

Supplementary information

Complete integration of carbene transfer chemistry into biosynthesis

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Supplementary Table 1 | Initially screened P450s

Protein	Mutations	Description
TbtJ1 ⁶⁵	NO	
TbtJ1 ⁶⁵	C340S	
P450-T2 ⁶⁶	NO	
CYP119 ⁶⁷	T213G, V254A, L155W, R256W	
CYP119 ⁶⁷	T213G, V254A, L155W, R256W, C317S	Mutant shown in Fig. 3a
P450 BM3 ⁶⁸	T268A, C400S, L437W, V78M, L181V	Only heme domain of P450 BM3
P450 BM3 ⁶⁸	T268A, C400S, L437W, V78M, L181V	Full length P450 BM3

Supplementary Table 2 | Plasmids used in this study

Name	Part ID ^a	Description
pAZA007	JBx_233142	Plasmid containing azaserine gene cluster from <i>S. fragilis</i> (other genes: apramycin resistance gene, phi C31 integrase gene). Individual genes in the azaserine gene cluster (aza1 to aza23) with Part ID from JBx_232920 to JBx_232942.
pAZA121 and pAZA138	JBx_233144 and JBx_236844	Plasmid containing genes for styrene biosynthesis in <i>S. albus</i> (other genes: spectinomycin resistance gene, VWB integrase gene)
pAZA128	JBx_233146	Plasmid containing evolved P50-T2-5 mutant gene and genes for styrene biosynthesis in <i>S. albus</i> (other genes: spectinomycin resistance gene, VWB integrase gene)
pAZA132	JBx_233148	Plasmid containing 2 copies of evolved P50-T2-5 mutant gene and genes for styrene biosynthesis in <i>S. albus</i> (other genes: spectinomycin resistance gene, VWB integrase gene)
pAZA037	JBx_233150	Plasmid containing P450-T2 WT gene under control of T7 promoter for expression in <i>E. coli</i>

pAZA076	JBx_233862	Plasmid containing CYP203A1 WT gene under control of T7 promoter for expression in <i>E. coli</i>
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^aThe accession code in the public version of JBEI registry (<http://public-registry.jbei.org>).

Supplementary Table 3 | Data collection and refinement statistics

P450-T2*	
<i>Data collection</i>	
Space group	P 2 21 21
Unit-Cell parameters (Å)	a=85.93 b=95.61 and c=100.43
Resolution range (Å)	41.78 - 1.53 (1.585 - 1.53)
R _{merge} (%)	0.059 (1.56)
<i>I</i> / σ <i>I</i>	15.7 (0.9)
Completeness (%)	100 (99.7)
Redundancy	7.0 (5.4)
CC _{1/2}	0.999 (0.367)
<i>Refinement</i>	
Resolution range (Å)	41.78 - 1.53 (1.585 - 1.53)
Reflections used in refinement	119251 (10768)
R _{work}	0.160 (0.238)
R _{free}	0.186 (0.283)
No. atoms	
Proteins	6188
Ligands/ion	146
Water	1035
RMS from ideal geometry	
Bond lengths (Å)	0.006
Bond angles (°)	0.85
Average B-factor	26.7
Macromolecules	25.4
Ligands	16.1
Solvent	34.3

* Data from a single crystal was used for P450-T2 structure.

Values in parentheses are for highest-resolution shell.

DNA and protein sequences

P450-T2 protein sequence (on pAZA037, residues underlined as N-terminal tag, residue in bold numbered as the 1st residue)

MKSSHHHHHHGSSGMMGLGSFHFDPYSPAIDADPFPSYKRLRDEFPCFWSEEAQMWILSR
YSDIVTAGQDWQTYSSASGNLMTELPGRAGATLGSSDPPKHDRLRGLIQHAFMKRNLM
ALEEPIRDVAKQVFAQVKGVKEFDKDVSSQFTVKVLMALGLPMGEDALVPEHEVRE
NAVLMVQSDARTRAKGPEHIAAYNWMQDYASKVIAMRRASPQNDLISNFALAEIDGDR
LDDREVLTTTTLIMAGVESLGGFMMMFAYNLATFDEARRAVVANPALLPDAIEESLRF
NTSAQRFRRRLMKDVTLHGQTMKEGDFVCLAYGSGNRDERQYPNPDVYDIARKPRGH
LGFGGGVHACLGTAIARLAVKIAFEFHQVVPDYRRVADQLPWMPSSSTFRSPLVLQLKA
Q*

Codon optimized DNA sequence of P450-T2 for expression in *E. coli*

ATGAAATCTTCTCACCATCACCATCACCATGGTAGTTCGGGCATGGGATTAGGTAGC
TTCCACTTCGACCCCTACAGTCCGGCGATCGACGCTGACCCCTTCCCTAGTTATAAA
CGCTTGCGCGATGAGTTCCCCTGCTTCTGGTCTGAAGAGGCCCAAATGTGGATTCTT
TCGCGCTACTCTGATATCGTCACTGCGGGTCAGGACTGGCAAACCTATTCATCGGCC
AGCGGGAACCTAATGACTGAATTGCCGGGTCGCGCAGGCGCAACTCTTGGGTCTTCC
GACCCACCGAAACACGATCGCTTGCCTGGGCTTATTCAGCACGCGTTCATGAAACGT
AACCTGATGGCGTTGGAAGAGCCAATTCGCGACGTCGCGAAACAGGTTTTTCGCGCA
AGTGAAAGGAGTAAAGGAGTTTGACTTTAAGGACGTATCTTCTCAGTTTACTGTCAA
GGTTTTGATGGCCGCGTTGGGGCTGCCCATGGGAGAAGATGCACTGGTACCAGAGC
ATGAAGTTCGCGAAAACGCAGTTCTGATGGTGCAATCGGACGCTCGCACTCGCGCG
AAGGGACCTGAGCACATTGCGGCATACTGGATGCAAGACTACGCATCAAAAGT
AATTGCTATGCGTCGCGCGAGCCCCAAAATGACCTGATTAGCAATTCGCGCTTGC
CGAGATTGATGGAGATCGTTTGGATGATCGCGAGGTGTTACTGACTACAACCACGCT
TATTATGGCCGGAGTGGAGAGCTTAGGTGGTTTTTCATGATGATGTTTCGCATACAATCT

GGCAACTTTCGACGAGGCCCGCCGTGCGGTGGTTGCGAATCCTGCGTTGTTGCCTGACGCGATCGAAGAGTCACTTCGTTTCAACACGTCGGCCCAACGCTTCCGTCGCCGCCTGATGAAAGATGTGACACTGCATGGCCAGACTATGAAGGAAGGTGATTTGTTTTGTCTGGCCTACGGTTCTGGGAACCGTGACGAGCGTCAATATCCCAACCCAGACGTTTATGACATTGCCCCGCAAGCCACGTGGGCATCTTGGCTTTGGAGGAGGTGTTTCATGCCTGTTTAGGCACAGCTATCGCACGCCTGGCGGTCAAGATCGCATTTGAAGAGTTTCACCAGGTAGTCCCCGATTACCGTCGCGTGGCCGATCAGTTGCCGTGGATGCCCTCCTCCACCTCCGTTACCTTTGGTGCTTCAGTTGAAAGCCCAGTAG

Codon optimized DNA sequence of P450-T2-5 for expression in *S. albus*

ATGGGGCTCGGCTCGTTCCACTTCGACCCCTACTCGCCCGCGATCGACGCGGACCCC
TTCCCGTCCTACAAGCGGCTGCGCGACGAATCCCTGCTTCTGGTCCGAAGAAGCC
CAGATGTGGATCCTCTCGCGGTACAGCGACATCGTGACCGCCGGCCAGGACTGGCA
GACCTACTCCTCCGCCAGCGGCAACCTCATGACGGAACCTCGACGGGCGCGCGGGGG
CGACCCTCGGGTCCTCGGACCCCCCGAAGCACGACCGGCTGCGCGGCCTGATCCAG
CACGCCTTCATGAAGCGCAACCTGATGGCGCTCGAGGAGCCGATCCGCGACGTGGC
CAAGCAGGTGTTTCGCCAGGTGAAGGGGGTCAAGGAATTCGACTTCAAGGACGTCT
CGAGCCAGTTCACCGTGAAGGTGCTGATGGCCGCGCTCGGCCTGCCGATGGGCGAG
GACGCGCTCGTCCCGGAACACGAAGTGCGGGAAAACGCCGTCTCATGGTCCAGTC
GGACGCGCGCACCCGGGCCAAGGGGCCCGAGCACATCGCCGCGTACAACCTGGATGC
AGGACTACGCCTCGAAGGTCATCGCCATGCGCCGCGCGTCCCCGCAGAACGACCTG
ATCTCGAACTTCGCCCTCGCCGAGATCGACGGCGACCGCCTCGACGACCGGGAAGT
GCTGCTGACCACGACCACCCTGATCATGGCGGGGGTTCGAGGTCCTCGGGGGCTTCAT
GATGATGTTTCGCGTACAACCTCGCGACCTTCGACGAAGCGCGGGCGCGCCGTCGTCGC
GAACCCGGCGCTGCTGCCCCGACGCCATCGAGGAATCCCTGCGTTCAACACCTCCGC
CCAGCGGTTCCGGCGCCGCCTGATGAAGGACGTCACGCTGCACGGGCAGACCATGA
AGGAAGGCGACTTCGTGTGCCTGGCCTACGGGAGCGGGAACCGGGACGAACGGCA
GTACCCCAACCCCGACGTGTACGACATCGCGCGGAAGCCCCGGGGGCACCTGGGGC
ACGGGGGTGGTGTCCACGCGTGCCTGGGTACGGCCATCGCCCGGCTGGCCGTCAAG
ATCGCGTTCGAAGAATTCCACCAGGTGGTCCCGGACTACCGGCGCGTCGCGGACCA

GCTCCCGTGGATGCCGTCCAGCGAGTTCCGGAGCCCCCTCGTCCTCCAGCTCAAGGC
GCAGTGA

1 **Synthesis of authentic standards for the product (aza-sty, 1, 2, 3, 4 compounds correspond**
2 **to P1, P2, P3, P4 in the manuscript) of the reaction of azaserine with styrene:**

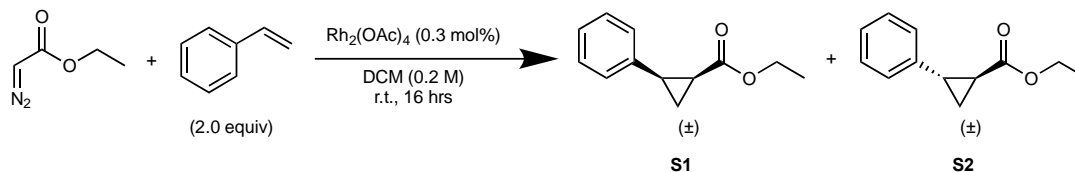
3 Unless stated otherwise, all chemicals, salts, and solvents were obtained from commercial
4 suppliers (e.g. Sigma-Aldrich, Ambeed, Strem Chemicals) and used without further purification.
5 Ethyl diazoacetate was purchased from Sigma-Aldrich as an 87 wt% solution in DCM and was
6 used without further purification. Tetrahydrofuran and dichloromethane were purified by passage
7 through a solvent column comprised of activated alumina, degassed over a copper column, and
8 stored over activated 4Å molecular sieves under an atmosphere of nitrogen for 24 h before use.
9 All air- and moisture-sensitive manipulations were conducted using standard Schlenk techniques
10 under an atmosphere of nitrogen. Solvents and solutions were transferred using air-tight syringes.
11 All flame-dried vessels were placed under vacuum and externally heated using a propane flame.
12 All reactions were performed in flame-dried glassware under an atmosphere of nitrogen and were
13 stirred using Teflon-coated magnetic stirring bars unless otherwise stated. Reactions were
14 monitored by thin layer chromatography (TLC) on Kieselgel 60 F254 glass plates precoated with
15 0.25 mm thickness of silica gel and visualized by UV irradiation. Flash column chromatography
16 was conducted with a Teledyne Isco CombiFlash R_f 200 System using SiliCycle SiliaSep Premium
17 25 µm columns.

18 Nuclear magnetic resonance (NMR) spectra were acquired on a Bruker NEO at 500 MHz
19 for ¹H and 126 MHz for ¹³C or on a Bruker AV-600 at 600 MHz for ¹H and 151 MHz for ¹³C at
20 the NMR facility of the College of Chemistry, University of California, Berkeley. Chemical shifts
21 were reported in ppm downfield of TMS and were referenced to residual solvent signal (¹H-NMR:
22 CDCl₃ δ = 7.76 ppm, CD₃C(O)OD = 2.03 ppm, CD₃OD = 3.31 ppm; ¹³C-NMR: CDCl₃ δ = 77.16
23 ppm, CD₃C(O)OD = 20.00 ppm, CD₃OD = 49.00 ppm). NMR Spectra are reported as follows:
24 chemical shift (multiplicity, coupling constants where applicable, number of nuclei). Splitting is
25 reported with the following symbols: s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet
26 of doublets, dt = doublet of triplets, td = triplet of doublets, m = multiplet. Coupling constants are
27 reported in Hz. High resolution mass spectrometry (HRMS) was performed on a Perkin Elmer
28 axION ESI TOF at the LBNL Catalysis Laboratory, University of California, Berkeley. HRMS
29 data only provided for newly reported compounds. Optical rotation was measured on a Perkin-
30 Elmer 241 Automatic Polarimeter. Sample concentration for polarimetry is given in c = g/mL.
31 Fourier Transform Infrared (FTIR) spectrometry was performed on a Bruker Vertex80 Time-

32 Resolved FTIR at the LBNL Catalysis Laboratory, University of California, Berkeley. FTIR
33 spectra are reported as follows: transmission wavenumber (cm^{-1}), relative intensity, and
34 characteristic bond (e.g. C=O). Relative transmission intensity is reported with the following
35 symbols: br = broad, s = strong, vs = very strong. Only selected resonances are reported. High
36 Performance Liquid Chromatography Mass Spectroscopy (HPLC-MS) analyses were performed
37 on either an Agilent 1260 infinity ii with mass selective detector iQ (MSD iQ) or Agilent 6545
38 with quadrupole time-of-flight (Q-TOF) with a MilliporeSigma Astec CYCLOBOND I 2000 HP-
39 RSP Chiral HPLC (5 μm , 25 cm x 4.6 mm) analytical column. The mobile phase consisted of 10
40 mM ammonium formate in water with 50 μL formic acid added per liter (solvent A) and 0.1%
41 (v/v) formic acid in acetonitrile (solvent B), and separations were performed as follows: held at
42 14% B from 0 min to 32 min. The flow rate was held at 0.35 mL/min from 0 min to 23 min,
43 increased to 0.8 mL/min in 0.2 min, held at 0.8 mL/min from 23.2 min to 32 min. Retention time
44 (T_r) is reported as detection time (in minutes) after sample injection.

45

46 **Synthesis of cis-ethyl-2-phenylcyclopropane-1-carboxylate (S1) and trans-ethyl-2-phenyl-**
47 **cyclopropane-1-carboxylate (S2)**

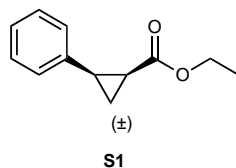


48

49 To a flame-dried, 500-mL round-bottom flask with magnetic stirring bar was added
50 $\text{Rh}_2(\text{OAc})_4$ (134 mg, 0.303 mmol, 0.3 mol%). The flask was placed under vacuum and backfilled
51 with nitrogen three times before 400 mL of dry, degassed dichloromethane (0.25 M) was added,
52 producing a light-green suspension of catalyst. The flask was then flushed with nitrogen for 10
53 min under constant stirring. Styrene (22.9 mL, 200 mmol, 2.00 equiv) was added to the reaction
54 flask and allowed to stir for 10 min at room temperature. Ethyl diazoacetate (12.1 mL, 100 mmol,
55 1.00 equiv) was then slowly added (0.80 mL per hour) over 15 h at room temperature under
56 nitrogen using a syringe pump. Once all ethyl diazoacetate had been added, the reaction was
57 allowed to stir under nitrogen for an additional 1 h, during which the reaction maintained a
58 consistent heterogenous blue-green color. The reaction mixture was concentrated to approximately
59 200 mL under reduced pressure and filtered through silica gel with 100 mL of dichloromethane,
60 giving a yellow-brown solution. This solution was then concentrated under reduced pressure to a

61 viscous, yellow oil. The crude residue was purified by flash column chromatography (gradient
62 0%→10% diethyl ether:hexanes) to yield **S1** (5.83 g, 30.7 mmol, 31% yield) as a colorless oil and
63 **S2** (9.00 g, 47.3 mmol, 47% yield) as a colorless, crystalline solid.

64



65

66 Data for cis-ethyl-2-phenylcyclopropane-1-carboxylate (**S1**)

67 ¹H NMR (500 MHz, CDCl₃) δ 7.29 – 7.22 (m, 4H), 7.18 (ddt, *J* = 8.6, 5.6, 2.9 Hz, 1H), 3.86 (q, *J*
68 = 7.1 Hz, 2H), 2.57 (td, *J* = 9.0, 7.5 Hz, 1H), 2.07 (ddd, *J* = 9.3, 7.8, 5.6 Hz, 1H), 1.77 – 1.65 (m,
69 1H), 1.31 (td, *J* = 8.2, 5.0 Hz, 1H), 0.96 (t, *J* = 7.1 Hz, 3H).

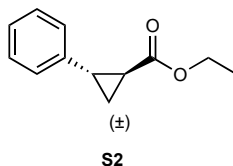
70 ¹³C NMR (126 MHz, CDCl₃) δ 171.09, 136.69, 129.42, 127.99, 126.75, 60.28, 25.58, 21.92,
71 14.13, 11.22.

72 FTIR (neat, cm⁻¹) *ν*_{max}: 1722 vs (C=O), 1175 vs (C–O)

73 *R*_f (10:90 ethyl acetate:hexanes): 0.40

74 ¹H-NMR and ¹³C-NMR of **S1** were consistent with those reported previously⁶⁹.

75



76

77 Data for trans-ethyl-2-phenylcyclopropane-1-carboxylate (**S2**)

78 ¹H NMR (500 MHz, CDCl₃) δ 7.26 (dd, *J* = 8.4, 6.8 Hz, 2H), 7.21 – 7.15 (m, 1H), 7.12 – 7.04 (m,
79 2H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.51 (ddd, *J* = 9.2, 6.5, 4.1 Hz, 1H), 1.89 (ddd, *J* = 8.3, 5.3, 4.1 Hz,
80 1H), 1.59 (dt, *J* = 9.5, 4.9 Hz, 1H), 1.40 – 1.15 (m, 4H).

81 ¹³C NMR (126 MHz, CDCl₃) δ 173.47, 140.21, 128.55, 126.55, 126.24, 60.77, 26.25, 24.27,
82 17.14, 14.36.

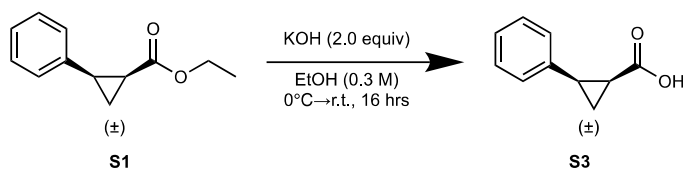
83 FTIR (neat, cm⁻¹) *ν*_{max}: 1714 vs (C=O), 1175 vs (C–O)

84 *R*_f (10:90 ethyl acetate:hexanes): 0.44

85 ¹H-NMR and ¹³C-NMR of **S2** were consistent with those reported previously⁷⁰.

86

87 **Synthesis of cis-2-phenylcyclopropane-1-carboxylic acid (S3)**



88

89 To a 50-mL, round-bottom flask with magnetic stirring bar under an atmosphere of air was

90 added potassium hydroxide (1.12 g, 20.0 mmol, 2.00 equiv). This material was dissolved in 23 mL

91 of absolute ethanol (final reaction concentration of 0.30 M) at room temperature under vigorous

92 stirring. Once the KOH had fully dissolved, the cloudy solution was cooled to 0 °C in an ice-water

93 bath for 15 min. **S1** (1.90 g, 10.0 mmol, 1.00 equiv) was dissolved in 7 mL of absolute ethanol and

94 was slowly added to the stirring ethanolic solution of KOH over 10 min. The reaction was allowed

95 to warm to room temperature overnight, during which time it turned light-orange. The reaction

96 mixture was diluted with diH₂O and transferred to a separatory funnel. The aqueous solution was

97 extracted three times with dichloromethane to remove uncharged impurities. The organic fractions

98 were combined and back-extracted with 0.5 M NaOH; the organic fractions were discarded. The

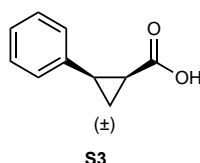
99 aqueous layers were combined and acidified to pH 1 with 6 N HCl, producing a cloudy, white

100 suspension. This suspension was extracted 5 times with dichloromethane. The organic fractions

101 were combined and sequentially washed with 1 N HCl and brine, dried over MgSO₄, and

102 concentrated under reduced pressure to yield a light-orange residue. This residue was recrystallized

103 from boiling pentanes to give **S3** (1.48 g, 9.14 mmol, 91% yield) as off-white needles.



105

106 Data for cis-2-phenylcyclopropane-1-carboxylic acid (**S3**)

107 **¹H NMR** (500 MHz, CDCl₃) δ 7.30 – 7.20 (m, 5H), 2.65 (q, *J* = 8.6 Hz, 1H), 2.05 (ddd, *J* = 9.2,

108 7.7, 5.6 Hz, 1H), 1.68 (dt, *J* = 7.7, 5.3 Hz, 1H), 1.39 (ddd, *J* = 8.7, 7.7, 5.0 Hz, 1H).

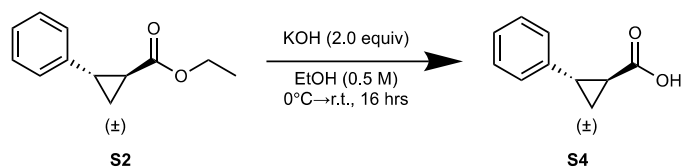
109 **¹³C NMR** (126 MHz, CDCl₃) δ 177.00, 136.01, 129.39, 128.08, 126.91, 26.70, 21.48, 12.18.

110 **FTIR** (neat, cm⁻¹) *ν*_{max}: 2936 br (O–H), 1688 vs (C=O), 1446 s (O–H)

111 **R_f** (20:80 ethyl acetate:hexanes): 0.17

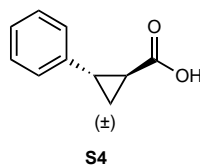
112 ¹H-NMR and ¹³C-NMR of **S3** were consistent with those reported previously⁷¹.

113 **Synthesis of trans-2-phenylcyclopropane-1-carboxylic acid (S4)**



114
 115 To a 100-mL, round-bottom flask with magnetic stirring bar under an atmosphere of air was
 116 added potassium hydroxide (4.49 g, 80.0 mmol, 2.00 equiv). This material was dissolved in 60 mL
 117 of absolute ethanol (final reaction concentration of 0.50 M) at room temperature under vigorous
 118 stirring. Once the KOH had fully dissolved, the cloudy solution was cooled to 0 °C in an ice-water
 119 bath for 15 min. **S2** (1.90 g, 10.0 mmol, 1.00 equiv) was dissolved in 20 mL of absolute ethanol
 120 and was slowly added to the stirring ethanolic solution of KOH over 10 min. The reaction was
 121 allowed to warm to room temperature overnight, during which time it became light yellow
 122 alongside formation of a white precipitate. The reaction mixture was diluted with diH₂O,
 123 dissolving the precipitate, and transferred to a separatory funnel. The aqueous solution was
 124 extracted three times with dichloromethane to remove uncharged impurities. The organic fractions
 125 were combined and back-extracted with 0.5 M NaOH; the organic fractions were discarded. The
 126 aqueous layers were combined and acidified to pH 1 with 6 N HCl, producing a cloudy, white
 127 suspension. This suspension was extracted 5 times with dichloromethane. The organic fractions
 128 were combined and sequentially washed with 1 N HCl and brine, dried over MgSO₄, and
 129 concentrated under reduced pressure to yield a yellow residue. This residue was recrystallized from
 130 boiling pentanes to give **S4** (5.38 g, 33.2 mmol, 83% yield) as a light-yellow crystalline solid.

131



132

133 Data for trans-2-phenylcyclopropane-1-carboxylic acid (**S4**)

134 ¹H NMR (500 MHz, CDCl₃) δ 11.81 (s, 1H), 7.26 (t, *J* = 7.6 Hz, 2H), 7.21 – 7.16 (m, 1H), 7.08
 135 (dd, *J* = 7.3, 1.8 Hz, 2H), 2.58 (ddd, *J* = 9.3, 6.7, 4.1 Hz, 1H), 1.88 (ddd, *J* = 8.8, 5.2, 4.0 Hz, 1H),
 136 1.64 (dt, *J* = 9.6, 4.9 Hz, 1H), 1.38 (ddd, *J* = 8.4, 6.7, 4.6 Hz, 1H).

137 ¹³C NMR (126 MHz, CDCl₃) δ 180.18, 139.62, 128.67, 126.84, 126.41, 27.25, 24.14, 17.65.

138 FTIR (neat, cm⁻¹) *ν*_{max}: 2938 br (O–H), 1687 vs (C=O), 1446 s (O–H)

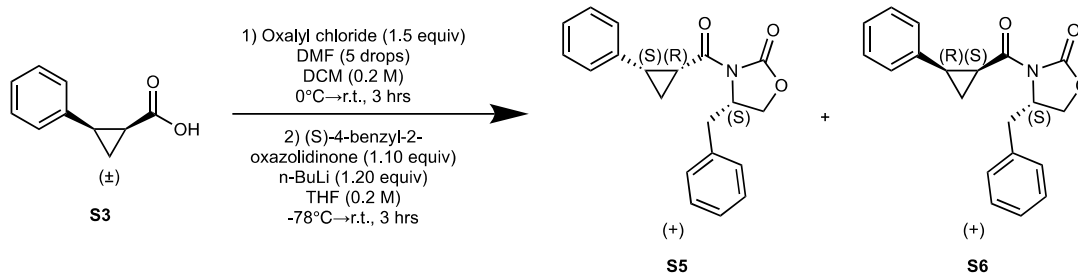
139 **R_f** (20:80 ethyl acetate:hexanes): 0.16

140 ¹H-NMR and ¹³C-NMR of **S4** were consistent with those reported previously⁷¹.

141

142 **Synthesis of (S)-4-benzyl-3-((1R,2S)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one**

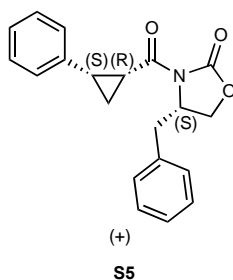
143 **(S5) and (S)-4-benzyl-3-((1S,2R)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one (S6)**



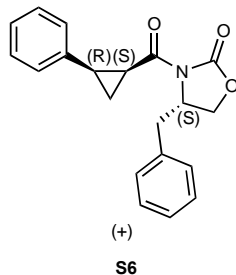
145 To a flame-dried, 50-mL round-bottom flask containing a magnetic stirring bar were added
146 **S3** (1.30 g, 8.00 mmol, 1.00 equiv) and 40 mL of dry, degassed dichloromethane (0.20 M). This
147 flask was flushed with nitrogen for 10 min under constant stirring, at which time the solution was
148 cooled to 0 °C in an ice-water bath for 15 min. Once cooled, 5 drops of dimethylformamide were
149 added, and the solution was allowed to stir for a further 5 min at 0 °C under an atmosphere of
150 nitrogen. Oxalyl chloride (1.03 mL, 12.0 mmol, 1.50 equiv) was slowly added dropwise to the
151 stirring reaction mixture over the course of 10 min, resulting in the yellowing of the reaction
152 mixture and evolution of gas. This reaction was allowed to warm to room temperature over 3 h
153 while stirring. The solution of acyl chloride was concentrated under reduced pressure and dried
154 under vacuum to give an orange oil. The crude acyl chloride was dissolved in 10 mL of dry,
155 degassed tetrahydrofuran.

