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

A Short Access to Oxaspiro[n,3,3]propellanes

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Experimental part

General working methods

The analytical data were obtained with the help of the following equipment.

NMR spectroscopy
^{1}H and ^{13}C NMR spectra were acquired on a Bruker Avance 300 (300 MHz), 400 (400 MHz) or 500 (500 MHz). in $CDCl_3$ as a solvent. The chemical shifts were reported relative to $CDCl_3$ (δ = ^{1}H: 7.26 ppm, ^{13}C: 77.16 ppm). The multiplicities of the signals are described using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, p = quintuplet, brd = broad. The spectra were evaluated with the software MestReNova.

Mass spectra were obtained on an electrospray (ESI) (Spectromètre amaZon SL Bruker or Spectromètre QTOF Impact II - Bruker).

IR spectra were measured on a JASCO FT/IR-4100 Spectrometer. Characteristic absorption bands are displayed in wavelengths $\tilde{\nu}$ in cm^{-1} and were analyzed with the software Spectral Manager from JASCO.

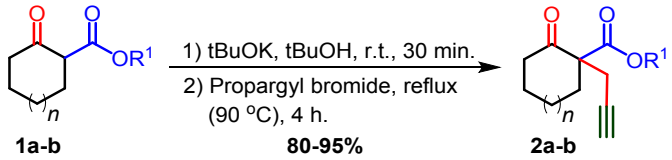
Melting points were measured on a B-540 from the company BÜCHI.

Chromatography Reaction progress was monitored by thin-layer chromatography on aluminium backed silica gel plates (silica gel 60 with fluorescent indicator UV_{254} from Macherey-Nagel (MN)), visualizing with UV light (λ = 254 nm). The plates were developed using $KMnO_4$ dip solution (3.0 g potassium permanganate, 5.0 mL NaOH-solution (5 w/w), 300 mL dest. water), cer dip solution (5.0 g phosphomolybdic acid, 16.0 mL conc. sulfuric acid, 200 mL dest. water, 2.0 g cer(IV)-sulfate) or an anisaldehyde solution (450 mL ethanol, 25.0 mL anisaldehyde, 25.0 mL conc. sulfuric acid, 8.0 mL acetic acid). Flash chromatography was performed using silica gel M60 from Macherey-Nagel (MN) (particle size: 40-63 μm).

Reagents and Solvents Reactions with air or moisture-sensitive substances were, if not otherwise indicated, carried out under an argon atmosphere with the help of the Schlenk technique. All other reagents and solvents were used as purchased from commercial suppliers unless otherwise noted. Anhydrous solvents were purified with the solvent purification system PURE SOLV (Innovative Technology (it)). Water-free DMF was purchased from Acros Organics in AcroSeal-bottles under Argon atmosphere with molecular sieves (4 A). The solvents (ethyl acetate, petroleum ether, pentane) used for column chromatography and workup were purified from commercially available technical grade solvents by distillation under reduced pressure with the help of rotatory evaporators (BÜCHI) at 40 °C water bath temperature.

Preparation of compounds

❖ α-propargyl β-ketoesters **2a-b**



General procedure: To a suspension of potassium *tert*-butoxide (49.1 mmol, 1.2 equiv.) in *tert*-butanol (200.0 ml) was added a solution of the chosen cyclic β-ketoester (42.8 mmol, 1.0 equiv.) in *tert*-butanol at room temperature and the mixture was stirred for 30 minutes. To this solution was added propargyl bromide (80% in toluene) (49.1 mmol, 1.2 equiv.) and then the mixture was refluxed for 4 hours. The reaction mixture was quenched by adding water, extracted with ether, washed with aqueous $NaHCO_3$ solution, and then dried over $MgSO_4$. Evaporation of the solvent gave a crude mixture, which was chromatographed on silica gel to give the desired α-propargyl β-ketoester.[1]

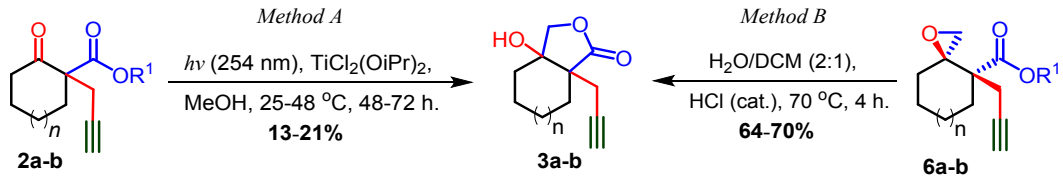
➢ Methyl 2-oxo-1-(prop-2-yn-1-yl)cyclopentane-1-carboxylate **2a**

$C_{10}H_{12}O_3$ (180.20), yellow oil; yield: 95% (2.4 g from **1a** (2 g)). $R_f =$ 0.375 (silica gel, Petroleum ether: EtOAc (88:12)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.71 (s, 3H), 2.71 (dd, J = 2.6, 1.2 Hz, 2H), 2.57 – 2.40 (m, 2H), 2.29 (m, 2H), 2.06 (m, 2H), 1.97 (t, J = 2.7 Hz, 1H). Spectroscopic data were in agreement with those previously reported in the literature.[2, 3]

➢ Ethyl 2-oxo-1-(prop-2-yn-1-yl)cyclohexane-1-carboxylate **2b**

$C_{12}H_{16}O_3$ (208.26), colourless oil; yield: 80% (7.82 g from **1b** (8 g)). $R_f =$ 0.378 (silica gel, Petroleum ether: EtOAc (95:5)). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.24 (q, J = 7.1 Hz, 2H), 2.82 – 2.71 (dd, J = 17.0, 2.7 Hz, 1H), 2.70 (dq, J = 13.7, 3.3 Hz, 1H), 2.58 (dd, J = 17.0, 2.7 Hz, 1H), 2.48 (m, 2H), 2.14 – 1.98 (m, 2H), 1.83 (m, 2H), 1.74 – 1.56 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H). Spectroscopic data were in agreement with those previously reported in the literature.[4]

❖ Alkynols **3a-b**



Method A

➢ Preparation of dichlorotitanium diisopropoxide **$TiCl_2(OiPr)_2$**

The reagent can either be obtained commercially or prepared by the reaction of $TiCl_4$ and $Ti(OiPr)_4$. As the quality of commercially supplied $TiCl_2(OiPr)_2$ can be variable, it is recommended to prepare the reagent freshly. To a solution of distilled $Ti(OiPr)_4$ (6.4 mL, 21.0 mmol, 1.1 equiv.) in a flame-dried Schlenk flask under an atmosphere of dry N_2 was added dry hexanes (20.0 mL), followed by the dropwise addition of $TiCl_4$ (2.2 mL, 20.0 mmol, 1.0 equiv.)

at room temperature. The warm solution was stirred for 15 minutes then left for crystallization (usually 2–3 hours). The colorless crystals were separated from the supernatant liquid by decantation under a stream of dry N_2 and washed with dry hexanes (5×2 mL). Drying in vacuum afforded the title compound (6.5 g, 69% yield) as colorless crystals. $TiCl_2(OiPr)_2$ can be handled on-air for weighting and can be kept in a closed container for several months without loss in performance. Upon extended exposure to moisture, crystals of $TiCl_2(OiPr)_2$ turn from a sticky paste into a liquid.[5]

- Photochemical hydroxymethylation of **2a-b**

General Procedure: Argon gas was passed through a solution of the chosen α-propargyl β-ketoester (5.2 mmol, 1.0 equiv.) in methanol (51.5 ml) containing titanium (IV) catalyst ($TiCl_2(OiPr)_2$) (2.6 mmol, 0.5 equiv.) for 15 min. The degassed solution was irradiated with UV light (254 nm) for 48-72 h at 40 ℃. After irradiation, the solution was concentrated, poured into water, and extracted four times with ethyl acetate. The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residual was purified via column chromatography.[6]

Method B

- Epoxide opening of **6a-b**

To a suspension of the chosen spiroepoxide (0.8 mmol, 1.0 equiv.) in H_2O/CH_2Cl_2 (1:1) (6.0 mL) was added HCl (15 mol%) at 70 °C for 4-5 h. After completion, the mixture was extracted with EtOAc, washed with brine, dried over $MgSO_4$, and then concentrated to give the crude product. Purification by silica gel flash column chromatography provided the desired bicyclic lactone.[7, 8]

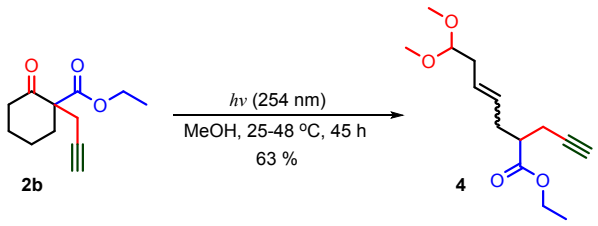
- 3a-hydroxy-6a-(prop-2-yn-1-yl)hexahydro-1H-cyclopenta[c]furan-1-one **3a**

$C_{10}H_{12}O_3$ (180.20), pale orange oil; *Method A:* yield: 13% (0.63 g from **2a** (4.81 g)). *Method B:* yield: 64% (66 mg isolated from **6a** (110 mg)). $R_f =$ 0.35 (silica gel, Petroleum ether: EtOAc (64:36)). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.32 (d, *J* = 9.9 Hz, 1H), 4.24 (d, *J* = 9.9 Hz, 1H), 2.70 (dd, *J* = 16.9, 2.7 Hz, 1H), 2.60 (dd, *J* = 16.9, 2.7 Hz, 1H), 2.55 (s, 1H), 2.22 (t, *J* = 2.7 Hz, 1H),2.22 – 2.10 (m, 2H), 2.08 – 1.94 (m, 2H), 1.90 – 1.80 (m, 1H), 1.54 – 1.40 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 180.0, 84.8, 80.6, 78.5, 72.0, 54.6, 42.2, 36.2, 22.4, 21.7. **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd for $C_{10}H_{12}NaO_3$: 203.0679; found 203.0672.

- 3a-hydroxy-7a-(prop-2-yn-1-yl)hexahydroisobenzofuran-1(*3H*)-one **3b**

$C_{11}H_{14}O_3$ (194.23), yellow-orange oil; *Method A:* yield: 21% (782 mg from **2b** (4 g)). *Method B:* yield: 70% (107 mg isolated from **6b** (175 mg)). $R_f =$ 0.288 (silica gel, Petroleum ether: EtOAc (65:35)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.17 (d, *J* = 9.6 Hz, 1H), 4.06 (d, *J* = 9.6 Hz, 1H), 2.62 – 2.52 (d, *J* = 2.8 Hz, 2H), 2.50 (broad, 1H), 2.09 (t, *J* = 2.8 Hz, 1H), 2.02 – 1.52 (m, 6H), 1.52 – 1.24 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.8, 80.4, 76.9, 74.1, 72.4, 47.9, 32.8, 31.0, 22.4, 20.8, 20.7. **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_3$: 217.0835; found 217.0838.

❖ **Compound 4**

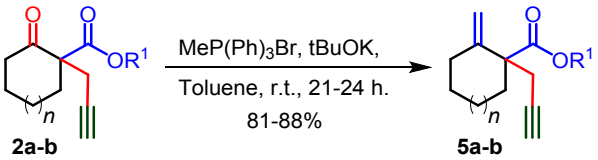


Argon gas was passed through a solution of the chosen α-propargyl β-ketoester **2b** (1.5 mmol, 1.0 equiv.) in methanol (15 ml) for 15 min. The degassed solution was irradiated with UV light (254 nm) for 45 h at 40 °C. After irradiation, the solution was concentrated, poured into water, and extracted four times with ethyl acetate. The organic phase was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residual was purified via column chromatography.[6]

➢ Ethyl 7,7-dimethoxy-2-(prop-2-yn-1-yl)hept-4-enoate **4**

$C_{14}H_{22}O_4$ (254.15), pale yellow oil; yield: 63% (240 mg from **2b** (312 g)). $R_f =$ 0.775 (silica gel, Petroleum ether: EtOAc (65:35)). *E*-isomer: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.72 – 5.53(dt, *J* = 15.41, 6.42 Hz, 1H), 5.53 – 5.32 (dt, *J* = 15.41, 8.16 Hz, 1H), 4.37 – 4.32 (t, *J* = 5.72 Hz, 1H), 4.21 – 4.06 (q, *J* = 7.18 Hz, 2H), 3.30 – 3.27 (s, 6H), 3.22 – 3.09 (q, *J* = 7.21 Hz, 1H), 2.65 – 2.34 (m, 2H), 2.22 – 2.03 (m, 2H), 1.96 (t, *J* = 2.54 Hz, 1H), 1.73 – 1.59 (m, 2H), 1.32 – 1.15 (t, *J* = 7.18 Hz, 3H). *Z*-isomer: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 5.72 – 5.53(m, 1H), 5.53 – 5.32 (m, 1H), 4.37 – 4.32 (t, *J* = 3.45 Hz, 1H), 4.21 – 4.06 (q, *J* = 7.18 Hz, 2H), 3.60 – 3.48 (m, 1H), 3.32 – 3.29 (s, 6H), 2.65 – 2.34 (m, 2H), 2.22 – 2.03 (m, 2H), 1.96 (t, *J* = 2.54 Hz, 1H), 1.73 – 1.59 (m, 2H), 1.32 – 1.15 (t, *J* = 7.18 Hz, 3H). *E*-isomer: **^{13}C NMR** (76 MHz, $CDCl_3$) δ 172.7, 133.5, 126.4, 103.8, 81.2, 69.9, 60.8, 52.7, 48.0, 31.8, 27.5, 21.9, 14.1. *Z*-isomer: **^{13}C NMR** (76 MHz, $CDCl_3$) δ 172.5, 133.0, 126.2, 103.8, 81.2, 69.8, 60.9, 52.6, 43.1, 32.1, 22.9, 21.9, 14.1. **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd for $C_{14}H_{22}NaO_4$: 277.1410; found 277.1409.

❖ Olefinic esters **5a-b**



General Procedure: To a well-stirred suspension of methyl triphenylphosphonium bromide (5.5 mmol, 2.0 equiv.) in anhydrous toluene (12.0 ml) under argon was added *t*-BuOK (5.5 mmol, 2.0 equiv.). The mixture was stirred at room temperature for one hour, then a solution of the chosen α-propargyl β-ketoester (2.8 mmol, 1.0 equiv.) in toluene was added dropwise. The mixture was kept stirring for 20-23 hours. After being poured to cold ether/water (1:1), the mixture was extracted by EtOAc, washed, dried and chromatographed on silica gel to give the desired olefinic esters.[9]

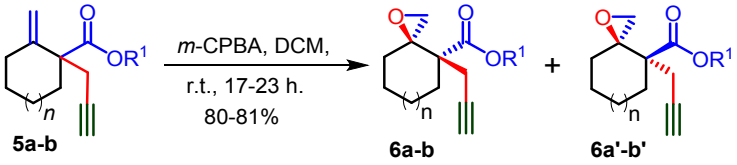
➢ Methyl 2-methylene-1-(prop-2-yn-1-yl)cyclopentane-1-carboxylate **5a**

$C_{11}H_{14}O_2$ (178.23), pale yellow oil; yield: 81% (398 mg from **2a** (500 mg)). $R_f =$ 0.675 (silica gel, Petroleum ether: EtOAc (80:20)). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 5.06 (t, *J* = 2.1 Hz, 1H), 5.04 (t, *J* = 2.1 Hz, 1H), 3.70 (s, 3H) 2.77 (dd, *J* = 16.7, 2.6 Hz, 1H), 2.50 – 2.42 (dd, *J* = 16.7, 2.6 Hz, 1H), 2.46 – 2.35 (m, 3H), 1.97 (m, 1H), 1.93 (t, *J* = 2.6 Hz, 1H), 1.90 – 1.78 (m, 1H), 1.72 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 174.7, 153.8, 108.0, 81.6, 69.3, 55.4, 52.3, 35.4, 34.0, 27.9, 24.1. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $C_{11}H_{14}NaO_2$: 201.0886; found 201.0894.

➢ Ethyl 2-methylene-1-(prop-2-yn-1-yl)cyclohexane-1-carboxylate **5b**

$C_{13}H_{18}O_2$ (206.29), yellow oil; yield: 88% (871 mg from **2b** (1 g)). $R_f =$ 0.788 (silica gel, Petroleum ether: EtOAc (80:20)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.93 (s, 1H), 4.83 (s, 1H), 4.20 (q, *J* = 7.0 Hz, 2H), 2.71 (dd, *J* = 16.5, 2.5 Hz, 1H), 2.55 (dd, *J* = 16.5, 2.5 Hz, 1H), 2.30 (m, 2H), 2.18 – 2.05 (m, 1H), 2.03 (t, *J* = 2.5 Hz, 1H), 1.78 – 1.56 (m, 3H), 1.53 – 1.31 (m, 2H), 1.26 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.6, 148.3, 109.2, 80.3, 71.1, 60.9, 52.4, 35.0, 34.5, 27.8, 26.8, 22.9, 14.2. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $C_{13}H_{18}NaO_2$: 229.119901; found 229.119978.

❖ Spiroepoxides **6a-a'** and **6b-b'**



General Procedure: *m*-CPBA (3.4 mmol, 3.0 equiv.) has been added in one portion to a solution of the chosen olefinic ester (1.1 mmol, 1.0 equiv.) at room temperature in DCM (12.0 ml). The resulting solution has been kept stirring for 17-23 hours before its classical work up.[10]

➢ Methyl 4-(prop-2-yn-1-yl)-1-oxaspiro[2.4]heptane-4-carboxylate **6a-a'**

$C_{11}H_{14}O_3$ (194.23), pale yellow oil; yield: 81% (175 mg from **5a** (200 mg)). $R_{f(2\ diastereoisomers)} =$ 0.375 (silica gel, Petroleum ether: EtOAc (90:10)). The ratio of the two inseparable diastereoisomers **6a**/**6a'** is 2.3:1. **6a**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.65 (s, 3H), 2.82 (d, *J* = 4.6 Hz, 1H), 2.78 (d, *J* = 4.6 Hz, 1H), 2.46 – 2.36 (dd, *J* = 16.9, 2.7 Hz, 1H), 2.33 – 2.23 (dd, *J* = 16.9, 2.7 Hz, 1H), 2.15 – 1.84 (m, 4H), 1.89 – 1.85 (t, *J* = 2.7 Hz, 1H) 1.82 – 1.63 (m, 2H). **6a'**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 3.64 (s, 3H), 2.88 (d, *J* = 4.3 Hz, 1H), 2.74 (d, *J* = 4.3 Hz, 1H), 2.56 (dd, *J* = 16.8, 2.8 Hz, 1H), 2.39 (dd, *J* = 16.8, 2.8 Hz, 1H), 2.14 – 1.92 (m, 4H), 1.89 (t, *J* = 2.8, Hz, 1H), 1.83 – 1.64 (m, 2H). **6a**: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 172.6, 79.3, 67.6, 65.2, 51.7, 50.3, 48.6, 33.7, 31.4, 20.4, 20.0. **6a'**: **^{13}C NMR** (126 MHz, $CDCl_3$) δ 170.2, 78.6, 68.1, 66.0, 52.3, 50.2, 47.7, 31.7, 31.0, 22.8, 20.2. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $C_{11}H_{14}NaO_3$: 217.0111; found 217.0123.

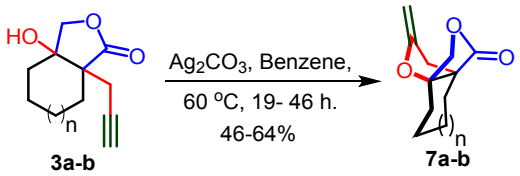
➢ Ethyl (*3S,4R*)-4-(prop-2-yn-1-yl)-1-oxaspiro[2.5]octane-4-carboxylate **6b**

$C_{13}H_{18}O_3$ (222.28), colourless oil; yield: 50% (755 mg from **5b** (1 g)). $R_f =$ 0.650 (silica gel, Petroleum ether: EtOAc (90:10)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.22 (q, *J* = 7.1 Hz, 2H), 3.18 (d, *J* = 4.0 Hz, 1H), 2.59 (d, *J* = 4.0 Hz, 1H), 2.41 (dd, *J* = 16.8, 2.7 Hz, 1H), 2.36 – 2.25 (m, 1H), 2.21 (dd, *J* = 16.8, 2.7 Hz, 1H), 2.03 – 1.9 (t, *J* = 2.7 Hz, 1H), 2.03 – 1.86 (m, 1H), 1.77 – 1.37 (m, 6H), 1.28 (t, *J* = 7.1 Hz, 3H**). ^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.9, 80.2, 71.1, 60.9, 59.5, 52.2, 50.1, 32.9, 32.7, 23.3, 23.1, 22.9, 14.2. **HRMS** (ESI): *m/z* [M + $Na]^+$ calcd for $C_{13}H_{18}NaO_3$: 245.1148; found 245.1148.

➢ Ethyl (*3R,4R*)-4-(prop-2-yn-1-yl)-1-oxaspiro[2.5]octane-4-carboxylate **6b'**

$C_{13}H_{18}O_3$, (222.28), white solid; yield: 30% (380 mg from **5b** (1 g)). $R_f =$ 0.525 (silica gel, Petroleum ether: EtOAc (90:10)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.21 (q, *J* = 7.1 Hz, 2H), 3.02 (d, *J* = 4.3 Hz, 1H), 2.65 (dd, *J* = 16.6, 2.7 Hz, 1H), 2.48 (d, *J* = 4.3 Hz, 1H), 2.48 – 2.30 (dd, *J* = 16.6, 2.7 Hz, 1H), 2.01 (t, *J* = 2.7 Hz, 1H), 1.86 – 1.41 (m, 8H), 1.29 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.4, 79.7, 71.1, 61.0, 59.9, 50.4, 50.2, 32.4, 31.4, 24.4, 23.1, 21.6, 14.1. **HRMS** (ESI): *m/z* [M + $Na]^+$ calcd for $C_{13}H_{18}NaO_3$: 245.1148; found 245.1148.

❖ Propellanes **7a-b**



General Procedure: To a stirred solution of the chosen alkynol (1.0 mmol, 1.0 equiv.) in benzene (15.0 ml), was added at room temperature silver carbonate (0.2 mmol, 0.2 equiv.). The mixture was heated at 60°C until TLC showed the disappearance of the starting acetylenic alcohol. The heterogeneous mixture, which gradually turned from green to brown then black, was filtered over Celite and concentrated in vacuo. The resulting crude mixture was then purified using column chromatography to afford the corresponding α-methylene heterocycle. (Remark: Triethylamine (1.0 vol%) was added to the used eluent before each purification to neutralize silica).[11]

➢ (6a*S*)-2-methylenetetrahydro-4*H*-3a,6a-(methanooxymethano)cyclopenta[b]furan-9-one **7a**

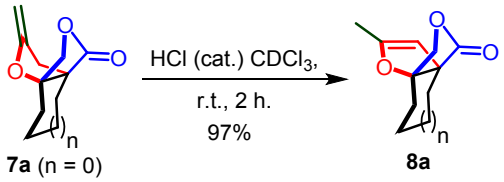
$C_{10}H_{12}O_3$ (180.20), pale yellow oil; yield: 54 % (278 mg from **3a** (520 mg)). $R_f =$ 0.35 (silica gel, Petroleum ether: EtOAc (85:15)). **^{1}H NMR** (400 MHz, DMSO) δ 4.39 (s, 2H), 4.18 (dd, *J* = 3.7, 1.7 Hz, 1H), 3.86 (dd, *J* = 3.7, 1.7 Hz, 1H), 2.95 (dt, *J* = 16.7, 1.5 Hz, 1H), 2.85 (dt, *J* = 16.7, 1.7 Hz, 1H), 2.03 (m, 2H), 1.96 – 1.84 (m, 3H), 1.82 – 1.70 (m, 1H). **^{1}H NMR** (300 MHz,

C_6D_6) δ 4.38 (d, *J* = 2.0 Hz, 1H), 3.96 (dd, *J* = 10.4, 1.7 Hz, 1H), 3.70 (d, *J* = 2 Hz, 1H), 3.46 (dd, *J* = 10.4, 3.9 Hz, 1H), 2.79 (d, *J* = 16.7 Hz, 1H), 2.19 (d, *J* = 16.7, 1H), 1.81 – 1.64 (m, 1H), 1.53 (m, 1H), 1.36 – 0.88 (m, 4H). **^{13}C NMR** (101 MHz, DMSO) δ 179.1, 162.0, 99.9, 81.9, 76.0, 59.0, 39.1, 36.3, 34.6, 26.3. **^{13}C NMR** (101 MHz, C_6D_6) δ 178.0, 161.8, 99.3, 82.4, 75.8, 58.9, 39.7, 37.2, 35.7, 26.2. **HRMS** (ESI): *m/z* $[M + H]^+$ calcd for $C_{10}H_{13}O_3$: 181.0859; found 181.0860.

- (7a*S*)-2-methylenehexahydro-3a,7a-(methanooxymethano)benzofuran-10-one **7b**

$C_{11}H_{14}O_3$ (194.23), pale yellow oil; yield: 51% (357 mg from **3b** (700 mg)). $R_f =$ 0.375 (silica gel, Petroleum ether: EtOAc (80:20)). **^{1}H NMR** (300 MHz, C_6D_6) δ 4.34 (d, *J* = 10.5 Hz, 1H), 4.28 (dt, *J* = 1.3, 2.2 Hz, 1H), 4.21 (d, *J* = 10.5 Hz, 1H), 3.91 (dt, *J* = 1.3, 2.2 Hz, 1H), 2.99 (dt, *J* = 16.4, 2.2 Hz, 1H), 2.78 (dt, *J* = 16.4, 2.2 Hz, 1H), 2.00 (m, 2H), 1.88 – 1.73 (m, 1H), 1.73 – 1.07 (m, 5H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.8, 158.2, 87.8, 82.7, 71.3, 50.2, 35.1, 29.1, 28.0, 22.5, 20.0. **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd for $C_{11}H_{14}NaO_3$: 217.0835; found 217.0834.

- Propellane **8a**

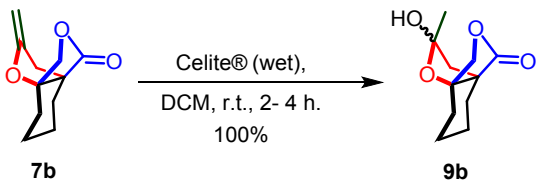


A catalytic amount of HCl ($\sim$10 mol%) was dissolved in a solution of the corresponding *exo* enol ether adduct **7a** (1 equiv.) in deuterated chloroform (0.07 M) at ambient temperature. Four hours later, a quantitative isomerization to its counterpart *endo* enol ether adduct **8a** has been observed by ^{1}H NMR analysis.

- (6a*S*)-2-methyl-5,6-dihydro-4*H*-3a,6a-(methanooxymethano)cyclopenta[b]furan-9-one **8a**

$C_{10}H_{12}O_3$ (180.20), colourless oil; yield: 97% (90 mg from **7a** (93 mg)). $R_f =$ 0.37 (silica gel, Petroleum ether: EtOAc (85:15)). **^{1}H NMR** (500 MHz, $CDCl_3$) δ = 4.71 (d, *J* = 1.1, 1H), 4.45 (d, *J*=10.3, 1H), 4.33 (d, *J*=10.3, 1H), 2.19 – 2.05 (m, 2H), 2.01 (m, 1H), 1.95 – 1.82 (m, 2H), 1.81 (d, *J*=1.1, 3H), 1.68 (dt, *J*=12.8, 6.5, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ = 178.5, 157.1, 99.5, 96.9, 77.9, 65.7, 39.2, 36.5, 26.0, 13.5. **HRMS** (ESI): *m/z* $[M + H]^+$ calcd for $C_{10}H_{13}O_3$: 181.0859; found 181.0856.

- Propellane **9b**

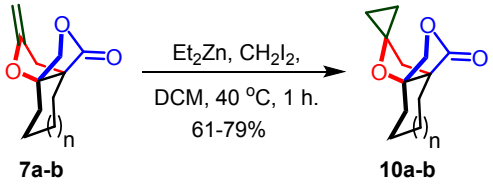


The chosen *exo* enol ether **7b** adduct (0.1 mmol, 1.0 equiv.) was added in one portion to a suspension of wet Celite® (100 mg) in dichloromethane (7 ml). After stirring for 4 h at room temperature, the reaction mixture was filtered, extracted and purified over silica gel to afford a mixture of inseparable diastereoisomers of the corresponding hemiacetal propellanes **9b**.[12]

- 2-hydroxy-2-methylhexahydro-3a,7a-(methanooxymethano)benzofuran-10-one **9b**.

$C_{11}H_{16}O_4$ (212,25), White solid; yield: 100% (20 mg from **7b** (19 mg)). $R_{f(2\ diastereoisomers)} =$ 0.350 (silica gel, Petroleum ether: EtOAc (50:50)). The ratio of the two inseparable diastereoisomers **9b'**/**9b''** is 1:1. **9b'**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.36 – 4.28 (d, *J* = 10.36 Hz, 1H), 4.20 – 4.13 (d, *J* = 10.36 Hz, 1H), 2.78 – 2.63 (brd, OH), 2.65 – 2.55 (d, *J* = 14.40 Hz, 1H), 2.40 – 2.30 (d, *J* = 14.40 Hz, 1H), 1.98 – 1.27 (m, 8H), 1.54 (s, 3H). **9b''**: **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.15 (s, 2H), 2.56 – 2.48 (d, *J* = 13.03 Hz, 1H), 2.56 – 2.42 (brd, OH), 2.15 – 2.05 (d, *J* = 13.03 Hz, 1H), 1.47 (s, 3H), 2.02 – 1.06 (m, 8H). **9b'**: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.4, 105.4, 86.7, 73.5, 52.5, 44.5, 31.2, 29.6, 28.2, 23.1, 19.8. **9b''**: **^{13}C NMR** (101 MHz, $CDCl_3$) δ 181.1, 104.0, 86.4, 71.5, 50.8, 44.4, 29.8, 28.2, 28.1, 21.8, 19.8. **HRMS** (ESI): *m/z* [M + Na] $^+$ calcd for $^{C_{11}H_{16}NaO_4}$: 235.0941; found 235.0934.

- Propellanes **10a-b**



7a-b **10a-b**

General Procedure: The chosen *exo* enol ether adduct (0.7 mmol, 1.0 equiv.), methylene iodide (3.4 mmol, 5.0 equiv.), and diethylzinc (1 M in hexane) (4.8 mmol, 7.0 equiv.) were stirred at reflux in anhydrous dichloromethane (8.0 ml) for 1 hour. After completion, the reaction mixture was quenched by adding water, extracted with diethyl ether, washed with aqueous $NaHCO_3$ solution, and then dried over $MgSO_4$. Evaporation of the solvent gave a crude mixture, which was chromatographed on silica gel to give the desired oxaspirocyclopropane [n,3,3]propellane.[13]

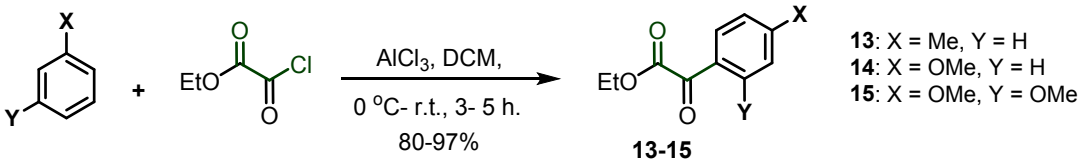
- Dihydro-3'*H*,4'*H*-spiro[cyclopropane-1,2'-[3a,6a](methanooxymethano)cyclopenta[*b*] furan]-9'-one **10a**

$C_{11}H_{14}O_3$ (194.23), colourless oil; yield: 61% (80 mg from **7a** (123 mg)). $R_f =$ 0.370 (silica gel, Petroleum ether: EtOAc (82:18)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 4.47 –4.41 (d, *J* = 10.20 Hz, 1H), 4.22 –4.18 (d, *J* = 10.20 Hz, 1H), 2.23 (s, 2H), 2.18 – 1.70 (m, 6H), 0.98 – 0.87 (ddd, *J* = 11.51, 6.58, 5.67 Hz, 1H), 0.85 – 0.75 (ddd, *J* = 11.51, 6.36, 5.10 Hz, 1H), 0.66 – 0.56 (ddd, *J* = 10.47, 6.36, 5.10 Hz, 1H), 0.53 – 0.43 (ddd, *J* = 10.47, 6.58, 5.67 Hz, 1H). **^{13}C NMR** (76 MHz, $CDCl_3$) δ 180.7, 97.3, 78.4, 65.6, 62.4, 43.7, 38.8, 36.3, 27.1, 10.6, 7.2. **HRMS** (ESI): *m/z* [M + Na] $^+$ calcd for $^{C_{11}H_{14}NaO_3}$: 217.0835; found 217.0837.

- Tetrahydro-3'*H*-spiro[cyclopropane-1,2'-[3a,7a](methanooxymethano)benzofuran]-10'-one **10b**

$C_{12}H_{16}O_3$ (208.26), colourless oil; yield: 79% (91 mg from **7b** (108 mg)). $R_f =$ 0.375 (silica gel, Petroleum ether: EtOAc (80:20)). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 4.26 – 4.19 (d, *J* = 10.50 Hz, 1H), 4.19 – 4.13 (d, *J* = 10.50 Hz, 1H), 2.40 – 2.33 (d, *J* = 12.44 Hz, 1H), 2.33 – 2.26 (d, *J* = 12.44 Hz, 1H), 2.12 – 1.99 (m, 1H), 1.88 – 1.11 (m, 7H), 0.90 – 0.84 (ddd, *J* = 11.50, 6.72, 5.44 Hz, 1H), 0.81 – 0.74 (ddd, *J* = 11.50, 6.68, 5.33 Hz, 1H), 0.60 – 0.53 (ddd, *J* = 10.84, 6.72, 5.33 Hz, 1H), 0.52 – 0.46 (ddd, *J* = 10.84, 6.68, 5.44 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 181.3, 85.6, 72.4, 62.4, 52.9, 39.2, 29.2, 28.5, 22.4, 20.2, 10.9, 10.8. **HRMS** (ESI): *m/z* [M + $Na]^+$ calcd for $^{C_{12}H_{16}NaO_3}$: 231.0992; found 231.0997.

- **α-ketoesters 13-15**



General Procedure: In a three-necked round-bottomed flask mounted with a cooling system under inert conditions, $AlCl_3$ (22 mmol, 2.2 equiv.) was suspended in CH_2Cl_2 (20 mL) at 0 °C. To this mixture mono-ethyl oxalyl chloride (22 mmol, 2.2 equiv.) was added dropwise over 15 min. at 0 °C an arene (10 mmol, 1.0 equiv.) was added dropwise in about 10 min., then the solution was stirred at r.t. for 2 h. After completion of the reaction, as determined by TLC, the mixture was cooled and carefully added 20 g of crushed ice and 20 mL of concentrated hydrochloric acid. Extraction was performed with CH_2Cl_2 (3 x 50 mL), the organic layer was collected and washed with 1 N NaOH (50 mL) and brine (50 mL). After the organic layer was separated and dried over Na_2SO_4, the solvent was evaporated, and the crude ethyl ester product was purified by column chromatography.[14]

- Ethyl 2-oxo-2-(p-tolyl)acetate **13**

$C_{11}H_{12}O_3$ (192.21), colourless oil; yield: 80% (500 mg from toluene (300 mg)). $R_f =$ 0.475 (silica gel, Petroleum ether: EtOAc (90:10)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.93 – 7.86 (d, *J* = 7.91 Hz, 2H), 7.33 – 7.27 (d, *J* = 7.91 Hz, 2H), 4.44 (q, *J* = 7.04 Hz, 2H), 2.46 – 2.37 (s, 3H), 1.41 (t, *J* = 7.04 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 186.1, 164.0, 146.2, 130.1, 130.0, 129.6, 62.2, 21.9, 14.1. Spectroscopic data were in agreement with those previously reported in the literature.[14]

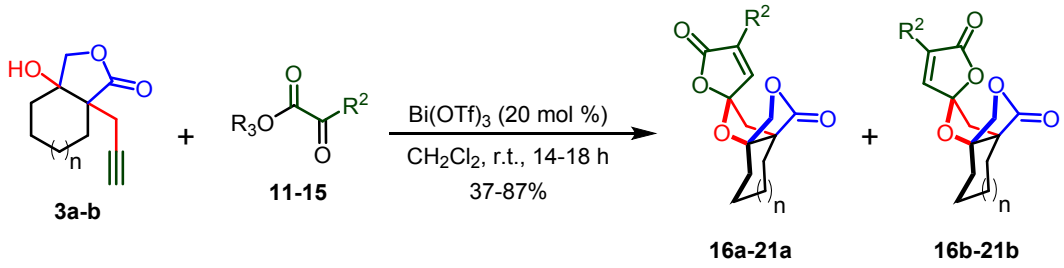
- Ethyl 2-(4-methoxyphenyl)-2-oxoacetate **14**

$C_{11}H_{12}O_4$ (208.21), yellow oil; yield: 84% (323 mg from anisole (200 mg)). $R_f =$ 0.35 (silica gel, Pentane: EtOAc (85:15)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.00 – 7.92 (d, *J* = 8.97 Hz, 2H), 6.97 – 6.89 (d, *J* = 8.97 Hz, 2H), 4.40 (q, *J* = 7.15 Hz, 2H), 3.85 (s, 3H), 1.38 (t, *J* = 7.15 Hz, 3H). **^{13}C NMR** (76 MHz, $CDCl_3$) δ 184.9, 165.0, 164.1, 132.5, 125.4, 114.2, 62.1, 55.6, 14.1. Spectroscopic data were in agreement with those previously reported in the literature.[14]

➢ Ethyl 2-(2,4-dimethoxyphenyl)-2-oxoacetate **15**

$C_{12}H_{14}O_5$ (238.24), violet oil; yield: 97% (630 mg from 1,3-dimethoxybenzene (375 mg)). R_f = 0.370 (silica gel, Petroleum ether: EtOAc (75:25)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.8 Hz, 1H), 6.60 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.44 (d, *J* = 2.3 Hz, 1H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 3.85 (s, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 185.0, 166.7, 166.0, 162.3, 132.9, 115.8, 106.7, 98.1, 61.6, 55.9, 55.7, 14.1. Spectroscopic data were in agreement with those previously reported in the literature.[15]

❖ **Propellanes 16-21(a-b)**



General Procedure: The chosen alkynol (0.66 mmol, 1.0 equiv.) and α-ketoester (0.66 mmol, 1.0 equiv.) were taken into a single neck round bottom flask, then dissolved in anhydrous CH_2Cl_2.(5.0 ml) $Bi(OTf)_3$ (0.13 mmol, 20 mol%) was then added under an argon atmosphere at room temperature (r.t.). The resulting reaction mixture was stirred at r.t. for respective reaction time. After completion of the reaction (typically after 14 h, monitored by TLC, visualized using UV and $KMnO_4$ staining solutions) the reaction was quenched with a saturated aqueous $NaHCO_3$ solution, then extracted with CH_2Cl_2 (2x10 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and filtered through sintered glass funnel. The filtrate was concentrated under reduced pressure and purified using silica-gel column chromatography to afford the corresponding oxaspirolactone[n,3,3]propellanes.

