

Enzyme-controlled stereoselective radical cyclization to arenes enabled by metalloredox biocatalysis

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Supplementary Methods

General methods

General. Unless otherwise noted, all chemicals and reagents were obtained from commercial suppliers (Sigma-Aldrich, VWR, Alfa Aesar, Combi-Blocks, AmBeed, Oakwood, and Enamine) and used without further purification. Silica gel chromatography was carried out using AMD Silica Gel 60, 230-400 mesh. ^1H and ^{13}C NMR spectra were recorded on a Varian 500, Varian 600, Bruker 400 or 500 MHz instrument in CDCl_3 or $\text{DMSO}-d_6$ and are referenced to residual solvent signals. ^{19}F NMR spectra (where applicable) were recorded on a Bruker 400 MHz and are referenced to CFCl_3 as the external standard. Data for ^1H NMR are reported as follows: chemical shift (δ : ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sext = sextet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, dq = doublet of quartets, ddd = doublet of doublet of doublets, ddt = doublet of doublet of triplets, brs = broad singlet), coupling constant (Hz), integration. Sonication on a small scale was performed using a BioLogics ultrasonic homogenizer (model 150VT) equipped with a stepped microtip. Sonication on a large scale was performed using a Branson Digital Sonifier 450 Ultrasonic Processor. All IR spectra were recorded on a Thermo Scientific Nicolet iS5 spectrometer (iD5 ATR, diamond). High-resolution mass spectrometry data was obtained at the Mass Spectral Facilities at the University of California Santa Barbara and the University of California Irvine. High-resolution accurate mass (HRAM) ESI data was analyzed on a Waters LCT Premier mass spectrometer with a LEAP PAL autosampler with isocratic MeOH flow (no column; direct injection). Molecular formulas (MF) were validated by lock mass calibration to sodiated polyethylene glycol polymer or sodiated monethylether polyethylene glycol polymer standards. High-resolution accurate mass (HRAM) EI data was acquired using a Waters LCT Premier time-of-flight (TOF) mass spectrometer. Masses of positively charged ions were calibrated using a methanol solution of polyethylene glycol or polyethylene glycol monomethyl ether as an internal standard. All samples were dissolved in methanol and were directly infused unless otherwise noted. Synthetic reactions were monitored by thin layer chromatography (TLC, Silicycle TLG-R10014BK-323 gel plates) using a UV-lamp or an appropriate TLC stain for visualization.

E. coli cells were grown using Luria-Bertani medium (LB) or Hyperbroth (AthenaES) (HB) with 0.1 mg/mL ampicillin (LB_{amp} or HB_{amp}). Primer sequences for site-saturation mutagenesis or site-directed mutagenesis are provided below. T5 exonuclease, Phusion DNA polymerase, and *Taq*

DNA ligase were purchased from New England Biolabs (NEB, Ipswich, MA). M9-N minimal medium (abbreviated as M9-N buffer; pH 7.4) was used as a buffering system for whole cells and lysates, unless otherwise specified. M9-N buffer was used without a nitrogen source; it contains 47.7 mM Na₂HPO₄, 22.0 mM KH₂PO₄, 8.6 mM NaCl, 2.0 mM MgSO₄, and 0.1 mM CaCl₂.

Chromatography. Analytical chiral HPLC was conducted using a Shimadzu i-series (66 MPa) instrument with hexanes and isopropanol as the mobile phase. Enantiomers were separated using a Chiralpak IC/IB-N5/IG column (4.6 × 250 mm, 5 micron) from Daicel. Gas chromatography-mass spectrometry (GC-MS) analyses were carried out using a Shimadzu GCMS-QP2020NX system with a GC-2030 front end and a J&W HP-5ms column (30 m × 0.320 mm, 0.25 µm film).

Cloning and site-saturation mutagenesis. pET-22b(+) was used as the cloning and expression vector for P450s used in this study as previously described.¹ The genes of haem proteins were cloned into pET-22b(+) between the Nde I and Xho I restriction sites. Site-saturation mutagenesis was performed using the “22 codon-trick” method as described by Kille et al.² The PCR products were digested with DpnI, gel purified, and ligated using a Gibson mix prepared from 5X isothermal (ISO) reaction buffer (25% PEG-8000, 500 mM Tris-HCl pH 7.5, 50 mM MgCl₂, 50 mM DTT, 1 mM each of the dNTPs, and 5 mM NAD), T5 exonuclease, Phusion DNA polymerase, and *Taq* DNA ligase.³ The ligation mixture was used directly to transform electrocompetent *E. coli* strain *E. coli* BL21(DE3) cells (Lucigen).

Expression of P450 variants in 96-well plates. Single colonies from LB_{amp} agar plates were picked using sterile toothpicks and cultured in deep-well 96-well plates containing LB_{amp} (400 µL/well) at 37 °C and 250 rpm shaking (12 h – 14 h) in an Eppendorf Innova 44R shaker. HB_{amp} (950 µL/well) in a deep-well 96-well plate was then inoculated with an aliquot (50 µL/well) of these overnight cultures and allowed to shake for 2.5 h at 37 °C and 250 rpm. The plates were cooled on ice for 20 min and the cultures were induced with 0.5 mM isopropyl β-D-1-thiogalactopyranoside (IPTG) and 1.0 mM 5-aminolevulinic acid (5-ALA) (final concentrations). Expression was conducted at 22 °C, 220 rpm for 22 h.

Reaction screening in 96-well plate format. *E. coli* (*E. coli* BL21(DE3)) cells in deep-well 96-well plates were pelleted (3,000 g, 3 min, 4 °C) using an Eppendorf tabletop centrifuge 5910R and resuspended in M9-N buffer (345 µL/well) by gentle shaking using a Fisher Scientific microplate shaker (800 rpm, 3-5 min). 40 µL of D-glucose stock solution (500 mM in M9-N buffer) was added to each well using an Eppendorf Xplorer plus, 12-channel, 15-300 µL electronic pipette. 96-well plates were then transferred into a Coy anaerobic chamber. In the anaerobic chamber, 15 µL of the substrate stock solution (267 mM in EtOH) was added into each well using an Eppendorf Xplorer 12-channel pipette (final concentration: 10 mM). The 96-well plate was sealed with an aluminum foil and shaken in a Corning digital microplate shaker at room temperature and 680 rpm in the anaerobic chamber. After 12–24 h, the 96-well plates were taken out of the anaerobic chamber, the seal was removed and analytical scale reactions were worked up following the appropriate method below.

Product formation screening and enantioselectivity screening using GC-MS or normal phase HPLC. After 12–24 h, a solution of 1 mM 1,3,5- trimethoxybenzene (internal standard) in a mixed solvent system (hexanes/ EtOAc = 1:1, 600 µL) was added using an Eppendorf Xplorer plus, 12-channel, 50-1000 µL electronic pipette. The plate was tightly sealed with a reusable silicone mat, shaken vigorously for 30 times, and centrifuged (4500 g, 5 min) to completely separate the organic and aqueous layers. The organic layers (350 µL/well) were transferred to 500 µL vial inserts using an Eppendorf Xplorer, 12-channel, 15-300 µL electronic pipette. The inserts were then placed in 2 mL vials and analyzed by GC-MS or normal phase HPLC. Chiral IC/IB-N5/IG columns were used for normal phase HPLC analysis.

Expression of P450 variants in 125 mL Erlenmeyer flasks. *E. coli* (*E. coli* BL21(DE3)) cells carrying plasmid encoding the appropriate P450 variant were grown overnight in 3 mL LB_{amp} (at 37 °C, 230 rpm, 12 h - 14 h). Preculture (1.5 mL) was used to inoculate 28.5 mL of HB_{amp} in a 125 mL Erlenmeyer flask. This culture was incubated in an Eppendorf Innova 44R shaker at 37 °C, 230 rpm for 2 h. It was then cooled on ice for 20 min and induced with 0.5 mM IPTG and 1.0 mM 5-aminolevulinic acid (final concentrations). Expression was conducted at 22 °C, 150 rpm for 20 h. *E. coli* cells were then transferred to a 50 mL conical centrifuge tube and pelleted by

centrifugation (3000 g, 5 min, 4 °C) using an Eppendorf 5910R tabletop centrifuge. Supernatant was removed and the resulting cell pellet was resuspended in M9-N buffer to $OD_{600} = 1\text{--}120$ (usually 15–35). An aliquot of this cell suspension (2 mL) was taken to determine protein concentration using the hemochrome assay after lysis by sonication. When applicable, the remaining cell suspension was further diluted with M9-N buffer to the OD_{600} used for the biotransformation and the concentration of P450 protein in the biotransformation was calculated accordingly.

Hemochrome assay for the determination of haem protein concentration.^{4,5} *E. coli* cells expressing haem protein resuspended in M9-N buffer were lysed by sonication using a BioLogics ultrasonic homogenizer (model 150 V/T) equipped with a stepped microtip (6 min in total, 1 sec on, 1 sec off, 40% amplitude, 2 cycles); samples were submerged in wet ice for this process. The resulting lysed solution was centrifuged (15,000 g, 10 min, 4 °C) using an Eppendorf 5424 R centrifuge to remove the cell debris. The supernatant (clarified lysate) was separated from the pellet and kept on ice until use.

In a conical tube, a solution of 0.2 M NaOH, 40% (v/v) pyridine, 0.5 mM $K_3Fe(CN)_6$ was prepared (**Solution I**: pyridine-NaOH- $K_3Fe(CN)_6$ solution). In another 1.5 mL centrifuge tube, a solution of 0.5 M $Na_2S_2O_4$ (sodium dithionite) was prepared in 0.1 M NaOH. 500 μ L of clarified lysate in M9-N buffer and 500 μ L of **Solution I** were transferred to a cuvette and carefully mixed. The UV-Vis spectrum of the oxidized Fe^{III} state was recorded immediately. To the cuvette was then added 10 μ L of the sodium dithionite solution (100 mg/mL). The cuvette was sealed with parafilm and the UV-Vis spectrum of the reduced Fe^{II} state was recorded immediately. A cuvette containing 500 μ L of M9-N and 500 μ L **Solution I** was used as a reference for all absorbance measurements. Concentrations of cytochromes P450 were determined using a published extinction coefficient for heme *b*, $\epsilon_{556(\text{reduced})} = 34.7 \text{ mM}^{-1}\text{cm}^{-1}$.

Analytical scale biotransformations using whole *E. coli* cells. Suspensions of *E. coli* (*E. coli* BL21(DE3)) cells expressing the appropriate haem protein variant in M9-N buffer (typically $OD_{600} = 30$) were kept on ice. In another conical tube, a solution of D-glucose (500 mM in M9-N) was prepared. To a 2 mL vial were added the suspension of *E. coli* cells expressing P450 (typically $OD_{600} = 30$, 345 μ L) and D-glucose (40 μ L of 500 mM stock solution in M9-N buffer). This 2 mL

vial was then transferred into an anaerobic chamber, where the organic substrate (15 μ L stock solution (267 mM in EtOH)) was added. Final reaction volume was 400 μ L; final concentrations were 10 mM substrate and 50 mM D-glucose. (Note: reaction performed with *E. coli* cells resuspended to OD₆₀₀ = 30 indicates that 345 μ L of OD₆₀₀ = 30 cells were added, and likewise for other reaction OD₆₀₀ descriptions.) The vials were sealed and shaken in a Corning digital microplate shaker at room temperature and 680 rpm for 12-24 h.

After 12–24 h, a solution of 1 mM 1,3,5- trimethoxybenzene (internal standard) in a mixed solvent system (hexanes/ EtOAc = 1:1, 600 μ L) was added. The mixture was transferred to a 1.5 mL centrifuge tube, vortexed (20 s for 3 times), and centrifuged (15000 g, 5 min) using an Eppendorf 5424 R centrifuge to completely separate the organic and aqueous layers. The organic layers (350 μ L/well) were transferred to 500 μ L vial inserts, which were then placed in 2 mL vials and analyzed by GC-MS or normal phase HPLC. Chiral IC/IB-N5/IG columns were used for normal phase HPLC analysis.

Preparative scale biotransformations using whole *E. coli* cells. HB_{amp} (1 L) in a 4 L flask was inoculated with an overnight culture (10 mL, 1% v/v, LB_{amp}) of *E. coli* (*E. coli* BL21(DE3)) cells containing a pET-22b(+) plasmid encoding the desired P450 variant. The cell culture was shaken at 37 °C and 230 rpm in an Eppendorf Innova 44R shaker for ca. 3.5 h (OD₆₀₀ around 2). The culture was placed on ice for 30 min. IPTG (0.5 mM final concentration) and 5-aminolevulinic acid (1.0 mM final concentration) were added. The culture was allowed to shake at 22 °C and 150 rpm for 20 h. Cells were pelleted by centrifugation (3,000 g, 5 min, 4 °C) using a Thermo Scientific Sorvall Lynx 6000 superspeed centrifuge, and resuspended in M9-N buffer (OD₆₀₀ = 30–40). An aliquot of cells (2 mL) was taken to determine P450 concentration using the hemochrome assay. Cell suspensions in M9-N buffer were kept on ice until use (Note: *leaving the cell suspension at room temperature for an extended period of time will lead to significantly reduced enzyme activity.*) To a 1 L Erlenmeyer flask equipped with a screw cap were added a suspension of *E. coli* cells in M9-N buffer expressing the desired enzyme variant and a D-glucose stock solution (500 mM in M9-N, 23.5 mL). The flask was transferred to an anaerobic chamber, where a stock solution of the organic substrate (1.0 g, 2.35 mmol, 267 mM in EtOH, 8.8 mL for substrate **1k**) were added. The flask was capped, sealed with parafilm, taken out of the anaerobic chamber and allowed to shake in an Eppendorf Innova 44R shaker at room temperature and 250 rpm for 12-24 h.

The reaction mixture was extracted with EtOAc. The mixture was transferred to a 500 mL centrifugation bucket and centrifuged (15000 g, 10 min) using a Lynx 6000 superspeed centrifuge to separate the organic layer from the aqueous layer. The aqueous layer was extracted with EtOAc for 5 times. Combined organic layers were dried over MgSO₄, concentrated *in vacuo* with the aid of a rotary evaporator and purified by column chromatography with the aid of a Biotage Isolera.

Normal phase HPLC and GC-MS calibration curve development. Stock solutions of authentic products (100 mM in EtOAc) were prepared. 1 L of extraction solvent with internal standard was freshly prepared (1 mmol (168 mg) of 1,3,5-trimethoxybenzene was added to a 1:1 mixture of hexanes and EtOAc (total volume = 1 L)). (Note: *It is critical to use a freshly prepared extraction mixture containing the internal standard due to the volatility of organic solvents. Use of aged extraction mixture will lead to inaccurate results.*) To a 1.5 mL microcentrifuge tube were added 400 μ L of M9-N buffer, 2, 4, 8, 16, 32, and 48 μ L product stock solution, respectively, and 600 μ L extraction solvent. The mixture was vortexed (20 s for 3 times) and centrifuged (15000 rpm, 5 min) to separate the organic and aqueous layers. The organic layer was transferred to a vial with an insert for normal phase HPLC and/or GC-MS analysis. The calibration curves detailed below plot product yield (y-axis) against the ratio of the peak area of product to the peak area of internal standard from HPLC/GC analysis (x-axis). In the development of our calibration curves, care was taken such that our calibration curve samples were prepared in a way similar to enzymatic samples.

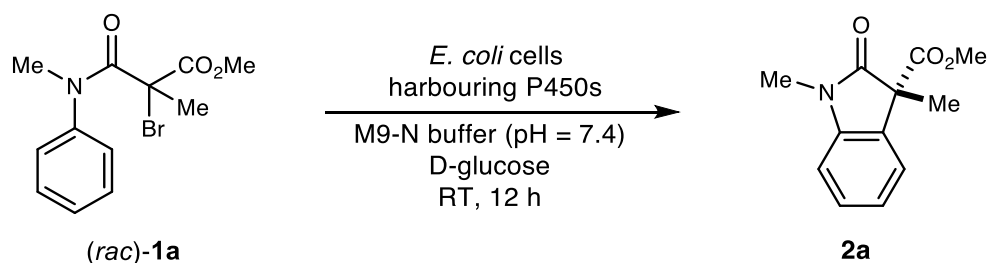
Protein purification. *E. coli* (*E. coli* BL21(DE3)) cells carrying plasmid encoding the desired P450 variant were grown overnight in 20 mL LB_{amp} (37 °C, 230 rpm). HB_{amp} (1 L) in a 4 L flask was inoculated with an overnight culture (10 mL, 1% v/v, LB_{amp}) of *E. coli* (*E. coli* BL21(DE3)) cells. The cell culture was shaken at 37 °C and 230 rpm in an Eppendorf Innova 44R shaker for ca. 3.5 h until OD₆₀₀ reached 2.0. The culture was placed on ice for 30 min. IPTG (0.5 mM final concentration) and 5-aminolevulinic acid (1.0 mM final concentration) were added. The culture was allowed to shake at 22 °C and 150 rpm for 20 h. Cultures were then centrifuged (3,000 g, 10 min, 4 °C) using a Thermo Scientific Lynx 6000 superspeed centrifuge and the cell pellets were flash frozen with liquid nitrogen. For purification, frozen cells were resuspended in HisTrap buffer A (25 mM Tris, 100 mM NaCl, 20 mM imidazole, pH 7.5 at 4 °C, 2-3 mL/g of cell wet weight) and lysed by sonication using a Branson Digital Sonifier 450 Ultrasonic Processor (12 min in total,

1 sec on, 1 sec off, 40% amplitude, 2 cycles); samples were submerged in wet ice for this process. To pellet cell debris, lysates were centrifuged using a Lynx 6000 superspeed centrifuge (15,000 g, 60 min, 4 °C). The protein containing a C-terminal 6×His-tag was purified with a Ni-NTA column (5 mL HisTrap HP, GE Healthcare, Piscataway, NJ) using an AKTA Start protein purification system (GE healthcare). Proteins were eluted on a linear gradient from HisTrap buffer A to HisTrap buffer B (25 mM Tris, 500 mM imidazole, 100 mM NaCl, pH 7.5 at 4 °C) over 10 column volumes (CV). Fractions containing the desired heme protein were combined, concentrated, and subjected to three exchanges of phosphate buffer (100 mM KPi, 10% glycerol, pH 7.4 at 4 °C) using ultra centrifugal filters (30 kDa molecular weight cut-off, Amicon Ultra, Sigma Millipore) to remove excess salt and imidazole. Protein concentration was measured with hemochrome assay and normalized to ca. 170 μ M. Concentrated proteins were aliquoted, flash-frozen in liquid nitrogen and stored at -80 °C until further use.

Supplementary Note 1. Evaluation of haem proteins for enantioconvergent radical cyclisation

At the outset of this study, we evaluated a diverse collection of haem proteins for this enantioconvergent radical cyclisation. A subset of our haem protein screening results is summarized below.

Supplementary Table 1. Selected screening results on the evaluation of haem proteins for enantioconvergent radical cyclisation^a



haem protein	mutations	yield of 2a	e.r. of 2a
wt <i>Rma</i>		38	50:50

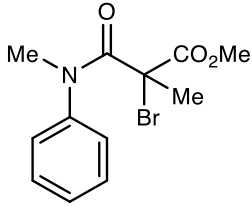
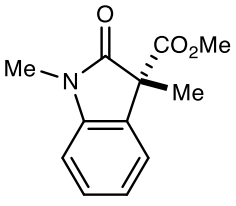
<i>cytochrome c</i>				
<i>Rma cyt c</i>	V75T M100D M103E	26	50:50	
TDE				
wt <i>Rma</i> nitric oxide dioxygenase		41	50:50	
sperm whale myoglobin H64V V68A		25	50:50	
wt hell's gate globin I		31	50:50	
P411-CIS T438S (P)	P450 _{BM3} V78A, F87V, P142S, T175I, A184V, S226R, H236Q, E252G, T268A, A290V, L353V, I366V, C400S, T438S, E442K	40	48:52	
"E267D"	P-I263F V87A A328V A268G A82L A78V F263L E267D	52	41:59	
P411 _{Diane1}	P450 _{BM3} A74G, V78L, A82L, F87A, P142S, T175I, M177L, A184V, S226R, H236Q, E252G, I263Y, T268G, A290V, T327I, A328V, L353V, I366V, C400S, T436L, L437Q, E442K ΔFAD	35	50:50	
P411 _{Diane1} I327P Y263W	P450 _{BM3} A74G, V78L, A82L, F87A, P142S, T175I, M177L, A184V, S226R, H236Q, E252G, I263W, T268G, A290V, T327P, A328V, L353V, I366V, C400S, T436L, L437Q, E442K ΔFAD	40	57:43	
P411 _{Diane2}	P450 _{BM3} A74G, V78L, A82L, F87A, P142S, T175I, M177L, A184V, S226R, H236Q, E252G, I263W, T268G, A290V, T327P, A328V, L353V, I366V, C400S, T436L, L437F, E442K ΔFAD	43	66:34	
P411 _{Diane3}	P450 _{BM3} A74G, V78A, A82L, F87G, P142S, T175I, M177L, A184V, S226R, H236Q, E252G, I263Y,	52	36:64	

	T268G, A290V, T327V, A328V, L353V, I366V, C400S, T436L, L437G, E442K ΔFAD		
P-I263F F263Y	P450 _{BM3} V78A, F87V, P142S, T175I, A184V, S226R, H236Q, E252G, I263Y, T268A, A290V, L353V, I366V, C400S, T438S, E442K	45	43:57
“E10”	P-I263F V87A A328V A268G A82L A78V F263L	49	44:56
"A82L" A78L F263Y T327I	P-I263F V87A A328V A268G A82L A78L F263Y T327I	40	46:54
“P-4 A87I”	P-I263F V87I, A268G, A328V	42	56:44
P411 _{Diane2} P327C		43	60:40
P411 _{Diane2} P327C S400A		33	55:45
P411 _{Diane2} P327C S400A T438Q		36	50:50
P411 _{Diane2} P327C S400A T438Q L181V		54	54:46

^aInitial screening was performed using whole-cell biocatalysts in a 96-well plate in an anaerobic chamber. Haem enzymes were induced with IPTG and 5-ALA. When induced with IPTG and 5-ALA, control experiment using *E. coli* cells carrying an empty pET-22b(+) vector provided the product in ca. 30% yield in a racemic manner, due to free haemin activity as detailed below. Thus, enantioselectivity (i.e., formation of enantioenriched product) was used as the selection criterion to identify enzyme-based activity. With evolved P450_{arc}'s that are highly enantioselective, whole-cell transformations provided the same e.r. as purified enzyme transformations, indicating substantially faster enzyme kinetics and minimal background activity in these whole-cell reactions.

Supplementary Note 2. Directed evolution

Supplementary Table 2. Summary of directed evolution of P411_{Diane2} W263Q L181M T438G H266L (P450_{arc1})

 (rac)-1a <i>E. coli</i> cells harbouring P450s M9-N buffer (pH = 7.4) D-glucose RT, 12 h  2a			
Parent	Sites targeted by SSM	Selection criteria	Beneficial mutation
P411 _{Diane2}	W263X	enantioselectivity and activity	W263Q
P411 _{Diane2} W263Q	L78X, A87X, L181X, T438X	enantioselectivity	L181M L78M, T438G
P411 _{Diane2} W263Q L181M	L78X, F437X, T438X	enantioselectivity	T438G
P411 _{Diane2} W263Q L181M T438G	H266X, E267X, T269X, A330X	enantioselectivity	H266L

Supplementary Table 3. Primers used for site-saturation mutagenesis (22c trick) for the engineering of P411_{Diane2} W263Q L181M T438G H266L (P450_{arc1})

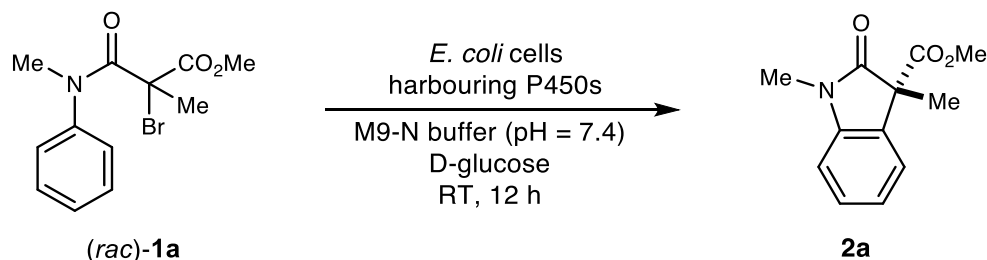
DNA template	Primer name	Primer sequence
P411 _{Diane2}	W263X_fwd_TGG	CTATCAAATTATTACATTCTTATGGGCGGGACACG AAG
	W263X_fwd_NDT	CTATCAAATTATTACATTCTTANDTGC GGGACACG AAG
	W263X_fwd_VHG	CTATCAAATTATTACATTCTTAVHGGCGGGACACG AAG
	W263X_rev	GAATGTAATAATTTGATAGCGAATGTTCCCGTC

P411 _{Diane2} W263Q	L78X_fwd_TGG	GATAAAAACTTAAGTCAAGGTCTGAAATTTTGGC GTGATTTTC
	L78X_fwd_NDT	GATAAAAACTTAAGTCAAGGTCTGAAATTTNDTC GTGATTTTC
	L78X_fwd_VHG	GATAAAAACTTAAGTCAAGGTCTGAAATTTVHGC GTGATTTTC
	L78X_rev	CAGACCTTGACTTAAGTTTTTATCAAAGCGTG
P411 _{Diane2} W263Q	A87X_fwd_TGG	CTGCGTGATTTTCTTGGAGACGGGTATGGACAAG CTGGAC
	A87X_fwd_NDT	CTGCGTGATTTTCTTGGAGACGGGTANDTACAAG CTGGAC
	A87X_fwd_VHG	CTGCGTGATTTTCTTGGAGACGGGTAVHGACAA GCTGGAC
	A87X_rev	GTCTCCAAGAAAATCACGCAGAAATTTTCAGAC
P411 _{Diane2} W263Q	L181X_fwd_TGG	CATTTATTATAAGTCTGGTCCGTGCATGGGATGAA GTAATG
	L181X_fwd_NDT	CATTTATTATAAGTCTGGTCCGTGCANDTGATGAA GTAATG
	L181X_fwd_VHG	CATTTATTATAAGTCTGGTCCGTGCAVHGGATGAA GTAATG
	L181X_rev	GCACGGACCAGACTTATAATAAATGGATGAG
P411 _{Diane2} W263Q	T438X_fwd_TGG	CATACAAACTACGAGCTCGATATTAAAGAACTGT TTTGGTTAAAACCTAAAG
	T438X_fwd_NDT	CATACAAACTACGAGCTCGATATTAAAGAACTGT TTNDTTTAAAACCTAAAG
	T438X_fwd_VHG	CATACAAACTACGAGCTCGATATTAAAGAACTGT TTVHGTAAAACCTAAAG
	T438X_rev	CAGTTCTTTAATATCGAGCTCGTAGTTTGTATG
P411 _{Diane2} W263Q	L78X_fwd_TGG	GATAAAAACTTAAGTCAAGGTCTGAAATTTTGGC GTGATTTTC

L181M	L78X_fwd_NDT	GATAAAACTTAAGTCAAGGTCTGAAATTTNDTC GTGATTTTC
	L78X_fwd_VHG	GATAAAACTTAAGTCAAGGTCTGAAATTTVHGC GTGATTTTC
	L78X_rev	CAGACCTTGACTTAAGTTTTTATCAAAGCGTG
P411 _{Diane2} W263Q L181M	F437X_fwd_TGG	CATACAAACTACGAGCTCGATATTAAAGAACTGT GGACGTTAAAC
	F437X_fwd_NDT	CATACAAACTACGAGCTCGATATTAAAGAACTGN DTACGTTAAAC
	F437X_fwd_VHG	CATACAAACTACGAGCTCGATATTAAAGAACTGV HGACGTTAAAC
	F437X_rev	CAGTTCTTTAATATCGAGCTCGTAGTTTGTATG
P411 _{Diane2} W263Q L181M	T438X_fwd_TGG	CATACAAACTACGAGCTCGATATTAAAGAACTGT TTTGGTTAAACCTAAAG
	T438X_fwd_NDT	CATACAAACTACGAGCTCGATATTAAAGAACTGT TTNDTTTAAACCTAAAG
	T438X_fwd_VHG	CATACAAACTACGAGCTCGATATTAAAGAACTGT TTVHGTAAACCTAAAG
	T438X_rev	CAGTTCTTTAATATCGAGCTCGTAGTTTGTATG
P411 _{Diane2} W263Q L181M T438G	H266X_fwd_TGG	CAAATTATTACATTCTTACAGGCGGGATGGGAAG GTACAAG
	H266X_fwd_NDT	CAAATTATTACATTCTTACAGGCGGGANDTGAAG GTACAAG
	H266X_fwd_VHG	CAAATTATTACATTCTTACAGGCGGGAVHGGAAG GTACAAG
	H266X_rev	CCTGTAAGAATGTAATAATTTGATAGCGAATGTTC
P411 _{Diane2} W263Q L181M T438G	E267X_fwd_TGG	CAAATTATTACATTCTTACAGGCGGGACACTGGG GTACAAGTG
	E267X_fwd_NDT	CAAATTATTACATTCTTACAGGCGGGACACNDTG GTACAAGTG

	E267X_fwd_VHG	CAAATTATTACATTCTTACAGGCGGGACACVHGG GTACAAGTG
	E267X_rev	CCTGTAAGAATGTAATAATTTGATAGCGAATGTTC
P411 _{Diane2} W263Q L181M T438G	T269X_fwd_TGG	CTTACAGGCGGGACACGAAGGTTGGAGTGGTCTT TTATC
	T269X_fwd_NDT	CTTACAGGCGGGACACGAAGGTNDTAGTGGTCTT TTATC
	T269X_fwd_VHG	CTTACAGGCGGGACACGAAGGTVHGAGTGGTCTT TTATC
	T269X_rev	CCTTCGTGTCCCGCCTGTAAGAATG
P411 _{Diane2} W263Q L181M T438G	A330X_fwd_TGG	CTGCGCTTATGGCCACCGGTTCTTGGTTTTCCCT ATATG
	A330X_fwd_NDT	CTGCGCTTATGGCCACCGGTTCTNDTTTTCCCT ATATG
	A330X_fwd_VHG	CTGCGCTTATGGCCACCGGTTCTVHGTTTTCCCT ATATG
	A330X_rev	GGAACCGGTGGCCATAAGCGCAG

Supplementary Table 4. Directed evolution of P411_{Diane2} W263Q L181M T438G H266L (P450_{arc1}) enzyme activity and selectivity summary^a

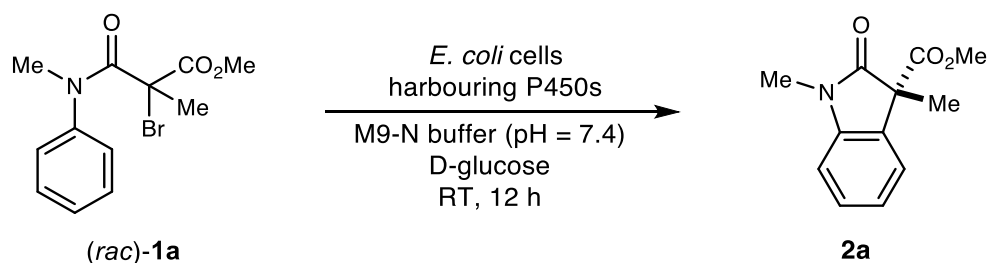


Enzyme variant	e.r.	yield (%)	TTN
P411 _{Diane2}	66:34	53 ± 1	1350 ± 30
P411 _{Diane2} W263Q	80:20	90 ± 4	2700 ± 100
P411 _{Diane2} W263Q L181M	84:16	88.0 ± 0.3	1810 ± 10

P411 _{Diane2} W263Q L181M T438G	90:10	64 ± 1	1450 ± 10
P411 _{Diane2} W263Q L181M T438G H266L (P450_{arc1})	96:4	77 ± 3	1330 ± 50

^aAll the *in vitro* reactions using P450 variants were run in triplicate and averaged yields and TTNs with SD (standard deviation) were described here.

Supplementary Table 5. Summary of directed evolution of P411_{Diane3} G437A V327P N70S A330F G74P (P450_{arc2})



Parent	Sites targeted by SSM	Selection criteria	Beneficial mutation
P411 _{Diane3}	A78X, Y263X, V327X, G437X	enantioselectivity and activity	G437A, A78C Y263L, V327T
P411 _{Diane3} G437A	A78X, L181X, Y263X, V327X	enantioselectivity and activity	V327P A78C
P411 _{Diane3} G437A V327P	N70X, A78X, G87X, E267X	enantioselectivity and activity	N70S
P411 _{Diane3} G437A V327P N70S	T269X, A330X, L436X, T438X	enantioselectivity	A330F L436R, T438C
P411 _{Diane3} G437A V327P N70S A330F	L436X, T438X, L262X, H266X, I401X, F261X, G74X, L75X	enantioselectivity	G74P G74V

Supplementary Table 6. Primers used for site-saturation mutagenesis (22c trick) for the engineering of P411_{Diane3} G437A V327P N70S A330F G74P (P450_{arc2})

DNA template	Primer name	Primer sequence
P411 _{Diane3}	A78X_fwd_TGG	GATAAAAACTTAAGTCAAGGTCTGAAATTTTGGC GTGATTTTCTTG
	A78X_fwd_NDT	GATAAAAACTTAAGTCAAGGTCTGAAATTTNDTC GTGATTTTCTTG
	A78X_fwd_VHG	GATAAAAACTTAAGTCAAGGTCTGAAATTTVHGC GTGATTTTCTTG
	A78X_rev	CAGACCTTGACTTAAGTTTTTATCAAAGCGTG
P411 _{Diane3}	Y263X_fwd_TGG	CATTCGCTATCAAATTATTACATTCTTATGGGCGG GACACG
	Y263X_fwd_NDT	CATTCGCTATCAAATTATTACATTCTTANDTGCGG GACACG
	Y263X_fwd_VHG	CATTCGCTATCAAATTATTACATTCTTAVHGGCGG GACACG
	Y263X_rev	GAATGTAATAATTTGATAGCGAATGTTCCCGTC
P411 _{Diane3}	V327X_fwd_TGG	CGAAGCGCTGCGCTTATGGCCATGGGTTTCCTGCGT TTTC
	V327X_fwd_NDT	CGAAGCGCTGCGCTTATGGCCANDTGTTTCCTGCGT TTTC
	V327X_fwd_VHG	CGAAGCGCTGCGCTTATGGCCAVHGGTTCCTGCG TTTTTC
	V327X_rev	CCATAAGCGCAGCGCTTCGTTTAAG
P411 _{Diane3}	G437X_fwd_TGG	CATACAAACTACGAGCTCGATATTAAAGAACTGT GGACGTAAAAAC
	G437X_fwd_NDT	CATACAAACTACGAGCTCGATATTAAAGAACTGN DTACGTAAAAAC

	G437X_fwd_VHG	CATACAAACTACGAGCTCGATATTAAAGAACTGV HGACGTTAAAAAC
	G437X_rev	CAGTTCTTTAATATCGAGCTCGTAGTTTGTATG
P411 _{Diane3} G437A	A78X_fwd_TGG	GATAAAAACTTAAGTCAAGGTCTGAAATTTTGGC GTGATTTTCTTG
	A78X_fwd_NDT	GATAAAAACTTAAGTCAAGGTCTGAAATTTNDTC GTGATTTTCTTG
	A78X_fwd_VHG	GATAAAAACTTAAGTCAAGGTCTGAAATTTVHGC GTGATTTTCTTG
	A78X_rev	CAGACCTTGACTTAAGTTTTTATCAAAGCGTG
P411 _{Diane3} G437A	Y263X_fwd_TGG	CATTCGCTATCAAATTATTACATTCTTATGGGCGG GACACG
	Y263X_fwd_NDT	CATTCGCTATCAAATTATTACATTCTTANDTGCGG GACACG
	Y263X_fwd_VHG	CATTCGCTATCAAATTATTACATTCTTAVHGGCGG GACACG
	Y263X_rev	GAATGTAATAATTTGATAGCGAATGTTCCCGTC
P411 _{Diane3} G437A	V327X_fwd_TGG	CGAAGCGCTGCGCTTATGGCCATGGGTTTCCTGCGT TTTC
	V327X_fwd_NDT	CGAAGCGCTGCGCTTATGGCCANDTGTTTCCTGCGT TTTC
	V327X_fwd_VHG	CGAAGCGCTGCGCTTATGGCCAVHGGTTCCTGCG TTTTTC
	V327X_rev	CCATAAGCGCAGCGCTTCGTTTAAG
P411 _{Diane3} G437A	L181X_fwd_TGG	CATTTATTATAAGTCTGGTCCGTGCATGGGATGAA GTAATG
	L181X_fwd_NDT	CATTTATTATAAGTCTGGTCCGTGCANDTGATGAA GTAATG
	L181X_fwd_VHG	CATTTATTATAAGTCTGGTCCGTGCAVHGGATGAA GTAATG

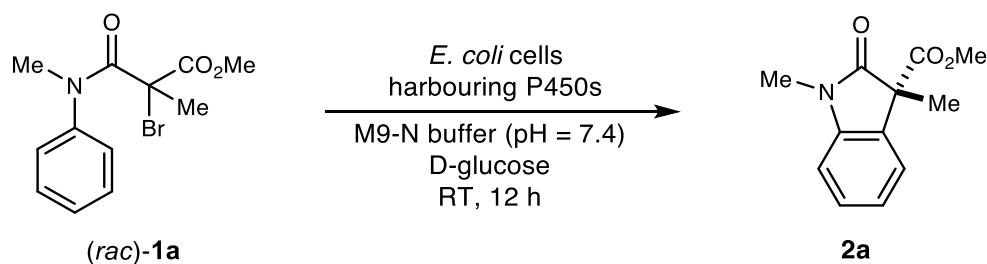
	L181X_rev	GCACGGACCAGACTTATAATAAATGGATGAG
P411 ^{Diane3} G437A V327P	N70X_fwd_TGG	CATGCGATGAATCACGCTTTGATAAATGGTTAAGT CAAGGTCTG
	N70X_fwd_NDT	CATGCGATGAATCACGCTTTGATAAANDTTTAAGT CAAGGTCTG
	N70X_fwd_VHG	CATGCGATGAATCACGCTTTGATAAAVHGTTAAG TCAAGGTCTG
	N70X_rev	CAAAGCGTGATTCATCGCATGCTTC
P411 ^{Diane3} G437A V327P	A78X_fwd_TGG	GATAAAAACCTTAAGTCAAGGTCTGAAATTTTGGC GTGATTTTCTTG
	A78X_fwd_NDT	GATAAAAACCTTAAGTCAAGGTCTGAAATTTNDTC GTGATTTTCTTG
	A78X_fwd_VHG	GATAAAAACCTTAAGTCAAGGTCTGAAATTTVHGC GTGATTTTCTTG
	A78X_rev	CAGACCTTGACTTAAGTTTTTATCAAAGCGTG
P411 ^{Diane3} G437A V327P	G87X_fwd_TGG	CGTGATTTTCTTGGAGACGGGTTATGGACAAGCTG GAC
	G87X_fwd_NDT	CGTGATTTTCTTGGAGACGGGTTANDTACAAGCTG GAC
	G87X_fwd_VHG	CGTGATTTTCTTGGAGACGGGTTAVHGACAAGCT GGAC
	G87X_rev	CGTCTCCAAGAAAATCACGCGCAAATTCAGAC
P411 ^{Diane3} G437A V327P	E267X_fwd_TGG	CTATCAAATTATTACATTCTTATATGCGGGACACT GGGGTACAAGTGGTC
	E267X_fwd_NDT	CTATCAAATTATTACATTCTTATATGCGGGACACN DTGGTACAAGTGGTC
	E267X_fwd_VHG	CTATCAAATTATTACATTCTTATATGCGGGACACV HGGGTACAAGTGGTC
	E267X_rev	GTGTCCCGCATATAAGAATGTAATAATTTGATAGC GAATG

P411 _{Diane3} G437A V327P N70S	T269X_fwd_TGG	CTTATATGCGGGACACGAAGGTTGGAGTGGTCTTT TATC
	T269X_fwd_NDT	CTTATATGCGGGACACGAAGGTNDTAGTGGTCTTT TATC
	T269X_fwd_VHG	CTTATATGCGGGACACGAAGGTVHGAGTGGTCTT TTATC
	T269X_Rev	CCTTCGTGTCCCGCATATAAGAATG
P411 _{Diane3} G437A V327P N70S	A330X_fwd_TGG	CTGCGCTTATGGCCACCGGTTCTTGGTTTTCCCT ATATG
	A330X_fwd_NDT	CTGCGCTTATGGCCACCGGTTCTNDTTTTCCCT ATATG
	A330X_fwd_VHG	CTGCGCTTATGGCCACCGGTTCTVHGTTTTCCCT ATATG
	A330X_rev	GGAACCGGTGGCCATAAGCGCAG
P411 _{Diane3} G437A V327P N70S	L436X_fwd_TGG	CTACGAGCTCGATATTAAAGAATGGGCGACGTTA AAAC
	L436X_fwd_NDT	CTACGAGCTCGATATTAAAGAANDTGGCGACGTTA AAAC
	L436X_fwd_VHG	CTACGAGCTCGATATTAAAGAAVHGGCGACGTTA AAAC
	L436X_Rev	CTTTAATATCGAGCTCGTAGTTTGTATGATC
P411 _{Diane3} G437A V327P N70S	T438X_fwd_TGG	CTACGAGCTCGATATTAAAGAACTGGCGTGGTTA AAACCTAAAG
	T438X_fwd_NDT	CTACGAGCTCGATATTAAAGAACTGGCGNDTTTA AAACCTAAAG
	T438X_fwd_VHG	CTACGAGCTCGATATTAAAGAACTGGCGVHGTTA AAACCTAAAG
	T438X_rev	CAGTTCTTTAATATCGAGCTCGTAGTTTGTATG
P411 _{Diane3} G437A	L436X_fwd_TGG	CTACGAGCTCGATATTAAAGAATGGGCGACGTTA AAAC

V327P N70S A330F	L436X_fwd_NDT	CTACGAGCTCGATATTAAAGAANDTGCGACGTAA AAAC
	L436X_fwd_VHG	CTACGAGCTCGATATTAAAGAAVHGGCGACGTAA AAAC
	L436X_Rev	CTTTAATATCGAGCTCGTAGTTTGTATGATC
P411 _{Diane3} G437A V327P N70S A330F	T438X_fwd_TGG	CTACGAGCTCGATATTAAAGAACTGGCGTGGTTA AAACCTAAAG
	T438X_fwd_NDT	CTACGAGCTCGATATTAAAGAACTGGCGNDTTTA AAACCTAAAG
	T438X_fwd_VHG	CTACGAGCTCGATATTAAAGAACTGGCGVHGTAA AAACCTAAAG
	T438X_rev	CAGTTCTTTAATATCGAGCTCGTAGTTTGTATG
P411 _{Diane3} G437A V327P N70S A330F	L262X_fwd_TGG	CATTCGCTATCAAATTATTACATTCTGGTATGCGG GACACG
	L262X_fwd_NDT	CATTCGCTATCAAATTATTACATTCNDTTATGCGG GACACG
	L262X_fwd_VHG	CATTCGCTATCAAATTATTACATTCVHGTATGCGG GACACG
	L262X_rev	GTAATAATTTGATAGCGAATGTTCCCGTCATC
P411 _{Diane3} G437A V327P N70S A330F	H266X_fwd_TGG	CAAATTATTACATTCTTATATGCGGGATGGGAAG GTACAAGTGG
	H266X_fwd_NDT	CAAATTATTACATTCTTATATGCGGGANDTGAAG GTACAAGTGG
	H266X_fwd_VHG	CAAATTATTACATTCTTATATGCGGGAVHGGGAAG GTACAAGTGG
	H266X_rev	GCATATAAGAATGTAATAATTTGATAGCGAATGT TCC
P411 _{Diane3} G437A	I401X_fwd_TGG	GGAAACGGTCAGCGTGCGTCTTGGGGTCAGCAGT TC

V327P N70S A330F	I401X_fwd_NDT	GGAAACGGTCAGCGTGCGTCTNDTGGTCAGCAGT TC
	I401X_fwd_VHG	GGAAACGGTCAGCGTGCGTCTVHGGGTCAGCAGT TC
	I401X_rev	GACGCACGCTGACCGTTTCCAAAC
P411 _{Diane3} G437A V327P N70S A330F	F261X_fwd_TGG	CATTCGCTATCAAATTATTACATGGTTATATGCGG GACACG
	F261X_fwd_NDT	CATTCGCTATCAAATTATTACANDTTTATATGCGG GACACG
	F261X_fwd_VHG	CATTCGCTATCAAATTATTACAVHGTTATATGCGG GACACG
	F261X_rev	GTAATAATTTGATAGCGAATGTTCCCGTCATC
P411 _{Diane3} G437A V327P N70S A330F	G74X_fwd_TGG	CTTTGATAAAAAGTTTAAGTCAATGGCTGAAATTTG CGCGTG
	G74X_fwd_NDT	CTTTGATAAAAAGTTTAAGTCAANDTCTGAAATTTG CGCGTG
	G74X_fwd_VHG	CTTTGATAAAAAGTTTAAGTCAAVHGCTGAAATTTG CGCGTG
	G74X_rev	GACTTAAACTTTTATCAAAGCGTGATTCATCG
P411 _{Diane3} G437A V327P N70S A330F	L75X_fwd_TGG	CTTTGATAAAAAGTTTAAGTCAAGGTTGGAAATTTG CGCGTG
	L75X_fwd_NDT	CTTTGATAAAAAGTTTAAGTCAAGGTNDTAAATTTG CGCGTG
	L75X_fwd_VHG	CTTTGATAAAAAGTTTAAGTCAAGGTVHGAAATTT GCGCGTG
	L75X_rev	GACTTAAACTTTTATCAAAGCGTGATTCATCG

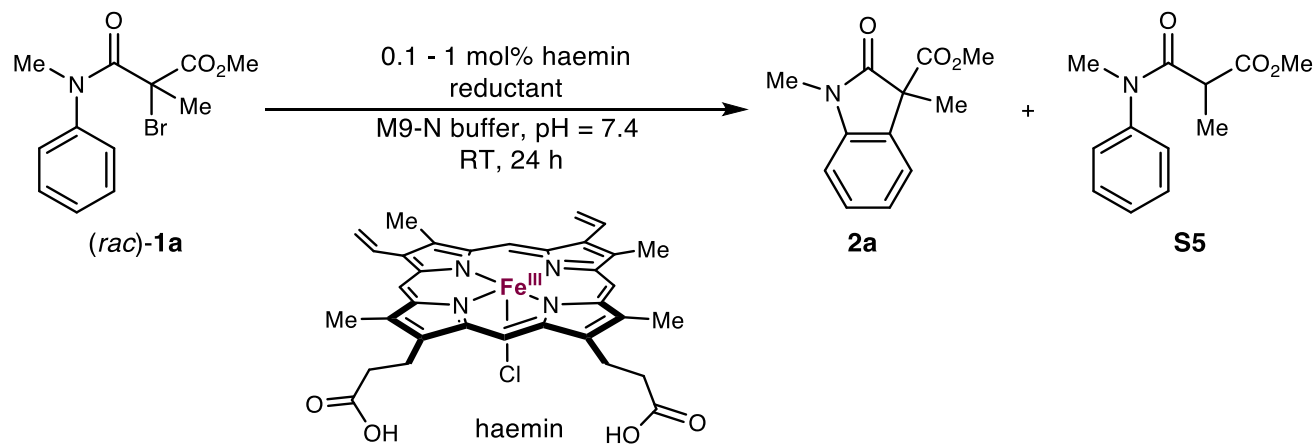
Supplementary Table 7. Directed evolution of P411_{Diane3} G437A V327P N70S A330F G74P (P450_{arc2}) enzyme activity and selectivity summary^a



Enzyme Variant	e.r.	yield (%)	TTN
P411 _{Diane3}	36:64	49 ± 1	1090 ± 20
P411 _{Diane3} G437A	22:78	81 ± 1	2230 ± 40
P411 _{Diane3} G437A V327P	20:80	94 ± 1	2460 ± 40
P411 _{Diane3} G437A V327P N70S	15:85	97 ± 1	2100 ± 30
P411 _{Diane3} G437A V327P N70S A330F	14:86	77 ± 3	1840 ± 20
P411 _{Diane3} G437A V327P N70S A330F G74P (P450 _{arc2})	12:88	88 ± 1	1890 ± 30

^aAll the *in vitro* reactions using P450 variants were run in triplicate and averaged yields and TTNs with SD (standard deviation) were described here.

Supplementary Table 8. Control experiments with cofactor^a



haemin loading (mol %)	reductant	yield of 2a (%) ^b	ee of 2a (%)	yield of S5 (%) ^b
1	0.1 eq L-ascorbic acid	38	0	<5%
1	1.0 eq L-ascorbic acid	62	0	<5%
0.1	1.0 eq L-ascorbic acid	21	0	<5%
0	1.0 eq L-ascorbic acid	6	0	<5%
1	1.0 eq Na ₂ S ₂ O ₄	5	0	80
0.1	1.0 eq Na ₂ S ₂ O ₄	3	0	83
0	1.0 eq Na ₂ S ₂ O ₄	2	0	81

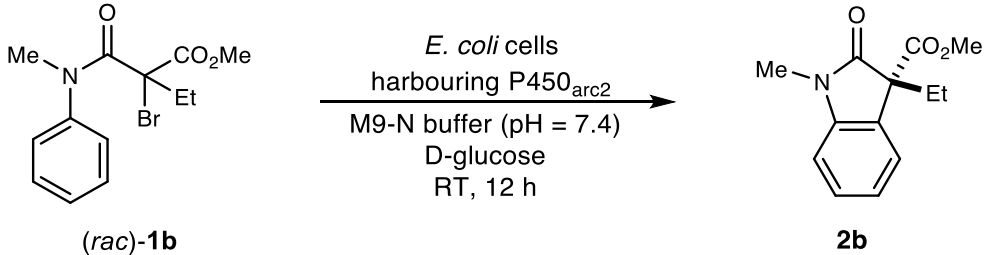
^aAll reactions were conducted in triplicate with 4 μ mol **1a** in a M9-N buffer. ^bYields were determined by GC-MS and HPLC.

Discussion

These results demonstrate that ferrous haemin catalyses this radical cyclisation with low to moderate levels of activity in a racemic fashion. Our evolved enzymes displayed a substantially higher activity (TTNs up to 10,000) and excellent enantiocontrol under the same conditions. With

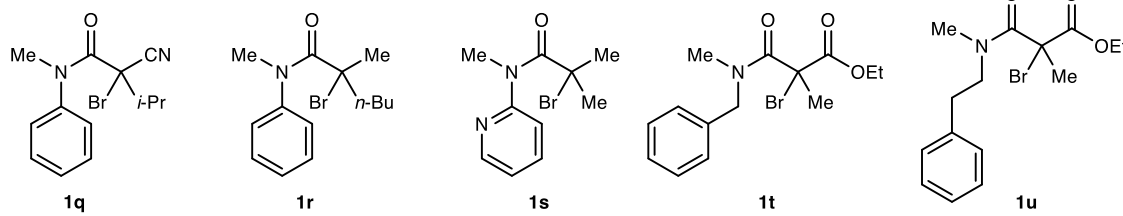
evolved P450_{arc}'s, whole-cell transformations provided the same e.r. as purified enzyme transformations, indicating minimal background activity in these whole-cell reactions.

Supplementary Table 9. High TTN experiments using whole *E. coli* cells harboring P411_{Diane3} G437A V327P N70S A330F G74P (P450_{arc2})

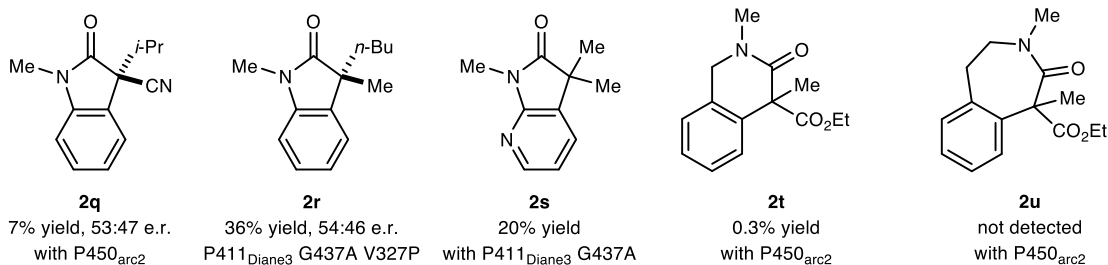
			
OD ₆₀₀ ^a	e.r.	Yield (%)	TTN
30	97:3	87 ± 1	1990 ± 20
20	97:3	85 ± 2	2910 ± 60
10	97:3	82 ± 3	5600 ± 200
5	97:3	86 ± 2	11800 ± 320

^a OD₆₀₀ here refers to the OD₆₀₀ of *E. coli* cell suspension used for catalysis and not the final OD₆₀₀ of whole-cell biotransformation. See **Supplementary Methods** above for details. All the *in vitro* reactions using P450 variants were run in triplicate and averaged yields and TTNs with SD (standard deviation) were described here.

Other types of substrates tested:



Products:



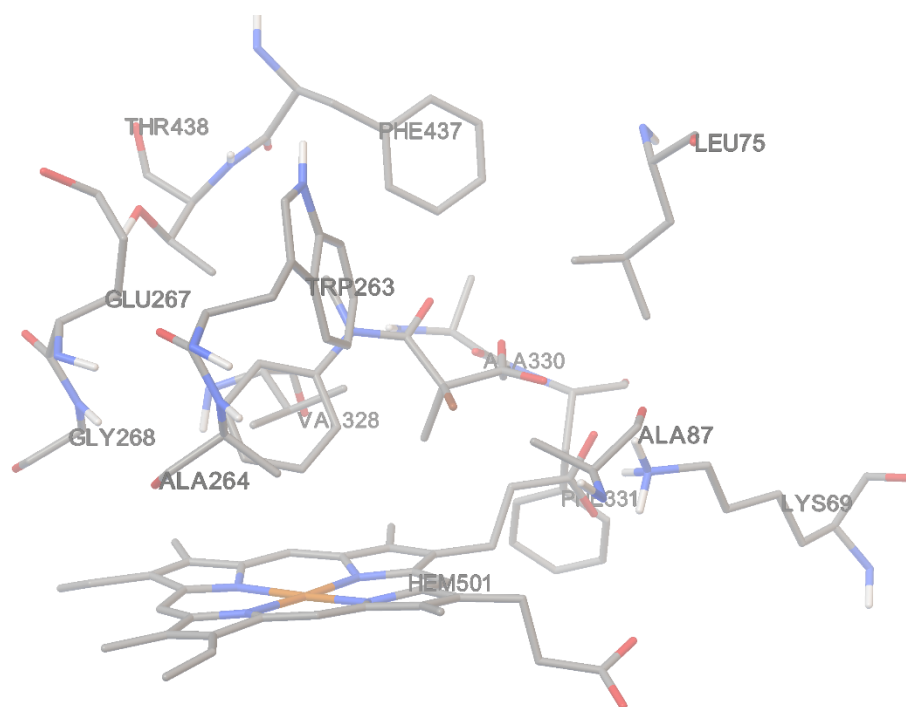
Supplementary Scheme 1. Preliminary results of additional substrates tested.

Docking studies

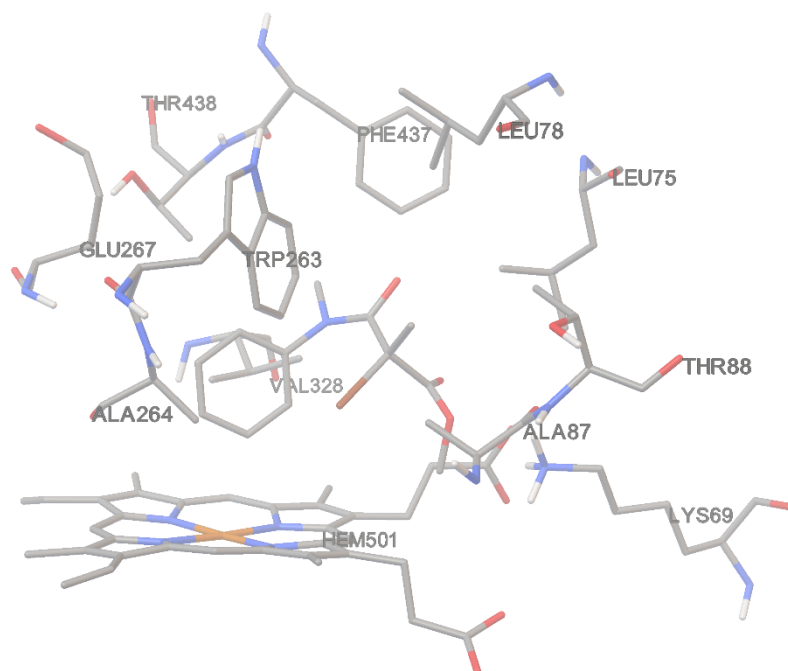
Prior to the start of our protein engineering work, we performed molecular docking using AutoDock^{6,7} to identify key active-site residues that are in close contact with the substrates. These residues and residues next to them are first subjected to site-saturation mutagenesis (SSM) and screening.

In the current enantioconvergent radical cyclization, as both the (*R*)- and the (*S*)-enantiomeric substrate are converted into the same major enantiomeric product, we docked both the (*R*)- and (*S*)- substrate (i.e., (***R***)-**1a** and (***S***)-**1a**) into the starting variant of P450_{arc1}, namely P411_{Diane2}. As the structure of the key radical intermediate pre-organized toward the cyclization step should resemble the cyclization product, in our docking studies, the major enantiomeric product (***S***)-**2a** was also docked into the starting enzyme variant to gain insights into the protein-radical intermediate interactions.

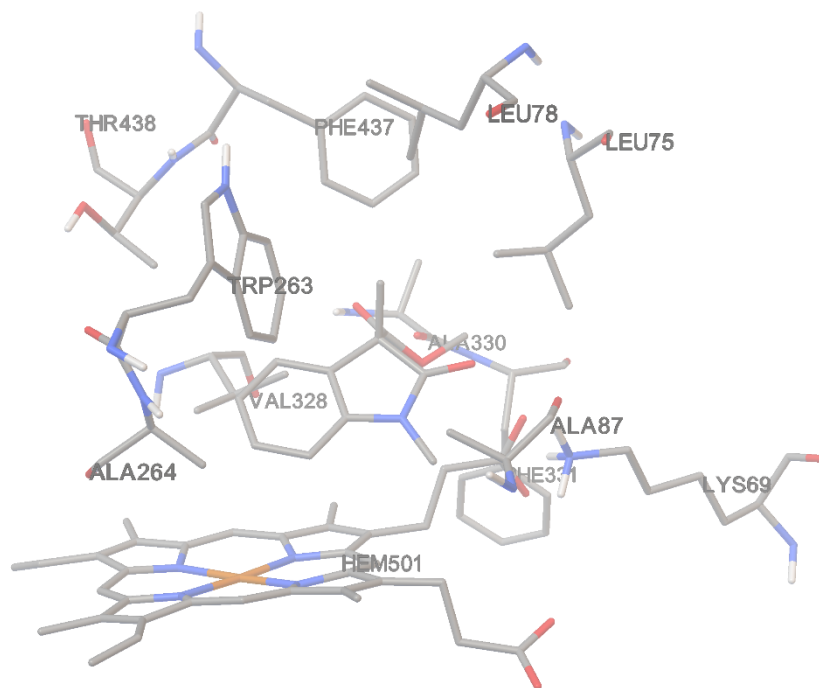
As no crystal structure of the starting variant P411_{Diane2} is known, we used the PDB structure of a closely related enzyme variant of P411_{Diane2} (PDB ID: 5UCW) as the protein structure file. PyMOL⁸ mutagenesis was used to introduce mutations to convert this structure into the actual starting variant for docking. The geometry of all the substrates and products were optimized by DFT using Gaussian (see Computational Details below). In our docking studies, each clustered conformation from AutoDock was analyzed individually to identify active-site residues that are in close contact with the substrate. Representative docking models that are likely relevant to enzyme catalysis are provided below (see **Supplementary Figure 1-3**).



Supplementary Figure 1. Representative docking model for P411_{Diane2} and (*S*)-1a



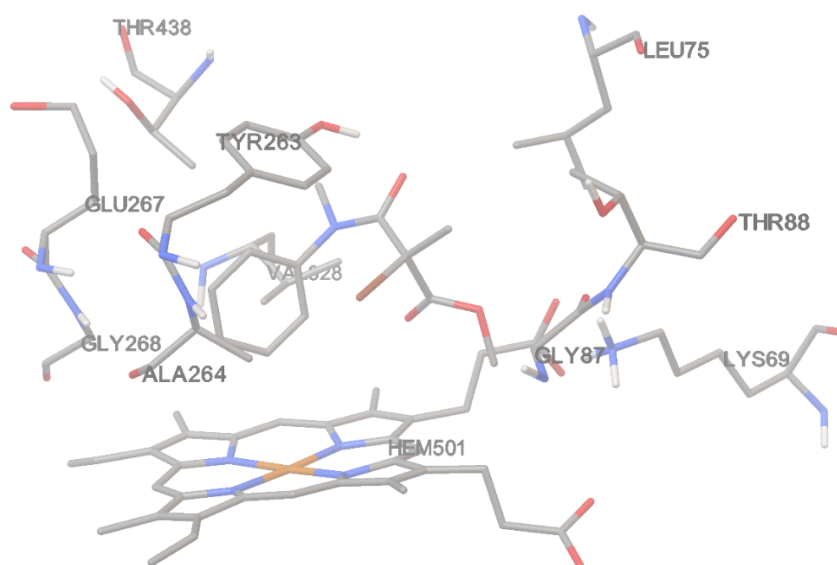
Supplementary Figure 2. Representative docking model for P411_{Diane2} and (*R*)-1a



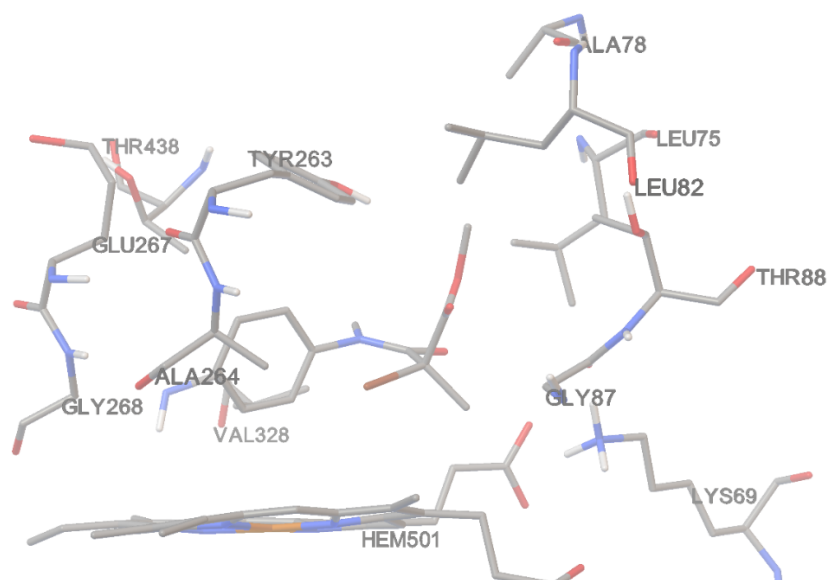
Supplementary Figure 3. Representative docking model for P411_{Diane2} and (*S*)-2a

Together, these docking studies revealed key active site residues that are in close contact with the substrate and the reactive intermediate. These residues include L75, L78, A87, W263, A264, E267, G268, V328, A330, F437, and T438. In directed evolution, these key residues and residues next to them (e.g., H266) are first subjected to site-saturation mutagenesis and screening. For P450_{arc1}, all the beneficial mutations identified from directed evolution (W263Q, T438G and H266L) except L181M are from this short list of key residues. Residue 181 is in close contact to key residues 437 and 438 and it resides in the substrate tunnel. In previous protein engineering of CYP102A1, residue 181 was also found to play an important role.⁹

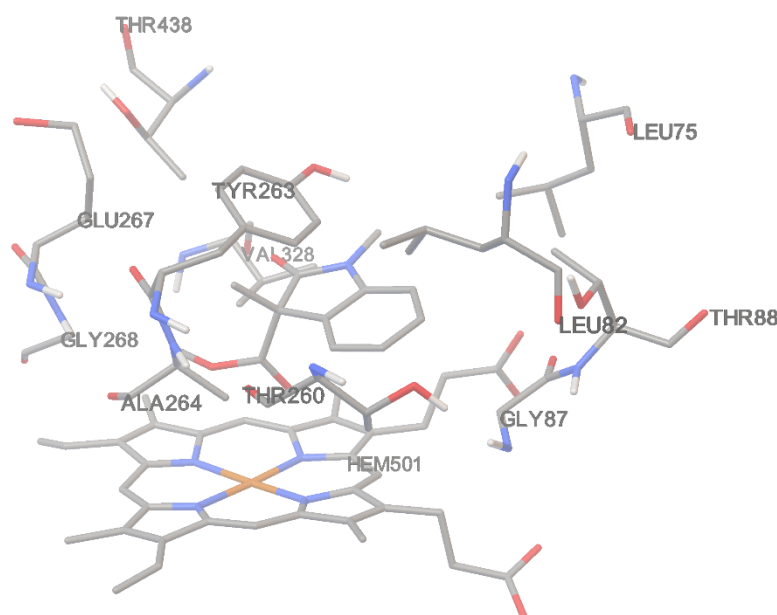
Similarly, representative docking models for the starting variant of P450_{arc2}, namely P411_{Diane3}, are provided below (see **Supplementary Figure 4-6**). These models also played an essential role in the selection of residues for SSM and screening. Based on these docking models, for P411_{Diane3}, active-site residues that are in close contact are L75, A78, L82, G87, Y263, A264, E267, G268, V328, and T438.



Supplementary Figure 4. Representative docking model for P411_{Diane3} and **(S)-1a**



Supplementary Figure 5. Representative docking model for P411_{Diane3} and **(R)-1a**



Supplementary Figure 6. Representative docking model for P411_{Diane2} and (*R*)-**2a**

Supplementary Note 3. Steady-state kinetics

Steady-state kinetic studies were carried out with both the evolved enzyme P450_{arc1} and its parent P411_{Diane2} using purified proteins. P450_{arc1} and P411_{Diane2} were purified using the above general procedure. The protein concentrations were measured using the hemochrome assay as described above (175 μ M for P411_{Diane2} and 172 μ M for P450_{arc1}).

Stock solutions of **1a** in 150 μ L EtOH with different concentrations were prepared by serial dilution (426.7 mM, 213.3 mM, 106.7 mM, 53.3 mM, 26.7 mM, 13.3 mM, 6.7 mM, and 3.3 mM; corresponding to a final concentration of 16 mM, 8 mM, 4 mM, 2 mM, 1 mM, 0.5 mM, 0.25 mM, and 0.125 mM, respectively, when 15 μ L of the stock solution was used for each reaction). A stock solution of sodium dithionite (10 mM) was prepared in 100 mM KPi buffer (pH = 7.4 at room temperature) before use.

The steady-state kinetic study using P411_{Diane2} were performed in 400 μ L KPi buffer (100 mM, pH 7.4 at RT) containing P411_{Diane2} (8 μ M final concentration), sodium dithionite (200 μ M final concentration), and substrate **1a** (15 μ L) in a deep well 96-well plate at 680 rpm with a microplate shaker for 5 min. 200 μ L of 100 mM KPi buffer was added to each well in C1–C12, followed by a stock solution of the substrate (15 μ L, each data point was run in triplicate). Then

P411_{Diane2} (175 μ M, 329.4 μ L) and a stock solution of sodium dithionite (10 mM, 144 μ L) were diluted in 100 mM KPi (2.857 mL) in a 15 mL centrifuge tube (VWR) and mixed by inverting the tube several times at room temperature. Then this ferrous enzyme solution (185 μ L) was added to each well at the same time using an Eppendorf Xplorer 12-channel electronic pipette (15-300 μ L). The reaction plate was shaken in a Corning digital microplate shaker at room temperature and 680 rpm for 5 min. At this time, a mixed organic solvent (Hexanes/EtOAc = 1/1, 1.0 mM 1,3,5-trimethoxybenzene, 600 μ L for reactions with a substrate concentration $\geq$ 2 mM; 300 μ L for reactions with a substrate concentration of 0.125 mM to 1 mM) was added to each well to stop the reaction using a 12-channel electronic pipette (15-300 μ L).

The steady-state kinetic study using P450_{arc1} were performed in 400 μ L KPi buffer (100 mM, pH 7.4 at RT) containing P450_{arc1} (4 μ M final concentration), sodium dithionite (100 μ M final concentration), and substrate **1a** in a deep well 96-well plate shaking at 680 rpm for 2 min. 200 μ L 100 mM KPi buffer was added to each well in C1–C12, followed by a stock solution of the substrate (15 μ L, each data point was run in triplicate). Then P450_{arc1} (172 μ M, 167.4 μ L) and a stock solution of sodium dithionite (10 mM, 72 μ L) were diluted in 100 mM KPi (3.09 mL) in a 15 mL centrifuge tube (VWR) and mixed by inverting the tube several times at room temperature. Then this ferrous enzyme solution (185 μ L) was added to each well at the same time using a 12-channel electronic pipette. The reaction plate was shaken in a Corning digital microplate shaker at room temperature and 680 rpm for 2 min. The workup procedure was described above.

The mixture was transferred to a 1.5 mL centrifugation tube, vortexed (20 s for 3 times), and centrifuged (15,000 rpm, 5 min) using an Eppendorf 5424 R centrifuge to separate the organic and aqueous layers. The organic layer (150 – 300 μ L/well) was transferred to a 500 μ L vial insert, which was then placed in a 2 mL vial and analyzed by normal phase HPLC.

Supplementary Table 10. Steady-state kinetic parameters using P450_{arc1} and its parent P411_{Diane2} using purified enzymes.^a

Variant	K_M [mM]	V_{max} [μ M/min]	k_{cat} [s^{-1}]	k_{cat}/K_M [$M^{-1}s^{-1}$]
P411 _{Diane2}	2.1 ± 0.7	$(1.7 \pm 0.2) \times 10$	$(3.6 \pm 0.4) \times 10^{-2}$	$(1.7 \pm 0.8) \times 10$
P450 _{arc1}	2.3 ± 0.5	$(1.30 \pm 0.07) \times 10^2$	$(5.4 \pm 0.3) \times 10^{-1}$	$(2.3 \pm 0.7) \times 10^2$

^aData are presented as mean values $\pm$ SD, with n = 3 (sample size).

Supplementary Table 11. Steady-state kinetic data for P411_{Diane2}.^a

[S] (mM)	[P] (mM)	V (μM/min)
0.125	0.013	2.7 ± 0.2
0.25	0.012	2.5 ± 0.1
0.5	0.015	3.1 ± 0.1
1	0.021	4.1 ± 0.3
2	0.050	10.1 ± 0.4
4	0.051	10.2 ± 0.4
8	0.068	13.6 ± 0.7

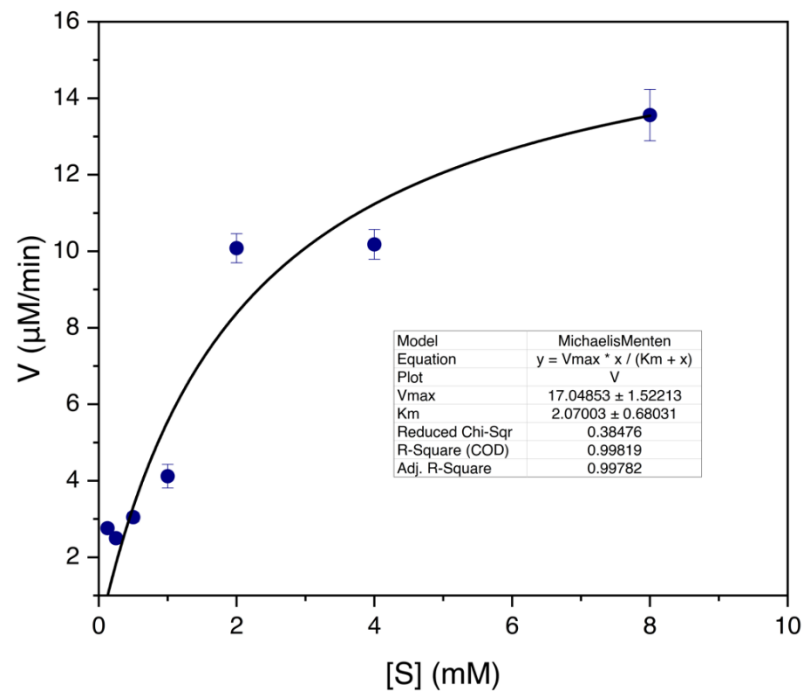
^aData are presented as mean values ± SD, with n = 3 (sample size).

Supplementary Table 12. Steady-state kinetic data for P450_{arc1}.^a

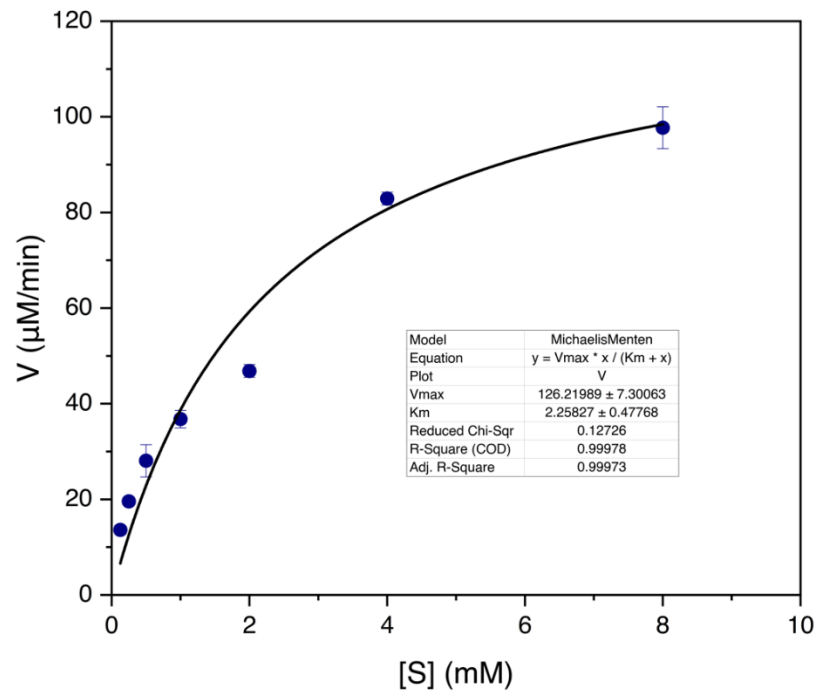
[S] (mM)	[P] (mM)	V(μM/min)
0.125	0.027	13.6 ± 0.7
0.25	0.039	19.6 ± 0.6
0.5	0.056	28 ± 3
1	0.074	37 ± 2
2	0.094	47 ± 1
4	0.17	83 ± 1
8	0.20	98 ± 4

^aData are presented as mean values ± SD, with n = 3 (sample size).

Simulated steady-state kinetics for P411_{Diane2}:

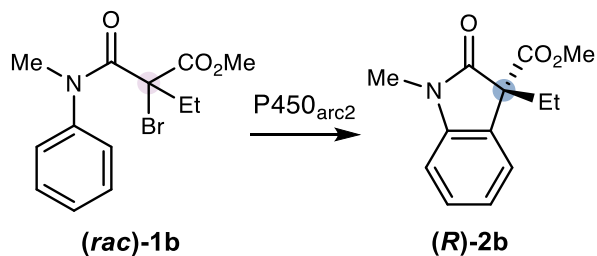


Simulated steady-state kinetics for P450_{arc1}:



Time-course studies

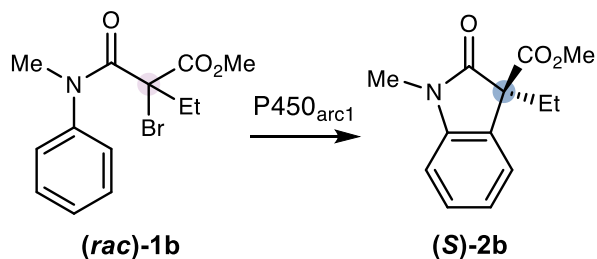
Supplementary Table 13. Time course of P450_{arc2}-catalysed enantioconvergent radical cyclisation of **1b**^a



Time	Conversion (%)	% of major enantiomer (1b)	% of major enantiomer (2b)
10 min	9	51	97
20 min	22	52	97
40 min	33	54	97
1 h	45	57	97
2 h	73	63	97
3 h	92	71	97
6 h	>99		97

^aAll reactions were conducted in triplicate using P450_{arc2} (OD₆₀₀ = 15) with 4 μmol **1b** in a M9-N buffer and averaged yields were described here.

Supplementary Table 14. Time course of P450_{arc1}-catalysed enantioconvergent radical cyclisation of **1b**^a

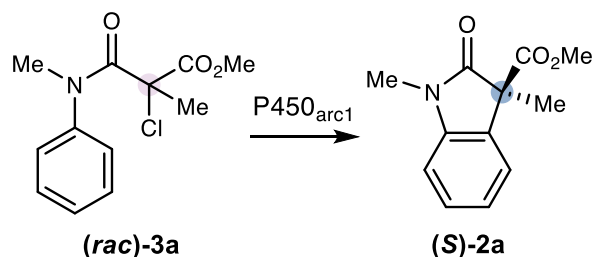


Time	Conversion (%)	% of major enantiomer (1b)	% of major enantiomer (2b)
10 min	17	53	78
20 min	28	55	78
40 min	33	56	79

1 h	50	61	79
2 h	85	75	80
3 h	>99		81

^aAll reactions were conducted in triplicate using P450_{arc1} (OD₆₀₀ = 30) with 4 μmol **1b** in a M9-N buffer and averaged yields were described here.

Supplementary Table 15. Time course of P450_{arc1}-catalysed enantioconvergent radical cyclisation of **3a**^a



Time	Conversion (%)	% of major enantiomer (3a)	% of major enantiomer (2a)
30 min	10	53	97
1 h	24	59	97
2 h	42	66	97
4 h	69	77	96
8 h	97	75	96
10 h	>99		95

^aAll reactions were conducted in triplicate using P450_{arc1} (OD₆₀₀ = 30) with 4 μmol **3a** in a M9-N buffer and averaged yields were described here.

Discussion

These results uncovered three possible product e.r. evolution patterns. These results also demonstrated that the chloride substrate underwent slower transformations relative to bromide substrate with the same enzyme variant due to the higher BDE for the activating C-Cl bond, which is consistent to our computational results.

Supplementary Note 4. DNA and protein sequences

DNA and amino acids sequence of P450_{arc1}:

DNA sequence

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Protein sequence

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DNA and protein sequence of P450_{arc2}:

DNA sequence

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Protein sequence

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DNA and protein sequence of P450_{arc1} G438T L266H L78C V328E S332A G74P:

DNA sequence

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Protein sequence

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DNA and protein sequence of P450_{arc2} P74G F330E L436R:

DNA sequence

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Protein sequence

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DNA and protein sequence of P450_{arc2} G74P F330E L436R H266C G268P:

DNA sequence

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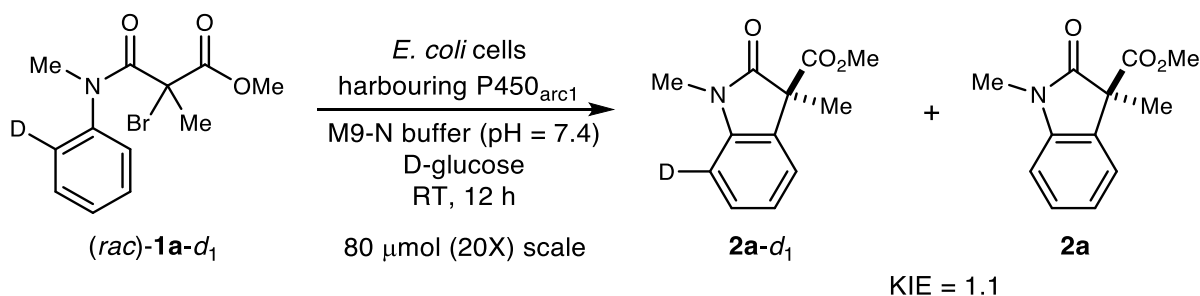
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Supplementary Note 5. Mechanistic studies

Deuterium-labeling experiment

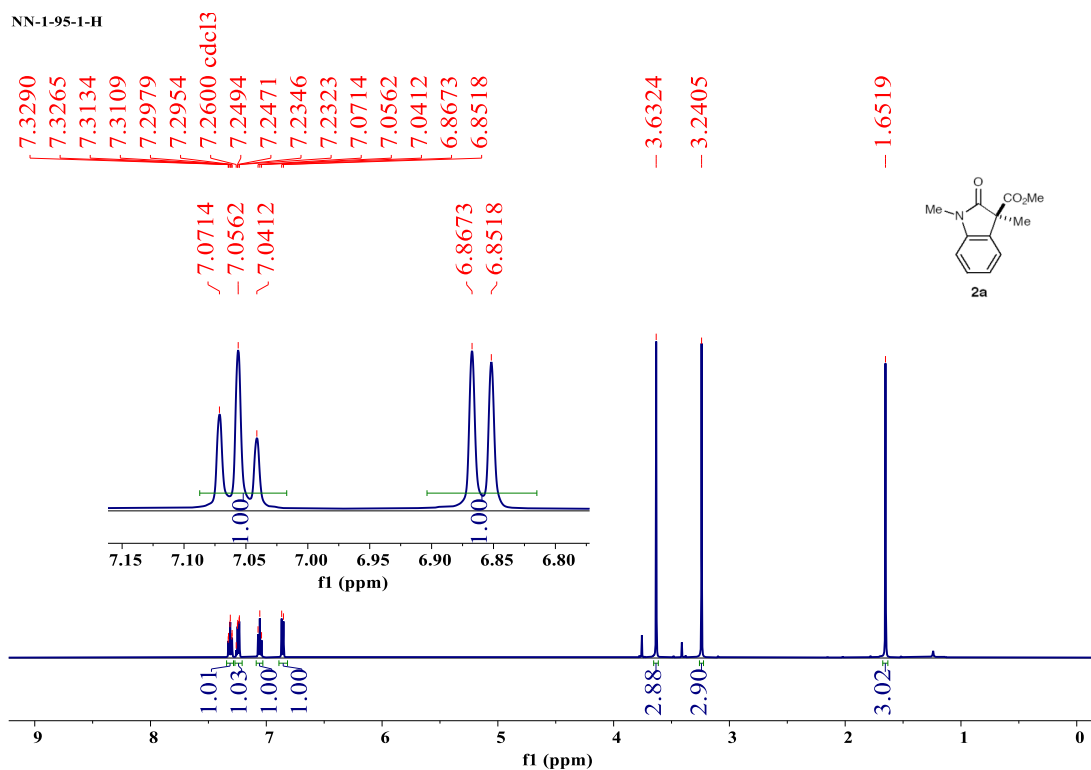


Supplementary Figure 7. Intramolecular KIE study with *(rac)*-**1a-d₁** and P450_{arc1}

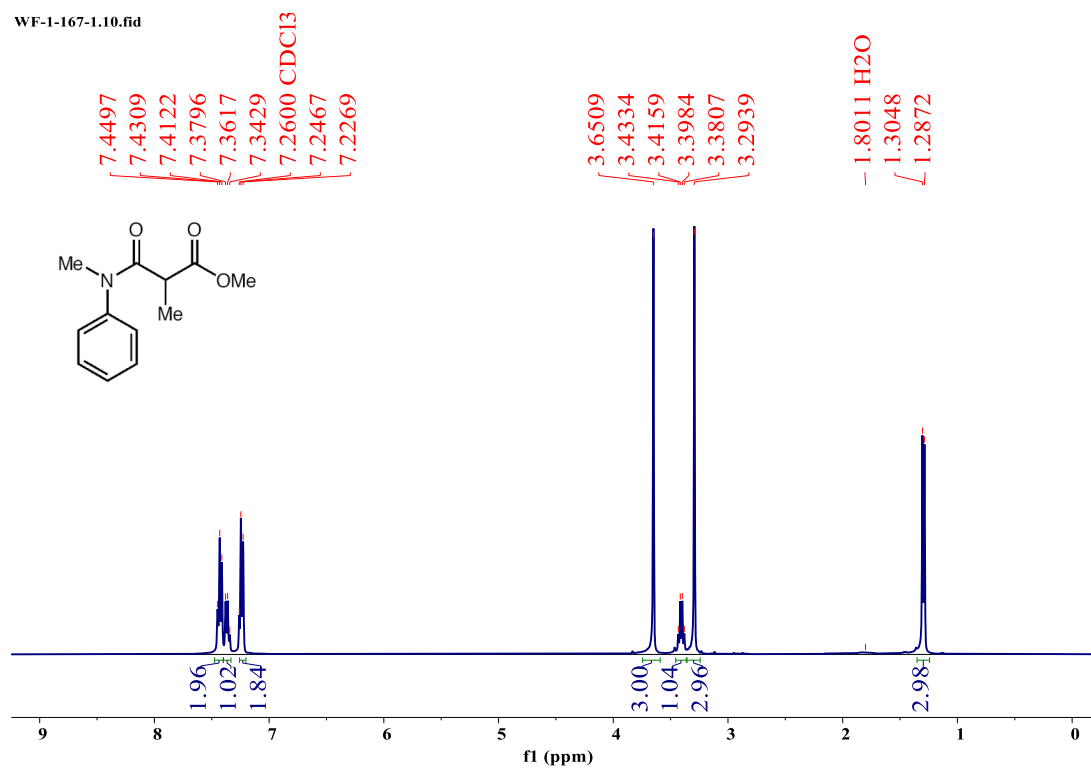
With *(rac)*-**1a-d₁** as the substrate, KIE of this intramolecular whole-cell biotransformation with P450_{arc1} is ca 1.1 (**Supplementary Figure 7**, KIE was calculated with the ratio of **2a** to **2a-d₁** based on ¹H NMR spectroscopic analysis, see **Supplementary Figure 8-10**). The KIE study indicates that C–H bond cleavage is not involved in the step that determines the selectivity between **2a** and **2a-d₁**, which is consistent with the reaction pathways computed by DFT calculations (**Fig. 6**). The DFT calculations indicated that the trapping of the cyclised radical intermediate via radical-polar crossover is kinetically facile. Thus, the radical cyclisation step is irreversible and determines

Supplementary Figure 8. Crude ^1H NMR spectrum for the enzymatic reaction with P450_{arc1}





Supplementary Figure 9. ¹H NMR spectrum for product **2a**

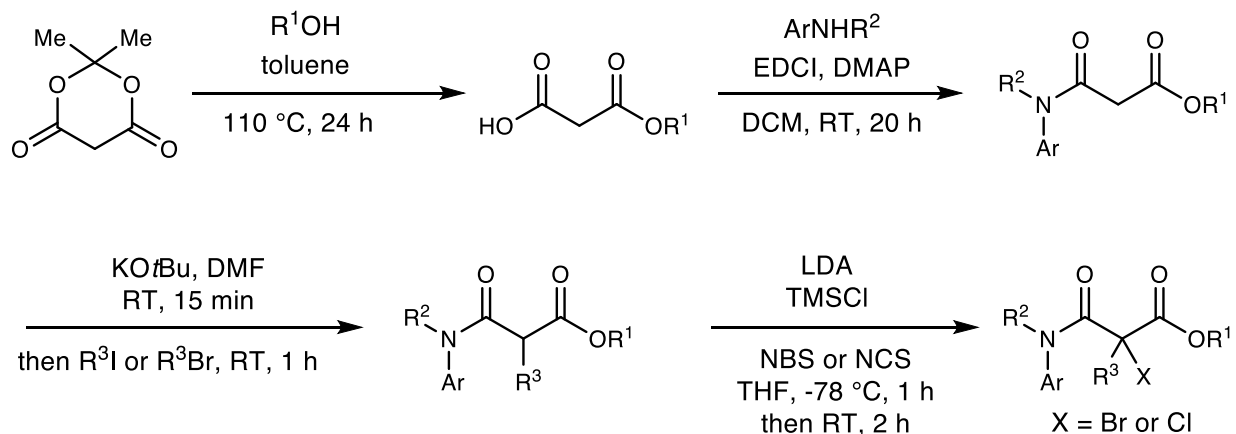


Supplementary Figure 10. ¹H NMR spectrum for reduced product **S5**

Supplementary Note 6. Synthesis and characterization of substrates

General procedure for the synthesis of substrates

Route A



General Procedure A

This procedure is modified from a previously described procedure.¹⁰ To a solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (5.8 g, 50 mmol, 1.0 eq) in toluene (50 mL) was added the alcohol (500 mmol, 10 eq) and the reaction mixture was heated at reflux for 24 h. After 24 h, the mixture was allowed to cool down to room temperature and concentrated *in vacuo* with the aid of a rotary evaporator to obtain the crude malonic acid monoester, which was used directly for the next step without further purification.

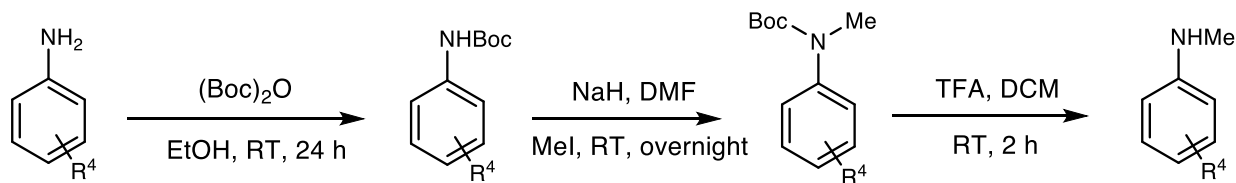
To a CH₂Cl₂ solution (60 mL) of aniline (30 mmol, 1.0 eq), EDCI·HCl (66 mmol, 2.2 eq), and DMAP (6 mmol, 0.2 eq) was added the malonic acid monoester (45 mmol, 1.5 eq) dropwise at 0 °C under nitrogen. The reaction mixture was allowed to warm to room temperature, stirred for ca. 20 h. The mixture was then diluted with CH₂Cl₂, washed with 1 M HCl (3 times) and brine. The combined organic layers were dried over MgSO₄ and concentrated *in vacuo*. The resulting mixture was purified by column chromatography with the aid of a Biotage Isolera to afford the amide product.

To a solution of the amide (20 mmol, 1.0 eq) in anhydrous DMF (40 mL) was added KO^tBu (2.69 g, 24 mmol, 1.2 eq) at room temperature under nitrogen. After 15 min, the alkyl halide R³I/R³Br (MeI, EtI, *n*PrBr, allyl bromide, and *i*PrI) (20 mmol, 1.0 eq) was added dropwise to the reaction mixture. After 1 h, the reaction was quenched with H₂O and extracted with EtOAc for 3 times.

The combined organic layers were washed with brine, dried over MgSO_4 , concentrated *in vacuo*, and purified by flash column chromatography with the aid of a Biotage Isolera.

To a solution of diisopropylamine (22.5 mmol, 1.5 eq) in anhydrous THF was added *n*BuLi (21 mmol, 1.4 eq, 2.5 M in hexanes) dropwise at 0 °C under nitrogen. The mixture was stirred for 15 min and cooled to -78 °C. A solution of the amide (15 mmol, 1.0 eq) in anhydrous THF (30 mL) was added slowly, and the mixture was allowed to stir at -78 °C for 2 h. Trimethylsilyl chloride (TMSCl, 19.5 mmol, 1.3 eq) was then added dropwise. The mixture was stirred at -78 °C for 1 h, warmed to room temperature, and stirred for another 2 h. The mixture was cooled to -78 °C and NBS (22.5 mmol, 1.5 eq) was added in one portion under nitrogen. After stirring at -78 °C for 1 h, the reaction mixture was allowed to warm to room temperature and stirred for another 2 h. The reaction was quenched with saturated NH_4Cl aqueous solution and extracted with EtOAc for 3 times. The combined organic layers were washed with 1 M HCl (3 times) and brine, dried over MgSO_4 , concentrated *in vacuo*, and purified by flash column chromatography with the aid of a Biotage Isolera.

Route B



N-methylaniline and *N*-ethylaniline were purchased from Combi-Blocks and used directly without further purification. Other *N*-methylanilines were prepared using **Route B**.

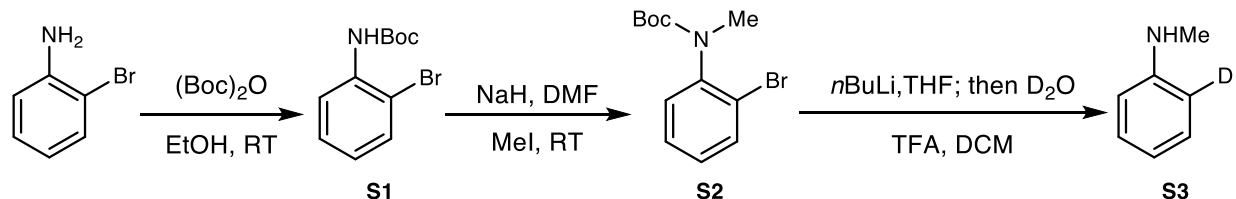
To a solution of aniline (60 mmol, 1.1 eq) in EtOH was added $(\text{Boc})_2\text{O}$ (54.55 mmol, 1.0 eq) at room temperature for 24 h. The reaction mixture was concentrated *in vacuo* and the resulting residue was diluted with EtOAc, washed with 1 M HCl (3 times) and brine, dried over MgSO_4 , concentrated *in vacuo* to afford the crude *N*-Boc aniline, which was used directly for the next step without further purification.

A solution of the *N*-Boc aniline in anhydrous DMF (20 mL) was added to the suspension of NaH (60 mmol, 1.1 eq, 60% in mineral oil) in anhydrous DMF (50 mL) at 0 °C under nitrogen. The reaction mixture was stirred at room temperature for 30 min, and MeI (3.73 mL, 60 mmol, 1.1 eq) was added slowly at 0 °C. The reaction was allowed to warm to room temperature, stirred overnight,

quenched with H₂O, and extracted with EtOAc (3 times). The combined organic layers were washed with brine, dried over MgSO₄, concentrated *in vacuo*, and used directly for the next step without further purification.

To a solution of *N*-Boc-*N*-methylaniline in CH₂Cl₂ (100 mL) was added CF₃COOH (TFA, 20.9 mL, 272.8 mmol, 5.0 eq) at room temperature and the reaction mixture was stirred for 2 h. the reaction was concentrated *in vacuo*, diluted with CH₂Cl₂, quenched with saturated Na₂CO₃ aqueous solution, and extracted with CH₂Cl₂ for 3 times. The combined organic layers were washed with brine, dried over MgSO₄, concentrated *in vacuo* to obtain the *N*-methylaniline product, which was used directly without further purification.

Route C



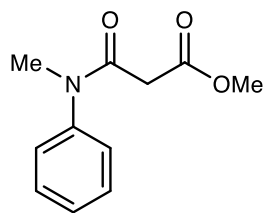
N-methylbenzen-2-*d*-amine (**S3**) was prepared using **Route C**. *Tert*-butyl (2-bromophenyl)(methyl)carbamate (**S2**) was prepared using procedures described above.

To a solution of *tert*-butyl (2-bromophenyl)(methyl)carbamate (**S2**, 3.4 g, 11.9 mmol, 1.0 eq) in 50 mL anhydrous THF was added *n*-BuLi (5.7 mL, 14.3 mmol, 1.2 eq, 2.5 M in hexanes) dropwise at -78 °C under nitrogen. After 1 h, D₂O (2.2 mL, 118.9 mmol, 10 eq) was added to the reaction at -78 °C and the reaction mixture was warmed to room temperature, quenched with H₂O, and extracted with EtOAc for 3 times. The combined organic layers were washed with brine, dried over MgSO₄, concentrated *in vacuo*, and used directly for next step without further purification.

To a solution of the above residue in CH₂Cl₂ (20 mL) was added CF₃COOH (TFA, 10 mL, 11 eq) at room temperature. After 2 h, the reaction was concentrated under reduced pressure, diluted with CH₂Cl₂, quenched with an aqueous solution of Na₂CO₃ (saturated), and extracted with CH₂Cl₂ for 3 times. The combined organic layers were washed with brine, dried over MgSO₄, and concentrated *in vacuo* to afford the product **S3**, which was used directly without further purification.

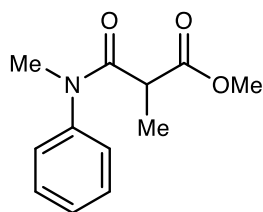
Characterization data for organic substrates

Methyl 3-(methyl(phenyl)amino)-3-oxopropanoate (S4)



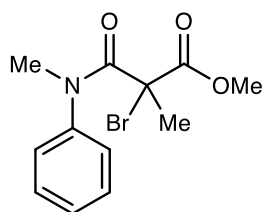
Purified by Biotage (100 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a pale yellow oil (88 mmol scale, 13.4 g, 73% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.46 – 7.32 (m, 3H), 7.25 – 7.17 (m, 2H), 3.67 (s, 3H), 3.31 (s, 3H), 3.22 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.0, 165.8, 143.3, 129.9, 128.2, 127.1, 52.1, 41.2, 37.3 ppm. Spectral data match those previously reported.¹¹

Methyl 2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (S5)



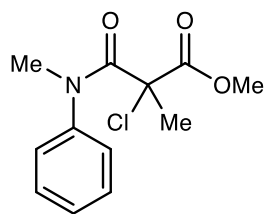
Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a pale yellow oil (20 mmol scale, 3.3 g, 72% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.47 – 7.33 (m, 3H), 7.25 – 7.22 (m, 2H), 3.65 (s, 3H), 3.41 (q, J = 7.0 Hz, 1H), 3.29 (s, 3H), 1.30 (d, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.2, 170.1, 143.5, 130.0, 128.3, 127.4, 52.3, 43.4, 37.6, 14.2 ppm. Spectral data match those previously reported.¹¹

Methyl 2-bromo-2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (1a)



Purified by Biotage (100 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (16 mmol scale, 2.56 g, 64% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 7.45 – 7.39 (m, 2H), 7.37 – 7.32 (m, 1H), 7.31 – 7.26 (m, 2H), 3.60 (s, 3H), 3.21 (s, 3H), 1.98 (s, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 168.7, 165.7, 142.8, 129.5, 128.7, 128.5, 59.1, 54.1, 40.6, 29.8 ppm. IR: 1756 (C=O, ester), 1655 (C=O, amide), 1494, 1375, 1275, 1231, 1110, 780, 700 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{12}\text{H}_{15}\text{BrNO}_3$ requires 300.0235 and 302.0216, observed 300.0229 and 302.0220.

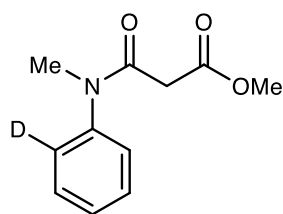
Methyl 2-chloro-2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (**3a**)



Purified by Biotage (100 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a white solid (15 mmol scale, 2.0 g, 53% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.41 – 7.13 (m, 5H), 3.43 (brs, 3H), 3.27 (s, 3H), 1.88 (s, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.8, 165.8, 141.3, 129.7, 129.1, 128.7, 66.1, 53.4, 40.6, 28.9 ppm. Spectral data match those previously reported.¹⁰ Signal broadening was observed for room temperature NMR due to the presence of amide rotamers. Thus, NMR data was also recorded at 80 °C. ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 7.45 – 7.40 (m, 2H), 7.38 – 7.33 (m, 1H), 7.31 – 7.26 (m, 2H), 3.61 (s, 3H), 3.23 (s, 3H), 1.82 (s, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 167.8, 164.6, 141.7, 128.6, 128.0, 127.6, 66.2, 53.0, 39.4, 27.9 ppm. HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) of the mixture resulting from the enzymatic reaction using P450_{arc3} indicated 45% starting material in 6:94 e.r.: t_R = 12.5 (*S*, minor), 13.2 (*R*, major) min.

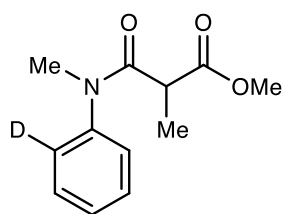
Preparative scale kinetic resolution using whole-cell biocatalysts with 300 mg (*rac*)-**3a** and P450_{arc3} provided 109 mg recovered (*R*)-**3a** (36%, 2:98 e.r.). $[\alpha]_D^{20}$ = -60.7 (c = 0.004 g/mL, CHCl_3). The absolute stereochemistry was determined by X-ray diffraction analysis (CCDC: 2184586).

Methyl 3-(methyl(phenyl-2-*d*)amino)-3-oxopropanoate (**S4-*d*₁**)



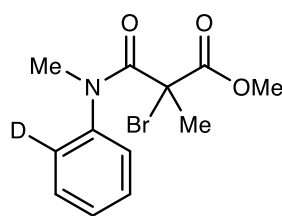
Purified by Biotage (100 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a pale yellow oil (11 mmol scale, 2.2 g, 96% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.39 – 7.31 (m, 2H), 7.31 – 7.26 (m, 1H), 7.18 – 7.13 (m, 1H), 3.57 (s, 3H), 3.22 (s, 3H), 3.13 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.0, 165.8, 143.3, 129.8, 129.7, 128.2, 127.1, 126.8 (t, J = 24.5 Hz), 52.1, 41.2, 37.3 ppm. IR: 2949, 1744 (C=O, ester), 1661 (C=O, amide), 1587, 1482, 1383, 550 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+$ $\text{C}_{11}\text{H}_{13}\text{DNO}_3$ requires 209.1036, observed 209.1034.

Methyl 2-methyl-3-(methyl(phenyl-2-*d*)amino)-3-oxopropanoate (S5-*d*₁)



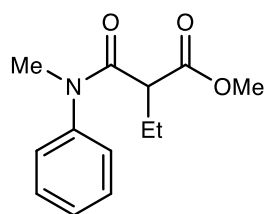
Purified by Biotage (100 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a yellow oil (9.6 mmol scale, 1.3 g, 62% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.48 – 7.27 (m, 3H), 7.23 – 7.17 (m, 1H), 3.60 (s, 3H), 3.37 (q, *J* = 7.0 Hz, 1H), 3.25 (s, 3H), 1.25 (d, *J* = 7.0 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 171.2, 170.1, 143.5, 130.0, 129.8, 128.3, 127.4, 127.1 (t, *J* = 24.4 Hz), 52.3, 43.4, 37.6, 14.2 ppm. IR: 3015, 1745 (C=O, ester), 1651 (C=O, amide), 1591, 1478, 1386, 1215, 1091, 666, 631 cm⁻¹. HRMS (GC-MS, EI TOF) (*m/z*) for [M]⁺ C₁₂H₁₆DNO₃ requires 223.1193, observed 223.1191.

Methyl 2-bromo-2-methyl-3-(methyl(phenyl-2-*d*)amino)-3-oxopropanoate (1a-*d*₁)



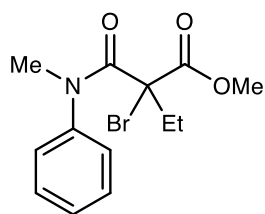
Purified by Biotage (50 g SNAP cartridge, 0-10% EtOAc/hexanes for 8 CV, then 10% EtOAc/hexanes for 5 CV) to afford the product as a brown oil (7 mmol scale, 710 mg, 51% yield). ¹H NMR (400 MHz, DMSO-*d*₆, 80 °C) δ: 7.48 – 7.39 (m, 2H), 7.39 – 7.27 (m, 2H), 3.61 (s, 3H), 3.23 (s, 3H), 1.99 (s, 3H) ppm. ¹³C NMR (101 MHz, DMSO-*d*₆) δ: 167.8, 164.7, 141.9, 128.6, 128.5, 127.8, 127.5 (two overlapping signals), 58.3, 53.2, 39.7, 29.0 ppm. IR: 3015, 1755 (C=O, ester), 1656 (C=O, amide), 1478, 1443, 1376, 1279, 1232, 1113, 749, 632, 565 cm⁻¹. HRMS (ESI) (*m/z*) for [M+H]⁺ C₁₂H₁₄DBrNO₃ requires 301.0298 and 303.0279, observed 301.0309 and 303.0292.

Methyl 2-(methyl(phenyl)carbamoyl)butanoate (S6)



Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (14.5 mmol scale, 2.9 g, 86% yield). ¹H NMR (400 MHz, CDCl₃) δ: 7.47 – 7.31 (m, 3H), 7.22 (d, *J* = 7.9 Hz, 2H), 3.65 (s, 3H), 3.30 (s, 3H), 3.25 (t, *J* = 7.4 Hz, 1H), 1.96 – 1.76 (m, 2H), 0.81 (t, *J* = 7.5 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 170.4, 169.0, 143.5, 129.8, 128.2, 127.6, 52.1, 50.4, 37.6, 22.8, 11.8 ppm. Spectral data match those previously reported.¹⁰

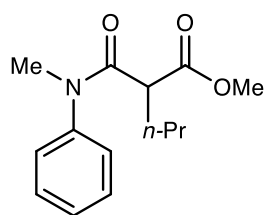
Methyl 2-bromo-2-(methyl(phenyl)carbamoyl)butanoate (1b)



Purified by Biotage (100 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 8 CV) to afford the product as a brown oil (16 mmol scale, 3.8 g, 74% yield). ^1H NMR (500 MHz, DMSO- d_6 , 80 °C) δ : 7.46 – 7.40 (m, 2H), 7.37 – 7.32 (m, 1H), 7.32 – 7.26 (m, 2H), 3.59 (s, 3H), 3.22 (s, 3H), 2.26 – 2.15 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H) ppm.

^{13}C NMR (126 MHz, DMSO- d_6 , 80 °C) δ : 166.77, 164.37, 141.88, 128.63, 127.91, 127.58, 65.61, 52.99, 39.63, 33.31, 8.91 ppm. ^{13}C NMR (126 MHz, DMSO- d_6 , 90 °C) δ : 166.7, 164.3, 141.9, 128.5, 127.8, 127.5, 78.6, 65.6, 52.9, 39.6, 33.2, 8.8 ppm. Spectral data match those previously reported.¹⁰

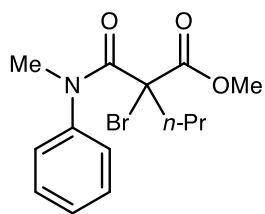
Methyl 2-(methyl(phenyl)carbamoyl)pentanoate (S7)



Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a pale yellow oil (20 mmol scale, 3.5 g, 70% yield). ^1H NMR (500 MHz, CDCl₃) δ : 7.45 – 7.38 (m, 2H), 7.37 – 7.32 (m, 1H), 7.24 – 7.18 (m, 2H), 3.64 (s, 3H), 3.32 (dd, J = 8.5, 6.1 Hz, 1H), 3.29 (s, 3H), 1.90 – 1.72 (m, 2H), 1.28 – 1.06 (m, 2H), 0.77 (t, J = 7.4 Hz, 3H) ppm.

^{13}C NMR (126 MHz, CDCl₃) δ : 170.7, 169.3, 143.6, 130.0, 128.3, 127.7, 52.3, 48.9, 37.7, 31.7, 20.6, 13.8 ppm. IR: 2959, 1740 (C=O, ester), 1656 (C=O, amide), 1595, 1496, 1382, 1195, 1172, 1112, 727, 701 cm⁻¹. HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+$ C₁₄H₁₉NO₃ requires 249.1365, observed 249.1377.

Methyl 2-bromo-2-(methyl(phenyl)carbamoyl)pentanoate (1c)

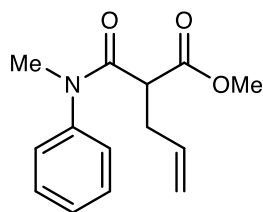


Purified by Biotage (50 g SNAP cartridge, 0-10% EtOAc/hexanes for 8 CV, then 10% EtOAc/hexanes for 8 CV) to afford the product as a pale yellow oil (14 mmol scale, 2.8 g, 61% yield). ^1H NMR (500 MHz, DMSO- d_6 , 80 °C) δ : 7.45 – 7.39 (m, 2H), 7.37 – 7.32 (m, 1H), 7.31 – 7.24 (m, 2H), 3.58 (s, 3H), 3.20 (s, 3H), 2.19 – 2.07 (m, 2H), 1.51 – 1.36 (m, 1H), 1.26 – 1.13 (m, 1H), 0.89 (t, J = 7.3 Hz, 3H) ppm.

^{13}C NMR (126 MHz, DMSO- d_6 , 80 °C) δ : 167.1, 164.5, 142.0, 128.8, 128.0, 127.8, 64.7, 53.1, 42.1, 39.9, 17.8, 13.2 ppm. IR: 2967, 1757 (C=O, ester),

1656 (C=O, amide), 1595, 1494, 1368, 1207, 1123, 906, 727, 699, 648 cm^{-1} . HRMS (ESI) (m/z) for $[M+H]^+$ $\text{C}_{14}\text{H}_{19}\text{BrNO}_3$ requires 328.0548 and 330.0529, observed 328.0532 and 330.0524.

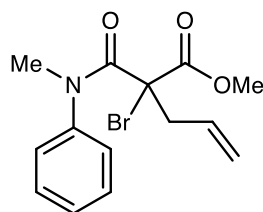
Methyl 2-(methyl(phenyl)carbamoyl)pent-4-enoate (S8)



Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (20 mmol scale, 4.1 g, 84% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.44 – 7.29 (m, 3H), 7.20 (d, J = 7.6 Hz, 2H), 5.60 (m, 1H), 5.04 – 4.92 (m, 2H), 3.63 (s, 3H), 3.43 – 3.35 (m, 1H), 3.26 (s, 3H), 2.64 – 2.48 (m, 2H) ppm.

^{13}C NMR (126 MHz, CDCl_3) δ : 170.1, 168.5, 143.4, 134.6, 129.9, 128.3, 127.8, 117.4, 52.4, 48.9, 37.7, 33.6 ppm. Spectral data match those previously reported.¹²

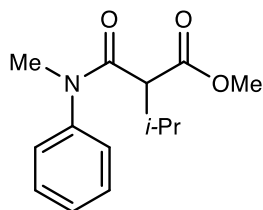
Methyl 2-bromo-2-(methyl(phenyl)carbamoyl)pent-4-enoate (1d)



Purified by Biotage (100 g SNAP cartridge, 0-8% EtOAc/hexanes for 8 CV, then 8% EtOAc/hexanes for 10 CV) to afford the product as a pale yellow solid (16 mmol scale, 1.6 g, 31% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 7.45 – 7.40 (m, 2H), 7.38 – 7.33 (m, 1H), 7.30 (d, J = 7.2 Hz, 2H), 5.77 – 5.66 (m, 1H), 5.18 – 5.11 (m, 2H), 3.56 (s, 3H), 3.23 (s, 3H), 3.03 –

2.93 (m, 2H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 166.2, 164.2, 141.8, 131.7, 128.6, 127.9, 127.6, 119.2, 62.8, 52.9, 44.4, 39.6 ppm. IR: 2959, 1758 (C=O, ester), 1655 (C=O, amide), 1594, 1494, 1368, 1267, 1201, 1124, 922, 699 cm^{-1} . HRMS (ESI) (m/z) for $[M+H]^+$ $\text{C}_{14}\text{H}_{17}\text{BrNO}_3$ requires 326.0392 and 328.0373, observed 326.0384 and 328.0370.

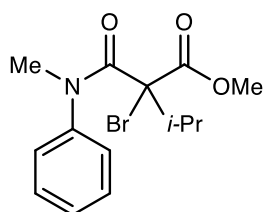
Methyl 3-methyl-2-(methyl(phenyl)carbamoyl)butanoate (S9)



Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (11 mmol scale, 2.3 g, 85% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.45 – 7.32 (m, 3H), 7.21 – 7.15 (m, 2H), 3.65 (s, 3H), 3.27 (s, 3H), 3.06 (d, J = 9.6 Hz, 1H), 2.48 – 2.38 (m, 1H), 0.88 (d, J = 6.7 Hz, 3H), 0.80 (d, J = 6.7

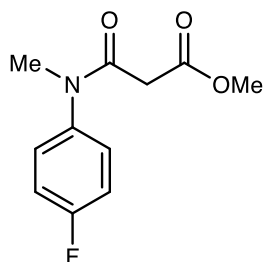
Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 170.0, 168.3, 143.6, 129.9, 128.2, 127.9, 56.4, 52.1, 37.8, 29.7, 20.6, 20.6 ppm. Spectral data match those previously reported.¹³

Methyl 2-bromo-3-methyl-2-(methyl(phenyl)carbamoyl)butanoate (1e)



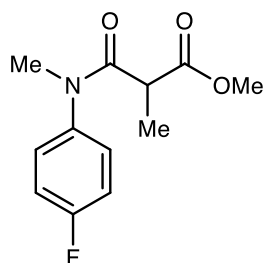
Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 8 CV) to afford the product as a green oil (8.4 mmol scale, 2.6 g, 90% yield). ^1H NMR (500 MHz, DMSO- d_6 , 80 °C) δ : 7.44 – 7.39 (m, 2H), 7.36 – 7.31 (m, 1H), 7.30 – 7.25 (m, 2H), 3.61 (s, 3H), 3.23 (s, 3H), 2.63 – 2.54 (m, J = 6.0 Hz, 1H), 1.10 (d, J = 6.4 Hz, 3H), 0.96 (d, J = 6.5 Hz, 3H) ppm. ^{13}C NMR (126 MHz, DMSO- d_6 , 80 °C) δ : 166.3, 164.4, 142.4, 128.5, 127.7, 127.2, 70.6, 52.7, 39.8, 36.0, 19.5, 18.6 ppm. IR: 2980, 1721 (C=O, ester), 1655 (C=O, amide), 1594, 1494, 1362, 1214, 1104, 1023, 697 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{14}\text{H}_{19}\text{BrNO}_3$ requires 328.0548 and 330.0529, observed 328.0534 and 330.0517.

Methyl 3-((4-fluorophenyl)(methyl)amino)-3-oxopropanoate (S10)



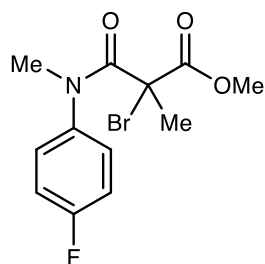
Purified by Biotage (50 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (20 mmol scale, 2.3 g, 51% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.21 – 7.14 (m, 2H), 7.12 – 7.03 (m, 2H), 3.62 (s, 3H), 3.23 (s, 3H), 3.16 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.0, 166.0, 162.0 (d, J = 248.7 Hz), 139.5 (d, J = 3.4 Hz), 129.2 (d, J = 8.8 Hz), 116.9 (d, J = 22.7 Hz), 52.3, 41.2, 37.6 ppm. ^{19}F NMR (376 MHz, CDCl_3) δ : -112.32 – -112.73 (m) ppm. Spectral data match those previously reported.¹⁴

Methyl 3-((4-fluorophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S11)



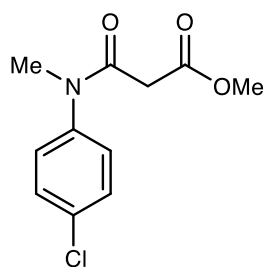
Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (9.2 mmol scale, 1.6 g, 73% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.24 – 7.16 (m, 2H), 7.13 – 7.05 (m, 2H), 3.62 (s, 3H), 3.35 (q, J = 7.1 Hz, 1H), 3.24 (s, 3H), 1.27 (d, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.1, 170.1, 162.0 (d, J = 248.7 Hz), 139.6 (d, J = 3.3 Hz), 129.4 (d, J = 8.7 Hz), 117.0 (d, J = 22.7 Hz), 52.4, 43.5, 37.8, 14.2 ppm. ^{19}F NMR (376 MHz, CDCl_3) δ : -112.50 – -112.73 (m) ppm. Spectral data match those previously reported.¹²

Methyl 2-bromo-3-((4-fluorophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (1f)



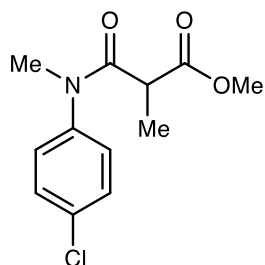
Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 8 CV) to afford the product as a pale yellow solid (5.4 mmol scale, 1.5 g, 86% yield). ^1H NMR (500 MHz, DMSO- d_6 , 80 °C) δ : 7.38 – 7.30 (m, 2H), 7.25 – 7.17 (m, 2H), 3.62 (s, 3H), 3.20 (s, 3H), 1.98 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO- d_6 , 80 °C) δ : 167.9, 165.1, 161.0 (d, J = 245.8 Hz), 138.2 (brs), 130.4 (brs), 115.6 (d, J = 22.8 Hz), 58.2, 53.5, 39.9, 29.1 ppm. ^{19}F NMR (376 MHz, DMSO- d_6 , 80 °C) δ : -113.46 (brs) ppm. IR: 1755 (C=O, ester), 1658 (C=O, amide), 1505, 1443, 1376, 1276, 1224, 1110, 846, 610 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{12}\text{H}_{14}\text{BrFNO}_3$ requires 318.0141 and 320.0122, observed 318.0143 and 320.0070.

Methyl 3-((4-chlorophenyl)(methyl)amino)-3-oxopropanoate (S12)

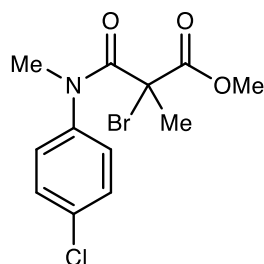


Purified by Biotage (50 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (20 mmol scale, 4.5 g, 93% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.39 – 7.28 (m, 2H), 7.15 (dd, J = 8.5, 1.2 Hz, 2H), 3.63 (s, 3H), 3.23 (s, 3H), 3.17 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.0, 165.8, 141.9, 134.2, 130.2, 128.7, 52.4, 41.2, 37.5 ppm. Spectral data match those previously reported.¹⁴

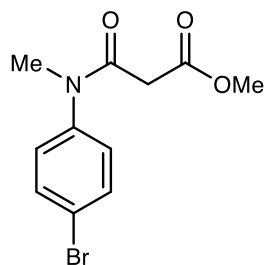
Methyl 3-((4-chlorophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S13)



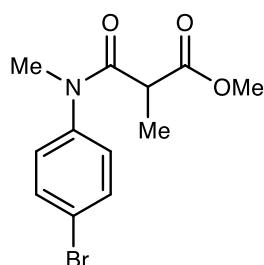
Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (19 mmol scale, 3.3 g, 69% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.38 (d, J = 8.2 Hz, 2H), 7.17 (d, J = 8.2 Hz, 2H), 3.63 (s, 3H), 3.36 (q, J = 7.0 Hz, 1H), 3.24 (s, 3H), 1.27 (d, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.0, 170.0, 142.1, 134.2, 130.2, 128.9, 52.4, 43.5, 37.7, 14.2 ppm. Spectral data match those previously reported.¹²

Methyl 2-bromo-3-((4-chlorophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (1g)

Purified by Biotage (50 g SNAP cartridge, 0-8% EtOAc/hexanes for 8 CV, then 8% EtOAc/hexanes for 8 CV) to afford the product as a white solid (12 mmol scale, 3.3 g, 80% yield). ^1H NMR (500 MHz, $\text{DMSO-}d_6$, 80 $^\circ\text{C}$) δ : 7.50 – 7.45 (m, 2H), 7.36 – 7.30 (m, 2H), 3.66 (s, 3H), 3.22 (s, 3H), 2.00 (s, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO-}d_6$, 80 $^\circ\text{C}$) δ : 167.8, 164.8, 140.9, 132.1, 129.6, 128.7, 57.9, 53.4, 39.4, 28.9 ppm. IR: 2954, 1755 (C=O, ester), 1658 (C=O, amide), 1490, 1443, 1374, 1279, 1231, 1110, 1092, 1015, 725, 646, 564, 527 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{12}\text{H}_{14}\text{BrClNO}_3$ requires 335.9824, observed 335.9829.

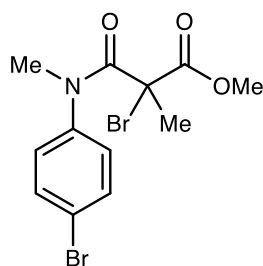
Methyl 3-((4-bromophenyl)(methyl)amino)-3-oxopropanoate (S14)

Purified by Biotage (50 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (30 mmol scale, 7.9 g, 93% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.57 – 7.51 (m, 2H), 7.14 – 7.08 (m, 2H), 3.66 (s, 3H), 3.26 (s, 3H), 3.20 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.0, 165.8, 142.6, 133.3, 129.1, 122.3, 52.5, 41.3, 37.6 ppm. Spectral data match those previously reported.¹⁴

Methyl 3-((4-bromophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S15)

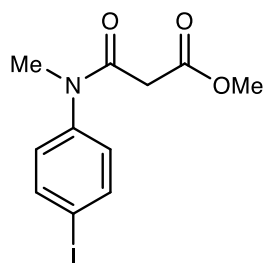
Purified by Biotage (100 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (27 mmol scale, 6.2 g, 77% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.57 – 7.52 (m, 2H), 7.15 – 7.09 (m, 2H), 3.64 (s, 3H), 3.37 (q, J = 7.0 Hz, 1H), 3.25 (s, 3H), 1.28 (d, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.0, 170.0, 142.7, 133.3, 129.3, 122.2, 52.5, 43.5, 37.7, 14.3 ppm. Spectral data match those previously reported.¹²

Methyl 2-bromo-3-((4-bromophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (1h)



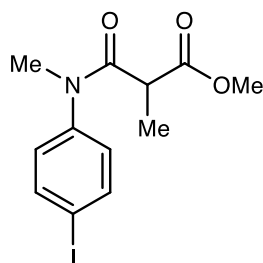
Purified by Biotage (50 g SNAP cartridge, 0-8% EtOAc/hexanes for 8 CV, then 8% EtOAc/hexanes for 10 CV) to afford the product as a brown solid (20 mmol scale, 6.6 g, 88% yield). ^1H NMR (500 MHz, DMSO- d_6 , 80 °C) δ : 7.64 – 7.58 (m, 2H), 7.30 – 7.22 (m, 2H), 3.66 (s, 3H), 3.21 (s, 3H), 2.00 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO- d_6 , 80 °C) δ : 167.8, 164.8, 141.3, 131.6, 129.9, 120.5, 57.8, 53.4, 39.4, 28.9 ppm. IR: 1762 (C=O, ester), 1658 (C=O, amide), 1487, 1376, 1280, 1234, 1111, 1071, 904, 723, 648 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{12}\text{H}_{14}\text{Br}_2\text{NO}_3$ requires 379.9321, observed 379.9312.

Methyl 3-((4-iodophenyl)(methyl)amino)-3-oxopropanoate (S16)



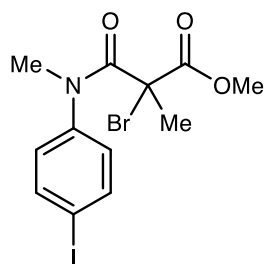
Purified by Biotage (100 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (30 mmol scale, 4.5 g, 45% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.74 – 7.68 (m, 2H), 6.99 – 6.93 (m, 2H), 3.62 (s, 3H), 3.23 (s, 3H), 3.17 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 167.9, 165.6, 143.1, 139.2, 129.2, 93.6, 52.4, 41.2, 37.4 ppm. Spectral data match those previously reported.¹⁴

Methyl 3-((4-iodophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S17)



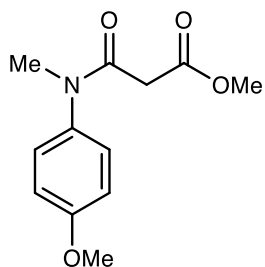
Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (13.6 mmol scale, 2.6 g, 55% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.77 – 7.70 (m, 2H), 7.01 – 6.95 (m, 2H), 3.63 (s, 3H), 3.36 (q, J = 7.0 Hz, 1H), 3.24 (s, 3H), 1.26 (d, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.0, 169.9, 143.3, 139.2, 129.5, 93.6, 52.4, 43.4, 37.6, 14.2 ppm. IR: 2949, 1742 (C=O, ester), 1652 (C=O, amide), 1482, 1383, 1203, 1090, 1008, 906, 721, 554 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+$ $\text{C}_{12}\text{H}_{14}\text{INO}_3$ requires 347.0018, observed 347.0033.

Methyl 2-bromo-3-((4-iodophenyl)(methyl)amino)-2-methyl-3-oxopropanoate (1i)



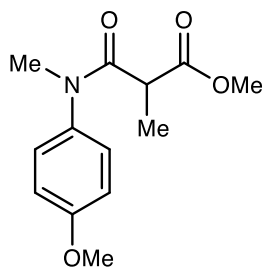
Purified by Biotage (50 g SNAP cartridge, 0-8% EtOAc/hexanes for 8 CV, then 8% EtOAc/hexanes for 10 CV) to afford the product as a brown solid (4 mmol scale, 1.0 g, 60% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 90 $^\circ\text{C}$) δ : 7.82 – 7.75 (m, 2H), 7.14 – 7.08 (m, 2H), 3.66 (s, 3H), 3.21 (s, 3H), 2.00 (s, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 90 $^\circ\text{C}$) δ : 167.7, 164.7, 141.9, 137.5, 129.8, 92.8, 57.8, 53.3, 39.3, 28.8 ppm. IR: 2959, 1754 (C=O, ester), 1656 (C=O, amide), 1484, 1374, 1278, 1232, 1110, 1008, 908, 727, 646 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{12}\text{H}_{14}\text{BrINO}_3$ requires 425.9202 and 427.9182, observed 425.9207 and 427.9211.

Methyl 3-((4-methoxyphenyl)(methyl)amino)-3-oxopropanoate (S18)



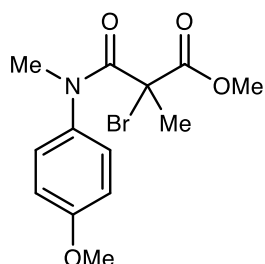
Purified by Biotage (50 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (27.7 mmol scale, 5.8 g, 89% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.12 – 7.07 (m, 2H), 6.91 – 6.84 (m, 2H), 3.78 (s, 3H), 3.62 (s, 3H), 3.22 (s, 3H), 3.17 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.3, 166.3, 159.2, 136.2, 128.3, 115.0, 55.5, 52.3, 41.2, 37.6 ppm. Spectral data match those previously reported.¹¹

Methyl 3-((4-methoxyphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S19)



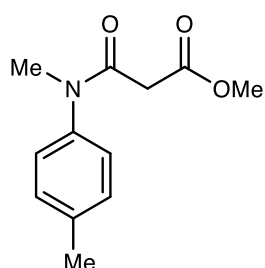
Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (24.6 mmol scale, 5.2 g, 84% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.16 – 7.09 (m, 2H), 6.93 – 6.87 (m, 2H), 3.80 (s, 3H), 3.63 (s, 3H), 3.40 (q, J = 7.1 Hz, 1H), 3.23 (s, 3H), 1.26 (d, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.4, 170.5, 159.3, 136.3, 128.6, 115.1, 55.6, 52.3, 43.4, 37.8, 14.2 ppm. Spectral data match those previously reported.¹²

Methyl 2-bromo-3-((4-methoxyphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (1j)



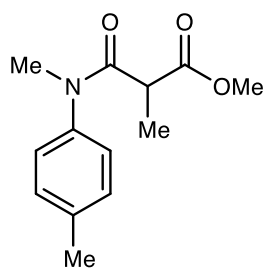
Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a brown solid (12.9 mmol scale, 3.0 g, 71% yield). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ : 7.26 – 7.16 (m, 2H), 7.00 – 6.91 (m, 2H), 3.80 (s, 3H), 3.59 (s, 3H), 3.18 (s, 3H), 1.97 (s, 3H) ppm. ^{13}C NMR (101 MHz, $\text{DMSO}-d_6$) δ : 167.6, 165.0, 158.5, 134.3, 129.5, 113.9, 58.6, 56.3, 55.1, 53.1, 29.1 ppm. IR: 2959, 1757 ($\text{C}=\text{O}$, ester), 1653 ($\text{C}=\text{O}$, amide), 1443, 1376, 1508, 1279, 1245, 1108, 1030, 839, 732, 613 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{13}\text{H}_{17}\text{BrNO}_4$ requires 330.0341 and 332.0322, observed 330.0329 and 332.0273.

Methyl 3-(methyl(*p*-tolyl)amino)-3-oxopropanoate (S20)



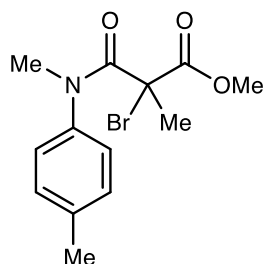
Purified by Biotage (50 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a yellow oil (30 mmol scale, 3.6 g, 68% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.19 (d, $J = 8.0$ Hz, 2H), 7.10 – 7.04 (m, 2H), 3.64 (s, 3H), 3.25 (s, 3H), 3.18 (s, 2H), 2.34 (s, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.3, 166.1, 140.9, 138.4, 130.6, 127.0, 52.3, 41.3, 37.5, 21.1 ppm. Spectral data match those previously reported.¹⁴

Methyl 2-methyl-3-(methyl(*p*-tolyl)amino)-3-oxopropanoate (S21)



Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (16 mmol scale, 2.9 g, 85% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.20 (d, $J = 8.0$ Hz, 2H), 7.09 (d, $J = 8.0$ Hz, 2H), 3.63 (s, 3H), 3.40 (q, $J = 7.0$ Hz, 1H), 3.25 (s, 3H), 2.36 (s, 3H), 1.27 (d, $J = 7.0$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.3, 170.3, 141.0, 138.3, 130.6, 127.2, 52.3, 43.4, 37.7, 21.2, 14.3 ppm. IR: 2959, 1743 ($\text{C}=\text{O}$, ester), 1655 ($\text{C}=\text{O}$, amide), 1514, 1384, 1202, 1177, 1090, 907, 724, 559 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+$ $\text{C}_{13}\text{H}_{17}\text{NO}_3$ requires 235.1208, observed 235.1208.