156 To a flame-dried, 100-mL round-bottom flask equipped with magnetic stirring bar were
157 added (S)-4-benzyl-2-oxazolidine (1.56 g, 8.80 mmol, 1.10 equiv) and 30 mL of dry, degassed
158 tetrahydrofuran (final reaction concentration of 0.20 M). This solution was flushed with nitrogen
159 for 10 min under constant stirring at room temperature, at which time the solution was cooled to -
160 78 °C in a dry ice/acetone bath for 20 min. A 2.5 M solution of n-butyl lithium in hexanes (3.84
161 mL, 9.60 mmol, 1.20 equiv) was added dropwise over 10 min, generating a white precipitate. This
162 reaction mixture was allowed to warm to room temperature under nitrogen over 1 h before cooling
163 the reaction mixture to -78 °C in a dry ice/acetone bath for 20 min. Simultaneously, the solution
164 of acyl chloride in THF was cooled to -78 °C in a dry ice/acetone bath under an atmosphere of
165 nitrogen for 20 min. Once cooled, the solution of acyl chloride was added slowly to the stirring

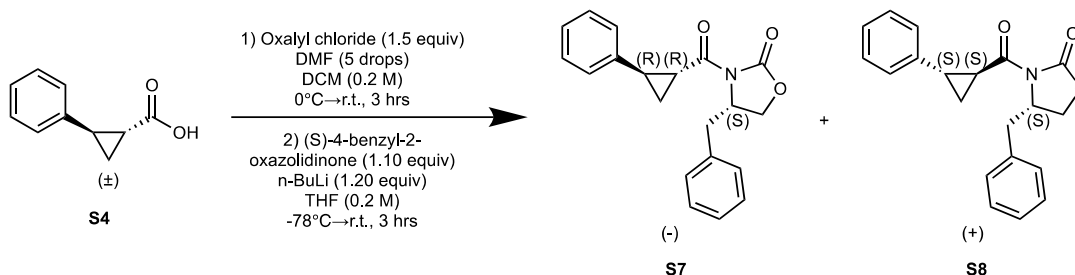
166 solution of lithiated oxazolidinone over the course of 5 min, during which time the reaction became
167 light yellow/orange. The reaction mixture was allowed to stir at -78 °C under an atmosphere of
168 nitrogen for 1 h before warming to room temperature over an additional 1 h. The reaction was
169 quenched with the addition of 20 mL of diH₂O, and the resulting mixture was allowed to stir for
170 10 min. This mixture was transferred to a separatory funnel and extracted 5 times with
171 dichloromethane. The organic layers were combined and sequentially washed with 1 N NaOH, 1
172 N HCl, diH₂O, and brine. The organic layer then was dried over MgSO₄ and concentrated to a
173 light-brown solid. The residue was purified by column chromatography (5%→15% ethyl
174 acetate:hexanes) to give **S5** (1.04 g, 3.22 mmol, 81% yield with respect to starting enantiomer of
175 **S3**) as a granular, colorless solid, and **S6** (1.11 g, 3.44 mmol, 86% yield with respect to starting
176 enantiomer of **S3**) as a colorless, crystalline solid.
177



178
179 Data for (*S*)-4-benzyl-3-((1*R*,2*S*)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one (**S5**)
180 ¹H NMR (500 MHz, CDCl₃) δ 7.35 – 7.21 (m, 7H), 7.20 – 7.14 (m, 1H), 7.00 – 6.94 (m, 2H), 4.51
181 – 4.38 (m, 1H), 4.18 – 4.08 (m, 1H), 4.04 (dd, *J* = 9.1, 2.3 Hz, 1H), 3.36 (ddd, *J* = 9.8, 7.3, 5.9 Hz,
182 1H), 2.90 (dt, *J* = 9.7, 7.8 Hz, 1H), 2.51 (dd, *J* = 13.5, 3.3 Hz, 1H), 2.15 – 2.02 (m, 2H), 1.45 (ddd,
183 *J* = 8.4, 7.3, 5.2 Hz, 1H).
184 ¹³C NMR (126 MHz, CDCl₃) δ 169.17, 153.68, 135.92, 135.66, 129.37, 129.19, 128.89, 128.08,
185 127.17, 126.92, 66.02, 55.47, 37.28, 27.15, 24.19, 10.33.
186 FTIR (neat, cm⁻¹) ν_{max}: 1769 vs (C=O), 1687 vs (C=O)
187 HRMS (ESI): *m/z* for C₂₀H₁₉NNaO₃⁺ [M+Na]⁺ calcd.: 344.1257, found: 344.1268.
188 [α]_D²⁵ = +152 degrees (c = 0.010, CHCl₃)
189 R_f (20:80 ethyl acetate:hexanes): 0.28
190



191
 192 Data of (*S*)-4-benzyl-3-((1*S*,2*R*)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one (**S6**)
 193 **¹H NMR** (500 MHz, CDCl₃) δ 7.34 – 7.17 (m, 8H), 7.17 – 7.08 (m, 2H), 4.31 (ddt, *J* = 9.5, 7.9,
 194 3.3 Hz, 1H), 4.03 (dd, *J* = 9.0, 3.1 Hz, 1H), 3.92 (t, *J* = 8.5 Hz, 1H), 3.40 (ddd, *J* = 9.6, 7.5, 5.9
 195 Hz, 1H), 3.19 (dd, *J* = 13.4, 3.5 Hz, 1H), 2.81 (q, *J* = 8.4 Hz, 1H), 2.70 (dd, *J* = 13.4, 9.6 Hz, 1H),
 196 2.02 (dt, *J* = 7.4, 5.5 Hz, 1H), 1.47 (td, *J* = 8.0, 5.1 Hz, 1H).
 197 **¹³C NMR** (126 MHz, CDCl₃) δ 169.51, 153.80, 136.18, 135.33, 129.51, 128.97, 128.95, 128.16,
 198 127.34, 126.84, 65.99, 55.06, 37.97, 27.23, 23.83, 11.18.
 199 **FTIR** (neat, cm⁻¹) *ν*_{max}: 1771 vs (C=O), 1685 vs (C=O)
 200 **HRMS** (ESI): *m/z* for C₂₀H₁₉NNaO₃⁺ [M+Na]⁺ calcd.: 344.1257, found: 344.1249.
 201 **[α]_D²⁵** = +14.3 degrees (c = 0.014, CHCl₃)
 202 **R_f** (20:80 ethyl acetate:hexanes): 0.49
 203
 204 **Synthesis of (*S*)-4-benzyl-3-((1*R*,2*R*)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one**
 205 **(*S7*) and (*S*)-4-benzyl-3-((1*S*,2*S*)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one (*S8*)**

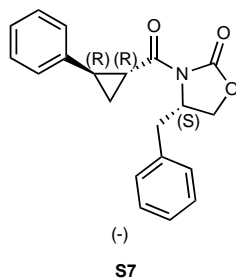


206
 207 To a flame-dried, 100-mL round-bottom flask containing a magnetic stirring bar were
 208 added **S4** (2.17 g, 13.4 mmol, 1.00 equiv) and 70 mL of dry, degassed dichloromethane (0.2 M).
 209 This flask was flushed with nitrogen for 10 min under constant stirring, at which time the solution
 210 was cooled to 0 °C in an ice-water bath for 15 min. Once cooled, 10 drops of dimethylformamide
 211 were added, and the solution was allowed to stir for a further 5 min at 0 °C under an atmosphere
 212 of nitrogen. Oxalyl chloride (1.73 mL, 20.1 mmol, 1.50 equiv) was slowly added dropwise to the

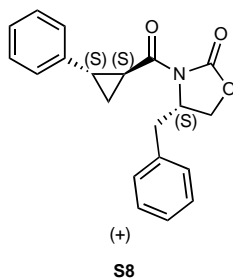
213 stirring reaction mixture over the course of 10 min, resulting in the yellowing of the reaction
214 mixture and evolution of gas. This reaction was allowed to warm to room temperature over 3 h
215 while stirring. The solution of acyl chloride was concentrated under reduced pressure and dried
216 under vacuum to give a dark-red oil. The crude acyl chloride was dissolved in 15 mL of dry,
217 degassed tetrahydrofuran.

218 To a flame-dried, 100-mL round-bottom flask equipped with magnetic stirring bar were
219 added (S)-4-benzyl-2-oxazolidine (2.60 g, 14.7 mmol, 1.10 equiv) and 50 mL of dry, degassed
220 tetrahydrofuran (final reaction concentration of 0.2 M). This solution was flushed with nitrogen
221 for 10 min under constant stirring at room temperature, at which time the solution was cooled to -
222 78 °C in a dry ice/acetone bath for 20 min. A 2.5 M solution of n-butyl lithium in hexanes (6.43
223 mL, 16.1 mmol, 1.20 equiv) was added dropwise over 10 min, generating a white precipitate. This
224 reaction mixture was allowed to warm to room temperature under nitrogen over 1 h before cooling
225 the reaction mixture to -78 °C in a dry ice/acetone bath for 20 min. Simultaneously, the solution
226 of acyl chloride in THF was cooled to -78 °C in a dry ice/acetone bath under an atmosphere of
227 nitrogen for 20 min. Once cooled, the solution of acyl chloride was added slowly to the stirring
228 solution of lithiated oxazolidinone over the course of 5 min, during which time the reaction became
229 red/orange in color. The reaction mixture was allowed to stir at -78 °C under an atmosphere of
230 nitrogen for 1 h before warming to room temperature over an additional 1 h. The reaction was
231 quenched with the addition of 30 mL of diH₂O, and the resulting mixture was allowed to stir for
232 10 min. This mixture was transferred to a separatory funnel and extracted 5 times with
233 dichloromethane. The organic layers were combined and sequentially washed with 1 N NaOH, 1
234 N HCl, diH₂O, and brine. The organic layer then was dried over MgSO₄ and concentrated to a
235 light-brown solid. The residue was purified by column chromatography (5%→20% ethyl
236 acetate:hexanes) to give **S7** (2.02 g, 6.30 mmol, 94% yield with respect to starting enantiomer of
237 **S4**) as a colorless, fibrous solid and **S8** (1.63 g, 5.08 mmol, 76% yield with respect to starting
238 enantiomer of **S4**) as a colorless, needle-like solid.

239



240
 241 Data of (*S*)-4-benzyl-3-((1*R*,2*R*)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one (**S7**)
 242 **¹H NMR** (500 MHz, CDCl₃) δ 7.38 – 7.22 (m, 10H), 4.75 (ddt, *J* = 9.4, 7.7, 3.2 Hz, 1H), 4.30 –
 243 4.15 (m, 2H), 3.62 (ddd, *J* = 8.3, 5.2, 4.2 Hz, 1H), 3.33 (dd, *J* = 13.4, 3.5 Hz, 1H), 2.84 (dd, *J* =
 244 13.4, 9.5 Hz, 1H), 2.77 (ddd, *J* = 9.3, 6.6, 4.1 Hz, 1H), 1.81 (ddd, *J* = 9.3, 5.2, 4.1 Hz, 1H), 1.48
 245 (ddd, *J* = 8.3, 6.6, 4.1 Hz, 1H).
 246 **¹³C NMR** (126 MHz, CDCl₃) δ 172.78, 153.89, 139.82, 135.42, 129.55, 129.06, 128.63, 127.44,
 247 126.78, 126.68, 66.20, 55.60, 38.16, 29.10, 23.09, 19.26.
 248 **FTIR** (neat, cm⁻¹) *ν*_{max}: 1781 vs (C=O), 1674 vs (C=O)
 249 **HRMS** (ESI): *m/z* for C₂₀H₁₉NNaO₃⁺ [M+Na]⁺ calcd.: 344.1257, found: 344.1244.
 250 **[α]_D²⁵** = -156 degrees (c = 0.011, CHCl₃)
 251 **R_f** (20:80 ethyl acetate:hexanes): 0.37
 252



253
 254 Data of (*S*)-4-benzyl-3-((1*S*,2*S*)-2-phenylcyclopropane-1-carbonyl)oxazolidin-2-one (**S7**)
 255 **¹H NMR** (500 MHz, CDCl₃) δ 7.46 – 7.17 (m, 10H), 4.74 (ddt, *J* = 10.3, 6.8, 3.3 Hz, 1H), 4.29 –
 256 4.13 (m, 2H), 3.63 (ddd, *J* = 8.1, 5.2, 4.1 Hz, 1H), 3.37 (dd, *J* = 13.4, 3.4 Hz, 1H), 2.85 (dd, *J* =
 257 13.4, 9.6 Hz, 1H), 2.75 (ddd, *J* = 9.2, 6.6, 4.2 Hz, 1H), 1.86 (ddd, *J* = 9.3, 5.3, 4.1 Hz, 1H), 1.55
 258 (ddd, *J* = 8.3, 6.6, 4.1 Hz, 1H).
 259 **¹³C NMR** (126 MHz, CDCl₃) δ 172.75, 153.91, 139.78, 135.48, 129.56, 129.08, 128.61, 127.46,
 260 126.77, 126.60, 66.18, 55.81, 38.10, 28.99, 23.11, 19.42.
 261 **FTIR** (neat, cm⁻¹) *ν*_{max}: vs 1758 (C=O), 1673 vs (C=O)

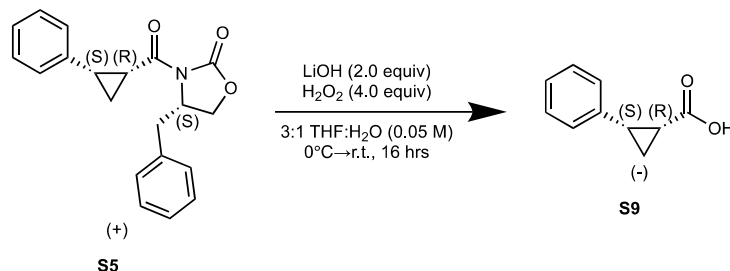
262 **HRMS** (ESI): m/z for $C_{20}H_{20}NO_3^+$ $[M+H]^+$ calcd.: 322.1438, found: 322.1424.

263 $[\alpha]_D^{25} = +302$ degrees ($c = 0.011$, $CHCl_3$)

264 **R_f** (20:80 ethyl acetate:hexanes): 0.46

265

266 **Synthesis of (1*R*,2*S*)-2-phenylcyclopropane-1-carboxylic acid (S9)**

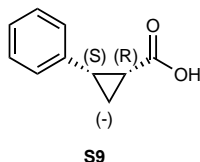


267

268 Procedure modified from Evans *et al*⁷². To a 50-mL, round-bottom flask containing a
269 magnetic stirring bar under an atmosphere of air were added **S5** (0.579 g, 1.80 mmol, 1.0 equiv)
270 and 36 mL of 3:1 THF:H₂O (0.05 M). This solution was allowed to stir at room temperature for 5
271 min before 30% H₂O₂ (0.735 mL, 7.20 mmol, 4.0 equiv) was added. LiOH (86.2 mg, 3.60 mmol,
272 2.0 equiv) was then added to the reaction mixture as one portion and allowed to stir at room
273 temperature for 16 h. Sodium sulfite (998 mg, 7.92 mmol, 4.4 equiv) was dissolved in 5 mL of
274 diH₂O and added to the reaction mixture. The resulting solution was allowed to stir at room
275 temperature for an additional 10 min. The reaction mixture was transferred to a separatory funnel,
276 10 mL of 1 N NaOH was added, and the aqueous layer was extracted with dichloromethane twice
277 to remove neutral organic products. The organic layers were combined and back-extracted with
278 0.5 N NaOH twice; the organic fraction was then discarded. The aqueous fractions were combined,
279 acidified to pH 1 with 6 N HCl, producing a cloudy, white suspension, and extracted 5 times with
280 dichloromethane. The organic fractions were combined and washed with 1 N HCl and brine, then
281 dried over MgSO₄ and concentrated under reduced pressure to give a colorless solid. This residue
282 was recrystallized from boiling pentanes to give **S9** (0.249 g, 1.54 mmol, 85% yield) as a fibrous,
283 colorless solid.

284

285



286

287 Data for (1*R*,2*S*)-2-phenylcyclopropane-1-carboxylic acid (**S9**)

288 ¹H NMR (500 MHz, CDCl₃) δ 11.04 (s, 1H), 7.32 – 7.20 (m, 5H), 2.64 (q, *J* = 8.6 Hz, 1H), 2.05
 289 (ddd, *J* = 9.3, 7.7, 5.6 Hz, 1H), 1.68 (dt, *J* = 7.8, 5.4 Hz, 1H), 1.38 (ddd, *J* = 8.7, 7.7, 5.0 Hz, 1H).

290 ¹³C NMR (500 MHz, CDCl₃) δ 177.47, 136.02, 129.37, 128.05, 126.87, 26.68, 21.54, 12.16.

291 FTIR (neat, cm⁻¹) ν_{max}: 2939 br (O–H), 1684 vs (C=O), 1442 s (O–H)

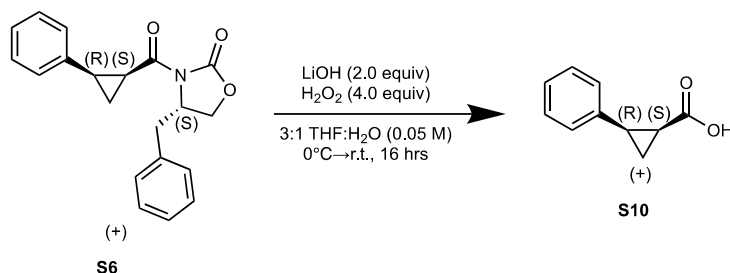
292 [α]_D²⁵ = -30.0 degrees (c = 0.010, CHCl₃)

293 R_f (20:80 ethyl acetate:hexanes): 0.17

294 ¹H-NMR and ¹³C-NMR, and [α]_D²⁵ of **S9** were consistent with those reported previously⁷³.

295

296 **Synthesis of (1*S*,2*R*)-2-phenylcyclopropane-1-carboxylic acid (**S10**)**

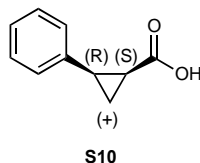


297

298 Procedure modified from Evans *et al*⁷². To a 50-mL, round-bottom flask containing a
 299 magnetic stirring bar under an atmosphere of air were added **S6** (0.656 g, 2.04 mmol, 1.0 equiv)
 300 and 41 mL of 3:1 THF:H₂O (0.05 M). This solution was allowed to stir at room temperature for 5
 301 min before 30% H₂O₂ (0.833 mL, 8.17 mmol, 4.0 equiv) was added. LiOH (171 mg, 4.08 mmol,
 302 2.0 equiv) was then added to the reaction mixture as one portion and allowed to stir at room
 303 temperature for 16 h. Sodium sulfite (1.13 g, 8.98 mmol, 4.4 equiv) was dissolved in 10 mL of
 304 diH₂O and added to the reaction mixture. The resulting solution was allowed to stir at room
 305 temperature for an additional 10 min. The reaction mixture was transferred to a separatory funnel,
 306 10 mL of 1 N NaOH was added, and the aqueous layer was extracted with dichloromethane twice
 307 to remove neutral organic products. The organic layers were combined and back-extracted with
 308 0.5 N NaOH twice; the organic fraction was then discarded. The aqueous fractions were combined,
 309 acidified to pH 1 with 6 N HCl, producing a cloudy, white suspension, and extracted 5 times with

310 dichloromethane. The organic fractions were combined and washed with 1 N HCl and brine, then
311 dried over MgSO₄ and concentrated under reduced pressure to give a colorless solid. This residue
312 was recrystallized from boiling pentanes to give **S10** (0.254 g, 1.56 mmol, 77% yield) as a fibrous,
313 colorless solid.

314



315

316 Data for (1*S*,2*R*)-2-phenylcyclopropane-1-carboxylic acid (**S10**)

317 ¹H NMR (500 MHz, CDCl₃) δ 10.66 (s, 1H), 7.32 – 7.13 (m, 5H), 2.60 (q, *J* = 8.6 Hz, 1H), 2.01
318 (ddd, *J* = 9.4, 7.7, 5.6 Hz, 1H), 1.64 (dt, *J* = 7.7, 5.3 Hz, 1H), 1.34 (ddd, *J* = 8.9, 7.7, 5.0 Hz, 1H).

319 ¹³C NMR (500 MHz, CDCl₃) δ 177.41, 136.03, 129.38, 128.06, 126.87, 26.68, 21.54, 12.16.

320 FTIR (neat, cm⁻¹) *ν*_{max}: 3026 br (O–H), 1683 vs (C=O), 1441 s (O–H)

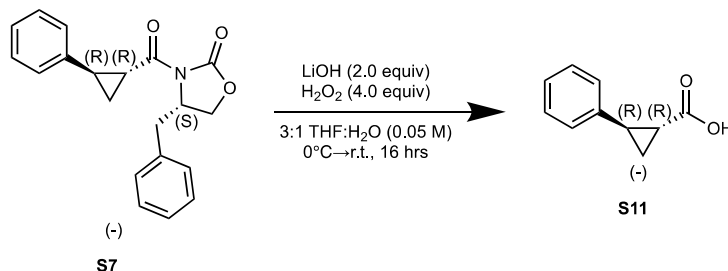
321 [α]_D²⁵ = +28.7 degrees (c = 0.010, CHCl₃)

322 *R*_f (20:80 ethyl acetate:hexanes): 0.17

323 ¹H-NMR and ¹³C-NMR, and [α]_D²⁵ of **S10** were consistent with those reported previously⁷³.

324

325 **Synthesis of (1*R*,2*R*)-2-phenylcyclopropane-1-carboxylic acid (**S11**)**

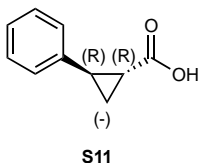


326

327 Procedure modified from Evans *et al*⁷². To a 100-mL, round-bottom flask containing a
328 magnetic stirring bar under an atmosphere of air were added **S7** (1.01 g, 3.14 mmol, 1.0 equiv)
329 and 60 mL of 3:1 THF:H₂O (0.05 M). This solution was allowed to stir at room temperature for 5
330 min before 30% H₂O₂ (1.28 mL, 12.6 mmol, 4.0 equiv) was added. LiOH (264 mg, 6.28 mmol,
331 2.0 equiv) was then added to the reaction mixture as one portion and allowed to stir at room
332 temperature for 16 h. Sodium sulfite (1.74 g, 13.8 mmol, 4.4 equiv) was dissolved in 10 mL of
333 diH₂O and added to the reaction mixture. The resulting solution was allowed to stir at room

334 temperature for an additional 10 min. The reaction mixture was transferred to a separatory funnel,
335 10 mL of 1 N NaOH was added, and the aqueous layer was extracted with dichloromethane twice
336 to remove neutral organic products. The organic layers were combined and back-extracted with
337 0.5 N NaOH twice; the organic fraction was then discarded. The aqueous fractions were combined,
338 acidified to pH 1 with 6 N HCl, producing a cloudy, white suspension, and extracted 5 times with
339 dichloromethane. The organic fractions were combined and washed with 1 N HCl and brine, then
340 dried over MgSO₄ and concentrated under reduced pressure to give a colorless solid. This residue
341 was purified by column chromatography (5%→15% ethyl acetate:hexanes) to give **S11** (0.265 g,
342 1.63 mmol, 52% yield) as a viscous, light-yellow oil.

343



344

345 Data for (1*R*,2*R*)-2-phenylcyclopropane-1-carboxylic acid (**S11**)

346 ¹H NMR (500 MHz, CDCl₃) δ 11.69 (s, 1H), 7.26 (td, *J* = 7.2, 1.3 Hz, 2H), 7.22 – 7.16 (m, 1H),
347 7.11 – 7.05 (m, 2H), 2.58 (ddd, *J* = 9.2, 6.7, 4.1 Hz, 1H), 1.88 (ddd, *J* = 8.2, 5.2, 4.1 Hz, 1H),
348 1.64 (dt, *J* = 9.6, 4.9 Hz, 1H), 1.38 (ddd, *J* = 8.3, 6.7, 4.6 Hz, 1H).

349 ¹³C NMR (500 MHz, CDCl₃) δ 179.85, 139.84, 128.62, 126.72, 126.39, 27.00, 24.37, 17.57.

350 FTIR (neat, cm⁻¹) ν_{max}: 3029 br (O–H), 1689 vs (C=O), 1427 s (O–H)

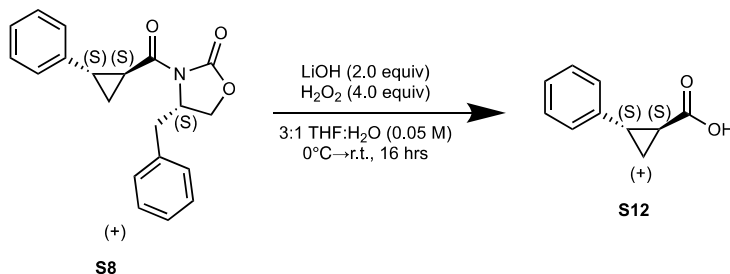
351 [α]_D²⁵ = -378 degrees (c = 0.011, CHCl₃)

352 R_f (20:80 ethyl acetate:hexanes): 0.16

353 ¹H-NMR and ¹³C-NMR, and [α]_D²⁵ of **S11** were consistent with those reported previously⁷³.

354

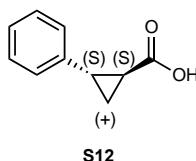
355 **Synthesis of (1*S*,2*S*)-2-phenylcyclopropane-1-carboxylic acid (**S12**)**



356

357 Procedure modified from Evans *et al*⁷². To a 100-mL, round-bottom flask containing a
358 magnetic stirring bar under an atmosphere of air were added **S8** (0.972 g, 3.02 mmol, 1.0 equiv)
359 and 60 mL of 3:1 THF:H₂O (0.05 M). This solution was allowed to stir at room temperature for 5
360 min before 30% H₂O₂ (1.23 mL, 12.1 mmol, 4.0 equiv) was added. LiOH (254 mg, 6.05 mmol,
361 2.0 equiv) was then added to the reaction mixture as one portion and allowed to stir at room
362 temperature for 16 h. Sodium sulfite (1.68 g, 13.3 mmol, 4.4 equiv) was dissolved in 10 mL of
363 diH₂O and added to the reaction mixture. The resulting solution was allowed to stir at room
364 temperature for an additional 10 min. The reaction mixture was transferred to a separatory funnel,
365 10 mL of 1 N NaOH was added, and the aqueous layer was extracted with dichloromethane twice
366 to remove neutral organic products. The organic layers were combined and back-extracted with
367 0.5 N NaOH twice; the organic fraction was then discarded. The aqueous fractions were combined,
368 acidified to pH 1 with 6 N HCl, producing a cloudy, white suspension, and extracted 5 times with
369 dichloromethane. The organic fractions were combined and washed with 1 N HCl and brine, then
370 dried over MgSO₄ and concentrated under reduced pressure to give a colorless solid. This residue
371 was purified by column chromatography (5%→15% ethyl acetate:hexanes) give **S12** (0.328 g,
372 2.02 mmol, 67% yield) as a viscous, colorless liquid which solidified to a colorless solid after
373 standing for 2 days.

374



375
376 Data for (1*S*,2*S*)-2-phenylcyclopropane-1-carboxylic acid (**S12**)
377 ¹H NMR (500 MHz, CDCl₃) δ 11.33 (s, 1H), 7.26 (td, *J* = 7.3, 1.4 Hz, 2H), 7.22 – 7.16 (m, 1H),
378 7.11 – 7.05 (m, 2H), 2.58 (ddd, *J* = 9.3, 6.7, 4.1 Hz, 1H), 1.88 (ddd, *J* = 8.3, 5.2, 4.1 Hz, 1H), 1.64
379 (dt, *J* = 9.6, 4.9 Hz, 1H), 1.38 (ddd, *J* = 8.4, 6.7, 4.6 Hz, 1H).

380 ¹³C NMR (500 MHz, CDCl₃) δ 180.00, 139.64, 128.67, 126.84, 126.41, 27.24, 24.13, 17.64.

381 FTIR (neat, cm⁻¹) ν_{max}: 3029 br (O–H), 1686 vs (C=O), 1444 s (O–H)

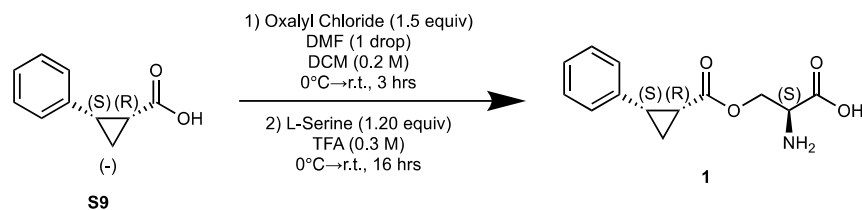
382 [α]_D²⁵ = +388 degrees (c = 0.011, CHCl₃)

383 R_f (20:80 ethyl acetate:hexanes): 0.16

384 ¹H-NMR and ¹³C-NMR, and [α]_D²⁵ of **S12** were consistent with those reported previously⁷³.

