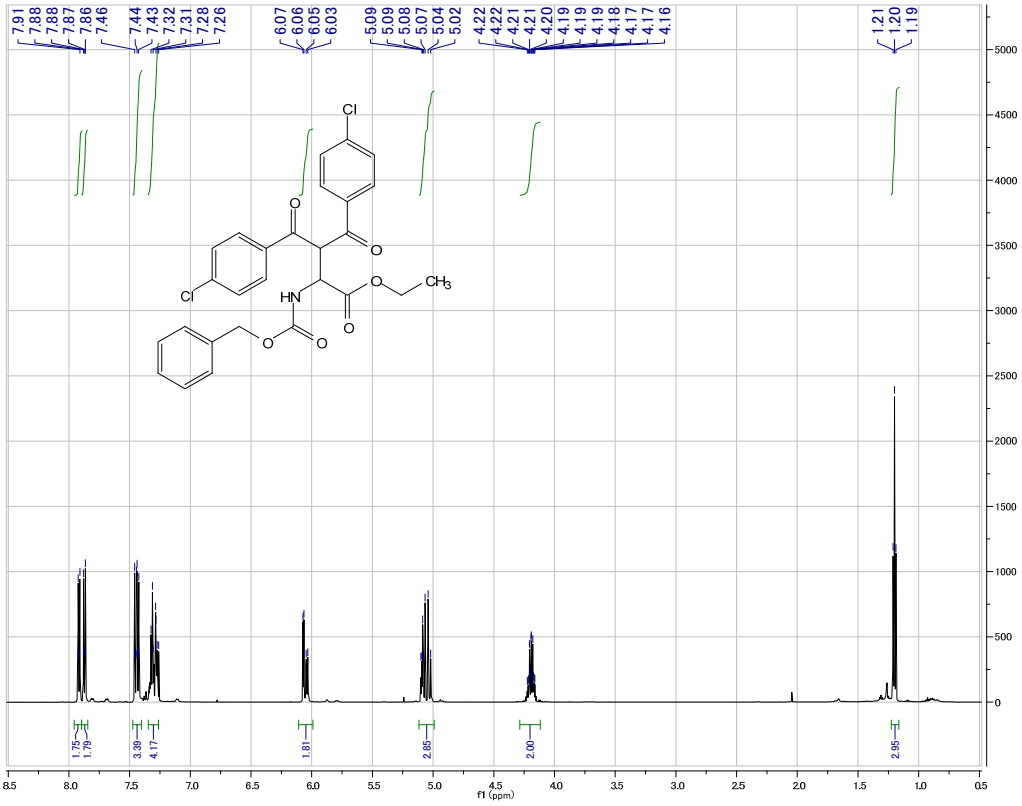
O
O
Cl
HN
O
CH3
O
O
O
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)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7.31
7.28
7.26
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6.06
6.05
6.03
5.09
5.09
5.08
5.07
5.04
5.02
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4.22
4.21
4.21
4.20
4.19
4.19
4.19
4.18
4.17
4.17
4.16
1.21
1.20
1.19
Cl
O
O
O
Cl
HN
O
CH3
O
O
1.75
1.79
3.39
4.17
1.81
2.85
2.00
2.95
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
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8.0
7.5
7.0
6.5
6.0
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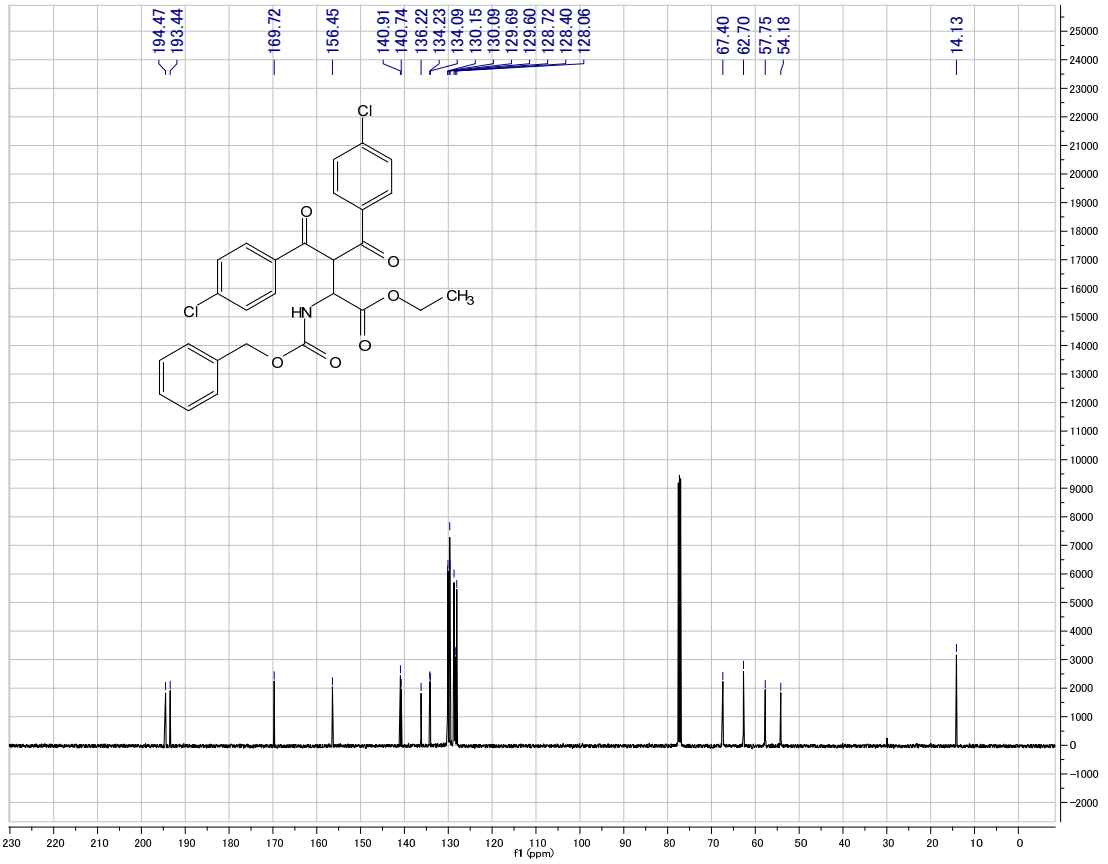
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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128.72
128.40
128.06
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54.18
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Cl
HN
O
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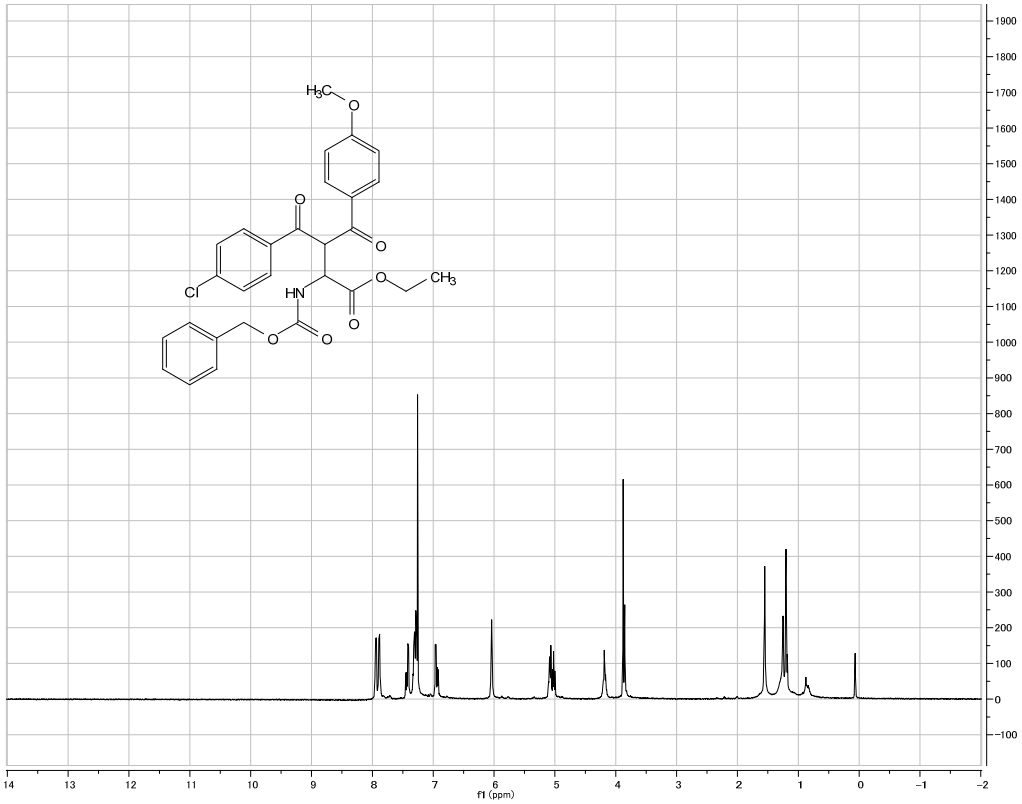
O
O
CH3
f1 (ppm)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O
Cl
HN
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CH3
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O
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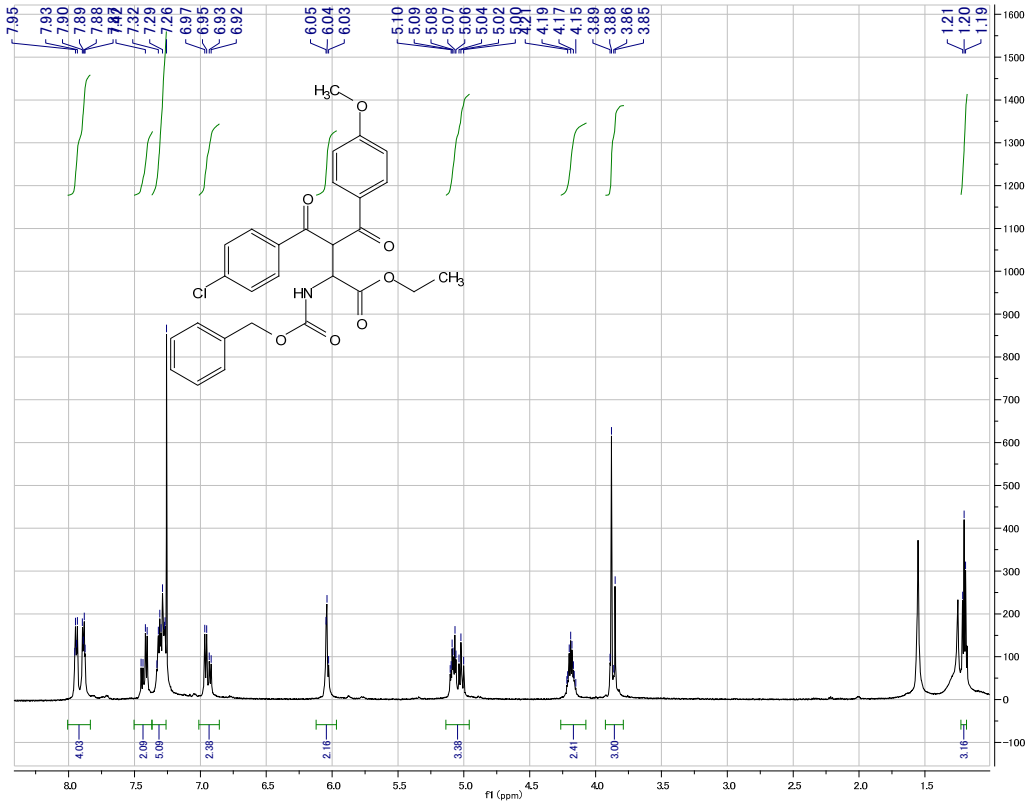
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6.93
6.92
6.05
6.04
6.03
5.10
5.09
5.08
5.07
5.06
5.04
5.02
4.19
4.17
4.15
3.89
3.88
3.86
3.85
1.21
1.20
1.19
H3C
O
O
O
Cl
HN
O
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2.09
5.09
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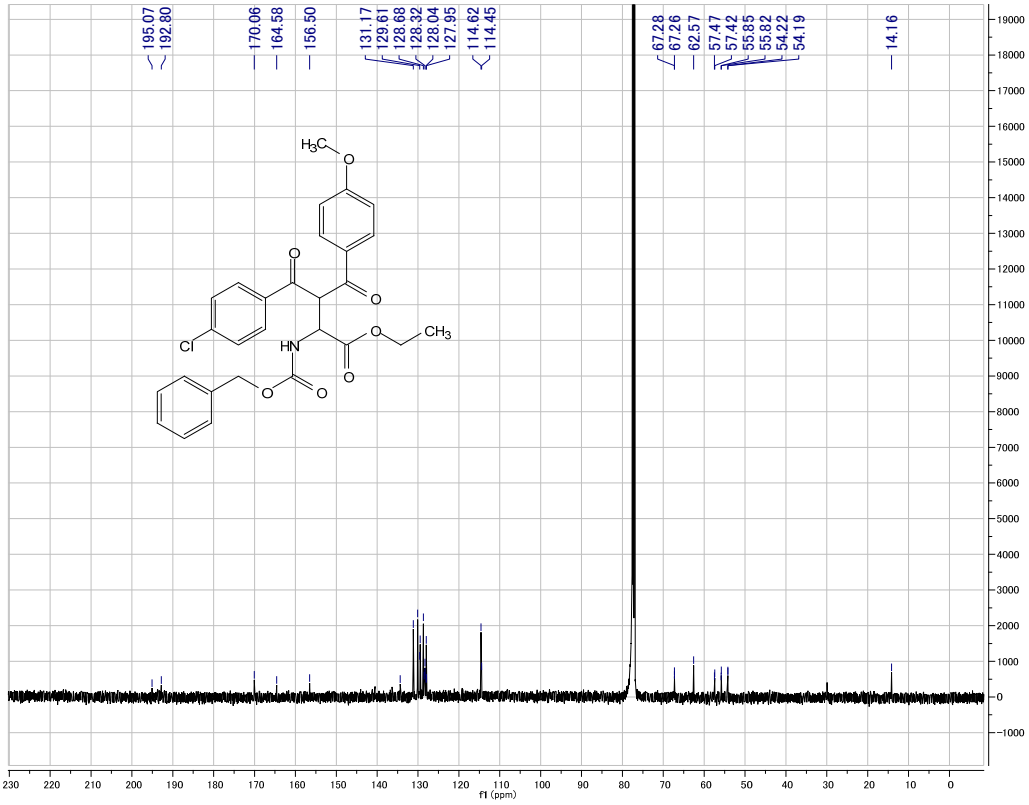
3.38
2.41
3.00
3.16
f1 (ppm)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128.04
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114.45
67.28
67.26
62.57
57.47
57.42
55.85
55.82
54.22
54.19
14.16
H3C
O
O
O
Cl
HN
O
CH3
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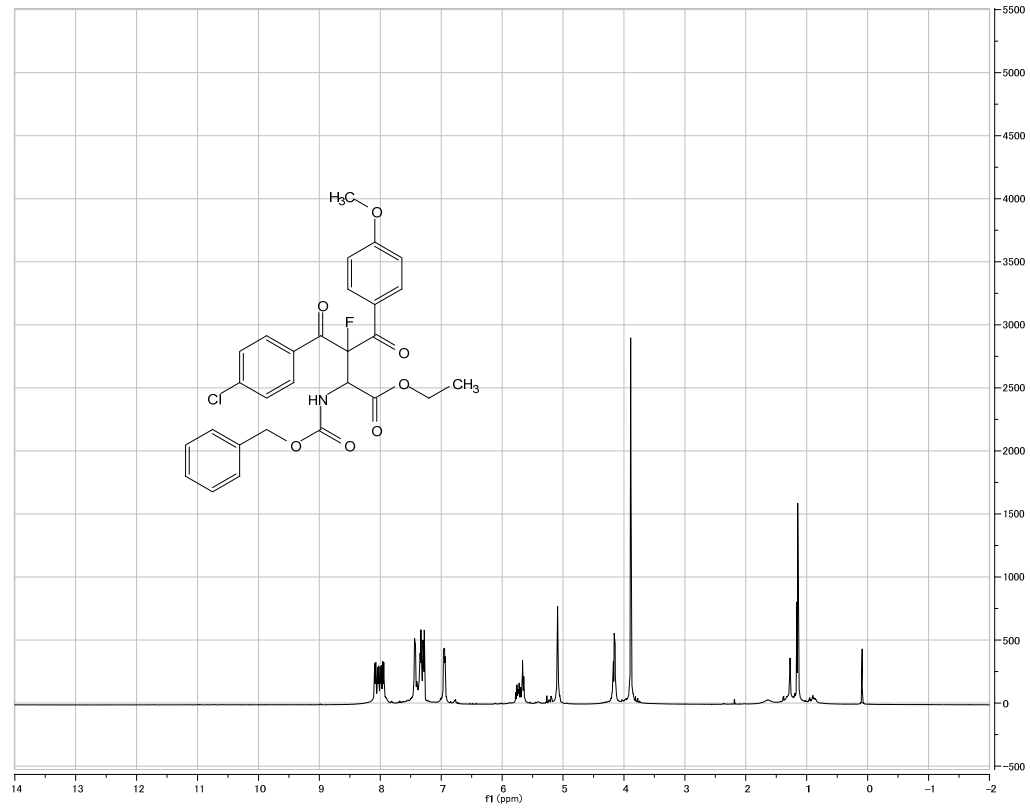
O
O
f1 (ppm)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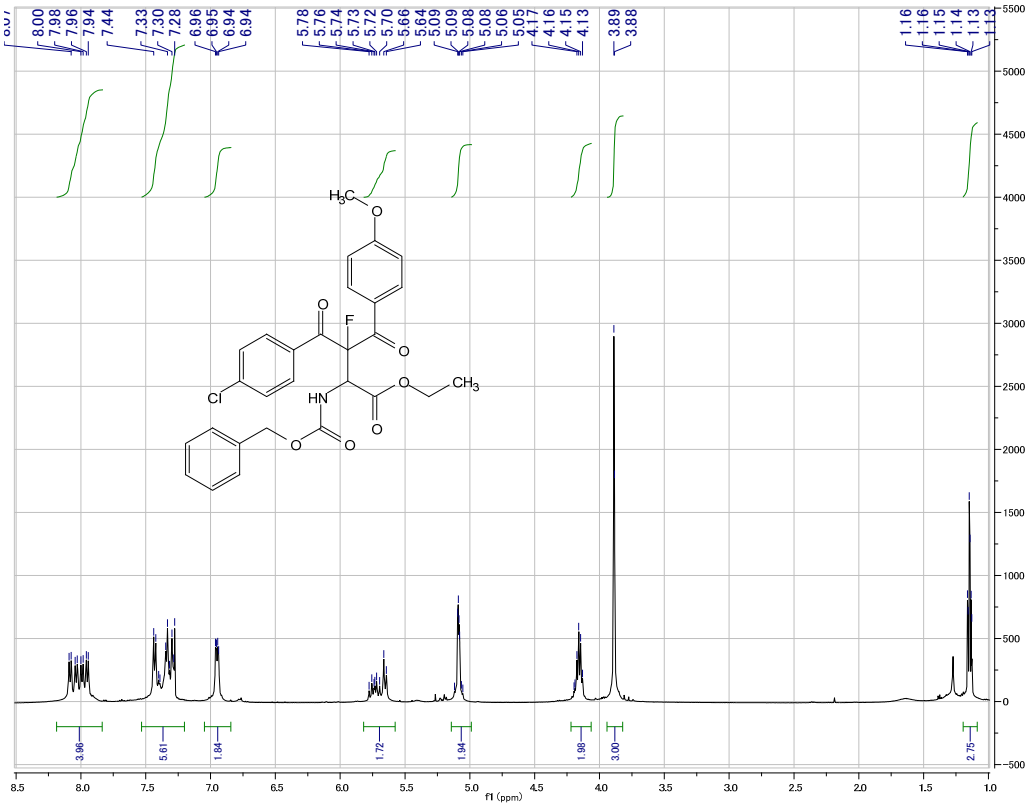
