Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Combining Iminium and Supramolecular Catalysis for the [4 + 2] Cycloaddition of *E*-Cinnamaldehydes

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Supporting Information

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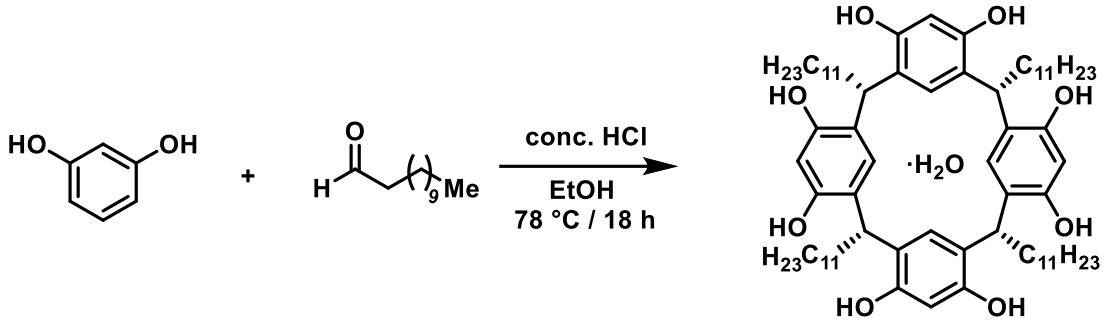
1. General Information

^{1}H, ^{13}C, and ^{19}F spectra were recorded on either a Varian Inova 400 MHz NMR spectrometer, a Varian Inova 600 MHz NMR spectrometer, or a Bruker Avance 600 MHz NMR spectrometer, and were processed using MestReNova by Mestrelab Research S.L. Proton (^{1}H) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane (TMS, δ=0), and referenced internally with respect to the protio solvent impurity.[1] Fluorine (^{19}F) chemical shifts are reported in parts per million (δ) and referenced internally with respect to hexafluorobenzene included in an insert tube (C_6F_6, δ= −161.64).[2] Mass spectra were recorded on a Waters SYNAPT G2-Si High Definition Mass Spectrometer. Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. All other materials were obtained from Sigma-Aldrich Chemical Company, St. Louis, MO, Combi-Blocks, San Diego, CA, Oakwood Chemical, Estill, SC, Alfa Aesar, Ward Hill, MA, Acros Organic, Geel, Belgium, or TCI, Tokyo, Japan, and were used as received.

2. Synthesis of Reactants

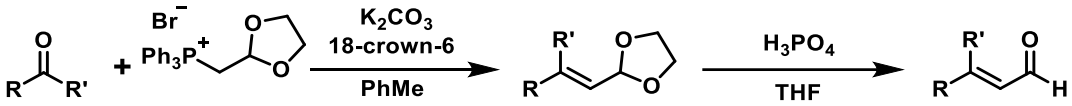
A) Synthesis of Resorcin[4]arene A



Resorcin[4]arene **A** was synthesized according to a literature procedure.[3] To a 100-mL round bottom flask charged with a stir bar was added resorcinol (4.00 g, 36.3 mmol, 1.1 equiv.), anhydrous ethanol (15 mL), followed by 37% aqueous HCl (5 mL). The reaction was stirred at 0 °C for 15 min, and a solution of dodecanal (6.09 g, 33.0 mmol, 1 equiv.) in absolute ethanol (9 mL) was added dropwise into the reaction mixture. After complete addition, the resulting solution was allowed to warm to rt, followed by heating under reflux for 18 h. The resulting dark red solution was cooled to rt, and a yellow precipitate formed that was collected using a fritted filter followed by washing with cold MeOH until the washings were light yellow. The resulting solid was air dried, then recrystallized from MeOH, washed again with cold MeOH (30 mL), then cold water (100 mL), followed by air drying until the residual organic solvents were completely removed. Compound **A** (8.5 g, 91%) was obtained as an off-white powder. The spectroscopic data matched those reported in the literature.

Note: Too low water content in compound gives a gel like mixture when dissolved in $CDCl_3$.

B) General Procedure for Synthesis of Cinnamaldehydes via Wittig Reaction/Deprotection

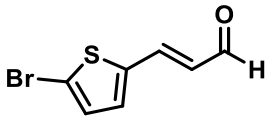


Based on our previously published procedure, carbonyl compound (1.0 equiv.), 18-crown-6 (2 mol%), (1,3-dioxolan-2-ylmethyl)triphenylphosphonium bromide (1.5 equiv.), K_2CO_3 (1.5 equiv.), and toluene (15 mL) were combined in a 40 mL reaction vial. The vial was sealed with a PTFE lined cap and the reaction mixture was heated in a pie-block at 100 ºC with stirring for 18 h. After cooling to rt, the solvent was evaporated *in vacuo*. The reaction mixture was then diluted with deionized water (20 mL), followed by extraction with dichloromethane (2 x 20 mL). The combined organic phases were dried over Na_2SO_4, then concentrated *in vacuo* to give the crude acetal product, which was used in the next step without any further purification.

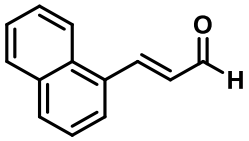
The crude acetal (assumed as 1.0 equiv.) was added to tetrahydrofuran (10 mL), followed by 1 mL of 85% H_3PO_4. The reaction was then heated at 80 ºC for 16 h. After cooling to RT, the solvent was evaporated *in vacuo*. The reaction mixture was diluted with deionized water (20 mL), followed by extraction with dichloromethane (2 x 20 mL).

The combined organic phases were dried over Na_2SO_4, then concentrated *in vacuo*. The crude reaction mixture was then purified by flash chromatography over silica to give the desired cinnamaldehyde product.

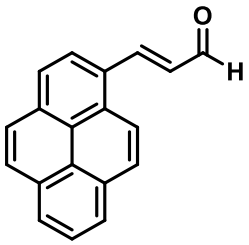
C) Cinnamaldehyde Characterization Data



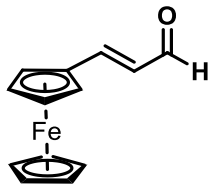
(*E*)-3-(4-Bromothiophen-2-yl)acrylaldehyde (*S*-1): Following the general procedure,[4] 4-bromothiophene-2-carbaldehyde (573 mg) was used. Product recovered as an orange solid (498 mg, 77% yield). R_f = 0.4 (hexanes/EtOAc = 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.64 (d, *J* = 7.6 Hz, 1H), 7.48 (d, *J* = 15.7 Hz, 1H), 7.38 (s, 1H), 7.27 (d, *J* = 1.3 Hz, 1H), 6.50 (dd, *J* = 15.7, 7.6 Hz, 1H).



(*E*)-3-(Napthalen-1-yl)acrylaldehyde (*S*-2): Following the general procedure,[4] 1-naphthaldehyde (468 mg) was used. Product recovered as a white solid (464 mg, 85% yield). R_f = 0.5 (hexanes/EtOAc = 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.86 (d, *J* = 7.7 Hz, 1H), 8.35 (d, *J* = 15.7 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 8.2 Hz, 1H), 7.92 (dd, *J* = 8.1, 0.6 Hz, 1H), 7.83 (d, *J* = 7.2 Hz, 1H), 7.63 (dt, *J* = 8.4, 6.8, Hz, 1H), 7.57 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 6.85 (dd, *J* = 15.7, 7.7 Hz, 1H).



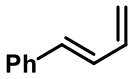
(*E*)-3-(Pyren-1-yl)acrylaldehyde (*S*-3): Following the general procedure,[4] 1-pyrenecarboxaldehyde (506 mg) was used. Product recovered as a yellow solid (310 mg, 55% yield). R_f = 0.3 (hexanes/EtOAc = 8:2). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.90 (d, *J* = 7.6 Hz, 1H), 8.53 (d, *J* = 15.6 Hz, 1H), 8.38 (d, *J* = 9.2 Hz, 1H), 8.23 (dd, *J* = 7.8, 3.4 Hz, 3H), 8.17 (d, *J* = 9.2 Hz, 1H), 8.12 (t, *J* = 8.5 Hz, 2H), 8.07 – 8.02 (m, 2H), 6.97 (dd, *J* = 15.6, 7.6 Hz, 1H).



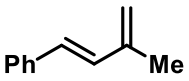
(*E*)-3-(Ferrocenyl)acrylaldehyde (*S*-4): Following the general procedure,[4] ferrocenecarbaldehyde (700 mg) was used. Product recovered as a red solid (471 mg, 60% yield). R_f = 04(hexanes/EtOAc = 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.56 (d, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 15.6 Hz, 1H), 6.34 (dd, *J* = 15.5, 8.0 Hz, 1H), 4.54 (d, *J* = 20.7 Hz, 4H), 4.17 (s, 5H).

D) Synthesis and Characterization of Dienes

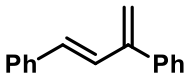
Cyclopenta-1,3-diene (*S*-5): Cyclopenta-1,3-diene was prepared by cracking dicyclopentadiene in the presence of heat. An oven-dried round bottom flask was charged with dicyclopentadiene (5.00 g) and connected to a distillation condenser with a receiving round bottom flask immersed in an ice bath. The temperature was raised to reflux (170 ºC), and distillation performed until a sufficient amount of diene had been collected. The freshly distilled cyclopentadiene (1.60 g, 32% yield) was immediately used in a reaction or stored in a freezer at -20 °C.



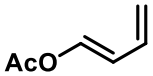
(*E*)-Buta-1,3-dien-1-ylbenzene (*S*-6): Compound ***S*-6** was synthesized according to a literature procedure.[5] To a mixture of methyltriphenylphosphonium bromide (2.68 g, 7.5 mmol, 1.5 equiv.) and potassium *tert*-butoxide (0.90 g, 8 mmol, 1.6 equiv.) was added THF (0.33 equiv. relative to aldehyde) at 0 ºC under a N_2 atmosphere. The bright yellow solution was warmed to rt and stirred for 2 h, upon which cinnamaldehyde (0.66 g, 5 mmol, 1 equiv.) was added and the reaction stirred for an additional 24 h. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ and THF was removed *in vacuo*. Hexanes was added to the solution, followed by filtration through celite, then rinsing with additional hexanes. The filtrate was diluted with brine, followed by extraction in a separatory funnel. The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to give the crude diene. The crude reaction was purified by silica plug, eluting with hexanes to give ***S*-6** as a clear oil (498 mg, 76% yield. R_f = 0.60 (hexanes). ^{1}H NMR (600 MHz, $CDCl_3$) δ) 7.45 (d, 2H, J = 7.3 Hz); 7.36 (t, 2H, J = 7.3 Hz); 7.27 (m, 1H); 6.84 (dd, 1H, J = 15.1, 10.3 Hz); 6.61 (d, 1H, J = 16.1 Hz); 6.56 (ddd, 1H, J = 17.3, 10.3, 10.3 Hz); 5.38 (d, 1H, J = 17.1 Hz); 5.22 (d, 1H, J = 9.8 Hz).



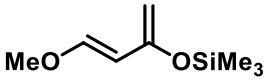
(*E*)-(3-Methylbuta-1,3-dien-1-yl) benzene (*S*-7): Compound ***S*-7** was synthesized according to a literature procedure.[5] To a mixture of methyltriphenylphosphonium bromide (2.68 g, 7.5 mmol, 1.5 equiv.) and potassium *tert*-butoxide (0.90 g, 8 mmol, 1.6 equiv.) was added THF (0.33 equiv. relative to aldehyde) at 0 ºC under a N_2 atmosphere. The bright yellow solution was warmed to rt and stirred for 2 h, upon which 4-phenyl-3-butene-2-one (0.73 g, 5 mmol, 1 equiv.) was added and the reaction was stirred for an additional 24 h. The reaction was quenched with saturated $NH_4Cl_{(aq)}$ and THF was removed *in vacuo*. Hexanes was added to the solution, followed by filtration through celite, then rinsing with additional hexanes. The filtrate was diluted with brine, followed by extraction in a separatory funnel. The combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo* to give the crude diene. The crude reaction was purified by silica plug eluting with hexanes to give ***S*-7** as a clear oil (532 mg, 74% yield). R_f = 0.65 (hexanes). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.46 (d, J = 7.4 Hz, 2H), 7.33-7.37 (m, 2H), 7.23-7.27 (m, 1H), 6.91 (d, J = 16.2 Hz, 1H), 6.57 (d, J = 16.2 Hz, 1H), 5.15 (s, 1H), 5.12 (s, 1H), 2.01 (s, 3H).



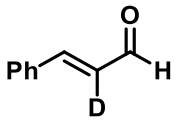
(*E*)-Buta-1,3-diene-1,3-diyldibenzene (*S*-8): Compound ***S*-8** was prepared based on a literature procedure.[5] To a mixture of methyltriphenylphosphonium bromide (2.68 g, 7.5 mmol, 1.5 equiv.) and potassium *tert*-butoxide (0.90 g, 8 mmol, 1.6 equiv.) was added THF (0.33 equiv. relative to aldehyde) at 0 ºC under a N_2 atmosphere. The bright yellow solution was warmed to rt and stirred for 2 h, upon which chalcone (1.04 g, 5 mmol, 1 equiv.) was added and stirred for an additional 24 hr. The reaction was quenched with saturated NH_4Cl and THF was removed *in vacuo*. Hexanes were added to the solution and filtered through celite, rinsing with hexanes to remove the solid Ph_3PO. The filtrate was diluted with brine, followed by extraction in a separatory funnel. The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo* to give the crude diene. The crude reaction was purified by silica plug, eluting with hexanes to give ***S*-8** as a clear oil. Note: The product contained impurities (~18%) but was used without any further purification due to the difficulty in removing these via chromatography. NMR spectra matched with previous reports.[6] R_f = 0.45 (hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.23 (m, 10H), 7.11-7.08 (m, 1H), 6.52 (m, 1H), 5.46 (s, 1H), 5.28 (s, 1H).



(*E*)-Buta-1,3-dien-1-yl acetate (*S*-9): Compound ***S*-9** was synthesized according to a literature procedure.[7] A 50 mL RBF was charged with crotonaldehyde (1 mL, 12.1 mmol, 1 equiv.), DMAP (0.295 g, 2.41 mmol, 0.2 equiv.), Et_3N (3.50 mL, 25.1 mmol, 2.08 equiv.), and Ac_2O (5.80 ml, 61.7 mmol, 5.11 equiv.). The reaction was stirred at rt under nitrogen atmosphere for 24 h. The reaction mixture was diluted with water (20 ml), extracted with ether (50 mL), washed with $NaHCO_3$ (3x 20 ml), dried (Na_2SO_4) and concentrated in *vacuo*. The residue was purified by column chromatography (pentane/ether, 97:3) giving the title compound as a colorless oil (1037 mg, 77%). The spectroscopic data matched those reported in the literature. R_f = 0.3 (pentane/Ether = 97:3). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 12.4 Hz, 1H), 6.23 (dt, *J* = 16.9, 10.7 Hz, 1H), 6.00 (t, *J* = 11.7 Hz, 1H), 5.18 (d, *J* = 17.0 Hz, 1H), 5.05 (d, *J* = 10.3 Hz, 1H), 2.11 (s, 3H).



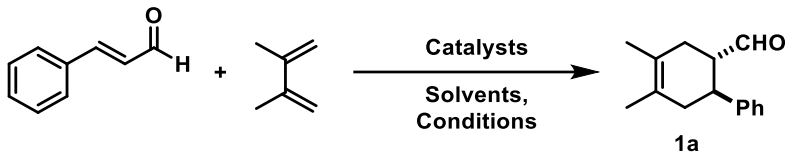
(*E*)-((4-Methoxybuta-1,3-dien-2-yl) oxy)trimethylsilane (*S*-10): Compound ***S*-10** was synthesized according to a literature procedure.[8] A 50 ml RBF with Et_3N (3 mL, 22 mmol, 2.2 equiv.) was added anhydrous $ZnCl_2$ (68 mg, 0.5 mmol, 0.5 equiv) and the reaction mixture was stirred at rt for 1 h. A solution of (*E*)-4-methoxybut-3-en-2-one (1 g, 10 mmol, 1 equiv.) in benzene was added to this homogeneous solution, followed by addition of TMSCl (2.53 mL, 19.96 mmol, 2 equiv.) within 30 min. The reaction mixture was stirred for 24 h at 40 ºC, cooled to rt, and quenched with anhydrous diethyl ether (30 mL). The formed mixture was filtered through alumina pad and washed with $NaHCO_3$ (20 ml), H_2O (20 mL) and brine (20 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in *vacuo* to give 1.36 gm diene (81%). Spectroscopic data for the crude compound matched those reported in the literature. R_f = 0.25 (hexanes/EtOAc = 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 6.84 (d, *J* = 12.4 Hz, 1H), 5.34 (d, *J* = 12.4 Hz, 1H), 4.10 (s, 1H), 4.07 (s, 1H), 3.54 (s, 3H), 0.23 (s, 9H)



Cinnamaldehyde-2-*d* (*S*-11): Following our previously published procedure,[4] commercially available cinnamaldehyde (119 mg, 0.9 mmol) was used in the deuteration reaction. A 40 mL vial was charged with cinnamaldehyde, isopropylamine (160 mg, 2.7 mmol), D_2O (1.5 mL), and AcOD (1.5 mL). The vial was sealed with a PTFE-lined cap, followed by heating to 100 ºC for 24 h in a pie-block on a heating/stirring plate. After cooling to rt, reaction was quenched with water. The aqueous layer was extracted with dichloromethane (2 x 40 mL), followed by subsequent washing with 1.2 M hydrochloric acid (2 x 30 mL). After drying over Na_2SO_4, the organic layer was concentrated *in vacuo* to give deuterated (*E*)-cinnamaldehyde-2-*d* as a yellow oil (103 mg, 86% yield). R_f = 0.4 (hexanes/EtOAc = 95:5). On the basis of internal proton integrations with non-deuterated peaks, the level of deuteration was determined to be 95% at the α-position. The spectroscopic data matched those reported in the literature. ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (s, 1H), 7.57 (dd, *J* = 7.1, 2.4 Hz, 2H), 7.49 – 7.46 (m, 1H), 7.46 – 7.42 (m, 3H), 6.73 (dd, *J* = 15.9, 7.7 Hz, 0.05H). ^{2}H NMR (92 MHz, $CDCl_3$) δ 6.77. ^{13}C NMR (151 MHz, $CDCl_3$) δ 193.9, 152.9, 134.1, 131.4, 129.2, 128.6, 128.5, 128.4 (t, *J* = 24.5 Hz).

3. Optimization and Synthesis of Cyclohexenes

A) Procedure (and Results) for Optimization Experiments for [4 + 2] Cycloaddition of Cinnamaldehydes:



1a

Entry	Reaction Conditions	Yield (%)
1	Standard conditions	86
2	Proline and cage omitted	0
3	Cage omitted	0
4	Proline omitted	4
5	DCM, 1 mL	65
6	Toluene, 1 mL	4
7	1:1 Toluene/$CDCl_3$, 1 mL	49
8	$PhCF_3$, 1 mL	46
9	1,2-DCE, 1 mL	37
10	1,1,2,2-TCE, 1 mL	60
11	MTBE, 1 mL	0
12	MeCN, 1 mL	0
13	EtOH, 1 mL	0
14	At 22 °C (Room Temp.)	34
15	At 60 °C	67
16	MacMillan Catalyst-Derivative Used	73
17	20 mol% proline and 10 mol% cage	38
18	10 mol% proline and 20 mol% cage	73
19	10 mol% proline and 10 mol% cage	67
20	1.0 eq. of 2,3-dimethylbutadiene	53

Table *S*-1. Optimization for [4 + 2] Cycloaddition of Cinnamaldehydes

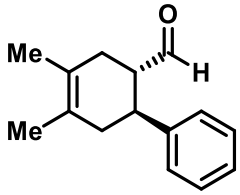
Optimization Procedure: Reactions were setup in triplicate. A 7.5 mL vial was charged with *L*-proline (2.3 mg, 0.02 mmol, 0.2 equiv.), **A** (135 mg, 0.02 mmol, 0.2 equiv.), cinnamaldehyde (13.2 mg, 0.1 mmol, 1.0 equiv.), 2,3-dimethylbutadiene (32.9 mg, 0.4 mmol, 4 equiv.) and $CDCl_3$ (1 mL). The vial was sealed with a PTFE lined cap and stirred at 40°C for 5 d in a pie-block. After 5 d of stirring, the reaction mixture was cooled to rt, then ^1H NMR analysis

was performed on the crude reaction mixture using dimethyl isophthalate as an internal standard, and the average yield reported.

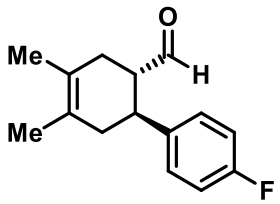
B) General Procedure for the Substrate Scope Studies

Reactions were setup in triplicate unless otherwise stated. A 7.5 mL vial was charged with *L*-proline (2.3 mg, 0.02 mmol, 0.2 equiv.), **A** (135 mg, 0.02 mmol, 0.2 equiv.), aldehyde (0.1 mmol, 1.0 equiv.), diene (0.4 mmol, 4 equiv.) and $CDCl_3$ (1 mL). The vial was sealed with a PTFE lined cap and stirred at 40ºC for 5 d in a pie-block. After 5 d of stirring, the reaction mixture was cooled to rt and 3 mL acetonitrile was added. The vial was cooled to -25 °C to precipitate **A**. The precipitate was then removed by centrifugation. Supernatant was collected after washing the precipitate with additional acetonitrile and concentrated *in vacuo*. All reactions were then combined and the crude reaction mixture was then purified by column chromatography (hexane:ethyl acetate, 500:1-250:1) over silica to give the desired product. The average yields are reported after combining the individual reaction runs.

C) Product Characterization Data

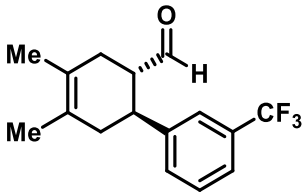


(1*S*,2*S*)-4,5-Dimethyl-1,2,3,6-tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (1a): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and (*E*)-cinnamaldehyde (13.2 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (54.6 mg, 85% yield), which was found to give spectral data matching that reported in the literature.[9] The *trans*/*cis d.r.* was determined from the crude NMR to be 91:9, while the %*ee* of the major isomer was determined to be 82% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.62 (hexane:ethyl acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.46 (d, *J* = 3.0 Hz, 1H), 7.33 – 7.28 (m, 2H), 7.24 – 7.19 (m, 3H), 3.08 (ddd, *J* = 10.2, 9.3, 6.3 Hz, 1H), 2.80 (dddd, *J* = 10.3, 9.6, 5.6, 3.0 Hz, 1H), 2.32 – 2.26 (m, 1H), 2.26 – 2.21 (m, 2H), 2.08 (ddd, *J* = 16.7, 3.7, 1.2 Hz, 1H), 1.70 (d, *J* = 0.8 Hz, 3H), 1.66 (d, *J* = 0.6 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.7, 143.6, 128.9, 127.6, 126.9, 125.8, 123.5, 52.2, 41.6, 39.6, 31.2, 18.9, 18.9. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{15}H_{19}O$ 215.1430; found 215.1411.

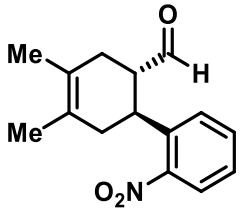


(1*S*,2*S*)-4'-Fluoro-4,5-dimethyl-1,2,3,6-tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (1b): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and (*E*)-4-fluorocinnamaldehyde (15 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (47.5 mg, 68% yield). The *trans*/*cis d.r.* was

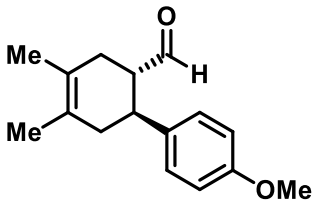
determined from the crude NMR to be 88:12, while the %*ee* of the major isomer was determined to be 20% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.50 (Hexane:Ethyl acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.46 (d, *J* = 3.0 Hz, 1H), 7.16 (dd, *J* = 8.6, 5.3 Hz, 2H), 6.99 (dd, *J* = 9.7, 7.7 Hz, 2H), 3.08 (td, *J* = 9.8, 5.8 Hz, 1H), 2.75 (dddd, *J* = 10.2, 9.5, 5.6, 3.0 Hz, 1H), 2.33 – 2.24 (m, 1H), 2.24 – 2.20 (m, 1H), 2.20 – 2.13 (m, 1H), 2.11 – 2.04 (m, 1H), 1.69 (s, 3H), 1.65 (s, 3H).). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.4, 161.7 (d, *J* = 244.8 Hz), 139.3 (d, *J* = 3.2 Hz), 129.0 (d, *J* = 7.9 Hz), 125.7, 123.6, 115.9 (d, *J* = 21.1 Hz), 52.3, 40.7, 39.5, 31.1, 18.9, 18.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ = −116.615. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{15}H_{18}FO$ 233.1336; found 233.1212.



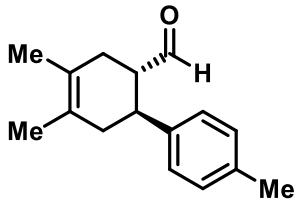
(1*S*,2*S*)-4,5-Dimethyl-3'-(trifluoromethyl)-1,2,3,6-tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (1c): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and (*E*)-3-(trifluoromethyl) cinnamaldehyde (20.0 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (59.2 mg, 70% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 89:11, while the %*ee* of the major isomer was determined to be 30% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.4 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.49 (d, *J* = 2.7 Hz, 1H), 7.49 – 7.44 (m, 2H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.7 Hz, 1H) , 3.18 (td, *J* = 9.6, 5.8 Hz, 1H), 2.86 – 2.79 (m, 1H), 2.33 – 2.24 (m, 2H), 2.23 – 2.06 (m, 2H), 1.70 (s, 3H), 1.66 (s, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ 203.9, 144.8, 131.2 (q, *J* = 32.1 Hz), 130.9 (q, *J* = 0.9 Hz), 129.4, 125.6, 124.4 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.3), 123.8 (q, *J* = 4.1 Hz), 123.75, 52.0, 41.1, 39.1, 30.9, 19.0, 18.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ = −62.927. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{16}H_{18}F_3O$ 283.1304; found 283.1290.



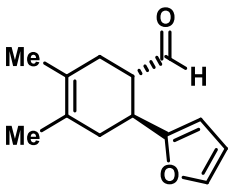
(1*S*,2*S*)-4,5-Dimethyl-2'-nitro-1,2,3,6-tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (1d): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and (*E*)-2-nitrocinnamaldehyde (18.0 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a white solid (29.8 mg, 38% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 92:8, while the %*ee* of the major isomer was determined to be 68% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.26 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.46 (d, *J* = 2.9 Hz, 1H), 7.75 (dd, *J* = 8.1, 1.3 Hz, 1H), 7.57 – 7.52 (m, 1H), 7.41 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.35 (ddd, *J* = 8.2, 7.4, 1.3 Hz, 1H), 3.66 (td, *J* = 9.5, 5.8 Hz, 1H), 2.89 (tdd, *J* = 9.5, 5.6, 2.9 Hz, 1H), 2.40 (dd, *J* = 17.4, 5.2 Hz, 1H), 2.35 – 2.25 (m, 1H), 2.16 – 2.09 (m, 2H), 1.71 (s,3H), 1,66 (s,3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.1, 150.3, 138.1, 133.1, 128.9, 127.6, 125.6, 124.4, 123.7, 51.9, 38.8, 35.1, 31.0, 18.9,18.9. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{15}H_{18}NO_3$ 260.1281; found 260.1282.



(1*S*,2*S*)-4'-Methoxy-4,5-Dimethyl-1,2,3,6-tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (1e): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and (*E*)-4-methoxycinnamaldehyde (16.2 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (40.3 mg, 55% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 89:11, while the %*ee* of the major isomer was determined to be 14% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.59 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.45 (d, *J* = 3.1 Hz, 1H), 7.13 – 7.11 (m, 2H), 6.85 – 6.83 (m, 2H), 3.05 – 2.99 (m, 1H), 2.78 – 2.71 (m, 1H), 2.32 – 2.25 (m, 1H), 2.22 – 2.13 (m, 2H), 2.06 (dd, *J* = 17.8, 4.3 Hz, 1H), 1.69 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.9, 158.5, 135.6, 128.5, 125.8, 123.5, 114.3, 55.4, 52.5, 40.8, 39.9, 31.3, 18.9,18.9. HRMS (ESI - MS): $[M+Na]^+$ Calculated for $C_{16}H_{20}NaO_2$ 267.1356; found 267.1361.

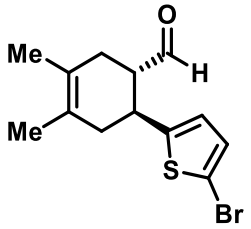


(1*S*,2*S*)-4,4',5-Trimethyl-2'-nitro-1,2,3,6-tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (1f): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9, 0.4 mmol) and (*E*)-4-methylcinnamaldehyde (14.62 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a white solid (26 mg, 30% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 85:15, while the %*ee* of the major isomer was determined to be 34% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.57 (Hexane: Ethyl acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ. 9.45 (d, *J* = 3.1 Hz, 1H), 7.18 – 7.04 (m, 4H), 3.03 (ddd, *J* = 10.3, 9.1, 6.5 Hz, 1H), 2.77 (tdd, *J* = 9.9, 5.6, 3.1 Hz, 1H), 2.31 (s, 4H), 2.29 – 2.25 (m, 1H), 2.21 (dd, *J* = 2.9, 0.9 Hz, 2H), 2.06 (dd, *J* = 17.3, 4.8 Hz, 1H), 1.69 (s, 3H), 1.65 (s, 3H) ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.9, 140.6, 136.4, 129.6, 127.6, 125.9, 123.5, 52.3, 41.2, 39.9, 31.3, 21.2, 18.9. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{16}H_{21}O$ 229.1587; found 229.1588.

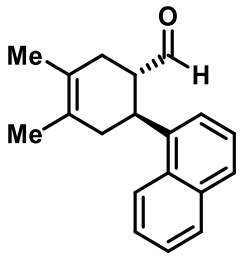


(1*S*,6*S*)-6-(Furan-2-yl)-3,4-dimethylcyclohex-3-en-1-carbaldehyde (1g): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and *E*-3-(Furan-2-yl)acrylaldehyde (12.21 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (24.6 mg, 40% yield), which was found to give spectral data matching that reported in the literature.[9] The *trans*/*cis d.r.* was determined from the crude NMR to be 71:29, while the %*ee* of the major isomer was determined to be 70% by reduction of the aldehyde and conversion to

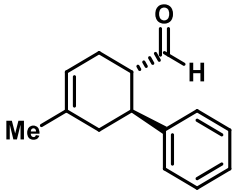
the Mosher ester.[10] R_f = 0.52 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.57 (d, *J* = 2.7 Hz, 1H), 7.31 (dd, *J* = 1.8, 0.8 Hz, 1H), 6.28 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.03 (d, *J* = 3.2 Hz, 1H), 3.24 (dt, *J* = 9.5, 7.4 Hz, 1H), 2.79 – 2.72 (m, 1H), 2.30 – 2.22 (m, 3H), 2.04 (dd, *J* = 16.8, 4.6 Hz, 1H), 1.66 (s,3H),1.64 (s,3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.1, 156.8, 141.5, 124.80, 123.3, 110.3, 105.4, 50.7, 35.7, 34.4, 30.5, 18.9,18.9. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{13}H_{17}O_2$ 205.1223; found 205.1223.



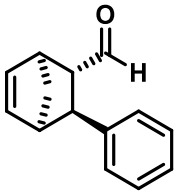
(1*S*,6*S*)-6-(5-Bromothiophen-2-yl)-3,4-dimethylcyclohex-3-en-1-carbaldehyde (1h): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and **S-1** (21.80 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (23 mg, 25% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 74:26, while the %*ee* of the major isomer was determined to be 34% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.57 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.57 (d, *J* = 2.3 Hz, 1H), 7.06 (d, *J* = 1.4 Hz, 1H), 6.75 – 6.74 (m, 1H), 3.45 (td, *J* = 8.5, 5.8 Hz, 1H), 2.69 (tdd, *J* = 8.3, 6.0, 2.3 Hz, 1H), 2.38 – 2.10 (m, 4H), 1.68 (s, 3H), 1.64 (s, 3H).. ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.5, 148.8, 127.0, 124.9, 123.8, 121.1, 109.3, 52.8, 38.9, 36.1, 30.5, 19.0, 18.9. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{13}H_{16}BrOS$ 299.0100; found 298.9962.



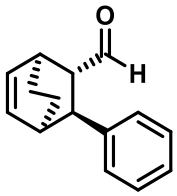
(1*S*,6*S*)-3,4-Dimethyl-6-(naphthalene-1-yl)cyclohex-3-ene-1-carbaldehyde (1i): Reaction was setup in triplicate. 2,3-Dimethylbutadiene (32.9 mg, 0.4 mmol) and ***S*-2** (18.22 mg, mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (13.7 mg, 17% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 83:17, while the %*ee* of the major isomer was determined to be 15% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.53 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.49 (d, *J* = 2.9 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.87 (d, *J* = 8.7 Hz, 1H), 7.73 (d, *J* = 8.2 Hz, 1H), 7.53 (ddd, *J* = 8.4, 6.8, 1.4 Hz, 1H), 7.51 – 7.47 (m, 1H), 7.46 – 7.42 (m, 1H), 7.35 (d, *J* = 7.0 Hz, 1H), 4.05 (d, *J* = 6.3 Hz, 1H), 3.02 (d, *J* = 8.1 Hz, 1H), 2.49 (dd, *J* = 17.5, 4.5 Hz, 1H), 2.36 (dd, *J* = 17.2, 8.4 Hz, 1H), 2.24 (d, *J* = 14.6 Hz, 1H), 2.12 (dd, *J* = 17.2, 3.8 Hz, 1H), 1.74 (s, 3H), 1.69 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.6, 139.8, 134.1, 131.5, 129.3, 127.3, 126.4, 125.9, 125.7, 123.6, 122.9, 51.6, 38.7, 31.2. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{19}H_{21}O$ 265.1587; found 265.1588.



