Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Asymmetric [2+2] Photocycloaddition via Charge Transfer Complex for the Synthesis of Tricyclic Chiral Ethers

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General Information

The ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a *Bruker Avance 300 MHz spectrometer* at 300, 75 and 282 MHz, respectively. The chemical shifts (δ) for ^{1}H NMR are reported relative to the tetramethylsilane signal at 0 ppm or relative to the residual signal of the solvent ($CDCl_3$ at 7.26 ppm), while for ^{13}C NMR are given in ppm relative to the residual signal of the solvent ($CDCl_3$ at 77.16 ppm). ^{13}C NMR spectra were acquired on a broadband decoupled mode. Coupling constants are given in Hz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; hept, heptet; m, multiplet; br, broad signal.

Optical rotations were recorded on a *Perkin Elmer 241 MC* Polarimeter in a 10 cm path length cell in HPLC grade $CHCl_3$ (concentration in g/100 mL).

Enantiomeric ratios were determined by Supercritical Fluid Chromatography (SFC) on chiral columns on an *Agilent Technologies 1260 Infinity Series* instrument, employing *Daicel Chiralpak* IA, IB-3, IC, ID-3 and IG-3 columns and a UV-Vis detector. The exact conditions for the analyses are specified in each case.

High-Resolution Mass Spectra (HRMS) were obtained on an *Agilent Technologies 6120 Quadrupole LC/MS* coupled with an SFC *Agilent Technologies 1260 Infinity Series* instrument for the ESI-MS (Electrospray Ionization). *MassWorks* software version 4.0.0.0 (*Cerno Bioscience*) was used for the formula identification. *MassWorks* is an MS calibration software which calibrates isotope profiles to achieve high mass accuracy and enables elemental composition determination on conventional mass spectrometers of unit mass resolution allowing highly accurate comparisons between calibrated and theoretical spectra.[1]

UV-Vis measurements were carried out on an *Agilent 8453 UV-Visible Spectroscopy System* controlled by *UV-Visible ChemStation Software*. Diethyl ether and a Teflon-top 10x10 mm precision cell made of Quartz SUPRASIL® were used for all absorption measurements. The solution concentration used for recording the absorption spectra was 0.05 M (0.1 mmol of **1a**, 0.02 mmol of catalyst **3**, 0.1 mmol of TFA, and 2 mL of solvent).

Materials and Methods

Commercial grade reagents and solvents were purchased from Sigma-Aldrich, Alfa Aesar, Fluorochem, Acros Organics, TCI Chemicals, Strem Chemicals and used without further purifications while anhydrous solvents were taken from a SPS solvent dispenser. Chromatographic purification of products was accomplished using flash chromatography (FC) on Merck Geduran® Si 60 silica gel (40-63 μm). Thin layer chromatography (TLC) was performed on Merck precoated TLC plates (silica gel 60 F254).

Photoreactor Setup

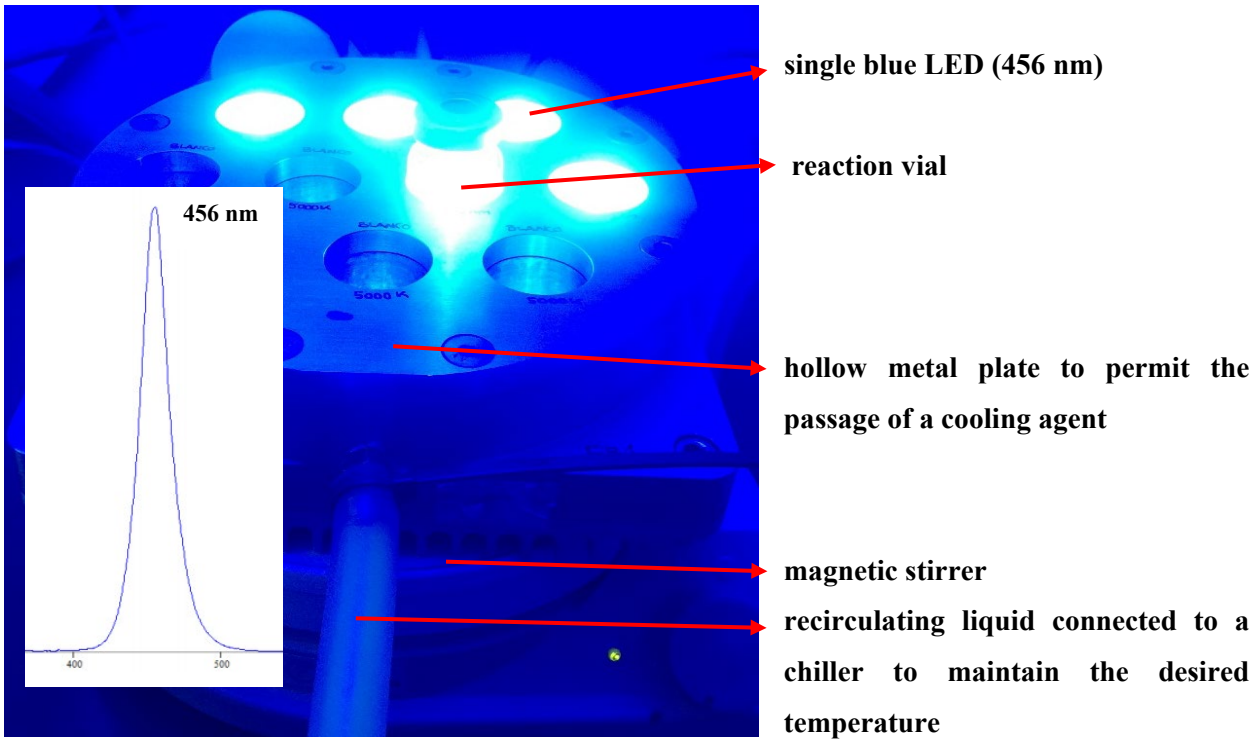


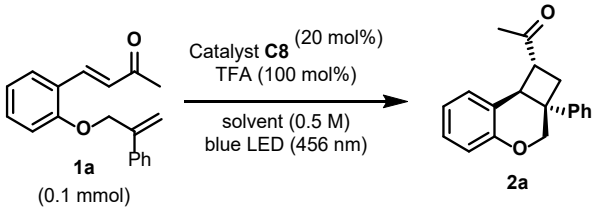
Figure S1: Photoreactor setup.

Catalyst Synthesis

The synthesis of the diamine catalysts was carried out according to the procedures reported in the literature.[2]

Optimization and Decomposition Studies

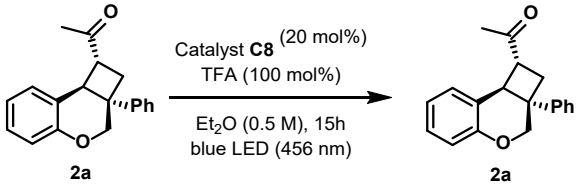
Table S1: Solvent screening (selected examples)



Solvent	Conversion[a](%)	yield	er [b]
DCE	60	27	62:38
THF	40	25	82:18
C_6F_6	84	37	80.20
i-PrOH	90	17	73:27
dioxane	57	31	80:20
i-Pr_2O	100	22	83:17
Ph_2O	100	37	82:18
Et_2O	**100**	**52**	**83:17**

[a] Determined by ^{1}H NMR of the crude mixture after 15h.
[b] Determined by chiral SFC analysis of the isolated product.

Table S2: Decomposition studies (selected examples)

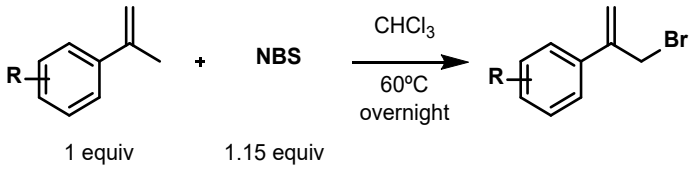


deviation from above conditions	yield[a]
none	36
no catalyst	45
no catalyst and no TFA	52

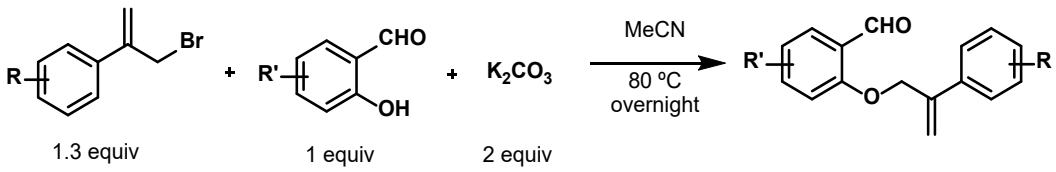
[a] Determined by ^{1}H NMR with 9-bromo-phenanthrene as the internal standard

General procedure A for the synthesis of substrates 1a-l

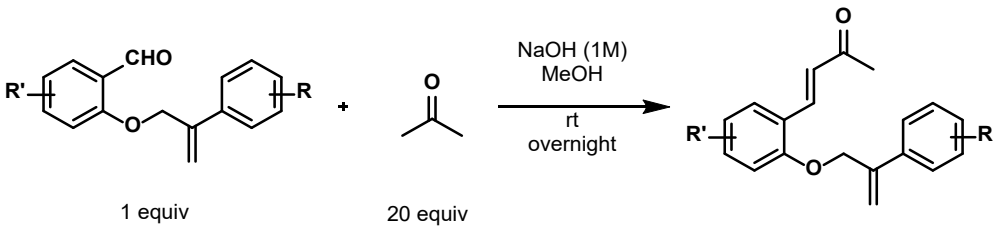
Step 1: To a solution of styrene derivative (1 equiv) in chloroform (0.15 mL/mmol) was added *N*-bromosuccinimide (1.15 equiv). The reaction mixture was stirred overnight at 60 ºC in a sealed tube. Then, after cooling, diethyl ether was added and the organic phase separated. The aqueous phase was extracted with diethyl ether, while the combined organic phases were washed with brine and dried over magnesium sulfate. After flash chromatography the corresponding allyl bromide was obtained as a pure product.



Step 2: An acetonitrile mixture (1 mL/mmol) of the corresponding salicylaldehyde derivative (1 equiv) and the corresponding allyl bromide (1.3 equiv) was stirred overnight at 80 ºC in a sealed tube in the presence of potassium carbonate (2 equiv). After cooling, diethyl ether was added and the organic phase separated. The aqueous phase was extracted with diethyl ether, while the combined organic phases were washed with brine and dried over magnesium sulfate. After removal of the solvents under reduced pressure, the crude product was obtained, which was used in the next step without further purification

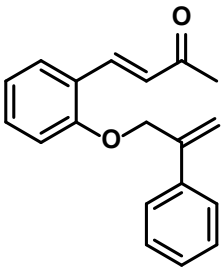


Step 3: A solution of the corresponding aldehyde (1 equiv) in methanol (1 mL/mmol) was added dropwise to a stirring mixture of acetone (20 equiv) and 1 M sodium hydroxide solution (5 mL/mmol). After overnight stirring, diethyl ether was added and the organic phase separated. The aqueous phase was extracted with diethyl ether, whereas the combined organic phases were washed with brine and dried over magnesium sulfate. After removal of the solvents under reduced pressure, the crude mixture was purified by flash chromatography to obtain the corresponding enone.



Characterization data for enones (1a-l)

(*E*)-4-(2-((2-phenylallyl)oxy)phenyl)but-3-en-2-one (1a)



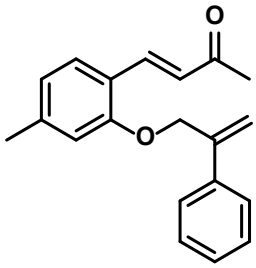
Compound **1a** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (9.1 mmol) and 2-hydroxybenzaldehyde (7 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 80:20) to obtain 1.14 g as a colorless oil (58% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16.5 Hz, 1H), 7.57 – 7.43 (m, 3H), 7.38 – 7.31 (m, 4H), 7.01 – 6.96 (m, 2H), 6.62 (d, *J* = 16.5 Hz, 1H), 5.60 (br s, 1H), 5.45 (br s, 1H), 4.99 (br s, 2H), 2.17 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 199.0, 157.1, 143.0, 138.5, 138.1, 131.6, 128.5 (2C), 128.4, 128.1, 127.8, 126.1 (2C), 123.9, 121.2, 115.0, 112.8, 70.4, 26.8.

HRMS (ESI): calculated for $C_{19}H_{18}O_2^+$ [M+H]+ = 279.1380; found = 279.1398.

(*E*)-4-(4-methyl-2-((2-phenylallyl)oxy)phenyl)but-3-en-2-one (1b)



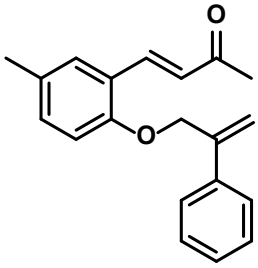
Compound **1b** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (2.0 mmol) and 2-hydroxy-4-methylbenzaldehyde (1.7 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 80:20) to obtain 323 mg as a pale yellow oil (65% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 16.5 Hz, 1H), 7.56 – 7.44 (m, 2H), 7.43 (d, *J* = 8.2 Hz, 1H), 7.42 – 7.29 (m, 3H), 6.85 – 6.77 (m, 2H), 6.60 (d, *J* = 16.5 Hz, 1H), 5.62 (br s, 1H), 5.45 (br s, 1H), 4.99 (br s, 2H), 2.38 (s, 3H), 2.17 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 199.1, 157.2, 143.1, 142.5, 138.6, 138.2, 128.5 (2C), 128.3, 128.1, 126.9, 126.1 (2C), 122.2, 121.2, 115.0, 113.6, 70.4, 26.7, 21.9.

HRMS (ESI): calculated for $C_{20}H_{20}O_2^+$ [M+H]+ = 293.1536; found = 293.1570.

(*E*)-4-(5-methyl-2-((2-phenylallyl)oxy)phenyl)but-3-en-2-one (1c)



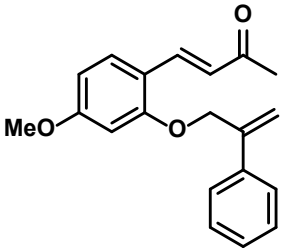
Compound **1c** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (2.0 mmol) and 2-hydroxy-5-methylbenzaldehyde (1.6 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 80:20) to obtain 292 mg as a pale yellow oil (64% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.71 (d, *J* = 16.5 Hz, 1H), 7.52 – 7.43 (m, 2H), 7.43 – 7.30 (m, 4H), 7.21 – 7.11 (m, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.62 (d, *J* = 16.5 Hz, 1H), 5.64 – 5.57 (m, 1H), 5.48 – 5.41 (m, 1H), 4.98 (br s, 2H), 2.31 (s, 3H), 2.18 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 199.1, 155.2, 143.2, 138.7, 138.2, 132.2, 130.6, 128.7, 128.5 (2C), 128.1, 127.7, 126.2 (2C), 123.7, 115.0, 113.0, 70.7, 26.8, 20.5.

HRMS (ESI): calculated for $C_{20}H_{20}O_2^+$ [M+H]+ = 293.1536; found = 293.1550.

(*E*)-4-(4-methoxy-2-((2-phenylallyl)oxy)phenyl)but-3-en-2-one (1d)



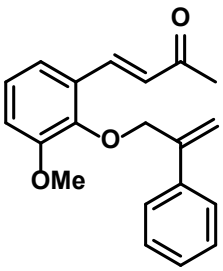
Compound **1d** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (1.6 mmol) and 2-hydroxy-4-methoxybenzaldehyde (1.2 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 80:20) to obtain 250 mg as a pale yellow oil (68% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.67 (d, *J* = 16.5 Hz, 1H), 7.52 – 7.42 (m, 3H), 7.43 – 7.28 (m, 3H), 6.59 – 6.51 (m, 3H), 5.61 (br s, 1H), 5.46 (br s, 1H), 4.98 (br s, 2H), 3.84 (s, 3H), 2.16 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 199.1, 162.8, 158.6, 142.9, 138.6, 138.2, 129.8, 128.5 (2C), 128.2, 126.2 (2C), 125.7, 117.0, 115.2, 106.1, 99.9, 70.5, 55.5, 26.8.

HRMS (ESI): calculated for $C_{20}H_{23}O_3^+$ [M+H]+ = 309.1485; found = 309.1500.

(*E*)-4-(3-methoxy-2-((2-phenylallyl)oxy)phenyl)but-3-en-2-one (1e)



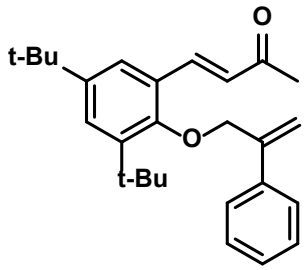
Compound **1e** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (8.5 mmol) and 2-hydroxy-3-methoxybenzaldehyde (6.6 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 50:50) to obtain 154 mg as a pale yellow oil (76% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.64 (d, *J* = 16.7, 1H), 7.58 – 7.51 (m, 2H), 7.38 – 7.28 (m, 3H), 7.14 (dd, *J* = 7.9, 1.9 Hz, 1H), 7.06 (td, *J* = 7.9, 2.3 Hz, 1H), 6.96 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.51 (d, *J* = 16.7, 1H), 5.61 – 5.57 (m, 1H), 5.41 – 5.37 (m, 1H), 5.01 – 4.98 (m, 2H), 3.90 (s, 3H), 2.07 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 199.2, 152.9, 146.9, 143.7, 138.7, 138.3, 129.1, 128.6, 128.5 (2C), 128.1, 126.1 (2C), 124.2, 118.7, 116.2, 114.1, 75.2, 55.9, 26.1.

HRMS (ESI): calculated for $C_{20}H_{23}O_3^+$ [M+H]+ = 309.1485; found = 309.1498.

(*E*)-4-(3,5-di-*tert*-butyl-2-((2-phenylallyl)oxy)phenyl)but-3-en-2-one (1f)



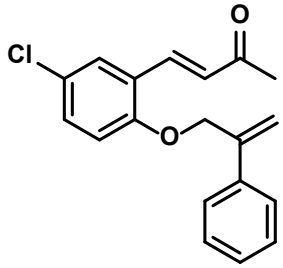
Compound **1f** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (1.6 mmol) and 3,5-di-tert-butyl-2-hydroxybenzaldehyde (1.3 mmol). The crude aldehydic intermediate was used in the subsequent aldol reaction which was performed at 40 ºC (instead of rt). After purification by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 90:10) 270 mg of product were obtained as a pale orange solid (69% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16.5 Hz, 1H), 7.37 (s, 2H), 7.34 – 7.19 (m, 5H), 6.60 (d, *J* = 16.5 Hz, 1H), 5.66 (d, *J* = 1.6 Hz, 1H), 5.55 (d, *J* = 1.5 Hz, 1H), 4.66 – 4.62 (m, 2H), 2.17 (s, 3H), 1.35 (s, 9H), 1.24 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 199.0, 155.8, 146.3, 143.9, 142.7, 140.5, 138.4, 128.5 (2C), 128.2, 128.1, 127.8, 126.9, 125.9 (2C), 122.7, 112.8, 76.3, 35.3, 34.6, 31.4 (3C), 30.9 (3C), 26.4.

HRMS (ESI): calculated for $C_{27}H_{34}O_2^+$ [M+H]+ = 391.2632; found = 391.2640.

(*E*)-4-(5-chloro-2-((2-phenylallyl)oxy)phenyl)but-3-en-2-one (1g)



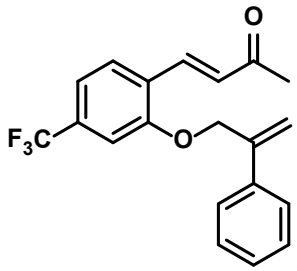
Compound **1g** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (2.54 mmol) and 5-chloro-2-hydroxybenzaldehyde (2 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 80:20) to obtain 232 mg as a colorless solid (37% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 16.6 Hz, 1H), 7.49 – 7.42 (m, 3H), 7.38 – 7.31 (m, 3H), 7.28 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 16.5 Hz, 1H), 5.61 – 5.59 (m, 1H), 5.44 – 5.41 (m, 1H), 4.98 (br s, 2H), 2.17 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.5, 155.6, 142.7, 137.9, 136.9, 131.0, 128.7, 128.5 (2C), 128.2, 127.9, 126.4, 126.1 (2C), 125.6, 115.3, 114.3, 70.9, 27.0.

HRMS (ESI): calculated for $C_{19}H_{17}ClO_2^+$ [M+H]+ = 313.0990; found = 313.1010.

(*E*)-4-(2-((2-phenylallyl)oxy)-4-(trifluoromethyl)phenyl)but-3-en-2-one (1h)



Compound **1h** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (2.7 mmol) and 2-hydroxy-4-(trifluoromethyl)benzaldehyde (2.1 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 50:50) to obtain 346 mg as a pale yellow oil (48% yield).

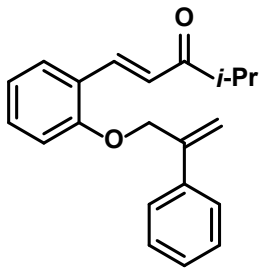
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.59 (d, *J* = 16.7 Hz, 1H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.38 – 7.24 (m, 3H), 7.23 – 7.12 (m, 2H), 6.60 (d, *J* = 16.5 Hz, 1H), 5.61 – 5.54 (m, 1H), 5.45 – 5.38 (m, 1H), 4.99 (br s, 2H), 2.09 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.6, 156.9, 142.6, 137.9, 136.8, 132.9 (q, $^{2}J_{C\text{-}F}$ = 32.6 Hz), 129.8, 128.9, 128.6 (2C), 128.3, 127.4 (q, $^{4}J_{C\text{-}F}$ = 1.4 Hz), 126.2 (2C), 123.6 (q, $^{1}J_{C\text{-}F}$ = 272.6 Hz), 118.0 (q, $^{3}J_{C\text{-}F}$ = 3.9 Hz), 115.8, 109.6 (q, $^{3}J_{C\text{-}F}$ = 3.9 Hz), 70.9, 27.1.

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.9.

HRMS (ESI): calculated for $C_{20}H_{17}F_3O_2^+$ [M+H]+ = 347.1253; found = 347.1280.

(*E*)-4-methyl-1-(2-((2-phenylallyl)oxy)phenyl)pent-1-en-3-one (1i)



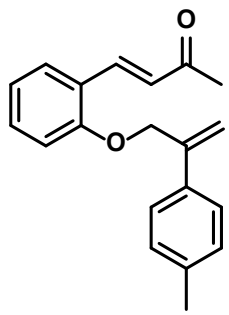
Compound **1i** was synthetized according to the general procedure A. The reaction was performed employing 2-phenylallyl bromide (7.6 mmol) and 2-hydroxybenzaldehyde (5.8 mmol). The aldol condensation was performed employing methyl isopropyl ketone instead of acetone and subsequent treatment with mesityl chloride (1.1 equiv) and pyridine (0.5M). It was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 90:10) to obtain 90 mg as a colorless solid (5% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.81 (d, *J* = 16.3 Hz, 1H), 7.56 – 7.46 (m, 3H), 7.43 – 7.29 (m, 4H), 7.04 – 6.95 (m, 2H), 6.77 (d, *J* = 16.2 Hz, 1H), 5.68 – 5.59 (m, 1H), 5.51 – 5.44 (m, 1H), 5.00 (br s, 2H), 2.75 (hept, *J* = 6.9 Hz, 1H), 1.07 (d, *J* = 6.9 Hz, 6H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 204.6, 157.5, 142.9, 138.2, 137.7, 131.3, 129.3, 128.5 (2C), 128.1, 126.1 (2C), 125.8, 124.2, 121.2, 115.2, 112.6, 70.4, 38.5, 18.6 (2C).

HRMS (ESI): calculated for $C_{21}H_{22}O_2^+$ [M+H]+ = 307.1693; found = 307.1598.

(*E*)-4-(2-((2-(*p*-tolyl)allyl)oxy)phenyl)but-3-en-2-one (1j)



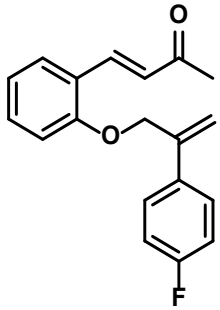
Compound **1j** was synthetized according to the general procedure A. The reaction was performed employing 2-(4-tolyl)allyl bromide (3.8 mmol) and 2-hydroxybenzaldehyde (3.15 mmol). The product derived from the subsequent aldol reaction was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 90:10) to obtain 438 mg as a pale yellow solid (48% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 16.5 Hz, 1H), 7.40 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.28 – 7.19 (m, 3H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.89 – 6.84 (m, 2H), 6.52 (d, *J* = 16.5 Hz, 1H), 5.45 (br s, 1H), 5.30 – 5.27 (m, 1H), 4.85 (br s, 2H), 2.23 (s, 3H), 2.06 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.9, 157.1, 142.7, 138.5, 137.8, 135.1, 131.5, 129.1 (2C), 128.3, 127.7, 125.9 (2C), 123.8, 121.1, 114.1, 112.8, 70.4, 26.6, 21.0.

HRMS (ESI): calculated for $C_{20}H_{20}O_2^+$ [M+H]+ = 293.1536; found = 293.1600.

(*E*)-4-(2-((2-(4-fluorophenyl)allyl)oxy)phenyl)but-3-en-2-one (1k)



Compound **1k** was synthetized according to the general procedure A. The reaction was performed employing 1-(3-bromoprop-1-en-2-yl)-4-fluorobenzene (5 mmol) and 2-hydroxybenzaldehyde (4.2 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 80:20) to obtain 592 mg as a pale yellow solid (48% yield).

