Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information for

Biocatalytic synthesis of chiral cyclopropanes from ethyl diazopyruvate: A platform access to high-value chiral derivatives.

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Supplementary Tables

Table S1. Optimization of reaction conditions for the cyclopropanation of styrene with EDPv **1**.

Entry	Mb (H64V, V68G) (OD_{600})	Styrene (mM)	EDP (mM)	Yield[a] (%)	de (%)
1	20	10	5	43	>99
2	40	10	5	33	>99
3	60	10	5	30	>99
4	10	50	10	39	>99
5	20	50	10	>99	>99
6	20	25	5	85	>99
7	20	50	5	>99	>99
8[b]	20	50	10	61%	>99

Reaction Conditions: 50 mM potassium phosphate (pH 7) buffer (KPi) with 10% ethanol, room temperature under anaerobic conditions. a) yield is determined by GC compared with authentic standards. b) reaction performed on 50 mL scale (scale-up reaction)

Table S2. Optimization of the photochemical rearrangement using ethyl 2-diazo-2-((1S,2S)-2-phenylcyclopropyl) acetate

Entry	Solvent	Time (h)	Yield[a] (%)	Regio-isomer ratio A/B
1	DCM	3h30	46	65/35
2	DCM	4h	48 (50)	65/35
3	MeCN	3h30	46	70/30
4[b,c]	MeCN	3h30	27	66/33
5	$CHCl_3$	3 h 30	52	64:36
6	C_6H_{12}	3h30	30	57/43
7	DMF	3h30	27	64/36
8	PhMe	3h30	51	57/43
9	Et_2O	3h30	58	55/45
10	THF	3 h 30	44	57:43
11[c]	Et_2O	3h30	57	56/44
12[c]	MeCN	3h30	50	68/32
13[c]	MeCN	6h	51	68/32
14[c]	Et_2O	6h	51	58/42

[a] ^1H NMR yield (in bracket isolated yield); [b] Sealed vial under argon ; [c] Sealed vial.

Table S3. Activity of myoglobin variants toward cyclopropanation of styrene with EDPv.

Entry	Variant	Yield %
1	Mb (F43V,H64V, V68G)	>3
2	Mb (H64V, V68G,I28V)	0
3	Mb (H64V,V68G,I111V)	0
4	Mb (L29T,H64V,V68F)	0
5	Mb (L29T,H64V,V68F,I107L)	0

Conditions: 50 mM olefin, 10 mM of EDPv **1**, OD_{600} = 20; 50 mM potassium phosphate (pH 7) buffer (KPi) with 10% ethanol, room temperature under anaerobic conditions. a) yield is determined by GC compared with authentic standards.

Supplementary Figures

Figure S1. Time-course experiment for Mb-catalyzed formation of ethyl 2-oxo-2-((1S,2S)-2-phenylcyclopropyl)acetate **2a**.

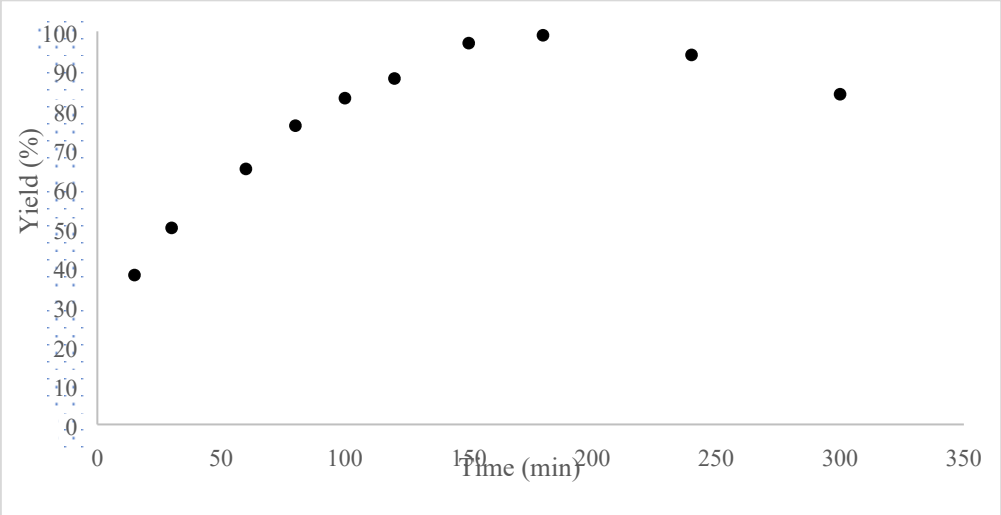


Figure S2. Absorbance spectra of ethyl 2-diazo-2-((1S,2S)-2-phenylcyclopropyl)acetate **3a** in DCM

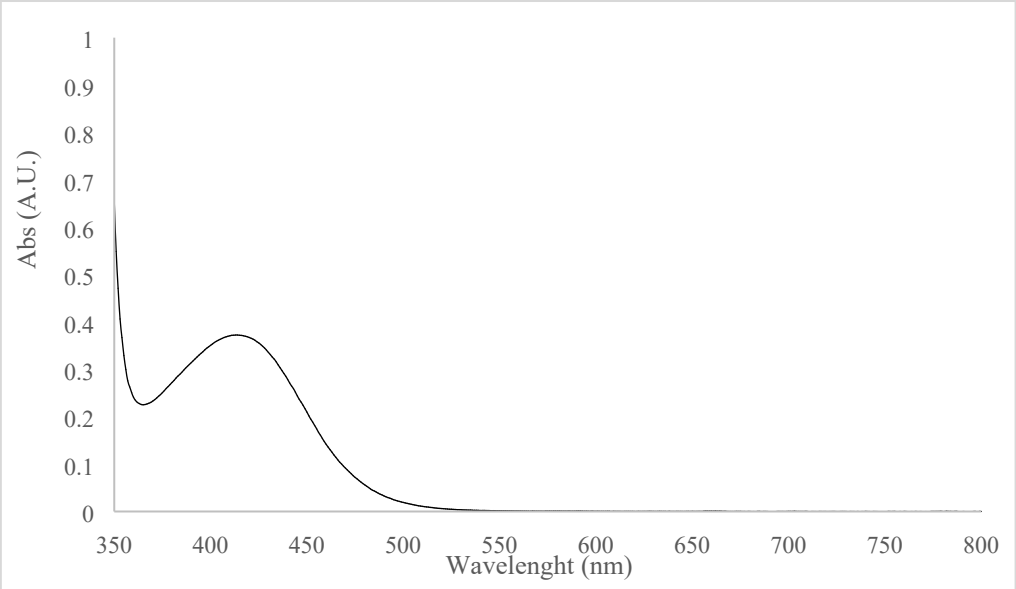
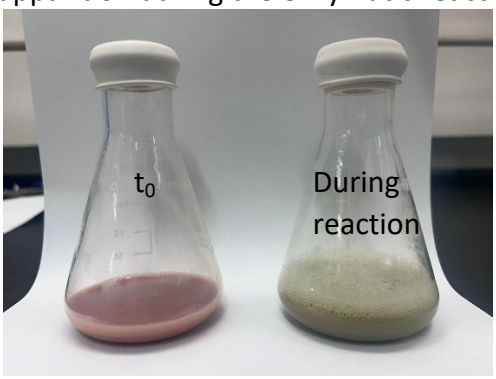


Figure S3. Green colors apparition during the enzymatic reaction on preparative scale.



Experimental Procedures

General information.

All chemicals and reagents were purchased from commercial suppliers (Sigma-Aldrich, Alfa Aeser, J.T. Baker, Acros, Oakwood) and used without any further purification, unless otherwise stated. Tetrahydrofuran and Toluene was distilled from sodium and benzophenone and dichloromethane was distilled from calcium hydride. All reactions were carried out under argon pressure in ovendried glassware with magnetic stirring using standard gas-tight syringes, cannulae, and septa. ^{1}H, ^{19}F and ^{13}C NMR spectra were measured on a Bruker DXC-300 instrument (operating at 300 MHz (^{1}H), 75 MHz (^{13}C) and 282 MHz (^{19}F)) Bruker DPX-400 instrument (operating at 400 MHz (^{1}H), 376 MHz (^{19}F) and 100 MHz (^{13}C)) or a Bruker DPX instrument (operating at 500 MHz (^{1}H) and 125 MHz (^{13}C)).The multiplicity signals were indicated with the common abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad) and the combinations thereof. Column chromatography purification was carried out using AMD Silica Gel 60 Å 230-400 mesh. Thin Layer Chromatography (TLC) was carried out using Merck Millipore TLC silica gel 60 F254 glass plates. Gas chromatography (GC) analyses were carried out using a Shimadzu GC-2010 gas chromatograph equipped with a FID detector, and a CyclosilB column (30 m x 0.25 mm x 0.25µm film). HRMS were recorded on a Waters LCP 1er XR spectrometer.

Protein Expression and Purification.

Wild-type and engineered myoglobin variants were expressed in E. coli C41(DE3) cells as follows. After transformation, cells were grown in TB medium (ampicillin, 100 mg/L) at 37°C (200 rpm) until OD600 reached 0.8. Cells were then induced with 0.25 mM isopropyl-β-D-1-thiogalactopyranoside (IPTG) and 0.3 mM γ-aminolevulinic acid (ALA). After induction, cultures were shaken at 180 rpm and 27 °C and harvested after 20 h by centrifugation at 4,000 rpm at 4°C. The cells were resuspended in 20 mL of Ni-NTA Lysis Buffer (50 mM KPi, 250 mM NaCl, 10 mM histidine, pH 8.0). Resuspended cells were frozen and stored at -80°C until purification. Cell suspensions were thawed at room temperature, lysed by sonication, and clarified by centrifugation (14,000 rpm, 50 min, 4 °C). The clarified lysate was transferred to a Ni-NTA column equilibrated with Ni-NTA Lysis Buffer. The resin was washed with 50 mL of Ni-NTA Lysis Buffer and then 50 mL of Ni-NTA Wash Buffer (50 mM KPi, 250 mM NaCl, 20 mM histidine, pH 8.0). Proteins were eluted with Ni-NTA Elution Buffer (50 mM KPi, 250 mM NaCl, 250 mM histidine, pH 7.0). After elution from the Ni-NTA column, the protein was buffer exchanged against 50 mM KPi buffer (pH 7.0) using 10 kDa Centricon filters. The concentration of the Mb variants (ferric form) was determined using ε_{410}=156 $mM^{-1}cm^{-1}$ as the extinction coefficients.

General procedure for enzymatic cyclopropanation reactions.

Enzymatic cyclopropanation reactions were carried out at a 400 µL-scale using Mb variant, alkenes and ethyl 3-diazo-2-oxopropanoate. Reactions were initiated by addition of buffered solution, followed by the addition of Mb solutions, then alkene (from a 1 M stock solution in ethanol), finishing by the addition of ethyl 3-diazo-2-oxopropanoate (from a 0.2 M stock solution in ethanol), and the reaction mixture was stirred for 3 hours at room temperature, into an anaerobic chamber. Reactions were quenched using a solution of 1,3-benzodioxole in DCM (40 µL, solution at 100 mM) as internal standard then 400 µL of DCM was added. Mixtures were transferred in an Eppendorf tube, mixed and centrifuged. Organic phases were removed for analysis. Analytical yield was determined by calibration curve using a sample of the pure corresponding cyclopropane. The TON for the whole-cell reactions were calculated based on Mb concentration in the reaction mixture as measured via UV-vis spectroscopy (ε_{410}= $mM^{-1}cm^{-1}$) after cell lysis.

α-substituted olefins with a fluorinated group (-CFH_2, -CF_2H, -CF_3) were prepared according to literature procedure.[1]

Product analysis.

The reactions were analyzed by adding 40 µL of internal standard (benzodioxole, 50 mM in methanol) to the reaction mixture, followed by extraction with 400 µL of dichloromethane (DCM) and analyzed by gas chromatography using a Shimadzu GC-2010 gas chromatograph equipped with a FID detector, and a Cyclosil-B column (30 m x 0.25 mm x 0.25 µm film) method: 1 µL injection, injector temp.: 140°C, detector temp: 300°C. Gradient: column temperature set at 80°C for 2 minutes, then to 245° at 65°C/min for 10 minutes. Total time was 14.54 min. Calibration curves of the different cyclopropane products were constructed using synthetically produced authentic standards. Calibration curves for the different cyclopropane products were constructed using pure racemic standards. All measurements were performed at least in duplicate. Stereoisomer resolution was performed by High pressure liquid chromatography (HPLC) using an AGILENT 1200 SERIES G312B With a Diode array and multiple wavelength detector instrument equipped with a column oven at 25 °C and Dionex Ultimate 3000 equipped with an RS pump, an RS autosampler, and an RS diode array detector. A Daicel Chiralpak® IB, IC, ID, IG and Phenomenex Lux® cellulose-2 column (0.46 cm ID × 25 cm L ; 5 µm) was used for separation of enantiomers. Samples were eluted at normal phase using isocratic or

[1] Carminati, D. M.; Decaens, J.; Couve-Bonnaire, S.; Jubault, P.; Fasan, R. *Angew. Chem. Int. Ed.* **2021**, *60*, 7072–7076.

gradient solvent system of isopropanol (IPA) as modifier in hexane and detected at λ = 210 ; 220 or 254 nm depending on the compound.

General procedure A for preparative-scale enzymatic reaction.

In an anaerobic chamber, in 50 round bottom flask was added successively, under stirring, KPI buffer 50 mM pH 7.0 (15.8 mL), a solution of Mb H64V V68G variant in KPI buffer 50 mM pH 7.0 (180 OD_{600}, 2.22 mL), the corresponding alkene in ethanol (solution of 1 M, 1 mL, slowly dropwise to the mixture until each drop are completely dissolved in the aqueous phases) and then a solution of the diazo compound in ethanol (solution of 0.2 M, 1 mL, slowly dropwise to the mixture until each drop are completely dissolved in the aqueous phases). The reaction is stirred for 3h at room temperature. After 3 hours, the reaction was quenched with DCM (15 mL). The two phases were mixed then centrifuged and the organic phase is removed. The aqueous phase is extracted with DCM (2 x 15 mL) with the same procedure. Organic phase dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude is purified by silica gel chromatography (n-Hexane:EtOAc) to afford corresponding cyclopropane.

Kinetic experiments

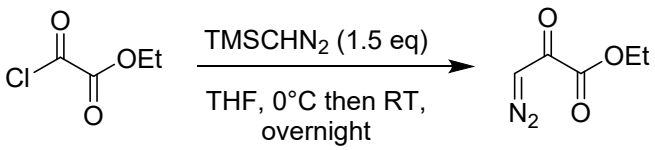
For the kinetic measurement with Mb(H64V, V68G), reactions were carried out on a 400 µL-scale in oxygen-free KPi buffer 50 mM (pH 7.0) using 20 OD Mb variant, 50 mM styrene (from a 1 M stock solution in ethanol) and 10 mM ethyl 3-diazo-2-oxopropanoate **1** (from a 0.2 M stock solution in ethanol). Reactions was stirred during a predetermined time and quenched using a solution of 1,3-benzodioxole in DCM (40 µL, solution at 100 mM) as internal standard then 400 µL of DCM was added. Mixtures were transferred in an Eppendorf tube, mixed and centrifuged. Organic phases were removed to analysis. Analytical yield was determined by calibration curve using isolated Ethyl 2-oxo-2-((1S,2S)-2-phenylcyclopropyl)acetate **2a** compound. Each reaction was triplicate.

General procedure for the preparation of racemic cyclopropanes.

To a stirred solution of alkene (2.5 eq.) and $Rh_2(OAc)_4$ (1 mol%, 0.6 mg) in DCM (300 µL) under argon at 0 °C was added dropwise (syringe-pump 5h) a solution of EDP (0.1 mmol, 14.2 mg) in DCM (500 µL). The solution was stirred one additional hour and then the solvent was evaporated. The crude mixture was purified by silica gel chromatography (n-Hexane: EtOAc) to afford the expected cyclopropane as a mixture of diastereoisomers.

Synthetic Procedures and Compound Characterization Data

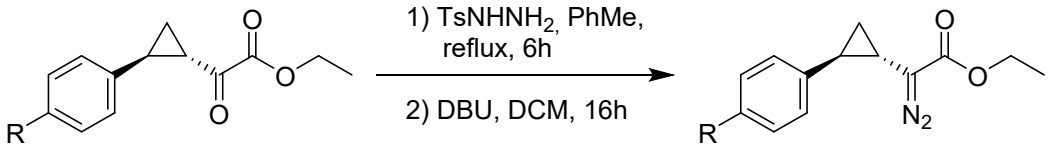
Synthesis of **ethyl 3-diazo-2-oxopropanoate (1):**



To a stirred solution of ethyl oxalyl chloride in THF (0.33 M) at 0°C was added, with a syringe pump over 30 min, a solution of $TMSCHN_2$ (solution in hexane, 2M, 1.5 eq). After the end of the addition the ice bath was let warm up and the reaction was stirred overnight at room temperature. The solvent is removed *in vacuo* and the crude mixture was purified under silica gel chromatography : n-

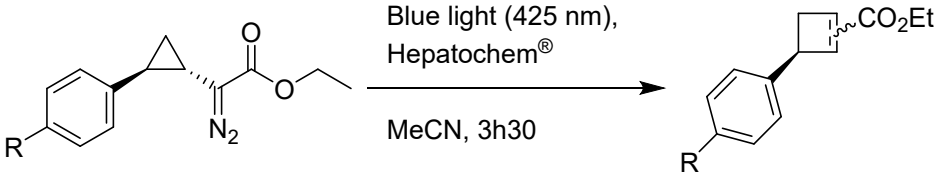
Hexane:EtOAc 80:20. The diazo compound was obtained as a pale yellow solid (65%) according to the literature.[2]

General procedure **B** for the synthesis of **α-cyclopropyldiazo derivatives (3):**



Tosyl hydrazine (1.4 eq.) was added to a solution of the corresponding α-cyclopropylpyruvate compound **2** in toluene (0.07 M) under argon. The mixture was heated in reflux during 5h, then concentrated *in vacuo* and the resulting crude mixture was directly used for the next step. The round bottom flask was protected with aluminum foil and DCM (0.07 M) was added following by DBU (4 eq.) under argon. The mixture is stirred overnight at room temperature. Brine is added (DCM:Brine 1:1 v:v). The two phases were separated and the aqueous phase was extracted with 3x DCM (DCM:Brine 0.5:1 v:v). Organic phases were combined and filtered through a pad of $MgSO_4$ (top) and silica (bottom). The solvent was evaporated and the crude mixture was purified by silica gel chromatography (EP:EtOAC 97:03). Each diazo compound, synthesized using this procedure, was obtained as a yellow oil and stored protected from light (aluminum foil) at -20 °C.

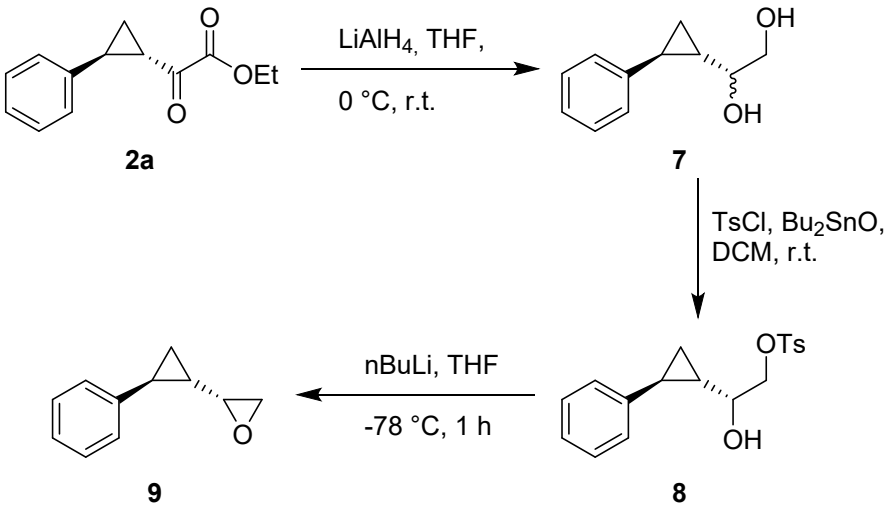
General procedure **C** for the synthesis of **cyclobutenoates (4):**



In a microwave vial was added the corresponding diazo compound then MeCN (0.1 M). The vial was sealed under air and stirred until total conversion of the diazo compound (~3 h 30). The solvent was directly evaporated and the crude mixture was purified by silica gel chromatography (Pentane:Et_2O 97:03). Regioisomeric ration were determined on ^1H NMR crude.

General procedure for the synthesis of **2-((1S,2S)-2-phenylcyclopropyl)oxirane (9)**:

[2] Qi, H.; Li, X.; Xu, J. *Org. Biomol. Chem.* **2011**, *9*, 2702–2714.



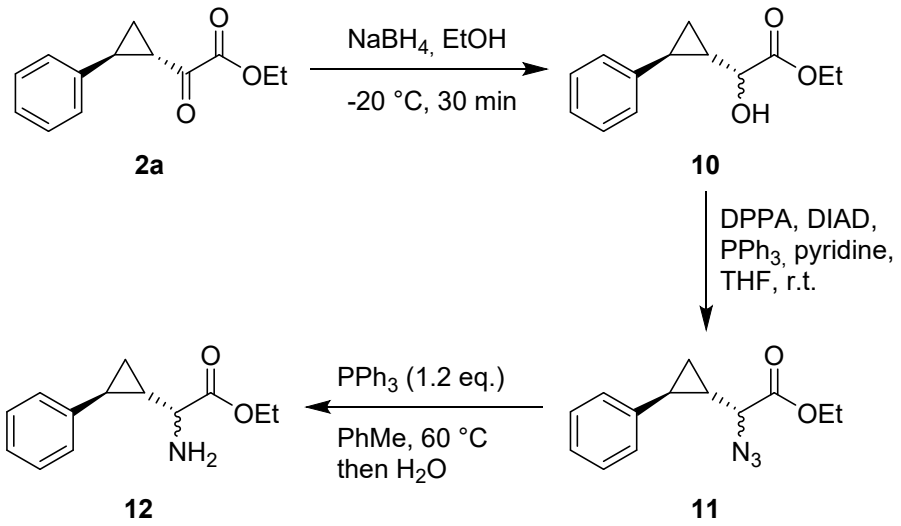
2a **7** **8** **9**

To a solution of cyclopropylpyruvate **2a** (0.15 mmol, 32.28mg) in THF (750 µL) at 0 °C was added dropwise LAH (0.525 mmol, 1M solution in THF, 525 µL). The reaction mixture was stirred during 3h at room temperature. Then, the reaction mixture was quenched with 900 µL EtOH:H_2O:EtOAc (1:1:1 v:v:v). EtOAC was added (4.5 mL) and the mixture was filtered through a pad of silica. The crude reaction mixture was concentrated *in vacuo* and purified by silica gel chromatography (EP: EtOAc 70:30 => 60:40 => 50:50). The expected diol compound **7** was obtained as a colorless oil (97 %, 25.8 mg).

The resulting diol **7** (0.132 mmol, 23.6 mg) was dissolved in DCM (1 mL) and Bu_2SnO (0.264 mmol, 65.2 mg) was added. The reaction mixture was stirred during 1 h at room temperature. Then Et_3N (0.132 mmol, 17.8 µL) and TsCl (0.132 mmol, 25.2 mg) were added and the reaction was stirred during 18 h. The reaction mixture was quenched with H_2O (5 mL) and DCM (5 mL). The two phases were separated and the organic phase was washed with $NaCl_{sat}$, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by preparative silica chromatography (DCM:EtO_2 95:05 (eluting two times)). Two separable diastereoisomers **8a** et **8b** were obtained as white solids (yield 66 %, ratio 65:35, 28.2 mg).

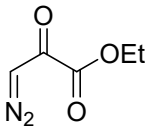
A solution of n-BuLi (0.054 mmol, 0.5 M in hexanes:THF 1:3, 108 µL) was added dropwise to a solution of the corresponding alcohol **8a** (0.054 mmol, 18 mg) in THF at -78 °C. The bath was removed and the reaction was stirred at room temperature during 30 min. The reaction was quenched with H_2O and hexanes was added. The two layers were separated and the organic phase was concentrated *in vacuo*. The crude was purified by silica gel chromatography (EP:EtOAc 80:20). The corresponding epoxide x was obtained as a colorless oil (90 %, 7.5 mg). Warning : the compound is slightly volatile.

General procedure for the synthesis of **ethyl 2-amino-2-((1S,2S)-2-phenylcyclopropyl)acetate (12)**:



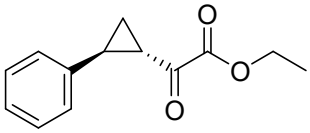
To a solution of cyclopropylpyruvate **2a** (0.15 mmol, 32.7 mg) in EtOH (910 µL) at -20 °C (ice + NaCl) was added $NaBH_4$ (0.09 mmol, 3.4 mg). The mixture was stirred during 30 min. The reaction mixture was quenched with acetone. The reaction mixture was concentrated and directly purified on silica gel chromatography (EP:EtOAc 85:15). The product **10** was obtained as a pale yellow oil (89 %, 29.3 mg).
To a solution of PPh_3 (0.268 mmol, 70.4 mg) in THF (450 µL) at 0 °C was added successively DIAD (0.268 mmol, 53 µL), DPPA (0.268 mmol, 58 µL) and pyridine (0.268 mmol, 21.6 µL). The mixture was stirred 1 min at 0 °C and a solution of the corresponding alcohol **10** (0.134 mmol, 29.5 mg) in THF (450 µL) was added to the mixture at 0 °C. The ice bath was removed and the reaction was stirred during 16 h at room temperature. The reaction mixture was concentrated and purified by flash silica chromatography (PE:EtOAC 90:10). Azide compound **11** was obtained as a faded yellow oil (70 %, 23 mg).
The corresponding azide compound **11** (0.071 mmol, 17.5 mg)) and PPh_3 (0.086 mmol, 22.5 mg) were dissolved in PhMe (710 µL). The mixture is vigorously stirred at 60 °C until almost full conversion of azide (~1h30). H_2O was then added and the reaction was stirred during 6 h. The solvent was evaporated and the crude was directly purified by silica (pre-packed with 1% of Et_3N) gel chromatography (DCM:EtOAC (+ Et_3N) 60:40 (+ 1%)). The two diastereoisomers were isolated (as a mixture with triphenylphosphine oxide (>95%, 16 mg). The diastereoisomeres were separated using reverse phases (H_2O + 0.1% formic acid:CAN 95:5 to 0:100 over 35 min). The corresponding amine fractions were combined and $NaCO_{3\ sat}$ solution was added until pH = 8. The aqueous phase was extracted with 3xDCM, dried over Na_2SO_4, filtered and concentrated. The two resulting diastereoisomers were separated using silica (pre-packed with 1% of Et_3N) gel chromatography (DCM:EtOAC (+ Et_3N) 60:40 (+ 1%)). The two diastereoismers **12a** and **12b** were isolated as a yellowish oil (Global yield: 64%, 10 mg)

Ethyl 3-diazo-2-oxopropanoate 1



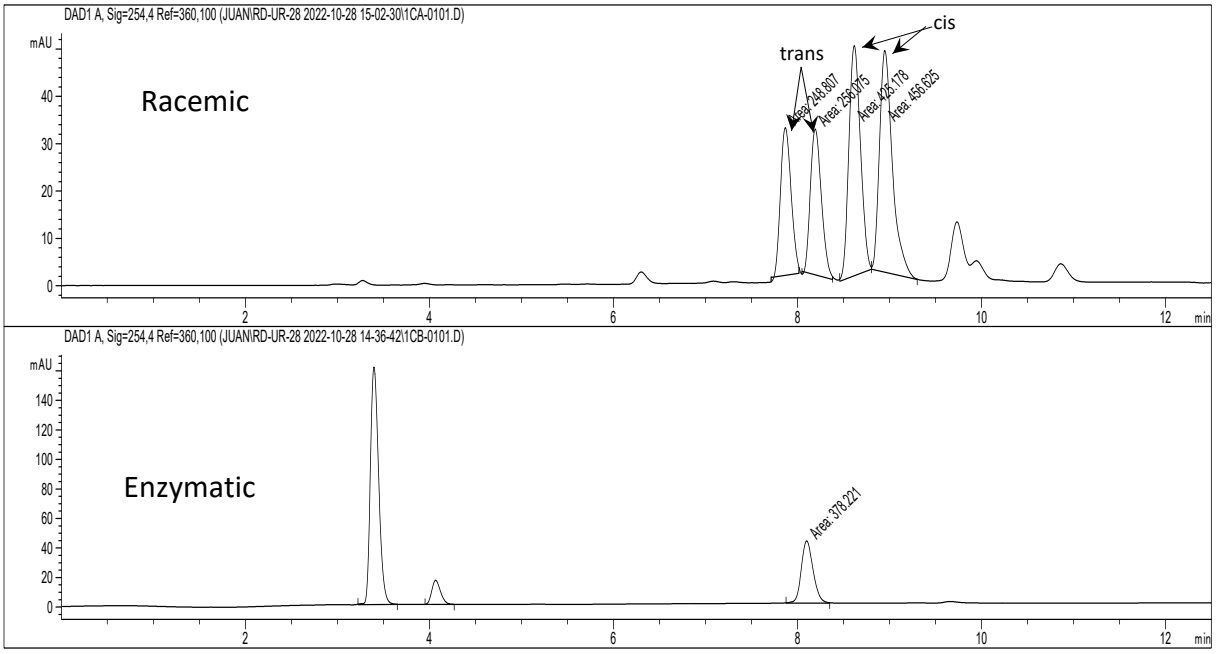
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.17 (s, 1H), 4.34 (q, *J* = 7.1 Hz, 3H), 1.38 (t, *J* = 7.1 Hz, 4H).
The data are in agreement with those described in the literature.[2]

Ethyl 2-oxo-2-((1S,2S)-2-phenylcyclopropyl)acetate 2a

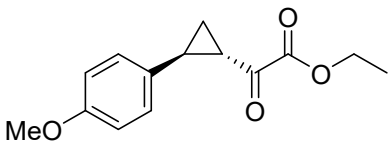


Following the general procedure A using styrene, *trans* isomer **2a** was isolated as a colorless oil (66.7 mg, 61%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34 – 7.27 (m, *J* = 7.3 Hz, 2H), 7.26 – 7.20 (m, 1H), 7.14 (d, *J* = 7.2 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.03 (ddd, *J* = 8.2, 5.2, 4.0 Hz, 1H), 2.72 (ddd, *J* = 9.2, 7.0, 4.0 Hz, 1H), 1.87 (ddd, *J* = 9.4, 5.3, 4.3 Hz, 1H), 1.65 (ddd, *J* = 8.1, 7.0, 4.1 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). The data are in agreement with those described in the literature.[3]
HPLC analysis: Obtained using Daicel Chiralpak® IA® Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 13 minute. (flow rate = 0.65 mL/min) **Tr** *trans* = 8.12 min



Ethyl 2-((1S,2S)-2-(4-methoxyphenyl)cyclopropyl)-2-oxoacetate 2b



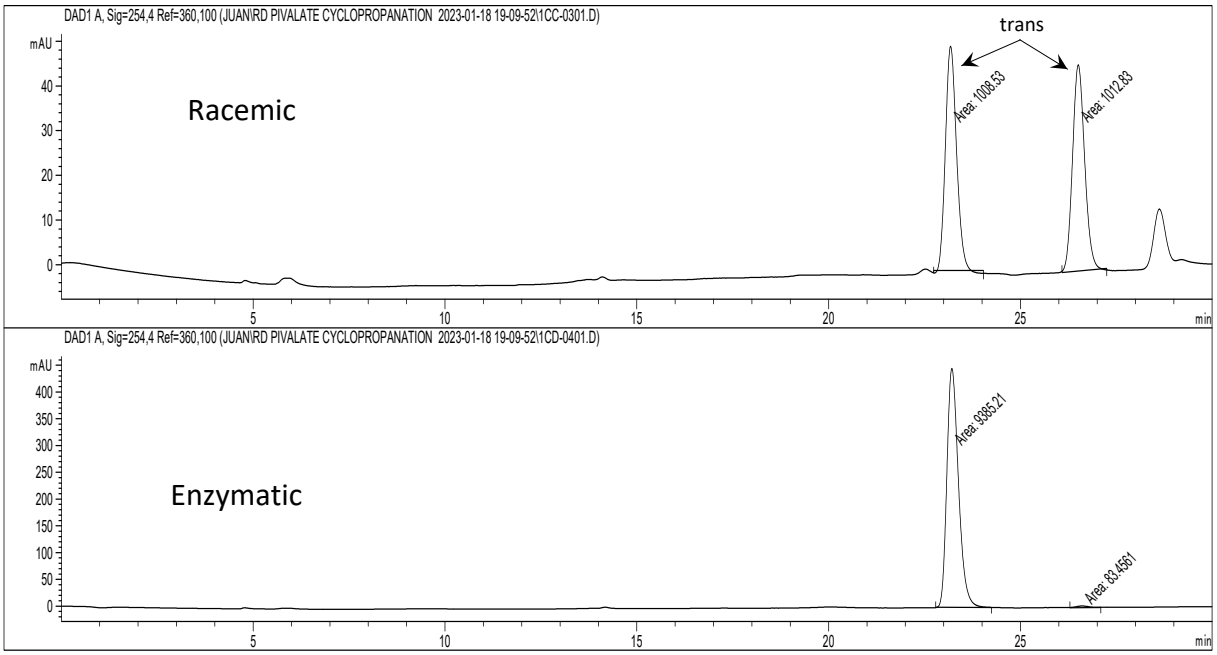
[3] Xu, H.; Zhang, W.; Shu, D.; Werness, J. B.; Tang, W. *Angew. Chem. Int. Ed.* **2008**, *47*, 8933–8936.

Following the general procedure A using 4-methoxy styrene, *trans* isomer **2b** was isolated as a colorless oil (18.3 mg, 37%).

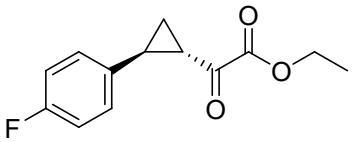
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.07 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 2.95 (ddd, *J* = 8.7, 4.9, 4.1 Hz, 1H), 2.68 (ddd, *J* = 9.2, 7.1, 4.0 Hz, 1H), 1.87 – 1.81 (m, 1H), 1.60 (app. td, *J* = 7.5, 4.2 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 192.5 (1C), 158.8 (1C), 131.4 (1C), 127.6 (2C), 114.1 (2C), 62.7 (2C), 55.5 (1C), 32.6 (1C), 29.7 (1C), 21.5 (1C), 14.2 (1C).