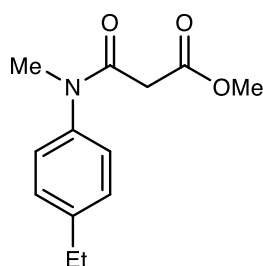
Methyl 2-bromo-2-methyl-3-(methyl(*p*-tolyl)amino)-3-oxopropanoate (1k)



Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a brown solid (12.3 mmol scale, 2.7 g, 69% yield). ¹H NMR (500 MHz, DMSO-*d*₆, 80 °C) δ: 7.21 (d, *J* = 7.9 Hz, 2H), 7.19 – 7.13 (m, 2H), 3.58 (s, 3H), 3.18 (s, 3H), 2.32 (s, 3H), 1.96 (s, 3H) ppm. ¹³C NMR (126 MHz, DMSO-*d*₆, 80 °C) δ: 167.9, 165.0, 139.4, 137.4, 129.3, 127.9, 58.6, 53.3, 40.0, 29.2, 20.3 ppm.

IR: 2954, 1731 (C=O, ester), 1656 (C=O, amide), 1511, 1375, 1232, 1109, 908, 826, 724, 647, 568 cm⁻¹. HRMS (ESI) (*m/z*) for [M+H]⁺ C₁₃H₁₇BrNO₃ requires 314.0392 and 316.0373, observed 314.0396 and 316.0353.

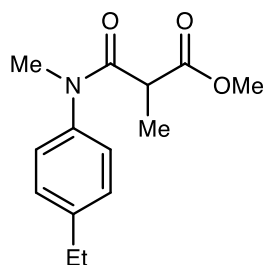
Methyl 3-((4-ethylphenyl)(methyl)amino)-3-oxopropanoate (S22)



Purified by Biotage (100 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a pale yellow oil (50 mmol scale, 9.7 g, 83% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.23 – 7.18 (m, 2H), 7.13 – 7.06 (m, 2H), 3.63 (s, 3H), 3.25 (s, 3H), 3.19 (s, 2H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 168.3, 166.1, 144.6, 141.1, 129.4, 127.0, 52.3, 41.3,

37.5, 28.5, 15.4 ppm. IR: 2970, 1742 (C=O, ester), 1657 (C=O, amide), 1510, 1382, 1247, 1158, 1120, 906, 727, 844 cm⁻¹. HRMS (GC-MS, EI TOF) (*m/z*) for [M]⁺ C₁₃H₁₇NO₃ requires 235.1208, observed 235.1206.

Methyl 3-((4-ethylphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S23)

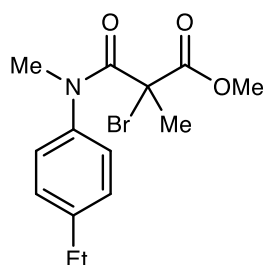


Purified by Biotage (100 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (28.7 mmol scale, 4.5 g, 63% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.22 (d, *J* = 8.3 Hz, 2H), 7.15 – 7.08 (m, 2H), 3.63 (s, 3H), 3.41 (q, *J* = 7.1 Hz, 1H), 3.25 (s, 3H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.27 (d, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.6 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ:

171.4, 170.3, 144.5, 141.1, 129.4, 127.3, 52.3, 43.4, 37.7, 28.5, 15.4, 14.3 ppm. IR: 2970, 1744

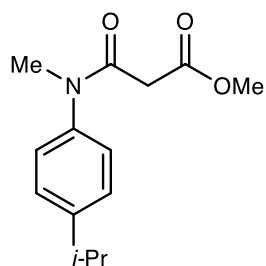
(C=O, ester), 1657 (C=O, amide), 1509, 1384, 1201, 1122, 1179, 1090, 844, 729 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+ \text{C}_{14}\text{H}_{19}\text{NO}_3$ requires 249.1365, observed 249.1372.

Methyl 2-bromo-3-((4-ethylphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (11)



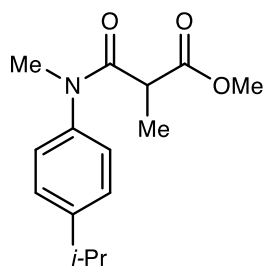
Purified by Biotage (100 g SNAP cartridge, 0-10% EtOAc/hexanes for 8 CV, then 10% EtOAc/hexanes for 10 CV) to afford the product as a white solid (17 mmol scale, 4.0 g, 72% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 7.26 (d, $J = 8.1$ Hz, 1H), 7.21 (d, $J = 8.1$ Hz, 1H), 3.59 (s, 1H), 3.21 (s, 1H), 2.66 (q, $J = 7.6$ Hz, 1H), 1.99 (s, 1H), 1.22 (t, $J = 7.6$ Hz, 1H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 167.7, 164.8, 143.4, 139.4, 127.9 (two overlapping signals), 58.4, 53.1, 39.7, 29.0, 27.3, 14.7 ppm. IR: 1731 (C=O, ester), 1656 (C=O, amide), 1509, 1444, 1376, 1232, 1111, 905, 727, 843, 648, 575 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+ \text{C}_{14}\text{H}_{19}\text{BrNO}_3$ requires 328.0548 and 330.0529, observed 328.0539 and 330.0529.

Methyl 3-((4-isopropylphenyl)(methyl)amino)-3-oxopropanoate (S24)



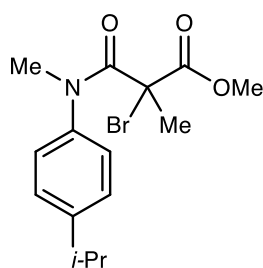
Purified by Biotage (100 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (60 mmol scale, 10 g, 70% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.26 (d, $J = 8.0$ Hz, 2H), 7.12 (d, $J = 8.0$ Hz, 2H), 3.67 (s, 3H), 3.28 (s, 3H), 3.22 (s, 2H), 2.98 – 2.87 (m, 1H), 1.25 (d, $J = 6.9$ Hz, 6H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.3, 166.1, 149.2, 141.1, 127.9, 127.0, 52.2, 41.3, 37.5, 33.8, 23.9 ppm. IR: 2964, 1742 (C=O, ester), 1659 (C=O, amide), 1509, 1380, 1246, 1157, 1120, 1018, 845, 585 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+ \text{C}_{14}\text{H}_{19}\text{NO}_3$ requires 249.1365, observed 249.1357.

Methyl 3-((4-isopropylphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S25)



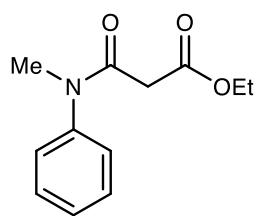
Purified by Biotage (100 g SNAP cartridge, 0-10% EtOAc/hexanes for 8 CV, then 10% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (20 mmol scale, 2.6 g, 49% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.30 – 7.25 (m, 2H), 7.19 – 7.12 (m, 2H), 3.44 (q, J = 7.1 Hz, 1H), 3.28 (s, 3H), 3.00 – 2.89 (m, 1H), 1.30 (d, J = 7.1 Hz, 3H), 1.27 (d, J = 6.9 Hz, 6H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.4, 170.4, 149.1, 141.2, 128.0, 127.3, 52.3, 43.4, 37.7, 33.8, 24.0, 14.3 ppm. IR: 2959, 1744 (C=O, ester), 1652 (C=O, amide), 1509, 1385, 1204, 905, 844, 726, 648, 588 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+$ $\text{C}_{14}\text{H}_{19}\text{NO}_3$ requires 249.1365, observed 249.1372.

Methyl 2-bromo-3-((4-isopropylphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (1m)



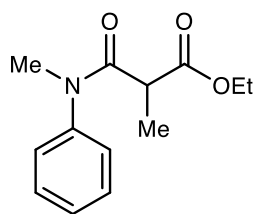
Purified by Biotage (50 g SNAP cartridge, 0-7% EtOAc/hexanes for 8 CV, then 7% EtOAc/hexanes for 10 CV) to afford the product as a brown oil (7.8 mmol scale, 1.8 g, 69% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 7.29 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.2 Hz, 2H), 3.56 (s, 3H), 3.20 (s, 3H), 2.98 – 2.89 (m, 1H), 1.98 (s, 3H), 1.23 (d, J = 6.9 Hz, 6H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 167.7, 164.9, 148.0, 139.4, 127.8, 126.4, 58.3, 53.1, 39.7, 32.6, 29.1, 23.2, 23.1 ppm. IR: 2959, 1725 (C=O, ester), 1657 (C=O, amide), 1509, 1444, 1376, 1278, 1232, 1111, 905, 727, 648, 587 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{15}\text{H}_{21}\text{BrNO}_3$ requires 342.0705 and 344.0686, observed 342.0718 and 344.0699.

Ethyl 3-(methyl(phenyl)amino)-3-oxopropanoate (S26)



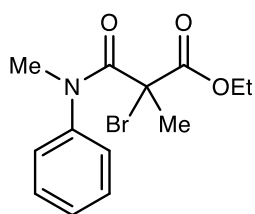
Purified by Biotage (100 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a brown oil (30 mmol scale, 4.5 g, 68% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.45 – 7.38 (m, 2H), 7.38 – 7.31 (m, 1H), 7.25 – 7.19 (m, 2H), 4.10 (q, J = 7.1 Hz, 2H), 3.29 (s, 3H), 3.19 (s, 2H), 1.21 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 167.8, 166.1, 143.6, 130.0, 128.3, 127.3, 61.3, 41.6, 37.5, 14.1 ppm. Spectral data match those previously reported.¹¹

Ethyl 2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (S27)



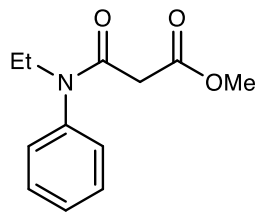
Purified by Biotage (50 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (8.8 mmol scale, 1.4 g, 70% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.44 – 7.37 (m, 2H), 7.37 – 7.30 (m, 1H), 7.24 – 7.18 (m, 2H), 4.13 – 4.00 (m, 2H), 3.37 (q, $J = 7.0$ Hz, 1H), 3.27 (s, 3H), 1.26 (d, $J = 7.0$ Hz, 3H), 1.19 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 170.8, 170.2, 143.7, 130.0, 128.2, 127.6, 61.2, 43.6, 37.7, 14.2, 14.1 ppm. Spectral data match those previously reported.¹⁵

Ethyl 2-bromo-2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (1n)



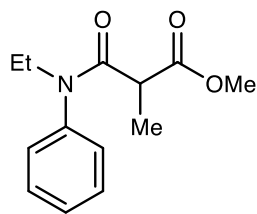
Purified by Biotage (50 g SNAP cartridge, 0-10% EtOAc/hexanes for 8 CV, then 10% EtOAc/hexanes for 10 CV) to afford the product as a white solid (5 mmol scale, 0.86 g, 52% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 7.42 (m, 2H), 7.38 – 7.27 (m, 3H), 4.11 – 3.99 (m, 2H), 3.24 (s, 3H), 2.00 (s, 3H), 1.20 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 167.3, 164.8, 142.2, 128.6, 127.6, 127.4, 62.4, 58.4, 39.6, 28.9, 13.0 ppm. Spectral data match those previously reported.¹⁶

Methyl 3-(ethyl(phenyl)amino)-3-oxopropanoate (S28)



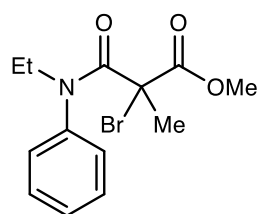
Purified by Biotage (100 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a pale yellow oil (30 mmol scale, 3.4 g, 55% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.46 – 7.33 (m, 3H), 7.19 (d, $J = 7.1$ Hz, 2H), 3.77 (q, $J = 7.1$ Hz, 2H), 3.66 (s, 3H), 3.16 (s, 2H), 1.13 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.2, 165.3, 141.7, 129.8, 128.4, 128.3, 52.2, 44.2, 41.7, 12.8 ppm. Spectral data match those previously reported.¹⁷

Methyl 3-(ethyl(phenyl)amino)-2-methyl-3-oxopropanoate (S29)



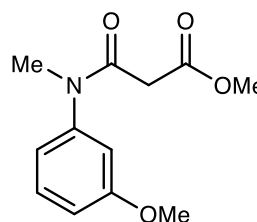
Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (15 mmol scale, 3.4 g, 94% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.40 – 7.34 (m, 2H), 7.34 – 7.29 (m, 1H), 7.15 (d, $J = 7.1$ Hz, 2H), 3.77 – 3.63 (m, 2H), 3.57 (s, 3H), 3.26 (d, $J = 7.1$ Hz, 1H), 1.22 (d, $J = 7.1$ Hz, 3H), 1.05 (t, $J = 7.2$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.2, 169.4, 141.7, 129.8, 128.4, 128.3, 52.1, 44.2, 43.7, 14.1, 12.8 ppm. Spectral data match those previously reported.¹⁸

Methyl 2-bromo-2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (1o)



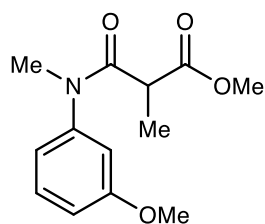
Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (14 mmol scale, 1.5 g, 34% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 7.47 – 7.41 (m, 2H), 7.41 – 7.35 (m, 1H), 7.27 (d, $J = 7.2$ Hz, 2H), 3.70 (m, 1H), 3.60 (m, 1H), 3.54 (s, 3H), 1.96 (s, 3H), 1.03 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 °C) δ : 168.5, 165.1, 140.2, 130.4, 129.4, 128.9, 59.7, 53.9, 47.2, 30.0, 12.6 ppm. IR: 2944, 1723 (C=O, ester), 1652 (C=O, amide), 1494, 1395, 1279, 1230, 1114, 729, 700, 647 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+$ $\text{C}_{13}\text{H}_{17}\text{BrNO}_3$ requires 314.0392 and 316.0373, observed 314.0398 and 316.0392.

Methyl 3-((3-methoxyphenyl)(methyl)amino)-3-oxopropanoate (S30)



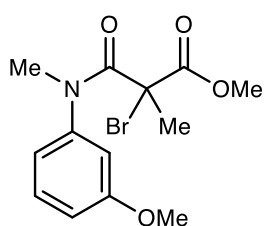
Purified by Biotage (100 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (30 mmol scale, 6.3 g, 86% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.27 (dd, $J = 8.1$, 8.1 Hz, 1H), 6.85 (dd, $J = 8.1$, 2.4 Hz, 1H), 6.75 (d, $J = 8.1$ Hz, 1H), 6.72 (dd, $J = 2.4$, 2.4 Hz, 1H), 3.76 (s, 3H), 3.62 (s, 3H), 3.23 (s, 3H), 3.19 (s, 2H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 168.2, 165.9, 160.7, 144.5, 130.7, 119.2, 113.9, 112.9, 55.4, 52.2, 41.2, 37.3 ppm. IR: 2954, 1739 (C=O, ester), 1658 (C=O, amide), 1599, 1589, 1488, 1220, 1156, 1114, 1037, 701 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+$ $\text{C}_{12}\text{H}_{15}\text{NO}_4$ requires 237.1001, observed 237.0996.

Methyl 3-((3-methoxyphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (S31)



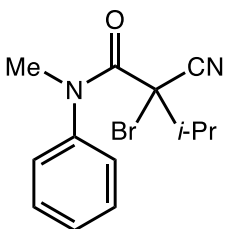
Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 10 CV) to afford the product as a colorless oil (25.7 mmol scale, 4.7 g, 73% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.29 (dd, $J = 8.1, 8.1$ Hz, 1H), 6.87 (dd, $J = 8.1, 2.4$ Hz, 1H), 6.78 (d, $J = 8.1$ Hz, 1H), 6.74 (dd, $J = 2.4, 2.4$ Hz, 1H), 3.78 (s, 3H), 3.62 (s, 3H), 3.42 (q, $J = 7.0$ Hz, 1H), 3.24 (s, 3H), 1.26 (d, $J = 7.0$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 171.3, 170.1, 160.7, 144.6, 130.7, 119.5, 113.7, 113.3, 55.5, 52.3, 43.4, 37.5, 14.3 ppm. IR: 2954, 1744 (C=O, ester), 1656 (C=O, amide), 1599, 1589, 1488, 1384, 1218, 1203, 1043, 703 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+ \text{C}_{13}\text{H}_{17}\text{NO}_4$ requires 251.1158, observed 251.1149.

Methyl 2-bromo-3-((3-methoxyphenyl)(methyl)amino)-2-methyl-3-oxopropanoate (1p)



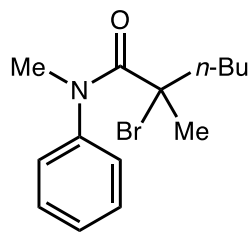
Purified by Biotage (100 g SNAP cartridge, 0-15% EtOAc/hexanes for 8 CV, then 15% EtOAc/hexanes for 10 CV) to afford the product as a brown oil (18.7 mmol scale, 3.9 g, 63% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 7.33 (dd, $J = 8.2, 8.2$ Hz, 1H), 6.94 (ddd, $J = 8.2, 2.5, 0.9$ Hz, 1H), 6.92 – 6.82 (m, 2H), 3.61 (s, 3H), 3.22 (s, 3H), 1.99 (s, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ : 167.8, 164.8, 159.4, 143.0, 129.4, 120.0, 114.0, 113.5, 58.4, 55.1, 53.2, 39.7, 29.0 ppm. IR: 2954, 2255, 1756 (C=O, ester), 1656 (C=O, amide), 1600, 1486, 1231, 1112, 1042, 905, 726, 703, 648 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{H}]^+ \text{C}_{13}\text{H}_{17}\text{BrNO}_4$ requires 330.041 and 332.0322, observed 330.0355 and 332.0274.

2-Bromo-2-cyano-*N*,3-dimethyl-*N*-phenylbutanamide (1q)



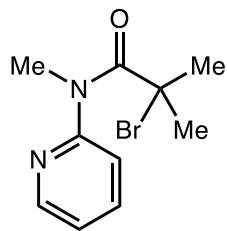
Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 8 CV) to afford the product as a pale-yellow oil (13 mmol scale, 1.6 g, 42% yield). ^1H NMR (400 MHz, $\text{Chloroform}-d$) δ 7.75 – 7.29 (m, 5H), 3.38 (s, 3H), 3.04 – 2.82 (m, 1H), 1.24 (d, $J = 6.8$ Hz, 3H), 1.08 (d, $J = 6.6$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, $\text{Chloroform}-d$) δ 162.7, 141.7, 129.9, 128.5, 113.8, 50.4, 41.4, 38.6, 18.5, 18.4 ppm. IR: 2971, 1652, 1593, 1495, 1373, 1275, 1129, 1054, 1033, 837, 697, 565 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{Na}]^+ \text{C}_{13}\text{H}_{15}\text{BrN}_2\text{O}_2$ requires 317.0266 and 319.0246, observed 317.0284 and 319.0284.

2-Bromo-*N*,2-dimethyl-*N*-phenylhexanamide (1r)



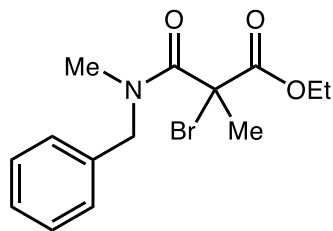
Purified by Biotage (50 g SNAP cartridge, 0-8% EtOAc/hexanes for 8 CV, then 8% EtOAc/hexanes for 8 CV) to afford the product as a pale-yellow oil (8.3 mmol scale, 1.6 g, 66% yield). ¹H NMR (500 MHz, Chloroform-*d*) δ 7.41 – 7.13 (m, 5H), 3.24 (s, 3H), 2.07 – 1.89 (m, 1H), 1.89 – 1.73 (m, 1H), 1.63 (s, 3H), 1.36 – 1.04 (m, 4H), 0.79 (t, *J* = 7.2 Hz, 3H) ppm. ¹³C NMR (126 MHz, Chloroform-*d*) δ 169.4, 144.1, 128.9, 128.0, 127.8, 62.5, 43.8, 41.7, 30.2, 28.0, 22.4, 13.7 ppm. IR: 2957, 2933, 1642, 1594, 1494, 1361, 1033, 774, 698, 633, 580 cm⁻¹. HRMS (ESI) (*m/z*) for [M+Na]⁺ C₁₄H₂₀BrNONa requires 320.0626 and 322.0607, observed 320.0637 and 322.0622.

2-Bromo-*N*,2-dimethyl-*N*-(pyridin-2-yl)propanamide (1s)



Purified by Biotage (100 g SNAP cartridge, 0-25% EtOAc/hexanes for 8 CV, then 25% EtOAc/hexanes for 8 CV) to afford the product as a pale-yellow solid (10 mmol scale, 2.2 g, 84% yield). ¹H NMR (500 MHz, DMSO-*d*₆, 80 °C) δ 9.44 (d, *J* = 6.3 Hz, 1H), 8.60 – 8.53 (m, 1H), 8.01 (d, *J* = 8.7 Hz, 1H), 7.75 – 7.68 (m, 1H), 3.38 (s, 3H), 1.84 (s, 6H) ppm. ¹³C NMR (126 MHz, DMSO-*d*₆, 80 °C) δ 172.9, 151.1, 146.6, 136.8, 119.6, 110.9, 67.4, 26.8, 23.1 ppm. IR: 2957, 2933, 1642, 1594, 1494, 1361, 1033, 774, 698, 633, 580 cm⁻¹. HRMS (ESI) (*m/z*) for [M+H]⁺ C₁₀H₁₄BrN₂O requires 257.0290 and 259.0270, observed 257.0286 and 259.0273.

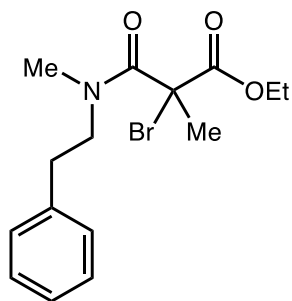
Ethyl 3-(benzyl(methyl)amino)-2-bromo-2-methyl-3-oxopropanoate (1t)



Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 8 CV) to afford the product as a pale-yellow oil (10 mmol scale, 1.0 g, 30% yield). ¹H NMR (500 MHz, DMSO-*d*₆) δ 7.45 – 7.16 (m, 5H), 4.72 (d, *J* = 15.0 Hz, 1H), 4.46 (d, *J* = 15.0 Hz, 1H), 4.38 – 4.14 (m, 2H), 2.84 (s, 3H), 2.04 (s, 3H), 1.18 (t, *J* = 7.0 Hz, 3H) ppm. ¹³C NMR (126 MHz, DMSO-*d*₆) δ 168.3, 165.5, 136.8, 128.4, 127.2, 127.2, 63.4, 57.4, 51.5, 35.5, 28.9, 13.6 ppm. IR: 2993, 2938, 1748, 1651, 1444, 1399, 1232, 1108, 1085,

734, 698, 639 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{Na}]^+$ $\text{C}_{14}\text{H}_{18}\text{BrNO}_3\text{Na}$ requires 350.0368 and 352.0349, observed 350.0352 and 352.0367.

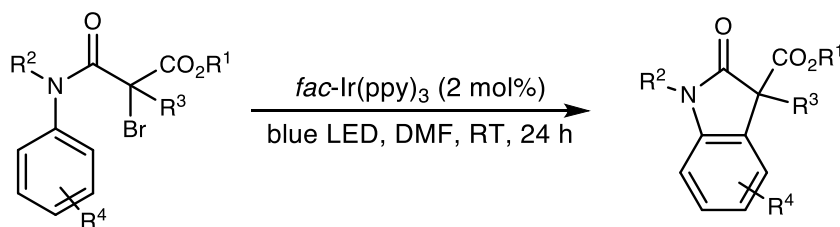
Ethyl 2-bromo-2-methyl-3-(methyl(phenethyl)amino)-3-oxopropanoate (1u)



Purified by Biotage (50 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 8 CV) to afford the product as a pale-yellow oil (10 mmol scale, 1.0 g, 29% yield). ^1H NMR (500 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ 7.34 – 7.18 (m, 5H), 4.29 – 4.21 (m, 2H), 3.62 – 3.45 (m, 2H), 2.89 (s, 3H), 2.87 – 2.79 (m, 2H), 2.02 (s, 3H), 1.23 (t, $J = 7.1$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, $\text{DMSO}-d_6$, 80 $^\circ\text{C}$) δ 167.9, 164.6, 138.3, 128.2, 127.9, 125.8, 62.7, 57.4, 50.5, 35.4, 32.1, 28.5, 13.1 ppm. IR: 2944, 1747, 1650, 1400, 1231, 1108, 1088, 1046, 748, 700, 643 cm^{-1} . HRMS (ESI) (m/z) for $[\text{M}+\text{Na}]^+$ $\text{C}_{15}\text{H}_{20}\text{BrNO}_3\text{Na}$ requires 364.0524 and 366.0505, observed 364.0523 and 366.0504.

Supplementary Note 7. Synthesis and characterization of products

General procedure for the synthesis of racemic products

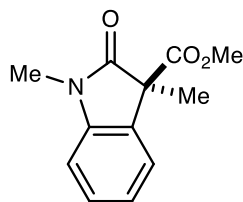


Racemic products were synthesized on a 0.2 – 1.0 mmol scale using 2 mol% *fac*-Ir(ppy)₃ with blue light at room temperature for 24 h according to literature procedure.¹⁹ Substrate (0.5 mmol, 1.0 eq), *fac*-Ir(ppy)₃ (0.01 mmol, 2 mol%), and 10 mL anhydrous DMF were added to a reaction tube (Fisherbrand tube, screw thread with marking spot, 20 X 125 MM) under nitrogen. Then the reaction tube was sealed and irradiated with Blue LED strip purchased from Super Bright LED for 24 hours with fan cooling. The reaction was then diluted with H₂O and extracted with EtOAc for 3 times. The combined organic layers were washed with brine, dried over MgSO₄, concentrated *in vacuo*, and purified by column chromatography with the aid of a Biotage Isolera.

Enantioenriched enzymatic products were synthesized by preparative scale enzymatic reactions using the general procedure described above.

Characterization data for products

Methyl -1,3-dimethyl-2-oxoindoline-3-carboxylate (2a)

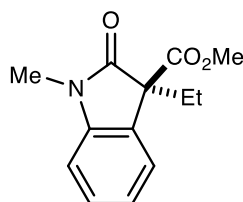


Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.2 mmol scale, 35 mg, 80% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.34 – 7.28 (m, 1H), 7.24 (d, $J = 7.4$ Hz, 1H), 7.08 – 7.02 (m, 1H), 6.86 (d, $J = 7.7$ Hz, 1H), 3.63 (s, 3H), 3.24 (s, 3H), 1.65 (s, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 175.1, 170.3, 143.6, 130.0, 129.1, 123.1, 123.0, 108.5, 54.9, 53.0, 26.6, 20.2 ppm. Spectral data match those previously reported.^{20,11}

With bromide substrate **1a**, HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 74% yield, 96:4 e.r. using P450_{arc1}: $t_R = 15.5$ (*S*, major), 17.5 (*R*, minor) min. HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 79% yield, 12:88 e.r. using P450_{arc2}: $t_R = 15.6$ (*S*, minor), 17.7 (*R*, major) min.

With chloride substrate **3a**, HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 85% yield, 94:6 e.r. using P450_{arc1}: $t_R = 15.6$ (*S*, major), 17.8 (*R*, minor) min. HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 64% yield, 12:88 e.r. using P450_{arc2} P74G L436R F330V: $t_R = 15.6$ (*S*, minor), 17.7 (*R*, major) min. The absolute stereochemistry was determined by comparison with **2i**.

Methyl (*R*)-3-ethyl-1-methyl-2-oxoindoline-3-carboxylate (2b)

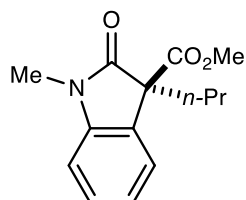


Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.5 mmol scale, 102 mg, 87% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.36 – 7.28 (m, 1H), 7.28 – 7.20 (m, 1H), 7.13 – 7.02 (m, 1H), 6.85 (d, $J = 7.8$ Hz, 1H), 3.64 (s, 3H), 3.24 (s, 3H), 2.38 – 2.18 (m, 2H), 0.63 (t, $J = 7.4$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 173.9, 169.8, 144.1, 128.9, 127.5, 123.1, 122.7, 108.2, 59.7, 52.6, 27.3, 26.2, 7.8 ppm. Spectral data match those previously reported.¹⁰

Large scale whole-cell biotransformation using P450_{arc2} provided 668 mg product (90% yield, 2:98 e.r.). $[\alpha]_{\text{D}}^{20} = -91.1$ ($c = 0.02$ g/mL, CHCl_3).

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 88% yield, 3:97 e.r. using P450_{arc2}: t_R = 7.9 (*S*, minor), 9.3 (*R*, major) min. The absolute stereochemistry was determined by comparison with **2i**.

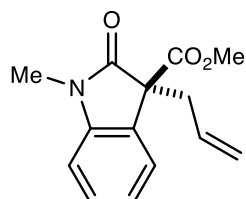
Methyl (*R*)-1-methyl-2-oxo-3-propylindoline-3-carboxylate (**2c**)



Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.5 mmol scale, 100 mg, 81% yield). ¹H NMR (500 MHz, CDCl₃) δ : 7.38 – 7.30 (m, 1H), 7.30 – 7.24 (m, 1H), 7.13 – 7.06 (m, 1H), 6.87 (d, J = 7.8 Hz, 1H), 3.67 (s, 3H), 3.26 (s, 3H), 2.32 – 2.14 (m, 2H), 1.12 – 0.88 (m, 2H), 0.84 (t, J = 7.2 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ : 174.4, 170.2, 144.2, 129.1, 128.3, 123.5, 123.0, 108.4, 59.6, 53.0, 36.5, 26.5, 17.1, 14.1 ppm. Spectral data match those previously reported.^{10,21}

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 78% yield, 12:88 e.r. using P450_{arc2}: t_R = 6.6 (*S*, minor), 7.2 (*R*, major) min.

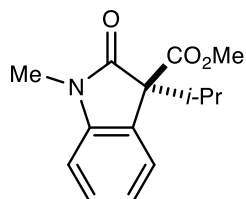
Methyl (*R*)-3-allyl-1-methyl-2-oxoindoline-3-carboxylate (**2d**)



Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.5 mmol scale, 107 mg, 87% yield). ¹H NMR (500 MHz, CDCl₃) δ : 7.34 – 7.23 (m, 2H), 7.09 – 7.04 (m, 1H), 6.84 (d, J = 7.9 Hz, 1H), 5.41 – 5.28 (m, 1H), 5.06 – 4.98 (m, 1H), 4.95 – 4.86 (m, 1H), 3.65 (s, 3H), 3.22 (s, 3H), 3.04 – 2.90 (m, 2H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ : 173.7, 169.6, 144.2, 131.0, 129.2, 127.6, 123.8, 122.9, 119.9, 108.4, 59.2, 53.1, 38.5, 26.5 ppm. Spectral data match those previously reported.^{10,11}

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 76% yield, 7:93 e.r. using P450_{arc2}: t_R = 7.0 (*S*, minor), 8.1 (*R*, major) min.

Methyl (*R*)-3-isopropyl-1-methyl-2-oxoindoline-3-carboxylate (**2e**)

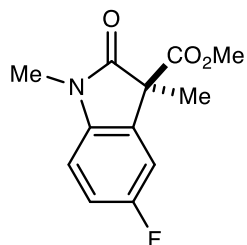


Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a colorless oil (1.0 mmol scale, 183 mg, 74% yield). ¹H NMR (500 MHz, CDCl₃) δ : 7.35 – 7.27 (m, 2H), 7.10 – 7.03 (m, 1H), 6.82 (d, J = 7.8 Hz, 1H), 3.68 (s, 3H),

3.21 (s, 3H), 2.83 – 2.71 (m, 1H), 1.02 (d, $J = 6.7$ Hz, 3H), 0.79 (d, $J = 6.9$ Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 173.2, 169.8, 144.1, 128.9, 127.5, 124.3, 122.7, 108.1, 63.3, 52.9, 35.0, 26.3, 17.2, 17.2 ppm. Spectral data match those previously reported.¹⁰

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 77% yield, 8:92 e.r. using P450_{arc2}: $t_R = 10.9$ (*S*, minor), 12.1 (*R*, major) min.

Methyl (*S*)-5-fluoro-1,3-dimethyl-2-oxoindoline-3-carboxylate (**2f**)

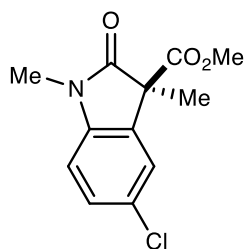


Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.4 mmol scale, 85 mg, 89% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.06 – 6.98 (m, 2H), 6.81 – 6.75 (m, 1H), 3.66 (s, 3H), 3.23 (s, 3H), 1.65 (s, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 174.8, 169.8, 159.4 (d, $J = 241.7$ Hz),

139.6 (d, $J = 2.2$ Hz), 131.5 (d, $J = 8.4$ Hz), 115.4 (d, $J = 23.4$ Hz), 111.6 (d, $J = 25.2$ Hz), 109.1 (d, $J = 8.0$ Hz), 55.3 (d, $J = 1.8$ Hz), 53.3, 26.8, 20.3 ppm. ^{19}F NMR (376 MHz, CDCl_3) δ : -119.75 – -119.83 (m) ppm. Spectral data match those previously reported.¹²

HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 76% yield, 90:10 e.r. using P450_{arc1} G438T L266H L78C V328E S332A G74P: $t_R = 12.5$ (*S*, major), 13.8 (*R*, minor) min.

Methyl (*S*)-5-chloro-1,3-dimethyl-2-oxoindoline-3-carboxylate (**2g**)

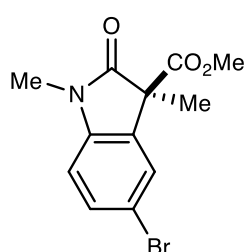


Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.5 mmol scale, 102 mg, 80% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.29 (dd, $J = 8.3, 2.1$ Hz, 1H), 7.23 (d, $J = 2.1$ Hz, 1H), 6.78 (d, $J = 8.3$ Hz, 1H), 3.66 (s, 3H), 3.23 (s, 3H), 1.65 (s, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ :

174.7, 169.7, 142.3, 131.6, 129.1, 128.4, 123.8, 109.5, 55.1, 53.3, 26.8, 20.3 ppm. Spectral data match those previously reported.¹²

HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 86% yield, 92:8 e.r. using P450_{arc1} G438T L266H L78C V328E S332A G74P: $t_R = 11.4$ (*S*, major), 12.8 (*R*, minor) min.

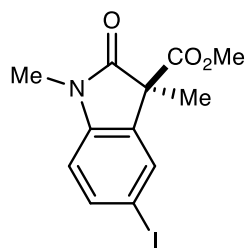
Methyl (S)-5-bromo-1,3-dimethyl-2-oxoindoline-3-carboxylate (2h)



Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.5 mmol scale, 139 mg, 93% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.43 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.35 (d, *J* = 2.0 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 3.65 (s, 3H), 3.21 (s, 3H), 1.64 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 174.5, 169.7, 142.7, 132.0, 131.9, 126.5, 115.5, 110.0, 55.0, 53.3, 26.7, 20.3 ppm. Spectral data match those previously reported.¹²

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 87% yield, 95:5 e.r. using P450_{arc1} G438T L266H L78C V328E S332A G74P: *t*_R = 8.7 (*S*, major), 9.5 (*R*, minor) min.

Methyl (S)-5-iodo-1,3-dimethyl-2-oxoindoline-3-carboxylate (2i)

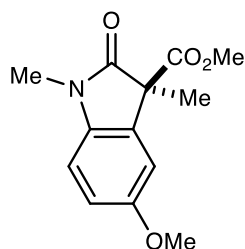


Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.5 mmol scale, 151 mg, 88% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.63 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.52 (d, *J* = 1.7 Hz, 1H), 6.64 (d, *J* = 8.2 Hz, 1H), 3.67 (s, 3H), 3.22 (s, 3H), 1.64 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 174.4, 169.7, 143.4, 138.0, 132.2, 132.0, 110.6, 85.3, 54.8, 53.3, 26.7, 20.3 ppm. IR: 2959, 2255, 1742, 1713, 1487, 1342, 1243, 1110, 905, 809, 725, 648 cm⁻¹. HRMS (GC-MS, EI TOF) (*m/z*) for [M]⁺ C₁₂H₁₂INO₃ requires 344.9862, observed 344.9865.

Large scale whole-cell biotransformation using P450_{arc1} G438T L266H L78C V328E S332A G74P provided 590 mg product (73% yield, 93:7 e.r.). [α]_D²⁰ = + 14.9 (*c* = 0.01 g/mL, CHCl₃). The absolute stereochemistry was determined by X-ray diffraction analysis (CCDC: 2184585).

HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 68% yield, 93:7 e.r. using P450_{arc1} G438T L266H L78C V328E S332A G74P: *t*_R = 11.7 (*S*, major), 13.5 (*R*, minor) min.

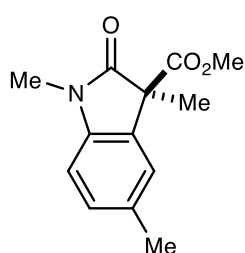
Methyl (*R*)-5-methoxy-1,3-dimethyl-2-oxindoline-3-carboxylate (**2j**)



Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.4 mmol scale, 68 mg, 68% yield). ¹H NMR (500 MHz, CDCl₃) δ: 6.89 – 6.82 (m, 2H), 6.77 (d, *J* = 8.4 Hz, 1H), 3.79 (s, 3H), 3.66 (s, 3H), 3.23 (s, 3H), 1.66 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 174.9, 170.4, 156.4, 137.1, 131.3, 113.5, 110.5, 108.9, 56.0, 55.4, 53.2, 26.8, 20.4 ppm. Spectral data match those previously reported.¹²

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 79% yield, 10:90 e.r. using P450_{arc2} P74G L436R F330E: *t*_R = 11.8 (*S*, minor), 13.8 (*R*, major) min.

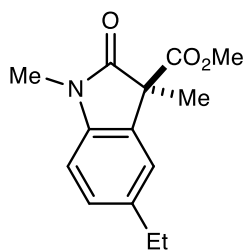
Methyl (*R*)-1,3,5-trimethyl-2-oxindoline-3-carboxylate (**2k**)



Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.5 mmol scale, 76 mg, 66% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.11 (d, *J* = 8.0 Hz, 1H), 7.07 (s, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 3.65 (s, 3H), 3.23 (s, 3H), 2.33 (s, 3H), 1.65 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 175.2, 170.6, 141.3, 132.7, 130.2, 129.4, 124.0, 108.3, 55.1, 53.1, 26.7, 21.2, 20.4 ppm. IR: 2959, 2255, 1741, 1708, 1499, 1375, 1351, 1237, 1112, 905, 726, 649 cm⁻¹. HRMS (GC-MS, EI TOF) (*m/z*) for [M]⁺ C₁₃H₁₅NO₃ requires 233.1052, observed 233.1056.

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 87% yield, 14:86 e.r. using P450_{arc2} P74G L436R F330E: *t*_R = 9.1 (*S*, minor), 11.2 (*R*, major) min.

Methyl (*R*)-5-ethyl-1,3-dimethyl-2-oxindoline-3-carboxylate (**2l**)

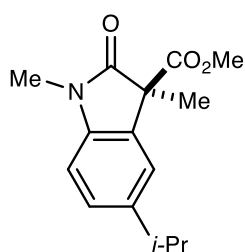


Purified by Biotage (25 g SNAP cartridge, 0-10% EtOAc/hexanes for 8 CV, then 10% EtOAc/hexanes for 5 CV) to afford the product as a colorless oil (0.5 mmol scale, 93 mg, 75% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.13 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.08 (d, *J* = 1.7 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 3.63 (s, 3H), 3.22 (s, 3H), 2.61 (q, *J* = 7.6 Hz, 2H), 1.64 (s, 3H), 1.20 (t, *J* = 7.6 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 175.2, 170.5, 141.4, 139.3, 130.1, 128.2, 122.7, 108.3, 55.0, 53.0, 28.6, 26.6, 20.3, 15.9 ppm. IR: 2975, 1741, 1709, 1498, 1375, 1351, 1233, 1113,

905, 727, 628 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+ \text{C}_{14}\text{H}_{17}\text{NO}_3$ requires 247.1208, observed 247.1204.

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 94% yield, 10:90 e.r. using P450_{arc2} P74G L436R F330E H266C G268P: t_R = 9.0 (*S*, minor), 11.2 (*R*, major) min.

Methyl (*R*)-5-isopropyl-1,3-dimethyl-2-oxoindoline-3-carboxylate (**2m**)

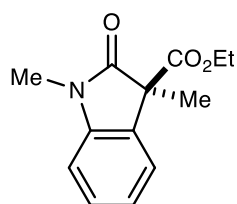


Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a colorless oil (0.5 mmol scale, 107 mg, 82% yield). ^1H NMR (400 MHz, CDCl_3) δ : 7.18 (d, J = 8.0 Hz, 1H), 7.12 (s, 1H), 6.78 (d, J = 8.0 Hz, 1H), 3.64 (s, 3H), 3.22 (s, 3H), 2.95 – 2.81 (m, 1H), 1.65 (s, 3H), 1.23 (d, J = 6.9 Hz, 6H) ppm. ^{13}C

NMR (126 MHz, CDCl_3) δ : 175.3, 170.6, 144.1, 141.5, 130.1, 126.8, 121.4, 108.3, 55.1, 53.1, 33.9, 26.6, 24.3, 24.2, 20.4 ppm. IR: 2964, 1741, 1712, 1497, 1451, 1373, 1348, 1231, 1111, 1056, 817 cm^{-1} . HRMS (GC-MS, EI TOF) (m/z) for $[\text{M}]^+ \text{C}_{15}\text{H}_{19}\text{NO}_3$ requires 261.1365, observed 261.1365.

HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 73% yield, 20:80 e.r. using P450_{arc2} P74G L436R F330E H266C G268P: t_R = 8.3 (*S*, minor), 10.3 (*R*, major) min.

Ethyl 1,3-dimethyl-2-oxoindoline-3-carboxylate (**2n**)



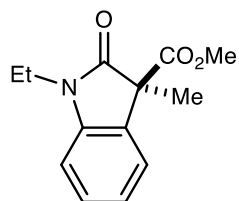
Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a colorless oil (0.5 mmol scale, 87 mg, 75% yield). ^1H NMR (500 MHz, CDCl_3) δ : 7.34 – 7.27 (m, 1H), 7.24 (dd, J = 7.4, 0.6 Hz, 1H), 7.09 – 7.02 (m, 1H), 6.85 (d, J =

7.8 Hz, 1H), 4.18 – 4.03 (m, 2H), 3.24 (s, 3H), 1.65 (s, 3H), 1.14 (t, J = 7.1 Hz, 3H) ppm. ^{13}C NMR (126 MHz, CDCl_3) δ : 175.3, 169.8, 143.7, 130.3, 129.0, 123.1, 122.9, 108.5, 62.0, 55.2, 26.6, 20.2, 14.0 ppm. Spectral data match those previously reported.¹¹

HPLC analysis (IC column, 90:10 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 79% yield, 91:9 e.r. using P450_{arc1}: t_R = 14.3 (*S*, major), 16.8 (*R*, minor) min. HPLC analysis (IC column, 90:10

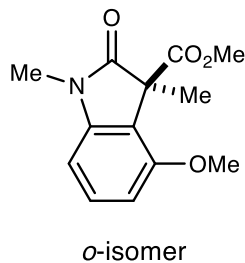
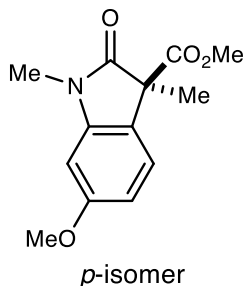
hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 80% yield, 10:90 e.r. using P450_{arc2}: *t*_R = 14.4 (*S*, minor), 16.9 (*R*, major) min.

Methyl (*S*)-1-ethyl-3-methyl-2-oxoindoline-3-carboxylate (**2o**)



Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a white solid (0.6 mmol scale, 110 mg, 79% yield). ¹H NMR (500 MHz, CDCl₃) δ: 7.30 (ddd, *J* = 7.8, 7.6, 1.3 Hz, 1H), 7.24 (d, *J* = 7.5 Hz, 1H), 7.04 (dd, *J* = 7.6, 7.5 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 3.78 (q, *J* = 7.2 Hz, 2H), 3.63 (s, 3H), 1.65 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 174.8, 170.4, 142.8, 130.4, 129.1, 123.3, 122.7, 108.7, 55.0, 53.1, 35.0, 20.2, 12.6 ppm. IR: 2985, 1740, 1708, 1352, 1376, 1241, 1209, 1106, 906, 728 cm⁻¹. HRMS (ESI) (*m/z*) for [M+H]⁺ C₁₃H₁₆NO₃ requires 234.1134, observed 234.1130. HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 98% yield, 94:6 e.r. using P450_{arc1}: *t*_R = 7.8 (*S*, major), 9.0 (*R*, minor) min.

Methyl (*R*)-4-methoxy-1,3-dimethyl-2-oxoindoline-3-carboxylate (*o*-isomer, major) and methyl (*R*)-6-methoxy-1,3-dimethyl-2-oxoindoline-3-carboxylate (*p*-isomer, minor) (**2p**)



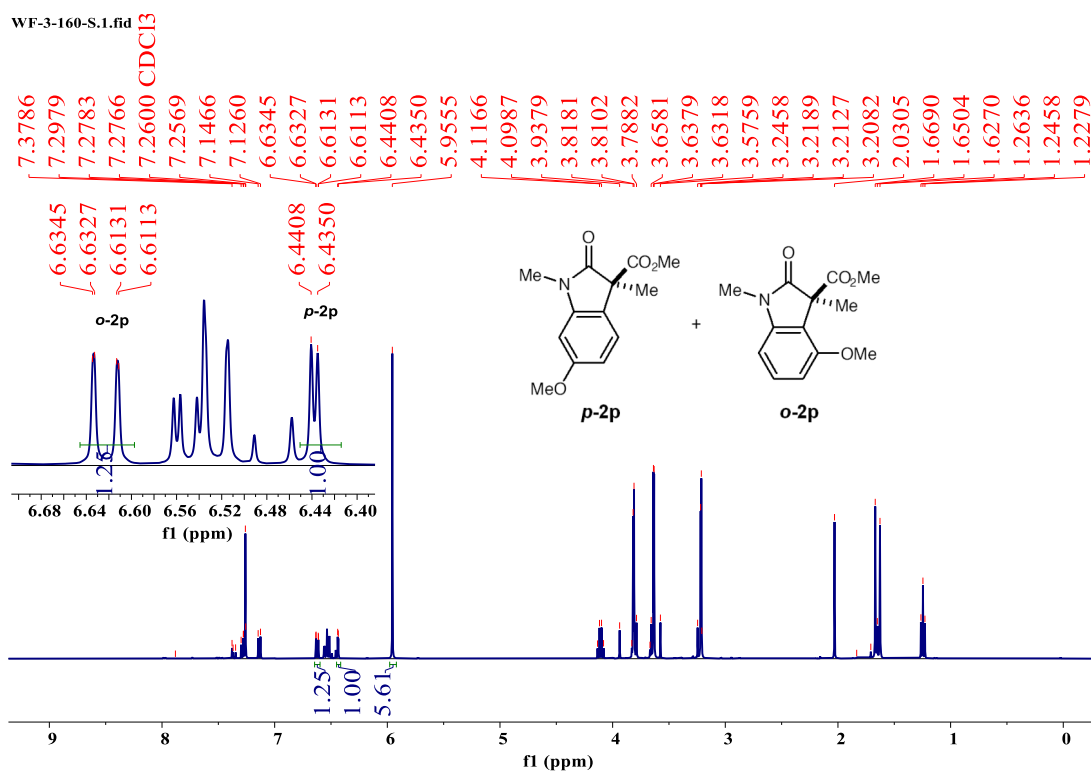
Purified by Biotage (25 g SNAP cartridge, 0-20% EtOAc/hexanes for 8 CV, then 20% EtOAc/hexanes for 5 CV) to afford the product as a colorless oil (0.5 mmol scale, 80% NMR yield with 1,1,2,2-tetrachloroethane as internal standard, 79 mg, 63% yield, inseparable mixture of two isomers, *p*-isomer : *o*-isomer = 44:56. ¹H NMR with crude and isolated product is shown in **Supplementary Figure 11-12**). Major *o*-isomer: ¹H NMR (500 MHz, CDCl₃) δ: 7.29 (dd, *J* = 8.5, 7.8 Hz, 1H), 6.63 (dd, *J* = 8.5, 0.8 Hz, 1H), 6.53 (dd, *J* = 7.8, 0.8 Hz, 1H), 3.82 (s, 3H), 3.64 (s, 3H), 3.22 (s, 3H), 1.68 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 175.4, 169.6, 155.7, 145.1, 130.2, 122.1, 106.3, 101.8, 55.7, 54.5, 53.0, 27.0, 18.2 ppm. Minor *p*-isomer: ¹H NMR (500 MHz, CDCl₃) δ: 7.14 (d, *J* = 8.2 Hz, 1H), 6.56 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.44 (d, *J* = 2.3 Hz, 1H), 3.83 (s, 3H), 3.65 (s, 3H), 3.23 (s, 3H), 1.64 (s, 3H) ppm. ¹³C NMR (126 MHz, CDCl₃) δ: 175.8, 170.7, 161.0, 145.0, 123.9, 116.8, 106.7, 96.7, 55.7, 54.5, 53.1, 26.7, 20.4 ppm. IR: 2949, 1746 (C=O,

ester), 1710 (C=O, amide), 1608, 1475, 1264, 1233, 1102, 1066, 904, 727 cm⁻¹. HRMS (GC-MS, EI TOF) (m/z) for [M]⁺ C₁₃H₁₅NO₄ requires 249.1001, observed 249.0991.

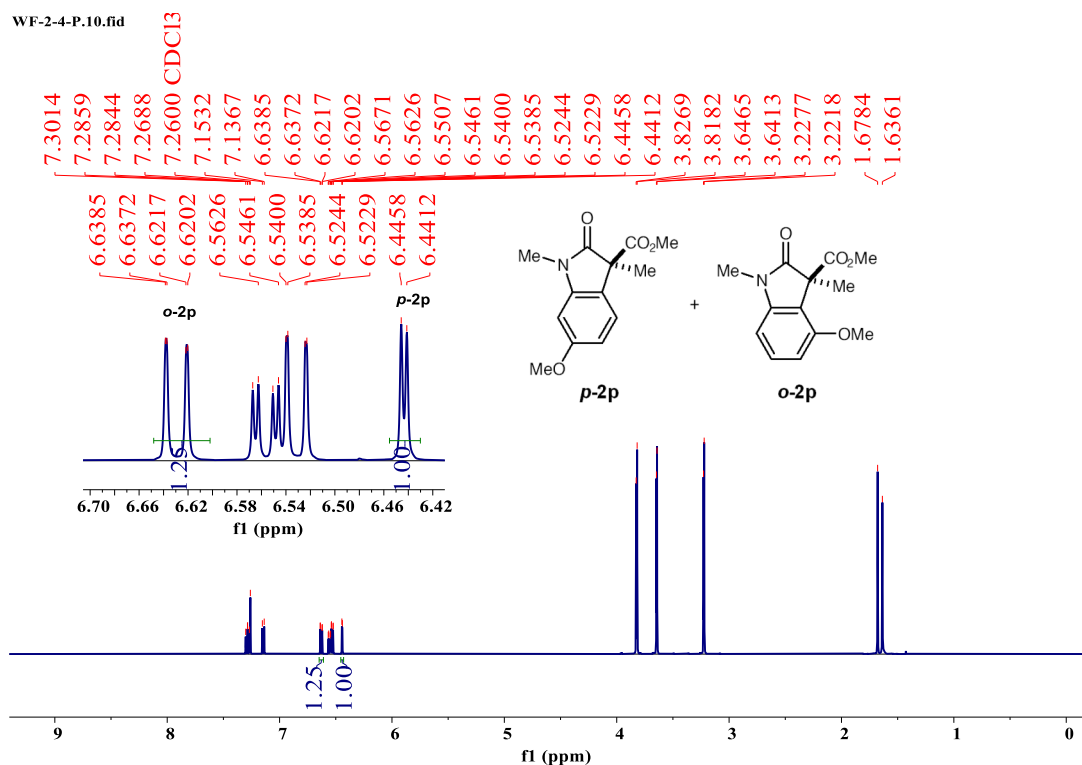
Reaction with CuBr (30 mol%), tris(2-pyridylmethyl)amine (TPA, 30 mol%) in toluene at 110 °C for 20 h provided the product as a mixture (0.2 mmol scale, 67% NMR yield with 1,1,2,2-tetrachloroethane as internal standard, inseparable mixture of two isomers, *p*-isomer : *o*-isomer = 39:61. Crude ¹H NMR is shown in **Supplementary Figure 13**).

Whole cell biotransformation with P450_{arc2} provided *p*-isomer as the major product (12 mg, 67% yield, *p*-isomer: *o*-isomer = 78:22 based on ¹H NMR, showed in **Supplementary Figure 14**).

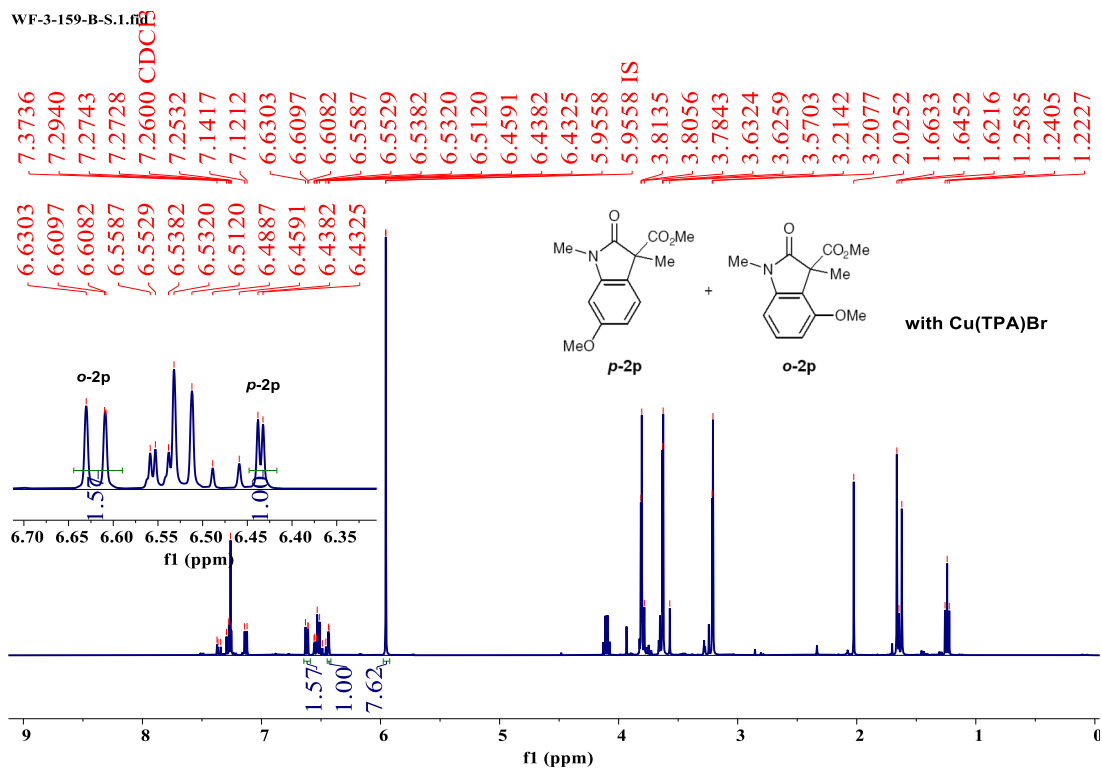
HPLC analysis (IC column, 80:20 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 46% yield, 85:15 e.r. (*p*-isomer) and 13% yield, 42:58 e.r. (*o*-isomer) using P450_{arc2}: *t*_R = 11.7 (*p*-isomer, major), 12.7 (*p*-isomer, minor), 14.6 (*o*-isomer, minor), 17.4 (*o*-isomer, major) min.



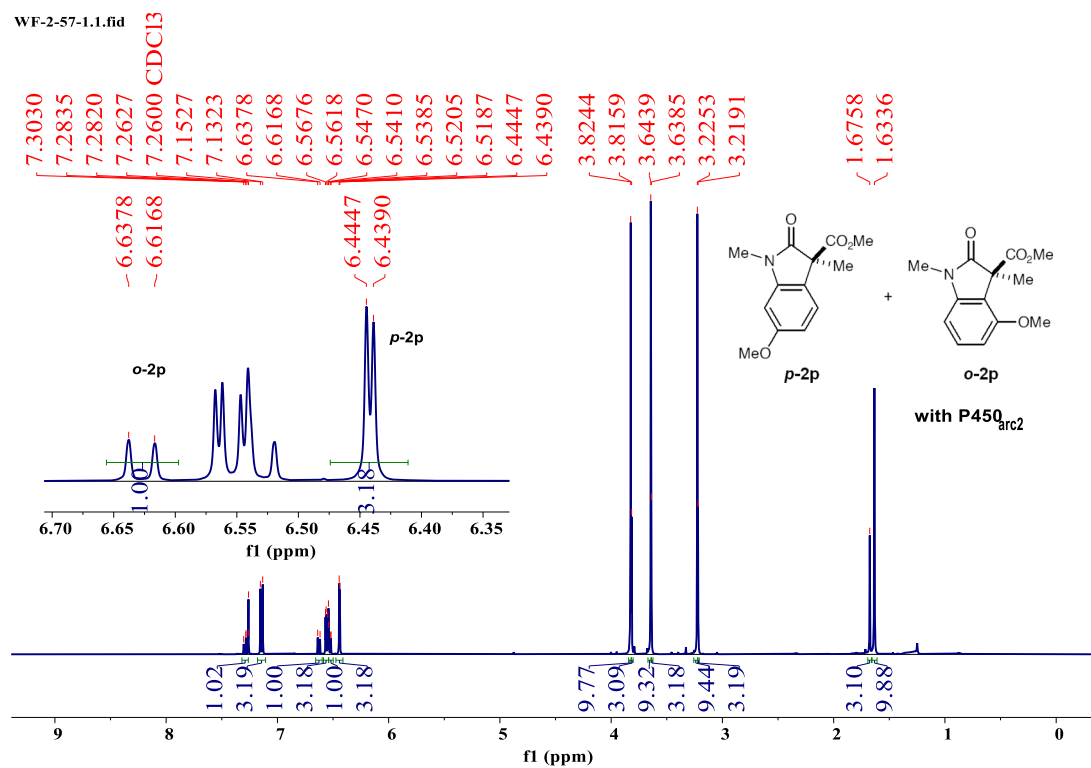
Supplementary Figure 11. Crude ¹H NMR spectrum for the reaction with *fac*-Ir(ppy)₃



Supplementary Figure 12. ^1H NMR spectrum for the isolated product from reaction with *fac*- $\text{Ir}(\text{ppy})_3$ (isolated product has the same ratio, *p*-isomer: *o*-isomer = 44:56).

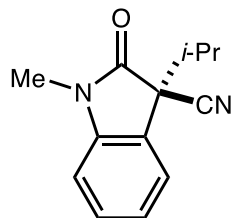


Supplementary Figure 13. Crude ^1H NMR spectrum for the reaction with CuBr/TPA



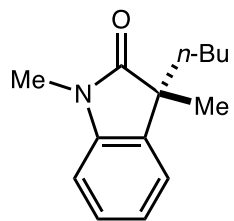
Supplementary Figure 14. ^1H NMR spectrum for the reaction with P450_{arc2}

3-Isopropyl-1-methyl-2-oxoindoline-3-carbonitrile (2q)



Purified by Biotage (25 g SNAP cartridge, 0-12% EtOAc/hexanes for 8 CV, then 12% EtOAc/hexanes for 8 CV) to afford the product as a white solid (0.5 mmol scale, 60 mg, 56% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 7.47 – 7.34 (m, 2H), 7.21 – 7.10 (m, 1H), 6.89 (d, J = 7.8 Hz, 1H), 3.24 (s, 3H), 2.65 – 2.50 (m, 1H), 1.18 (d, J = 6.8 Hz, 3H), 0.90 (d, J = 6.7 Hz, 3H) ppm. ^{13}C NMR (126 MHz, Chloroform-*d*) δ 170.3, 143.6, 130.3, 124.7, 123.9, 123.5, 117.2, 109.0, 51.3, 36.2, 26.8, 17.5, 16.5 ppm. IR: 2972, 1720, 1607, 1491, 1461, 1366, 1260, 1055, 1033, 762, 691, 542 cm^{-1} . HRMS (TOF MS EI+) (m/z) for $[\text{M}]^+$ $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}$ requires 214.1106, observed 214.1107. HPLC analysis (IB-N5 column, 98:2 hexanes: *i*-PrOH, 1.2 mL/min, 40 °C) indicated 7% yield, 53:47 e.r. using P450_{arc2}: t_{R} = 9.8 (major), 11.6 (minor) min.

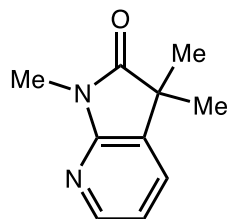
3-Butyl-1,3-dimethylindolin-2-one (2r)



Purified by preparative TLC (EtOAc/hexanes = 3/1) to afford the product as a colorless oil (0.5 mmol scale, 70 mg, 65% yield). ^1H NMR (500 MHz, Chloroform-*d*) δ 7.26 – 7.19 (m, 1H), 7.14 (d, J = 7.1 Hz, 1H), 7.04 (dd, J = 7.4, 7.4 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 3.19 (s, 3H), 1.87 (td, J = 12.8, 4.5 Hz, 1H), 1.70 (td, J = 12.9, 4.3 Hz, 1H), 1.32 (s, 3H), 1.23 – 1.08 (m, 2H), 0.99 – 0.69 (m, 5H) ppm. ^{13}C NMR (126 MHz, Chloroform-*d*) δ 180.9, 143.4, 134.3, 127.5, 122.5, 122.4, 107.8, 48.4, 38.3, 26.6, 26.1, 23.8, 22.8, 13.9 ppm. IR: 2958, 2929, 1705, 1612, 1492, 1469, 1376, 1347, 1121, 1084, 1033, 753, 542, 486 cm^{-1} . HRMS (TOF MS EI+) (m/z) for $[\text{M}]^+$ $\text{C}_{14}\text{H}_{19}\text{NO}$ requires 217.1467, observed 217.1476.

HPLC analysis (IG column, 95:5 hexanes: EtOH, 1.2 mL/min, 40 °C) indicated 36% yield, 54:46 e.r. using P411_{Diane3} G437A V327P: t_{R} = 4.4 (major), 4.7 (minor) min.

1,3,3-Trimethyl-1,3-dihydro-2H-pyrrolo[2,3-b]pyridin-2-one (2s)

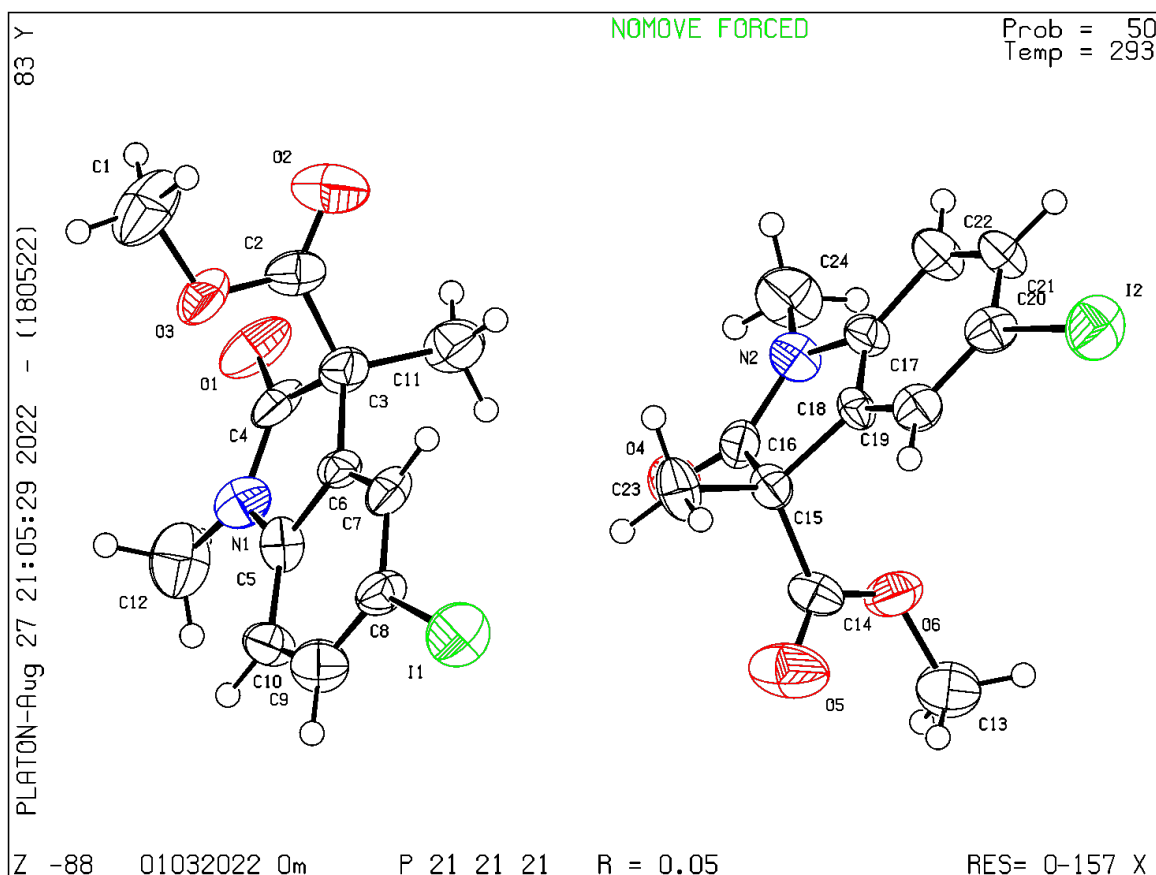
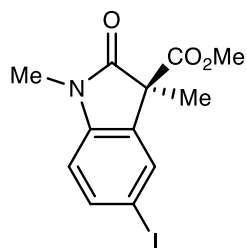


Purified by preparative TLC (EtOAc/hexanes = 3/1) to afford the product as a white solid (0.5 mmol scale, 40 mg, 45% yield). ^1H NMR (400 MHz, Chloroform-*d*) δ 8.13 (dd, J = 5.3, 1.6 Hz, 1H), 7.39 (dd, J = 7.2, 1.6 Hz, 1H), 6.92 (dd, J = 7.2, 5.3 Hz, 1H), 3.26 (s, 3H), 1.35 (s, 6H) ppm. ^{13}C NMR (126

MHz, Chloroform-*d*) δ 180.9, 156.3, 146.7, 130.1, 129.7, 118.1, 43.9, 25.4, 24.0 ppm. IR: 2973, 1716, 1592, 1470, 1382, 1340, 1141, 1033, 782, 551, 495 cm^{-1} . HRMS (TOF MS EI+) (m/z) for $[\text{M}]^+$ $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}$ requires 176.0950, observed 176.0952.

Supplementary Note 8. X-ray crystal structures for the determination of absolute stereochemistry

Methyl (*S*)-5-iodo-1,3-dimethyl-2-oxoindoline-3-carboxylate (2i) (CCDC 2184585)



Checkcif report:

Datablock: 01032022_0m

Bond precision:	C-C = 0.0194 Å	Wavelength=0.71073
Cell:	a=12.070(3) b=13.081(3) c=16.311(4)	
	alpha=90 beta=90 gamma=90	
Temperature:	293 K	
	Calculated	Reported
Volume	2575.3(11)	2575.4(11)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C12 H12 I N O3	?
Sum formula	C12 H12 I N O3	C12 H12 I N O3
Mr	345.13	345.13
Dx,g cm-3	1.780	1.780
Z	8	8
Mu (mm-1)	2.483	2.483
F000	1344.0	1344.0
F000'	1340.77	
h,k,lmax	14,15,19	14,15,19
Nref	4737[2681]	4696
Tmin,Tmax	0.742,0.780	0.677,0.745
Tmin'	0.609	
Correction method=	# Reported T Limits: Tmin=0.677 Tmax=0.745	
AbsCorr =	MULTI-SCAN	
Data completeness=	1.75/0.99	Theta(max)= 25.382
R(reflections)=	0.0548(2469)	wR2(reflections)= 0.0848(4696)
S =	0.946	Npar= 314

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

● **Alert level C**

● [PLAT242_ALERT_2_C](#) Low "ainMol"Ueq as Compared to Neighbors of C14
Check

[PLAT342_ALERT_3_C](#) Low Bond Precision on C-C Bonds 0.01935 Ång.

[PLAT911_ALERT_3_C](#) Missing FCF Refl Between Thmin & STh/L= 0.600 9 Report

● **Alert level G**

[PLAT199_ALERT_1_G](#) Reported _cell_measurement_temperature (K) 293 Check

[PLAT200_ALERT_1_G](#) Reported _diffn_ambient_temperature (K) 293 Check

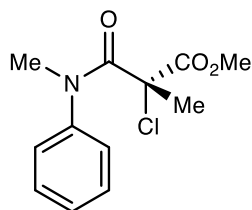
PLAT791 ALERT 4 G Model has Chirality at C3 (Sohnke SpGr) S Verify
PLAT791 ALERT 4 G Model has Chirality at C15 (Sohnke SpGr) S Verify
PLAT883 ALERT 1 G No Info/Value for _atom_sites_solution_primary . Please Do !
PLAT912 ALERT 4 G Missing # of FCF Reflections Above STh/L= 0.600 2 Note
PLAT941 ALERT 3 G Average HKL Measurement Multiplicity 4.0 Low
PLAT978 ALERT 2 G Number C-C Bonds with Positive Residual Density. 0 Info

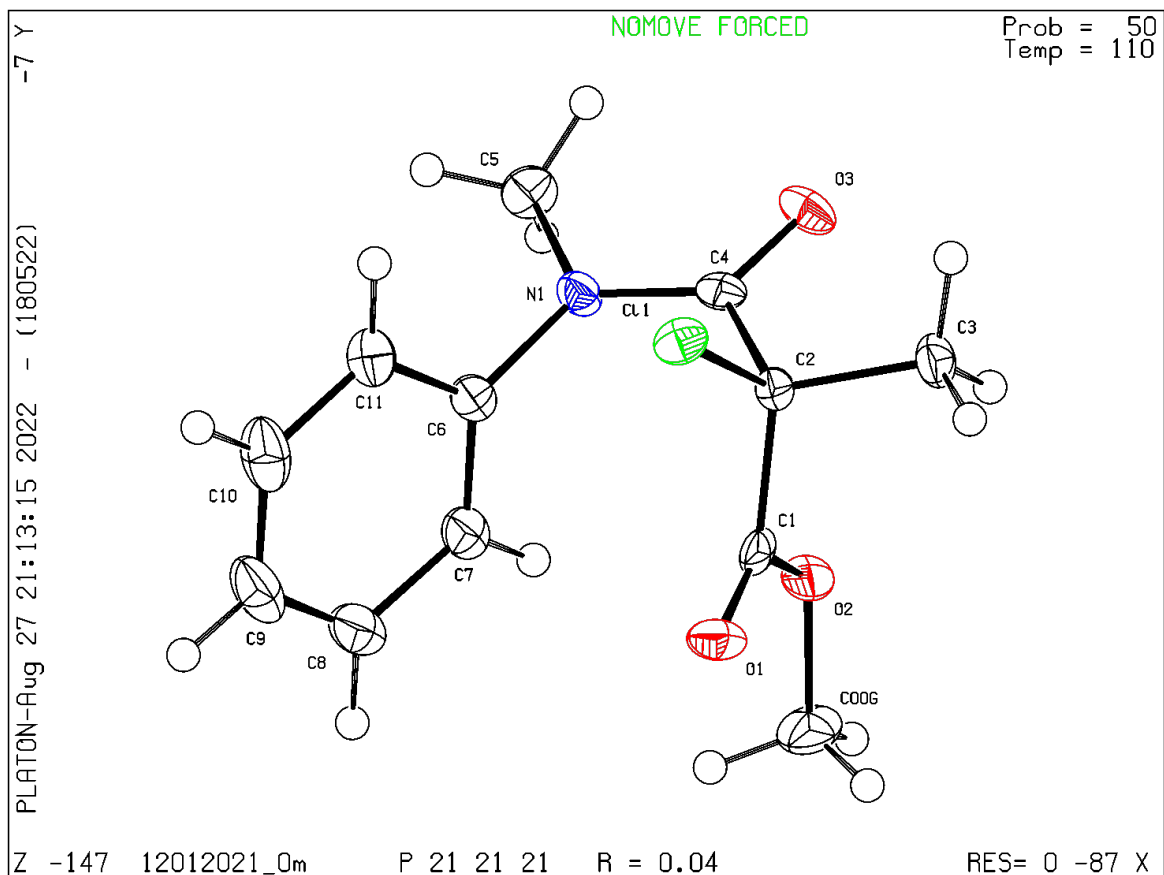
0 **ALERT level A** = Most likely a serious problem --resolve or explain
 0 **ALERT level B** = A potentially serious problem, consider carefully
 3 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight
 8 **ALERT level G** = General information/check it is not something unexpected

3 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
 2 ALERT type 2 Indicator that the structure model may be wrong or deficient
 3 ALERT type 3 Indicator that the structure quality may be low
 3 ALERT type 4 Improvement, methodology, query or suggestion
 0 ALERT type 5 Informative message, check

PLATON version of 18/05/2022; check.def file version of 17/05/2022

Methyl (*R*)-2-chloro-2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate (3a) (CCDC 2184586)





Checkcif report:

Datablock: 12012021_0m

Bond precision:	C-C = 0.0069 Å	Wavelength=0.71073
Cell:	a=7.8535(19) b=11.405(3) c=13.717(4)	
	alpha=90 beta=90 gamma=90	
Temperature: 110 K		
	Calculated	Reported
Volume	1228.6(6)	1228.6(6)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C12 H14 Cl N O3	?
Sum formula	C12 H14 Cl N O3	C12 H14 Cl N O3
Mr	255.69	255.69
Dx, g cm ⁻³	1.382	1.382
Z	4	4
Mu (mm ⁻¹)	0.307	0.307

F000	536.0	536.0
F000''	536.84	
h,k,lmax	9,13,16	9,13,16
Nref	2114[1242]	2113
Tmin,Tmax	0.926,0.955	0.681,0.745
Tmin''	0.926	

Correction method= # Reported T Limits: Tmin=0.681 Tmax=0.745
AbsCorr = MULTI-SCAN
Data completeness= 1.70/1.00 Theta(max)= 24.778
R(reflections)= 0.0447(1668) wR2(reflections)=
0.0880(2113)
S = 1.010 Npar= 157

The following ALERTS were generated. Each ALERT has the format

test-name_ALERT_alert-type_alert-level.

Click on the hyperlinks for more details of the test.

● **Alert level C**

[THETM01_ALERT_3_C](#) The value of sine(theta_max)/wavelength is less than 0.590

Calculated sin(theta_max)/wavelength = 0.5897

[PLAT340_ALERT_3_C](#) Low Bond Precision on C-C Bonds 0.00689 Ang.

● **Alert level G**

[PLAT432_ALERT_2_G](#) Short Inter X.I Contact Cl1 ..C7 . 3.20 Ang.

1-x,1/2+y,1/2-z = 3_655 Check

[PLAT720_ALERT_4_G](#) Number of Unusual/Non-Standard Labels 4 Note

[PLAT791_ALERT_4_G](#) Model has Chirality at C2 (Sohnke SpGr) R Verify

[PLAT883_ALERT_1_G](#) No Info/Value for _atom_sites_solution_primary . Please Do !

[PLAT909_ALERT_3_G](#) Percentage of I>2sig(I) Data at Theta(Max) Still 50% Note

[PLAT978_ALERT_2_G](#) Number C-C Bonds with Positive Residual Density. 3 Info

0 **ALERT level A** = Most likely a serious problem --resolve or explain

0 **ALERT level B** = A potentially serious problem, consider carefully

2 **ALERT level C** = Check. Ensure it is not caused by an omission or oversight

6 **ALERT level G** = General information/check it is not something unexpected

1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data

2 ALERT type 2 Indicator that the structure model may be wrong or deficient

3 ALERT type 3 Indicator that the structure quality may be low

2 ALERT type 4 Improvement, methodology, query or suggestion

0 ALERT type 5 Informative message, check

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so

attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that [full publication checks](#) are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 18/05/2022; check.def file version of 17/05/2022

Supplementary Note 9. Computational studies

Computational details

Density Functional Theory (DFT) Calculations: All density functional theory (DFT) calculations were carried out using the Gaussian 16 program.²² Geometries of intermediates and transition states were optimized using the dispersion-corrected (U)B3LYP-D3 functional^{23–25} with a mixed basis set of LANL2DZ for Fe and 6-31G(d) for other atoms in the gas phase. Vibrational frequency calculations were performed for all stationary points to confirm if each optimized structure is a local minimum or a transition state structure. All optimized transition state structures have only one imaginary (negative) frequency, and all minima (reactants, products, and intermediates) have no imaginary frequencies. The (U)B3LYP-D3 functional with a mixed basis set of LANL2TZ(f)²⁶ for Fe and 6-311+G(d,p) for other atoms was used for single-point energy calculations in solution. Solvation energy corrections were calculated in chlorobenzene ($\epsilon=5.6968$) solvent with the refined SMD18²⁷ continuum solvation model (SMD with a refined Coulomb radius of 2.60 Å for Br)²⁸ based on the gas-phase optimized geometries. The solvent environment was chosen based on recommendations from previous computational studies of enzymatic reactions to mimic the relative permittivity in enzyme active sites.^{29,30} The C–Br and C–Cl bond dissociation enthalpies (BDEs) at 298 K were calculated at the same level of theory [(U)B3LYP-D3/LANL2TZ(f)–6-311+G(d,p)/SMD(chlorobenzene)//(U)B3LYP-D3/LANL2DZ–6-31G(d)]. Gibbs free energies were calculated at the standard conditions (298 K, 1 M solution). Truhlar’s quasi-harmonic corrections³¹ were applied for vibrational entropy calculations using 100 cm⁻¹ as the frequency cutoff using GoodVibes.³² 3D images of optimized structures were prepared using CYLView.³³ For each Fe complex and transition state, wavefunction stability tests were carried out with the “stable=opt” keyword to ensure all the open-shell calculations adopted stable wavefunctions.

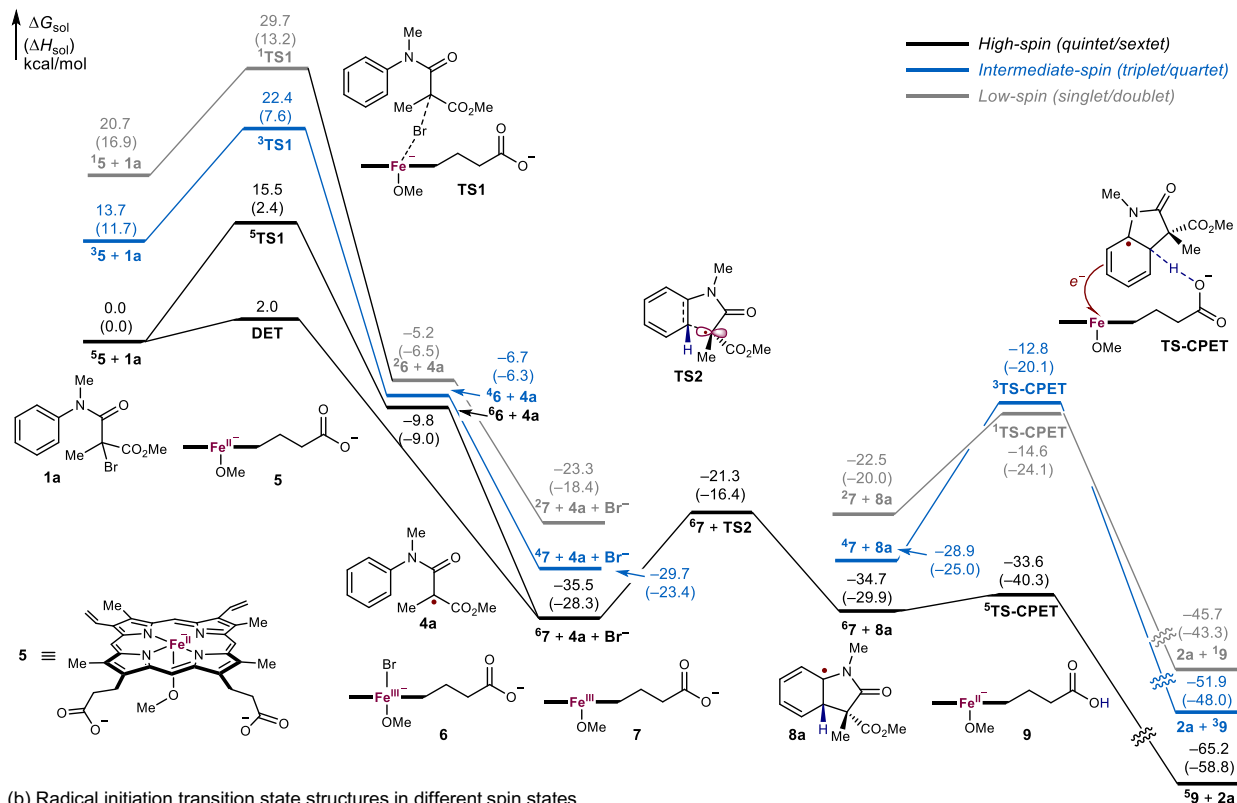
Classical Molecular Dynamics (MD) Simulations: Classical molecular dynamics (MD) simulations were performed with P450_{arc1}, which forms (S)-products. The initial geometry of P450_{arc1} used in the modeling was generated by modifying the X-ray crystal structure of a closely related P450 variant (PDB ID: 5UCW). Ten mutations (A74G, V78L, M177L, L181M, L263Q, H266L, T327P, T436L, L437F, and S438G) were introduced into 5UCW using the mutagenesis tool in PyMOL⁸ to prepare P450_{arc1}. Classical MD simulations were carried out using the pmemd

module of the GPU-accelerated Amber 20 package.³⁴ Force field parameters for the iron–porphyrin complex were generated using the MCPB.py module³⁵ with the general Amber force field (gaff).³⁶ Parameters for substrates **(R)-1a**, **(S)-1a**, and radical intermediate **4a** were generated using the gaff force field, whereas the Amber ff14SB force field³⁷ was used for standard residues and TIP3P for solvent water molecules. First, three replicas³⁸ of independent 500 ns MD simulations were performed in the holo state of P450_{arc1} in the absence of substrate **1**. The classical MD simulations follow four stages, including geometry optimization, heating, equilibration, and production runs. The geometry optimization first optimizes the positions of solvent molecules and ions by imposing positional restraints on the solute with a harmonic potential with a force constant of 500 kcal·mol⁻¹·Å⁻² and then optimizes the positions of all the atoms in the simulation cell. Then, the systems were gently heated using six 50 ps steps with a time step of 2 fs, increasing the temperature by 50 K in each step (*i.e.*, from 0–300 K) under constant volume and periodic boundary conditions. Harmonic restraints of 30 kcal·mol⁻¹ were applied to the solute and the Andersen thermostat was used. Water molecules were treated with the SHAKE algorithm such that the bonds involving hydrogen are constrained. Long-range electrostatic effects were modelled using the Particle-Mesh Ewald method.³⁹ An 8 Å cutoff was applied to Lennard–Jones and electrostatic interactions. Each system was then equilibrated for 5 ns with a 2 fs time step at a constant volume. Production trajectories were then run for an additional 500 ns under the same simulation conditions as system equilibration. Clustering analysis based on the root-mean-square deviation (RMSD) of backbone was carried out using the cpptraj module⁴⁰ to identify the most populated protein conformation in the MD simulations of all three replicas. A representative snapshot of the most visited structure was used for docking calculations with substrates **(R)-1a**, **(S)-1a**, and radical intermediate **4a** using the AutoDock package.⁷ Then, MD simulations of substrate- and **4a**-bound P450_{arc1} were performed to study the preferred substrate binding pose and the possible interaction modes between activate site residues and the substrate following the same four-step computational approach described above. For the substrate-bound enzyme, three replicas of 500 ns production trajectory simulations were performed and the most representative snapshot was extracted (**Supplementary Figure 19**). For the radial intermediate, one 400 ns simulation was performed. Relevant structural parameters (*e.g.*, dihedral angles and number of hydrogen bonds) were extracted along the production MD simulations to study hydrogen bonding interactions involving propionate groups (**Supplementary Figure 18**).

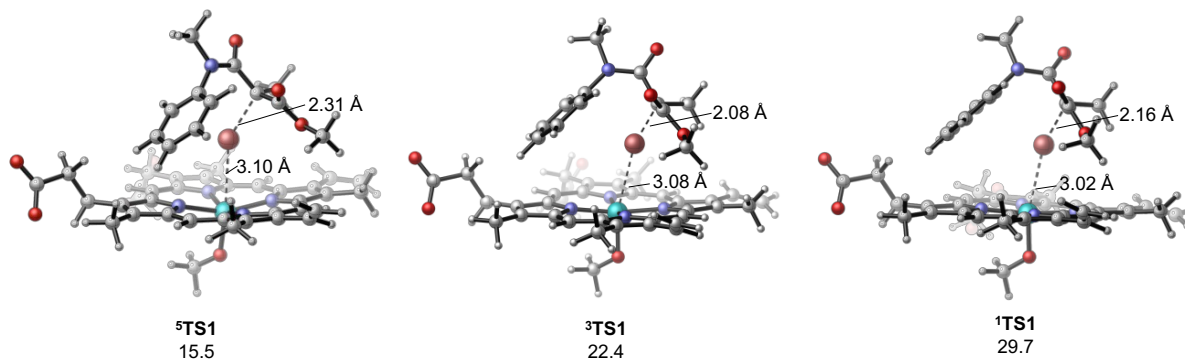
Reaction energy profile of biocatalytic radical cyclisation using a methoxy-ligated Fe porphyrin model system

The model Fe porphyrin complex (**5**) used in the DFT calculations is shown in **Supplementary Figure 15a**. The deprotonated methoxy was used as an axial ligand. In previous computational studies of axial serine-ligated Fe-porphyrin complexes, the deprotonated state of the axial ligand is typically used.¹ The high-spin (quintet/sextet), intermediate-spin (triplet/quartet), and low-spin (singlet/doublet) states of each intermediate and transition-state structure were calculated at the (U)B3LYP-D3/6-311+G(d,p)–LANL2TZ(f)/SMD(chlorobenzene)//(U)B3LYP-D3/LANL2DZ–6-31G(d) level of theory. The same method was applied in our previous studies as it predicted the correct spin states for Fe porphyrin intermediates and provided good agreement with the PNO-LCCSD(T)-F12 spin-state energies. Consistent with previous studies,^{1,41} the Fe porphyrin catalyst remains high spin throughout the catalytic cycle in this biocatalytic radical cyclisation process.

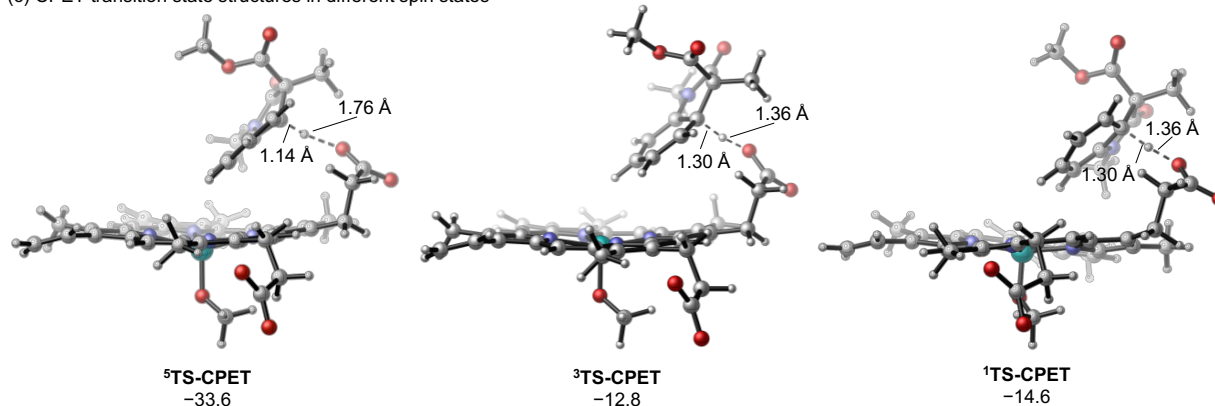
(a) Reaction energy profile for biocatalytic radical cyclisation to arenes



(b) Radical initiation transition state structures in different spin states



(c) CPET transition state structures in different spin states

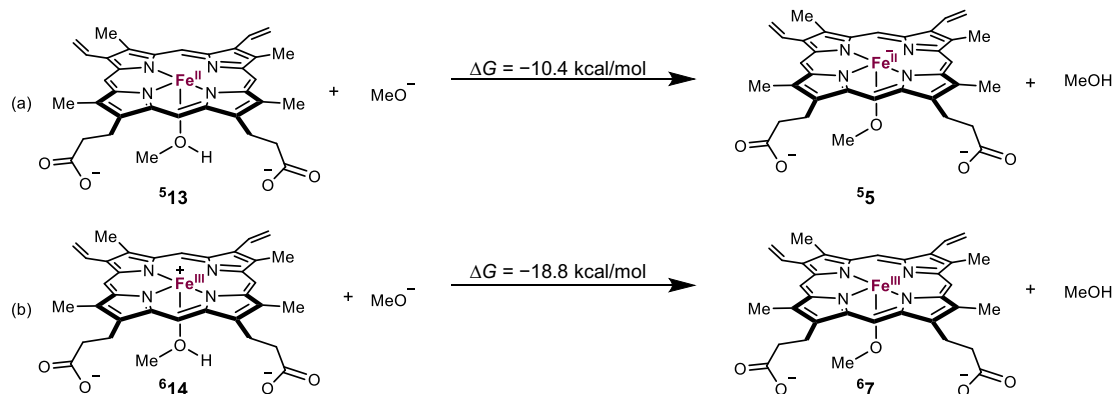


Supplementary Figure 15. Reaction energy profile of the biocatalytic radical cyclisation using a

model system for the axial serine-ligated Fe-porphyrin catalyst. All Gibbs free energies and enthalpies are with respect to separated Fe porphyrin complex **55** and substrate **1a**.

Protonation state of the axial ligand

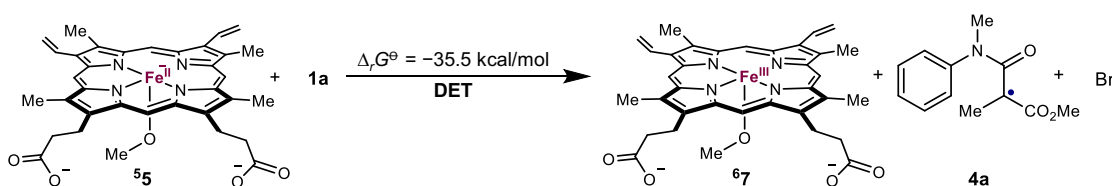
The axial position of the haem cofactor is bound to the hydroxy group of the serine residue. Although the serine hydroxy group has a relatively high pK_a, its deprotonation can be promoted by coordination to the Lewis acidic haem cofactor. To investigate the protonation state of the axial ligand, we compared the relative acidity of an iron-bound serine hydroxy group and a free hydroxy group in methanol, using the computational approach previously applied by Hong and Arnold⁴² (Supplementary Figure 16). Based on the computed Gibbs free energies of reactions (a) and (b) ($\Delta G = -10.4$ and 18.8 kcal/mol, respectively), the MeOH-bound Fe(II) and Fe(III) haem complexes **13** and **14** are much more acidic than free MeOH. These calculations suggest the pK_a values of **13** and **14** are 7.6 and 13.8 lower than methanol, respectively. It should be noted that the computed solvation free energy for anions may have error of up to a few kcal/mol, the relative pK_a values of **13** and **14** with respect to MeOH may have error of several pK_a numbers. In addition, the acidities of **13** and **14** are also affected by the enzyme environment. Nonetheless, these model DFT calculations suggest that coordination to the haem Fe center, especially to the Fe(III) center in **14**, significantly promotes the serine hydroxy group deprotonation. Therefore, the deprotonated serine axial ligand was used our computational studies. This deprotonated serine model was also used in previous studies by us⁴¹ and others.^{43–46}



Supplementary Figure 16. Gibbs free energies of deprotonation of MeOH-bound Fe(II) and Fe(III) haem complexes computed at the [(U)B3LYP-D3/LANL2TZ(f)–6-311+G(d,p)/SMD(water)//(U)B3LYP-D3/LANL2DZ–6-31G(d)] level.

SET radical initiation pathway

We used the modified Marcus theory to estimate the barriers for the outer-sphere dissociative electron transfer (DET) pathway.^{47,48} Geometry optimization of the radical anion of the alkyl bromide substrate **1a** leads to direct dissociation of the C–Br bond to form an alkyl radical and a bromide anion, indicating that the radical anion of **1a** is unstable and the outer-sphere electron transfer would lead to separated alkyl radical and bromide anion in a concerted process, known as dissociative electron transfer (DET)⁴⁸ or concerted outer-sphere electron transfer (OSET-C).⁴⁹ Therefore, we used Saveant's modified Marcus theory⁵⁰ to calculate the activation free energy of this dissociative electron transfer pathway.



Supplementary Figure 17. Dissociative electron transfer (DET) mechanism.

In the DET pathway (**Supplementary Figure 17**), the electron transfer occurs with simultaneous alkyl halide bond dissociation to form radical **4a** and the Br^- anion. The activation Gibbs free energy of the DET step is given by

$$\Delta G_{DET}^\ddagger = \Delta G_0^\ddagger \left(1 + \frac{\Delta_r G^\ominus - D_p}{4\Delta G_0^\ddagger} \right)^2$$

$$\Delta G_0^\ddagger = \frac{(\sqrt{BDE_{1a}} - \sqrt{D_p})^2 + \lambda_0}{4}$$

where $\Delta G_0^\ddagger$ is the intrinsic barrier; $\Delta_r G^\ominus = -35.5 \text{ kcal/mol}$ is the DFT-calculated reaction energy of the DET process; D_p is the interaction energy between **4a** and Br^- in the solvent cage. As there is no available experimental data of D_p (usually a small value close to 0), $D_p = 0 \text{ kcal/mol}$ was used in our calculation;⁵¹ $BDE_{1a} = 47.6 \text{ kcal/mol}$ is the bond dissociation enthalpy of the $\text{C}(sp^3)\text{--Br}$ bond of **1a**; λ_0 is the solvent reorganization energy^{52,53} that can be calculated as follows:

$$\lambda_0 = \frac{N_A e^2}{4\pi\epsilon_0} \left(\frac{1}{n_D^2} - \frac{1}{\epsilon_s} \right) \left(\frac{1}{2r_D} + \frac{1}{2r_A} - \frac{1}{R} \right)$$

where $n_D = 1.52$ and $\epsilon_s = 5.6968$ are refractive index and dielectric constants of chlorobenzene solvent, respectively. E_0 is the vacuum permittivity. R_D and r_A are the hard-sphere radii of the

electron donor (**5**, 5.8 Å) and acceptor (**1a**, 3.8 Å), respectively, calculated using the “volume” keyword in Gaussian 16.

Thus,

$$\lambda_0 = \frac{6.02 \times 10^{23} \times (1.6 \times 10^{-19})^2 \times 2.39 \times 10^6}{4\pi \times (8.85 \times 10^{-12})} \left(\frac{1}{1.52^2} - \frac{1}{5.6968} \right) \left(\frac{1}{2 \times 5.8} + \frac{1}{2 \times 3.8} - \frac{1}{5.8 + 3.8} \right) = 9.4 \text{ kcal/mol}$$

$$\Delta G_0^\ddagger = \frac{(\sqrt{BDE_{2a}} - \sqrt{D_p})^2 + \lambda_0}{4} = \frac{(\sqrt{47.6} - \sqrt{0})^2 + 9.4}{4} = 14.3 \text{ kcal/mol}$$

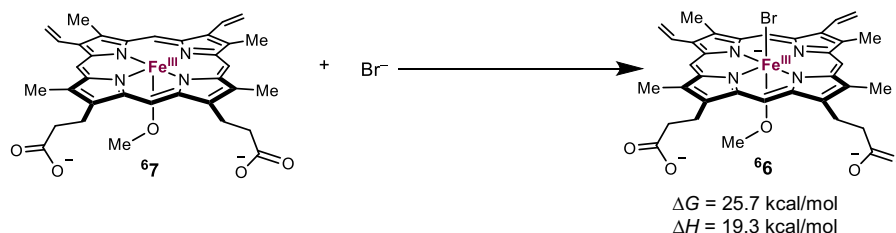
$$\Delta G_{DET}^\ddagger = \Delta G_0^\ddagger \left(1 + \frac{\Delta_r G^\ominus - D_p}{4\Delta G_0^\ddagger} \right)^2 = 14.3 \times \left(1 + \frac{-35.5}{4 \times 14.3} \right)^2 = 2.0 \text{ kcal/mol}$$

These results suggest that the DET pathway requires a low activation free energy of 2.0 kcal/mol with respect to **5** and **1a**. In contrast, in our previous computational studies of the Fe porphyrin catalyzed atom transfer radical cyclisation of alkyl bromide,^{1,54} as the substrate has a stronger C–Br bond with a higher BDE (BDE = 56.4 kcal/mol), the DET pathway requires a higher barrier ($\Delta G^\ddagger$ = 14.4 kcal/mol). In this system, the DET pathway is more favorable, because the substrate has a weaker C–Br bond (BDE_{1a} = 47.6 kcal/mol), providing a greater driving force for DET. Thus, the overall substrate activation of **1a** via DET is kinetically more favorable than the C–Br cleavage of *N*-allyl-*N*-benzyl-2-bromo-2-methylpropanamide substrate used in the previous study. It should be noted that different Fe porphyrin complexes were used in these two computational studies—an unsubstituted porphyrin was employed in the previous study whereas a porphyrin with two propionate groups was used in the present study. The computed barriers and reaction energies of the C–Br bond activation step may be affected by whether the negatively charged propionate groups were included in the computational model.

Br[−] coordination to the Fe(III) haem

After the substrate C–Br cleavage via dissociative electron transfer (DET), a five-coordinated Fe(III) complex **7** is formed. To investigate whether the Br[−] anion formed in the DET process can coordinate to the empty coordination site of **7** to form octahedral complex **6**, we computed the Gibbs free energy of association of Br[−] anion to the Fe(III) haem **7** (**Supplementary Figure 18**).

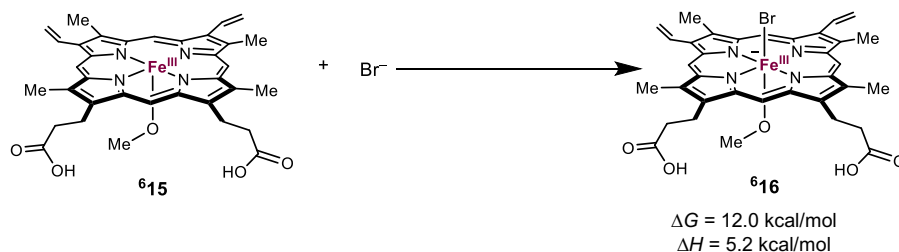
These DFT calculations indicate that the Br^- association is highly endergonic ($\Delta G = 25.7$ kcal/mol), suggesting the octahedral 18-electron complex **6** is less stable than the axially vacant 16-electron complex **7**. Cytochrome P450 enzymes with axially vacant Fe(III) center have been reported previously.^{55–58}



Supplementary Figure 18. Association of Br^- anion to Fe(III) haem **67**.

We recognize two potential sources of error in the computed Br^- association energy shown above: (a) solvation free energy of Br^- anion and (b) the lack of other active site residues in the simple DFT model. To obtain more reliable solvation free energy of Br^- anion, we used the "SMD18" solvation model in the present study, which includes modified atomic radius for Br to provide better solvation energy for Br-containing compounds.²⁸ Among active site residues that may impact the Br^- association energy, we surmised that hydrogen bond donor residues that interact with the pendant haem carboxylate groups would decrease their partial negative charges and therefore lead to diminished field effects. This means the computed endergonicity of Br^- association may be overestimated. To investigate the magnitude of this field effect on Br^- association energy, we computed the Br^- association energy using a haem model with fully protonated carboxylate groups (**15**, **Supplementary Figure 19**). With this model, the Br^- association is still computed to be endergonic, albeit to a lesser extent ($\Delta G = 12.0$ kcal/mol). These results indicate that even in the absence of the field effect of carboxylate groups, the Br^- dissociation process from Fe(III) is still energetically favorable.

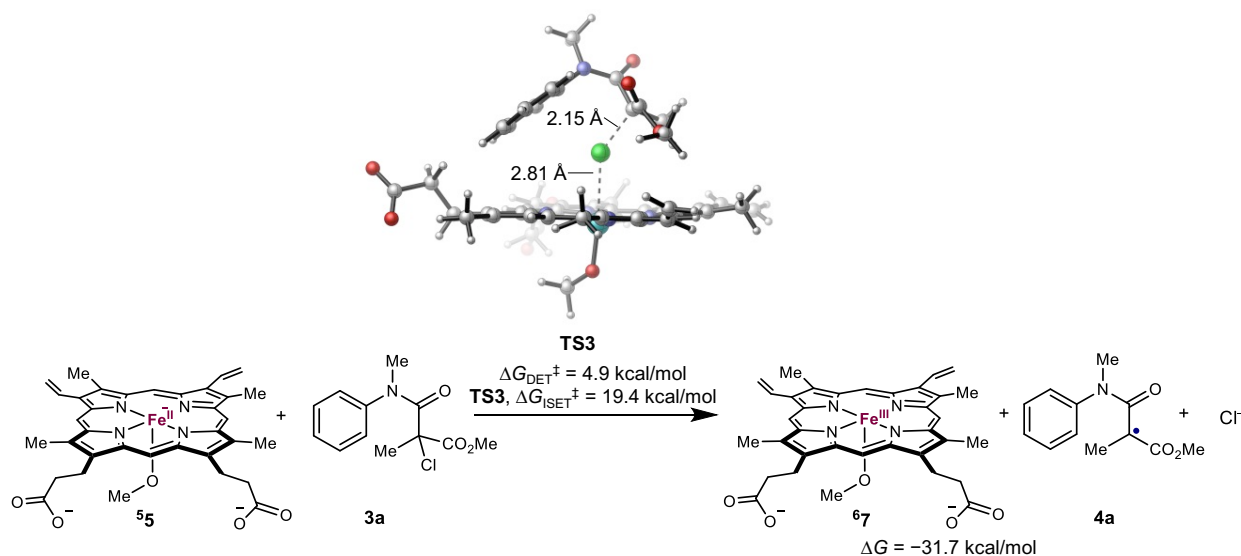
Taken together, these computational results suggest that association of Br^- to the axial position of **7** is unfavorable and the axially vacant 16-electron complex **7** is likely involved during the subsequent radical cyclisation event.



Supplementary Figure 19. Association of Br^- anion to Fe(III) complex **615** with protonated carboxylate groups.

Radical initiation with **3a**

The radical initiation of **3a** also prefers an outer-sphere dissociative electron transfer mechanism (DET, $\Delta G_{\text{DET}}^\ddagger = 4.9 \text{ kcal/mol}$) over the inner-sphere electron transfer pathway (**TS3**, $\Delta G_{\text{ISET}}^\ddagger = 19.4 \text{ kcal/mol}$). Because **3a** has a higher BDE (59.5 kcal/mol) for the activating C–Cl bond than the C–Br bond in **1a**, the activation free energies for both pathways with **3a** are higher than the corresponding barriers with **1a**.

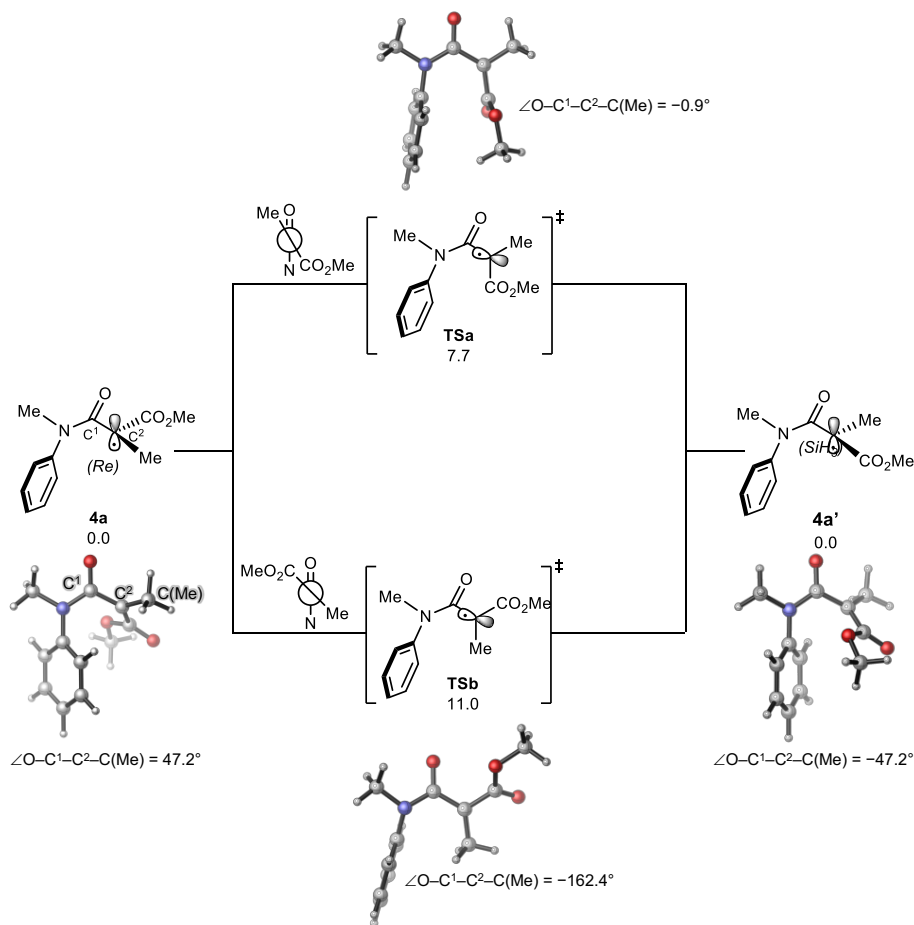


Supplementary Figure 20. Radical initiation pathways with **3a**.

C–C bond rotation of radical intermediate **4a**

Rotation about the C(carbonyl)–C(α) bond in **4a** leads to rotamer **4a'**. Intermediates **4a** and **4a'** are a pair of enantiomers—in **4a**, the (*Re*)-face of the α -carbonyl radical points towards the *N*-phenyl group, whereas in **4a'**, the (*Si*)-face of the α -carbonyl radical points towards the *N*-phenyl

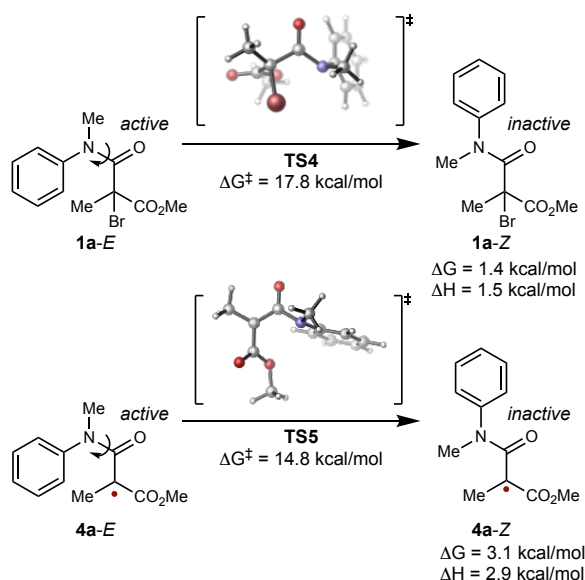
group. Therefore, **4a** and **4a'** would lead to two enantiomeric products after radical cyclisation and proton/electron transfer. To investigate whether **4a** and **4a'** may rapidly interconvert, we computed the C(carbonyl)–C(α) bond rotation transition states (**TSa** and **TSb**) (**Supplementary Figure 21**). These calculations indicate that the most favourable C–C bond rotation transition state to interconvert rotamers **4a** and **4a'** requires an activation free energy of 7.7 kcal/mol (**TSa**). The less favourable C–C bond rotation transition state requires 11.0 kcal/mol (**TSb**). Because the rotational barrier (**TSa**, $\Delta G^\ddagger = 7.7$ kcal/mol) is lower than the barrier of radical cyclisation (**TS2**, $\Delta G^\ddagger = 14.2$ kcal/mol with respect to **4a**), these results suggest **4a** and **4a'** can rapidly interconvert prior to the subsequent radical cyclisation step, leading to the Curtin–Hammett condition, where the product enantioselectivity is determined by the radical cyclisation transition states. It should be noted that the relative rates of cyclisation and C–C bond rotation will be affected by enzyme active site residues. Therefore, more careful calculations using the entire enzyme are needed to confirm if the C–C bond rotation is indeed faster than cyclisation.



Supplementary Figure 21. C(carbonyl)–C(α) bond rotation in α -carbonyl radical intermediate **4a**.

Amide bond rotation

Both the *E* (*i.e.* the "active" conformer directly leading to the cyclisation products) and *Z* ("inactive" conformer) rotamers of the amide substrate **1a** and the alkyl radical intermediate **4a** were calculated (**Supplementary Figure 22**). We have also calculated the activation free energies of the amide bond rotation involving these compounds. The active conformers (**1a-E** and **4a-E**) are more stable than the inactive conformers (**1a-Z** and **4a-Z**), consistent with previous literature reports.^{59,60} The amide bond rotation requires activation free energies of 17.8 kcal/mol (**TS4**, with respect to **1a-E**) and 14.8 kcal/mol (**TS5**, with respect to **4a-E**), respectively. Because the active *E* conformer (**1a-E**) is more stable, it will lead to the *E* conformer **4a-E** upon radical initiation, which then can undergo cyclisation directly via radical addition to the phenyl group. Only the more stable and "active" *E* conformers are reported in the reaction energy profiles in the paper.

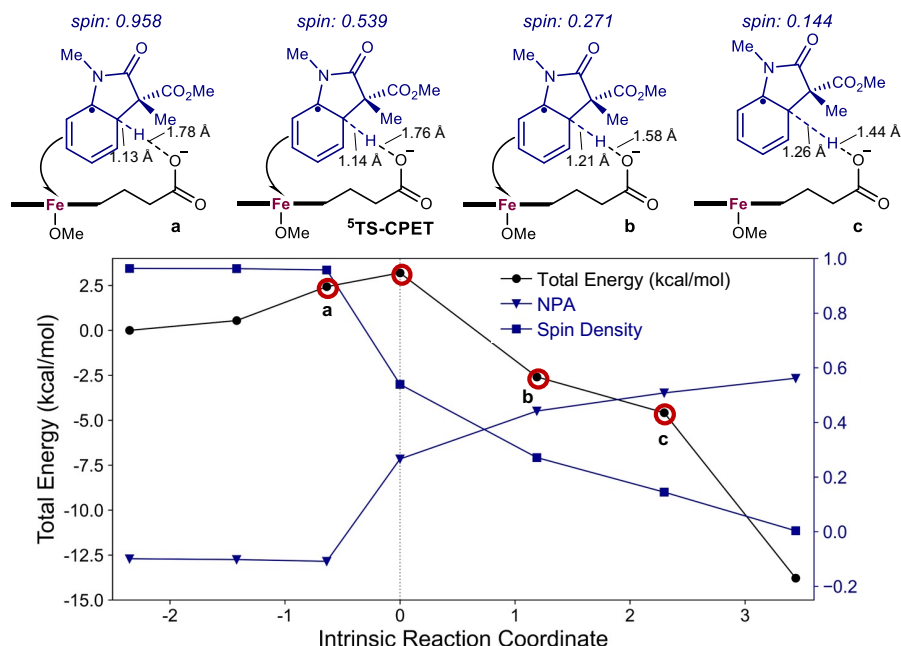


Supplementary Figure 22. Amide bond rotation barriers of **1a** and the radical intermediate **4a**.

Intrinsic reaction coordinate (IRC) calculations of TS-CPET

To confirm the reaction pathway of the concerted proton–electron transfer involving **TS-CPET**, intrinsic reaction coordinate (IRC) calculations were performed at (U)B3LYP-D3/LANL2DZ–6-31G(d) level of theory. Mulliken spin density and NPA charges of the substrate in several

structures along the IRC path were computed and shown in **Supplementary Figure 23**. The IRC calculations indicate that the $1e^-/1H^+$ proton-coupled electron transfer is a concerted process—the proton transfer to the remote carboxylate group and the electron transfer to the Fe centre take place simultaneously without an intermediate. While the proton is being transferred from the dearomatized radical intermediate to the carboxylate, the spin density on the substrate decreases and the NPA charge of the substrate increases, suggesting that the substrate is being oxidized. It should be noted the sum of NPA partial atomic charges shown in **Supplementary Figure 23** includes the proton being transferred. The sum of NPA charges excluding the H atom being transferred also increases along the IRC path.

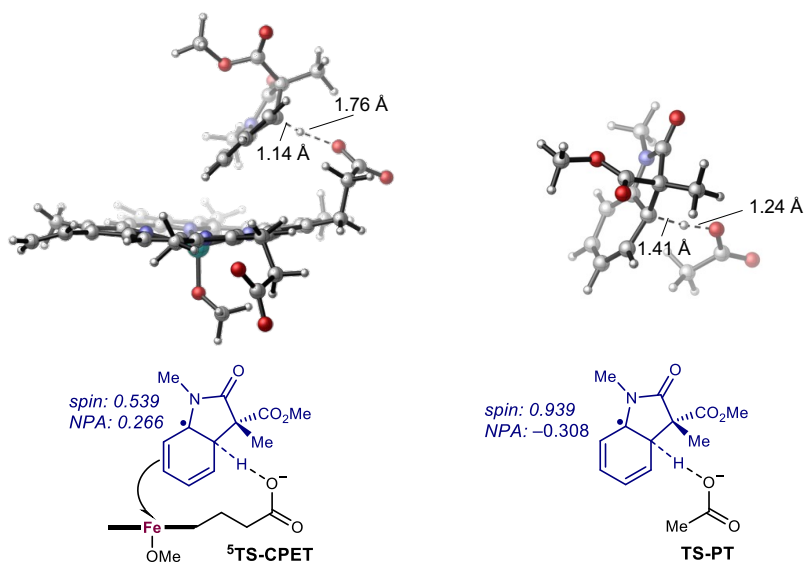


Supplementary Figure 23. Mulliken spin density and NPA charges of the substrate (atoms highlighted in blue) in select structures along the intrinsic reaction coordinate involving ⁵TS-CPET.

Reaction free energy and activation free energy of the stepwise proton-transfer/electron transfer (PT/ET) pathway

The stepwise reaction pathway involving proton transfer from the dearomatized radical intermediate **8a** to the propionate group of Fe(III) complex **67** to form radical anion **11** was computed. The reaction Gibbs free energy of **8a** and **67** to form **11** and **610** is endergonic by 9.1 kcal/mol, which is already higher in energy than the CPET transition state. The activation free

energy of the proton transfer from **8a** to the propionate side chain in the absence of electron transfer to the Fe centre was estimated by computing the transition state of proton transfer from **8a** to an acetate anion in the absence of Fe porphyrin (**TS-PT**, **Supplementary Figure 24**). The proton transfer transition state **TS-PT** is much later and requires a much higher activation free energy ($\Delta G^\ddagger = 13.2$ kcal/mol with respect to **8a** and the acetate anion) than the concerted proton–electron transfer transition state (**⁵TS-CPET**) with the Fe porphyrin complex ($\Delta G^\ddagger = 1.1$ kcal/mol with respect to **8a** and **67**). In **TS-PT**, the substrate bears a spin density close to unity (0.939), indicating that the radical character remains on the substrate in this proton transfer transition state. In contrast, in the CPET pathway (**Supplementary Figure 23**), whereas the spin density on **8a** is close to unity prior to the TS (*e.g.* point **a**), the spin density on the substrate decreases to 0.539 at the concerted proton–electron transfer transition state (**⁵TS-CPET**), indicating a substantial electron transfer from the substrate to the Fe centre at the concerted transition state.

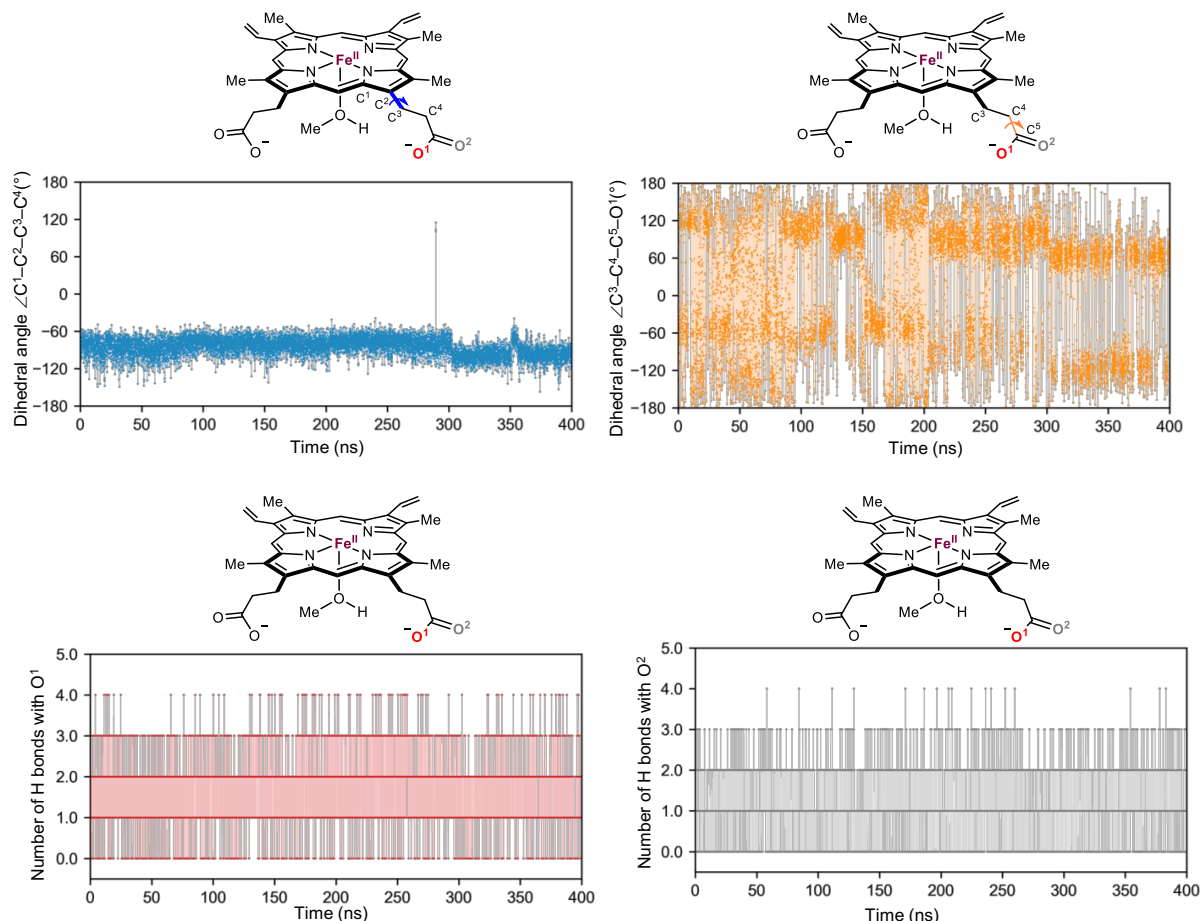


Supplementary Figure 24. Optimized geometries of the concerted proton–electron transfer transition state (**⁵TS-CPET**) and proton transfer transition state (**TS-PT**) to acetate anion to model the stepwise proton transfer to the propionate side chain in the absence of electron transfer with the Fe porphyrin catalyst.

Classical MD simulations

To investigate whether one of the propionate groups on the haem cofactor can serve as the base in the CPET with cyclised radical intermediate **8a**, we performed classical MD simulations to

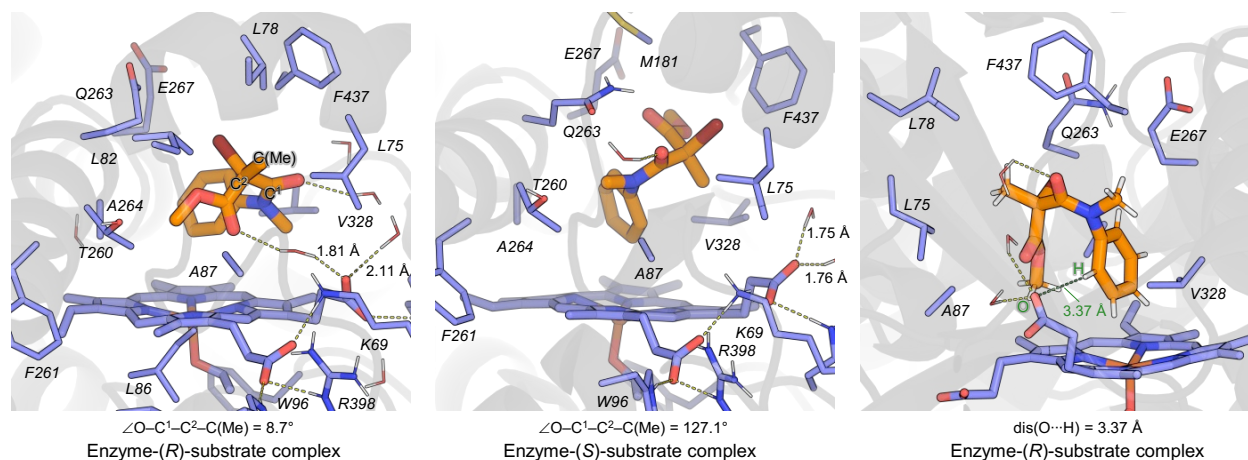
investigate the orientations of the propionate groups and whether the propionate groups form strong hydrogen bonds with the enzyme. We surmised that the propionate group serving as proton acceptor must be oriented on the same side as **8a** (*i.e.*, opposite from the axial serine residue) and it cannot form strong hydrogen bonds with other active site residues. Throughout the MD trajectory of a 400 ns simulation with the α -carbonyl radical intermediate (**Supplementary Figure 25**), one of the propionate groups on the haem cofactor always stays above the porphyrin plane (*i.e.*, on the same side as the substrate), as can be seen from the $\angle C^1-C^2-C^3-C^4$ dihedral angle (staying within $-120^\circ - -60^\circ$). The $\angle C^3-C^4-C^5-O^1$ dihedral angle indicates that the carboxylate group itself is conformationally flexible with fast rotation about C^4-C^5 . During most of the MD trajectory, the propionate group forms hydrogen bonds with water molecules, rather than with an active site residue directly. The lack of well-defined hydrogen bonds with the propionate group is further evidenced by the variation of total number of hydrogen bonds along the MD trajectory. These results suggest the propionate above the haem plane has relatively weak interactions with the protein scaffold and may serve as a proton acceptor in the CPET process.



Supplementary Figure 25. Dihedral angles ($\angle C^1-C^2-C^3-C^4$ and $\angle C^3-C^4-C^5-O^1$) and hydrogen bonding interactions involving a propionate side chain along a 400 ns unrestrained MD simulation.

Classical MD simulations of the enzyme–substrate complexes with (*S*)-**1a** and (*R*)-**1a**, respectively, were performed to study the substrate binding pose and hydrogen bonding interactions with carboxylate group. In the representative snapshots shown in **Supplementary Figure 26**, the (*S*)- and (*R*)-enantiomers of **1a** adopt different conformations and different binding poses. In the complex with (*R*)-**1a**, the C–Br bond is anticlinal to the amide carbonyl ($\angle O-C^1-C^2-C(Me) = 8.7^\circ$) whereas in the complex with (*S*)-**1a**, the C–Br bond is synperiplanar with the amide carbonyl ($\angle O-C^1-C^2-C(Me) = 127.1^\circ$). The orientations of the pendant propionate groups on the haem cofactor are similar to those observed in the MD simulations of the radical intermediate—one of the propionate groups stays on the same side of the porphyrin ring as the substrate and it only forms hydrogen bonding interactions with waters. In selected structures along the MD trajectory, a relatively short distance between the pendant propionate group and the ortho C–H bond

of the substrate was observed (see **Supplementary Figure 26**, right). These results suggest that the carboxylate oxygen is positioned to potentially act as the base in the CPET process after the radical cyclisation.



Supplementary Figure 26. Representative snapshots from classical MD simulations of enzyme–substrate complexes with (*R*)-**1a** (left) and (*S*)-**1a** (middle). An additional snapshot with a relatively short distance between one of the haem propionate groups and an ortho C–H bond of (*R*)-**1a** is shown (right).