- **16**

Yield: 86% (117 mg from **3b** (100 mg)) (System of isomers **16a/16b** (1:1)).

➢ (2*S*,7a'*S*)-4-methyl-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **16a**

$C_{14}H_{16}O_5$ (264.28), white solid; R_f = 0.688 (silica gel, Petroleum ether: EtOAc (50:50)). **m.p.** = 145–147 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.62 (q, *J* = 1.66 Hz, 1H), 4.32 – 4.24 (d, *J* = 10.74 Hz, 1H), 4.24 – 4.21 (d, *J* = 10.74 Hz, 1H), 2.91 – 2.83 (d, *J* = 14.71 Hz, 1H), 2.67 – 2.58 (d, *J* = 14.71 Hz, 1H), 2.15 – 1.83 (m, 5H), 1.90 –1.87 (d, *J* = 1.66 Hz, 3H), 1.53 – 1.37 (m, 3H). **^{13}C NMR** (76 MHz, $CDCl_3$) δ 180.3, 171.1, 145.0, 131.8, 111.1, 89.0, 70.9, 52.3, 40.8, 28.4, 28.0, 22.8, 19.6, 10.1. **IR**: $\tilde{\nu}$ = 3081, 2960, 2861, 2170, 1977, 1760, 1460, 768 cm^{-1}. **HRMS** (ESI): *m/z* $[M + Na]^+$ calcd for $^{C_{14}H_{16}NaO_5}$: 287.0890; found 287.0890.

➢ (2*R*,7a'*S*)-4-methyl-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **16b**

$C_{14}H_{16}O_5$ (264.28), white solid; $R_f =$ 0.219 (silica gel, Petroleum ether: EtOAc (50:50)). **m.p.** = 194–196 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.64 – 6.60 (q, *J* = 1.60 Hz, 1H), 4.48 – 4.40 (d, *J* = 10.67 Hz, 1H), 4.25 – 4.16 (d, *J* = 10.67 Hz, 1H), 2.68 – 2.59 (d, *J* = 13.49 Hz, 1H), 2.48 – 2.39 (d, *J* = 13.49 Hz, 1H), 2.19 – 1.98 (m, 2H), 1.96 – 1.86 (d, *J* = 1.60 Hz, 3H), 1.84 – 1.45 (m, 5H), 1.29 – 1.19 (m, 1H).**^{13}C NMR** (76 MHz, $CDCl_3$) δ 179.0, 170.1, 143.4, 134.0, 110.3, 88.8, 73.5, 50.4, 42.3, 31.0, 28.3, 21.2, 19.5, 10.5. **IR**: $\tilde{\nu}$ = 2930, 2865, 2170, 1976, 1766, 1449, 766 cm^{-1}. **HRMS** (ESI): *m/z* [M + $Na]^+$ calcd for $^{C_{14}H_{16}NaO_5}$: 287.0890; found 287.0890.

- **17**

Yield: 61% (102 mg from **3b** (100 mg)) (System of isomers **17a/17b** (1:1)).

- (2S,7a'S)-4-phenyl-4',5',6',7'-tetrahydro-3'H,5H-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **17a**

$C_{19}H_{18}O_5$ (326.35), white solid; $R_f =$ 0.488 (silica gel, Petroleum ether: EtOAc (50:50)). **m.p.** = 168–170 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.84 – 7.75 (m, 2H), 7.44 – 7.35 (m, 3H), 7.08 (s, 1H), 4.35 – 4.29 (d, *J* = 10.70 Hz, 1H), 4.28 – 4.22 (d, *J* = 10.70 Hz, 1H), 3.04 – 2.94 (d, *J* = 14.84 Hz, 1H), 2.77 – 2.69 (d, *J* = 14.84 Hz, 1H), 2.21 – 1.86 (m, 4H), 1.78 – 1.35 (m, 4H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 180.3, 168.9, 143.2, 132.7, 130.0, 128.7, 128.3, 127.5, 110.3, 89.3, 70.9, 52.5, 41.0, 28.4, 28.0, 22.8, 19.6. **IR**: $\tilde{\nu}$ = 2937, 2170, 1977, 1767, 1460, 779 cm^{-1}. **HRMS** (ESI): *m/z* [M + $Na]^+$ calcd for $^{C_{19}H_{18}NaO_5}$: 349.1046; found 349.1043.

- (2*R*,7a'*S*)-4-phenyl-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **17b**

$C_{19}H_{18}O_5$ (326.35), pale yellow solid; $R_f =$ 0.363 (silica gel, Petroleum ether: EtOAc (50:50)). **m.p.** = 200–202 °C. **^{1}H NMR** (300 MHz, $CDCl_3$) δ 7.86 –7.76 (m, 2H), 7.44 – 7.35 (m, 3H), 7.10 (s, 1H), 4.51 – 4.45 (d, *J* = 10.63 Hz, 1H), 4.27 – 4.22 (d, *J* = 10.63 Hz, 1H), 2.77 – 2.69 (d, *J* = 13.59 Hz, 1H), 2.60 – 2.53 (d, *J* = 13.59 Hz, 1H), 2.20 – 2.01 (m, 3H), 1.90 – 1.77 (m, 1H), 1.75 – 1.52 (m, 4H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.1, 167.8, 141.8, 134.7, 130.0, 128.7, 128.5, 127.5, 109.6, 89.1, 73.1, 50.5, 42.4, 31.0, 28.3, 21.4, 19.6. **IR**: $\tilde{\nu}$ = 3080, 2942, 2866, 2170, 1977, 1762, 1496, 747 cm^{-1}. **HRMS** (ESI): *m/z* [M + $Na]^+$ calcd for $^{C_{19}H_{18}NaO_5}$: 349.1046; found 349.1043.

- **18**

Yield: 74% (128 mg from **3b** (100 mg)) (System of isomers **18a/18b** (1:1)).

- (2*S*,7a'*S*)-4-(p-tolyl)-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **18a**

$C_{20}H_{20}O_5$ (340.38), white solid; $R_f =$ 0.625 (silica gel, Petroleum ether: EtOAc (65:35)). **m.p.** = 140–142 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.73 – 7.68 (d, *J* = 8.27 Hz, 2H), 7.22 – 7.18 (d, *J* = 8.27 Hz, 2H), 7.03 (s, 1H), 4.34 – 4.29 (d, *J* = 10.70 Hz, 1H), 4.27 – 4.24 (d, *J* = 10.70 Hz, 1H), 3.00 – 2.95 (d, *J* = 14.80 Hz, 1H), 2.75 – 2.70 (d, *J* = 14.80 Hz, 1H), 2.36 (s, 3H), 2.23 – 1.87 (m, 4H), 1.77 – 1.69 (m, 1H), 1.54 – 1.40 (m, 2H), 1.30 – 1.18 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 180.3, 169.0, 142.2, 140.3, 132.6, 129.4, 127.4, 125.4, 110.3, 89.2, 70.9, 52.5,

41.1, 28.4, 28.0, 22.8, 21.4, 19.6. **IR**: $\tilde{\nu}$ = 2937, 1976, 1766, 1126, 821.69 cm^{-1}. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $C_{20}H_{20}NaO_5$: 363.1203; found 363.1191.

- (2*R*,7a'*S*)-4-(p-tolyl)-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **18b**

$C_{20}H_{20}O_5$ (340.38), white solid; R_f = 0.240 (silica gel, Petroleum ether: EtOAc (65:35)). **m.p.** = 197–199 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.67 – 7.62 (d, *J* = 7.91 Hz, 2H), 7.15 – 7.11 (d, *J* = 7.91 Hz, 2H), 6.98 (s, 1H), 4.43 – 4.39 (d, *J* = 10.98 Hz, 1H), 4.20 – 4.15 (d, *J* = 10.98 Hz, 1H), 2.68 – 2.62 (d, *J* = 13.47 Hz, 1H), 2.52 – 2.47 (d, *J* = 13.47 Hz, 1H), 2.29 (s, 3H), 2.12 – 1.98 (m, 2H), 1.82 – 1.72 (m, 1H), 1.68 – 1.47 (m, 4H), 1.39 – 1.26 (m, 1H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.1, 168.0, 140.7, 140.3, 134.6, 129.4, 127.4, 125.7, 109.6, 89.0, 73.2, 50.5, 42.5, 31.1, 28.3, 21.4, 21.3, 19.6. **IR**: $\tilde{\nu}$ = 2945, 2169, 1976, 1764, 962, 661 cm^{-1}. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $C_{20}H_{20}NaO_5$: 363.1203; found 363.1191.

- **19**

Yield: 69% (99 mg isolated from **3a** (76 mg)) (System of isomers **19a/19b** (1:1)).

- (2*S*,6a'*S*)-4-(4-methoxyphenyl)-5',6'-dihydro-3'*H*,4'*H*,5*H*-spiro[furan-2,2'-[3a,6a](methanooxymethano)cyclopenta[b]furan]-5,9'-dione **19a**

$C_{19}H_{18}O_6$ (342.35), orange oil; R_f = 0.775 (silica gel, Pentane: EtOAc (54:46)). **^{1}H NMR** (500 MHz, $CDCl_3$) δ 8.05 – 7.96 (d, *J* = 8.80 Hz, 2H), 7.26 (s, 1H), 7.00 – 6.95 (d, *J* = 8.28 Hz, 2H), 4.56 – 4.51 (d, *J* = 10.21 Hz, 1H), 4.31 – 4.26 (d, *J* = 10.21 Hz, 1H), 3.89 (s, 3H), 3.16 – 3.09 (d, *J* = 16.80 Hz, 1H), 2.93 – 2.85 (d, *J* = 16.80 Hz, 1H), 2.31 – 2. 7. (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 180.5, 165.0, 164.1, 132.2, 131.8, 128.5, 109.1, 97.4, 80.0, 62.1, 55.6, 41.9, 39.9, 38.4, 36.7, 29.7, 27.1. **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{19}H_{19}O_6$: 343.1176; found 343.1177 and *m/z* [M + Na]$^+$ calcd for $C_{19}H_{18}NaO_6$: 365.0996; found 365.0994.

- (2*R*,6a'*S*)-4-(4-methoxyphenyl)-5',6'-dihydro-3'*H*,4'*H*,5*H*-spiro[furan-2,2'-[3a,6a](methanooxymethano)cyclopenta[b]furan]-5,9'-dione **19b**

$C_{19}H_{18}O_6$ (342.11), yellow solid; R_f = 0.350 (silica gel, Pentane: EtOAc (54:46)). **m.p.** = 195–197 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 – 7.78 (d, *J* = 8.28 Hz, 2H), 7.06 (s, 1H), 6.95 – 6.90 (d, *J* = 8.28 Hz, 2H), 4.74 – 4.69 (d, *J* = 11.88 Hz, 1H), 4.34 – 4.69 (d, *J* = 11.88 Hz, 1H), 3.84 (s, 3H), 2.87 – 2.79 (d, *J* = 13.68 Hz, 1H), 2.37 – 2.32 (d, *J* = 13.68 Hz, 1H), 2.31 – 2. 7. (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 178.6, 168.1, 161.1, 137.6, 129.1, 120.9, 114.2, 113.8, 100.2, 78.6, 61.0, 55.3, 48.8, 46.7, 39.7, 37.2, 27.3. **IR**: $\tilde{\nu}$ =2952, 1981, 1760, 1617, 1268, 827 cm^{-1}. **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{19}H_{19}O_6$: 343.1176; found 343.1177 and *m/z* [M + Na]$^+$ calcd for $C_{19}H_{18}NaO_6$: 365.0996; found 365.0994.

- **20**

Yield: 87% (146 mg from **3b** (91 mg)) (System of isomers **20a/20b** (1:1)).

- (2*S*,7a'*S*)-4-(4-methoxyphenyl)-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **20a**

$C_{20}H_{20}O_6$ (356.37), white solid; $^{R_f} =$ 0.775 (silica gel, Petroleum ether: EtOAc (50:50)). **m.p.** = 161–163 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.81 – 7.76 (d, *J* = 9.05 Hz, 2H), 6.96 (s, 1H), 6.94 – 6.89 (d, *J* = 9.05 Hz, 2H), 4.34 – 4.30 (d, *J* = 10.84 Hz, 1H), 4.28 – 4.24 (d, *J* = 10.84 Hz, 1H), 3.83 (s, 3H), 3.00 – 2.95 (d, *J* = 14.51 Hz, 1H), 2.75 – 7.70 (d, *J* = 14.51 Hz, 1H), 2.21 – 2.05 (m, 2H), 2.03 – 1.89 (m, 2H), 1.75 (m, 1H), 1.54 – 1.43 (m, 2H), 1.25 (m, 1H).**^{13}C NMR** (126 MHz, $CDCl_3$) δ 180.4, 169.2, 160.9, 140.8, 132.1, 129.0, 120.8, 114.1, 110.3, 89.1, 70.9, 55.3, 52.5, 41.1, 28.5, 28.0, 22.8, 19.6. **IR**: $\tilde{\nu}$ = 2947, 2160, 1978, 1772, 1630, 1511, 1001, 849 cm^{-1}. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $^{C_{20}H_{20}NaO_6}$: 379.1152; found 379.1145.

- (2*R*,7a'*S*)-4-(4-methoxyphenyl)-4',5',6',7'-tetrahydro-3'H,5H-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **20b**

$C_{20}H_{20}O_6$ (356.37), pale yellow solid; $^{R_f} =$ 0.425 (silica gel, Petroleum ether: EtOAc (50:50)). **m.p.** = 201–203 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.82 – 7.78 (d, *J* = 8.80 Hz, 2H), 6.97 (s, 1H), 6.94 – 6.89 (d, *J* = 8.80 Hz, 2H), 4.51 – 4.46 (d, *J* = 10.75 Hz, 1H), 4.26 – 4.22 (d, *J* = 10.75 Hz, 1H), 3.83 (s, 3H), 2.74 – 2.70 (d, *J* = 13.67 Hz, 1H), 2.56 – 7.52 (d, *J* = 13.67 Hz, 1H), 2.17 – 2.04 (m, 2H), 1.87 – 1.78 (m, 1H), 1.72 – 1.55 (m, 4H), 1.46 – 1.37 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.1, 168.1, 161.0, 139.1, 134.1, 129.0, 121.1, 114.1, 109.6, 88.9, 73.2, 55.3, 50.5, 42.6, 31.1, 28.3, 21.3, 19.6. **IR**: $\tilde{\nu}$ = 2949, 1977, 1764, 1612, 1268, 824 cm^{-1}. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $^{C_{20}H_{20}NaO_6}$: 379.1152; found 379.1145.

- **21**

Yield: 37% (61 mg from **3b** (82 mg)) (System of isomers **21a/21b** (1:1)).

- (2*S*,7a'*S*)-4-(2,4-dimethoxyphenyl)-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **21a**

$C_{21}H_{22}O_7$ (386.40), white solid; $^{R_f} =$ 0.613 (silica gel, Petroleum ether: EtOAc (50:50)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.27 – 8.18 (d, *J* = 8.72 Hz, 1H), 7.35 (s, 1H), 6.53 – 6.50 (dd, *J* = 8.72, 2.47 Hz, 1H), 6.50 – 6.46 (d, *J* = 2.47 Hz, 1H), 4.37 – 4.30 (d, *J* = 10.75 Hz, 1H), 4.25 – 4.21 (d, *J* = 10.75 Hz, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 3.04 – 2.95 (d, *J* = 14.78 Hz, 1H), 2.74 – 2.65 (d, *J* = 14.78 Hz, 1H), 2.26 – 2.09 (m, 2H), 2.03 – 1.83 (m, 2H), 1.65 – 1.37 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 180.6, 170.2, 161.8, 159.8, 144.2, 130.9, 127.2, 110.6, 110.4, 104.3, 98.5, 89.0, 71.0, 55.4, 55.4, 52.5, 41.4, 28.5, 28.2, 22.8, 19.6. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $^{C_{21}H_{22}NaO_7}$: 409.1258; found 409.1251.

- (2*R*,7a'*S*)-4-(2,4-dimethoxyphenyl)-4',5',6',7'-tetrahydro-3'*H*,5*H*-spiro[furan-2,2'-[3a,7a](methanooxymethano)benzofuran]-5,10'-dione **21b**

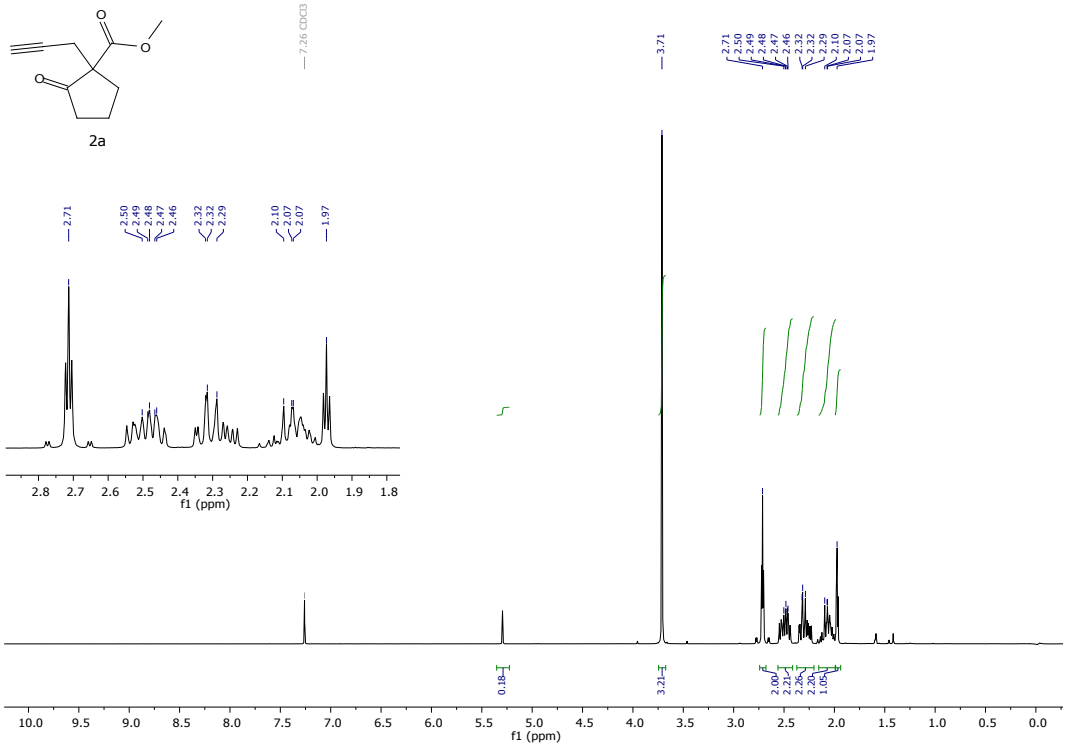
$C_{21}H_{22}O_7$ (386.40), pale yellow solid; $^{R_f} =$ 0.313 (silica gel, Petroleum ether: EtOAc (50:50)). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 8.30 – 8.22 (d, *J* = 9.00 Hz, 1H), 7.35 (s, 1H), 6.57 – 6.51 (dd, *J* = 9.00, 2.57 Hz, 1H), 6.51 – 6.47 (d, *J* = 2.57 Hz, 1H), 4.53 – 4.46 (d, *J* = 11.03 Hz, 1H), 4.27 – 4.20 (d, *J* = 11.03 Hz, 1H), 3.88 (s, 3H), 3.83 (s, 3H), 2.75 – 2.66 (d, *J* = 14.29 Hz, 1H), 2.58 – 2.49 (d, *J* = 14.29 Hz, 1H), 2.19 – 2.04 (m, 2H), 1.76 – 1.52 (m, 4H), 1.35 – 1.19 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ 179.2, 169.0, 161.8, 159.7, 142.5, 131.1, 129.2, 110.7, 109.7, 104.3, 98.6, 88.6, 73.3, 55.4, 55.4, 50.6, 42.7, 31.1, 28.4, 21.2, 19.6. **HRMS** (ESI): *m/z* [M + Na]$^+$ calcd for $^{C_{21}H_{22}NaO_7}$: 409.1258; found 409.1251.

References

1. N. Tzvetkov, P. Waske, B. Neumann, H. Stammler and J. Mattay, *Tetrahedron Lett.*, 2008, **49**, 1710-1713.
2. X. Lu, M. Lyu, X. Peng and H. Wong, *Angew. Chem.*, 2018, **130**, 11535-11538.
3. L. Teixeira, E. Barreiro and C. Fraga, *Synth. Commun.*, 1997, **27**, 3241-3257.
4. M. Blümel, R. Crocker, J. Harper, D. Enders and T. Nguyen, *Chem. Commun.*, 2016, **52**, 7958-7961.
5. M. Peifer, R. l. Berger, V. Shurtleff, J. Conrad and D. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 5900-5903.
6. A. Griesbeck and M. Reckenthäler, *Beilstein J. Org. Chem.*, 2014, **10**, 1143-1150.
7. R. Parker and N. Isaacs, *Chem. Rev.*, 1959, **59**, 737-799.
8. G. Olah, P. Iyer and G. Prakash, *Synthesis*, **1986**, 513-531.
9. H. Lee, D. Moon and J. Bahn, *Tetrahedron Lett.*, 2005, **46**, 1455-1458.
10. L. Pehlivan, M. Jacolot, N. Coia, N. Monteiro, D. Bouyssi and G. Balme, *Tetrahedron Lett.*, 2011, **52**, 4716-4719.
11. P. Pale and J. Chuche, *Eur. J. Org. Chem.*, **2000**, 1019-1025.
12. S. Baskaran, I. Islam, M. Raghavan and S. Chandrasekaran, *Chem. Lett.*, 1987, **16**, 1175-1178.
13. A. Charette, A. Beauchemin and S. Francoeur, *J. Am. Chem. Soc.*, 2001, **123**, 8139-8140.
14. S. Xie, D. Li, H. Huang, F. Zhang and Y. Chen, *J. Am. Chem. Soc.*, 2019, **141**, 16237-16242.
15. D. Kambale, S. Thorat, M. Pratapure, R. Gonnade and R. Kontham, *Chem. Commun.*, 2017, **53**, 6641-6644.

NMR spectra

- **2a**



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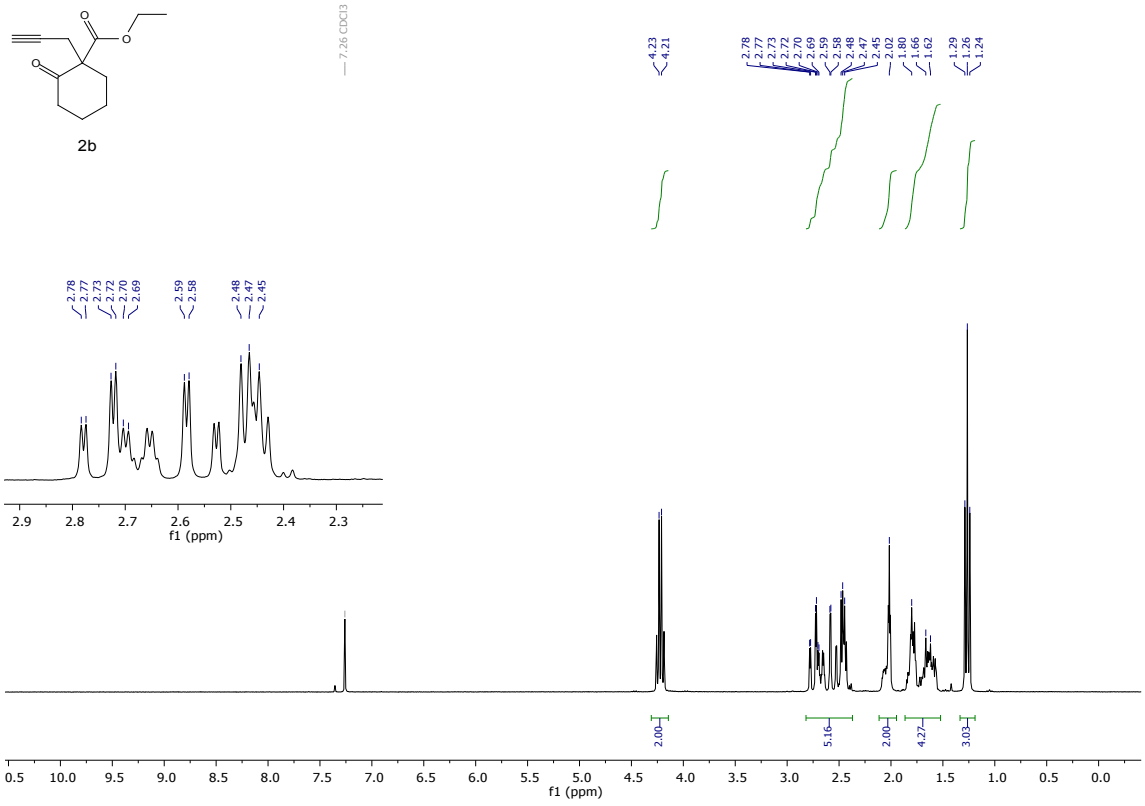
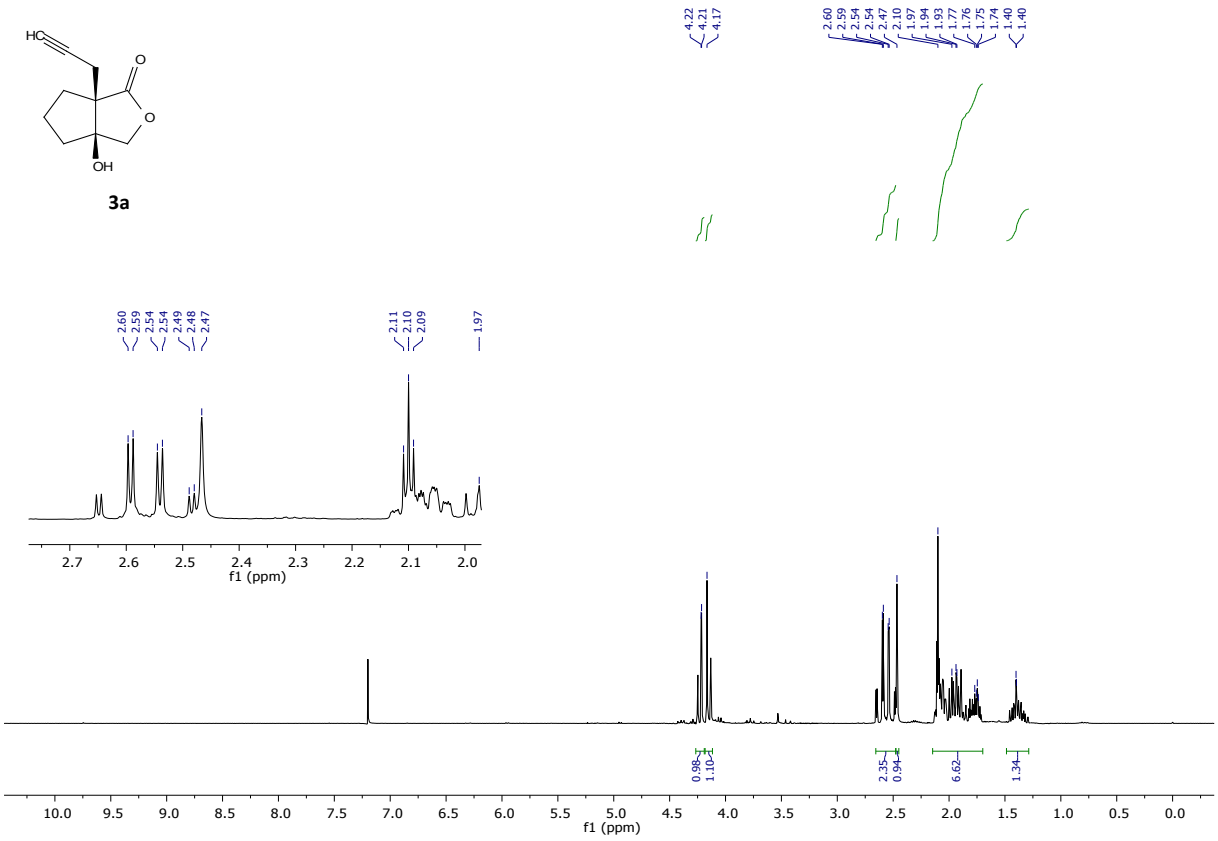


- **3a**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OH
3a
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2.59
2.54
2.54
2.47
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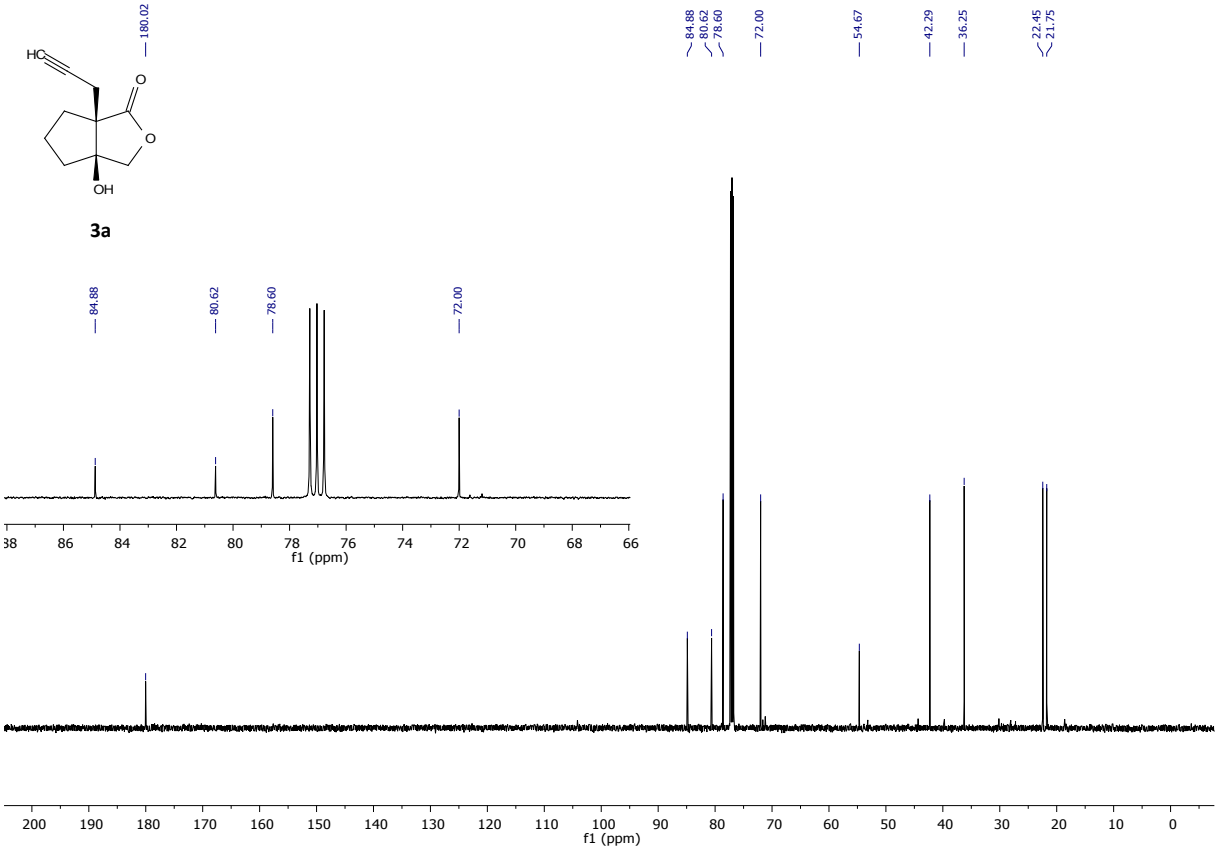
1.97
1.94
1.93
1.77
1.76
1.75
1.74
1.40
1.40
2.60
2.59
2.54
2.54
2.49
2.48
2.47
2.11
2.10
2.09
1.97
f1 (ppm)
0.98
1.10
2.35
0.94
6.62
1.34
f1 (ppm)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O
OH
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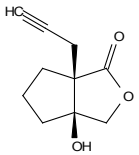
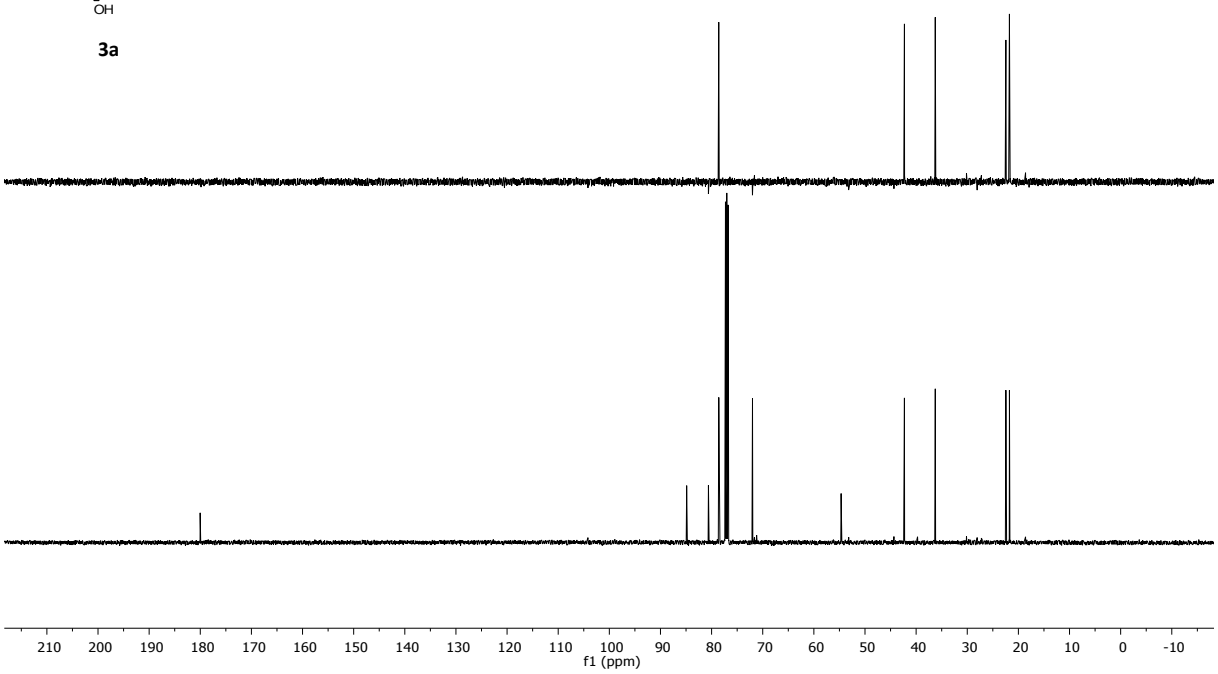
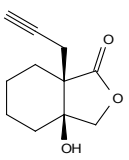
80.62
78.60
72.00
f1 (ppm)
f1 (ppm)


HC
O
O
OH

3a

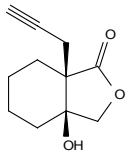

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

- **3b**

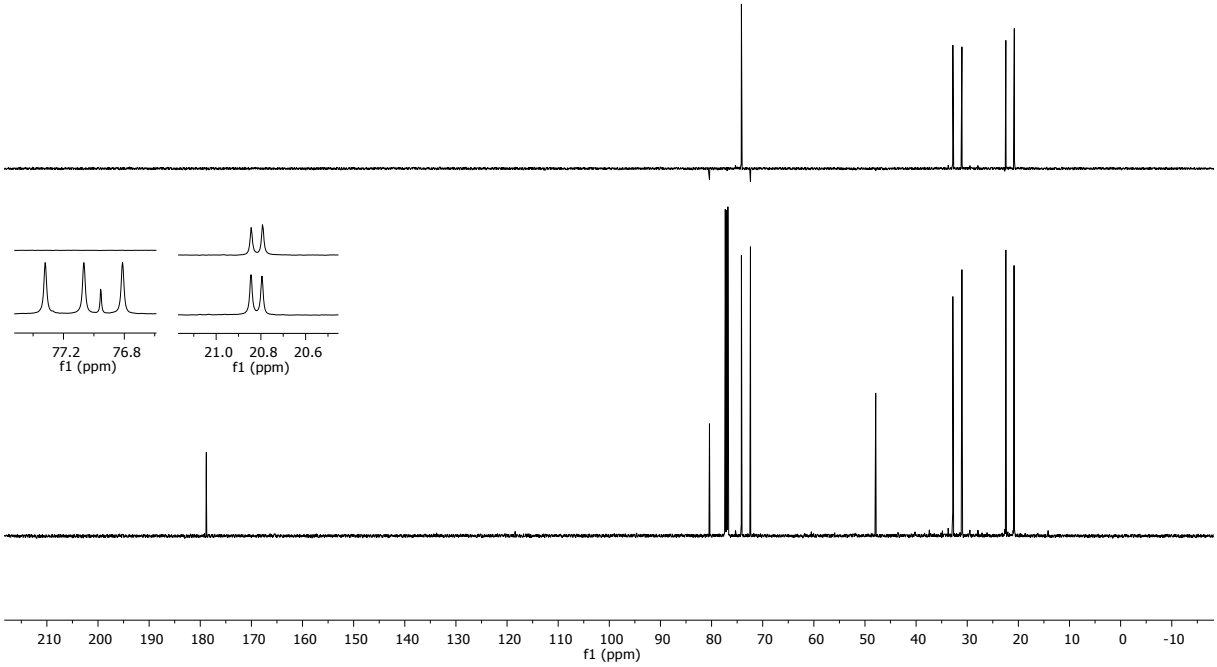

O
O
OH

3b

4.24
4.21
4.13
4.10
2.63
2.62
2.62
2.62
2.55
2.54
2.14
1.96
1.96
1.94
1.69
1.65
1.49
1.48
1.47
1.46
1.46
2.63
2.62
2.62
2.62
2.55
2.54
2.15
2.14
2.14
2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1
f1 (ppm)
0.97
1.00
1.80
0.95
0.93
6.49
2.76
10.5 10.0 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
f1 (ppm)


O
O
OH

3b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76.8
f1 (ppm)
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20.8
20.6
f1 (ppm)
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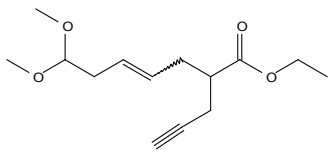
f1 (ppm)