385

386 **Synthesis of *O*-((1*R*,2*S*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**1**)**

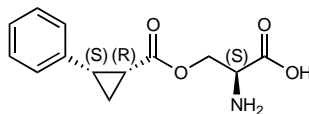


387

388 To a flame-dried, 1-dram (3.7 mL) vial equipped with magnetic stirring bar was added **S9**
 389 (73.6 mg, 0.454 mmol, 1.0 equiv). The vial was placed under vacuum and backfilled with nitrogen
 390 3 times. To the vial was added 2.3 mL of dry, degassed dichloromethane (0.2 M), and this solution
 391 was allowed to stir at room temperature under an atmosphere of nitrogen for 5 min. One drop of
 392 dimethylformamide was added to the reaction mixture, and the resulting mixture was allowed to
 393 stir for 2 min. The vial was allowed to cool to 0 °C in an ice-water bath for 10 min before oxalyl
 394 chloride (58 μL, 0.681 mmol, 1.5 equiv) was added dropwise over 5 min. The reaction was allowed
 395 to warm to room temperature over 3 h under an atmosphere of nitrogen. The reaction mixture was
 396 concentrated under reduced pressure to an orange residue and dried under vacuum to give a orange
 397 oil. This oil was dissolved in 0.5 mL of trifluoroacetic acid.

398 To a separate, flame-dried, 1-dram vial containing a magnetic stirring bar was added L-
 399 serine (57.3 mg, 0.545 mmol, 1.2 equiv). The vial was placed under vacuum and backfilled with
 400 nitrogen 3 times. To the vial was added 1 mL of trifluoroacetic acid (final reaction concentration
 401 0.3 M), and the resulting mixture was allowed to stir at room temperature until all of the L-serine
 402 had dissolved. The L-serine solution was then cooled to 0 °C in an ice-water bath under nitrogen
 403 for 30 min. In a separate vessel, the acyl chloride solution was allowed to cool to 0 °C in an ice-
 404 water bath under nitrogen for 30 min. The solution of acyl chloride was slowly added dropwise to
 405 the L-serine solution over 5 min, and this reaction mixture was allowed to warm to room
 406 temperature under an atmosphere of nitrogen for 16 h. After completion of the reaction, the
 407 reaction mixture was transferred to a beaker containing 10 mL of cold diethyl ether, causing
 408 precipitation of a yellow solid. The yellow solid was filtered through a fine glass frit and washed
 409 with diethyl ether. To this crude solid was added 5 mL of diH₂O, producing a yellow solution.
 410 Saturated NaHCO₃ was added until the solution reached pH 5.5, causing a light yellow solid to
 411 precipitate. The mother liquor was removed, and the yellow solid was recrystallized from boiling
 412 diH₂O to give **1** (22.6 mg, 0.091 mmol, 20% yield) as colorless, reflective crystals.

413



1

414

415 Data for *O*-((1*R*,2*S*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**1**)

416 ¹H NMR (500 MHz, acetic acid-d₄) δ 7.31 – 7.13 (m, 5H), 4.42 (dd, *J* = 12.3, 3.0 Hz, 1H), 4.25
 417 (dd, *J* = 12.4, 5.3 Hz, 1H), 4.21 – 4.13 (m, 1H), 2.68 (q, *J* = 8.5 Hz, 1H), 2.18 (ddd, *J* = 9.1, 7.6,
 418 5.5 Hz, 1H), 1.68 (dt, *J* = 7.5, 5.4 Hz, 1H), 1.41 (td, *J* = 8.2, 4.9 Hz, 1H).

419 ¹³C NMR (126 MHz, acetic acid-d₄) δ 172.55, 171.53, 137.29, 130.27, 129.02, 127.73, 63.45,
 420 54.87, 27.11, 21.93, 12.32.

421 FTIR (neat, cm⁻¹) ν_{max}: 3192 br (N–H), 2982 br (O–H), 1729 s (C=O), 1603 s (C=O)

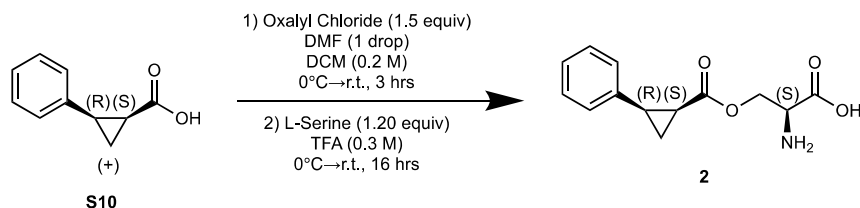
422 HRMS (ESI): *m/z* for C₁₃H₁₅NNaO₄⁺ [M+Na]⁺ calcd.: 272.0893, found: 272.0893.

423 T_r (HPLC-MS): 18.1 min

424 The absolute configuration of the product is determined by the correlation to the known absolute
 425 configuration of the reactants.

426

427 **Synthesis of *O*-((1*S*,2*R*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**2**)**

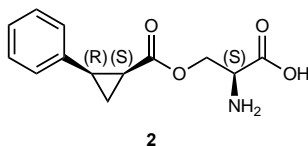


428

429 To a flame-dried, 10-mL conical flask equipped with magnetic stirring bar was added **S10**
 430 (200 mg, 1.23 mmol, 1.0 equiv). The flask was placed under vacuum and backfilled with nitrogen
 431 3 times. To the flask was added 6.2 mL of dry, degassed dichloromethane (0.2 M), and this solution
 432 was allowed to stir at room temperature under an atmosphere of nitrogen for 5 min. Five drops of
 433 dimethylformamide were added to the reaction mixture, and the resulting mixture was allowed to
 434 stir for 2 min. This solution was allowed to cool to 0 °C in an ice-water bath for 10 min before
 435 oxalyl chloride (0.158 mL, 1.85 mmol, 1.5 equiv) was added dropwise over 5 min. The reaction
 436 was allowed to warm to room temperature over 3 h under an atmosphere of nitrogen. The reaction
 437 mixture was concentrated under reduced pressure to an orange residue and dried under vacuum to
 438 give an orange oil. This oil was dissolved in 1.0 mL of trifluoroacetic acid.

439 To a separate, flame-dried, 5-mL conical flask containing a magnetic stirring bar was added
440 L-serine (0.155 g, 1.48 mmol, 1.2 equiv). The flask was placed under vacuum and backfilled with
441 nitrogen 3 times. To the flask was added 3.0 mL of trifluoroacetic acid (final reaction concentration
442 0.3 M), and the resulting mixture was allowed to stir at room temperature until all of the L-serine
443 had dissolved. The L-serine solution was then cooled to 0 °C in an ice-water bath under nitrogen
444 for 30 min. In a separate vessel, the acyl chloride solution was allowed to cool to 0 °C in an ice-
445 water bath under nitrogen for 30 min. The solution of acyl chloride was slowly added dropwise to
446 the L-serine solution over 5 min, and this reaction mixture was allowed to warm to room
447 temperature under an atmosphere of nitrogen for 16 h. After completion of the reaction, the
448 reaction mixture was transferred to a beaker containing 20 mL of cold diethyl ether, causing
449 precipitation of an off-white solid. The crude solid was filtered through a fine glass frit and washed
450 with diethyl ether. To the crude solid was added 5 mL of diH₂O, producing a light-yellow solution.
451 Saturated NaHCO₃ was added until the solution reached pH 5.5, causing a light yellow solid to
452 precipitate. The mother liquor was removed, and the crude material was recrystallized from boiling
453 diH₂O to give **2** (123 mg, 0.493 mmol, 40% yield) as colorless, reflective crystals.

454



455

456 Data for *O*-((1*S*,2*R*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**2**)

457 ¹H NMR (500 MHz, acetic acid-d₄) δ 7.33 – 7.12 (m, 5H), 4.37 – 4.26 (m, 2H), 4.17 (dd, *J* = 4.9,
458 3.6 Hz, 1H), 2.70 (q, *J* = 8.5 Hz, 1H), 2.26 – 2.12 (m, 1H), 1.70 (dt, *J* = 7.7, 5.4 Hz, 1H), 1.43 (td,
459 *J* = 8.2, 5.1 Hz, 1H).

460 ¹³C NMR (126 MHz, acetic acid-d₄) δ 172.67, 171.12, 136.97, 129.99, 128.87, 127.60, 63.19,
461 54.58, 27.08, 22.00, 12.29.

462 FTIR (neat, cm⁻¹) *ν*_{max}: 2982 br (O–H), 1728 s (C=O), 1601s (C=O)

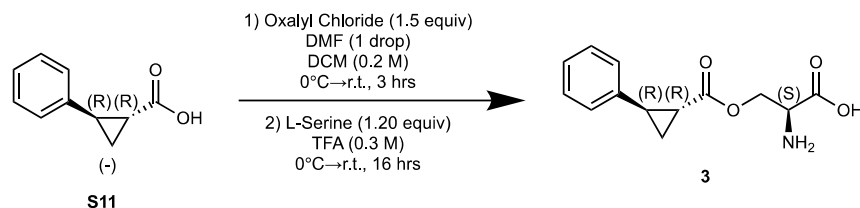
463 HRMS (ESI): *m/z* for C₁₃H₁₅NNaO₄⁺ [M+Na]⁺ calcd.: 272.0893, found: 272.0894.

464 T_r (HPLC-MS): 19.7 min

465 The absolute configuration of the product is determined by the correlation to the known absolute
466 configuration of the reactants.

467

468 **Synthesis of *O*-((1*R*,2*R*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**3**)**

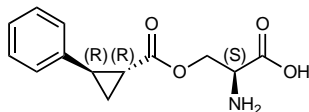


469

470 To a flame-dried, 10-mL conical flask equipped with magnetic stirring bar was added **S11**
 471 (200 mg, 1.23 mmol, 1.0 equiv). The flask was placed under vacuum and backfilled with nitrogen
 472 3 times. To the flask was added 6.2 mL of dry, degassed dichloromethane (0.2 M), and this solution
 473 was allowed to stir at room temperature under an atmosphere of nitrogen for 5 min. Five drops of
 474 dimethylformamide were added to the reaction mixture, and the resulting mixture was allowed to
 475 stir for 2 min. This solution was allowed to cool to 0 °C in an ice-water bath for 10 min before
 476 oxalyl chloride (0.158 mL, 1.85 mmol, 1.5 equiv) was added dropwise over 5 min. The reaction
 477 was allowed to warm to room temperature over 3 h under an atmosphere of nitrogen. The reaction
 478 mixture was concentrated under reduced pressure to an orange residue and dried under vacuum to
 479 give an orange oil. This oil was dissolved in 1.0 mL of trifluoroacetic acid.

480 To a separate, flame-dried, 5-mL conical flask containing a magnetic stirring bar was added
 481 L-serine (0.155 g, 1.48 mmol, 1.2 equiv). The flask was placed under vacuum and backfilled with
 482 nitrogen 3 times. 3.0 mL of trifluoroacetic acid (final reaction concentration 0.3 M) was added to
 483 the flask, and the resulting mixture was allowed to stir at room temperature until all of the L-serine
 484 had dissolved. The L-serine solution was then cooled to 0 °C in an ice-water bath under nitrogen
 485 for 30 min. In a separate vessel, the acyl chloride solution was allowed to cool to 0 °C in an ice-
 486 water bath under nitrogen for 30 min. The solution of acyl chloride was slowly added dropwise to
 487 the L-serine solution over 5 min, and this reaction mixture was allowed to warm to room
 488 temperature under an atmosphere of nitrogen for 16 h. After completion of the reaction, the
 489 reaction mixture was transferred to a beaker containing 20 mL of cold diethyl ether, causing
 490 precipitation of an off-white solid. The crude solid was filtered through a fine glass frit and washed
 491 with diethyl ether. 5 mL of diH₂O were added to the crude solid, producing a colorless solution.
 492 Saturated NaHCO₃ was added until the solution reached pH 5.5, causing an off-white solid to
 493 precipitate. The mother liquor was removed, and the crude material was recrystallized from boiling
 494 diH₂O to give **3** (24.1 mg, 0.097 mmol, 9% yield) as colorless, reflective crystals.

495



3

496

497 Data for *O*-((1*R*,2*R*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**3**)

498 ¹H NMR (500 MHz, acetic acid-d₄) δ 7.26 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.4 Hz, 1H), 7.10 (d, *J*
499 = 7.6 Hz, 1H), 4.71 – 4.56 (m, 1H), 2.62 – 2.48 (m, 1H), 1.94 (dt, *J* = 9.0, 4.9 Hz, 1H), 1.60 (dt,
500 *J* = 9.7, 5.0 Hz, 1H), 1.41 (q, *J* = 6.7 Hz, 1H).

501 ¹³C NMR (126 MHz, acetic acid-d₄) δ 180.24, 139.73, 128.77, 126.95, 126.52, 27.36, 24.24,
502 17.75.

503 FTIR (neat, cm⁻¹) ν_{max}: 3286 br (N–H), 3027 br (O–H), 1713 s (C=O), 1582 vs (C=O)

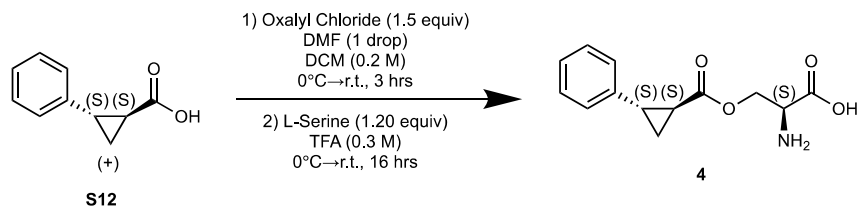
504 HRMS (ESI): *m/z* for C₁₃H₁₅NNaO₄⁺ [M+Na]⁺ calcd.: 272.0893, found: 272.0888.

505 T_r (HPLC-MS): 28.1 min

506 The absolute configuration of the product is determined by the correlation to the known absolute
507 configuration of the reactants.

508

509 **Synthesis of *O*-((1*S*,2*S*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**4**)**

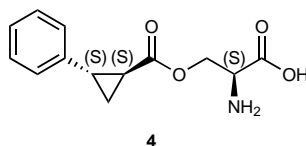


510

511 To a flame-dried, 10-mL conical flask equipped with magnetic stirring bar was added **S12**
512 (200 mg, 1.23 mmol, 1.0 equiv). The flask was placed under vacuum and backfilled with nitrogen
513 3 times. To the flask was added 6.2 mL of dry, degassed dichloromethane (0.2 M), and this solution
514 was allowed to stir at room temperature under an atmosphere of nitrogen for 5 min. Five drops of
515 dimethylformamide were added to the reaction mixture, and the resulting mixture was allowed to
516 stir for 2 min. This solution was allowed to cool to 0 °C in an ice-water bath for 10 min before
517 oxalyl chloride (0.158 mL, 1.85 mmol, 1.5 equiv) was added dropwise over 5 min. The reaction
518 was allowed to warm to room temperature over 3 h under an atmosphere of nitrogen. The reaction
519 mixture was concentrated under reduced pressure to an orange residue and dried under vacuum to
520 give an orange oil. This oil was dissolved in 1.0 mL of trifluoroacetic acid.

521 To a separate, flame-dried, 5-mL conical flask containing a magnetic stirring bar was added
522 L-serine (0.155 g, 1.48 mmol, 1.2 equiv). The flask was placed under vacuum and backfilled with
523 nitrogen 3 times. To the flask was added 3.0 mL of trifluoroacetic acid (final reaction concentration
524 0.3 M), and the resulting mixture was allowed to stir at room temperature until all of the L-serine
525 had dissolved. The L-serine solution was then cooled to 0 °C in an ice-water bath under nitrogen
526 for 30 min. In a separate vessel, the acyl chloride solution was allowed to cool to 0 °C in an ice-
527 water bath under nitrogen for 30 min. The solution of acyl chloride was slowly added dropwise to
528 the L-serine solution over 5 min, and this reaction mixture was allowed to warm to room
529 temperature under an atmosphere of nitrogen for 16 h. After completion of the reaction, the
530 reaction mixture was transferred to a beaker containing 20 mL of cold diethyl ether, causing
531 precipitation of an off-white solid. The crude solid was filtered through a fine glass frit and washed
532 with diethyl ether. To the crude solid was added 5 mL of diH₂O, producing a colorless solution.
533 Saturated NaHCO₃ was added until the solution reached pH 5.5, causing an off-white solid to
534 precipitate. The mother liquor was removed, and the crude material was recrystallized from boiling
535 diH₂O to give **4** (60.0 mg, 0.241 mmol, 20% yield) as colorless, reflective crystals.

536



537

538 Data for *O*-((1*S*,2*S*)-2-phenylcyclopropane-1-carbonyl)-L-serine (**4**)

539 ¹H NMR (500 MHz, acetic acid-d₄) δ 7.27 (t, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 7.11 (d, *J*
540 = 7.5 Hz, 2H), 4.73 – 4.54 (m, 2H), 4.36 (dd, *J* = 5.2, 2.9 Hz, 1H), 2.53 (ddd, *J* = 10.1, 6.7, 4.0 Hz,
541 1H), 1.95 (dt, *J* = 8.8, 4.7 Hz, 1H), 1.61 (dt, *J* = 9.6, 4.9 Hz, 1H), 1.46 – 1.36 (m, 1H).

542 ¹³C NMR (126 MHz, acetic acid-d₄) δ 174.70, 171.62, 140.55, 129.38, 127.47, 126.84, 63.86,
543 54.82, 27.49, 24.59, 18.02.

544 FTIR (neat, cm⁻¹) ν_{max}: 3013 br (O–H), 1717 s (C=O), 1603 s (C=O)

545 HRMS (ESI): *m/z* for C₁₃H₁₆NO₄⁺ [M+H]⁺ calcd.: 250.1074, found: 250.1076.

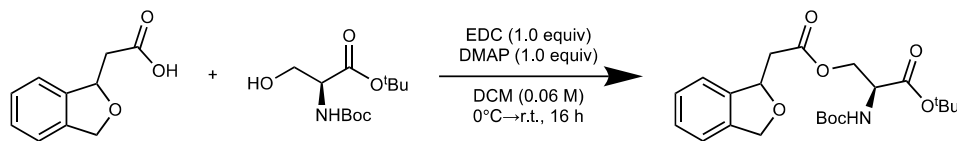
546 T_r (HPLC-MS): 30.1 min

547 The absolute configuration of the product is determined by the correlation to the known absolute
548 configuration of the reactants.

549

550 **Synthesis of standard for the product (aza-phtha, compound 5, mixture of C1 and C2**
551 **diastereomers in Fig. 3d) of the reaction of azaserine with phthalan**

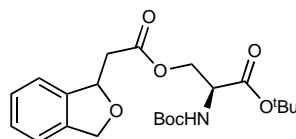
552
553 **Synthesis of *tert*-butyl *N*-(*tert*-butoxycarbonyl)-*O*-(2-(1,3-dihydroisobenzofuran-1-yl)acetyl)-**
554 ***L*-serinate (**S13**)**



S13

555
556 To a stirred solution of 2-(1,3-dihydroisobenzofuran-1-yl)acetic acid (222 mg, 1.25 mmol)
557 in anhydrous dichloromethane (20 mL) at 0 °C under nitrogen was added EDC (239 mg, 1.25
558 mmol) and the resulting reaction mixture was continued to stir for 30 mins. Then *tert*-butyl (*tert*-
559 *butoxycarbonyl*)-*L*-serinate (326 mg, 1.25 mmol) was added, followed by the addition of DMAP
560 (152 mg, 1.25 mmol). The ice bath was removed, and the reaction mixture was stirred at room
561 temperature for 16 h. After evaporation of the solvent under reduced pressure, the residue was
562 subjected to purification by column chromatography to give 409 mg of compound **S13** (*tert*-butyl
563 *N*-(*tert*-butoxycarbonyl)-*O*-(2-(1,3-dihydroisobenzofuran-1-yl)acetyl)-*L*-serinate) as a mixture of
564 two inseparable diastereomers (coelute from flash chromatography) in 78% yield.

565



S13

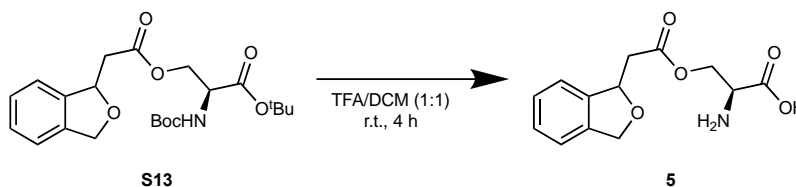
566
567 Data of *tert*-butyl *N*-(*tert*-butoxycarbonyl)-*O*-(2-(1,3-dihydroisobenzofuran-1-yl)acetyl)-*L*-
568 serinate (**S13**):

569 ¹**H-NMR** (600 MHz, CDCl₃) δ (ppm) 7.32-7.27 (m, 4H), 7.25-7.22 (m, 2H), 7.19-7.16 (m, 2H),
570 5.65-5.60 (m, 2H), 5.50-5.45 (m, 1H), 5.37-5.32 (m, 1H), 5.17-5.12 (m, 2H), 5.09-5.05 (dd, 2H, J
571 = 12.2, 6.4 Hz), 4.50-4.37 (m, 6H), 2.86-2.81 (dd, 1H, J = 17.2, 4.6 Hz), 2.83-2.78 (dd, 1H, J =
572 17.2, 4.6 Hz), 2.74-2.68 (m, 2H), 1.50-1.43 (m, 36H).

573 ¹³**C NMR** (151 MHz, CDCl₃) δ 170.29, 170.17, 168.78, 168.71, 155.24, 155.30, 140.45, 140.40,
574 139.14, 139.12, 127.98, 127.53, 121.15 (2C), 121.10, 121.08, 82.67, 82.65, 80.22, 80.12,
575 79.99(2C), 79.94(2C), 72.68, 72.64, 64.98, 64.94, 53.46, 53.39, 41.39, 41.37, 28.3(6C), 27.9 (2C).

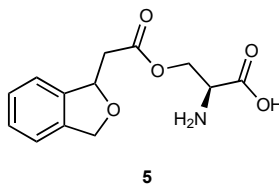
576 **HRMS (ESI)** [M+Na]⁺ calculated for C₂₂H₃₁NO₇Na: 444.1993, found 444.1996.

577 **Synthesis of O-(2-(1,3-dihydroisobenzofuran-1-yl)acetyl)-L-serine (5)**



578
 579 To a stirred solution of *tert*-butyl *N*-(*tert*-butoxycarbonyl)-*O*-(2-(1,3-
 580 dihydroisobenzofuran-1-yl)acetyl)-*L*-serinate (**S13**, 15 mg, 0.036 mmol) in dichloromethane (1.0
 581 mL) was added trifluoroacetic acid (1 mL, 13 mmol) and the resulting reaction mixture was
 582 continued to stir for 4 h at room temperature. After evaporation of the solvent under reduced
 583 pressure, the residue (13 mg) was obtained in 99% yield as a mixture of two diastereomers (with
 584 1:1 ratio), which could not be separated by flash column chromatography. The compounds **5** were
 585 used directly without further purification.

586

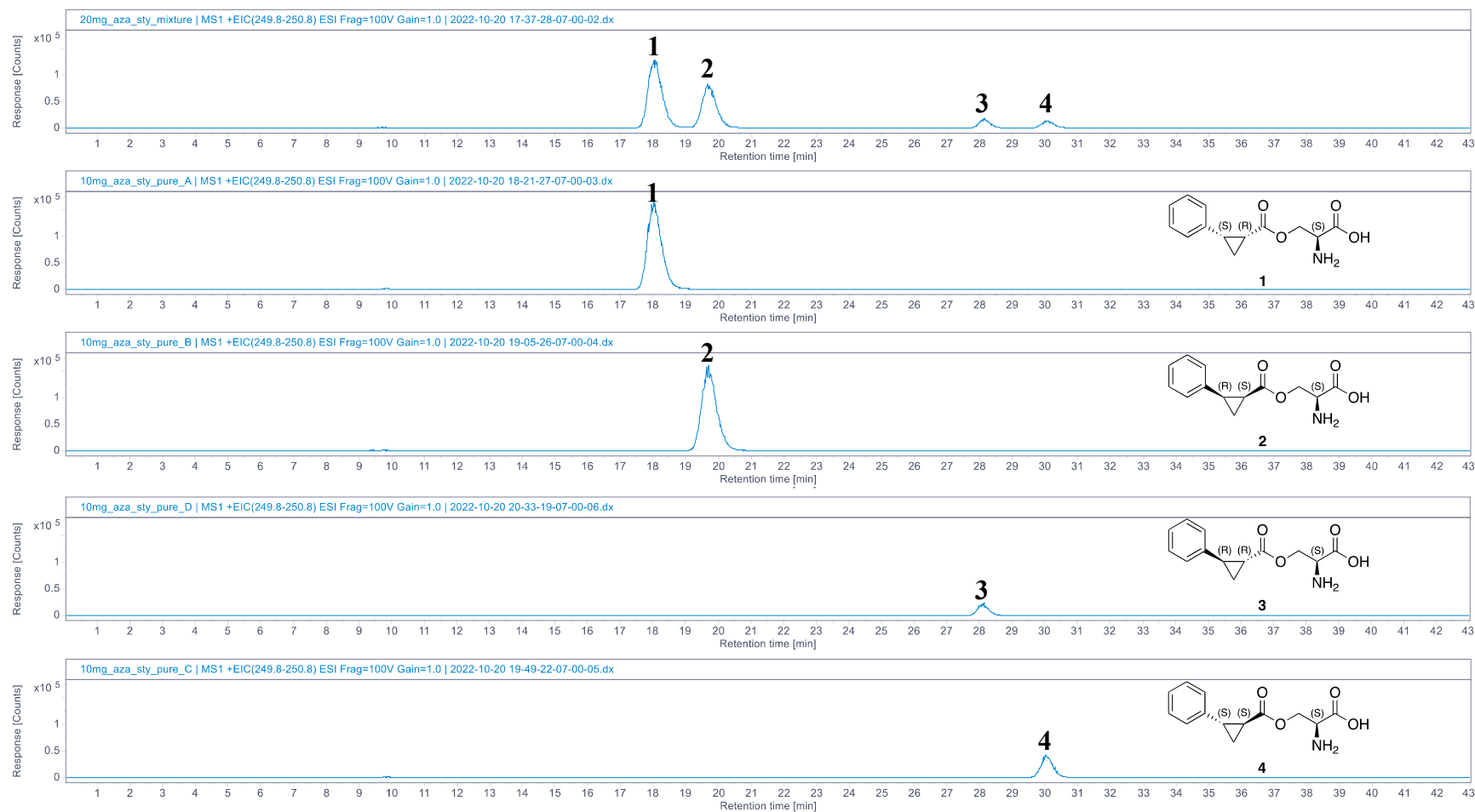


587
 588 Data of *O*-(2-(1,3-dihydroisobenzofuran-1-yl)acetyl)-*L*-serine (**5**):

589 ¹H-NMR (600 MHz, CD₃OD) δ (ppm) 7.35-7.18 (m, 8H), 5.62-5.56 (m, 2H), 5.12-5.05 (dd, 2H,
 590 J = 12.0, 2.4 Hz), 5.02-4.98 (d, 2H, J = 2.4 Hz), 4.60-4.56 (dd, 2H, J = 12.4, 3.3 Hz), 4.55-4.50
 591 (ddd, 2H, J = 12.3, 4.8, 1.4 Hz), 4.35-4.31 (m, 2H), 2.97-2.92 (dd, 2H, J = 15.8, 4.1 Hz), 2.72-2.66
 592 (ddd, 2H, J = 15.8, 8.6, 0.7 Hz).