The data are in agreement with those described in the literature.[3]

HPLC analysis: Obtained using Daicel Chiralpak® IG Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 30 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 24.15 min



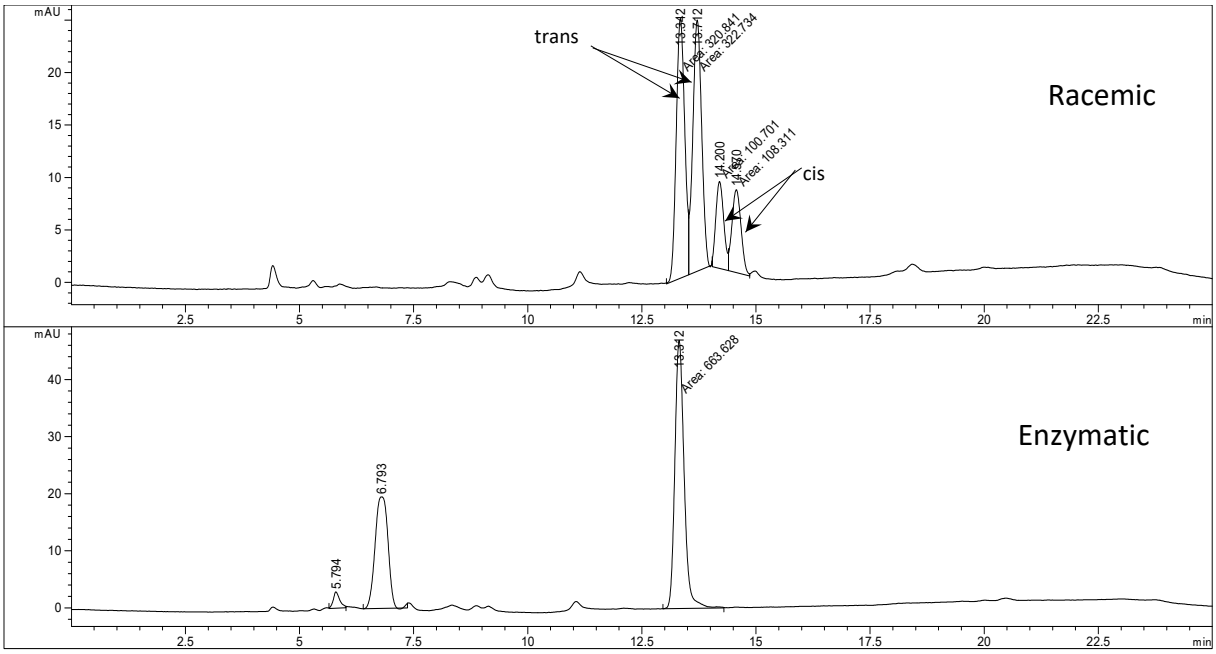
Ethyl 2-((1S,2S)-2-(4-fluorophenyl)cyclopropyl)-2-oxoacetate 2c



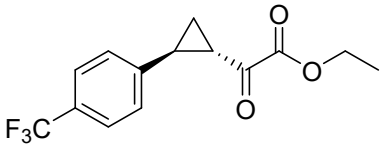
Following the general procedure A using 4-fluoro styrene, *trans* isomer **2c** was isolated as a colorless oil (16.6 mg, 35%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.11 (dd, *J* = 8.6, 5.3 Hz, 2H), 6.99 (t, *J* = 8.6 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.03 – 2.93 (m, 1H), 2.69 (ddd, *J* = 9.3, 7.0, 4.0 Hz, 1H), 1.85 (app. dt, *J* = 9.2, 4.7 Hz, 1H), 1.59 (app.td, *J* = 7:.4, 4.4 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -115.62 (s). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 192.3 (1C), 162.0 (d, *J* = 245.6 Hz, 1C), 161.1 (1C), 135.1 (1C), 128.1 (d, *J* = 8.1 Hz, 1C), 115.6 (d, *J* = 21.6 Hz, 1C), 62.8 (1C), 31.9 (1C), 29.4 (1C), 21.5 (1C), 14.2 (1C). **HRMS** (ESi$^+$-TOF) m/z: calculated for $C_{13}H_{12}O_3FNa^+$ $[M+Na]^+$ 223.0770, found 223.0780 (note : product has been trans-esterified by MeOH in HPLC vial). **R_f** = 0.34 (Hexane:EtOAc 80:20)

HPLC analysis: Obtained using Daicel Chiralpak® IA Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 25 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 13.312 min



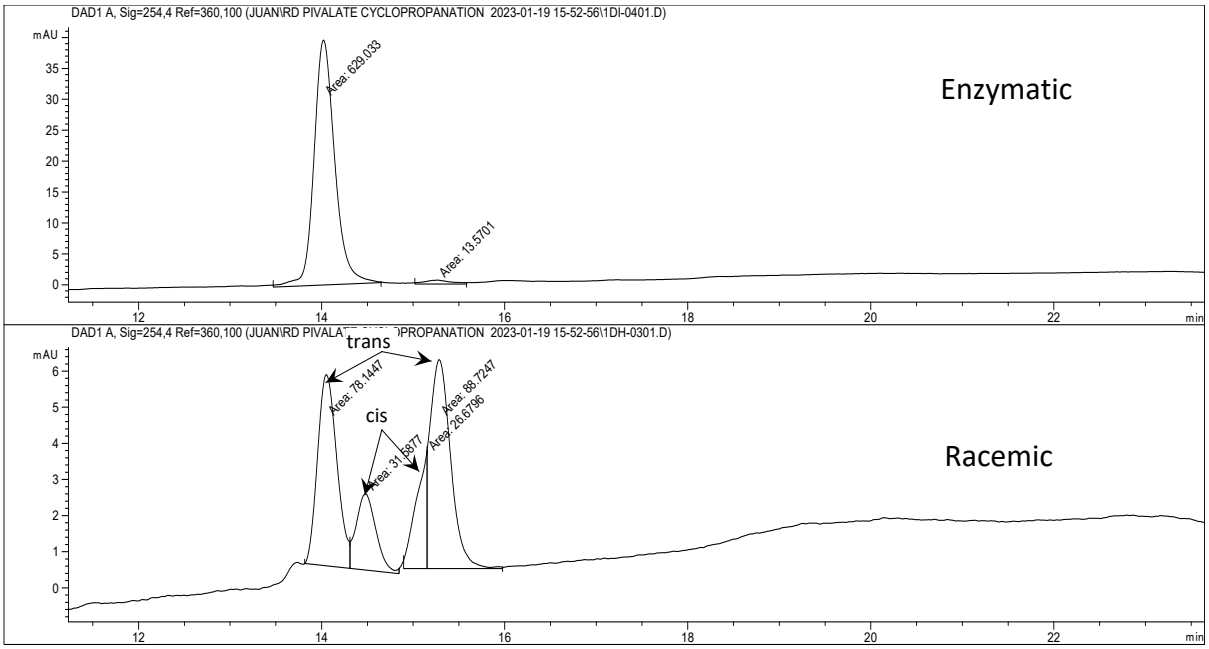
Ethyl 2-oxo-2-((1S,2S)-2-(4-(trifluoromethyl)phenyl)cyclopropyl)acetate 2d



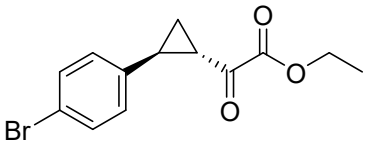
Following the general procedure A using 4-trifluoro styrene, *trans* isomer **2d** was isolated as a colorless oil (12.2 mg, 21%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.1 Hz, 2H), 7.24 (d, *J* = 8.1 Hz, 2H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.07 (ddd, *J* = 8.4, 5.3, 4.3 Hz, 1H), 2.74 (ddd, *J* = 9.3, 6.9, 4.1 Hz, 1H), 1.90 (ddd, *J* = 9.4, 5.1, 4.6 Hz, 1H), 1.65 (ddd, *J* = 8.1, 7.0, 4.4 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR** (376 MHz, $CDCl_3$): δ -63.38 (s). **^{13}C NMR** (101 MHz, $CDCl_3$): δ 192.0 (1C), 160.9 (1C), 143.5 (1C), 126.7 (2C), 125.7 (1C), 125.7 (1C), 63.0 (1C), 31.7 (1C), 29.9 (1C), 29.5 (1C), 21.7 (1C), 14.2 (1C). **HRMS** (ESi^{+}-TOF) m/z: calculated for $C_{14}H_{13}O_3F_3Na^{+}$ $[M+Na]^{+}$ 309.0709, found 309.0707. **R_f** = 0.39 (Hexane:EtOAc 85:15)

HPLC analysis: Obtained using Daicel Chiralpak® IG Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 25 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 14.03 min



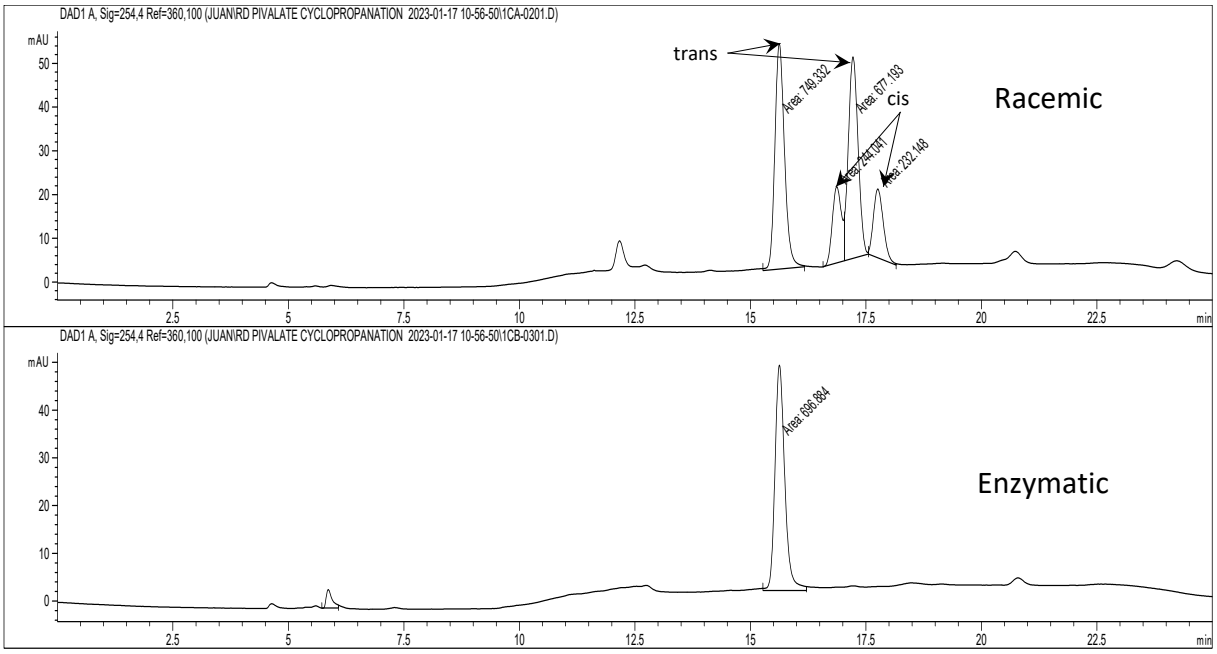
Ethyl 2-((1S,2S)-2-(4-bromophenyl)cyclopropyl)-2-oxoacetate 2e



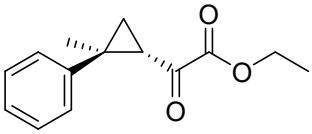
Following the general procedure A using 4-bromo styrene, *trans* isomer **2e** was isolated as a white solid (32 mg, 22%).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (d, *J* = 8.5 Hz, 2H), 7.01 (d, *J* = 8.3 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 1H), 3.00 (ddd, *J* = 8.2, 5.3, 4.0 Hz, 1H), 2.66 (ddd, *J* = 9.1, 6.9, 4.0 Hz, 1H), 1.86 (ddd, *J* = 9.2, 5.3, 4.3 Hz, 1H), 1.60 (ddd, *J* = 8.3, 6.9, 4.3 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 2H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 191.9 (1C), 160.8 (1C), 138.3 (1C), 131.6 (2C), 128.0 (2C), 120.7 (1C), 62.7 (1C), 31.6 (1C), 29.3 (1C), 21.3 (1C), 14.0 (1C). **HRMS** (ESi$^+$-TOF) m/z: calculated for $C_{13}H_{13}O_3BrNa^+$ $[M+Na]^+$ 318.9940, found 318.9937. $\mathbf{R_f}$ = 0.44 (Hexane:EtOAc 75:25)

HPLC analysis: Obtained using Daicel Chiralpak® IG Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 25 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 15.62 min



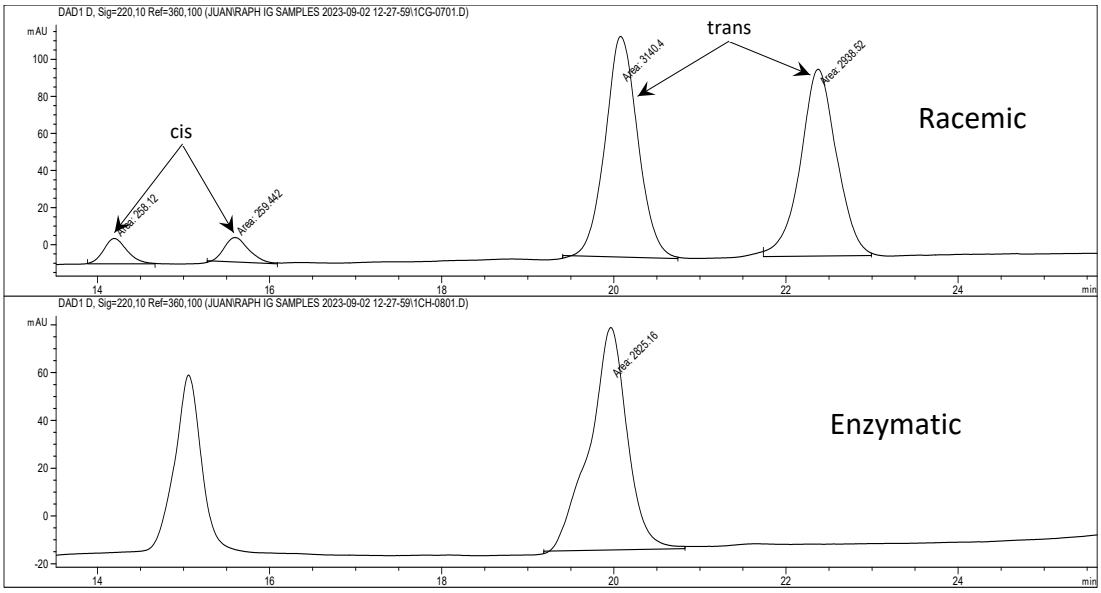
Ethyl 2-((1S,2S)-2-methyl-2-phenylcyclopropyl)-2-oxoacetate 2f



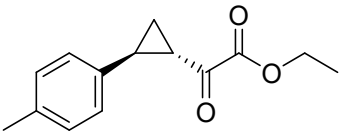
Following the general procedure A using α-methyl styrene, *trans* isomer **2f** was isolated as a faded yellow oil (40.3 mg, 35%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.30 (m, 2H), 7.28 – 7.22 (m, 1H), 4.37 (app. qd, *J* = 7.1, 2.0 Hz, 2H), 3.06 (dd, *J* = 7.8, 6.2 Hz, 1H), 1.78 (dd, *J* = 6.2, 4.4 Hz, 1H), 1.65 (dd, *J* = 7.8, 4.4 Hz, 1H), 1.45 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 192.0 (1C), 161.8 (1C), 145.3 (1C), 128.8(1C), 127.7 (1C), 127.0 (1C), 62.6 (1C), 38.4 (1C), 33.2 (1C), 29.9 (1C), 23.9 (1C), 19.6 (1C), 14.2 (1C). **HRMS** (ESi^+-TOF) m/z: calculated for $C_{14}H_{16}O_3Na^+$ $[M+Na]^+$ 255.0992, found 255.0990. $\mathbf{R_f}$ = 0.40 (Hexane:EtOAc 85:15)

HPLC analysis: Obtained using Daicel Chiralpak® IG Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 3% in 30 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 19.94 min



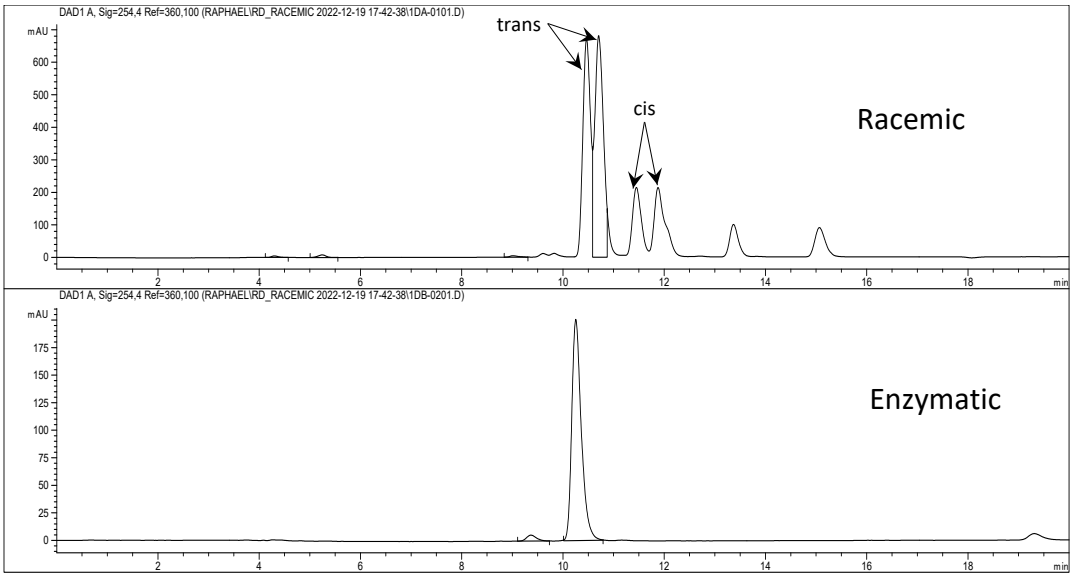
Ethyl 2-oxo-2-((1S,2S)-2-(p-tolyl)cyclopropyl)acetate 2g



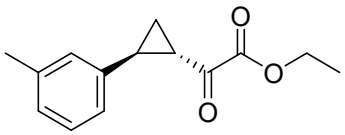
Following the general procedure A using 4-methyl styrene, *trans* isomer **2g** was isolated as a faded yellow oil (30 mg, 26%).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11 (d, *J* = 7.9 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.03 – 2.92 (m, 1H), 2.69 (ddd, *J* = 9.6, 7.2, 4.0 Hz, 1H), 2.32 (s, 3H), 1.85 (app. dt, *J* = 9.2, 4.6 Hz, 1H), 1.65 – 1.59 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 192.5 (1C), 161.1 (1C), 136.9 (1C), 136.3 (1C), 129.4 (2C), 126.4 (2C), 62.7 (1C), 32.7 (1C), 29.7 (1C), 21.6 (1C), 21.2 (1C), 14.2 (1C). **HRMS** (ESi$^+$-TOF) m/z: calculated for $C_{14}H_{16}O_3Na^+$ $[M+Na]^+$ 255.0992, found 255.0991. **R_f** = 0.32 (Hexane:EtOAc 85:15)

HPLC analysis: Obtained using Daicel Chiralpak® IG Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 25 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 10.26 min



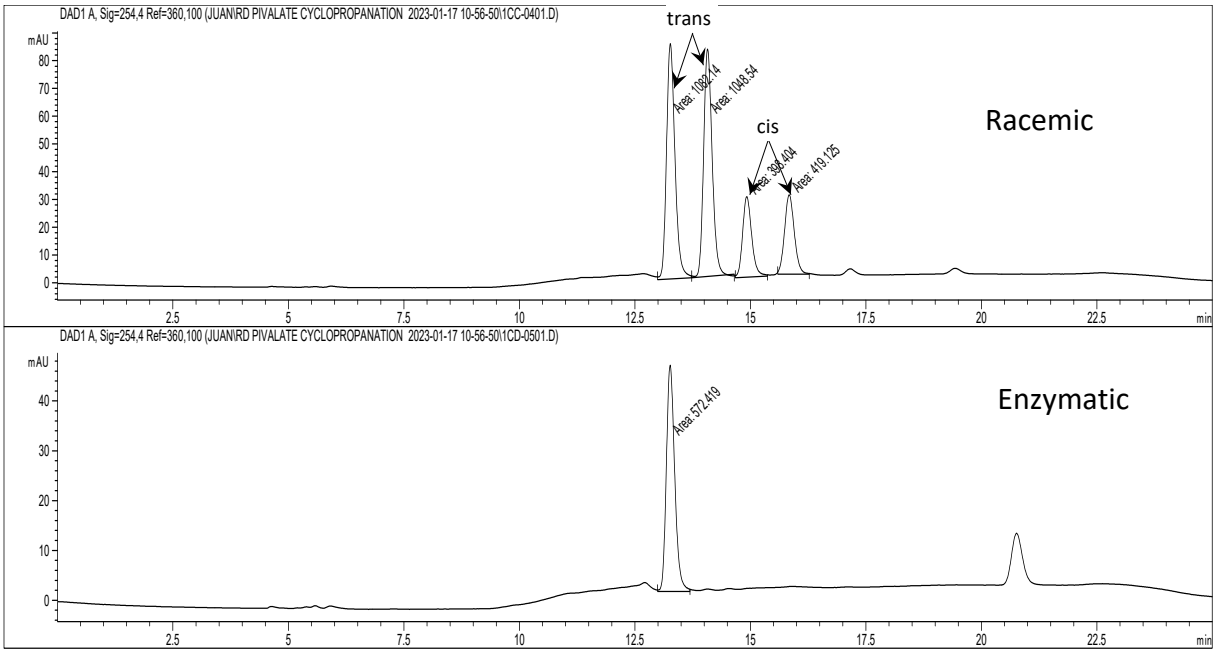
Ethyl 2-oxo-2-((1S,2S)-2-(m-tolyl)cyclopropyl)acetate 2h



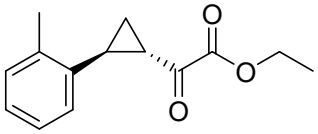
Following the general procedure A using 3-methyl styrene, *trans* isomer **2h** was isolated as a faded yellow oil (17.2 mg, 37%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (t, *J* = 7.5 Hz, 1H), 7.05 (d, *J* = 7.5 Hz, 1H), 6.97 – 6.90 (m, *J* = 7.8 Hz, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.02 (ddd, *J* = 8.4, 5.2, 4.1 Hz, 1H), 2.68 (ddd, *J* = 9.2, 7.0, 4.0 Hz, 1H), 2.33 (s, 3H), 1.85 (ddd, *J* = 9.2, 5.1, 4.2 Hz, 1H), 1.64 (ddd, *J* = 8.1, 7.1, 4.1 Hz, 1H), 1.38 (t, *J* = 7.1 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 192.5 (1C), 161.1 (1C), 139.3 (1C), 138.4 (1C), 128.6 (1C), 127.9 (1C), 127.2 (1C), 123.4 (1C), 62.7 (1C), 32.8 (1C), 29.6 (1C), 21.7 (1C), 21.5 (1C), 14.2 (1C). **HRMS** (ESi^+-TOF) m/z: calculated for $C_{14}H_{16}O_3Na^+$ $[M+Na]^+$ 255.0992, found 255.0991. $\mathbf{R_f}$ = 0.44 (Hexane:EtOAc 85:15)

HPLC analysis: Obtained using Daicel Chiralpak® IG Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 25 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 13.26 min



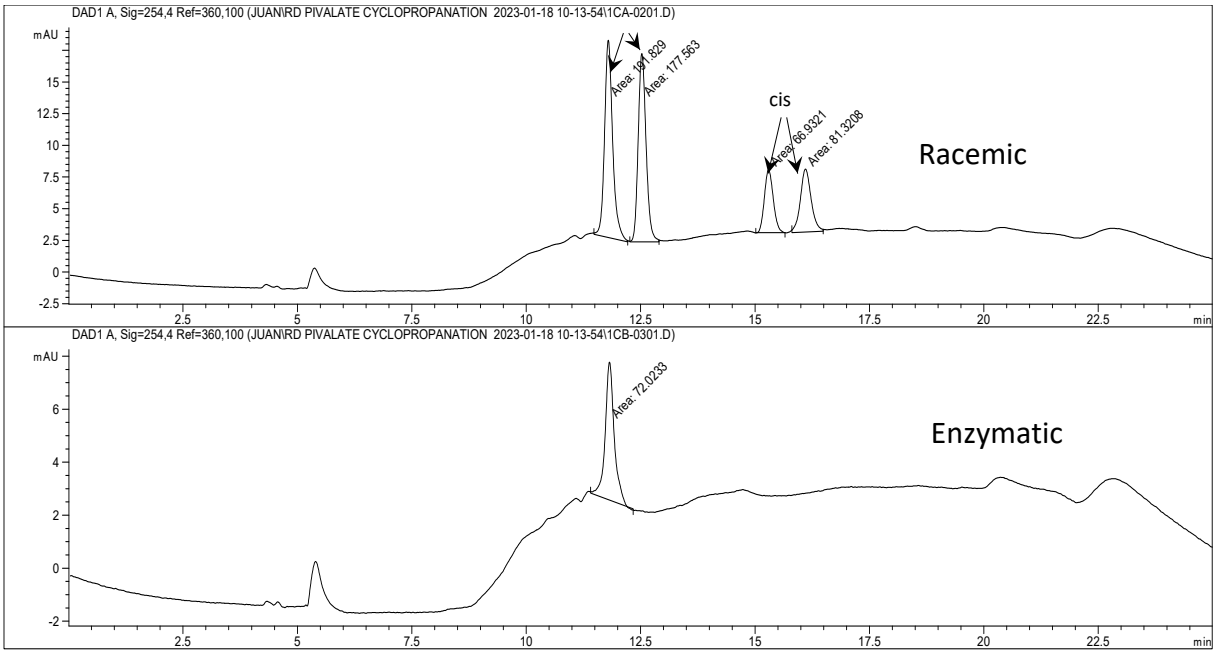
Ethyl 2-oxo-2-((1S,2S)-2-(o-tolyl)cyclopropyl)acetate 2i



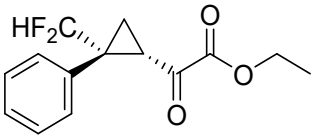
Following the general procedure A using 2-methyl styrene, *trans* isomer **2i** was isolated as a faded yellow oil (15 mg, 32%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.30 – 7.19 (m, 3H), 7.14 (d, *J* = 6.5 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 2H), 3.02 – 2.94 (m, 1H), 2.80 (app. td, *J* = 8.0, 4.2 Hz, 1H), 1.94 (ddd, *J* = 8.9, 5.0, 0.9 Hz, 1H), 1.75 (app. td, *J* = 7.7, 4.0 Hz, 1H), 1.48 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 193.0 (1C), 161.2 (1C), 138.2 (1C), 137.3 (1C), 130.2 (1C), 127.4 (1C), 126.2 (1C), 126.0 (1C), 62.8 (1C), 31.2 (1C), 28.0 (1C), 20.3 (1C), 19.7 (1C), 14.2 (1C). **HRMS** (ESi$^+$-TOF) m/z: calculated for $C_{14}H_{16}O_3Na^+$ $[M+Na]^+$ 255.0992, found 255.0990. **R_f** = 0.54 (Hexane:EtOAc 85:15).

HPLC analysis: Obtained using Daicel Chiralpak® IG Column at 25°C, eluted using Gradient of Isopropyl alcohol as modifier in hexane going from 1% to 8% in 25 minutes. (flow rate = 0.65 mL/min) **Tr** *trans* = 11.82 min

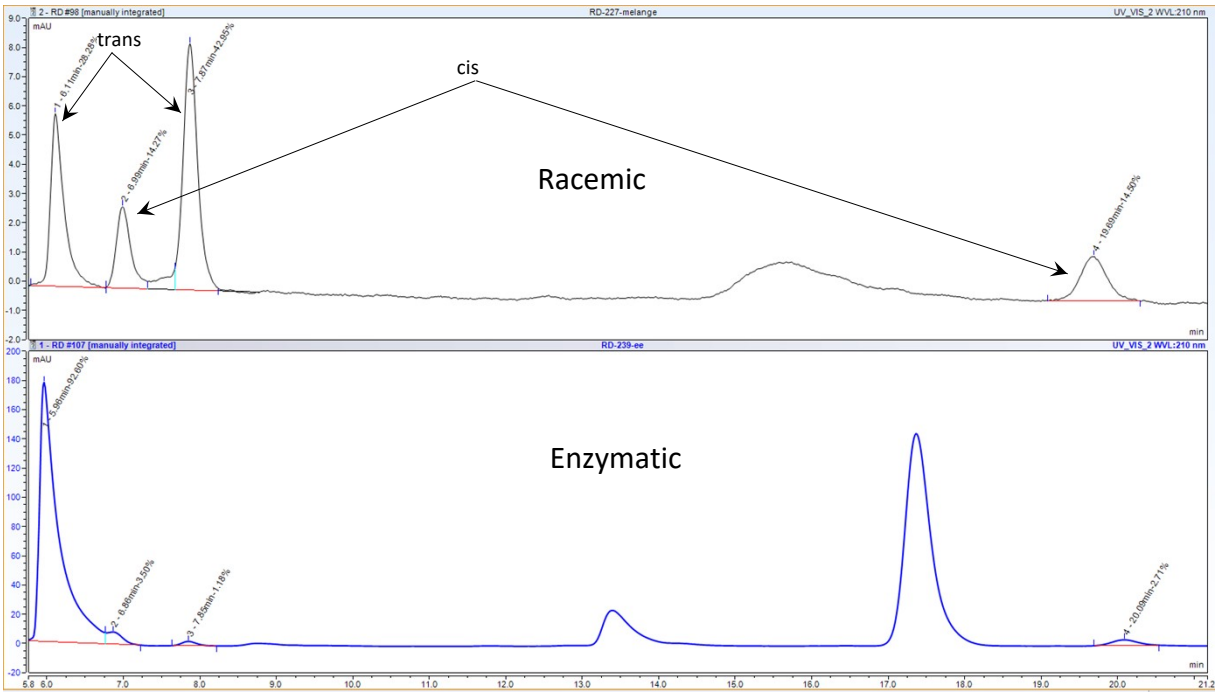


ethyl 2-((1S,2R)-2-(difluoromethyl)-2-phenylcyclopropyl)-2-oxoacetate 2k

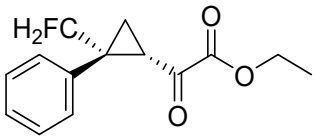


^{1}H NMR (300 MHz, $CDCl_3$): δ 7.53 – 7.43 (m, 2H), 7.42 – 7.32 (m, 3H), 5.84 (t, *J* = 55.1 Hz, 1H), 4.42 (q, *J* = 7.1 Hz, 2H), 3.30 (ddd, *J* = 8.0, 6.5, 2.9 Hz, 1H), 2.06 (ddt, *J* = 6.5, 5.2, 1.4 Hz, 1H), 1.76 (ddd, *J* = 7.9, 7.0, 5.1 Hz, 1H), 1.43 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ -111.81 (d, *J* = 288.2 Hz), -120.38 (d, *J* = 288.2 Hz). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 191.0 (1C), 160.6 (1C), 135.3 (1C), 131.2 (1C), 128.8 (2C), 128.7 (2C), 114.80 (t, *J* = 238.9 Hz, 1C), 63.2 (1C), 41.36 (t, *J* = 27.5 Hz, 1C), 29.4 (1C), 19.83 (d, *J* = 7.2 Hz, 1C), 14.16 (1C). **HRMS** (EI^{+}-TOF) m/z: calculated for $C_{14}H_{14}F_2O_2^{+}$ $[M]^{+}$ 268.0911, found 268.0914. **R_f** = 0.32 (Hexane:EtOAc 85:15)

HPLC analysis: Obtained using Daicel Chiralpak® IB column at 15 °C with Heptane:^{i}PrOH 95:05 (flow rate = 1 mL/min). **Tr** *trans* = 5.96 min.

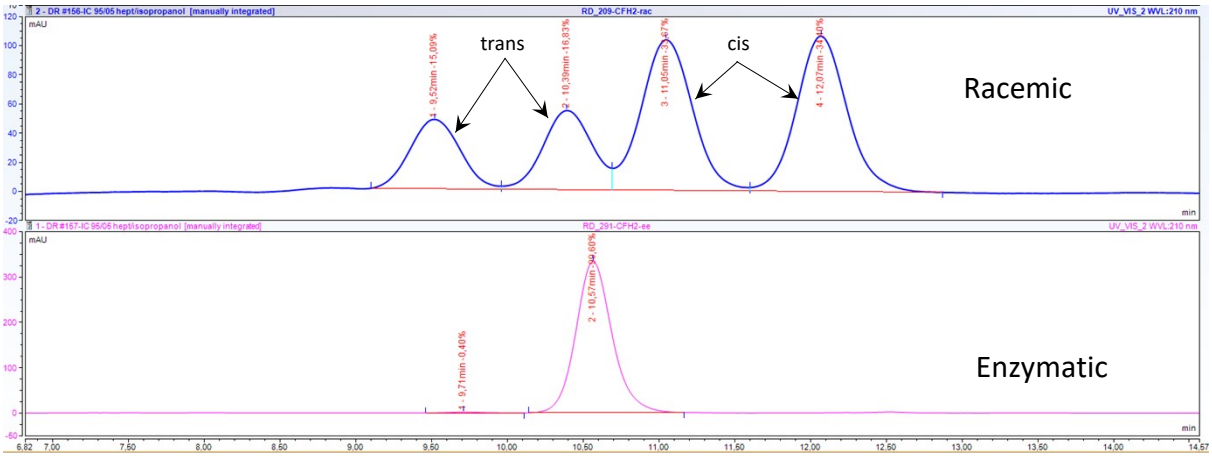


ethyl 2-((1S,2R)-2-(fluoromethyl)-2-phenylcyclopropyl)-2-oxoacetate 2l

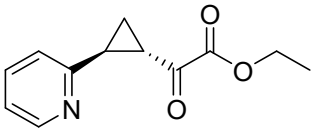


^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51 – 7.41 (m, 2H), 7.41 – 7.29 (m, 3H), 4.75 (dd, *J* = 47.9, 10.1 Hz, 1H), 4.50 (dd, *J* = 46.9, 9.8 Hz, 1H), 4.40 (q, *J* = 7.3 Hz, 2H), 3.35 – 3.24 (m, 1H), 1.93 (ddd, *J* = 6.6, 4.8, 2.1 Hz, 1H), 1.69 – 1.61 (m, 1H), 1.42 (t, *J* = 7.1 Hz, 3H). **^{19}F NMR** (282 MHz, $CDCl_3$): δ -211.07. **^{13}C NMR** (75 MHz, $CDCl_3$): 190.8 (1C), 160.9 (1C), 140.6 (1C), 129.0 (2C), 128.8 (2C), 128.0 (1C), 84.1 (d, *J* = 171.1 Hz, 1C) , 62.9 (1C), 41.2 (d, *J* = 21.5 Hz, 1C), 30.5 (d, *J* = 3.8 Hz, 1C), 20.6 (d, *J* = 7.8 Hz, 1C), 14.2 (1C). **R_f** = 0.29 (Hexane:EtOAc 85:15)

HPLC analysis: Obtained using Daicel Chiralpak® IC column at 20 °C with Heptane:^{i}PrOH 95:05 (flow rate = 1 mL/min). **Tr** *trans* = 10.57 min



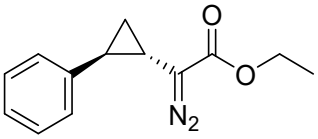
ethyl 2-oxo-2-((1S,2S)-2-(pyridin-2-yl)cyclopropyl)acetate 2m



Following the general procedure A using 2-vinyl pyridine, *trans* isomer **2m** was isolated as a faded yellow oil (15 mg, 32%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J* = 4.8 Hz, 1H), 7.58 (td, *J* = 7.7, 1.9 Hz, 1H), 7.23 (d, *J* = 7.8 Hz, 1H), 7.15 – 7.08 (m, 1H), 4.33 (q, *J* = 7.2 Hz, 2H), 3.35 – 3.28 (m, 1H), 2.79 – 2.75 (m, 1H), 1.98 – 1.91 (m, 1H), 1.81 (m, 1H), 1.36 (t, *J* = 6.8 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 192.8 (1C), 161.1 (1C), 158.1 (1C), 149.7 (1C), 136.3 (1C), 122.8 (1C), 121.9 (1C), 62.7 (1C), 32.9 (1C), 29.6 (1C), 21.8 (1C), 14.15 (1C). **HRMS** (ESi^+-TOF) m/z: calculated for $C_{12}H_{13}NO_3H^+$ $[M+H]^+$ 220.0968, found 220.0969. **R_f** = 0.26 (Hexane:EtOAc 70:30)

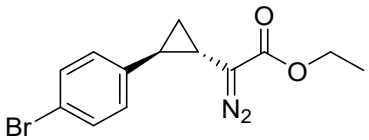
ethyl 2-diazo-2-((1S,2S)-2-phenylcyclopropyl)acetate 3a



The product **3a** was obtained following the general procedure B using Ethyl 2-oxo-2-((1S,2S)-2-phenylcyclopropyl)acetate (0.2 mmol, 63.7 mg) as a yellow oil (87 %, 58 mg).

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 – 7.26 (m, 2H), 7.24 – 7.13 (m, 3H), 4.24 (qd, *J* = 7.1, 3.9 Hz, 2H), 2.16 – 2.10 (m, 1H), 1.88 (ddd, *J* = 8.4, 5.3, 4.4 Hz, 1H), 1.36 (app. dt, *J* = 8.4, 5.7 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.18 (app. dt, *J* = 9.1, 5.4 Hz, 1H). The data are in agreement with those described in the literature.[3]

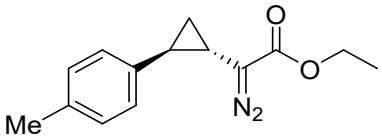
ethyl 2-((1S,2S)-2-(4-bromophenyl)cyclopropyl)-2-diazoacetate 3b



The product **3b** was obtained following the general procedure B using Ethyl 2-oxo-2-((1S,2S)-2-phenylcyclopropyl)acetate (0.11 mmol, 32 mg) as a yellow oil (59 %, 19.5 mg).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 8.3 Hz, 2H), 4.23 (qd, *J* = 7.1, 2.8 Hz, 2H), 2.14 – 2.01 (m, 1H), 1.83 (ddd, *J* = 8.4, 5.4, 4.3 Hz, 1H), 1.37 – 1.23 (m, 2H), 1.22 – 1.12 (m, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 167.3 (1C), 140.0 (1C), 131.5 (2C), 128.4 (2C), 120.0 (1C), 60.9 (1C), 25.8 (1C), 15.6 (1C), 15.2 (1C), 14.6 (1C). **R_f** = 0.29 (EP:EtOAc 90:10). **HRMS** : Diazo peak cannot be observed using EI or API ionization sources. Only rearrangement product (without -N_2) was observed.