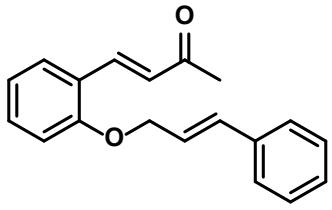
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.61 (d, *J* = 16.5 Hz, 1H), 7.41 – 7.37 (m, 1H), 7.35 – 7.28 (m, 2H), 7.23 (ddd, *J* = 8.3, 7.4, 1.7 Hz, 1H), 6.96 – 6.82 (m, 4H), 6.51 (d, *J* = 16.6 Hz, 1H), 5.43 (d, *J* = 1.0 Hz, 1H), 5.37 – 5.27 (m, 1H), 4.83 (d, *J* = 1.1 Hz, 2H), 2.07 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.6, 162.4 (d, $^1J_{C\text{-}F}$ = 247.4 Hz), 156.8, 141.8, 138.2, 134.0 (d, $^4J_{C\text{-}F}$ = 3.4 Hz), 131.5, 128.2, 127.7 (d, $^3J_{C\text{-}F}$ = 8.1 Hz, 2C), 127.6, 123.7, 121.1, 115.2 (d, $^2J_{C\text{-}F}$ = 21.4 Hz, 2C), 115.0 (d, $^5J_{C\text{-}F}$ = 1.5 Hz), 112.6, 70.2, 26.6.

^{19}F NMR (282 MHz, $CDCl_3$) δ -113.7.

HRMS (ESI): calculated for $C_{19}H_{17}FO_2^+$ [M+H]+ = 297.1285; found = 297.1185.

(*E*)-4-(2-(cinnamyloxy)phenyl)but-3-en-2-one (1l)



Compound **1l** was synthetized according to the general procedure A. The reaction was performed employing 3-phenylallyl bromide (5.2 mmol) and 2-hydroxybenzaldehyde (4.0 mmol). The final product was purified by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 80:20) to obtain 786 mg as a pale yellow solid. (72% yield).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.95 (d, *J* = 16.4 Hz, 1H), 7.55 (d, *J* = 7.7, 1H), 7.45 – 7.37 (m, 2H), 7.37 – 7.21 (m, 4H), 7.02 – 6.91 (m, 2H), 6.80 – 6.69 (m, 2H), 6.42 (dt, *J* = 16.0, 5.7 Hz, 1H), 4.79 – 4.74 (m, 2H), 2.37 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 198.9, 157.2, 138.5, 136.2, 133.2, 131.7, 128.6 (2C), 128.2, 128.0, 127.7, 126.5 (2C), 123.9, 123.7, 121.0, 112.6, 69.1, 27.1.

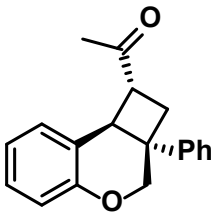
HRMS (ESI): calculated for $C_{19}H_{18}O_2^+$ [M+H]+ = 279.1380; found = 279.1307.

General procedure B for the enantioselective [2+2] photocycloaddition

An oven-dried 10 mL vial, equipped with a magnetic stir bar, was charged with catalyst **C8** (0.02 mmol), and the corresponding enone **1** (0.10 mmol). Then, 200 µL of a TFA solution (0.10 mmol, 0.5 M) in diethyl ether were added. The vial was closed with a PTFE/rubber septum and the reaction mixture was deoxygenated by three cycles of "freeze-pump-thaw". The reaction mixture was stirred at 20 ºC under 456 nm LED irradiation (8.2460 W/m^2 intensity) in a photoreactor, until reaction completion (as judged by TLC or ^{1}H NMR). The solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography to afford the corresponding cyclobutane **2** in stated yield and enantiomeric purity.

Characterization data for enantioenriched cyclobutanes (2a-l)

1-((1*R*,2a*R*,8b*S*)-2a-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2a)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2a** was obtained in 52% yield as a pale yellow oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IA column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 3.0 mL/min, λ = 210 nm, τ_{major} = 6.16 min, τ_{minor} = 6.91 (*er* = 83:17).

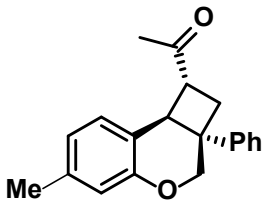
[α] $^{20}_{D}$ = - 93.0 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.19 – 7.13 (m, 3H), 7.11 – 7.04 (m, 1H), 7.03 – 6.97 (m, 2H), 6.93 (dd, *J* = 8.1, 1.3 Hz, 1H), 6.71 (td, *J* = 7.5, 1.2 Hz, 1H), 6.49 (dd, *J* = 7.8, 1.6 Hz, 1H), 5.41 (d, *J* = 11.0 Hz, 1H), 4.10 and 3.94 (AB system, *J* = 9.4 Hz, 2H), 3.38 (q, *J* = 9.5 Hz, 1H), 2.90 (dd, *J* = 11.6, 9.7 Hz, 1H), 2.78 (dd, *J* = 11.7, 8.4 Hz, 1H), 2.11 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.0, 157.0, 138.7, 129.9, 129.5, 128.4 (2C), 127.8 (3C), 126.8, 122.3, 117.4, 77.6, 50.6, 45.2, 41.4, 27.9, 26.0.

HRMS (ESI): calculated for $C_{19}H_{18}O_2^+$ [M+H]+ = 279.1380; found = 279.1398.

1-((1*R*,2a*R*,8b*S*)-6-methyl-2a-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2b)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2b** was obtained in 63% yield as a pale brown oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak ID-3 column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 2.0 mL/min, λ = 210 nm, τ_{major} = 7.36 min, τ_{minor} = 7.82 (*er* = 85:15).

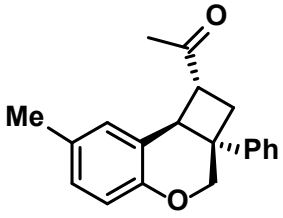
[α] $^{20}_{D}$ = - 47.0 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.20 – 7.12 (m, 3H), 7.03 – 6.96 (m, 2H), 6.75 (s, 1H), 6.52 (d, *J* = 7.8 Hz, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 5.33 (d, *J* = 11.0 Hz, 1H), 4.07 and 3.90 (AB system, *J* = 9.6 Hz, 2H), 3.33 (q, *J* = 9.7 Hz, 1H), 2.88 (dd, *J* = 11.8, 9.7 Hz, 1H), 2.75 (dd, *J* = 11.7, 8.4 Hz, 1H), 2.19 (s, 3H), 2.09 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.2, 156.9, 138.9, 137.8, 129.2, 128.5 (2C), 127.8 (2C), 126.8, 126.7, 123.0, 118.4, 77.8, 50.6, 45.5, 41.3, 27.8, 25.8, 21.1.

HRMS (ESI): calculated for $C_{20}H_{20}O_2^+$ [M+H]+ = 293.1536; found = 293.1550.

1-((1*R*,2a*R*,8b*S*)-7-methyl-2a-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2c)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2c** was obtained in 46% yield as a pale yellow oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IB-3 column: CO_2/MeOH gradient from 95/5 to 70/30 in 8 minutes, flow rate 2.0 mL/min, λ = 210 nm, τ_{major} = 6.18 min, τ_{minor} = 6.38 (*er* = 82:18).

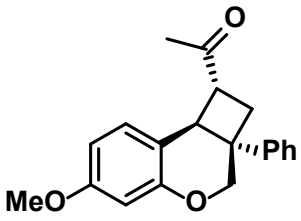
[α] $^{20}_{D}$ = -17.4 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.20 – 7.13 (m, 3H), 7.01 – 6.95 (m, 2H), 6.87 – 6.77 (m, 2H), 6.16 (d, *J* = 2.3 Hz, 1H), 5.39 (d, *J* = 11.1 Hz, 1H), 4.05 and 3.86 (AB system, *J* = 9.5 Hz, 2H), 3.34 (td, *J* = 10.2, 8.3 Hz, 1H), 2.89 (dd, *J* = 11.8, 9.9 Hz, 1H), 2.77 (dd, *J* = 11.6, 8.5 Hz, 1H), 2.12 (s, 3H), 1.97 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.4, 154.9, 138.7, 131.4, 130.3, 129.4, 128.5 (2C), 128.1, 127.7 (2C), 126.8, 117.3, 77.7, 50.7, 45.5, 41.1, 27.8, 25.8, 20.6.

HRMS (ESI): calculated for $C_{20}H_{20}O_2^+$ [M+H]+ = 293.1536; found = 293.1552.

1-((1*R*,2a*R*,8b*S*)-6-methoxy-2a-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2d)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2d** was obtained in 62% yield as a pale yellow oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IA column: CO_2/MeOH 80:20, flow rate 3.0 mL/min, λ = 210 nm, τ_{major} = 10.69 min, τ_{minor} = 12.47 (*er* = 91:9).

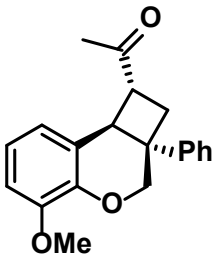
[α] $^{20}_{D}$ = - 74.7 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.21 – 7.15 (m, 3H), 7.04 – 6.97 (m, 2H), 6.49 (d, *J* = 2.4 Hz, 1H), 6.33 (d, *J* = 8.7 Hz, 1H), 6.27 (dd, *J* = 8.6, 2.4 Hz, 1H), 5.30 (d, *J* = 11.1 Hz, 1H), 4.06 and 3.90 (AB system, *J* = 9.5 Hz, 2H), 3.68 (s, 3H), 3.38 – 3.24 (m, 1H), 2.85 (dd, *J* = 11.7, 9.8 Hz, 1H), 2.75 (dd, *J* = 11.7, 8.4 Hz, 1H), 2.10 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.2, 159.5, 157.8, 138.7, 130.1, 128.5 (2C), 127.9 (2C), 126.8, 122.0, 107.8, 103.7, 77.7, 55.3, 50.6, 45.7, 41.1, 27.9, 25.8.

HRMS (ESI): calculated for $C_{20}H_{20}O_3^+$ [M+H]+ = 309.1485; found = 309.1520.

1-((1*R*,2a*R*,8b*S*)-5-methoxy-2a-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2e)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2e** was obtained in 38% yield as a pale yellow oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak ID-3 column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 2.0 mL/min, λ = 210 nm, τ_{major} = 3.97 min, τ_{minor} = 3.55 (*er* = 66:34).

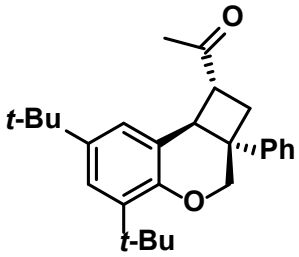
[α]$^{20}_{D}$ = - 12.2 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.30 – 7.25 (m, 2H), 7.23 – 7.17 (m, 1H), 7.15 – 7.08 (m, 2H), 6.99 – 6.91 (m, 1H), 6.89 – 6.79 (m, 2H), 4.29 and 4.14 (AB system, *J* = 11.1 Hz, 2H), 3.89 (s, 3H), 3.92 – 3.84 (m, 1H), 3.28 – 3.14 (m, 1H), 2.73 – 2.54 (m, 2H), 2.15 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 207.4, 149.0, 145.5, 145.3, 128.5 (2C), 127.9, 126.6, 125.4 (2C), 121.6, 120.3, 110.0, 75.4, 55.9, 51.1, 41.6, 40.9, 31.4, 27.9.

HRMS (ESI): calculated for $C_{20}H_{20}O_3^+$ [M+H]+ = 309.1485; found = 309.1490.

1-((1*R*,2a*R*,8b*S*)-5,7-di-tert-butyl-2a-phenyl-1,2a,3,8b-tetrahydro-2H-cyclobuta[c]chromen-1-yl)ethan-1-one (2f)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 60:40), compound **2f** was obtained in 58% yield as a pale yellow solid. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IC column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 3.0 mL/min, λ = 210 nm, τ_{major} = 3.87 min, τ_{minor} = 3.18 (*er* = 65:35).

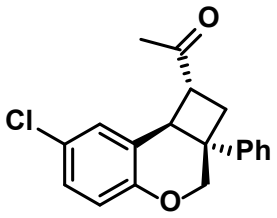
$[\alpha]^{20}_D$ = -5.8 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.33 – 7.13 (m, 6H), 7.09 (d, *J* = 2.3 Hz, 1H), 4.24 and 3.81 (AB system, *J* = 11.0 Hz, 2H), 3.80 (d, *J* = 7.9 Hz, 1H), 3.21 (td, J = 9.2, 7.6 Hz, 1H), 2.75 (dd, J = 11.6, 8.9 Hz, 1H), 2.62 (dd, J = 11.6, 9.4 Hz, 1H), 2.13 (s, 3H), 1.40 (s, 9H), 1.34 (s, 9H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 207.7, 153.3, 145.9, 143.9, 138.3, 128.4 (2C), 128.2, 126.4, 125.5 (2C), 122.8, 122.2, 75.4, 50.8, 43.2, 43.1, 34.8, 34.5, 31.6 (3C), 31.0, 29.9 (3C), 27.9.

HRMS (ESI): calculated for $C_{27}H_{34}O_2^+$ [M+H]+ = 391.2632; found = 391.2660.

1-((1*R*,2a*R*,8b*S*)-7-chloro-2a-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2g)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2g** was obtained in 38% yield as a pale brown oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IA column: CO_2/MeOH 80:20, flow rate 3.0 mL/min, λ = 210 nm, τ_{major} = 10.42 min, τ_{minor} = 11.55 (*er* = 87:13).

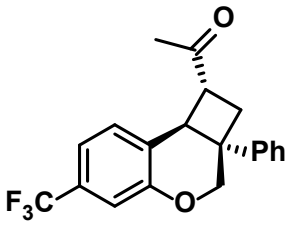
$[\alpha]^{20}_D$ = - 63.0 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 3H), 7.06 – 6.97 (m, 3H), 6.84 (d, *J* = 8.7 Hz, 1H), 6.35 (d, *J* = 2.6 Hz, 1H), 5.33 (d, *J* = 11.0 Hz, 1H), 4.09 and 3.90 (AB system, *J* = 9.4 Hz, 2H), 3.32 (q, *J* = 9.2 Hz, 1H), 2.82 (d, *J* = 9.2 Hz, 2H), 2.14 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.4, 155.4, 137.9, 131.8, 129.6, 128.3 (2C), 128.1 (2C), 127.7, 127.5, 127.3, 118.5, 77.7, 50.5, 45.2, 40.9, 28.0, 26.3.

HRMS (ESI): calculated for $C_{19}H_{17}ClO_2^+$ [M+H]+ = 313.0990; found = 313.0993.

1-((1*R*,2a*R*,8b*S*)-2a-phenyl-6-(trifluoromethyl)-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2h)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2h** was obtained in 51% yield as a pale brown oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IC column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 3.0 mL/min, λ = 210 nm, τ_{major} = 2.88 min, τ_{minor} = 3.24 (*er* = 81:19).

$[\alpha]^{20}_D$ = -21.9 (*c* 1.0, $CHCl_3$).

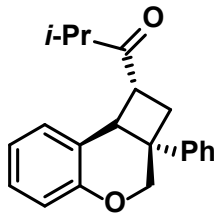
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.24 – 7.17 (m, 3H), 7.16 (d, *J* = 1.8 Hz, 1H), 7.03 – 6.94 (m, 3H), 6.57 (d, *J* = 8.1 Hz, 1H), 5.44 (d, *J* = 10.8 Hz, 1H), 4.20 and 3.99 (AB system, *J* = 9.5 Hz, 2H), 3.41 (td, *J* = 10.3, 8.5 Hz, 1H), 2.94 – 2.80 (m, 2H), 2.15 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 208.1, 156.9, 137.7, 133.9 (q, $^4J_{C\text{-}F}$ = 1.1 Hz), 130.2 (q, $^2J_{C\text{-}F}$ = 32.5 Hz), 130.0, 128.3 (2C), 128.1 (2C), 127.3, 123.7 (q, $^1J_{C\text{-}F}$ = 272.2 Hz), 118.9 (q, $^3J_{C\text{-}F}$ = 3.5 Hz), 114.1 (q, $^3J_{C\text{-}F}$ = 3.6 Hz), 77.7, 50.6, 45.1, 40.9, 27.9, 26.7.

^{19}F NMR (282 MHz, $CDCl_3$) δ -62.5.

HRMS (ESI): calculated for $C_{20}H_{17}F_3O_2^+$ [M+H]+ = 347.1253; found = 347.1263.

2-methyl-1-((1*R*,2a*R*,8b*S*)-2a-phenyl-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[c]chromen-1-yl)propan-1-one (2i)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 70:30), compound **2i** was obtained in 39% yield as a pale yellow oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IG-3 column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 2.0 mL/min, λ = 210 nm, τ_{major} = 3.84 min, τ_{minor} = 3.42 (*er* = 78:22).

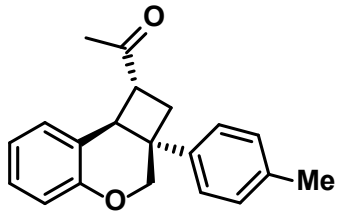
[α] $^{20}_D$ = -42.2 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.19 – 7.15 (m, 2H), 7.07 – 6.98 (m, 4H), 6.91 (dd, *J* = 8.2, 1.3 Hz, 1H), 6.70 (t, *J* = 7.4 Hz, 1H), 6.51 – 6.42 (m, 1H), 5.41 (d, *J* = 10.9 Hz, 1H), 4.12 (d, *J* = 8.8 Hz, 1H), 3.92 (d, *J* = 9.4 Hz, 1H), 3.50 (q, *J* = 10.3, 9.7 Hz, 1H), 2.95 – 2.83 (m, 1H), 2.76 (dd, *J* = 11.6, 8.3 Hz, 1H), 2.65 (hept, *J* = 6.9 Hz, 1H), 1.06 (dd, *J* = 6.9 Hz, 3H), 1.00 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 214.4, 157.0, 139.0, 130.1, 129.5, 128.4 (2C), 127.75 (2C), 127.68, 126.7, 122.1, 117.3, 77.7, 50.6, 43.2, 41.1, 38.2, 30.9, 18.7, 18.1.

HRMS (ESI): calculated for $C_{21}H_{22}O_2^+$ [M+H]+ = 307.1693; found = 307.1725.

1-((1*R*,2a*R*,8b*S*)-2a-(*p*-tolyl)-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2j)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2j** was obtained in 54% yield as a pale yellow oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IG-3 column: CO_2/MeOH gradient from 95/5 to 65/35 in 20 minutes 95:5, flow rate 2.0 mL/min, λ = 210 nm, τ_{major} = 7.51 min, τ_{minor} = 6.62 (*er* = 80:20).

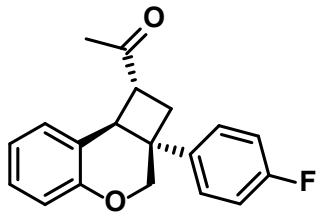
[α] $^{20}_D$ = -37.1 (*c* 1.0, $CHCl_3$).

^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.08 (ddd, *J* = 8.8, 7.3, 1.6 Hz, 1H), 7.00 – 6.82 (m, 5H), 6.73 (td, *J* = 7.5, 1.2 Hz, 1H), 6.52 (dd, *J* = 7.8, 1.7 Hz, 1H), 5.38 (d, *J* = 11.0 Hz, 1H), 4.06 and 3.89 (AB system, *J* = 9.5 Hz, 2H), 3.36 (q, *J* = 9.7 Hz, 1H), 2.87 (dd, *J* = 11.6, 9.8 Hz, 1H), 2.75 (dd, *J* = 11.6, 8.4 Hz, 1H), 2.27 (s, 3H), 2.11 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.2, 157.0, 136.4, 135.6, 130.0, 129.6, 128.5 (2C), 128.3 (2C), 127.7, 122.2, 117.4, 77.7, 50.3, 45.3, 41.3, 27.8, 26.0, 20.9.

HRMS (ESI): calculated for $C_{20}H_{20}O_2^+$ [M+H]+ = 293.1536; found = 293.1573.

1-((1*R*,2a*R*,8b*S*)-2a-(4-fluorophenyl)-1,2a,3,8b-tetrahydro-2*H*-cyclobuta[*c*]chromen-1-yl)ethan-1-one (2k)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 90:10 to 50:50), compound **2k** was obtained in 42% yield as a pale brown oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IC column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 3.0 mL/min, λ = 210 nm, τ_{major} = 5.29 min, τ_{minor} = 5.86 (*er* = 84:16).

[α] $^{20}_{D}$ = - 45.7 (*c* 1.0, $CHCl_3$).

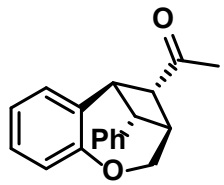
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.13 – 7.06 (m, 1H), 6.98 – 6.81 (m, 5H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.50 (dd, *J* = 7.7, 1.6 Hz, 1H), 5.34 (d, *J* = 10.9 Hz, 1H), 4.09 and 3.85 (AB system, *J* = 9.4 Hz, 2H), 3.38 (q, *J* = 9.6 Hz, 1H), 2.86 (dd, *J* = 11.8, 9.8 Hz, 1H), 2.73 (dd, *J* = 11.8, 8.4 Hz, 1H), 2.12 (s, 3H).

^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.2, 161.6 (d, $^{1}J_{C\text{-}F}$ = 246.2 Hz), 156.9, 134.4 (d, $^{4}J_{C\text{-}F}$ = 3.3 Hz), 130.0 (d, $^{3}J_{C\text{-}F}$ = 7.8 Hz, 2C), 129.6, 129.4, 128.0, 122.5, 117.5, 114.6 (d, $^{2}J_{C\text{-}F}$ = 21.0 Hz, 2C), 77.9, 50.0, 45.0, 41.4, 28.0, 26.3.

^{19}F NMR (282 MHz, $CDCl_3$) δ -115.8.

HRMS (ESI): calculated for $C_{19}H_{17}FO_2^+$ [M+H]+ = 297.1285; found = 297.1300.

1-((3*S*,4*S*,5*R*,10*R*)-10-phenyl-2,3,4,5-tetrahydro-3,5-methanobenzo[*b*]oxepin-4-yl)ethan-1-one (2l)



Following the general procedure B, after purification by flash chromatography (CyHex/EtOAc gradient = from 100:0 to 60:40), compound **2l** was obtained in 30% yield as a pale yellow oil. The enantiomeric excess was determined by SFC on a Daicel Chiralpak IA column: CO_2/MeOH gradient from 95/5 to 60/40 in 8 minutes, flow rate 3.0 mL/min, λ = 210 nm, τ_{major} = 4.69 min, τ_{minor} = 4.49 (*er* = 93:7).

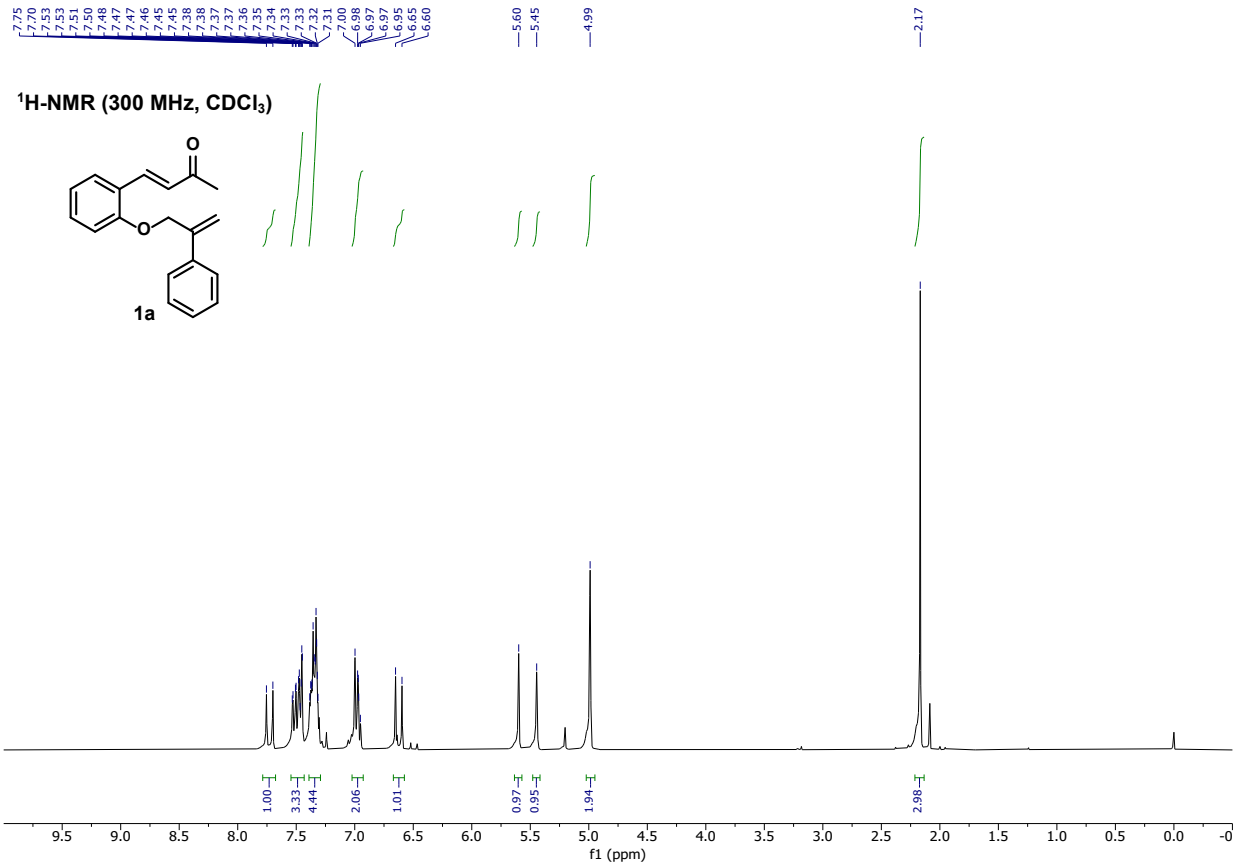
[α] $^{20}_{D}$ = -35.3 (*c* 1.0, $CHCl_3$).