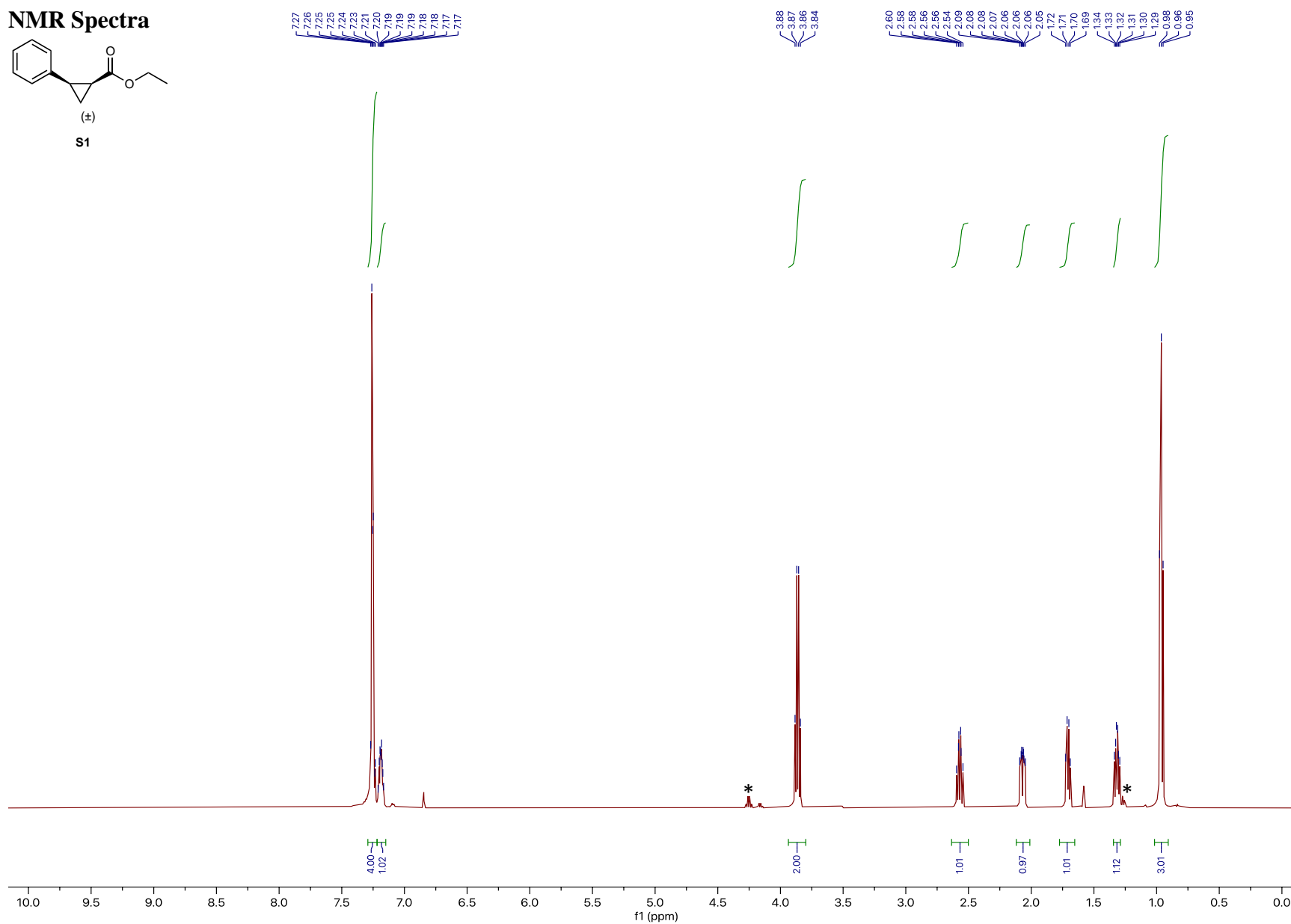
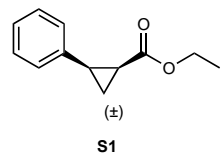
593 ¹³C NMR (151 MHz, CD₃OD) δ 170.2, 170.1, 167.6 (2C), 140.0, 138.7, 127.8 (2C), 127.3 (2C),
 594 120.83, 120.82, 120.79, 120.78, 80.2, 80.1, 72.2 (2C), 61.55, 61.54, 52.0 (2C), 40.6, 40.5.

595 **HRMS (ESI)** [M+H]⁺ calculated for C₁₃H₁₆NO₅: 266.1023, found 266.1025.

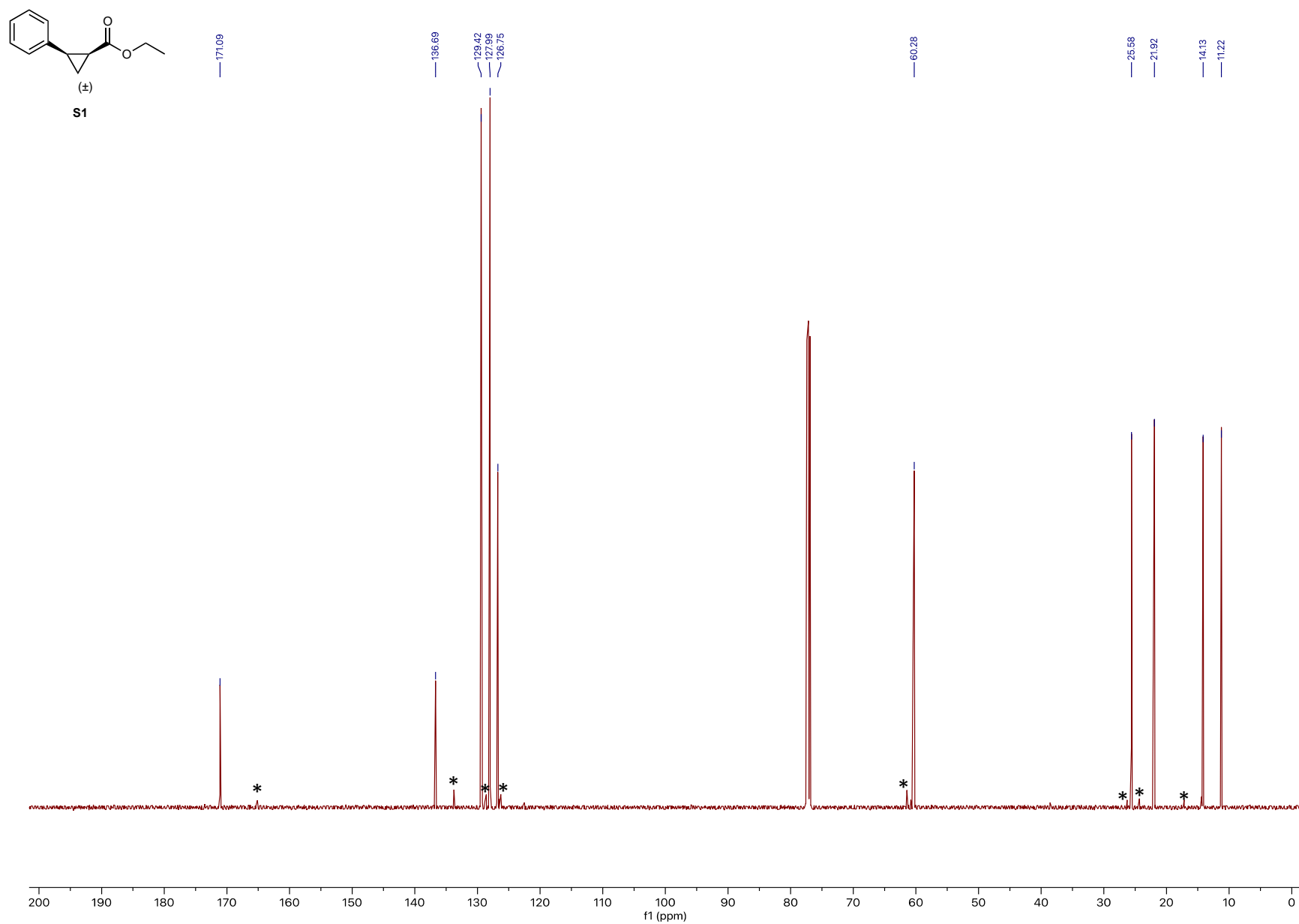


Supplementary Fig. 1 | LC-MS traces of authentic aza-sty products. Extracted ion chromatograms for synthetic aza-sty products (1, 2, 3, 4 correspond to P1, P2, P3, P4 peaks in the manuscript) (m/z $[\text{M}+\text{H}]^+ = 249.8\text{-}250.8$) by standard HPLC-MS method.

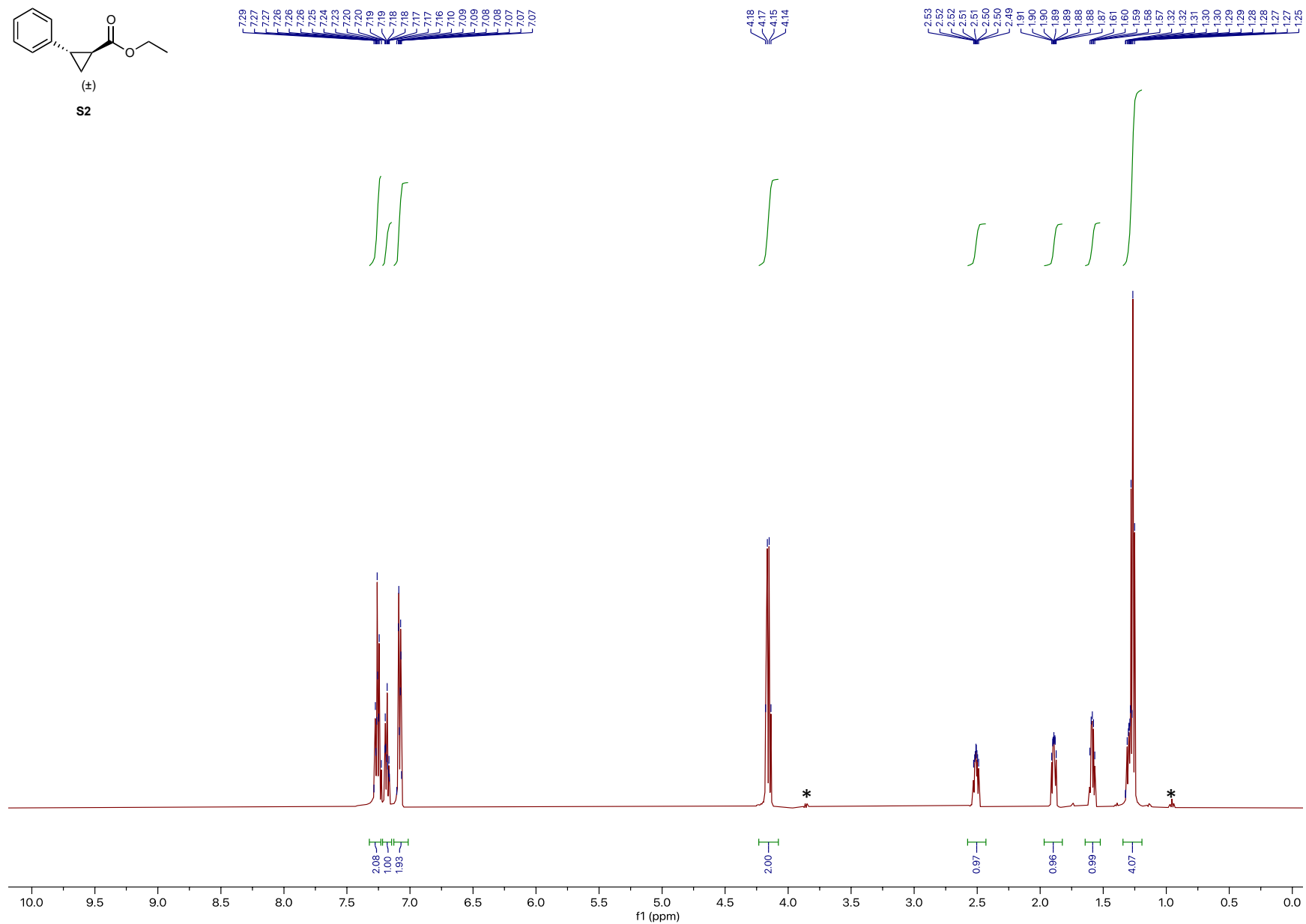
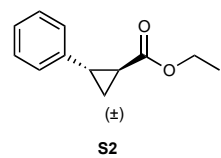
NMR Spectra



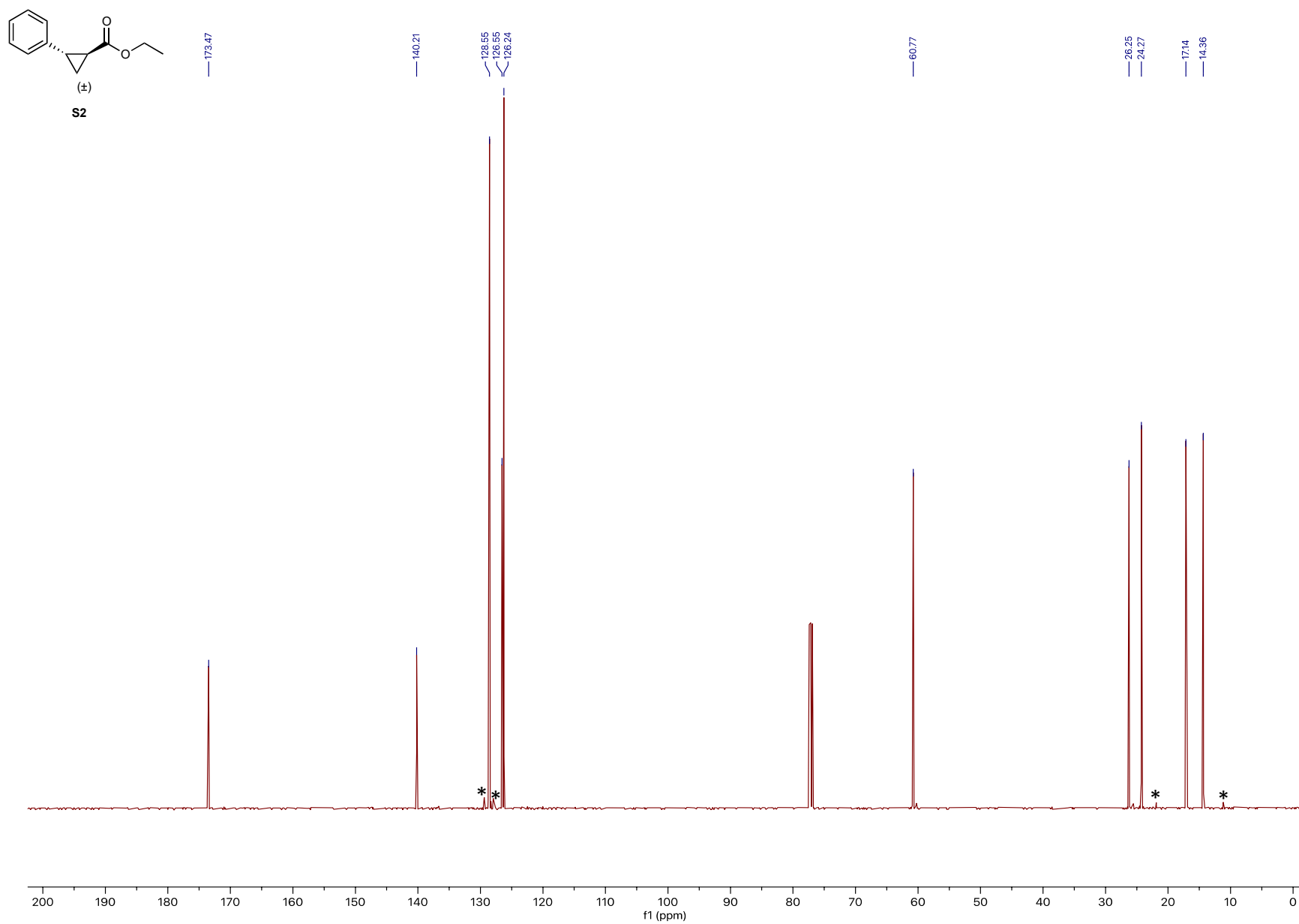
Supplementary Fig. 2 | ¹H-NMR (500 MHz, CDCl₃) of S1. *Impurity resulting from diastereomer S2, which is removed in later steps of the sequence.



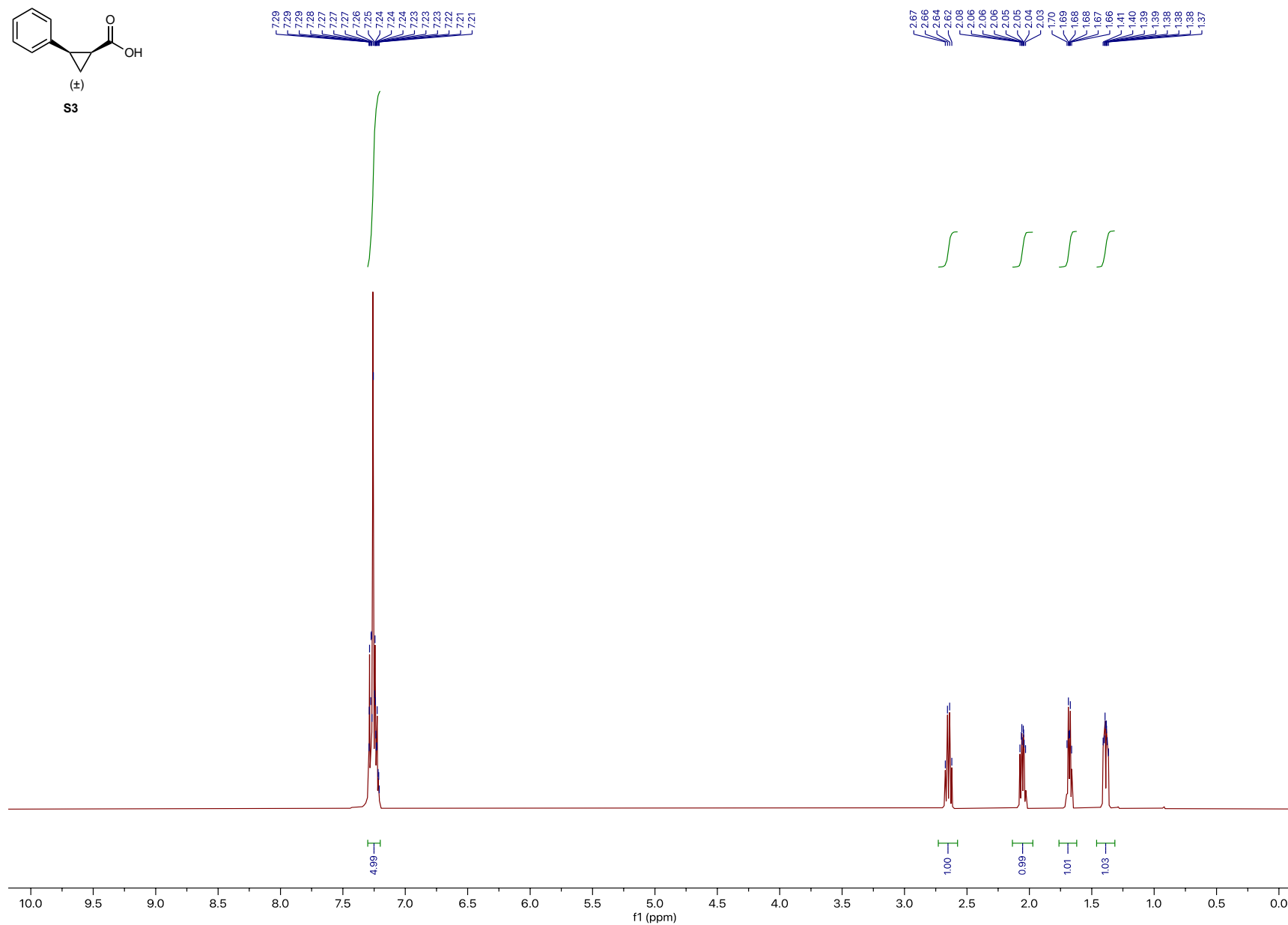
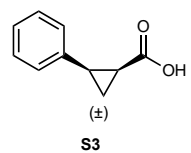
Supplementary Fig. 3 | ¹³C-NMR (126 MHz, CDCl₃) of S1. *Impurity resulting from diastereomer S2, which is removed in later steps of the sequence.



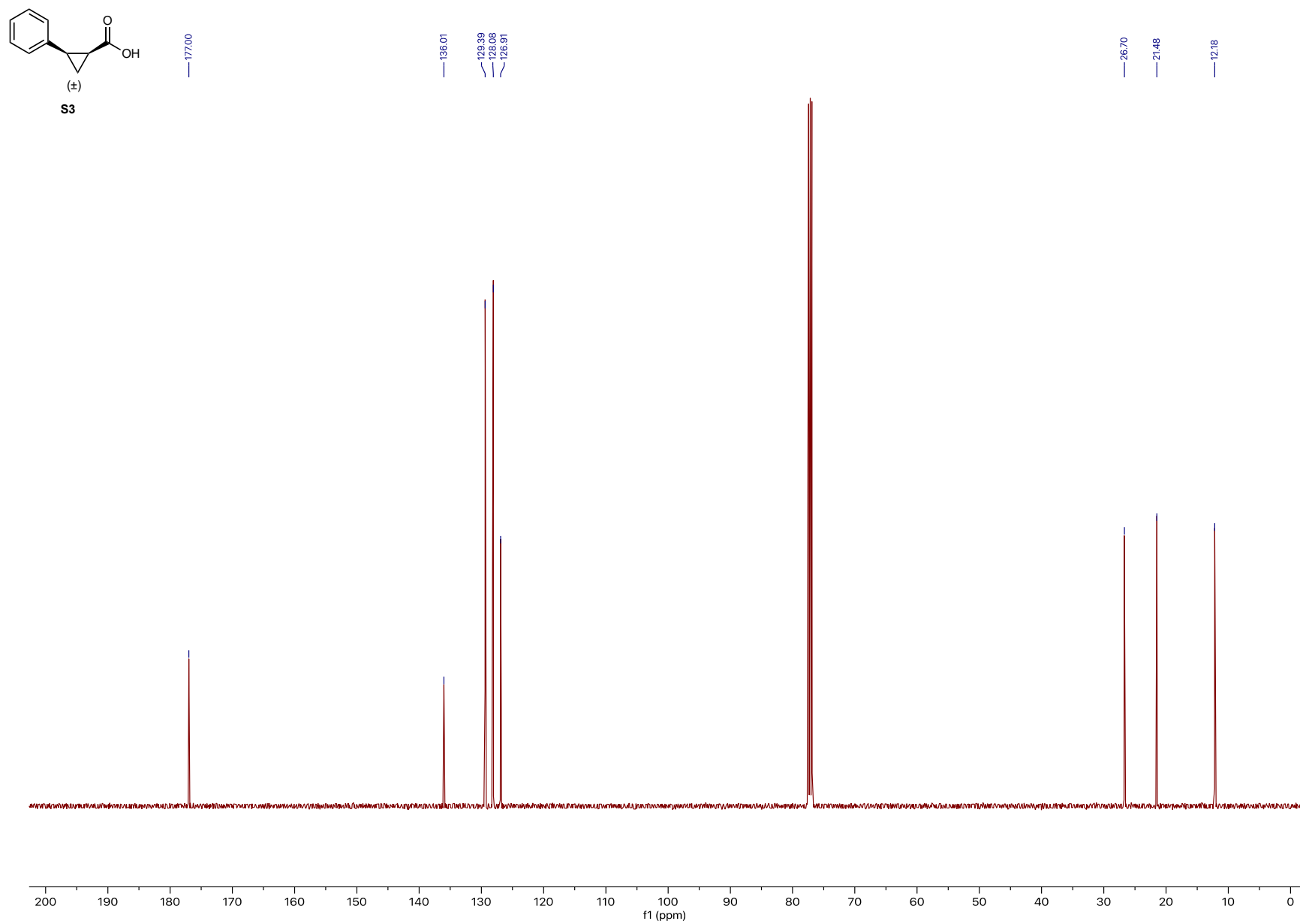
Supplementary Fig. 4 | ¹H-NMR (500 MHz, CDCl₃) of S2. *Impurity resulting from diastereomer S1, which is removed in later steps of the sequence.



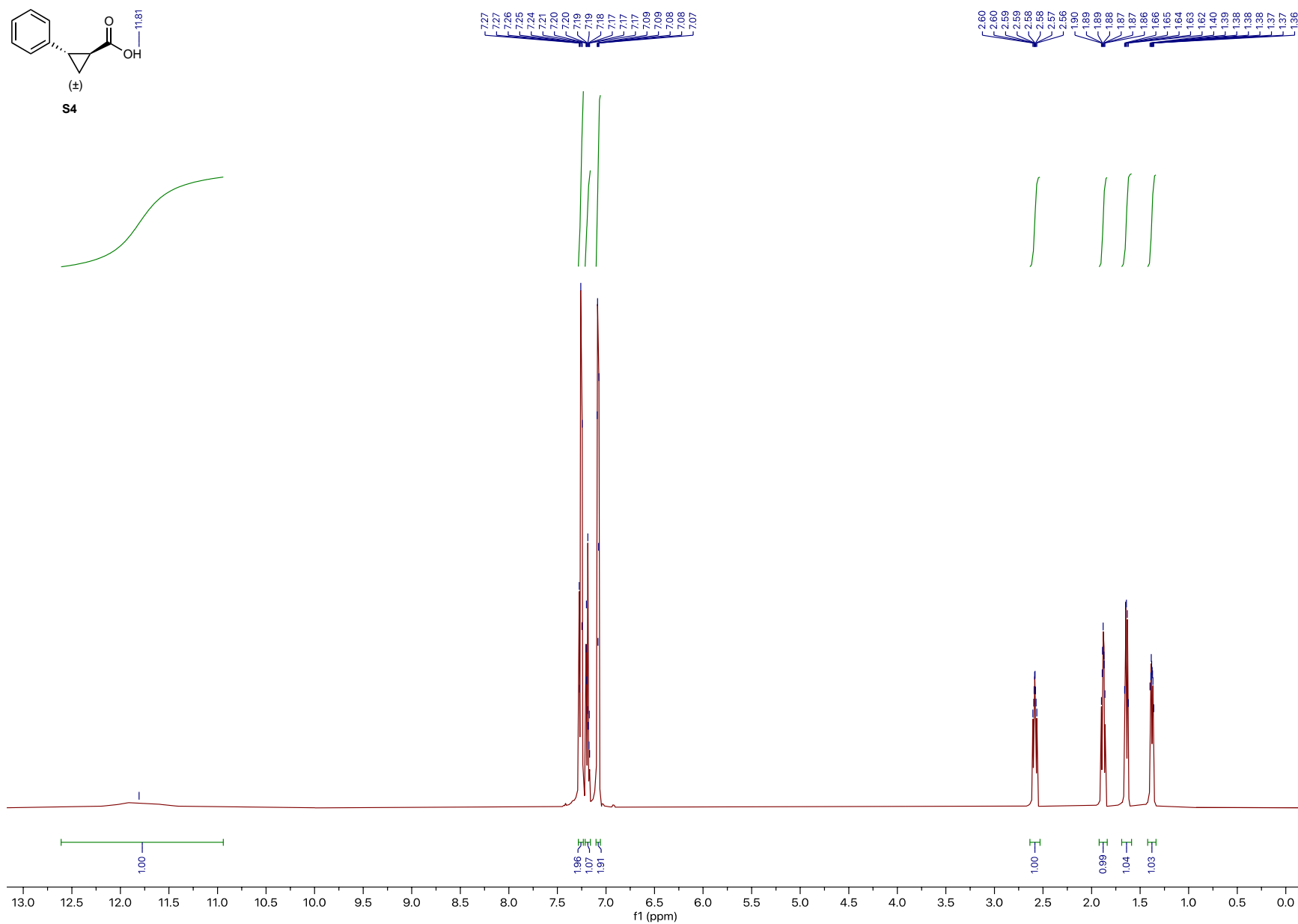
Supplementary Fig. 5 | $^{13}\text{C-NMR}$ (126 MHz, CDCl_3) of **S2**. *Impurity resulting from diastereomer **S1**, which is removed in later steps of the sequence.