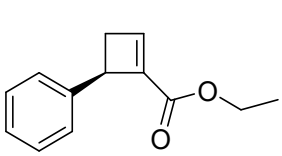
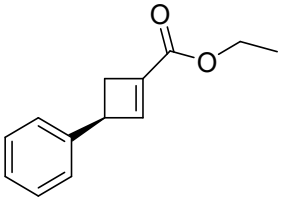
ethyl 2-diazo-2-((1S,2S)-2-(p-tolyl)cyclopropyl)acetate 3c



The product **3c** was obtained following the general procedure B using Ethyl 2-oxo-2-((1S,2S)-2-(p-tolyl)cyclopropyl)acetate (0.128 mmol, 29.7 mg) as a yellow oil (49 %, 15.2 mg).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.14 – 7.03 (m, 4H), 4.24 (qd, *J* = 7.1, 2.4 Hz, 2H), 2.31 (s, 3H), 2.14 – 2.04 (m, 1H), 1.84 (ddd, *J* = 8.4, 5.3, 4.4 Hz, 1H), 1.37 – 1.23 (m, 4H), 1.14 (dt, *J* = 9.1, 5.3 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 167.4 (1C), 137.8 (1C), 135.9 (1C), 129.0 (2C), 126.5 (2C), 60.8 (1C), 25.7 (1C), 21.0 (1C), 15.3 (1C), 15.2 (1C), 14.6 (1C). **R_f** = 0.32 (EP:EtOAc 90:10). **HRMS** : Diazo peak cannot be observed using EI or API ionization sources. Only rearrangement product (without -N_2) was observed.

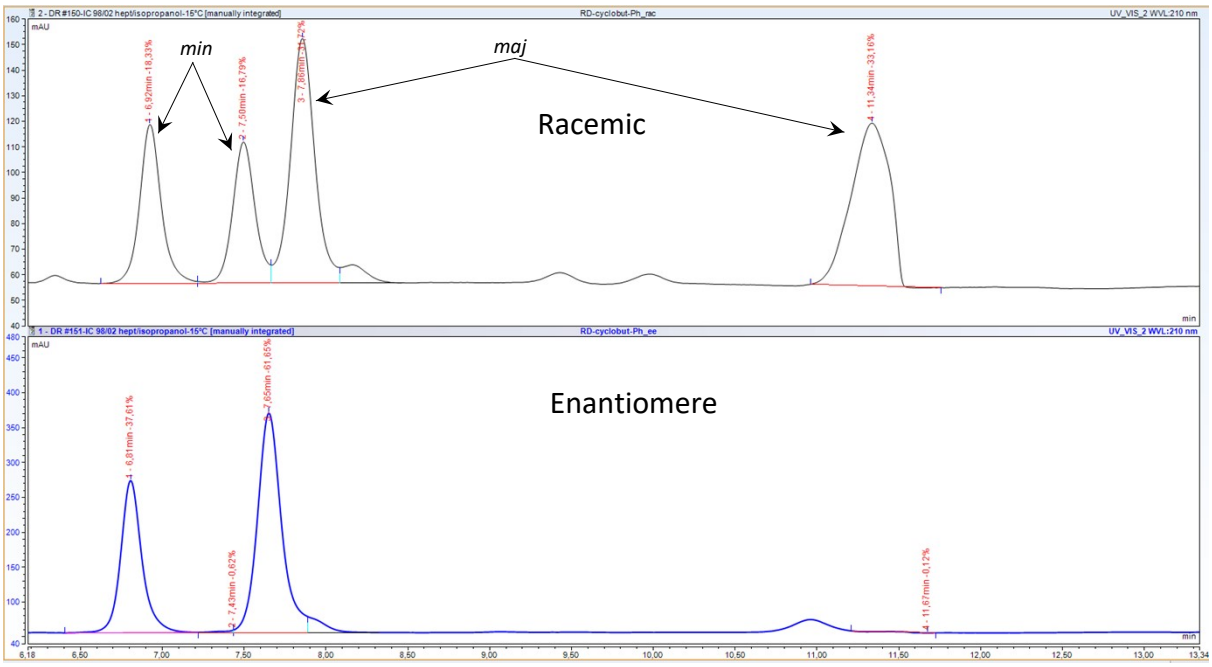
ethyl (R)- 4-phenylcyclobut-1-ene-1-carboxylate 4a (maj.)
ethyl (R)- 3-phenylcyclobut-1-ene-1-carboxylate 4b (*min.*)

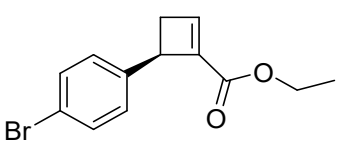
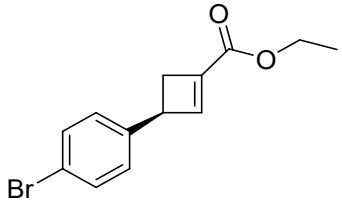
The products were obtained following the general procedure C using ethyl 2-diazo-2-((1S,2S)-2-phenylcyclopropyl)acetate (0.1 mmol, 23.0 mg). They were obtained as two regioisomers with a ratio 70:30 as a colorless oil (46 %, 9.3 mg).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 – 7.16 (m, 10H), 7.02 (*maj*, s, 1H), 6.98 (*min*, d, *J* = 0.8 Hz, 0.5H), 4.31 – 4.06 (m, 4H), 3.94 (*min*, d, *J* = 4.7 Hz, 0.5H), 3.22 (*min,* dd, *J* = 13.4, 4.7 Hz, 0.5H), 2.97 (*maj,* ddd, *J* = 15.5, 4.6, 1.3 Hz, 1H), 2.60 (*min*, dd, *J* = 13.3, 1.8 Hz, 0.5H), 2.43 – 2.30 (*maj*, m, 1H), 1.32 (*min*, t, *J* = 7.1 Hz, 2H), 1.21 (*maj*, t, *J* = 7.1 Hz, 3H). The data are in agreement with those described in the literature.[3]

HPLC analysis: Obtained using Daicel Chiralpak® IC column at 15 °C with Heptane:^{i}PrOH 98:02 (flow rate = 1 mL/min). **Tr** *maj* = 7.65 min ; **Tr** *min* = 6.81 min



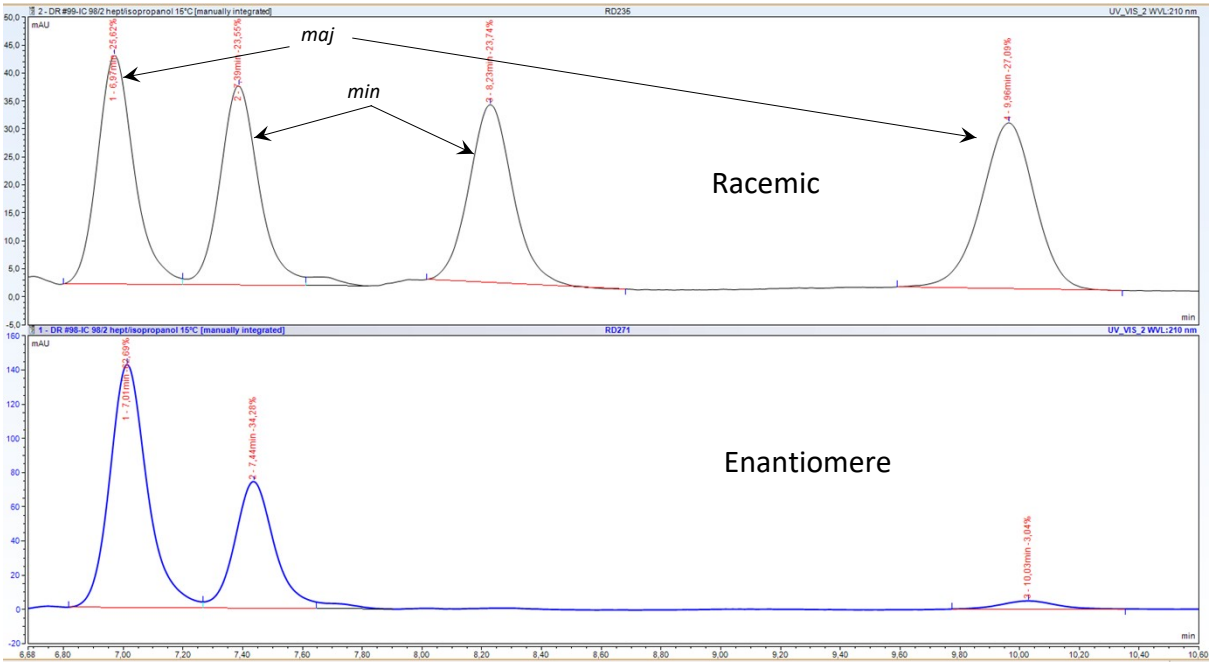
ethyl (R)- 4-(4-bromophenyl)cyclobut-1-ene-1-carboxylate 5a (*maj.*)
ethyl (R)- 3-(4-bromophenyl)cyclobut-1-ene-1-carboxylate 5b (*min.*)

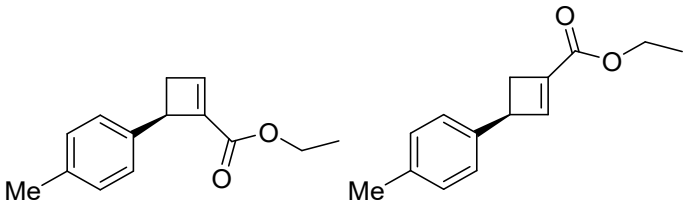
The products were obtained following the general procedure C using ethyl 2-((1S,2S)-2-(4-bromophenyl)cyclopropyl)-2-diazoacetate (0.1 mmol, 30.8 mg). They were obtained as two regioisomers with a ratio 70:30 as a colorless oil (43 %, 12.1 mg).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.47 – 7.38 (m, 2.9H), 7.16 – 7.07 (m, 2.8H), 7.01 (*maj*, s, 1H), 6.92 (*min*, d, *J* = 0.7 Hz, 0.4H), 4.23 (*min*, q, *J* = 7.1 Hz, 1.2H), 4.18 – 4.10 (*maj*, m, 3H), 3.88 (*min,* d, *J* = 4.6 Hz, 0.5H), 3.22 (min, dd, *J* = 13.5, 4.7 Hz, 0.5H), 2.97 (*maj*, ddd, *J* = 15.5, 4.6, 1.3 Hz, 1H), 2.55 (*min*, dd, *J* = 13.4, 1.5 Hz, 0.5H), 2.36 – 2.28 (*maj*, m, 1H), 1.32 (*min*, t, *J* = 7.1 Hz, 1.8H), 1.22 (*maj*, t, *J* = 7.1 Hz, 3H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 161.9 (*min*, 1C), 161.8 (*maj*, 1C), 147.2 (*min*, 1C), 146.9 (*maj*, 1C), 141.1 (*min*, 1C), 140.1 (*maj*, 2C), 131.7 (*min*, 2C), 131.6 (*maj*, 1C), 128.7 (*min*, 1C), 128.6 (*maj*, 1C), 120.6 (*min*, 1C), 120.4 (*maj*, 1C), 60.6 (*min*, 1C), 60.4 (*maj*, 1C), 46.1 (*maj*, 1C), 43.2 (*min*, 1C), 38.7 (*min*, 1C), 37.4 (*maj*, 1C), 14.4 (*min*, 1C), 14.3 (*maj*, 1C). **HRMS** (EI^{+}-TOF) m/z: calculated for $C_{13}H_{13}O_2{}^{79}Br^{+}$ $[M]^{+}$ 280.0097, found 280.0099. **R_f** = 0.32-0.38 (EP:Et_2O 90:10)

HPLC analysis: Obtained using Daicel Chiralpak® IC column at 15 °C with Heptane:^{i}PrOH 98:02 (flow rate = 1 mL/min). **Tr** *maj* = 7.01 min ; **Tr** *min* = 7.44 min

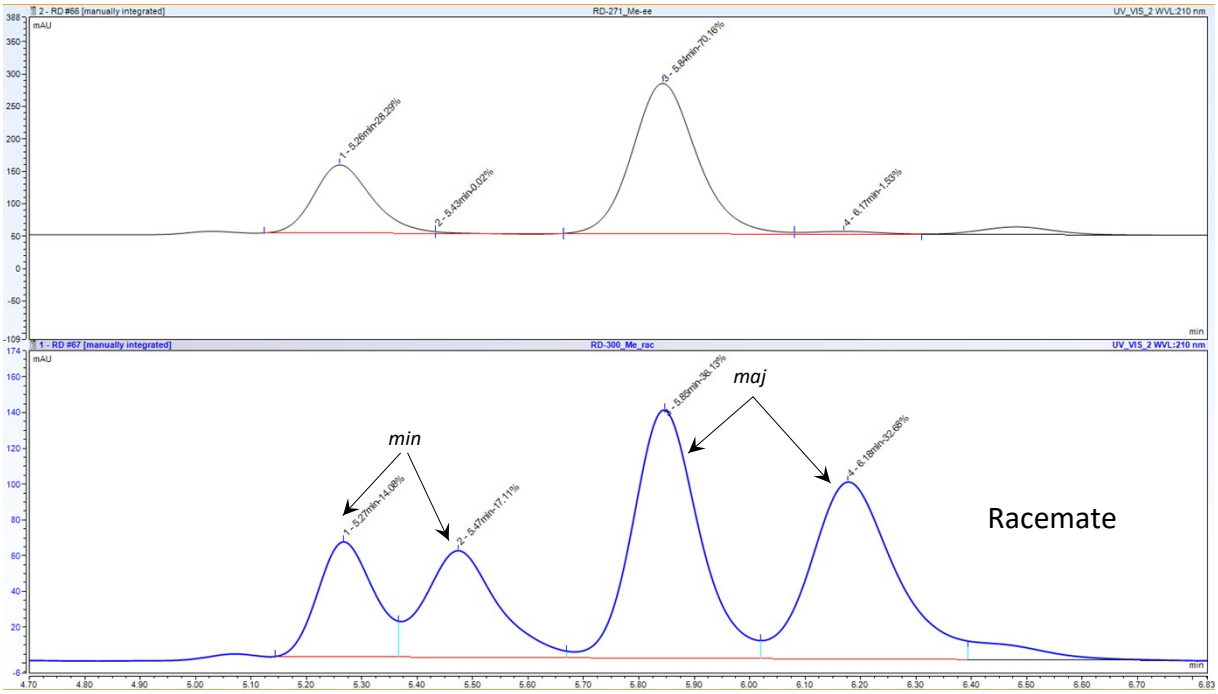


ethyl (R)- 4-(p-tolyl)cyclobut-1-ene-1-carboxylate 6a (*maj.*)
ethyl (R)- 4-(p-tolyl)cyclobut-1-ene-1-carboxylate 6b (*min.*)

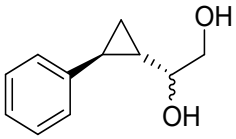


The products were obtained following the general procedure C using ethyl 2-((1S,2S)-2-(4-methylphenyl)cyclopropyl)-2-diazoacetate (0.1 mmol, 24.4 mg). They were obtained as two regioisomers with a ratio 75:25 as colorless oil (48 %, 10.4 mg).

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19 – 7.05 (m, 5.7zH), 7.01 (*maj*, t, *J* = 1.1 Hz, 1H), 6.96 (*min*, d, *J* = 0.9 Hz, 0.4H), 4.23 (*min*, q, *J* = 7.1 Hz, 0.9H), 4.19 – 4.09 (m, 1H), 3.90 (*min*, dt, *J* = 4.5, 1.5 Hz, 1H), 3.20 (*min*, dd, *J* = 13.3, 4.6 Hz, 0.4H), 2.95 (*min*, ddd, *J* = 15.5, 4.6, 1.3 Hz, 1H), 2.57 (*min*, dd, *J* = 13.4, 1.5 Hz, 1H), 2.41 – 2.28 (m, H), 1.32 (*min*, t, *J* = 7.1 Hz, 1.4H), 1.22 (*maj*, t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 162.7 (*min*, 1C), 162.1 (*maj*, 1C), 148.2 (*min*, 1C), 146.6 (*maj*, 1C), 141.6 (*maj*, 1C), 138.9 (*min*, 1C), 138.2 (*min*, 1C), 138.1 (*maj*, 1C), 136.5 (*min*, 1C), 136.2 (*maj*, 1C), 129.3 (*min*, 2C), 129.2 (*maj*, 2C), 126.8 (*min*, 2C), 126.6 (*maj*, 2C), 60.5 (*min*, 1C), 60.2 (*maj*, 1C), 46.4 (*maj*, 1C), 43.5 (*min*, 1C), 38.8 (*min*, 1C), 37.6 (*maj*, 1C), 21.2 (*maj*, 1C), 21.2 (*min*, 1C), 14.4 (*min*, 1C), 14.3 (*maj*, 1C). **HRMS** (EI^+-TOF) m/z: calculated for $C_{14}H_{16}O_2^+$ $[M]^+$ 216.11480, found 216.11503. **R_f** = 0.41-0.47 (EP:Et_2O 90:10).
HPLC analysis: Obtained using Daicel Chiralpak® ID column at 15 °C with Heptane:^{i}PrOH 98:02 (flow rate = 1 mL/min). **Tr** *maj* = 5.85 min ; **Tr** *min* = 5.27 min



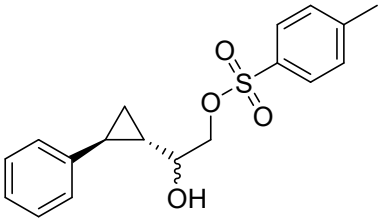
1-((1S,2S)-2-phenylcyclopropyl)ethane-1,2-diol 7



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30 – 7.22 (m, 4H), 7.20 – 7.12 (m, 1.75H), 7.12 – 7.02 (m, 3.4H), 3.89 – 3.74 (m, 1.6H), 3.72 – 3.58 (m, 1.6H), 3.37 – 3.22 (m, 1.6H), 2.11 (*min*., d, *J* = 3.6 Hz, 0.6H), 2.04 (*maj*, d, *J* = 3.7 Hz, 1H), 2.02 – 1.92 (m, 2H), 1.92 – 1.82 (m, 1.6H), 1.34 – 1.16 (m, 3.9H), 1.11 – 1.05 (*min,* m, 0.6H), 1.05 – 1.00 (*maj*, m, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 142.5 (*maj,* 1C), 142.1 (*min,* 1C), 128.5 (*min,* 2C), 128.5 (*maj,* 2C), 126.0 (*min,* 2C), 125.9 (*maj,* 1C), 125.9 (*min,* 1C), 125.8 (*maj,* 1C), 76.0 (*maj,* 1C), 75.8 (*min,* 1C), 66.6 (*min,* 1C), 66.3 (*maj,* 1C), 25.4 (*maj,* 1C), 25.2 (*min,* 1C), 20.9 (*maj,* 1C), 20.5 (*min,* 1C), 13.3 (*min,* 1C), 13.1 (*maj,* 1C). **HRMS** (EI^+-TOF) m/z: calculated for $C_{11}H_{14}O_2^+$ $[M]^+$ 178.0994, found 178.1004. **R_f** = 0.15 (DCM:Et_2O 50:50) The data are in agreement with those described in the literature.[4]

[4] Landais, Y.; Parra-Rapado, L. *Eur. J. Org. Chem* **2000**, 401–418.

2-hydroxy-2-((1S,2S)-2-phenylcyclopropyl)ethyl 4-methylbenzenesulfonate 8



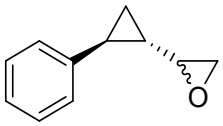
8a (*maj*):

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.29 – 7.20 (m, 3H), 7.19 – 7.11 (m, 1H), 7.07 – 6.99 (m, 2H), 4.18 (dd, *J* = 10.2, 3.2 Hz, 1H), 4.04 (dd, *J* = 10.2, 7.0 Hz, 1H), 3.50 (app. td, *J* = 7.2, 3.2 Hz, 1H), 2.45 (s, 3H), 2.33 – 2.07 (m, 1H), 1.98 (td, *J* = 8.9, 5.0 Hz, 1H), 1.22 – 1.11 (m, 1H), 1.01 – 0.87 (m, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 145.20 (1C), 141.90 (1C), 132.83 (1C), 130.1 (2C), 128.5 (2C), 128.1 (2C), 126.1 (2C), 126.0 (1C), 73.5 (1C), 72.6 (1C), 24.6 (1C), 21.8 (1C), 20.7 (1C), 12.6 (1C). **HRMS** (ESI$^+$-TOF) m/z: calculated for $C_{18}H_{21}O_4S^+$ $[M]^+$ 332.1082, found 332.1330. **R_f** = 0.66 (DCM:Et_2O 70:30)

8b (*min*):

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 – 7.70 (m, 2H), 7.39 – 7.21 (m, 5H), 7.21 – 7.12 (m, 1H), 7.06 – 6.93 (m, 2H), 4.18 (dd, *J* = 10.2, 3.3 Hz, 1H), 4.02 (dd, *J* = 10.2, 7.4 Hz, 1H), 3.52 (td, *J* = 7.4, 3.1 Hz, 1H), 2.44 (s, 3H), 2.20 (s, 1H), 1.93 – 1.78 (m, 1H), 1.20 – 1.11 (m, 1H), 1.11 – 1.03 (m, 1H), 0.97 (dt, *J* = 8.5, 5.2 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 145.2 (1C), 141.6 (1C), 132.7 (1C), 130.1 (2C), 128.6 (2C), 128.1 (2C), 126.1 (1C), 126.0 (2C), 73.5 (1C), 72.5 (1C), 24.7 (1C), 21.8 (1C), 20.3 (1C), 13.2 (1C). **HRMS** (ESI$^+$-TOF) m/z: calculated for $C_{18}H_{21}O_4S^+$ $[M]^+$ 333.1161, found 333.2171. **R_f** = 0.58 (DCM:Et_2O 70:30)

2-((1S,2S)-2-phenylcyclopropyl)oxirane 9a

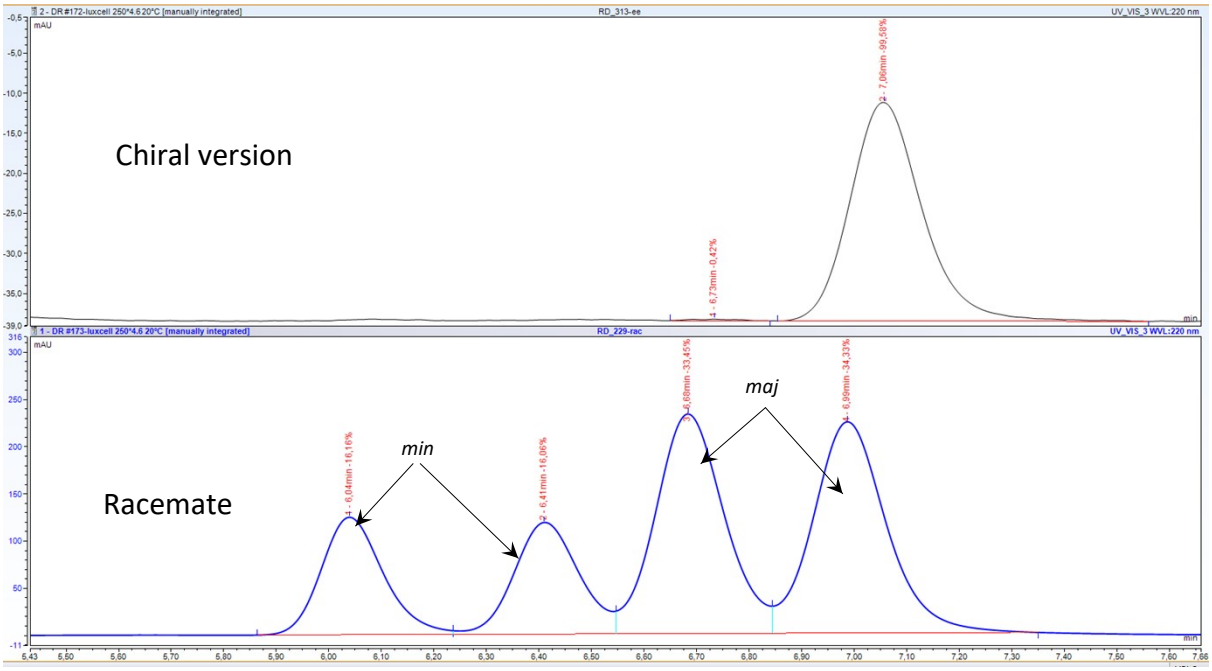


^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30 – 7.21 (m, 2H), 7.20 – 7.12 (m, 1H), 7.10 – 7.03 (m, 2H), 2.97 (ddd, *J* = 4.8, 4.0, 2.7 Hz, 1H), 2.80 (dd, *J* = 4.9, 4.0 Hz, 1H), 2.60 (dd, *J* = 4.9, 2.7 Hz, 1H), 1.98 – 1.88 (m, 1H), 1.32 – 1.22 (m, 1H)[1], 1.09 – 0.96 (m, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 142.1 (1C), 128.8 (2C), 126.1 (2C), 125.9 (2C), 53.3 (1C), 46.7 (1C), 23.2 (1C), 20.0 (1C), 12.5 (1C). **HRMS** (EI$^+$-TOF) m/z: calculated for $C_{11}H_{12}O_1^+$ $[M]^+$ 160.0888, found 160.0902. **R_f** = 0.5 (EP:EtOAc 75:25) The data are in agreement with those described in the literature.[5]

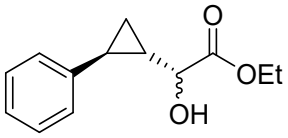
[1]The integration on ^{1}H NMR spectra integrate for more than one proton due to overlapping with "grease". The proton was observed clearly using ^{1}H COSY experiment.

HPLC analysis: Obtained using Phenomenex Lux® cellulose-2 column at 20 °C with Heptane:^{i}PrOH 95:05 (flow rate = 1 mL/min). **Tr** = 7.06 min

[5] Miller, V. P.; Fruetel, J. A.; Ortiz de Montellano, P. R. *Archives of Biochemistry and Biophysics* **1992**, *298*, 697–702.

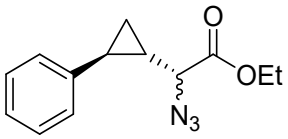


ethyl 2-hydroxy-2-((1S,2S)-2-phenylcyclopropyl)acetate 10



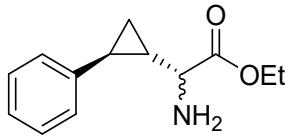
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29 – 7.20 (m, 4H), 7.19 – 7.11 (m, 1.8H), 7.11 – 7.02 (m, 3.3H), 4.32 – 4.22 (m, 3.5H), 4.08 – 3.98 (m, 1.7H), 2.84 (*min*, d, *J* = 5.9 Hz, 0.7H), 2.80 (*maj*, d, *J* = 6.1 Hz, 1H), 2.18 – 2.08 (*min*, m, 1H), 2.06 – 1.97 (*maj*, m, 1H), 1.49 – 1.35 (m, 1.8H), 1.28 (app. q, *J* = 7.1 Hz, 5.7H), 1.24 – 1.15 (m, 1.6H), 1.15 – 1.06 (m, 1H), 1.02 – 0.91 (m, 1.8H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 174.8 (*min*, 1C), 174.7 (*maj*, 1C), 142.1 (*min*, 1C), 142.0 (*min*, 1C), 128.4 (*min*, 1C), 128.4 (*maj*, 1C), 126.3 (*maj*, 1C), 126.2 (*min*, 1C), 125.9 (*min*, 1C), 125.9 (*maj*, 1C), 71.3 (*maj*, 1C), 71.1 (*min*, 1C), 62.1 (*min*, 1C), 62.0 (*maj*, 1C), 25.9 (*min*, 1C), 25.72, 19.8 (*min*, 1C), 19.5 (*maj*, 1C), 14.3 (2C), 12.03 (*maj*, 1C), 11.5 (*min*, 1C). **HRMS** (EI^+-TOF) m/z: calculated for $C_{13}H_{16}O_3^+$ $[M]^+$ 220.1099, found 220.1094. **R_f** = 0.24 (EP:EtOAc 80:20)

ethyl 2-azido-2-((1S,2S)-2-phenylcyclopropyl)acetate 11



^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37 – 7.23 (m, 4H), 7.22 – 7.15 (m, 1.9H), 7.14 – 7.01 (m, 3.4H), 4.39 – 4.17 (m, 3.5H), 3.49 (d, *J* = 8.6 Hz, 1.7H), 2.18 – 2.09 (*maj*, m, 1H), 2.09 – 2.00 (*min*, m, 0.7H), 1.64 – 1.49 (m, 2H), 1.38 – 1.25 (m, 5.6H), 1.23 – 1.07 (m, 4H). **^{13}C NMR** (75 MHz, $CDCl_3$): δ 169.9 (*maj*, 1C), 169.8 (*min*, 1C), 140.9 (*min*, 1C), 140.8 (*maj*, 1C), 128.6 (*min*, 2C), 128.6 (*maj*, 2C), 126.4 (*min*, 1C), 126.4 (*maj*, 1C), 126.3 (2C), 65.5 (*min*, 1C), 65.0 (*maj*, 1C), 62.0 (2C), 23.4 (*maj*, 1C), 23.3 (*min*, 1C), 21.9 (*min*, 1C), 21.3 (*maj*, 1C), 14.3 (2C), 13.4 (*maj*, 1C), 13.1 (*min*, 1C). **HRMS** (API^+-TOF) m/z: calculated for $C_{13}H_{14}O_2^+$ $[M-H]^+$ 244.1086, found 244.1345. **R_f** = 0.56 (EP:EtOAc 80:20)

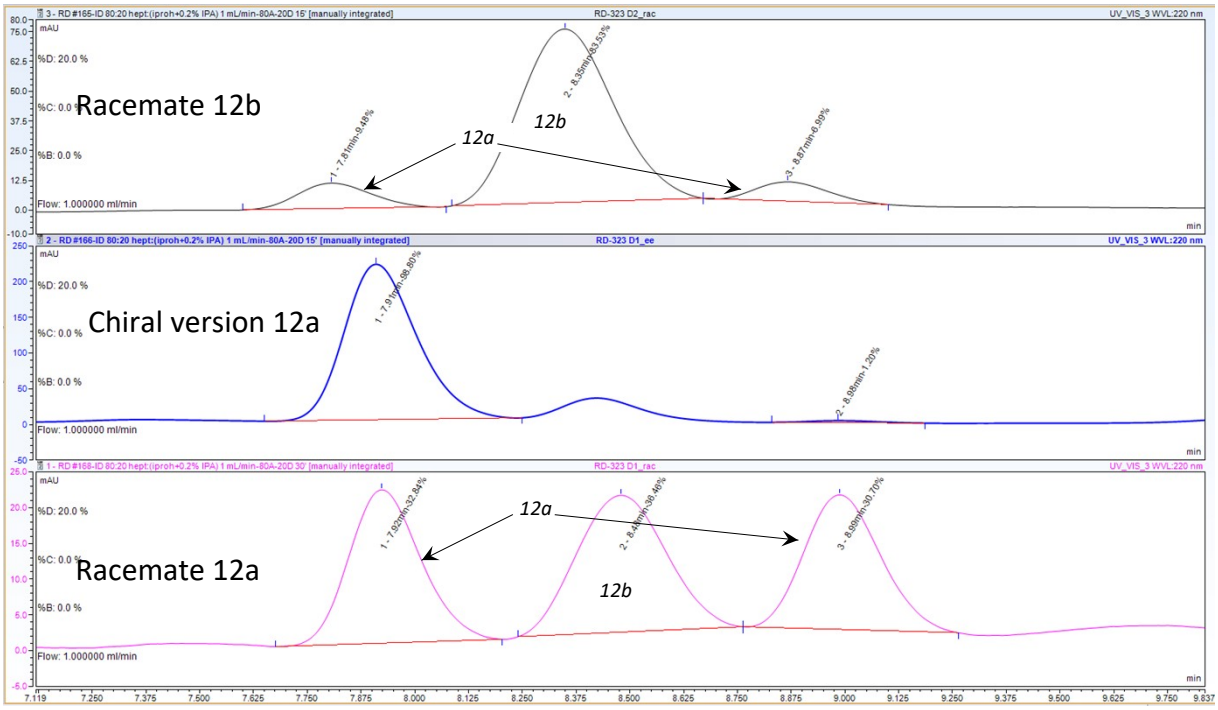
ethyl 2-amino-2-((1S,2S)-2-phenylcyclopropyl)acetate 12



12a

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25 – 7.14 (m, 3H), 7.14 – 7.04 (m, 1H), 7.04 – 6.98 (m, 2H), 4.15 (qd, *J* = 7.2, 2.5 Hz, 2H), 3.07 (d, *J* = 7.9 Hz, 1H), 2.36 (s, 1H), 1.86 (dt, *J* = 9.6, 5.0 Hz, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 1.08 (dt, *J* = 9.0, 5.4 Hz, 1H), 0.91 (dt, *J* = 8.7, 5.3 Hz, 1H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ 142.3 (1C), 128.5 (2C), 126.1 (2C), 125.9 (1C), 61.4 (1C), 57.8 (1C), 27.6 (1C), 21.4 (1C), 14.4 (1C), 13.6 (1C). **HRMS** (API^{+}-TOF) m/z: calculated for $C_{13}H_{18}NO_2^{+}$ $[M]^{+}$ 220.1338, found 244.1334. **R_f** = 0.33 (DCM:EtOAc 60:40 + 1% Et_3N)

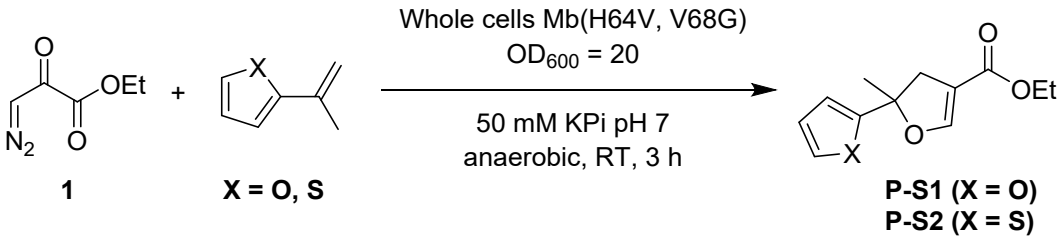
HPLC analysis: Obtained using Daicel Chiralpak® ID column at 20 °C with Heptane:(^{i}PrOH+0.2% IsoPropylAmine) 98:02 (flow rate = 1 mL/min). **Tr** = 7.91 min



12b

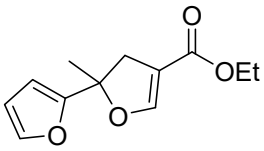
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.31 – 7.20 (m, 2H), 7.19 – 7.11 (m, 1H), 7.10 – 7.03 (m, 2H), 4.20 (qd, *J* = 7.1, 2.2 Hz, 2H), 3.15 (d, *J* = 7.3 Hz, 1H), 2.14 – 2.01 (m, 1H), 1.73 (s,1H), 1.40 – 1.18 (m, 5H). **^{13}C NMR** (75 MHz, $CDCl_3$) ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.1 (1C), 128.5 (1C), 126.2 (1C), 125.9 (1C), 61.2 (1C), 57.4 (1C), 27.4 (1C), 21.2 (1C), 14.4 (1C), 13.1 (1C). **HRMS** (API^{+}-TOF) m/z: calculated for $C_{13}H_{18}NO_2^{+}$ $[M]^{+}$ 220.1338, found 244.1329. **HRMS** (API^{+}-TOF) m/z: calculated for $C_{13}H_{18}NO_2^{+}$ $[M]^{+}$ 220.1338, found 244.1334. **R_f** = 0.14 (DCM:EtOAc 60:40 + 1% Et_3N)

Cloke-Wilson rearrangement product:



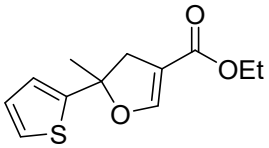
Obtained by following the general procedure A.

ethyl 2-methyl-2,3-dihydro-[2,2'-bifuran]-4-carboxylate P-S1:



^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 – 7.38 (m, 1H), 6.36 – 6.30 (m, 1H), 5.92 (t, *J* = 2.9 Hz, 1H), 4.27 (q, *J* = 7.1 Hz, 1H), 3.26 (dd, *J* = 17.5, 2.8 Hz, 1H), 2.75 (dd, *J* = 17.4, 2.9 Hz, 1H), 1.76 (s, 1H), 1.32 (t, *J* = 7.1 Hz, 2H).

ethyl 5-methyl-5-(thiophen-2-yl)-4,5-dihydrofuran-3-carboxylate P-S2:



^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.02 (dd, *J* = 3.5, 1.1 Hz, 1H), 6.95 (dd, *J* = 5.0, 3.6 Hz, 1H), 4.29 (qd, *J* = 7.1, 1.5 Hz, 3H), 3.14 (dd, *J* = 17.5, 3.0 Hz, 1H), 2.96 (dd, *J* = 17.5, 2.9 Hz, 1H), 1.84 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 4H).