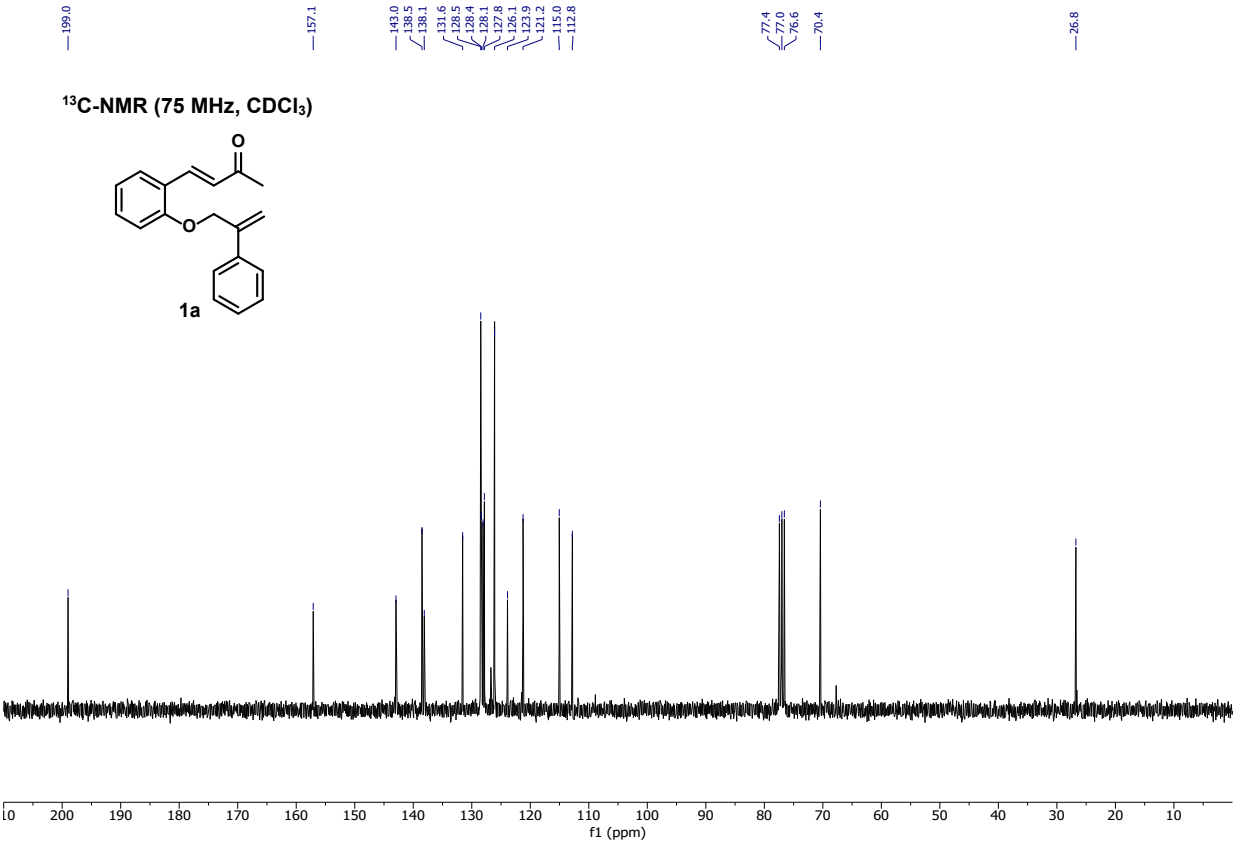
^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.21 – 7.00 (m, 6H), 6.83 (d, *J* = 8.1 Hz, 1H), 6.58 (t, *J* = 7.5 Hz, 1H), 6.46 (dd, *J* = 7.6, 1.7 Hz, 1H), 5.95 (dd, *J* = 12.7, 9.6 Hz, 1H), 4.96 (d, *J* = 9.0 Hz, 1H), 4.19 – 4.08 (m, 2H), 3.85 (dd, *J* = 12.7, 9.1 Hz, 1H), 3.41 (br d, *J* = 9.3 Hz, 1H), 2.03 (s, 3H).

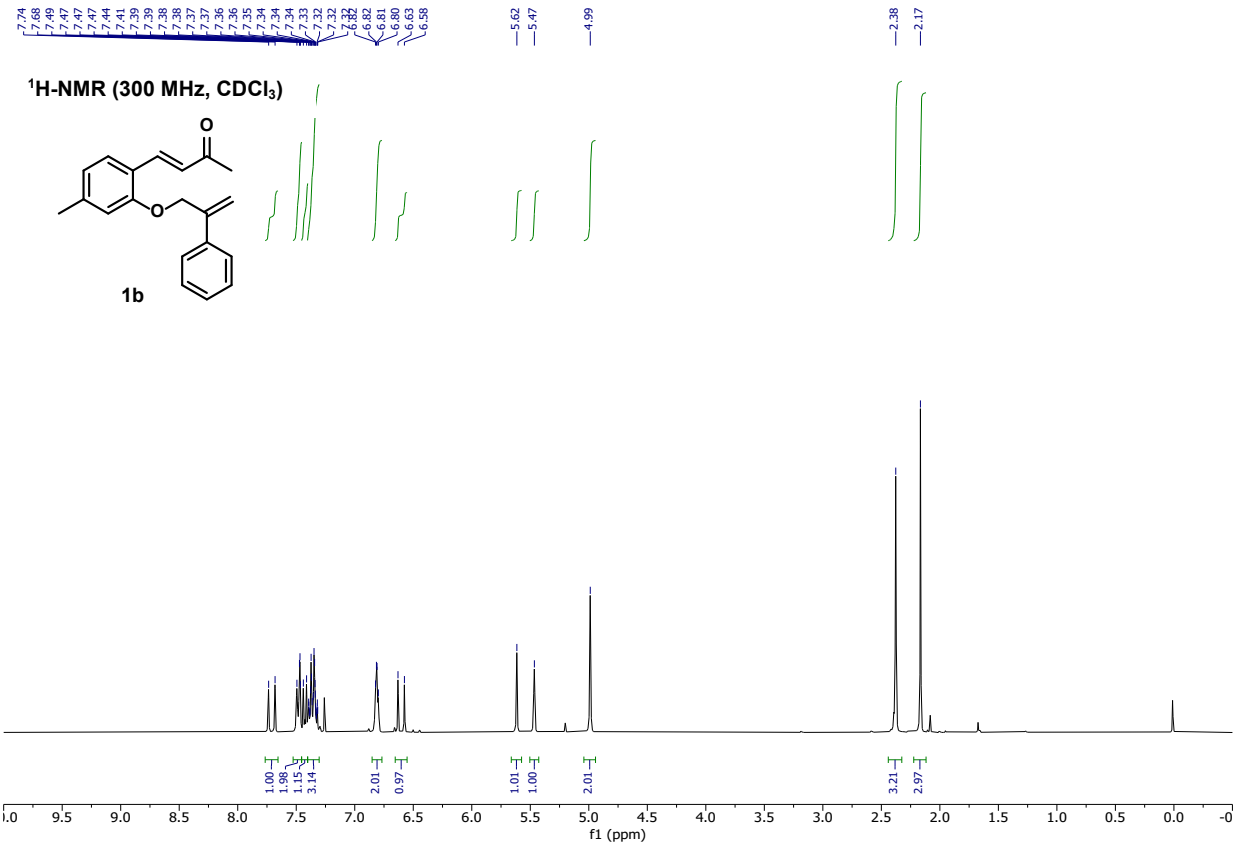
^{13}C-NMR (75 MHz, $CDCl_3$) δ 209.7, 157.3, 139.1, 128.3 (2C), 127.9 (2C), 127.6, 127.4, 127.2, 126.3, 120.3, 111.4, 67.1, 49.3, 45.9, 39.9, 38.6, 28.1.

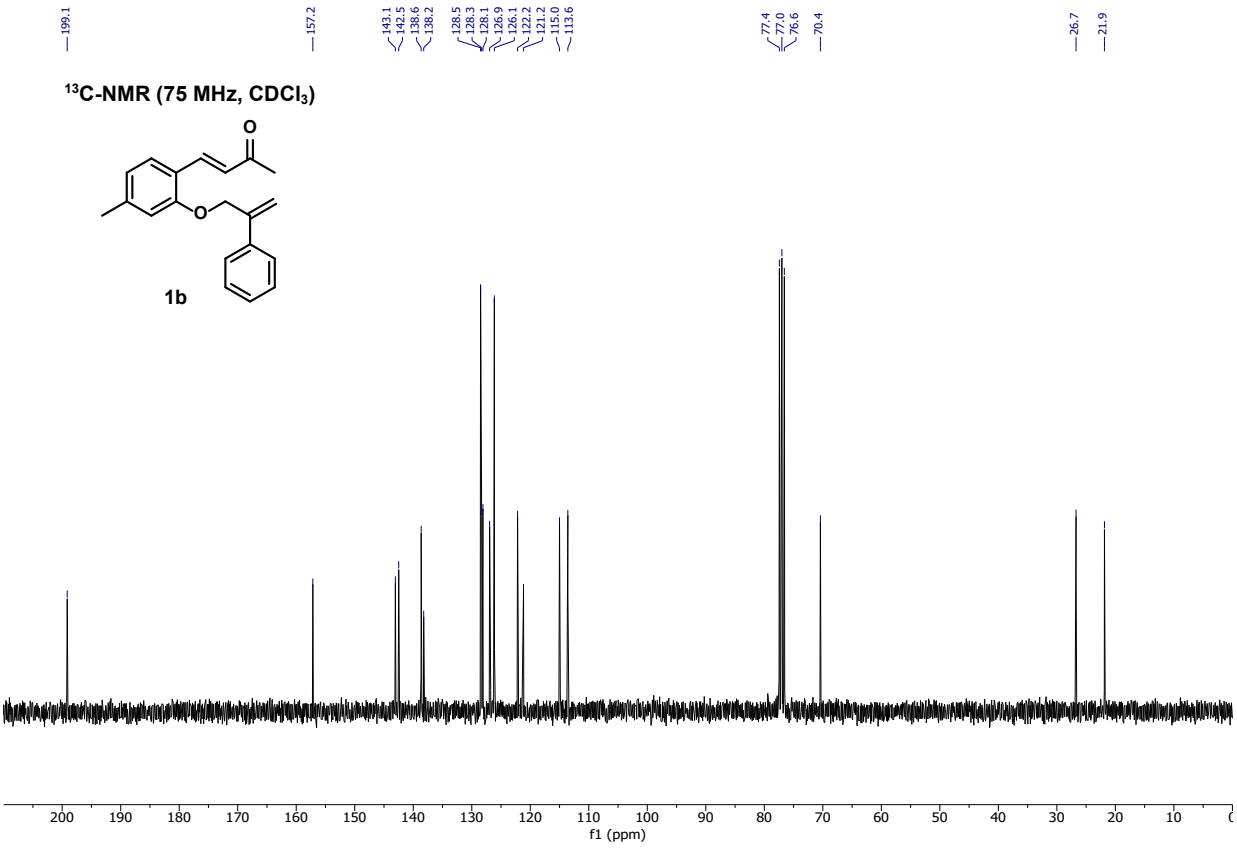
HRMS (ESI): calculated for $C_{19}H_{18}O_2^+$ [M+H]+ = 279.1380; found = 279.1401.

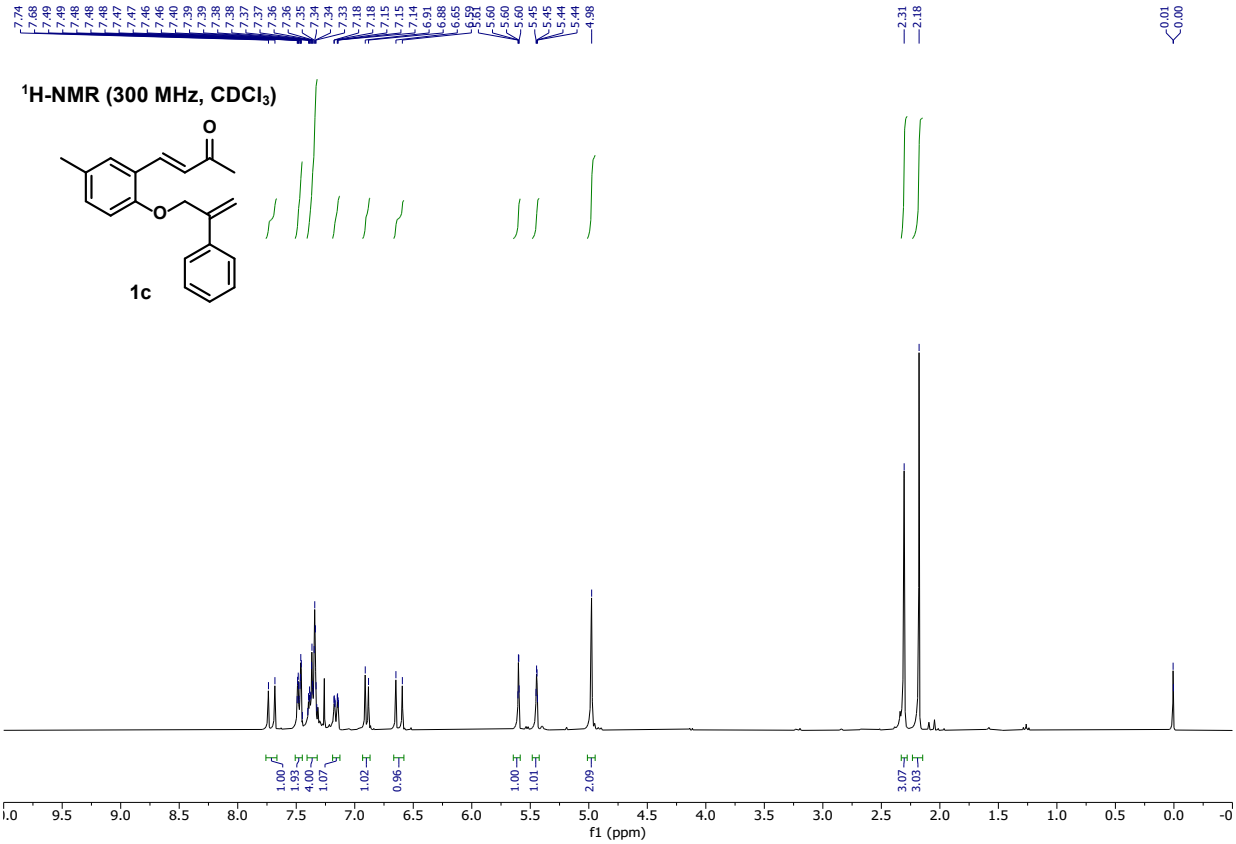
NMR spectra

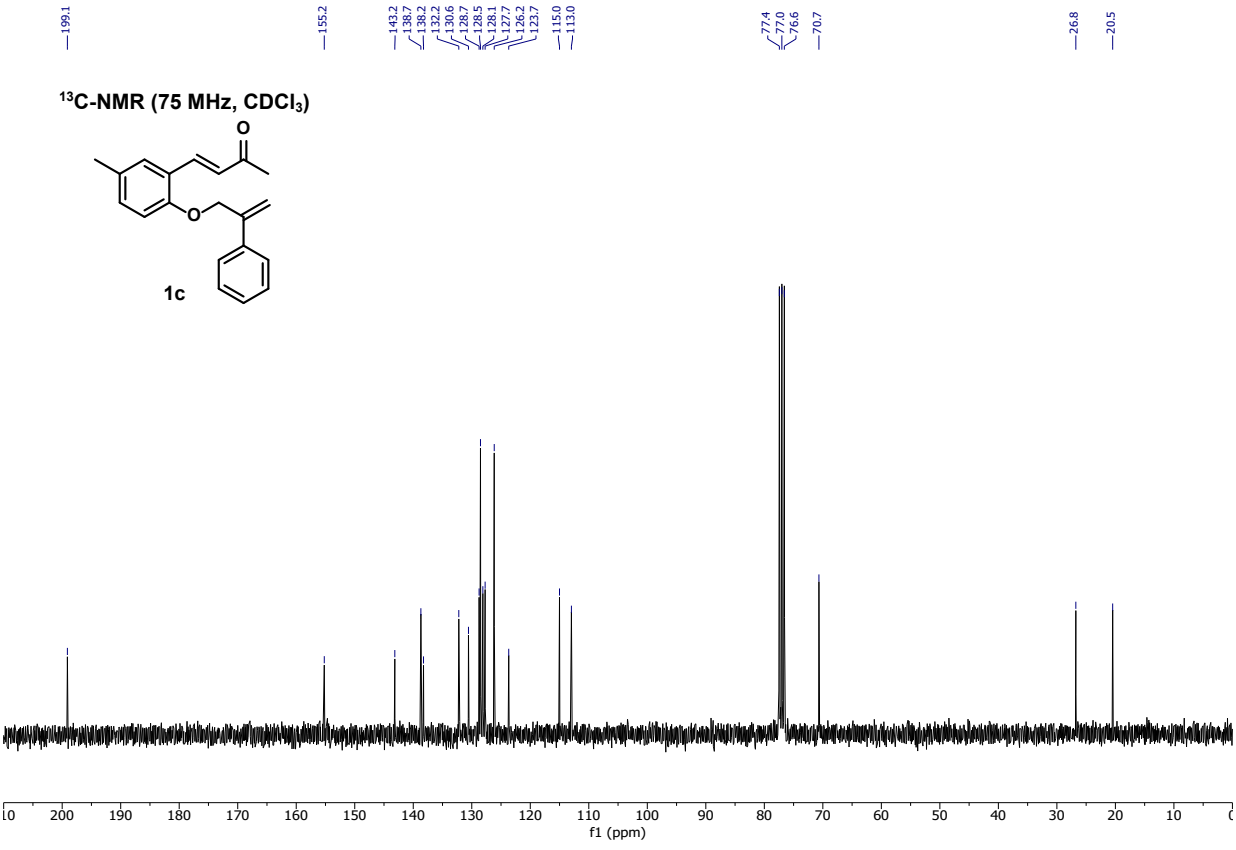

7.75
7.70
7.53
7.53
7.51
7.50
7.48
7.47
7.47
7.46
7.45
7.45
7.38
7.38
7.37
7.37
7.36
7.35
7.34
7.33
7.33
7.32
7.31
7.00
6.98
6.97
6.97
6.95
6.65
6.60
5.60
5.45
4.99
2.17
1H-NMR (300 MHz, CDCl3)
O
O
1a
1.00
3.33
4.44
2.06
1.01
0.97
0.95
1.94
2.98
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

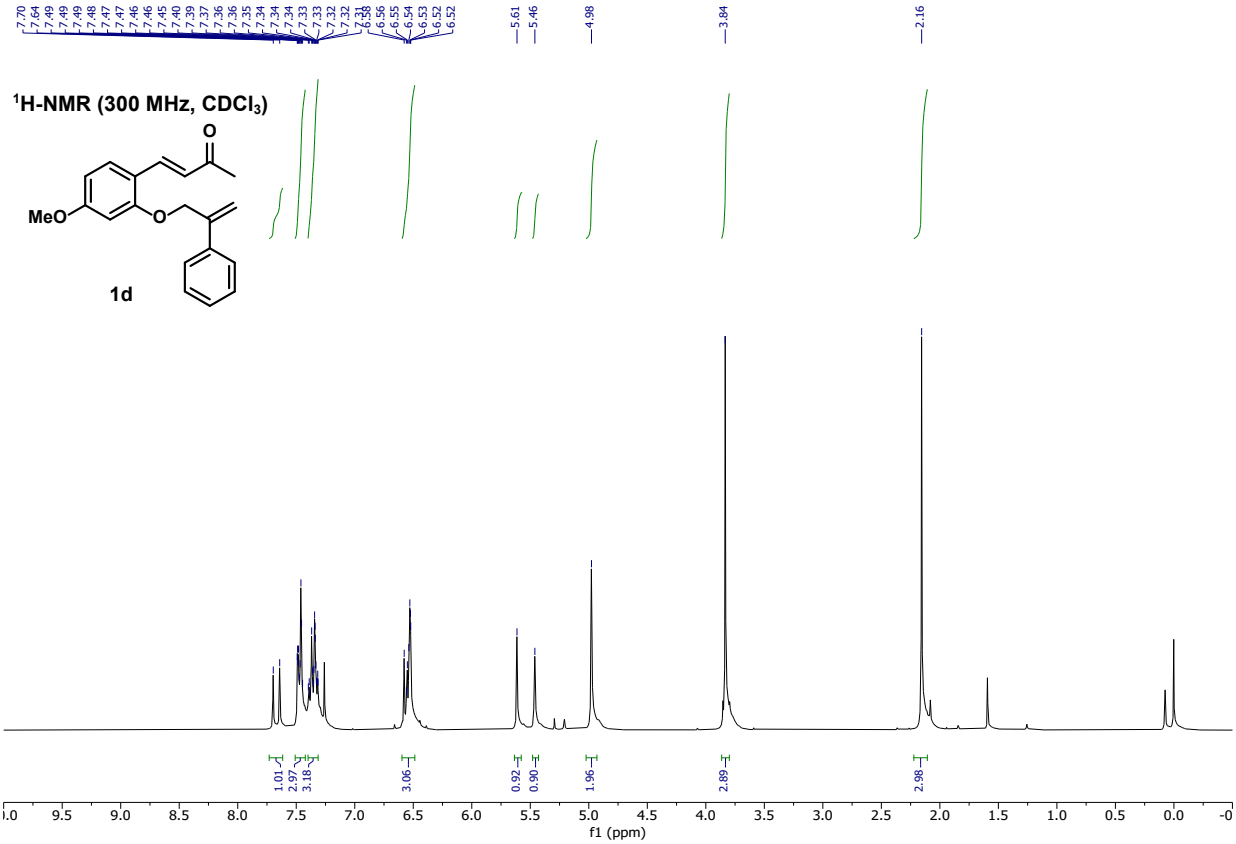

199.0
157.1
143.0
138.5
138.1
131.6
128.5
128.4
128.1
127.8
126.1
123.9
121.2
115.0
112.8
77.4
77.0
76.6
70.4
26.8
13C-NMR (75 MHz, CDCl3)
O
O
1a
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

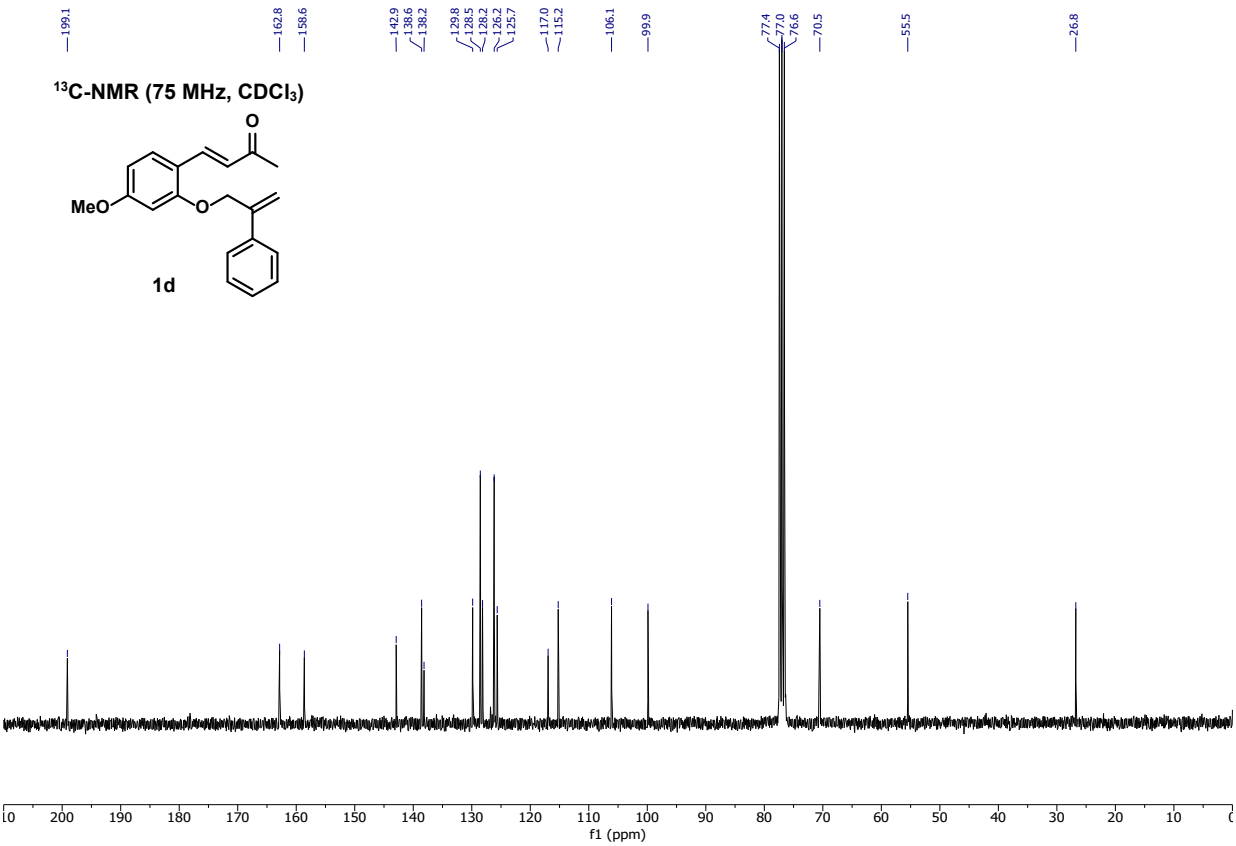

7.74
7.68
7.49
7.47
7.47
7.47
7.44
7.41
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.34
7.34
7.33
7.32
7.32
6.82
6.82
6.81
6.80
6.63
6.58
5.62
5.47
4.99
2.38
2.17
1H-NMR (300 MHz, CDCl3)
O
O
1b
1.00
1.98
1.15
3.14
2.01
0.97
1.01
1.00
2.01
3.21
2.97
f1 (ppm)