- **4**


O
O
O
O

4

5.62
5.60
5.58
5.50
5.48
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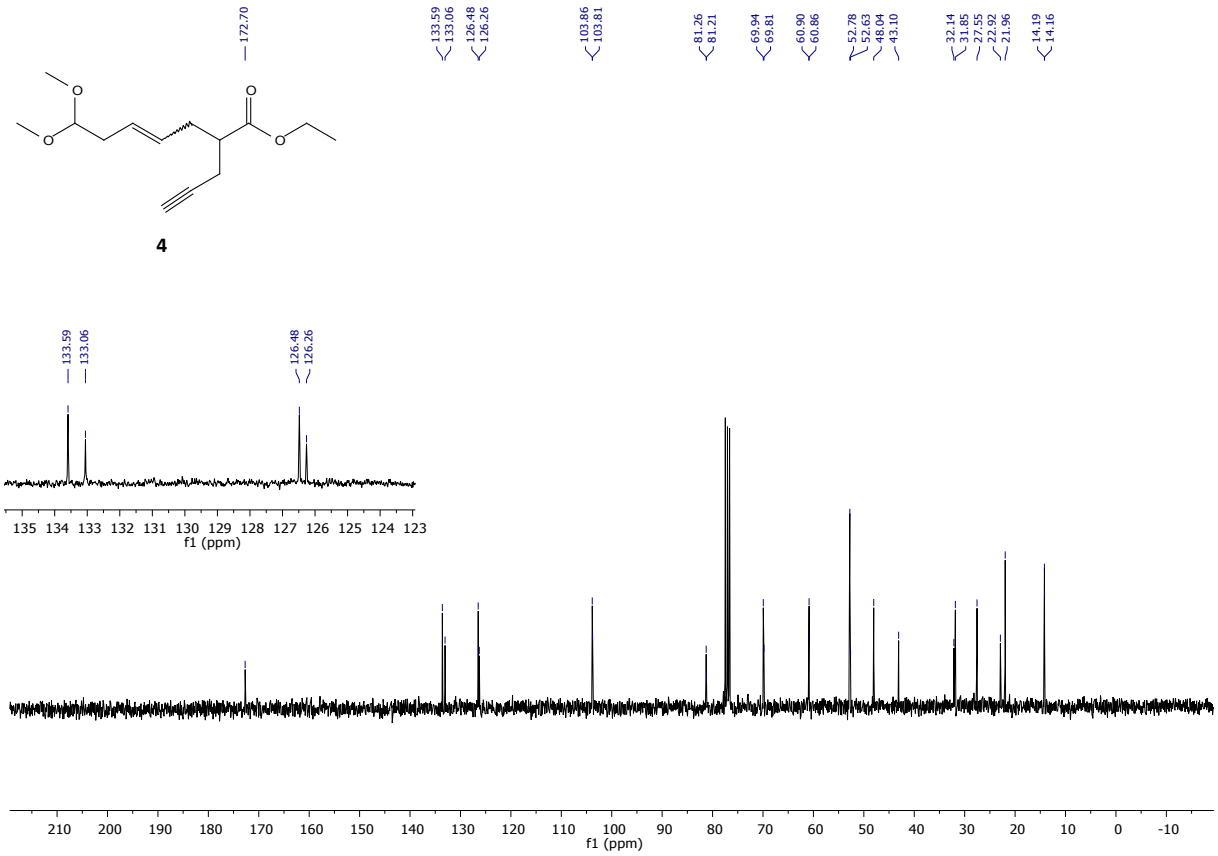
4.13
3.30
3.29
1.96
1.67
1.27
1.24
1.24
1.22
5.67
5.65
5.64
5.64
5.63
5.62
5.60
5.58
5.56
5.50
5.48
5.45
5.43
5.41
5.38
5.34
5.75 5.70 5.65 5.60 5.55 5.50 5.45 5.40 5.35 5.30
f1 (ppm)
3.04
1.50
3.27
0.41
0.64
8.91
0.97
1.80
1.85
3.18
1.35
3.71
5.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


172.70
133.59
133.06
126.48
126.26
103.86
103.81
81.26
81.21
69.94
69.81
60.90
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52.78
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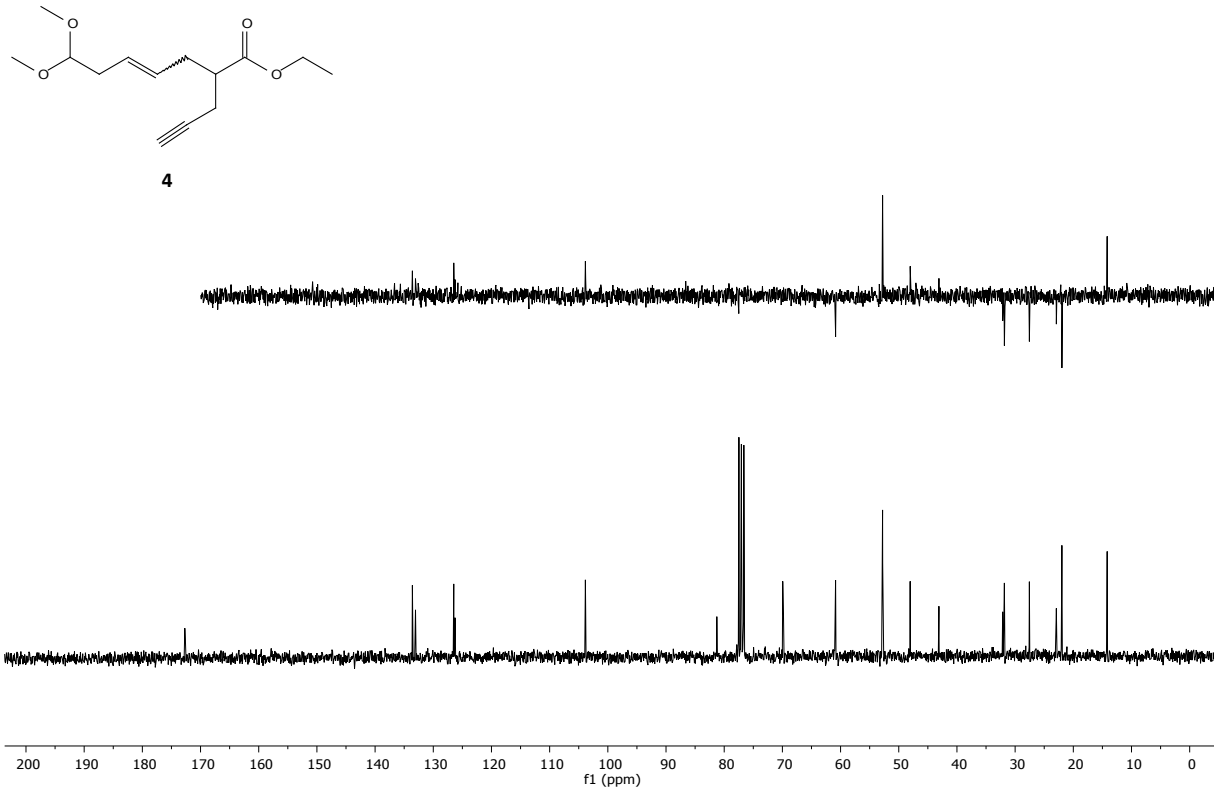
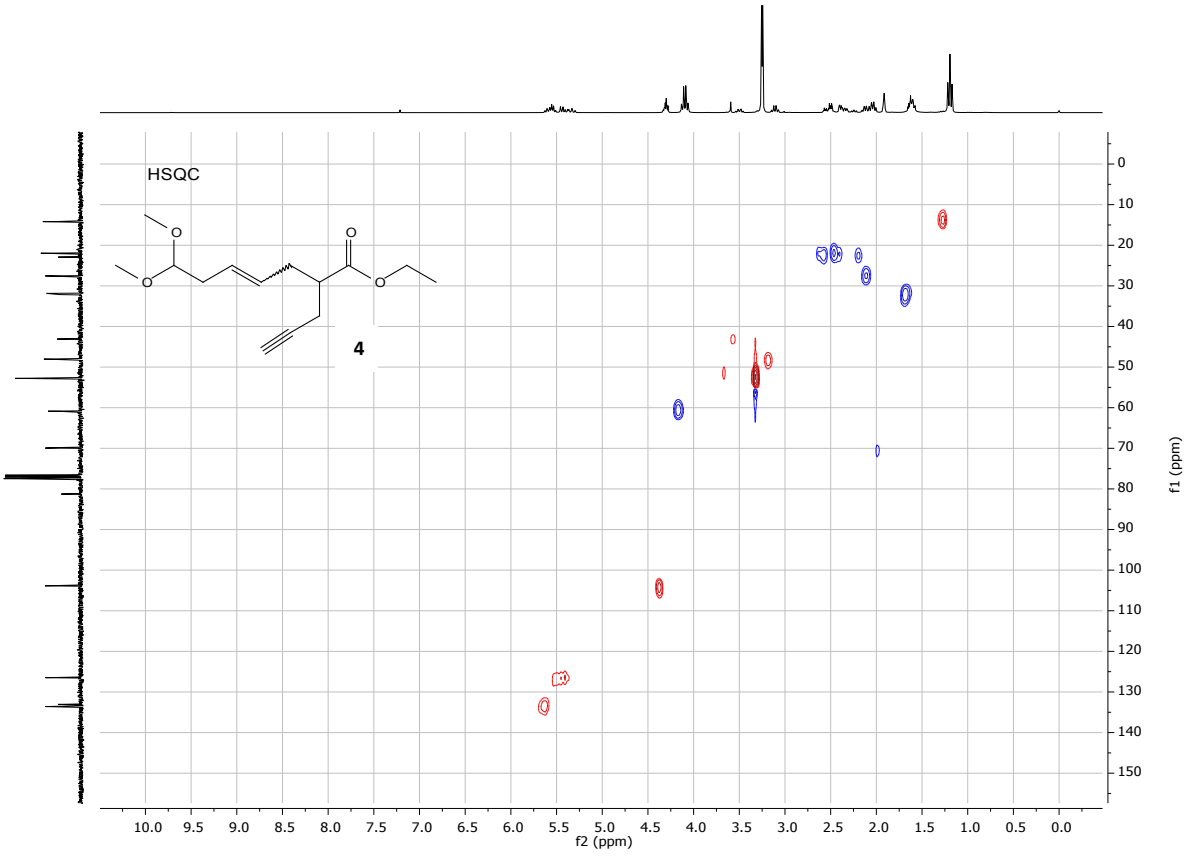
22.92
21.96
14.19
14.16
f1 (ppm)

4


f1 (ppm)

4



Acquisition Parameter

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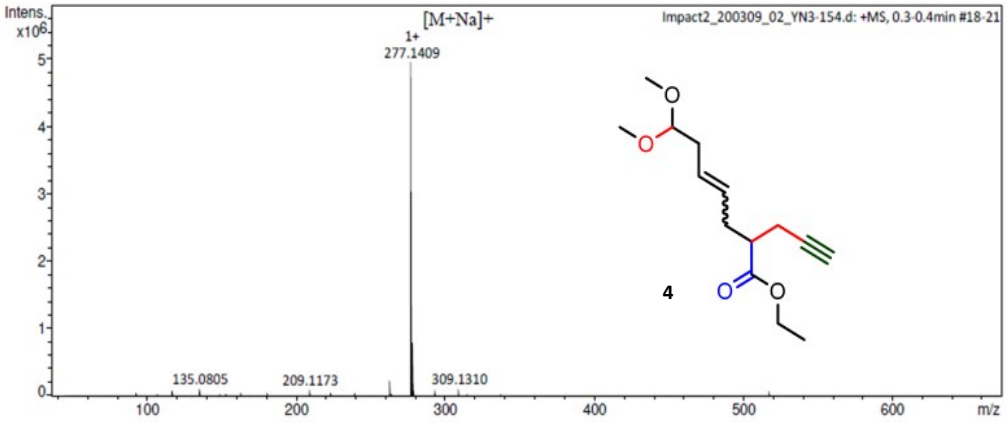
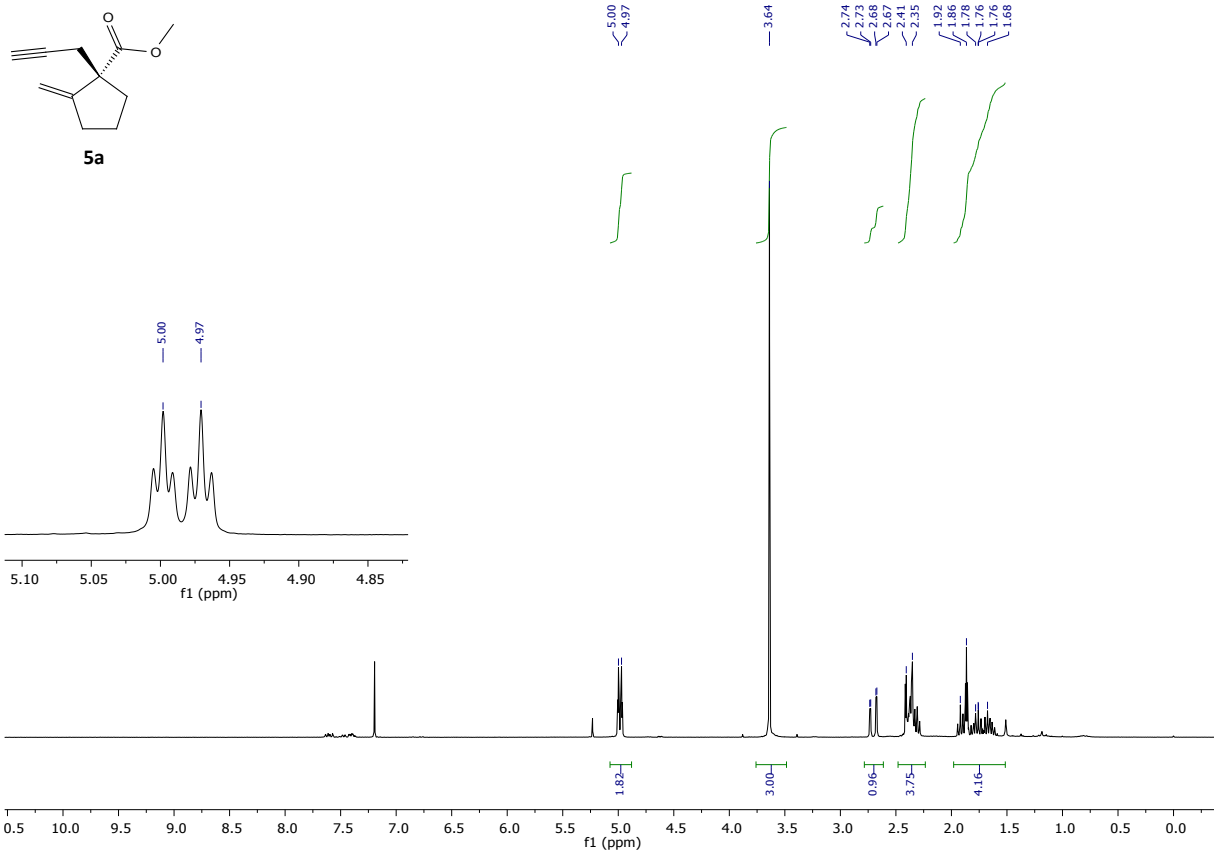


- **5a**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2.41
2.35
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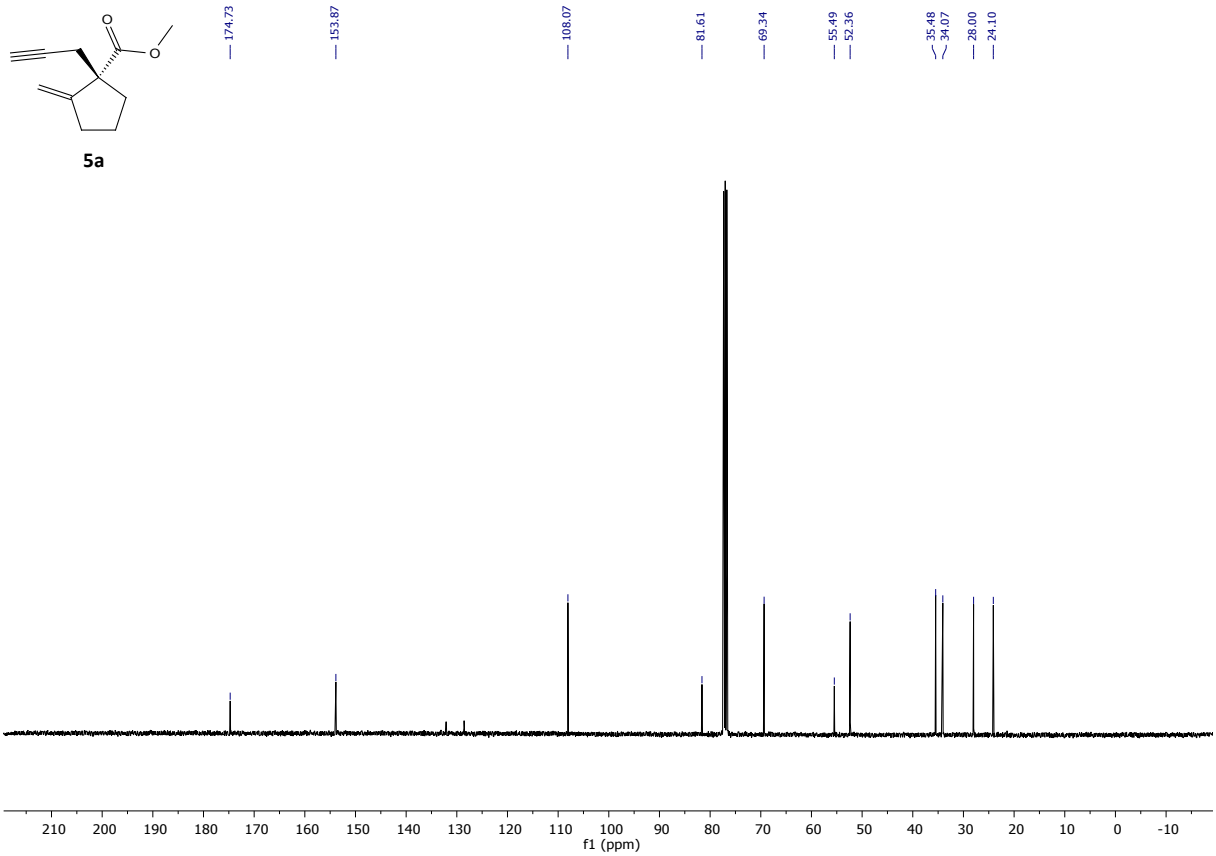
1.78
1.76
1.76
1.68
1.82
3.00
0.96
3.75
4.16
f1 (ppm)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52.36
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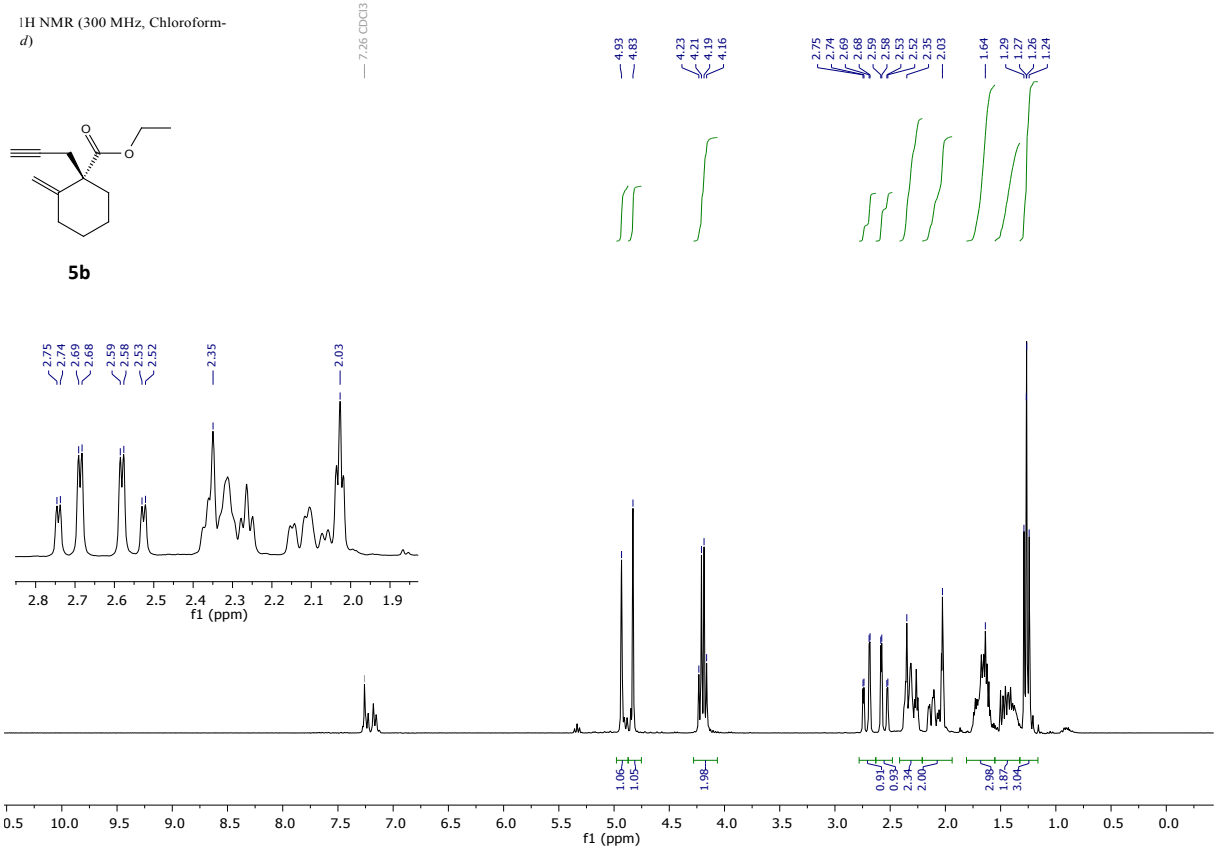
34.07
28.00
24.10
f1 (ppm)

- **5b**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4.83
4.23
4.21
4.19
4.16
2.75
2.74
2.69
2.68
2.59
2.58
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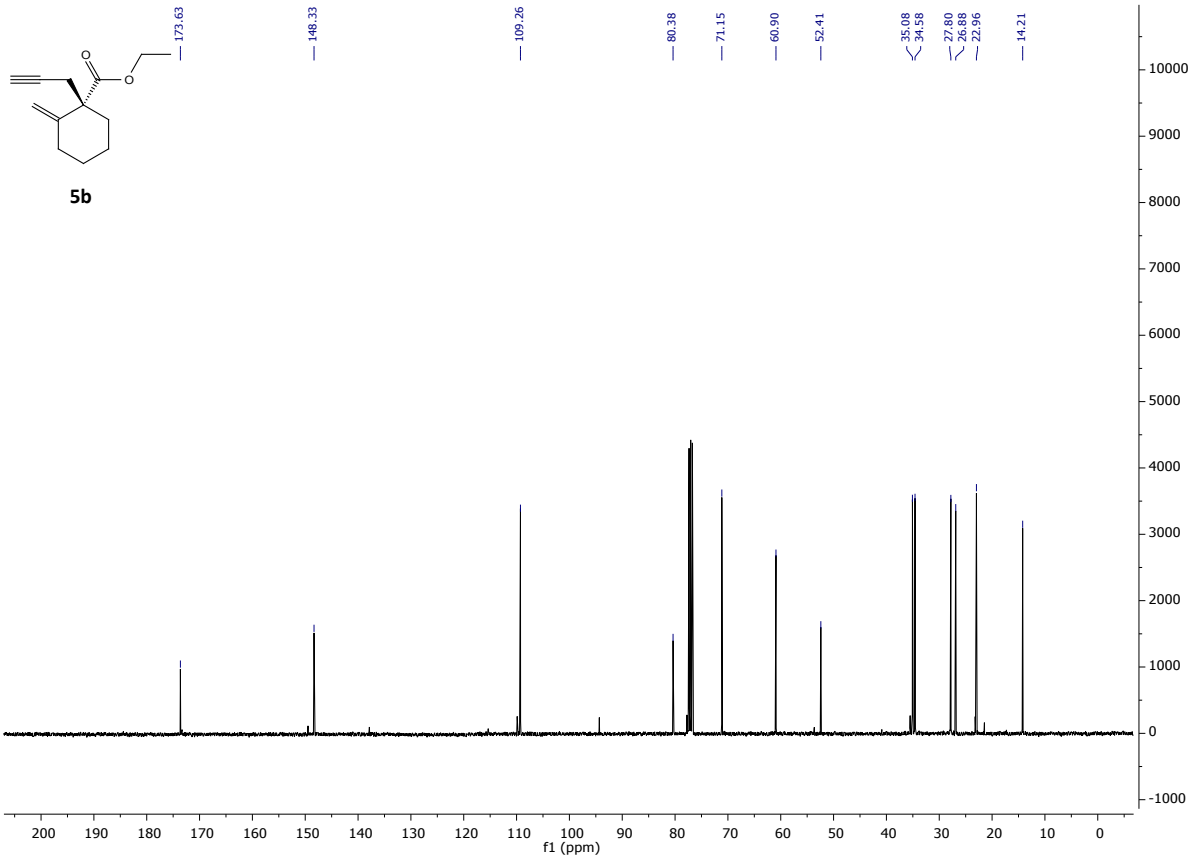
1.29
1.27
1.26
1.24
5b
f1 (ppm)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80.38
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60.90
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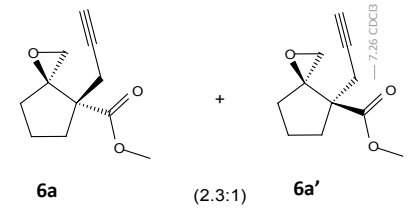
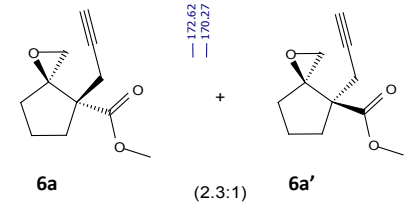
35.08
34.58
27.80
26.88
22.96
14.21
5b
f1 (ppm)

- **6a**


7.26 CDCl3

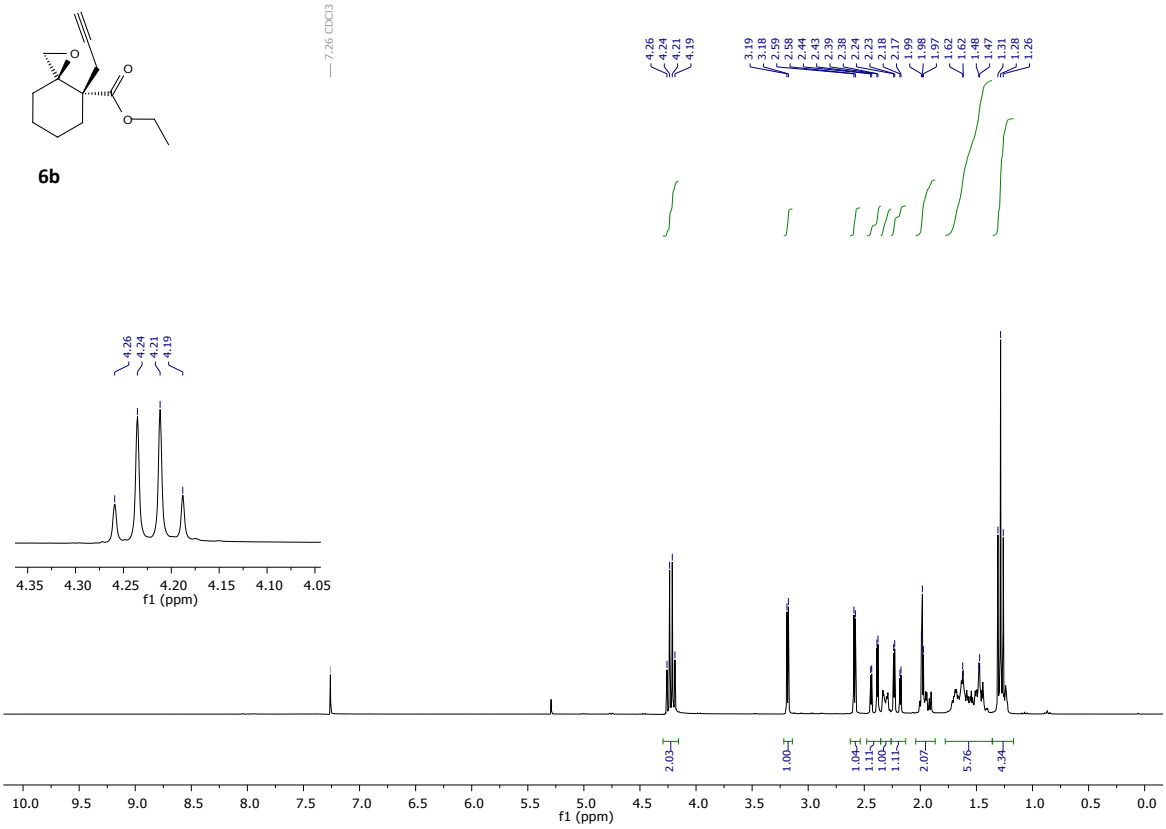
6a (2.3:1) **6a'**

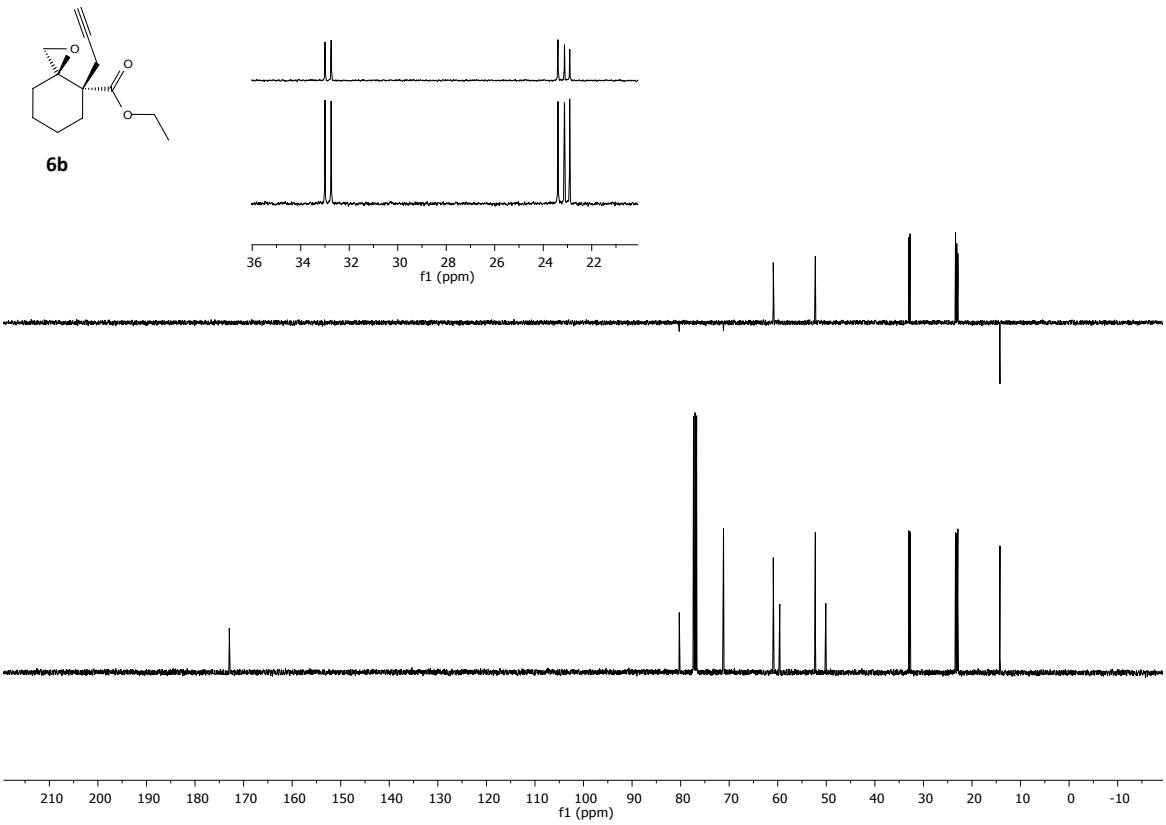
3.71
3.70
2.94
2.89
2.87
2.85
2.83
2.81
2.80
2.51
2.45
2.45
2.40
2.38
2.37
2.36
2.03
2.00
1.96
1.95
1.94
1.93
1.92
1.84
1.83
1.82
1.82
1.81
1.80
1.80
1.80
1.79
1.78
2.98
1.21
2.99
4.31
6.25
4.45
f1 (ppm)


3.80
3.75
3.70
3.65
3.60
3.55
f1 (ppm)

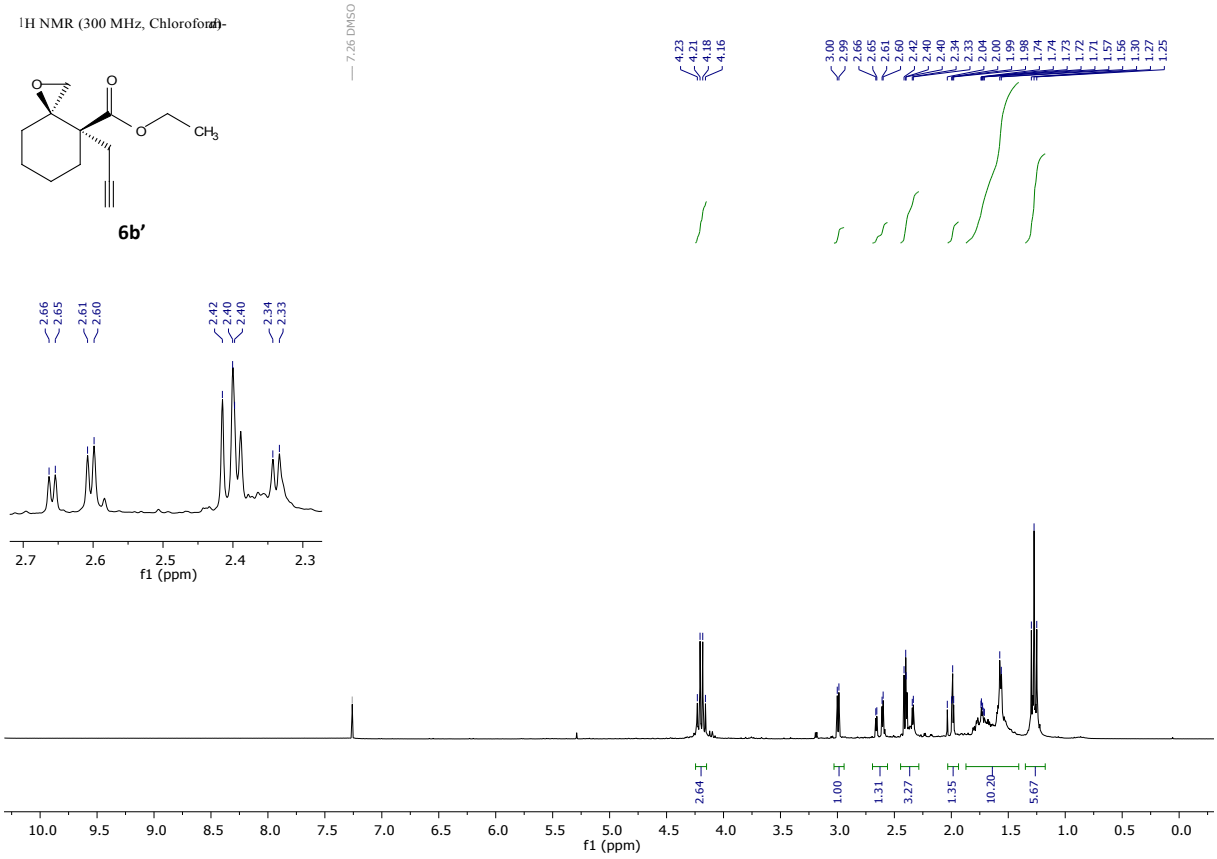
172.62
170.27
79.33
78.68
68.14
67.67
66.07
65.22
52.37
51.77
50.39
50.29
48.69
47.72
33.78
31.77
31.45
31.03
30.02
27.79
27.45
22.88
20.92
20.78
20.45
20.09
f1 (ppm)

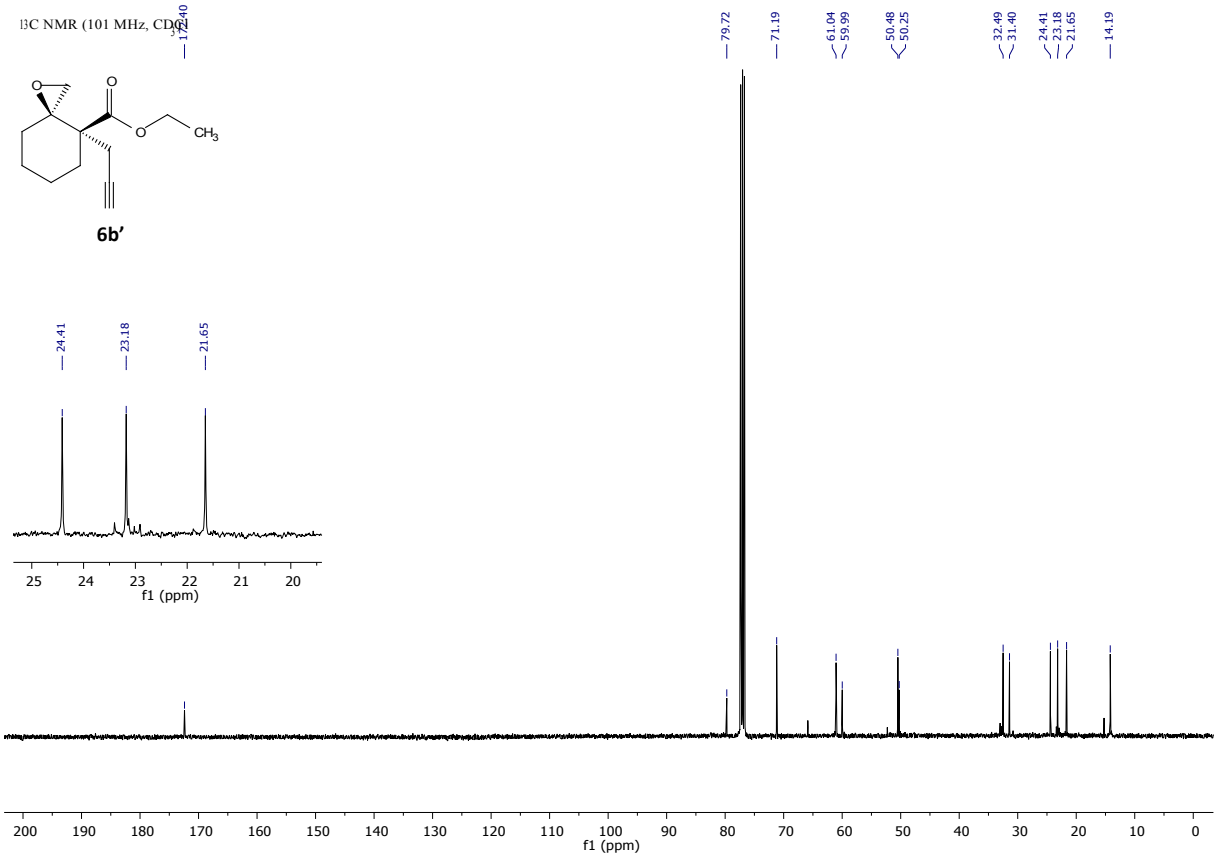
- **6b**


6b
7.26 CDCl3
4.26
4.24
4.21
4.19
3.19
3.18
2.59
2.58
2.44
2.43
2.39
2.38
2.34
2.23
2.18
2.17
1.99
1.98
1.97
1.62
1.62
1.48
1.47
1.31
1.28
1.26
2.03
1.00
1.04
1.11
1.00
1.11
2.07
5.76
4.34
f1 (ppm)