X-ray crystallographic analyses

A crystal (0.124 x 0.107 x 0.08 mm3) was placed onto a thin glass optical fiber or a nylon loop and mounted on a Rigaku XtaLAB Synergy-S Dualflex diffractometer equipped with a HyPix-6000HE HPC area detector for data collection at 100.00(10) K. A preliminary set of cell constants and an orientation matrix were calculated from a small sampling of reflections.1 A short pre-experiment was run, from which an optimal data collection strategy was determined. The full data collection was carried out using a PhotonJet (Cu) X-ray source with a frame time of 0.05 seconds and a detector distance of 34.0 mm. Series of frames were collected in 0.50º steps in *w* at different 2*q*, *k*, and *f* settings. After the intensity data were corrected for absorption, the final cell constants were calculated from the xyz centroids of 17668 strong reflections from the actual data collection after integration.

The structure was solved using SHELXT2 and refined using SHELXL.3. The space group $P2_1$ was determined based on systematic absences and intensity statistics. Most or all non-hydrogen atoms were assigned from the solution. Full-matrix least squares / difference Fourier cycles were performed which located any remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters.

Figure S4. ORTEP of **Ethyl 2-((1S,2S)-2-(4-bromophenyl)cyclopropyl)-2-oxoacetate** with ellipsoids drawn at the 50% probability level. Hydrogen atoms were located in the difference Fourier map and refined freely. They are represented here as spheres of arbitrary radius for clarity.

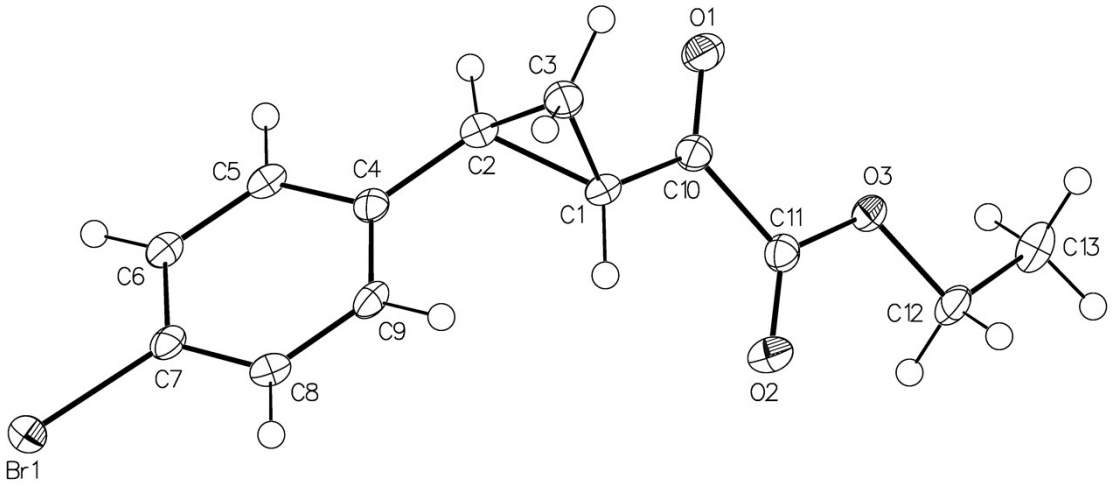


Table S3. Crystal data and structure refinement for

Identification code	fasrd01	
Empirical formula	C13 H13 Br O3	
Formula weight	297.14	
Temperature	100.00(10) K	
Wavelength	1.54184 Å	
Crystal system	monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 5.88458(4) Å	α = 90°
	b = 7.18609(5) Å	β = 101.2289(6)°
	c = 14.65407(9) Å	γ = 90°
Volume	607.816(7) Å^3	
Z	2	
Density (calculated)	1.624 Mg/m^3	
Absorption coefficient	4.570 mm^{-1}	
F(000)	300	
Crystal color, morphology	colourless, block	
Crystal size	0.124 x 0.107 x 0.08 mm^3	
Theta range for data collection	6.158 to 80.022°	
Index ranges	$-7 \le h \le 7$, $-9 \le k \le 9$, $-18 \le l \le 18$	

Reflections collected	20597
Independent reflections	2596 [R(int) = 0.0316]
Observed reflections	2589
Completeness to theta = 74.504°	99.8%
Absorption correction	Multi-scan
Max. and min. transmission	1.00000 and 0.90894
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2596 / 1 / 155
Goodness-of-fit on F^2	1.164
Final R indices [I>2sigma(I)]	$R1$ = 0.0198, $wR2$ = 0.0468
R indices (all data)	$R1$ = 0.0199, $wR2$ = 0.0468
Absolute structure parameter	-0.008(9)
Largest diff. peak and hole	0.364 and -0.505 e.Å^{-3}

References

[1] Carminati, D. M.; Decaens, J.; Couve-Bonnaire, S.; Jubault, P.; Fasan, R. *Angew. Chem. Int. Ed.* **2021**, *60*, 7072–7076.

[2] Qi, H.; Li, X.; Xu, J. *Org. Biomol. Chem.* **2011**, *9*, 2702–2714.

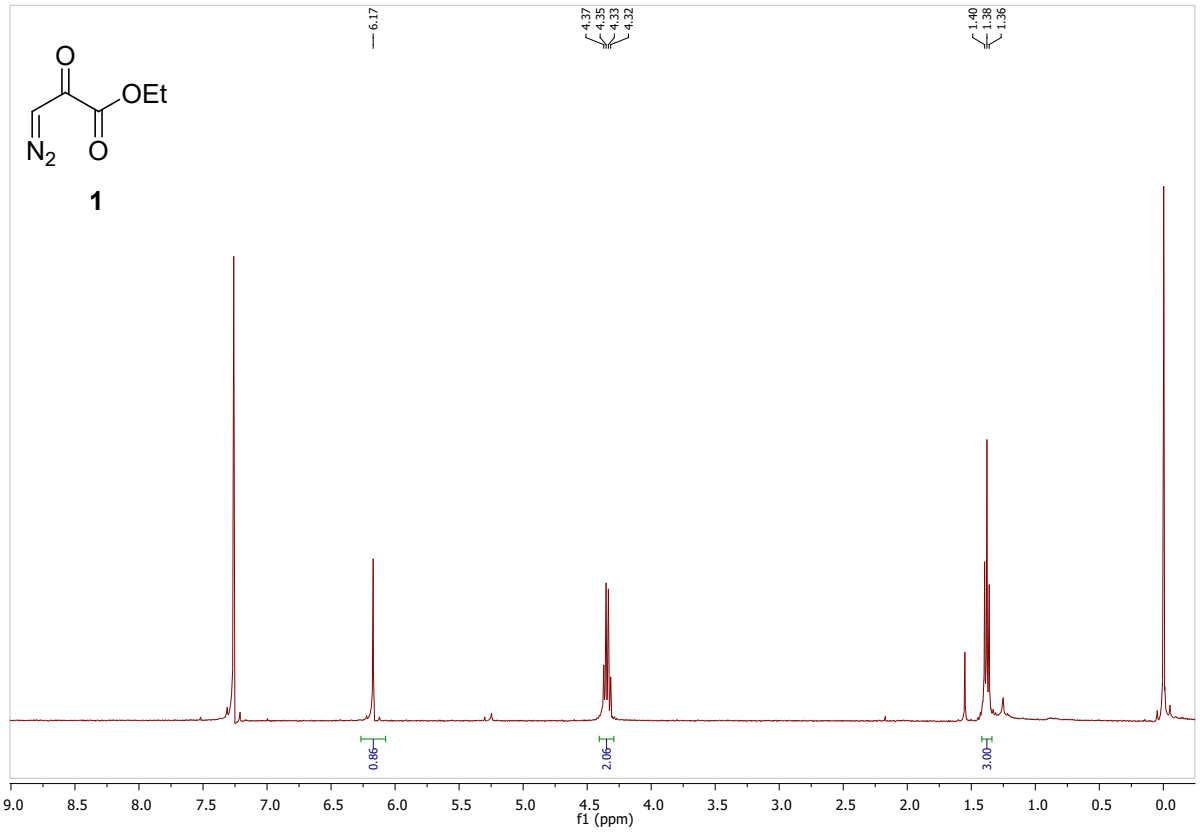
[3] Xu, H.; Zhang, W.; Shu, D.; Werness, J. B.; Tang, W. *Angew. Chem. Int. Ed.* **2008**, *47*, 8933–8936.

[4] Landais, Y.; Parra-Rapado, L. *Eur. J. Org. Chem.* **2000**, *2000*, 401–418.

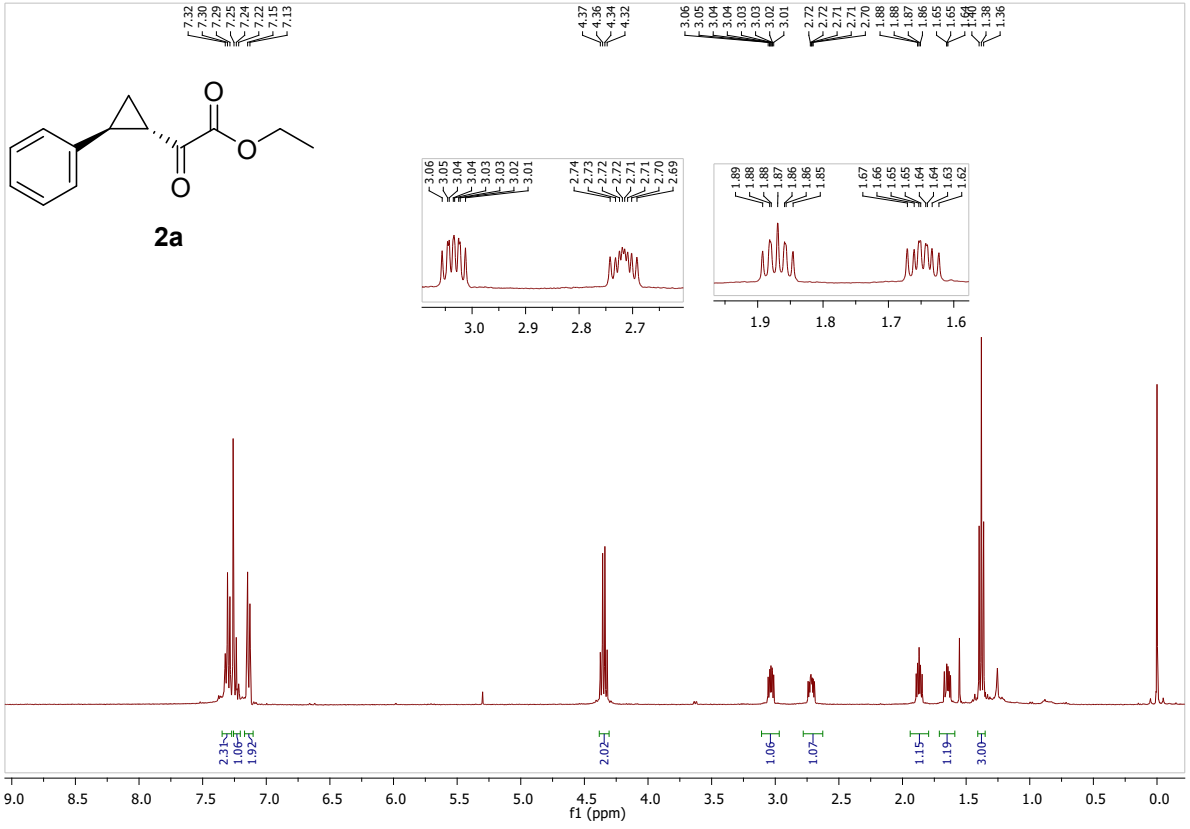
[5] Miller, V. P.; Fruetel, J. A.; Ortiz de Montellano, P. R. *Archives of Biochemistry and Biophysics* **1992**, *298*, 697–702.

NMR spectra

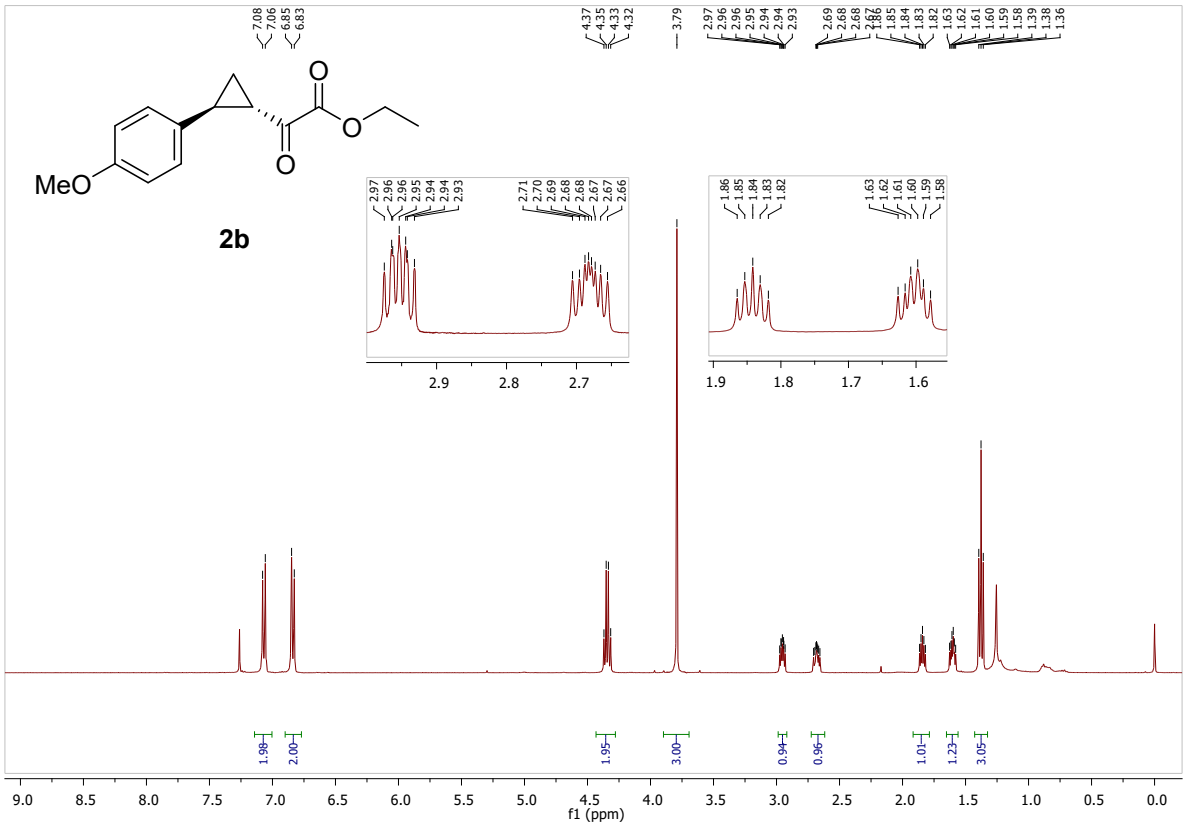
^{1}H NMR (400 MHz, $CDCl_3$)



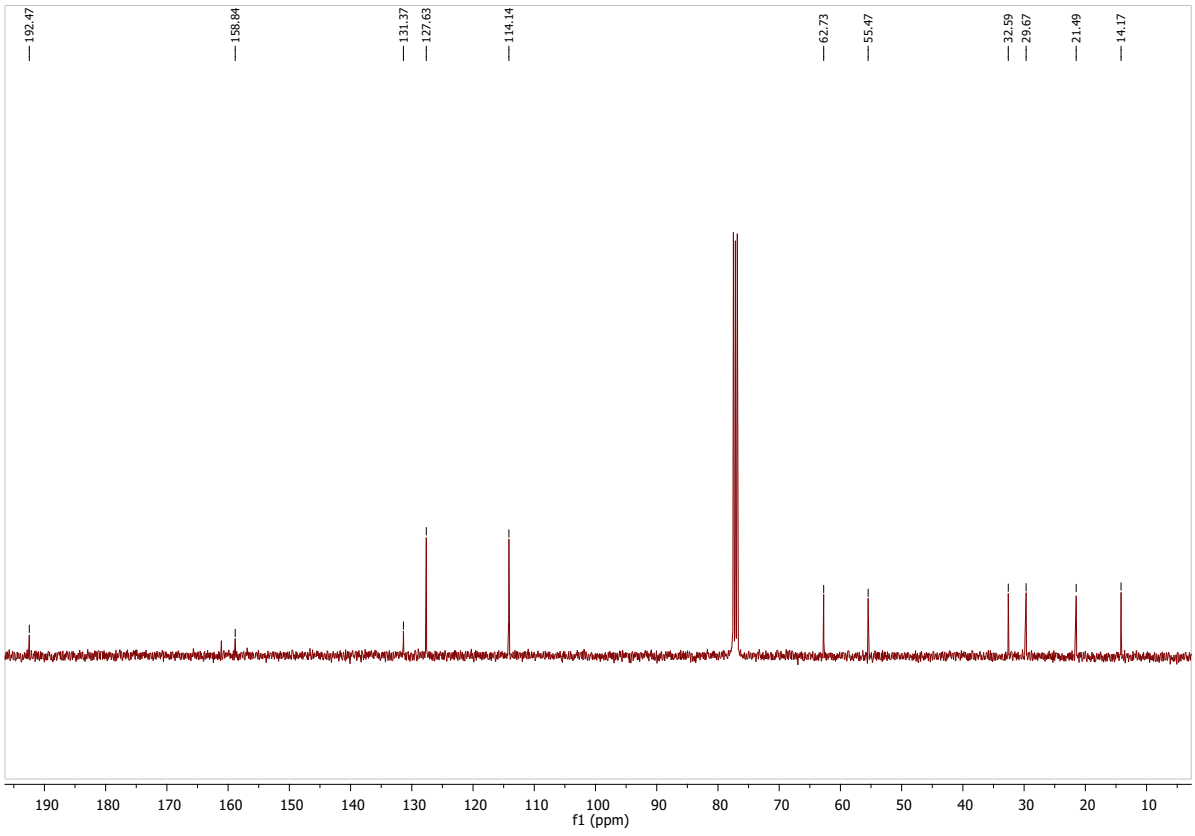
^{1}H NMR (400 MHz, $CDCl_3$)



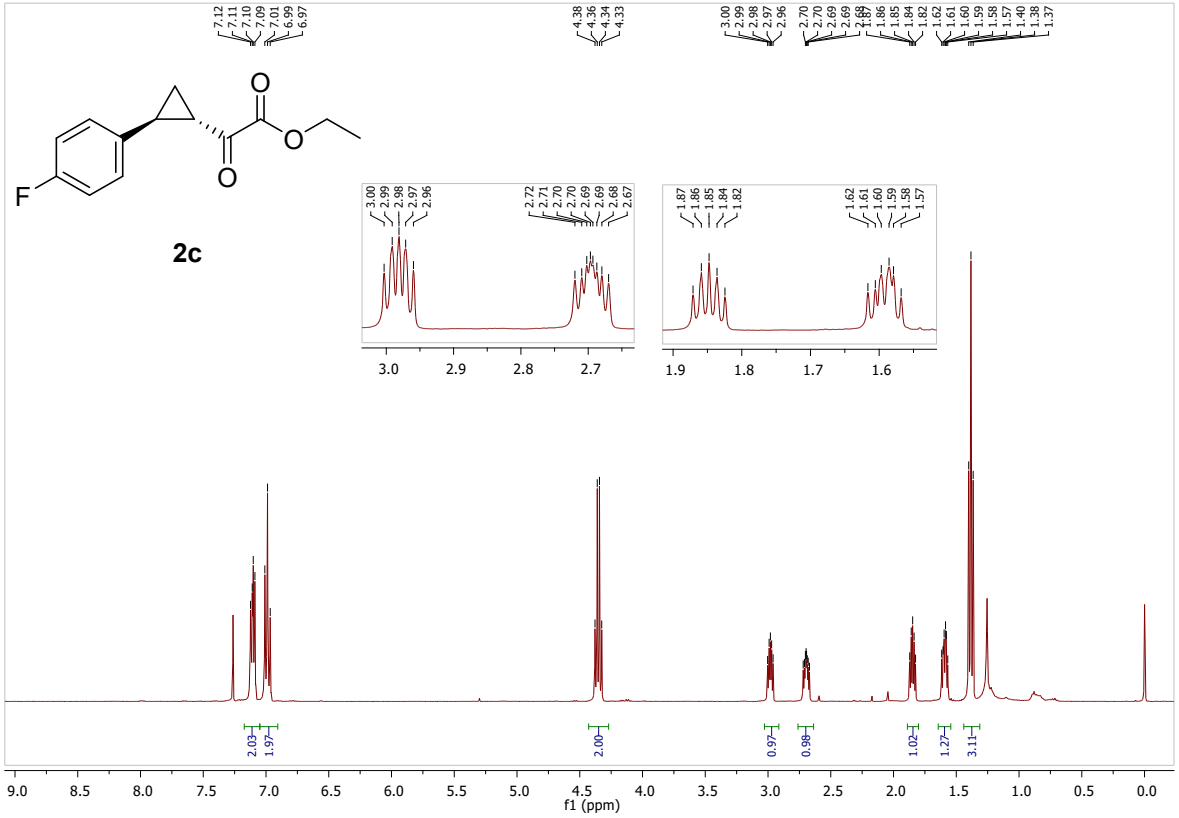
^{1}H NMR (400 MHz, $CDCl_3$)



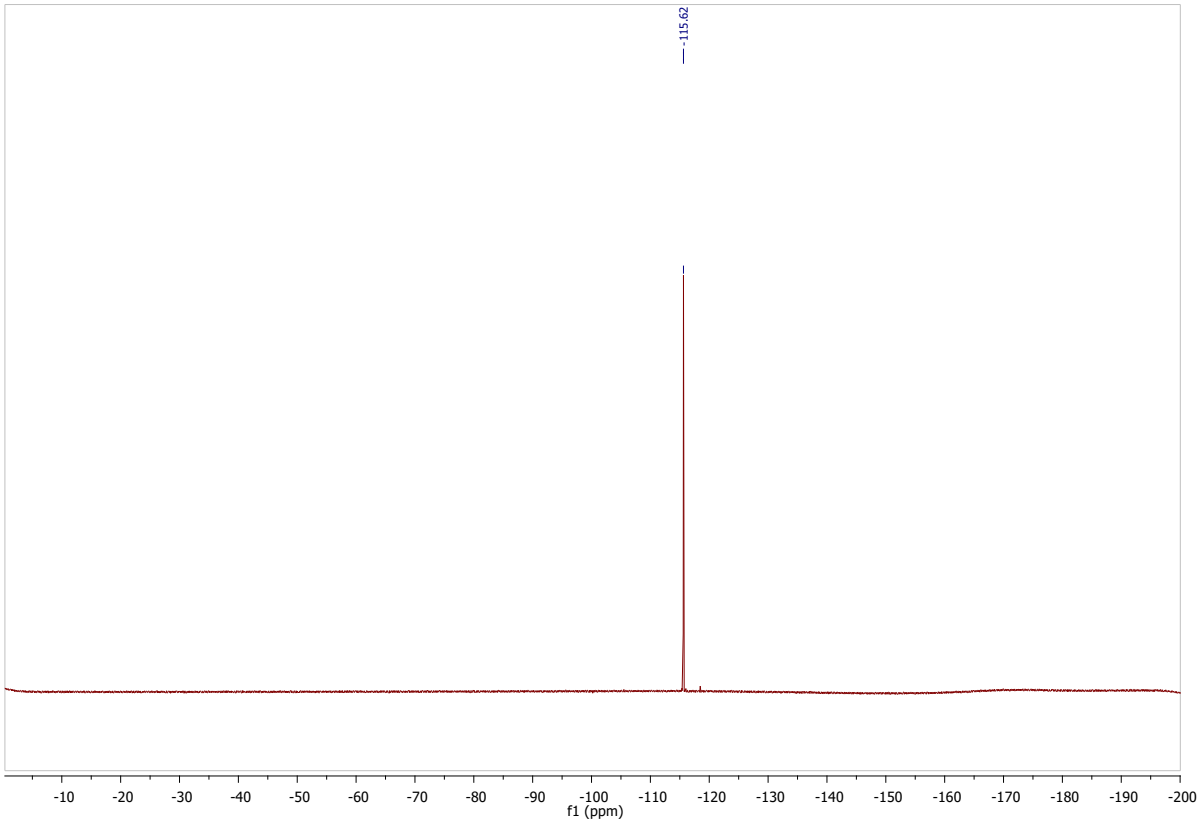
^{13}C NMR (101 MHz, $CDCl_3$)



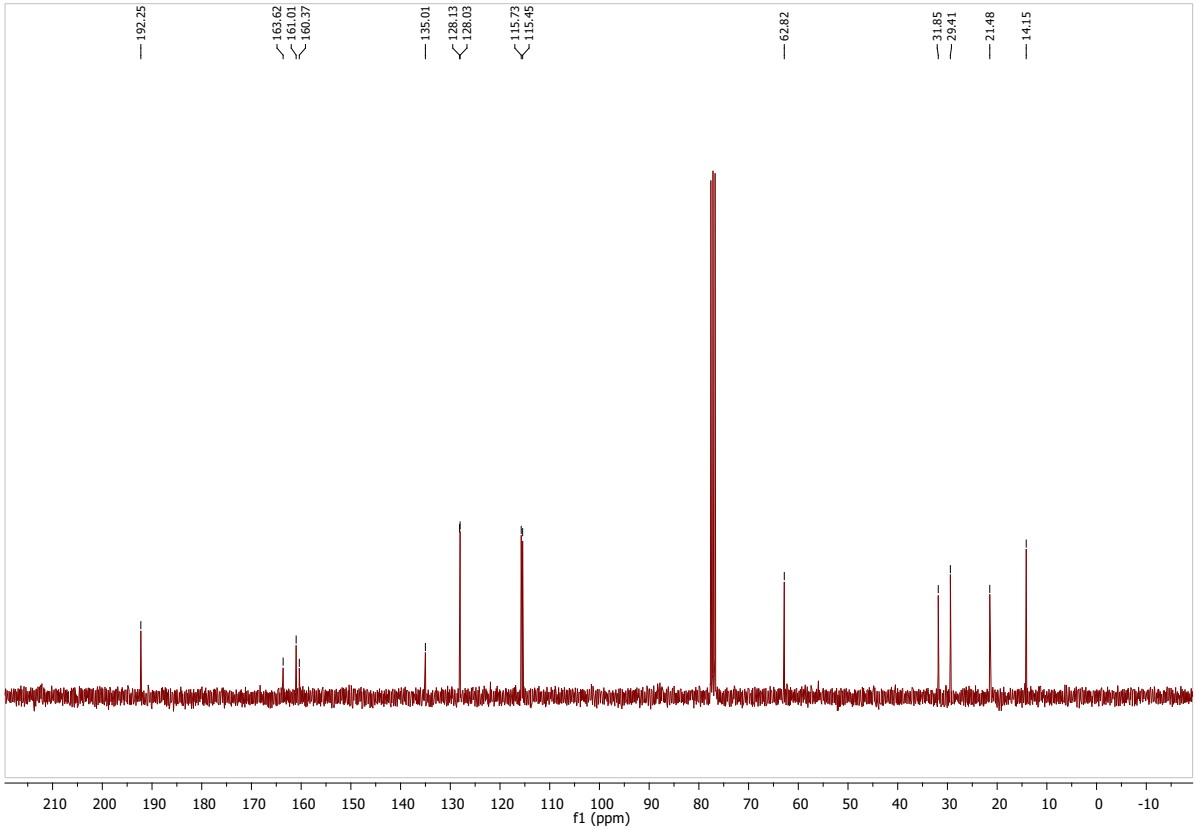
^{1}H NMR (400 MHz, $CDCl_3$)



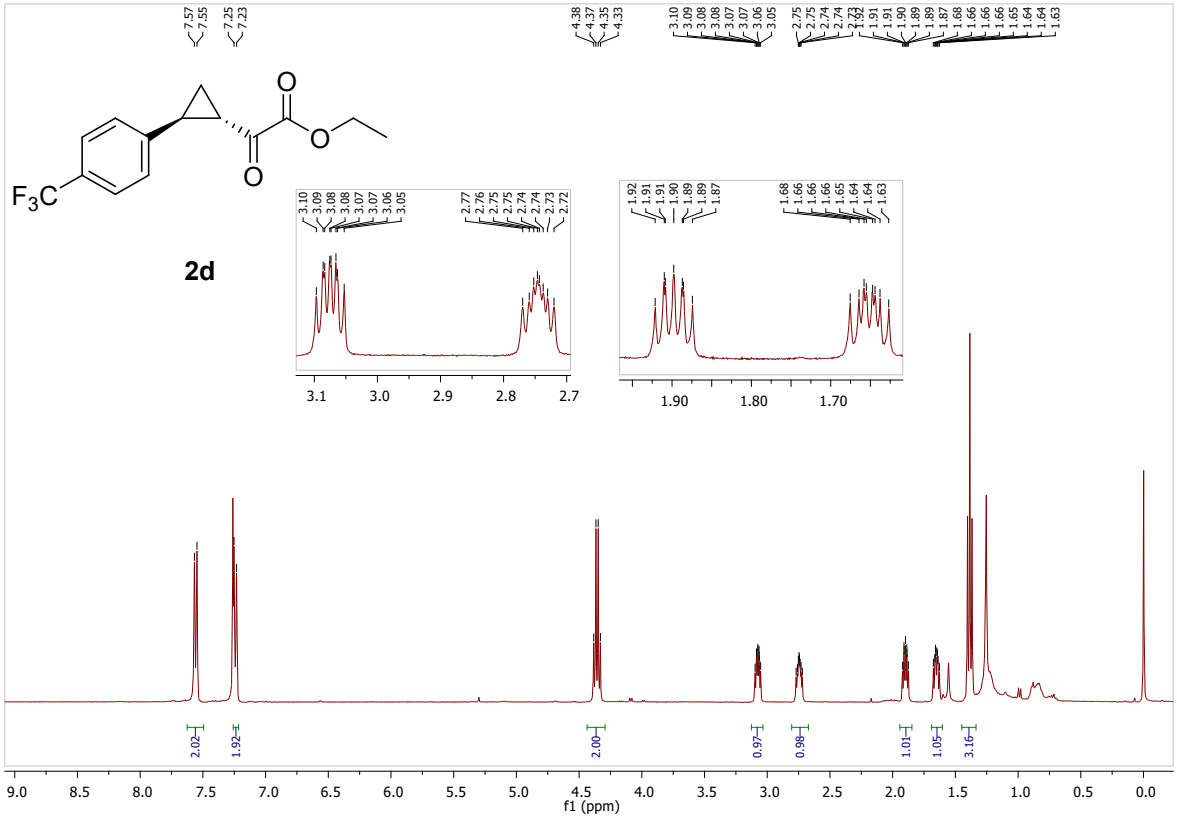
^{19}F NMR (376 MHz, $CDCl_3$)



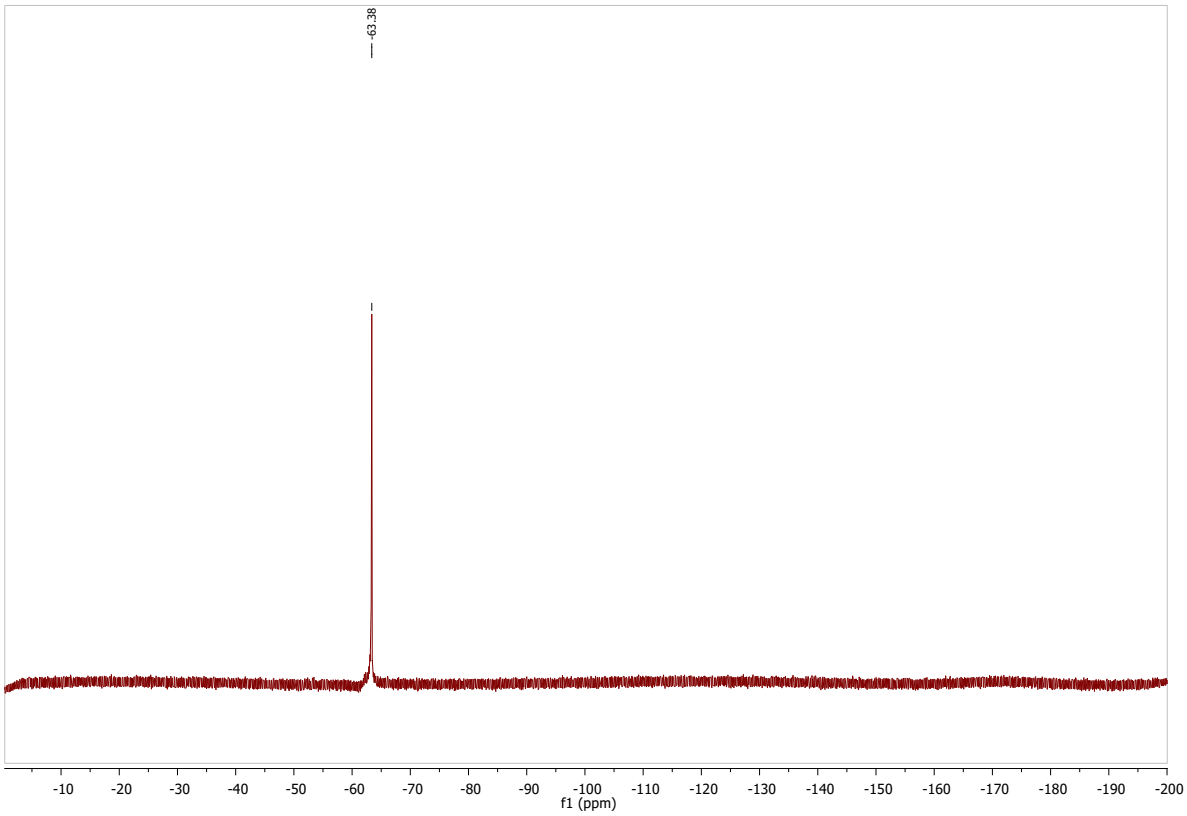
^{13}C NMR (75 MHz, $CDCl_3$)



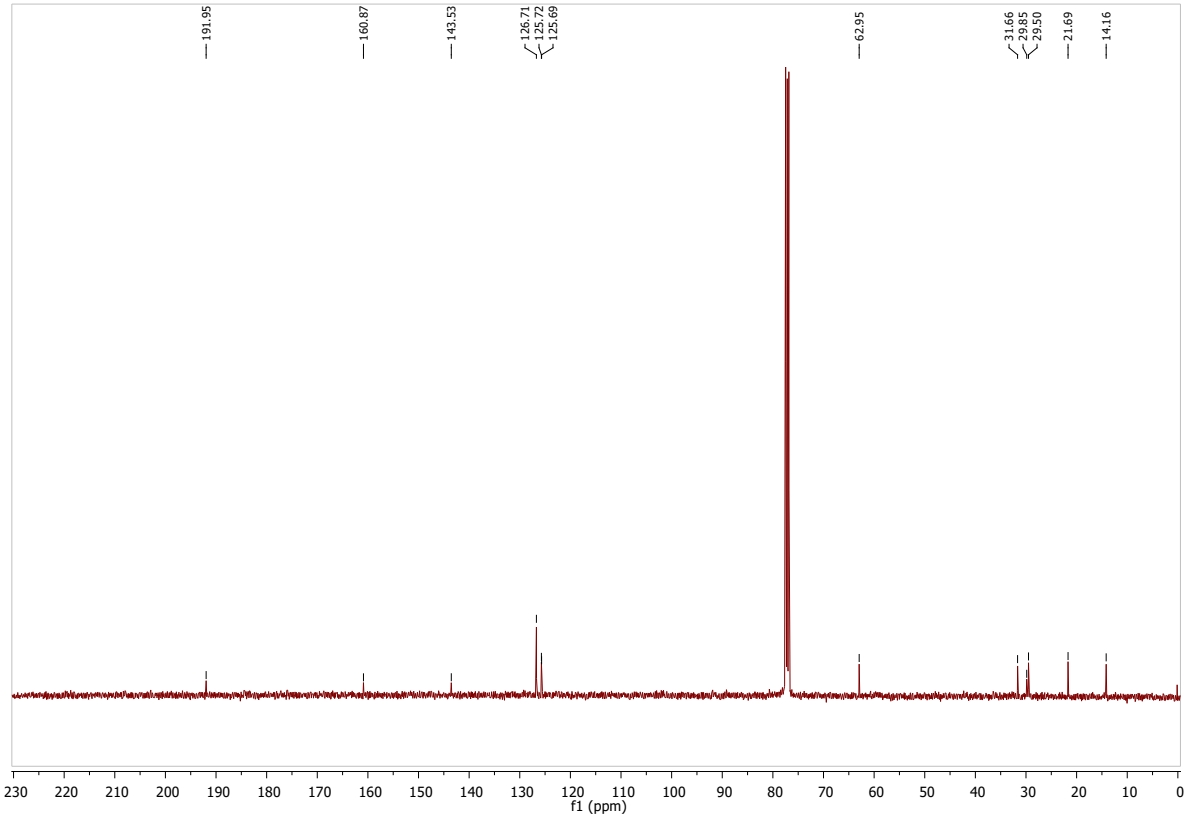
^{1}H NMR (400 MHz, $CDCl_3$)