(1*S*,2*S*)-5-Methyl-1,2,3,6-(tetrahydro-[1,1'-biphenyl]-2-carbaldehyde (2a): Reaction was setup in triplicate. Isoprene (27.29 mg, 0.4 mmol) and (*E*)-cinnamaldehyde (13.2 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (50.6 mg, 84% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 88:12, while the %*ee* of the major isomer was determined to be 80% by reduction of the aldehyde and conversion to the Mosher ester.[10] R_f = 0.57 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.48 (d, *J* = 2.9 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.24 – 7.20 (m, 3H), 5.49 (dd, *J* = 2.7, 1.5 Hz, 1H), 3.15 (td, *J* = 9.4, 5.9 Hz, 1H), 2.78 – 2.71 (m, 1H), 2.36 – 2.13 (m, 4H), 1.71 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.8, 143.7, 134.3, 128.9, 127.6, 126.9, 118.7, 51.4, 41.1, 37.7, 25.1, 23.4. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{14}H_{17}O$ 201.1274; found 201.1274.

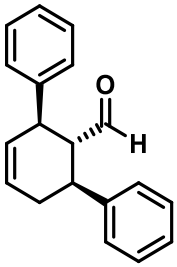


(1*S*,2*S*,3*S*,4*R*)-5-Methyl-3-phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde (2b): Reaction was setup in triplicate. ***S*-5** (26.5 mg, 0.4 mmol) and (*E*)-cinnamaldehyde (13.2 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (53.7 mg, 90% yield). The *trans*/*cis d.r.* with respect to the aldehyde and phenyl group was determined from the crude NMR to be >20:1, while the %*ee* of the major isomer was determined to be 70% by reduction of the aldehyde and conversion to the Mosher ester.[10] The *endo*/*exo* ratio was determined to be 31:69 from the crude NMR. R_f = 0.53 (Hexane: Ethyl acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.92 (d, *J* = 2.1 Hz, 1H), 7.14-7.26 (m, 5H), 6.34 (dd, *J* = 5.5, 3.4 Hz, 1H), 6.07 (dd, *J* = 5.5, 3.1 Hz, 1H), 3.72 (dd, *J* = 5.1, 3.4 Hz, 1H), 3.24 – 3.20 (m, 2H), 2.60 (m, 1H), 1.63 – 1.54 (m, 2H).. ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.0, 142.7, 136.7, 136.5, 128.3, 128.1, 126.5, 59.6, 48.6, 47.8, 45.7, 45.6. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{14}H_{15}O$ 199.1117; found 199.1118.

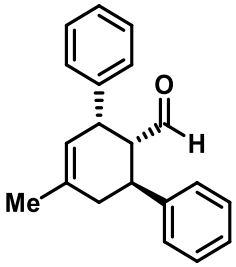


(1*S*,2*S*,3*S*,4*R*)-3-phenylbicyclo[2.2.1]oct-5-ene-2-carbaldehyde (2c): Reaction was setup in quintuplicate. Cyclohexa-1,3-diene (32.1 mg, 0.4 mmol) and (*E*)-cinnamaldehyde (13.2 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (37.0 mg, 58 % yield). The *trans*/*cis d.r.* with respect to the aldehyde and phenyl group was determined from the crude NMR to be >20:1, while the %*ee* of the major isomer was determined to be 87% by reduction of the aldehyde and conversion to the Mosher ester.[10] The *endo*/*exo* ratio was determined to be 35:65 from the crude NMR. R_f = 0.50 (Hexane: Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ

9.85 (s, 1H), 7.32 – 7.29 (m, 3H), 7.27 – 7.21 (m, 3H), 6.57 – 6.53 (m, 1H), 6.47 – 6.43 (m, 1H), 3.47 (dd, *J* = 6.6, 1.3 Hz, 1H), 3.17 (ddtd, *J* = 6.7, 3.4, 2.3, 1.3 Hz, 1H), 2.81 (ddd, *J* = 4.7, 2.2, 0.9 Hz, 1H), 2.66 – 2.63 (m, 1H), 1.78 – 1.72 (m, 1H), 1.60 – 1.54 (m, 1H), 1.39 (tdd, *J* = 12.1, 4.4, 3.1 Hz, 1H), 1.33 – 1.29 (m, 1H).. ^{13}C NMR (151 MHz, $CDCl_3$) δ 203.1, 146.3, 134.7, 133.7, 128.5, 127.7, 126.4, 60.8, 43.0, 36.8, 31.2, 26.8, 20.3. HRMS (ESI - MS): $[M+Na]^+$ Calculated for $C_{15}H_{16}NaO$ 235.1093; found 235.1083.



(1*R*,2'*R*,3'*S*)-1',2',3',4'-Tetrahydro-1[1,1':3',1"-terphenyl]-2'-carbaldehyde (2d): Reaction was setup in triplicate. ***S*-6** (52 mg, 0.4mmol) and (*E*)-cinnamaldehyde (13.2 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (27.8 mg, 35% yield). The *trans*/*cis d.r.* was determined from the crude NMR to be 95:5, while the %*ee* of the major isomer was determined to be 72% by reduction of the aldehyde and conversion to the Mosher ester.[10] The *endo*/*exo* ratio was determined to be 10:90 from the crude NMR. R_f = 0.47 (Hexane:Ethyl Acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.36 (d, *J* = 3.4 Hz, 1H), 7.32 – 7.28 (m, 5H), 7.25 – 7.20 (m, 5H), 5.95 (ddt, *J* = 7.4, 5.3, 2.7 Hz, 1H), 5.76 – 5.72 (m, 1H), 3.91 – 3.87 (m, 1H), 3.18 (ddd, *J* = 11.6, 9.9, 6.7 Hz, 1H), 3.08 (ddd, *J* = 11.7, 10.2, 3.4 Hz, 1H), 2.45 – 2.41 (m, 2H. ^{13}C NMR (151 MHz, $CDCl_3$) δ 204.3, 143.0, 142.5, 130.0, 129.9, 129.1, 128.9, 128.4, 127.7, 127.2, 127.1, 126.8, 59.6, 44.0, 43.0, 34.40. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{19}H_{19}O$ 263.1430; found 263.1466.

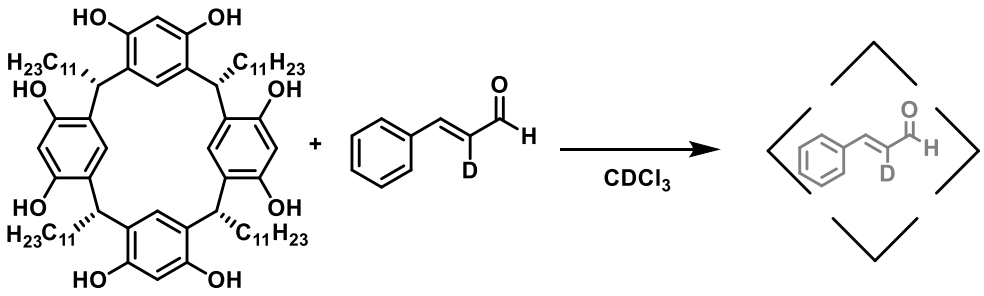


(1*S*,2'*R*,3'*S*)-5'-Methyl-1',2',3',4'-tetrahydro-1[1,1':3',1"-terphenyl]-2'-carbaldehyde (2e): Reaction was setup in triplicate. ***S*-7** (58 mg, 0.4 mmol) and (*E*)-cinnamaldehyde (13.2 mg, 0.1 mmol) were used. Reaction time was 120 h. Product was recovered as a colorless oil (74.3 mg, 94% yield). The *trans*/*cis d.r.* with respect to the aldehyde and phenyl group was determined from the crude NMR to be >20:1, while the %*ee* of the minor diastereomer was determined to be 90% by reduction of the aldehyde and conversion to the Mosher ester.[10] The *endo*/*exo* ratio was determined to be 56:44 from the crude NMR. R_f = 0.53 (Hexane:Ethyl acetate, 9:1). ^{1}H NMR (600 MHz, $CDCl_3$) (mixture of isomers) δ 9.39 (d, *J* = 3.6 Hz, 1H), 8.96 (d, *J* = 4.3 Hz, 1H), 7.45 – 7.01 (m, 20H), 5.65 – 5.61 (m, 1H), 5.46 (s, 1H), 3.90 – 3.83 (m, 2H), 3.49 – 3.40 (m, 1H), 3.22 (td, *J* = 11.6, 5.4 Hz, 1H), 3.02 (ddd, *J* = 11.7, 10.3, 3.6 Hz, 1H), 2.95 (ddd, *J* = 10.4, 6.0, 4.3 Hz, 1H), 2.48 (dd, *J* = 18.2, 5.8 Hz, 1H), 2.44 – 2.37 (m, 1H), 2.31 (dd, *J* = 17.6, 5.3 Hz, 1H), 2.25 (ddd, *J* = 18.1, 9.1, 1.0 Hz, 1H), 1.88 (s, 4H), 1.80 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 206.5,

204.6, 143.5, 143.4, 142.6, 139.8, 135.6, 134.1, 129.8, 129.0, 128.9, 128.8, 128.6, 128.3, 127.9, 127.7, 127.2, 127.2, 127.0, 124.1, 122.4, 59.5, 55.3, 44.4, 43.3, 42.7, 39.3, 37.7, 36.9, 23.5, 23.3. HRMS (ESI - MS): $[M+H]^+$ Calculated for $C_{20}H_{21}O$ 277.1587; found 277.1553.

4. NMR, Kinetic, and Scale-Up Studies

A) Simple NMR Guest Binding Studies (Cinnamaldehyde-2-*d*)



Resorcin[4]arene **A** (16.0 mg, 0.0024 mmol) was combined with **S-*12*** (41.0 mg, 0.31 mmol) in $CHCl_3$ (700 μL) in a 5 mm NMR tube with $CDCl_3$ (70 μL) added. The mixture was analyzed by ^1H and ^2H NMR.

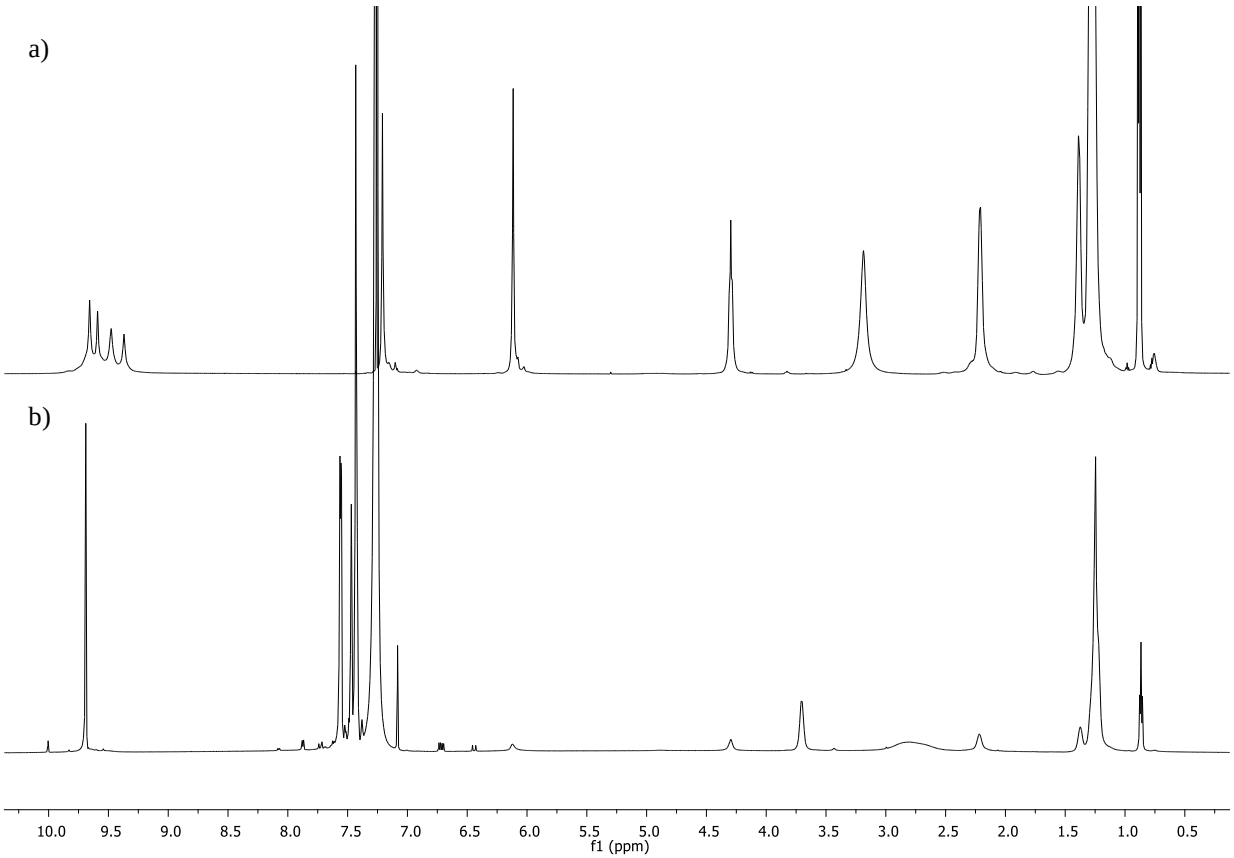
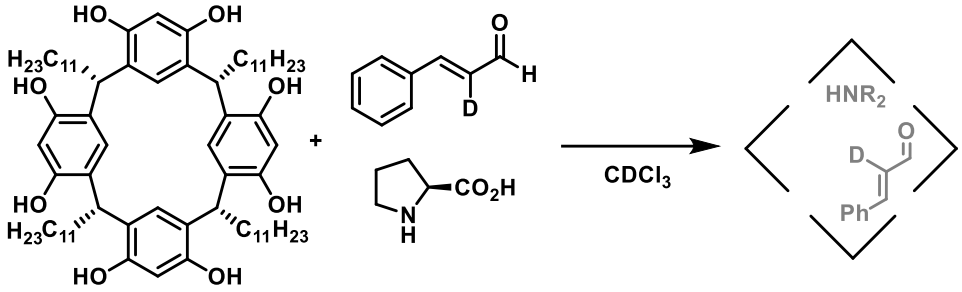


Figure S1. ^1H NMR spectrum of a) **A** and b) **A** + Cinnamaldehyde-2-*d* ($CDCl_3$, 600 MHz, 298 K)

B) Simple NMR Guest Binding Studies (Cinnamaldehyde-2-*d* + L-Proline)



Resorcin[4]arene **A** (16.0 mg, 0.0024 mmol) was combined with **S-*12*** (41.0 mg, 0.31 mmol) in $CHCl_3$ (700 μL) in a 5 mm NMR tube with $CDCl_3$ (70 μL) added, followed by *L*-proline (10 mg, 0.086 mmol), which was observed to settle on the bottom of the NMR tube rather than dissolving. The mixture was analyzed by ^1H and ^2H NMR.

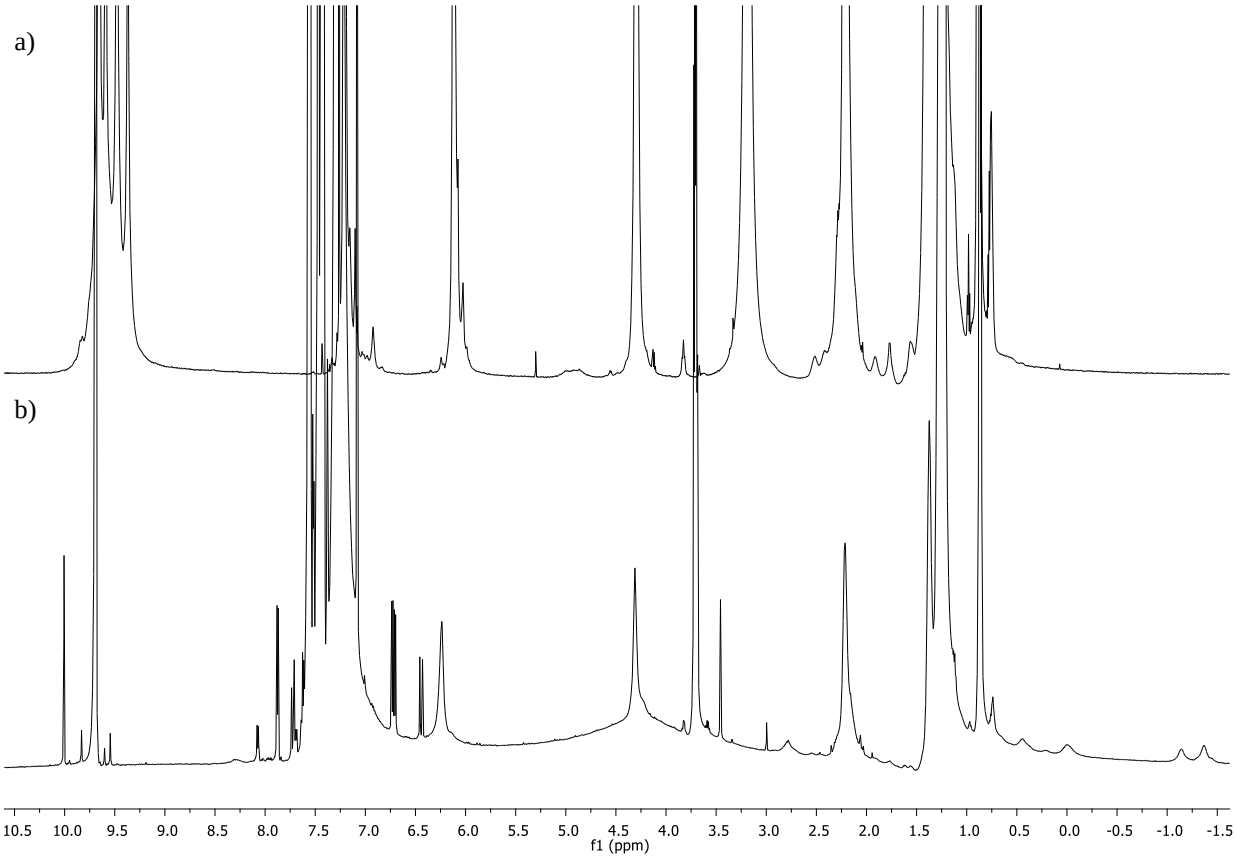
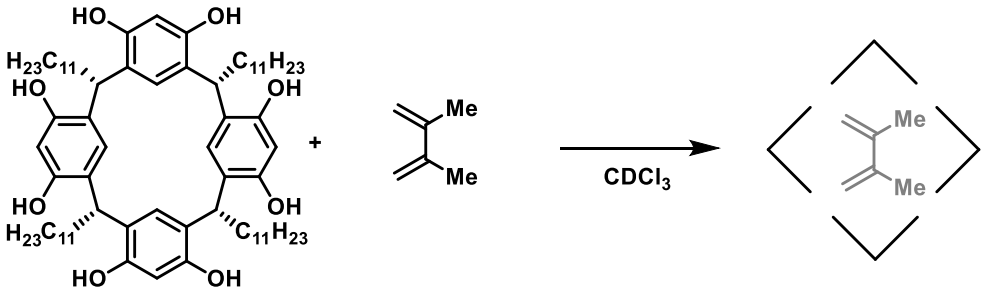


Figure S*2.** ^1H NMR spectrum of a) **A** and b) **A** + **S-*11 ($CDCl_3$, 600 MHz, 298 K)

C) Simple NMR Guest Binding Studies (Diene)



Resorcin[4]arene **A** (16.0 mg, 0.0024 mmol) was combined with 2,3-dimethylbutadiene (32.0 mg, 0.39 mmol) in $CDCl_3$ (700 μL) in a 5 mm NMR tube. The mixture was analyzed by ^1H NMR.

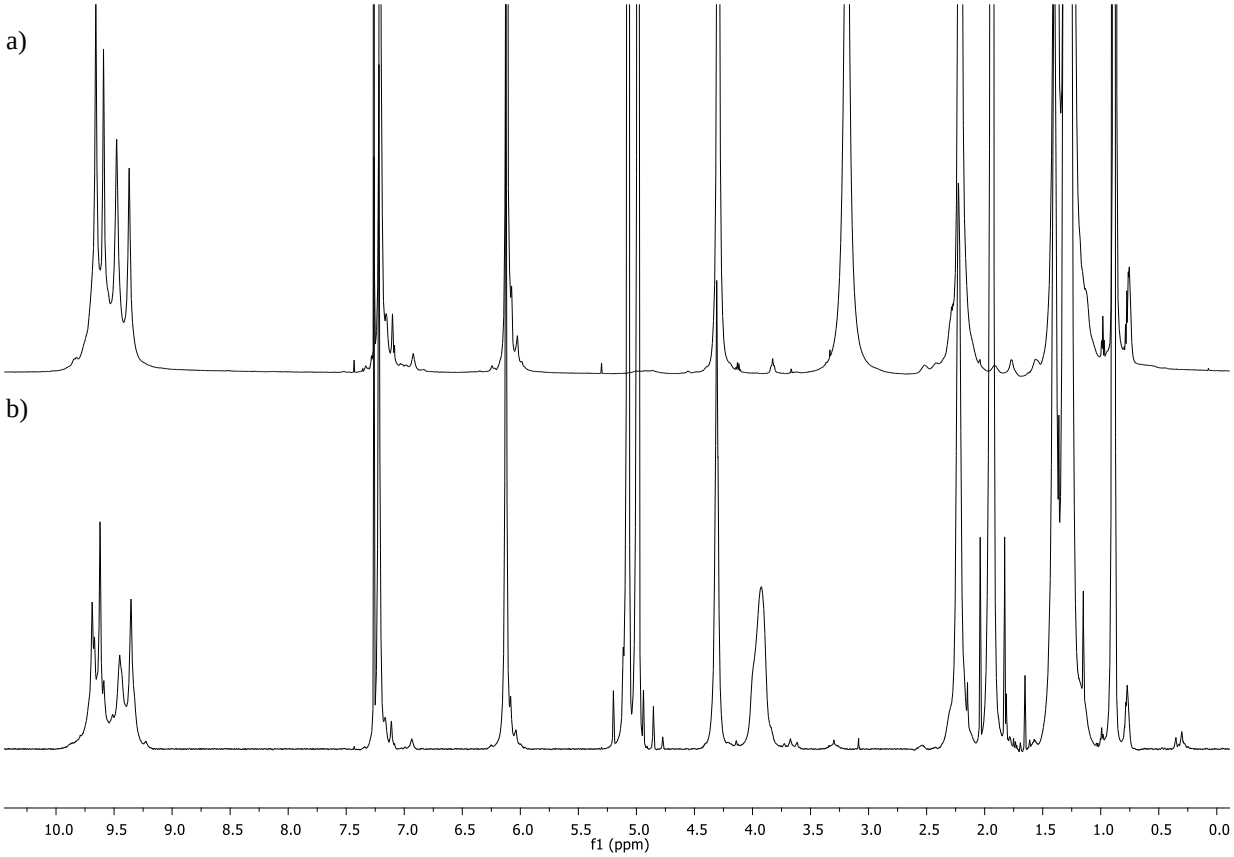
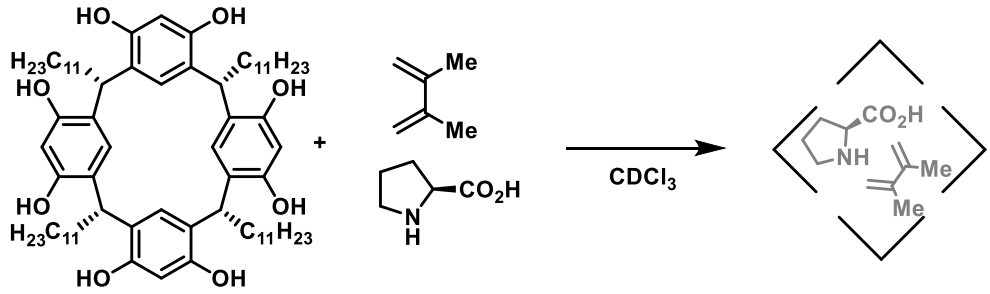


Figure S3. ^1H NMR spectrum of a) **A** and b) **A** + 2,3-Dimethylbutadiene ($CDCl_3$, 600 MHz, 298 K)

D) Simple NMR Guest Binding Studies (Diene + L-Proline)



Resorcin[4]arene **A** (16.0 mg, 0.0024 mmol) was combined with 2,3-dimethylbutadiene (32.0 mg, 0.39 mmol) and then L-proline (2.3 mg, 0.002 mmol) in $CDCl_3$ (700 μL) in a 5 mm NMR tube. The mixture was analyzed by ^{1}H NMR.

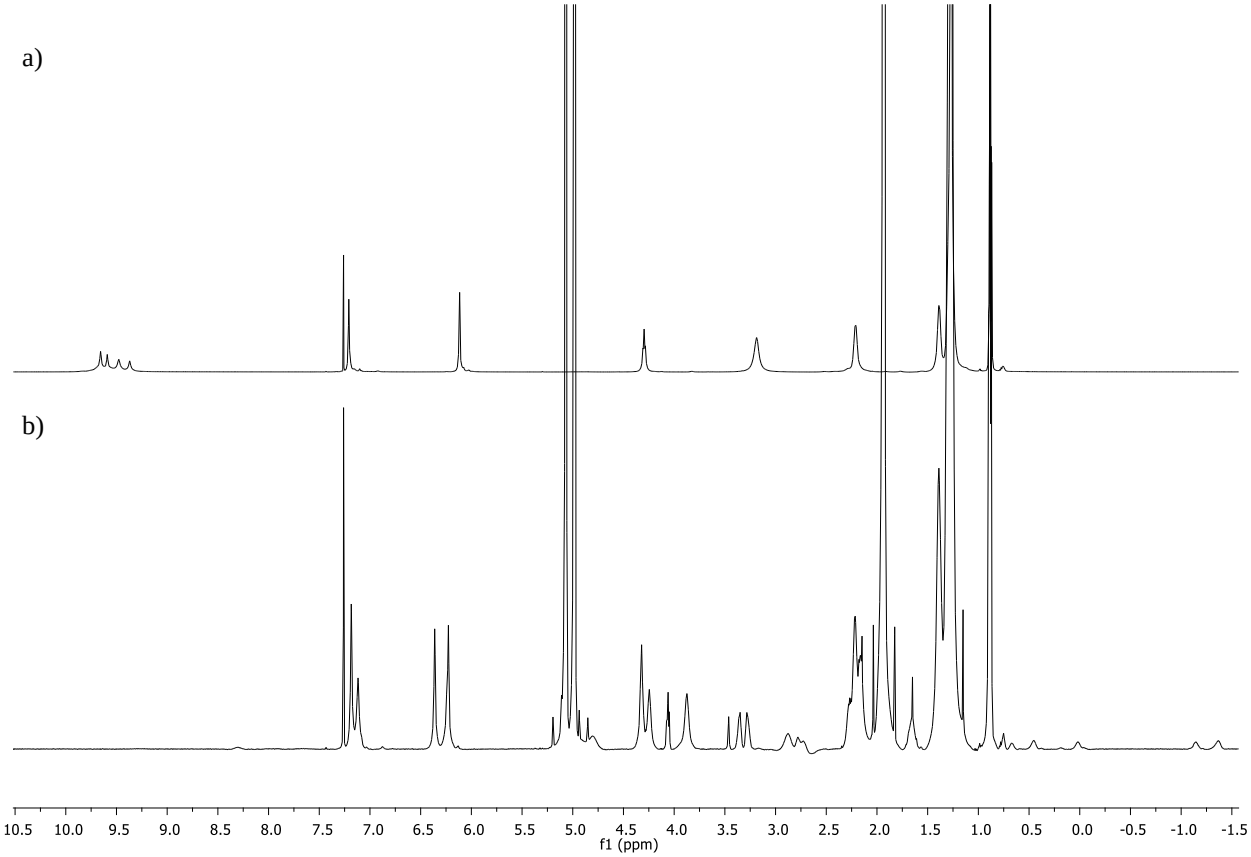
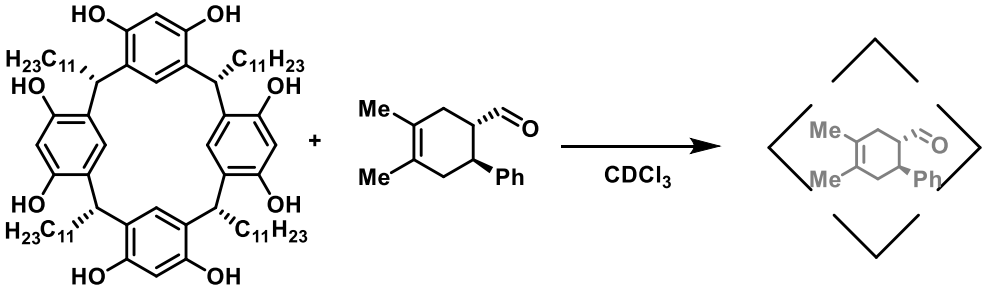


Figure S4. ^{1}H NMR spectrum of a) **A** and b) **A** + 2,3-Dimethylbutadiene + L-Proline ($CDCl_3$, 600 MHz, 298 K)

E) Simple NMR Guest Binding Studies (Product)



Resorcin[4]arene **A** (16.0 mg, 0.0024 mmol) was combined with **1a** (12.0 mg, 0.056 mmol) in $CDCl_3$ (700 μL) in a 5 mm NMR tube. The mixture was analyzed by ^1H NMR.

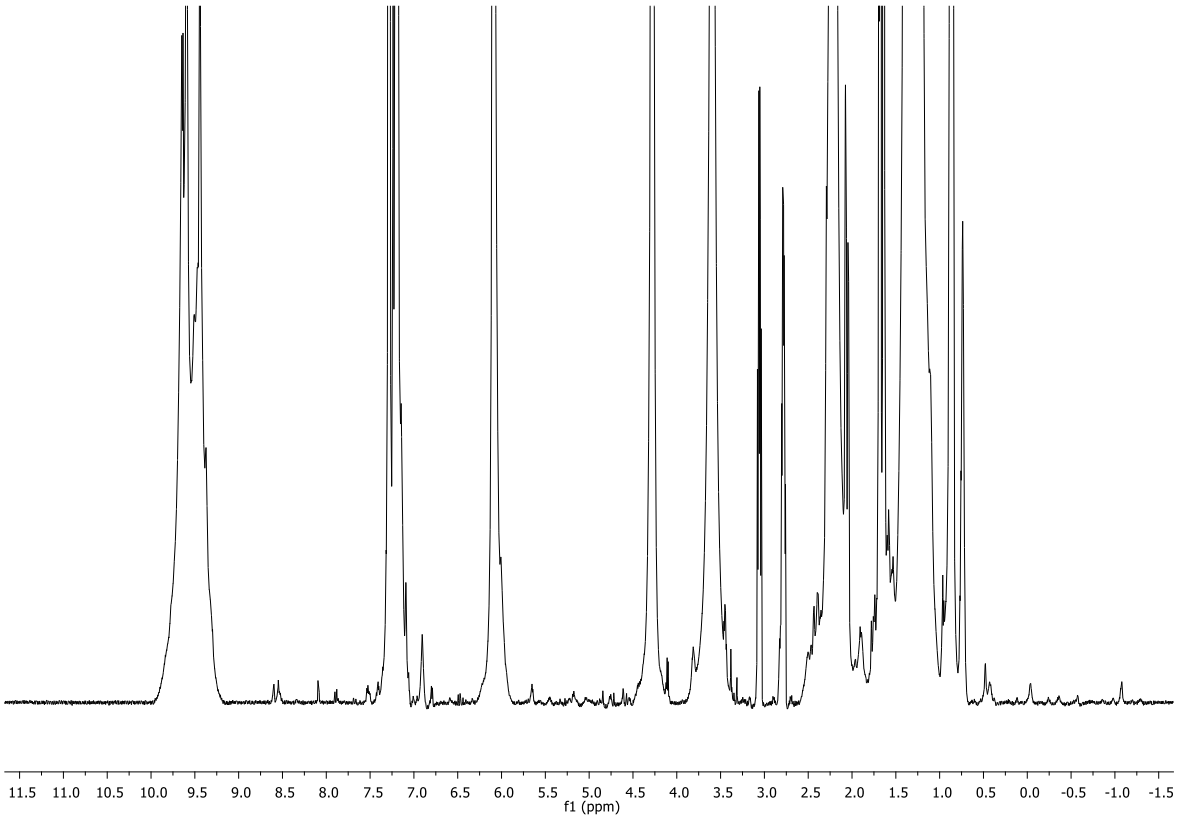
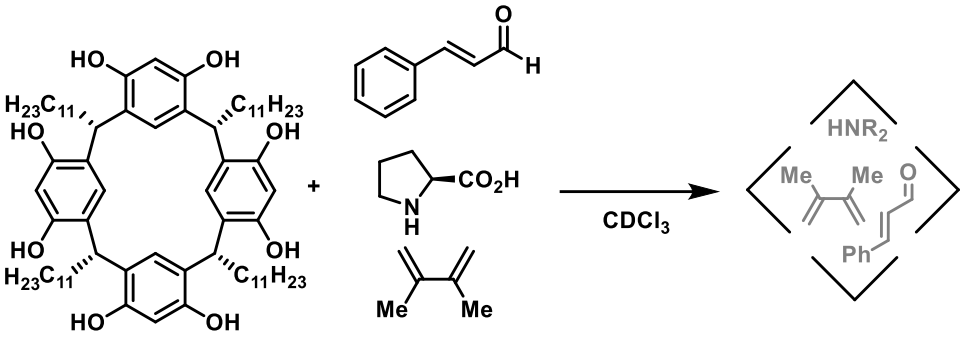


Figure S*5.** ^1H NMR spectrum of **A** + **S-*12 ($CDCl_3$, 600 MHz, 298 K)

F) NMR Guest Binding Studies (NOESY)



Resorcin[4]arene **A** (10.0 mg, 0.0015 mmol) was combined with *E*-cinnamadlehyde (2.0 mg, 0.015 mmol), 2,3-dimethylbutadiene (2.0 mg, 0.024 mmol), and *L*-proline (2.0 mg, 0.017 mmol) in $CDCl_3$ (700 µL) in a 5 mm NMR tube. The mixture was analyzed by NOESY NMR.