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7.30
7.28
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6.95
6.94
6.94
5.78
5.76
5.74
5.73
5.72
5.70
5.66
5.64
5.09
5.09
5.08
5.08
5.06
5.05
4.17
4.16
4.15
4.13
3.89
3.88
1.16
1.16
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1.84
1.72
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1.98
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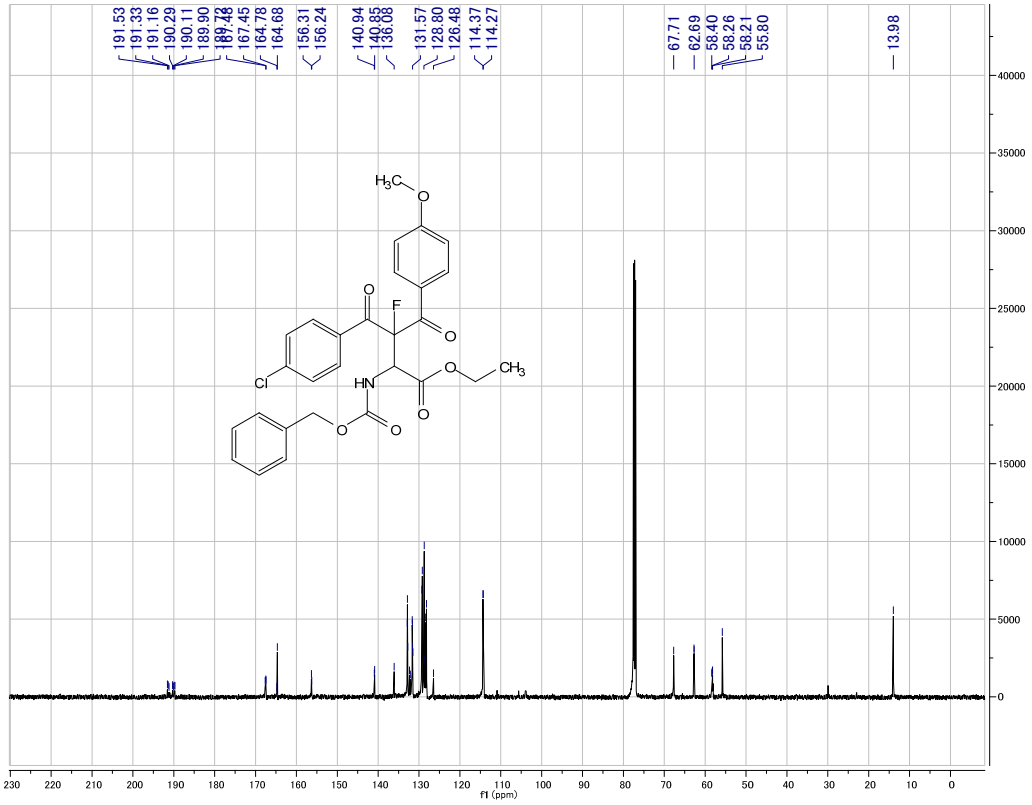
f1 (ppm)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156.24
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136.08
131.57
128.80
126.48
114.37
114.27
67.71
62.69
58.40
58.26
58.21
55.80
13.98
H3C
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O
F
O
Cl
HN
O
CH3
O
O
O
40000
35000
30000
25000
20000
15000
10000
5000
0
230
220
210
200
190
180
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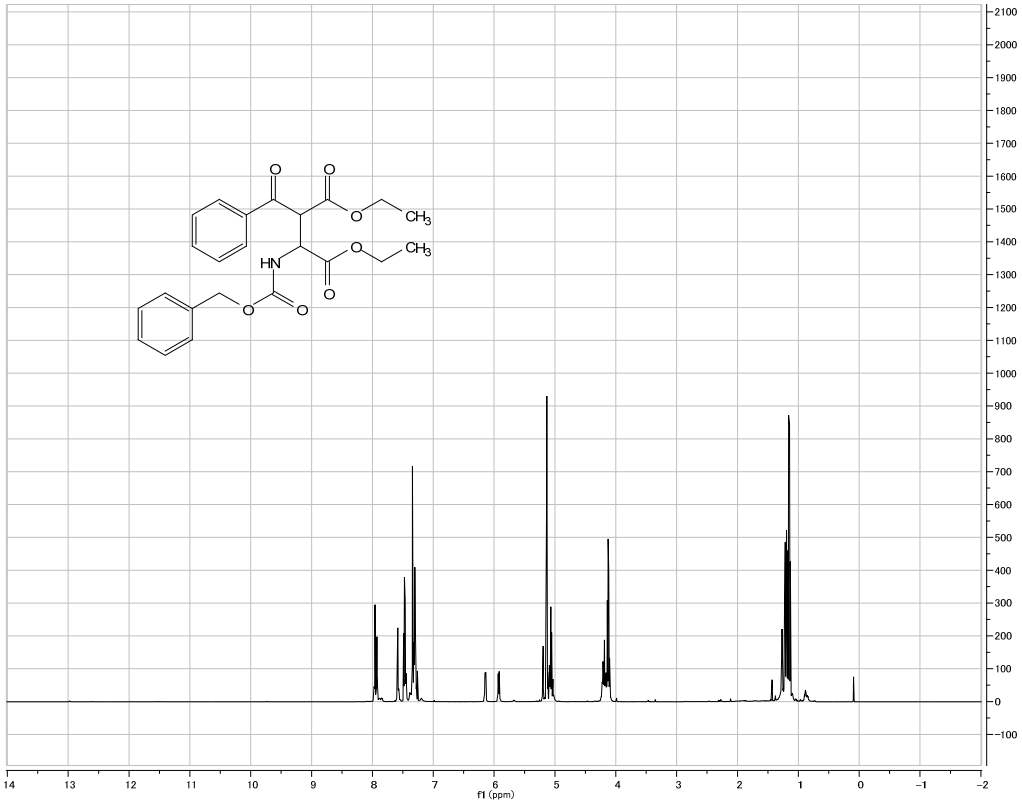
f1 (ppm)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CH3
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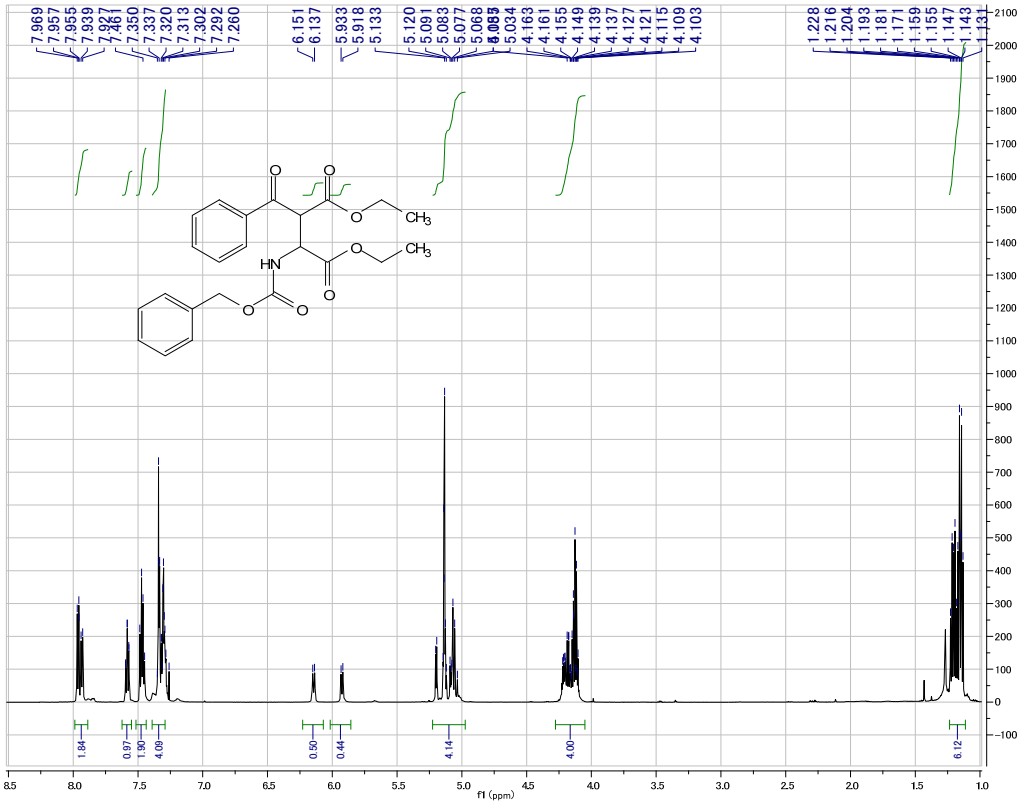
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7.292
7.260
6.151
6.137
5.933
5.918
5.133
5.120
5.091
5.083
5.077
5.068
5.034
4.163
4.161
4.155
4.149
4.139
4.137
4.127
4.121
4.115
4.109
4.103
1.228
1.216
1.204
1.193
1.181
1.171
1.159
1.155
1.147
1.143
1.131
O
O
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CH3
HN
O
CH3
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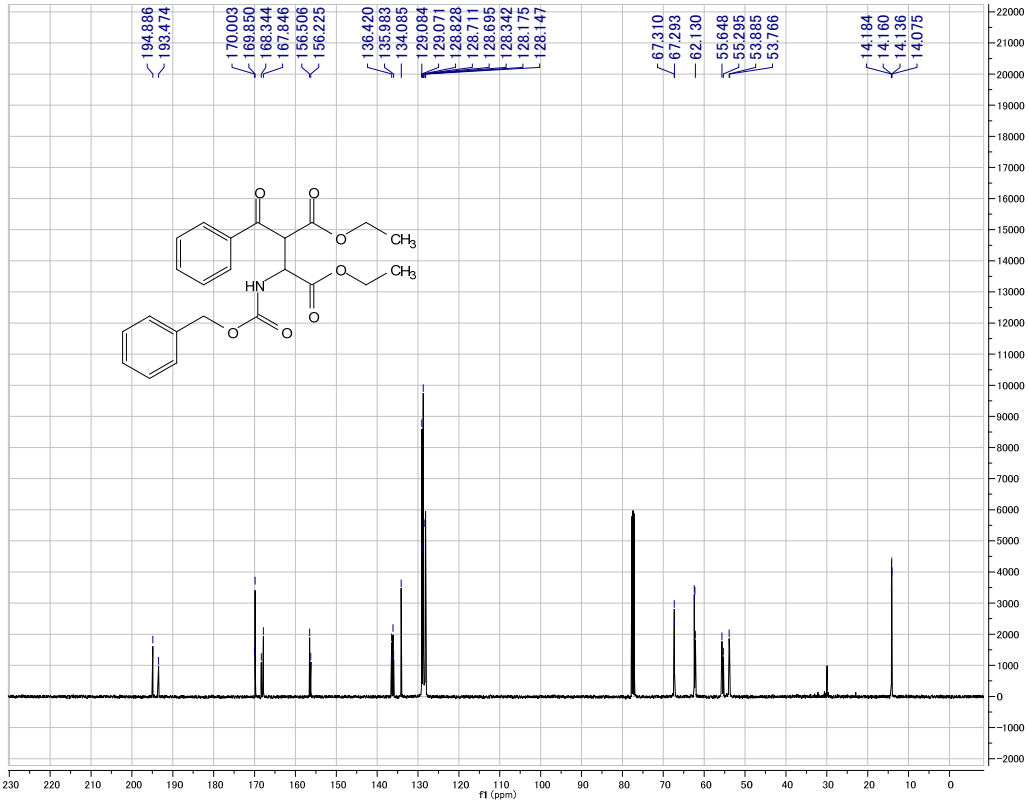
6.12
f1 (ppm)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167.846
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156.225
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135.983
134.085
129.084
129.071
128.828
128.711
128.695
128.342
128.175
128.147
67.310
67.293
62.130
55.648
55.295
53.885
53.766
14.184
14.160
14.136
14.075
O
O
O
CH3
HN
O
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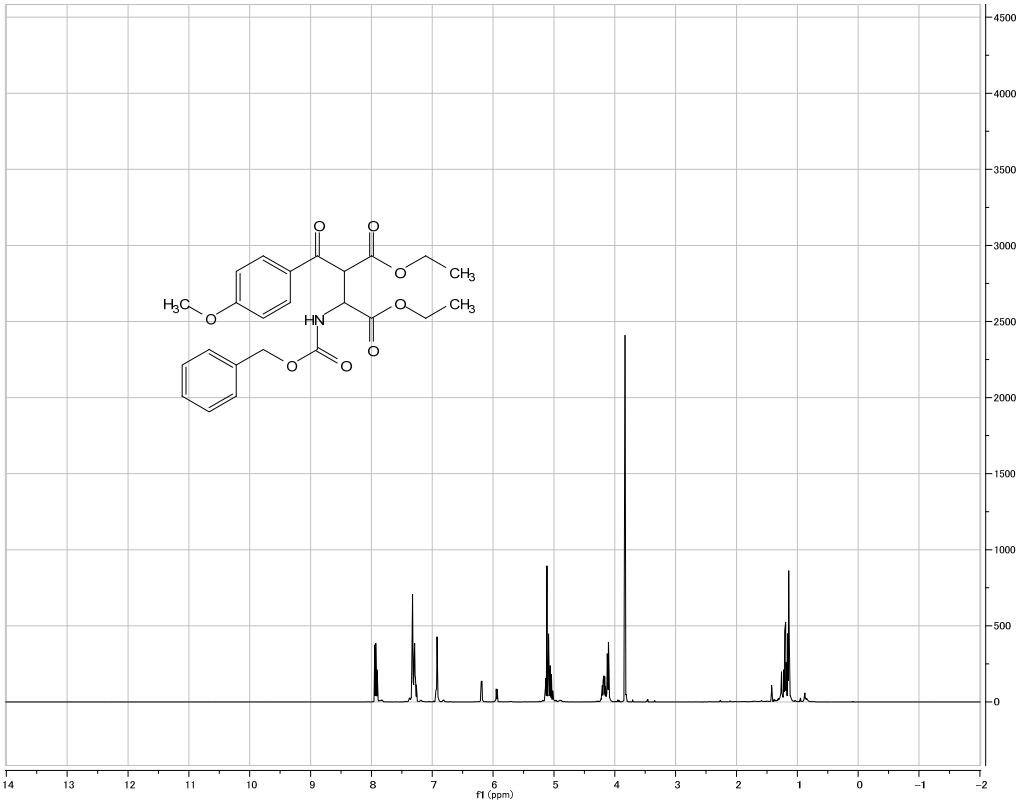
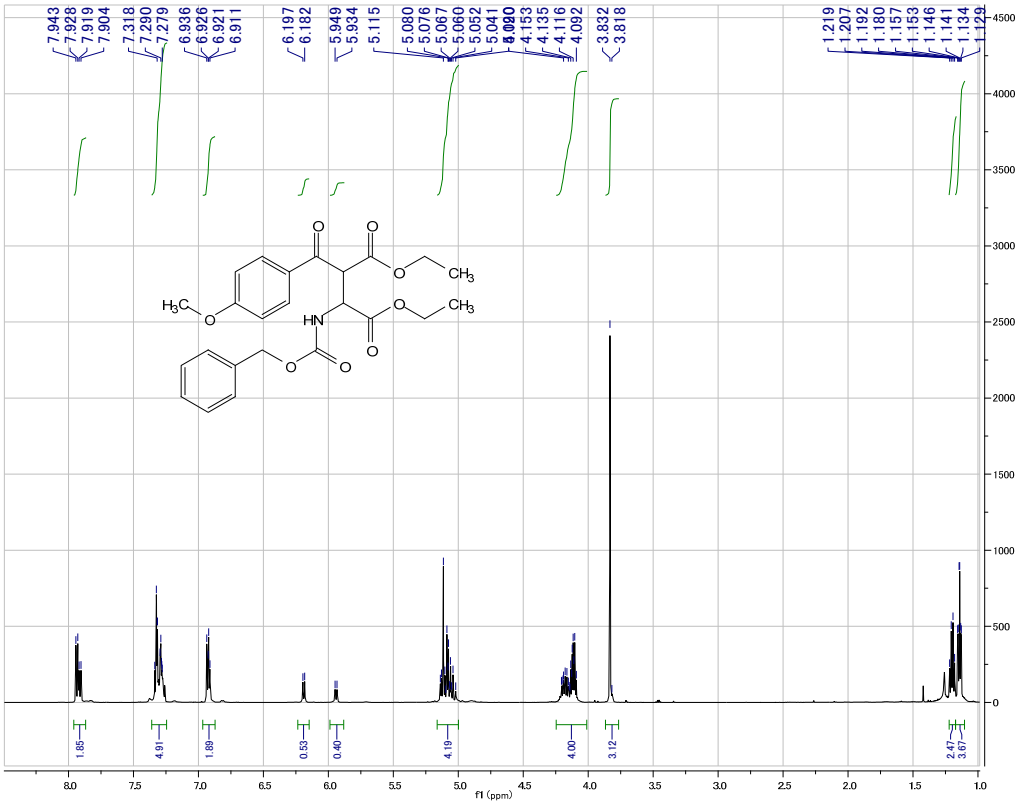
CH3
O
O
f1 (ppm)