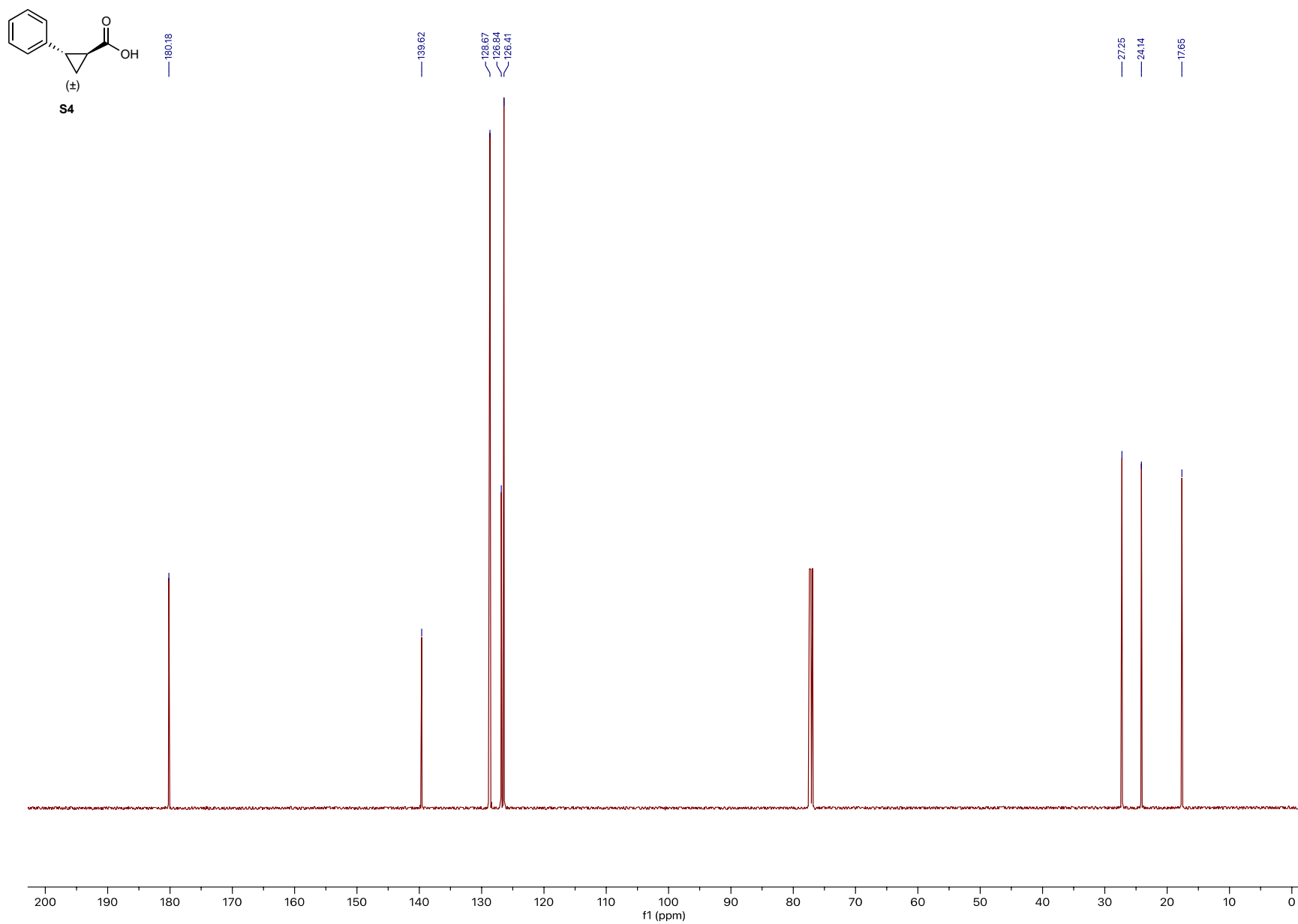
Supplementary Fig. 6 | $^1\text{H-NMR}$ (500 MHz, CDCl_3) of S3.



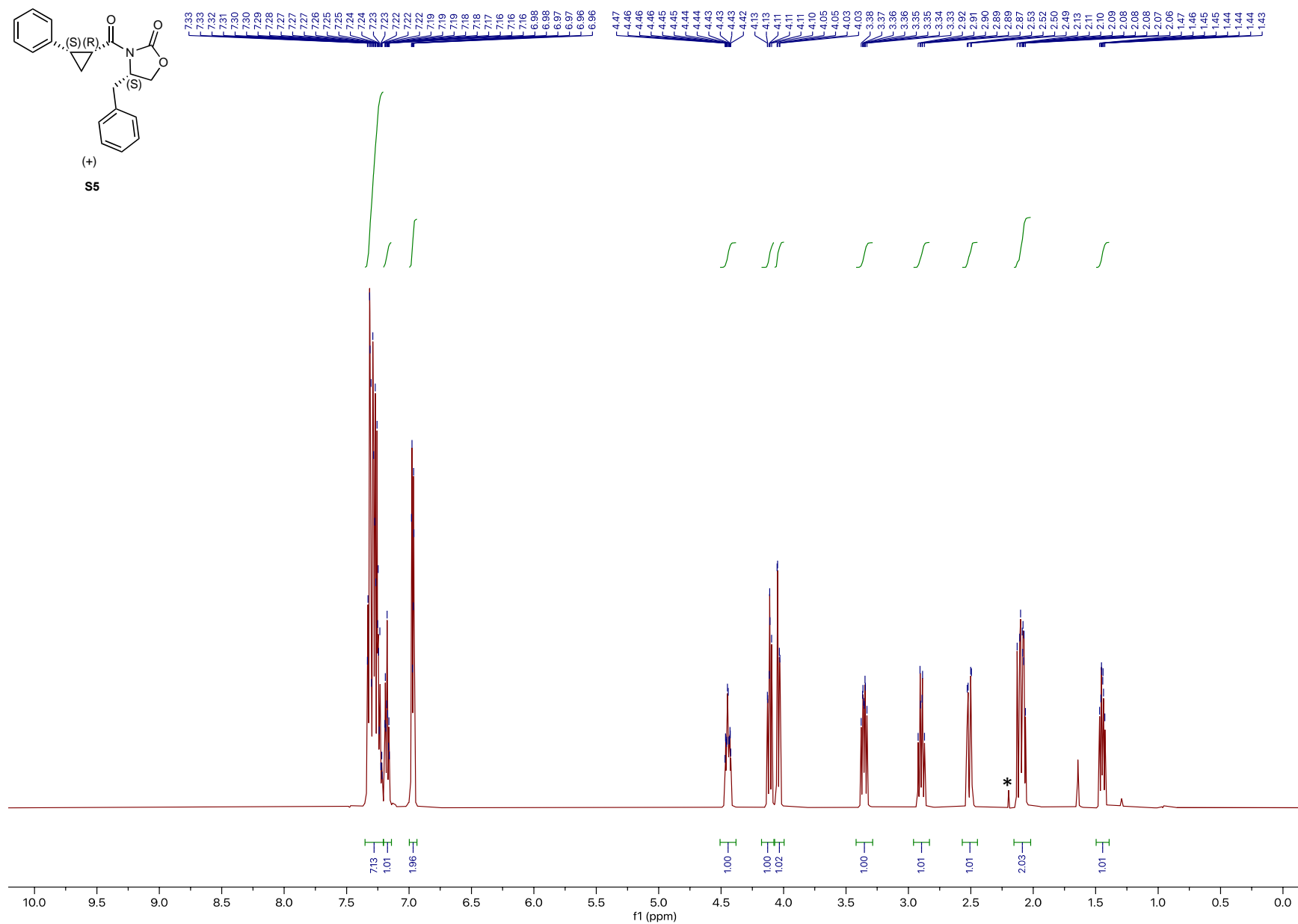
Supplementary Fig. 7 | ¹³C-NMR (126 MHz, CDCl₃) of S3.



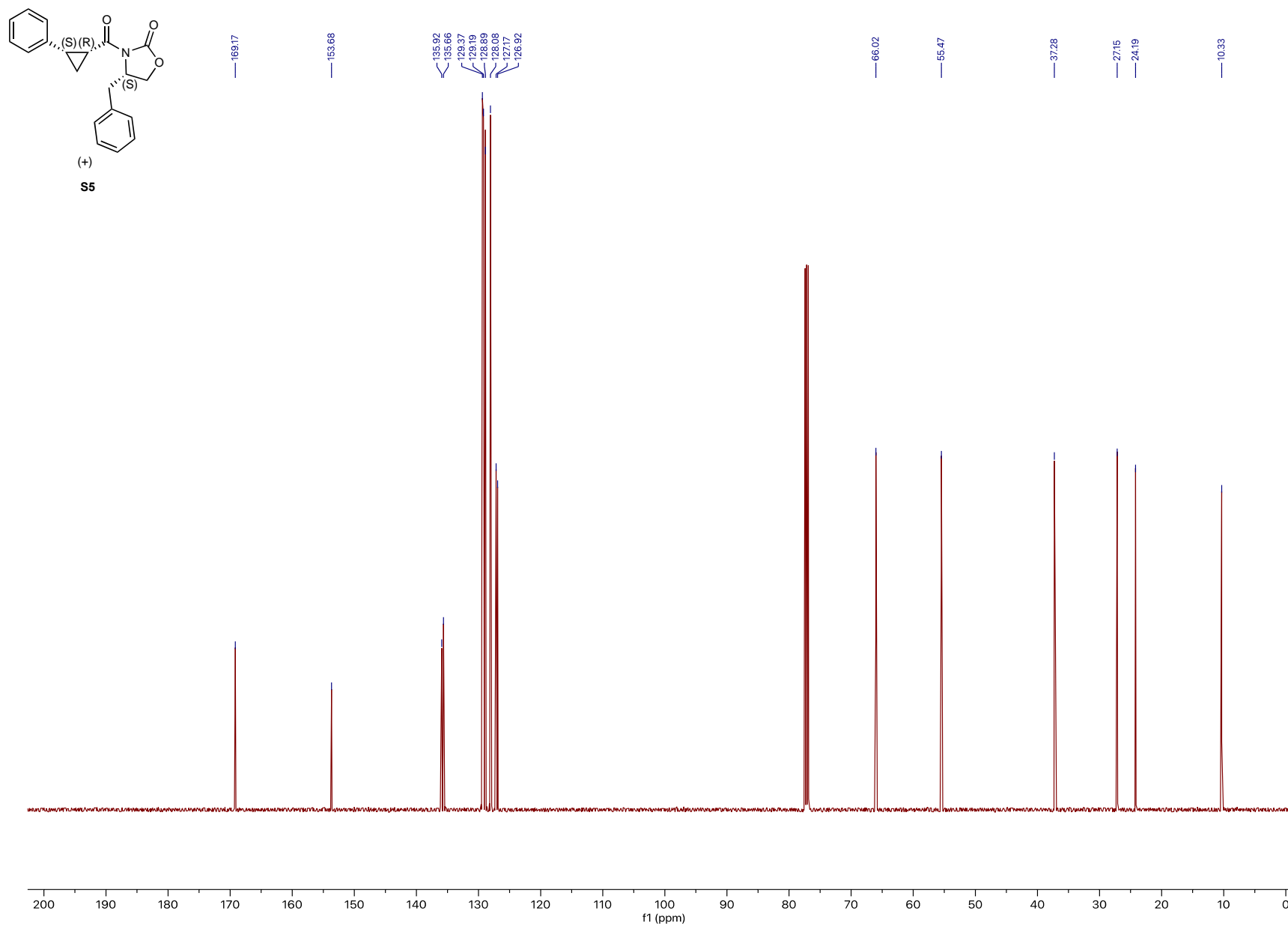
Supplementary Fig. 8 | ¹H-NMR (500 MHz, CDCl₃) of S4.



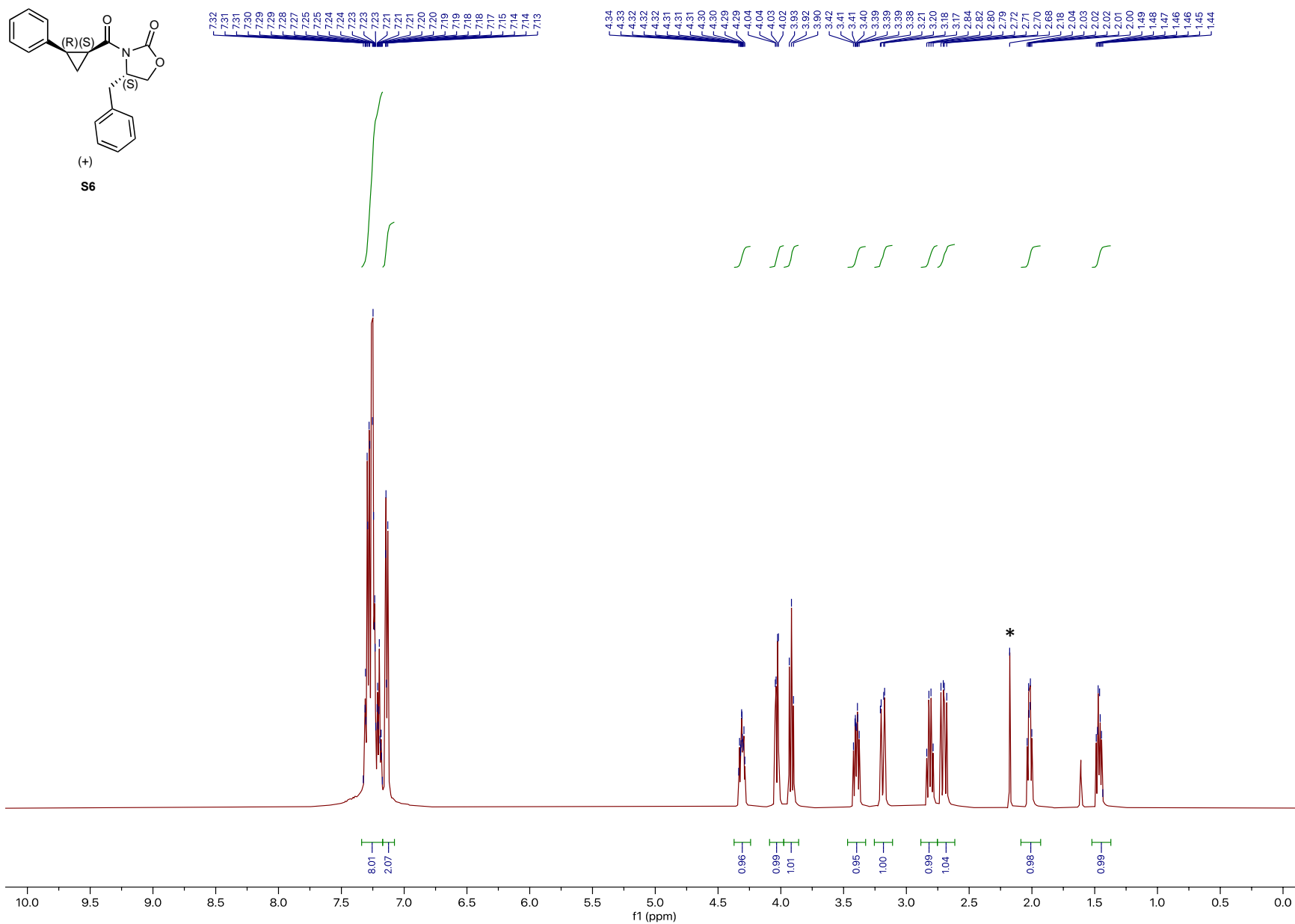
Supplementary Fig. 9 | ¹³C-NMR (126 MHz, CDCl₃) of S4.



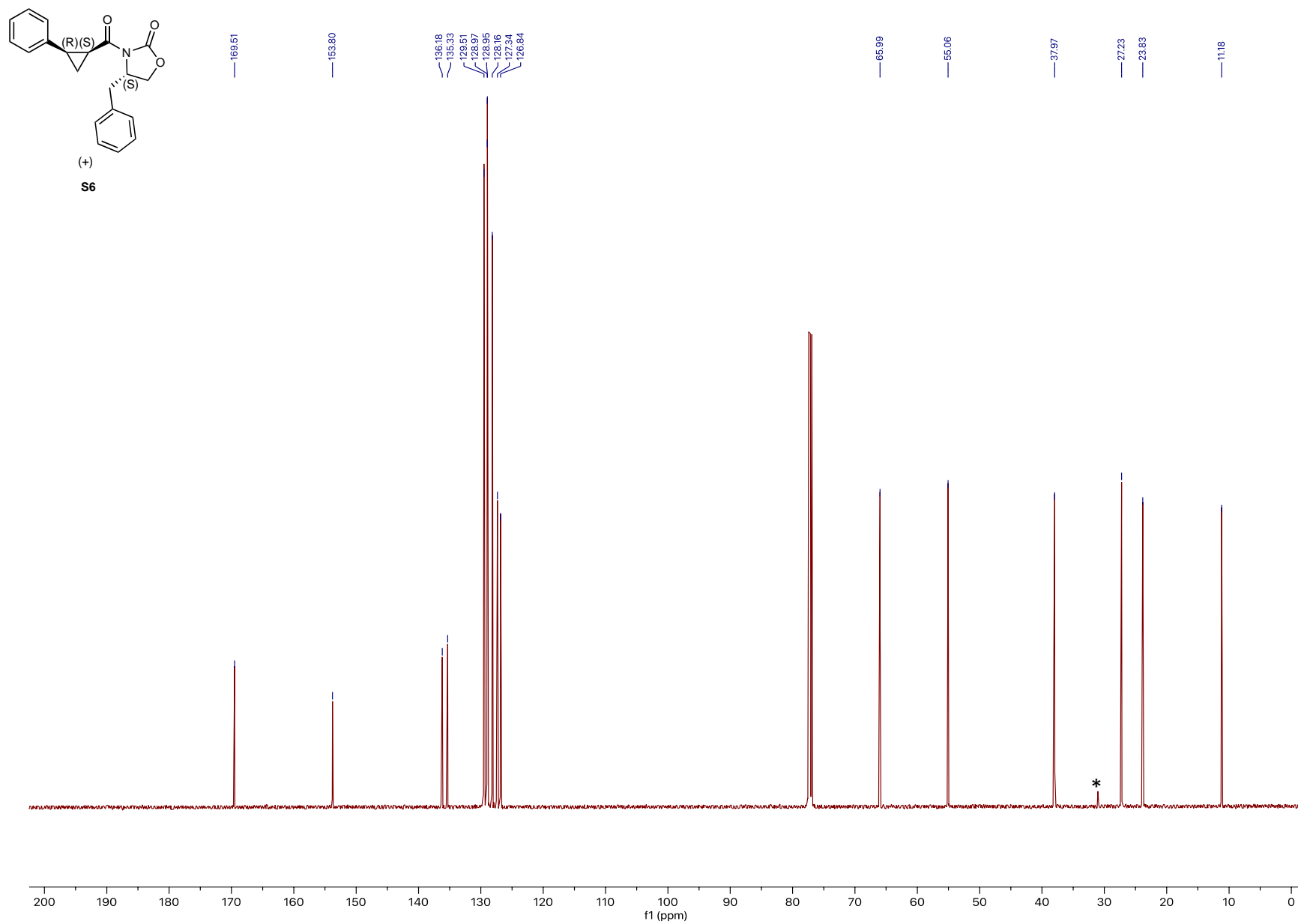
Supplementary Fig. 10 | ¹H-NMR (500 MHz, CDCl₃) of S5. *Impurity the result of acetone.



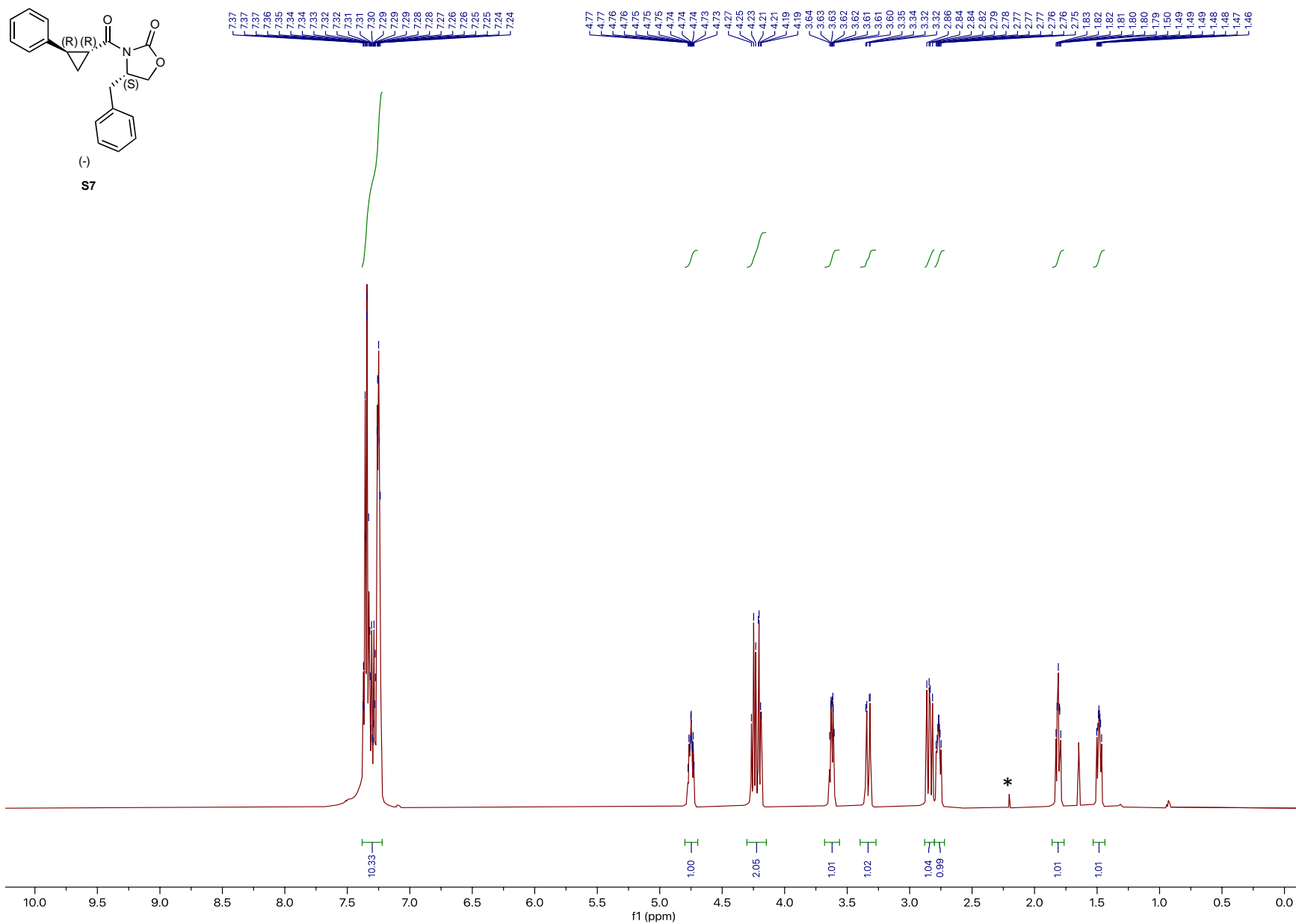
Supplementary Fig. 11 | ^{13}C -NMR (126 MHz, CDCl_3) of S5.



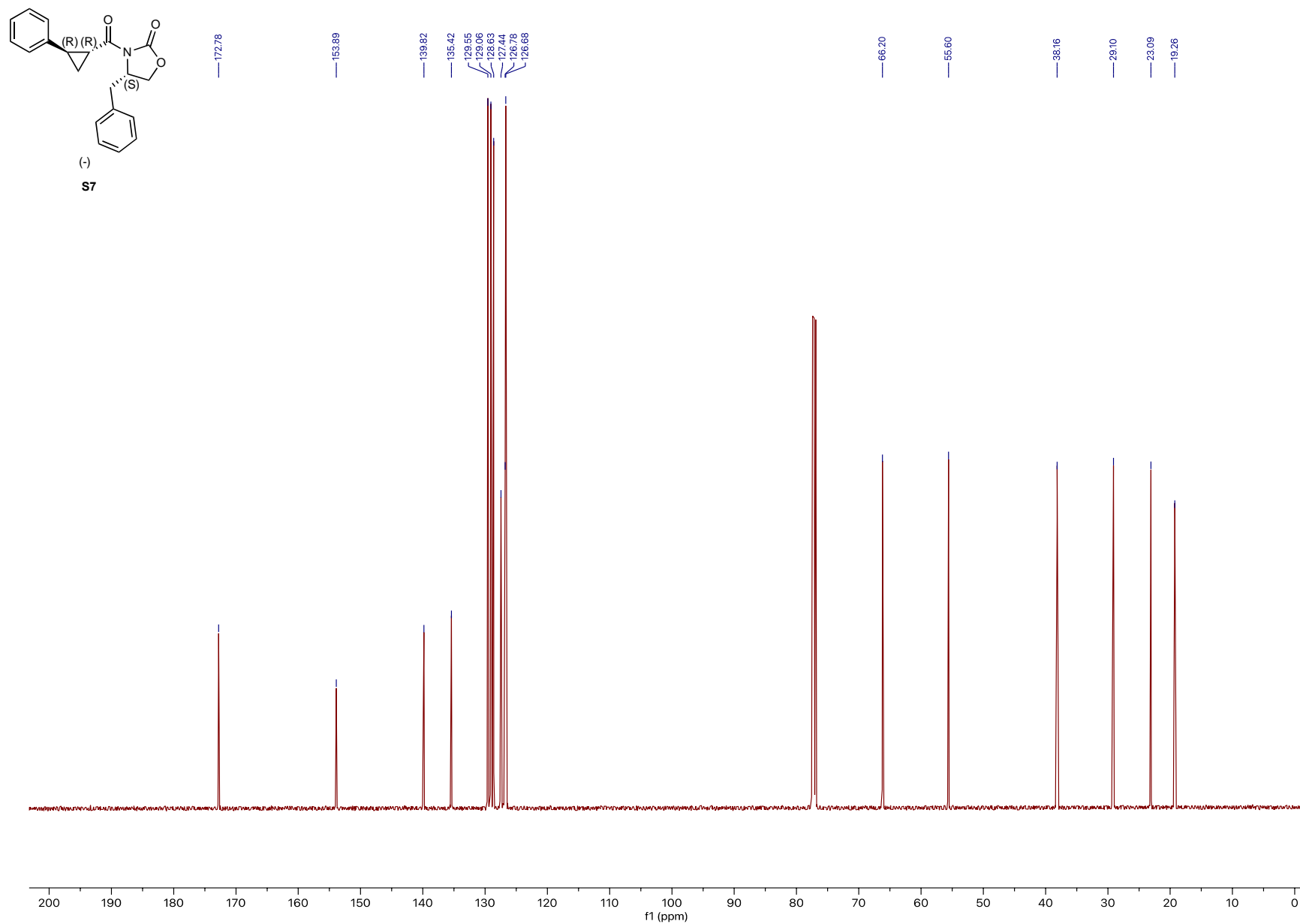
Supplementary Fig. 12 | ¹H-NMR (500 MHz, CDCl₃) of S6. *Impurity the result of acetone.