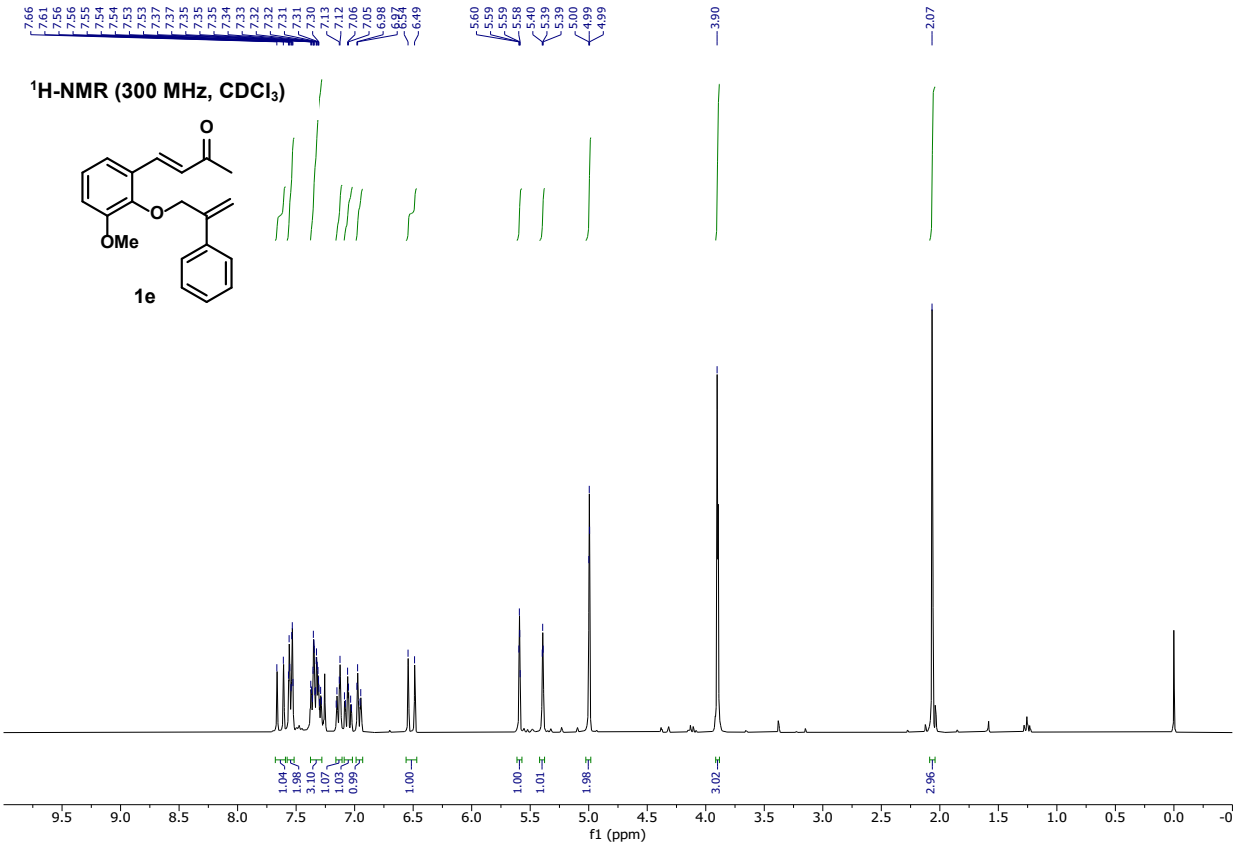

199.1
157.2
143.1
142.5
138.6
138.2
128.5
128.3
128.1
126.9
126.1
122.2
121.2
115.0
113.6
77.4
77.0
76.6
70.4
26.7
21.9
13C-NMR (75 MHz, CDCl3)
O
O
1b
f1 (ppm)

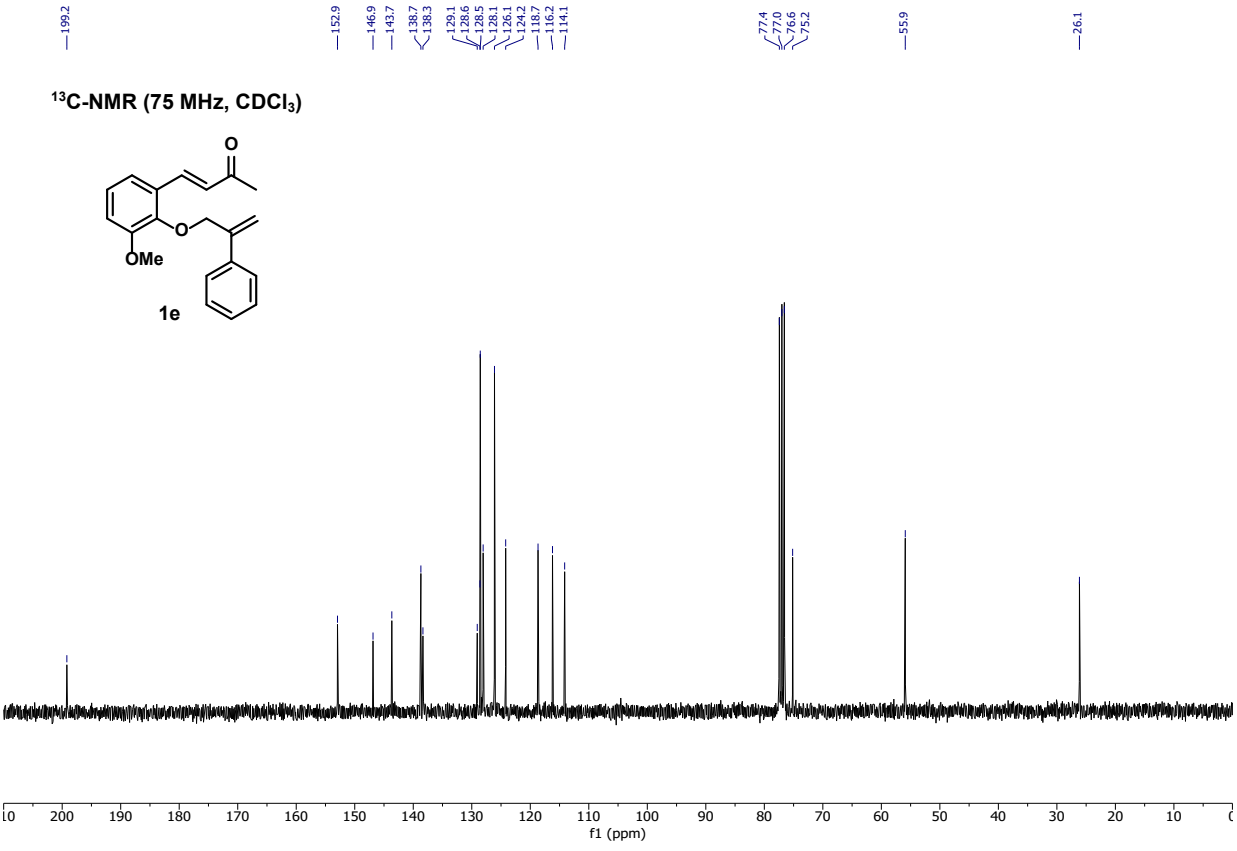

7.74
7.68
7.49
7.49
7.48
7.48
7.48
7.47
7.47
7.46
7.46
7.40
7.39
7.39
7.38
7.38
7.37
7.37
7.36
7.36
7.35
7.34
7.34
7.33
7.18
7.15
7.15
7.14
6.91
6.88
6.65
6.61
5.60
5.60
5.60
5.45
5.45
5.44
5.44
4.98
2.31
2.18
0.01
0.00
1H-NMR (300 MHz, CDCl3)
O
O
1c
1.00
1.93
4.00
1.07
1.02
0.96
1.00
1.01
2.09
3.07
3.03
f1 (ppm)

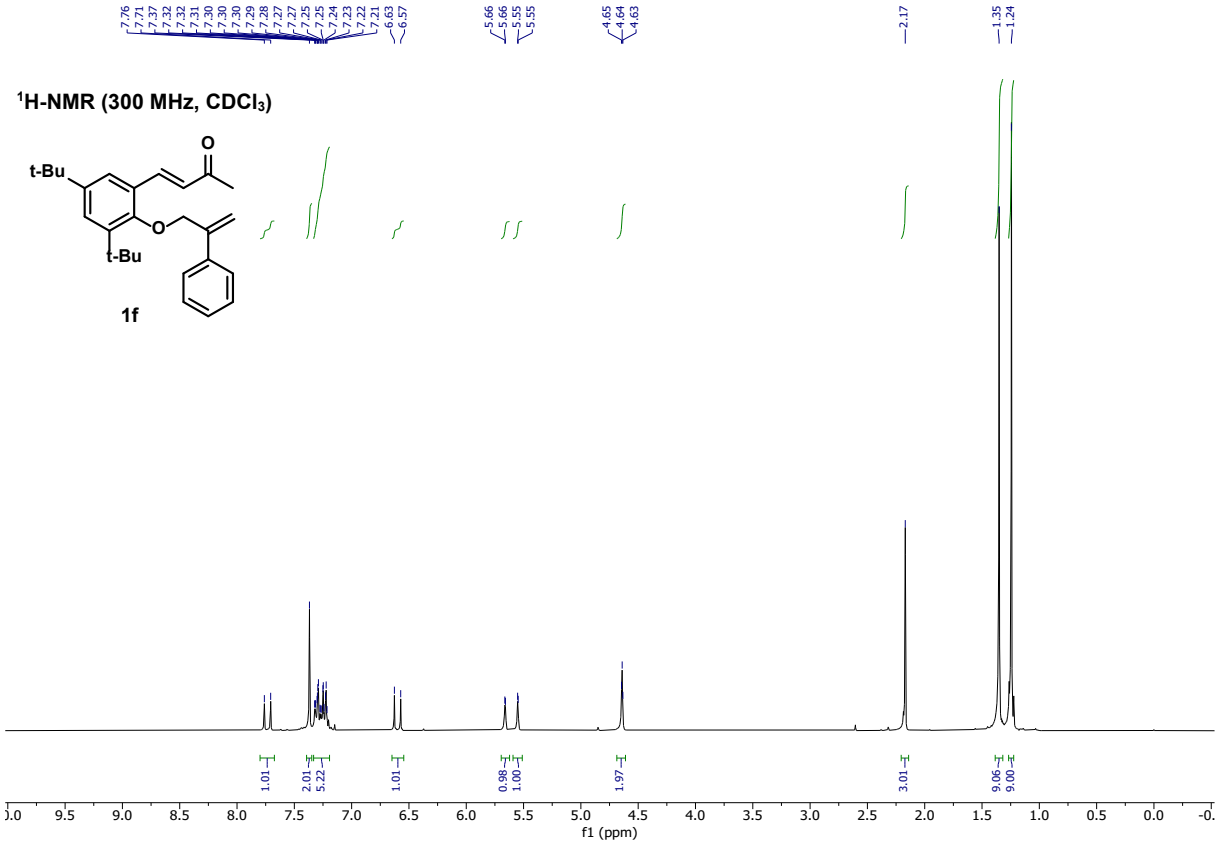

199.1
155.2
143.2
138.7
138.2
132.2
130.6
128.7
128.5
128.1
127.7
126.2
123.7
115.0
113.0
77.4
77.0
76.6
70.7
26.8
20.5
13C-NMR (75 MHz, CDCl3)
O
O
1c
f1 (ppm)


7.70
7.64
7.49
7.49
7.49
7.48
7.47
7.47
7.46
7.46
7.45
7.40
7.39
7.37
7.36
7.36
7.35
7.34
7.34
7.34
7.33
7.33
7.32
7.32
7.31
6.58
6.56
6.55
6.54
6.53
6.52
6.52
5.61
5.46
4.98
3.84
2.16
1H-NMR (300 MHz, CDCl3)
O
MeO
O
1d
1.01
2.97
3.18
3.06
0.92
0.90
1.96
2.89
2.98
f1 (ppm)


199.1
162.8
158.6
142.9
138.6
138.2
129.8
128.5
128.2
126.2
125.7
117.0
115.2
106.1
99.9
77.4
77.0
76.6
70.5
55.5
26.8
13C-NMR (75 MHz, CDCl3)
O
MeO
O
1d
f1 (ppm)

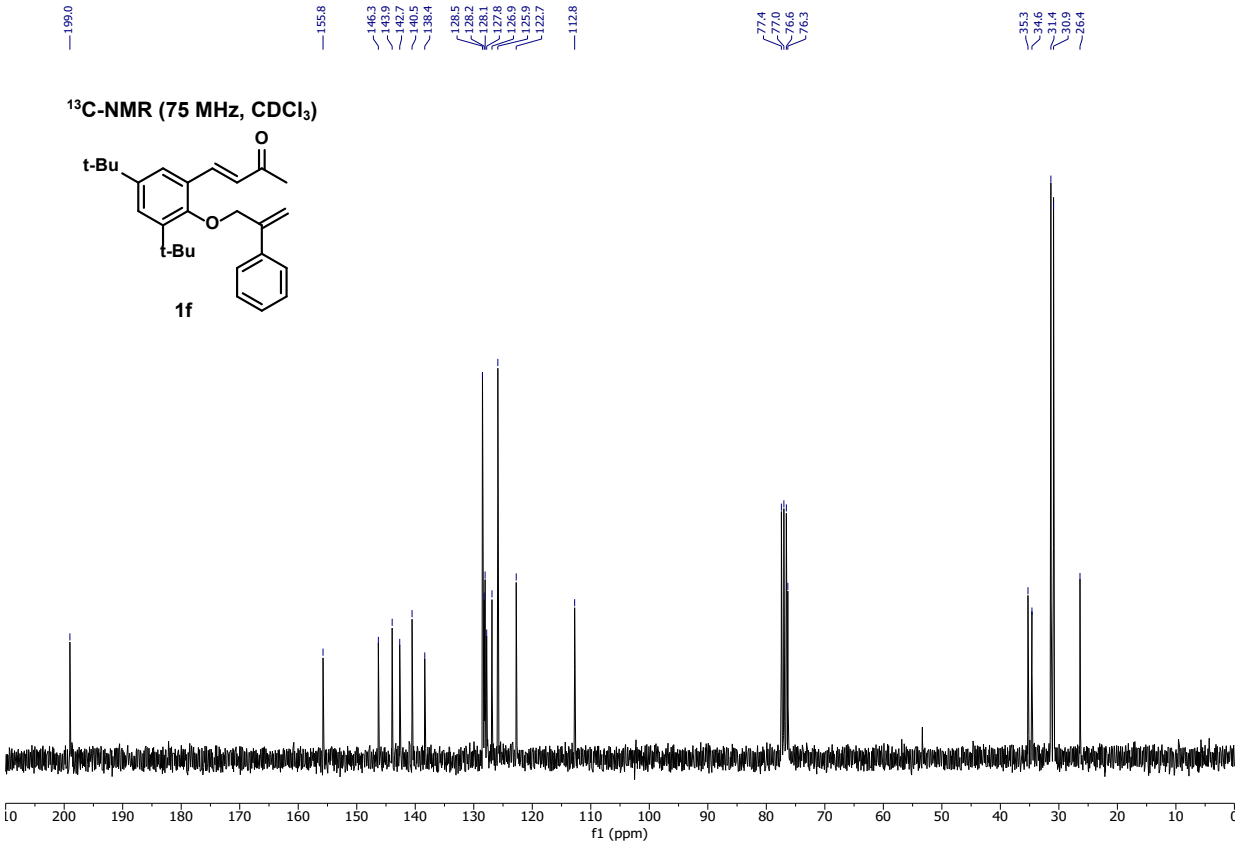

7.66
7.61
7.56
7.56
7.55
7.54
7.54
7.53
7.53
7.37
7.37
7.35
7.35
7.35
7.34
7.33
7.32
7.32
7.31
7.31
7.30
7.13
7.12
7.06
7.05
6.98
6.54
6.49
5.60
5.59
5.59
5.58
5.40
5.39
5.39
5.00
4.99
4.99
3.90
2.07
1H-NMR (300 MHz, CDCl3)
O
O
OMe
1e
1.04
1.98
3.10
1.07
1.03
0.99
1.00
1.00
1.01
1.98
3.02
2.96
f1 (ppm)


199.2
152.9
146.9
143.7
138.7
138.3
129.1
128.6
128.5
128.1
126.1
124.2
118.7
116.2
114.1
77.4
77.0
76.6
75.2
55.9
26.1
13C-NMR (75 MHz, CDCl3)
O
O
OMe
1e
f1 (ppm)



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

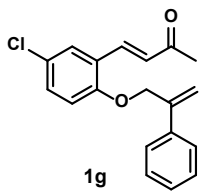
1f



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

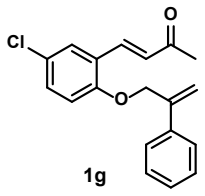
1f

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



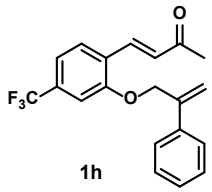
1g

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



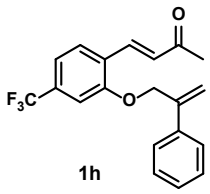
1g

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



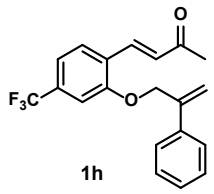
1h

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

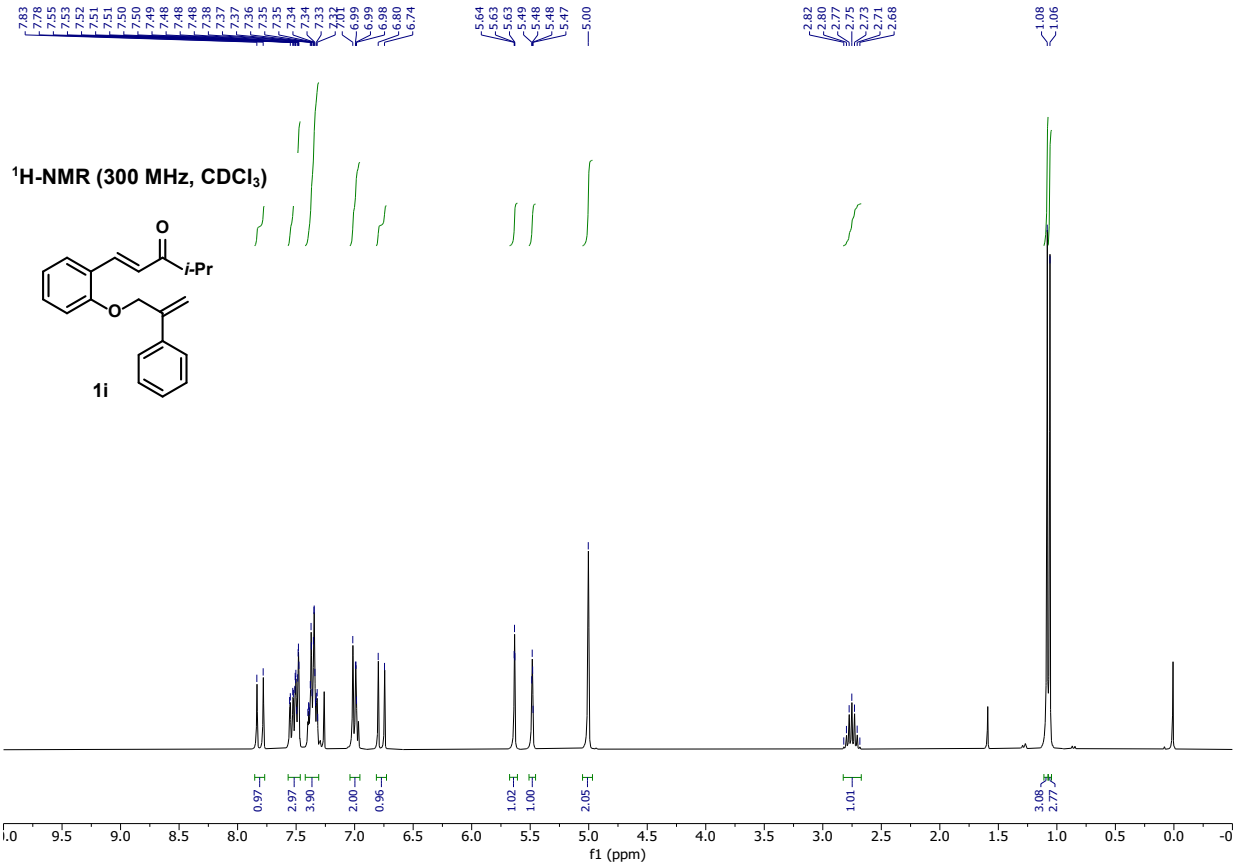


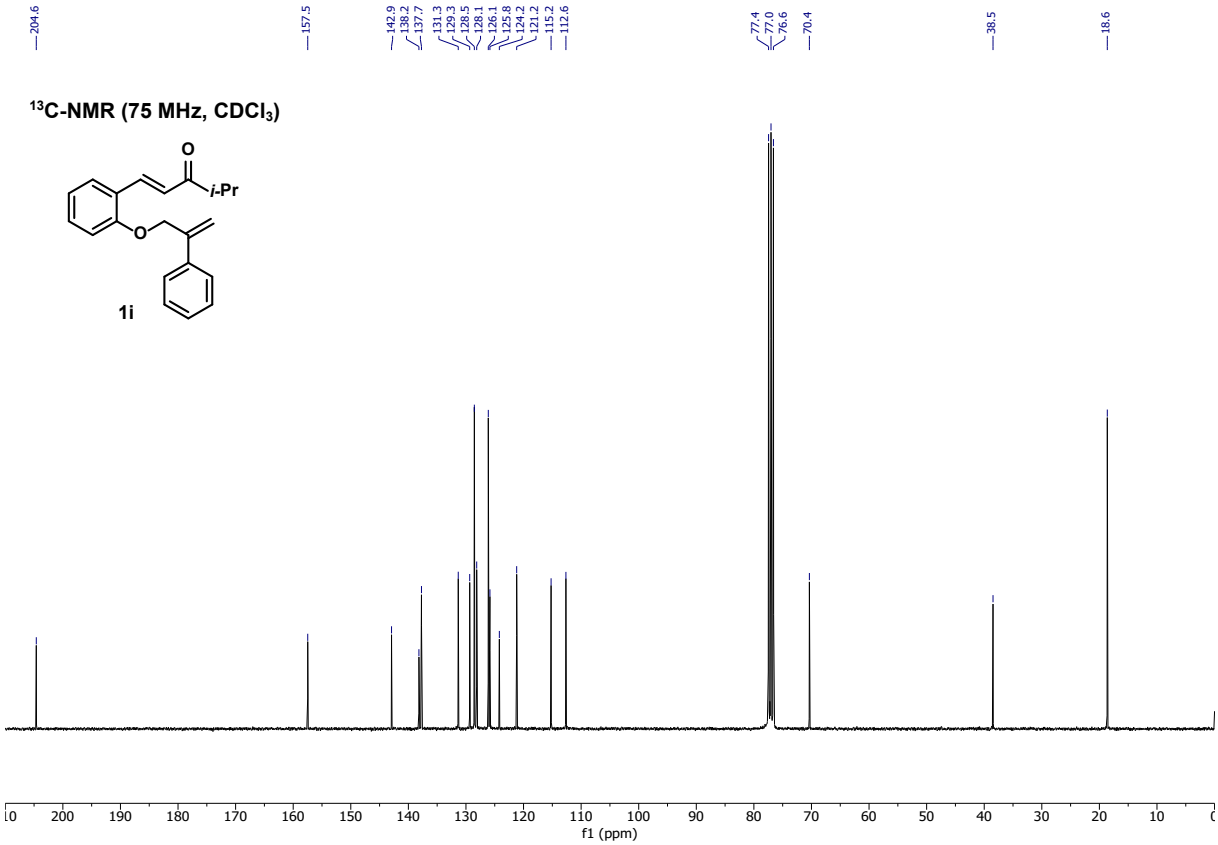
1h

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

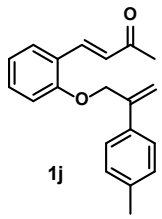


1h


7.83 7.78 7.55 7.53 7.52 7.51 7.51 7.50 7.50 7.49 7.48 7.48 7.48 7.38 7.37 7.37 7.36 7.35 7.35 7.34 7.34 7.33 7.32 7.01 6.99 6.99 6.98 6.80 6.74
5.64 5.63 5.63 5.49 5.48 5.48 5.47 5.00
2.82 2.80 2.77 2.75 2.73 2.71 2.68
1.08 1.06
1H-NMR (300 MHz, CDCl3)
O
i-Pr
O
1i
0.97 2.97 3.90 2.00 0.96 1.02 1.00 2.05 1.01 3.08 2.77
f1 (ppm)

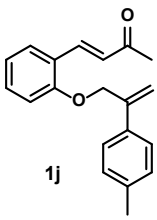

204.6
157.5
142.9 138.2 137.7 131.3 129.3 128.5 128.1 126.1 125.8 124.2 121.2 115.2 112.6
77.4 77.0 76.6 70.4
38.5
18.6
13C-NMR (75 MHz, CDCl3)
O
i-Pr
O
1i
f1 (ppm)