f1 (ppm)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7.904
7.318
7.290
7.279
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6.926
6.921
6.911
6.197
6.182
5.949
5.934
5.115
5.080
5.076
5.067
5.060
5.052
5.041
4.153
4.135
4.116
4.092
3.832
3.818
1.219
1.207
1.192
1.180
1.157
1.153
1.146
1.141
1.134
1.123
1.85
4.91
1.89
0.53
0.40
4.19
4.00
3.12
2.47
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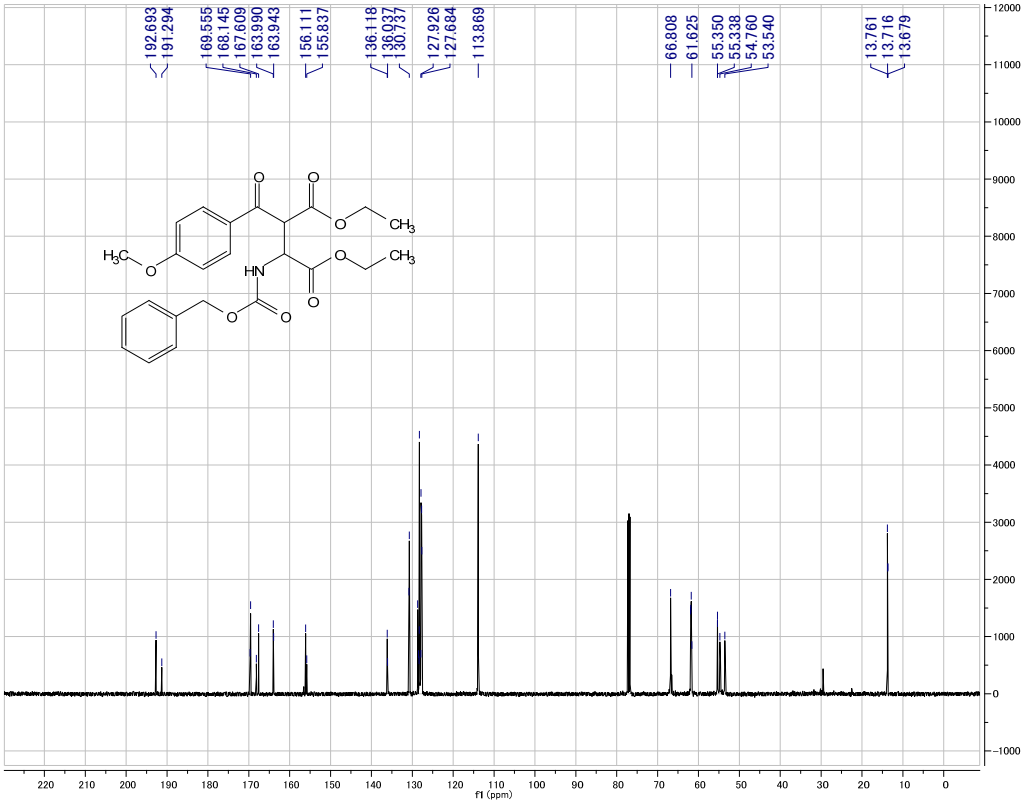
f1 (ppm)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127.684
113.869
66.808
61.625
55.350
55.338
54.760
53.540
13.761
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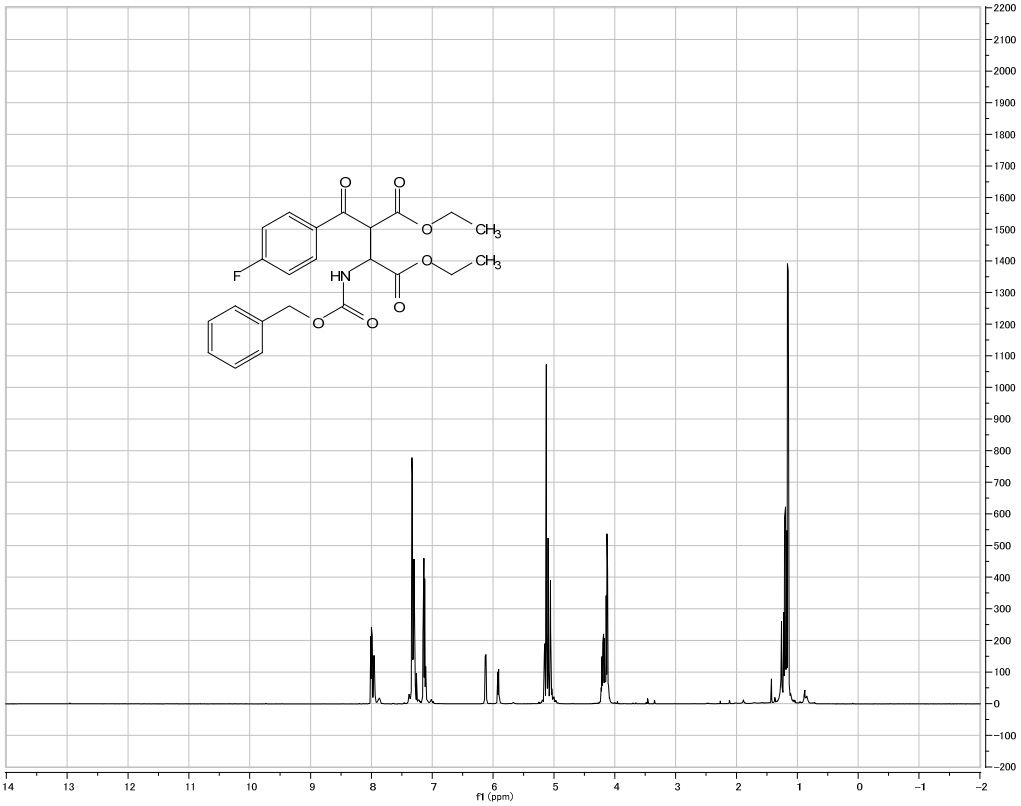
O
O
CH3
H3C
O
HN
O
CH3
O
O
O
f1 (ppm)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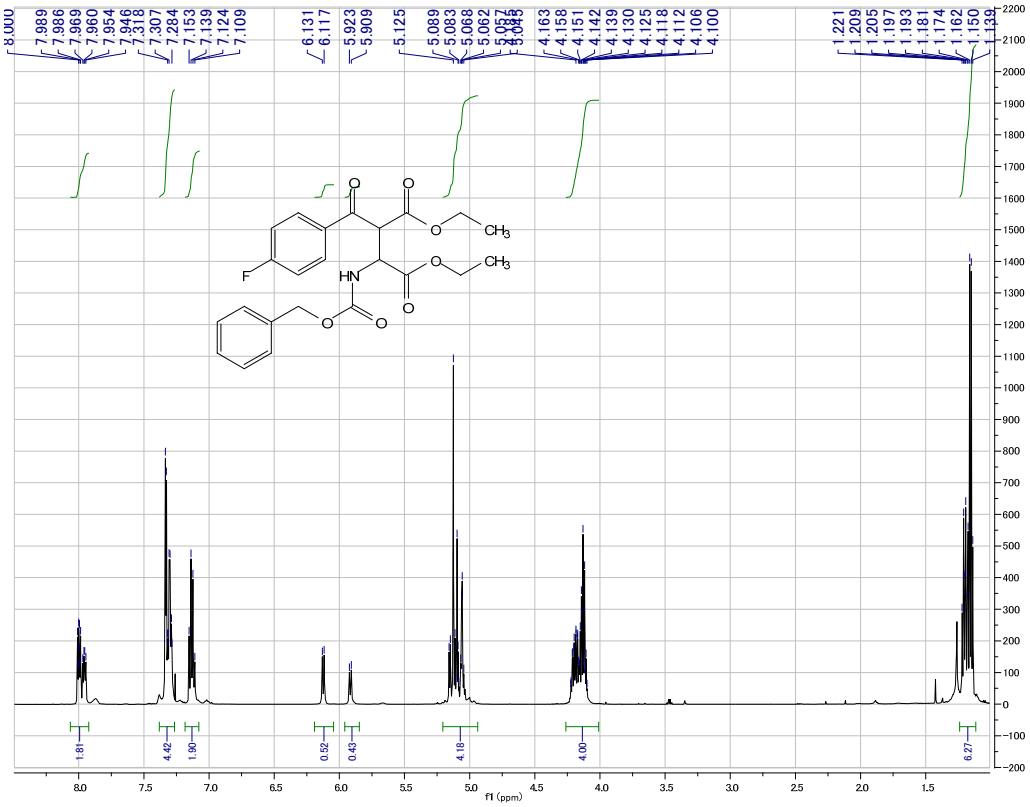
CH3
f1 (ppm)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7.139
7.124
7.109
6.131
6.117
5.923
5.909
5.125
5.089
5.083
5.068
5.062
4.163
4.158
4.151
4.142
4.139
4.130
4.125
4.118
4.112
4.106
4.100
1.221
1.209
1.205
1.197
1.193
1.181
1.174
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1.150
1.139
1.61
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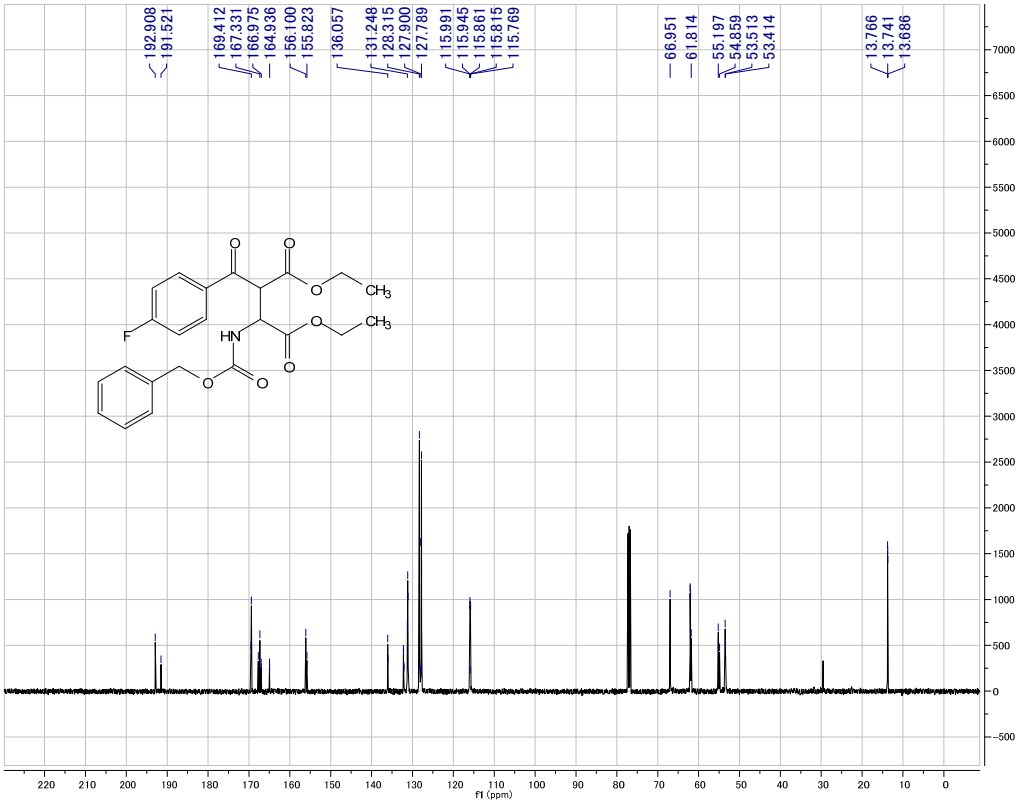
f1 (ppm)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127.789
115.991
115.945
115.861
115.815
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55.197
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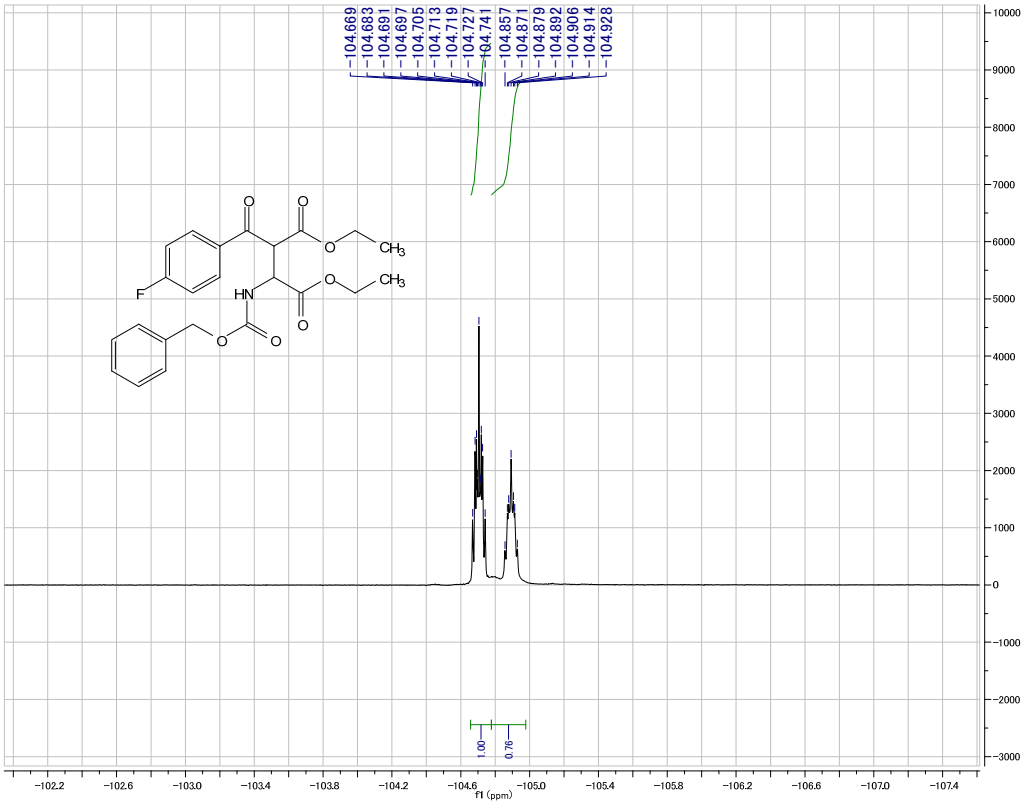
53.414
13.766
13.741
13.686
f1 (ppm)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104.727
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104.879
104.892
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104.928
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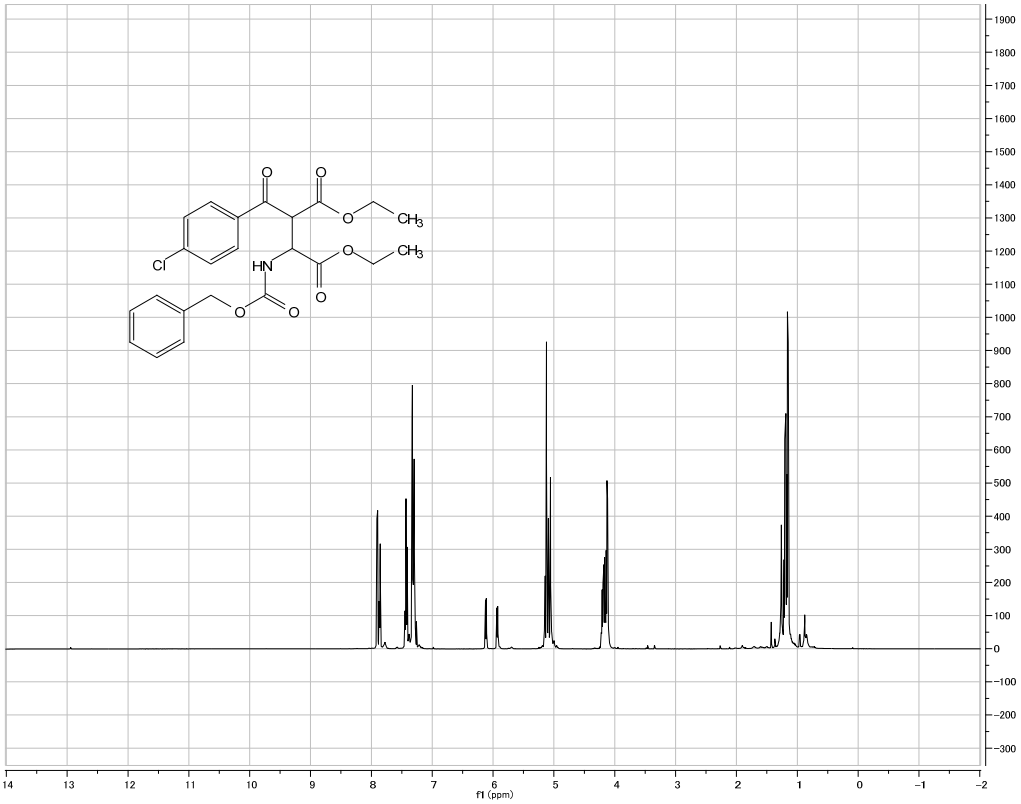
0.76
f1 (ppm)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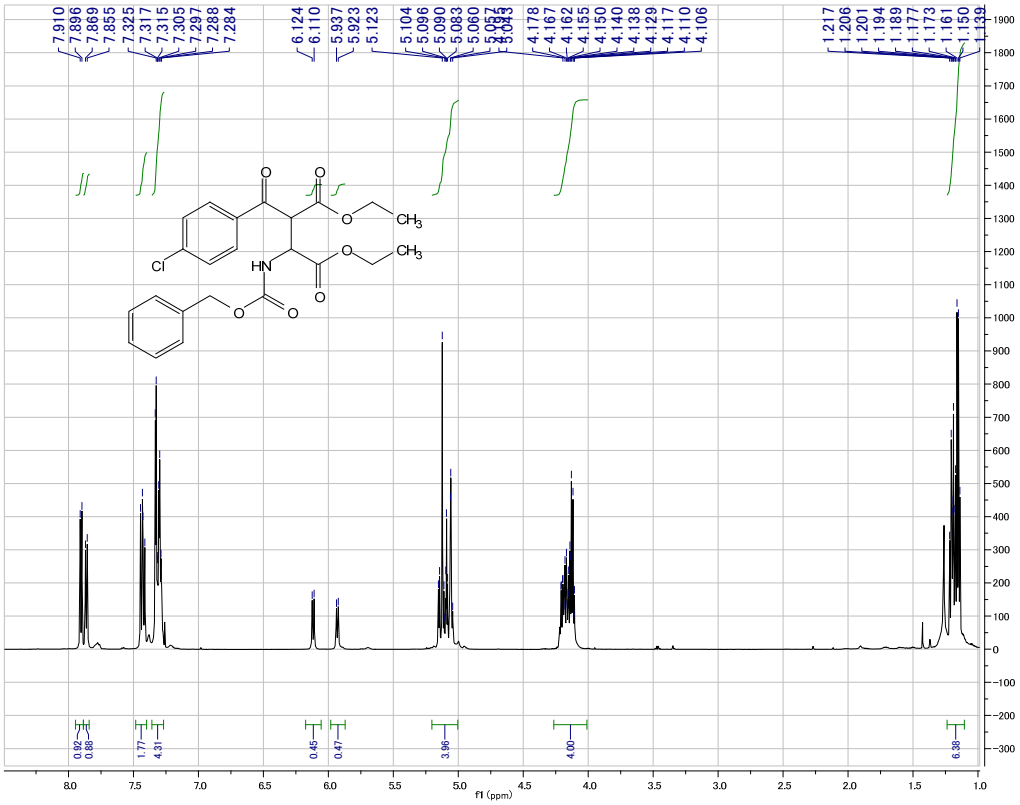
O
O
CH3
Cl
HN
O
CH3
O
O
O
O
f1 (ppm)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6.110
5.937
5.923
5.123
5.104
5.096
5.090
5.083
5.060
4.178
4.167
4.162
4.155
4.150
4.140
4.138
4.129
4.117
4.110
4.106
1.217
1.206
1.201
1.194
1.189
1.177
1.173
1.161
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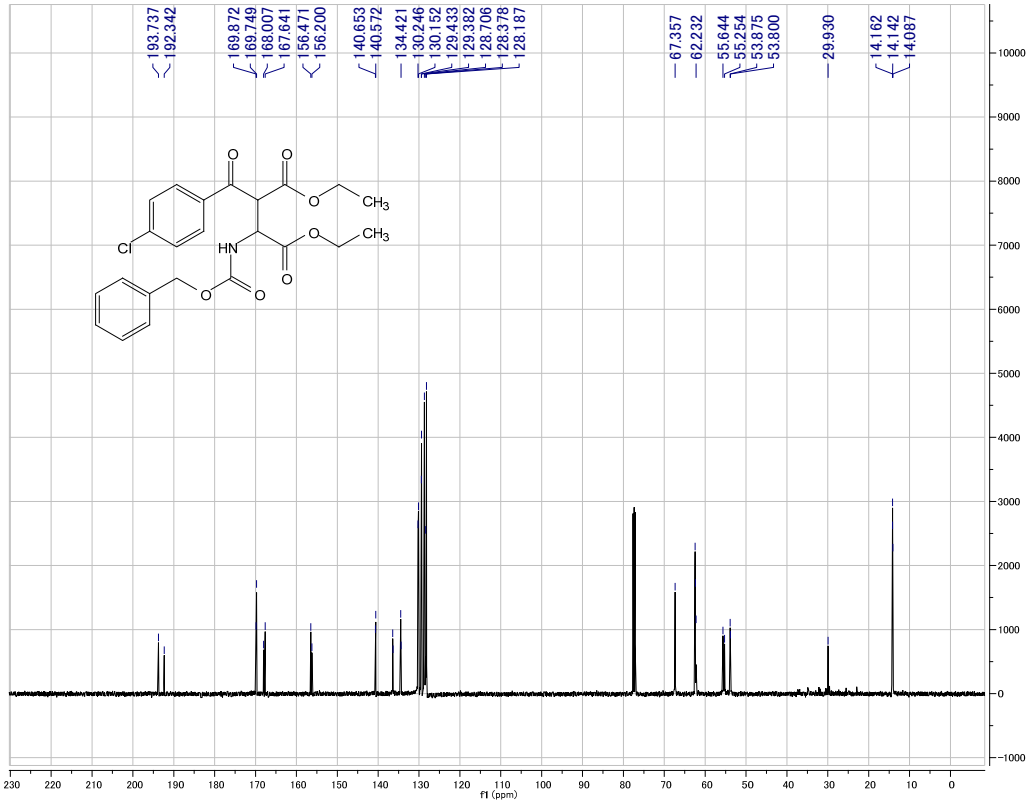
f1 (ppm)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130.152
129.433
129.382
128.706
128.378
128.187
67.357
62.232
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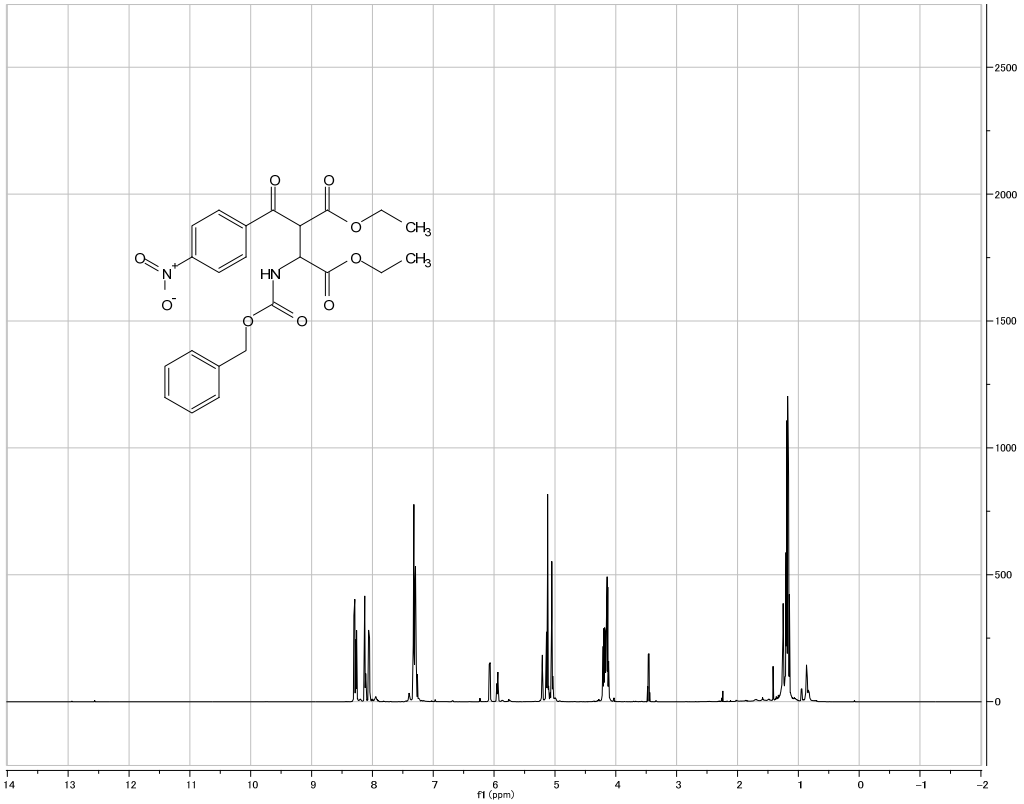
53.875
53.800
29.930
14.162
14.142
14.087
Cl
HN
O
CH3
f1 (ppm)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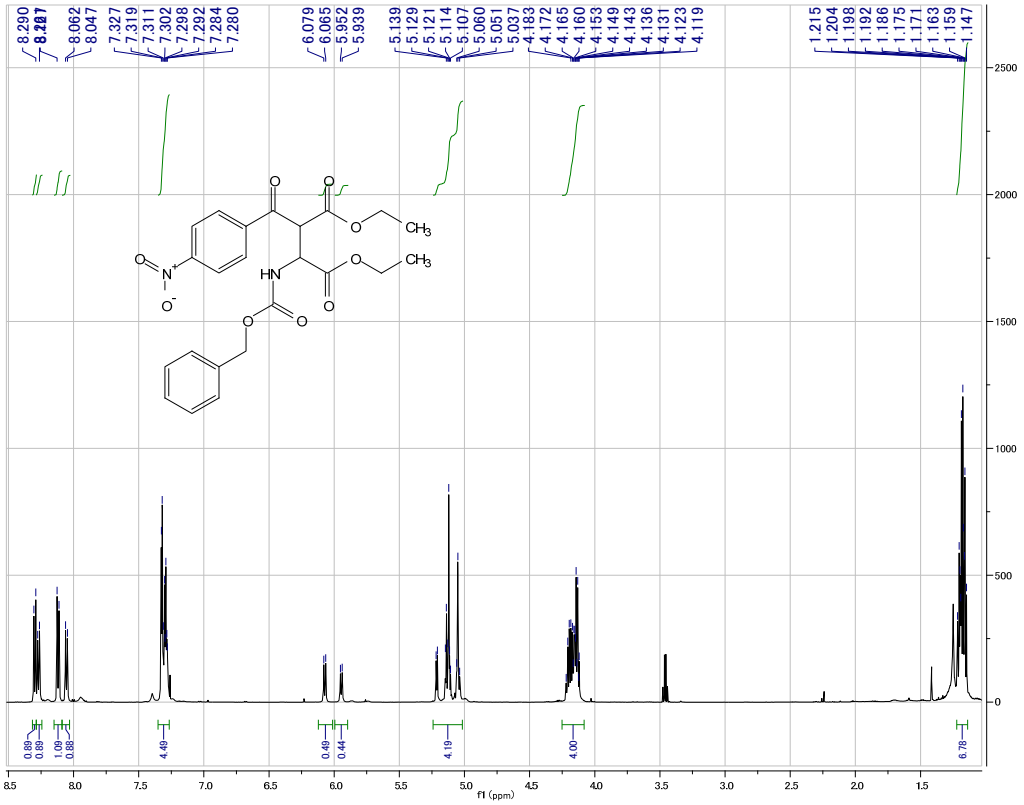
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7.302
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7.292
7.284
7.280
6.079
6.065
5.952
5.939
5.139
5.129
5.121
5.114
5.107
5.060
5.051
5.037
4.183
4.172
4.165
4.160
4.153
4.149
4.143
4.136
4.131
4.123
4.119
1.215
1.204
1.198
1.192
1.186
1.175
1.171
1.163
1.159
1.147
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0.89
1.08
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0.49
0.44
4.19
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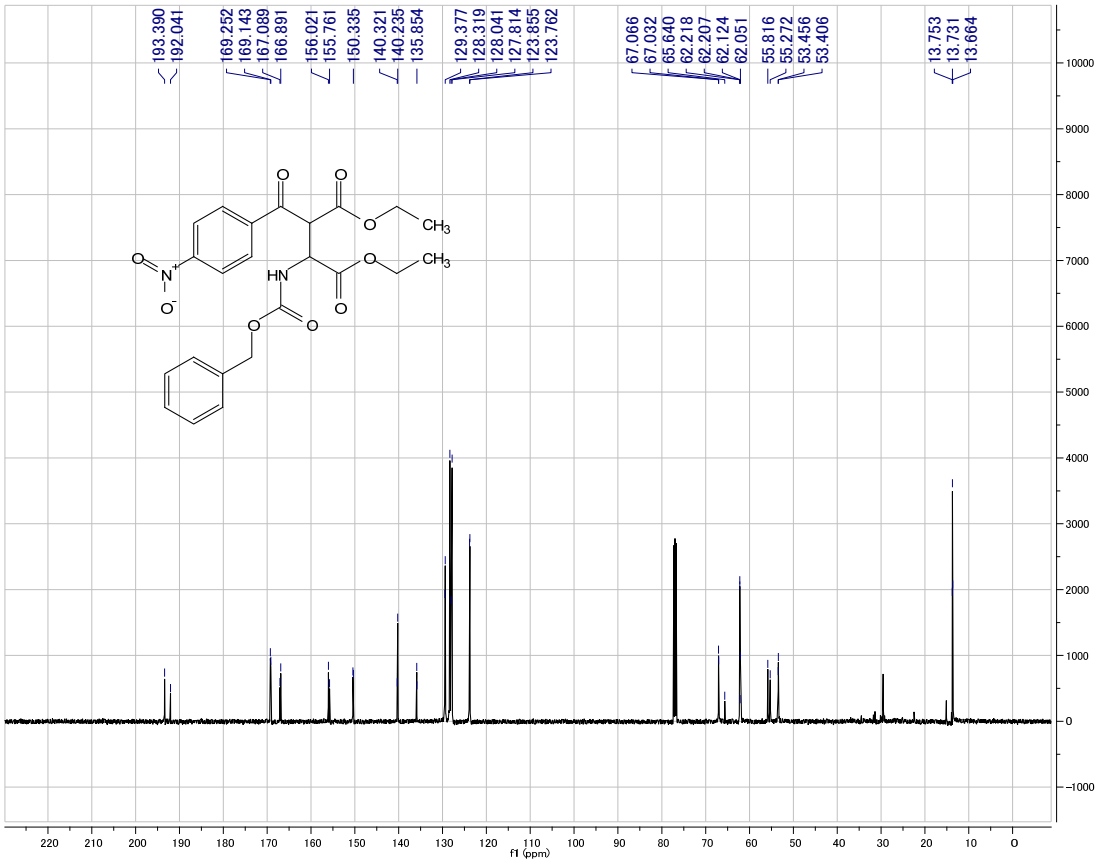
6.78
f1 (ppm)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140.235
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128.319
128.041
127.814
123.855
123.762
67.066
67.032
65.640
62.218
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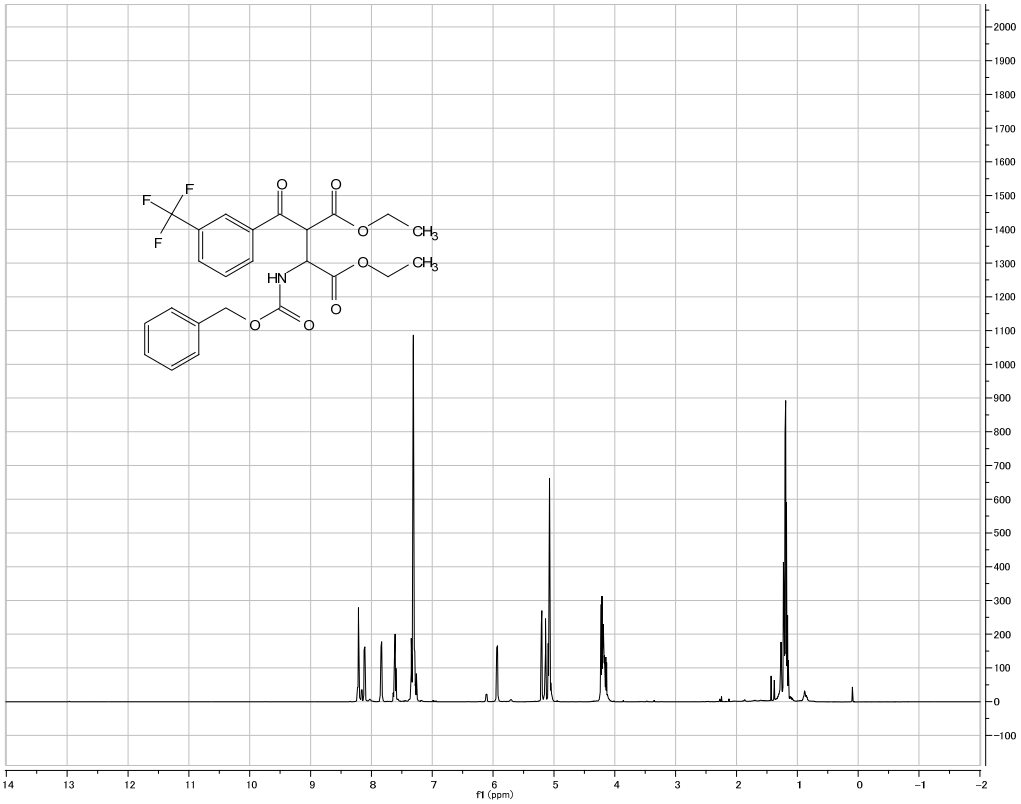
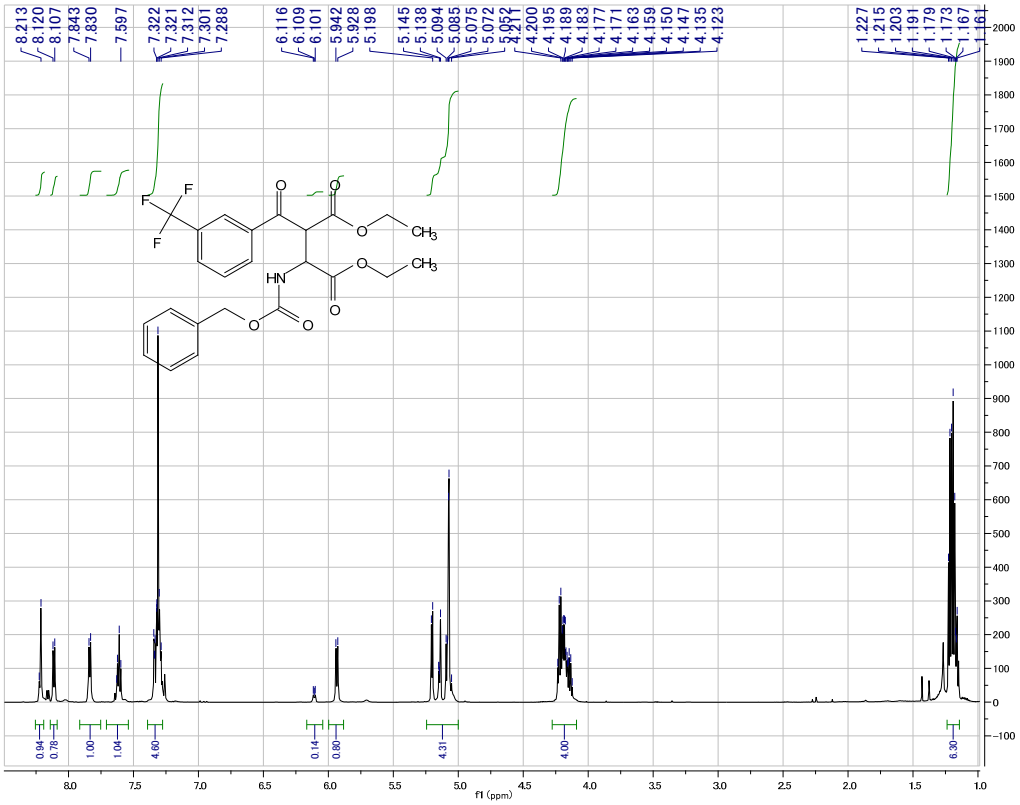
55.816
55.272
53.456
53.406
13.753
13.731
13.664
f1 (ppm)