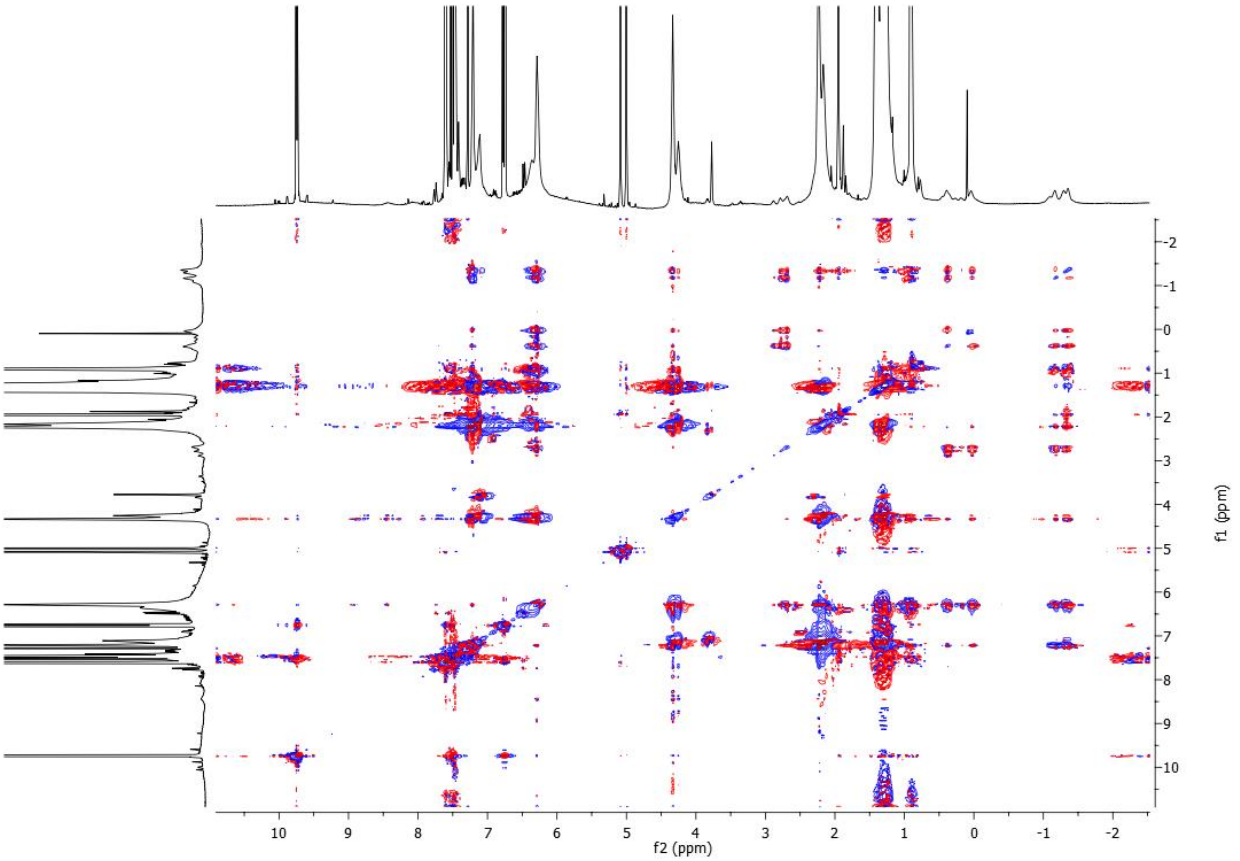
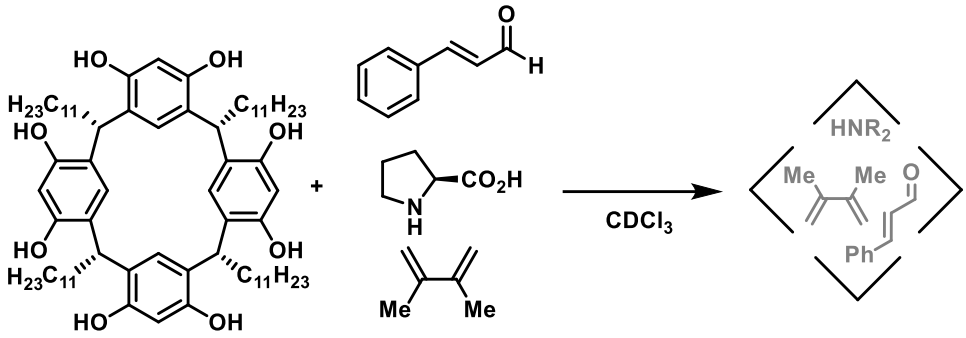


Figure S6. NOESY NMR spectrum of reaction mixture (**A** + cinnamaldehyde + L-proline + 2,3-dimethylbutadiene) ($CDCl_3$, 600 MHz, 298 K)

G) NMR Guest Binding Studies (DOSY)



Resorcin[4]arene **A** (10.0 mg, 0.0015 mmol) was combined with *E*-cinnamadlehyde (2.0 mg, 0.015 mmol), 2,3-dimethylbutadiene (2.0 mg, 0.024 mmol), and *L*-proline (2.0 mg, 0.017 mmol) in $CDCl_3$ (700 µL) in a 5 mm NMR tube. The mixture was analyzed by DOSY (1edbpgp2s) using diffusion delay of 150 ms, gradient pulse of 1400 ms, and a recover delay of 0.2 ms.

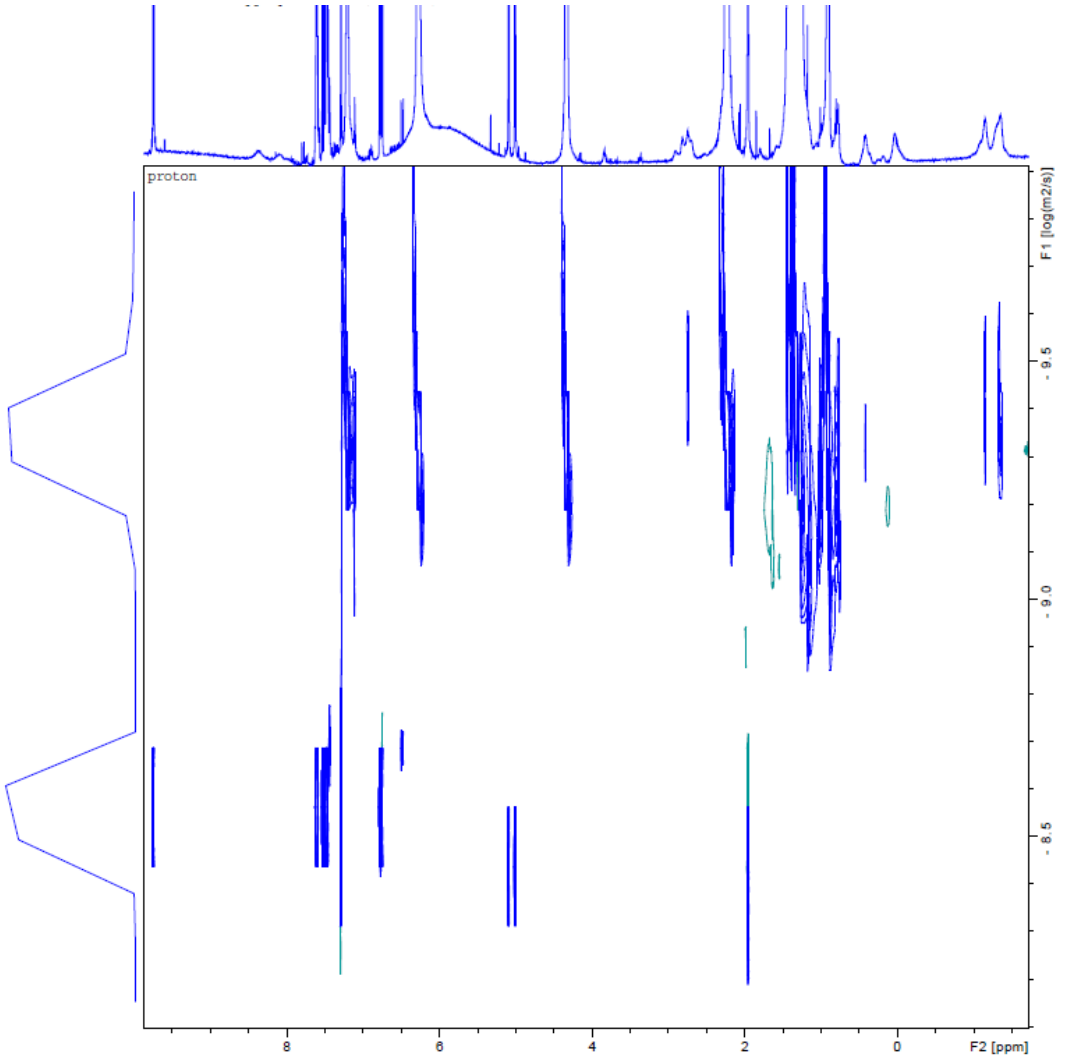
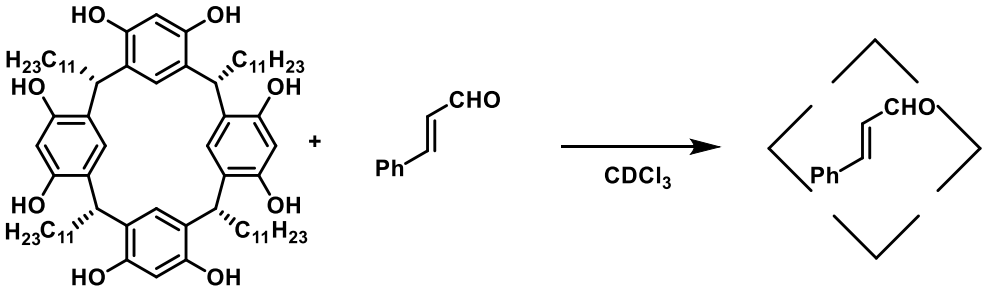


Figure S7. DOSY NMR spectrum of reaction mixture (**A** + cinnamaldehyde + L-proline + 2,3-dimethylbutadiene) ($CDCl_3$, 600 MHz, 298 K)

H) Titration NMR Guest Binding Studies (Cinnamaldehyde)



Resorcin[4]arene **A** (16.0 mg, 0.0024 mmol) in $CDCl_3$ (700 µL) in a 5 mm NMR tube was titrated with cinnamaldehyde. The mixture was analyzed by ^{1}H NMR, with minor peaks observed in the ^{1}H NMR spectrum between 5.5 and 8.5 ppm, but none further upfield. These are expected to be a mixture of encapsulated cinnamaldehyde resonances as well as from the encapsulating hexamer.

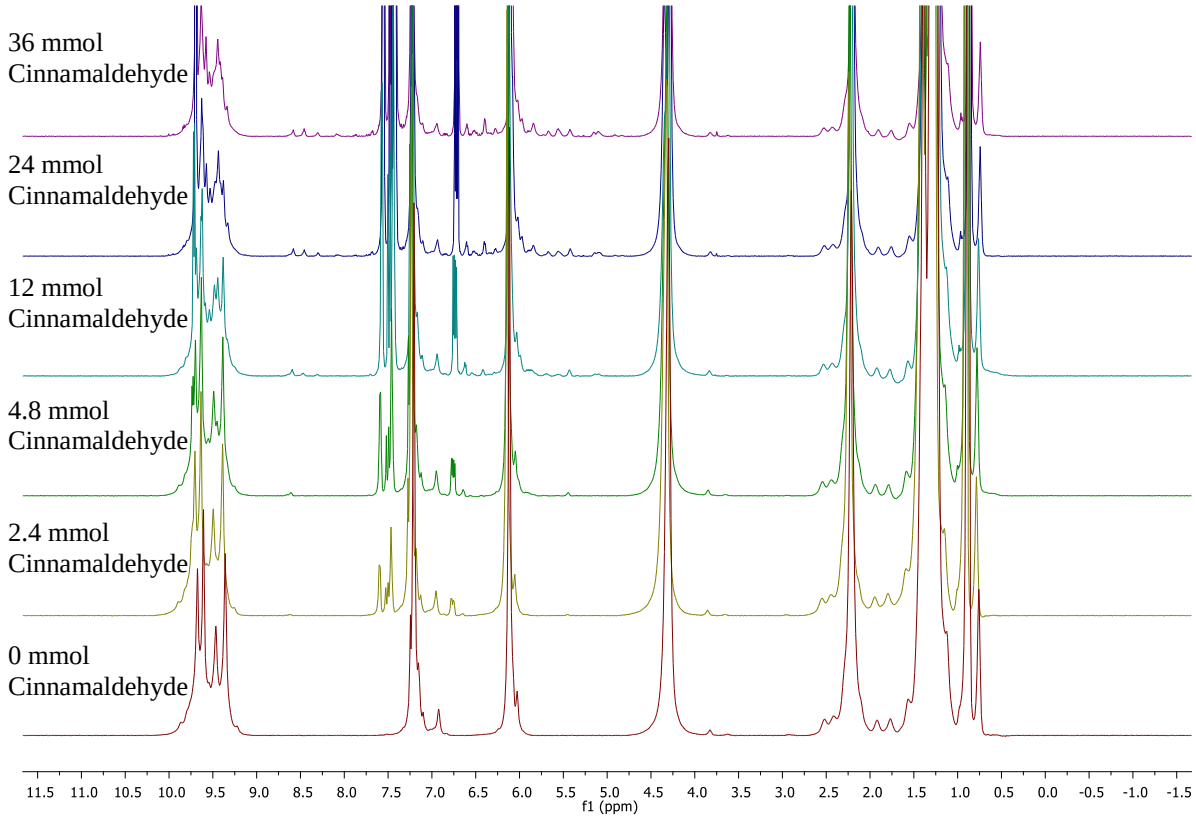
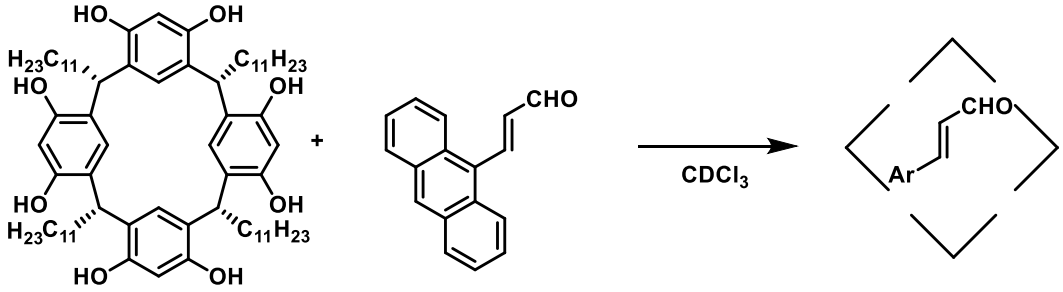


Figure S8. ^{1}H NMR spectra of **A** titrated with cinnamaldehyde ($CDCl_3$, 600 MHz, 298 K)

I) Titration NMR Guest Binding Studies (Cinnamaldehyde)



Resorcin[4]arene **A** (23 mg, 0.0034 mmol) in $CDCl_3$ (700 µL) in a 5 mm NMR tube was treated with (*E*)-3-(anthracen-1-yl)acrylaldehyde (6.0 mg, 0.026 mmol). The mixture was analyzed by ^{1}H NMR, with minor peaks observed in the ^{1}H NMR spectrum at 9.27 ppm and 6.73 ppm which would be consistent with an upfield shift due to shielding of the encapsulated aldehyde.

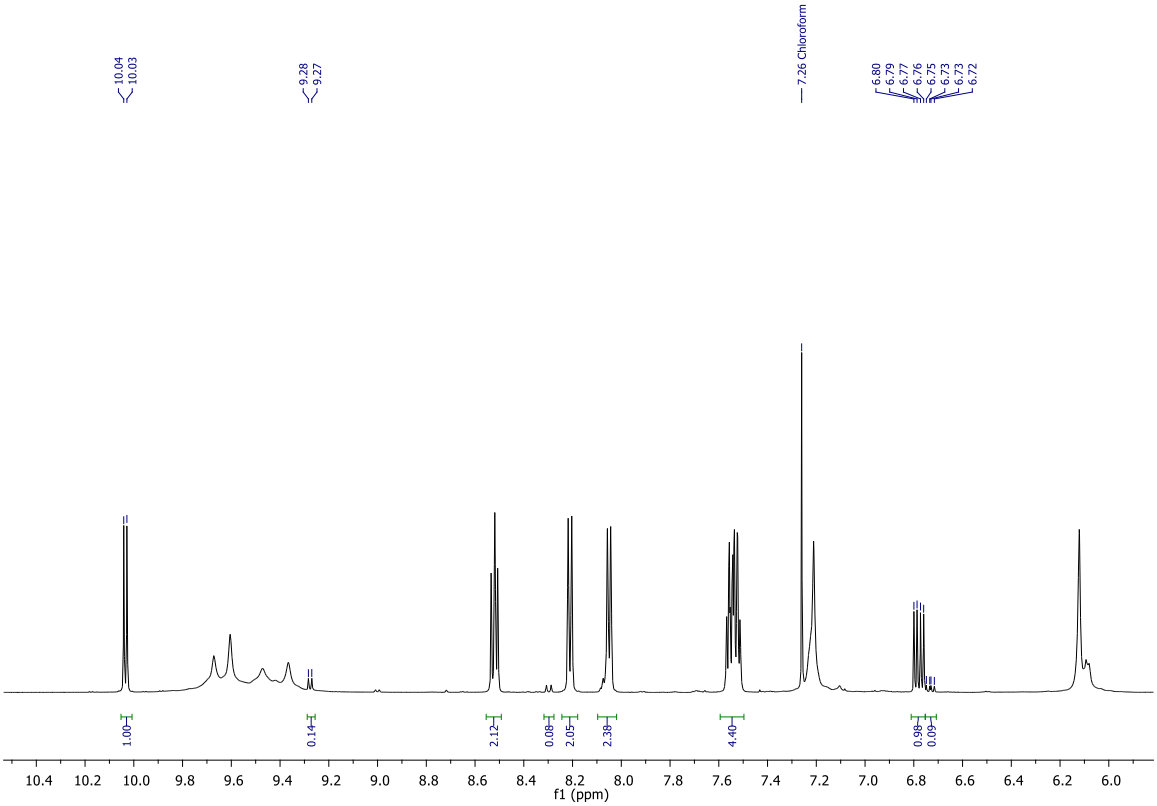
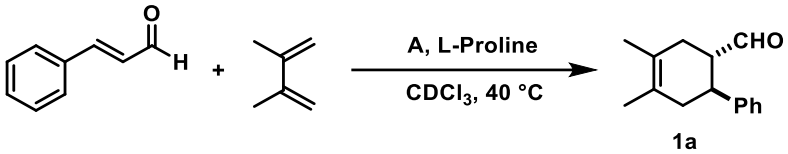


Figure S9. ^{1}H NMR spectrum of **A** with (*E*)-3-(anthracen-1-yl)acrylaldehyde ($CDCl_3$, 600 MHz, 298 K)

J) Procedure for Kinetics by NMR (Diene)



Resorcin[4]arene **A** (135 mg, 0.02 mmol) was combined with cinnamaldehyde (13.2 mg, 0.1 mmol), 2,3-dimethylbutadiene (between 0.2 and 0.6 mmol), and *L*-proline (2.3 mg, 0.02 mmol) in $CDCl_3$ (1000 µL) in a 5 mm NMR tube, followed by addition of 1,2-dichloroethane as a standard (performed in triplicate). Reactions were heated, cooled, then immediately analyzed by ^1H NMR at intervals, followed by continued heating/analysis.

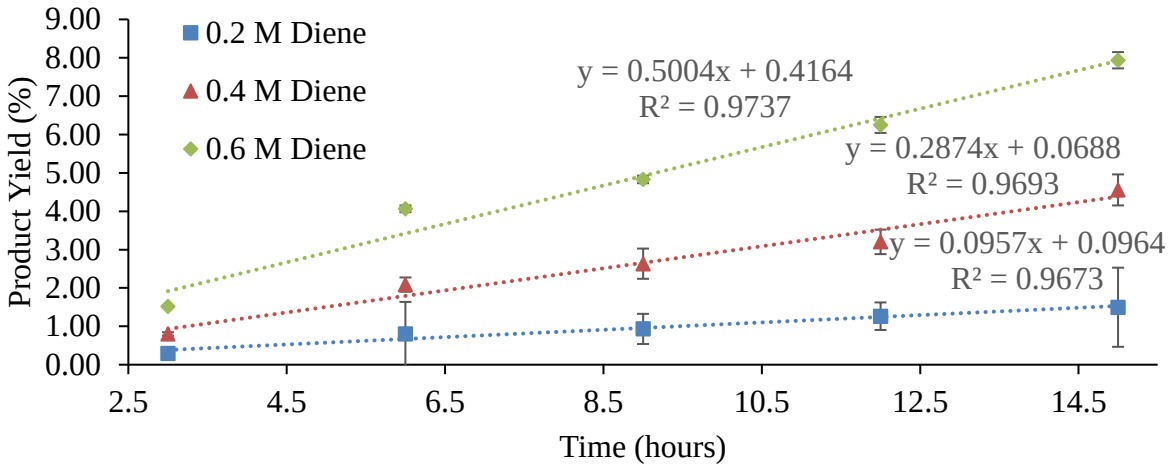
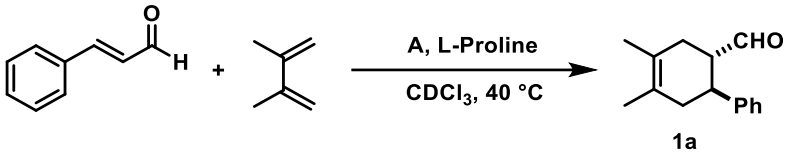


Figure S10. Reaction Kinetics Based on Diene Concentration Determined by ^1H NMR (1,2-Dichloroethane as internal standard).

K) Procedure for Kinetics by NMR (Cinnamaldehyde)



1a

Resorcin[4]arene **A** (135 mg, 0.02 mmol) was combined with cinnamaldehyde (between 0.05 and 0.2 mmol), 2,3-dimethylbutadiene (32.9 mg, 0.4 mmol), and *L*-proline (2.3 mg, 0.02 mmol) in $CDCl_3$ (1000 µL) in a 5 mm NMR tube, followed by addition of 1,2-dichloroethane as a standard (performed in triplicate). Reactions were heated, cooled, then immediate analyzed by ^{1}H NMR at intervals, followed by continued heating/analysis.

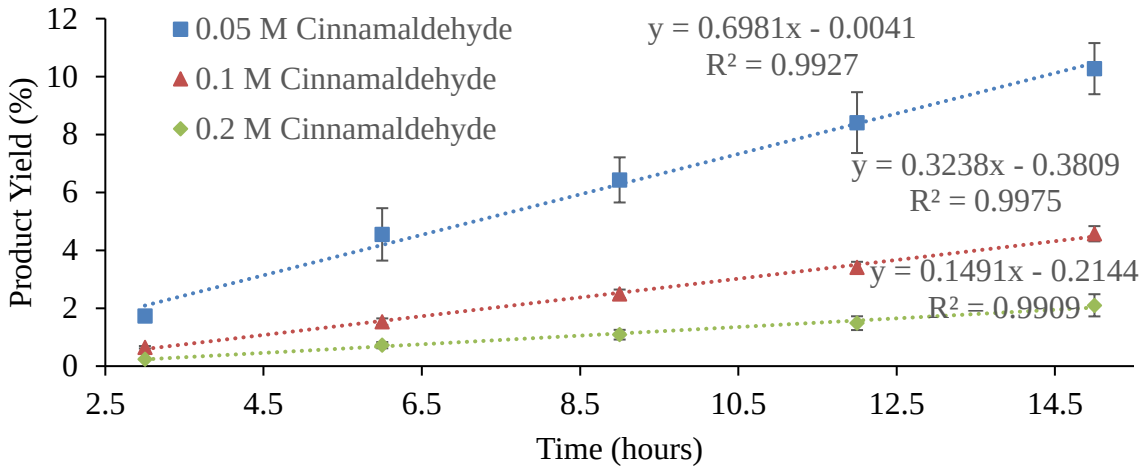
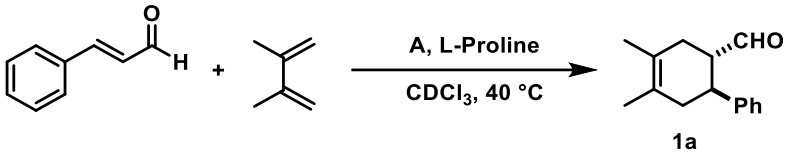


Figure S11. Reaction Kinetics Based on Cinnamaldehyde Concentration Determined by ^{1}H NMR (1,2-Dichloroethane as internal standard).

L) Procedure for Kinetics by NMR (Inhibition)



1a

Resorcin[4]arene **A** (135 mg, 0.02 mmol) was combined with cinnamaldehyde (13.2 mg, 0.1 mmol), 2,3-dimethylbutadiene (32.9 mg, 0.4 mmol), product **1a** (3.0 mg, 0.014 mmol), and *L*-proline (2.3 mg, 0.02 mmol) in $CDCl_3$ (1000 µL) in a 5 mm NMR tube, followed by addition of 1,2-dichloroethane as a standard (performed in triplicate). Reactions were heated, cooled, then immediately analyzed by ^1H NMR at intervals, followed by continued heating/analysis (reference was taken from the cinnamaldehyde kinetics using the same concentrations).

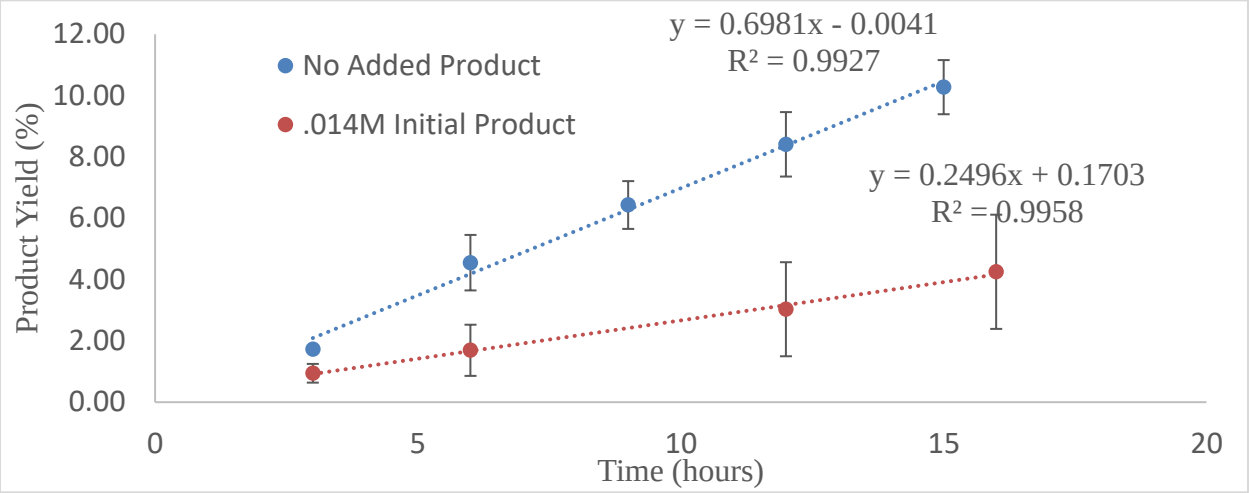


Figure S12. Reaction Kinetics Based on Product Concentration Determined by ^1H NMR (1,2-Dichloroethane as internal standard).

M) Procedure for Reaction Scale-Up and Catalyst Recovery

A 40 mL vial was charged with *L*-proline (23 mg, 0.2 mmol, 0.2 equiv.), hexamer **A** (1350 mg, 0.2 mmol, 0.2 equiv.), aldehyde (132 mg, 1 mmol, 1.0 equiv), 2,3-dimethylbutadiene (330 mg, 4 mmol, 4 equiv.) and $CDCl_3$ (10 mL). The vial was sealed with a PTFE lined cap and stirred at 40 ºC for 120 h in a pie-block. After 120 h of stirring, the reaction mixture was cooled to rt and 10 mL acetonitrile was added. The vial was cooled to -25 °C to complete the precipitation of the cage. The precipitate was removed by centrifugation. The supernatent was collected and the precipitate was washed with additional acetonitrile, followed by combining the solvent fractions and removal of solvent *in vacuo*. The crude reaction mixture was then purified by column chromatography (Hexane: Ethyl Acetate, 500:1) over silica to give product as colorless oil (176.4 mg, 82% yield).

The precipitate during the workup was collected, dried, and weighed, giving a recovery of 90% of the catalyst.