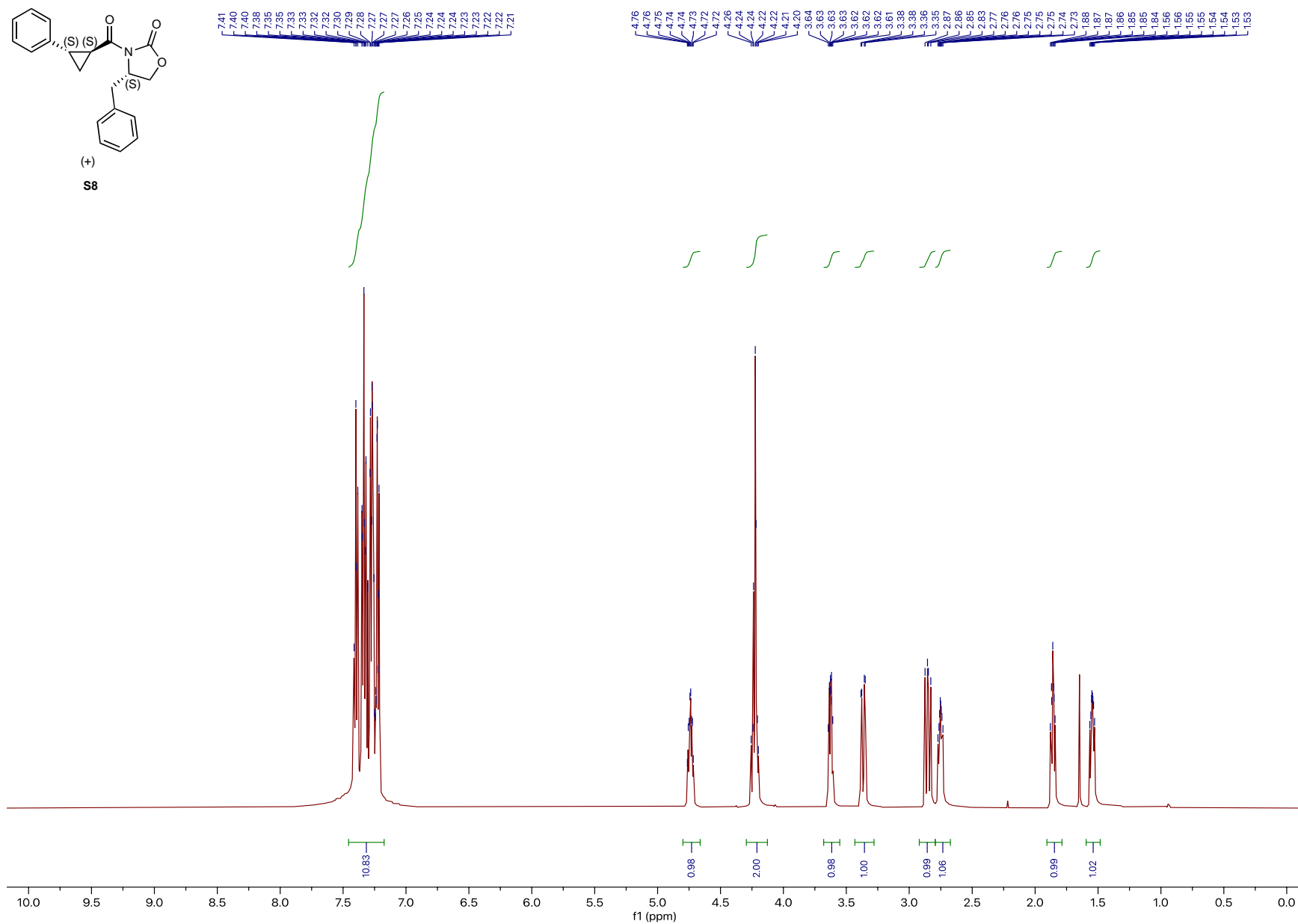
Supplementary Fig. 13 | ^{13}C -NMR (126 MHz, CDCl_3) of S6. *Impurity the result of acetone.



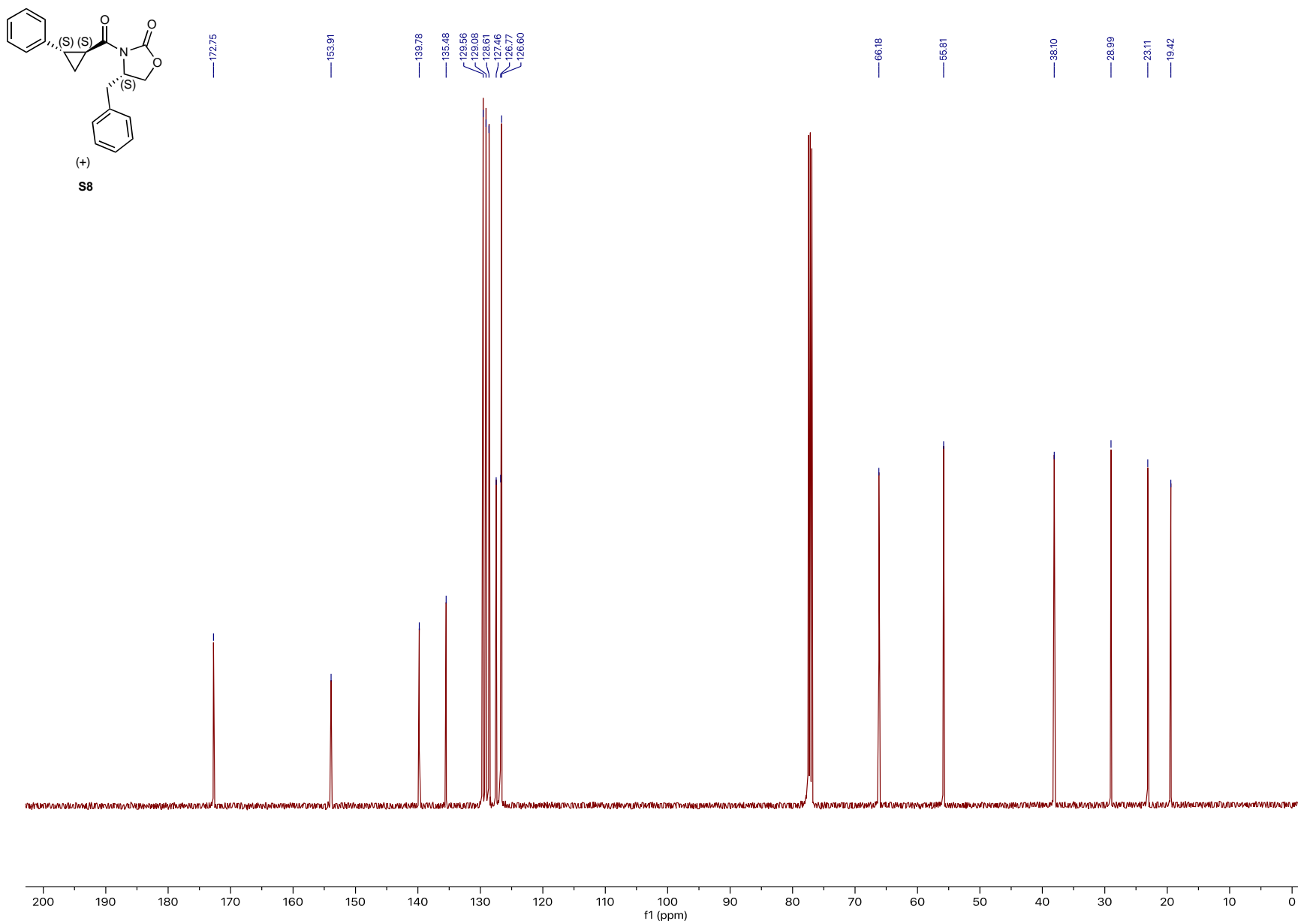
Supplementary Fig. 14 | ¹H-NMR (500 MHz, CDCl₃) of S7. *Impurity the result of acetone.



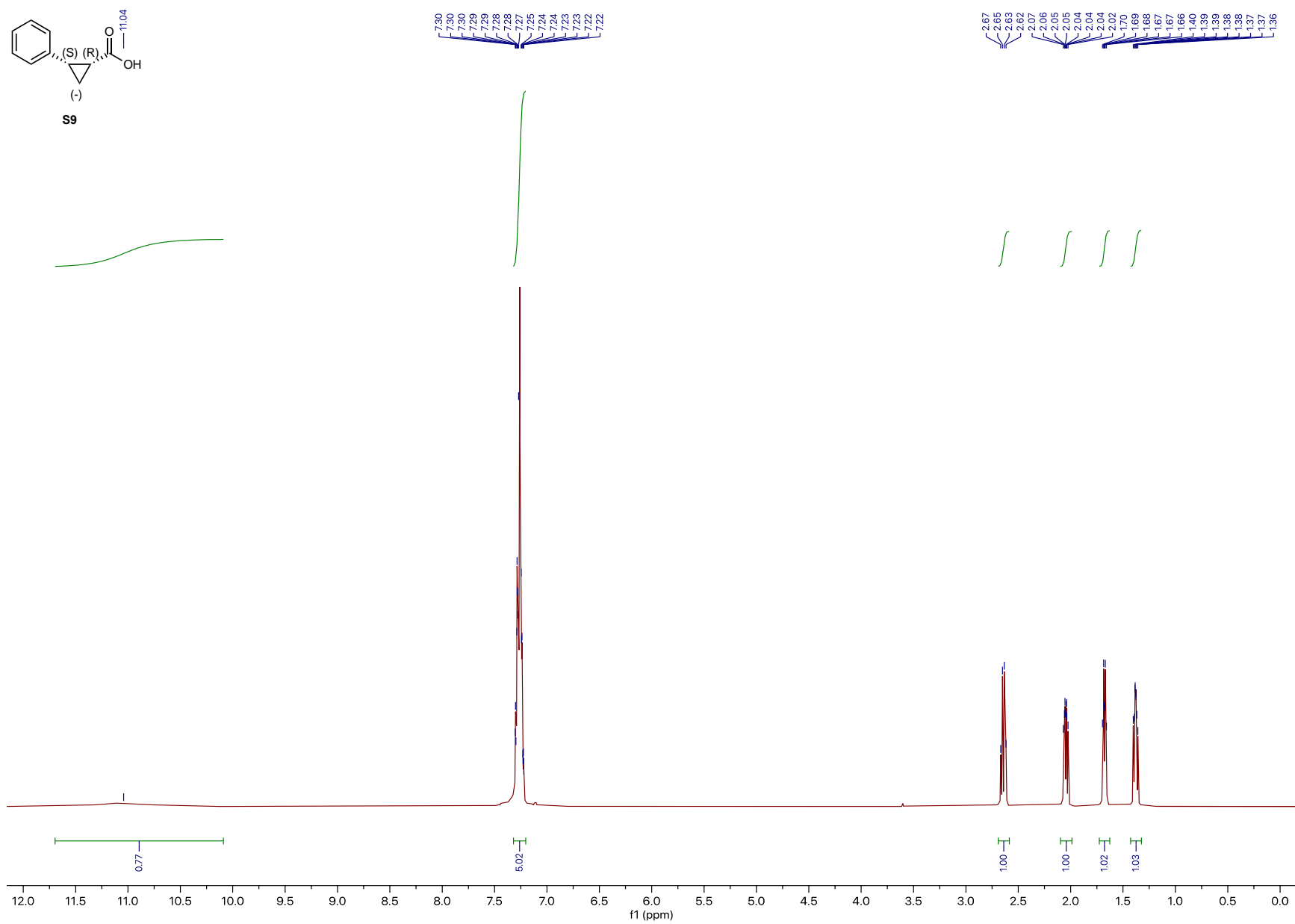
Supplementary Fig. 15 | ^{13}C -NMR (126 MHz, CDCl_3) of **S7**.



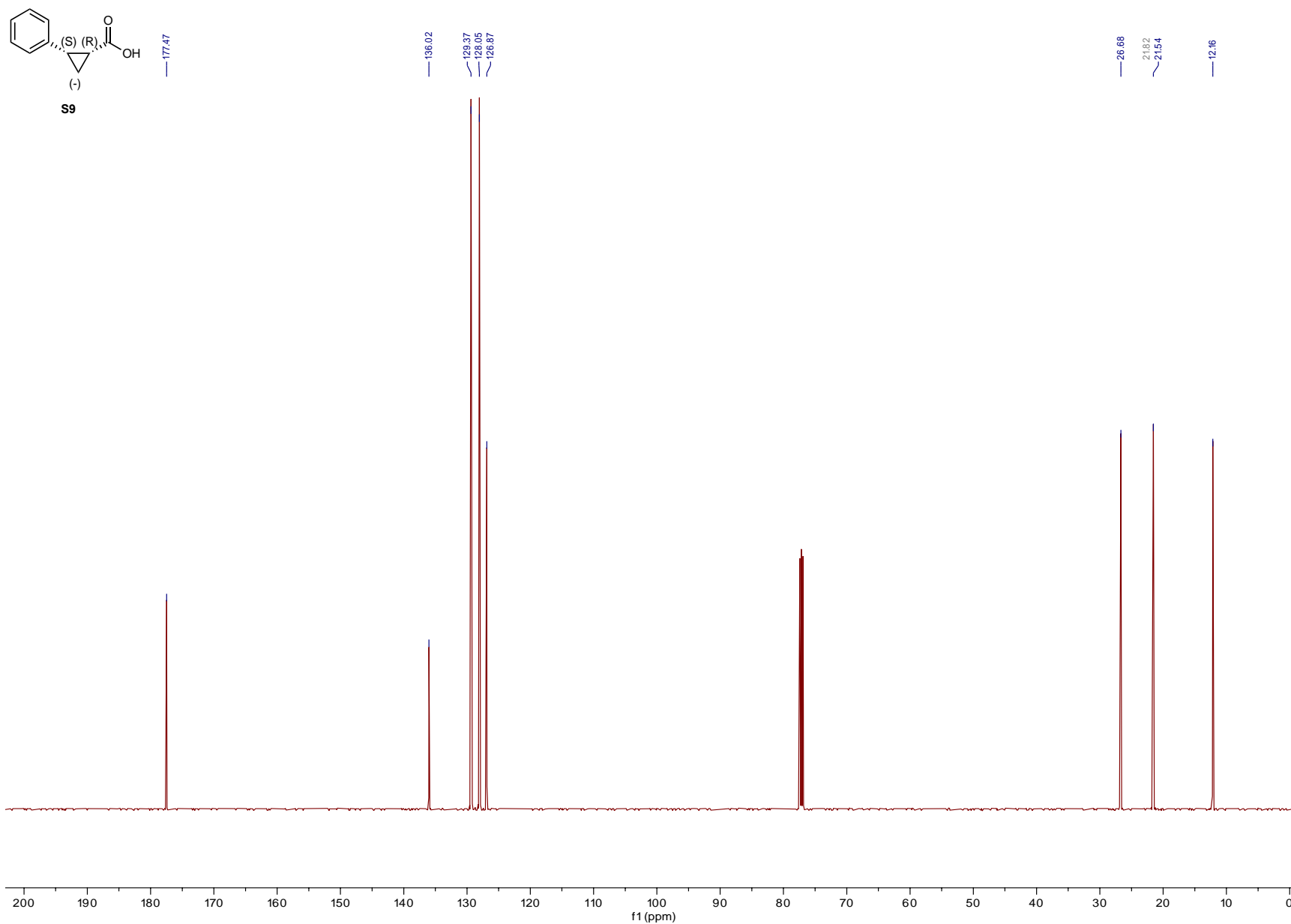
Supplementary Fig. 16 | ¹H-NMR (500 MHz, CDCl₃) of S8.



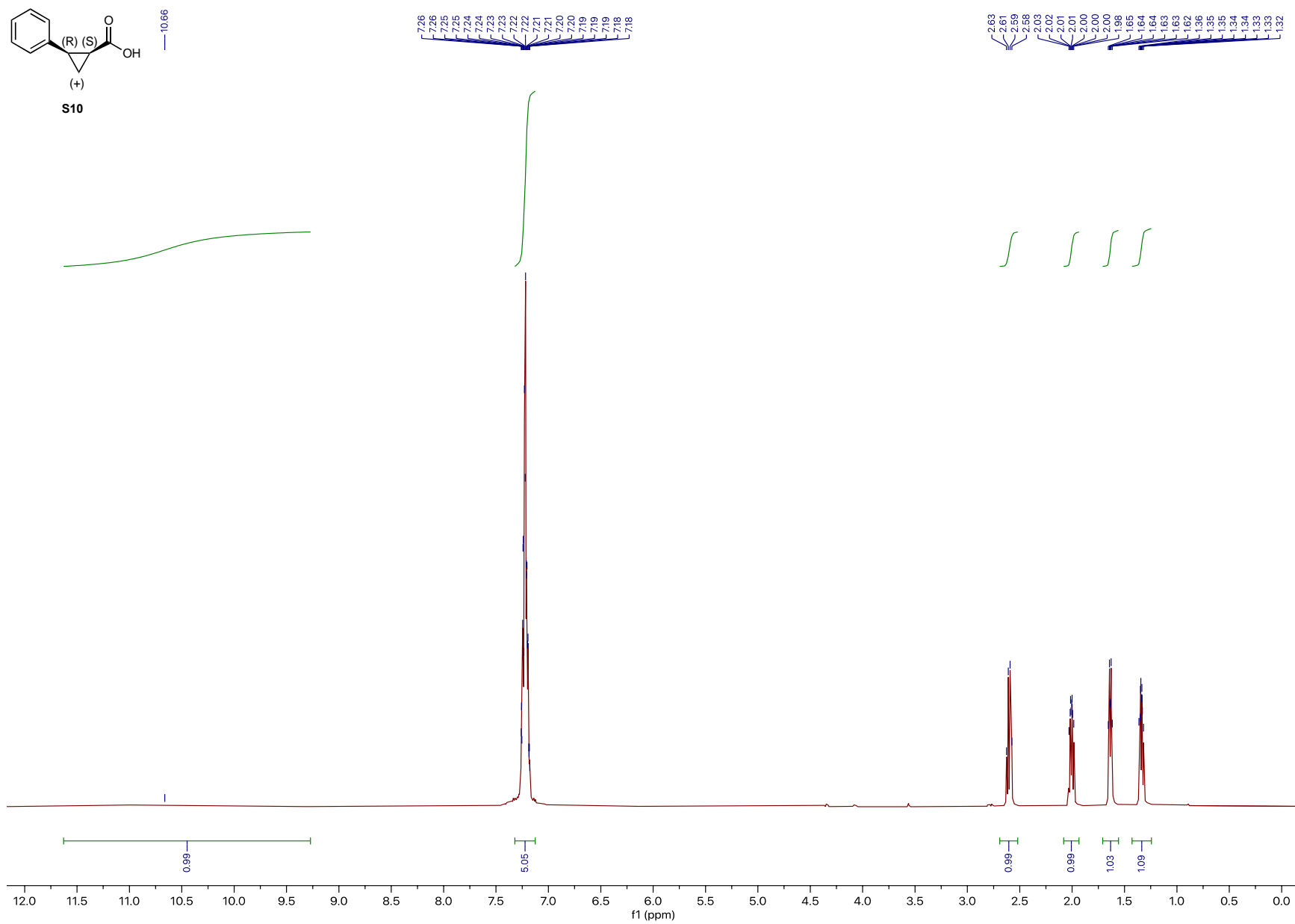
Supplementary Fig. 17 | ^{13}C -NMR (126 MHz, CDCl_3) of S8.



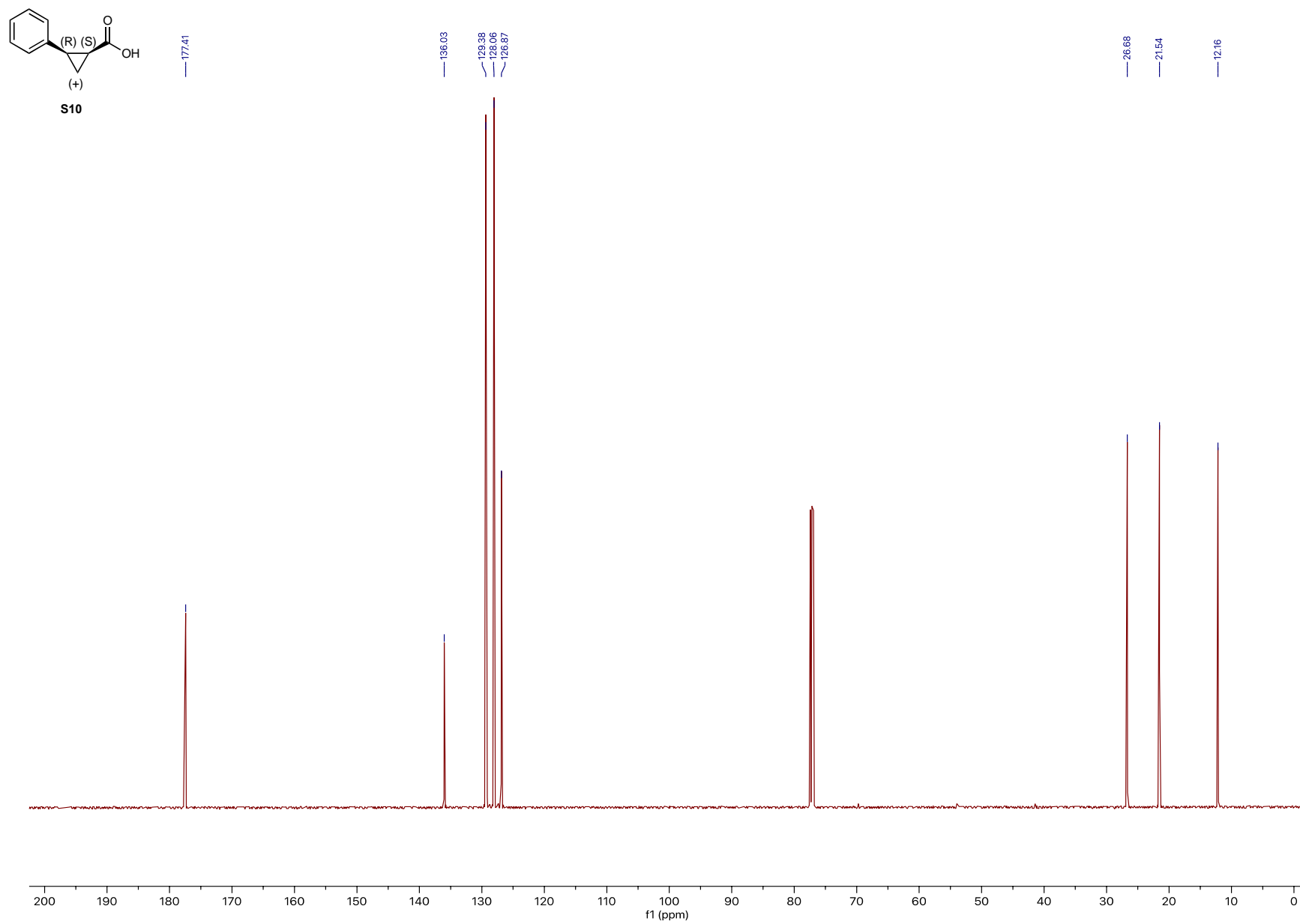
Supplementary Fig. 18 | ¹H-NMR (500 MHz, CDCl₃) of S9.



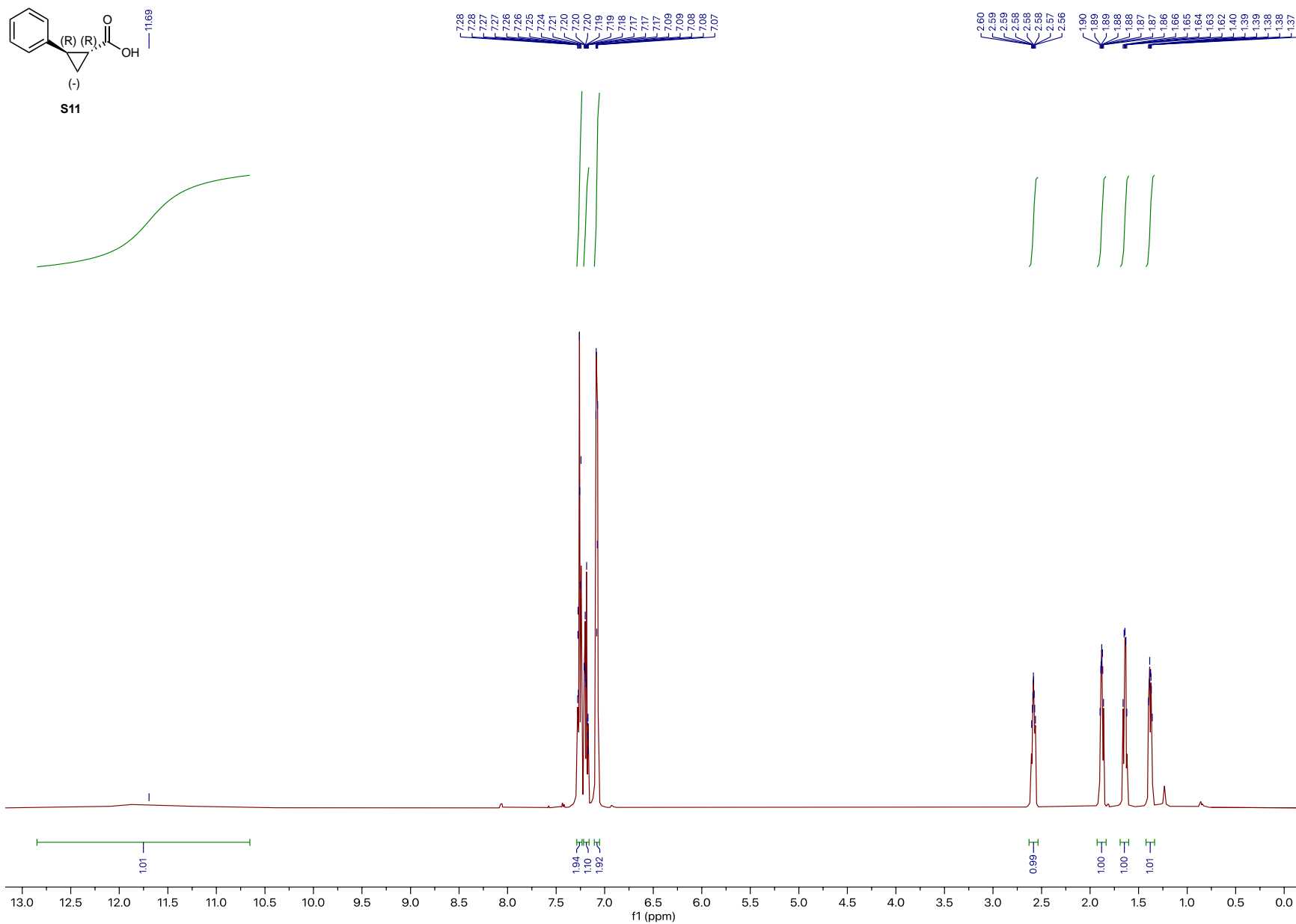
Supplementary Fig. 19 | ¹³C-NMR (126 MHz, CDCl₃) of S9.



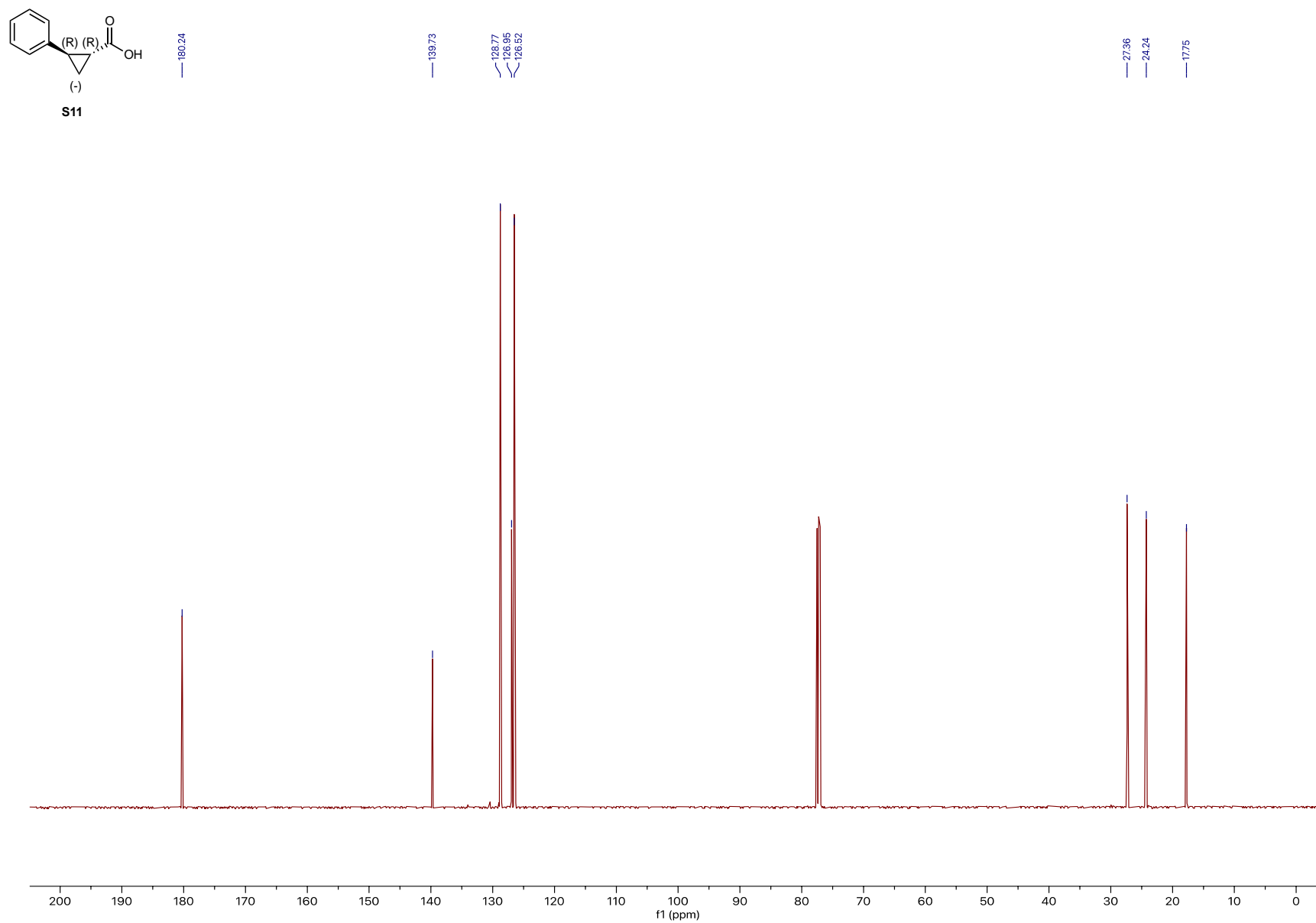
Supplementary Fig. 20 | ¹H-NMR (500 MHz, CDCl₃) of S10.