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

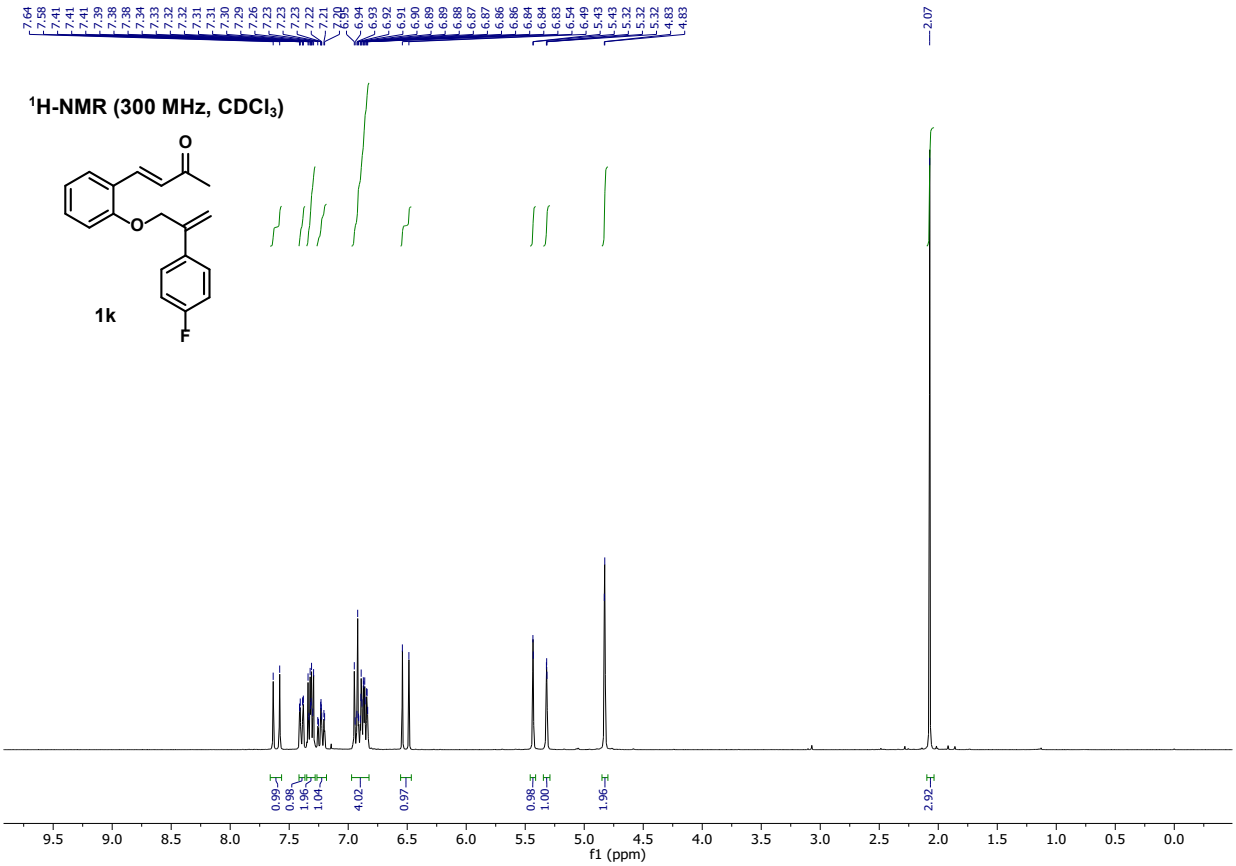


1j

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

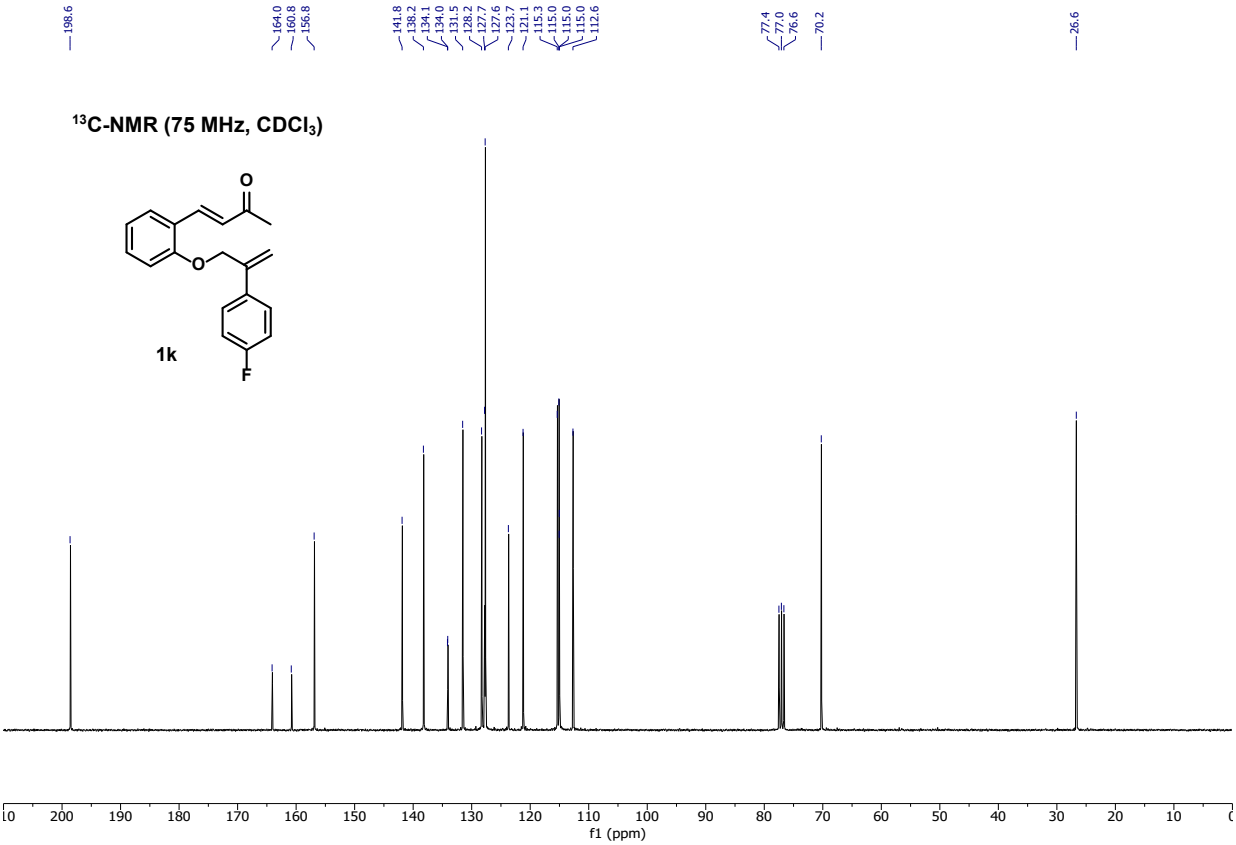


1j



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

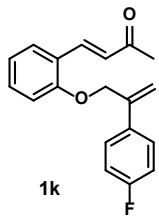
1k



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

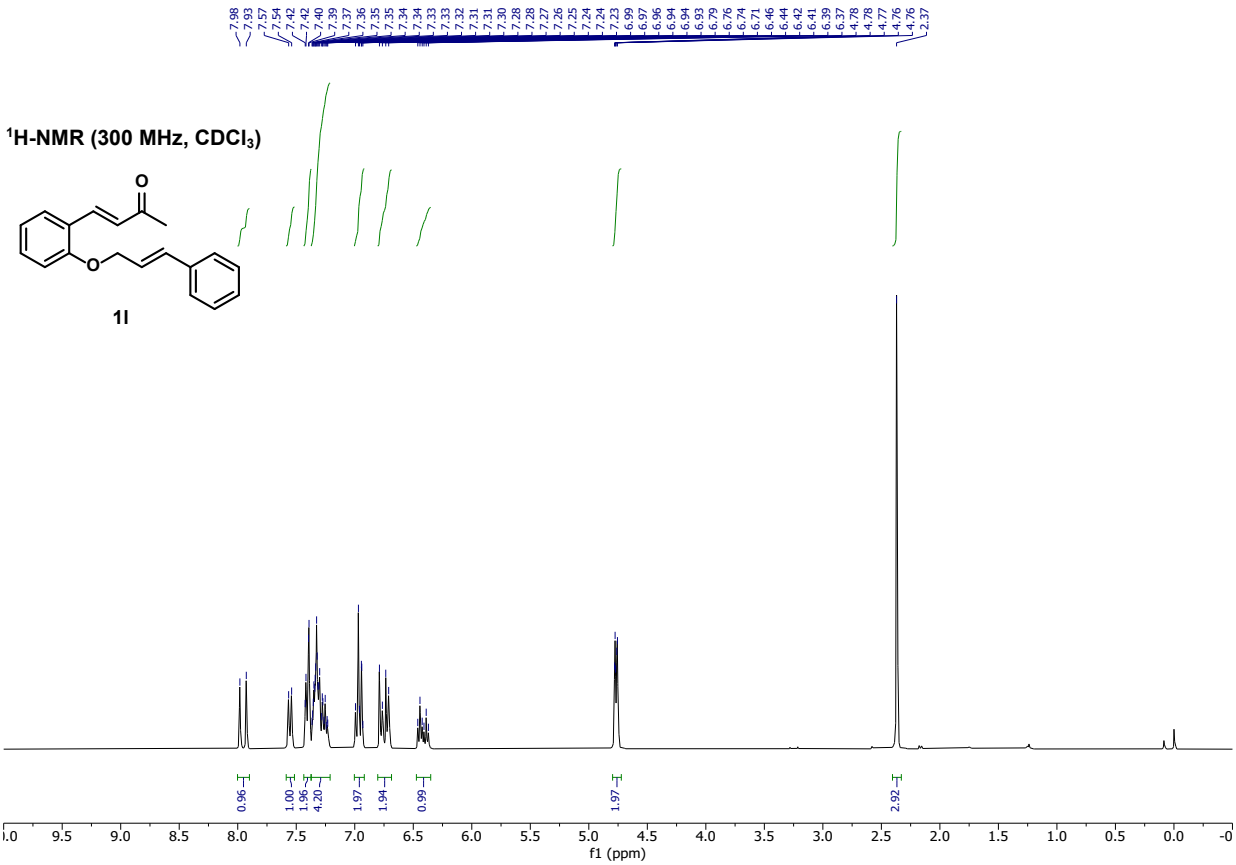
1k

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



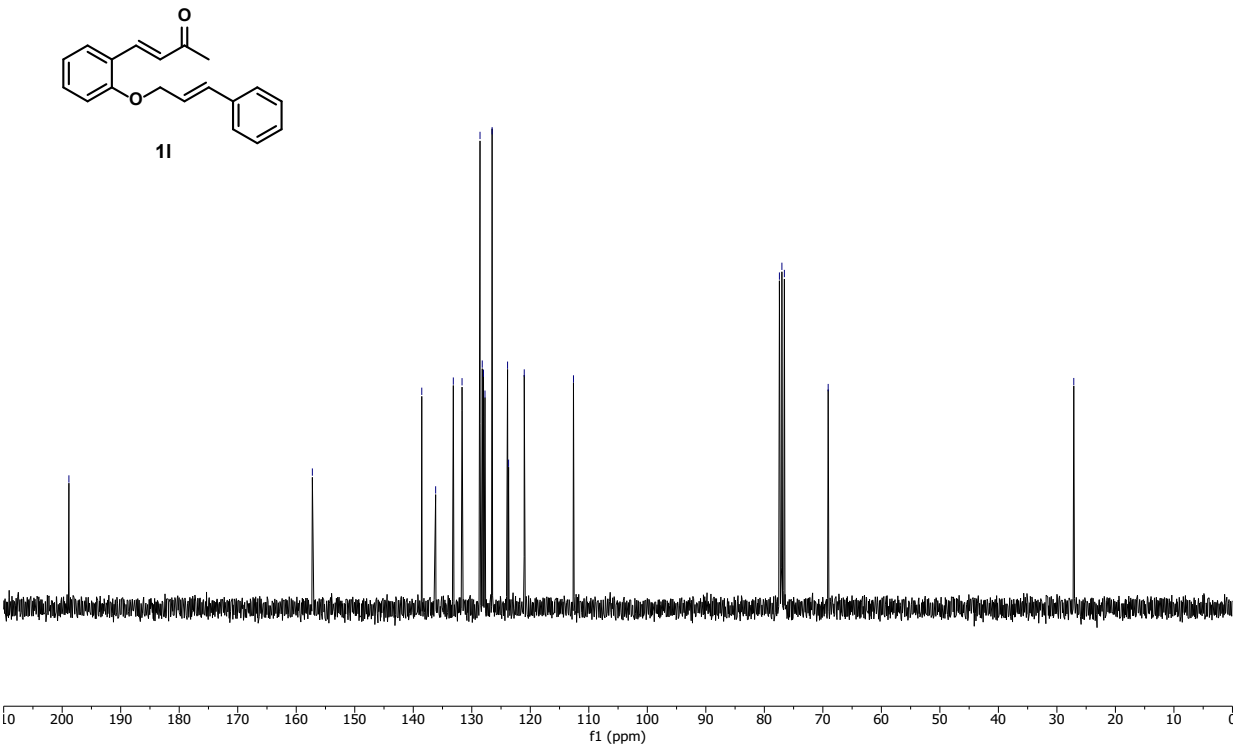
1k

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

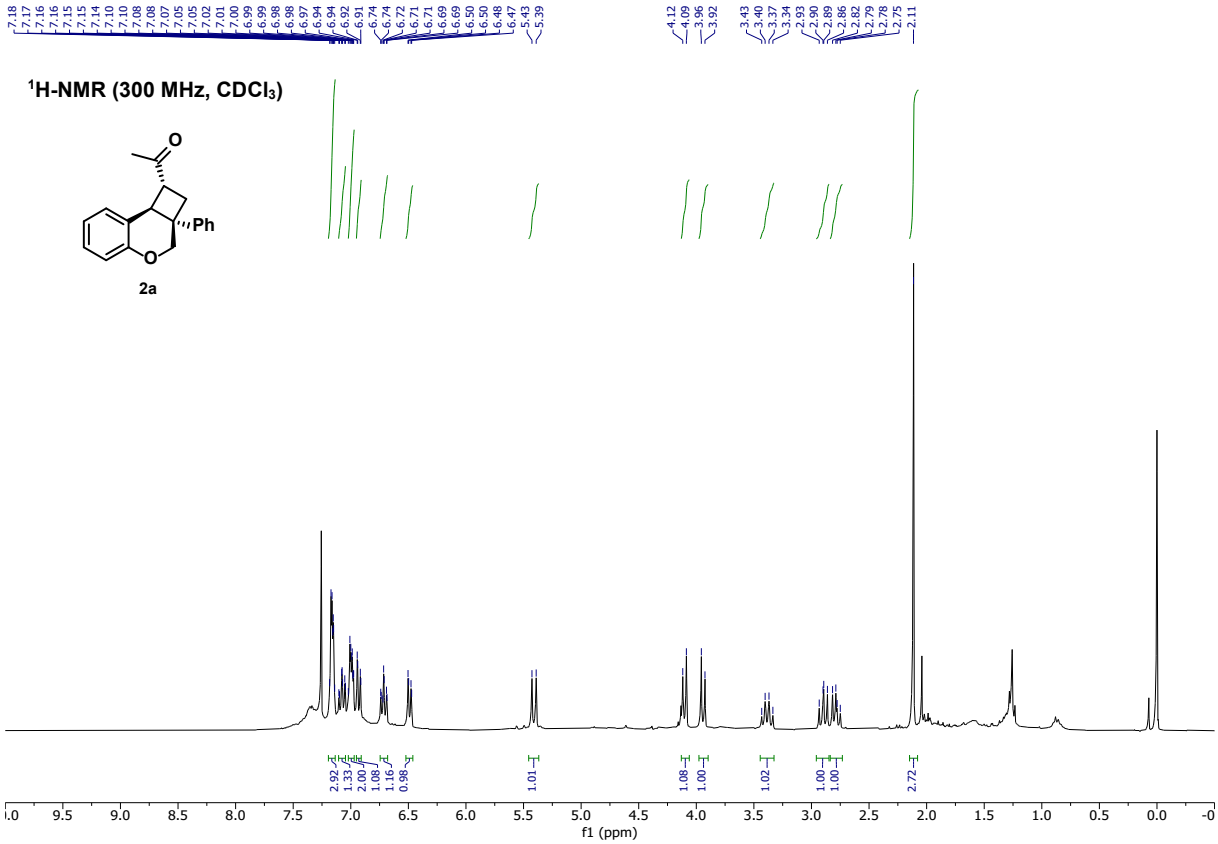


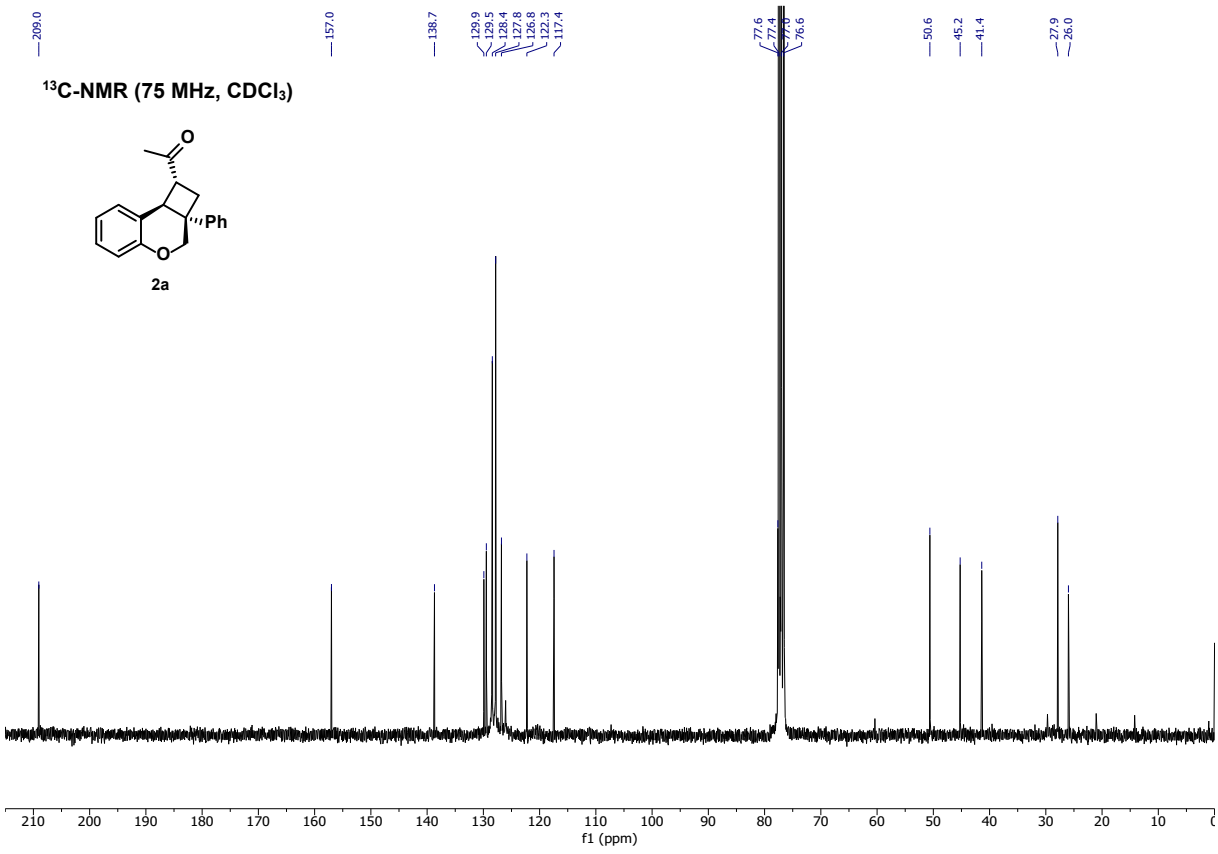
1l

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

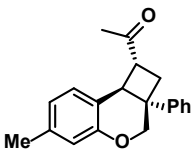


1l


7.18 7.17 7.16 7.16 7.15 7.15 7.14 7.10 7.10 7.08 7.08 7.07 7.05 7.05 7.02 7.01 7.00 6.99 6.99 6.98 6.98 6.97 6.94 6.94 6.92 6.91 6.74 6.74 6.72 6.71 6.71 6.69 6.69 6.50 6.50 6.48 6.47 5.43 5.39
4.12 4.09 3.96 3.92
3.43 3.40 3.37 3.34 2.93 2.90 2.89 2.86 2.82 2.79 2.78 2.75 2.11
1H-NMR (300 MHz, CDCl3)
O
Ph
O
2a
2.92 1.33 2.00 1.08 1.16 0.98 1.01 1.08 1.00 1.02 1.00 1.00 2.72
f1 (ppm)

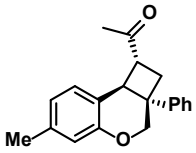

209.0
157.0
138.7
129.9 129.5 128.4 127.8 126.8 122.3 117.4
77.6 77.4 77.0 76.6
50.6
45.2
41.4
27.9 26.0
13C-NMR (75 MHz, CDCl3)
O
Ph
O
2a
f1 (ppm)