Cartesian coordinates (Å) and energies of optimized structures from DFT calculations

1a

B3LYP-D3 SCF energy:	-3317.56791267 a.u.
B3LYP-D3 enthalpy:	-3317.303934 a.u.
B3LYP-D3 free energy:	-3317.369303 a.u.
B3LYP-D3 SCF energy in solution:	-3320.55270295 a.u.
B3LYP-D3 enthalpy in solution:	-3320.288724 a.u.
B3LYP-D3 free energy in solution:	-3320.354093 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	-1.355037	0.512136	0.178335
C	-2.559951	1.388734	0.544039
H	-2.272588	2.072292	1.347447
H	-3.378804	0.762621	0.897488
H	-2.879988	1.963049	-0.329540
C	-0.247814	1.432044	-0.361038
O	0.108794	1.561214	-1.504797
O	0.212077	2.179833	0.668594
C	1.197447	3.164794	0.308112
H	2.072858	2.676536	-0.127220
H	0.780840	3.871171	-0.414961
H	1.455819	3.671167	1.238604
C	-0.961575	-0.361779	1.404892
O	-1.748698	-0.455267	2.336848
N	0.226454	-1.050272	1.392731
C	1.315311	-0.841688	0.478938
C	1.377227	-1.540637	-0.729124
C	2.464707	-1.352492	-1.583232
C	3.502619	-0.492256	-1.222125
C	3.457221	0.179859	0.002665
C	2.366496	0.004693	0.853306
H	2.306352	0.532928	1.799816
H	4.269131	0.840805	0.294157
H	4.347366	-0.348300	-1.889883
H	2.499221	-1.880888	-2.531478
H	0.566108	-2.206182	-0.997840
C	0.515667	-1.898467	2.555115
H	-0.417983	-2.312296	2.936865
H	1.183612	-2.702999	2.239159
H	0.997446	-1.326279	3.358141
Br	-1.946453	-0.734789	-1.261553

1a-Z

B3LYP-D3 SCF energy:	-3317.56318910 a.u.
B3LYP-D3 enthalpy:	-3317.299147 a.u.
B3LYP-D3 free energy:	-3317.365125 a.u.
B3LYP-D3 SCF energy in solution:	-3320.55034465 a.u.
B3LYP-D3 enthalpy in solution:	-3320.286303 a.u.
B3LYP-D3 free energy in solution:	-3320.352281 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	-1.361903	-0.119254	0.733258
C	-1.947019	-0.219818	2.145954
H	-1.579578	0.622273	2.739894
H	-1.614861	-1.143953	2.618858
H	-3.038779	-0.192188	2.099416
C	-1.786190	1.232401	0.158004
O	-1.153488	2.236644	0.413900
O	-2.917769	1.210673	-0.551909
C	-3.367748	2.496168	-1.024338
H	-3.558805	3.165606	-0.181464
H	-2.611896	2.946338	-1.673601
H	-4.284623	2.294962	-1.577732
C	0.187719	-0.236164	0.792480
O	0.712053	-0.538272	1.853479
N	0.913354	-0.004450	-0.349422
C	2.346275	0.041712	-0.217579
C	2.946748	1.080625	0.497732
C	4.337056	1.145935	0.582328
C	5.125846	0.182957	-0.053359
C	4.520469	-0.852008	-0.769342
C	3.128707	-0.926243	-0.849246
H	2.642564	-1.733885	-1.389373
H	5.129613	-1.606804	-1.259014
H	6.209055	0.237813	0.011945
H	4.805018	1.950548	1.142802
H	2.316949	1.817779	0.985837
C	0.389463	0.458486	-1.635835
H	0.418921	1.552628	-1.700792
H	1.009084	0.039833	-2.432819
H	-0.630225	0.108829	-1.796920

Br -2.052824 -1.685994 -0.315005

2a

B3LYP-D3 SCF energy:	-745.57773037 a.u.
B3LYP-D3 enthalpy:	-745.327754 a.u.
B3LYP-D3 free energy:	-745.386121 a.u.
B3LYP-D3 SCF energy in solution:	-745.81754900 a.u.
B3LYP-D3 enthalpy in solution:	-745.567573 a.u.
B3LYP-D3 free energy in solution:	-745.625940 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.671385	-0.005618	-0.844437
C	-0.649120	-0.623242	-0.426154
C	-1.110997	-1.925236	-0.519242
C	-2.399837	-2.221928	-0.047114
C	-3.194879	-1.217186	0.507631
C	-2.734672	0.104048	0.609101
C	-1.455854	0.378023	0.137295
N	-0.777630	1.603290	0.119514
C	0.485814	1.476905	-0.434087
O	1.286750	2.377562	-0.597551
C	-1.308072	2.855128	0.614556
H	-2.224778	3.126933	0.077926
H	-0.548013	3.620971	0.450723
H	-1.531653	2.783580	1.685576
H	-3.356102	0.881960	1.041454
H	-4.190644	-1.458216	0.869560
H	-2.778320	-3.237581	-0.113376
H	-0.481662	-2.701284	-0.946825
C	1.806308	-0.644150	-0.037172
O	2.598270	-1.446713	-0.477622
O	1.775439	-0.239478	1.246482
C	2.771757	-0.824647	2.102622
H	2.649481	-1.910814	2.142655
H	2.608759	-0.381508	3.085258
H	3.774615	-0.591633	1.734669
C	0.968954	-0.103729	-2.346795
H	1.851679	0.496268	-2.585251
H	0.118006	0.269803	-2.924109
H	1.163647	-1.142697	-2.622541

3a

B3LYP-D3 SCF energy:	-1206.35530624 a.u.
B3LYP-D3 enthalpy:	-1206.090963 a.u.
B3LYP-D3 free energy:	-1206.154871 a.u.
B3LYP-D3 SCF energy in solution:	-1206.63123906 a.u.
B3LYP-D3 enthalpy in solution:	-1206.366896 a.u.
B3LYP-D3 free energy in solution:	-1206.430804 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	-1.623691	-0.279901	0.268495
C	-2.999667	-0.870606	-0.066735
H	-3.006798	-1.196788	-1.109456
H	-3.766899	-0.107705	0.064976
H	-3.202704	-1.722417	0.588078
C	-0.581615	-1.401349	0.109593
O	-0.018647	-2.002614	0.988831
O	-0.466088	-1.686873	-1.207045
C	0.415178	-2.782498	-1.513536
H	1.425651	-2.558891	-1.162292
H	0.061279	-3.699722	-1.035217
H	0.392326	-2.879067	-2.599379
C	-1.374371	0.977829	-0.621211
O	-2.314587	1.462407	-1.235042
N	-0.124525	1.545168	-0.644459
C	1.084655	0.937046	-0.162588
C	1.476843	1.083675	1.170152
C	2.673881	0.514122	1.606570
C	3.492371	-0.176042	0.711433
C	3.115981	-0.293352	-0.629688
C	1.914901	0.263049	-1.067276
H	1.598360	0.164653	-2.101081
H	3.755669	-0.819605	-1.333150
H	4.423133	-0.618405	1.055206
H	2.965339	0.611593	2.648233
H	0.834163	1.623133	1.855236
C	0.042326	2.757629	-1.454599
H	-0.883878	3.332296	-1.431768
H	0.861600	3.345563	-1.034563
H	0.274822	2.512372	-2.498684

Cl -1.663915 0.272696 2.007497

4a

B3LYP-D3 SCF energy:	-746.12070277 a.u.
B3LYP-D3 enthalpy:	-745.861101 a.u.
B3LYP-D3 free energy:	-745.924355 a.u.
B3LYP-D3 SCF energy in solution:	-746.36432581 a.u.
B3LYP-D3 enthalpy in solution:	-746.104724 a.u.
B3LYP-D3 free energy in solution:	-746.167978 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	-1.708485	-0.388632	-0.471924
C	-2.664852	-0.667799	-1.581860
H	-2.335373	-0.191660	-2.517589
H	-2.756891	-1.742110	-1.750438
H	-3.643524	-0.235336	-1.340443
C	-1.611961	1.016164	0.017629
O	-2.650991	1.633827	0.250641
N	-0.365725	1.583950	0.194394
C	-1.042312	-1.507077	0.194304
O	-0.990103	-2.641218	-0.258300
C	-0.301476	2.874085	0.883106
H	-0.242289	2.744572	1.971091
H	0.577425	3.421675	0.536154
H	-1.208337	3.434628	0.652833
C	0.845021	0.939114	-0.175821
C	1.903759	0.851142	0.738428
C	0.997477	0.399982	-1.460734
C	3.087722	0.210937	0.377117
H	1.784019	1.260443	1.736440
C	2.175988	-0.262368	-1.807247
H	0.197620	0.511851	-2.185514
C	3.225395	-0.358867	-0.892303
H	3.900713	0.144425	1.095090
H	2.276912	-0.687133	-2.801876
H	4.145810	-0.865823	-1.167087
O	-0.482117	-1.152422	1.378373
C	0.312192	-2.169138	2.003587
H	1.162393	-2.430431	1.366172
H	0.660182	-1.733037	2.940738

H -0.283714 -3.066460 2.192258

4a'

B3LYP-D3 SCF energy:	-746.12070584 a.u.
B3LYP-D3 enthalpy:	-745.861097 a.u.
B3LYP-D3 free energy:	-745.924313 a.u.
B3LYP-D3 SCF energy in solution:	-746.36430468 a.u.
B3LYP-D3 enthalpy in solution:	-746.104696 a.u.
B3LYP-D3 free energy in solution:	-746.167912 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.728256	-1.314185	1.336817
C	1.769225	-2.310227	1.722612
H	1.875129	-2.326167	2.814234
H	1.508274	-3.303386	1.353057
H	2.753559	-2.031340	1.317447
C	0.829402	0.051682	1.925536
O	1.025145	0.160881	3.135965
N	0.702456	1.151843	1.100811
C	-0.422868	-1.753707	0.549209
O	-0.473647	-2.813888	-0.056852
C	0.582310	2.464486	1.737537
H	0.977538	3.227022	1.062975
H	-0.462377	2.698727	1.977855
H	1.153899	2.451982	2.666381
C	0.593298	1.058661	-0.312772
C	1.517833	0.303335	-1.047351
C	-0.432911	1.735865	-0.985631
C	1.385430	0.187726	-2.431834
H	2.341860	-0.180126	-0.532717
C	-0.544034	1.637014	-2.371284
H	-1.154564	2.313845	-0.417259
C	0.356650	0.853729	-3.099499
H	2.100781	-0.411018	-2.988322
H	-1.346044	2.162510	-2.882650
H	0.261116	0.770906	-4.178244
O	-1.438767	-0.853948	0.560077
C	-2.532373	-1.161610	-0.314506
H	-2.967748	-2.133272	-0.065105
H	-3.259946	-0.363009	-0.164752
H	-2.192407	-1.177043	-1.354516

4a-Z

B3LYP-D3 SCF energy:	-746.11438277 a.u.
B3LYP-D3 enthalpy:	-745.854810 a.u.
B3LYP-D3 free energy:	-745.918131 a.u.
B3LYP-D3 SCF energy in solution:	-746.35967707 a.u.
B3LYP-D3 enthalpy in solution:	-746.100104 a.u.
B3LYP-D3 free energy in solution:	-746.163425 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	1.938232	0.997276	-0.167112
C	2.603238	2.319098	-0.352832
H	2.260174	3.044456	0.398693
H	3.687894	2.217820	-0.283578
H	2.329016	2.730250	-1.332974
C	0.469730	0.907588	-0.428321
O	0.065969	1.289994	-1.525507
N	-0.358427	0.418148	0.551599
C	2.753529	-0.204345	-0.027517
O	3.967087	-0.212496	0.121093
C	0.120360	-0.004805	1.865646
H	-0.593850	0.301710	2.634357
H	0.247876	-1.092249	1.907547
H	1.079343	0.471019	2.081963
C	-1.722936	0.121556	0.224529
C	-2.759349	0.689735	0.970542
C	-2.015028	-0.763058	-0.819065
C	-4.085412	0.365184	0.680696
H	-2.526450	1.392346	1.765764
C	-3.341591	-1.074140	-1.112530
H	-1.199797	-1.188620	-1.394098
C	-4.379783	-0.516011	-0.361528
H	-4.887375	0.809818	1.263560
H	-3.564700	-1.757813	-1.927003
H	-5.412557	-0.763980	-0.590173
O	2.006546	-1.344140	-0.074937
C	2.751452	-2.562624	0.057751
H	3.271249	-2.595440	1.020267
H	2.015314	-3.364656	-0.009153
H	3.491383	-2.651290	-0.743103

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B3LYP-D3 SCF energy:	-2072.27130724 a.u.
B3LYP-D3 enthalpy:	-2071.616098 a.u.
B3LYP-D3 free energy:	-2071.737134 a.u.
B3LYP-D3 SCF energy in solution:	-2073.26324008 a.u.
B3LYP-D3 enthalpy in solution:	-2072.608031 a.u.
B3LYP-D3 free energy in solution:	-2072.729067 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-1.137587	0.065210	1.796790
Fe	-0.906157	-0.028003	-0.069264
C	3.963965	-2.996720	0.010956
C	-5.919323	-2.553579	-0.343848
C	-3.377520	4.949190	-0.855747
C	4.172032	2.546490	-0.463431
N	0.475675	-1.492485	-0.043620
C	4.457422	-3.722107	-1.272824
C	-6.731681	-3.579970	-0.008947
C	-4.444435	5.759649	-0.688312
C	4.780987	3.294514	0.755594
N	-2.392392	-1.415265	-0.173629
C	5.141486	-5.125024	-1.038691
C	5.606976	4.591040	0.402061
N	0.578709	1.317116	-0.303115
C	2.521475	-0.164509	-0.187904
C	-1.019747	-3.427618	0.123514
C	-4.319614	0.068249	-0.425452
C	-0.768273	3.356502	-0.500529
C	1.591188	-5.086303	0.286260
C	-3.752390	-4.913777	0.033259
C	-5.766069	2.783030	-0.850124
C	1.963702	4.813715	-0.637237
C	1.843246	-1.374712	-0.076202
C	-2.247614	-2.771400	-0.020242
C	-3.646372	1.284872	-0.498551
C	0.438050	2.682051	-0.420695
O	5.825811	-5.539266	-2.006430
O	5.340242	5.149839	-0.701142
C	2.491124	-2.687358	0.038698
C	-3.527547	-3.434253	-0.047062
C	-4.294990	2.561735	-0.667009

C	1.736724	3.337512	-0.488284
O	4.905732	-5.700119	0.062421
O	6.419033	4.956751	1.286770
C	1.477413	-3.596001	0.150397
C	-4.481924	-2.441688	-0.213444
C	-3.287870	3.513522	-0.680368
C	2.679804	2.351011	-0.416828
C	0.231468	-2.842906	0.088547
C	-3.738394	-1.186648	-0.286213
C	-2.037095	2.773508	-0.529442
C	1.935894	1.092478	-0.294428
N	-2.276845	1.435069	-0.423297
H	4.542077	-2.078842	0.173382
H	4.198450	-3.674908	0.840973
H	-6.406181	-1.678840	-0.779015
H	-2.448705	5.430149	-1.165139
H	4.672851	1.580741	-0.602719
H	4.416747	3.163595	-1.337568
H	5.157121	-3.096479	-1.840430
H	3.607632	-3.902202	-1.945970
H	5.419521	2.632392	1.352557
H	3.974319	3.617305	1.428508
H	3.604880	-0.205318	-0.193694
H	-1.041962	-4.505741	0.248126
H	-5.403465	0.108828	-0.459714
H	-0.708548	4.438089	-0.566681
H	-6.371636	-4.484512	0.469888
H	-7.803157	-3.519545	-0.189730
H	-5.406261	5.402171	-0.334633
H	-4.362713	6.828268	-0.875942
H	-4.058869	-5.237393	1.040399
H	-2.847787	-5.474208	-0.224533
H	-4.549565	-5.225748	-0.654867
H	-6.268187	1.878903	-1.212822
H	-5.951935	3.584925	-1.576968
H	-6.268679	3.080242	0.083984
H	1.120408	-5.439582	1.217054
H	1.076543	-5.602163	-0.538891
H	2.640494	-5.407340	0.283605
H	3.033393	5.047200	-0.711260
H	1.460665	5.205277	-1.535235
H	1.551324	5.369584	0.218582
C	-0.067445	0.550065	2.522420

H	0.137970	1.630633	2.358666
H	-0.270030	0.428603	3.609012
H	0.886339	0.021780	2.319625

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B3LYP-D3 SCF energy:	-2072.27733714 a.u.
B3LYP-D3 enthalpy:	-2071.623586 a.u.
B3LYP-D3 free energy:	-2071.747578 a.u.
B3LYP-D3 SCF energy in solution:	-2073.27006280 a.u.
B3LYP-D3 enthalpy in solution:	-2072.616312 a.u.
B3LYP-D3 free energy in solution:	-2072.740304 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-1.005177	0.137315	1.927890
Fe	-0.920578	-0.005646	0.027058
C	3.954598	-2.983364	-0.013346
C	-5.920001	-2.537437	-0.283672
C	-3.374395	4.960298	-0.937046
C	4.144725	2.551554	-0.431942
N	0.472601	-1.488673	-0.090986
C	4.464996	-3.698813	-1.295844
C	-6.732061	-3.576394	0.028177
C	-4.450220	5.777665	-0.872341
C	4.736501	3.278704	0.807896
N	-2.399230	-1.379967	-0.116801
C	5.148316	-5.101867	-1.062034
C	5.553012	4.590259	0.487509
N	0.553011	1.312219	-0.289872
C	2.518922	-0.151530	-0.185604
C	-1.028229	-3.420265	0.093867
C	-4.350726	0.086455	-0.373859
C	-0.779691	3.365812	-0.548991
C	1.584305	-5.079606	0.210912
C	-3.753068	-4.887345	0.058297
C	-5.789035	2.797576	-0.872133
C	1.937970	4.807889	-0.654901
C	1.838604	-1.368273	-0.103658
C	-2.252056	-2.754115	0.006251
C	-3.680934	1.310066	-0.498577
C	0.407680	2.685370	-0.433525

O	5.856710	-5.503793	-2.017149
O	5.299273	5.161925	-0.612058
C	2.481460	-2.673491	-0.001212
C	-3.522755	-3.407531	-0.006839
C	-4.318051	2.573351	-0.694393
C	1.709346	3.333512	-0.495014
O	4.886987	-5.689876	0.026749
O	6.345080	4.950701	1.391717
C	1.463225	-3.588396	0.086675
C	-4.488226	-2.415115	-0.151957
C	-3.295039	3.529437	-0.743973
C	2.652892	2.352399	-0.403013
C	0.223100	-2.844949	0.032254
C	-3.753433	-1.153476	-0.221991
C	-2.062022	2.795787	-0.583519
C	1.917509	1.090208	-0.278425
N	-2.308692	1.456610	-0.445423
H	4.530440	-2.066960	0.163968
H	4.178077	-3.667518	0.814889
H	-6.412831	-1.657507	-0.701394
H	-2.423779	5.441621	-1.169962
H	4.649589	1.590266	-0.583895
H	4.396804	3.185599	-1.291441
H	5.169789	-3.067874	-1.850953
H	3.623418	-3.876094	-1.980134
H	5.377591	2.610405	1.395050
H	3.922300	3.579434	1.481975
H	3.601284	-0.184725	-0.182869
H	-1.054118	-4.499347	0.204256
H	-5.434042	0.118611	-0.385584
H	-0.706641	4.443946	-0.640065
H	-6.373569	-4.489873	0.490859
H	-7.802430	-3.514992	-0.158401
H	-5.444104	5.429219	-0.611898
H	-4.343721	6.844469	-1.058151
H	-4.089407	-5.213993	1.054587
H	-2.846616	-5.452806	-0.179990
H	-4.534597	-5.189133	-0.651772
H	-6.309575	1.868885	-1.132746
H	-5.982929	3.521295	-1.675853
H	-6.274798	3.197123	0.033483
H	1.111051	-5.441244	1.136686
H	1.075712	-5.589838	-0.620848

H	2.635268	-5.395618	0.211799
H	3.009006	5.043918	-0.692262
H	1.465957	5.184461	-1.575368
H	1.491197	5.370607	0.178300
C	0.143394	0.383940	2.663630
H	0.595898	1.369114	2.438151
H	-0.075207	0.368326	3.751877
H	0.934306	-0.369637	2.482851

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B3LYP-D3 SCF energy:	-2072.29875041 a.u.
B3LYP-D3 enthalpy:	-2071.645398 a.u.
B3LYP-D3 free energy:	-2071.772724 a.u.
B3LYP-D3 SCF energy in chlorobenzene:	-2073.28828134 a.u.
B3LYP-D3 enthalpy in chlorobenzene:	-2072.634929 a.u.
B3LYP-D3 free energy in chlorobenzene:	-2072.762255 a.u.
B3LYP-D3 SCF energy in water:	-2073.37744832 a.u.
B3LYP-D3 enthalpy in water:	-2072.724173 a.u.
B3LYP-D3 free energy in water:	-2072.851064 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.984051	0.198697	2.392526
Fe	-0.946393	0.044062	0.503001
C	3.963747	-3.001078	0.025500
C	-5.970350	-2.557535	-0.376517
C	-3.412801	4.976657	-0.982278
C	4.175937	2.580140	-0.489903
N	0.480656	-1.511778	0.028618
C	4.465104	-3.692642	-1.273827
C	-6.780078	-3.605809	-0.114249
C	-4.480497	5.796964	-0.887419
C	4.795846	3.385797	0.686533
N	-2.464720	-1.421688	-0.069188
C	5.152774	-5.098423	-1.070207
C	5.614653	4.666508	0.264576
N	0.591041	1.380308	-0.221576
C	2.504319	-0.141026	-0.104877
C	-1.047326	-3.427042	0.093875
C	-4.366467	0.095278	-0.349965
C	-0.790535	3.382473	-0.524274

C	1.595727	-5.105394	0.188386
C	-3.798868	-4.925576	-0.105537
C	-5.810831	2.825115	-0.897043
C	1.972411	4.840029	-0.768624
C	1.837183	-1.372582	-0.005402
C	-2.294547	-2.776241	-0.006491
C	-3.703626	1.329275	-0.432429
C	0.435407	2.724914	-0.414294
O	5.846229	-5.485606	-2.042350
O	5.340749	5.168650	-0.863645
C	2.490711	-2.693514	0.056427
C	-3.576357	-3.443419	-0.091538
C	-4.344831	2.604173	-0.675894
C	1.740213	3.375378	-0.535674
O	4.909727	-5.702061	0.014101
O	6.429118	5.077948	1.126519
C	1.475291	-3.610735	0.120272
C	-4.534952	-2.443859	-0.215674
C	-3.330216	3.552046	-0.726068
C	2.684458	2.389861	-0.419278
C	0.223341	-2.854957	0.091630
C	-3.796741	-1.178567	-0.210865
C	-2.079986	2.815285	-0.516266
C	1.934516	1.134339	-0.226355
N	-2.346524	1.498012	-0.330442
H	4.538127	-2.085613	0.213647
H	4.196504	-3.699903	0.838985
H	-6.455276	-1.660606	-0.766084
H	-2.474105	5.437807	-1.291819
H	4.671823	1.606287	-0.583666
H	4.416135	3.151971	-1.395513
H	5.164763	-3.050549	-1.822556
H	3.618928	-3.858776	-1.955019
H	5.443119	2.753553	1.306053
H	3.996207	3.737587	1.353305
H	3.588461	-0.184793	-0.122672
H	-1.070498	-4.511740	0.153505
H	-5.450054	0.133025	-0.414089
H	-0.730641	4.458566	-0.660188
H	-6.420556	-4.535675	0.313692
H	-7.849645	-3.540459	-0.304404
H	-5.453601	5.461248	-0.543701
H	-4.389155	6.854145	-1.127897

H	-4.135414	-5.307883	0.870931
H	-2.883411	-5.466668	-0.366114
H	-4.572523	-5.200170	-0.835488
H	-6.316514	1.899021	-1.192681
H	-5.980852	3.568670	-1.687404
H	-6.321030	3.200145	0.004201
H	1.104641	-5.502807	1.090153
H	1.102223	-5.582954	-0.671868
H	2.646069	-5.423061	0.195618
H	3.042092	5.066728	-0.862427
H	1.463666	5.181441	-1.683558
H	1.566659	5.443518	0.057475
C	0.206634	0.226982	3.099676
H	0.868465	1.067794	2.805681
H	0.028849	0.335358	4.192981
H	0.811376	-0.695295	2.971355

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B3LYP-D3 SCF energy:	-4643.74831592 a.u.
B3LYP-D3 enthalpy:	-4643.088588 a.u.
B3LYP-D3 free energy:	-4643.215727 a.u.
B3LYP-D3 SCF energy in solution:	-4647.48895215 a.u.
B3LYP-D3 enthalpy in solution:	-4646.829224 a.u.
B3LYP-D3 free energy in solution:	-4646.956363 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-1.042567	0.153600	1.519117
Fe	-0.898530	-0.010194	-0.290295
C	3.968305	-2.952224	0.041137
C	-5.929499	-2.528062	-0.279526
C	-3.393294	4.977947	-0.820936
C	4.161320	2.587861	-0.501877
N	0.488027	-1.464592	-0.168157
C	4.512078	-3.805112	-1.139240
C	-6.722000	-3.538515	0.134756
C	-4.447011	5.783646	-0.576005
C	4.731199	3.230994	0.793858
N	-2.410004	-1.387605	-0.223849
C	5.210224	-5.156561	-0.721280
C	5.501893	4.592866	0.587237

N	0.584344	1.340386	-0.423955
C	2.529805	-0.132253	-0.305430
C	-1.017878	-3.389070	0.042366
C	-4.339479	0.093307	-0.445159
C	-0.783444	3.370539	-0.576369
C	1.589088	-5.035050	0.299784
C	-3.744170	-4.882747	0.037277
C	-5.789078	2.816277	-0.796307
C	1.935208	4.845750	-0.669808
C	1.850879	-1.340159	-0.182068
C	-2.247978	-2.735753	-0.072841
C	-3.665965	1.307322	-0.526429
C	0.424747	2.697783	-0.519257
O	5.980913	-5.640115	-1.585419
O	5.270807	5.222378	-0.484869
C	2.495638	-2.646420	-0.012184
C	-3.528385	-3.403013	-0.056278
C	-4.314361	2.590375	-0.656638
C	1.719840	3.364523	-0.567295
O	4.894622	-5.632326	0.407838
O	6.242437	4.923466	1.544896
C	1.477924	-3.552093	0.099849
C	-4.486699	-2.413558	-0.199548
C	-3.304998	3.537144	-0.680155
C	2.670837	2.385047	-0.504896
C	0.233192	-2.802789	-0.007747
C	-3.749930	-1.157757	-0.306480
C	-2.053319	2.790172	-0.578212
C	1.936365	1.119354	-0.412521
N	-2.303587	1.460168	-0.482975
H	4.540999	-2.021476	0.131062
H	4.168396	-3.541459	0.945380
H	-6.431130	-1.676598	-0.742170
H	-2.481031	5.461528	-1.171480
H	4.667909	1.637731	-0.710111
H	4.424184	3.277225	-1.313881
H	5.215834	-3.231667	-1.754032
H	3.685247	-4.077986	-1.809500
H	5.400278	2.539840	1.320514
H	3.911435	3.442538	1.494456
H	3.612551	-0.168727	-0.300291
H	-1.036434	-4.465528	0.175579
H	-5.423151	0.132182	-0.460394

H	-0.724811	4.451907	-0.634956
H	-6.337117	-4.415616	0.644800
H	-7.799181	-3.495306	-0.013113
H	-5.388161	5.416355	-0.179062
H	-4.376201	6.855929	-0.745311
H	-3.976546	-5.209732	1.062956
H	-2.859136	-5.439516	-0.287242
H	-4.587189	-5.192389	-0.593859
H	-6.296853	1.926858	-1.185661
H	-5.989850	3.646477	-1.485553
H	-6.270171	3.073358	0.160646
H	1.044641	-5.355912	1.201064
H	1.148836	-5.584145	-0.546033
H	2.637149	-5.345299	0.399086
H	3.004629	5.092295	-0.668404
H	1.484585	5.249802	-1.589193
H	1.462201	5.374796	0.171082
C	0.085527	0.222482	2.335932
H	0.714964	1.102872	2.123798
H	-0.248642	0.295112	3.386977
H	0.731182	-0.667626	2.251341
Br	-0.917168	-0.241552	-2.850446

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B3LYP-D3 SCF energy:	-4643.73626441 a.u.
B3LYP-D3 enthalpy:	-4643.077065 a.u.
B3LYP-D3 free energy:	-4643.206908 a.u.
B3LYP-D3 SCF energy in solution:	-4647.48819470 a.u.
B3LYP-D3 enthalpy in solution:	-4646.828995 a.u.
B3LYP-D3 free energy in solution:	-4646.958838 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.948157	0.164440	1.713493
Fe	-0.906663	-0.002983	-0.210566
C	3.959210	-2.948071	0.069432
C	-5.937139	-2.519159	-0.258918
C	-3.403249	4.979060	-0.880337
C	4.154845	2.581301	-0.498748
N	0.478354	-1.479693	-0.177341
C	4.530200	-3.788926	-1.106677

C	-6.725205	-3.531854	0.155268
C	-4.450309	5.789252	-0.625943
C	4.708283	3.237948	0.797616
N	-2.415043	-1.398228	-0.193575
C	5.227836	-5.138411	-0.681209
C	5.479574	4.598630	0.584256
N	0.576856	1.351966	-0.433335
C	2.516912	-0.131364	-0.277297
C	-1.025383	-3.411014	-0.004674
C	-4.339663	0.101088	-0.375050
C	-0.786500	3.383681	-0.620024
C	1.590210	-5.049372	0.242903
C	-3.759880	-4.891517	-0.045642
C	-5.794135	2.817644	-0.760322
C	1.941581	4.843729	-0.739650
C	1.840948	-1.343480	-0.168714
C	-2.254560	-2.751874	-0.091808
C	-3.669099	1.316144	-0.476148
C	0.421262	2.709812	-0.555042
O	6.024257	-5.609231	-1.528174
O	5.261716	5.213900	-0.498763
C	2.487289	-2.648656	-0.009900
C	-3.538084	-3.410346	-0.086593
C	-4.318010	2.595469	-0.631200
C	1.717709	3.366148	-0.608432
O	4.885591	-5.624618	0.435770
O	6.206472	4.941414	1.547532
C	1.472070	-3.563927	0.067817
C	-4.492340	-2.410993	-0.186934
C	-3.310001	3.542680	-0.696424
C	2.664975	2.382450	-0.515663
C	0.226117	-2.822983	-0.041563
C	-3.754475	-1.155447	-0.261832
C	-2.056302	2.804308	-0.590350
C	1.927795	1.121543	-0.404588
N	-2.306722	1.476809	-0.450342
H	4.525921	-2.016035	0.179862
H	4.142280	-3.545338	0.972185
H	-6.439586	-1.663189	-0.711666
H	-2.503282	5.451054	-1.275258
H	4.661659	1.627986	-0.690254
H	4.428444	3.261788	-1.314624
H	5.241859	-3.206681	-1.703502

H	3.718411	-4.062700	-1.794611
H	5.372031	2.552690	1.338251
H	3.880657	3.455538	1.486922
H	3.599323	-0.166918	-0.257784
H	-1.044940	-4.490335	0.100347
H	-5.423128	0.141104	-0.379891
H	-0.727660	4.462966	-0.705679
H	-6.334334	-4.411896	0.655783
H	-7.803572	-3.488855	0.017183
H	-5.376675	5.431450	-0.187609
H	-4.388965	6.855863	-0.830353
H	-3.963773	-5.257834	0.972572
H	-2.887336	-5.437785	-0.418178
H	-4.622004	-5.170930	-0.664384
H	-6.304050	1.921699	-1.130844
H	-6.001309	3.636362	-1.460809
H	-6.264924	3.089186	0.197490
H	1.023145	-5.390589	1.122136
H	1.179006	-5.584656	-0.625847
H	2.637658	-5.353153	0.366516
H	3.011966	5.085942	-0.724010
H	1.509121	5.228185	-1.675734
H	1.456013	5.391892	0.081311
C	0.183169	0.208600	2.510073
H	0.845652	1.059536	2.260345
H	-0.090028	0.311215	3.579908
H	0.802343	-0.704899	2.418350
Br	-1.116947	-0.254846	-3.132412

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B3LYP-D3 SCF energy:	-4643.73879139 a.u.
B3LYP-D3 enthalpy:	-4643.080907 a.u.
B3LYP-D3 free energy:	-4643.211271 a.u.
B3LYP-D3 SCF energy in solution:	-4647.49112403 a.u.
B3LYP-D3 enthalpy in solution:	-4646.833240 a.u.
B3LYP-D3 free energy in solution:	-4646.963604 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.911949	0.159090	1.723240
Fe	-0.916323	-0.000116	-0.163422

C	3.984447	-2.985164	0.051619
C	-5.975033	-2.551051	-0.248259
C	-3.433542	5.004338	-0.902327
C	4.180942	2.615043	-0.493210
N	0.513770	-1.516490	-0.159618
C	4.545123	-3.824372	-1.130709
C	-6.764959	-3.579168	0.124455
C	-4.486588	5.820430	-0.692506
C	4.735089	3.277814	0.799863
N	-2.467782	-1.426336	-0.150095
C	5.247665	-5.174334	-0.715289
C	5.511705	4.634531	0.580920
N	0.613997	1.388516	-0.415527
C	2.529620	-0.131398	-0.270394
C	-1.031526	-3.418416	0.009717
C	-4.369429	0.104220	-0.349372
C	-0.792649	3.393687	-0.607200
C	1.614075	-5.082195	0.231362
C	-3.792727	-4.917286	-0.043357
C	-5.829535	2.851404	-0.772274
C	1.966309	4.872720	-0.738118
C	1.869260	-1.365435	-0.162364
C	-2.283412	-2.774732	-0.064573
C	-3.712534	1.339376	-0.451987
C	0.438077	2.738567	-0.542385
O	6.033499	-5.644342	-1.572887
O	5.297238	5.245856	-0.504884
C	2.512686	-2.680294	-0.015213
C	-3.570673	-3.435749	-0.072008
C	-4.355452	2.623695	-0.629646
C	1.740447	3.395700	-0.601863
O	4.919533	-5.662104	0.405158
O	6.238898	4.979156	1.543634
C	1.493796	-3.595765	0.064725
C	-4.531866	-2.436616	-0.169607
C	-3.342031	3.570997	-0.699091
C	2.691376	2.411491	-0.507614
C	0.241726	-2.851626	-0.031336
C	-3.799701	-1.171245	-0.229782
C	-2.083800	2.832918	-0.572326
C	1.956867	1.142411	-0.391965
N	-2.356626	1.515788	-0.413544
H	4.552387	-2.052950	0.157600

H	4.176038	-3.583678	0.951820
H	-6.478395	-1.678608	-0.668035
H	-2.520097	5.471404	-1.271955
H	4.687705	1.660239	-0.679148
H	4.455097	3.291176	-1.312534
H	5.250672	-3.241007	-1.733844
H	3.726732	-4.097442	-1.811129
H	5.395169	2.593562	1.346415
H	3.906704	3.502937	1.485962
H	3.613459	-0.167449	-0.257940
H	-1.052852	-4.499909	0.105392
H	-5.454128	0.143304	-0.367537
H	-0.735319	4.473396	-0.704904
H	-6.377209	-4.479276	0.590173
H	-7.843059	-3.528882	-0.013811
H	-5.429212	5.471315	-0.283075
H	-4.414075	6.884615	-0.906081
H	-4.036802	-5.286024	0.965270
H	-2.904471	-5.460943	-0.381090
H	-4.629185	-5.198971	-0.696061
H	-6.344360	1.942620	-1.103000
H	-6.031982	3.639937	-1.508484
H	-6.300677	3.168363	0.171504
H	1.047643	-5.428517	1.109267
H	1.200705	-5.613122	-0.639306
H	2.661218	-5.388171	0.351318
H	3.036322	5.116344	-0.725394
H	1.531681	5.254650	-1.674514
H	1.481332	5.424024	0.081336
C	0.218587	0.207458	2.527143
H	0.868379	1.063855	2.274369
H	-0.064171	0.302416	3.592762
H	0.836938	-0.701995	2.423258
Br	-1.063490	-0.244496	-2.947589

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B3LYP-D3 SCF energy:	-2072.36524624 a.u.
B3LYP-D3 enthalpy:	-2071.706980 a.u.
B3LYP-D3 free energy:	-2071.828698 a.u.
B3LYP-D3 SCF energy in solution:	-2073.18724301 a.u.
B3LYP-D3 enthalpy in solution:	-2072.528977 a.u.

B3LYP-D3 free energy in solution:

-2072.650695 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-1.015980	0.249186	1.655506
Fe	-0.865872	0.000019	-0.096605
C	3.997793	-2.867201	0.067383
C	-5.874500	-2.553102	-0.283047
C	-3.360657	4.924312	-1.023552
C	4.178994	2.485016	-0.597923
N	0.493691	-1.456688	-0.087921
C	4.548188	-3.273394	-1.320470
C	-6.672571	-3.487145	0.264619
C	-4.420294	5.709398	-0.760056
C	4.822231	2.718724	0.790456
N	-2.349103	-1.392955	-0.171936
C	4.583543	-4.828161	-1.592547
C	5.022968	4.235057	1.183122
N	0.587074	1.315493	-0.455189
C	2.545168	-0.143164	-0.314998
C	-0.984813	-3.375278	0.293487
C	-4.287073	0.048202	-0.564119
C	-0.760008	3.355483	-0.620575
C	1.621951	-5.001299	0.551247
C	-3.703546	-4.862136	0.334882
C	-5.731061	2.733115	-1.086974
C	1.948681	4.824013	-0.715659
C	1.866700	-1.339532	-0.132220
C	-2.205648	-2.731129	0.104415
C	-3.614381	1.256158	-0.676290
C	0.445001	2.685581	-0.544748
O	4.753070	-5.138206	-2.791669
O	4.928394	5.079349	0.245051
C	2.516618	-2.625440	0.089496
C	-3.485171	-3.394677	0.126005
C	-4.263058	2.527899	-0.867343
C	1.738700	3.344300	-0.602318
O	4.489019	-5.580325	-0.579048
O	5.302300	4.421392	2.387115
C	1.507125	-3.530864	0.282894
C	-4.432032	-2.424125	-0.144037
C	-3.263503	3.482329	-0.851893
C	2.684359	2.354442	-0.564774

C	0.260309	-2.793642	0.175964
C	-3.697972	-1.182913	-0.321729
C	-2.015733	2.757810	-0.675647
C	1.949631	1.100241	-0.449605
N	-2.245943	1.412382	-0.579856
H	4.510886	-1.972088	0.443658
H	4.242139	-3.696671	0.739705
H	-6.351944	-1.797916	-0.908635
H	-2.464038	5.410851	-1.407194
H	4.602933	1.593807	-1.079760
H	4.456309	3.354563	-1.203812
H	5.586804	-2.922151	-1.408396
H	3.993315	-2.787646	-2.131753
H	5.822659	2.262264	0.803443
H	4.253024	2.223663	1.586117
H	3.627022	-0.180126	-0.320415
H	-1.005551	-4.435502	0.516081
H	-5.368772	0.079317	-0.623147
H	-0.710770	4.436453	-0.674157
H	-6.298801	-4.252946	0.936564
H	-7.741671	-3.491066	0.067668
H	-5.339133	5.325603	-0.328026
H	-4.379098	6.779596	-0.945291
H	-3.907695	-5.105073	1.387863
H	-2.830143	-5.447720	0.030869
H	-4.563669	-5.210997	-0.248554
H	-6.196954	1.854363	-1.546266
H	-5.905003	3.590698	-1.747288
H	-6.269159	2.934313	-0.149077
H	1.412784	-5.229100	1.607640
H	0.897725	-5.567992	-0.048981
H	2.627483	-5.359506	0.291660
H	2.991345	5.080899	-0.484003
H	1.700422	5.183431	-1.726205
H	1.301984	5.367596	-0.013826
C	0.151756	0.459388	2.412439
H	0.613009	1.433545	2.197213
H	-0.139137	0.437293	3.473700
H	0.907273	-0.320395	2.245201

B3LYP-D3 SCF energy:	-2072.36768123 a.u.
B3LYP-D3 enthalpy:	-2071.710279 a.u.
B3LYP-D3 free energy:	-2071.834364 a.u.
B3LYP-D3 SCF energy in solution:	-2073.19432819 a.u.
B3LYP-D3 enthalpy in solution:	-2072.536926 a.u.
B3LYP-D3 free energy in solution:	-2072.661011 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.935521	0.247350	1.833677
Fe	-0.884746	0.004563	-0.007927
C	3.976936	-2.881196	0.140964
C	-5.900953	-2.528008	-0.246574
C	-3.350594	4.925044	-1.097382
C	4.176203	2.467211	-0.553838
N	0.477636	-1.476604	-0.070633
C	4.578669	-3.243556	-1.238636
C	-6.687487	-3.486464	0.274334
C	-4.392330	5.731843	-0.829036
C	4.781300	2.821188	0.828377
N	-2.368517	-1.397249	-0.163140
C	4.654479	-4.790511	-1.545260
C	5.062449	4.358457	1.059803
N	0.581224	1.312007	-0.435711
C	2.531380	-0.152999	-0.223131
C	-1.007532	-3.411746	0.177952
C	-4.306101	0.072254	-0.461749
C	-0.755055	3.351437	-0.702297
C	1.594447	-5.042990	0.432869
C	-3.731086	-4.881347	0.170830
C	-5.742323	2.761306	-0.986743
C	1.960145	4.796738	-0.840534
C	1.848428	-1.351149	-0.071705
C	-2.224559	-2.751019	0.030314
C	-3.628059	1.275289	-0.595557
C	0.445017	2.676363	-0.593649
O	4.886600	-5.066813	-2.742024
O	4.963651	5.114561	0.050228
C	2.495635	-2.644154	0.117758
C	-3.507083	-3.405362	0.043110
C	-4.270005	2.546617	-0.809661
C	1.740578	3.324994	-0.660580
O	4.523026	-5.569719	-0.556698

O	5.393047	4.644341	2.230853
C	1.483602	-3.561961	0.229309
C	-4.453970	-2.413945	-0.142020
C	-3.261173	3.490327	-0.868413
C	2.682246	2.334589	-0.551639
C	0.239356	-2.824242	0.116839
C	-3.717839	-1.169276	-0.271747
C	-2.015258	2.762137	-0.702799
C	1.940718	1.088437	-0.395808
N	-2.257874	1.425295	-0.539831
H	4.473075	-1.997210	0.562962
H	4.199807	-3.731281	0.795034
H	-6.391704	-1.738412	-0.816555
H	-2.464065	5.384804	-1.533645
H	4.616877	1.542200	-0.947327
H	4.468107	3.285061	-1.222230
H	5.611581	-2.869179	-1.286860
H	4.038860	-2.750443	-2.055506
H	5.747122	2.309555	0.944105
H	4.149373	2.458926	1.648042
H	3.612758	-0.191062	-0.203531
H	-1.032896	-4.482504	0.340469
H	-5.388399	0.110476	-0.490879
H	-0.698114	4.427974	-0.807282
H	-6.298327	-4.288338	0.893357
H	-7.762012	-3.475132	0.110073
H	-5.298153	5.376713	-0.347873
H	-4.347642	6.792848	-1.060354
H	-3.906732	-5.185230	1.212968
H	-2.871281	-5.452804	-0.192818
H	-4.610170	-5.189245	-0.407231
H	-6.234572	1.870701	-1.392091
H	-5.929441	3.593179	-1.675674
H	-6.243491	3.008249	-0.039514
H	1.332282	-5.321302	1.464964
H	0.905903	-5.583260	-0.230460
H	2.614452	-5.384835	0.210218
H	3.007610	5.057134	-0.635751
H	1.700334	5.113856	-1.862083
H	1.327071	5.374959	-0.154055
C	0.211946	0.356727	2.620590
H	0.827996	1.224119	2.330670
H	-0.068010	0.478978	3.680461

H 0.851072 -0.538982 2.539235

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B3LYP-D3 SCF energy:	-2072.37065613 a.u.
B3LYP-D3 enthalpy:	-2071.714157 a.u.
B3LYP-D3 free energy:	-2071.839559 a.u.
B3LYP-D3 SCF energy in chlorobenzene:	-2073.20126843 a.u.
B3LYP-D3 enthalpy in chlorobenzene:	-2072.544769 a.u.
B3LYP-D3 free energy in chlorobenzene:	-2072.670171 a.u.
B3LYP-D3 SCF energy in water:	-2073.25417012 a.u.
B3LYP-D3 enthalpy in water:	-2072.597428 a.u.
B3LYP-D3 free energy in water:	-2072.720415 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.846564	0.293049	2.019152
Fe	-0.891355	0.037180	0.211312
C	3.992264	-2.906953	0.107657
C	-5.930312	-2.546090	-0.220309
C	-3.373315	4.933801	-1.170374
C	4.193125	2.481610	-0.558981
N	0.498165	-1.498048	-0.036183
C	4.579147	-3.261526	-1.281019
C	-6.715499	-3.523780	0.266406
C	-4.416458	5.751412	-0.941978
C	4.795869	2.765919	0.838230
N	-2.408120	-1.409236	-0.097878
C	4.682016	-4.807318	-1.586710
C	4.959623	4.295718	1.192099
N	0.603041	1.343095	-0.418502
C	2.535400	-0.148842	-0.206572
C	-1.013477	-3.417167	0.178505
C	-4.330211	0.081267	-0.404702
C	-0.761316	3.357603	-0.727192
C	1.610194	-5.070516	0.379130
C	-3.755033	-4.900428	0.143926
C	-5.770349	2.783300	-0.995422
C	1.984740	4.811687	-0.901204
C	1.865059	-1.363578	-0.056200
C	-2.247433	-2.764139	0.058421
C	-3.662591	1.297050	-0.554838

C	0.455834	2.699612	-0.608399
O	4.931901	-5.077557	-2.781444
O	4.899222	5.108672	0.224184
C	2.511442	-2.665561	0.103416
C	-3.532241	-3.421407	0.053809
C	-4.299600	2.567207	-0.807101
C	1.756915	3.345201	-0.690026
O	4.549283	-5.590505	-0.601734
O	5.181989	4.522909	2.401020
C	1.497569	-3.585646	0.206332
C	-4.484455	-2.427524	-0.110411
C	-3.285904	3.507592	-0.894162
C	2.698495	2.354511	-0.559812
C	0.248822	-2.844634	0.121357
C	-3.753288	-1.173791	-0.213957
C	-2.037421	2.782568	-0.703707
C	1.957417	1.107204	-0.382707
N	-2.296096	1.457136	-0.495481
H	4.494036	-2.025226	0.528109
H	4.222445	-3.760882	0.754271
H	-6.423067	-1.738348	-0.762696
H	-2.480112	5.378228	-1.609202
H	4.626618	1.569864	-0.991597
H	4.491490	3.325533	-1.190182
H	5.602658	-2.865543	-1.349778
H	4.015130	-2.782917	-2.090148
H	5.803469	2.327822	0.887907
H	4.214916	2.282335	1.632556
H	3.617907	-0.187444	-0.197120
H	-1.039878	-4.492862	0.312166
H	-5.413211	0.118082	-0.442405
H	-0.706869	4.431264	-0.866398
H	-6.325796	-4.346374	0.857169
H	-7.789926	-3.508493	0.101692
H	-5.330112	5.414623	-0.462571
H	-4.365220	6.804408	-1.206310
H	-3.947583	-5.228628	1.175751
H	-2.886944	-5.460756	-0.217429
H	-4.623278	-5.198408	-0.455649
H	-6.267754	1.876525	-1.356304
H	-5.953339	3.581644	-1.724327
H	-6.270458	3.079628	-0.061785
H	1.350243	-5.370136	1.405951

H	0.918465	-5.596442	-0.292716
H	2.629342	-5.409491	0.148615
H	3.010561	5.082990	-0.616264
H	1.813264	5.092238	-1.951892
H	1.293388	5.408923	-0.292059
C	0.333984	0.461641	2.758796
H	0.870880	1.371245	2.450718
H	0.092323	0.544631	3.829359
H	1.015859	-0.391454	2.619747

8a

B3LYP-D3 SCF energy:	-746.12514761 a.u.
B3LYP-D3 enthalpy:	-745.865527 a.u.
B3LYP-D3 free energy:	-745.924764 a.u.
B3LYP-D3 SCF energy in solution:	-746.36696683 a.u.
B3LYP-D3 enthalpy in solution:	-746.107346 a.u.
B3LYP-D3 free energy in solution:	-746.166583 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.942124	0.028275	-0.852995
C	1.846573	-0.059924	-2.079310
H	1.886064	-1.086761	-2.451222
H	1.475552	0.598348	-2.871645
H	2.860246	0.254563	-1.817152
C	0.937817	1.450885	-0.251411
O	1.906418	2.167607	-0.086971
N	-0.370496	1.774289	0.091736
C	1.393209	-0.982669	0.206634
O	2.053496	-1.970783	-0.023354
C	-0.692378	2.940504	0.890339
H	0.195157	3.573757	0.926843
H	-1.525133	3.489596	0.439260
H	-0.971059	2.640435	1.908044
C	-1.254891	0.739647	-0.174100
C	-0.581338	-0.202855	-1.136307
C	-2.499912	0.518396	0.345438
C	-1.160409	-1.585637	-1.081198
H	-0.737944	0.202262	-2.157899
C	-3.117974	-0.738305	0.110485
H	-2.977906	1.254116	0.985896

C	-2.402415	-1.782113	-0.538210
H	-0.613182	-2.393560	-1.557687
H	-4.107952	-0.930710	0.510986
H	-2.854177	-2.770329	-0.585728
O	0.900530	-0.672644	1.421827
C	1.161035	-1.635268	2.457940
H	2.237536	-1.765316	2.597166
H	0.700540	-1.227101	3.357827
H	0.713528	-2.598380	2.197299

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B3LYP-D3 SCF energy:	-2072.95693610 a.u.
B3LYP-D3 enthalpy:	-2072.288100 a.u.
B3LYP-D3 free energy:	-2072.410103 a.u.
B3LYP-D3 SCF energy in solution:	-2073.77465954 a.u.
B3LYP-D3 enthalpy in solution:	-2073.105823 a.u.
B3LYP-D3 free energy in solution:	-2073.227826 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.994336	-0.412028	1.498059
Fe	-0.631251	-0.341558	-0.368809
C	4.422631	-2.758555	0.200625
C	-5.358661	-3.209688	-1.303262
C	-3.434149	4.484845	-0.966067
C	4.271523	2.467721	-0.524621
N	0.862595	-1.712369	-0.316040
C	5.210420	-2.419337	-1.097258
C	-6.114019	-4.294502	-1.040100
C	-4.567730	5.177038	-0.741316
C	5.045215	2.418222	0.811699
N	-1.965695	-1.828046	-0.699132
C	6.684180	-2.184114	-0.821454
C	5.319066	3.837236	1.464066
N	0.744913	1.131184	-0.409565
C	2.779212	-0.201710	-0.195171
C	-0.475216	-3.758887	-0.400668
C	-3.980192	-0.477539	-1.023656
C	-0.724692	3.075646	-0.572895
C	2.240616	-5.194836	0.051909
C	-3.052444	-5.424366	-0.891323

C	-5.624702	2.144125	-1.323707
C	1.942703	4.719821	-0.483662
C	2.195627	-1.464859	-0.166334
C	-1.725659	-3.179801	-0.631703
C	-3.413235	0.790865	-0.942090
C	0.524079	2.488824	-0.466623
O	6.994548	-1.031013	-0.171181
O	4.996363	4.845858	0.776625
C	2.936828	-2.704091	0.005472
C	-2.943625	-3.930705	-0.835827
C	-4.155808	2.026143	-1.051874
C	1.788826	3.228579	-0.450825
O	7.568651	-2.960007	-1.109032
O	5.864993	3.783254	2.587857
C	2.017325	-3.716564	-0.056271
C	-3.950318	-3.001118	-1.020369
C	-3.234204	3.047120	-0.908918
C	2.781920	2.293582	-0.422786
C	0.723523	-3.078613	-0.258534
C	-3.308062	-1.691942	-0.927120
C	-1.937799	2.397490	-0.729766
C	2.108959	0.998847	-0.348371
N	-2.073699	1.041455	-0.750361
H	4.711709	-2.049422	0.988321
H	4.739671	-3.747762	0.550919
H	-5.858888	-2.373149	-1.793772
H	-2.547126	5.065438	-1.221445
H	4.650707	1.700273	-1.219608
H	4.494932	3.444914	-0.964196
H	4.771912	-1.527971	-1.559718
H	5.126293	-3.243257	-1.809682
H	6.036171	1.958809	0.657921
H	4.529326	1.798281	1.555294
H	3.853126	-0.134093	-0.065956
H	-0.434056	-4.842140	-0.337049
H	-5.056473	-0.521676	-1.152224
H	-0.751932	4.160091	-0.564828
H	-5.730342	-5.161259	-0.511639
H	-7.162147	-4.325478	-1.328688
H	-5.492351	4.702035	-0.429233
H	-4.584788	6.260306	-0.834587
H	-3.340692	-5.859896	0.077519
H	-2.103575	-5.887443	-1.184045

H	-3.815207	-5.731387	-1.617835
H	-6.010188	1.262034	-1.847435
H	-5.835061	3.023588	-1.945018
H	-6.214200	2.256177	-0.401113
H	1.660538	-5.632222	0.876129
H	1.933994	-5.719997	-0.863885
H	3.296233	-5.430262	0.227883
H	2.945376	4.995128	-0.133017
H	1.788492	5.127364	-1.495261
H	1.206214	5.205393	0.170792
C	-0.023669	0.086334	2.345175
H	0.125850	1.183892	2.262202
H	-0.301352	-0.114209	3.402074
H	0.977783	-0.370391	2.195000
H	6.212256	-0.471080	-0.014988

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B3LYP-D3 SCF energy:	-2072.96059019 a.u.
B3LYP-D3 enthalpy:	-2072.292549 a.u.
B3LYP-D3 free energy:	-2072.416994 a.u.
B3LYP-D3 SCF energy in solution:	-2073.78137368 a.u.
B3LYP-D3 enthalpy in solution:	-2073.113332 a.u.
B3LYP-D3 free energy in solution:	-2073.237777 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.879924	-0.375729	1.608573
Fe	-0.650632	-0.330717	-0.274479
C	4.421397	-2.755116	0.154424
C	-5.355881	-3.201066	-1.265602
C	-3.424020	4.492481	-1.024500
C	4.245145	2.464160	-0.492663
N	0.866538	-1.717655	-0.349508
C	5.207817	-2.397525	-1.140502
C	-6.114302	-4.275316	-0.968716
C	-4.569216	5.199573	-0.925132
C	5.012839	2.395844	0.845818
N	-1.967663	-1.803694	-0.643538
C	6.681560	-2.166235	-0.864832
C	5.248667	3.802552	1.537650
N	0.720311	1.115925	-0.388422

C	2.779524	-0.198281	-0.195588
C	-0.483472	-3.761892	-0.412776
C	-4.003672	-0.477001	-0.994508
C	-0.730649	3.084184	-0.583891
C	2.240230	-5.198487	-0.016902
C	-3.051449	-5.404676	-0.872136
C	-5.633589	2.147433	-1.358206
C	1.918550	4.708404	-0.453988
C	2.199386	-1.470120	-0.190269
C	-1.722748	-3.169121	-0.598598
C	-3.437323	0.804330	-0.947833
C	0.496928	2.486209	-0.452460
O	6.991606	-1.022357	-0.196972
O	4.932943	4.822112	0.863045
C	2.935573	-2.699745	-0.036646
C	-2.942811	-3.911495	-0.798921
C	-4.165995	2.024987	-1.080866
C	1.763593	3.217513	-0.425268
O	7.567107	-2.936497	-1.164539
O	5.763795	3.730376	2.674757
C	2.009383	-3.719511	-0.111208
C	-3.951112	-2.985342	-0.972029
C	-3.231705	3.057845	-0.953888
C	2.756108	2.285145	-0.396571
C	0.728119	-3.089562	-0.297498
C	-3.318800	-1.669795	-0.876475
C	-1.954244	2.414643	-0.758659
C	2.092759	0.985774	-0.328266
N	-2.092962	1.053161	-0.762629
H	4.714590	-2.057273	0.951127
H	4.740366	-3.748876	0.490219
H	-5.847392	-2.383020	-1.794568
H	-2.512806	5.070920	-1.179353
H	4.627043	1.708092	-1.198305
H	4.466832	3.448751	-0.915886
H	4.768147	-1.498628	-1.587545
H	5.121106	-3.210566	-1.864983
H	6.015152	1.965279	0.682798
H	4.509527	1.742526	1.569044
H	3.851852	-0.123512	-0.067556
H	-0.449445	-4.845500	-0.362198
H	-5.079244	-0.532376	-1.114825
H	-0.744985	4.168023	-0.586904

H	-5.736650	-5.117716	-0.397672
H	-7.157473	-4.321596	-1.272692
H	-5.532163	4.740382	-0.728676
H	-4.557818	6.283434	-1.012413
H	-3.293964	-5.853813	0.102606
H	-2.116344	-5.860657	-1.215390
H	-3.846979	-5.699722	-1.566944
H	-6.046414	1.220533	-1.771803
H	-5.828631	2.949240	-2.082310
H	-6.217137	2.387440	-0.455609
H	1.677011	-5.646771	0.813339
H	1.923933	-5.720003	-0.931557
H	3.299784	-5.429074	0.141189
H	2.916610	4.981355	-0.088703
H	1.777582	5.115309	-1.467387
H	1.173274	5.192620	0.190900
C	0.134846	0.035687	2.462328
H	0.401391	1.100440	2.329764
H	-0.167400	-0.098280	3.519558
H	1.068470	-0.541619	2.316155
H	6.207376	-0.468174	-0.030904

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B3LYP-D3 SCF energy:	-2072.98113641 a.u.
B3LYP-D3 enthalpy:	-2072.313806 a.u.
B3LYP-D3 free energy:	-2072.442933 a.u.
B3LYP-D3 SCF energy in solution:	-2073.79792532 a.u.
B3LYP-D3 enthalpy in solution:	-2073.130595 a.u.
B3LYP-D3 free energy in solution:	-2073.259722 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.910679	-0.365835	2.122449
Fe	-0.715746	-0.354087	0.245487
C	4.425112	-2.874531	0.059351
C	-5.411913	-3.217435	-1.323653
C	-3.376690	4.489894	-1.173863
C	4.299061	2.517093	-0.150632
N	0.856950	-1.786537	-0.174309
C	5.079937	-2.513611	-1.305501
C	-6.170419	-4.315502	-1.137717

C	-4.502760	5.217471	-1.046731
C	4.830671	3.080952	1.194251
N	-2.039296	-1.884982	-0.580364
C	6.581207	-2.345756	-1.174928
C	5.492344	4.512447	1.086389
N	0.782199	1.133698	-0.240995
C	2.769120	-0.258182	0.004712
C	-0.513445	-3.805056	-0.404362
C	-4.007963	-0.477293	-0.955493
C	-0.696389	3.053552	-0.567230
C	2.239439	-5.277539	-0.173158
C	-3.118219	-5.455844	-0.986423
C	-5.598841	2.175279	-1.464565
C	1.984354	4.697682	-0.477289
C	2.185064	-1.533651	-0.043959
C	-1.784130	-3.228312	-0.588833
C	-3.435260	0.798906	-0.888223
C	0.559681	2.475034	-0.378853
O	6.993760	-1.188138	-0.588132
O	5.260429	5.165373	0.029082
C	2.930390	-2.790644	-0.005907
C	-3.003567	-3.967693	-0.850244
C	-4.147915	2.044620	-1.113253
C	1.827218	3.211435	-0.348590
O	7.401625	-3.171840	-1.505272
O	6.160337	4.846344	2.090975
C	2.006910	-3.797082	-0.126366
C	-4.008225	-3.024156	-1.006076
C	-3.209885	3.056573	-1.001105
C	2.817317	2.275941	-0.205054
C	0.703552	-3.143967	-0.232156
C	-3.363288	-1.719069	-0.842861
C	-1.931071	2.395075	-0.716358
C	2.132062	0.977292	-0.127627
N	-2.112426	1.052172	-0.639834
H	4.804249	-2.189863	0.829938
H	4.757816	-3.877668	0.350750
H	-5.905298	-2.352049	-1.768704
H	-2.467080	5.031979	-1.434136
H	4.829773	1.588381	-0.415410
H	4.570231	3.264656	-0.906330
H	4.624112	-1.590538	-1.682334
H	4.883994	-3.307427	-2.029887

H	5.565302	2.405137	1.650026
H	4.010671	3.163675	1.919631
H	3.845966	-0.220055	0.139847
H	-0.468045	-4.890780	-0.420642
H	-5.079042	-0.508123	-1.130316
H	-0.707736	4.137235	-0.635438
H	-5.793878	-5.214325	-0.660345
H	-7.215108	-4.326967	-1.439812
H	-5.449252	4.783718	-0.740098
H	-4.492768	6.291158	-1.218326
H	-3.452032	-5.936820	-0.054444
H	-2.159092	-5.910073	-1.258401
H	-3.849019	-5.722346	-1.760649
H	-5.982153	1.263009	-1.935119
H	-5.757900	3.007954	-2.161235
H	-6.225925	2.373078	-0.582199
H	1.669994	-5.799857	0.607723
H	1.923959	-5.706692	-1.134639
H	3.297619	-5.526040	-0.033701
H	3.033326	4.996584	-0.353755
H	1.631473	5.053114	-1.457566
H	1.386376	5.223178	0.281233
C	0.203350	-0.286027	2.942728
H	0.817157	0.618442	2.755819
H	-0.084262	-0.256534	4.014984
H	0.890625	-1.151367	2.825950
H	6.239744	-0.599266	-0.408300

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B3LYP-D3 SCF energy:	-2072.98358629 a.u.
B3LYP-D3 enthalpy:	-2072.312987 a.u.
B3LYP-D3 free energy:	-2072.437800 a.u.
B3LYP-D3 SCF energy in solution:	-2073.69597650 a.u.
B3LYP-D3 enthalpy in solution:	-2073.025377 a.u.
B3LYP-D3 free energy in solution:	-2073.150190 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.524464	-0.066642	1.641737
Fe	-0.570904	-0.245194	-0.155832
C	4.503800	-2.754667	-0.088140

C	-5.378388	-3.166786	-0.964434
C	-3.360463	4.520727	-1.355578
C	4.302943	2.563432	-0.202752
N	0.935858	-1.690555	-0.449155
C	5.237377	-2.461007	-1.424302
C	-6.108661	-4.202082	-0.517359
C	-4.459825	5.237858	-1.070493
C	4.615791	2.245761	1.279506
N	-1.951270	-1.797383	-0.610295
C	6.736996	-2.305033	-1.231678
C	3.679364	3.115543	2.194383
N	0.839712	1.192910	-0.689852
C	2.853733	-0.167378	-0.405546
C	-0.434693	-3.721849	-0.395172
C	-3.963752	-0.429339	-0.921040
C	-0.656245	3.119723	-0.874621
C	2.306034	-5.167424	-0.110509
C	-3.060854	-5.382988	-0.639986
C	-5.586994	2.188295	-1.417988
C	2.023578	4.770984	-0.536030
C	2.276093	-1.435494	-0.367922
C	-1.703380	-3.146736	-0.530437
C	-3.387268	0.838857	-0.972608
C	0.603727	2.548638	-0.739060
O	7.129118	-1.206298	-0.527138
O	3.797424	4.357030	2.003968
C	3.012139	-2.680116	-0.218904
C	-2.939291	-3.889642	-0.633125
C	-4.112657	2.074346	-1.179180
C	1.856052	3.284825	-0.618984
O	7.566811	-3.084801	-1.633117
O	2.910940	2.490407	2.961334
C	2.084275	-3.689686	-0.224484
C	-3.948584	-2.955215	-0.780658
C	-3.173714	3.088375	-1.161639
C	2.847969	2.345477	-0.500324
C	0.783237	-3.052958	-0.361316
C	-3.302292	-1.649914	-0.775046
C	-1.880030	2.447230	-0.957364
C	2.195044	1.049861	-0.539142
N	-2.043432	1.095787	-0.842783
H	4.832967	-2.037947	0.676544
H	4.814067	-3.741408	0.272153

H	-5.899467	-2.390381	-1.525072
H	-2.505578	5.053649	-1.771187
H	4.929914	1.966888	-0.886360
H	4.549371	3.616802	-0.362622
H	4.828682	-1.546107	-1.870152
H	5.071927	-3.277795	-2.130001
H	5.667306	2.496006	1.477268
H	4.459460	1.182275	1.498199
H	3.927547	-0.109143	-0.279786
H	-0.394221	-4.803252	-0.317510
H	-5.043584	-0.471070	-1.007285
H	-0.691435	4.201910	-0.911080
H	-5.683796	-4.995383	0.089453
H	-7.172603	-4.266695	-0.728399
H	-5.337790	4.799456	-0.606719
H	-4.495013	6.305653	-1.267906
H	-3.222245	-5.789204	0.368597
H	-2.159845	-5.859047	-1.041268
H	-3.911395	-5.698457	-1.254582
H	-5.988650	1.288137	-1.895637
H	-5.807425	3.043101	-2.067123
H	-6.145891	2.338879	-0.483654
H	1.777275	-5.587267	0.754957
H	1.938506	-5.697407	-0.999174
H	3.367877	-5.407847	0.000718
H	2.515051	5.005897	0.419317
H	2.666683	5.142023	-1.345404
H	1.069543	5.303955	-0.597604
C	0.592323	0.174918	2.473298
H	1.073235	1.139940	2.266058
H	0.268254	0.168223	3.522614
H	1.348103	-0.612850	2.333593
H	6.367749	-0.654760	-0.277556

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B3LYP-D3 SCF energy:	-745.54486551 a.u.
B3LYP-D3 enthalpy:	-745.300574 a.u.
B3LYP-D3 free energy:	-745.360476 a.u.
B3LYP-D3 SCF energy in solution:	-745.85545308 a.u.
B3LYP-D3 enthalpy in solution:	-745.611162 a.u.
B3LYP-D3 free energy in solution:	-745.671064 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	0.813326	0.053648	-0.906915
C	1.392448	-0.057138	-2.323136
H	1.545609	-1.111238	-2.572935
H	0.709182	0.394641	-3.052226
H	2.357581	0.461292	-2.365807
C	0.707907	1.507949	-0.434425
O	1.563213	2.387103	-0.538785
N	-0.544616	1.687229	0.139208
C	1.697578	-0.797268	0.056298
O	2.016376	-1.970929	-0.177497
C	-0.943024	2.907191	0.785635
H	-0.116441	3.614780	0.683899
H	-1.846780	3.327416	0.321226
H	-1.153459	2.738429	1.851428
C	-1.322711	0.525725	0.048050
C	-0.586442	-0.444868	-0.694654
C	-2.587676	0.291962	0.547907
C	-1.163706	-1.722315	-0.868472
C	-3.170010	-0.982802	0.327530
H	-3.128108	1.067132	1.088924
C	-2.441161	-1.971918	-0.369403
H	-0.600691	-2.502321	-1.374318
H	-4.166632	-1.196377	0.706980
H	-2.890760	-2.952819	-0.524338
O	1.631331	-0.311630	1.365583
C	1.872864	-1.289491	2.360783
H	2.877896	-1.724616	2.271027
H	1.775272	-0.778074	3.324308
H	1.145929	-2.109254	2.297791

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B3LYP-D3 SCF energy:	-745.91345394 a.u.
B3LYP-D3 enthalpy:	-745.651563 a.u.
B3LYP-D3 free energy:	-745.710418 a.u.
B3LYP-D3 SCF energy in solution:	-746.20597266 a.u.
B3LYP-D3 enthalpy in solution:	-745.944082 a.u.
B3LYP-D3 free energy in solution:	-746.002937 a.u.

Cartesian coordinates

ATOM	X	Y	Z
C	-0.703875	0.061647	0.869051
C	-1.541065	-0.034019	2.144280
H	-2.516307	0.425795	1.977427
H	-1.046936	0.488233	2.968955
C	-0.535954	1.520462	0.398692
O	-1.319892	2.425232	0.444851
N	0.778564	1.626483	-0.184268
C	-1.325816	-0.670492	-0.349304
O	-0.635878	-1.178833	-1.210521
C	1.200927	2.813070	-0.932669
H	2.161639	3.168404	-0.553045
H	1.281788	2.570801	-1.996092
H	0.438351	3.578550	-0.786088
C	1.475627	0.500870	-0.015846
C	0.775538	-0.393684	0.959625
C	2.689023	0.131106	-0.613832
C	1.169993	-1.826463	0.875140
H	1.141783	-0.065551	1.953358
C	3.080166	-1.187286	-0.473573
H	3.248383	0.822182	-1.234080
C	2.312891	-2.175306	0.232761
H	0.584655	-2.553175	1.430593
H	3.994714	-1.508362	-0.965586
H	2.658130	-3.203493	0.230123
O	-2.646567	-0.621308	-0.331337
C	-3.328781	-1.228310	-1.463828
H	-3.071942	-2.287875	-1.524505
H	-4.389193	-1.090344	-1.261688
H	-3.033517	-0.721932	-2.385198
H	-1.694855	-1.078909	2.428781

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B3LYP-D3 SCF energy:	-2073.00819298 a.u.
B3LYP-D3 enthalpy:	-2072.340125 a.u.
B3LYP-D3 free energy:	-2072.463040 a.u.
B3LYP-D3 SCF energy in water:	-2073.86917070 a.u.
B3LYP-D3 enthalpy in water:	-2073.201103 a.u.
B3LYP-D3 free energy in water:	-2073.324018 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	0.045112	0.744070	1.781410
Fe	-0.704755	0.195812	-0.098823
C	4.112502	-2.836098	-0.321782
C	-5.801213	-2.304578	0.449214
C	-3.334342	4.962906	-1.709667
C	4.061499	2.605961	-0.041330
N	0.612662	-1.427892	-0.335783
C	4.619950	-3.344541	-1.695372
C	-6.537056	-3.231095	1.091704
C	-4.359451	5.816511	-1.527281
C	3.832041	2.298039	1.465726
N	-2.277115	-1.247059	0.026910
C	4.887670	-4.899210	-1.784158
C	2.712654	3.222735	2.025399
N	0.697538	1.427611	-1.064273
C	2.610464	-0.066049	-0.647705
C	-0.883115	-3.271631	0.236507
C	-4.199372	0.257457	-0.209835
C	-0.680533	3.431562	-1.299529
C	1.760702	-4.960586	0.263392
C	-3.635758	-4.676678	0.708991
C	-5.700621	2.896367	-0.975680
C	2.055844	4.932108	-0.932335
C	1.967739	-1.293544	-0.459424
C	-2.114611	-2.590590	0.252592
C	-3.553778	1.438072	-0.601844
C	0.548623	2.785872	-1.179193
O	5.234441	-5.289273	-2.921962
O	3.003642	4.434298	2.098166
C	2.633255	-2.586393	-0.252326
C	-3.401501	-3.215048	0.474228
C	-4.218583	2.677669	-0.938509
C	1.838074	3.450933	-1.017267
O	4.757055	-5.567674	-0.718918
O	1.594980	2.689182	2.333879
C	1.630985	-3.491724	-0.009978
C	-4.353446	-2.212865	0.358425
C	-3.220015	3.584445	-1.262780
C	2.745224	2.460024	-0.747302
C	0.375739	-2.744018	-0.042665
C	-3.619619	-0.987701	0.053799
C	-1.956387	2.866100	-1.125691
C	2.022873	1.194206	-0.832103
N	-2.194332	1.583707	-0.727647

H	4.639230	-1.915697	-0.034229
H	4.386768	-3.612257	0.401824
H	-6.347413	-1.515535	-0.069504
H	-2.470952	5.340076	-2.258521
H	4.832280	1.939107	-0.453859
H	4.426596	3.634993	-0.124982
H	5.571093	-2.853845	-1.946224
H	3.925601	-3.074013	-2.500159
H	4.761535	2.491182	2.017636
H	3.561156	1.244438	1.588532
H	3.694132	-0.082232	-0.597780
H	-0.910758	-4.332635	0.464090
H	-5.279023	0.314496	-0.116451
H	-0.645393	4.504954	-1.454443
H	-6.091796	-4.030837	1.674586
H	-7.623534	-3.192897	1.068121
H	-5.244429	5.557832	-0.955112
H	-4.318807	6.826115	-1.928819
H	-3.710714	-4.920124	1.779413
H	-2.824600	-5.284678	0.295622
H	-4.573710	-5.000562	0.241439
H	-6.243505	1.953859	-1.105951
H	-5.974768	3.560332	-1.805063
H	-6.077558	3.364757	-0.054099
H	1.544728	-5.190475	1.318483
H	1.042478	-5.534786	-0.338569
H	2.771435	-5.314425	0.020899
H	1.987437	5.259802	0.112259
H	3.057980	5.200412	-1.287342
H	1.328063	5.488233	-1.535906
C	0.530820	-0.293476	2.627379
H	1.520296	-0.639044	2.303521
H	0.591139	0.065557	3.662634
H	-0.166710	-1.133704	2.567458
H	0.701546	1.540380	1.877409

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B3LYP-D3 SCF energy:	-2072.96724541 a.u.
B3LYP-D3 enthalpy:	-2072.297071 a.u.
B3LYP-D3 free energy:	-2072.422411 a.u.
B3LYP-D3 SCF energy in water:	-2073.72584068 a.u.
B3LYP-D3 enthalpy in water:	-2073.055666 a.u.
B3LYP-D3 free energy in water:	-2073.181006 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.791105	0.677508	1.911144
Fe	-0.841573	-0.054747	-0.309918
C	4.029455	-2.881628	0.059484
C	-5.871919	-2.520596	0.002662
C	-3.323659	4.883229	-1.277017
C	4.206350	2.427894	-0.463870
N	0.526054	-1.512321	-0.127701
C	4.661485	-2.950285	-1.347078
C	-6.630596	-3.414562	0.658672
C	-4.338209	5.703000	-0.955198
C	4.596422	2.278941	1.027402
N	-2.326544	-1.412555	-0.137391
C	4.457384	-4.308822	-2.027233
C	3.922040	3.368650	1.865947
N	0.632559	1.277149	-0.649601
C	2.572599	-0.194080	-0.386086
C	-0.964234	-3.419771	0.239520
C	-4.267841	0.054032	-0.432185
C	-0.715405	3.308676	-0.897332
C	1.658591	-5.056161	0.475563
C	-3.698926	-4.863976	0.442819
C	-5.717581	2.733015	-1.017525
C	2.031601	4.769894	-0.892783
C	1.893505	-1.387082	-0.181504
C	-2.183539	-2.755677	0.116724
C	-3.594673	1.251885	-0.641389
C	0.493756	2.638769	-0.793300
O	4.430962	-4.334462	-3.292665
O	4.180985	4.573068	1.610223
C	2.542794	-2.670524	0.042702
C	-3.472913	-3.399508	0.222755
C	-4.240602	2.520442	-0.881359
C	1.794123	3.292150	-0.793351
O	4.373707	-5.358380	-1.344769
O	3.107746	3.024808	2.769089
C	1.540271	-3.584112	0.217716
C	-4.419075	-2.413312	0.029854
C	-3.230819	3.454503	-1.004714
C	2.723941	2.296844	-0.659281
C	0.289103	-2.846292	0.114208
C	-3.679250	-1.181822	-0.200713
C	-1.980312	2.726137	-0.852843
C	1.984069	1.050113	-0.571741
N	-2.222749	1.395392	-0.629370

H	4.504318	-2.069846	0.626217
H	4.268390	-3.812607	0.581442
H	-6.385945	-1.789387	-0.621916
H	-2.469553	5.319746	-1.794645
H	4.743753	1.678561	-1.060349
H	4.542079	3.410730	-0.807650
H	5.747596	-2.798685	-1.268813
H	4.273883	-2.160727	-1.999360
H	5.684989	2.379790	1.129817
H	4.299148	1.296131	1.407306
H	3.655280	-0.232420	-0.375164
H	-0.996975	-4.483384	0.445065
H	-5.350761	0.094298	-0.428300
H	-0.668883	4.384477	-1.017110
H	-6.208617	-4.148908	1.337536
H	-7.711617	-3.417173	0.548256
H	-5.206233	5.364694	-0.398018
H	-4.311156	6.755668	-1.223025
H	-3.774312	-5.114356	1.510512
H	-2.884423	-5.465103	0.025523
H	-4.633036	-5.184710	-0.031271
H	-6.217712	1.842548	-1.413345
H	-5.925010	3.566664	-1.697511
H	-6.193762	2.973561	-0.056242
H	1.502728	-5.293028	1.537768
H	0.908606	-5.617692	-0.094238
H	2.640357	-5.424001	0.167477
H	2.952033	5.045591	-0.371879
H	2.099346	5.099830	-1.939369
H	1.219824	5.336083	-0.423439
C	0.499554	0.928546	2.498202
H	1.004651	1.791699	2.056609
H	0.407811	1.078817	3.581099
H	1.097034	0.036810	2.303217
H	-1.265052	1.519061	1.820502

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B3LYP-D3 SCF energy:	-2073.54281401 a.u.
B3LYP-D3 enthalpy:	-2072.857744 a.u.
B3LYP-D3 free energy:	-2072.987639 a.u.
B3LYP-D3 SCF energy in solution:	-2074.19608538 a.u.
B3LYP-D3 enthalpy in solution:	-2073.511015 a.u.
B3LYP-D3 free energy in solution:	-2073.640910 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-0.970965	0.353714	1.979195
Fe	-1.043479	0.046923	0.189194
C	3.847130	-2.875681	0.105492
C	-6.069339	-2.534032	-0.137583
C	-3.513364	4.905638	-1.331573
C	4.049660	2.444796	-0.583716
N	0.360786	-1.502851	-0.006246
C	4.392270	-2.856043	-1.345654
C	-6.840515	-3.439613	0.484050
C	-4.521504	5.731011	-1.009706
C	4.572102	2.426173	0.875634
N	-2.533858	-1.409453	-0.075370
C	5.900561	-2.932385	-1.391759
C	6.081101	2.393396	0.948554
N	0.469426	1.337193	-0.484678
C	2.397855	-0.153250	-0.214865
C	-1.156888	-3.414640	0.258258
C	-4.453830	0.076516	-0.411940
C	-0.898306	3.340834	-0.862528
C	1.468382	-5.058281	0.461374
C	-3.905143	-4.885370	0.289232
C	-5.903385	2.757299	-1.061873
C	1.843211	4.782454	-1.056864
C	1.723619	-1.360361	-0.036480
C	-2.383375	-2.760546	0.123908
C	-3.786391	1.285865	-0.601332
C	0.319652	2.682575	-0.721070
O	6.640603	-2.089946	-1.848582
C	2.364664	-2.652395	0.141607
C	-3.676270	-3.412140	0.146522
C	-4.430388	2.551692	-0.887093
C	1.622487	3.320630	-0.812367
O	6.748043	1.525161	1.465570
C	1.358831	-3.575376	0.275480
C	-4.618089	-2.419898	-0.042317
C	-3.420578	3.485008	-1.012595
C	2.555261	2.331296	-0.632787
C	0.108180	-2.840823	0.183401
C	-3.877988	-1.173128	-0.189199
C	-2.169112	2.765987	-0.811216
C	1.818157	1.095506	-0.427996
N	-2.421924	1.444809	-0.558867
H	4.359331	-2.100515	0.689827
H	4.107653	-3.831845	0.568340

H	-6.561191	-1.801472	-0.777270
H	-2.670936	5.323304	-1.882710
H	4.509708	1.617429	-1.138982
H	4.386823	3.365445	-1.068398
H	4.092625	-1.939739	-1.858484
H	3.973603	-3.707655	-1.894690
H	4.197665	1.550203	1.409605
H	4.209787	3.321786	1.394289
H	3.481412	-0.192832	-0.201365
H	-1.190997	-4.486616	0.419093
H	-5.536379	0.112076	-0.447276
H	-0.850843	4.409662	-1.038999
H	-6.434602	-4.173053	1.173705
H	-7.916436	-3.452748	0.336113
H	-5.374483	5.405007	-0.422769
H	-4.505690	6.775177	-1.308317
H	-4.005277	-5.185131	1.341389
H	-3.080163	-5.465381	-0.137578
H	-4.826771	-5.182820	-0.221811
H	-6.389356	1.865485	-1.471245
H	-6.097160	3.591401	-1.744339
H	-6.400147	2.992448	-0.110686
H	0.943321	-5.389141	1.366222
H	1.026453	-5.601138	-0.384143
H	2.511361	-5.376281	0.548525
H	2.908442	5.023160	-1.118618
H	1.374053	5.107195	-1.994200
H	1.411683	5.392289	-0.252822
C	0.186487	0.486219	2.757689
H	0.790069	1.344965	2.424798
H	-0.090223	0.639679	3.810052
H	0.815565	-0.414664	2.687660
O	6.633317	3.473874	0.336267
H	7.600322	3.362813	0.407542
O	6.358844	-4.081064	-0.827692
H	7.332720	-4.038150	-0.874990

⁶16

B3LYP-D3 SCF energy:	-4645.04678136 a.u.
B3LYP-D3 enthalpy:	-4644.360180 a.u.
B3LYP-D3 free energy:	-4644.494735 a.u.
B3LYP-D3 SCF energy in solution:	-4648.50858780 a.u.
B3LYP-D3 enthalpy in solution:	-4647.821986 a.u.
B3LYP-D3 free energy in solution:	-4647.956541 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-1.019680	0.344685	1.807627
Fe	-1.033372	0.005623	-0.044015
C	3.873329	-2.905255	0.152812
C	-6.072305	-2.556074	-0.126161
C	-3.509313	4.914270	-1.361237
C	4.086148	2.483623	-0.508699
N	0.407051	-1.519146	0.133765
C	4.377274	-2.876642	-1.315195
C	-6.864251	-3.498682	0.414194
C	-4.542711	5.746441	-1.143781
C	4.598243	2.506218	0.955183
N	-2.561197	-1.424880	0.023023
C	5.869728	-3.068883	-1.409329
C	6.101739	2.581186	1.054667
N	0.520411	1.381590	-0.390282
C	2.421448	-0.141448	-0.108928
C	-1.146253	-3.407679	0.351541
C	-4.451044	0.081240	-0.379779
C	-0.880475	3.350333	-0.823112
C	1.495685	-5.074789	0.511246
C	-3.908649	-4.899407	0.330968
C	-5.901225	2.769592	-1.104261
C	1.883108	4.800926	-1.037418
C	1.755503	-1.361392	0.079253
C	-2.386900	-2.765051	0.210177
C	-3.791554	1.303790	-0.570207
C	0.351020	2.706031	-0.657444
O	6.680179	-2.262664	-1.812691
C	2.395775	-2.665530	0.229608
C	-3.681947	-3.424239	0.203982
C	-4.432401	2.568192	-0.891977
C	1.660509	3.344701	-0.761751
O	6.828747	1.788158	1.613386
C	1.387927	-3.587539	0.360543
C	-4.627525	-2.435321	0.000056
C	-3.420838	3.503462	-1.014956
C	2.593308	2.358643	-0.561967
C	0.132993	-2.844164	0.294297
C	-3.887864	-1.177701	-0.128830
C	-2.165444	2.787240	-0.776301
C	1.853234	1.120088	-0.331904
N	-2.441103	1.486523	-0.501495
H	4.414866	-2.141608	0.726690

H	4.135278	-3.871865	0.595143
H	-6.552771	-1.784341	-0.728366
H	-2.627471	5.329361	-1.850343
H	4.558219	1.645095	-1.036825
H	4.420427	3.395927	-1.012387
H	4.125635	-1.924580	-1.786390
H	3.877429	-3.676850	-1.872806
H	4.270456	1.612350	1.490040
H	4.170604	3.380382	1.461434
H	3.506663	-0.184014	-0.108548
H	-1.180275	-4.483685	0.492644
H	-5.533320	0.113330	-0.446579
H	-0.830173	4.415131	-1.028130
H	-6.481210	-4.278183	1.065287
H	-7.936088	-3.497387	0.233930
H	-5.442459	5.434287	-0.622953
H	-4.501566	6.783447	-1.466727
H	-4.074213	-5.206807	1.373969
H	-3.051875	-5.469835	-0.043671
H	-4.793219	-5.205348	-0.239298
H	-6.382450	1.853812	-1.464038
H	-6.080834	3.558822	-1.843279
H	-6.417503	3.067973	-0.180135
H	0.966615	-5.428309	1.406240
H	1.053091	-5.596600	-0.347816
H	2.538407	-5.399304	0.592576
H	2.948814	5.040061	-1.116128
H	1.403241	5.107576	-1.976027
H	1.460408	5.430616	-0.242704
C	0.075042	0.464691	2.651196
H	0.733487	1.300331	2.351720
H	-0.251606	0.648787	3.689756
H	0.696077	-0.449073	2.648774
Br	-0.903352	-0.509028	-2.768755
O	6.249116	-4.296960	-0.950976
H	7.221742	-4.313189	-1.023747
O	6.595781	3.681088	0.418165
H	7.564784	3.627153	0.516802

Br⁻

B3LYP-D3 SCF energy:

-2571.46438018 a.u.

B3LYP-D3 enthalpy:

-2571.462020 a.u.

B3LYP-D3 free energy:

-2571.480556 a.u.

B3LYP-D3 SCF energy in solution:

-2574.32158865 a.u.

B3LYP-D3 enthalpy in solution:	-2574.319228 a.u.
B3LYP-D3 free energy in solution:	-2574.337764 a.u.

Cartesian coordinates

ATOM	X	Y	Z
Br	0.000000	0.000000	0.000000

Cl⁻

B3LYP-D3 SCF energy:	-460.24873168 a.u.
B3LYP-D3 enthalpy:	-460.246371 a.u.
B3LYP-D3 free energy:	-460.263754 a.u.
B3LYP-D3 SCF energy in solution:	-460.39344412 a.u.
B3LYP-D3 enthalpy in solution:	-460.391083 a.u.
B3LYP-D3 free energy in solution:	-460.408466 a.u.

Cartesian coordinates

ATOM	X	Y	Z
Cl	3.713312	-0.136612	0.742523

MeO⁻

B3LYP-D3 SCF energy:	-115.06987678 a.u.
B3LYP-D3 enthalpy:	-115.031459 a.u.
B3LYP-D3 free energy:	-115.057523 a.u.
B3LYP-D3 SCF energy in water:	-115.26715174 a.u.
B3LYP-D3 enthalpy in water:	-115.228734 a.u.
B3LYP-D3 free energy in water:	-115.254798 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-4.812146	-0.412329	9.856003
C	-4.548848	-1.374358	10.703180
H	-3.516276	-1.905842	10.616397
H	-4.546442	-1.112165	11.837843
H	-5.254525	-2.301058	10.710172

MeOH

B3LYP-D3 SCF energy:	-115.71332646 a.u.
B3LYP-D3 enthalpy:	-115.657670 a.u.
B3LYP-D3 free energy:	-115.684615 a.u.

B3LYP-D3 SCF energy in water:	-115.77376088 a.u.
B3LYP-D3 enthalpy in water:	-115.718104 a.u.
B3LYP-D3 free energy in water:	-115.745049 a.u.

Cartesian coordinates

ATOM	X	Y	Z
O	-4.839501	-0.433610	9.846744
C	-4.511518	-1.448064	10.782582
H	-3.518229	-1.890487	10.602893
H	-4.549859	-1.095650	11.826133
H	-5.259130	-2.237941	10.665243
H	-4.185805	0.275751	9.936041

TSa

B3LYP-D3 SCF energy:	-746.10942838 a.u.
B3LYP-D3 enthalpy:	-745.851161 a.u.
B3LYP-D3 free energy:	-745.913122 a.u.
B3LYP-D3 SCF energy in solution:	-746.35236265 a.u.
B3LYP-D3 enthalpy in solution:	-746.094095 a.u.
B3LYP-D3 free energy in solution:	-746.156056 a.u.
Imaginary frequency:	-49.5857 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
C	0.541273	-1.147885	1.606371
C	0.616769	-2.238007	2.628318
H	-0.386147	-2.631926	2.845935
H	1.211245	-3.080628	2.245258
H	1.072344	-1.863156	3.545734
C	1.134907	0.161171	1.934912
O	1.658326	0.321724	3.044163
N	1.079096	1.205049	1.022691
C	-0.074707	-1.572700	0.315853
O	0.544147	-2.076171	-0.598398
C	1.679912	2.487498	1.391971
H	2.611081	2.655949	0.835343
H	0.983526	3.299483	1.156322
H	1.895650	2.475796	2.459453
C	0.594055	1.124178	-0.322923
C	1.468686	0.795576	-1.364034
C	-0.735587	1.454575	-0.604406
C	1.009973	0.779817	-2.680223
H	2.494744	0.531304	-1.127564
C	-1.191809	1.442106	-1.923797

H	-1.401188	1.704280	0.216028
C	-0.319476	1.105160	-2.962202
H	1.687494	0.508251	-3.484531
H	-2.226201	1.695655	-2.139466
H	-0.675142	1.095187	-3.988908
O	-1.416726	-1.440550	0.336288
C	-2.091809	-1.888186	-0.854861
H	-1.891187	-2.948201	-1.033168
H	-3.153127	-1.722446	-0.666903
H	-1.755642	-1.305616	-1.716039

TSb

B3LYP-D3 SCF energy:	-746.10544834 a.u.
B3LYP-D3 enthalpy:	-745.846910 a.u.
B3LYP-D3 free energy:	-745.907017 a.u.
B3LYP-D3 SCF energy in solution:	-746.34906049 a.u.
B3LYP-D3 enthalpy in solution:	-746.090522 a.u.
B3LYP-D3 free energy in solution:	-746.150629 a.u.
Imaginary frequency:	-30.4849 cm-1

Cartesian coordinates

ATOM	X	Y	Z
C	-0.531675	-1.027845	0.635933
C	-0.015375	-1.623758	-0.638418
H	-0.260936	-0.996671	-1.502756
H	1.077356	-1.721602	-0.634895
H	-0.440286	-2.619438	-0.777801
C	-0.245746	0.321525	1.177965
O	-0.459877	0.571859	2.365943
N	0.177252	1.346550	0.325176
C	-1.335437	-1.953192	1.478739
O	-1.111955	-3.152717	1.522670
C	0.240534	2.678662	0.940926
H	1.105454	2.773177	1.610631
H	0.320188	3.421278	0.143760
H	-0.663622	2.851722	1.526470
C	1.050792	1.162059	-0.794705
C	2.327788	0.617085	-0.616348
C	0.647160	1.586096	-2.065752
C	3.180299	0.461672	-1.710519
H	2.637434	0.310598	0.379170
C	1.505758	1.439817	-3.155569
H	-0.344487	2.012345	-2.187480
C	2.770808	0.871357	-2.981554

H	4.165860	0.027012	-1.568322
H	1.184300	1.762179	-4.142086
H	3.435542	0.752004	-3.832423
O	-2.358331	-1.367865	2.123588
C	-3.126754	-2.240252	2.964808
H	-2.496168	-2.668331	3.749530
H	-3.905473	-1.612750	3.399346
H	-3.565924	-3.055290	2.381189

TS1¹

B3LYP-D3 SCF energy:	-5389.87918649 a.u.
B3LYP-D3 enthalpy:	-5388.959312 a.u.
B3LYP-D3 free energy:	-5389.123838 a.u.
B3LYP-D3 SCF energy in solution:	-5393.82252356 a.u.
B3LYP-D3 enthalpy in solution:	-5392.902649 a.u.
B3LYP-D3 free energy in solution:	-5393.067175 a.u.
Imaginary frequency:	-389.3166 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
O	-1.003180	0.442298	1.732999
Fe	-0.846369	0.027171	-0.083356
C	3.622003	-3.439607	0.634452
C	-6.117297	-1.912585	-0.361790
C	-2.681360	5.185794	-1.301851
C	4.508982	1.940746	-0.483988
N	0.346984	-1.592257	0.115570
C	4.103945	-4.445875	-0.447494
C	-6.958479	-2.902234	-0.726477
C	-3.648750	6.123098	-1.229090
C	5.160787	2.626392	0.749472
N	-2.491721	-1.183658	-0.114145
C	4.627112	-5.828137	0.109682
C	6.108734	3.843433	0.415447
N	0.799733	1.159421	-0.366294
C	2.541794	-0.523362	-0.052239
C	-1.377574	-3.315437	0.375522
C	-4.218558	0.492066	-0.566316
C	-0.300456	3.324841	-0.703666
C	1.006370	-5.201708	0.981453
C	-4.260575	-4.473882	0.273140
C	-5.306709	3.310370	-1.303095

C	2.588563	4.441545	-0.865529
C	1.719960	-1.626387	0.160235
C	-2.507123	-2.537259	0.108993
C	-3.407010	1.619538	-0.677026
C	0.817381	2.520774	-0.564026
O	5.367475	-6.464308	-0.677041
O	5.953448	4.392145	-0.713310
C	2.198766	-2.972028	0.488797
C	-3.854742	-3.049409	0.045253
C	-3.887273	2.944279	-0.991980
C	2.186563	3.013514	-0.641991
O	4.212614	-6.166209	1.255418
O	6.896970	4.160121	1.338670
C	1.077275	-3.742195	0.638407
C	-4.675353	-1.963436	-0.214798
C	-2.774518	3.768596	-1.009221
C	3.005025	1.930166	-0.484468
C	-0.064331	-2.875947	0.384440
C	-3.793457	-0.804244	-0.301541
C	-1.632365	2.902440	-0.722658
C	2.115989	0.778540	-0.297515
N	-2.044001	1.623194	-0.518540
H	4.297451	-2.577031	0.676740
H	3.718146	-3.969892	1.590330
H	-6.567945	-0.939946	-0.155727
H	-1.695534	5.525664	-1.620757
H	4.889819	0.918151	-0.596779
H	4.856421	2.511631	-1.354369
H	4.887774	-4.011544	-1.079548
H	3.276245	-4.692837	-1.126609
H	5.728921	1.907303	1.351669
H	4.377080	3.017360	1.413058
H	3.611837	-0.688284	0.002550
H	-1.531959	-4.373463	0.560789
H	-5.283655	0.643262	-0.707841
H	-0.109035	4.382813	-0.849172
H	-6.610220	-3.893458	-0.999295
H	-8.031486	-2.730630	-0.779239
H	-4.652235	5.905145	-0.877079
H	-3.441988	7.156042	-1.500189
H	-5.247933	-4.525970	0.748904
H	-3.545991	-4.996101	0.918473
H	-4.325498	-5.046715	-0.664807

H	-5.871905	2.447573	-1.673624
H	-5.344673	4.091202	-2.073100
H	-5.846145	3.701194	-0.425846
H	0.399430	-5.367277	1.884154
H	0.528246	-5.781380	0.175937
H	2.006583	-5.620605	1.151230
H	3.680671	4.548759	-0.881297
H	2.186965	4.823247	-1.816796
H	2.192999	5.094218	-0.072915
C	0.031949	0.095578	2.590509
H	1.015626	0.478678	2.264261
H	-0.164823	0.521426	3.594790
H	0.144075	-0.999921	2.718745
C	-1.722333	0.129767	-5.006804
C	-2.218432	1.562943	-5.207139
H	-1.365984	2.240690	-5.280850
H	-2.792445	1.636758	-6.139182
H	-2.841174	1.858039	-4.361317
C	-0.756377	-0.276466	-6.117222
O	-0.680148	0.435555	-7.125356
N	0.013073	-1.412437	-6.036914
C	-2.872252	-0.829884	-4.851811
O	-3.063528	-1.822222	-5.539091
C	0.876317	-1.652419	-7.194837
H	0.285063	-1.635458	-8.116095
H	1.652875	-0.881778	-7.284340
H	1.346715	-2.629439	-7.071059
C	0.233019	-2.266682	-4.896224
C	1.387438	-2.082505	-4.125454
C	-0.635289	-3.322255	-4.614494
C	1.654733	-2.929400	-3.054214
H	2.038651	-1.240839	-4.340438
C	-0.366958	-4.163221	-3.531164
H	-1.522005	-3.450624	-5.221443
C	0.773408	-3.971299	-2.752557
H	2.525484	-2.764046	-2.429296
H	-1.059360	-4.966955	-3.291311
H	0.976178	-4.610065	-1.900896
O	-3.733688	-0.427610	-3.898862
C	-4.808572	-1.325390	-3.607906
H	-5.367852	-1.572473	-4.516745
H	-4.421895	-2.241522	-3.153330
H	-5.433833	-0.806949	-2.884108

Br -0.725245 0.255229 -3.093993

TS1³

B3LYP-D3 SCF energy:	-5389.88281392 a.u.
B3LYP-D3 enthalpy:	-5388.963429 a.u.
B3LYP-D3 free energy:	-5389.131019 a.u.
B3LYP-D3 SCF energy in solution:	-5393.83098842 a.u.
B3LYP-D3 enthalpy in solution:	-5392.911603 a.u.
B3LYP-D3 free energy in solution:	-5393.079193 a.u.
Imaginary frequency:	-108.0859 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
O	-1.024998	0.335420	1.974977
Fe	-0.800372	0.011894	0.068112
C	3.659708	-3.462459	0.774578
C	-6.055452	-1.959872	-0.460641
C	-2.611100	5.144296	-1.289797
C	4.564154	1.899829	-0.389587
N	0.391761	-1.606984	0.246552
C	4.169391	-4.410373	-0.346587
C	-6.894832	-2.954364	-0.820217
C	-3.579817	6.079886	-1.229909
C	5.227142	2.639168	0.806101
N	-2.447039	-1.217022	-0.084007
C	4.657510	-5.830650	0.144273
C	6.183266	3.830052	0.408477
N	0.850751	1.137205	-0.249951
C	2.589388	-0.547408	0.092101
C	-1.331858	-3.342727	0.424681
C	-4.156864	0.457073	-0.579220
C	-0.241780	3.297730	-0.627782
C	1.039107	-5.235790	1.047150
C	-4.207148	-4.519773	0.206641
C	-5.225240	3.258616	-1.362549
C	2.652847	4.397532	-0.819702
C	1.760823	-1.644559	0.307268
C	-2.461421	-2.571089	0.125108
C	-3.345195	1.584465	-0.637377
C	0.874084	2.491471	-0.475894
O	5.385751	-6.442551	-0.672505

O	6.015632	4.333581	-0.739720
C	2.236569	-2.996829	0.624338
C	-3.799096	-3.091865	0.006067
C	-3.818344	2.904743	-0.986573
C	2.243960	2.976576	-0.564680
O	4.235662	-6.215422	1.272239
O	6.989041	4.176685	1.305343
C	1.114580	-3.768582	0.741055
C	-4.619300	-2.007184	-0.274643
C	-2.708199	3.730153	-0.977832
C	3.059700	1.893550	-0.382082
C	-0.025275	-2.896795	0.482799
C	-3.739112	-0.844761	-0.317050
C	-1.572520	2.873616	-0.643100
C	2.166221	0.751273	-0.173563
N	-1.987382	1.597262	-0.418883
H	4.326597	-2.597682	0.872631
H	3.742121	-4.038571	1.704694
H	-6.507720	-0.980928	-0.291097
H	-1.624221	5.479949	-1.609726
H	4.941715	0.872220	-0.457820
H	4.907463	2.428931	-1.287769
H	4.983469	-3.951257	-0.920442
H	3.367379	-4.603910	-1.072195
H	5.791291	1.945445	1.440796
H	4.449490	3.069071	1.452555
H	3.658388	-0.715287	0.152893
H	-1.484004	-4.404398	0.590271
H	-5.214374	0.608385	-0.767599
H	-0.049084	4.352461	-0.793122
H	-6.549168	-3.955454	-1.057305
H	-7.964900	-2.776287	-0.902604
H	-4.582671	5.862435	-0.875328
H	-3.375939	7.110256	-1.512865
H	-5.190338	-4.579395	0.690838
H	-3.489107	-5.059559	0.832855
H	-4.285070	-5.070227	-0.743669
H	-5.755138	2.396819	-1.784371
H	-5.235304	4.057902	-2.113862
H	-5.816944	3.617188	-0.505458
H	0.432449	-5.422905	1.945787
H	0.558301	-5.791284	0.226472
H	2.038475	-5.662032	1.202928

H	3.745095	4.495947	-0.862109
H	2.232243	4.766828	-1.767495
H	2.280051	5.065554	-0.029001
C	0.049435	0.108312	2.812519
H	0.975859	0.626035	2.486499
H	-0.160612	0.466816	3.845052
H	0.318802	-0.966350	2.905718
C	-1.852711	0.095640	-4.914689
C	-2.251596	1.566549	-5.087252
H	-1.353664	2.189271	-5.089541
H	-2.772873	1.706536	-6.039744
H	-2.890160	1.873963	-4.258288
C	-0.925327	-0.337221	-6.068054
O	-1.073973	0.230166	-7.155416
N	0.047503	-1.290287	-5.930558
C	-3.057657	-0.817850	-4.838755
O	-3.181803	-1.874635	-5.435695
C	0.849500	-1.529255	-7.133415
H	0.246922	-2.002775	-7.919705
H	1.232669	-0.584594	-7.530242
H	1.678353	-2.185385	-6.864029
C	0.301220	-2.159807	-4.809431
C	1.470720	-1.976177	-4.062605
C	-0.569803	-3.207505	-4.509570
C	1.748391	-2.816728	-2.989043
H	2.120478	-1.136752	-4.292505
C	-0.288869	-4.041761	-3.424908
H	-1.471924	-3.328440	-5.095735
C	0.864523	-3.850712	-2.665923
H	2.627909	-2.651301	-2.376049
H	-0.984373	-4.835891	-3.164284
H	1.074497	-4.481539	-1.810386
O	-4.008471	-0.319894	-4.027300
C	-5.072034	-1.217602	-3.690210
H	-5.599354	-1.553854	-4.589410
H	-4.678925	-2.079543	-3.146258
H	-5.732304	-0.654167	-3.032825
Br	-1.021118	0.026195	-3.004604

TS1⁵

B3LYP-D3 SCF energy:

-5389.88687272 a.u.

B3LYP-D3 enthalpy:	-5388.968718 a.u.
B3LYP-D3 free energy:	-5389.139607 a.u.
B3LYP-D3 SCF energy in solution:	-5393.83799414 a.u.
B3LYP-D3 enthalpy in solution:	-5392.919839 a.u.
B3LYP-D3 free energy in solution:	-5393.090728 a.u.
Imaginary frequency:	-441.5159 cm-1

Cartesian coordinates

ATOM	X	Y	Z
O	-0.678166	0.334812	2.161600
Fe	-0.755084	0.132334	0.296951
C	3.904397	-3.234804	0.565572
C	-5.884901	-2.106608	-0.692254
C	-2.762275	5.197382	-1.261139
C	4.566492	2.263065	-0.211795
N	0.553811	-1.522109	0.193598
C	4.415813	-4.169883	-0.565468
C	-6.624382	-3.111963	-1.202821
C	-3.768433	6.094105	-1.243597
C	5.153137	2.911898	1.073851
N	-2.368949	-1.196248	-0.019105
C	4.969718	-5.566327	-0.079823
C	6.016081	4.212975	0.838170
N	0.896356	1.358794	-0.160755
C	2.677743	-0.304661	0.092528
C	-1.121195	-3.295441	0.328949
C	-4.126933	0.433088	-0.525166
C	-0.315118	3.449630	-0.537565
C	1.376836	-5.140927	0.784112
C	-3.913961	-4.603925	-0.135201
C	-5.306899	3.228304	-1.309208
C	2.560931	4.693984	-0.630580
C	1.918930	-1.476221	0.230086
C	-2.293389	-2.560937	0.078667
C	-3.374149	1.611934	-0.582200
C	0.853206	2.708116	-0.363947
O	5.696981	-6.157399	-0.912542
O	5.878158	4.797346	-0.274494
C	2.460976	-2.825496	0.457737
C	-3.595871	-3.140498	-0.152820
C	-3.889801	2.915666	-0.935962
C	2.207731	3.251310	-0.419850
O	4.596284	-5.957770	1.063500

O	6.730316	4.544556	1.814592
C	1.374381	-3.657783	0.555834
C	-4.463762	-2.084466	-0.398980
C	-2.806900	3.784066	-0.932544
C	3.065201	2.195261	-0.252927
C	0.188666	-2.826671	0.375906
C	-3.659953	-0.867886	-0.305719
C	-1.637545	2.977718	-0.585259
C	2.215716	1.003636	-0.095126
N	-2.024396	1.692862	-0.357515
H	4.538987	-2.343429	0.636402
H	4.038738	-3.801725	1.495944
H	-6.412383	-1.176143	-0.473856
H	-1.780737	5.568597	-1.556654
H	4.986746	1.260448	-0.358473
H	4.917815	2.885858	-1.043772
H	5.195335	-3.683286	-1.163305
H	3.600276	-4.392455	-1.268365
H	5.768894	2.197224	1.633255
H	4.338483	3.197276	1.753591
H	3.754525	-0.426743	0.136771
H	-1.236665	-4.370077	0.428790
H	-5.188621	0.536294	-0.722369
H	-0.170802	4.513210	-0.699851
H	-6.192664	-4.059885	-1.506398
H	-7.694224	-2.991173	-1.358786
H	-4.774431	5.842699	-0.922851
H	-3.594472	7.128279	-1.532119
H	-4.928443	-4.782325	0.242879
H	-3.213927	-5.160698	0.496999
H	-3.858782	-5.044257	-1.142213
H	-5.842462	2.332959	-1.643442
H	-5.341259	3.962987	-2.123623
H	-5.879633	3.654278	-0.470568
H	0.729736	-5.412550	1.631150
H	0.988256	-5.680344	-0.093509
H	2.390513	-5.513434	0.980447
H	3.646067	4.850530	-0.578776
H	2.202414	5.050443	-1.608545
H	2.086384	5.331804	0.129853
C	0.474503	0.299443	2.935547
H	1.202937	1.076218	2.639652
H	0.235179	0.463624	4.004627

H	0.998450	-0.671673	2.862605
C	-1.501228	0.044760	-4.890956
C	-1.470791	1.562437	-5.014336
H	-0.437791	1.913205	-4.997142
H	-1.918426	1.875884	-5.967870
H	-2.017364	2.015836	-4.186908
C	-0.609205	-0.627213	-5.908198
O	-0.136334	0.053434	-6.827878
N	-0.336417	-1.982878	-5.871255
C	-2.870378	-0.523755	-4.781770
O	-3.301009	-1.505167	-5.374561
C	0.505602	-2.475302	-6.961768
H	0.156077	-2.067002	-7.913390
H	1.556200	-2.178550	-6.834039
H	0.443610	-3.566318	-6.975267
C	-0.456248	-2.887513	-4.754835
C	0.615668	-3.017642	-3.863619
C	-1.566994	-3.724843	-4.634382
C	0.565671	-3.956022	-2.836432
H	1.464850	-2.348952	-3.954909
C	-1.618484	-4.660583	-3.597685
H	-2.388526	-3.606041	-5.328071
C	-0.556969	-4.776635	-2.700124
H	1.380412	-4.017728	-2.122551
H	-2.496626	-5.294689	-3.490073
H	-0.605049	-5.492218	-1.884257
O	-3.667240	0.219832	-3.972716
C	-4.976717	-0.307049	-3.769198
H	-5.503296	-0.433919	-4.722471
H	-4.932897	-1.269628	-3.253000
H	-5.487275	0.422348	-3.139522
Br	-0.586923	-0.180560	-2.782291

TS2

B3LYP-D3 SCF energy:	-746.10039256 a.u.
B3LYP-D3 enthalpy:	-745.842373 a.u.
B3LYP-D3 free energy:	-745.901638 a.u.
B3LYP-D3 SCF energy in solution:	-746.34379861 a.u.
B3LYP-D3 enthalpy in solution:	-746.085779 a.u.
B3LYP-D3 free energy in solution:	-746.145044 a.u.
Imaginary frequency:	-492.1011 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
C	1.111988	-0.679801	-0.624695
C	1.881378	-1.390890	-1.703973
H	1.363896	-2.308694	-1.992515
H	2.017901	-0.751741	-2.583907
H	2.880507	-1.655649	-1.335295
C	1.712306	0.620916	-0.132810
O	2.894733	0.760992	0.130917
N	0.771398	1.646586	-0.022457
C	0.472975	-1.554033	0.382689
O	0.174953	-2.720354	0.197700
C	1.073256	2.830257	0.764249
H	2.154452	2.972843	0.751024
H	0.574836	3.700883	0.329326
H	0.744814	2.706645	1.804718
C	-0.530183	1.261172	-0.357409
C	-0.550286	0.282793	-1.415740
C	-1.668488	1.570925	0.368641
C	-1.773676	-0.421960	-1.638263
H	0.079660	0.470045	-2.284424
C	-2.860384	0.878264	0.099950
H	-1.623741	2.293921	1.176991
C	-2.892446	-0.141412	-0.869374
H	-1.821240	-1.157498	-2.435334
H	-3.754873	1.112332	0.669539
H	-3.818581	-0.680621	-1.048316
O	0.177378	-0.880769	1.524299
C	-0.605756	-1.611667	2.478089
H	-0.090295	-2.526594	2.782748
H	-0.733496	-0.940258	3.328201
H	-1.576880	-1.874931	2.048535

TS3⁵

B3LYP-D3 SCF energy:	-3278.66376167 a.u.
B3LYP-D3 enthalpy:	-3277.745748 a.u.
B3LYP-D3 free energy:	-3277.913818 a.u.
B3LYP-D3 SCF energy in solution:	-3279.91026934 a.u.
B3LYP-D3 enthalpy in solution:	-3278.992256 a.u.
B3LYP-D3 free energy in solution:	-3279.160326 a.u.

Imaginary frequency:

-497.8236 cm⁻¹

Cartesian coordinates

ATOM	X	Y	Z
O	-0.728025	0.328360	2.169841
Fe	-0.819550	0.054830	0.305328
C	3.671497	-3.475104	0.926361
C	-6.119480	-1.909301	-0.068512
C	-2.609081	5.112276	-1.498514
C	4.593336	1.913915	-0.298257
N	0.411256	-1.655266	0.326117
C	4.216856	-4.493919	-0.112011
C	-6.979681	-2.897590	-0.390667
C	-3.563036	6.064021	-1.504310
C	5.228509	2.649956	0.915119
N	-2.505549	-1.197796	0.151660
C	4.741780	-5.852097	0.499307
C	6.154151	3.875802	0.549850
N	0.887065	1.194037	-0.143258
C	2.586754	-0.533501	0.215251
C	-1.347525	-3.342066	0.541231
C	-4.202146	0.506533	-0.324408
C	-0.234552	3.301475	-0.682346
C	1.061994	-5.271772	1.105649
C	-4.261003	-4.488135	0.478565
C	-5.251142	3.275032	-1.339801
C	2.698641	4.393328	-0.905525
C	1.774564	-1.662152	0.403505
C	-2.497321	-2.556487	0.335429
C	-3.388380	1.632207	-0.507749
C	0.901110	2.521299	-0.459226
O	5.547590	-6.480087	-0.227000
O	6.030714	4.359503	-0.611742
C	2.251960	-3.020493	0.714292
C	-3.849470	-3.060450	0.282588
C	-3.843802	2.929335	-0.958047
C	2.280445	2.992116	-0.570622
O	4.260989	-6.183697	1.620976
O	6.898116	4.259882	1.484021
C	1.130574	-3.804556	0.798924
C	-4.675942	-1.965219	0.055116
C	-2.716696	3.735254	-1.050782
C	3.089788	1.915093	-0.319674

C	-0.015835	-2.934629	0.549325
C	-3.796060	-0.802121	-0.031085
C	-1.581266	2.899093	-0.666743
C	2.187533	0.780820	-0.059686
N	-2.029706	1.658917	-0.328344
H	4.335290	-2.604305	0.985896
H	3.728271	-3.988535	1.894915
H	-6.555921	-0.926835	0.120777
H	-1.625889	5.398493	-1.872913
H	4.963465	0.882677	-0.354412
H	4.962985	2.438717	-1.187985
H	5.015794	-4.057451	-0.723155
H	3.421541	-4.774781	-0.815308
H	5.813343	1.960540	1.536066
H	4.437805	3.041180	1.570025
H	3.656491	-0.700910	0.281645
H	-1.510690	-4.405083	0.692018
H	-5.265424	0.657953	-0.480542
H	-0.041466	4.339943	-0.933238
H	-6.651965	-3.900469	-0.644119
H	-8.050740	-2.711044	-0.429783
H	-4.560565	5.895701	-1.110195
H	-3.352661	7.059656	-1.888394
H	-5.212753	-4.548990	1.021926
H	-3.511043	-5.047929	1.047125
H	-4.403372	-5.016405	-0.476545
H	-5.808322	2.383594	-1.649061
H	-5.262546	3.984770	-2.176218
H	-5.812389	3.742322	-0.515280
H	0.398696	-5.465016	1.961869
H	0.647316	-5.838003	0.257001
H	2.054423	-5.679974	1.336446
H	3.790890	4.499120	-0.886505
H	2.335921	4.686730	-1.902636
H	2.272801	5.114014	-0.191612
C	0.408361	0.269380	2.963404
H	1.184674	0.985946	2.638258
H	0.165180	0.504264	4.018639
H	0.876840	-0.732501	2.950705
C	-1.559408	0.056072	-4.371295
C	-1.916994	1.523349	-4.193398
H	-1.005353	2.112298	-4.073612
H	-2.451251	1.893953	-5.077614

H	-2.536819	1.653242	-3.306545
C	-0.586434	-0.164336	-5.513557
O	-0.504015	0.702713	-6.393108
N	0.177698	-1.306808	-5.624174
C	-2.716363	-0.875204	-4.382893
O	-2.849795	-1.863571	-5.096740
C	1.031920	-1.367522	-6.809822
H	0.450804	-1.113586	-7.700834
H	1.870689	-0.660506	-6.746145
H	1.424822	-2.383242	-6.895133
C	0.470501	-2.276687	-4.598685
C	1.641153	-2.133129	-3.844647
C	-0.356090	-3.383130	-4.403825
C	1.960327	-3.068278	-2.864900
H	2.259096	-1.251810	-3.988429
C	-0.032756	-4.317048	-3.416157
H	-1.262244	-3.468622	-4.989153
C	1.117796	-4.161150	-2.643799
H	2.840133	-2.932517	-2.244753
H	-0.694957	-5.162169	-3.240132
H	1.356855	-4.871624	-1.859651
O	-3.679621	-0.491528	-3.507725
C	-4.762969	-1.404676	-3.351631
H	-5.256840	-1.599106	-4.310961
H	-4.409610	-2.350756	-2.930564
H	-5.446005	-0.933637	-2.646103
Cl	-0.608468	-0.314577	-2.474463

TS4

B3LYP-D3 SCF energy:	-3317.54105924 a.u.
B3LYP-D3 enthalpy:	-3317.278667 a.u.
B3LYP-D3 free energy:	-3317.344134 a.u.
B3LYP-D3 SCF energy in solution:	-3320.52411597 a.u.
B3LYP-D3 enthalpy in solution:	-3320.261724 a.u.
B3LYP-D3 free energy in solution:	-3320.327191 a.u.
Imaginary frequency:	-55.3145 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
C	-1.416859	0.474172	0.586369
C	-2.528435	0.631957	1.615105

H	-2.087306	0.906090	2.577701
H	-3.069237	-0.309192	1.736034
H	-3.215043	1.417964	1.299055
C	-0.746613	1.835956	0.311243
O	-1.304422	2.901247	0.426791
O	0.532174	1.669982	-0.044655
C	1.289745	2.859241	-0.329493
H	0.857077	3.382574	-1.186365
H	1.291065	3.524704	0.537843
H	2.295261	2.504431	-0.554169
C	-0.360354	-0.572032	1.016998
O	-0.242584	-0.818459	2.197806
N	0.419268	-1.182425	-0.016044
C	1.828851	-0.898546	-0.021113
C	2.448373	-0.825562	-1.276737
C	3.807839	-0.537153	-1.378101
C	4.562335	-0.294619	-0.225750
C	3.945229	-0.360177	1.024218
C	2.587587	-0.673332	1.134030
H	2.117798	-0.738956	2.108185
H	4.523507	-0.178599	1.926529
H	5.619815	-0.057425	-0.303267
H	4.274525	-0.482909	-2.358240
H	1.841026	-0.973866	-2.164838
C	0.071906	-2.604329	-0.189414
H	-1.001975	-2.691556	-0.379704
H	0.606693	-2.985825	-1.062410
H	0.338365	-3.210318	0.689164
Br	-2.240935	-0.051791	-1.166161

TS5

B3LYP-D3 SCF energy:	-746.09636003 a.u.
B3LYP-D3 enthalpy:	-745.838435 a.u.
B3LYP-D3 free energy:	-745.900011 a.u.
B3LYP-D3 SCF energy in solution:	-746.34107888 a.u.
B3LYP-D3 enthalpy in solution:	-746.083154 a.u.
B3LYP-D3 free energy in solution:	-746.144730 a.u.
Imaginary frequency:	-59.3741 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
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C	2.048288	0.557762	-0.463955
C	3.260394	1.123426	-1.121594
H	3.124844	2.184692	-1.338373
H	4.135989	0.966303	-0.480908
H	3.466566	0.602843	-2.069124
C	0.826748	1.328002	-0.372189
O	0.642672	2.347630	-1.031897
N	-0.120651	0.891811	0.633583
C	2.166035	-0.788441	0.154169
O	3.118411	-1.122943	0.834503
C	-0.080246	1.732961	1.830116
H	-0.736671	2.611332	1.751420
H	-0.368266	1.146823	2.708435
H	0.946743	2.074518	1.983374
C	-1.353097	0.366623	0.206436
C	-2.481316	0.367310	1.046548
C	-1.470639	-0.219761	-1.070163
C	-3.678673	-0.212403	0.623465
H	-2.436618	0.819096	2.030608
C	-2.670533	-0.790748	-1.479462
H	-0.615851	-0.235340	-1.736799
C	-3.787169	-0.795831	-0.637949
H	-4.535098	-0.197570	1.292872
H	-2.732743	-1.233893	-2.470110
H	-4.722786	-1.240878	-0.963456
O	1.133571	-1.589665	-0.152987
C	1.122481	-2.876712	0.487669
H	1.110272	-2.758041	1.574752
H	0.208335	-3.360089	0.143627
H	2.004361	-3.456365	0.200592

TS-CPET¹

B3LYP-D3 SCF energy:	-2818.53379934 a.u.
B3LYP-D3 enthalpy:	-2817.618328 a.u.
B3LYP-D3 free energy:	-2817.773803 a.u.
B3LYP-D3 SCF energy in solution:	-2819.56087588 a.u.
B3LYP-D3 enthalpy in solution:	-2818.645405 a.u.
B3LYP-D3 free energy in solution:	-2818.800880 a.u.
Imaginary frequency:	-1278.7030 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
O	-0.632235	-0.530814	0.956635
Fe	0.069901	-0.608670	-0.684841
C	5.301827	-2.489150	0.275236
C	-3.904100	-4.122306	-2.544416
C	-3.057940	3.745349	-2.252917
C	4.394899	2.888076	0.287736
N	1.645398	-1.755861	-0.281885
C	6.029000	-2.841228	-1.047111
C	-4.628596	-5.230702	-2.305589
C	-4.293034	4.260856	-2.399411
C	4.633262	3.133245	1.798913
N	-0.976050	-2.269037	-1.213684
C	5.978088	-4.358957	-1.304550
C	4.556232	4.645480	2.251529
N	1.232896	0.996428	-0.569904
C	3.382442	-0.041875	-0.050898
C	0.542609	-3.948740	-0.280595
C	-2.914471	-1.235815	-2.294946
C	-0.451246	2.721297	-1.001039
C	3.334646	-5.056412	0.342995
C	-1.685214	-5.959547	-1.085799
C	-4.663430	1.130838	-3.254355
C	1.774823	4.709623	-0.210156
C	2.957007	-1.366305	-0.101797
C	-0.668821	-3.560127	-0.850614
C	-2.541204	0.091327	-2.141519
C	0.809163	2.307261	-0.605529
O	5.297627	-4.791327	-2.324085
O	4.448662	5.511500	1.336256
C	3.804644	-2.517850	0.146109
C	-1.709902	-4.471094	-1.256831
C	-3.361073	1.211679	-2.517655
C	1.890314	3.216204	-0.265529
O	6.553463	-5.098145	-0.498735
O	4.645793	4.809691	3.488051
C	2.978209	-3.611709	0.164458
C	-2.670836	-3.705308	-1.896145
C	-2.689221	2.347812	-2.102417
C	3.003677	2.444078	-0.059561
C	1.641217	-3.122736	-0.114580
C	-2.198488	-2.334483	-1.842909
C	-1.442771	1.885303	-1.508342

C	2.572870	1.062961	-0.222237
N	-1.367318	0.519916	-1.545869
H	5.628762	-1.499780	0.614383
H	5.634993	-3.207332	1.033371
H	-4.273347	-3.447350	-3.317551
H	-2.225787	4.449371	-2.241937
H	5.110200	2.152002	-0.104275
H	4.603992	3.845514	-0.202911
H	7.087444	-2.571248	-0.941852
H	5.605696	-2.263466	-1.872844
H	5.635670	2.778491	2.077501
H	3.930847	2.556547	2.412780
H	4.425960	0.141305	0.173285
H	0.683328	-5.001444	-0.065092
H	-3.882590	-1.425228	-2.744348
H	-0.643504	3.787295	-0.979043
H	-4.369321	-5.942484	-1.528676
H	-5.527935	-5.441575	-2.878777
H	-5.189842	3.650075	-2.371865
H	-4.436929	5.331221	-2.522416
H	-2.220954	-6.284289	-0.181595
H	-0.662558	-6.343016	-1.008534
H	-2.164331	-6.455090	-1.938596
H	-4.728532	0.221027	-3.861136
H	-4.780230	1.991433	-3.923654
H	-5.528725	1.132768	-2.575168
H	2.643615	-5.559043	1.032761
H	3.305848	-5.583636	-0.618606
H	4.353839	-5.173938	0.717587
H	2.669331	5.148973	0.250927
H	1.640517	5.136624	-1.216167
H	0.901154	5.012887	0.383229
C	0.207522	-0.157719	2.019123
H	0.494319	0.903093	1.968461
H	-0.350058	-0.322752	2.954763
H	1.129322	-0.756252	2.056741
C	4.331404	-4.466916	-5.350546
C	5.628382	-5.276352	-5.353170
H	6.466904	-4.635859	-5.641011
H	5.809519	-5.683634	-4.357301
H	5.548033	-6.092673	-6.078291
C	3.104249	-5.358295	-5.044052
O	2.884973	-6.468522	-5.504040

N	2.279785	-4.670512	-4.173091
C	4.142490	-3.772921	-6.699388
O	5.032587	-3.487497	-7.474595
C	0.973556	-5.149803	-3.769068
H	0.866997	-6.171074	-4.138167
H	0.885934	-5.123985	-2.680539
H	0.182904	-4.517561	-4.191574
C	2.785994	-3.416392	-3.856919
C	4.193023	-3.365300	-4.254170
C	2.121462	-2.355349	-3.292533
C	4.743903	-2.018531	-4.376150
H	4.779015	-3.933184	-3.239033
C	2.800445	-1.118471	-3.213847
H	1.106056	-2.447741	-2.922448
C	4.079774	-0.956936	-3.798961
H	5.724649	-1.890014	-4.826823
H	2.304865	-0.271987	-2.750332
H	4.540453	0.028056	-3.783432
O	2.852837	-3.407414	-6.897738
C	2.621728	-2.560066	-8.026078
H	2.911897	-3.060111	-8.955946
H	1.551370	-2.348088	-8.020638
H	3.194602	-1.632593	-7.929328

TS-CPET³

B3LYP-D3 SCF energy:	-2818.53042946 a.u.
B3LYP-D3 enthalpy:	-2817.615603 a.u.
B3LYP-D3 free energy:	-2817.775372 a.u.
B3LYP-D3 SCF energy in solution:	-2819.55387810 a.u.
B3LYP-D3 enthalpy in solution:	-2818.639052 a.u.
B3LYP-D3 free energy in solution:	-2818.798821 a.u.
Imaginary frequency:	-1258.7234 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
O	-0.543005	-0.414422	1.338842
Fe	-0.017403	-0.633104	-0.442752
C	5.145494	-2.761447	0.535269
C	-4.396411	-3.927685	-1.693156
C	-2.866987	3.825886	-2.314577
C	4.599602	2.590290	0.053393

N	1.544533	-1.885199	-0.127765
C	5.936140	-3.086196	-0.757778
C	-5.138211	-4.980847	-1.305138
C	-4.052602	4.456171	-2.417154
C	4.861828	2.989091	1.527542
N	-1.193960	-2.245468	-0.849969
C	5.908018	-4.598670	-1.053600
C	4.907453	4.545373	1.799611
N	1.282649	0.880549	-0.563974
C	3.356224	-0.253068	0.080188
C	0.347043	-4.032381	-0.172419
C	-3.206278	-1.113949	-1.677453
C	-0.246819	2.691303	-1.204409
C	3.107172	-5.270065	0.355618
C	-2.060932	-5.901150	-0.676797
C	-4.856797	1.305161	-2.690010
C	2.162605	4.547989	-0.726846
C	2.856288	-1.552872	0.094281
C	-0.897409	-3.564211	-0.567527
C	-2.707757	0.186091	-1.719856
C	0.974720	2.212411	-0.787821
O	5.343993	-5.003336	-2.151610
O	4.856389	5.304754	0.789683
C	3.656911	-2.740439	0.329946
C	-2.038249	-4.409284	-0.814794
C	-3.460577	1.329552	-2.146754
C	2.138654	3.056960	-0.575532
O	6.403136	-5.357160	-0.213287
O	5.024007	4.844800	3.008067
C	2.797097	-3.807425	0.252940
C	-3.051508	-3.582524	-1.259472
C	-2.621626	2.427894	-2.004441
C	3.175055	2.227093	-0.247099
C	1.488314	-3.261219	-0.028150
C	-2.500804	-2.235313	-1.280850
C	-1.365442	1.909909	-1.503177
C	2.622525	0.875728	-0.223988
N	-1.431467	0.552873	-1.342887
H	5.478611	-1.795834	0.931418
H	5.418556	-3.516858	1.280703
H	-4.842939	-3.244704	-2.416794
H	-1.973846	4.427840	-2.481657
H	5.249665	1.757159	-0.246299

H	4.885232	3.463043	-0.544410
H	6.987885	-2.814368	-0.601901
H	5.547674	-2.491789	-1.589883
H	5.833159	2.589812	1.851830
H	4.116956	2.546594	2.199969
H	4.404535	-0.113144	0.309611
H	0.456080	-5.099084	-0.018166
H	-4.242937	-1.252645	-1.959979
H	-0.330348	3.764074	-1.329094
H	-4.799354	-5.687017	-0.553688
H	-6.129443	-5.147566	-1.719344
H	-4.999192	3.962181	-2.223657
H	-4.098563	5.511625	-2.672906
H	-2.391454	-6.221053	0.322056
H	-1.069804	-6.335984	-0.843954
H	-2.751846	-6.345072	-1.402763
H	-5.111405	0.325422	-3.108720
H	-4.973725	2.050155	-3.486366
H	-5.609955	1.536874	-1.922053
H	2.377925	-5.795249	0.986419
H	3.096621	-5.733104	-0.638987
H	4.107806	-5.440803	0.759020
H	3.085034	4.962412	-0.298204
H	2.090880	4.842021	-1.785201
H	1.309840	5.007336	-0.208858
C	0.345214	0.018545	2.323185
H	0.709062	1.042586	2.132917
H	-0.150583	0.014627	3.309678
H	1.233752	-0.633338	2.390538
C	5.124992	-3.949459	-5.173425
C	6.621154	-3.963824	-4.860380
H	6.971519	-2.946340	-4.665930
H	6.802465	-4.585691	-3.982405
H	7.174496	-4.365794	-5.714689
C	4.603639	-5.367365	-5.502972
O	5.149148	-6.194035	-6.217956
N	3.391142	-5.539234	-4.859777
C	4.842446	-3.006551	-6.342541
O	5.565870	-2.103356	-6.707215
C	2.587005	-6.730062	-5.001749
H	3.153862	-7.441021	-5.605627
H	2.374469	-7.161752	-4.017142
H	1.636710	-6.497805	-5.499814

C	3.013542	-4.410281	-4.140850
C	4.179778	-3.537706	-4.003612
C	1.773604	-4.092662	-3.642120
C	3.873030	-2.156929	-3.642926
H	4.767411	-4.105419	-2.996193
C	1.583914	-2.794656	-3.114719
H	0.945176	-4.794123	-3.685482
C	2.624659	-1.836552	-3.154981
H	4.663766	-1.412303	-3.680027
H	0.619489	-2.517336	-2.705797
H	2.426684	-0.838298	-2.774965
O	3.619059	-3.231701	-6.881346
C	3.181065	-2.253820	-7.829656
H	3.859119	-2.211332	-8.688182
H	2.184648	-2.571554	-8.141278
H	3.137261	-1.264820	-7.363584

TS-CPET⁵

B3LYP-D3 SCF energy:	-2818.54630858 a.u.
B3LYP-D3 enthalpy:	-2817.629122 a.u.
B3LYP-D3 free energy:	-2817.789206 a.u.
B3LYP-D3 SCF energy in solution:	-2819.58845080 a.u.
B3LYP-D3 enthalpy in solution:	-2818.671264 a.u.
B3LYP-D3 free energy in solution:	-2818.831348 a.u.
Imaginary frequency:	-141.2318 cm ⁻¹

Cartesian coordinates

ATOM	X	Y	Z
O	-0.515094	-0.616996	1.447296
Fe	0.067810	-0.807821	-0.281035
C	5.377966	-2.760001	0.605785
C	-3.935944	-4.334360	-2.277311
C	-2.798906	3.544505	-2.514473
C	4.640373	2.596942	0.188455
N	1.747744	-2.039313	-0.066119
C	6.147607	-3.016608	-0.714349
C	-4.631492	-5.463626	-2.052356
C	-4.008013	4.118510	-2.645995
C	4.851141	2.978886	1.673955
N	-0.956880	-2.524646	-1.027183
C	6.084669	-4.524415	-1.080783

C	4.719310	4.520730	1.990851
N	1.395264	0.802366	-0.488172
C	3.469693	-0.312093	0.179633
C	0.648916	-4.221421	-0.259535
C	-2.915307	-1.433972	-2.017634
C	-0.189462	2.510287	-1.236428
C	3.448472	-5.352525	0.418385
C	-1.611021	-6.219212	-1.079109
C	-4.609861	0.944634	-3.108785
C	2.174347	4.478593	-0.706288
C	3.034950	-1.639678	0.176696
C	-0.599171	-3.823581	-0.761237
C	-2.497462	-0.103059	-1.969434
C	1.048782	2.106512	-0.750118
O	5.385704	-4.851823	-2.097677
O	4.699101	5.305059	0.998545
C	3.888338	-2.801701	0.417357
C	-1.656249	-4.723404	-1.160440
C	-3.270767	1.023497	-2.441018
C	2.183105	2.991043	-0.520827
O	6.678768	-5.299476	-0.304207
O	4.694220	4.790225	3.211375
C	3.078305	-3.903998	0.323457
C	-2.668110	-3.934150	-1.687074
C	-2.506633	2.153133	-2.202975
C	3.235591	2.191921	-0.148801
C	1.744973	-3.410490	0.006492
C	-2.201930	-2.557672	-1.596187
C	-1.262161	1.686094	-1.602332
C	2.718776	0.822690	-0.124297
N	-1.290779	0.327546	-1.468084
H	5.671605	-1.793300	1.032885
H	5.695593	-3.531100	1.317135
H	-4.362608	-3.622801	-2.985141
H	-1.927162	4.184702	-2.649367
H	5.321194	1.785942	-0.104729
H	4.914553	3.486505	-0.389136
H	7.200854	-2.751502	-0.555195
H	5.744690	-2.382488	-1.512799
H	5.865378	2.686721	1.982593
H	4.165973	2.429744	2.330826
H	4.513002	-0.143879	0.417876
H	0.804392	-5.286849	-0.128790

H	-3.908188	-1.611628	-2.416019
H	-0.314992	3.577312	-1.383105
H	-4.313846	-6.213226	-1.335066
H	-5.565511	-5.654682	-2.574640
H	-4.933741	3.576566	-2.480270
H	-4.098889	5.172297	-2.896331
H	-2.100894	-6.599599	-0.171055
H	-0.582831	-6.594736	-1.071924
H	-2.127184	-6.669519	-1.935408
H	-4.754215	-0.019573	-3.608337
H	-4.713278	1.734362	-3.862254
H	-5.438413	1.069251	-2.396314
H	2.733650	-5.910992	1.037940
H	3.476552	-5.798977	-0.582236
H	4.454954	-5.483367	0.822020
H	3.041169	4.931538	-0.205959
H	2.193583	4.746221	-1.774070
H	1.263288	4.921176	-0.281622
C	0.339482	-0.274697	2.503753
H	0.798292	0.714707	2.349775
H	-0.225183	-0.247460	3.449802
H	1.157824	-1.005078	2.613660
C	4.286995	-4.155595	-5.210951
C	5.635861	-4.871781	-5.206161
H	6.435620	-4.159194	-5.428081
H	5.808698	-5.312540	-4.221487
H	5.640478	-5.649706	-5.976683
C	3.113182	-5.146157	-5.028559
O	2.984674	-6.226611	-5.581115
N	2.199701	-4.580903	-4.152769
C	4.096664	-3.367975	-6.505717
O	4.982513	-3.014876	-7.255647
C	0.898033	-5.160327	-3.894946
H	0.890472	-6.163207	-4.324595
H	0.716871	-5.201476	-2.818553
H	0.108277	-4.553074	-4.355376
C	2.585704	-3.314573	-3.742344
C	4.042431	-3.168360	-4.010991
C	1.796425	-2.309116	-3.247678
C	4.489325	-1.752138	-4.066865
H	4.581248	-3.684989	-3.147686
C	2.359554	-1.019546	-3.128397
H	0.761357	-2.476473	-2.968188