F
F
F
O
O
O
CH3
HN
O
CH3
O
O
O
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
f1 (ppm)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5.138
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5.075
5.072
4.200
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4.189
4.183
4.177
4.171
4.163
4.159
4.150
4.147
4.135
4.123
1.227
1.215
1.203
1.191
1.179
1.173
1.167
1.161
F
F
F
O
O
O
CH3
HN
O
CH3
O
O
O
0.94
0.78
1.00
1.04
4.60
0.14
0.80
4.31
4.00
6.30
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
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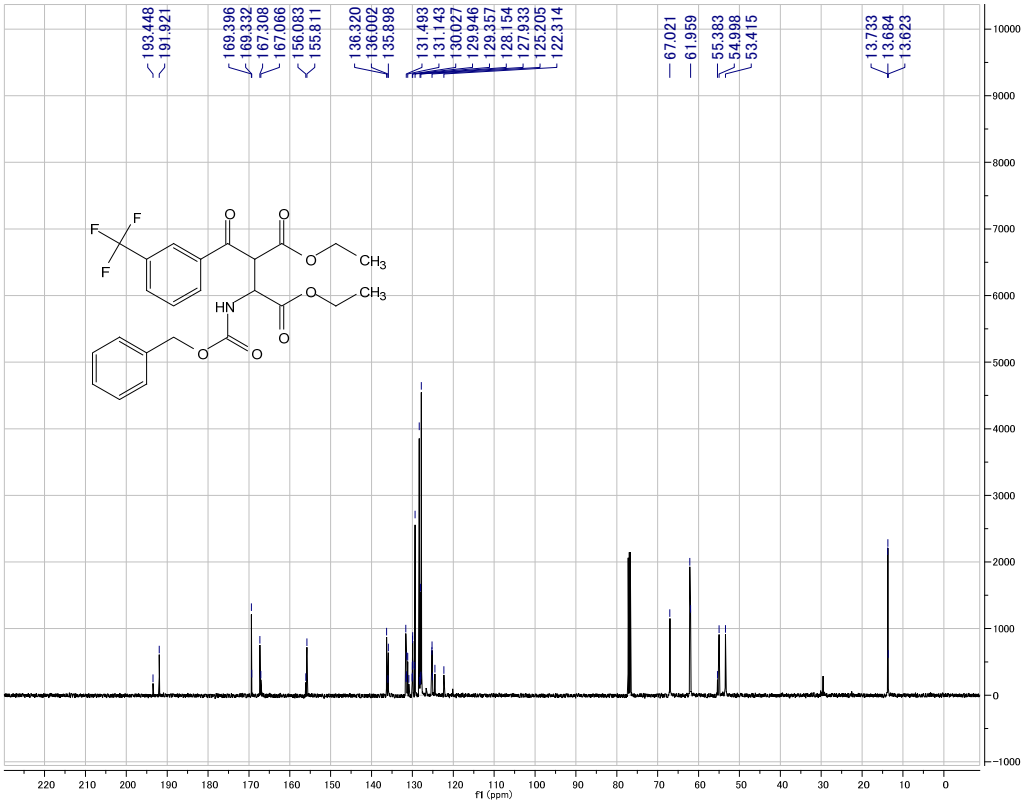
1.5
1.0
f1 (ppm)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130.027
129.946
129.357
128.154
127.933
125.205
122.314
67.021
61.959
55.383
54.998
53.415
13.733
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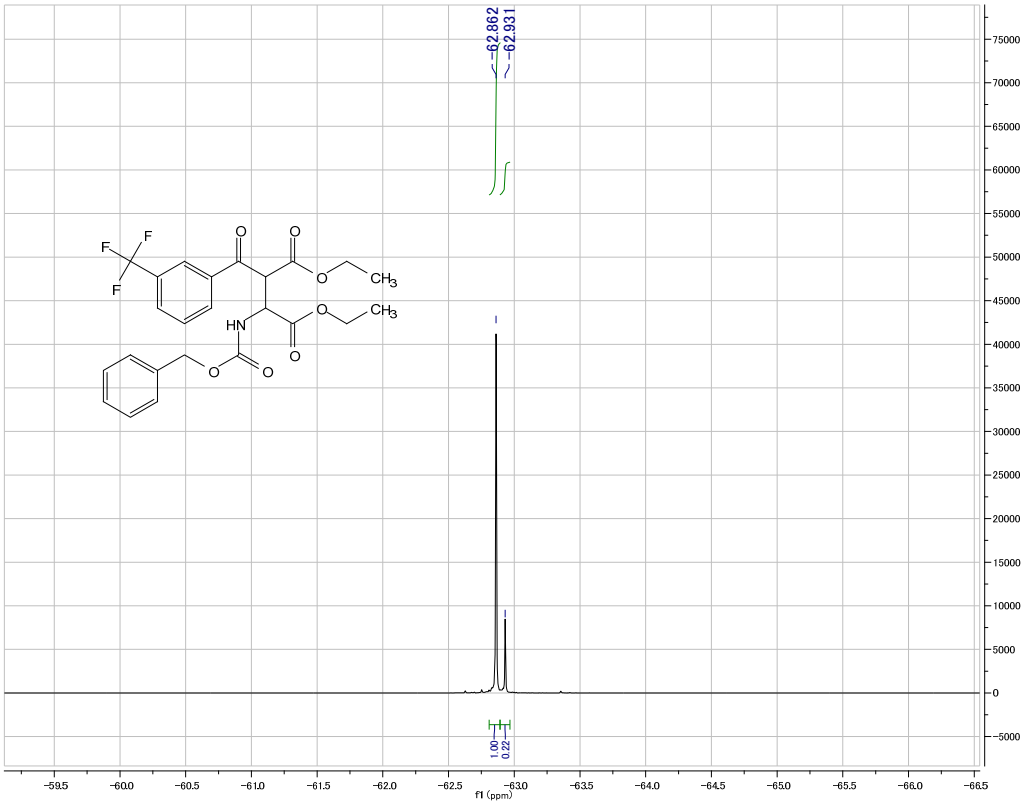
F
F
F
O
O
O
CH3
HN
O
CH3
O
O
O
f1 (ppm)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F
F
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O
O
CH3
HN
O
CH3
O
O
O
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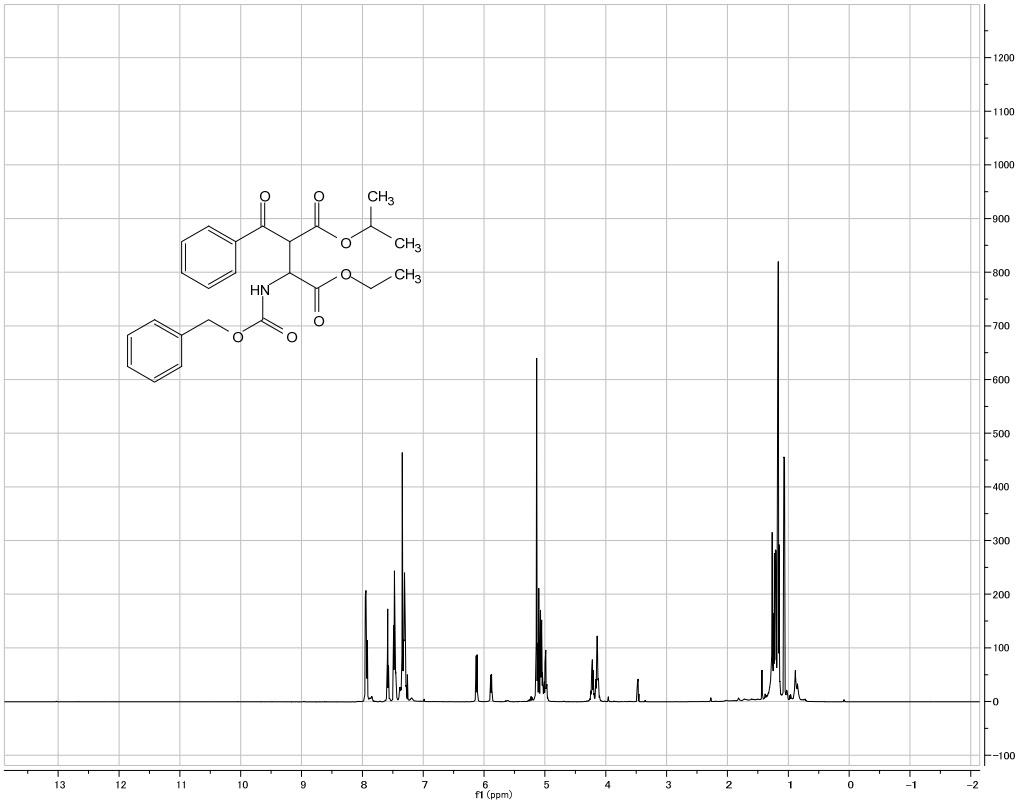
0.22
f1 (ppm)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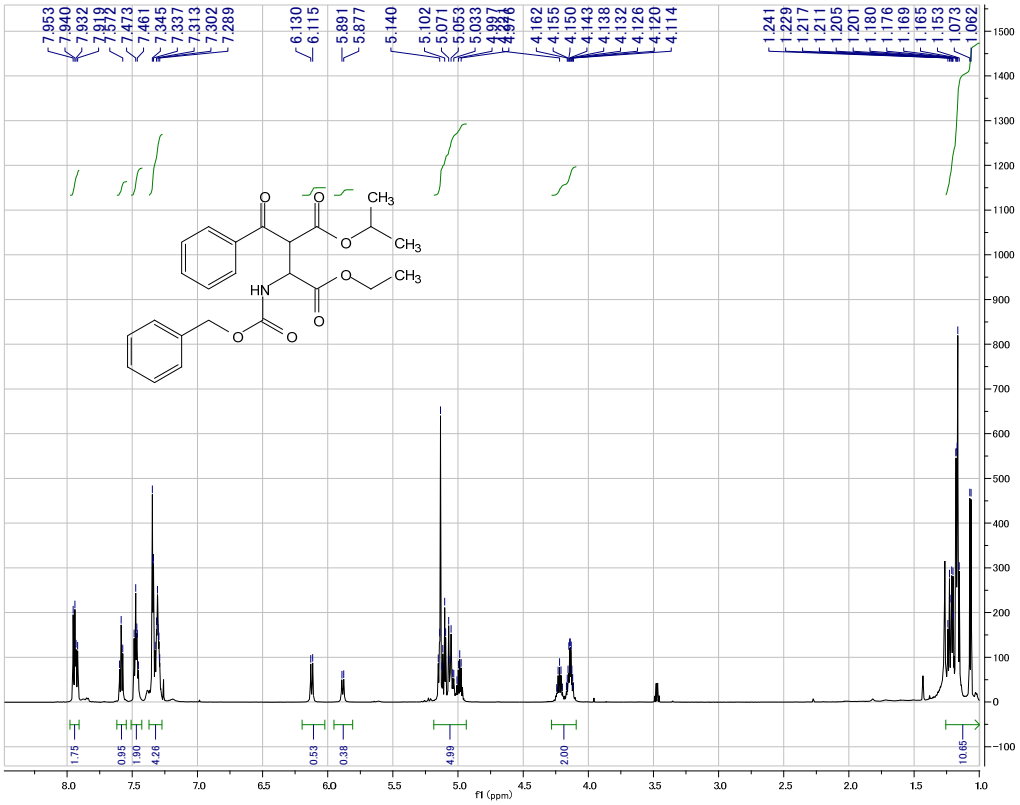
CH3
O
CH3
HN
O
O
CH3
O
O
f1 (ppm)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6.115
5.891
5.877
5.140
5.102
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5.053
5.033
4.162
4.155
4.150
4.143
4.138
4.132
4.126
4.120
4.114
1.241
1.229
1.217
1.211
1.205
1.201
1.180
1.176
1.169
1.165
1.153
1.073
1.062
O
O
CH3
O
CH3
HN
O
O
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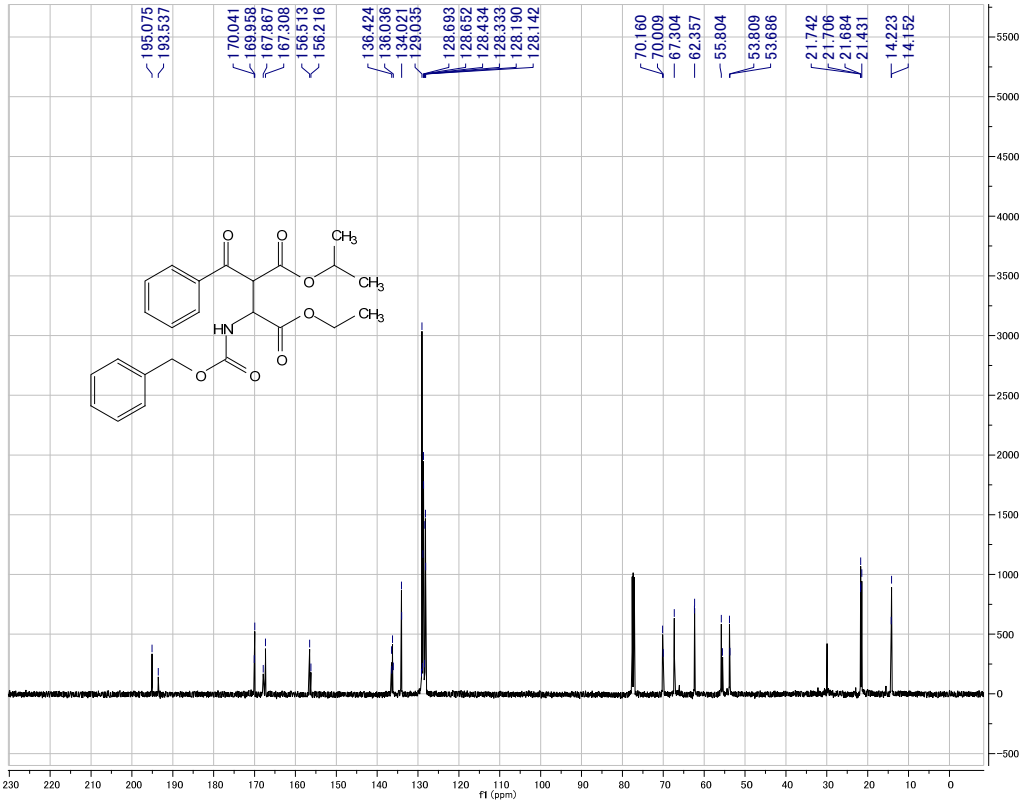
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70.009
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21.431
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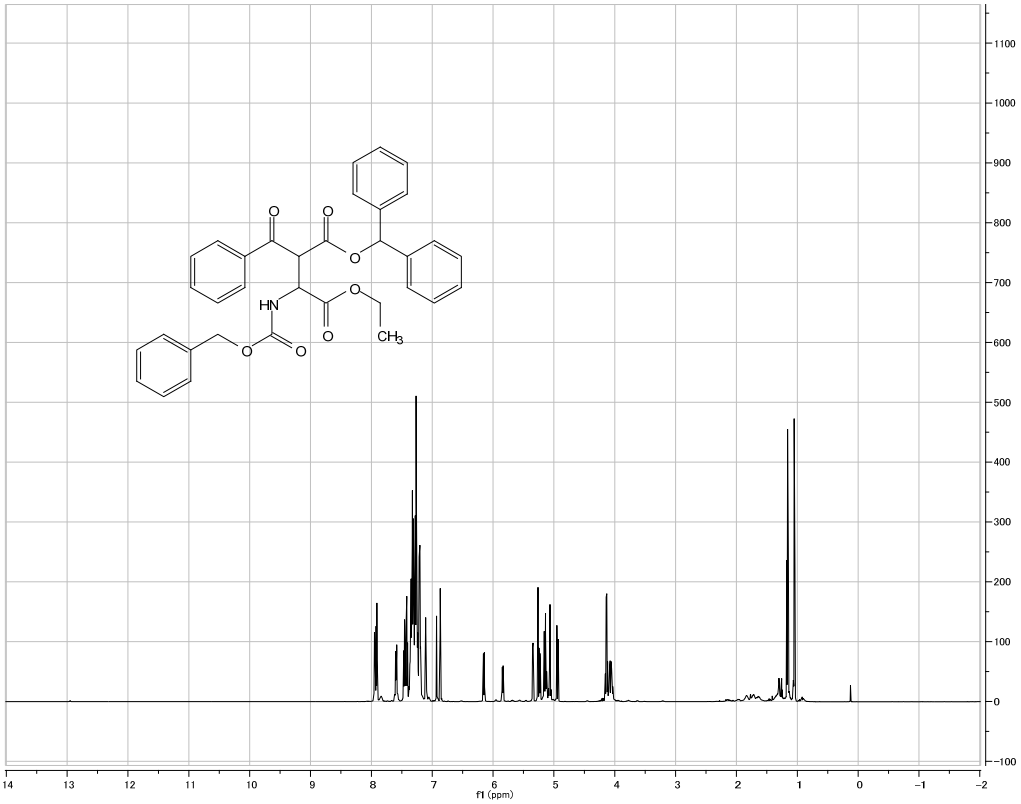
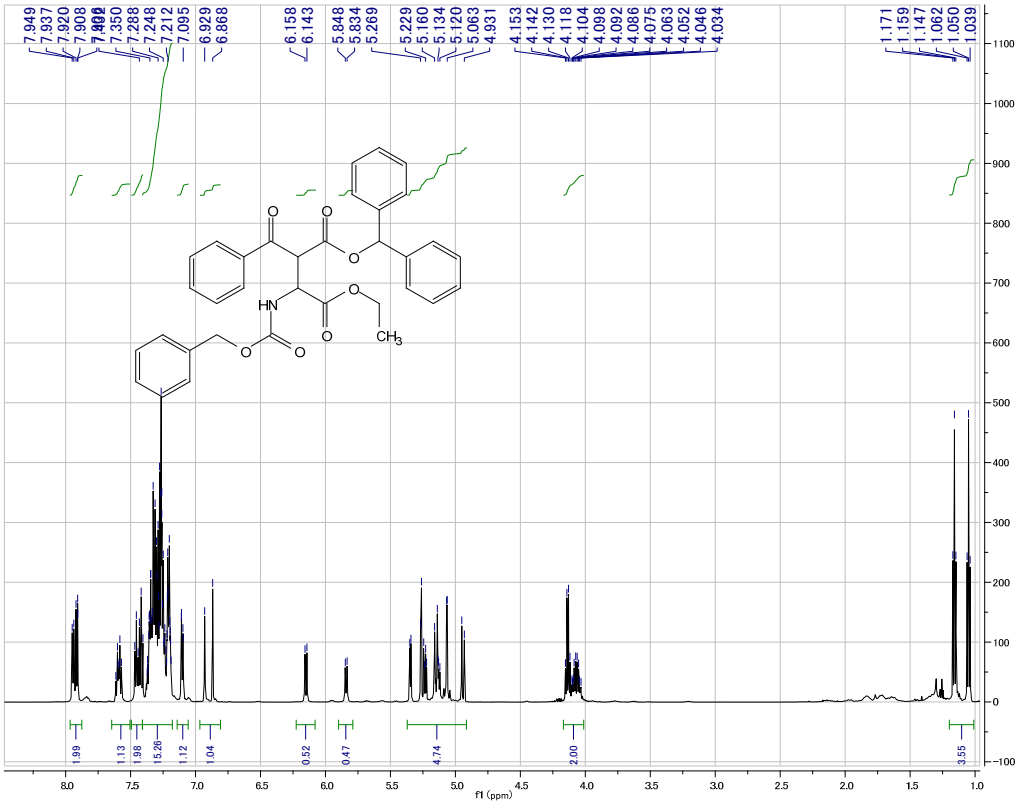
f1 (ppm)