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

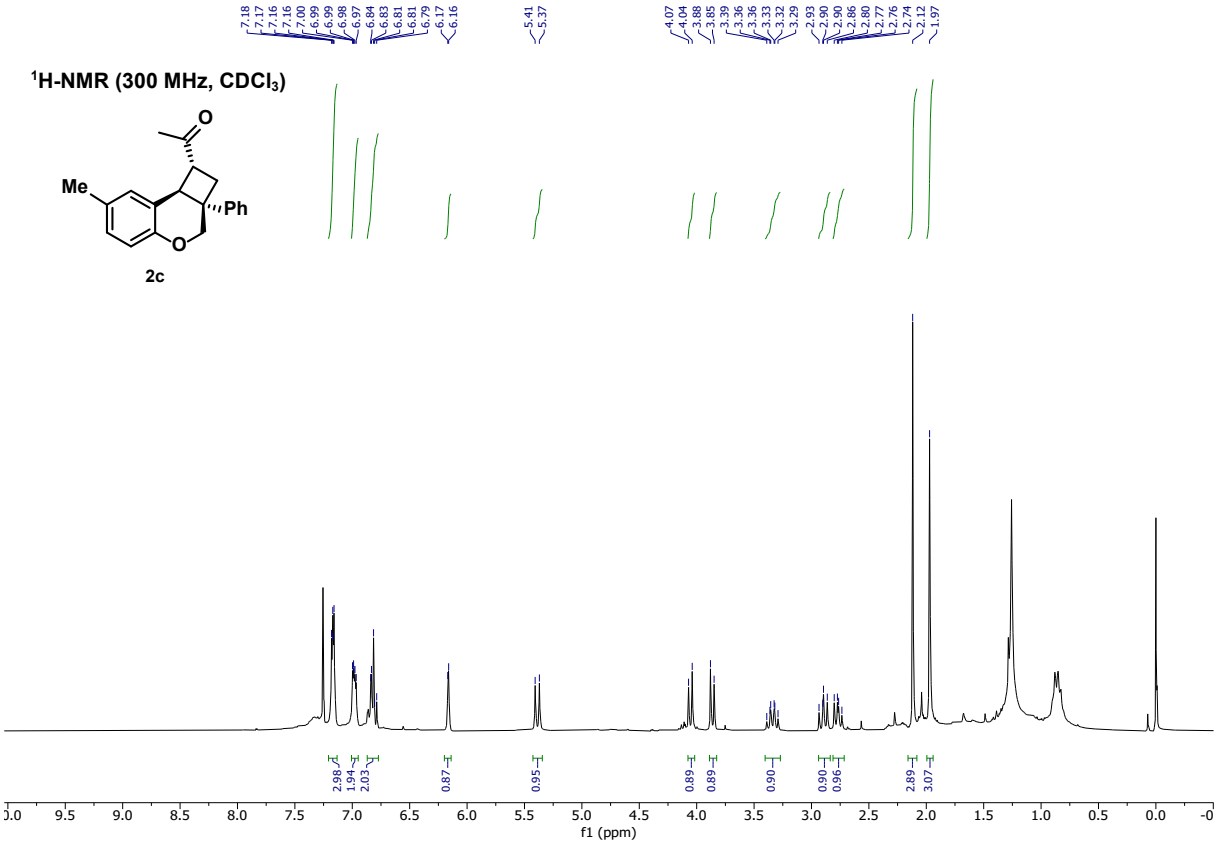


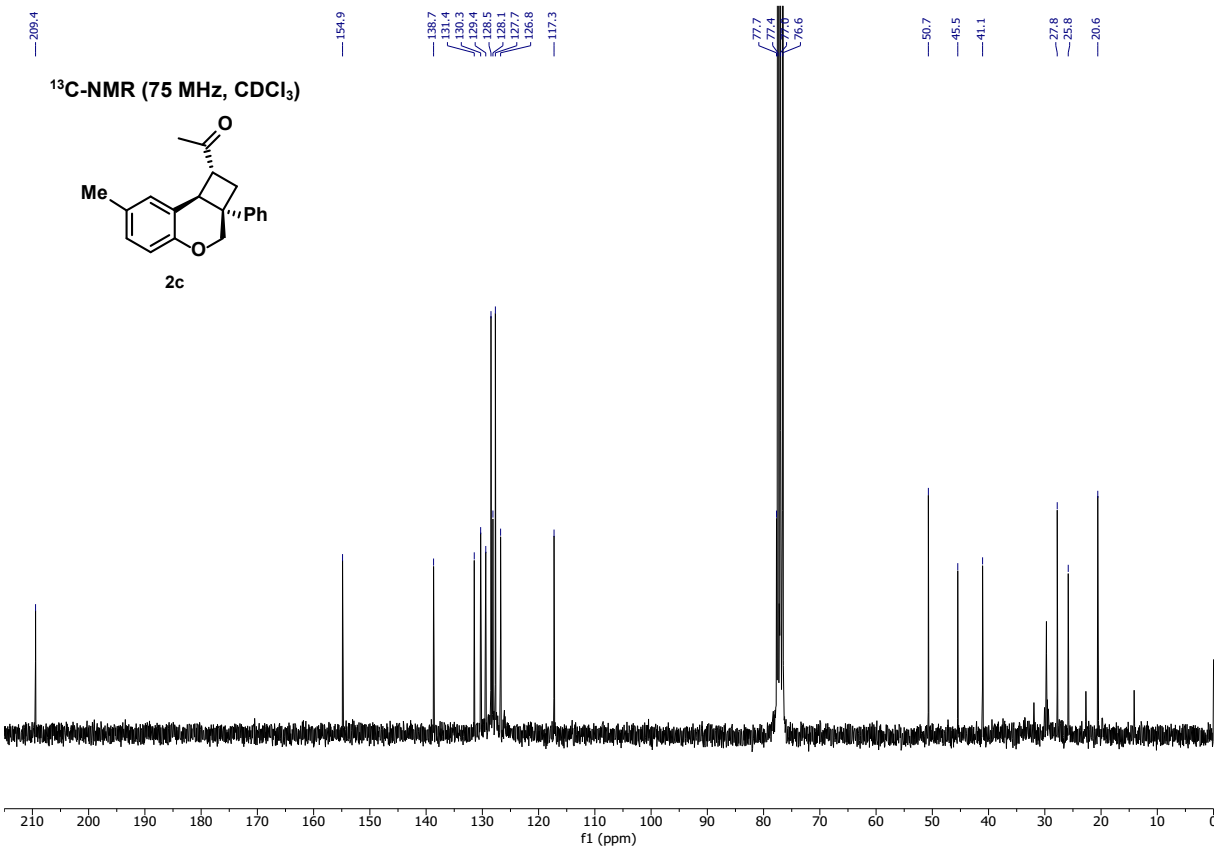
2b

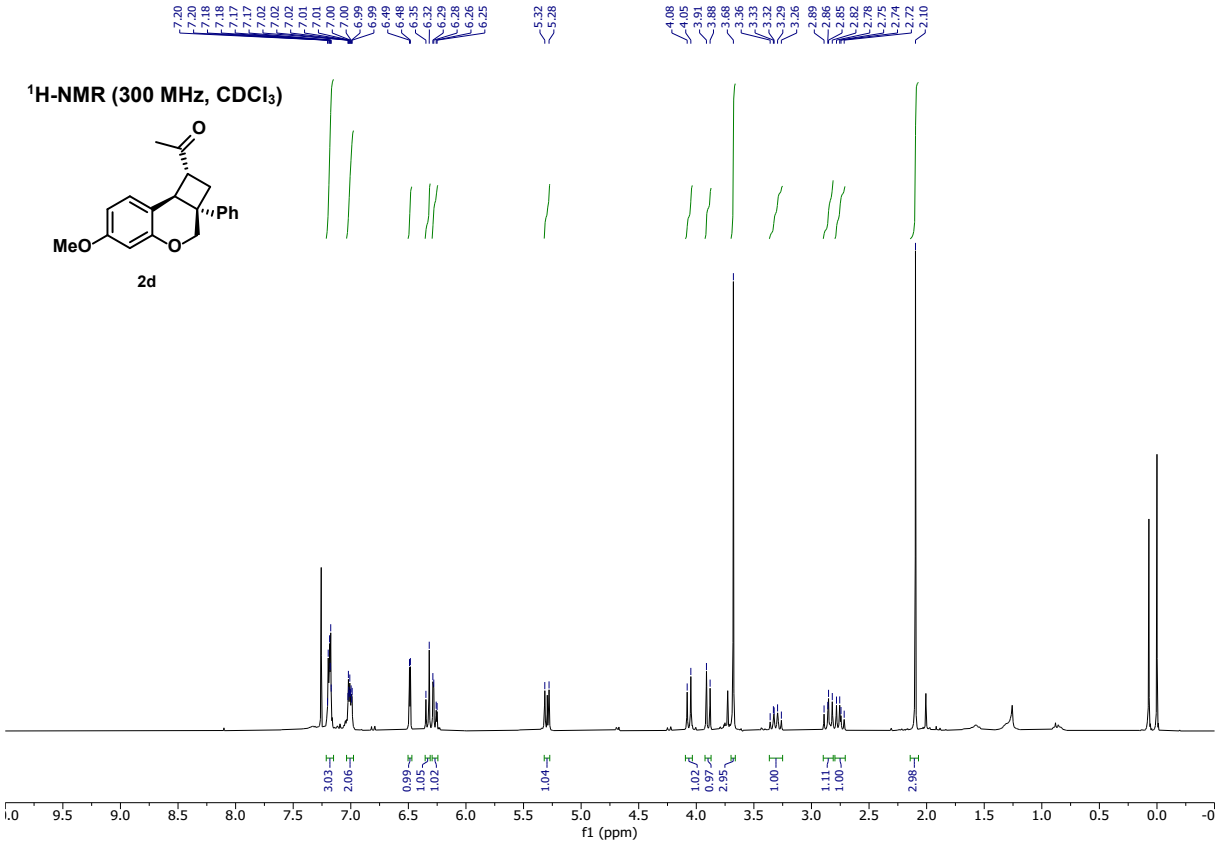
^{13}C-NMR (75 MHz, $CDCl_3$)

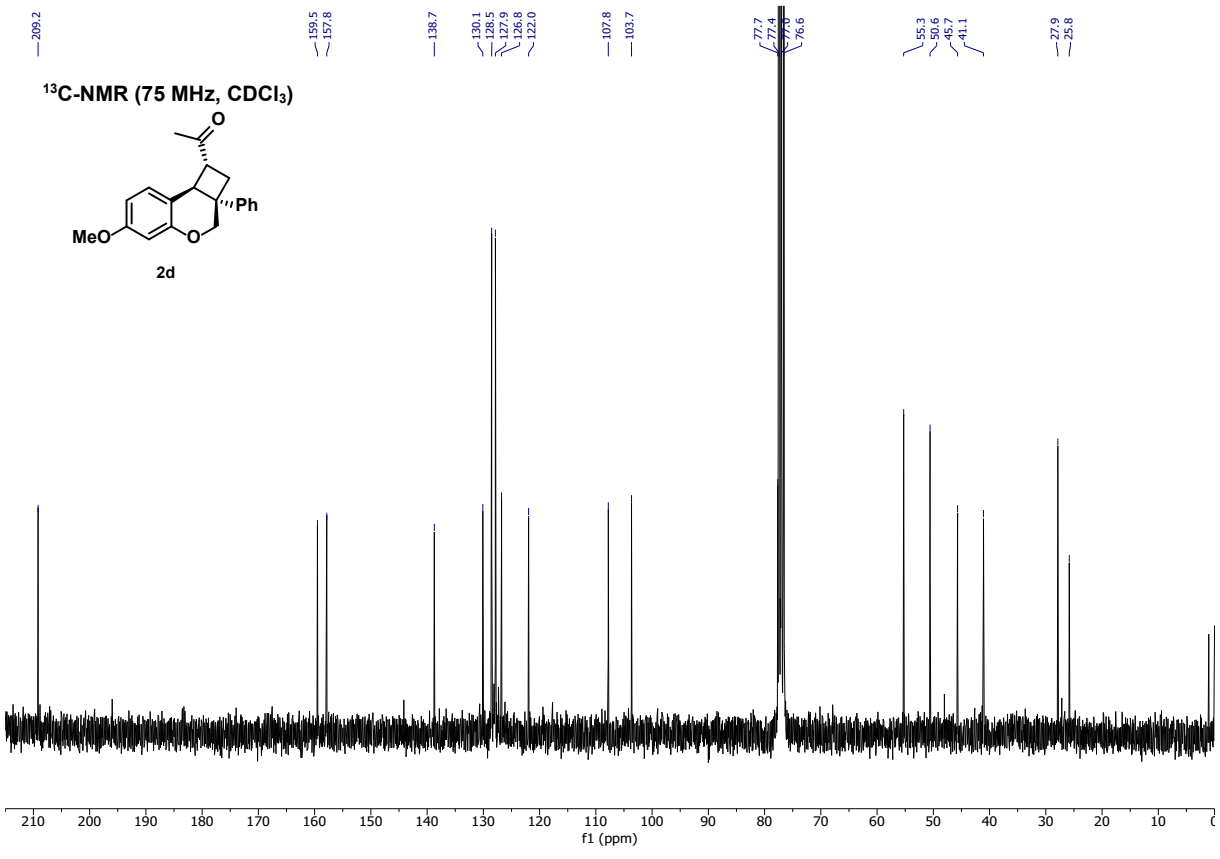


2b

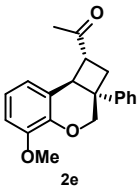

7.18
7.17
7.16
7.16
7.16
7.00
6.99
6.99
6.98
6.97
6.84
6.83
6.81
6.81
6.79
6.17
6.16
5.41
5.37
4.07
4.04
3.88
3.85
3.39
3.36
3.36
3.33
3.32
3.29
2.93
2.90
2.90
2.86
2.80
2.77
2.76
2.74
2.12
1.97
1H-NMR (300 MHz, CDCl3)
O
Me
Ph
O
2c
2.98
1.94
2.03
0.87
0.95
0.89
0.89
0.90
0.90
0.96
2.89
3.07
f1 (ppm)


209.4
154.9
138.7
131.4
130.3
129.4
128.5
128.1
127.7
126.8
117.3
77.7
77.4
77.0
76.6
50.7
45.5
41.1
27.8
25.8
20.6
13C-NMR (75 MHz, CDCl3)
O
Me
Ph
O
2c
f1 (ppm)

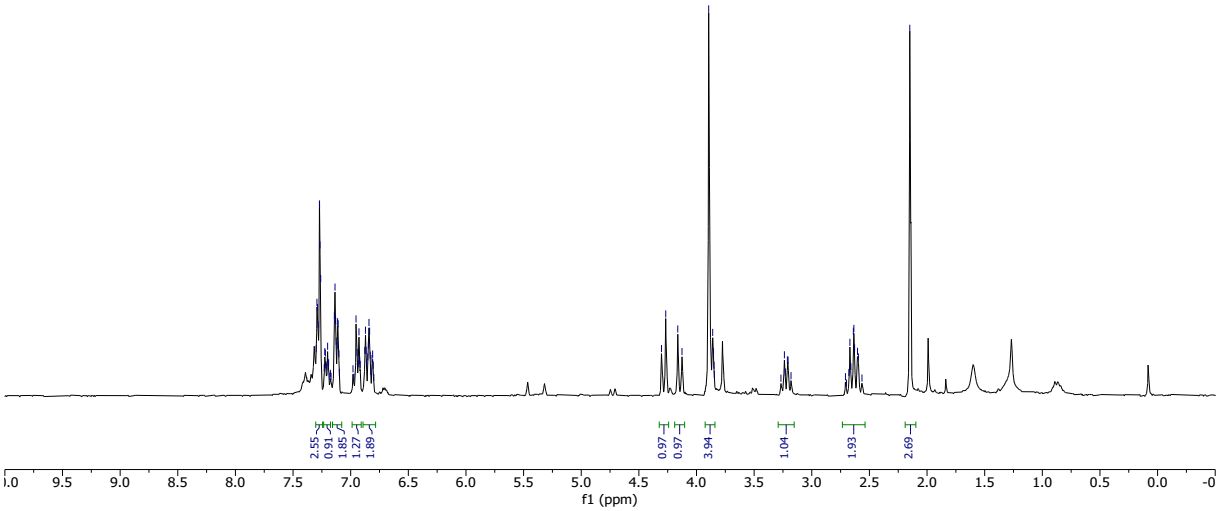

7.20
7.20
7.18
7.18
7.17
7.17
7.02
7.02
7.02
7.01
7.01
7.00
7.00
6.99
6.99
6.49
6.48
6.35
6.32
6.29
6.28
6.26
6.25
5.32
5.28
4.08
4.05
3.91
3.88
3.68
3.36
3.33
3.32
3.29
3.26
2.89
2.86
2.85
2.82
2.78
2.75
2.74
2.72
2.10
1H-NMR (300 MHz, CDCl3)
O
Ph
MeO
O
2d
3.03
2.06
0.99
1.05
1.02
1.04
1.02
0.97
2.95
1.00
1.11
1.00
2.98
f1 (ppm)


209.2
159.5
157.8
138.7
130.1
128.5
127.9
126.8
122.0
107.8
103.7
77.7
77.4
77.0
76.6
55.3
50.6
45.7
41.1
27.9
25.8
13C-NMR (75 MHz, CDCl3)
O
Ph
MeO
O
2d
f1 (ppm)

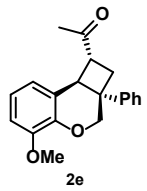
^{1}H-NMR (300 MHz, $CDCl_3$)



2e

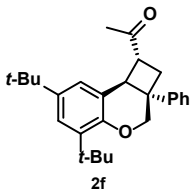


^{13}C-NMR (75 MHz, $CDCl_3$)



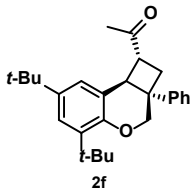
2e

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

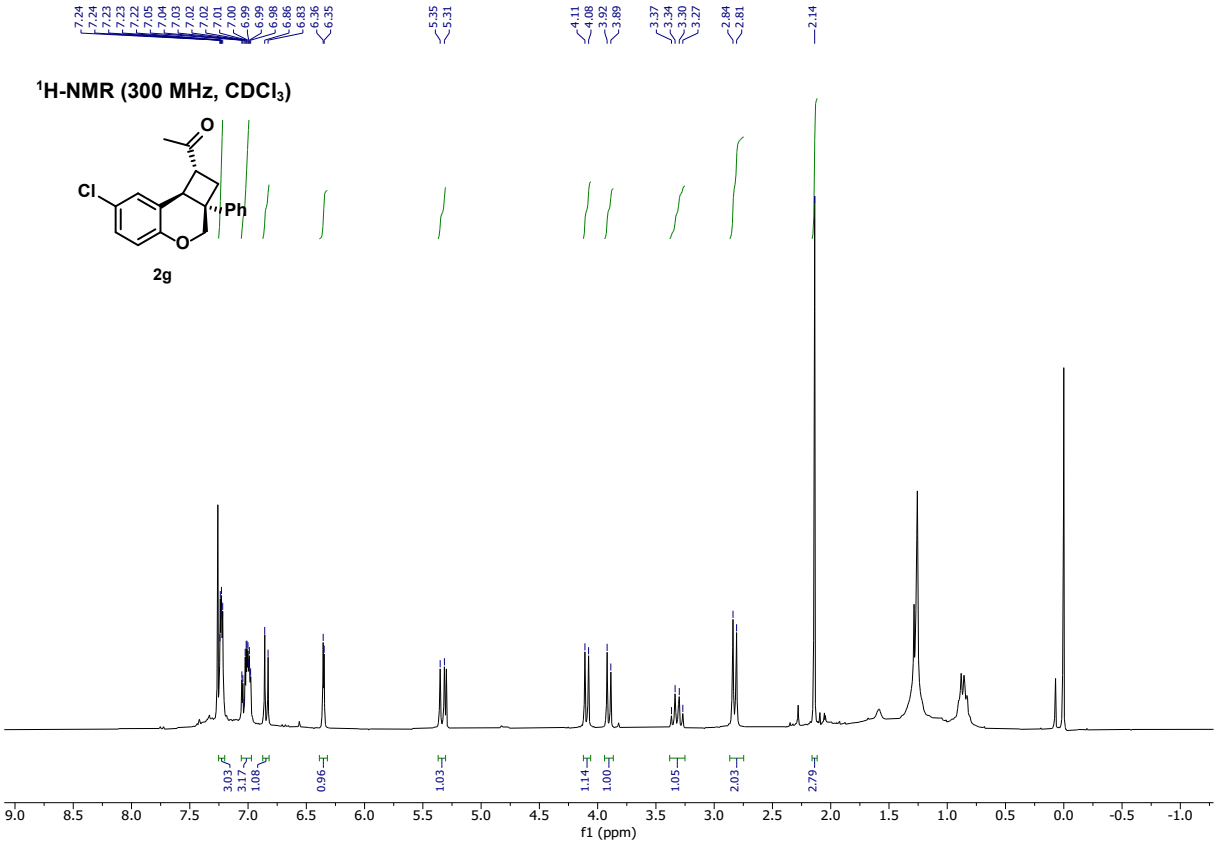


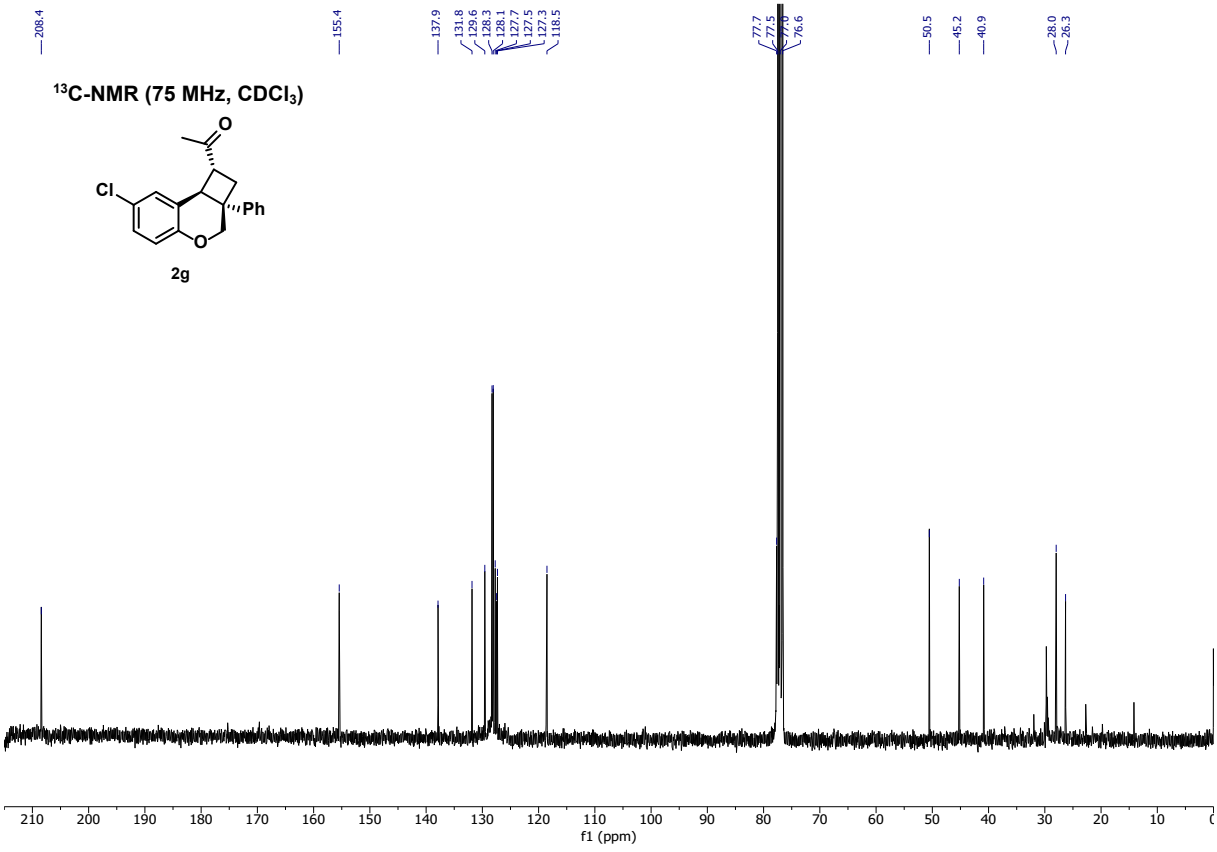
2f

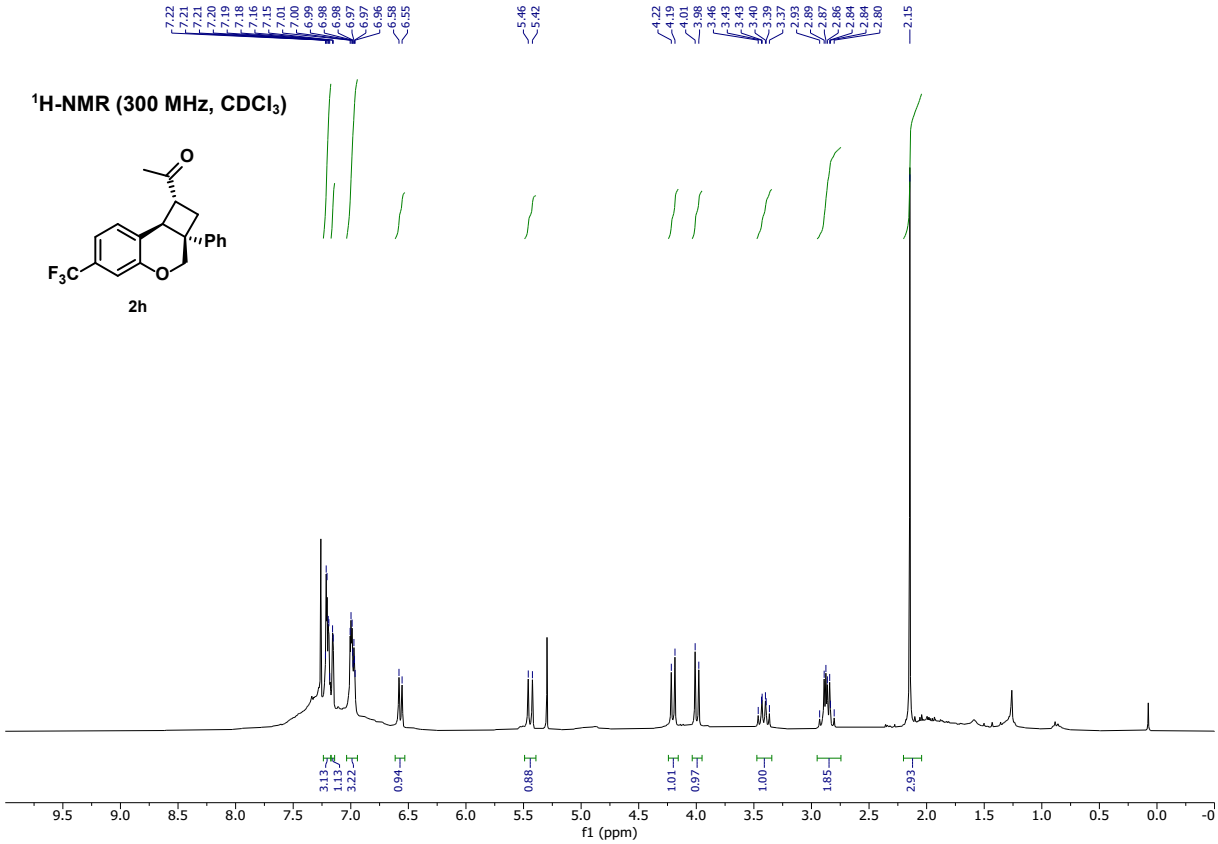
^{13}C-NMR (75 MHz, $CDCl_3$)



2f

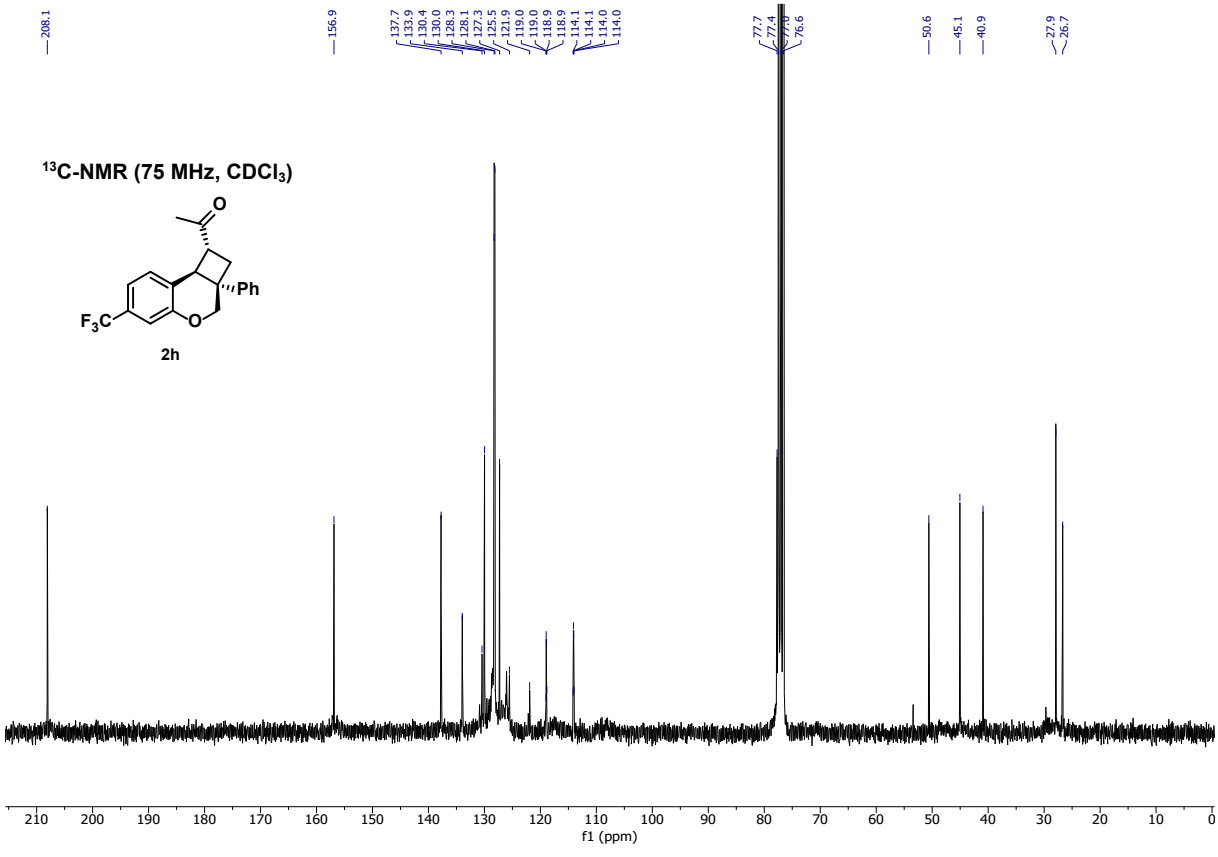

7.24
7.24
7.23
7.23
7.23
7.22
7.05
7.04
7.03
7.02
7.02
7.01
7.00
6.99
6.99
6.98
6.86
6.83
6.36
6.35
5.35
5.31
4.11
4.08
3.92
3.89
3.37
3.34
3.30
3.27
2.84
2.81
2.14
1H-NMR (300 MHz, CDCl3)
Cl
O
Ph
O
2g
3.03
3.17
1.08
0.96
1.03
1.14
1.00
1.05
2.03
2.79
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)


208.4
155.4
137.9
131.8
129.6
128.3
128.1
127.7
127.5
127.3
118.5
77.7
77.5
77.0
76.6
50.5
45.2
40.9
28.0
26.3
13C-NMR (75 MHz, CDCl3)
Cl
O
Ph
O
2g
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)