C	3.683177	-0.757475	-3.576140
H	5.504093	-1.544794	-4.395507
H	1.761255	-0.217631	-2.711859
H	4.056253	0.262251	-3.515193
O	2.799752	-3.017827	-6.687690
C	2.556230	-2.094105	-7.751820
H	2.863357	-2.516786	-8.713945
H	1.481431	-1.906470	-7.738219
H	3.107395	-1.164414	-7.580347

TS-PT

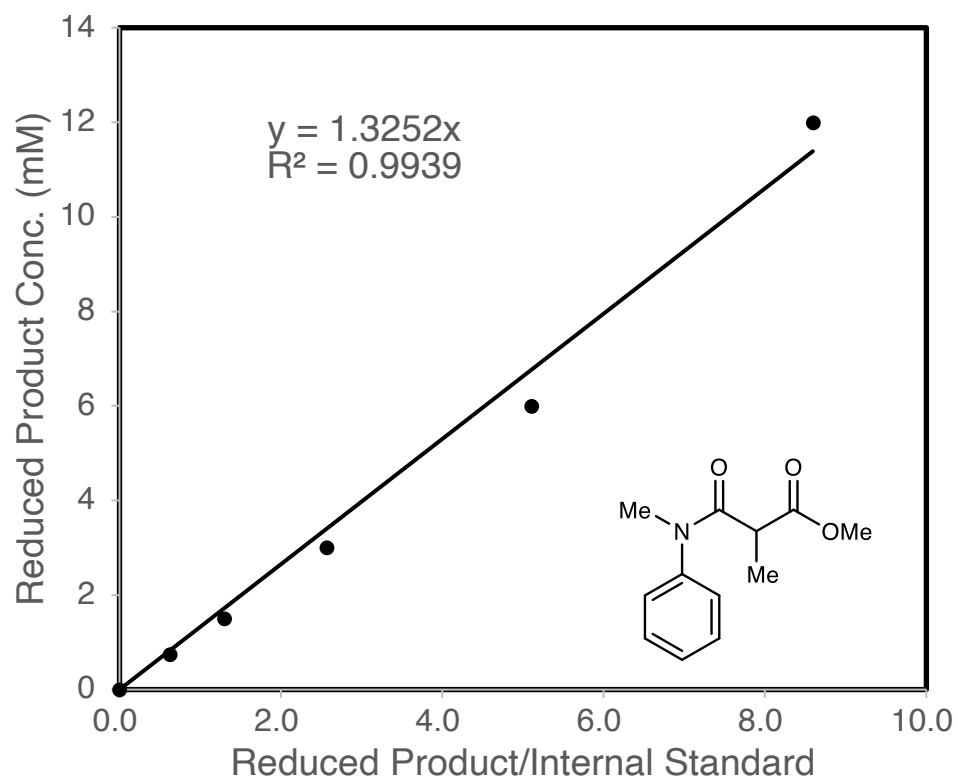
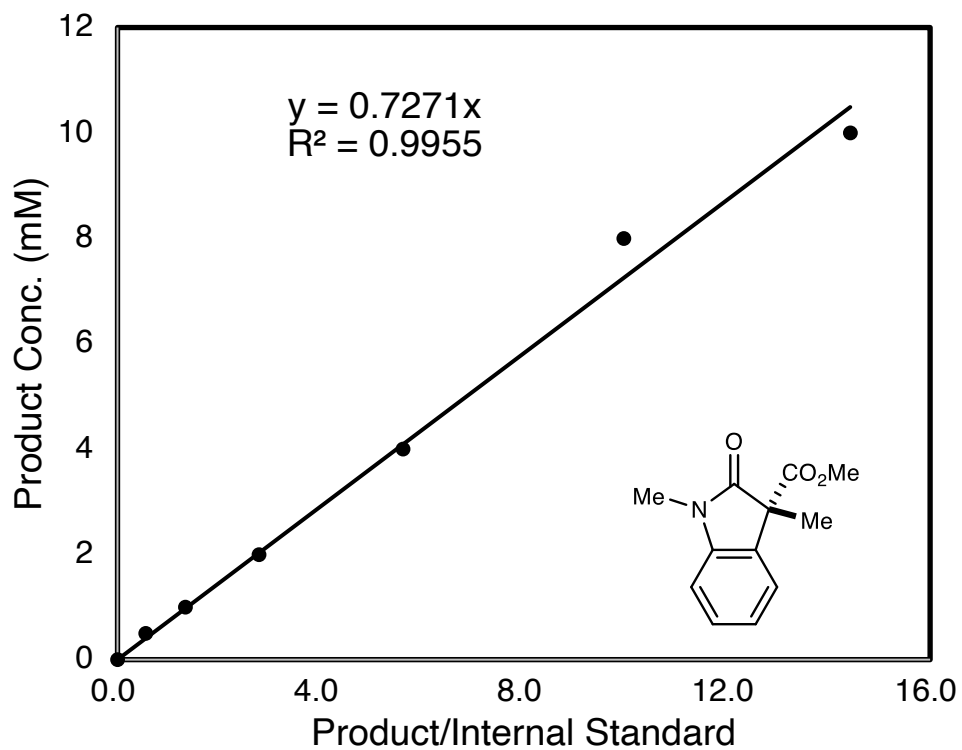
B3LYP-D3 SCF energy:	-974.65219490 a.u.
B3LYP-D3 enthalpy:	-974.342266 a.u.
B3LYP-D3 free energy:	-974.415167 a.u.
B3LYP-D3 SCF energy in solution:	-975.04158152 a.u.
B3LYP-D3 enthalpy in solution:	-974.731653 a.u.
B3LYP-D3 free energy in solution:	-974.804554 a.u.
Imaginary frequency:	-1250.7495 cm ⁻¹

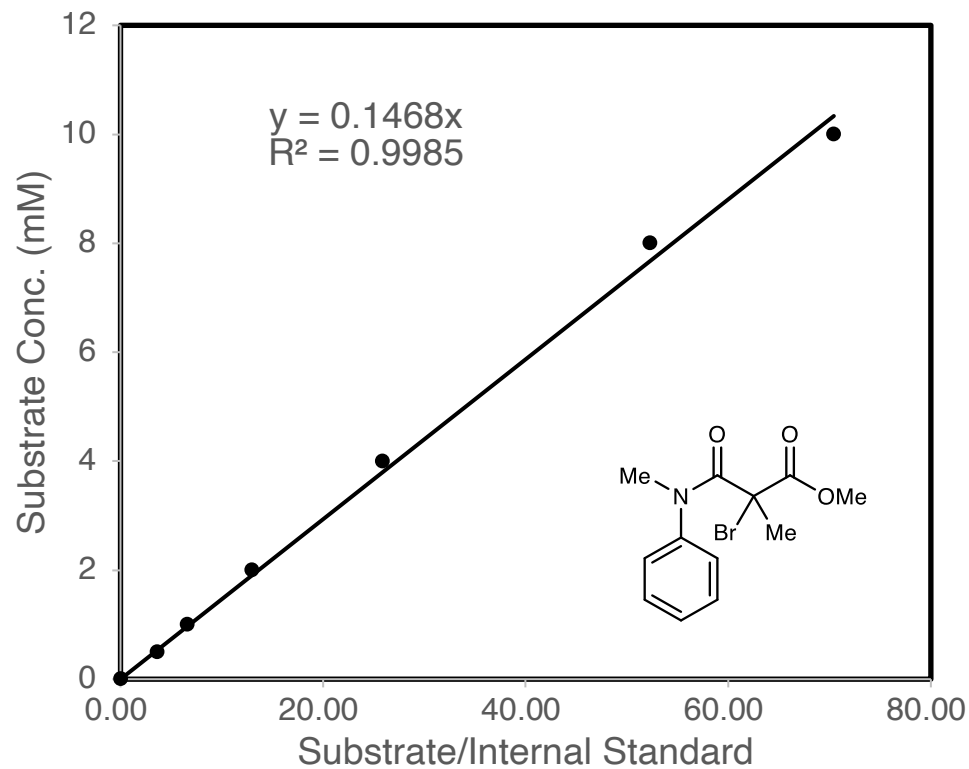
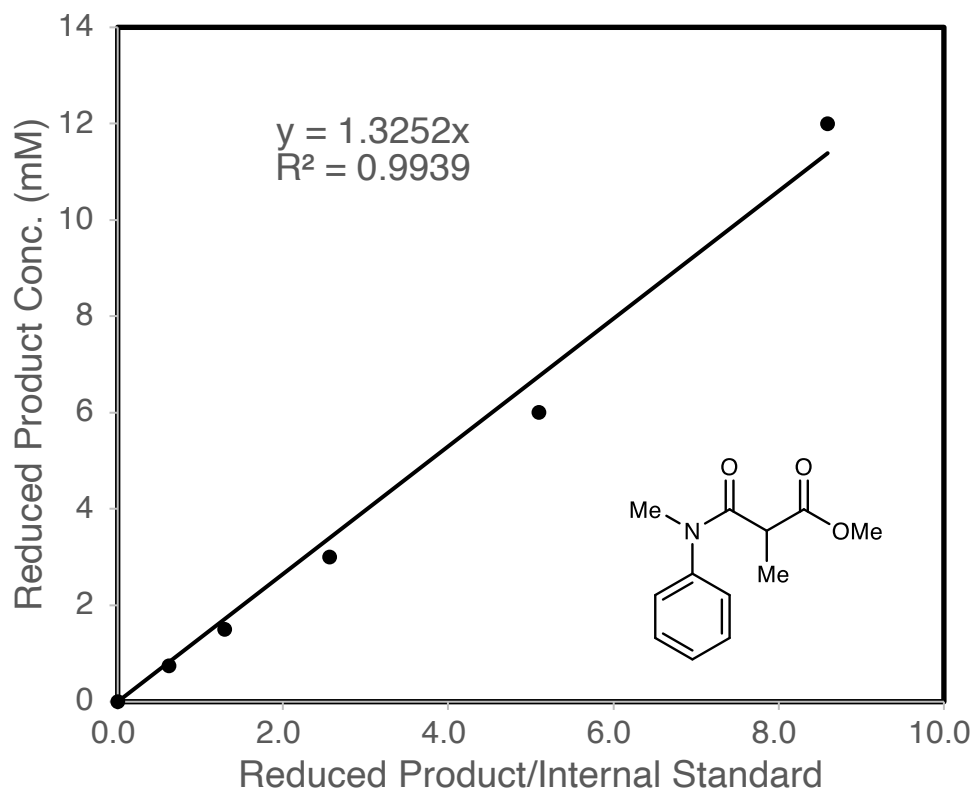
Cartesian coordinates

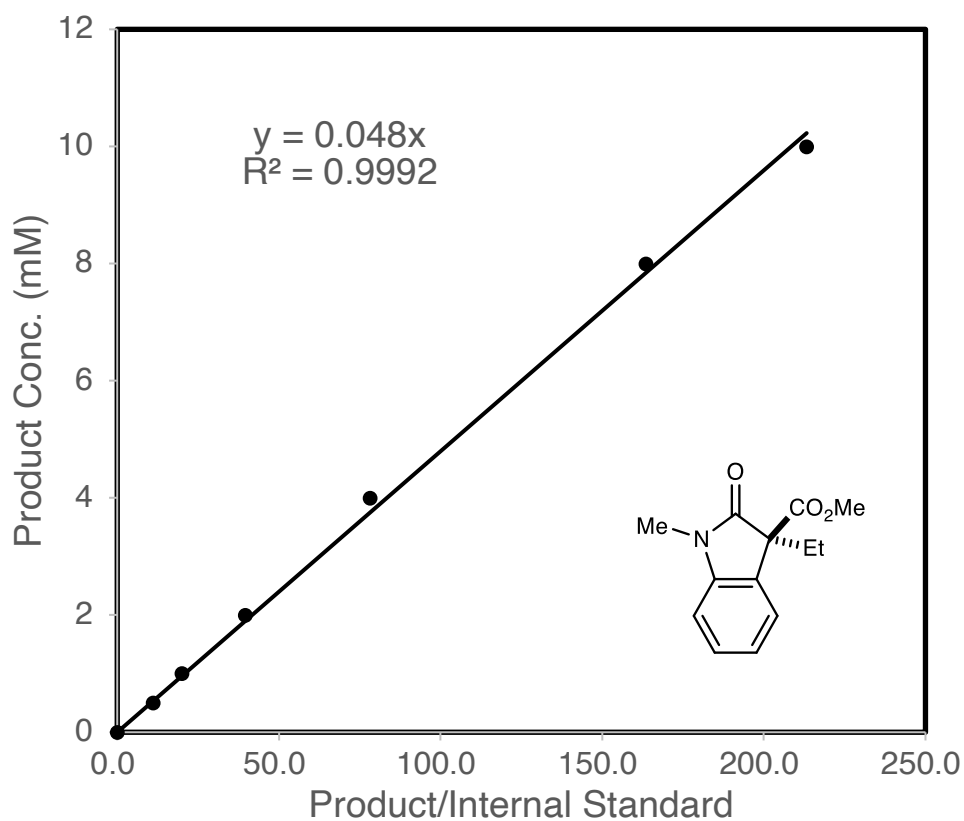
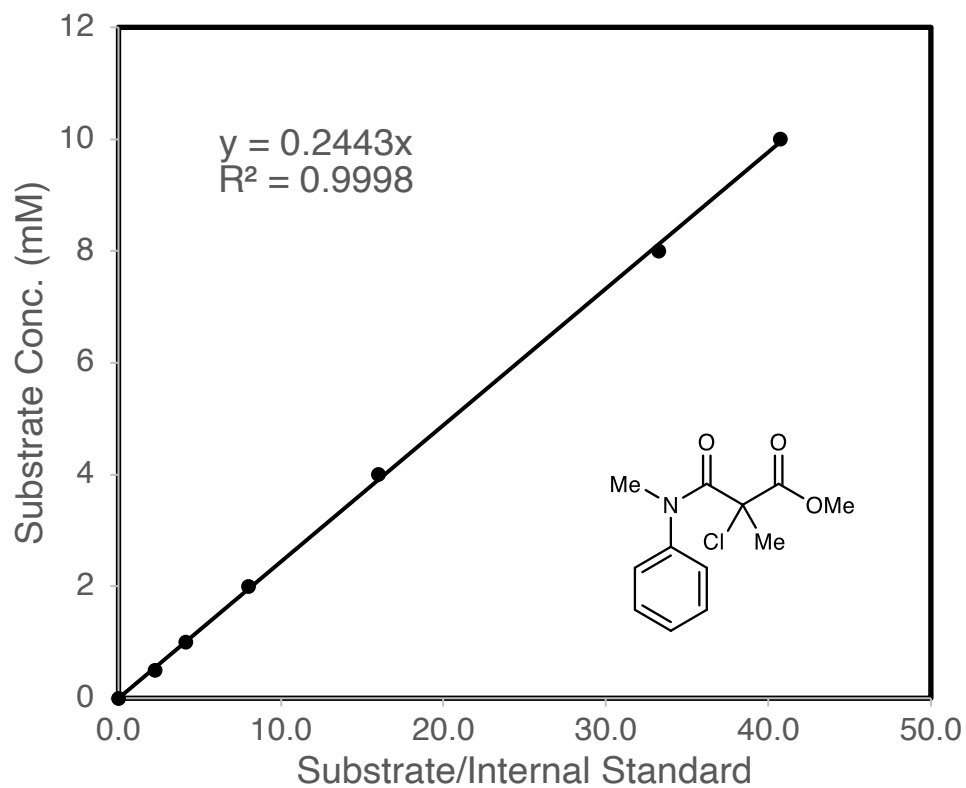
ATOM	X	Y	Z
C	-1.347449	-1.002448	-0.498474
C	-1.197676	-1.898509	-1.729804
H	-1.679353	-1.427691	-2.591432
H	-0.140864	-2.056435	-1.950787
H	-1.680094	-2.864187	-1.543462
C	-0.779019	-1.674085	0.770378
O	-0.924229	-2.843828	1.101393
N	-0.094848	-0.717916	1.493462
C	-2.814723	-0.646228	-0.290165
O	-3.646449	-0.540097	-1.171464
C	0.438893	-0.970666	2.808402
H	0.329978	-2.038020	3.010854
H	1.497555	-0.688115	2.853053
H	-0.109460	-0.394749	3.567042
C	-0.133930	0.538794	0.877664
C	-0.560318	0.347648	-0.513330
C	0.122510	1.759741	1.442461
C	-1.063464	1.571487	-1.144402
H	0.629694	-0.056864	-1.157427
C	-0.171092	2.933080	0.683990

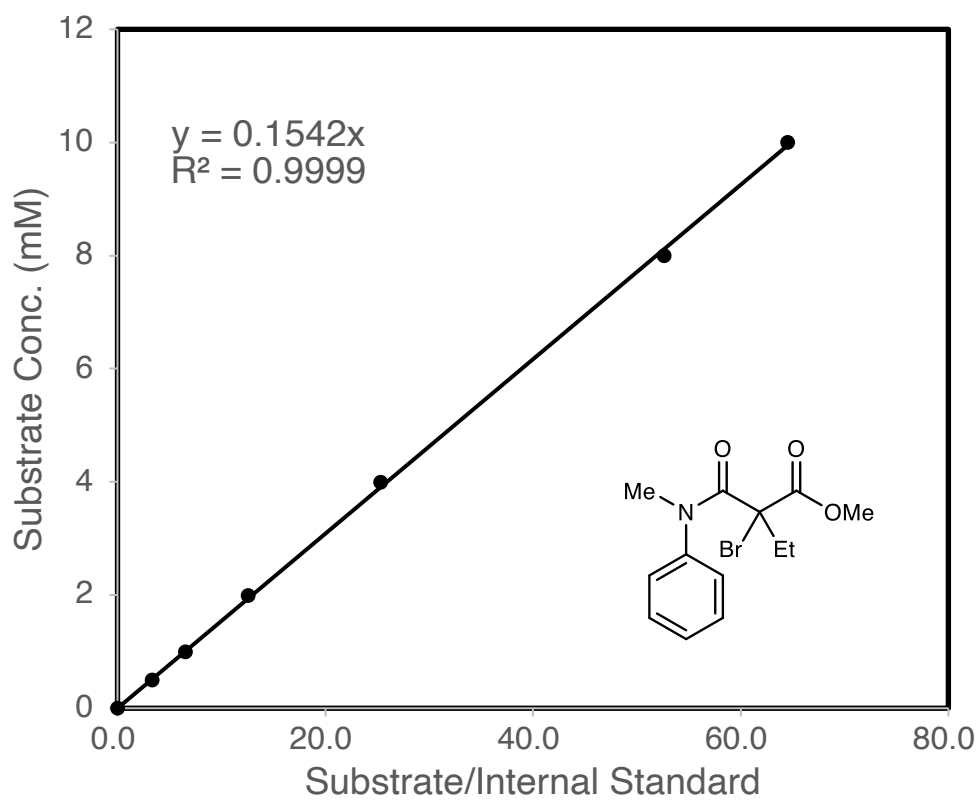
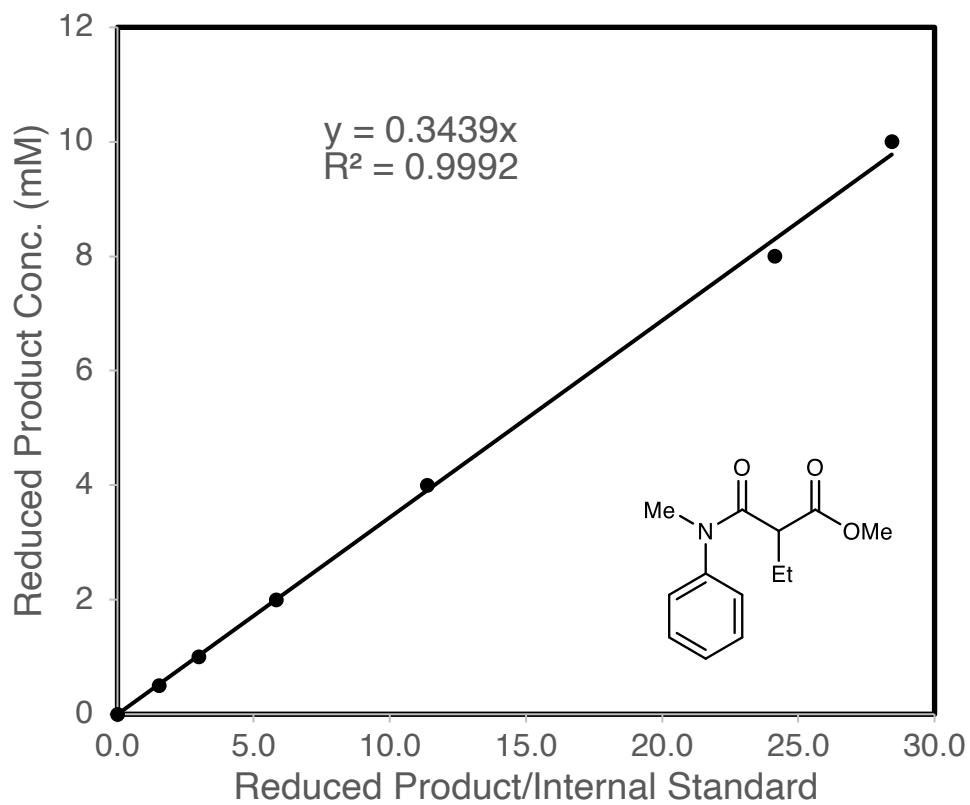
H	0.497287	1.838200	2.460927
C	-0.806223	2.803855	-0.574610
H	-1.573167	1.498150	-2.101954
H	0.031282	3.914858	1.102530
H	-1.102987	3.707295	-1.107367
O	-3.077686	-0.302896	1.000341
C	-4.351109	0.304796	1.215692
H	-5.164453	-0.375688	0.941330
H	-4.392022	0.538336	2.281670
H	-4.442980	1.219666	0.621502
C	2.667181	0.173954	-1.867291
O	1.620515	-0.589239	-1.668938
O	3.717904	-0.227652	-2.363861
C	2.514888	1.635172	-1.435514
H	2.284486	1.695601	-0.366341
H	3.433443	2.186071	-1.652988
H	1.666305	2.099657	-1.949316

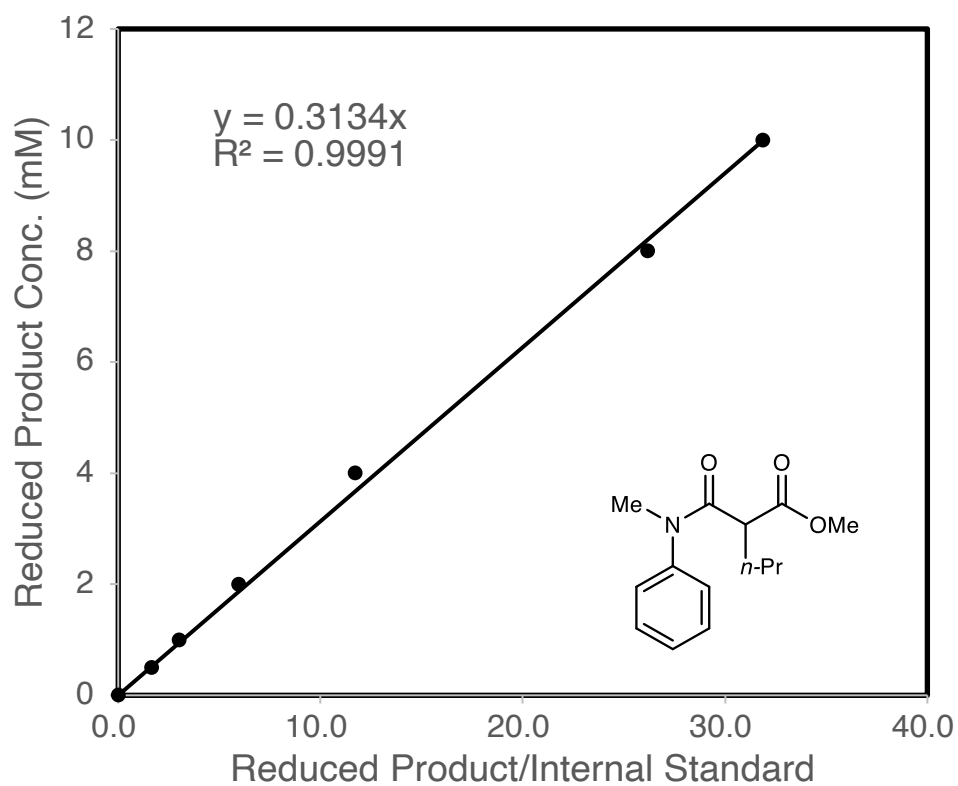
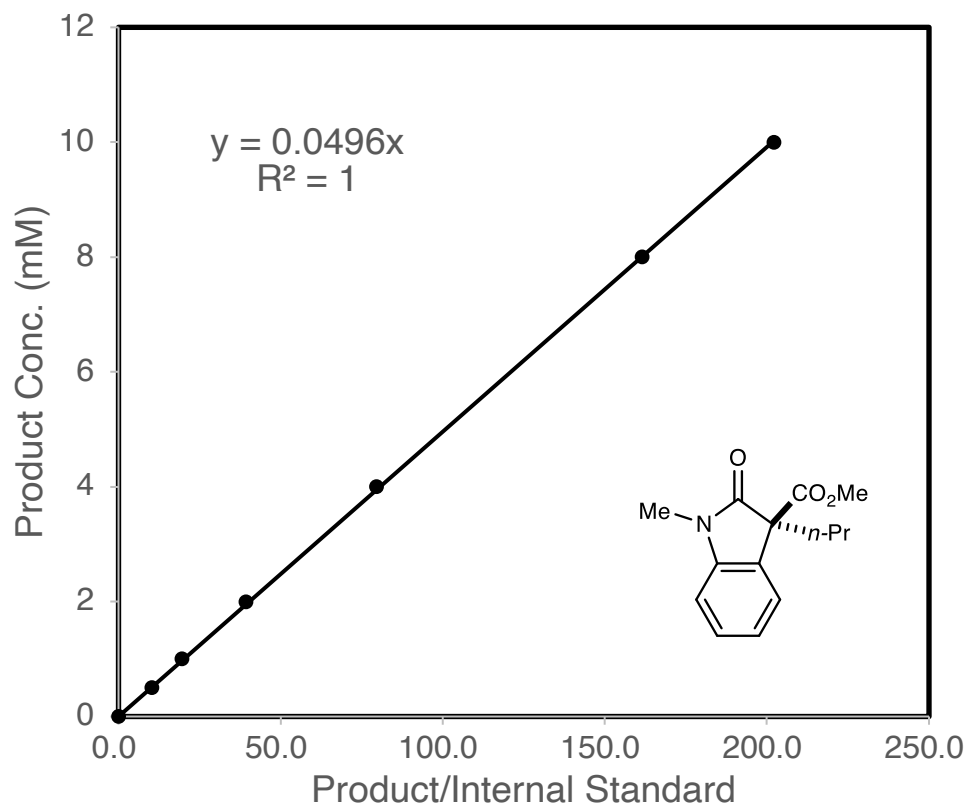
Supplementary Note 10. Product HPLC calibration curves

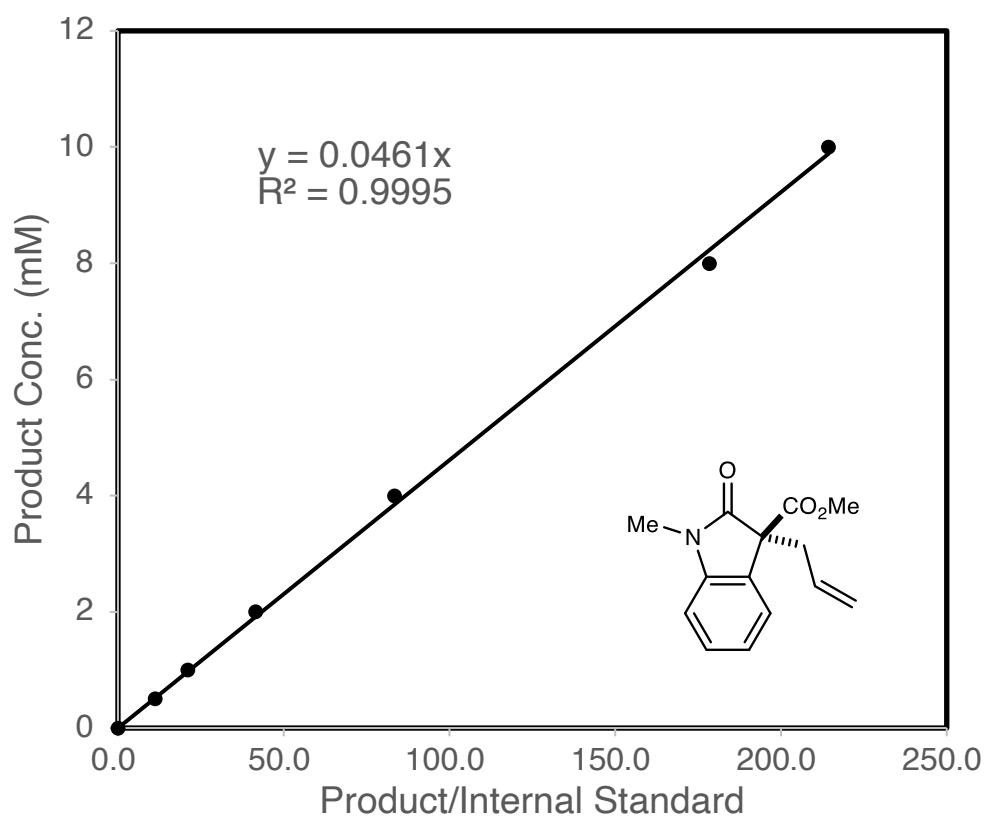
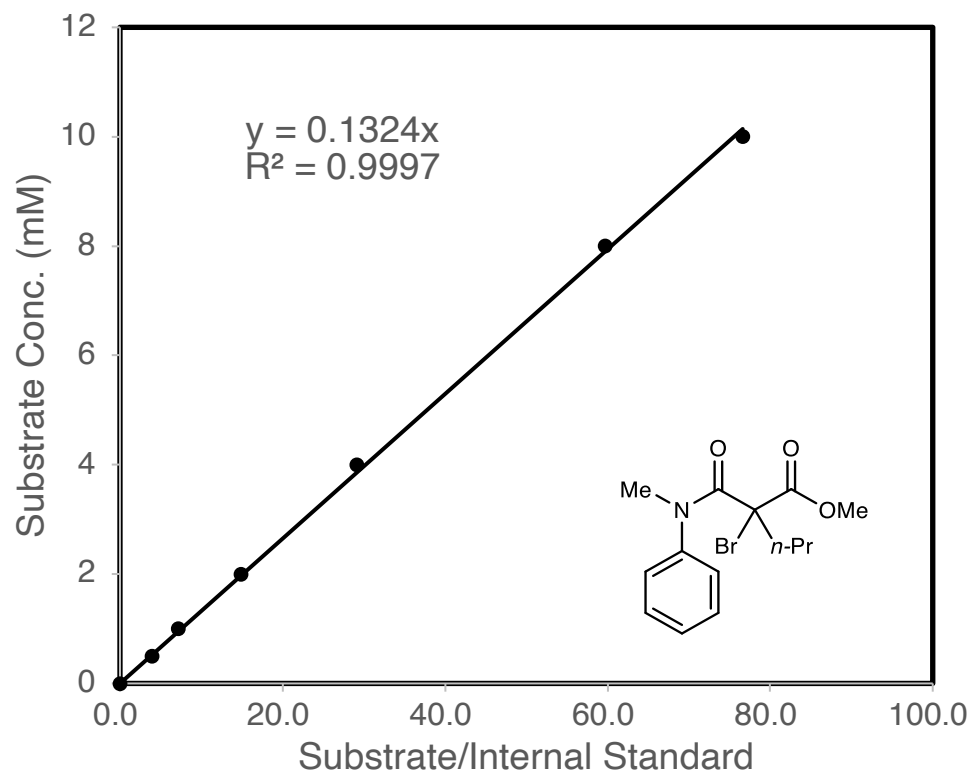


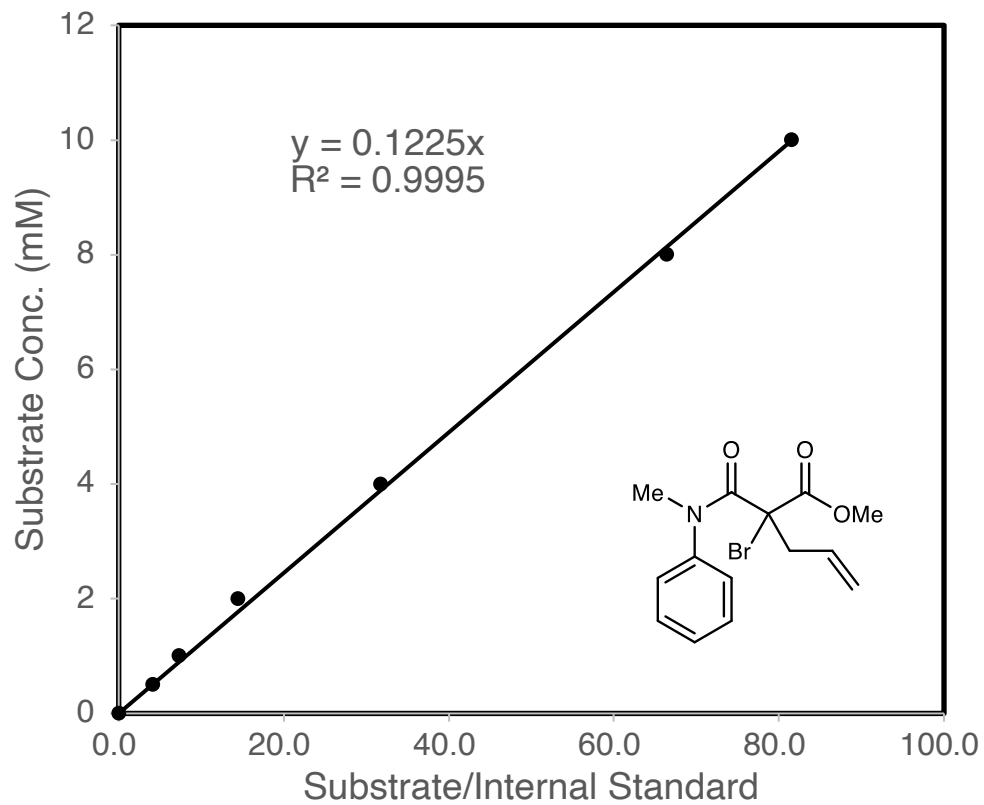
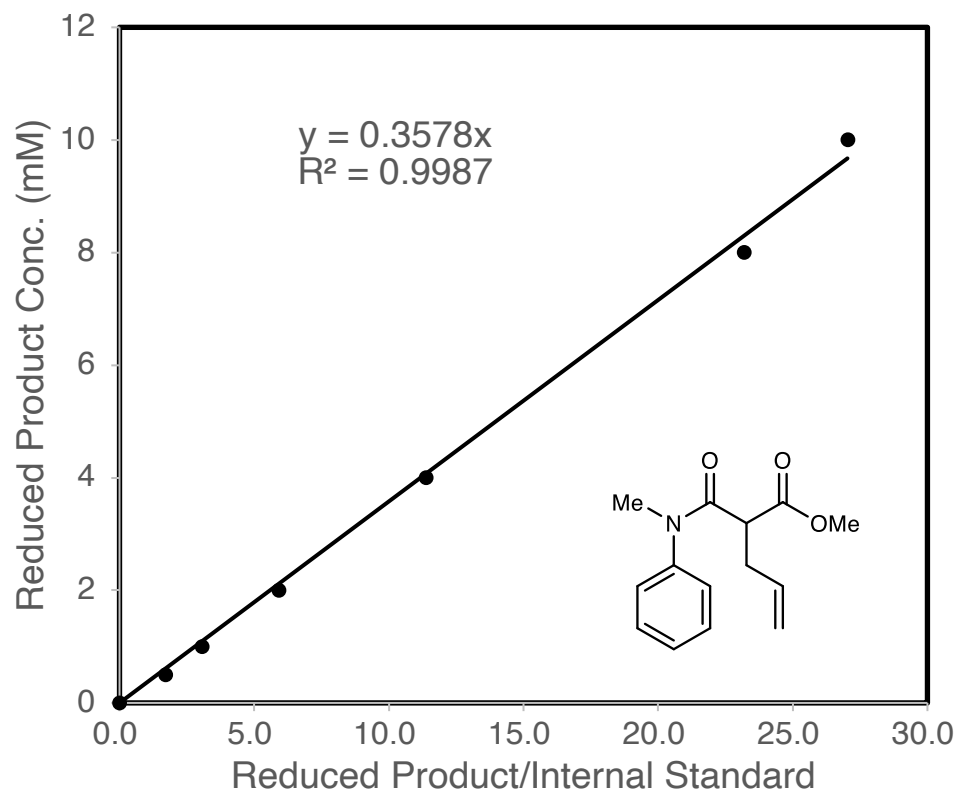


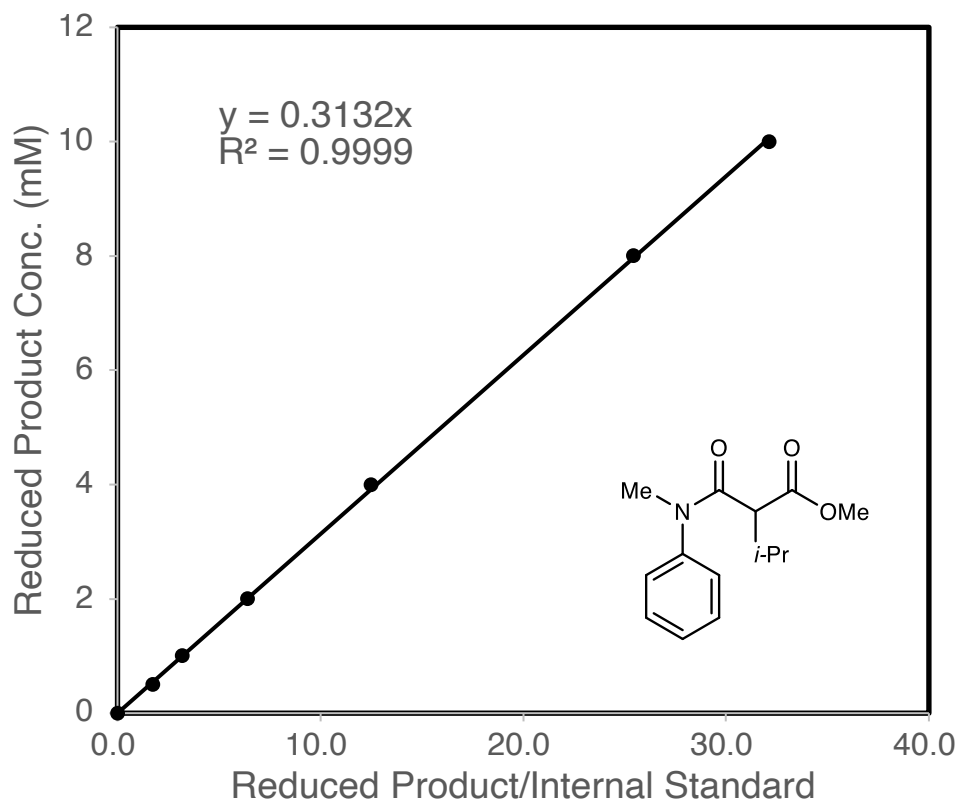
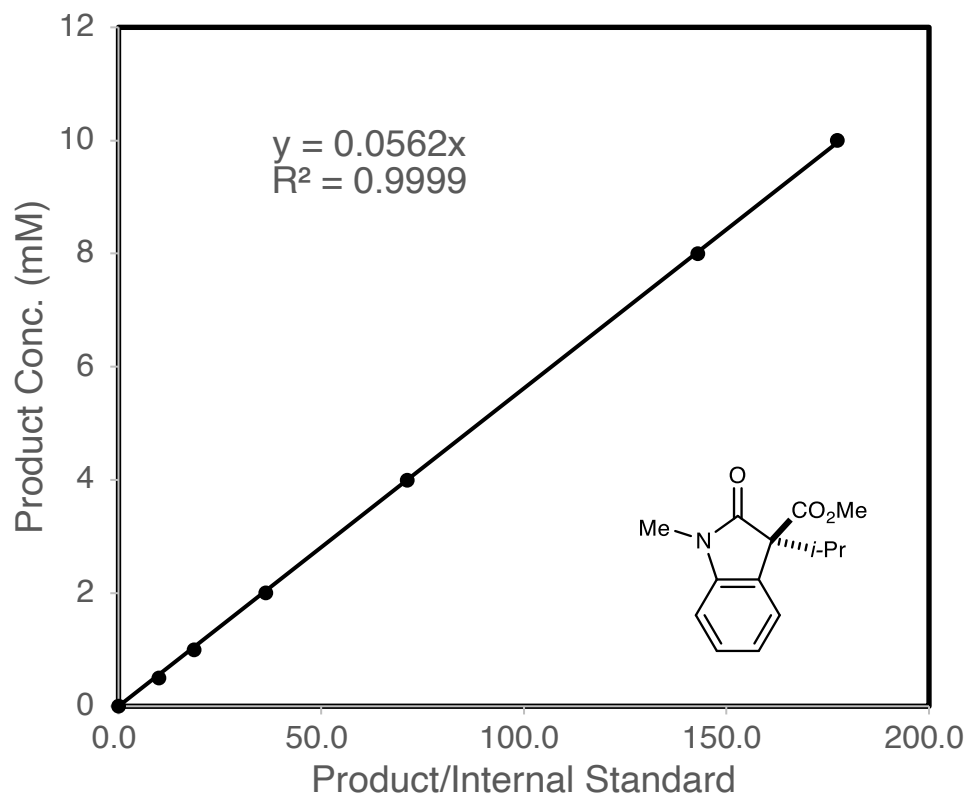


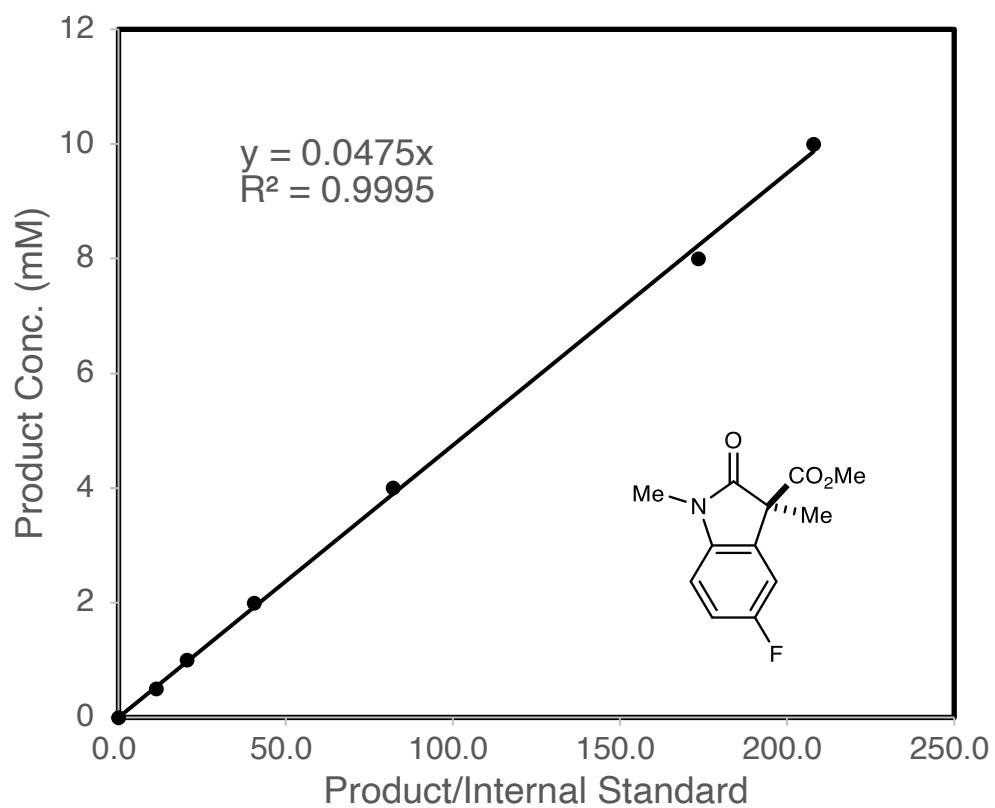
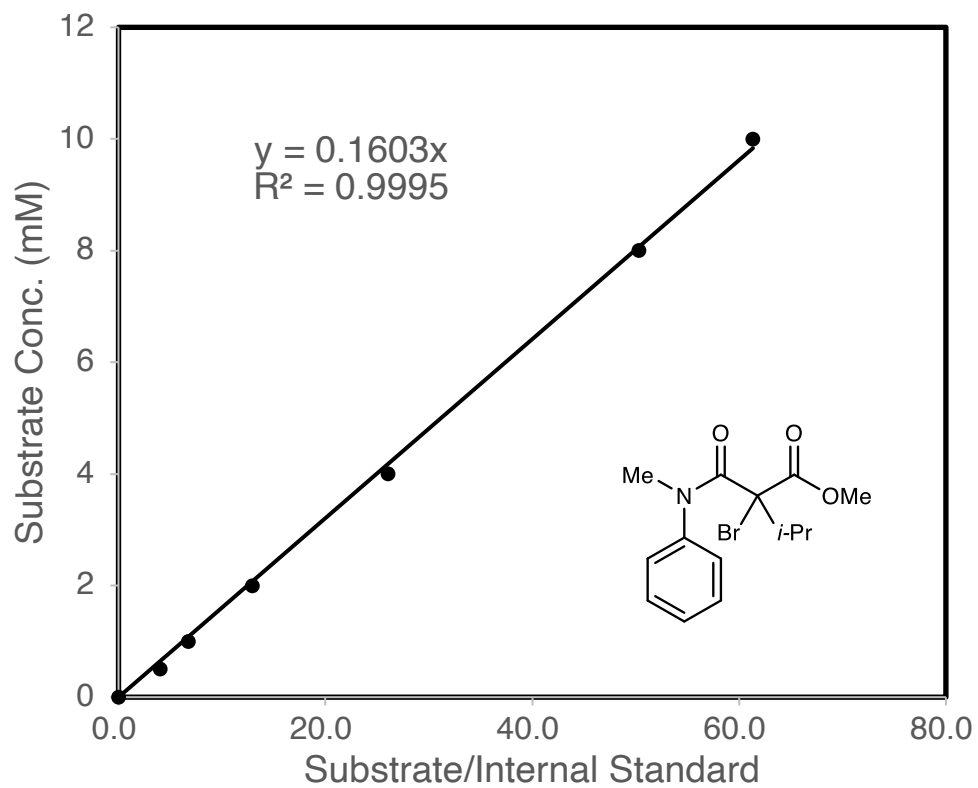


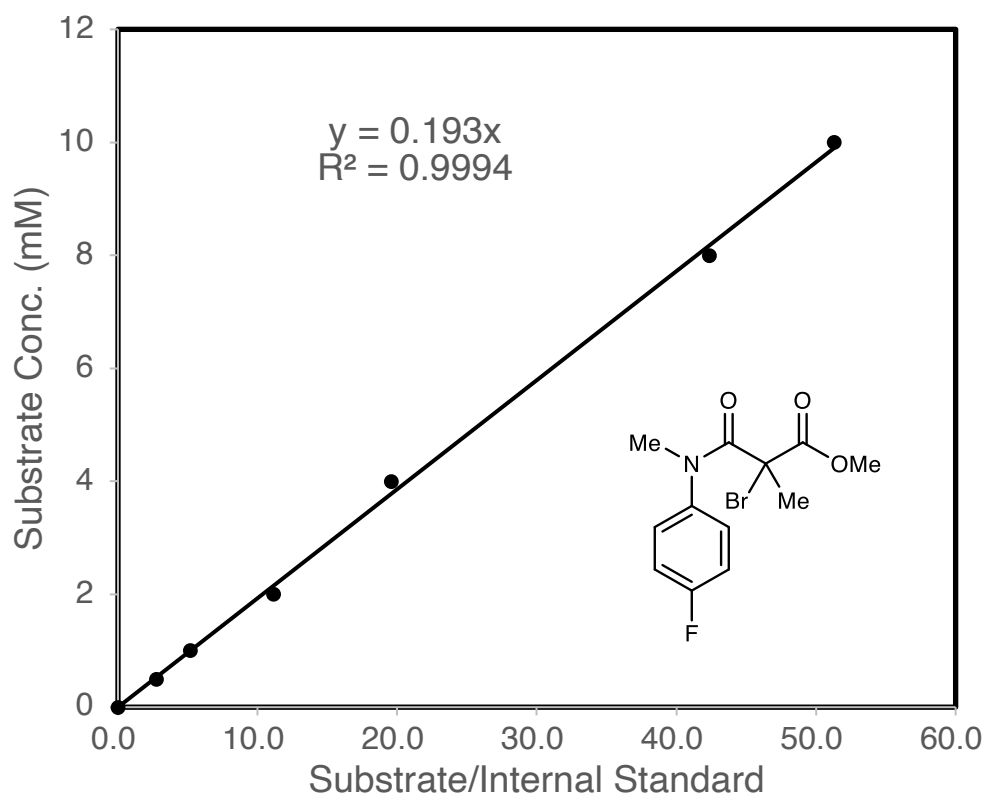
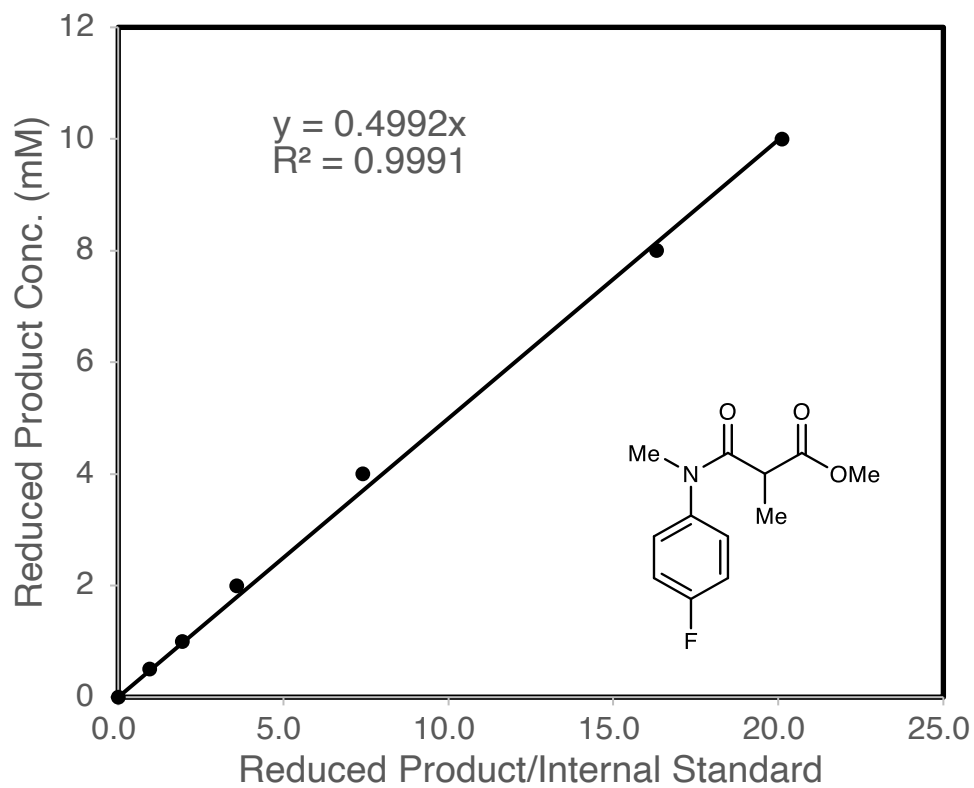


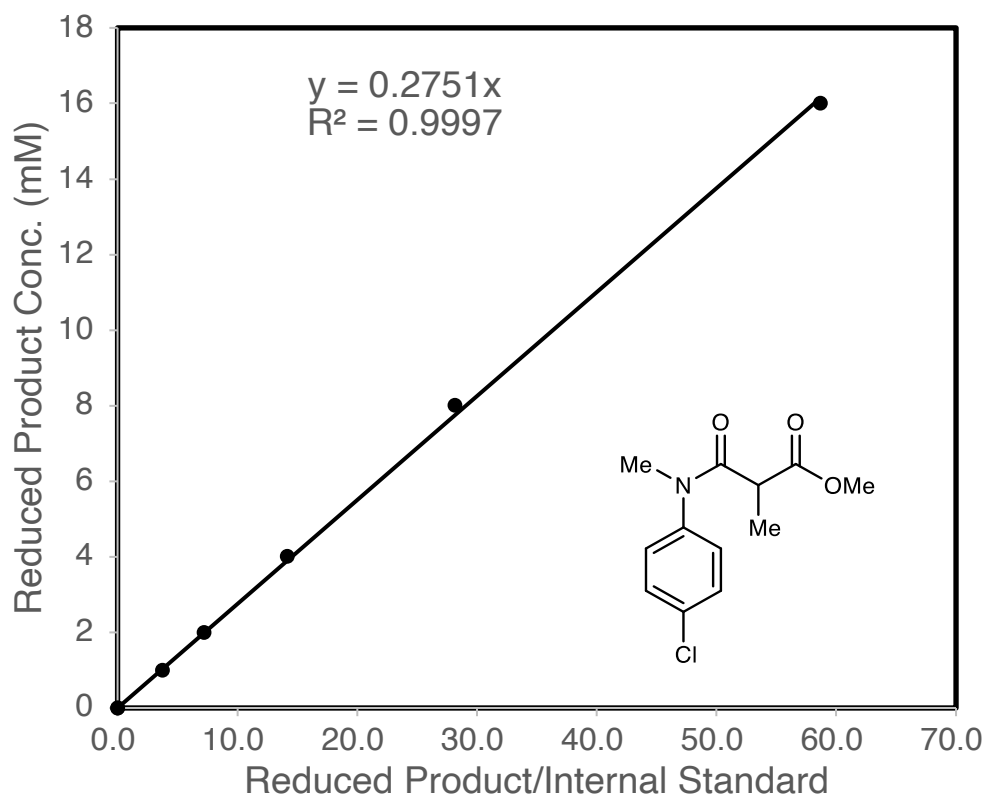
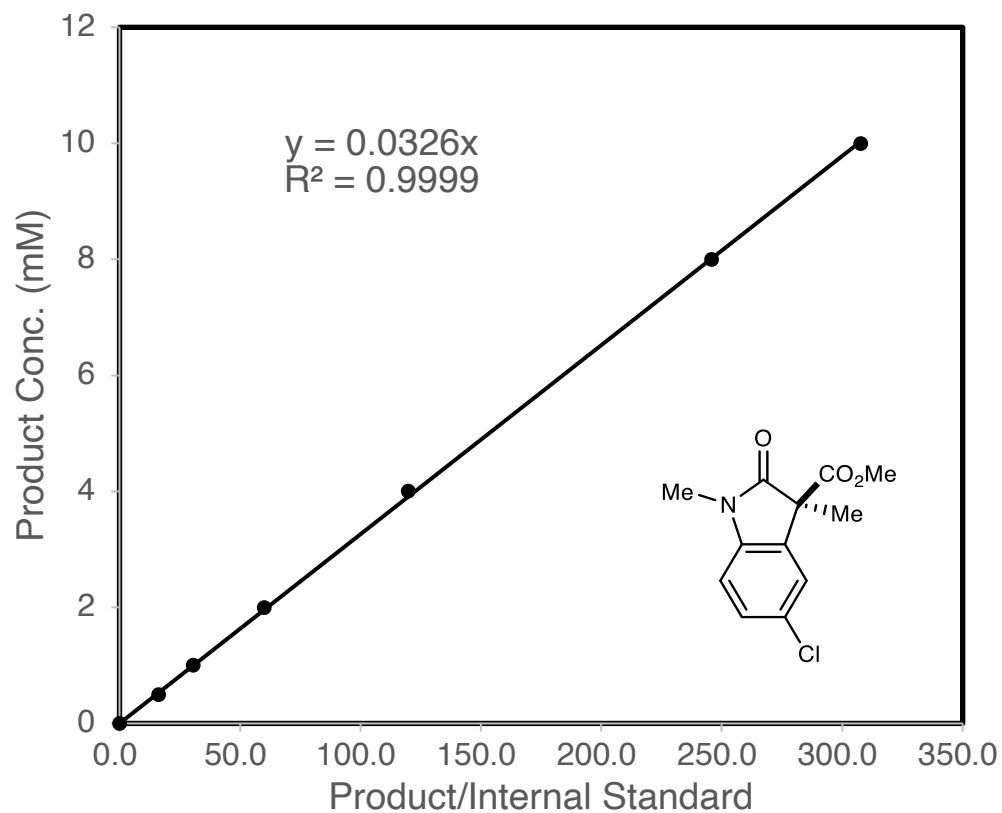


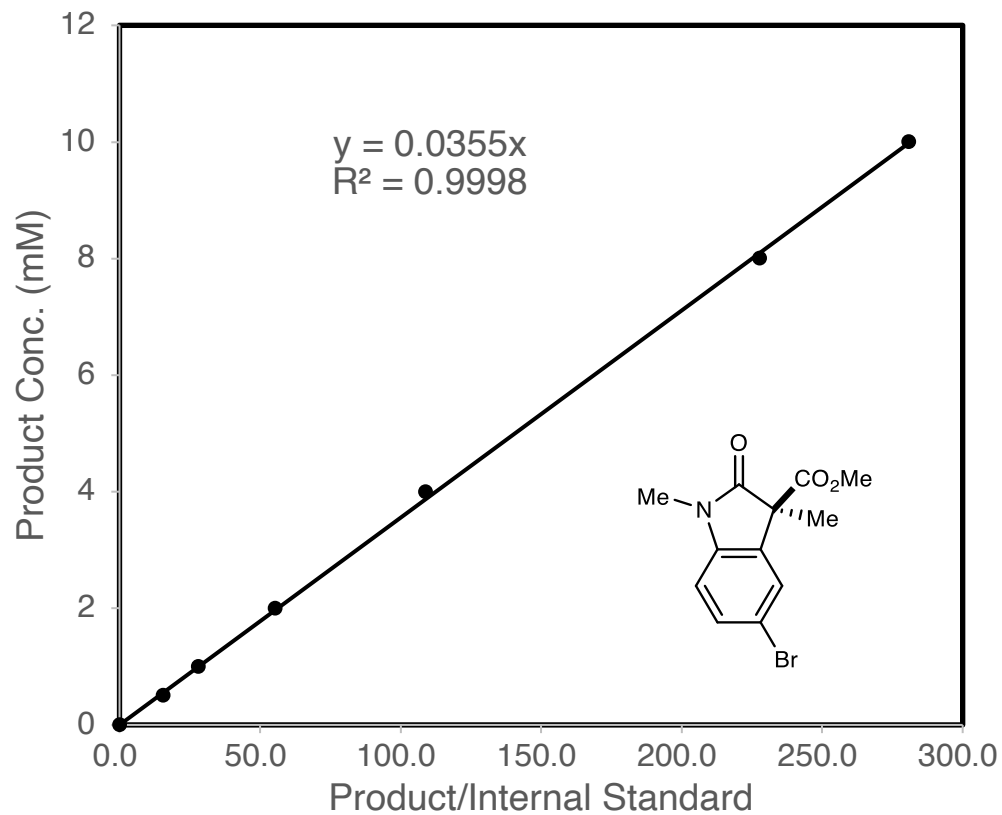
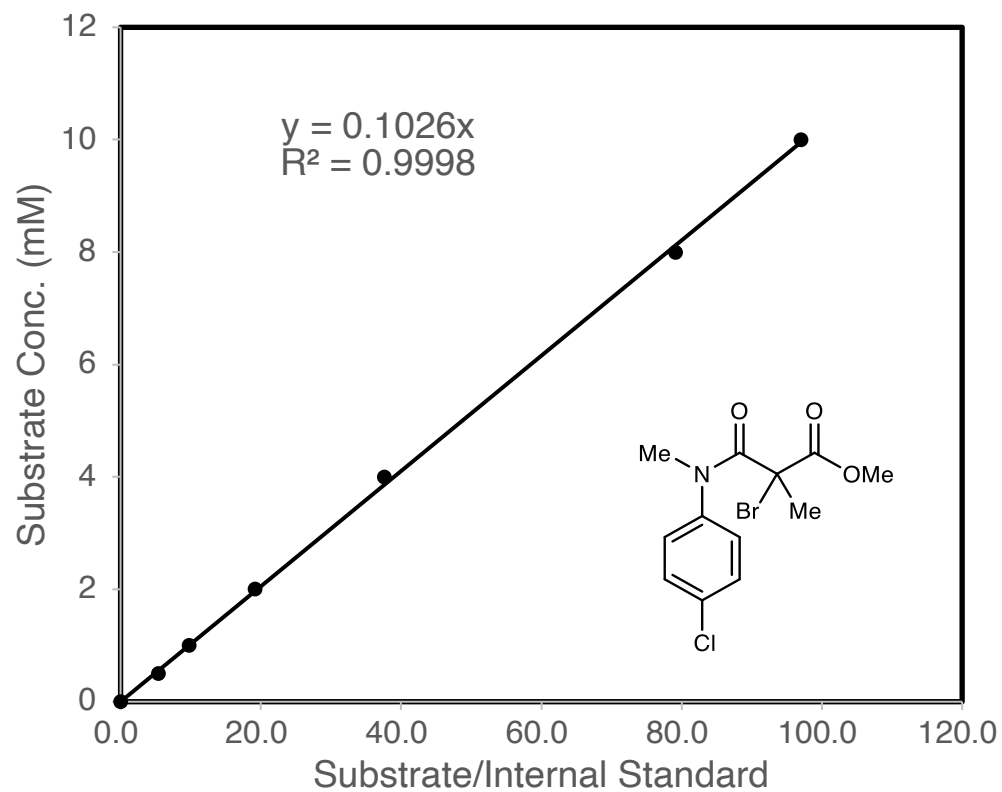


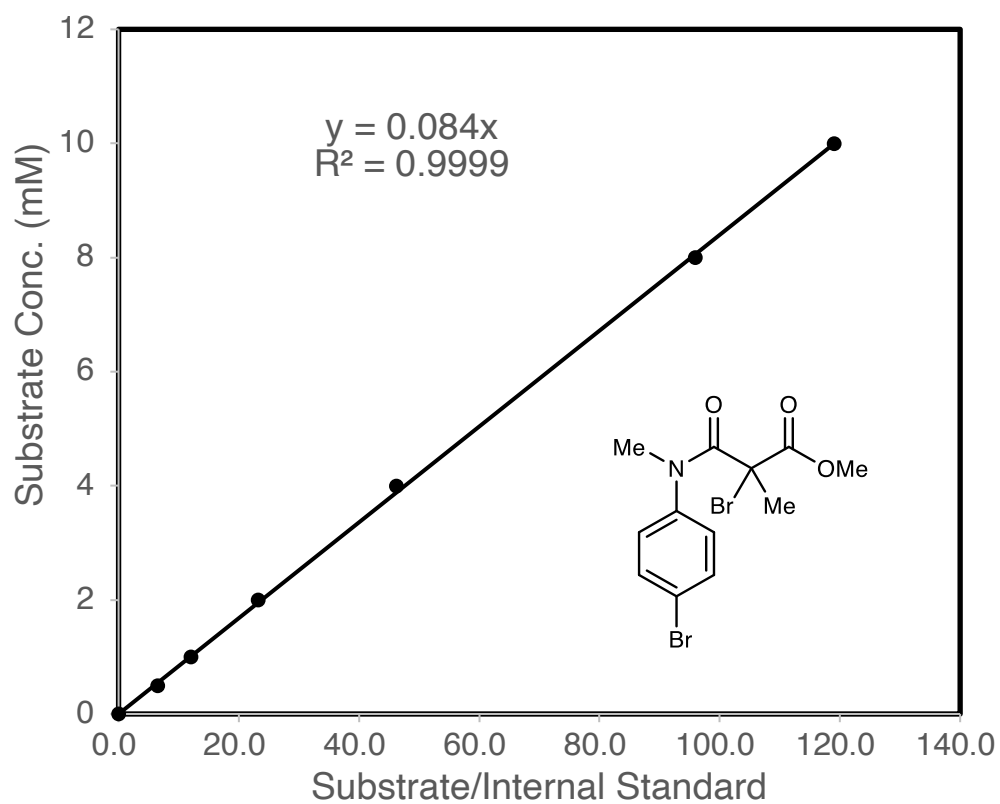
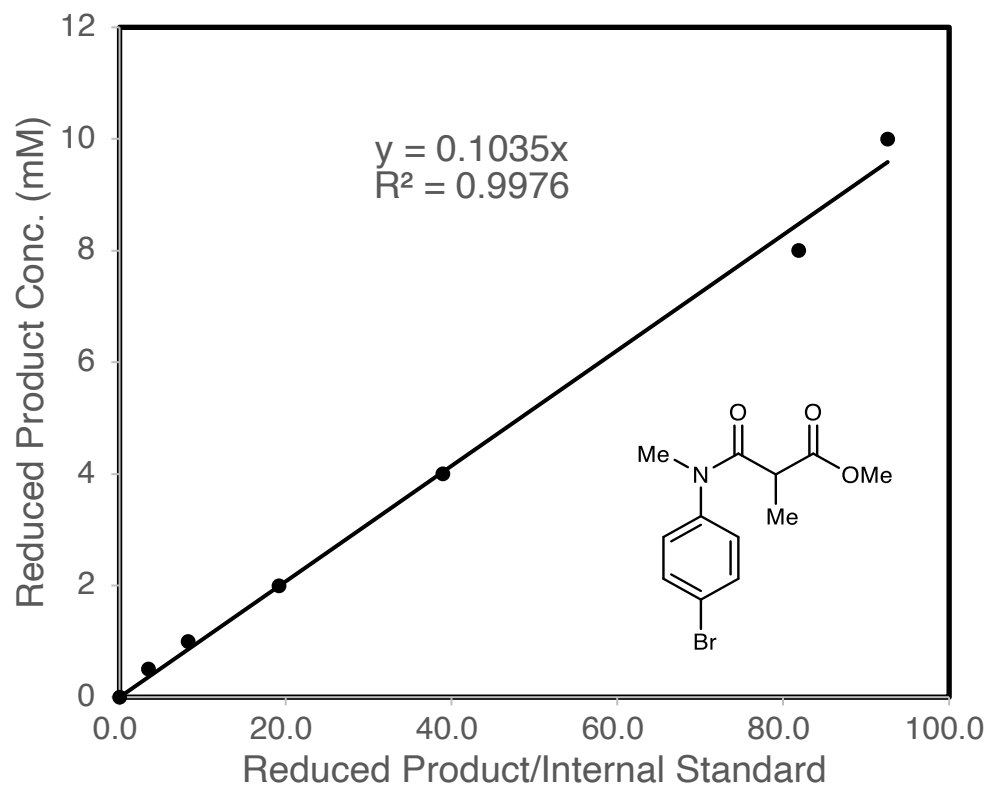


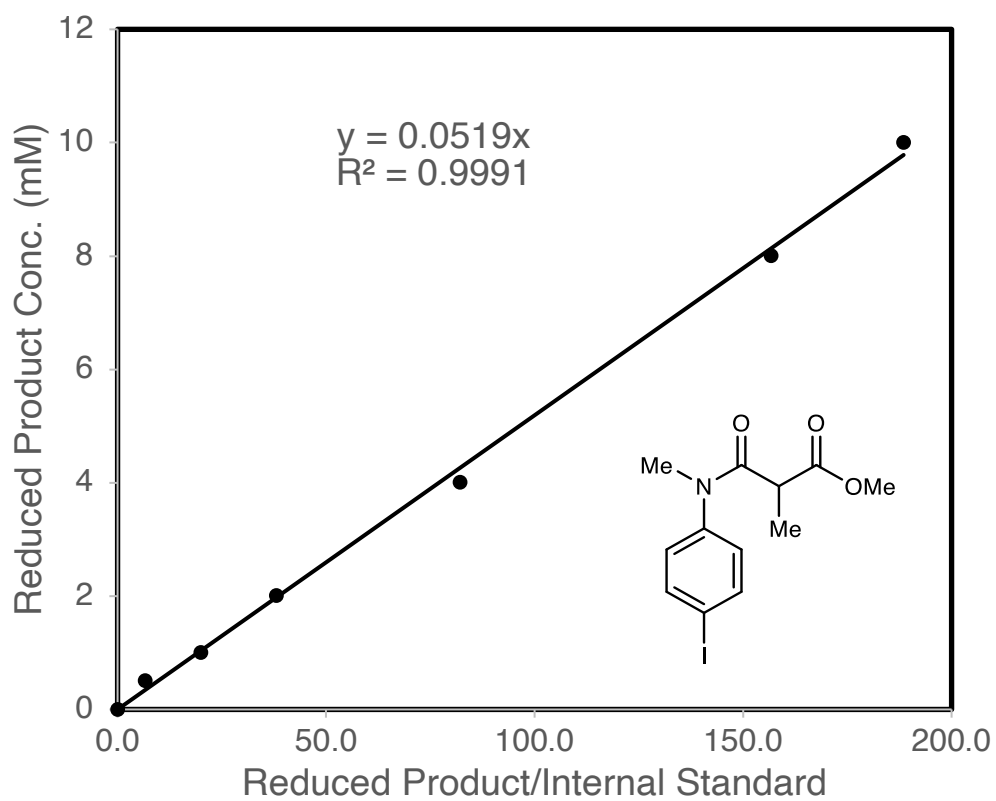
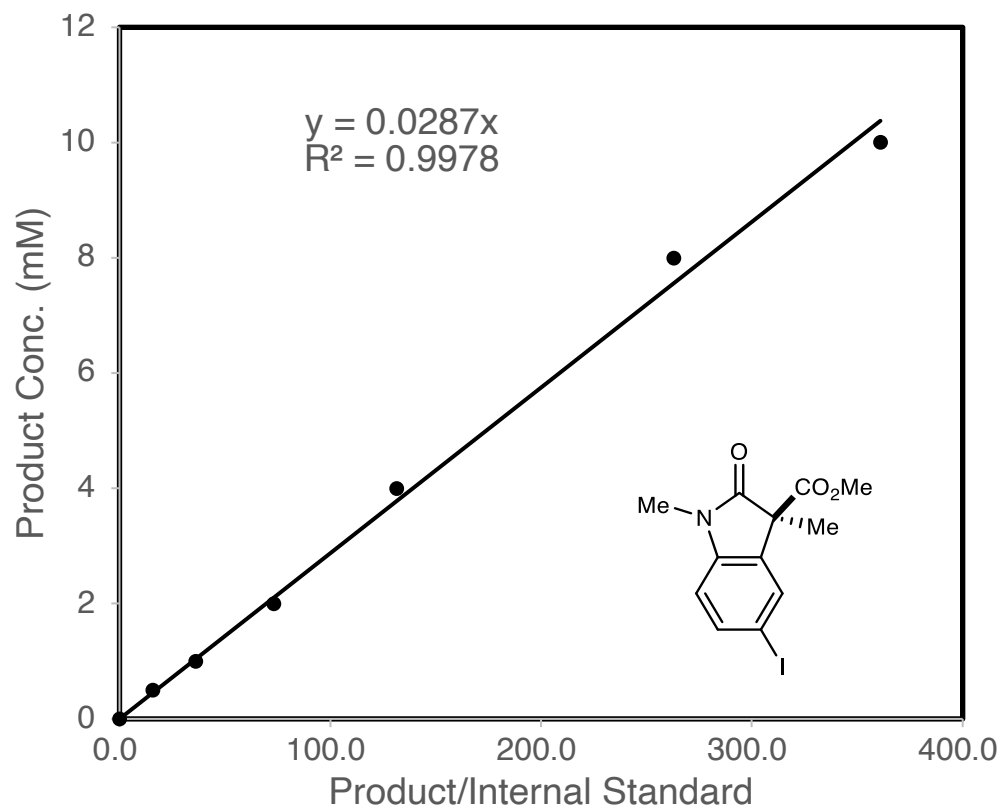


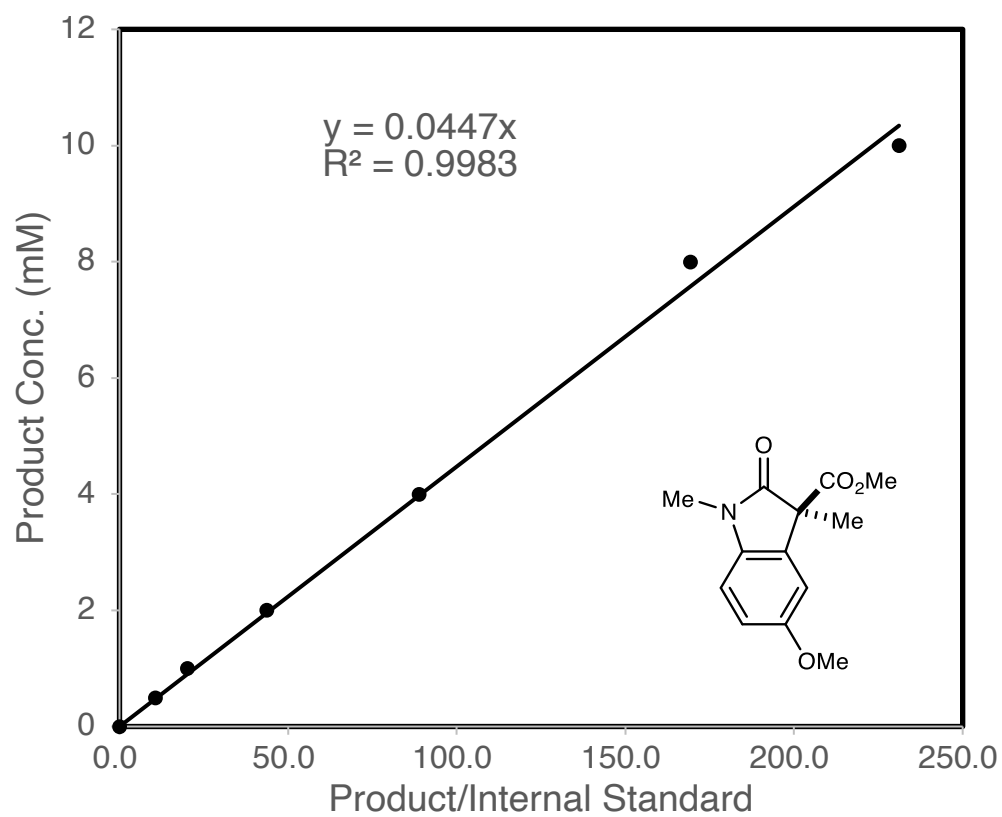
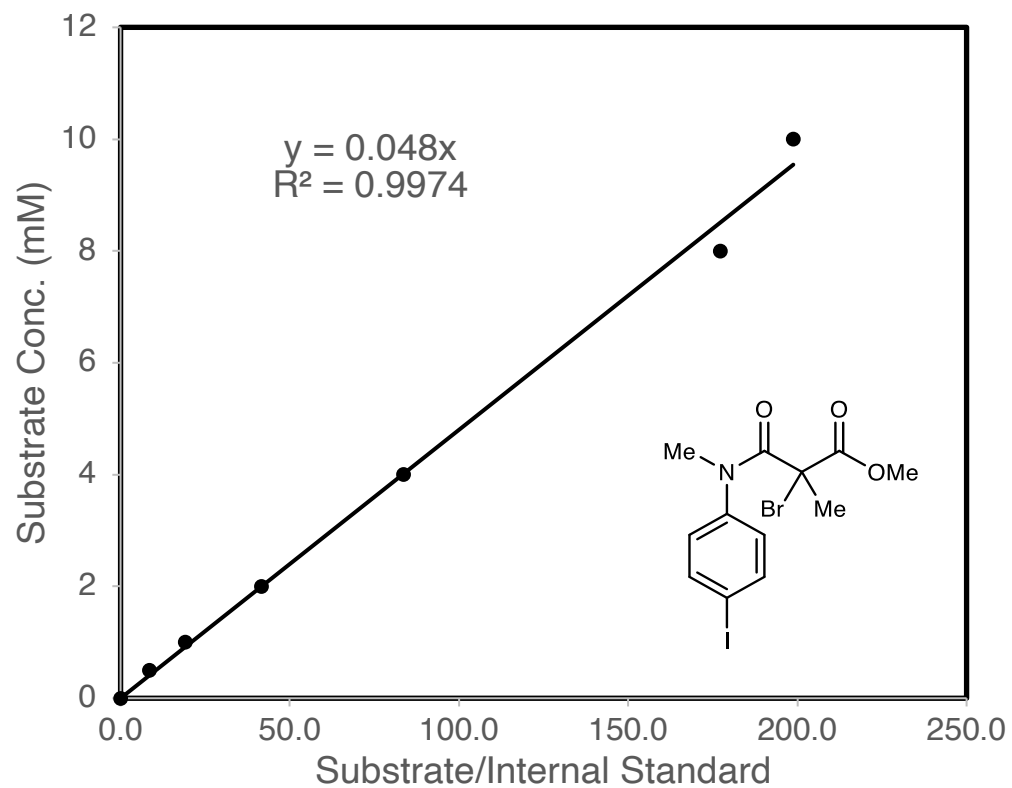


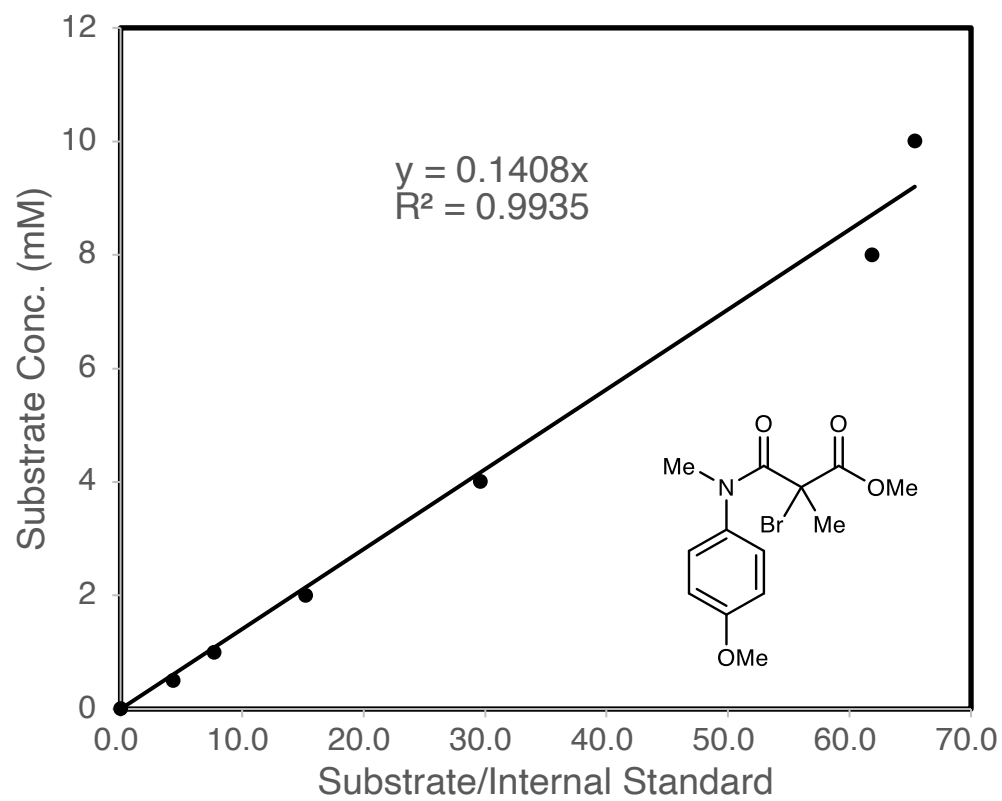
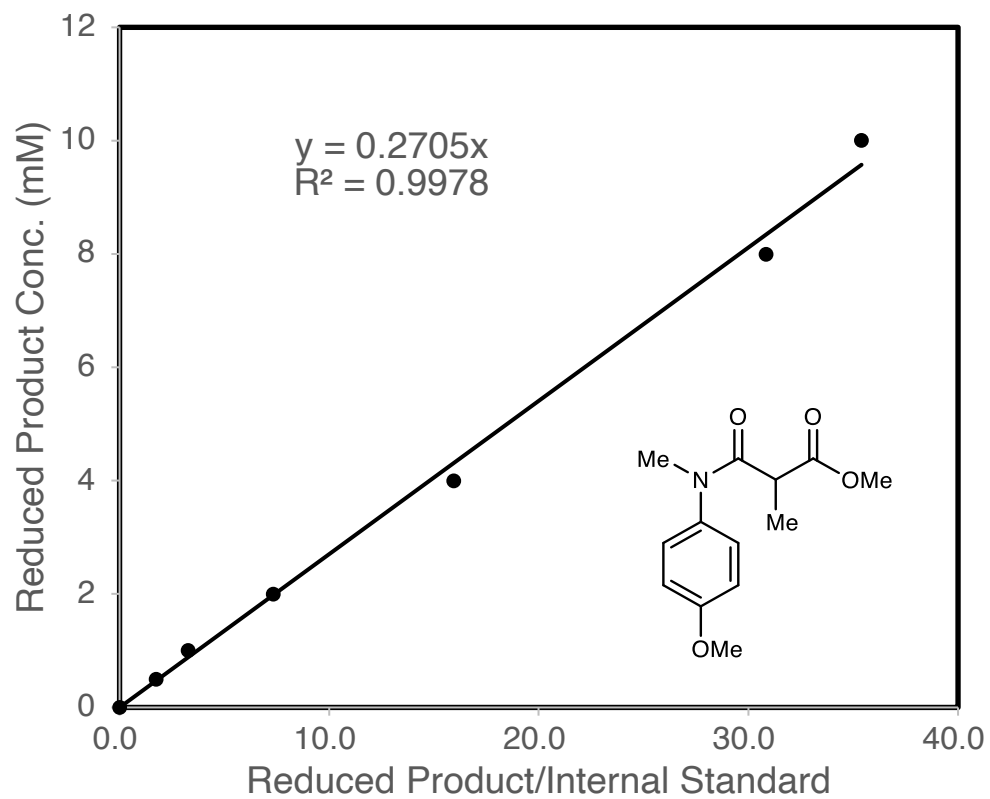


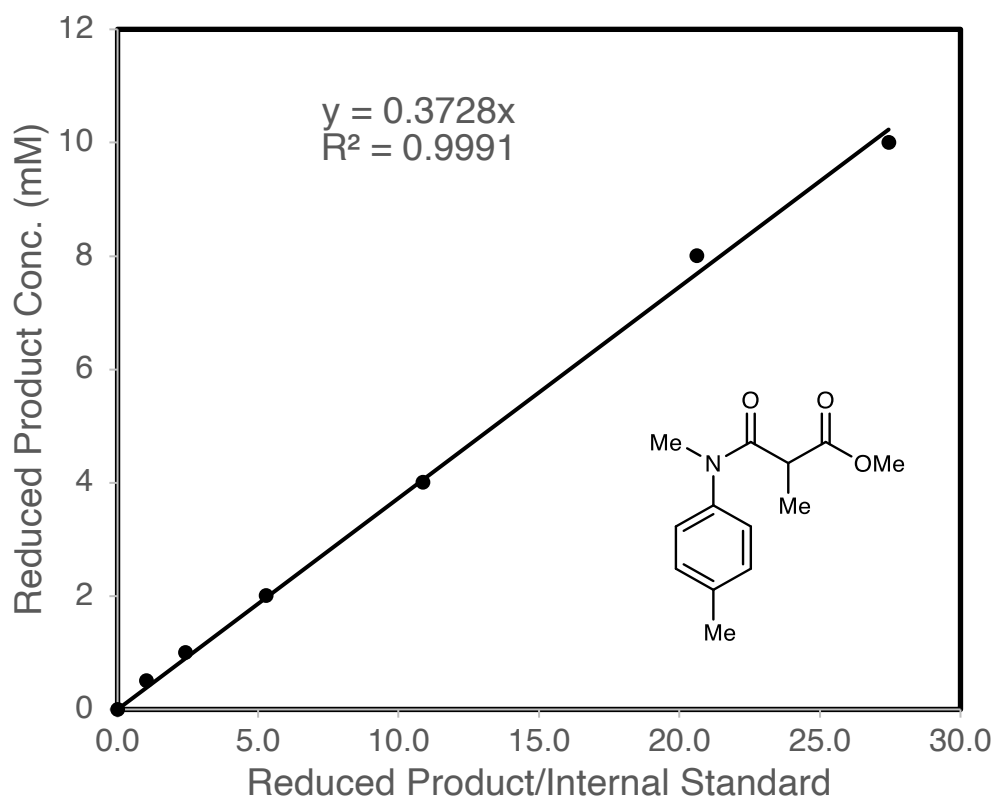
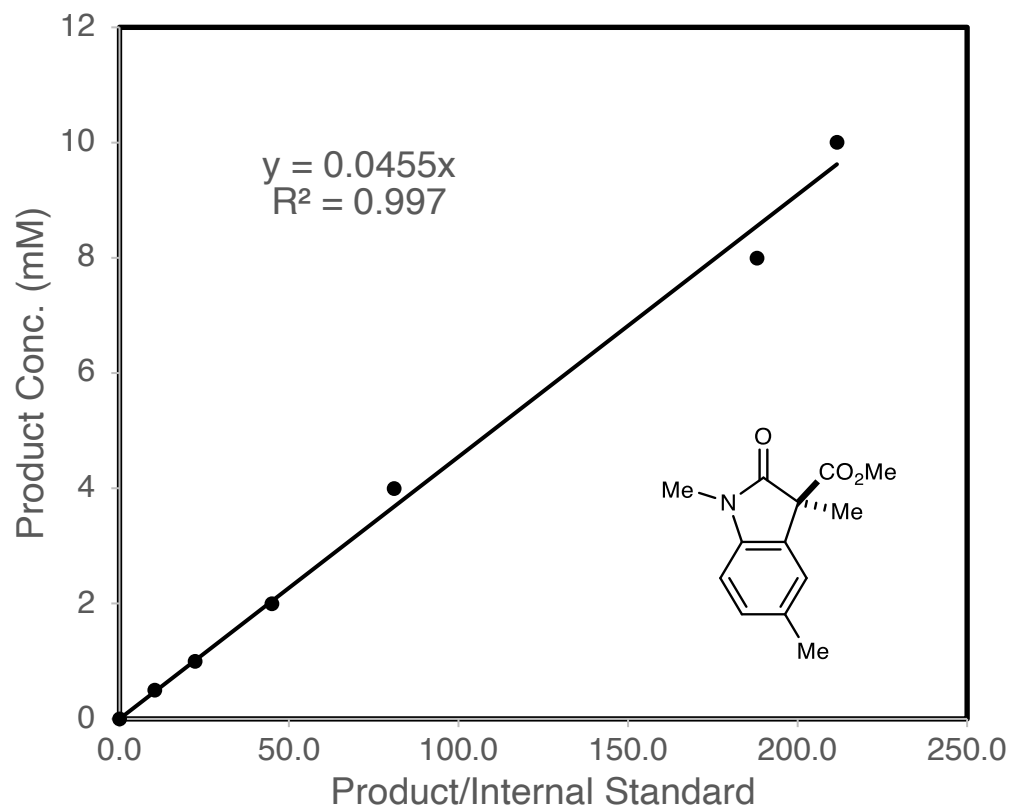


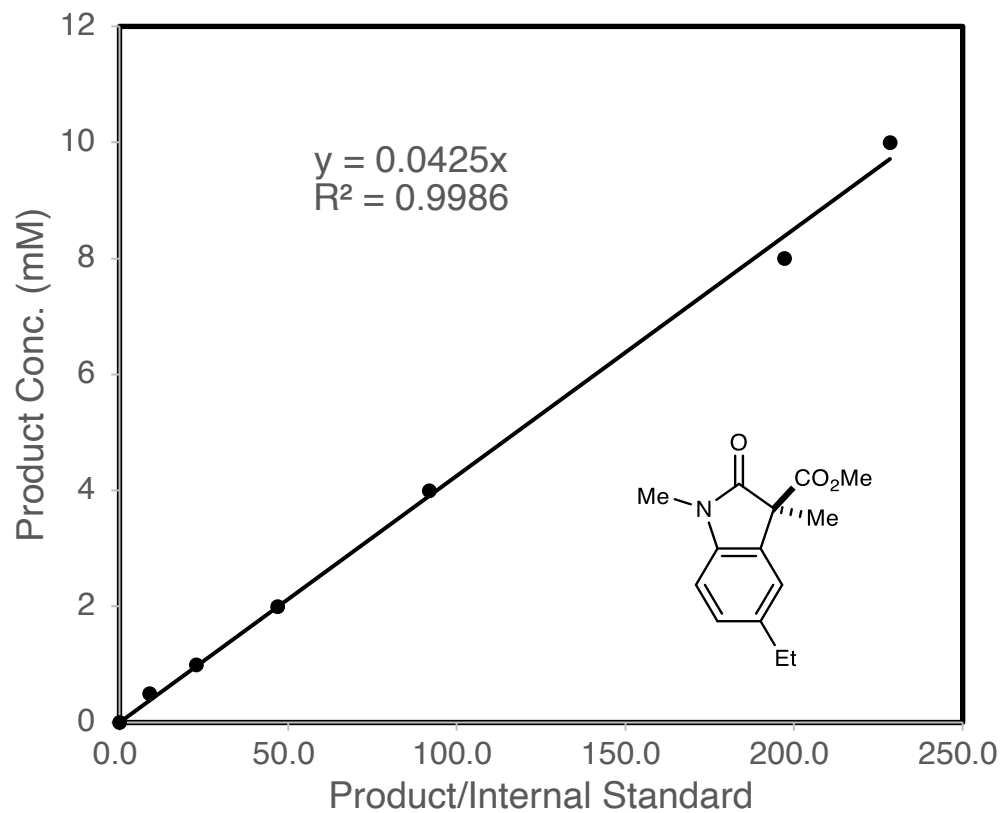
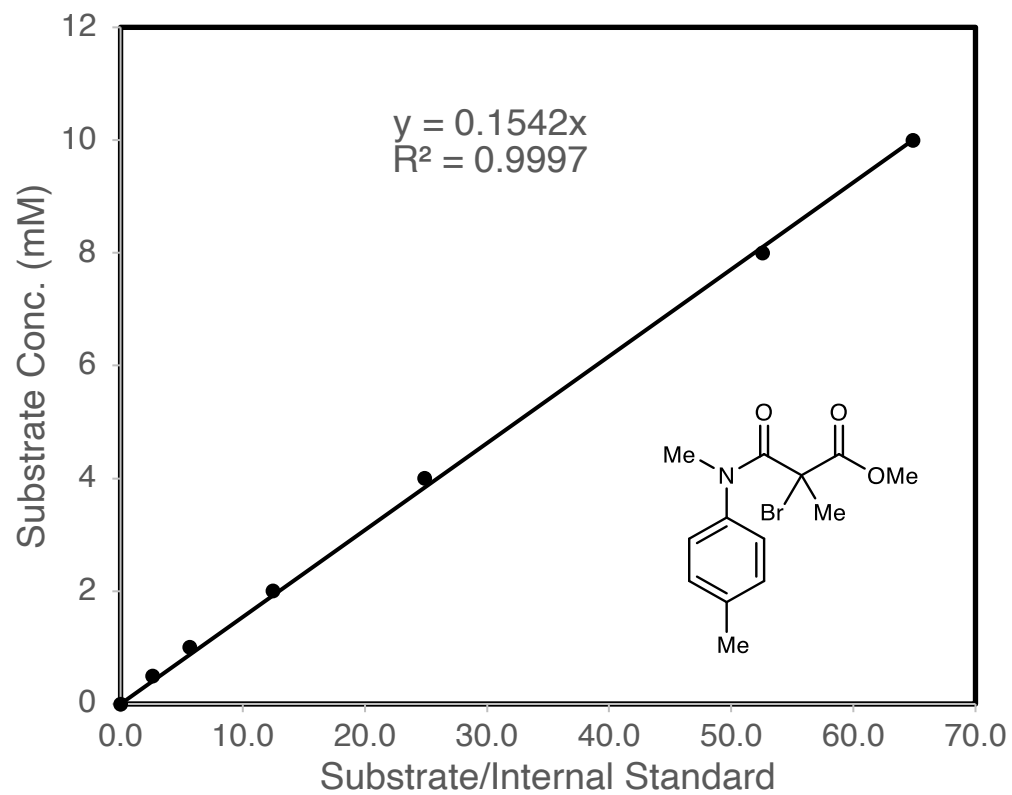


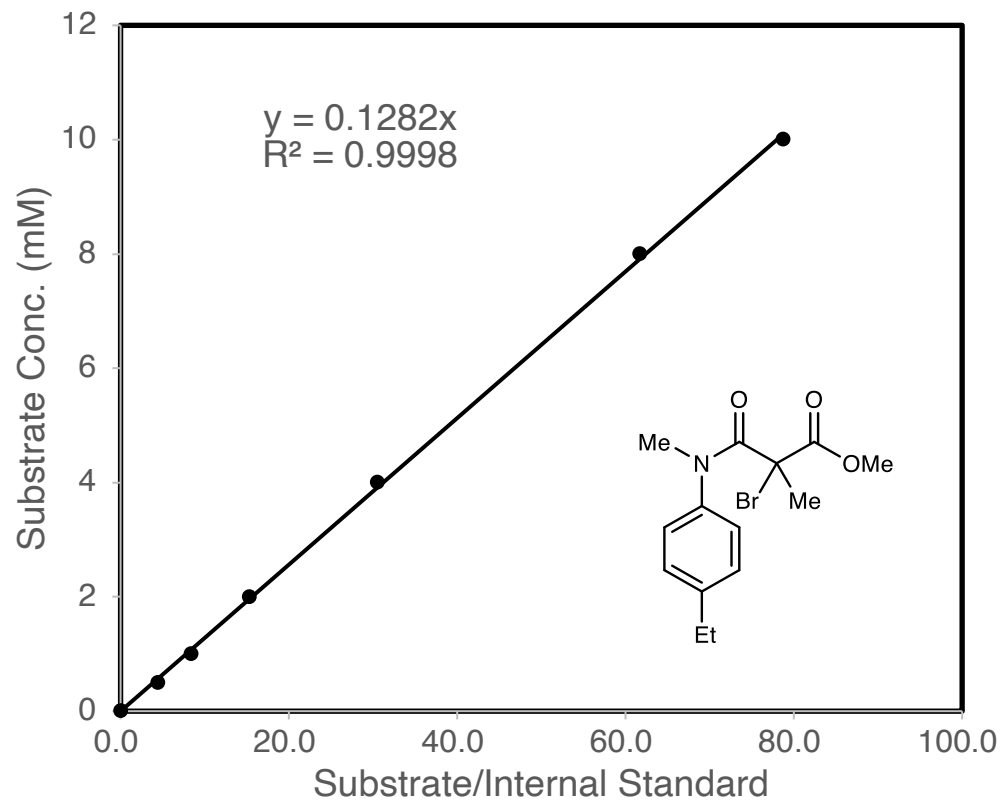
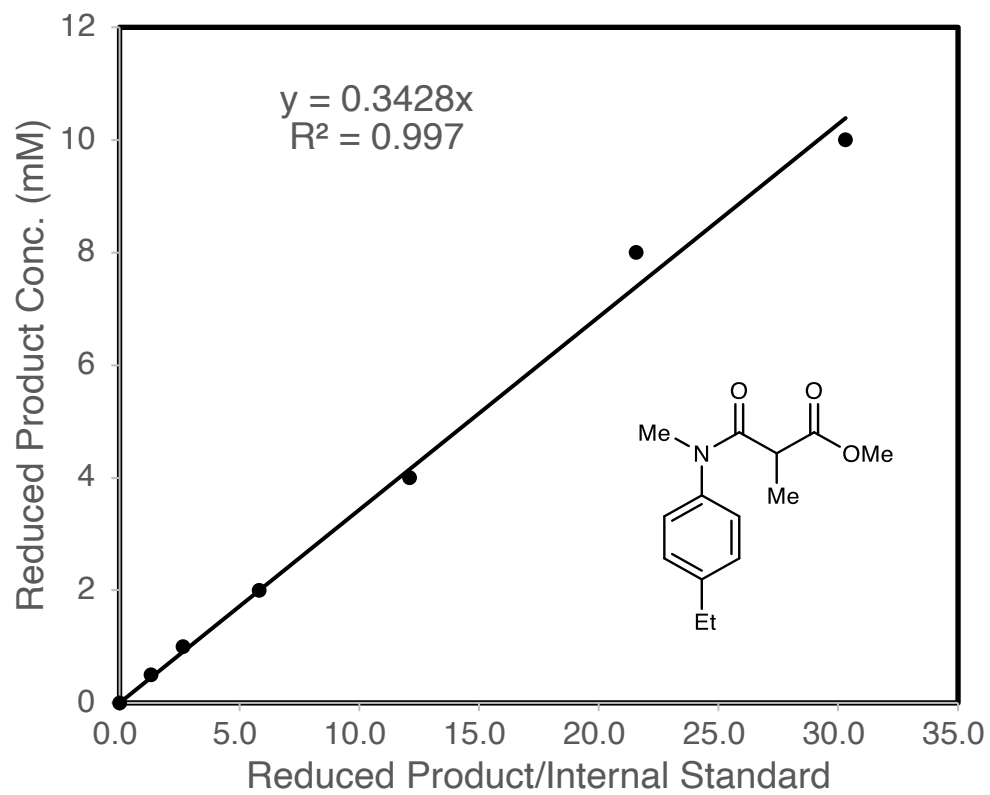


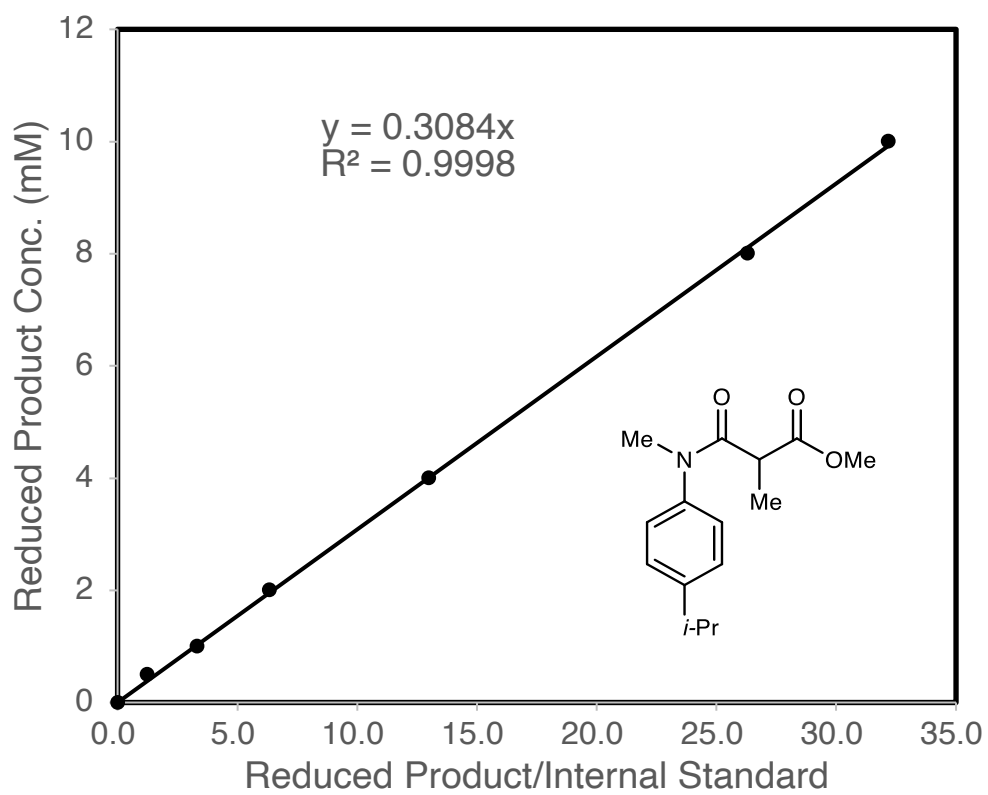
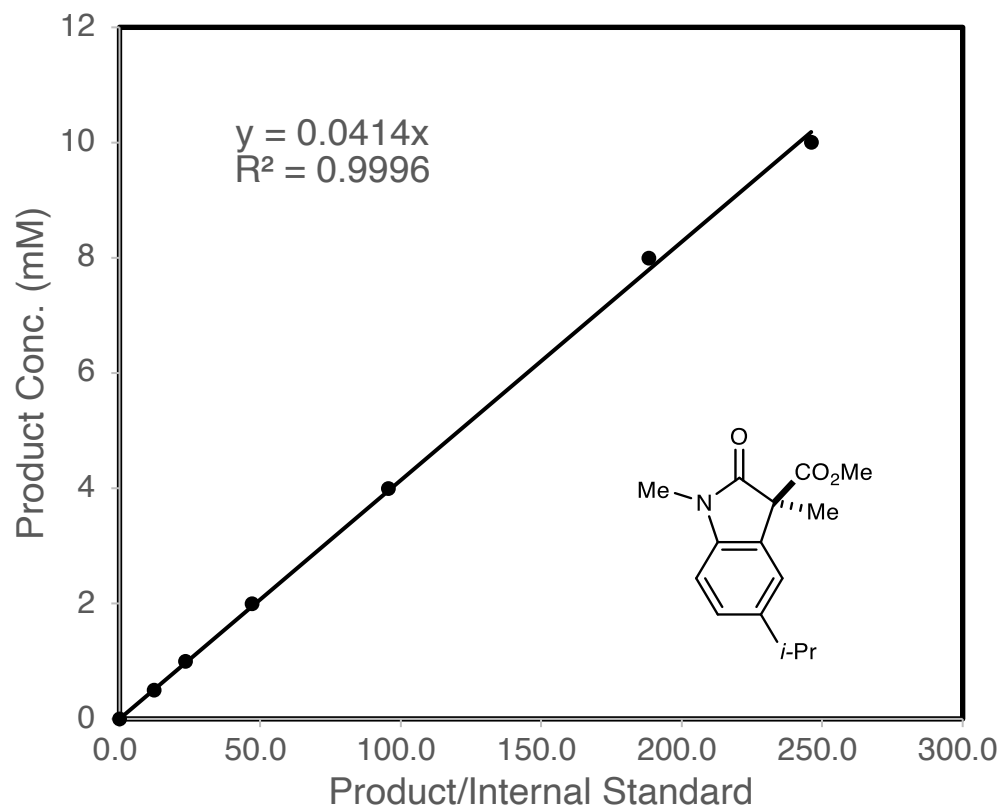


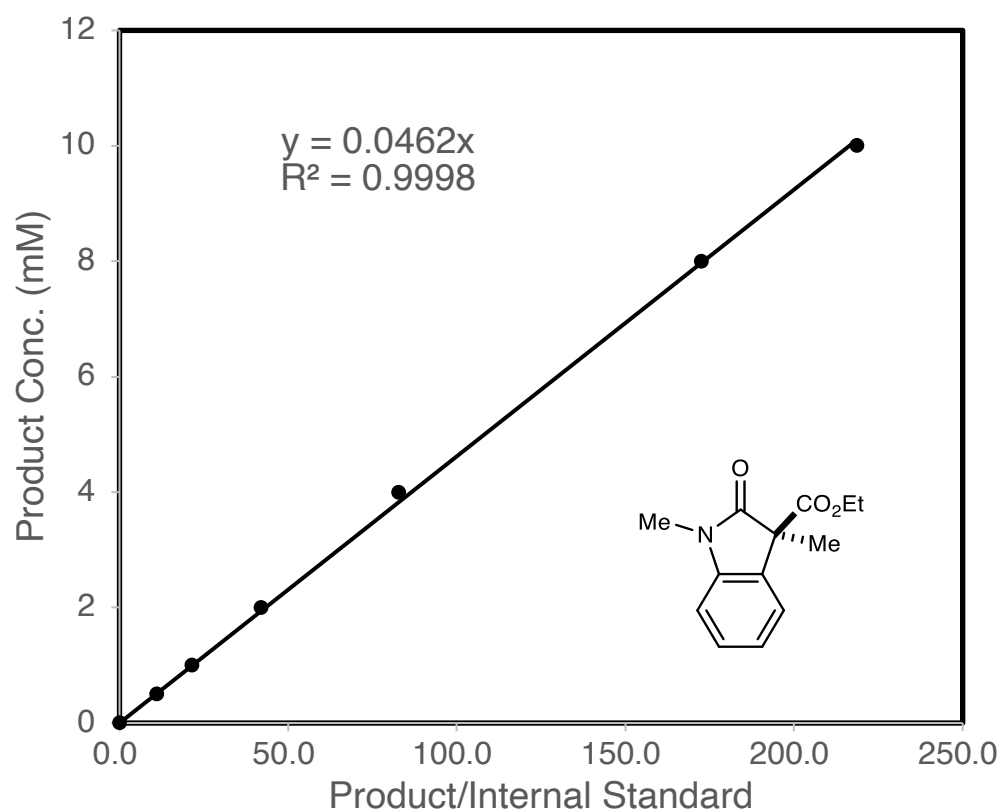
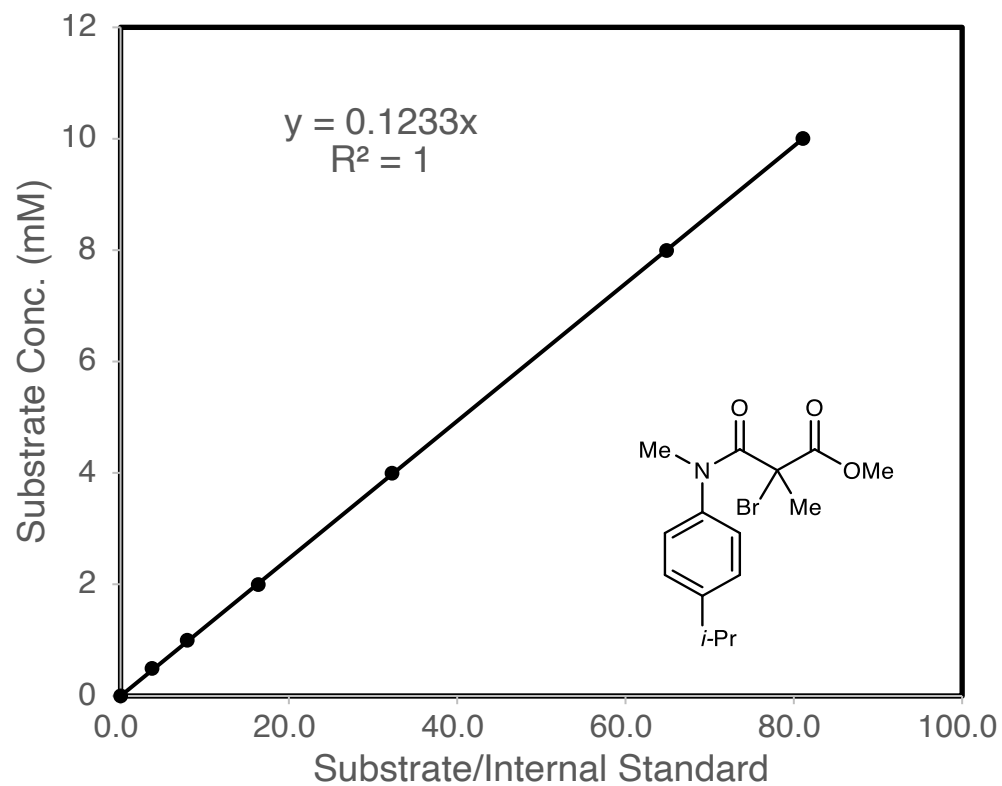


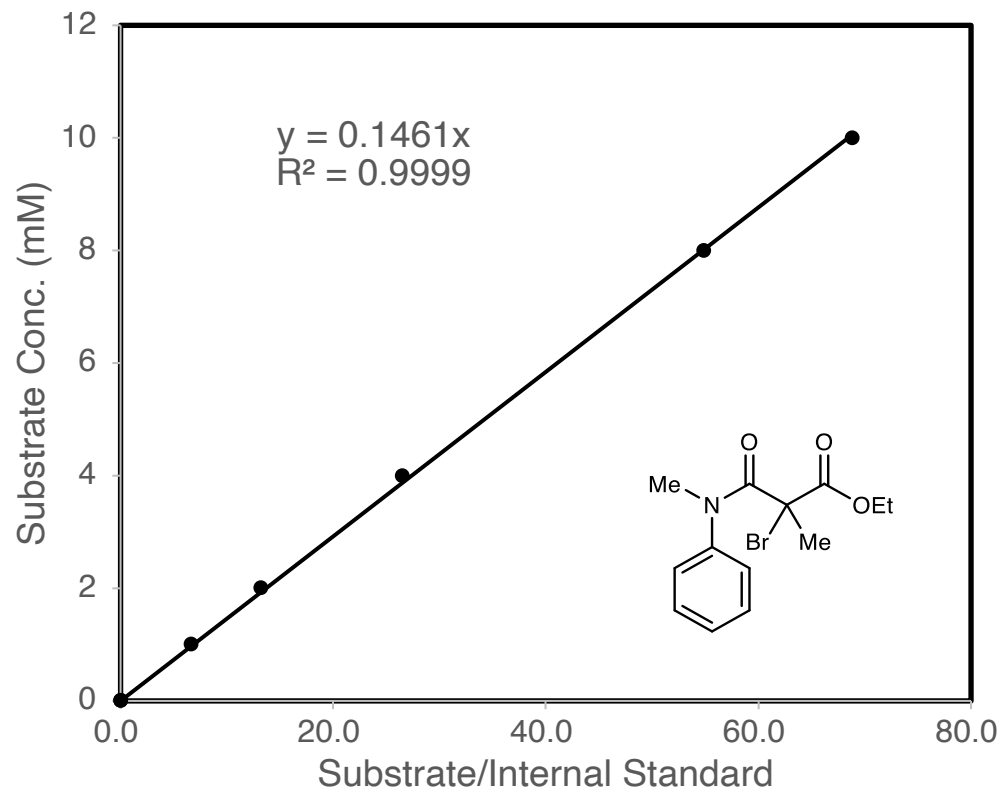
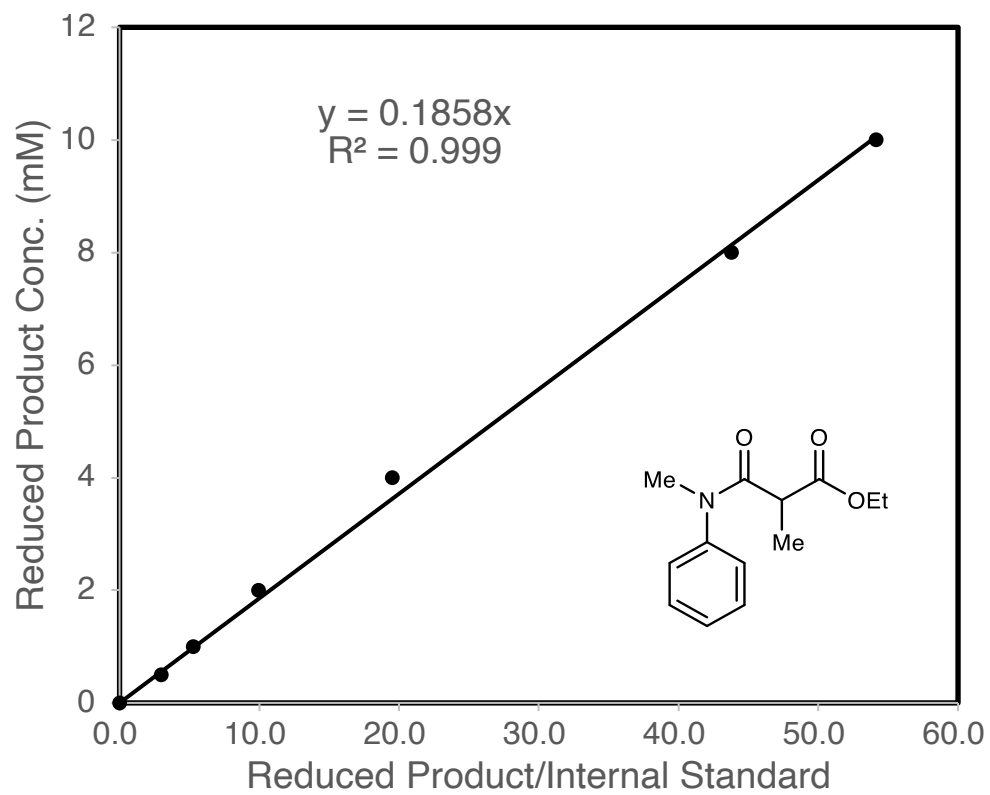


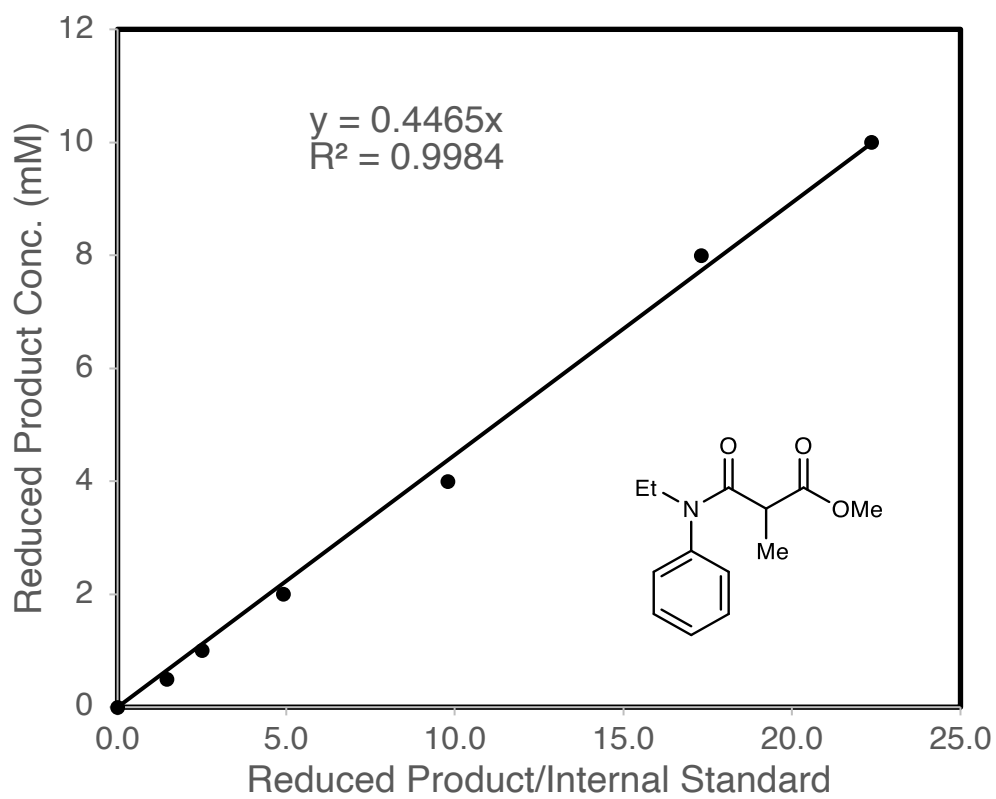
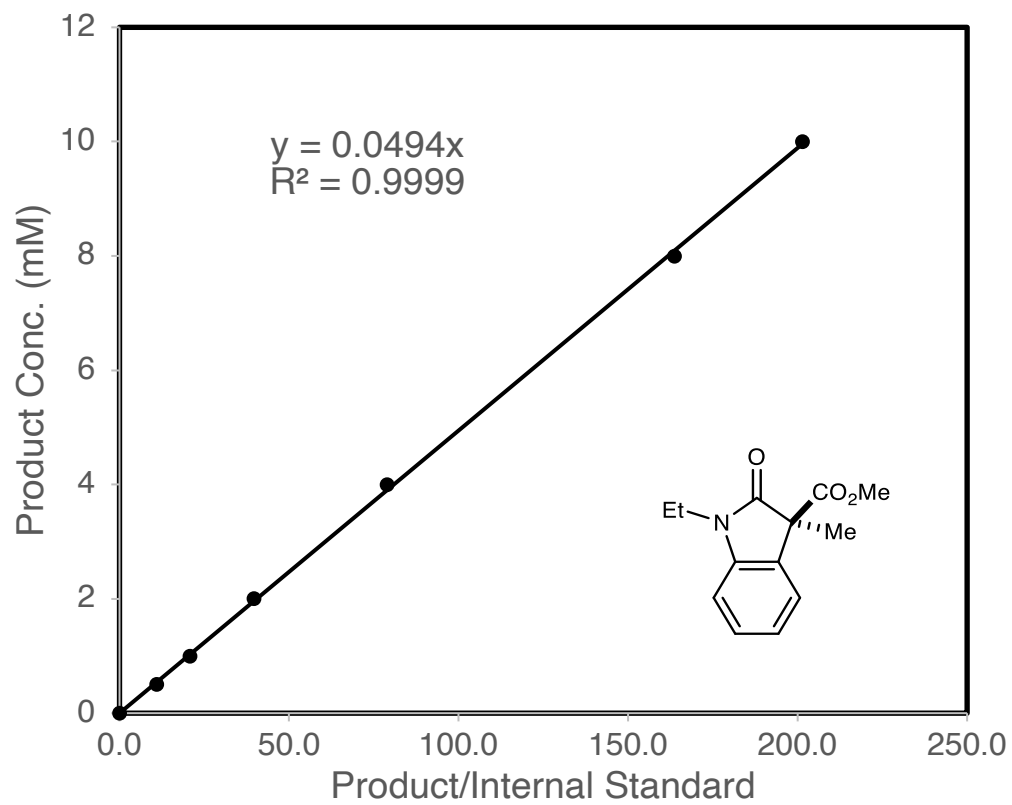


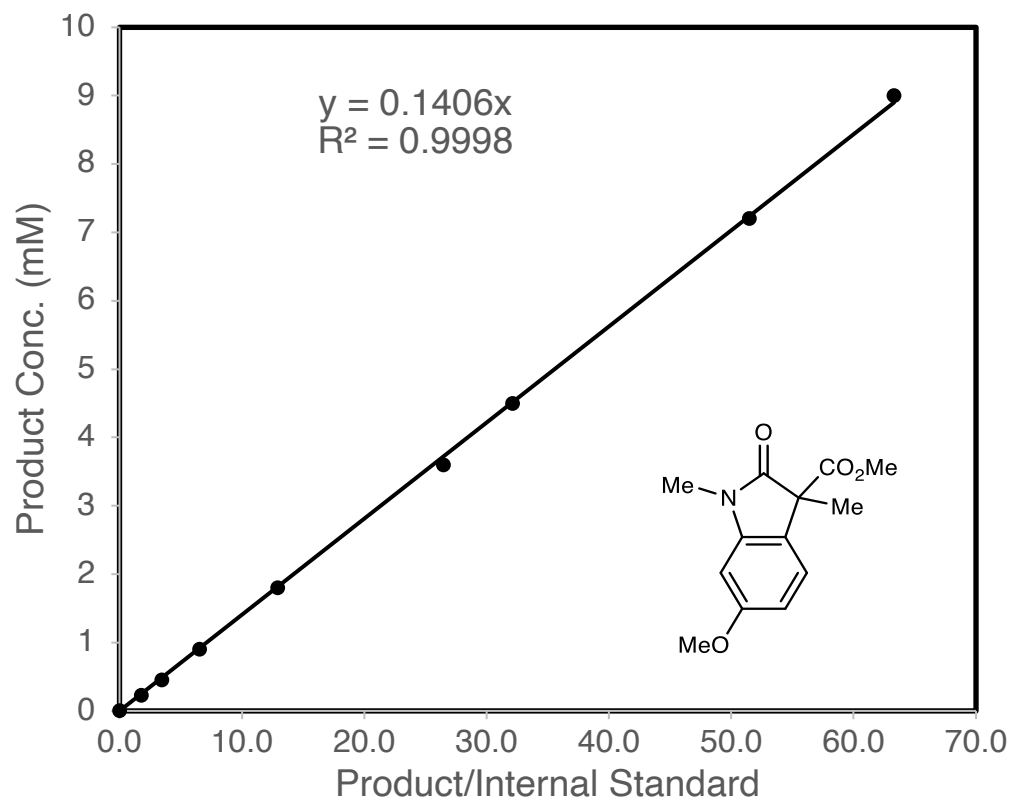
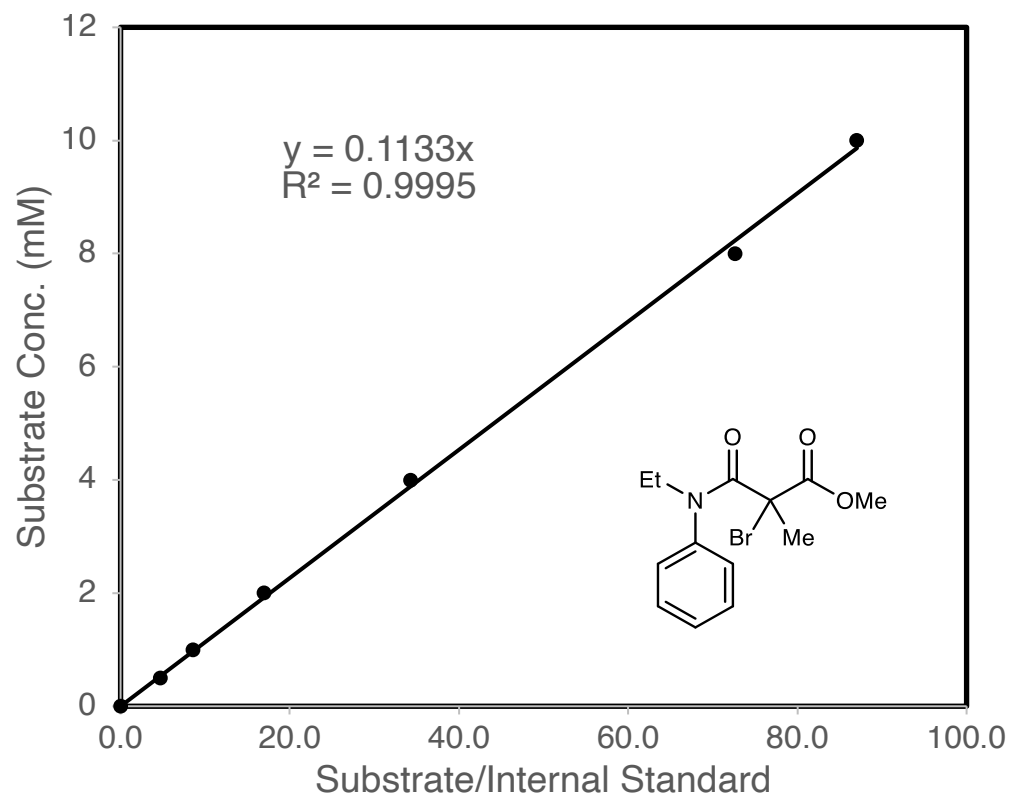


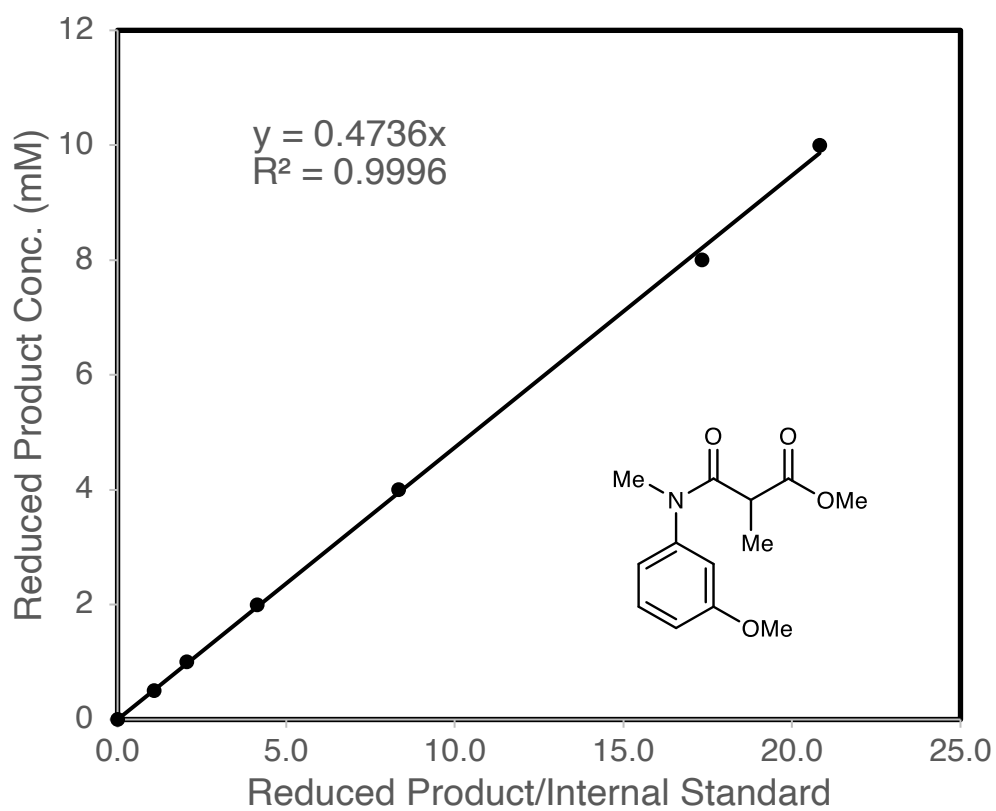
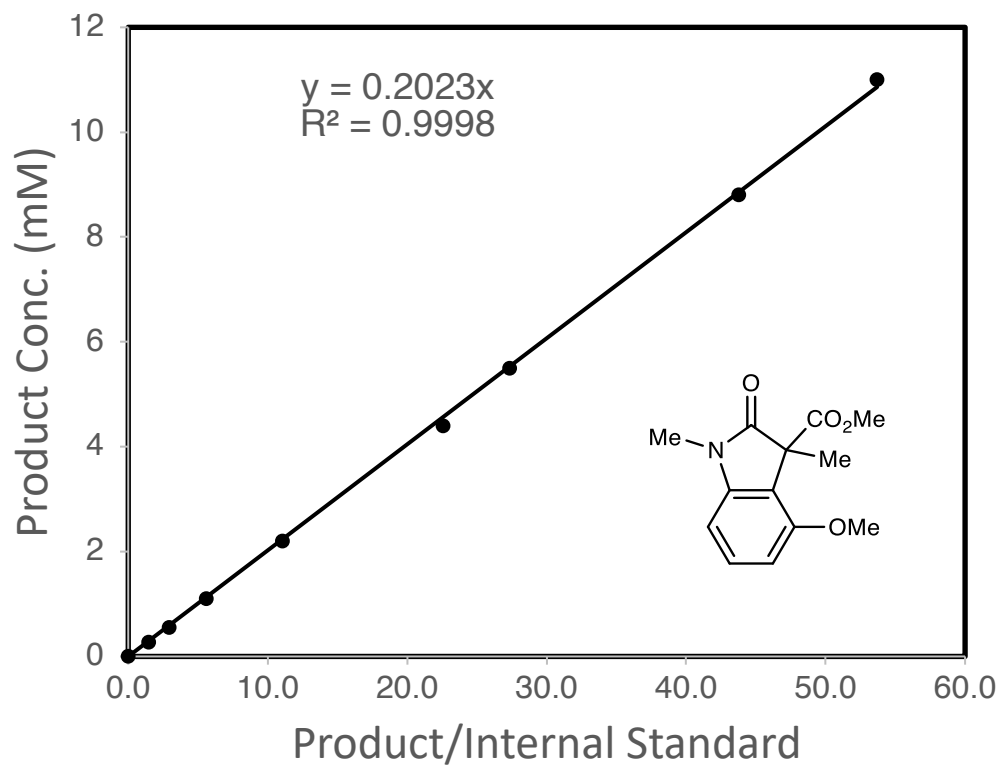


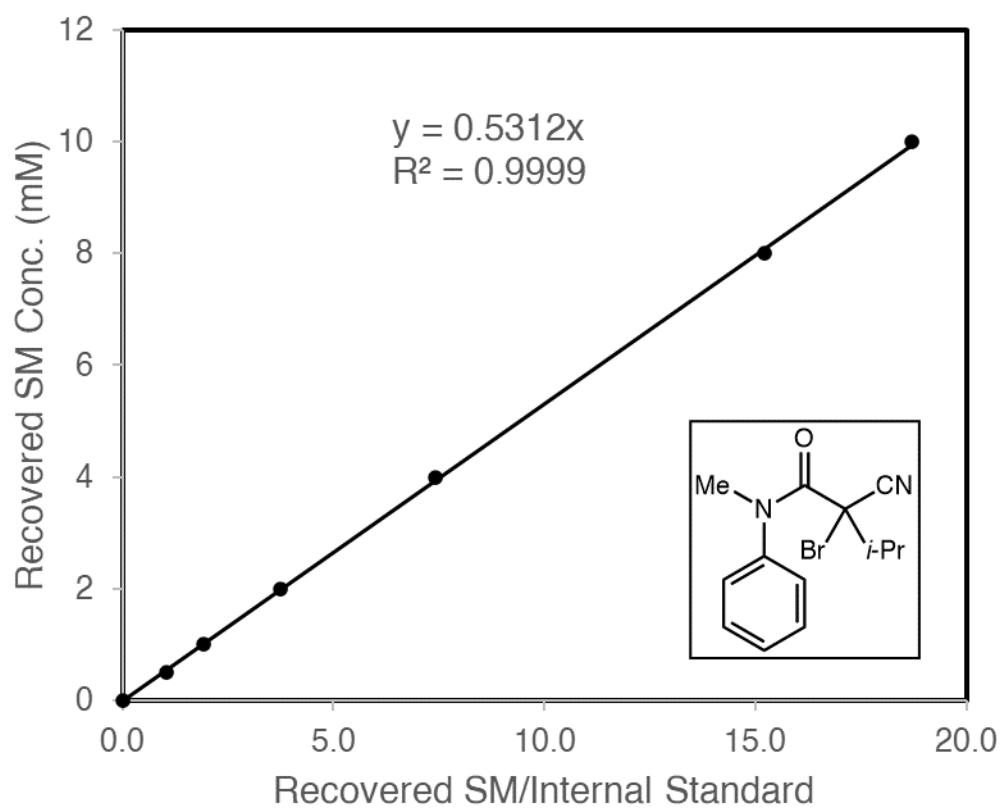
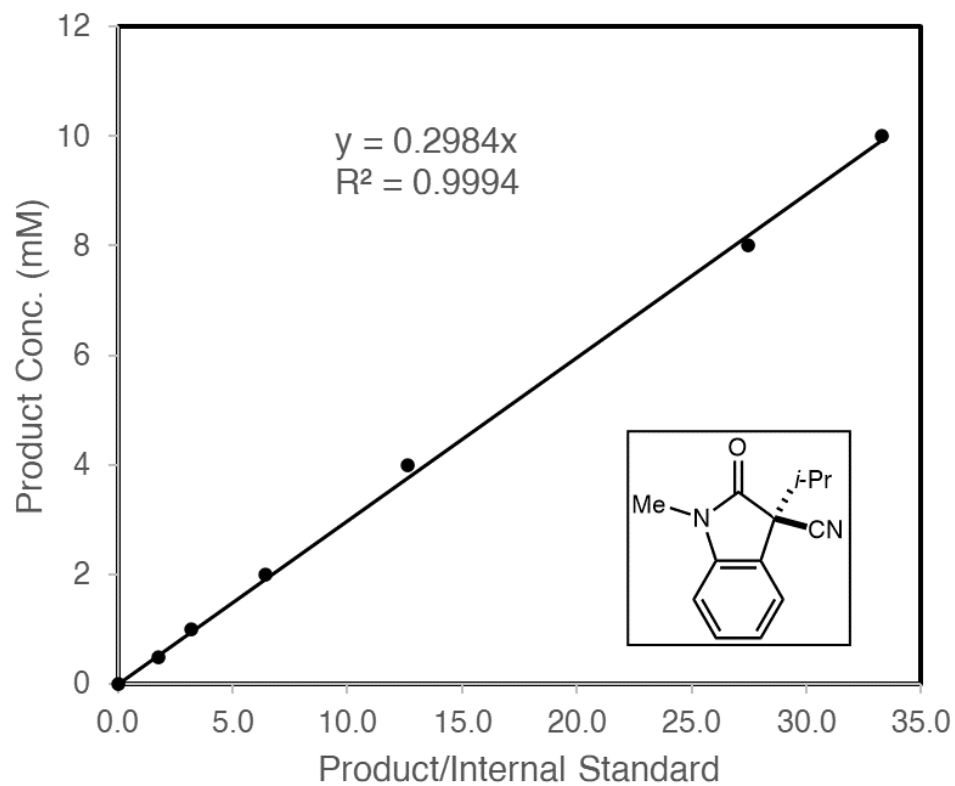


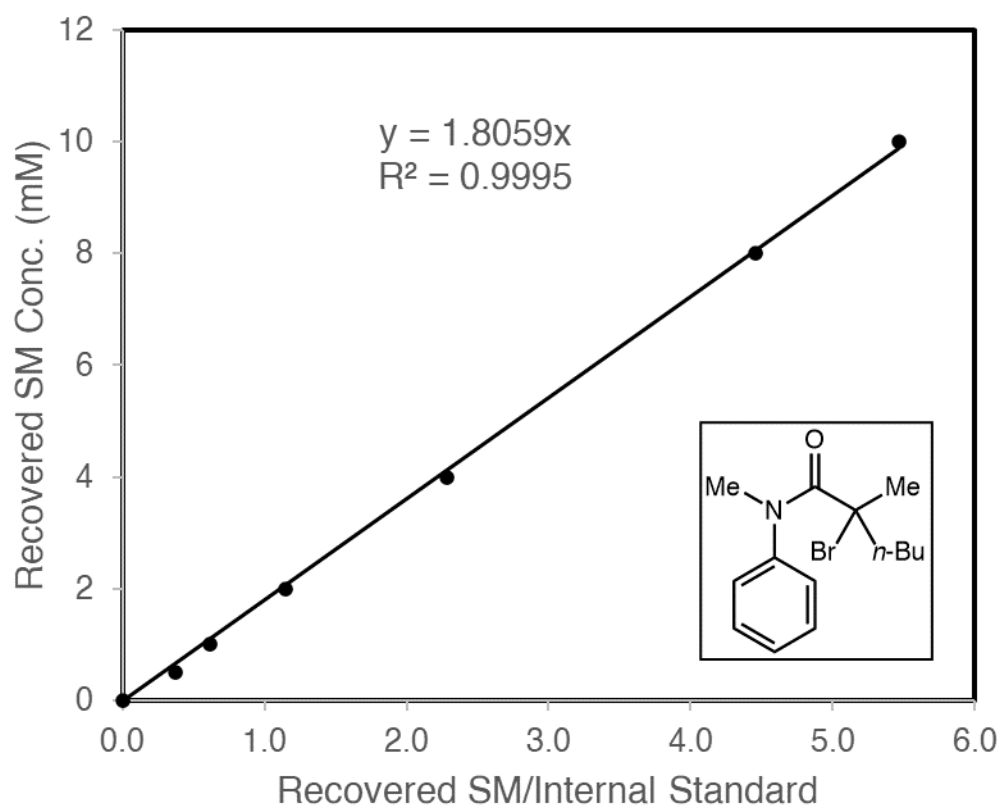
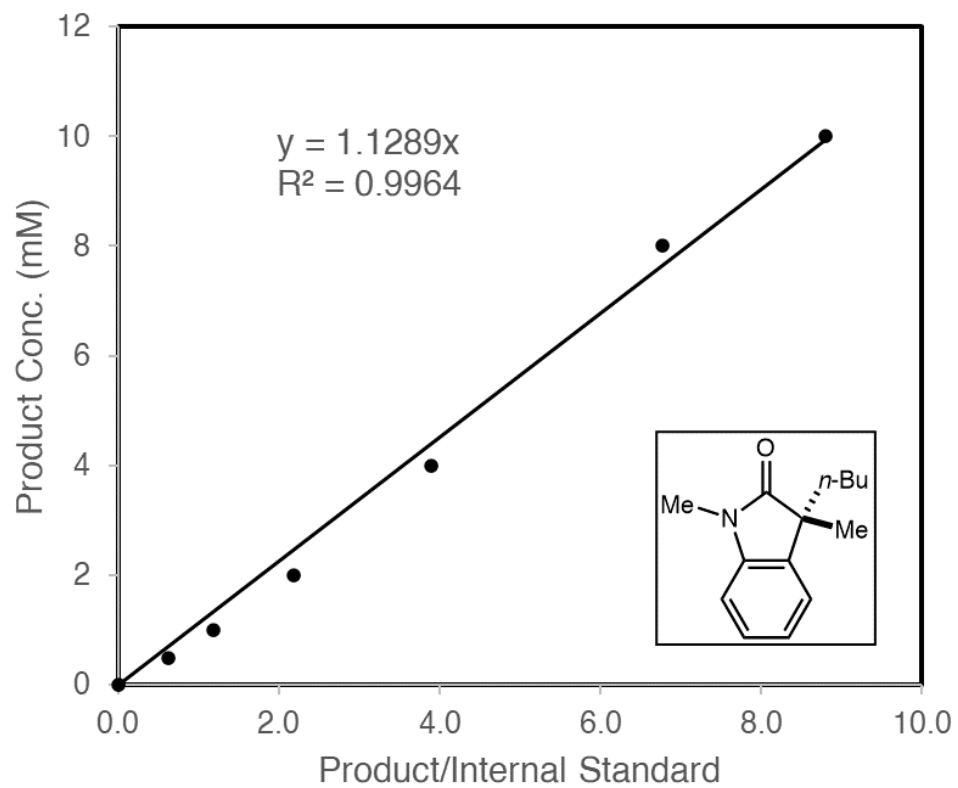


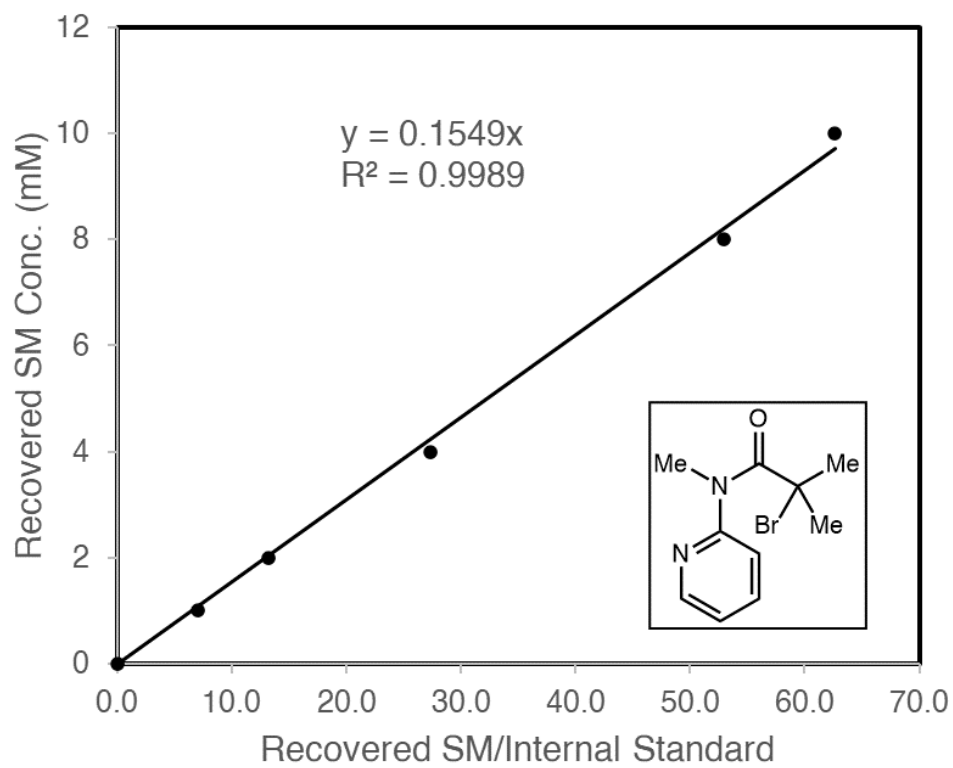
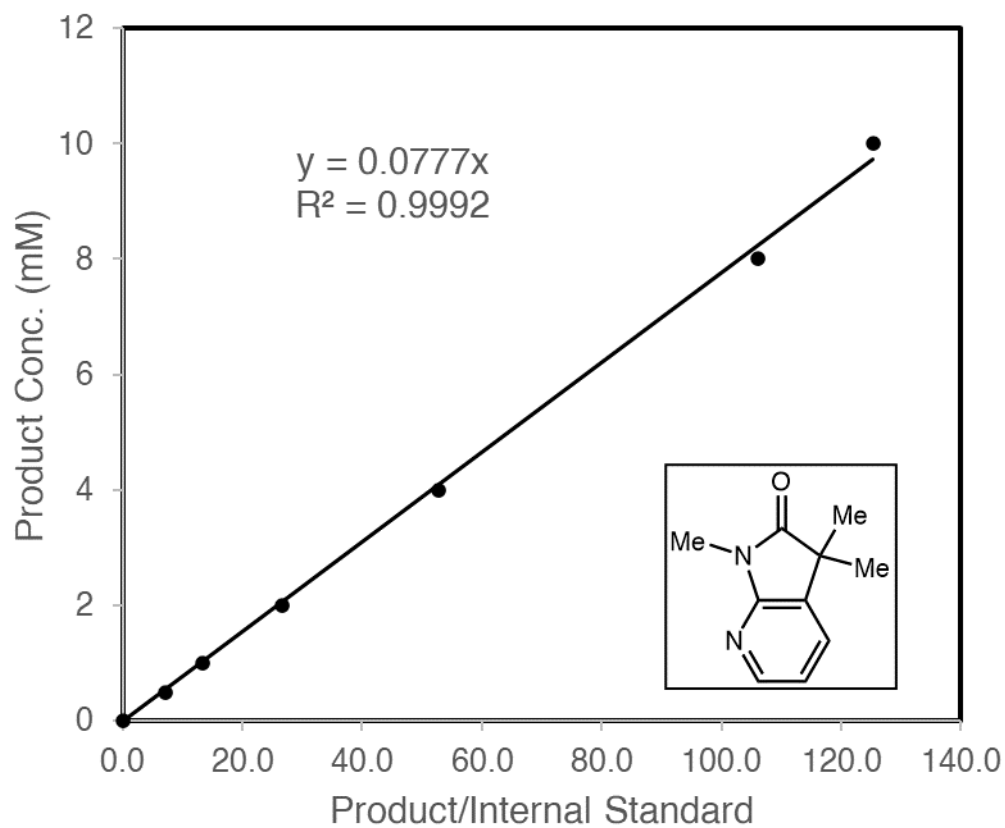






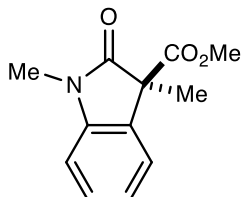




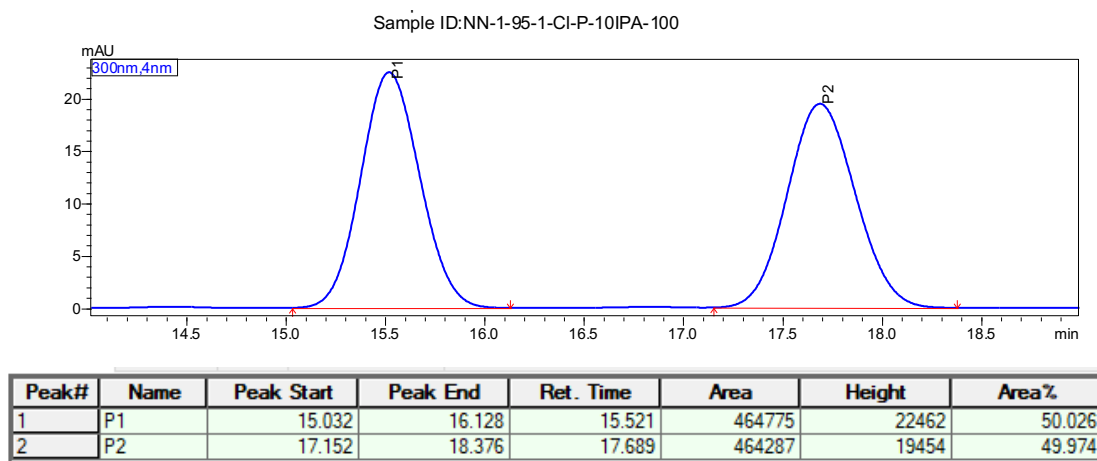


Supplementary Note 11. HPLC traces

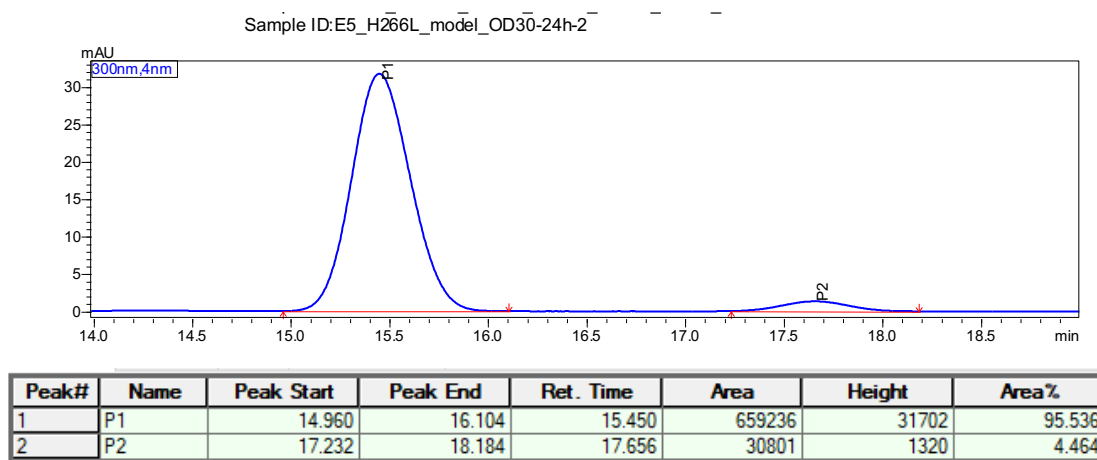
Methyl 1,3-dimethyl-2-oxoindoline-3-carboxylate



Racemic **2a** (HPLC analysis):

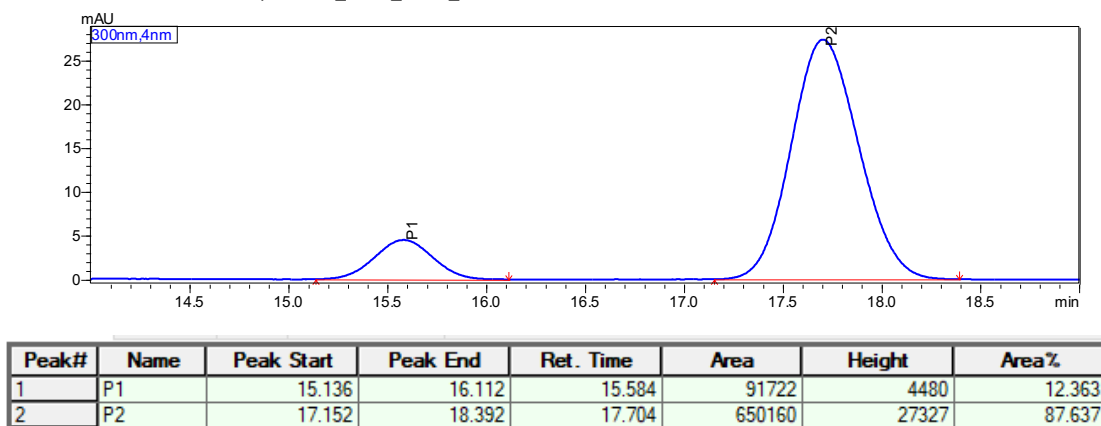


Enantioenriched **2a** obtained using P450_{arc1} (HPLC analysis): 96:4 e.r.