5. ^{1}H and ^{13}C Spectra of Compounds

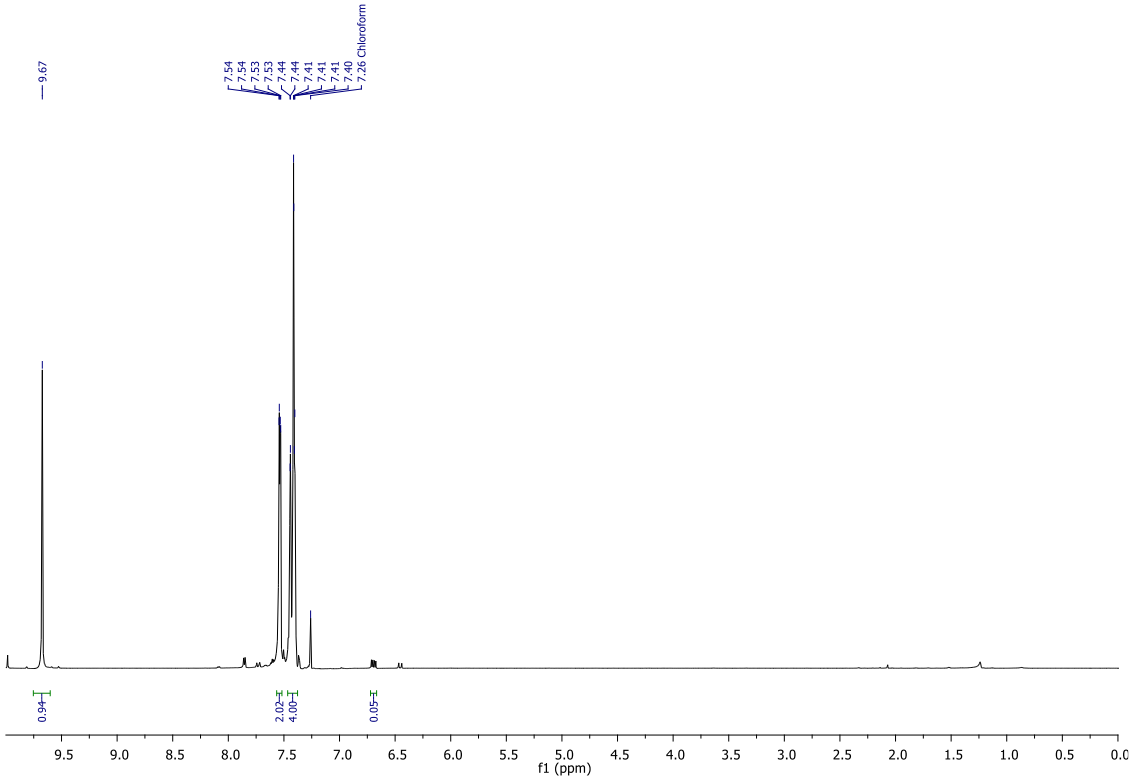


Figure S13. ^{1}H NMR spectrum of ***S*-11** ($CDCl_3$, 600 MHz, 298 K)

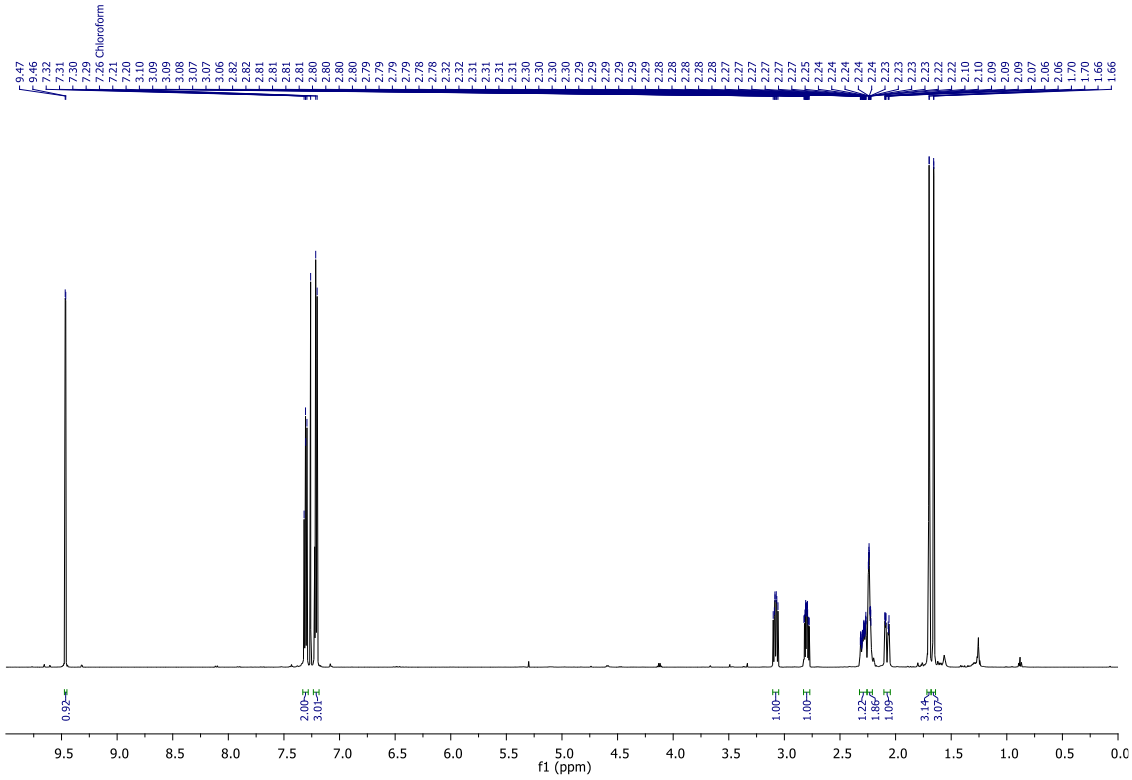


Figure S14. ^{1}H NMR spectrum of **1a** ($CDCl_3$, 600 MHz, 298 K)

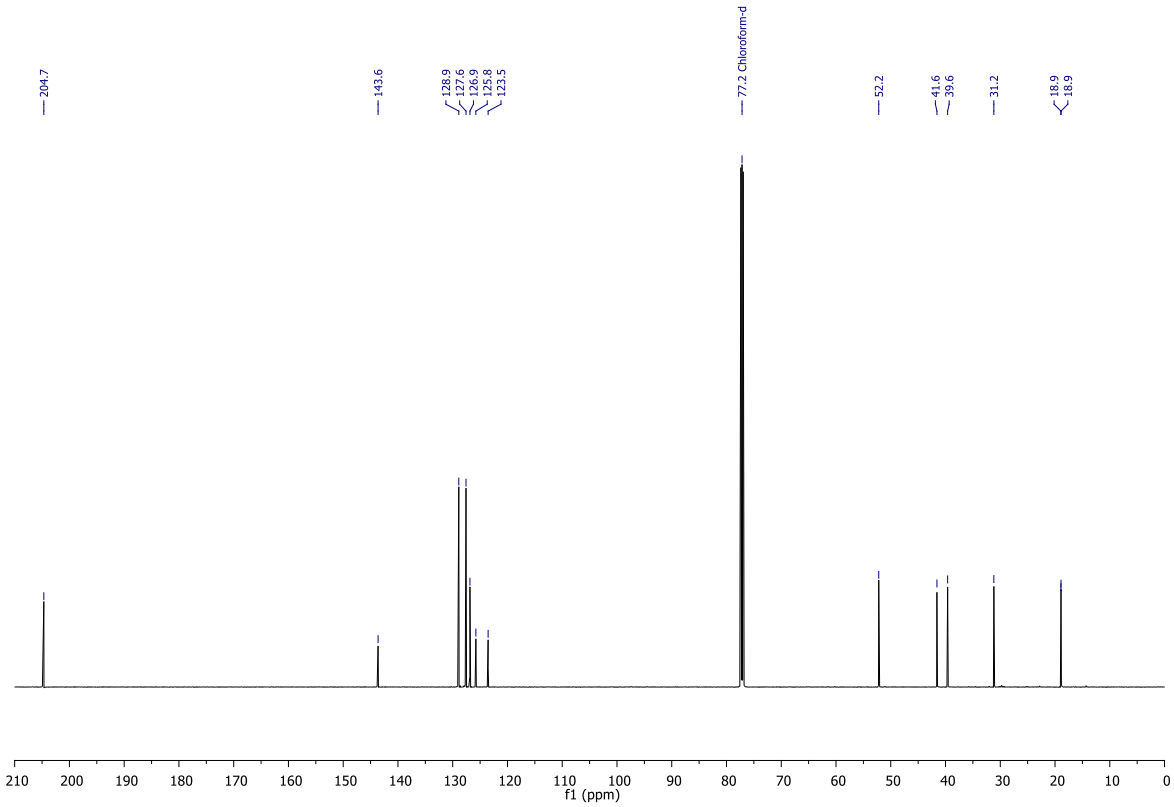


Figure S15. ^{13}C NMR spectrum of **1a** ($CDCl_3$, 151 MHz, 298 K)

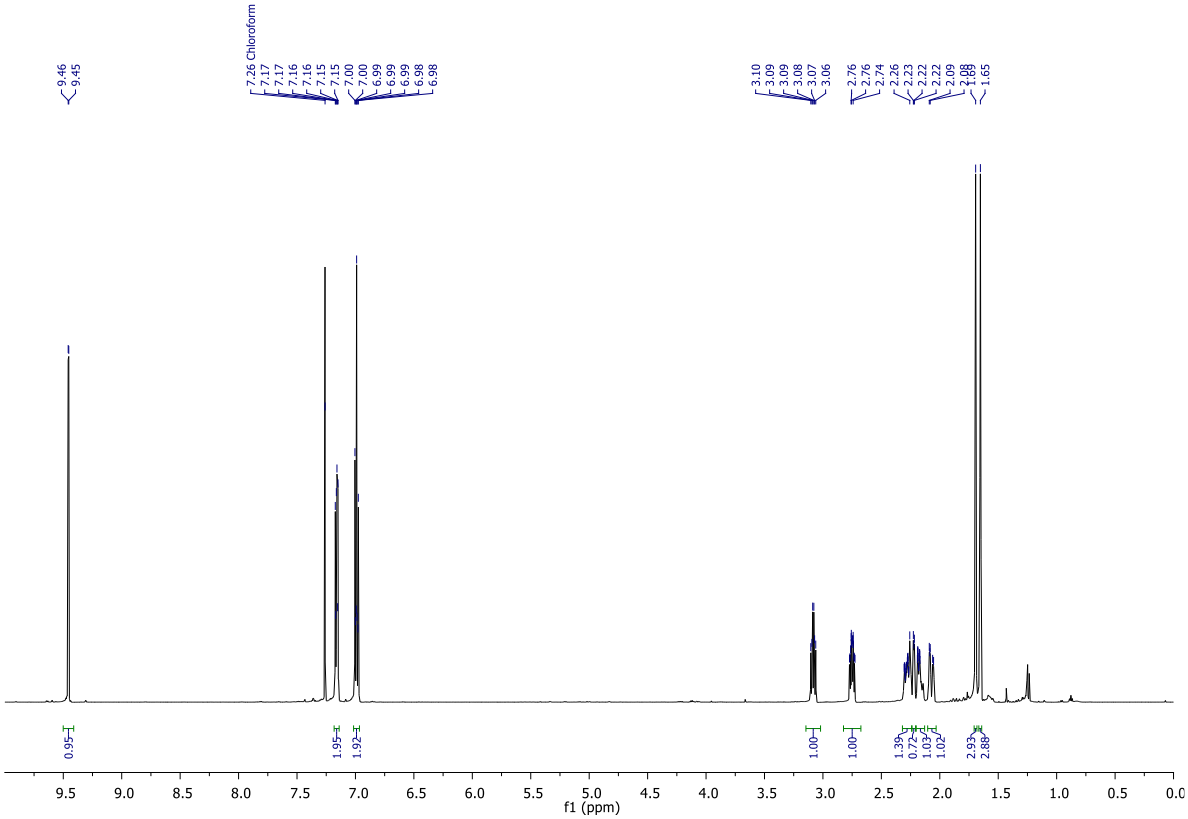


Figure S16. ^{1}H NMR spectrum of **1b** ($CDCl_3$, 600 MHz, 298 K)

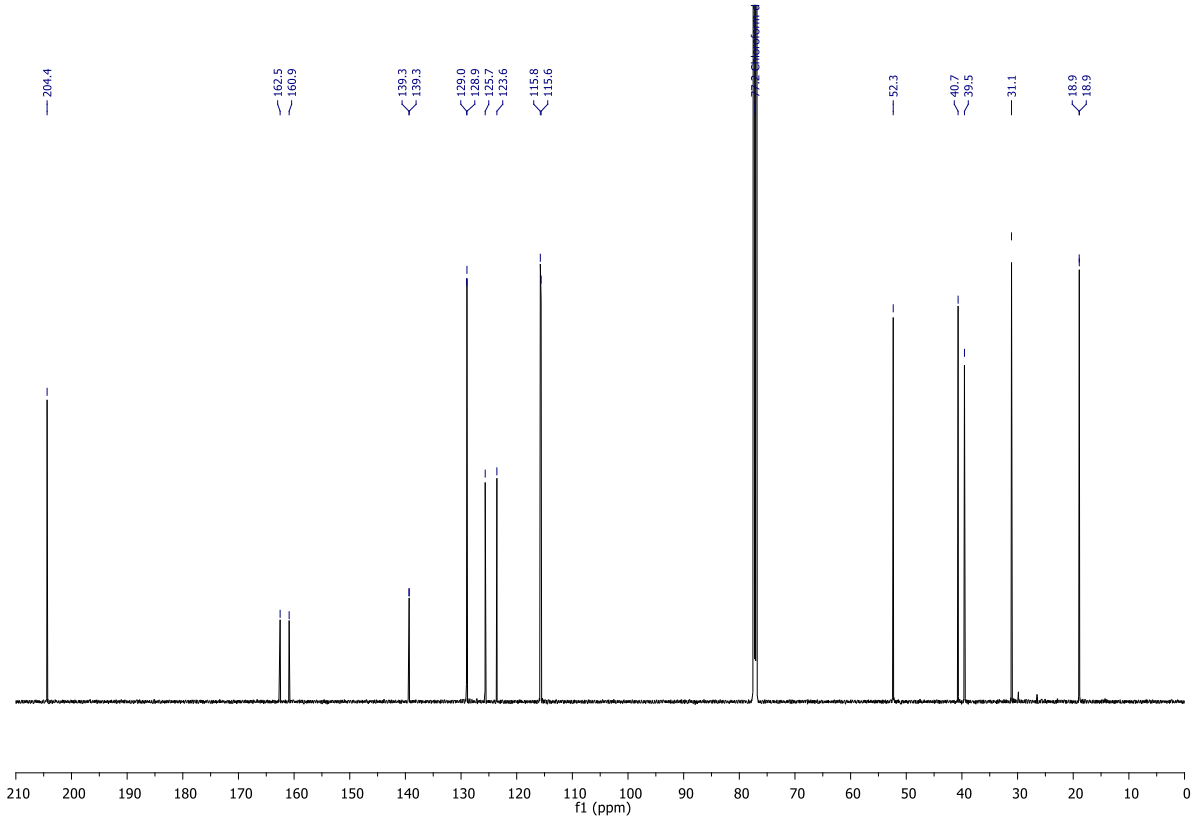


Figure S17. ^{13}C NMR spectrum of **1b** ($CDCl_3$, 151 MHz, 298 K)

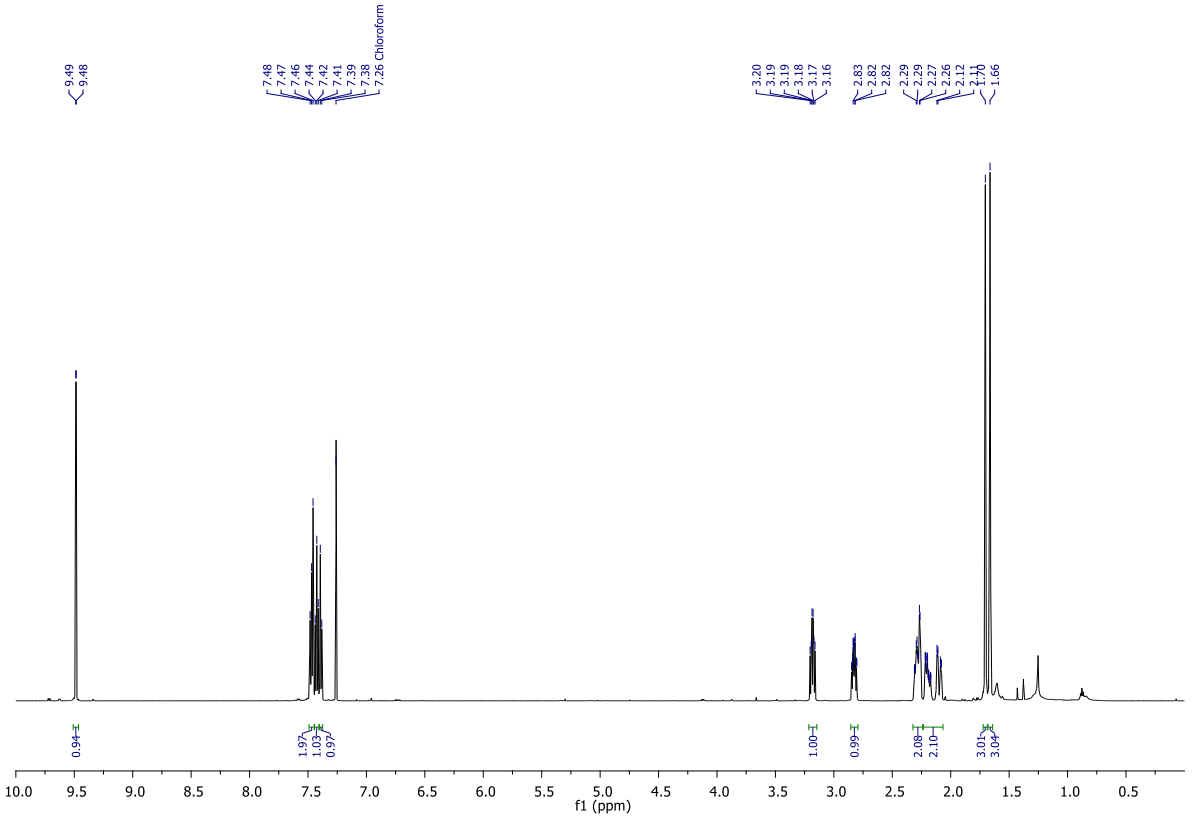


Figure S18. ^{1}H NMR spectrum of **1c** ($CDCl_3$, 600 MHz, 298 K)

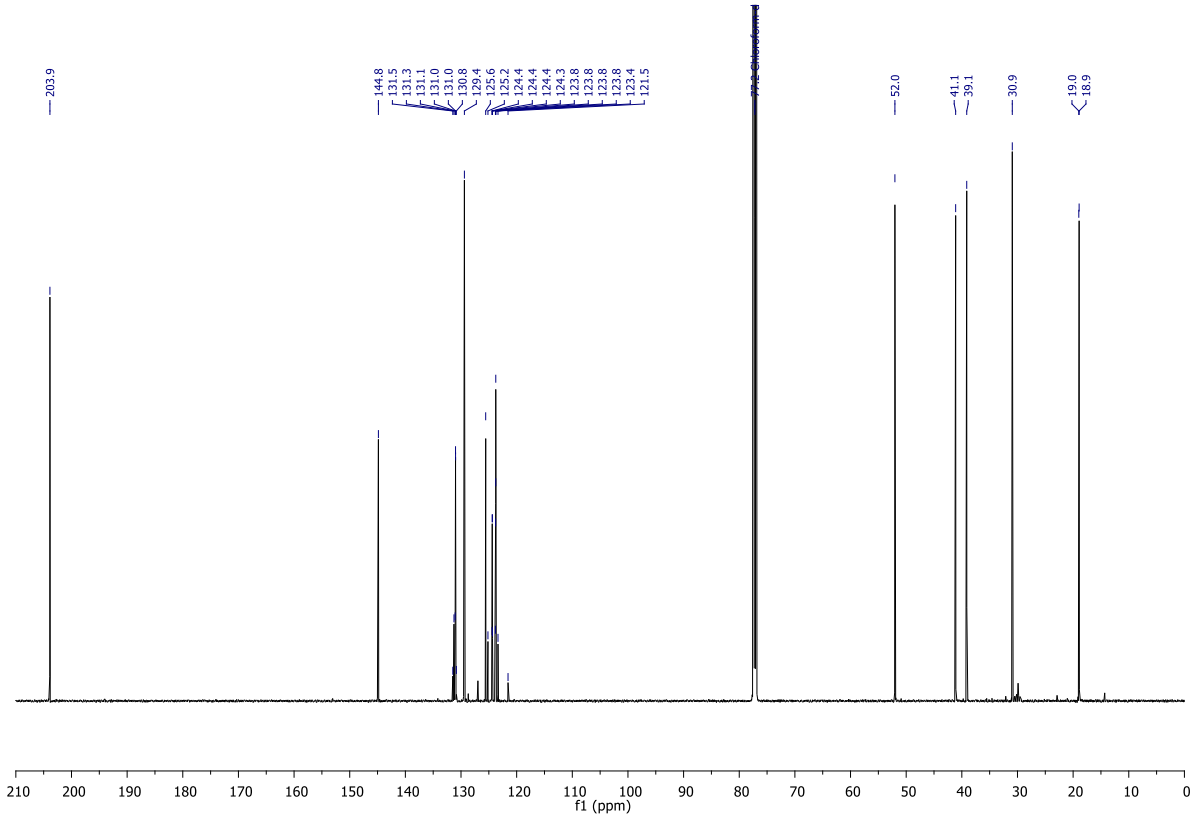


Figure S19. ^{13}C NMR spectrum of **1c** ($CDCl_3$, 151 MHz, 298 K)

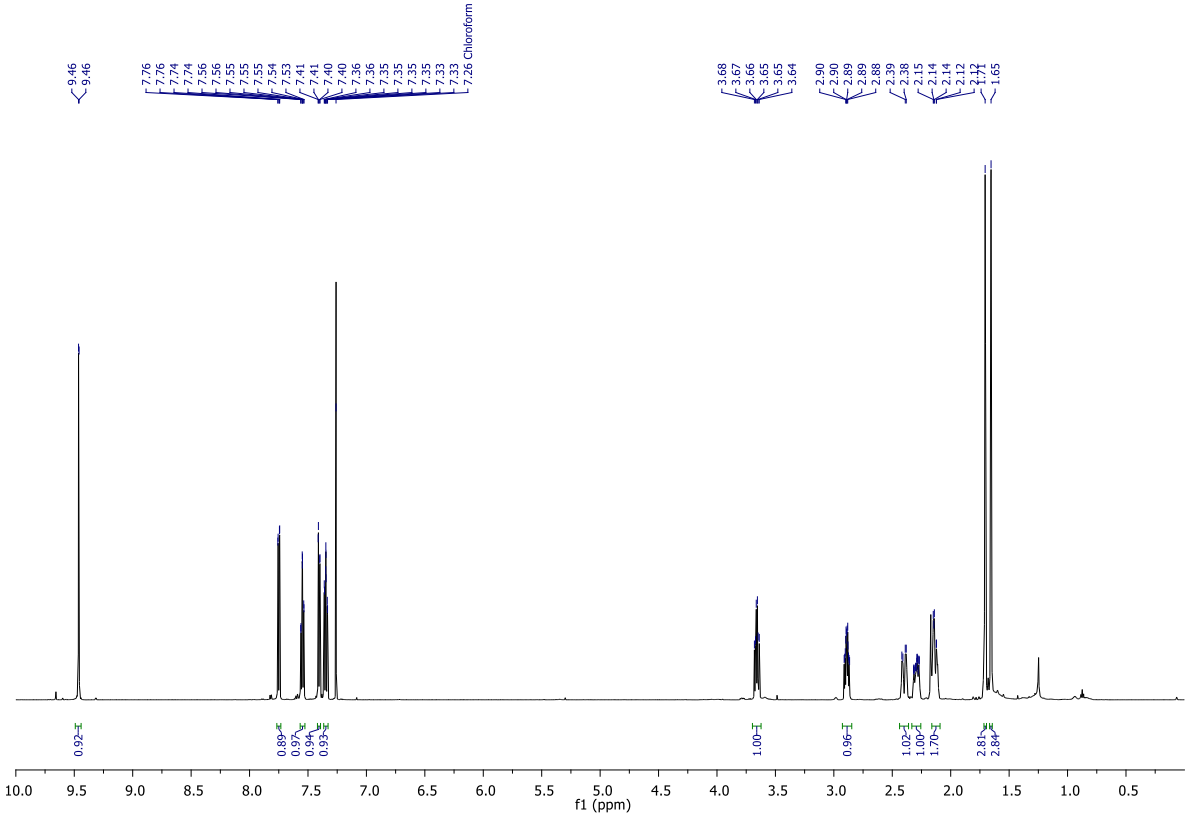


Figure S20. ^{1}H NMR spectrum of **1d** ($CDCl_3$, 600 MHz, 298 K)

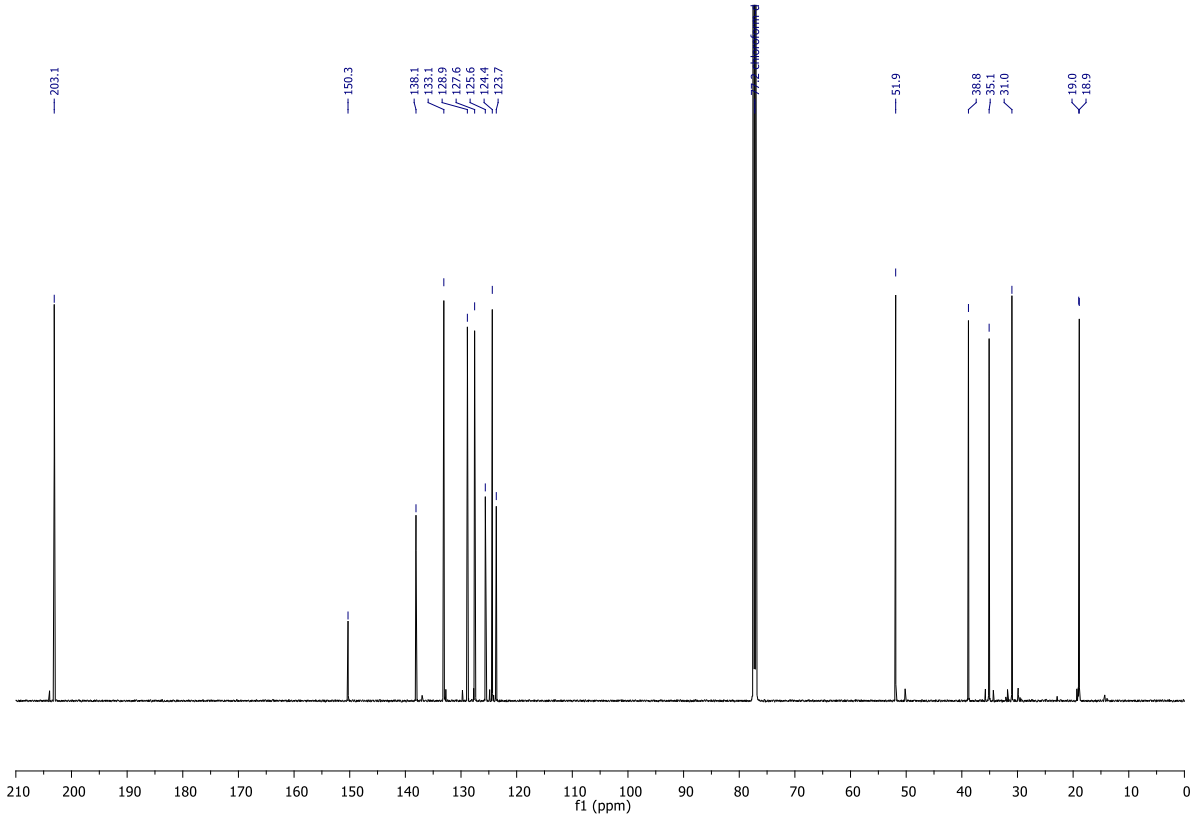


Figure S21. ^{13}C NMR spectrum of **1d** ($CDCl_3$, 151 MHz, 298 K)

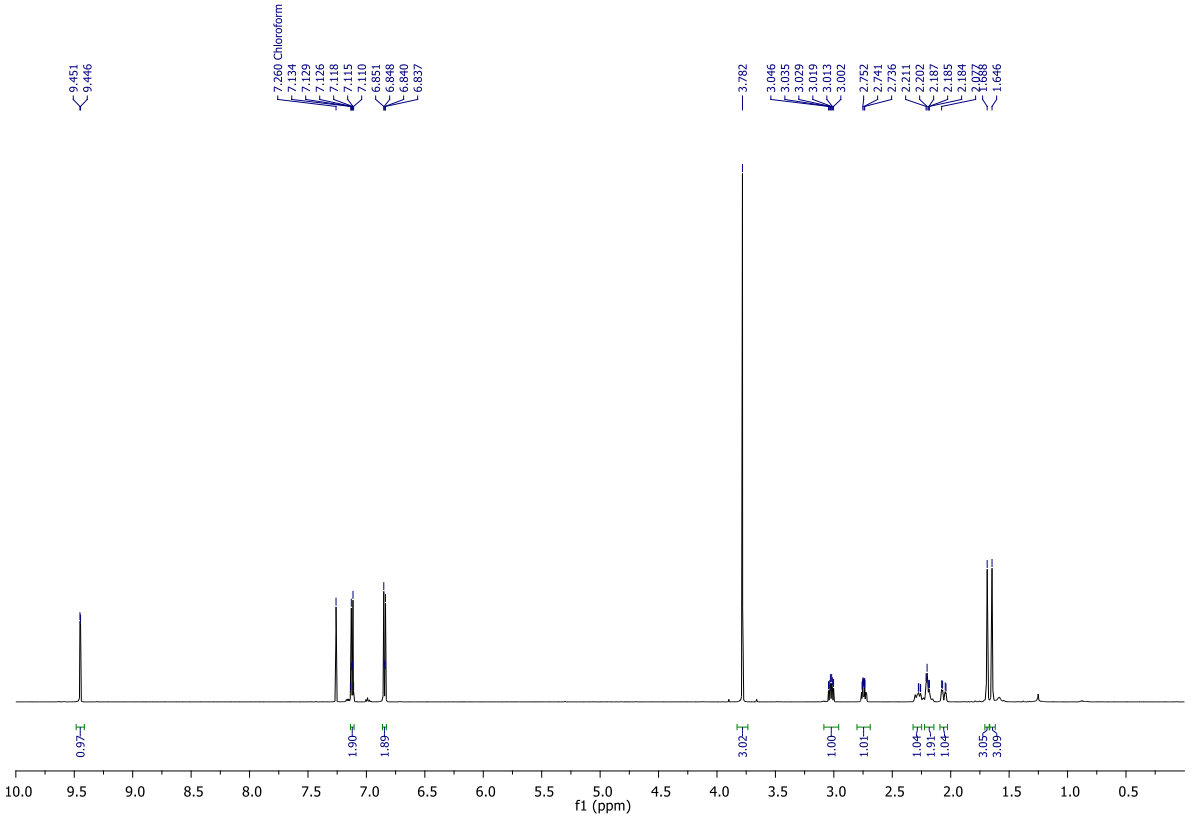


Figure S22. ^{1}H NMR spectrum of **1e** ($CDCl_3$, 600 MHz, 298 K)

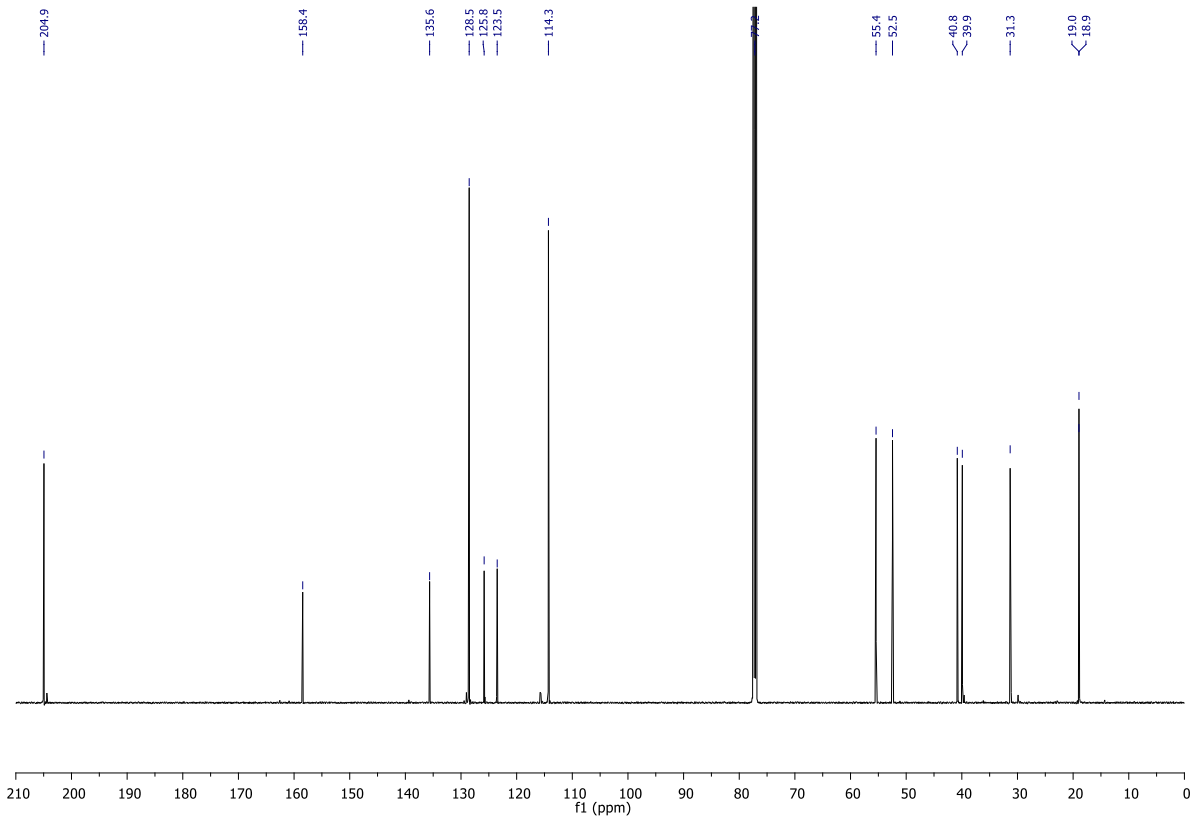


Figure S23. ^{13}C NMR spectrum of **1e** ($CDCl_3$, 151 MHz, 298 K)

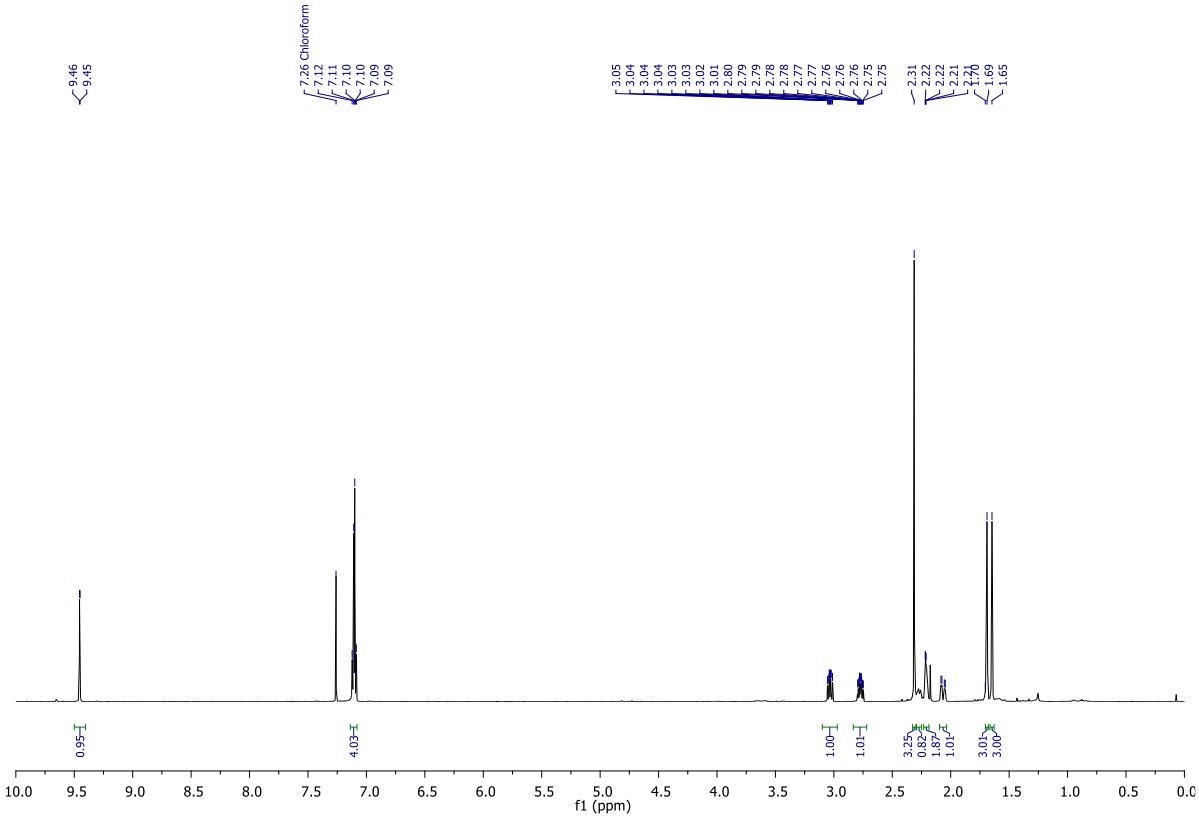


Figure S24. ^{1}H NMR spectrum of **1f** ($CDCl_3$, 600 MHz, 298 K)