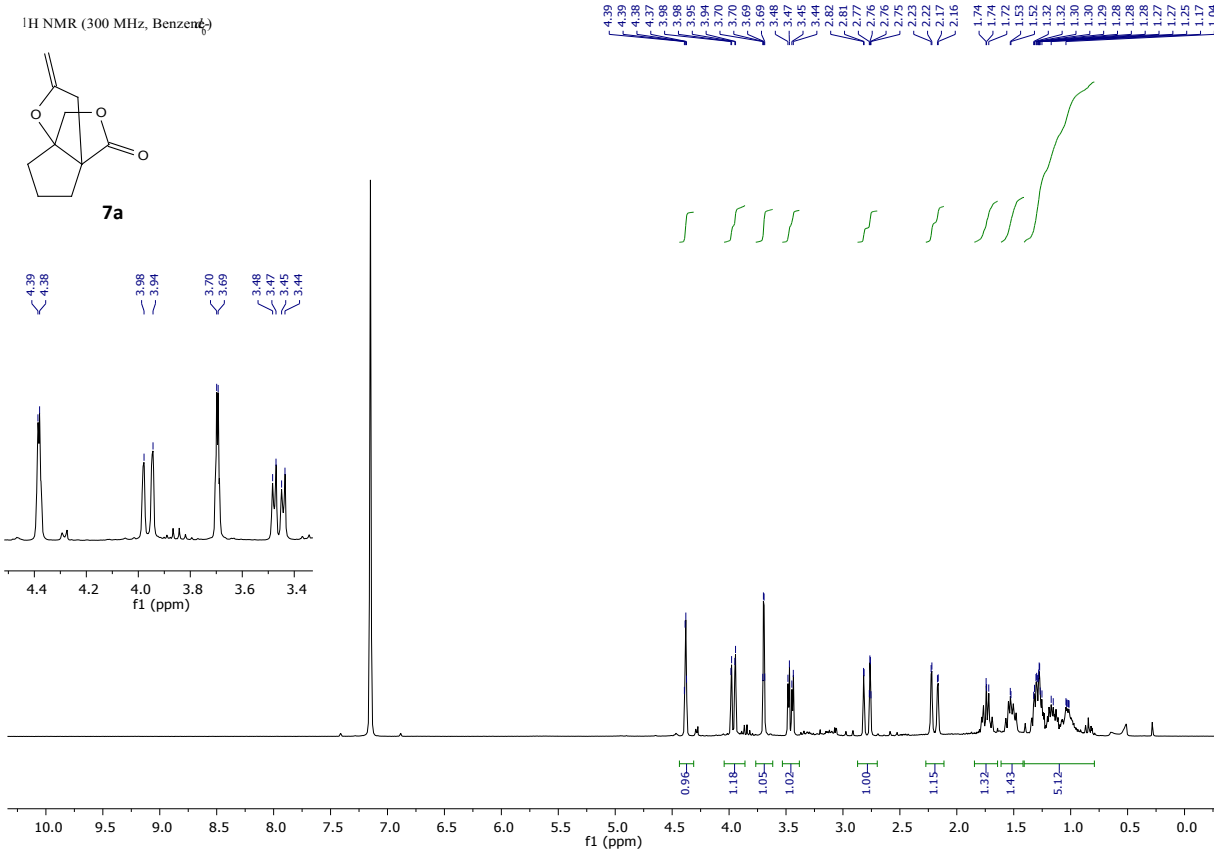

6b
f1 (ppm)

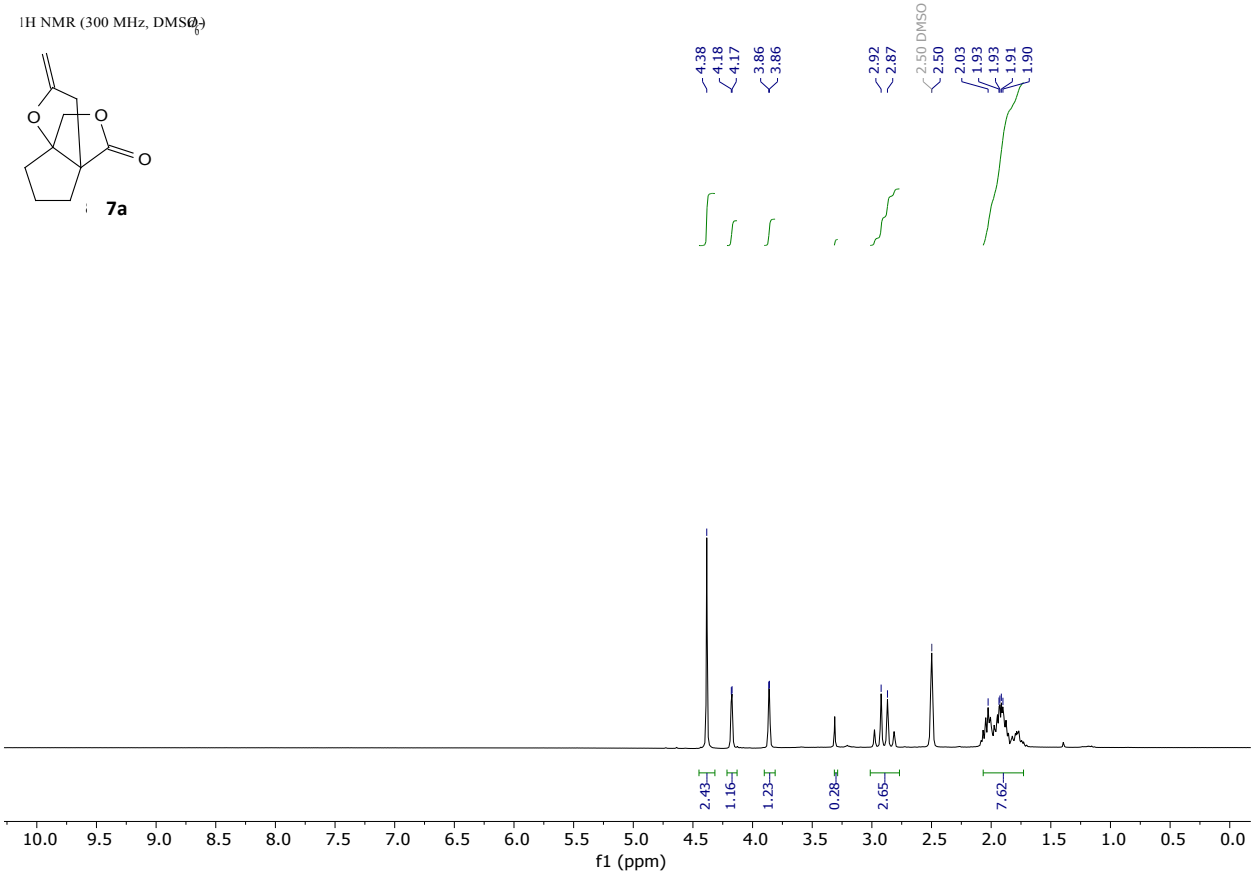
- **6b’**

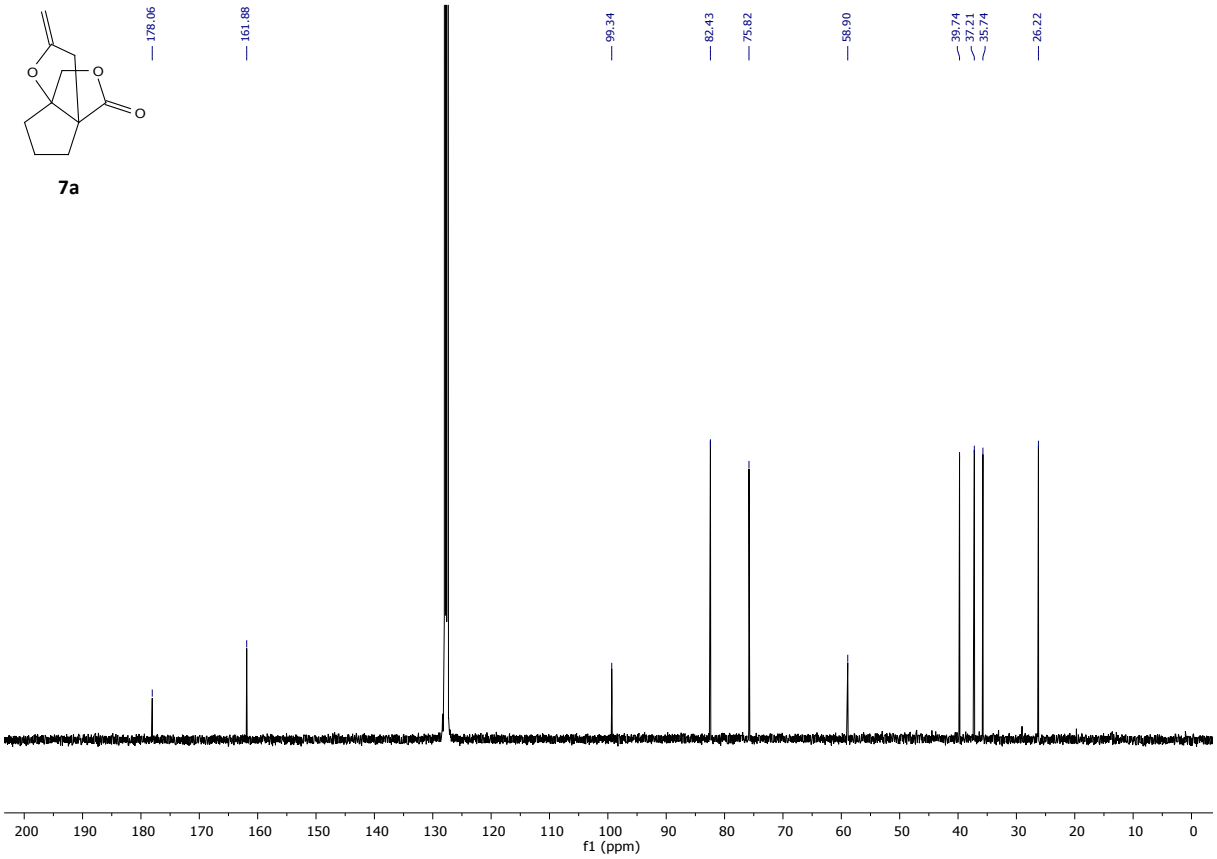

1H NMR (300 MHz, Chloroform-d)
7.26 DMSO
6b’
4.23
4.21
4.18
4.16
3.00
2.99
2.66
2.65
2.61
2.60
2.42
2.40
2.40
2.34
2.33
2.04
2.00
1.99
1.98
1.74
1.74
1.73
1.72
1.71
1.57
1.56
1.30
1.27
1.25
2.66
2.65
2.61
2.60
2.42
2.40
2.40
2.34
2.33
2.7
2.6
2.5
2.4
2.3
f1 (ppm)
2.64
1.00
1.31
3.27
1.35
10.20
5.67
10.0
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
f1 (ppm)

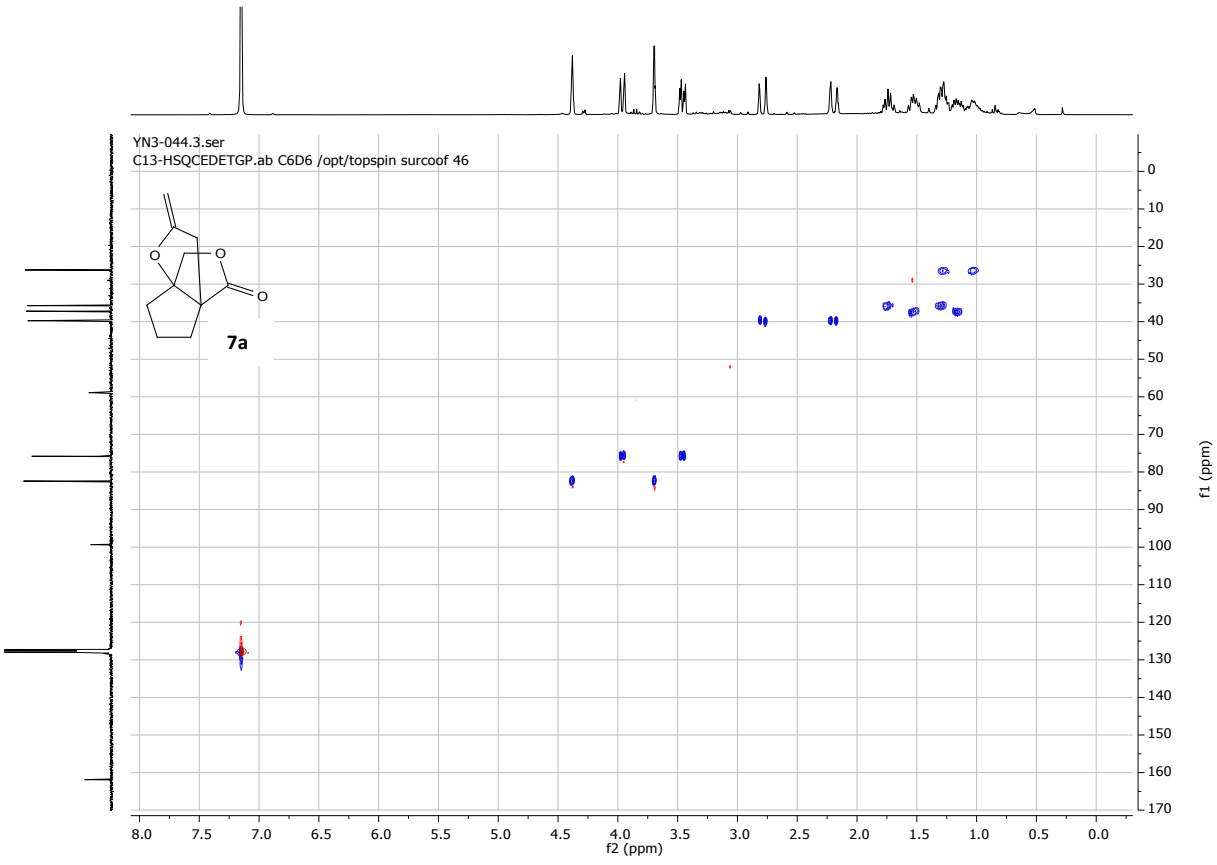

13C NMR (101 MHz, CDCl3)
172.40
79.72
71.19
61.04
59.99
50.48
50.25
32.49
31.40
24.41
23.18
21.65
14.19
6b’
24.41
23.18
21.65
25
24
23
22
21
20
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

- **7a**

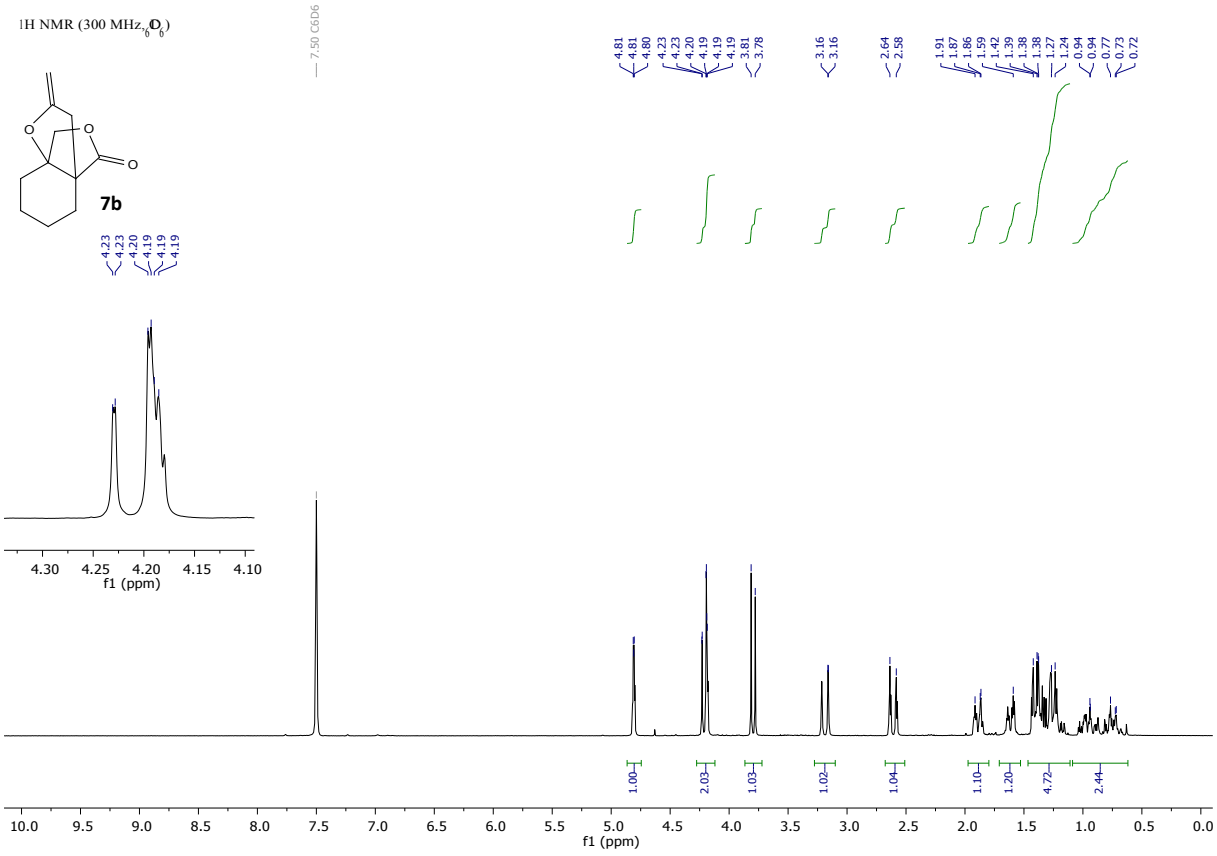

1H NMR (300 MHz, Benzene-d6)
7a
4.4
4.2
4.0
3.8
3.6
3.4
f1 (ppm)
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

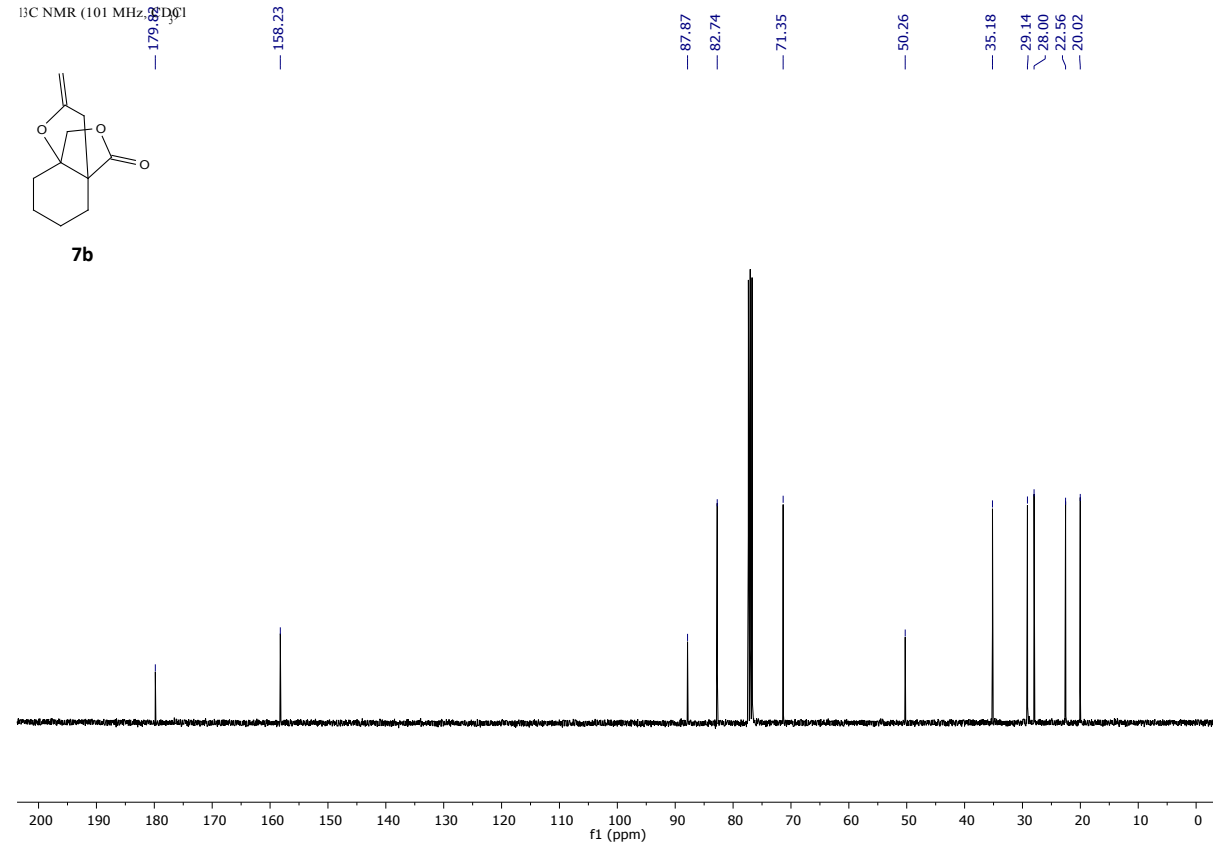

1H NMR (300 MHz, DMSO-d6)
7a
2.50 DMSO
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

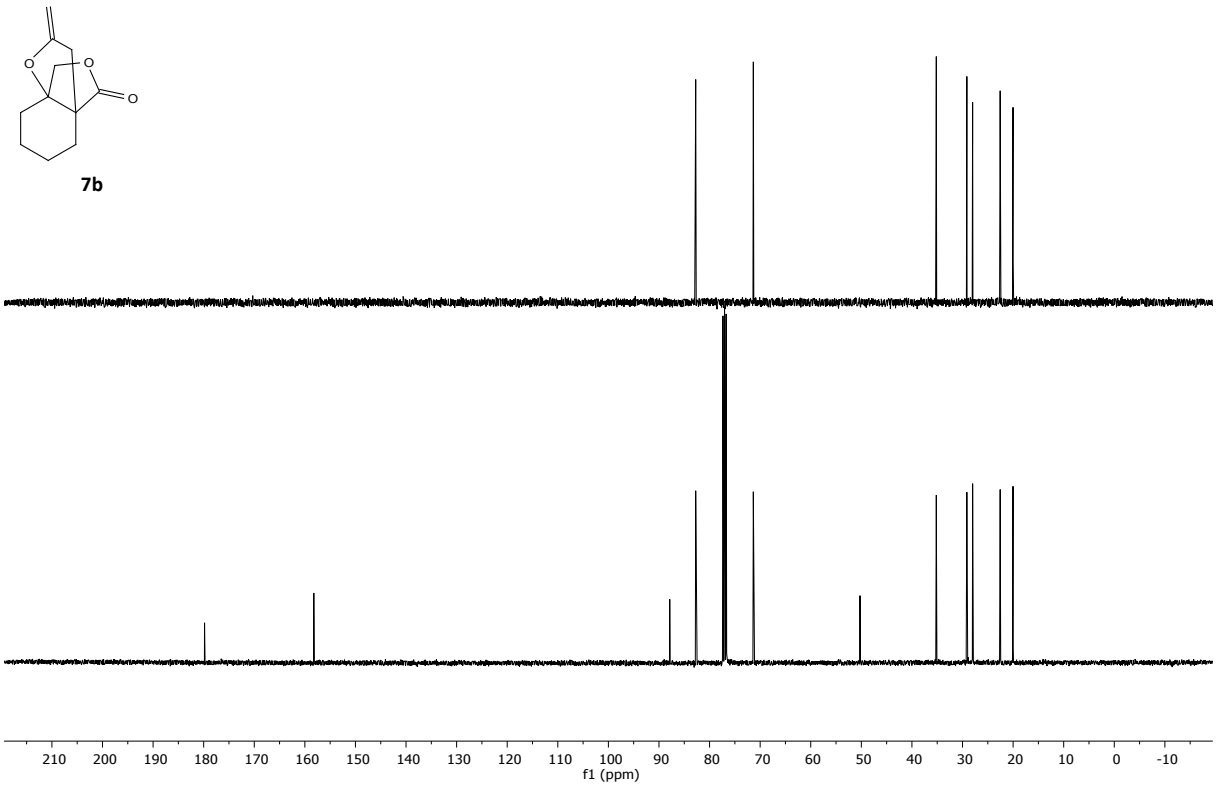

178.06
161.88
99.34
82.43
75.82
58.90
39.74
37.21
35.74
26.22
O
O
O
7a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


YN3-044.3.ser
C13-HSQCEDETGP.ab C6D6 /opt/topspin surcoof 46
O
O
O
7a
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
f2 (ppm)
0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170
f1 (ppm)

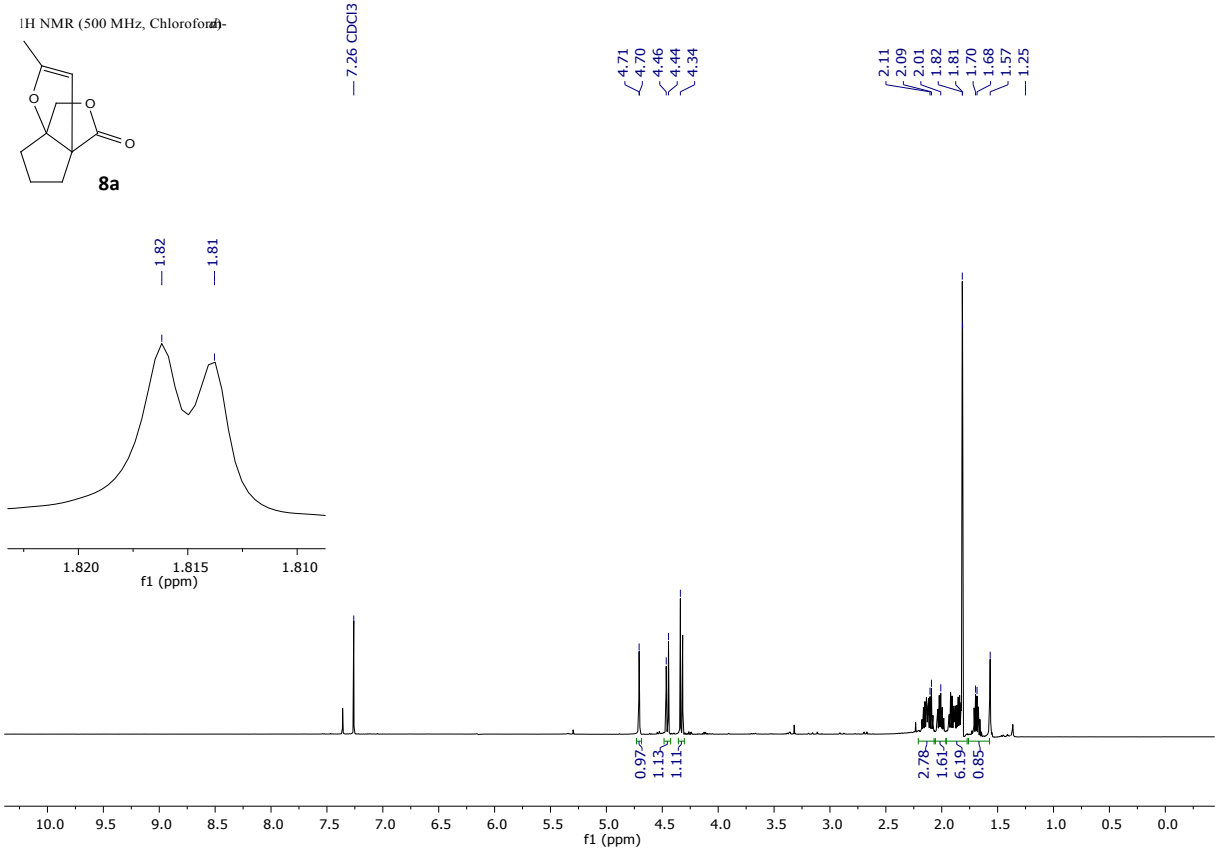
- **7b**

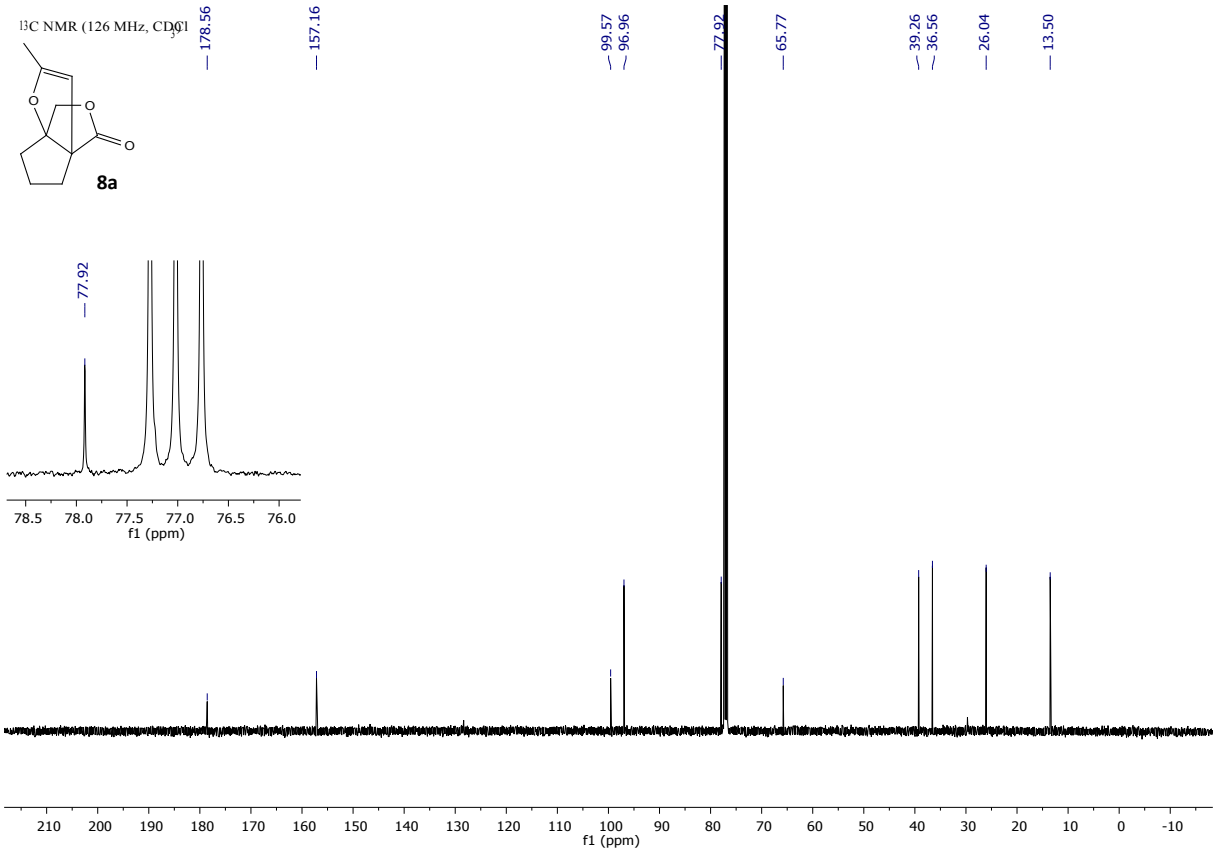

1H NMR (300 MHz, C6D6)
7.50 C6D6
7b
4.81 4.81 4.80 4.23 4.23 4.20 4.19 4.19 3.81 3.78 3.16 3.16 2.64 2.58 1.91 1.87 1.86 1.59 1.42 1.39 1.38 1.38 1.27 1.24 0.94 0.94 0.77 0.73 0.72
4.23 4.23 4.20 4.19 4.19 4.19
4.30 4.25 4.20 4.15 4.10
f1 (ppm)
1.00 2.03 1.03 1.02 1.04 1.10 1.20 4.72 2.44
10.0 9.5 9.0 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
f1 (ppm)

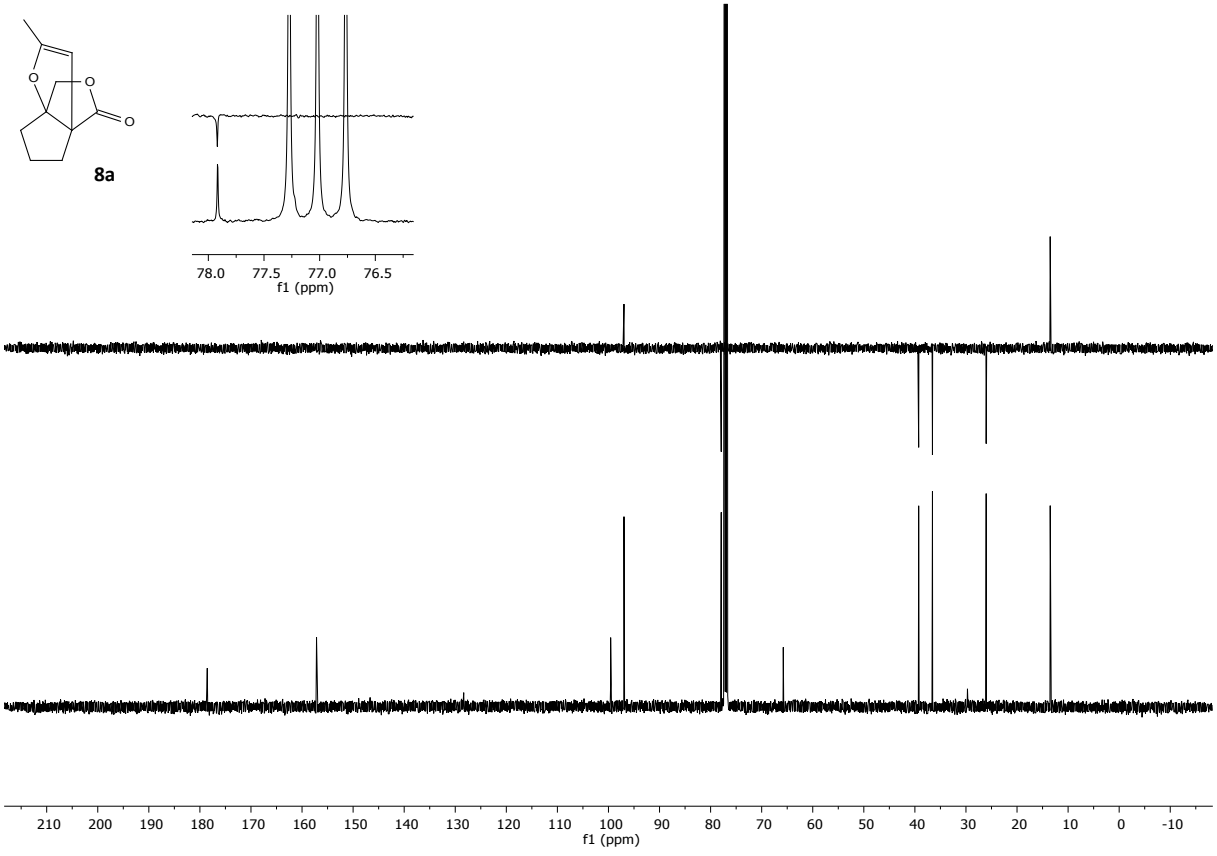

13C NMR (101 MHz, CDCl3)
179.82
158.23
87.87
82.74
71.35
50.26
35.18
29.14
28.00
22.56
20.02
7b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