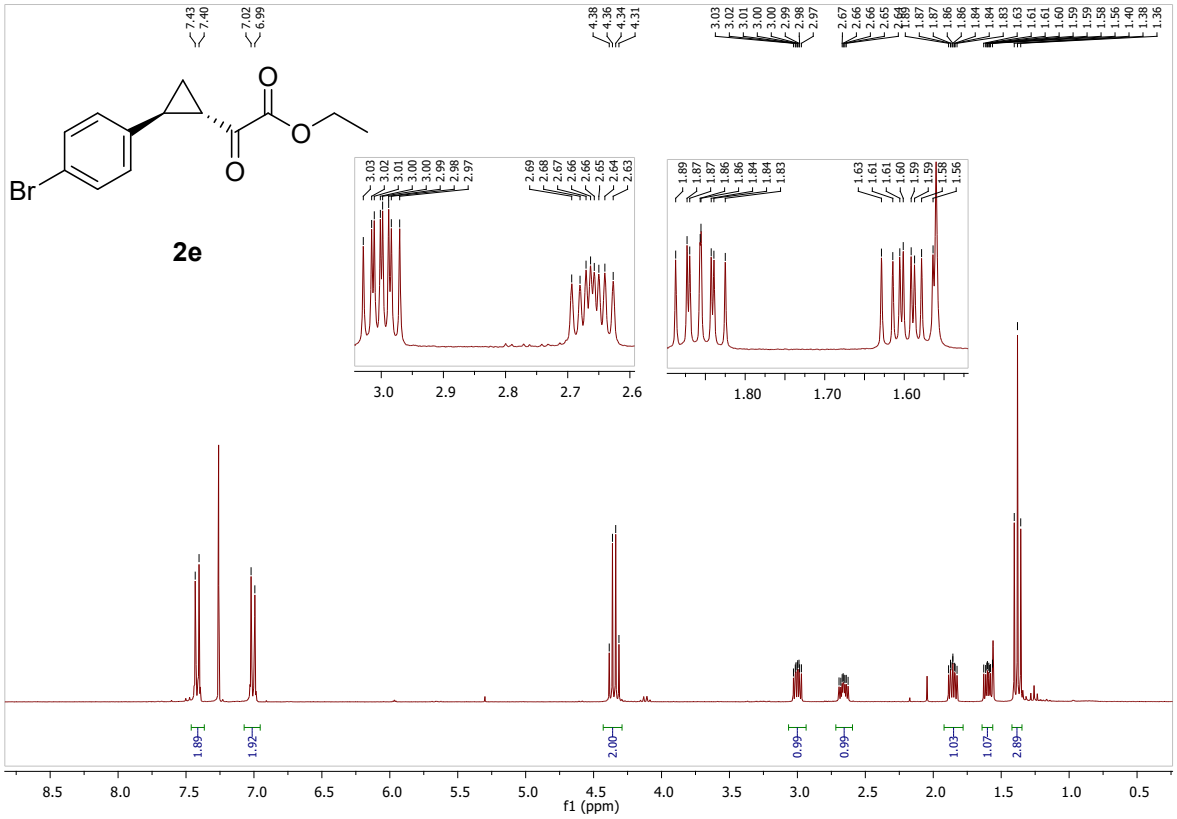
^{19}F NMR (376 MHz, $CDCl_3$)



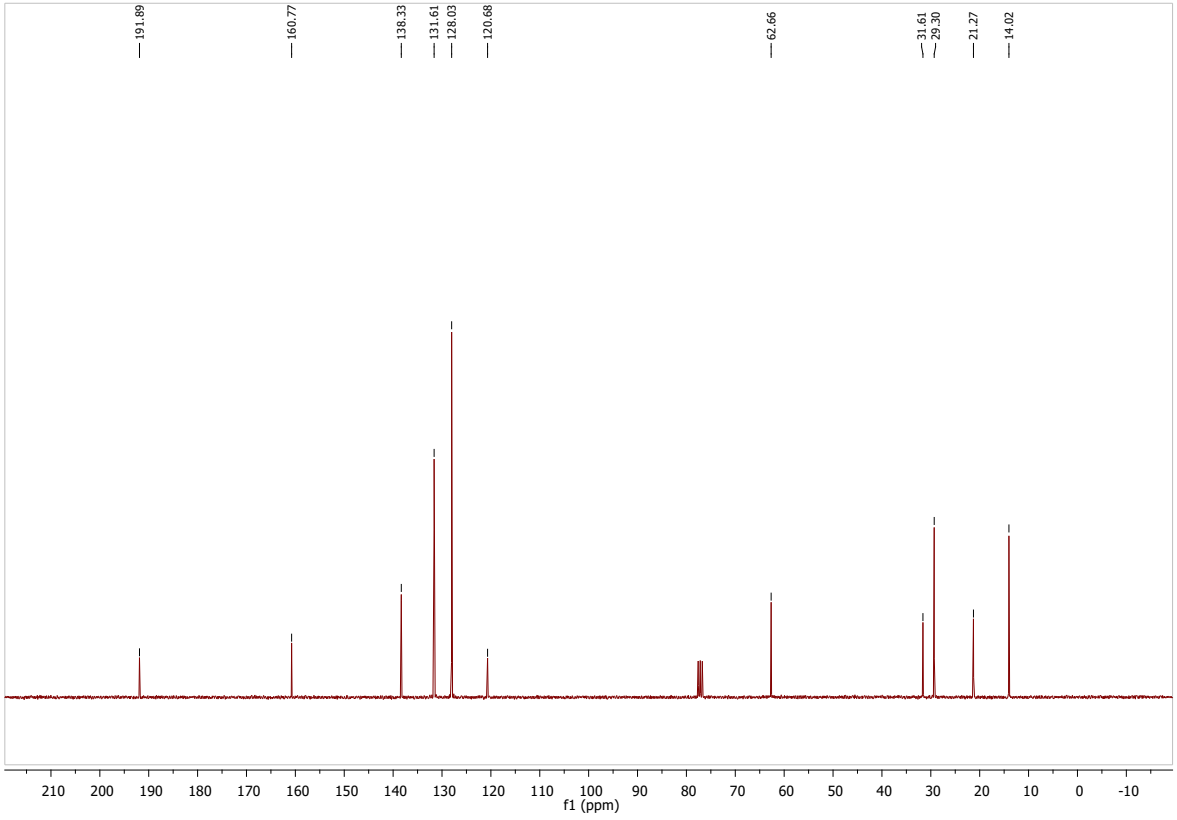
^{13}C NMR (101 MHz, $CDCl_3$)



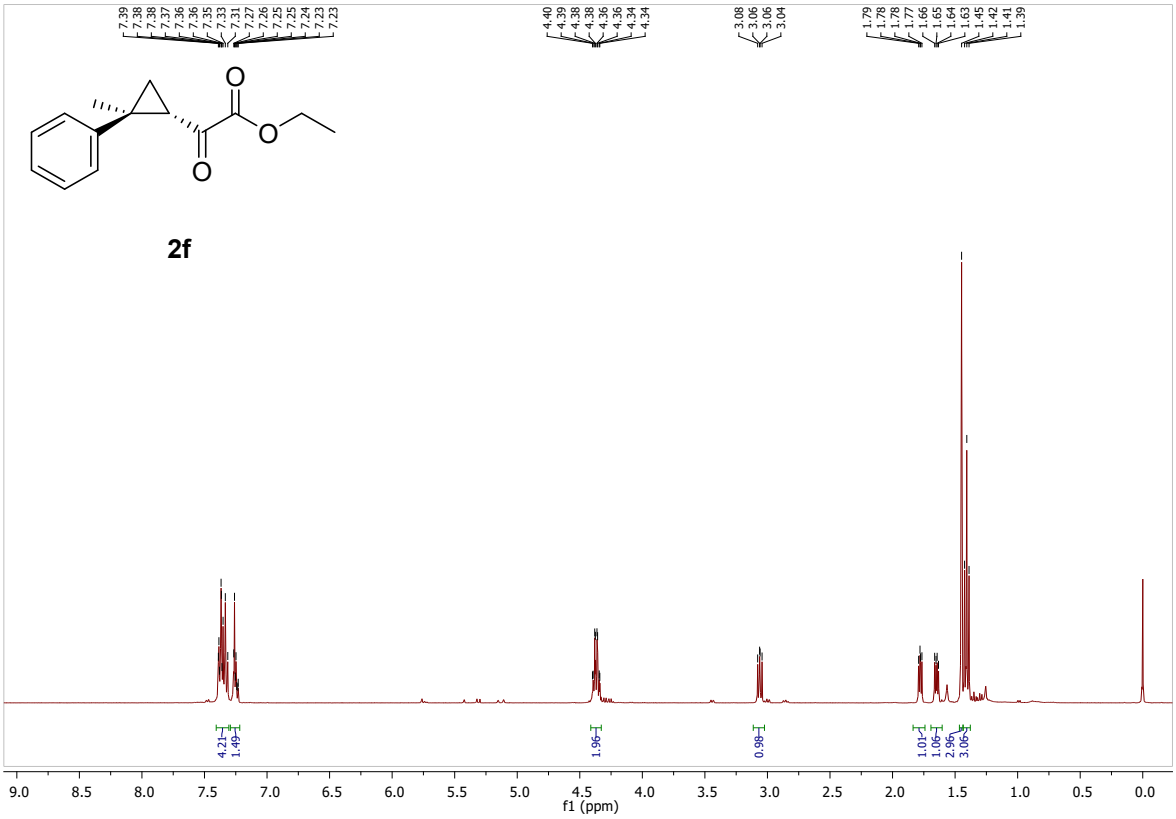
^{1}H NMR (300 MHz, $CDCl_3$)



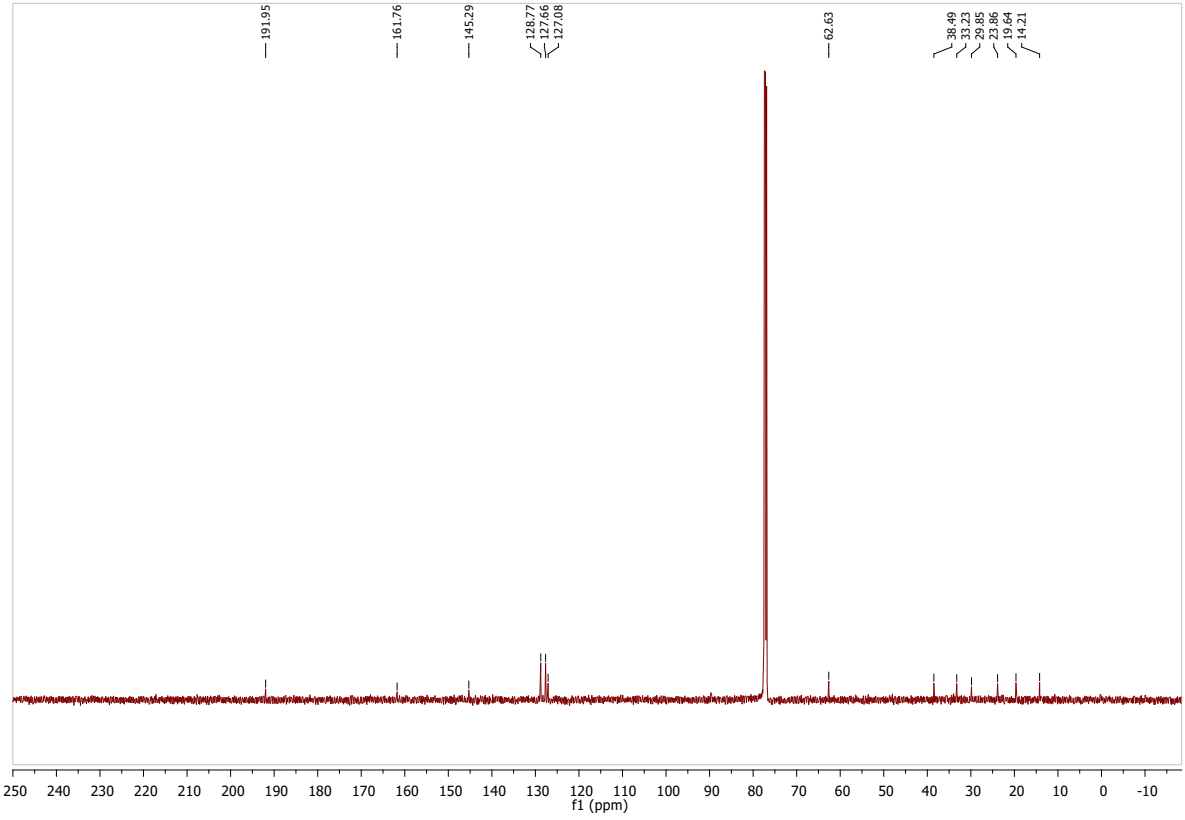
^{13}C NMR (75 MHz, $CDCl_3$)



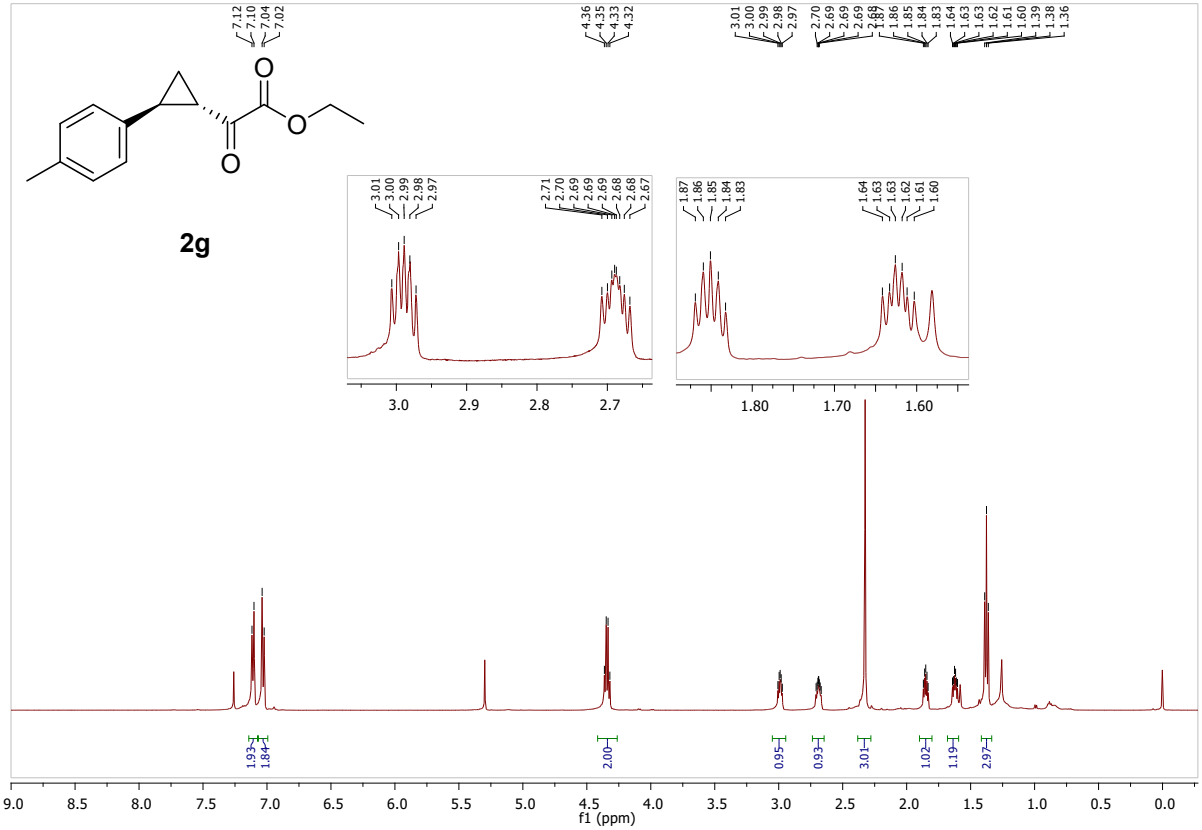
^{1}H NMR (400 MHz, $CDCl_3$)



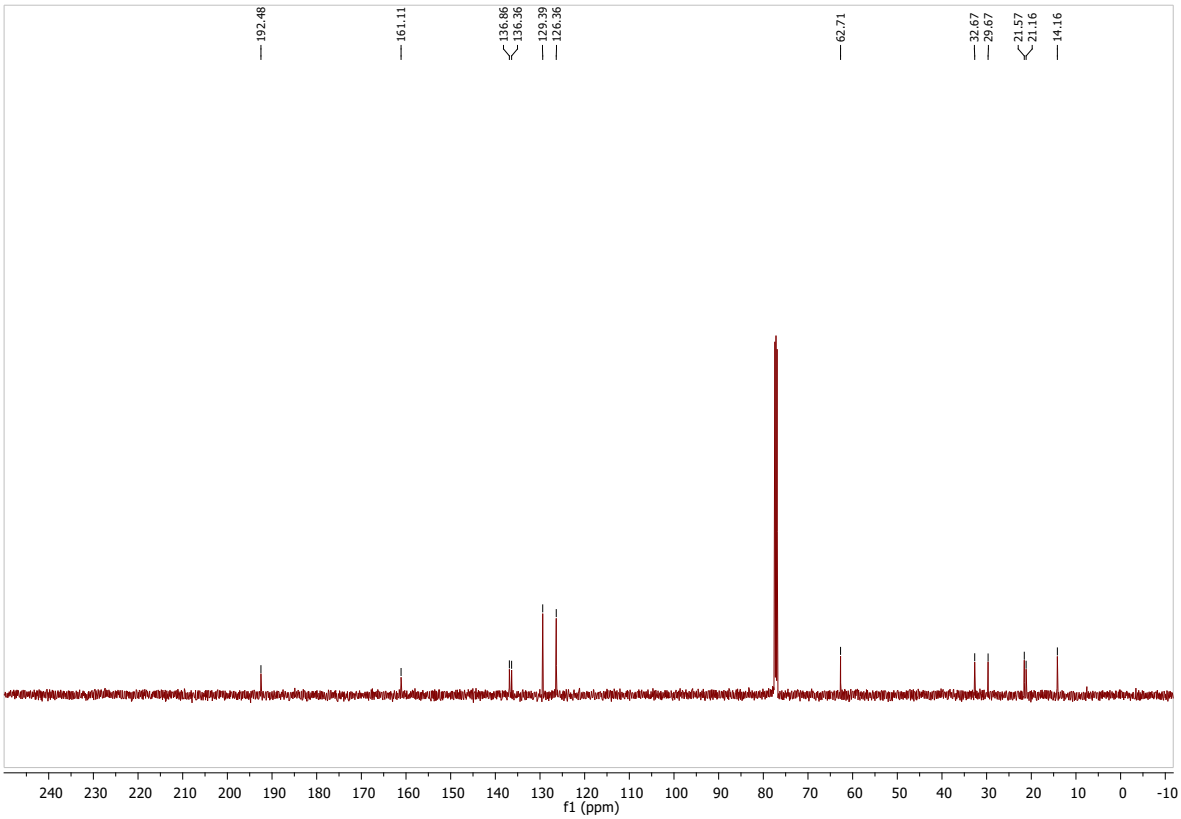
^{13}C NMR (126 MHz, $CDCl_3$)



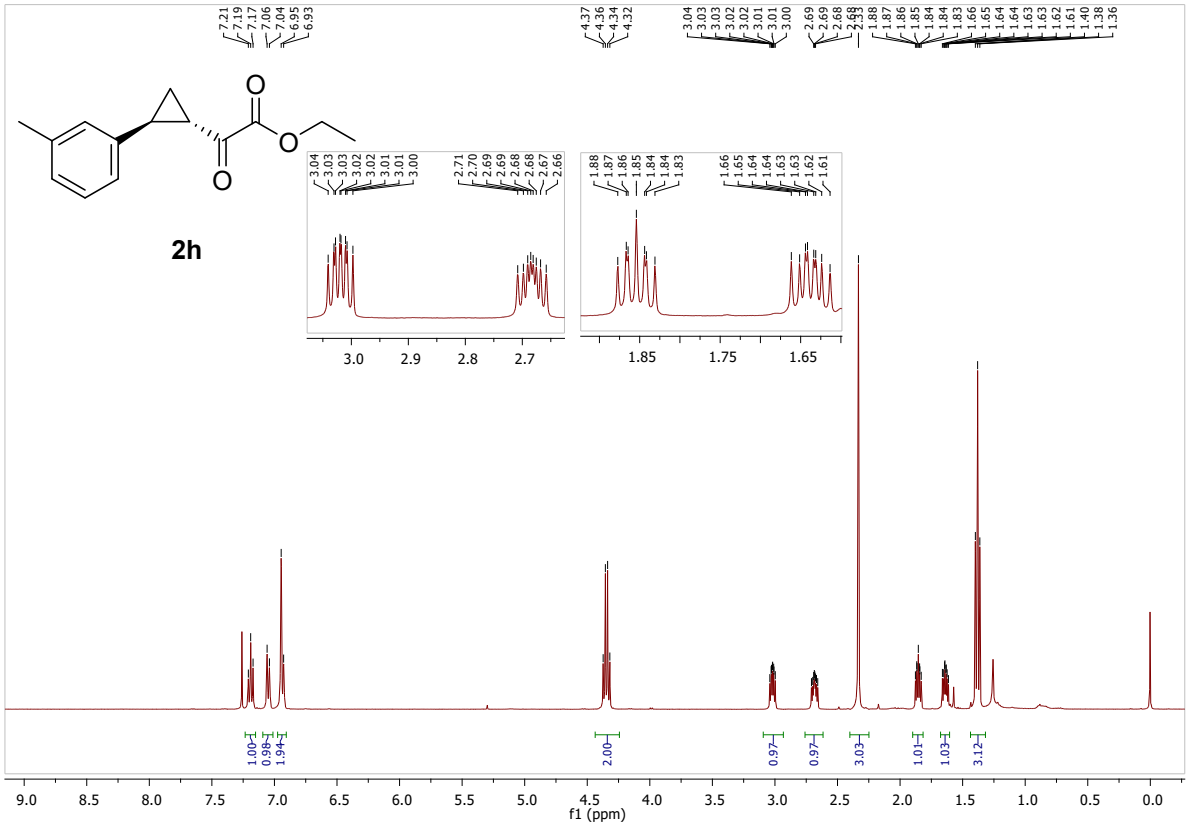
^{1}H NMR (500 MHz, $CDCl_3$)



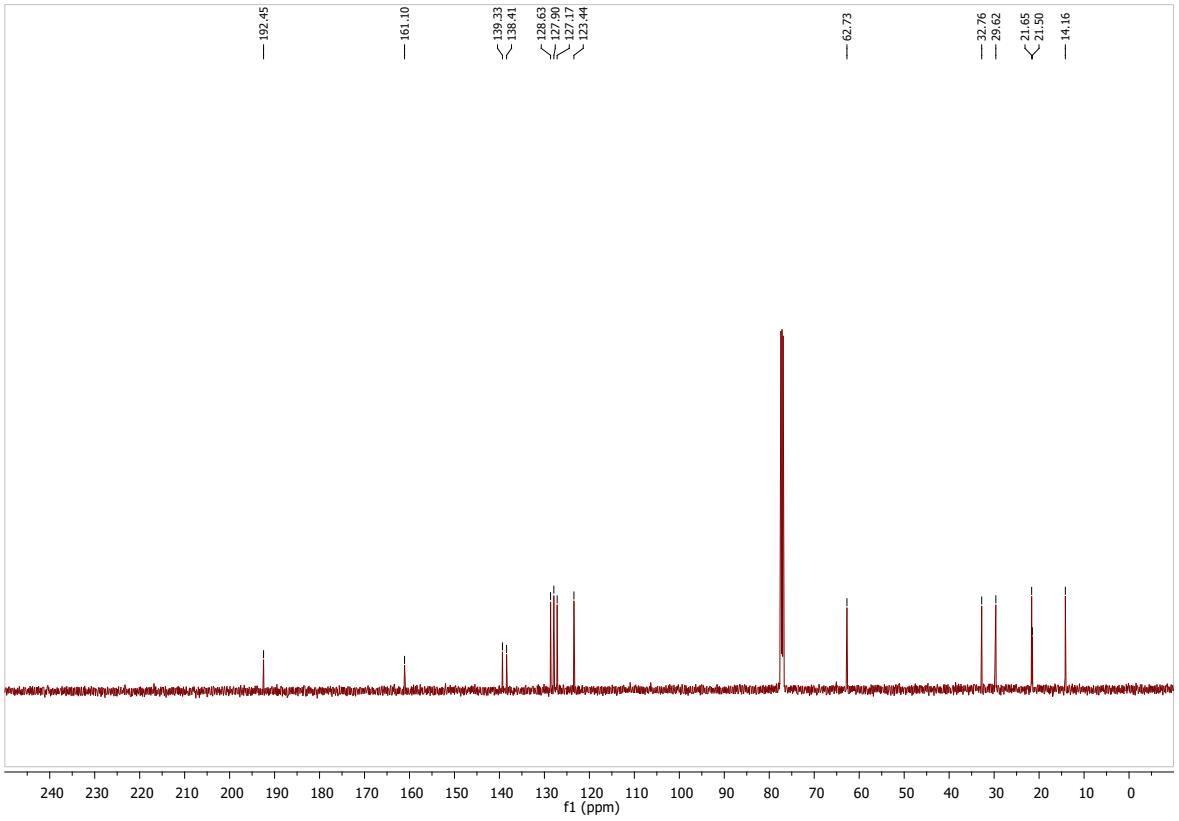
^{13}C NMR (126 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)



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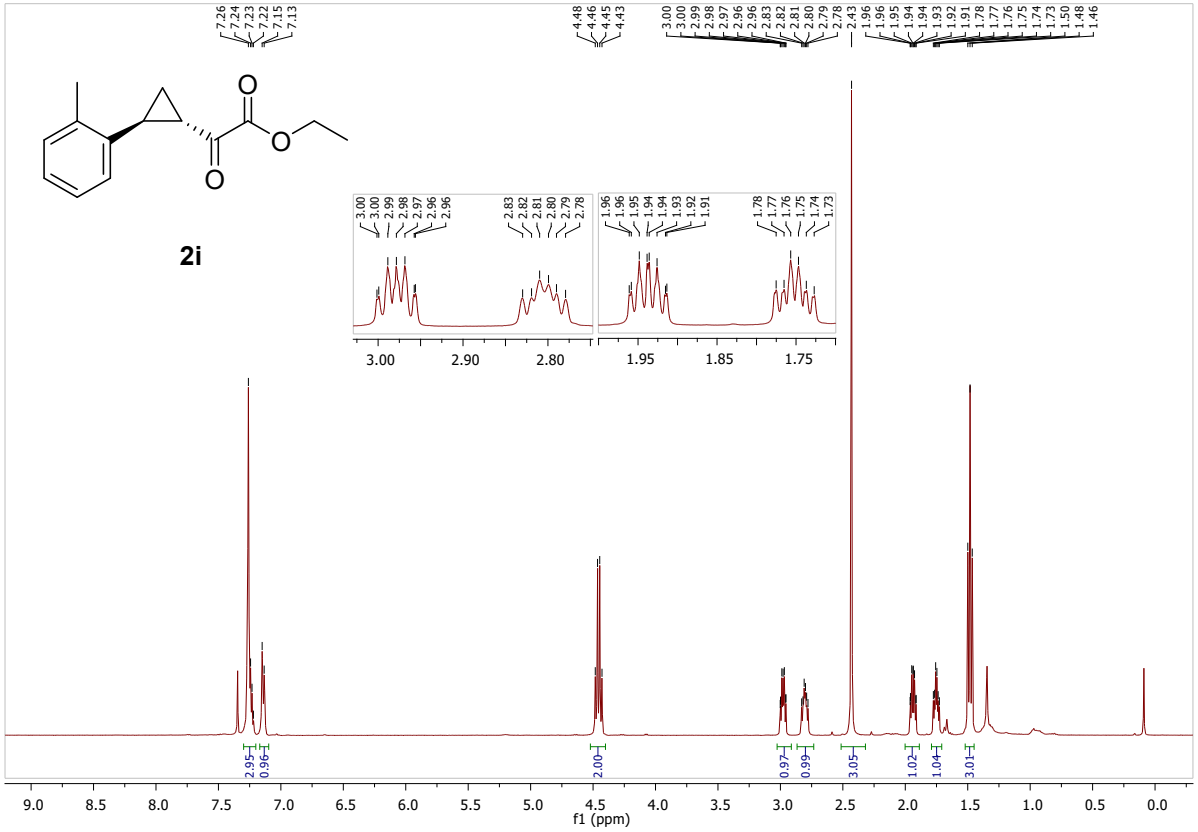
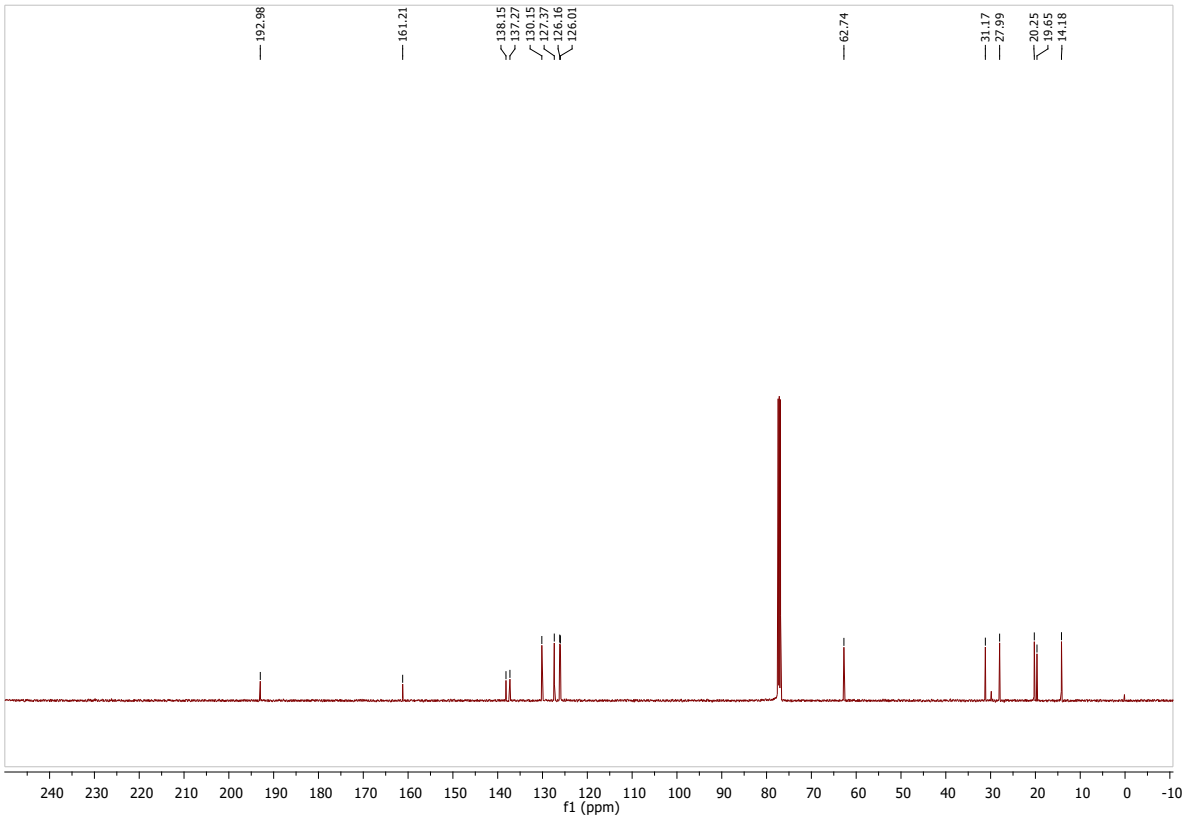
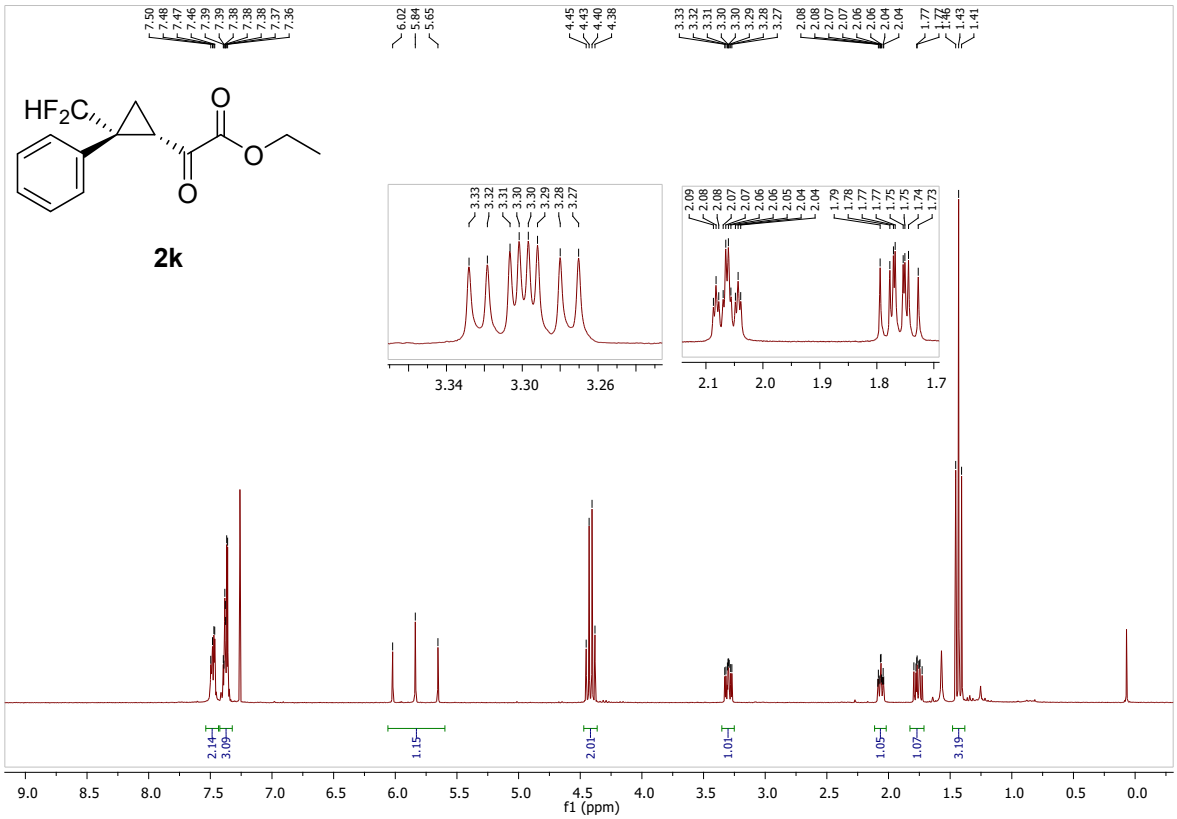


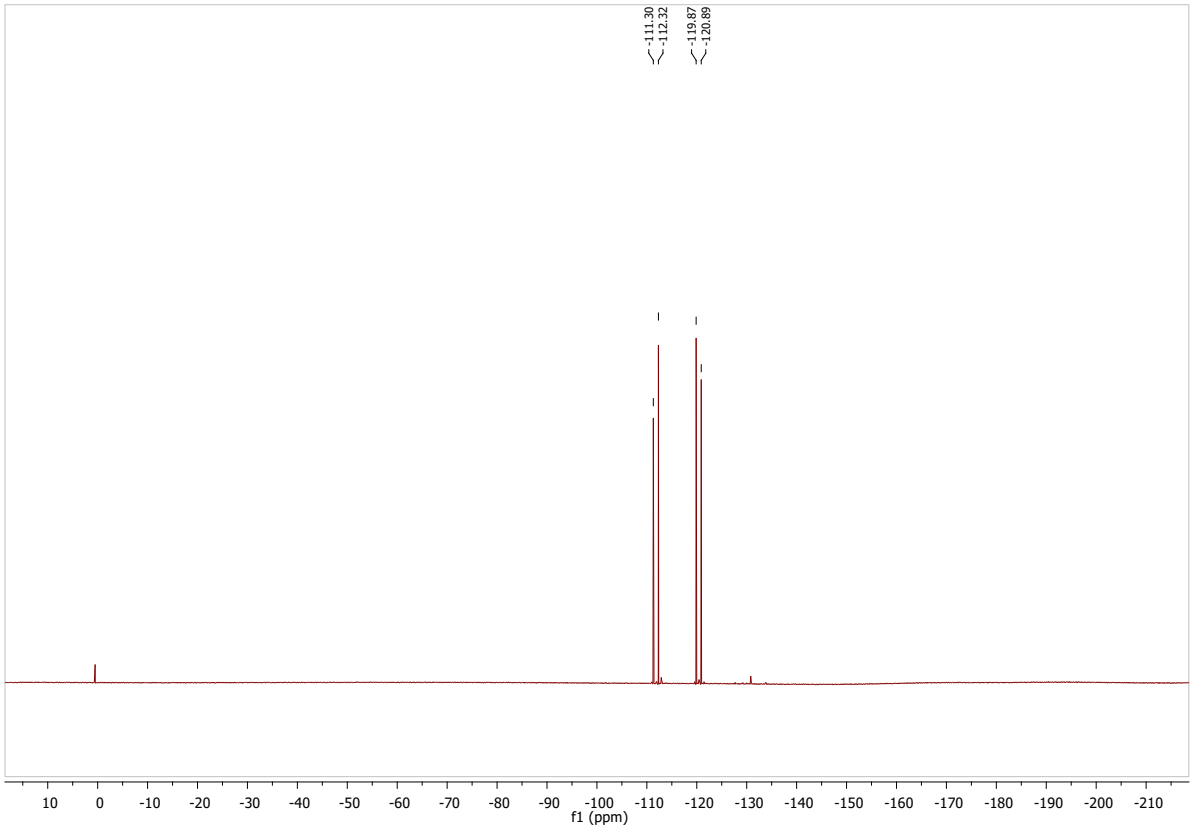
^{13}C NMR (126 MHz, $CDCl_3$)