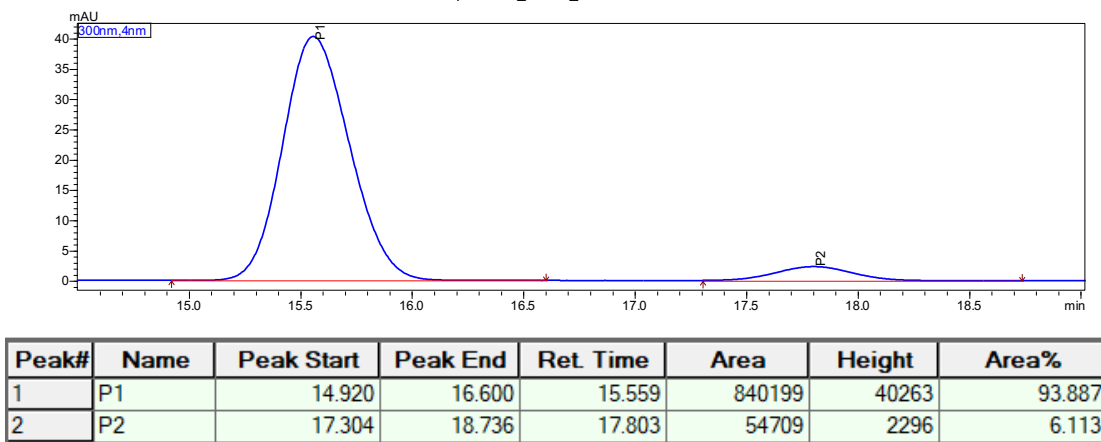
Enantioenriched **2a** obtained using P450_{arc2} (HPLC analysis): 12:88 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330F_G74P_OD30_model-24h-1.lcd
Sample Name:E8_G437A_V327P_N70S_A330F_G74P_OD30_model-24h-1
Sample ID:E8_G74P_OD30_model-24h-1

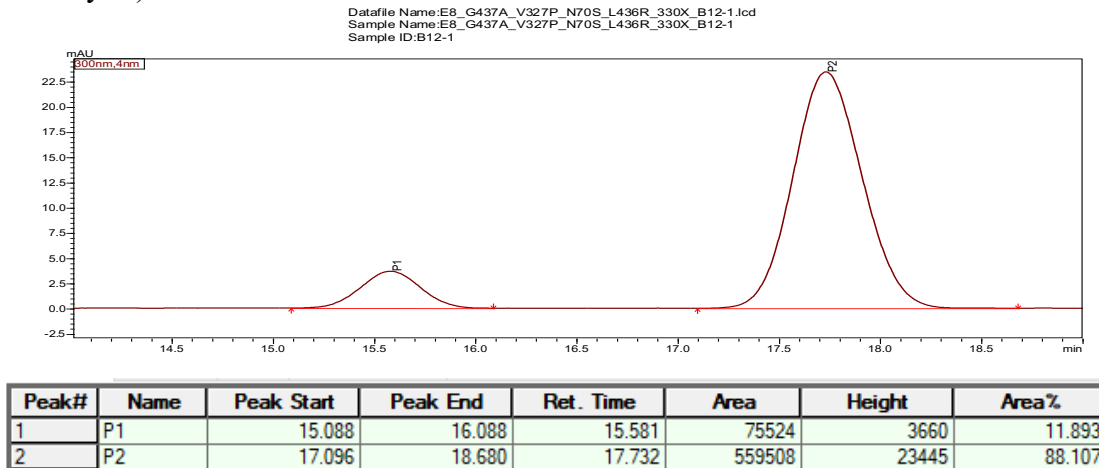


Enantioenriched **2a** obtained from chloride substrate **3a** using P450_{arc1} (HPLC analysis): 94:6 e.r.

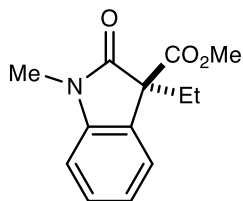
Datafile Name:E5_H266L_OD120-1.lcd
Sample Name:E5_H266L_OD120-1
Sample ID:E5_H266L_OD120-1



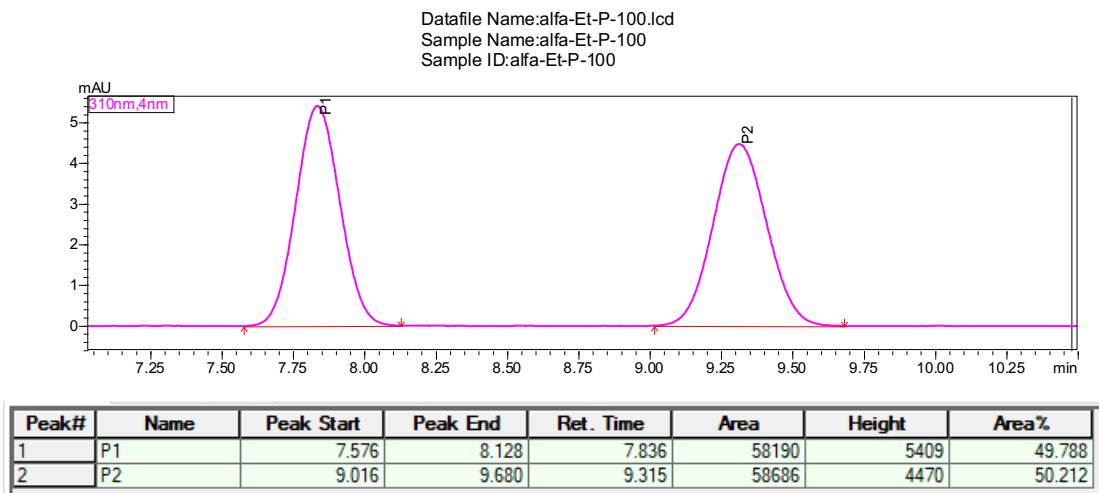
Enantioenriched **2a** obtained from chloride substrate **3a** using P450_{acr2} P74G L436R F330V (HPLC analysis): 12:88 e.r.



Methyl (*R*)-3-ethyl-1-methyl-2-oxindoline-3-carboxylate

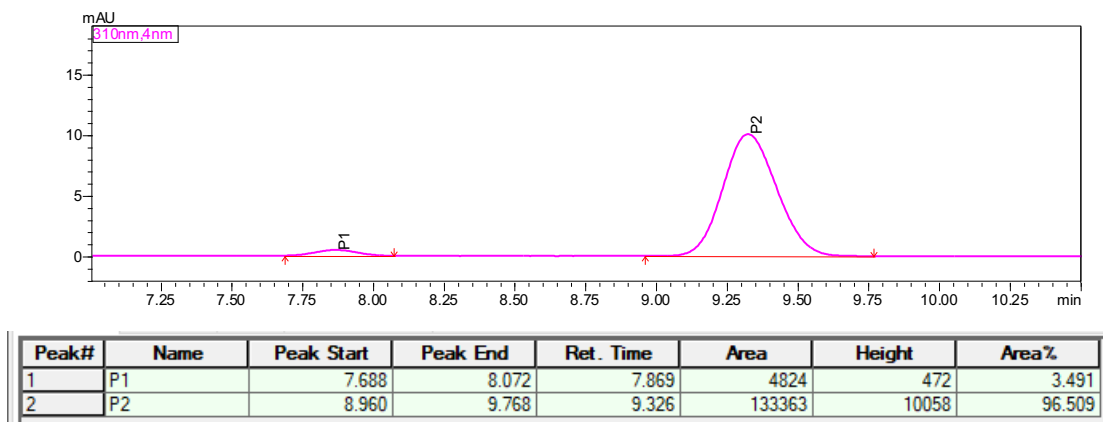


Racemic **2b** (HPLC analysis):



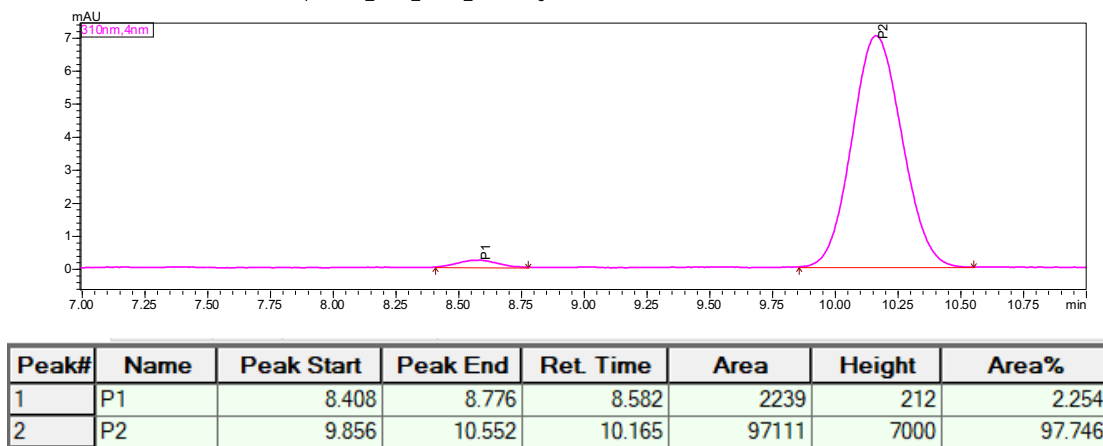
Enantioenriched **2b** obtained using P450_{arc2} (HPLC analysis): 3:97 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330F_G74P_OD15_alfa-Et-1.lcd
Sample Name:E8_G437A_V327P_N70S_A330F_G74P_OD15_alfa-Et-1
Sample ID:E8_G74P_OD15_alfa-Et-1

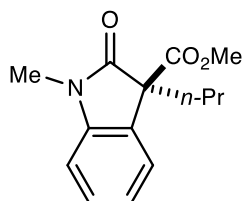


Enantioenriched **2b** obtained using P450_{arc2} (gram-scale, HPLC analysis): 2:98 e.r.

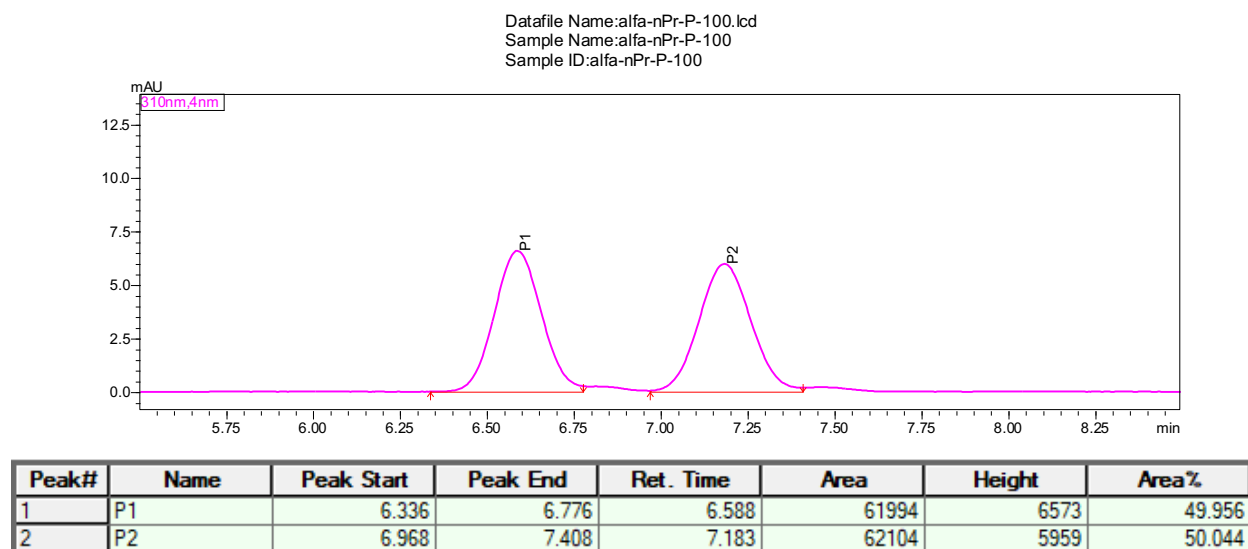
Datafile Name:E8_G437A_V327P_N70S_A330F_G74P_alfa-Et_OD30-Large scale.lcd
Sample Name:E8_G437A_V327P_N70S_A330F_G74P_alfa-Et_OD30-Large scale
Sample ID:E8_G74P_alfa-Et_OD30-Large scal



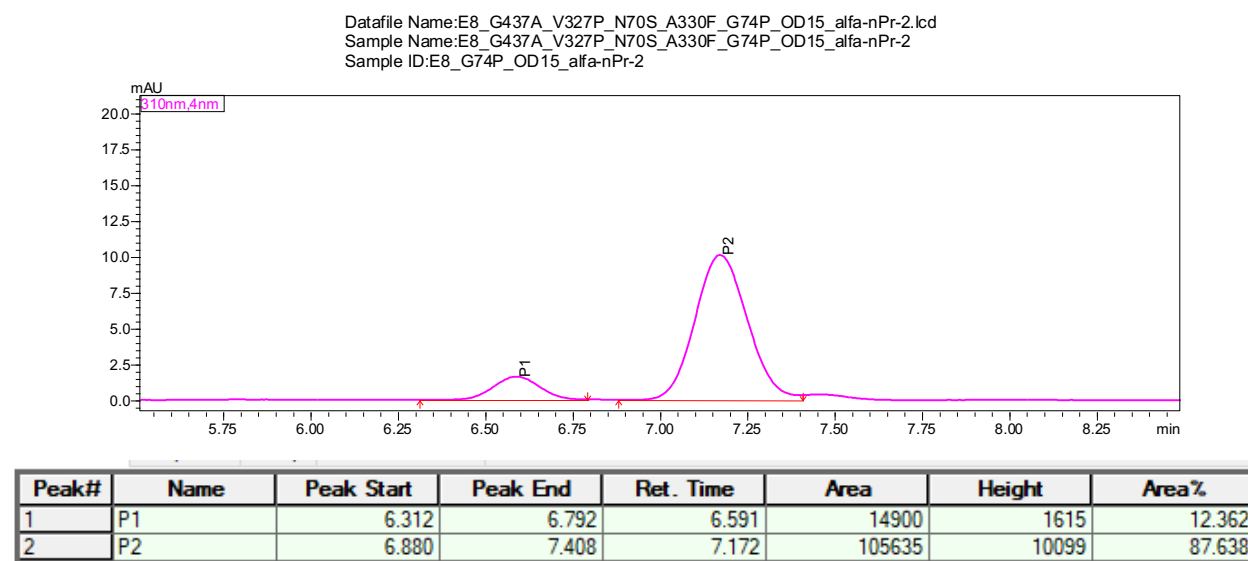
Methyl (*R*)-1-methyl-2-oxo-3-propylindoline-3-carboxylate



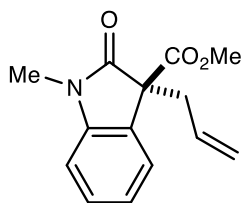
Racemic **2c** (HPLC analysis):



Enantioenriched **2c** obtained using P450_{arc2} (HPLC analysis): 12:88 e.r.

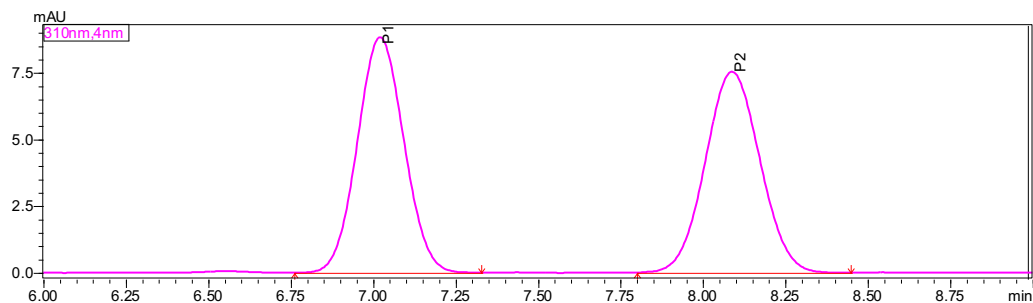


Methyl (*R*)-3-allyl-1-methyl-2-oxindoline-3-carboxylate



Racemic **2d** (HPLC analysis):

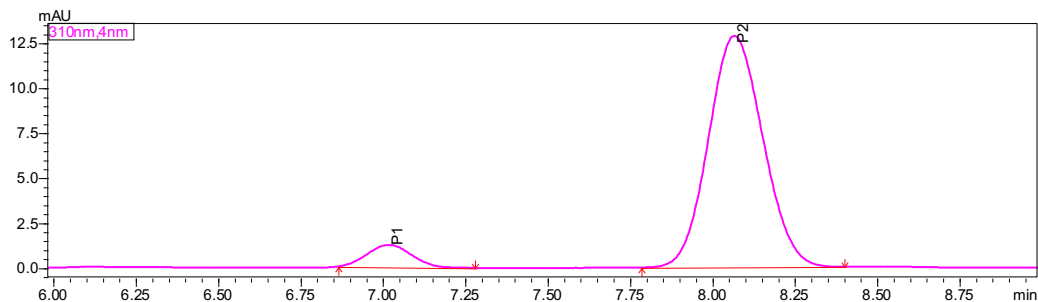
Datafile Name:alfa-allyl-P-100.lcd
Sample Name:alfa-allyl-P-100
Sample ID:alfa-allyl-P-100



Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	6.760	7.328	7.021	86744	8824	49.949
2	P2	7.800	8.448	8.089	86920	7530	50.051

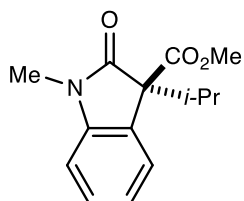
Enantioenriched **2d** obtained using P450_{arc2} (HPLC analysis): 7:93 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330F_G74P_OD15_alfa-allyl-2.lcd
Sample Name:E8_G437A_V327P_N70S_A330F_G74P_OD15_alfa-allyl-2
Sample ID:E8_G74P_OD15_alfa-allyl-2



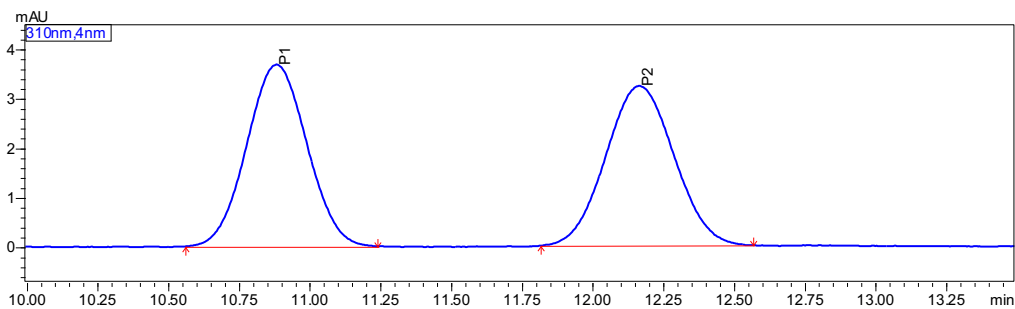
Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	6.864	7.280	7.018	11492	1230	7.212
2	P2	7.784	8.400	8.067	147864	12845	92.788

Methyl (*R*)-3-isopropyl-1-methyl-2-oxoindoline-3-carboxylate



Racemic **2e** (HPLC analysis):

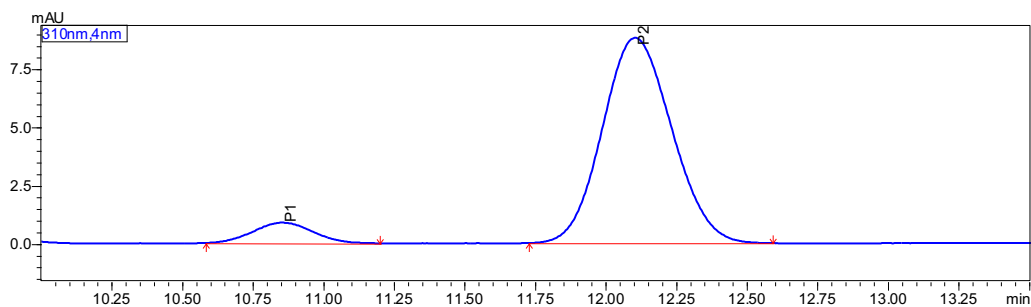
Datafile Name:WF-2-19-1-alfa-iPr-IC-10IPA.lcd
Sample Name:WF-2-19-1-alfa-iPr-IC-10IPA
Sample ID:WF-2-19-1-alfa-iPr-IC-10IPA



Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	10.560	11.240	10.884	54404	3672	50.073
2	P2	11.816	12.568	12.166	54246	3223	49.927

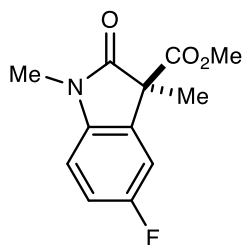
Enantioenriched **2e** obtained using P450_{arc2} (HPLC analysis): 8:92 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330F_G74P_OD15_alfa-iPr-1.lcd
Sample Name:E8_G437A_V327P_N70S_A330F_G74P_OD15_alfa-iPr-1
Sample ID:E8_G74P_OD15_alfa-iPr-1

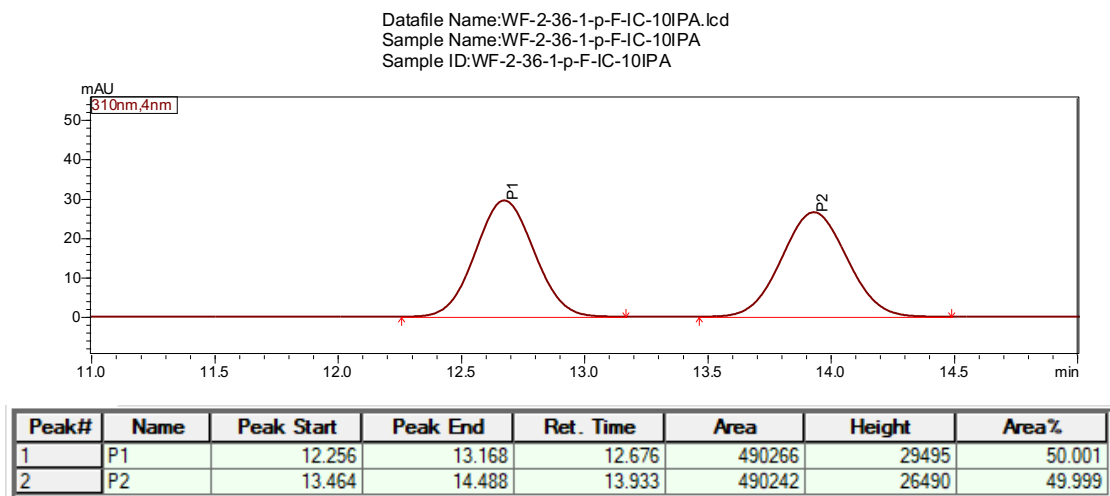


Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	10.584	11.200	10.855	12928	880	7.900
2	P2	11.728	12.592	12.105	150724	8810	92.100

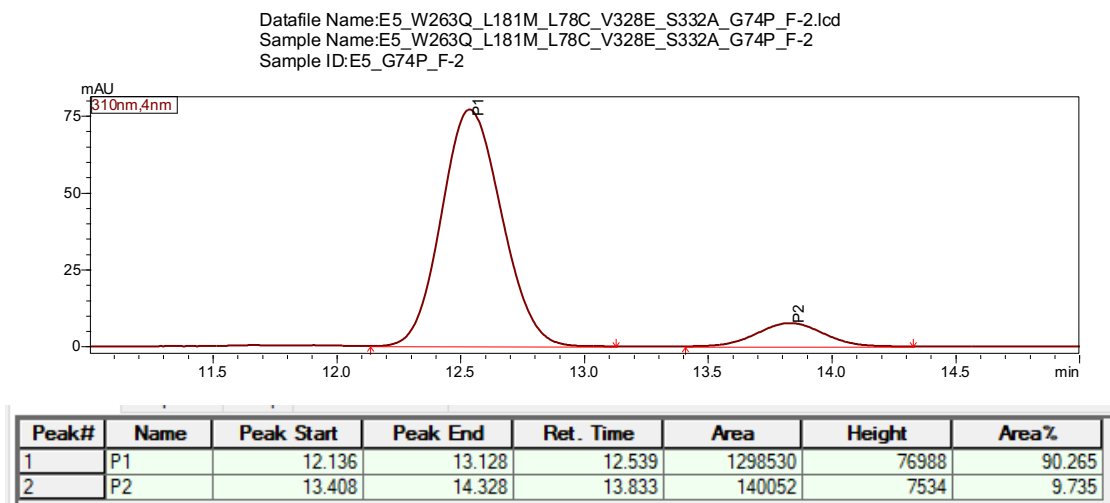
Methyl (S)-5-fluoro-1,3-dimethyl-2-oxindoline-3-carboxylate



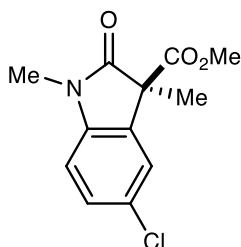
Racemic **2f** (HPLC analysis):



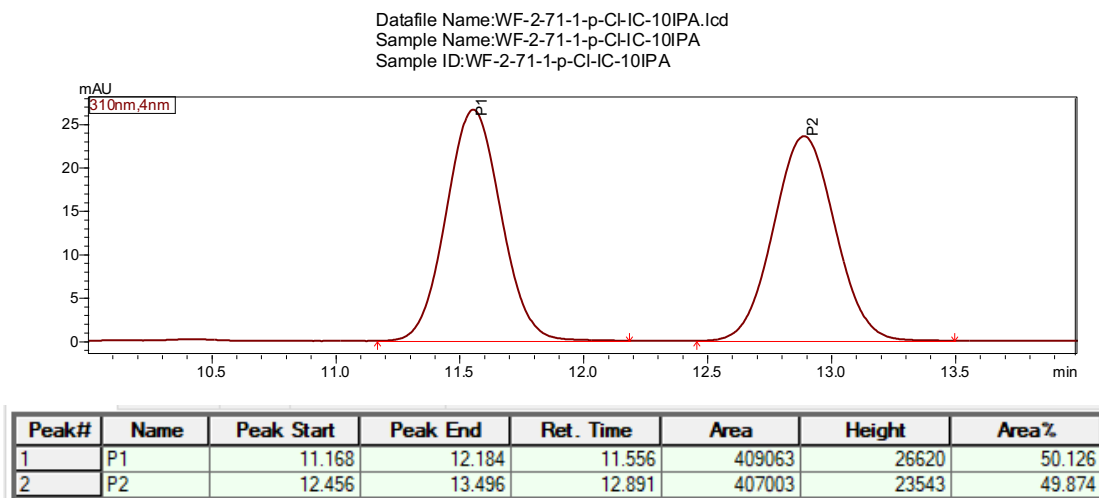
Enantioenriched **2f** obtained using P450_{arc1} G438T L266H L78C V328E S332A G74P (HPLC analysis): 90:10 e.r.



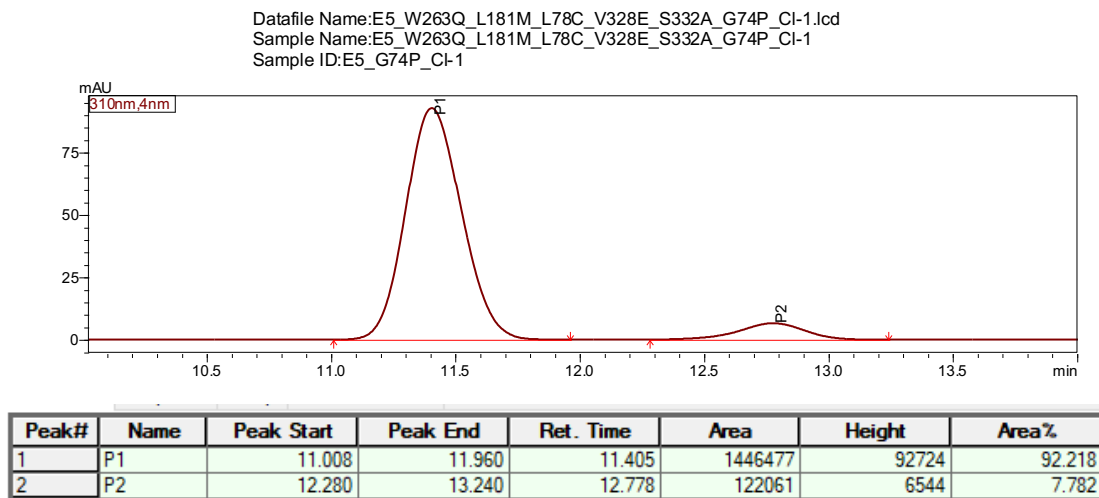
Methyl (S)-5-chloro-1,3-dimethyl-2-oxoindoline-3-carboxylate



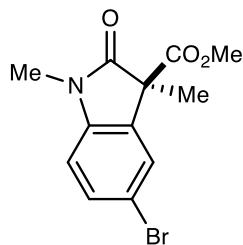
Racemic **2g** (HPLC analysis):



Enantioenriched **2g** obtained using P450_{arc1} G438T L266H L78C V328E S332A G74P (HPLC analysis): 92:8 e.r.

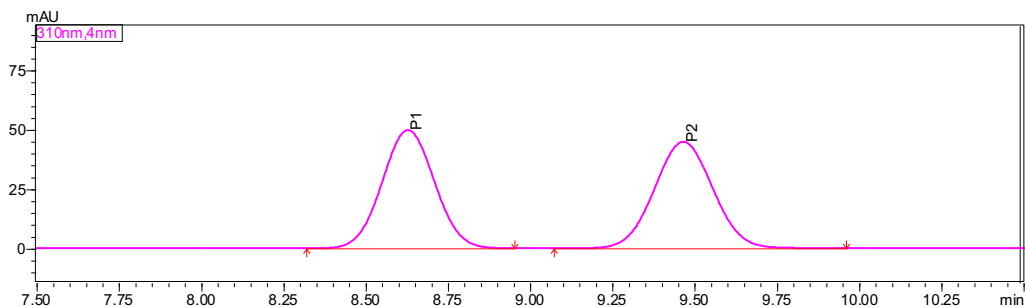


Methyl (*S*)-5-bromo-1,3-dimethyl-2-oxindoline-3-carboxylate



Racemic **2h** (HPLC analysis):

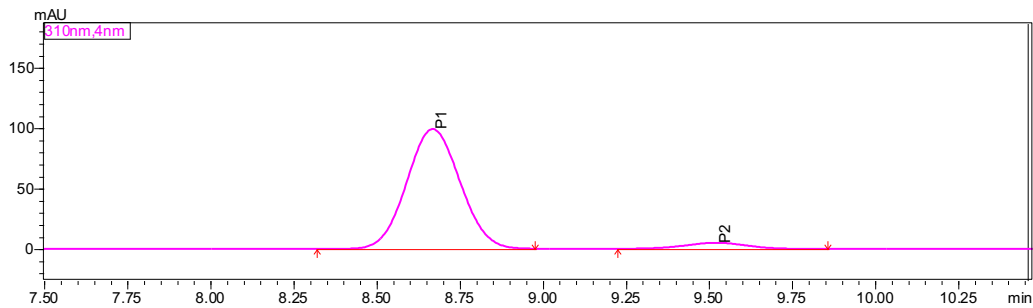
Datafile Name:p-Br-P-100.lcd
Sample Name:p-Br-P-100
Sample ID:p-Br-P-100



Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	8.320	8.952	8.629	553083	49731	49.859
2	P2	9.072	9.960	9.466	556205	44680	50.141

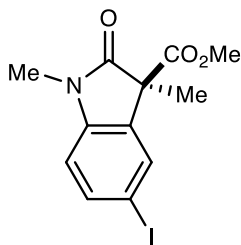
Enantioenriched **2h** obtained using P450_{arc1} G438T L266H L78C V328E S332A G74P (HPLC analysis): 95:5 e.r.

Datafile Name:E5-G74P_p-Br-2.lcd
Sample Name:E5-G74P_p-Br-2
Sample ID:E5-G74P_p-Br-2

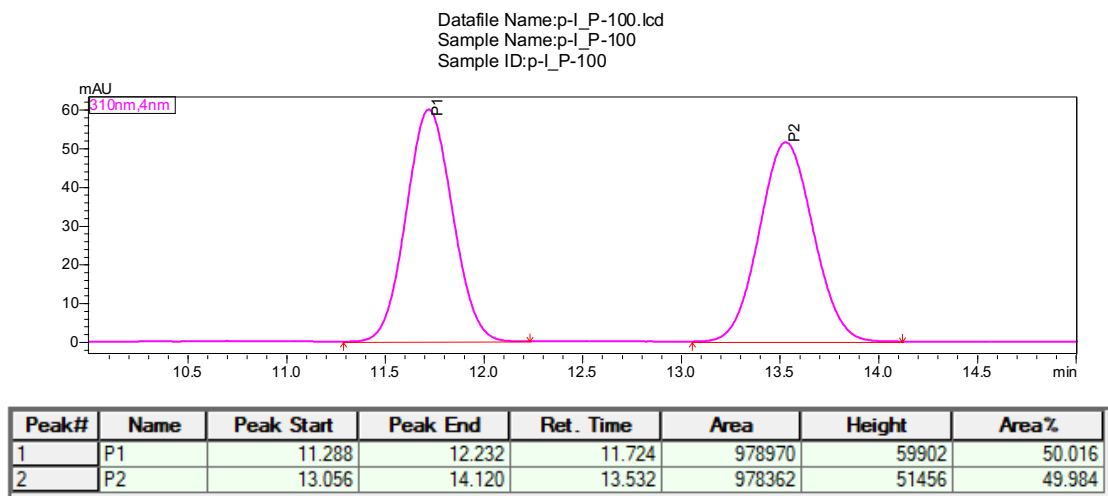


Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	8.320	8.976	8.669	1105087	98932	94.511
2	P2	9.224	9.856	9.523	64179	4989	5.489

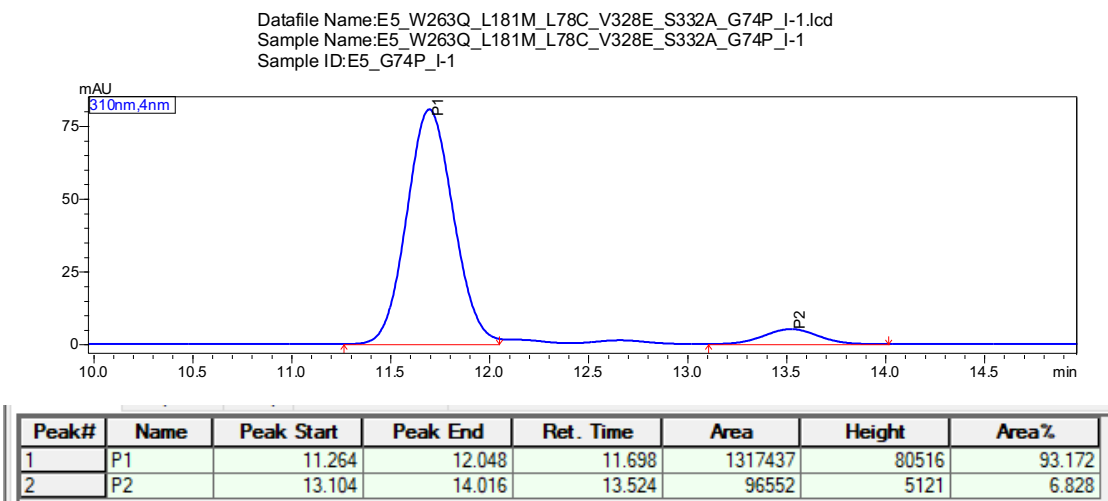
Methyl (*S*)-5-iodo-1,3-dimethyl-2-oxindoline-3-carboxylate



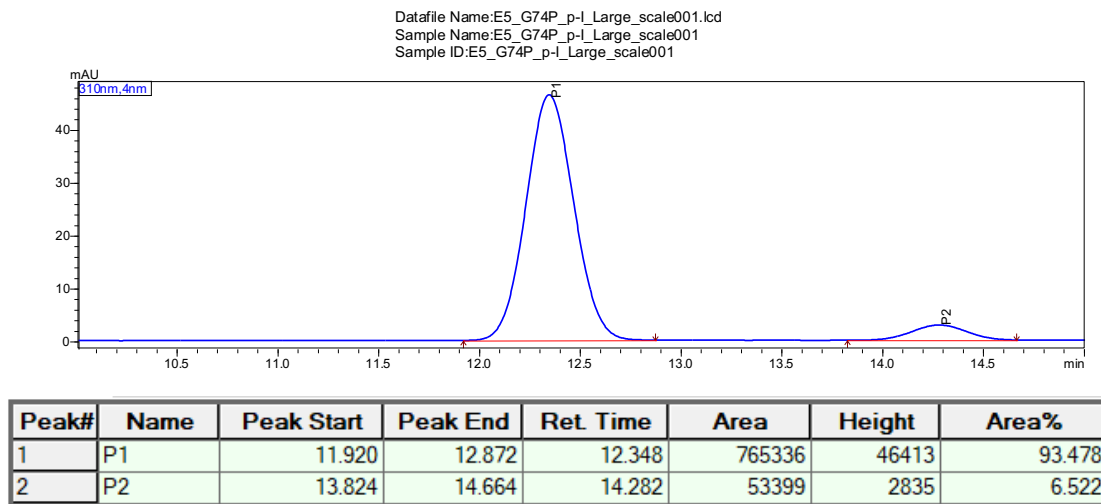
Racemic **2i** (HPLC analysis):



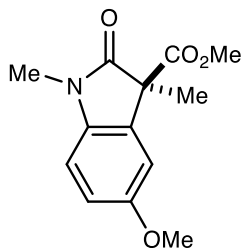
Enantioenriched **2i** obtained using P450_{arc1} G438T L266H L78C V328E S332A G74P (HPLC analysis): 93:7 e.r.



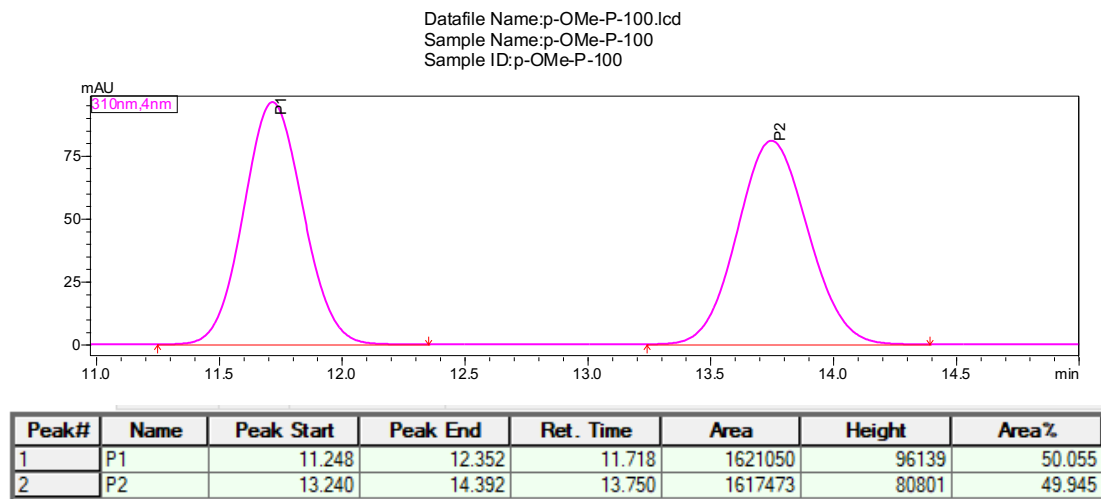
Enantioenriched **2i** obtained using P450_{arc1} G438T L266H L78C V328E S332A G74P (gram-scale, HPLC analysis): 93:7 e.r.



Methyl (*R*)-5-methoxy-1,3-dimethyl-2-oxoindoline-3-carboxylate

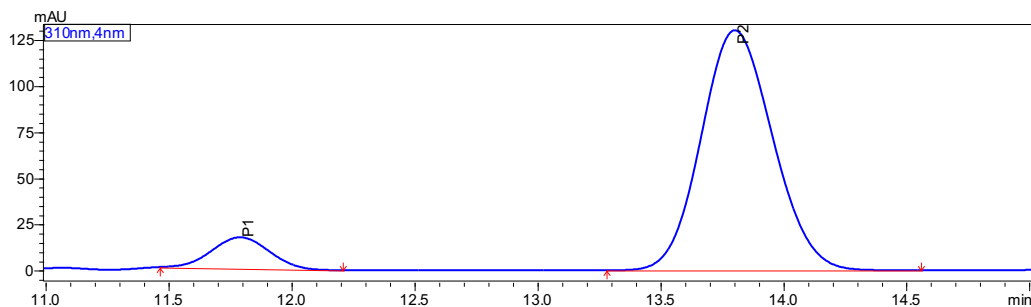


Racemic **2j** (HPLC analysis):



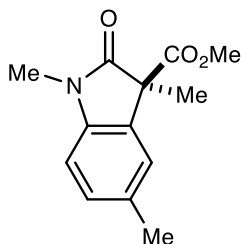
Enantioenriched **2j** obtained using P450_{arc2} P74G L436R F330E (HPLC analysis): 10:90 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330E_L436R_OD30-p-OMe-24h-1.lcd
 Sample Name:E8_G437A_V327P_N70S_A330E_L436R_OD30-p-OMe-24h-1
 Sample ID:E8_L436R_OD30-p-OMe-24h-1



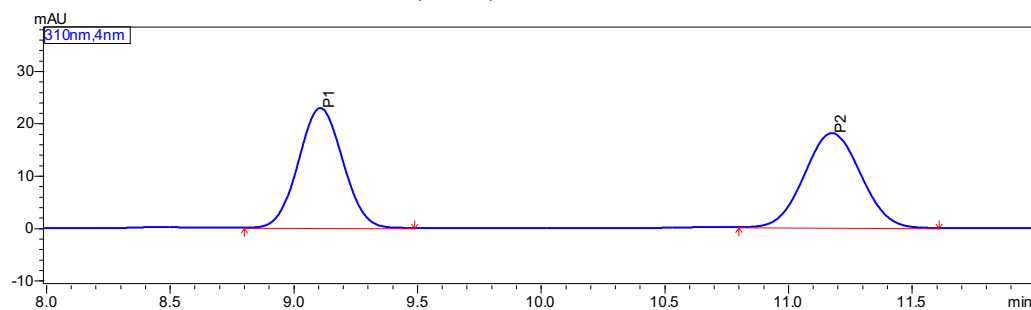
Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	11.464	12.208	11.791	272612	16864	9.401
2	P2	13.280	14.560	13.803	2627159	130052	90.599

Methyl (*R*)-1,3,5-trimethyl-2-oxoindoline-3-carboxylate



Racemic **2k** (HPLC analysis):

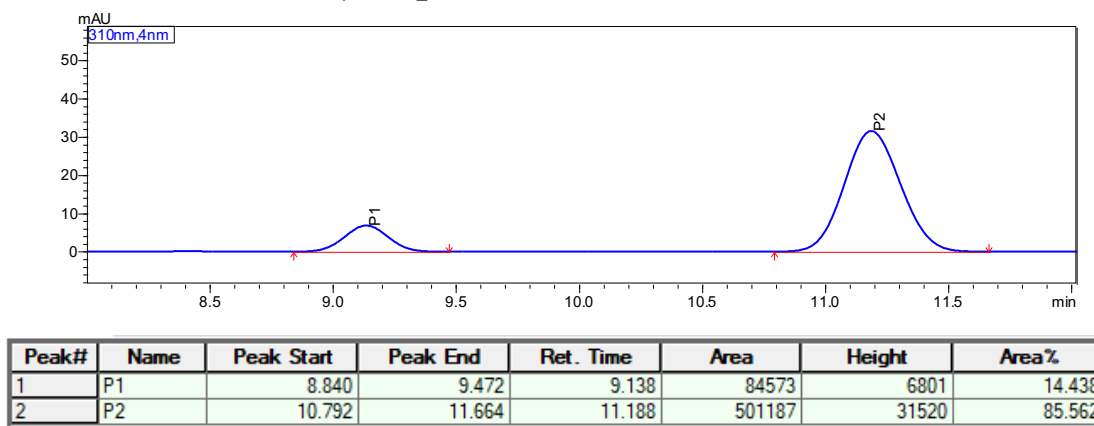
Datafile Name:P-p-Me-100.lcd
 Sample Name:P-p-Me-100
 Sample ID:P-p-Me-100



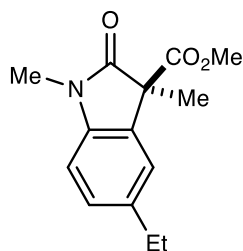
Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	8.800	9.488	9.109	285081	22853	50.046
2	P2	10.800	11.608	11.179	284555	18024	49.954

Enantioenriched **2k** obtained using P450_{arc2} P74G L436R F330E (HPLC analysis): 14:86 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330E_L436R-1.lcd
 Sample Name:E8_G437A_V327P_N70S_A330E_L436R-1
 Sample ID:E8_L436R-1

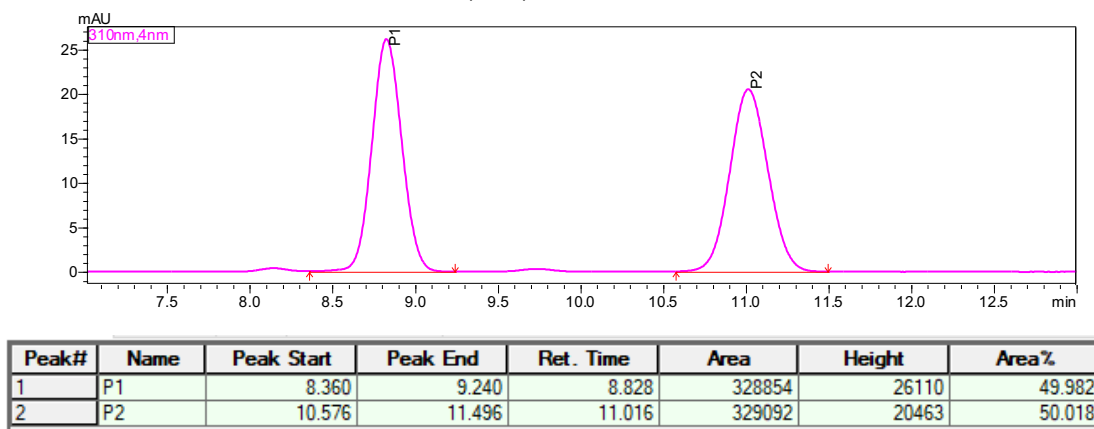


Methyl (*R*)-5-ethyl-1,3-dimethyl-2-oxoindoline-3-carboxylate

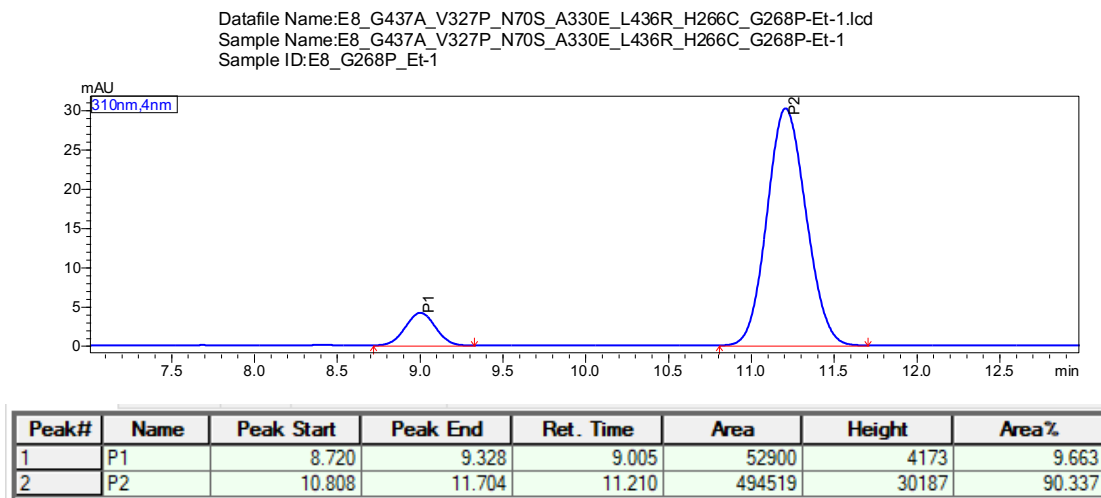


Racemic **2l** (HPLC analysis):

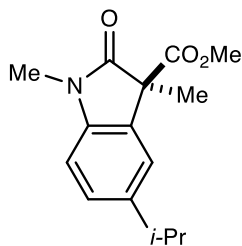
Datafile Name:p-Et-P-100.lcd
 Sample Name:p-Et-P-100
 Sample ID:p-Et-P-100



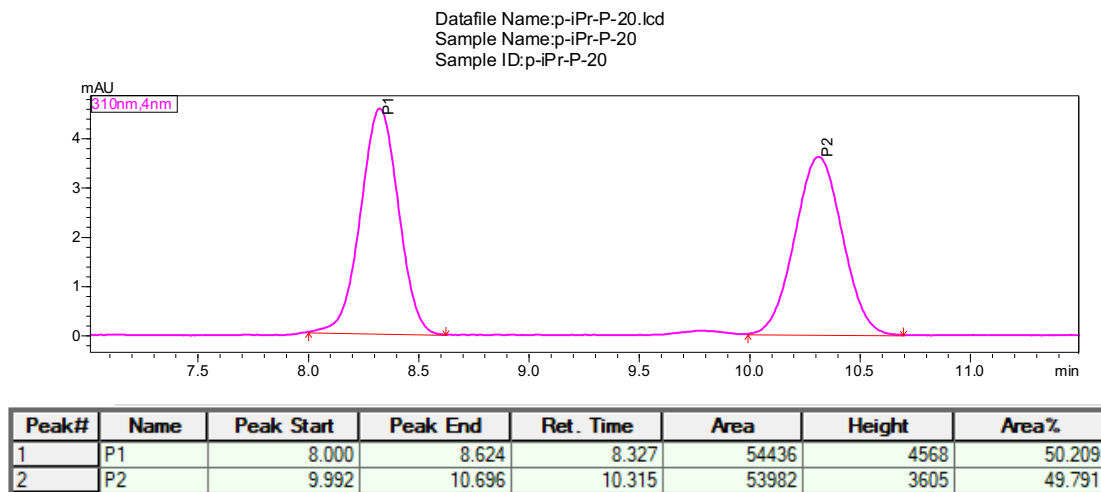
Enantioenriched **2l** obtained using P450_{arc2} P74G L436R F330E H266C G268P (HPLC analysis):
10:90 e.r.



Methyl (*R*)-5-isopropyl-1,3-dimethyl-2-oxoindoline-3-carboxylate

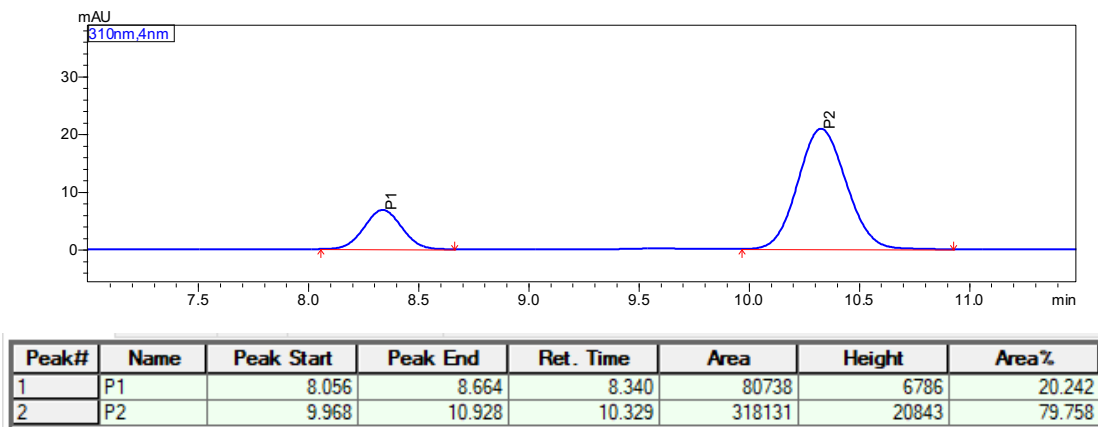


Racemic **2m** (HPLC analysis):

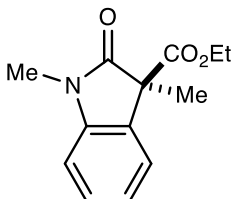


Enantioenriched **2m** obtained using P450_{arc2} P74G L436R F330E H266C G268P (HPLC analysis):
20:80 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330E_L436R_H266C_G268P-iPr-3.lcd
Sample Name:E8_G437A_V327P_N70S_A330E_L436R_H266C_G268P-iPr-3
Sample ID:E8_G268P_iPr-3

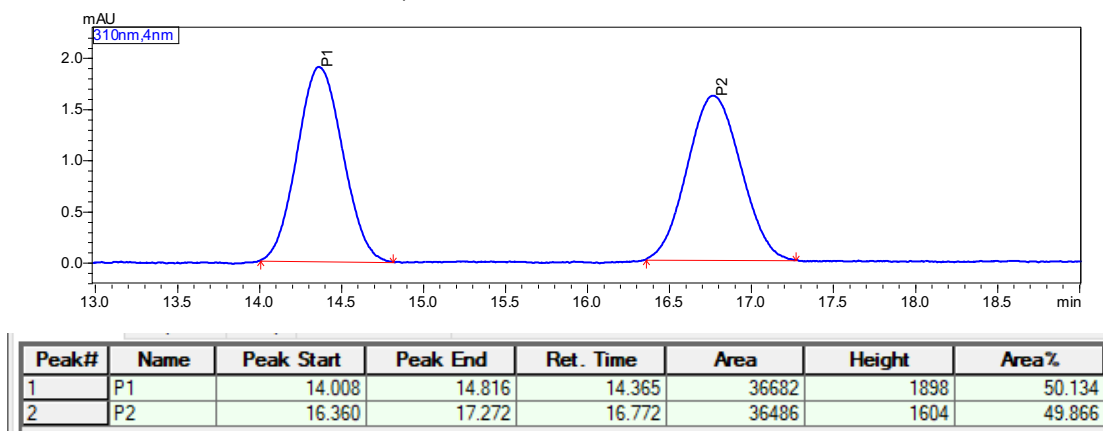


Ethyl 1,3-dimethyl-2-oxoindoline-3-carboxylate



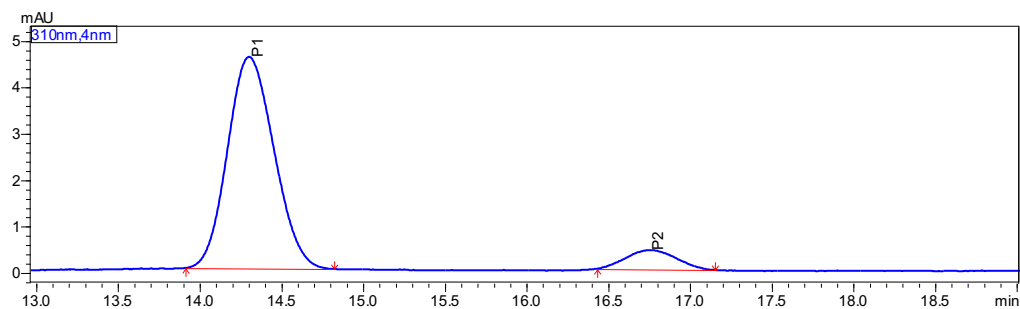
Racemic **2n** (HPLC analysis):

Datafile Name:NN-1-36-1-CO2Et-IC-10IPA.lcd
Sample Name:NN-1-36-1-CO2Et-IC-10IPA
Sample ID:NN-1-36-1-CO2Et-IC-10IPA



Enantioenriched **2n** obtained using P450_{arc1} (HPLC analysis): 91:9 e.r.

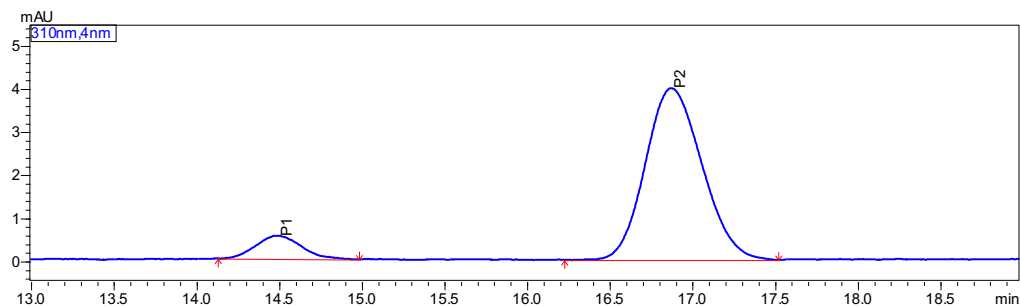
Datafile Name: E5_W263Q_L181M_T438G_H266L_CO2Et_OD30-24h-1.lcd
 Sample Name: E5_W263Q_L181M_T438G_H266L_CO2Et_OD30-24h-1
 Sample ID: E5_H266L_CO2Et_OD30-24h-1



Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	13.912	14.824	14.304	90290	4562	91.051
2	P2	16.432	17.152	16.753	8874	416	8.949

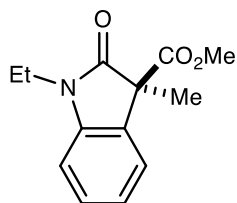
Enantioenriched **2n** obtained using P450_{arc2} (HPLC analysis): 10:90 e.r.

Datafile Name: E8_G437A_V327P_N70S_A330F_G74P_OD30-CO2Et-24h-2.lcd
 Sample Name: E8_G437A_V327P_N70S_A330F_G74P_OD30-CO2Et-24h-2
 Sample ID: E8_G74P_OD30-CO2Et-24h-2



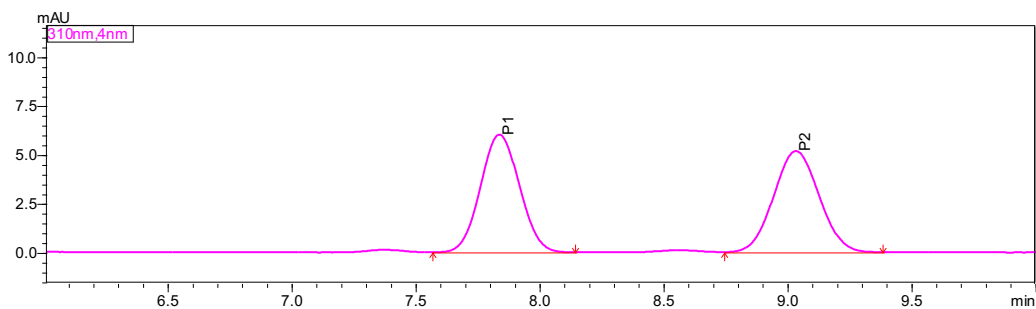
Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	14.128	14.984	14.496	10264	538	9.778
2	P2	16.224	17.520	16.873	94703	3973	90.222

Methyl (S)-1-ethyl-3-methyl-2-oxoindoline-3-carboxylate



Racemic **2o** (HPLC analysis):

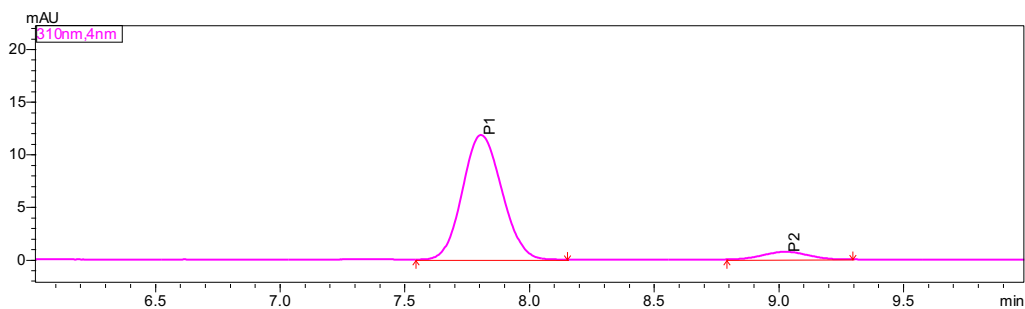
Datafile Name:N-Et-P-100.lcd
Sample Name:N-Et-P-100
Sample ID:N-Et-P-100



Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	7.568	8.144	7.839	65945	6018	50.016
2	P2	8.744	9.384	9.035	65903	5164	49.984

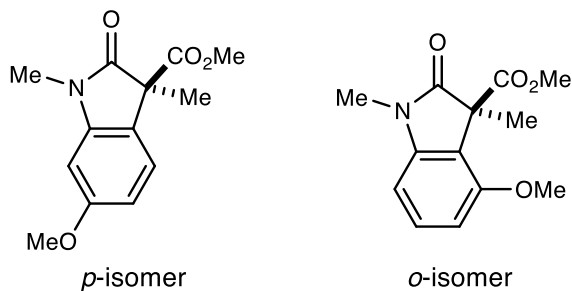
Enantioenriched **2o** obtained using P450_{arc1} (HPLC analysis): 94:6 e.r.

Datafile Name:E5_W263Q_L181M_T438G_H266L_N-Et_OD30-24h-3.lcd
Sample Name:E5_W263Q_L181M_T438G_H266L_N-Et_OD30-24h-3
Sample ID:E5_H266L_N-Et_OD30-24h-3



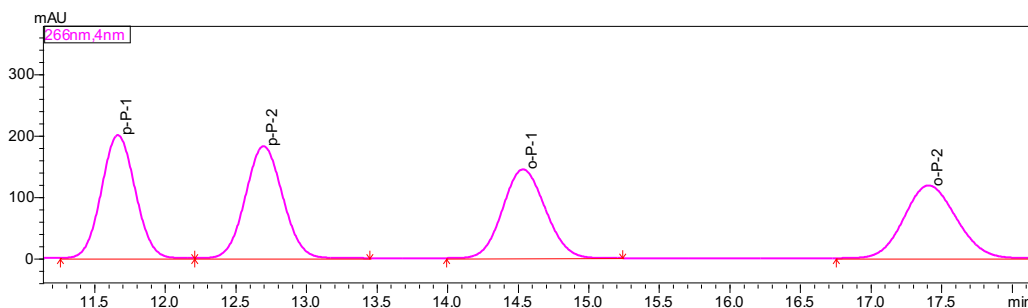
Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	P1	7.544	8.152	7.809	129729	11809	93.561
2	P2	8.792	9.296	9.030	8927	721	6.439

Methyl (*R*)-4-methoxy-1,3-dimethyl-2-oxoindoline-3-carboxylate (*p*-isomer) and methyl (*R*)-6-methoxy-1,3-dimethyl-2-oxoindoline-3-carboxylate (*o*-isomer)



Racemic **2p** (HPLC analysis):

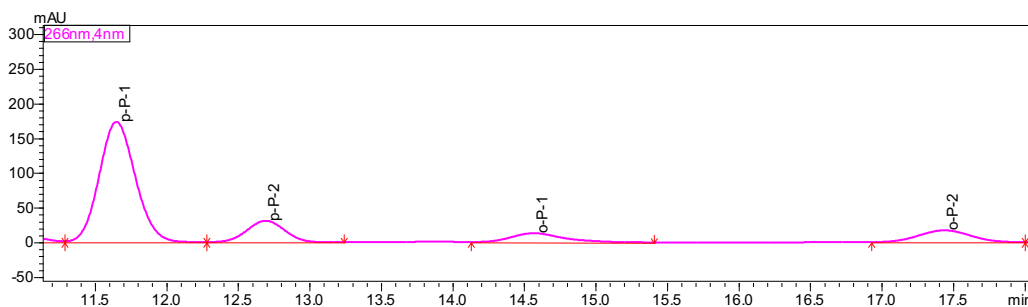
Datafile Name:WF-2-4-1-m-OMe-IC-20IPA.lcd
 Sample Name:WF-2-4-1-m-OMe-IC-20IPA
 Sample ID:WF-2-4-1-m-OMe-IC-20IPA



Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	p-P-1	11.256	12.208	11.669	3327353	200529	26.100
2	p-P-2	12.208	13.448	12.701	3340417	182475	26.203
3	o-P-1	13.992	15.240	14.539	3038911	144574	23.838
4	o-P-2	16.752	18.256	17.413	3041686	118543	23.859

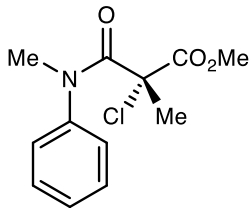
Enantioenriched **2p** obtained using P450_{arc2} (HPLC analysis): *p*-isomer, 85:15 e.r.; *o*-isomer, 42:58 e.r.

Datafile Name:E8_G437A_V327P_N70S_A330F_G74P_OD30-m-OMe-24h-1.lcd
 Sample Name:E8_G437A_V327P_N70S_A330F_G74P_OD30-m-OMe-24h-1
 Sample ID:E8_G74P_OD30-m-OMe-24h-1



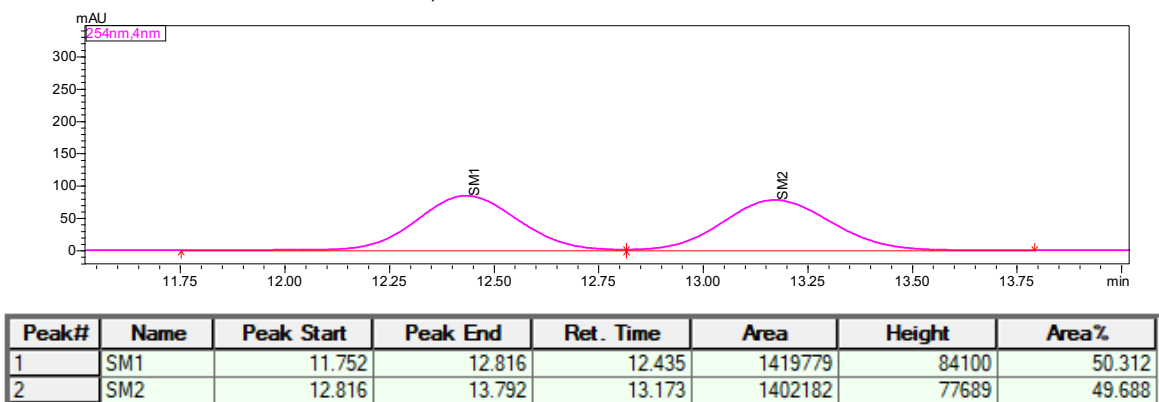
Peak#	Name	Peak Start	Peak End	Ret. Time	Area	Height	Area%
1	p-P-1	11.288	12.280	11.652	3050839	173469	69.754
2	p-P-2	12.280	13.240	12.696	569104	30934	13.012
3	o-P-1	14.128	15.408	14.570	321222	12912	7.344
4	o-P-2	16.928	18.000	17.440	432552	17066	9.890

Methyl (*R*)-2-chloro-2-methyl-3-(methyl(phenyl)amino)-3-oxopropanoate



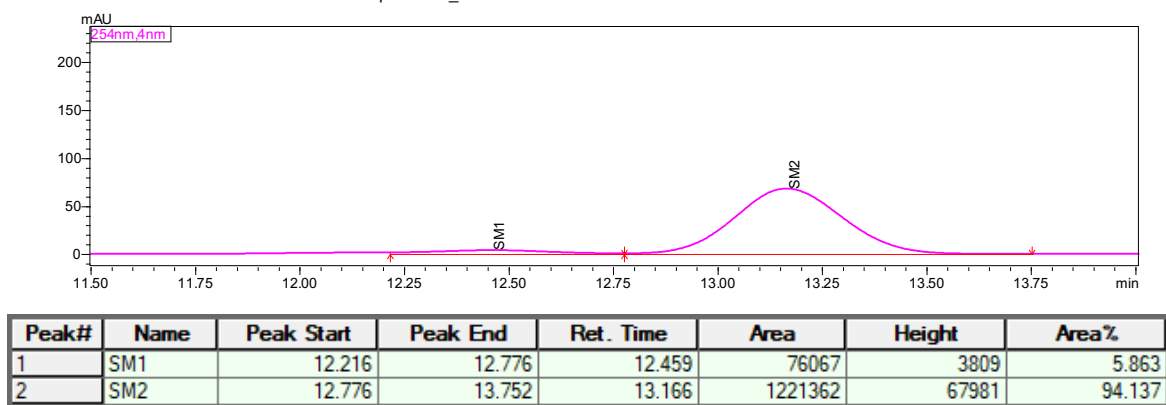
Racemic **3a** (HPLC analysis):

Datafile Name: NN-1-64-1-CI-SM-10IPA-100.lcd
 Sample Name: NN-1-64-1-CI-SM-10IPA-100
 Sample ID: NN-1-64-1-CI-SM-10IPA-100



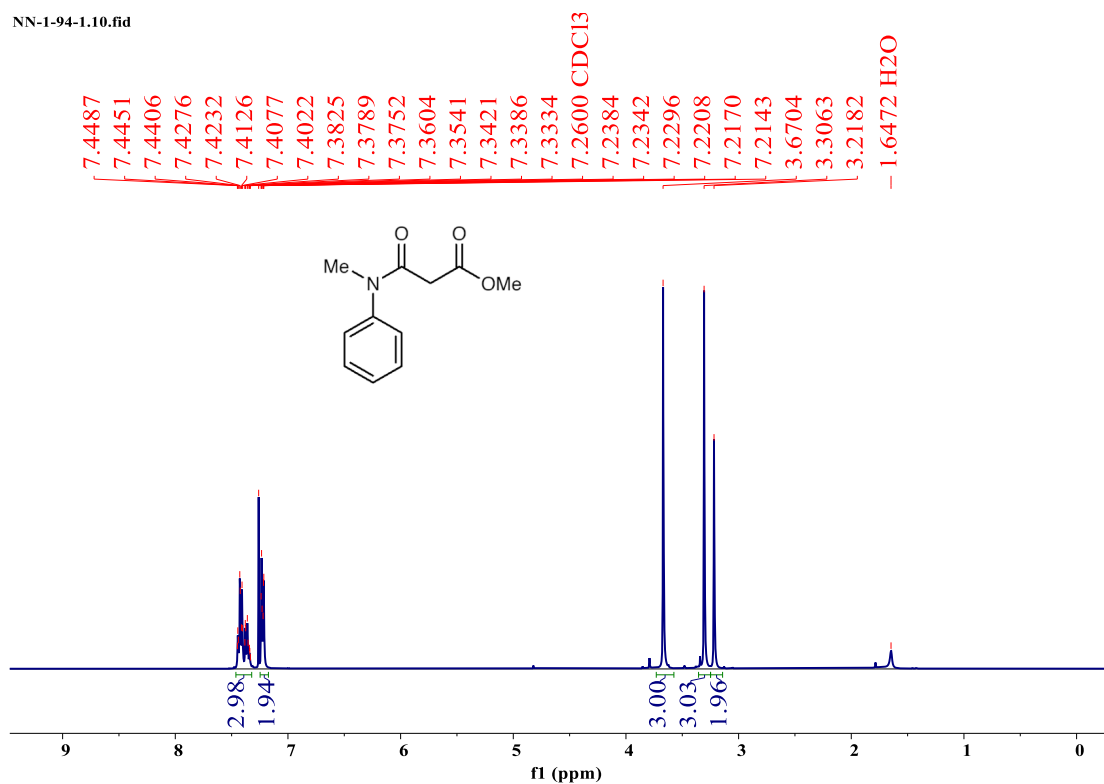
Enantioenriched **3a** obtained using P450_{arc3} (HPLC analysis): 6:94 e.r.

Datafile Name: E5_W263Q_L181M_L78C_V328E_S332A-2.lcd
 Sample Name: E5_W263Q_L181M_L78C_V328E_S332A-2
 Sample ID: E5_S332A-2

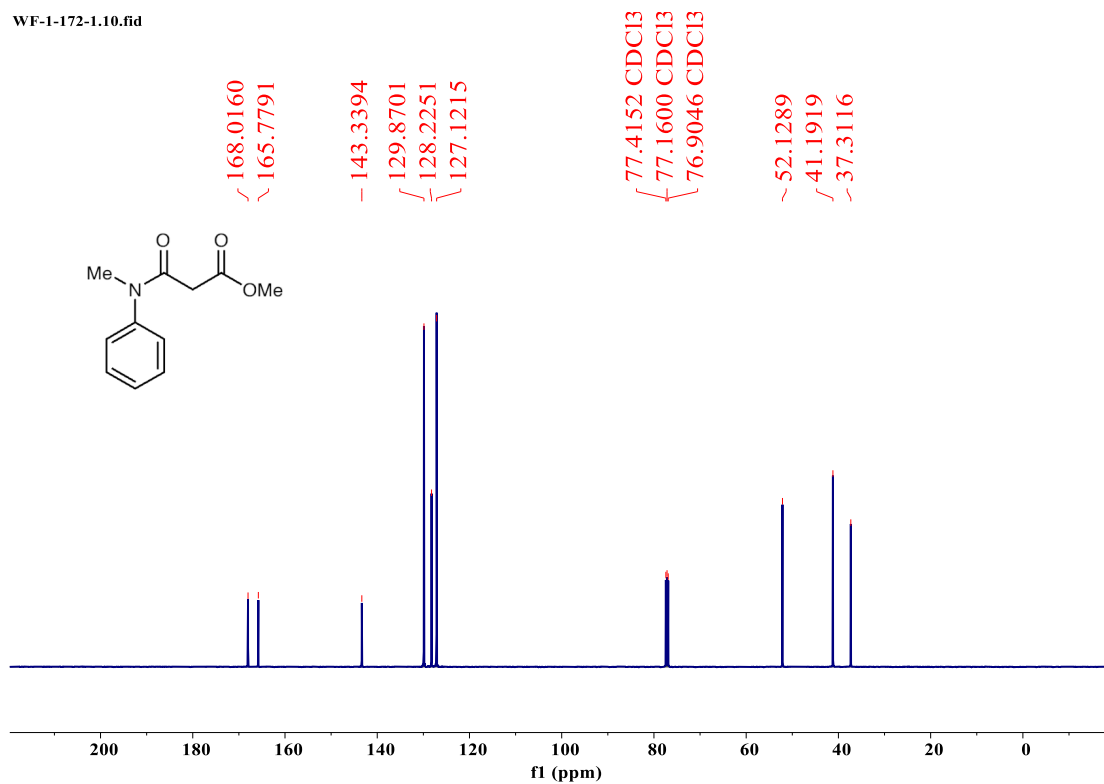


Supplementary Note 12. ^1H , ^{19}F , ^{13}C NMR spectra of compounds

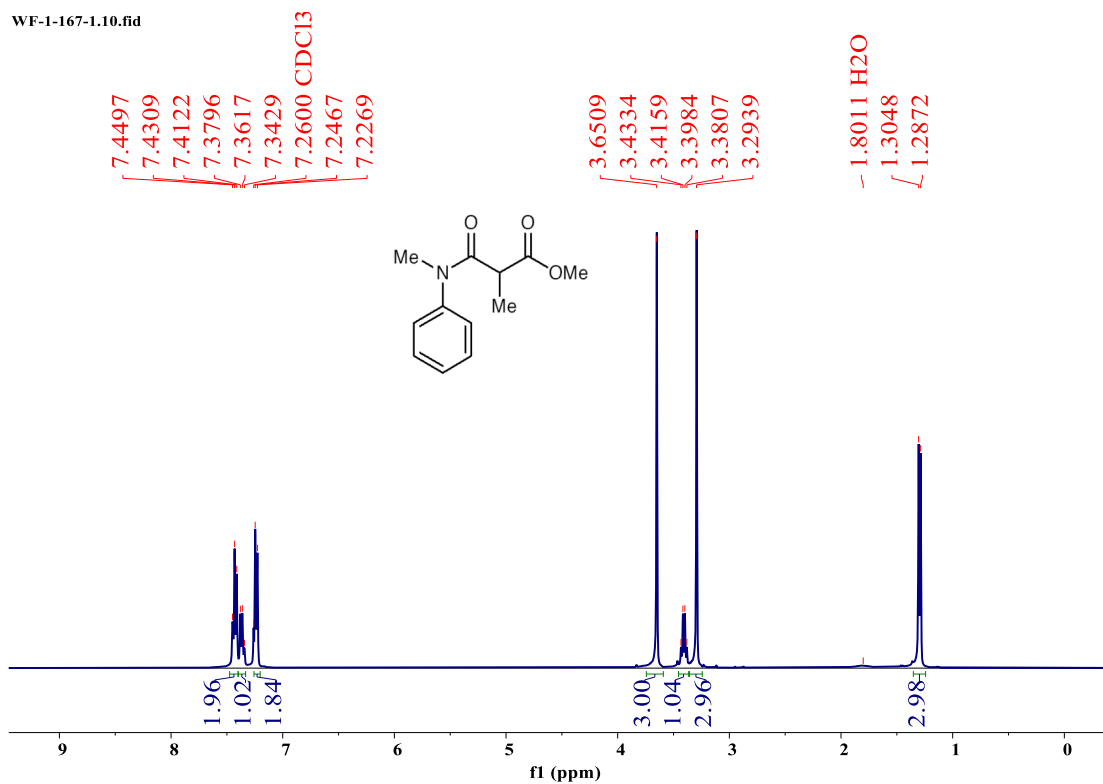
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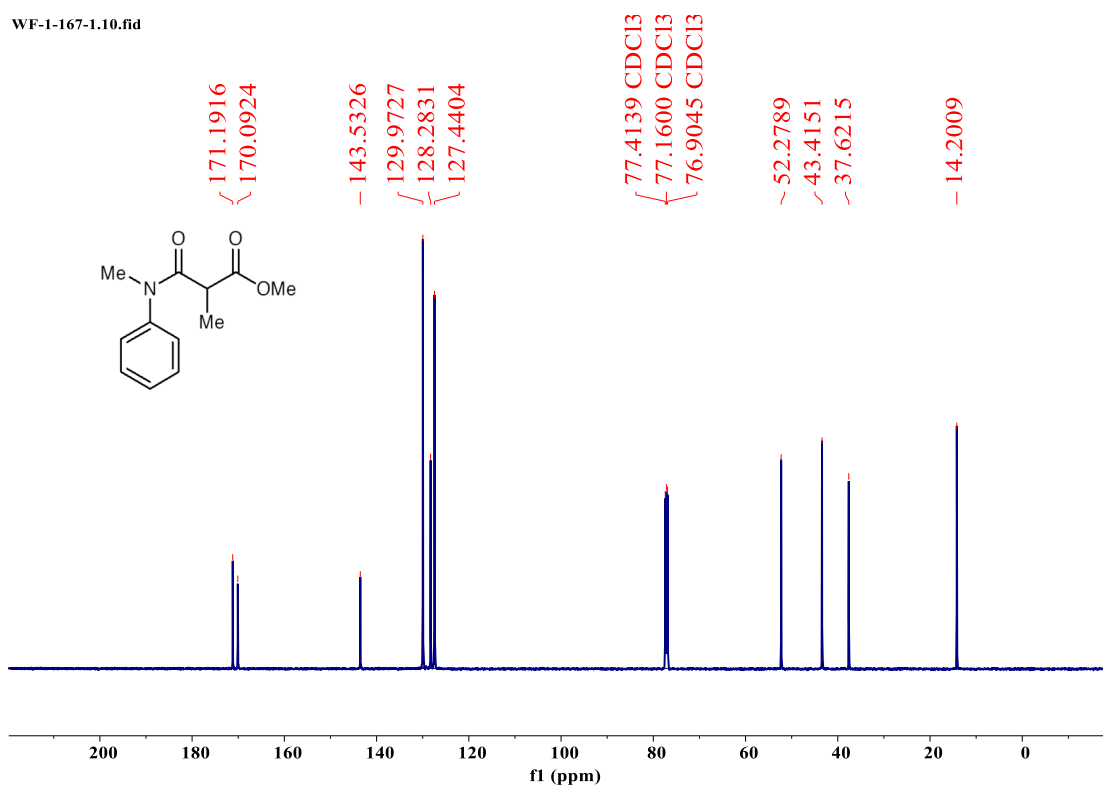
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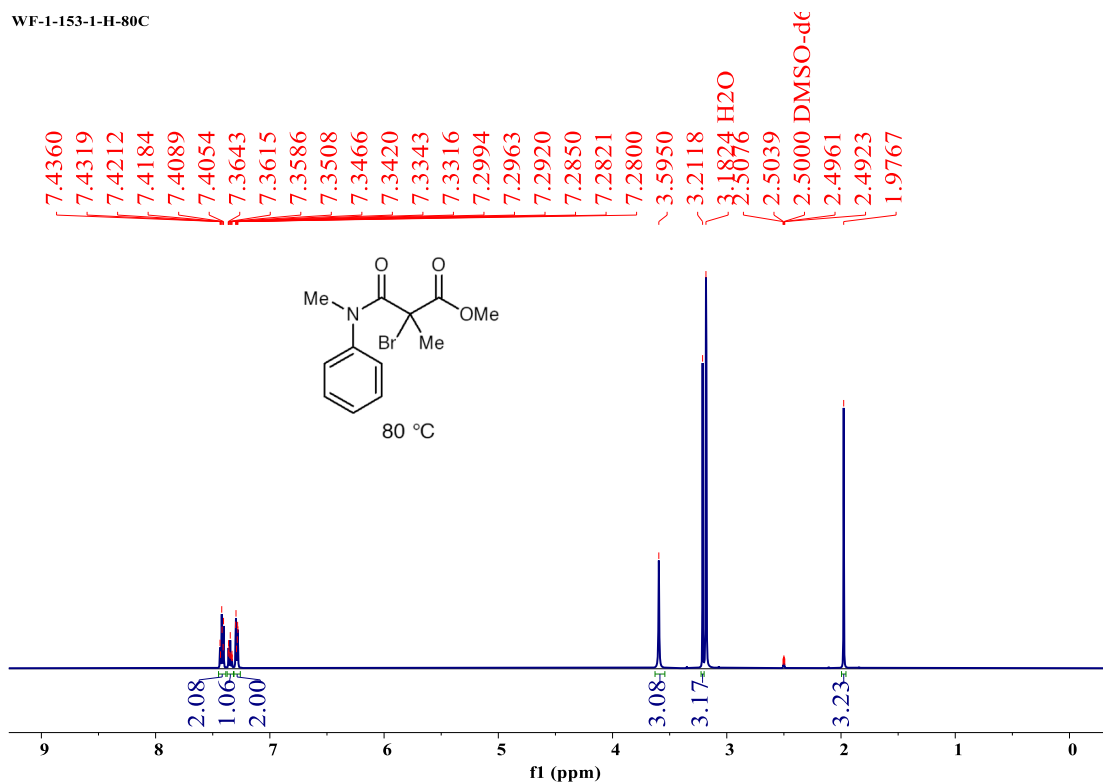
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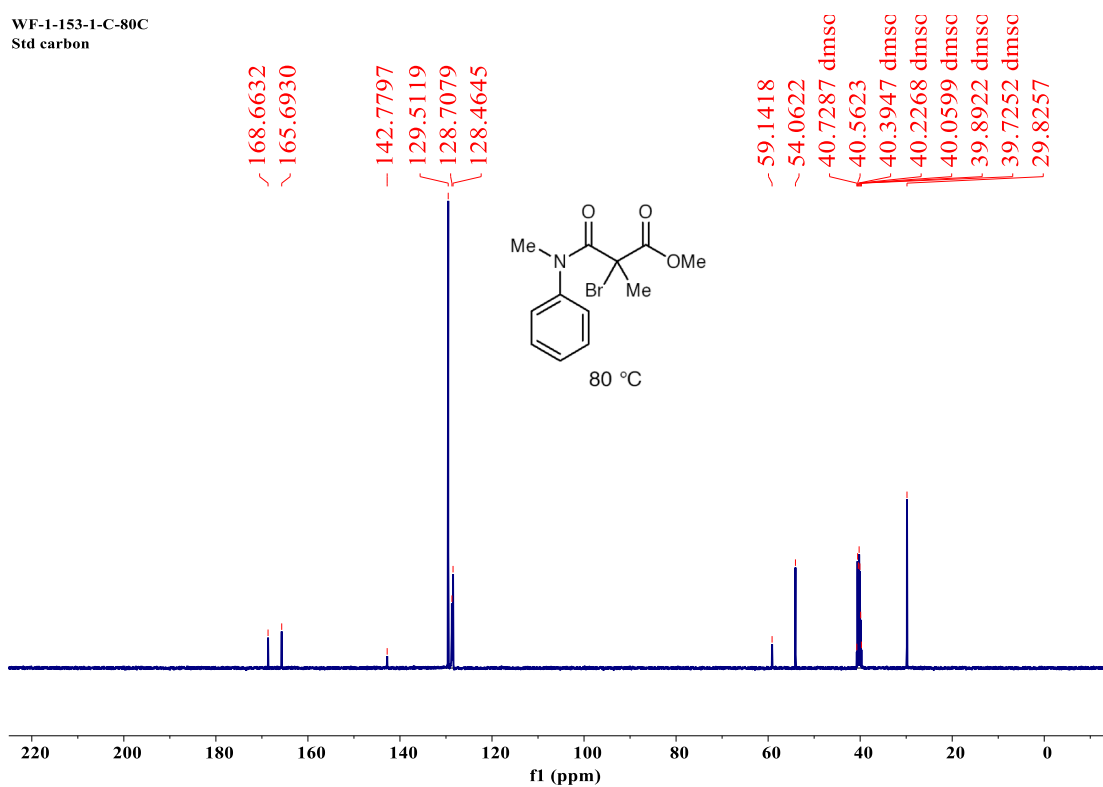
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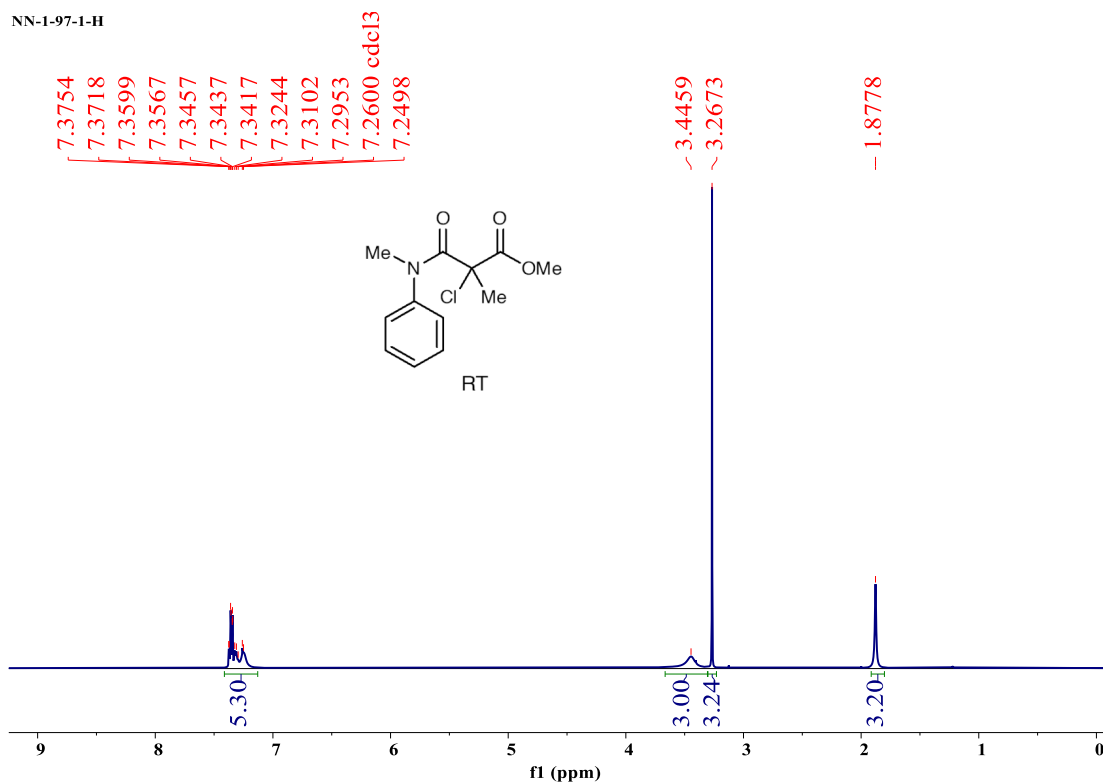
WF-1-153-1-H-80C



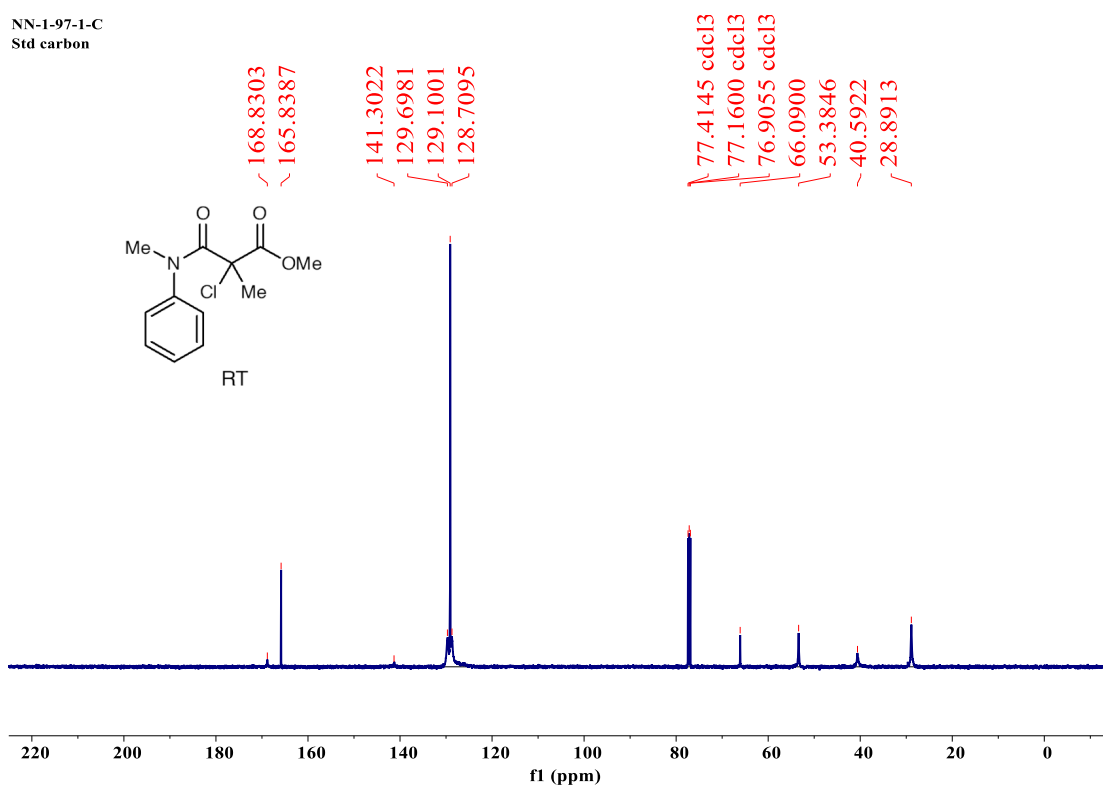
WF-1-153-1-C-80C
Std carbon



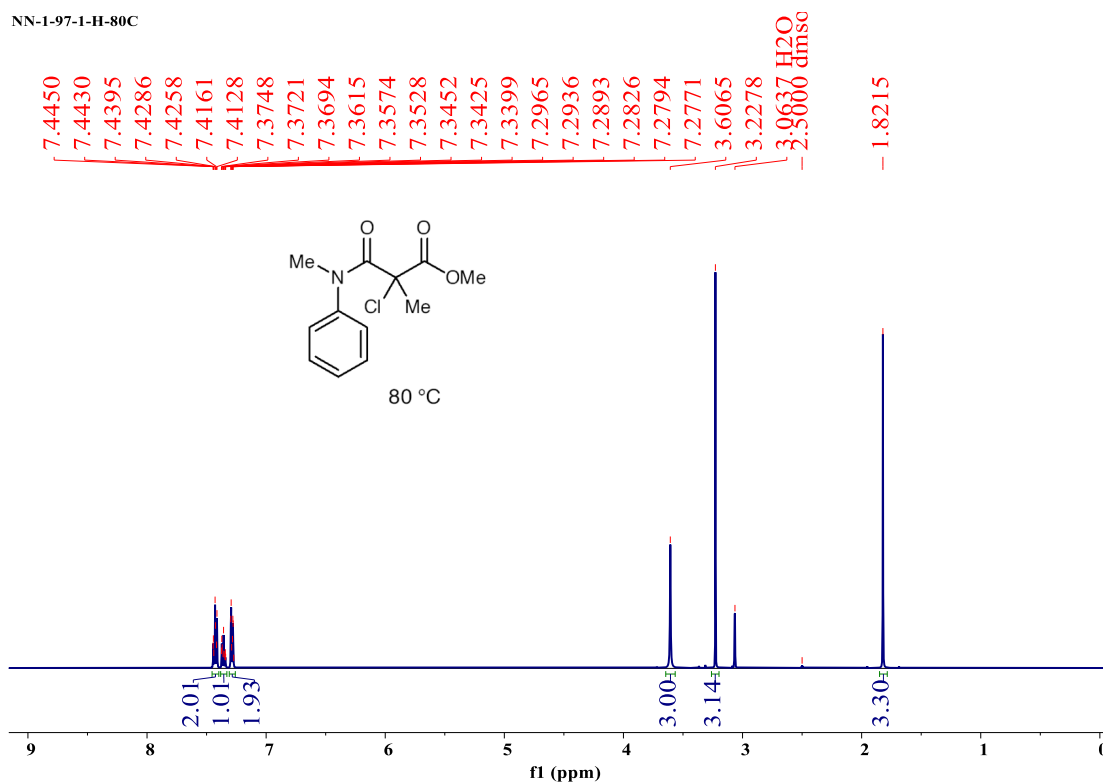
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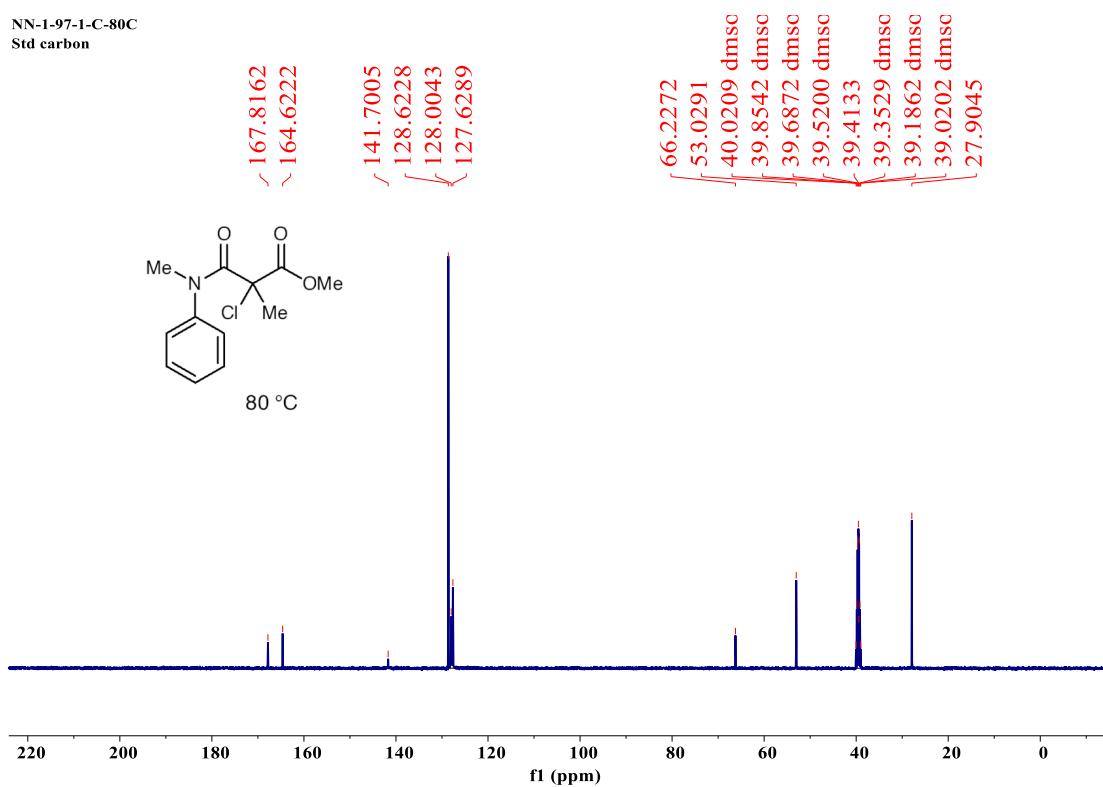
NN-1-97-1-C
Std carbon



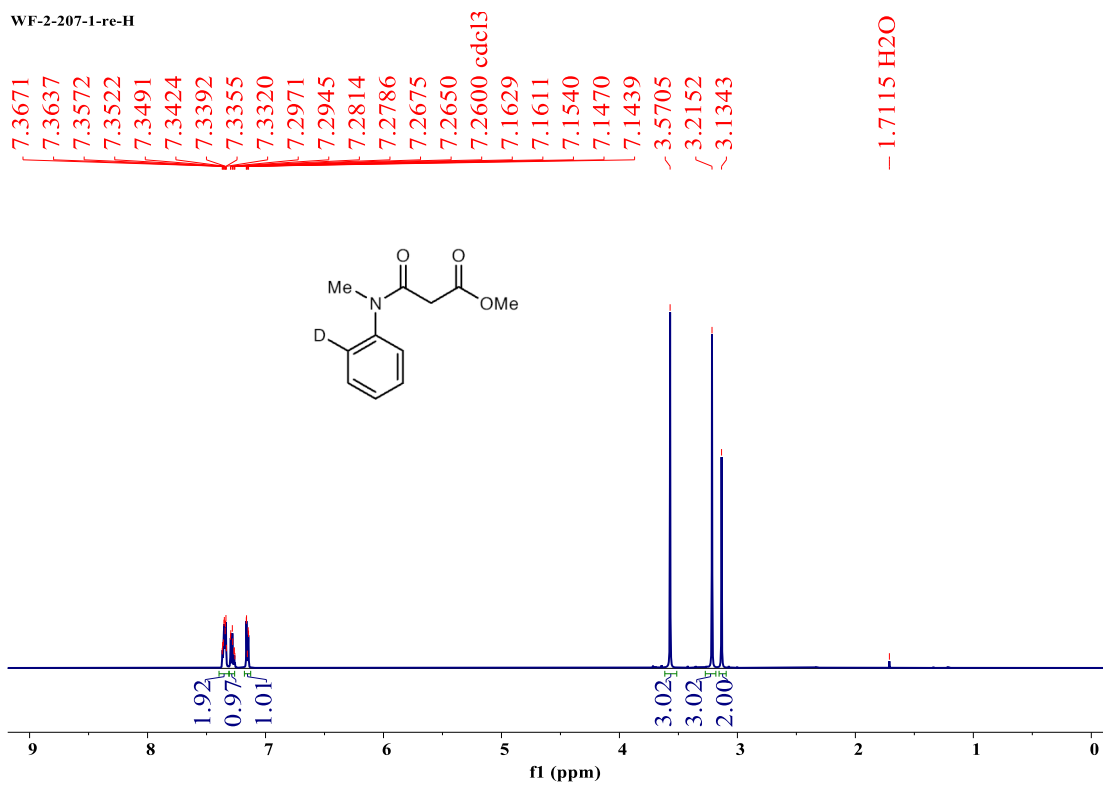
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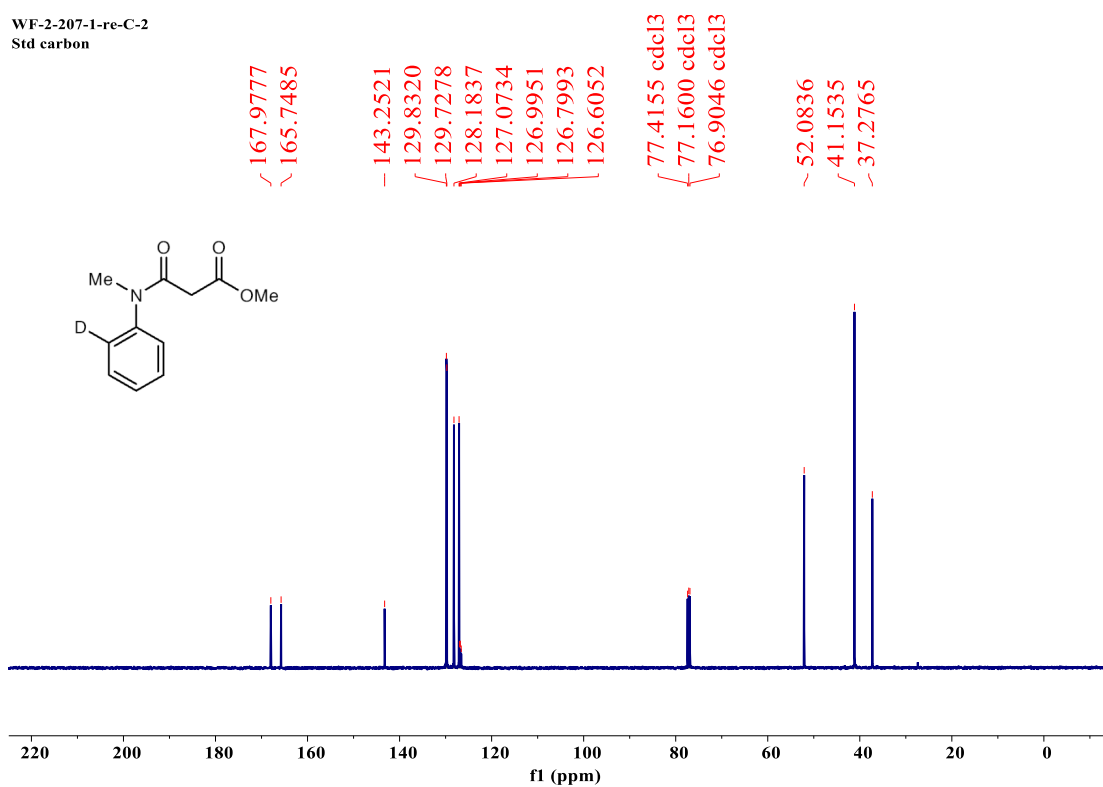
NN-1-97-1-C-80C
Std carbon



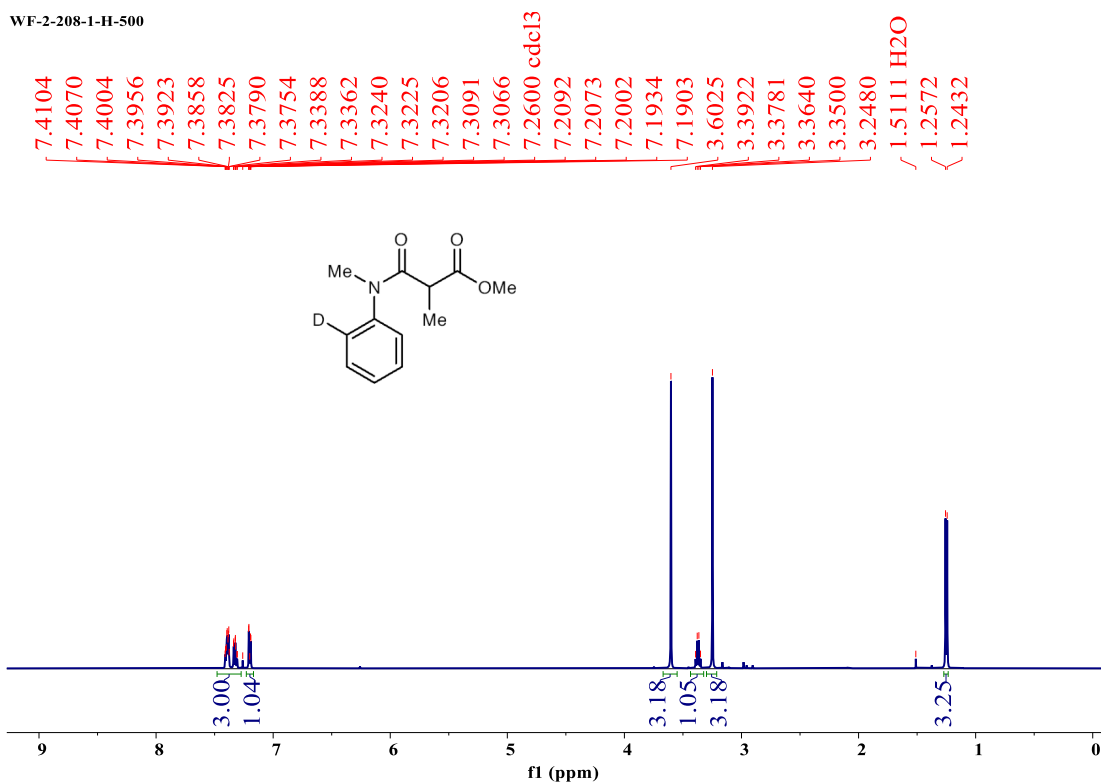
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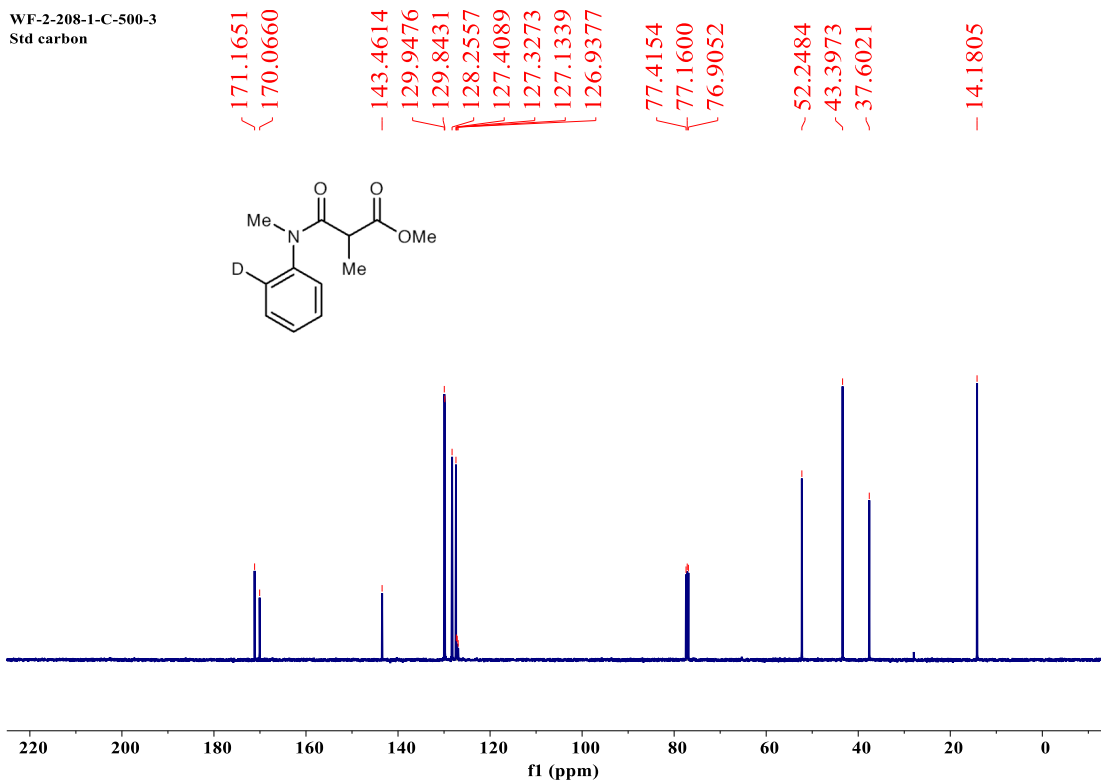
WF-2-207-1-re-C-2
Std carbon