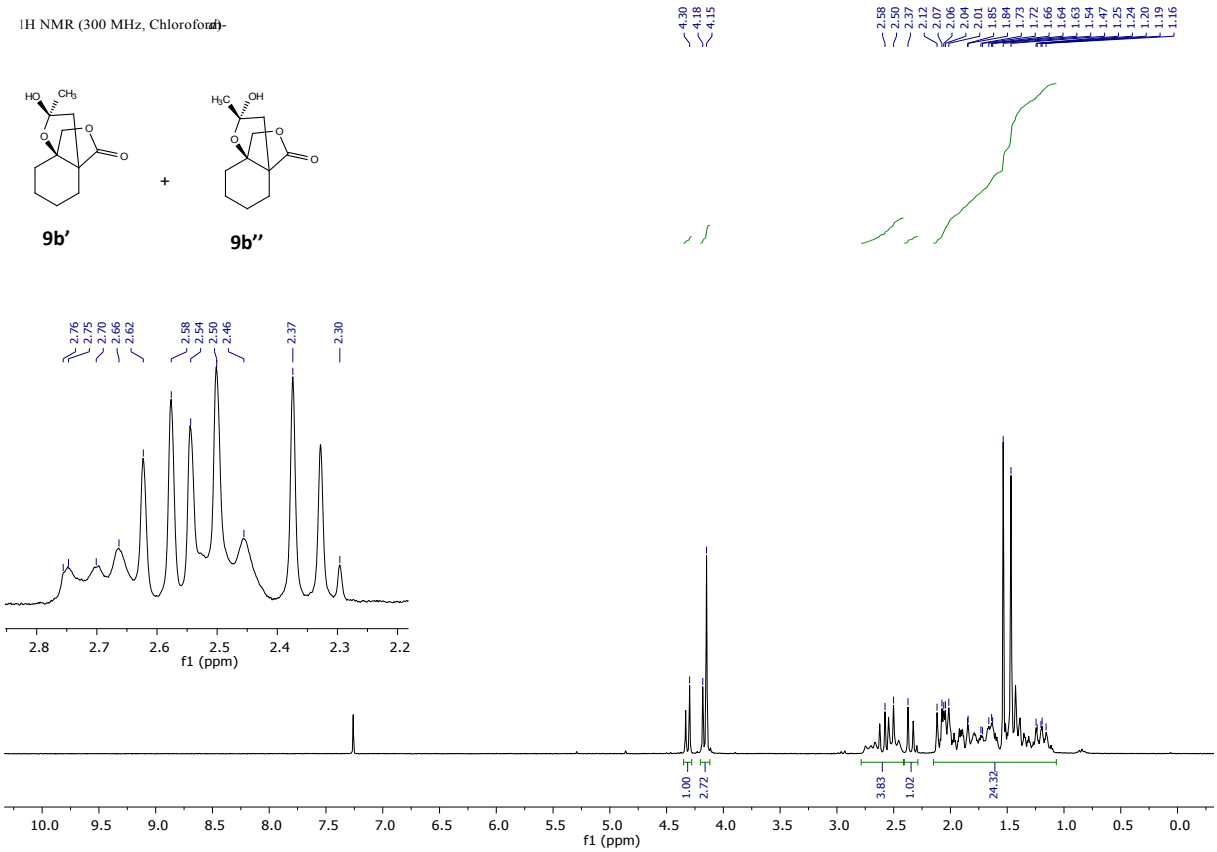
- **8a**

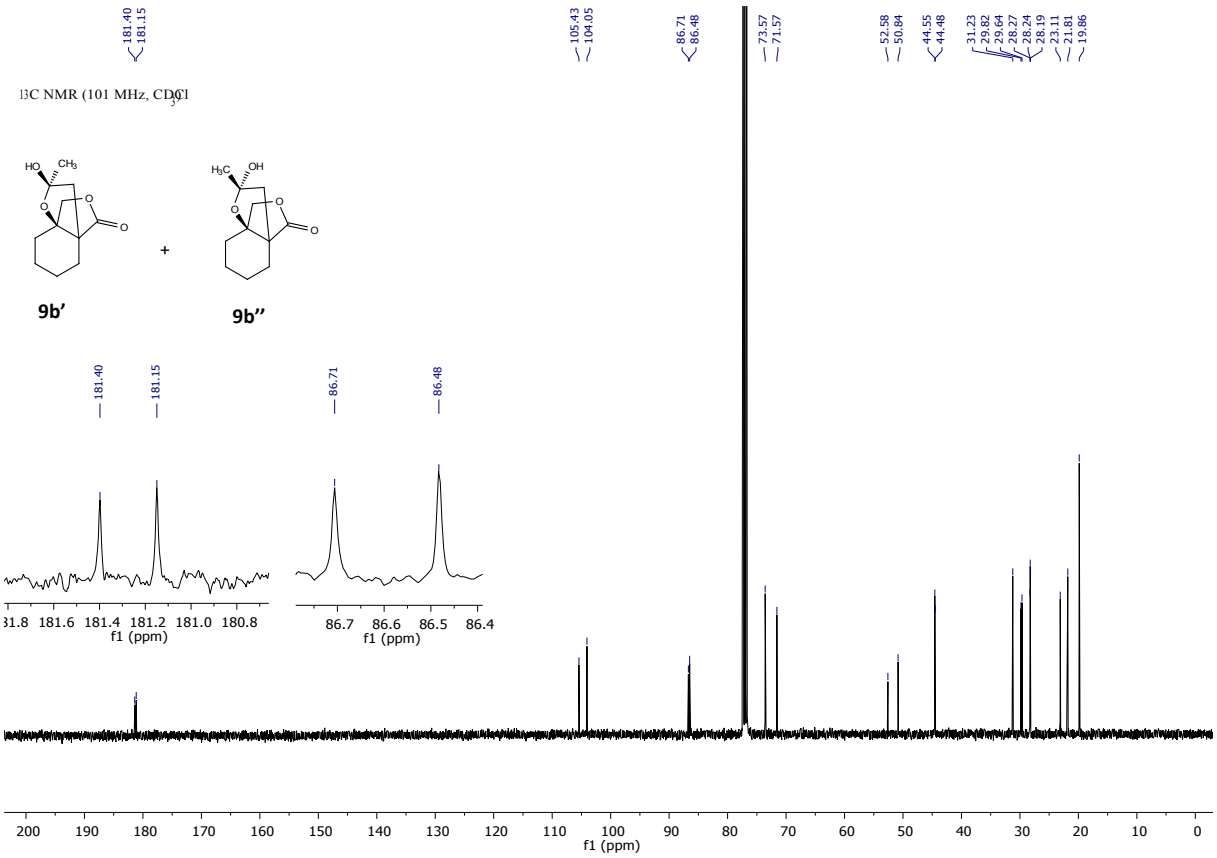

1H NMR (500 MHz, Chloroform-d)
8a
7.26 CDCl3
4.71
4.70
4.46
4.44
4.34
2.11
2.09
2.01
1.82
1.81
1.70
1.68
1.57
1.25
0.97
1.13
1.11
2.78
1.61
6.19
0.85
1.820 1.815 1.810
f1 (ppm)
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


13C NMR (126 MHz, CDCl3)
178.56
157.16
99.57
96.96
77.92
65.77
39.26
36.56
26.04
13.50
8a
77.92
78.5 78.0 77.5 77.0 76.5 76.0
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

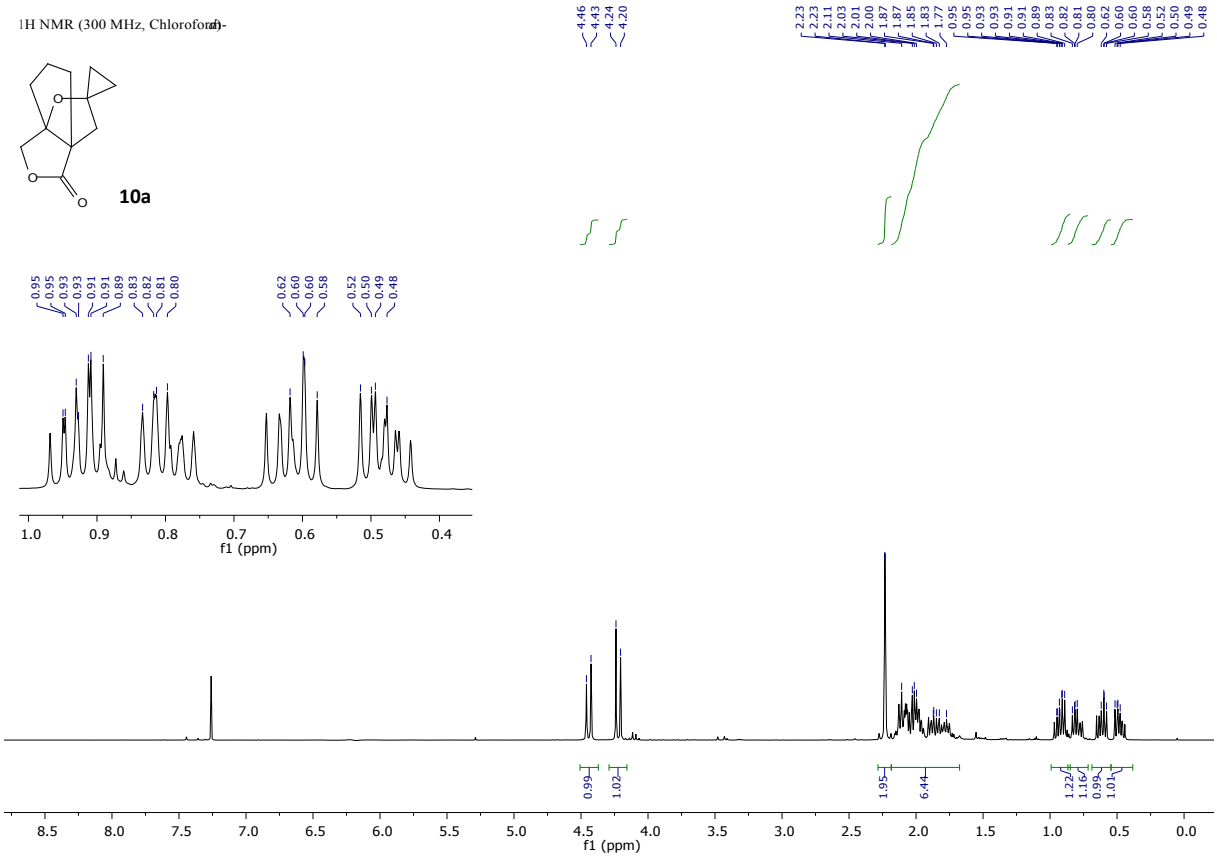

8a
78.0 77.5 77.0 76.5
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

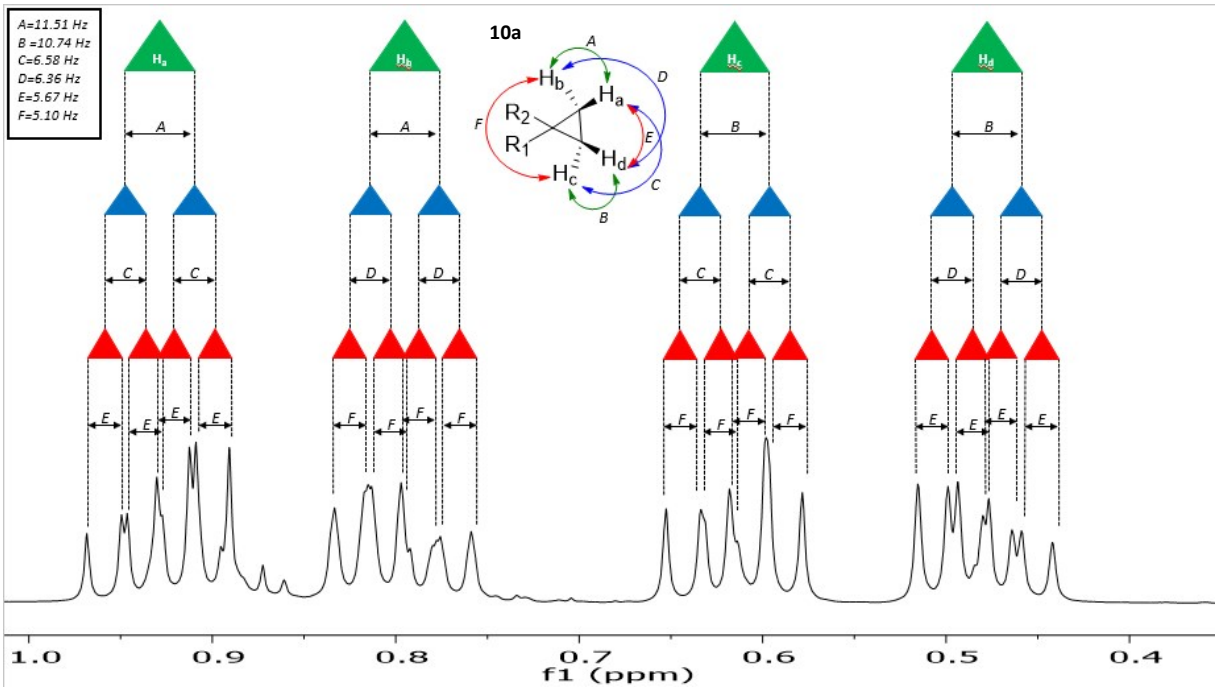
- **9b**

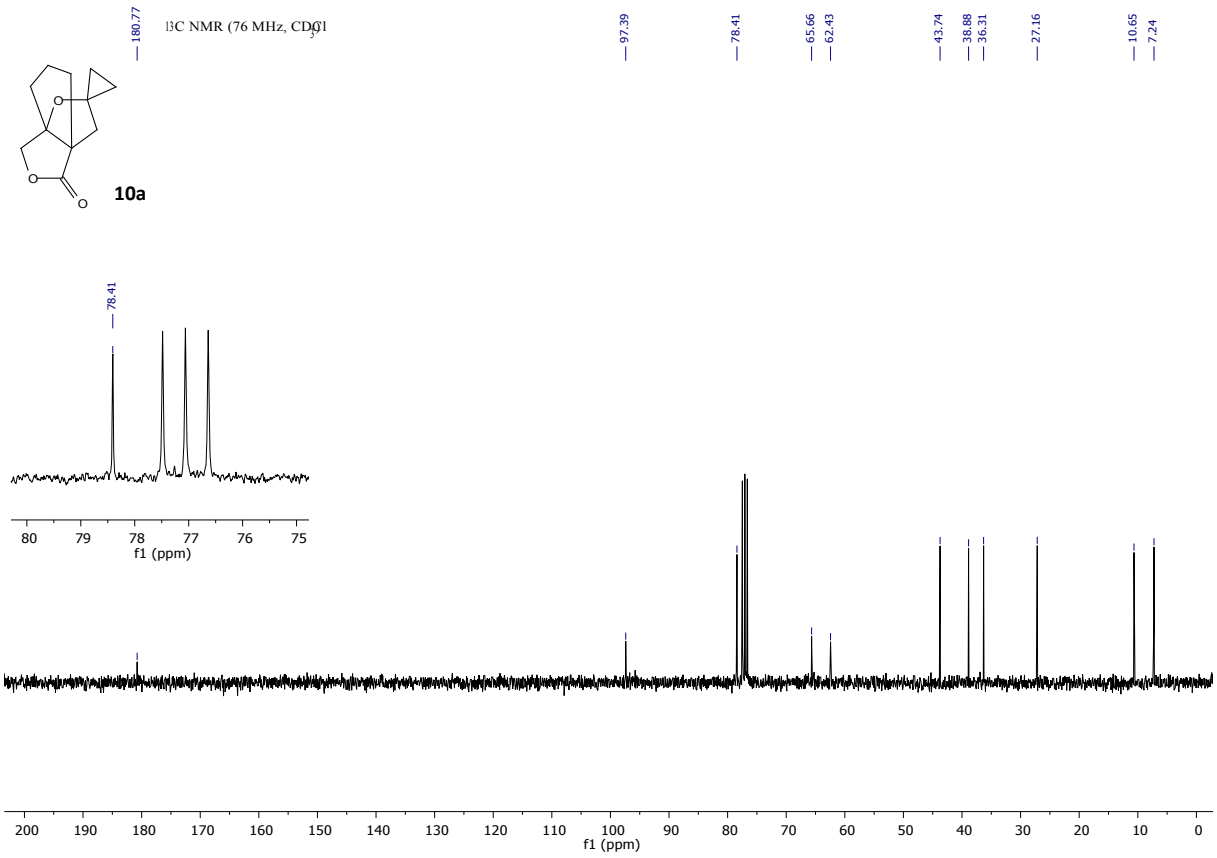

1H NMR (300 MHz, Chloroform-d)
9b'
9b''
f1 (ppm)

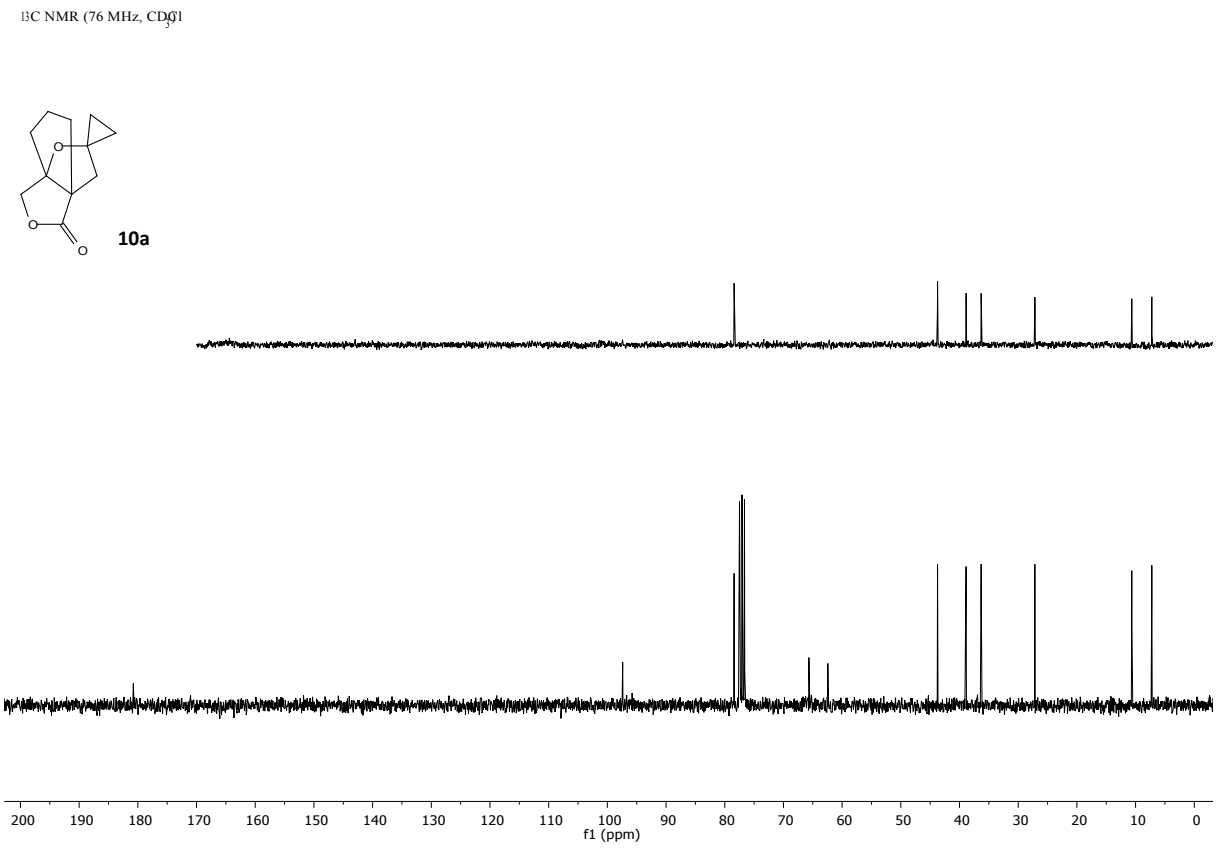

13C NMR (101 MHz, CDCl3)
9b'
9b''
f1 (ppm)

- **10a**

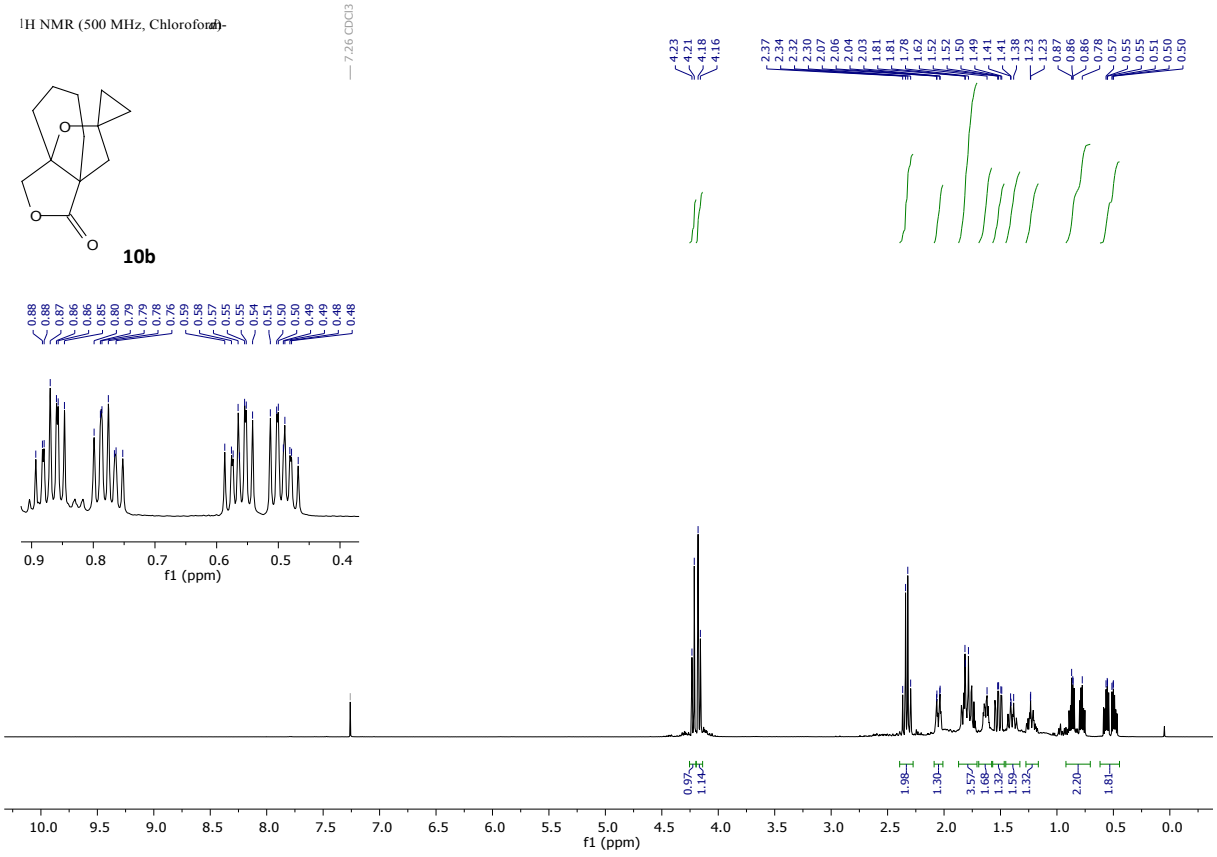

1H NMR (300 MHz, Chloroform-d)
10a
f1 (ppm)

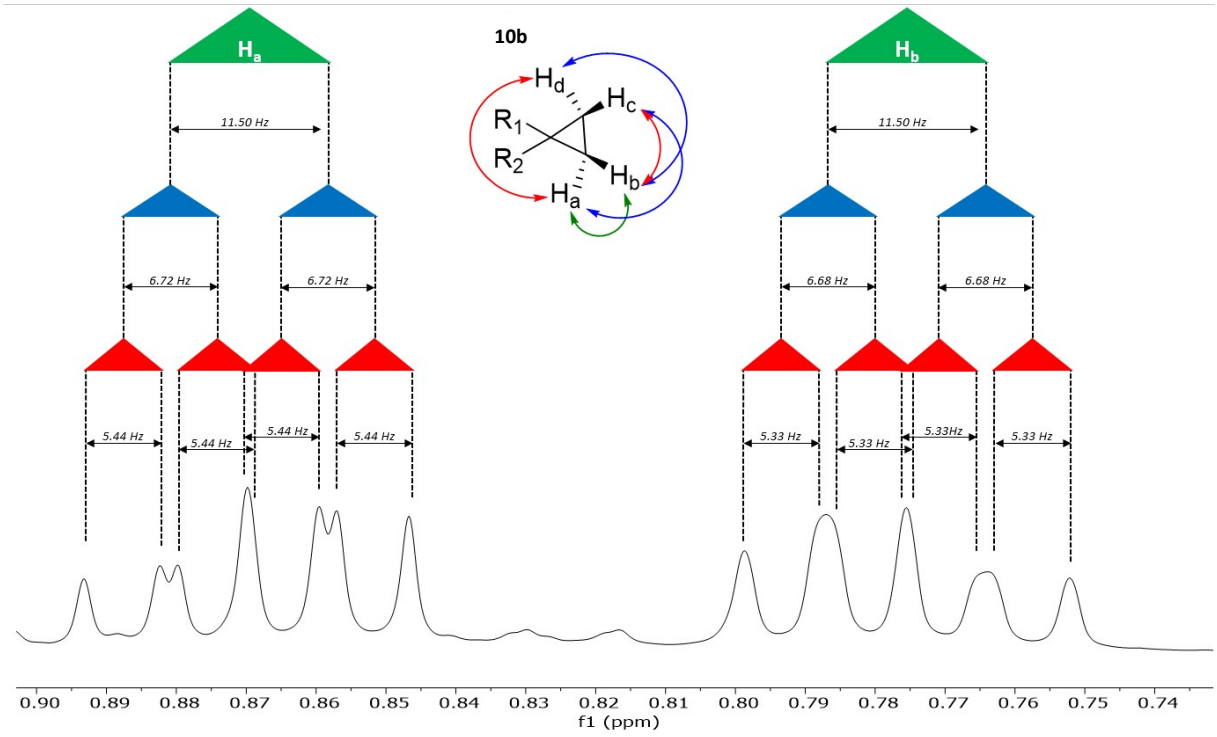

A=11.51 Hz
B =10.74 Hz
C=6.58 Hz
D=6.36 Hz
E=5.67 Hz
F=5.10 Hz
10a
f1 (ppm)

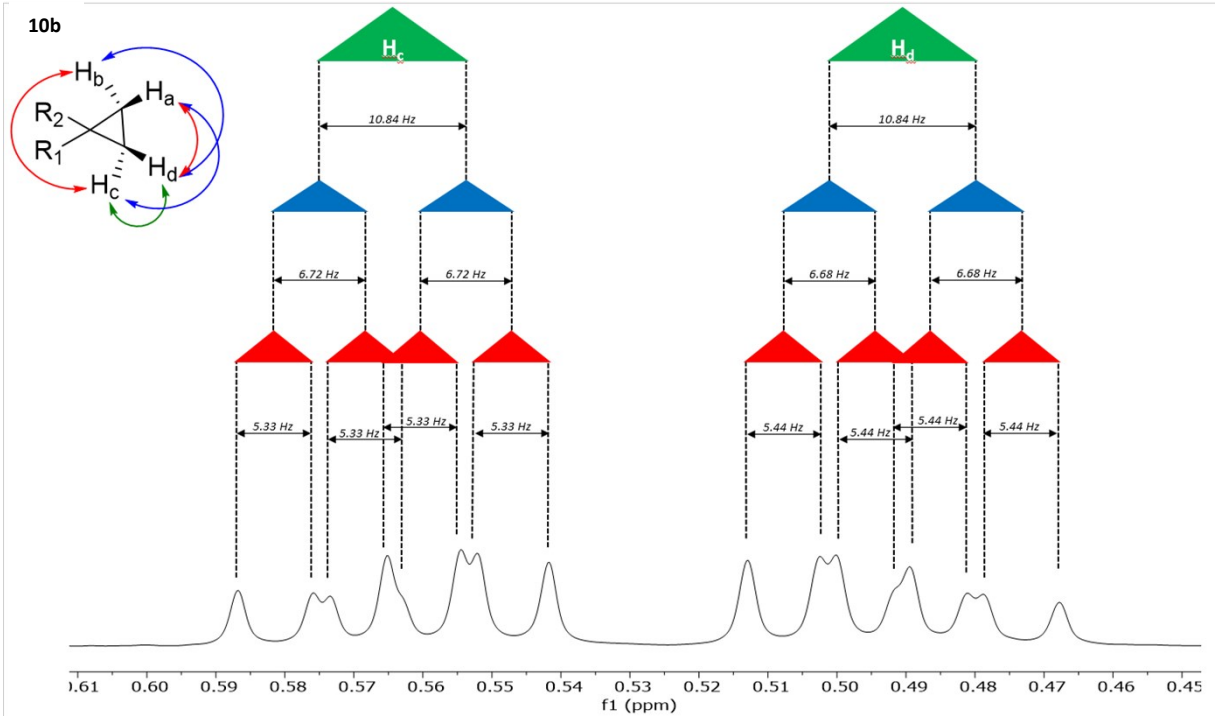

13C NMR (76 MHz, CDCl3)
180.77
97.39
78.41
65.66
62.43
43.74
38.88
36.31
27.16
10.65
7.24
10a
78.41
80 79 78 77 76 75
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

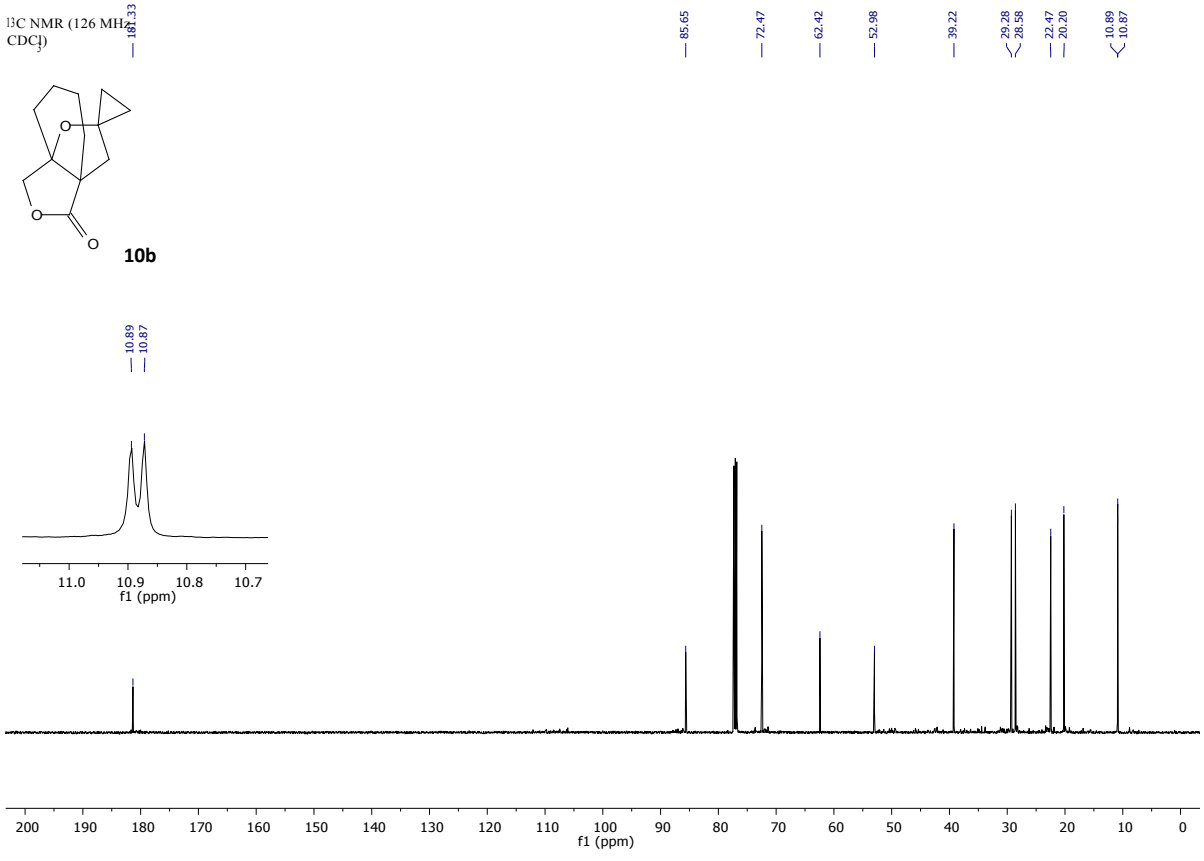

13C NMR (76 MHz, CDCl3)
10a
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

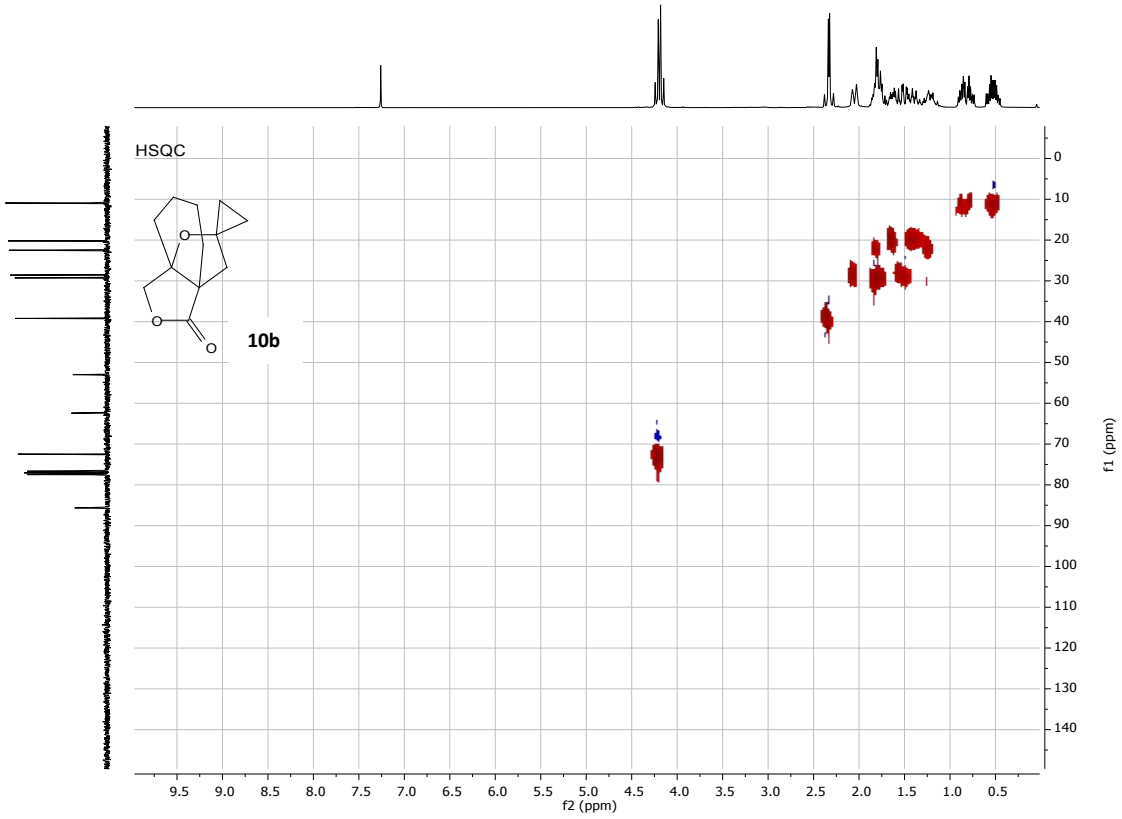
- **10b**


1H NMR (500 MHz, Chloroform-d)
7.26 CDCl3
10b
f1 (ppm)

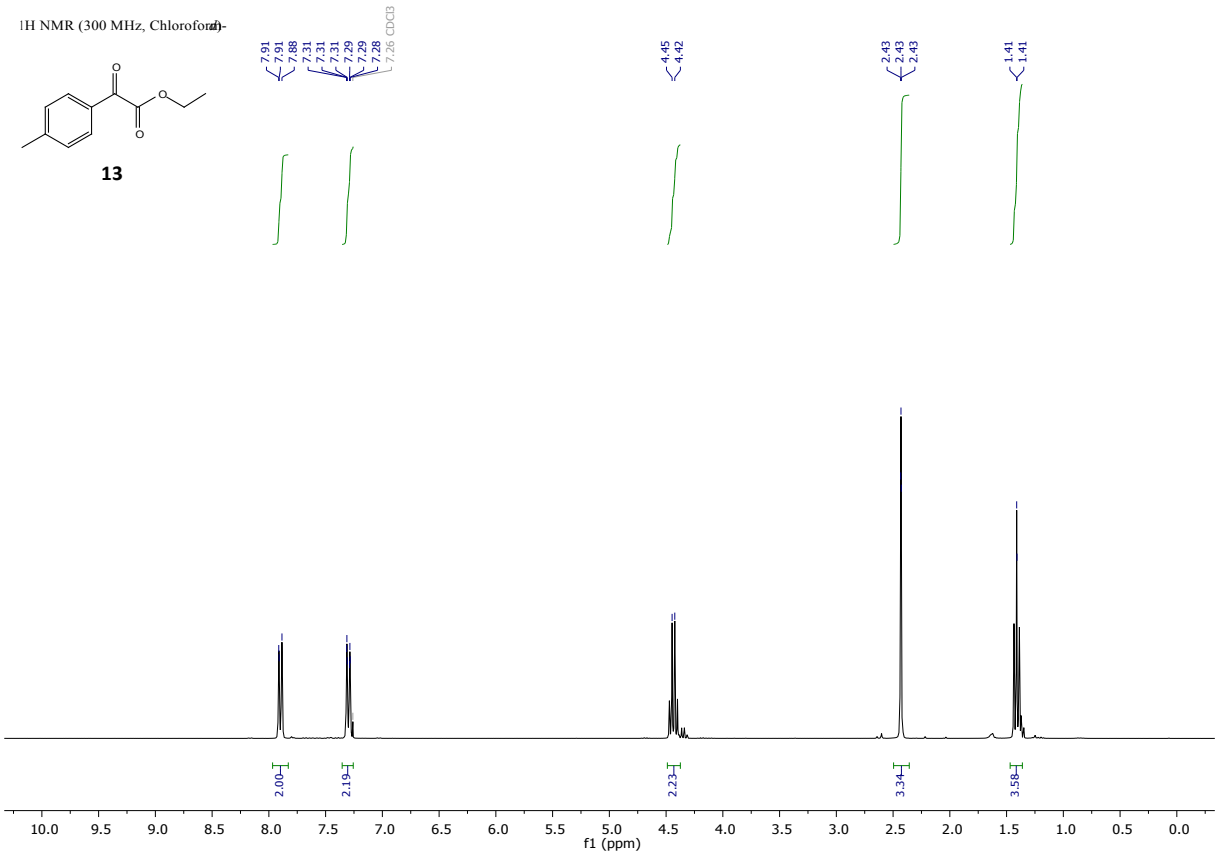

10b
Ha
Hb
Hc
Hd
R1
R2
11.50 Hz
6.72 Hz
6.68 Hz
5.44 Hz
5.33 Hz
5.33Hz
f1 (ppm)

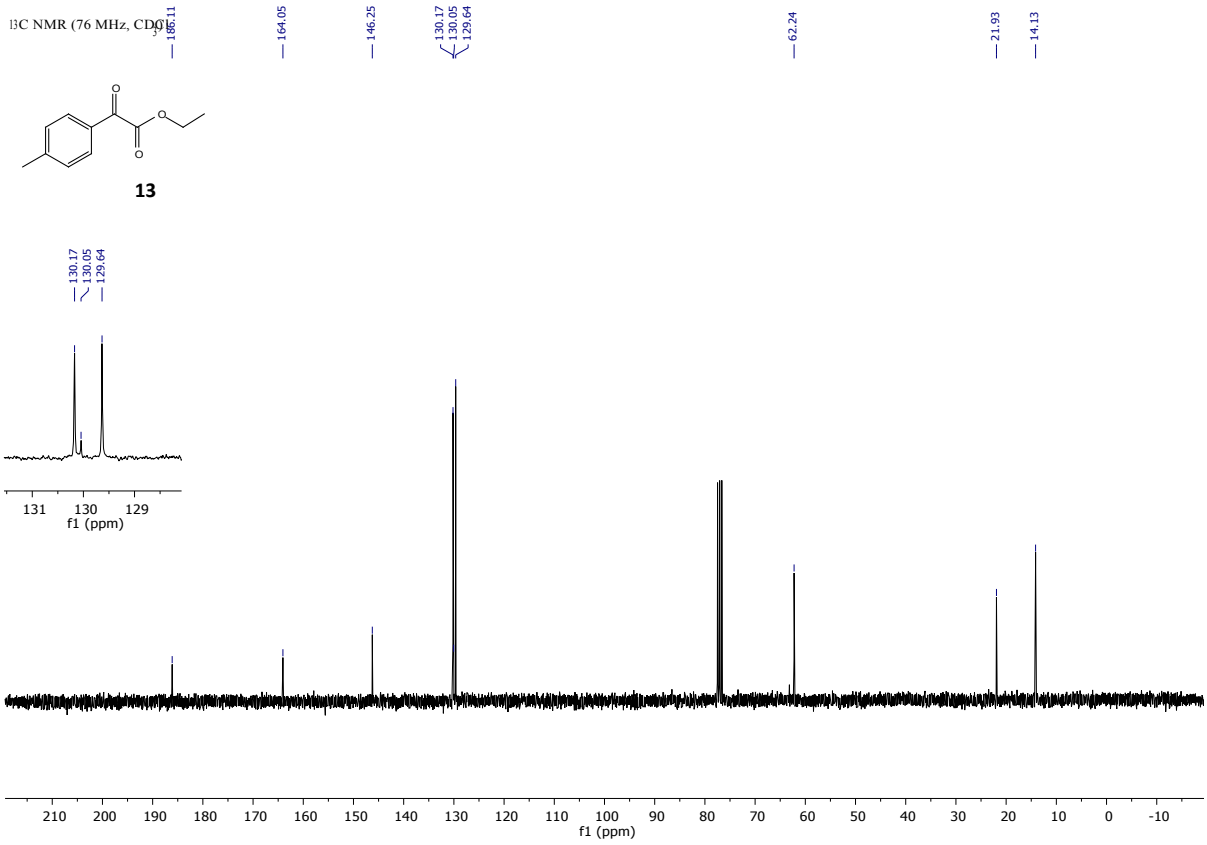

10b
Hb
Ha
R2
R1
Hd
Hc
Hc
Hd
10.84 Hz
10.84 Hz
6.72 Hz
6.72 Hz
6.68 Hz
6.68 Hz
5.33 Hz
5.33 Hz
5.33 Hz
5.33 Hz
5.44 Hz
5.44 Hz
5.44 Hz
5.44 Hz
f1 (ppm)