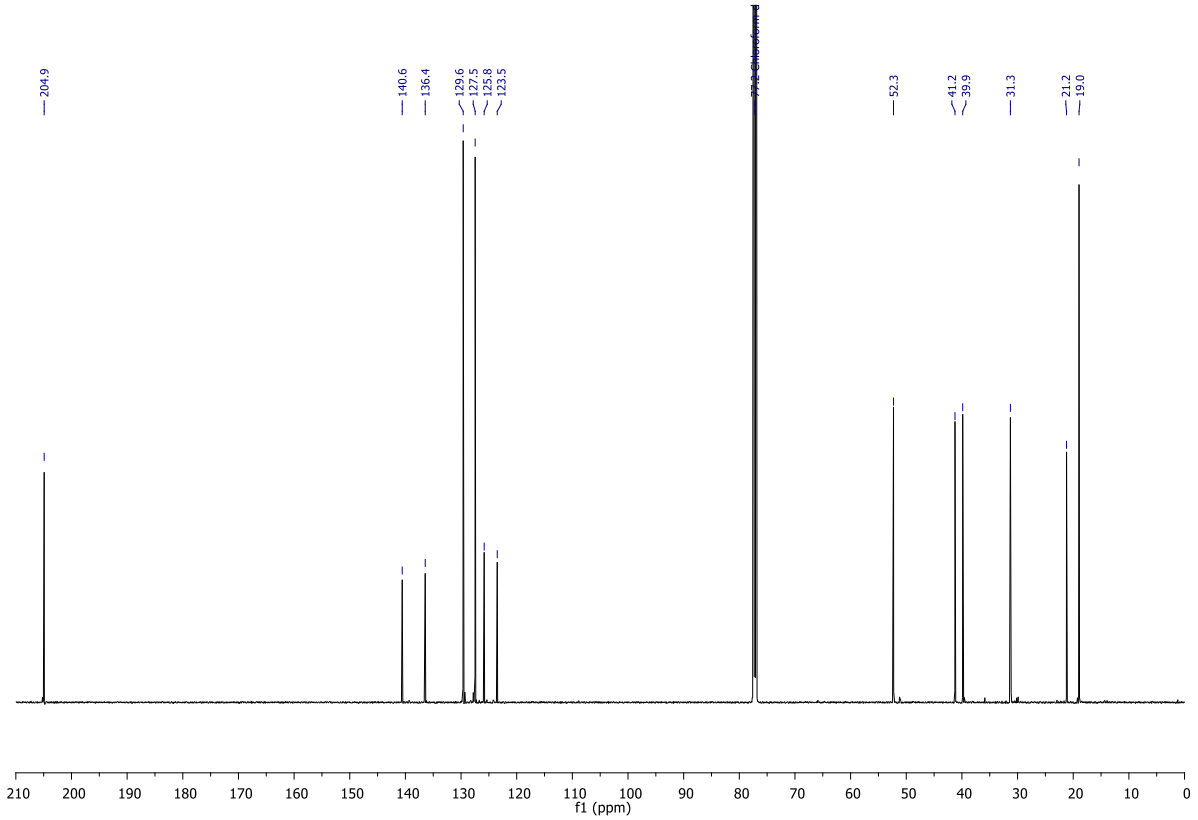


Figure S25. ^{13}C NMR spectrum of **1f** ($CDCl_3$, 151 MHz, 298 K)

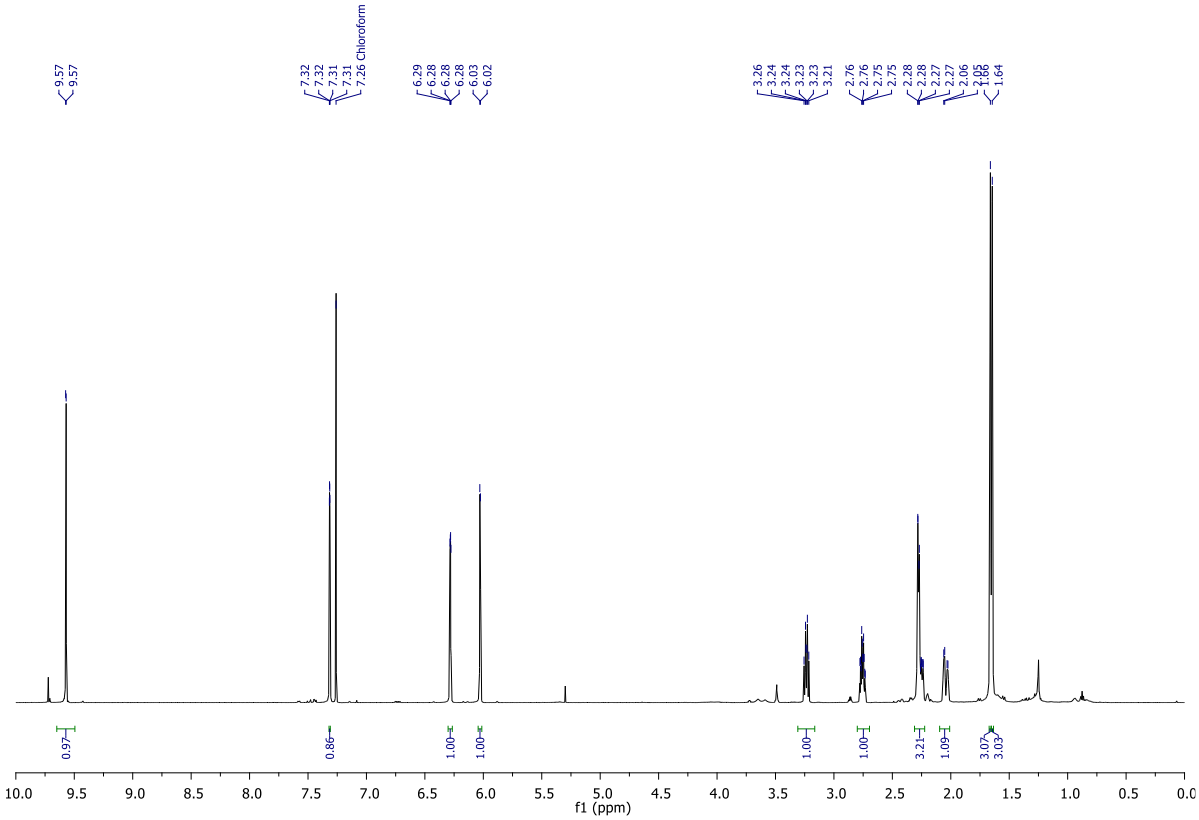


Figure S26. ^{1}H NMR spectrum of **1g** ($CDCl_3$, 600 MHz, 298 K)

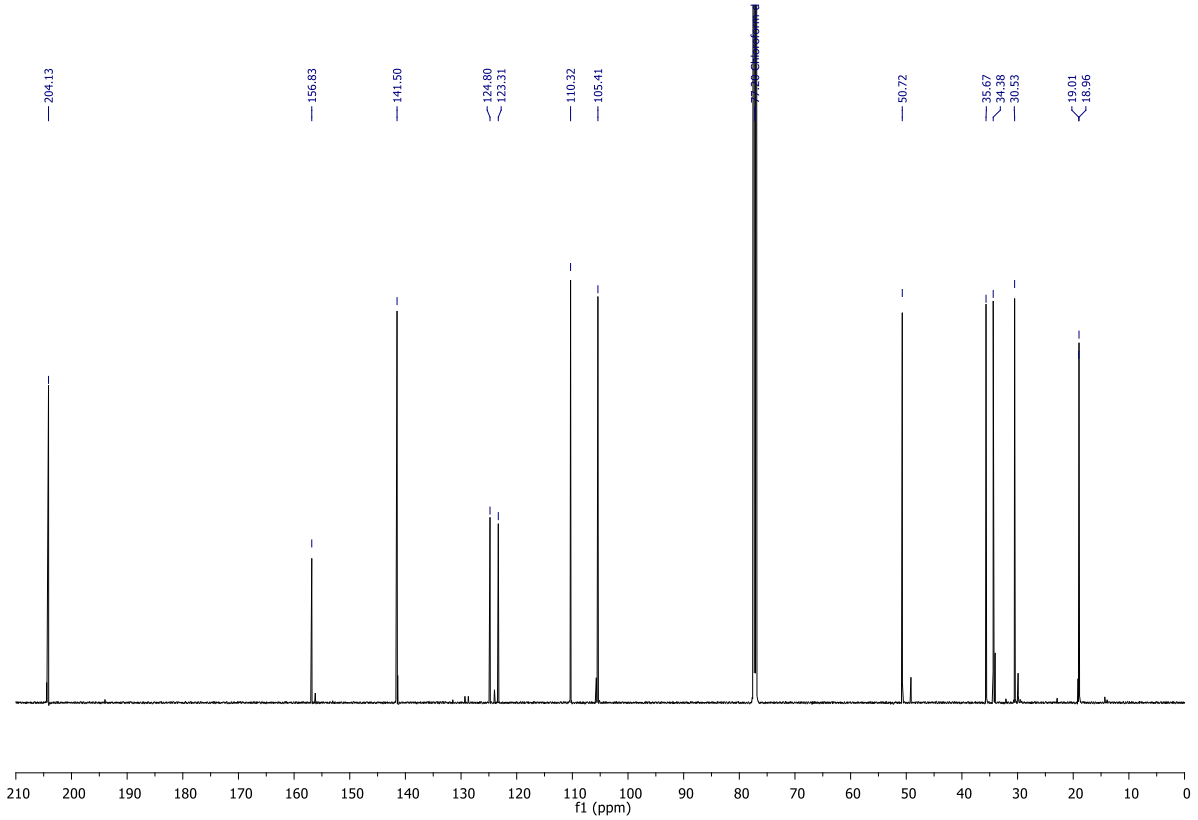


Figure S27. ^{13}C NMR spectrum of **1g** ($CDCl_3$, 151 MHz, 298 K)

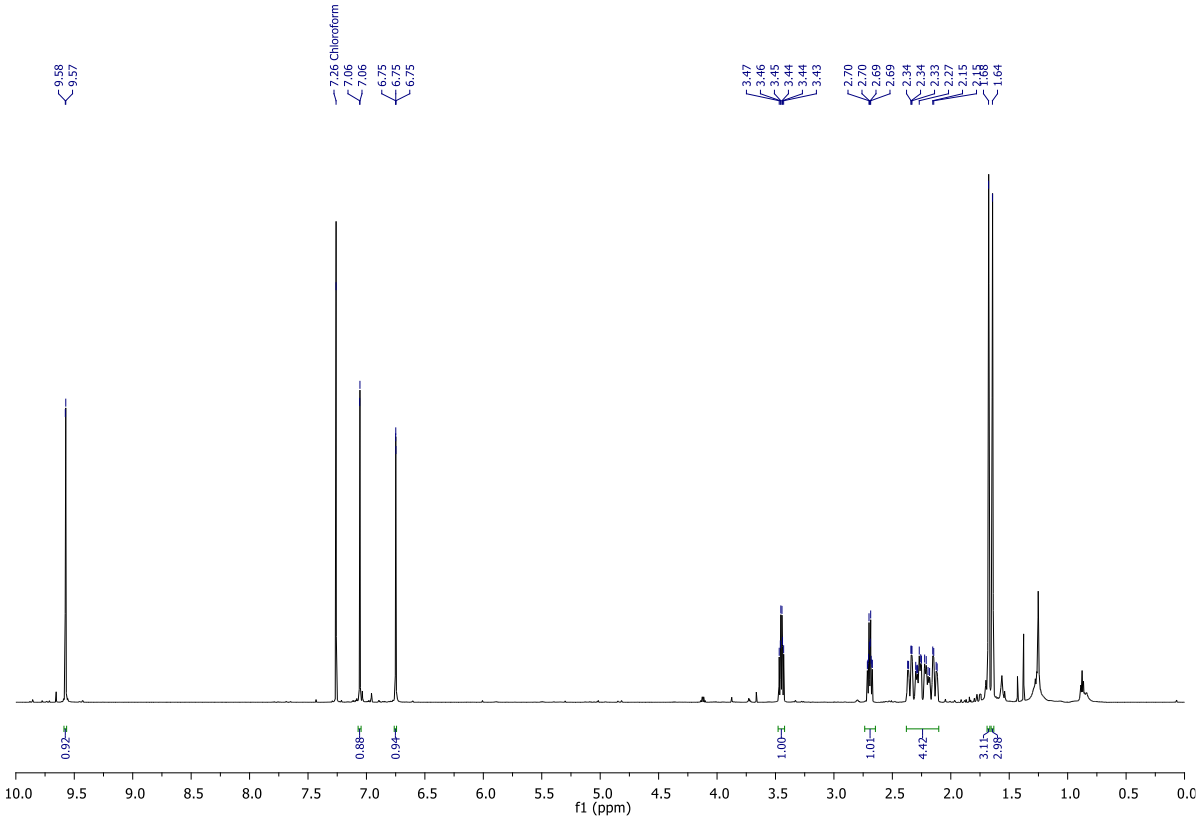


Figure S28. ^{1}H NMR spectrum of **1h** ($CDCl_3$, 600 MHz, 298 K)

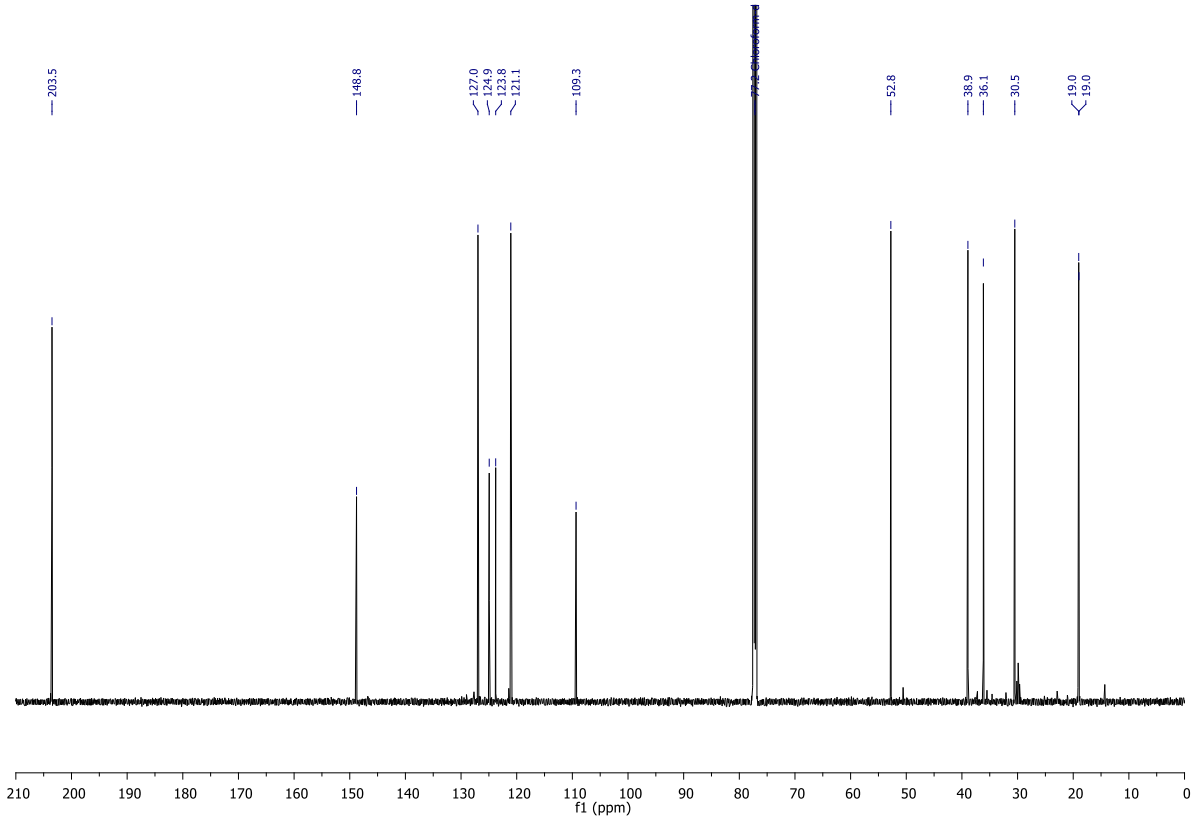


Figure S29. ^{13}C NMR spectrum of **1h** ($CDCl_3$, 151 MHz, 298 K)

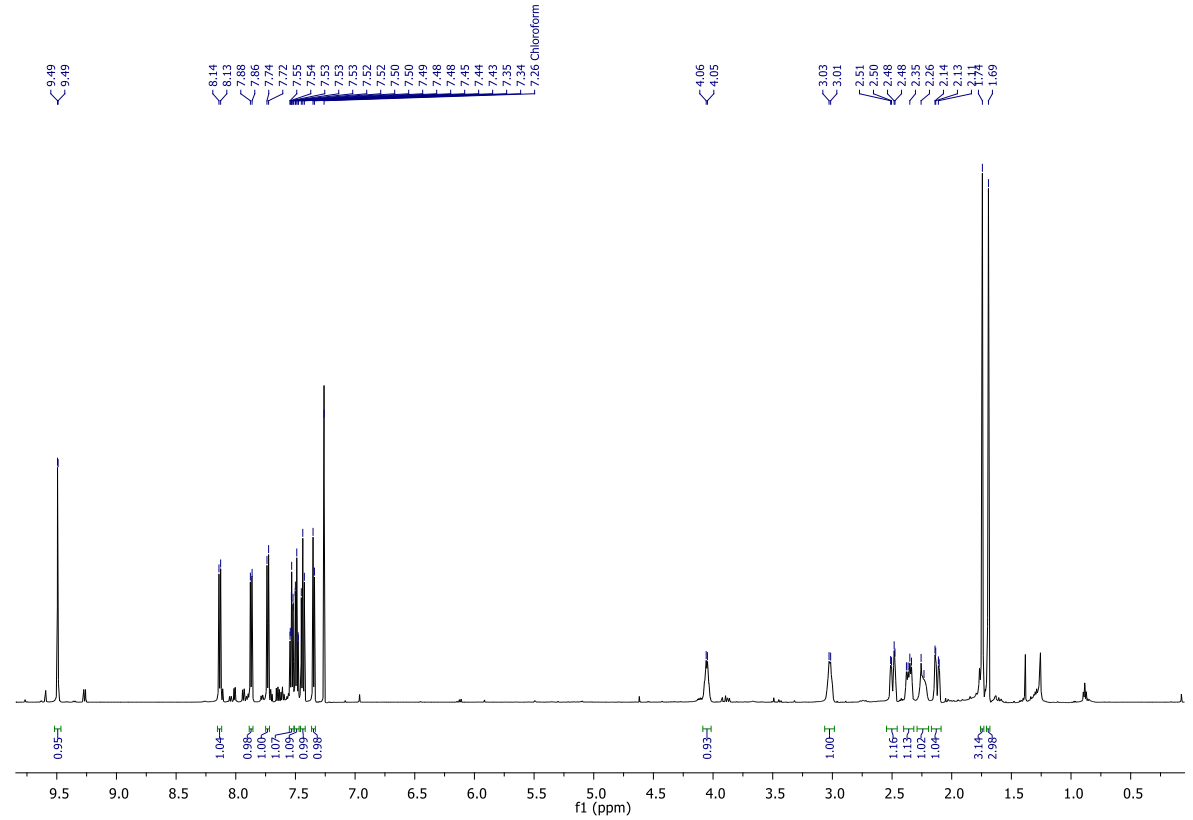


Figure S30. ^{1}H NMR spectrum of **1i** ($CDCl_3$, 600 MHz, 298 K)

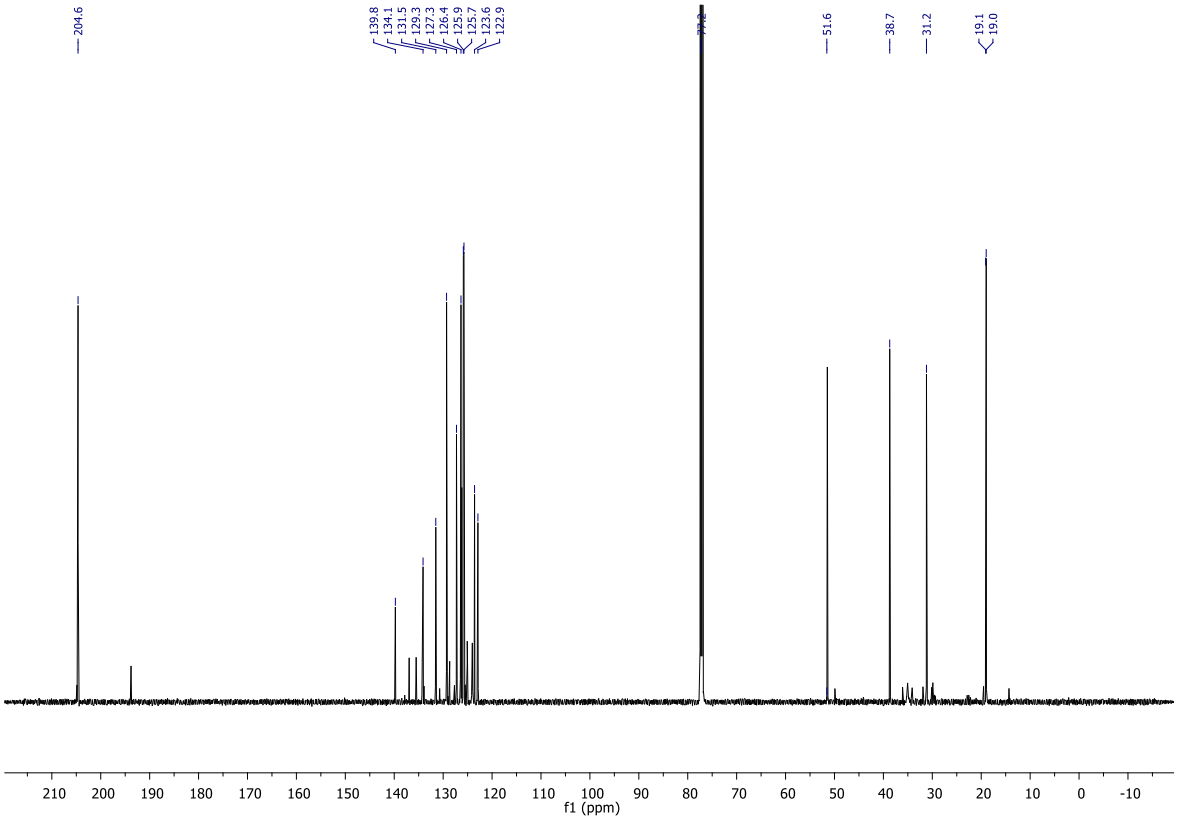


Figure S31. ^{13}C NMR spectrum of **1i** ($CDCl_3$, 151 MHz, 298 K)

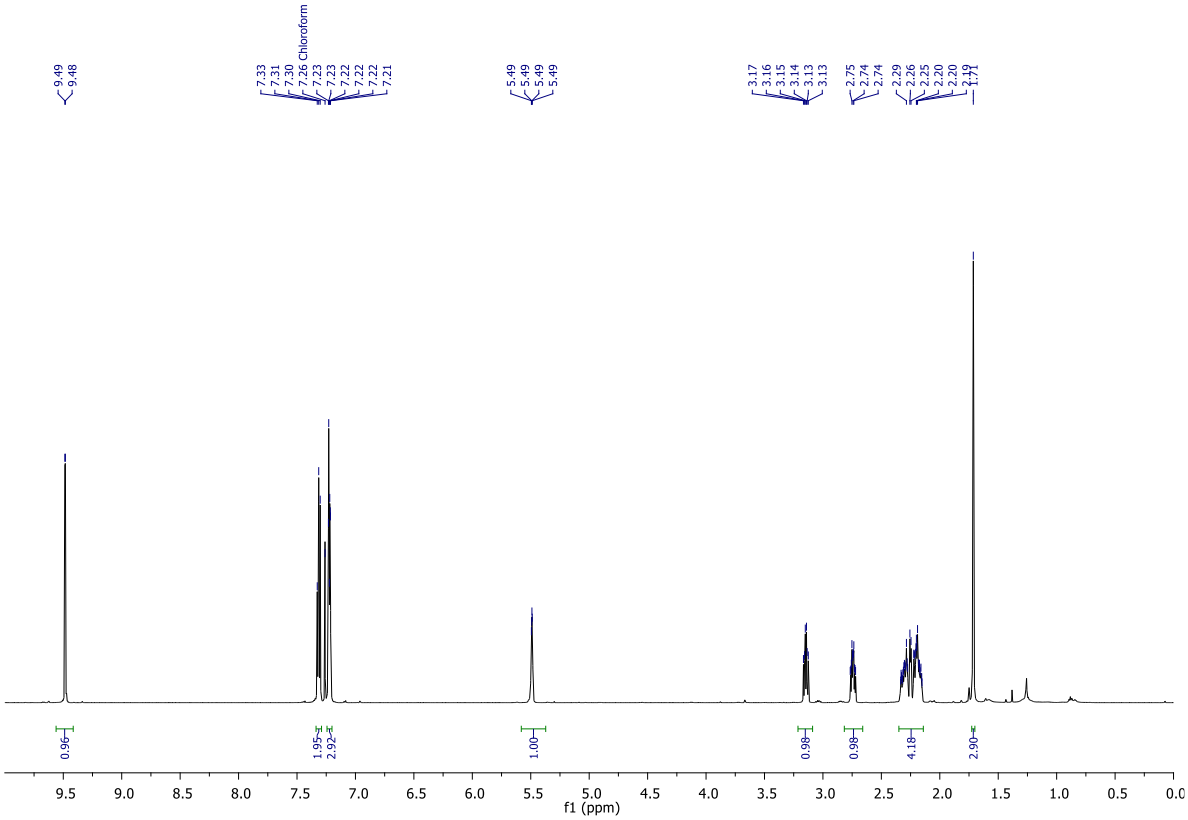


Figure S32. ^{1}H NMR spectrum of **2a** ($CDCl_3$, 600 MHz, 298 K)

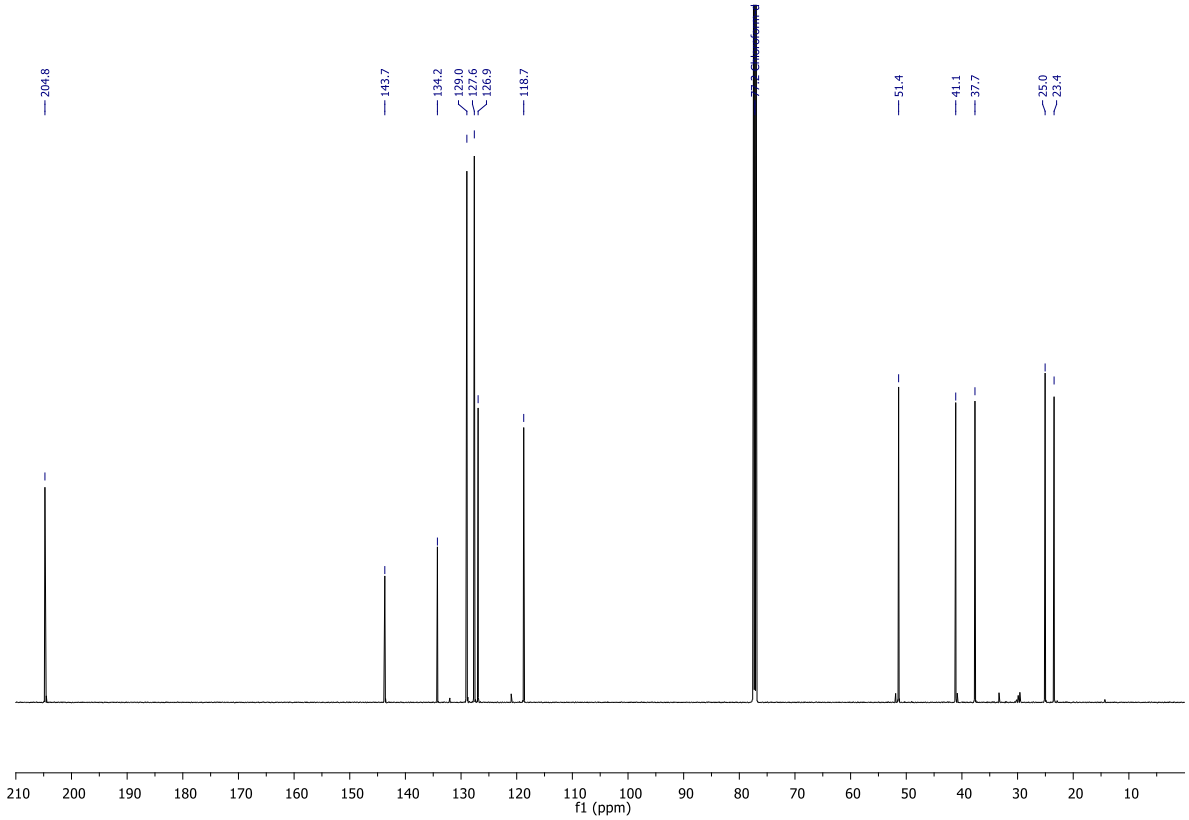


Figure S33. ^{13}C NMR spectrum of **2a** ($CDCl_3$, 151 MHz, 298 K)

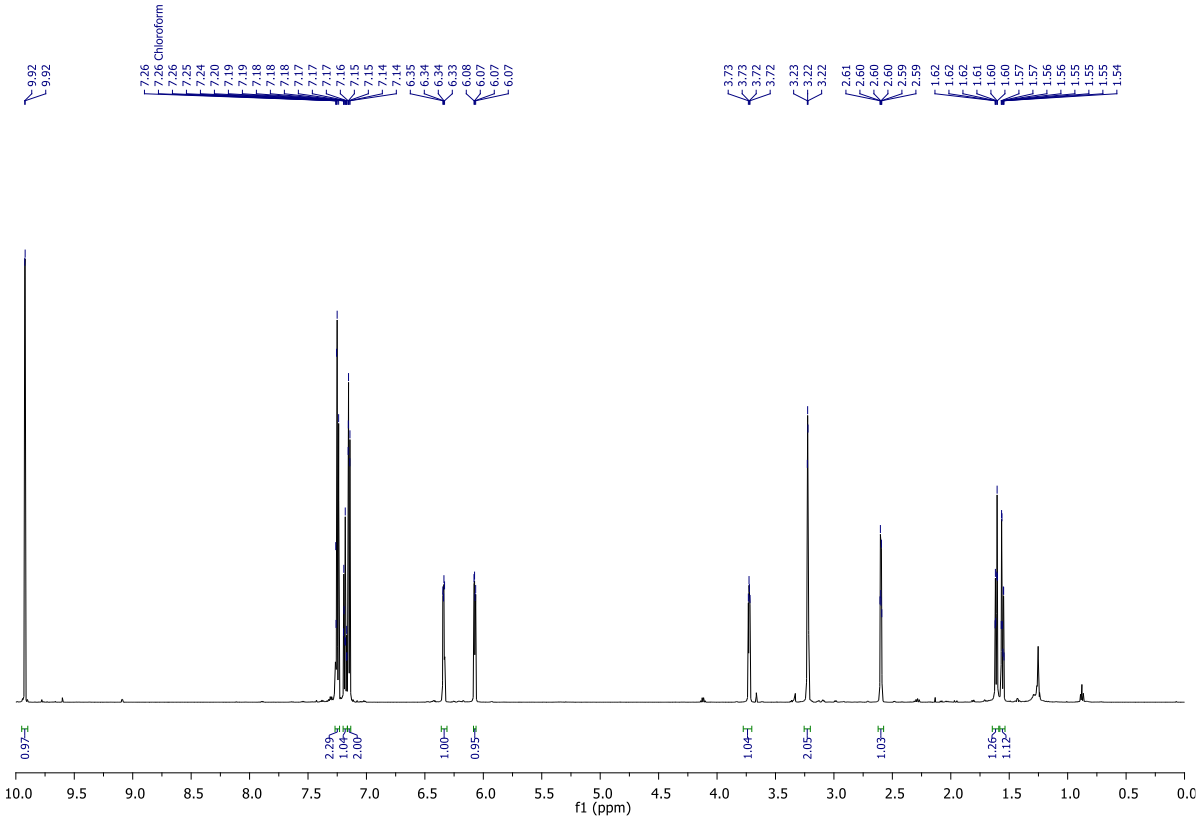


Figure S34. ^{1}H NMR spectrum of **2b** ($CDCl_3$, 600 MHz, 298 K)