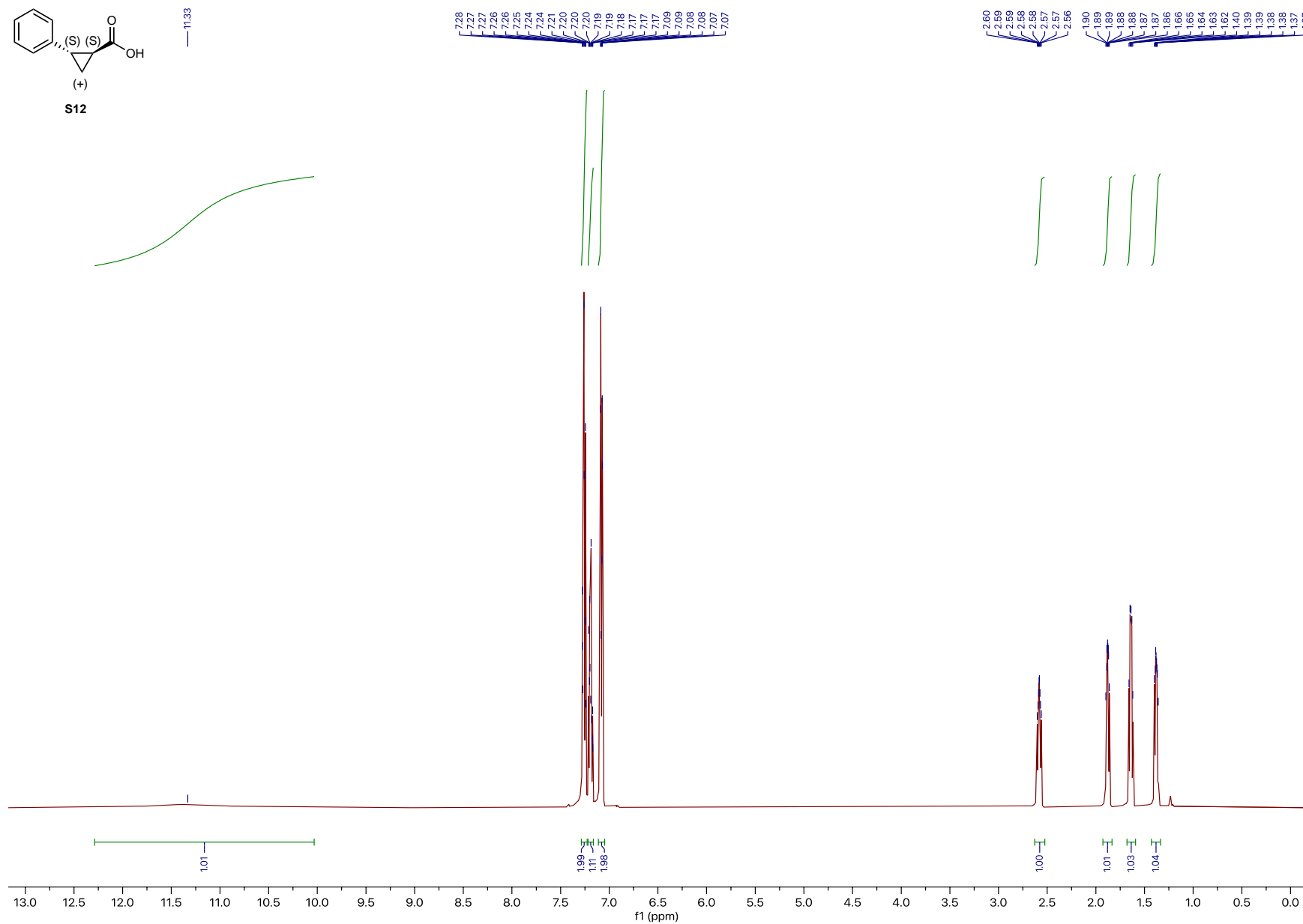
Supplementary Fig. 21 | ¹³C-NMR (126 MHz, CDCl₃) of S10.



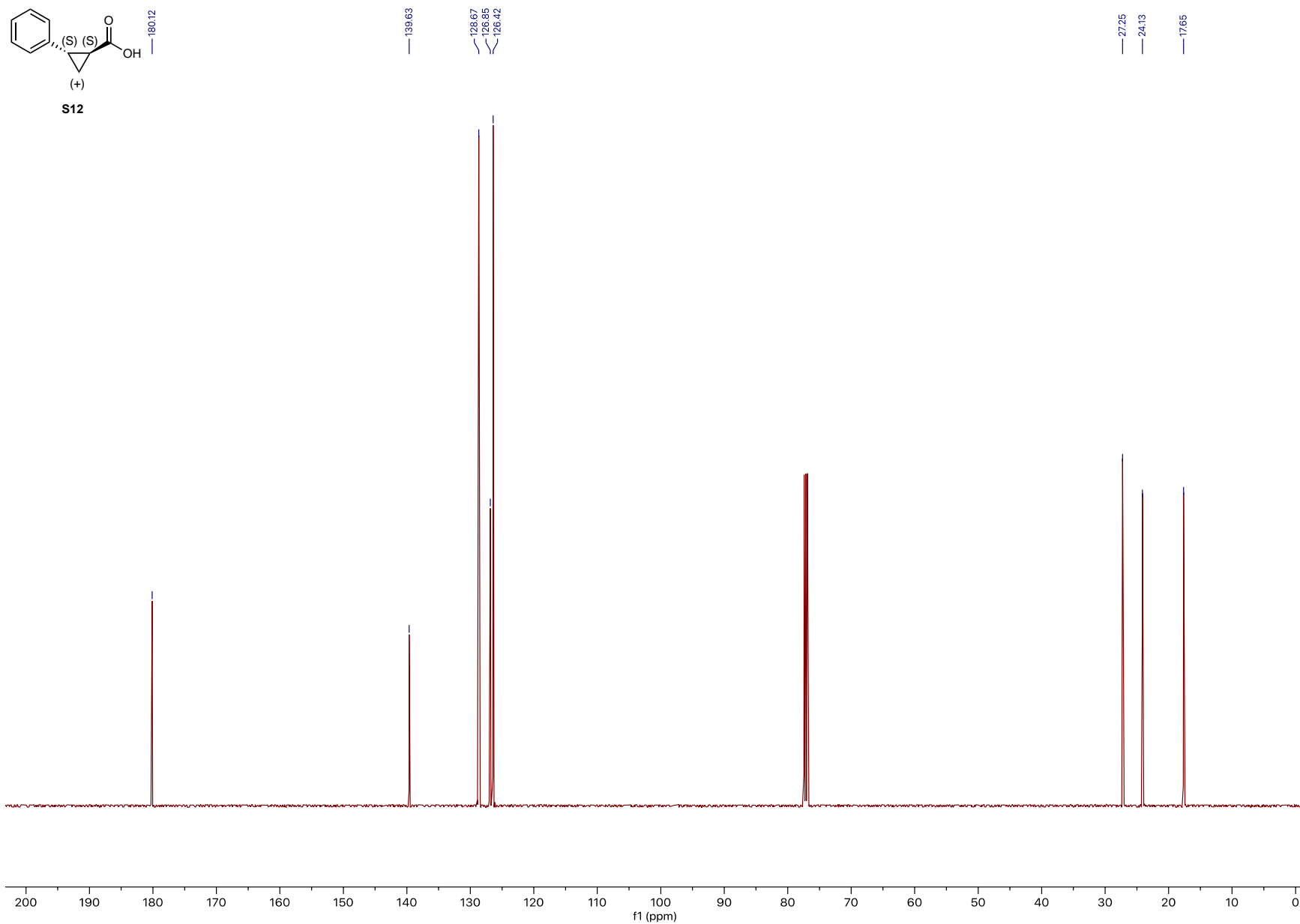
Supplementary Fig. 22 | ¹H-NMR (500 MHz, CDCl₃) of S11.



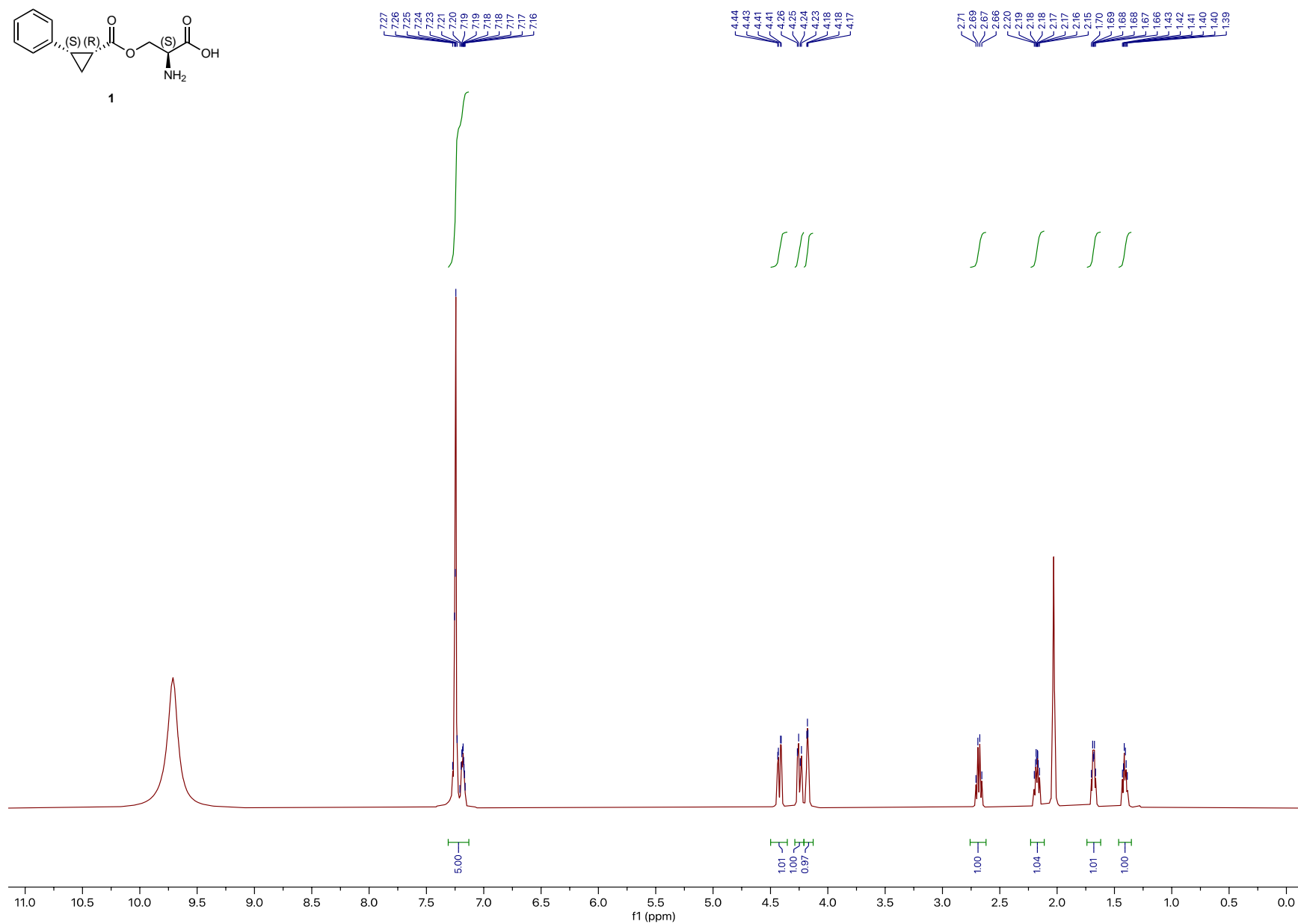
Supplementary Fig. 23 | ¹³C-NMR (126 MHz, CDCl₃) of S11.



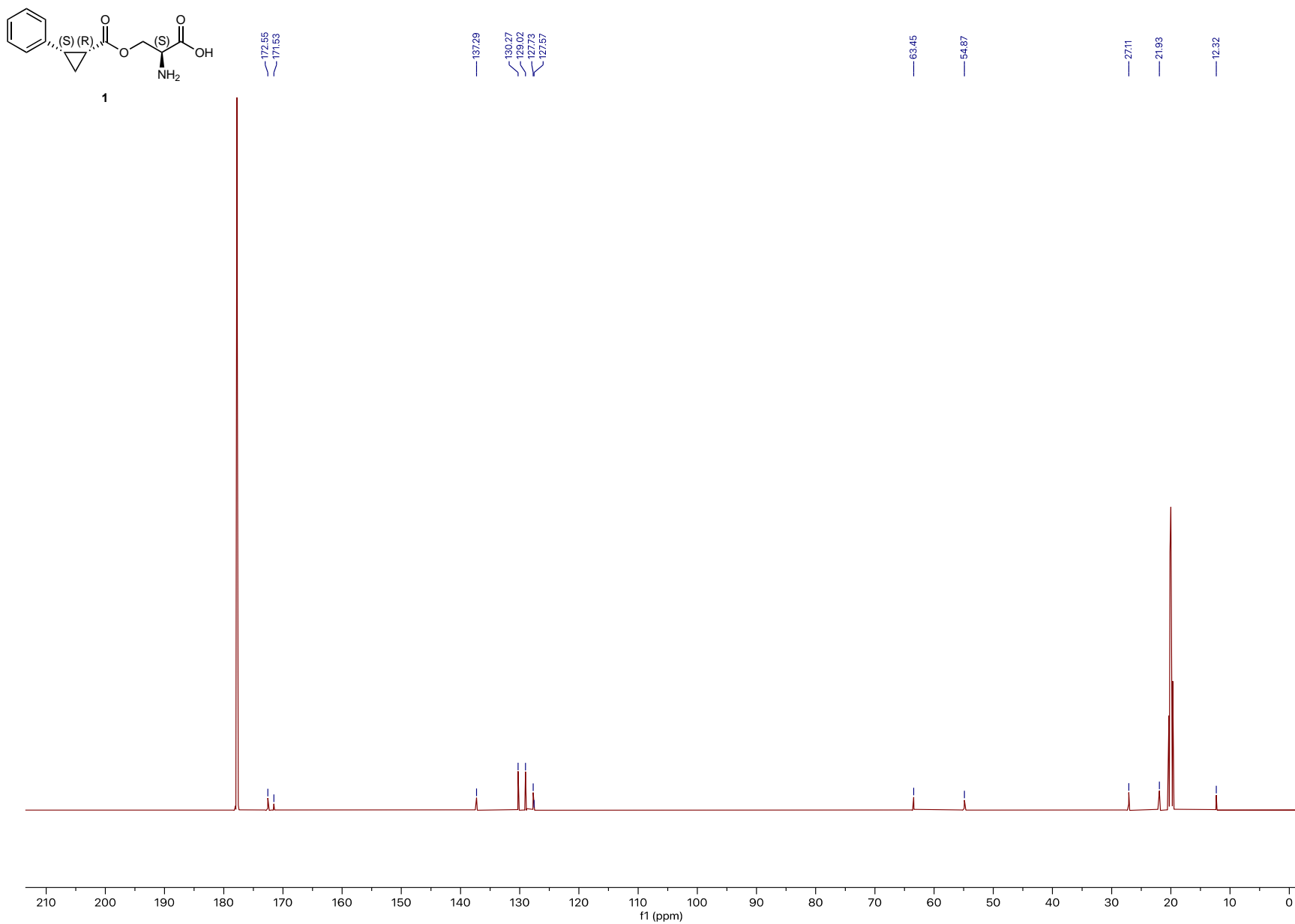
Supplementary Fig. 24 | ¹H-NMR (500 MHz, CDCl₃) of S12.



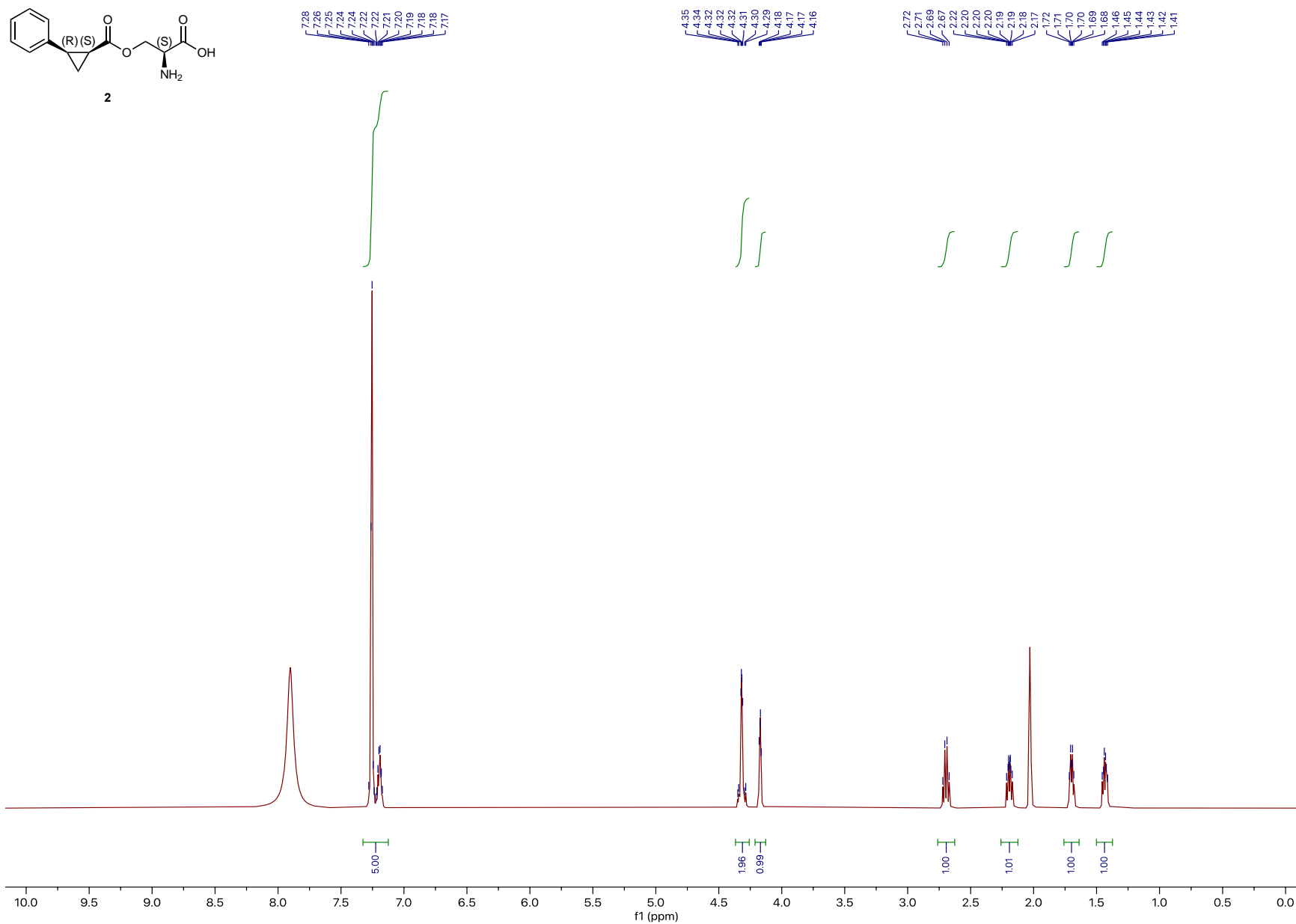
Supplementary Fig. 25 | ¹³C-NMR (126 MHz, CDCl₃) of S12.



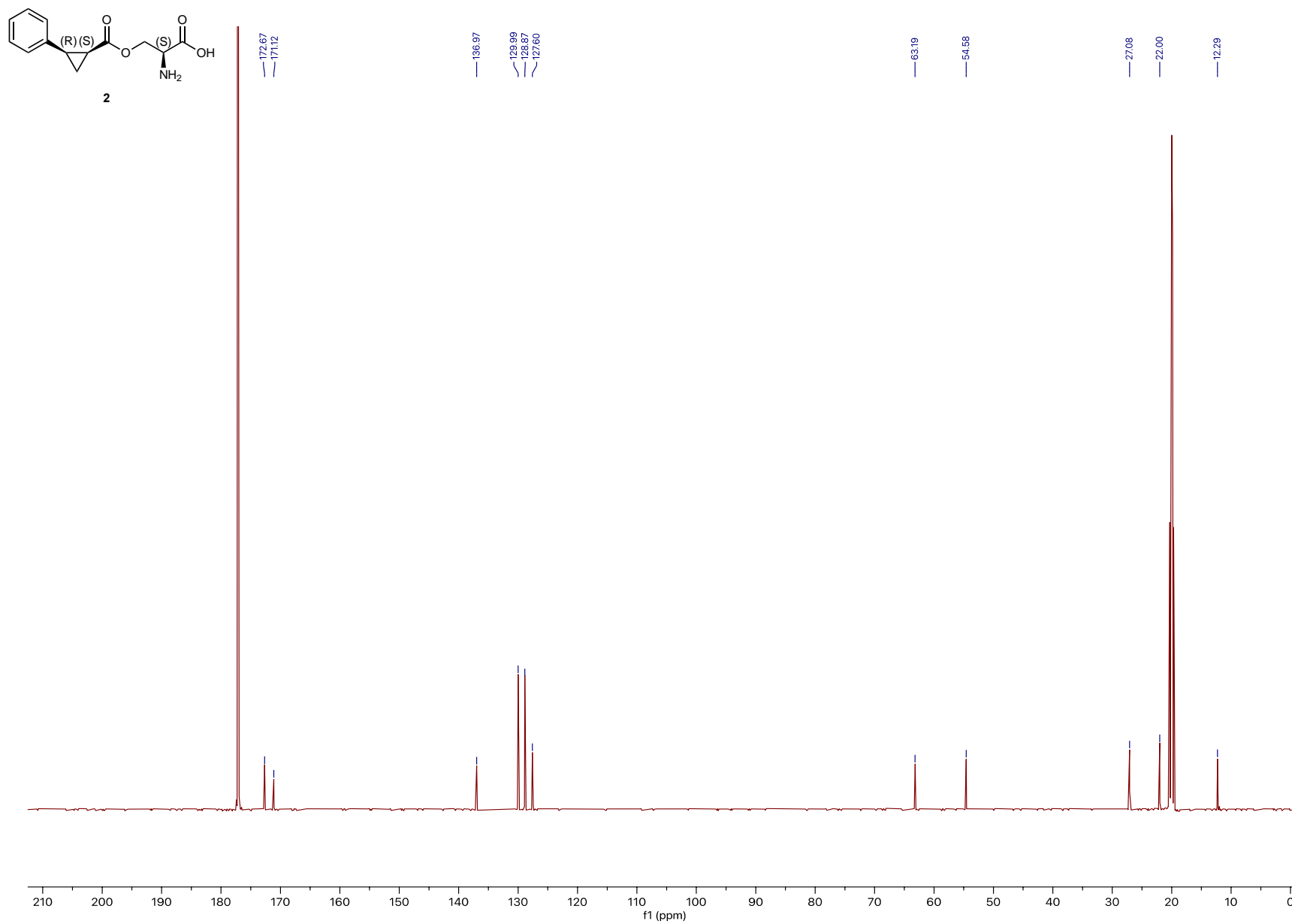
Supplementary Fig. 26 | $^1\text{H-NMR}$ (500 MHz, $\text{d}_4\text{-acetic acid}$) of **1**.



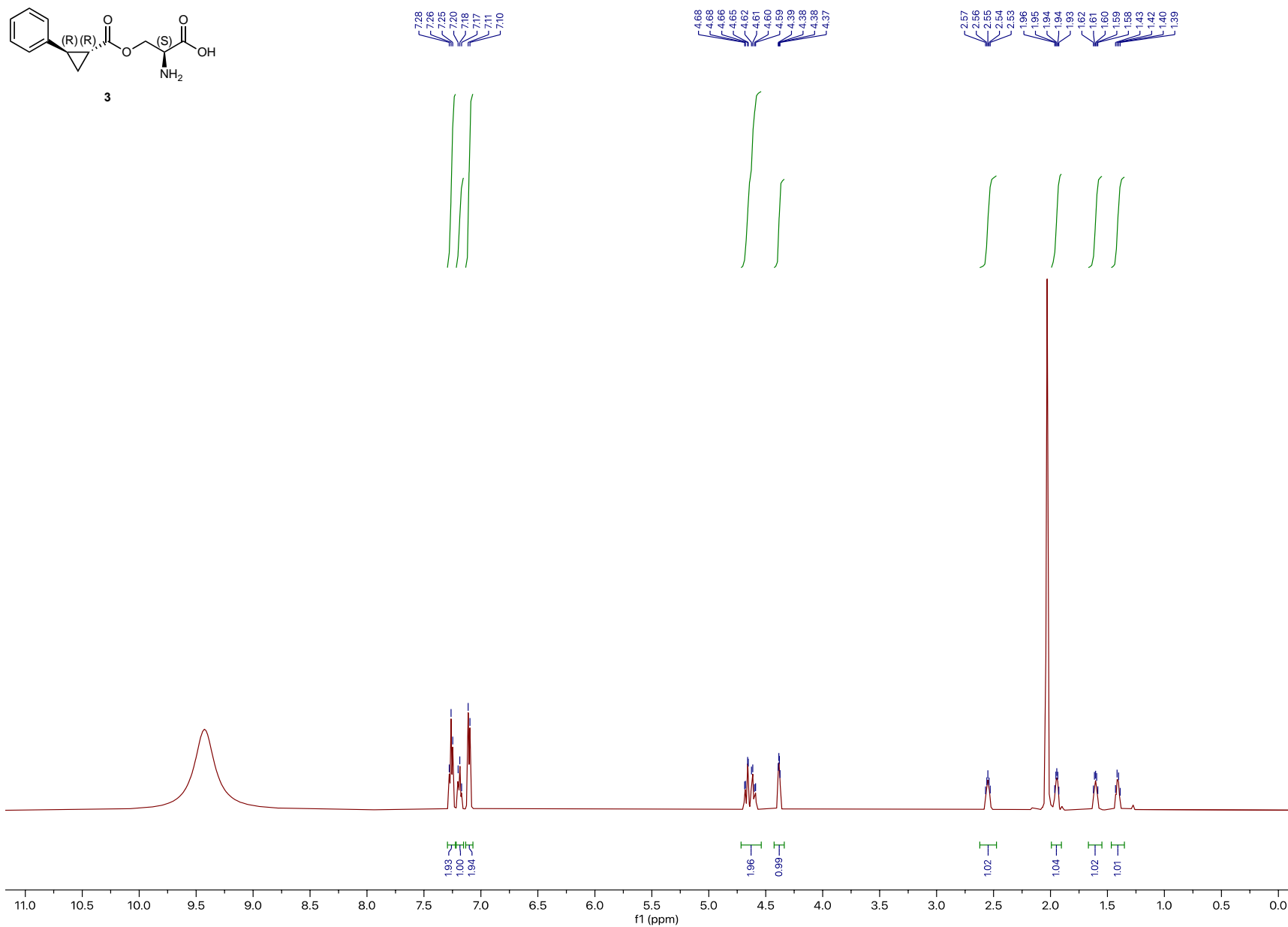
Supplementary Fig. 27 | ¹³C-NMR (126 MHz, d₄-acetic acid) of 1.