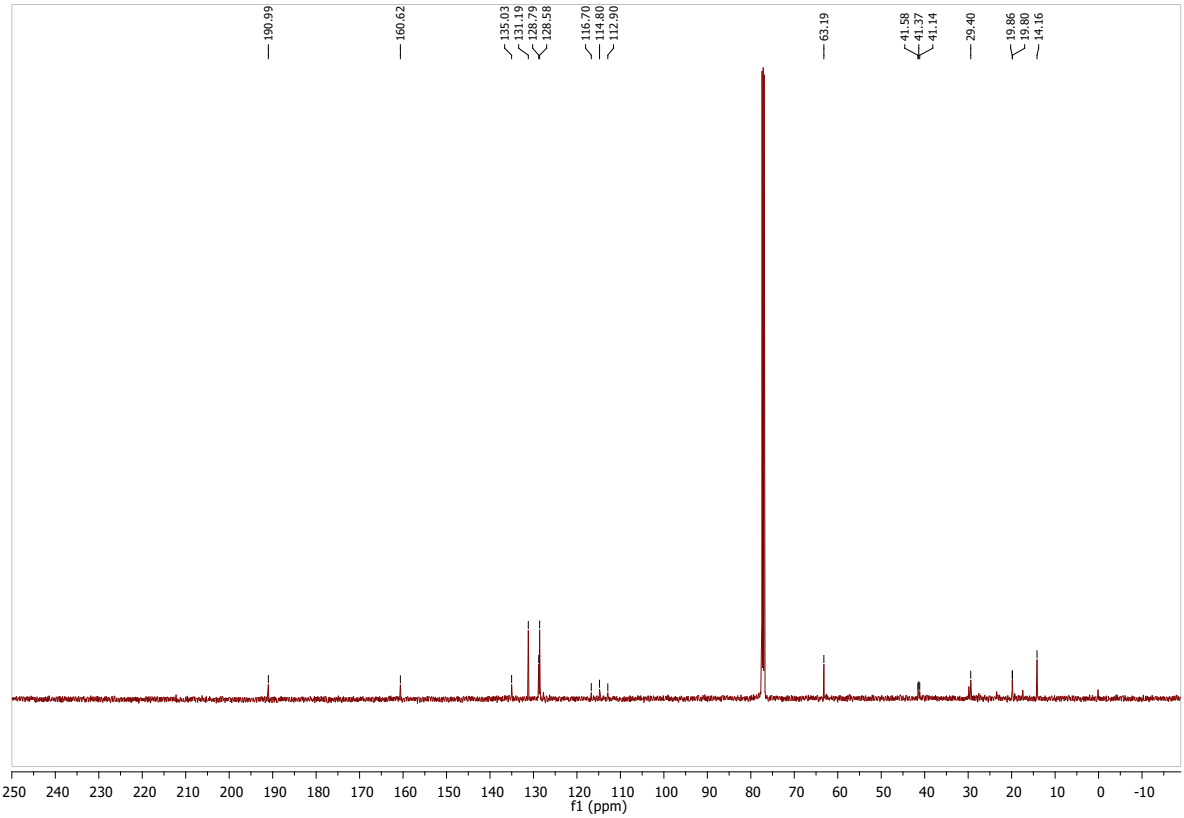
^{1}H NMR (300 MHz, $CDCl_3$)



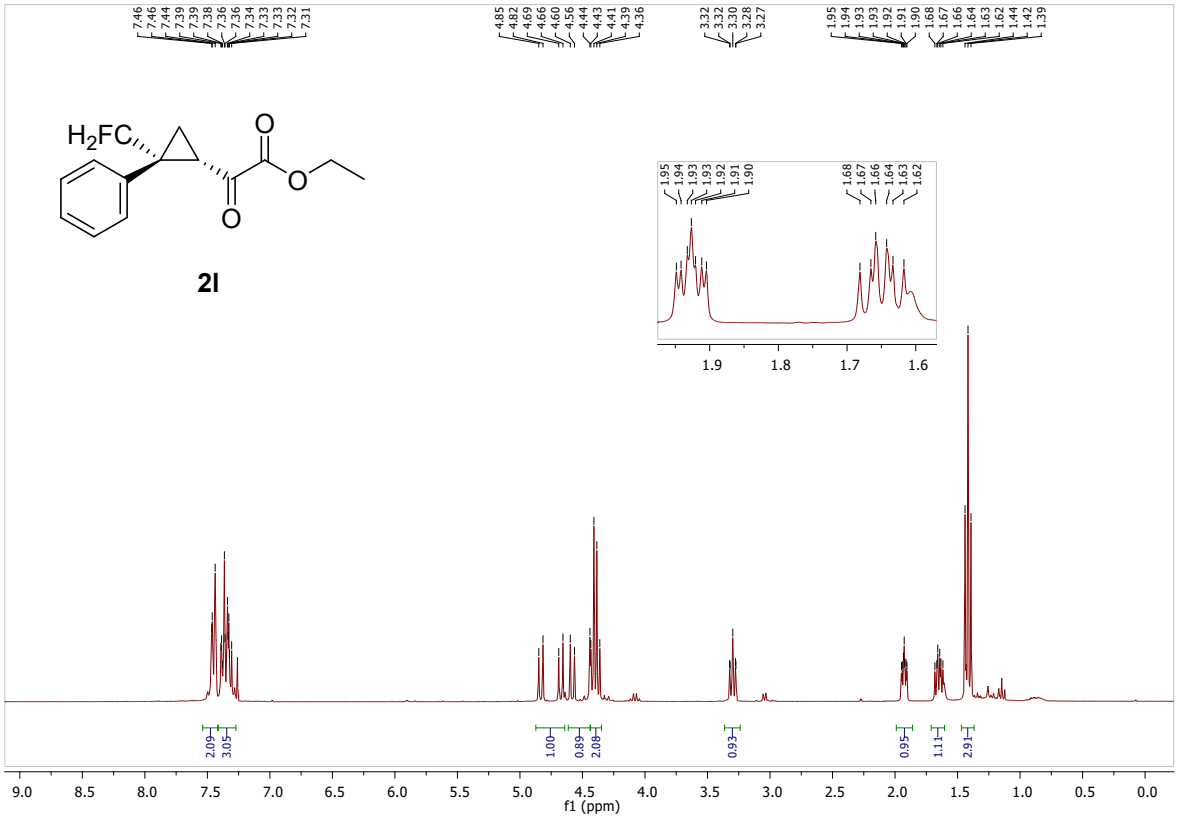
^{19}F NMR (282 MHz, $CDCl_3$)



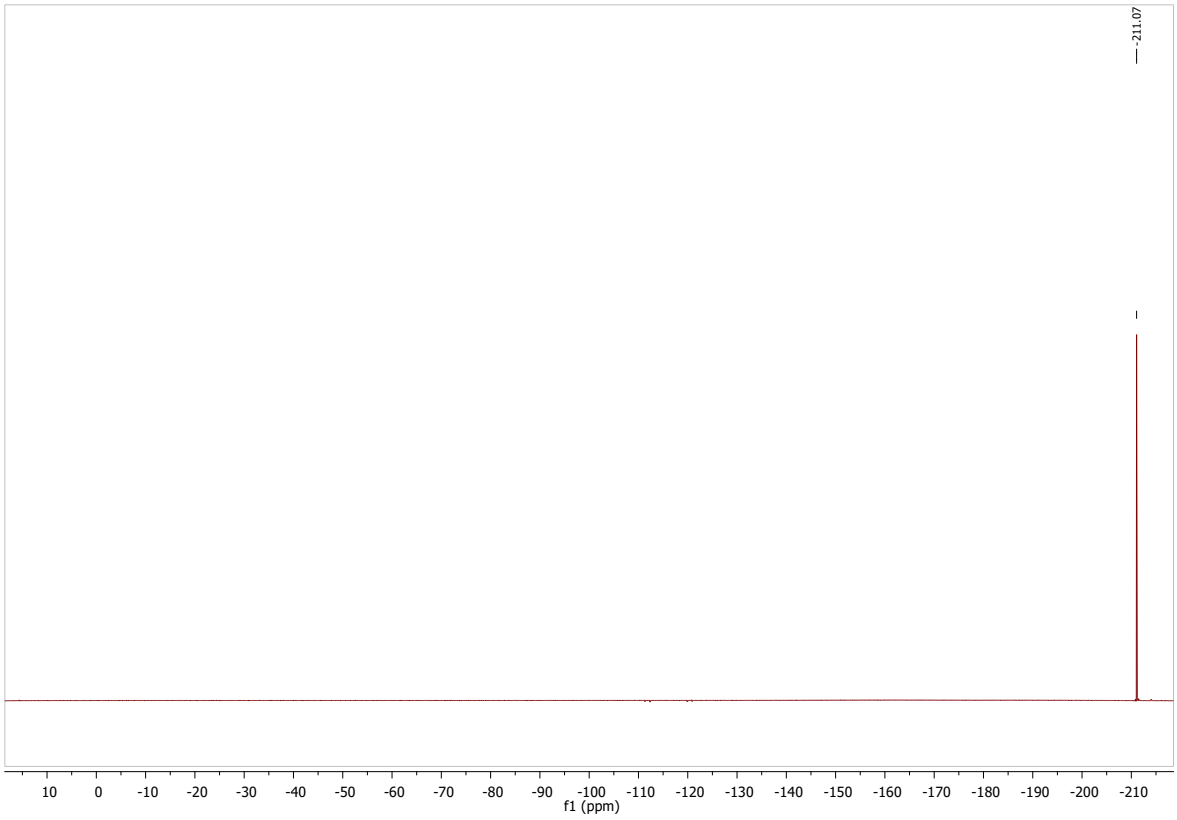
^{13}C NMR (75 MHz, $CDCl_3$)



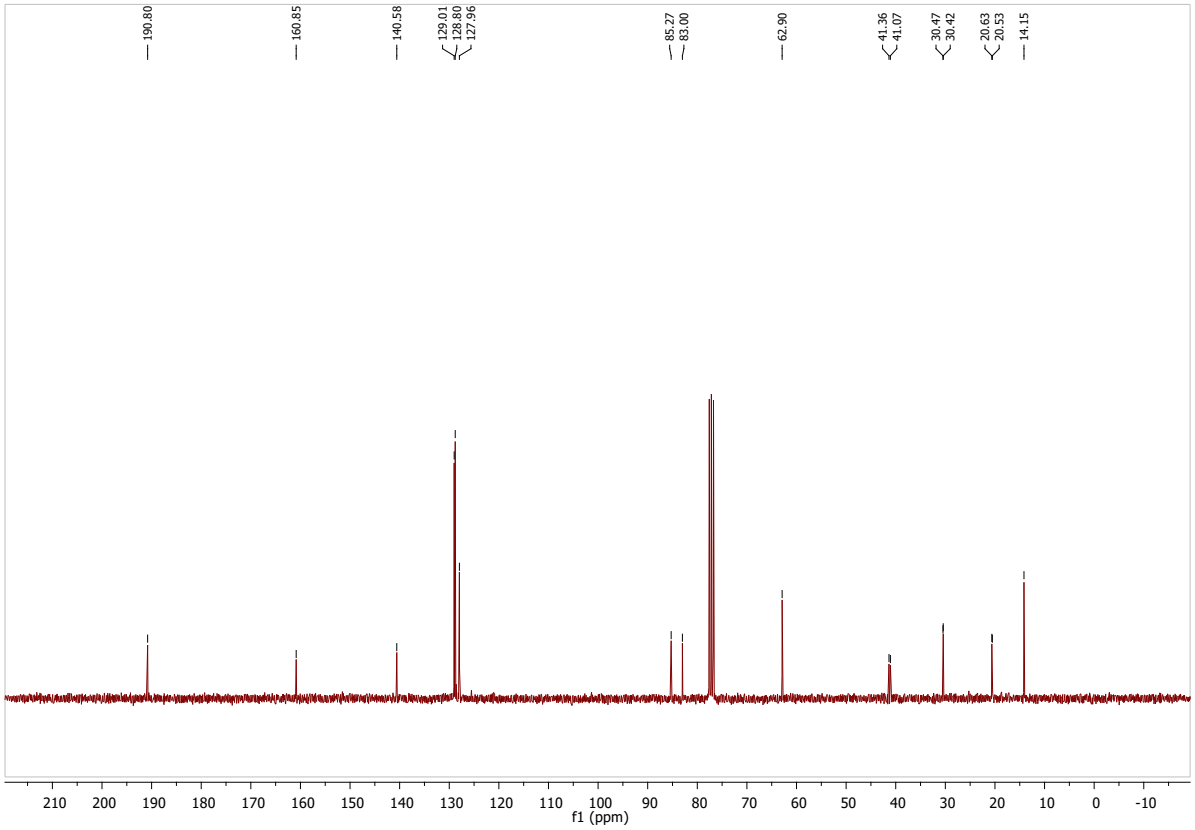
^{1}H NMR (300 MHz, $CDCl_3$)



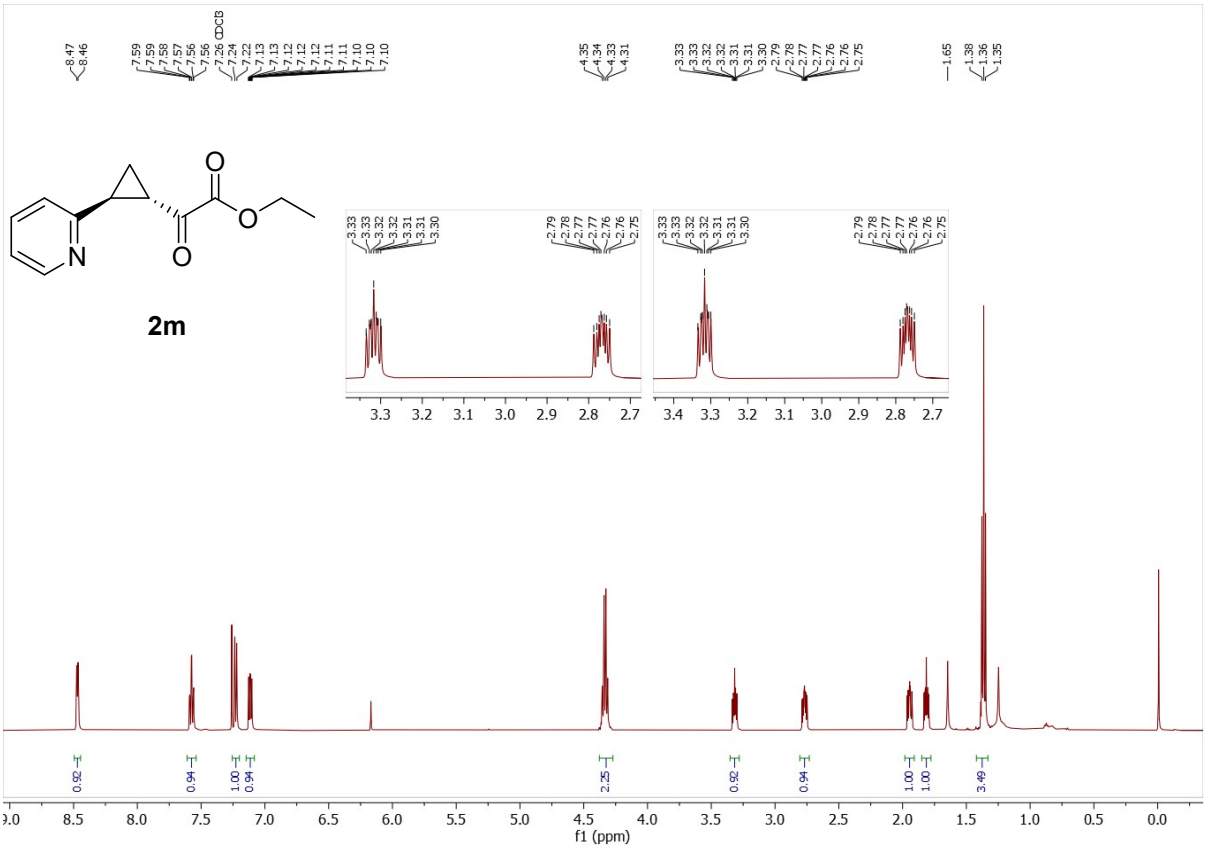
^{19}F NMR (282 MHz, $CDCl_3$)



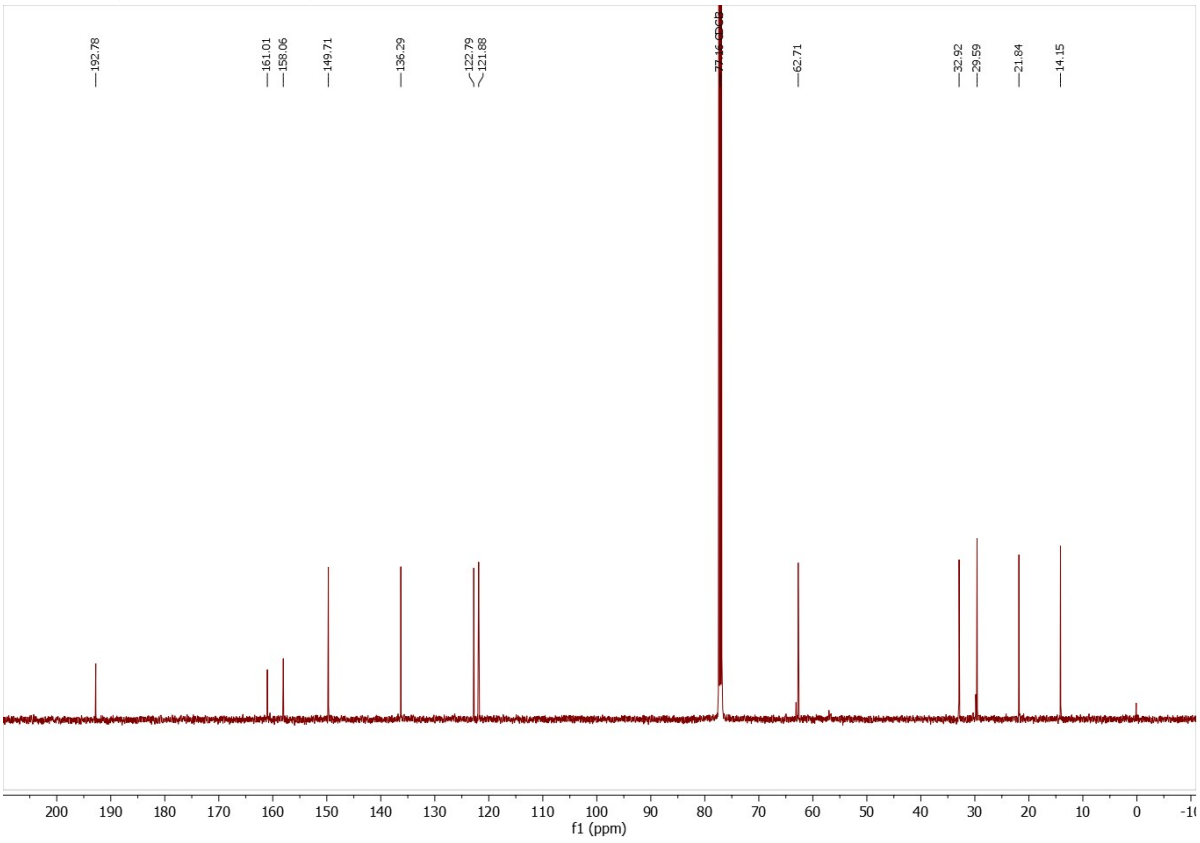
^{13}C NMR (75 MHz, $CDCl_3$)



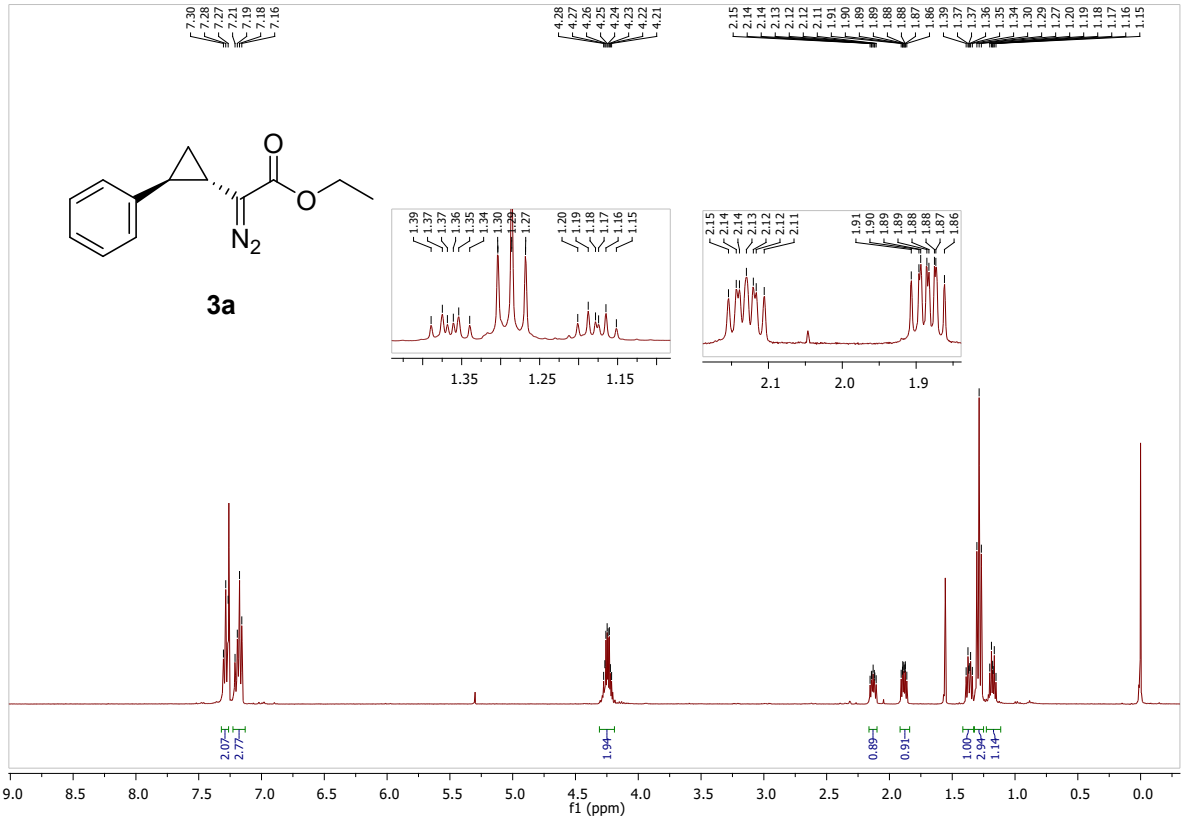
^{1}H NMR (400 MHz, $CDCl_3$)



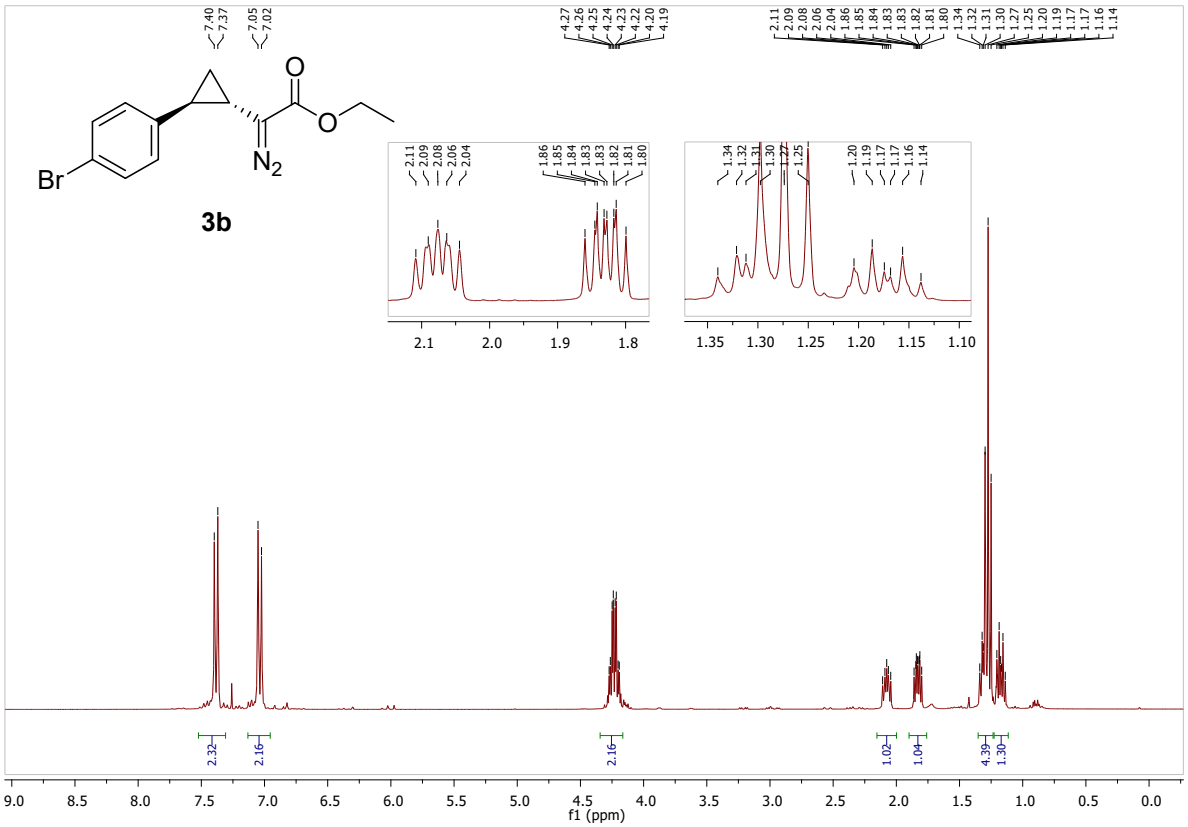
^{13}C NMR (101 MHz, $CDCl_3$)



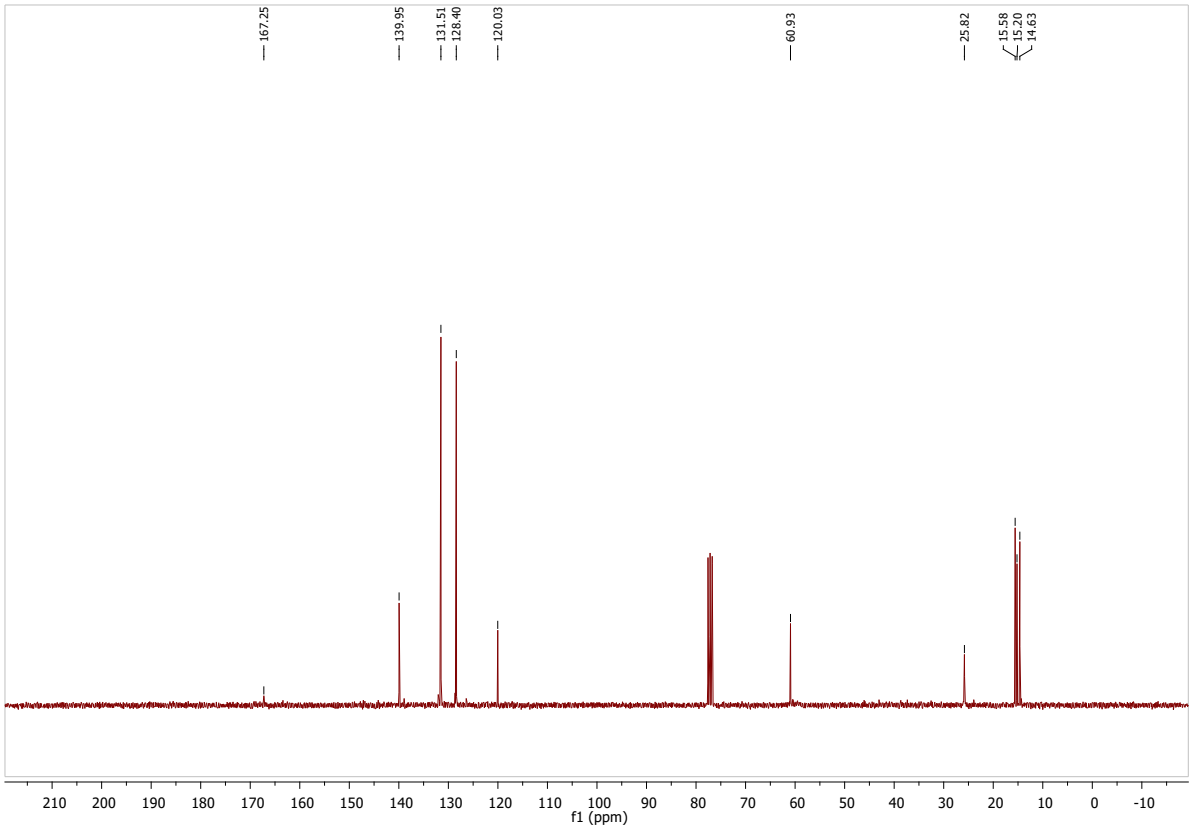
^{1}H NMR (400 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



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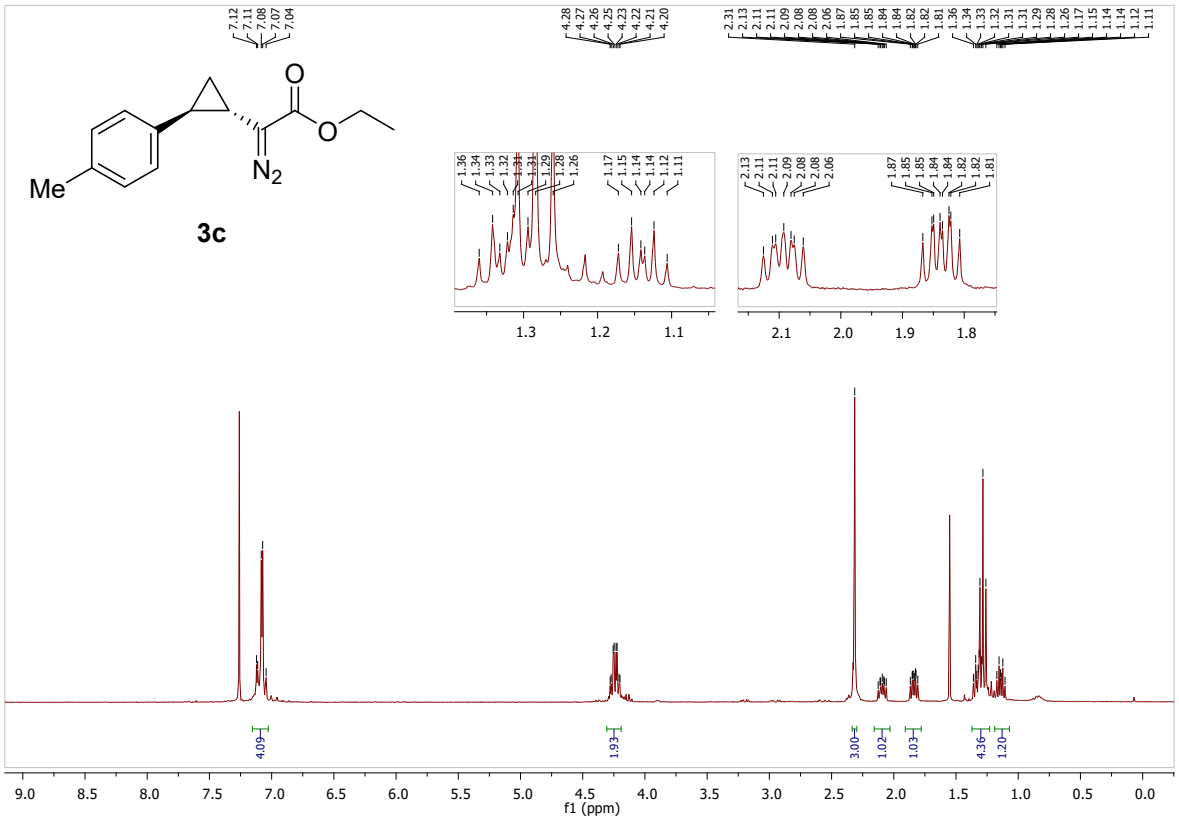