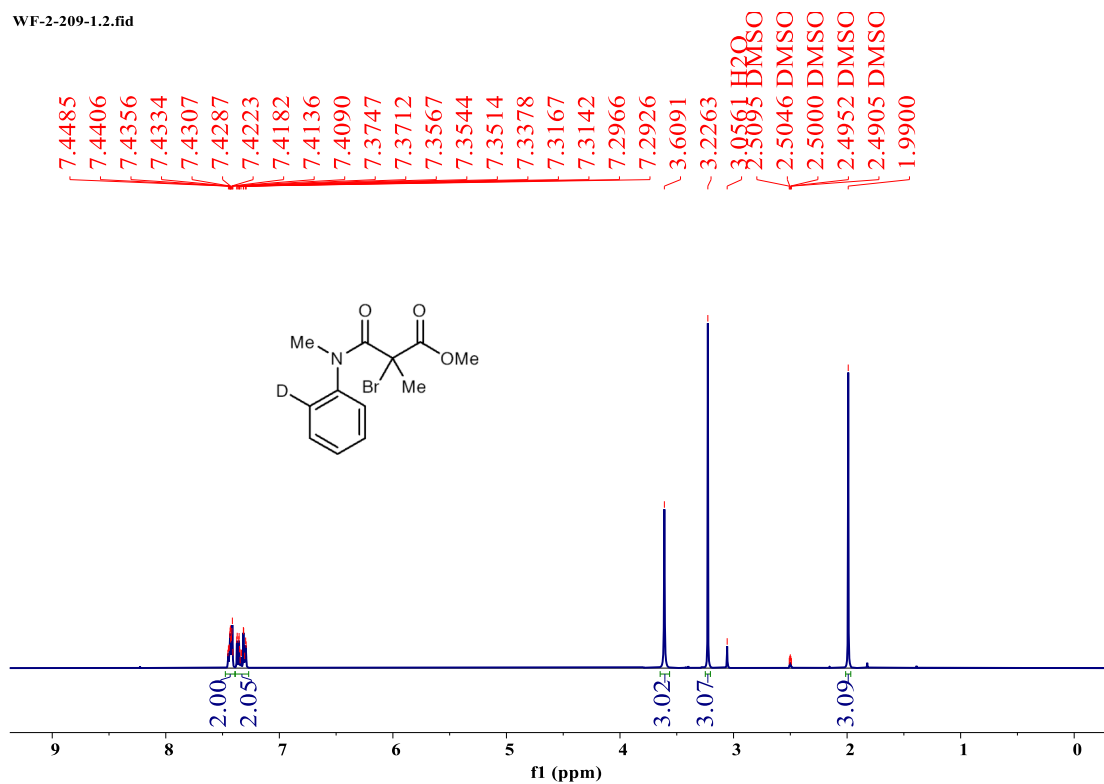
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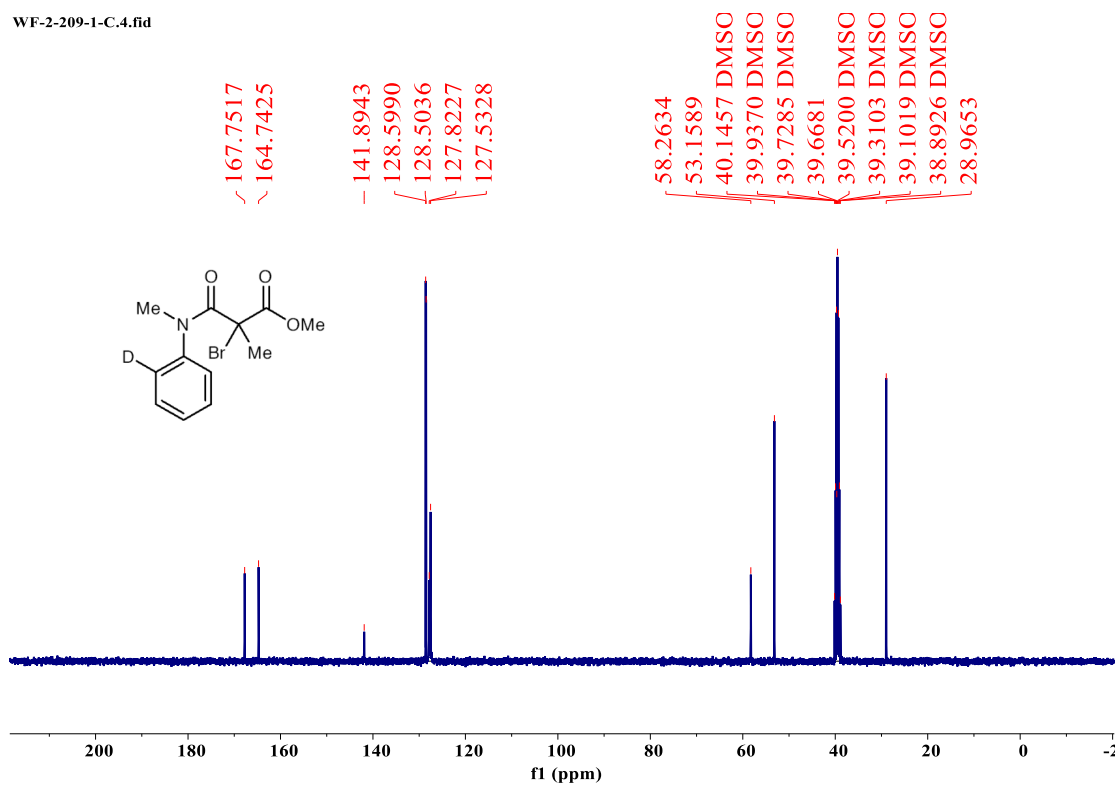
WF-2-208-1-C-500-3
Std carbon



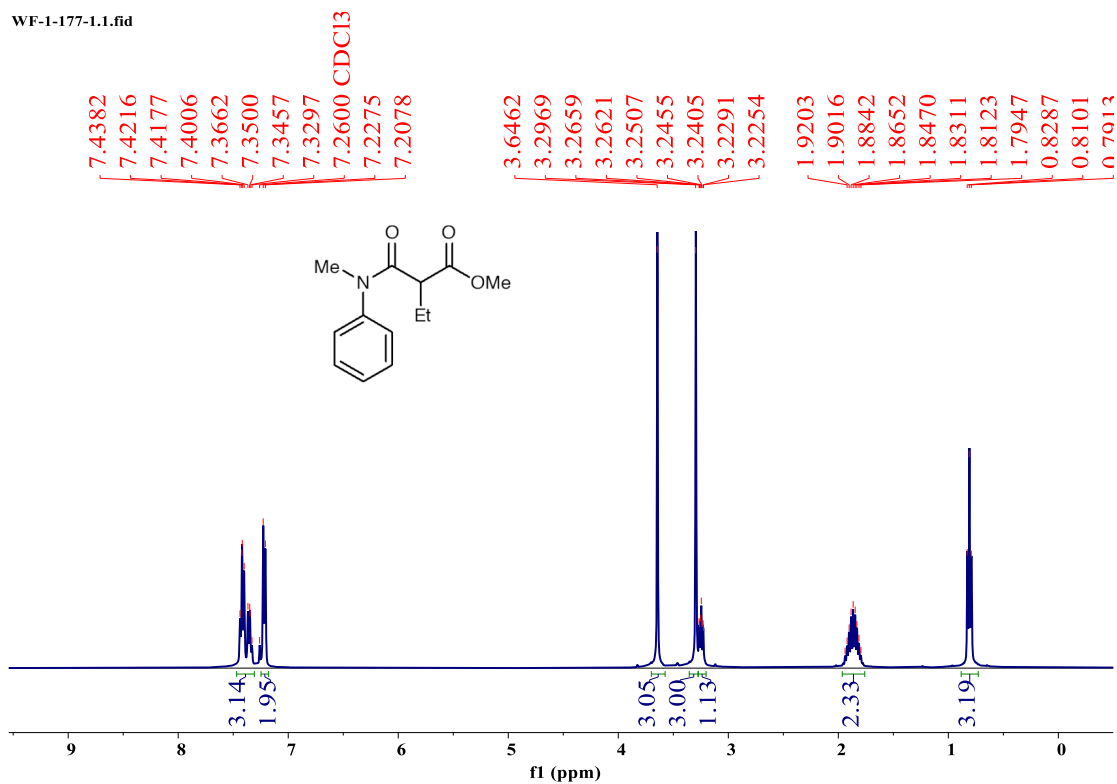
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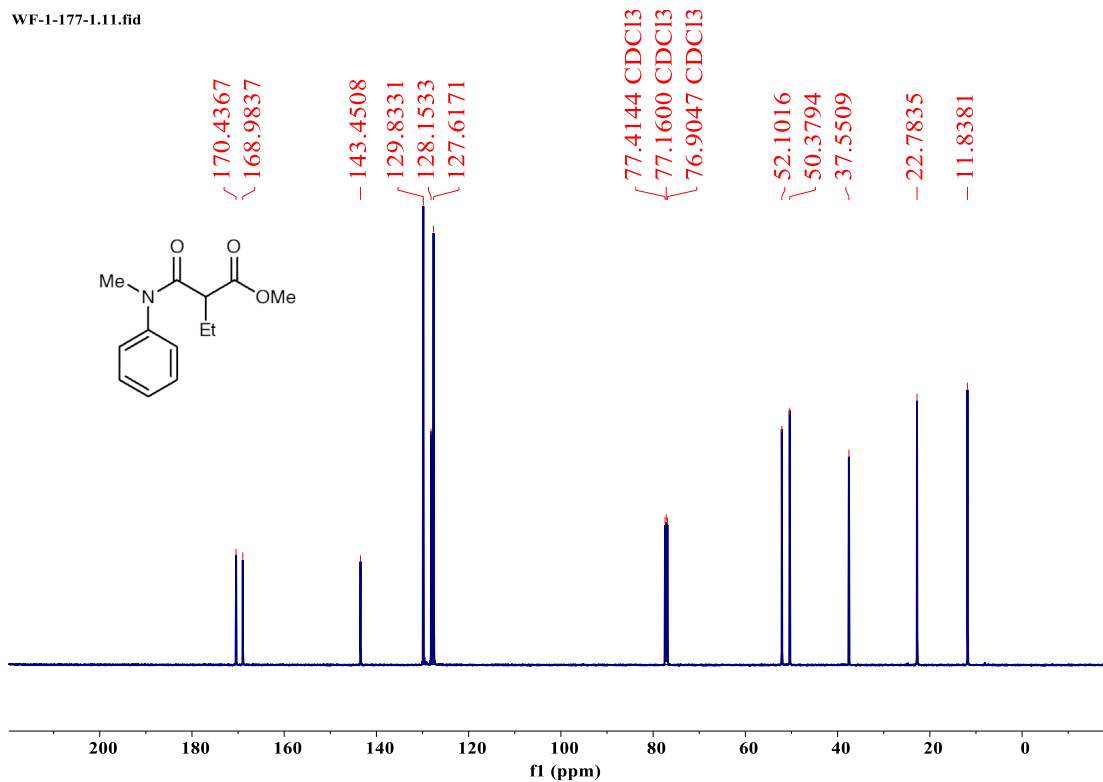
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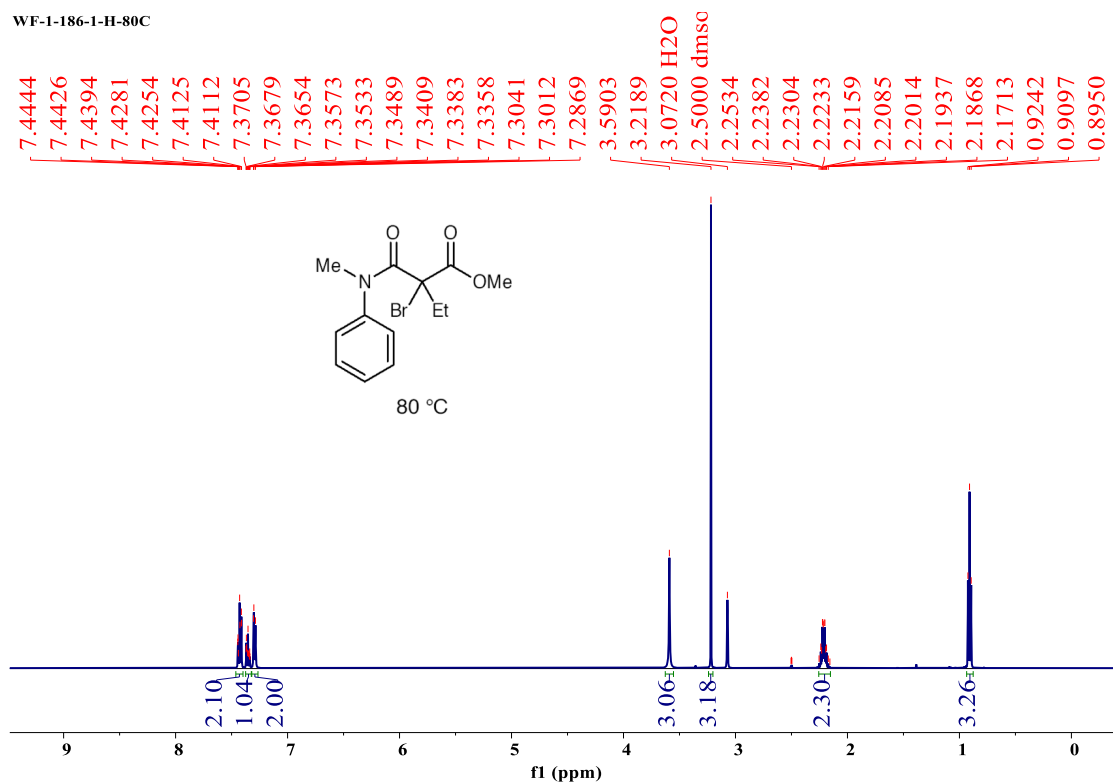
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WF-1-177-1.11.fid

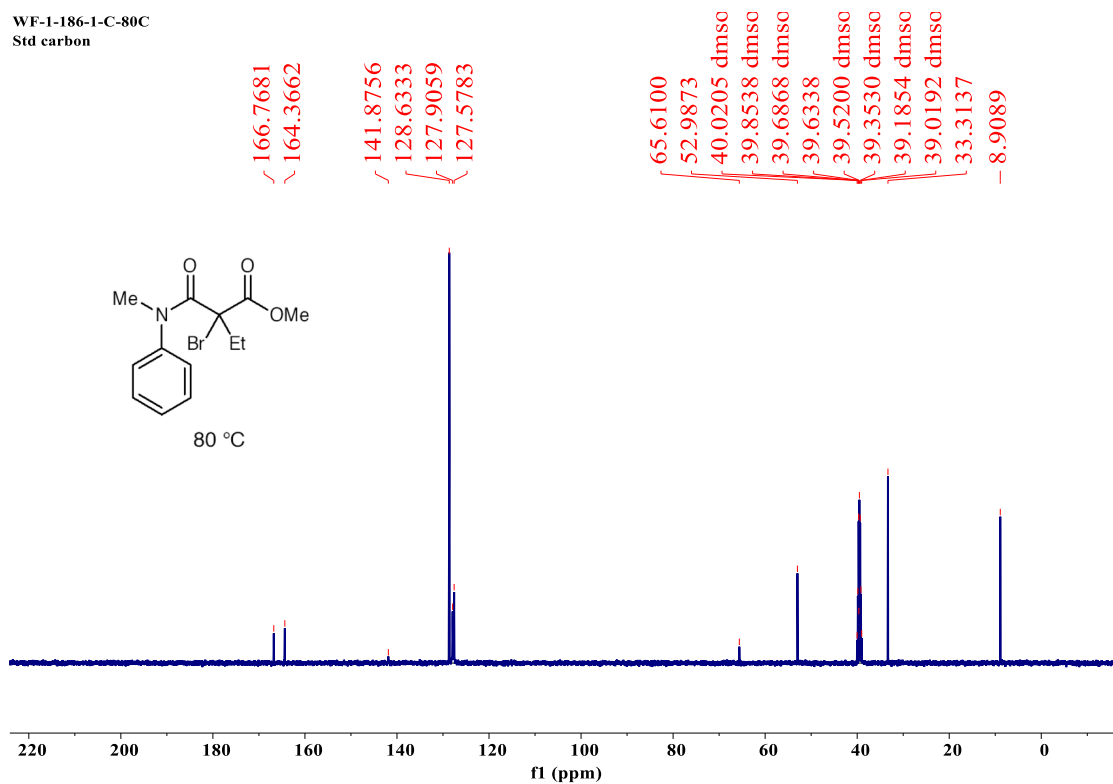


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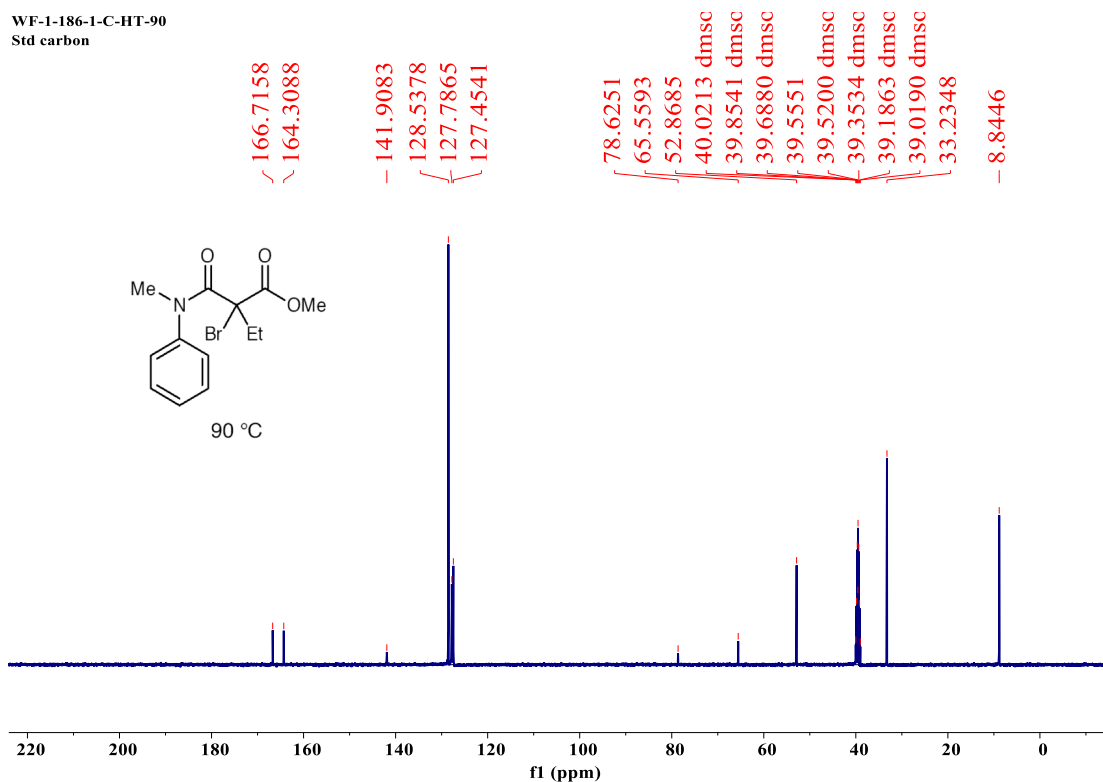


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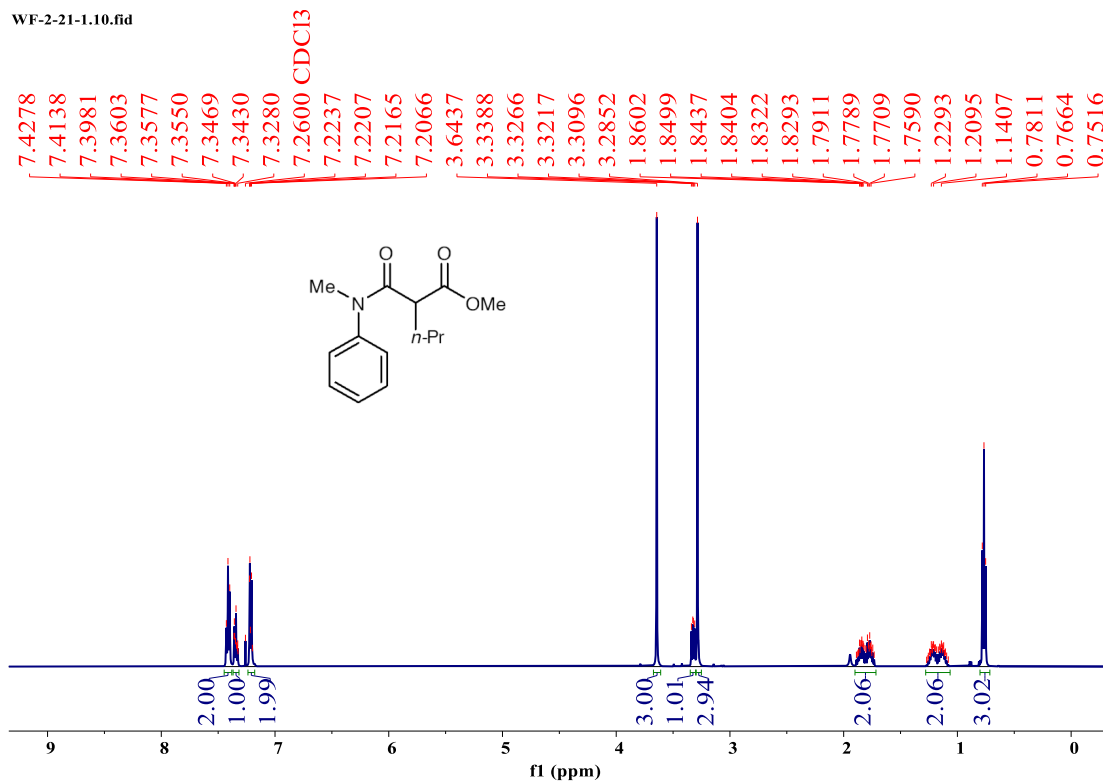
Std carbon



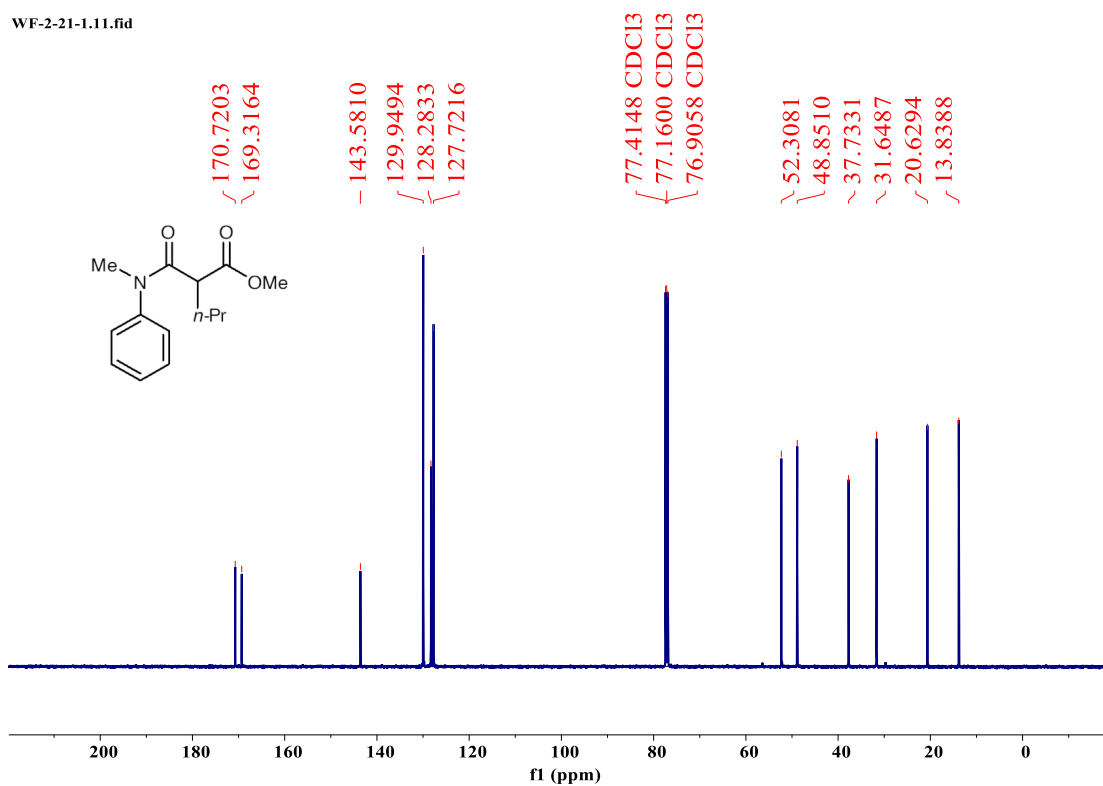
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Std carbon



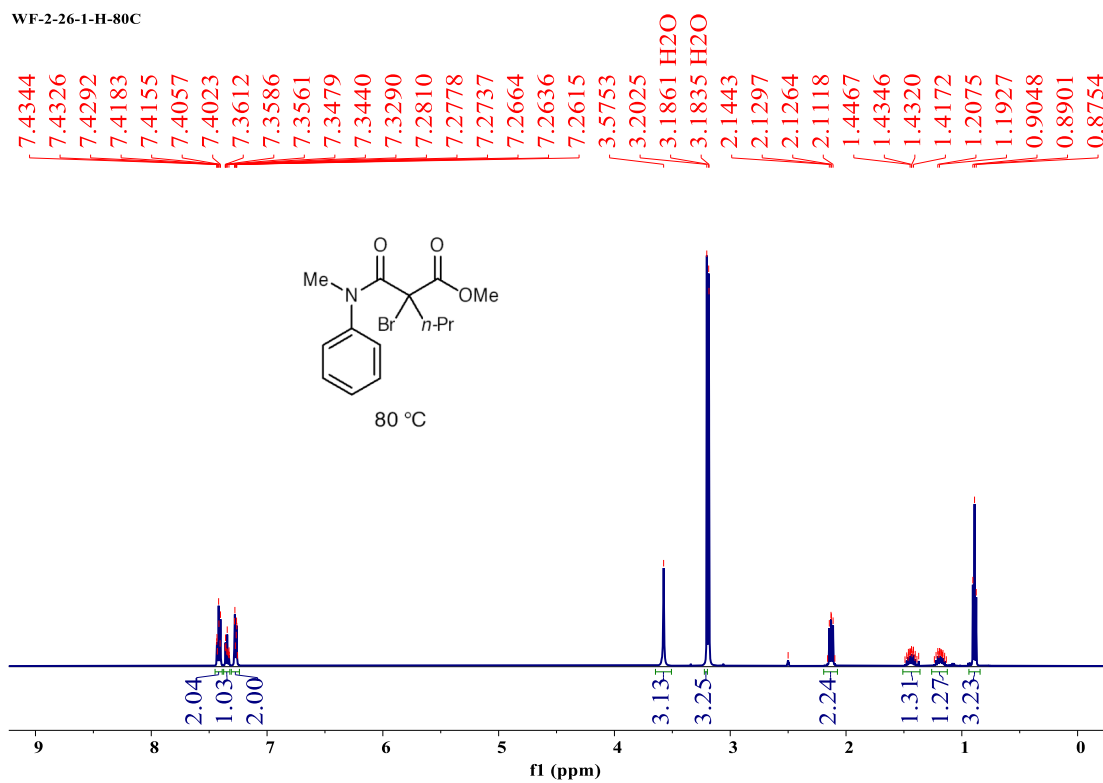
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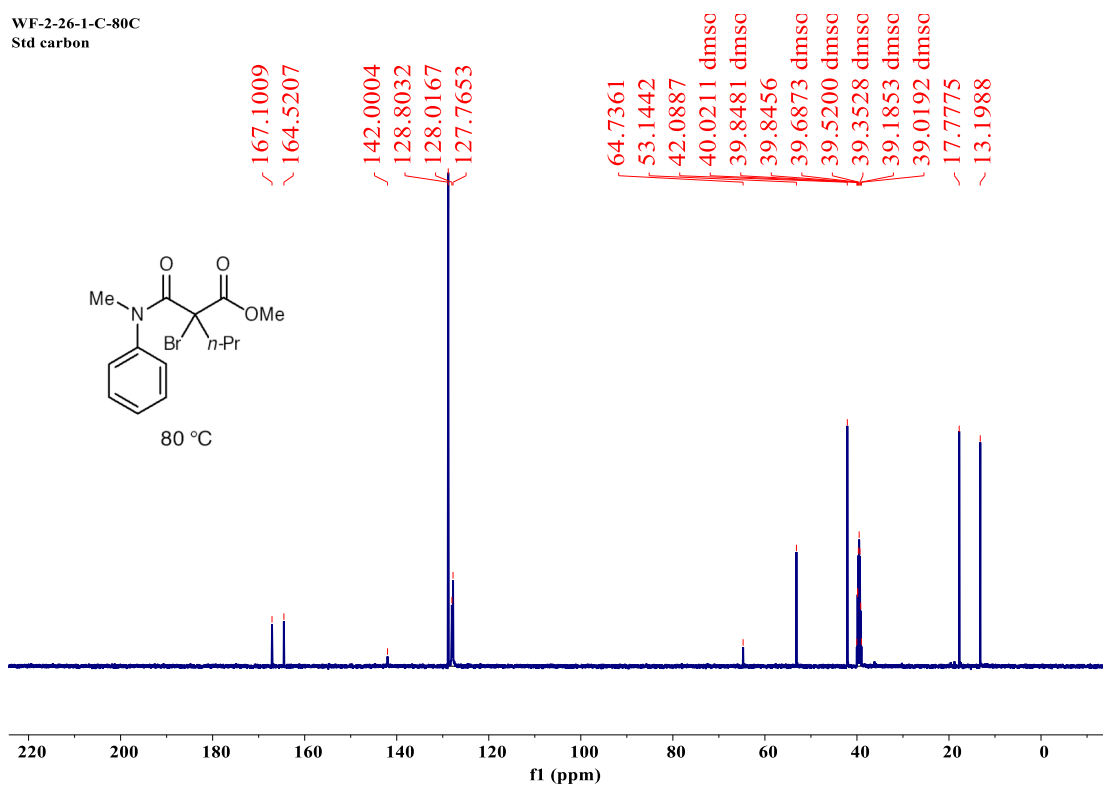
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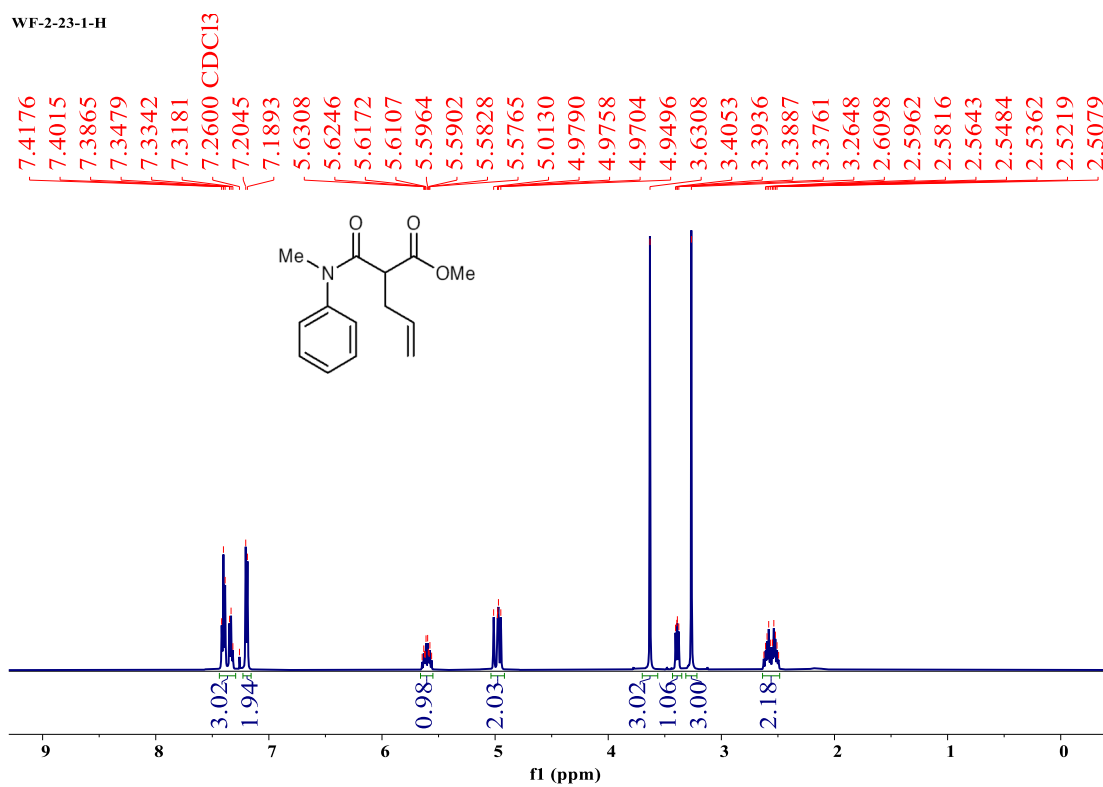
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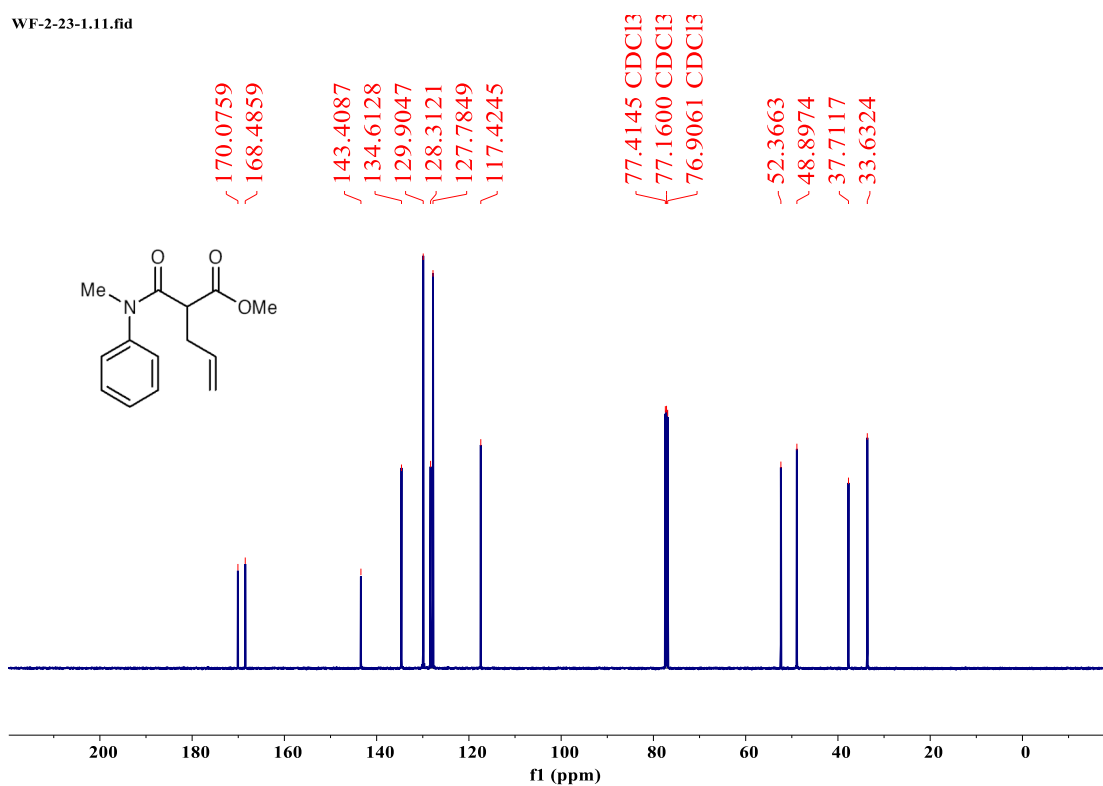
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Std carbon



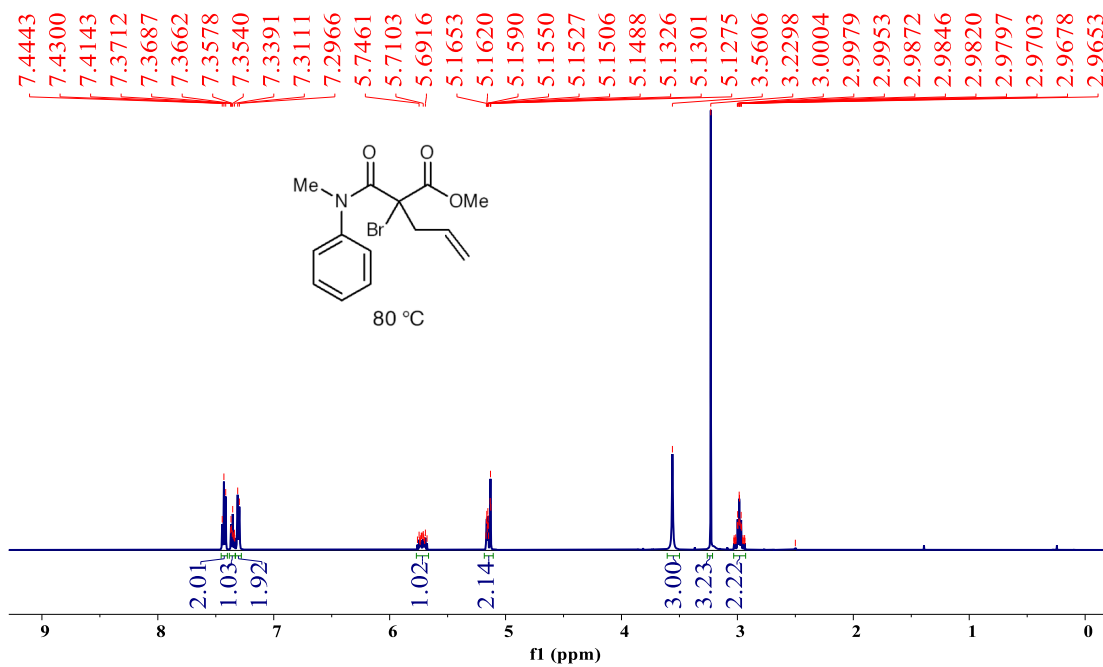
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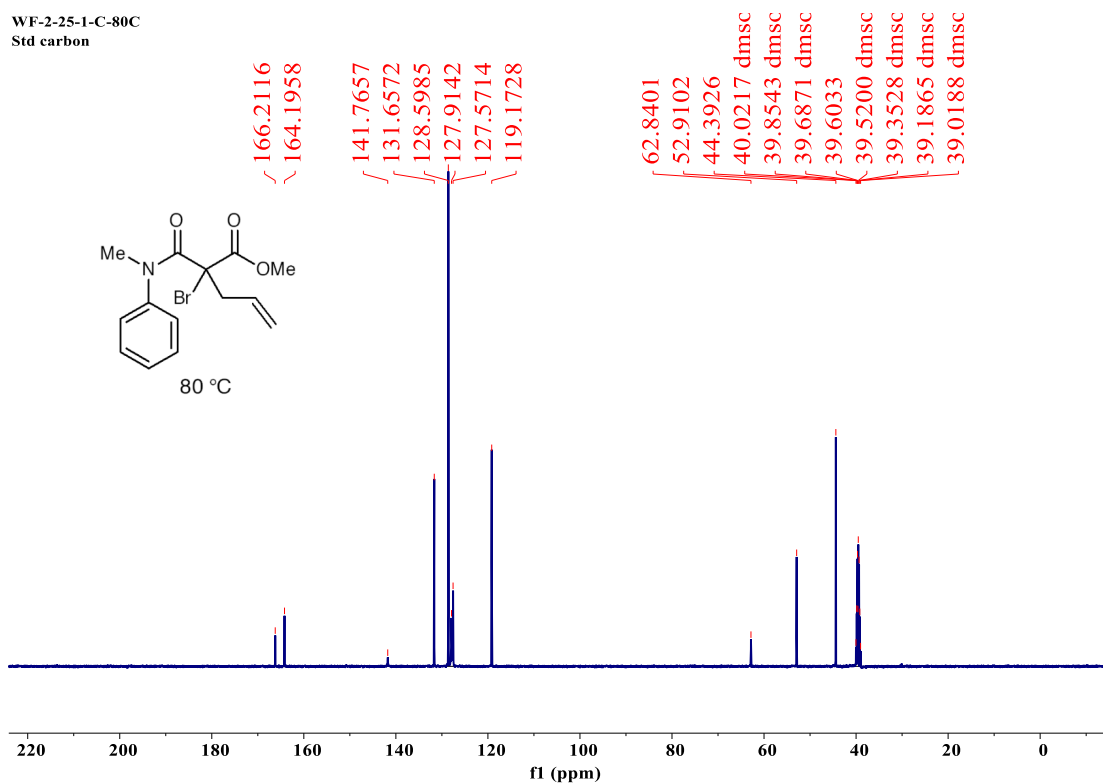
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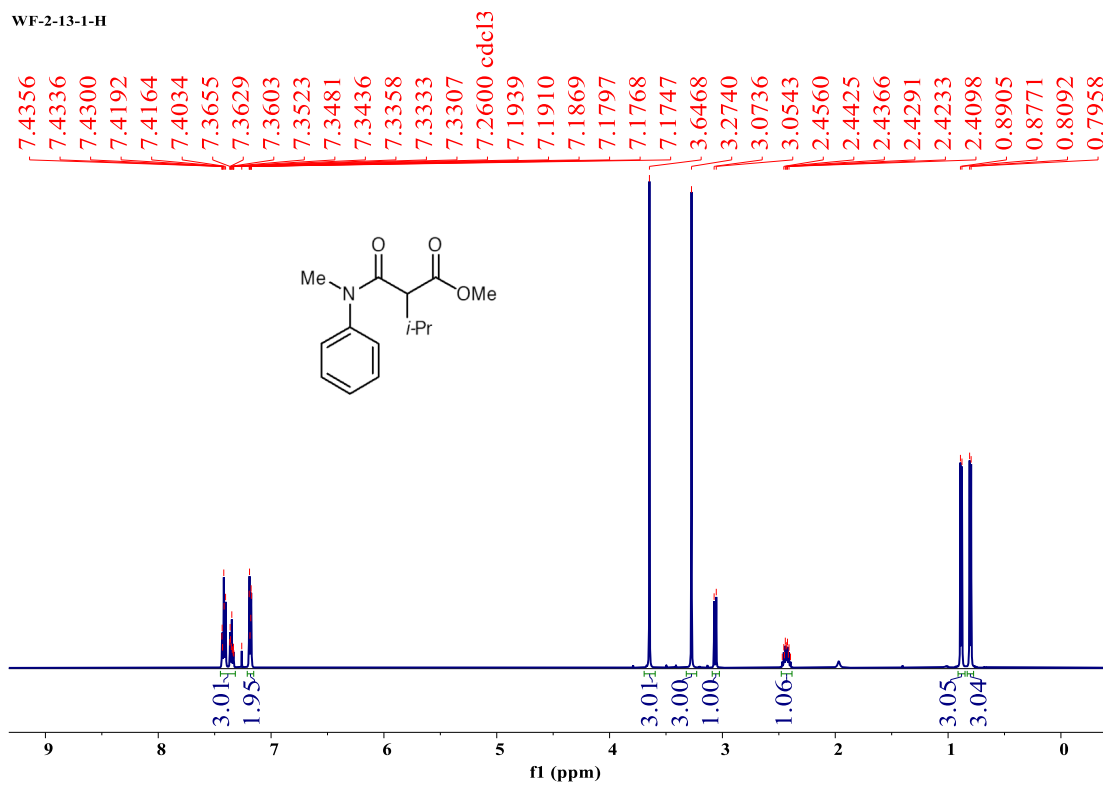
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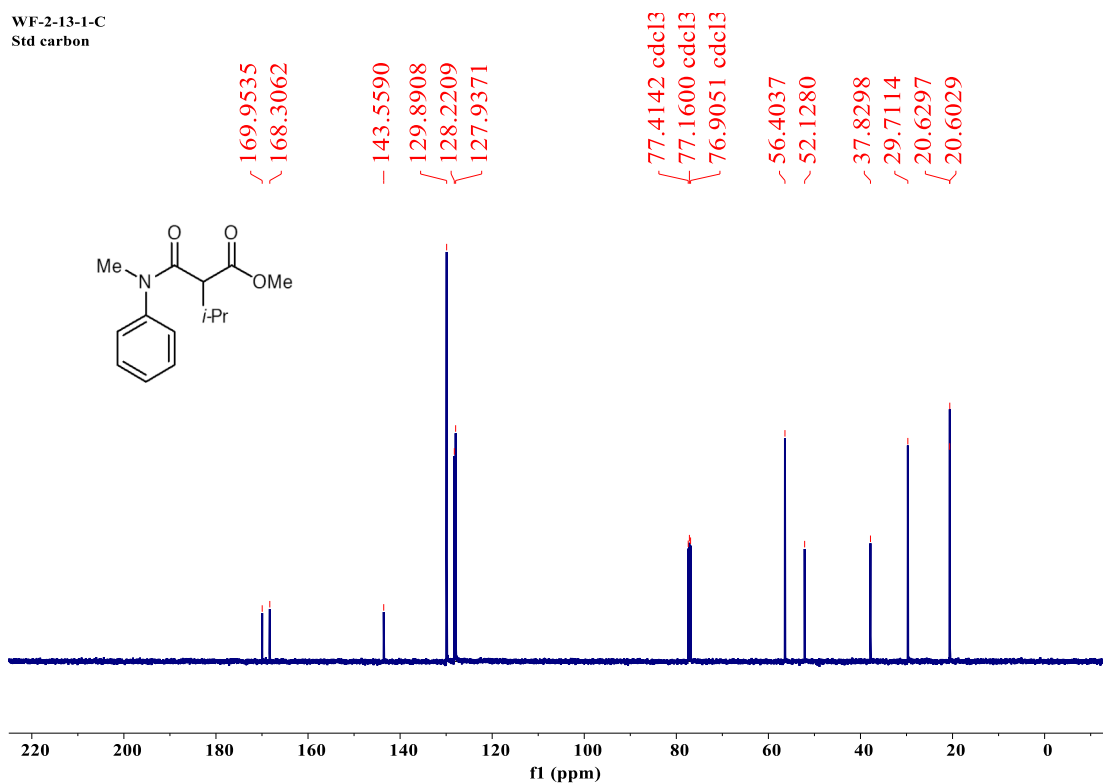
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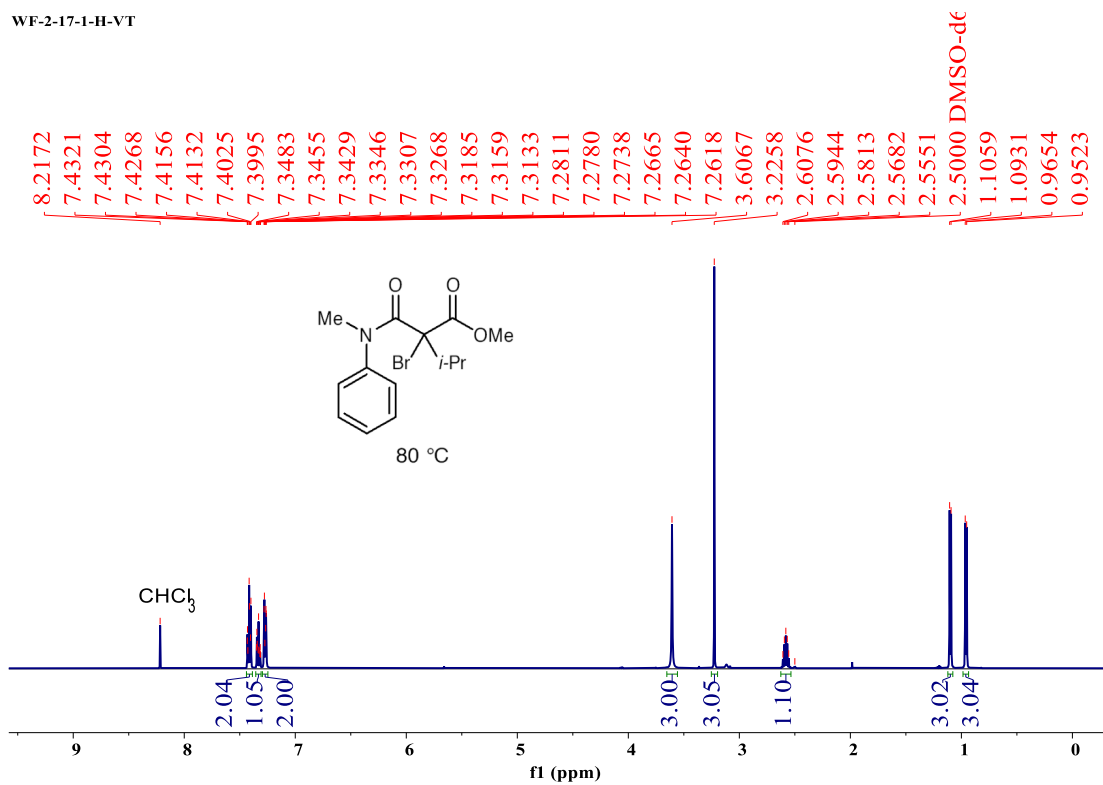
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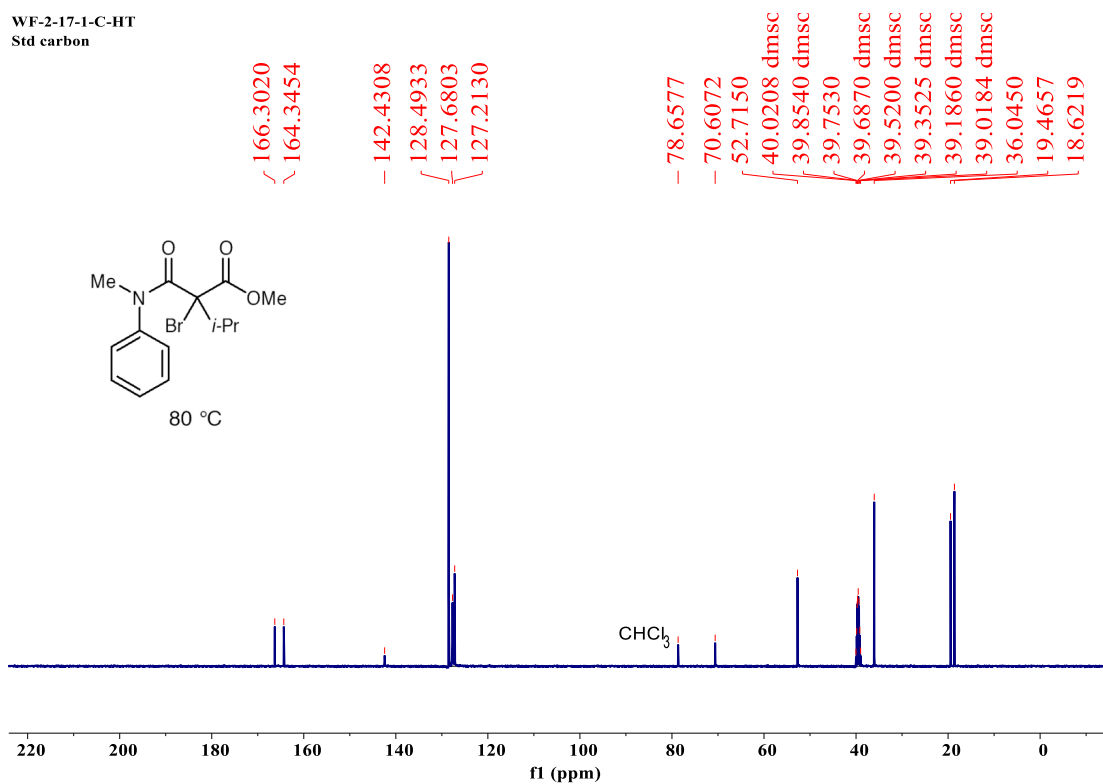
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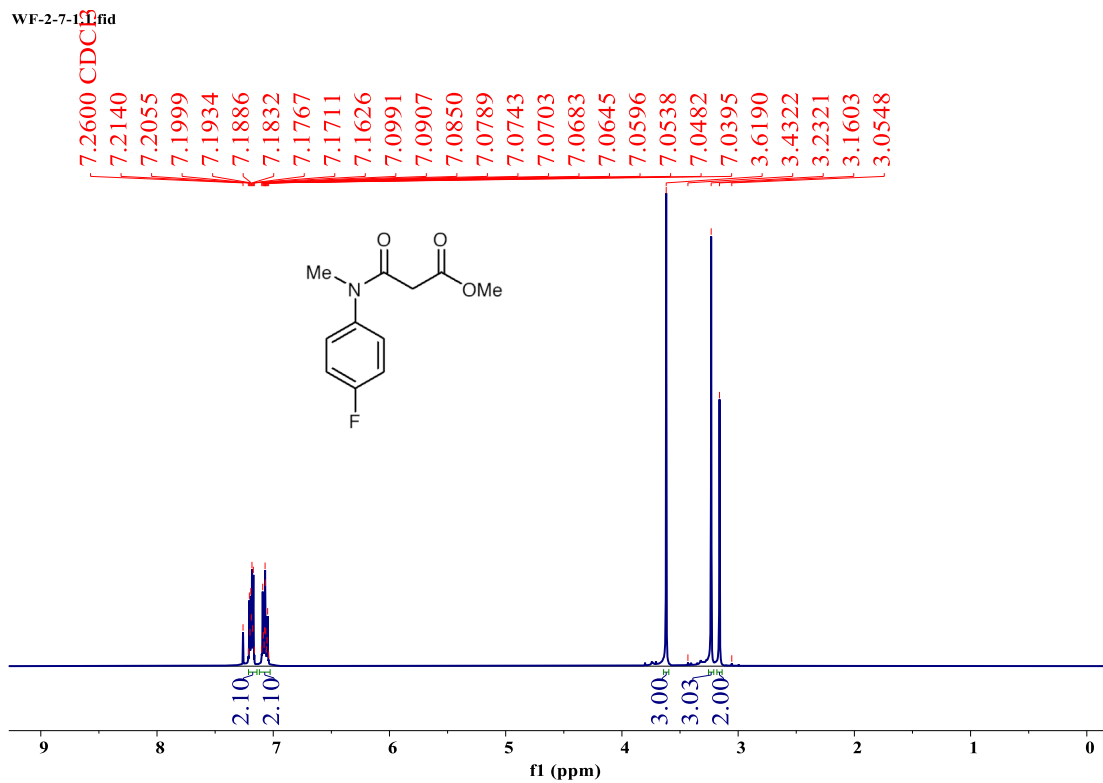
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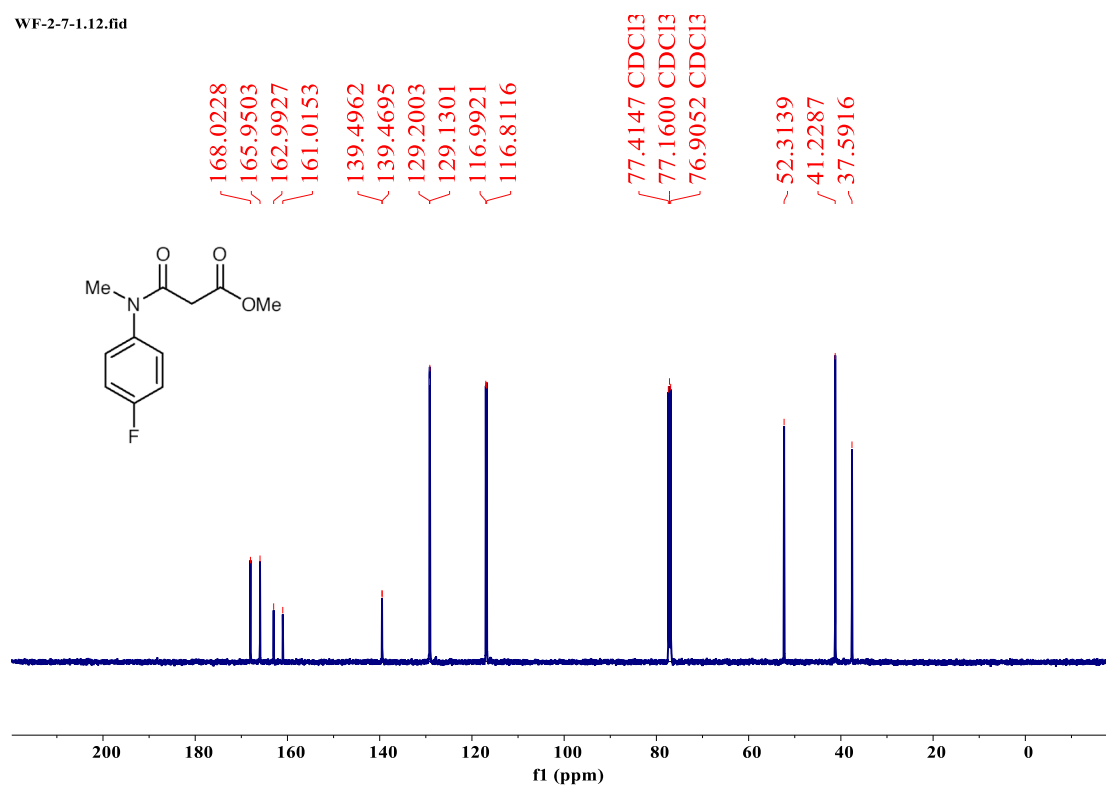
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Std carbon



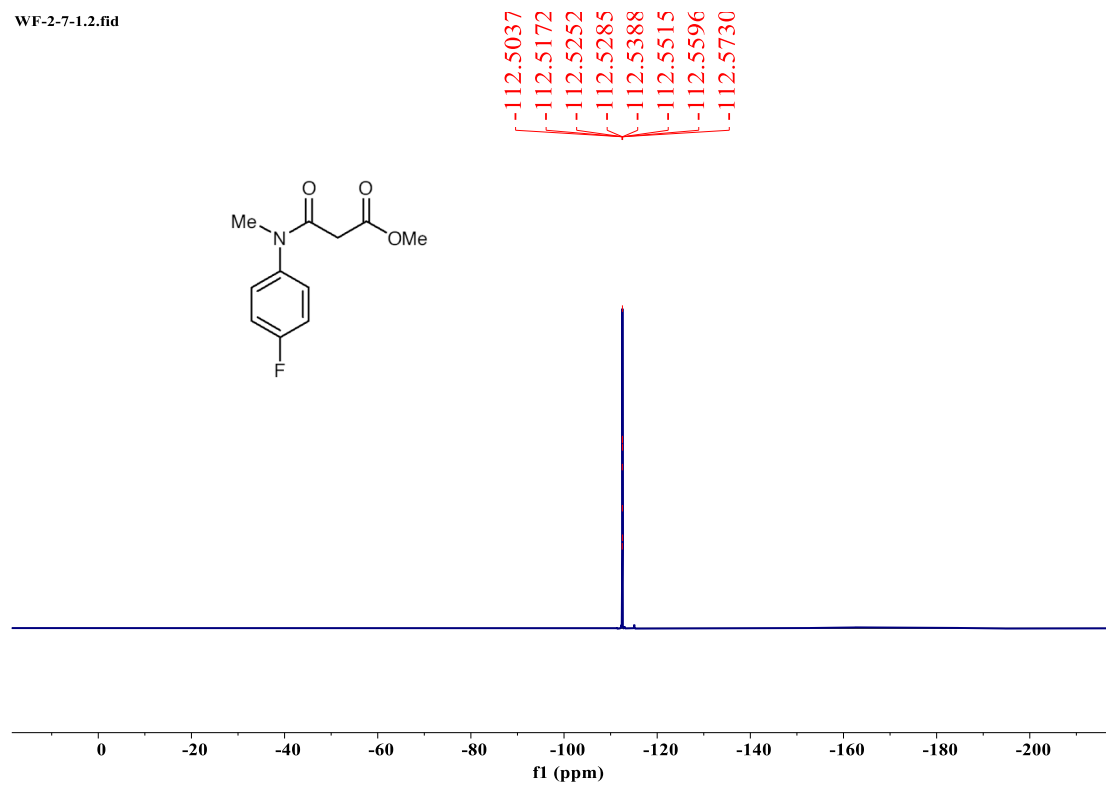
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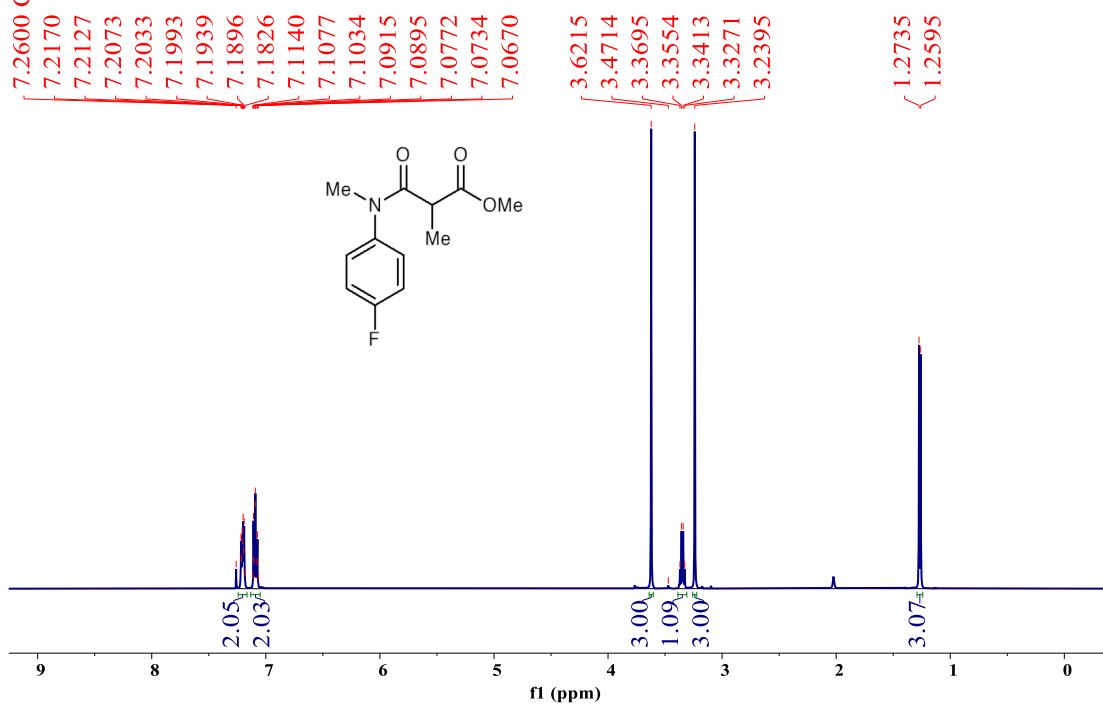
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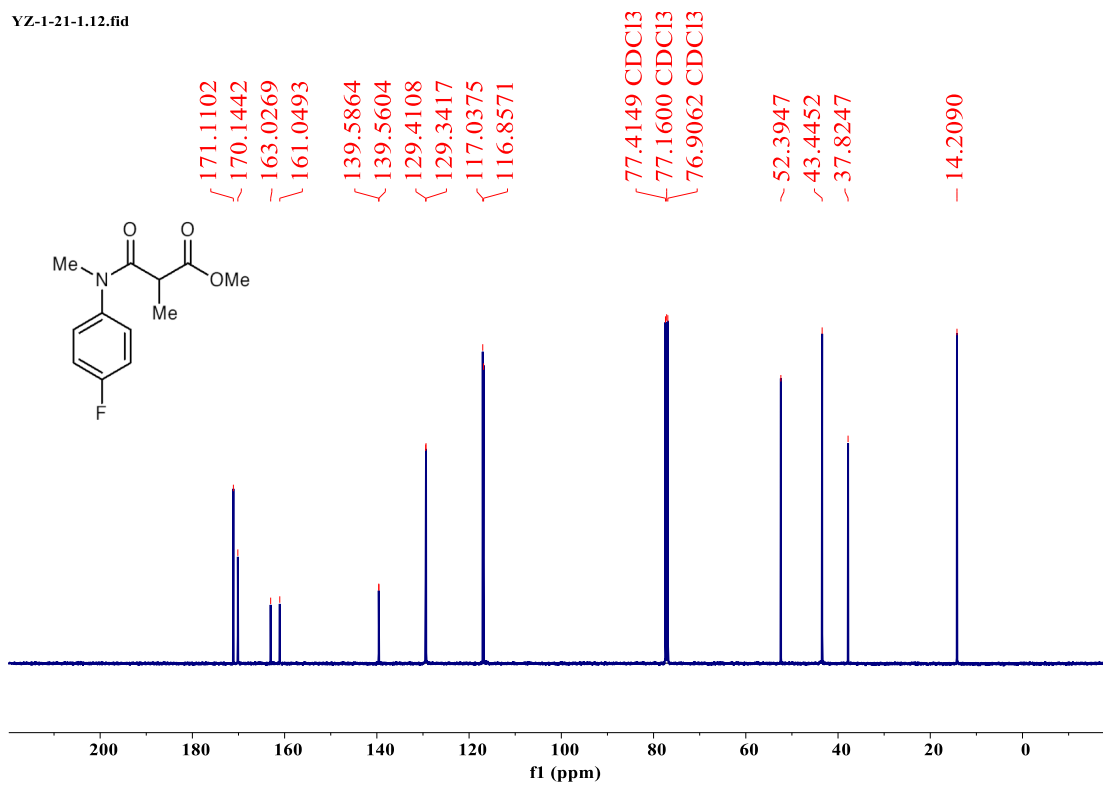
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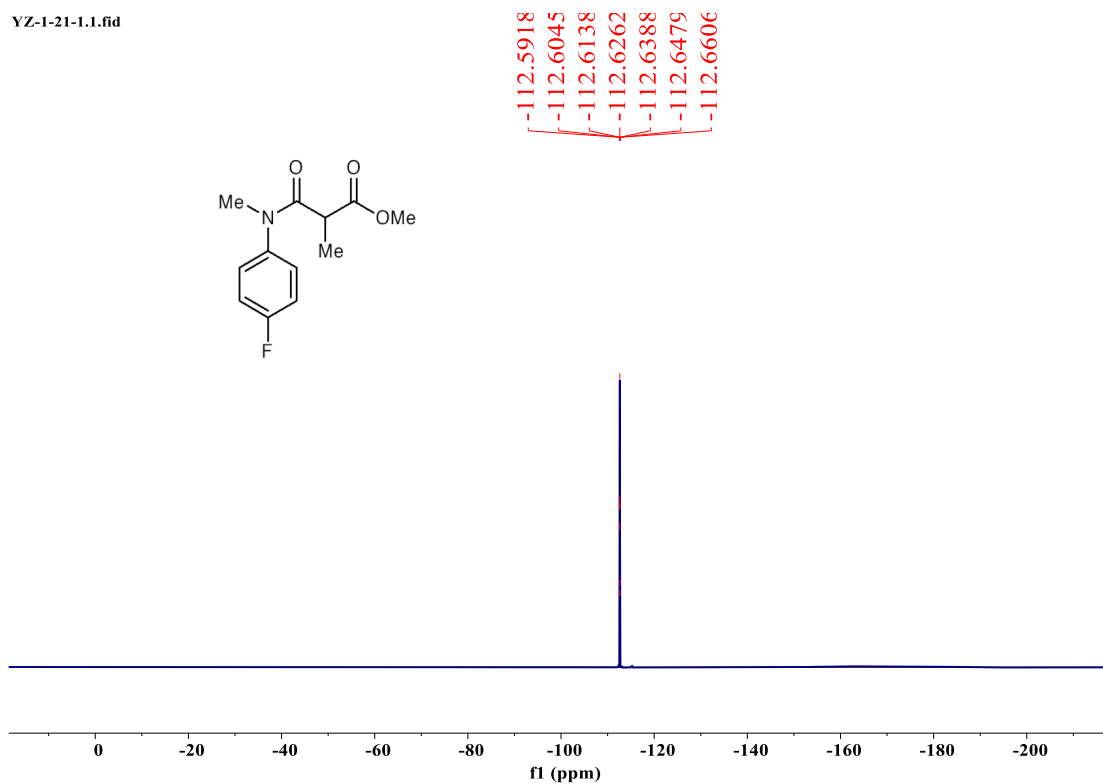
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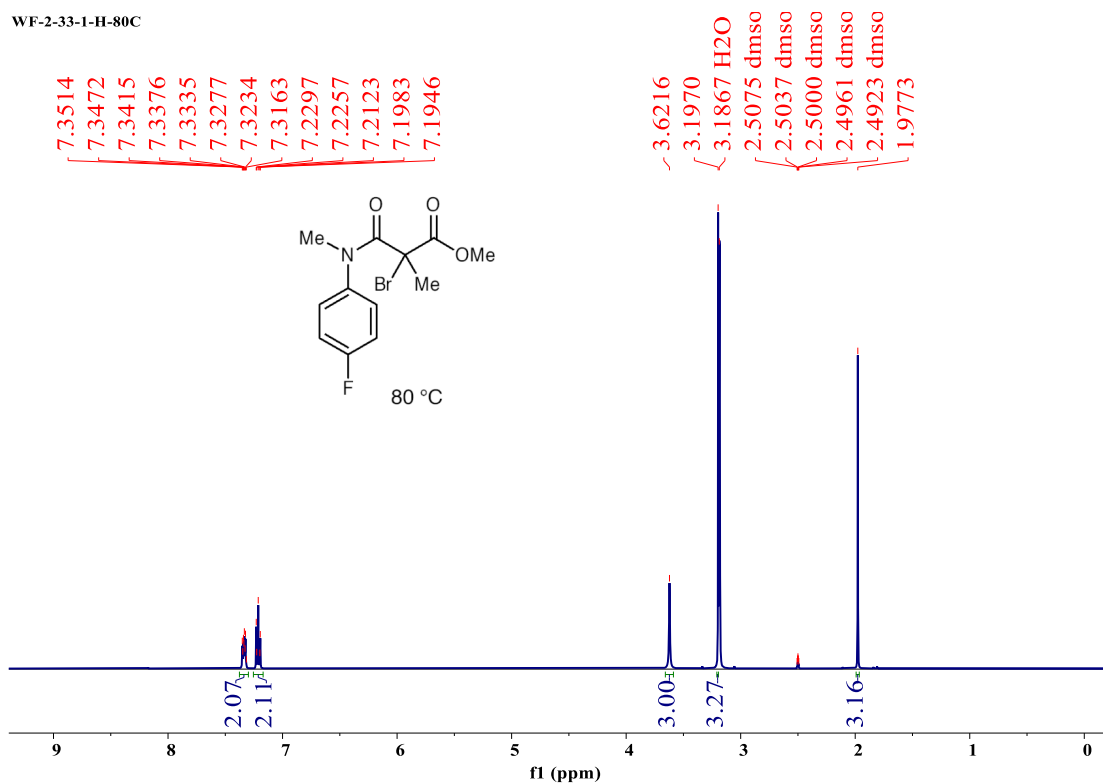
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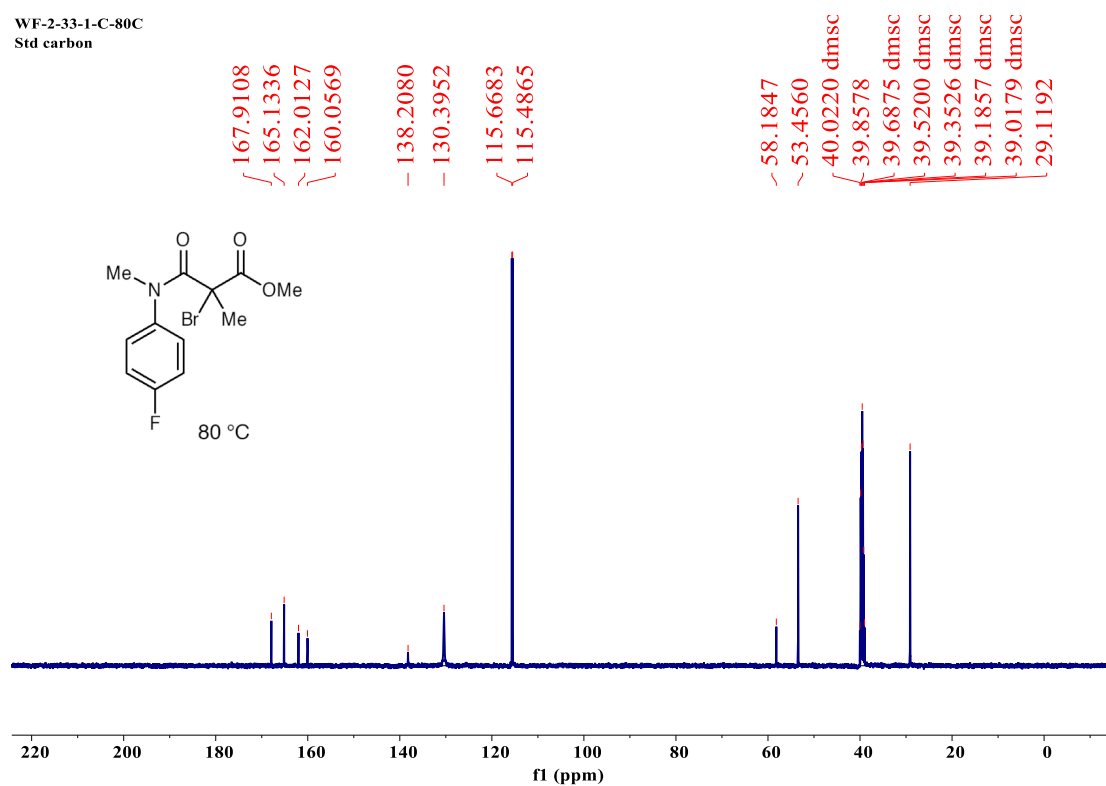
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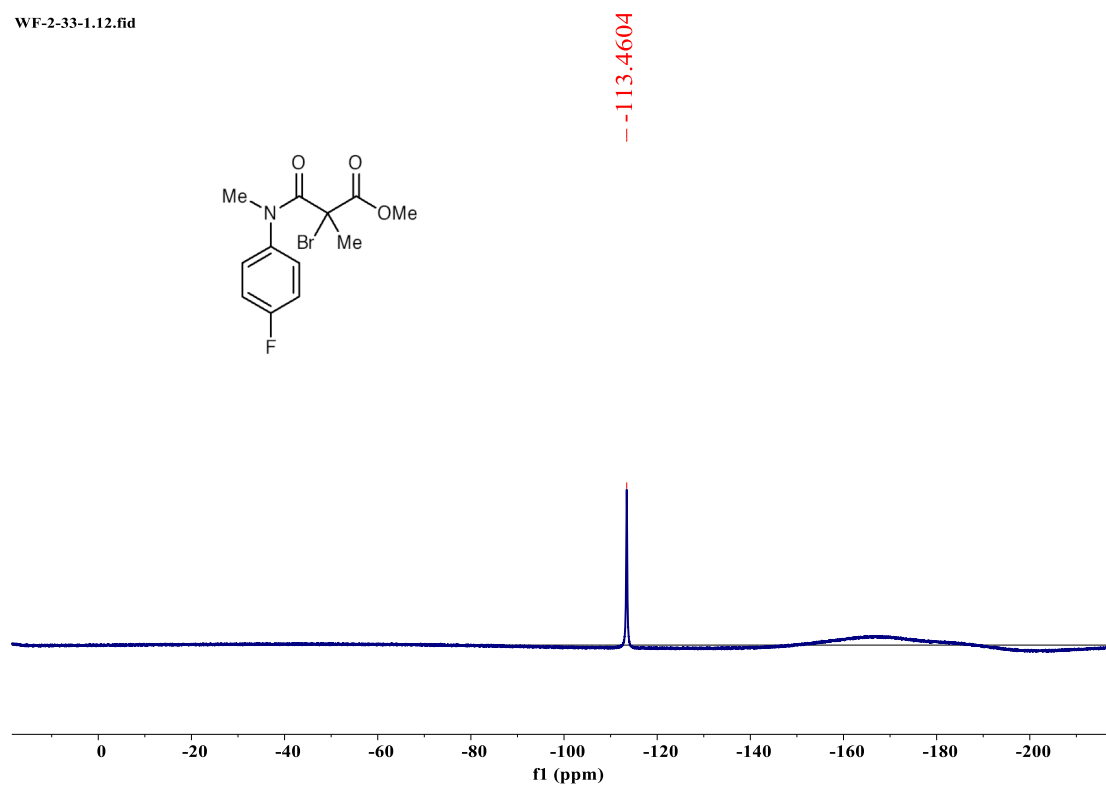
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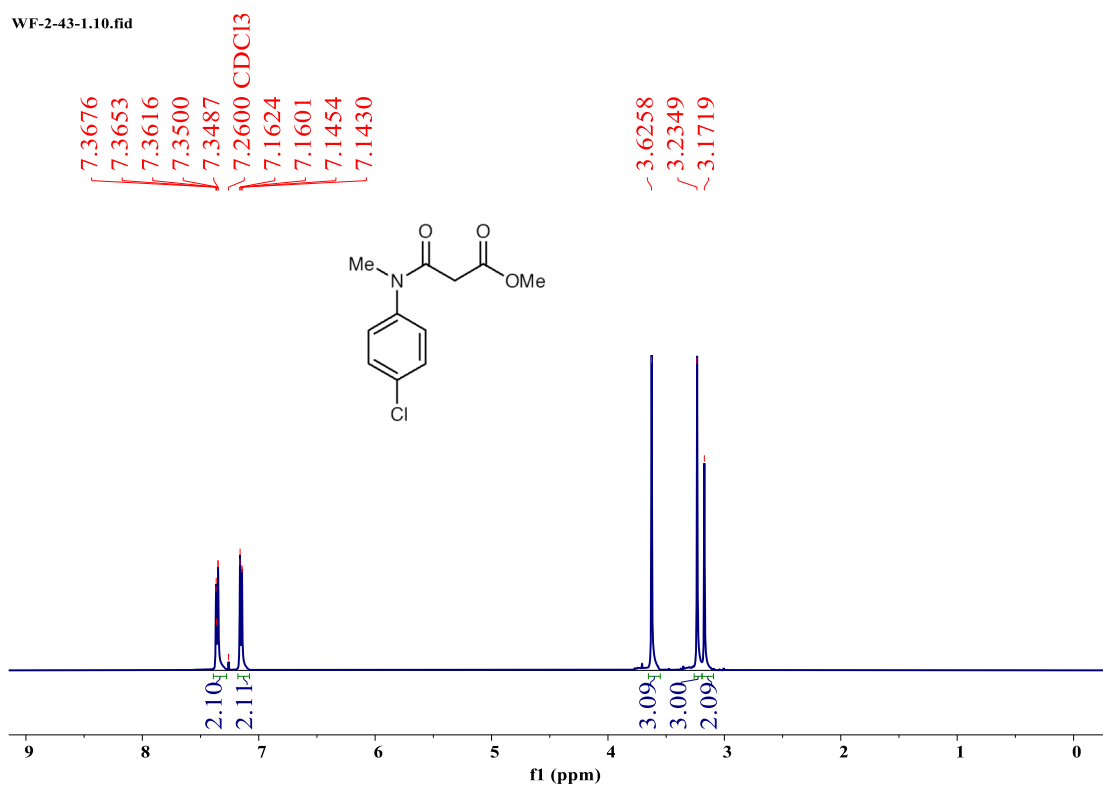
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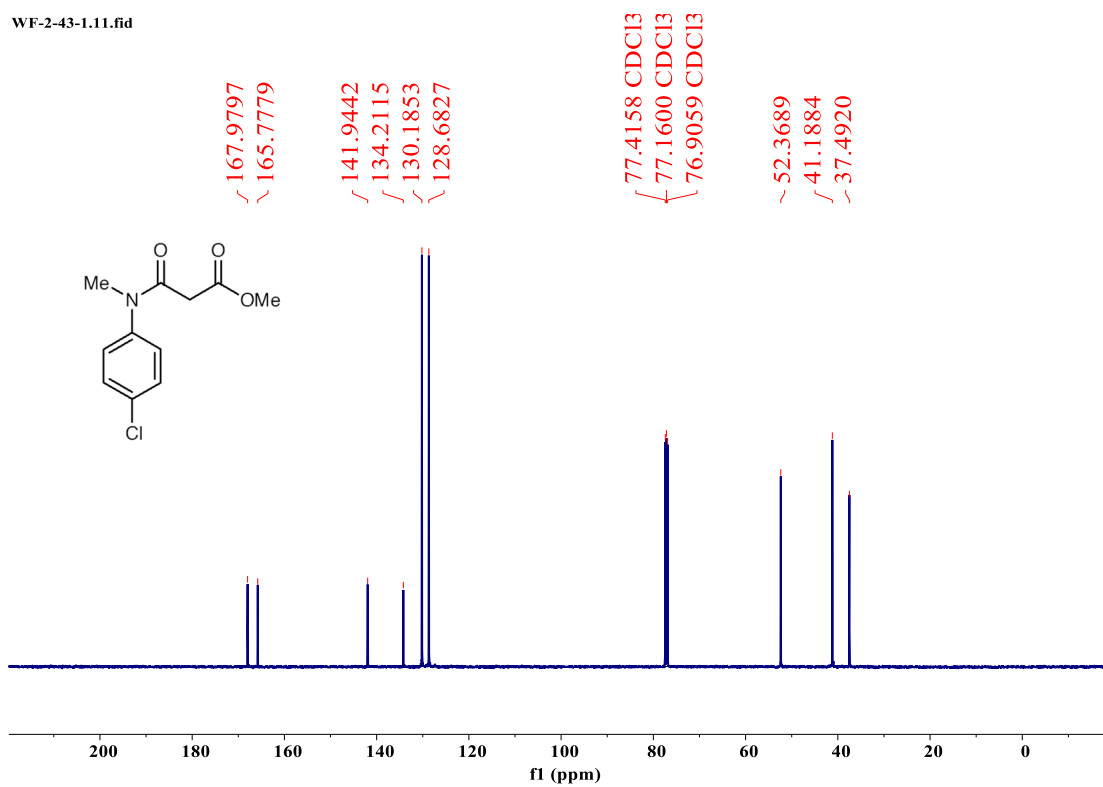
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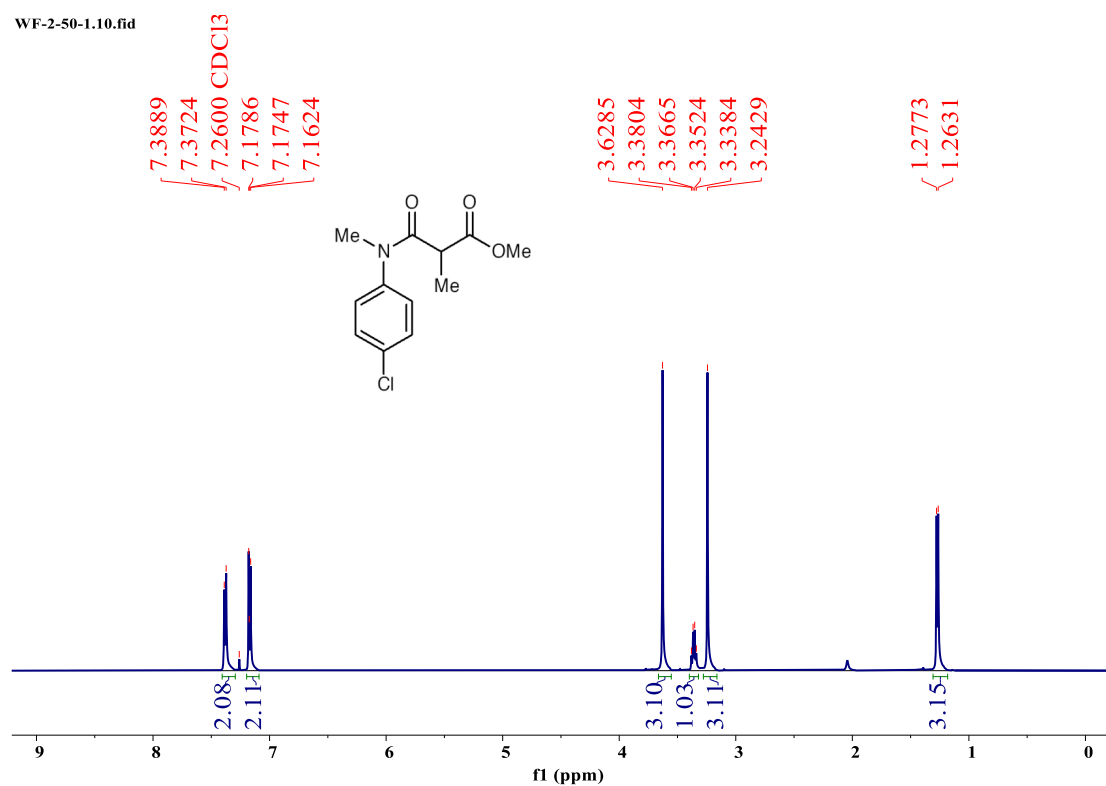
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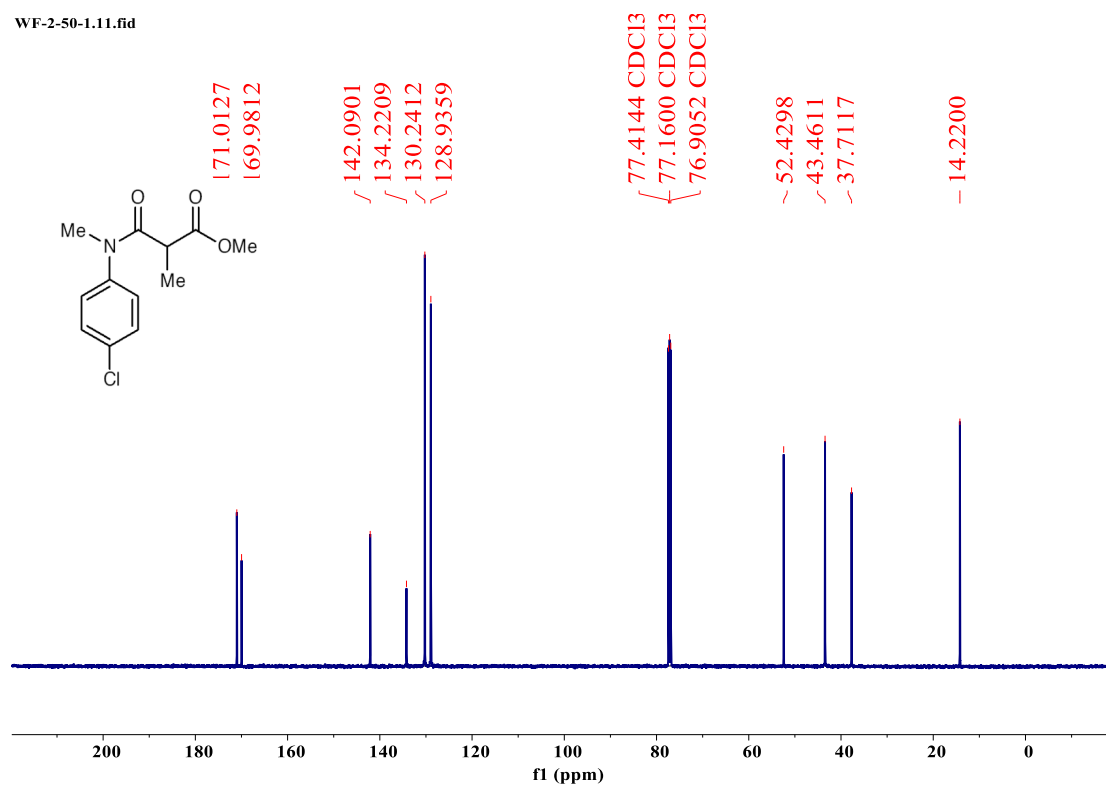
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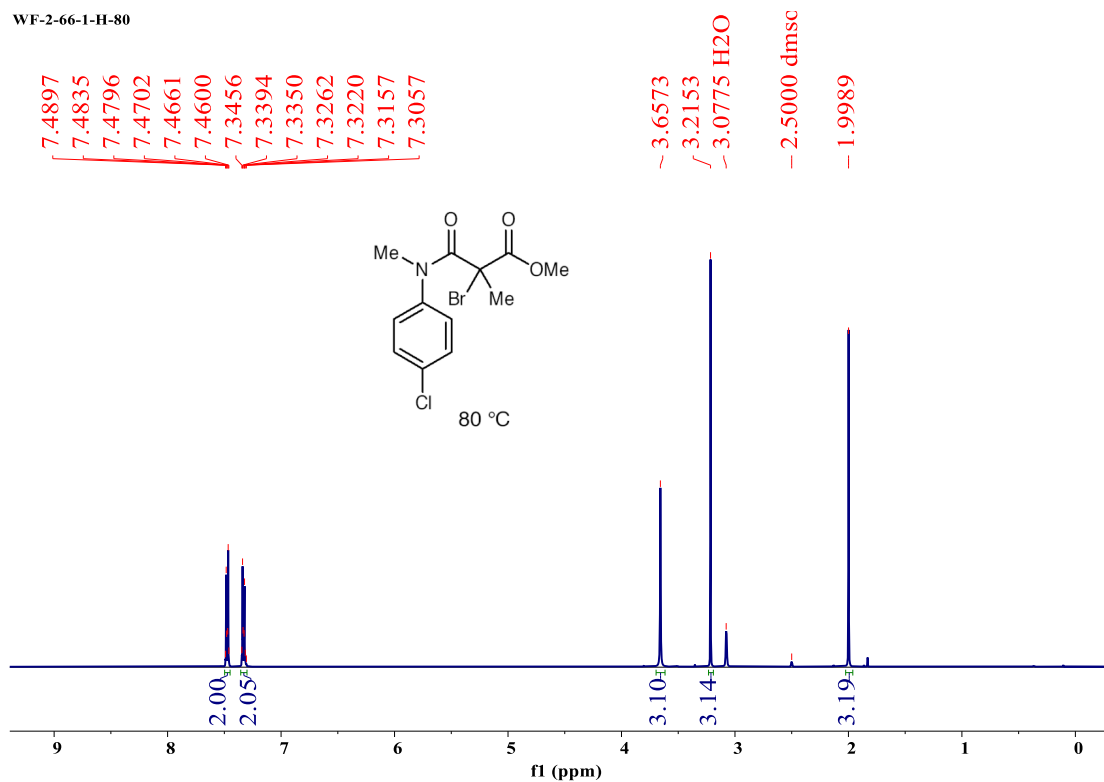
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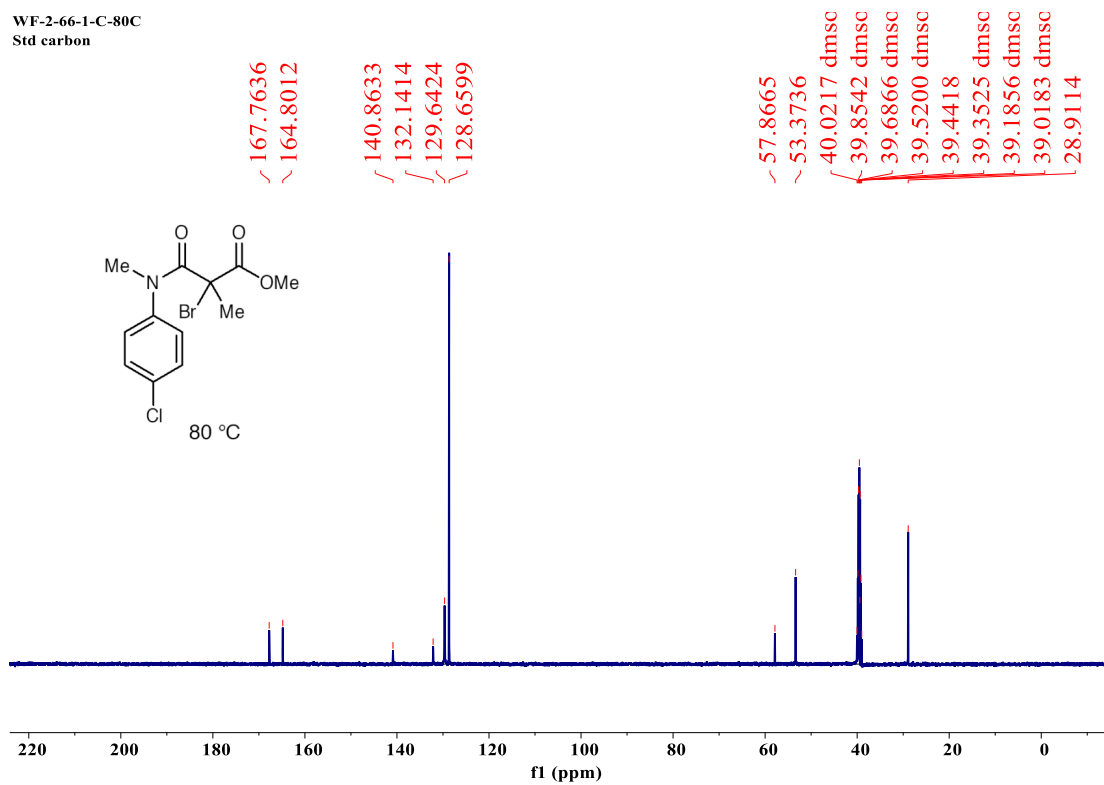
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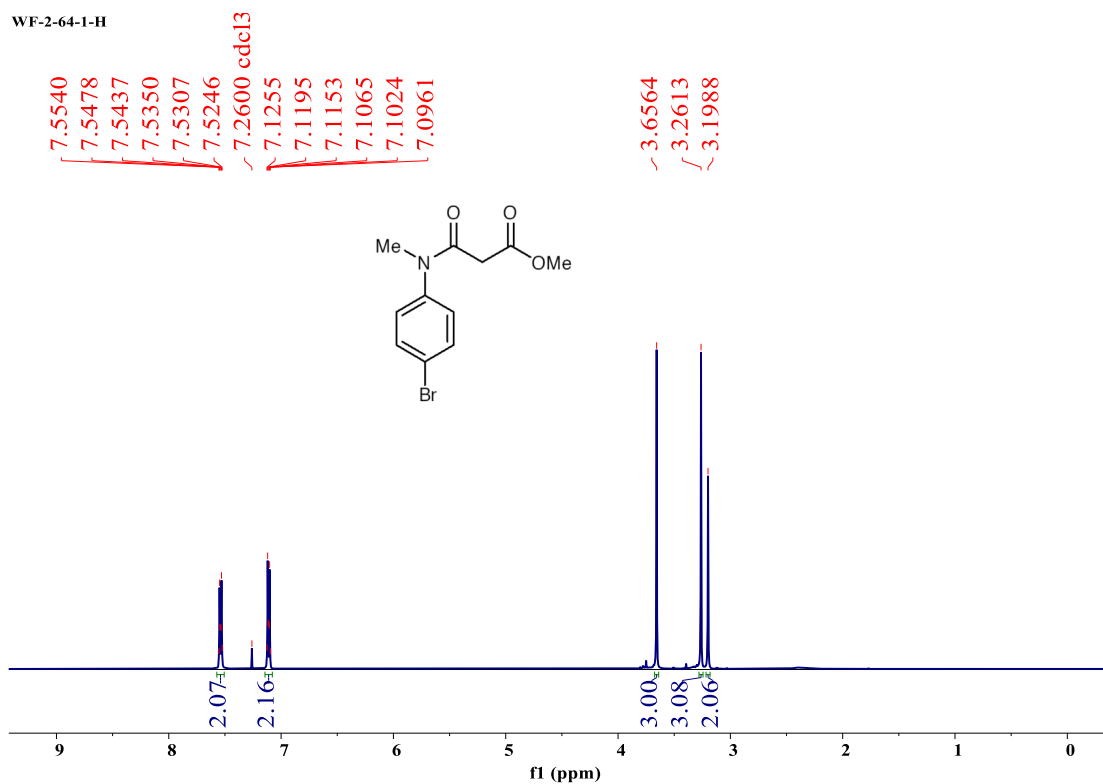
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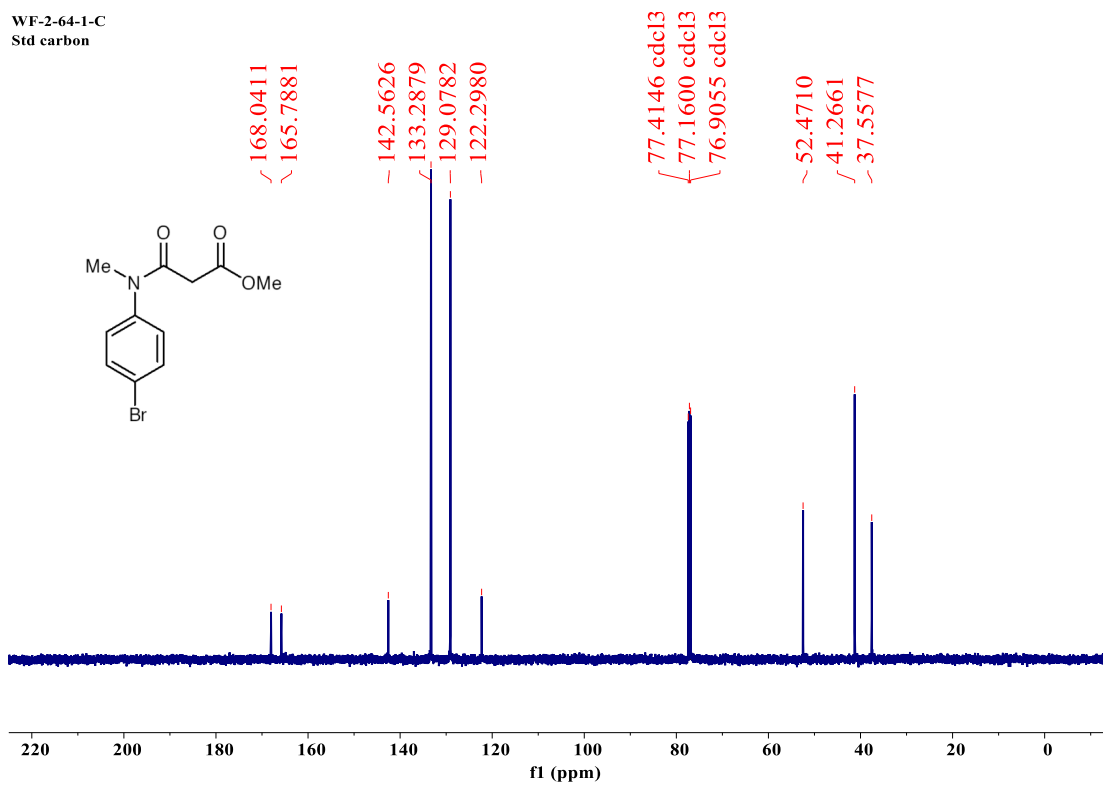
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Std carbon



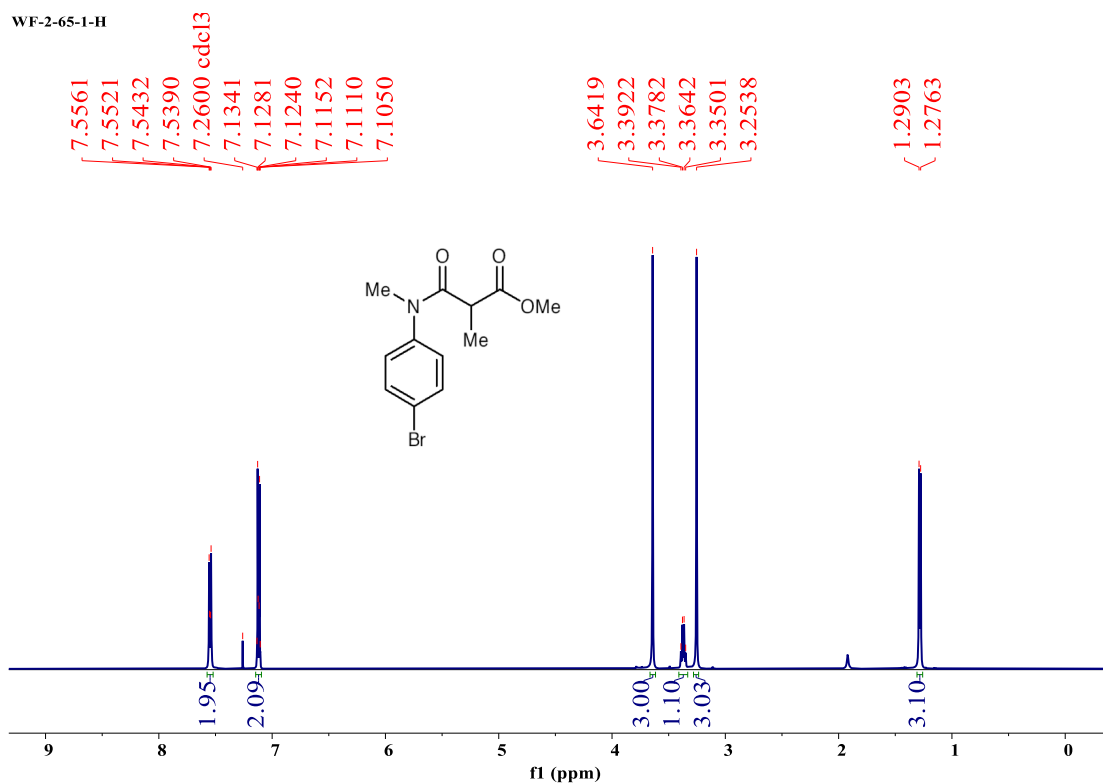
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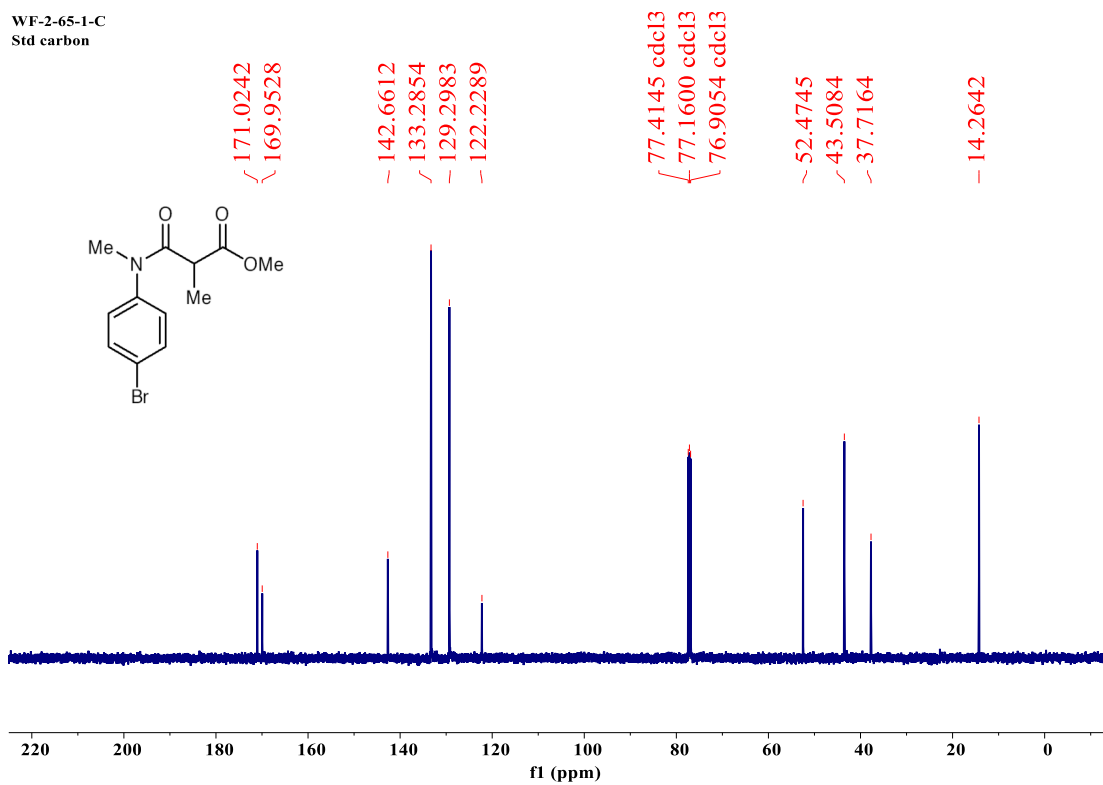
WF-2-64-1-C
Std carbon



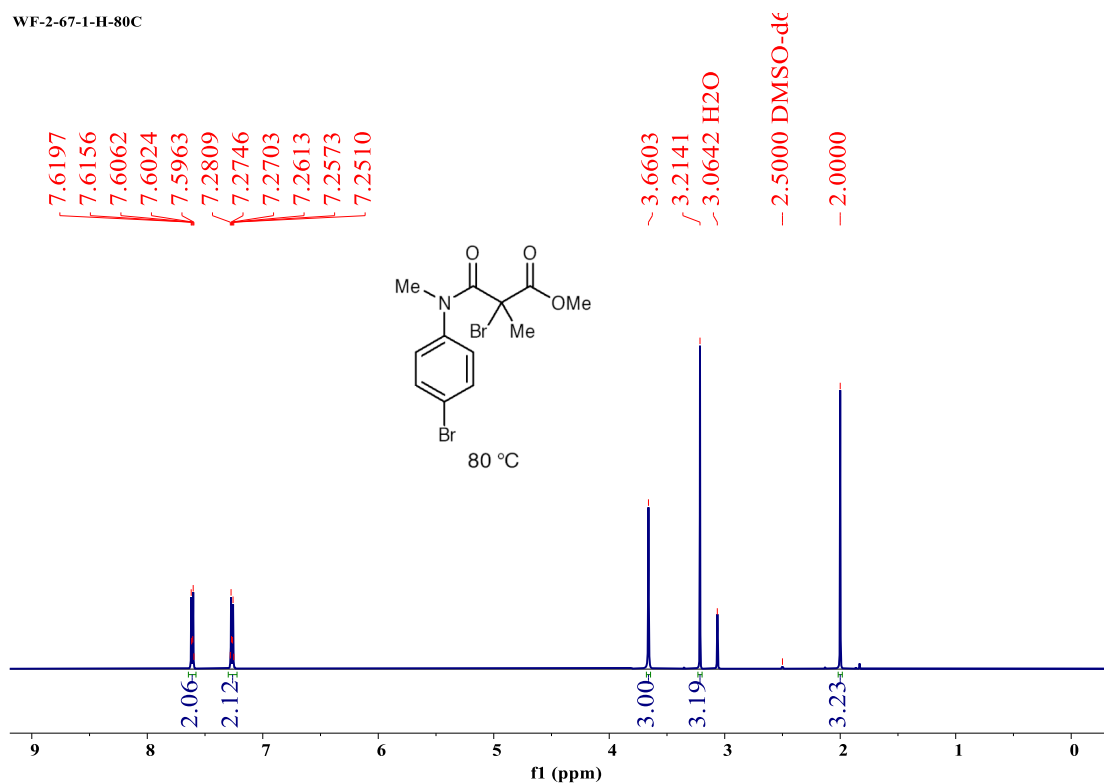
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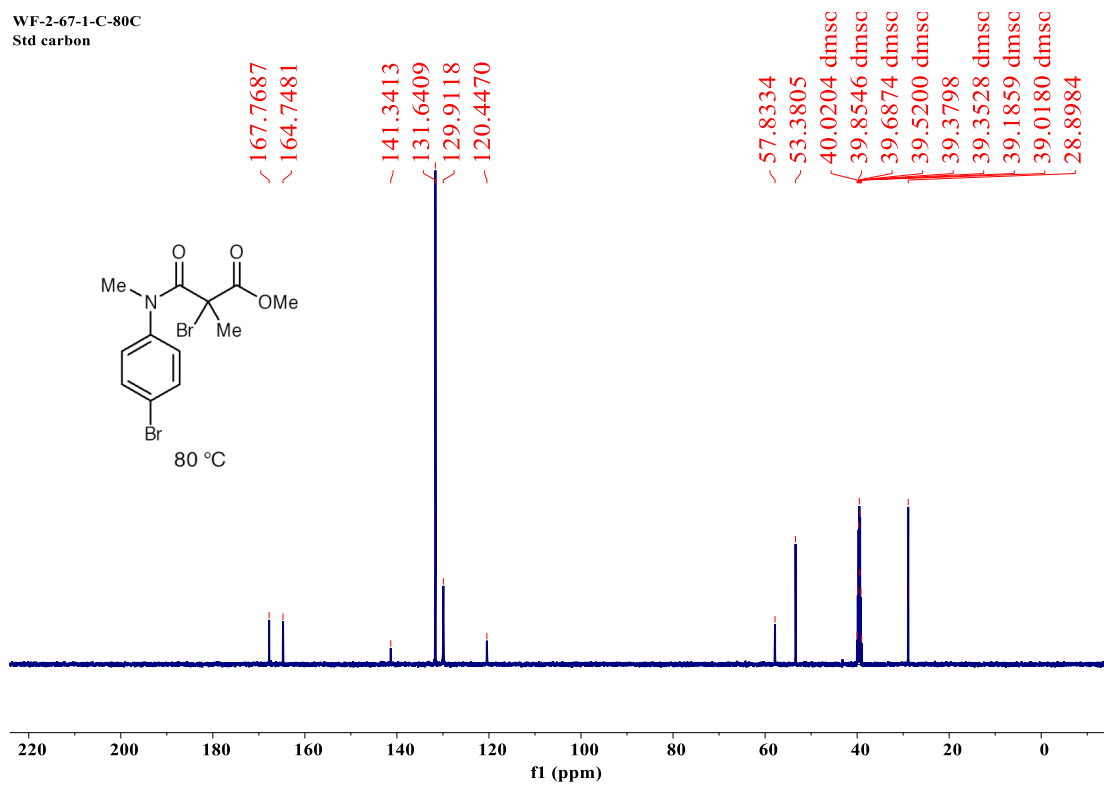
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Std carbon



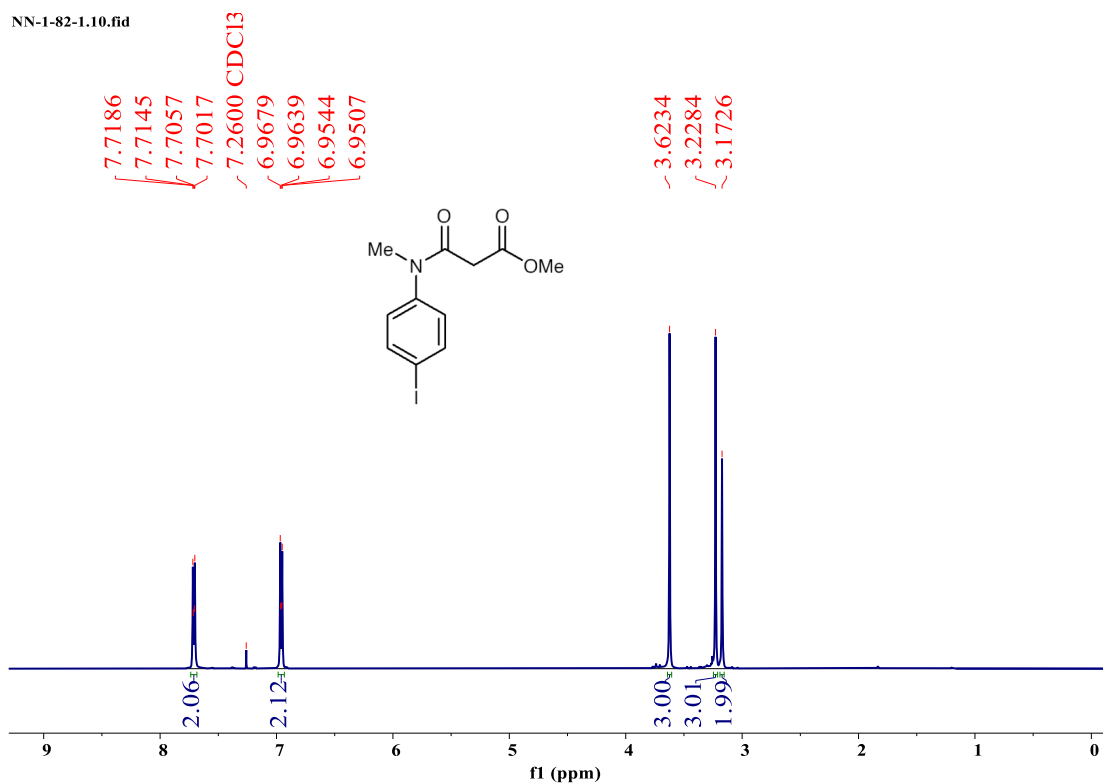
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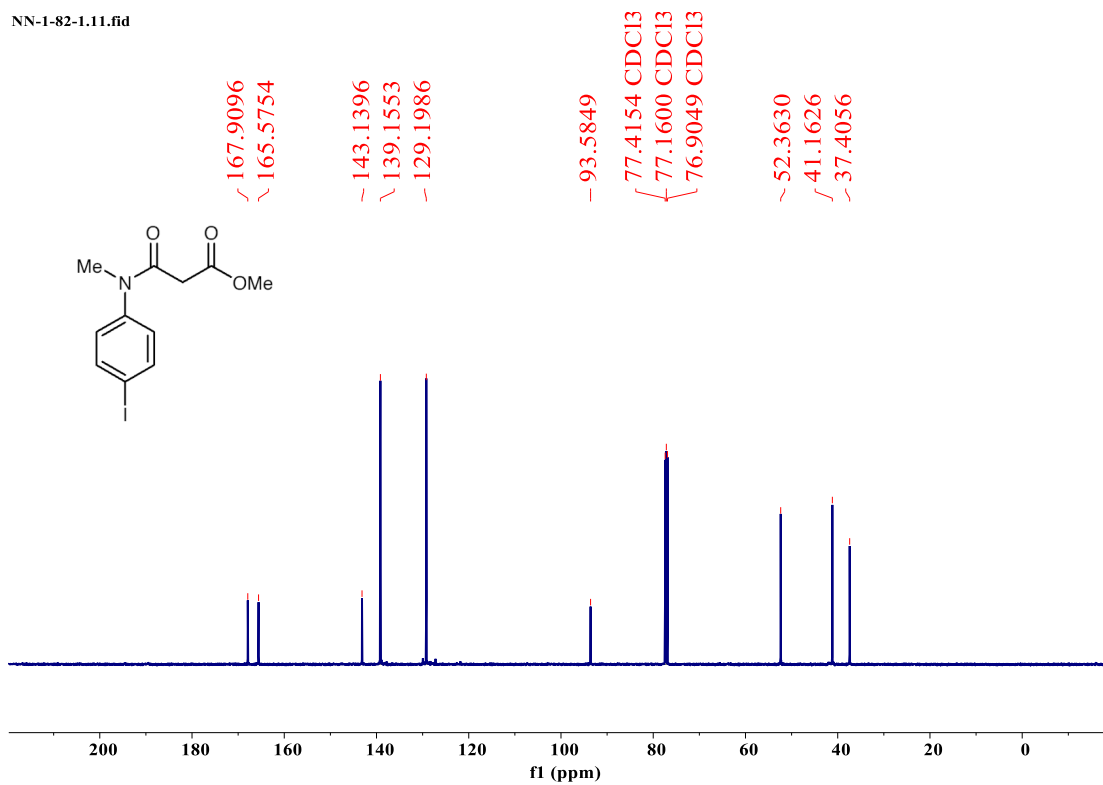
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Std carbon



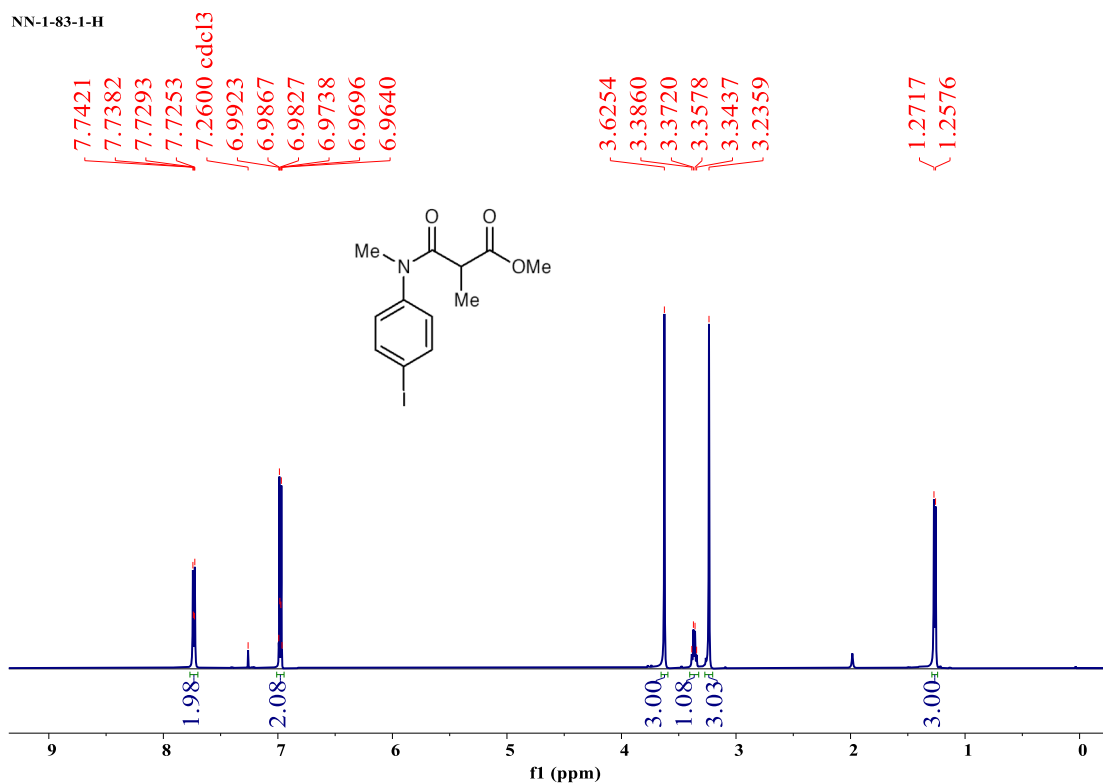
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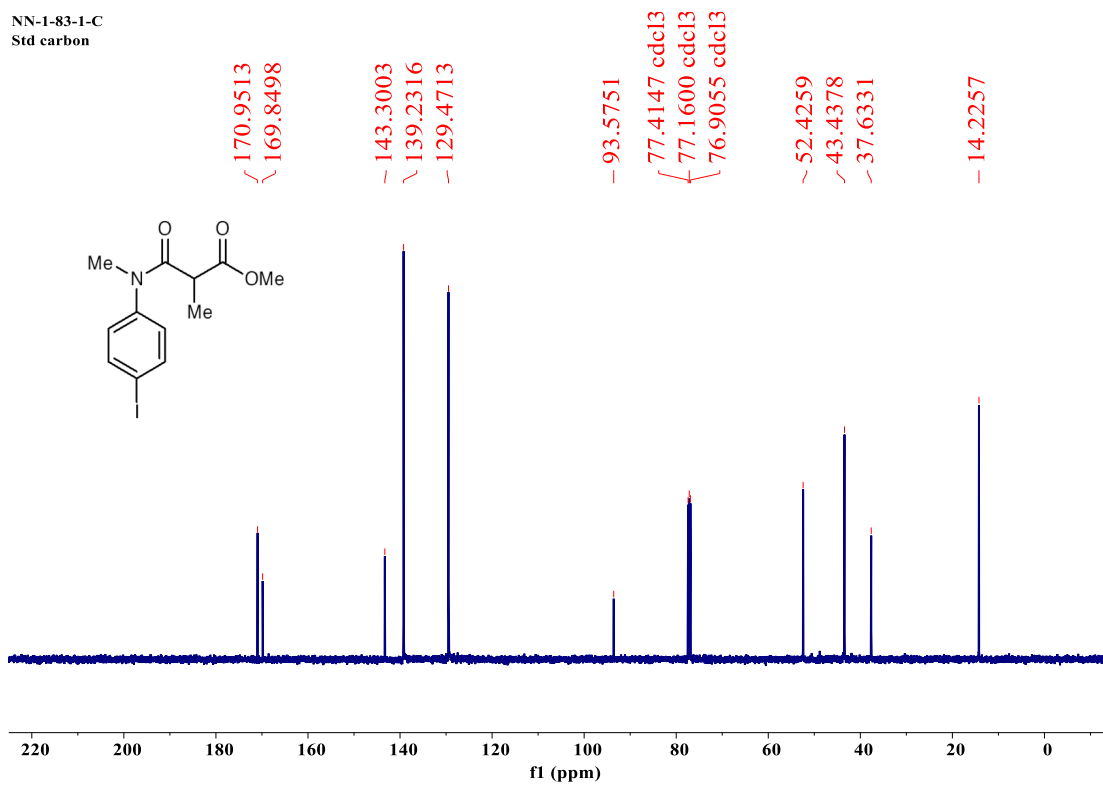
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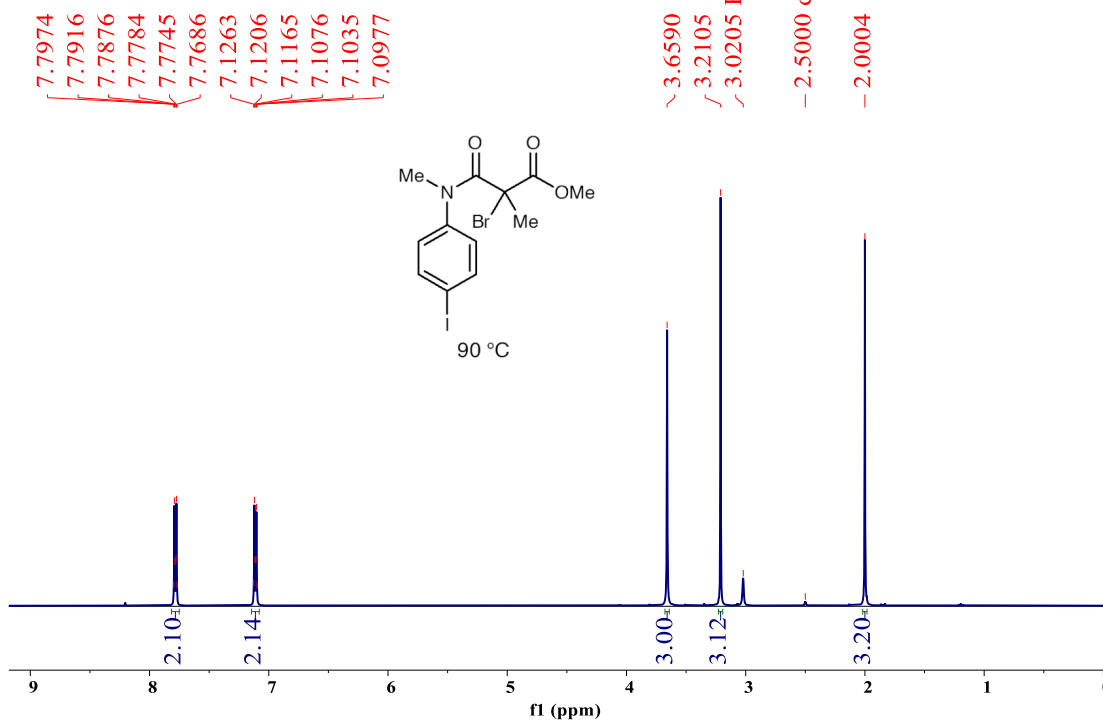
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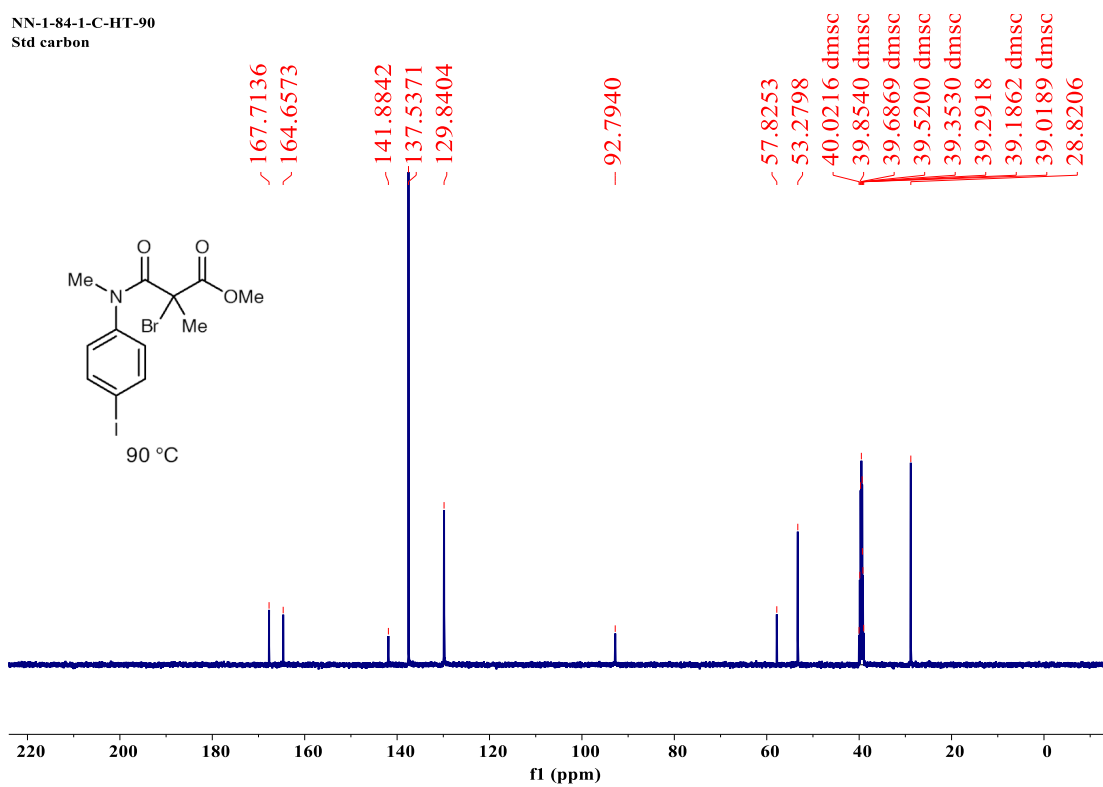
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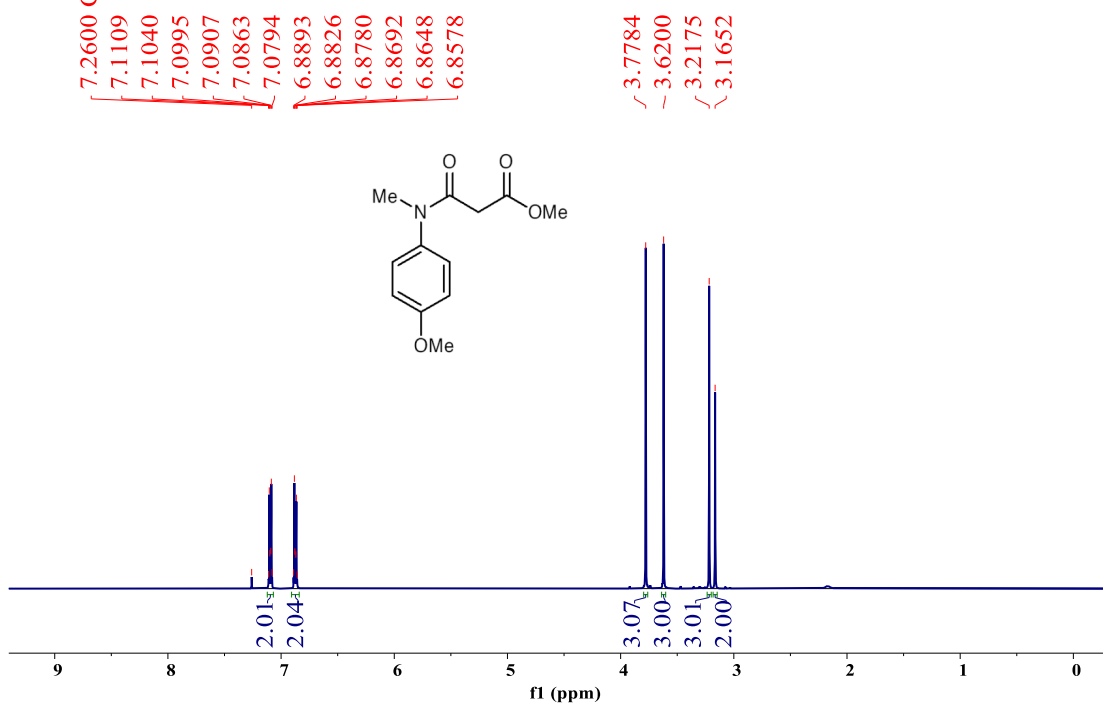
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H1_CDCL3



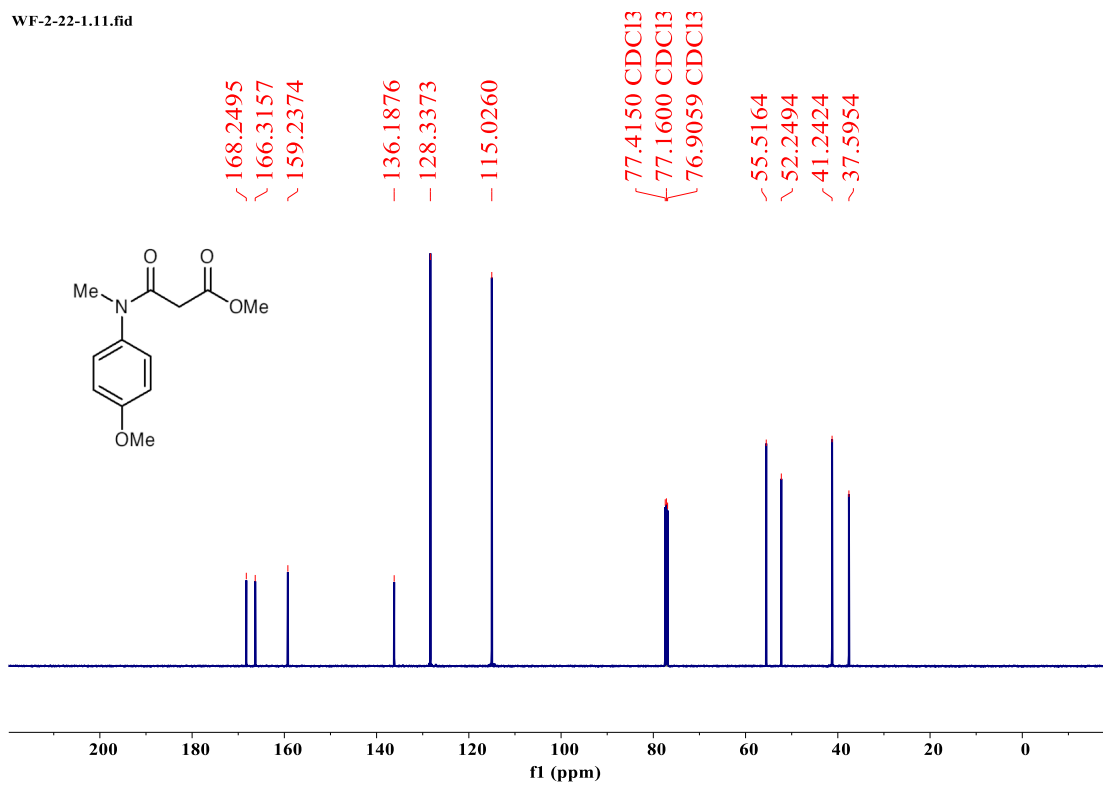
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Std carbon