HN
O
CH3
f1 (ppm)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6.143
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5.834
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5.120
5.063
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4.142
4.130
4.118
4.104
4.098
4.092
4.086
4.075
4.063
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4.046
4.034
1.171
1.159
1.147
1.062
1.050
1.039
HN
O
CH3
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3.55
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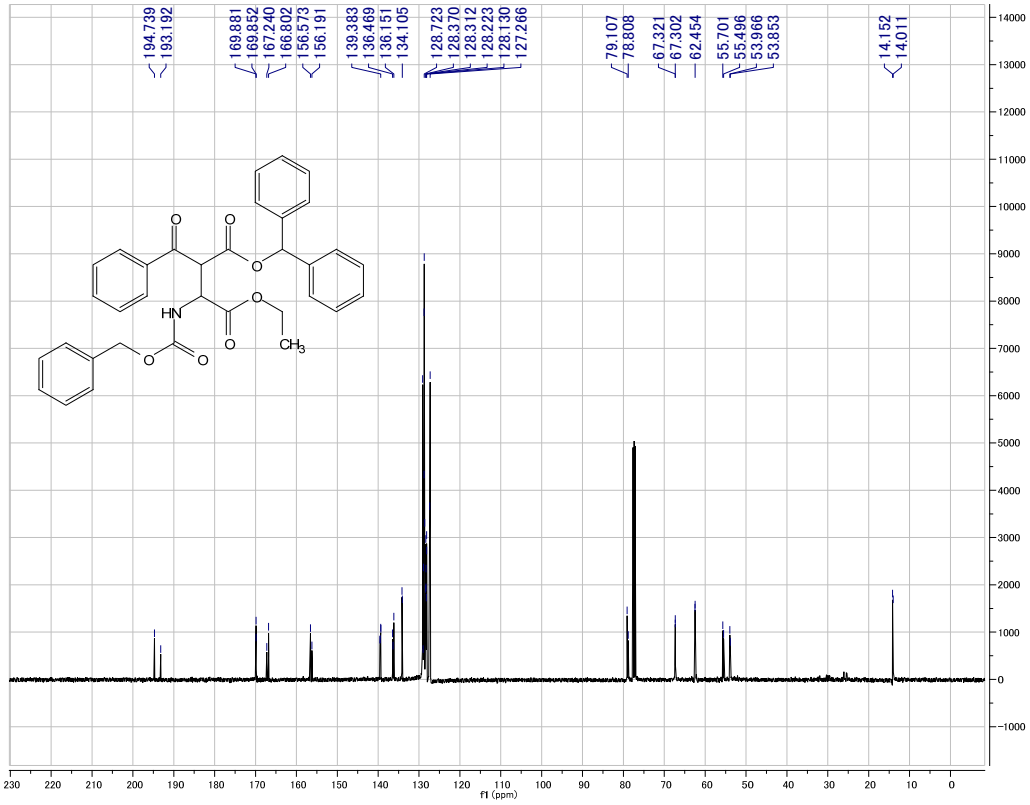
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128.130
127.266
79.107
78.808
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53.853
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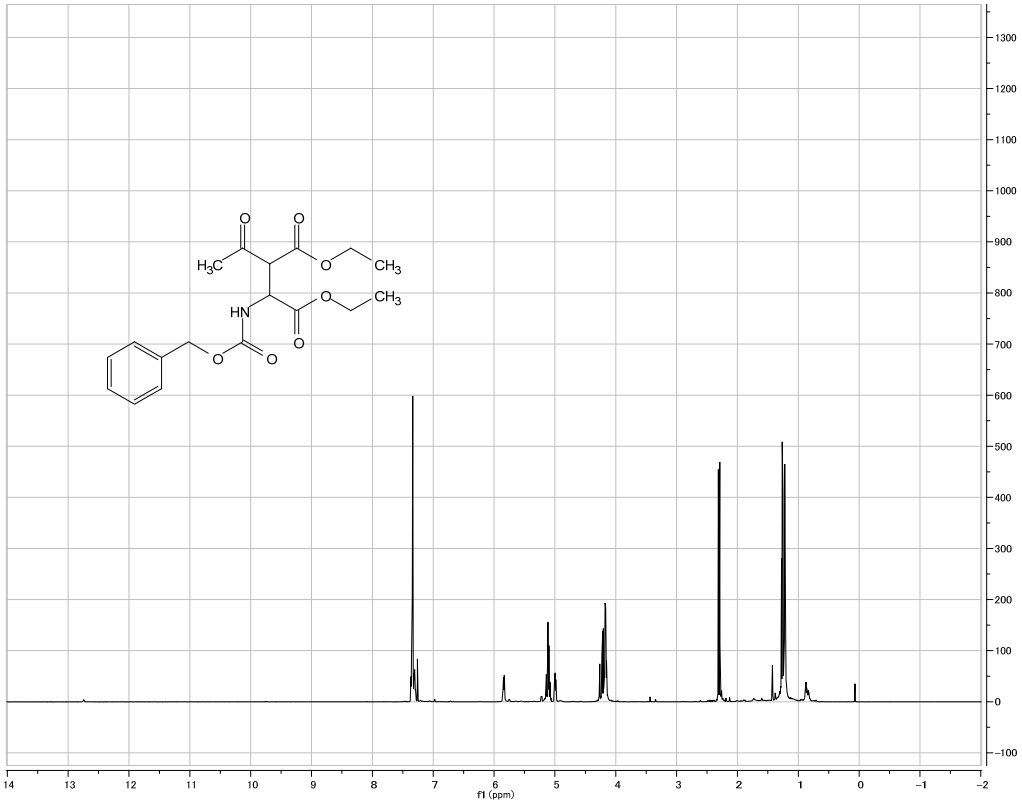
14.011
HN
O
CH3
f1 (ppm)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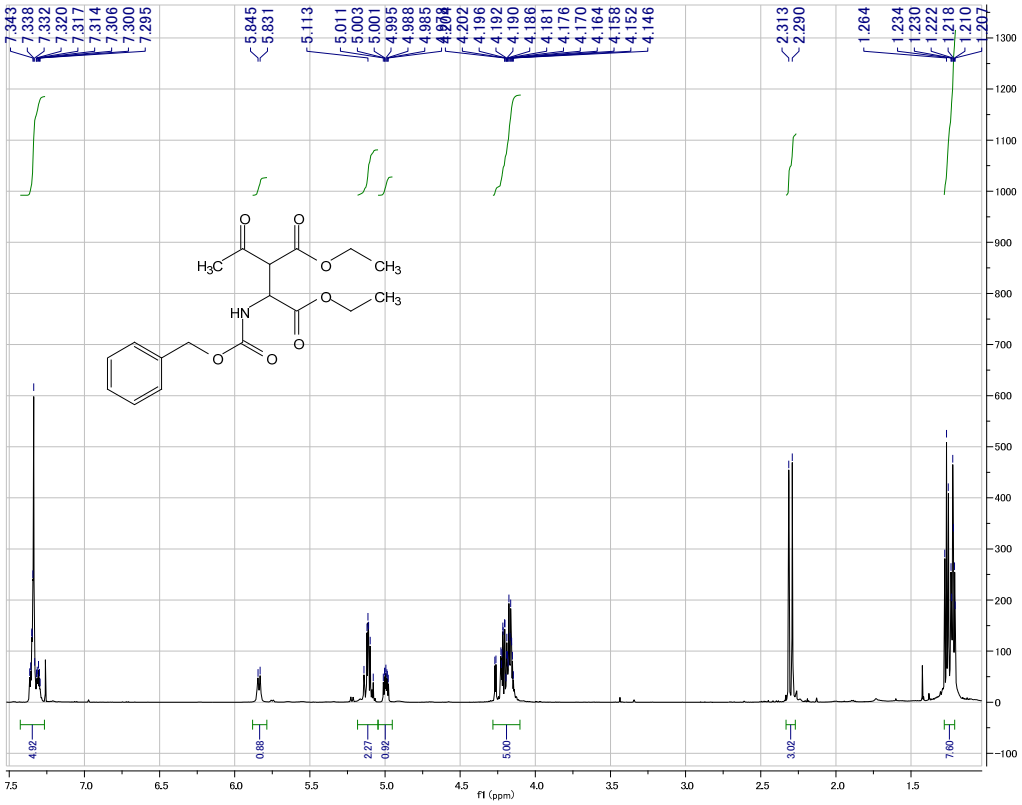
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7.300
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5.831
5.113
5.011
5.003
5.001
4.995
4.988
4.985
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4.196
4.192
4.190
4.186
4.181
4.176
4.170
4.164
4.158
4.152
4.146
2.313
2.290
1.264
1.234
1.230
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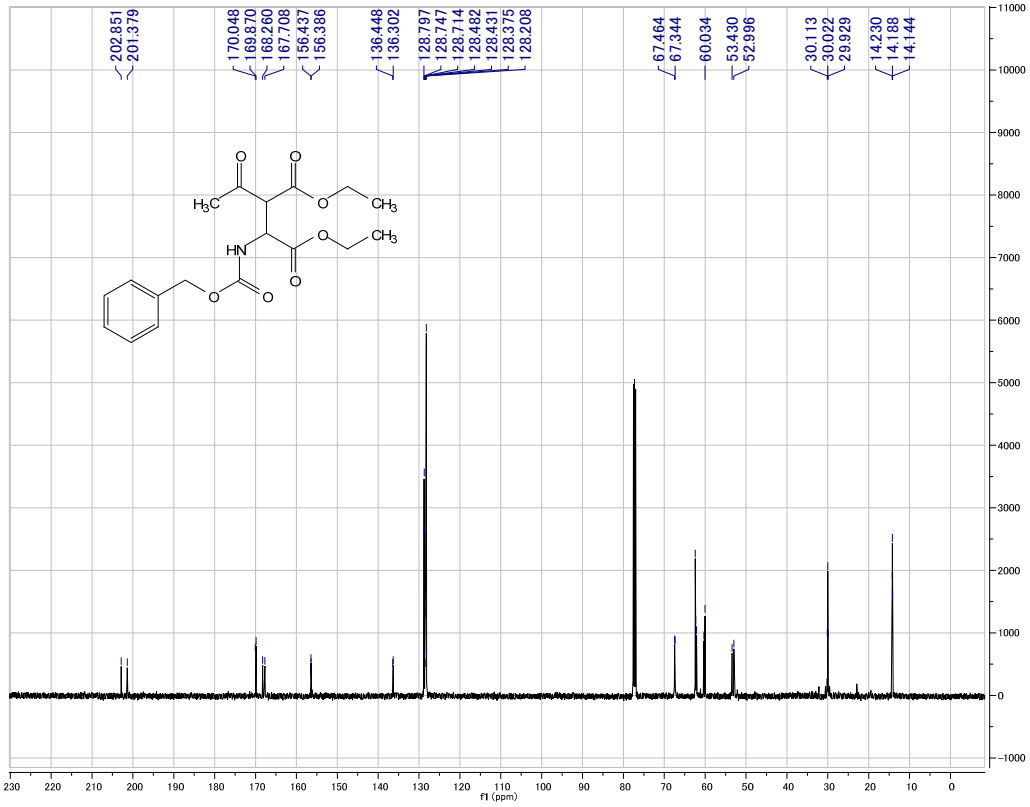
5.00
3.02
7.60
f1 (ppm)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128.431
128.375
128.208
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30.113
30.022
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14.230
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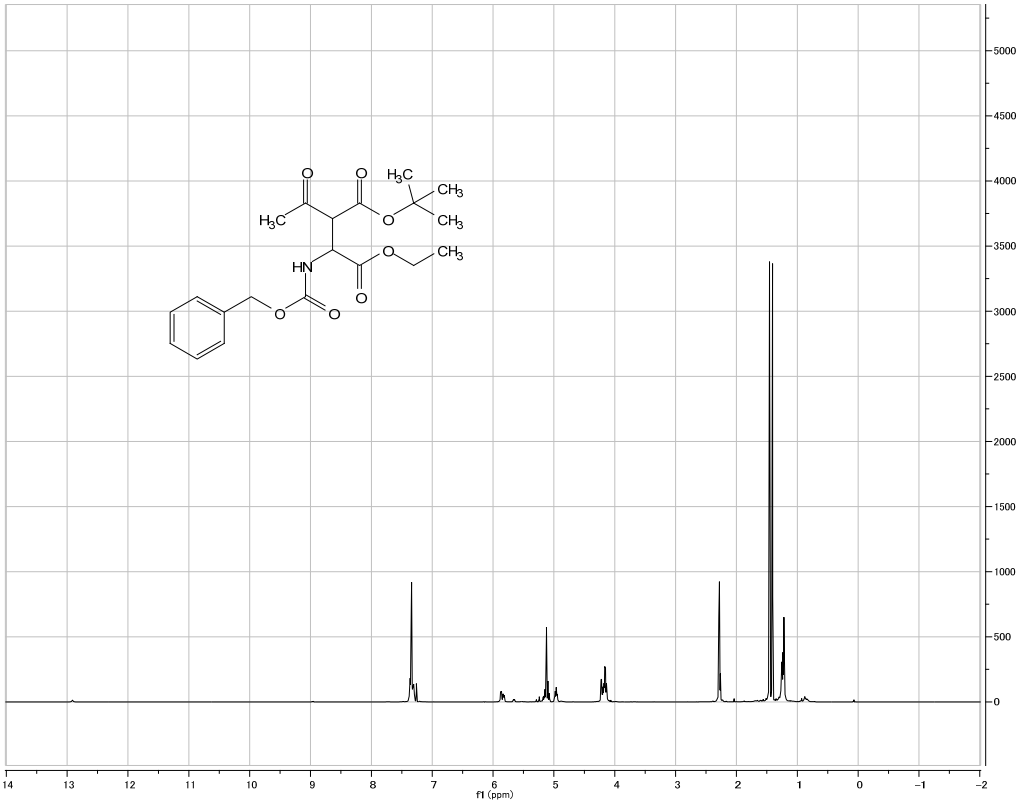
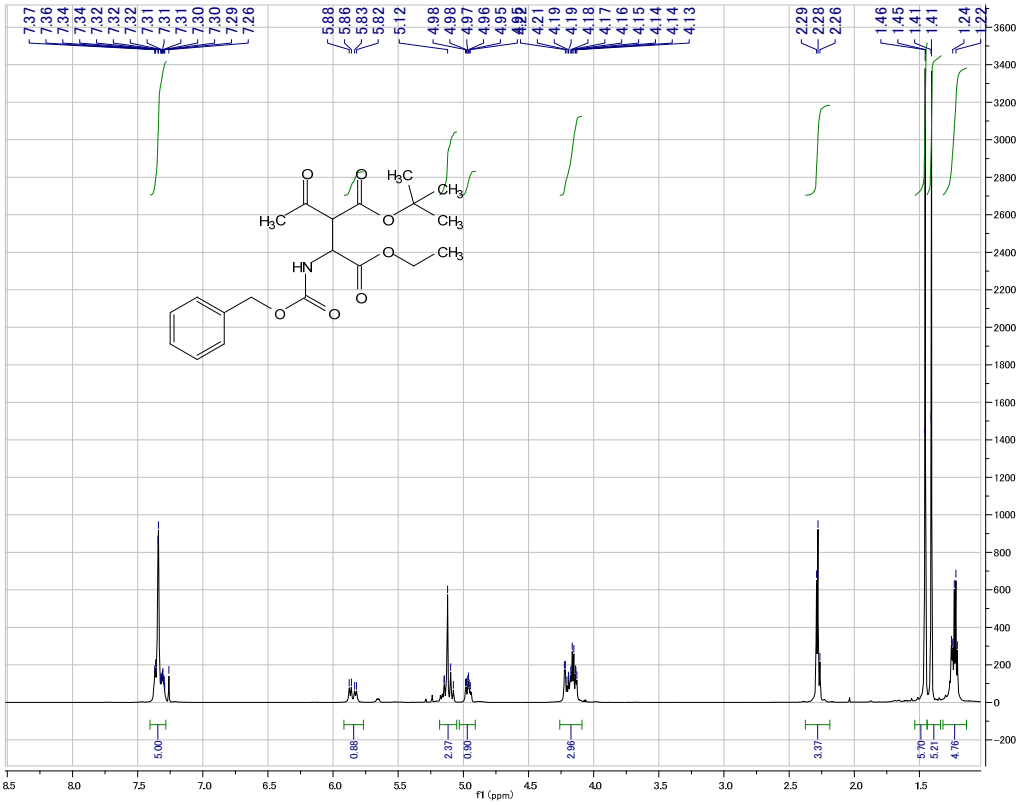
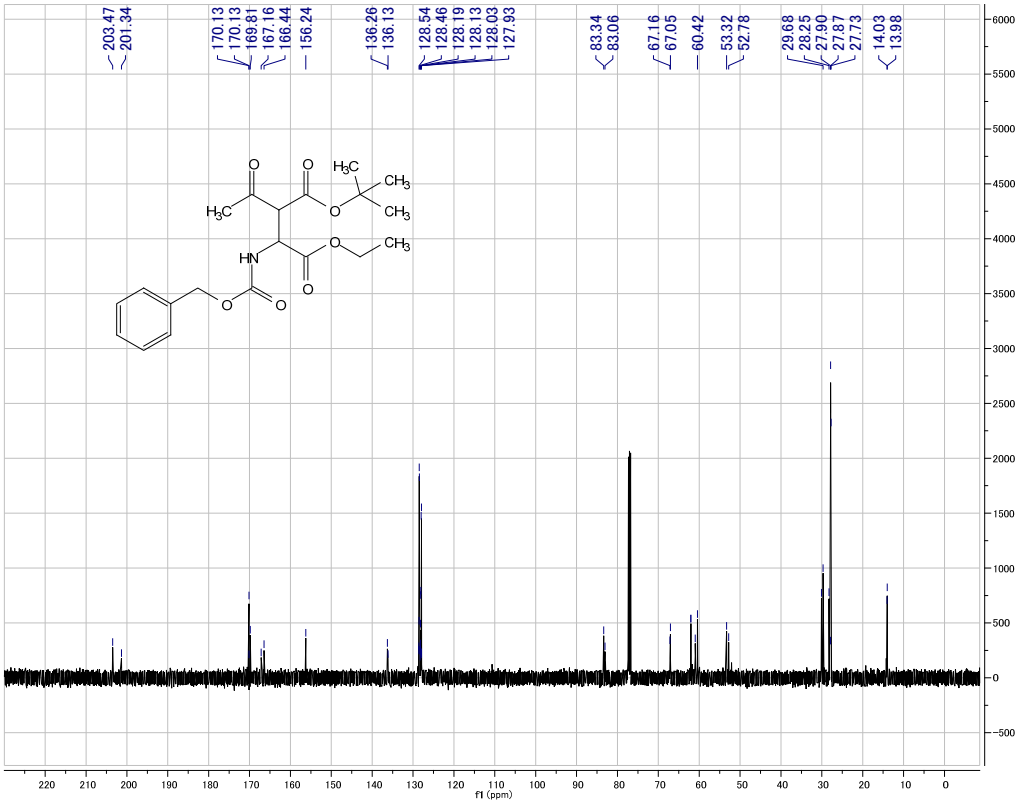
14.144
f1 (ppm)