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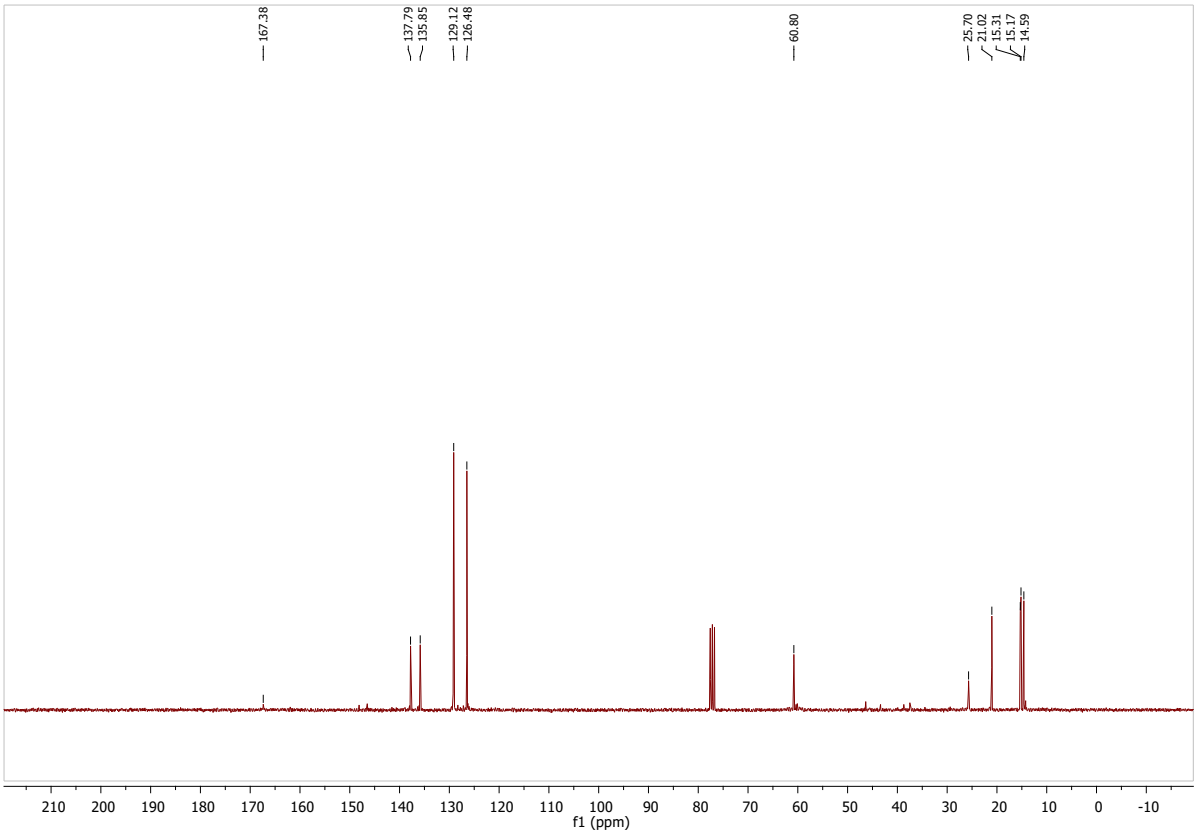
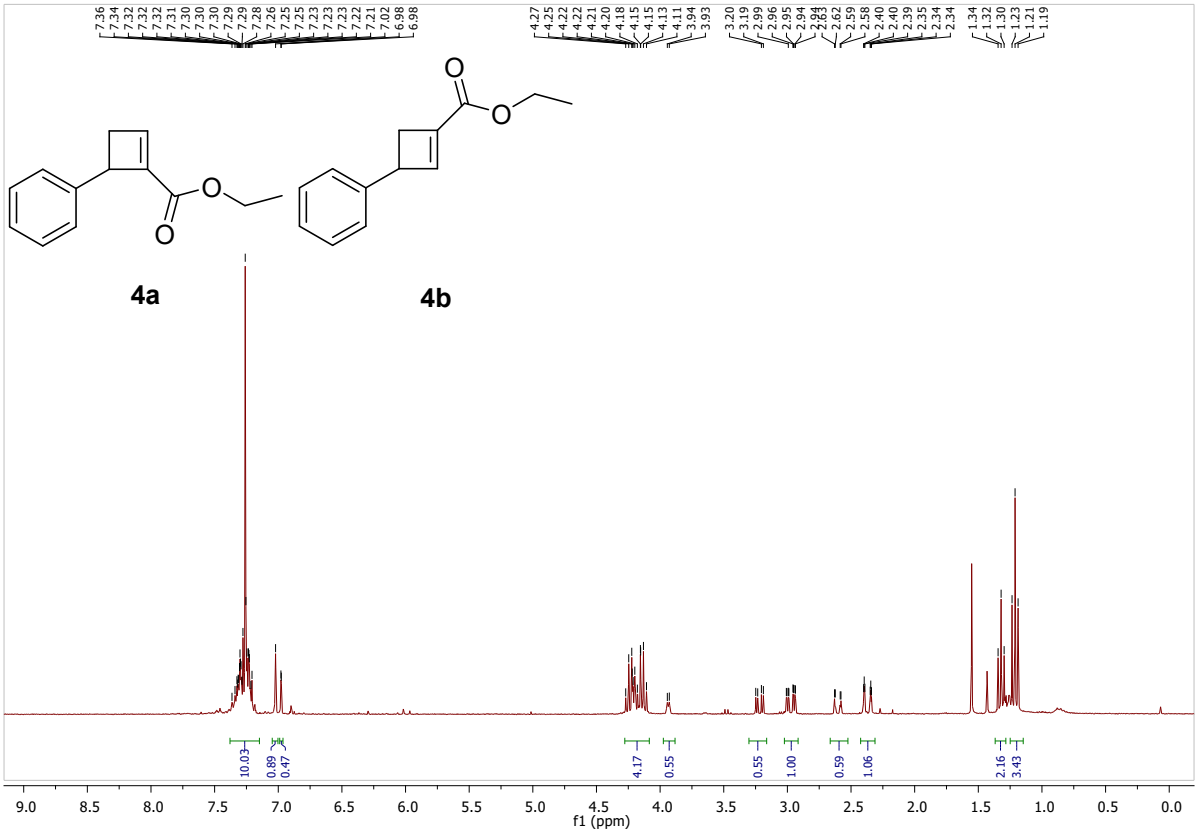
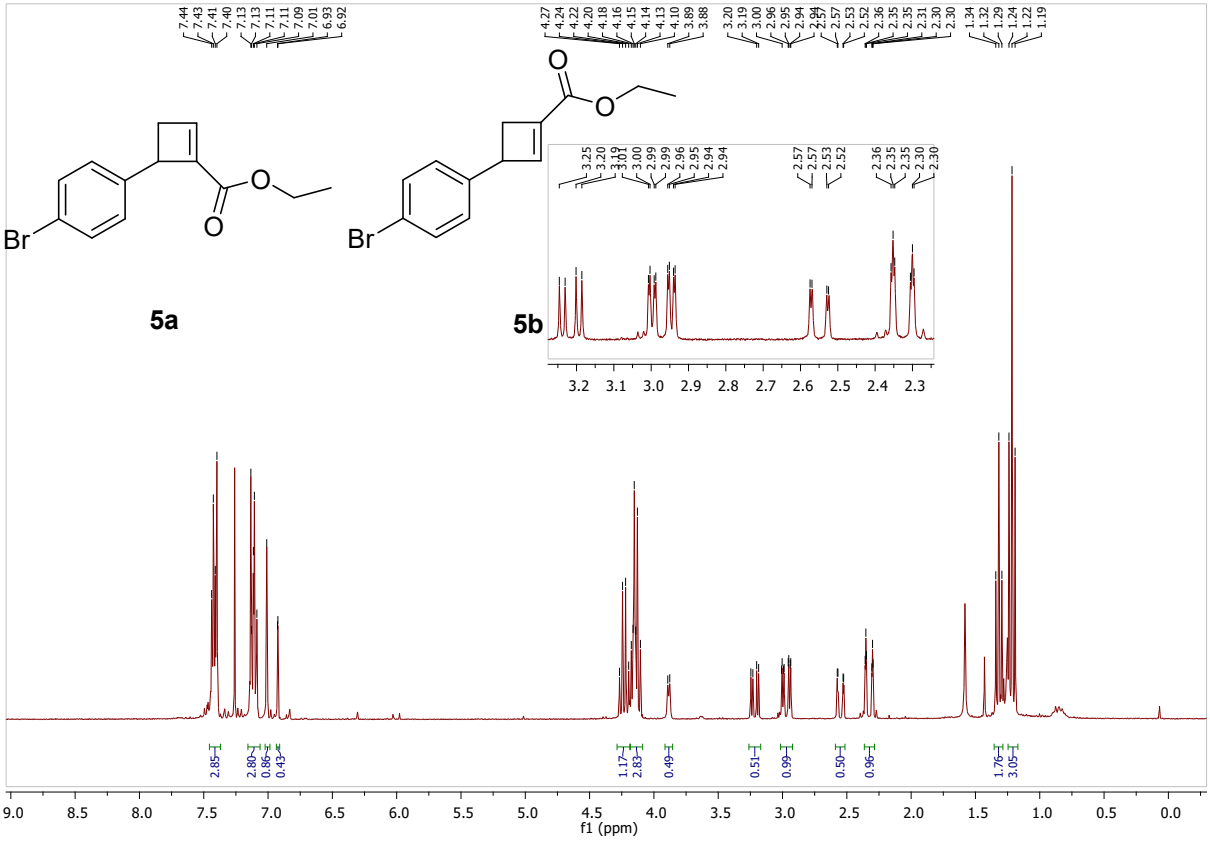


^{1}H NMR (400 MHz, $CDCl_3$)



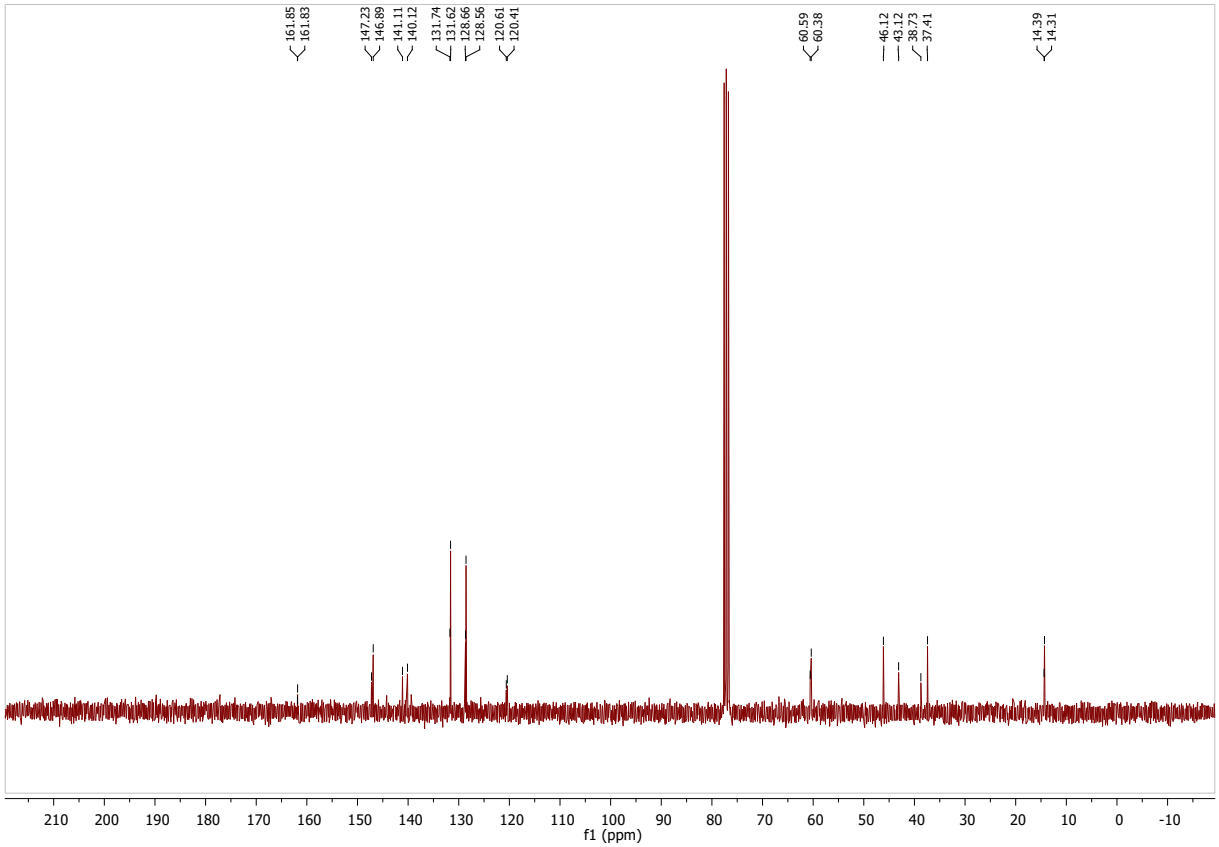
Isolated as a mixture of regioisomers.

^{1}H NMR (300 MHz, $CDCl_3$)

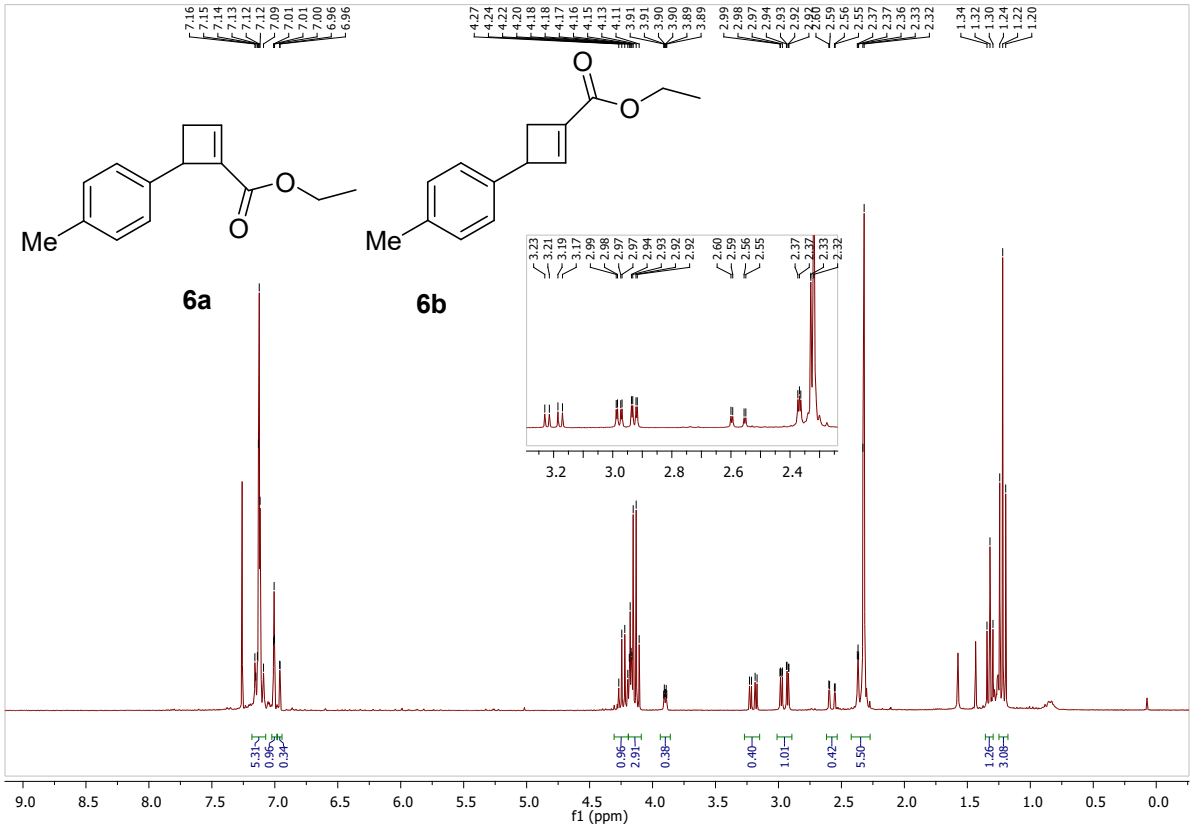


Isolated as a mixture of regioisomers.

^{13}C NMR (75 MHz, $CDCl_3$)

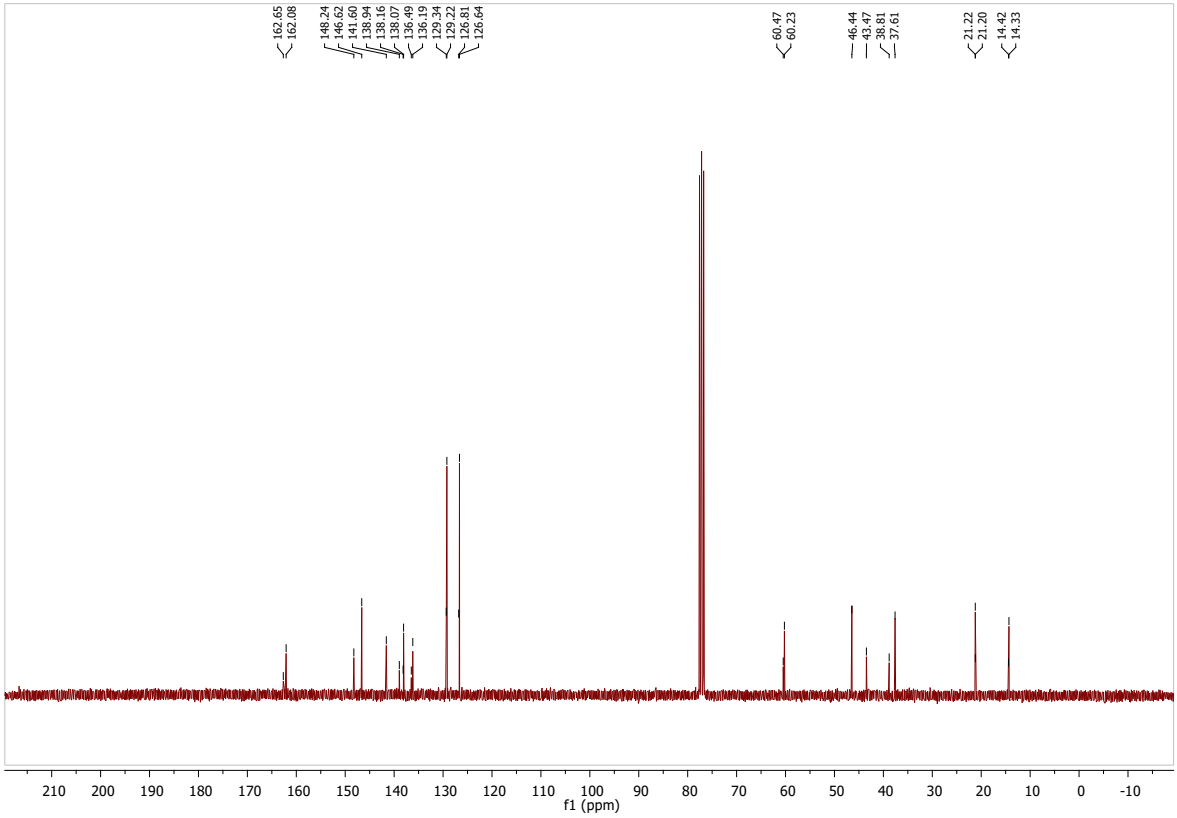


^{1}H NMR (300 MHz, $CDCl_3$)

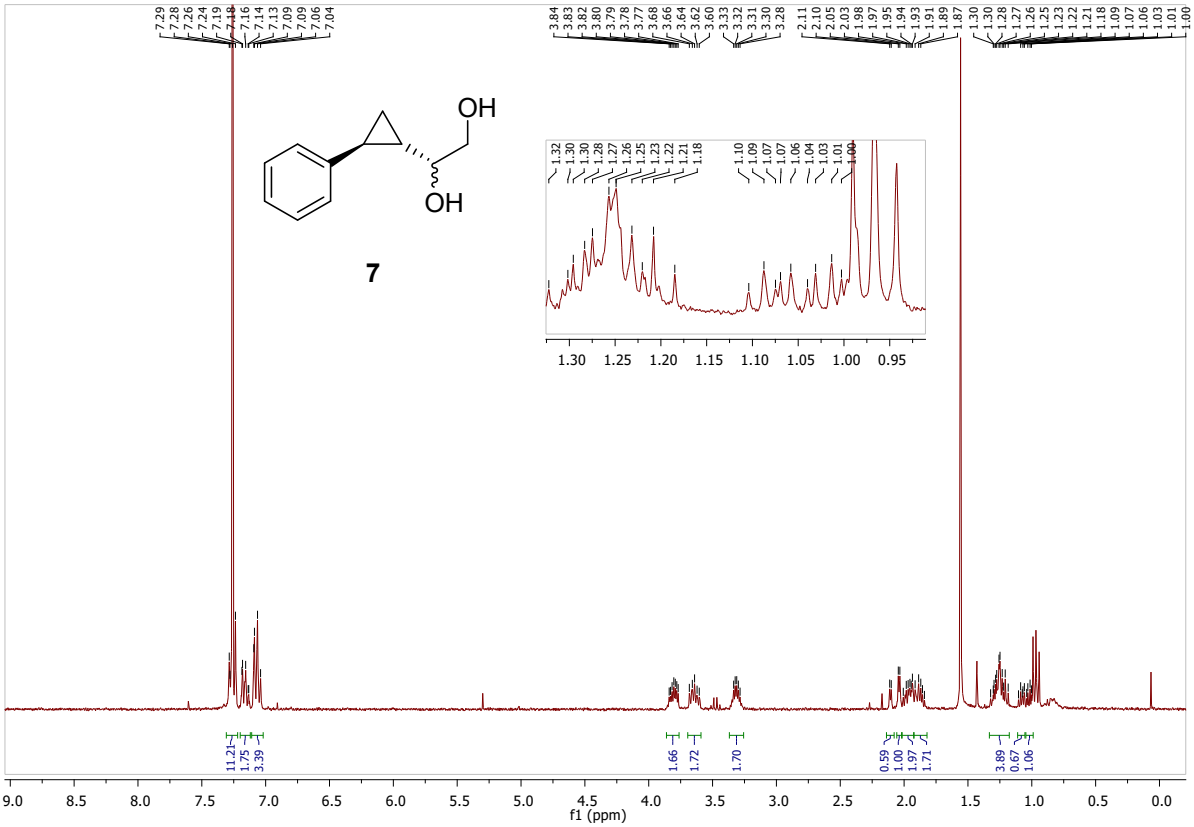


Isolated as a mixture of regioisomers.

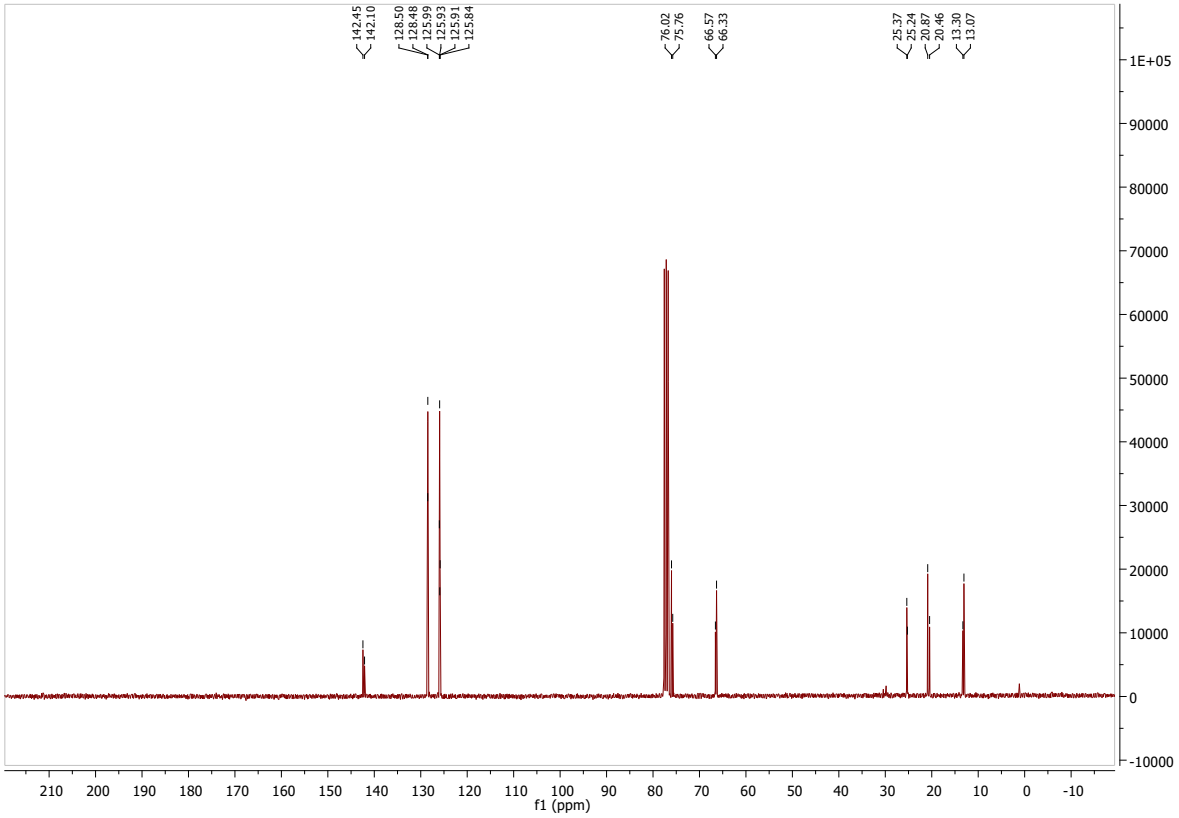
^{13}C NMR (75 MHz, $CDCl_3$)



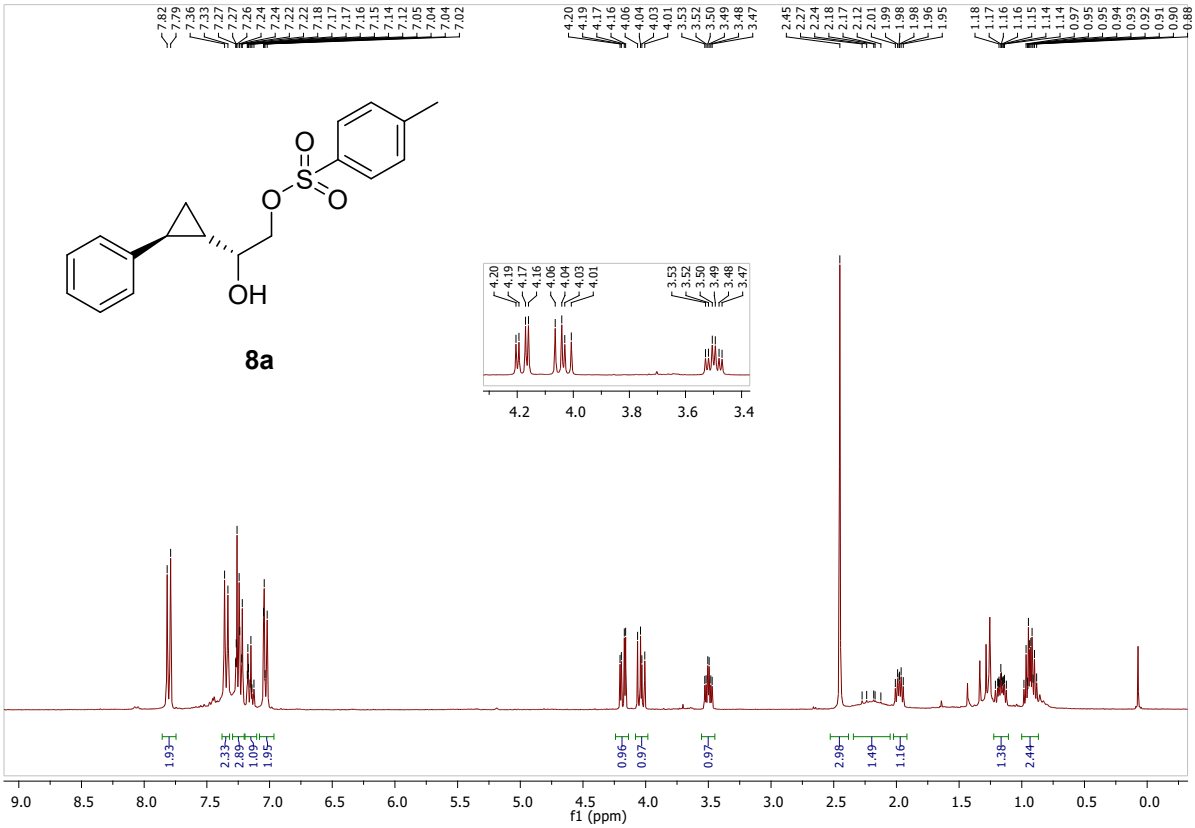
^{1}H NMR (300 MHz, $CDCl_3$)



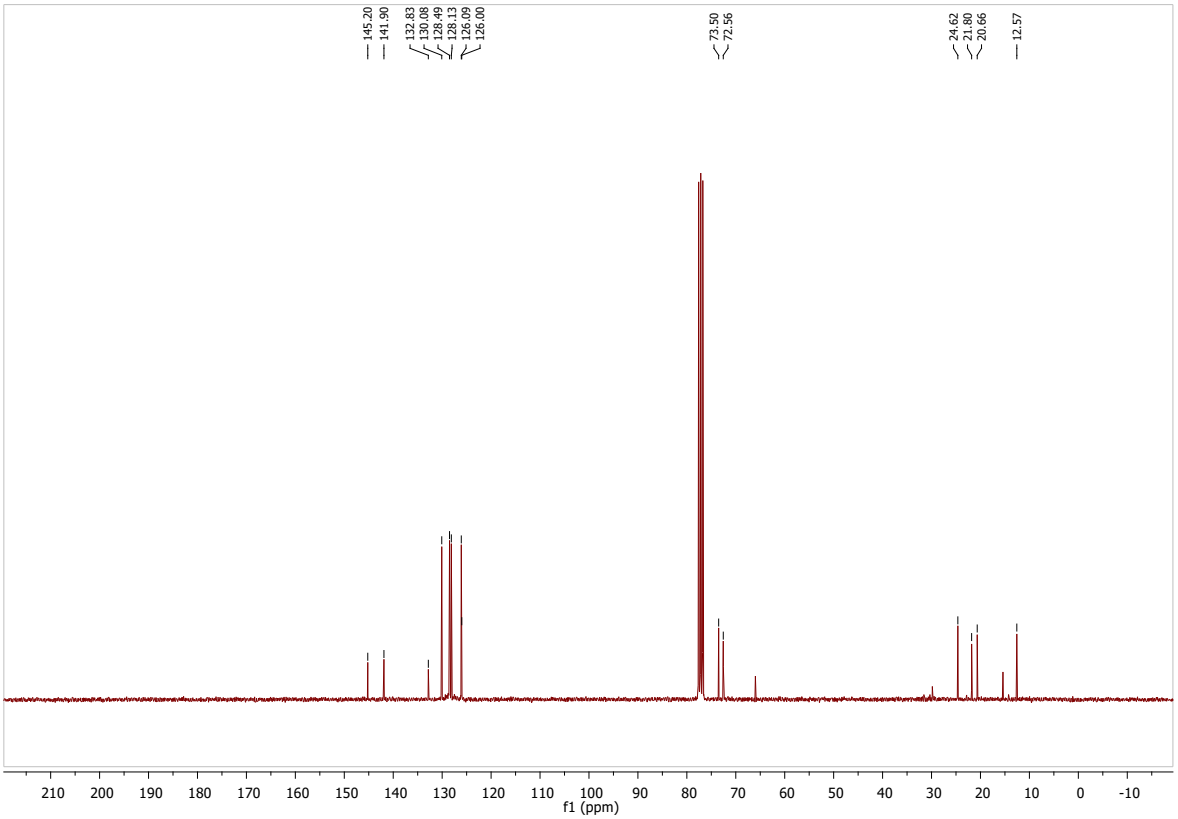
^{13}C NMR (75 MHz, $CDCl_3$)



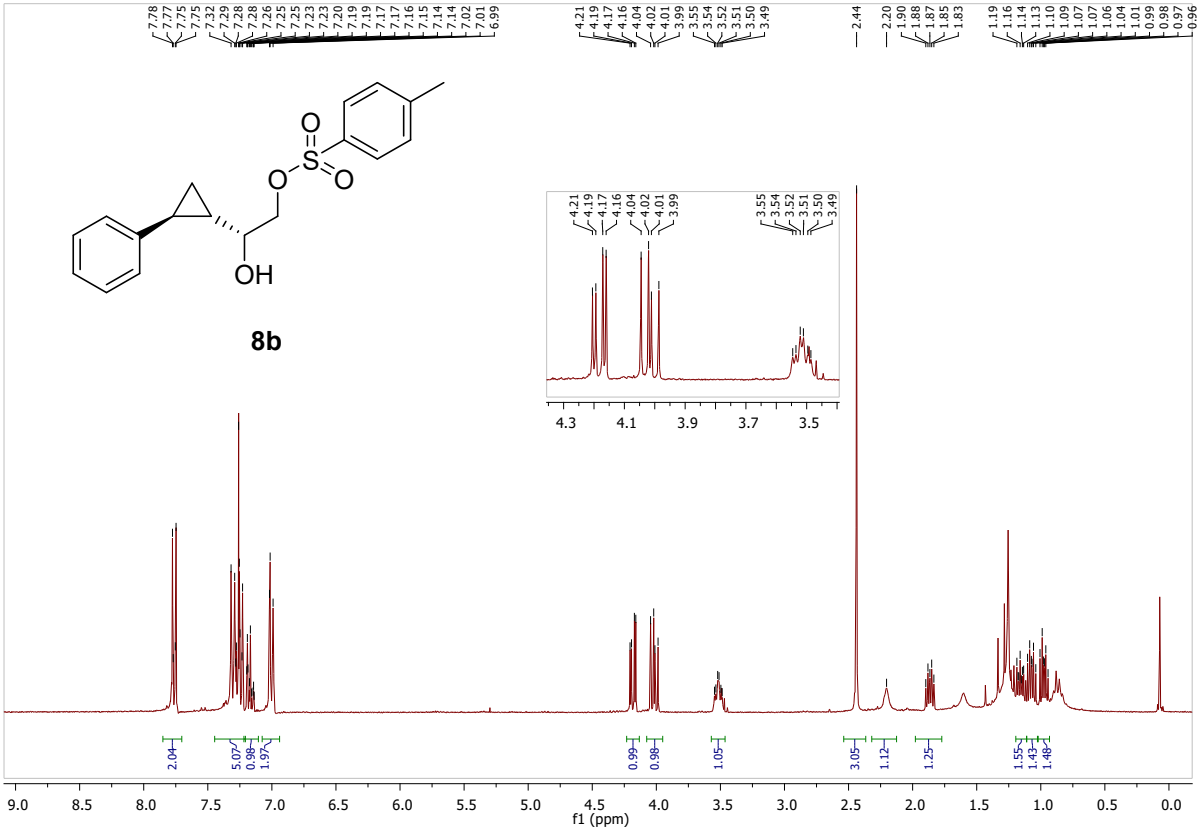
^{1}H NMR (300 MHz, $CDCl_3$)



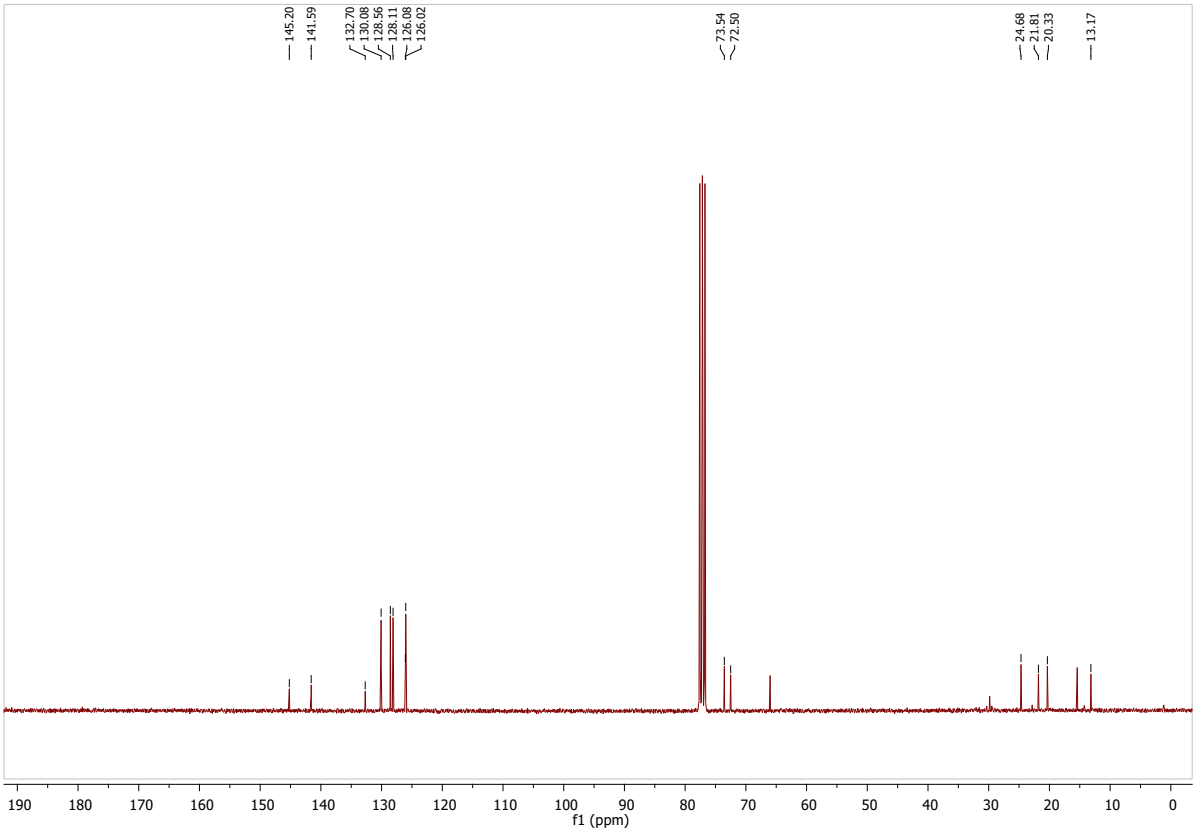
^{13}C NMR (75 MHz, $CDCl_3$)



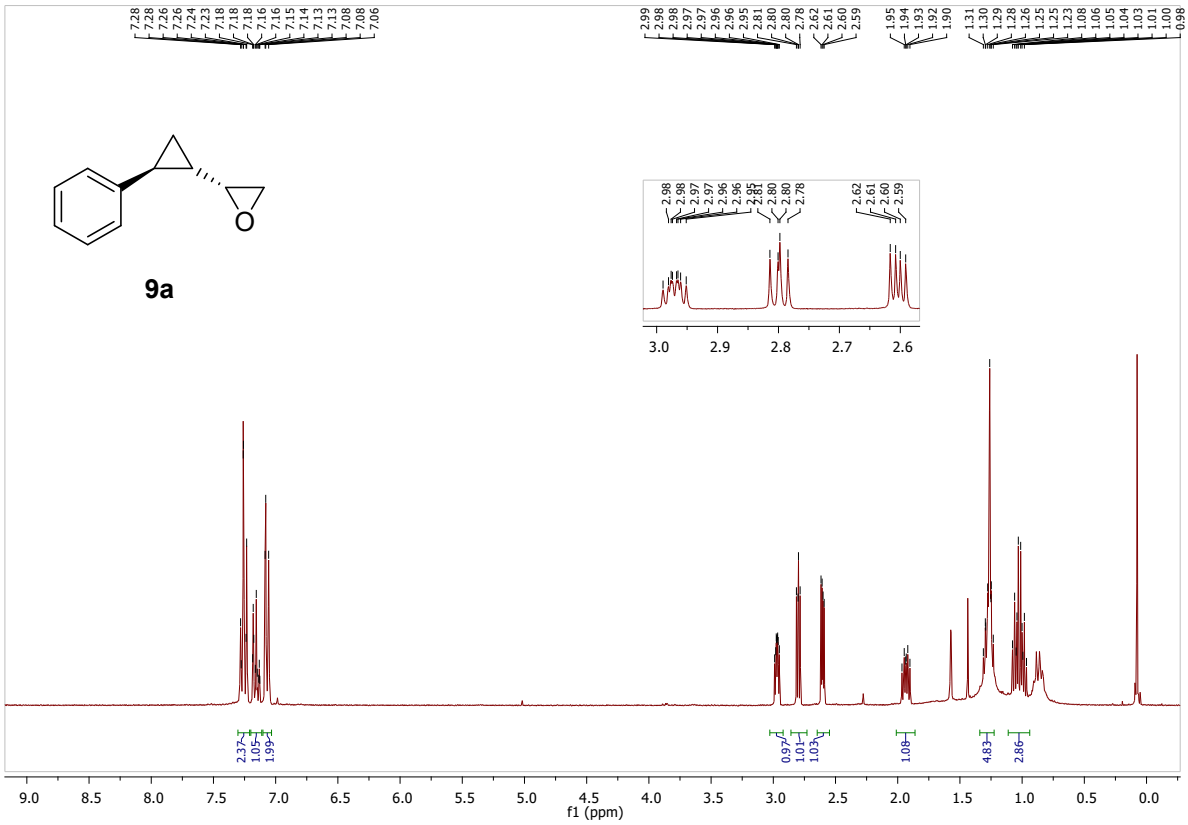
^{1}H NMR (300 MHz, $CDCl_3$)