13C NMR (126 MHz, CDCl3)
187.33
85.65
72.47
62.42
52.98
39.22
29.28
28.58
22.47
20.20
10.89
10.87
O
O
O
10b
10.89
10.87
11.0
10.9
10.8
10.7
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


HSQC
10b
f2 (ppm)
f1 (ppm)

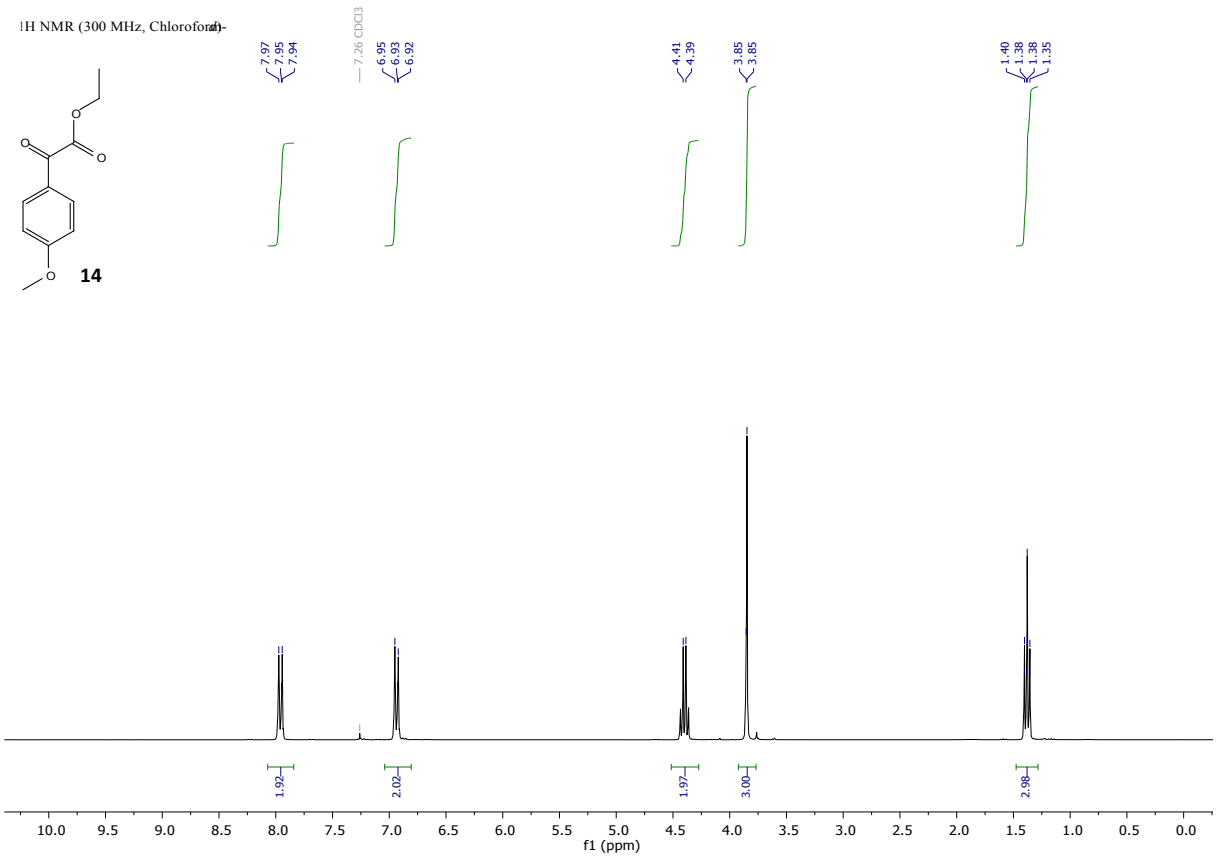
- **13**


1H NMR (300 MHz, Chloroform-d)
13
7.91
7.91
7.88
7.31
7.31
7.31
7.29
7.29
7.28
7.26 CDCl3
4.45
4.42
2.43
2.43
2.43
1.41
1.41
2.00
2.19
2.23
3.34
3.58
f1 (ppm)

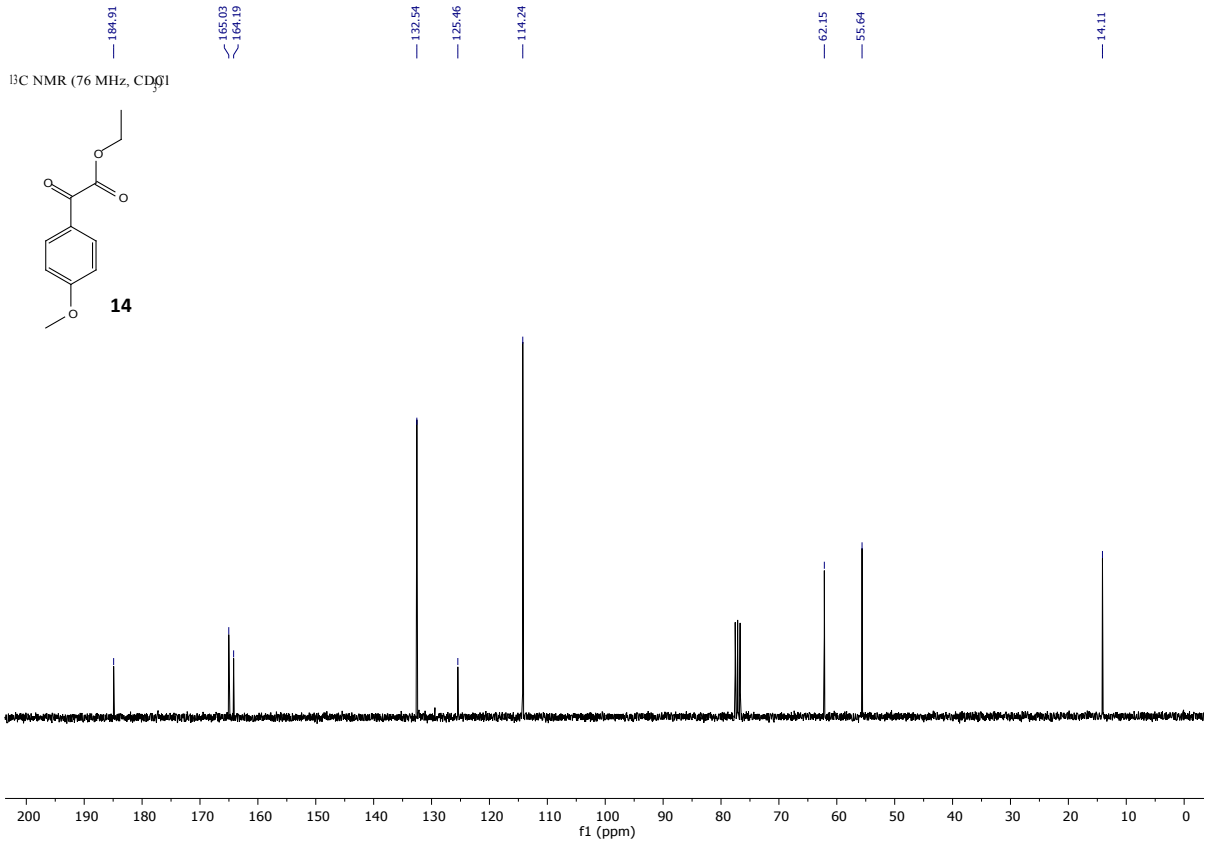

13C NMR (76 MHz, CDCl3)
166.11
164.05
146.25
130.17
130.05
129.64
62.24
21.93
14.13
131
130
129
f1 (ppm)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

13

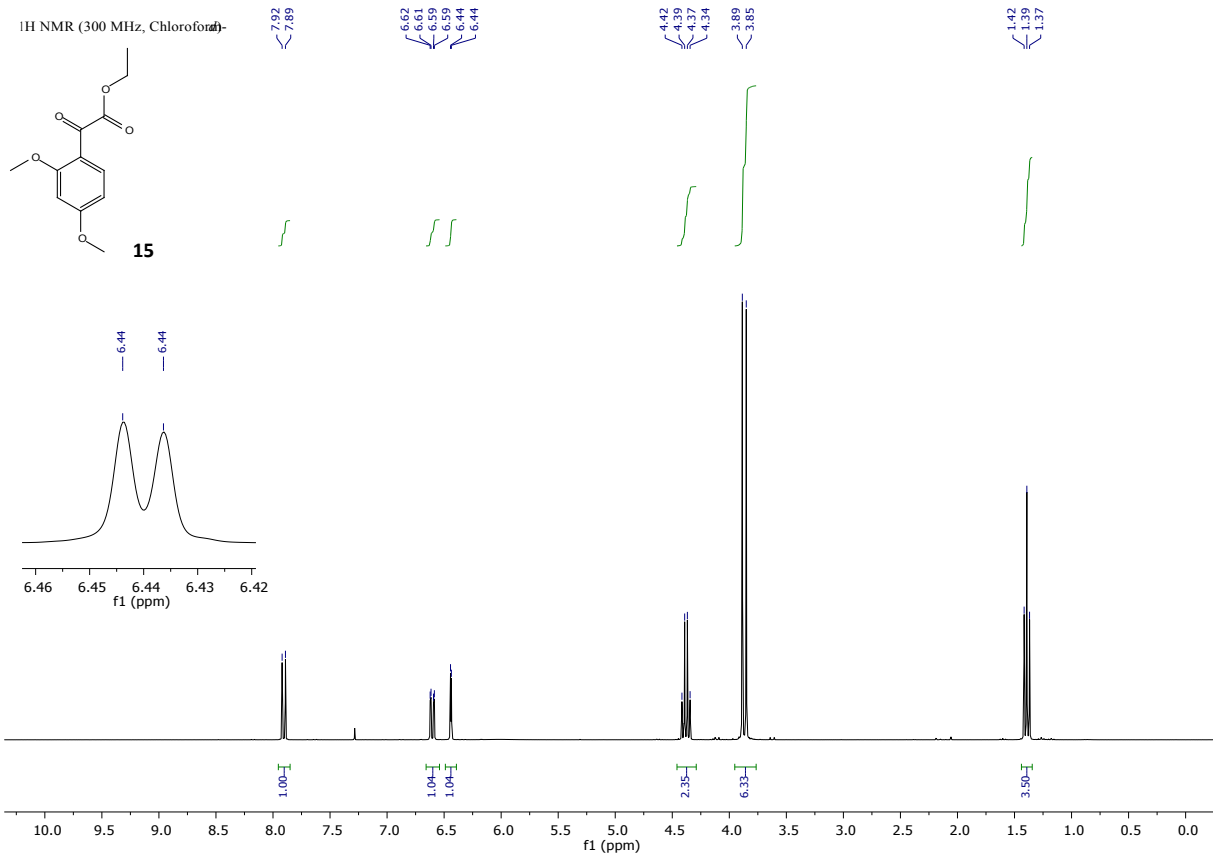
- **14**

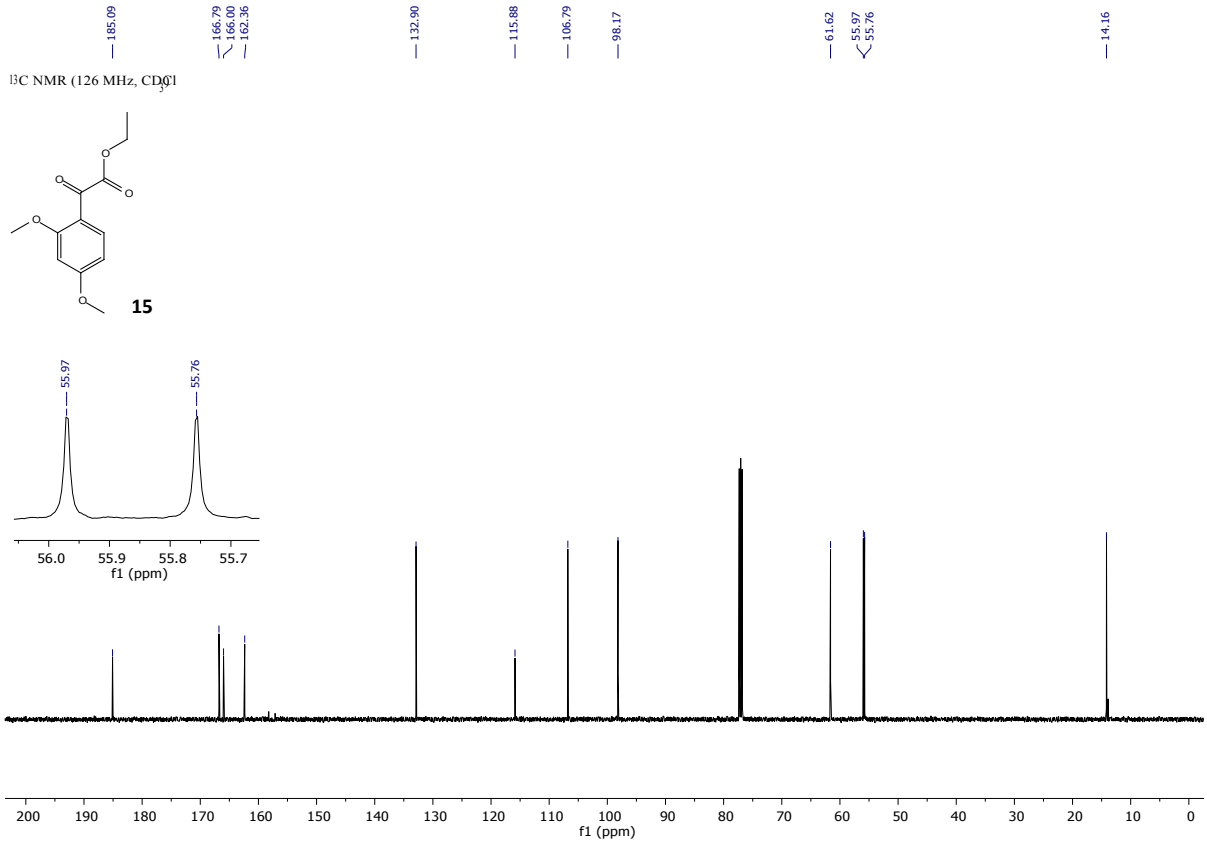

1H NMR (300 MHz, Chloroform-d)
7.97
7.95
7.94
7.26 CDCl3
6.95
6.93
6.92
4.41
4.39
3.85
3.85
1.40
1.38
1.38
1.35
1.92
2.02
1.97
3.00
2.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

14

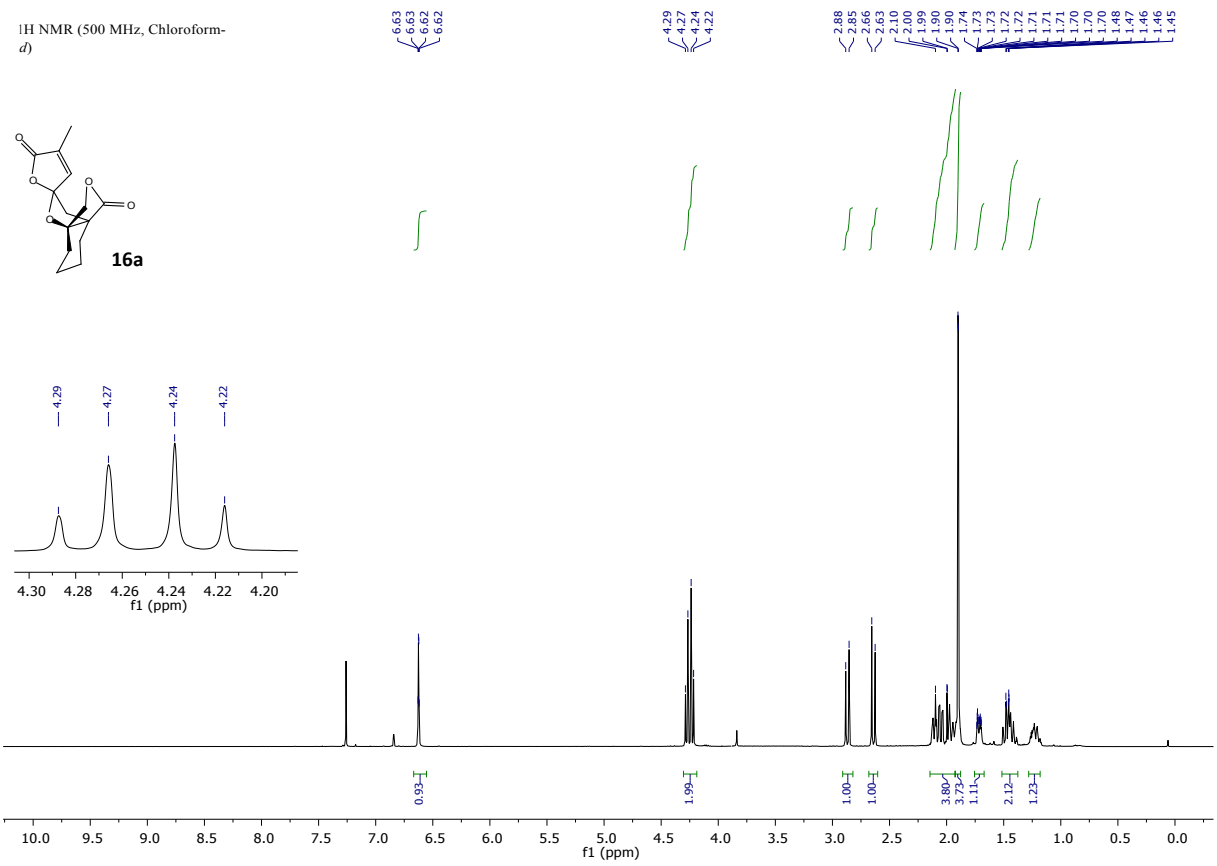

184.91
165.03
164.19
132.54
125.46
114.24
62.15
55.64
14.11
13C NMR (76 MHz, CDCl3)
14
f1 (ppm)

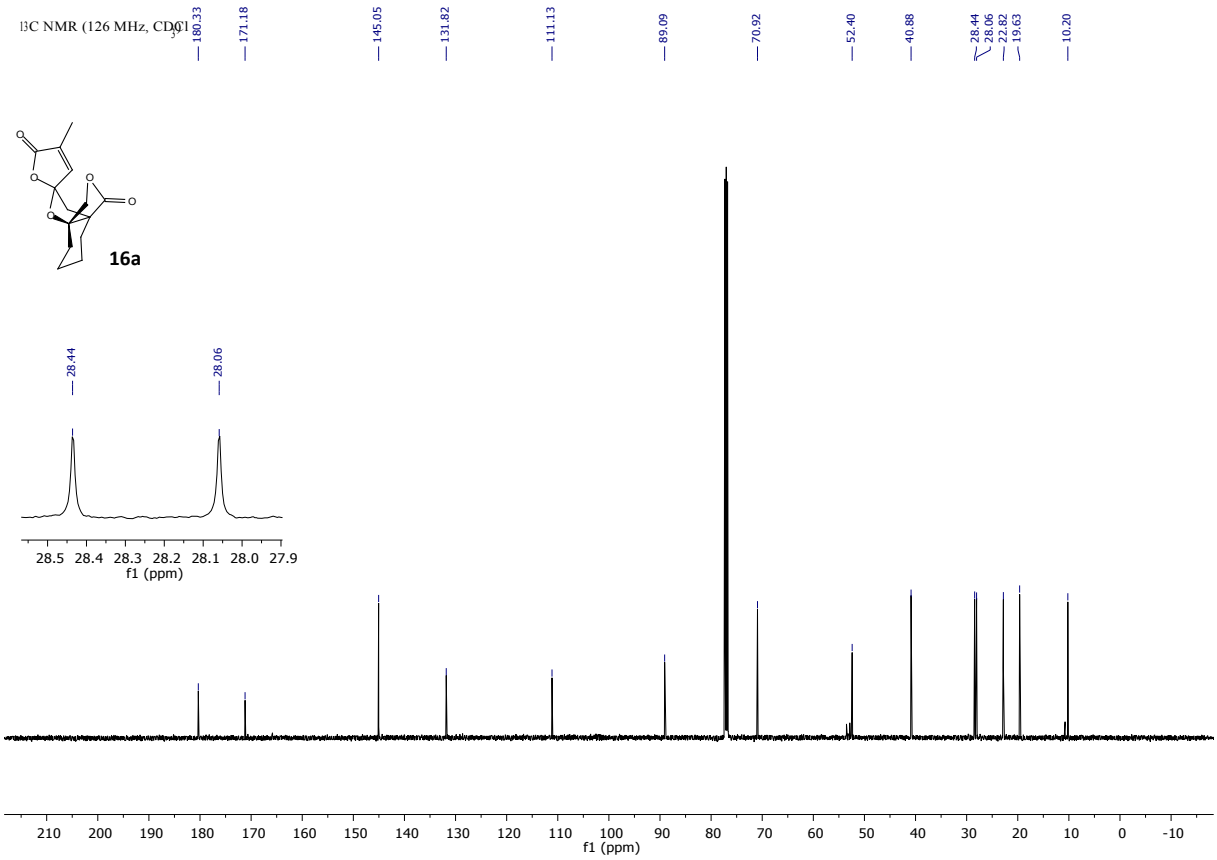
- **15**


1H NMR (300 MHz, Chloroform-d)
7.92
7.89
6.62
6.61
6.59
6.59
6.44
6.44
4.42
4.39
4.37
4.34
3.89
3.85
1.42
1.39
1.37
15
6.44
6.44
6.46
6.45
6.44
6.43
6.42
f1 (ppm)
1.00
1.04
1.04
2.35
6.33
3.50
f1 (ppm)

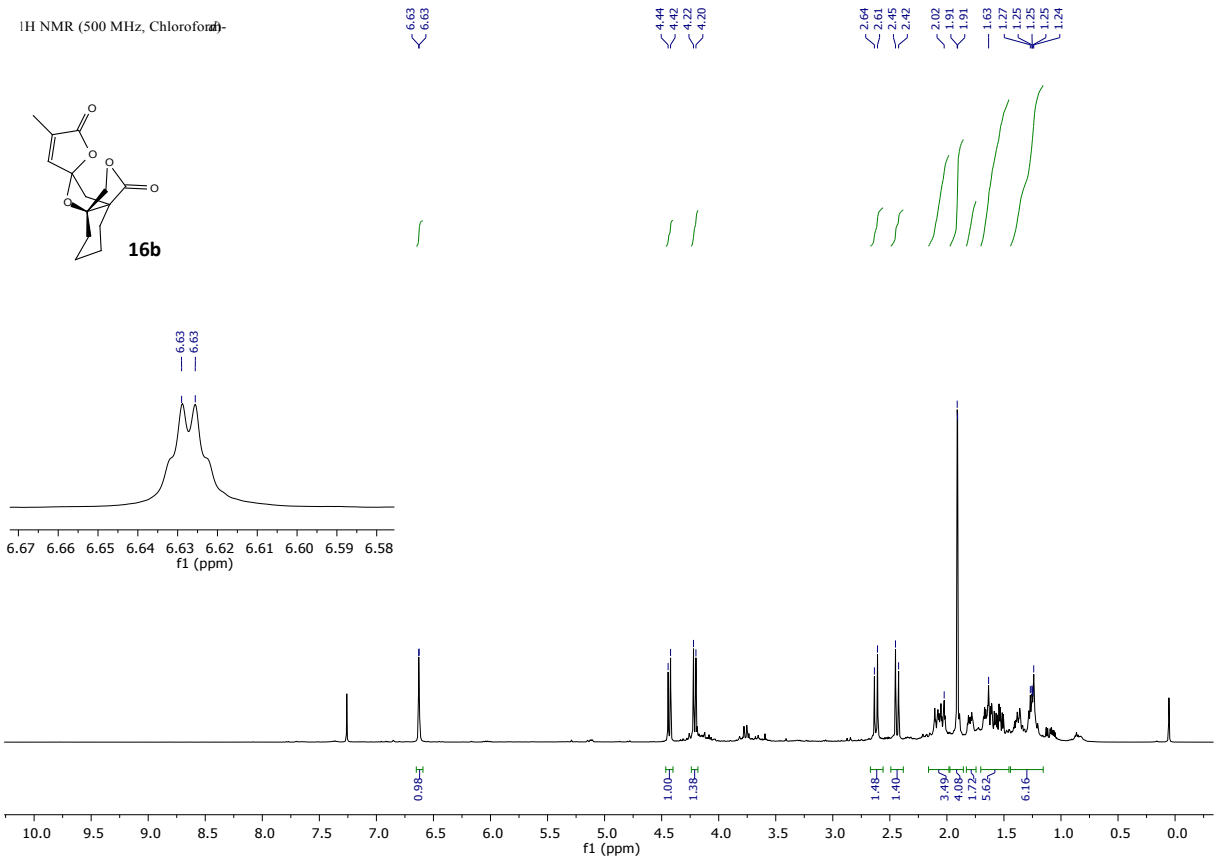

185.09
166.79
166.00
162.36
132.90
115.88
106.79
98.17
61.62
55.97
55.76
14.16
13C NMR (126 MHz, CDCl3)
15
55.97
55.76
56.0
55.9
55.8
55.7
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

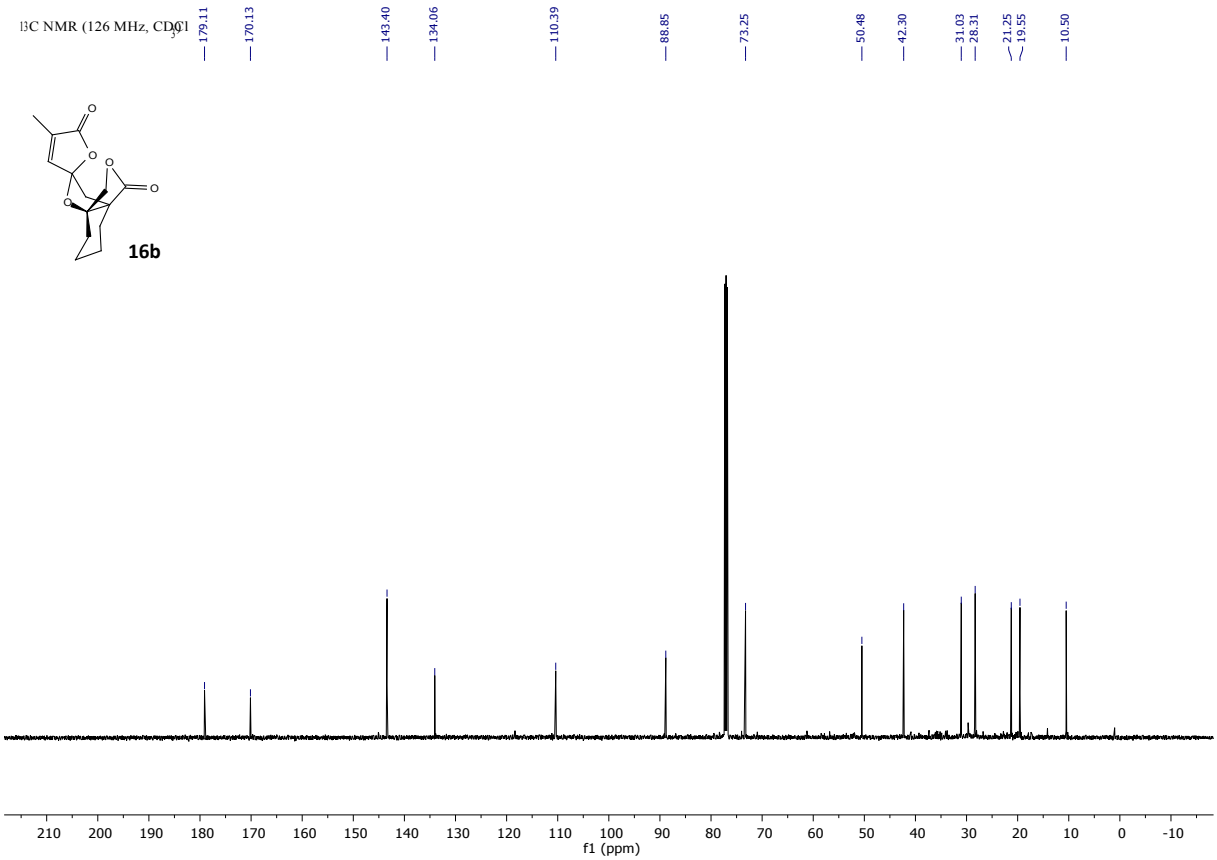
- **16a**

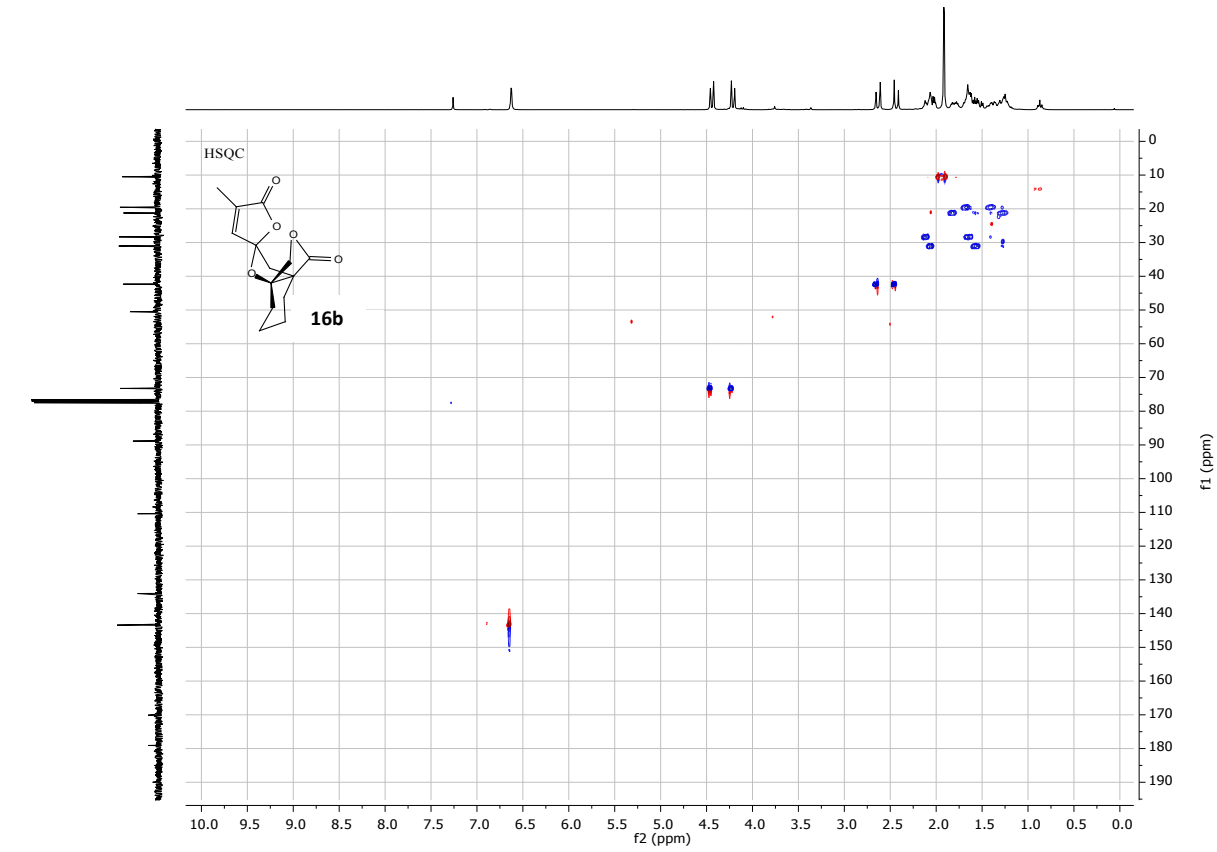

1H NMR (500 MHz, Chloroform-d)
6.63
6.63
6.62
6.62
4.29
4.27
4.24
4.22
2.88
2.85
2.66
2.63
2.10
2.00
1.99
1.90
1.90
1.74
1.73
1.73
1.72
1.72
1.71
1.71
1.71
1.70
1.70
1.70
1.48
1.47
1.46
1.46
1.45
16a
4.29
4.27
4.24
4.22
4.30
4.28
4.26
4.24
4.22
4.20
f1 (ppm)
0.93
1.99
1.00
1.00
3.80
3.73
1.11
2.12
1.23
10.0
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
f1 (ppm)

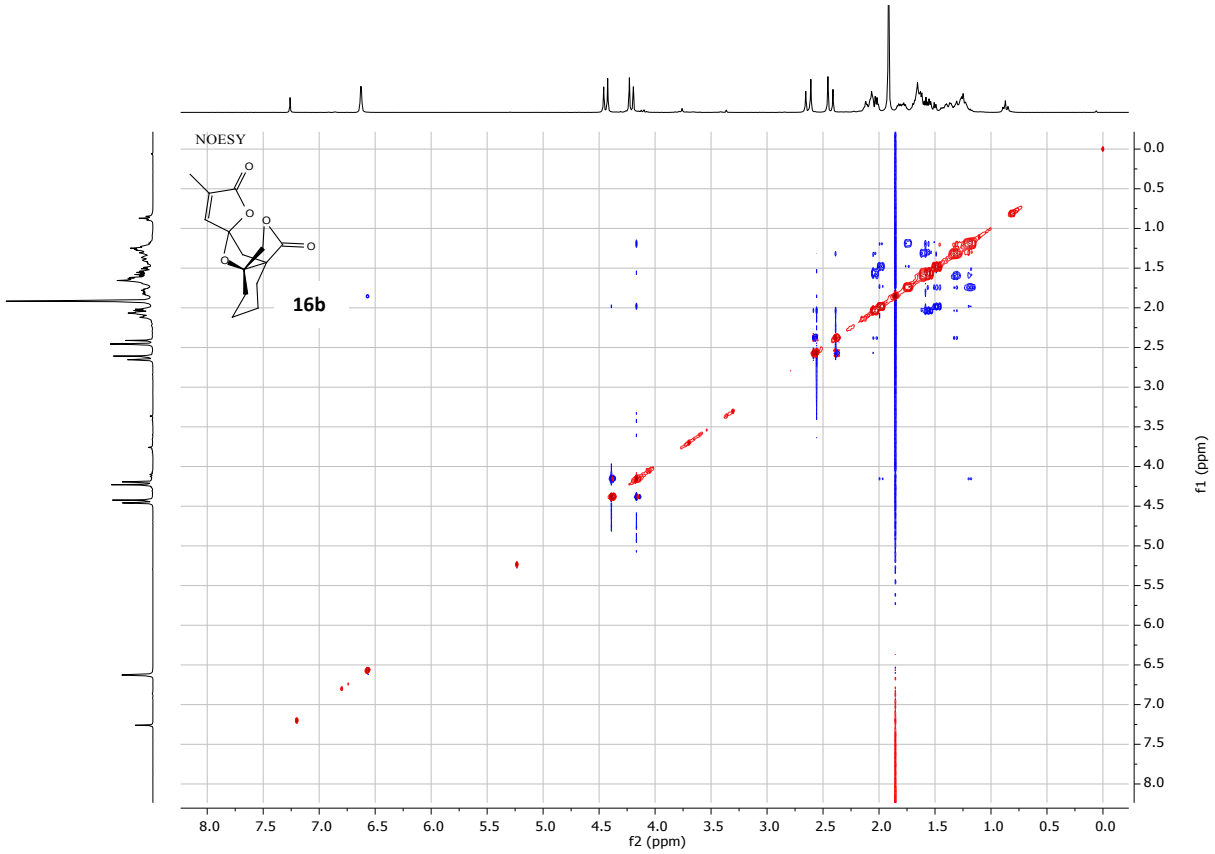

13C NMR (126 MHz, CDCl3)
180.33
171.18
145.05
131.82
111.13
89.09
70.92
52.40
40.88
28.44
28.06
22.82
19.63
10.20
16a
28.44
28.06
28.5 28.4 28.3 28.2 28.1 28.0 27.9
f1 (ppm)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

- **16b**

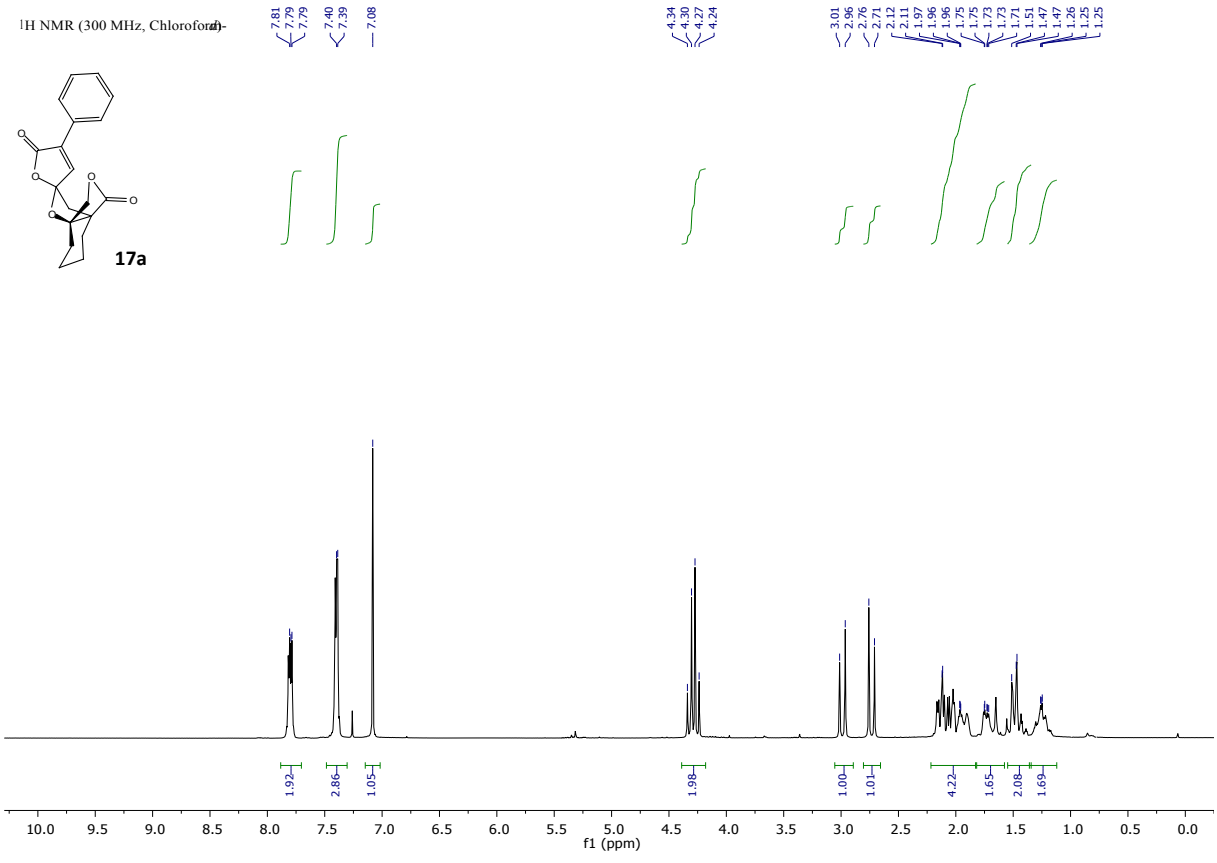

1H NMR (500 MHz, Chloroform-d)
6.63
6.63
4.44
4.42
4.22
4.20
2.64
2.61
2.45
2.42
2.02
1.91
1.91
1.63
1.27
1.25
1.25
1.25
1.24
16b
6.63
6.63
6.67 6.66 6.65 6.64 6.63 6.62 6.61 6.60 6.59 6.58
f1 (ppm)
0.98
1.00
1.38
1.48
1.40
3.49
4.08
1.72
5.62
6.16
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