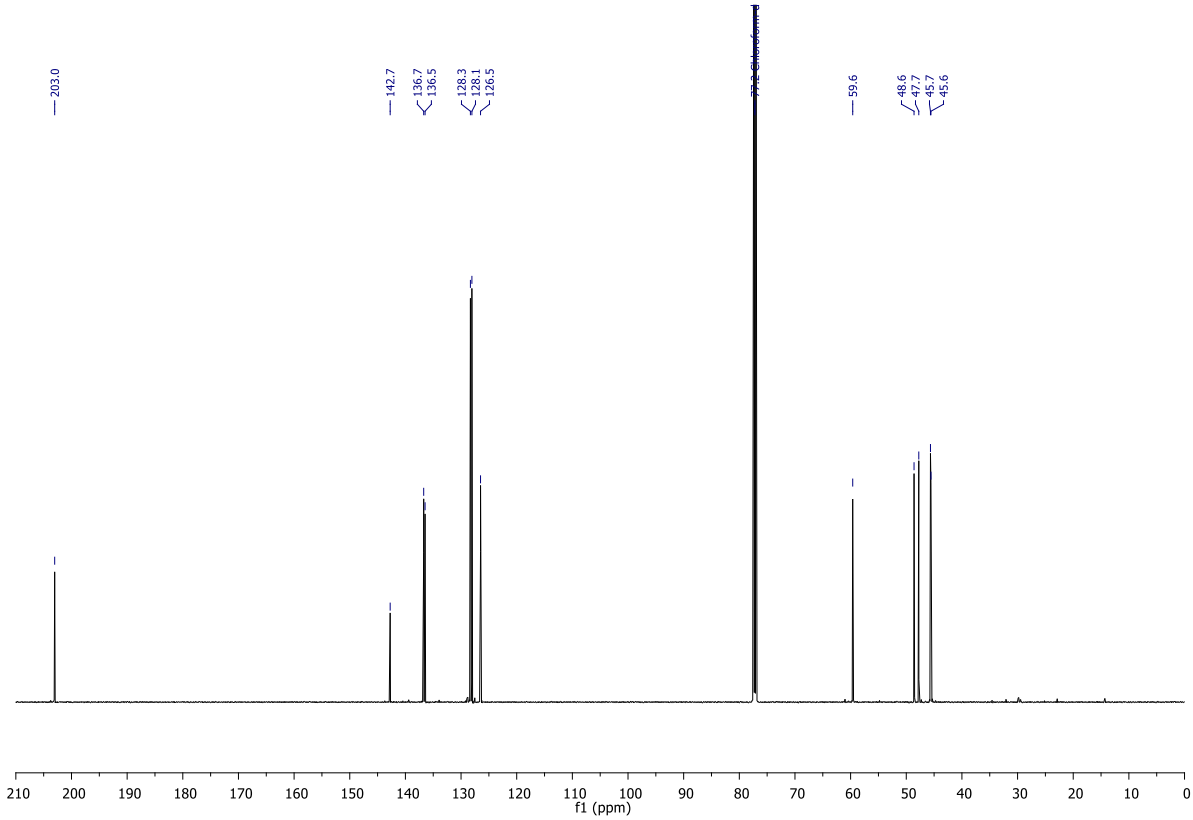


Figure S35. ^{13}C NMR spectrum of **2b** ($CDCl_3$, 151 MHz, 298 K)

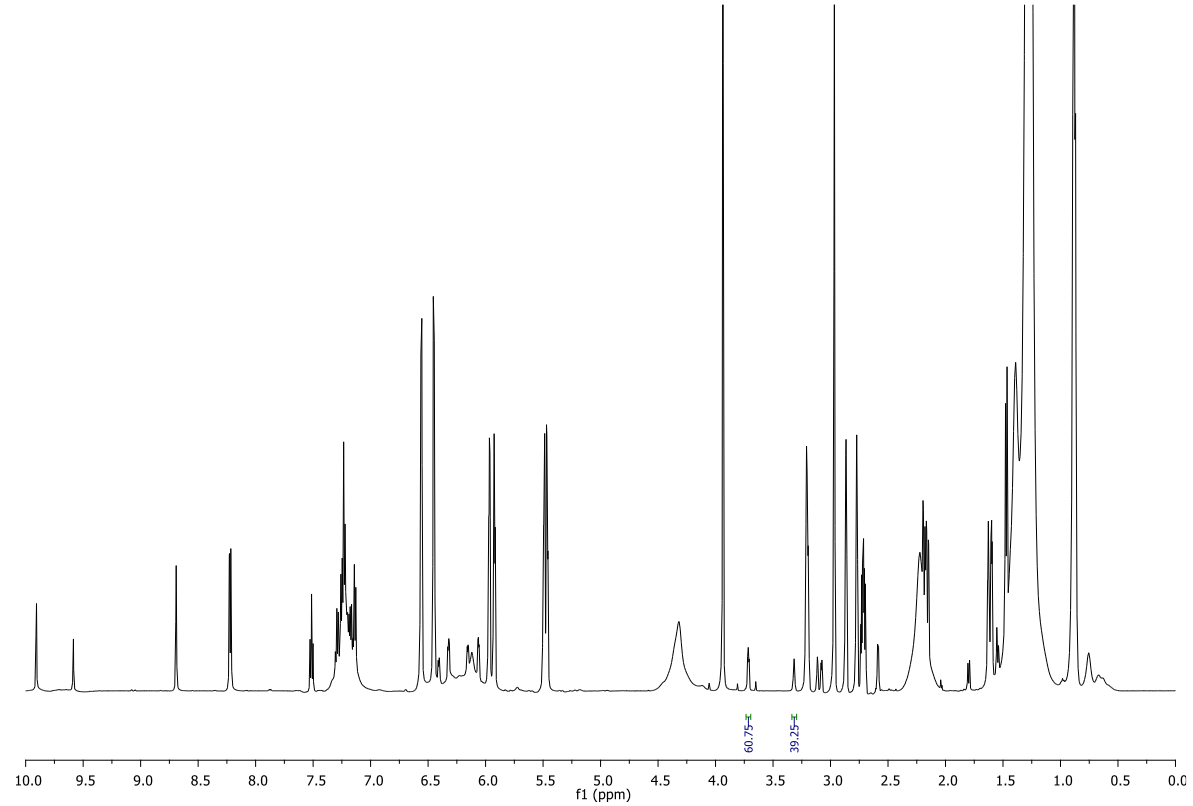


Figure S36. ^{1}H NMR spectrum of crude **2b** denoting diastereomeric ratio ($CDCl_3$, 600 MHz, 298 K)

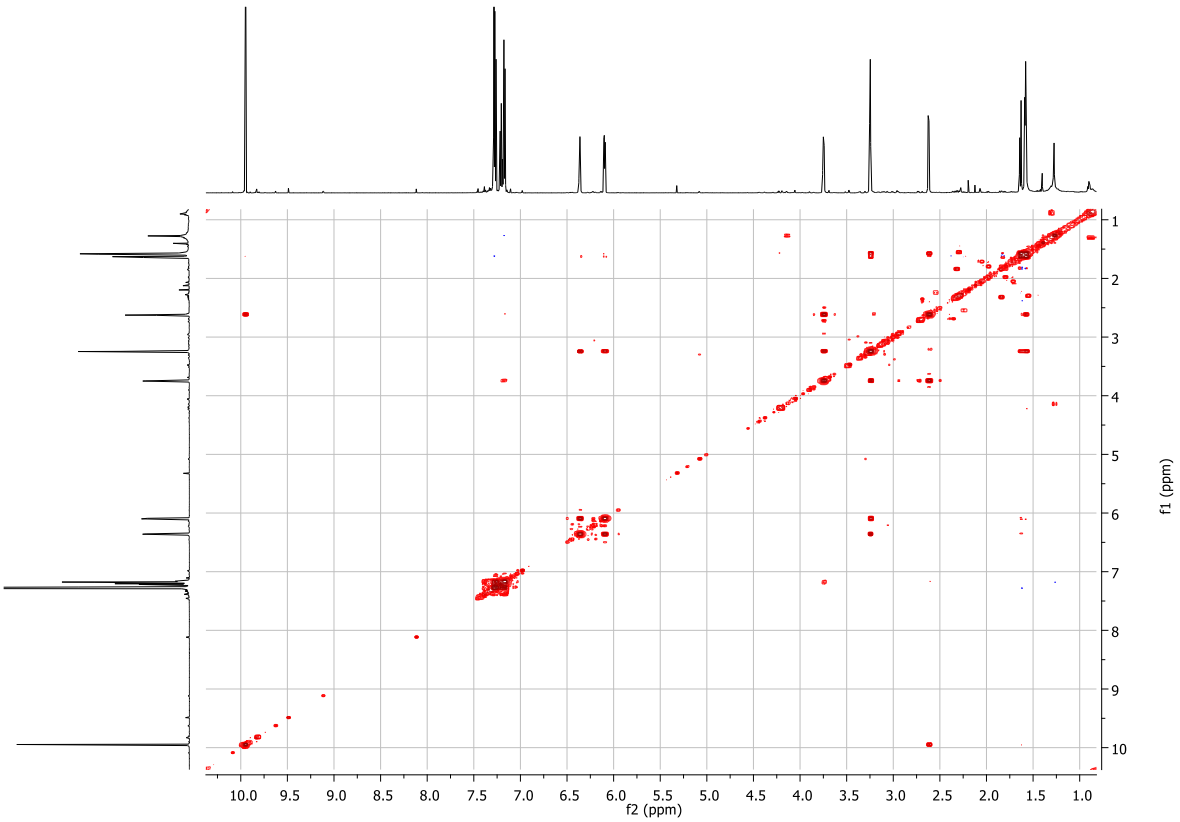


Figure S37. COSY spectrum of **2b** ($CDCl_3$, 600 MHz, 298 K)

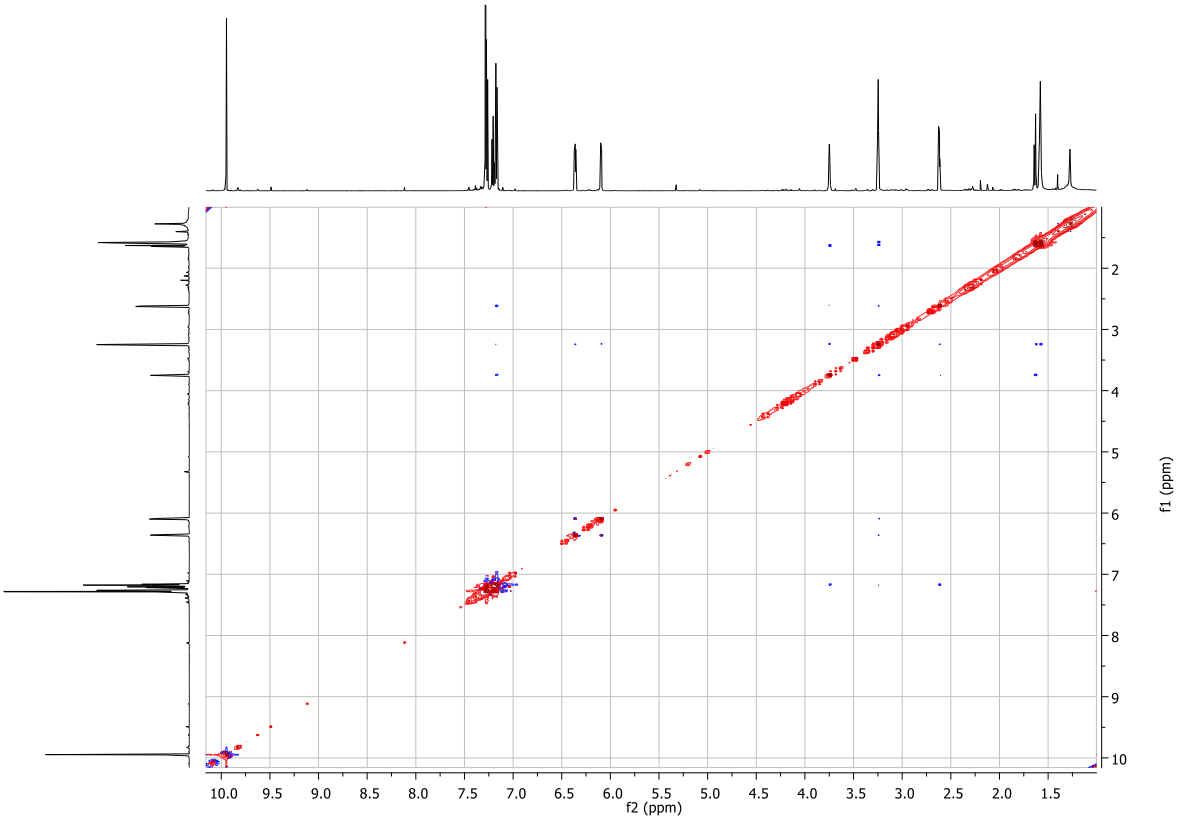


Figure S38. NOESY spectrum of **2b** ($CDCl_3$, 600 MHz, 298 K)

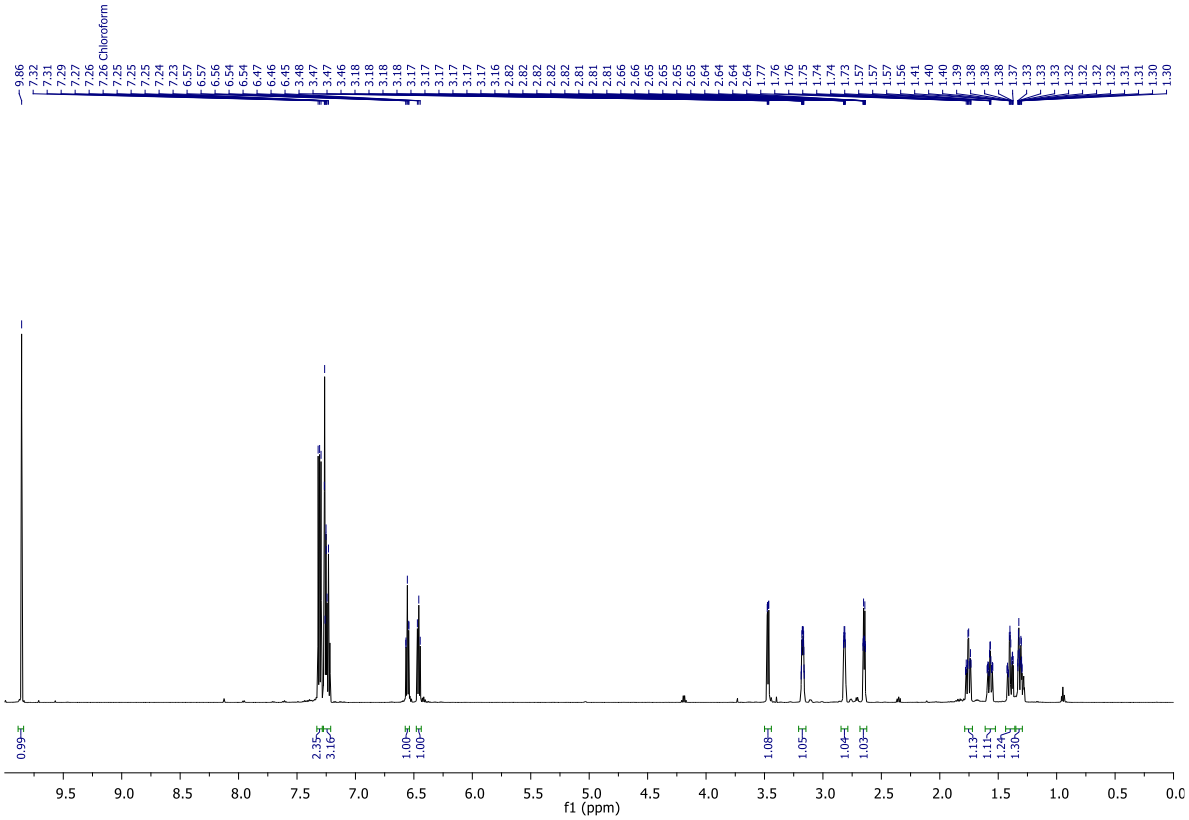


Figure S39. ^{1}H NMR spectrum of **2c** ($CDCl_3$, 600 MHz, 298 K)

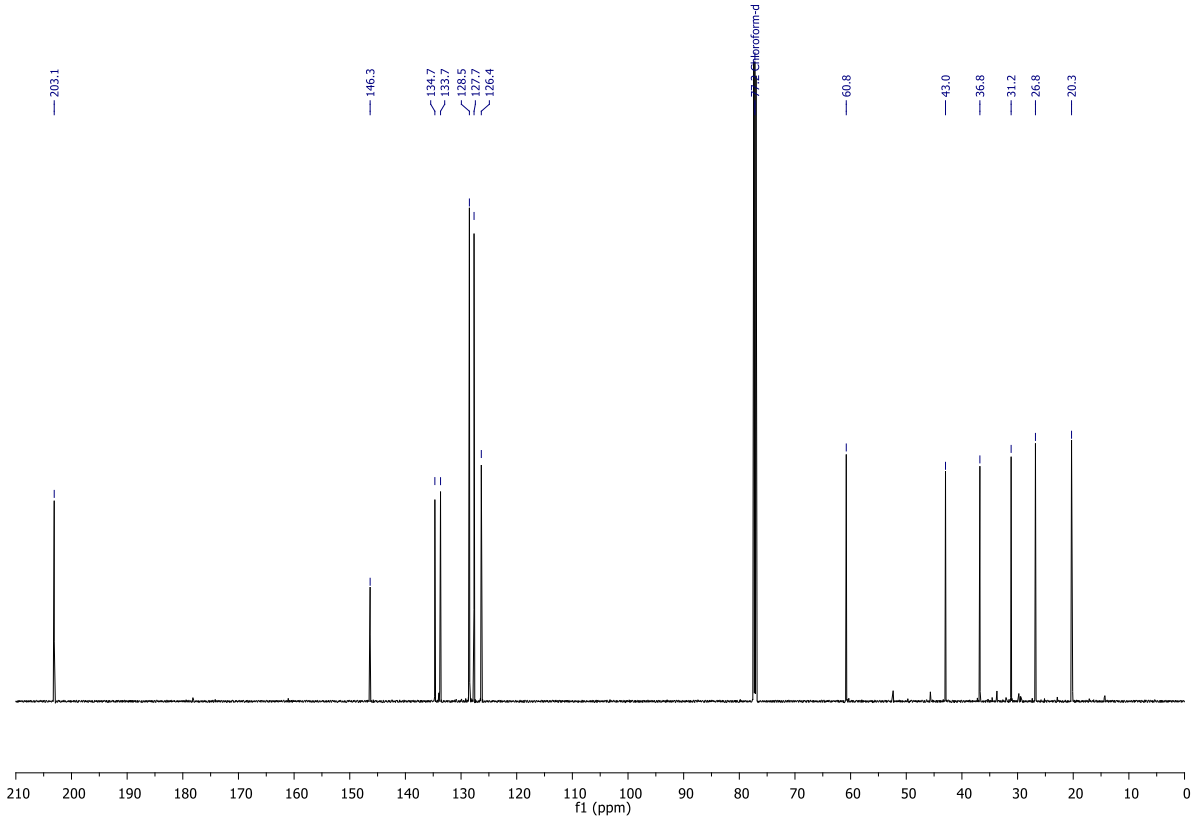


Figure S40. ^{13}C NMR spectrum of **2c** ($CDCl_3$, 151 MHz, 298 K)

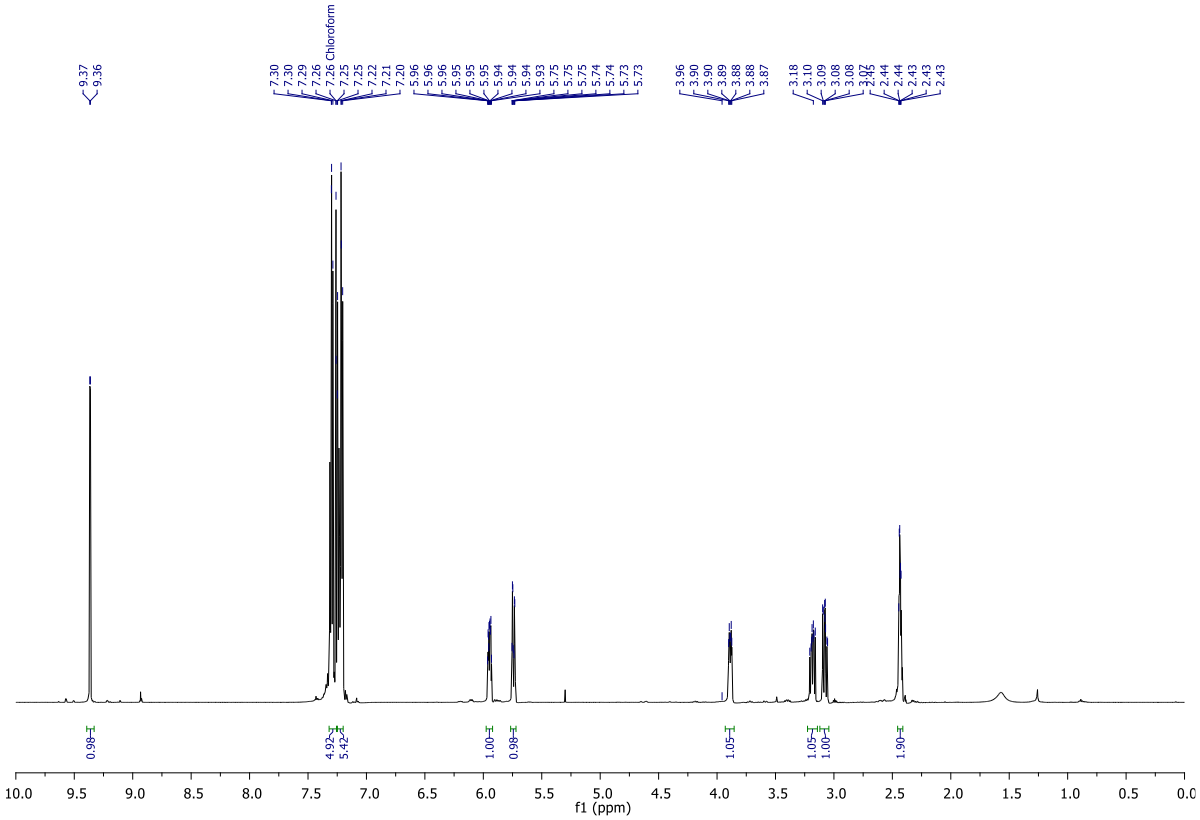


Figure S41. ^{1}H NMR spectrum of **2d** ($CDCl_3$, 600 MHz, 298 K)

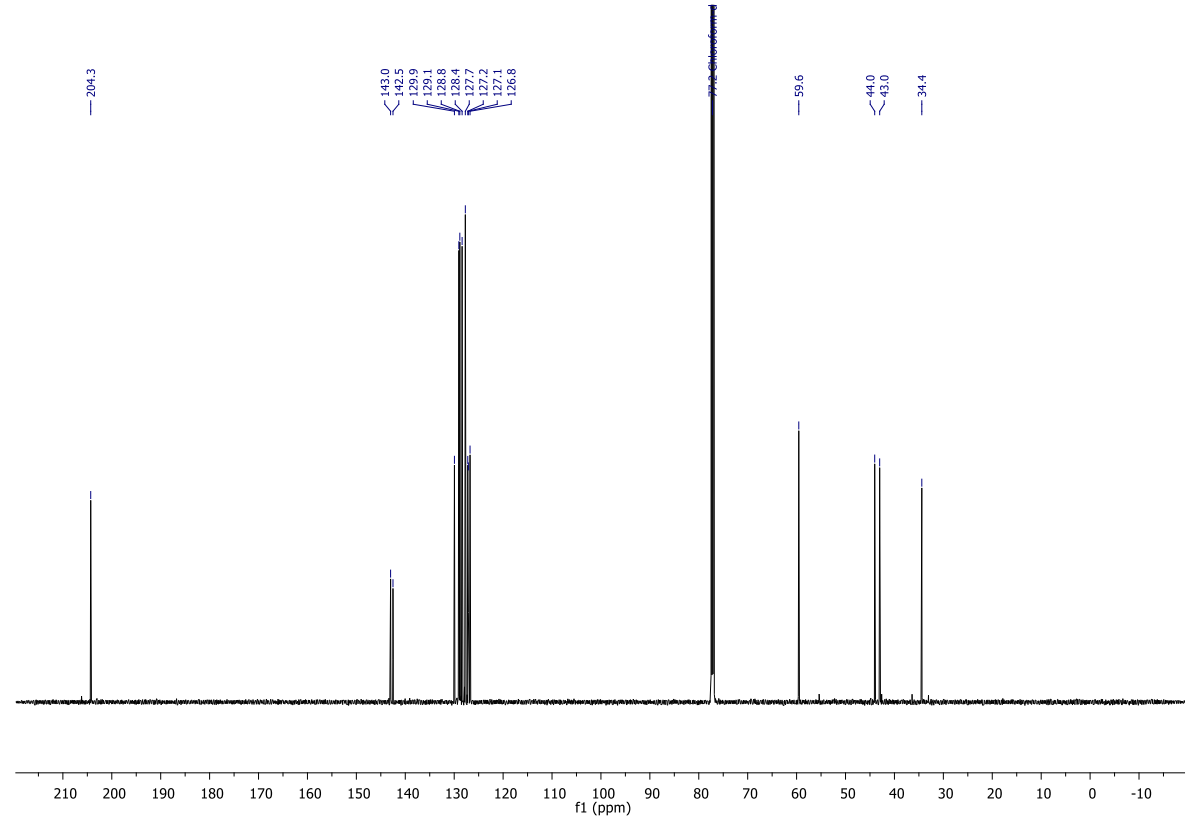


Figure S42. ^{13}C NMR spectrum of **2d** ($CDCl_3$, 151 MHz, 298 K)

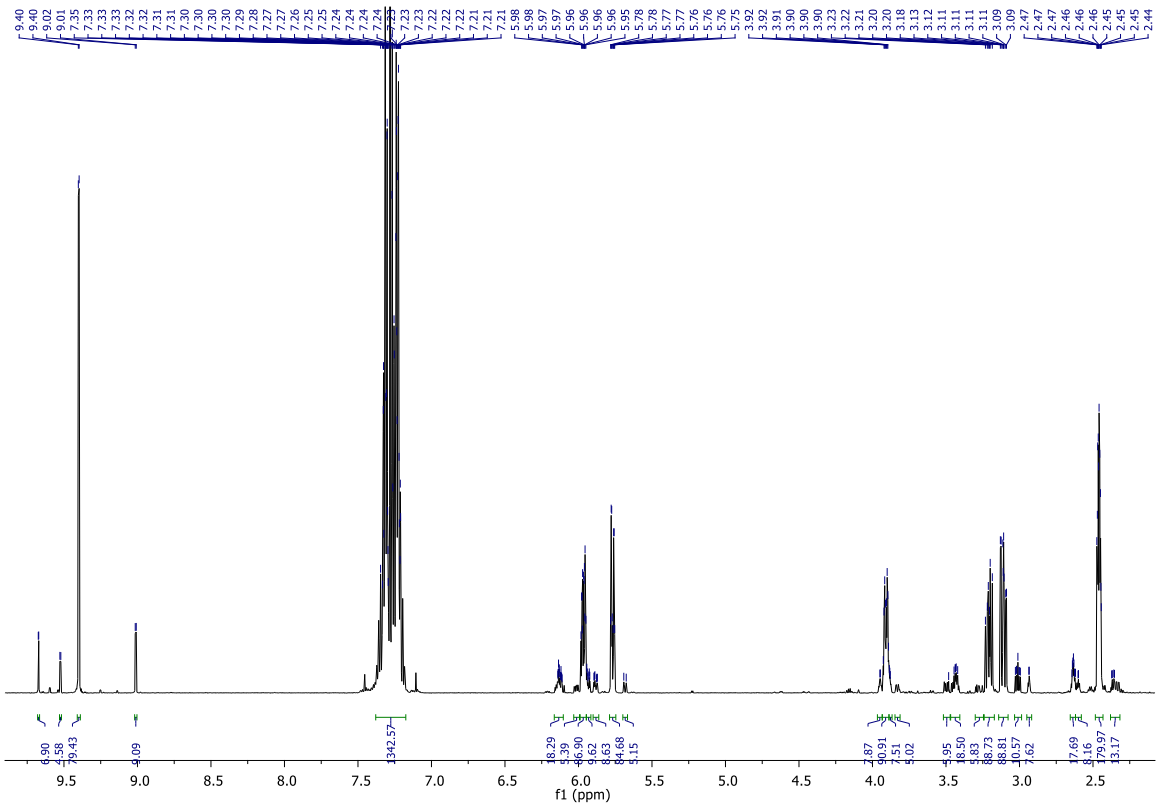


Figure S43. ^{1}H NMR spectrum of crude **2d** denoting diastereomeric ratio ($CDCl_3$, 600 MHz, 298 K)

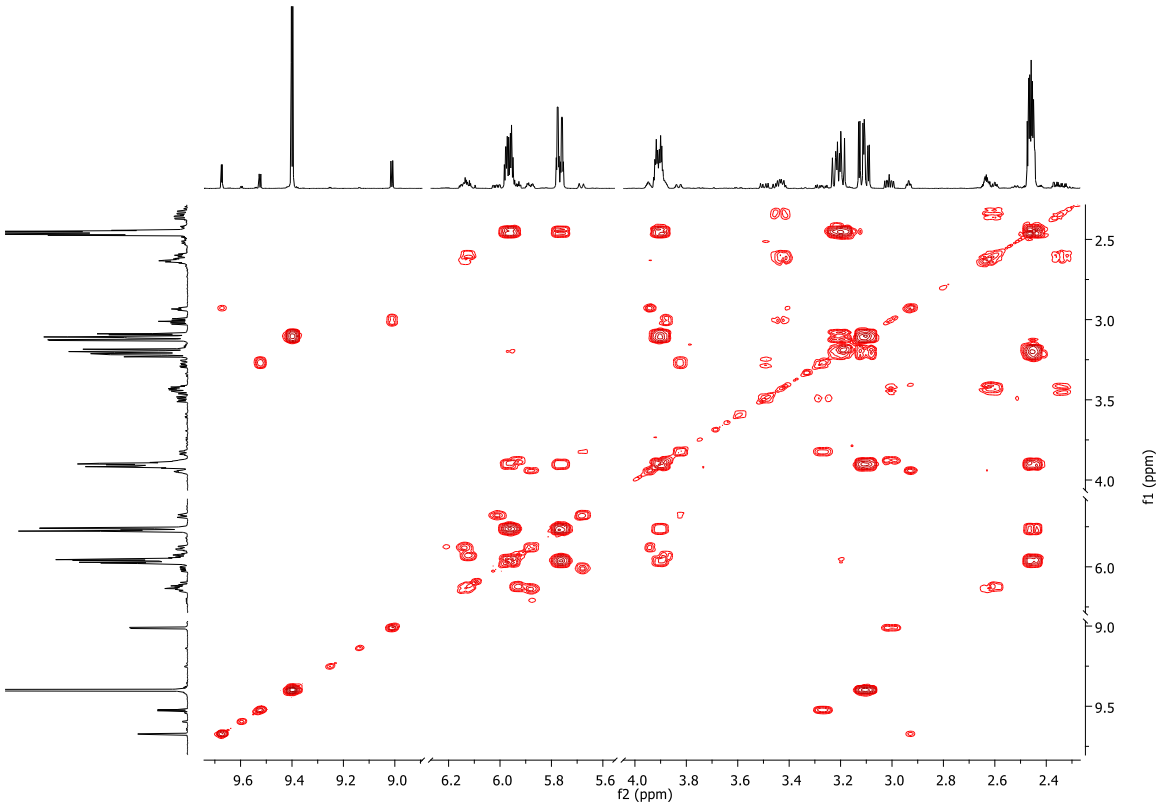


Figure S44. COSY NMR spectrum of crude **2d** ($CDCl_3$, 600 MHz, 298 K)