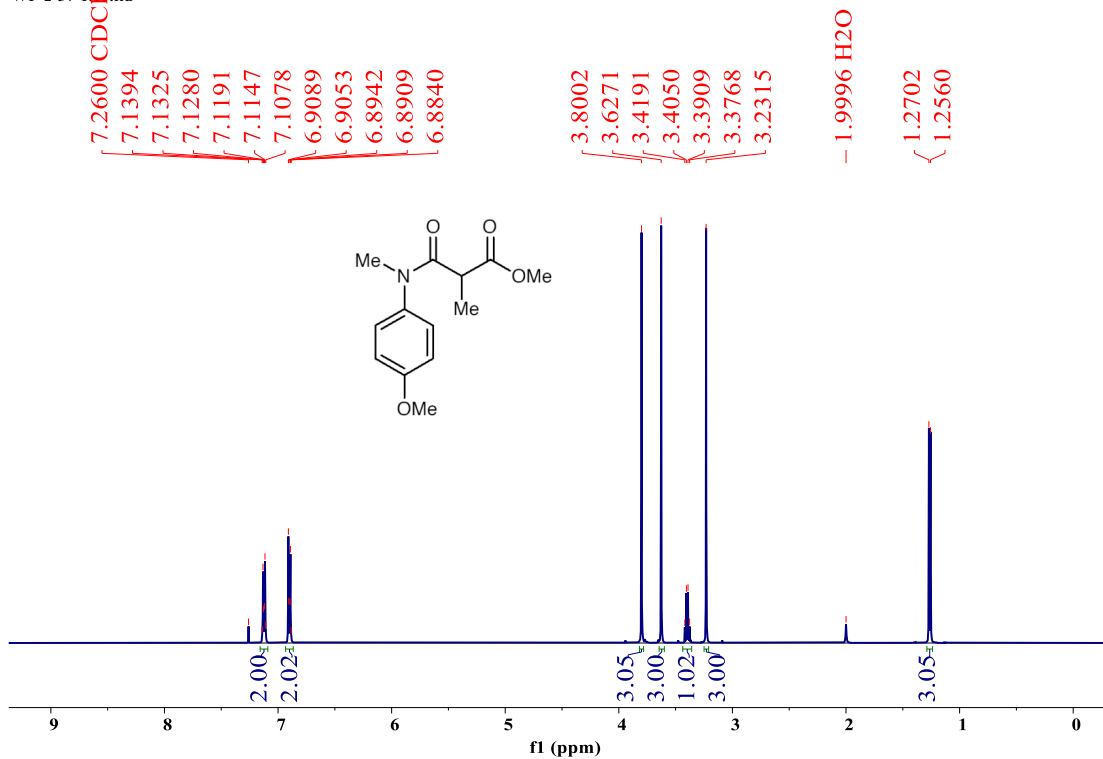
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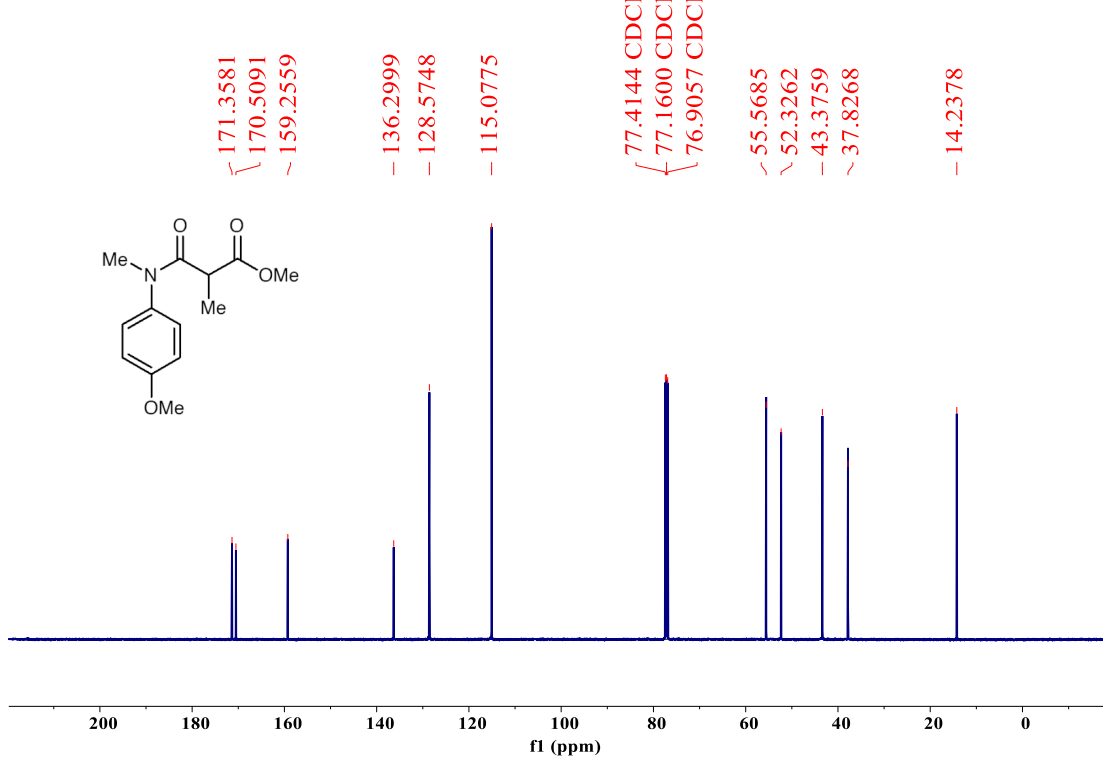
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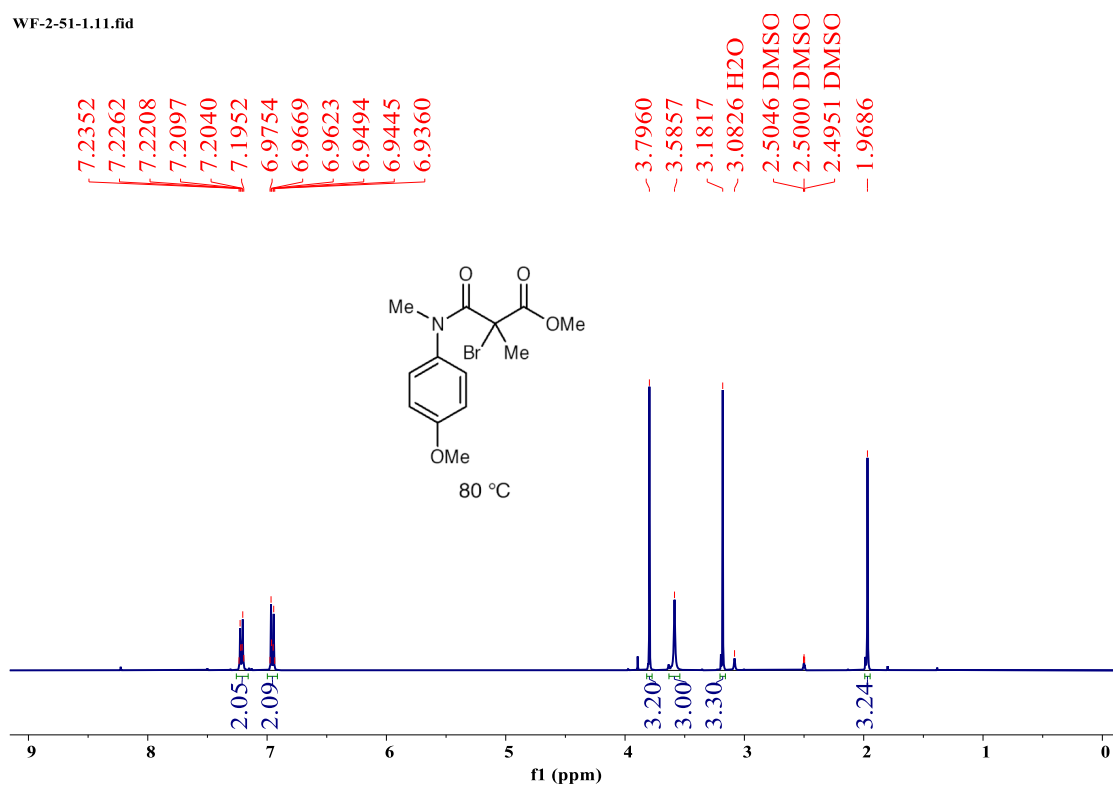
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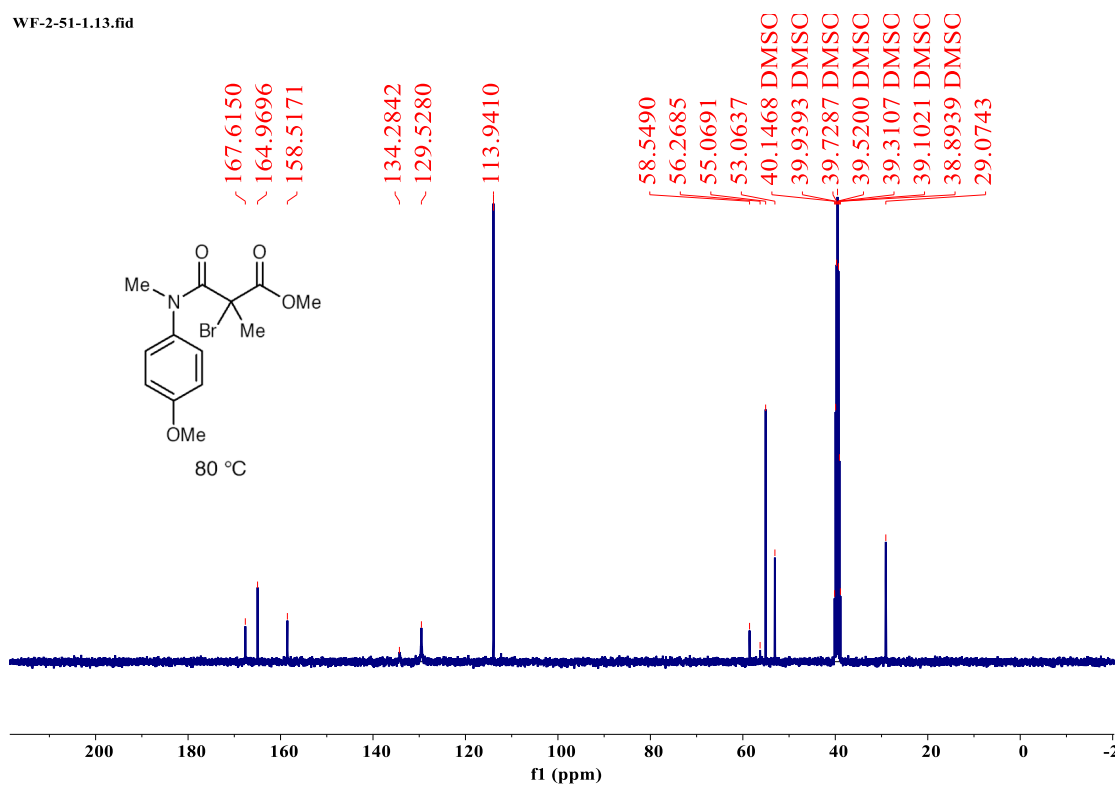
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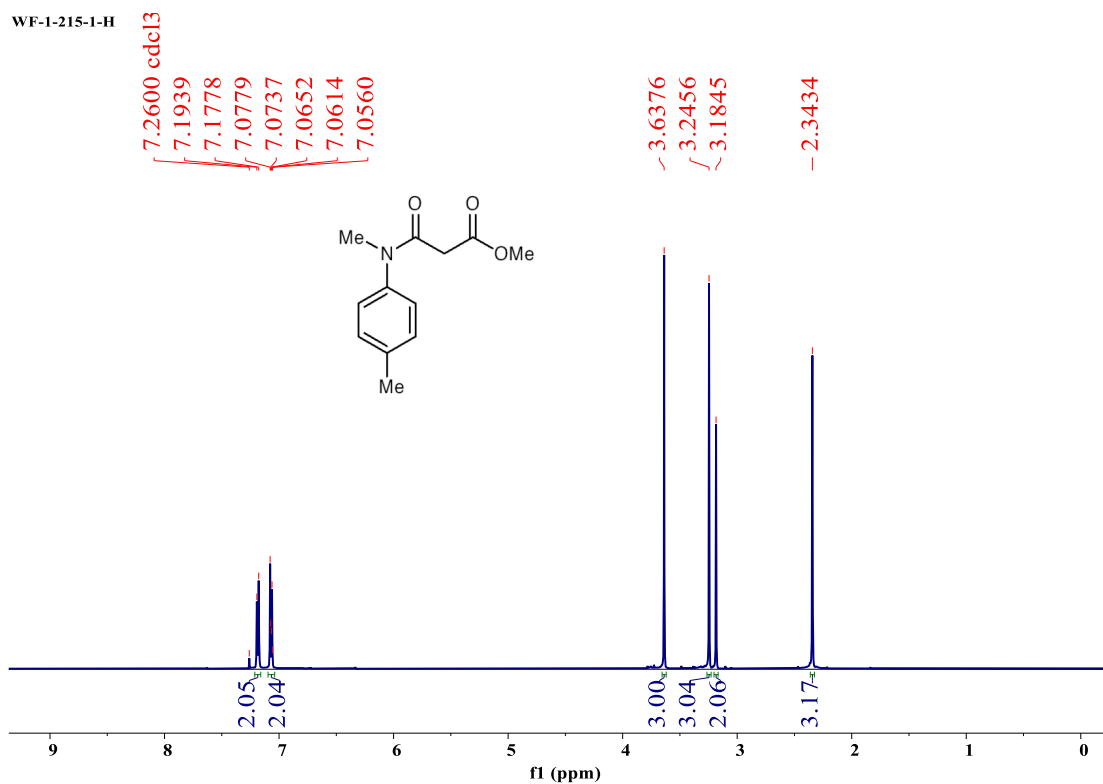
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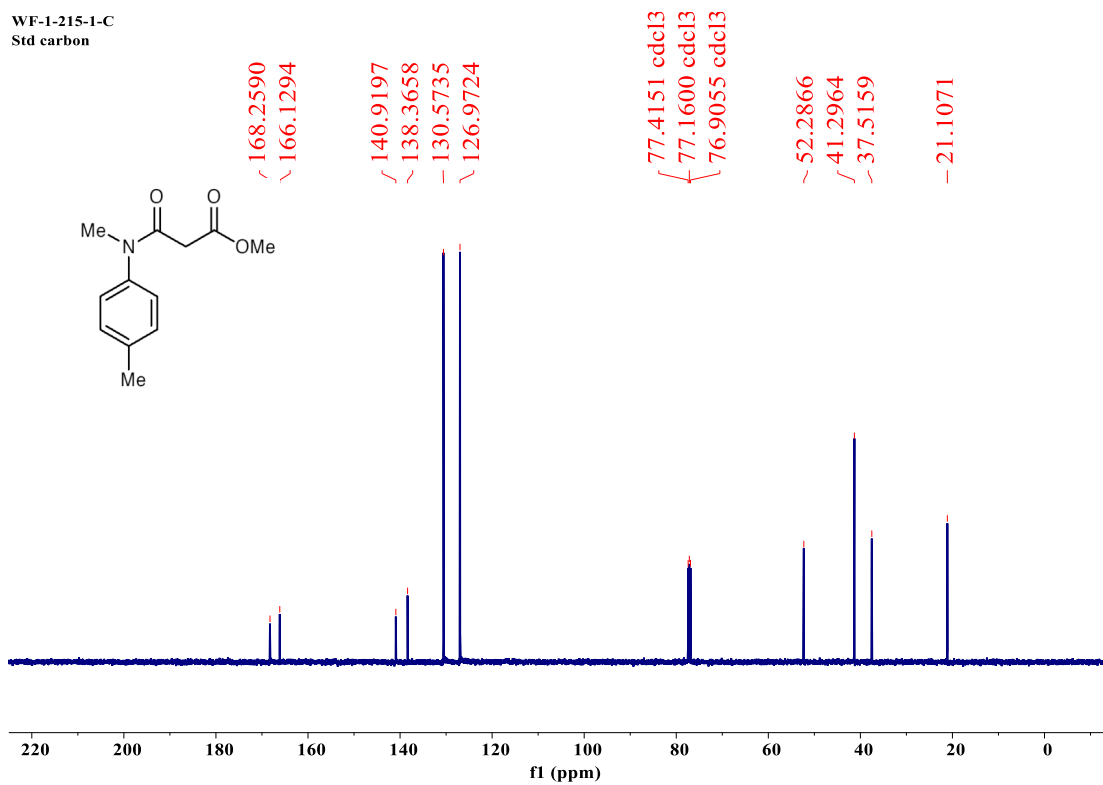
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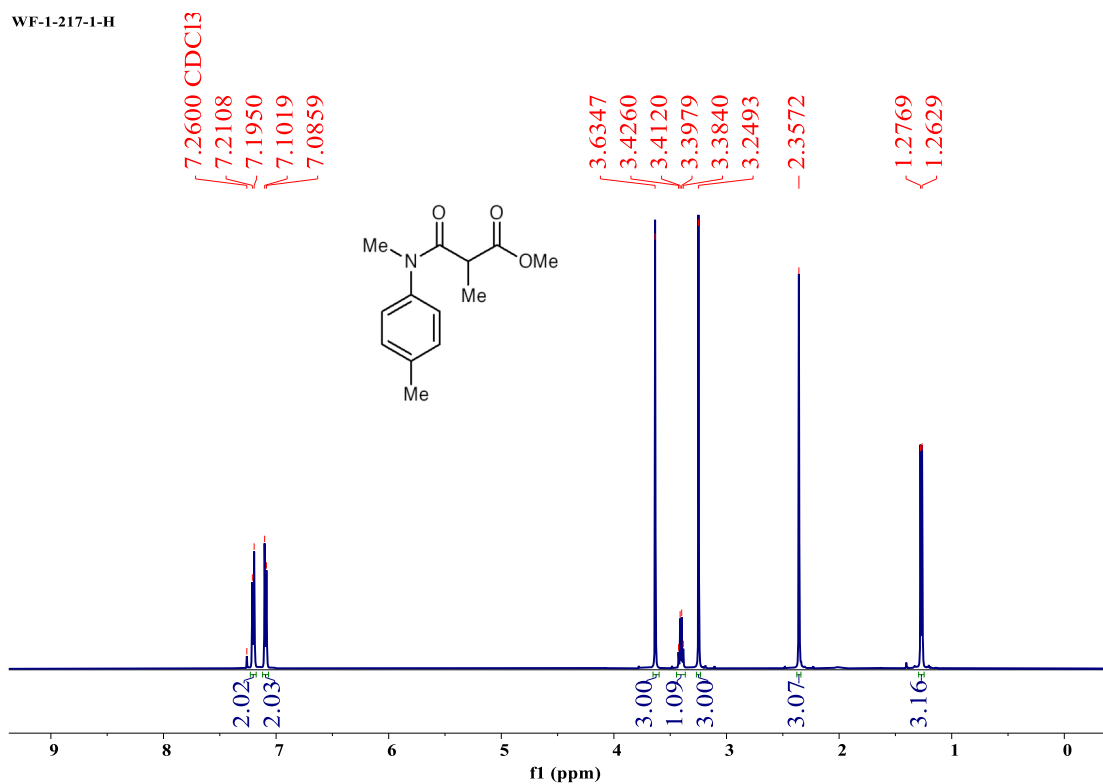
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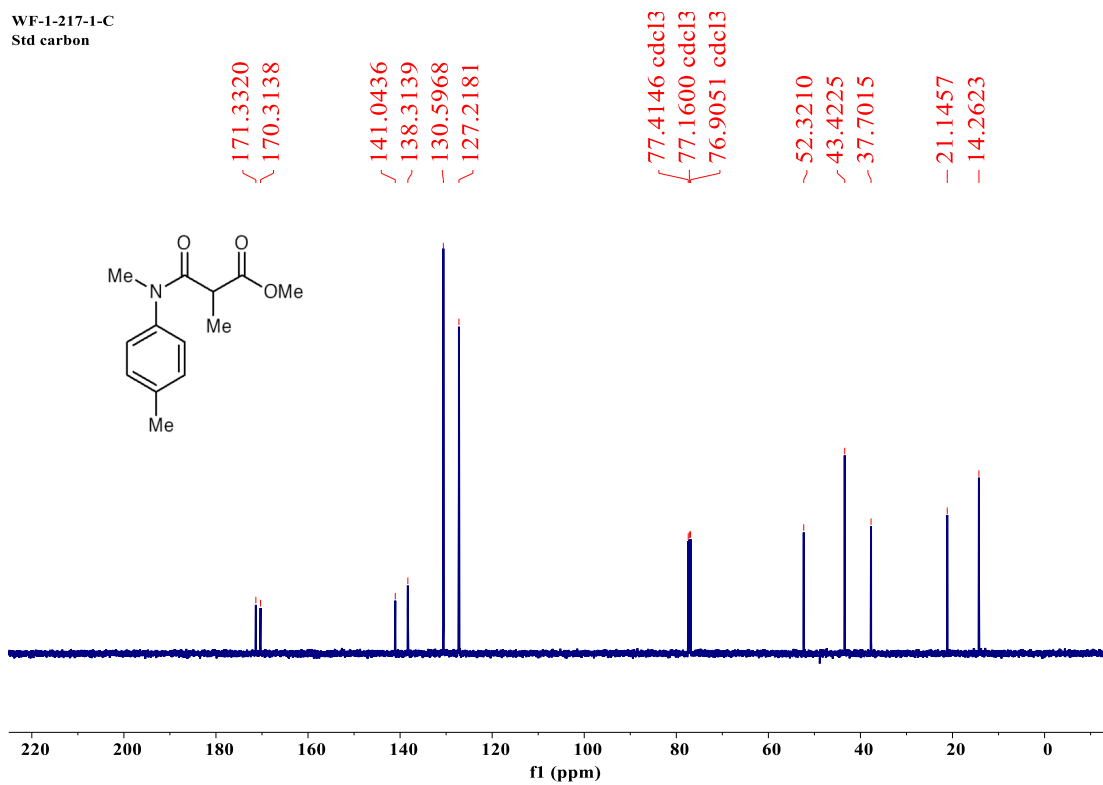
WF-1-215-1-C
Std carbon



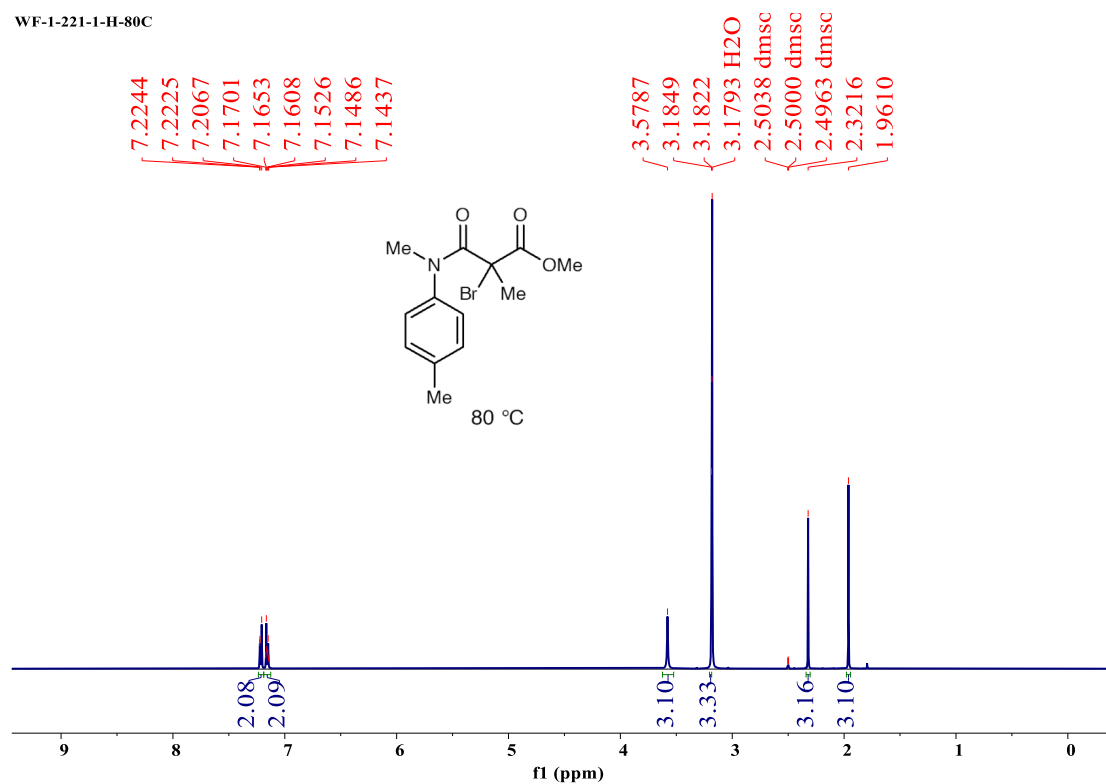
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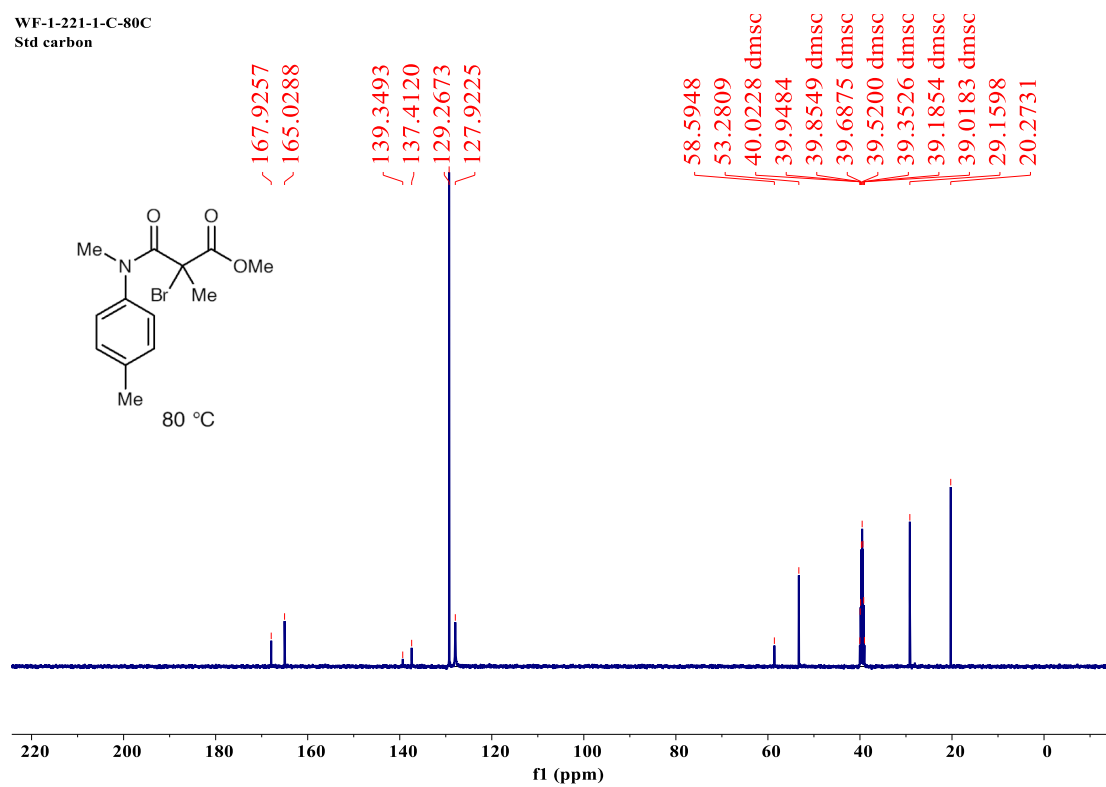
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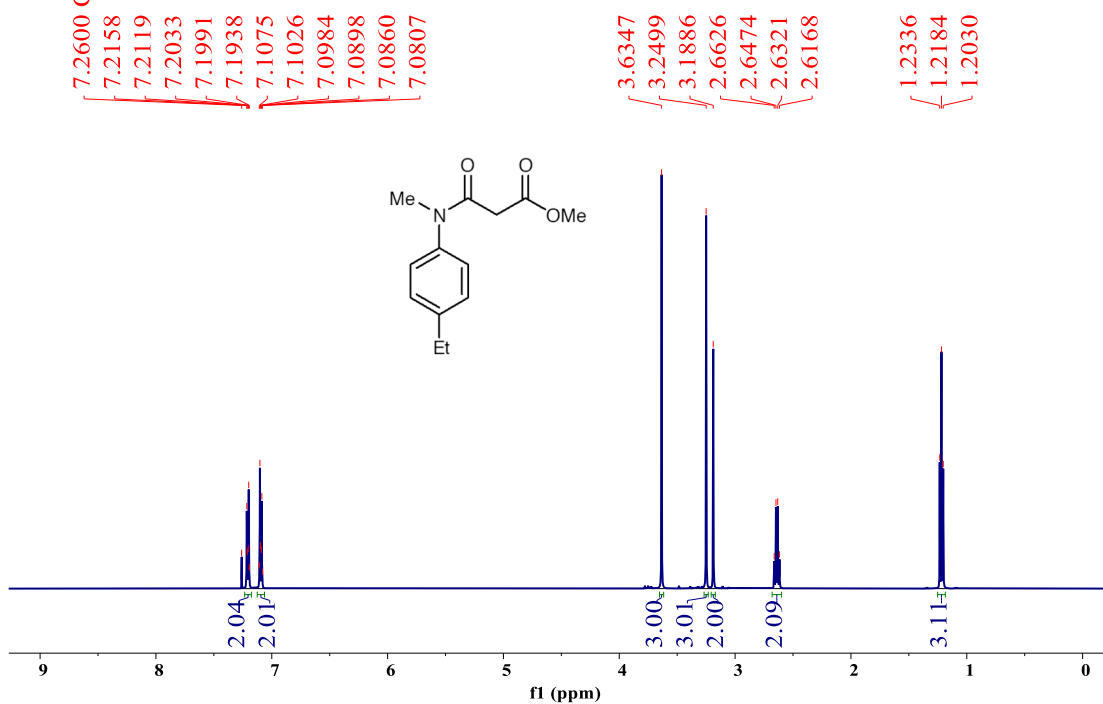
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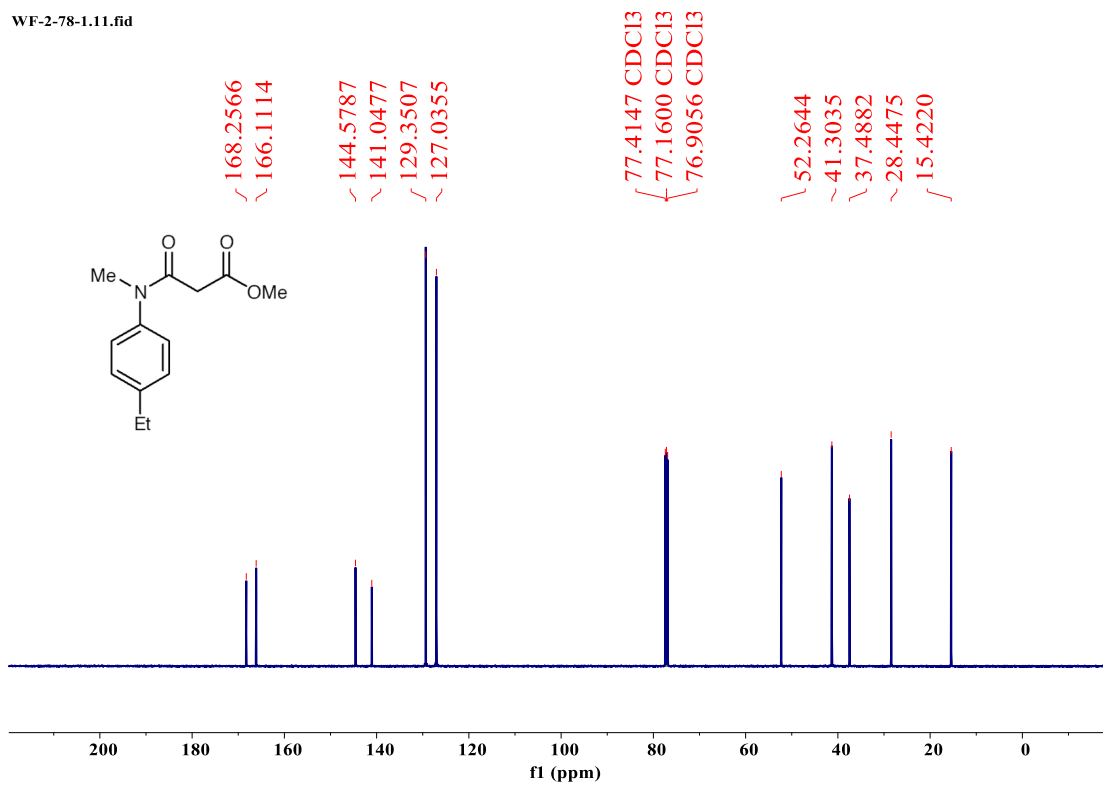
WF-1-221-1-C-80C
Std carbon



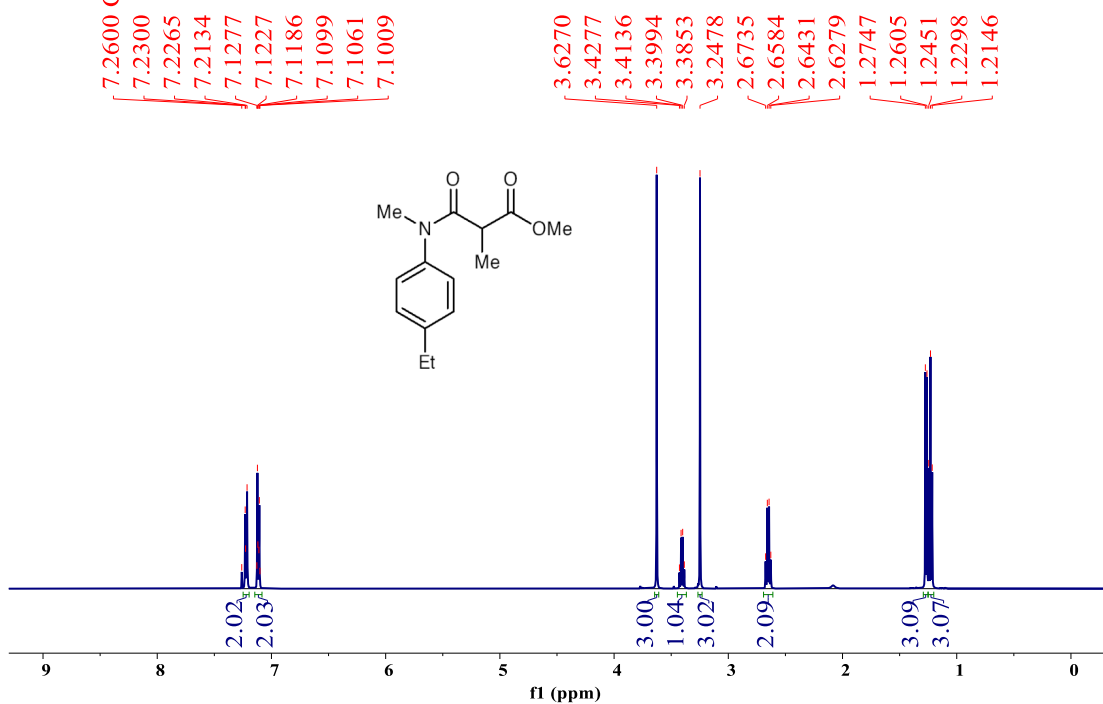
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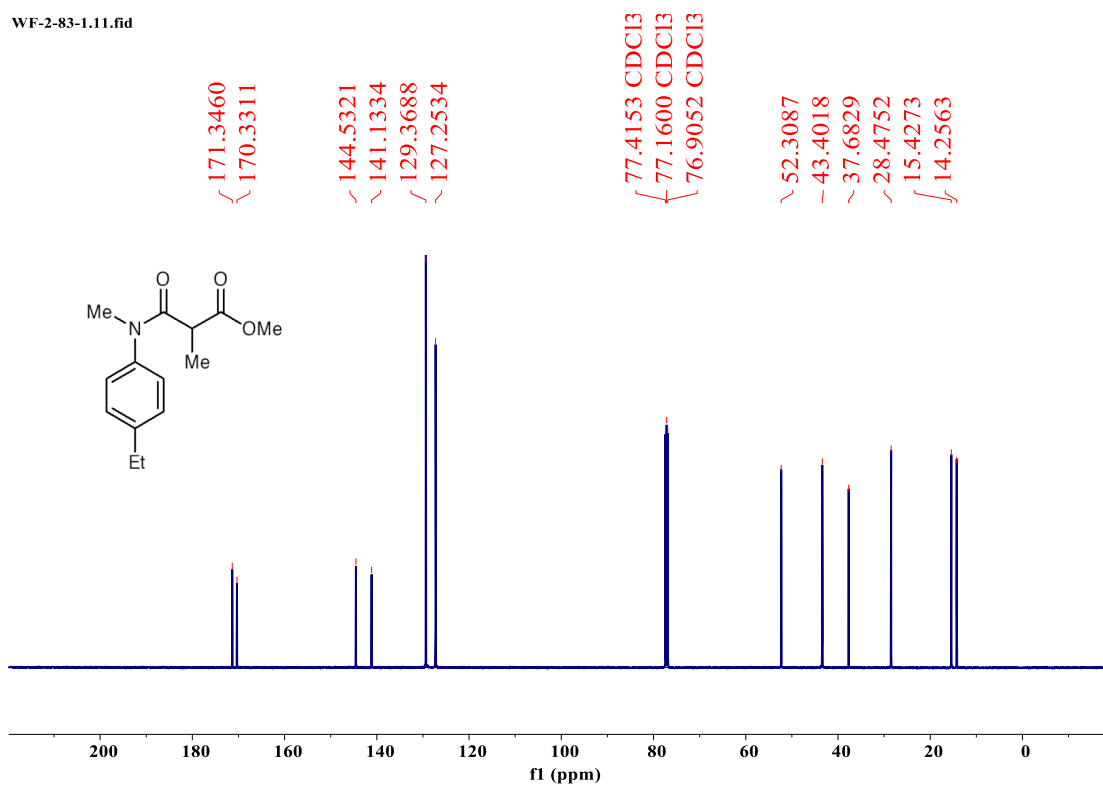
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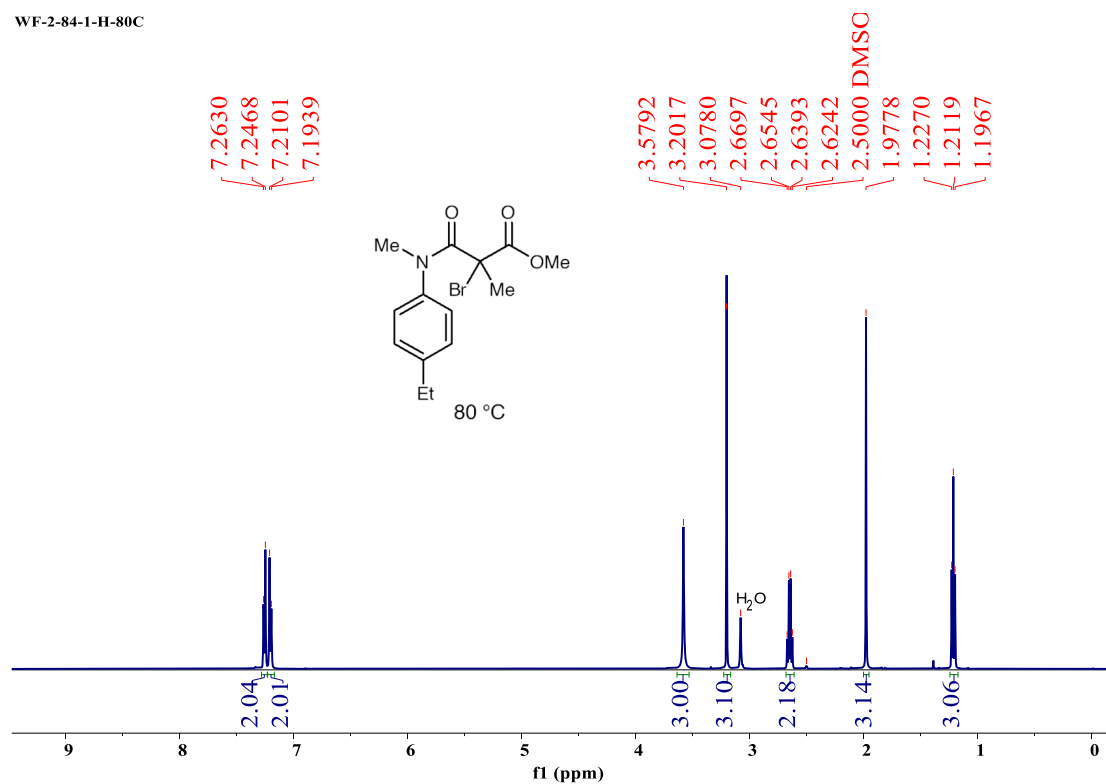
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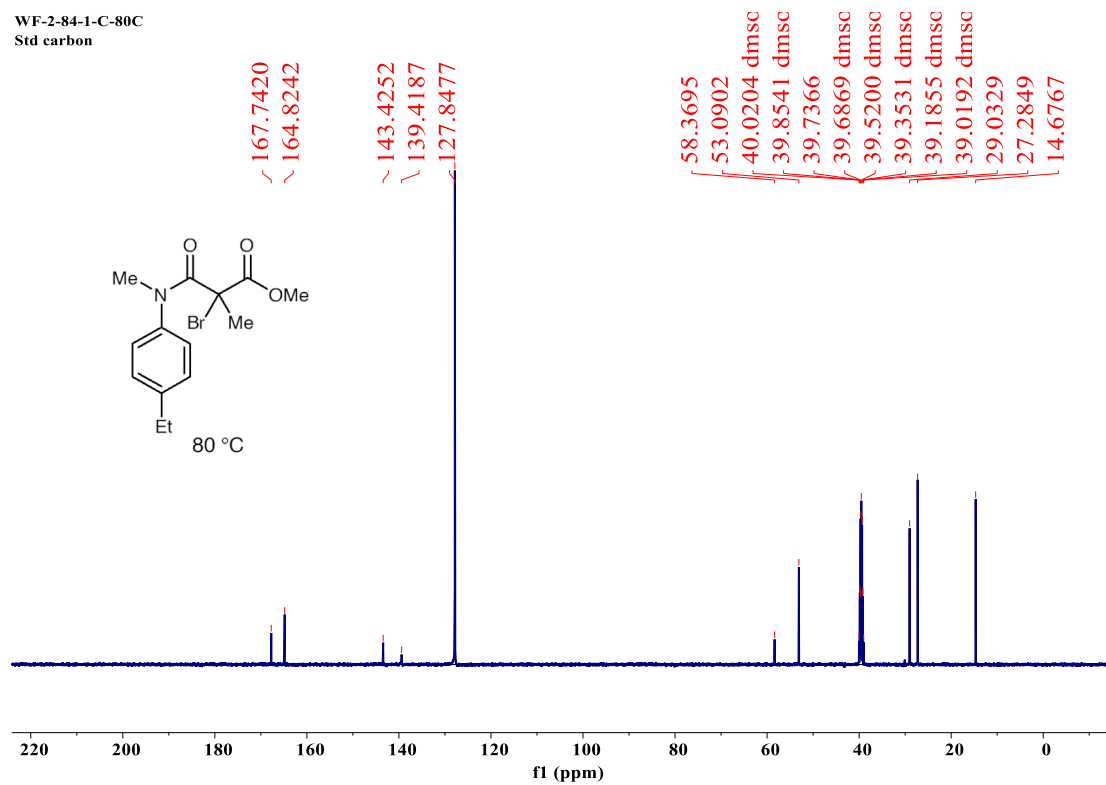
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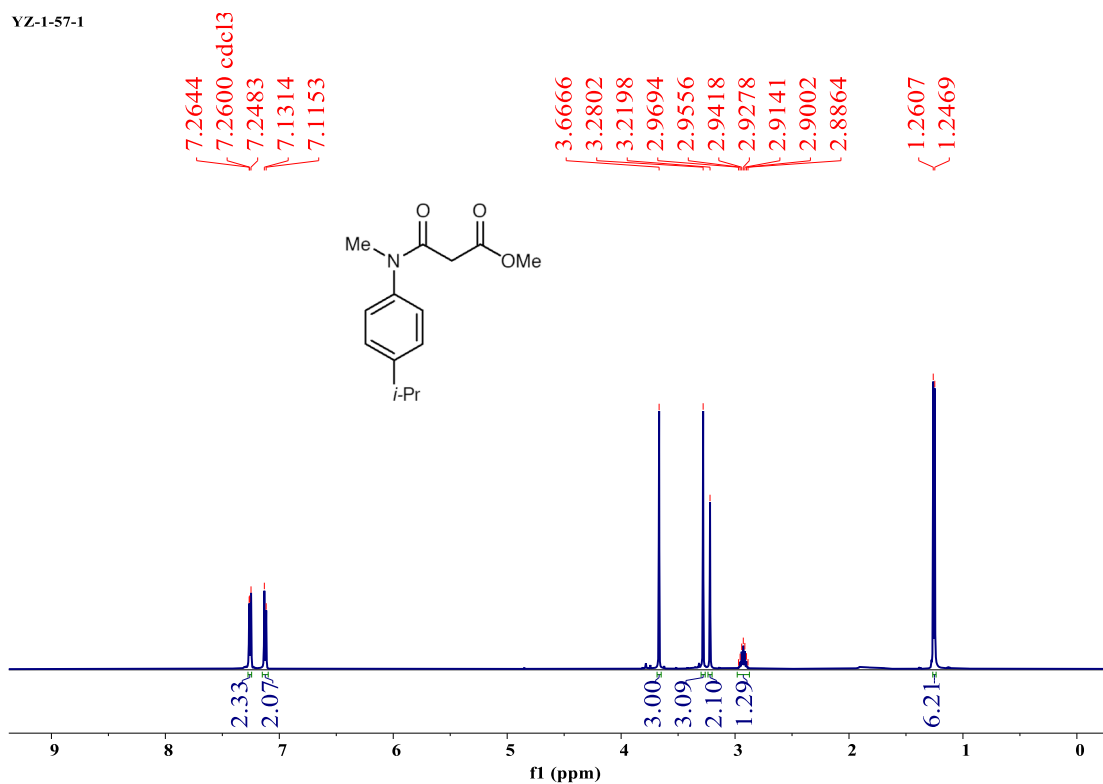
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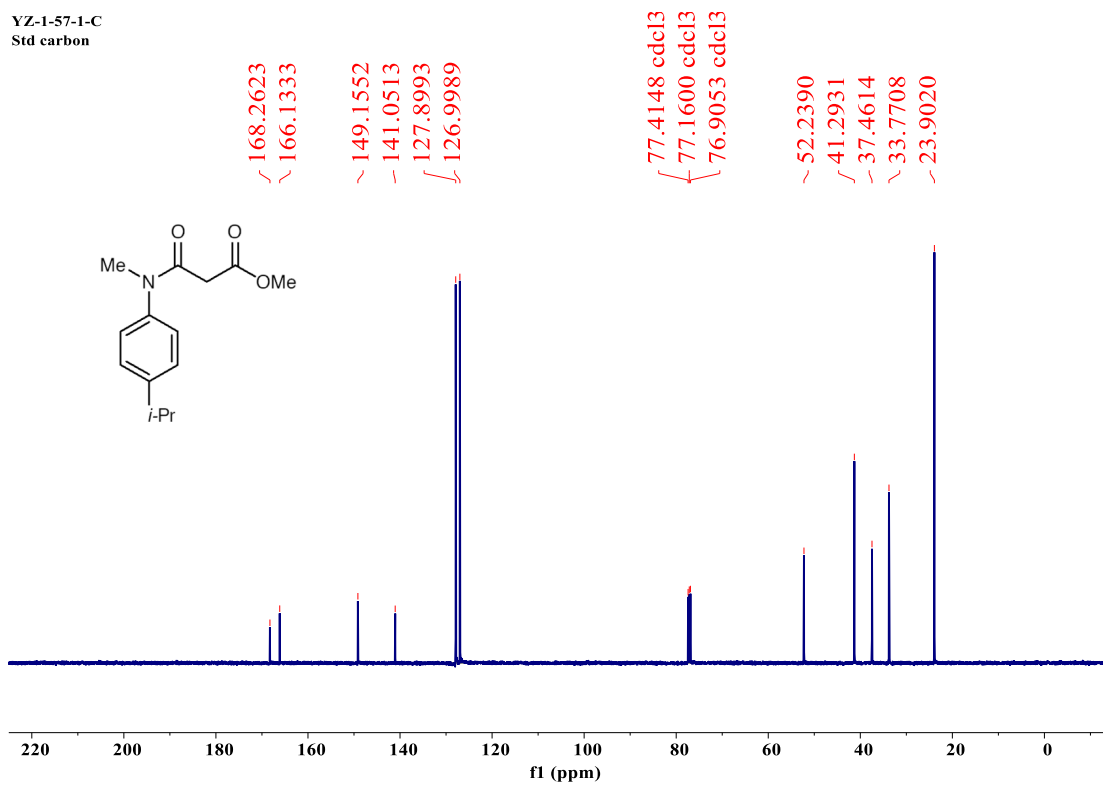
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YZ-1-57-1



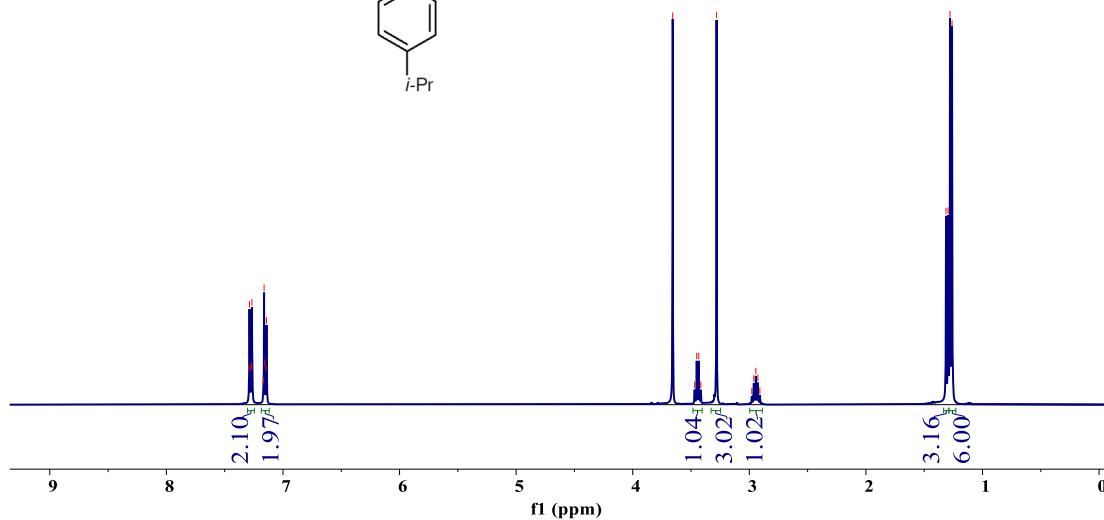
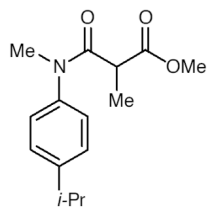
YZ-1-57-1-C
Std carbon



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3.4158
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1.2785
1.2612

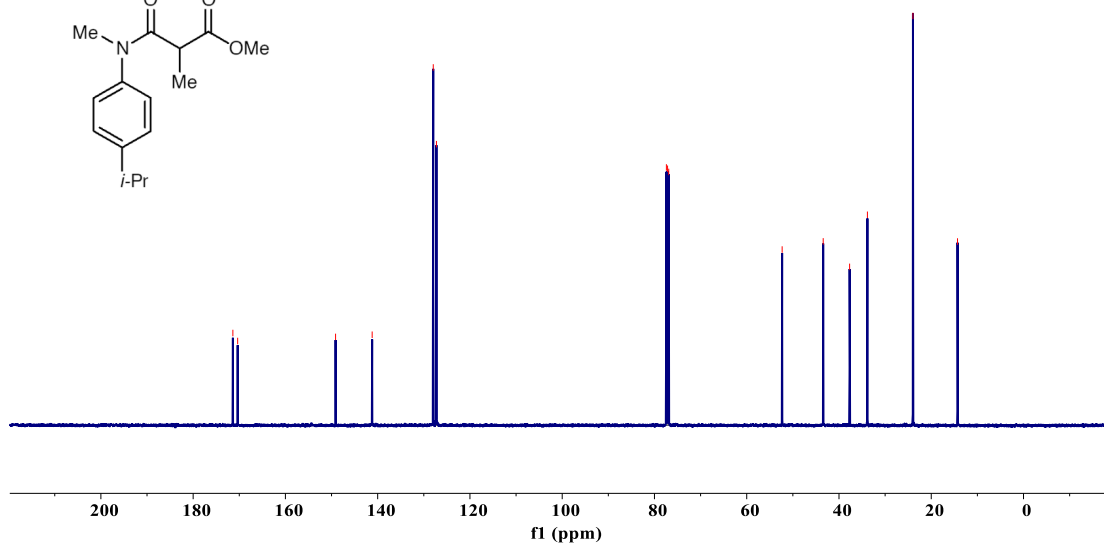
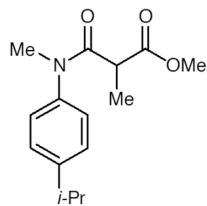


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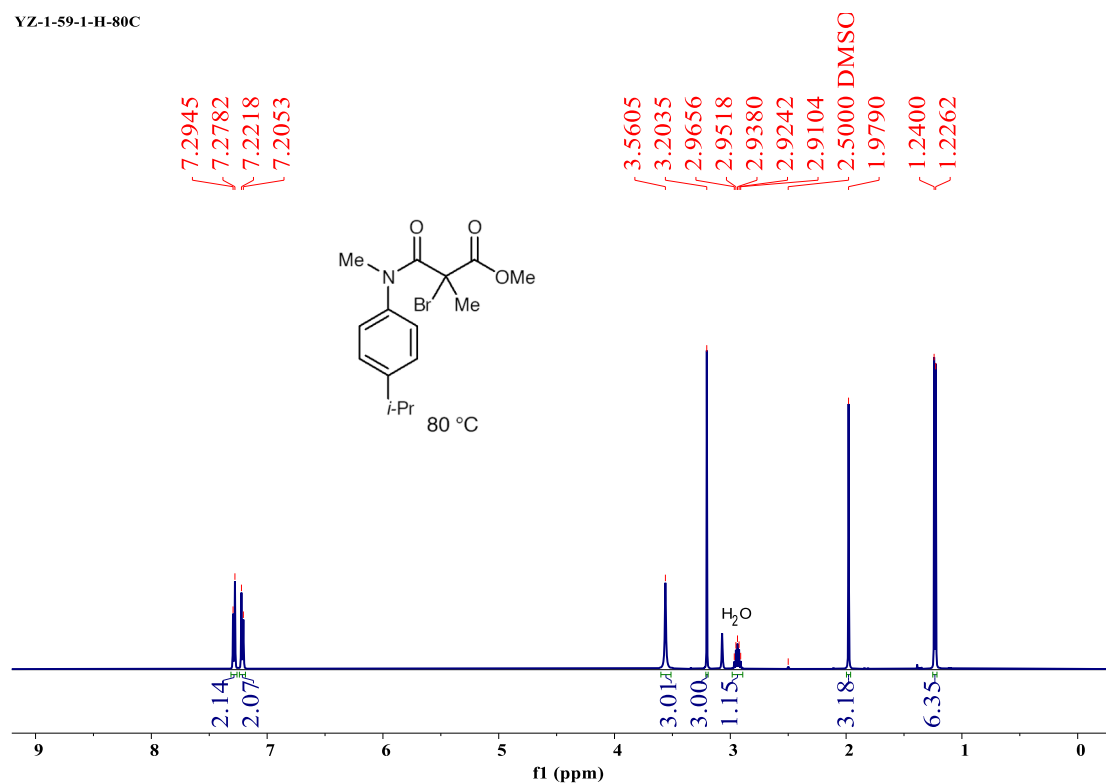
171.3882
 170.3505
 — 149.1275
 — 141.1942
 127.9502
 127.2603

77.4145 CDCl₃
77.1600 CDCl₃
76.9057 CDCl₃

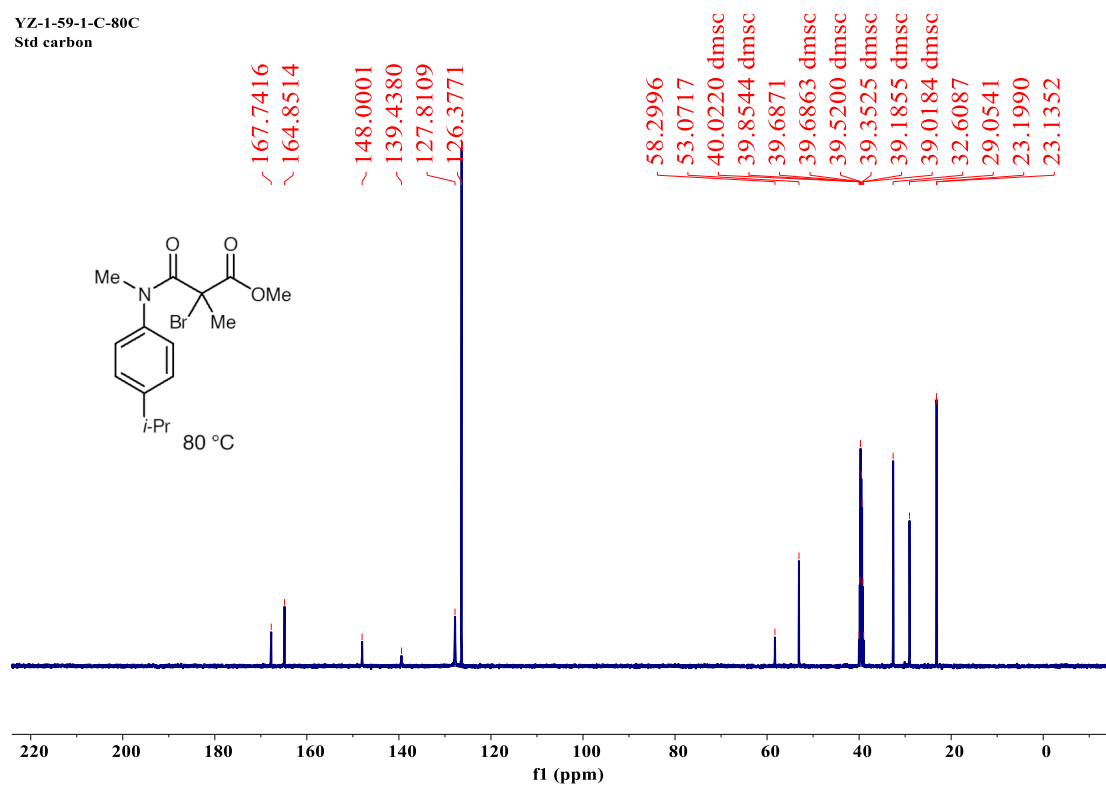
$\wedge$ 52.3221
 $-$ 43.4227
 $\sim$ 37.6963
 $\wedge$ 33.8376
 $\sim$ 23.9697
 $\wedge$ 14.3068



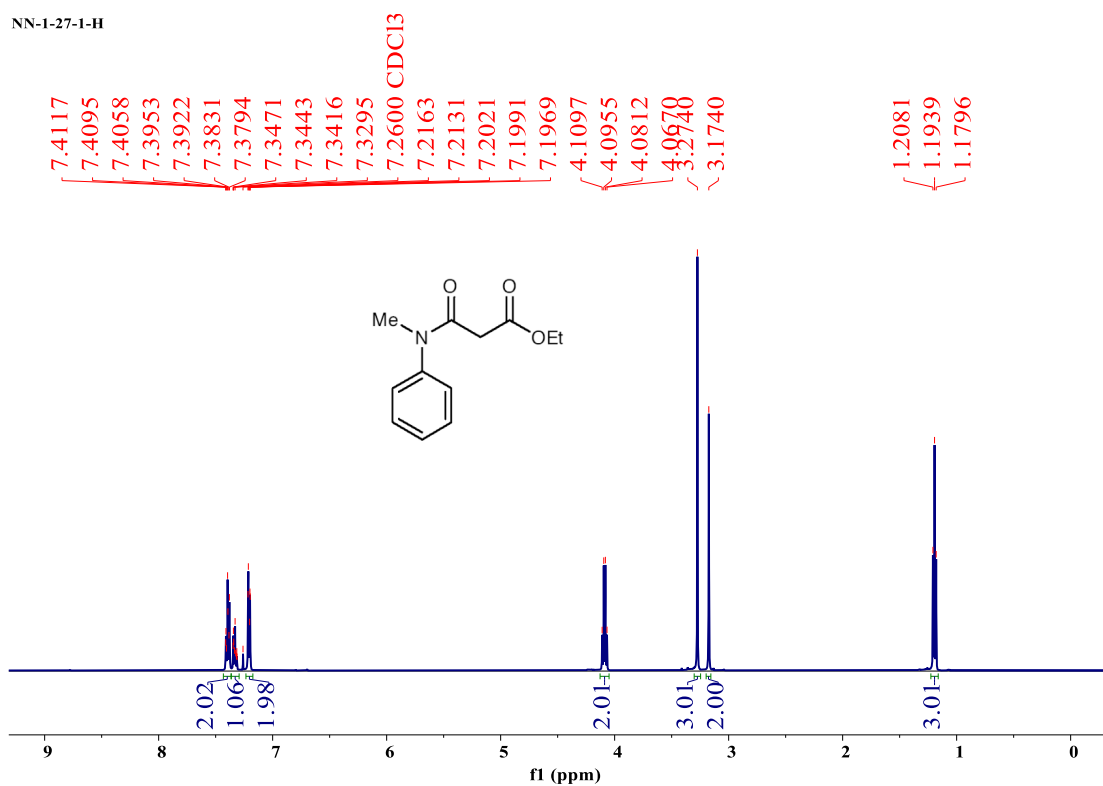
YZ-1-59-1-H-80C



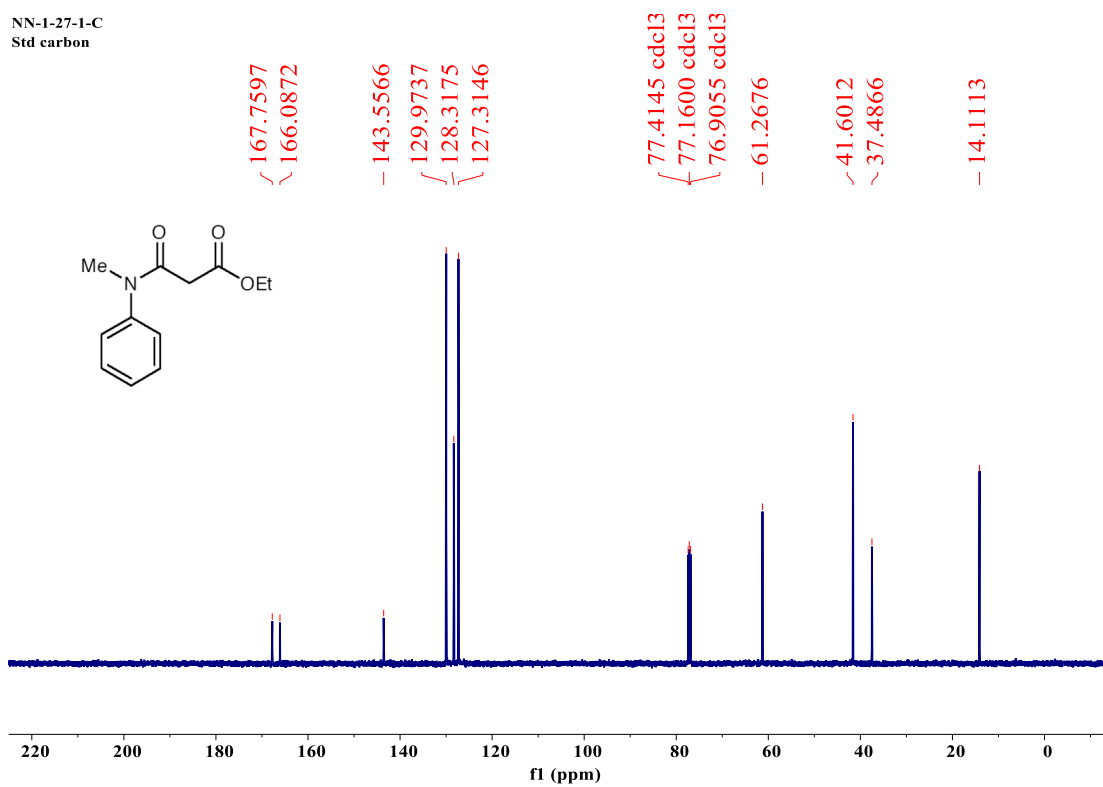
YZ-1-59-1-C-80C
Std carbon



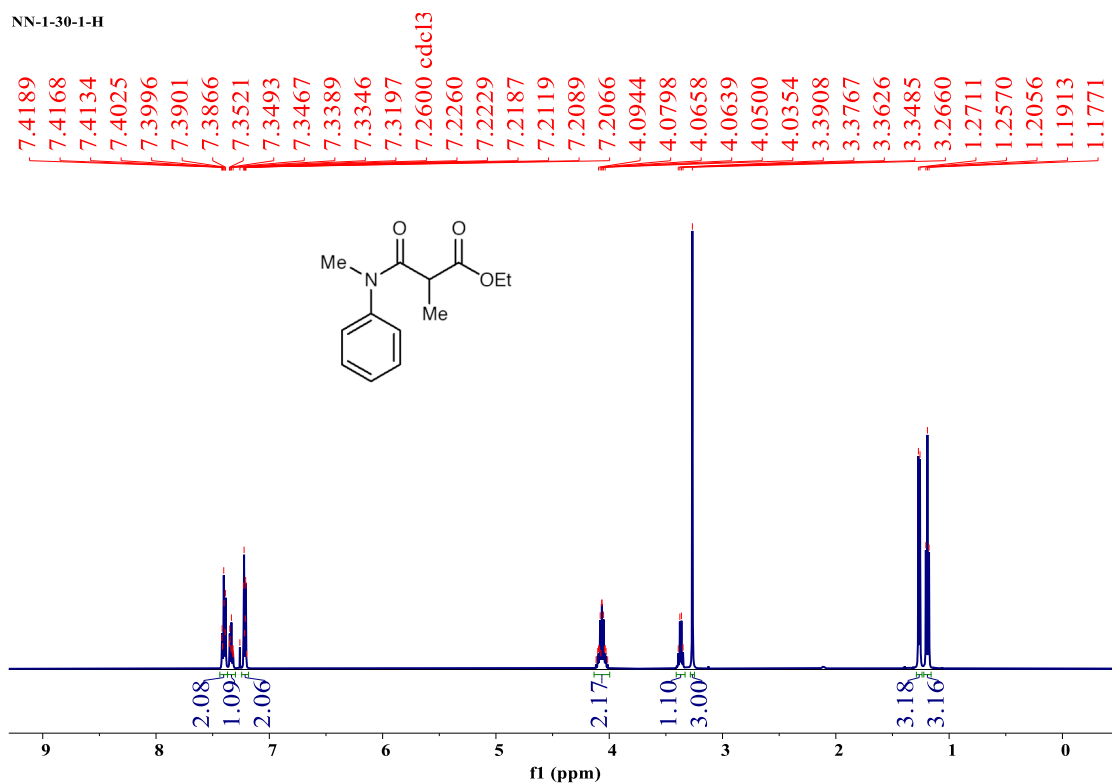
NN-1-27-1-H



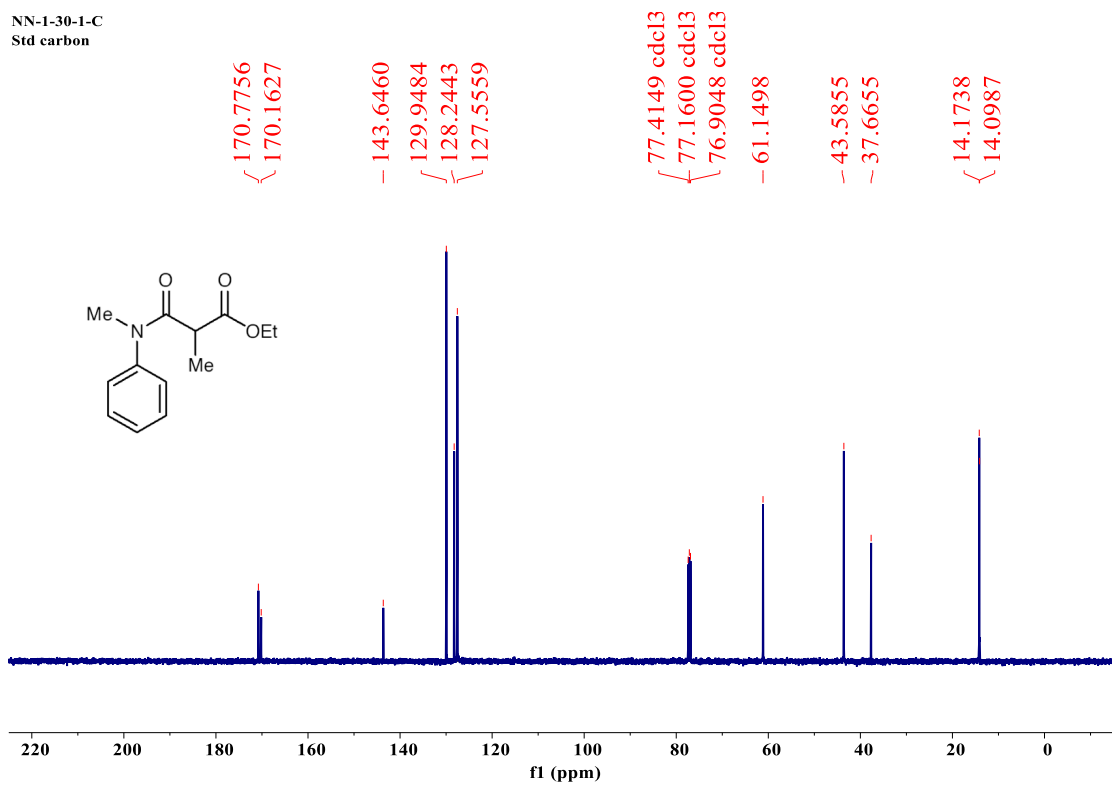
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Std carbon



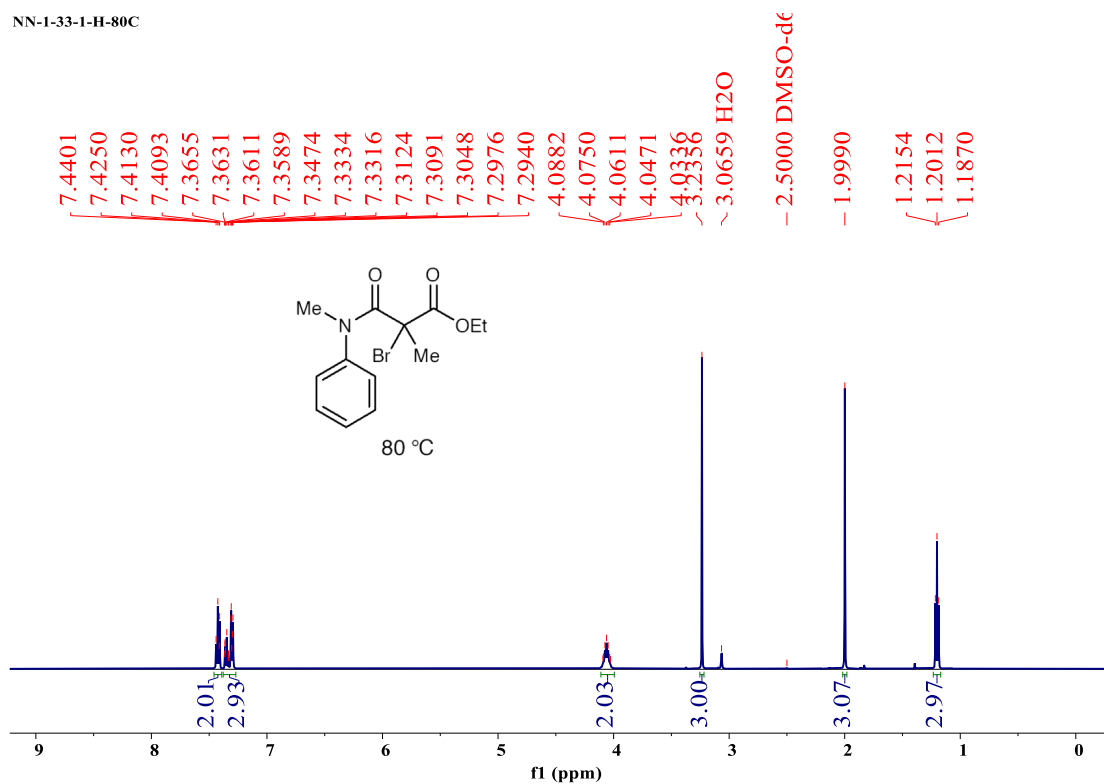
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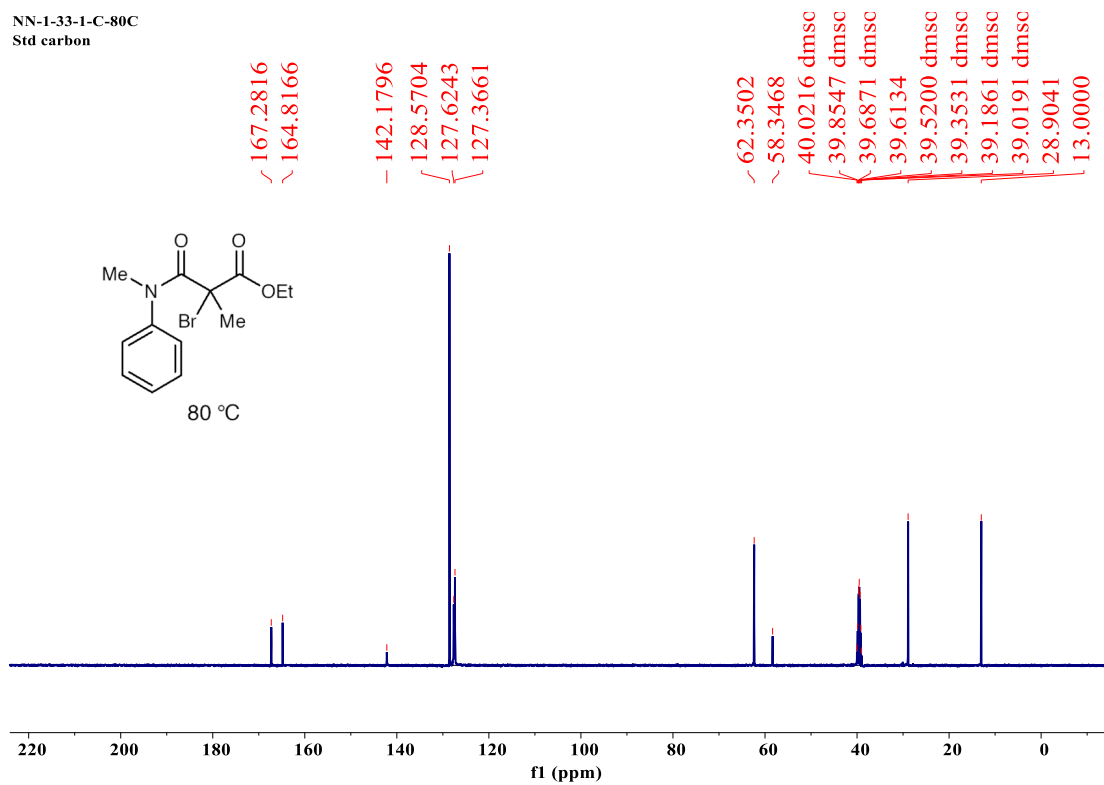
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Std carbon



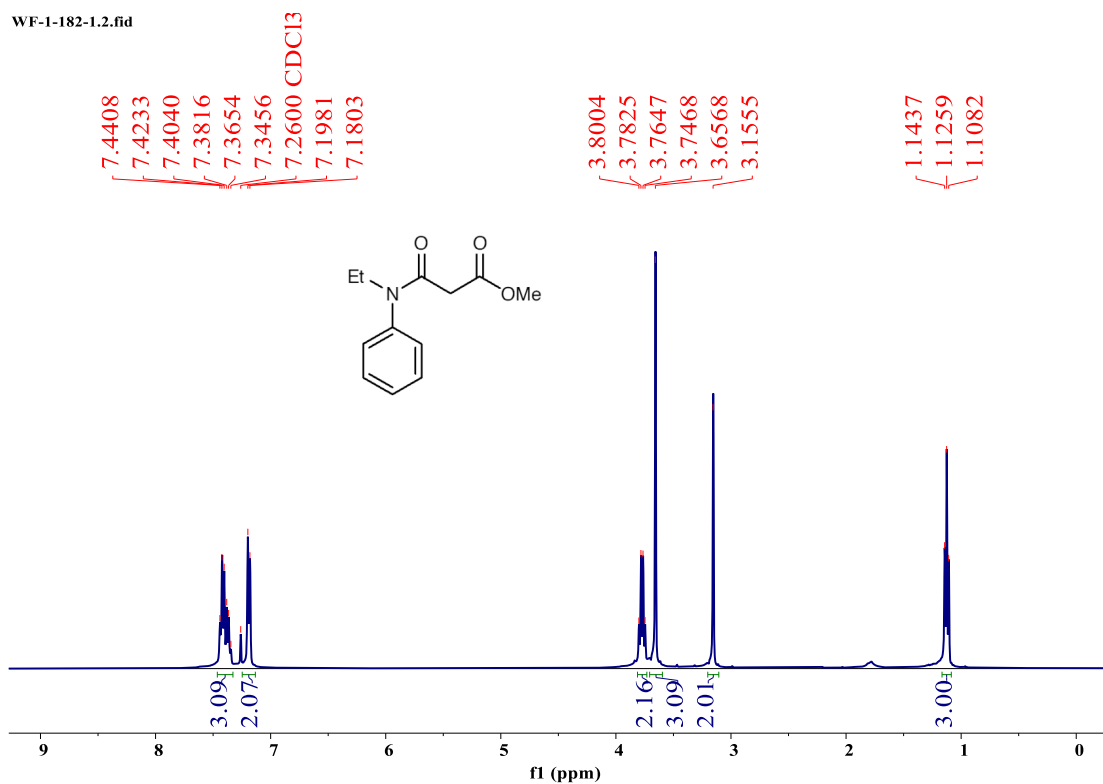
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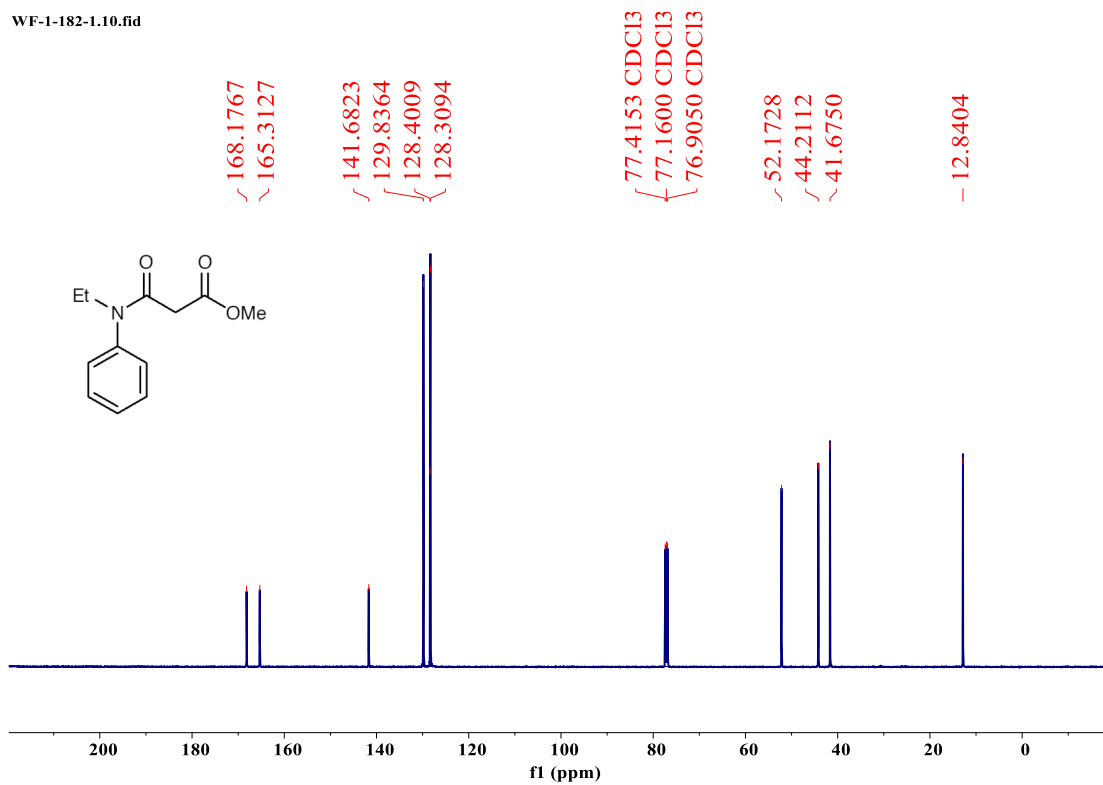
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Std carbon



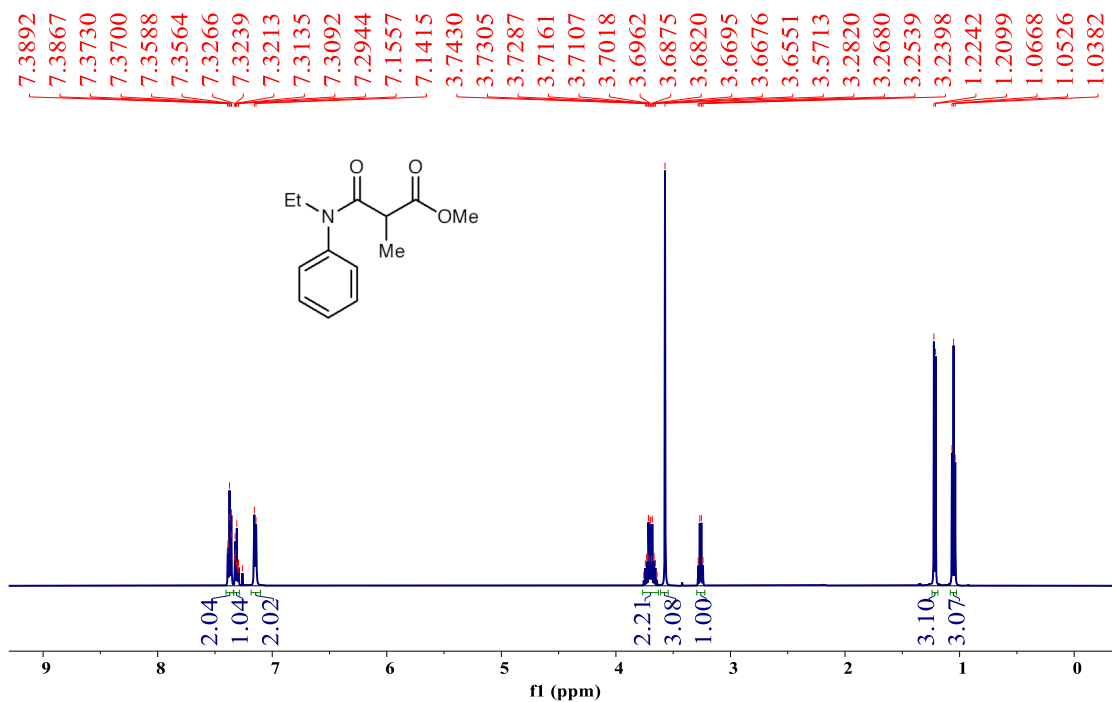
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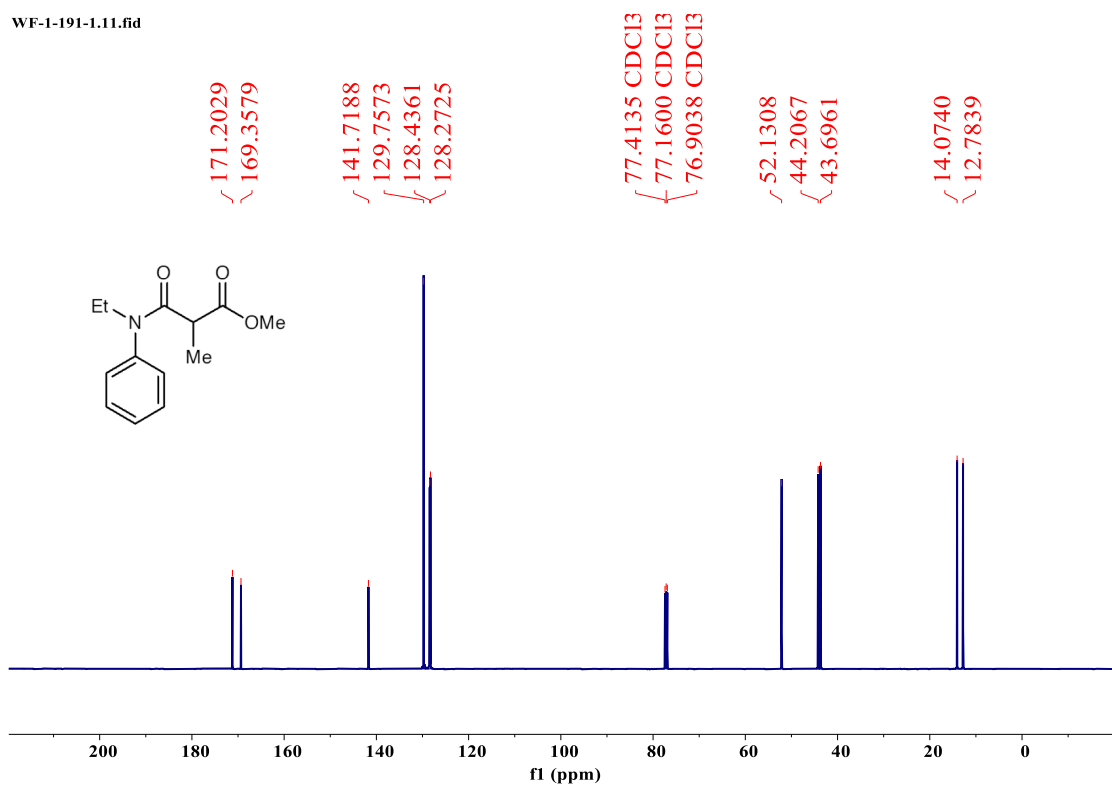
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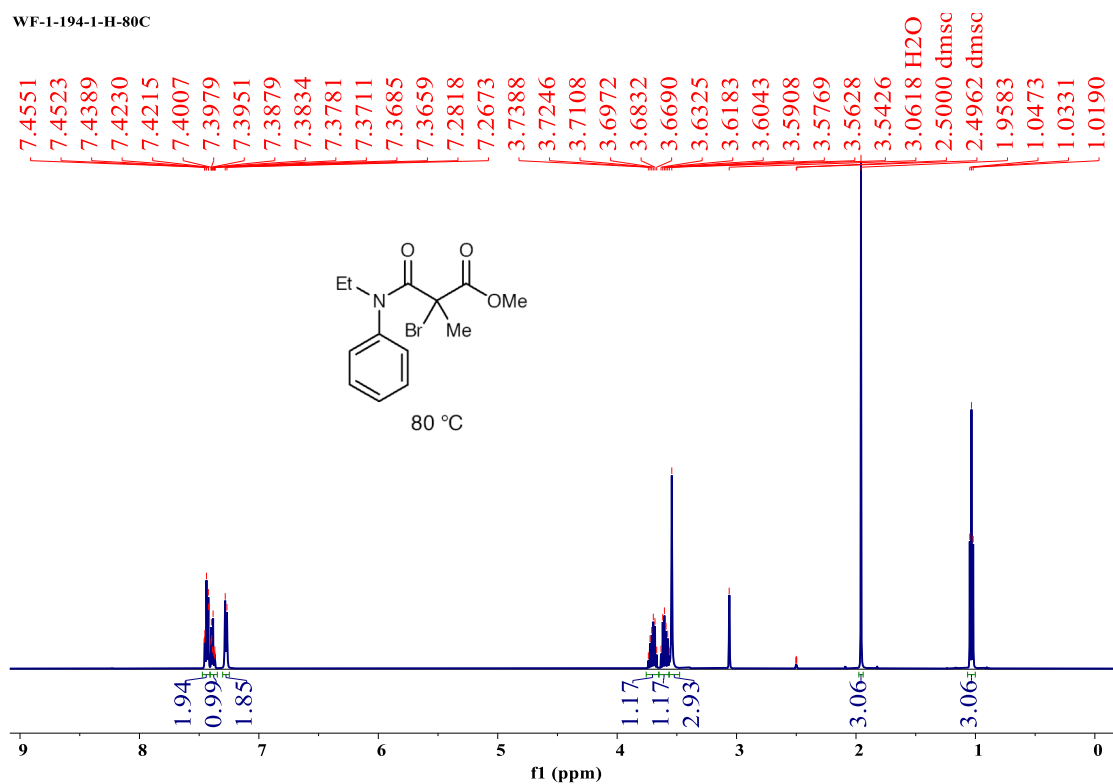
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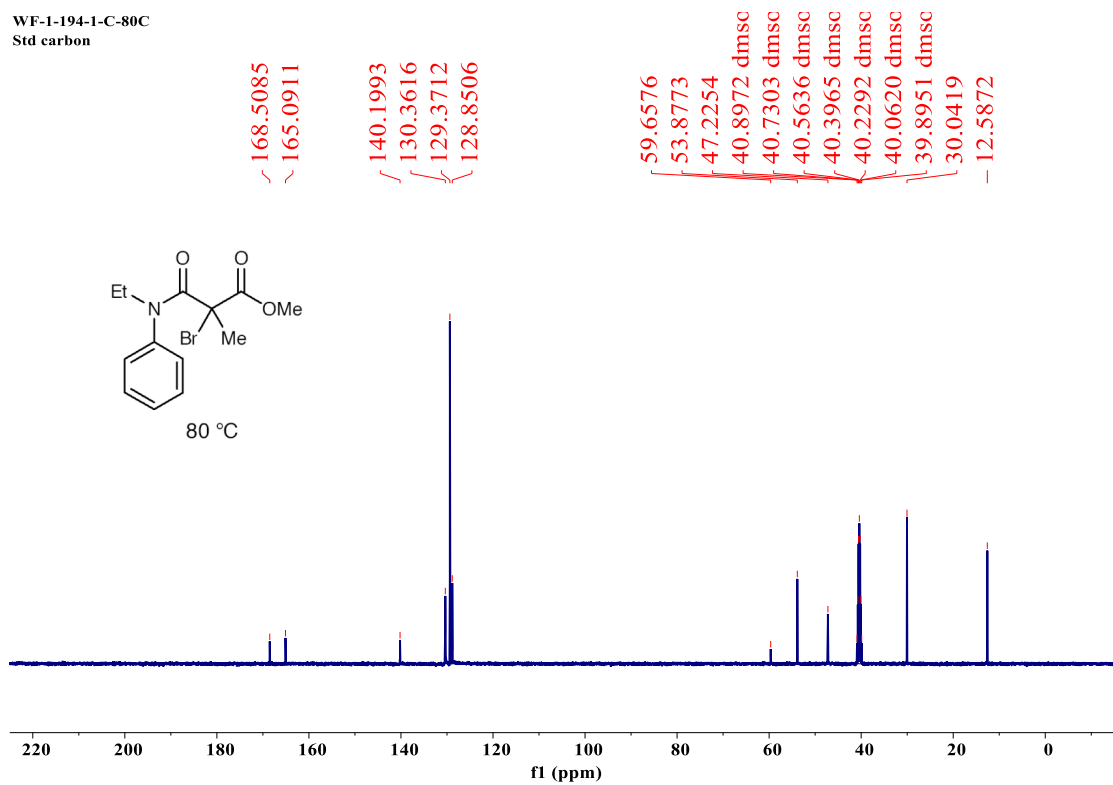
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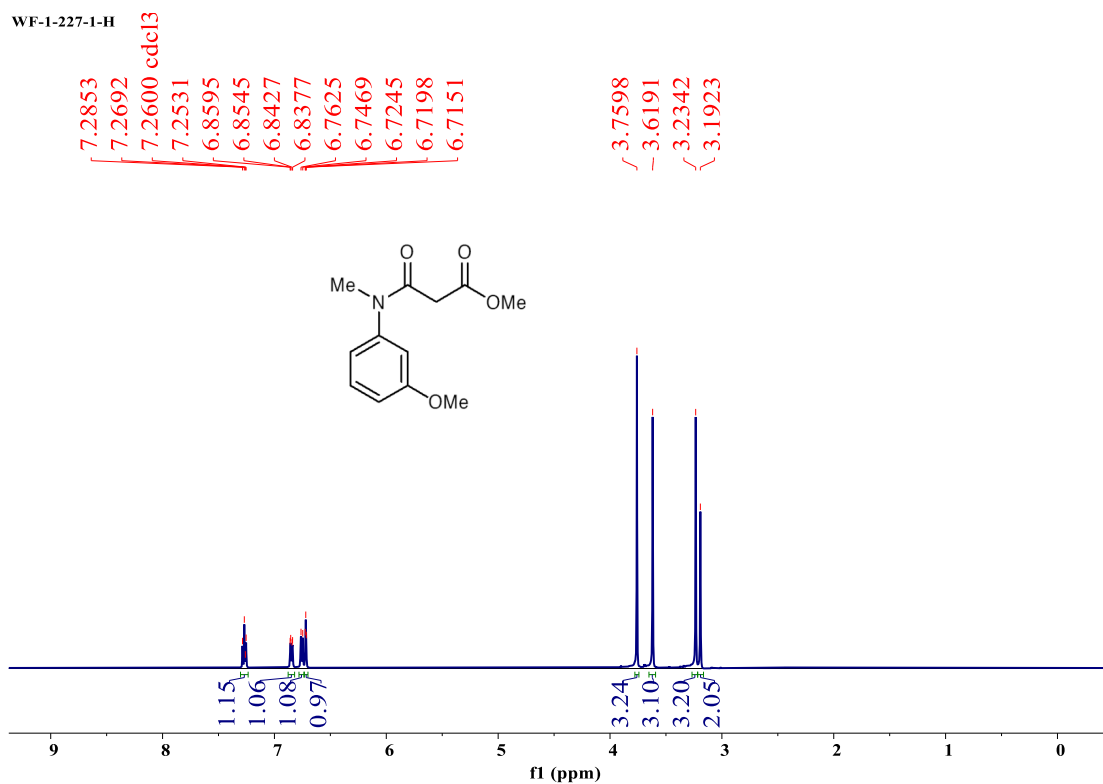
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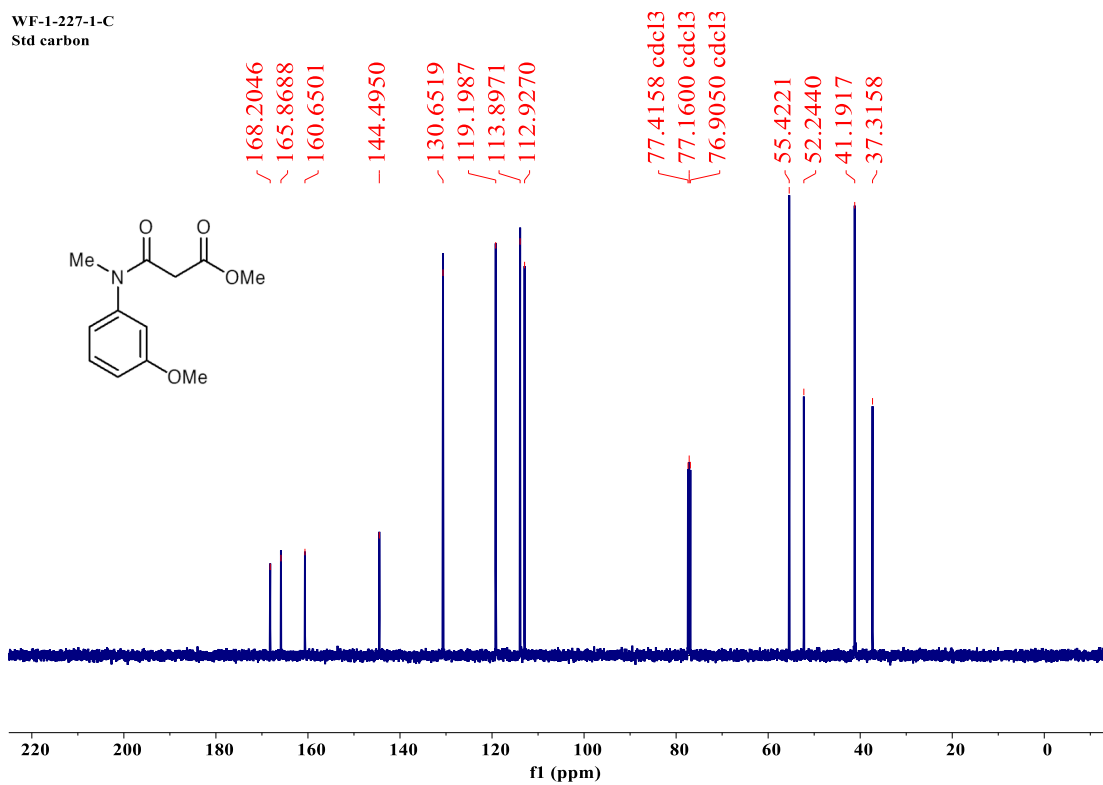
WF-1-194-1-C-80C
Std carbon



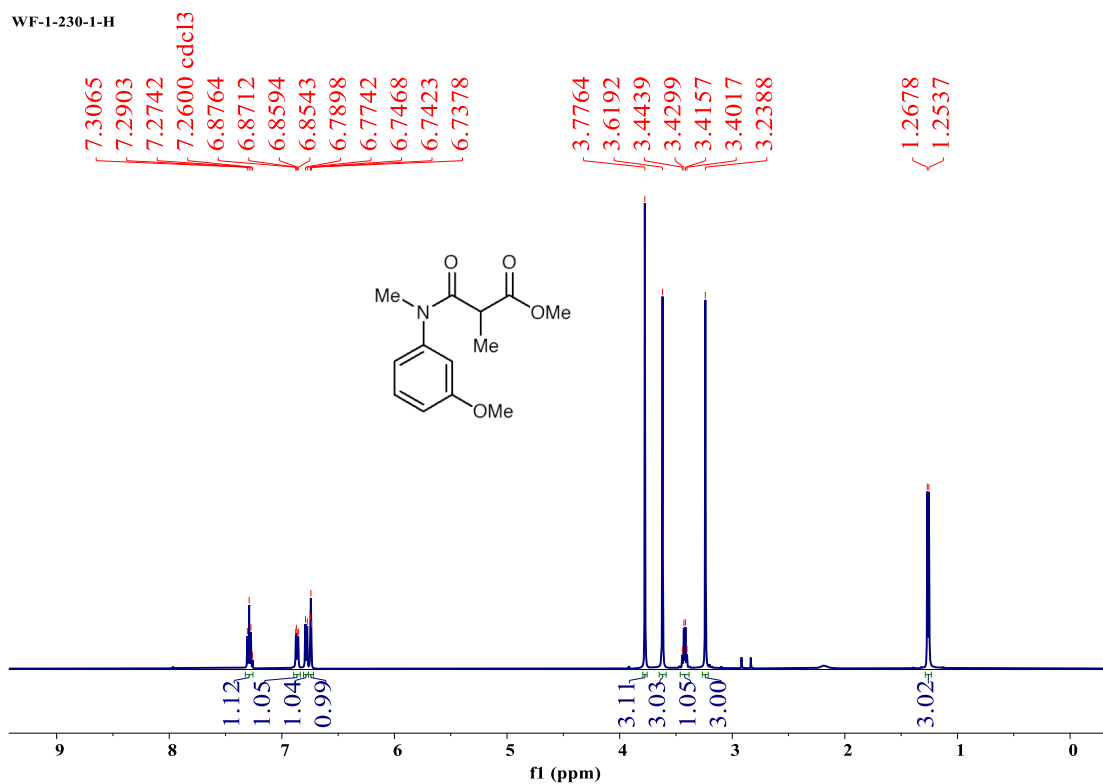
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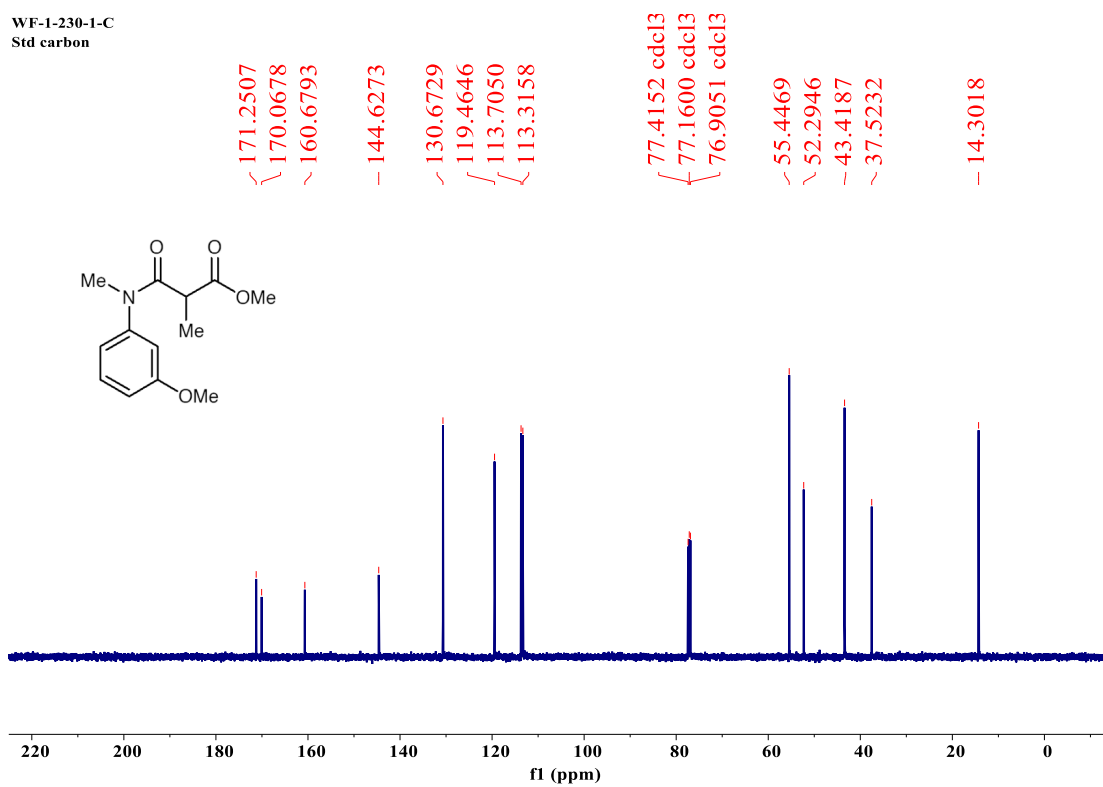
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Std carbon



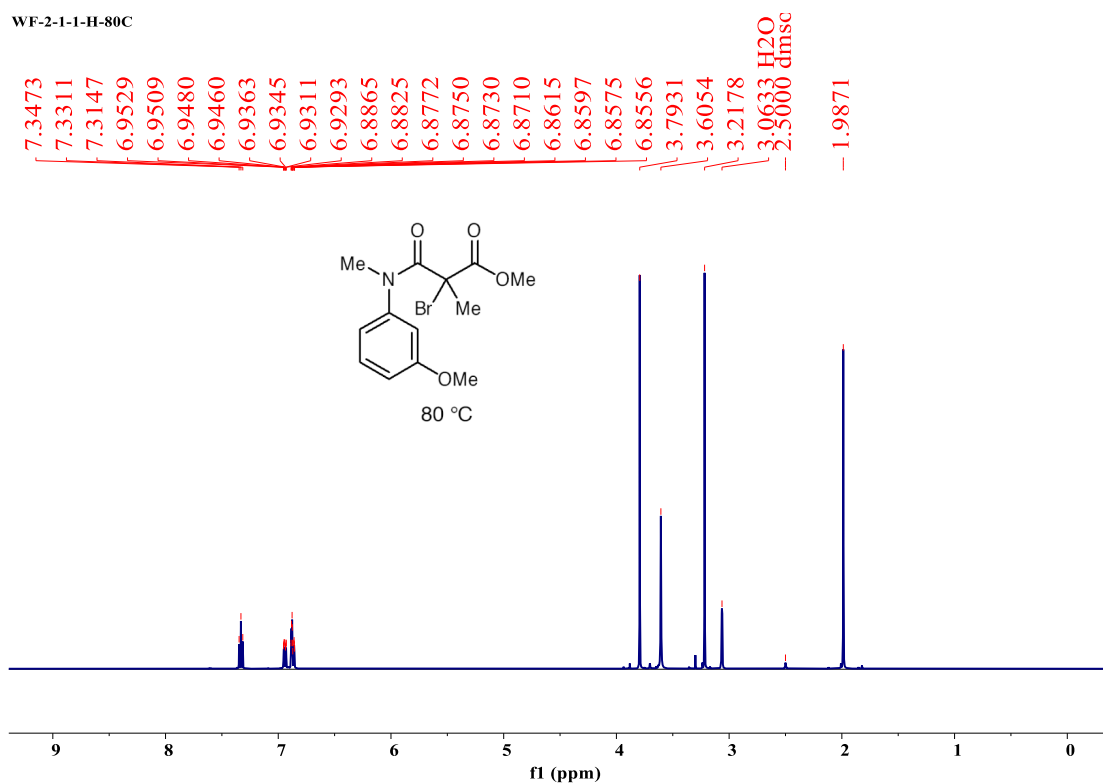
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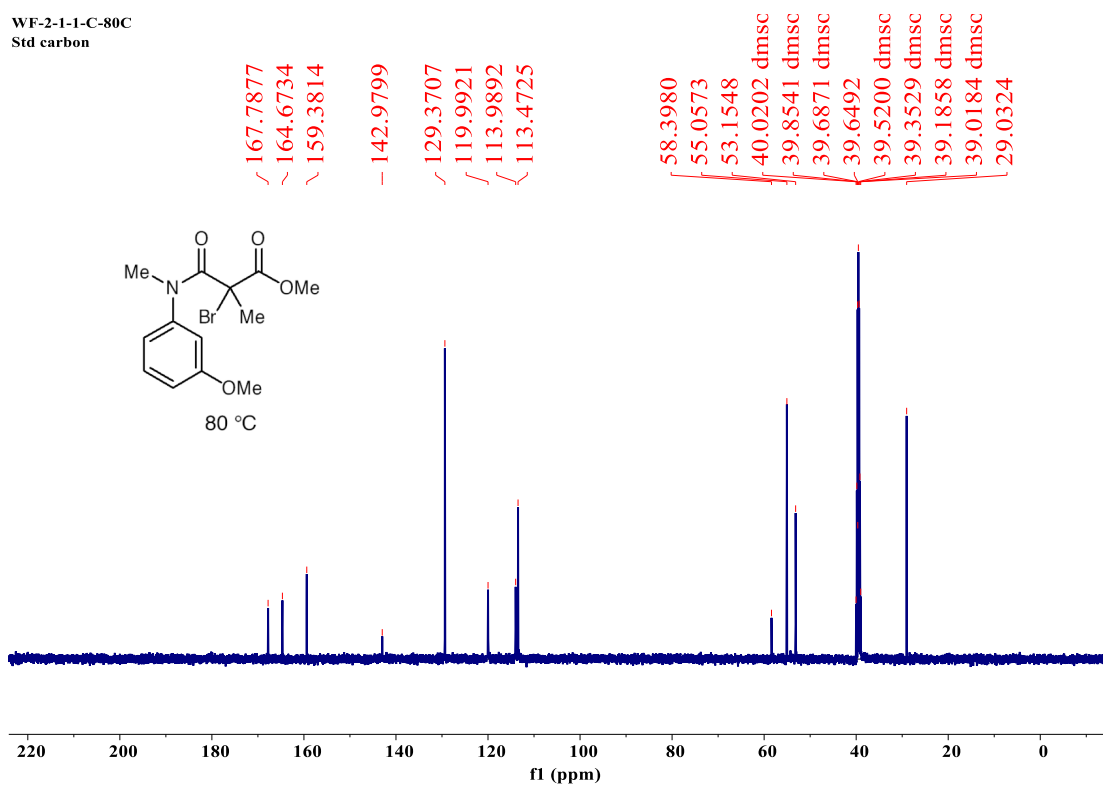
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Std carbon



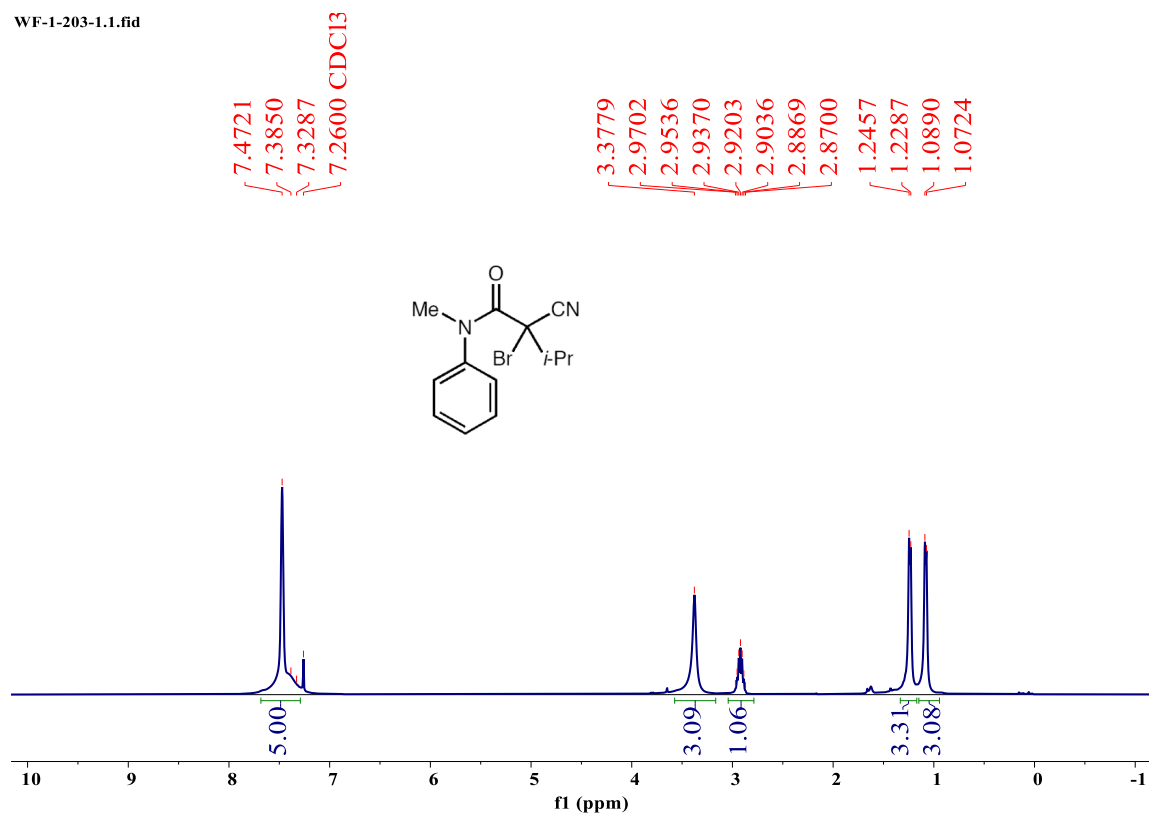
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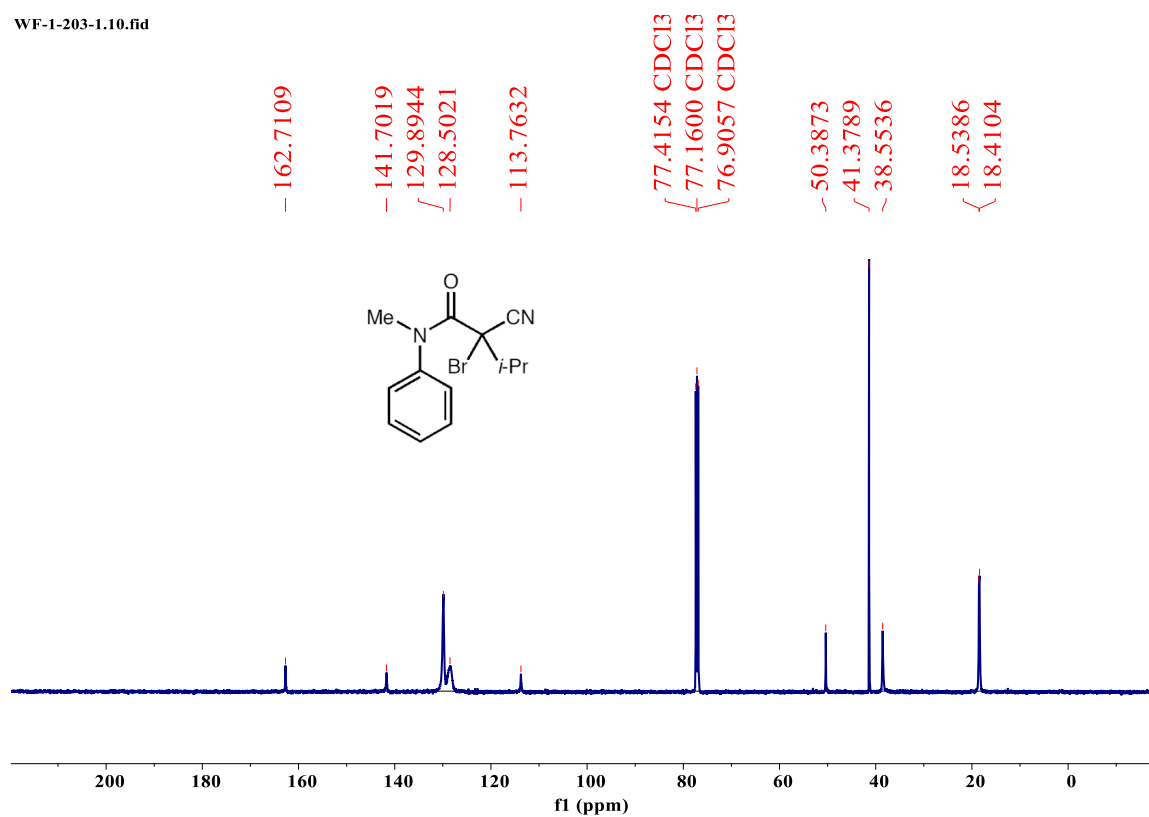
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Std carbon