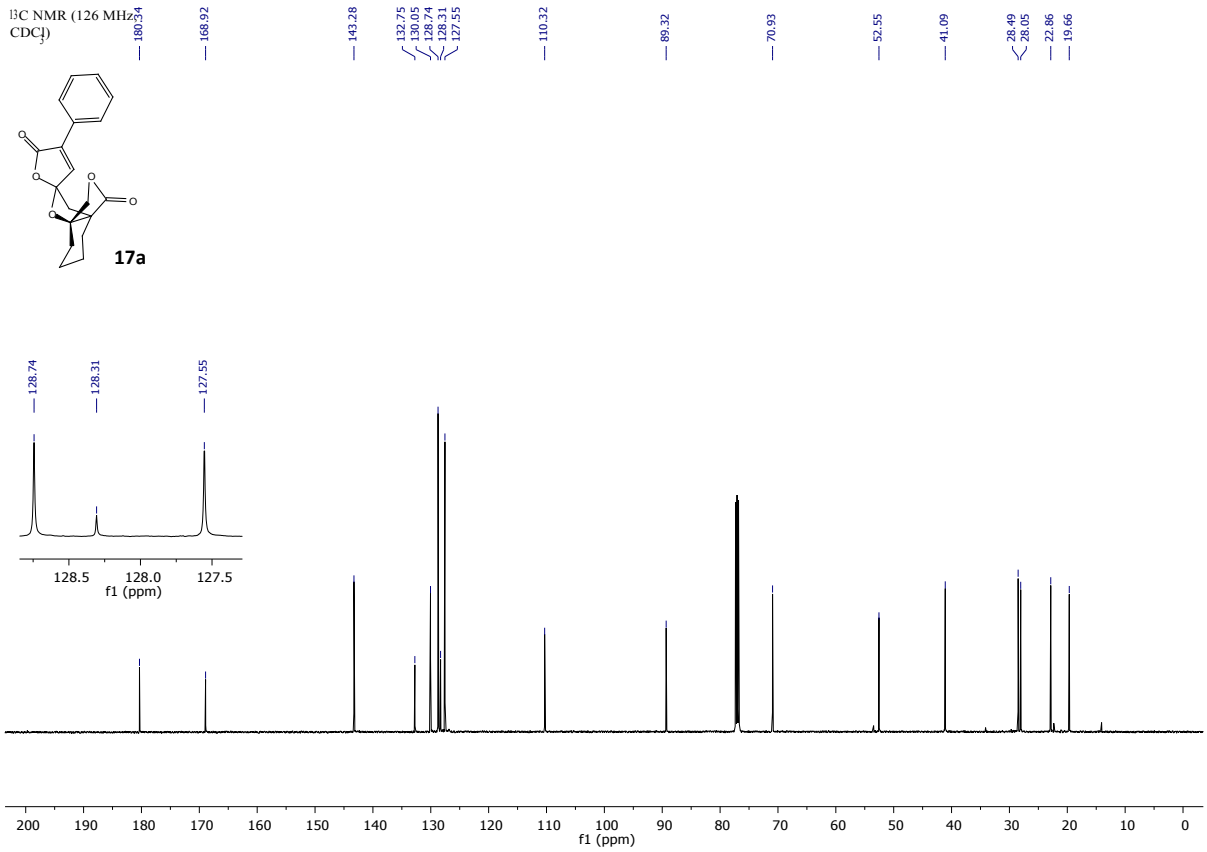

13C NMR (126 MHz, CDCl3)
179.11
170.13
143.40
134.06
110.39
88.85
73.25
50.48
42.30
31.03
28.31
21.25
19.55
10.50
16b
f1 (ppm)

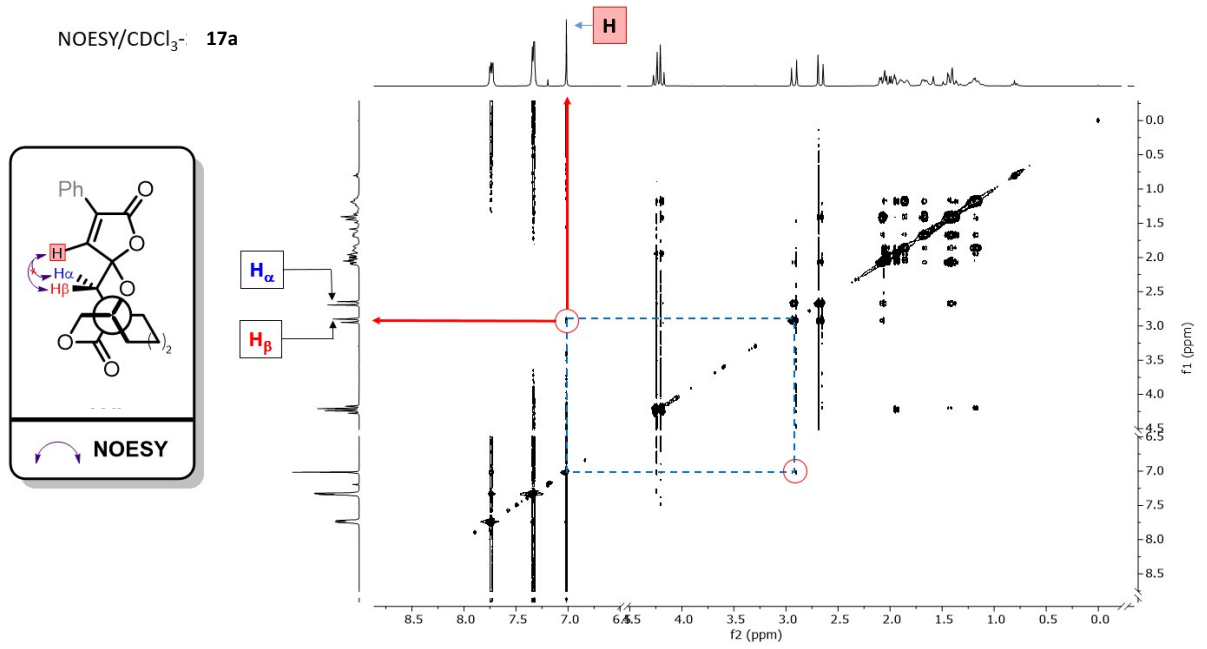

HSQC
16b
f2 (ppm)
f1 (ppm)



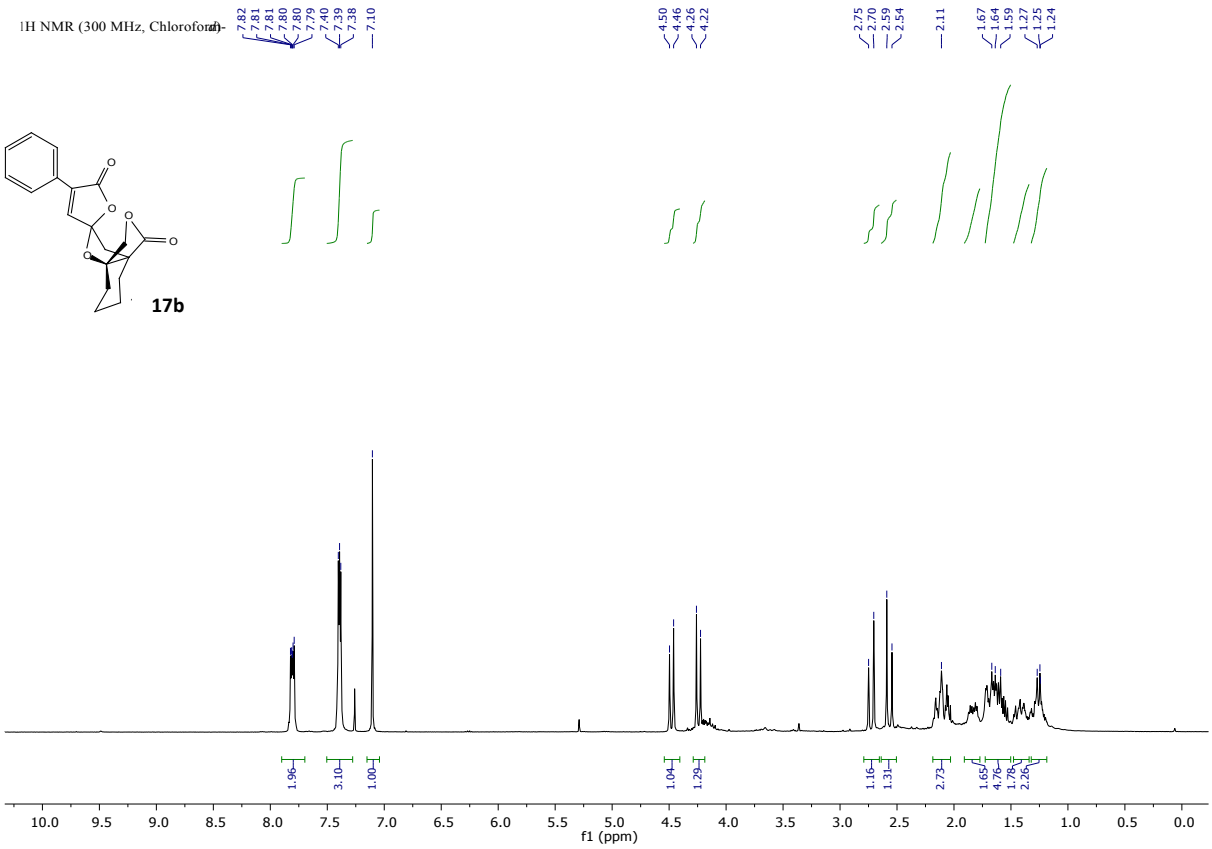
- **17a**

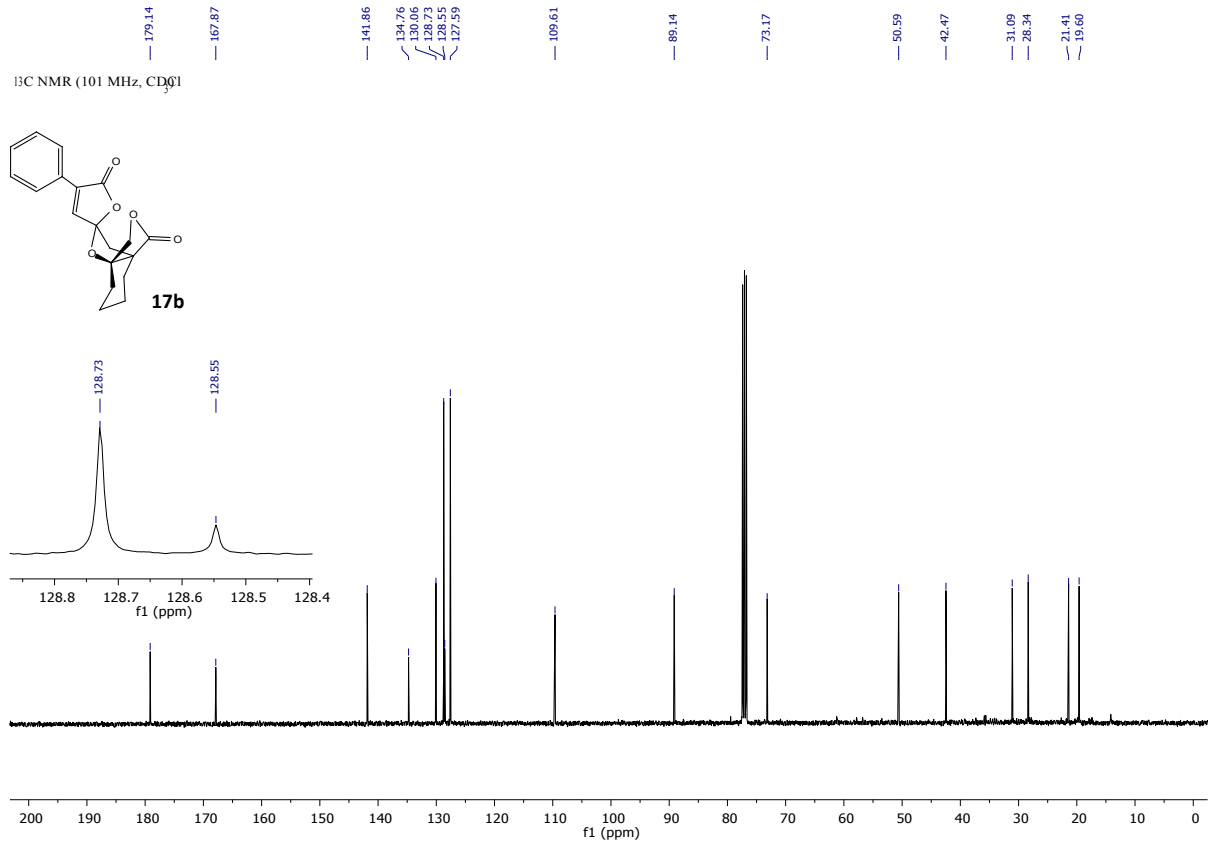


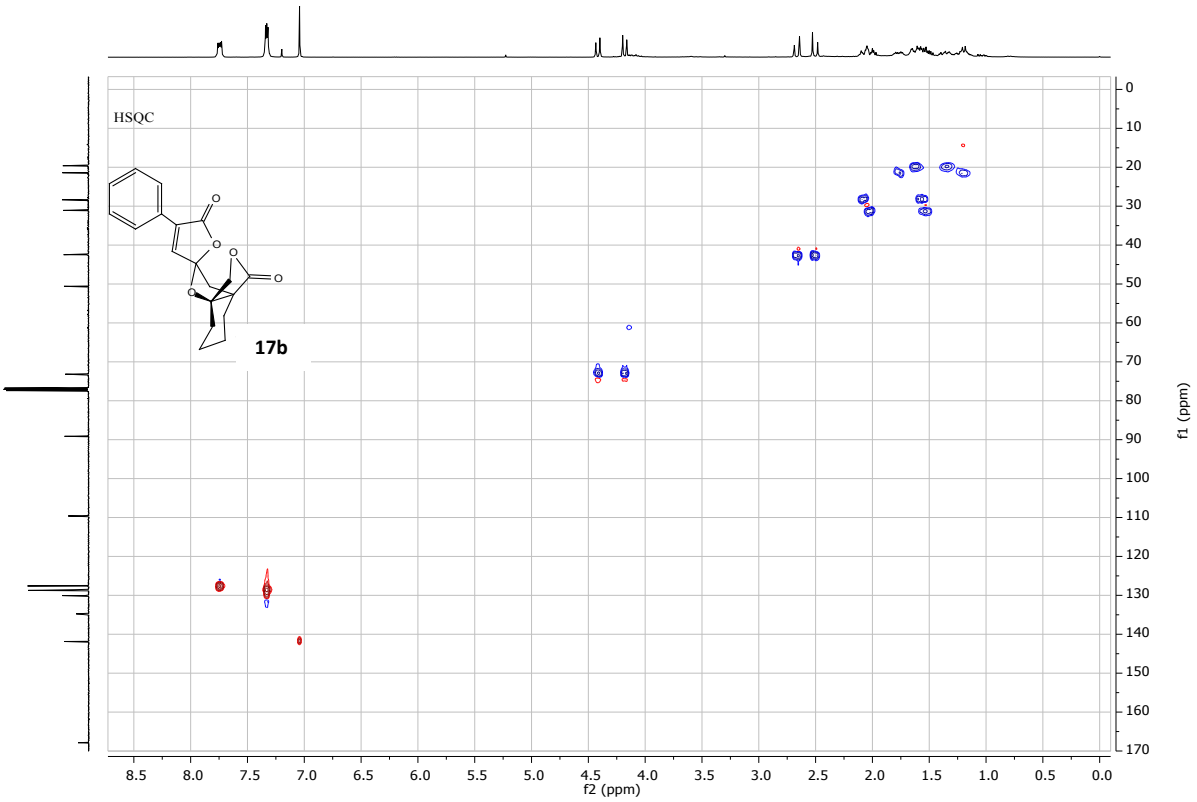

13C NMR (126 MHz, CDCl3)
180.34
168.92
143.28
132.75
130.05
128.74
128.31
127.55
110.32
89.32
70.93
52.55
41.09
28.49
28.05
22.86
19.66
17a
128.74
128.31
127.55
128.5
128.0
127.5
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

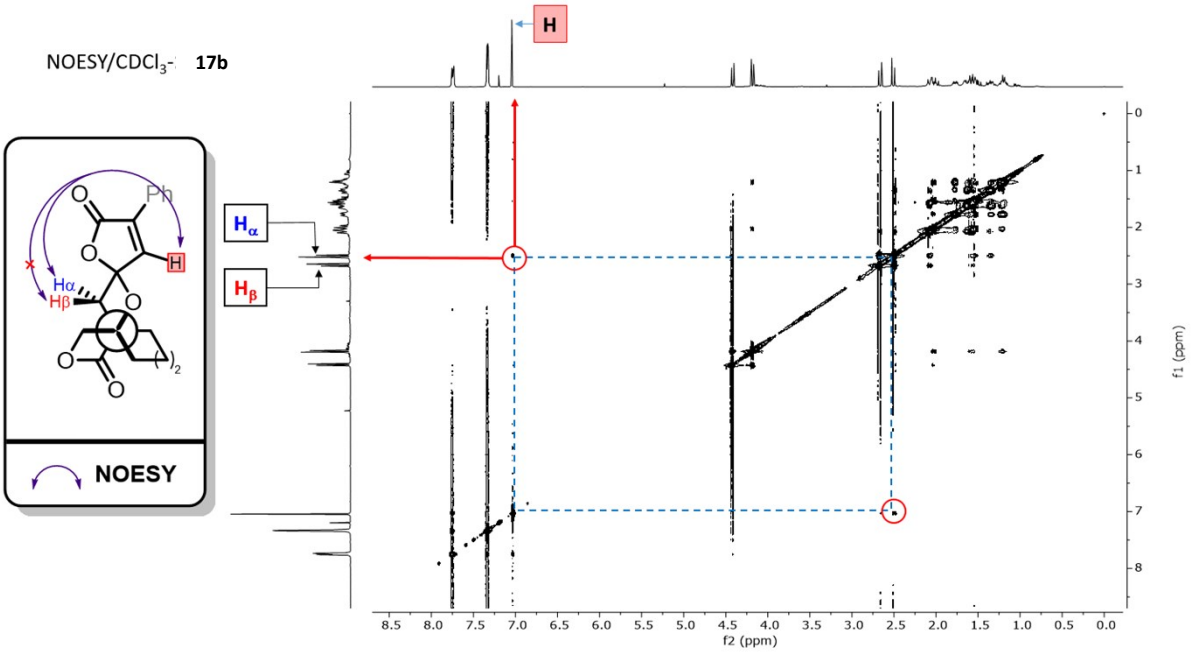

NOESY/CDCl3- 17a
H
Hα
Hβ
Ph
NOESY
f2 (ppm)
f1 (ppm)

- **17b**

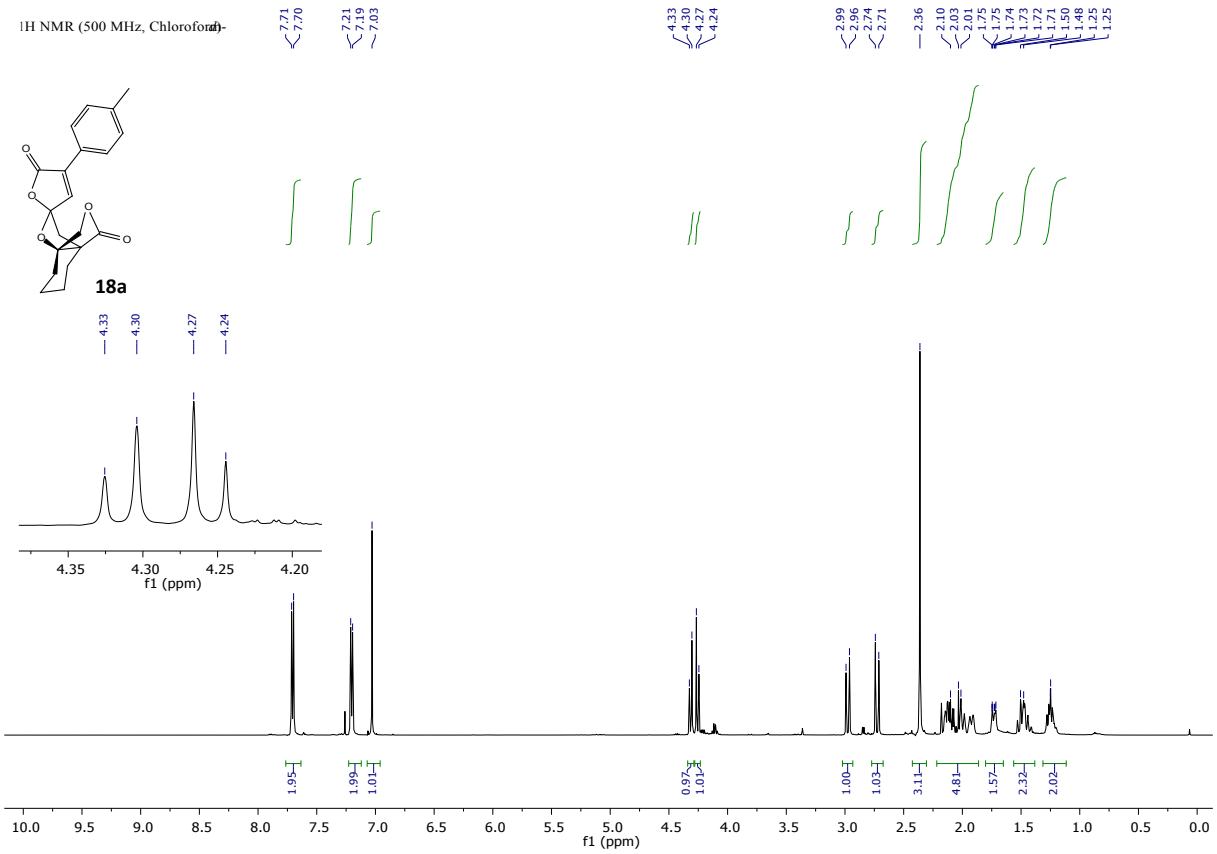

1H NMR (300 MHz, Chloroform-d)
7.82
7.81
7.81
7.80
7.80
7.79
7.40
7.39
7.38
7.10
4.50
4.46
4.26
4.22
2.75
2.70
2.59
2.54
2.11
1.67
1.64
1.59
1.27
1.25
1.24
17b
1.96
3.10
1.00
1.04
1.29
1.16
1.31
2.73
1.65
4.76
1.78
2.26
f1 (ppm)

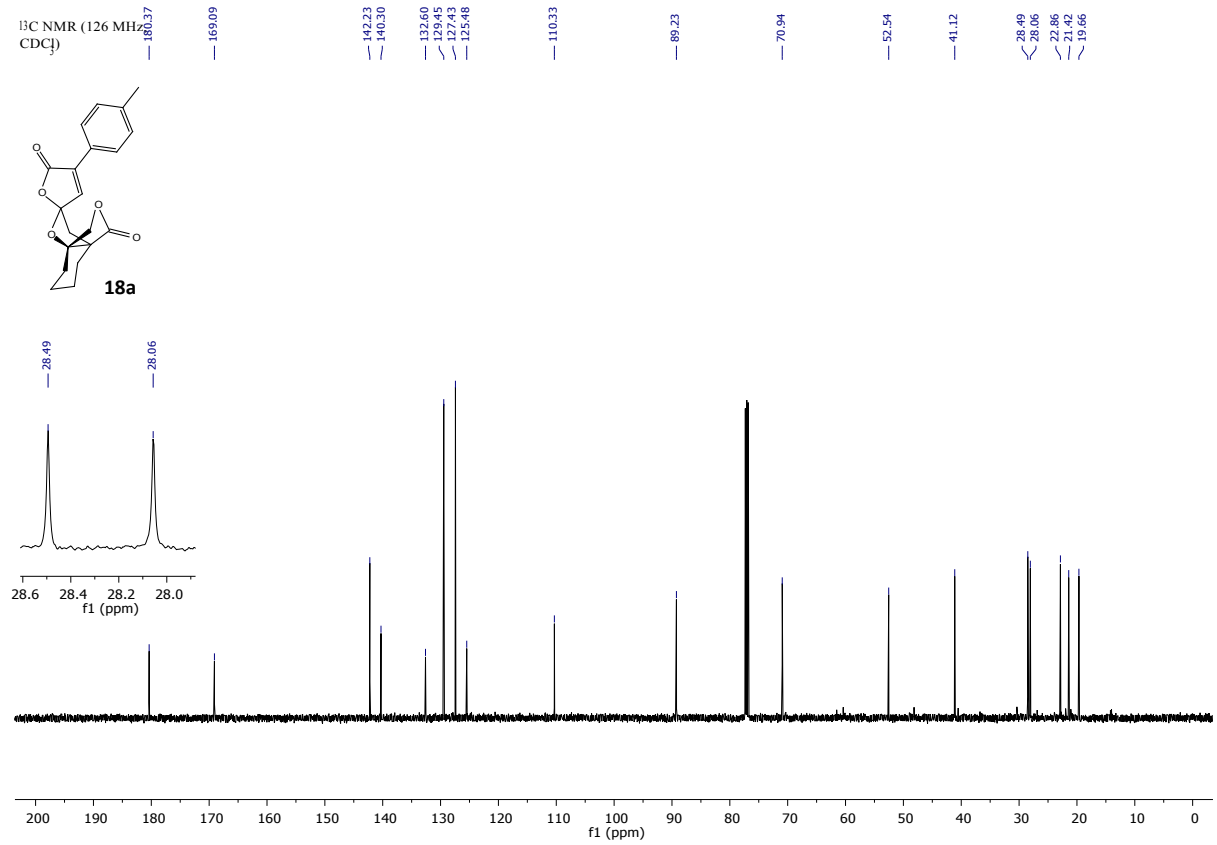

13C NMR (101 MHz, CDCl3)
179.14
167.87
141.86
134.76
130.06
128.73
128.55
127.59
109.61
89.14
73.17
50.59
42.47
31.09
28.34
21.41
19.60
17b
128.73
128.55
f1 (ppm)

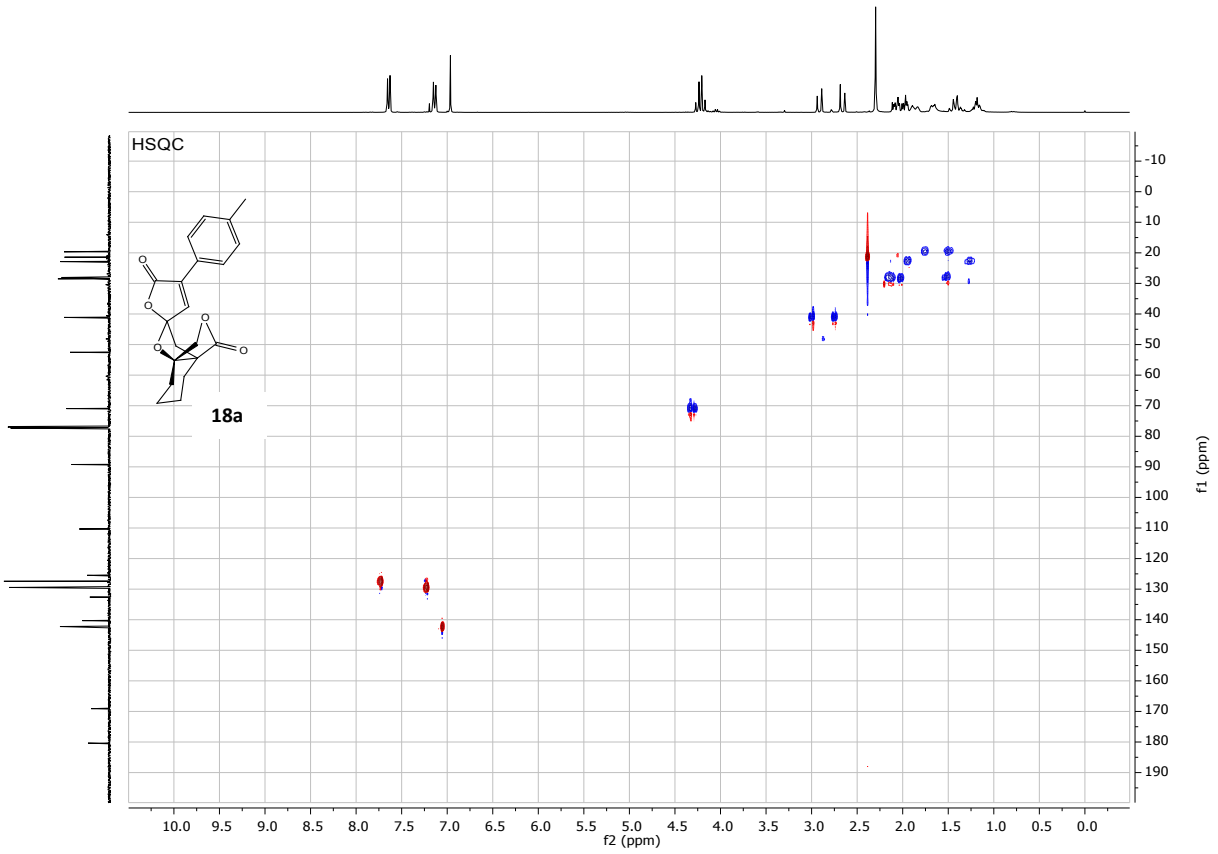

HSQC
17b
f2 (ppm)
f1 (ppm)


NOESY/CDCl3- 17b
H
Hα
Hβ
Ph
NOESY
f2 (ppm)
f1 (ppm)

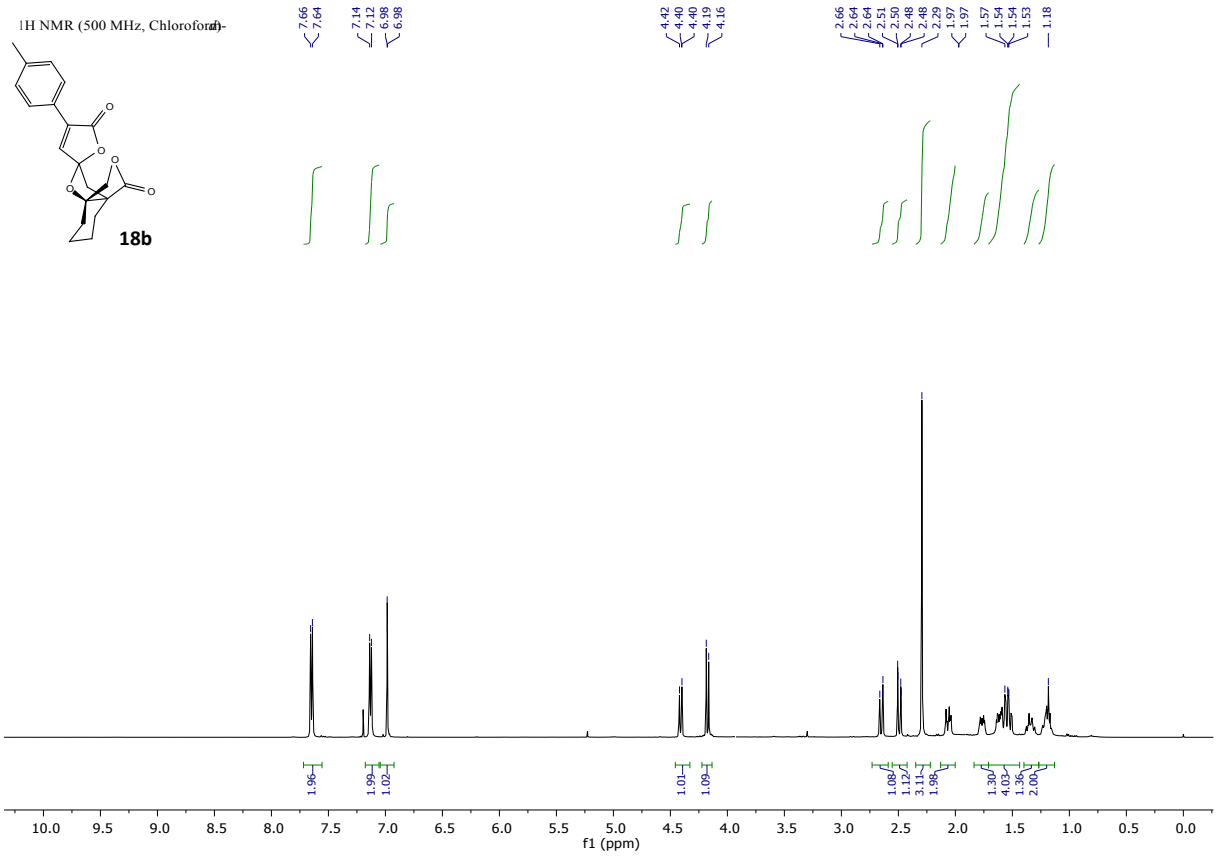
- **18a**

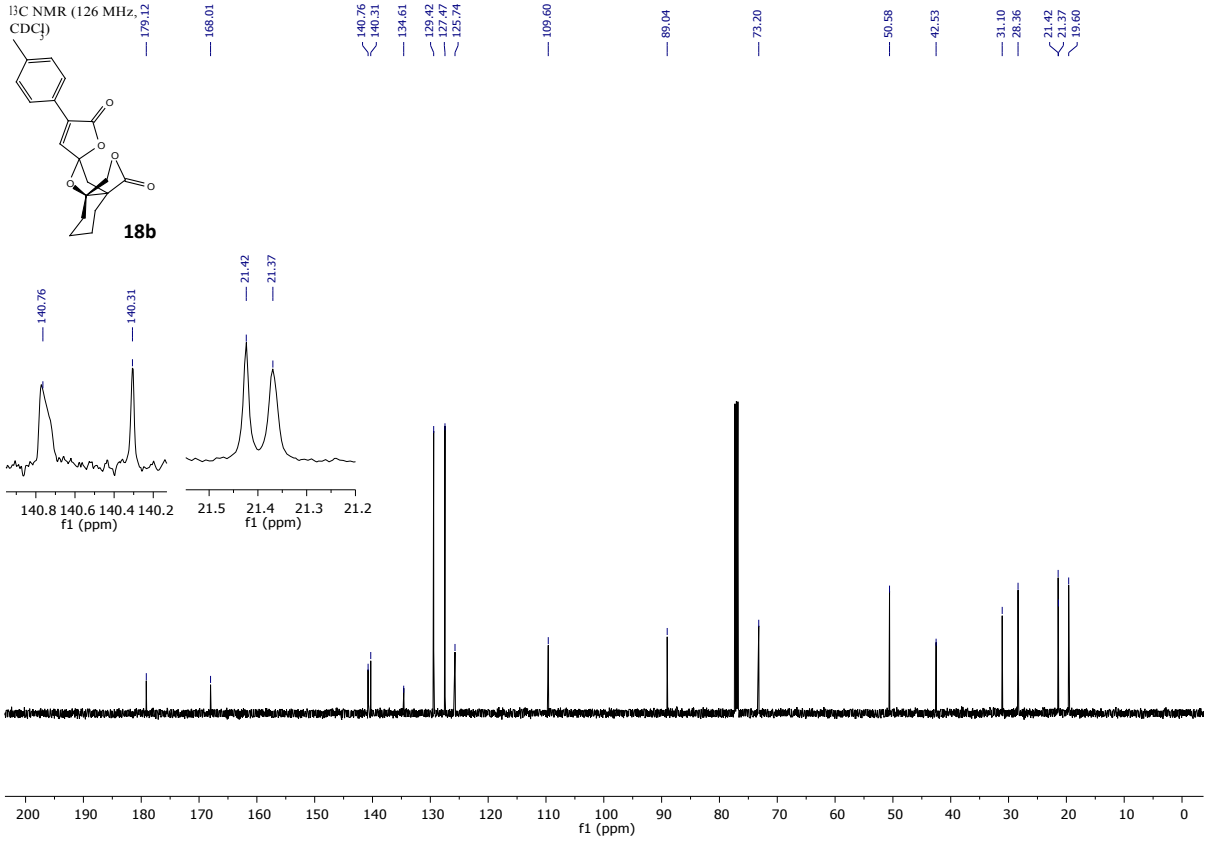

1H NMR (500 MHz, Chloroform-d)
18a
f1 (ppm)


13C NMR (126 MHz, CDCl3)
18a
f1 (ppm)