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128.13
128.03
127.93
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83.06
67.16
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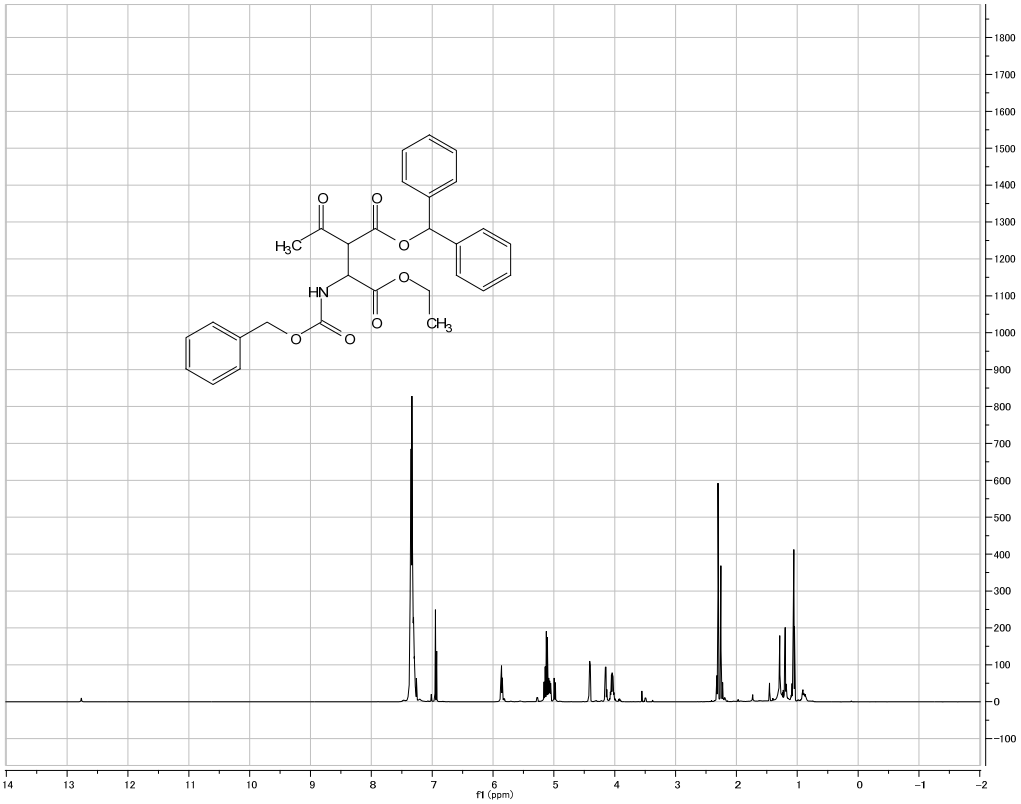
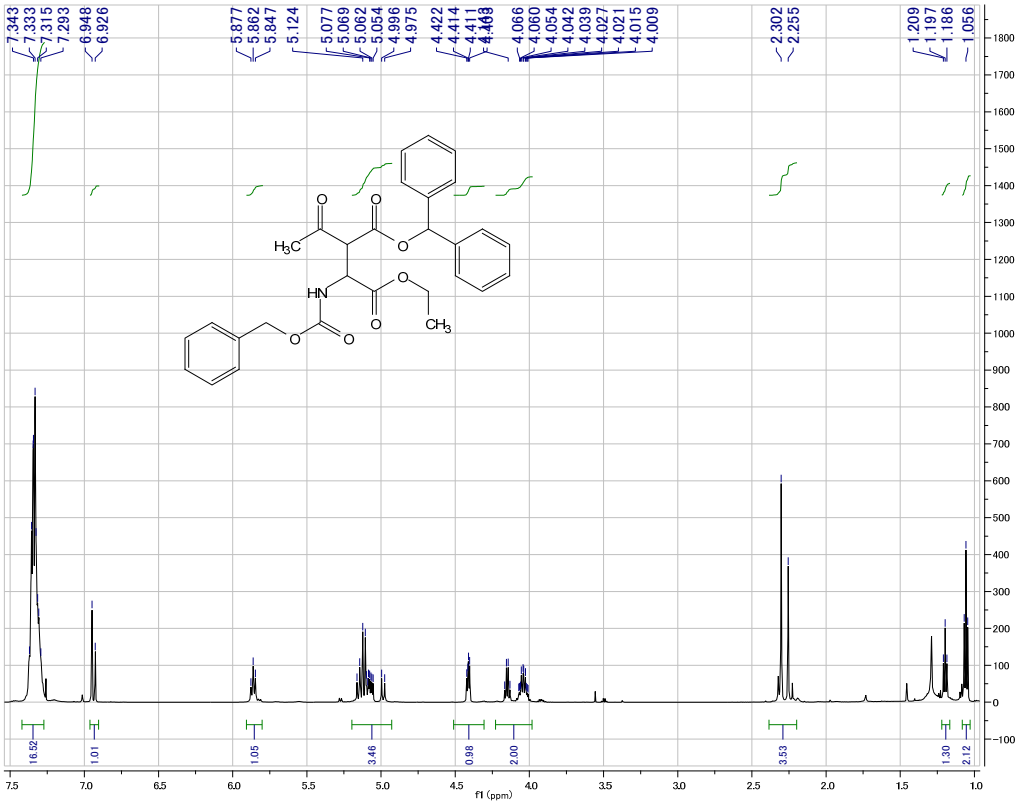
13.98
f1 (ppm)