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

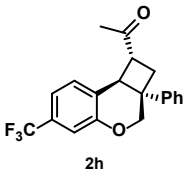
2h



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

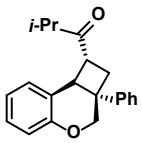
2h

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



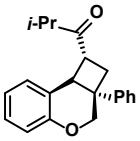
2h

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

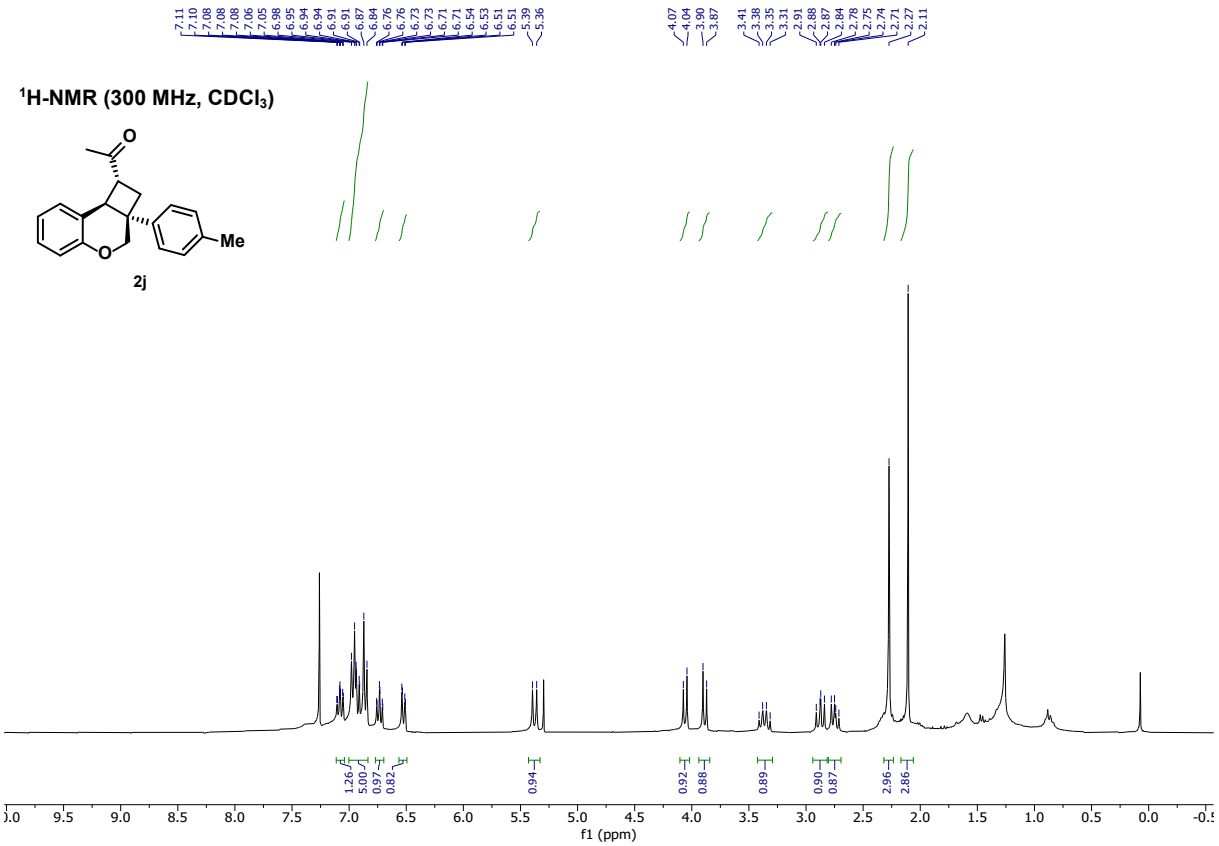


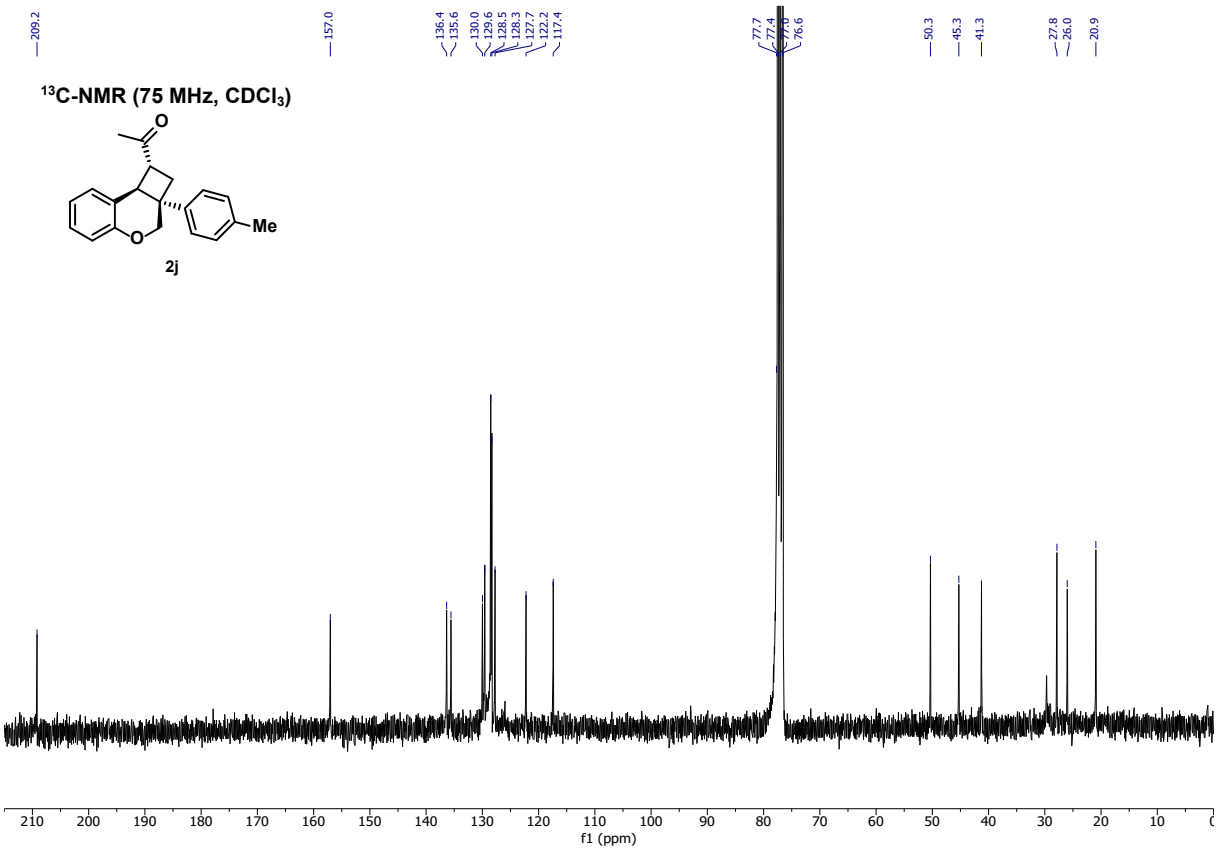
2i

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

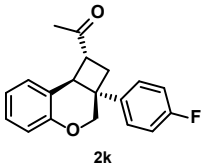


2i


7.11
7.10
7.08
7.08
7.08
7.06
7.05
6.98
6.95
6.94
6.94
6.91
6.91
6.87
6.84
6.76
6.76
6.73
6.73
6.71
6.71
6.54
6.53
6.51
6.51
5.39
5.36
4.07
4.04
3.90
3.87
3.41
3.38
3.35
3.31
2.91
2.88
2.87
2.84
2.78
2.75
2.74
2.71
2.27
2.11
1H-NMR (300 MHz, CDCl3)
O
Me
O
2j
1.26
5.00
0.97
0.82
0.94
0.92
0.88
0.89
0.90
0.87
2.96
2.86
f1 (ppm)

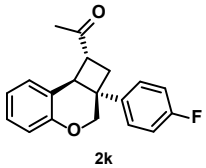

209.2
157.0
136.4
135.6
130.0
129.6
128.5
128.3
127.7
122.2
117.4
77.7
77.4
77.0
76.6
50.3
45.3
41.3
27.8
26.0
20.9
13C-NMR (75 MHz, CDCl3)
O
Me
O
2j
f1 (ppm)

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



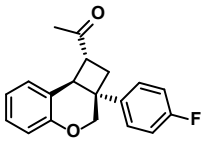
2k

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



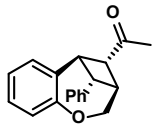
2k

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



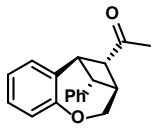
2k

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



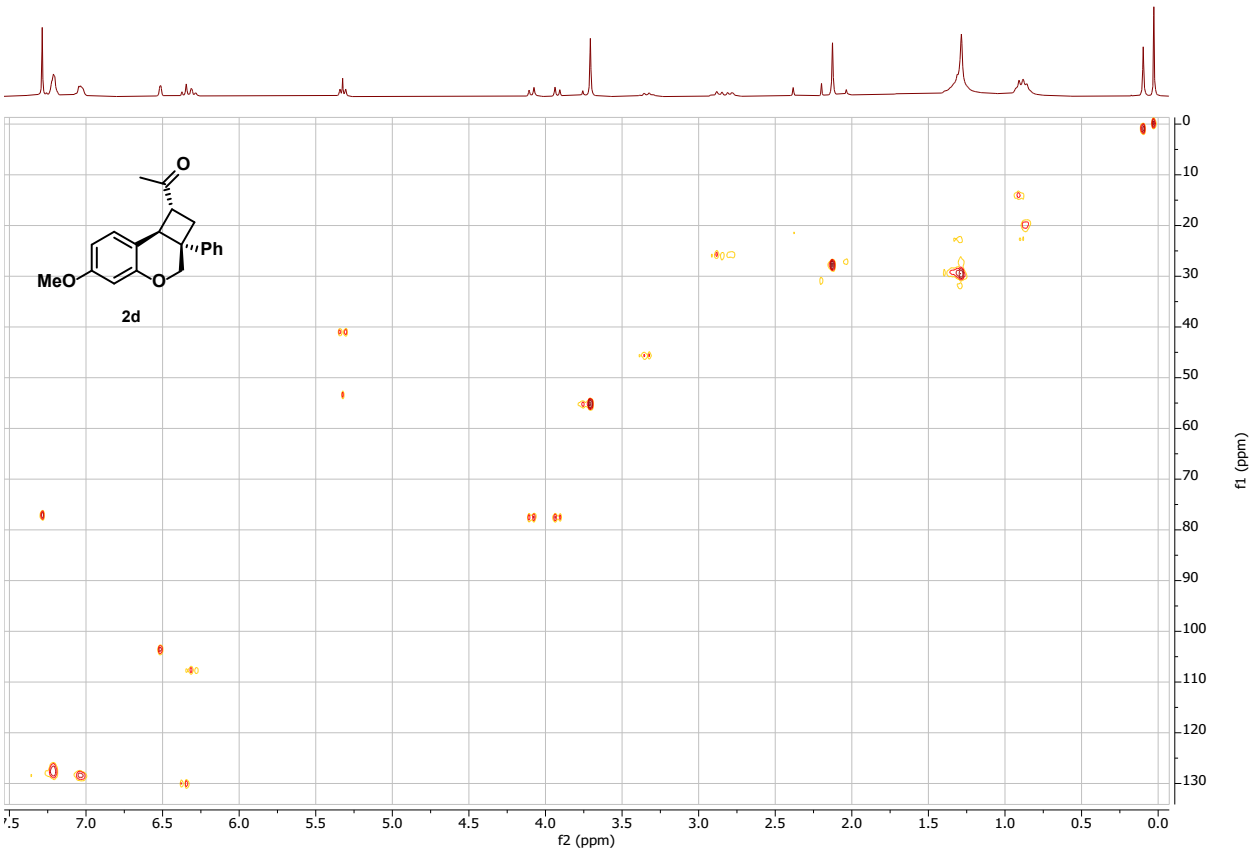
2l

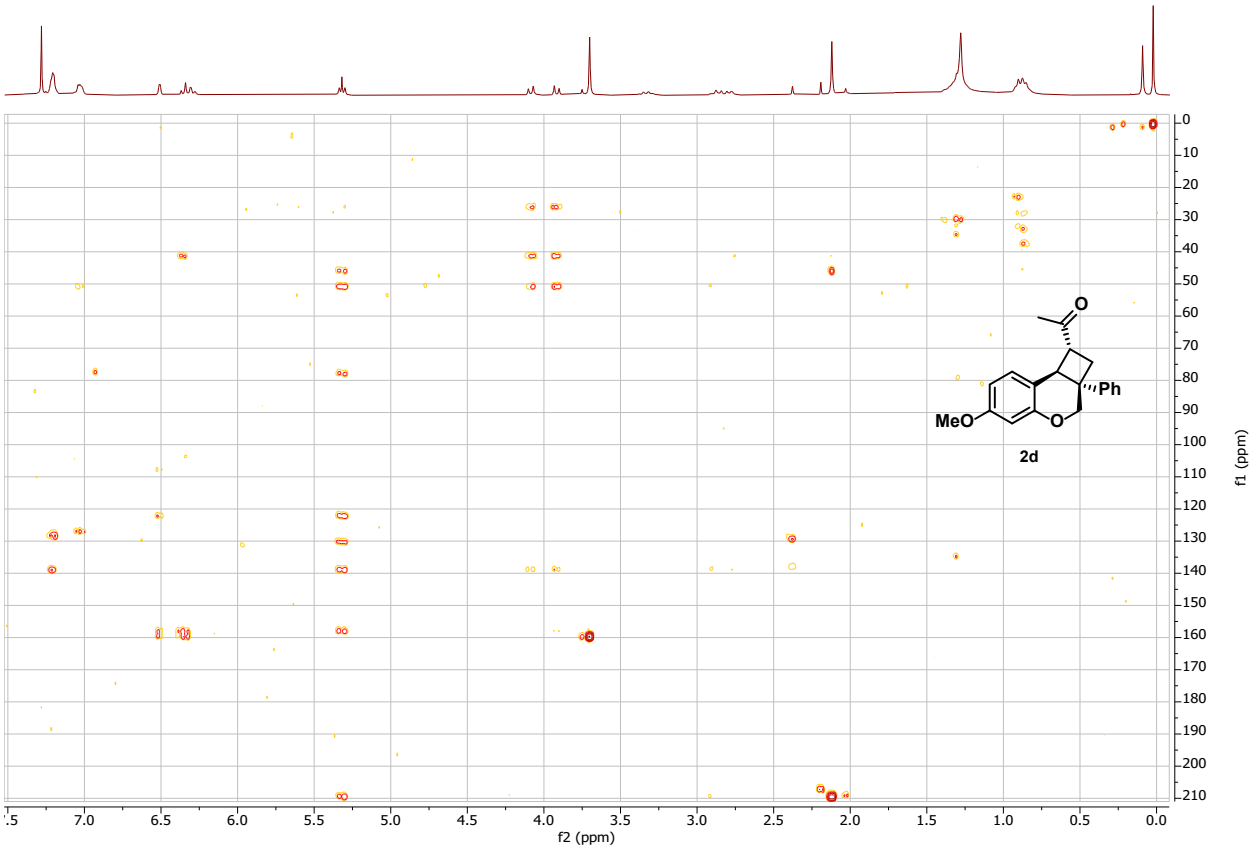
^{13}C-NMR (75 MHz, $CDCl_3$)



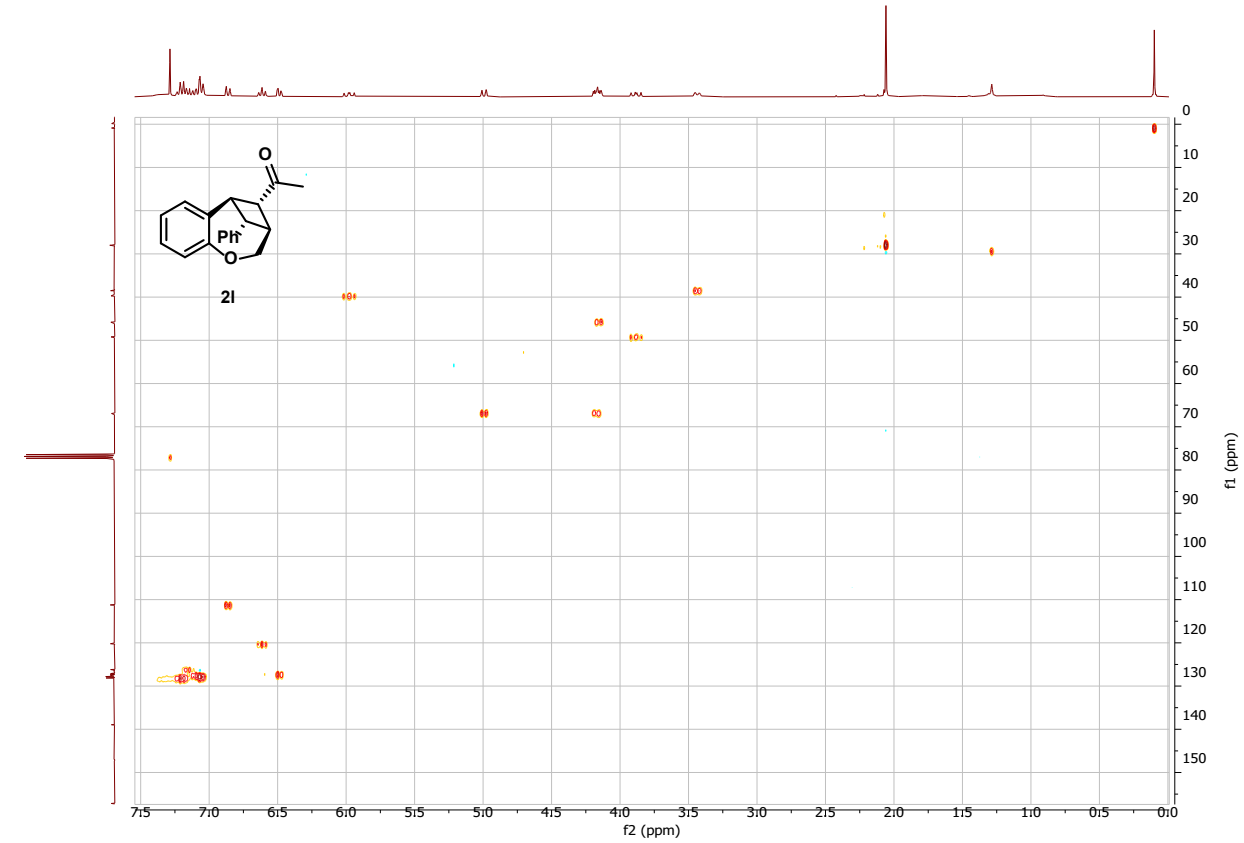
2l

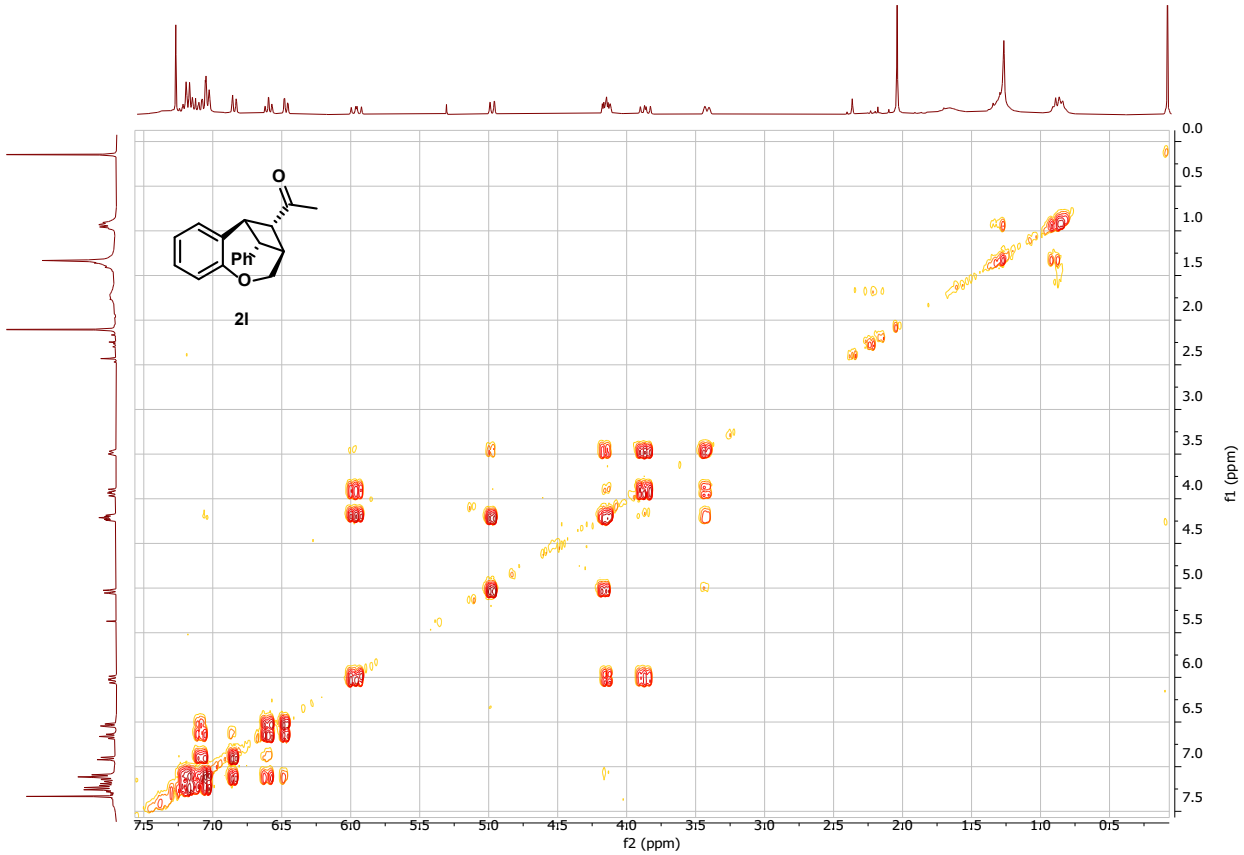
2D NMR experiments for cyclobutane 2d (HSQC, HMBC)

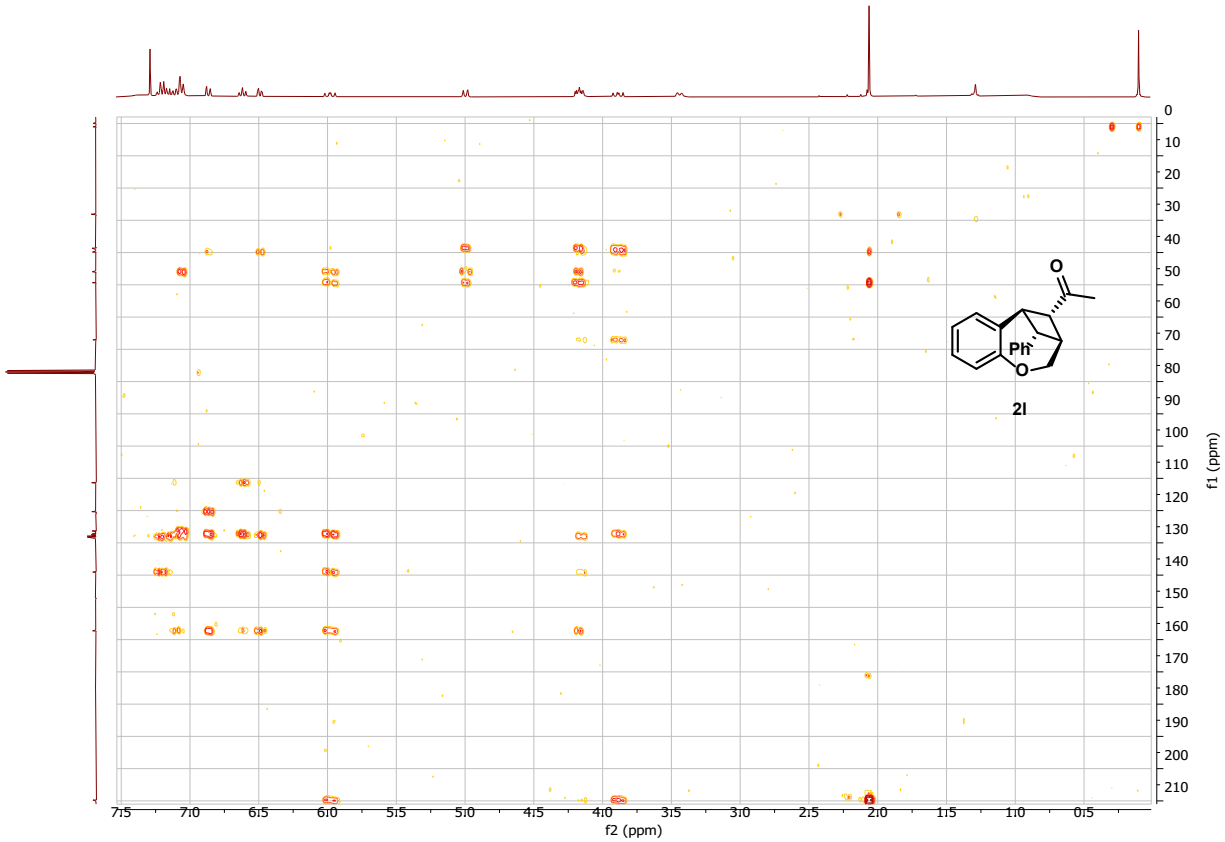




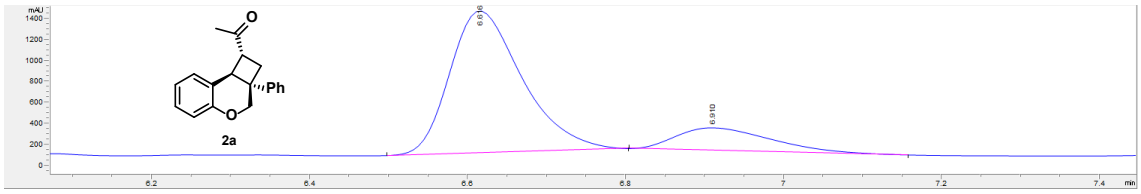
2D NMR experiments for cyclobutane 2l (HSQC, COSY, HMBC)






O
Ph
O
2l
f1 (ppm)
f2 (ppm)

SFC traces



#	Time	Type	Area	Height	Width	Area%	Symmetry
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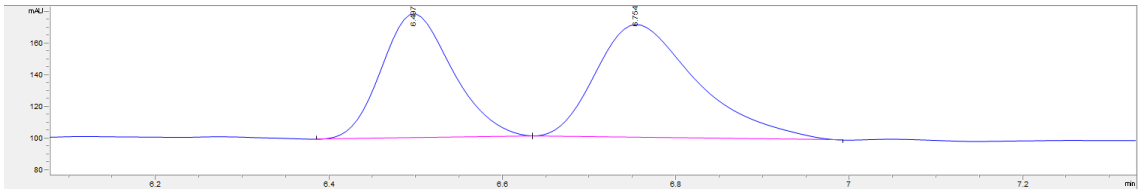
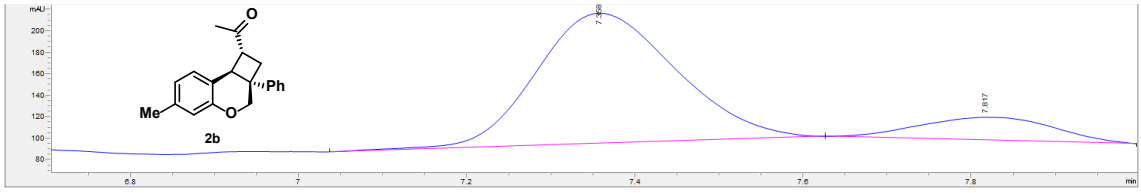
2	6.91	BB	1802.6	214.8	0.1319	17.358	0.57

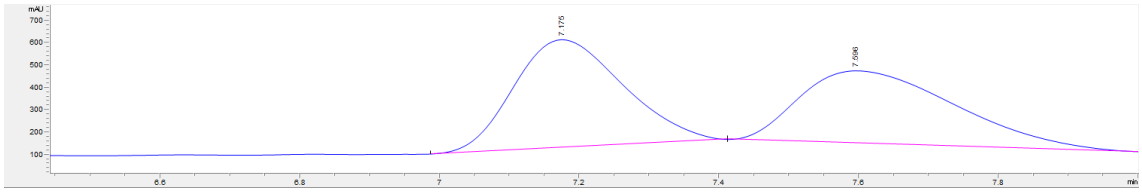


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.497	BB	442.6	77.9	0.0863	43.625	0.8
2	6.754	BB	572	70.8	0.1242	56.375	0.62

Figure S2: SFC chromatograms for compound **2a** (enantioenriched and racemic samples).