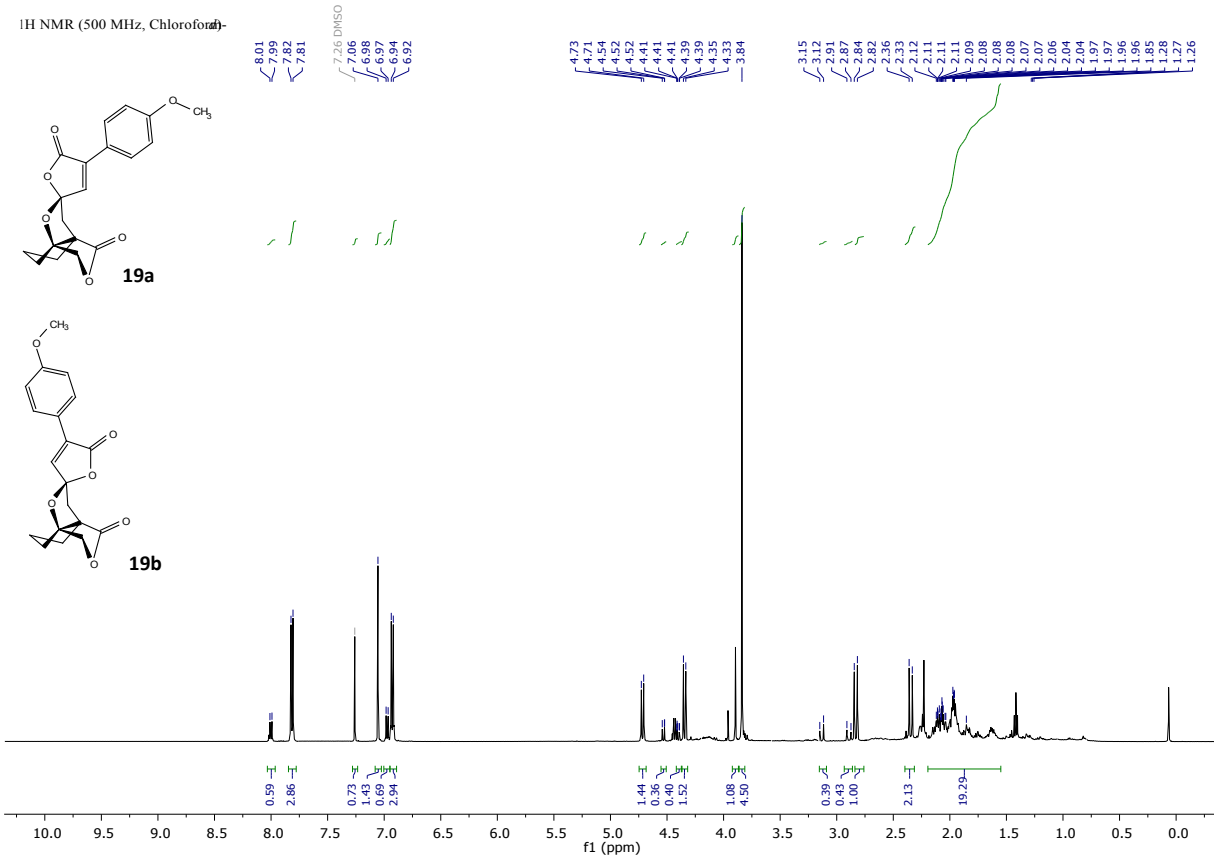


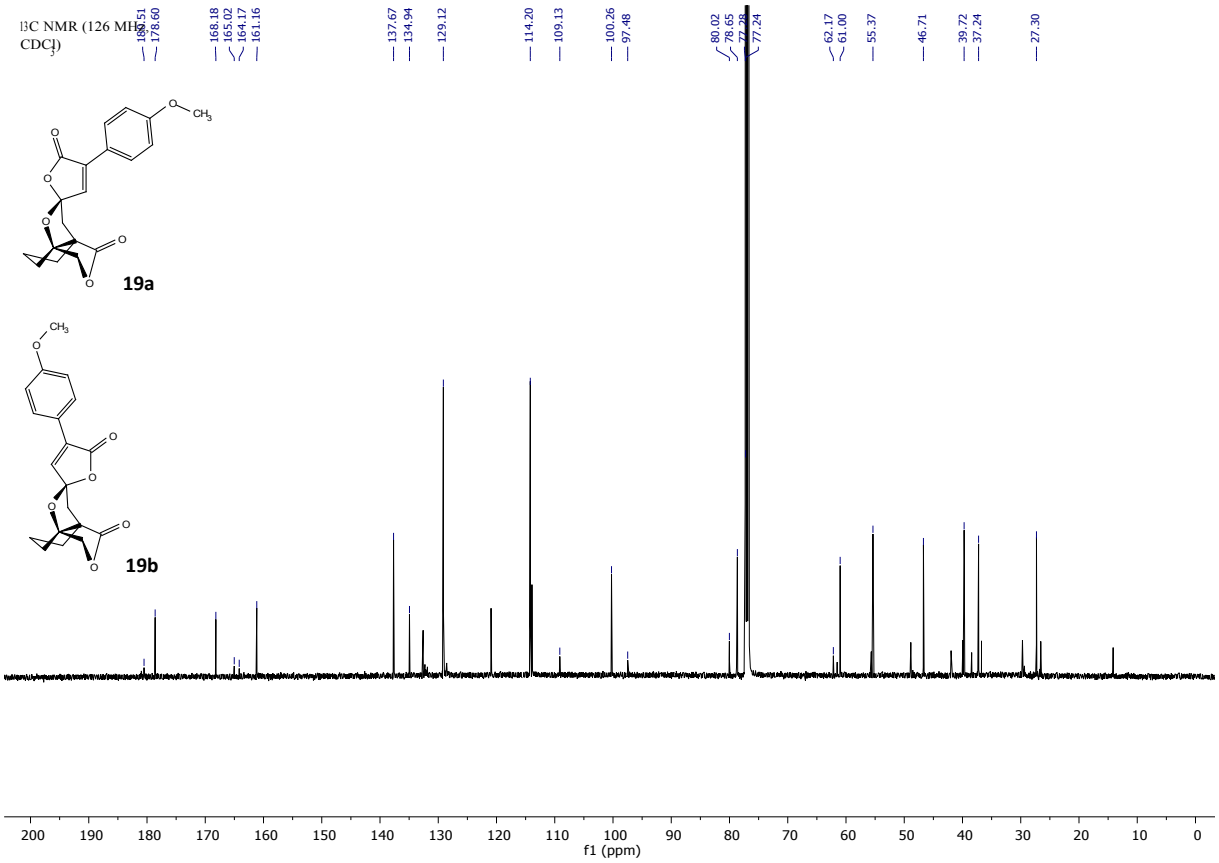
- **18b**



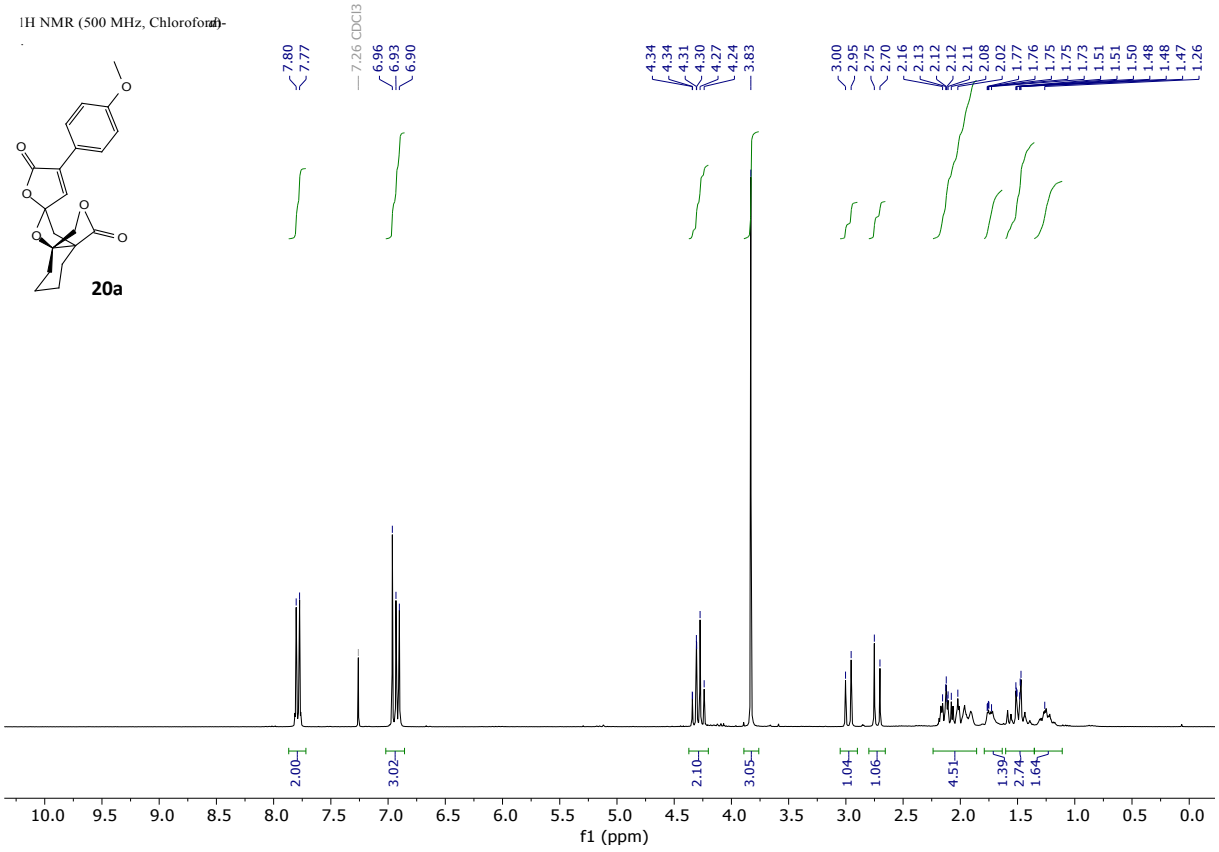

13C NMR (126 MHz, CDCl3)
179.12
168.01
140.76
140.31
134.61
129.42
127.47
125.74
109.60
89.04
73.20
50.58
42.53
31.10
28.36
21.42
21.37
19.60
18b
140.76
140.31
21.42
21.37
140.8 140.6 140.4 140.2
f1 (ppm)
21.5 21.4 21.3 21.2
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

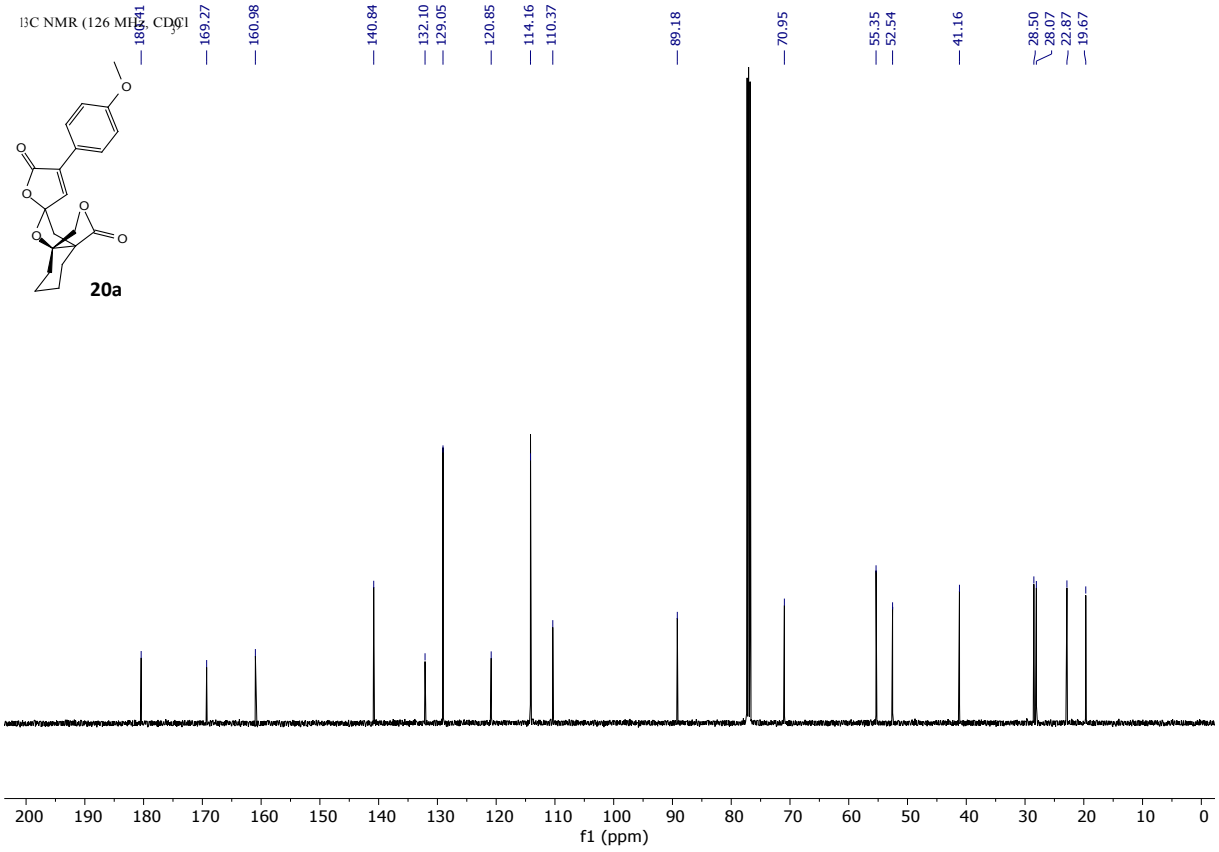
- **19a-b**

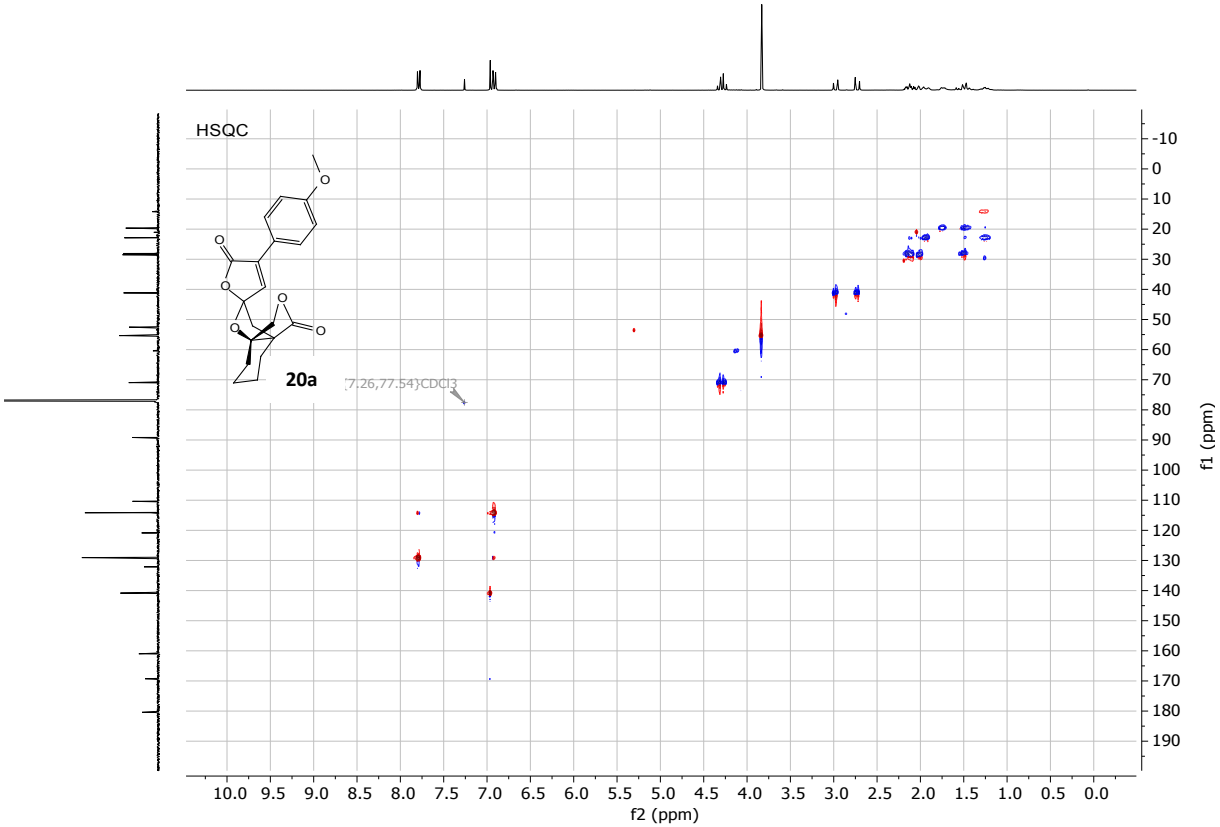

1H NMR (500 MHz, Chloroform-d)
8.01
7.99
7.82
7.81
7.26 DMSO
7.06
6.98
6.97
6.94
6.92
4.73
4.71
4.54
4.52
4.52
4.41
4.41
4.41
4.39
4.39
4.35
4.33
3.84
3.15
3.12
2.91
2.87
2.84
2.82
2.36
2.33
2.12
2.11
2.11
2.11
2.09
2.08
2.08
2.08
2.07
2.07
2.06
2.04
2.04
2.04
1.97
1.97
1.96
1.96
1.85
1.28
1.27
1.26
19a
19b
0.59
2.86
0.73
1.43
0.69
2.94
1.44
0.36
0.40
1.52
1.08
4.50
0.39
0.43
1.00
2.13
19.29
10.0 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
f1 (ppm)


13C NMR (126 MHz, CDCl3)
168.51
178.60
168.18
165.02
164.17
161.16
137.67
134.94
129.12
114.20
109.13
100.26
97.48
80.02
78.65
77.38
77.24
62.17
61.00
55.37
46.71
39.72
37.24
27.30
19a
19b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

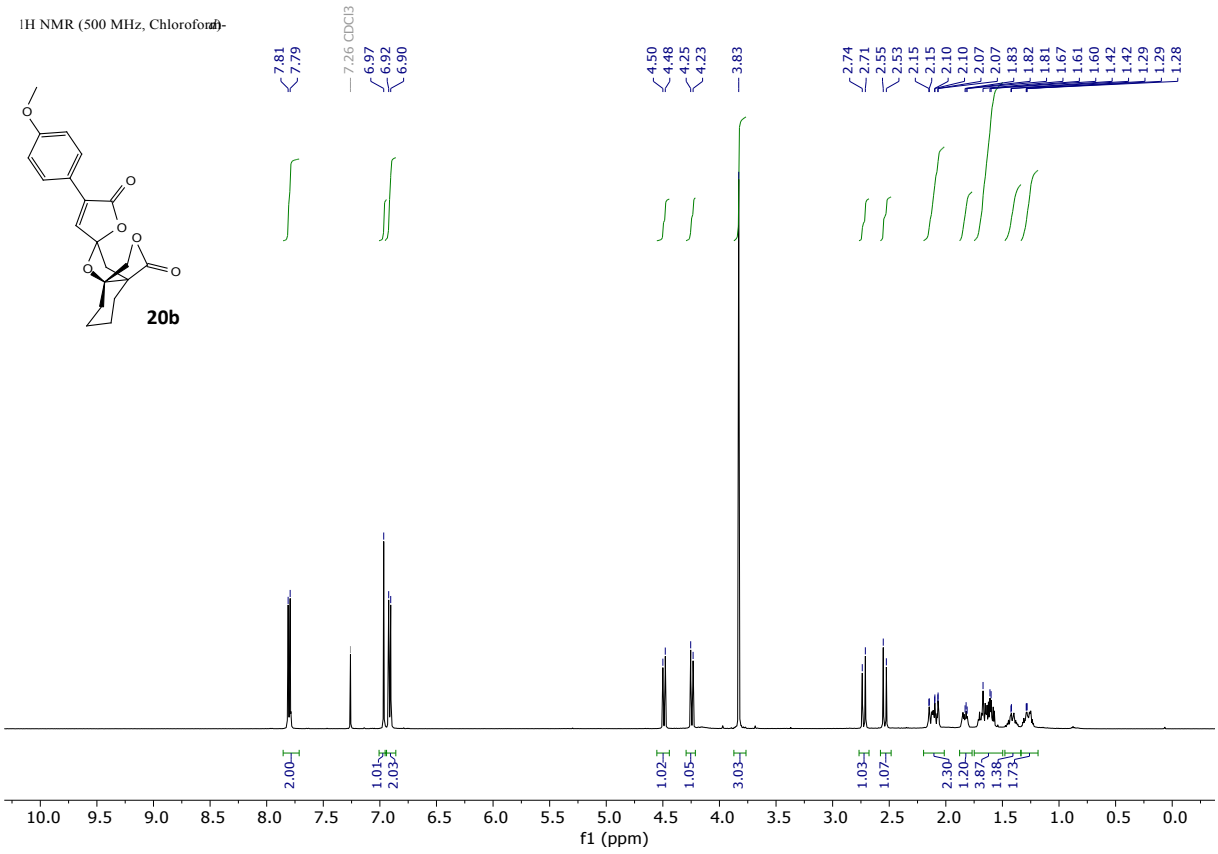
- **20a**

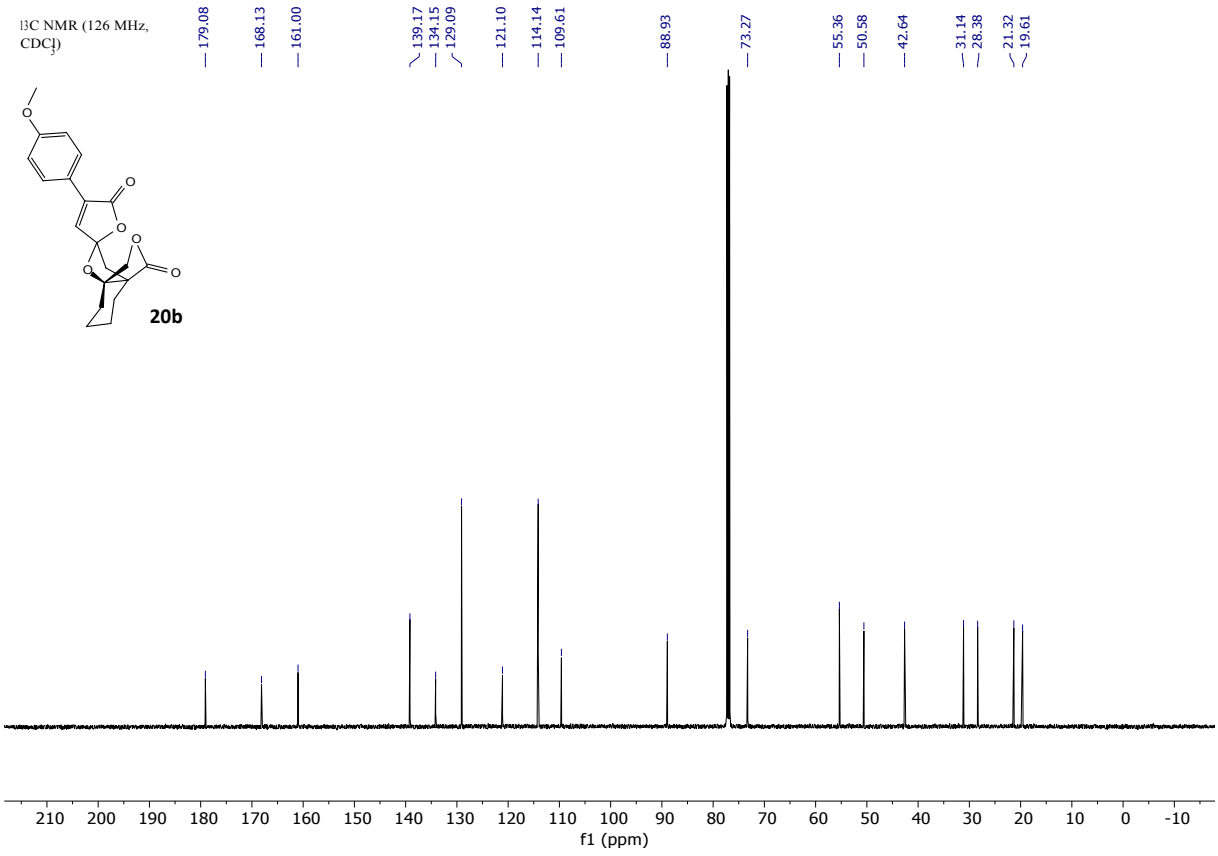

1H NMR (500 MHz, Chloroform-d)
7.26 CDCl3
7.80
7.77
6.96
6.93
6.90
4.34
4.34
4.31
4.30
4.27
4.24
3.83
3.00
2.95
2.75
2.70
2.16
2.13
2.12
2.12
2.11
2.08
2.02
1.77
1.76
1.75
1.75
1.73
1.51
1.51
1.50
1.48
1.48
1.47
1.26
20a
2.00
3.02
2.10
3.05
1.04
1.06
4.51
1.39
2.74
1.64
f1 (ppm)


13C NMR (126 MHz, CDCl3)
180.41
169.27
160.98
140.84
132.10
129.05
120.85
114.16
110.37
89.18
70.95
55.35
52.54
41.16
28.50
28.07
22.87
19.67
20a
f1 (ppm)

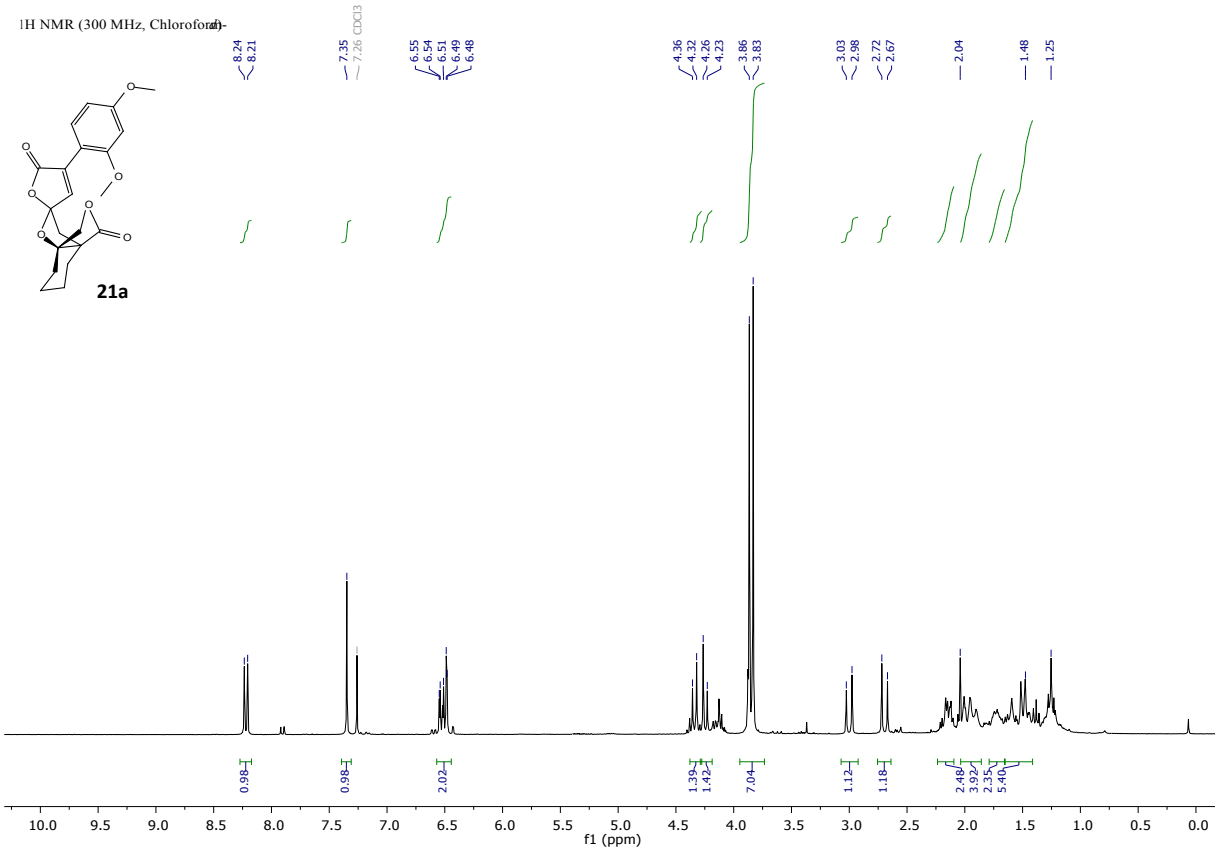


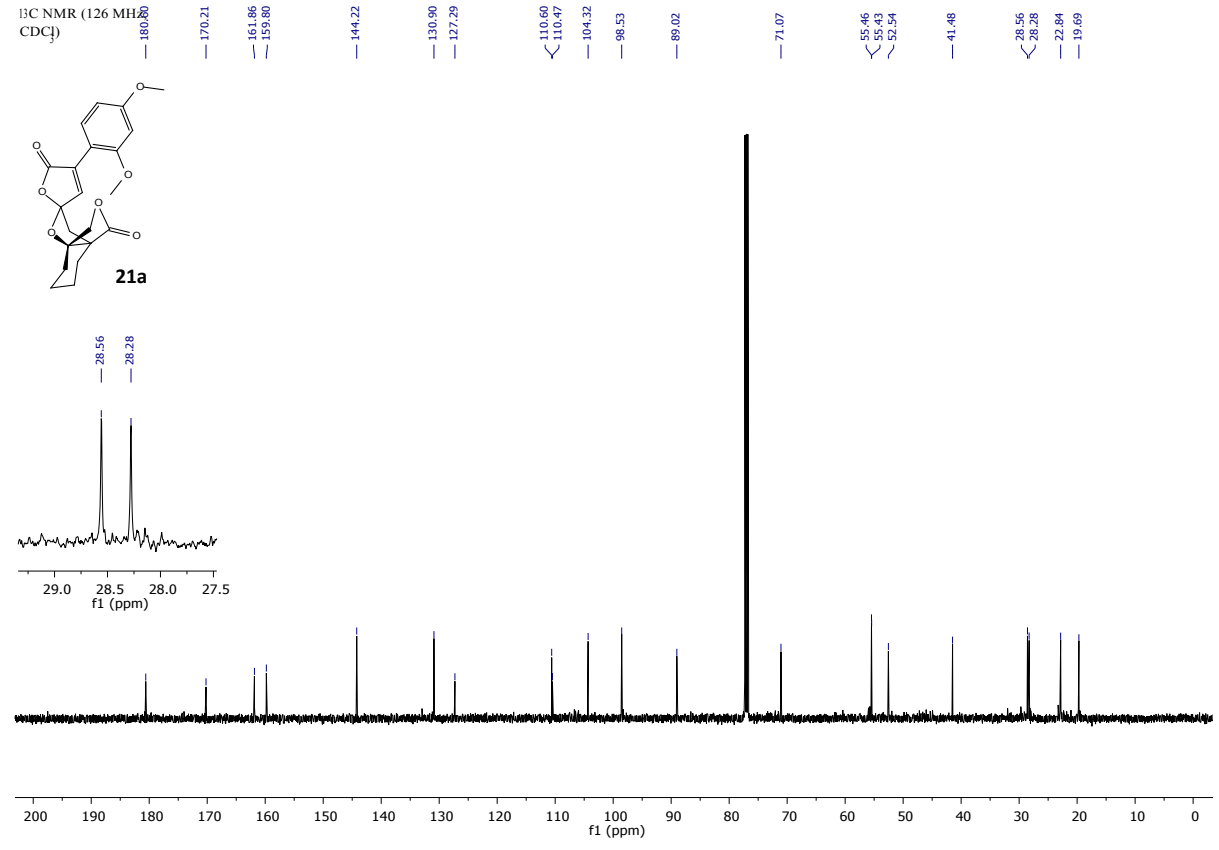
- **20b**


1H NMR (500 MHz, Chloroform-d)
7.26 CDCl3
7.81
7.79
6.97
6.92
6.90
4.50
4.48
4.25
4.23
3.83
2.74
2.71
2.55
2.53
2.15
2.15
2.10
2.10
2.07
2.07
1.83
1.82
1.81
1.67
1.61
1.60
1.42
1.42
1.29
1.29
1.28
20b
2.00
1.01
2.03
1.02
1.05
3.03
1.03
1.07
2.30
1.20
3.87
1.38
1.73
f1 (ppm)

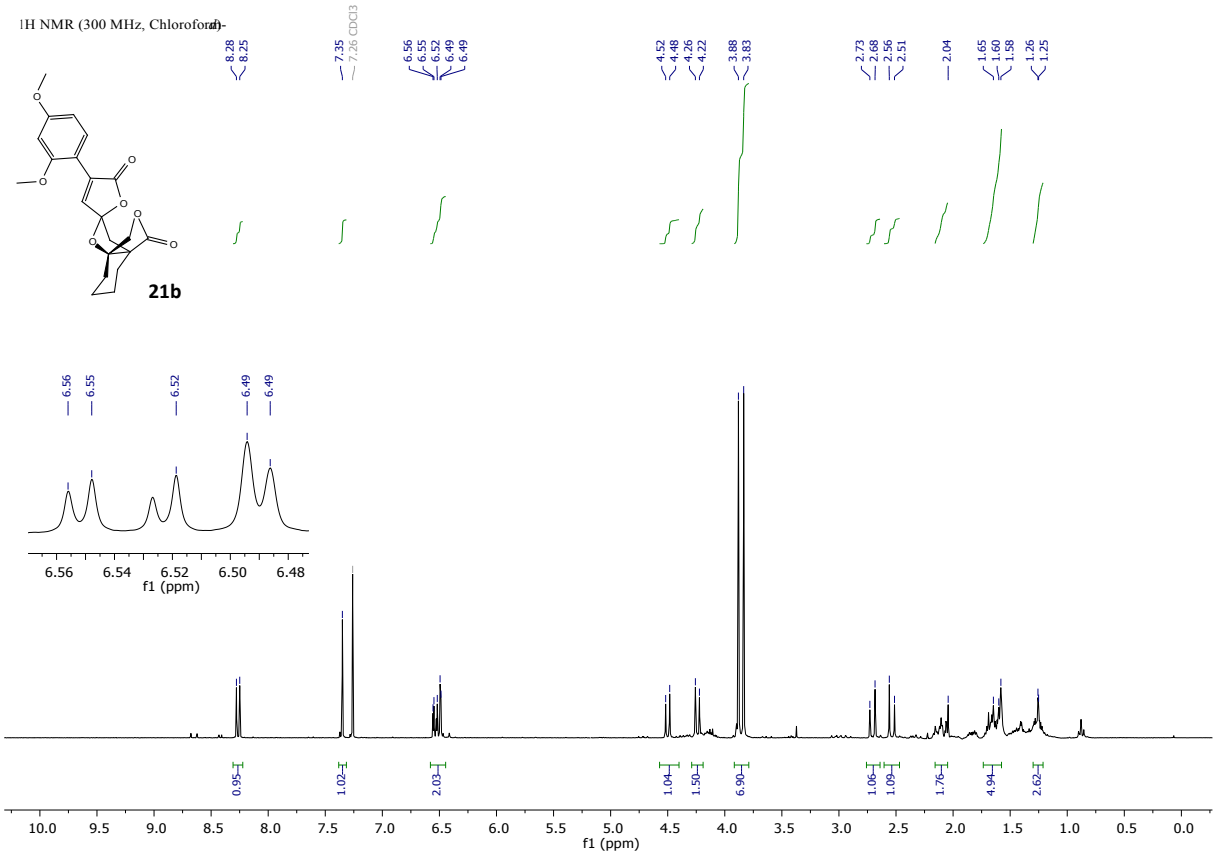

13C NMR (126 MHz, CDCl3)
179.08
168.13
161.00
139.17
134.15
129.09
121.10
114.14
109.61
88.93
73.27
55.36
50.58
42.64
31.14
28.38
21.32
19.61
20b
f1 (ppm)

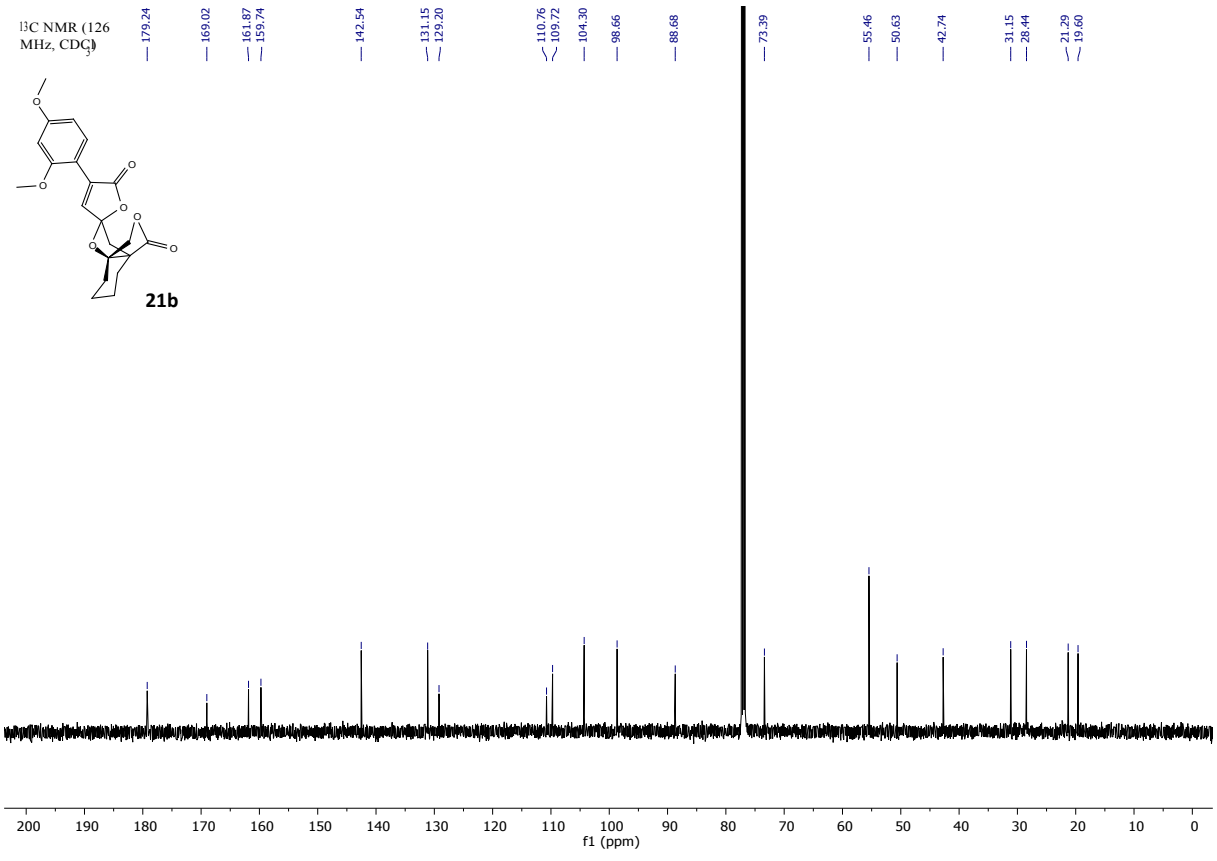
- **21a**


1H NMR (300 MHz, Chloroform-d)
21a
f1 (ppm)


13C NMR (126 MHz, CDCl3)
21a
f1 (ppm)

- **21b**


1H NMR (300 MHz, Chloroform-d)
21b
8.28
8.25
7.35
7.26 CDCl3
6.56
6.55
6.52
6.49
6.49
4.52
4.48
4.26
4.22
3.88
3.83
2.73
2.68
2.56
2.51
2.04
1.65
1.60
1.58
1.26
1.25
6.56
6.55
6.52
6.49
6.49
6.56 6.54 6.52 6.50 6.48
f1 (ppm)
0.95
1.02
2.03
1.04
1.50
6.90
1.06
1.09
1.76
4.94
2.62
10.0 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
f1 (ppm)


13C NMR (126 MHz, CDCl3)
21b
179.24
169.02
161.87
159.74
142.54
131.15
129.20
110.76
109.72
104.30
98.66
88.68
73.39
55.46
50.63
42.74
31.15
28.44
21.29
19.60
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)