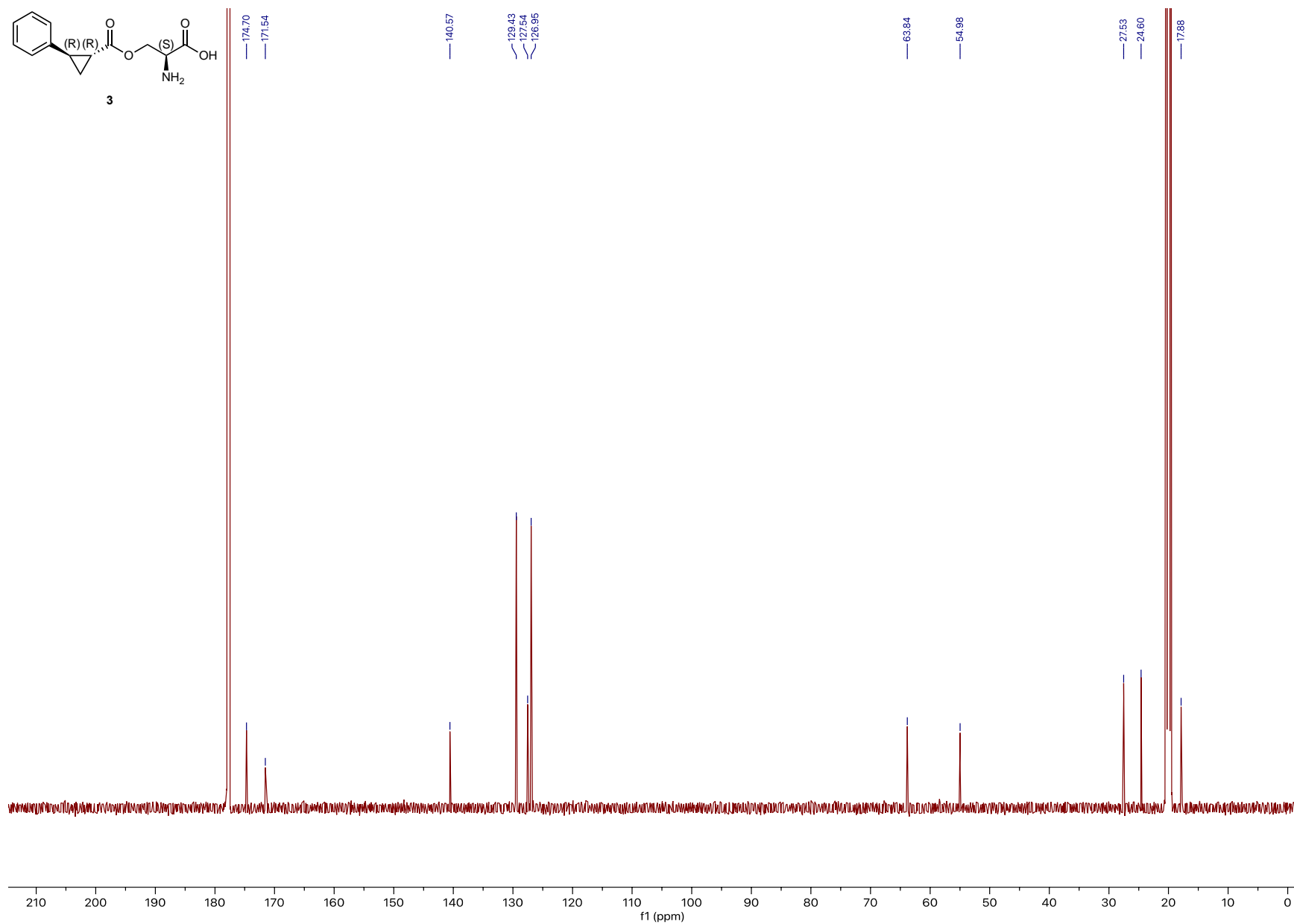
Supplementary Fig. 28 | ¹H-NMR (500 MHz, d₄-acetic acid) of 2.



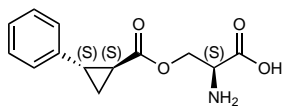
Supplementary Fig. 29 | ¹³C-NMR (126 MHz, CDCl₃) of 2.



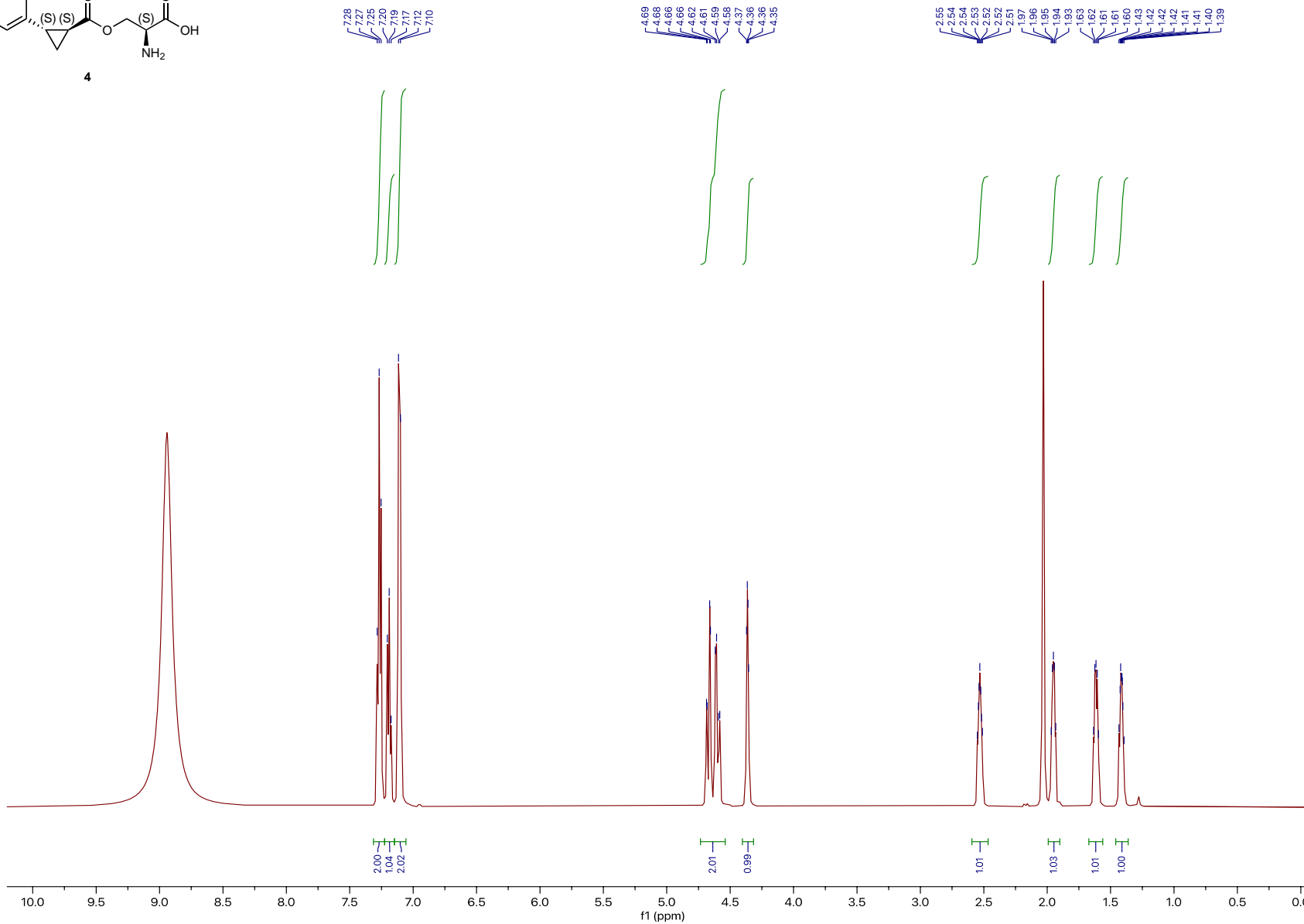
Supplementary Fig. 30 | ¹H-NMR (500 MHz, d₄-acetic acid) of 3.



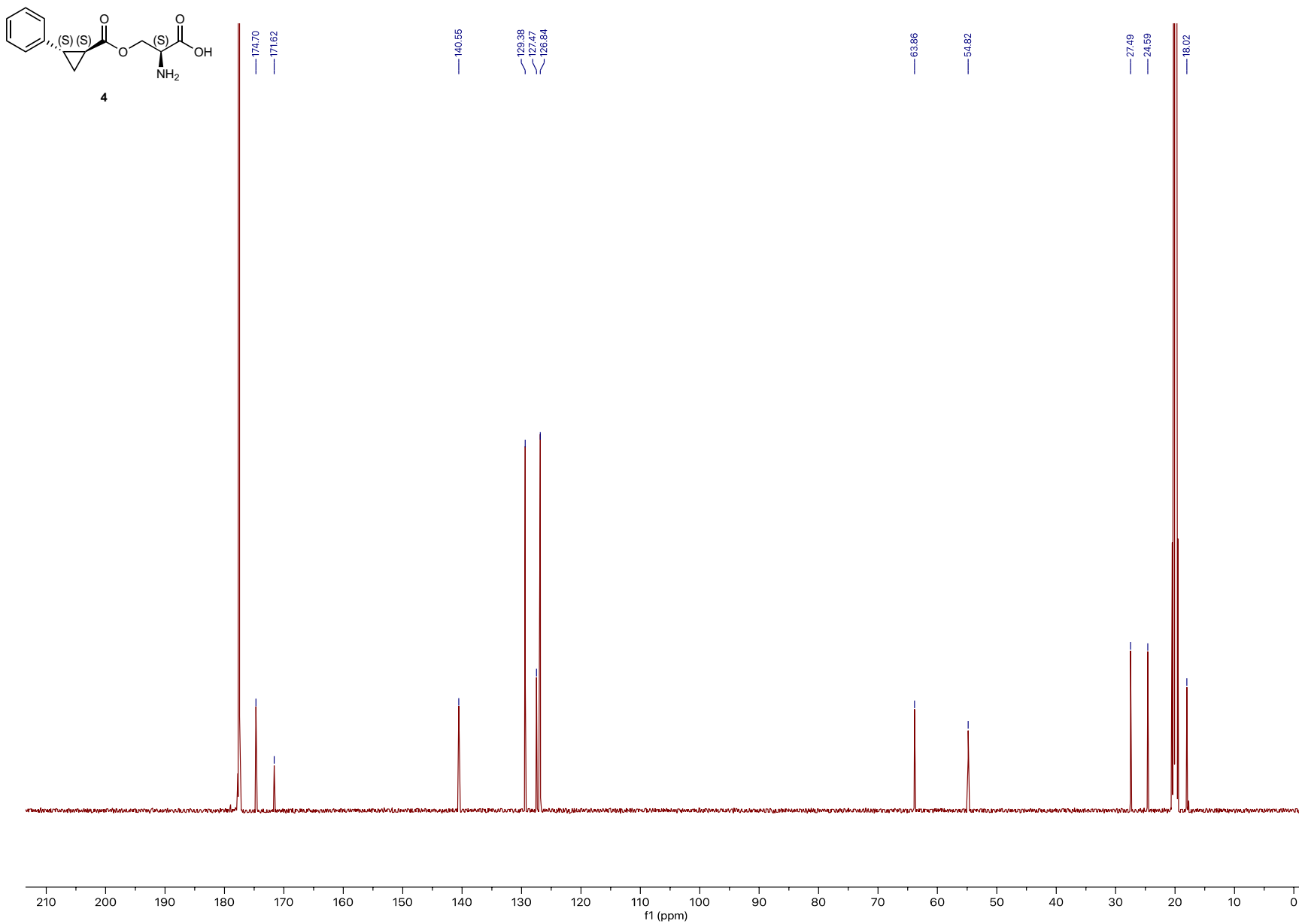
Supplementary Fig. 31 | ¹³C-NMR (126 MHz, d₄-acetic acid) of 3.



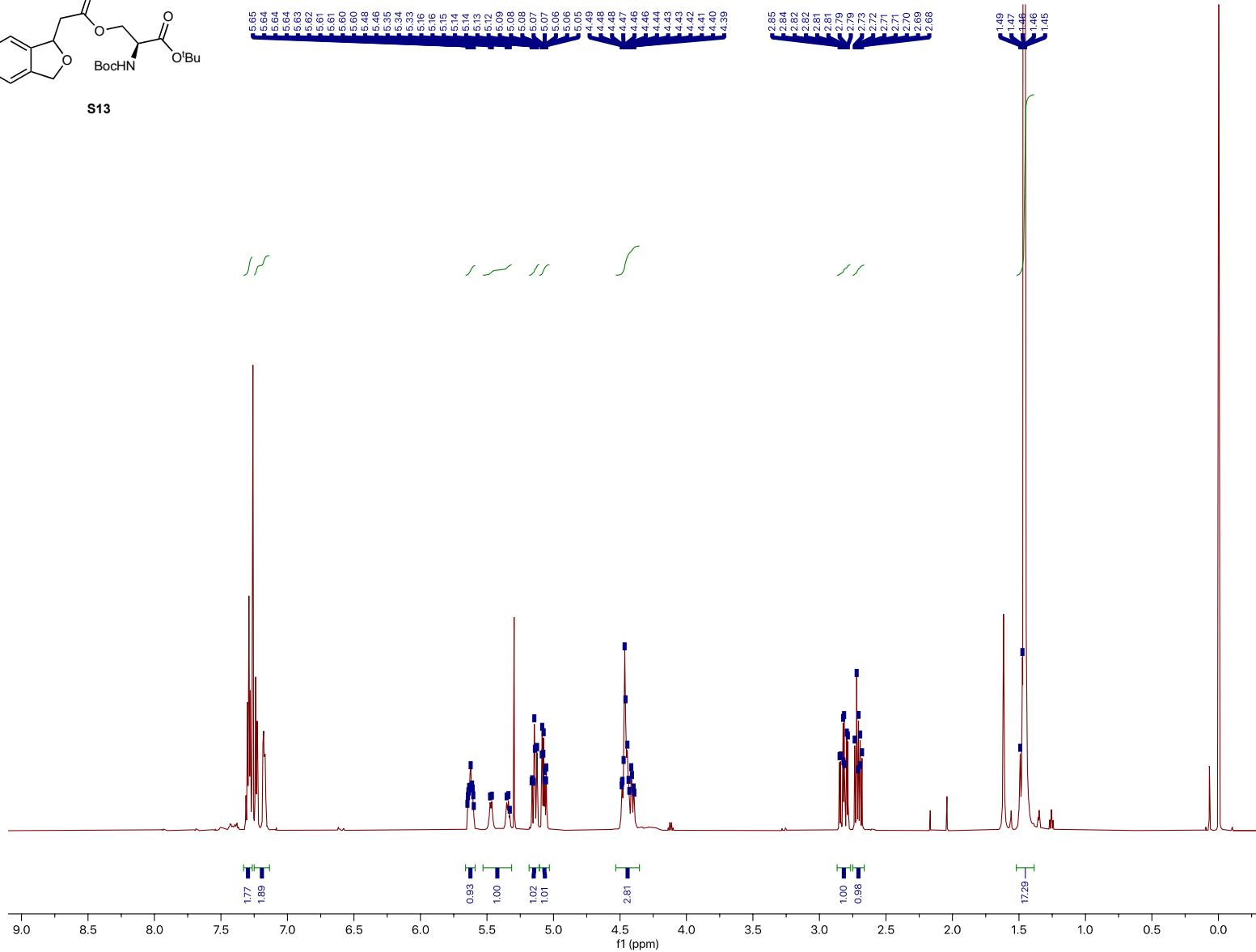
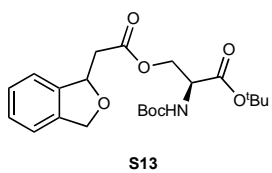
4



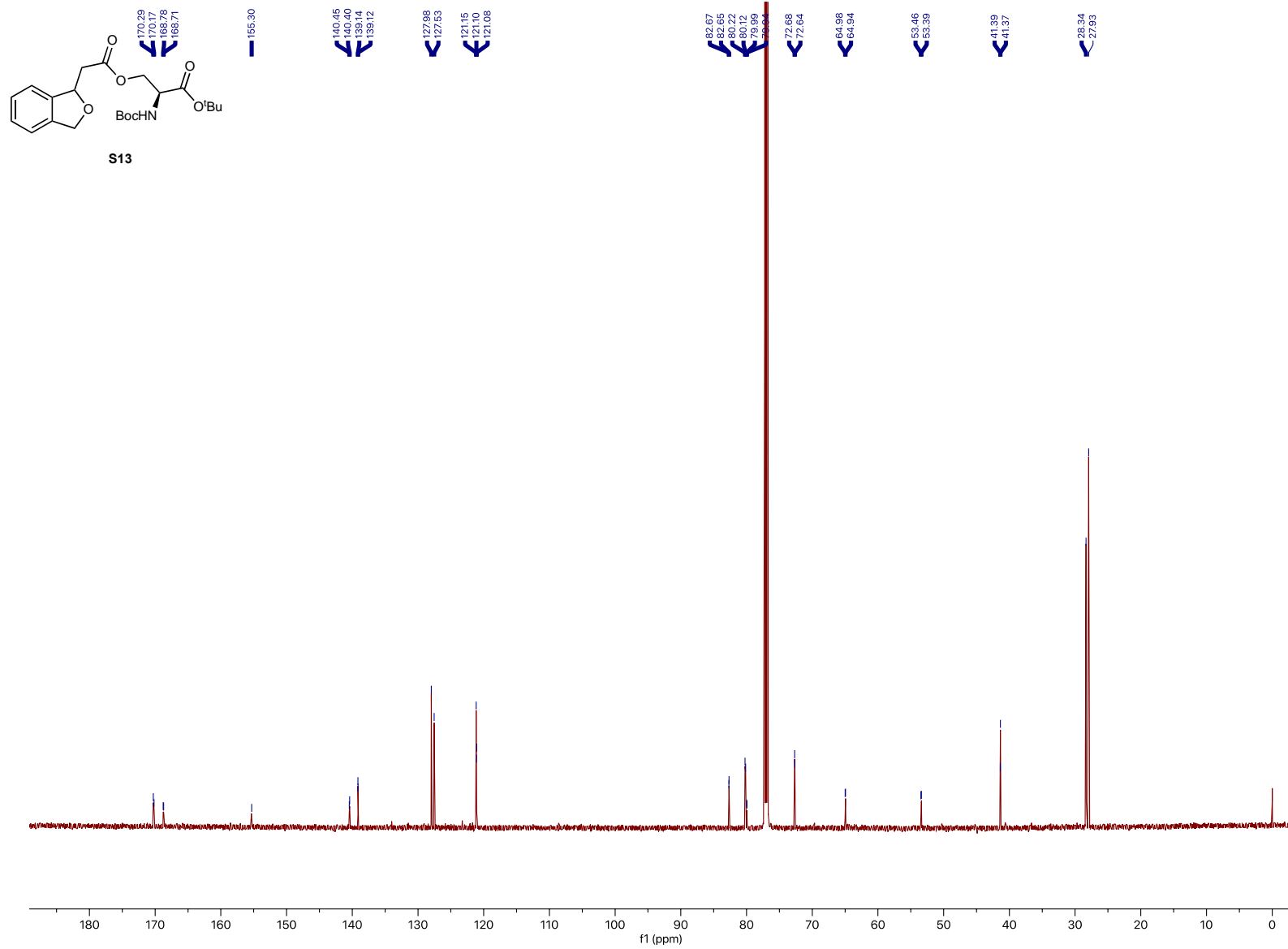
Supplementary Fig. 32 | ¹H-NMR (500 MHz, d₄-acetic acid) of 4.



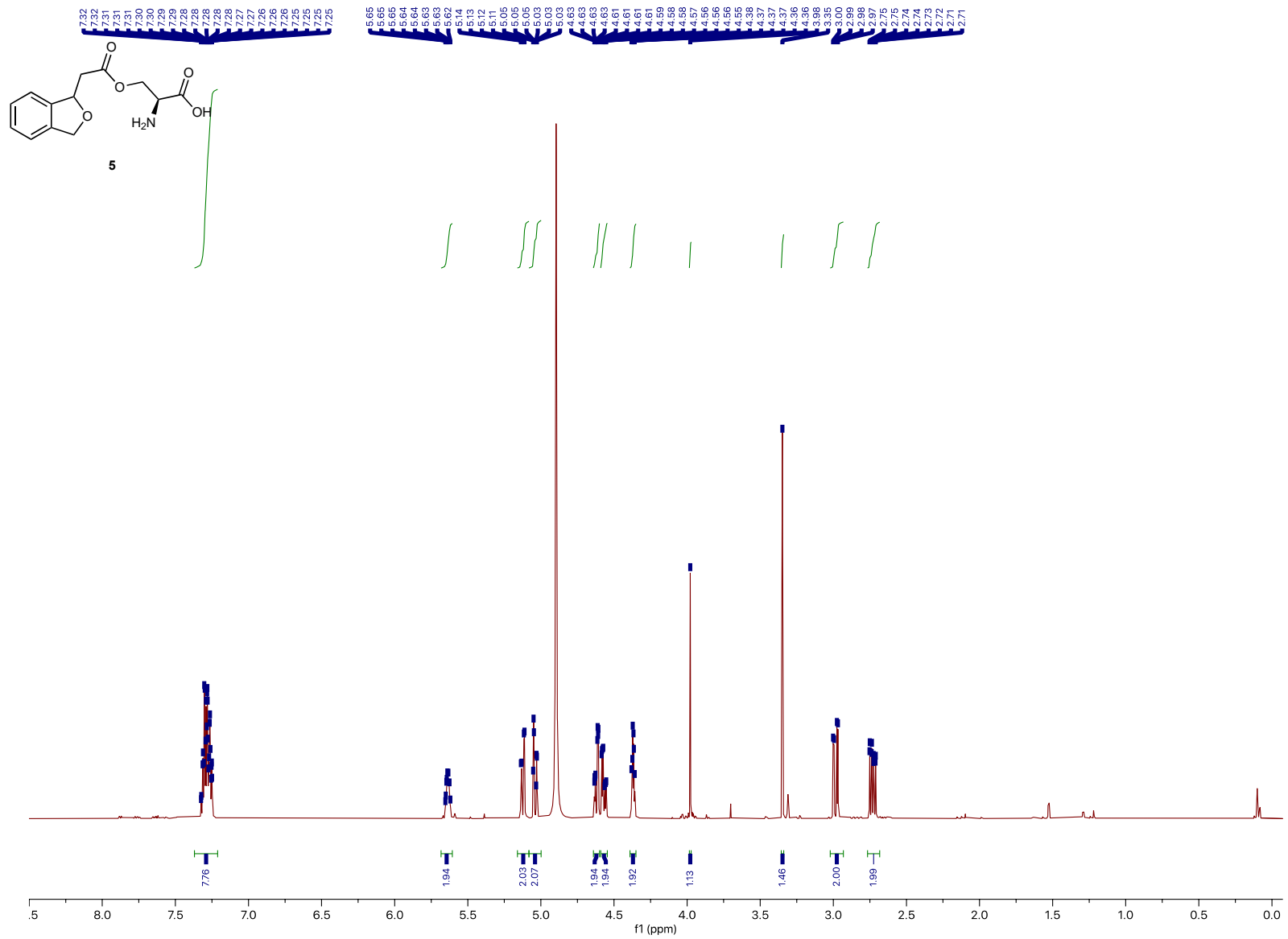
Supplementary Fig. 33 | ¹³C-NMR (126 MHz, d₄-acetic acid) of 4.



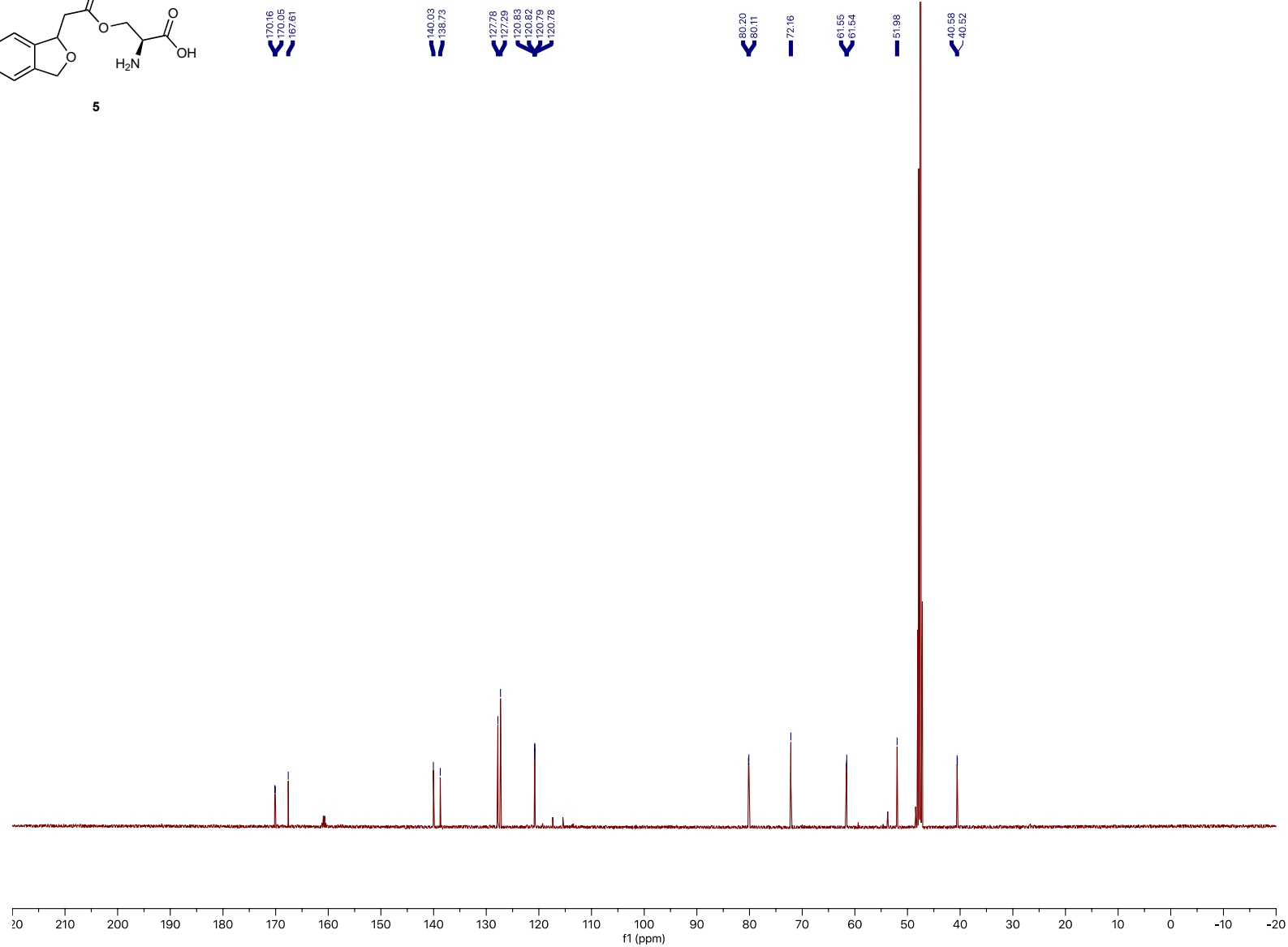
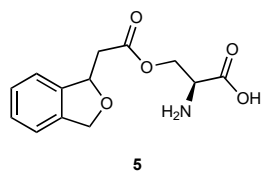
Supplementary Fig. 34 | ¹H-NMR (600 MHz, CDCl₃) of S13.



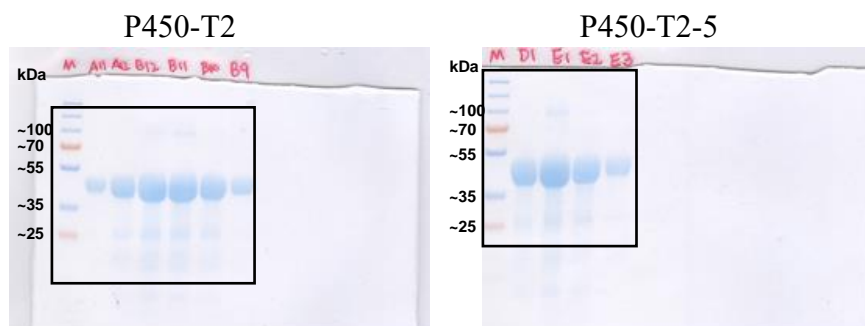
Supplementary Fig. 35 | ¹³C-NMR (151 MHz, CDCl₃) of S13.



Supplementary Fig. 36 | ¹H-NMR (600 MHz, CD₃OD) of 5.



Supplementary Fig. 37 | ^{13}C -NMR (151 MHz, CD_3OD) of 5.



Supplementary Fig. 38 | Raw gel image for Extended Data Fig. 5a. Region in black rectangle was displayed.

Supplementary References

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