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4.996
4.975
4.422
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4.054
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4.039
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4.021
4.015
4.009
2.302
2.255
1.209
1.197
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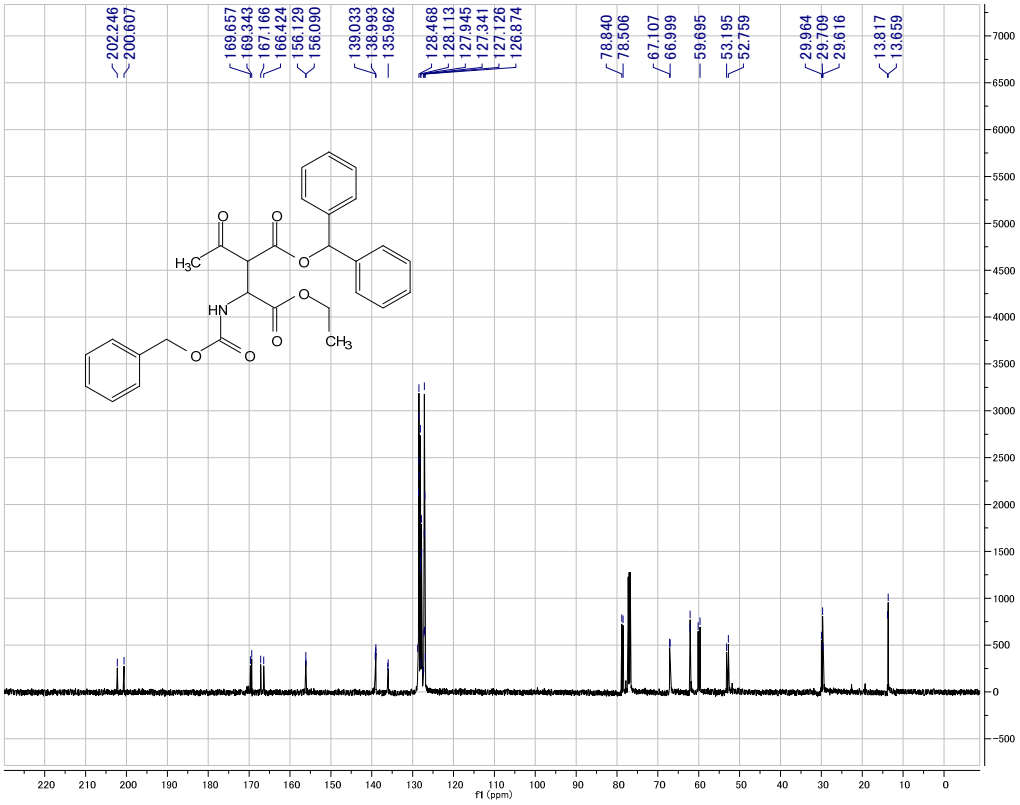
f1 (ppm)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138.993
135.962
128.468
128.113
127.945
127.341
127.126
126.874
78.840
78.506
67.107
66.999
59.695
53.195
52.759
29.964
29.709
29.616
13.817
13.659
O
O
H3C
O
HN
O
O
CH3
O
O
f1 (ppm)