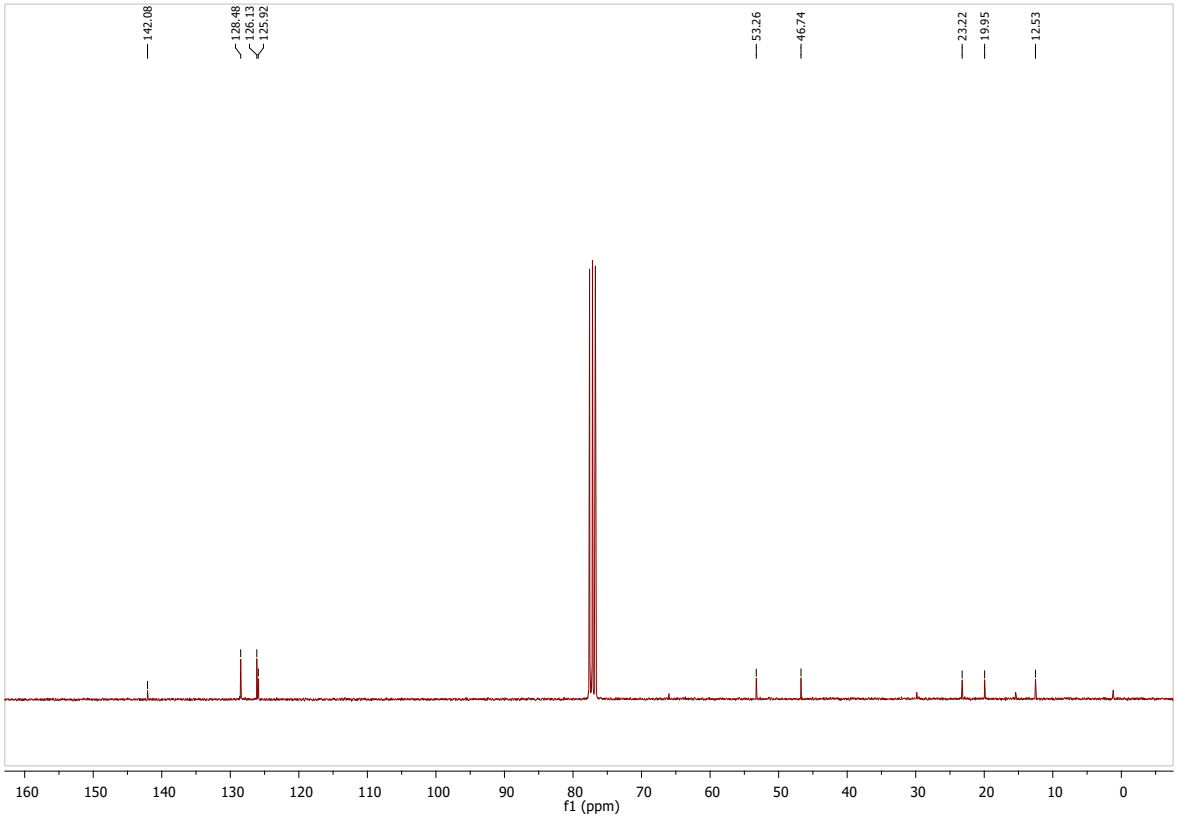
^{13}C NMR (75 MHz, $CDCl_3$)



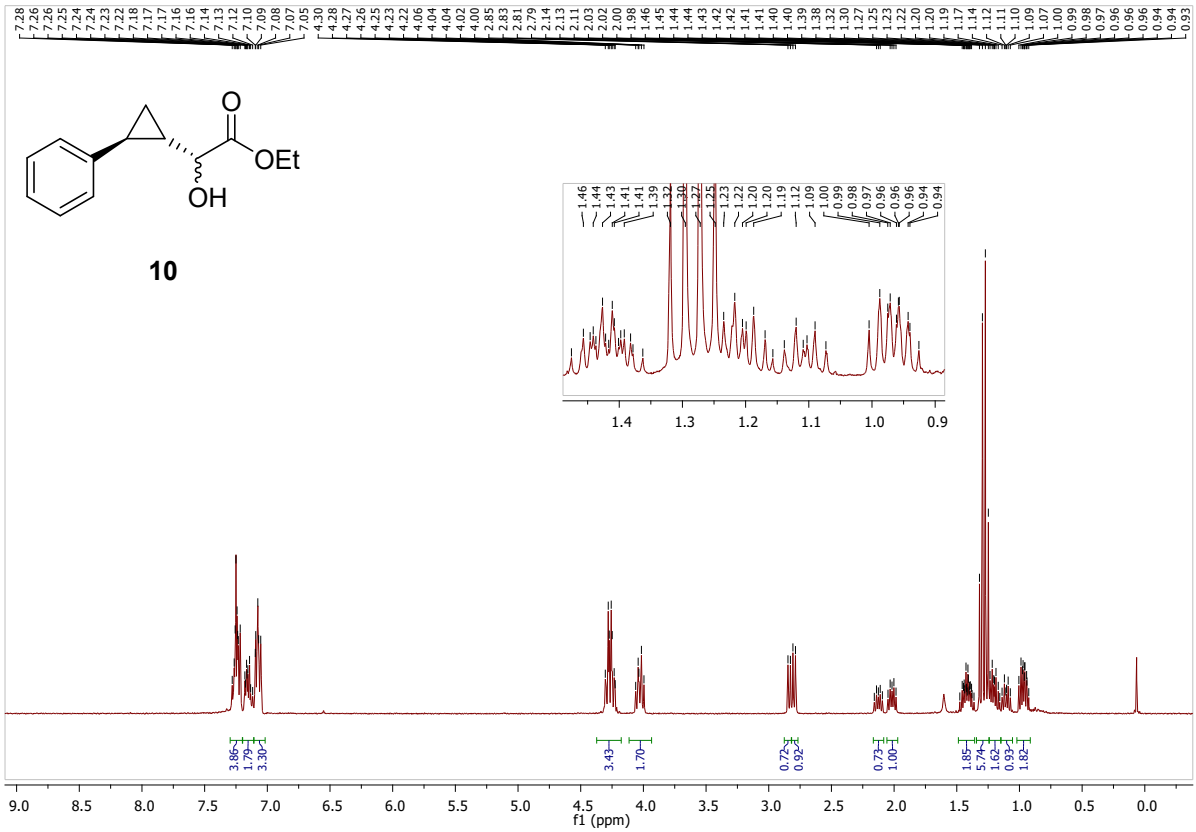
^{1}H NMR (300 MHz, $CDCl_3$)



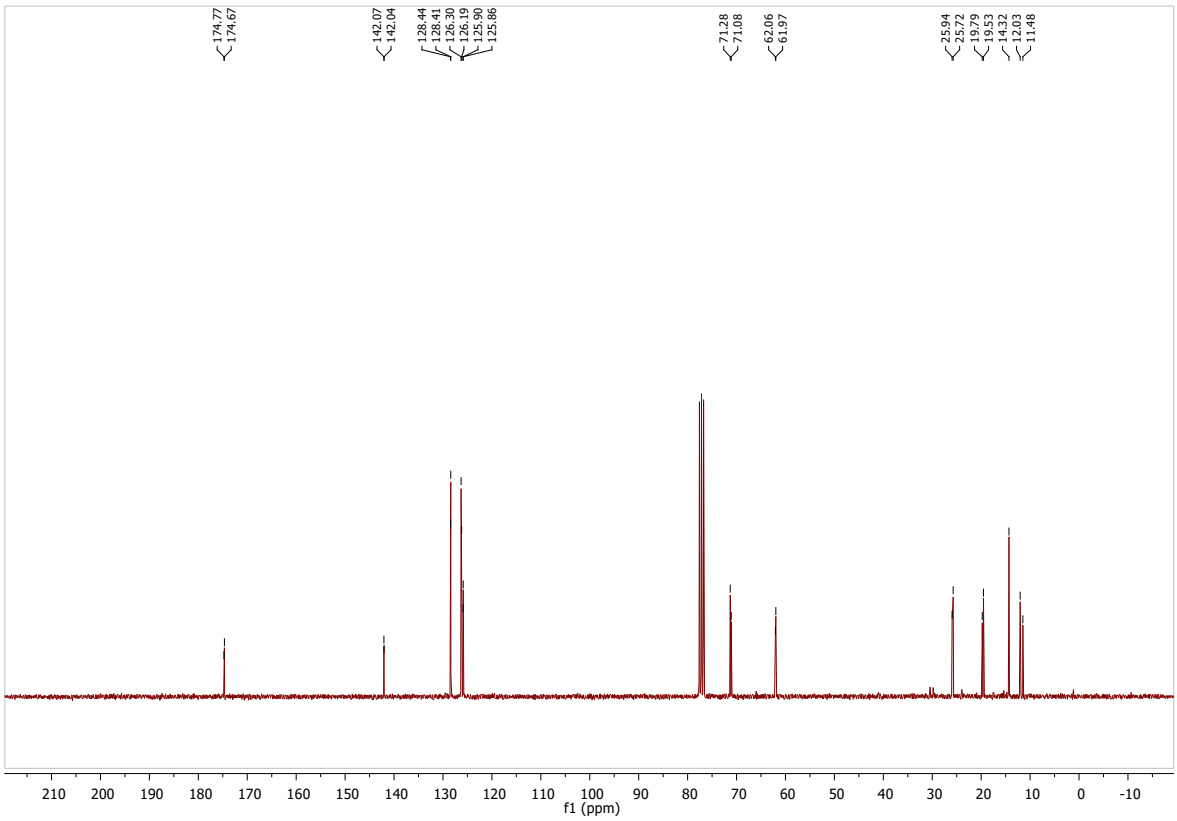
^{13}C NMR (75 MHz, $CDCl_3$)



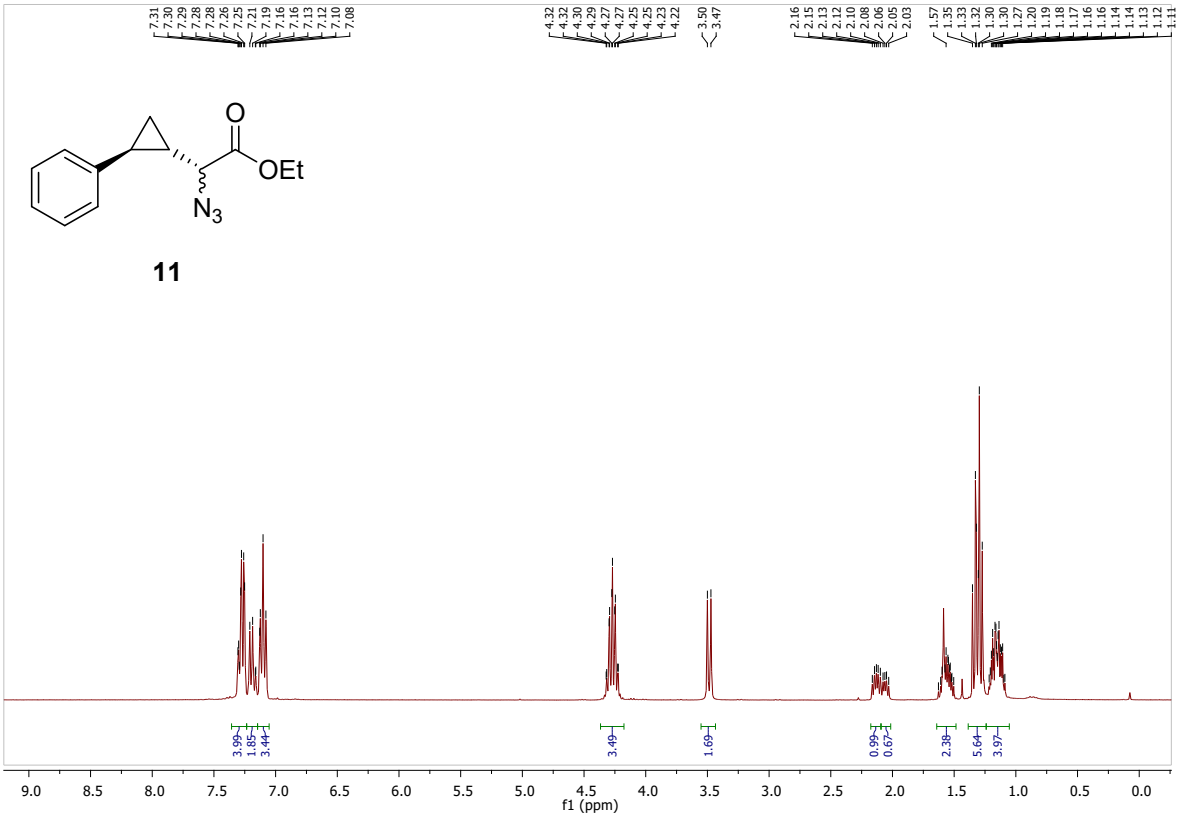
^{1}H NMR (300 MHz, $CDCl_3$)



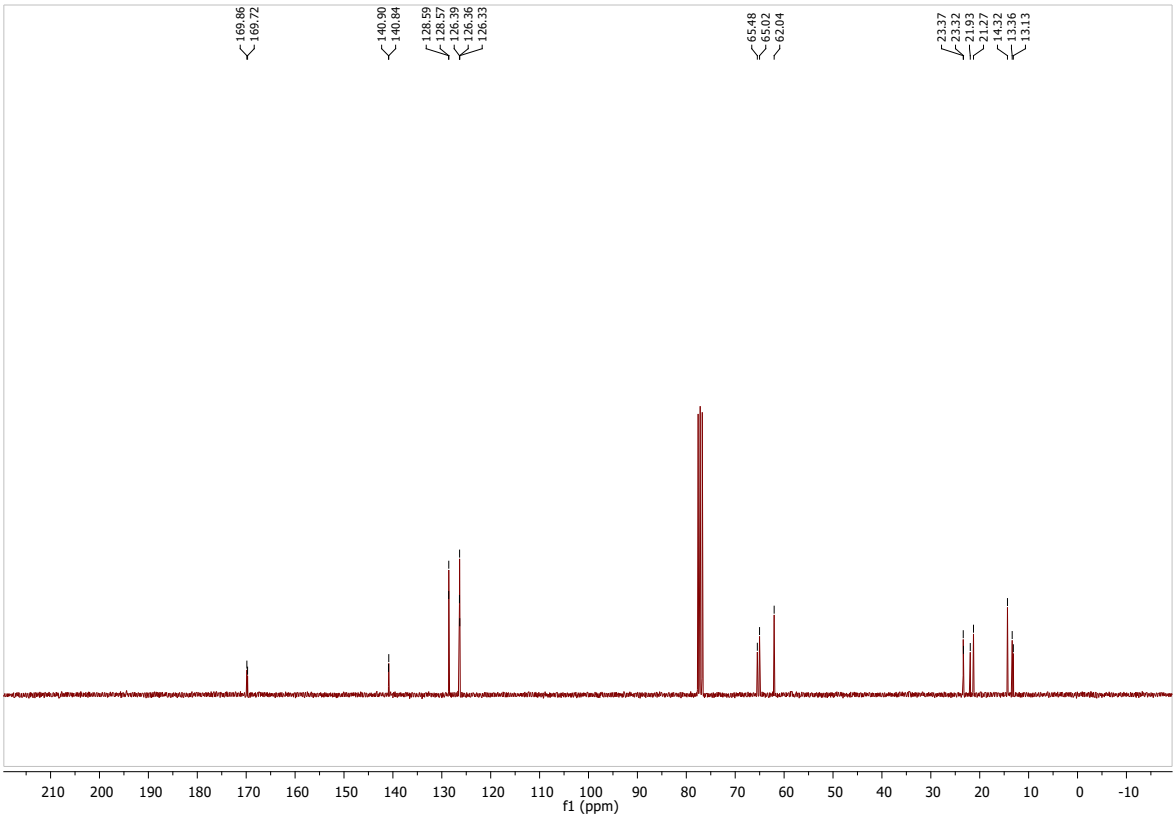
^{13}C NMR (75 MHz, $CDCl_3$)



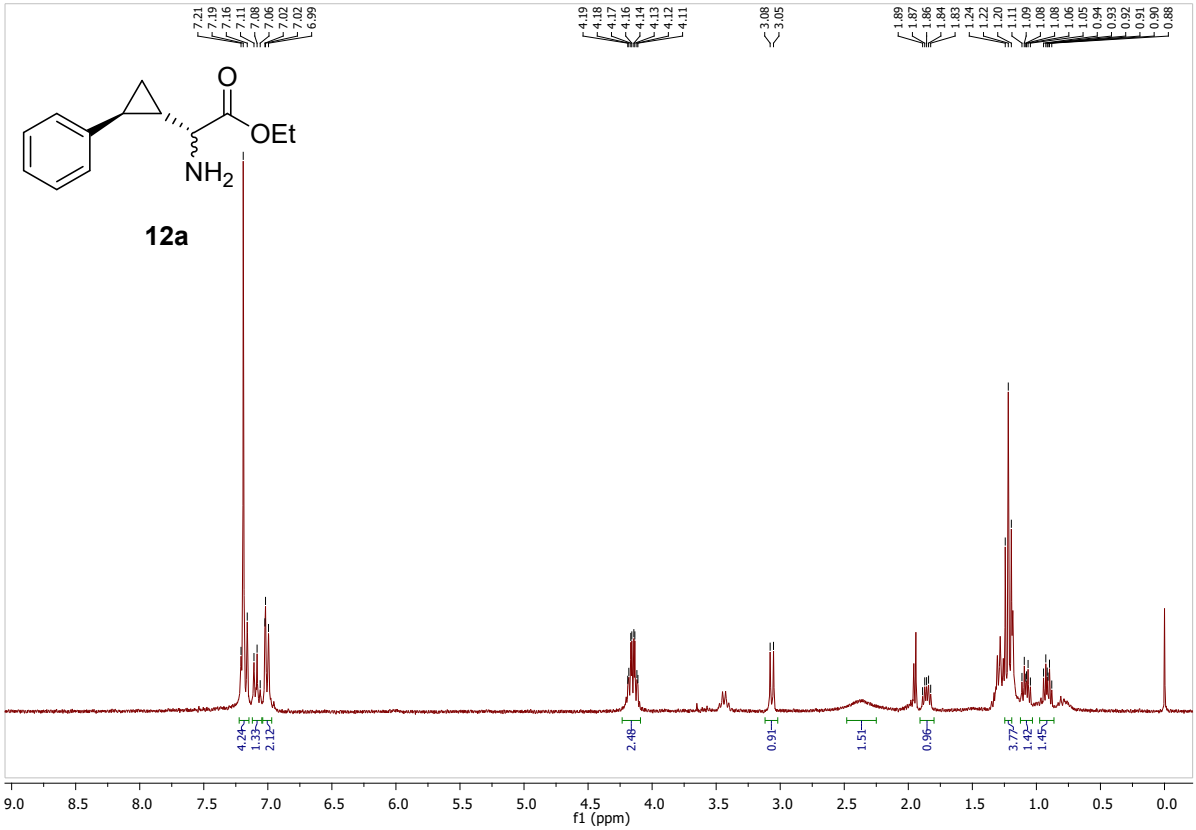
^{1}H NMR (300 MHz, $CDCl_3$)



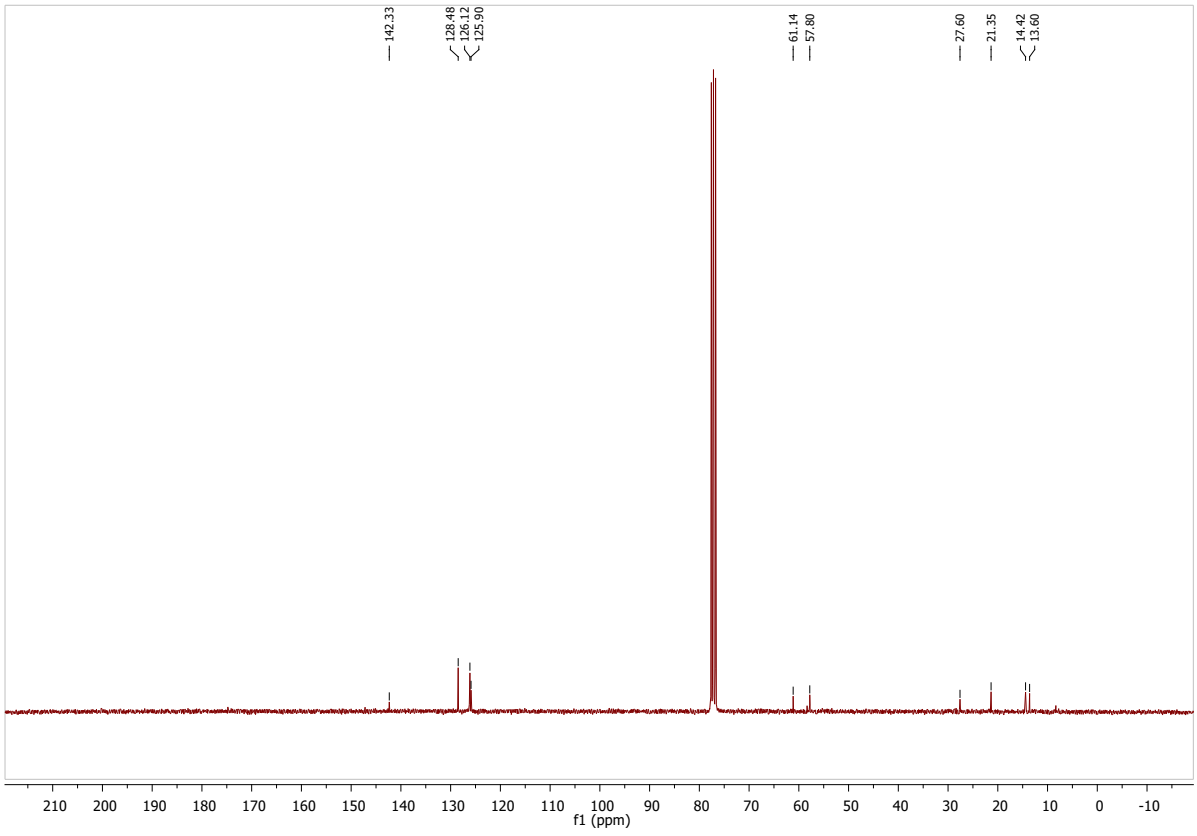
^{13}C NMR (75 MHz, $CDCl_3$)



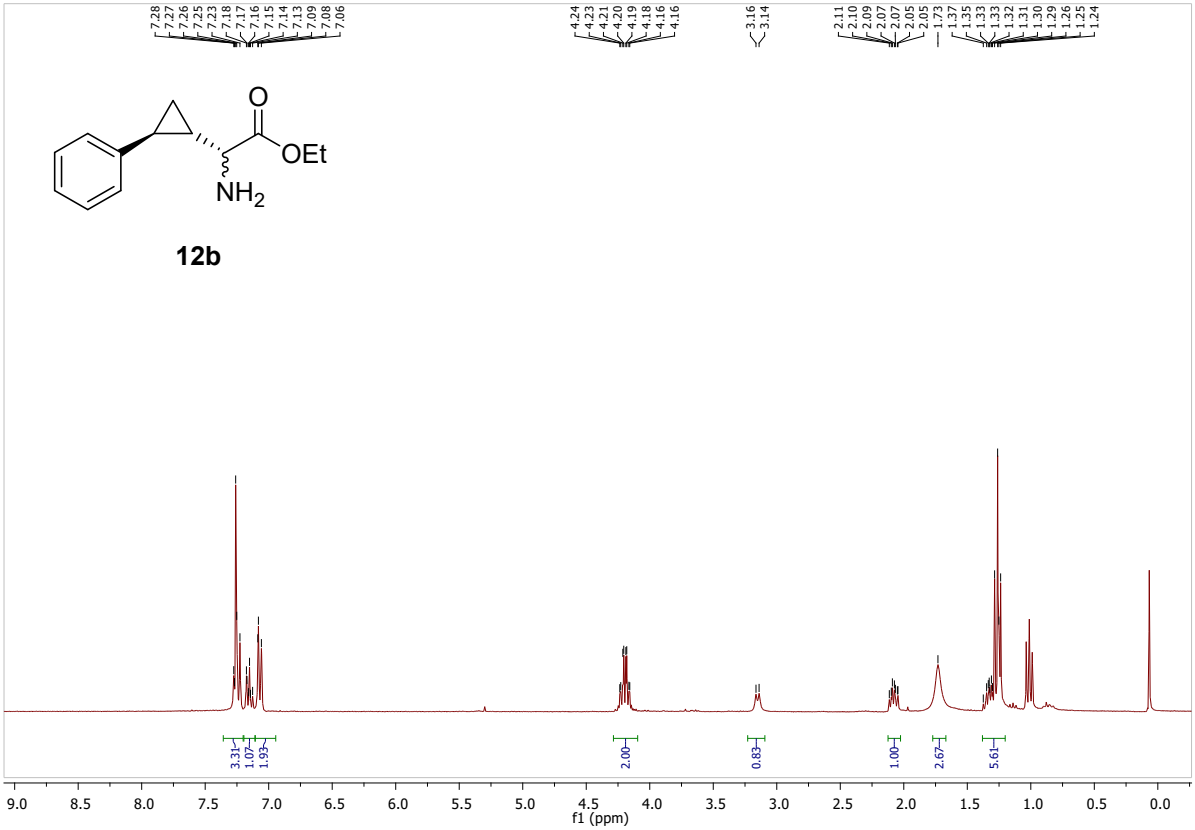
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)

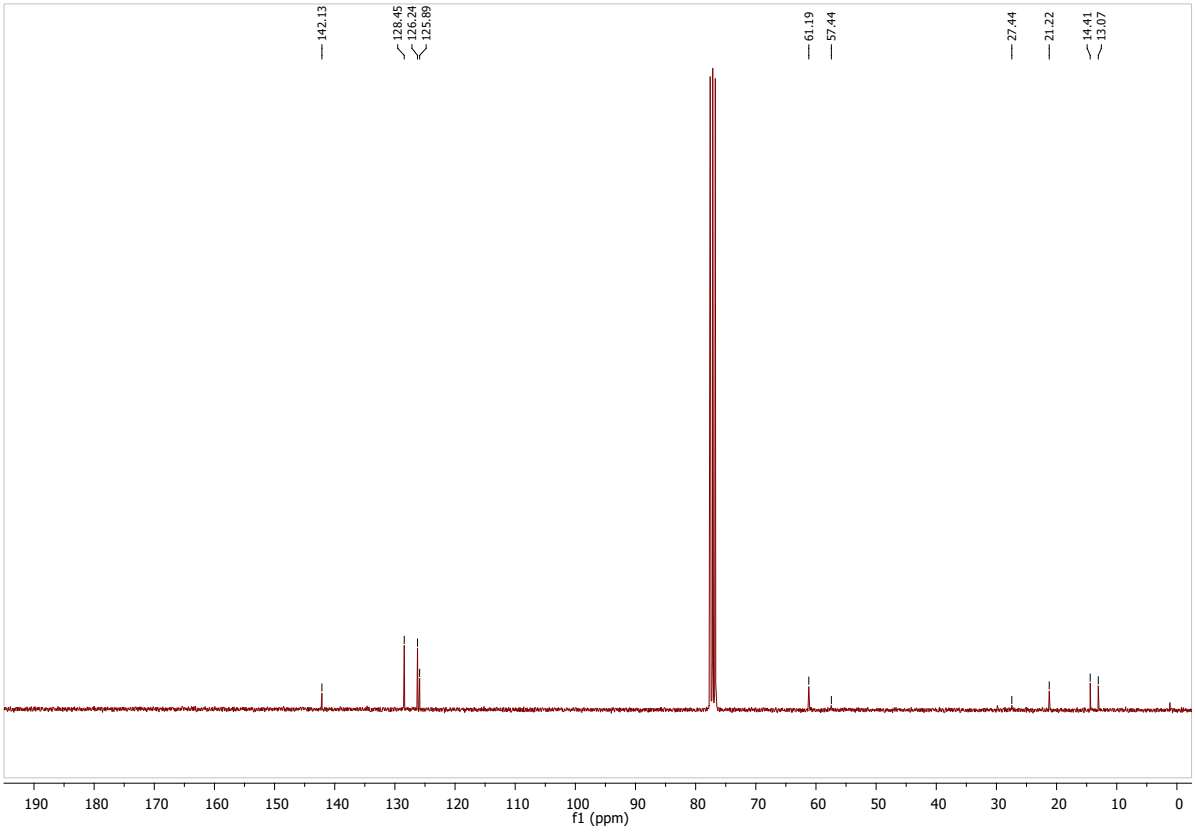


^{1}H NMR (300 MHz, $CDCl_3$)

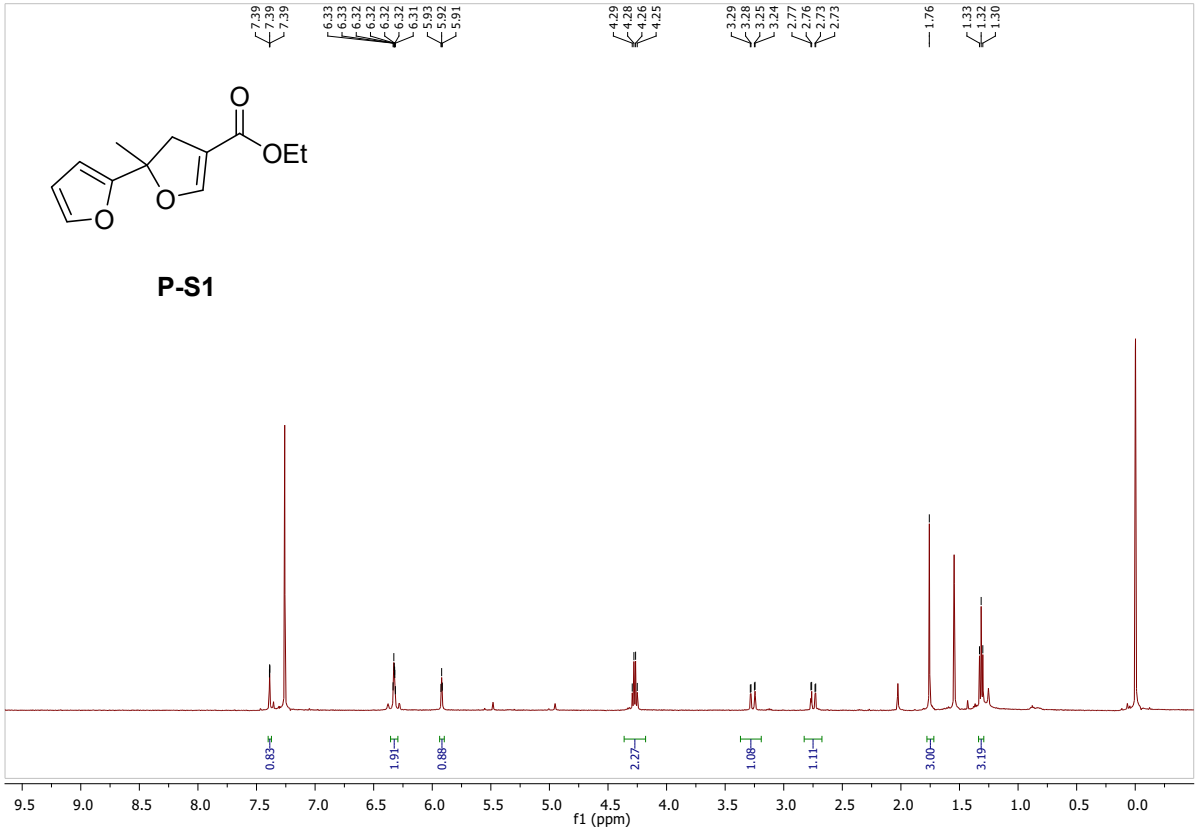


12b

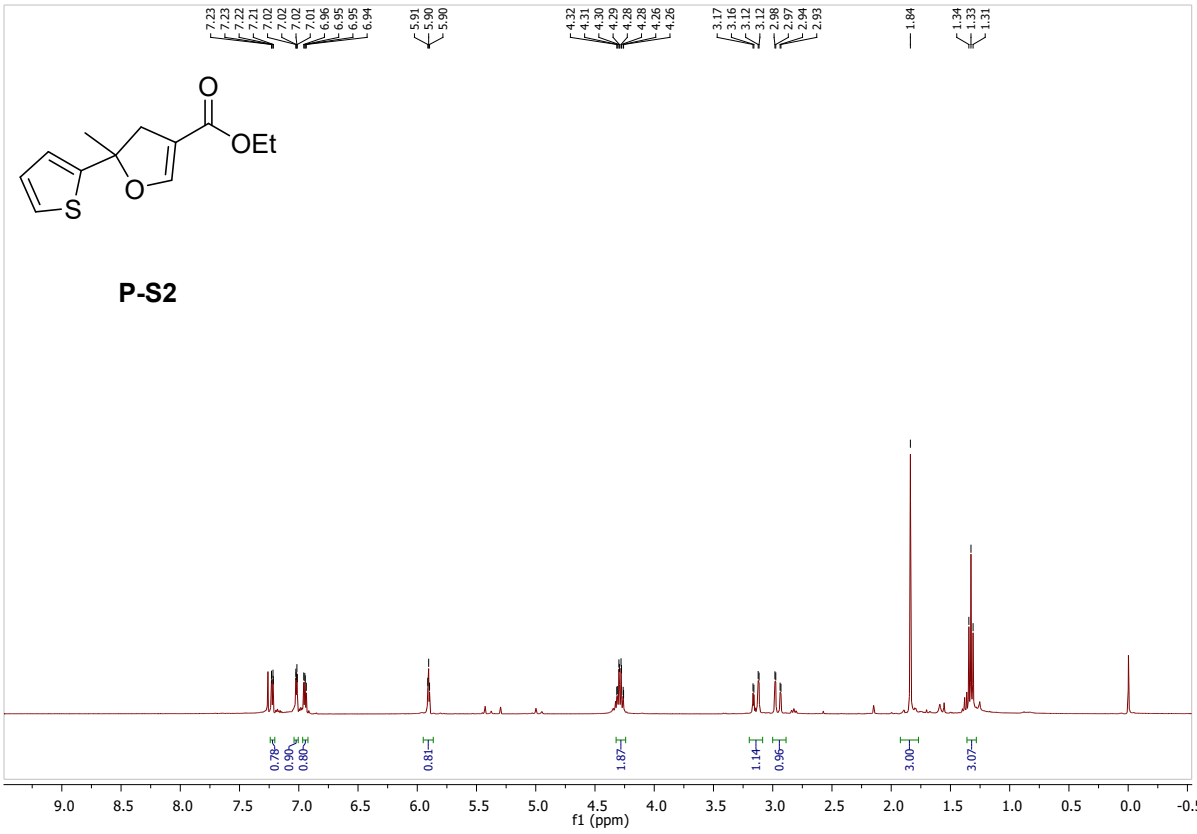
^{13}C NMR (75 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)



^{1}H NMR (400 MHz, $CDCl_3$)


7.23
7.23
7.22
7.21
7.02
7.02
7.02
7.01
6.96
6.95
6.95
6.94
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5.90
5.90
4.32
4.31
4.30
4.29
4.28
4.28
4.26
4.26
3.17
3.16
3.12
3.12
2.98
2.97
2.94
2.93
1.84
1.34
1.33
1.31
O
OEt
O
S
0.78
0.90
0.80
0.81
1.87
1.14
0.96
3.00
3.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

P-S2