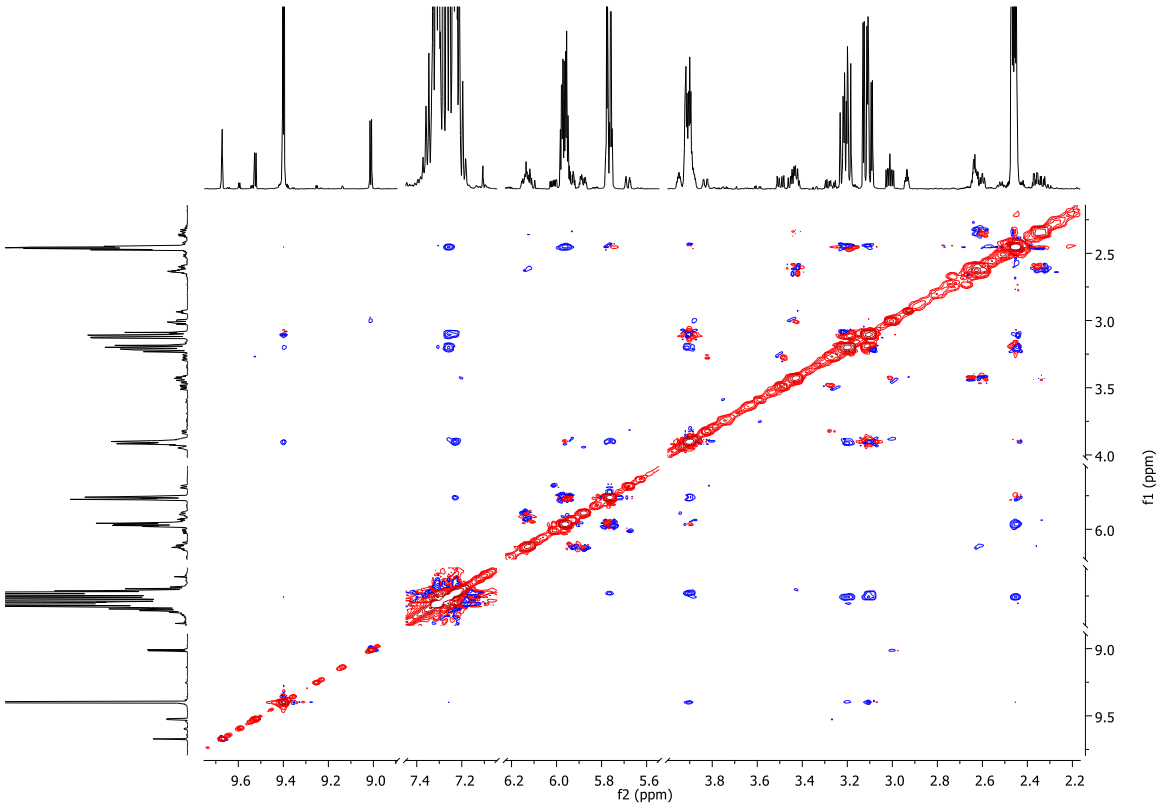


Figure S45. COSY NMR spectrum of crude **2d** ($CDCl_3$, 600 MHz, 298 K)

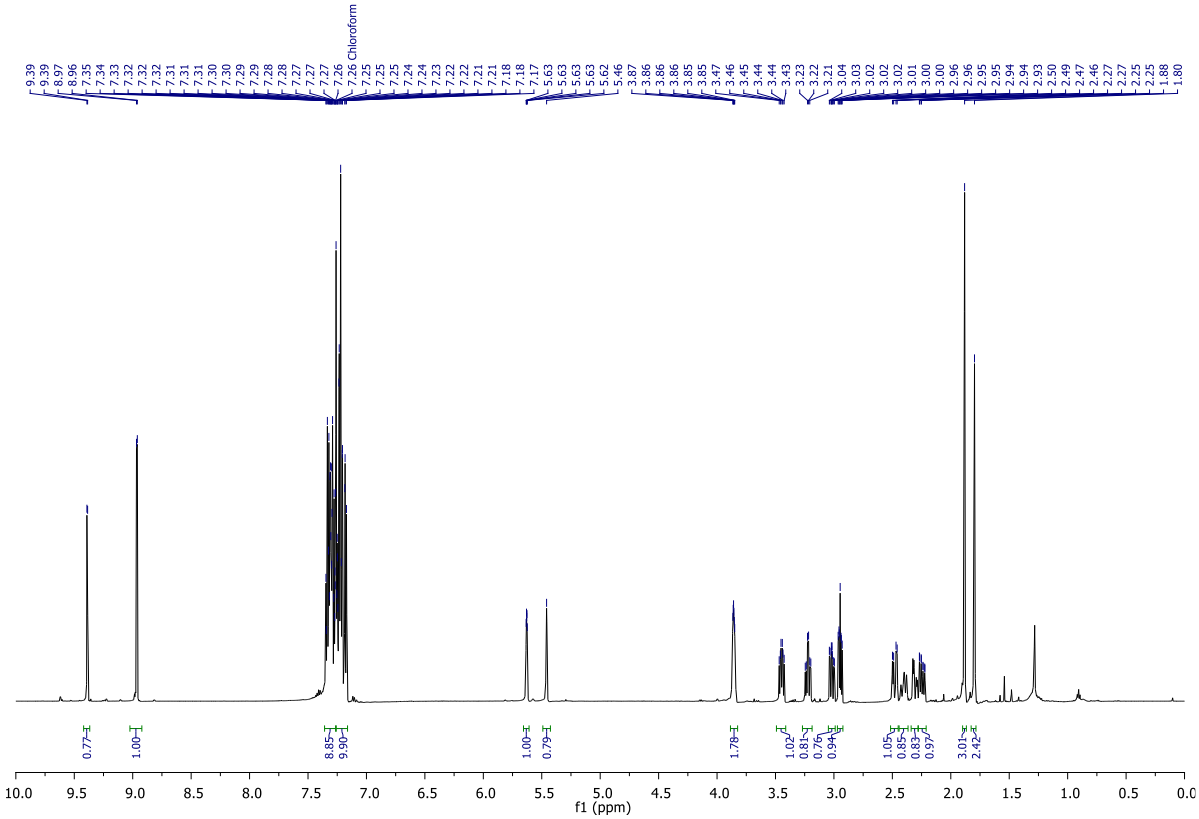


Figure S46. ^1H NMR spectrum of **2e** ($CDCl_3$, 600 MHz, 298 K)

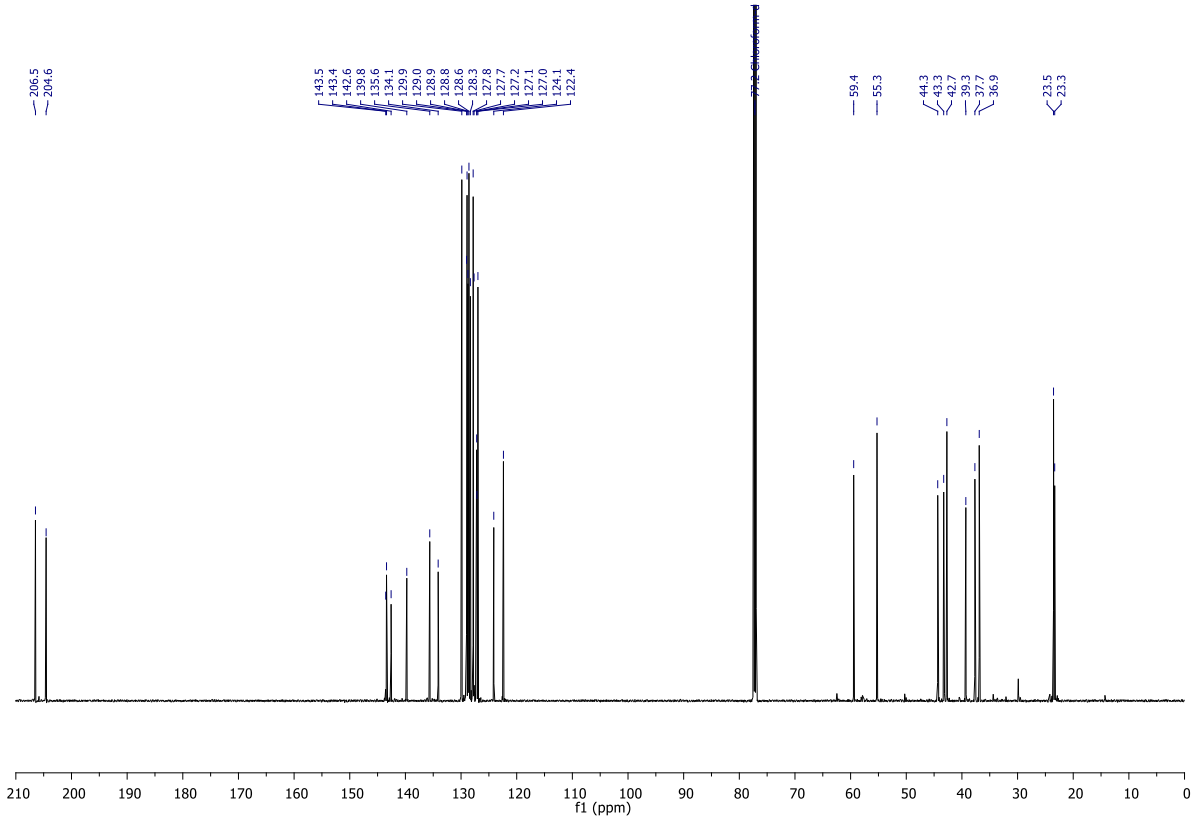


Figure S47. ^{13}C NMR spectrum of **2e** ($CDCl_3$, 151 MHz, 298 K)

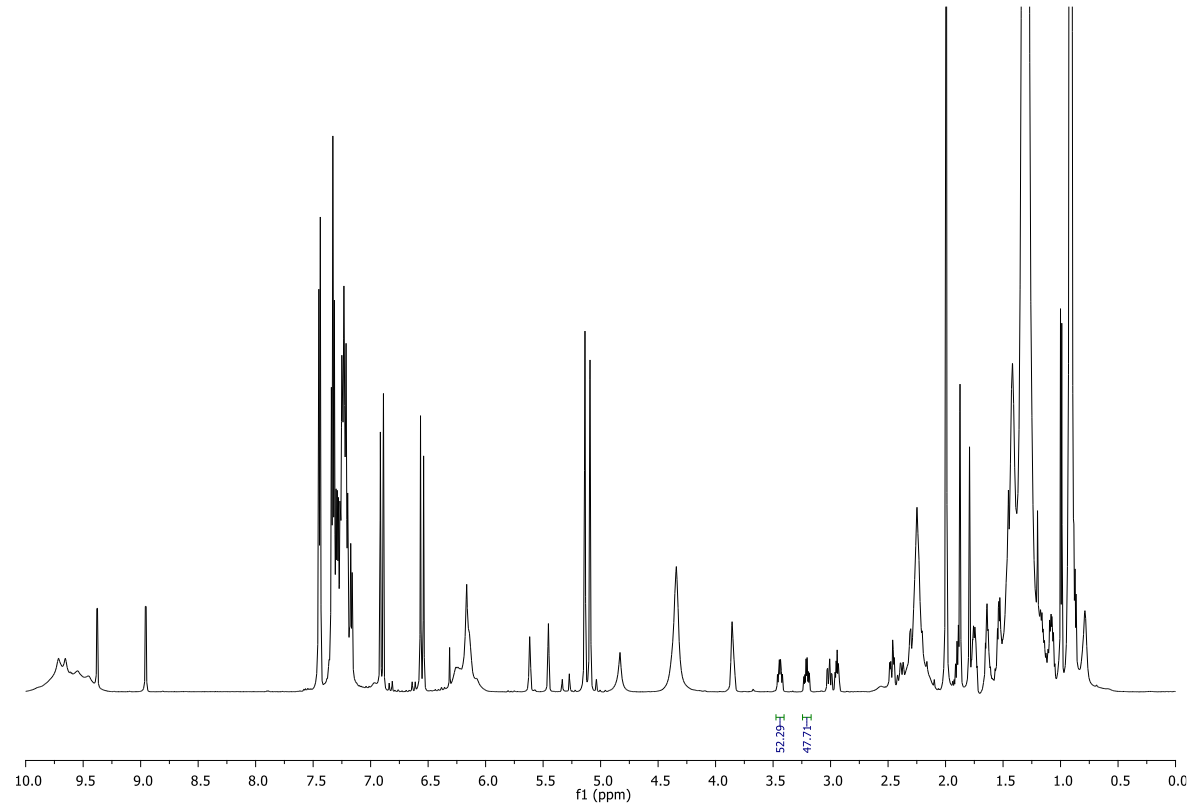


Figure S48. ^{1}H NMR spectrum of crude **2e** denoting diastereomeric ratio ($CDCl_3$, 600 MHz, 298 K)

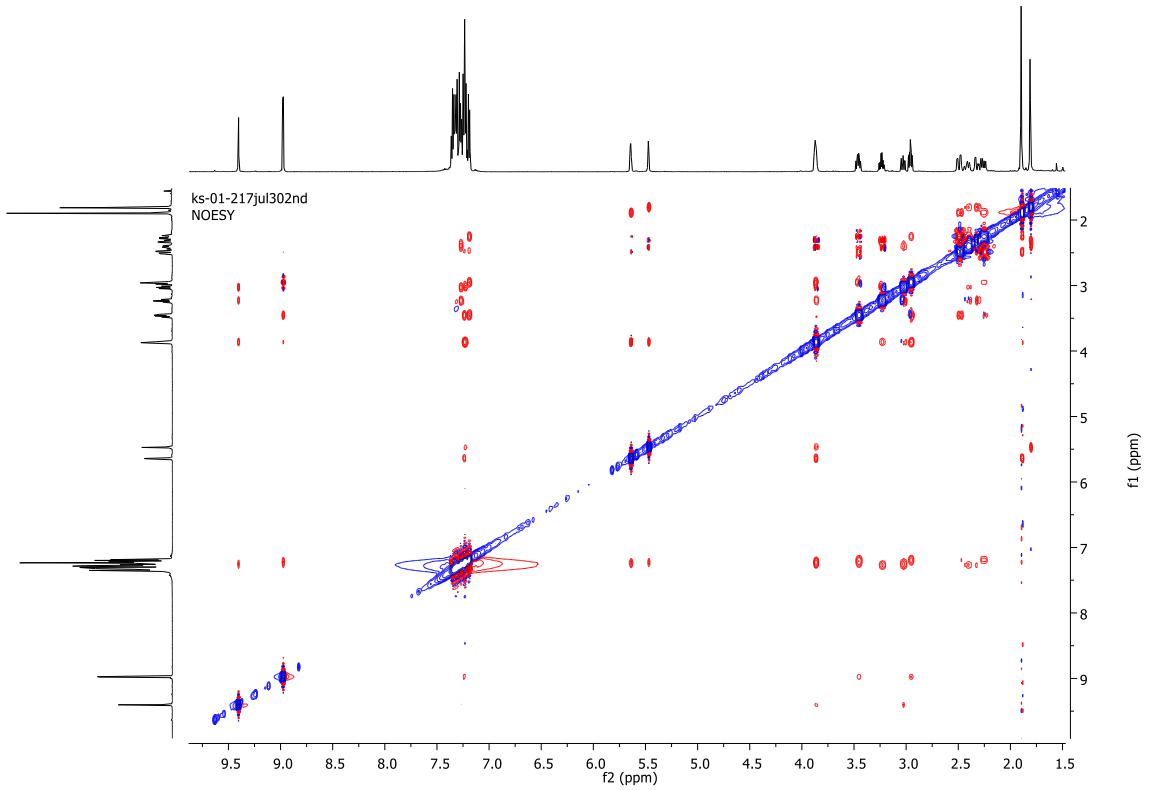


Figure S49. NOESY NMR spectrum of **2e** diastereomers ($CDCl_3$, 600 MHz, 298 K)

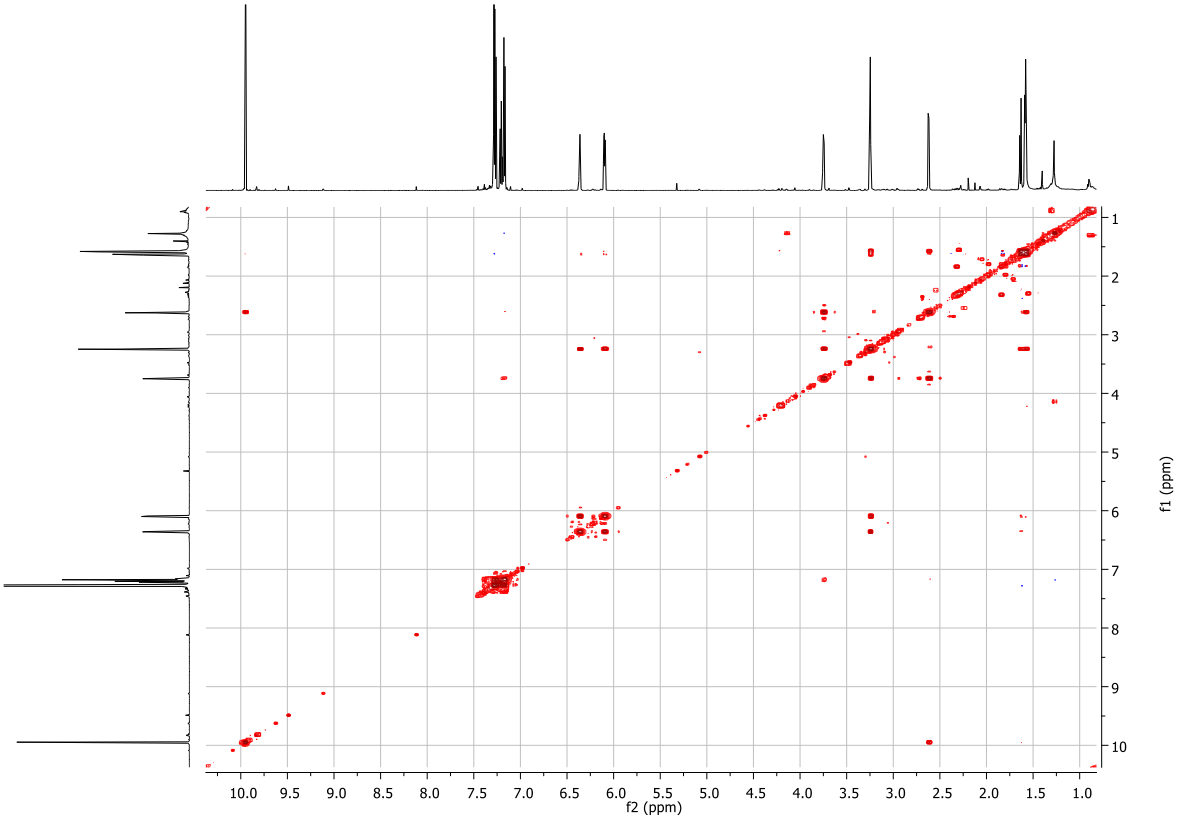


Figure S50. COSY spectrum of **2e–OH (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

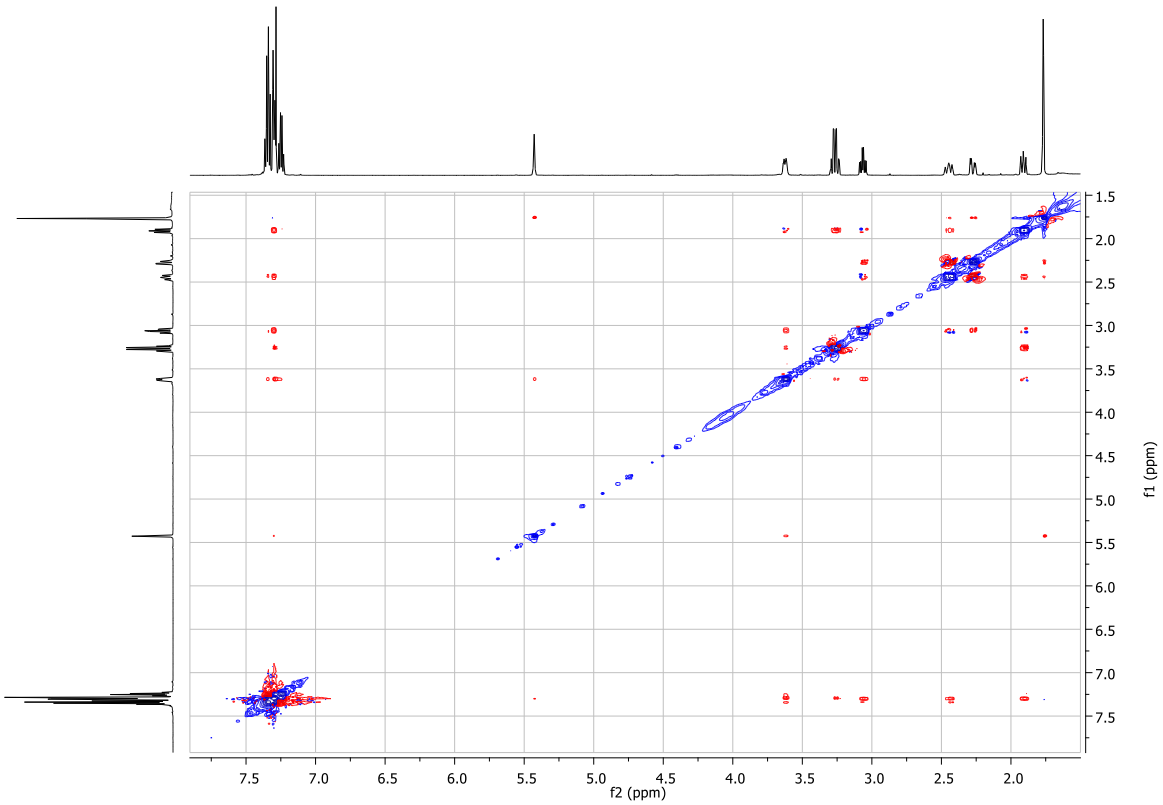


Figure S51. NOESY spectrum of **2e–OH (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

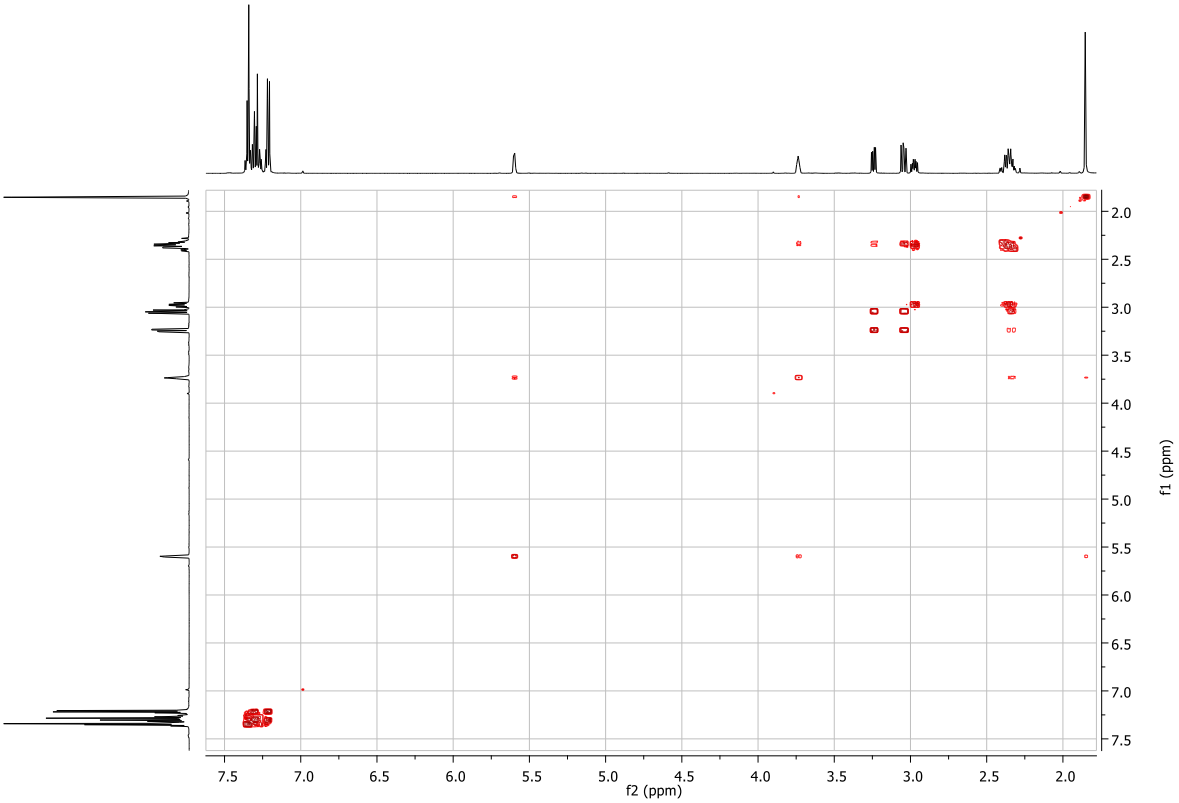


Figure S52. COSY spectrum of **2e–OH (Minor Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

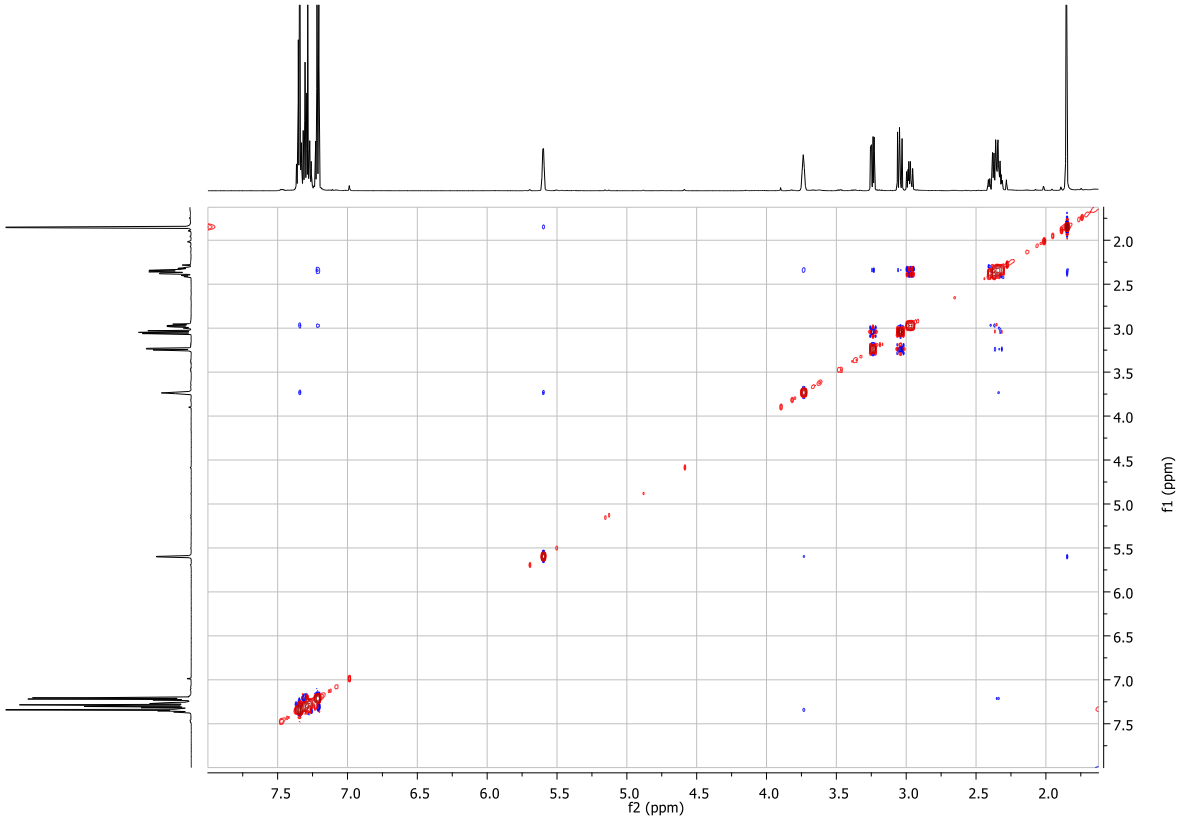


Figure S53. NOESY spectrum of **2e–OH (Minor Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

6. ^{1}H or ^{19}F Data of Mosher Esters

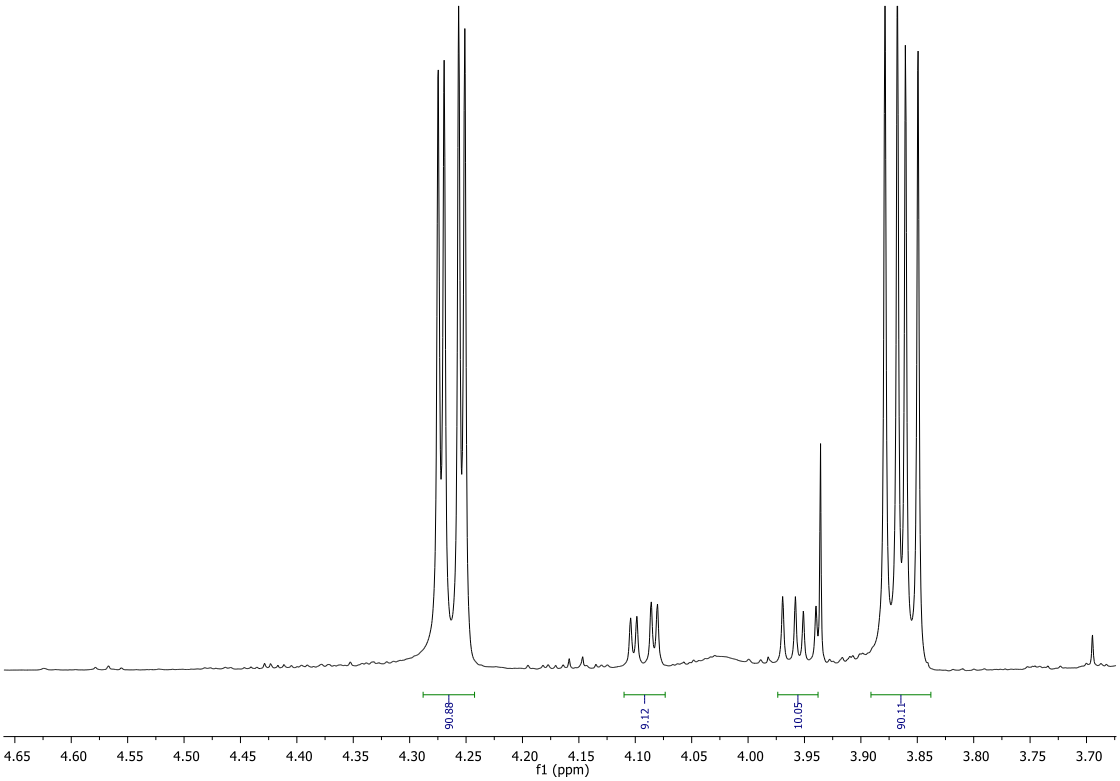


Figure S54. ^{1}H Spectrum of **1a-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

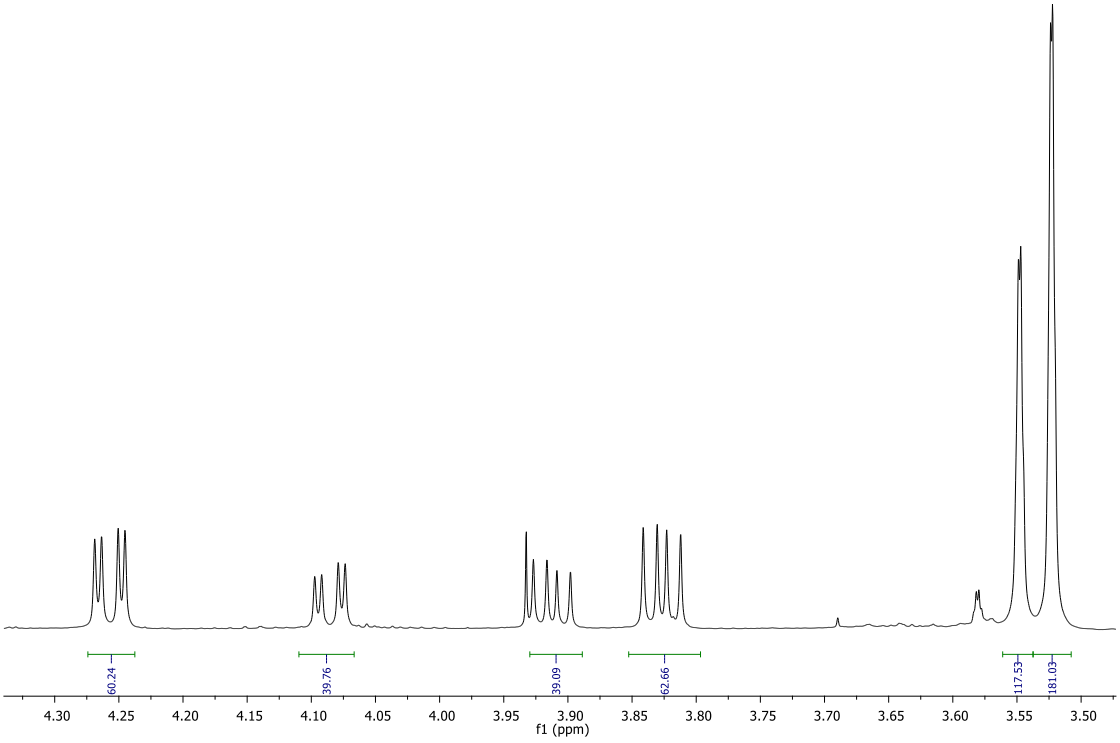


Figure S55. ^{1}H Spectrum of **1b-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