X-Ray Structure of 4h

Experimental

A crystal mounted on a diffractometer was collected data at 100 K. The intensities of the reflections were collected by means of a Bruker APEX II DUO CCD diffractometer ($Cu_{K\alpha}$ radiation, λ=1.54178 Å), and equipped with an Oxford Cryosystems nitrogen flow apparatus. The collection method involved 1.0° scans in ω at 30°, 55°, 80° and 115° in 2θ. Data integration down to 0.84 Å resolution was carried out using SAINT V7.46 A (Bruker diffractometer, 2009) with reflection spot size optimisation. Absorption corrections were made with the program SADABS (Bruker diffractometer, 2009). The structure was solved by the direct methods procedure and refined by least-squares methods again F^2 using SHELXS-97 and SHELXL-97 (Sheldrick, 2008) with OLEX 2 interface (Dolomanov, et al., 2009). Non-hydrogen atoms were refined anisotropically, and hydrogen atoms were allowed to ride on the respective atoms. Crystal data as well as details of data collection and refinement are summarized in Table S3. The Ortep plots produced with SHELXL-97 program, and the other drawings were produced with Accelrys DS Visualizer 2.0 (Accelrys, 2007).

Table S3. Crystal Data and Structure Refinement

Chemical formula	$C_{34}H_{31}NO_7$
M_r	565.60
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	100
a, *b*, *c* (Å)	5.2357 (6), 45.397 (5), 11.9994 (13)
b (°)	94.399 (6)
V (Å^3)	2843.7 (5)
Z	4
Radiation type	Cu *K*a
m (mm^{-1})	0.76

Crystal size (mm)	0.25 × 0.16 × 0.12
Data collection	
Diffractometer	Bruker D8 goniometer with CCD area detector diffractometer
Absorption correction	Multi-scan *SADABS*
T_{min}, T_{max}	0.833, 0.915
No. of measured, independent and observed [$I > 2s(I)$] reflections	52512, 9238, 9005
R_{int}	0.060
$(\sin q/l)_{max}$ (Å^{-1})	0.597
Refinement	
$R[F^2 > 2s(F^2)]$, $wR(F^2)$, S	0.032, 0.077, 1.05
No. of reflections	9238
No. of parameters	762
No. of restraints	2
H-atom treatment	H atoms treated by a mixture of independent and constrained refinement
$D\rho_{max}$, $D\rho_{min}$ (e Å^{-3})	0.13, -0.16
Absolute structure	Flack H D (1983), Acta Cryst. A39, 876-881
Absolute structure parameter	-0.15 (10)

Computer programs: *APEX2* v2009.3.0 (Bruker-AXS, 2009), *SAINT* 7.46A (Bruker-AXS, 2009), *SHELXS97* (Sheldrick, 2008), *SHELXL97* (Sheldrick, 2008), Bruker *SHELXTL* (Sheldrick, 2008).

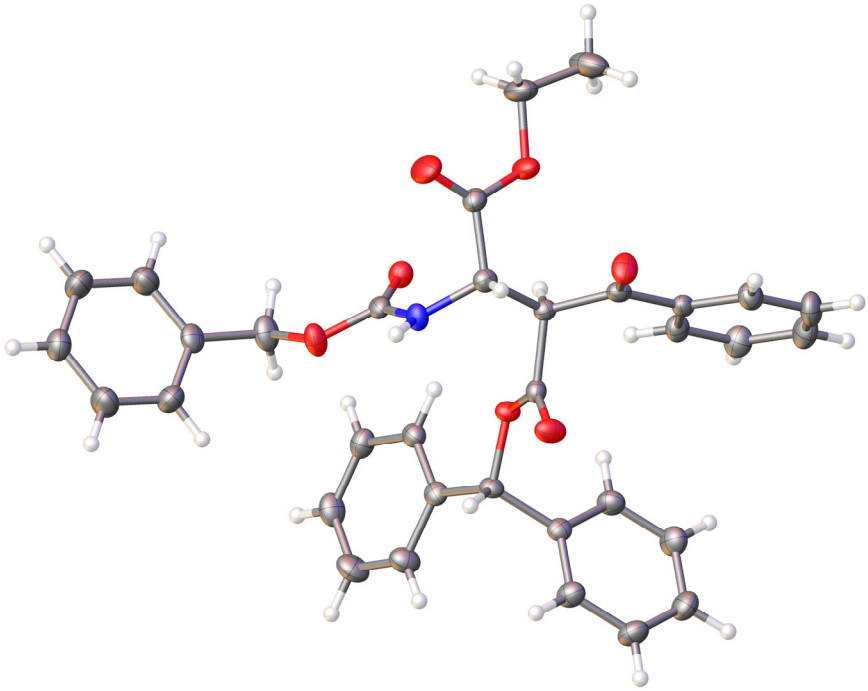

Figure S1. Perspective views showing 50% probability displacement.

References:

1. Bruker AXS APEX II, Bruker AXS, Madison, Wisconsin, 2009.
2. Accelrys DS Visualizer v2.0.1, Accelrys Software. Inc., 2007.
3. Sheldrick, G. M. *Acta Cryst.* **2008**, *A64*, 112-122.
4. Dolomanov, O.V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst.* **2009**, *42*, 339-341.