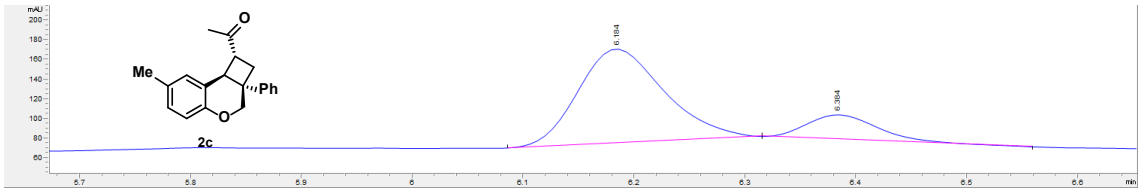


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	7.358	BB	1407.4	121.9	0.1767	85.460	0.815
2	7.817	BBA	239.5	21.5	0.1601	14.540	0.969

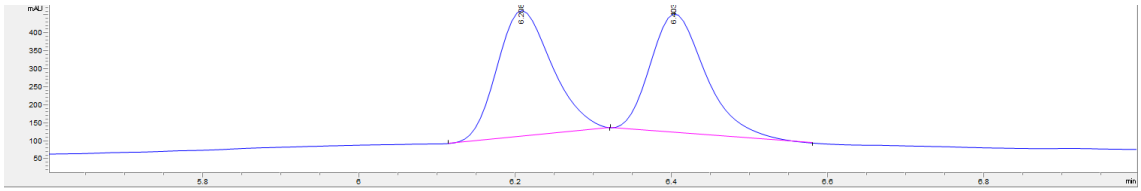


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	7.175	BB	5251.8	483.7	0.1687	50.973	0.766
2	7.596	BBA	5051.2	324.8	0.2454	49.027	0.552

Figure S3: SFC chromatograms for compound **2b** (enantioenriched and racemic samples).

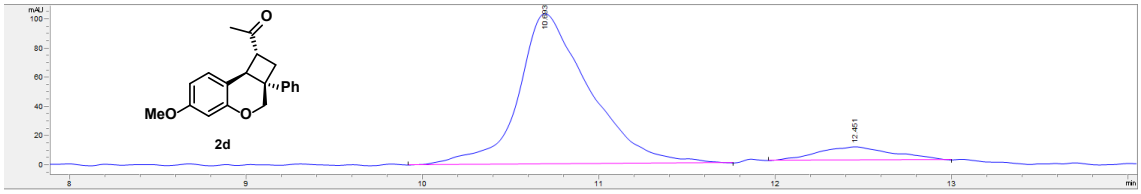


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.184	BB	520.5	96.4	0.083	82.155	0.771
2	6.384	BB	113.1	25.1	0.0705	17.845	0.706

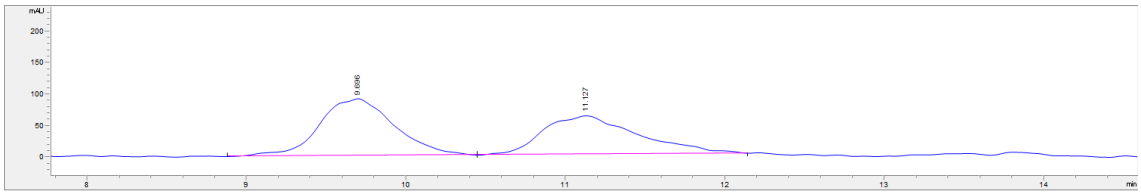


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.208	BB	1721.5	351.4	0.0752	51.331	0.781
2	6.403	BB	1632.2	331.7	0.0754	48.669	0.726

Figure S4: SFC chromatograms for compound **2c** (enantioenriched and racemic samples).

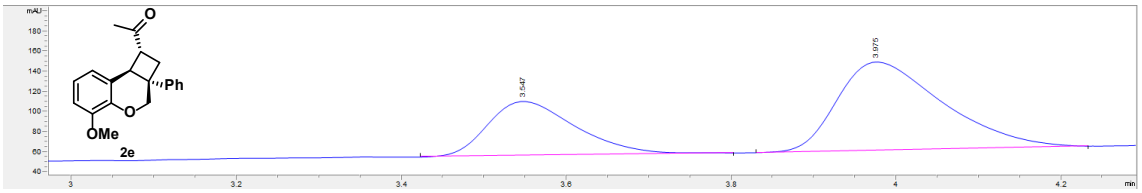


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.693	BB	2907	103.7	0.3871	91.331	0.602
2	12.451	BB	275.9	9.2	0.3778	8.669	0.944

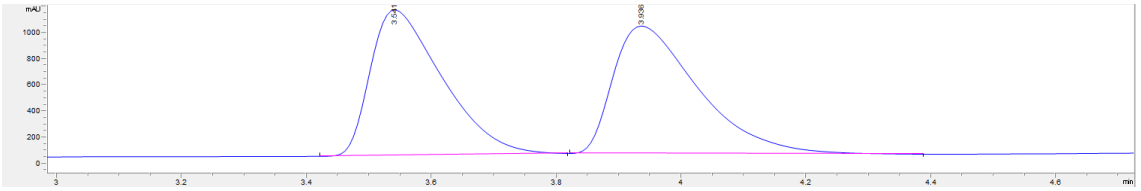


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.696	BB	2976.6	90.6	0.4091	53.900	1.03
2	11.127	BB	2545.8	61.2	0.5309	46.100	0.781

Figure S5: SFC chromatograms for compound **2d** (enantioenriched and racemic samples).

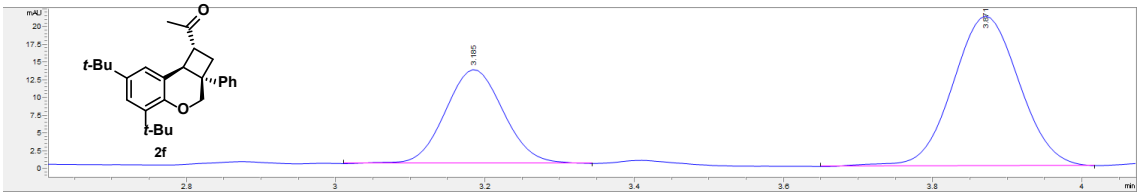


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.547	BB	402.4	54.2	0.1126	33.944	0.648
2	3.975	BB	783.1	88.2	0.1355	66.056	0.563

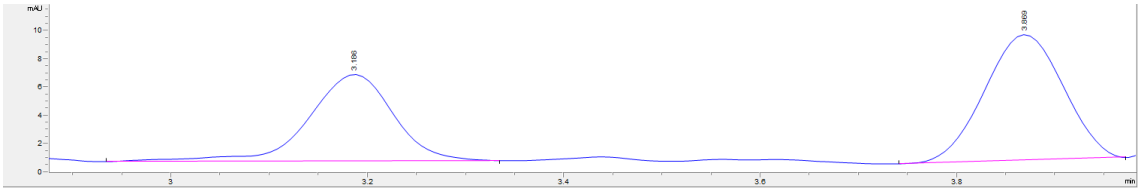


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.541	BB	8869.3	1111.8	0.1211	48.976	0.482
2	3.936	BB	9240	974.5	0.1446	51.024	0.462

Figure S6: SFC chromatograms for compound **2e** (enantioenriched and racemic samples).

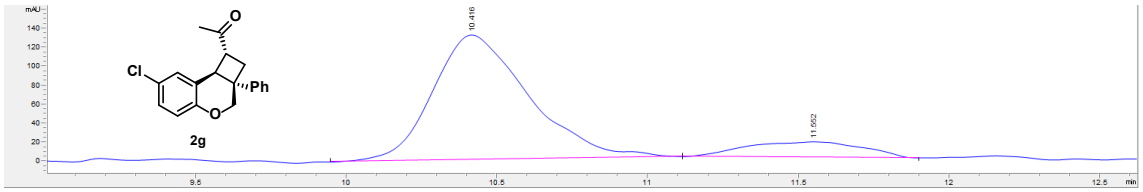


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.185	BB	72.4	13.3	0.0854	35.475	0.944
2	3.871	BB	131.6	21.2	0.0963	64.525	0.966

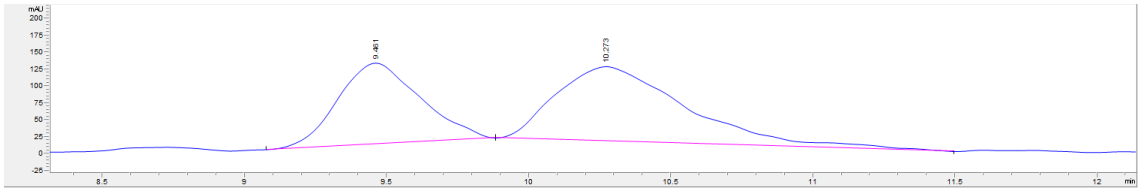


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.186	BB	36.9	6.1	0.0921	42.637	1.181
2	3.869	BB	49.7	8.9	0.089	57.363	1.006

Figure S7: SFC chromatograms for compound **2f** (enantioenriched and racemic samples).

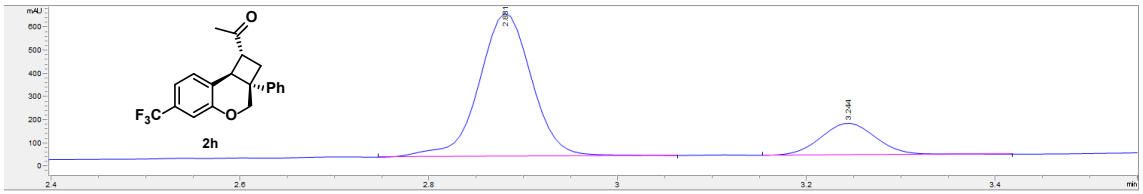


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	10.416	BB	2905.3	131.1	0.3484	86.880	0.661
2	11.552	BB	438.7	16.2	0.3297	13.120	1.334

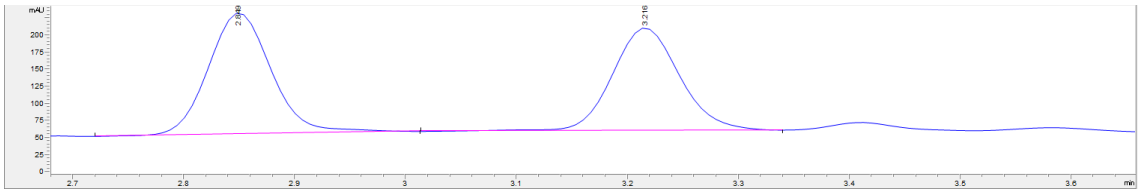


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	9.461	BB	2431.1	120.3	0.2998	40.585	0.824
2	10.273	BB	3559	110.9	0.4485	59.415	0.58

Figure S8: SFC chromatograms for compound **2g** (enantioenriched and racemic samples).

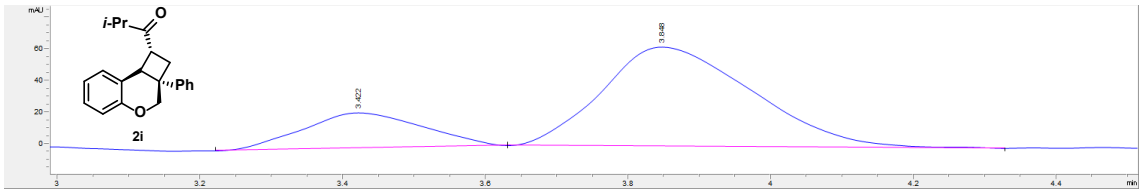


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.881	BB	2382.1	615.9	0.0591	81.152	0.993
2	3.244	BB	553.3	136.1	0.0634	18.848	0.924

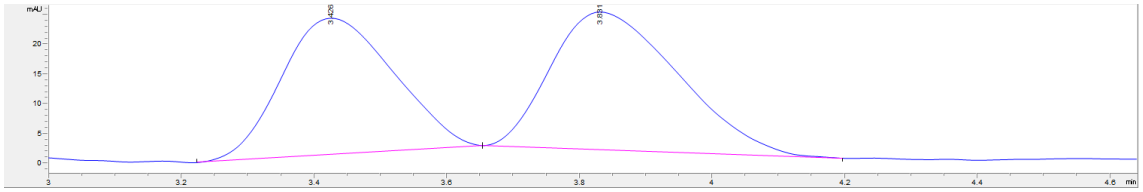


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	2.849	BB	705.1	178.1	0.0622	52.474	0.878
2	3.216	BB	638.6	150.7	0.0654	47.526	0.91

Figure S9: SFC chromatograms for compound **2h** (enantioenriched and racemic samples).

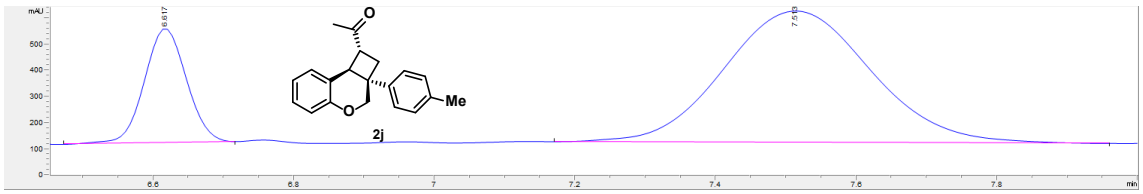


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.422	BB	264.3	22.6	0.1727	22.081	0.867
2	3.848	BB	932.6	63.3	0.2198	77.919	0.646

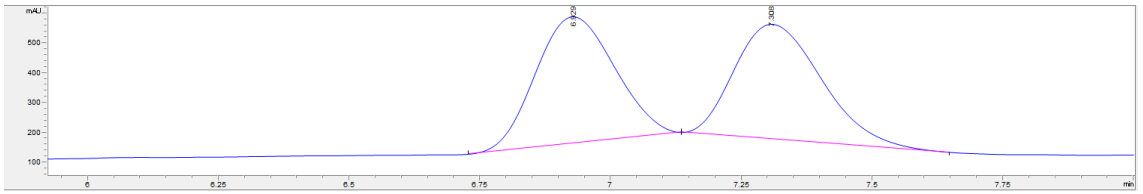


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	3.426	BB	267.4	22.8	0.1829	46.537	0.791
2	3.831	BB	307.2	23	0.2178	53.463	0.605

Figure S10: SFC chromatograms for compound **2i** (enantioenriched and racemic samples).

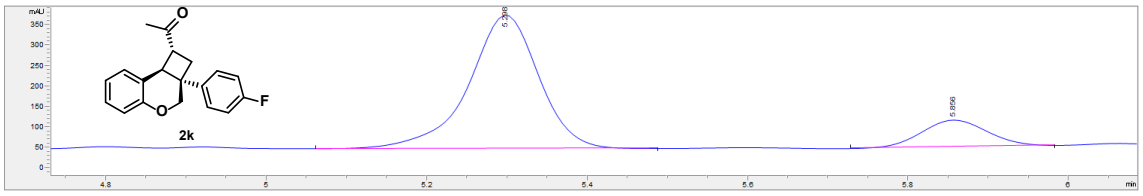


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.617	BB	1810.4	436	0.0644	19.875	0.953
2	7.513	BB	7298.5	500.9	0.226	80.125	0.922

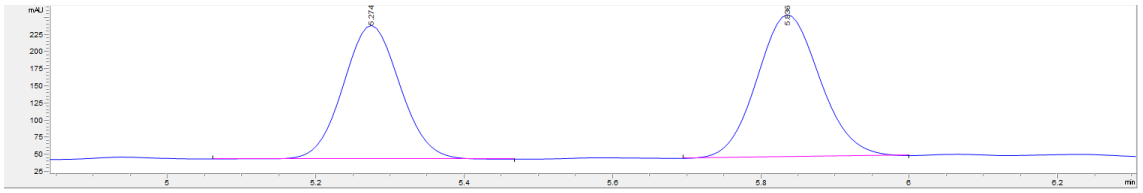


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	6.929	BB	4498.9	428	0.1686	49.995	0.884
2	7.308	BB	4499.7	388	0.1853	50.005	0.708

Figure S11: SFC chromatograms for compound **2j** (enantioenriched and racemic samples).

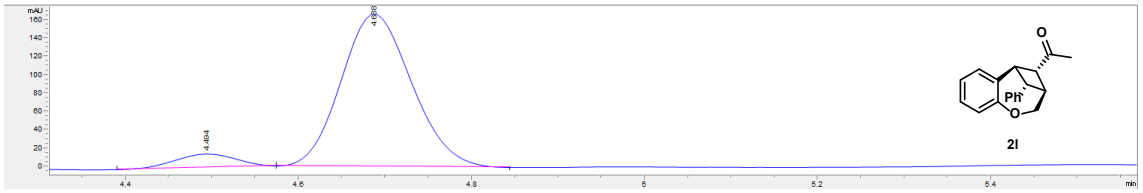


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.298	BB	1976.4	326.1	0.0907	84.096	1.107
2	5.856	BB	373.8	65.6	0.0885	15.904	0.942

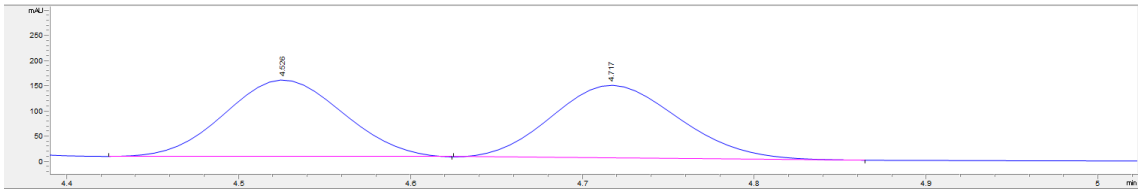


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.274	BB	1040.7	195.2	0.0842	45.872	0.932
2	5.836	BB	1228	207.9	0.0909	54.128	0.904

Figure S12: SFC chromatograms for compound **2k** (enantioenriched and racemic samples).



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.494	BB	71.9	14.7	0.079	7.072	1.123
2	4.688	BB	944.3	166.4	0.0902	92.928	0.846



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	4.526	BB	724.7	151.8	0.0757	49.495	0.933
2	4.717	BB	739.5	144.2	0.0818	50.505	0.845

Figure S13: SFC chromatograms for compound **2l** (enantioenriched and racemic samples).

Computed Electronic Circular Dichroism

Calculations have been carried out with the Gaussian16 package.[3] Geometry optimization was performed using the density functional theory (DFT); in particular with the hybrid exchange-correlation B3LYP functional[4-6] and the 6-311+G(d,p) basis set.[7,8] Over this geometry, UV-VIS and Electronic Circular Dichroism (ECD) spectra were simulated with electronic excited state calculations computed by using the time-dependent DFT method (TD-DFT);[9-12] in this case we employed the CAM-B3LYP functional,[13] which introduces a long-range correction, and the same basis set. To mimic the experimental conditions, solvent effects (acetonitrile) were introduced in both type of simulations (geometry optimization and electronic excited states) by using the Integral Equation Formalism of the Polarizable Continuum Model (IEFPCM).[14-16]

Simulated electronic circular dichroism spectra are presented in **Fig S14** together with the experimental measured one for compound **2d**. We consider the two enantiomers shown in the figure to unequivocally assign the absolute configuration. The enantiomer in the upper panel reproduces the main transitions in the experimental ECD. The simulated spectrum of this conformation is slightly shifted, by approximately 25 nm, with respect to the experimental one, and underestimate the intensity of the band at 280nm; but the positive doublet structure at 230 nm and the negative sharp peak at 200 nm confirms the assignation to the enantiomer in the upper panel.

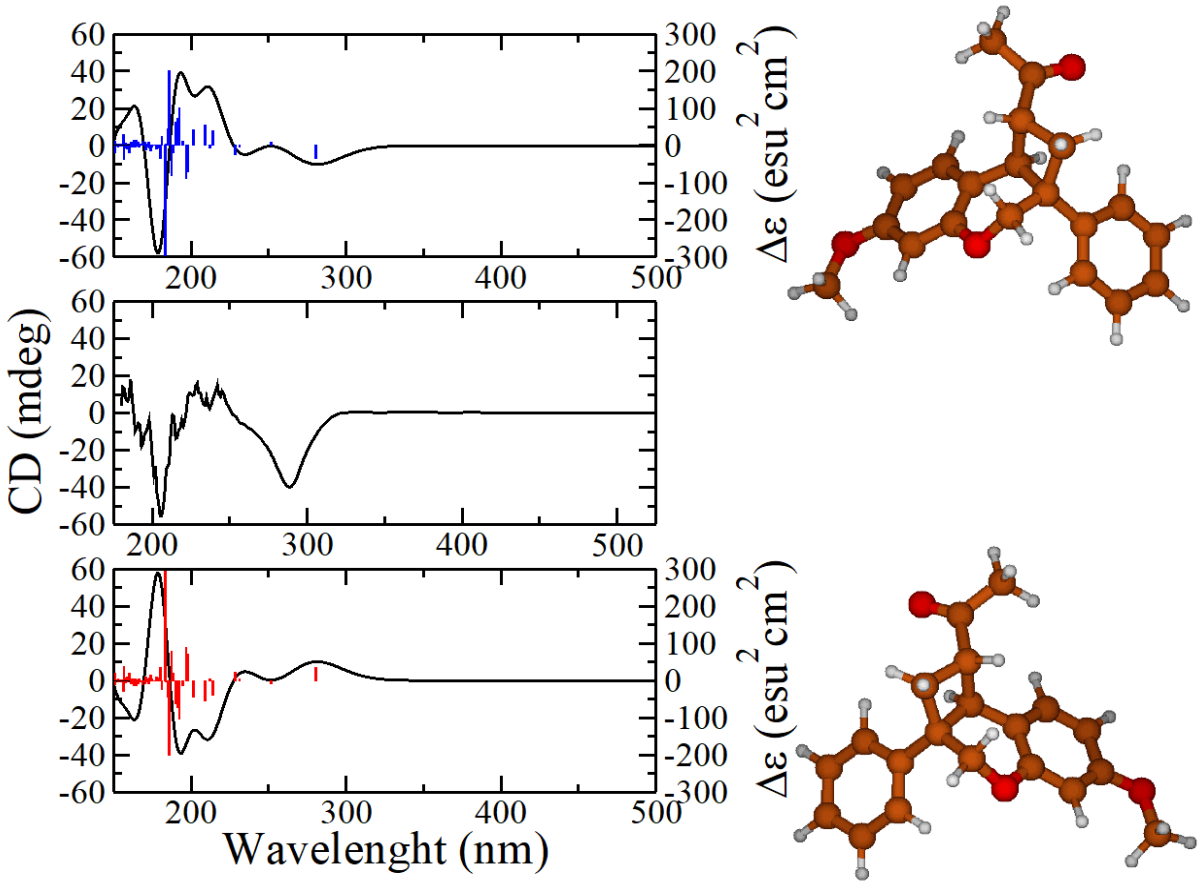


Figure S14: Electronic Circular Dichroism spectra for compound **2d**. Central panel experimentally measured ECD spectra. Upper and lower panels simulated ECD spectra for the enantiomers shown in at the right of each spectra. Transitions are shown in blue and red bars for each enantiomer. The simulated spectra were computing by introducing a peak half-width of 0.3 eV. Notice that the wavelength scale in the computed spectra are shifted by 25 nm with respect to the experimental one.

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