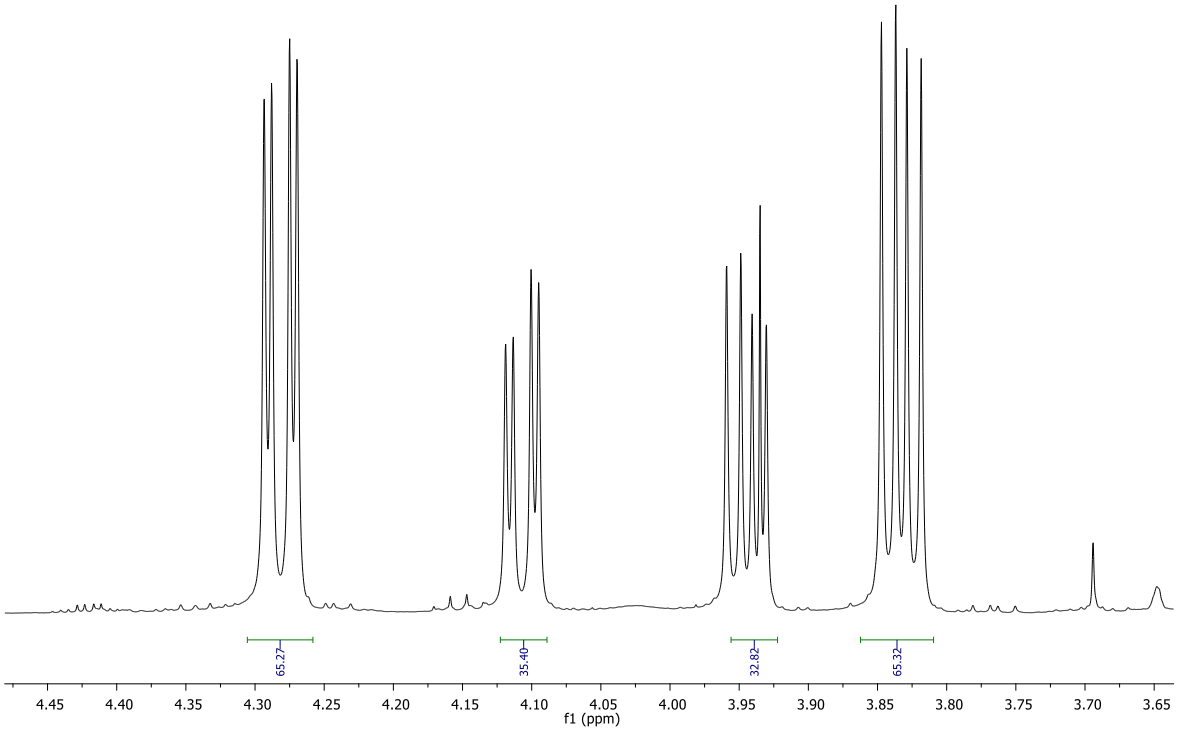


Figure S56. ^{1}H Spectrum of **1c-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

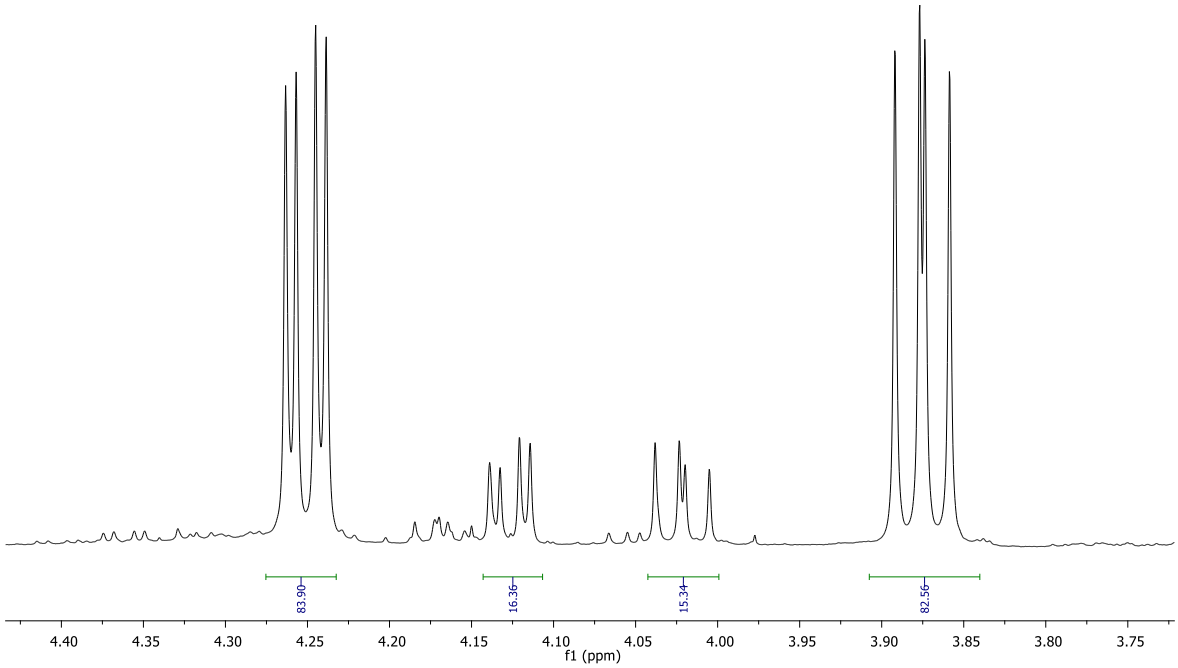


Figure S57. ^{1}H Spectrum of **1d-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

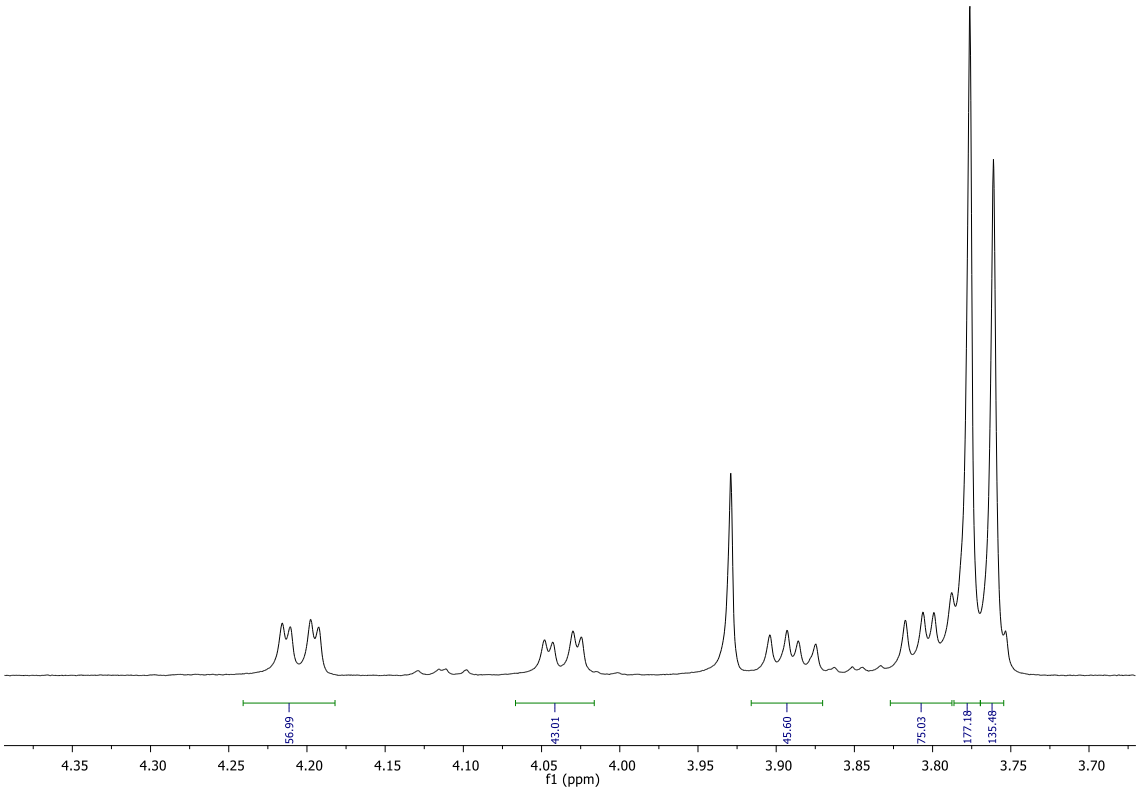


Figure S58. ^{1}H Spectrum of **1e-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

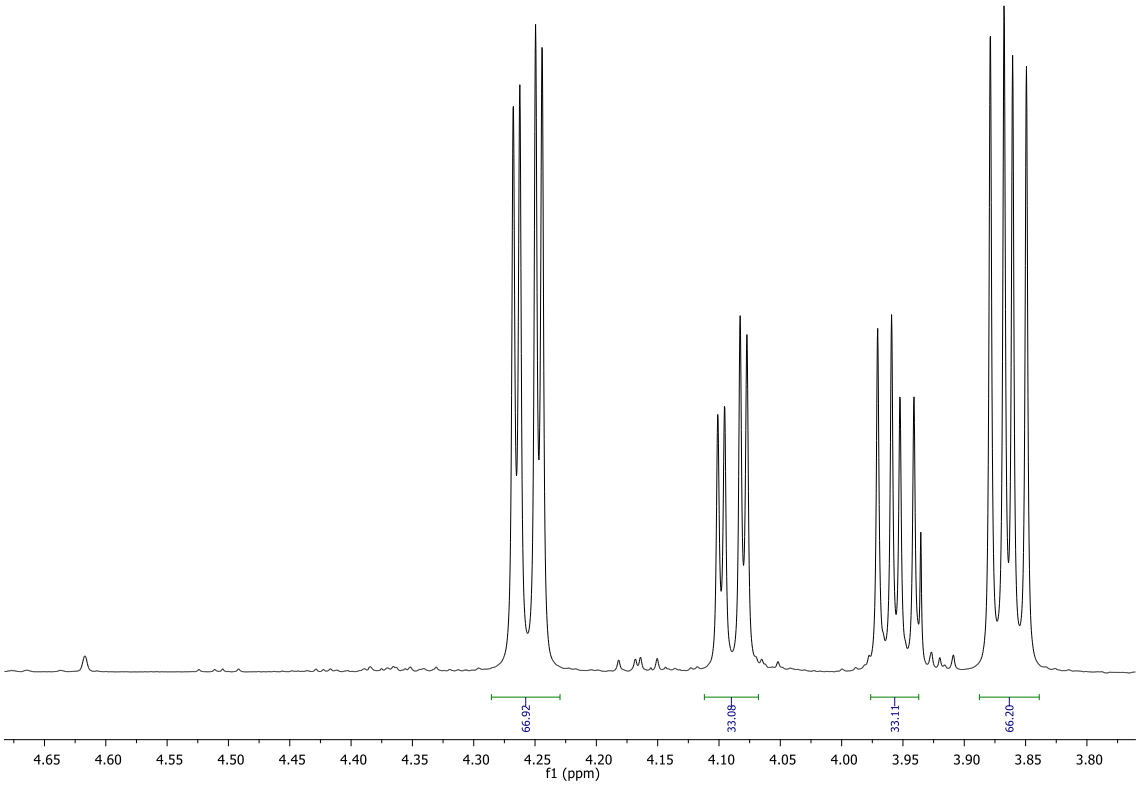


Figure S59. ^{1}H Spectrum of **1f-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

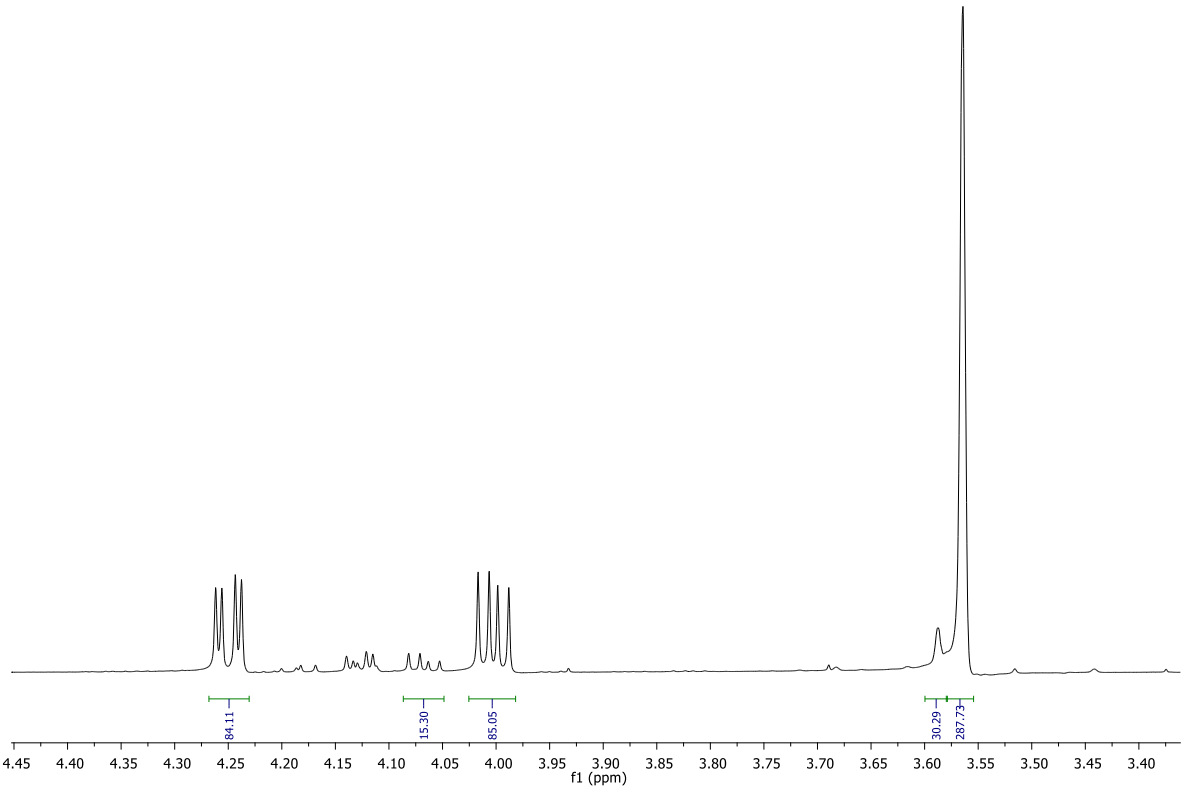


Figure S60. ^{1}H Spectrum of **1g-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

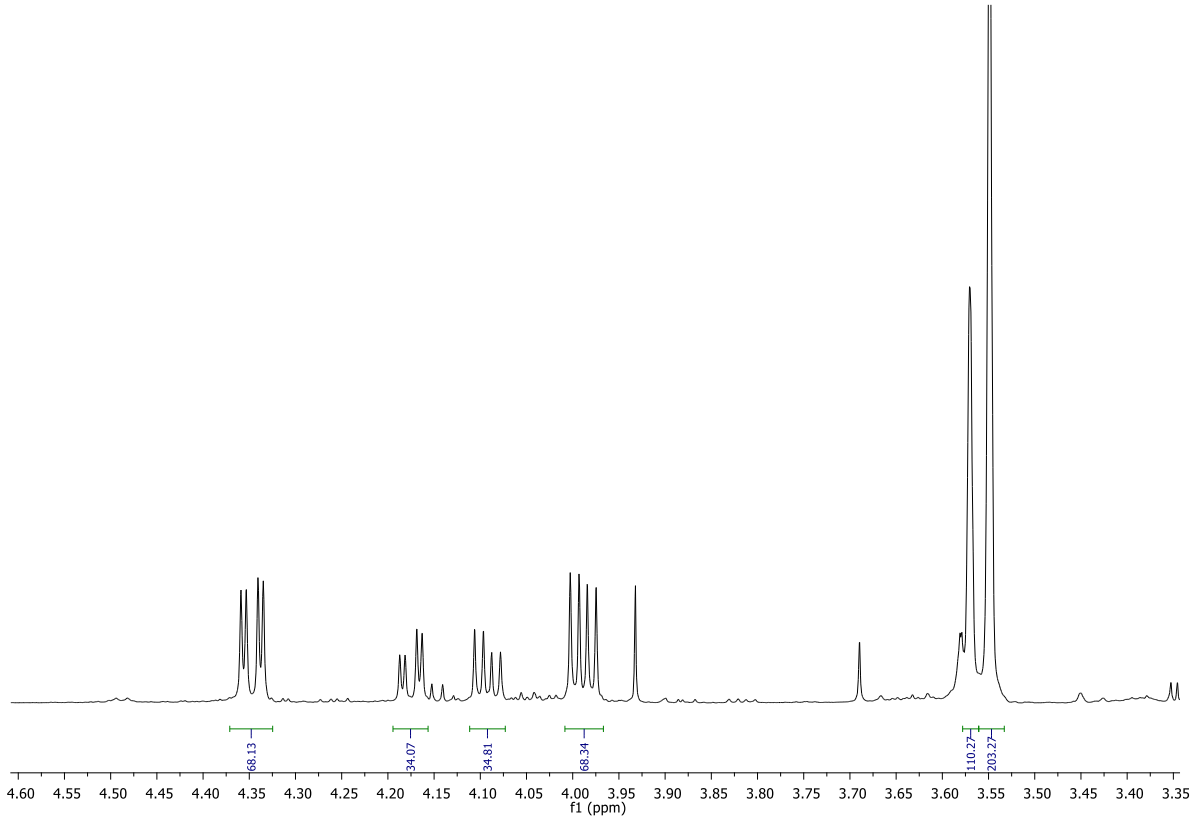


Figure S61. ^{1}H Spectrum of **1h-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

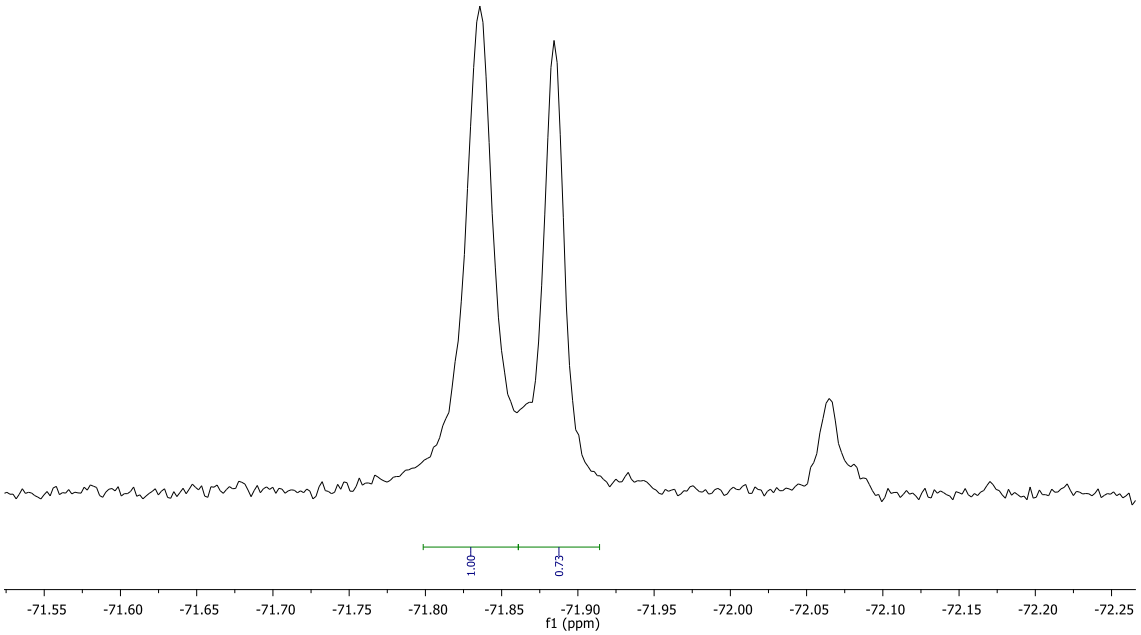


Figure S62. ^{19}F Spectrum of **1i-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 376 MHz, 298 K)

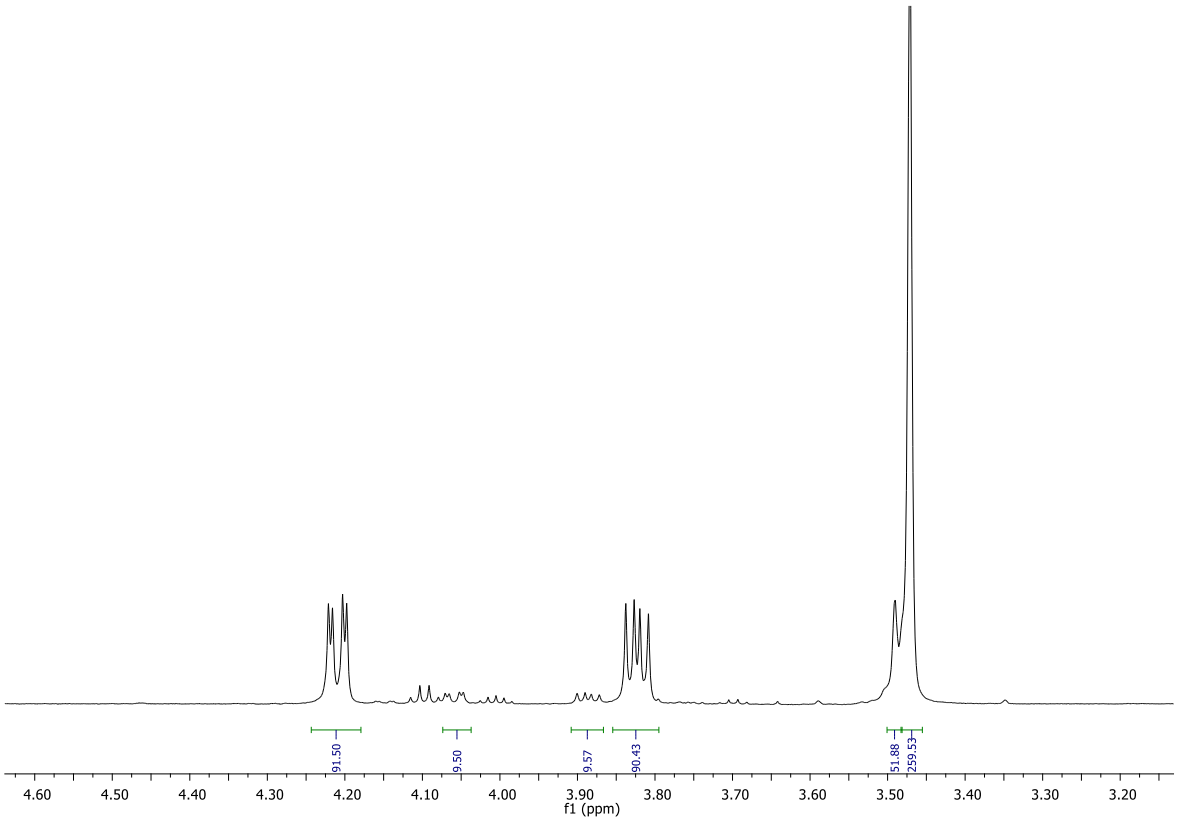


Figure S63. ^{1}H Spectrum of **2a-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz or 376 MHz, 298 K)

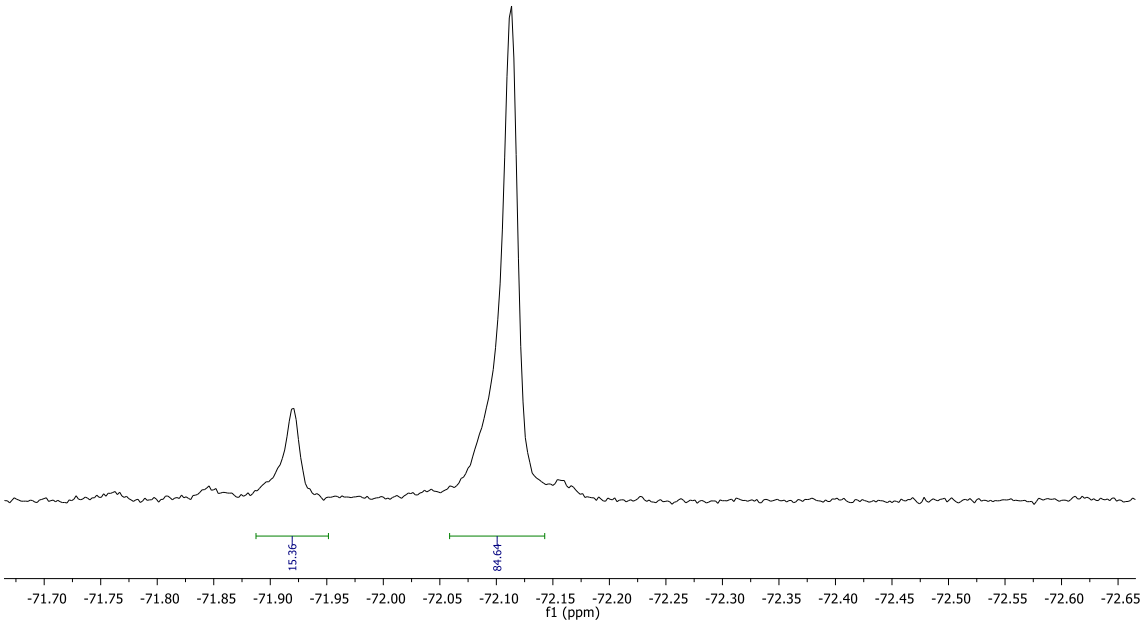


Figure S64. ^{19}F Spectrum of **2b-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 376 MHz, 298 K)

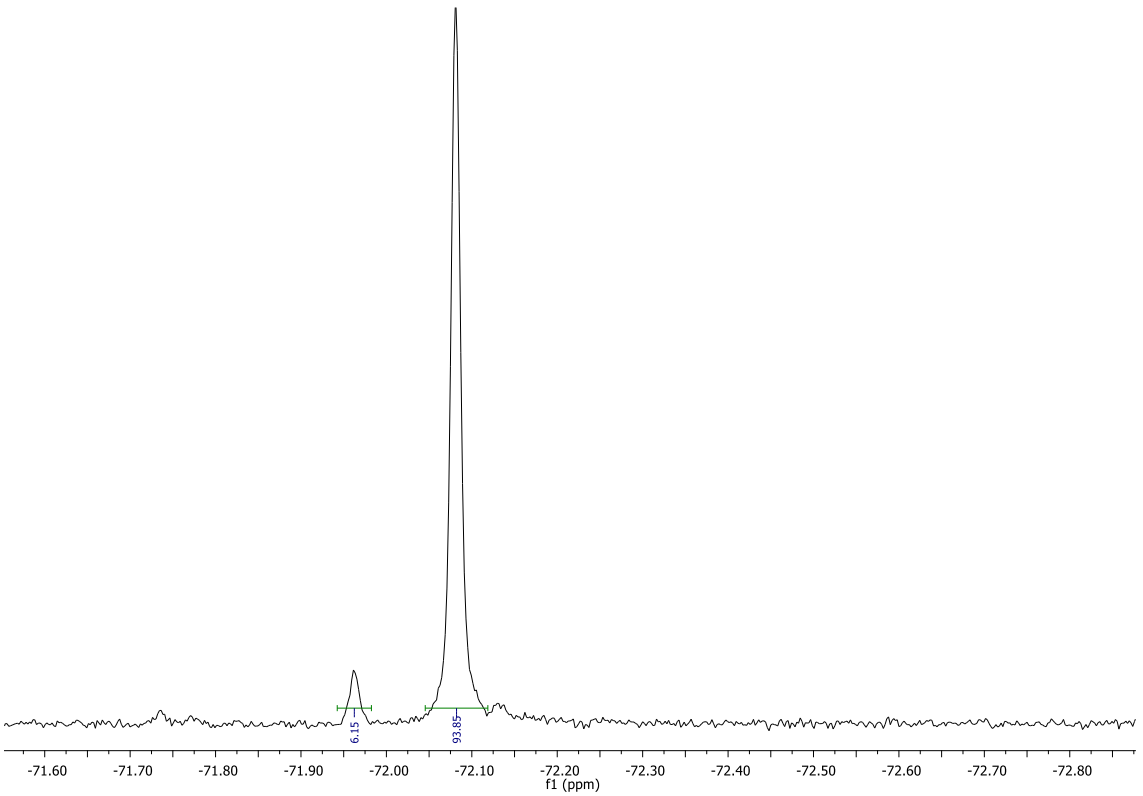


Figure S65. ^{19}F Spectrum of **2c-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 376 MHz, 298 K)

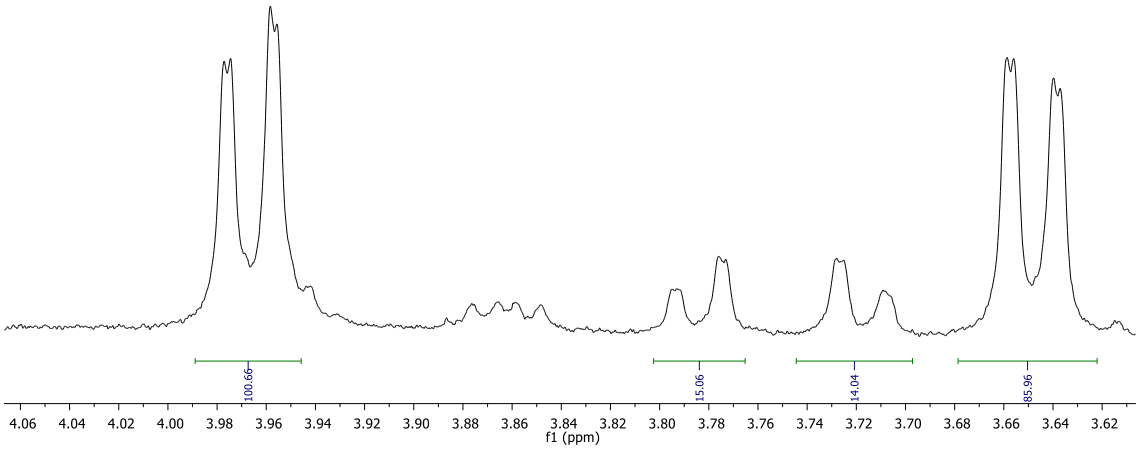


Figure S66. ^{1}H Spectrum of **2d-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

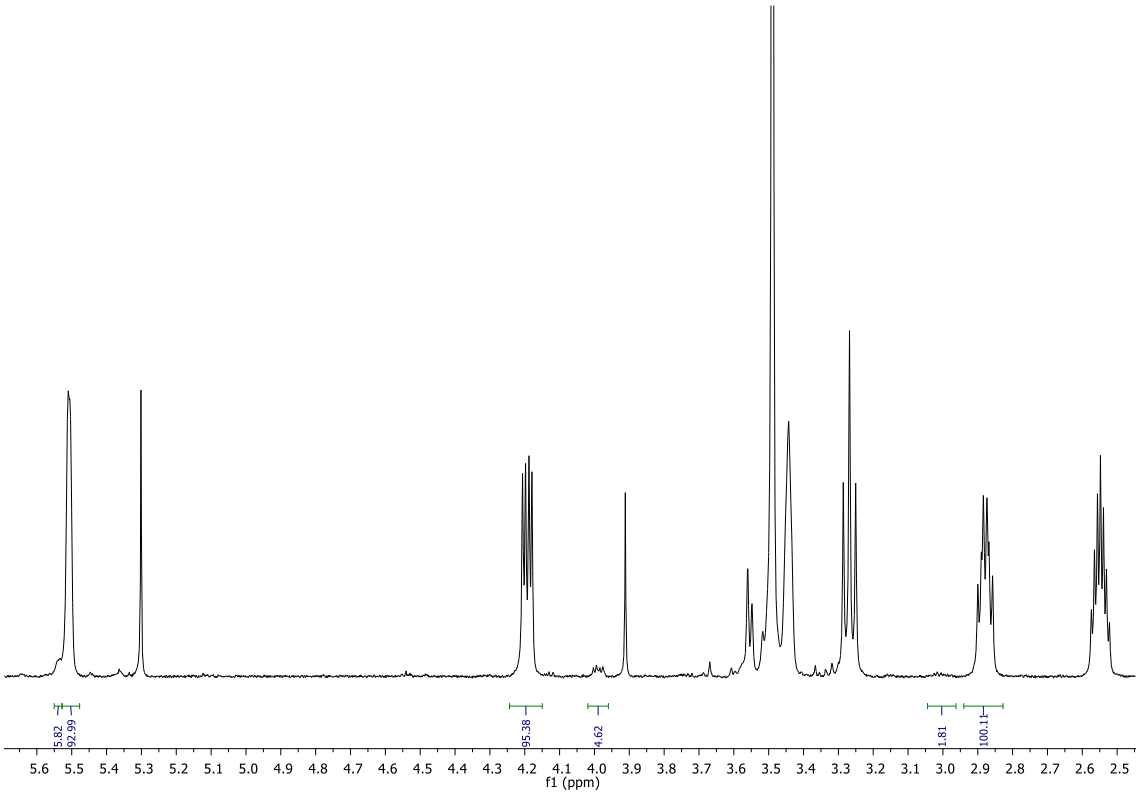


Figure S67. ^{1}H Spectrum of **2f-Mosher Ester (Major Diastereomer)** ($CDCl_3$, 600 MHz, 298 K)

7. References

[1] G. R. Fulmer, A. J. M. Miller, N. H. Sherden, H. E. Gottlieb, A. Nudelman, B. M. Stoltz, J. E. Bercaw and K. I. Goldberg, *Organometallics*, 2010, **29**, 2176-2179.

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