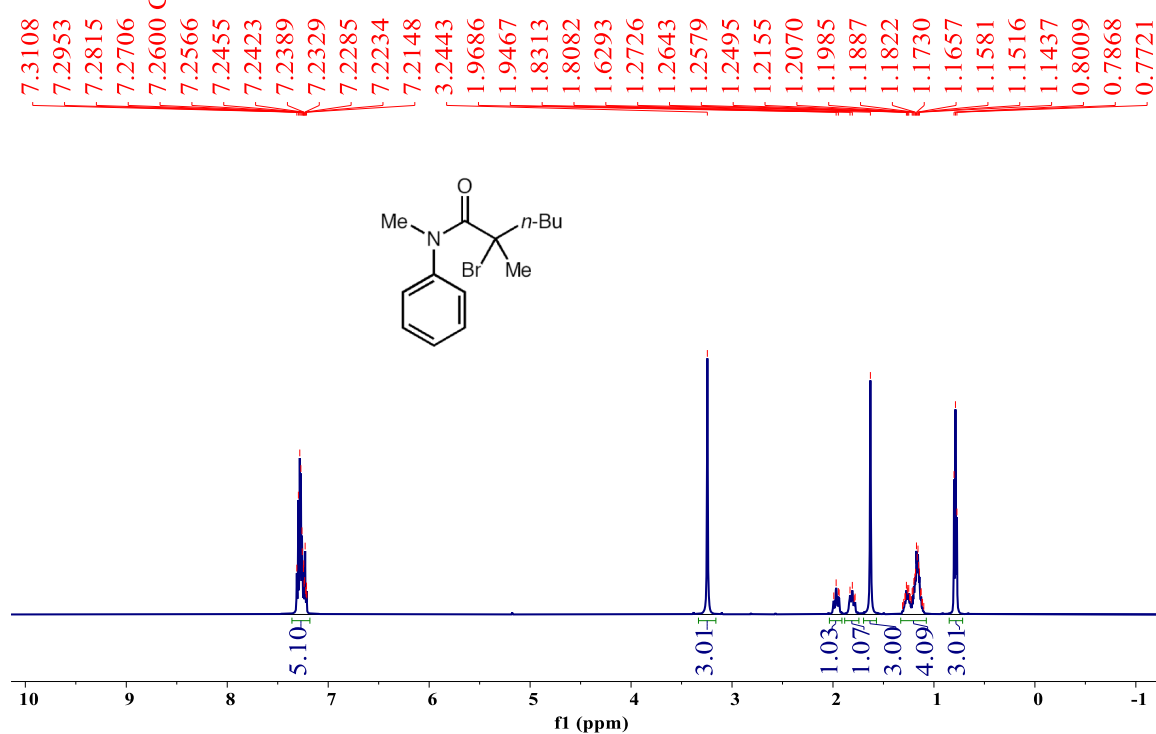
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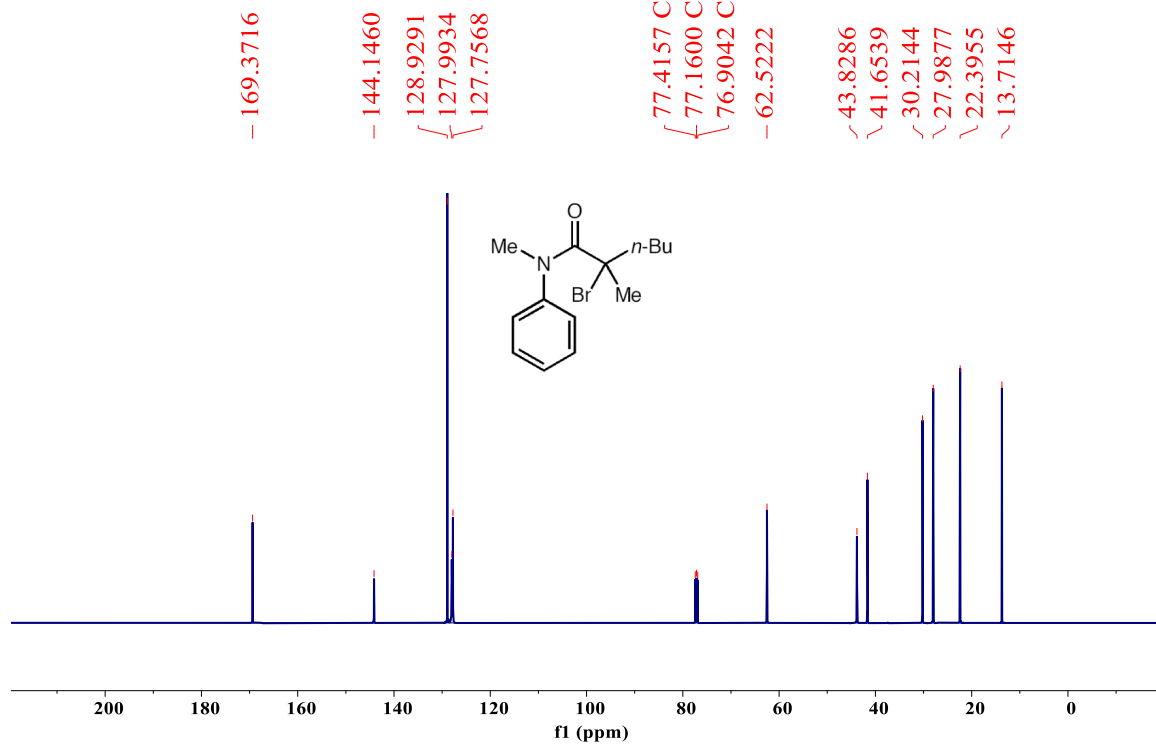
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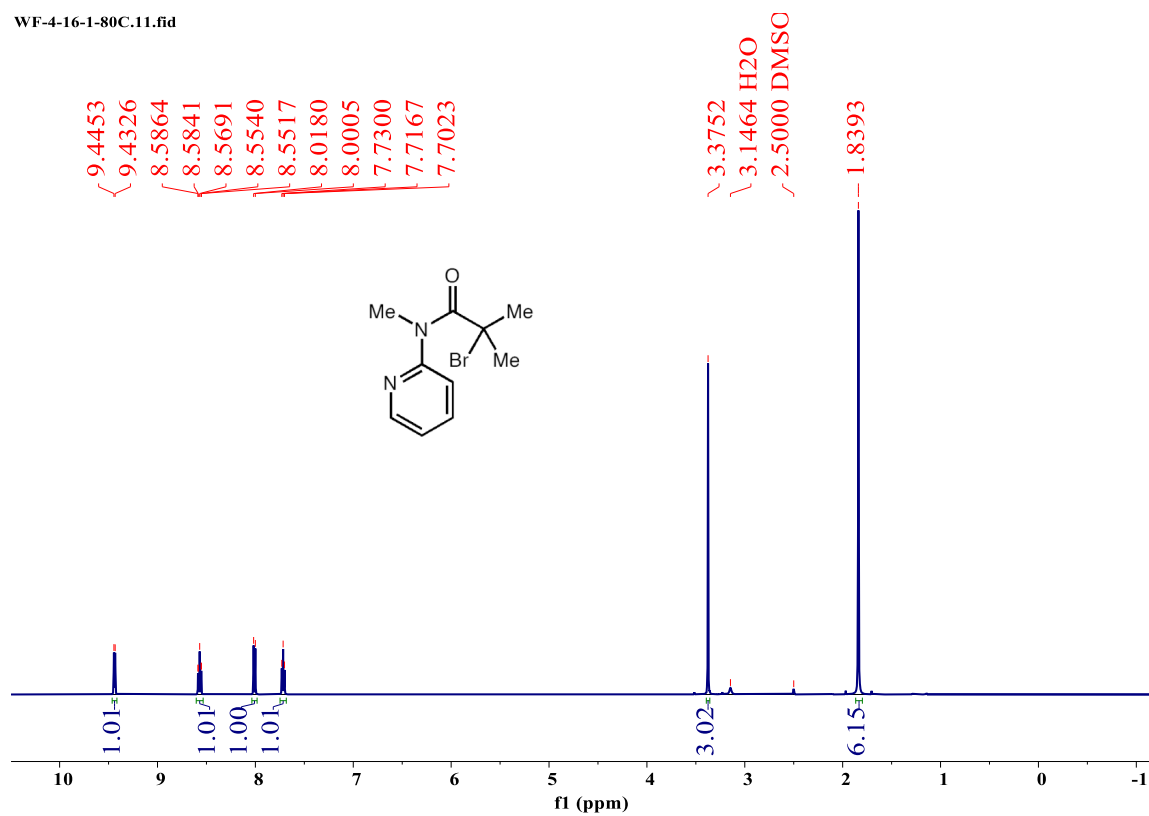
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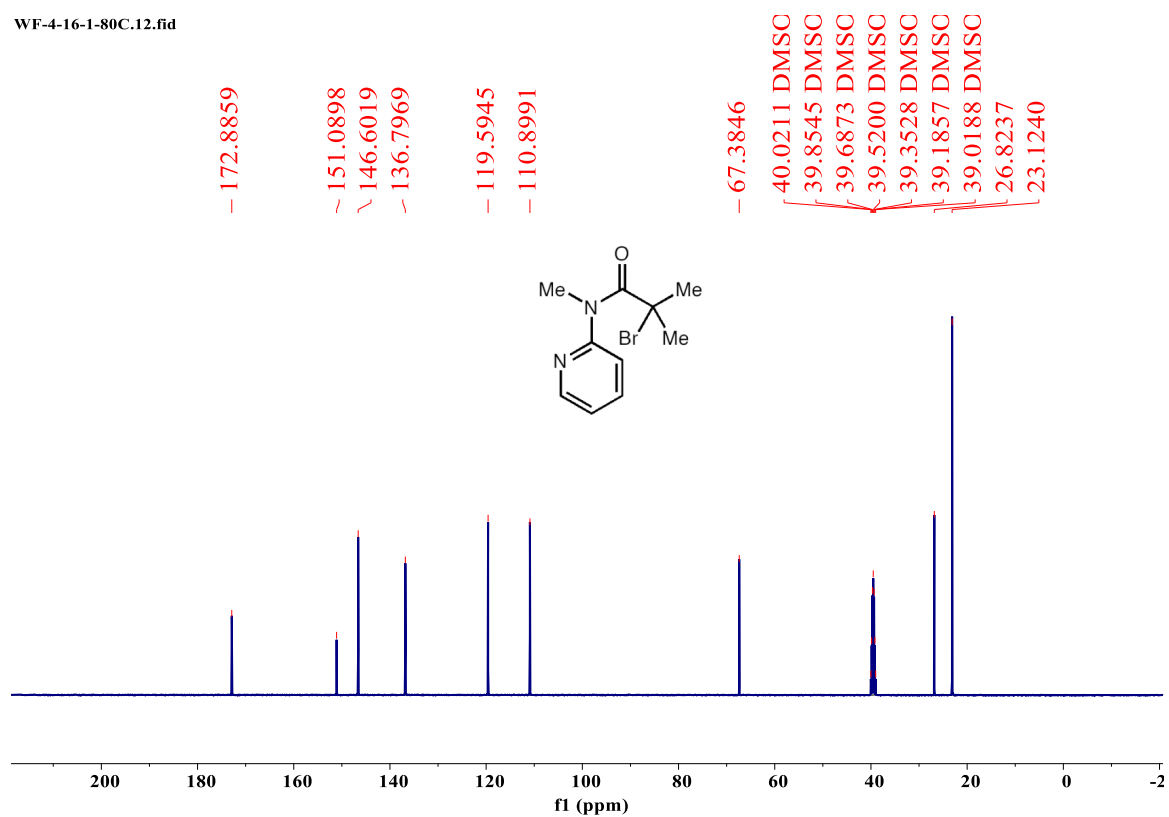
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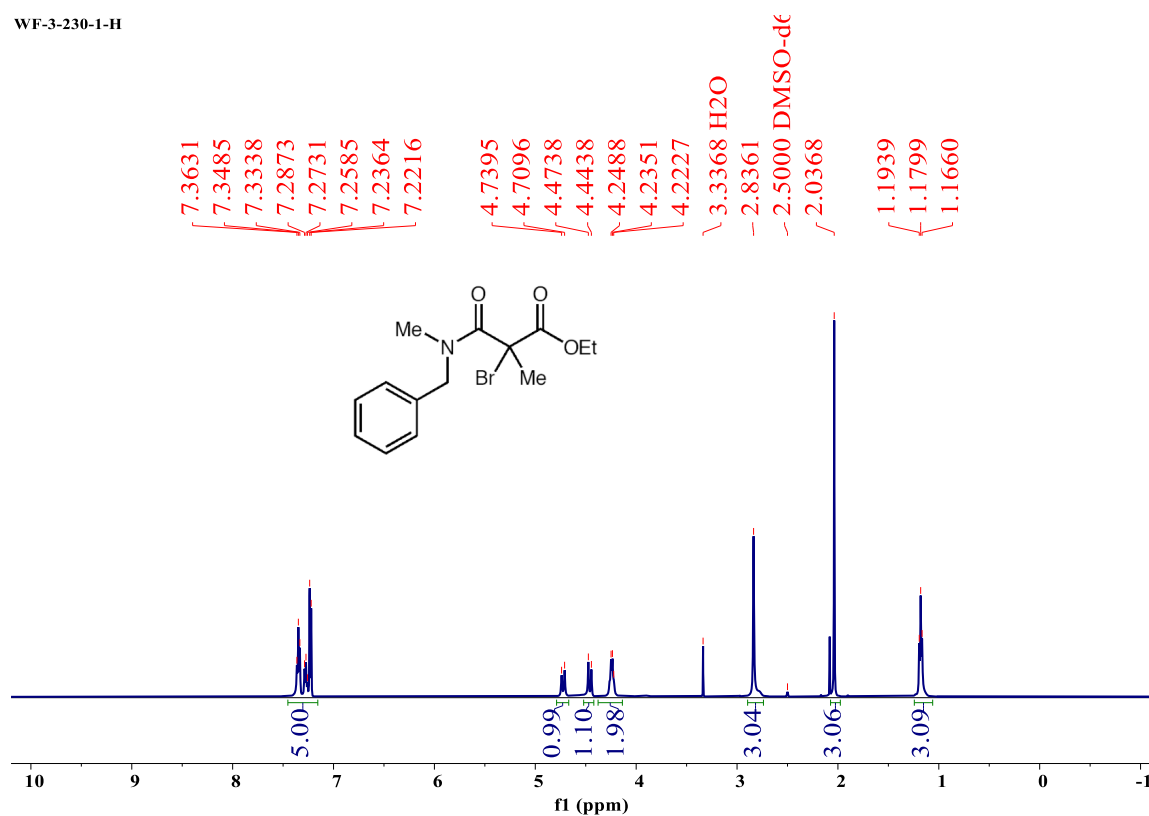
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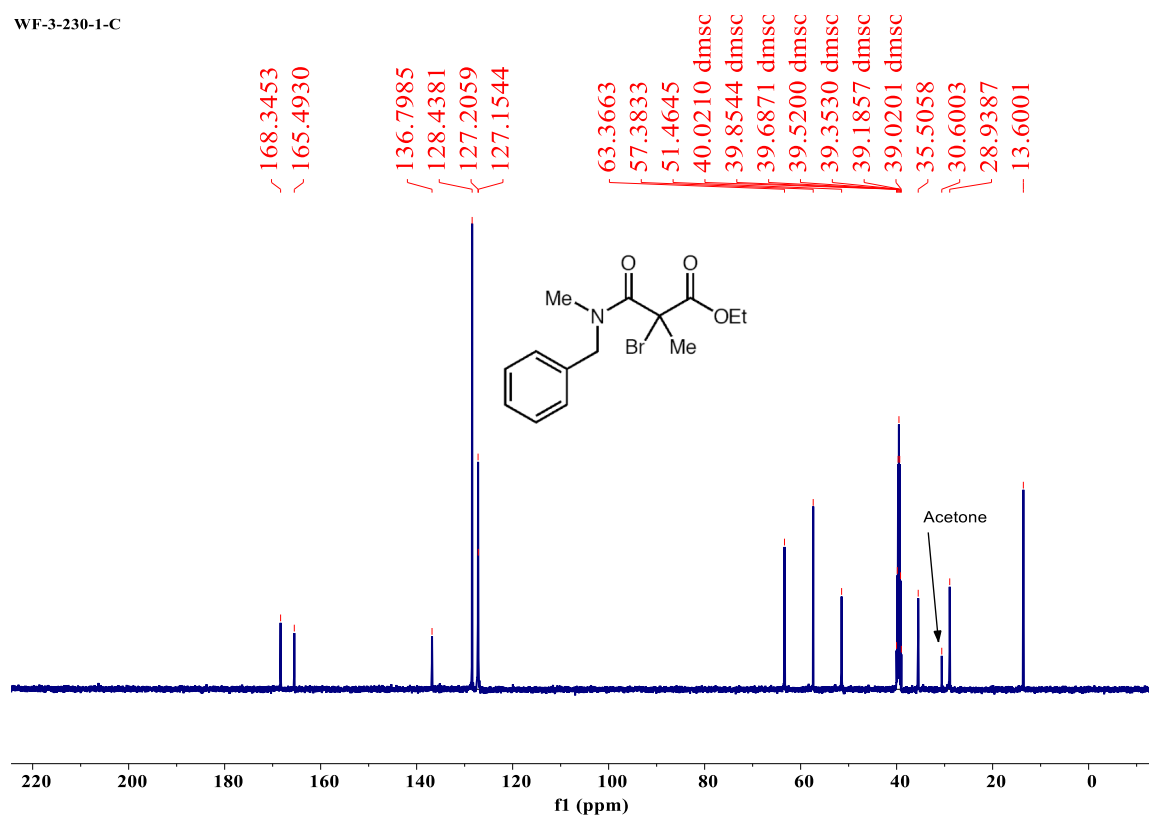
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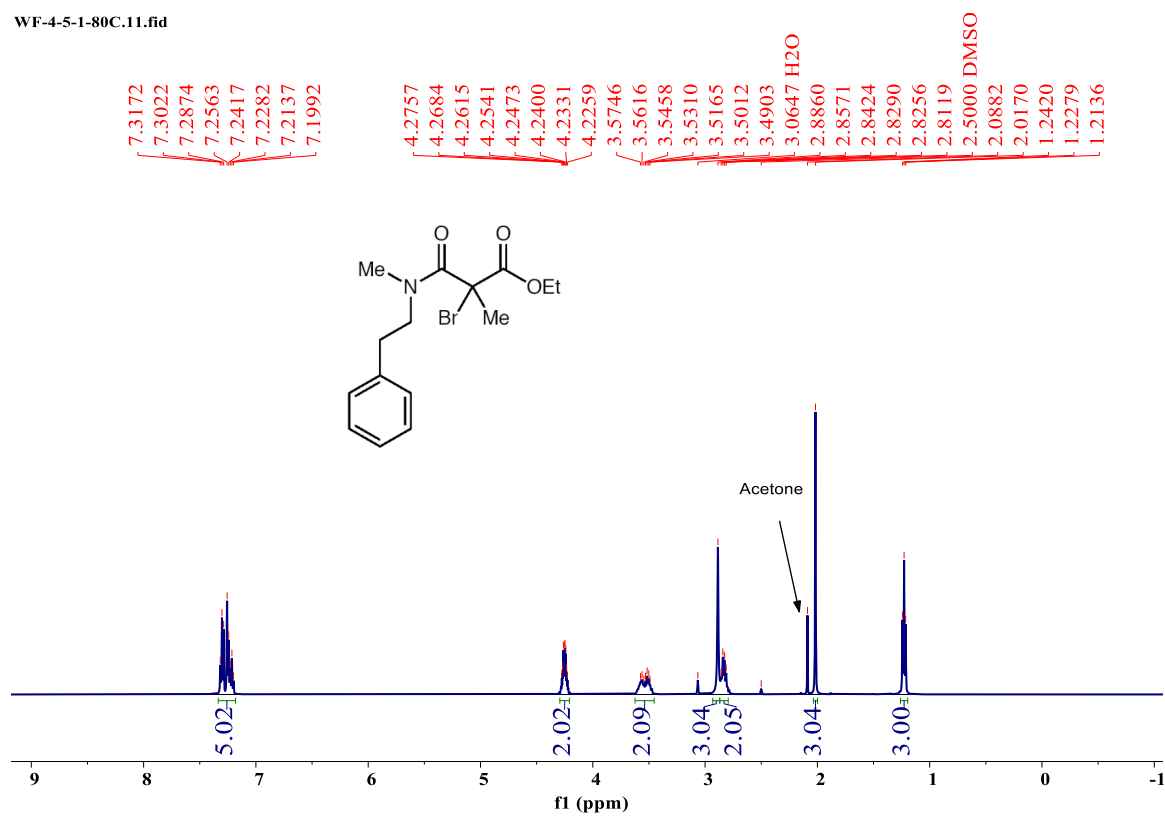
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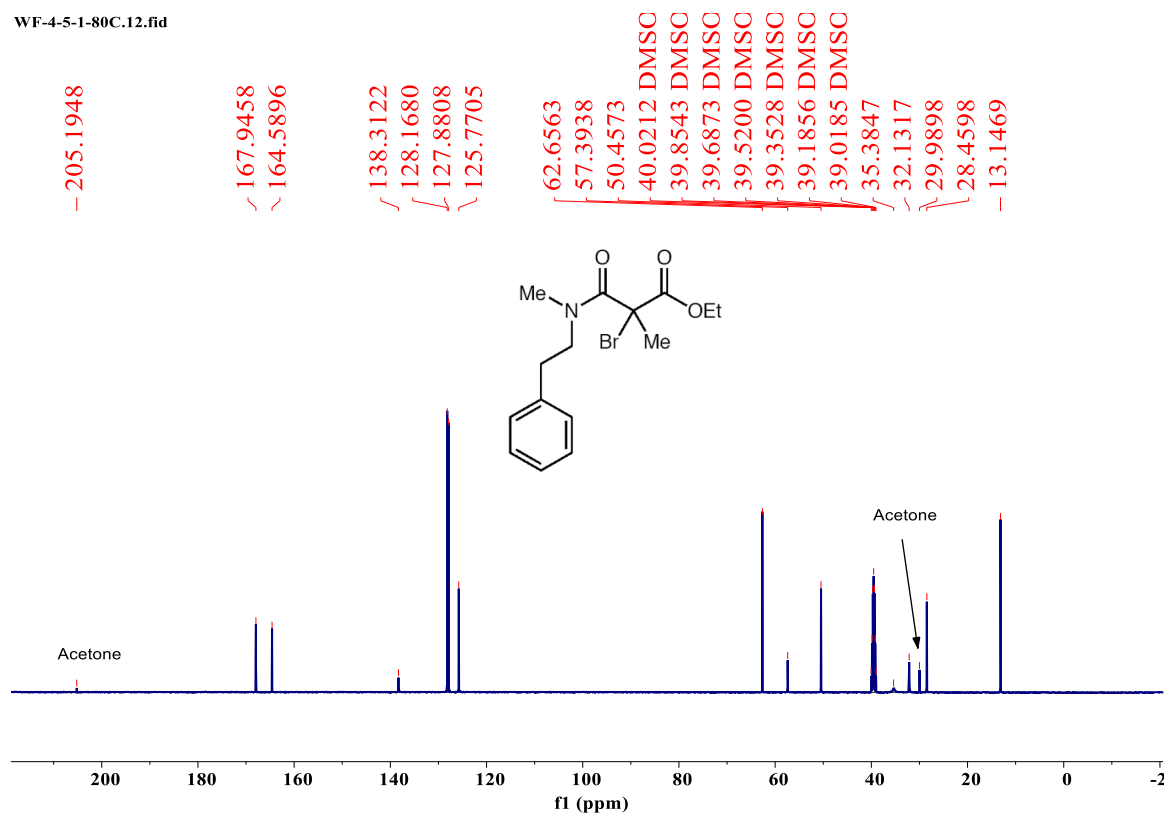
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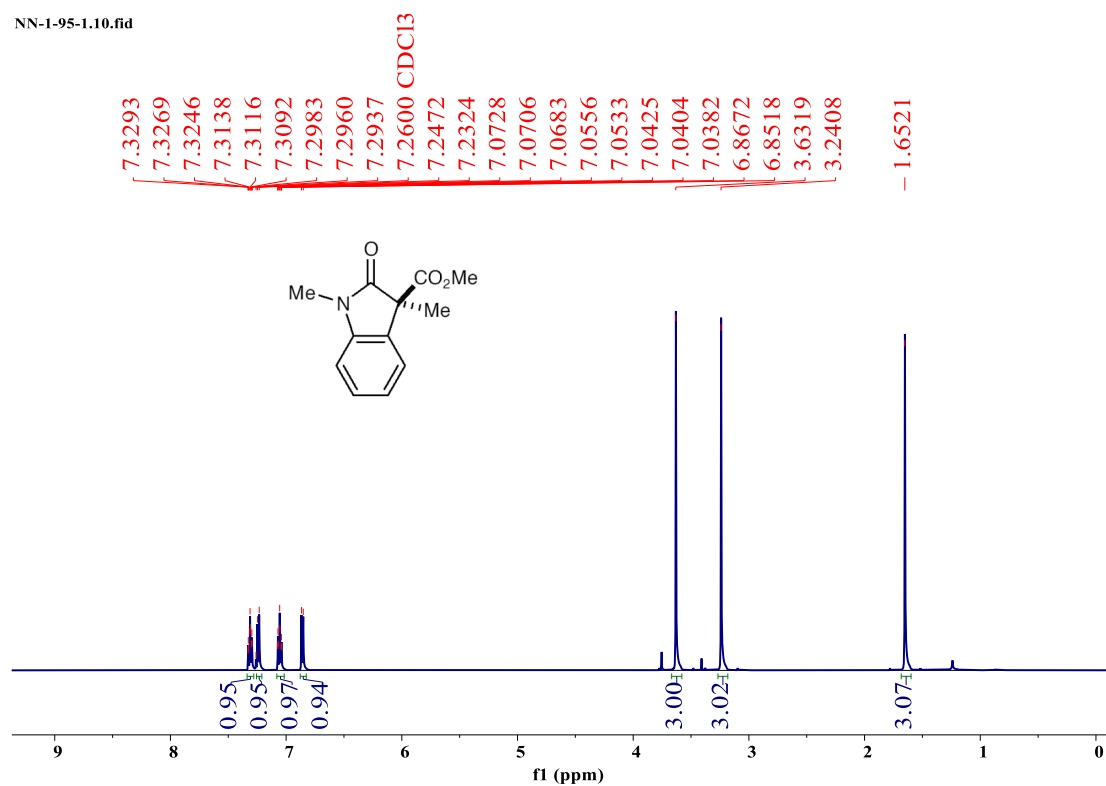
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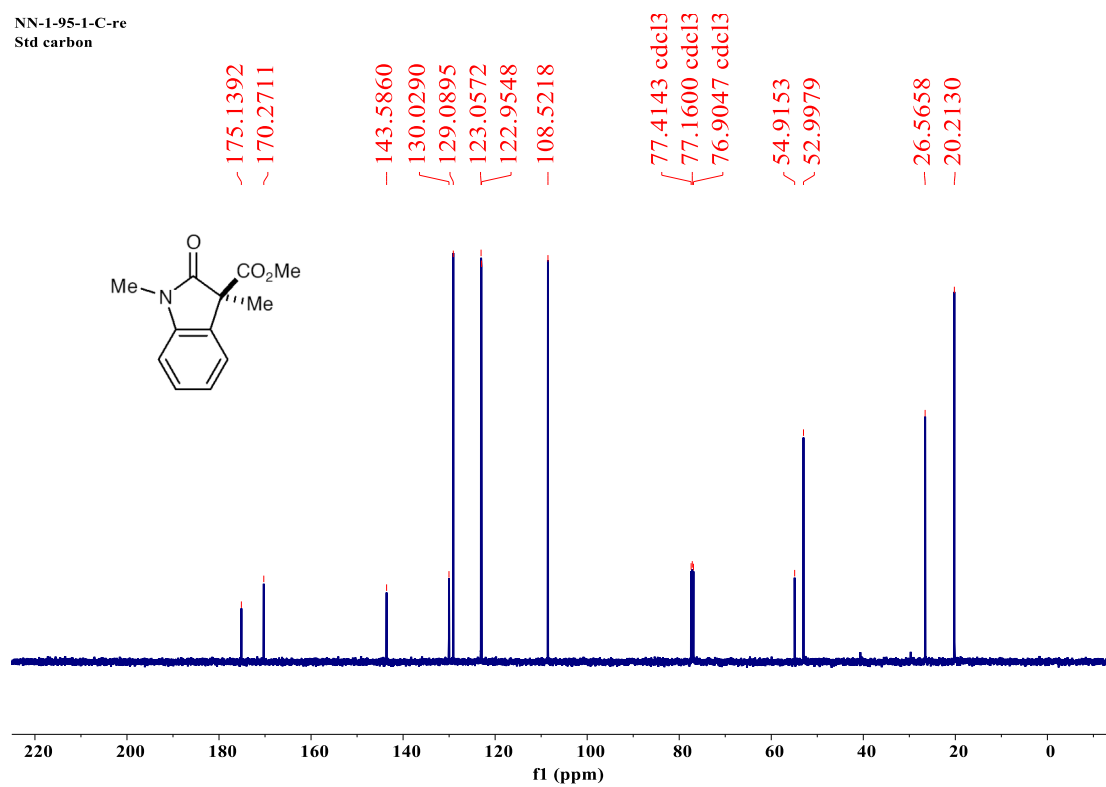
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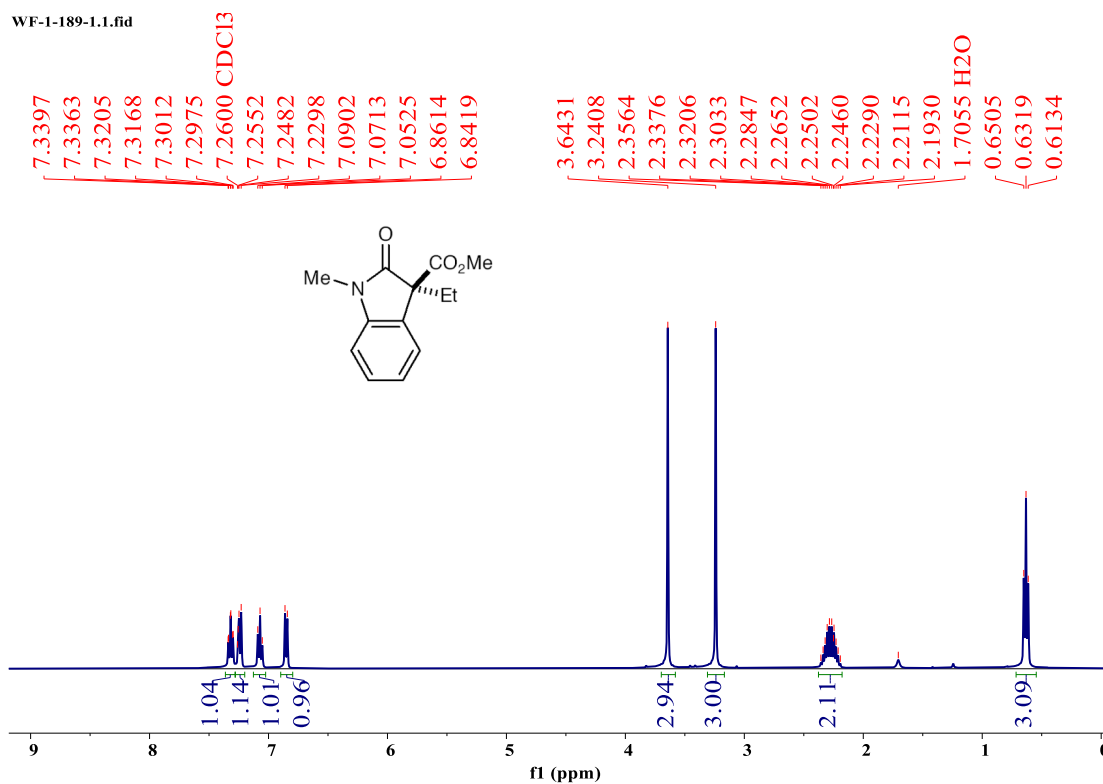
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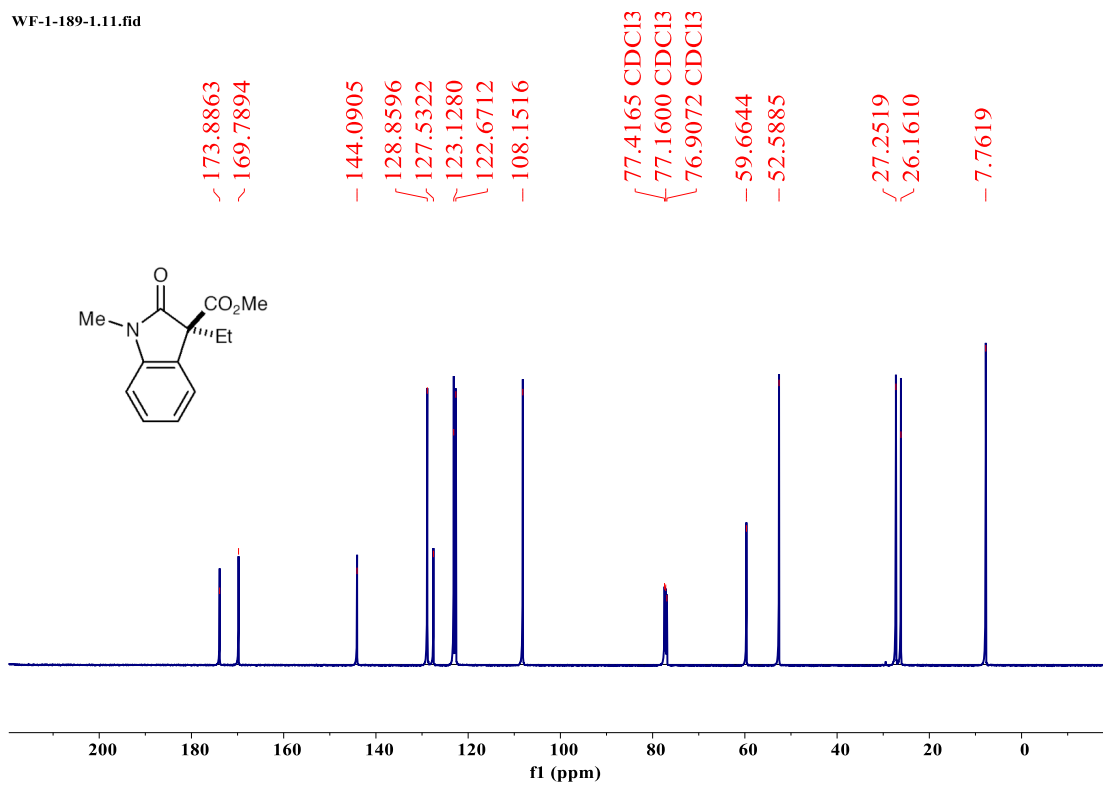
NN-1-95-1-C-re
Std carbon



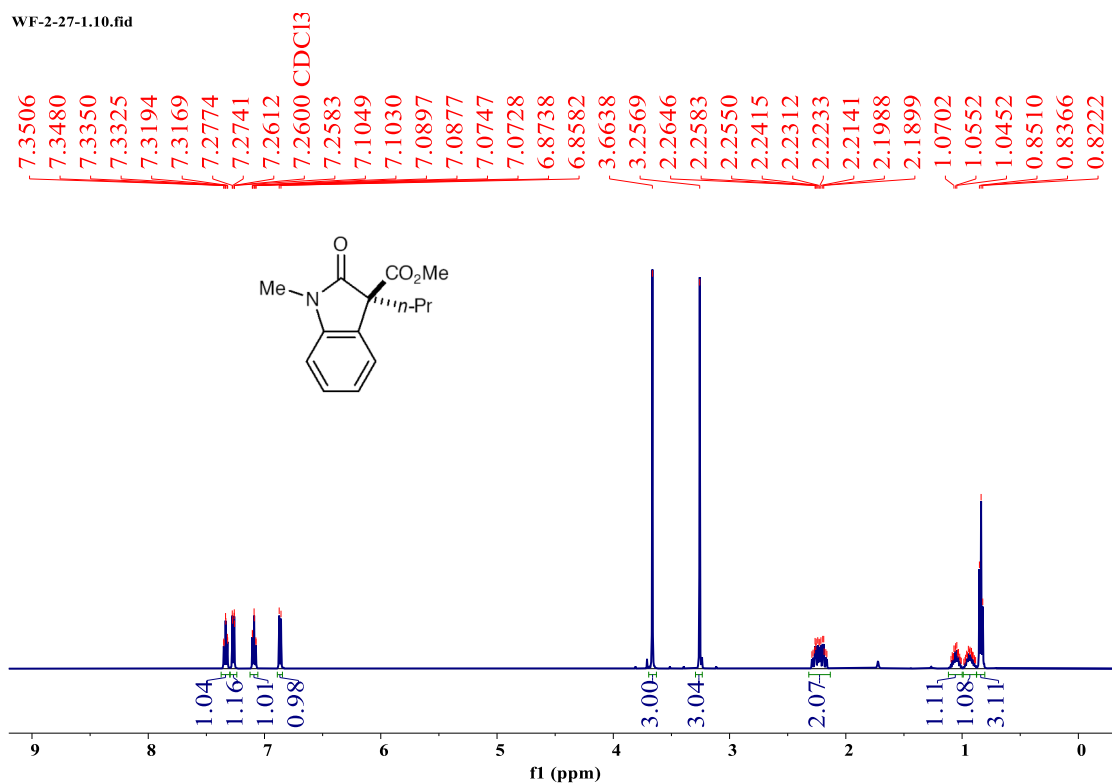
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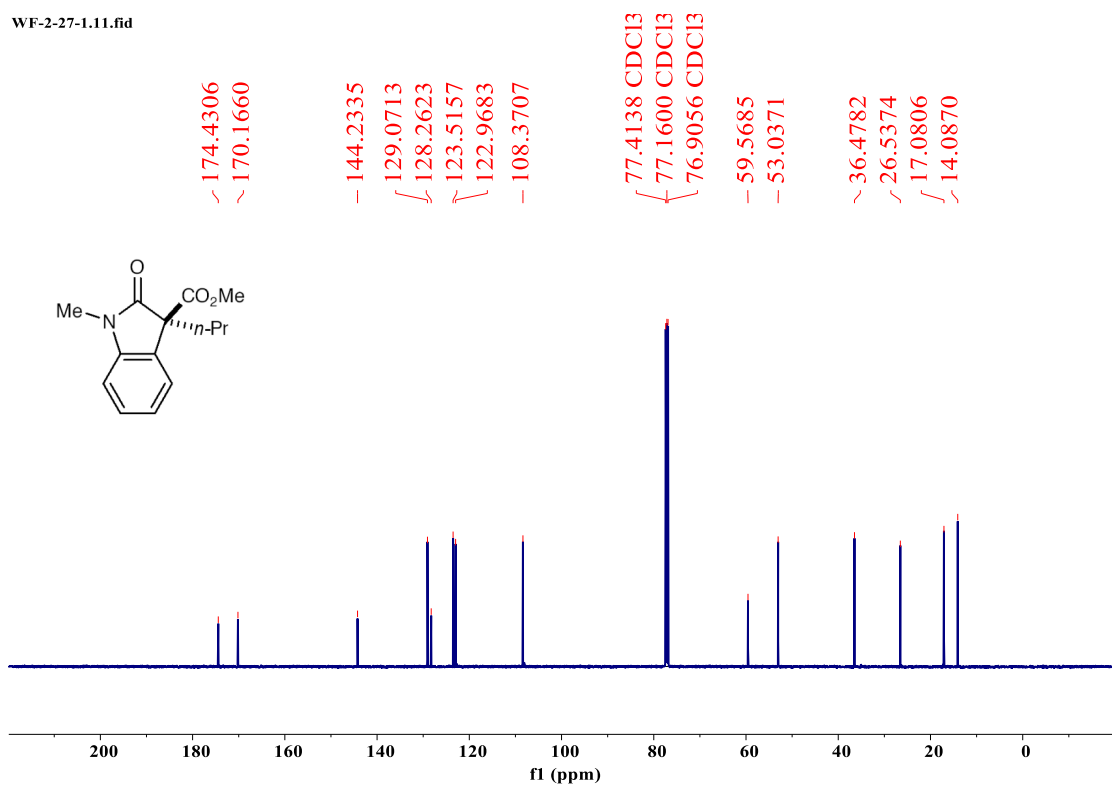
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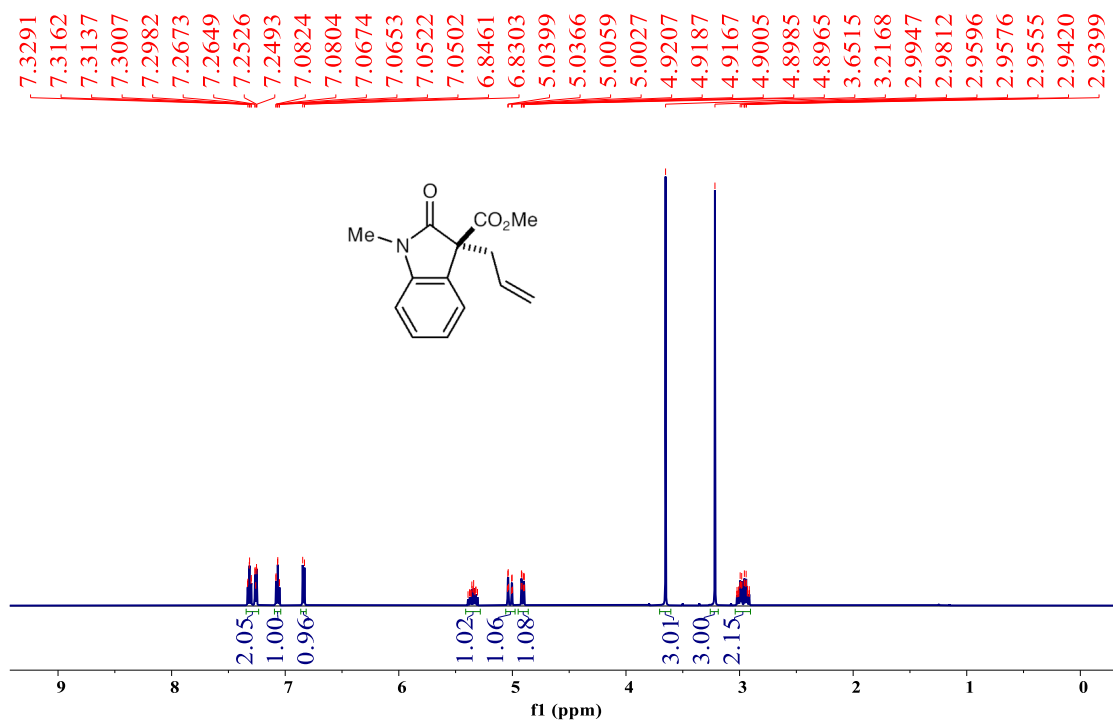
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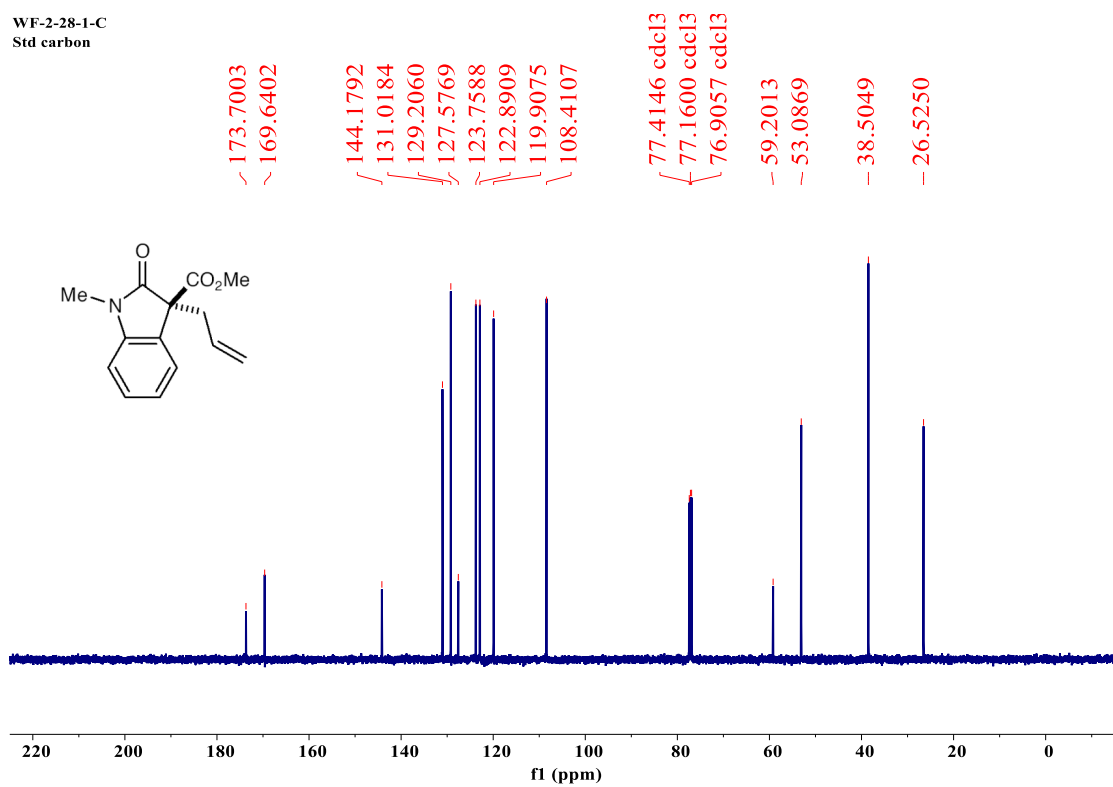
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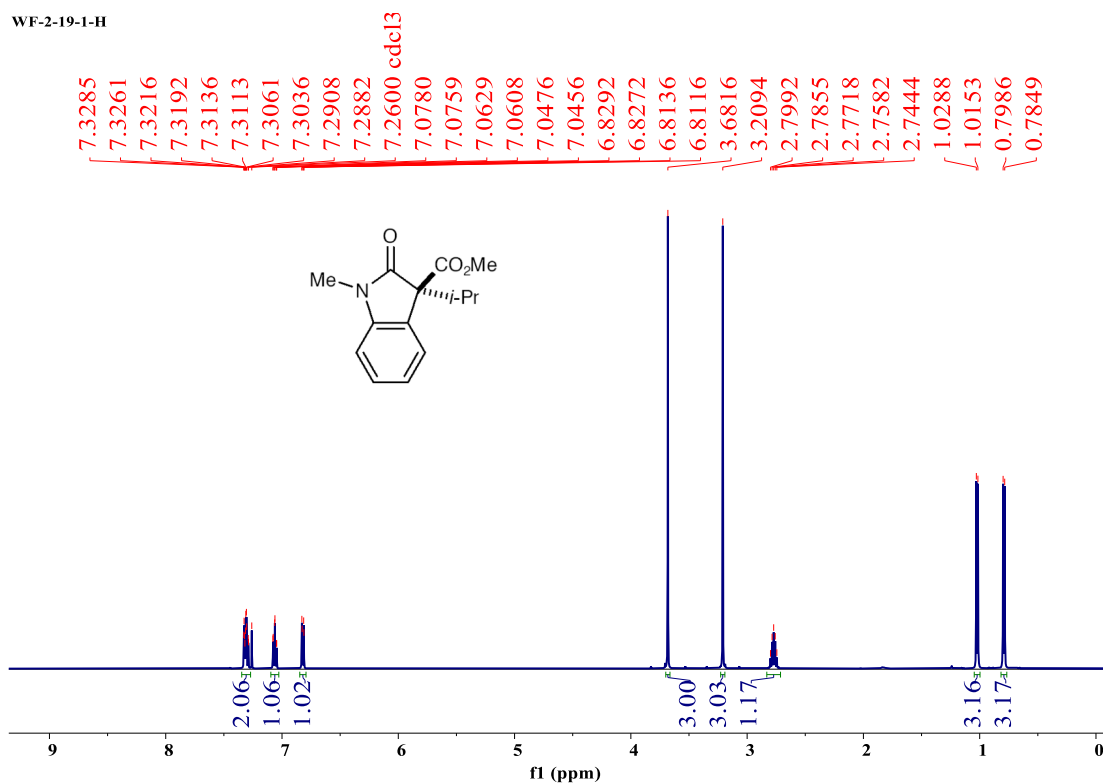
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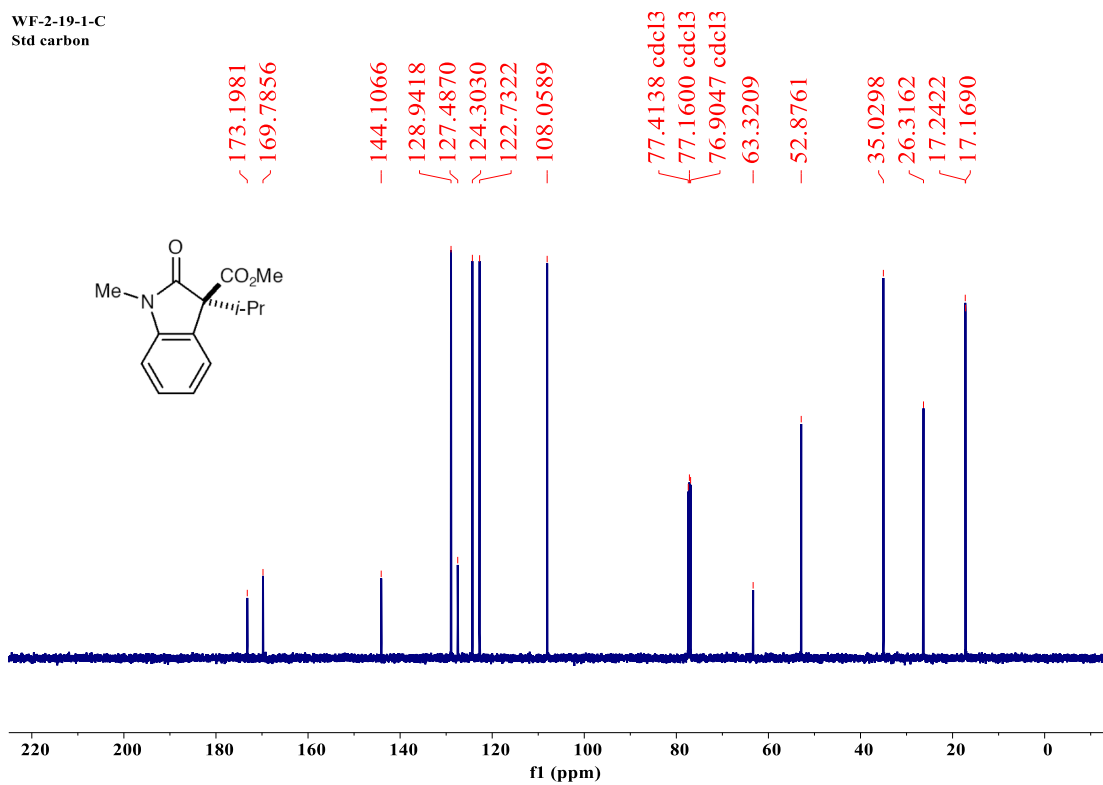
WF-2-28-1-C
Std carbon



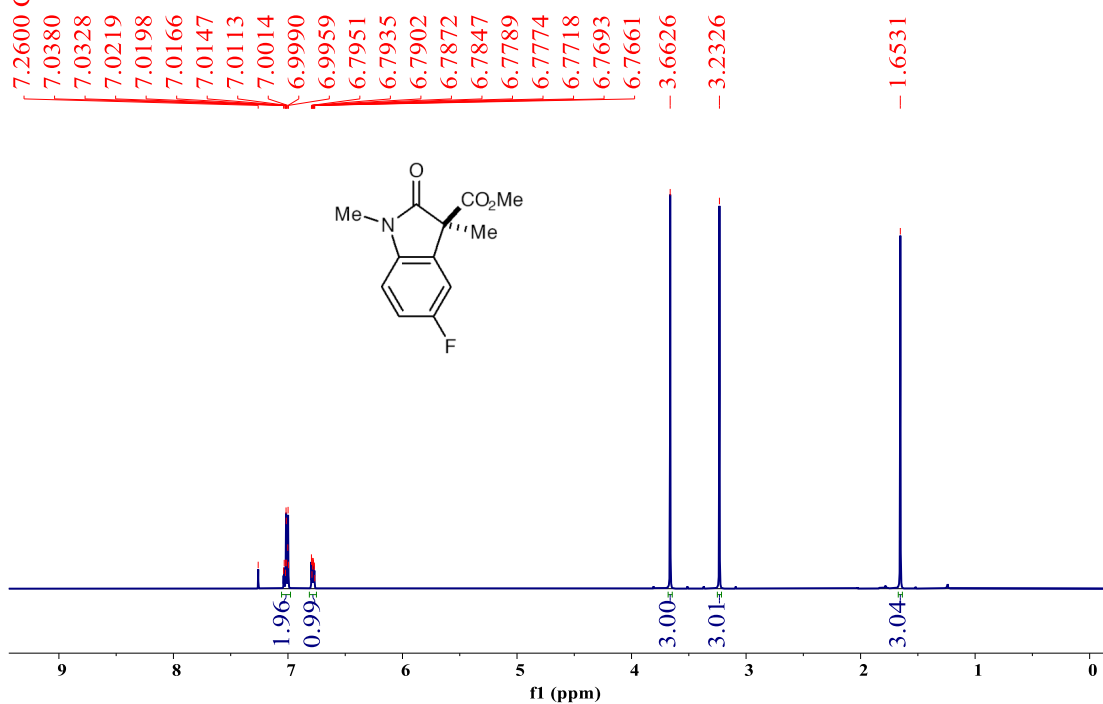
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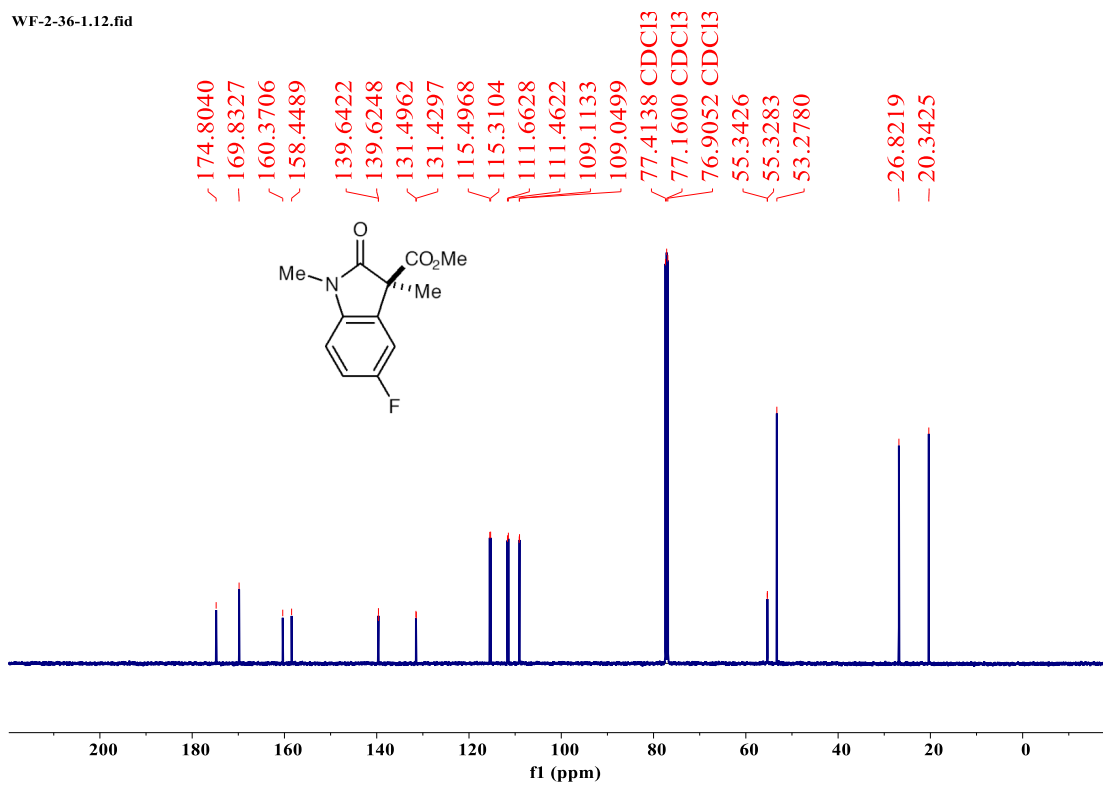
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Std carbon



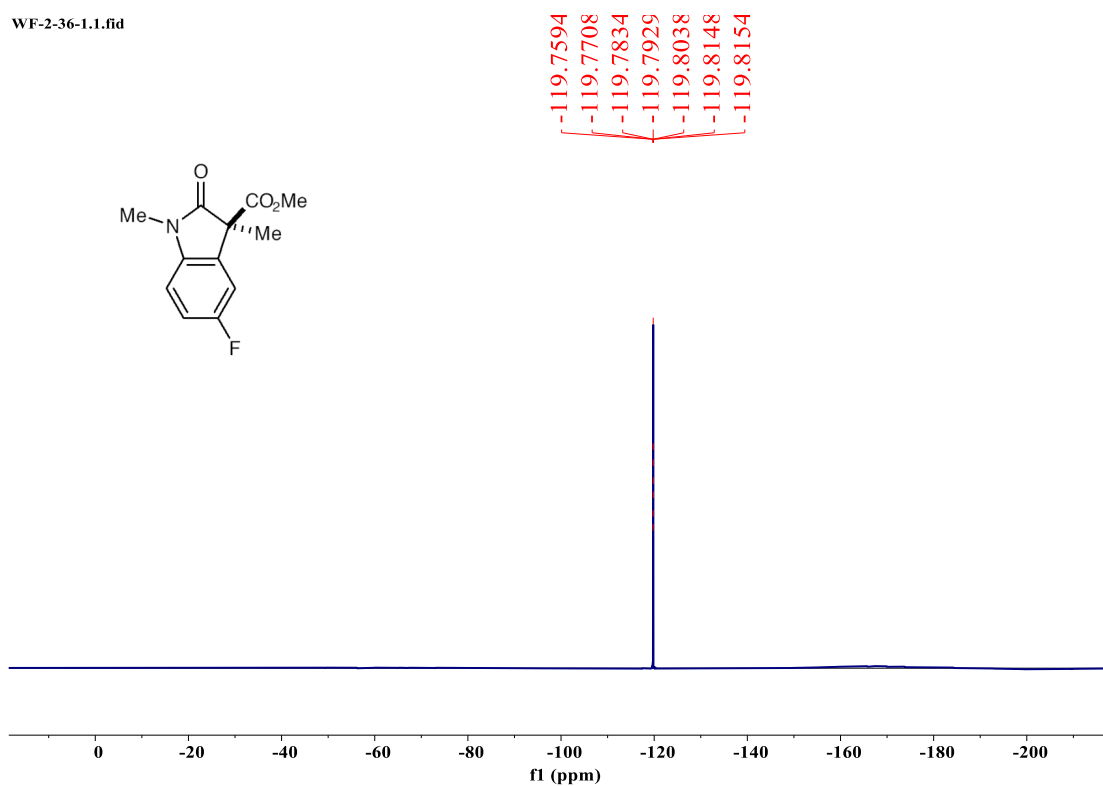
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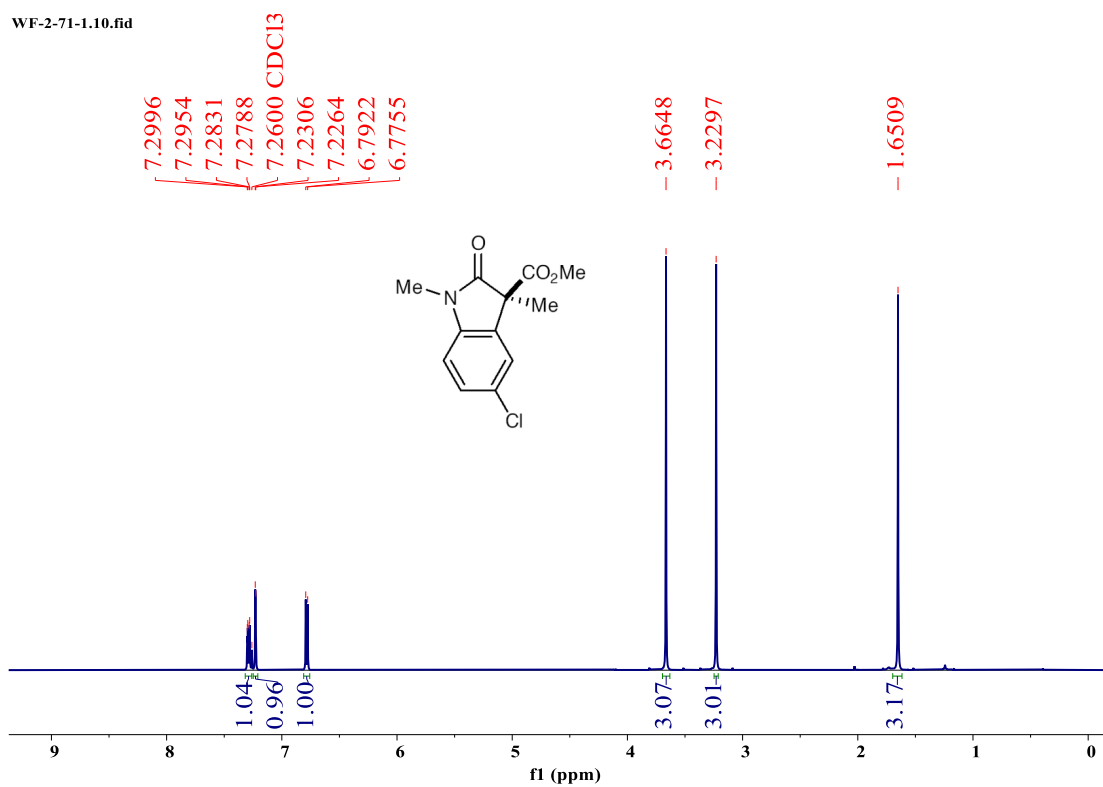
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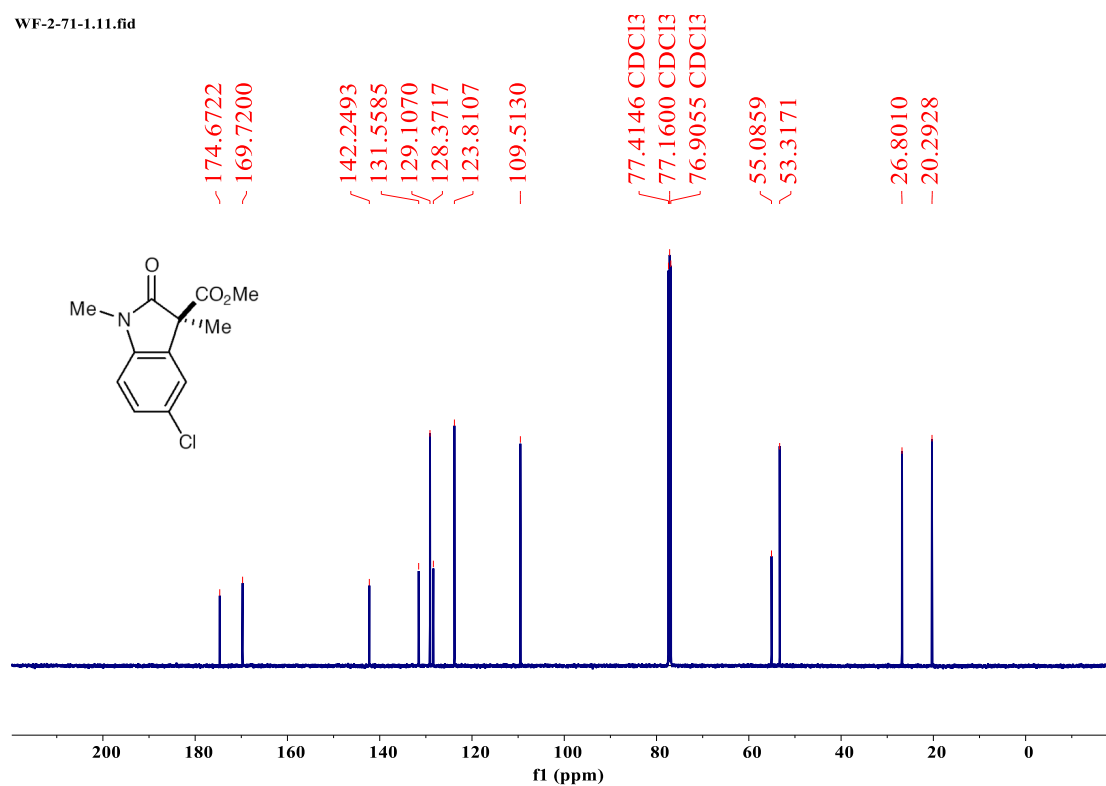
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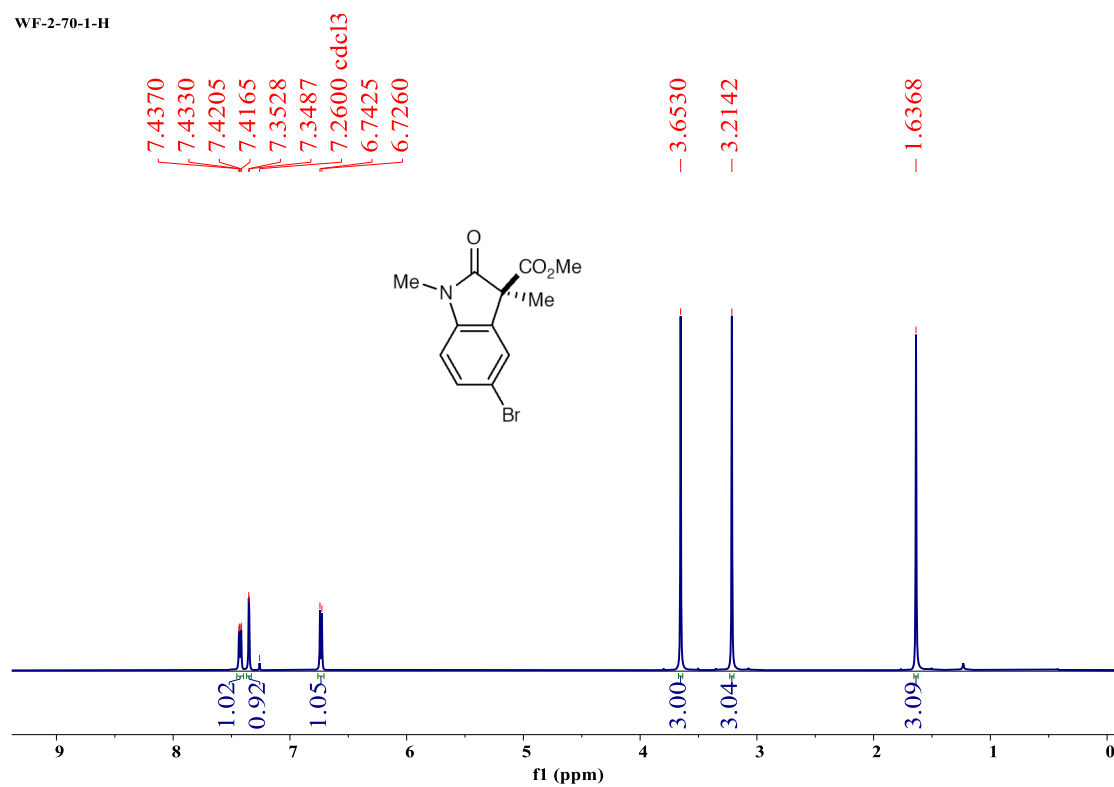
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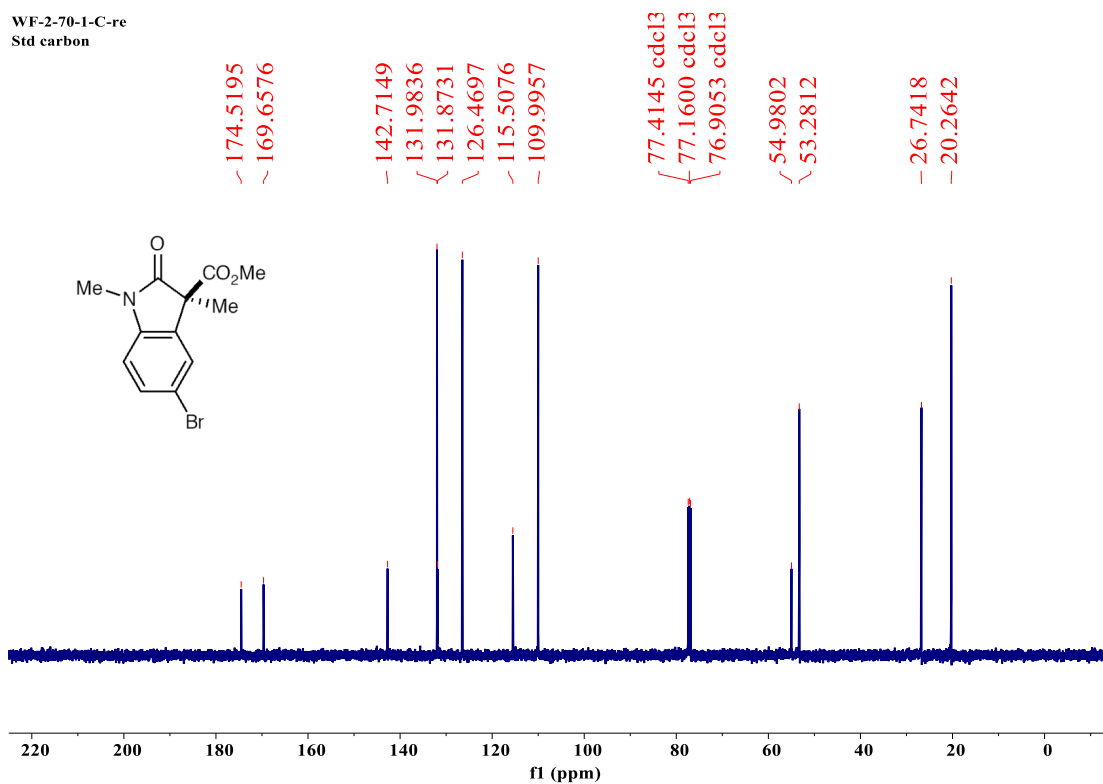
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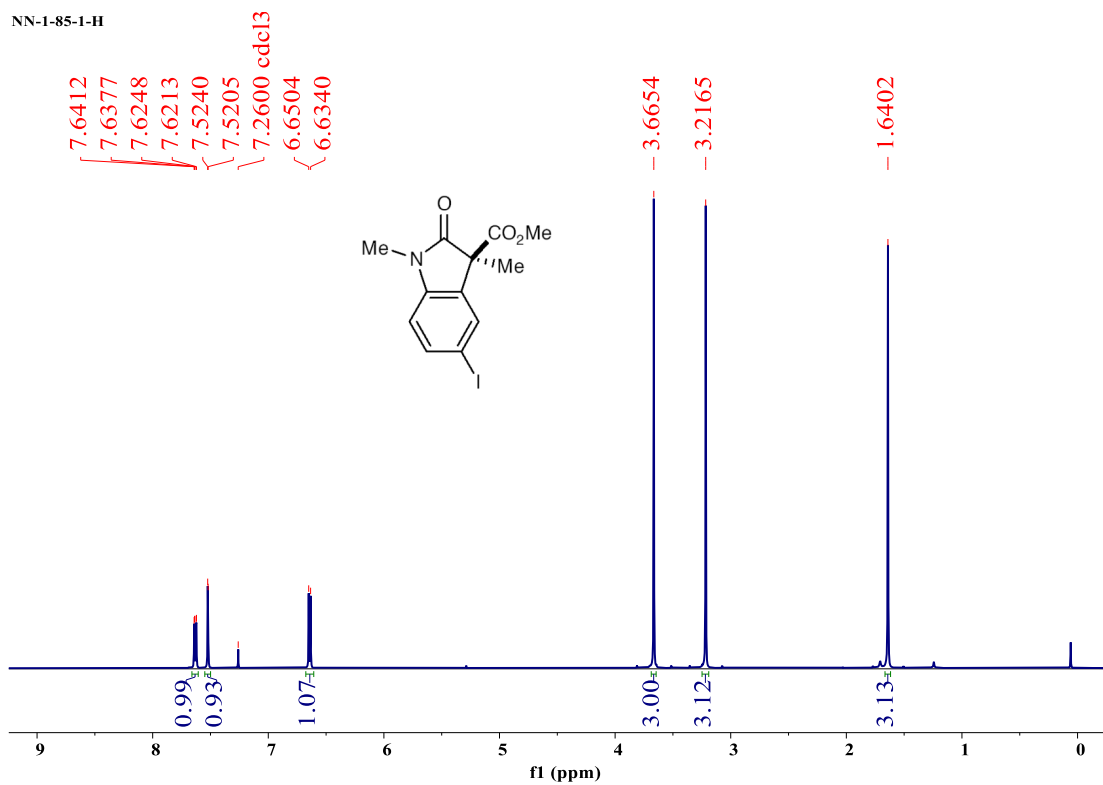
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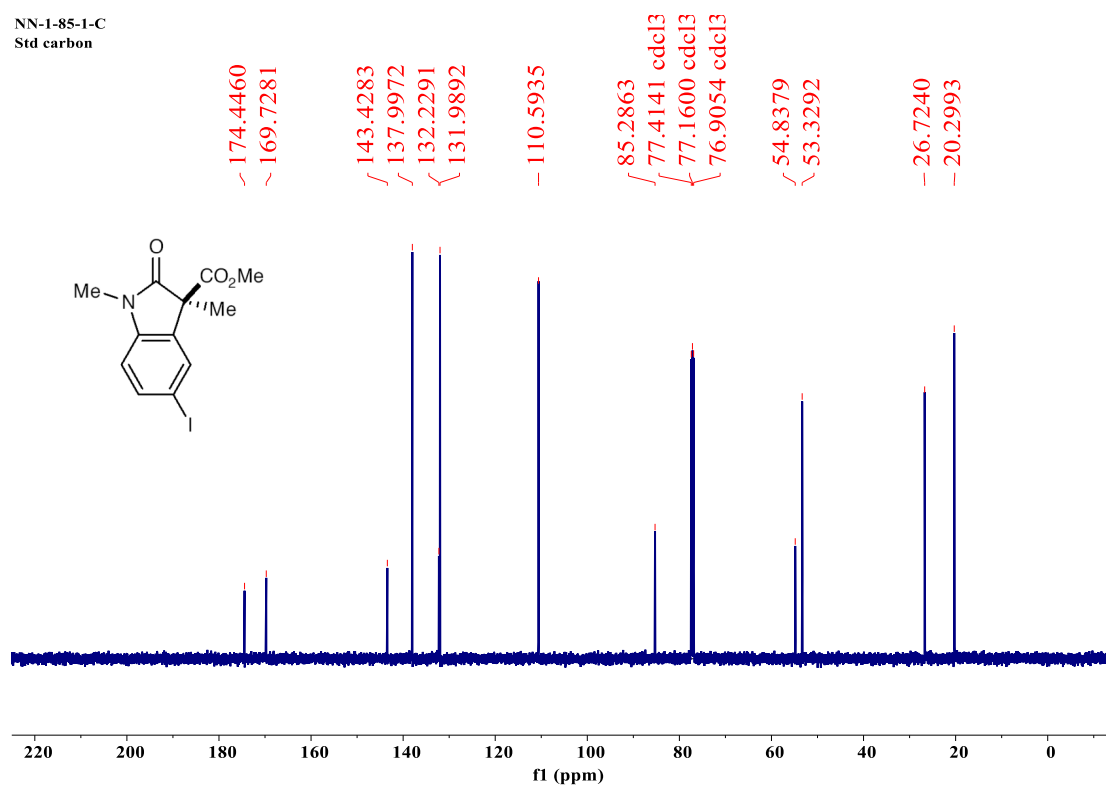
WF-2-70-1-C-re
Std carbon



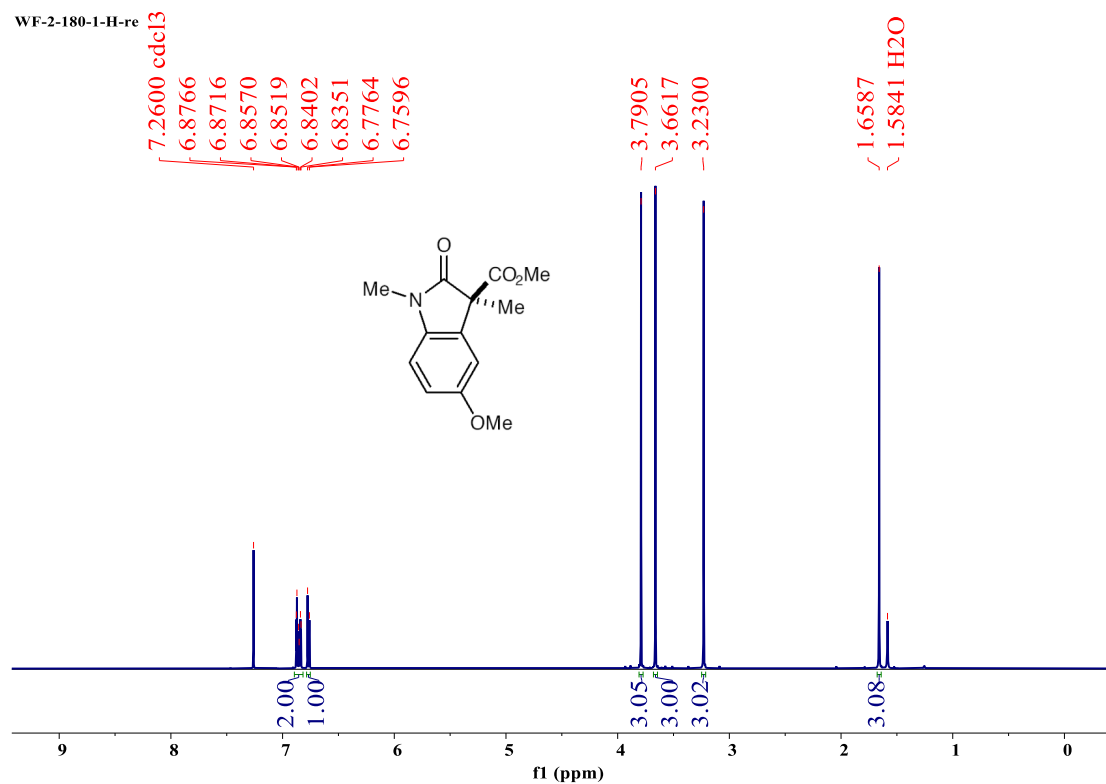
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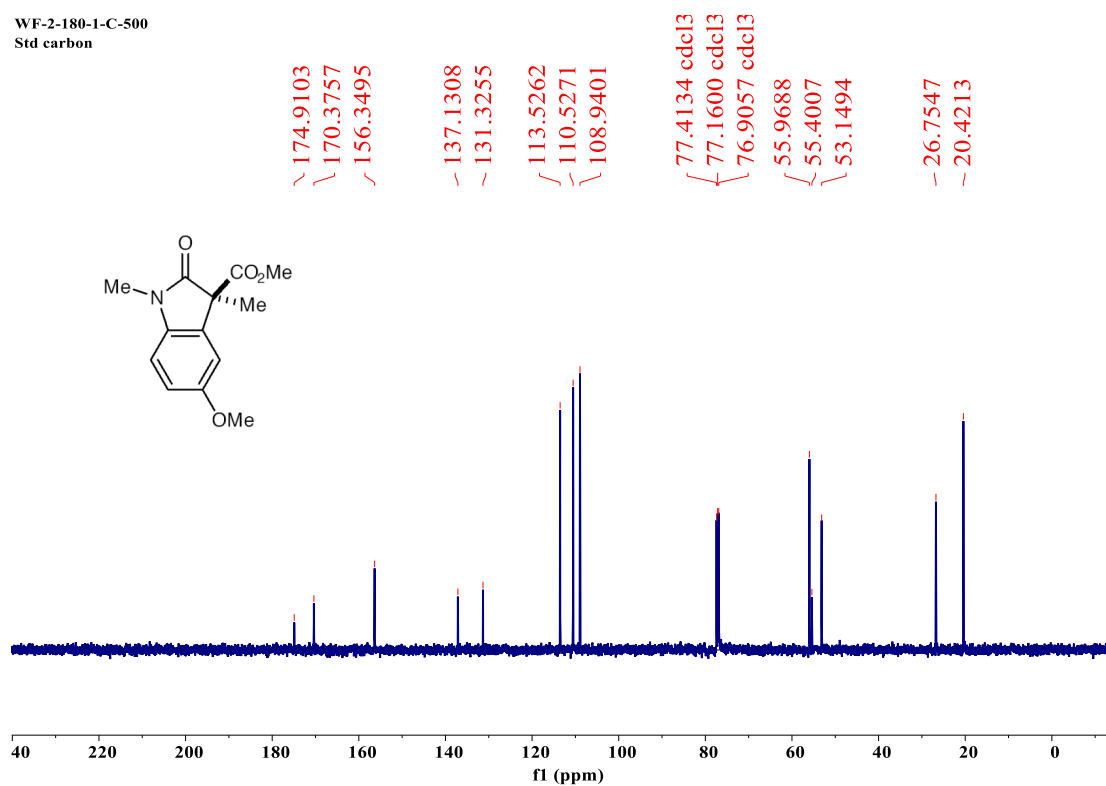
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Std carbon



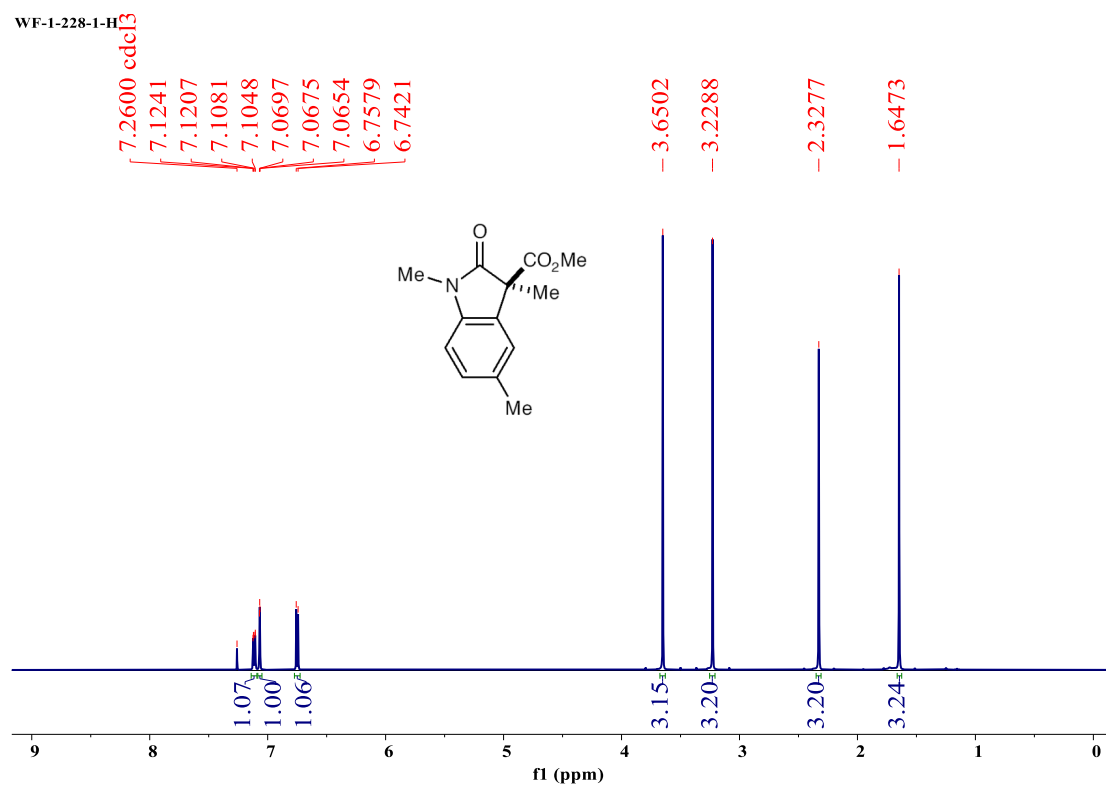
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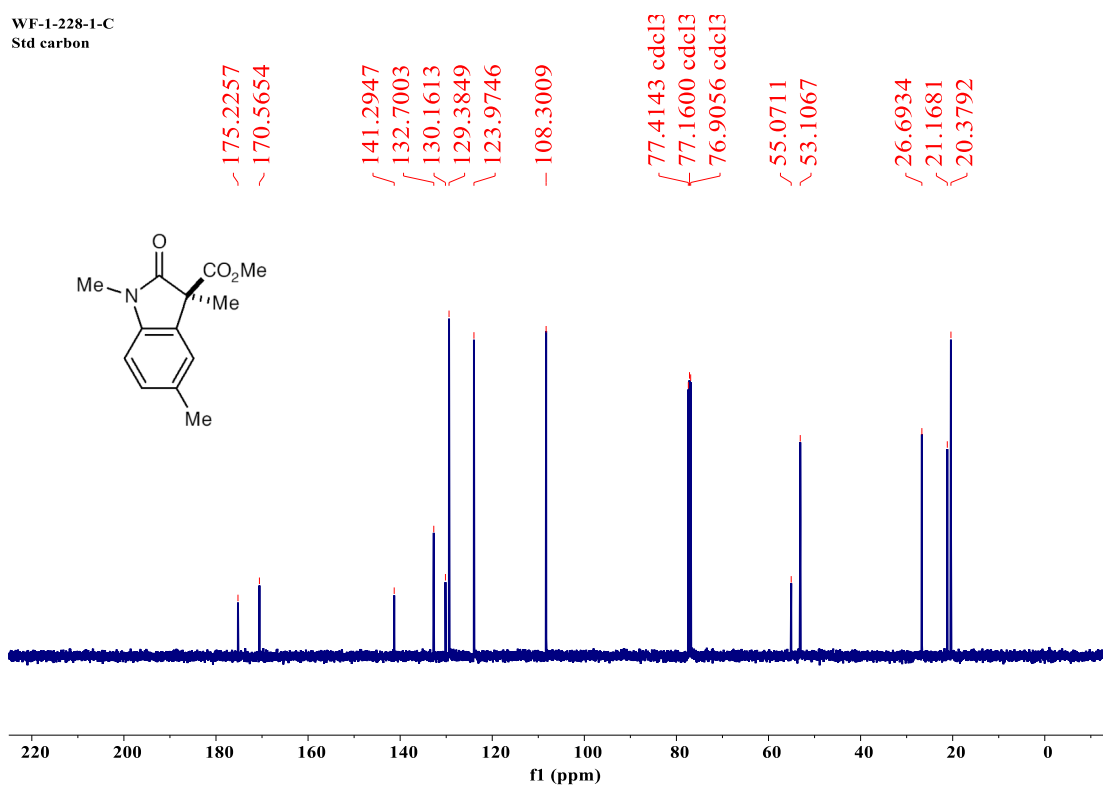
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Std carbon



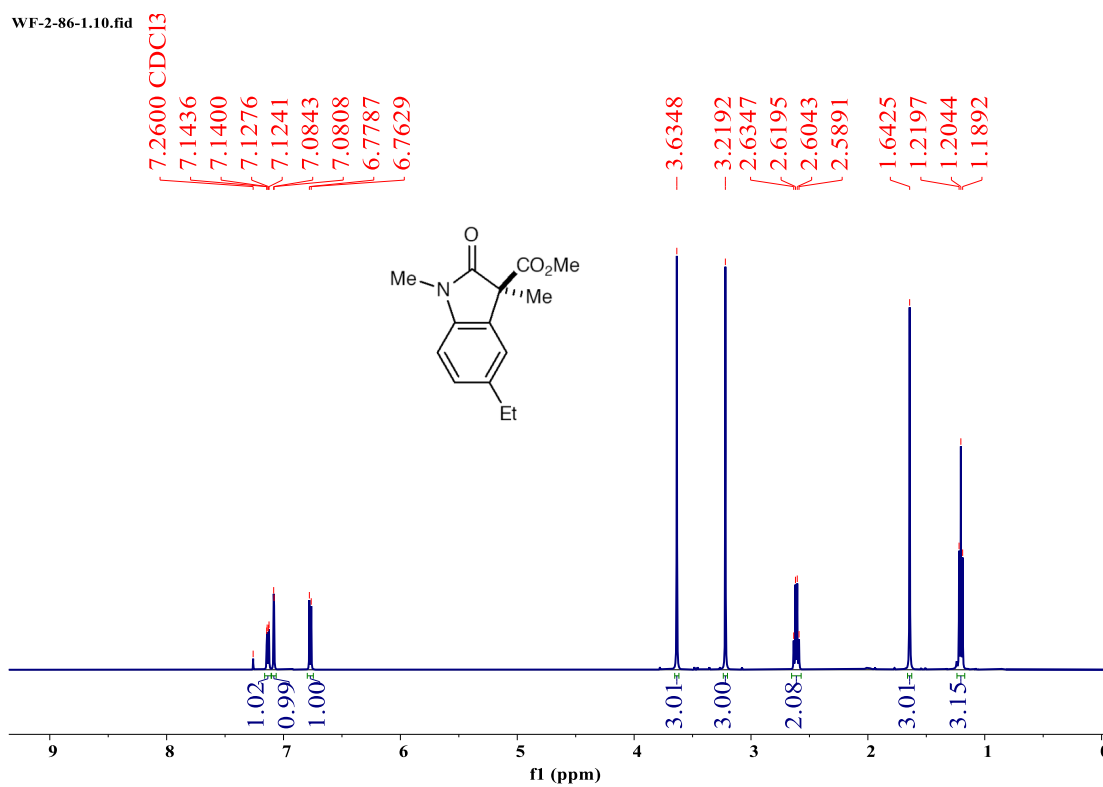
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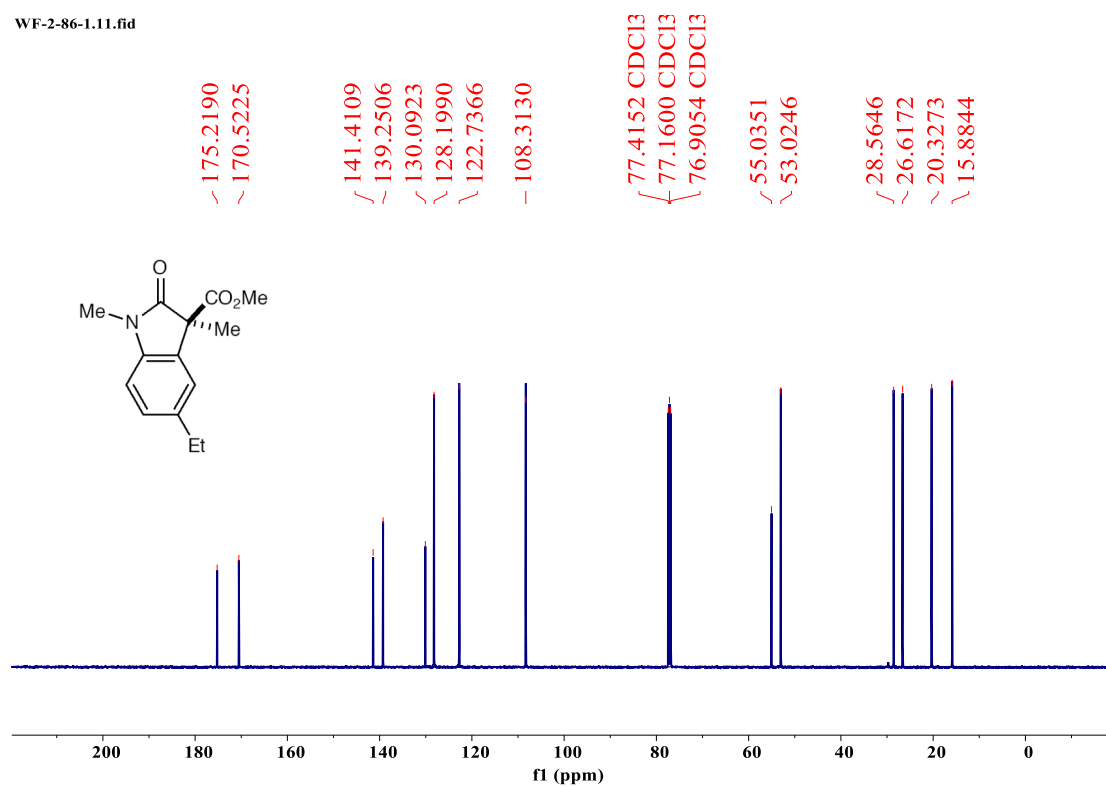
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Std carbon



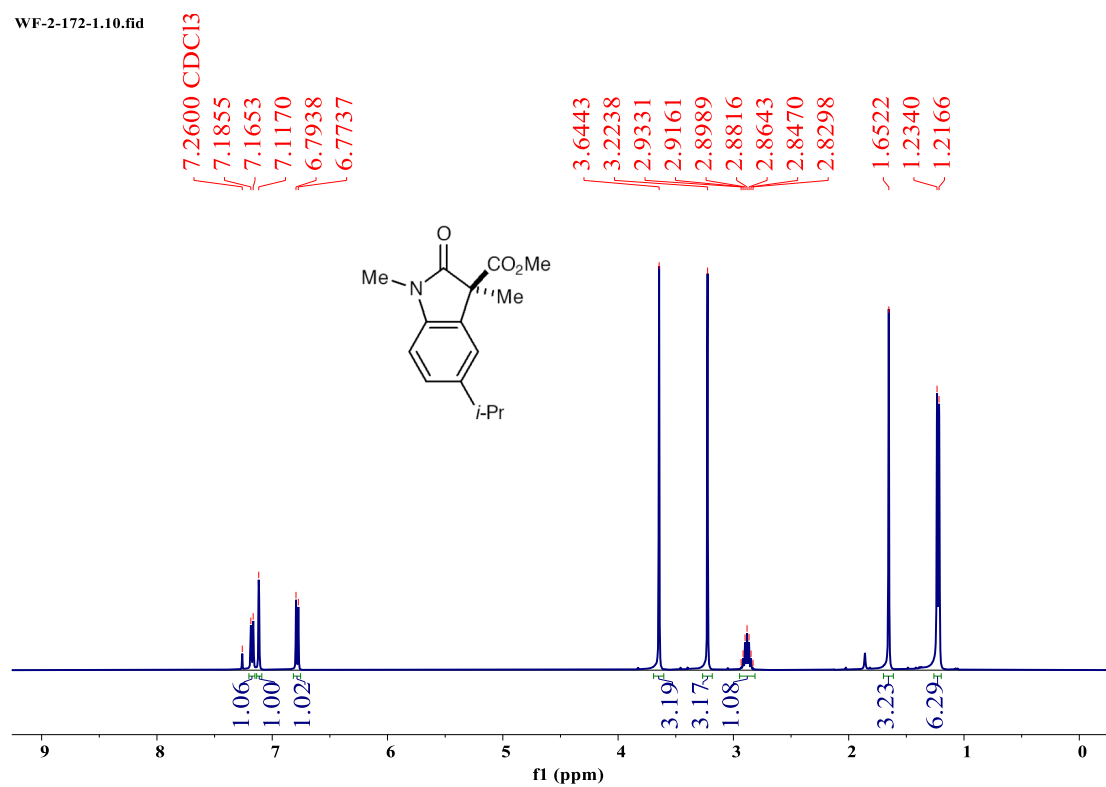
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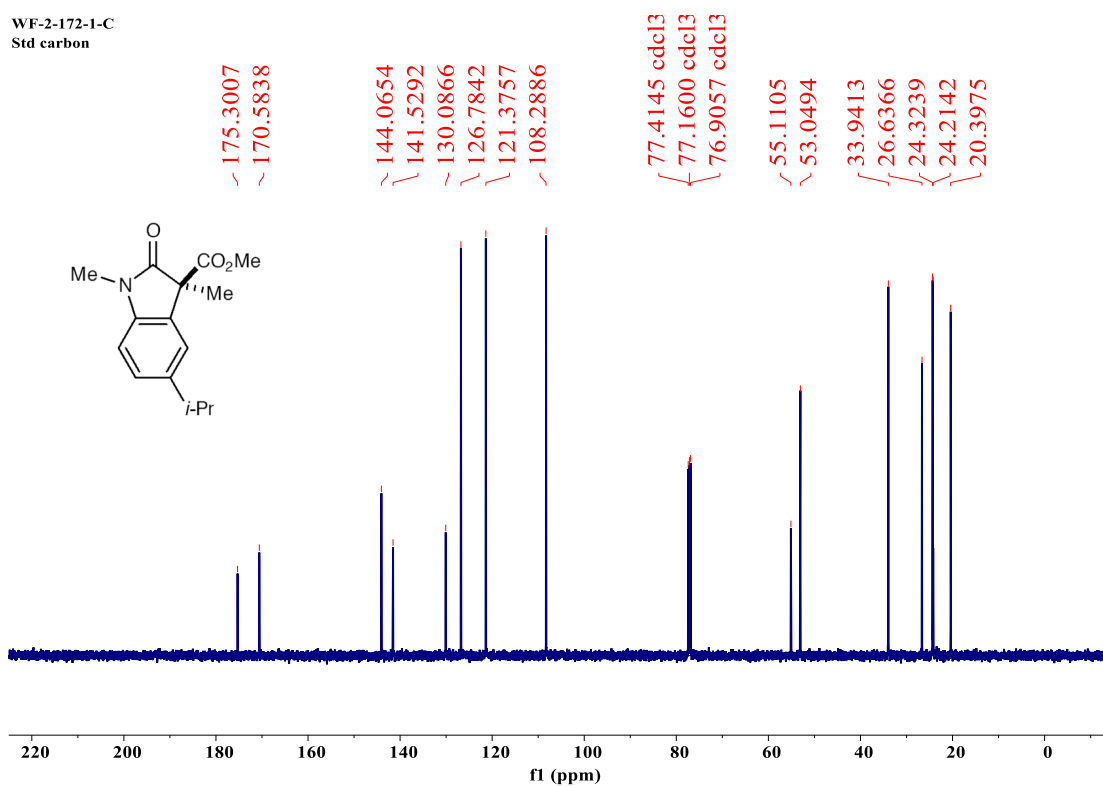
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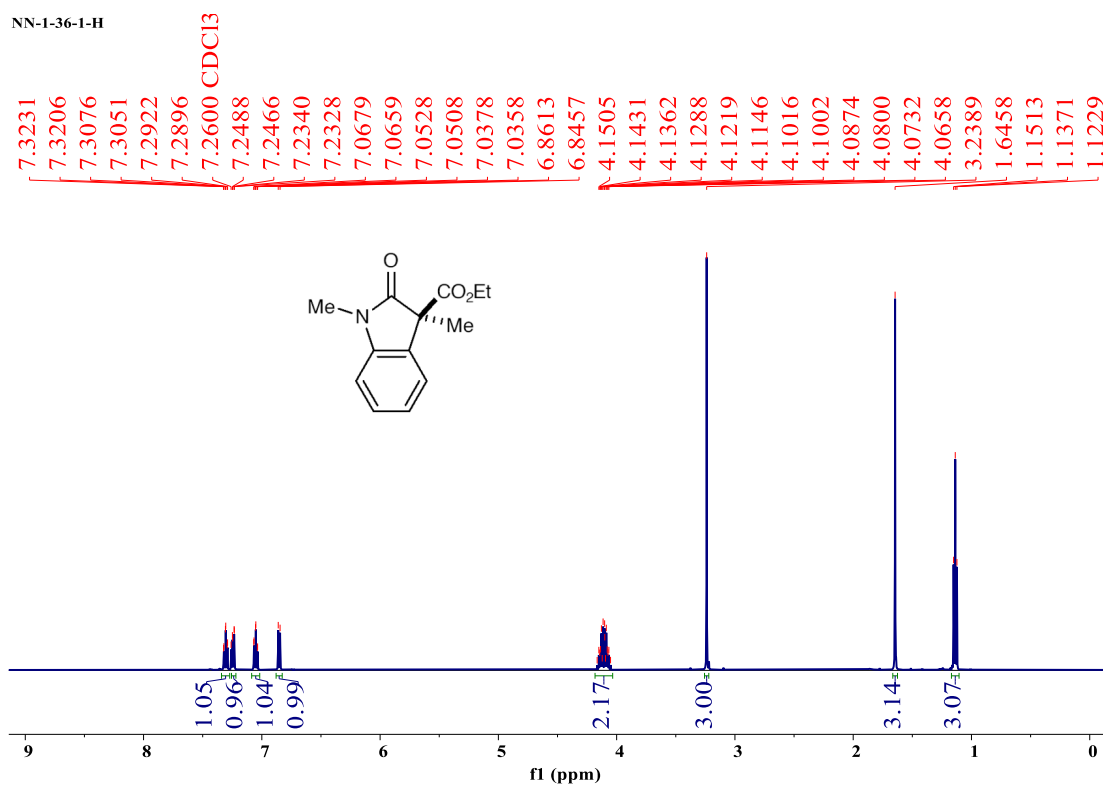
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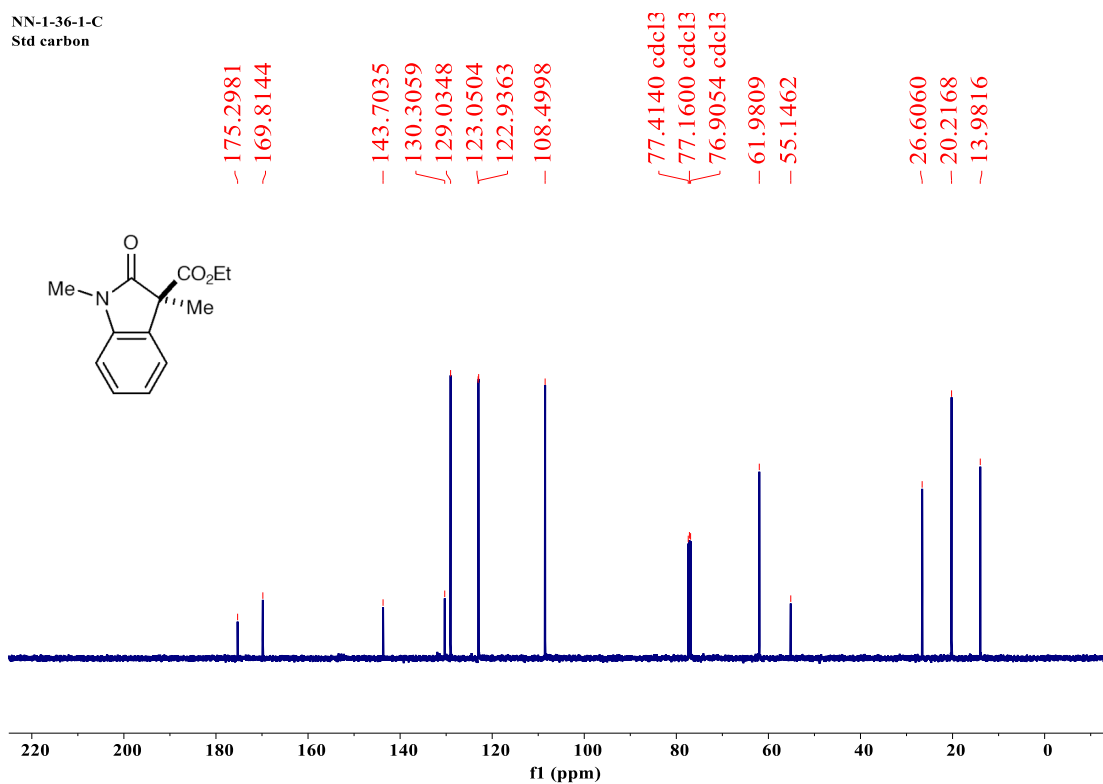
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Std carbon



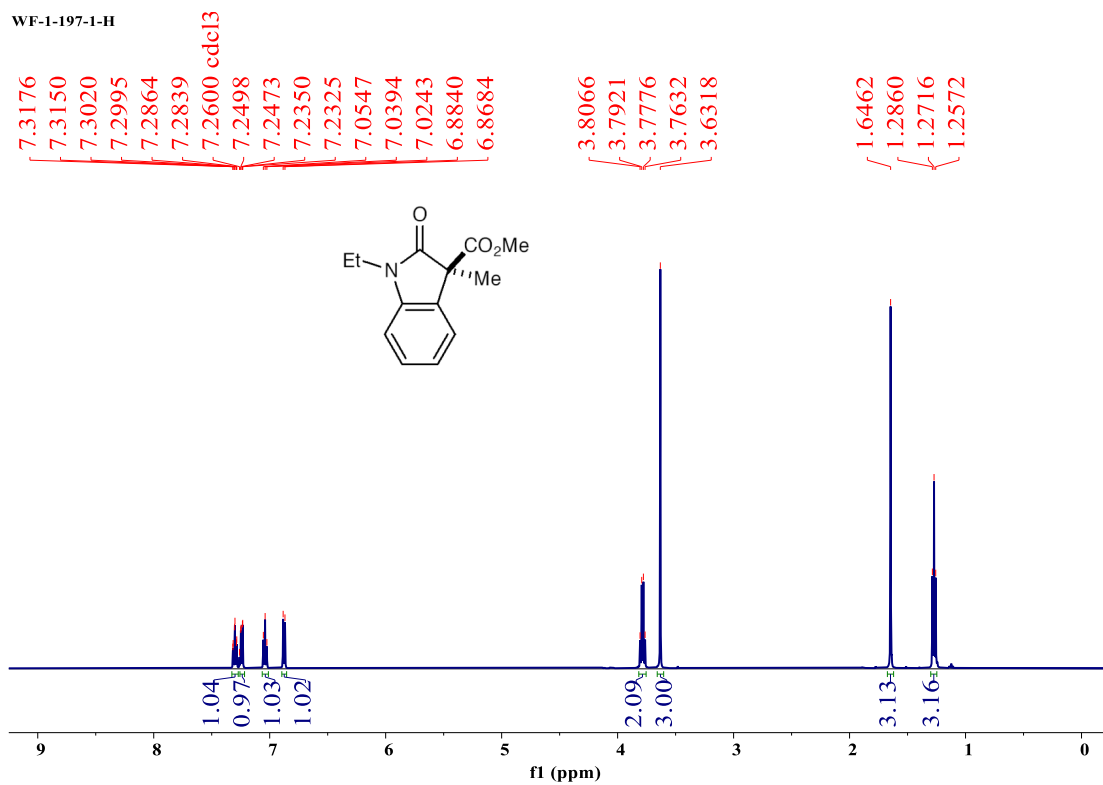
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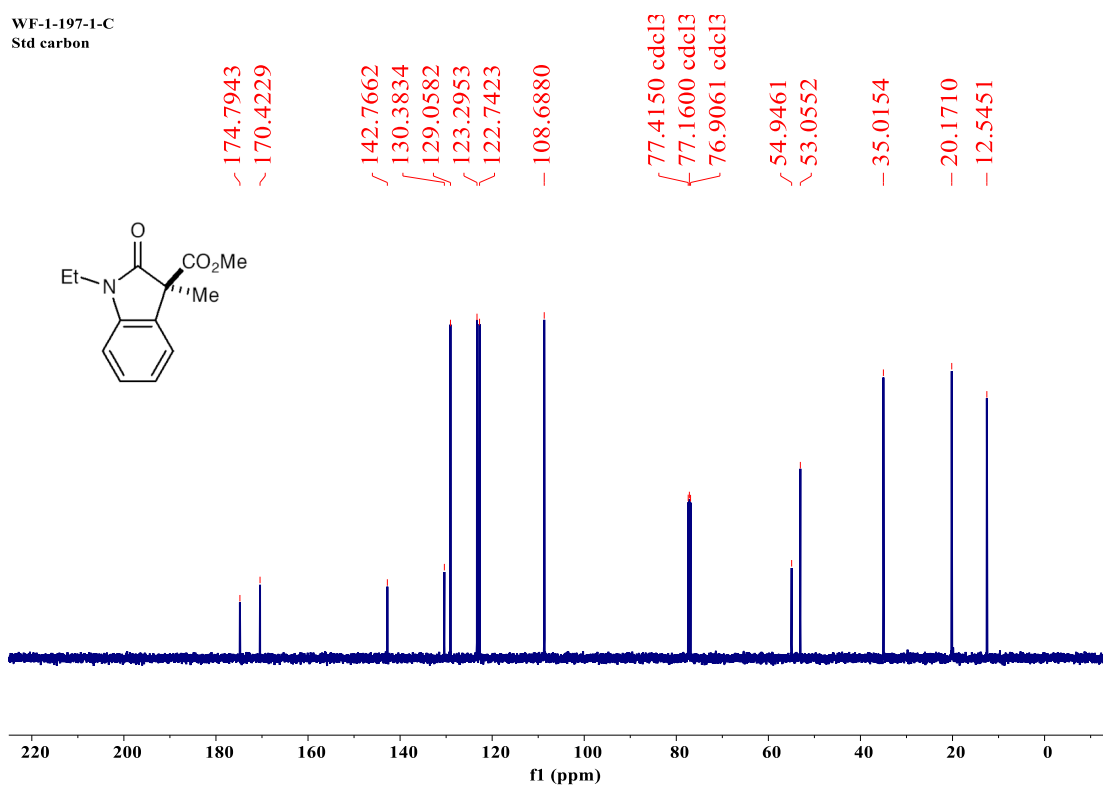
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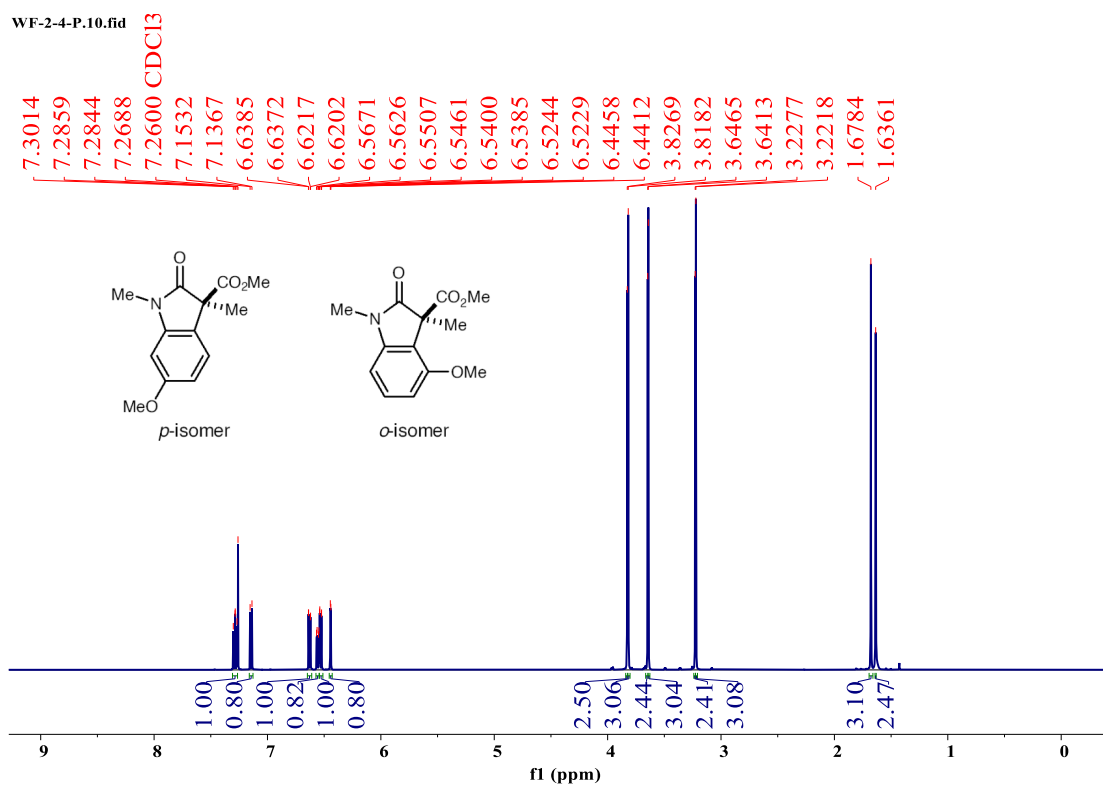
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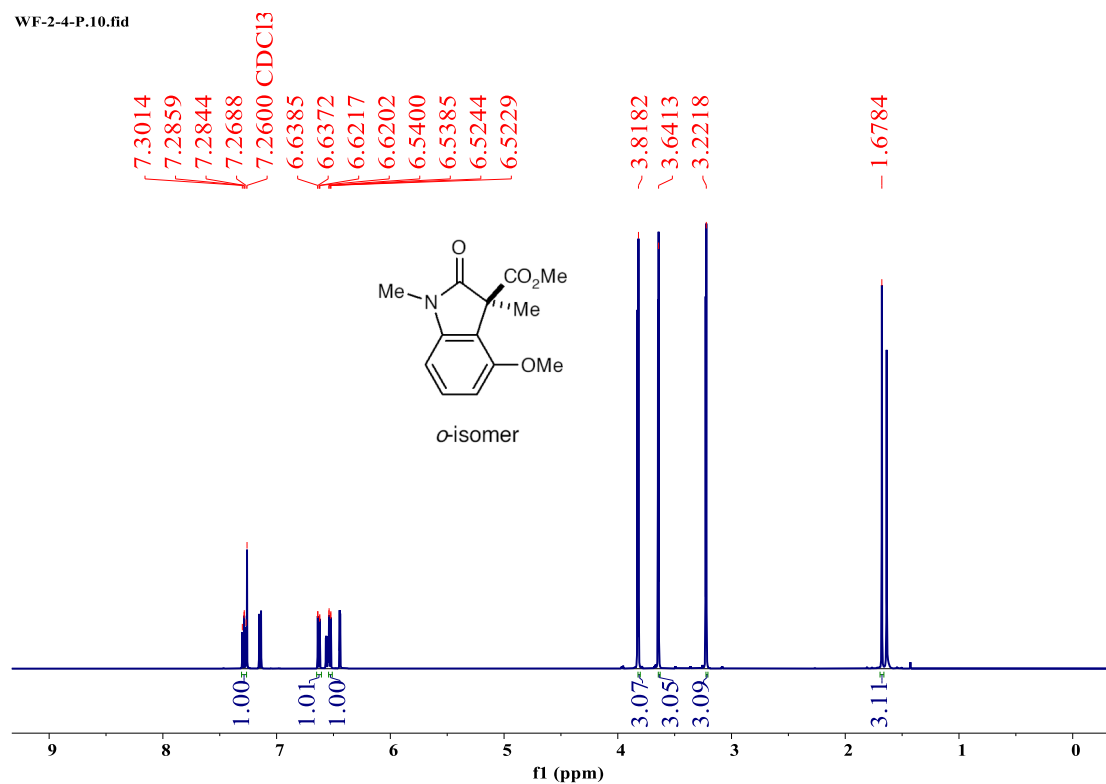
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Std carbon



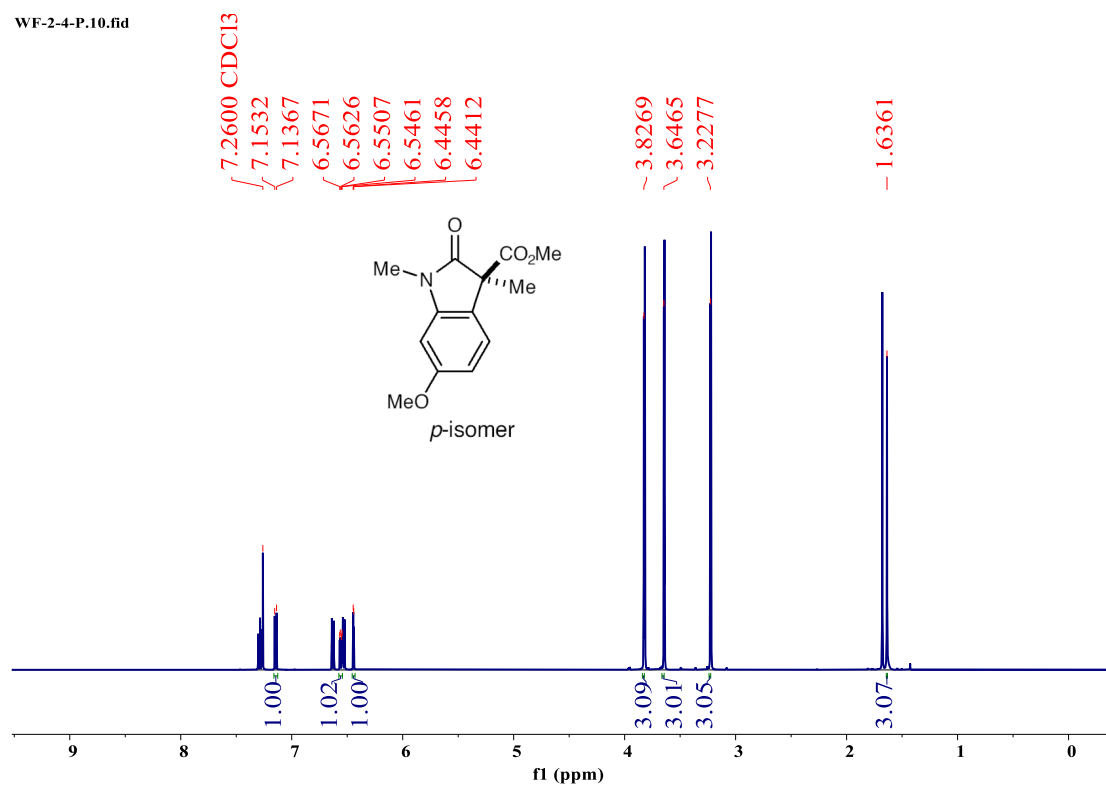
WF-2-4-P-10.fid



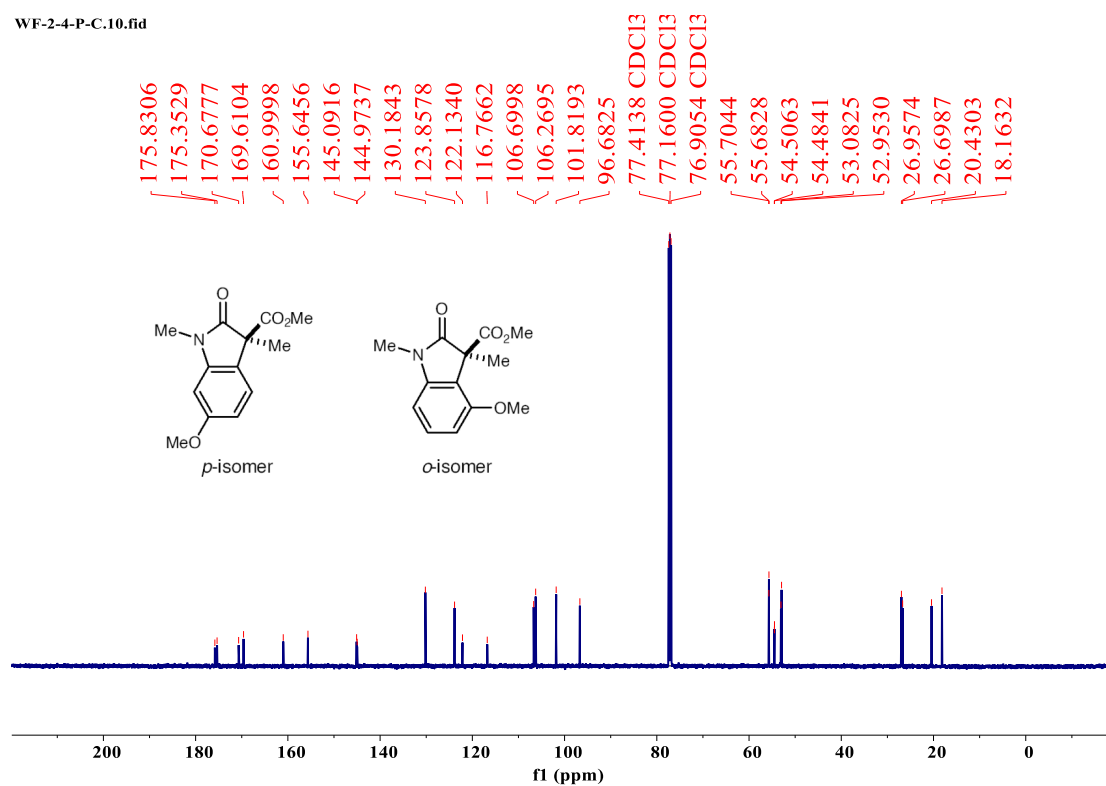
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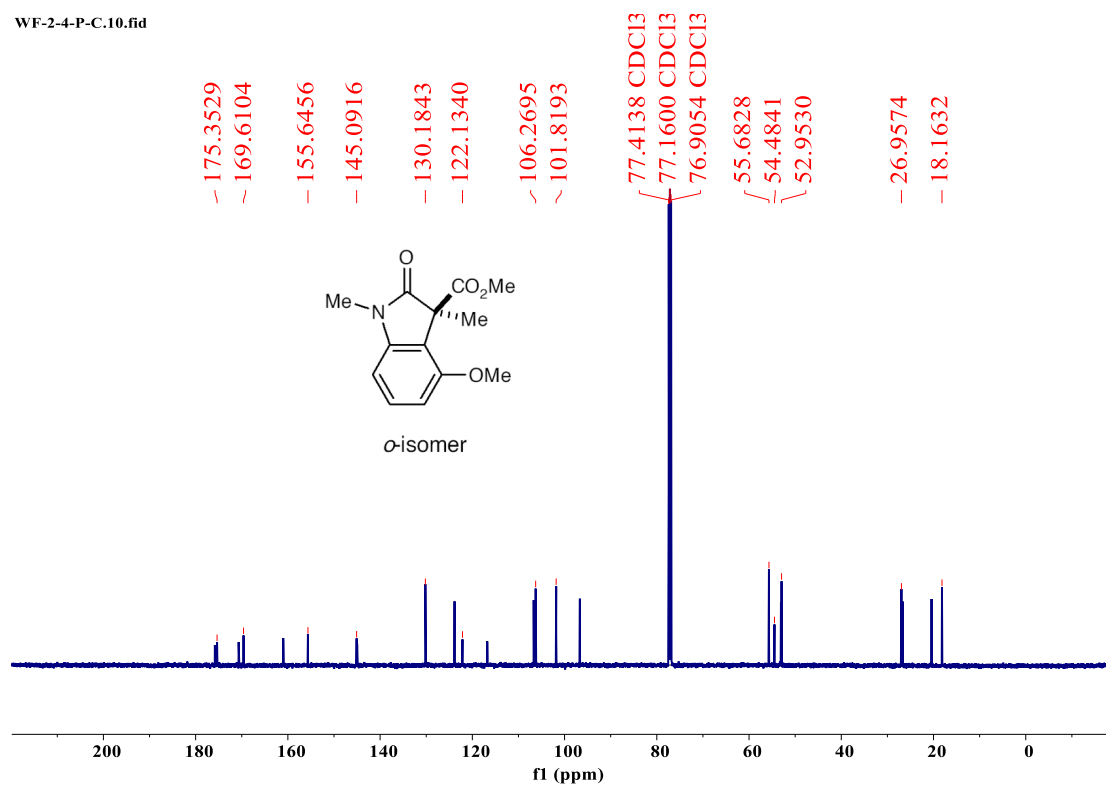
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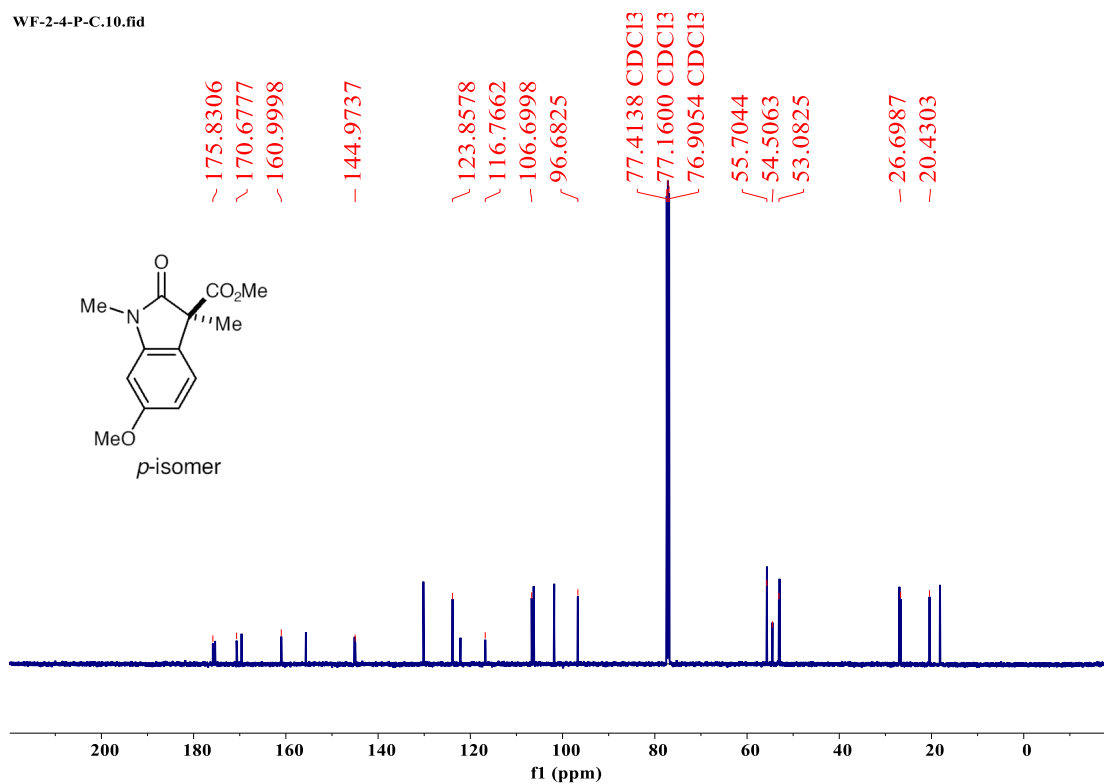
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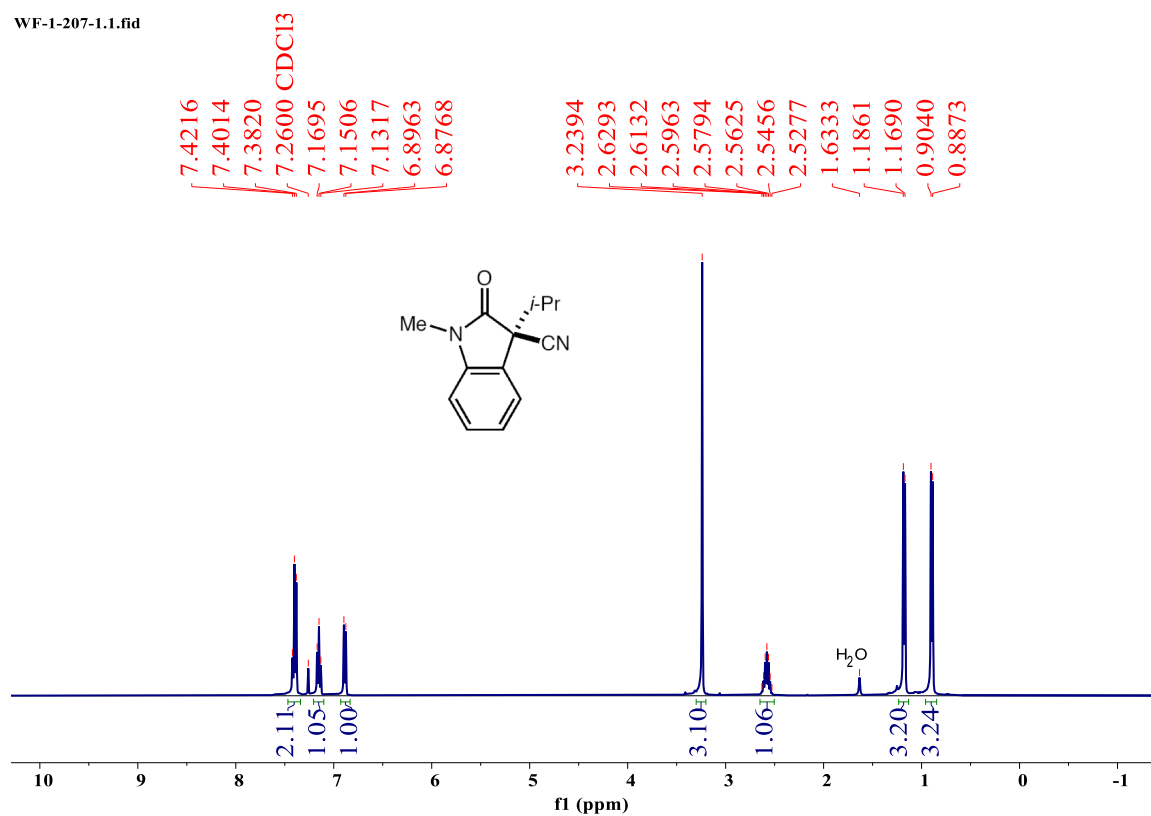
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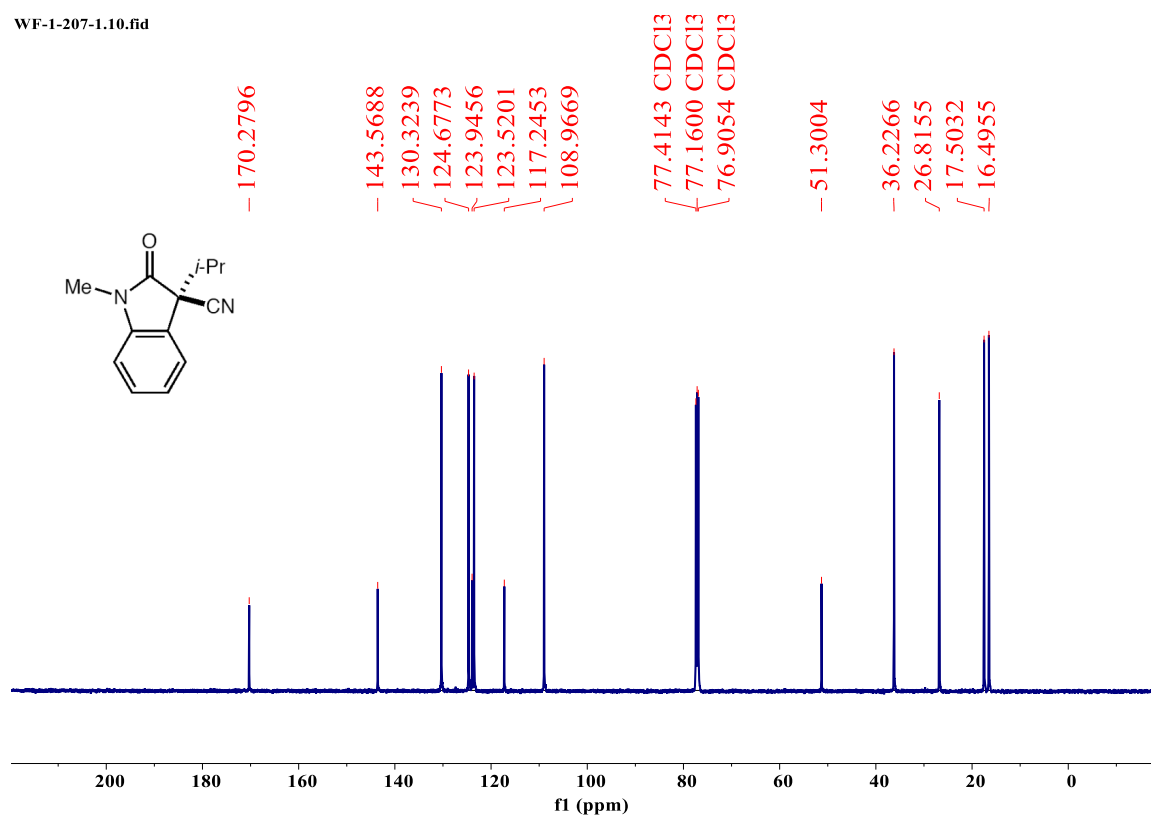
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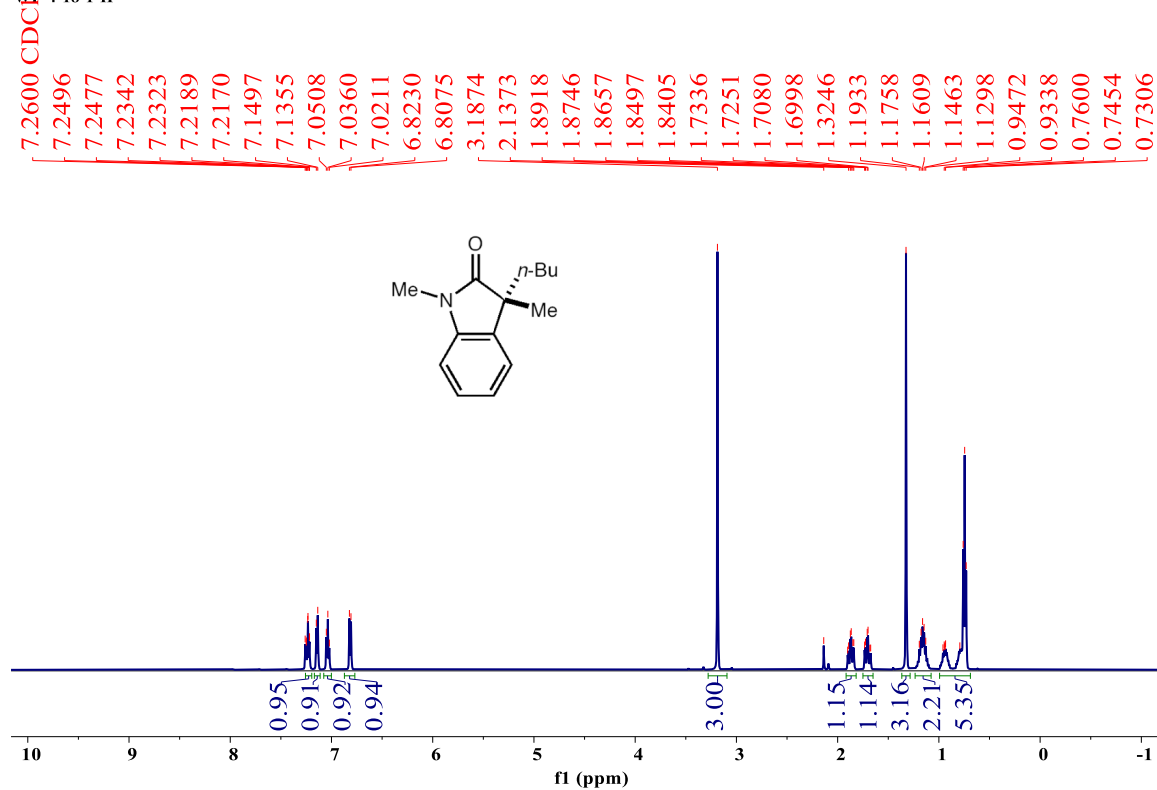
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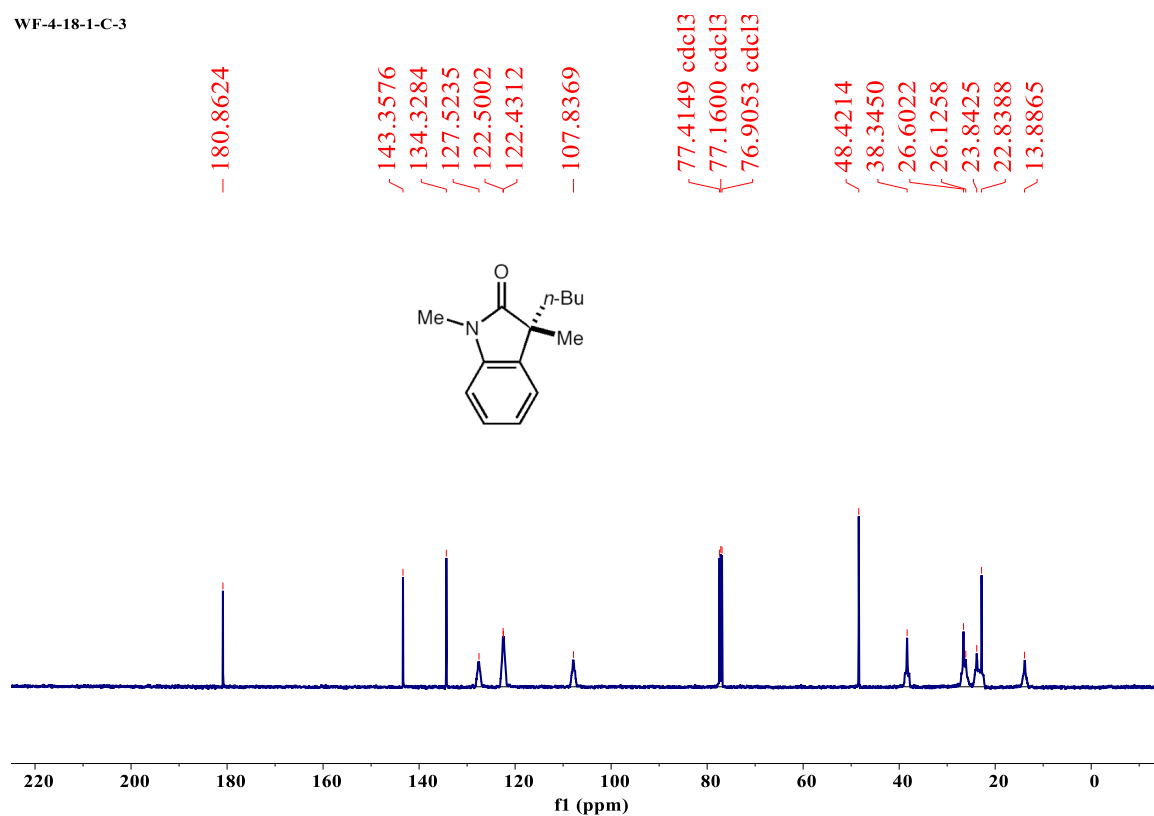
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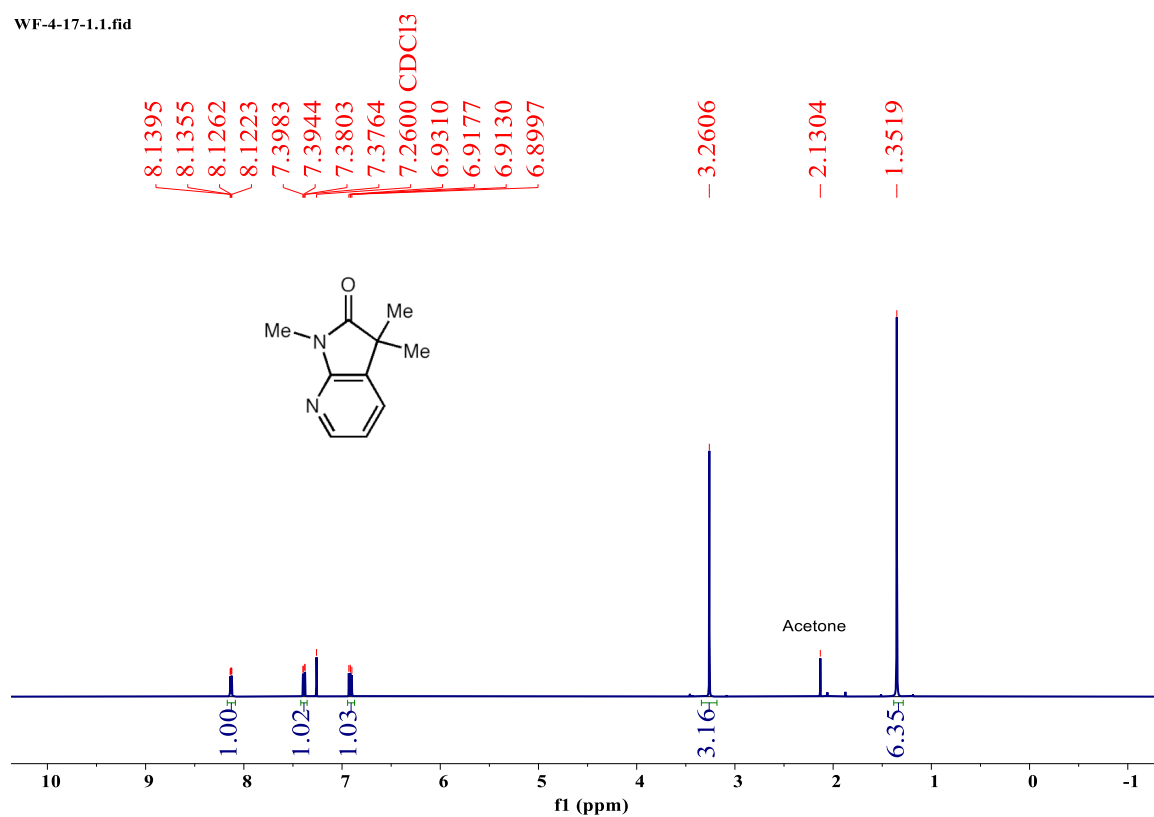
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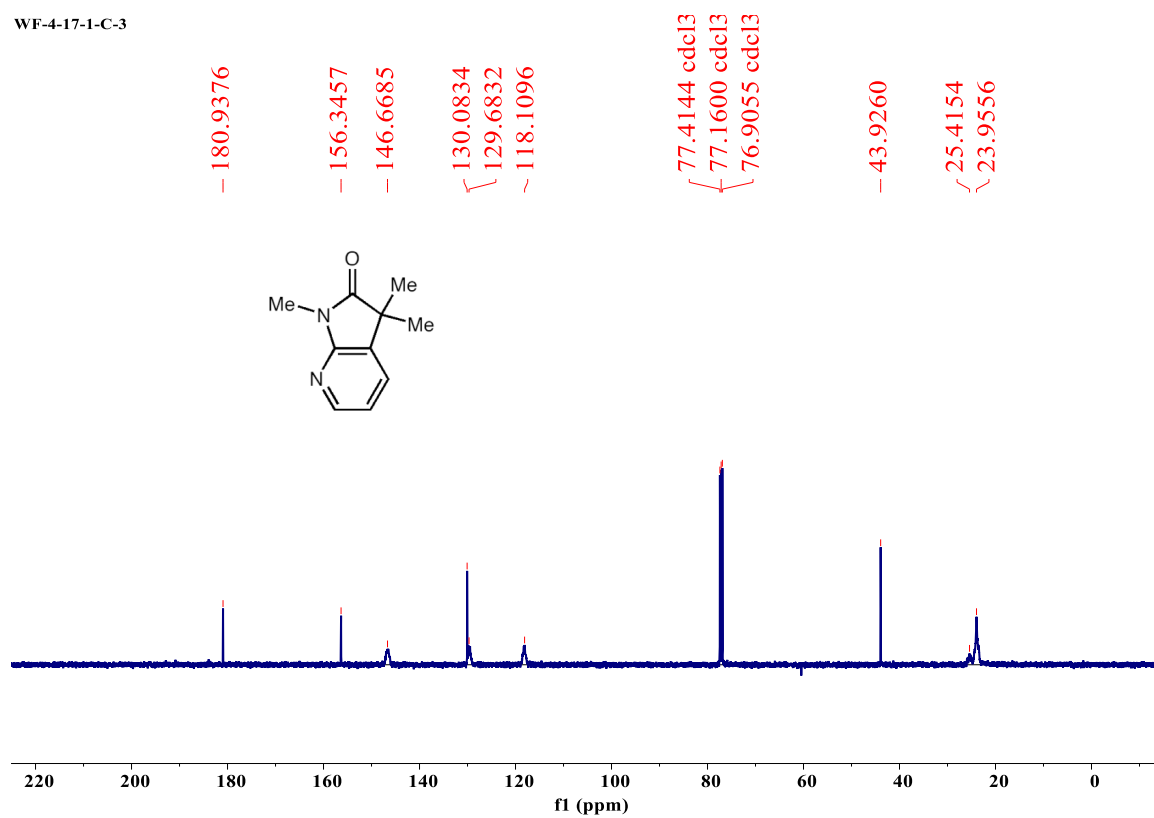
WF-4-18-1-C-3



WF-4-17-1.1.fid



WF-4-17-1-C-3



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